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ABSTRACT SUPPLEMENT

ACR Convergence 2021

November 5–9, 2021

Virtual

American College of Rheumatology
Empowering Rheumatology Professionals

WILEY

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Abstract Number: 0001

Autoantigenic Properties Indicated for the Entire Aminoacyl tRNA Synthetase Family in Idiopathic Inflammatory Myopathies

Charlotta Preger[1], Antonella Notarnicola[1], Cecilia Hellström[2], Edvard Wigren[1], Catia Cerqueira[3], Peter Nilsson[2], Ingrid E Lundberg[1], Helena Persson[4], Susanne Gräslund[1] and Per-Johan Jakobsson[5], [1]Karolinska Institutet, Karolinska University Hospital, Division of Rheumatology, Department of Medicine Solna, Stockholm, Sweden, Stockholm, Sweden, [2]Division of Affinity Proteomics, Department of Protein Science, KTH Royal Institute of Technology & SciLifeLab, Stockholm, Sweden, [3]4Dcell, Montreuil, France, [4]Drug Discovery and Development Platform, SciLifeLab & School of Engineering Sciences in Chemistry, Biotechnology and Health, Royal Institute of Technology (KTH), Solna, Sweden, [5]Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Autoantibodies are thought to play a key role in the pathogenesis of idiopathic inflammatory myopathies (IIM). However, 40% of IIM patients, even those with clinical manifestations of anti-synthetase syndrome (ASS), test seronegative to all known myositis specific autoantibodies (MSAs). Therefore, we hypothesized the existence of new potential autoantigens and we included all human cytoplasmic aminoacyl tRNA synthetases (aaRS) in an autoantibody screening of patients with IIM.

Methods: Plasma samples and clinical data from 217 IIM patients were collected from the Karolinska University Hospital myositis cohort. Fulfillment of the 2017 classification criteria (1) for IIM and Connor's criteria (2) for ASS was verified for all patients. Patients were divided into two groups based on the ASS status (not available for 2/217 patients) and clinical manifestations were compared. Autoantibodies (MSAs and myositis associated autoantibodies (MAAs)) were tested in the clinic by standardized immunoassays (ELISA, line lot or immunoprecipitation). The 217 plasma samples were screened, using a multiplex bead array assay, for the presence of autoantibodies against a panel of 118 recombinant protein variants, representing 33 myositis-related proteins, including all 20 cytoplasmic aaRS.

Results: Fifty patients with and 165 without ASS were identified. In the non-ASS group, 69% were seronegative for MSAs. Frequency of muscle and skin involvement did not statistically differ between the two groups, while Raynaud's phenomenon, arthritis, ILD and cardiac disease were statistically more frequent in the ASS group. On the contrary, dysphagia was statistically more prevalent among the non-ASS patients. By performing the multiplex assay, we could confirm reactivity to Jo1, PL-12, PL-7, and EJ in 44/49 patients with ASS, but not to OJ (1 patient) in the ASS group. We identified patients positive for anti-Zo (n=5), -KS (n=2) and -HA (n=3), 9/10 from the non-ASS group. In addition, we identified 12 patients positive for autoantibodies targeting other aaRS (3 from the ASS group, and 9 from the non-ASS group). These novel reactivities could be confirmed by ELISA. Ten of 22 reactivities were identified in patients previously known as seronegative.

Conclusion: Our results suggest that all aaRS may become autoantigenic. Autoantibodies against new aaRS might be found in plasma of patients previously classified as seronegative with potential high clinical relevance.

References

1. Lundberg IE, Tjärnlund A, Bottai M, Werth VP, Pilkington C, de Visser M, et al. 2017 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Adult and Juvenile Idiopathic Inflammatory Myopathies and Their Major Subgroups. Arthritis & Rheumatology. 2017;69(12):2271-82.
2. Connors GR, Christopher-Stine L, Oddis CV, Danoff SK. Interstitial Lung Disease Associated With the Idiopathic Inflammatory Myopathies: What Progress Has Been Made in the Past 35 Years? Chest. 2010;138(6):1464-74.

Disclosure: C. Preger, None; **A. Notarnicola**, None; **C. Hellström**, None; **E. Wigren**, None; **C. Cerqueira**, None; **P. Nilsson**, None; **I. Lundberg**, Corbus Pharmaceutical,, 2, EMD Serono Research & Development Institute, 2, Argenx, 2, Bristol Myers Squibb, 2, Janssen, 2, Kezaar, 2, Octapharma, 1, Orphazyme, 1, Roche, 11, Novartis, 11; **H. Persson**, None; **S. Gräslund**, None; **P. Jakobsson**, None.

Abstract Number: 0002

Salivary Sodium Levels in the Parotid Salivary Gland of SS Patients Suggest B-cell Mediated Epithelial Sodium Channel Disruption

Sarah Pringle[1], Bas Berkhof[1], Martha S. van Ginkel[2], Silvia Liefers[1], Bert van der vegt[2], Fred Spijkervet[2], Hendrika Bootsma[1], Arjan Vissink[1] and Frans Kroese[1], [1]University Medical Center Groningen, Groningen, Netherlands, [2]University of Groningen, University Medical Center Groningen, Groningen, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with Sjögren's syndrome (SS) suffer from significantly reduced saliva production. Saliva is important for oral health. A careful of sodium, chloride, potassium and phosphate ions in saliva is essential for this. Studies have suggested that salivary levels of sodium are increased in SS patients but no mechanism for the increased sodium has been suggested. We aimed to perform an extensive characterization of sialochemical parameters in SS patient saliva compared to non-SS sicca patients, correlate this with SS histopathology, and investigate potential mechanisms underpinning any differences observed.

Methods: Unstimulated and stimulated submandibular/sublingual (SmSl), and stimulated parotid (Par) saliva was collected from 32 SS patients diagnosed according to the 2016 ACR-EULAR criteria. For comparison, 62 non-SS sicca control patients were analysed. Sodium, chloride, phosphate and potassium ion concentration, α-amylase activity and total protein content were measured as sialochemical parameters. CD45, CD20 and CD3 percentage positive cell area in parotid biopsies were quantified, and determination of lymphoepithelial lesion (LEL) severity was carried out as published (1,2). Epithelial sodium channel (ENaC) immunostaining was performed according to standard protocols.

Results: Sodium concentrations were significantly higher in unstimulated SmSl ($p< 0.0001$), stimulated SmSl ($p=0.002$), and stimulated Par saliva ($p< 0.0001$) of pSS patients, compared to non-SS controls (Fig1A). No other sialochemical readout was so significantly different between in saliva from pSS and controls. Stimulated Par saliva sodium levels positively correlated with the percentage of $CD45^+$ infiltration ($r=0.69$, $p< 0.001$; Fig1B) and $CD20^+$ B cells in pSS patient parotid glands ($r=0.73$, $p< 0.0001$; Fig1C) and maximum LEL severity score ($r=0.46$, $p=0.02$; Fig1D) in patient parotid glands. Percentage area of $CD3^+$ T cells were only fairly correlated with salivary sodium ($r=0.23$, $p=0.015$). No significant correlation between other sialochemical parameters and infiltration was observed.

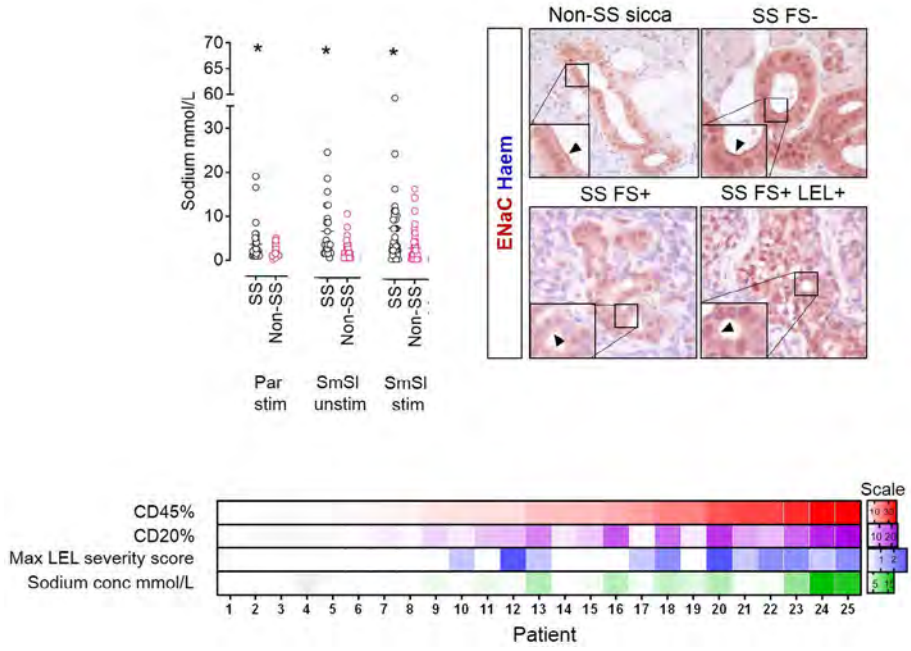


Figure 1. *Salivary sodium levels in pSS patients suggest a role for B cells in dysregulation of epithelial sodium channels.* A) Sodium concentration in stimulated parotid saliva, unstimulated submandibular/sublingual saliva and stimulated submandibular/sublingual saliva, in SS and non-SS patients B-D) Heatmaps of CD45 percentage area (B), CD20+ cell percentage area (C) and maximum lymphoepithelial lesions (LEL) score (D), matched with patient salivary sodium concentration. Scales for each parameters are given to the right of each parameter. E-H) Immunohistochemical staining for the epithelial sodium transporter channel ENaC, in E) non-SS parotid gland tissue, F) SS tissue with a negative focus score (FS) G) SS tissue with a positive FS and H) SS tissue with a positive FS and presence of a LEL.

In non-SS control parotid tissue, ENaC, responsible for transport of sodium out of saliva, into ductal cells, was clearly localized at the apical membrane of the luminal striated duct cells (Fig1E,F). In tissue from SS patients with a positive FS, and SS patients with positive FS and presence of LELs, ENaC appeared to be absent from the apical membrane of the ductal cells (Fig1G,H).

Conclusion: We confirm that salivary sodium levels are increased in patients with SS and extend this observation by correlating these levels with the percentage of $CD45^+$ and $CD20^+$ infiltration. In SG tissue of SS patients with inflammatory foci (with and without LELs), the ENaC protein does not appear to be present at the apical membrane of the ductal cells. We hypothesize that B cell-related cytokines in SS are directly responsible for the dysregulation of sodium transport channels in SS and may represent a larger driving force behind decreased oral health in SS patients than previously appreciated.

N/A

Disclosure: S. Pringle, None; **B. Berkhof**, None; **M. van Ginkel**, None; **S. Liefers**, None; **B. van der vegt**, None; **F. Spijkervet**, None; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2; **A. Vissink**, None; **F. Kroese**, Bristol Myers Squibb, 5, Roche, 5.

Abstract Number: 0003

Clinically Identifiable Autoreactivity Is Common in Severe SARS-CoV-2 Infection

Richard Ramonell[1], Matthew Woodruff[2], Mark Rudolph[3], F. Eun-Hyung Lee[1] and Iñaki Sanz[4], [1]Emory University, Atlanta, GA, [2]Emory University, Decatur, GA, [3]Exagen Inc., Vista, CA, [4]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: A massive expanson of plasmablasts or antibody secreting cells (ASC) have been shown in severe patients with SARS-CoV-2 infection and in patients with autoimmune disease i.e. Systemic Lupus Erythematosus (SLE). The ASC responses in severe SARS-CoV-2 infections are associated with an intense extrafollicular (EF) B cell response reminiscent of flares in SLE patients. Additionally, autoantibodies against phospholipids, type-I interferons, and other targets have been reported in SARS-CoV-2 infection. These observations raise the possibility that severe SARS-CoV-2 infection results in breaks of self-tolerance to autoantigens.

Methods: Peripheral blood was prospectively collected from two groups of patients with COVID-19: 26 critically ill and 18 outpatients together with 15 healthy adults. Plasma from these samples was tested for a variety of autoimmune serologies. Additionally, we retrospectively collected data from 31 critically ill patients with COVID-19 who had autoimmune serologies ordered by their treatment team in the course of their ICU care in two academic ICUs in Atlanta, Georgia, USA.

Results: In the prospective cohort, autoantibodies were found more frequently in the plasma of critically ill subjects compared to healthy donors. Although there was no significant difference between dsDNA levels or ANA titers between groups, there were significantly higher levels of anti-carbamylated antibodies in the critically ill group. Notably, these levels were similar to levels in donors with SLE. In the retrospective cohort, 44% of patients had positive levels of ANA at ≥ 1:80 in a predominantly speckled pattern (50%). Of positive tests, 81% displayed titers of ≥1:160, with the higher titers ranging from 1:320-1:640. Anti-RNP and anti-centromere IgG titers were detected in 2 of 22 ANA+ patients. Reactivity against rheumatoid factor (10/52), phospholipids (3/52), prothrombin (2/52), and c-ANCA (2/52), with or without ANA reactivity, suggests broad autoimmune targeting. 59% of ANA+ patients displayed at least one other positive auto-reactive antibody test. Longitudinal data in seven patients showed that two subjects had increased ANA titers, one remained at 1:360, and one became negative.

Conclusion: Our findings invite two interpretations. Either patients with undocumented and pre-existing autoimmunity comprise the majority of the critical illness within our cohort or, more likely, the immunological environment of serious COVID-19 infection is sufficient to drive de novo autoreactivity against a variety of self-antigens. Longitudinal study of recovered patients will be critical in understanding the persistence of this autoreactive state, its role in the increasingly documented cases of 'lingering' COVID-19, and its propensity for conversion into self-sustaining autoimmunity.

Disclosure: R. Ramonell, None; **M. Woodruff**, None; **M. Rudolph**, Exagen, Inc, 3, 11; **F. Lee**, MicoBPlex, 8; **I. Sanz**, None.

Abstract Number: 0004

Unappreciated Systemic Metabolic Functions of the Canonical B Cell Cytokines, BAFF and APRIL: Regulation of Lipolysis and Non-shivering Thermogenesis and Protection from Obesogenic Diet Induced Weight Gain

Isaac Harley[1], Calvin Chan[2], Paul Pfluger[3], Trompette Aurelien[4], Traci Stankiewicz[5], Jessica Allen[5], Maria Moreno-Fernandez[5], Michelle Damen[5], Jarren Oates[5], Pablo Alarcon[5], Jessica Doll[6], Matthew Flick[7], Leah Flick[8], Juan Sanchez-Gurmaches[9], Rajib Mukherjee[9], Rebekah Karns[10], Michael Helmrath[11], Thomas Inge[12], Stuart Weisberg[13], Sunje Pamp[14], David Relman[15], Randy Seeley[16], Matthias Tschoep[17], Chris Karp[18] and Senad Divanovic[8], [1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]University of Cincinnati, Cincinnati, OH, [3]Technical University of Munich, Munich, Germany, [4]Le Centre hospitalier universitaire vaudois, Lausanne, Switzerland, [5]Cincinnati Children's Hospital Medical Center, Division of Immunobiology, Cincinnati, OH, [6]Cincinnati Children's Hospital Medical Center, Division of Immunobiology, Cincinn, OH, [7]Division of Experimental Hematology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Division of Immunobiology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [9]Division of Endocrinology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [10]Division of Gastroenterology, Hepatology and Nutrition, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [11]Pediatric General and Thoracic Surgery, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [12]Department of Surgery, Children's Hospital Colorado, Aurora, CO, [13]Columbia University Medical Center, New York, NY, USA, New York, NY, [14]Danmarks Tekniske Universitet, Lyngby, Denmark, [15]Department: Medicine - Med/Infectious Diseases - Stanford University, Stanford, [16]Department of Surgery, Internal Medicine and Nutritional Sciences, University of Michigan, Ann Arbor, MI, [17]Division of Metabolic Diseases, Technische Universität München, Munich, Germany, [18]Division of Molecular Immunology, Cincinnati Children's Hospital Medical Center, Cincinnati

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The impact of immune mediators on weight homeostasis and systemic metabolism remains underdefined. Interrogation of resistance to diet-induced obesity in mice lacking a negative regulator of Toll-like receptor signaling serendipitously uncovered a role for B cell activating factor (BAFF). Here, we sought to define noncanonical roles for role BAFF and the BAFF homolog, A proliferation-inducing ligand (APRIL), as regulators of systemic metabolism and weight homeostasis.

Methods: Multiple murine genetic models with variable levels of BAFF and APRIL sufficiency/overexpression were examined in the context of an *in vivo* model of obesogenic diet-induced obesity. Direct effects of BAFF on murine white adipose tissue and brown adipose tissue adipocytes were examined *in vitro* and *in vivo*. Whether these effects on murine metabolism were relevant to humans was assessed by examining plasma BAFF and APRIL levels with BMI change in response to bariatric surgery in obese individuals. Similarly, the direct effects on human white adipose tissue were assessed by examining the expression of orthologous human genes on white adipose tissue adipocytes in response to treatment with recombinant human BAFF and APRIL.

Results: Overexpression of BAFF in multiple mouse models associates with protection from weight gain, approximating a log-linear dose response relation to BAFF concentrations. Gene expression analysis of BAFF-stimulated adipocytes unveils upregulation of lipid metabolism pathways, with BAFF inducing white adipose tissue (WAT) lipolysis. Brown adipose tissue (BAT) from BAFF-overexpressing mice exhibits increased Ucp1 expression and BAFF promotes brown adipocyte respiration and energy expenditure. A proliferation-inducing ligand (APRIL), a BAFF homolog, similarly modulates WAT and BAT lipid handling. Genetic deletion of both BAFF and APRIL augments diet-induced

obesity. Importantly, BAFF/APRIL effects are conserved in human adipocytes and higher BAFF/APRIL levels correlate with BMI decrease after bariatric surgery. Finally, preliminary results suggest that the critical source BAFF in these models is intestinal epithelial cells.

Conclusion: Together, our results define the BAFF/APRIL axis as a multifaceted immune regulator of weight gain and adipose tissue function. The percentage change in BAFF sufficient to modify obesity in murine models is comparable to levels that increase risk of Lupus and Multiple Sclerosis in humans. Thus, these findings will inform our understanding of the unexpected potential metabolic effects of B-cell targeted therapies in humans.

Disclosure: I. **Harley**, None; **C. Chan**, None; **P. Pfluger**, None; **T. Aurelien**, None; **T. Stankiewicz**, None; **J. Allen**, N/A, 12, Patent on BAFF and APRIL; **M. Moreno-Fernandez**, None; **M. Damen**, None; **J. Oates**, None; **P. Alarcon**, None; **J. Doll**, None; **M. Flick**, None; **L. Flick**, None; **J. Sanchez-Gurmaches**, None; **R. Mukherjee**, None; **R. Karns**, None; **M. Helmrath**, None; **T. Inge**, None; **S. Weisberg**, None; **S. Pamp**, None; **D. Relman**, None; **R. Seeley**, consultant to Novo Nordisk, Sanofi, Scohia, GuidePoint Consultants, Kintai Therapeutics, and Ionis., 2, Novo Nordisk, Zafgen, Astra Zeneca, Redesign Health, Ionis and Pfizer, 12, research support or equity; **M. Tschoep**, Novo Nordisk and ERX, 1; **C. Karp**, N/A, 12, Patent on BAFF and APRIL; **S. Divanovic**, N/A, 12, Patent on BAFF and APRIL, Janssen Research & Development, 2.

Abstract Number: 0005

Maturation and Dysfunction of Autoreactive B Cell Clones in Tissues of Patients with Sjögren's Syndrome

Mathijs Broeren[1], Giulia Balzaretti[2], Jing Wang[3], Patricia Groenen[1], Barbera van Schaik[4], Tim Chataway[3], Charlotte Kaffa[1], Sander Bervoets[1], Konnie Hebeda[1], Gergana Bounova[5], Ger Pruijn[1], Tom Gordon[3], Niek De Vries[6] and **Rogier Thurlings**[7], [1]Radboud University Medical Center, Nijmegen, Netherlands, [2]Amsterdam, Netherlands, [3]Flinders University, Adelaide, Australia, [4]Amsterdam University Medical Centers, Amsterdam, Netherlands, [5]Enpicom BV, Den Bosch, Netherlands, [6]Amsterdam UMC, Amsterdam, Netherlands, [7]Radboud University Medical Centre, Nijmegen, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren's syndrome (SjS) involves chronic inflammation of exocrine glands that can be complicated by extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT). We analyze the generation of the antinuclear (ANA) and rheumatoid factor (RF)-specific B cell repertoires, and their interaction in patient tissues before and at disease relapse after rituximab treatment.

Methods: We analyzed blood and tissues of 6 SjS patients with anti-Ro60, anti-Ro52, anti-La and RF autoantibodies. We analyzed the tissues of 2 patients that had been diagnosed with MALT lymphoma and were subsequently treated with rituximab monotherapy. We analyzed anti-Ro60, anti-Ro52, anti-La and RF clones using a combination of new, partly self-developed tools to analyze autoreactive B cell receptors at DNA, RNA, protein and single cell level.

Results: In affected tissues anti-Ro52, anti-La and anti-Ro60 clones outnumbered RF clones. Compared to ANA clones affinity maturation of RF clones was IgM directed and depended on the structural integrity of the frame work regions of preferred variable immunoglobulin segments. In MALT lymphoma tissues lymphomatous clones were

solitary large RF clones using shared sequence motifs and displaying high intra-clonal diversification. These co-occurred with a high number of ANA clones. At clinical relapse after rituximab treatment dominant persistent MALT or other RF clones proliferated in a memory, intra-clonal diversification directed recall response. In the same tissues many small ANA clones displayed a plasma cell directed recall response.

Conclusion: We find divergent affinity maturation of RF compared to ANA clones, that exacerbates in RF-clone derived MALT lymphomas and at regeneration of disease manifestations after rituximab.

Disclosure: M. Broeren, None; **G. Balzaretti**, None; **J. Wang**, None; **P. Groenen**, None; **B. van Schaik**, None; **T. Chataway**, None; **C. Kaffa**, None; **S. Bervoets**, None; **K. Hebeda**, None; **G. Bounova**, None; **G. Pruijn**, None; **T. Gordon**, None; **N. De Vries**, None; **R. Thurlings**, None.

Abstract Number: 0006

Metabolic Characteristics of Age-related B Cells in Lupus-prone Mice and Effects on Follicular Helper T Cells

Ivan Ramirez[1], Betty Diamond[2] and Sun Jung Kim[3], [1]Northwell, Little Neck, NY, [2]Northwell Health, Manhasset, NY, [3]Feinstein Institutes for Medical Research, Manhasset, NY

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Since the description of age-associated B cells (ABC), there has been a growing interest in the role of these cells in autoimmunity. Evidence suggests that ABC are involved in antigen presentation, autoantibody production and demonstrates a particular response to Toll-like receptor stimulation[1,2]. The study of lymphocyte metabolism in SLE has revealed that metabolic pathways are hyperactivated in lupus-prone mice compare to controls and that the treatment with metabolic inhibitors reverses these changes[3,4]. In this study, we test the hypothesis that ABC cells show increased metabolic activity and the altered metabolism in ABCs is responsible for the promotion of Tfh cell differentiation.

Methods: ABC cells were identified by the definition of CD11c+/ CD11b+ in CD19+ B cells by flow cytometry analysis. For the metabolism study, ABCs were isolated from spleens of 10–12-month old lupus-prone mice, triple congenital *sle1,2,3* (TC) and B6.lpr, and age-matched C57BL/6 controls, and metabolism (oxygen consumption (OCR) and extracellular acidification rate (ECAR)) was analyzed by the seahorse assay with XFp cell mito stress kit. Tfh differentiation was conducted by co-culture of naïve CD4+ T cells and isolated ABCs or follicular B cells (FO B) for 3 days. After the co-culture, Tfh cells were identified by CXCR5+/PD1+ CD4+, and activation of T cells were measured by the expression of CD44 on T cells by flow cytometry analysis. Under similar co-culture condition of ABC and Naïve CD4+ T cells, the effects of various agents, Metformin, Etomoxir and N-Acetyl cysteine on differentiation was assessed.

Results: We observed that ABCs have increased mitochondrial metabolism (but not glycolysis measured by ECAR) in lupus-prone mice compared to ABC from age-matched controls. No difference in metabolism was found in FO B cells between lupus mice and controls. After 72 hours of coculture condition naïve CD4 T cells with B cells, both FO B and ABCs induced T cell activation and proliferation equally, but there was a higher percentage of activated T cells differentiated into CXCR5+ PD1+ Tfh cells by ABCs compared to T cells with FO B. The differentiation and activation of T cells were suppressed by metformin treatment.

Conclusion: ABC cells show an increase in mitochondrial metabolism measured by OCR compared to controls. Coculture of ABCs with naïve CD4 T cells induced differentiation to T cells with makers of Tfh cells. Blocking of mitochondrial activation by metformin could suppress Tfh differentiation. This data suggests that this increase in metabolic activity might correspond with the inflammatory profile of ABCs.

Disclosure: I. Ramirez, None; **B. Diamond**, ISD, 2, nextcure, 2, J5J, 2, astlia, 2, dbv, 2, cyxone, 2; **S. Kim**, None.

Abstract Number: 0007

Divergent Reactivities of Rheumatoid Factors and Anti-Modified Protein Antibodies Converge on IgG Epitopes

Aisha Mergaert[1], Zihao Zheng[1], Michael Denny[1], Maya Amjadi[1], Janna Bashar[1], Michael Newton[1], Vivianne Malmström[2], Caroline Grönwall[2], Sara McCoy[1] and **Miriam Shelef**[1], [1]University of Wisconsin, Madison, WI, [2]Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) patients often develop rheumatoid factors (RFs), antibodies that bind IgG Fc, and anti-modified protein antibodies (AMPAs), multi-reactive autoantibodies that commonly bind citrullinated, homocitrullinated, and acetylated antigens. Recently, antibodies that bind citrulline-containing IgG epitopes were discovered in RA, suggesting that additional undiscovered IgG epitopes could exist and that IgG could be a shared antigen for RFs and AMPAs. The objective of this study was to reveal new IgG epitopes in rheumatic disease and to determine if cross-reactive AMPAs bind IgG.

Methods: Using RA, lupus, Sjögren's syndrome, and spondyloarthropathy sera, IgG binding to native, citrulline-containing, and homocitrulline-containing linear epitopes of the IgG constant region were evaluated by peptide array with novel epitopes further evaluated by ELISA. Monoclonal AMPA binding to IgG-derived peptides and IgG Fc was evaluated by ELISA.

Results: Seropositive RA sera had high IgG binding to multiple citrulline- and homocitrulline-containing IgG-derived peptides, whereas only anti-SSA+ Sjögren's Syndrome had consistent binding to a single linear native epitope of IgG. AMPAs bound citrulline- and homocitrulline-containing IgG peptides and modified IgG Fc.

Conclusion: The repertoire of epitopes bound by AMPAs includes modified IgG epitopes, positioning IgG as a common antigen that connects the divergent reactivities of RFs and AMPAs.

Disclosure: A. Mergaert, None; **Z. Zheng**, None; **M. Denny**, None; **M. Amjadi**, None; **J. Bashar**, None; **M. Newton**, None; **V. Malmström**, None; **C. Grönwall**, None; **S. McCoy**, BMS, 2, Novartis, 1, Boehringer Ingelheim, 6; **M. Shelef**, None.

Abstract Number: 0008

Jo-1-Binding and Clonally-Expanded Memory B Cells Express Germline and Somatically-Mutated B Cell Receptors in Anti-tRNA Synthetase Syndrome Patients

Erin Wilfong, Alberto Cisneros, **Jennifer Young-Glazer**, Scott Smith, Leslie Crofford and Rachel Bonami, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-tRNA synthetase syndrome (ARS) is a severe systemic autoimmune disease associated with myositis, interstitial lung disease, rash, and arthritis. ARS is associated with autoantibodies towards the tRNA synthetases, the most common being anti-histidyl tRNA synthetase (Jo-1). We previously showed Jo-1-binding B cells (JoBCs) isolated from Jo-1 autoantibody+ (Jo-1 ARS) patients are skewed towards a non-class-switched B cell subset that has phenotypic features of autoreactive-prone memory B cells. Mutated JoBC B cell receptors (BCRs), which dictate antigen specificity, would imply a requirement for T cell selection, whereas germline BCRs would point to T cell-independent mechanisms of JoBC expansion. Our objective was to define BCR V gene usage and mutation among BCRs expressed by JoBCs and determine phenotypic and BCR repertoire features of highly expanded B cell clones in ARS patients.

Methods: We applied human hybridoma technology to identify Jo-1 autoantigen-binding B cells. Additionally, single-cell, tandem RNAseq/BCRseq and a modified Seurat and IMGT/HighVQUEST-based pipeline was used to identify and analyze expanded B cell clones isolated from Jo-1 ARS, non-Jo-1 ARS, and healthy control peripheral blood (n=5 donors per group). BCR gene structure and phenotypic attributes were determined.

Results: JoBC hybridoma clones expressed germline and mutated BCRs. VH4-34 and VH3-21 were identified among JoBC hybridomas as well as clonally expanded B cells in our single-cell dataset isolated from distinct donors. Clonally-expanded B cells were biased towards memory and plasmablast subsets in both Jo-1 ARS and non-Jo-1 ARS patients. The majority of Jo-1 ARS expanded clones were not class-switched, whereas IgG and IgA class-switched clones were more predominant in non-Jo-1 ARS.

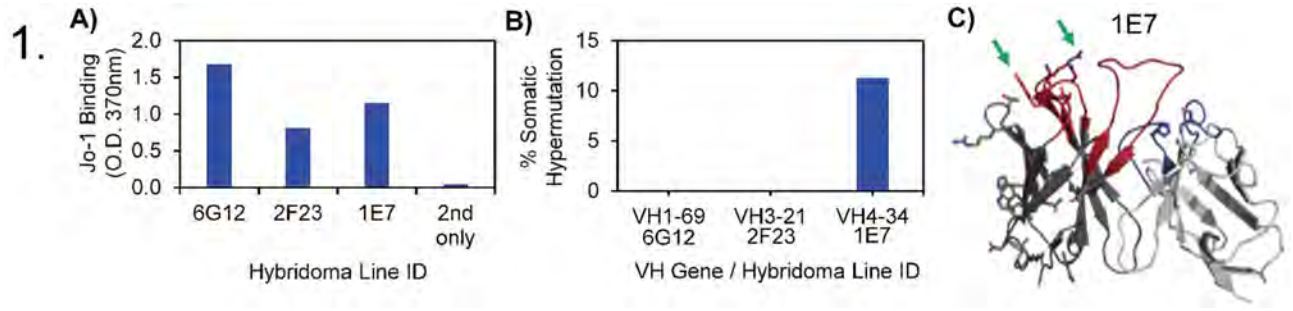


Figure 1. Somatically-mutated as well as germline BCRs confer Jo-1 autoantigen recognition. A) Jo-1 reactivity of representative JoBC monoclonal hybridoma lines is shown by ELISA. B) % Somatic hypermutation (y-axis) and VH gene identity (x-axis) is shown. C) BCR structural model of JoBC hybridoma line 1E7 depicts amino acid mutations as sticks (e.g., arrows). VH CDR loops (red), VL CDR loops (blue).

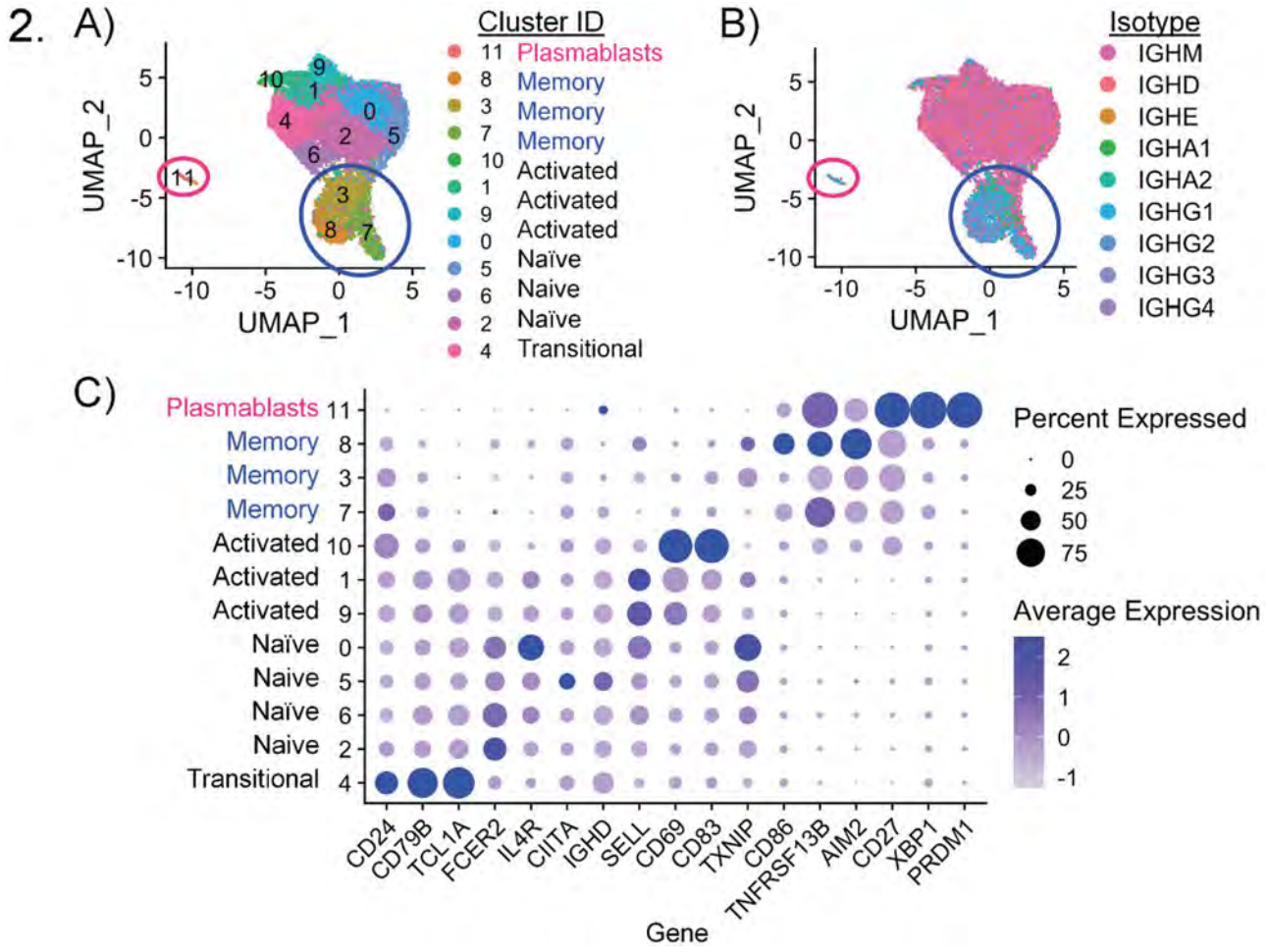


Figure 2. Single-cell transcriptomics identifies distinct B cell subsets in peripheral blood. Single-cell RNAseq and BCRseq technology was used to profile purified B cells isolated from ~5x106 cryopreserved PBMCs per donor from Jo-1 ARS patients, Non-Jo-1 ARS patients, and healthy controls (n=5 donors per group). Seurat was used to determine A) RNAseq-based B cell clusters, B) BCR isotype, and C) specific gene expression profiles to define B cell cluster identities (expression of selected genes is shown). Memory B cell (blue circles) and plasmablast subsets (pink circles) are highlighted in panels A-B.

Conclusion: These data suggest B cell clones can expand, enter memory, and differentiate into plasmablasts prior to class-switching, particularly in Jo-1 ARS patients. Our approaches to identify autoantigen-specific and clonally-expanded B cells could be used to track B cell perturbations as correlates of conventional or experimental immune therapy responsiveness. Improved monitoring of deleterious expansion of autoantigen-specific B cells could improve disease management in ARS patients and other rheumatic diseases. Germline VH4-34 cross-reacts with commensal bacteria, providing a potential mechanism for JoBC immune tolerance breach prior to somatic hypermutation and T cell selection.

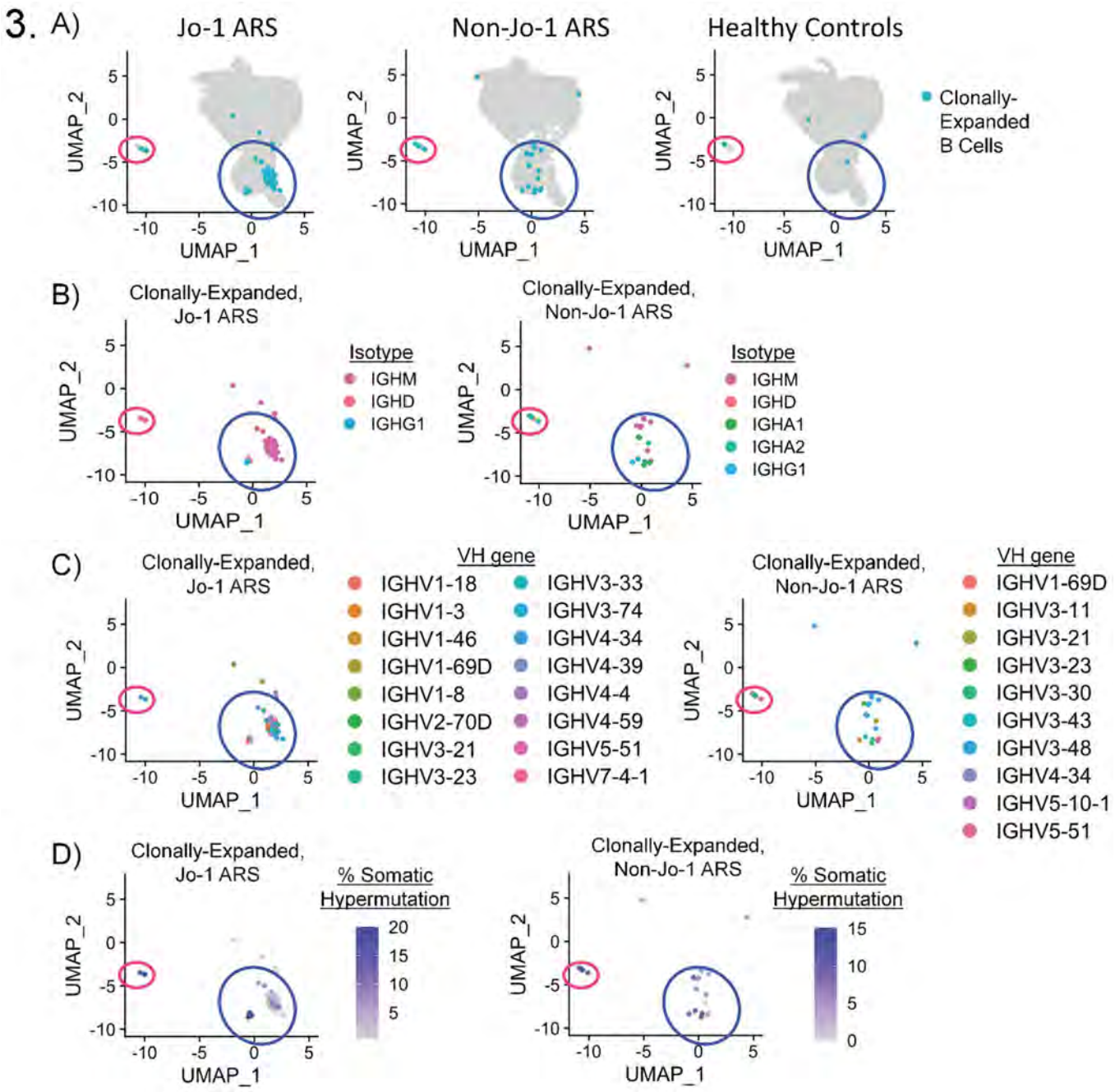


Figure 3. Clonally expanded, memory B cells isolated from Jo-1 ARS and non-Jo-1 ARS patients express both minimally and highly mutated BCRs, which are skewed towards non-class-switched isotypes in Jo-1 ARS patients. B cell subsets were identified as in Fig. 2; memory B cell (blue circles) and plasmablast subsets (pink circles) are highlighted. A) Integrated Seurat and IMGT/HighV-QUEST BCR gene analysis identified clonally expanded B cells (n≥3 clones per clonotype, teal) among Jo-1 ARS (left), non-Jo-1 ARS (middle), or healthy controls (right), n=5 participants per group. B-D) Data filtered on clonally-expanded B cells from Jo-1 ARS or Non-Jo-1 ARS patients show: B) BCR isotypes, C) BCR V gene usage, and D) BCR somatic hypermutation (depicted by heat scale).

Disclosure: E. Wilfong, Boehringer-Ingelheim, 1, 5; **A. Cisneros**, None; **J. Young-Glazer**, None; **S. Smith**, None; **L. Crofford**, Boehringer-Ingelheim, 5, UpToDate, 9; **R. Bonami**, Boehringer-Ingelheim, 5.

Abstract Number: 0009

Humoral Immune Responses to SARS-CoV2 Infections and upon Vaccination Against SARS-CoV2

STEPHANIE FINZEL[1], Nicole Peter[2], Chiara Brand[2], Beate Fischer[2], Bärbel Keller[2], Sebastian Weigang[3], Georg Kochs[3], Martin Schwemmle[3], Siegbert Rieg[4], Philipp Mathé[4], Winfried Kern[4], Lia van der Hoek[5], Kathrin de la Rosa[6], Hans-Martin Jäck[7], Klaus Warnatz[2], Reinhard Voll[8] and Hermann Eibel[2], [1]University Clinic of Freiburg, Department of Rheumatology and Clinical Immunology, Freiburg, Germany, [2]Department of Rheumatology and Clinical Immunology, Medical Faculty, University of Freiburg and Center for Chronic Immunodeficiency, Medical Center, University of Freiburg, Freiburg, Germany, [3]Institute of Virology, University of Freiburg, Freiburg, Germany, [4]Department of Infectiology, Medical Faculty, University of Freiburg, Freiburg, Germany, [5]Laboratory of Experimental Virology, Department of Medical Microbiology, Center for Infection and Immunity Amsterdam (CINIMA), Academic Medical Center of the University of Amsterdam, Amsterdam, Netherlands, [6]Max-Delbrück-Centrum für Molekulare Medizin (MDC), Berlin, Germany, [7]Department of Medicine 3. Division of Immunology, Friedrich-Alexander-University Erlangen, Erlangen, Germany, [8]Department of Rheumatology and Clinical Immunology, University Medical Center, Faculty of Medicine, Albert-Ludwigs-University of Freiburg, Freiburg, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: We compared humoral immune responses against SARS-CoV-2 to responses against spike-antigen after vaccination.

Methods: 800 health-care workers from University Medical Center Freiburg, Germany, were pursued for 9 months; 120/800 had COVID-19 infections. IgM, IgG and IgA responses against spike, nucleocapsid, ORF3A, ORF8 were determined by ELISA. Spike-specific and neutralizing antibody concentrations were quantified by functional assays. IgM, IgA, IgG and neutralizing antibody titers against Wuhan, B1.17 and B1.351 spike variants were measured after BNT162b2-vaccination.

Results: While acute infection induced robust and strong IgM, IgG and IgA response against viral spike and nucleocapsid proteins, antibody titers and neutralizing antibody concentrations decreased over time in ~50% of samples. IgM, IgG, IgA antibodies against ORF3A/ORF8 were also found in non-infected individuals. Furthermore, SARS-CoV2 infections induced strong humoral response against endemic coronaviruses HCoV-229E, -OC43, -NL63 and -HKU1. Spike-specific IgG+ memory B-cells were detected in ≤ 1/1000 B-cells also in convalescents with low virus-specific antibody titers indicating that SARS-CoV-2-directed memory B-cell formation may differ from humoral anti-viral responses. BNT162b2 prompted strong primary immune response against the Wuhan, B1.17 and B1.351 variants starting 1.5 weeks post vaccination. Inhibition of ACE2-binding and virus neutralization assays revealed higher neutralizing activity against Wuhan and B1.17 than against B1.351.

Conclusion: Humoral response against SARS-CoV-2 often subsides within nine months, whereas memory B-cells apparently uphold immune response. Cross-reactivity of anti-SARS-CoV-2 IgG with endemic coronaviruses could bias interpretation of POC tests. ORF3A and ORF8-antibodies are detectable in non-infected individuals and therefore not indicative of SARS-CoV-2 infections. Vaccination with BNT162b2 elicits higher anti-spike antibody titers than infection with SARS-CoV-2.

Disclosure: S. FINZEL, None; **N. Peter**, None; **C. Brand**, None; **B. Fischer**, None; **B. Keller**, None; **S. Weigang**, None; **G. Kochs**, None; **M. Schwemmle**, None; **S. Rieg**, None; **P. Mathé**, None; **W. Kern**, None; **L. van der Hoek**, None; **K. de la Rosa**, None; **H. Jäck**, None; **K. Warnatz**, None; **R. Voll**, None; **H. Eibel**, None.

Abstract Number: 0010

Relaxed Peripheral Tolerance Drives Broad *de Novo* Autoreactivity in Severe COVID-19

Matthew Woodruff[1], Richard Ramonell[2], Ankur Singh Saini[2], Mark Rudolph[3], F. Eun-Hyung Lee[2] and Iñaki Sanz[4], [1]Emory University, Decatur, GA, [2]Emory University, Atlanta, GA, [3]Exagen Inc., Vista, CA, [4]Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (0001–0010)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: An emerging feature of COVID-19 is the identification of autoreactivity in patients with severe disease that may contribute to disease pathology, however the origins of these responses remain unclear. Previously, we identified extrafollicular B cell activation as a shared immune feature between severe COVID-19 and active rheumatic disease. In autoimmune settings, this pathway is associated with relaxed peripheral tolerance in the antibody secreting cell compartment and the generation of *de novo* autoreactive responses.

Methods: To further investigate these responses in COVID-19, we performed single-cell B-cell repertoire analysis on 7 patients with severe disease to understand the nature of the antibody secreting cell compartment. We paired these data with cytometry-based and serological assays to detail the nature of these cells, and their contribution to antiviral, and autoreactive responses.

Results: In these patients, we identify a unique low-mutation IgG1 fraction of the antibody secreting cell compartment that lacks surface-expressed B cell receptor, and thus cannot be studied through traditional antigen-labeling studies. These cells are not memory derived, display very low levels of selective pressure, and are enriched for autoreactivity-prone V gene *IGHV4-34*. Within this compartment, we identify B cell lineages that display specificity to both SARS-CoV-2 and autoantigens, and describe progressive, broad, clinically relevant autoreactivity within these patients including emerging reactivity against the glomerular basement membrane. While progressive early in acute infection, we identify the contraction of this pathway 6 months post-recovery, and a re-establishment of tolerance standards coupled with a concomitant loss of acute-derived responders irrespective of antigen specificity.

Conclusion: In total, this study reveals the origins, breadth, and resolution of emerging autoreactivity in severe COVID-19, with significant implications in both acute-phase rheumatologic interventions and potential treatment of patients with post-COVID sequelae.

Disclosure: M. Woodruff, None; **R. Ramonell**, None; **A. Singh Saini**, None; **M. Rudolph**, Exagen, Inc, 3, 11; **F. Lee**, MicoBPlex, 8; **I. Sanz**, None.

Abstract Number: 0011

Differential Inflammation-mediated Function of Prokineticin 2 in the Synovial Fibroblasts of Patients with Rheumatoid Arthritis Compared to Osteoarthritis

Kentaro Noda, Bianca Dufner and Rainer Straub, Laboratory of Experimental Rheumatology and Neuroendocrine Immunology, Department of Internal Medicine I, University Hospital Regensburg, Regensburg, Germany

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Prokineticin 2 (PK2) is a secreted protein involved in several pathological and physiological processes, including the regulation of inflammation, sickness behaviors, and the circadian rhythm. Recently, it was reported that PK2 is associated with the pathogenesis of collagen-induced arthritis in mice. However, whether PK2 influences the pathogenesis of rheumatoid arthritis (RA) or osteoarthritis (OA) remains unknown.

Methods: We collected synovial tissue, plasma, and synovial fluid from RA and OA patients. Fibroblast-like synoviocytes (FLS) were induced from synovial tissue. We examined the expressions of PK2 and its receptors prokineticin receptor (PKR) 1 and 2 in RA and OA synovial tissues and FLS using immunohistochemistry and measured the concentration of PK2 in plasma and synovial fluid using ELISA. To study the cellular expression of PK2, PKR1, and PKR2

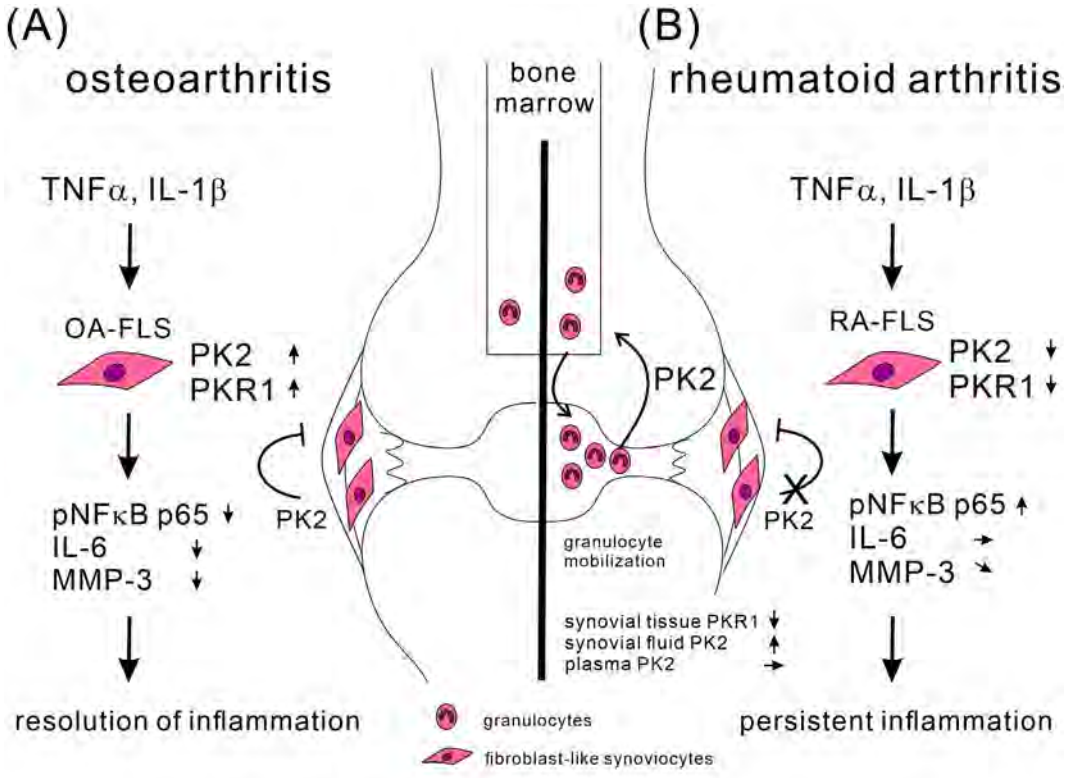


Figure Model describing the dysregulation of endogenous inflammation by PK2 in RA.

under proinflammatory conditions, we stimulated FLS with TNFa (10 ng/ml), IL-1b (200 pg/ml), and TGFb (10 ng/ml) for 24 and 48 h and examined the expression of PK2, PKR1, and PKR2 using cell-based ELISA. Finally, we analyzed the effect of PK2 on TNFa-pretreated FLS using IL-6 and MMP-3 ELISAs.

Results: PK2, PKR1, and PKR2 were expressed in RA and OA synovial tissues. PKR1 expression in RA synovial tissue was downregulated compared with OA synovial tissue. PK2 and PKR1 were expressed in RA and OA-FLS. However, PKR2 was not expressed in FLS. PK2 expression in RA-FLS was downregulated at 24 h after stimulation with TNFa, IL-1b, and TGFb. PKR1 expression was upregulated at 48 h after stimulation with TNFa and TGFb in OA-FLS and downregulated at 48 h after stimulation with IL-1b in RA-FLS. PKR2 expression in OA- and RA-FLS was upregulated at 24 and 48 h after stimulation with TGFb and at 48 h after stimulation with TNFa in RA-FLS. The PK2 concentration was higher in RA synovial fluid than in OA synovial fluid but similar between RA and OA plasma. PK2 suppressed the production of IL-6 and MMP-3 from TNFa-prestimulated OA-FLS, and this effect was attenuated in TNFa-prestimulated RA-FLS.

Conclusion: We demonstrated that PK2, PKR1, and PKR2 were expressed in synovial tissue. This indicates that PK2 acts locally. Indeed, PK2 had an anti-inflammatory effect on OA-FLS that was likely mediated through the PKR1 pathway, whereas this anti-inflammatory effect was attenuated in RA-FLS because of PKR1 downregulation. This study provides a new model to explain some aspects regarding the chronicity of inflammation in RA.

In OA, exposure to proinflammatory cytokines upregulates the expression of PKR1. PK2 secreted from OA-FLS acts on PKR1 in an autocrine or paracrine manner and reduces the secretion of IL-6 and MMP-3 from OA-FLS (A). In contrast, in RA-FLS, exposure to proinflammatory cytokines downregulates the expression of PK2 and PKR1 (B). Therefore, PK2 does not exhibit a similarly strong anti-inflammatory effect in RA-FLS compared with OA-FLS. Indeed, the expression of PKR1 in RA synovial tissue was decreased compared with OA synovial tissue. This dysregulation in the endogenous inflammation-mediated modulation of PK2 in RA-FLS may be associated with the chronicity of inflammation in the pathogenesis of RA.

Disclosure: K. Noda, None; **B. Dufner**, None; **R. Straub**, None.

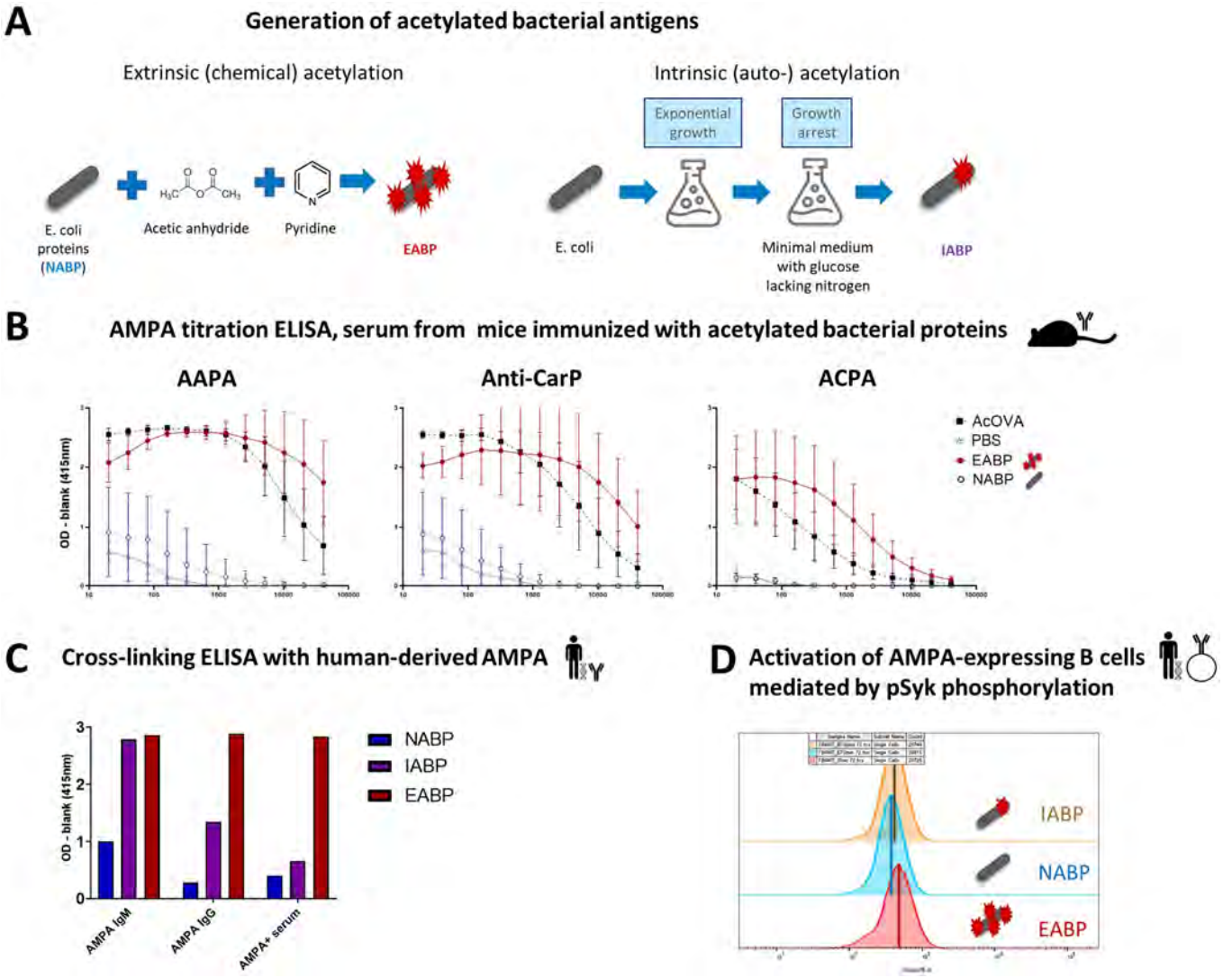
Abstract Number: 0012

A Novel Mechanism Linking Mucosal Bacteria with Autoantibody Responses in RA: Acetylated Bacterial Lysate as a Model Antigen

Mikhail Volkov, Arieke Kampstra, Karin van Schie, Joanneke Kwekkeboom, Tom WJ Huizinga, René Toes and Diane van der Woude, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by autoantibodies against post-translationally modified proteins (AMPA) such as citrullinated, carbamylated and acetylated proteins. Importantly, these antibodies are highly multireactive, as they often recognize more than one of these post-translational modifications. Despite extensive research, the antigens inducing the breach of tolerance remain unknown, although microbial antigens are often suspected. Various bacteria are known to be capable of acetylation, therefore, it is intriguing to know which



A: Methods of E. coli proteins acetylation. B: AMPA reactivities in mice immunized with extrinsically (chemically) acetylated bacterial proteins and control antigens. Delta OD values measured with titrated mice serum on modified fibrinogen ELISA are depicted. C: Recognition of bacterial protein samples by AMPA derived from RA patients. Delta OD obtained with cross-linking ELISA are depicted. D: Activation of AMPA IgG expressing B cells as measured by Syk phosphorylation assay using flow cytometry. Histograms visualizing mean fluorescence intensity values of stimulated cells stimulated with different bacterial protein samples are depicted.

mechanisms underlie the breach of tolerance towards acetylated proteins and development of AMPA. The aim of this project was to investigate whether acetylated proteins of bacterial origin (1) are recognized by human derived AMPA and AMPA-expressing B cells; and (2) can induce AMPA development when used to immunize mice.

Methods: Acetylated E. coli proteins were acquired with two separate methods (Figure A): by culturing E. coli in a condition promoting auto-acetylation (intrinsically acetylated bacterial proteins, IABP), or by directly acetylating lysate-derived proteins via a chemical reaction (extrinsically acetylated BP, EABP). Acetylated ovalbumin (AcOVA) served as positive control for AMPA induction in mice, while non-acetylated BP (NABP) and phosphate buffer saline (PBS) served as negative control. Mice were immunized with these proteins and the resulting antibody response was studied by ELISA. Furthermore, EABP/IABP/NABP were investigated for recognition by human-derived AMPA with ELISA and AMPA-expressing B cells with spleen tyrosine kinase (Syk) phosphorylation assay; acetylated human fibrinogen and native fibrinogen served as positive and negative control.

Results: Intrinsic acetylation resulted in partial, while extrinsic/chemical acetylation resulted in complete acetylation of E. coli proteins. Repetitive immunization of mice with EABP resulted in an AMPA response recognizing acetylated, carbamylated and citrullinated proteins, which was not observed in mice immunized with NABP or IABP (Figure B). Human-derived AMPA recognized EABP and IABP (Figure C). B cell activation (measured by Syk phosphorylation) assay indicated that AMPA-expressing B cells recognized EABP and (to a lesser extent) IABP, but not NABP (Figure D).

Conclusion: Acetylated bacterial proteins are potent antigens that can induce cross-reactive AMPA responses in mice, and can be recognized by human AMPA and AMPA-expressing B cells. This suggests that acetylated bacterial proteins could potentially be involved in the breach of tolerance in RA.

Disclosure: M. Volkov, None; **A. Kampstra**, None; **K. van Schie**, None; **J. Kwekkeboom**, None; **T. Huizinga**, None; **R. Toes**, None; **D. van der Woude**, None.

Abstract Number: 0013

Cyclin Dependent Kinase 4 and 6 Determine the Cytokine Responsiveness by Stabilizing JUN in Rheumatoid Arthritis Synovial Fibroblasts

Tadashi Hosoya[1], Tetsuya Saito[2], Hiroyuki Baba[2], Nao Tanaka[2], Seiji Noda[2], Yoji Komiya[2], Yasuhiro tagawa[2], Akio Yamamoto[2] and Shinsuke Yasuda[2], [1]Tokyo Medical and Dental University(TMDU), Tokyo, Japan, [2]Tokyo Medical and Dental University (TMDU), Tokyo, Japan

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Although current inflammation-targeted therapy improved the outcome of patients with rheumatoid arthritis (RA), the achievement of complete disease remission was still challenging. Since synovial fibroblasts (SFs) in RA are epigenetically altered, acquiring invasiveness, and excessive cytokine-producing and proliferating capacity, SFs-targeted therapy was expected to be alternative or complementally therapeutic strategy. This study was designed for discerning the underlying mechanisms involved in cyclin-dependent kinase (CDK) 4/6-mediated regulation of inflammatory mediators, including matrix metalloproteinases.

Methods: CDK4/6 activity in RASFs was inhibited or enhanced using a small-molecule CDK4/6 inhibitor (CDKI) or gene transduction. The gene and protein expressions were evaluated with quantitative PCR and ELISA under the combination treatment with IL-1β and TNFα (0.2 ng/ml, respectively) as a stimulation in the presence (10%) or absence (0.5%) of fetal bovine serum (FBS). The nuclear protein binding to the DNA sequence was assessed with an electrophoresis mobility shift assay. Protein expression and ubiquitination were assessed with Western blotting using specific antibodies. Gene knockdown was performed using RNA interfering. RNA-Seq was performed to identify genes affected by CDKI treatment in cytokine stimulation using RASFs from 5 individuals.

Results: In RASFs, cytokine productions induced with the combination of IL-1β and TNFα were enhanced in the presence of FBS. Among them, CDKI suppressed the production of MMP-1 and MMP-3, but not MMP-2, CXCL8 and IL-6. MMP-1 and MMP-3 shared AP-1 binding motif in their promoter region. CDKI impaired the binding of AP-1 components to DNA. CDK4/6 protected JUN, one of the AP-1 components, from proteasome-dependent degradation by inhibiting ubiquitination, indicating that CDK4/6 inhibition would result in the repression of a set of genes regulated by AP-1. The RNA-Seq analysis confirmed the hypothesis, namely, the AP-1 motif was enriched in a set of genes

suppressed by CDKI treatment. Interestingly, according to the KEGG pathway classification, these CDKI-repressing inflammatory genes were also enriched in RA associated genes (Q value 0.03), Cytokine-cytokine receptor interaction (Q value 0.07), and IL-17 signaling (Q value 0.07).

Conclusion: The active CDK4/6 enhanced transcriptional activity of AP-1 via JUN stabilization, indicating that CDK4/6 would determine the cytokine hyper-responsiveness of RASFs. We have revealed that inhibition of CDK 4/6 prevented joint destruction in animal models of arthritis by inhibiting synovial cell proliferation and by synergizing with TNF inhibition or IL-6 inhibition. Since the pharmacologic inhibition of CDK4/6 was established as tolerable in the cancer treatment, it would exert anti-arthritic effects to attenuate pathogenic characteristics of RASFs in addition to suppressing synovial hyperplasia.

Disclosure: T. **Hosoya**, GlaxoSmithKline, 5; **T. Saito**, None; **H. Baba**, None; **N. Tanaka**, None; **S. Noda**, None; **Y. Komiya**, None; **Y. tagawa**, None; **A. Yamamoto**, None; **S. Yasuda**, Abbvie, 5, 6, Asahi Kasei Corporation, 5, 6, Chugai Pharmaceutical, 5, 6, Bristol Myers Squibb, 5, 6, Ono pharmaceuticals, 5, 6, Eisai, 5, 6, Tanabe-Mitsubishi Pharmaceutical, 5, 6, Eli Lilly, 5, 6, GlaxoSmithKline, 6, Pfizer, 6.

Abstract Number: 0014

Low Baseline Expression of Pyruvate Kinase and Succinate Dehydrogenase Genes in the Peripheral Blood of Rheumatoid Arthritis Patients Treated with Tofacitinib Is Associated with Clinical Remission at the End of Follow-up

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease of unknown etiology, which is characterized by erosive arthritis and systemic inflammation. Tofacitinib (TFCN) is a Janus kinase (JAK) inhibitor that targets JAK1/JAK3. Presently it is not possible to predict TFCN efficacy in every patient while some patients are non-responsive to the drug that may produce adverse effects. However, identification of patients sensitive to TFCN before treatment could significantly improve therapy outcome. TFCN function in RA patients has been recently associated with alterations in bioenergetics, mitochondrial function, and ATP production [McGarry et al. Arthritis Rheumatol, 2018; 70:1959.]. Therefore, we hypothesized that baseline metabolic status of RA patients prior to drug administration can predict the therapeutic outcome. We aimed to investigate the importance of baseline expression of genes involved in energy generation in RA patients, which could serve prognostic biomarkers for treatment response to tofacitinib.

Methods: Peripheral blood of 28 RA patients aged 52.2±15.6 years old, average disease duration 3.5 years (range 0.6-19) treated with TFCN (5-10 mg twice a day) during three months and 26 healthy age-matched control subjects were examined. Clinical response was assessed by serum levels of ACPA antibodies, rheumatoid factor (RF), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and disease activity score (DAS28-ESR). Clinical remis-

sion was assessed according to ACR criteria and DAS28 (DAS28 < 2.6). Protein concentrations were measured using ELISA. Total RNA was isolated and used in gene expression studies performed with quantitative real-time RT-PCR.

Results: All of the patients were Steinbrocker's radiographic stage II-III at baseline. The majority of patients demonstrated erosive arthritis (23 out of 28), they were ACPA- (25 out of 28) and RF- (24 out of 28) positive. TFCN treatment significantly decreased the disease activity according to DAS28. At the end of the study, the majority of patients demonstrated moderate disease activity (3.2< DAS28 < 5.1), four patients retained high disease activity while 8, attained remission (DAS28 < 2.6). This was accompanied by significant decrease in CRP and the number of swollen and tender joints. ESR values were not changed significantly. Gene and protein expression analysis revealed that RA patients, which attained clinical remission after TFCN treatment demonstrated significantly lower baseline expression of genes associated with glycolysis (pyruvate kinase) and oxidative phosphorylation (succinate dehydrogenase) compared to other examined RA patients. Moreover, in RA patients who attained clinical remission these gene expressions were tending to increase while in other examined patients, to downregulate in the course of follow-up.

Conclusion: Our preliminary study demonstrated that clinical remission attainment in RA patients treated with tofacitinib was associated with lower baseline expression of genes related to energy generation pathways (pyruvate kinase and succinate dehydrogenase) compared to other examined subjects.

Disclosure: E. Tchetina, None; **A. Satybaldyev**, None; **G. Markova**, None; **A. Lila**, None.

Abstract Number: 0015

Rheumatoid Factor Recognizes Specific Domains of IgG Heavy Chain Complexed with HLA Class II Molecules

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid factor (RF) is an autoantibody that binds to IgG Fc region (C_H2 and C_H3 domains) and is detectable in patients with rheumatoid arthritis (RA). We previously reported that IgG heavy chain (IgGH) was transported to the cell surface by HLA class II molecule via association with the peptide binding groove and that IgGH / HLA class II complex could be specifically recognized by RF. However, its mechanisms have not been fully understood. Here we tried to identify the binding sites of IgGH to HLA class II and recognition sites of IgGH by RF.

Methods: The heavy chain of IgG contains a variable region (V_H) and 3 constant regions (C_H). Each single domain (V_H, C_H1, C_H2, and C_H3) or 2~3 contiguous domains of human IgGH were sub-cloned and transfected with HLA-DR4 into HEK293T cells. The Flag-tagged IgGH domains presented by the HLA-DR molecules on the cell surface were detected by anti-Flag antibody using flow cytometry (FCM). Next, RF recognition to IgGH domains / HLA-DR complex was evaluated by FCM after RA patients' sera and anti-human IgM antibody staining. We also made constructs of IgGH single domains linked to Cw3 peptide which binds strongly to HLA-DR4 peptide binding groove. We co-transfected

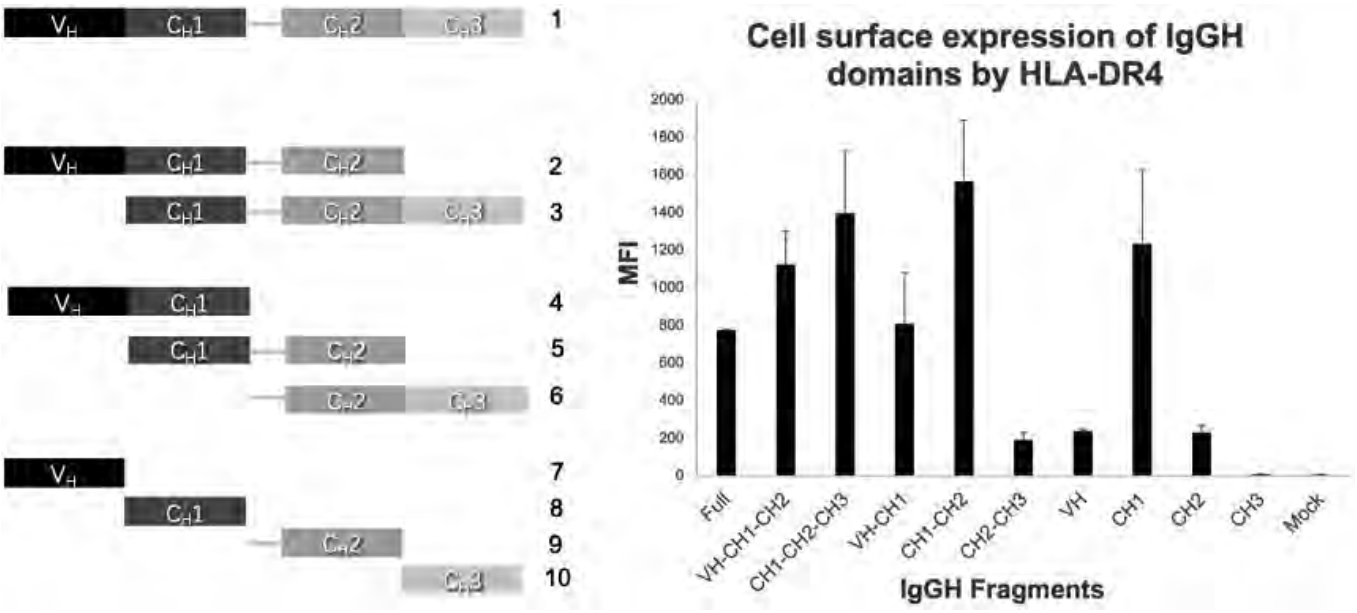

Figure 1. Each fragment of human IgGH was transfected with HLA-DR4 into HEK293T cells. The Flag-tagged IgGH domains presented by the HLA-DR molecules on the cell surface were detected by anti-Flag antibody using flow cytometry.

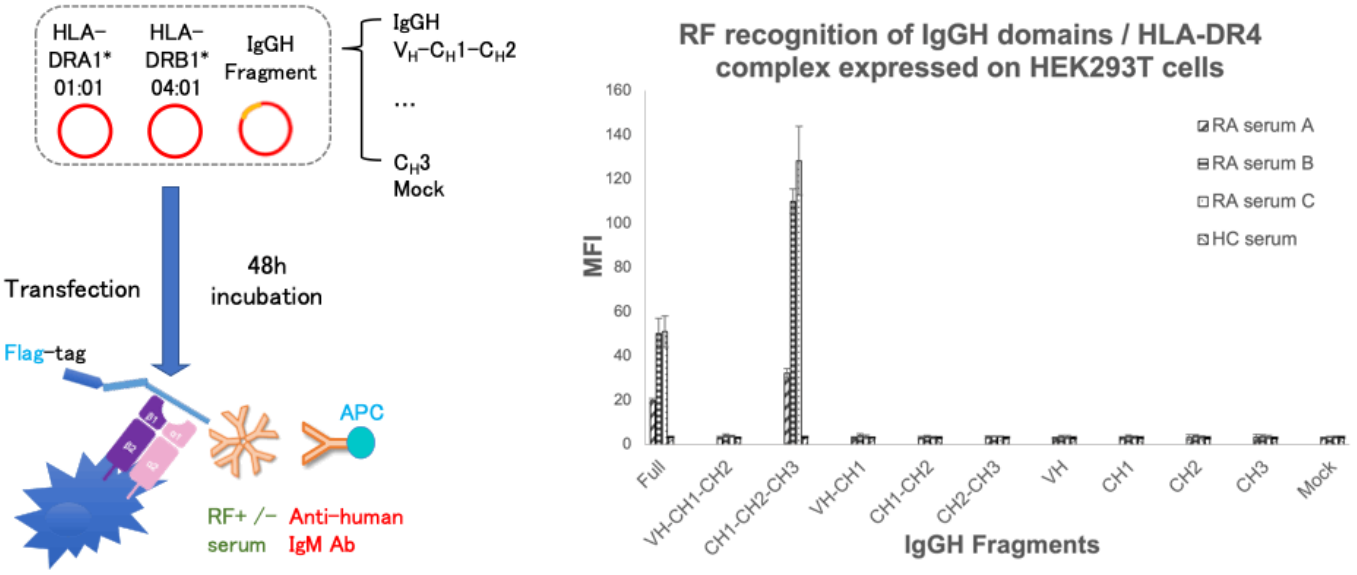

Figure 2. IgGH fragments and HLA-DR4 were co-transfected into HEK293T cells and binding of RF to IgGH domains / HLA-DR4 complex was evaluated by RA patients' sera using flow cytometry.

the HLA-DR4 and IgGH single domains with or without Cw3 peptide then compared the IgGH fragment expression and RF reactivity.

The RF positive sera were obtained from the patients diagnosed with RA based on the ACR / EULAR criteria for RA in 2010.

Results: The expression of fragments containing C_H1 on the cell surface by HLA-DR4 were equal to or rather higher than the full IgGH's expression, while fragments without C_H1 (C_H2-C_H3, V_H, C_H2 and C_H3) were presented at a far lower level compared with full IgGH, especially the C_H3 domain (Figure 1).

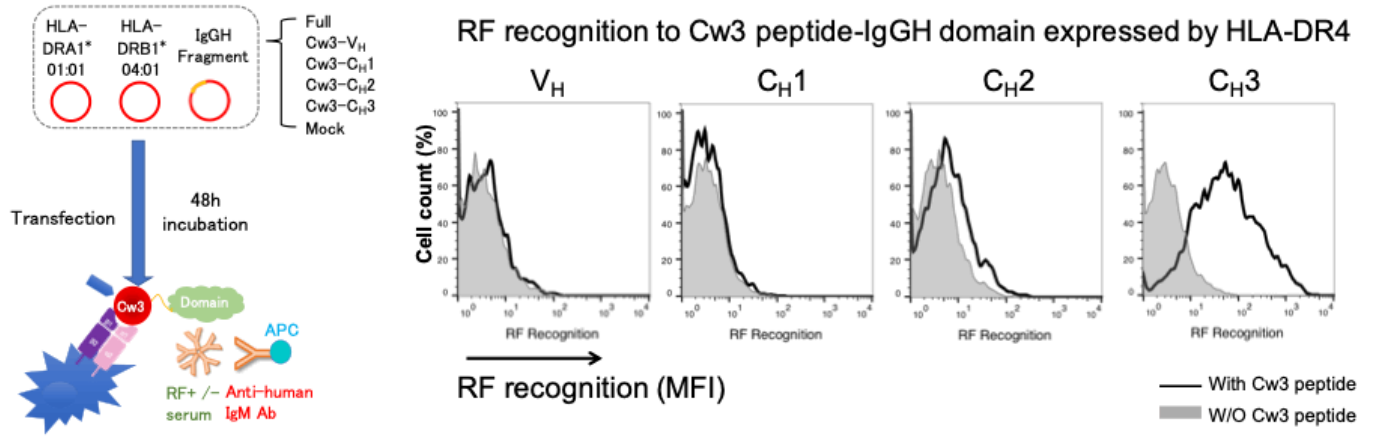

Figure 3. IgGH fragments with or without Cw3 peptide were transfected with HLA-DR4 into HEK293T cells and RF reactivity to the complex with HLA-DR4 complex were compared by RA patients' sera using flow cytometry.

Next, among all the fragments, RF only recognized C_H1-C_H2-C_H3 fragment besides full IgGH chain (Figure 2). On the other hand, Cw3 peptide-linked IgGH domain study revealed that RF recognized C_H3 single domain linked to Cw3 peptide presented by HLA-DR4 but none of other Cw3-linked single domains were recognized (Figure 3). All of the sera from 43 RF-positive RA patients showed the same results.

Conclusion: Our data suggest that HLA-DR presents IgG heavy chain mainly by binding to C_H1 domain, while RFs recognize the epitope on C_H3 domain.

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Abstract Number: 0016

Structural and Functional Neurobiological Alterations of Salience and Sensorimotor Networks in Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is a common childhood illness, characterized by inflammation of the joint, chronic pain and decreased physical functioning. To date, the underlying neurobiological mechanisms that drive pain and sensorimotor dysfunction are unclear and understudied. Thus, in this pilot study, we explored the morphology and functionality of salience and sensorimotor structures in JIA patients.

Methods: Nine JIA patients (12.4 ± 2.8 years of age) and 13 control subjects matched by age, gender and handedness were enrolled. All JIA patients were on active treatment and had prior or ongoing symptoms in hand-wrist joints. High-resolution structural magnetic resonance imaging (MRI), diffusion tensor imaging (DTI), functional MRI (fMRI), and Pseudo-continuous arterial spin labelling (ASL) were performed. In addition, clinical lab tests and the 9-hole peg test for hand-motor function were administered.

Results: Morphology: Morphological analysis (Freesurfer v7.1.1) of the structural neuroimaging data revealed a significant decrease ($P < 0.05$) of cortical thickness in the left hemisphere insular cortex in JIA patients (**Figure 1**). Furthermore, cortical volume of the caudate nucleus (CN) was negatively correlated with patient-reported pain severity (Left CN: $P = 0.04$, $R = -0.70$; Right CN: $P = 0.03$, $R = -0.71$). Functional connectivity: In JIA patients, seed-based functional connectivity analysis (CONN-fMRI v18.b and SPM 12) showed altered connectivity from anterior insula (AI) subregions, as defined by Deen et al., to key hubs of the salience (e.g., anterior cingulate cortex (ACC)) and sensorimotor (e.g., pre- and postcentral gyri) networks. The most robust finding was that of decreased functional connectivity from the dorsal AI (dAI) to angular/ supramarginal gyrus regions in JIA patients (**Figure 1)**. Structural connectivity: Probabilistic tractography (FMRIB's Software Library v6.0.4) revealed higher connectivity from the left and right AI to several ipsilateral and contralateral regions of the salience network in JIA patients. Connectivity from the left ventral AI (vAI) to the left ACC, which is associated with affective processes, was increased in JIA patients ($P = 0.015$), and left vAI to right ACC was correlated to erythrocyte sedimentation rate (ESR) and pain (ESR: $P = 0.03$, Pain: $P = 0.01$) (**Figure 1**). Cerebral blood flow (CBF): CBF analysis (BASIL toolbox) did not reveal significant group differences for the insular cortex or other regions of the salience network (**Figure 1**). However, assessment of regional CBF in JIA patients and controls revealed significantly higher CBF values in multiple subcortical areas within the sensorimotor network for the JIA group (**Figure 2**). These values were positively correlated with left to right hand ratio motor performance, calculated from subjects' time score on the 9-hole peg test (**Figure 3**).

Conclusion: This pilot study points toward several structural and functional alterations in salience and sensorimotor networks, which could be at the core of pain and sensorimotor deficits in JIA. Future studies may focus on whether

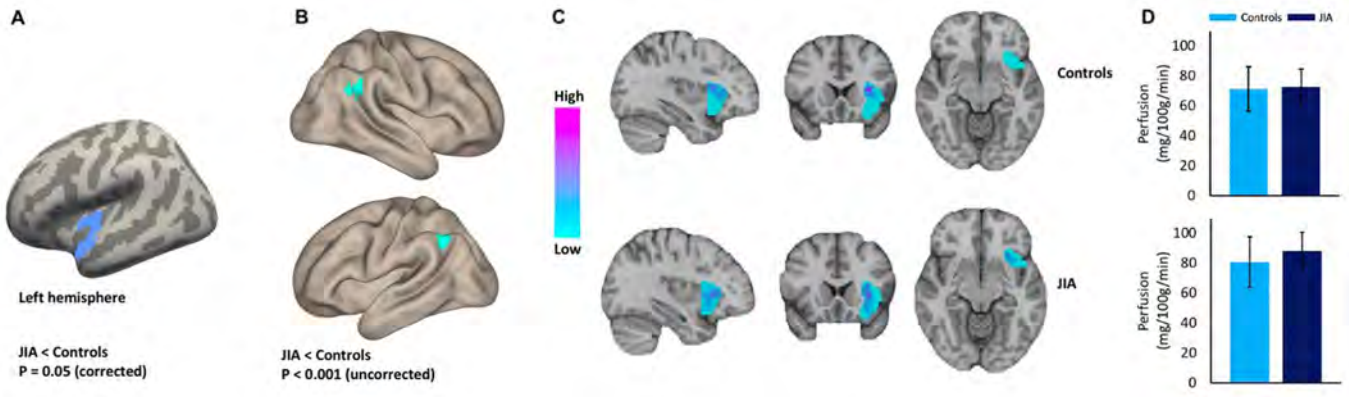

Figure 1. Anterior Insula Alterations in JIA patients. A. Insular cortex regions (blue cluster) showing a significant decrease in cortical thickness in JIA patients vs. healthy controls. Only the left-hemisphere insular cluster remained significant after correction for multiple comparisons. B. Significantly decreased seed-based functional connectivity from the left dAI to bilateral angular gyrus/ supramarginal gyrus regions (blue clusters) in JIA patients vs. healthy controls. C. Increased structural connectivity of AI to the left anterior cingulum: AI connectivity map for controls and JIA patients. D. rCBF in the AI in the left (top) and right (bottom) hemisphere.

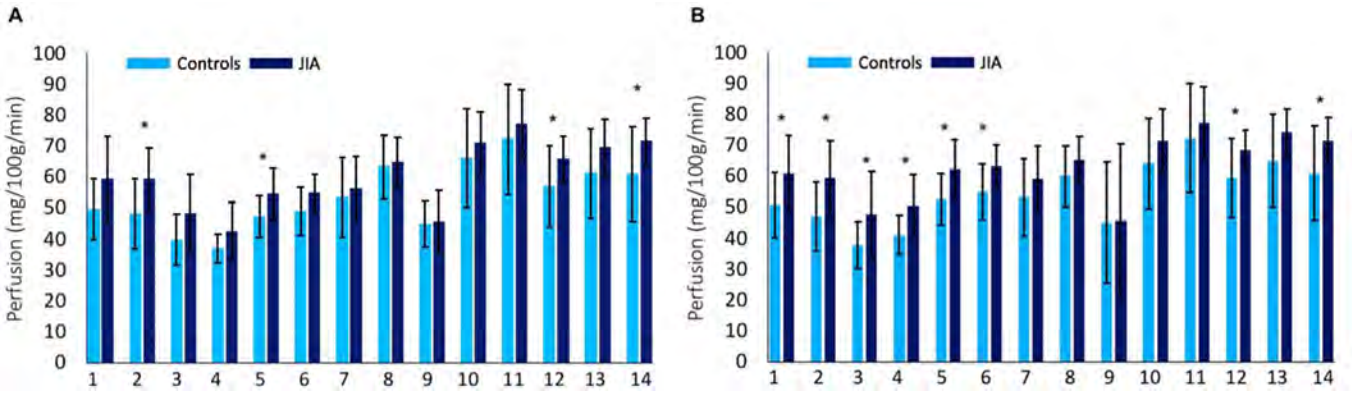

Figure 2. rCBF Differences in Sensorimotor Areas. rCBF values (mg/100g/min) for (A) left and (B) right hemisphere. (1) Red Nucleus, (2) SNpc, (3) SNpr, (4) Thalamus VA, (5) Thalamus VL, (6) Thalamus VPL, (7) Caudate, (8) Putamen, (9) Pallidum, (10) Postcentral Gyrus, (11) Precentral Gyrus, (12) Cerebellum lobule V, (13) Cerebellum lobule VI, (14) Vermis. Asterisk (*) indicates significant ($P < 0.05$) group differences. Error bars represent standard deviations.

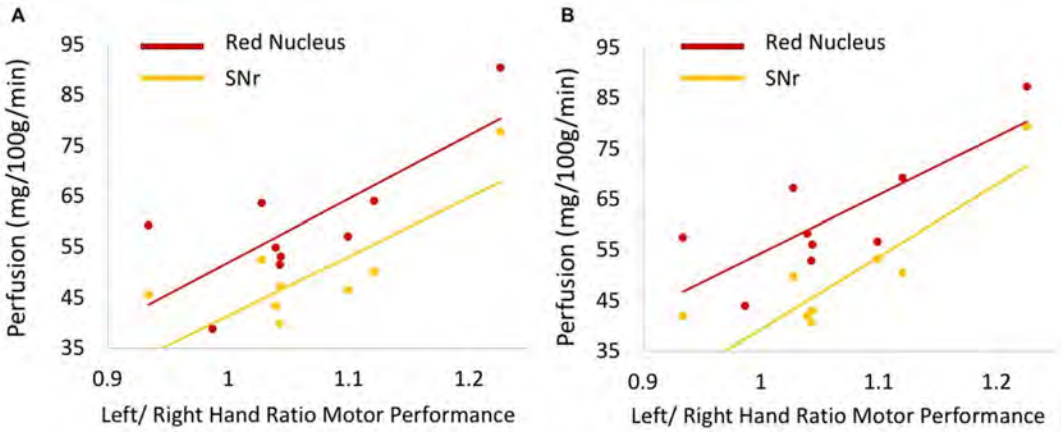

Figure 3. Left to Right Hand Ratio Correlations to rCBF in Sensorimotor Areas. Significant correlations are shown for (A) left hemisphere Red Nucleus ($P = 0.0094$, $R = 0.7547$) and SNpr ($P = 0.0064$, $R = 0.7821$), and for the (B) right hemisphere Red Nucleus ($P = 0.0063$, $R = 0.7829$) and SNpr ($P = 0.0014$, $R = 0.8610$). Ratio was calculated with time (s) to complete the 9-hole Peg Test with each hand.

central changes are maladaptive or adaptive in nature, and how CNS properties are impacted by standard of care and novel therapies.

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Abstract Number: 0017

Lessons Learnt from Associations Between Anti-modified Protein Antibodies and Risk Factors: Human Leukocyte Antigen - Shared Epitope Alleles Solely Associate with Anti-citrullinated Protein Antibodies

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by the presence of auto-antibodies to post translationally modified proteins (anti-modified protein antibodies (AMPA)): anti-citrullinated protein antibodies (ACPA), anti-carbamylated protein antibodies (anti-CarP) and anti-acetylated protein antibodies (AAPA). ACPA is unique since an association with the risk factors smoking and the human leukocyte antigen (HLA) - shared epitope (SE) is found only in the ACPA positive patients. However the association of SE and smoking with all three AMPA has remained unstudied. Nonetheless, this association is of great interest, since it would increase our understanding if the pathological mechanisms underlying the development of these auto-antibodies are unique of shared.

Objective: To investigate the association of SE and smoking with the different kinds of AMPA.

Methods: 648 RA patients fulfilling the 1987 RA criteria from the Leiden Early Arthritis Cohort, of whom data were available on the presence of ACPA, AAPA and anti-CarP, smoking and SE status were included. SE positivity was defined as having ≥1 of the following HLA alleles: DRB1*01:01, *01:02, *04:01, *04:04, *04:05, *04:08 and*10:01. Healthy controls (n=1211) for SE analysis were randomly selected from the collection of the section of Immunogenetics and Transplantation Immunology from the Leiden University Medical Center. The association between auto-antibodies and SE and smoking was assessed by logistic regression analysis.

Results: When investigating the association of smoking with the presence of the various combinations of AMPA, a significant association was only found in the triple positive patients (OR 1.67 (1.08 – 2.60), p0.02), table 1. There was no association with smoking for patients positive for one or two auto-antibodies.

SE was solely associated with ACPA positive patients, whereas the association with SE was similar among patients who were single-positive for ACPA compared to patients harboring 1 or 2 additional auto-antibodies (AAPA and/or anti-CarP), indicating that SE is only associated with ACPA.

Table 1 Association of smoking with anti-modified protein antibodies

Autoantibody status	Smoking neg n (%)	Smoking pos n (%)	OR (95% CI)	p-value
ACPA-AAPA-CarP-	198 (78.3)	55 (23.7)	1 (ref)	-
ACPA+AAPA-CarP-	32 (69.6)	14 (30.4)	1.58 (0.79 – 3.16)	0.20
ACPA-**AAPA+**CarP-	3 (75.00)	1 (25.0)	0.84 (0.35 – 2.02)	0.69
ACPA-AAPA-**CarP+**	30 (81.01)	7 (18.9)	1.20 (0.12 – 11.76)	0.89
ACPA+AAPA-**CarP+**	49 (74.2)	17 (25.8)	1.25 (0.67 – 2.34)	0.70
ACPA+AAPA+CarP+	30 (81.1)	7 (18.9)	0.84 (0.35 – 2.02)	0.70
ACPA-**AAPA+CarP+**	0 (0.0)	0 (0.0)	-	-
ACPA+AAPA+CarP+	114 (68.3)	53 (31.7)	**1.67 (1.08 – 2.60)**	**0.02**

Table 2 Association of SE with anti-modified protein antibodies

			Reference = healthy controls		Reference = single ACPA pos patients	
Autoantibody status	**SE neg n(%)**	**SE pos n(%)**	**OR (95% CI)**	**p-value**	**OR (95% CI)**	**p-value**
Healthy controls	674 (55.7)	537 (44.3)	1 (ref)	-		
ACPA-AAPA-CarP-	132 (51.8)	123 (48.2)	1.17 (0.89 – 1.53)	0.26		
ACPA+AAPA-CarP-	10 (21.7)	36 (78.3)	**4.52 (2.22 – 9.19)**	**0.000**	1 (ref)	-
ACPA-**AAPA+**CarP-	1 (25.0)	3 (75.0)	3.77 (0.39 – 36.30)	0.25		
ACPA-AAPA-**CarP+**	21 (56.8)	16 (43.3)	0.96 (0.49 – 1.85)	0.89		
ACPA+AAPA+CarP-	9 (24.3)	28 (75.7)	**3.90 (1.83 – 8.35)**	**0.000**	0.86 (0.31 – 2.41)	0.78
ACPA+AAPA-**CarP+**	15 (22.7)	51 (77.3)	**4.27 (2.37 – 7.67)**	**0.000**	0.94 (0.38 – 2.34)	0.90
ACPA-AAPA+**CarP+**	0 (0.0)	0 (0.0)	-	-	-	-
ACPA+AAPA+CarP+	32 (19.2)	171 (80.3)	**5.30 (3.52 – 7.91**	**0.000**	1.17 (0.53 – 2.61)	0.70

Conclusion: This in-depth analysis of the exact association between risk factors and AMPA presence revealed striking differences regarding the associations for smoking versus SE. Since smoking is associated with the concurrent presence of multiple AMPA, this implies that smoking is involved in a general process of auto-antibody development. However SE is solely associated with the presence of ACPA, and not with anti-CarP or AAPA. This suggests that, despite the similarity in antigenic targets and partial cross reactivity between AMPA responses, the pathophysiological mechanisms underlying their development differ for the various AMPA.

Disclosure: T. van wesemael, None; **A. Dorjee**, None; **T. Huizinga**, None; **A. van der Helm-van Mil**, None; **R. Toes**, None; **D. van der Woude**, None.

Abstract Number: 0018

Caspase-8 Variant G Regulates Rheumatoid Arthritis Fibroblast-Like Synoviocyte Aggressive Behavior

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS) display an aggressive phenotype, including abnormal migration and invasion. Using data from our previous studies defining the epigenetic landscape of RA FLS, *CASP8* (encoding caspase-8) was identified as a gene of interest in RA that might be implicated in this behavior due to abnormal epigenetic marks. Caspase-8 has proteolytic functions that regulate apoptosis and non-proteolytic functions that affect cell movement. However, the specific isoforms responsible for the latter are unknown. In this study, we identified the mechanisms of caspase-8 function in RA FLS and identified the specific isoform responsible.

Methods: RA FLS lines were obtained from synovial tissues at arthroplasty and used at passage 5-8 (n=20). *CASP8* deficiency was induced with siRNA to deplete either all isoforms or individual isoforms; non-targeting siRNA was used as control. RT-qPCR and western blot were used to assess gene and protein expression, respectively. PDGF-induced migration (scratch assay), invasion (through Matrigel membrane), and adhesion to fibronectin and collagen type II in CASP8-deficient and control cells were assessed. Talin cleavage was measured by western blot and calpain cleavage activity assessed via fluorescent assay. Analysis of *CASP8* epigenetic marks and transcript isoforms in RA and osteoarthritis (OA) FLS was evaluated using public databases (ChIPseq and RNAseq). Crystal structures of variant B and G were determined.

Results: Silencing total *CASP8* reduced RA FLS migration (36.7%±7.2, n=6, P=0.008) and invasion (41.6±6.3%, n=4, P=0.01) after PDGF stimulation, and lower adhesion to fibronectin and collagen type II (n=4; P=0.002 and P=0.005 respectively). Decreased migration after PDGF stimulation was associated with decreased talin cleavage and calpain activity. The caspase enzymatic inhibitor Z-IETD-FM did not affect FLS migration nor invasion. Of the 20 known alternatively spliced variants of caspase-8, only variant C and G are expressed in FLS, with G > >C. Epigenetic analysis found enhanced H3K4me1 and H3K27ac peaks in the promoter region of variant G and C in RA FLS compared

with OA. Expression of caspase-8 variant G, but not other variants, was induced by PDGF (1.5±0.1 fold increase at 6h, n=6, *P*=0.003). Selective silencing of variant G showed that this isoform is solely responsible for the effect of caspase-8 on FLS invasion and calpain activity (n=6, $P \leq 0.01$). The crystal structures of caspase-8 isoform G and B were identical aside for a unique unstructured 59aa N-terminal domain in variant G.

Conclusion: Non-enzymatic functions of caspase-8 regulate key activities associated with aggressive RA FLS behavior. RA FLS have a restricted pattern of *CAPS8* alternative splicing, and variant G is solely responsible for this function. Because caspase-8 variant G has a unique amino acid tail, selective targeting could potentially inhibit FLS invasion without the deleterious effects of blocking caspase-8-mediated apoptosis.

Disclosure: C. Ansalone, None; **G. Nygaard**, None; **R. Ainsworth**, None; **R. Ai**, None; **D. Hammaker**, None; **N. Perumal**, Eli Lilly and Company, 3; **K. Weichert**, Eli Lilly & Company, 3; **F. Tung**, Eli Lilly & Company, 3; **L. Kodandapani**, None; **M. Sauder**, Eli Lilly & Company, 3; **E. Mertsching**, Eli Lilly, 3; **R. Benschop**, Eli Lilly & company, 3, 10, 11; **W. Wang**, None; **D. Boyle**, None; **G. Firestein**, Eli Lilly, 5.

Abstract Number: 0019

Increased Circulating CD39+FoxP3+CD4+ Treg Cells in Early Rheumatoid Arthritis Facilitate the Antiinflammatory Action of Methotrexate

Laura Nuño[1], Alejandro Villalba[1], Marta Novella-Navarro[2], Irene Monjo[1], Diana Peitado[1], Sara Garcia-Carazo[1], Alejandro Balsa[2] and **Maria-Eugenia Miranda-Carus**[1], [1]Hospital La Paz - IdiPAZ, Madrid, Spain, [2]Immuno-Rheumatology Research Group, Hospital La Paz Institute for Health Research-IdiPAZ, Rheumatology, La Paz University Hospital, Madrid, Spain

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Inhibition of AICAR transformylase by MTX results in augmented release of adenine nucleotides to the extracellular space; these are rapidly hydrolysed by ectonucleotidases CD39 and CD79 rendering the antiinflammatory agent adenosine. CD39, the rate-limiting enzyme in this cascade, is highly expressed by a subset of human FoxP3+CD4+ regulatory T cells (Treg39+)[2-4] and MTX may act synergistically with Tregs in the control of inflammation. Our objective was to study the expression of CD39 on circulating Treg cells of untreated early RA (ERA) patients and its relation with the ex vivo effect of MTX.

Methods: Peripheral blood was drawn from 30 DMARD- and steroid- naïve ERA (disease duration < 24 weeks), 15 longstanding RA patients (LRA, duration > 2 years) and 45 healthy controls (HC). LRA patients were naïve for biologicals and received low-dose weekly MTX. 10 ERA patients who achieved remission 12 months after initiating MTX were re-evaluated (ERA-R). The frequency of Treg cell subsets was determined by flow cytometry. CD4+CD25+CD127- (total T reg), CD4+CD27+CD127-CD39+ Treg (Treg39+) and CD4+CD25-CD39- responder T (Tresp39-) cells were isolated by sorting. The suppressor potency of Tregs was assessed in cocultures with Tresp, at different Treg/Tresp ratios. Proliferation was determined by CFSE dilution and cytokine secretion by ELISA of culture supernatants.

Results: ERA but not LRA patients demonstrated a superior frequency of circulating Treg (CD4+CD25+CD127-FoxP3+) cells. In addition, the proportion of Tregs that expressed CD39 (Treg39+) was increased in ERA but not LRA. Total ERA Tregs were more potent suppressors of proliferation, TNFα and IFNγ secretion when compared with HC

or LRA, and this difference was downmodulated in the presence of adenosine deaminase (ADA), or the adenosine A2A receptor (A2AR) antagonists DMPX (3,7-dimethyl-1-propargylxanthine) or ZM 241385, but not of the adenosine A1 receptor antagonist DPCPX (8-cyclopentyl-dipropylxanthine). When adding MTX, the suppressor potency of total Tregs was further enhanced in all 3 groups of patients, and this enhancement was significantly higher in ERA total Treg/Tresp39- cocultures as compared with HC or LRA. This effect of MTX was significantly abrogated by ADA, DMPX or ZM 241385 but not DPCPX. We then tested the suppressor potency of isolated Treg39+ together with the enhancer effect of MTX on this potency, and observed that there were no longer differences among ERA, LRA and HC; this further suggests that the differences observed in assays using total Tregs can be attributable to the increased Treg39+ proportions present in ERA. The frequency and function of ERA-R Treg cells were not different from HC or LRA Tregs.

Conclusion: The suppressor action of CD39+Tregs is mediated at least in part by adenosine trough A2AR ligation, and the superior suppressive potency of total ERA Tregs is associated with their higher proportion of TregCD39+ cells. The augmented suppressor effect observed in the presence of MTX is partly mediated by an increased adenosine production acting on A2AR and is more marked in ERA patients reflecting again their higher proportion of Treg39+ cells. This indicates that MTX cooperates with Treg39+ cells in the control of inflammation.

Disclosure: L. Nuño, None; **A. Villalba**, Janssen, 6; **M. Novella-Navarro**, None; **I. Monjo**, Roche, 2, 6, UCB, 6, Gedeon Richter, 6, Novartis, 6; **D. Peitado**, Janssen, 6, Nordic, 6, Lilly, 6, Novartis, 6, Abbvie, 6; **S. Garcia-Carazo**, BMS, 5, Actelion pharmaceuticals, 5; **A. Balsa**, BMS, 5, 6, Gebro Pharma, 5, Pfizer, 5, 6, Roche, 5, 6, UCB, 5, 6, Novartis, 5, 6, Abbvie, 6, MSD, 6, Lilly, 6, Nordic, 6, Galapagos, 6, Gilead, 6, Sandoz, 6; **M. Miranda-Carus**, Gebro-Pharma, 5, BMS, 5, UCB, 12, EULAR Meeting registration financial support.

Abstract Number: 0020

Citrullination Drives the Expression of Pro-fibrotic Genes in Rheumatoid Arthritis Fibroblast-like Cells

Peter Maloley, Evan Ryan, Nozima Aripova, Michael Duryee, Bryant England, Ted Mikuls and Geoffrey Thiele, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The pathophysiology of rheumatoid arthritis (RA) is hallmarked by joint inflammation, thickening of the pannus, and resultant joint destruction. Within the synovial tissue, citrullinated antigens and malondialdehyde-acetaldehyde (MAA)-modified proteins co-localize, implicating a potential synergistic role in the induction of immune and pro-fibrotic responses. To further elucidate the mechanisms by which these modifications contribute to RA pathogenesis, we studied fibrotic gene expression by human fibroblast-like synoviocytes from RA patients (HFLS-RA) in response to stimulation with citrullinated and/or MAA-modified fibrinogen.

Methods: HFLS-RA cells were treated with native fibrinogen versus citrullinated and/or MAA-modified fibrinogen for 8 hours with sham treated HFLS-RA cells as reference, and mRNA was isolated. Expression of 763 genes was quantified using the NanoString® nCounter® Human Fibrosis Panel. Comparisons of gene expression across treatment groups were performed using differential expression analysis. Only genes with increased or decreased expression

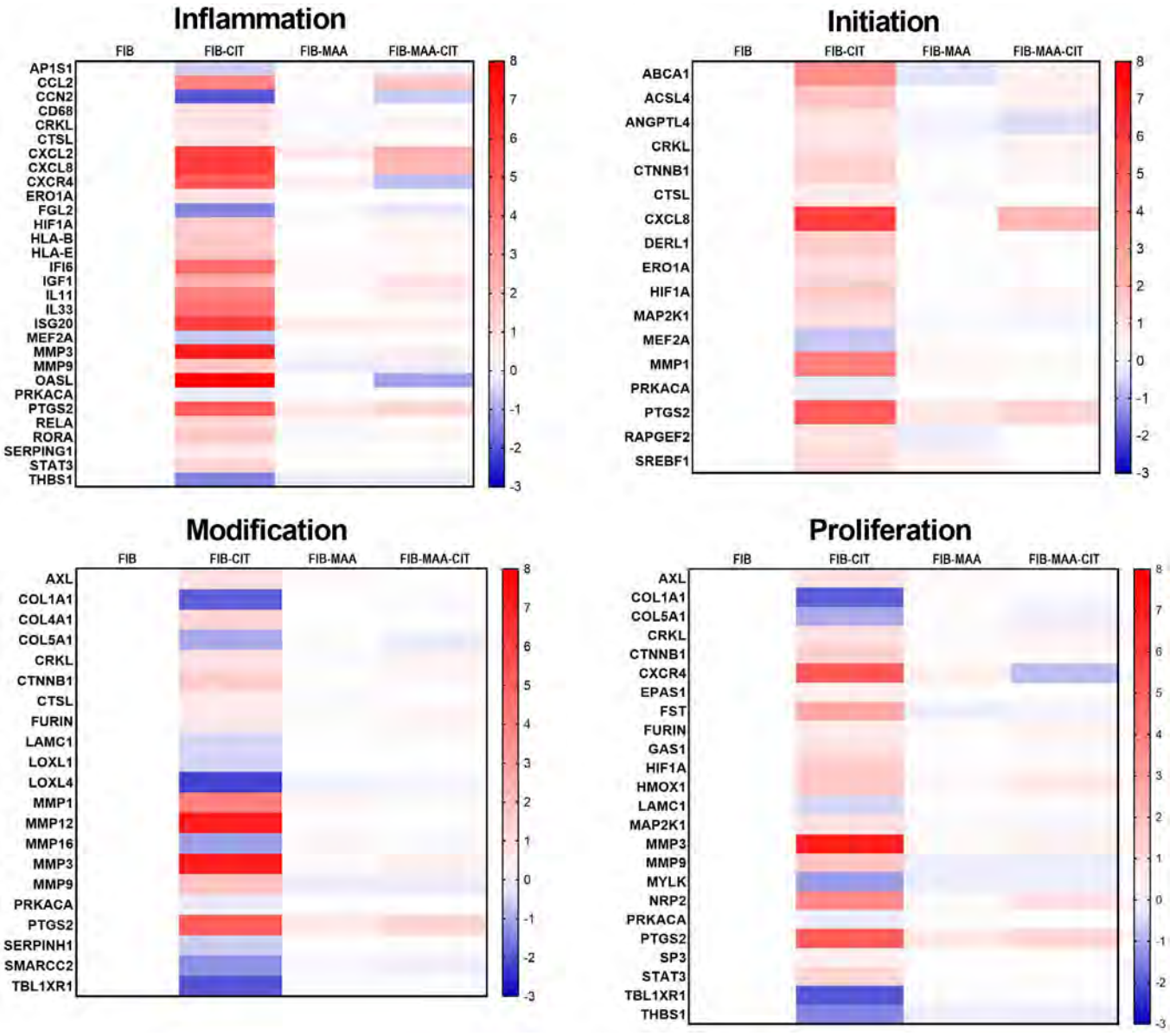

Figure 1. Heat map (red = increased; blue = decreased) of significant genes expressed following 8-hour treatment of HFLS-RA cells with native fibrinogen (control), citrullinated fibrinogen, MAA-modified fibrinogen, or MAA-modified and citrullinated fibrinogen. Gene profiles were categorized into inflammation, initiation, modification, and proliferation. The heat map bar on the right is expressed as fold-change compared to control.

compared to untreated HFLS-RA cells were reported in the final results. Data was reported using $\log_2$ of normalized ratio with the sham group as reference.

Results: The gene responses of treated HFLS-RA cells were categorized based on their role in the fibrotic pathway (inflammation, initiation, modification, and proliferation) with many genes having influence on multiple pathways. Of the 763 genes analyzed, 58 demonstrated differential expression when exposed to modified antigen (Figure 1). Forty genes exhibited significantly increased expression when treated with citrullinated-fibrinogen alone compared to native unmodified fibrinogen (Figure 2). Of these 40 genes, four also demonstrated increased expression after treatment with fibrinogen co-modified with citrulline and MAA (Figure 3). One gene, CCL2 (inflammation), yielded increased gene expression in response to co-modified fibrinogen but not to citrullinated antigen alone (Figure 3). Treatment with MAA-modified fibrinogen alone did not generate any significant differential expression.

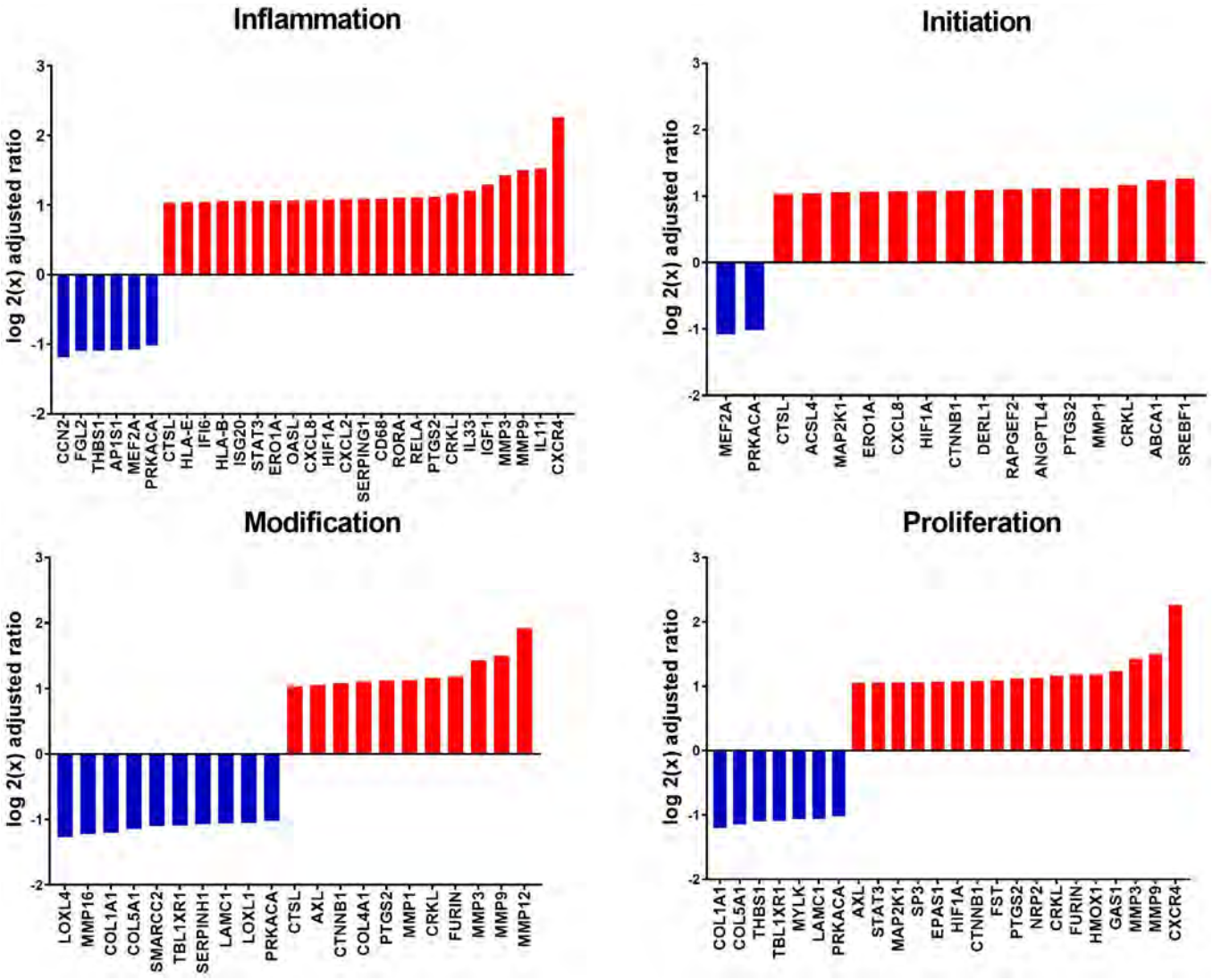

Figure 2. Genes that were significantly increased (red) or decreased (blue) by citrullinated fibrinogen were extracted from the heat maps and expressed as the log2 ratio compared to native fibrinogen (control). Gene profiles were categorized into inflammation, initiation, modification, and proliferation. Data is expressed as fold-change compared to control.

Conclusion: In this study, citrullinated fibrinogen augmented gene expression most conspicuously, whereas MAA-modification alone did not. Interestingly, co-modification did demonstrate a synergistic pro-fibrotic synovial response in one gene (CCL2) that was not seen with either single modification alone. Many of the genes identified have previously been shown to correlate with anti-citrullinated antibodies and RA disease activity, and thus, these post-translationally modified proteins may play a role in the development of fibrosis that contributes to joint pathology in RA. We would benefit from further elucidation of the synergistic role MAA and citrulline play and if that could be a target of diagnostic and/or therapeutic clinical practice.

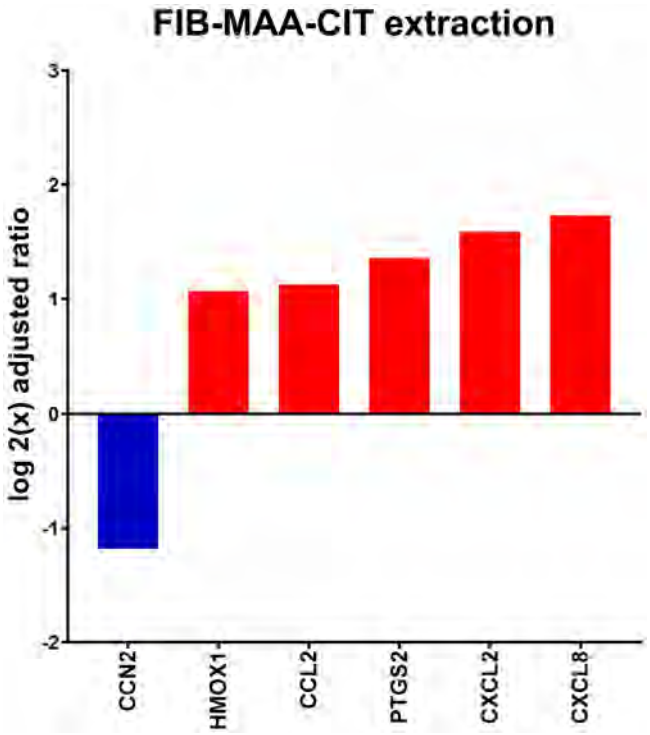

Figure 3. Genes that were significantly increased (red) or decreased (blue) by co-modification of fibrinogen with MAA and citrulline (Fib-MAA-CIT) were extracted from the heat maps and expressed as the log2 ratio compared to native fibrinogen (control). Data is expressed as fold-change compared to control.

Disclosure: P. Maloley, None; **E. Ryan**, None; **N. Aripova**, None; **M. Duryee**, None; **B. England**, Boehringer-Ingelheim, 2; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6.

Abstract Number: 0021

Unique Alterations in Circulating T Peripheral Helper Cells Are Found in Different Ethnic Groups of ACPA+ Individuals Both At-risk for and with Classified RA

Hideto Takada[1], Yuko Okamoto[2], Yasuhiro Katsumata[3], Jennifer Seifert[4], Kristen Demoruelle[5], Jill Norris[6], Kevin Deane[7], Masayoshi Harigai[3] and V. Michael Holers[8], [1]Tokyo Women's Medical University School of Medicine, Shinjuku-ku, Japan, [2]Tokyo Women's Medical University Division of Rheumatology, 10-22 Kawada-cho, Shinjyuku-ku, Tokyo, Japan, [3]Tokyo Women's Medical University School of Medicine, Tokyo, Japan, [4]University of Colorado School of Medicine, Littleton, CO, [5]University of Colorado Anschutz Medical Campus, Aurora, CO, [6]Colorado School of Public Health, Aurora, CO, [7]University of Colorado Denver, Denver, CO, [8]University of Colorado, Denver, CO

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Production of autoantibodies following pathogenic T and B cell interactions precede the development of RA. T follicular helper (Tfh) cells and T peripheral helper (Tph) cells are capable of providing B-cell

Table 1. Demographic characteristics of the study subjects

	CU population			TWMU population		
	HC (N=14)	ARI (N=14)	RA (N=15)	HC (N=15)	ARI (N=10)	RA (N=10)
Age, median (range) years	56 (35–70)	66 (35–72)	52 (35–65)	46 (29–68)	56 (31–67)	48 (21-69)
Women	9 (60)	8 (60)	7 (60)	13 (90)	9 (90)	8 (80)
Serum IgM-RF						
Positivity	0	5 (40)	11 (73)	0	5 (50)	10 (100)
Median (range) IU/ml	0.25 (0.3–3.1)	0.44 (0.3–68.7)	97.7 (0.3–104.8)	0.25 (0.3–0.3)	10.6 (0.3–104.8)	79.9 (7.6–104.8)
Serum CCP3.0						
Positivity	0	12 (86)	12 (80)	0	9 (90)	10 (100)
Median (range) U/ml	3.8 (3.8–3.8)	39.1 (3.8–165.6)	261.7 (3.8–261.7)	3.9 (3.9–3.9)	231.5 (3.9–261.7)	261.7 (253.8–261.7)
Serum CCP3.1						
Positivity	0	13 (93)	15 (100)	0	10 (100)	10 (100)
Median (range) U/ml	3.8 (3.8–7.8)	46.5 (19.7–261.7)	261.7 (38.1–261.7)	3.9 (3.9–3.9)	228.6 (3.9–261.7)	261.7 (255.2–261.7)

All values are number (%) unless otherwise noted.
Serum IgM-RF, CCP3.0, and CCP3.1 were measured using ELISA assay (Inova Diagnostics).

help and both are increased in the peripheral blood in patients with seropositive RA. However, it is unknown whether these cell populations are expanded and/or altered in the peripheral blood prior to the onset of clinically apparent RA. Moreover, the contribution of these cells to the pathogenesis of RA may differ according to genetic and environmental backgrounds. Herein, we explored circulating Tph (cTph) cells and circulating Tfh (cTfh) cells from anti-citrullinated protein antibodies (ACPA)+ individuals both before and after development of RA in two ethnically distinct populations.

Methods: We recruited 14 and 10 ACPA+ individuals without arthritis but at-risk of future RA (ARI), 15 and 10 ACPA+ patients with early RA (2010 criteria and < 1 year from diagnosis), and 14 and 15 healthy controls (HC) from the Studies of the Etiologies of RA (SERA) population at University of Colorado (CU) and the rheumatology outpatient clinic at Tokyo Women's Medical University (TWMU) in Japan, respectively (Table 1). Cryopreserved peripheral blood mononuclear cells were analyzed by flow cytometry to quantify cTph cells (PD-1^{hi}CXCR5^{-}CD4^{+} memory T cells) and cTfh cells (PD-1^{hi}CXCR5^{+}CD4^{+} memory T cells). We also assessed the expression of activation markers, HLA-DR and ICOS, on these cells.

Results: In both ethnic populations, cTph cells were significantly increased in RA but not in ARI compared to HC (Figure 1A and 2A). In the CU population, the frequency of cTph cells was moderately correlated with serum IgM-RF levels in both ARI (Spearman's ρ=0.56, p=0.04) and RA (Spearman's ρ=0.68, p=0.005) (Figure 1B), while no correlation was observed between the frequencies of cTph cells and serum ACPA levels in either ARI or RA. There were no significant differences in the expressions of HLA-DR and ICOS on cTph cells or cTfh cells between CU study groups (Figure 1C). Unlike the CU population, the TWMU population did not show positive correlation between the frequency of cTph cells and serum IgM-RF levels in either ARI or RA (Figure 2B). In that population, however, the expression of HLA-DR on cTph cells was increased in both ARI and RA (Figure 2C).

Conclusion: cTph cells were expanded in RA but not in ARI in both ethnic populations, suggesting a relationship of these cells with clinically-apparent inflammatory arthritis. In addition, unique alterations in cTph cells among ACPA+ individuals with different ethnic backgrounds and in relationship to IgM-RF suggest their shared importance but potentially different roles in the future transition of ACPA+ ARI to early RA.

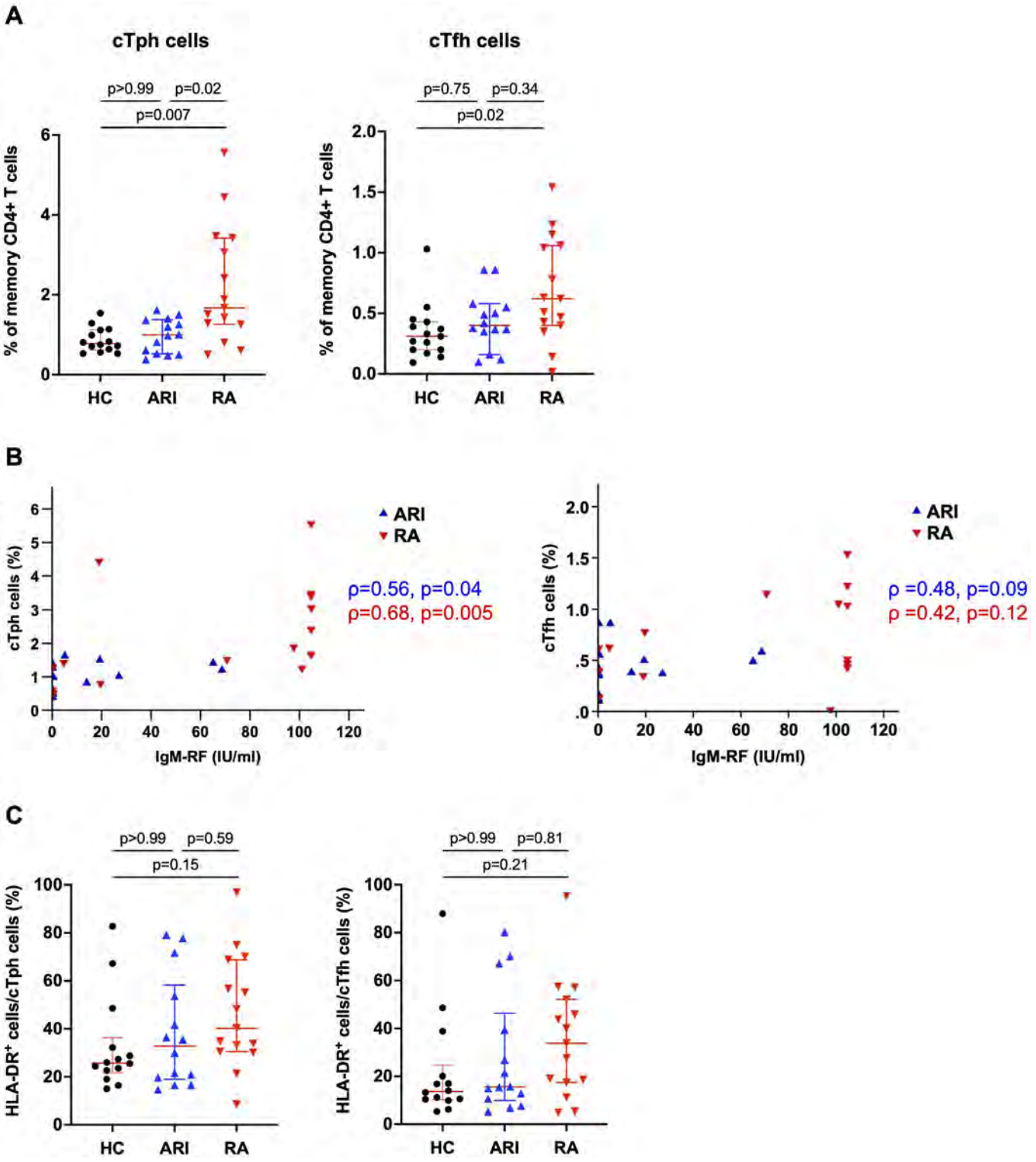

Figure 1. Flow cytometry analysis of cTph and cTfh cells in ACPA+ individuals at-risk of future RA (ARI) and ACPA+ early RA patients, and healthy controls (HC) at University of Colorado. A) Frequencies of cTph and cTfh cells in each study group. B) Correlation between frequencies of cTph or cTfh cells and serum IgM-RF levels in ARI and RA. C) Expression of HLA-DR on cTph or cTfh cells in each study group. P-values were calculated using Kruskal-Wallis one-way analysis of variance followed by Dunn's multiple comparisons test (Panel A and C) and Spearman's rank correlation (Panel B).

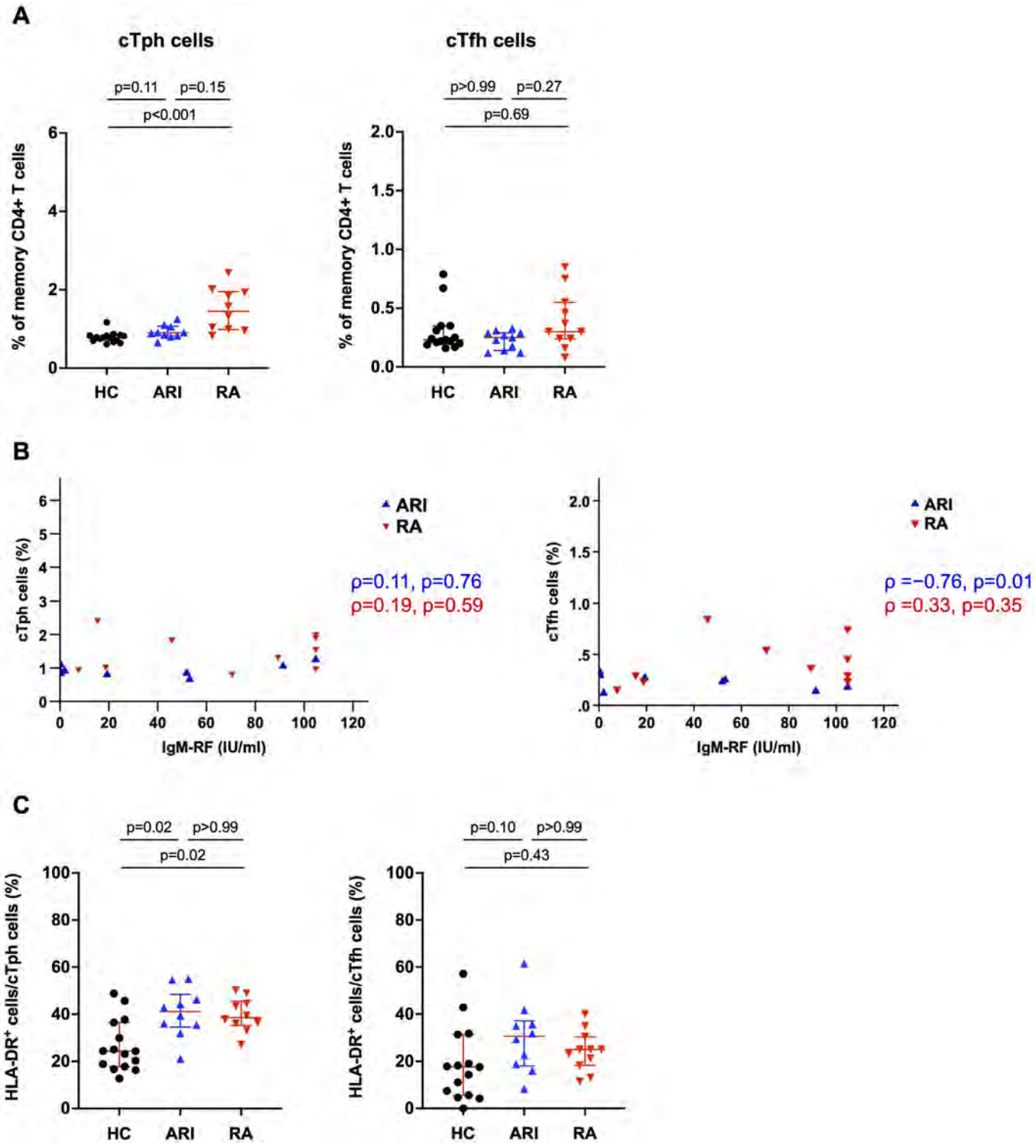

Figure 2. Flow cytometry analysis of cTph and cTfh cells in ACPA+ individuals at-risk of future RA (ARI) and ACPA+ early RA patients, and healthy controls (HC) at Tokyo Women's Medical University. A) Frequencies of cTph and cTfh cells in each study group. B) Correlation between frequencies of cTph or cTfh cells and serum IgM-RF levels in RA and ARI. C) Expression of HLA-DR on cTph or cTfh cells in each study group. P-values were calculated using Kruskal-Wallis one-way analysis of variance followed by Dunn's multiple comparisons test (Panel A and C) and Spearman's rank correlation (Panel B).

Disclosure: H. Takada, None; **Y. Okamoto**, None; **Y. Katsumata**, Glaxo-Smithkline K.K., 6, Sanofi K.K., 6, Astra-Zeneca K.K., 6, Chugai Pharmaceutical Co., Ltd., 6, Pfizer Japan Inc., 6, Astellas Pharma Inc., 6, Mitsubishi Tanabe Pharma Corporation, 6, Janssen Pharmaceutical K.K., 6; **J. Seifert**, None; **K. Demoruelle**, Pfizer, 5; **J. Norris**, None; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, im-aware, 2, ThermoFisher, 2, 5, Medscape, 6; **M. Harigai**, None; **V. Holers**, Jansson, 5.

Abstract Number: 0022

The Effects of MAA-Modified and/or Citrullinated Proteins on Calcium Influx and Peptidyl Arginine Deiminase (PAD) Expression in Macrophage

Andrew Gerber, Michael Duryee, Nozima Aripova, Bryant England, James O'Dell, Ted Mikuls and Geoffrey Thiele, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Expressed in synovial fluid mononuclear and other inflammatory cells, peptidyl arginine deiminase (PAD) catalyzes post-translational citrullination of synovial proteins in a calcium (Ca2+)-dependent manner. Prior reports have demonstrated that post-translational modification of proteins with malondialdehyde-acetaldehyde (MAA) are also common in the RA synovium where they co-localize with citrullinated antigen. However, little is known about the effects of MAA modified proteins on PAD expression or intracellular Ca2+ concentrations. The purpose of this study was to examine the intracellular Ca2+ levels, and the PAD-4 mRNA and protein levels in macrophages following treatment with a MAA-modified antigen.

Methods: THP-1 human macrophage cells were treated with unmodified fibrinogen (Fib) as a negative control or MAA-modified fibrinogen (Fib-MAA) for 24 hours. Cells were washed and incubated with a Fluo-4 AM calcium-binding protein for 30 minutes and subjected to live cell imaging on a 710 Ziess confocal microscope. Images were

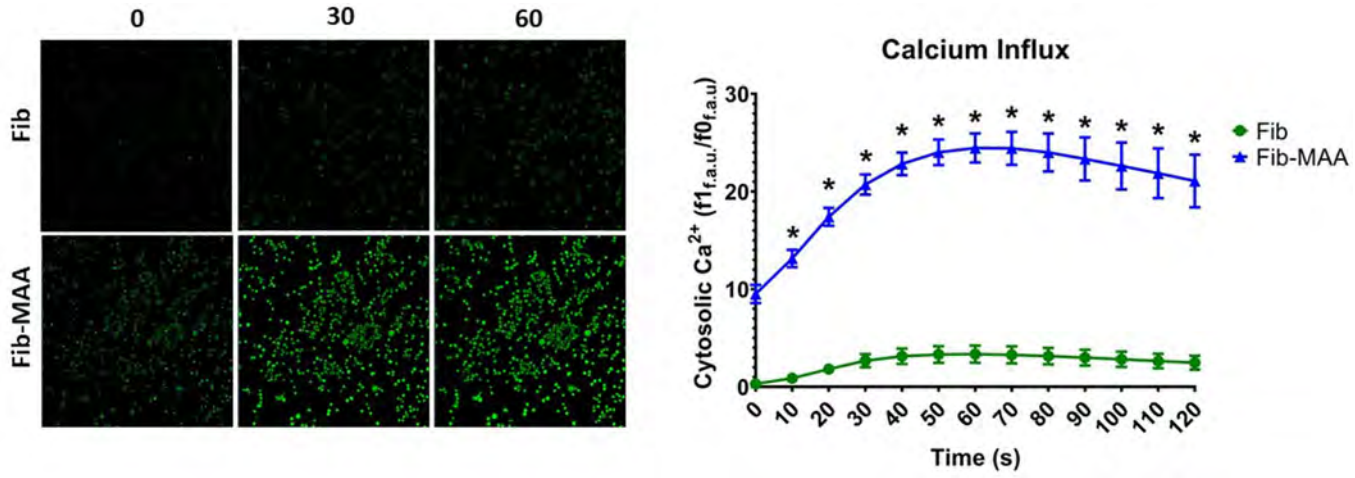

Figure 1. Intracellular calcium increase following 24 hour treatment of THP-1 macrophage with native fibrinogen or MAA modified fibrinogen. Data is expressed as fluorescence of cells with no treatment divided by time 0 fluorescence. *p<0.001 significantly increased compared to Fib. N=5.

acquired in 10-second intervals for 120 seconds and analyzed using Image J. RTPCR was performed on the cells to determine the expression of PAD-4 as well as the calcium binding proteins Inositol 1,4,5-triphosphate receptor-3 (ITPR3) and calcium/calmodulin-dependent protein kinase (CAMKK)-2. THP-1 cells were subjected to Western Blot for protein expression of PAD-4 using an anti-PAD antibody. Group differences were examined using ANOVA with a post-hoc test to account for multiple comparisons.

Results: Human macrophages incubated with Fib-MAA significantly increased ($p < 0.001$) the Ca2+ influx compared to unmodified Fib (**Figure 1**). Exposure to Fib-MAA had no meaningful impact on ITPR3 expression ($p > 0.05$) (**Figure 2**). In contrast, CAMKK2 expression was significantly ($p < 0.001$) increased in macrophages stimulated with Fib-MAA compared to cells stimulated with unmodified Fib. Likewise, PAD-4 mRNA expression was significantly ($p < 0.01$) increased in only the Fib-MAA vs. native Fib. In contrast to the mRNA expression, Western Blot revealed a decrease in PAD-4 protein expression for Fib-MAA vs. unmodified Fib, suggesting protein depletion (**Figure 3**).

Conclusion: The increase in Ca2+ influx following treatment with a MAA-modified antigen provides a critical element needed for PAD-mediated protein citrullination in human macrophages, while the observed increase in PAD-4 expression provides the requisite catalyst. The lack of effect seen on ITPR3 (which promotes intracellular movement from the endoplasmic reticulum) suggests that the overall increase likely stems from extracellular sources. The increased expression of CAMKK2 following Fib-MAA exposure could account for changes in cellular activity such as cell differentiation, changes in cell cycle and/or cytoskeletal architecture even though the source of calcium is different. Taken together, these data for the first time implicate MAA-modified proteins as promoters of macrophage-mediated citrul-

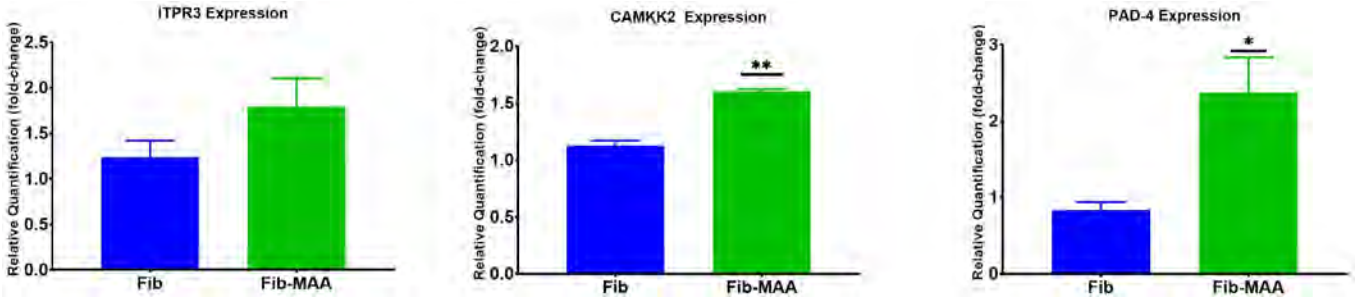

Figure 2. Expression of mRNA by RTPCR following 24 hour treatment of THP-1 macrophage with native fibrinogen or MAA modified fibrinogen. ITPR3 expression was not significant compared to Fib. CAMKK2 expression **p<0.01 significantly increased compared to Fib treatment. PAD-4 expression *p<0.01 significantly increased compared to Fib treatment. N=5.

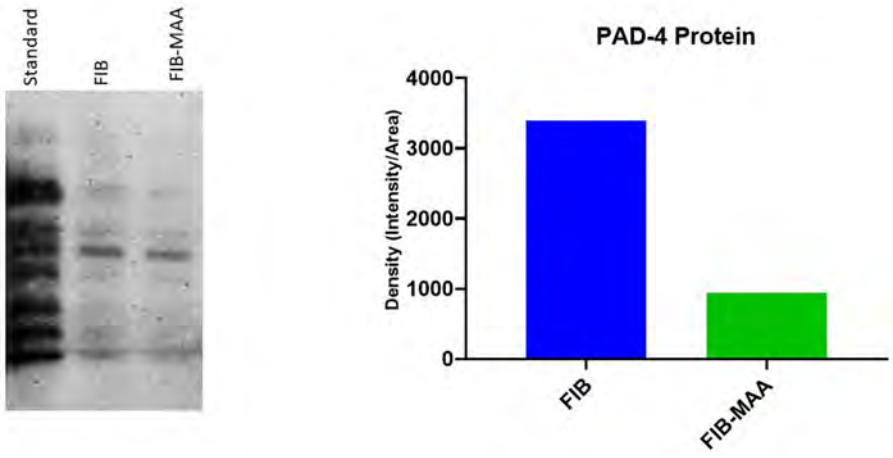

Figure 3. Western Blot analysis of THP-1 macrophage cell lysates following 24 hour treatment with native fibrinogen or MAA modified fibrinogen.

lination, a process that is critical in RA pathogenesis and that appears to be dependent on increases in both Ca2+ influx and increased PAD expression.

Disclosure: A. Gerber, None; **M. Duryee**, None; **N. Aripova**, None; **B. England**, Boehringer-Ingelheim, 2; **J. O'Dell**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6.

Abstract Number: 0023

Investigating Temporal Changes in Pregnancy Among Women with Rheumatoid Arthritis and Healthy Women Using Co-expression Network Analysis

Matthew Wright[1], Dana Goin[2], Mette Smed[3], J Lee Nelson[4], Nicholas Jewell[5], Jorn Olsen[6], Merete Hetland[7], Vibeke Zoffmann[3] and **Damini Jawaheer**[8], [1]UCSF Benioff Children's Hospital Oakland, Oakland, CA, [2]University of California San Francisco, San Francisco, CA, [3]Juliane Marie Center, Rigshospitalet, Copenhagen, Denmark, [4]Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA, [5]University of California Berkeley, Berkeley, CA, [6]Aarhus University Hospital, Aarhus, Denmark, [7]DANBIO and COPECARE, Centre for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, Denmark, [8]UCSF Benioff Children's Hospital Oakland / University of California San Francisco, Oakland, CA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA), while still an incurable disease, can often improve naturally during pregnancy. The specific mechanism(s) underlying this pregnancy-induced improvement, however, are not known. Our goal was to use our prospective pregnancy cohort (a) to identify genes whose expression are modulated during pregnancy in healthy women and in RA, as the disease improves, and (b) to investigate their functional enrichment using co-expression network analysis.

Methods: Data and samples were collected at pre-pregnancy (T0) and each trimester (T1, T2, T3) from women with RA who improved during pregnancy (n=14) and healthy women (n=15) enrolled in our prospective pregnancy cohort. Total RNA samples from whole blood were sequenced (RNA-seq). Following alignment (HISAT2) and transcript assembly (StringTie), gene-level expression was quantified (featureCounts) and normalized (edgeR). Cell type proportions were inferred through deconvolution (CIBERSORTx). Generalized Estimating Equation (GEE) models were used to assess modulation of gene expression across pregnancy in each group of women, adjusting for changes in cell type proportions across time points. Thresholds of FDR< 0.05 and fold-change >=2 (vs T0) were used to determine significance. Functional enrichment analysis (Webgestalt, Enrichr) and co-expression network analysis (WGCNA) were also performed.

Results: Temporal changes were observed in the proportions of neutrophils, resting NK cells, and resting CD4 memory T cells among healthy women only, and of monocytes among the women with RA. Numerous genes (334 protein-coding and 115 non-coding) were significantly up- or down-regulated during pregnancy among the women with RA, some demonstrating significant changes starting from early pregnancy (T1: n=26) or mid-pregnancy (T2: n=262) or during late-pregnancy (T3: n=161). Of those, 116 demonstrated similar temporal expression patterns among healthy women; another 112 genes were modulated during pregnancy only in the healthy group. The genes whose expres-

sion were modulated during pregnancy as RA improved were enriched in specific co-expression network modules related to neutrophil activation (upregulated in early pregnancy), binding of erythroid transcription factors (upregulated in mid-pregnancy), immunoglobulin constant and variable chain genes (downregulated in mid-pregnancy), and translation (mostly ribosomal genes, upregulated in late pregnancy). Similar enrichment in co-expression modules were observed in healthy pregnancy, except for the module related to binding of erythroid transcription factors which seemed to be specific to the RA group. Additionally, a module related to interferon signaling was enriched in genes modulated only in healthy pregnancy.

Conclusion: In our pregnancy cohort, multiple co-expression modules overlapped between the RA and healthy pregnancies. However, there were also differences including a specific module related to binding of erythroid transcription factors that was unique to RA, and a module related to interferon signaling that was unique to healthy pregnancy. It remains to be investigated how those differences may influence improvement of the disease during pregnancy.

Disclosure: M. Wright, None; **D. Goin**, None; **M. Smed**, None; **J. Nelson**, None; **N. Jewell**, None; **J. Olsen**, None; **M. Hetland**, Biogen, 2, 5, 6, Celltrion, 2, 6, Janssen Biologics B.V, 2, 6, MSD, 2, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, 6, AbbVie, 5, BMS, 5, Eli Lilly Denmark A/S, 5, 12, personal fees, Lundbeck Fond, 5, Roche, 5, Sandoz, 5, Novartis, 5, Merck, 5, Orion Pharma, 12, personal fees, Medac, 6; **V. Zoffmann**, None; **D. Jawaheer**, None.

Abstract Number: 0024

Heterogeneity of Inflammatory HLA-DR$^+$ Synovial Fibroblasts in Rheumatoid Arthritis Is Driven by Responses to Leukocyte-Derived Cytokines

Melanie Smith[1], Alejandro Kochen[1], Vianne Gao[2], Michail Schizas[2], Edward DiCarlo[1], Susan Goodman[1], Christina Leslie[3], Laura Donlin[1] and Alexander Rudensky[4], [1]Hospital for Special Surgery, New York, NY, [2]Memorial Sloan Kettering Cancer Center, New York, NY, [3]Computational and Systems Biology Program Memorial Sloan Kettering Cancer Center, New York, NY, [4]Memorial Sloan Kettering Cancer Center / Howard Hughes Medical Institute, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Treatment-refractory rheumatoid arthritis (RA) represents a major unmet need with substantial societal burden. Targeting RA-associated fibroblast-like synoviocytes (FLS) may provide a less-immunosuppressive therapeutic option. Recent single cell RNA-sequencing (scRNA-seq) studies of RA synovial tissue have identified distinct fibroblast subsets, including a population of HLA-DR$^+$ FLS that are expanded in RA and express pro-inflammatory cytokines as well as interferon gamma (IFNg) and tumor necrosis factor alpha (TNFa) response signatures (1). Donors with an expansion of HLA-DR$^+$ FLS have an expansion of inflammatory monocytes, which express interleukin 1 beta (IL-1b), and CD8$^+$ T cells, which express both TNFa and IFNg (1). TNFa stimulated macrophages that produce IL-1b induce key genes expressed by HLA-DR$^+$ FLS, including IL6 (2). Here we explored the ability of distinct combinations of cytokines predominant in RA to impart gene expression features observed in HLA-DR$^+$ FLS and localize these FLS within the inflamed synovium.

Methods: Synovial tissue was obtained from a prospective cohort of RA patients undergoing arthroplasty or synovectomy who are screened for active RA at the time of surgery (HSS IRB no. 2014-233). For cultured FLS, synovial

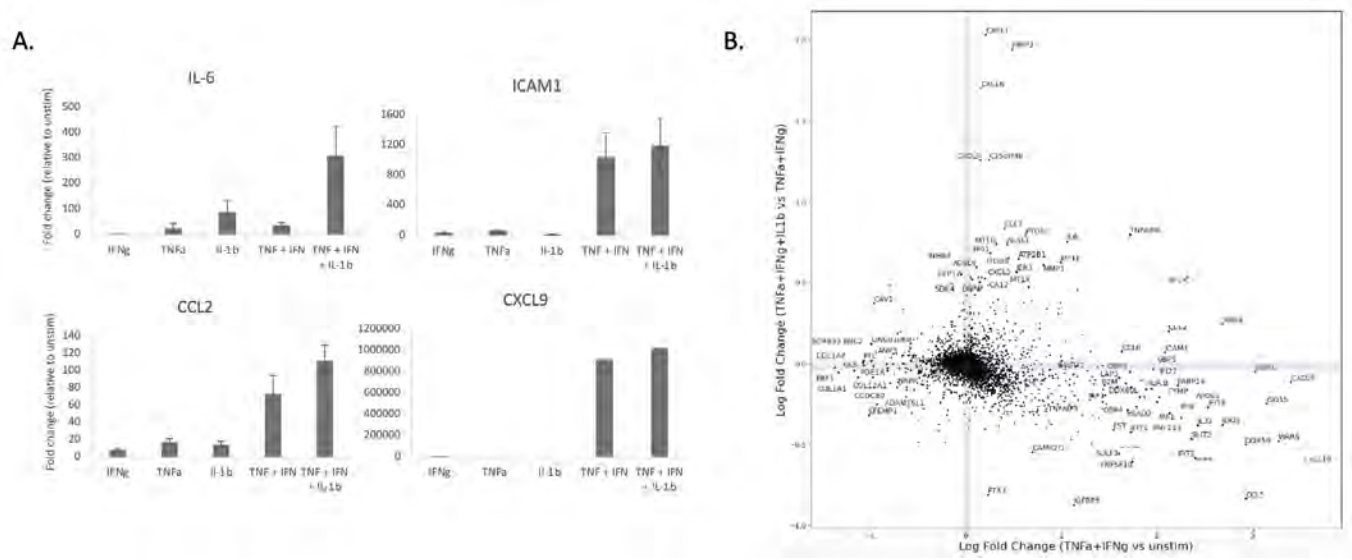

Figure 1. Stimulation of cultured FLS with combinations of dominant RA cytokines reveals marked synergy and distinct gene signatures driven by either TNFa + IFNg ± IL-1b. A. qPCR on cultured, cytokine-stimulated FLS. n = 3 donors. Mean ± SD. B. Differential expression analysis from scRNA-seq of cultured, cytokine-stimulated FLS derived from single RF+/CCP+ patient on methotrexate monotherapy with active disease.

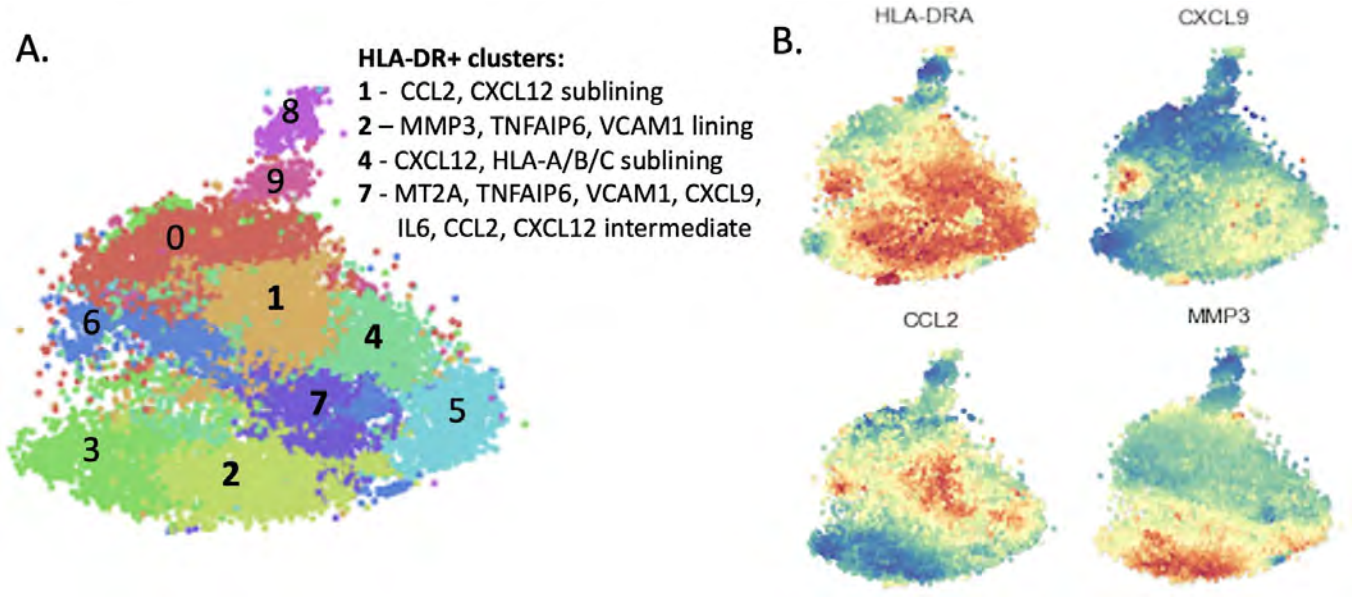

Figure 2. Heterogeneity of HLA-DR+ FLS including clusters with expression of genes induced cytokine combinations. ScRNA-seq of freshly dissociated, sorted FLS from same patient as in Fig 1. A. t-SNE showing clusters of transcriptionally similar FLS in which clusters 2 and 3 are lining, 5 and 7 are intermediate sublining/lining and 0, 1, 4, 6, 8, and 9 are sublining. B. Expression of HLA-DRA as well as genes induced by IFNg + TNFa (CXCL9), IL-1b (MMP3) or IFNg + TNFa + IL-1b (CCL2).

tissue was dissociated and cultured as in (2). FLS were cultured with cytokines for 24 hours. ScRNA-seq was performed on sorted FLS ($CD45^-$, $CD31^-$, $PDPN^+$) from dissociated synovial tissue. Multiparameter immunofluorescence (IF) was carried out using Iterative Bleaching Extends Multiplexity (IBEX) (3).

Results: The combination of IFNg, TNFa +/- IL-1b induced FLS expression of genes characteristic of HLA-DR^+ FLS such as IL6, CCL2, CXCL9 and ICAM1 (Fig 1A). Differential gene expression analysis of cytokine-stimulated FLS revealed distinct transcriptional features elicited by IFNg + TNFa vs IL-1b (Fig 1B). When used in combination, the cytokines were able to exert a synergistic effect on FLS gene expression with a small set of genes induced by the

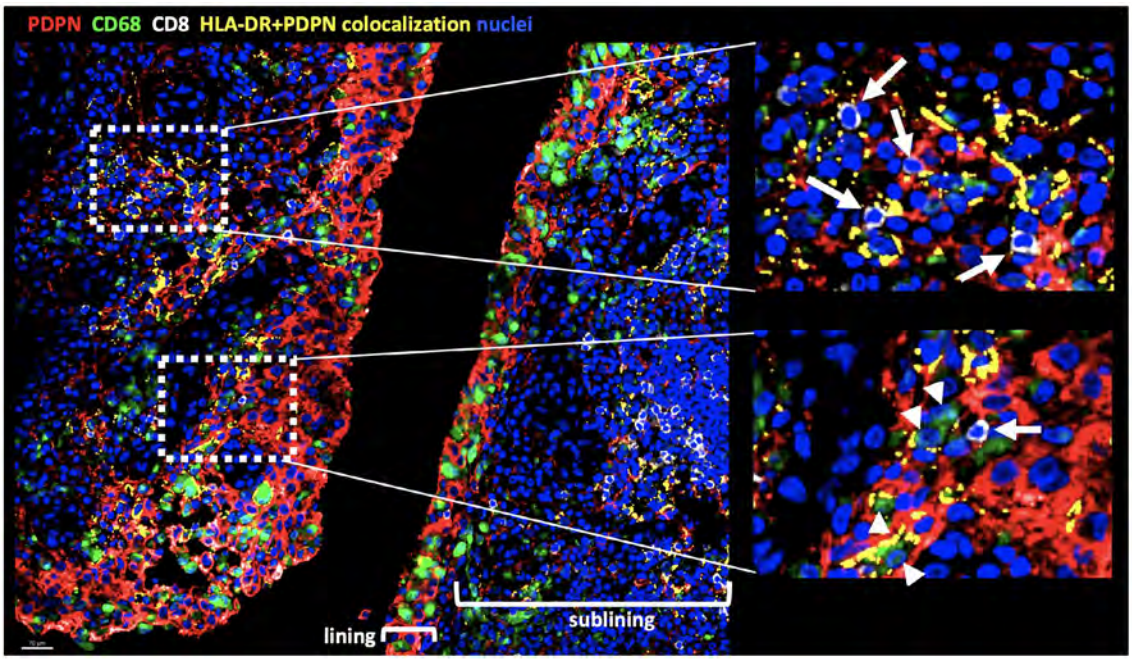

Figure 3. HLA-DR+ FLS are found within both synovial sublining and lining. IF of RA synovial tissue from same patient as in Fig 1 and 2 where HLA-DR+ FLS can be found near both CD68+ macrophages (arrow heads) and CD8+ T cells (arrows). Black space in full sized image represents synovial fluid space between two hypertrophied villi of the inflamed synovium.

combination of all three cytokines (IL6, TNFAIP6, MT2A, CCL2, MT1E). Unsupervised clustering analysis of gene expression of freshly dissociated FLS shows heterogeneity of HLA-DR$^+$ FLS with expression in both lining and sublining clusters as well as in clusters with an intermediate lining/sublining phenotype (Fig 2A). Clusters have differential expression of genes driven by TNFa + IFNg (CXCL9), IL-1b (MMP3) or all three cytokines (CCL2) (Fig 2B). IF analysis of inflamed synovium revealed localization of HLA-DR$^+$ FLS to both the lining and sublining areas in proximity to CD68$^+$ macrophages and CD8$^+$ T cells, respectively, (Fig 3).

Conclusion: Pro-inflammatory cytokine exposure of FLS accounts in part for the HLA-DR$^+$ FLS heterogeneity observed in the arthritic synovium *in situ*. Our analyses suggest that gene expression patterns observed in HLA-DR$^+$ FLS, which we were able to reconstruct with combinatorial cytokine stimulation *in vitro,* may originate from interacting CD8$^+$ T cells and inflammatory macrophages in the synovium.

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2) Kuo D, et al. Sci Transl Med. 2019;11(491):eaau8587.
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Disclosure: M. Smith, None; **A. Kochen**, None; **V. Gao**, None; **M. Schizas**, None; **E. DiCarlo**, None; **S. Goodman**, UCB, 1, NOvartis, 5; **C. Leslie**, None; **L. Donlin**, Karius, Inc., 5, Stryker, 2, 6; **A. Rudensky**, Takeda, 5, 10, Surface Oncology, 2, 11, RAPT Therapeutics, 2, 11, Sonoma Biotherapeutics, 2, 11, Vedanta Biosciences, 2, 11, BioInvent AB, 2.

Abstract Number: 0025

The Modulatory Capacity of Galectin-3 on the Programmed Death-1 Signaling Axis in Rheumatoid Arthritis

Kathrine Pedersen[1], Morten Aagaard Nielsen[2], Malene Hvid[1], Bent Deleuran[1] and Stinne Greisen[1], [1]Aarhus University, Aarhus, Denmark, [2]Aarhus University / Aarhus University Hopital, Aarhus, Denmark

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disease characterized by inflammation of the synovium. Despite a variety of treatments, 30-40% of RA patients fail to respond to any of the approved treatment options. Thus, improving the understanding of the molecular background and complex disease mechanisms in RA is of utmost importance.

Programmed death 1 (PD-1) is an inhibitory glycosylated immune checkpoint receptor that dampens immune responses, and high PD-1 expression is considered desirable in RA. However, the exact effects of the PD-1 signaling axis in RA remains to be elucidated.

Extracellular Galectin-3 (Gal-3) is suggested to be associated with RA disease severity and inflammation. In contrast, Gal-3 has immune suppressing capabilities in cancer. Thus, effects of Gal-3 are complex, but could potentially be explained by Gal-3s diverse effect on immune checkpoint receptors.

Here, we aimed to investigate whether Gal-3 is a binding partner to PD-1, and how this interaction affects PD-1 signaling as well as inflammatory markers.

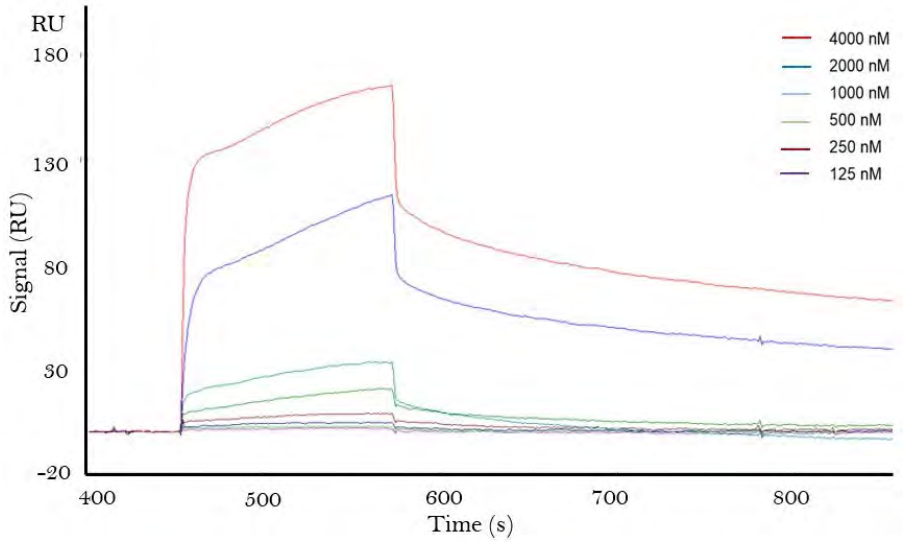


Figure 1. Surface plasmon resonance data. Recombinant human PD-1 coupled to Protein G and immobilized onto a sensor chip, while recombinant human Gal-3 is added to the buffer and run over the sensor chip. PD-1 and Gal-3 interaction will give rise to increased signal (Response Units (RU)). Here increasing concentrations of rhGal-3 is run over the sensor chip and demonstrating how rhGal-3 can interact with rhPD-1.

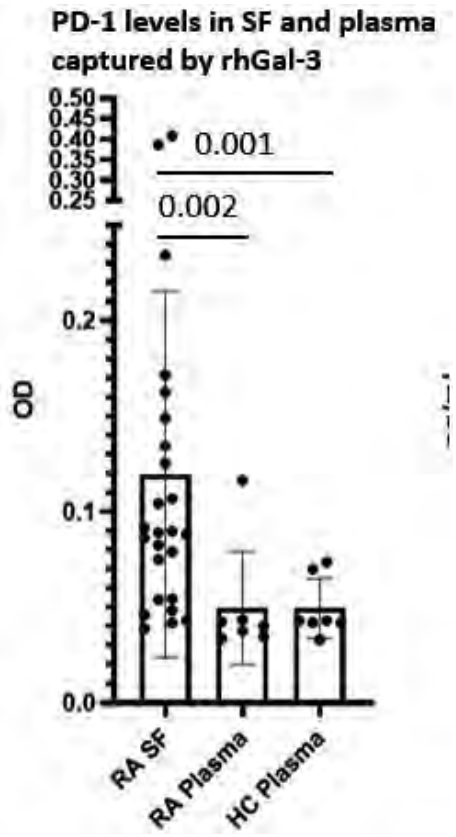


Figure 2. ELISA data. Visualizing levels of soluble PD-1 captured by rhGal-3 in synovial fluid and plasma samples from RA patients as well as plasma samples from healthy controls (HC). Significantly higher levels of PD-1 was detected in synovial fluid compaired to both RA plasma ($p<0.01$) and HC plasma ($p<0.01$).

Methods: Patient material consisted of synovial fluid (SF, n=25), plasma, peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) from chronic (c) RA patients. Patients presented with a disease flare when samples were obtained. Surface Plasmon Resonance (SPR) was performed using recombinant human (rh) Gal-3 and PD-1 to investigate potential binding. PD-1 and Gal-3 interaction in patient samples was measured by ELISA. Surface expression of Gal-3 and PD-1 on PBMCs and SFMCs, as well as intracellular IL-2 levels upon stimulation were assessed by flow cytometry. Statistical analysis and graphs were performed using GraphPad Prism 9.0.2 Software.

Results: Using SPR, we demonstrated that Gal-3 binds PD-1 as well as PD-L1 with an estimated K_D of 10^{-6} and 10^{-5}, respectively (Fig. 1). This binding was confirmed in SF and plasma samples from RA patients, where rhGal-3 could capture soluble PD-1 (Fig. 2). Significantly higher levels of PD-1 were detected by rhGal-3 in SF (n=25) compared to plasma samples from both RA (n=7, p=0.002) and healthy controls (n=7, p=0.001).

RA PBMCs (n=6) and SFMCs (n=6) were stimulated using anti-CD3/anti-CD28 stimulation. Significantly higher levels of cells expressing either PD-1 (p=0.007), as well cells positive for both PD-1 and Gal-3 (p=0.04), were observed in SFMCs compared to PBMCs, supporting the effects of Gal-3 in the local inflamed microenvironment. Treating stimulated CD4+ cells with rhPD-L1, caused IL-2 levels to decrease (p=0.059). When rhGal-3 was administered alone it also resulted in decreased IL-2 levels (p=0.02), however, treating stimulated CD4+ cells with both rhPD-L1 and rhGal-3 the effect of each treatment was repelled (p=0.03), which could be explained by Gal-3s capability to interact directly with PD-1 and its ligands (Fig. 3).

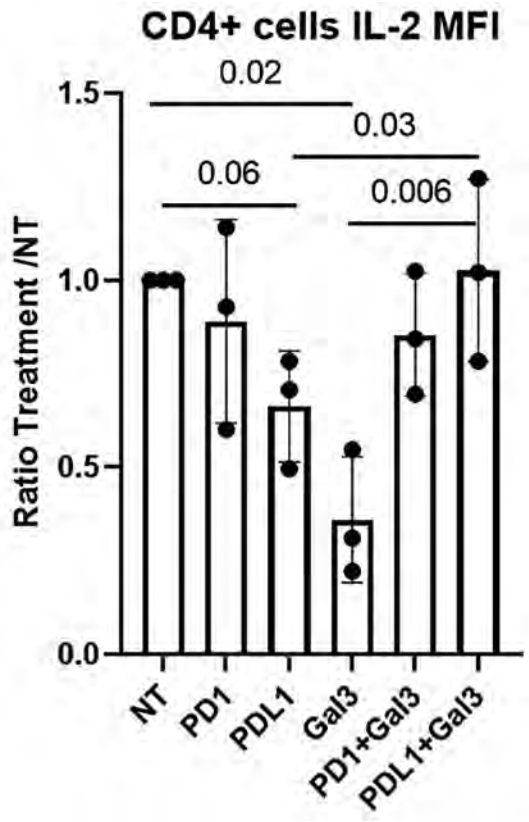


Figure 3. Flow cytometry and intracellular staining for IL-2. The ratio between IL-2 mean fluorescence intensity (MFI) on CD4+ T cells in cells stimulated with anti-CD3 and anti-CD28 and given various treatments. Treating cells with rhPD-L1 resulted in decreased IL-2 MFI (p=0.0591). IL-2 MFI is also decreased when treating cells with rhGal-3 (p=0.02). However, when cells are treated with rhPDL1 and rhGal-3, the effect is repelled (PD-L1 vs PD-L1+Gal-3, p=0.03; NT+s vs PD-L1+Gal-3, p=0.9).

Conclusion: Here we showed how Gal-3 binds PD-1. Data support that the effect of Gal-3 on PD-1 signaling are more pronounced in a local inflammatory milieu in the synovium. Finally, when both Gal-3 and PDL1 were present, the anti-inflammatory effect of PD-1 signaling in decreasing IL-2 was repelled by high levels of local Gal-3.

Disclosure: K. Pedersen, None; **M. Nielsen**, None; **M. Hvid**, None; **B. Deleuran**, None; **S. Greisen**, None.

Abstract Number: 0026

Synovial Fibroblasts Acquire a Proinflammatory and Destructive Phenotype After Exposure to αS1-Casein (CSN1S1)

Nadine Honke[1], Tim Appel[1], Matthias Schneider[2] and Georg Pongratz[3], [1]Department of Rheumatology, Hiller Research Center Rheumatology, University Hospital Düsseldorf, Germany (* contributed equally), Düsseldorf, Germany, [2]Policlinic & Hiller Research Unit Rheumatology, UKD, Heinrich-Heine University, Düsseldorf, Germany, [3]Polyclinic and Functional Area for Rheumatology & Hiller Research Center Rheumatology, University Hospital Düsseldorf, Düsseldorf, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The milk protein αS1-Casein (CSN1S1) was described to be overexpressed in synovial tissue of patients with rheumatoid arthritis (RA) and osteoarthritis (OA). Recently we were able to show that αS1-Casein is capable of inducing the secretion of proinflammatory cytokines in human monocytic cells. Since synovial fibroblasts are known to regulate propagation of inflammation and contribute to cartilage and bone destruction in RA, our aim was to investigate whether αS1-Casein increases the pathogenic potential of RA and OA synovial fibroblasts (RASF and OASF).

Methods: Fibroblasts were isolated from synovial tissues obtained from patients diagnosed with RA and OA who underwent synovectomy due to total joint replacement. RASF and OASF were cultivated in the presence or absence of procaryotic recombinant human αS1-Casein and LPS. Polymyxin B (5µg/ml, Px5) was added to cultured cells to rule out any LPS-effects. After 24 hours fibroblast-derived IL-6, IL-8 and MMP-3 were measured in the supernatant by ELISA.

Results: ELISA analysis showed that synovial fibroblasts from RA and OA patients acquire a proinflammatory and destructive phenotype after treatment with αS1-Casein. This proinflammatory phenotype was induced by αS1- Casein in a concentration-dependent manner with elevated secretion of IL-6 (Ctrl. vs. αS1-Casein (500ng/ml); n=5-6, RA: p***=0.0001; OA: p**=0.0048), IL-8 (Ctrl. vs. αS1-Casein (500ng/ml); n=5, RA: p****< 0.0001; OA: p*=0.0179) and MMP3 (Ctrl. vs. αS1-Casein (500ng/ml); n=5-6, RA: p***=0.0007; OA: n.s.). LPS treatment alone increased the levels of IL-6 (Ctrl. vs. LPS 1ng/ml; n=5-6, RA: p*=0.0455, OA: n.s.; Ctrl. vs. LPS 10ng/ml; n=5-6, RA: p**=0.0039; OA: p**=0.0014), IL-8 (Ctrl. vs. LPS 1ng/ml; n=4-5, RA: p**=0.0037, OA: p**=0,0094; Ctrl. vs. LPS 10ng/ml; n=4-5, RA: p***=0.0005; OA: p***=0.0002) and MMP3 (Ctrl. vs. LPS 1ng/ml; n=5-6, RA: n.s; OA: p*=0.0433; Ctrl. vs. LPS 10ng/ml; n=5-6, RA: p*=0,0287; OA: p**=0.002). Addition of polymyxin B to αS1-Casein-treated fibroblasts did not significantly influence the secretion of the investigated factors (IL-6, IL-8, MMP3: αS1-Casein vs. αS1-Casein+Px5, n=4-6) while polymyxin B completely blunted the LPS-induced secretion (IL-6: LPS 10ng/ml vs. LPS 10ng/ml +Px5, n=5, RA: p*=0.0326; OA: p*=0.014; IL-8: LPS 10ng/ml vs. LPS 10ng/ml +Px5, n=5-6, RA: p**=0.0038; OA: p****< 0.0001; MMP3: LPS 10ng/ml vs. LPS 10ng/ml +Px5, n=6, RA: p*=0.0287; OA: n.s.). Furthermore, by using immunofluorescence histology of synovial tissue from RA and OA patients, we demonstrated that infiltration of casein-positive cells occurs mainly in RA and not OA patients.

Conclusion: In conclusion, our results suggest that casein-positive infiltrating cells are responsible for inducing a proinflammatory phenotype in RASF and augment their destructive capability. αS1-Casein might therefore be part of the pathomechanism of RA.

Disclosure: N. Honke, None; **T. Appel**, None; **M. Schneider**, GlaxoSmithKline, 2, 5, 6, UCB, 5, 6, AbbVie, 2, 5, Alexion, 2, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, Janssen-Cilag, 2, 6, Lilly, 2, 6, Novartis, 2, Pfizer, 2, 6, Roche, 2, Sanofi-Aventis, 2, Biogen, 6, BMS, 6, Celgene, 6, Chugai, 6; **G. Pongratz**, None.

Abstract Number: 0027

Metabolomic Study of Rheumatoid Arthritis Using ^{1}H Nuclear Magnetic Resonance (^{1}H NMR)

Konstantina Tsezou, Dimitra Benaki, Katerina iliou, Emmanuel Mikros and Panayiotis Vlachoyiannopoulos, National and Kapodistrian University of Athens, Athens, Greece

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A

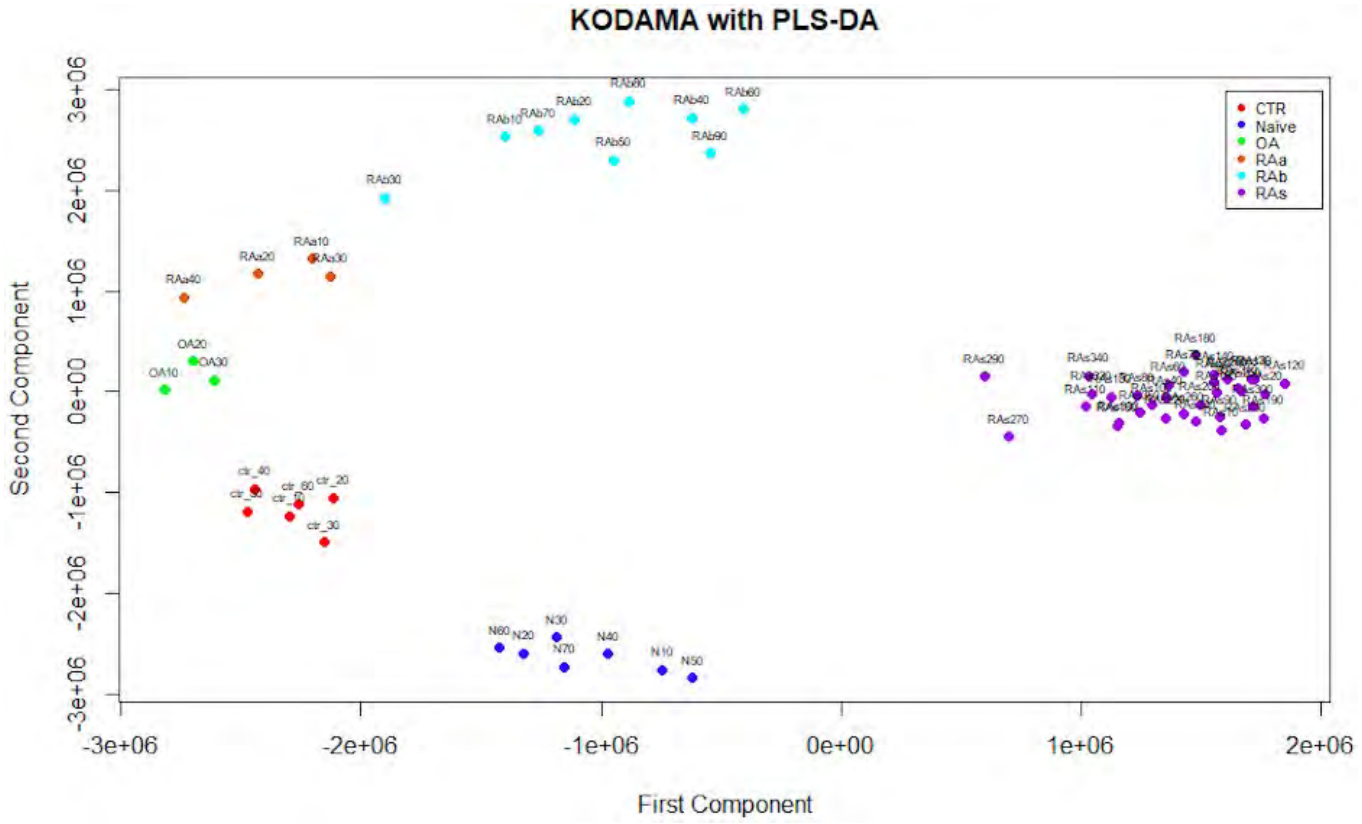


Figure 1. KODAMA is a supervised multivariate statistical analysis. This graph shows that the 6 experimental groups show a characteristic clustering, hence suggesting that each group has a unique metabolic fingerprint.

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) remains a disease with high morbidity. Biologic agents revolutionized the therapy of RA, but they are withdrawn in 50% of patients in 5 years due to loss of efficacy or side-effects. Predictive biomarkers for drug efficacy or side effects are missing while a personalized approach in RA therapy is imperative. Several reports support the notion that specific metabolomics profiles are good predictors for response to TNF blockers. However, the results of many studies are inconclusive due to the small sample size, lack of sequential samples and synchronization of sample collection with initiation or change of therapy.

The aim is to create a metabolic profile for RA patients at different time-points of therapy (DMARDs/bDMARDs), identify biomarkers related to therapy-response, monitor the disease progression, and predict the optimal disease management.

Methods: Plasma was collected from fasted RA patients according to their therapy timepoint: newly diagnosed Naïve (N, n=5) without therapy, before (RAb, n=9) and after (RAa, n=4) therapy (follow up of Naïve and RAb), and patients on standard therapy (RAs, n=35) either DMARD/bDMARD being in a stable condition. Osteoarthritis (OA, n=3) patients and healthy controls (ctr, n=6) were also included in the study. Metabolomic profiling was carried out with 1H NMR spectroscopy. Uni- and multivariate statistical analyses were done to investigate clustering of the experimental groups and define the responsible metabolites. Knowledge Discovery by Accuracy Maximization (KODAMA) was applied for feature extraction in an unsupervised and semi-supervised approach, using principal component analysis-canonical analysis with k-Nearest Neighbor (PCA-CA-kNN) and Partial least squares discriminant analysis (PLS-DA) as classifiers.

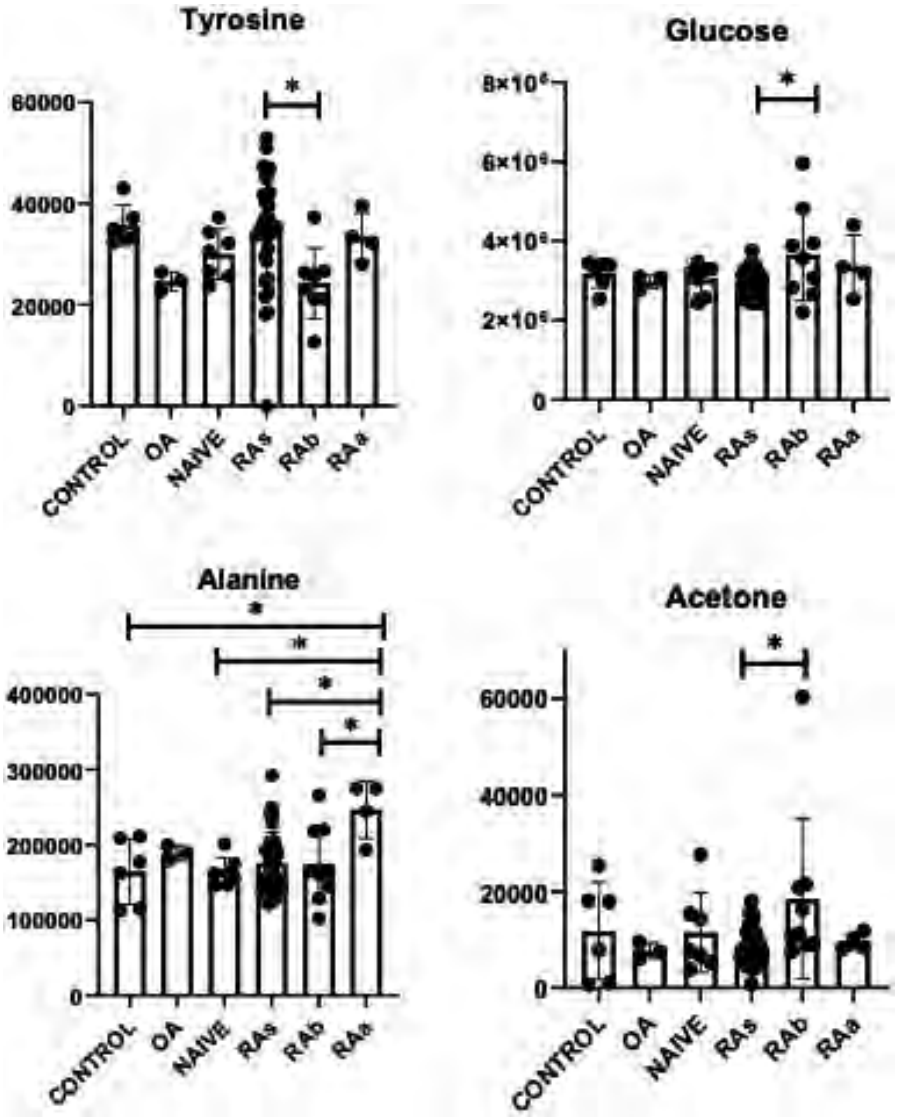


Figure 2. Univariate analysis showed statistical significance (p>0.05) of the metabolites Tyrosine, Alanine, Glucose, and Acetone.

Results: Multivariate analysis using KODAMA revealed distinct metabotypes for the six groups, with acetone, tyrosine and alanine, posing the highest importance for discriminating RA patients. Pairwise comparisons using Orthogonal PLS-DA could also differentiate Naïve patients from ctr and RAa patients, as well as RAb from RAa patients. Univariate study showed that RAa patients are characterized by elevated alanine levels compared to the other groups (mean ± SD, 103) 246.8±38.5 in RAa, 174.1±51.2 in RAb, 175.6±40.4 in RAs, 163.9±19.3 in Naïve; p< 0.01. Tyrosine was significantly increased in RAs compared to RAb, 35.5±8.8 vs 24.3±6.9 respectively; p=0.005, while glucose (2943.5±316.0, 3659.8±1166.8; p=0.01) and acetone were decreased (2943.5±316.0, 3659.8±1166.8; p=0.01). Significant alterations were also observed in macromolecule signals attributed to VLDL and LDL, indicating a putative role of these lipoproteins in differentiating Naïve from RAa and RAs patients.

Conclusion: These data confirm that the metabolic profile of RA patients from Greek populations shows differences related to therapeutic treatment. Biomarkers like alanine and tyrosine can help evaluate the response to therapy. Lastly, the lipoprotein profile is expected to provide additional biomarkers to improve patient classification helping the treatment planning.

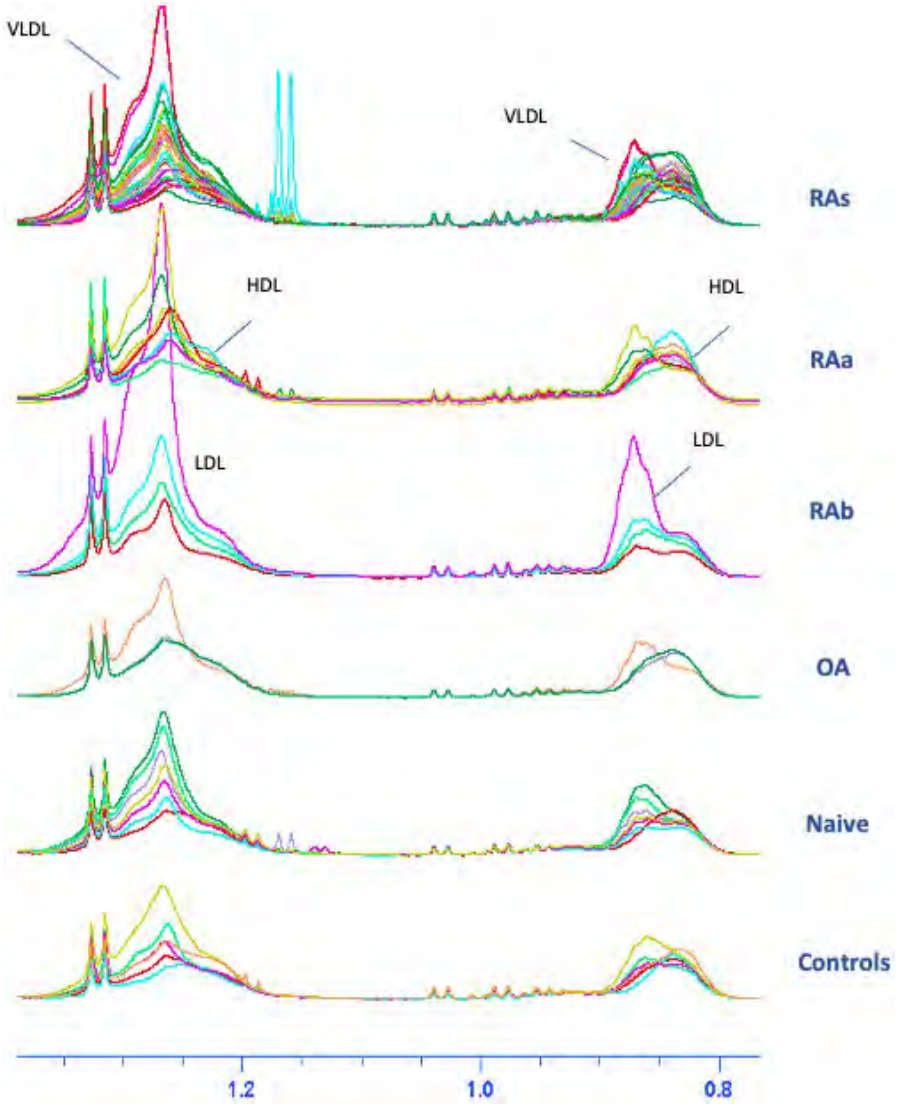


Figure 3. Changes in the lipoprotein signal on the NMR spectra between the experimental groups.

Disclosure: K. Tsezou, Pharmagnose S.A., 3; **D. Benaki**, None; **K. iliou**, None; **E. Mikros**, Pharmagnose S.A., 3; **P. Vlachoyiannopoulos**, None.

Abstract Number: 0028

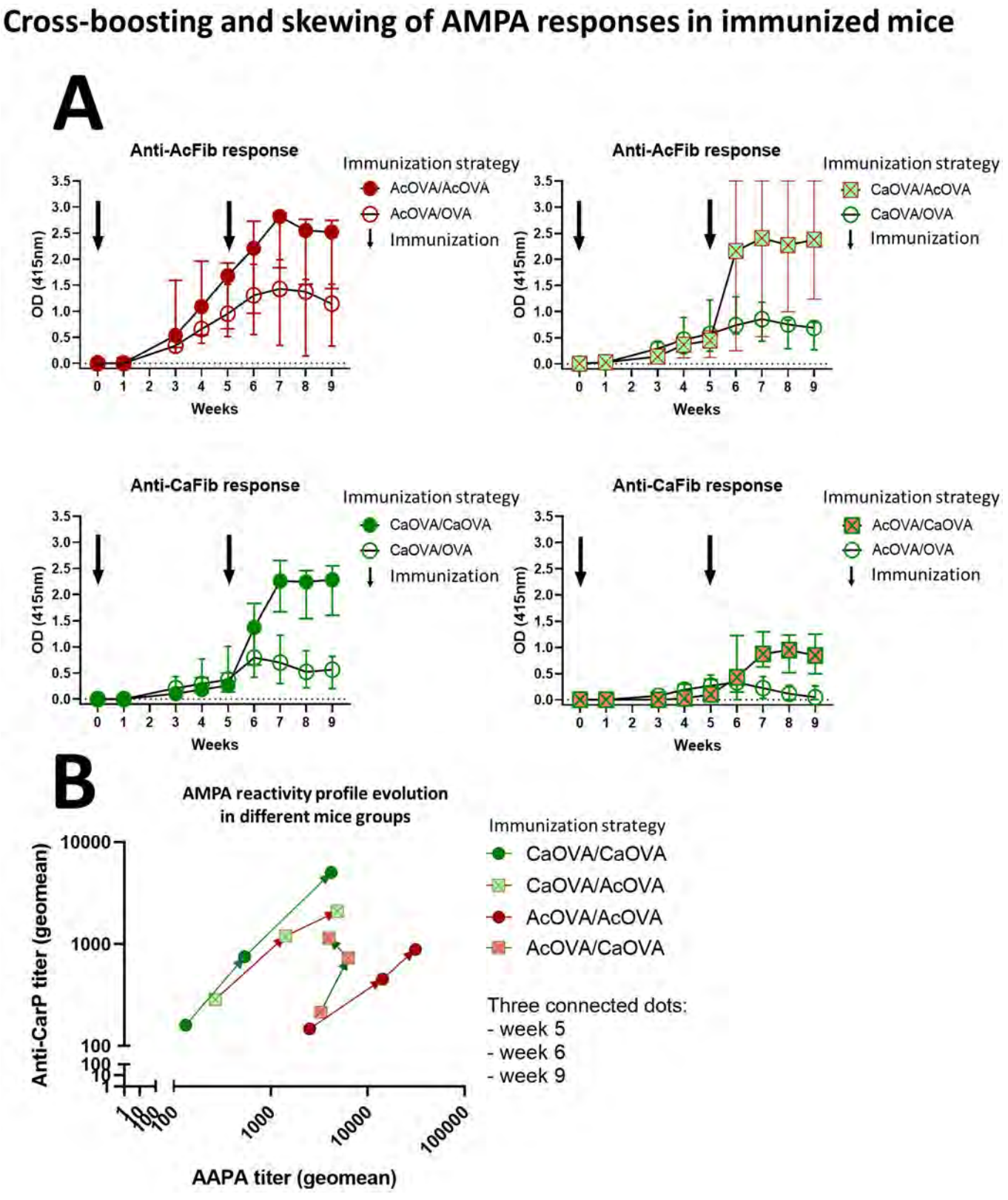
Evolution of Anti-modified Protein Antibody Responses Can Be Driven by Consecutive Exposure to Different Post-translational Modifications

Mikhail Volkov, Arieke Kampstra, Karin van Schie, Tom WJ Huizinga, René Toes and Diane van der Woude, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Besides anti-citrullinated protein antibodies (ACPA), rheumatoid arthritis patients (RA) often display autoantibody reactivities against other post-translationally modified (PTM) proteins, more specifically carbamylated and acetylated proteins. Immunizing mice with one particular PTM results in an anti-modified protein antibody (AMPA) response recognizing multiple PTMs. Furthermore, human AMPA, isolated based on their reactivity



to one PTM, cross-react with other PTMs at the monoclonal and polyclonal level. However, it is unclear whether the AMPA reactivity profile is "fixed" in time, or whether consecutive exposure to different PTMs can shape the evolving AMPA-response. In this work, we aimed to investigate the evolution of the AMPA response in mice with controlled exposure to PTMs as well as in humans at risk of RA and with early RA.

Methods: Mice were immunized with acetylated (or carbamylated) protein (ovalbumin) twice or cross-immunized with an acetylated and then a carbamylated protein (or vice versa) and their serum was analyzed for AMPA responses using a different backbone protein (fibrinogen) bearing the same modifications. Longitudinally collected serum samples of human individuals at risk of RA and with early RA were tested to investigate the evolution of the AMPA responses over time.

Results: Mice immunized twice with either solely acetylated or solely carbamylated ovalbumin (AcOVA or CaOVA) developed reactivity against both acetylated and carbamylated antigens. Irrespective of the PTM used for the first immunization, a booster immunization with the other PTM resulted in increased titers to the second/booster PTM (Figure A), indicating that immunization with a defined PTM-antigen leads to the generation of anti-PTM memory B cells able to cross-recognize other PTMs. Furthermore, immunizing with CaOVA and boosting with AcOVA (or vice versa) skewed the overall AMPA-response profile towards a relatively higher reactivity against the "booster" PTM (Figure B). Human data also illustrated dynamic changes in AMPA reactivity profiles in both individuals at risk of RA and in early RA patients (not shown).

Conclusion: The relationship between different reactivities within the AMPA response is dynamic. The initial exposure to a PTM antigen induces cross-reactive response that can be boosted by this or other PTMs. The overall reactivity pattern can be shaped by subsequent exposure to other PTMs. These data might explain temporal differences in the AMPA-response profile and point to the possibility that the PTM responsible for the initiation of the AMPA response may differ from the PTM predominantly recognized later in time.

Disclosure: M. Volkov, None; **A. Kampstra**, None; **K. van Schie**, None; **T. Huizinga**, None; **R. Toes**, None; **D. van der Woude**, None.

Abstract Number: 0029

JAK1 Regulates Autophagy and Reinforces the Inflammatory and Autoimmune Potentials in Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Background/Purpose: Rheumatoid arthritis (RA) is pathologically characterized by autoimmunity against citrullinated proteins, proliferative synovitis, and ultimately joint destruction. Synovial fibroblasts (SFs) are, when activated, capable of hyperproliferating and producing large amounts of proinflammatory mediators including IL-6, thus considered to be

the key effector cells in RA pathogenesis. SFs obtained from RA patients have high autophagy activity, probably contributing their active phenotype [1]. Besides, our recent study suggests SFs' autoimmune potential by demonstrating the increase of citrullinated vimentin and its interaction with MHC class II when treated with IFN-γ and autophagy inducers [2]. JAK1 is an emerging therapeutic target in RA, but its roles in the active phenotype of SFs remain to be elucidated. To clarify the role of JAK1 in the regulation of autophagy and in the inflammatory and autoimmune potentials in SFs.

Methods: SFs were derived from synovial tissue specimens obtained from RA patients during joint replacement surgery and used between passages 4-8 for all experiments. To inhibit JAK1, SFs were treated with its selective inhibitor upadacitinib for 6-24 h with the optimal concentration determined by BrdU assay. To induce autophagy, SFs were starved using serum-free medium for 2h or treated with 10μM of the proteasome inhibitor MG132 for 24h in the presence or absence of 5mM of the autophagy inhibitor 3-methyladenin. The expression of autophagy-related proteins/genes, including LC3-II, *BECN1*, *ATG5* and *ATG7*, were analyzed by Western blotting or real-time PCR. The expression of IL-6 was measured in cell culture supernatants by ELISA. The interaction between citrullinated vimentin and MHC class II (HLA-DR) were analyzed by *in situ* proximity ligation assays. P values were calculated by ratio paired t-test and considered significant when less than 0.05.

Results: JAK1 inhibition with upadacitinib resulted in the significantly decreased expression of LC-3II ($p = 0.016$ triplicated, $n = 3$), *BECN1* ($p = 0.01$, $n = 5$), *ATG5* ($p = 0.03$, $n = 5$) and *ATG7* ($p = 0.02$, $n = 5$) in starved SFs. Similar results were obtained in SFs treated with IFN-γ. The treatment of SFs with 100 ng/mL of IFN-γ for 24 h increased the expression of IL-6 in cell culture supernatants ($p = 0.017$, $n = 3$), which was inhibited by upadacitinib ($p = 0.02$, $n = 5$). The interaction between citrullinated vimentin and MHC class II was increased in SFs following treatment with starvation and IFN-γ (100ng/mL, 24h) ($p = 0.003$, $n = 6$). The effect was cancelled by the addition of upadacitinib ($p = 0.009$, $n = 6$) or 3-methyladenin ($p = 0.02$, $n = 6$).

Conclusion: Our current results indicate that JAK1 positively regulates autophagy and reinforces the inflammatory and autoimmune potentials in SFs. The mode of action of JAK inhibitors would include the mitigation of SFs' active phenotype.

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Abstract Number: 0030

Interleukin-9 Enhances the Osteoclastogenesis in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Rheumatoid Arthritis (RA) is a chronic inflammatory disease characterized by synovial inflammation leading to bone destruction. Bone erosion in RA results from excessive resorption of bone by osteoclasts and inadequate formation of bone by osteoblasts. Osteoclasts are specialized multinucleated cells that are derived from cells of monocyte-macrophage lineage. The pro-inflammatory cytokines exert their influence on the biology of osteoclast and thereby enhances the joint destruction in RA. Recently, our group and others have observed increased levels of interleukin-9 (IL-9) in the synovial fluid of patients with RA. Therefore, we investigated the impact of IL-9 on *in vitro* osteoclastogenesis in RA.

Methods: The study was conducted in active RA patients, diagnosed based on American College of Rheumatology (ACR), 1987 criteria. Peripheral blood (PB) was collected in heparinized vial. For TRAP assay, Mononuclear cells were stimulated with 50 ng/ml recombinant(r) human sRANKL, 50 ng/ml M-CSF and 100ng/ml of rIL-9 for 21 days. Cells were then fixed and stained using Acid Phosphatase, Leukocyte Kit. Tartrate resistant acid phosphatase (TRAP)-positive cells with three or more nuclei were scored as osteoclasts. Quantitative RT-PCR of osteoclast specific gene was performed after 3 days of stimulation as indicated using the QuantStudio® 5 Real-Time PCR System. Whole transcriptome analysis was performed using Illumina HiSeq X10 sequencing platform. Bone samples were obtained under sterile conditions from patients undergoing orthopedic surgery for non-pathological fractures and immediately placed in phosphate buffer saline (PBS) containing antibiotics. Samples were broken into tiny pieces and cultured in complete αMEM medium. Bone explant cultures were performed in six well plates with one piece of bone in a final volume of 6 ml, and in the presence or absence of 100ng/ml IL-9.

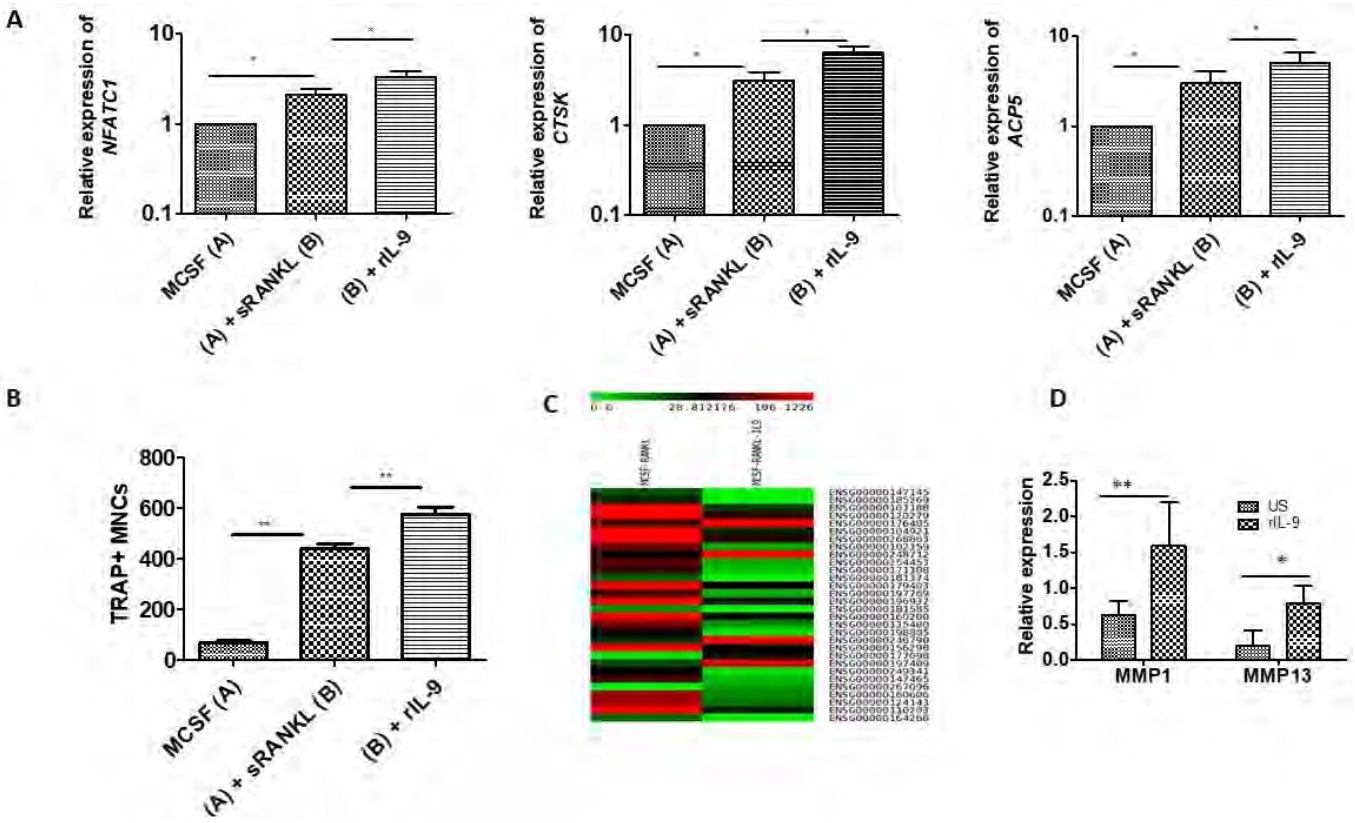

Figure 1. Impact of IL-9 on Osteoclast formation and Matrix metalloproteinases (A) Quantitative Real-Time PCR (RT-PCR) of osteoclast specific genes, nuclear factor of activated T-cells, cytoplasmic 1 (NFATc1), cathepsin K (CTSK) and acid phosphatase 5, tartrate-resistant (ACP5) was performed after 3 days of stimulation as indicated (* $p<0.05$). (B)Tartrate resistant acid phosphatase (TRAP) positive multinucleated cells (MNCs) were scored as osteoclasts (** $p<0.005$). (C) Heat map of RNA-Seq transcriptome analysis for top 30 genes at 2 foldchange and p value 0.05 of samples treated with MCSF+RANKL in presence or absence of IL-9. Differential expression analysis was done using DESEQ software. (D) Quantitative RT-PCR of MMP-1 and MMP13 was performed after 5 days of stimulation with or without rIL-9 (** $p<0.005$* $p<0.05$).

Results: We observed that rIL-9 stimulation along with M-CSF/sRANKL significantly enhanced the expression of nuclear factor of activated T-cells, cytoplasmic 1 (*NFATc1*), acid phosphatase 5, tartrate-resistant (*ACP5*) and cathepsin K (*CTSK*) as compared to M-CSF/sRANKL stimulation. Furthermore, we observed significant increase in the number of osteoclasts with rIL-9 stimulation along with M-CSF/sRANKL. Next, we performed transcriptome analysis between IL-9/M-CSF/sRANKL treated samples and M-CSF/sRANKL treated samples. Transcriptome analysis revealed differential gene expression with rIL-9 stimulation along with M-CSF/sRANKL as compared to stimulation with M-CSF/sRANKL. Using trabecular bone explant, we checked the effect of rIL-9 on matrix metalloproteinases (MMPs), which are critical regulators of extracellular matrix (ECM) proteolysis. We observed that IL-9 modulates the expression of collagenases *MMP1* and *MMP13,* which plays critical role in bone and cartilage degradation.

Conclusion: Our observations indicate towards the IL-9 mediated structural damage in the RA by the enhancing the differentiation of osteoclasts and modulating the expression of MMPs. Thus, blocking IL 9 pathway might be an attractive immunotherapeutic target for RA.

Disclosure: S. Kar, None; **D. Mitra**, None; **V. D**, None; **S. Chakraborty**, None.

Abstract Number: 0031

A New Pharmacostatistical Model to Assess MTX-adherence in RA Patients

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SESSION INFORMATION
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Background/Purpose: Methotrexate (MTX) is the first-line therapy for rheumatoid arthritis (RA). While therapeutic adherence is essential to the successful management of the patient, an estimated 40% of patients are thought to be non-adherent. Adherence to MTX is challenging to monitor as no objective MTX assay is currently available.

Our objective was to describe the urinary kinetics of MTX and its major 7-OH-MTX metabolite in treated patients and to evaluate the possibility to use one or both of these markers as an objective MTX-adherence assay.

Methods: Fifty-nine patients with RA (2010 ACR/EULAR criteria) treated with subcutaneous MTX were recruited.

Patients underwent urinary MTX pharmacokinetic assessment using high-performance liquid chromatography-mass spectrometry (HPLC-MS/MS) analysis. The urine sample was analyzed before and after subcutaneous injection (from 2 hours to 10 days after injection). Confirmed administration at hospital therapy was the reference of MTX-adherence.

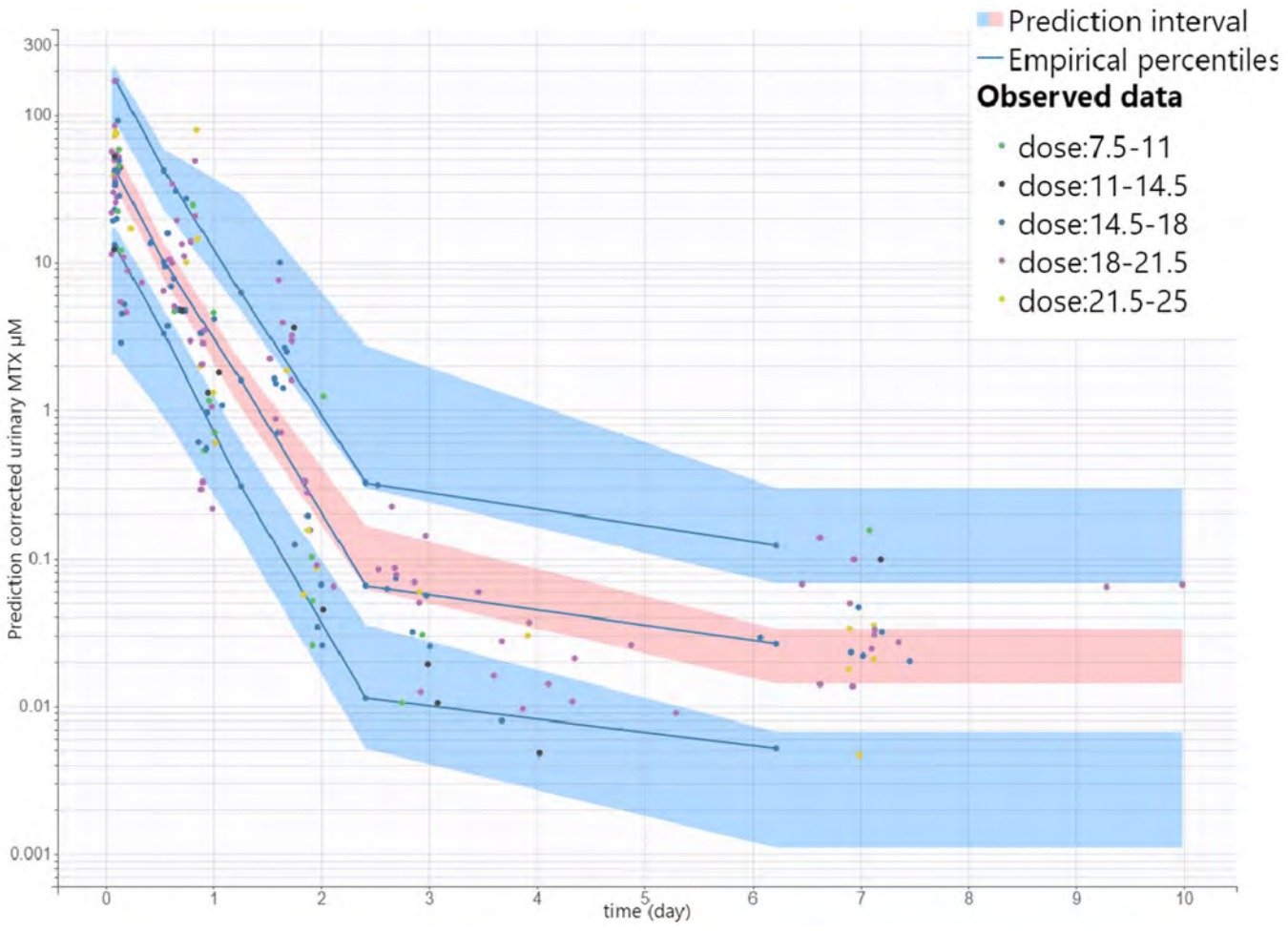
MTX and 7-OH-MTX concentrations were analyzed, and a population pharmacokinetic model was developed to describe the kinetics of MTX as a function of time and weekly dose.

From this model, the urinary MTX concentrations in treated patients were compared with the urinary concentrations of controls (n = 18 referent patient adherent and 10 patient with undifferentiated inflammatory arthritis without mtx treatment).

Results: A total of 363 urine samples (range 2-6 per patient) were obtained from patients treated with subcutaneous MTX. The average weekly dose of MTX was 17.2 mg/week (7.5-25mg)

A 2-compartment model with nonlinear renal elimination kinetic best described the urine MTX concentration versus time curves. This model allowed us to characterize the standard kinetic profiles of the observant patients as a function of different associated factors. Thus, 95% of MTX urine concentration values were above 0.9 nM regardless of the delay between MTX injection and urine sampling and independently associated MTX-adherence. A discriminatory cut-off value of 0.9 nM (v.s control group 0.22, CI95% [0.19-0.25] µM) made it possible to have an assay sensitivity and specificity of more than 93% and an AUC-ROC above 96 %, regardless of the MTX doses.

Conclusion: Using urine MTX concentration, we developed a pharmacostatistical model to monitor subcutaneous MTX adherence of RA patients. This allowed us to propose a new and objective MTX-adherence assay, which could help in current practice to differentiate patients who do not respond to methotrexate from non-adherent patients. After further validation, this test could therefore improve patient management by avoiding unnecessary intensification in non-adherent patients.



Visual predictive check of urinary MTX model with observed data (dot). Prediction intervals (95 %) for each percentile are estimated across all simulated data and displayed as colored areas (pink for the 50th percentile, blue for the 10th and 90th percentiles).

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Abstract Number: 0032

IL-40: A New B-cell Associated Cytokine Up-regulated in Rheumatoid Arthritis Decreases Following the Rituximab Therapy and Correlates with Disease Activity, Autoantibodies and NETosis

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Background/Purpose: Interleukin 40 (IL-40) is recently identified B cell - associated cytokine implicated in humoral immune responses and in B cell development and homeostasis. As B cells play a pivotal role in autoimmunity, we aimed to investigate the function of IL-40 in rheumatoid arthritis (RA).

Methods: IL-40 expression was determined in the synovial tissue from RA and osteoarthritis (OA) patients. IL-40 was analysed in the serum and synovial fluid of patients with RA (n=50), systemic lupus erythematosus (SLE, n=69), OA (n=44), and in healthy controls (HC, n=50). All patients met the ACR-EULAR criteria of the particular disease (1,2,3). We also assessed the changes of IL-40 levels in RA patients following the B-cell depletion therapy by rituximab (n=33) or after the TNF inhibition by adalimumab (n=25). We examined the relationship between IL-40, disease activity, autoantibodies, cytokines and markers of NETosis. The effect of IL-40 on synovial fibroblasts was determined.

Results: We observed increased expression of IL-40 in the RA synovial tissue compared to OA, particularly in synovial lining cells and infiltrating immune cells. The levels of IL-40 were up-regulated in the synovial fluid of RA compared to OA patients ($p< 0.0001$). Similarly, IL-40 was increased in the serum of RA patients compared to HC, OA or SLE patients ($p< 0.0001$ for all) and decreased after 16 and 24 weeks ($p< 0.01$ and $p< 0.01$) following rituximab treatment. No significant effect of adalimumab on serum IL-40 was observed. IL-40 levels in RA patients correlated with rheumatoid factor-IgM and anti-*cyclic* citrullinated peptides (anti-CCP) in the serum ($p< 0.0001$ and $p< 0.01$), as well as in the synovial fluid ($p< 0.0001$ and $p< 0.001$). Synovial fluid IL-40 was also associated with DAS28 ($p< 0.05$), synovial fluid leukocyte count ($p< 0.01$), neutrophil attractants IL-8 ($p< 0.01$), MIP-1α ($p< 0.01$), and markers of NETosis such as proteinase 3 ($p< 0.0001$) and neutrophil elastase ($p< 0.0001$). RA synovial fibroblasts exposed to recombinant IL-40 increased the secretion of IL-8 ($p< 0.01$), MCP-1 ($p< 0.05$) and MMP-13 ($p< 0.01$) compared to the unstimulated cells.

Conclusion: We show the up-regulation of IL-40 in RA and its decrease following B-cell depletion therapy. The association of IL-40 with autoantibodies, chemokines and markers of NETosis may imply its potential involvement in RA development. Moreover, IL-40 up-regulates the secretion of chemokines and MMP-13 in synovial fibroblasts, indicating its role in the regulation of inflammation and tissue destruction in RA.

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Abstract Number: 0033

Impaired Adipose Tissue Function in Rheumatoid Arthritis: Association with Autoimmunity, Disease Activity and Therapeutic Response

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SESSION INFORMATION
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Background/Purpose: 1) to evaluate the relationship among adipose tissue dysfunction, autoimmunity and disease activity in rheumatoid arthritis (RA) patients; 2) to analyze the direct effect of antibodies to citrullinated protein antigens (ACPAs) on the adipose tissue (AT) function and 3) to evaluate the role of insulin resistance (IR) and adipocytokines in the therapeutic response with biological treatments.

Methods: 1) Design: cross-sectional study (150 RA patients and 50 healthy donors (HDs)) and longitudinal study (122 RA patients treated with anti-TNF-a (45), anti-IL6R (22) and anti-CD20 (55) therapies after 6 months of treatment). Patients were classified in responders or non-responders based on EULAR criteria. Disease activity (DAS-28), autoimmunity, acute phase reactants (CRP and ESR) and cardiovascular disease (CVD) risk factors were evaluated. The serum levels of adipocytokines (TNF-a, IL-1b, IL-6, leptin, adiponectin, resistin, visfatin, omentin and vaspin) were measured by ELISA. Next, in vitro experiments with human AT and adipocyte and macrophage cell lines treated with G immunoglobulins isolated from HDs and RA patients were performed. The expression of genes related to inflammation, lipid accumulation and adipogenesis was analyzed in all experiments; 3) a collagen induced arthritis (CIA) mice was developed. Plasma and AT were analyzed.

Results: The levels of adipocytokines were significantly altered in RA serum and associated with disease activity. Likewise, homeostatic model assessment of insulin resistance (HOMA-IR) correlated to DAS28. On the other hand, ACPAs levels correlated with adipocytokine profile suggesting a role of ACPAs in the dysregulation of AT. AT of lean CIA mice showed higher gene expression of specific markers of B and plasmatic cells and M1 macrophages as disease activity increased. Furthermore, the *in vitro* treatment of human AT with ACPAs could promote the adipose tissue dysfunction promoting an inflammatory state through the M1 polarization of macrophages and the blockage of adipocyte differentiation. Next, RA patients with higher levels of HOMA-IR presented a worse response to biological treatments. Besides, levels of vaspin and visfatin were significantly increased before the treatment in the non-responders group. Although, all treatments significantly reduced disease activity after 6 months of treatment, the effect of each one was different being the anti-CD20 treatment which modified a higher number of adipocytokines.

Conclusion: 1) IR and the altered adipocytokine profile in RA patients is associated with disease activity, the presence of autoimmunity and a worse response to therapy; 2) adipose tissue in the context of RA is altered in parallel with the disease progression, characterized by an inflammatory state due to the infiltration of macrophages and B and plasmatic cells; 3) ACPAs could be at least partially the responsible of adipose tissue dysfunction inducing inflammation and IR in macrophages and promoting a defective adipocyte differentiation.

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Disclosure: I. **Arias de la Rosa**, None; **a. Escudero**, None; **C. Román-Rodriguez**, None; **R. Guzmán-Ruiz**, None; **M. Malagón**, None; **C. Pérez-Sánchez**, None; **C. Plasencia-Rodríguez**, None; **A. Martinez-Feito**, None; **M. Ábalos-Aguilera**, None; **A. Patiño-Trives**, None; **J. Calvo**, None; **R. Ortega**, None; **E. Collantes-Estevez**, None; **C. Lopez-Pedrera**, None; **N. Barbarroja**, None.

Abstract Number: 0034

Immune Complexes Contain Novel Acetylated Antigens in the Synovial Fluid of RA Patients

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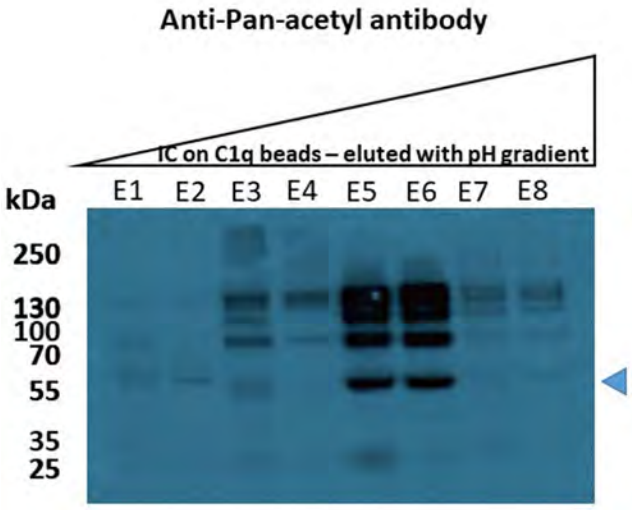
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease characterized by genetic predisposition and associated immunological features including the production of autoantibodies against various epitopes. Several pathways have been implicated in the induction of autoantibodies against novel epitopes through post-translational modifications such as citrullination, carbamylation and acetylation. However, the spectrum of these antibodies and their contributions in the pathogenesis e.g. by the formation of immune complexes in the synovial fluid has not been fully uncovered.

Methods: Synovial fluids (SF) were collected from 17 RA patients and 40 individuals from a disease control (CG) including reactive arthritis and psoriasis arthritis. Paired serum and SF samples were used from 16 RA and 19 CG compared to serum from 70 healthy donors (HD). ELISA kits for anti CCP-IgG, anti-mutated citrullinated vimentin



(MCV)-IgG, anti-acetylated Lysine Antibody (anti-HC55)-IgG and anti-carbamylated vimentin (carbVim)-IgG were used to test reactivity against modified proteins. Immune complexes (IC) were purified from sera and SF by applying a technique using purified human C1q, which was immobilised on magnetic tosylactivated microparticles (Dynabeads M-280) according to the manufacturer's recommendations for activation of amine groups. C1q beads were washed and incubated with 20 µL serum or SF in an Eppendorf microliter tube for 1.5 hours on shaker (600 rpm) at 37°C. Antibodies from the C1q-bound IC were recovered in a two-step procedure- first with 0.1 M glycine–HCl, pH 2.5, followed by 25% methanol, pH 11.5. Fractions were neutralized immediately. Extracted antigens from the IC were investigated with Western blot for specific modifications or individual antigens with the corresponding antibodies. Citrullinated and acetylated vimentin was identified as part of IC via mass spectroscopy. Purified anti modified protein antibodies (AMPAs) from serum or SF (isolated from IC or as soluble antibodies) were investigated on a custom-made LineBlot array containing 24 different antigens either citrullinated, carbamylated, acetylated or unmodified/native counterparts.

Results: Titers of anti-CCP and anti-acetylated (anti-HC55) reactivity were higher in SF of RA patients compared to CG. In contrast, no significant differences were detected in the titers of anti-carbVim and anti-MCV in SF of both groups. AMPAs were detected in SF in immune complexes as well as free antibodies. Surprisingly, in addition to citrullinated vimentin, the acetelylated form was also detected in the eluted fractions. Like carbamylated proteins, haptoglobin and fibrinogen fragments were identified in small concentrations. The spectrum of identified acetylated proteins included human proteins such as histones as well as fragments of bacterial filament proteins.

Conclusion: AMPAs recognize different modified antigens and form immune complexes in the SF of RA patients. The higher titers of anti-acetylated protein antibodies and immune complexes in the synovium point to their contribution in the pathogenesis of RA.

The identification of acetylated antigens in the synovium of RA patients is especially intriguing, as infections (bacteria) are known to not only acetylate their own proteins, but also modify host proteins. Acetylated vimentin (MW 57 kDa) was detected in eluted fractions (arrow). IC: immune complexes.

Disclosure: K. Ghannam, None; **H. Bang**, Orgentec Diagnostika GmbH, 3; **T. Häupl**, None; **E. Feist**, R-Pharm, 2, 6, Abbvie, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, AB2Bio, 6, BMS, 6, Celgene, 6, Janssen, 6, Eli Lilly, 2, 5, 6, Medac, 6, MSD, 6, Roche/Chugai, 2, 5, 6, Sanofi, 6, Sobi, 6, UCB, 6; **G. Burmester**, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6.

Abstract Number: 0035

Bromodomain Protein-regulated Stress Response in Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Hypoxia and subsequent oxidative stress are early events in the RA joint and contribute to the activation of synovial fibroblasts (SF). Small molecule inhibitors targeting the members of the bromodomain and extra-terminal (BET) protein family (BRD2, BRD3, BRD4) have anti-inflammatory properties in RA. Here we analyzed the potential of BET inhibitors in regulating stress response pathways in RA SF.

Methods: SF were obtained from shoulder and hand joints of RA patients undergoing joint replacement surgery. We mimicked hypoxic conditions by treatment of SF with dimethyloxalylglycine (DMOG; 0.5 mM, 24 h). Stabilization of HIF1α and GLUT1 protein expression were assessed by Western blotting. Oxidative stress was induced by treatment of SF with 4-hydroxynonenal (4-HNE; 5 μM, 48h), a lipid peroxidation product present in synovial fluids, and TNF (10 ng/ml, 48h). Experiments were performed in absence and presence of the pan-BET inhibitor I-BET151 (1 μM). The expression of hypoxic response (*VEGFA, PDK1, GLUT1, HK2*) and oxidative stress response genes (*CAT, GPX1, SOD2, HMOX1*) was measured by Real-time PCR (n=7-10). Autophagy was assessed by Western blotting using LC3B-II as an autophagy marker (n=7).

Results: Treatment of SF with DMOG stabilized HIF1α protein. I-BET treatment suppressed the DMOG-induced expression of the hypoxic response genes *VEGFA, PDK1, GLUT1* and *HK2* (Figure 1A). Hypoxic conditions induced the GLUT1 protein expression by 101.8-fold (± 108.2-fold), which was suppressed by 62.2% (± 32.1%) in presence of I-BET ($p< 0.05$). TNF treatment induced the expression of all measured stress response genes. Oxidative stress further induced the TNF-induced expression of *VEGFA, PDK1, GLUT1, HK2* and *CAT* (Figure 1B). In contrast to results obtained under hypoxic conditions, I-BET treatment further increased the expression of hypoxia response genes under oxidative stress conditions. We have detected similarities and differences regarding the BET-meditated regulation of oxidative stress response genes under different stress conditions. I-BET increased basal *HMOX1* and *CAT* expression in all conditions, and suppressed *GPX1* expression under hypoxia and oxidative stress. In contrast, BET inhibition decreased the expression of *SOD2* only during oxidative stress but not under hypoxia. I-BET further increased the expression of *HMOX1* during oxidative stress, but suppressed the expression of *HMOX1* during hypoxia. I-BET induced the accumulation of LC3B-II protein by 2.7 (± 1.4)-fold, which was further increased to 4.5 (± 2.9)-fold in presence of DMOG ($p< 0.05$). Oxidative stress conditions did not further induce the I-BET-induced expression of LC3B-II.

Conclusion: BET protein inhibition affects stress-response target genes in a stimulus-dependent manner. Our data suggest that hypoxia and oxidative stress conditions regulate individual stress response genes via distinct enhancers. Furthermore, we have identified BET proteins as regulators of autophagy.

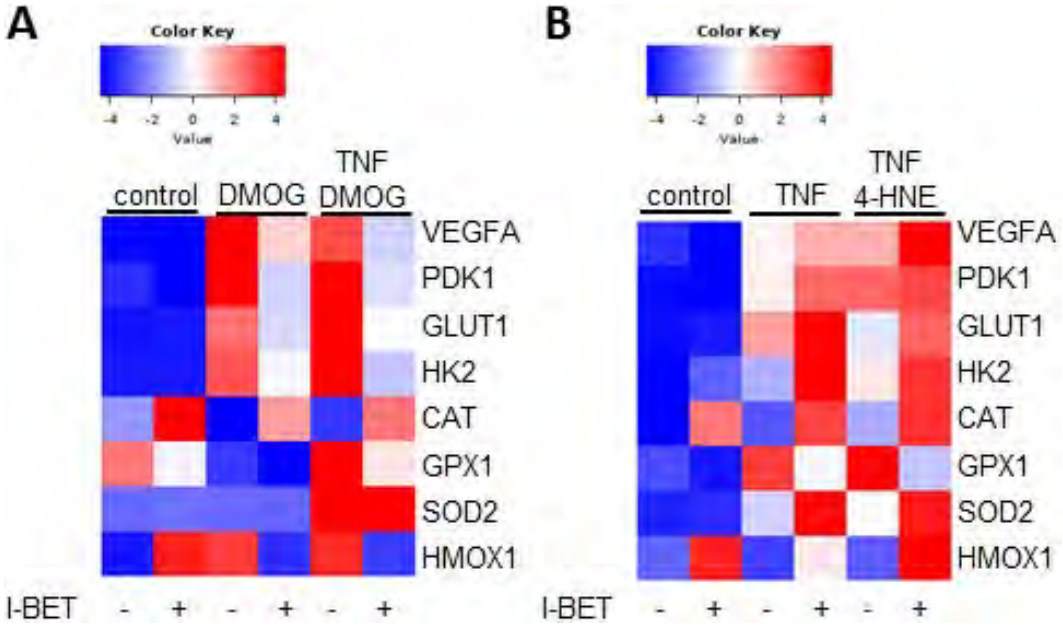

Figure 1. Expression of stress response genes in synovial fibroblasts after treatment with A. DMOG +/- TNF and B. TNF +/- 4-HNE in absence and presence of the bromodomain inhibitor I-BET.

Disclosure: T. Seifritz, None; **T. Züllig**, None; **L. Moser**, None; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2; **C. Ospelt**, Novartis Foundation for Biomedical Research, 5; **K. Klein**, Novartis Foundation, 5.

Abstract Number: 0036

The NAD$^+$ Metabolism Is Altered in Rheumatoid Arthritis and Its Modulation with NAD$^+$ Boosters Exhibits Key Anti-Inflammatory and Anti-Oxidant Effects

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: NAD$^+$ is a key cofactor and second messenger for multiple cellular processes that exhibits antioxidant, anti-apoptotic, and anti-inflammatory properties. Numerous publications and clinical trials have shown the beneficial effects of NAD$^+$ boosters in different diseases. However, to date no studies have evaluated the NAD$^+$ metabolism and the therapeutic effects of NAD$^+$ boosters in RA patients.

Aims: 1- To study the NAD^+ metabolism in RA patients and its association with key clinical features; 2-To evaluate the effect of anti-TNF therapy in the NAD^+ metabolism; 3- To analyze the beneficial effects of NAD^+ boosters in leukocytes from active RA patients.

Methods: Plasma and PBMCs were purified from 100 RA patients and 50 healthy donors (HDs). NAD^+ levels were determined by using the NAD/NADH-Glo Assay. Gene expression analysis of markers related to the synthesis (NAMPT, NMNAT2, NRK1), transport (Cx43) and consumption of NAD^+ (PARP-1, Sirtuin-1, CD157, CD38 y CD73) were performed in PBMCs by RT-PCR.

Moreover, in a second cohort of 50 RA patients treated with anti-TNF therapy, changes in the levels of NAD^+ were analyzed before and after 6 months of treatment.

In parallel, PBMCs from a third cohort of 10 active RA patients were treated *ex vivo* with 1 mM of NAD^+ boosters including nicotinamide (NAM), nicotinamide riboside (NR), and nicotinamide mononucleotide (NMN). After 24 hours, intracellular reactive oxygen species (ROS) levels and the % of apoptotic PBMCs were assessed by flow cytometry. Finally, a panel of key pro-inflammatory genes was evaluated by RT-PCR.

Results: NAD^+ levels were significantly reduced in plasma of RA patients compared with HDs, and directly related to disease activity. Accordingly, the expression levels of genes involved in the consumption of NAD^+ such as SIRT-1, CD38 and PARP-1 were found up-regulated in PBMCs from RA patients. The levels of NAMPT and Cx43 were found increased suggesting a compensatory response of the organism against the depletion of NAD^+ levels. The altered metabolism of NAD^+ was associated with the increased expression of several cytokines such as TNF, IL6, IL1, IL8 and CCL2 highlighting the role of inflammation in the altered NAD^+ metabolism.

Anti-TNF therapy restored the altered NAD^+ levels towards those showed by HDs. Furthermore, the clinical response promoted by anti-TNF therapy correlated with changes in NAD^+ levels.

In vitro treatments of PBMCs isolated from active RA patients with NAD^+ boosters significantly increased the NAD^+ levels and promoted a deep reduction of intracellular ROS levels, the percentage of apoptotic cells and the expression levels of key inflammatory mediators, such as IL-6, IL-8, IL-1b, TNF-α, CCL2, IL-23, and STAT-3.

Conclusion: 1. NAD^+ metabolism is altered and associated with the disease activity and the pro-inflammatory status of RA patients. 2. Anti-TNF therapy restored NAD^+ levels, which was directly linked to the clinical effectiveness. 3. NAD^+ boosters reduced the oxidative, apoptotic, and inflammatory profile of RA leukocytes through the parallel increase of intracellular NAD^+ levels. Thus, NAD^+ boosters might be considered novel therapeutic tools for RA patients.

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Disclosure: C. **Pérez-Sánchez**, None; **L. Sanchez-Mendoza**, None; **N. Barbarroja**, None; **M. Abalos-Aguilera**, None; **M. Luque-Tevar**, None; **A. Patiño-Trives**, None; **I. Arias de la Rosa**, None; **C. Román-Rodriguez**, None; **J. Moreno**, None; **M. Buron**, None; **J. Gonzalez-Reyes**, None; **M. Rojas-Gimenez**, None; **E. Collantes-Estevez**, None; **a. Escudero**, None; **J. Villalba**, None; **C. lopez-pedrera**, None.

Abstract Number: 0037

Identification and Validation of Four Circulating Autoantibodies Associated with the ACPA Status in Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The presence of anti-citrullinated protein antibodies (ACPAs) is a highly specific hallmark of rheumatoid arthritis (RA), that is present also in early disease. However, 20% of RA subjects test negative for ACPA and thus their early diagnosis and treatment may be delayed. Furthermore, despite the high specificity of the cyclic citrullinated tests, their low sensitivity indicates that a negative result does not rule out the disease. Therefore, an increased knowledge about the presence of other circulating biomarkers related with early RA is needed to improve its diagnosis and to better understand the pathogenic mechanisms underlying the different RA subsets. In this study, we aimed to search for plasma autoantibodies associated with ACPA status that could be useful to assist the early diagnosis of RA.

Methods: We firstly profiled the plasma IgG and IgA repertoire of 80 ACPA positive and 80 ACPA negative subjects entering the Epidemiological Investigation of Rheumatoid Arthritis (EIRA) early RA cohort. To this end, we employed an antigen suspension bead array built with 260 protein fragments within Human Protein Atlas and selected from an initial untargeted screening on planar arrays. A validation phase using a suspension bead array including 27 antigens was carried out on another set of samples from EIRA which included 386 ACPA positive, 358 ACPA negative and 372 age and sex-matched control subjects. A sample-specific threshold was selected to determine the reactivity of all the samples. The Wilcoxon rank sum test and Fisher's test were applied for the comparison of autoantibody levels and reactivity frequencies between the sample groups.

Results: Reactivities towards four different antigens were significantly associated to ACPA status (Figure 1 and Figure 2). IgG autoantibody levels towards Testis-specific Y-encoded-like protein 4 (TSPYL4) were higher in ACPA negative subjects compared to controls (Figure 1A). The prevalence of IgG autoantibodies towards TSPYL4 was also higher in ACPA negative compared to ACPA positive (8% *vs*. 3%) (Figure 1B). Higher IgG autoantibody levels towards dual specificity mitogen-activated protein kinase kinase 6 (MAP2K6), were also observed in ACPA negative subjects

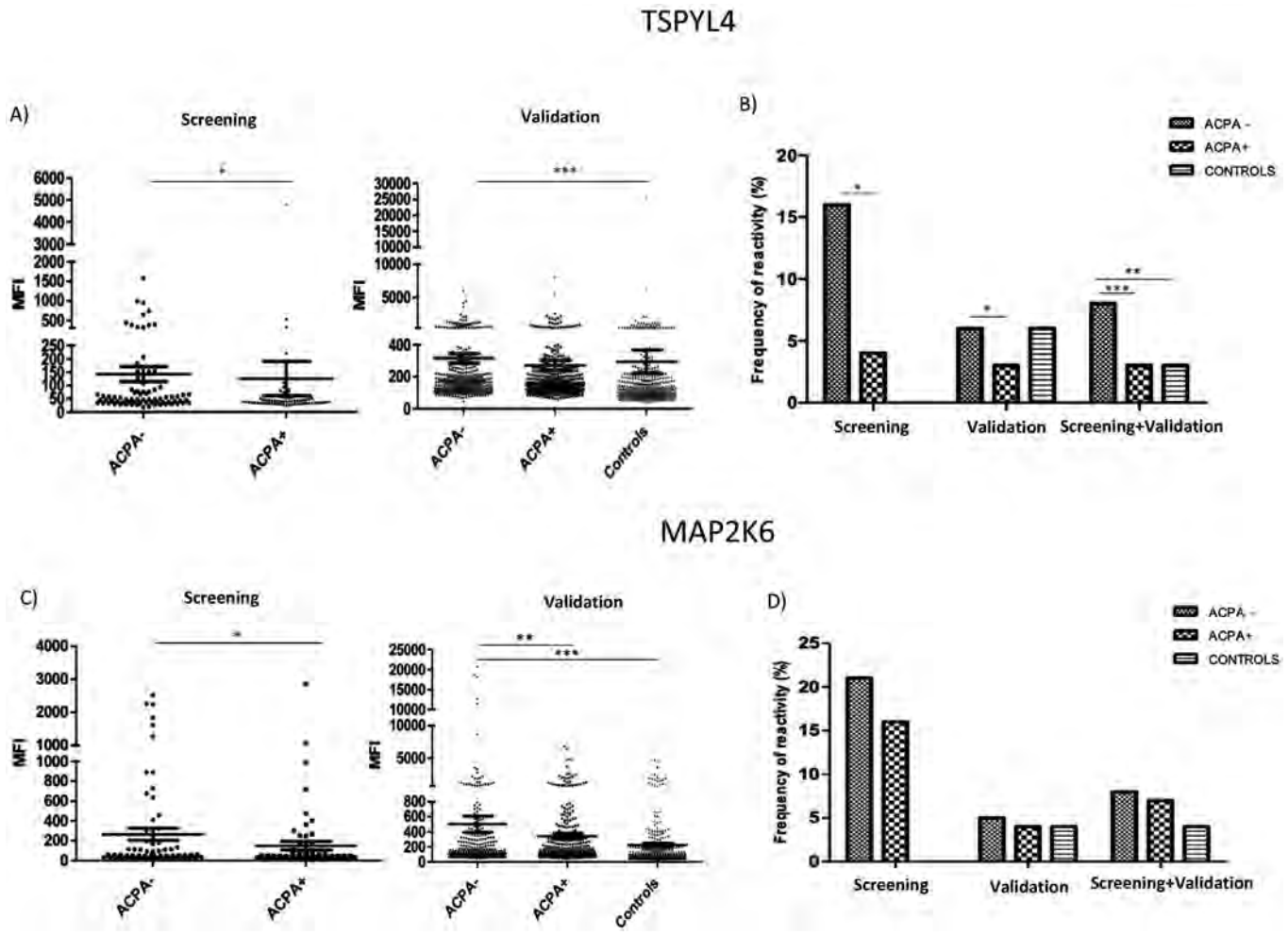

Figure 1. IgG autoantibodies associated with ACPA negative status. MFI: median fluorescence intensity.*P<0.05;**P<0.01;***P<0.001.

compared to ACPA positive and controls, but no differences were observed on their prevalence (Figure 1C,1D). In contrast, higher IgG autoantibody levels towards muscle related coiled-coil protein (MURC) and Anosmin-1 (ANOS-1) were observed in ACPA positive individuals compared to ACPA negative and controls (Figure 2A, 2C). The prevalence of IgG autoantibodies towards ANOS-1 was also higher in ACPA positive subjects compared with ACPA negative and controls (22%, 9% and 6% respectively) (Figure 2D). Interestingly, three out of the four antigens discovered are highly expressed in lungs and heart, two of the extraarticular sites affected in RA. No significant differences were validated at IgA reactivity levels for any of the antigens analyzed.

Conclusion: Although further validation in other early RA sample cohorts is needed, our data suggest the measurement of these four autoantibodies might be useful to assist the early diagnosis of RA and give insight into its pathogenesis.

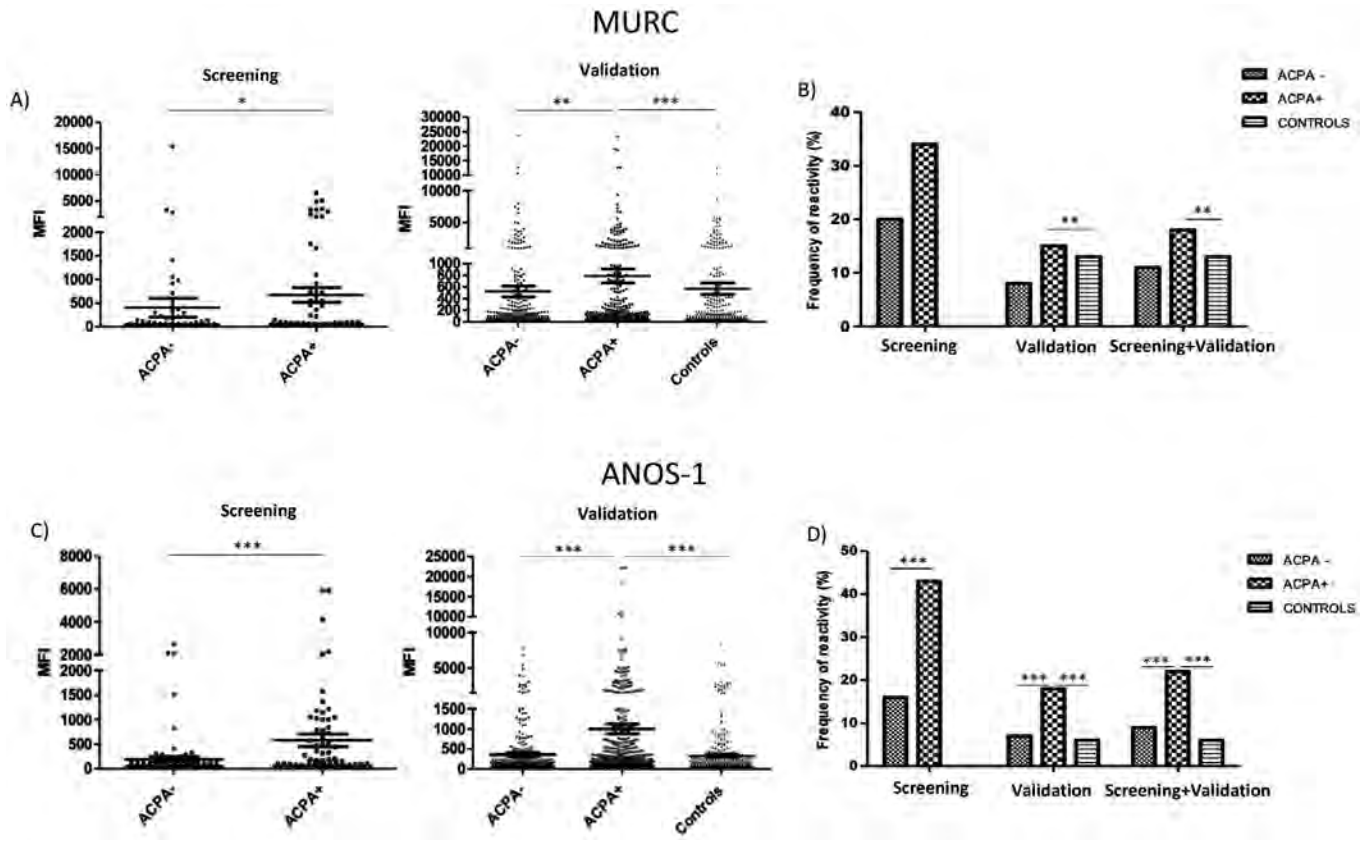

Figure 2. IgG autoantibodies associated with ACPA positive status. MFI: median fluorescence intensity.*P<0.05;**P<0.01;***P<0.001.

Disclosure: L. Lourido, None; **C. Ruiz-Romero**, None; **L. Collado**, None; **M. Hansson**, None; **L. Klareskog**, None; **R. Sjöberg**, None; **E. Pin**, None; **P. Nilsson**, None; **F. Blanco-García**, None.

Abstract Number: 0038

Arthritis Progression in at Risk Individuals Is Associated with ACPAs Not AMPAs

Alexandra Circiumaru[1], Yogan Kisten[2], Monika Hansson[2], Heidi Wähämaa[3], Meng Sun[3], Vijay Joshua[3], Hamed Rezaei[4], Erik Af Klint[4], Aleksandra Antovic[1], Anca Catrina[3] and Aase Haj Hensvold[5], [1]Division for Rheumatology, Karolinska Institutet; Center for Rheumatology, Academic Specialist Center, Stockholm Region, Stockholm, Sweden, [2]Division for Rheumatology, Karolinska Institutet, Stockholm, Sweden, [3]Karolinska Institutet and Karolinska university Hospital, Stockholm, Sweden, [4]Division for Rheumatology, Karolinska Institutet; Department of Rheumatology, Karolinska University Hospital, Stockholm, Sweden, [5]Karolinska Institutet, Division for Rheumatology; & Center for Rheumatology, Academic Specialist Center, Stockholm Region, Stockholm, Sweden

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Individuals with anti citrullinated protein antibodies (ACPA) and musculoskeletal complaints are at high risk for developing rheumatoid arthritis (RA) and often seek medical attention due to a symptom burden

Table 1. Main antibody differences between individuals developing arthritis and those who remain arthritis free – univariate analysis		
ACPA specificities		p value
	cit-enolase	0.0009
	cit-fibrinogen 36-52	0.001
	cit-filaggrin 302-324	<0.0001
	cit-vimentin 2-17	0.0006
	cit-vimentin 60-75	0.0006
	cit-tenascin 5	0.005
AMPA reactivities		
	acetylated-histone4 peptide	0.05
	carbamylated-filaggrin 307-324	0.0001
	acetylated-filaggrin 307-324	0.02

comparable to that of already diagnosed patients [1] We aimed to investigate the autoimmunity to other autoantibodies, beside ACPA, and study its importance in relation to clinical variables and inflammatory proteins, in risk stratification of predisposed individuals.

Methods: ACPA-positive individuals with musculoskeletal complaints referred from primary care (93%) and other specialist (7%), to a rheumatology clinic were recruited in the Risk-RA Karolinska research program and followed-up for up to 3 years or until arthritis diagnosis (April 2014 and February 2020). In order to investigate early disease mechanisms all individuals lacked both clinical arthritis and subclinical arthritis (measured by ultrasound according to EULAR-OMERACT definitions) in hands, feet and any other symptomatic joints. Blood samples collected at inclusion were analyzed for 14 ACPA specificities along with their arginine counterparts as well as 5 anti-modified protein antibodies (AMPA) against homocitrulline-, acetyl- and lysine- modified filaggrin 307-324 along with acetylated- histone 2B and histone 4 peptides, using custom made peptide array. We further screened for 92 inflammation-associated protein biomarkers (by multiplex immunoassay with Olink extension technology) and HLA-SE (DR low resolution kit). Statistical analysis used univariate and multivariate models with backwards selection and cox regression.

Results: 267 individuals (median age 48 CI: 36-58) were recruited, out of which 210 (78%) were females and with mean presence of 5 ACPA and 1 AMPA reactivities. 79 (30%) developed arthritis within 11 (4-21) months of follow-up compared to 21 (14-28) months median follow-up in those remaining arthritis free. In univariate models, specific ACPAs and AMPAs were associated with progression towards arthritis (Table 1.) Rheumatoid factor positivity (p 0.0003), presence of HLA-SE (p 0.005) and levels of certain inflammatory proteins (CCL20, CXCL6, CXCL9, IL6, IL15, IL17, DNER and TWEAK) associated with arthritis development. In multivariate (backwards selection) cox regression analysis the presence of anti-cit-filaggrin 307-324 (HR 2.1, 95% CI 1.2-3.7, p 0.005), IL6 levels (HR 1.4, 95% CI 1.2-1.7, p< 0.001) and tenosynovitis (HR 2.9, 95% CI 1.7-5.0, p < 0.001) remained significant predictors for arthritis onset. All other types of AMPA for filaggrin lost significance.

Conclusion: Risk-RA phase is characterized by several types of ACPAs and AMPAs, however anti-cit-filaggrin and ACPA reactivities show the strongest risk for progression to arthritis along with inflammatory proteins and ultrasound-detected tenosynovitis. The biological mechanisms need to be further explored in detail.

References

[1] Studenic P., et al. Symptoms characteristics of seropositive individuals at-risk for developing rheumatoid arthritis are versatile and comparable to those in people with early rheumatoid arthritis, accepted abstract EULAR 2021

Disclosure: A. Circiumaru, None; **Y. Kisten**, None; **M. Hansson**, None; **H. Wähämaa**, None; **M. Sun**, None; **V. Joshua**, None; **H. Rezaei**, None; **E. Af Klint**, None; **A. Antovic**, None; **A. Catrina**, None; **A. Haj Hensvold**, None.

Abstract Number: 0039

Elevated IgA Subclass Levels in Rheumatoid Arthritis Patients: Indications of a Mucosal Origin?

Veerle Derksen, Cornelia F. Allaart, Annette H.M van der Helm-van Mil, Tom WJ Huizinga, René Toes and Diane van der Woude, Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Mucosal surfaces may be involved in the pathophysiology of rheumatoid arthritis (RA) (1). IgA is the most abundant class of immunoglobulin at mucosal sites and has an important function in intestinal homeostasis. Therefore, it is worthwhile to study this isotype in more detail in the context of RA. Humans have two IgA subclasses, IgA1 and IgA2, which are not evenly distributed. IgA1 is dominant in serum, whereas IgA1 and IgA2 are more balanced at mucosal surfaces (2). Besides these differences in location, IgA2 has also been ascribed pro-inflammatory properties (3). As IgA subclasses might provide insights into mucosal involvement and potential pro-inflammatory mechanisms in RA, we measured total and autoantibody specific IgA subclasses in sera of rheumatoid arthritis patients.

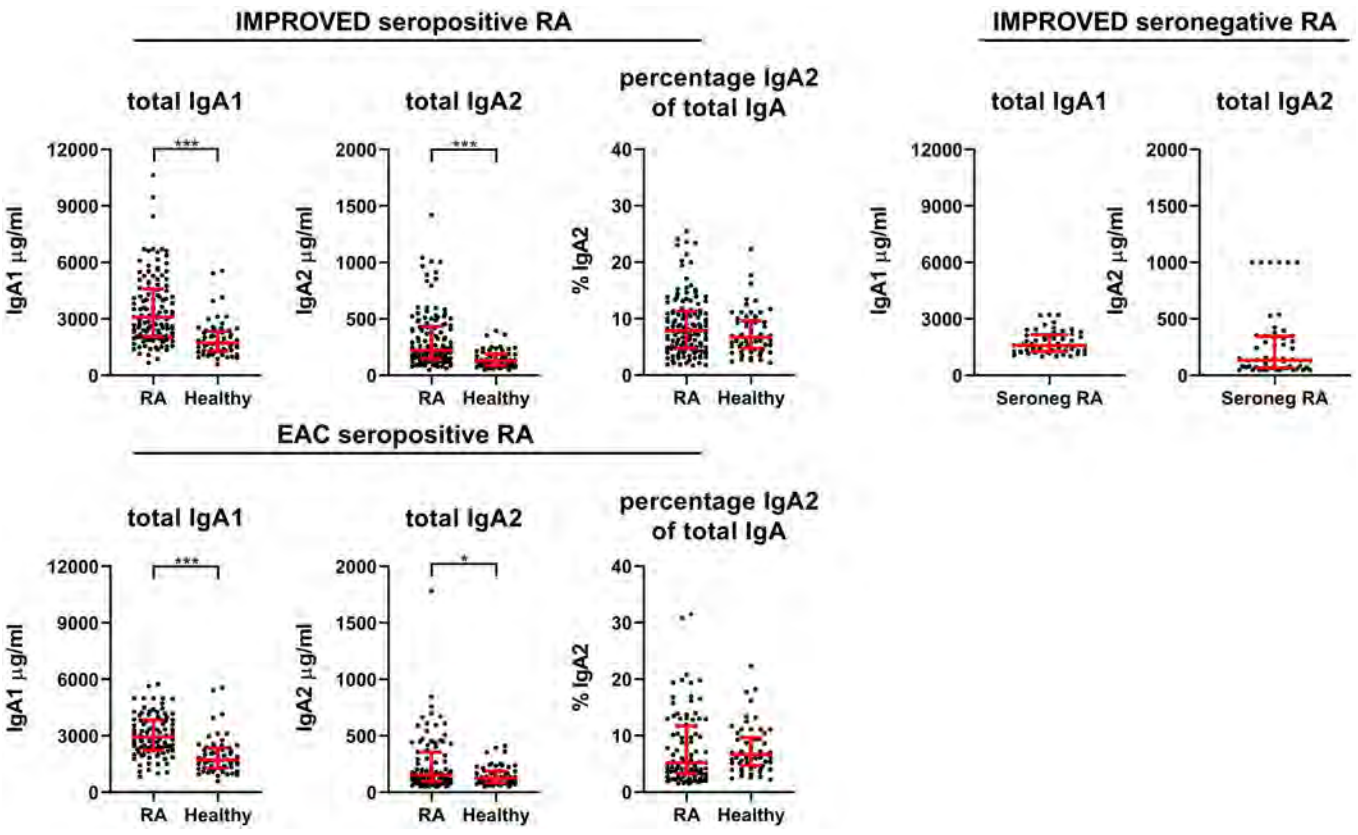

Figure 1. Total IgA1 and IgA2 levels in seropositive and seronegative RA patients.

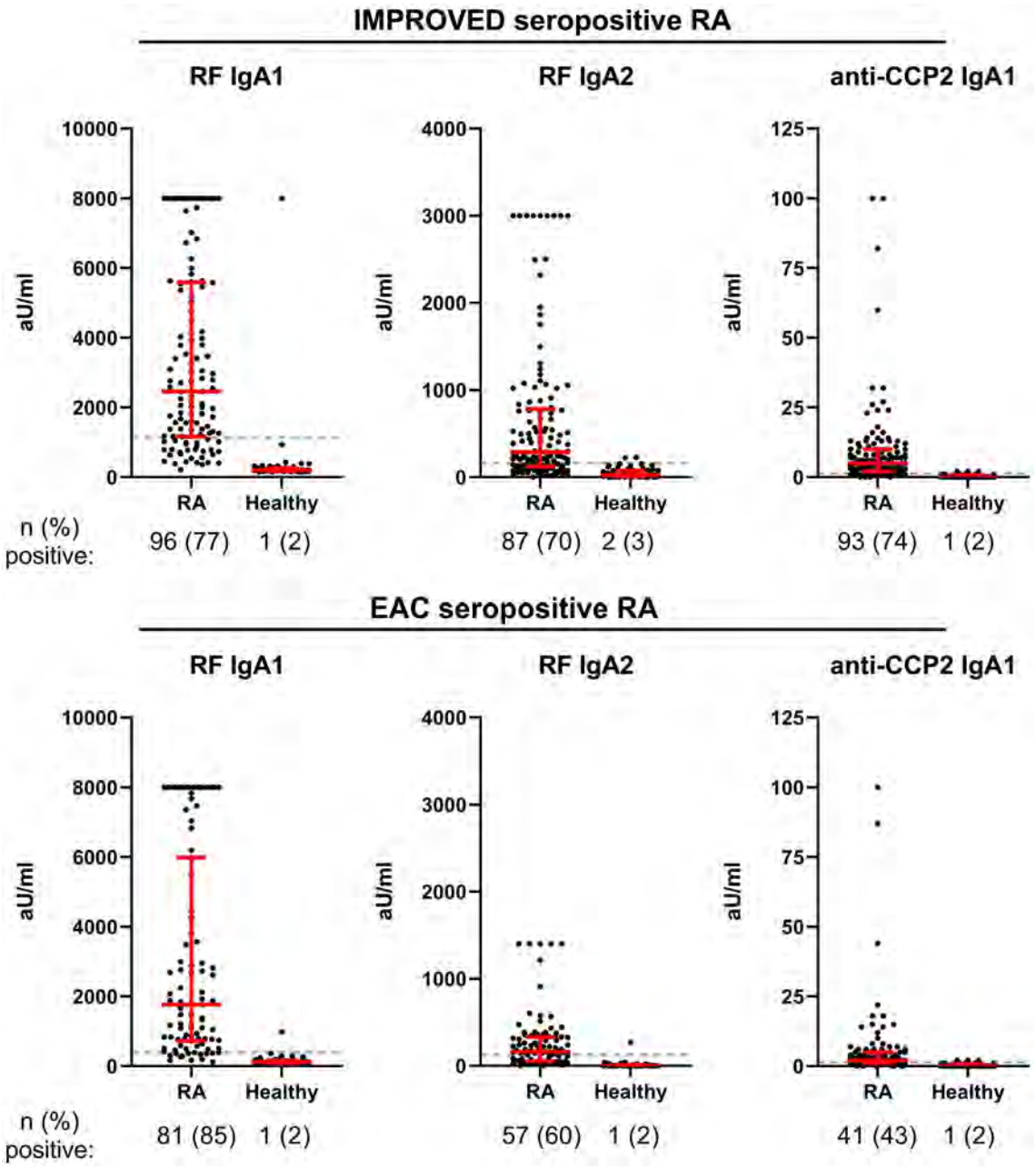

Figure 2. RF IgA1 & IgA2 levels and anti-CCP2 IgA1 levels in RA patients.

Methods: RA patients from two cohorts, the IMPROVED and the EAC, were selected based on previous autoantibody measurements. Samples were collected at baseline in the IMPROVED study and at the 1-year visit in the EAC. All patients fulfilled the 1987 (EAC) or 2010 (IMPROVED) ACR criteria for RA. Rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA) and total IgA subclasses were measured in these sera using in-house ELISA's, and compared to healthy donors. The association of IgA subclass levels with CRP, disease activity score (DAS) and smoking was investigated using Spearman's rank correlation and Mann–Whitney U tests.

Results: Both total IgA1 and IgA2 were increased in seropositive RA, but not in seronegative RA patients in the IMPROVED (Figure 1). In seropositive RA, both IgA subclasses were raised to the same extent. RF and ACPA IgA1 and IgA2 were also detected in seropositive RA patients (Figure 2), but measurements of ACPA IgA2 levels proved challenging due to interference of RF IgA and are therefore not depicted. Although IgA2 has been postulated to be

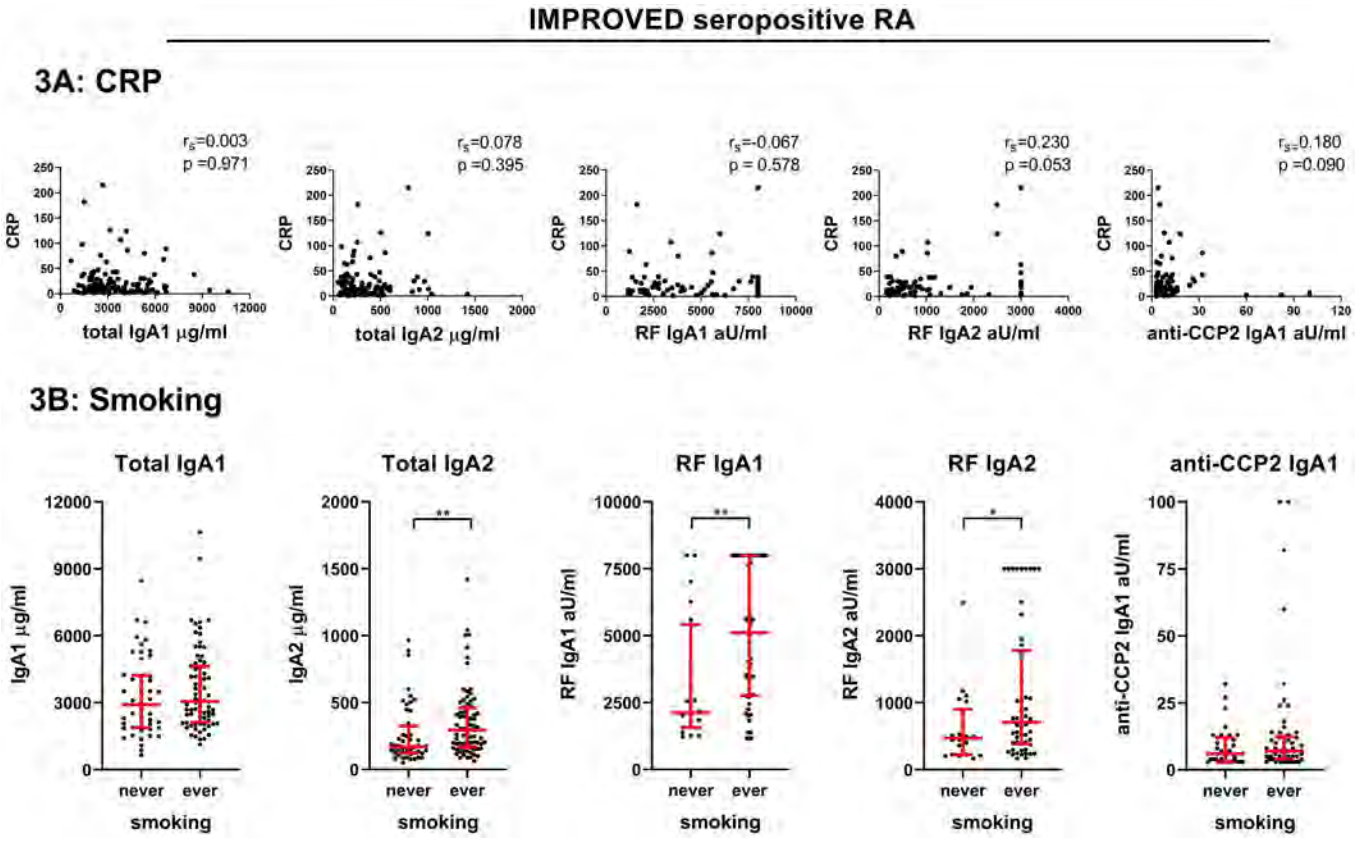

Figure 3. A) Association of total and autoantibody IgA subclasses with CRP in IMRPOVED B) Association of total and autoantibody IgA subclasses with smoking in IMPROVED.

more proinflammatory, no relevant associations were found between total, RF and ACPA IgA subclass levels and CRP (Figure 3A, IMPROVED only) or DAS. In smoking seropositive RA patients, a selective minor increase in total IgA2, RF IgA1 and RF IgA2 was seen in both cohorts (Figure 3B, IMPROVED only), although all were non-significant in the EAC.

Conclusion: Seropositive RA patients have equally raised IgA1 and IgA2 levels and can also harbor RF and ACPA IgA subclasses. No indications of a mucosal source, such as a predominance of total IgA2, were found, although smokers might have slightly increased total IgA2. However, these results do consolidate the concept that seropositive versus seronegative RA have different pathophysiological traits, with seropositive patients perhaps displaying more aspecific B cell hyperreactivity.

References

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(3) Steffen, Nat commun 2020

Disclosure: V. Derksen, None; **C. Allaart**, Dutch College of Health Insurances, 5, Schering-Plough BV, 5, Centocor Inc., 5, Eli Lilly, 5; **A. van der Helm-van Mil**, None; **T. Huizinga**, None; **R. Toes**, None; **D. van der Woude**, None.

Abstract Number: 0040

M1-M2 Polarization by CTLA4-Ig (Abatacept) on Cultured Circulating Monocytes from Rheumatoid Arthritis Patients and Healthy Subjects

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disorder affecting 1% of the population worldwide [1]. Monocytes/macrophages are known to play a crucial role in modulating the immune inflammatory response through their possible polarization into “pro-inflammatory” (M1) or “anti-inflammatory” (M2) phenotypes [2]. In RA, CTLA4-Ig fusion protein (abatacept) has been found to reduce the proinflammatory activity of macrophages, by interacting with the costimulatory molecule CD86 [3,4].

This study aimed to investigate the *in vitro* capability of CTLA4-Ig to induce the M2 phenotype in cultured monocyte-derived macrophages (MDMs) obtained from RA patients and in M1-polarized MDMs obtained from healthy subjects (HSs).

Methods: Five RA patients (mean age 54±13 years), who fulfilled the 2010 ACR/EULAR Classification Criteria for RA, and ten age-matched HSs were enrolled for the study after signed informed consent and local EC approval. Cultured MDMs were obtained from circulating blood mononuclear cells and stimulated with phorbol myristate acetate (PMA, 5ng/ml) for 24 hours (hrs). HS MDMs were then stimulated with lipopolysaccharide (LPS, 1mg/mL) for 4 hrs to induce a pro-inflammatory M1-MDM phenotype. Therefore, both RA-MDMs and M1-MDMs were treated with CTLA4-Ig (100μg/mL or 500μg/mL) for 3, 12, 24 and 48 hrs. Gene expression of CD80, CD86 and TLR4 (M1 markers), CD163, CD204 and CD206 (M2 markers) were evaluated by qRT-PCR. Moreover, protein synthesis of M2 markers was investigated by Western blotting. The statistical analysis was performed by non-parametric Wilcoxon t-test.

Results: In LPS induced M1-MDMs (HS), CTLA4-Ig (100μg/mL and 500μg/mL) significantly downregulated the gene expression of all M1 phenotype markers (CD80, CD86, TLR4: 3 hrs $p< 0.01$; 12 hrs $p< 0.05$ for all) and significantly upregulated all M2 markers after 12 hrs of treatment (CD163: $p< 0.01$ and $p< 0.05$; CD206: $p< 0.05$ and $p< 0.01$; CD204: $p< 0.05$ by CTLA4-Ig 100μg/mL). Accordingly, CTLA4-Ig (500μg/mL) increased the protein synthesis of M2 markers, significantly after 48 hrs of treatment ($p< 0.05$).

On the other hands, in RA-MDMs, CTLA4-Ig generally downregulated the gene expression of M1 markers at both concentrations and all timing, but in a significant manner only that of TLR4 and CD80 and only by the highest dose (500μg/mL, 12 hrs, $p< 0.05$). Of note, CTLA4-Ig (100μg/mL) upregulated significantly the gene expression of CD163 (M2 phenotype marker; $p< 0.05$). However, gene expression and protein synthesis of all the investigated M2 markers at both concentrations increased in a non-significant manner compared to untreated cells.

Conclusion: CTLA4-Ig seems to induce the *in vitro* polarization, from M1 to M2, of cultured MDMs obtained from RA patients and of M1-MDMs from HSs, therefore proving a new aspect for the anti-inflammatory activity exerted by abatacept in RA pts.

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Disclosure: S. tardito, None; **S. Soldano**, None; **E. Gotelli**, None; **P. Montagna**, None; **R. Campitiello**, None; **S. Paolino**, None; **C. Pizzorni**, None; **A. Sulli**, Saviopharma, 5, Laboratori Baldacci, 5; **V. Smith**, Boehringer Ingelheim, 2, 6, Janssens, 2, 6; **M. Cutolo**, Bristol Myers Squibb, 5, Boehringer Ingelheim, 5, Celltrion, 6, Janssen, 6.

Abstract Number: 0041

Vascularized 'Synovium-on-a-Chip' - A Novel and Adaptable Model for Dissecting Inflammatory Biology Underlying Rheumatoid Arthritis

Theresa Wampler Muskardin[1], Chao Ma[2], Benteng Ma[2], Kayla Van Buren[3], Timothy Niewold[4] and Weiqiang Chen[2], [1]Colton Center for Autoimmunity, NYU School of Medicine, New York, NY, [2]New York University, New York, NY, [3]Mnemo Therapeutics, New York, NY, [4]Colton Center for Autoimmunity NYU School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a common multisystem inflammatory condition, affecting approximately 1% of the world population. The mechanisms underlying RA are still incompletely defined and current therapies, such as TNF-alpha inhibition, are mainly applied to mitigate the abnormal inflammation with limited success. RA fibroblast-like synoviocytes (FLS) in the synovium release cytokines that drive inflammation and attract immune cells, particularly monocytes, to the synovium microenvironment. These monocytes can further polarize to inflammatory macrophages, exacerbate the tissue inflammation and contribute to joint destruction. Herein, we engineered an organotypic, perfusable 'Synovium-on-a-Chip' to recapitulate the *in vivo* pathophysiology of RA synovial microenvironments and to dissect the RA FLS and monocyte associated inflammatory mechanisms that contribute to RA.

Methods: The microfluidic Synovium-on-a-Chip was constructed using a polydimethylsiloxane (PDMS)-based soft lithography technique. The chip contains two areas (**Fig. 1A**). The inner ring was infused with endothelial cells to form a 3D vascularized sublining layer. The outer ring was inoculated with RA FLS which aligned to form a synovial lining layer in a fibrin hydrogel (**Fig. 1B-D**). Monocytes were isolated from peripheral blood mononuclear cells and then loaded into the 3D vasculature (**Fig. 1C**). We analyzed cellular architecture and motility, gene expression, and cytokine secretion. Flow cytometry was used to assess cells after culture.

Results: We found that RA FLS released several cytokines, such as IL-6, CCL5, and CCL8, which facilitate the monocyte recruitment and drive inflammation in the RA niche (**Fig. 1D**). We confirmed that TNF-α (a major pathogenic

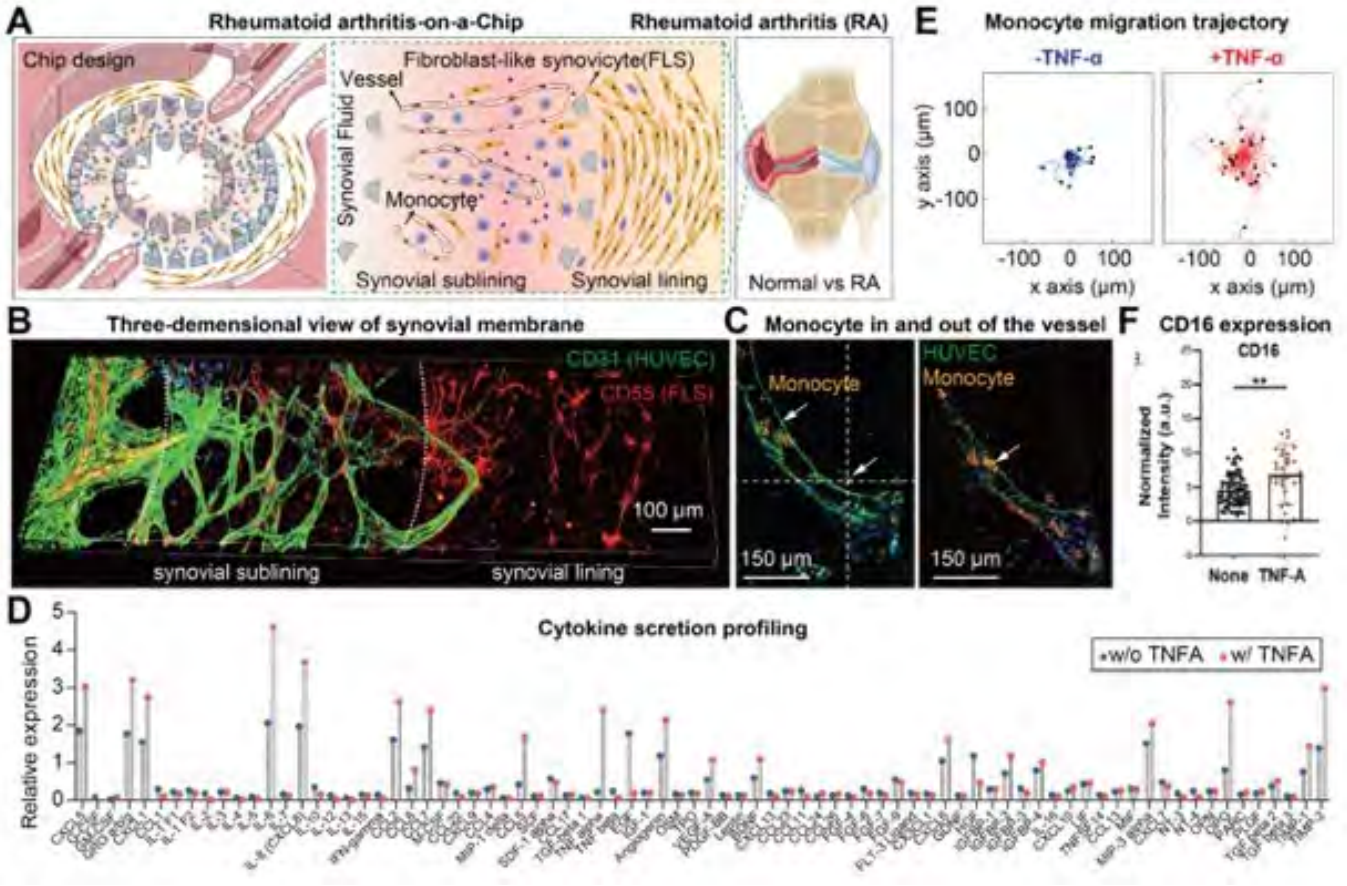

Figure 1. An organotypic Synovium-on-a-Chip. (A) Schematic of the RA niche and microfluidic design and (B) the resultant RA chip. (C) 3D view of monocytes loaded into the vascular network. (D) Cytokine profile of the RA niche identified inflammatory cytokines. (E) Migration trajectory of monocyte into RA niche treated with or without TNF-α. (F) TNF-α promoted non-classical monocyte emergence. **p < 0.01.

cytokine in RA) induced inflammatory cytokine production and enhanced monocyte migration in the inflammatory environment (**Fig. 1E**). We also observed RA FLS and TNF-α treatment enhanced intermediate/non-classical CD16+ monocyte emergence (**Fig. 1F**).

Conclusion: We engineered a biomimetic 'Synovium-on-a-Chip' system that reconstitutes *in vivo* RA pathophysiology and dissected interactions between RA FLS and peripheral blood monocytes and their associated inflammatory milieu involved in RA. To our knowledge, ours is the first vascularized device used in biomimetic synovial culture and testing.

Disclosure: T. Wampler Muskardin, None; **C. Ma**, None; **B. Ma**, None; **K. Van Buren**, None; **T. Niewold**, None; **W. Chen**, None.

Abstract Number: 0042

High-throughput Testing for Modified-protein Antibodies in Patients Diagnosed with "Seronegative" Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antibodies to citrullinated and other modified proteins play a critical role in the pathogenesis of rheumatoid arthritis (RA). The prevalence and degree of multi-site peptide reactivity of these antibodies in patients classified as "seronegative" is unclear.

Methods: An ultra-dense peptide array consisting of two million sequences was manufactured using photolithography. The peptide library was random but biased to include the sequences of filaggrin, fibrinogen, vimentin, collagen II, enolase, histones, and 14-3-3 eta with native, citrullinated, and carbamylated epitopes. A machine-learning algorithm identified 314 RA-specific peptides from a testing cohort of 140 RA patients, 480 healthy controls, and 136 disease controls based on signal-to-noise ratio. A validation cohort of 249 patients with RA (Table 1) was then analyzed on the basis of anti-cyclic citrullinated peptide (CCP) and rheumatoid factor (RF) positivity.

Results: The validation cohort included 106 patients (43%) who were negative for both CCP and RF ("seronegative"). Within this group, 25% had antibody binding to at least one site in the library of 314 peptides, compared with 98% of patients in the CCP and RF positive group ($p < 0.0001$). Only one control patient (1%) had any positive result. A heat-map of peptide reactivity is shown in Figure 1. Multi-site reactivity was more limited among the "seronegative" patients, with only 4% having antibody binding to at least 50 sites, compared to 80% in the CCP and RF positive group ($p < 0.0001$) (Figure 2). There was no significant difference in the ratio of antibodies to carbamylated vs. citrullinated proteins between "seronegative" and CCP positive patients. The presence of any HLA shared epitope allele was associated with positivity in this assay, with odds ratios of 3.56 (95%CI 1.99-6.37) for any binding and 4.22 (95%CI 2.22-6.37) for binding to greater than 50 sites.

Conclusion: This high-throughput assay demonstrated the presence of modified protein antibodies in a subset of "seronegative" patients, though multi-site reactivity was rare relative to CCP positive patients. This suggests that the mechanisms driving polyreactivity are features of seropositive RA and "seronegative" disease may have unique pathogenic features even when autoantibodies are present.

Table 1. Demographics of the validation cohort

	CCP+ RF+ (N=69)	CCP+ RF- (N=30)	CCP- RF+ (N=44)	"Seronegative" (N=106)	Controls (N=89)
Age at draw (mean±SD)	55 (11)	52 (14)	56 (13)	56 (15)	51 (15)
Age at diagnosis(mean±SD)	42 (18)	39 (16)	39 (10)	49 (18)	-
Female	46 (67%)	26 (87%)	37 (84%)	79 (75%)	59 (66%)
Ever smoker	32 (46%)	7 (23%)	12 (27%	Collaborate on this presentation with others.	0%)
HLA "Shared epitope" allele	47 (68%)	22 (73%)	12 (27%)	27 (26%)	23 (26%)
CCP titer, U/ml (mean±SD)	244 (216)	216 (330)	-	-	-
RF titer, U/ml (mean±SD)	333 (665)	-	150 (166)	-	-
DAS-28 CRP at draw (mean±SD)	2.8 (1.3)	2.8 (1.0)	2.7 (1.1)	2.9 (1.4)	-
Erosive disease	26 (38%)	14 (46%)	6 (14%)	10 (9%)	-
Any biologic use	45 (65%)	21 (70%)	12 (27%)	41 (39%)	-

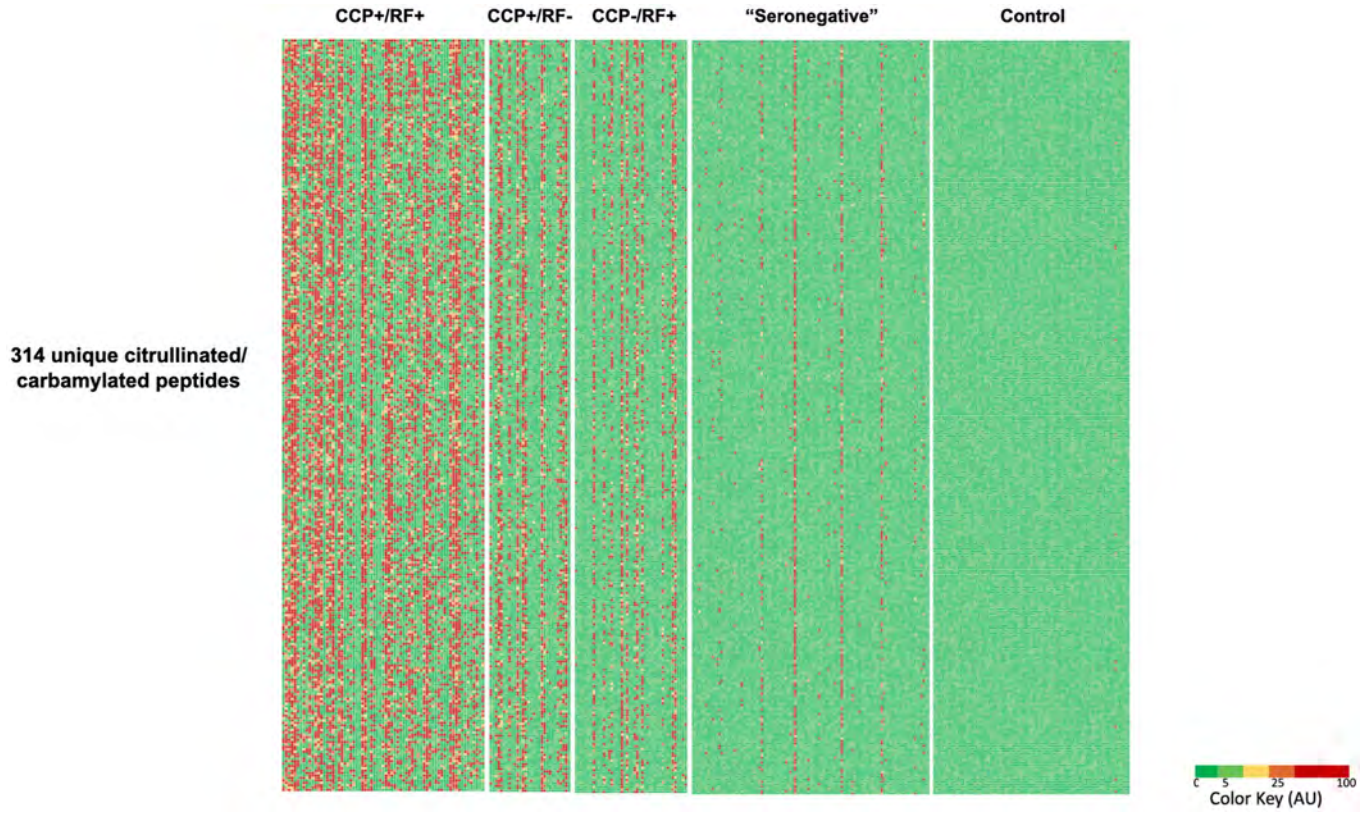

Figure 1. Heat-map of peptide reactivity. Results determined through immunofluorescence with tyramide signal amplification. Columns represent individual patients with rows showing antibody binding to each peptide.

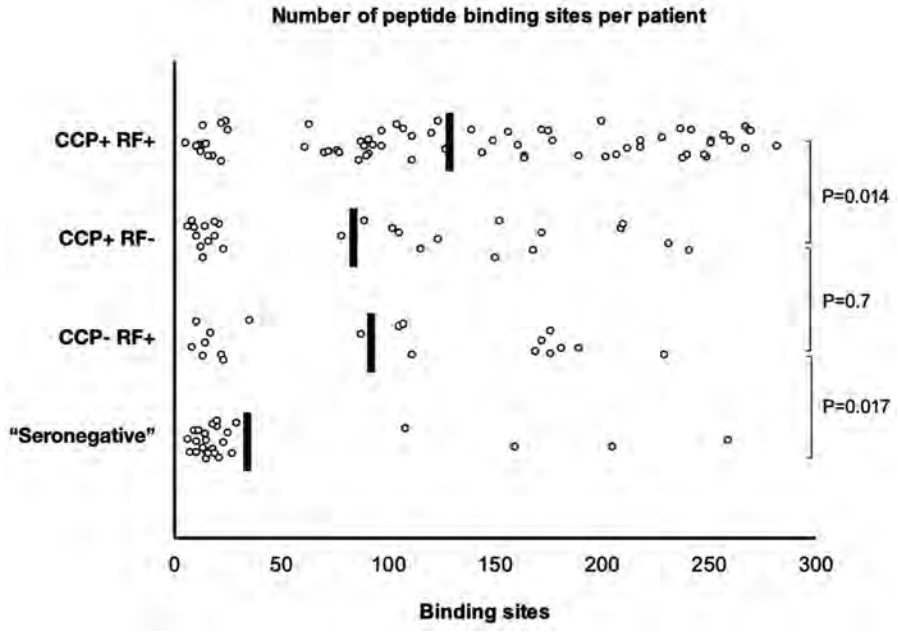

Figure 2. Number of peptide binding sites for every patient with at least one positive result. Each circle represents an individual patient.

Disclosure: M. Richter, None; **H. Krishnamurthy**, None; **S. Posso**, Janssen R&D, 5; **J. Carlin**, None; **J. Buckner**, Janssen R&D, 5.

Abstract Number: 0043

Takinib Inhibits IL-1β-Induced Activation of Signal Transducer and Activator of Transcription 3 (STAT3) in Human Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Interleukin-1 (IL-1) is a crucial mediator of inflammatory cartilage and bone destruction in rheumatoid arthritis (RA). IL-1β signaling relies on the activation of TGF-beta activated kinase 1 (TAK1), a serine/threonine kinase that centrally regulates the mitogen activated protein kinase (MAPK) and nuclear factor kappa B (NF-κB) pathways, which makes it an attractive therapeutic target. Takinib is a small molecule inhibitor proposed to inhibit TNF-α-induced inflammation by targeting TAK1, however, its efficacy against IL-1β-driven inflammation and the underlying mechanism of its action remains to be tested. In the present study, we evaluated the effect of takinib on IL-1β-activated RA synovial fibroblasts (RASFs).

Methods: Human RASFs isolated from RA synovial tissue were serum starved overnight followed by two-hour pre-treatment with takinib at various concentrations (0.1-10 μM) before treatment with IL-1β (10 ng/mL) for 24 hours to determine the cell viability and the production of soluble proteins by ELISA, or for 30 minutes to evaluate the effect on IL-1β-activated signaling pathways. Irreversible type I (5z-7-oxozeaenol; 5Z-7o; 1 μM) and reversible type II (NG-25; 1 μM) inhibitors of TAK1 served as experimental controls. Effect of takinib on the kinome was determined using a human proteome profiler phospho-kinase array. Conditioned media was used for ELISA, whole cell lysates and nuclear/cytoplasmic extract were used for Western blot analysis. Effect on the cell viability was determined using an MTT-based assay. Molecular docking of Takinib as a ligand was performed on human STAT3 protein.

Results: Human phospho-kinase array results from RASFs identified phosphorylation of STAT3 at Ser^{727} and Tyr^{705} as a primary target of takinib (10 μM) in response to IL-1β stimulation. Pretreatment of RASFs with takinib (0.1-10 μM) showed a dose-dependent reduction in ENA-78/CXCL5, IL-6, IL-8 and MCP-1/CCL2 production, which were completely abrogated by 5Z-7o and NG-25 at 1 μM ($n=3$; $p< 0.05$). We also observed a significant reduction in cell viability by takinib at 10 μM ($n=4$; $p< 0.05$). Evaluation of the signaling pathways in RASFs further confirmed that takinib abrogates the non-canonical activation of STAT3 in response to IL-1β stimulation by suppressing Ser^{727} and Tyr^{705} activation. Surprisingly, takinib showed a dose-dependent increase in IL-1β-induced phospho-TAK1 at its kinase domain ($Thr^{184/187}$) in human RASFs. In corroboration of the kinome results, Western blot analysis showed that takinib inhibited the nuclear translocation of IL-1β-induced STAT3, but not of NF-κBp65, in human RASFs ($n=3$; $p< 0.05$). Molecular docking of takinib with STAT3 protein suggests binding of takinib at Gln^{644} and Tyr^{657} residues in the DNA binding domain. These may be essential for STAT3 activation and translocation to the nuclear compartment.

Conclusion: Our findings suggest STAT3 is an important target of takinib in the IL-1β signaling pathway, which may further be utilized for therapeutic purposes.

Disclosure: A. singh, None; **P. Panipinto**, None; **R. Siegel**, None; **F. Shaikh**, None; **M. Chourasia**, None; **S. Ahmed**, None.

Abstract Number: 0044

Autoantibodies Against Malondialdehyde-modifications Promote Osteoclast Development by Reprogramming Cellular Metabolism

Koji Sakuraba[1], Akilan Krishnamurthy[1], Alexandra Circiumaru[2], Jitong Sun[1], Vijay Joshua[1], Heidi Wähämaa[1], Marianne Engström[1], Meng Sun[1], Xiaowei Zheng[1], Cheng Xu[1], khaled amara[1], Vivianne Malmström[1], Sergiu Catrina[1], Caroline Grönwall[1], Anca Catrina[1] and **Bence Réthi**[1], [1]Karolinska Institutet and Karolinska University Hospital, Stockholm, Sweden, [2]Division for Rheumatology, Karolinska Institutet; Center for Rheumatology, Academic Specialist Center, Stockholm Region, Stockholm, Sweden

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Malondialdehyde (MDA) is a highly reactive compound generated during lipid-peroxidation in conditions associated with oxidative stress. MDA can irreversibly modify proteins (e.g. lysine, arginine and histidine residues). In addition, acetaldehyde can further react with the MDA adducts to form malondialdehyde-acetaldehyde (MAA) modification. Such protein modifications can lead to immunogenic neo-epitopes that are recognized by autoantibodies. In fact, anti-MDA/MAA IgG levels are increased in the serum of patients with autoimmune diseases, such as rheumatoid arthritis (RA).

Very little is known about the pathogenic pathways induced by different types of autoantibodies in RA. Interestingly, anti-MDA/MAA antibodies have been shown to promote osteoclast (OC) differentiation in cell culture, suggesting a potential role for these antibodies in bone damage associated with RA. Here we elucidated the pathways specifically triggered by anti-MDA/MAA autoantibodies in developing osteoclasts.

Methods: Recombinant human monoclonal anti-MDA/MAA antibodies, which were previously cloned from single synovial B cells of RA patients, or control antibodies were added to different OC assays. OCs were generated from monocyte-derived macrophages in the presence of RANK-L and M-CSF. OC development was monitored by light microscopy following tartrate-resistant acid phosphatase (TRAP) staining and in erosion assays using calcium phosphate-coated plates. Bone morphometrics were analyzed in anti-MDA/MAA-injected mice using X-ray microscopy. Cellular metabolism was analyzed by mass spectrometry, Seahorse XF Analyzer and a colorimetric L-Lactate assay.

Results: Anti-MDA/MAA antibodies induced a robust OC differentiation *in vitro* and bone *loss in vivo*. The anti-MDA/MAA antibodies acted on developing OCs by increasing glycolysis through an Fcγ receptor I-mediated pathway and the upregulation of the transcription factors HIF-1α and Myc. Such regulation of cellular metabolism was exclusively observed in the presence of the osteoclastogenic anti-MDA/MAA antibodies, but not in the presence of other autoantibodies (e.g. ACPA or other anti-MDA/MAA). The anti-MDA/MAA treatment induced a shift in the tricarboxylic acid (TCA) cycle activity in developing OCs, increasing citrate production. Interestingly, osteoclast differentiation was in general associated with the accumulation of citrate/aconitate in the cells, which suggested intense lipid biosynthesis. Indeed, we detected a profound shift in cellular lipid compositions in developing OCs and we showed that phosphoglyceride/triacylglyceride biosynthesis was essential for osteoclast development.

Conclusion: We described a novel type of autoantibody-induced pathway in RA, which could contribute to increased OC activation and a consequent bone loss. Our results showed that anti-MDA/MAA antibodies promoted osteoclast development by increasing glycolysis and modulating the TCA cycle through a signaling pathway that included Fcγ receptor I and transcription factors acting on glycolysis. A TCA cycle bias towards citrate production suggested that anti-MDA/MAA antibodies might stimulate osteoclastogenesis via increasing lipid biosynthesis.

Disclosure: K. Sakuraba, None; **A. Krishnamurthy**, None; **A. Circiumaru**, None; **J. Sun**, None; **V. Joshua**, None; **H. Wähämaa**, None; **M. Engström**, None; **M. Sun**, None; **X. Zheng**, None; **C. Xu**, None; **k. amara**, None; **V. Malmström**, None; **S. Catrina**, None; **C. Grönwall**, None; **A. Catrina**, None; **B. Réthi**, None.

Abstract Number: 0045

Endothelial Cells from Patients with DMARD Naïve, Active Inflammatory Arthritis Demonstrate Pro-inflammatory Sensitisation That Is Reversed by Therapy Initiation

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Etiology & Pathogenesis Poster (0011–0045)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory arthritides (IA) including rheumatoid arthritis are associated with increased cardiovascular disease (CVD) mortality. Although inflammation-driven endothelial dysfunction is considered a major factor, the mechanisms driving this risk are incompletely understood. Endothelial colony forming cells (ECFC) are endothelial cells derived from peripheral blood. Due to their implied role in vessel repair, ECFC frequency in the circulation has been proposed as a marker of vascular dysfunction. Furthermore, these patient-derived EC provide an opportunity to study endothelial functions relevant to vascular injury in IA. In this ongoing study, we assessed inflammation-driven endothelial dysfunction in IA by measuring ECFC frequency and phenotype in patients before and after initiation of DMARD therapy.

Methods: ECFC were isolated from healthy controls (HC) (n=30) and patients with clinically active, IA naïve to DMARDs (n=37) (Table 1). In patients who commenced DMARDs (MTX+HCQ n=12, MTX, n=6), ECFC were isolated 4 months post initiation (n=16). ECFC frequency was evaluated by colony count normalised to number of PBMC seeded. After confirmation of endothelial purity by flow cytometry ($CD31^+/CD144^+/CD146^+/CD45^-/CD14^-$), ECFC phenotype was interrogated at passage 5 using proliferation and pro-inflammatory activation assays, and by transcriptional analysis of 85 key endothelial genes (Qiagen qPCR arrays). Data is presented as median [IQR]. Non-parametric statistical comparisons were made.

Results: ECFC frequency did not differ between treatment-naïve IA patients and controls (0.59 [0.27-0.75] and 0.75 [0.28-1.35] colonies/10^7 PBMC respectively) and no correlation was observed between frequency and DAS28, ESR or CRP. DMARD initiation led to a non-significant increase in ECFC frequency (1.49 [0.95-4.89] fold, p=0.083), but was unrelated to treatment response (DAS28, ESR, CRP).

Table 1. Basic Characteristics.

	Inflammatory Arthritis	Healthy Controls
N	37	30
Age (yr)	53.3 (48.4-61.4)	47.7 [36.8-58.5]
Female (%)	28 (76%)	20 (51.3%)
Caucasian (%)	20 (54%)	22 (56.4%)
Disease Duration		
≤6 months	21 (57%)	
<12 months	4 (11%)	
>12 months	12 (32%)	
Diagnosis		
Rheumatoid Arthritis	28 (76%)	
Other	9 (24%)	
Rheum. Factor+	18 (49%)	
CCP+	33 (62%)	
Elevated CRP (>5mg/L)	22 (59%)	
Elevated ESR (>23mm/h)	24 (65%)	
Disease Activity (DAS28-ESR)		
Low (≤3.2)	4 (10.8%)	
Moderate (>3.2 and ≤5.1)	9 (24.3%)	
High (>5.1)	22 (56.7%)	

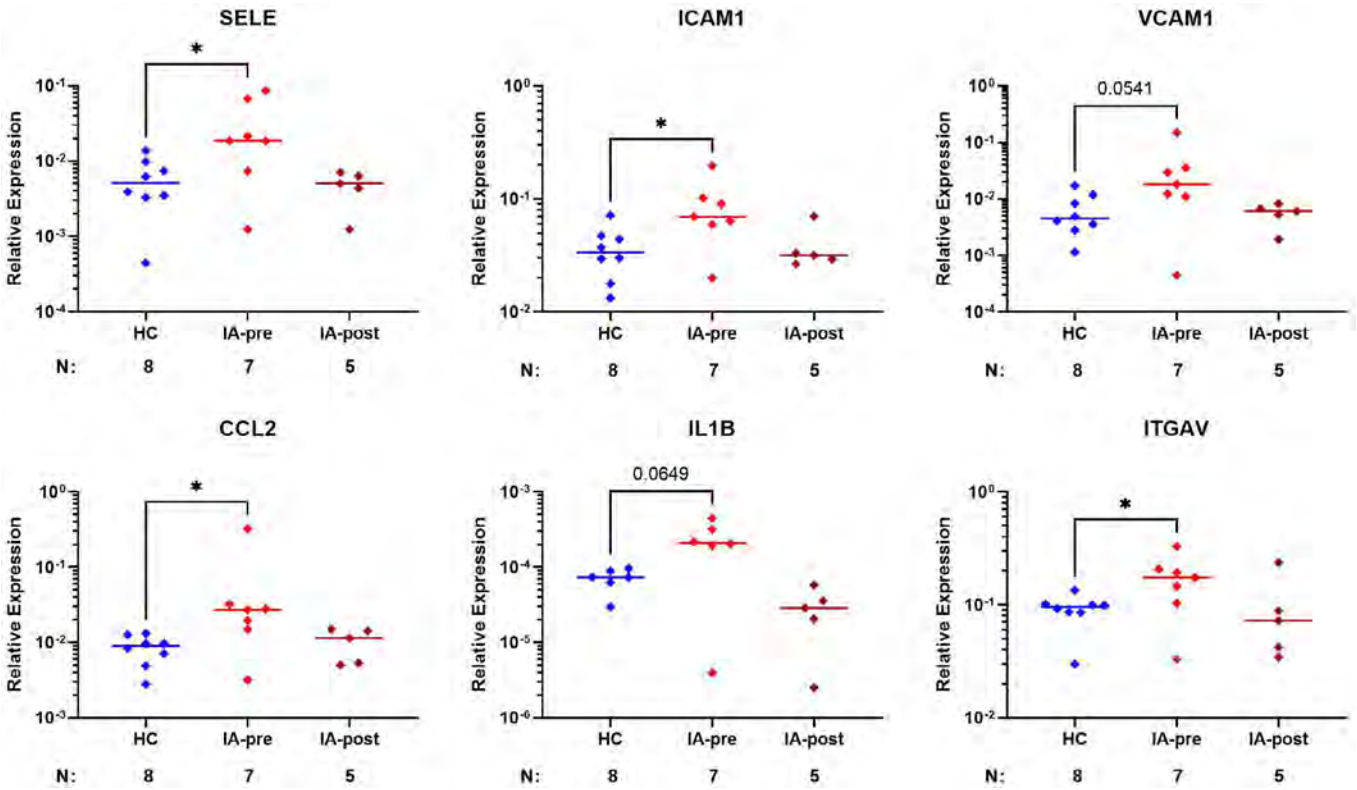

Figure 1. Gene expression Results. *P<0.05.

In comparison to HC, ECFC from treatment-naïve IA patients tended to be less proliferative and had significantly increased expression of CCL2, ICAM1, SELE, ITGAV and a non-significant increase in VCAM1 and IL1B suggesting a primed pro-inflammatory state (Fig. 1). Treatment-naïve ECFC were also more sensitive to pro-inflammatory activation (TNFα), expressing 3.7-13-fold higher mRNA levels of VCAM1 (p=0.0012), ICAM1 (*p*=0.0006) and E-selectin

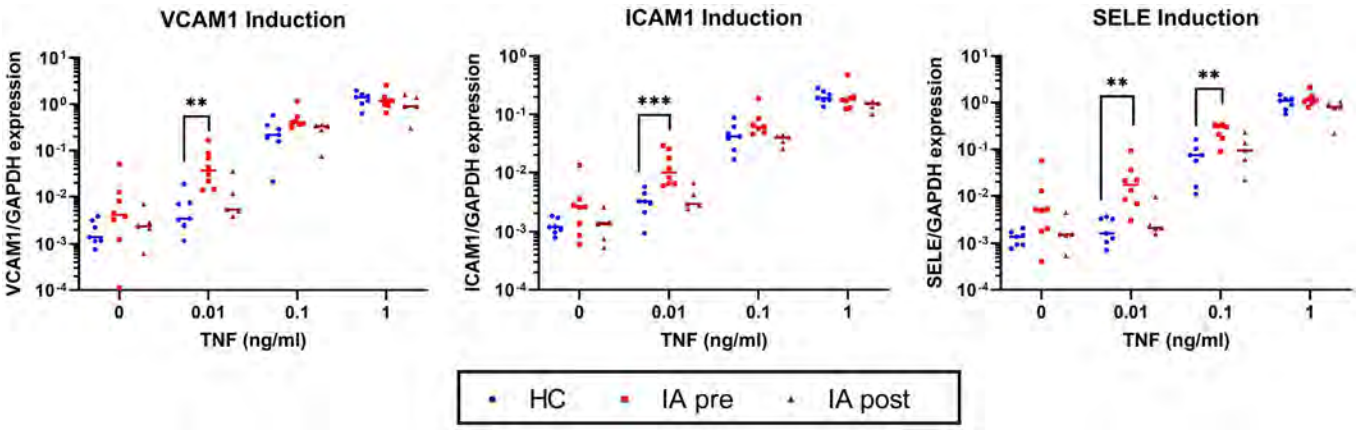

Figure 2. TNF stimulation. *P<0.05, **P<0.01, ***P<0.005.

(p=0.0041) with low dose TNFα stimulation. Of note, ECFC isolated after DMARD initiation demonstrated a reversal in this primed state, as exhibited by a reduction in pro-inflammatory gene expression (Fig. 1) and normalisation of TNFα sensitivity (Fig. 2).

Conclusion: Our data do not support an association between ECFC frequency and severity of inflammation or disease activity in IA. Increased ECFC frequency following DMARD initiation proved to be unrelated to inflammatory changes and may reflect a direct action of the medications. Evaluation of ECFC phenotype demonstrated a pro-inflammatory state that persisted despite *ex vivo* culture and which was reversed following DMARD initiation. These findings have mechanistic implications for inflammatory-driven vascular dysfunction and further analysis may highlight avenues for therapeutic targeting.

Disclosure: R. Maughan, None; **M. Lang**, None; **A. Olsson**, None; **A. Porter**, None; **A. Greeves**, None; **T. Youngstein**, None; **C. Pericleous**, None; **J. Mason**, None.

Abstract Number: 0046

Psoriatic Arthritis Skin Is Transcriptionally Different to Psoriasis Skin and Enriched in Immunoglobulin Transcripts

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Up to 30% of patients with psoriasis develop psoriatic arthritis (PsA). The traditional assumption is that the skin disease is the same in both conditions, although a previous proteomic analysis found differences[1]. The aim of this project was to investigate and compare the skin transcriptome in PsA and psoriasis.

Methods: Full thickness skin biopsies were obtained from healthy controls (HC) and paired lesional and uninvolved skin from patients with PsA. Libraries for bulk RNA sequencing were prepared from polyA selected RNA and

sequenced on NovaSeq 6000. Sequencing data were analysed using Searchlight2. Read counts of HC, lesional and uninvolved skin from patients with psoriasis without PsA obtained by Tsoi et al 2019 [2](GEO accession GSE121212) were analysed using Searchlight2. Results from the two analyses were compared. Read counts of patients with PsA from the Tsoi cohort were used for validation.

Results: The PsA cohort had 9 participants and the psoriasis cohort 16 participants in each group. The Tsoi PsA cohort had 4 participants. Both PsA skin lesions (PsA L) and psoriasis skin lesions (PsO L) formed distinct populations in the respective principal component analysis plot. While the HC and PsA uninvolved skin (PsA U) populations were mixed, the psoriasis uninvolved skin (PsO U) population was skewed from the HC population toward the PsO L population. Consistent with this, there were 15 differentially expressed genes between the PsA U and HC groups, and 124 differentially expressed genes between the PsO U and HC groups. All but one overlapped with genes differentially expressed in PsO L versus HC and pathway analysis showed enrichment of pathways also enriched in PsO L.

In lesional skin, most enriched pathways were shared between PsA L and PsO L. However, PsA L skin was enriched in immunoglobulin genes while PsO L skin was not. Increased expression of immunoglobulin genes was also seen in PsA L skin in the Tsoi cohort.

Conclusion: This study found differences in the transcriptomes of psoriasis and PsA skin. PsA U skin is closer to healthy skin than PsO U skin, which shares some transcriptomic changes with PsO L skin. Although PsA L and PsO L skin share many inflammatory pathways, transcriptomic changes suggest differences in immunoglobulin pathways.

1. Cretu, D., et al., Clin Proteomics, 2015. **12**(1): p. 1.

2. Tsoi, L.C., et al., J Invest Dermatol, 2019. **139**(7): p. 1480-1489.

Disclosure: H. Johnsson, Eli Lilly, 12, Attendance at course and conference; **J. Cole**, None; **S. Siebert**, AbbVie, 5, 6, Biogen, 6, Amgen (previously Celgene), 5, 6, Bristol Myers Squibb, 5, Boehringer-Ingelheim, 5, Novartis, 5, 6, UCB, 5, 6, Janssen, 1, 5, 6, GlaxoSmithKline, 5; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **G. Graham**, None.

Abstract Number: 0047

A Role for Neutrophils in Disease Onset and Severity of Spondyloarthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Spondyloarthritis (SpA) is a group of inflammatory diseases that includes axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA). AxSpA patients have irregular neutrophil responses, as indicated clinically by neutrophilia, increased neutrophil to lymphocyte ratios, and aberrant neutrophil activation. However, the role of

neutrophils in disease pathogenesis remains unknown. Here we employed an experimental model of SpA (SKG mice) in tandem with SpA patient data to determine the role of neutrophils in SpA.

Methods: Arthritis was induced in SKG mice by intraperitoneal injection of 1.5mg β-glucan (zymosan). Splenic CD4+ T cells were stimulated *in vitro* with PMA/ionomycin and the Th17 response was quantified by flow cytometry. Neutrophils were depleted in SKG mice with anti-Ly6G (1A8) or isotype control (2A3) beginning 24h prior to zymosan and every 2d for 5d. For mouse studies, three independent experiments were performed (n=5-6 mice/genotype), and data analyzed using non-parametric statistics. SpA patients with axSpA or PsA from the Program to Understand the Long term Outcomes in Spondyloarthritis Registry (Pulsar) were included. Regression was used to assess for associations of absolute neutrophil count (ANC) and neutrophil percentage, with measures of functional capacity determined using the Bath Ankylosing Spondylitis Functional Index (BASFI) Test.

Results: We induced disease in neutrophil-sufficient or -deficient SKG mice. Five days post-zymosan (disease induction), neutrophil-sufficient SKG mice developed autoreactive Th17 responses and arthritis; however, neutrophil-deficient SKG mice had decreased Th17 responses and no signs of arthritis, indicating a role for neutrophils in induction of arthritis. Conversely, 8 weeks post-zymosan neutrophil depletion resulted in worsened disease indicating neutrophils play a protective role during established/chronic disease. In human subjects, both absolute neutrophil count (ANC) ($p=0.002$) and neutrophil percentage ($p=0.008$) were associated with increased disease severity, as indicated by BASFI scores. On average, for every increasing increment of 5,000 neutrophils/mm^3, disability status worsened by approximately 15% (ΔBASFI of 1.5). These associations were also present in treatment-naïve SpA subjects, further supporting a role for neutrophils in SpA pathogenesis rather than an artifact of treatment. In corroboration with SKG mice, treatment-naïve SpA subjects within 5 years of diagnosis (earlier disease) had greater ANC than controls ($p < 0.001$), whereas subjects with more established disease demonstrated lower ANCs.

Conclusion: Our data suggest neutrophils may play a role in initiation of pathogenic Th17 responses and disease in Spa patients. Future studies aimed at understanding how dysregulation of neutrophil numbers and function contributes to SpA will inform development of novel therapeutics.

Disclosure: H. **Rosenzweig**, None; **E. Vance**, None; **R. sen**, None; **L. Caplan**, None; **R. Napier**, None.

Abstract Number: 0048

A Novel Technology to Study the Role of Intestinal Biology in Spondyloarthritis Pathogenesis: Human Colonic Organoids and Epithelial Monolayers

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Ankylosing spondylitis (AS) is a complex genetic disease with strong association to the human leukocyte antigen (HLA)-B27. Several observations including frequent, occult histologic evidence for inflamma-

tion, clinical overlap with Crohn's disease, and microbial dysbiosis point to the gut as a potential primary cause of spondyloarthritis. However, the role of HLA-B27 associated gut epithelial biology or host-microbe interaction is not clear in spondyloarthritis pathogenesis. While immortalized cell-lines transfected with HLA-B27 can be studied, they cannot mimic the complexity of the epithelial tissue. In addition, animal and cell line models cannot recapitulate the interindividual variability of the human population. To counter these issues, we have developed human colonic organoids and epithelial monolayers from colon biopsies of HLA-B27 positive and negative healthy individuals to study the effect of HLA-B27 on host-microbe interactions and epithelial cell biology.

Methods: To generate colonic organoids, frozen biopsies from healthy individuals undergoing elective colonoscopies were used. These biopsies were minced and the tissue digested on a shaker to release the crypts. The crypts were washed and resuspended in undiluted Cultrex reduced-growth-factor basement membrane extract. The organoids were expanded after ~1 week by mechanical disruption and splitting. After 2-5 passages, these organoids were frozen during exponential growth phase for optimal recovery. To generate epithelial monolayers, organoids were washed and mechanically disrupted and cells were plated over Matrigel matrix coated transwells to form monolayers.

Results: We have developed colonic organoids and epithelial monolayers from multiple HLA-B27 positive and negative individuals and are in the process of generating colonic organoids from AS patients. We have shown that organoids maintain their stemness after being frozen, as confirmed by the presence of spheroids (early-stage organoids), and their ability to differentiate into mature (lobular) organoids and epithelial monolayers. These organoids have been characterized for the presence of goblet cells, and experiments using various proliferation markers to confirm recapitulation of key aspects of *in vivo* sample are underway. Monolayers will be used to study HLA-B27 associated alteration of epithelial cell biology. In addition, organoids/monolayers will be cultured with either microbial products (e.g., lipopolysaccharide) or HLA-B27 associated microbes as determined in our previous studies, and the loss of barrier function will be analyzed by global gene expression, tight-junction proteins, and production of antimicrobial peptides.

Conclusion: To our knowledge, we are amongst the first groups to use human colonic organoids to study the role of intestinal epithelial cells in barrier function and host-microbe interaction in any rheumatic disease. Using organoids developed from HLA-B27 positive AS patients and healthy individuals and HLA-B27 negative controls, we will be able to functionally assay whether HLA-B27 is associated with altered barrier function and host-microbe interactions.

Disclosure: M. Rodriguez, None; **A. Furst**, None; **J. Rosenbaum**, AbbVie, 2, UCB, 2, Novartis, 2, Gilead, 2, Corvus, 2, Roivant, 2, Revolo, 2, Neoleukin, 2, Affibody, 2, Santen, 2, Celgene, 2, Bristol Myers, 2, Pfizer, 5, Horizon, 5, UpToDate, 9; **T. Gill**, None.

Abstract Number: 0049

CC-99677, a Novel, Selective, Oral MK2 Inhibitor, Sustainably Reduces Pro-inflammatory Cytokine Production and Ameliorates Inflammation in the Mannan-Induced Murine Model of Psoriasis and Psoriatic Arthritis

Rajula Gaur, Kofi Mensah, Jason Stricker, Anastasia Parton, Dorota Cedzik and Francisco Ramírez-Valle, Bristol Myers Squibb, Princeton, NJ

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Mitogen-activated protein kinase-activated protein kinase-2 (MK2), a direct downstream target of p38, has been identified as a promising candidate for treatment of inflammatory diseases. Activation of the p38 pathway leads to increased production of pro-inflammatory cytokines via MK2-mediated increases in the stability and translation of their mRNA (eg, TNF, IL-17, IL-6). Previously, p38 inhibitors were investigated for the treatment of autoimmune diseases, but tachyphylaxis was observed with the lack of sustained inhibition of inflammation despite continuous treatment.[1,2] MK2 inhibition is hypothesized to avoid the negative feedback network that may have limited p38 inhibitors. CC-99677 is a novel covalent MK2 inhibitor being developed for the treatment of inflammatory diseases.

Methods: In the *in vitro* model of tachyphylaxis, CC-99677 and p38 inhibitors similarly decreased TNF production at early time points. However, on day 9, loss of TNF inhibition was noted for all p38 inhibitors tested. In contrast, the MK2 inhibitor, CC-99677, sustainably suppressed TNF production throughout the treatment period. MK2 inhibition with CC-99677 resulted in reduced TNF and IL-17A/F production in *in vitro*-stimulated PBMCs from patients with PsA. In the animal model of psoriasis and PsA, a new cumulative score based on paw swelling, ear thickness, skin flaking, and joint severity score was devised: Psoriatic Arthritis Severity Index (PsASI). CC-99677 reduced the PsASI score in a dose-dependent manner.

Results: In the *in vitro* model of tachyphylaxis, CC-99677 and p38 inhibitors similarly decreased TNF production at early time points. However, on day 9, loss of TNF inhibition was noted for all p38 inhibitors tested. In contrast, the MK2 inhibitor, CC-99677, sustainably suppressed TNF production throughout the treatment period. MK2 inhibition with CC-99677 resulted in reduced TNF and IL-17A/F production in *in vitro*-stimulated PBMCs from patients with PsA. In the animal model of psoriasis and PsA, a new cumulative score based on paw swelling, ear thickness, skin flaking, and joint severity score was devised: Psoriatic Arthritis Severity Index (PsASI). CC-99677 reduced the PsASI score in a dose-dependent manner.

Conclusion: CC-99677 is an MK2 inhibitor that exhibits sustained inhibition of TNF *in vitro* and effectively reduces TNF production in stimulated immune cells from patients with PsA. In the *in vivo* MIP model of psoriasis and PsA, MK2 inhibition was efficacious in reducing skin and joint inflammation, reflected in a dose-dependent reduction in PsASI score. These data extend previous results demonstrating reduction in cytokine production in stimulated PBMCs from patients with AS and efficacy in the rat HLA-B27 transgenic model of AS.[5] Thus, our *in vitro* and *in vivo* data support investigating CC-99677 in clinical studies planned in patients with spondyloarthritis.

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Disclosure: R. Gaur, Bristol Myers Squibb, 3, 11; **K. Mensah**, Bristol Myers Squibb, 3, 11; **J. Stricker**, Bristol Myers Squibb, 3, 11; **A. Parton**, Bristol Myers Squibb, 3, 11; **D. Cedzik**, Bristol Myers Squibb, 3, 11; **F. Ramírez-Valle**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0050

Integrative Analysis of mRNAs to Identify Sex Differences in Th-17 Mediated Inflammation in Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Gender has been shown to impact disease expression in ankylosing spondylitis. Men with AS are more likely to develop radiographic joint damage, while women have latter onset of disease, higher symptomatic burden but slow progression of structural damage and impaired response to treatment. An important observation was made in a recent study which showed that male patients with AS had a distinctive up-regulation of the Th17 signature,

Table1. Disease Activity and Function Outcome Measures in Patients

Variable	AS female patients (n=10) Mean ± SD	AS male patients (n=10) Mean ± SD
Age	48 ± 17	45 ± 13
HLAB27+	7	10
BASDAI	4.1 ± 3.1	3.0 ± 2.1
BASFI	3.6 ± 2.6	3.6 ± 2.6
ASDAS-ESR	3.0 ± 1.1	2.3 ± 1.2
RAPID-3	10.9 ±8.6	10.1 ± 6.9
Patient Global	3.8 ± 3.2	4.2 ± 3.3
Physician Global	4.2 ± 3.4	4.1 ± 2.9
ESR (mm/hr)	27.9 ± 15.2	18.9 ± 15.7
Uveitis	40%	60%
TNF-a blockers	60%	50%

Symbol	LogFoldChange	*p*-value
S100A2	1.42	0.005
S100A6	1.28	0.007
S100A10	0.93	0.014
S100A4	1.22	0.023
S100B	1.34	0.035
CCL17	1.437	0.002
TNFSF12 (TWEAK)	1.093	0.011
TNFRSF18 (GITR)	1.126	0.030
TNFRSF4 (CD134)	1.085	0.025
HLA-B	0.899	0.010
PTGES2	0.737	0.038
PTGR2	0.832	0.048
IL23R	*-1.131*	*0.028*
IL12RB2	*-1.122*	*0.012*
IL6R	*-0.734*	*0.024*
JAK2	*-0.990*	*0.024*
JAK1	*-0.637*	*0.010*
STAT3	*-0.424*	*0.021*
CCR4 (CD194)	*-0.916*	*0.039*

Figure 1. Dysregulated differential genes in AS male vs AS female.

while female patients with AS had Th17 cell profiles comparable with those of the healthy control subjects (1). We propose that mRNAs are differentially expressed in IL-17 producing cells between males and females with AS and disparately regulate the genes in males and females and subsequently contribute to the difference in disease phenotype.

Methods: 10 female and 10 male subjects ≥18 years of age with AS based on NYCS, were enrolled. Patients were recruited as per approved IRB protocol. Peripheral blood samples (30 ml) were obtained in the Clinical Research Unit of MetroHealth Medical Center. The PBMCs obtained were stimulated with CytoStim for 4 h (Miltenyi Biotec GmbH, Bergisch Gladbach, Germany). After stimulation, the cells were processed through the interleukin (IL)-17-phycoerythrin (PE) cytokine secretion assay enrichment kit (Miltenyi Biotec). The IL-17 positive cells were counted and total RNA was extracted as per Takara kit (Takara Biotech, Japan). Changes in mRNA expression were identified using next

generation RNA-sequencing (RNA-seq). To proceed 500 ng of RNA from each sample was sent to Novogene for sequencing. Analysis of the data was done using Ipathway guide by Advaita Bioinformatics (ipathwayguide.advaitabio.com). Genes were identified using a threshold of 0.05 for statistical significance (p-value) and a log fold change of expression with absolute value of at least 0.6. These data were analyzed in the context of pathways obtained from the KEGG database, miRNAs from the miRBase and TARGETSCAN databases, network of regulatory relations from BioGRID, and diseases from the KEGG database.

Results: Patient demographics and disease activity and functional outcomes are reported in table 1. In this experiment, 2,373 differentially expressed (DE) genes B were identified out of a total of 15,294 genes with measured expression as in Fig 1. 613Gene Ontology (GO) terms, 40 miRNAs, 201 upstream regulators, and 14 diseases were found to be significantly enriched before the correction for multiple comparisons. In summary, 15 pathways were found to be significantly impacted.

Conclusion: The study revealed multiple cytokine genes were found to be dysregulated between men and women with AS. The IL23R, IL12R, IL6R, JAK, STAT and TYK2 genes were downregulated in men compared to women while S100A2, S100A4, S100A6, S100B, chemokine CCL-17 and PGE2 related genes were upregulated. These data need to be confirmed by RTPCR and may provide clues for understanding the pathogenesis and phenotypic differences.

1.Gracey E, Yao Y, Green B, Qaiyum Z, Baglaenko Y, Lin A, Anton A, Ayearst R, Yip P, Inman RD. Sexual Dimorphism in the Th17 Signature of Ankylosing Spondylitis. Arthritis Rheumatol. 2016 Mar;68(3):679-89. https://doi.org/10.1002/art.39464. PMID: 26473967.

Disclosure: M. Haghiac, None; **M. Breitman**, None; **R. Chan**, None; **A. Khalil**, None; **M. Magrey**, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5.

Abstract Number: 0051

Identification of Biomarkers and Deregulated Pathways in Psoriatic Arthritis Through Proteomic Analysis of Synovial Fluid

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory arthritis that currently lacks diagnostic biomarkers. We hypothesized that there are differences in the protein intensities in the synovial fluid (SF) of patients with osteoarthritis (OA), rheumatoid arthritis (RA) and PsA. We aimed to identify markers for PsA by proteomic analysis of knee joint SF. Our objectives were to identify proteins and pathways differentially expressed between:

1. OA and the inflammatory arthritides (PsA and RA).
2. PsA and RA.

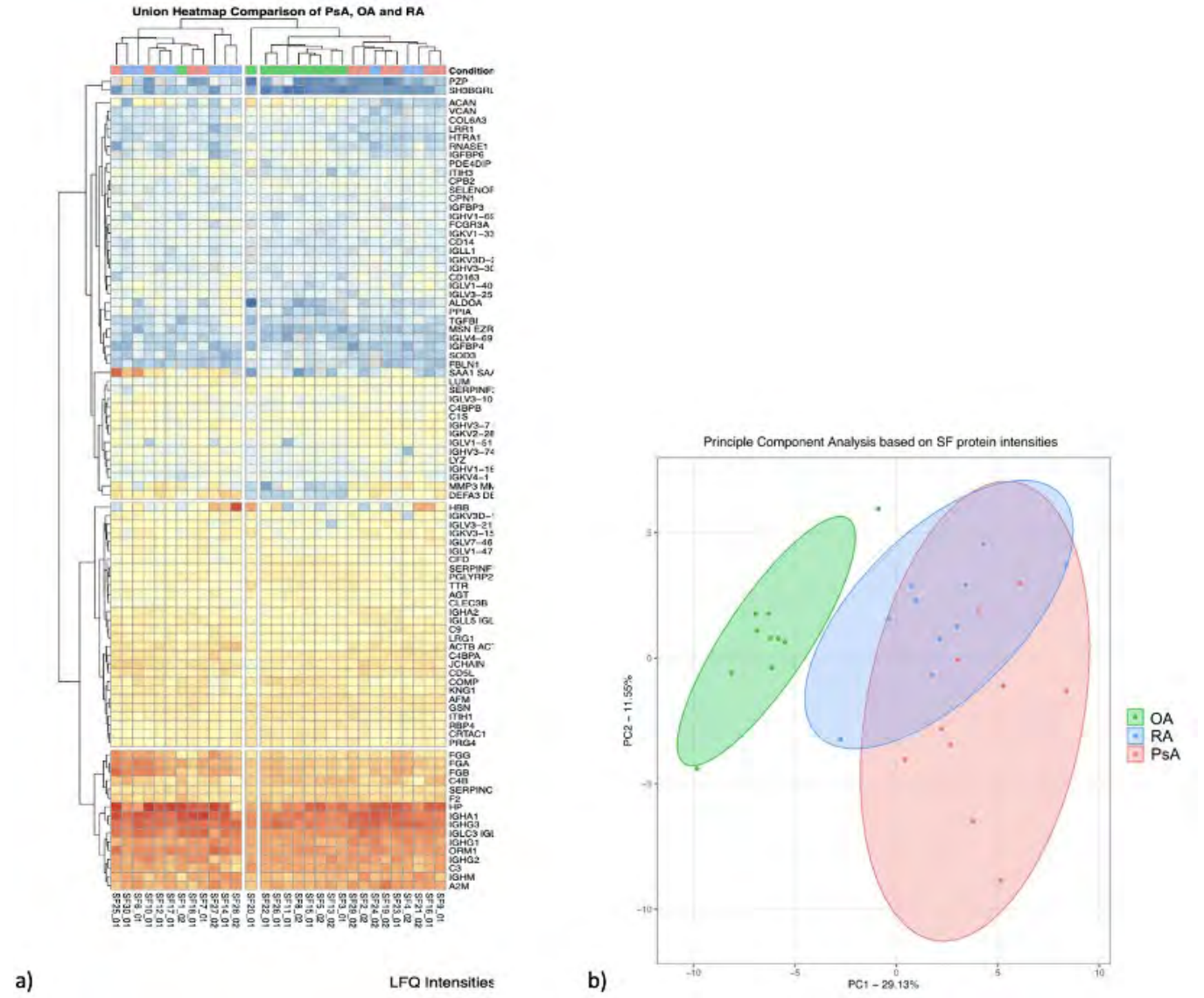

Figure 1. Hierarchical clustering (a) and principal component analysis (b) distinguish OA from the inflammatory arthritides based on mass spectrometry data of proteins with significant differential intensities in at least one of the three comparisons.

Methods: Mass spectrometry was used to identify the SF proteome from 10 OA, 10 PsA, and 10 RA patients. All patients satisfied the classification criteria for their disease. First, we used student's t-test for differential intensity analysis (p-value < 0.05; fold change > 1.5) to identify potential protein biomarkers of each disease. Next, we performed protein-protein interaction (PPI) network and pathway enrichment analysis to obtain biological insights on systems biology of these diseases.

Results: Aim 1: 4 proteins were present and 45 were absent in OA SF compared to PsA and RA. Among those present in all conditions, we detected 56 and 66 proteins with differential intensities in OA compared to PsA and RA, respectively. Hierarchical clustering and principal component analysis confirmed the power of these proteins in distinguishing OA from the inflammatory arthritides (Fig 1). In both comparisons, enriched pathways were involved in inflammation and immune response. Additionally, PPI network analysis of both lists revealed connected subnetworks of proteins with high fold change enriched in immune-system and extracellular matrix (Fig 2a,b). In both comparisons, VIM showed the highest fold change and was central in connecting other high fold change proteins.

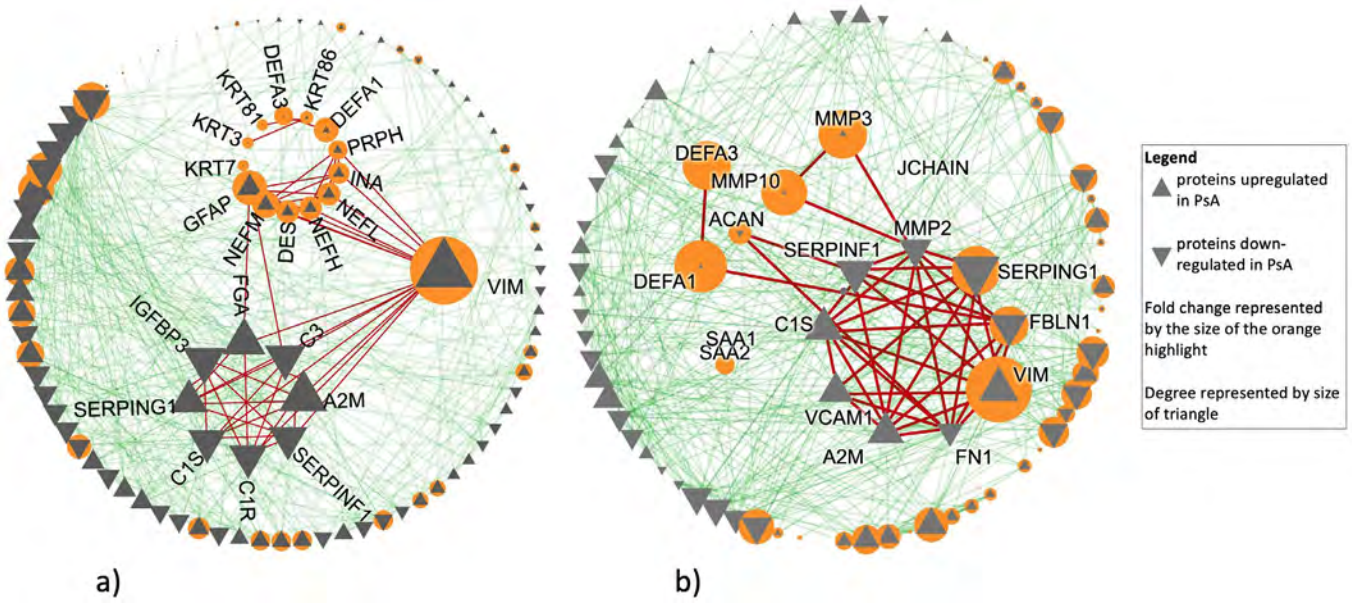

Figure 2. Comparison between OA and the inflammatory arthritides a) OA vs RA b) OA vs PsA. To build the network, we first annotated the physical PPI network (obtained from http://iid.ophid.utoronto.ca) with differential intensities. We expanded the list of differential proteins by relaxing the thresholds for fold change and p-value. Instead, they must interact with at least another differential protein. Next, we selected proteins whose PPI count (degree) and/or fold change was within the top 10th percentile of protein degrees and/or fold changes in each network. Finally, we arranged all other proteins in a big circular layout around these selected proteins. Selected proteins with a high degree form a densely connected network module in both comparisons. In addition, they maintain physical connectivity among proteins with high fold change. PPIs within the proteins inside the large circular layout are shown in red. Networks are visualized in http://navigator.ophid.utoronto.ca/navigatorwp.

Aim 2: 22 proteins with differential intensities between PsA and RA were identified. In addition to immune system pathways, these proteins were enriched in cell metabolism pathways, such as glycolysis which has been previously suggested to distinguish PsA and RA. PPI analysis identified three densely connected network modules (Fig 3a). All upregulated proteins in PsA formed one dense module enriched in complement and clotting pathways (Fig 3b). We identified one highly densely connected subnetwork enriched in transcription-related pathways (Fig 3c) which has four interactions with one upregulated protein (VCAM1). All other proteins were downregulated and have many interactions with the upregulated module. These proteins were highly enriched in glycolysis and glycogenesis, followed by immune pathways (Fig 3d). Previous research has shown interplay between glycolysis and complement pathways. Unlike in Aim 1, VIM shows small but statistically significant differences.

Conclusion: We have identified differential proteins and pathways between PsA, OA, and RA. VIM was a central protein in connecting proteins with differential intensities between OA and the inflammatory arthritides. Additionally, we identified three large network modules enriched in complement, transcription, and glycolysis pathways that may distinguish PsA from RA. Our results suggest disrupted interplay between complement and glycolysis pathways in PsA vs RA.

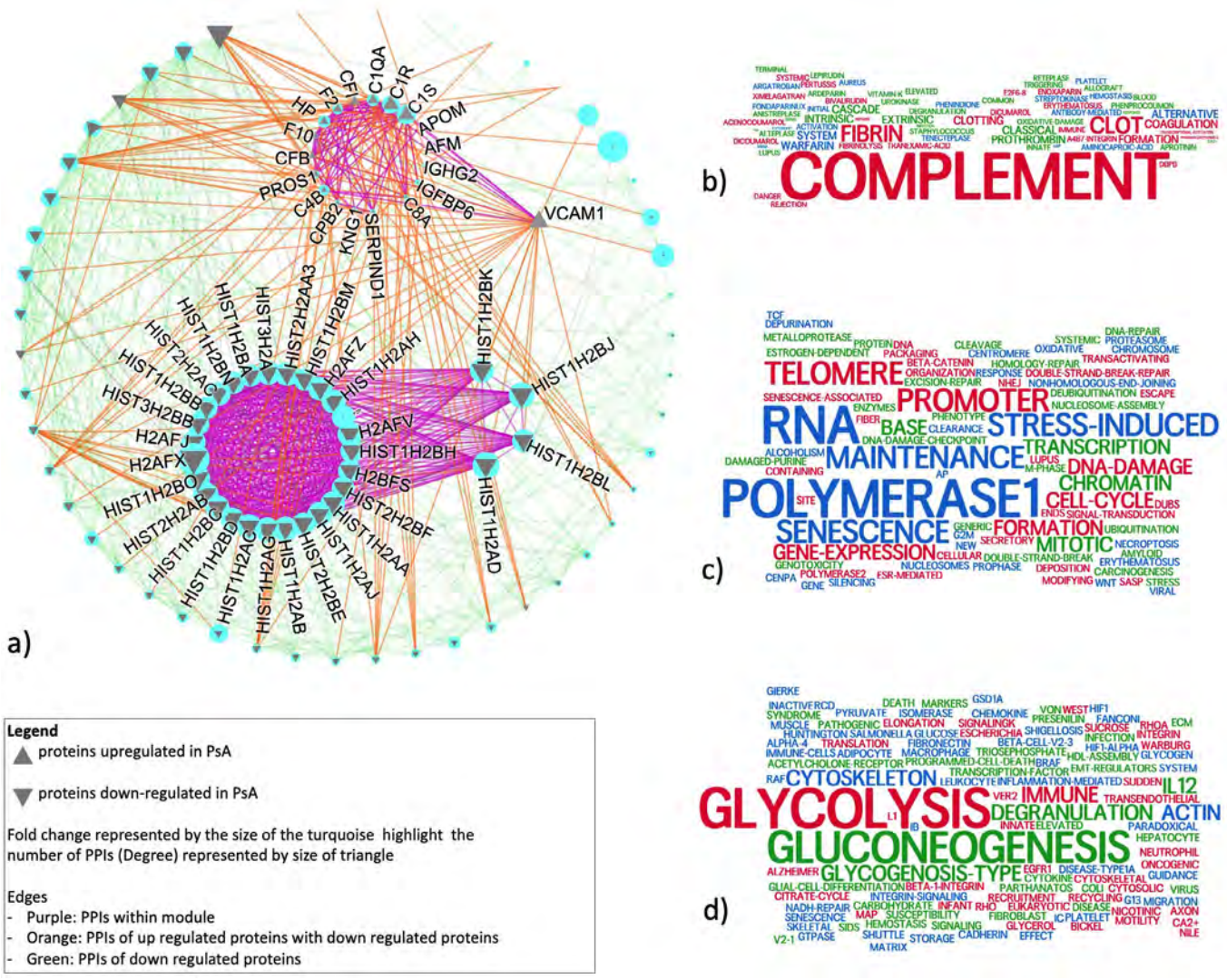

Figure 3. Network and pathway analysis of differential proteins between SF of PsA vs RA. a) To build the network, we first annotated the physical PPI network with differential intensities. We expanded the list of differential proteins by relaxing the thresholds for fold change and p-value. Instead, they must interact with at least another differential protein. Analysis of this network revealed three densely connected modules involved in different pathway groups. Module 1: covers all of the upregulated proteins in PsA compared to RA (arranged in the smallest circular subnetwork); module 2: consists of downregulated proteins with high intra-module connectivity (formed mainly by histone proteins); and module 3: includes all downregulated proteins not in module 2 (arranged on the large network circle). Most of these proteins have interactions with at least one upregulated protein (module 1). b) Key-terms in titles of pathways enriched in proteins of module 1 shows strong enrichment in complement pathways. c) Module 2 is enriched in pathways related to transcription. Polymerase, RNA, and Promoter are three major keywords in the titles of these pathways. This module was also connected to only one upregulated protein in the whole network - VCAM1. d) Proteins in module 3 are enriched in glycolysis and gluconeogenesis. Most proteins in module 3 have PPIs with proteins in module 1 that suggest differential interplay between complement and glycolysis pathways in PsA vs RA. Pathway and key-term analysis are done by http://ophid.utoronto.ca/pathDIP/ and word-clouds are made by http://www.edwordle.net.

Disclosure: J. Lai, None; **S. Rahmati**, None; **R. Sivakumar**, None; **K. Oikonomopoulou**, None; **F. Abji**, None; **V. Chandran**, Abbvie, 1, 2, 5, Amgen, 1, 2, 5, Eli Lilly, 1, 2, 5, BMS, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, AstraZeneca, 12, Spousal employment, Celgene, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 0052

HLA-B27 Is Associated with Altered Mucosal IgA Response to Oral and Fecal Microbiota in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (AxSpA) is immune-mediated inflammatory arthritis, which affects the sacroiliac and spinal joints, and is associated with gut inflammation. Disease pathogenesis is associated with host genetics (HLA-B27), environmental factors, and gut microbial dysbiosis. Previous studies have shown HLA-B27-associated microbial dysbiosis in ankylosing spondylitis patients as well in experimental models of spondyloarthritis. However, not all microbial changes might drive the chronic inflammatory response or elicit host IgA responses. Here, we report the presence of specific IgA-coated microbes that may be disease contributors in AxSpA patients.

Methods: Microbial community structure and IgA coating from feces and saliva samples from AxSpA patients (n=17) and healthy controls (n=12-14) were determined by 16S rRNA sequencing (16S sequencing) and IgA sequencing (IgA-SEQ) respectively. IgA-SEQ involves sorting IgA-coated microbes using flow cytometry and performing 16S sequencing on the IgA positive and negative fractions. Correlation analyses were performed to determine the disease association between IgA-coated microbes in AxSpA patients and the disease activity score. Furthermore, metagenomic contribution of IgA positive and negative microbes was estimated by using the bioinformatic tool PICRUSt2

Results: 16S sequencing of oral and fecal microbiota showed distinct microbial community composition in AxSpA patients as compared with the healthy controls. AxSpA patients showed a significant decrease in oral microbial diversity, whereas the decrease in fecal microbial diversity was not significant. However, the lack of microbial differences in diversity in fecal samples did not suggest a lack of immunological impact of the gut microbes. AxSpA patients had many microbes at a genus level with increased IgA coating (e.g., *Akkermansia*, *Klebsiella*, *Ruminococcus*, *Lachnospira*, *Pseudomonas*) in comparison with the healthy controls. Despite significant changes in microbial diversity in the saliva of AxSpA patients, only a few microbes such as Prevotellaceae*,* NK3831 group, and *Alloprevotella* were enriched in IgA coating. We also found a positive correlation between IgA-coated *Clostridium Family XIII* and the disease activity. Predictive metagenomic analysis of IgA coated microbes showed perturbation of pathways belonging to propanoate and glutathione metabolism, biosynthesis of secondary metabolites, and bacterial secretion system in AxSpA patients. Analysis of individual genes showed the alterations of the genes belonging to the tryptophan and butanoate pathways, further emphasizing the importance of IgA coating in targeting immune responsive bacteria.

Conclusion: We show that the immune response to oral and fecal microbes is altered in AxSpA patients, with IgA coated *Clostridium* positively correlating with disease activity. Predictive metagenome analysis revealed perturbations of metabolic and oxidative stress-related pathways in AxSpA patients. Taken together, our results suggest that

HLA-B27-associated increase in IgA coated microbes may indicate an aberrant immune response to gut commensal microbes, which may contribute to the development of AxSpA.

Disclosure: T. Gill, None; **P. Stauffer**, None; **M. Asquith**, None; **T. Laderas**, None; **T. Martin**, None; **S. Davin**, None; **C. Ramirez**, None; **I. Lindquist**, None; **J. Nguyen**, None; **s. Planck**, None; **C. Shaut**, None; **S. Diamond**, None; **J. Rosenbaum**, AbbVie, 2, UCB, 2, Novartis, 2, Gilead, 2, Corvus, 2, Roivant, 2, Revolo, 2, Neoleukin, 2, Affibody, 2, Santen, 2, Celgene, 2, Bristol Myers, 2, Pfizer, 5, Horizon, 5, UpToDate, 9; **L. Karstens**, None.

Abstract Number: 0053

Susceptibility Factors for Psoriatic Arthritis Single-cell RNA-Sequencing of Patients with Psoriatic Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory musculoskeletal disease that affects 30% of patients with psoriasis. Thus, early diagnosis of this subgroup is crucial to reduce disease progression and prevent joint destruction. GWAS and epigenome studies have identified major susceptibility genes albeit having low odds ratios. Single cell RNA-seq provides increased resolution to identify novel cell types and cell-specific differential gene expression. We aim to identify a set of genes that can lead to an earlier diagnosis of PsA.

Methods: Three PsA patients, three cutaneous psoriasis (PsC) patients and two healthy control samples were profiled with 10X genomics single cell RNA-seq. The patients recruited were recently diagnosed with PsA and were not treated with biologics. The gene profiles of peripheral blood mononuclear cells (PBMC) were selected for sequencing. The raw data were processed using the CELLRANGER pipeline. R version 4.0.1 was used for secondary analysis using the following packages: SingleCellExperiment, scran, scater and Seurat. These packages were used to cluster the cells and perform differential gene expression analysis. Cell clusters were manually annotated based on canonical markers generated from the 'findallmarkers' function in Seurat and differentially expressed genes were selected in each cluster. A ranking was assigned to genes in each cluster to identify suitable targets for validation by considering the results of the differential gene expression analysis, network analysis using the Integrated Interactions Database version 2018-11, GO and pathway over-representation analysis which was conducted using Pathdip 4.0. A score was assigned to every gene based on their log fold change difference, adjusted p-value in the differential gene expression analysis, closeness centrality and connectivity in the protein interaction network.

Results: The aggregated data revealed the presence of 18 clusters with 15 unique cell types. In the T-Cell and Classical Monocyte populations pathways related to inflammation, cell migration and apoptosis were enriched. Genes belonging to the AP-1 transcription factor JUN, JUNB, and FOS were ranked highly across both T-Cell and Monocyte clusters. Interestingly, the classical monocyte population included several highly ranked genes that are responsive

to interferon-alpha: MNDA and IFI6. The genes that are listed above were found to be consistently differentially expressed across healthy controls and either PSA or PsC.

Conclusion: Several genes were identified in specific cell types; these will be validated using multiple gene and protein assays.

Disclosure: A. Garrido, None; **R. Machhar**, None; **O. Cruz Correa**, None; **D. Ganatra**, None; **S. Crome**, None; **J. Wither**, None; **I. Jurisica**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5.

Abstract Number: 0054

TCR Immune Profiling of Patients with Psoriatic Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: $CD8^+$ and $CD4^+$ T cell subsets have been implicated in the pathogenesis of psoriatic disease. Here, we explore the T-cell repertoire in psoriatic disease using single-cell RNA sequencing to identify novel susceptibility markers of disease by focusing on T cells with clonal expansion.

Methods: We profiled frozen peripheral blood mononuclear cells derived from 3 psoriasis, 3 psoriatic arthritis (biologic naïve, matched for age, gender and disease duration) and 2 healthy control samples using 10X genomics 5' single cell gene expression technology. TCR immune cell profiling was employed, and sequencing data was processed using the CELLRANGER pipeline. We identified 4579 TCRs in psoriasis, 3323 in psoriatic arthritis, and 1843 in healthy control samples. Secondary analysis of TCR beta and alpha chains was conducted in R version 4.0.1 using scran, scater, SingleCellExperiment, Seurat, scREPERTOIRE and Immunarch. The online tool GLIPH2.0 was used to cluster the TCR beta CDR3 amino acid sequences based on motif similarity and VDJdb was used to predict antigen specificity. VDJ gene differential expression analysis was conducted across multiple groups using the Dunn.test function in R.

Results: The shared motifs from the clustering results from GLIPH2.0 comprising only psoriatic arthritis and/or psoriasis patients had a predicted antigen specificity for Cytomegalovirus (CMV) proteins Immediate-Early1 (IE1) or pp65. The variable beta chain genes TRBV2 (FC= 0.14, p-value= 0.033), TRBV7-2(FC=1.49, p-value= 0.0098), TRBV7-7(FC=1.00, p-value= 0.018) and TRBV6-3 (FC= 1.17, p-value=0.033) were elevated and significantly differentially expressed in psoriatic arthritis patients when compared to psoriasis patients. A clonal expansion of $CD8^+$ cytotoxic T-cells was observed in a psoriatic arthritis patient. It accounted for approximately 7% of all clonotypes for that individual. The predicted antigen was IE1 from CMV.

Conclusion: Antigen selection may be occurring in psoriatic arthritis patients. Further investigation is required to determine if the predicted antigens pp65 and IE1 are relevant in the pathogenesis of psoriatic arthritis.

Disclosure: A. Garrido, None; **R. Machhar**, None; **O. Cruz Correa**, None; **S. Crome**, None; **J. Wither**, None; **I. Jurisica**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5.

Abstract Number: 0055

Time Course of Intestinal Permeability and Intestinal Inflammation in Rat Adjuvant-induced Arthritis

Sophie Hecquet[1], Perle Totoson[2], Marie-Paule Algros[3], Hélène Martin[2], Célian Peyronnel[2], Maude Tournier[2], Clement Prati[1], Daniel Wendling[1], Céline Demougeot[2] and Frank Verhoeven[1], [1]Service de rhumatologie, CHU de Besançon, Besançon, France, [2]PEPITE EA4267, FHU INCREASE, Bourgogne Franche-Comté University, Besançon, France, [3]Service d'anatomopathologie, CHU de Besançon, Besançon, France

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

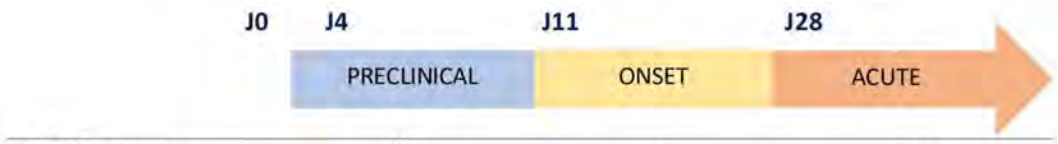
Session Time: 8:30AM–10:30AM

Background/Purpose: Intestinal inflammation (I-Inf) and increased intestinal permeability (IP) and intestinal damage (ID) have been observed in patients with spondyloarthritis (SpA). However, whether these changes might be causal or are the consequence of SpA is unknown. To answer this question, the present study investigated the time-course of I-Inf and IP in a rat model of reactive arthritis, a subgroup of SpA, the adjuvant-induced arthritis model.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by injection at the base of the tail of *Mycobacterium butyricum* in incomplete Freund's adjuvant (Day 0). Control rats received saline. I-Inf and IP were studied at 3 phases of arthritis: pre-arthritic phase (Day 4, AIA-preclinical), onset of arthritis (Day 11, AIA-onset) and acute inflammatory phase (Day 28, AIA-acute). IP was assessed by measuring plasma levels of zonulin (ELISA) and ileal mRNA expression of zonulin and occludin (RT-qPCR). Ileal inflammation was assessed by TCD4+ and TCD8+ lymphocyte count from rat ileum (immunohistochemistry) and by measuring ileal mRNA expression of IL-8, IL-33, IL-17, IL-23p19 and TNF-α (RT-qPCR). The integrity of the intestinal barrier was evaluated by measuring plasma levels of intestinal fatty acid binding protein (iFABP) by ELISA. Joint damage was assessed by determination of an arthritis score (Sa) and of a radiographic score (Sr) of hind paws.

Results: AIA induced arthritis symptoms beginning at day 11, leading to a severe clinical and radiographic arthritic disease at day 28 (Sa=3.9±1.0; Sr=23.8±8.1). Compared to control rats, plasma levels of zonulin increased at pre-clinical phase, at onset but not at the acute phase. While ileal zonulin mRNA expression was enhanced at the onset phase, no change in occludin mRNA expression was observed. Plasma levels of iFABP levels were increased in AIA rats at all stages of arthritis course. Regarding inflammation, preclinical phase was characterized by increased mRNA expression of IL-8, IL-33 and IL-17. At the onset phase, TNF-α, IL-23p19 and IL-8 mRNA expression were increased. No changes in cytokines mRNA expression were observed at the acute phase. Consistent with these findings, increased TCD4+ and TCD8+ number was measured in AIA ileum as compared to controls at Day 4 and Day D11. No correlation was found between clinical and radiographic arthritis scores and zonulin levels. A negative correlation was observed between intestinal IL-8 mRNA expression and Sa. A positive correlation was observed between Sa and the CD4 lymphocyte count.

Conclusion: Intestinal changes associated to reactive arthritis occurred prior the development of articular symptoms. These data are in favour of the "causative" hypothesis of intestinal changes in SpA.



Arthritis score	0	+	++
Radiographic score	0	+	++
Intestinal inflammation	++	++	0
Intestinal permeability	+	++	0
Alteration of intestinal integrity	+	++	++

Disclosure: S. Hecquet, None; **P. Totoson**, None; **M. Algros**, None; **H. Martin**, None; **C. Peyronnel**, None; **M. Tournier**, None; **C. Prati**, None; **D. Wendling**, None; **C. Demougeot**, None; **F. Verhoeven**, None.

Abstract Number: 0056

Peripheral Blood Immune Cell Profiling in Psoriatic Arthritis: Comparison of Patients with Healthy Controls

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Heterogeneity in immune cell populations among patients with psoriatic arthritis (PsA) may determine disease expression and treatment response. The objective of this study was to compare peripheral blood immune cell profiles in patients with PsA (before- and after- advanced therapy) and healthy controls using mass cytometry.

Methods: Patients with PsA who were initiating treatment with advanced therapies for active peripheral musculoskeletal disease were recruited along with healthy controls. We performed mass cytometry (CyTOF) using a panel of 30 metal-tagged antibodies (Maxpar Direct, Fluidigm) to characterize over 37 immune cell populations in whole blood from patients (before- and 3 months after therapy) and controls. The frequencies of the different immune cells populations were automatically quantified for each sample based on combinations of their associated canonical cellular markers using Probability State Modelling algorithms in a commercially available automated analysis system (MaxparPathsetter, Fluidigm). The levels (counts per 100 cells) of the different cell populations were compared between PsA patients vs. controls and among patients with PsA (before- and after- therapy) using Mann-Whitney U test and cluster analysis was performed using differential cell population levels.

Results: A total of 37 samples from 12 patients with PsA (14 treatment periods) and 9 controls were analyzed. In general, large variability was found in the different cell populations across patients with PsA, while the levels were more homogenous across the controls (Figure 1). Most variability was found in the lymphocytic cells populations, in

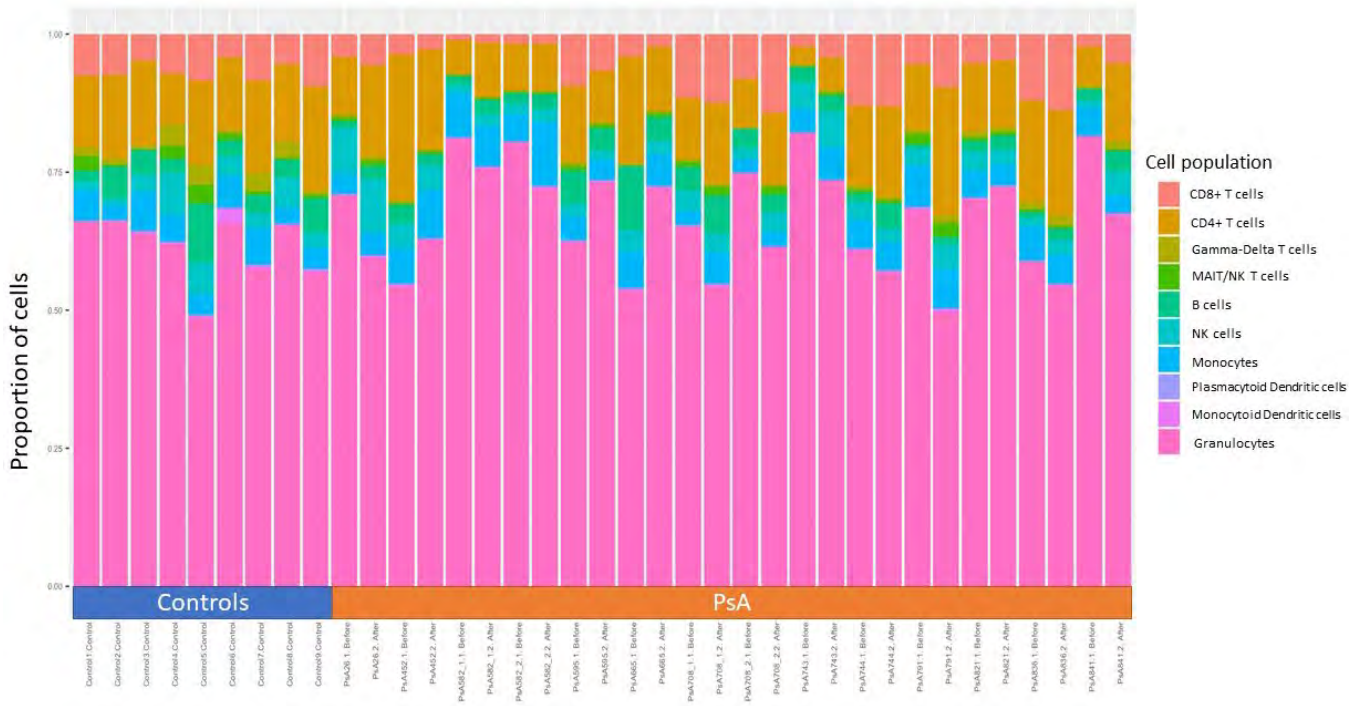

Figure 1. Distribution of the different immune cell populations in PsA and controls.

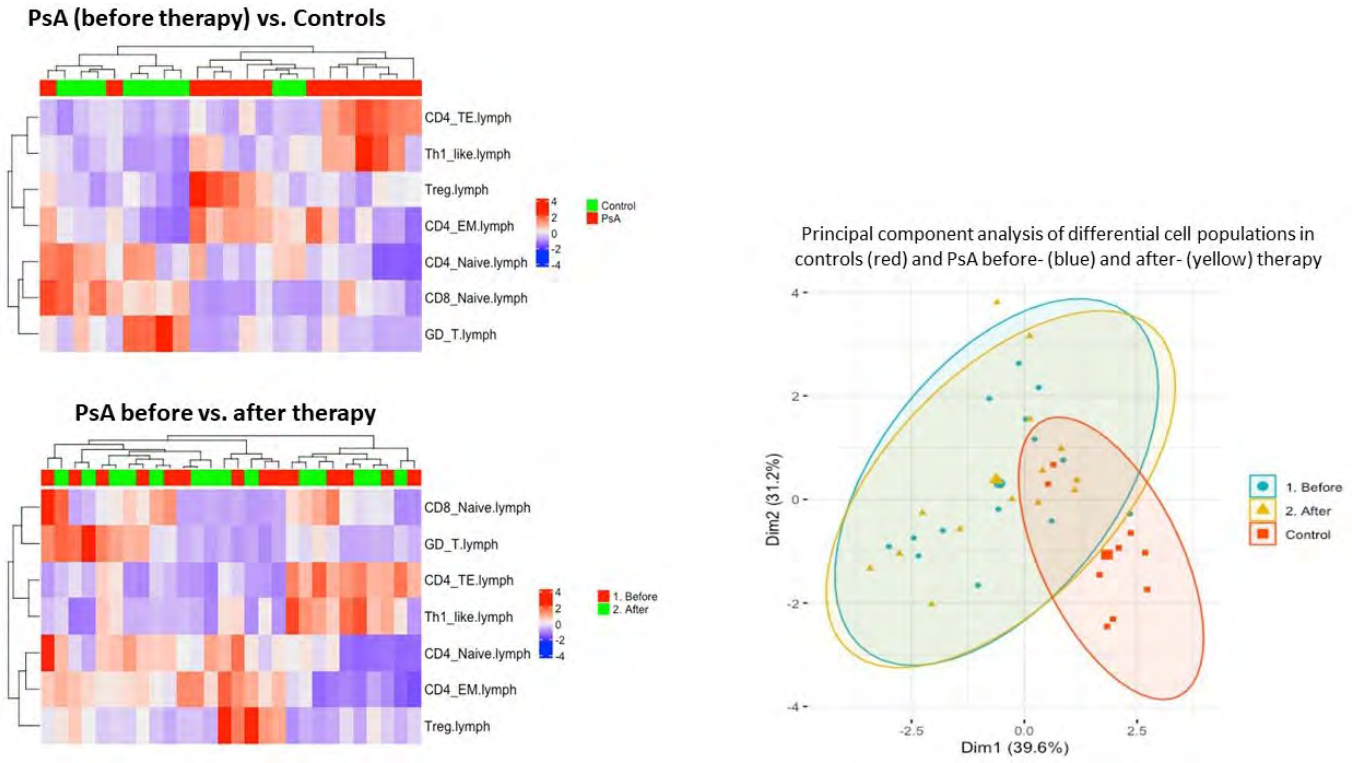

Figure 2. Clustering of PsA (before and after therapy) and controls of differential cell population levels.

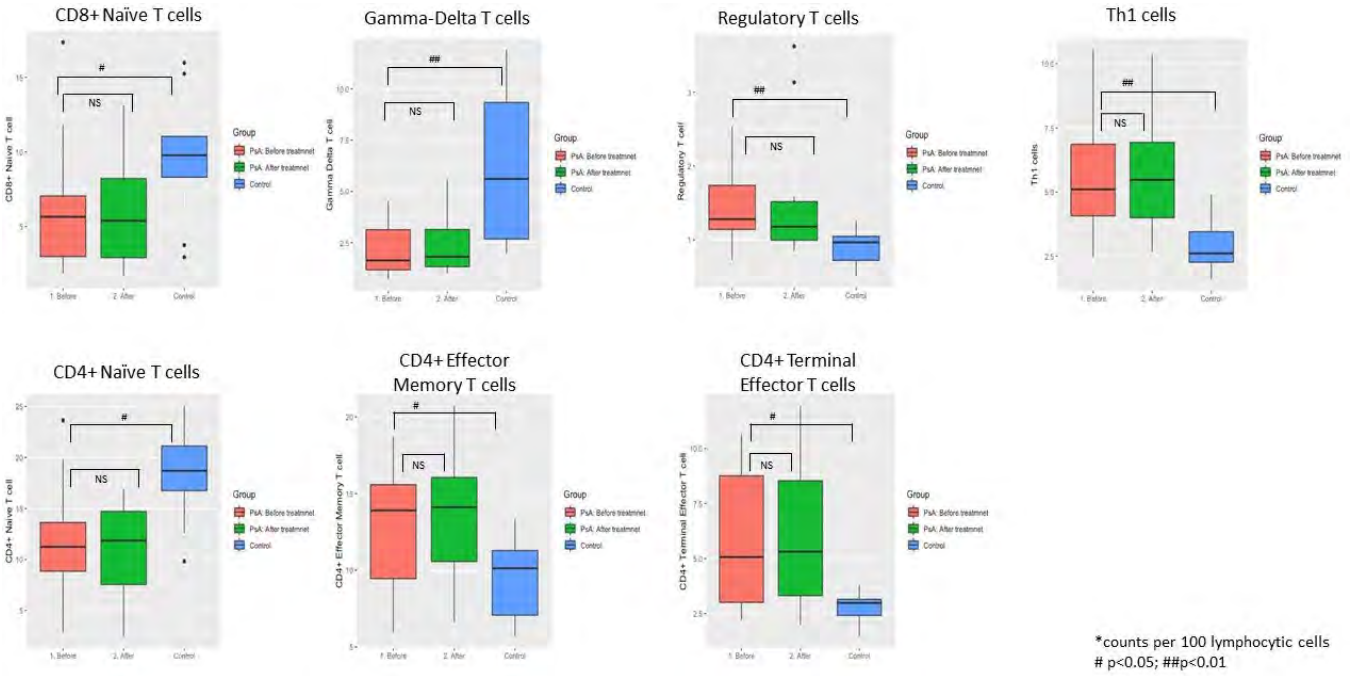

Figure 3. Differences in T cell sub-populations between PsA (before and after therapy) and controls*.

particular among the T cell sub-populations, thus the analysis was restricted to lymphocytic cells. We found significant differences in T cell sub-populations between PsA and controls (Figures 2). Patients with PsA had higher levels of CD4+ Terminal effector and CD4+ Effector memory T cells, CD4+ Th1 cells and CD4+ regulatory T cells, while higher levels of CD8+ and CD4+ Naïve T cells and gamma-delta T cells were found in controls (Figure 3). No significant differences were found in lymphocytic cell populations before and after advanced therapy. In addition, no significant differences were found in the levels of the following cell types and their sub populations between PsA vs. controls and among PsA patients before and after treatment: B cells, NK cells, granulocytes, monocytes and dendritic cells.

Conclusion: Considerable variability was found in T cell sub-populations among patients with PsA. Differences in the levels of specific T cell populations with a shift towards terminal and memory T cells as well as Th1 axis was seen in patients with PsA compared to control. Whether immune cell profile predict response to advanced therapy in PsA remains to be examined.

Disclosure: L. Eder, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5; **D. Ganatra**, None; **V. Chandran**, Abbvie, 1, 2, 5, Amgen, 1, 2, 5, Eli Lilly, 1, 2, 5, BMS, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, AstraZeneca, 12, Spousal employment, Celgene, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 0057

Molecular Profiling of Radiographic Axial Spondyloarthritis Patients Reveals an Association Between Innate and Adaptive Cell Populations and Therapeutic Response to Adalimumab

Rita Torres[1], Daniel Sobral[2], Ana Fernandes[3], Atlas Sardoo[4], Miguel Bernardes[5], Patrícia Pinto[6], Helena Santos[7], João Gomes[8], Jose Tavares-Costa[9], José Silva[10], João Dias[11], Alexandra Bernardo[5], Jean Gailard[12], Jean Armengaud[13], Vladimir Benes[14], Lúcia Domingues[15], Sara Maia[16], Jaime Branco[17], Ana Varela[18] and Fernando Santos[19], [1]Rheumatology Department, Hospital de Egas Moniz, Centro Hospitalar Lisboa Ocidental, Lisbon, Portugal, [2]Faculdade Ciências e Tecnologia, Lisboa, Lisboa, Portugal, [3]Instituto de Tecnologia Química e Biológica, Lisboa, Portugal, [4]CEDOC, NOVA Medical School, UNL, Lisboa, Lisboa, Portugal, [5]Rheumatology Department, Centro Hospitalar Universitário de São João EPE, Porto, Portugal, [6]Centro Hospitalar de Vila Nova de Gaia/Espinho, Vila Nova de Gaia, Portugal, [7]Portuguese Institute of Rheumatology, Lisbon, Portugal, [8]Hospital Egas Moniz, Lisboa, Lisboa, Portugal, [9]Rheumatology Department - Unidade Local de Saude do Alto Minho, Ponte de Lima, Portugal, [10]Centro Hospitalar e Universitário de Coimbra, Coimbra, Portugal, [11]Centro Hospitalar Médio Tejo, Abrantes, Portugal, [12]Centre dénergie atomique; Service de Pharmacologie et Immunoanalyse (SPI), Paris, France, [13]Service de Pharmacologie et Immunoanalyse (SPI), Paris, France, [14]The European Molecular Biology Laboratory, Heidelberg, Germany, [15]CEDOC - Chronic Diseases Research Center - Nova Medical School|Faculdade de Ciências Médicas, Lisboa, Lisboa, Portugal, [16]NOVA Medical School, Nova University of Lisbon, Lisboa, Lisboa, Portugal, [17]EpiDoC Unit, CEDOC, Nova Medical School, Comprehensive Health Research Centre (CHRC), Lisbon, Portugal, [18]Instituto Tecnologia Química e Biológica; Universidade NOVA de Lisboa, Lisboa, Lisboa, Portugal, [19]Hospital Egas Moniz, Lisboa, Portugal

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

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Session Time: 8:30AM–10:30AM

Background/Purpose: The response to treatment in spondylarthropaties is heterogeneous, due to factors yet to be better described. For that reason, it is important to find tools that might help clinicians to decide what is the best available therapeutic option for each patient.

The goal of this study is to use comprehensive molecular profiling to characterize clinical response to therapy in a real-world setting. Specifically, to identify molecular biomarkers differentiating good responders and non-responders to TNF inhibitors (TNFi) treatment, using adalimumab, in radiographic axial spondyloarthritis | ankylosing spondylitis (r-axSpA|AS) patients context.

Methods: Whole-blood mRNA and plasma proteins were measured in a cohort of biologic naïve r-axSpA|AS patients (n = 35) from the Bioefficacy study (Biomarkers identification of anti-TNF alpha agent efficacy in AS patients using RNA sequencing and mass spectrometry), pre and post (14 weeks) TNFi treatment using adalimumab. Response to treatment was categorized according to ASAS20. Results of differential expression analysis were used to identify the most enriched pathways and in predictive models to distinguish responses to TNFi.

Results: A treatment-related signature, independent of the type of response, suggests a reduction in inflammatory disease activity. We found genes and proteins robustly differentially expressed between baseline and week 14 in responders, including the GWAS AS-associated genes *TNFRSF1A, FCGR2A, TYK2, TBKBP1, IL1R1, IL6R, ICOSLG, IL7R, HHAT and LTBR*. Moreover, CRP and HP proteins showed strong and early decrease in the plasma of AS patients, while a cluster of apolipoproteins (APO1, APO2, APO3) showed an increased expression at week 14. Good responders to TNFi treatment tend to have higher expression of innate immunity genes at baseline, and lower expression of markers associated with adaptive immunity, particularly B-cells. A logistic regression model incorporating

ASDAS-CRP, gender and *Gene x*, the top differentially expressed gene at baseline between responders and non-responders, enabled an accurate prediction of response to adalimumab in our cohort (AUC=0.97).

Conclusion: Differences in disease activity and/or innate/adaptive immune cell type composition at baseline may be a major contributor to response to adalimumab in r-axSpA|AS. Alternatively, a model including clinical and gene expression variables could be considered, particularly in patients with mild disease activity.

Disclosure: R. Torres, None; **D. Sobral**, None; **A. Fernandes**, None; **A. Sardoo**, None; **M. Bernardes**, Lilly, 1, Janssen, 1, Abbvie, 1; **P. Pinto**, None; **H. Santos**, None; **J. Gomes**, None; **J. Tavares-Costa**, None; **J. Silva**, None; **J. Dias**, None; **A. Bernardo**, None; **J. Gailard**, None; **J. Armengaud**, None; **V. Benes**, None; **L. Domingues**, None; **S. Maia**, None; **J. Branco**, None; **A. Varela**, None; **F. Santos**, None.

Abstract Number: 0058

Effect of Anti-inflammatory Drugs on Intestinal Epithelial Damage and Bacterial Translocation in the Adjuvant-induced Arthritis Model

Sophie Hecquet[1], Perle Totoson[2], Maude Tournier[2], Clement Prati[1], Daniel Wendling[1], Céline Demougeot[2] and Frank Verhoeven[1], [1]Service de rhumatologie, CHU de Besançon, Besançon, France, [2]PEPITE EA4267, FHU INCREASE, Bourgogne Franche-Comté University, Besançon, France

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The intestine is no longer considered as an organ targeted by spondyloarthritis (SpA) but also an actor of the disease alongside environmental and immunological phenomena. In patients with SpA, increased intestinal permeability (IP) and bacterial translocation (BT) has been described. Whereas anti-inflammatory drugs (non- steroidal anti-inflammatory drugs, NSAIDs, or glucocorticoids, GCs) are known to induce deleterious intestinal changes in the general population, their effects in case of arthritis have been poorly studied. This aim of this study was to determine the effect of NSAIDs and GC on bacterial translocation and intestinal integrity in rats with adjuvant-induced arthritis (AIA).

Methods: AIA was induced in 6-week-old male Lewis rats by injection at the base of the tail of *Mycobacterium butyricum* in incomplete Freund's adjuvant. At first signs of arthritis, rats were treated daily with naproxen (10 mg/kg/day, i.p.), diclofenac (5mg/kg twice daily, i.p.), celecoxib (3 mg/kg/day, i.p.), prednisolone (10 mg/kg/day, i.p.) or vehicle (saline). After 21 days of treatment, intestinal damage was assessed by measure of plasma levels of intestinal Fatty Acid Binding Protein (iFABP, ELISA) and bacterial translocation by measure of serum levels of soluble CD14 (sCD14, ELISA). Joint damage was assessed by the determination of an arthritis score (Sa).

Results: Compared to vehicle, all treatments reduced arthritis score in AIA rats ($p< 0.05$). Compared to AIA-vehicle, treatment with prednisolone and naproxen significantly decreased both circulating iFABP and sCD14 levels. Celecoxib decreased sCD14 but had no effect on iFABP levels. Diclofenac changed neither sCD14 nor iFABP levels.

Conclusion: This study demonstrated that NSAIDs and GC induced changes in intestinal damage and bacterial translocation in arthritis. Contrary to what is observed in healthy population, none anti-inflammatory drug enhanced intestinal damage or bacterial translocation but on the contrary, prednisolone and naproxen decreased these two

parameters. Of interest, our data showed that the effect of NSAIDs is not a class-effect but depends on the balance of cyclooxygenase 1/2 inhibition.

Disclosure: S. Hecquet, None; **P. Totoson**, None; **M. Tournier**, None; **C. Prati**, None; **D. Wendling**, None; **C. Demougeot**, None; **F. Verhoeven**, None.

Abstract Number: 0059

Deep Immune Cell Profiling of Tissue Microenvironment Using Imaging Mass Cytometry in Psoriatic Disease

Lihi Eder[1], Stephane Caucheteux[1], Somi Afiuni[2], Adriana Krizova[1], James Limacher[1], Hartland Jackson[1] and Vincent Piguet[1], [1]University of Toronto, Toronto, ON, Canada, [2]Lunenfeld Tanenbaum Research Institute, Sinai Health System, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cross talk between different cell types, such as T cell subsets and other immune cell populations, is important in psoriatic disease. Imaging Mass Cytometry (IMC) is a novel technology that enables comprehensive analysis of cellular phenotypes and their interrelationships at the tissue level. We performed a multi-parameter

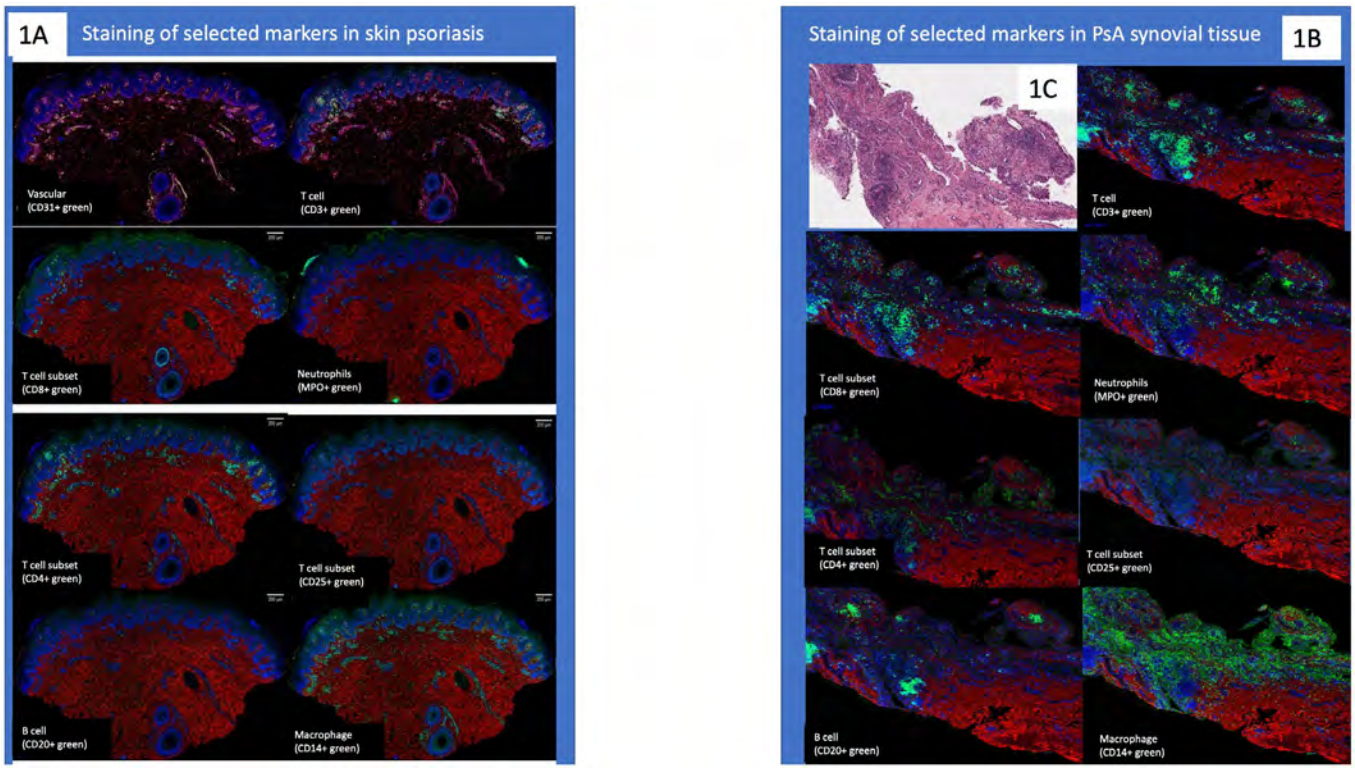

Figure 1. Staining of selected cellular markers using imaging mass cytometry in skin psoriasis (1A) and PsA synovial tissue (1B). Red=Collagen, blue=DNA and green=selected marker. (1C). H&E staining of the same synovial section.

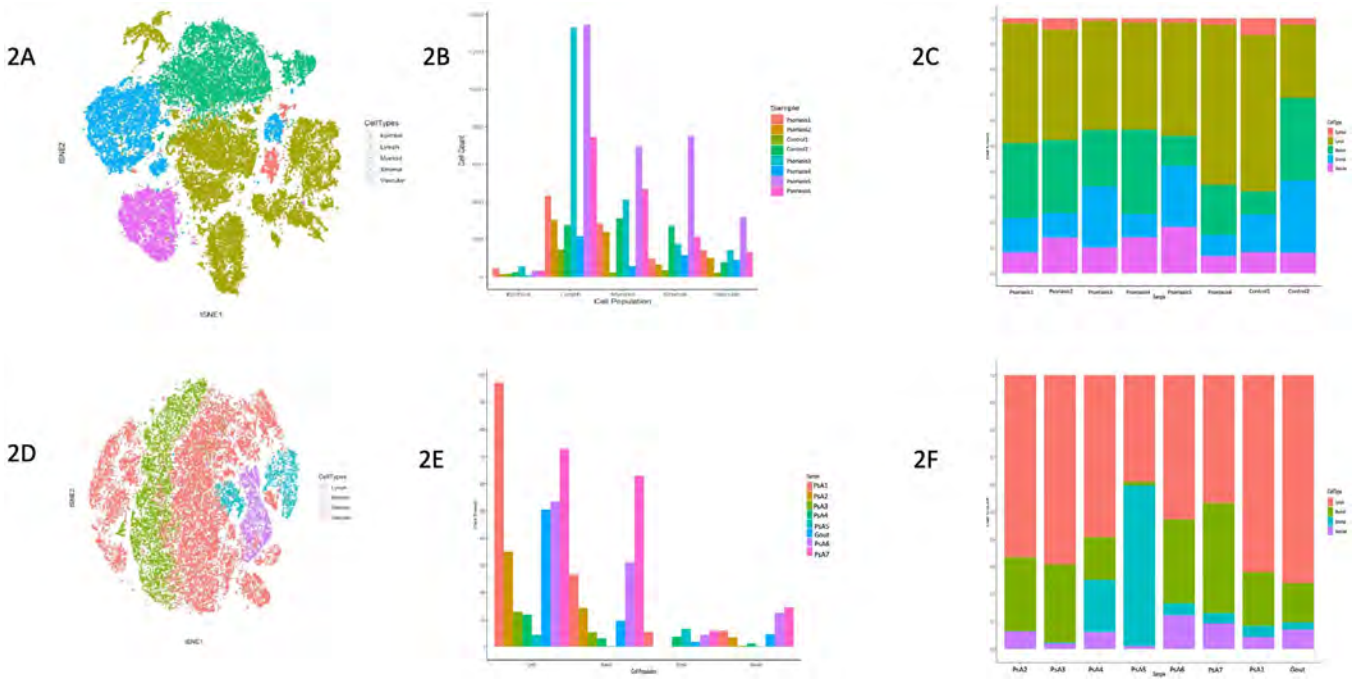

Figure 2. Immune and non-immune cells in skin and synovial tissue in patients with psoriasis and PsA. 2A t-SNE plot of all cell types in psoriasis skin; 2B Distribution of cell population counts in psoriasis skin samples; 2C Proportion of the various cell population types in psoriasis skin samples; 2D t-SNE plot of all cell types in PsA synovium; 2E Distribution of cell population counts in PsA synovium samples; 2F Proportion of the various cell population types in PsA synovial samples.

characterization of various immune cell populations and assessed their spatial interactions in skin and synovial tissue samples from patients with psoriatic disease.

Methods: A total of 6 skin and 7 synovial formalin-fixed, paraffin embedded samples from patients with plaque psoriasis and psoriatic arthritis (PsA), respectively, were analyzed. Additionally, 1 synovial sample from a gout patients and a skin sample from a control patient were analyzed. We used a panel of 36 of metal-tagged antibodies to stain different cell populations. IMC was performed using the Hyperion Imaging System (Fluidigm). Tissue of 5-μm thickness was ablated with Nd:YAG 213 mm laser and analyzed in a Fluidigm CyTOF mass cytometer. Images were analyzed using MCD Viewer. Data were converted to TIFF format and segmented into single cells using previously developed methods. Individual cells were segmented using a combination of in-house program and CellProfiler to classify pixels on the basis of a combination of antibody stains to identify membranes and nuclei. The maps were then segmented into single-cell object masks using CellProfiler. Cell were classified into cell categories based on pre-specified markers (epithelial, vascular, stromal, myeloid and lymphoid) and further classified into immune cells types (T cell, macrophage, B cell, neutrophils, plasma cells). Single-cell marker expressions were summarized by mean pixel values for each channel. To visualize the number of cells per image the cell counts were normalized by the image area (total number of pixels) and displayed as cell density.

Results: Markers identifying stromal and immune cell types performed well and correlated with the expected location and morphological features of the various cell types (Figure 1). Among all cell types in the skin and synovium, lymphoid cells accounted for the most prevalent cell type followed by myeloid cells (Figure 2A-2B). Large degree of inter-patient heterogeneity was found in the prevalence of the various immune cell population across the different skin and synovial samples (Figure 3A-3B). T cells accounted for the largest immune cell type in both skin and synovial samples followed by macrophages and lower counts of neutrophils, B cells and plasma cells. Neighborhood analysis

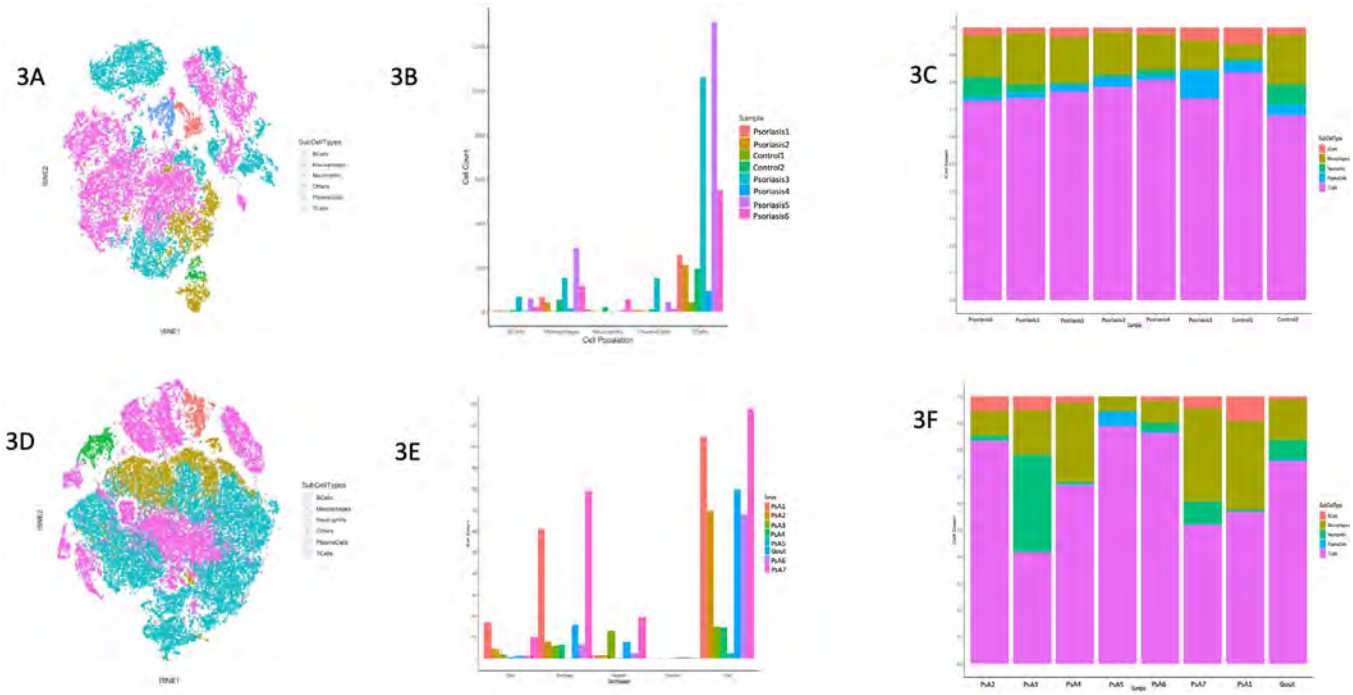

Figure 3. Immune cells in skin and synovial tissue in patients with psoriasis and PsA. 3A t-SNE plot of immune types in psoriasis skin; 3B Distribution of immune cell population counts in psoriasis skin samples; 3C Proportion of various immune cell population types in psoriasis skin samples; 3D t-SNE plot of all cell types in PsA synovium; 3E Distribution of cell population counts in PsA synovium samples; 3F Proportion of the various cell population types in PsA synovial samples.

showed high correlation between CD20+, CD3+, CD4+ and CD8+ in the synovial tissue, which suggest close physical proximity and cross-talk between these T cell subsets and B cells in the synovium.

Conclusion: Innate and adaptive immune cells can be reliably identified using IMC in skin and synovial tissue. Cross talk between T cell subsets and innate immune cells in the skin and synovial tissue plays a role in psoriatic disease. IMC technology provides opportunities for exploring the underlying mechanisms driving psoriasis and PsA.

Disclosure: L. Eder, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5; **S. Caucheteux**, None; **S. Afiuni**, None; **A. Krizova**, None; **J. Limacher**, Sanofi Genzyme, 2; **H. Jackson**, GlaxoSmithKline, 7, Fluidigm, 6, Abcam, 12, Collaboration; **V. Piguet**, None.

Abstract Number: 0060

Lipidomic Profiling Identifies Different Expression of Oxylipins Between Synovial Tissue and Plasma of Patients with Rheumatoid and Psoriatic Arthritis

Abha Singh[1], Jessica Murillo Saich[2], **Roxana Coras**[3], Julio Ramirez[4], Eric Chang[2], Raquel Celis[5], Aaron Armando[2], Oswald Quehenberger[2], Arthur Kavanaugh[2], Juan D Cañete[6] and Monica Guma[7], [1]University of California San Diego, San Diego, CA, [2]University of California San Diego, La Jolla, CA, [3]University of California San Diego/Department of Medicine, Autonomous University of Barcelona, San Diego, CA, [4]Arthritis Unit, Rheumatology Department, Hospital Clinic and IDIBAPS, Barcelona, Spain, [5]Hospital Clinic and IDIBAPS, Barcelona, Spain, [6]Rheumatology Department, Hospital Clinic, Barcelona, Spain, [7]University of California San Diego/San Diego VA Healthcare Service/Department of Medicine, Autonomous University of Barcelona, La Jolla, CA

SESSION INFORMATION

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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Oxylipins are bioactive lipids derived from polyunsaturated fatty acids (PUFAs) that modulate inflammation. Oxylipins derived from n-6 PUFA precursors, such as arachidonic acid (AA), linoleic acid (LA), and dihomo-ylinolinic acid (DGLA), are known for their proinflammatory effects. Oxylipins, derived from the n-3 PUFA precursors such as decosahexanoic acid (DHA), eicosapentanoic acid (EPA), and α-linoleic acid (ALA), have inflammation resolving properties. Several studies have suggested that these mediators in plasma might be biomarkers of synovial pathology. The goal of this study is to evaluate the expression of oxylipins in synovial biopsies obtained from patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA), and correlate oxylipin levels between synovial tissue and plasma.

Methods: Thirteen patients with established RA and 11 patients with established PsA with active disease in at least one knee or one wrist were recruited, and synovial tissue (ST) was collected by either arthroscopy or ultrasound-guided synovial biopsy. 9 patients with RA and 8 patients with PsA had blood collected at the time of the procedure. Oxylipins in plasma and ST were determined by liquid chromatography with tandem mass spectrometry (LC-MS-MS) and were classified into groups according to their precursor: AA, LA, ALA, DHA, EPA and DGLA. The levels of oxylipins are expressed in pmoles/ml. Data were analyzed using SPSS v27.0 Results were considered significant if the 2-sided P value was less than 0.05.

Results: We included a total of 24 ST and 17 plasma samples. A total of seventy-five oxylipins where identified in ST but only 39 were identified in plasma (Figure 1). While most of the proinflammatory AA-derived oxylipins were detected in both synovial tissue and plasma, several of the anti-inflammatory EPA- DHA- and LA-derived oxylipins

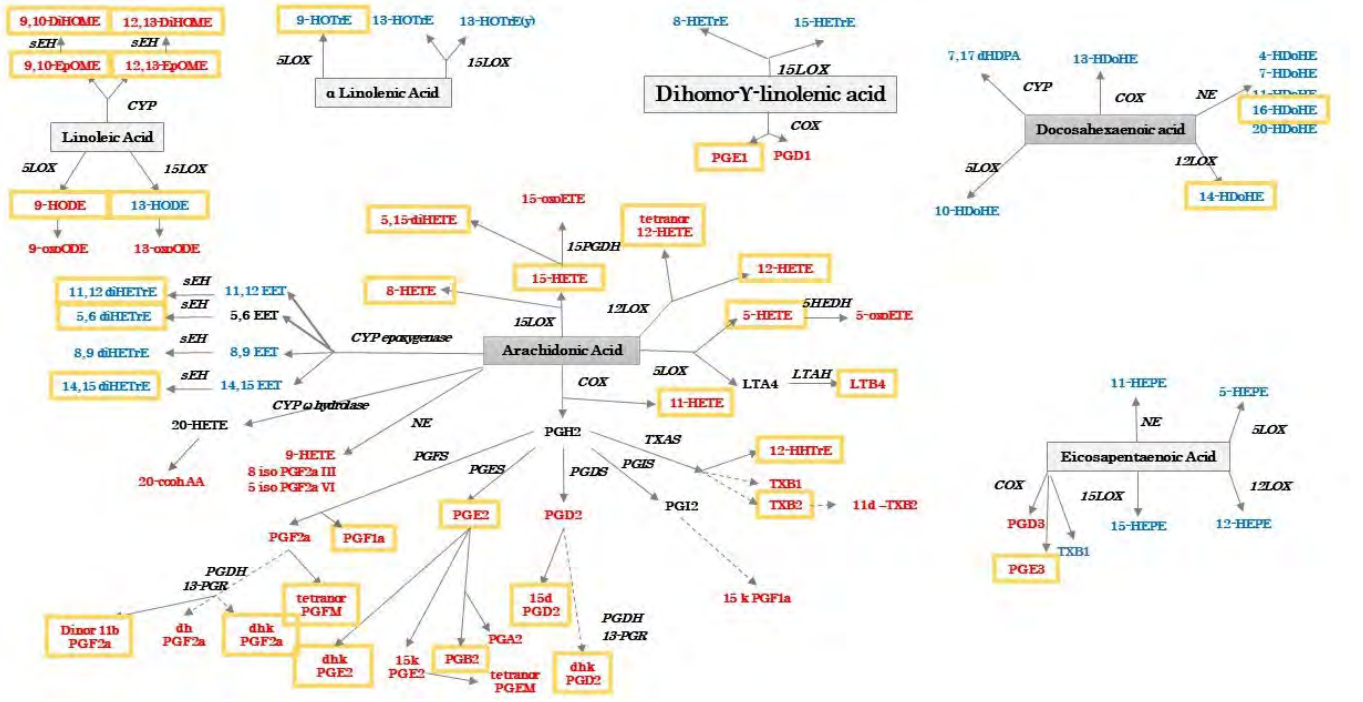


Figure 1. Oxylipins expressed in synovial tissue (n=24). Proinflammatory oxylipins are marked in red and oxylipins associated with resolution of inflammation are marked in blue. In italic, key enzymes involved in oxylipin metabolism. Only 39 oxylipins (in yellow box) were also found in plasma (n=17).

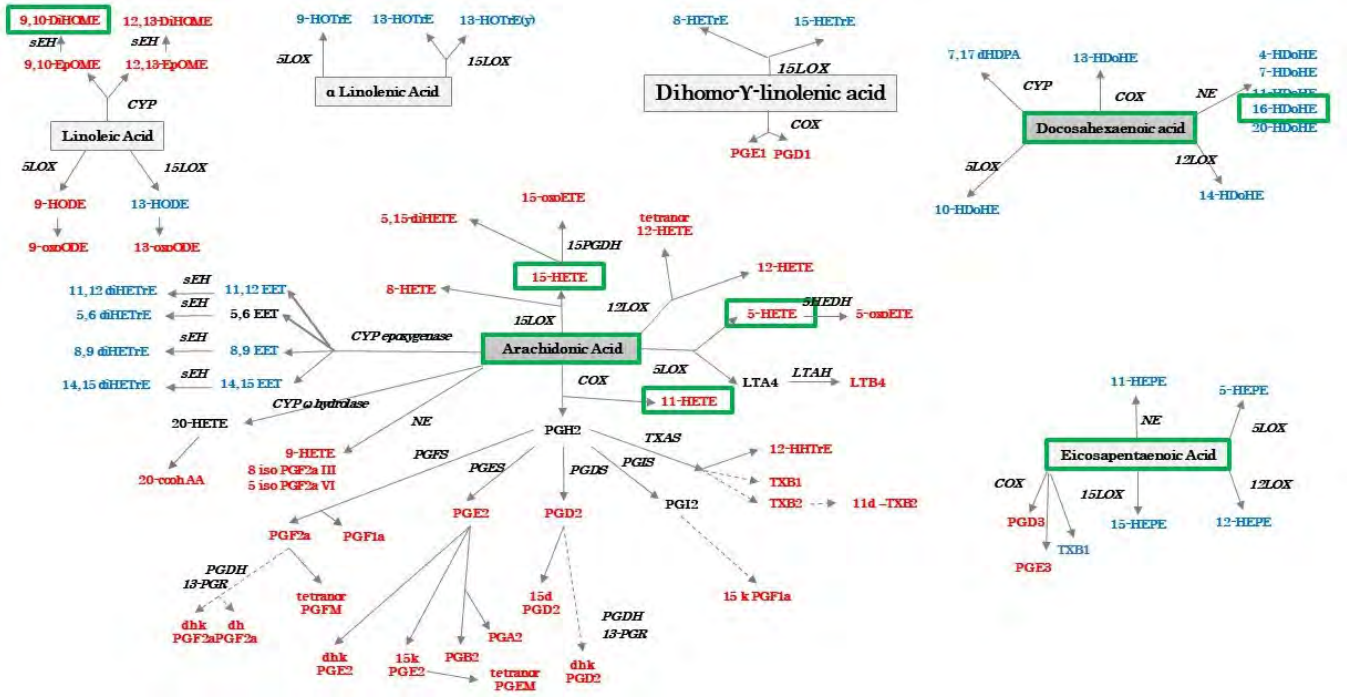


Figure 2. Pearson correlation of oxylipins between synovial tissue and plasma (n=17). Proinflammatory oxylipins are marked in red and oxylipins associated with resolution of inflammation are marked in blue. In italic, key enzymes involved in oxylipin metabolism. Oxylipins with a statistically significant Pearson correlation between ST and plasma are highlighted with a green box.

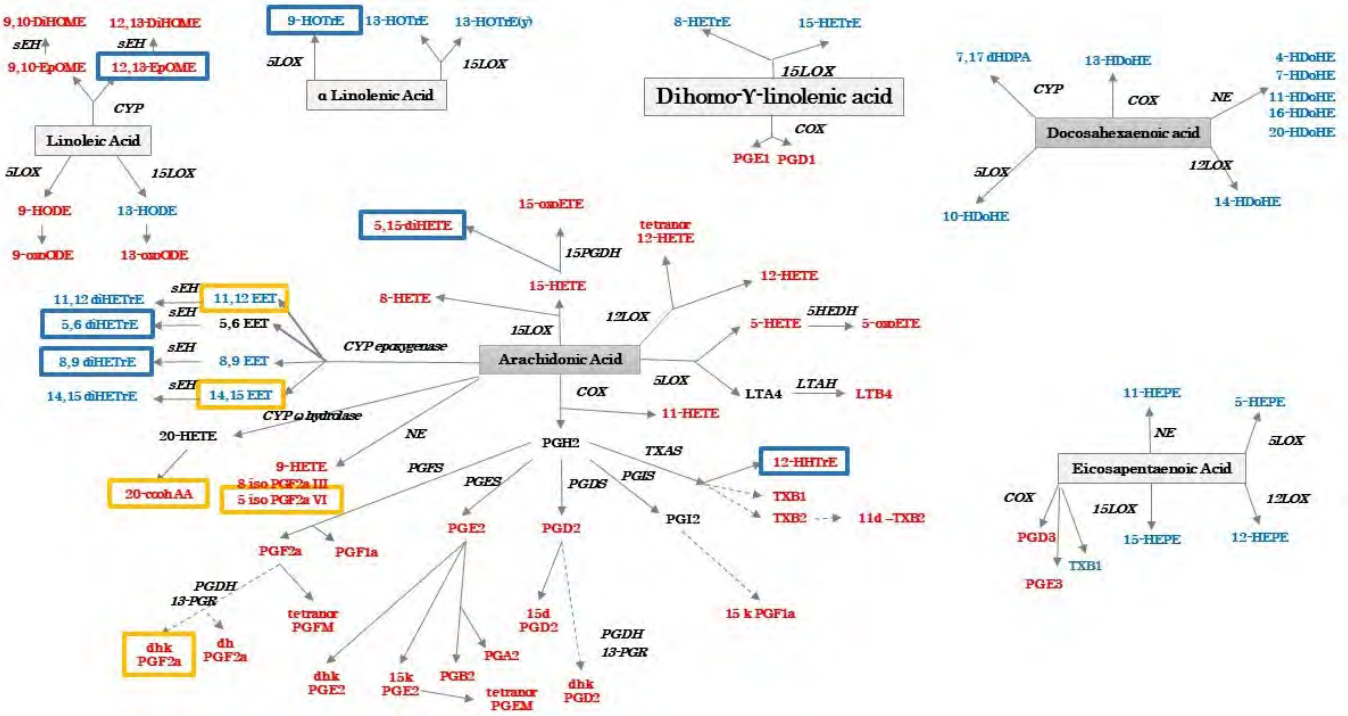


Figure 3. Oxylipin profile in ST from RA and PsA patients. Proinflammatory oxylipins are marked in red and oxylipins associated with resolution of inflammation are marked in blue. In italic, key enzymes involved in oxylipin metabolism. Oxylipins, whose level were higher in RA than PsA are highlighted with a yellow box, whereas the ones whose levels are higher in PsA than RA are highlighted with a blue box.

were only detected in ST (Figure 1). Only levels of 11-HETE, 5-HETE, 15-HETE, 9,10-DiHOME and 16-HDoHE had a statistically significant positive correlation between plasma and ST (Figure 2). In addition, while several oxylipins were different in ST between RA and PsA patients (Figure 3) only the levels of 9-HOTrE and 5,15-diHETE were different between both diseases in plasma.

Conclusion: Lipidomic profiling detected almost twice the number of oxylipin species in synovial tissue as compared with plasma. More importantly, levels of only a few oxylipins correlated between plasma and synovial tissue. This work suggests that lipidomic profiling in synovial tissue can more accurately identify biomarkers than in plasma. Further studies with early, non-treated arthritis patients are needed to determine whether lipidomic profiling of synovial tissue can identify new therapeutic targets in inflammatory arthritis.

Disclosure: A. Singh, Novartis, 5, Pfizer, 5; **J. Murillo Saich**, None; **R. Coras**, None; **J. Ramirez**, None; **E. Chang**, None; **R. Celis**, None; **A. Armando**, None; **O. Quehenberger**, None; **A. Kavanaugh**, AbbVie, 5, 12, Expert advice, Amgen, 5, 12, Expert advice, Bristol Myers Squibb, 5, 12, Expert advice, Janssen, 5, 12, Expert advice, Pfizer, 5, 12, Expert advice, UCB, 5, 12, Expert advice, AstraZeneca, 5, 12, Expert advice, Celgene, 5, 12, Expert advice, Roche, 5, 12, Expert advice, Novartis, 5; **J. Cañete**, Abbvie, 6, Pfizer, 6, Janssen, 6; **M. Guma**, novartis, 5, pfizer, 5, gilled, 5, genentech, 6.

Abstract Number: 0061

Harnessing Spatially-Resolved Gene Expression to Characterize the Transcriptional Landscape of Psoriatic Skin

Rochelle Castillo[1], Ikjot Sidhu[1], Di Yan[1], Piotr Konieczny[1], Rebecca Haberman[1], Brandon Hsieh[1], Andrea Neimann[1], Shruti Naik[1] and Jose Scher[2], [1]NYU Langone Health, New York, NY, [2]New York University School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The skin is recognized as a window into the immunopathogenic mechanisms in the psoriatic arthritis (PsA) joint. This is evidenced by the fact that skin disease precedes joint involvement in ~90% of PsA patients and by the greater degree of overlap between gene expression in the synovial tissue of PsA and lesional skin in psoriasis (PsO) compared to synovium in other forms of inflammatory arthritis.[1] Thus, the study of the psoriatic skin transcriptome has the potential to yield revolutionary insights into the immunopathogenesis of PsA. Spatial transcriptomics (ST) is a ground-breaking technology that allows for mRNA sequencing from histologically-intact tissue sections, facilitating precise localization of the site of gene expression (Fig. 1). A platform for ST (Visium Spatial Gene Expression Solution by 10X Genomics) has been made available; however, it remains to be optimized for human skin tissue, which is inherently challenging to use in transcriptomic studies due in part to its preponderance of RNAses.[2,3] To date, there are no published studies on ST in either healthy or psoriatic human skin. Through a multidisciplinary collaboration, we have successfully optimized both healthy and psoriatic human skin tissue for use with ST.

Methods: Workflow

1. Skin biopsy
2. Cryopreservation

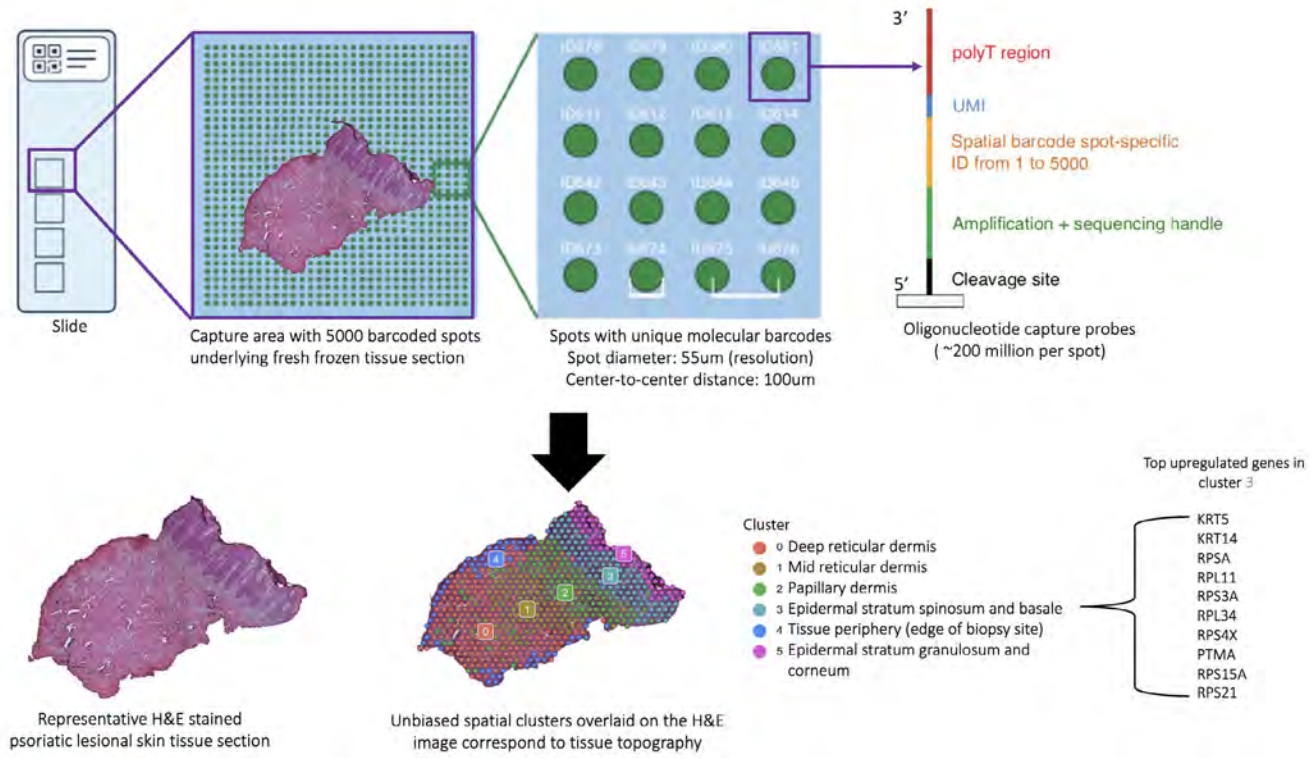


Figure 1. Overview of spatial transcriptomics. The spatial transcriptomics platform utilizes a slide containing four capture areas, each with 5000 molecularly barcoded, spatially encoded spots over which an intact fresh frozen tissue section is placed, stained, imaged, and permeabilized. Permeabilization results in the release of mRNA transcripts from the tissue that are then captured by ~200 million oligonucleotide capture probes. The unique spatial barcode allows the transcripts to be mapped to their exact location in the tissue section. Imaging and RNA sequencing data are processed together, resulting in whole transcriptome gene expression mapped to the tissue image. Each generated spatial cluster represents unbiased grouping based on gene expression and should ideally correlate with tissue topography. Gene expression in each cluster can then be explored.

3. Sectioning and staining
4. Confirmation of RNA integrity
5. Optimization of permeabilization
6. Sequencing
7. Data analysis

Results: To date, we have accrued samples from 3 controls, 4 PsA patients, and 6 PsO patients. All samples met the platform's quality control (QC) metrics for spots and mapping, with reads in spots under tissue >50% (range: 63.1 to 87.1) and reads mapped confidently to exonic regions >30% (range: 80.1 to 91.5). The expected biological variation in transcriptional activity as evidenced by molecular counts (which correlate strongly with unique genes)[4] across disease states and tissue regions was observed, with gene expression strikingly greater in the cell-dense epidermis and in appendageal structures than in the dermis and in psoriatic lesional skin compared to non-lesional and control skin (Fig. 2A). To detect technical variation, two contiguous sections from the same control sample were run on separate slides (Fig. 2B). Clustering and the Uniform Manifold Approximation and Projection (UMAP) plot architecture were consistent between the two replicates. Importantly, accuracy of spatial localization of gene expression and biological consistency of unbiased clustering was observed, with concordance of histopathologically annotated regions with gene-expression based clustering (Fig. 3).

Conclusion: Successful optimization of both healthy and psoriatic human skin tissue for ST was achieved, with all samples meeting the platform's QC metrics. The expected biological variance in transcriptional activity across tissue

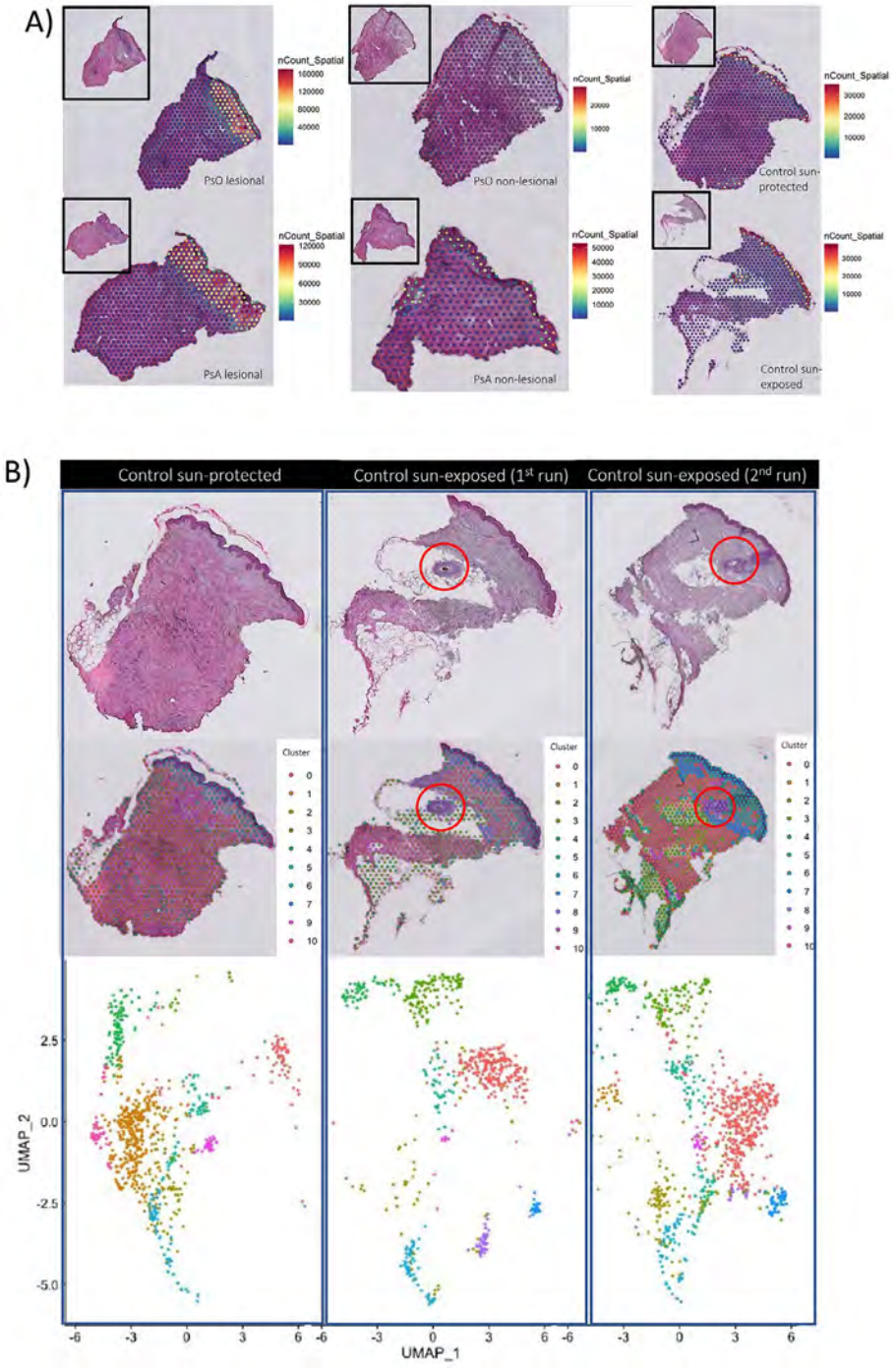
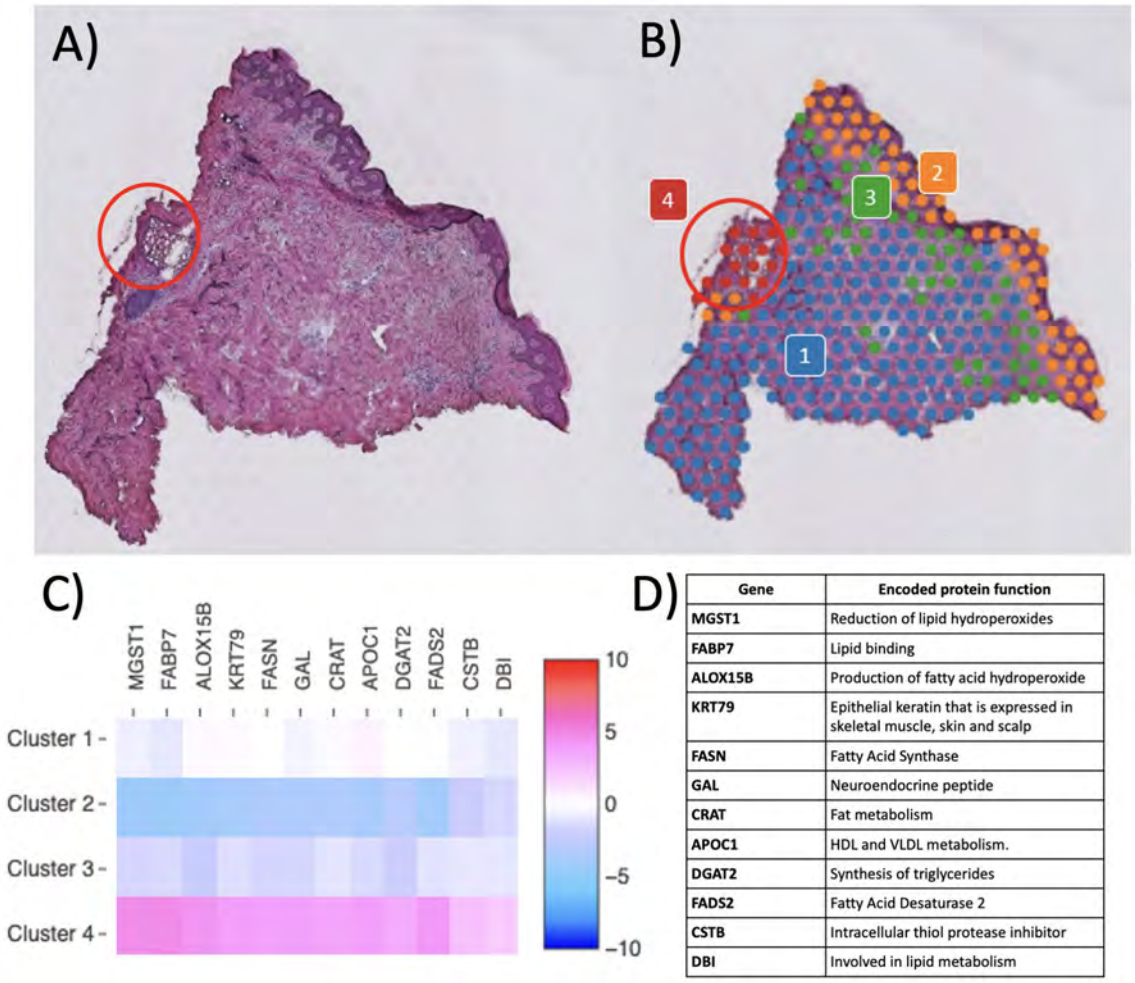


Figure 2. Transcriptional activity and reproducibility of spatial transcriptomics in control (non-psoriatic) and psoriatic skin. A.) Molecular counts mapped to each spot across disease states (psoriatic lesional, non-lesional, control) and tissue regions. Across all disease states, the epidermis and appendageal structures (hair follicles, sebaceous glands) were found to be more transcriptionally active than the dermis, consistent with the much higher cell density in these regions compared to the dermis, which consists mostly of collagen and elastic fibers and ground substance. Lesional skin from PsO and PsA patients was strikingly more transcriptionally active than non-lesional skin and control skin, which is consistent with epidermal hyperproliferation characteristic of psoriatic disease. B.) Determining reproducibility across runs. To detect technical variation, two contiguous sections from the same control sun-exposed skin sample (center and right panel) were run on the ST platform on separate slides. For comparison, results from a separate control sample are also shown (left panel). All three sections were computationally merged to render the clusters comparable. Identical clusters (middle row) and largely similar overall UMAP plot architecture (bottom row) was noted, save for an increase in the density of spots in the second run, which can be attributed to an increase in the volume of tissue overlying the spots. Of note, cluster 8, which contains the hair follicle (encircled in red), does not appear in the control sun-protected sample, which is devoid of hair follicles, and supports accuracy of spatial localization of gene expression.



Gene	Encoded protein function
MGST1	Reduction of lipid hydroperoxides
FABP7	Lipid binding
ALOX15B	Production of fatty acid hydroperoxide
KRT79	Epithelial keratin that is expressed in skeletal muscle, skin and scalp
FASN	Fatty Acid Synthase
GAL	Neuroendocrine peptide
CRAT	Fat metabolism
APOC1	HDL and VLDL metabolism.
DGAT2	Synthesis of triglycerides
FADS2	Fatty Acid Desaturase 2
CSTB	Intracellular thiol protease inhibitor
DBI	Involved in lipid metabolism

Figure 3. Concordance of histopathologic annotation with unbiased gene expression-based clustering. A.) H&E stained non-lesional skin section with sebaceous gland manually annotated (encircled in red). B.) Unbiased clustering of spots by gene expression results in unique segregation of sebaceous gland region (Cluster 4) (k means=4). C.) Heatmap of top globally differentially expressed genes (DEG) in the cluster containing the sebaceous glands (Cluster 4). D.) Description of DEG in cluster containing the sebaceous glands. The vast majority are involved in the metabolism of various lipids such as cholesterol, fatty acids, triglycerides which make up sebum, the production and secretion of which is the primary function of sebaceous glands.

regions and disease states was noted, the quantity, quality, and location of reads was biologically consistent, and there was no technical variation between samples. Thus, spatial profiling of gene expression in psoriatic skin through spatial transcriptomics can be performed and has the potential to offer invaluable insights into the immunopathogenesis of psoriatic disease.

Disclosure: R. Castillo, None; **I. Sidhu**, None; **D. Yan**, None; **P. Konieczny**, None; **R. Haberman**, Janssen, 1; **B. Hsieh**, None; **A. Neimann**, BMS, 12, Advisory Board, Celgene, 12, Advisory Board, Abbot, 11, Abbvie, 11, janssen, 11, Pfizer, 11; **S. Naik**, Seed Health, Inc, 1; **J. Scher**, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, AbbVie, 2, Sanofi, 2, Kaleido, 2, UCB, 2.

Abstract Number: 0062

Axial Spondyloarthritis and Its Related Immune-Mediated Diseases Share a Gut Microbiome Signature Besides Their Own Distinctive Profile

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Deep profiling of gut microbiota may reveal new pathways of how SpA and its related diseases such as Crohn's disease (CD) and acute anterior uveitis (AAU) are initiated and perpetuated. The aim of our study was to characterize a shared gut microbiota signature for SpA and its related diseases, as well as for each individual disease, compared with individual controls.

Methods: Patients were recruited with a definite diagnosis of axial SpA, AAU or CD, and were compared with controls (patients with back pain and previously ruled out SpA/CD/AAU diagnosis). Fecal samples were collected, and microbiota composition was determined by 16S rRNA gene sequencing, followed by computational analysis using the LotuS pipeline (v1.62) and referencing the taxonomic classification by the SILVA (v138), Greengenes (v13.5) and HITdb (v1.0.0) databases. Nonparametric Wilcoxon tests were used to calculate differential abundances between binary groups, and the Spearman correlation was used with continuous covariates. Nested linear models and likelihood ratio tests were used to assess confounding with respect to patient characteristics, HLA-B27 expression, inflammatory markers, and the presence of other immune-mediated diseases.

Results: A total of 300 patients were recruited for the study: 111 axial SpA, 110 AAU, and 79 CD patients and were compared with 63 control individuals. The average age was 39.1±12.3 years (mean±SD) and 53% were males. The prevalence of HLA-B27 was 63.0% by all patients (87.4% in axial SpA, 77.3% in AAU and 8.9% in CD patients) compared to 7.9% by control individuals.

At the phylum level, patients with axial SpA, AAU and CD were dominated by Firmicutes, followed by Bacteroidetes and Actinobacteria, except for CD patients who were richer in Proteobacteria than Actinobacteria. At the genus level, patients displayed a shared gut microbiome signature differing from that of control individuals including enrichments in *Veillonella* and *Lactobacillus* (that correlated with increased CRP) and a strong depletion of *Blautia* and other Firmicutes such as *Fusicatenibacter*, *Lachnospiraceae FCS020* and *Roseburia*. By looking at each separate disease phenotype, CD patients differed significantly from the control individuals with respect to many genera. These primarily consisted of depletions in Clostridiales (*Roseburia*, *Coprococcus*, *Ruminococcaceae*), and enrichments of pathogen-harboring genera such as *Escherichia-Shigella* and *Fusobacterium*. Axial SpA patients were uniquely enriched in *Collinsella* and depleted in *Cupriavidus*. HLA-B27+ individuals were enriched in several Firmicutes, most

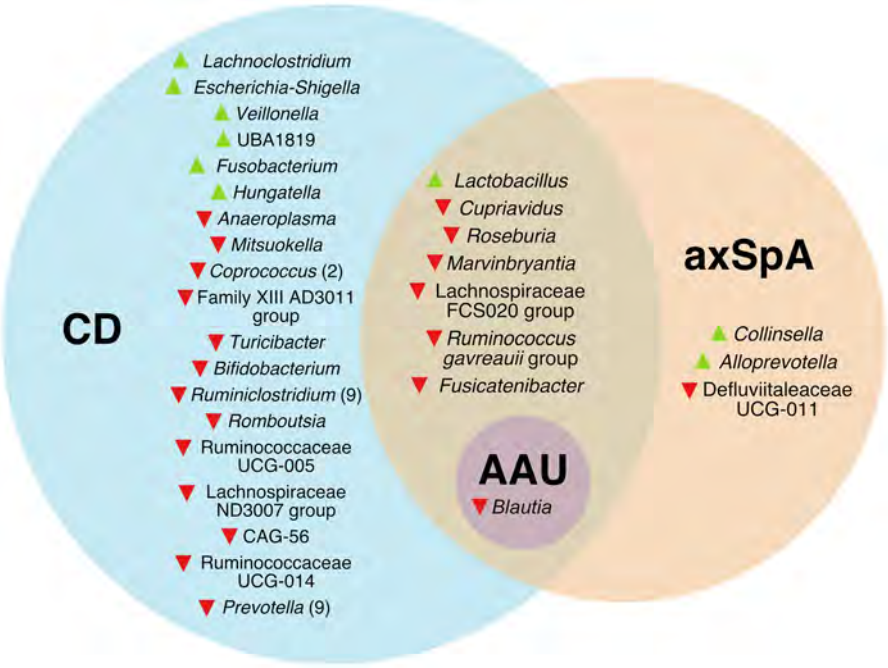

Figure 1. Taxa associations within and between the groups resulting from comparing each with the control group and accounting for disease concomitance and patient characteristics (FDR ≤ 0.05). AAU, anterior acute uveitis; CD, Crohn's disease; SpA, spondyloarthritis.

notably *Faecalibacterium, but also Rominococcaceae* and *Lachnospiraceae NK4A136*. AAU patients shared many of the same enrichments, including a significant increase in *Coprococcus*.

Conclusion: There is a robust shared taxonomic signature among related immune-mediated diseases, in addition to individual disease phenotype signatures. Patients shared a strong depletion in *Blautia* and enrichment in *Veillonella* and *Lactobacillus*. SpA patients were uniquely enriched in *Collinsella*.

Disclosure: V. Rios Rodriguez, None; **M. Essex**, None; **J. Rademacher**, None; **F. Proft**, Novartis, 1, 5, 6, Eli Lilly and Company, 1, 5, UCB, 1, 5, 6, AbbVie, 1, 6, Amgen, 1, 6, Bristol-Myers Squibb, 1, 6, Hexal, 1, 6, MSD, 1, 6, Pfizer, 1, 6, Roche, 1, 6; **U. Löber**, None; **L. marko**, None; **U. Pleyer**, AbbVie, 2, 6, Alcon, 6, Allergan, 2, 6, Dompé, 6, Novartis, 2, 6, Pfizer, 6, Santen, 2, 6, Shire, 6, Thea, 2, 6, Winzer, 6; **B. Siegmund**, AbbVie, 2, 6, Boehringer Ingelheim, 2, Celgene, 2, Dr. Falk Pharma GmbH, 2, 6, Janssen, 2, 6, Eli Lilly & Co., 2, Pfizer Inc., 2, Prometheus Laboratories Inc., 2, Takeda, 2, 6, CED Service GmbH, 6, Novartis, 6, Ferring Pharmaceuticals, 6; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **S. Forslund**, None.

Abstract Number: 0063

Development of a Novel Cartilage Model Co-cultured with Conditioned Medium from Th17 Cells to Explore the Effect of IL-17A on Joint Tissue Remodeling

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

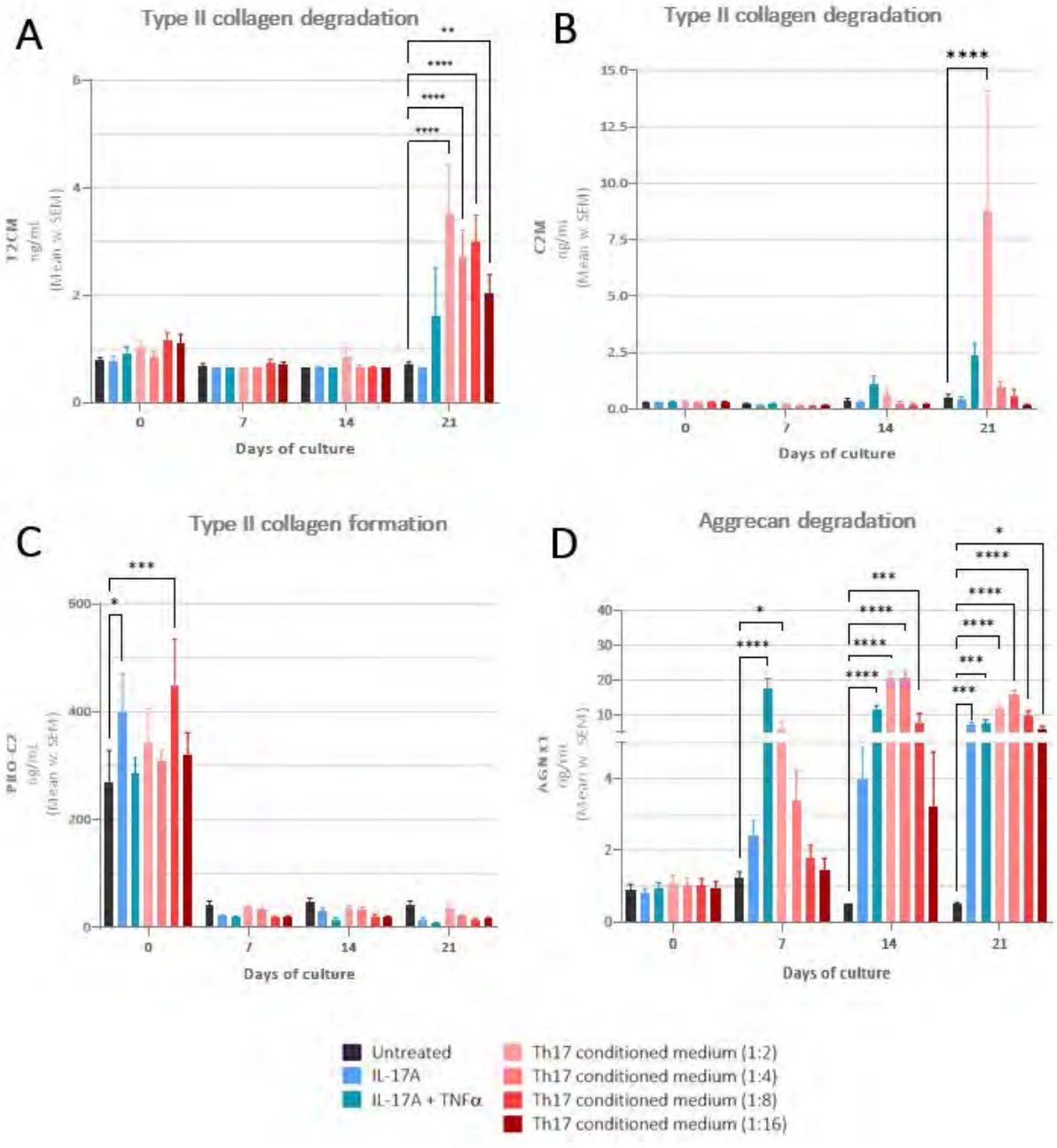
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: In spondyloarthritis (SpA) Th17 cells play a critical role in activating the pathogenic chain leading to manifestations related to skin, joints and entheses. Elevated levels of both Th17 cells and IL-17A have been detected in skin lesions, blood, and synovial fluid from patients with psoriatic arthritis (PsA) and ankylosing

Fig. 1



Extracellular matrix biomarkers quantified in supernatant from bovine cartilage explant model.

spondylitis (AS). The important role of IL-17A in SpA manifestations is reflected by the suppression of disease activity seen with IL-17A inhibitors in psoriasis, PsA and AS. However, it is still not well understood how IL-17A affects the extracellular matrix (ECM) of the joint. The aim of this study is to establish a cartilage model co-cultured with conditioned medium from Th17 cells to explore the effect of IL-17A on joint tissue remodeling.

Methods: $CD4^+$ T cells were isolated from healthy human buffy coat and differentiated into Th17 cells. After 5 days of incubation conditioned medium from Th17 cells was harvested. The Th17 differentiation was confirmed by flow cytometry. Cytokine concentrations were quantified in conditioned medium by ELISA. Bovine cartilage explants (BEX) were cultured for 21 days with 7 different treatments; 1) Culture medium, 2) IL-17A [9.25 ng/mL], 3) IL-17A + TNF-α [9.25 + 20 ng/mL], 4-10) 2-fold titration of Th17 supernatant from 1:2 to 1:16 [9.25 to 0.58 ng/mL]. Each group comprised of 6 replicates. The BEX supernatant-harvest and addition of new treatment were repeated 3 times a week. Metabolic activity was measured by AlamarBlue. Neo-epitope biomarkers of type II collagen formation (PRO-C2) and degradation (T2CM, C2M), together with aggrecan degradation (AGNx1) were quantified in BEX supernatant by ELISA. Differences between groups were compared by two-way RM ANOVA with Dunnett's multiple comparisons test.

Results: The cytokine concentrations of IL-17A/F/AF, IL-22 and TNF-α were quantified to 18.57, 0.05, 2.82, 1.58 and 12.8 ng/mL. In the BEX model, the metabolic activity was stable throughout study. T2CM and C2M were significantly upregulated in groups treated with Th17 conditioned medium at day 21 (Fig.1A-B), while PRO-C2 was downregulated in all groups compared to untreated (Fig.1C). Furthermore, on day 21 the AGNx1 release was significantly increased in all groups compared to untreated (Fig.1D).

Conclusion: The conditioned medium from Th17 cells showed to significantly increase the degradation of type II collagen and aggrecan, while type II collagen formation was decreased. Translational ECM biomarkers combined with *ex vivo* models can have great potential as output for describing joint disease mechanisms and predicting structural effect of treatment on bone and cartilage. Thus, this model may provide early indications of structural treatment efficacy in a clinical setting.

Disclosure: S. Groen, None; **C. Thudium**, Nordic Bioscience, 3, 11; **M. Karsdal**, Nordic Bioscience, 3, 4, 11; **A. Bay-Jensen**, Nordic Biosciences, 3, 11; **S. Nielsen**, Nordic Bioscience, 3.

Abstract Number: 0064

Prevalence, Incidence and Predictor Features of Uveitis in Spondyloarthritis in a Canadian Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Spondyloarthritis (SpA) encompasses Ankylosing Spondylitis (AS), Psoriatic Arthritis (PsA), Inflammatory bowel disease- associated spondyloarthritis (IBD-SpA), Reactive Arthritis (ReA), and undifferentiated

Table 1

Variable	axSpA	PsA	p-value
n	1724	1582	
UV	521 (30)	121 (8)	<0.001
age	38.3 (13.2)	44.9 (13.2)	<0.001
sex	1117 (65)	882 (56)	<0.001
Caucasian	1135 (66)	1350 (85)	<0.001
Alcohol	808 (47)	703 (44)	0.16
HLA-B27+	1169 (68)	201 (16)	<0.001
Tender	2.6 (6.1)	6.9 (8.7)	<0.001
Swollen	1.3 (3.3)	3.3 (4.8)	<0.001
Active	3.8 (7.9)	9.0 (9.8)	<0.001
Damaged	3.6 (8.2)	2.6 (6.7)	0.004
Peripheral Arthritis	48 (3)	87 (5)	<0.001
NSAIDs	917 (53)	1035 (65)	<0.001
DMARDs	217 (13)	574 (36)	<0.001
Biologics	435 (25)	140 (9)	<0.001

NSAID: non-steroidal anti-inflammatory drugs, DMARD: Disease modifying rheumatic drug

Table 2

PsA		Univariate		Multivariate Full Model			Multivariate Reduced Model		
Covariates	HR	CL	p-value	HR	CL	p-value	HR	CL	p-value
Clinical Model:									
age at baseline				1.007	(0.951, 1.0671)	0.809	1.023	(0.989, 1.058)	0.181
PsA Duration				1.051	(0.982, 1.124)	0.155	0.996	(0.952, 1.0415)	0.850
sex (male)				6.187	(1.446, 26.463)	0.014	1.395	(0.610, 3.193)	0.431
alcohol	2.454	(1.054, 5.713)	0.037	0.637	(0.164, 2.479)	0.516			
HLA-B27+	3.372	(1.481, 7.677)	0.004	2.046	(0.479, 8.736)	0.334	3.085	(1.342, 7.089)	0.008
BASFI	0.855	(0.7112, 1.028)	0.095	0.849	(0.658, 1.095)	0.207			
Biologics	5.208	(2.335, 11.617)	< 0.0001	0.704	(0.191, 2.599)	0.598			
BMI	0.919	(0.839, 1.0059)	0.067	0.921	(0.774, 1.0956)	0.352			
DMARDS	0.287	(0.1066, 0.775)	0.014	0.139	(0.0234, 0.824)	0.030	0.262	(0.0966, 0.714)	0.009
University Education	3.571	(1.510, 8.445)	0.004	0.997	(0.167, 5.956)	0.997			

PsA: Psoriatic arthritis, BASFI: Bath Ankylosisng Spondylitis Funtional Index, DMARD: Disease modifying anti-rheuamtic drug

Table 3

axSpA analysis		Univariate		Multivariate Full Model			Multivariate Reduced Model		
Covariates	HR	CL	p-value	HR	CL	p-value	HR	CL	p-value
Clinical Model:									
age at baseline				1.003	(0.988, 1.019)	0.690	0.997	(0.982, 1.012)	0.702
AS Duration				0.990	(0.969, 1.011)	0.345	0.983	(0.966, 1.0018)	0.077
sex (male)				0.976	(0.682, 1.398)	0.896	0.960	(0.679, 1.357)	0.817
Biologics	0.693	(0.502, 0.957)	0.026	0.743	(0.528, 1.046)	0.089	0.703	(0.501, 0.985)	0.040
Cardiomyopathy	6.464	(0.869, 48.081)	0.068	4.656	(0.612, 35.403)	0.137			
CRP	1.010	(1.0035, 1.0165)	0.002	1.010	(1.0007, 1.019)	0.034	1.009	(1.0029, 1.016)	0.004
ESR	1.009	(0.999, 1.0174)	0.058	0.999	(0.986, 1.011)	0.828			
UV duration	0.979	(0.958, 1.0005)	0.055	0.980	(0.958, 1.003)	0.090			

UV: uveitis, AS: ankilosing spondyitis. CRP: c-reactive protein, ESR: Erythrosedimentation rate

spondyloarthritis. These conditions share a number of extra musculoskeletal manifestations, the most common being acute anterior uveitis.

To determine the frequency and characteristics of SpA associated uveitis, to elucidate associated clinical features of SpA in patients with uveitis, and to identify SpA features that can predict flares of uveitis (UV).

Uveitis occurs more commonly in axial SpA (axSpA) than in PsA

Methods: Patients followed in the axSpA and PsA clinics at a single centre from January 2004 to December 2020 at 6–12-month intervals, according to a standard protocol including demographic and clinical variables, treatment and acute phase reactants.

T and chi-squared tests were performed at baseline visits on demographic and clinical factors on both the SpA and PsA populations, to compare patients with and without UV. Cox proportional-hazard models with time-dependent covariates were performed on patients with UV, with their first instance of a UV flare as the outcome event. Univariate analysis was done for each clinical and demographic factor, controlling for age, sex, and disease duration. Factors significant (< 0.1) in the univariate analysis were included in a multivariate analysis, controlling for age, sex and disease duration.

Results: A total of 3306 patients were included, 1724 patients with axSpA and 1582 patients with PsA. 30.2% of the axSpA cohort having uveitis (UV), vs 7.6% in the PsA. The rate of flares per person years at risk was 12.12% in the axSpA cohort, vs 1.71% in the PsA.

Demographic and clinical features are depicted in Table 1. There were more men in the total cohort (axSpA 65% and PsA 56%). More men with UV in the axSpA cohort (65% compared to 47% in the PsA). Most patients were Caucasian (axSpA 67%, 94% PsA)

Among axSpA patients 1169 (68%) were HLA*B27+, and 435 had UV. Among PsA patients 201 (16%) patients were HLA*B27+, and 32 had UV.

The multivariate analysis of the axSpA cohort showed that higher CRP (HR 1.009 p=0.004) increased the risk of a flare, while biologic agents decrease risk of flare (HR 0.702 p=0.040) in patients with UV. In the PsA cohort, being HLA*B27+ (HR 3.084 p=0.007) increased the risk of a UV flare, while being on a DMARD decreased the risk of a flare in patients with UV (HR 0.262 p=0.0088)

Conclusion: The results confirm the hypothesis that uveitis is more common in the axSpA than in the PsA population. New onset of UVs was also more commonly seen in the axSpA cohort. Factors that increase the risk of new uveitis flare were elevated ESR and CRP in the axSpA cohort and being a male or HLA-B27+ in the PsA population.

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Abstract Number: 0065

Altered Expression of Several miRNAs in Axial Spondyloarthritis Patients with High Disease Activity

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Recent studies have shown that microRNAs (miRNAs) play a role in various disorders, including immune mediated inflammatory diseases. Therefore, we studied relationship between miRNA profiles, disease activity and selected clinical manifestations of axial spondyloarthritis (axSpA).

Methods: We studied the whole miRNome in peripheral blood mononuclear cells (PBMC) of patients with non-radiographic (n=38) and radiographic (n=38) axSpA. The miRNA expression was profiled by massive parallel sequencing. The expression of particular miRNAs was correlated with disease activity (ASDAS, BASDAI and CRP) and selected clinical manifestations (e.g. uveitis). Sequencing data were analysed using DESeq2 algorithm, which additionally assessed the relationship of miRNA expression with BASDAI or the presence of uveitis, and the relationship with ASDAS and CRP were analysed using generalized linear modelling with negative binomial assumption (GLM-NB).

Results: Although DESeq2 did not reveal associations between miRNA expression, BASDAI or uveitis; the expression of several miRNAs correlated with the levels of CRP ($p < 0.05$). The pairwise comparison of ASDAS levels by Dunnett`s test revealed that 14 miRNAs were significantly different in axSpA patients with high and very high disease activity compared to patients with inactive disease. The pathway enrichment analysis by MIENTURNET revealed a list of pathways, with emphasis on interleukin (e.g., IL-4, IL-6, IL-10), JAK-STAT and NOTCH signalling pathways, in which dysregulated miRNAs are potentially involved. Additionally, the screening revealed that miR-1246 was differently expressed between radiographic and non-radiographic axSpA patients.

Conclusion: Our results revealed altered expression of several miRNAs in patients with high disease activity of axSpA, which may affect their target genes associated with pathogenesis of the disease.

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Abstract Number: 0066

Characterization of αβTCR of HLA-B*27-Restricted CD8 T-Cell Clones Associated with Spondyloarthropathies

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The mechanism by which HLA-B27 induces Ankylosing Spondylitis (AS) and related disease is unknown, but a leading hypothesis is that it presents 'arthritogenic epitopes' to CD8 T-lymphocytes. Supporting this hypothesis, we have previously demonstrated clonal expansions of CD8 TRB clones adhering to the CASSVG(V/I/L)(Y/F)STDTQYF CDR3 motif in AS patients (PMID: 32162785), which have also been reported by 2 recent independent studies in AS, as well as in samples from patients with bacterial-induced reactive arthritis (PMID: 10201900; 12472659; 28002888). The presence of those clones exclusively in *HLA-B*27*+ve disease points to a common antigen engaged by receptors of similar structure. The aim of our study was to obtain the paired αβTCR carried by these cells, characterize their phenotype, and, furthermore, to determine whether such clones reside at the normal enthesis.

Methods: We used PBMCs of 2 AS donors screened in our previous study and flow-sorted memory CD8 T-lymphocytes carrying the relevant TRBV genes (TRBV9 and TRBV27) to enrich for our low-frequency target population. Using single-cell RNA sequencing, the whole transcriptome and targeted VDJ sequences were obtained. Healthy enthesal tissue (n=3) was obtained from patients undergoing elective spinal surgery and the peri-enthesal bone (PEB) and the enthesis soft tissue (EST) were disaggregated by mechanical and enzymatic digestion. PEB and EST single-cell suspensions were analyzed by flow cytometry.

Results: The analysis of the enriched memory CD8 T cells from AS patients captured 8 different clonal expansions containing the same TRB consensus CDR3 sequence CASSVGL(Y/F)STDTQYF, and all carried the TRBV9 TCRB. These clones all paired with the same TRAV gene and presented similar TRA-CDR3 sequences. These cells were characterized by the expression of KLRB1, LGALS3, DUSP1, GNLY, ID2, FOS, and JUN whilst lacking HLA-II expression, a marker of activation. Higher expression of inflammatory genes was also observed, including the upregulation of CD69, NFKBIA, TNFAIP3, and PDE4D, an AS-relevant therapeutic target. The analysis of the healthy enthesal tissue confirmed the presence of TRBV9 carriers amongst the memory CD8 and CD4 T cell populations in both the PEB and the EST.

Conclusion: This study confirms the identification of expanded CD8 clonotypes in AS patients, carrying highly conserved TCRB CDR3 sequences, and also demonstrates restriction of the clonotypic TCRA carriage to a single TRAV gene in patients studied thus far. This is consistent with AS being driven by exposure to a common antigen presented by HLA-B27 ie the 'arthritogenic peptide' theory of causation of AS. On-going analysis will determine whether the AS-associated clonal expansions resemble the T cell clones that populate the healthy spinal enthesis PEB and EST.

Disclosure: J. Garrido-Mesa, None; **N. Harvey**, None; **A. Hanson**, None; **T. Kenna**, None; **C. Wong**, None; **C. Bridgewood**, None; **D. McGonagle**, Novartis, 5, 6, Roche, 6, Sobi, 6; **M. Brown**, None.

Abstract Number: 0067

Mendelian Randomisation Analysis of Protein Quantitative Trait Loci with Ankylosing Spondylitis Reveals Causative Involvement of Key Effector Proteins and Pathways

Nicholas Harvey[1], Zhixiu Li[2], Jose Garrido-Mesa[3], Jie Zheng[4], Paul Wordsworth[5], John Reveille[6], Mario Falchi[3], Niccolo Rossi[3], Alessia Visconti[3], David Evans[7] and Matthew Brown[3], [1]Molecular Genetics, London, United Kingdom, [2]Queensland University of Technology, Brisbane, Australia, [3]King's College London, London, United Kingdom, [4]Bristol University, Bristol, United Kingdom, [5]Oxford University, Oxford, United Kingdom, [6]Division of Rheumatology, The University of Texas Health Science Center at Houston, Houston, TX, [7]University of Queensland, Brisbane, Australia

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

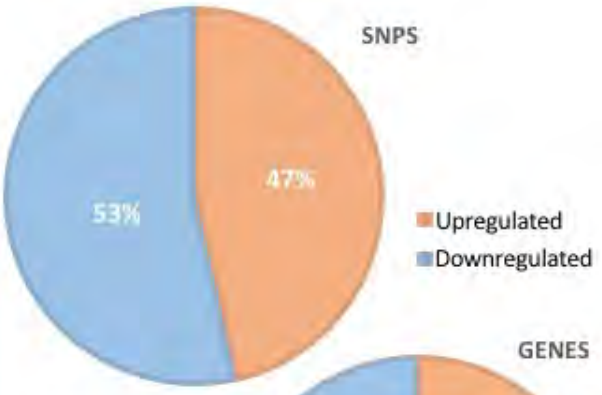
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Susceptibility to ankylosing spondylitis (AS) is known to be highly influenced by genetic factors, with heritability assessed in twins of >90%, with >115 genetic variants having been demonstrated to be associated with the disease. Assignment of causality from association studies remains challenging, and for many AS-associated loci the key gene and associated protein involved remain unclear. Using large-scale proteomic data-sets and Mendelian randomisation approaches, potential disease-causative associations, where disease-associated

Beta	P	Protein
1.38	2.56E-63	CFB
1.16	6.72E-35	IL23R
0.69	3.78E-15	ERAP1
0.47	2.29E-12	AGER
0.40	0.0093	LANCL1
0.32	0.0052	IL1R1
0.29	0.0011	DLL1
0.22	0.00015	IL12B
0.22	0.0010	GLTD2
0.20	0.00055	CCL25
0.20	1.50E-06	ICAM5
0.11	0.0032	CLEC1B
0.11	0.0074	TLR4;LY96
0.07	0.00035	IL1RL1
0.06	0.0038	IL18R1



Beta	P	Protein
-0.78	7.76E-16	IL27
-0.44	0.00094	GSTM3
-0.39	7.95E-05	TYMP
-0.33	0.0038	IL5RA
-0.28	0.0022	FAM3D
-0.27	0.0029	ISLR2
-0.23	0.00045	HDGF
-0.22	0.0027	MAPK13
-0.22	0.0041	MFGE8
-0.19	0.0033	CREB3L4
-0.16	0.00024	FLRT3
-0.16	1.48E-06	IGFLR1
-0.14	0.00087	CLPS
-0.13	0.0017	WISP1
-0.11	3.40E-09	FCGR2B
-0.11	2.28E-13	IL6R
-0.11	0.00023	FCGR2A;FCGR2B
-0.11	9.20E-05	HIBCH
-0.11	0.0013	FAH
-0.10	0.011	IL1RL1
-0.08	0.0023	ERAP2
-0.07	4.91E-05	CFHR1
-0.07	0.0016	IL27RA

Figure 1. Summary of results obtained from pQTL MR analysis. The direction of regulation was determined from association beta estimates.

genes operate through effects on protein levels to cause the disease concerned, can be investigated. We aimed to identify possible plasma protein level and pathway level changes that may influence the development of AS.

Methods: For the selection of protein exposures, we used an established pipeline (Zheng J et al, 2020). Briefly, this pipeline consisted of five plasma-based pQTL studies of European individuals, in which pQTLs of 1,064 proteins were pooled and used as exposure instruments for MR analysis. We also included a sixth study from a subset of the TwinsUK dataset (n=184, 33 pQTLs) to increase the number of available pQTL exposure instruments in our analysis. To determine AS outcome data for the MR analysis, we used a large-scale GWAS of Caucasian AS cases (n=11,352) vs controls (n=35,446). We performed Mendelian randomisation (MR) using the '*TwoSampleMR*' package in R v4.0.2 to estimate the putative causal effect of the 1,097 plasma proteins on AS incidence. To ascertain the biological effect of the protein changes, we conducted over-representation analysis (ORA) using the GOBP function of the '*clusterProfiler*' package in R to determine pathway changes resulting from likely pQTLs.

Results: We identified 37 plasma proteins showed putative causal link with AS using MR (FDR< 0.05).

Of these, n=19 (45%) SNPs were likely to increase the effector protein, whereas n=23 (55%) were predicted to have a limiting effect on protein expression. Upregulated proteins included ERAP1 (rs27033, rs17482078, rs469735), IL-23R (rs11581607), IL-12B (rs4921484), and IL-1RL1 (rs10179654). Downregulated proteins included IL-27 (rs181209), GSTM3 (rs115929572), IL-5RA (rs77400868), IL-6R (rs4129267), and ERAP2 (rs17408150). The pQTLs corresponded to immune based gene ontology terms such as 'GO:0032693 - negative regulation of IL-10 production', 'GO:0002697 - regulation of immune effector processes', and 'GO:0051707 - response to other organism'.

Conclusion: The results obtained strengthen the hypothesis that immune proteins, particularly cytokines in the IL-23 pathway (including IL-12, IL-23 and IL-27) and their receptor (IL-23R), as well as novel pathways such as the IL-33 pathway, are inherently dysregulated in AS patients. In addition, the 'response to other organism' processes may indicate a possible mechanism for gut dysbiosis in AS. These findings point to novel potential therapeutic targets in AS, and support further research targeting proteins upstream of IL-23R for therapy or prevention of AS.

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Abstract Number: 0068

Gut Bacteria Causing Ankylosing Spondylitis Identified Through Mendelian Randomization Studies

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Basic Science Poster (0046–0068)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: There is strong evidence from animal models, human microbiome profiling studies, genetic analyses, and from the model of reactive arthritis, that AS is caused by interaction of the gut mucosal immune system with the gut microbiome. We and others have recently confirmed expansion of CD8 T-lymphocyte clonotypes, in AS patients but not HLA-B27 matched healthy controls, that are also known to be expanded in bacterial-induced reactive arthritis. As disturbance of the gut microbiome can potentially result from either effects of the microbiome on disease or the converse, we sought to examine the causal impact of the gut microbiome on AS using Mendelian randomisation (MR) methodology.

Methods: We utilised MR analysis to investigate potential causal associations between AS genetics and gut microbiome composition. To determine outcome instruments for MR analysis, we used a large-scale GWAS of Caucasian AS cases (n=11,352) vs controls n=35,446). For the exposure instruments, we obtained publicly available data for genomewide significant microbe QTLs as identified by *Kurilshikov A et al*, 2021 (PMID 33462485). Briefly, the study performed GWAS on a meta-analysed population of European host gut microbiomes as determined by 16S ribosomal sequencing.

Results: We identified a significant protective (β=-0.96, FDR=0.011) causal relationship between presence of *Ruminococcus torques* and AS through the rs35866622 variant, which tags the *FUT2* gene determining secretor status, the ability to secrete ABO blood group antigens and other fucosylated mucus glycans in the gastrointestinal mucosa.

Conclusion: Using MR analysis, we demonstrate that the bacterium *Ruminococcus torques* is associated with the gene *FUT2* to influence the risk of developing AS. The observed negative correlation is consistent with previous findings demonstrating reduced carriage of this taxon in the stool microbiome of AS cases (PMID 31377126; 31662318), and with similar Mendelian randomization study findings in inflammatory bowel disease (PMID 33462485). These results support the hypothesis that AS is a gut microbiome driven disease and encourage the evaluation of novel therapeutic approaches targeting the gut microbiome. Correcting the underlying dysbiosis as part of AS clinical management could result in direct improvement for patients, and we hypothesize could be used as a preventative treatment in individuals at high risk of the disease.

Disclosure: N. **Harvey**, None; **J. Garrido-Mesa**, None; **Z. Li**, None; **D. Evans**, None; **P. Sternes**, None; **M. Brown**, None.

Abstract Number: 0069

First and Recurrent Thrombosis Risk After 3842 Patient-Years of Follow-Up: Prospective Results from AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Antiphospholipid Syndrome Poster (0069–0083)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: APS ACTION "Registry" was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL)-positive patients with/without other systemic autoimmune diseases (SAIDx). The objective of this study was to update the incident first and recurrent thrombosis risk in persistently aPL-positive registry patients, previously reported in 2018 as 1.53% and 2.75%, respectively (*Arthritis Rheumatol*.2018;70[suppl 10]).

Methods: A web-based data capturing system is used to store patient demographics, history, and medications. The inclusion criteria are positive aPL according to Updated Sapporo Classification Criteria tested within one year prior to the enrollment. Patients are followed every 12±3m with clinical data and blood collection; they also receive counseling on cardiovascular disease (CVD) and venous thromboembolism (VTE) prevention at each visit. In this prospective analysis, based on patients who completed 1-8-year follow-up visits, we report the incident thrombosis risk in persistently aPL-positive patients without and with a history of thrombosis. We also compare the demographic and clinical characteristics of patients with and without new thrombosis.

Results: As of March 2021, 886 patients were included: aPL/APS without SAIDx: 546 (aPL without APS classification: 101; thrombotic APS [TAPS]: 320; obstetric APS [OAPS]: 59; and TAPS+OAPS: 66]; and aPL/APS associated with SAIDx: 340 [aPL without APS: 91; TAPS: 178; OAPS: 21; and TAPS+OAPS: 50]). Of 886 patients, 705, 605, 527, 456, 401, 328, 200 and 49 completed 1, 2, 3, 4, 5, 6, 7, and 8-year follow-up, respectively. Mean follow-up was 4.67 years (1270 patient-years [pt-y]) and 4.19 years (2572 pt-y) for those without and with a history of thrombosis, respectively. Based on *13 initial events in 13 patients,* and *67 recurrent events in 54 patients* (Tables 1 and 2), the incident throm-

Table 1: Clinical and Laboratory Characteristics of Patients (Baseline) with Initial and Recurrent Thrombosis Since the Inception of APS ACTION Registry

N (%)	aPL-positive Patients with Initial Events n: 13*	APS Patients with Recurrent Events n: 54**
Mean age ± SD (registry entry)	42.92 ± 13.2	44.63 ± 14.6
Female	11 (85%)	38 (70%)
Systemic Autoimmune Disease	8 (61%)	21 (39%)
aPL Profile		
· Triple aPL-positive	2 (15%)	27 (50%)
· Double aPL-positive	3 (23%)	10 (18%)
· Single aPL positive (aCL or $a\beta_2GPI$)	2 (15%)	3 (5%)
· Single aPL positive (LA)	6 (46%)	14 (26%)
· LA-positive with/without aCL/$a\beta_2GPI$	11 (85%)	46 (85 %)

*3, 2, 5, 2, and 1 initial events reported in 13 patients during the 1st, 2nd, 3rd, 4th and 5th year follow-up periods, respectively. ** 18, 13, 10, 10, 8, 3 , 4, and 1 recurrent events (total: 67) reported in 54 patients during the 1st, 2nd, 3rd, 4th, 5th, 6th, 7th and 8th year follow-up periods, respectively

The APS ACTION registry was created using REDCAP provided by the Clinical and Translational Science Center at Weill Cornell Medical College (CTSC grant UL1 TR000457).

bosis risk was 1.02 and 2.09 per 100 pt-y in patients without and with a history of thrombosis, respectively. Demographics, concomitant lupus, aPL-profile, medications, and non-aPL thrombosis risk factors were not different between aPL-positive patients with (n=13) or without (n=259) first thrombosis, and between APS patients with (n=54) or without (n=560) recurrent thrombosis except APS patients with recurrence were younger and more likely to have triple aPL positivity compared to those without recurrence (42.1 ± 14.1 vs 46.6 ± 13.3, p 0.02, and 31% vs 50%, p 0.006).

Conclusion: Based on approximately 4000 patient-years of follow-up, the incident thrombosis risk in persistently aPL-positive patients remains relatively low (1.02 and 2.09 per 100 pt-y in patients without and with a history of thrombosis, respectively). Lupus anticoagulant and/or triple aPL-positivity, sub-therapeutic international normalized ratios, and additional CVD and VTE risk factors were relatively common at the time of the new events. Future Cox proportional hazards analysis will help us better define the risk and protective factors for thrombosis in persistently aPL-positive patients.

Table 2: Clinical and Laboratory Characteristics of Patients (at the time of events) with Initial and Recurrent Thrombosis Since the Inception of APS ACTION Registry

N (%)	Initial Events n: 13	Recurrent Events n: 67*
New Events**		
· Venous Thrombosis	6 (46%)	31 (46%)
· Arterial Thrombosis	6 (46%)	31 (46%)
· Catastrophic APS	-	1 (2%)
· Microthrombosis***	1 (8%)	3 (4%)
· Transient Ischemic Attack	-	1 (2%)
Antiplatelet & Anticoagulant Treatment		
· VKA Only	1 (8%)	38 (57%)
· LMWH Only	–	8 (12%)
· VKA + Antiplatelet Agent	–	4 (6%)
· LMWH + Antiplatelet Agent	–	3 (4%)
· Antiplatelet Agent only	7 (54%)	9 (13%)
. Direct Oral Anticoagulants	–	9 (13%)
· None	5 (38%)	5 (7%)
Other Treatments		
· Hydroxychloroquine	4 (31%)	27 (40%)
· Statin	–	25 (37%)
Non-aPL Risk Factors at the Time of Events		
· Sub-therapeutic INR (<2)****	–	19/42 (45%)
· CVD Risk Factors*****	6 (46%)	52 (77%)
· Prolonged Immobilization/Surgery/Travel	3 (23%)	9 (13%)
· Homozygous MTHFR Polymorphism	–	1/15 (7%)
· Estrogen-containing OC Use	1 (8%)	1 (1%)

LA: lupus anticoagulant; **aCL:** anticardiolipin antibody; **aβ$_2$GPI**: anti-β2-glycoprotein-I antibody; **VKA:** vitamin K antagonists; **LMWH:** low-molecular-weight heparin; **INR:** international normalized ratio; **CVD:** cardiovascular disease; **OC:** oral contraceptive. *: 2 events in 4 patients, 3 in 3, 4 in 1, and 6 in 1; **: Deep vein thrombosis with/without pulmonary embolism in 6/13 (39%) and 28/67 (42%), stroke in 2/13 (15%) and 13/67 (19%), and myocardial infarction in 2/13 (15%) and 10/67 (15%). ***: Microvascular events include aPL-nephropathy (2), adrenal hemorrhage (1), diffuse alveolar hemorrhage (1). ****: Mean INR for those with subtheraputic levels = 1.57; *****: CVD risk factors include hypertension, hyperlipidemia, diabetes mellitus, obesity, current smoking, family history of early CVD, and renal failure.

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Abstract Number: 0070

Pregnancy Outcomes of Antiphospholipid Antibody Positive Patients: Prospective Results from AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: APS ACTION Registry was created to study the natural course of disease over 10 years in persistently antiphospholipid antibody (aPL) positive patients with or without systemic autoimmune diseases. The objective of this analysis was to describe the new pregnancy outcomes of the aPL-positive patients since the inception of the registry.

Methods: A web-based data capture system is used to store patient demographics, history, and medications. The inclusion criteria are positive aPL according to Updated Sapporo Classification Criteria tested within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection. We identified patients recorded as "pregnant" during prospective follow-up; new "*aPL-related composite pregnancy morbidity*" was defined as: a) preterm live birth (PTLB) at or before 37th week due to (pre)eclampsia (PEC) and/or small-for-gestational age (SGA); and b) fetal death (FD) after the 10th week. In addition to descriptive characteristics, we analyzed pregnancy outcomes based on different aPL-related histories.

Results: Since the inception of the registry in 2012, 77 completed pregnancies were recorded in 55 patients (mean maternal age: 33.4 ± 5.2y; primary aPL/APS: 41 [75%]; and SLE: 14 [25%]) (Table 1). Of 55 patients, 15 (27%) did not

Table 1: Clinical and Laboratory Characteristics of Newly Pregnant Patients Included in APS ACTION Registry, by Pregnancy Outcomes

N= 77 Pregnancies	TLB ≥ 37.0 w n: 36 (47%)	PTLB 34.0 – 36.6w n:6 (8%)	PTLB < 34.0 w n:6 (8%)	FD >20.0w n:5 (6%)	FD 10.0-19.6w n:4 (5%)	PELS[a] <10.0w n:20 (26%)
Additional Pregnancy Morbidity						
• SGA and PEC	1	1[b]	-	-	-	-
• SGA	1	-	1[d]	-	-	-
• PEC	1	3[c]	2[e]	-	-	-
History of Systemic Lupus Erythematosus[f]	6 (17%)	4(67%)	2 (33%)	3 (60%)	2 (50%)	6 (30%)
History of Thrombosis	22 (61%)	2 (33%)	5 (83%)	3 (60%)	2 (50%)	15 (75%)
• Arterial	7 (19%)	-	1 (17%)	1 (20%)	-	3 (15%)
• Venous	18 (50%)	2	4 (67%)	3(60%)	2 (50%)	14 (70%)
• Arterial and Venous	3 (8%)	-	-	1 (20%)	-	2 (10%)
History of Pregnancy	28 (78%)	1 (17%)	4 (67%)	3(60%)	2 (50%)	15 (75%)
History of Pregnancy Morbidity	21(58%)	1 (17%)	4 (67%)	3(60%)	2 (50%)	13 (65%)
• ≥1 Fetal Death ≥ 10w	15 (42%)	-	2 (33%)	2 (40%)	1 (25%)	8 (40%)
• ≥1 Preterm Delivery ≤ 34w	6 (17%)	-	-	-	1 (25%)	4 (20%)
• ≥1 Pre-Emb/Emb Loss < 10w	11 (31%)	-	2 (33%)	2 (40%)	1 (25%)	8 (40%)
Laboratory Category						
• LA (+) Only	13 (36%)	3 (50%)	3 (50%)	4 (80%)	1 (25%)	8 (40%)
• Double aPL (+)	9 (25%)	1 (17%)	1 (17%)	1 (20%)	2 (50%)	5 (25%)
• Triple aPL (+)	11 (31%)	2 (33%)	2 (33%)	-	1 (25%)	5 (25%)
Treatment During Pregnancy						
• No LDA / LMWH	2 (6%)	-	-	-	2 (50%)	6 (30%)
• LDA alone	2 (6%)	1 (17%)	-	1 (20%)	1 (25%)	2(10%)
• LMWH alone	5 (14%)	-	-	-	1 (25%)	-
• LDA + LMWH	27 (75%)	5 (83%)	6 (100%)	4 (80%)	-	12 (60%)
• Hydroxychloroquine	21 (58%)	2 (33%)	3 (50%)	2 (40%)	2 (50%)	8 (40%)
Hypertension	1 (3%)	-	-	-	1 (25%)	1 (5%)
Obesity	5 (14%)	-	3 (50%)	-	1 (25%)	3 (15%)

TLB: term live birth; **PTLB**: preterm live birth; **FD**: fetal death; **PELS:** pre-embryonic or embryonic loss; **SGA**: small for gestational age; **PEC**: preeclampsia; **LDA:** Low-dose aspirin; **LMWH**: Low-molecular-weight-heparin; **LA**: lupus anticoagulant. [a]: 3rd consecutive loss only for one patient; [b]: gestational age (GA) at 36 weeks (w); [c]: GA 34w, 35w and 36w; [d]: GA 24w; [e]: GA 33.6w and 26w; [f]: pregnancy outcomes (n: 23) in 14 SLE patients were 6 for TLB (1 SGA), 6 PTLB ([3 PEC at GA 36w in two, 34w in two, 27w in one, and 26w in one), 5 FD (GA 12,15,20,23 and 24w), and 6 PELS.

fulfill the clinical APS classification criteria, 8 (15%) had obstetric APS (OAPS) only, 18 (33%) thrombotic APS (TAPS) only, and 14 (25%) both OAPS+TAPS. Pregnancy outcomes are reported in Table 1. Sixty-seven of 77 (87%) pregnancies were treated with low dose aspirin (LDA) and/or low-molecular weight heparin (LMWH) (54 with LDA+LMWH): 9/77 (12%) were due to OAPS only (LDA+LMWH: 7); 21/77 (27%) TAPS only (LDA+LMWH: 18); 21/77 (27%) OAPS and TAPS (LDA+LMWH: 19); and 16/77 (21%) despite no APS classification (LDA+LMWH: 10). Table 2 demonstrates TLB, PTLB, FD, and PELS rates based on the history of thrombotic APS (vs not), obstetric APS (vs not), and APS (vs not); 93% of all patients were lupus anticoagulant [LA] positive (as well as 100% of those who developed aPL-related composite pregnancy morbidity).

Conclusion: In our multi-center international prospective aPL-positive cohort, of 77 pregnancies in 55 patients observed prospectively, 20 (26%) were complicated by (pre)embryonic losses. Of the remaining 57 pregnancies,

Table 2: Pregnancy Outcomes Based on Antiphospholipid Antibody -related History

N=77 Pregnancies	History of Thrombotic APS		History of Obstetric APS		History of APS		History of Positive LA	
	Yes (N=49)	No (N=28)	Yes (N=33)	No (N=44)	Yes (N=58)	No (N=19)	Yes (N=72)	No (N=5)
TLB (N=36)	22 (45%)	14 (50%)	17 (52%)	19 (43%)	27 (47%)	9 (47%)	33 (46%)	3 (60%)
PTLB (N=12)	7 (14%)	5 (18%)	4 (12%)	8 (18%)	8 (14%)	4 (21%)	12 (17%)	-
FD (N=9)	5 (10%)	4 (14%)	3 (9%)	6 (14%)	6 (10%)	3 (16%)	9 (13%)	-
PELS (N=20)	15 (31%)	5 (18%)	9 (27%)	11 (25%)	17 (29%)	3 (16%)	18 (25%)	2 (40%)

TLB: term live birth; **PTLB**: preterm live birth; **FD**: fetal death; **PELS:** pre-embryonic or embryonic loss; **LA:** lupus anticoagulant.

Acknowledgment: The APS ACTION registry was created using REDCAP provided by the Clinical and Translational Science Center at Weill Cornell Medical College (CTSC grant UL1 TR000457).

aPL-related composite pregnancy morbidity was observed in 16/57 (28%) of pregnancies including 7/57 (12%) preterm live births with SGA and/or PEC, and 9/57 (16%) fetal deaths.

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Abstract Number: 0071

Damage Accrual Measured by DIAPS in Antiphospholipid Antibody (aPL)-positive Patients: Results from AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Antiphospholipid Syndrome Poster (0069–0083)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Damage Index in APS (DIAPS) is a scoring system developed to assess long-term damage in thrombotic primary antiphospholipid syndrome (PAPS), which also correlates with impaired quality of life (EuroQoL) in Latin Americans. DIAPS is not validated in aPL-positive patients without thrombosis. Our primary objective was to quantify damage accrual measured by DIAPS in aPL-positive patients with or without a history of thrombosis in an international cohort. Secondly, we aimed to identify clinical and laboratory characteristics associated with damage in aPL-positive patients.

Methods: In this cross-sectional study, we analyzed the baseline damage, measured by DIAPS, in APS ACTION Registry patients. The inclusion criteria were positive aPL according to Updated Sapporo Classification Criteria tested within one year prior to enrollment. We excluded patients with other autoimmune diseases. We analyzed the demographic, clinical, and laboratory characteristics of patients based on two subgroups: (1) thrombotic APS patients with high (DIAPS ≥3) *versus* low damage (DIAPS < 3); and (2) non-thrombotic aPL-positive patients with damage (DIAPS >0) *versus* without damage (DIAPS=0). Chi-square, Fisher's exact test, Mann-Whitney U and Student t test were used when applicable. In the multivariate analysis, our model included age, gender, race and variables with $p < 0.10$ in the univariate analysis.

Results: Of the 826 aPL-positive patients included in the registry as of April 2020, 576 with no other systemic autoimmune diseases were included in the analysis (412 thrombotic and 164 non-thrombotic [108 aPL only and 56 obstetric]). Baseline demographic, clinical and laboratory characteristics are summarized in Table 1. *For the thrombotic group*, the most frequent domains contributing to damage were peripheral vascular (n=260, 63% - mainly deep vein

Table 1. Demographic, clinical and laboratory characteristics of aPL-positive patients. For thrombotic PAPS, patients were compared regarding the presence of high (DIAPS ≥3) and low damage (DIAPS <3). For the non-thrombotic group, patients were compared based on the presence (DIAPS >0) or absence (DIAPS=0) of damage.

	Thrombotic PAPS (N=412)			Non-Thrombotic patients (aPL+OAPS) (N=164)		
	Patients with high damage (DIAPS ≥3) (N=110)	Patients with low damage (DIAPS <3) (N=302)	Adjusted p-value	Patients with damage (DIAPS >0) (N=34)	Patients without damage (DIAPS=0) (N=130)	Adjusted p-value
Demographics						
Age	54.9±13.2	51.4±13.6	**.022**	52.6±13.9	48.5±12.3	.260
Female	59 (53.6%)	204 (67.5%)	**.008**	29 (85.3%)	115 (88.5%)	.615
White	72 (65.5%)	198 (65.6%)	.522	25 (73.5%)	88 (67.7%)	.581
Cardiovascular Disease Risk Factors						
Hypertension	50 (45.5%)	89 (29.5%)	**.002**	14 (41.2%)	20 (15.4%)	**.001**
Diabetes	8 (7.3%)	18 (6.0%)	.628	2 (5.9%)	5 (3.8%)	.601
Hyperlipidemia	42 (38.2%)	79 (26.2%)	**.018**	11 (32.4%)	10 (7.7%)	**<.001**
Obesity	40 (36.7%)	66 (21.9%)	**.002**	7 (20.6%)	25 (19.2%)	.859
Criteria Manifestations						
Arterial event	60 (54.5%)	145 (48.0%)	.266	NA	NA	NA
Venous event	82 (74.5%)	165 (54.6%)	**<.001**	NA	NA	NA
Microvascular event or CAPS	14 (12.7%)	24 (7.9%)	.138	NA	NA	NA
Obstetric event	19/59 (32.2%)	55/204 (27%)	.826	7 (20.6%)	49 (37.7%)	.061
Non-criteria Manifestations						
Livedo	20 (18.2%)	36 (11.9%)	.101	3 (8.8%)	12 (9.2%)	.942
Thrombocytopenia	24 (21.8%)	45 (14.9%)	.096	7 (20.6%)	21 (16.2%)	.541
Autoimmune hemolytic anemia	3 (2.7%)	8 (2.6%)	.965	0	4 (3.1%)	.300
Skin ulcer*	20 (18.2%)	3 (1.0%)	**<.001**	3 (8.8%)	0	NA
MS-like disease	1 (0.9%)	1 (0.3%)	.455	1 (2.9%)	0	NA

*Biopsy-proven microthrombosis: 6 (26.1%).
CAPS: catastrophic APS; MS: multiple sclerosis.
The APS ACTION registry was created using REDCAP provided by the Clinical and Translational Science Center at Weill Cornell Medical College (CTSC grant UL1 TR000457).

thrombosis), neuropsychiatric (n=107, 30% - mainly ischemic stroke with sequelae) and cardiovascular (n=57, 14% - mainly heart valve disease). Older age, male gender, hypertension, hyperlipidemia and obesity were associated with high damage (Table 1). In the multivariate analysis, male gender (OR 1.73, 95%CI 1.10-2.71, p=.018) and hypertension (OR 1.90, 95%CI 1.21-2.99, p=.006) were independently correlated with high damage. *For the non-thrombotic group*, the most frequent domains contributing to damage were neuropsychiatric (n=25, 15% - mainly cognitive impairment) and cardiovascular (n=13, 8% - mainly heart valve disease). Hypertension and hyperlipidemia were independently associated with damage in the multivariate analysis (OR 2.72, 95%CI 1.09-6.80, p=.032 and OR 4.48, 95%CI 1.62-12.29, p=.004, respectively). There was no correlation between aPL profile (triple vs double vs single aPL) and damage in either group.

Conclusion: DIAPS was able to discriminate damage in a large multicenter cohort of aPL-positive patients. Traditional cardiovascular risk factors, namely older age, male gender, hypertension, hyperlipidemia and obesity, correlate with higher damage in thrombotic primary APS patients. Hypertension and hyperlipidemia also correlate with damage in aPL-positive patients without a history of thrombosis.

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Alexion Inc., 6, TEIJIN PHARMA LIMITED., 5, 6, Novartis Pharma K.K., 2, 5, 6, Eli Lilly Japan K.K., 5, 6, Kyowa Kirin Co., Ltd., 5, 6, AbbVie Inc., 2, 5, 6, NIPPON SHINYAKU CO.,LTD., 5, TAIHO PHARMACEUTICAL CO.,LTD., 5, Nippon Boehringer Ingelheim Co.,Ltd., 5, 6, Amgen Inc., 5, 6, UCB Japan Co. Ltd., 5, 6, Astra Zeneca plc, 2, 6, ONO Pharmaceutical Co., Ltd., 2, 5, Byaer Yakuhin, Ltd., 5; **H. Cohen**, Bayer Healthcare, 5, 6, 12, Support to attend scientific meetings; Honoraria for lectures at symposia paid to University College London Hospitals Charity, UCB Biopharma, 2, 12, Consultancy fees paid to University College London Hospitals Charity; **G. de Jesus**, None; **D. Branch**, UCB Pharmaceuticals, 1, 5; **C. Nalli**, None; **N. Kello**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **E. Rodriguez-Almaraz**, None; **G. Barilaro**, None; **J. Knight**, None; **B. Artim-Esen**, None; **R. Willis**, Louisville APL Diagnostic Inc, 2; **M. Bertolaccini**, None; **R. Roubey**, None; **D. Erkan**, ACR/EULAR, 5, LCTC, 5, NIH/NIAID, 5, GSK, 5, 6, Exagen, 5, Alexion, 2, UCB, 2, UpToDate, 9, APS ACTION, 4; **D. De Andrade**, None; **o. APS ACTION**, None.

Abstract Number: 0072

Immunosuppression Use in Primary Antiphospholipid Antibody Positive Patients: Descriptive Analysis of the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Antiphospholipid Syndrome Poster (0069–0083)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The APS ACTION Registry was created to study the natural course of antiphospholipid syndrome (APS) over 10 years in persistently antiphospholipid antibody (aPL) positive patients with or without systemic autoimmune diseases (SAIDx). Given data to support the role of immunosuppression (IS) in the management of APS patients with certain clinical phenotypes, e.g, diffuse alveolar hemorrhage (DAH), our primary objective was to characterize IS use in aPL-positive patients without other SAIDx.

Table: Immunosuppressive Medications Recorded (ever) in 50 Primary Antiphospholipid Antibody-positive Patients (Pts) with Selected Non-criteria Manifestations (NCM)[1] (*some patients had more than one NCM simultaneously or at different time points; thus, medications reported were not necessarily used only for the individual NCM*)

Medications (# of Pts)	DAH	aPL-N*	LV**	TP***	HA	VD
Only NCM (# of Pts)	**3**	**3**	**15**	**58**	**6**	**17**
Total NCM (# of Pts)	**5**	**15**	**26**	**85**	**12**	**35**
IVIG (n:26 pts)	3	0	2	19	5	4
RTX (n: 17 pts)	4	4	4	11	2	1
MMF (n: 8 pts)	2	3	4	3	0	0
AZT (n:9 pts)	0	0	1	5	2	3
PE (n:4 pts)	1	0	0	5	0	2
Other (n:6 pts)****	0	0	3	2	0	2
Hydroxychloroquine	2	6	17	38	7	13
Anticoagulation	4	9	23	65	7	31
-Thrombosis Hx (+)	(4)	(9)	(22)	(54)	(5)	(23)
-Thrombosis Hx (-)	(0)	(0)	(1)	(11)	(2)	(8)
Antiplatelet Agent alone	0	5	3	15	5	3
No Antiplatelet Agent + No Anticoagulation	1	0	0	5	0	1

DAH: diffuse alveolar hemorrhage; **aPL-N**: aPL- nephropathy; **LV**: livedoid vasculopathy; **TP**: persistent thrombocytopenia < 100 x 10^9/l; **HA**: hemolytic anemia; and **VD**: cardiac valve disease. **IVIG:** intravenous immunoglobulin; **RTX**: rituximab; **MMF:** mycophenolate mofetil; **AZT**: azathioprine; **PE**: plasma exchange; and **Hx**: history. * Biopsy proven aPL-N=15/15; ** Biopsy proven LV-related skin ulcer=6/26. ***: "Current" (N=27) and "Not Current" (N: 57) at baseline; mean platelet count at baseline: 85 x 10^9/L; ****: Cyclophosphamide (CYC), Cyclosporine, Methotrexate (MTX), Belimumab.

[1]**Potential additional indications in the remaining 20/70 (29%)** patients: lupus- like disease with musculoskeletal, renal, and/or neurologic involvement (n: 6, IVIG, MMF, AZT, CYC, MTX); infertility (n=1, IVIG); anticoagulation-resistant thrombosis (n=2, PE, RTX, AZT); arthralgia (n=2, MTX); autoimmune hepatitis (n=1, AZT); Crohn's disease (n=1, AZT), and unknown (n=7).

Acknowledgment: The APS ACTION registry was created using REDCAP provided by the Clinical and Translational Science Center at Weill Cornell Medical College (CTSC grant UL1 TR000457)

Methods: A central online database was used to collect detailed clinical data. The inclusion criteria were positive aPL based on the laboratory section of the current APS Classification Criteria, tested at least twice within one year prior to enrollment. For this descriptive analysis, we only included aPL-positive patients without other SAIDx and excluded those with catastrophic APS (CAPS). We retrieved data on demographics, aPL/APS-related history including selected non-criteria manifestations (DAH, antiphospholipid-nephropathy [aPL-N], livedoid vasculopathy-related skin ulcers [LV], thrombocytopenia [TP], hemolytic anemia [HA], and cardiac valve disease [VD]); and IS use (ever) (Table).

Results: As of 1/2021, 866 patients were included in the registry; 325 (38%) were excluded due to another SAIDx and an additional five due to CAPS. Of the remaining 536 patients (mean age at entry: 45±13y; 70% female; 70%

white; 432 [81%] meeting the APS Classification; and 143 [27%] with at least one selected non-criteria manifestations), 70 (13%) used IS (ever) excluding corticosteroids (CS) and hydroxychloroquine (HCQ). *Of 70 IS users* (non-CS/HCQ), 50 (71%) had at least one of the selected non-criteria manifestations. *Of 143 patients with at least one of the selected non-criteria manifestations*, 38 (27%) had no history of thrombosis; 19/38 (50%) received anticoagulation with/without antiplatelets, 15/38 (39%) antiplatelets alone, and 4/38 (11%) no antithrombotic agents. Four of 5 (80%) DAH patients, 6/15 (40%) aPL-N, 10/26 (39%) LV, 32/85 (38%) TP, 7/12 (58%) HA, and 9/35 (26%) VD patients were reported to receive non-CS/HCQ immunosuppression (Table).

Conclusion: In our multi-center international cohort, 13% of aPL-positive patients without other systemic autoimmune diseases, mostly those with selected non-criteria manifestations, were reported to use immunosuppressives other than corticosteroids and hydroxychloroquine. Given the inconsistent reporting of immunosuppression use in aPL-positive patients with non-criteria manifestations, systematic studies are urgently needed to better define the role of immunosuppression for different aPL-related non-criteria manifestations.

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Abstract Number: 0073

Anti-Domain 1 Antibody Fluctuation over Time in Patients with Persistently Positive Antiphospholipid Antibodies: Results from the Aps Action Clinical Database and Repository ("Registry")

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Antiphospholipid Syndrome Poster (0069–0083)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Data on fluctuation of antibodies against domain 1 (anti-D1) of β_2-glycoprotein I (β_2GPI) are scarce. Patients with antiphospholipid syndrome (APS) and all three criteria tests for antiphospholipid antibodies (aPL) display higher titers of anti-D1, which correlate with aβ_2GPI levels. This project aims at evaluating anti-D1 titers over time in a large international cohort of persistently aPL positive patients.

Methods: AntiPhospholipid Syndrome Alliance For Clinical Trials and InternatiOnal Networking (APS ACTION) Registry was created to study the course of persistently aPL-positive patients with or without autoimmune disorders over at least 10 years. Inclusion criteria are positive aPL by Updated Sapporo Criteria tested within one year prior to enrolment. Patients are followed up every 12±3 months with clinical data and blood collection. Patients with available blood samples from at least three time points were included in this analysis. Anti- β_2GPI and anti-D1 IgG were tested by chemiluminescence (BioFlash, INOVA Diagnostics) at APS ACTION core laboratories. Positive results were defined as >20 CU. Clinical data were retrieved from APS ACTION online database. Anti-D1 titers within the same subject were compared by Friedman's test. The association between categorical and continuous variables was assessed by chi-squared and Spearman's tests.

Results: In this longitudinal study, 1942 samples from 515 patients were tested for anti-D1 and aβ2GPI IgG; 230 patients with anti-D1 tested at ≥3 time points were included (Table). Patients with thrombotic APS had anti-D1 titers significantly higher than those without thrombosis (p=0.022). Among 135 patients with at least one anti-D1 positive result, anti-D1 titers varied significantly over time (Friedman statistics: 508.5, p< 0.0001; anti-D1 geometric mean [95%CI] at baseline 189.0 [115.9-308.3]; T1 132.3 [81.1-215.8]; T2 113.8 [69.8-185.5]; T3 109.2 [66.9-178.1]. Anti-D1 titers were significantly higher at baseline compared to T3 (p=0.029). Over time, anti-D1 titers significantly decreased in 107 patients, and increased in 28 (p< 0.0001). In 11.3% of patients, anti-D1 results changed from positive to neg-

Table: Demongrahic and Clinical Characteristics of 230 APS ACTION Registry Patients with anti-D1 tested ≥3 time points during the follow-up

Demographics	N (%)
Age in years, mean (SD)	12.7 (45.0)
Gender, %F (n)	159 (69.1)
Caucasian	179 (77.8)
APS Classification	
Thrombotic APS	124 (53.9)
Obstetric APS	21 (9.1)
Thrombotic and obstetric APS	26 (11.3)
Primary APS	105 (45.6)
APS with associated autoimmune disease	66 (28.7)
Positive aPL without APS	59 (25.7)
Positive aPL without associated autoimmune disease	30 (13.0)
Positive aPL with associated autoimmune disease	29 (12.6)
Positive criteria aPL (baseline)	
aCL IgG	143/227 (63.0)
aCL IgM	74/227 (32.6)
aβ$_2$GPI IgG	161/227 (70)
aβ$_2$GPI IgM	66/227 (29.1)
Lupus anticoagulant	126/173 (72.8)

ative (n: 20), or negative to positive (n: 6). (Mc Nemar's $\chi 2=6.5$; p=0.011). Anti- β2GPI titers correlated with anti-D1 titers and significantly reduced at T3 compared to baseline (aβ2GPI at baseline 187.1 [14.5-1586.5]; T1 150.8 [11.1-1379.2]; T2 124.9 [12.2-1304]; T3 117.6 [8.7-1136.6]; Friedman statistics=11.32, p=0.010).

Conclusion: Anti-D1 antibodies vary significantly overtime and approximately 10% may become negative during follow up. Our future analysis of the registry will demonstrate the clinical relevance of this variation, and the impact of treatment.

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Abstract Number: 0074

Association of Anti-phospholipid Antibodies (aPL) with Poor Clinical Outcomes in Hospitalized Patients with COVID-19

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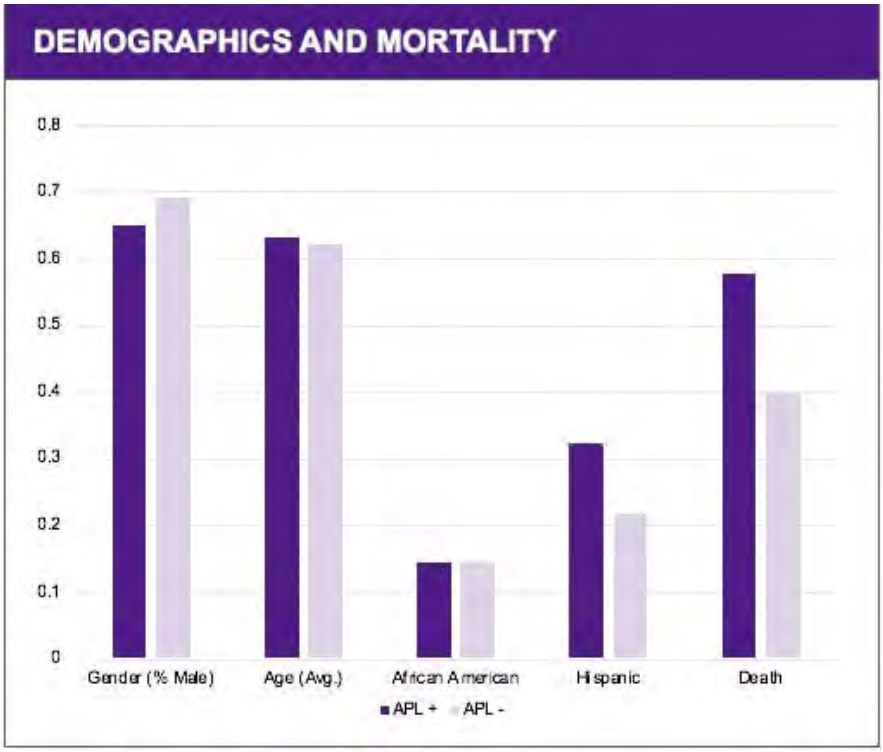
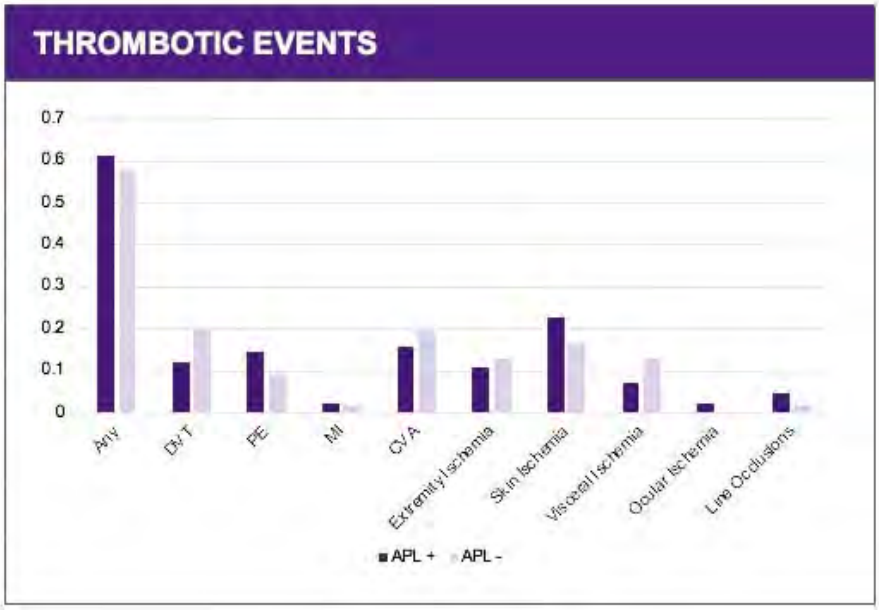
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Critically ill patients with COVID-19 infection have a profound hypercoagulable state and can often develop thromboses in many different vascular beds. Given the presence of anti-phospholipid antibodies among COVID-19 patients reported previously, we hypothesized that poor outcomes and thrombosis could also be promoted by autoimmunity. In this retrospective case control analysis, we aimed to evaluate associations between aPL titers, clinical outcomes and mortality in hospitalized patients admitted with COVID-19 infection.

Methods: We analyzed 138 electronic medical records of patients who were admitted to NYU Langone Hospital - Long Island between the months of March-April 2020 with findings of COVID-19 positivity via PCR and who had aPL titers determined. Patients with elevated titers of beta-2-Glycoprotein IgG, IgM, IgA and/or cardiolipin IgG, IgM, IgA were compared to those who were not elevated. Patients with positive lupus anticoagulant titers only were excluded due to prevalent use of anti-coagulation during this time.





KEY LABORATORY PARAMETERS

Parameter	APLA +	APLA -	P
C-Reactive protein (CRP) mg/L	283.1 (231.3, 358.6)	214.6 (153.7, 321.0)	**0.0007**
D-dimer (ng/ml)	10,805 (4764.5, 30,376.0)	7073 (2144.0, 12,316.0)	**0.04**
Ferritin (ng/ml)	2904.0 (1513.0, 6442.0)	2356.0 (1364.0, 4094.0)	0.31
Interleukin-6 (IL-6) (pg/ml)	227.0 (79.0, 478.0)	89.0 (30.0, 377.0)	**0.04**
Lactic dehydrogenase (LDH) (U/L)	895.0 (692.5, 1306.5)	747.0 (565.2, 1084.2)	**0.01**
Procalcitonin (ng/ml)	4.1 (1.0, 13.6)	3.1 (0.6, 13.6)	0.42
Troponin (ng/ml)	0.3 (0.1, 1.0)	0.2 (0.1, 0.8)	0.12

COVID-19 positive patients with aPL titers were assessed for clinical events (including DVT, PE, MI, CVA, extremity ischemia, skin ulcerations, visceral thrombosis and ocular and line occlusions) and mortality. The control group included patients that were negative for aPL antibody titers. Associations between Anti-Phospholipid (aPL) titer positivity and clinical events was assessed by Chi-square analysis using Fisher's exact test.

Results: The predominant aPL species that was noted in COVID-19 patients was anti-cardiolipin IgM. Of those patients with elevated antibody titers, cardiolipin IgM, IgG, IgA, and β2GPI antibodies were prevalent at rates of 98.9%, 26.7%, 19.2%, and 16.5%, respectively. Multiple aPL isotypes were detected in several patients.

There was a positive association between aPL positivity and elevations in IL-6, CRP, D-dimer, and LDH ($P < 0.05$). There was an increased incidence of clinical events in patients with COVID-19 and positive aPL titers (52/83 or 62%) compared to those who were aPL negative (32/55 or 58%), however this association was not statistically significant.

No significant association was detected between positive aPL titers and gender, age, or self-identified ethnicity. An increased incidence of ARDS and a rising serum creatinine was noted in the aPL positive group (P = 0.03 and P= 0.05 respectively). A significant increase in mortality was identified for the aPL positive group (P=0.01).

Conclusion: These findings suggest that aPL titers may provide insight into disease prognosis and outcome in hospitalized patients with COVID-19. Despite lack of significant association with discrete thrombotic events, association of aPL positivity with rising serum creatinine and ARDS suggest that aPL may contribute to end organ dysfunction through enhanced microthrombosis, resulting in increased mortality.

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Abstract Number: 0075

Endothelial Cell-activating Antibodies in COVID-19

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with COVID-19 are at high risk for occlusion of vascular beds of all sizes. Considering endothelial cell activation has regularly been described as part of the COVID-19 thrombo-inflammatory storm, we aimed to characterize potential upstream mediators of this activation including neutrophil extracellular traps (NETs) and antiphospholipid antibodies (aPL).

Methods: Cultured human umbilical vein endothelial cells (HUVECs) were exposed to sera from 118 patients hospitalized with COVID-19. Plasma samples from 100 non-COVID sepsis patients were also characterized alongside 72 COVID samples. Upregulation of surface cell adhesion molecules E-selectin, ICAM-1, and VCAM-1 was determined by in-cell ELISA. Soluble E-selectin was measured in serum. HUVECs were also stimulated with IgG purified from three COVID patients positive for anticardiolipin IgG and separately five positive for anti-PS/PT IgG.

Results: As compared with sera from 38 healthy controls, COVID sera triggered an activated HUVEC phenotype as evidenced by markedly increased surface expression of the cell adhesion molecules E-selectin (mean 1.67-fold increase, $p< 0.0001$), VCAM-1 (mean 1.89-fold increase, $p< 0.0001$), and ICAM-1 (mean 1.66-fold increase, $p< 0.0001$). While non-COVID sepsis plasma elicited higher expression of surface ICAM-1 than did control plasma, the effect was even more robust with COVID-19 plasma ($p< 0.05$ comparing COVID-19 to sepsis). Beyond the in-cell ELISA platform, we also found significantly higher levels of soluble E-selectin in COVID serum as compared with healthy controls ($p< 0.0001$), where it correlated with clinical parameters that track with COVID-19 severity including C-reactive protein ($r=0.31$, $p=0.005$), D-dimer ($r=0.31$, $p=0.008$), calprotectin ($r=0.29$, $p=0.003$), and oxygenation efficiency ($r=-0.31$, $p=0.002$). One marker of NET remnants, myeloperoxidase-DNA complexes, modestly correlated with the ability of serum to increase expression of both VCAM-1 ($r=0.26$, $p< 0.01$) and ICAM-1 ($r=0.28$, $p< 0.01$) on

Table 1: Correlation of HUVEC cell adhesion molecules with antiphospholipid antibodies in COVID patients

	E-selectin		ICAM-1		VCAM-1	
Spearman	r	p	r	p	r	p
Antiphospholipid antibodies						
IgG anticardiolipin	0.450	****	0.346	***	0.421	****
IgM anticardiolipin	0.365	****	0.357	****	0.252	**
IgG anti-β_2GPI	0.145	ns	0.076	ns	0.213	*
IgM anti-β_2GPI	0.017	ns	0.150	ns	0.047	ns
IgG anti-PS/PT	0.439	****	0.299	***	0.252	**
IgM anti-PS/PT	0.249	**	0.276	**	0.115	ns
Other biomarkers						
C-reactive protein	-0.008	ns	0.003	ns	0.173	ns
D-dimer	0.175	ns	0.258	*	0.133	ns
Calprotectin	0.187	*	0.197	*	0.203	*
ns=not significant; *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001						

HUVECs, while cell-free DNA and citrullinated histone H3 (additional markers of NETs) correlated with VCAM-1 only (r=0.24, p< 0.05 and r=0.22, p< 0.05, respectively). Interestingly, we detected robust correlations between various aPL in serum, especially anticardiolipin IgG/M and anti-phosphatidlyserine/prothrombin (anti-PS/PT) IgG/M, and the three markers of HUVEC activation (E-selectin, VCAM-1, and ICAM-1) (Table 1). As compared with mock depletion, IgG depletion strongly abrogated the ability of pooled COVID sera (anticardiolipin-positive and anti-PS/PT-positive) to upregulate HUVEC E-selectin (p< 0.01 and p< 0.05, respectively), VCAM-1 (p< 0.05 and p< 0.01) and ICAM-1 (p< 0.01 for both). Furthermore, IgG (100 µg/ml) purified from the anticardiolipin-positive and anti-PS/PT-positive COVID serum increased expression of ICAM-1 (p< 0.01 for both) when spiked into control serum.

Conclusion: These data are the first to suggest that patient antibodies are a driver of endothelial cell activation in COVID-19 and add important context regarding thrombo-inflammatory effects of aPL-like autoantibodies in severe COVID-19.

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Abstract Number: 0076

Predicting the Transitions Between Lupus Anticoagulant Status and Thrombosis in SLE Using a Multi-state Markov Model

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antiphospholipid syndrome (APS) is a significant cause of morbidity and mortality in patients with SLE and lupus anticoagulant (LAC) positivity is the best predictor of thrombosis. However, in SLE LAC positivity can fluctuate over time. We determined the probabilities of transitions between the lupus anticoagulant states and thrombosis, and identify predictors of these transitions.

Methods: SLE patients in a longitudinal cohort had LAC determined using ISTH guidelines at every visit. A dRVVT of 45 or more seconds and a positive confirm ratio of more than 1.4 were defined as positive for LAC. Missing values were handled using multiple imputation based largely on the degree of elevation of dRVVT. At each visit, patients were classified into state 1 (a negative LAC), state 2 (a positive LAC), or state 3 (thrombosis). Multistate Markov models were used to provide estimates of relative transitions rates and to identify predictors in these transitions. The multiply imputed datasets were analyzed for complete data by imputation. Then, the results were pooled from the multiple analyses.

Table 1. The observed transitions in states between visits for patients in the Hopkins Cohort

From \ To	LAC-	LAC+	Thrombosis
LAC-	32888 (97.6%)	626 (1.9%)	200 (0.6%)
LAC+	640 (35.5%)	1135(63%)	26 (1.5%)

Table 2. Transition probability between states after SLE diagnosis and expected time in each state. The table presents the estimated probability from state 1 (LAC-), state 2 (LAC+) to the LAC states and to first thrombotic event

	Estimated probabilities of being in the RVVT state			Estimated time spent in the RVVT state (in years)		
	LAC-	***LAC+***	***Thrombosis***	***LAC-***	***LAC+***	***Thrombosis***
Initial state						
1year						
LAC-	94.48%	3.98%	1.54%	0.9671	0.0253	0.008
LAC+	74%	23.00%	3.03%	0.4696	0.5133	0.0172
2 years						
LAC-	92.21%	4.67%	3.12%	1.8995	0.0696	0.031
LAC+	86.89%	8.24%	4.87%	1.2926	0.6501	0.0571
5 years						
LAC-	87.64%	4.63%	7.73%	4.5953	0.2106	0.1941
LAC+	85.97%	4.56%	9.47%	3.916	0.8107	0.2734

Table 3. Multivariable analysis on the predictors of transitions

Variables	LAC- to LAC+	LAC- to Thrombosis	LAC+ to LAC-	LAC+ to Thrombosis
Ethnicity				
Caucasian	Ref	Ref	Ref	Ref
African American	0.77 (0.62, 0.97)	1.26 (0.9, 1.78)	1.42 (1.12, 1.81)	2.35 (0.45, 12.21)
Other	1.01 (0.73, 1.4)	0.91 (0.46, 1.81)	0.87 (0.61, 1.25)	1.64 (0.2, 13.15)
Sex: Male	1.49 (1.07, 2.07)	1.09 (0.54, 2.21)	0.53 (0.39, 0.74)	2.52 (0.57, 11.23)
Smoking: ever	1.4 (1.12, 1.74)	1.45 (1.06, 1.97)	1.52 (1.2, 1.92)	1.46 (0.48, 4.41)
Obese (BMI>=30)	1.27 (1.01, 1.59)	1 (0.7, 1.43)	0.77 (0.62, 0.95)	8.39 (1.7, 41.5)
Prednisone use: yes	2.24 (1.78, 2.81)	2.11 (1.51, 2.96)	1.69 (1.34, 2.14)	1.8 (0.57, 5.71)
Plaquenil use: yes	0.63 (0.51, 0.77)	0.8 (0.57, 1.13)	1.34 (1.06, 1.69)	0.23 (0.07, 0.72)
Aspirin use: yes	1.6 (1.31, 1.94)	1.15 (0.81, 1.62)	0.54 (0.44, 0.66)	0.49 (0.13, 1.79)
Anti-hypertensive medications: yes	1.03 (0.84, 1.27)	1.8 (1.28, 2.52)	0.92 (0.74, 1.14)	1.79 (0.57, 5.67)
Cholesterol>=200	1.18 (0.96, 1.45)	1.69 (1.23, 2.32)	1.09 (0.89, 1.34)	0.4 (0.08, 1.93)
age at visit >=50	0.99 (0.79, 1.23)	1.47 (1.04, 2.07)	1.45 (1.16, 1.8)	1.05 (0.28, 3.94)
Low C3	0.97 (0.75, 1.25)	1.63 (1.13, 2.35)	0.62 (0.48, 0.81)	7.26 (2.07, 25.43)
SLEDAI (per 1 unit increase)	1.05 (1.01, 1.08)	1.09 (1.05, 1.13)	1 (0.96, 1.03)	0.82 (0.67, 1.02)

Results: 1781 patients (37296 clinic visits) were eligible to be included for this analysis. 93% were female, 41% were African American, 50% were Caucasian. The mean age at SLE diagnosis was 32 years (SD=13 years). Patients had the higher probability of improving (LAC+ to LAC-) than deteriorating (LAC- to LAC+), regardless of years after SLE diagnosis (Table 1, 2). In 5 years, the probability of remaining in the same state was 87.6% for state 1, and 4.6% for state 2. 7.7% of the patients initially in state 1 and 9.7% of the patients initially in state 2 transitioned to developing a thrombosis (Table 2). Multivariable regression results showed that African American ethnicity, normal C3, and being on hydroxychloroquine treatment were at higher rates of transitioning from positive LAC to negative LAC while male sex, SLEDAI, and obesity predicted higher rates of transition from LAC negative to positive states. For patients transitioning from positive LAC, obesity and low C3 levels were risk factors for thrombosis and being on hydroxychloroquine was protective against thrombosis (Table 3).

Conclusion: In SLE, transitions between LAC status could be estimated by multistate Markov model. We can estimate the risk of future thrombosis based on the baseline RVVT status, C3, ethnicity, gender, disease activity and obesity.

Disclosure: S. Demir, None; **J. Li**, None; **L. Magder**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2.

Abstract Number: 0077

Association of Lupus Nephritis and Other Clinical Features with Antiphospholipid Antibody Positivity Among Patients with Systemic Lupus Erythematosus

Prarthana Jain, Jim Oates, Dulaney Wilson and Diane Kamen, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antiphospholipid antibody (aPL) positivity is associated with elevated risk of thrombosis among patients with SLE, but other clinical associations are less well-known. The goal of our study was to determine clinical correlations with aPL seropositivity among patients with SLE to help inform risk factor prediction models and provide insights to improve management strategies.

Methods: We used data from a longitudinal research registry of patients with SLE seen at our institution between 2003-2020. Patients were selected using a case-control design based on having known aPL and/or lupus anticoagulant (LAC) status (normal or elevated). aPL status included IgM and IgG anticardiolipin and anti-b2glycoprotein, categorized by Ig level (any positive >20 GLP/MLP, or high positive >40 GLP/MLP). Demographic information, American College of Rheumatology (ACR) and SLICC classification criteria for SLE, SLICC Damage Index (SDI), and renal biopsies were evaluated. Statistical analysis was performed using Fisher's exact or Pearson's chi-squared testing.

Results: A total of 400 patients with SLE were evaluated, the majority black (69.9%) and female (93.9%). Table 1 compares aPL status by race, gender, and age of SLE diagnosis. Table 2 compares aPL and LAC status by presence of clinical characteristics. Lupus nephritis was more prevalent among black compared to non-black patients (59.3% vs. 26.4%, p< 0.01), childhood-onset SLE compared to those diagnosed in adulthood (67.1% vs. 45.8%, p< 0.01), and men compared to women (64.7% vs. 48.9%, p=0.07). Table 2 shows associations between clinical characteristics and any positive aPL, high positive aPL, and positive LAC. Positive aPL was associated with lupus nephritis in 58.6% of patients compared to 45.1% of those negative for aPL (p=0.03). After evaluating renal biopsy data, we found no significant difference in nephritis biopsy classes between those positive or negative for aPL or LAC. In addition to nephritis, discoid rash and neurologic disorder were significantly associated with positive aPL status. Serositis, thrombocytopenia and neurologic disorder were significantly associated with high positive aPL and neurologic disorder with positive LAC. High positive aPL was associated with disease damage, as measured by SDI,

Table 1. Demographic Characteristics for Patients with SLE by aPL Positivity (N=400)

		Any Positive aPL				
		No N=255		Yes N=145		p-values
Gender n (%)	Female	234	(91.8)	139	(95.9)	0.12
	Male	21	(8.2)	6	(4.1)	
Age at Diagnosis of SLE (years ± sd)		30.8	±13.1	28.9	±14.8	0.21
Race n (%)	White	62	(24.3)	41	(28.3)	0.63
	Black	184	(72.2)	98	(67.6)	
	Other	9	(3.5)	6	(4.1)	

Table 2. SLE Classification Criteria & Other Clinical Features by aPL Antibody Positivity

	aPL Status								
	Any Positive aPL (>20 GLP/MLP)			High Positive aPL (>40 GLP/MLP)			Positive LAC		
	No N=255	Yes N=145		No N=292	Yes N=108		No N=157	Yes N=23	
Clinical Features	n (%)	n (%)	P value	n (%)	n (%)	P value	n (%)	n (%)	P value
Childhood-onset SLE	46 (18.0)	37 (25.5)	0.07	56 (19.2)	27 (25.0)	0.17	39 (24.8)	2 (8.7)	0.11
Lupus Nephritis	115 (45.1)	85 (58.6)	**0.03**	139 (47.6)	58 (53.7)	0.28	86 (54.8)	14 (60.9)	0.58
Renal biopsy reviewed	52 (20.4)	30 (20.7)	0.94	61 (20.9)	21 (19.4)	0.75	29 (18.5)	3 (13.0)	0.52
Class I	7 (2.7)	3 (2.1)	0.27	8 (2.7)	2 (1.9)	0.43	5 (3.2)	1 (4.3)	0.88
Class II	8 (3.1)	3 (2.1)		11 (3.8)	0 (0.0)		3 (1.9)	1 (4.3)	
Class III	24 (9.4)	15 (10.3)		26 (8.9)	13 (12.0)		16 (10.2)	2 (8.7)	
Class IV	35 (13.7)	22 (15.2)		42 (14.4)	15 (13.9)		30 (19.1)	5 (21.7)	
Class V	8 (3.1)	10 (6.9)		12 (4.1)	6 (5.6)		8 (5.1)	0 (0.0)	
Class VI	1 (0.4)	1 (0.7)		1 (0.3)	1 (0.9)		(0.0)	(0.0)	
Malar Rash	101 (39.6)	69 (47.6)	0.12	124 (42.5)	46 (42.6)	0.98	73 (46.5)	8 (34.8)	0.29
Discoid Rash	41 (16.1)	39 (26.9)	**0.01**	54 (18.5)	26 (24.1)	0.22	36 (22.9)	6 (26.1)	0.74
Photosensitivity	101 (39.6)	65 (44.8)	0.24	119 (40.8)	47 (43.5)	0.55	59 (37.6)	11 (47.8)	0.33
Alopecia	92 (36.1)	58 (40.0)	0.31	107 (36.6)	43 (39.8)	0.57	56 (35.7)	8 (34.8)	0.89
Arthritis	164 (64.3)	93 (64.1)	0.97	186 (63.7)	71 (65.7)	0.71	90 (57.3)	16 (69.6)	0.27
Serositis	63 (24.7)	48 (33.1)	0.07	73 (25.0)	38 (35.2)	**0.04**	43 (27.4)	11 (47.8)	**0.05**
Neurologic Disorder	26 (10.2)	25 (17.2)	**0.04**	29 (9.9)	22 (20.4)	**<0.01**	17 (10.8)	7 (30.4)	**0.01**
Leukopenia	71 (27.8)	40 (27.6)	0.96	76 (26.0)	35 (32.4)	0.21	26 (16.6)	4 (17.4)	0.92
Thrombocytopenia	31 (12.2)	23 (15.9)	0.3	33 (11.3)	21 (19.4)	**0.03**	13 (8.3)	4 (17.4)	0.17
Low Complement Level	104 (40.8)	59 (40.7)	0.16	116 (39.7)	47 (43.5)	0.30	39 (24.8)	3 (13.0)	0.23
Autoimmune Disease Overlap	76 (29.8)	44 (30.3)	0.71	83 (28.4)	37 (34.3)	0.31	35 (22.3)	9 (39.1)	0.1
History of Thrombosis	42 (16.5)	34 (23.4)	0.12	51 (17.5)	25 (23.1)	0.25	27 (17.2)	4 (17.4)	0.97
SLICC Damage Index									
Any damage (>0)	153 (60.0)	95 (65.5)	0.29	173 (59.2)	75 (69.4)	**0.05**	88 (56.1)	15 (65.2)	0.54
High Damage (>1)	96 (37.6)	59 (40.7)	0.55	107 (36.6)	48 (44.4)	0.16	57 (36.3)	10 (43.5)	0.51

but no significant difference was seen with lower titer positive aPL or LAC positivity. Although no significant difference was seen in prevalence of thrombosis and aPL status, the use of low dose aspirin (45.5%) and warfarin (18.6%) were significantly higher among patients with any positive aPL compared to those negative for aPL ($p< 0.01$).

Conclusion: We found that within this predominately African American cohort of patients with SLE, elevated levels of aPL antibodies are associated with lupus nephritis, discoid rashes, and neurologic disorder. At high titers, aPL status was associated with serositis, neurologic disorder and thrombocytopenia. The strongest association of LAC was with neurologic disorder. Further studies will determine the timing of aPL status to these clinical manifestations and potential benefit of antiplatelet and/or anticoagulation on nonthrombotic manifestations such as lupus nephritis, when aPL antibodies are elevated.

Disclosure: P. Jain, None; **J. Oates**, None; **D. Wilson**, None; **D. Kamen**, None.

Abstract Number: 0078

Frequency and Clinical Characteristics of Secondary Antiphospholipid Syndrome in Systemic Lupus Erythematosus: The Georgia Lupus Registry

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Although APS was originally described in those with SLE, the epidemiology and clinical characteristics of secondary APS (2APS) has not been well described in SLE populations with large numbers of Blacks.

Methods: The Georgia Lupus Registry is a Centers for Disease Control and Prevention-funded population-based registry of validated SLE patients in Atlanta and was designed to determine SLE prevalence in 2002 and incidence in 2002–04. Diagnoses were validated through medical record and database review without the requirement of patient consent. Case definitions included those with ≥4 ACR criteria or 3 ACR criteria with a final diagnosis of SLE by a board-certified rheumatologist. Case finding efforts included searching for APS-related elements from medical records and labs. Validated prevalent and incident SLE cases were matched with the state Hospital Discharge Database from 2002–13, which captured all hospital admissions along with associated diagnoses and procedure codes. 2APS was defined by 1) the treating rheumatologist diagnosis and/or 2) ≥1 clinical and ≥1 laboratory criteria after SLE diagnosis using a modified Sydney classification criteria. Clinical criteria included vascular thromboses and pregnancy morbidity captured by medical record review and/or hospital diagnosis codes. Laboratory criteria for an-

Table 1. Frequency of Clinical and Laboratory Characteristics in Prevalent and Incident Systemic Lupus Erythematosus and by Secondary Antiphospholipid Syndrome Status

		Prevalent SLE (N=1353)				Incident SLE (N=336)			
Characteristic	Category	Total (n=1353)	+ APS Overall (n=194)	- APS Overall (n=1159)	P-value APS (+ vs -)	Total (n=336)	+ APS Overall (n=40)	- APS Overall (n=296)	P-value APS (+ vs -)
age [1], years±SD	Mean ± SD	45.7 ± 14.1	44.1 ± 13.1	46.0 ± 14.2	0.082	42.1 ± 16.3	44.1 ± 15.5	41.8 ± 16.4	0.4
SLE duration [1], years±SD	Mean ± SD	11.1 ± 8.0	11.1 ± 8.0	11.1 ± 8.0	0.97	1.5 ± 0.9	1.6 ± 0.8	1.5 ± 0.9	0.72
sex, n (%)	Male	136 (10.1)	24 (12.4)	112 (9.7)	0.25	44 (13.1)	5 (12.5)	39 (13.2)	0.91
	Female	1217 (89.9)	170 (87.6)	1047 (90.3)		292 (86.9)	35 (87.5)	257 (86.8)	
smoking, n (%)	Never	686 (62.3)	104 (62.3)	582 (62.2)	0.51	186 (69.4)	22 (61.1)	164 (70.7)	**0.049**
	Current	203 (18.4)	35 (21.0)	168 (18.0)		43 (16.0)	4 (11.1)	39 (16.8)	
	Former	213 (19.3)	28 (16.8)	185 (19.8)		39 (14.6)	10 (27.8)	29 (12.5)	
livedo reticularis, n (%)	No	1311 (96.9)	180 (92.8)	1131 (97.6)	**0.0004**	328 (97.6)	38 (95.0)	290 (98.0)	0.25
	Yes	42 (3.1)	14 (7.2)	28 (2.4)		8 (2.4)	2 (5.0)	6 (2.0)	
Raynaud's, n (%)	No/Unk	871 (64.4)	113 (58.2)	758 (65.4)	0.054	240 (71.4)	31 (77.5)	209 (70.6)	0.37
	Yes	482 (35.6)	81 (41.8)	401 (34.6)		96 (28.6)	9 (22.5)	87 (29.4)	
anticardiolipin Ab, n (%)	No/Unk	1093 (80.8)	64 (33.0)	1029 (88.8)	**<0.0001**	274 (81.5)	14 (35.0)	260 (87.8)	**<0.0001**
	Yes	260 (19.2)	130 (67.0)	130 (11.2)		62 (18.5)	26 (65.0)	36 (12.2)	
lupus anticoagulant, n (%)	No/Unk	1188 (87.8)	94 (48.5)	1094 (94.4)	**<0.0001**	302 (89.9)	19 (47.5)	283 (95.6)	**<0.0001**
	Yes	165 (12.2)	100 (51.5)	65 (5.6)		34 (10.1)	21 (52.5)	13 (4.4)	
anti-beta 2 glycoprotein I IgG or IgM, n (%)	No/Unk	1325 (97.9)	179 (92.3)	1146 (98.9)	**<0.0001**	326 (97.0)	35 (87.5)	291 (98.3)	**0.0002**
	Yes	28 (2.1)	15 (7.7)	13 (1.1)		10 (3.0)	5 (12.5)	5 (1.7)	
vascular thromboses, n (%)	No/Unk	1092 (80.7)	74 (38.1)	1018 (87.8)	**<0.0001**	277 (82.4)	14 (35.0)	263 (88.9)	**<0.0001**
	Yes	261 (19.3)	120 (61.9)	141 (12.2)		59 (17.6)	26 (65.0)	33 (11.1)	
pregnancy morbidity, n (%)	No/Unk	1249 (92.3)	151 (77.8)	1098 (94.7)	**<0.0001**	310 (92.3)	29 (72.5)	281 (94.9)	**<0.0001**
	Yes	104 (7.7)	43 (22.2)	61 (5.3)		26 (7.7)	11 (27.5)	15 (5.1)	
ACR Criteria, n (%)									
Malar Rash	Yes	458 (33.9)	60 (30.9)	398 (34.3)	0.35	64 (19.0)	7 (17.5)	57 (19.3)	0.79
Discoid Rash	Yes	333 (24.6)	37 (19.1)	296 (25.5)	0.053	48 (14.3)	3 (7.5)	45 (15.2)	0.19
Photosensitivity	Yes	382 (28.2)	54 (27.8)	328 (28.3)	0.89	61 (18.2)	8 (20.0)	53 (17.9)	0.75
Oral Ulcers	Yes	349 (25.8)	46 (23.7)	303 (26.1)	0.47	75 (22.3)	6 (15.0)	69 (23.3)	0.24
Arthritis	Yes	1009 (74.6)	136 (70.1)	873 (75.3)	0.12	220 (65.5)	20 (50.0)	200 (67.6)	**0.028**
Serositis	Yes	594 (43.9)	99 (51.0)	495 (42.7)	**0.031**	118 (35.1)	22 (55.0)	96 (32.4)	**0.005**
Renal Disorder	Yes	487 (36.0)	91 (46.9)	396 (34.2)	**0.0006**	103 (30.7)	16 (40.0)	87 (29.4)	0.17
Neurologic Disorder	Yes	216 (16.0)	58 (29.9)	158 (13.6)	**<0.0001**	31 (9.2)	6 (15.0)	25 (8.4)	0.18
Hematologic Disorder	Yes	1135 (83.9)	176 (90.7)	959 (82.7)	**0.0052**	282 (83.9)	36 (90.0)	246 (83.1)	0.27
anti-dsDNA and/or anti-Sm [2]	Yes	816 (60.3)	132 (68.0)	684 (59.0)	**0.017**	206 (61.3)	22 (55.0)	184 (62.2)	0.38
Antinuclear Antibody	Yes	1229 (90.8)	172 (88.7)	1057 (91.2)	0.26	321 (95.5)	33 (82.5)	288 (97.3)	**<0.0001**

[1] as of December 31, 2004; [2] Immunologic Disorder without antiphospholipid antibodies; SD=standard deviation; Unk=unknown

Table 2. Frequency of Clinical and Laboratory Characteristics in Prevalent and Incident Systemic Lupus Erythematosus with Secondary Antiphospholipid Syndrome by Race

Characteristic	Category	Prevalent SLE (N=1353)					Incident SLE (N=336)				
		Total (n=1353)	+ APS (n=194)				Total (n=336)	+ APS (n=40)			
			Overall (n=194)	Black (n=143)	Non-Black (n=51)	P-value		Overall (n=40)	Black (n=28)	Non-Black (n=12)	P-value
age [1], years±SD	Mean ± SD	45.7 ± 14.1	44.1 ± 13.1	42.4 ± 12.4	48.9 ± 13.9	**0.0022**	42.1 ± 16.3	44.1 ± 15.5	43.7 ± 15.2	45.1 ± 16.8	0.8
SLE duration [1], years±SD	Mean ± SD	11.1 ± 8.0	11.1 ± 8.0	11.0 ± 7.9	11.3 ± 8.2	0.86					
sex, n (%)	Male	136 (10.1)	24 (12.4)	17 (11.9)	7 (13.7)	0.8	44 (13.1)	5 (12.5)	2 (7.1)	3 (25.0)	0.15
	Female	1217 (89.9)	170 (87.6)	126 (88.1)	44 (86.3)		292 (86.9)	35 (87.5)	26 (92.9)	9 (75.0)	
smoking, n (%)	Never	686 (62.3)	104 (62.3)	79 (62.2)	25 (62.5)	0.63	186 (69.4)	22 (61.1)	16 (61.5)	6 (60.0)	0.57
	Current	203 (18.4)	35 (21.0)	25 (19.7)	10 (25.0)		43 (16.0)	4 (11.1)	2 (7.7)	2 (20.0)	
	Former	213 (19.3)	28 (16.8)	23 (18.1)	5 (12.5)		39 (14.6)	10 (27.8)	8 (30.8)	2 (20.0)	
livedo reticularis, n (%)	No/Unk	1311 (96.9)	180 (92.8)	137 (95.8)	43 (84.3)	**0.011**	328 (97.6)	38 (95.0)	27 (96.4)	11 (91.7)	0.52
	Yes	42 (3.1)	14 (7.2)	6 (4.2)	8 (15.7)		8 (2.4)	2 (5.0)	1 (3.6)	1 (8.3)	
Raynaud's, n (%)	No/Unk	871 (64.4)	113 (58.2)	84 (58.7)	29 (56.9)	0.87	240 (71.4)	31 (77.5)	23 (82.1)	8 (66.7)	0.41
	Yes	482 (35.6)	81 (41.8)	59 (41.3)	22 (43.1)		96 (28.6)	9 (22.5)	5 (17.9)	4 (33.3)	
anticardiolipin Ab, n (%)	No/Unk	1093 (80.8)	64 (33.0)	45 (31.5)	19 (37.3)	0.49	274 (81.5)	14 (35.0)	10 (35.7)	4 (33.3)	0.99
	Yes	260 (19.2)	130 (67.0)	98 (68.5)	32 (62.7)		62 (18.5)	26 (65.0)	18 (64.3)	8 (66.7)	
lupus anticoagulant, n (%)	No/Unk	1188 (87.8)	94 (48.5)	72 (50.3)	22 (43.1)	0.42	302 (89.9)	19 (47.5)	13 (46.4)	6 (50.0)	0.99
	Yes	165 (12.2)	100 (51.5)	71 (49.7)	29 (56.9)		34 (10.1)	21 (52.5)	15 (53.6)	6 (50.0)	
anti-beta 2 glycoprotein I IgG or IgM, n (%)	No/Unk	1325 (97.9)	179 (92.3)	136 (95.1)	43 (84.3)	**0.027**	326 (97.0)	35 (87.5)	26 (92.9)	9 (75.0)	0.15
	Yes	28 (2.1)	15 (7.7)	7 (4.9)	8 (15.7)		10 (3.0)	5 (12.5)	2 (7.1)	3 (25.0)	
vascular thromboses, n (%)	No/Unk	1092 (80.7)	74 (38.1)	48 (33.6)	26 (51.0)	**0.031**	277 (82.4)	14 (35.0)	9 (32.1)	5 (41.7)	0.72
	Yes	261 (19.3)	120 (61.9)	95 (66.4)	25 (49.0)		59 (17.6)	26 (65.0)	19 (67.9)	7 (58.3)	
pregnancy morbidity, n (%)	No/Unk	1249 (92.3)	151 (77.8)	110 (76.9)	41 (80.4)	0.7	310 (92.3)	29 (72.5)	19 (67.9)	10 (83.3)	0.45
	Yes	104 (7.7)	43 (22.2)	33 (23.1)	10 (19.6)		26 (7.7)	11 (27.5)	9 (32.1)	2 (16.7)	
ACR Criteria, n (%)											
Malar Rash	Yes	458 (33.9)	60 (30.9)	46 (32.2)	14 (27.5)	0.6	64 (19.0)	7 (17.5)	4 (14.3)	3 (25.0)	0.41
Discoid Rash	Yes	333 (24.6)	37 (19.1)	35 (24.5)	2 (3.9)	**0.0007**	48 (14.3)	3 (7.5)	3 (10.7)		0.54
Photosensitivity	Yes	382 (28.2)	54 (27.8)	34 (23.8)	20 (39.2)	**0.045**	61 (18.2)	8 (20.0)	3 (10.7)	5 (41.7)	**0.039**
Oral Ulcers	Yes	349 (25.8)	46 (23.7)	34 (23.8)	12 (23.5)	0.99	75 (22.3)	6 (15.0)	5 (17.9)	1 (8.3)	0.65
Arthritis	Yes	1009 (74.6)	136 (70.1)	105 (73.4)	31 (60.8)	0.11	220 (65.5)	20 (50.0)	16 (57.1)	4 (33.3)	0.3
Serositis	Yes	594 (43.9)	99 (51.0)	80 (55.9)	19 (37.3)	**0.023**	118 (35.1)	22 (55.0)	15 (53.6)	7 (58.3)	0.99
Renal Disorder	Yes	487 (36.0)	91 (46.9)	78 (54.5)	13 (25.5)	**0.0005**	103 (30.7)	16 (40.0)	14 (50.0)	2 (16.7)	0.079
Neurologic Disorder	Yes	216 (16.0)	58 (29.9)	46 (32.2)	12 (23.5)	0.29	31 (9.2)	6 (15.0)	5 (17.9)	1 (8.3)	0.65
Hematologic Disorder	Yes	1135 (83.9)	176 (90.7)	131 (91.6)	45 (88.2)	0.57	282 (83.9)	36 (90.0)	26 (92.9)	10 (83.3)	0.57
anti-dsDNA and/or anti-Sm [2]	Yes	816 (60.3)	132 (68.0)	103 (72.0)	29 (56.9)	0.055	206 (61.3)	22 (55.0)	18 (64.3)	4 (33.3)	0.093
Antinuclear Antibody	Yes	1229 (90.8)	172 (88.7)	130 (90.9)	42 (82.4)	0.12	321 (95.5)	33 (82.5)	25 (89.3)	8 (66.7)	0.17

[1] as of December 31, 2004; [2] Immunologic Disorder without antiphospholipid antibodies; SD=standard deviation; Unk=unknown

ticardiolipin (aCL), lupus anticoagulant (LA), and/or anti-b2 glycoprotein-I IgG or IgM (ab2) were captured by medical record and laboratory review. Frequency of clinical and laboratory characteristics were reported for prevalent and incident SLE cases overall and compared between SLE cases with (+APS) and without 2APS (-APS) and between Black and non-Black SLE cases +APS.

Results: In prevalent SLE, 14.3% (194/1353) had 2APS with no differences in age, SLE duration, or sex between APS status [Table 1]. In +APS, there were 67% aCL, 51.5% LA, and 7.7% ab2 (-APS: 11.2, 5.6, and 1.1%, respectively) with 61.9% vascular thromboses and 22.2% pregnancy morbidity. Anti-dsDNA and/or Sm, livedo reticularis, serositis, renal, neurologic, and hematologic disorder were also more frequent. In incident SLE, 11.9% (40/336) had 2APS with no differences in age, SLE duration, or sex between APS status. In +APS, there were 65% aCL, 52.5% LA, and 12.5% ab2 (-APS: 12.2, 4.4, and 1.7%, respectively) with 65% vascular thromboses and 27.5% pregnancy morbidity. There was also more smoking, arthritis, serositis, and ANA positivity. Blacks with prevalent SLE had 2APS less frequently than non-Blacks (143/1024 or 14.0% vs 51/329 or 15.5%) and were younger and had more vascular thromboses, discoid, serositis, and renal disorder but less livedo, ab2, and photosensitivity compared to non-Blacks [Table 2]. Blacks with incident SLE had 2APS less frequently than non-Blacks (28/247 or 11.3% vs. 12/89 or 13.5%) and had less photosensitivity.

Conclusion: The burden of 2APS in SLE in this population-based study ranged from 11.9 to 14.3%. There were notable differences in prevalent and incident SLE by APS status and by race, which may provide insight into the pathophysiology of 2APS. Further research is needed into this important subgroup.

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Abstract Number: 0079

Association Between Preconception Complement Levels and Use of Hydroxychloroquine with Pregnancy Outcome in Patients with Primary Antiphospholipid Syndrome and Carriers of Antiphospholipid Antibodies: An International Multicenter Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Antiphospholipid Syndrome Poster (0069–0083)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: APS is a rare autoimmune disease characterized by thrombotic events and/or pregnancy morbidities in the presence of confirmed positivity for aPL. Complement was demonstrated to be involved in aPL-related pregnancy loss in animal models and human disease. According to some authors, Hydroxychloroquine (HCQ) can control the activation of the complement system. HCQ has been shown to improve pregnancy outcome and to reduce aPL title. In murine model of obstetrical APS, HCQ was able to prevent placental and fetal abnormalities and to lower serum C5a levels. This study was conducted to verify the effect of HCQ in a multicenter cohort of Primary APS (PAPS) and aPL carriers pregnant women and possible correlation with preconception serum C3/C4 levels.

Methods: Medical records of pregnant women with confirmed positivity for aPL antibodies attending 12 referral centers from January 2010 to December 2020 were retrospectively evaluated. We considered as aPL-related adverse pregnancy outcome (APO): spontaneous abortions (< 10 weeks of gestation), fetal loss (≥10 weeks of gestation), neonatal death (death of a formed fetus alive at birth in the first 28 days of life), preterm delivery before 37 weeks of

gestation, preeclampsia, eclampsia or HELLP syndrome. The presence of one or more of them were considered for the definition of gestational outcome. No patients with SLE or other autoimmune disease were included.

Results: We have analyzed 164 singleton pregnancies (22 aPL carriers - 13%) in 128 patients: all the patients were treated with combination therapy (low dose aspirin, LDA + low molecular weight heparin, LMWH), and in 30 HCQ was added. 58 pregnancies (43%) had low levels of preconception C3 and/or C4. A triple aPL positivity was observed in 54 pregnancies (40%), 14 (26%) of them were treated with combination therapy + HCQ. When considering the whole cohort, the addition of HCQ did not significantly improved the gestational outcome (14/30, 47% vs 72/134, 54%, p=0.317, ns). Further stratification was performed on the basis of complement consumption. In the group of patients with preconception low C3 and/or C4 the addition of HCQ did not significantly improve pregnancy outcome (7/11, 64% vs 15/47, 32%, p=0.264, ns). We have lastly evaluated 40 pregnancies that were characterized by a high-risk profile (triple aPL positivity and complement consumption) to assess whether the administration of HCQ on the top of combination therapy during pregnancy could influence gestational outcome. HCQ significantly improved gestational outcome (7/10, 70% vs 7/30, 23%, p=0.018). This observation could not be confirmed in patients with single or double aPL positivity (p=1, ns).

Conclusion: The study shows that administering HCQ in addition to combination therapy can improve gestational outcome in aPL/APS high-risk patients defined as triple aPL positive, with decreased C3 and /or C4 levels. This observation confirms that HCQ exerts a beneficial effect on aPL pregnancies by complement inhibition as it was shown in animal models. In addition, our results provide the clinicians a useful tool to implement conventional treatment in patients at high risk of pregnancy complication or loss.

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Abstract Number: 0080

One Point Increase in the Initial Damage as Measured by the Damage Index for Antiphospholipid Syndrome Predicts Mortality in a Multi-Ethnic Group of Thrombotic Antiphospholipid Syndrome Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

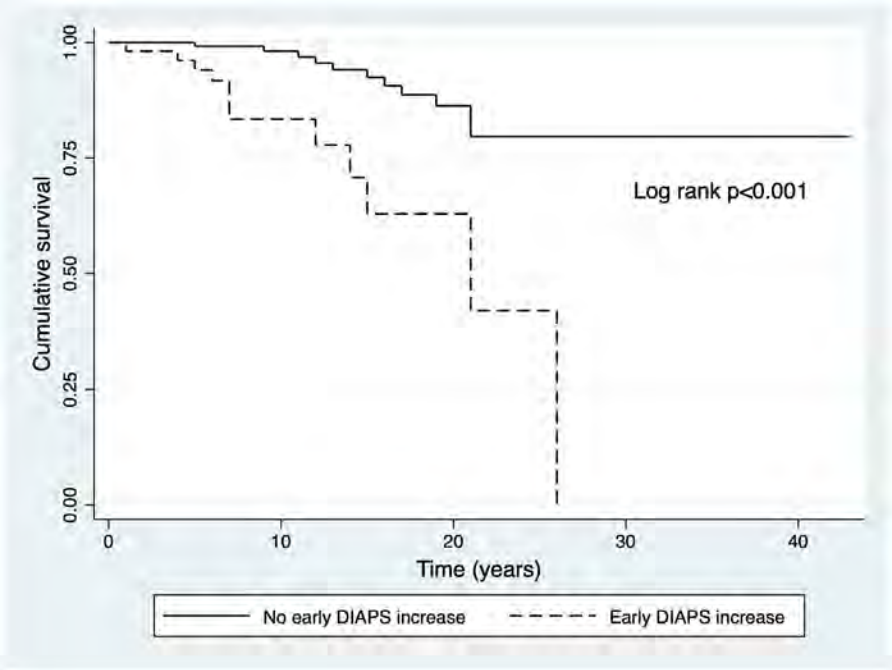

Figure 1. Kaplan–Meier curve showing cumulative survival according to the presence of early DIAPS increase.

Background/Purpose: The chronic and recurrent nature of antiphospholipid syndrome (APS) leads to damage accrual that impairs long-term functional status and survival. The Damage Index for Antiphospholipid Syndrome (DIAPS) is a validated instrument designed to capture the damage accrual in thrombotic APS, but it is not known whether it correlates with mortality. We aim to determine whether early damage, as measured by the DIAPS, predicts long-term mortality in thrombotic APS.

Methods: We carried out a retrospective analysis of all medical records to calculate the yearly DIAPS score of 197 thrombotic APS patients attending the Rheumatology and/or Haematology clinics at a tertiary hospital for up to 43 (median 10) years. Patients fulfilled the 2006 Sydney classification criteria. The disease onset was the time the first thrombotic event related to APS was diagnosed. Early damage refers to damage present at six months after the disease onset. Early DIAPS increase refers to the increase of at least one point from the initial DIAPS score within the first five years after the disease onset. DIAPS score is shown as median (interquartile range, IQR). We used logistic, and uni and multivariable Cox regression models to analyse risk factors affecting mortality. Survival was analysed through the Kaplan-Meier method.

Results: The median age at APS onset was 40 (IQR 51-28) years, with a female (71%) and primary APS (66%) preponderance. Caucasian ethnicity was the most prevalent (72%), followed by Asian (10%), Afro-Caribbean (9%) and other (9%). Damage developed in 143 (73%) patients with a median DIAPS score of 1 (IQR 2-0) at the last visit. Early damage was present in 69 (35%) patients. Early DIAPS scored low values in the whole group (0, IQR 1-0). We identified 23 fatalities (12%). Patients who died had higher last DIAPS (2, IQR 3-1 vs. 1, IQR 2-0, p=0.012) but similar early DIAPS score (0, IQR 1-0 vs. 0, IQR 1-0, p=0.318) compared to those who survived. Secondary APS (HR 3.07, 95% CI 1.32-7.12, p=0.009), male gender (HR 3.14, 95% CI 1.35-7.33, p=0.008) and age at APS onset ≥40 years (HR 5.34, 95% CI 1.96-14.53, p=0.001) were risk factors for death. Early damage was not associated with death (HR 1.65, 95% CI 0.73-3.78, p=0.231). Conversely, early DIAPS increase, present in 29% (53/181) of patients, was associated with death (HR 5.40, 95% CI 2.33-12.52, p< 0.001), even after adjusting individually for APS category (secondary, HR 5.05, 95% CI 2.18-11.72, p< 0.001), gender (male, HR 5.40, 95% CI 2.29-12.73, p< 0.001) and age at APS onset (≥40 years, HR 3.41, 95% CI 1.43-8.20, p=0.006). Figure 1 shows the survival analysis. Having a first arterial thrombotic

event was associated with early damage (OR 7.24, 95% CI 3.74-14.03, $p< 0.001$), but not with early DIAPS increase (OR 1.22, 95% CI 0.64-2.33, $p=0.539$) nor with the risk of death (HR 1.85, 95% CI 0.79-4.27, $p=0.151$).

Conclusion: These findings suggest that damage accrual accessed by DIAPS is associated with increased mortality in a large multi-ethnic group of APS patients. In particular, an increase of at least one point on DIAPS in the first five years after disease onset, but not early damage, is an important predictor of mortality regardless of the nature of the first thrombotic event, gender, APS category and age.

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Abstract Number: 0081

Thrombin Generation Assay and Lupus Anticoagulant Identify Different Populations of Patients with Antiphospholipid Antibodies

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Risk stratification in patients with antiphospholipid antibodies (aPL) remains a clinical challenge. We aim to evaluate the role of Thrombin Generation Assay (TGA) in distinguishing various populations of aPL positive patients (with and without lupus anticoagulant - LA) and its association with β2GPI-dependent and anti-phosphatidyl-serine/prothrombin (aPS/PT) antibodies.

Methods: One-hundred-and-eight patients were tested with TGA and divided as follows: 21 patients with aPS/PT IgG/IgM, 29 with aβ2GPI IgG/IgM, 31 with aPS/PT and aβ2GPI IgG/IgM, 27 with aPS/PT and/or aβ2GPI IgM low-titers. Table 1 resumes the clinical characteristics of the APS patients (excluding aPL asymptomatic). Thirty-one healthy donors (HDs) and 24 controls treated with VKA were also included.

Results: The most deranged TGA and LA profile was observed in patients with both aPS/PT and aβ2GPI when compared to those with an isolated positivity for aPS/PT or aβ2GPI and patients with aPS/PT and/or aβ2GPI IgM at low titres (Figure 1). Similarly, patients with aPS/PT and/or aβ2GPI at medium/high titres presented with the higher rate of clinical manifestations.

When comparing the TGA curves of APS patients, asymptomatic aPL positive (aPL+) subjects, HDs and controls treated with VKA, we observed that aPL+ patients (particularly those with a confirmed diagnosis of APS) showed a characteristic profile (Figure 2). Moreover, both in aPL+ subjects and in the control groups we observed a correlation between TGA and LA parameters.

	Group 1: isolated aPS/PT+ IgG/IgM (16)	Group 2: isolated aβ2GPI+ IgG/IgM (20)	Group 3: aPS/PT+ and aβ2GPI+ IgG/IgM (24)	Group 4: aPS/PT+ and/or aβ2GPI+ IgM low titres (15)
APS clinical manifestations				
Thrombosis (Y/N), n (%)	14 (87,5%)	16 (80%)	21 (87,5%)	13 (86,6%)
N of thrombotic events	21	23	36	15
Arterial thrombosis (Y/N), n (%)	10 (62,5%)	9 (45%)	14 (58,3%)	11 (73,3%)
Arterial events, n	13	10	21	12
Venous thrombosis (Y/N), n (%)	6 (37,5%)	10 (50%)	11 (45,8%)	3 (20%)
Venousevents, n	9	13	15	3
Pregnancy morbidity, n (%)	3 (18,8%)	4 (20%)	3 (12,5%)	2 (13,3%)
Stroke, n (%)	4 (25%)	4 (20%)	9 (37,5%)	7 (46,6%)
TIA, n (%)	1 (6,2%)	3 (15%)	4 (16,6%)	0
DVT, n (%)	4 (25%)	8 (40%)	11 (45,8%)	2 (13,3%)
PE, n (%)	2 (12,5%)	3 (15%)	2 (8,3%)	1 (6,6%)
Recurrent thrombosis (Y/N), n (%)	3 (18,8%)	3 (15%)	7 (29,1%)	0
Livedo reticularis, n (%)	1 (6,2%)	1 (5%)	4 (16,6%)	0
Thrombocytopenia, n (%)	4 (25%)	4 (20%)	6 (25%)	2 (13,3%)
Valvular, n (%)	1 (6,2%)	0	2 (8,3%)	0
Peripheral artery disease, n (%)	0	3 (15%)	4 (16,6%)	0
Diffuse alveolar hemorrhage, n (%)	0	0	1 (4,1%)	0

Conclusion: TGA seems a valuable approach to stratify aPL+ patients according to their risk profile. The differences among groups and different populations of autoantibodies specificities obtained from this test can be considered a translational validation of the increased thrombotic risk of patients with triple or tetra aPL positivity.

“Classical” and “Extra-criteria” APS clinical manifestations of each group (considering solely patients with a confirmed diagnosis of APS).

Graphical representation of the differences between TGA and LA profiles between groups. The differences between groups that reached statistical significance ($p<0,05$) are indicated in the graph. (aPS/PT - Anti-phosphatidylserine/prothrombin antibodies; aβ2GPI - Anti-β2-glycoprotein-I antibodies; Ig – Immunoglobulin; tLag – Lag time; tPeak – Time to peak; AUC – Area under the curve; sctScreen - Silica Clotting Time screening; sctMix - Silica Clotting Time mix; sctConf – Silica Clotting Time confirmation; dRVVTscreen - Dilute Russell’s viper venom time screening; dRVVTmix - Dilute Russell’s viper venom time mix; dRVVTconf - Dilute Russell’s viper venom time confirmation)

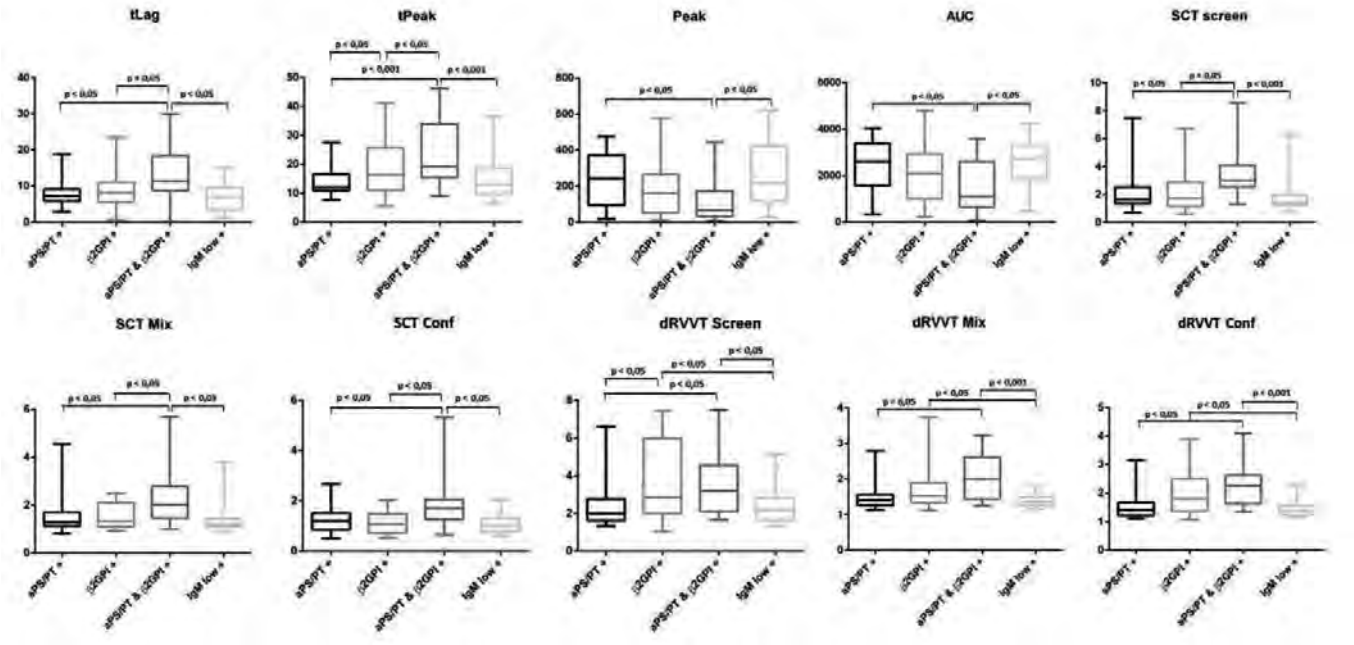

Figure 1

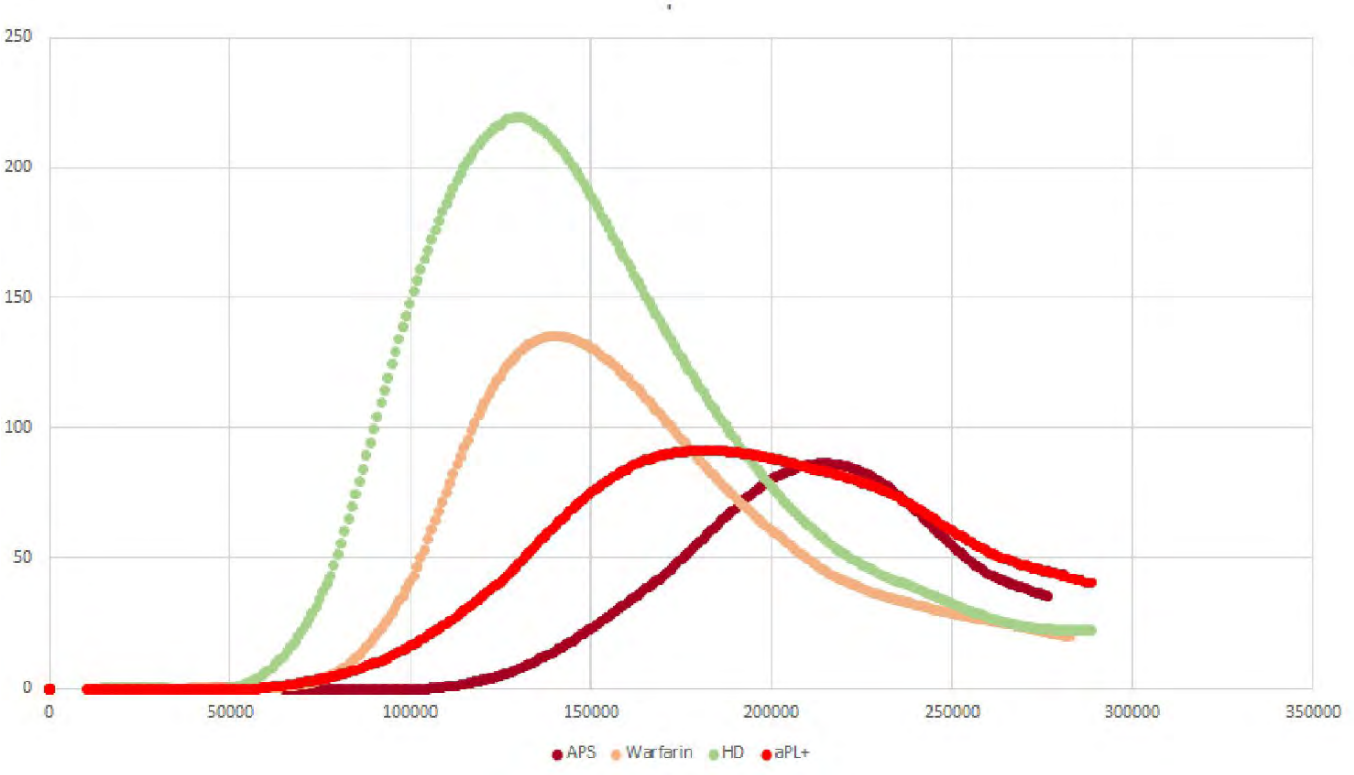

Figure 2

Representative Thrombin Generation Assay profile of APS patients, asymptomatic aPL+ patients, healthy controls and controls treated with Vitamin K antagonists. (TGA – Thrombin generation assay; APS – Antiphospholipid Syndrome; aPL – Antiphospholipid antibodies; HC – healthy controls)

Disclosure: M. Radin, None; **A. Barinotti**, None; **I. Cecchi**, None; **S. Foddai**, None; **E. Rubini**, None; **D. Roccatello**, None; **E. Menegatti**, None; **S. Sciascia**, None.

Abstract Number: 0082

Association of Current Cigarette Smoking and Obesity with Antiphospholipid Antibodies and Thrombosis in 1216 International Patients Evaluated for Suspected Antiphospholipid Syndrome (APS)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Few studies have evaluated the role of environmental factors in APS. While antiphospholipid antibodies (aPL) may be induced by environmental stiumuli, e.g., viruses, cardiovascular disease and venous thromboembolism (VTE) risk factors may contribute to thrombosis in aPL-positive patients. In particular, we hypothesized that cigarette smoking and obesity might be risk factors for aPL positivity and thrombosis development based on previous literature. Using international multi-center data on patients referred for "suspected APS", we tested the association of smoking and obesity with aPL positivity and thrombosis.

Methods: We collected 1216 cases of patients referred to 32 major centers in North America, South America, Europe, and Asia for suspected APS (aPL-positive/negative cases with/without history of thrombosis were collected as part of the new APS classification criteria development efforts, with additional questions specific for this project). Demographic, exposure, and clinical data were collected in a standardized format using an online secure REDCap database. For the current analysis, for each case, we also collected information related to current/past/never smoking history and most recent body mass index (BMI) at the office visit. We used t-tests or chi-square tests to evaluate associations of smoking (current versus former/never) and obesity (BMI≥ 30 versus < 30) with ever positive and most recent positive aPL (lupus anticoagulant [LA], anticardiolipin antibody [aCL] IgG, or anti-βeta-2-glycoprotein-I antibody [aβ2GPI] IgG) and with history of any thrombosis (including venous thromboembolism [VTE] or arterial thrombosis [AT]). aPL positivity was defined as test result above the laboratory normal range.

Results: Median age of 1216 cases was 42 years (IQR: 35, 55.5); 78.5% were female, 82.1% White, 10.4% Hispanic/Latinx, and 52.6% were European, and 37.7% North American. 64.2% of patients had positive LA tests, 42.9% had positive aβ2GPI IgG, and 53.6% had positive aCL IgG. 8.6% of patients were current smokers, while 22.8% had BMI≥ 30 kg/m2 at office visit (Table 1). We found no association of current smoking with history of ever or most recent positive LA, aCL IgG, aβ2GPI IgG as well as history of thrombosis overall, VTE, or AT (Table 2). However, obesity was associated with ever (but not most recent) positive LA (p=0.04) and history of thrombosis (p < 0.01), but not ever or most recent positive aCL or aB2GPI IgG positivity (Table 2). Obesity was specifically associated with VTE (p=0.01), but not AT.

Conclusion: Within a cohort of international cases referred for suspected APS, obesity was associated with a history of ever positive LA and with VTE. No clear association of current smoking was demonstrated, possibly due to

Table 1. Baseline Characteristics of 1216 International Cases Referred for Suspected APS	
Age in years, median (IQR)	42 (35, 55.5)
Gender	
• Female	955 (78.5%)
Race	
• White	998 (82.1%)
• Black	69 (5.7%)
• Other	149 (12.3%)
Ethnicity	
• Hispanic/Latin American	126 (10.4%)
• Not Hispanic/Latin American	821 (67.5%)
• Other	175 (14.4%)
Region	
• Europe	640 (52.6%)
• North America	459 (37.7%)
• South America	85 (7.0%)
• Asia	32 (2.6%)
Antiphospholipid Antibody Status	
Ever Positive	
• Lupus Anticoagulant positive (N=1,178)	756 (64.2%)
• Anticardiolipin IgG positive (N=1,178)	631 (53.6%)
• Anti-Beta-2-Glycoprotein-1 IgG positive (N=1,063)	456 (42.9%)
Most Recent	
• Lupus Anticoagulant positive (N=1,174)	598 (50.9%)
• Anticardiolipin IgG positive (N=1,173)	473 (40.3%)
• Anti-Beta-2-Glycoprotein-1 IgG positive (N=1063)	370 (34.8%)
History of Thrombosis (VTE or AT)*	623 (51.2%)
• Venous Thromboembolism (VTE)	422 (34.7%)
• Arterial Thrombosis (AT)	286 (23.5%)
Smoking Status (N=1,145)	
• Current	104 (9.1%)
• Former	180 (15.9%)
• Never	861 (75.2%)
Body Mass Index (N=995)	
• Obese (BMI ≥30 kg/m2)	227 (22.8%)
*85 individuals experienced both VTE and AT	

Table 2. Association of Current Cigarette Smoking and Obesity with Antiphospholipid Antibody Positivity and History of Thrombosis in 1216 International Cases Suspected of APS

N, % (p-values)	LA Positive* (Ever) N=756	aCL IgG Positive* (Ever) N=631	aB2GPI IgG** Positive (Ever) N=456	LA Positive* (Most Recent) N=598	aCL IgG Positive* (Most Recent) N=473	aB2GPI IgG Positive** (Most Recent) N=370	Any Thrombosis (AT or VTE) N=623	AT N=286	VTE N=422
Smoking Status* **									
Current Smoker (versus Former/Never)	59, 7.8% (p=0.21	52, 8.2% (p=0.75)	36, (7.9%) (p=0.48)	46, 7.7% (p=0.22)	40, 8.5% (p=0.94)	33, 8.9% (p=0.76)	53, 8.5% (p=0.86)	26, 9.0% (p=0.72)	38, 9.0% (p=0.75)
Body Mass Index (BMI**)**									
Obese (BMI ≥ 30) versus < 30 kg/m^2)	157, 20.8% **(p=0.04)**	129, 20.4% (p=0.12)	91, 20.0% (p=0.80)	119, 19.9% (p=0.09)	95, 20.1% (p=0.32)	78, 21.1% p=0.43	130, 20.9% **(p<0.0001)**	57, 19.9% (p=0.73)	96, 22.7% **(p=0.01)**

LA= lupus anticoagulant; aCL=anticardiolipin antibody; aB2GPI=anti-beta-2-glycoprotein-I antibody, AT=arterial thrombosis, VTE=venous thromboembolism.
*LA and aCL tested in 1178 of 1216; **aB2GPI IgG tested in 1063 of 1216; ***Smoking status available in 1145 of 1216; and ****BMI available in 995 of 1216. p-values from Chi squared tests. <0.05 considered significant. Missing values excluded from p-value calculation.

low prevalence in our cohort. These results are hypothesis-generating and are being pursued in further analyses, accounting for potential confounders such as sociodemographics, concomitant systemic rheumatic disease, and other thrombosis risk factors. Subgroup analyses will evaluate also the association of these environmental stimuli with other aPL isotypes.

Disclosure: M. Barbhaiya, None; **D. Jannat-Khah**, Cytodyn, 12, own shares of stock, Walgreens, 12, Own stock shares, AstraZeneca, 12, own stock shares, GW Pharmaceuticals, 12, stock ownership; **D. Erkan**, ACR/EULAR, 5, LCTC, 5, NIH/NIAID, 5, GSK, 5, 6, Exagen, 5, Alexion, 2, UCB, 2, UpToDate, 9, APS ACTION, 4; **K. Costenbader**, Neutrolis, 11, Merck, Exagen, Gilead, 5, Astra Zeneca, Neutrolis, 2; **O. Criteria Development Case Collectors**, None.

Abstract Number: 0083

Cardiac Valve Surgery Outcomes in the Antiphospholipid Syndrome

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Antiphospholipid Syndrome Poster (0069–0083)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiac valve involvement in the APS is prevalent, necessitating valve surgery in about 5% of the patients. Data regarding valve surgery outcomes in APS relies on small case series and case reports with a mortality rate ranging from 12.5% to 40%. We aimed to describe the outcome and prognosis of cardiac valve surgery in patients with primary and secondary APS, and to determine factors associated with outcome.

Methods: All patients with APS, (primary or secondary to SLE), who underwent valve surgery at the Sheba-Tel-Hashomer or Tel Aviv Sourasky medical centers in Israel in the last 3 decades were included in this retrospective analysis. Data regarding clinical characteristics, valve involvement, treatment before surgery, type of valve used and early and late complications were collected and analyzed.

Results: We identified 23 patients who underwent cardiac valve surgery from 1992-2021. Of whom, 17 (73.9%) were female, median age at surgery was 45 years (range 18-71). Ten patients (43.5%) had APS secondary to SLE. The median time from APS diagnosis to valve surgery was 17 years (range 0-40). Triple positive aPL were noted in 16 of 21 patients (76.2%), and 19 of 21 (90.5%) had a positive lupus anticoagulant (LA).

The mitral valve (MV) was the most common valve affected (n=15, 65.22%), followed by the aortic valve (n=7, 30.43%). Findings compatible with Libman-Sacks endocarditis (LSE) were noted in 13 (56.52%) of the patients. Moderate-severe pulmonary hypertension was evident in 50% of the patients before surgery, and the mean New-York Heart Association score was 2.09.

A mechanical valve was used in 14 of 23 (60.87%) patients, one patient underwent MV repair and one tricuspid valve repair. One patient required concomitant coronary bypass surgery (CABG).

Mean follow up following surgery was 66.59±80.12 months.

Thirteen patients (56.52%) had an early (30 day post-surgery) complication, including 8 severe complications - 2 deaths, 2 post-pericardiotomy syndrome, valve infection, valve thrombosis, stroke and major bleeding (one of each). Eight of 20 patients (40%) had a late complication - one death (4 years after MV replacement); valve thrombosis; stroke and major bleeding; newly developed LSE; major bleeding; stroke; E. coli bacteremia and chronic pericarditis (one of each). All mortality cases occurred in patients with mechanical valves.

In a univariate analysis pre-surgical warfarin treatment (p=0.02) and valve repair (p=0.03) were associated with a better outcome (no complications or death). Whereas a past history of DVT (p=0.02), pre-surgical heparin treatment (p=0.009), and CABG (p=0.008) were linked with mortality.

Conclusion: In this cohort of APS patients from two tertiary centers in Israel the mortality rate was 13.04%, which was lower than some previous case series. The total complication rate was 73.91%.

We have identified possible predictors of outcome, however valve surgery in APS patients continues to carry a guarded prognosis. Larger studies and registries are needed to define risk factors for severe valvular involvement, the best surgical approach and medical treatment post-surgery.

Disclosure: T. Eviatar, None; **S. Niznik**, None; **N. Agmon-Levin**, None; **D. Paran**, None.

Abstract Number: 0084

COVID-19 Pneumonia in Two Hospitals: Similar Outcomes Despite Differential Use of Tocilizumab

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
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Session Time: 8:30AM–10:30AM

Background/Purpose: A substantial number of patients with COVID-19 pneumonia develop a hyperinflammatory state. The anti-IL-6 receptor (IL-6R) mAb tocilizumab (TCZ) has been used in such setting. However, studies to date have had mixed results.

Our institution is unique in that nearly all services to two independent hospitals, Keck Medical Center (KMC, a private non-profit hospital owned and managed by USC) and the Los Angeles County + University of Southern California Medical Center (LAC+USC MC, a public hospital owned and managed by the County of Los Angeles), are provided by the same pool of physicians who follow similar protocols for management of COVID-19, with one crucial exception – patients admitted to LAC+USC MC do not receive TCZ, while those admitted to KMC are eligible to receive TCZ. This difference in access to TCZ results in two arms of “real-world” patients that are “quasi-randomized”, resulting in a setting that combines components of a randomized trial with real-world practice.

Methods: The records of patients with COVID-19 admitted to KMC or LAC+USC MC between March 1, 2020, and August 31, 2020 (COVID surge 1), and between February 20, 2021, and April 20, 2021 (COVID surge 2), were reviewed. Forty patients with severe COVID-19 pneumonia at KMC received at least a single TCZ dose (400 mg IV).

Table 1: Baseline (Day 0) Characteristics by Tocilizumab Exposure

Variable	Tocilizumab (n=40)	No tocilizumab (n=133)	p-value
Age	58.1 (15.3)	60.5 (13.7)	0.33
BMI (kg/m^2)	28.8 (5.7)	28.4 (4.9)	0.97
SOFA (Day 0)	4.6 (2.6)	3.8 (2.5)	0.08
SOFA (Admission)	2.7 (1.8)	3.4 (2.4)	0.06
Male	25 (62.5%)	77 (57.9%)	0.71
Hispanic	24 (60.0%)	110 (82.7%)	0.004
Race			
White	35 (87.5%)	115 (86.5%)	1.00
Black	0	6 (4.5%)	0.34
Asian	1 (2.5%)	11 (8.3%)	0.30
American Indian/Pacific Islander	0	2 (1.5%)	1.00
Hypertension	24 (60.0%)	71 (53.4%)	0.34
Diabetes	13 (32.5%)	64 (48.1%)	0.014
Smoking history	4 (10.0%)	26 (19.6%)	0.42
Hyperlipidemia	11 (27.5%)	41 (30.8%)	0.08
Ordinal scale			
Ambulatory (1, 2)	0	1 (0.8%)	0.29
Hospitalized, mild disease: No oxygen therapy (3)	0	12 (9.0%)	
Hospitalized, mild disease: Oxygen by mask or nasal prongs (4)	13 (32.5%)	40 (30.1%)	
Hospitalized, severe disease: non-invasive ventilation or high-flow oxygen (5)	13 (32.5%)	42 (31.6%)	
Hospitalized, severe disease: intubation and mechanical ventilation (6)	5 (12.5%)	20 (15.0%)	
Hospitalized, severe disease: ventilation+additional organ support (7)	9 (2.25%)	18 (13.5%)	
Survived	29 (72.5%)	94 (71.2%)	1.00
Other medications			
Steroid (n=172)	23 (59.0%)	88 (66.2%)	0.45
HCQ (n=170)	19 (48.7%)	11 (8.4%)	<0.0001
Azithromycin (n=173)	28 (70.0%)	113 (85.0%)	0.039
Convalescent plasma (n=173)	14 (35.0%)	32 (24.1%)	0.22
Mesenchymal stem cell therapy (n=172)	0	12 (9.1%)	0.07
Remdesivir (n=173)	9 (22.5%)	24 (18.0%)	0.50

Numbers are mean (SD) for continuous variables and frequency (percent) for categorical variables. Group comparisons by Wilcoxon rank sum test for continuous variables and Fisher's exact test for categorical variables.
BMI: body mass index. SOFA: sequential organ failure assessment. HCQ: hydroxychloroquine

These patients were matched to 133 LAC+USC MC controls on gender, age, and BMI, and, when feasible, the presence or absence of diabetes. Day 0 for KMC patients was the day of in-patient TCZ administration, and the matching day 0 for LAC+USC MC patients was the day of emergency room presentation + the number of days for which their matched KMC counterpart had been admitted prior to receiving TCZ. This numbering scheme ensured that disease timelines were similar. Outcomes were assessed at 72 hrs, day 14, and day 28. Primary outcome was ≥2-point improvement on the ordinal scale for clinical improvement (a 7-point scale based on hospitalization status, oxygen requirements, and presence of other organ support). Secondary outcome was survival at days 14 and 28.

Results: Demographics are shown in Table 1. The two populations were balanced in most baseline demographics and characteristics, although they differed in proportions of individuals of Hispanic ethnicity, presence of diabetes,

Table 2: Clinical Improvement: Improvement of at least 2 grades on COVID Ordinal Scale

Time Period Relative to Day 0	Tocilizumab (n=40)	No tocilizumab (n=133)	Unadjusted RR (95% CI)	Minimally adjusted RR (95% CI) [1]	RR Adjusted for Day SOFA [2]	RR Adjusted for admission SOFA [3]
72 hours	1 (2.5%)	23 (17.3%)	0.14 (0.02, 1.04)	0.13 (0.02, 0.92)	0.15 (0.02, 1.13)	0.13 (0.02, 0.96)
p-value	0.017 [4]		0.054	0.041	0.066	0.046
14 days	18 (45.0%)	69 (51.9%)	0.87 (0.59, 1.27)	0.86 (0.60, 1.23)	0.94 (0.65, 1.35)	0.82 (0.56, 1.20)
p-value	0.48		0.46	0.41	0.73	0.31
28 days (n=172)	23 (57.5%)	76 (57.6%)	1.00 (0.74, 1.35)	0.90 (0.68, 1.21)	0.96 (0.71, 1.30)	0.85 (0.62, 1.17)
p-value	1.00		0.99	0.49	0.78	0.32

Analysis by Poisson regression with robust standard errors. Rate ratios are tested by Wald tests.
1 Adjusted for age, BMI, sex, diabetes.
2 Adjusted for age, BMI, sex, diabetes, day 0 SOFA
3 Adjusted for age, BMI, sex, diabetes, admission SOFA
4 Fisher's exact p-value

Table 3: Survival at 14 and 28 days

Time Period Relative to Day 0	Tocilizumab (n=40)	No tocilizumab (n=132)*	Unadjusted OR (95% CI)	Minimally adjusted OR (95% CI) [1]	OR adjusted for Day 0 SOFA [2]	OR adjusted for admission SOFA [3]
14 days	37 (92.5%)	114 (86.4%)	1.73 (0.51, 5.83)	1.62 (0.44, 5.97)	1.80 (0.47, 6.91)	1.95 (0.44, 8.63)
p-value	0.41[2]		0.38	0.47	0.39	0.38
28 days	32 (80.0%)	101 (76.5%)	1.19 (0.50, 2.81)	1.00 (0.39, 2.56)	0.97 (0.37, 2.59)	0.90 (0.32, 2.49)
p-value	0.83[2]		0.70	1.00	0.96	0.83

Numbers (percent) survived.
Firth logistic regression used to estimate odds ratios and 95% confidence intervals
1 Minimally adjusted OR: adjusted for age, BMI, sex, diabetes.
2 Adjusted for age, BMI, sex, diabetes, Hispanic ethnicity, day 0 SOFA
3 Adjusted for age, BMI, sex, diabetes, Hispanic ethnicity, admission SOFA
*Full survival data missing for a single patient.

and use of hydroxychloroquine for treatment of COVID-19. Our findings failed to demonstrate improved clinical outcomes among patients receiving vs not receiving TCZ at any of the time points (Table 2). Moreover, there was also no difference between these cohorts in survival at days 14 and 28 (Table 3).

Conclusion: While our two hospitals are separate, the same physicians and similar treatment protocols (other than TCZ use) resulted in a natural experimental setting. In our study, use of TCZ for COVID-19 pneumonia did not lead to a significant benefit in this quasi-randomized, real-world environment. Moreover, clinical outcomes of patients in our public hospital were no worse than those in our private hospital. The hyperinflammatory state of severe COVID-19 is unlikely to be driven by a single inflammatory cytokine, and the risks of using any and all types of immunosuppression must be carefully weighed against the perceived benefits.

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Abstract Number: 0085

Association of CD20 Inhibitor Use with Severe COVID-19 Outcomes

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with immune-mediated diseases have similar risk of severe COVID-19 versus the general population but CD20 inhibitor users may be at increased risk of COVID-19-related death. We examined whether CD20 inhibitor users have worse COVID-19 outcomes than general population comparators.

Methods: We performed a comparative cohort study of CD20 inhibitor users in immune-mediated diseases and general population comparators for COVID-19 outcomes. We identified cases who used CD20 inhibitors for immune-mediated diseases (non-oncologic/non-transplant indication) within one year prior to index date of PCR-confirmed COVID-19 between January 31, 2020, and January 31, 2021, in a large healthcare system. Details regarding demographics, medical history, CD20 inhibitor treatment, and COVID-19 were extracted from the electronic health record. Comparators with COVID-19 were matched up to 5:1 by age, sex, and index date of PCR positivity. We estimated hazard ratios (HRs) and 95% confidence intervals (CIs) for hospitalization, mechanical ventilation, and death in CD20 inhibitor users versus comparators using Cox regression. We also assessed these associations among cases with rheumatic conditions and shorter (< 1 year) or longer (>1 year) CD20 inhibitor duration versus comparators.

Table 1. Clinical characteristics of immune-mediated cases on CD20 inhibitors with COVID-19 and age, sex, and COVID-19 diagnosis date-matched comparators.

Characteristic	CD20 Inhibitor-Treated Cases (n=114)	Matched Comparators (n=559)	p-value
Age, years, mean ± SD	55 ± 15	54 ± 15	0.44
Female, n (%)	80 (70)	391 (70)	0.96
Race, n (%)			0.43
White	69 (61)	316 (57)	
Black or African American	16 (14)	70 (13)	
Asian	4 (4)	12 (2)	
Other	25 (22)	161 (29)	
Hispanic or Latinx ethnicity, n (%)	6 (5)	46 (8)	0.28
Body mass index, kg/m^2, mean ± SD	28.7 ± 6.2	29.7 ± 6.7	0.16
Smoking status, n (%)			0.06
Never	66 (58)	271 (48)	
Former	29 (25)	126 (23)	
Current	3 (3)	18 (3)	
Unknown	16 (14)	144 (26)	
Charlson Comorbidity Index, median (IQR)	1 (0, 2)	0 (0, 1)	0.001
Comorbidities, n (%)			
Hypertension	45 (39)	120 (21)	<0.0001
Diabetes	13 (11)	56 (10)	0.66
Coronary artery disease	8 (7)	21 (4)	0.12
Heart failure	8 (7)	11 (2)	0.003
Asthma	10 (9)	32 (6)	0.22
Chronic obstructive pulmonary disease	6 (5)	6 (1)	0.002
Obstructive sleep apnea	2 (2)	25 (4)	0.18
Chronic kidney disease	12 (11)	26 (5)	0.01

COVID-19, Coronavirus Disease 2019; SD, standard deviation; IQR, interquartile range.

Results: We identified 114 cases with COVID-19 who used CD20 inhibitors for immune-mediated diseases and 559 matched comparators with COVID-19 (Table 1). Rheumatic disease (59 [52%]) and neurologic conditions (48 [42%]) were the most common indications for CD20 inhibition (Table 2). The total duration of CD20 inhibitor use was < 1 year in 33 (29%), 1-3 years in 51 (45%), and >3 years in 30 (26%). Forty-eight (42%) patients received a CD20 inhibitor dose within 3 months before COVID-19 onset. CD20 inhibitor-treated cases had higher mortality (aHR 2.16; 95% CI: 1.03 to 4.54) than matched comparators. Risks of hospitalization (aHR 0.88; 95% CI: 0.62 to 1.26) and mechanical ventilation (aHR 0.82; 95% CI: 0.36 to 1.87) were similar (Table 3). Approximately half of deceased patients in each group were not mechanically ventilated due to “Do Not Intubate” status. Deaths were numerically higher in patients on CD20 inhibitors for rheumatic diseases (7 [13%] vs. 15 [5%]), unadjusted HR 2.52; 95% CI: 1.07 to 5.90), which was attenuated in the adjusted model (aHR 1.76, 95% CI: 0.50 to 6.15). Short-term CD20 inhibitor users (< 1 year) had higher risk of death (7 [9%] vs. 11 [3%], unadjusted HR 2.82, 95% CI: 1.34 to 5.96) than comparators, which was attenuated in the adjusted model (aHR 2.33, 95% CI: 0.92 to 5.91). Lastly, those with long-term CD20 inhibitor use had numerically higher risk of death (5 [15%] vs. 10 [6%]) than comparators, and a similar trend in unadjusted (HR 2.92, 95% CI: 0.95 to 8.99) and adjusted (aHR 2.41, 95% CI: 0.66 to 8.87) models.

Conclusion: Patients who used CD20 inhibitors for immune-mediated diseases prior to COVID-19 infection had higher mortality than matched comparators. These results highlight the urgent need to mitigate excess risks in CD20 inhibitor users during the ongoing COVID-19 pandemic. Additional studies are needed to better stratify these risks and guide decision-making.

Table 2. Disease characteristics of immune-mediated cases with CD20 inhibitor use prior to COVID-19.

Characteristic	CD20 Inhibitor-Treated Cases (n=114)
Type of CD20 inhibitor, n (%)*	
Rituximab or biosimilar	90 (79)
Ocrelizumab	26 (23)
Indication for CD20 inhibitor, n (%)	
Rheumatic condition	59 (52)
Vasculitis	19 (17)
Inflammatory arthritis†	22 (19)
Systemic lupus erythematosus	7 (6)
Inflammatory myopathy	7 (6)
Other rheumatic condition‡	4 (4)
Neurologic condition	48 (42)
Multiple sclerosis	33 (29)
Neuromyelitis optica	4 (4)
Other neurologic condition§	6 (5)
Ocular inflammation	5 (4)
Hematologic condition	8 (7)
Thrombotic thrombocytopenic purpura	3 (3)
Other hematologic condition‖	5 (4)
Autoimmune hepatitis	3 (3)
Other conditions¶	3 (3)
Duration of CD20 inhibitor use, n (%)	
<1 year	33 (29)
1-3 years	51 (45)
>3 years	30 (26)
Most recent CD20 inhibitor dose prior to COVID-19 onset, n (%)	
<3 months	48 (42)
3-6 months	44 (39)
6-12 months	22 (19)
Concomitant immunomodulatory medications at COVID-19 onset, n (%)	
Mycophenolate mofetil	8 (7)
Methotrexate	6 (5)
Hydroxychloroquine	5 (4)
Leflunomide	3 (3)
Other immunomodulatory medication#	6 (5)
Oral glucocorticoid	35 (31)
Prednisone-equivalent daily dose mg, median (IQR)	7.5 (5.0, 15.0)

*No individuals were on obinutuzumab or ofatumumab. Two individuals were initially on rituximab and then transitioned to ocrelizumab.
†Includes rheumatoid arthritis, other inflammatory arthritis, and juvenile idiopathic arthritis.
‡Includes Sjögren's syndrome and IgG4-related disease.
§Includes myasthenia gravis, autoimmune encephalitis, acute disseminated encephalomyelitis, and small fiber polyneuropathy.
‖Includes antiphospholipid syndrome, immune thrombocytopenia, and autoimmune hemolytic anemia.
¶Includes pemphigus vulgaris, membranous nephropathy, and autoimmune interstitial lung disease.
#Includes azathioprine (n=1), cyclophosphamide (n=2), sulfasalazine (n=1), and tacrolimus (n=2).

Table 3. COVID-19 outcomes in immune-mediated cases treated with CD20 inhibitors versus matched comparators.

Outcomes	CD20 Inhibitor-Treated Cases (n=114)	Matched Comparators (n=559)
Hospitalization, n (%)	35 (31)	123 (22)
Total follow-up time (person-days)	11658	62942
Incidence rate/1000 days (95% CI)	3.0 (2.0, 4.0)	2.0 (1.6, 2.3)
Unadjusted HR (95% CI)	1.32 (0.96 to 1.80)	Ref
Adjusted HR (95% CI)*	0.88 (0.62 to 1.26)	Ref
Mechanical ventilation, n (%)	6 (5)	26 (5)
Total follow-up time (person-days)	14755	78729
Incidence rate/1000 days (95% CI)	0.4 (0.1, 0.7)	0.3 (0.2, 0.5)
Unadjusted HR (95% CI)	1.10 (0.48 to 2.52)	Ref
Adjusted HR (95% CI)	0.82 (0.36 to 1.87)	Ref
Death, n (%) †	12 (11)	21 (4)
Total follow-up time (person-days)	15818	84172
Incidence rate/1000 days (95% CI)	0.8 (0.3, 1.2)	0.2 (0.1, 0.4)
Unadjusted HR (95% CI)	**2.86 (1.51 to 5.41)**	Ref
Adjusted HR (95% CI)	**2.16 (1.03 to 4.54)**	Ref

HR, hazard ratio; CI, confidence interval; BMI, body mass index; CCI, Charlson comorbidity index.
*Adjusted for age, race, BMI, and CCI (dichotomized as <2 or ≥2).
†Of those who died, 6 (50%) in the CD20 inhibitor-treated immune-mediated cases and 10 (48%) in the matched comparators were not mechanically ventilated due to "Do Not Intubate" status.

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Abstract Number: 0086

SARS-CoV-2 Infection and COVID-19 Outcomes in Rheumatic Disease: A Systematic Literature Review

Richard Conway[1], Alyssa Grimshaw[2], Maximilian Konig[3], Michael Putman[4], Ali Duarte-Garcia[5], Candice Low[6], Shangyi Jin[7], Diego Cabrera[8], Yu Pei Eugenia Chock[9], Berk Degirmenci[10], Eimear Duff[11], Bugra Egeli[12], Elizabeth Graef[13], Akash Gupta[14], Patricia Harkins[15], Bimba Franziska Hoyer[16], Aruni Jayatilleke[17], Christopher Kasia[18], Aneka Khilnani[19], Adam Kilian[20], Alfred Kim[21], Chung Mun Alice Lin[22], Laurie Proulx[23], Sebastian Sattui[24], Namrata Singh[25], Jeffrey Sparks[26], Herman Tam[27], Leslie Yingzhijie Tseng[2], Manuel Ugarte-Gil[28], Natasha Ung[29], Leanna Wise[30], Ziyi Yang[31], Kristen Young[32], Jean Liew[33], Rebecca Grainger[34], Zachary Wallace[35] and Evelyn Hsieh[2], [1]St. James's University Hospital, Dublin, Ireland, [2]Yale School of Medicine, New Haven, CT, [3]The Johns Hopkins University School of Medicine, Baltimore, MD, [4]Medical College of Wisconsin, Brookfield, WI, [5]Mayo Clinic, Rochester, MN, [6]St. Vincent's University Hospital, Dublin, Ireland, [7]Department of Rheumatology and Clinical Immunology, Chinese Academy of Medical Sciences & Peking Union Medical College; National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [8]Yale School of Medicine, Lima, Peru, [9]Yale School of Medicine, Greenwich, CT, [10]St. Elizabeth's Medical Center, Boston, MA, [11]St. James's Hospital, Dublin, Ireland, [12]Boston Children's Hospital, Boston, MA, [13]Emerson Hospital, Concord, MA, [14]Department of Medicine, Yale University School of Medicine, New Haven, CT, [15]St James hospital, Dublin, Ireland, [16]Universittsklinikum Schleswig-Holstein, Kiel, Germany, [17]Temple University, Philadelphia, PA, [18]The Medical College of Wisconsin, Maywood, IL, [19]George Washington University School of Medicine and Health Sciences, Washington, DC, [20]George Washington University, Melbourne, FL, [21]Washington University School of Medicine, St. Louis, MO, [22]Newcastle University, Newcastle, United Kingdom, [23]Canadian Arthritis Patient Alliance, Ottawa, ON, Canada, [24]Hospital for Special Surgery, New York, NY, [25]University of Washington, Bellevue, WA, [26]Brigham and Women's Hospital, Boston, MA, [27]Stollery Children's Hospital, University of Alberta, Edmonton, AB, Canada, [28]Hospital Guillermo Almenara Irigoyen, Essalud/Universidad Científica del Sur, Lima, Peru,

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The relative risk of COVID-19 among patients with rheumatic and musculoskeletal disease (RMD) and the comparative severity of COVID-19 infection in RMD remain uncertain. This systematic review seeks to quantify the risk for SARS-CoV-2 infection and to describe the clinical course and outcomes of COVID-19 in people with RMD.

Methods: A systematic literature search was conducted across 14 databases from inception to February 13th 2021. We included observational studies and experimental trials in RMD patients reporting the following outcomes: 1) comparative rates of SARS-CoV-2 infection, 2) hospitalization, 3) oxygen supplementation/ICU admission/mechanical ventilation, and 4) mortality. Studies were screened, data extracted, and quality assessment performed by two independent reviewers with a third reviewer to resolve conflicts. The methodological quality of all included studies was evaluated using the Newcastle-Ottawa scale or JBI Critical Appraisal Tools.

Table 1. Studies reporting comparative rates of COVID-19 infection (n=47)

Authors	Design	n	Outcome and inference	Bias assessment	Direction of effect
So	Cross-sectional	39835 RMD 7460165 non-RMD	5/39835 (0.0126%) RMD vs 1067/7500000 (0.0142%) total population (including RMD)	Low risk	=
Gentry	Cohort	32109 RMD 9000000 non-RMD	109/32109 (0.3%) RMD vs 18560/9000000 (0.21%) 3.39/1000 non-RMD 31/10703 (0.3%) HCQ users vs 78/21406 (0.4%) non-HCQ users OR 0·79 (95%CI 0·52–1·20) (p=0·27)	Low Risk	=
Pablos	Cross-sectional	26131 RMD 2899935 non-RMD	Prevalence 199/26131 (0.76%) RMD vs 16820/2899935 (0.58%) non-RMD. OR 1.3 (95%CI 1.15% to 1.52%)	Low risk	+
Topless	Cohort	7820 RA 13105 Gout 473139 total	117/13105 (0.89%) gout vs 2001/460034 (0.43%) non-gout Adjusted OR 1.01 (95%CI 0.83-1.23) (p=0.92) 81/7850 (1.03%) RA vs 2037/465289 (0.44%) non-RA Adjusted OR 1.27 (95%CI 1.0-1.62) (p=0.051)	Low risk	=
Gluthorp	Cross-sectional	12789 RMD 5800000 General population	40/12789 (0.3%) RMD vs 12831/5800000 (0.22%) General population	Low risk	=
Flood	Cross-sectional	7500 RMD	78/7500 (1.04%) RMD Cumulative incidence 1083/100000 inflammatory RMD vs 940/100000 non-inflammatory RMD vs 887/100000 General population	Low risk	=
Zhong	Cohort	6228 RMD	27/43 (63%) RMD vs 28/83 (34%) non-RMD developed COVID-19 after exposure (OR 2·68 (95% CI 1·14–6·27; p=0·023)	Low risk	+
Bjornsson	Cohort	3184 RMD 36777 non-RMD	9/1438 (0.6%) bDMARD RMD vs 84/13815 (0.6%) comparators (to bDMARD) vs 5/1746 (0.3%) MTX RMD vs 134/22962 (0.6%) comparators (to MTX)	Low risk	=
Jung	Cohort	2066 RA/SLE	15/649 (2.3%) RA/SLE on HCQ vs 31/1417 (2.2%) RA/SLE not on HCQ Adjusted OR 1.131 (95%CI 0.570-2.244) p=0.7248	Low risk	=
Ferri	Cross-sectional	1636 SSc	14/1636 (1%) PCR+ 47/1636 (3%) clinical COVID+ in SSc vs 349/100000 General population (p=0.001)	Low risk	+
Carcianaeiia	Cross-sectional	1471 RMD	6/1471 (0.4%) (4.08/1000) RMD vs reported as similar to General population (no figures given)	Low risk	=
Quartuccio	Cross-sectional	1051 RMD 466700 General population	4/1051 (3.8/1000, 95%CI 1.5-9.7/1000) RMD on b/tsDMARD vs 937/466700 (2/1000, 95%CI 1.9-2.1/1000) General population (p=0.33)	Low risk	=
Michelena	Cross-sectional	959 RMD 672278 General population	11/959 (1.15%) RMD vs 3903/672278 (0.58%) Adjusted cumulative incidence rate 1.21% (95% CI 0.42-1.99%) RMD vs 0.58% (95% CI 0.56-0.60%) General population. Confirmed cases with pneumonia, adjusted cumulative incidence rate 0.48% (95%CI 0.09-0.87%) RMD vs 0.58% (95%CI 0.56-0.60%) General population	Low risk	=
Favalli	Cross-sectional	955 RMD 8726060 General population	6/955 RMD (0.62%) (95%CI0.25-1.4%) RMD vs 57592/8726060 (0.66%) General population (p=0.5)	Low risk	=
Andreica	Cross-sectional	917 RMD 17900000 General population	PCR+: 3/917 (0.33%) RMD vs 40153/17900000 (0.22%) General population IgG antibody+: 5/342 (1.42%) RMD vs 5/316 (1.6%) healthcare workers	Low risk	=
Zen	Cross-sectional	916 RMD 5697000 General population	2/916 (0.21%) RMD vs 17391/5797000 (0.3% (3/1000)) General population	Low risk	=
Goswami	Cross-sectional	840 RMD 21777954 General population	4/840 (0.476% (95%CI 0.19-1.22)) RMD vs 113193/21777954 (0.519% (95%CI 0.517-0.523)) General population (p=0.86)	Low risk	=
Costantino	Cohort	655 RA/PsA/SpA	45/655 (6.9%) (95%CI5.1–9.2%) RA/PsA/SpA Vs 9.9% (range:6.6–15.7) General population	Low risk	=
Chen	Cross-sectional	627 RMD 57237727 General population	8/627 (1.28% (95%CI 0.4–2.2%) RMD vs 67801/57237727 (0.12%) General population OR 10.898 (95% CI, 5.425–21.889 (p<0.001)	Low risk	+
Emmi	Cross-sectional	458 RMD 3729641 General population	Prevalence (1/458) 0.22% (95%CI0.01–1.21%) RMD vs General population 0.20% (95%CI 0.20–0.21%) (p=0.597)	Low risk	=
Ramirez	Cross-sectional	417 RMD 10000000 General population	5/417 (1.2%) RMD PCR+ vs 73000/10000000 (0.73%) General population	Low risk	+
Bourguiba	Cross-sectional	342 FMF	27/342 (7.8%) FMF vs 11% General population	Low risk	-
Zucchi	Cross-sectional	332 SLE	6/303 (1.8%) SLE vs 0.3% General population	Low risk	+
Polat	Cross-sectional	328 PsA	8/328 (2.4%) PsA vs 108749/15519267 (0.7%) General population	Low risk	+
Benfaremo	Cross-sectional	305 RMD 1525271 General population	2/305 (0.66%) RMD vs 6723/1525271 (0.44%) General population	Low risk	=
Benucci	Cross-sectional	295 RMD 1620952 General population	4/295 RMD taking bDMARD (1.4% (95% CI 0.4% to 3.4%)) vs 7393/1620952 (0.5% (95% CI 0.4% to 0.5%)) General population OR 3.01 (95% CI 1.13 to 8.09) (p=0.047)	Low risk	+
Moradi	Cross-sectional	249 RMD 207 non-RMD	9/249 (3.6%) RMD vs 18/207 (8.7%) non-RMD (p=0.028)	Low risk	-
Kant	Cross-sectional	206 AAV	3/206 (1.4%) AAV vs 1.2% General population	Low risk	=
Desbois	Cross-sectional	199 sarcoid	26/199 (13%) sarcoid vs 9.3-9.9% General population	Low risk	+
Fike	Case control	178 RMD	32/178 (18%) RMD incidence rate 17978/100000 RMD Latino population vs 4689-5809/100000 general Latino population	Low risk	+
Francesconi	Case control	40245 RMD 2589374 General population	98/28366 (0.35%) RA 23/11879 (0.19%) CTD 4581/2589374 (0.17%) General population (all groups aged >30) RA adjusted OR 1.64 (1.32–2.05) (p<0.001) CTD adjusted OR 1.09 (0.72–1.66) (p=ns)	Some concerns	+
Salvarani	Cohort	4408 RMD 2104319 General population	31/4408 (0.70%) RMD receiving HCQ/CQ vs 11563/2104319 (0.55%) General population Multivariable OR 0.94 (95% CI 0.66–1.34)	Some concerns	=
Khoubnasabjafari	Cross-sectional	1858 RA	34/1435 (2.2%) RA on HCQ vs 12/422 (2.8%) RA not on HCQ (p=0.344)	Some concerns	=
Ferri	Cross-sectional	1641 RMD	25/938 (1.5%) RMD total COVID (13/938 (0.7%) PCR+) vs 349/100,000 (0.3%) General population	Some concerns	+
Murray	Cross-sectional	1298 RMD	6/1298 (0.46%) RMD vs 0.44% General population	Some concerns	=
Kipps	Cross-sectional	887 RMD 285400 non-RMD	1/887 (0.113%) RMD vs 1001/285400 non-RMD (0.351%) RR 0.32 (95%CI 0.05–2.28) (p=ns)	Some concerns	=
Goyal	Cross-sectional	845 RMD 1380004385 General population	2/845 (0.24%) RMD vs 46711/1380004385 (0.003%) General population	Some concerns	+
Cassione	Cross-sectional	165 SLE	Incidence 4/165 (2.5%) SLE in vs 0.76% in Lombardy and 0.47% in Emilia Romagna (627.1 and 470.53 cases/100 000)) General population	Some concerns	+
Giardina	Cross-sectional	150 pSS 5524232 General population	Incidence 0/150 (0%) (0 cases per 100,000) pSS vs 6839/5524232 (123.8/100,000) General population	Some concerns	-
Comarmond	Cross-sectional	148 LVV	8/148 (5.4%) LVV vs 12.3% General population	Some concerns	-
Favalli	Cross-sectional	123 CTD	1/123 (0.62%) CTD vs 0.81% General population	Some concerns	=
Aries	Cross-sectional	11771 RMD (on DMARD) 1814000 non-RMD	30/11771 (0.25%) RMD (on DMARD) vs 5120/1814000 (0.28%) non-RMD	High risk	=
Bency	Cross-sectional	7600 RMD	27/7600 (0.4%) RMD vs 120–900/100000 (0.12%–1%) General population	High risk	=
Baughman	Cross-sectional	5200 sarcoid	116/5200 (2.23% or 22308 per million) sarcoid vs 1050-5197 per million General population	High risk	+
Favalli	Cross-sectional	914 RMD	Incidence 1/112 (0.89%) RMD HCQ-users vs 5/802 (0.62%) RMD non HCQ-users (p=0.64)	High risk	=
Holubar	Cohort	120 SLE 5808181 General population	8/120 (6.7%) SLE vs 6389/5808181 (0.11%) General population	High risk	=

Table 2. Studies reporting comparative hospitalization, oxygen supplementation, ventilation, ICU admission rates in RMD patients (n=16)

Authors	Design	n	Hospitalization	ICU Admission	O2 Supplementation	Mechanical Ventilation	Risk of Bias
Cordtz	Cohort	58052 RMD 4539177 Denmark Gen Population	69/58052 (0.12%) overall RMD population vs. 2536/459177 (0.06%) in overall general population aHR1 1.26 (1.26-2.03) aHR2 1.46 (1.15-1.86)	7/58052 (0.01%) overall RMD population vs. 348/4539177 (0.008%) in overall general pop (p=0.23)			Low risk
Bailey	Cohort	13846 RA/CTD 407973 Non-RMD	145/348 (41.7%) PCR+ for SARS-CoV2 in RMD Group vs. 2109/10774 (19.5%) in Non-RMD OR 2.9 (2.4-3.7) aOR 1.5 (1.1-1.9)	18/348 PCR+ (5.2%) in RMD group vs. 296/10774 (2.7%) in Non-RMD group (p=0.007)			Low risk
Flood	Cross-Sectional	4524 RMD 2976 Non-RMD	6/40 (15%) total COVID-19 cases in RMD group vs. 15/68 (22.1%) in Non-RMD group (p=0.37)				Low risk
D'Silva	Cohort	2379 RMD 142750 Non-RMD	620/2379 (26.1%) total COVID-19 cases in RMD group vs. 21501/142750 (15.1%) in Non-RMD group RR 1.73(1.62-1.85) aRR1 1.14 (1.03-1.26) aRR2 1.06 (0.96-1.17)	142/2379 (6.0%) total COVID-19 cases in RMD group vs. 4615/142750 (3.2%) in Non-RMD group. RR 1.85(1.57-2.17) aRR1 1.32 (1.03-1.68) aRR2 1.05 (0.84-1.32)		78/2379 (3.3%) total COVID-19 cases in RMD group vs. 2938/142750 (2.1%) in Non-RMD group. RR 1.28 (1.28-1.99) aRR1 1.05(0.77-1.44) aRR2 0.91 (0.67-1.23)	Low risk
Blomsson	Cohort	1438 RMD 13815 Non-RMD	3/9 (33.3%) PCR+ for SARS-CoV2 in RMD group vs. 3/84 (3.6%) in Non-RMD group RR 9.33 (2.20-39.6)		2/9 PCR+ (22.2%) for SARS-CoV2 in RMD group vs. 3/84 (3.6%) in Non-RMD group RR 6.22 (1.19–32.46)	0/9 PCR+ (0%) for SARS-CoV2 in RMD group vs. 1/84 (1.2%) in Non-RMD group (p=0.74)	Low risk
Emmi	Cross-sectional	458 RMD 3729641 Total Tuscany	1/13 (7.7%) total COVID-19 cases v. 225/7527 (3.0%) PCR+ for SARS-CoV2 in general population	1/13 (7.7%) total COVID-19 cases vs. 225/7527 (3.0%) PCR+ for SARS-CoV2 in general population (p=0.32)		1/13 total (7.7%) COVID-19 cases	Low risk
Pablos	Cohort	288 RMD 288 Non-RMD	162/228 (71.1%) PCR+ RMD vs 175/228 (76.8%) PCR+ Non-RMD (p=0.63)	15/228 PCR+ (6.6%) RMD vs 116/228 PCR+ (7.0%) Non-RMD (p=0.88)	117/228 PCR+ (51.3%) RMD vs 126/228 PCR+ (55.3%) Non-RMD (p=0.10)	8/228 PCR+ (3.5%) RMD vs 6/228 PCR+ (2.6%) Non-RMD (p=0.10)	Low risk
Veenstra	Cohort	213 IMID 15345 Total Tested in Health System				7/77 PCR+ (9.1%) for SARS-CoV2 in RMD group vs. 522/5881 (8.9%) in Non-RMD group OR = 1.03 (0.47-2.19)	Low risk
Serling-Boyd	Cohort	143 RMD 688 Non-RMD	58/143 (40.6) PCR+ in RMD group, vs. 295/688 PCR+ (42.9%) in Non-RMD group HR 0.95 (0.75-1.12) aHR1 0.89 (0.70-1.13) aHR2 0.86 (0.68-1.09) aHR3 = 0.87 (0.68-1.11)	28/143 PCR+ (19.6%) in RMD group, vs. 96/688 PCR+ (14.0%) in Non-RMD group HR 1.38 (0.95-2.00) aHR1 1.33 (0.91-1.94) aHR2 1.22 (0.83-1.79) aHR3 = 1.27 (0.86-1.86)		22/143 PCR+ (15.4%) in RMD group, vs. 63/688 PCR+ (9.2%) in Non-RMD group HR 1.75 (1.12-2.74) aHR 1.72 (1.07-2.76) aHR2 1.56 (0.97-2.50) aHR3 1.51 (0.93–2.44)	Low risk
D'Silva	Cohort	52 RMD 104 Non-RMD	23/52 (44.2%) total COVID-19 cases in RMD vs 42/104 (40.4%) in Non-RMD group OR 1.26 (0.64-2.48) aOR1 1.27 (0.61-2.64) aOR2 1.22(0.56-2.63) aOR3 1.10 (0.51-2.38)	11/52 total (21.2%) COVID-19 cases in RMD vs. 7/104 (6.7%) in Non-RMD OR 3.22 (1.16-8.92) aOR1 3.26 (1.17-9.09) aOR2 3.11 (1.07-9.05) aOR3 2.92 (1.002-8.49)	17/52 (32.7%) in RMD vs 26/104 (25%) in Non-RMD	11/52 total (21.2%) COVID-19 cases in RMD vs. 7/104 (6.7%) in Non-RMD OR 3.22 (1.16-8.92) aOR1 3.26 (1.17-9.09) aOR2 3.11 (1.07-9.05) aOR3 2.92 (1.002-8.49)	Low risk
Morgenthau	Cohort	37 Sarcoidosis 7330 Non- Sarcoidosis	22/37 (59.5%) PCR+ in RMD group vs. 5002/7330 PCR+ in Non-RMD group (p=0.29)			9/97 PCR+ (24.3%) in RMD group, vs 1150/7330 PCR+ (15.8%) in Non-RMD group (p=0.17)	Low risk
Huang	Cohort	17 RMD 1255 Total Patients		1/17 PCR+ (0.2%) for SARS-CoV2 in RMD vs 236/1255 (18.8%) in Non-RMD (p=0.17)	13/17 PCR+ (76.5%) for SARS-CoV2 in RMD group	0/17 PCR+ (0%) for SARS-CoV2 in RMD group	Low risk
Vazquez	Cohort	23 IA 23 (of 1514) Non-RMD	10/23 (43.5%) PCR+ in IA group, vs. 15/23 (65.2%) in age, sex, COVID-19 diagnosis matched Non-RMD (p=0.14)				Low risk
Mazzucchelli	Cohort	476 RMD 321 Derm/GI (All on bDMARDS)		0/2 PCR+ (0%) in RMD group, vs 1/2 (50%) in Non-RMD group (p=0.25)			Some concerns
Ansarin	Cohort	30 RMD 381 Non-RMD		7/30 total (23.3%) COVID-19 cases in RMD group vs. 89/381 (23.4%) in Non-RMD group (p=0.89)		12/30 total (40%) COVID-19 cases vs. 137/381 (36%) in Non-RMD group (p=0.89)	Some concerns
Aries	Cross-sectional	10771 RMD 1814000 General Population		3/30 PCR+ (10%) for SARS-CoV2 in RMD group vs. 227/5120 (4.4%) in General Population (p=0.14)			High risk

Results: Of 5799 abstracts screened, 528 articles underwent full text review, and 100 studies met criteria for inclusion. Most studies (54%) had low risk of bias. br>

47 studies reported comparative rates of SARS-CoV-2 infection in people with RMD, 15 showed increased rates, 28 no difference, and 4 decreased rates (Table 1). Adjusted comparative risk measures were reported in 8 studies; 4 reported increased risk, 4 showed no difference in risk.

70 studies reported hospitalization rates among RMD patients. Of the 11 studies providing comparative data (Table 2) 3 showed increased risk among patients with RMD, and 7 showed no significant effect. No studies found decreased risk for hospitalization. In 5 studies reporting adjusted analyses, 2 reported increased risk, whereas 3 found no significant differences.

In terms of oxygen supplementation (n=28 studies), 3 studies reported comparative findings: 1 showed increased risk among patients with RMD, while 2 found no significant difference. Regarding ICU admission (n=52 studies), 11 comparative studies were identified, 2 showed increased risk among RMD patients and the remainder showed no differences. For mechanical ventilation (n=42 studies), among 8 comparative studies, 7 showed no effect of RMD status and 1 showed a positive correlation. Only 2 studies reported adjusted risk estimates for ICU admission/mechanical ventilation, with 1 reporting a positive correlation, and the other, no effect.

Table 3. Studies reporting comparative mortality rates in RMD patients (n=16)

Authors	Design	N	Mortality and Inference	Bias assessment	Direction of effect
Williamson	Cohort	878475 RMD 16399917 total	962/878,475 (0.11%) RA/SLE/PsO vs 9964/16399917 (0.06%) total population HR 1.19 (95%CI 1.11–1.27)	Low risk	+
Cordtz	Cohort	58052 RMD 4539177 General population	16/47 (34%) RA vs 567/2536 (22%) in General population	Low risk	+
Topless	Cohort	7820 RA 13105 Gout 473139 total	RA 30/81 (37%) COVID+ (30/7820 total) vs 427/1565 COVID+ (27%) (427/465289 total) Gout 42/117 (36%) COVID+ (42/13105 total) vs 415/1541 COVID+ (27%) (415/460034 total) RA OR 1.8 [95%CI 1.2-2.7] Gout OR 1.2 [95%CI 0.9- 1.7]	Low risk	+
Reiley	Cohort	13846 RA/CTD 421819 Total	50/348 (8.7%) for RA/CTD vs 527/10774 (5.2%) in General population OR 0.9 (95%CI 0.6-1.3)	Low risk	=
D'Silva	Cohort	2379 RMD 142750 Non-RMD	94/2379 (4%) RMD vs 2972/142790 (2%) non-RMD RR 1.08 (95%CI 0.81-1.44)	Low risk	=
Harrison	Cohort	681 RMD 30780 non-RMD	54/681 (8%) RMD vs 1242/30780 (4%) non-RMD OR 1.17 (95%CI 0.85–1.60)	Low risk	=
Cleaton	Cross-sectional	10387 RMD 7415149 General population	12/10387 (0.12%) RMD vs 4131/7415149 (0.12%) General population	Low risk	=
Morgenthau	Cohort	37 sarcoid 7300 comparators	6/37 (16.2%) sarcoid vs 1502/7300 (20.6%) comparators (p=0.683)	Low risk	-
Vazquez	Cohort	23 IA 1514 Non-RMD	2/23 (9%) in RMD and in non-RMD controls	Low risk	=
Pablos	Cohort	288 RMD 288 Non-RMD	41/228 (18.1%) RMD vs 30/228 (13.2%) non-RMD (p=0.15)	Low risk	=
Serling-Boyd	Cohort	143 RMD 688 non-RMD	12/143 (8%) RMD vs 48/688 (7%) non-RMD HR 1.02 (95%CI 0.53–1.95)	Low risk	=
FAI2R	Cohort	Adult: 694 RMD 175 Non-RMD Pediatric: 13 RMD	58/694 (8%) RMD OR 1.45 (95% CI 0.87–2.42) vs non-RMD	Low risk	=
Chen	Cross-sectional	627 RMD 57237727 General population	3/8 (38%) RMD vs 3,163/67,801 (4.7%) General population	Low risk	+
Moradi	Cross-sectional	249 RMD 207 non-RMD	2/9 (22%) RMD vs 0/18 (0%) non-RMD (p=0.503)	Low risk	+
D'Silva	Cohort	52 RMD 104 non-RMD	3/52 (6%) RMD vs 4/104 (3%) non-RMD (p=0.69)	Low risk	=
Aries	Cross-sectional	11771 RMD (on DMARD) 1814000 non-RMD	0/30 (0%) DMARD-treated RMD vs 226/5120 (4.4%) in General population	High risk	-

71 studies reported mortality;16 reported comparative mortality rates (Table 3). Of these, 5 reported increased risk, 9 no difference, and 2 decreased risk in the RMD group; notably the 3 largest studies showed increased risk. 7 studies reported adjusted risk estimates. Compared to the general population, 2 studies reported increased mortality and 1 found no difference. Compared to non-RMD comparators 4 studies reported no difference in mortality.

Conclusion: This is the largest systematic review to date on COVID-19 in RMD. Although distillation of the overall results was limited by study heterogeneity, a similar number of studies reported increased risk or equal risk for RMD patients with few reporting decreased risk.

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Abstract Number: 0087

TNF Inhibitors and the Risk of Adverse COVID-19 Outcomes in Patients with Immune-Mediated Inflammatory Disease: Pooled Data from Three Global Registries

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: While tumor necrosis factor inhibitors (TNFi) are widely prescribed globally due to their high efficacy across immune-mediated inflammatory diseases (IMIDs), the impact of COVID-19 on individuals with IMIDs receiving TNFi remains poorly understood. The objective of this study was to assess the association between TNFi monotherapy and COVID-19-related hospitalization or death among individuals with IMIDs, compared to other commonly prescribed immunomodulatory regimens.

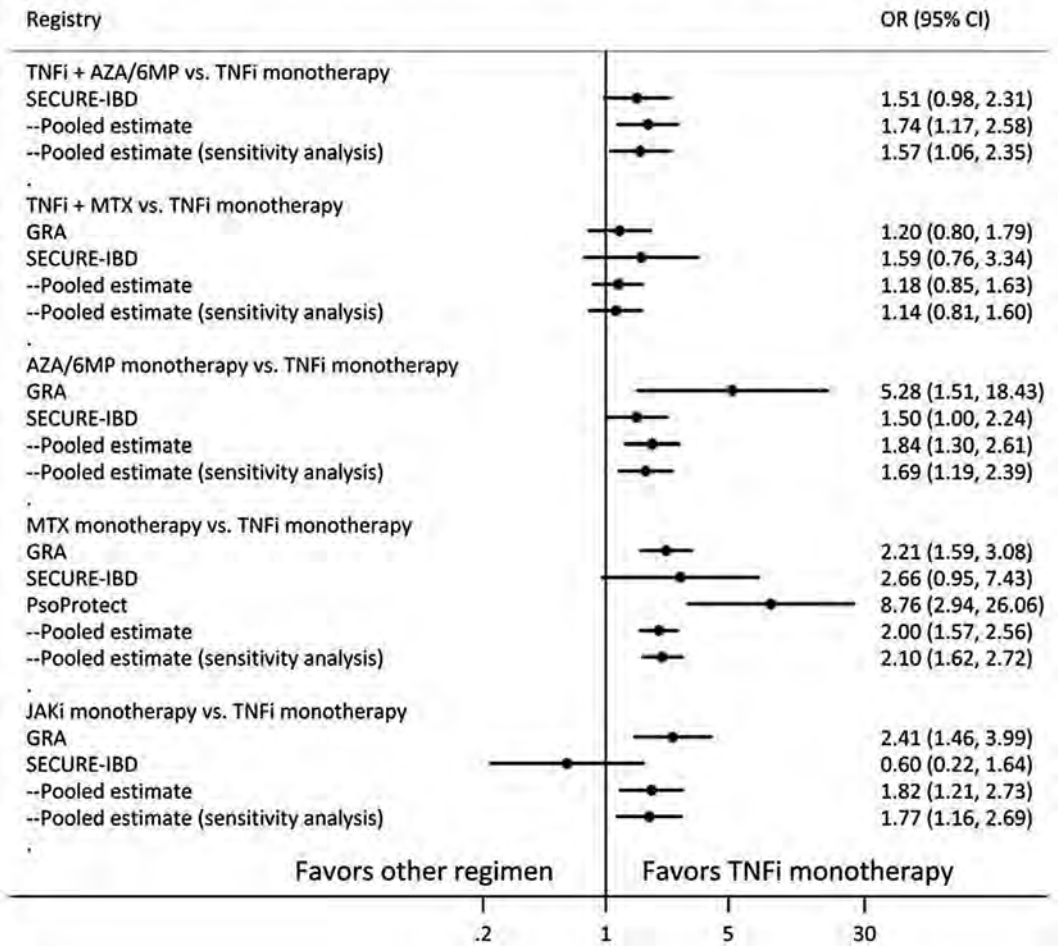
Table: Patient and clinical characteristics of the study population and COVID-19 outcomes.

	N (%) unless specified			
	GRA	**SECURE-IBD**	**PsoProtect**	**Pooled**
	N = 3,441	**N = 2,336**	**N = 300**	**N = 6,077**
Age, Mean (SD)	55.0 (14.4)	39.4 (15.4)	49.9 (12.6)	48.8 (16.5)
Sex*				
Male	1,144 (33.2)	1,139 (48.8)	185 (61.7)	2,468 (40.6)
Female	2,295 (66.7)	1,153 (49.4)	115 (38.3)	3,563 (58.6)
Unknown	2 (0.1)	44 (1.9)	0 (0)	46 (0.8)
Diagnoses*				
Rheumatoid arthritis only	2,146 (62.4)	-	-	2,146 (35.3)
Spondyloarthritis only	624 (18.1)	-	-	624 (10.3)
Psoriatic arthritis only	566 (16.4)	-	-	566 (9.3)
Other IA or >1 type of IA	105 (3.1)	-	-	105 (1.7)
Crohn's disease	-	1,537 (65.8)	-	1,537 (25.3)
IBD, unspecified	-	37 (1.6)	-	37 (0.6)
Ulcerative colitis	-	762 (32.6)	-	762 (12.5)
Psoriasis	-	-	300 (100)	300 (4.9)
Disease activity*				
Remission	1,067 (31.0)	1,369 (58.6)	75 (25.0)	2,511 (41.3)
Active disease	1,829 (53.2)	864 (37.0)	225 (75.0)	2,918 (48.0)
Unknown	545 (15.8)	103 (4.4)	0 (0)	648 (10.7)
Exposure regimens*				
TNFi monotherapy	1,183 (34.4)	1,445 (61.9)	216 (72.0)	2,844 (46.8)
TNFi + methotrexate	575 (16.7)	87 (3.7)	7 (2.3)	669 (11.0)
TNFi + Azathioprine/6MP	7 (0.2)	327 (14.0)	0 (0)	334 (5.5)
Methotrexate monotherapy	1,438 (41.8)	31 (1.3)	77 (25.7)	1,546 (25.4)
Azathioprine/6MP monotherapy	19 (0.6)	379 (16.2)	0 (0)	398 (6.5)
JAKi monotherapy	219 (6.4)	67 (2.9)	0 (0)	286 (4.7)
Hospitalization status*				
Not hospitalized	2,396 (69.6)	1,996 (85.4)	257 (85.7)	4,649 (76.5)
Hospitalized	939 (27.3)	316 (13.5)	42 (14.0)	1,297 (21.3)
Unknown	106 (3.1)	24 (1.0)	1 (0.3)	131 (2.2)
Death*				
Alive	3,266 (94.9)	2,282 (97.7)	297 (99.0)	5,845 (96.2)
Died	166 (4.8)	20 (0.9)	3 (1.0)	189 (3.1)
Unknown	9 (0.3)	34 (1.5)	0 (0)	43 (0.7)
Presumptive COVID-19 case**	752 (21.9)	0 (0)	112 (37.3)	864 (14.2)

Methods: We used data from three global COVID-19 registries of individuals with rheumatic diseases, IBD, and psoriasis. Healthcare providers reported COVID-19 outcomes and demographic and clinical characteristics of individuals with IMIDs with confirmed or suspected COVID-19. We included resolved adult COVID-19 cases with a diagnosis of inflammatory arthritis (IA), IBD, or psoriasis reported on or before February 1st, 2021. Medication exposure was defined as a categorical variable with the following categories: TNFi monotherapy (reference), TNFi in combination with MTX, TNFi in combination with AZA/6-mercaptopurine (AZA/6MP), MTX monotherapy, AZA/6MP monotherapy, and janus kinase inhibitor (JAKi) monotherapy. The outcome was COVID-19-related hospitalization or death. Registry-level analyses and a pooled analysis of data across the three registries were conducted using multilevel multivariable mixed-effects logistic regression, adjusting for demographics, clinical characteristics, comorbidities, concomitant immunomodulatory medications, and accounting for country, calendar-month, and registry-level correlations. In a sensitivity analysis we excluded patients whose COVID-19 diagnosis was based on symptoms alone.

Results: A total of 6,077 cases from 74 countries were included. Mean (SD) age was 48.8 (16.5) years and 58.6% were female (Table). The most common diagnoses were rheumatoid arthritis (35.3%) and Crohn's disease (25.3%).

Figure: Adjusted odds of COVID-19 related hospitalization or death for immunomodulatory treatment regimens compared with tumor necrosis factor inhibitor monotherapy in registry-specific and pooled analyses.



*Categories are mutually exclusive. **Presumptive diagnosis was based on symptoms alone. Abbreviations: GRA: Global Rheumatology Alliance; SECURE-IBD: Secure Epidemiology of Coronavirus Under Research Exclusion for Inflammatory Bowel Disease; PsoProtect: Psoriasis Patient Registry for Outcomes, Therapy and Epidemiology of COVID-19 Infection. JAKi: janus kinase inhibitor; 6MP: 6-mercaptopurine; TNFi: tumor necrosis factor inhibitor; HCQ: hydroxychloroquine; GC: glucocorticoid; IA: inflammatory arthritis; IBD: inflammatory bowel disease.

Over one-fifth (21.3%) of cases were hospitalized for COVID-19 and 3.1% died. In the pooled analysis, compared with TNFi monotherapy, higher odds of hospitalization or death were observed with TNFi in combination with AZA/6MP (odds ratio: 1.7, 95% CI: 1.2-2.6), AZA/6MP monotherapy (1.8, 1.3-2.6), MTX monotherapy (2.0, 1.6-2.6), and JAKi monotherapy (1.8, 1.2-2.7). ORs obtained from registry-specific analyses were generally in the same direction and of similar magnitude as those obtained from the pooled analysis (Figure). Similar findings were obtained after excluding patients whose COVID-19 diagnosis was based on symptoms alone.

Conclusion: Among individuals with IMIDs, TNFi monotherapy is associated with a lower risk of adverse COVID-19 outcomes compared with other commonly prescribed immunomodulatory regimens. These data can help inform treatment decisions for individuals with IMIDs during the pandemic.

TNFi monotherapy is the reference category. Pooled sensitivity analysis excludes COVID-19 diagnoses based on symptoms alone. Odds ratios derived using multilevel multivariable mixed-effects logistic regression. Registry-level

analyses adjusted for demographics, clinical characteristics, comorbidities, concomitant medications, and accounted for country and calendar-month correlations. Pooled analyses additionally accounted for registry-level correlations. Abbreviations: MTX: methotrexate; TNFi: tumor necrosis factor inhibitor; AZA/6MP: azathioprine/6-mercaptopurine; JAKi: janus kinase inhibitor. N = 3,523 (GRA); 2,336 (SECURE-IBD); 300 (PsoProtect); 6,159 (Pooled); 5,223 (Pooled, sensitivity analysis).

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Abstract Number: 0088

Evaluation of Patient Characteristics and Clinical Outcomes Among SARS-CoV-2-Diagnosed Patients with and Without RA or PsA Treated with Systemic Therapies: A Retrospective Cohort Study Using US Optum® COVID-19 Electronic Health Record Data

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with chronic rheumatic diseases are considered to be at increased risk for some infections, with prescribed immunomodulatory (IM) therapies increasing this risk further. It is unclear if patients with RA or PsA receiving IM therapies are at increased risk for SARS-CoV-2 infection, and if they experience more severe COVID-19 clinical outcomes compared with the general population. We describe the characteristics and COVID-19 clinical outcomes in this patient population.

Table. Baseline characteristics and IPs of clinical manifestations/outcomes in the RA, PsA, and comparator cohorts[a]

	RA cohort[b] (N=2,306)	PsA cohort[b] (N=421)	Comparator cohort[c] (N=311,563)
Baseline demographics[d]			
Age (yrs), median (range)	61 (19–89)	55 (22–89)	49 (18–89)
Female, n (%)	1,795 (77.8)	226 (53.7)	177,732 (57.1)
White, n (%)	1,634 (70.9)	367 (87.2)	218,293 (70.1)
Baseline IM therapy, n (%)[d]			
Tofacitinib	69 (3.0)	13 (3.1)	0 (0.0)
Any JAK inhibitors	96 (4.2)	13 (3.1)	0 (0.0)
TNFi	228 (9.9)	103 (24.5)	0 (0.0)
Non-TNFi biologic	278 (12.1)	75 (17.8)	0 (0.0)
csDMARD[e]	838 (36.3)	93 (22.1)	0 (0.0)
Corticosteroid use[f]	748 (32.4)	85 (20.2)	19,651 (6.3)
Baseline clinical characteristics, n (%)[d]			
Hypertension	1,088 (47.2)	146 (34.7)	67,995 (21.8)
Hyperlipidemia	827 (35.9)	123 (29.2)	54,225 (17.4)
History of hospitalization	410 (17.8)	36 (8.6)	17,144 (5.5)
Diabetes	479 (20.8)	78 (18.5)	34,210 (11.0)
Asthma	288 (12.5)	45 (10.7)	16,241 (5.2)
Coronary artery disease	356 (15.4)	35 (8.3)	15,684 (5.0)
CKD/dialysis	364 (15.8)	27 (6.4)	16,582 (5.3)
COPD	288 (12.5)	20 (4.8)	9,625 (3.1)
Serious infections (hospitalized)	201 (8.7)	13 (3.1)	6,952 (2.2)
Cancer	179 (7.8)	19 (4.5)	8,907 (2.9)
Other immune deficiencies	120 (5.2)	13 (3.1)	864 (0.3)
VTE	97 (4.2)	9 (2.1)	2,874 (0.9)
Liver disease	117 (5.1)	22 (5.2)	5,391 (1.7)
Interstitial lung disease	86 (3.7)	4 (1.0)	956 (0.3)
HIV/AIDS	<10 (< 1)	0 (0.0)	841 (0.3)
Primary endpoints, n; IP (95% CI)			
Hospitalization	585; 25.4 (23.6, 27.2)	50; 11.9 (8.9, 15.4)	45,712; 14.7 (14.6, 14.8)
ICU admission	135; 23.1 (19.7, 26.7)	9; 18.0 (8.8, 31.4)	9,353; 20.5 (20.1, 20.8)
Clinical manifestations/outcomes of interest, n; IP (95% CI)			
In-hospital death[g]	93; 15.9 (13.0, 19.1)	8; 16.0 (7.2, 29.1)	5,226; 11.4 (11.1, 11.7)
All-cause mortality[h]	118; 5.1 (4.3, 6.1)	10; 2.4 (1.1, 4.3)	7,937; 2.6 (2.5, 2.6)
Pneumonia[i]	519; 22.5 (20.8, 24.3)	54; 12.8 (9.8, 16.4)	41,296; 13.3 (13.1, 13.4)
Kidney failure[i]	210; 9.1 (8.0, 10.4)	19; 4.5 (2.7, 7.0)	15,700; 5.0 (5.0, 5.1)
Thrombotic event[i]	108; 4.7 (3.8, 5.6)	11; 2.6 (1.3, 4.6)	6,664; 2.1 (2.1, 2.2)
Acute respiratory distress syndrome[i]	368; 16.0 (14.5, 17.5)	35; 8.3 (5.9, 11.4)	26,709; 8.6 (8.5, 8.7)
Heart failure[i]	205; 8.9 (7.8, 10.1)	18; 4.3 (2.6, 6.7)	9,814; 3.2 (3.1, 3.2)
Sepsis/septic shock[i]	167; 7.2 (6.2, 8.4)	14; 3.3 (1.8, 5.5)	11,555; 3.7 (3.6, 3.8)
Mechanical ventilation/ECMO	70; 3.0 (2.4, 3.8)	5; 1.2(0.4, 2.8)	4,607; 1.5 (1.4, 1.5)
IV immunoglobulin	9; 0.4 (0.2, 0.7)	2; 0.5 (0.1, 1.7)	595; 0.2 (0.2, 0.2)

[a]Patients who did not have complete data, including encounter data, were excluded

[b]At least 1 diagnosis of RA or PsA and treatment with IM therapy (JAK inhibitor, TNFi, non-TNFi biologic, or csDMARD) within 2 yrs prior to SARS-CoV-2 diagnosis date

[c]Absence of a diagnosis of RA, PsA, or UC, and no IM therapy within 2 yrs prior to SARS-CoV-2 diagnosis date

[d]Baseline was defined as within 6 months prior to SARS-CoV-2 diagnosis date

[e]csDMARDs included aursnofin, aurothioglucose, azathioprine, chloroquine hydrochloride, chloroquine phosphate, cyclophosphamide, cyclosporine, gold sodium thiomalate, hydroxychloroquine sulfate, leflunomide, mercaptopurine, mesalamine, methotrexate, minocycline hydrochloride, n-acetylpenicillamine, penicillamine, primaquine, sulfasalazine, tacrolimus, and thalidomide

[f]Within 90 days prior to SARS-CoV-2 diagnosis date

[g]Denominator is the number of patients hospitalized within 30 days of SARS-CoV-2 diagnosis; defined as death during hospitalization

[h]Within 90 days of SARS-CoV-2 diagnosis date

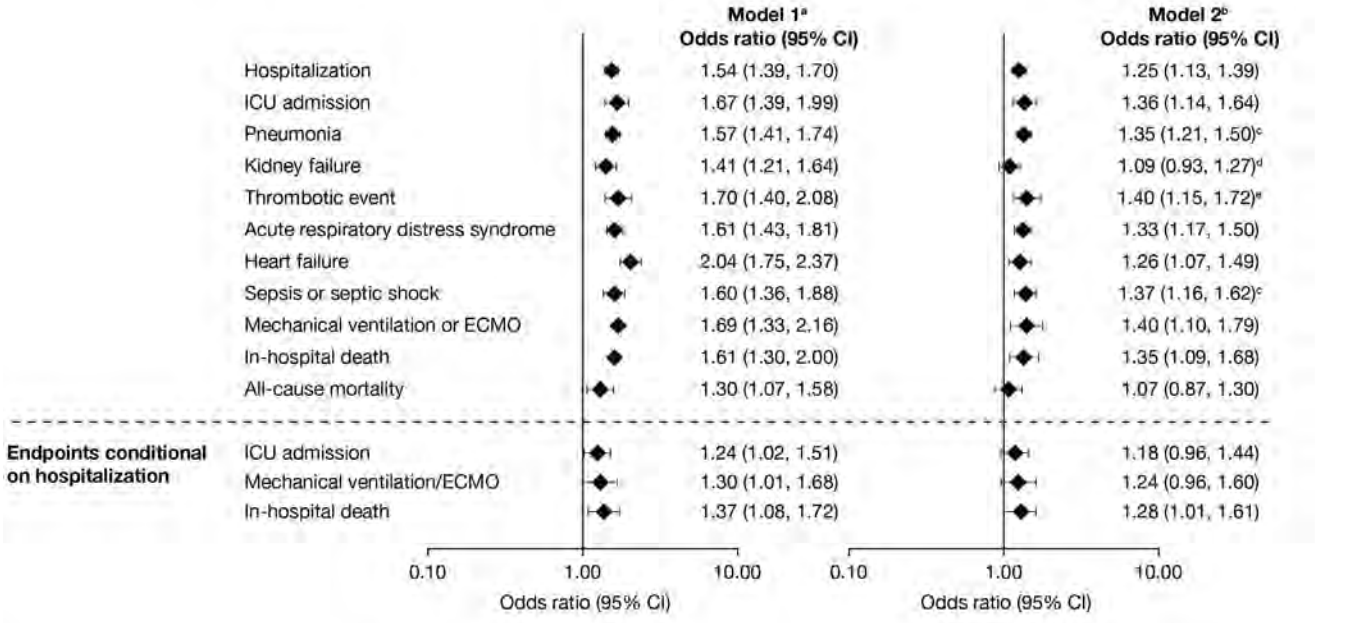
[i]Within 30 days of SARS-CoV-2 diagnosis date

CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; csDMARD, conventional synthetic DMARD; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; IM, immunomodulatory; IP, incidence proportion; IV, intravenous; JAK, Janus kinase; N, number of patients in the cohort; n, number of patients in the specified category; TNFi, TNF inhibitor; UC, ulcerative colitis; VTE, venous thromboembolism

Methods: This descriptive retrospective cohort study (a post-approval safety study of tofacitinib [approved for RA, PsA, and ulcerative colitis (UC) at the time of the study] in the context of the COVID-19 pandemic) used data from the US Optum® deidentified COVID-19 electronic health record dataset (2007–2020). Adults with a COVID-19 diagnosis (≥ 1 diagnosis code or positive SARS-CoV-2 laboratory test [including PCR, antibody, or antigen]) were stratified into 3 cohorts: patients with RA or PsA and evidence of treatment with IM therapy in the 2 yrs prior to COVID-19 diagnosis (RA and PsA cohorts); and patients without a diagnosis of RA, PsA, or UC and no record of IM therapy in the 2 yrs prior to COVID-19 diagnosis (comparator cohort). Baseline (SARS-CoV-2 diagnosis date) demographics, comorbidities, and IM therapy class were evaluated. The incidence proportions (IPs; with 95% confidence intervals) of primary endpoints (hospitalization and intensive care unit [ICU] admission) and COVID-19 clinical manifestations/outcomes of interest were calculated. Logistic regression was used in exploratory analyses to estimate the risk of endpoints, adjusting for demographics (age, sex, race, region), and demographics plus comorbidities.

Results: As of December 09, 2020, there were 2,306 patients in the RA cohort, 421 patients in the PsA cohort, and 311,563 patients in the comparator cohort. Compared with the comparator cohort, patients with RA and PsA were older and had a higher prevalence of baseline comorbidities (Table). Crude IP of hospitalization due to COVID-19 was higher in the RA cohort compared with the PsA and comparator cohorts (Table). ICU admission (conditional on hospitalization) was similar in the RA and comparator cohorts. Adjusting for demographics, COVID-19 patients with RA had an increased risk of hospitalization and in-hospital death, compared with the comparator cohort (Figure 1). The increased risk was also observed when adjusted for demographics plus comorbidities. Risk of hospitalization was lower in COVID-19 patients with RA receiving TNF inhibitors (TNFi) vs non-TNFi biologics and the comparator cohort

Figure 1. Adjusted odds ratios of each endpoint in the RA cohort



[a]Covariates included in logistic regression models were age, sex, race, and region

[b]Covariates included in logistic regression models were age, sex, race, region, lung disease (interstitial lung disease, asthma, and COPD), VTE, hypertension, coronary artery disease, serious infections (hospitalized), cancer, diabetes, CKD/dialysis, and liver disease

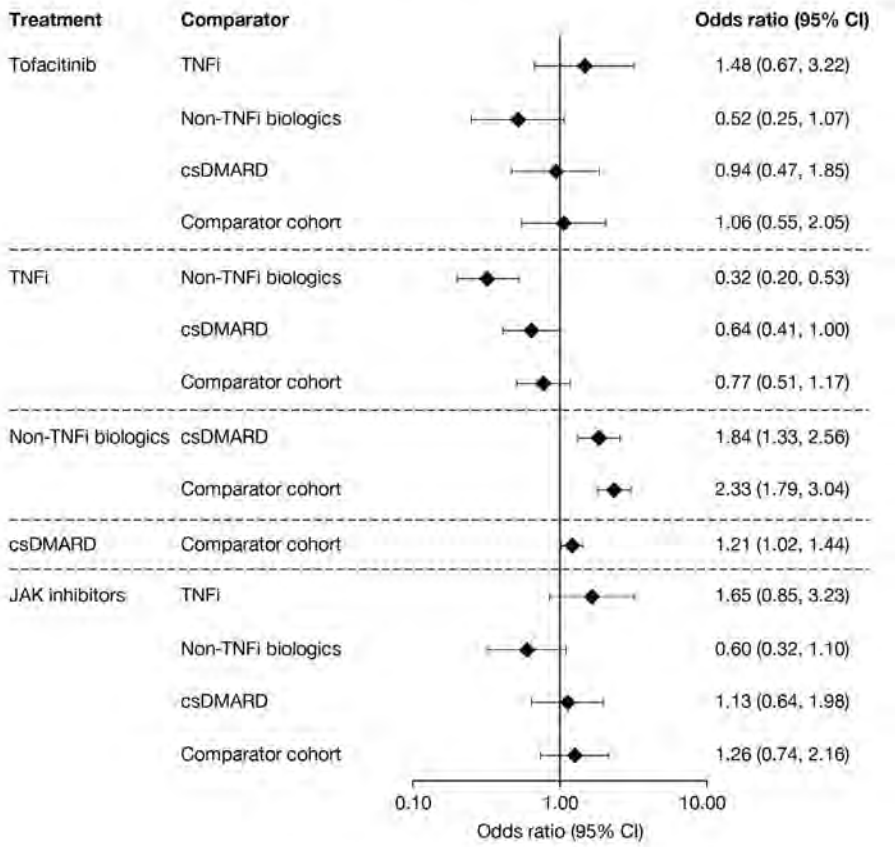
[c]Serious infections (hospitalized) was not included as a covariate

[d]CKD/dialysis was not included as a covariate

[e]VTE was not included as a covariate

CI, confidence interval; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; ECMO, extracorporeal membrane oxygenation; ICU, intensive care unit; VTE, venous thromboembolism

Figure 2. Adjusted odds ratios of hospitalization according to baseline systemic IM therapy in the RA cohort



Covariates included in logistic regression models were age, sex, race, region, hypertension, diabetes, and CKD/dialysis

CI, confidence interval; CKD, chronic kidney disease; csDMARD, conventional synthetic DMARD; IM, immunomodulatory; JAK, Janus kinase; TNFi, TNF inhibitor

(Figure 2). In the RA cohort, risk of hospitalization due to COVID-19 was similar between patients receiving tofacitinib and the comparator cohort (Figure 2).

Conclusion: Compared with the comparator cohort, patients with RA were at higher risk of more severe or critical COVID-19; except for non-TNFi biologics, immunosuppressive therapies such as TNFi did not further increase the risk.

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Abstract Number: 0089

SARS-CoV-2 Seroprevalence and Seroconversion in a Systemic Lupus Erythematosus Cohort and Comparison to General Population Controls

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: At the outset of the SARS-CoV-2 pandemic, it was speculated that SLE patients may be at significant risk of developing COVID-19 due to underlying immune dysregulation and use of immunomodulatory therapies. Our aims were to:

1. Compare SARS-CoV-2 seroprevalence pre- and intra-pandemic in a local SLE cohort to (a) ambulatory individuals tested for autoantibodies, and (b) a geographically similar general population.
2. Assess rates of RT-PCR testing and positivity.
3. Evaluate relationships between SARS-CoV-2 exposure and demographic and clinical features in the SLE cohort.

Methods: Sera from 173 SLE patients were included, with pre-pandemic samples biobanked prior to 01/01/2020 and intra-pandemic samples collected from 03/15/2020 to 01/31/2021. One hundred pre-pandemic and 148 intra-pandemic sequential, unselected sera from ambulatory individuals served as controls. All sera were tested for SARS-CoV-2 antibodies using two FDA early use authorized assays: an ELISA measuring IgA and IgG anti-spike 1 (S1) (Euroimmun AG, Lübeck, Germany) and an xMAP® assay detecting IgG antibodies to nucleocapsid (N), S1, and receptor-binding domain (RBD) of S1 (Luminex Corp., Austin, TX). The seroprevalence rate of a geographically similar general population was obtained from online published jurisdiction rates. RT-PCR testing was performed in the SLE cohort by a government-sanctioned laboratory. Differences in seropositivity between cohort and controls, and differences in demographic and clinical features between SLE patients with and without SARS-CoV-2 exposure (defined as positive RT-PCR and/or antibodies to SARS-CoV-2) were assessed using 95% confidence intervals (CI).

Table 1. Pre-pandemic demographic and clinical and features in the SLE cohort. Clinical features were measured at the time of the pre-pandemic serum sample date

Age (mean years (SD))	48.5 (14.7)
Sex (% Female)	94.8
Race/Ethnicity (% White)	57.2
Disease Duration (mean years (SD))	11.7 (11.3)
SLEDAI-2K Score (mean (SD))	2.9 (3.6)
Anti-malarials (% use)	85.5
CS (% use)	29.0
Other Immunomodulators[1] (% use)	44.5
Other Biologics (% use)	6.9

Abbreviations: SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; CS, corticosteroids.

[1] Azathioprine, Methotrexate, Cyclophosphamide IV, Cyclophosphamide PO, Mycophenolate Mofetil, Tacrolimus, or Mycophenolic Acid.

Table 2. Pre- and intra-pandemic SARS-CoV-2 antibodies in SLE patients and controls

	Pre-Pandemic SLE cohort, n = 173 Controls, n = 100				Intra-Pandemic SLE cohort, n = 173 Controls, n = 148			
	ELISA anti-S1		XMAP® anti-N, S1, or RBD S1	Patients with at least one SARS-CoV-2 antibody	ELISA anti-S1		XMAP® anti-N, S1, or RBD S1	Patients with at least one SARS-CoV-2 antibody
	IgA	IgG	IgG		IgA	IgG	IgG	
SLE Cohort (n (%))	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	4 (2.3)	3 (1.7)	6 (3.5)
Controls (n (%))	2 (2.0)	3 (3.0)	0 (0.0)	5 (5.0)	3 (2.0)	5 (3.4)	3 (2.0)	5 (3.4)
Difference[1] (% (95% CI))	-2.0 (-4.7%, 0.7%)	-3.0 (-6.3%, 0.3%)	0.0 (0.0%, 0.0%)	-5.0 (-9.3%, -0.7%)	-1.4 (-3.9%, 1.1%)	-1.1 (-4.8%, 2.6%)	-0.3 (-3.3%, 2.7%)	0.1 (-3.9%, 4.1)

Abbreviations: S1, spike 1; RBD, receptor-binding domain; N, nucleocapsid

[1] between cohort and controls.

Table 3. Comparison of pre-pandemic demographic and clinical features among those with and without SARS-CoV-2 exposure (defined as positive serology and/or positive RT-PCR) in the intra-pandemic SLE cohort

	Exposed (n = 9)	Non-exposed (n = 164)	Difference[1] (95% CI)
Age (mean years (SD))	46.7 (11.9)	48.6 (14.9)	-1.9 (-10.0, 6.2)
Sex (% Female)	88.9	95.1	-6.2 (-27.0, 14.6)
Ethnicity (% White)	55.6	57.3	-1.7 (-35.0, 31.6)
Disease Duration (mean years (SD))	10.3 (9.1)	11.8 (11.4)	-1.5 (-7.7, 4.7)
SLEDAI-2K Score (mean (SD))	4.2 (3.1)	2.9 (3.7)	1.3 (-0.8, 3.4)
Anti-malarials (% use)	77.8	84.8	-7.0 (-34.7, 20.7)
CS (% use)	33.3	28.7	4.6 (-27.0, 36.2)
Other Immunomodulators[2] (% use)	55.6	43.9	11.7 (-21.6, 45.0)
Other Biologics (% use)	0.0	7.3	-7.3 (-11.3, -3.3)

Abbreviations: SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; CS, corticosteroids.

[1] between exposed and non-exposed patients to SARS-CoV-2.

[2] Azathioprine, Methotrexate, Cyclophosphamide IV, Cyclophosphamide PO, Mycophenolate Mofetil, Tacrolimus, or Mycophenolic Acid.

Results: The SLE cohort was 95% female with a mean age of 48.5 years (SD 14.7) and mean disease duration of 11.7 years (SD 11.3) (Table 1). Eighty-six percent were using anti-malarials, 29% corticosteroids, and 45% other immunomodulators.

In the pre-pandemic samples, none of the SLE cohort vs. 5 (5%) of the ambulatory controls had at least one antibody to any SARS-CoV-2 antigens (difference (dif) -5.0%, 95% CI -9.3, -0.7%; Table 2). In the intra-pandemic samples, 6 (3.5%) SLE patients vs. 5 (3.4%) of the ambulatory controls (dif 0.1%, 95% CI -3.9%, 4.1%) and 2.9% of the geo-

graphically similar general population (dif 0.6%, 95% CI -2.2%, 3.4%) had at least one SARS-CoV-2 antibody. Eighty-one (47%) SLE patients received an RT-PCR test, of which 6/81 (7%) were positive.

Within the SLE cohort, the only significant difference in pre-pandemic characteristics between those with and without SARS-CoV-2 exposure was biologic use (0.0% vs. 7.3%; dif -7.3, 95% CI -11.3, -3.3) (Table 3).

Conclusion: Despite underlying immune dysregulation and frequent use of immunomodulatory therapies, our SLE patients did not appear to have higher exposure to SARS-CoV-2 or greater risk of developing COVID-19 compared to the general population. Further, none of the SLE patients had pre-pandemic (i.e., cross-reactive) antibodies to SARS-CoV-2 N, S1, or RBD proteins. More effective use of infection control principles may contribute to reducing SARS-CoV-2 infections in SLE.

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Abstract Number: 0090

Subcutaneous Sarilumab in Hospitalized Patients with Moderate-severe COVID-19 Infection Compared to the Standard Care: An Open-label Randomized Clinical Trial

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Many uncertainties remain for IL-6 blockers on the management of COVID-19 such as the optimal time of intervention, the schedule of administration and predictors of response. To date, data on the use of subcutaneous sarilumab (SAR) is scarce and no randomized controlled trial (RCT) results are available. Therefore, we aimed at evaluating the effect of subcutaneous SAR vs standard of care (SOC) in hospitalized patients with moderate to severe COVID-19.

Methods: Single center open-label RCT. We included admitted adult patients with documented COVID-19 infection with pneumonia confirmed by chest imaging, laboratory evidence of inflammatory phenotype and no need for invasive ventilation. Patients were randomized from March 14th to October 30th 2020, to receive SAR or SOC in a 2:1 proportion. The experimental arm received a single 400 mg dose of SAR in two 200 mg subcutaneous injections added to SOC. The control arm received usual supportive care as per local protocols.

The primary endpoints included 30-day mortality, mean change in clinical status at day 7 on an ordinal scale ranging from death (category1) to discharged (category 7), and duration of hospitalization. The primary efficacy analysis was conducted on the intention to-treat population. Secondary outcomes included time to became afebrile for 48 hours

Table 1. Baseline clinical characteristics of the study population AST: Aspartate amino-transferase; ALT: Alanine amino- transferase; COPD: Chronic obstructive pulmonary disease; CRP: C-reactive protein; GGT: Gamma-glutamyl transferase; IL-6: Interleukin-6; LDH: Lactate Dehydrogenase; NIV: noninvasive ventilation; PaO2/Fi02: partial pressure of arterial oxygen/fraction of inspired oxygen; PCT: Procalcitonin. a) O2 flow ≤ 15l/min e.g. by face mask, nasal cannula (NC); b) O2 flow >15l/min, e.g. by face mask, 'High Flow' devices (e.g. HFNC), CPAP or NIV including BiPAP and other devices; c) Corticosteroids: ≥ 30 mg Prednisone/d or equivalent; intravenous bolus of 6-Metilprednisolone 120-125 mg/d, except 1 patient 80 mg/d; d) All radiologic exams were assessed and reported by radiologists with pneumological expertise

	Total (n=30)	SAR + SOC (n=20)	SOC (n=10)
Median Age in years (IQR)	61.5 (56-72)	61.5 (50.5-72)	62 (58-71)
Male sex, n (%)	20 (67)	15 (75)	5 (50)
Coexisting Disorders, n (%)	19 (63)	14 (70)	5(50)
Hypertension	13(43)	8 (40)	5 (50)
Diabetes Mellitus	5 (17)	3 (15)	2 (20)
Obesity	3 (10)	2 (10)	1 (10)
Median days from symptom onset to randomization (IQR)	11 (8-16)	10.5 (8-12.5)	16 (12-23)
Median days from admission to randomization (IQR)	2 (1-4)	2 (1-4)	3 (1-6)
Fever ≥37,5 °C, n (%)	10 (33)	9 (45)	1 (10)
Oxygen support at randomization (7-category ordinal scale) n (%)			
5. No supplemental oxygen therapy	4 (13.3)	4 (20)	0 (0)
4. Low flow suppl oxygen therapy [a]	22 (73.3)	12 (60)	10 (100)
3. High flow suppl oxygen therapy or NIV [b]	4 (13.3)	4 (20)	0 (0)
Median PaO_2/FiO_2 mmHg (IQR) at randomization	318 (233-358)	298 (223-348)	341 (261-404)
Additional treatment during hospitalization			
Hydroxychloroquine	6 (20)	4 (20)	2 (20)
Lopinavir/Ritonavir	5 (17)	4 (20)	1 (10)
Azithromycin	18 (60)	12 (60)	6 (60)
Corticosteroids at randomization [c]	25 (83)	17 (85)	8 (80)
Methylprednisolone bolus at randomization [c]	17 (57)	14 (70)	3 (30)
Laboratory Values (median, IQR)			
Lymphocyte Count (cells/mm^3)	830 (680-1,130)	825 (680-1,070)	865 (680-1,580)
Creatinine. mg/dl	0.80 (0.63-0.98)	0.83 (0.71-0.99)	0.65 (0.59-0.87)
Bilirubin. mg/dl	0.40 (0.32-0.52)	0.38 (0.32-0.53)	0.49 (0.34-0.52)
AST. U/L	33 (26-54)	40 (27-53)	32 (25-93)
ALT. U/L	46 (24-61)	48 (29-57)	28 (21-97)
GGT. U/L	56 (34-117)	41 (30-119)	71 (55-108)
LDH. U/L	297 (238-349)	317 (263-350)	263 (222-333)
Inflammatory markers			
serum IL-6. pg/ml (n=24)	12 (3-21.5)	13.3 (7.5-24)	3 (1-16.5)
IL-6 ≥ 30 pg/ml, n (%)	4/24 (17)	3/16 (19)	1/8 (13)
Ferritin. ng/ml (n=29)	1,179 (735-1,511)	1,048 (664-1,511)	1,265 (735-1,532)
CRP. mg/dL	9.28 (5.06-19.73)	8.59 (4.17-18.1)	9.94 (6.19-19.73)
PCT. ng/ml (n=13)	0.11 (0.08-0.18)	0.11 (0.09-0.18)	0.12 (0.07-0.18)
D-dimer (µg/ml) (n=29)	0.49 (0.37-1.14)	0.49 (0.36-1.28)	0.51 (0.37-1.09)
Baseline radiologic findings (x ray and/or CT scan) [d]			
Alveolar pattern/ground glass opacities > 50%	14 (47)	11 (55)	3 (30)

without antipyretics, mean change in the mentioned ordinal scale at day 14, progression to non- invasive mechanical ventilation (NIMV) and invasive mechanical ventilation (IMV), time to oxygen supply independency, and adverse events (AE). To estimate the intervention effect size, hazard ratios (HR) were estimated when feasible.

Table 2. Primary and secondary outcomes IMV: invasive mechanical ventilation; NIMV: Noninvasive mechanical ventilation; SD: standard deviation; SOC: Standard of care. a) Accounting for survival status by treating patients who died as having a 30-day hospital stay; b) Eleven patients in the SAR arm and 5 in the SOC arm were febrile at randomization

Outcomes	SAR + SOC (n=20)	SOC (n=10)	HR (SE)	Log HR (SE)	*p*-value
Primary outcomes					
Median (IQR) change on the ordinal scale, day 7	2 (0-3)	3 (0-3)			0.32
Mean (SD) change on the ordinal scale, day 7	1.45 (1.93)	2.1 (1.45)			0.36
30-day mortality, n (%)	2 (10)	0		15.11 (22.64)	0.54
Duration of hospitalization, days from randomization a	7 (6-11)	6 (4-12)	0.65 (0.26)		0.27
Secondary Outcomes					
Median change on the ordinal scale, day 14	3 (3-3)	4 (2-4)			0.36
Time to became afebrile for at least 48 h, days[b]	3 (3-6)	4 (4-8)	1.60 (0.97)		0.39
Progression to NIMV, n (%)	4 (20)	0 (0)		15.09 (22.52)	0.27
Progression to IMV, n (%)	3 (15)	0 (0)		15.10 (22.52)	0.5
Time to suppl oxygen withdrawal, days from randomization	5.5 (3 -13)	4.5 (2-12)	0.83 (0.37)	-	0.83

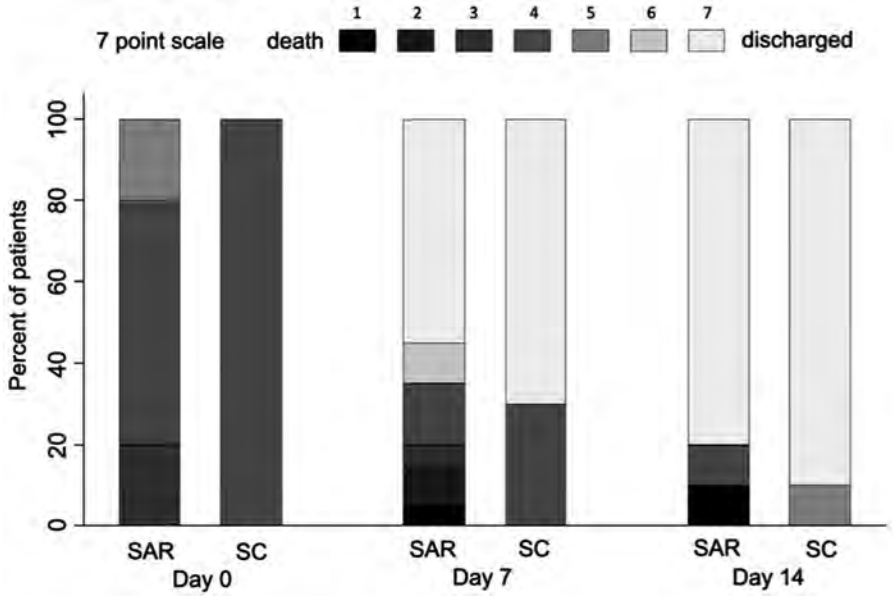

Figure 1. Evolution of clinical status in COVID-19 patients from baseline to day 14 according to the 7-category ordinal scale. Data are shown as the percentage of patients at each ordinal point.

Results: Thirty out of sixty-five screened patients underwent randomization: 20 to SAR and 10 to SOC. Most patients were male (20/30, 67%) with a median (interquartile range, IQR) age of 61.5 (56-72) **(Table 1)**.

At day 30, 2/20 patients died in the SAR and none in the SOC arm (Log HR 15.11, SD 22.64, p 0.54). At day 7, no significant differences were seen in the median change on a 7-category ordinal scale (2 [0-3] vs 3 [0-3], p 0.32) **(Figure 1)**. The median days to discharge were similar (7 [6-11] vs 6 [4-12]; HR 0.65, SD 0.26; p 0.27). No significant differences were seen for any of the secondary outcomes. In the SAR arm, 4/20 (20%) and 3/20 (15%) patients required NIMV and IMV respectively vs none in the SOC **(Table 2)**. Regarding safety, the rate of AE of special interest were similar in the SAR (50%) and SOC (40%) arms.

Conclusion: In our study, subcutaneous SAR added to SOC showed no additional benefit in 30-day mortality, clinical status at day 7, or hospital stay.

Disclosure: S. Rodriguez-García, None; **I. Gonzalez-Alvaro**, None; **F. Abad-Santos**, None; **A. Bautista-Hernández**, None; **L. García-Fraile**, None; **J. Baldivieso-Achá**, None; **J. Sanz-Sanz**, None; **R. Garcia de Vicuña**, None.

Abstract Number: 0091

Vaccination of Patients with Chronic Inflammatory Rheumatic Diseases: An Analysis of Barriers and Facilitators in a Prospective Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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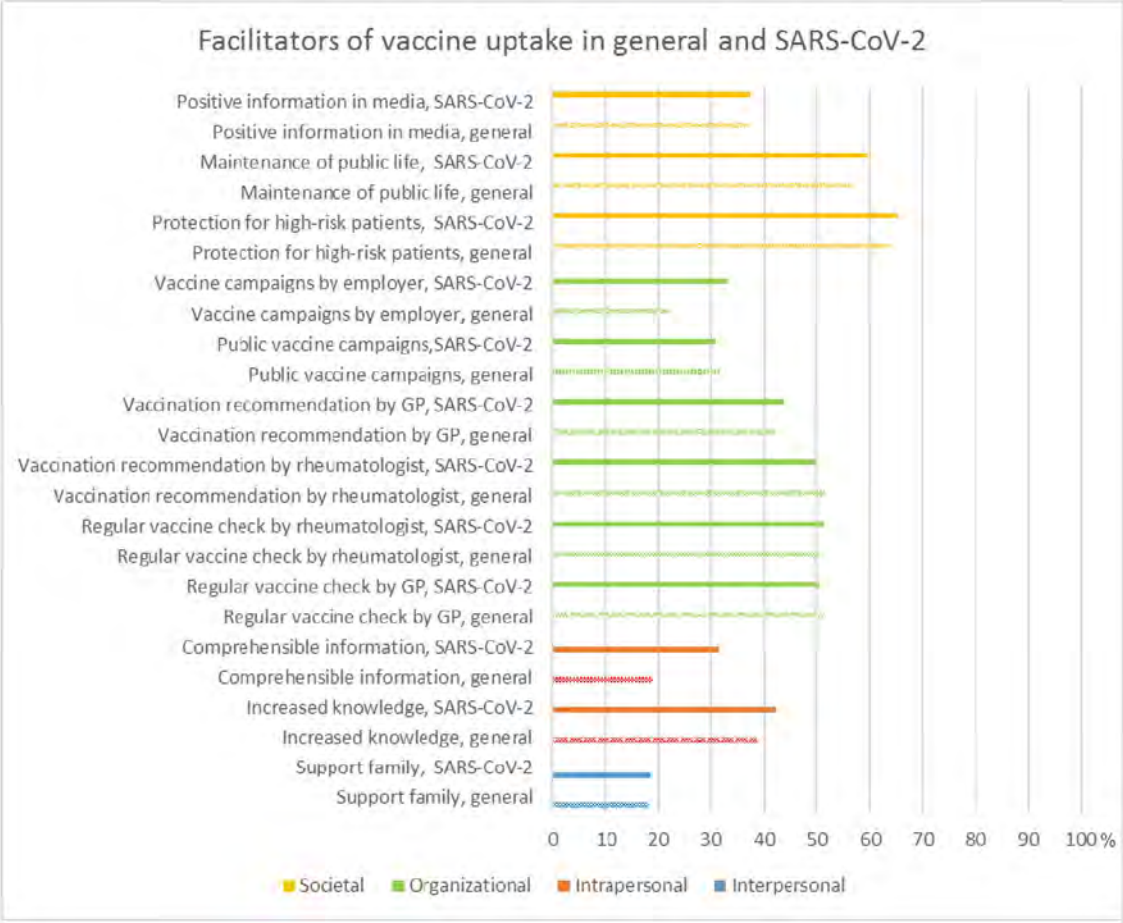


Figure 1. Facilitators of vaccine uptake in general and for SARS-CoV-2.

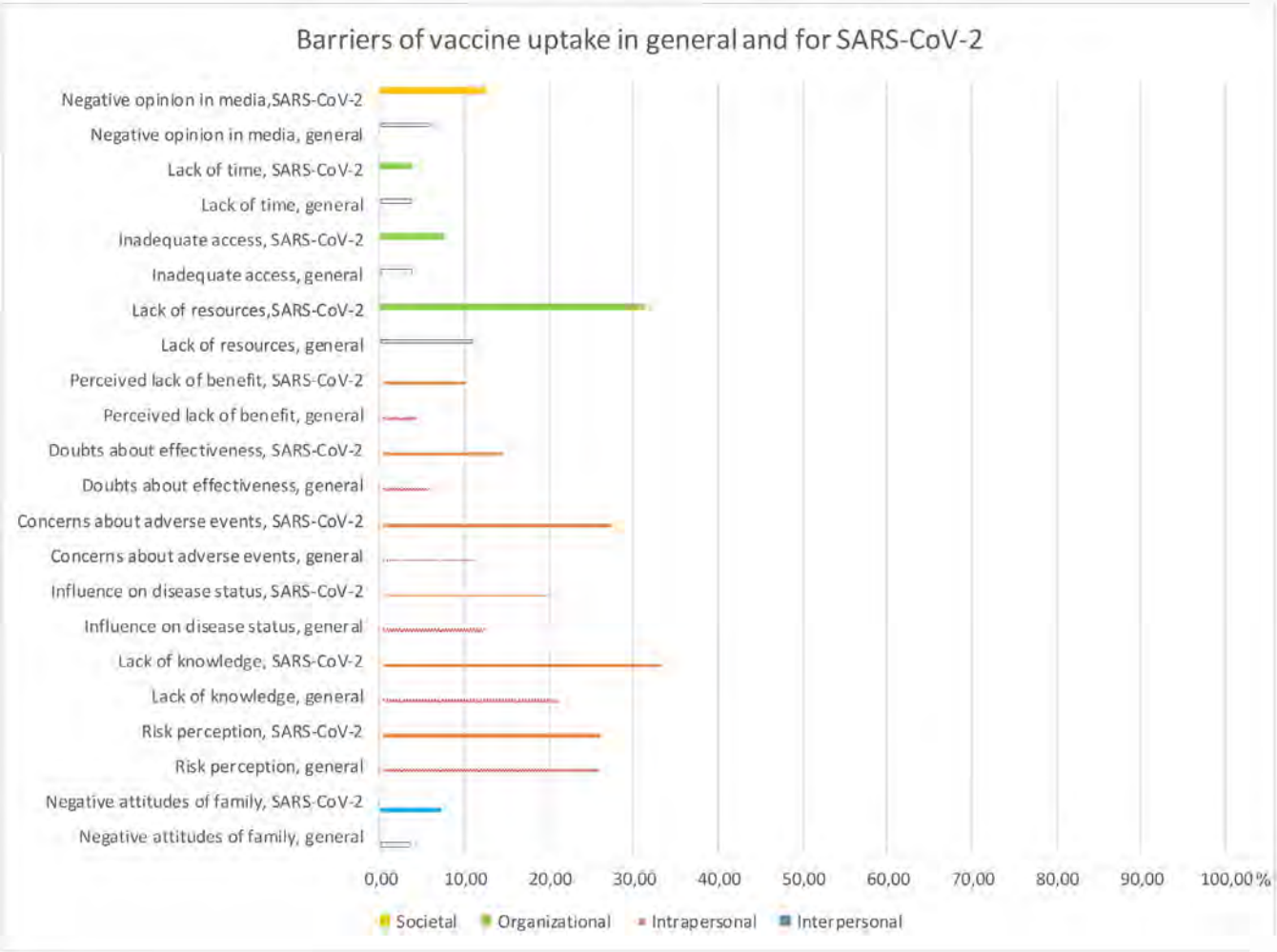


Figure 2. Barriers of vaccine uptake in general and for SARS-CoV-2.

Background/Purpose: Patients (pts.) with chronic inflammatory rheumatic diseases (CIRD) are often not adequately protected against infectious diseases. As shown in an earlier study, less than 50% of CIRD pts. were vaccinated against pneumococci and influenza before the SARS-CoV-2 pandemic started [1]. High vaccination rates are critical to achieve herd immunity. Knowledge on barriers and facilitators of vaccine uptake in CIRD pts. is limited. The aim of this study was to characterize barriers and facilitators towards vaccines in general and specifically against pneumococci, influenza and SARS-CoV-2 in adult CIRD pts..

Methods: In early 2021, consecutive CIRD pts. completed a structured questionnaire including knowledge on vaccination, attitudes, and perceived barriers and facilitators towards vaccination. A total of 12 facilitators and 11 barriers towards vaccination was assessed in general, and specifically for vaccination against pneumococci, influenza and SARS-CoV2. The Likert scales had 4 response options, ranging from 1 (completely disagree) to 4 (completely agree). Patient and disease characteristics, their vaccination history and attitudes towards vaccination against SARS-CoV-2 were assessed.

Results: Of 514 prospectively recruited pts., 441 responded (85.8%) to the questionnaire (table 1). Self-reported vaccine uptake was 48.8% against pneumococci and 66.2% against seasonal influenza. The majority (82.2%) was willing to be vaccinated against SARS-CoV-2. The majority (≥70%) had decent knowledge about vaccination, and

Table 1. Patient and disease characteristics Table legend on the bottom: variables as mean (SD)

Age, y	54.1 (12.6)
Women, No. (%)	272 (61.7)
Rheumatoid Arthritis, No. (%)	156 (35.4)
Axial Spondyloarthritis, No. (%)	120 (27.2)
Psoriatic Arthritis, No. (%)	61 (13.8)
Other diagnoses, No. (%)	104 (23.6))
Treatment, csDMARD, No. (%)	121 (27.4)
Treatment, bDMARD, No. (%)	280 (63.5)
Treatment, tsDMARD, No. (%)	24 (5.4)
CDAI, n=194	11.1 (9.0)
CRP, mg/L, n=440	0.4 (0.7)
HAQ score, n=317	1.1 (0.7)
BASDAI, n=118	3.8 (2.2)
BASFI, n=118	3.8 (2.3)
Patient global, NRS 0-10	4.1 (2.5)
HADS-A, n=436	6.6 (4.0)
HADS-D, n=436	5.8 (4.3)

variables as mean (SD)

only < 10% doubted its effectiveness. The level of knowledge did not differ between the studied 3 vaccinations. Pts. were more likely to rate statements about facilitators favorably compared to statements about barriers. Facilitators for SARS-CoV-2 vaccination did not differ from vaccination in general (figure 1). Societal and organizational facilitators such as public vaccine campaigns or protection for high risk pts. were more commonly named compared to inter- or intrapersonal facilitators. Protection of high-risk pts. was by far the most frequently cited facilitator. Most pts. indicated that they were likely to receive a vaccine if their health care professional would recommend it – without preference for GP or rheumatologist. The frequency of barriers was much lower compared to facilitators and more barriers towards SARS-CoV-2 vaccination were reported in comparison to vaccination in general or pneumococci and influenza, respectively. However, pts. frequently cited intrapersonal issues as barriers against vaccination. Importantly, the major barrier was an inadequate risk perception between the severity of COVID-19 and the potential adverse events of the vaccine.

Conclusion: A relatively high number of pts. was vaccinated against pneumococci and influenza, actually more than in our last study – a probable campaign success. Importantly, more than 80% of pts. were willing to be vaccinated against SARS-CoV-2. Facilitators were of greater significance than barriers. The high number of societal and organizational facilitators enables the implementation of effective strategies to increase future vaccination rates.

Reference: 1 Kiltz et al. RMD Open 2021

Disclosure: I. Andreica, None; **I. Roman**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5.

Abstract Number: 0092

Clinical Outcomes of Patients with Systemic Rheumatic Diseases Hospitalized for COVID-19 at a Large Academic Center in New York City

Caroline Siegel[1], Jacky Choi[2], Debra D'Angelo[2], Paul Christos[2], Lindsay Lally[1], Parag Goyal[2], Lisa Mandl[1] and Medha Barbhaiya[1], [1]Hospital for Special Surgery, New York, NY, [2]Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: While patients with systemic rheumatic diseases (SRDs) are in general more vulnerable to infections due to their underlying immune dysregulation and immunomodulatory therapies, data related to COVID-19 is conflicting. Early case series suggest that patients with SRD do not have more severe outcomes from COVID-19. This contrasts with data from retrospective cohort studies which suggest that patients with SRD have higher risk of mechanical ventilation or intensive care unit (ICU) admission than age- and sex- matched patients without SRD. Prior studies have been limited by sample size, lack of comparator groups, and/or appropriate statistical analysis. We used a large, multicenter cohort of patients hospitalized with COVID-19 in New York City during the first wave of the pandemic to determine whether patients with SRD hospitalized with COVID-19 were at increased risk of severe outcomes.

Methods: This retrospective observational cohort study included patients aged ≥18 years with confirmed SARS-CoV-2 infection hospitalized at any of three NewYork-Presbyterian hospital sites from March 3-May 15, 2020. We used chi-square tests and t-tests, as appropriate, to compare baseline characteristics, COVID-19-related symptoms, and outcomes between patients with and without SRD. Inverse probability of treatment weighting based on propensity scores (PS) was applied to a logistic regression model to assess the multivariable (MV) association between SRD status and the primary composite outcome of mechanical ventilation, admission to the ICU, or in-hospital death. Covariates with an absolute standardized mean (or proportion) difference (SMD) ≥0.10 in the PS model were adjusted for in the MV logistic regression outcome model (Figure 1).

Results: Out of 3,680 patients hospitalized with COVID-19, 92 (2.5%) had SRD. Mean age of the cohort was 63.7 [16.9] years, and 41% were female, 29% White, and 34% Hispanic/Latinx. Compared to patients without SRD, patients with SRD had similar age and BMI, but were more likely to be female, ever smokers, White or Black, and less likely to be Hispanic/Latinx (Table 1). Patients with SRD had a higher proportion of coronary artery disease, hypertension, and pulmonary disease, as well as use of hydroxychloroquine, corticosteroids, and immunosuppressive medications than patients without SRD (Table 1). Although presenting symptoms were similar, patients with SRD were more likely than those without SRD to be treated with steroids during hospitalization (51% vs. 17%, $p< 0.001$) (Table 2). In the weighted MV analysis, patients with SRD had an OR of 1.27 [95% CI 1.12-1.44, $p< 0.001$] for the composite

Table 1. Baseline Demographics, Comorbidities, and Outpatient Medications in Hospitalized Patients with COVID-19 with and without Systemic Rheumatic Disease[1]

	Overall N = 3,680[2]	SRD N = 92[2]	No SRD N = 3,588[2]	p-value[3]
Demographics				
Age	63.7 (16.9)	66.3 (16.5)	63.6 (17.0)	0.13
Female sex	1,509 (41%)	75 (82%)	1,434 (40%)	<0.01
Race				<0.01
• **White**	1,063 (29%)	37 (40%)	1,026 (29%)	
• **Asian**	689 (19%)	9 (9.8%)	680 (19%)	
• **Black**	438 (12%)	18 (20%)	420 (12%)	
• **Other**	1,246 (34%)	23 (25%)	1,223 (34%)	
• **Unknown**	244 (6.6%)	5 (5.4%)	239 (6.7%)	
Ethnicity				0.02
• **Hispanic/Latinx**	1,241 (34%)	24 (26%)	1,217 (34%)	
• **Not Hispanic/Latinx**	1,780 (48%)	55 (60%)	1,725 (48%)	
• **Other**	45 (1.2%)	3 (3.3%)	42 (1.2%)	
• **Unknown**	614 (17%)	10 (11%)	604 (17%)	
BMI (N=3,482)	28.2 (6.7)	28.2 (6.7)	28.2 (6.7)	>0.90
BMI ≥ 30 (N=3,482)	1,145 (33%)	31 (34%)	1,114 (33%)	0.70
Ever Smoker (N=3,675)	751 (20%)	29 (32%)	722 (20%)	0.01
Comorbidities				
Coronary Artery Disease	534 (15%)	20 (22%)	514 (14%)	0.05
Hypertension	2,019 (55%)	66 (72%)	1,953 (54%)	<0.01
Diabetes Mellitus	1,171 (32%)	27 (29%)	1,144 (32%)	0.60
Cerebral Vascular Accident	251 (6.8%)	6 (6.5%)	245 (6.8%)	>0.90
Chronic Kidney Disease	355 (9.6%)	10 (11%)	345 (9.6%)	0.70
Pulmonary Disease	600 (16%)	28 (30%)	572 (16%)	<0.01
Outpatient Medications				
Hydroxychloroquine	67 (1.8%)	21 (23%)	46 (1.3%)	<0.01
Systemic Corticosteroids	158 (4.3%)	35 (38%)	123 (3.4%)	<0.01
Immunosuppressive Medication	73 (2.0%)	15 (16%)	58 (1.6%)	<0.01
• **Azathioprine**	5 (0.1%)	1 (1.1%)	4 (0.1%)	0.12
• **Cyclosporine**	3 (<0.1%)	0 (0%)	3 (<0.1%)	>0.90
• **MTOR Inhibitor**	2 (<0.1%)	0 (0%)	2 (<0.1%)	>0.90
• **Methotrexate**	19 (0.5%)	15 (16%)	4 (0.1%)	<0.01
• **Mycophenolate**	55 (1.5%)	6 (6.5%)	49 (1.4%)	0.02
• **Tacrolimus**	53 (1.4%)	4 (4.3%)	49 (1.4%)	0.04
• **TNF-Alpha Inhibitor**	4 (0.1%)	3 (3.3%)	1 (<0.1%)	<0.01
• **Other Monoclonal Antibody**	11 (0.3%)	4 (4.3%)	7 (0.2%)	<0.01

[1]RA (50%), SLE (16.3%), Vasculitis/PMR/SSc/Myositis (16.3%), SLE-like/SS/MCTD/APS (12%), PsA (3.2%), Sarcoidosis (2.2%)
[2]Mean (SD); n (%)
[3]Welch Two Sample t-test; Pearson's Chi-squared test; Fisher's exact test

outcome of mechanical ventilation, ICU admission, or death compared to patients without SRD after adjustment for the remaining covariates with an absolute SMD ≥0.10.

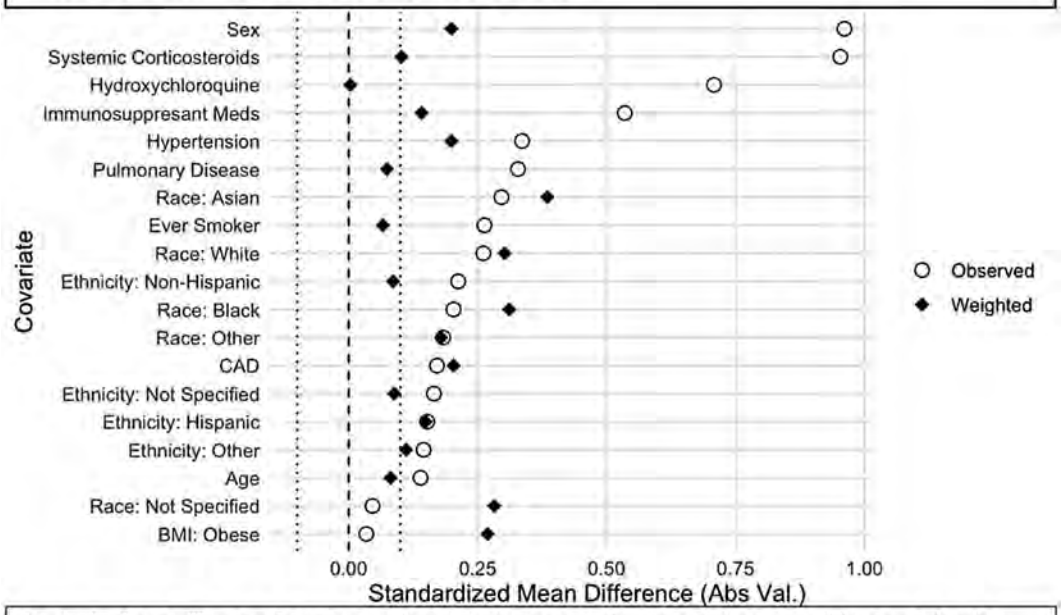
Conclusion: During the initial peak of the pandemic in New York City, patients with SRD hospitalized with COVID-19 were 1.27 times more likely to experience mechanical ventilation, ICU admission, or death than patients without SRD. Our findings, which used inverse weighting to balance covariates in a large observational inpatient cohort in a COVID-19 "hotspot", warrant confirmation in population-based cohorts.

Table 2. Symptoms on Presentation, In-hospital Treatment, and Clinical Outcomes in Hospitalized Patients with COVID-19 with and without Systemic Rheumatic Disease[1]

	Overall N = 3,680[2]	SRD N = 92[2]	No SRD N = 3,588[2]	p-value[3]
Clinical Presentation				
Presenting Symptom (N=3,666)				
• **Fever**	2,412 (66%)	61 (66%)	2,351 (66%)	>0.90
• **Cough**	2,479 (68%)	64 (70%)	2,415 (68%)	0.70
• **Dyspnea**	2,398 (65%)	62 (67%)	2,336 (65%)	0.70
• **Sore Throat**	209 (5.7%)	9 (9.8%)	200 (5.6%)	0.09
• **Rhinorrhea**	125 (3.4%)	6 (6.5%)	119 (3.3%)	0.13
• **Conjunctivitis**	4 (0.1%)	0 (0%)	4 (0.1%)	>0.90
• **Headache**	314 (8.6%)	7 (7.6%)	307 (8.6%)	0.70
• **Myalgia**	757 (21%)	16 (17%)	741 (21%)	0.40
• **Nausea**	623 (17%)	18 (20%)	605 (17%)	0.50
• **Diarrhea**	864 (24%)	24 (26%)	840 (24%)	0.60
• **Sputum**	263 (7.2%)	9 (9.8%)	254 (7.1%)	0.30
• **Presyncope**	169 (4.6%)	4 (4.3%)	165 (4.6%)	>0.90
• **Chest Pain**	466 (13%)	15 (16%)	451 (13%)	0.30
• **Abdominal Pain**	236 (6.4%)	3 (3.3%)	233 (6.5%)	0.20
• **Altered Mental Status**	442 (12%)	15 (16%)	427 (12%)	0.20
• **Anosmia**	83 (2.3%)	1 (1.1%)	82 (2.3%)	0.70
• **Ageusia**	115 (3.1%)	1 (1.1%)	114 (3.2%)	0.40
Symptom Onset to Admission (Days) (N=2,574)	6.0 (3.0, 9.0)	6.0 (3.2, 10.0)	6.0 (3.0, 9.0)	0.60
In-hospital Treatment				
Hydroxychloroquine	2,537 (69%)	70 (76%)	2,467 (69%)	0.13
Remdesivir	181 (4.9%)	6 (6.5%)	175 (4.9%)	0.50
Systemic Corticosteroids	653 (18%)	47 (51%)	606 (17%)	<0.01
Tocilizumab	165 (4.5%)	0 (0%)	165 (4.6%)	0.04
Sarilumab	24 (0.7%)	1 (1.1%)	23 (0.6%)	0.50
Anakinra	11 (0.3%)	0 (0%)	11 (0.3%)	>0.90
Convalescent Plasma	38 (1.0%)	0 (0%)	38 (1.1%)	>0.90
Clinical Outcomes				
Composite (ICU Admission/Mechanical Ventilation/Death)	1,286 (35%)	35 (38%)	1,251 (35%)	0.50
ICU Admission	775 (21%)	19 (21%)	756 (21%)	>0.90
Mechanical Ventilation	745 (20%)	20 (22%)	725 (20%)	0.70
Death	883 (24%)	24 (26%)	859 (24%)	0.60

[1] RA (50%), SLE (16.3%), Vasculitis/PMR/SSc/Myositis (16.3%), SLE-like/SS/MCTD/APS (12%), PsA (3.2%), Sarcoidosis (2.2%)
[2] Median (IQR); n (%)
[3] Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Figure 1. Standardized Mean Differences for Observed and Weighted Sample for Covariates Included in Propensity Score Model



Standardized mean differences for each covariate included in the propensity score model, as well as differences before (i.e., observed) and after (i.e., weighted) weighting. Weighted covariates with SMD ≥ 0.1 were additionally adjusted for in the multivariable logistic regression model.

Disclosure: C. Siegel, None; **J. Choi**, None; **D. D'Angelo**, None; **P. Christos**, None; **L. Lally**, None; **P. Goyal**, None; **L. Mandl**, Regeneron Pharmaceuticals, 5; **M. Barbhaiya**, None.

Abstract Number: 0093

The Association of General and Covid-19-Specific Stress with Changes in Patient-Reported Outcomes and Comorbidities

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: We previously showed that perceived stress during the COVID-19 pandemic was associated with concomitant increases in symptoms of depression and anxiety. In lupus alone, perceived stress during the pandemic was associated with concomitant increases in patient-reported disease activity, pain, fatigue, and cognitive functioning. We examined the role of both general and COVID-specific stress during the early stages of the pandemic with subsequent changes in patient-reported outcomes and comorbidities among individuals with rheumatic disease

Methods: Data are from FORWARD, The National Databank for Rheumatic Diseases, a longitudinal registry of individuals with rheumatic diseases. Data are regularly collected via semi-annual questionnaires. Participants with active emails were asked to respond to 5 COVID-19-specific questionnaires from March 25 through June 2, 2020. The COV-

Table 1. Characteristics of Participants	
	Total (n = 1135)
Age	66.4 ± 10.6
Female	84.9 (963)
Education (yrs)	15.4 ± 2.0
Rural residence	21.2 (240)
Disease duration (yrs)	23.4 ± 12.4
Pre-COVID Global severity rating	3.1 ± 2.4
Stress	
COVID-19-specific	6.0 ± 1.9
General (PSS)	2.4 ± 1.8
Patient-reported outcomes	
PAS2	2.9 ± 2.0
HAQ2	0.77 ± 0.59
Pain rating	3.2 ± 2.5
Fatigue rating	3.5 ± 2.8
Sleep problem rating	3.4 ± 2.9
Rheumatic Disease Comorbidity Index	2.4 ± 1.8
Global severity rating range 0 – 10 Both stress measures re-scaled for range 0 – 10.	

ID-19 questionnaire included an item about COVID-19-specific stress and the 4-item Perceived Stress Scale (PSS), which assesses general stress. Both stress scale scores were transformed to 0 – 10 scores to facilitate comparison. PROs examined were Patient Activity Score (PAS)-II, Health Assessment Questionnaire (HAQ)-II, and numeric rating scales for pain, fatigue, and sleep disturbance (0=no problem, 10=severe). Comorbidity burden was measured with the Rheumatic Disease Comorbidity Index (RDCI). Participant characteristics and baseline PRO scores were taken from the most recent pre-COVID-19 semi-annual questionnaire. Follow-up PRO scores were from the semi-annual questionnaire collected between July-December 2020. Predictors of PRO/RDCI worsening among respondents with rheumatoid arthritis (RA), osteoarthritis (OA), and lupus (SLE) were identified using multiple logistic regression, focusing on the role of COVID-19-specific stress and PSS, and controlling for age, sex, race, education, rural residence, disease duration, pre-COVID-19 global disease severity rating, and the pre-COVID PRO/RDCI outcome value.

Results: 7217 participants were invited for the COVID-19 questionnaire; 2000 (28%) responded. Of these, 1135 also responded to the July 2020 questionnaire and are included in analyses (Table 1). The frequency worsening of PROs ranged from 12.2% for the HAQ2 to 32.4% for sleep disturbance (Table 2). 16.5% had an increase in RDCI. General stress during the pandemic was associated with significantly greater odds of subsequent worsening of all PROs and an increase in RDCI (Table 2). COVID-specific stress was associated with significantly greater odds of subsequent worsening of PAS2, HAQ2, and fatigue.

Conclusion: Substantial portions of these individuals with rheumatic diseases experienced worsening in patient-reported outcomes and comorbid conditions. General stress levels early in the pandemic were significantly associated with those subsequent changes. Results suggest an important role for stress levels in patient outcomes and highlight the importance of the assessment of stress in clinical settings and identification of effective stress management techniques.

Table 2. Association of Stress with Worsening of Disease Activity and Symptoms and Comorbid Conditions

			Odds (95% CI) of worsening	
	Definition of worsening (increase in score)	% (n) with worsening	COVID-specific stress	General stress
PAS-II	≥0.50	27. (317)	1.15 (1.07, 1.25)	1.16 (1.06, 1.26)
HAQ-II	≥0.25	12.2 (146)	1.11 (1.01, 1.23)	1.12 (1.01, 1.25)
Pain (0-10 rating)	≥1	28.1 (352)	1.04 (0.96, 1.12)	1.09 (1.01, 1.19)
Fatigue (0-10 rating	≥1	30.6% (384)	1.11 (1.01, 1.23)	1.12 (1.01, 1.25)
Sleep problems (0-10 rating)	≥1	32.4% (362)	1.08 (0.996, 1.17)	1.09 (1.003, 1.19)
RDCI	≥1	16.5 (219)	1.05 (0.97, 1.15)	1.14 (1.03, 1.25)

Values are odds ratio (95% confidence interval) from multiple logistic regression analyses adjusting for age, sex, education, race, rural residence, and pre-COVID global severity rating, hydroxychloroquine use, and PHQ4 depression or anxiety score.

Disclosure: P. Katz, None; **K. Wipfler**, None; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Diseases, 3; **K. Michaud**, None.

Abstract Number: 0094

Characteristics Associated with Severe Outcomes in Patients with Systemic Rheumatic Diseases Hospitalized for COVID-19 in New York City

Caroline Siegel[1], Jacky Choi[2], Debra D'Angelo[2], Paul Christos[2], Lindsay Lally[1], Parag Goyal[2], Lisa Mandl[1] and Medha Barbhaiya[1], [1]Hospital for Special Surgery, New York, NY, [2]Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with systemic rheumatic diseases (SRD) are potentially at increased risk of severe outcomes from SARS-CoV-2 infection due to their underlying immune dysregulation and chronic use of immunosuppressive therapies. Older age, medical comorbidities, and steroid use have been identified as potential risk factors for COVID-19-related hospitalization in SRD patients, but still need to be confirmed. Our study aims to identify characteristics associated with severe COVID-19, characterized by mechanical ventilation, admission to an intensive care unit (ICU), or death, in patients with SRD hospitalized for COVID-19 in a U.S. "hotspot" during the initial wave of the pandemic.

Methods: This retrospective observational cohort study included patients aged ≥18 years with SRD hospitalized for COVID-19 at one of three NewYork-Presbyterian (NYP) hospital sites between March 3-May 15, 2020. Data were manually abstracted from the medical chart. We used chi-square tests and t-tests, as appropriate, to compare baseline demographics, comorbidities, outpatient medications, presenting symptoms, COVID-19 treatment, and laboratory values in patients hospitalized for COVID-19 with underlying SRD, stratified on the composite outcome of mechanical ventilation, ICU admission, or in-hospital death. We also examined the prevalence of secondary clinical outcomes in SRD patients.

Table 1. Baseline Demographics, Medical Comorbidities and Medication Use in Patients with Systemic Rheumatic Disease[1] Hospitalized with COVID-19, Stratified by Outcome[2]

	Overall N = 92[3]	SRD, Outcome[2] N = 35[3]	SRD, No Outcome[2] N = 57[3]	p-value[4]
Demographics				
Female	75 (82%)	24 (69%)	51 (89%)	0.01
Race				0.03
• **White**	37 (40%)	18 (51%)	19 (33%)	
• **Asian**	9 (9.8%)	6 (17%)	3 (5.3%)	
• **Black**	18 (20%)	4 (11%)	14 (25%)	
• **Other**	23 (25%)	5 (14%)	18 (32%)	
• **Unknown**	5 (5.4%)	2 (5.7%)	3 (5.3%)	
Ethnicity				0.13
• **Hispanic/Latinx**	24 (26%)	5 (14%)	19 (33%)	
• **Not Hispanic/Latinx**	55 (60%)	24 (69%)	31 (54%)	
• **Other**	3 (3.3%)	2 (5.7%)	1 (1.8%)	
• **Unknown**	10 (11%)	4 (11%)	6 (11%)	
BMI	28.2 (6.7)	27.0 (6.2)	29.0 (6.9)	0.20
BMI ≥ 30	31 (34%)	10 (30%)	21 (37%)	0.50
Ever smoker	29 (32%)	12 (34%)	17 (30%)	0.70
Comorbidities				
Coronary Artery Disease	20 (22%)	10 (29%)	10 (18%)	0.20
Hypertension	66 (72%)	25 (71%)	41 (72%)	>0.90
Diabetes	27 (29%)	10 (29%)	17 (30%)	0.90
Cerebral Vascular Accident	6 (6.5%)	5 (14%)	1 (1.8%)	0.03
Renal Disease	10 (11%)	3 (8.6%)	7 (12%)	0.70
Pulmonary Disease	28 (30%)	15 (43%)	13 (23%)	0.04
Active Cancer	2 (2.2%)	1 (2.9%)	1 (1.8%)	>0.90
HIV	1 (1.1%)	0 (0%)	1 (1.8%)	>0.90
Transplant	4 (4.3%)	0 (0%)	4 (7.0%)	0.30
Baseline Medications				
Hydroxychloroquine	21 (23%)	7 (20%)	14 (25%)	0.60
Systemic Corticosteroids	35 (38%)	12 (34%)	23 (40%)	0.60
Immunosuppressive Medication	15 (16%)	8 (23%)	7 (12%)	0.20
• Azathioprine	1 (1.1%)	1 (2.9%)	0 (0%)	0.40
• Methotrexate	15 (16%)	7 (20%)	8 (14%)	0.50
• Mycophenolate	6 (6.5%)	2 (5.7%)	4 (7.0%)	>0.90
• Tacrolimus	4 (4.3%)	0 (0%)	4 (7.0%)	0.30
• TNF-Alpha Inhibitor	3 (3.3%)	1 (2.9%)	2 (3.5%)	>0.90
• Other Monoclonal Antibody	4 (4.3%)	2 (5.7%)	2 (3.5%)	0.60

[1]RA (50%), SLE (16.3%), Vasculitis/PMR/SSc/Myositis (16.3%), SLE-like/SS/MCTD/APS (12%), PsA (3.2%), Sarcoidosis (2.2%)
[2]Composite Outcome of Intensive Care Unit Admission (N=19) or Mechanical Ventilation (N=20) or Death (N=24)
[3]Mean (SD); n (%)
[4]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test

Results: Among 3,680 patients included in the NYP COVID-19 registry, 92 had an SRD (mean age 66.3 [16.5] years; 82% female, 40% White, and 26% Hispanic/Latinx; mean BMI 28.2 [6.7]). Patients with SRD and severe COVID-19 (N=35) were more likely to be older (73.5 [12.8] versus 61.8 [17.1] years), male, White or Asian, and have history of pulmonary disease or stroke compared to patients without severe COVID-19 (Table 1). No difference in baseline medications was noted. Both groups predominantly presented with fever and dyspnea, although the frequency of these symptoms was higher in the non-severe group (Table 2). Patients with SRD and severe COVID-19 had higher peak white blood cell count, creatinine, aspartate aminotransferase, and alanine aminotransferase levels; they also had higher peak inflammatory markers, including erythrocyte sedimentation rate, C-reactive protein, ferritin, D-dimer, lactate dehydrogenase, and fibrinogen (Table 2). There were no differences in in-hospital treatments. Thromboses, respiratory coinfections, septic shock, cardiac complications, and renal dysfunction were more common in patients with severe COVID-19 (Table 2).

Conclusion: Among SRD patients who were hospitalized for COVID-19 during the peak of the pandemic in New York City, demographic factors and medical comorbidities, but not baseline immunosuppressive medication use, were associated with severe COVID-19 leading to mechanical ventilation, ICU admission, or death. We were underpowered to perform subgroup analyses by SRD type. Future analyses are needed to evaluate the role of social determinants of health, access to care, and geocoding.

Table 2. COVID-19 Presentation, Treatment, and Complications in Patients with Systemic Rheumatic Disease[1] Hospitalized with COVID-19, Stratified by Outcome[2]

	Overall N = 92[3]	SRD, Outcome[2] N = 35[3]	SRD, No Outcome[2] N = 57[3]	p-value[4]
Clinical Presentation				
Presenting Symptom				
• Fever	61 (66%)	16 (46%)	45 (79%)	0.001
• Cough	64 (70%)	20 (57%)	44 (77%)	0.042
• Dyspnea	62 (67%)	21 (60%)	41 (72%)	0.2
• Sore Throat	9 (9.8%)	4 (11%)	5 (8.8%)	0.7
• Rhinorrhea	6 (6.5%)	4 (11%)	2 (3.5%)	0.2
• Conjunctivitis	0 (0%)	0 (0%)	0 (0%)	>0.9
• Headache	7 (7.6%)	2 (5.7%)	5 (8.8%)	0.7
• Myalgia	16 (17%)	2 (5.7%)	14 (25%)	0.021
• Nausea	18 (20%)	6 (17%)	12 (21%)	0.6
• Diarrhea	24 (26%)	5 (14%)	19 (33%)	0.043
• Sputum	9 (9.8%)	3 (8.6%)	6 (11%)	>0.9
• Presyncope	4 (4.3%)	2 (5.7%)	2 (3.5%)	0.6
• Chest Pain	15 (16%)	2 (5.7%)	13 (23%)	0.031
• Abdominal Pain	3 (3.3%)	0 (0%)	3 (5.3%)	0.3
• Altered Mental Status	15 (16%)	9 (26%)	6 (11%)	0.056
• Anosmia	1 (1.1%)	0 (0%)	1 (1.8%)	>0.9
• Ageusia	1 (1.1%)	0 (0%)	1 (1.8%)	>0.9
Symptom Onset to Admission (Days)	8.1 (8.5)	7.0 (5.7)	8.7 (9.8)	0.7
Basic Laboratory Values[5]				
• WBC	13.4 (9.4)	20.4 (10.7)	8.9 (4.5)	<0.01
• Creatinine	2.4 (3.2)	3.2 (3.4)	1.9 (3.0)	<0.01
• AST	161.5 (642.0)	316.4 (1,015.2)	62.1 (43.1)	<0.01
• ALT	102.0 (268.1)	174.6 (416.9)	55.4 (54.1)	0.02
Inflammatory Markers[5]				
• ESR	97.7 (33.6)	112.5 (28.5)	86.8 (33.2)	<0.01
• CRP	16.2 (11.3)	21.2 (11.9)	11.7 (8.7)	<0.01
• Ferritin	1,907.0 (5,713.4)	3,394.1 (8,578.2)	802.2 (741.5)	<0.01
• D-Dimer	3,768.7 (8,952.8)	7,337.1 (12,822.6)	1,298.2 (3,048.8)	<0.01
• LDH	609.9 (561.1)	892.7 (767.1)	416.4 (209.5)	<0.01
• Fibrinogen	706.3 (284.3)	831.6 (262.8)	587.9 (257.2)	0.02
In-Hospital Treatment				
Hydroxychloroquine	70 (76%)	26 (74%)	44 (77%)	0.80
Remdesivir	6 (6.5%)	2 (5.7%)	4 (7.0%)	>0.90
Steroids	47 (51%)	20 (57%)	27 (47%)	0.40
Steroid Duration (Days)	11.0 (18.1)	18.1 (25.5)	5.6 (4.6)	0.10
Complications				
Thrombotic Events	6 (6.5%)	5 (14%)	1 (1.8%)	0.03
Respiratory Coinfection	11 (12%)	10 (29%)	1 (1.8%)	<0.01
Cardiac Complications[6]	12 (13%)	10 (29%)	2 (3.5%)	<0.01
New-onset Arrythmia	6 (6.5%)	5 (14%)	1 (1.8%)	0.03
Renal Complications[7]	31 (34%)	20 (57%)	11 (19%)	<0.01
Septic Shock	12 (13%)	10 (29%)	2 (3.5%)	<0.01

[1]RA (50%), SLE (16.3%), Vasculitis/PMR/SSc/Myositis (16.3%), SLE-like/SS/MCTD/APS (12%), PsA (3.2%), Sarcoidosis (2.2%)
[2]Outcome=Composite Outcome of Intensive Care Unit Admission or Mechanical Ventilation or Death
[3]Mean (SD); n (%)
[4]Wilcoxon rank sum test; Pearson's Chi-squared test; Fisher's exact test
[5]Peak values during hospitalization
[6]Myocardial infarction or heart failure
[7]Acute kidney injury or initiation of renal replacement therapy

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Abstract Number: 0095

Risk Factors for "Long Haul" COVID-19 in Rheumatology Outpatients in New York City

Medha Barbhaiya[1], Deanna Jannat-Khah[1], Jonah Levine[1], Huong Do[1], Jessica Gordon[1], Vivian Bykerk[2] and Lisa Mandl[1], [1]Hospital for Special Surgery, New York, NY, [2]Division of Rheumatology, Hospital for Special Surgery, New York City, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 'long-haulers' are individuals who experience persistent symptoms after COVID-19 diagnosis. Whether this is of particular concern for rheumatic disease patients, due to their underlying immune dysregulation and use of immunosuppressive medications, is poorly studied. We evaluated the prevalence of "long haul" COVID-19 symptoms as well as its potential risk factors in Rheumatology outpatients in New York City.

Methods: We emailed a secure web-based survey on March 5, 2021 to 7,505 patients aged ≥18 years evaluated at least once by a rheumatologist between 2018-2020 at a large Rheumatology center in New York City and who previously agreed to participate in surveys on COVID-19. We included patients who completed a questionnaire on COVID-19 history, and also collected data on sociodemographics, medical comorbidities, medication use, and health related quality of life using PROMIS-29. ICD-10 algorithms identified patients with SRD. COVID-19 status was confirmed (self-report of a positive nasopharyngeal PCR or antigen test) or suspected (told by a healthcare provider of a COVID-19 diagnosis); the latter was included as testing was not readily available early in the pandemic in New York. We defined COVID "long haul" as symptoms persistent for ≥3 months and used descriptive statistics to compare factors associated with this group compared to patients with COVID-19 symptoms < 1 month.

Results: Among 2572 patients (34.3%) who completed our COVID-19 questionnaire, 254 patients indicated a history of suspected/confirmed COVID-19. 142 (55.9%) patients indicated ≥3 months of COVID-19 symptoms and 112 (44.09%) had < 1 month. No differences in demographics were noted between the ≥3 months versus < 1 month groups (Mean age 55.1 [14.6] vs. 56.9 [14.3] years; 83.1% vs. 75% female; 93.7% vs. 86.6% White, and 9.9% vs. 5.4% Hispanic/Latinx) (Table 1). COVID-19 long-haulers were more likely to have ≥1 or more medical comorbidities (Table 1) and to be a current or former smoker. No difference in SRD or non-SRD status was observed; only 2 patients with long haul symptoms had Fibromyalgia. Patients with long-haul COVID-19 were more likely to have used corticosteroids for ≥3 months at time of COVID-19 diagnosis (p=0.002). The long-haul group had significantly higher frequency of most COVID-19 symptoms at presentation, most commonly chills, cough, fatigue/malaise, headache/migraine, loss of smell or taste, muscle aches, memory/concentration problems, joint pain, and shortness of breath (Table 2). PROMIS-29 T-scores demonstrated significantly and clinically worse anxiety, depression, fatigue and pain in the long hauler group (Table 2).

Conclusion: Over half of rheumatology outpatients with COVID-19 reported persistent symptoms for ≥3 months; these "long hauler" patients were more likely to have more medical comorbidities, a smoking history, and use chronic corticosteroids at time of COVID-19 diagnosis. COVID-19 symptoms at presentation were more common in long-haulers, who also reported worse quality of life. Future prospective analyses accounting for additional potential covariates are underway to identify risk factors in this vulnerable group.

Table 1. Baseline Characteristics of Rheumatology Outpatients with COVID-19 in New York City by "Long Haul" Status			
	Non Long-haulers (<1 month symptoms) N=112	**Long-haulers (≥3 months) N= 142**	**p-value**
Age, mean (SD)	56.9 (14.3)	55.1 (14.6)	0.32
Female Sex	84 (75.0%)	118 (83.1%)	0.12
Race			0.16
• Non-White*	9 (8.0%)	5 (3.5%)	
• White	97 (86.6%)	133 (9.4%)	
• Missing	6 (5.3%)	4 (2.8%)	
Ethnicity			0.35
• Hispanic/Latinx	6 (5.4%)	14 (9.9%)	
• Not Hispanic/Latinx	103 (92.0%)	126 (88.7%)	
• Missing	3 (2.7%)	2 (1.4%)	
Education			0.29
• High school grad or below	3 (2.7%)	8 (5.6%)	
• Any college	59 (52.7%)	64 (45.1%)	
• Masters, professional, doctorate	40 (35.7%)	59 (41.5%)	
• Missing	10 (8.9%)	11 (7.7%)	
BMI			0.72
• <25	52 (46.4%)	63 (44.4%)	
• 25-29	36 (32.1%)	43 (30.3%)	
• 30+	23 (20.5%)	36 (25.4%)	
• missing	1 (0.9%)	0 (0.0%)	
General Medical Comorbidities**			**<0.01**
• 0	74 (66.1%)	54 (38.0%)	
• 1	29 (25.9%)	55 (38.7%)	
• 2 or more	9 (8.0%)	33 (23.2%)	
Smoke			**0.01**
• Never	81 (72.3%)	85 (59.9%)	
• Current/former	19 (17.0%)	44 (31.0%)	
• Missing	12 (10.7%)	13 (9.2%)	
Any Systemic Rheumatic Disease	65 (58.0%)	87 (61.3%)	0.39
• Inflammatory Arthritis	29 (25.9%)	33 (23.2%)	0.76
• Spondyloarthritis	16 (14.3%)	17 (12.0%)	0.71
• Vasculitis/Scleroderma/Myositis	4 (3.6%)	9 (6.3%)	0.39
• SLE/Sjogren's/MCTD/UCTD	21 (18.8%)	36 (25.4%)	0.17
Any Non-Systemic Rheumatic Disease	35 (31.3%)	36 (25.4%)	0.39
• Osteoarthritis	8 (7.1%)	14 (9.9%)	0.49
• Gout/pseudogout	4 (3.6%)	3 (2.1%)	0.7
• Osteoporosis	6 (5.4%)	8 (5.6%)	1
• Fibromyalgia	0 (0.0%)	2 (1.4%)	0.5
• Other Musculoskeletal category	11 (9.8%)	15 (10.6%)	0.83
Chronic Steroid Use at COVID-19 diagnosis***	4	22	**<0.01**

*Includes American Indian/Alaskan Native/Native Hawaiian/Other,Asian/Indian Subcontinent and Black
**Comorbidities include any of the following identified by the Centers for Disease Control and Prevention in 2/2021 as being most relevant for COVID-19 risk: Asthma or lung disease, Cancer, Chronic Kidney Disease, Diabetes, Congestive Heart Failure or Myocardial Infarction, Ever smoking, Stroke
***≥3 months

Table 2: Clinical Presentation of Patients of Rheumatology Outpatients with COVID-19 in New York City by "Long Haul" Status			
	Non Long-haulers (<1 month symptoms) N=112	Long-haulers (≥3 months) N= 142	p-value
COVID-19 Symptoms at Time of Diagnosis*			
• Abdominal/Belly Pain	18 (16.1%)	39 (27.5%)	**0.03**
• Anxiety	6 (5.4%)	15 (10.6%)	0.17
• Chest Pain	18 (16.1%)	43 (30.3%)	**0.01**
• Chills	49 (43.8%)	83 (58.5%)	**0.02**
• Confusion/Irritability	2 (1.8%)	23 (16.2%)	**<0.01**
• Cough	51 (45.5%)	94 (66.2%)	**<0.01**
• Depression	0 (0.0%)	11 (7.7%)	**<0.01**
• Diarrhea	31 (27.7%)	58 (40.8%)	**0.03**
• Dizziness/lightheadedness	23 (20.5%)	65 (45.8%)	**<0.01**
• Fatigue or Malaise	64 (57.1%)	124 (87.3%)	**<0.01**
• Fever	57 (50.9%)	94 (66.2%)	**0.02**
• Hair loss	5 (4.5%)	22 (15.5%)	**<0.01**
• Headache or migraine	43 (38.4%)	93 (65.5%)	**<0.01**
• Heart racing/Palpitations	10 (8.9%)	24 (16.9%)	0.09
• Joint Pain	29 (25.9%)	71 (50.0%)	**<0.01**
• Loss of smell or taste	51 (45.5%)	85 (59.9%)	**0.03**
• Abnormal taste or smell	15 (13.4%)	38 (26.8%)	**0.01**
• Memory, concentration	9 (8.0%)	71 (50.0%)	**<0.01**
• Mood changes	1 (0.9%)	17 (12.0%)	**<0.01**
• Muscle Aches	39 (34.8%)	91 (64.1%)	**<0.01**
• Numbness and/or tingling	4 (3.6%)	28 (19.7%)	**<0.01**
• Rash	2 (1.8%)	14 (9.9%)	**0.01**
• Runny nose	33 (29.5%)	44 (31.0%)	0.89
• Shortness of Breath	18 (16.1%)	75 (52.8%)	**<0.01**
• Sleep problems	8 (7.1%)	37 (26.1%)	**<0.01**
• Sore throat or scratchy throat	26 (23.2%)	59 (41.5%)	**<0.01**
• Vomiting or Nausea	13 (11.6%)	36 (25.4%)	**<0.01**
• Other	6 (5.4%)	21 (14.8%)	**0.02**
PROMIS-29 Scores (within the last 7 days)			
• Anxiety, mean (SD)	50.0 (9.1)	56.0 (9.7)	**<0.01**
• Depression, mean (SD)	46.8 (7.3)	51.0 (9.1)	**<0.01**
• Fatigue, mean (SD)	48.1 (11.4)	58.0 (11.0)	**<0.01**
• Sleep, mean (SD)	51.0 (5.6)	52.6 (6.5)	0.06
• Pain, mean (SD)	50.3 (9.7)	56.3 (9.9)	**<0.01**
*Not mutually exclusive			

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Abstract Number: 0096

The True Prevalence of SARS-CoV-2 Infection in an Italian Cohort of Patients with Inflammatory Arthritis: A Seroepidemiological Study

Gabriella Maioli[1], **Ennio Giulio Favalli**[2], Elisa Pesce[3], Martina Biggioggero[2], Mauro Bombaci[3], Elena Agape[2], Martina Martinovic[3], Tanya Fabbris[3], Elena Zagato[3], Andrea Favalli[3], Andrea Gobbini[3], Sergio Abrignani[3], Renata Grifantini[3] and Roberto Caporali[4], [1]Università degli Studi di Milano, Department of Clinical Sciences and Community Health, Research Center for Adult and Pediatric Rheumatic Diseases, Milan, Italy, Milan, Italy, [2]ASST Gaetano Pini-CTO Institute, Division of Clinical Rheumatology, Milan, Italy, Milan, Italy, [3]Istituto Nazionale Genetica Molecolare, Padiglione Romeo ed Enrica Invernizzi, Milan, Italy, [4]Policlinico S. Matteo University, Pavia, Italy

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Observational data have shown that rheumatic patients seem not to be more susceptible to SARS-CoV-2 infection neither to worse outcomes. However, the true prevalence of COVID-19 is still unknown due to the high proportion of subclinical infection. In this scenario, measuring the seroprevalence of SARS-CoV-2 may be crucial to improve the knowledge about the impact of COVID-19 in rheumatic patients.

The aim of this study is to estimate the prevalence of anti-SARS-CoV-2 antibodies in a large cohort of patients with rheumatoid arthritis or spondyloarthritis treated with biologic (b-) or targeted synthetic (ts-) DMARDs, living in a COVID-19 high-endemic area (Lombardy, Italy).

Methods: A seroprevalence cross-sectional study was conducted in the period between 4th May and 16th June 2020, including consecutive patients with confirmed RA or SpA treated with b- or tsDMARDs. Enrolled patients were tested

Table 1. Prevalence of anti-SARS-CoV-2 antibodies

Antibodies	Posivite(n)	Seroprevalence (%)	(95% CI)
IgG	27	9%	(6.2 – 12.7)
IgG anti-N	26	8.6%	(5.9 – 12.3)
IgG anti-RBD	18	6%	(4.3 – 10)
IgM	41	13.6%	(10.2 – 18)
IgM anti-N	35	11.6%	(8.5 – 15.7)
IgM anti-RBD	25	8.3%	(5.7 – 12)
IgA	40	13.3%	(9.9 – 17.6)
IgA anti-N	37	12.3%	(9.0 – 16.5)
IgA anti-RBD	25	8.3%	(5.7 – 12)
IgG+IgM	23	7.6%	(5.1 – 11.2)
IgG+IgM+IgA	22	7.3%	(4.9 – 10.5)
IgG+IgA	24	8%	(5.4 – 11.6)
IgG/IgM/IgA	56	18.6%	(14.6 – 23.4)

Table 2. IgG Anti-RBD SARS-CoV-2 seroprevalence and associated factors

	Total	Positive cases (n)	(%)	Negative cases (n)	(%)	OR	95 % CI		P value
	300	18	6,0%	282	94,0%				
Age, mean (SD), years	53,4 (13,5)	54.4 (14,6)		52.6 (13.7)					
Age goup									
<65 years	229	12	5,2%	217	94,8%	0,60	0,2164	1,6588	0,3291
≥65 years	71	6	8,5%	65	91,5%	1,67	0,6029	4,6219	1,3533
Female, n (%)	188	10	5,3%	178	94,7%	0,73	0,2795	1,9087	1,3347
Diagnosis									
RA	158	11	7,0%	147	93,0%	1,44	0,5438	3,8300	0,4705
SpA	142	7	4,9%	135	95,1%	0,69	0,2611	1,8390	0,4705
Anti-rheumatic treatment									
bDMARDs	282	16	5,7%	266	94,3%	0,48	0,1017	2,2766	0,3623
tsDMARDs	22	1	4,5%	21	95,5%	0,73	0,0927	5,7663	1,1929
b/tsDMARDs monotherapy	160	11	6,9%	149	93,1%	1,40	0,5285	3,7227	0,5070
csDMARDs association	140	7	5,0%	133	95,0%	0,71	0,2686	1,8921	0,5070
MTX	112	4	3,6%	108	96,4%	0,46	0,1477	1,4348	0,1821
noMTX	188	14	7,4%	174	92,6%	2,17	0,6970	6,7713	0,1821
PDN – avarage dose	92 – 4,2 mg	8 - 5,75 mg	7,6%	97 - 3,8 mg	92,4%	1,52	0,6092	3,7737	0,3709
≤2.5 mg	40	2	5,0%	38	95,0%	0,80	0,1774	3,6305	0,7877
>2.5 mg	52	6	11,5%	46	88,5%	2,57	0,9161	7,1829	0,0726
>10 mg	5	2	40,0%	3	60,0%	11,63	1,8118	74,5877	0,0097
Comorbidities									
At least 1	76	11	14,5%	65	85,5%	5,25	1,9545	14,0811	0,0010
CHD	7	0	0,0%	7	100,0%	0,00			
DM II	5	1	20,0%	4	80,0%	4,09	0,4329	38,6099	0,2210
Hypertension	56	9	16,1%	47	83,9%	5,00	1,8849	13,2636	0,0013
Obesity	13	3	23,1%	10	76,9%	5,44	1,3536	21,8630	0,0169
None	224	7	3,1%	217	96,9%	0,19	0,0710	0,5116	0,0010
Current smokers	42	1	2,4%	41	97,6%	0,35	0,0448	2,6693	0,3130

RA rheumatoid arthritis, SpA spondyloarthritis, PDN prednisone, csDMARDs conventional synthetic disease-modifying anti-rheumatic drugs, b/tsDMARDs biological/targeted synthetic disease-modifying anti-rheumatic drugs, MTX methotrexate, CVD coronary heart disease, DM II diabetes mellitus type II.

for anti-SARS-CoV-2 IgG, IgM, and IgA antibodies against main viral antigens (nucleoprotein [N], receptor-binding domain [RBD]) using ELISA. Demographical and clinical data were also collected and patients were questioned about history of COVID-19 symptoms in order to identify potential factors that correlate with anti-SARS-CoV-2 positivity. Results were compared with those observed in the healthy population in the same period and region [1].

Results: The study population included 300 patients (62% females, mean age 53 years), diagnosed with RA (56%), psoriatic arthritis (23%), or ankylosing spondylitis (21%). Most patients were being treated with anti-TNF (57%), and the remainder were receiving abatacept (20%), anti-IL6 (11%), or JAK inhibitors (5%). Four patients (1.3%) referred a prior diagnosis of COVID-19 defined by nasopharyngeal swab. Immunoglobulin titers were evaluated resulting in 9%, 13.6%, and 13.3% positive patients for IgG, IgM, and IgA, respectively, with no significant difference to the healthy population. Among seropositive patients, 55.3% were asymptomatic, 16% had minor and 19.6% major symptoms, 7.1% were hospitalized. No deaths or admission to intensive care units occurred. No differences were found between seronegative and seropositive patients in relation to age, sex, rheumatic diagnosis, and treatments with b- or tsDMARDs. Conversely, corticosteroids therapy was associated with an increased risk of seropositivity in a dose-dependent manner with a significantly high OR for doses above 10 mg (OR 11.6, p 0.009). Relative increased risk was associated with the presence of at least one comorbidity (OR 5.25; 95%CI 1.95 – 14.08, p 0.001), especially hypertension (OR 5, p 0.001) and obesity (OR 5.4, p 0.01).

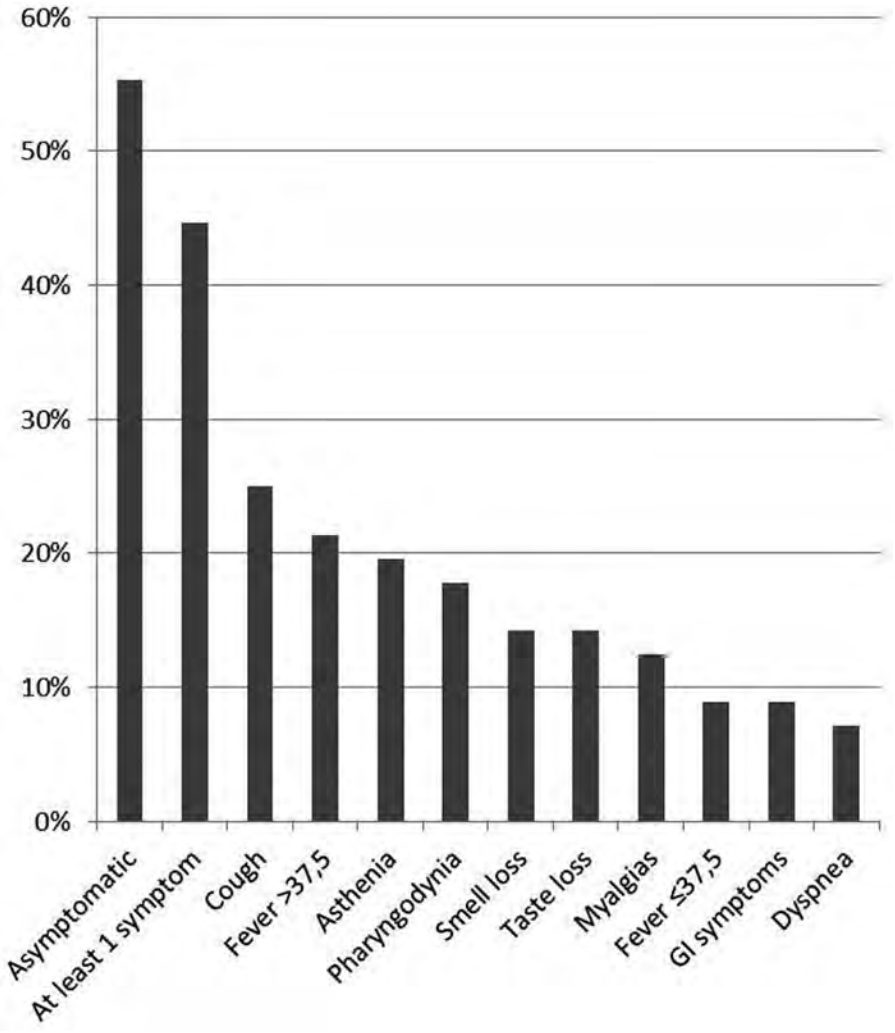

Figure 1. Clinical manifestations of seropositive patients.

Conclusion: This study confirms that, even in a cohort of rheumatic patients, the spread of SARS-CoV-2 infection is much greater than that observed by capturing only swab-diagnosed COVID-19 cases, but consistent with healthy population. The underlying rheumatic disease and ongoing therapy with b/tsDMARD do not seem to impact SARS-CoV-2 antibody positivity, which conversely seems to be associated with the presence of comorbidities and with CS therapy. The project was co-financed by Lombardy Region 2014-2020 Regional Operational Programme under the European Regional Development Fund.

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Abstract Number: 0097

Outcome of SARS-CoV-2 Infection in Patients with Rheumatoid Arthritis Under Treatment with Janus Kinase Inhibitors Compared to Tumour Necrosis Factor Inhibitors

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Janus kinase inhibitors (JAK-i) offer a potent mode of action to treat rheumatic diseases. Little is known on the course and outcome of SARS-CoV-2 infections in RA patients treated with JAK-i. The aim of this study is to describe the outcome of SARS-CoV-2 infection in RA patients treated with JAK-i in comparison to patients treated with TNF-inhibitors (TNF-i).

Methods: In the German COVID-19 registry for inflammatory rheumatic diseases, the course and outcome of proven SARS-CoV-2 infections are documented by treating rheumatologists. From March 30th, 2020 until April 5th, 2021 a total of 2253 cases was collected. 982 were reported with RA, of which 128 were treated with JAK-i and 190 with TNF-i. Patient characteristics and outcome of the SARS-CoV-2 infection were analysed descriptively. Differences in characteristics were tested by the Pearson Chi-Square-Test.

Results: Median age in both treatment groups was comparable (tab.1). Concomitant glucocorticoids (GC) were used in 50% of the JAK-i and 31% of the TNF-i patients ($p < 0.001$). Additional conventional synthetic (cs) disease-modifying anti-rheumatic drugs (DMARD) were used in 29% of the JAK-i and in 49% of the TNF-i patients ($p < 0.001$). Moderate and high disease activity before acquisition of the infection was more frequently reported in JAK-i patients than under TNF-i treatment ($p=0.042$). Comorbidities that were recently found to be associated with a higher risk of hospitalisation and death, namely cardiovascular disease and hypertension were also more frequent in patients with JAK-i. Hospitalisation due to COVID-19 was necessary for 33% of patients treated with JAK-i and 13% of patients treated with TNF-i , and oxygen treatment was required in 25% and 7% of the patients, respectively ($p < 0.001$). Eight versus none ($p < 0.001$) fatal cases were reported in the JAK-i versus the TNF-i group.

Conclusion: The higher rate of hospitalisation and death among RA patients treated with JAK-i compared to TNF-i is remarkable. However, this has to be interpreted with caution, since RA patients under JAK-i harboured some differences in potentially confounding *RA-related and unrelated* factors like disease activity, concomitant use of GCs, and certain comorbidities. To address this, further analyses with adjustments for baseline differences should follow.

Table 1. Characteristics of JAK-i and TNF-i treated patients with SARS-CoV-2 infections

	JAK-i (n=128)	TNF-i (n=190)
Baseline characteristics		
Female	85% (109)	74% (141)
Age (median) in years	58 (24-86)	57 (23-91)
BMI (median)	27 (19-56)	26 (18-47)
Disease activity (DA)		
No	41% (53)	57% (108)
Low	40% (51)	32% (60)
Moderate	13% (17)	7% (14)
High	5% (6)	3% (5)
Unknown	1% (1)	2% (3)
Immunomodulatory drugs		
GC	50% (64)	31% (58)
GC (≤5 mg prednisolone per day)	89% (50/64)	84% (41/58)
Prednisolone daily dose (median)	5 mg (1-20)	5 mg (1-30)
Concomitant use of csDMARD	29% (37)	49% (94)
Baricitinib	46% (59)	/
Tofacitinib	28% (36)	/
Upadacitinib	26% (33)	/
Adalimumab	/	26% (50)
Infliximab	/	3% (5)
Certolizumab	/	16% (31)
Golimumab	/	5% (10)
Etanercept	/	50% (94)
Comorbidities		
Cardiovascular disease	10% (13)	6% (12)
Hypertension	49% (38)	35% (67)
Bronchial Asthma	4% (5)	9% (5)
Chronic Obstructive Pulmonary Disease	7% (9)	3% (5)
Interstitial Lung Disease	0% (0)	3% (6)
Chronic Renal Failure	1% (1)	3% (6)
Osteoporosis	12% (15)	8% (10)
Diabetes Mellitus	10% (12)	11% (21)
Cancer	2% (2)	1% (2)
Other	14% (18)	17% (33)
No	45% (58)	46% (87)
≥2	39% (33)	28% (47)
COVID-19 symptoms		
Duration (median) in days	14 (range: 0-120)	10 (range: 0-70)
COVID-19 course		
Hospitalisation	33% (42)	13% (24)
Oxygen treatment	25% (32)	7% (13)
Invasive ventilation	10% (9)	1% (1)
Complications	12% (15)	4% (8)
Fatal courses	6% (8)	0% (0)
Characteristics of hospitalized patients		
Female	81% (34)	83% (20)
Age (median)	68 (36-86)	66 (35-84)
GC (combination)	60% (25)	54% (13)
csDMARD (combination)	19% (8)	63% (15)
Fatal courses	19% (8)	0% (0)

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Chugai, 2, 6, Gilead Sciences, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Pfizer Inc, 2, 6, Sanofi, 2, 6, Galapagos, 1, 2, UCB, 1, 2; **C. Specker**, AbbVie, 1, 6, Boehringer, 1, 6, Chugai, 2, 6, GSK, 1, 6, Lilly, 6, MSD, 6, Novartis, 1, 6, Pfizer, 6, Roche, 6, Sanofi, 6, Sobi, 1, 6; **U. Müller-Ladner**, Biogen, 6.

Abstract Number: 0098

Patients with Chronic Inflammatory Rheumatic Diseases Report a Lower Frequency of Infections Than Controls and They Protect Themselves Well Against SARS-CoV-2 Transmission

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Table 1. Patients and disease characteristics

	CIRD	Control group
Age, mean (years)	54.7 ± 12.8	55.6 ± 9.8
Women, No*. (%)	315 (61.3%)	83 (83.0%)
BMI**, mean	27.9 ± 5.9	30.4 ± 7.8
Disease duration, mean (years)	9.8 ± 8.9	4.05 ± 6.5
Educational level, No.* (%)		
< 8 years	50 (10.4 %)	9 (9.3%)
8-12 years	275 (57.4 %)	67 (69.1%)
>12 years	154 (32.2 %)	21 (21.6%)
CIRD, No.* (%)		
Rheumatoid arthritis	192 (37.3 %)	
Axial spondyloarthritis	134 (26.0 %)	
Psoriatic arthritis	72 (14.0 %)	
Connective tissue disease and vasculitis	106 (22.6 %)	
Therapy, No.* (%)		
bDMARD	316 (61.5 %)	
csDMARD	147 (28.6 %)	
tsDMARD	33 (6.4 %)	
no DMARDs	18 (3.5 %)	
Prednisolon		

*number of patients
**body mass index

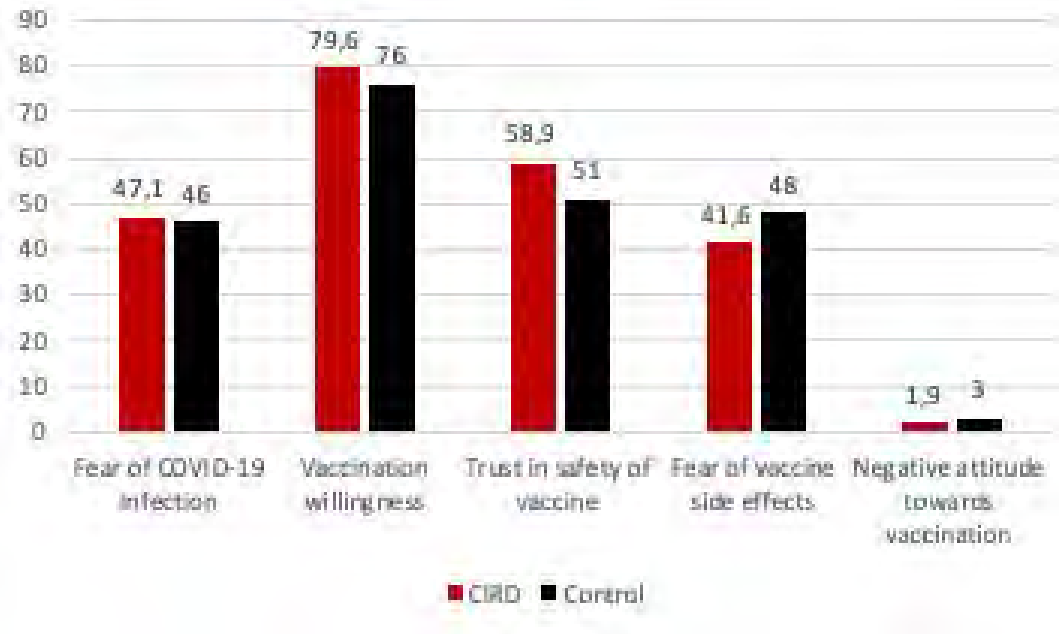

Figure 1. Vaccination willingness and its predictors as percentage.

Background/Purpose: The SARS-CoV-2 pandemic has affected life in most countries around the world for more than a year now. It is not entirely clear if patients with chronic inflammatory rheumatic diseases (CIRD) are at increased risk for COVID19, but some drugs seem to be associated with worse outcomes. Vaccination has now started but knowledge about patients' attitudes and acceptance to be vaccinated is limited.

To study the attitudes of patients with CIRD towards the pandemic and their acceptance to be vaccinated against SARS-CoV-2.

Methods: In preparation of this prospective cross-sectional study, a detailed questionnaire was developed. After approval by the ethical committee, patients of our tertiary rheumatology hospital were consecutively included to answer questions regarding the upcoming vaccination against SARS-CoV-2. A numerical rating scale (NRS) ranging from 0 (fully disagree) to 10 (fully agree) was used. A definite positive answer was assumed if ratings were ³ 7. Sociodemographic and comorbidity data, a detailed history of infections, disease characteristics, medication and compliance with hygiene rules were recorded. The data were compared with a control group consisting of patients without CIRD.

Results: A total of 514 CIRD and 100 controls were included (table 1). No significant differences were found in the history of infections or their severity between groups. Recurrent and/or severe infections were reported by 10.5% and 4.5% of CIRD patients vs. 16% and 13% in controls, respectively. A positive PCR test for SARS-CoV-2 was found in 4%-5% of both groups. A larger percentage of CIRD patients felt that they are at increased risk of COVID 19: 60.4% vs. 48.5% in controls (p=0.02), while 47.2% vs. 46.5%, respectively, stated to be afraid of COVID19. Only 63.7% of CIRD patients thought that their medication is 'immunosuppressive'. About 20% of patients in both groups reported to have experienced COVID 19 associated deaths in their acquaintance. The compliance with hygiene rules was similar with over 90% reporting strict adherence. More CIRD patients reported financial losses due to pandemic: 34% vs. 19%, respectively. Slightly more CIRD patients (79.6%) than controls (76%) were willing to be vaccinated against SARS-CoV-2. About 60% of CIRD patients thought that the vaccines are safe, while 42% were afraid of side effects (figure 1). A generally negative attitude towards vaccination was more often found in controls.

Conclusion: These data indicate that CIRD patients have less severe and recurrent infections than controls but most CIRD patients think that they are at increased risk of a COVID19 infection, but they are less often afraid of being infected. However, CIRD patients have adhered very well to hygiene protection measures, even though their knowledge about their medication seems to be limited. This study also confirms that 80% of CIRD patients are ready to be vaccinated against SARS-CoV-2 even though many admitted fear of side effects. Less than 5% of CIRD patients have been infected with SARS-CoV-2, not much different from the control group. More controls were general opponents of vaccination.

Disclosure: I. Roman, None; **I. Andreica**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5.

Abstract Number: 0099

First Results of the BELCOMID Study: BELgian Cohort Study of COVID-19 in Immune Mediated Inflammatory Diseases (IMID)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: It has been suggested that 100% of SARS-CoV2 infections leads to development of specific IgG antibodies that remain detectable for a long period of time. Targeted Immune-Modulating Therapies (TIMT) such as anti-TNF, anti-interleukins and Janus Kinase inhibitors (JAKi) for treatment of Immune Mediated Inflammatory diseases (IMID) could theoretically interfere with cytokine storm and humoral immune response against COVID19. We investigate the seroprevalence of SARS-CoV2 IgG in relation to previous exposure to COVID19 and ongoing IMID treatment in a Belgian, real-life population of IMID patients in the prevaccine era.

Methods: A cross-disciplinary, prospective, observational cohort study was set up at two university hospitals. Between 17/12/2020 and 28/02/2021, all patients with IMIDs of the joints (rheumatoid arthritis, psoriatic arthritis, spondyloarthritis, the gut (Crohn's disease (CD), ulcerative colitis (UC)), and skin (psoriasis, hidradenitis suppurativa, atopic dermatitis) visiting the respective clinics were asked to participate. Both patients under conventional treatment and/or TIMT were included. Patients were asked to fill out an electronic survey (REDCap®, based on WHO-ISARIC) and blood samples were drawn for serology testing (SARS-CoV-2 IgG Abbott – Architect kit®). Statistical analyses were performed with SPSS26.

Results: In total 2166 IMID patients consented to take part. Of these, 1913 responded to the survey, including 415 rheumatology patients, 1217 IBD patients (64.7% CD, 34.3% UC, 1% undifferentiated colitis) and 218 dermatology patients. There were 372 patients (19.5%) who reported having experienced symptoms suggestive of COVID19 (Fig.

1). Fatigue (61.3%), headache (48.1%), sore throat (46.9%) and dry cough (38.7%) were most frequent symptoms. Gastrointestinal symptoms such as diarrhoea or abdominal pain were present in less than 20.0% (Fig. 2). Ninety-six IMID patients (5.04%) had a positive SARS-CoV2 PCR test on nasal or throat swab. In 44/96 (45.8%) anti-SARS-CoV2 IgG seroconversion was confirmed. There was no significant difference in seroconversion rate between patients treated with TIMT compared to conventional therapy (P=0.192). Of the seroconverted group, 75.0% were treated with TIMT. The interval between reported positive PCR date and serology test date ranged from 3 to 24 weeks with a mean of 10 weeks. Of all survey responders, 25 were hospitalized for respiratory symptoms since 01/02/2020, six of these had positive SARS-CoV2 PCR.

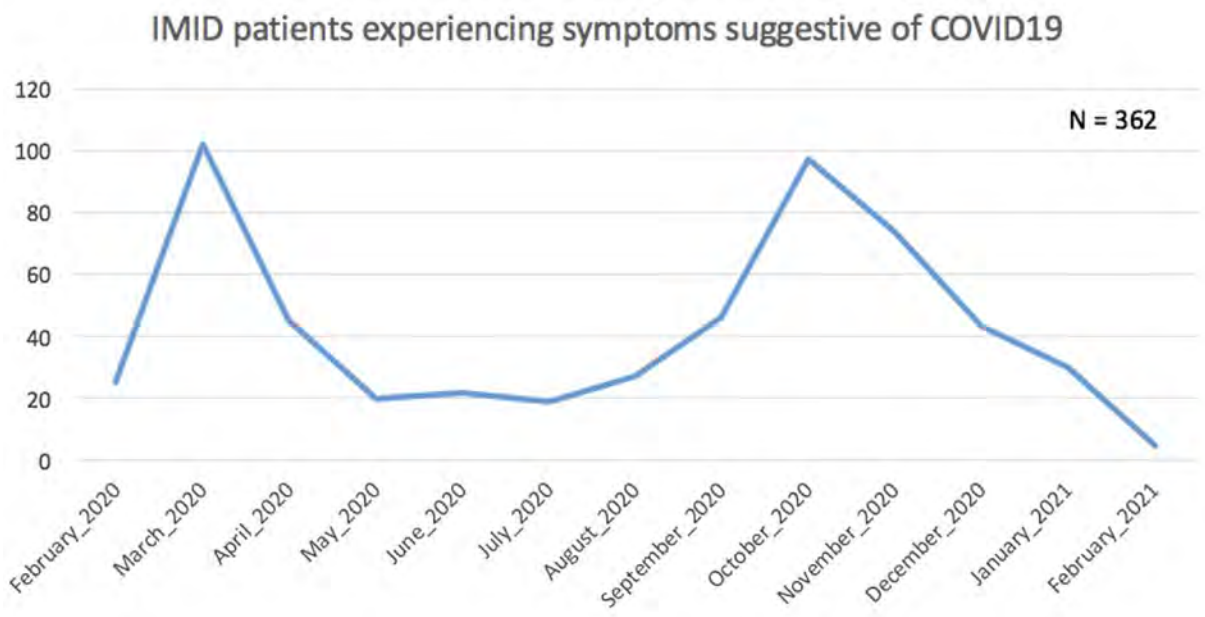

Figure 1. Number of IMID patients experiencing symptoms suggestive of COVID19 per month.

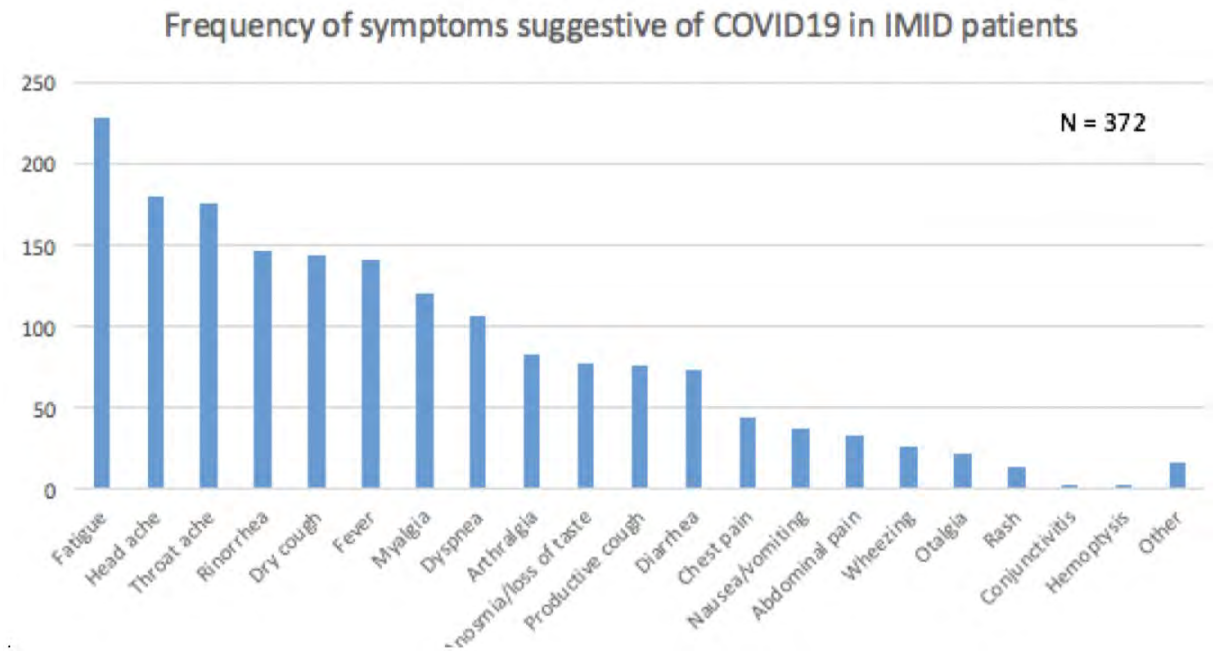

Figure 2. Frequency of experienced symptoms suggestive of COVID19 in IMID patients.

Conclusion: Prevalence of COVID19 symptoms and number of confirmed COVID19 cases by PCR in this cohort of IMID patients remain low regardless of treatment modality. There was no significant difference in SARS-CoV2 IgG seroconversion rate between TIMT or conventional treatment in patients with positive PCR.

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Abstract Number: 0100

Safety of COVID-19 Vaccines After First Vaccination in Patients with Rheumatic Diseases in a Patient Reported Survey

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Among patients with rheumatic and musculoskeletal diseases (RMDs) and their treating physicians, concerns prevail about the effectiveness and safety of vaccination against COVID-19, especially with respect to triggering RMD flares. The aim of our study was to collect safety data among RMD patients receiving COVID-19 vaccines.

Methods: The German COVID-19 vaccination registry is an observational longitudinal study launched February 8th, 2021. Data are entered voluntarily by RMD patients who have received at least 1 vaccination against SARS-CoV-2. The characteristics of all patients registered until May 29th, 2021 is presented here.

Table 1. Characteristics of COVID-19 vaccinated RMD patients.

Total, n	866	
Age (years, median)	54	Range: 18-86
Female	702	81%
Inflammatory rheumatic diseases (multiple selections possible)		
Rheumatoid Arthritis	432	50%
Spondyloarthritides	272	31%
Connective tissue disease	250	29%
ANCA-associated vasculitides	18	2%
Polymyalgia/ Giant cell arteritis	27	3%
Other inflammatory rheumatic diseases	45	5%
Osteoarthritis	182	21%
Fibromyalgia	77	9%
Small Fiber-Neuropathy	13	2%
Days with diseases flares within 12 months prior to COVID-19 vaccination	1 (Median)	Range: 0-365
Immunomodulation (multiple selections possible)		
Glucocorticoids	286	33%
Methotrexate	278	32%
Azathioprine	36	4%
Cyclosporine	2	0%
Leflunomide	39	5%
Hydroxychloroquine	109	13%
Sulfasalazine	39	5%
Janus kinase inhibitors	73	8%
TNF-inhibitors	186	22%
Interleukin 17-inhibitors	42	5%
Interleukin 6-inhibitors	23	3%
Interleukin 1-inhibitors	3	0%
Abatacept	18	2%
Rituximab	26	3%
Ustekinumab/guselkumab	14	2%
Belimumab	17	2%
Mycophenolate	24	3%
Cyclophosphamide	1	1%
Immunoglobulins	12	1%
Apremilast	3	0%
Other immunomodulation	86	20%
No immunomodulation	76	9%
Comorbidities (multiple selections possible)		
Cardiovascular diseases (e.g. heart failure, heart attack, coronary artery disease)	50	6%
Arrhythmia	56	7%
Arterial hypertension	284	33%
Asthma	108	13%
COPD	24	3%
Pulmonal arterial hypertension	7	1%
Interstitial lung disease	38	4%
Cancer	46	5%
Liver diseases	3	0%
Osteoporosis	103	12%
Diabetes	52	6%
Depression	109	13%
No Comorbidities	347	40%

Ever vaccination prior to COVID-19 vaccination (multiple selections possible)		
Influenza	670	77%
Pneumococcal	493	57%
Tuberculosis	139	16%
Measles, mumps, rubella	316	37%
Shingles	145	17%
Diphtheria	347	40%
No vaccination	65	8%
Unknown	11	1%
Other	154	17%
COVID-19 vaccines		
Moderna	75	9%
Pfizer-BioNTech	552	64%
AstraZeneca	238	28%
Johnson & Johnson's Janssen	1	0%
Concern regarding COVID-19 vaccination		
No	369	43%
Few	316	37%
Moderate	139	16%
Many	32	4%
Very many	10	1%
Discontinuation of immunomodulation		
No	606	70%
Yes	260	30%
Side effects after COVID-19 vaccination (multiple selections possible)		
Pain at injection site	617	71%
Fever	63	7%
Fatigue	351	41%
Vomiting	93	11%
Shivering	122	14%
Headache	282	33%
Abdominal pain	32	4%
Arthralgia	206	24%
Allergic reaction	8	1%
Other	129	15%
No	129	15%
Duration (days, median)	2	0-99
Disease flare after COVID-19 vaccination	115	13%
Strength of disease flare (median)	5	Range: 1-10
Duration of disease flares (days, median)	14	Range: 1-99
Change of immunomodulation due to disease flare	**(n=115)**	
No change of treatment	61	53%
Addition of low dose prednisolone (≤ 5 mg/day) or use of NSAIDs	26	23%
Addition of > 5 mg prednisolone/day	21	18%
Change of immunomodulating treatment	2	0%
Addition of another DMARD	5	1%

Results: So far, 866 patients reported their experience after the first COVID-19 vaccination. Median age was 54 years (range 18-86) and 81% of the participants were female (table 1). Most of the patients (50%) were diagnosed with rheumatoid arthritis, followed by spondyloarthritides (31%). At the time of vaccination, 33% were treated with glucocorticoids, 59% with conventional synthetic DMARDs, 23% with TNF-inhibitors, 9% with JAK-inhibitors, and 5% with IL17-inhibitors. No immunomodulatory therapy was reported from 9% of the patients. Within the last 12 months, 42% of the patients reported no disease activity and 40% did not state further comorbidities. The most common comorbidity was arterial hypertension (33%). Prior to COVID-19 vaccination, 77% of the patients had received ever influenza and 57% pneumococcal vaccinations. The majority of the patients were vaccinated with Pfizer-BioNTech vaccine (67%), followed by AstraZeneca vaccine (28%). Most of the participants reported no or low concerns regarding COVID-19 vaccination (80%) and 70% did not change their immunomodulation around the vaccination period. The most common side effect was pain at the injection site (71%), followed by fatigue (41%), headache (33%), and arthralgia (24%). Only 1% of the patients reported allergic reactions. Side effects lasted in median for two days (range 0-99 days) and 15% reported no relevant side effects. Disease flares after first COVID-19 vaccination as reported by patients on a 1-10 scale was indicated in 13% of the patients. In these patients, 6% needed a change of their immunomodulation treatment. In 41% of the cases with disease flares, increasing the GC dose was sufficient to cope with the flares.

Conclusion: The first COVID-19 vaccination was well tolerated by the majority of RMD patients. Adverse events were similar to those observed in the general population. Only in 13% of the patients, self-reported disease flare was indicated and in these patients, only 6% needed changes in their immunomodulatory therapy. These preliminary results support the recommendation for COVID-19 vaccination in RMD patients.

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Abstract Number: 0101

Herpes Zoster Recombinant Zoster Vaccination Among Adults Age ≥50 Years with Immune Mediated Inflammatory Diseases in the United States

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Recombinant Zoster Vaccine (RZV) 1 and 2 dose Vaccination in Persons with Immune Mediated Inflammatory Diseases (IMIDs)

	MarketScan (50–64-Year-Olds) 2018–2019, N=54,270			CMS Medicare (≥65-Year-Olds) 2018–2019, N=160,521		
Immune Mediated Inflammatory Diseases (IMIDs)	N	≥1-dose # (%)	2-dose completion (%)[a]	N	≥1-dose # (%)	2-dose completion (%)[a]
RA	22631	3,898 (17.2%)	76.0%	89,498	43,730 (48.9%)	85.1%
AS	171	34 (19.9%)	73.7%	78	44 (56.4%)	85.7%
SPA	200	43 (21.5%)	73.9%	95	54 (56.8%)	88.2%
PsA	6991	1,144 (16.4%)	76.8%	15,845	6,448 (40.7%)	85.5%
PsO	10323	1,198 (11.6%)	75.7%	23,495	5,907 (25.1%)	85.0%
IBD	13013	1,693 (13.0%)	78.8%	31,097	12,012 (38.6%)	87.3%
CD	5322	682 (12.8%)	77.4%	13,086	5,094 (38.9%)	86.8%
UC	7764	1,045 (13.5%)	80.3%	18,321	7,024 (38.3%)	87.7%
SLE	4482	576 (12.9%)	75.4%	8,746	4,022 (46.0%)	84.3%
Any	54778	8,099 (14.8%)	76.6%	160,521	69,325 (43.2%)	85.5%

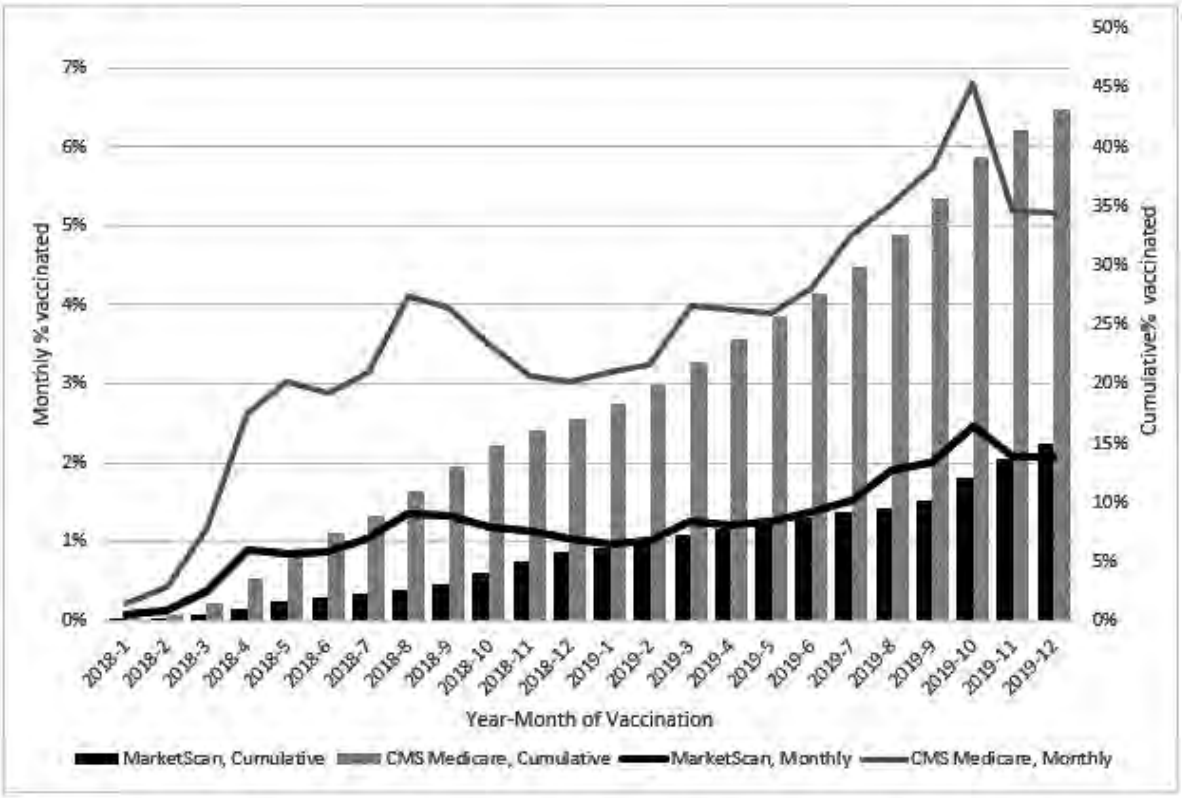
[a]2-dose RZV vaccination completion within 6 months of receipt of their first dose of RZV among persons who received their first dose before July 1, 2019 to allow for a 6-month follow-up period.

Background/Purpose: Persons with immune mediated Inflammatory diseases (IMIDs) are at increased risk of developing herpes zoster (HZ) and postherpetic neuralgia. In 2018, CDC recommended a highly efficacious (>90% efficacy) adjuvanted recombinant zoster vaccine (RZV, Shingrix) that was licensed as a two-dose series for prevention of HZ for immunocompetent persons age ≥50 years. In a 2018 national survey, ~2.4% of adults age ≥50 years self-reported receipt of RVZ, but RZV coverage in persons with IMIDs is unknown. We estimated the proportion of adults with selected IMIDs who received RZV vaccination between 2018–2019.

Methods: We used medical claims data from the 2017–2019 IBM® MarketScan® (persons age 50–64 years) and 2017–2019 Centers for Medicare and Medicaid Services Medicare (persons age ≥65 years) databases to examine RZV vaccination in persons with IMIDs (Rheumatoid Arthritis, RA; Ankylosing Spondylitis, AS; Axial Spondyloarthritis, SpA; Psoriatic Arthritis, PsA; Psoriasis, PsO; Inflammatory Bowel Disease, IBD; Crohn's Disease, CD; Ulcerative Colitis, UD; Systemic lupus erythematosus, SLE). Vaccine coverage was defined as receipt of ≥1 RZV dose. IMIDs were defined using all 3 of the following criteria: (a) ≥2 outpatient visits for their respective conditions, and (b) ≥1 claim for disease-specific medications, and (c) ≥1 visit to a relevant specialist (rheumatologist for RA, AS, SpA, PsA, SLE; gastroenterologist for IBD, CD, UC; dermatologist for PsO). RZV vaccination was defined using NDC and CPT codes.

Results: Among the 54,270 MarketScan enrollees with IMIDs, 14.8% received ≥1 dose of RZV, ranging from 11.6–21.5% depending on condition [Table 1]. There were 160,521 Medicare enrollees with IMIDs, among whom 43.2% had received ≥1 dose of RZV, ranging from 25.1–56.8% depending on the condition. Persons with RA, AS, and SPA

Figure 1. Monthly (Line graph) and Cumulative (Bar graph) Recombinant Zoster Vaccine (RZV) Coverage in Persons with Immune Mediated Inflammatory Diseases (IMIDs), MarketScan, 50–64-year-olds, and CMS Medicare, ≥65-year-olds, 2018–2019



Disclaimer: *The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention, US Department of Health and Human Services.*

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had the highest proportion vaccinated and persons with PsO had the lowest proportion. Among persons who initiated RZV vaccination, two-dose series completion within 6 months was 76.6% in MarketScan enrollees as compared to 85.5% in Medicare enrollees. Cumulative RZV vaccination and frequency of persons vaccinated monthly steadily increased during 2018–2019 [Figure 1]. When provider specialty prescribing vaccination was known among ≥65 year-olds (90% of vaccine doses), it was most frequently prescribed by physicians in family practice or internal medicine (52.9%) and pharmacists, (14.3%), and uncommonly by rheumatologists, dermatologists, or gastroenterologists (< 1% each).

Conclusion: A substantial proportion of adults age ≥50 years with IMIDs have received RZV vaccination; approximately 15–25% who received the first dose of RZV did not complete the 2-dose series within 6 months. RZV vaccination with at least one dose and 2-dose series completion was higher in ≥65 year-olds than 50–64 year-olds. Coverage in persons with IMIDs and in older ages may be higher than the general or younger populations because of physician recommendation for RZV or patient perception of increased risk for HZ. Additional data on efficacy and safety of RZV vaccination in this population, and vaccine policy recommendations may help to further increase RZV coverage.

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Abstract Number: 0102

Differential Impact of TNFi, JAKi and Rituximab on the Outcome of SARS-CoV-2 Infection in RMD Patients

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Due to the impressive efforts of the global scientific rheumatology community, increasing evidence about inflammatory rheumatic and musculoskeletal diseases (RMD) specific risk factors in the pandemic has been achieved. In this analysis from the German COVID19-Rheuma registry, we analysed the risk factors for the outcome of SARS-CoV-2 infection in patients with RMD, specifically focusing on the impact of the RMD treatment.

Methods: Data from the German physician-reported COVID-19 registry for RMD from March 30th, 2020 until April 9th, 2021 were analysed. Ordinal outcome of SARS-CoV-2 infection severity was defined in three groups: neither hospitalized, ventilated nor deceased; hospitalized with or without non-invasive ventilation, but neither invasively ventilated

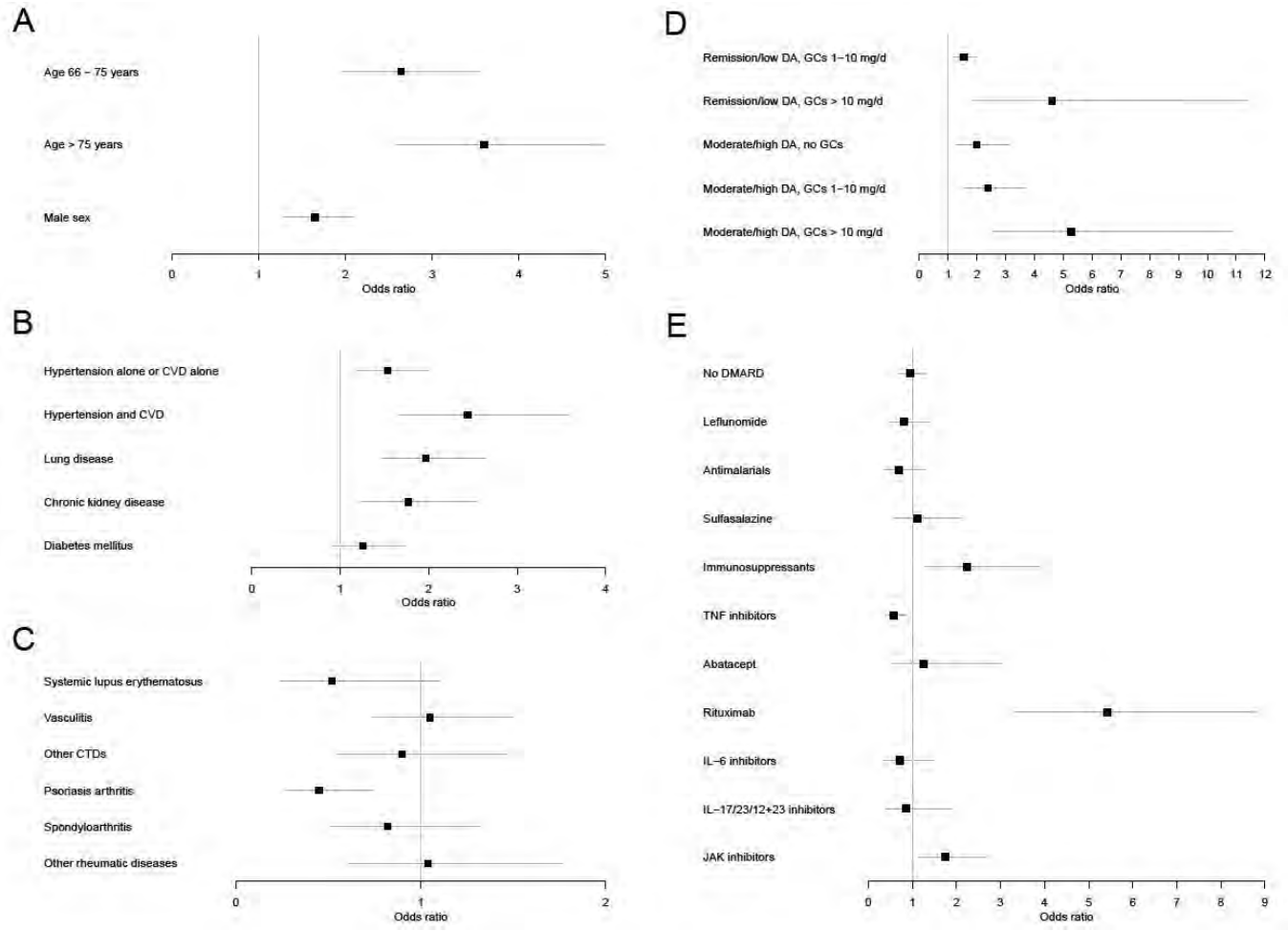

Figure 1A-E. Results of the ordinal regression analysis. Shown are multivariable-adjusted ORs for the outcome SARS-CoV-2 infection severity with 95% CIs, assessing the association with (A) general patient characteristics, (B) comorbidities, (C) rheumatic disease diagnoses (RMD), (D) disease activity and glucocorticoids, and (E) rheumatic disease medications.

nor deceased; invasively ventilated or deceased. Independent associations between demographic and disease features and SARS-CoV-2 infection-related severity were estimated by multivariable ordinal logistic regression using the proportional odds model and reported as odds ratio (OR) and 95% confidence interval (CI).

Results: 2,274 patients were included. Baseline characteristics are shown in table 1. 83 patients died, resulting in a case fatality rate of 3.6%.

In the ordinal regression analysis, age, male sex, cardiovascular disease, hypertension, chronic lung diseases, and chronic kidney disease were independently associated with a worse outcome of SARS-CoV-2 infection (fig. 1 a, b). Compared to RA, patients with PsA showed a lower OR (fig. 1c). Disease activity and glucocorticoids (GC) were associated with severity of SARS-CoV-2 infection as shown in figure 1d.

For the analysis of the impact of RMD treatment, MTX monotherapy was used as reference. TNFi showed a significant association with a better outcome of SARS-CoV-2 infection. In contrast, immunosuppressants (mycophenolate mofetil, azathioprine, cyclophosphamid, ciclosporin), JAKis and rituximab were independently associated with a worse outcome of SARS-CoV-2 infection (figure 1e).

Table 1. Baseline characteristics stratified by SARS-CoV-2 infection severity

Parameter	Not hospitalized, no death	Hospitalized, no invasive ventilation or death	Invasive ventilation or death	Total
N	**1771**	**374**	**129**	**2274**
General				
Age [years]	55 (18)	67 (19)	71 (19)	57 (19)
Male sex	546 (30.8)	130 (34.8)	67 (51.9)	743 (32.7)
Ever smoker	115 (96.6) *(N=119)* *(Missing=1652)*	21 (100) *(N=21)* *(Missing=353)*	9 (100) *(N=9)* *(Missing=120)*	145 (97.3) *(N=149)* *(Missing=2125)*
Inflammatory joint diseases				
Rheumatoid arthritis (RA)	781 (44.1)	193 (51.6)	76 (58.9)	1050 (46.2)
Spondyloarthritis	251 (14.2)	28 (7.5)	6 (4.7)	285 (12.5)
Psoriatic arthritis (PsA)	287 (16.2)	19 (5.1)	9 (7)	315 (13.9)
Total Inflammatory joint diseases	1313 (74.1)	238 (63.6)	90 (69.8)	1641 (72.2)
Connective tissue diseases (CTD)/ Vasculitis				
Systemic lupus erythematosus	91 (5.1)	12 (3.2)	2 (1.6)	105 (4.6)
Connective tissue diseases (other than SLE)	134 (7.6)	29 (7.8)	13 (10.1)	176 (7.7)
Vasculitis	145 (8.2)	81 (21.7)	29 (22.5)	255 (11.2)
Total CTD/ Vasculitis	364 (20.6)	121 (32.4)	43 (33.3)	528 (23.2)
Disease activity	*N=1751* *(Missing=20)*	*N=355* *(Missing=19)*	*N=109* *(Missing=20)*	*N=2215* *(Missing=59)*
Remission	939 (53.6)	165 (46.5)	37 (33.9)	1141 (51.5)
Minimal/low disease activity	603 (34.4)	112 (31.5)	44 (40.4)	759 (34.3)
Moderate disease activity	169 (9.7)	57 (16.1)	12 (11)	238 (10.7)
Severe/high disease activity	40 (2.3)	21 (5.9)	16 (14.7)	77 (3.5)
Comorbidities				
Hypertension	524 (29.6)	186 (49.7)	83 (64.3)	793 (34.9)
Cardiovascular disease	121 (6.8)	97 (25.9)	51 (39.5)	269 (11.8)
Chronic lung disease	168 (9.5)	72 (19.3)	43 (33.3)	283 (12.4)
Chronic kidney disease	64 (3.6)	71 (19)	35 (27.1)	170 (7.5)
Obesity (BMI ≥ 30)	355 (20)	87 (23.3)	31 (24)	473 (20.8)
Diabetes	137 (7.7)	67 (17.9)	31 (24)	235 (10.3)
Cancer	50 (2.8)	25 (6.7)	10 (7.8)	85 (3.7)
DMARD therapies				
csDMARDs monotherapy	576 (32.5)	115 (30.7)	35 (27.1)	726 (31.9)
csDMARDs combination therapy	327 (18.5)	58 (15.5)	17 (13.2)	402 (17.7)
Methotrexate monotherapy	381 (21.5)	84 (22.5)	22 (17.1)	487 (21.4)
Methotrexate combination therapy	278 (15.7)	50 (13.4)	15 (11.6)	343 (15.1)
Leflunomide monotherapy	53 (3)	12 (3.2)	8 (6.2)	73 (3.2)
Leflunomide combination therapy	34 (1.9)	5 (1.3)	1 (0.8)	40 (1.8)
Sulfasalazine monotherapy	37 (2.1)	7 (1.9)	3 (2.3)	47 (2.1)
Sulfasalazine combination therapy	21 (1.2)	7 (1.9)	1 (0.8)	29 (1.3)
Antimalarial monotherapy	105 (5.9)	12 (3.2)	2 (1.6)	119 (5.2)
Antimalarial combination therapy	70 (4)	9 (2.4)	2 (1.6)	81 (3.6)
Immunosuppressants monotherapy	42 (2.4)	32 (8.6)	8 (6.2)	82 (3.6)
Immunosuppressants combination therapy	24 (1.4)	12 (3.2)	2 (1.6)	38 (1.7)
Mycophenolate mofetil monotherapy	8 (0.5)	12 (3.2)	2 (1.6)	22 (1)
Mycophenolate mofetil combination therapy	9 (0.5)	6 (1.6)	1 (0.8)	16 (0.7)
Azathioprine monotherapy	33 (1.9)	15 (4)	6 (4.7)	54 (2.4)
Azathioprine combination therapy	10 (0.6)	5 (1.3)	0	15 (0.7)
Cyclophosphamide monotherapy	1 (0.1)	4 (1.1)	0	5 (0.2)
Cyclophosphamide combination therapy	1 (0.1)	1 (0.3)	1 (0.8)	3 (0.1)
Cyclosporin monotherapy	0	1 (0.3)	0	1 (0)
Cyclosporin combination therapy	5 (0.3)	1 (0.3)	0	6 (0.3)
bDMARDs monotherapy	440 (24.8)	57 (15.2)	29 (22.5)	526 (23.1)

Conclusion: Known general risk factors for severity of SARS-CoV-2 infection such as age, male sex, and certain comorbidities play a similar role in RMD patients. PsA patients have a better outcome of SARS-CoV-2 infection compared to RA. The influence of disease activity is of great importance as patients in high disease activity - even without GCs - have a worse outcome. Regarding RMD treatment, patients on TNFi show a better outcome of SARS-CoV-2 infection than MTX patients. The negative impact of sulfasalazin shown in the global rheumatology alliance analysis

Table 1. Baseline characteristics stratified by SARS-CoV-2 infection severity, cont

bDMARDs combination therapy	213 (12)	45 (12)	12 (9.3)	270 (11.9)
TNF inhibitors monotherapy	300 (16.9)	23 (6.1)	6 (4.7)	329 (14.5)
TNF inhibitors combination therapy	139 (7.8)	20 (5.3)	0	159 (7)
Abatacept monotherapy	6 (0.3)	5 (1.3)	0	11 (0.5)
Abatacept combination therapy	15 (0.8)	3 (0.8)	1 (0.8)	19 (0.8)
B-cell-targeted bDMARDs monotherapy	16 (0.9)	12 (3.2)	17 (13.2)	45 (2)
B-cell-targeted bDMARDs combination therapy	30 (1.7)	17 (4.5)	10 (7.8)	57 (2.5)
Rituximab monotherapy	15 (0.8)	11 (2.9)	17 (13.2)	43 (1.9)
Rituximab combination therapy	22 (1.2)	17 (4.5)	9 (7)	48 (2.1)
Belimumab monotherapy	1 (0.1)	1 (0.3)	0	2 (0.1)
Belimumab combination therapy	8 (0.5)	0	1 (0.8)	9 (0.4)
IL-6 inhibitors monotherapy	38 (2.1)	7 (1.9)	3 (2.3)	48 (2.1)
IL-6 inhibitors combination therapy	9 (0.5)	2 (0.5)	0	11 (0.5)
IL-1 inhibitors monotherapy	18 (1)	3 (0.8)	2 (1.6)	23 (1)
IL-1 inhibitors combination therapy	3 (0.2)	0	1 (0.8)	4 (0.2)
IL-17, Il-23, Il-12/23 inhibitors monotherapy	62 (3.5)	7 (1.9)	1 (0.8)	70 (3.1)
IL-17, Il-23, Il-12/23 inhibitors combination therapy	17 (1)	3 (0.8)	0	20 (0.9)
tsDMARDs monotherapy	72 (4.1)	26 (7)	9 (7)	107 (4.7)
tsDMARDs combination therapy	36 (2)	7 (1.9)	5 (3.9)	48 (2.1)
JAK inhibitors monotherapy	65 (3.7)	26 (7)	9 (7)	100 (4.4)
JAK inhibitors combination therapy	36 (2)	6 (1.6)	5 (3.9)	47 (2.1)
Apremilast monotherapy	7 (0.4)	0	0	7 (0.3)
Apremilast combination therapy	0	1 (0.3)	0	1 (0)
No DMARD therapies	311 (17.6)	79 (21.1)	29 (22.5)	419 (18.4)
Further therapies				
Glucocorticoids (#)	485 (27.5) *(N=1759) (Missing=12)*	198 (52.9) *(N=373) (Missing=1)*	78 (60.5) *(N=129) (Missing=0)*	761 (33.6) *(N=2261) (Missing=13)*
0 mg/d < Glucocorticoids <= 10 mg/d	453 (25.8) *(N=1759) (Missing=12)*	179 (48) *(N=373) (Missing=1)*	60 (46.5) *(N=129) (Missing=0)*	692 (30.6) *(N=2261) (Missing=13)*
Glucocorticoids > 10 mg/d	24 (1.4 *(N=1759) (Missing=12)*	18 (4.8) *(N=373) (Missing=1)*	18 (14) *(N=129) (Missing=0)*	60 (2.7) *(N=2261) (Missing=13)*

Data are N (column %) for categorical variables or mean (SD) for continuous variables. Table includes all patients with a non-missing outcome and non-missing values for age, sex and disease-modifying anti-rheumatic drugs (DMARDs) (4 patients excluded). Data refers to patients with non-missing values for the respective variable; total N for patients with non-missing values is given in parentheses for variables with missing values; the total number of missing values is also given in parenthesis, for the applicable variables. (#) Includes patients with a missing glucocorticoid dosage.

bDMARD, biological disease-modifying anti-rheumatic drugs; BMI, body mass index; csDMARD, conventional synthetic disease-modifying anti-rheumatic drugs; CTD, connective tissue diseases; DMARD, disease-modifying anti-rheumatic drugs; IL, interleukin; JAK, Janus kinase; JIA, juvenile idiopathic arthritis; N, number; NSAID, non-steroidal anti-inflammatory drugs; SLE, Systemic lupus erythematosus; TNF; tumour necrosis factor; tsDMARD, targeted synthetic disease-modifying anti-rheumatic drugs.

[1] was not reproduced in this analysis. This might be due to the larger homogeneity in our data deriving from one country, resulting in less bias. The signals showing a less favorable outcome of SARS-CoV-2 infection for immunosuppressants, rituximab, and JAKi could be reproduced. These associations with a worse outcome of SARS-CoV-2 infection may be attributed to residual and unmeasured confounding due to higher burden of comorbidity or cumulative effect of therapies. However, the data show that the individual risk/benefit ratios for the different RMD treatments should be carefully considered and further evaluated.

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Abstract Number: 0103

Patients with Inflammatory Rheumatic Diseases Are at Increased Risk of COVID-19 Related Hospitalization: Data from a Prospective Controlled Cohort Study

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Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Retrospective studies have suggested that patients with rheumatic diseases may be at increased risk of severe COVID-19 related disease, and that this risk may partly be related to specific antirheumatic therapies. We investigated this in a large prospective controlled cohort study. The primary objective of the study was to investigate whether patients with rheumatic diseases are at increased risk of developing severe COVID-19 manifestations, defined as hospitalizations, compared to the general population. Secondary objectives were to analyze associations between anti-rheumatic treatment and disease severity of COVID-19, and to monitor the sustainability of SARS-CoV-2 specific IgG antibody titers over time.

Methods: All adult patients with inflammatory rheumatic diseases from the Amsterdam Rheumatology & Immunology Center, Amsterdam and Amsterdam UMC were invited to participate in the study (Netherlands Trial Register, trial ID NL8513). Patients were asked to register their own healthy control subject who were of the same sex and comparable age. During follow-up, participants received three digital questionnaires assessing patient and COVID-19 related characteristics. Serum samples were collected at two different time points, and analyzed for the presence of SARS-CoV-2 specific antibodies using a highly sensitive RBD-Ab bridging ELISA. COVID-19 cases were defined as participants with at least one positive PCR or a positive antibody test result.

Results: Between April, 2020, and March, 2021, 3279 rheumatic patients and 1110 healthy controls were included in the study. The mean age of patients and controls was 58 ± 13 and 56 ± 13 years respectively, and 1647 (63%) patients and 626 (69%) controls were female. Diagnosis of COVID-19 was confirmed in 307 (9%) patients and 128 (12%) healthy controls. The COVID-19 related hospitalization rate was significantly higher in patients compared to controls; 18 (6%) patients and 1 (1%) healthy control were hospitalized (*P* 0.02). Table 1 compares characteristics of non-hospitalized and hospitalized rheumatic patients with a confirmed COVID-19 diagnosis. It can be seen that patients with older age, male sex, a history of chronic pulmonary disease or diabetes, and patients who were treated with prednisone or rituximab were more frequently hospitalized. In contrast, patients treated with hydroxychloroquine or TNF-inhibitors were less frequently hospitalized.

Table 1. Characteristics of rheumatic patients: non-hospitalized vs. hospitalized COVID-19 cases.		
Patient characteristics	**Non-hospitalized patients (n=307)**	**Hospitalized patients (n=18)**
Age (years) – mean ± SD	54 ± 13	60 ± 12
Female sex – no. (%)	216 (67)	7 (39)
BMI – mean ± SD	26 ± 5	27 ± 5
Coexisting conditions – no. (%)		
Cardiovascular disease	18 (6)	1 (6)
Chronic pulmonary disease	23 (6)	2 (11)
Diabetes	11 (4)	4 (22)
Immunosuppressive medication – no. (%)		
Methotrexate	119 (38)	6 (33)
Hydroxychloroquine	43 (14)	1 (6)
TNF inhibitor	97 (32)	3 (17)
Tocilizumab	5 (2)	0 (0)
Abatacept	6 (2)	0 (0)
Rituximab	4 (1)	2 (12)
Oral glucocorticoids	32 (10)	3 (17)

Values are displayed as mean ± standard deviation (SD) or frequencies with corresponding percentages (%). BMI = Body mass index.

Conclusion: Our data suggest, albeit based on a limited number of patients in the hospitalization group, that patients with rheumatic diseases are at increased risk of COVID-19 related hospitalization. In addition, treatment with rituximab or prednisone seems to increase the risk of COVID-19 related hospitalization, while treatment TNF-inhibitors and hydroxychloroquine may have protective effects.

Disclosure: L. Boekel, None; **F. Hooijberg**, None; **E. Vogelzang**, None; **M. Leeuw**, None; **S. Atiqi**, None; **R. van Vollenhoven**, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, UCB, 2, 5, 6, Pfizer, 2, 6, 12, Support for educational programs; institutional grants, Roche, 12, Support for educational programs; institutional grants, Janssen, 2, 6, AbbVie, 2, 6, AstraZeneca, 2, Biotest, 2, GlaxoSmithKline, 2, 6, Biogen, 2, Galapagos, 2, 6, Gilead, 2, Sanofi, 2, Servier, 2, Vielabio, 2; **A. Voskuyl**, None; **I. van der Horst-Bruinsma**, None; **W. Lems**, None; **T. Kuijpers**, None; **M. van Ham**, None; **L. Wieske**, None; **F. Eftimov**, None; **M. Steenhuis**, None; **S. Keijzer**, None; **O. Christianawati**, None; **F. Loeff**, None; **S. Tas**, None; **M. Nurmohamed**, Abbvie, 4, Eli Lilly, 2, Celltrion, 2, GSK, 2, Novartis, 5, Janssen, 6, Pfizer, 5, Galapagos, 5; **T. Rispens**, None; **G. Wolbink**, None.

Abstract Number: 0104

Adverse Events of First SARS-CoV-2 Vaccinations Are Comparable for Patients with Autoimmune Diseases and the General Population

Laura Boekel[1], Laura Kummer[2], Koos van Dam[2], Femke Hooijberg[1], Zoé van Kempen[2], Erik Vogelzang[2], Luuk Wieske[2], Filip Eftimov[2], Ronald van Vollenhoven[3], Taco Kuijpers[2], Marieke van Ham[4], Sander Tas[5], Joep Killestein[2], Maarten Boers[6], Mike Nurmohamed[7], Theo Rispens[4] and Gertjan Wolbink[1], [1]Reade, Amsterdam, Netherlands, [2]Amsterdam UMC, Amsterdam, Netherlands, [3]Department of Rheumatology and Clinical Immunology, Amsterdam University Medical Center, Amsterdam Rheumatology Center, Amsterdam, Netherlands, [4]Sanquin, Amsterdam, Netherlands, [5]Amsterdam UMC, locatie AMC, Utrecht, Netherlands, [6]Amsterdam UMC, Vrije Universiteit, Amsterdam, Netherlands, [7]Reade; Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Clinical trials on efficacy and safety of SARS-CoV-2 vaccines did not include patients with autoimmune diseases. We previously demonstrated that concerns of adverse events and disease exacerbations due to SARS-CoV-2 vaccinations are important reasons for vaccine hesitancy in this patient group. Consequently, data on effects of SARS-CoV-2 vaccinations on patients with autoimmune diseases are urgently needed. The primary objective was to compare the frequency and severity of adverse events following SARS-CoV-2 vaccinations between patients with autoimmune diseases and healthy controls. Secondary objectives were to assess whether autoimmune disease activity was influenced by SARS-CoV-2 vaccinations, and whether any vaccine (AstraZeneca, Pfizer/BionN-Tech or Moderna) would be preferable for patients with autoimmune diseases.

Methods: On April 14th, 2021, a digital questionnaire evaluating consequences of SARS-CoV-2 vaccinations was sent to patients with systemic autoimmune diseases and healthy controls, who were enrolled in two ongoing prospective cohort studies of the Amsterdam Rheumatology & Immunology Center, Amsterdam and Amsterdam UMC (Netherlands Trial Register, trial ID NL8513 and NCT04498286). Mild adverse events were defined as annoying but not limiting daily activities, moderate adverse events as limiting daily activities, and severe adverse events as necessity of a visit to a medical expert. Multivariable logistic regression analyses were used to compare the occurrence of any adverse event, and the occurrence of moderate/severe adverse events following SARS-CoV-2 vaccinations between patients and controls. Effect modification was investigated for gender and vaccine type.

Results: On April 25th, 2021, 501 patients (420 patients with rheumatic diseases and 81 patients with multiple sclerosis) and 184 healthy controls were vaccinated against SARS-CoV-2 and included for analyses. The mean age of patients and controls was 63 (SD 11) and 64 (SD 11) years respectively, and 329 (66 %) patients and 119 (65%) controls were female. AstraZeneca and Pfizer/BioNTech were the most commonly applied vaccines in both patients and controls. The majority of patients and controls experienced at least one mild adverse event (56% vs. 58%), a minority at least one moderate adverse event (23% vs. 21%), and severe adverse events were rare (1% vs. 0%). A small proportion of patients (5%) reported to experience a deterioration of their autoimmune disease following SARS-CoV-2 vaccination. Results of the regression analyses are shown in table 1. After adjusting for age, gender and vaccine type, the odds for patients and healthy controls to experience any, systemic or moderate/severe adverse event(s) following the first SARS-CoV-2 vaccination were comparable. No effect modification by gender or vaccine type was demonstrated.

Conclusion: Our data demonstrate that patients with autoimmune diseases are not at an increased risk of experiencing adverse events from vaccination with AstraZeneca, Moderna or Pfizer/BioNTech compared to the general population, and that the impact of these vaccines on autoimmune disease activity is minimal.

Table 1. The risk of adverse events following the first SARS-CoV-2 vaccination in patients with autoimmune diseases compared to healthy controls.

	Any adverse event			Systemic adverse event			Moderate/severe adverse event		
First vaccination									
All patients	1.1	(0.7 – 1.6)	P = 0.73	1.1	(0.8 – 1.6)	P = 0.60	1.1	(0.8 – 1.8)	P = 0.48
RA patients	0.9	(0.6 – 1.4)	P = 0.54	1.0	(0.6 – 1.6)	P = 0.94	1.0	(0.6 – 1.7)	P = 0.96
MS patients	1.2	(0.6 – 2.4)	P = 0.55	1.5	(0.8 – 2.9)	P = 0.18	1.4	(0.7 – 2.8)	P = 0.32

Values are displayed as odds ratios with corresponding 95% confidence intervals and P-values. Odds ratios are adjusted for age, gender and vaccine type. RA = rheumatoid arthritis, MS = multiple sclerosis.

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Abstract Number: 0105

Most Patients with Spondylitis Accept COVID-19 Vaccination and Few Experience Disease Exacerbation After Immunization

Rachel Higgins[1], Hedley Hamilton[2], Michael Weisman[3], John Reveille[4], Kimbery Ogle[1], Cassie Shafer[5], Elin Aslanyan[5], Richard Howard[5], Dongseok Choi[1], James T. Rosenbaum[6] and Kevin Winthrop[1], [1]Oregon Health & Science University, Portland, OR, [2]Any-3 Ltd, London, United Kingdom, [3]Adjunct Professor of Medicine, Stanford University; Distinguished Professor of Medicine Emeritus, David Geffen School of Medicine at UCLA, Los Angeles, CA, [4]Division of Rheumatology, The University of Texas Health Science Center at Houston, Houston, TX, [5]Spondylitis Association of America, Encino, CA, [6]Departments of Ophthalmology, Medicine, and Cell Biology, Oregon Health & Sciences University and Chair Emeritus, Legacy Devers Eye Institute, Portland, OR

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatic and musculoskeletal diseases (RMDs) remain at an increased risk of morbidity and mortality from vaccine preventable infections, often as a result of disease activity, comorbidities, and immunosuppressive medication.[1] Despite increased risk, vaccine uncertainty and hesitancy remain ongoing

Table 1. Impact of COVID-19 vaccination on SpA symptoms

Do you believe taking the COVID-19 vaccine affected your SpA symptoms? (N=1292)	
Response:	**Count (n [%])**
Receiving the vaccine has not affected my SpA symptoms	997 (77.2)
My disease activity changed but I believe this was the result of something other than the vaccine, such as holding medication	116 (9.0)
The 2nd shot made my disease significantly worse	71 (5.5)
The 1st shot made my disease significantly worse	63 (4.9)
Both shots made the disease significantly worse	33 (2.6)
The 1st shot made my disease significantly better	<10 (<0.8)
Both shots made the disease significantly better	<10 (<0.8)
The 2nd shot made my disease significantly better	<10 (<0.8)

Table 2. Medication modifications due to COVID-19 vaccination

Did you modify your medications due to vaccination? And if so, which medicines were reduced or stopped temporarily?* (N=1539)	
Response:	**Count (n [%])**
No, I did not modify medication	1020 (66.3)
Yes, I modified biologics	222 (14.4)
Yes, I modified NSAIDs	129 (8.4)
Yes, I modified MTX	92 (6.0)
Yes, I modified another medication	40 (2.6)
Yes, I modified prednisone	17 (1.1)
Yes, I modified SSZ	<10 (<0.6)
Yes, I modified a JAK inhibitor	<10 (<0.6)
Yes, I modified HCQ	<10 (<0.6)
*Participants may select multiple responses	

challenges among this population and continue to be observed during the COVID-19 pandemic.[2] Even as COVID-19 vaccinations become more accessible, relatively low acceptance of the vaccine among the general population may negatively impact RMD populations, who would benefit from increased protection against COVID-19 illness.[3]

Methods: We conducted a web-based follow-up survey of spondyloarthritis (SpA) patients in the U.S. and Canada who had previously participated in a Spondylitis Association of America-sponsored COVID-19 survey. Fifteen multiple-choice questions were designed to capture information related to COVID-19 vaccine acceptance, attitudes, medication modification, perceived impact of vaccination on disease activity, past and present vaccine hesitancy or refusal, and COVID-19 vaccine information sources among SpA patients. Beginning April 1st 2021, participants were prompted to complete the follow-up questions via an email blast and social media posts.

Results: Between April 1st and April 27th, 1745 self-reported SpA participants responded to the survey. Overall, 1430 (81.9%) indicated they had received at least one dose of a COVID-19 vaccine and 10.1% planned to be vaccinated in the future. Fifty-one (2.9%) were undecided about receiving a COVID-19 vaccination and only 88 (5%) did not intend to receive the vaccine in the future. Among the 1539 responses from vaccinated participants (multiple selections possible), 1020 (66.3%) did not modify their SpA treatment due to vaccination, 222 (14.4%) modified a biologic, 129 (8.4%) modified an NSAID, 92 (6%) modified MTX, and 73 (4.9%) modified another medication. Among 1292 vaccinated participants, 997 (77.2%) indicated the COVID-19 vaccine had no effect on their SpA symptoms, 167 (12.9%) reported worsening symptoms after the first, second, or both vaccines, and 116 (9%) indicated a change in disease activity that they attributed to another factor, such as modified medication. Among 194 unvaccinated participant responses (multiple selections possible), 61 (31.4%) indicated fear of potential vaccine side effects as their main reason to decline, 39 (20.1%) indicated that the vaccine wasn't mandated and it was their right to decline, and 36 (18.6%) indicated fear of worsened disease symptoms.

Conclusion: Willingness to receive the COVID-19 vaccine was high and uncertainty and hesitancy were low among survey participants; over half of respondents were eager to be vaccinated. Nearly 80% of vaccinated participants indicated that the vaccine had no effect on their SpA symptoms, and only 1/3 modified their SpA treatment due to vaccination. These findings highlight the lower impact of vaccination on SpA disease activity, and may encourage other hesitant or unsure SpA patients concerned about increased disease activity to get vaccinated against SARS-CoV-2.

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Abstract Number: 0106

COVID-19 Mortality and Hospitalization Risk in Patients with Rheumatic Diseases: A Single Center Retrospective Cohort Study

Mousa Albalwi, Ben Brintz, Srinivasan Beddhu, Guo Wei and Julie Thomas, University of Utah, Salt Lake City, UT

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Following SARS-CoV-2 infection, patients with rheumatic diseases seem to have similar or slightly poorer outcomes compared with those without rheumatic disease. However, robust data is lacking to inform our understanding of mortality and morbidity following COVID-19 infection in patients with rheumatic diseases.

Methods: The University of Utah COVID-19 database identifies all adult patients that tested positive with Covid-19 at a University of Utah facility throughout the state of Utah. This database was used to identify and glean data from all Covid-19 positive patients retrospectively from January 1, 2020 to March 26, 2021. Patients with rheumatic diseases testing positive for Covid-19 were identified from this database using ICD-10 codes of the most common rheumatic diseases, including rheumatoid arthritis, lupus, inflammatory myositis, vasculitis, spondyloarthritis, sarcoidosis, and gout. Outcomes of interest included mortality, hospitalization, and length of stay. For each outcome, we conducted univariable analysis and used weighted (propensity scores) and unweighted multivariable logistic regression to estimate odds ratio (ORs) and 95% confidence interval (CI) based on the presence of rheumatic diseases. Age, sex, Charleson Comorbidity Index (CCI) and BMI were included as covariates in multivariable logistic regression models. Subgroup analysis was performed for glucocorticoids, conventional synthetic disease modifying agents (cDMARDs) and biological disease modifying agents (bDMARDs) medications.

Results: The University of Utah COVID-19 database identified 39,114 patients with confirmed COVID-19 infection with 195 deaths (0.5 %) from January 1, 2020 to March 26, 2021. 979 patients were identified with rheumatic diseases (2.5%) (see Table 1). In weighted and unweighted multivariable logistic regression, rheumatic disease was associated with higher odds of death (OR 1.5, 95% CI 1.01 to 2.22) and (OR 1.57, 95% CI 1.02 to 2.39), respectively. Rheumatic disease was also associated with higher odds of hospitalization (OR 1.77, 95% CI 1.48 to 2.13). Independent factors associated with COVID-19-related death were age (OR 1.08, 95% CI 1.07 to 1.1), male sex (2.52, 1.83 to 3.47) and CCI (1.27, 1.21 to 1.32). In the immunosuppressants subgroup analysis, there was no evidence for a difference in odds of death in glucocorticoids (OR 0.65, 95% CI 0.23 to 1.84), conventional synthetic DMARDs (OR 0.39, 95% CI 0.13 to 1.22) and biological DMARDs (OR 1.13, 95% CI 0.12 to 10.43).

Table 1. Summary of Group Characteristics in a Univariate Analysis

Variable		No Rheumatic Diseases (N=38135)	Rheumatic Diseases (N=979)	P-value
Gender :	Female	19494 (51.1%)	531 (54.2%)	0.16[f]
	Male	18618 (48.8%)	448 (45.8%)	-
Race :	White	18278 (47.9%)	336 (34.3%)	<0.001[c]
	Non-white	19857 (52.1%)	643 (65.7%)	-
Age :	Mean (SD)	38.9 (15.1)	52.5 (16.5)	<0.001[t]
BMI :	Mean (SD)	29.7 (8.8)	31.7 (8.2)	<0.001[t]
Charleson Comorbidity Score :	Mean (SD)	0.4 (1.3)	3.0 (3.1)	-
Death from COVID :	No	37976 (99.6%)	943 (96.3%)	<0.001[f]
	Yes	159 (0.4%)	36 (3.7%)	-
Hospitalization :	No	36181 (94.9%)	759 (77.5%)	<0.001[c]
	Yes	1954 (5.1%)	220 (22.5%)	-
Length of Stay in Days *:	- Mean (SD)	5.77 (8.8)	8.57 (9.9)	-

[f] Fisher's exact test, [c] Chi-squared test, [t] T-test, [w] Wilcoxon rank sum test.
**Based on only patients who have at least an overnight stay in the hospital*

Conclusion: Among patients with COVID-19 infection, persons with rheumatic diseases have an increased odds of death and hospitalization compared to persons without rheumatic diseases.

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Abstract Number: 0107

Acceptability of the COVID-19 Vaccine in Patients with Rheumatic Diseases and Healthcare Professionals in 19 Arab Countries

Lina El Kibbi[1], Mona Metawee[1], Ihsane Hmamouchi[2], Nizar Abdulateef[3], Hussein Halabi[4], Mervat Eissa[5], Manal El Rakawi[6], Basel Masri[7], Fatemah Abutiban[8], Wafa Hamdi[9], Asal Adnan[3], Antonella Abi Najm[10], Renaud Felten[11], Laurent Arnaud[11] and Nelly Ziade[12], [1]Specialized Medical Center, Riyadh, Saudi Arabia, [2]Rheumatology Unit, Temara Hospital, Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, [3]Rheumatology Unit, Department of Medicine, College of Medicine, University of Baghdad, Baghdad, Iraq, [4]King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia, [5]Cairo University, Cairo, Egypt, Cairo, Egypt, [6]Rheumatology Department, Douera Hospital, Faculty of Medicine, Saad Dahlab, Blida, Algeria, [7]Jordan Hospital, Amman, Jordan, [8]Rheumatology Unit, Department of Medicine, Jaber Alahmed Alsabah Hospital, Kuwait City, Kuwait, [9]Rheumatology Department, Kassab Institute of Orthopedics, UR17SP04, Faculty of Medicine of Tunis, Tunis El Manar University, Tunis, Tunisia, [10]Faculty of Medicine, Saint-Joseph University, Beirut, Lebanon, [11]Department of Rheumatology, French National Reference Center for Autoimmune Diseases (CRMR RESO), Strasbourg, France, [12]Rheumatology Department, Saint-Joseph Medical University and Hotel-Dieu de France Hospital, Beirut, Lebanon

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The first COVID-19 vaccines were authorized in December 2020. However, their acceptability remains debated and has never been evaluated in patients with chronic rheumatic disease and health care professionals (HCPs) in the Arab countries. The primary objective of this study was to assess the acceptability of COVID-19 vaccines in patients with chronic rheumatic disease and HCPs in the Arab countries and to evaluate the factors associated with acceptability.

Table 1. Characteristics of the Participants in the Arab COVID-19 Perceptions (ARCOVAX) study and Vaccination status

	Patients	Health Care Professionals	All Participants
Number	1595	1517	3176
Age, mean [SD]*	39.0 [13.0]	40.4 [11.7]	39.6 [12.4]
Female Gender, N (%)**	1159 (72.7)	900 (59.3)	2073 (65.3)
GDP Region, N(%)**			
- *High income*	577 (36.2)	227 (15.0%)	808 (25.4)
- *Middle High income*	546 (34.1)	689 (45.4%)	1286 (40.5)
- *Middle Low and Low income*	472 (29.6)	601 (39.6%)	1082 (34.1)
Rheumatic Diagnosis, N (%)			
Rheumatoid Arthritis	745 (46.7)	-	-
Systemic Lupus Erythematosus	342 (21.4)	-	-
Spondylarthritis	143 (9.0)	-	-
Psoriatic Arthritis	79 (4.9)	-	-
Myositis	33 (2.1)	-	-
Health Professionals, N (%)			
Rheumatologist	-	860 (56.7)	-
Other Physicians	-	474 (31.2)	-
Other Health Care Professionals	-	183 (12.1)	-
Relevant Comorbidities, N (%)**			
High Blood Pressure	236 (14.8)	160 (10.5)	396 (12.5)
Obesity	179 (11.2)	119 (7.8)	299 (9.4)
Respiratory Diseases	105 (6.6)	58 (3.8)	163 (5.1)
Diabetes	97 (6.1)	80 (5.3)	177 (5.6)
Smoker (ever), N (%)	350 (21.9)	297 (19.6)	0.104
University Education, N (%)**	284 (17.8)	1076 (70.9)	1360 (43.7)
Use of Oral Glucocorticoids, N (%)	632 (39.6)	-	-
Use of Immunosuppressive Drugs, N (%)	975 (61.1)	-	-
Vaccine Hesitancy			
Have taken influenza vaccination in the past 3 years, N (%)**	481 (30.1)	632 (41.7)	1121 (35.3)
Have previously refused a recommended vaccine for self or children, N (%)**	108 (6.8)	112 (7.4)	221 (7.0)
COVID-19			
Previous COVID-19 infection, N (%)*	313 (19.6)	533 (35.1)	867 (27.3)
Close contact with severe COVID-19, N (%)**	887 (55.6)	1067 (70.3)	2000 (63.0)
Afraid of COVID-19 on a 0-10 scale, median [IQR]**	7 [5-10]	7 [5-9]	7 [5-9]
Afraid of severe COVID-19 on a 0-10 scale, median [IQR]	8 [5-10]	7 [5-10]	7 [5-10]

*p-value<0.01, **p-value≤0.001
GDP: Gross Domestic Product, classified according to the World Bank; IQR: Interquartile range; SD: Standard Deviation.

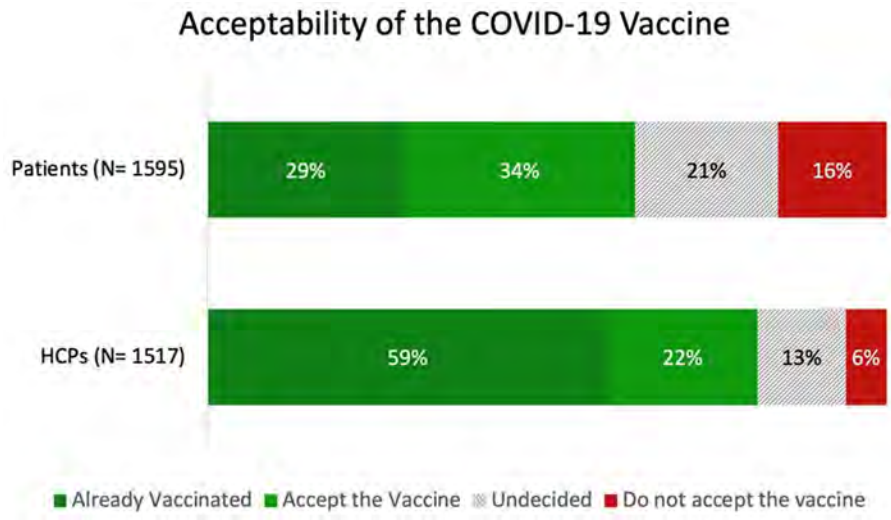

Figure 1. Acceptability of the COVID-19 Vaccination in Patients and in Health Care Professionals (HCPs).

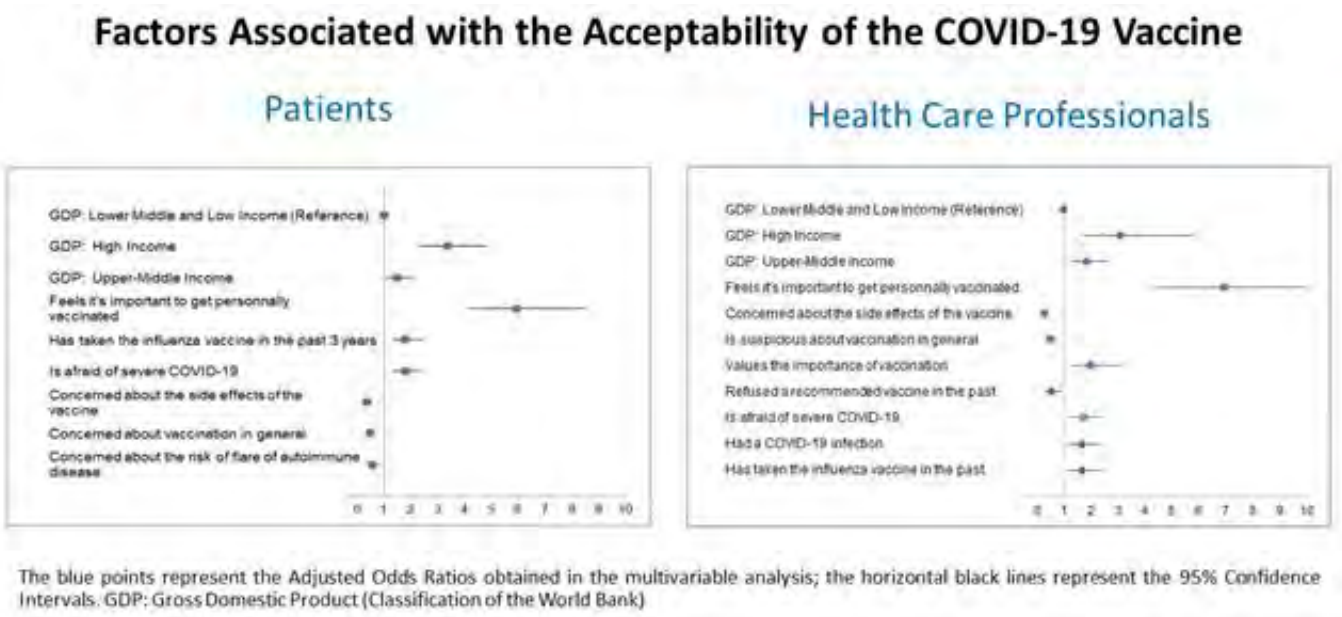

Figure 2. Factors associated with the acceptability of the COVID-19 vaccine in patients and health care professionals in the multivariable analysis.

Methods: The ARCOVAX (Arab League of Associations for Rheumatology (ArLAR) COVID Vaccination study) utilized an anonymous web-based survey that was adapted from the VAXICOV study (1), translated to Arabic by the authors, and validated by the scientific committee of the ArLAR. The survey was disseminated online in three languages: Arabic, English, and French between April 13th and May 11th, 2021, through multiple social media platforms (Facebook, Twitter, Instagram, Snapchat), patients' associations, mass emails from ArLAR and AAAA (Arab Adult Arthritis Awareness) group, WhatsApp messages to rheumatologists and patients, and direct invitation to patients while in the waiting room. Acceptability was defined by participants who were already vaccinated or willing to get vaccinated; non-acceptability was defined by participants who were undecided or refused to get vaccinated. Demographic and disease data, perceptions about COVID-19 vaccines were presented in numbers and percentages for categorical variables and means and standard deviations or medians and interquartile ranges for continuous variables, as appropriate. The factors associated with acceptability were evaluated using two separate binary logistic regression models for patients and HCPs, respectively.

Results: A total of 3,176 participants from 19 Arab countries completed the survey (1,594 patients and 1,517 HCPs). The mean age of the patients was 39 years, 73% were female and 18% had a university degree (Table 1). Twenty-nine percent of the patients were already vaccinated, versus 59% of the HCPs. Acceptability was significantly lower in patients (63%) compared to HCPs (81%), p< 0.001 (Figure 1), and remained significantly lower when considering the non-vaccinated participants only (p=0.006). Among the patients who were not vaccinated, 57% of the undecided and 40% of those who refused the vaccine would be willing to get vaccinated if it were recommended by their physician. In both patients and HCPs, acceptability was associated with a higher country gross domestic product, the feeling that it is important to be personally vaccinated, previous Influenza vaccination, fear of COVID-19 and lower levels of concerns regarding the vaccines side effects (Figure 2).

Conclusion: Acceptability of the COVID-19 by patients (63%) was significantly lower than HCPs (81%) but may be substantially improved if the vaccine was recommended by the doctor. Addressing the main determinants of acceptability, i.e., perceptions regarding vaccination and concerns regarding the side effects of the COVID-19 vaccines may facilitate the uptake of the vaccine in patients and in HCPs.

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Abstract Number: 0108

Efficacy of *SARS-CoV-2* Vaccine in Patients with Rheumatic Diseases: A Systematic Review and Meta-Analysis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The mRNA-based *SARS-CoV-2* vaccine has shown efficacy in large vaccine trials. However, patients on immunosuppressive therapies including those with rheumatic disease (RD) were excluded. Recent studies have examined the immunogenicity of *SARS-CoV-2* vaccination in immunocompromised patients. We thus conducted a systematic review and meta-analysis on the humoral immune response of *SARS-CoV-2* vaccination in patients with rheumatic disease.

Methods: We systematically searched Pubmed/Medline, Scopus, and MedRxiv from January 1, 2021- May 30, 2021 to identify eligible studies that examined the immunogenicity of *SARS-CoV-2* vaccination in RD patients. Included studies provided information on proportion of RD patients who developed an immune response following the second dose of the vaccine. Immune response was defined as development of IgG antibodies to *SARS-CoV-2* S anti-receptor binding domain (RBD) or neutralizing antibodies with cutoffs established by manufacturer. Information on RD type and immunosuppressant use was also obtained from each study. Meta-Analysis was performed using Comprehensive Meta-Analysis.

Results: Our meta-analysis included eight studies (3 observational studies, 5 case-control studies) which was comprised of 1482 RD patients. The pooled response rate following vaccination against *SARS-CoV-2* was 0.88 (95% CI 0.75-0.94). Compared to non-RD patients, RD patients had significantly decreased response to *SARS-CoV-2* vaccination (RR 0.88, 95% 0.84-0.93). Patients on rituximab (37%), mycophenolate (70.8%), prednisone (86.6%), and methotrexate (91.9%) showed lower vaccine response. On the other hand, patients on TNF (100%), JAK (96.3%), and IL-17 inhibitors (92.9%) showed higher vaccine response.

Conclusion: In this systematic review and meta-analysis, majority of RD patients developed an immune response following second dose of *SARS-CoV-2* vaccine. However, the vaccine response rate was significantly lower in RD patients compared to controls. This is likely driven by certain immunosuppressants particularly B-cell depleting therapy which can hamper the humoral immune response. Future studies need to examine the use and timing of these immunosuppressants prior to *SARS-CoV-2* vaccination.

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

Abstract Number: 0109

COVID-19 Infection and Outcomes in Patients with Rheumatic Diseases: A Systematic Review and Meta-Analysis

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Early studies published at the beginning of COVID-19 pandemic suggested lower risk of COVID-19 and less severe disease course in patients with rheumatic diseases (RD). Subsequent studies have been published worldwide since the onset of the COVID-19 pandemic with studies showing mixed results. We thus conducted a systematic review and meta-analysis on the prevalence and outcomes of COVID-19 in patients with rheumatic diseases.

Methods: PubMed/Medline and Scopus were systematically searched from January 1, 2020 to April 31, 2021 to identify observational and case-control studies that reported prevalence and outcomes of confirmed *SARS-CoV-2* infection (by polymerase chain reaction or serologies) among patients with inflammatory and autoimmune rheumatic diseases (RD). The secondary outcomes measured were hospitalization, admission to Intensive Care Unit (ICU), use of mechanical ventilation, and death. Additional information including demographics and medication use were obtained from each of the studies. Medications were classified by conventional synthetic disease-modifying antirheumatic drugs (csDMARD), biologic/targeted synthetic DMARD (b/tsDMARD), and glucocorticoids (GC).

Results: Our meta-analysis included 35 observational studies composed of 68,537 patients with rheumatic disease. The pooled prevalence of COVID-19 was 0.016 (95% CI 0.008-0.031). The hospitalization rate was 0.54 (95% CI 0.46-0.62); admission to ICU was 0.12 (95% CI 0.09-0.17); death was 0.12 (95% CI 0.10-0.15). Both csDMARDs (OR 2.21 (95% CI 1.55-3.14) and glucocorticoids (OR 2.55 (95% CI 1.13-3.61) were associated with increased risk for hospitalization. Patients on biologic/targeted synthetic DMARDs had decreased risk for hospitalization (OR 0.56,

95% CI 0.40-0.78). Meta-analysis of 16 case control studies showed that RD patients were at increased risk for COVID-19 infection compared to general population (OR 1.57, 95% CI 1.35-1.82). The risk for hospitalization was not increased compared to controls (OR 1.01, 95% CI 0.62-1.63). However, among those hospitalized, patients with RD—compared to non-RD controls—were at increased risk for admission to intensive care unit (OR 1.05, 95% CI 0.75-1.48), use of mechanical ventilation (OR 1.20, 95% CI 0.80-1.80) and death (OR 1.17, 95% CI 1.01-1.36).

Conclusion: In this systematic review and meta-analysis, patients with rheumatic diseases had similar rate of COVID-related hospitalization as non-RD controls. However, hospitalized RD patients had poorer in-hospital outcomes and higher mortality. The poor in-hospital outcomes in RD population with COVID-19 may—at least in part—reflect the use of immunomodulating medications such as glucocorticoids and csDMARDs. A counterintuitive finding from our meta-analysis is the association of b/tsDMARDs with lower risk for hospitalization due to COVID-19. Future studies are necessary to closely examine the risk and protective factors for severe outcomes in RD patients with COVID-19.

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

Abstract Number: 0110

Mortality in 2020 Due to COVID-19 in U.S. Adults with Rheumatic Diseases: Data from a Large, National, Multi-Rheumatic Disease Registry

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Recent studies have detailed the excess death due to COVID-19 during the pandemic, yet few have examined these rates within a rheumatic disease population predisposed to COVID-19 and with extensive disease characterization. We sought to investigate the risk of mortality among patients with rheumatic diseases during 2020, and further examine aspects of those who died of COVID-19.

Methods: We studied non-deceased participants in FORWARD, The National Databank for Rheumatic Diseases, a longitudinal observational study following patients through biannual questionnaires as of January 1, 2020. Primary rheumatic disease diagnosis was confirmed through physicians and categorized as either inflammatory (Inflam) or non-inflammatory (Non-Inflam) and, in a large subset, RA vs Non-Inflammatory Rheumatic Disease (NIRD) that excludes primary fibromyalgia. Mortality was confirmed through US National Death Index-matched death records from 1/1999 through recently released 12/2020. Death records were classified by conditions that appeared concomitantly with COVID-19 to better identify possible misclassification of non-COVID-19 cases earlier in the pandemic (1). Patients were characterized at baseline or study enrollment in Forward. Cox regressions with baseline covariables were used to investigate the risk of mortality by diagnoses. Secondary analyses examined respiratory specific causes and those who died of COVID-19 during 2020. Finally, deaths that occurred in 2020 were compared to a similar cohort of deaths that occurred in 2019.

Results: Among 37,853 participants, 1100 died during 2020 (2.9%) and are characterized in Table 1. Those who died were older, more frequently had a diagnosis of RA, had worse socioeconomic status and disease measures,

and completed fewer questionnaires. By cause of death, those with inflammatory disease or RA had increased respiratory-specific cause of death, while those with NIRD had increased deaths related to heart failure, dementia, and renal failure (Table 2). Deaths from COVID-19 were found in 81 patients, most frequently together with respiratory-specific and diabetes diagnoses. Predictors of mortality were studied among Inflam vs Non-Inflam and also RA vs NIRD. Adjusting for baseline confounders such as sex, age age^2, disease severity, comorbidities, smoking and socioeconomic status, HRs were 1.31 (1.09 – 1.58) for Inflam vs Non-Inflam and 1.28 (1.02-1.60) for RA vs NIRD. For respiratory-specific deaths, the same HR were 1.72 (1.07 – 2.80) and 1.66 (0.92 – 3.00), respectively. There were 1074 deaths in 2019 and the causes of death were similar between 2019 and 2020 with the exceptions of COVID-19 and reduced other causes of death not associated with COVID-19 in 2020.

Conclusion: Using a large, multi-rheumatic disease registry and expedited NDI data, we found COVID-19 to be recorded in 8% of all 2020 deaths and was associated with respiratory failure, diabetes, renal failure, and disassoci-

Table 1. Baseline characterization by 2020 mortality status, % (N) or mean (SD)

Variable	Alive (N=37,853)	Died in 2020 (N=1,100)	P-value	Covid-19 Deaths (N=81)
Diagnosis				
Inflammatory disease	75.20 (27638)	78.18 (860)	0.024	74.07 (60)
Rheumatoid arthritis (RA)	72.50 (25465)	76.89 (822)	0.001	70.51 (55)
Lupus	6.52 (2396)	3.73 (41)	<0.001	7.41 (6)
Spondyloarthritis	2.12 (779)	1.64 (18)	0.271	0.00 (0)
Non-Inflammatory RDs	14.38 (5285)	15.82 (174)	0.181	20.99 (17)
Fibromyalgia	11.71 (4114)	6.83 (73)	<0.001	5.13 (4)
Osteoarthritis (OA)	16.53 (5799)	18.37 (196)	0.112	20.51 (16)
Male sex	15.38 (5441)	20.54 (221)	<0.001	26.92 (21)
Age, yrs	54.33(12.76)	63.67(10.97)	<0.001	62.75 (12.54)
Race/Ethnicity				
White, not of Hispanic origin	86.62 (28366)	88.51 (878)	0.085*	78.46 (51)
Black, not of Hispanic origin	5.79 (1897)	6.25 (62)	0.138	16.92 (11)
Asian or Pacific Islander	1.26 (411)	0.81 (8)	.	1.54 (1)
American Indian/Alaska Native	1.00 (328)	0.91 (9)	.	0.00 (0)
Hispanic	4.34 (1420)	2.82 (28)	.	3.08 (2)
Other	1.00 (326)	0.71 (7)	.	0.00 (0)
Married	68.38 (22133)	65.84 (613)	0.101	58.46 (38)
Education, yrs	13.99 (2.36)	13.35(2.51)	<0.001	13.36 (2.52)
Annual household income, $1000	54.25 (32.93)	43.80 (28.75)	<0.001	43.42 (347.1)
Employed	39.30 (14445)	20.45 (225)	<0.001	27.16 (22)
Disease duration, yrs (SD)	30.95 (10057)	26.25 (258)	.	12.22 (13.39)
Rural vs urban location	24.71 (8904)	27.54 (298)	.	17.95 (14)
Past smoker	32.25 (11173)	37.76 (387)	<0.001	37.31 (25)
Current smoker	12.35 (4278)	14.24 (146)	.	8.96 (6)
RD Comorbidity Index (0-9)	1.71 (1.56)	1.96 (1.62)	<0.001	1.92 (1.47)
Pain VAS (0-10)	4.30 (2.88)	4.27 (2.88)	0.701	4.37 (2.68)
HAQ (0-3)	0.94 (0.69)	1.08 (0.69)	<0.001	1.08 (0.71)
Patient global assessment (0-10)	3.81 (2.61)	3.88 (2.59)	0.460	4.30 (2.52)
Fatigue VAS (0-10)	4.84 (3.13)	4.62 (3.16)	0.032	4.63 (3.06)
Calendar year	2007 (6.21)	2005 (5.90)	<0.001	2006 (5.27)

*Comparison White vs other

Table 2. Primary cause of death in 2020 for conditions most often associated with COVID-19 by rheumatic disease diagnosis group and COVID-19 deaths

N=1,100	Non-Inflam. (N=240)	Inflam. (N=860)	NIRD (N=174)	RA (N=822)	COVID-19 (N=81)
Respiratory system					
Influenza and pneumonia	4.6 (11)*	9.2 (79)*	4.0 (7)*	9.3 (76)*	43.2 (35) §
Chronic lower respiratory	7.1 (17)	10.6 (91)	5.8 (11)	10.7 (88)	13.6 (11)
Other resp. system	14.2 (34)	19.5 (168)	13.2 (23)*	20.2 (166)*	46.91 (38) §
Circulatory system					
Hypertensive disease	19.6 (46)	17.6 (151)	20.1 (36)	17.8 (146)	18.52 (15)
Ischemic heart disease	18.3 (42)	16.9 (145)	19.0 (32)	17.3 (142)	8.64 (7)
Heart failure	17.1 (40)	12.8 (110)	20.1 (36)*	12.9 (106)*	6.17 (5)
Cerebrovascular disease	7.1 (17)	8.4 (72)	6.3 (12)	8.5 (70)	8.64 (7)
Other circul. system	25.4 (60)	24.4 (209)	27.0 (48)	24.4 (200)	23.46 (19)
Malignant neoplasms	14.6 (35)	15.7 (135)	13.1 (23)	15.0 (123)	7.41 (6) §
Alzheimer and dementias	19.8 (47)*	13.4 (114)*	22.2 (39)*	13.7 (112)*	11.11 (9)
Other causes					
Sepsis	5.8 (13)	8.7 (75)	2.8 (5)*	9.0 (74)*	8.74 (75)
Diabetes	10.4 (25)	8.0 (69)	11.9 (21)	8.2 (67)	18.52 (15) §
Obesity	2.5 (6)	1.6 (14)	2.3 (4)	1.6 (13)	3.70 (3)
Renal failure	7.1 (17)	5.7 (49)	9.1 (16)*	5.2 (43)*	9.88 (8) §
Injury, poison and other AE	7.1 (17)	5.1 (44)	6.8 (12)	5.1 (42)	2.47 (2)
All other conditions§§	33.3 (79)*	42.3 (363)*	31.3 (55)*	41.8 (343)*	37.04 (30)
COVID-19	8.8 (21)	7.0 (60)	9.7 (17)	6.7 (55)	---

*P<0.05 §P<0.05 comparing COVID-19 deaths versus other deaths
§§All other conditions include ICD10 codes: A00-A39 A42-B99 D00-E07 E15-E68 E70-E90 F00 F02 F04-G26 G31-H95 K00-K93 L00-M99 N00-N16, N20-N98, O00–O99 P00–P96 Q00–Q99

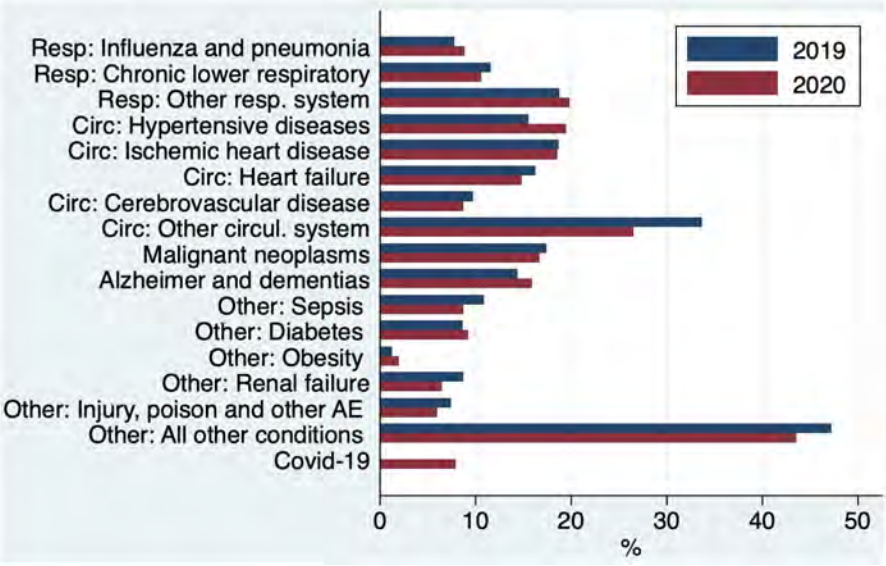

Figure 1. Percentage of deaths in study cohort by primary cause/condition comparing 2019 vs 2020. Among 37,290 participants, 1,074 deaths occurred in 2019 while 1,110 deaths occurred among 37,853 participants in 2020.

ated with malignancies. After accounting for confounders, risks of respiratory death in 2020 were increased among inflammatory rheumatic diseases including RA. Follow-up analyses will formally quantify the excess mortality from COVID-19 in patients with rheumatic diseases.

Disclosure: K. Michaud, None; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Diseases, 3; **R. Schumacher**, None; **M. Kumar**, None; **B. England**, Boehringer-Ingelheim, 2; **A. Freifeld**, None.

Abstract Number: 0111

Risk of Hospitalization, Admission to Intensive Care and Mortality Due to COVID-19 in Patients with Rheumatic Diseases: A Population-based Matched Cohort Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
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Background/Purpose: New cases of the novel coronavirus disease (COVID-19) continue to occur even one year since the declaration of a global pandemic. Although most people will experience mild-to-moderate symptoms, some patients will experience severe and potentially fatal outcomes. Patients with rheumatic diseases may be at higher risk of experiencing severe outcomes compared to the general population. The purpose of this study was to compare the risk of hospitalization, admission to intensive care and mortality due to COVID-19 in patients with rheumatic diseases compared to the general population.

Methods: We used administrative health data from British Columbia (BC), Canada (population 5.1M) to conduct a population-based matched cohort study. Among all COVID-19 cases in BC between February 6, 2020 and April 15, 2021, we used ICD codes to identify all individuals with a rheumatic disease including: rheumatoid arthritis (RA), psoriasis/psoriatic arthritis (PsO/PsA), ankylosing spondylitis (AS), gout, systemic lupus erythematosus (SLE), and other systemic autoimmune rheumatic diseases (SARDs, including systemic sclerosis, Sjogren's syndrome, myopathy, undifferentiated connective disease, and adult systemic vasculitides). All cases of COVID-19 were confirmed by a positive SARS-CoV-2 PCR test from the provincial Centre for Disease Control. Each individual with a rheumatic disease was matched with up to 5 individuals without rheumatic disease of similar age (± 5 years), sex, month and year of COVID-19 diagnosis and health authority. The risk of COVID-19 related hospitalization, intensive care unit (ICU) admission, mortality after COVID-19 diagnosis, and mortality with COVID-19 listed as primary cause were compared using multivariate logistic regression adjusting for age and Charlson Comorbidity Index score.

Results: Among the 104,508 cases of COVID-19 in BC up to April 15th, 2021, we matched 1581 individuals with RA, 1950 PsO/PsA, 378 AS, 1773 gout, 179 SLE, and 660 other SARDs to individuals without rheumatic disease. There was a statistically significant increase in the adjusted risk of hospitalization due to COVID-19 for individulas with RA (OR: 1.58),PsO/PsA (OR: 1.39), AS (OR: 2.16), gout (OR: 1.43), and other SARDs excluding SLE (OR: 1.71). While the risk of ICU admissions was significantly increased only for individuals with RA (OR: 1.43), AS (OR: 2.29) and other

Table 1. Baseline characteristics of rheumatic disease and general population cohorts

	Mean age (SD)	% Female	Mean Charlson Commorbidity Index score (SD)
RA (n=1581)	61.1 (18.4)	69.5	0.75 (1.50)
Non-RA (n=7807)	60.2 (18.2)	69.4	0.64 (1.40)
PsO/PsA (n=1950)	51.7 (18.7)	47.3	0.57 (1.40)
Non-PsO/PsA (n=9699)	51.3 (18.6)	47.2	0.44 (1.22)
AS (n=378)	50.5 (16.2)	50.3	0.52 (1.32)
Non-AS (n=1184)	50.1 (16.1)	50.3	0.34 (1.01)
Gout (n=1773)	62.8 (15.9)	18.3	1.00 (1.83)
Non-gout (n=8787)	62.1 (15.9)	18.3	0.71 (1.49)
SLE (n=179)	51.9 (15.6)	85.5	0.93 (1.68)
Non-SLE (n=887)	51.5 (15.6)	85.3	0.42 (1.20)
Other SARD (n=660)	58.0 (18.1)	70.9	0.84 (1.47)
Non-SARD (n=3267)	57.4(18.0)	71.1	0.58 (1.39)

SARDs excluding SLE (OR: 1.90). Lastly, the risk of mortality was not significantly increased for individuals with rheumatic diseases compared to the general population.

Conclusion: Compared to individuals without a rheumatic disease, individuals with RA, PsO/PsA, AS, gout and SARDs excluding SLE were more likely to experience severe outcomes of COVID-19 including admissions to hospital and ICU. Furthermore, SLE was not associated with an increased risk of severe outcomes of COVID-19 when compared to the general population. Our findings have important implications for patients with certain rheumatic diseases and could inform targeted preventive measures, such as differential isolation measures, priority testing and optimization of vaccination schedules.

Table 2. Association between rheumatic disease status and COVID-19 outcomes

	COVID-19 Hospitalization		COVID-19 ICU Admission		Deaths after COVID-19 diagnosis		Deaths due to COVID-19	
	N	OR (95% CI)*	N	OR (95% CI)	N	OR (95% CI)	N	OR (95% CI)
RA (n=1581)	193	1.58 (1.30, 1.92)	48	1.43 (1.01, 2.02)	95	1.057 (0.82, 1.40)	74	1.14 (0.85, 1.53)
Non-RA (n=7807)	669	1.00 (ref.)	166	1.00 (ref.)	428	1.00 (ref.)	316	1.00 (ref.)
PsO/PsA (n=1950)	158	1.39 (1.13, 1.70)	30	0.90 (0.60, 1.34)	65	0.92 (0.67, 1.28)	47	0.96 (0.66, 1.38)
Non-PsO/PsA (n=9699)	573	1.00 (ref.)	161	1.00 (ref.)	314	1.00 (ref.)	230	1.00 (ref.)
AS (n=378)	35	2.16 (1.38, 3.40)	13	2.29 (1.11, 4.72)	14	1.96 (0.93, 4.15)	11	2.18 (0.97, 4.93)
Non-AS (n=1184)	90	1.00 (ref.)	31	1.00 (ref.)	40	1.00 (ref.)	28	1.00 (ref.)
Gout (n=1773)	261	1.43 (1.20, 1.69)	69	1.15 (0.87, 1.53)	139	1.16 (0.92, 1.47)	96	0.99 (0.75, 1.29)
Non-gout (n=8787)	919	1.00 (ref.)	282	1.00 (ref.)	544	1.00 (ref.)	419	1.00 (ref.)
SLE (n=179)	17	1.57 (0.80, 3.09)	7	3.15 (0.87, 11.43)	6	2.75 (0.67, 11.27)	≤5	N/A†
Non-SLE (n=887)	45	1.00 (ref.)	7	1.00 (ref.)	13	1.00 (ref.)	9	1.00 (ref.)
Other SARD (n=660)	76	1.71 (1.25, 2.32)	21	1.90 (1.10, 3.38)	40	1.44 (0.95, 2.19)	31	1.40 (0.89, 2.20)
Non-SARD (n=3267)	237	1.00 (ref.)	58	1.00 (ref.)	158	1.00 (ref.)	120	1.00 (ref.)

*Multivariable models adjusted for age and Charlson Comorbidity Index

† Unable to report due to policy that impedes publishing small cell sizes

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Abstract Number: 0112

A Randomized Trial Showing No Differences in Patient Satisfaction with Telemedicine Delivered by Phone or Video During COVID-19 in Rheumatology and Other Medical Specialty Clinics

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Demographic characteristics of participants who completed phone surveys and were included in the modified intent to treat analysis; p < 0.05 in bold font.

	Telemedicine Video (N=96)	Telemedicine Phone (N=104)	p
Age, years, median (Q 25-Q 75)	66.75 (62.10-72.45)	62.25 (53.60-68.45)	**0.001**
Age group No. (%)			0.074
<65 years	39 (40.6)	63 (60.6)	
≥65 years	57 (59.4)	41 (39.4)	
Sex, female, No. (%)	67 (69.8)	69 (66.3)	0.71
Race, No. (%)			0.97
White	51 (53.1)	56 (53.8)	
Black	42 (43.8)	44 (42.3)	
Other	3 (3.1)	4 (3.9)	
Insurance plans, No. (%)			**0.03**
Medicare	25 (26.0)	16 (15.4)	
Medicaid	65 (67.7)	71 (68.3)	
Other*	6 (6.2)	17 (16.3)	
Specialty, No. (%)			0.13
Cardiology	28 (29.2)	18 (17.3)	
Family medicine	39 (40.6)	51 (49.0)	
Rheumatology	29 (30.2)	35 (33.7)	
Health status, excellent or very good, No. (%)	70 (72.9)	69 (66.3)	0.48
Education, some college or more, No. (%)	73 (76.0)	75 (72.1)	0.64
Health literacy, inadequate**, No. (%)	23 (24.0)	20 (19.2)	0.52
Employment status, unemployed$, No. (%)	73 (76.0)	83 (79.8)	0.64
Annual income, No. (%)			0.40
Low, < $29,999	14 (14.6)	21 (20.2)	
Medium, $30,000-79,999	28 (29.2)	29 (27.9)	
High, > $80,000	16 (16.7)	10 (9.6)	
Prefer not to answer	38 (39.6)	44 (42.3)	
Area deprivation index (ADI) ranking, state decile, median (Q 25-Q 75)#	5.00 [2.00, 8.00]	5.00 [2.00, 7.75]	0.95
Area deprivation index (ADI) ranking, national percentile, median (Q 25-Q 75)##	67.00 [41.00, 85.00]	69.00 [40.00, 84.75]	0.95

* Viva, Blue Cross Blue Shield, United Health Care, Tricare; **Inadequate health literacy grouped the following answers: "Somewhat", "A little bit", and "Not at all"; $Employed is full-time, part-time, or temporary work; #State decile from 1 (least disadvantaged) to 10 (most disadvantaged); ##National percentile from 1 (least disadvantaged) to 100 (most disadvantaged), missing for 9 participants.

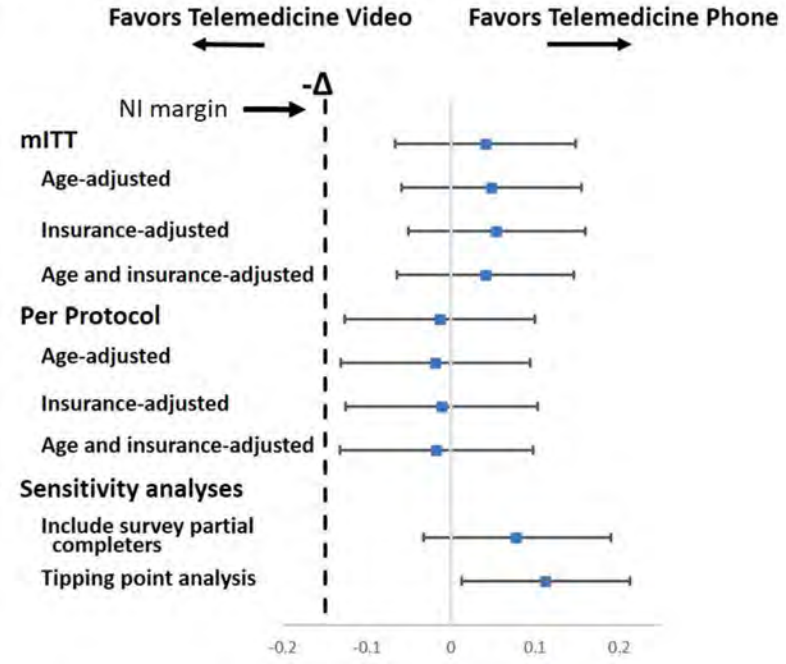
Background/Purpose: The COVID-19 pandemic has led to a significant shift to home-based telemedicine including video and phone-only visits in many medical specialties. However, patients may be agnostic about the relative value and satisfaction with one form of telemedicine compared to another. Thus, the goal of our study was to determine if patient satisfaction with phone-only visits was noninferior to video visits in rheumatology and two other medical clinics at a large tertiary referral center in the Deep South, a region which is home to many socioeconomically disadvantaged older individuals.

Methods: We conducted a parallel group, randomized (1:1), single-blind, noninferiority trial comparing satisfaction rates for two telemedicine delivery methods: phone-only (intervention group) and video visits (standard group). Adults, age >= 60 years or with public insurance (Medicare/Medicaid) were recruited from rheumatology, family medicine,

Table 2. Patient experience with telemedicine phone or video, modified intent-to-treat (mITT) and per protocol analyses; No (%) represented unless otherwise stated.

	Modified Intent-to-treat			Per Protocol		
	Telemedicine Video (N=96)	Telemedicine Phone (N=104)	*p*	Telemedicine Video (N=66)	Telemedicine Phone (N=79)	*p*
Primary Outcome						
Satisfaction rate, score ≥ 9	75 (78.1)	88 (84.6)	0.32	56 (84.8)	66 (83.5)	1
Satisfaction, median (IQR)	10 (9, 10)	10 (9, 10)	0.26	10 (9, 10)	10 (9, 10)	0.52
Secondary Outcomes						
Preference for next visit			0.65			0.35
Telemedicine, same type	29 (30.2)	29 (27.9)		27 (40.9)	27 (34.2)	
Telemedicine, different type	13 (13.5)	19 (18.3)		4 (6.1)	10 (12.7)	
In-office	54 (56.2)	56 (53.8)		35(53.0)	42 (53.2)	
Would recommend telemedicine			0.44			0.62
Yes, definitely	69 (71.9)	74 (71.2)		51 (77.3)	58 (73.4)	
Yes, somewhat	21 (21.9)	25 (24.0)		12 (18.2)	17 (21.5)	
No	6 (6.2)	3 (2.9)		3 (4.5)	2 (2.5)	
No answer	0 (0.0)	2 (1.9)		0 (0.0)	2 (2.5)	
Medical concerns addressed			0.22			0.09
All	80 (83.3)	94 (90.4)		53 (80.3)	71 (89.9)	
Most	12 (12.5)	9 (8.7)		10 (15.2)	8 (10.1)	
Some	4 (4.2)	1 (1.0)		3 (4.5)	0 (0.0)	

Figure 1. Satisfaction (scores of 9 or 10) rates (95% confidence intervals) from modified intent-to-treat (mITT), per protocol, and sensitivity analyses; NI, noninferiority margin.



cardiology clinics. The primary outcome was visit satisfaction rate (9 or 10 on a 0-10 satisfaction scale). Noninferiority was determined if satisfaction with phone-only (intervention) versus video visits (comparator) was no worse by a -15% noninferiority margin. We performed modified intent-to-treat (mITT) and per protocol analysis. We also examined preference for the next visit type, whether patient concerns were addressed during the visit, and whether patients recommended telemedicine.

Results: A total of 200 participants (87.3%), including 96 assigned to video group and 104 assigned to phone-only group, completed surveys on average 2.7 (3.4) days post-visit. A third of the participants were recruited from the rheumatology clinic. This population defines the modified intent-to-treat (mITT) analysis. Overall, participants who completed the surveys were predominately women (N=136, 68%), 86 (43%) were Black with a mean age in the early sixties consistent with the inclusion criteria, and the majority had at least some college education (N=148, 74%) (Table 1).The satisfaction rates were higher than anticipated in both groups (78.1% for video vs 84.6% for phone-only) and not significantly different, (p = 0.32) (Table 2). In the mITT analysis, phone-only visits were noninferior by an adjusted difference of 3.2% (95% CI, -7.6% to 14%). In the per protocol analysis, phone-only were noninferior by an adjusted difference of -4.1% (95% CI, -14.8% to 6.6%) (Figure 1). The proportion of participants who indicated they preferred the same type of telemedicine visit as their next clinic visit were similar (30.2% versus 27.9% video versus phone-only group, p = 0.78) and a majority said their medical concerns were addressed and would recommend a telemedicine visit.

Conclusion: Among a group of diverse, medically at-risk patients seen in rheumatology and two other medical clinics the satisfaction rate for phone-only was noninferior to video visits. Our findings provide added data on patients' acceptance and satisfaction with different types of telemedicine in populations of concern, which can inform clinical, regulatory, and administrative context of telemedicine and related reimbursement policies for medical care of patients with chronic diseases during and beyond the COVID-19 era.

Disclosure: M. **Danila**, Boehringer Ingelheim, 5, Amgen, 1, Amgen, 5, AbbVie, 1, Pfizer, 5, Pfizer, 11, Horizon, 5, Novartis, 1, WebMD, 12, writer; **D. Sun**, None; **L. Jackson**, None; **G. Cutter**, Mitsubishi Tanabe Holdings DSMB, 1, Clinical Trial Solutions LLC, 2; **E. Jackson**, Amgen, 5, Uptodate, 9, McKesson, 2; **E. Ford**, None; **E. DeLaney**, None; **A. Mudano**, None; **J. Foster**, None; **G. Rosas**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5.

Abstract Number: 0113

Reactogenicity of the SARS-CoV-2 Vaccines Associates with Immunogenicity in Patients with Autoimmune and Inflammatory Disease

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Little is known about the reactogenicity and related SARS-CoV-2 vaccine response in patients with chronic inflammatory disease (CID). While researchers have hypothesized increased symptomatology following vaccine would indicate a more robust vaccine response, this has not been demonstrated in the general population. Our objective was to characterize the adverse event (AE) profile in patients with CID receiving the SARS-CoV-2 vaccines and to better understand the relationship between reactogenicity and immunogenicity of the SARS-CoV-2 vaccines in patients with CID.

Methods: This study was part of a larger prospective study examining the immunogenicity and safety profile of the SARS-CoV-2 vaccines in patients with CID. Adults with CID and healthy controls eligible to receive the SARS-CoV-2 vaccine were enrolled. Subjects participated in 3 study visits (pre-vaccine, after dose 1, after dose 2) where blood and clinical data were collected. Assessment of AEs including local and systemic symptoms were solicited within 7 days

Table 1. Demographic and Clinical Characteristics of Participants

Demographic Data	CID (n=134)	Control (n=44)	P-value
Age [years], mean (SD)	46.1 ± 16.3	37.5 ± 18.3	0.003
<65 (%)	85.7	91.1	0.38
65+ (%)	14.3	8.9	
Gender (%female)	74.4	69.9	0.60
Race (%white)	88.0	77.1	0.07
Vaccine			
Pfizer (%)	85.0	95.6	0.06
Moderna (%)	15.0	4.4	
Immunologic Diagnosis			N (%)
Inflammatory Bowel Disease			42 (31.6)
Rheumatoid Arthritis			38 (28.6)
Spondyloarthritis			20 (15.0)
Systemic Lupus Erythematosus			15 (11.3)
Other Connective Tissue Disease			12 (9.0)
Vasculitis			5 (3.8)
Multiple Sclerosis			9 (6.8)
Autoinflammatory Syndrome			2 (1.5)
NMO			1 (0.8)
IgG4-Related Disease			2 (1.5)
Medications			N (%)
Prednisone			17 (12.8)
Disease Modifying Antirheumatic Drug			
Methotrexate			29 (21.8)
Hydroxychloroquine			30 (22.6)
Mycophenolate Mofetil			9 (6.8)
Azathioprine			4 (3.0)
Leflunomide			2 (1.5)
Sulfasalazine			7 (5.3)
Janus Kinase inhibitors			11(8.3)
Biological therapies			
Tumor Necrosis Factor inhibitors			38 (28.6)
B cell depleting therapies			10 (7.5)
Belimumab			3 (2.3)
Vedolizumab			12 (9.0)
Interleukin 12/23 or 23 inhibitors			10 (7.5)
Other			4 (3.0)
Nonsteroidal Anti-inflammatory Drugs			27 (20.3)

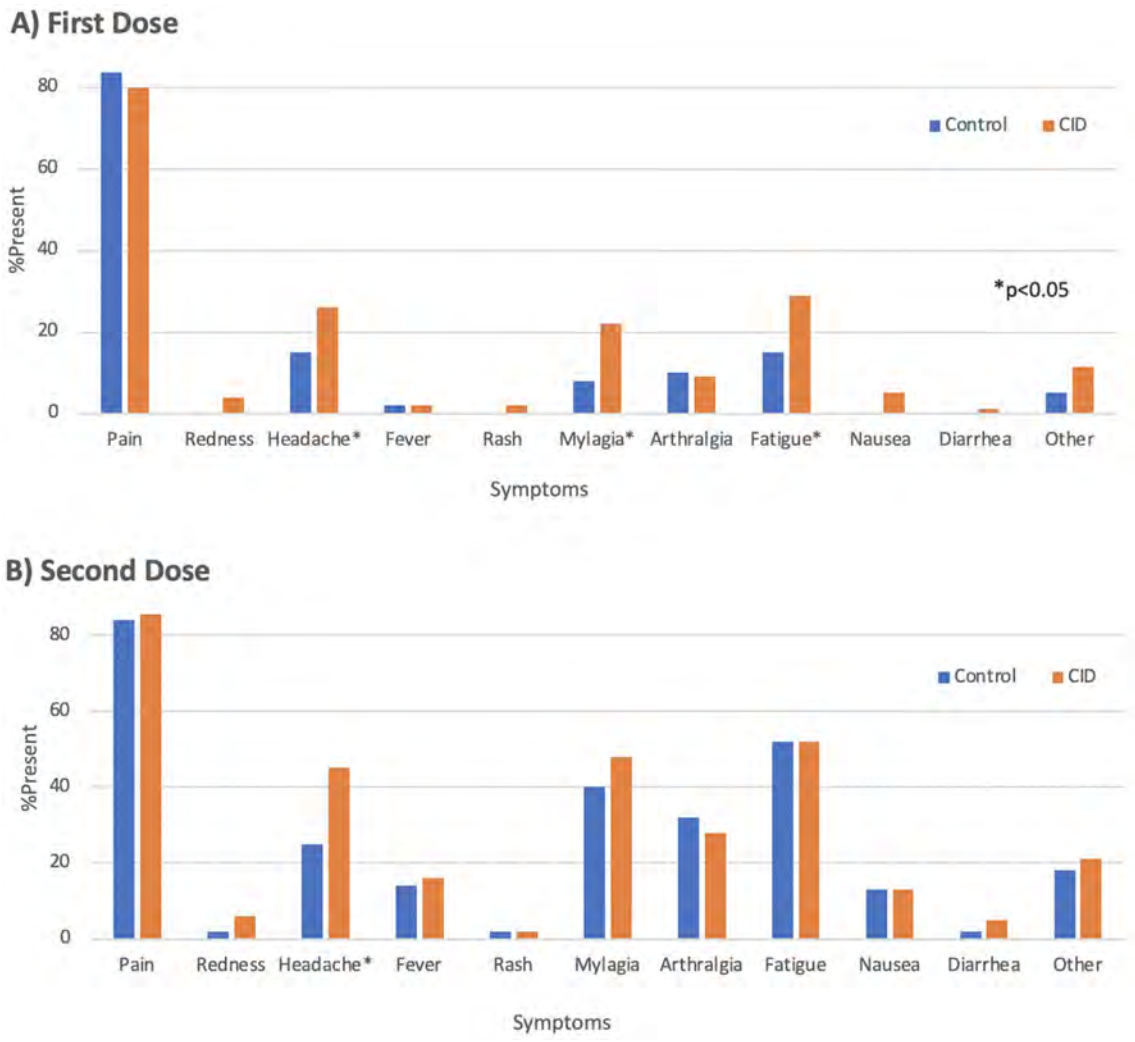

Figure 1. Solicited Symptoms among Control vs. CID Patients.

of receiving each vaccine dose. Serum anti-SARS-CoV-2 spike (S) IgG$^{\pm}$ antibody titerswere quantified to assess the magnitude of the humoral response following vaccination. Statistical analysis of solicited symptoms was performed utilizing two sample t-test and z-test. To study reactogenicity impact on vaccine antibody response, tobit regressions adjusting for patient status, age, gender, and vaccine type were utilized to account for left-censoring below the response detect limit.

Results: 178 participants were included in this study including 134 patients with CID and 44 healthy controls. Demographic and clinical characteristics are shown in Table 1. Solicited symptoms among controls and CID patients are shown in Figure 1. CID patients experienced significantly more symptoms after the 1st dose of vaccine compared to controls (p=0.04), including more headache, myalgia and fatigue (p< 0.05). For immunogenicity, after adjustment for covariates, a higher number of reported symptoms after the second dose was associated with higher antibody titers (p=0.028). Each increase of one endorsed symptom was associated with 15.9% increase in antibody titer. Among all individual symptoms (Table 2), the most strongly associated at each dose included site pain after 1st dose (p=0.04) with 118% increase in antibody titer when present and fatigue after 2nd dose (p=0.02) with 91.6% change in antibody titer when present.

Table 2. Symptom measures associated with increased SARs-CoV-2 antibody titers

Symptom (Dose)	CID Antibody Titer (x10³)	Control Antibody Titer(x10³)	%Change§	P value
Site Pain (1)			118.0%	0.037
Present	6.0 ± 12.0	8.6 ± 6.8		
Absent	2.6 ± 3.2	7.5 ± 4.9		
Fatigue (2)			91.6%	0.023
Present	6.8 ± 14.4	9.8 ± 6.9		
Absent	3.9 ± 4.6	6.6 ± 5.6		
Nausea (2)			130.4%	0.043
Present	12.5 ± 27.1	9.7 ± 3.9		
Absent	4.4 ± 5.0	8.0 ± 6.9		
Myalgia (2)			67.4%	0.074
Present	6.9 ± 14.9	10.2 ± 6.8		
Absent	4.0 ± 4.8	6.3 ± 5.6		

SARS-CoV-2 Antibody Titer reported as 10^3. §Percent change in SARS-CoV-2 antibody titer if the symptom is present vs absent after adjusting for patient status, age, gender and vaccine type.

Conclusion: This study is one of the first to examine reactogenicity of the novel SARS-CoV-2 vaccines among patients with CID and the relationship between reactogenicity and vaccine response. We demonstrated that patients with CID have a distinct reactogenicity profile from their healthy control counterparts with CID patients having more numerous symptoms following 1st dose of vaccine. Furthermore, we demonstrated an association between reactogenicity and immunogenicity in CID patients. This finding, thus far not seen in the general population, may speak to the more variable immunogenicity in patients with CID and could be an important indicator of vaccine response to the novel SARS-CoV-2 vaccines.

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Abstract Number: 0114

The Safety Profile of SARS-CoV-2 Vaccines Among Patients with Immune-Mediated Rheumatic Diseases

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Cohort of patients with IMRD vaccinated against SARS-CoV-2

	N=285	%
Gender (Female)	193	67.7
Mean age (years), SD	53.2 ± 14.5	range 18-92
Underlying IMRD		
RA	126	44.2
PsA	46	16.1
Spa	61	21.4
SLE	21	7.4
Palindromic rheumatism	4	1.4
Juvenil idiopathic arthritis	4	1.4
Polymyalgia rheumatica	4	1.4
Other inflammatory arthritis	5	1.8
Other systemic autoimmune diseases *	10	3.5
Other autoinflammatory diseases**	4	1.4
Underlying treatment		
DMARD	160	56.9
MTX	72	25.2
Antimalarials	26	9.1
bDMARD	207	73.1
Targeted therapies (bFAMEs/JAK inhibs)	**N=218**	%
Anti-TNF	146	66.9
Anti-IL6	34	15.5
Anti-IL17/IL-23	16	7.3
Jak Inhibs	11	5.0
Rituximab	7	3.2
Belimumab	3	1.3
Anakinra	1	0.4
Stop/delay of DMARD after vaccination	29/160	18
Stop/delay of targeted therapy after vaccination	15/208	7.2

(*) Systemic sclerosis N=3, Sjögren syndrome N=2, Mixed connective tissue disease N=1, Poliautoimmune syndrome N=1, Evans syndrome N=1, Morphea N=1,Sarcoidosis N=1.
(**) Behçet syndrome= 2, SAPHO=1; hyper IgD syndrome =1

Background/Purpose: The best strategy for the prevention of SARS-CoV-2 infection is vaccination. Both mRNA and vector vaccines have demonstrated a satisfactory safety profile in general population but information about their utility in patients with immune-mediated rheumatic diseases (IMRD) is scarce. Both mRNA and viral vector vaccines have demonstrated a satisfactory safety profile in general population but information about their utility in patients with immune-mediated rheumatic diseases (IMRD) is scarce.

Methods: Observational prospective study conducted in a tertiary University center in Catalonia, Spain in patients with IMRD vaccinated between January to May 2021. Patient's information was obtained during clinical visits and follow-up was made by telephonic interviews. Vaccination was confirmed using the electronic clinical records of the local health system. We considered as fully vaccinated those patients with 2 doses of mRNA vaccines and 1 for vector or patients with previous SARS-CoV-2 infection who received 1 dose. Descriptive analysis was done. This study was approved by our hospital's Ethical Committee.

Results: At the end of May, 285 patients with IMRD were registered. Most of the patients were female 193 (67%) with a mean age of 53.2 ± 14.5 years (range 18-92). Main IMRD were rheumatoid arthritis in 126 (42%), followed by spondyloarthropathies in 61 (21%), psoriatic arthritis in 46 (16%) and systemic lupus erythematosus in 21 (7.4%) among others (See Table).

Eight percent of patients had previous SARS-CoV-2 infection before vaccination. At the moment of the first dose, 73% of patients were in remission, 17% with low disease activity, 3% with moderate activity and only 2% with high disease activity.

A total of 160 (57%) patients were under DMARD treatment and 65 (22%) with glucocorticoids (mean dose 6.0 ± 4.4 mg/d), 218 (76%) were under targeted therapies (207 bDMARD and 11 with JAK inhibitors). The main bDMARD used are described in detail in Table.

A total of 128 (45%) of patients were fully vaccinated. Vaccines received included: Moderna in 73%, Pfizer/BioNTech in 17.5%, Astra Zeneca in 9 % and Janssen in 0.4%. Eighteen and 8% of patients stop or delayed DMARD and bDMARD, respectively after vaccination.

Underlying IMRD flare was reported in 16 (5.6%) of patients all of them mild or moderate. Main symptoms included arthralgias (9), arthritis (4), inflammatory back pain (2), and psoriasis (1). Only 1 patient had COVID-19 infection 1 week after first vaccine dose. A total of 153 (53%) patients reported any symptom related to vaccination, basically injection site pain (48%), myalgias (11%), and fever (8%). One patient had oral herpes after vaccination.

Conclusion: Among patients with IMRD, the safety profile of vaccines for SARS-CoV-2 was satisfactory. Disease flares were uncommon (5%) and mostly mild. Vaccination side effects were similar to expected for the general population reassuring the importance of SARS-CoV2 vaccination in patients with IMRD.

Disclosure: J. Gomez-Puerta, Abbvie, 6, BMS, 6, GSK, 6, Galapagos, 1, Janssen, 6, Pfizer, 6, Roche, 6, Sanofi, 1, Lilly, 6, MSD, 6; **N. Sapena**, None; **J. Sarmiento-Monroy**, None; **A. Azuaga**, None; **V. Ruiz-Esquide**, Lilly, 6, Abbvie, 6, Pfizer, 6, Roche, 6; **B. Frade-Sosa**, Abbvie, 6; **M. Bassas**, None; **R. Morlà**, None; **A. Ponce**, Pfizer, 6, Lilly, 6; **J. Cañete**, Abbvie, 6, Pfizer, 6, Janssen, 6; **J. Ramirez**, Abbvie, 6, Janssen, 6, Lilly, 6, Pfizer, 6, MSD, 6; **A. Villella**, None; **A. Trilla**, None; **R. Sanmarti**, Abbvie, 6, BMS, 5, BMS, 6, Sandoz, 6, Pfizer, 6, Roche, 6, MSD, 6.

Abstract Number: 0115

Rheumatic Disease Management by Resilient Rheumatology Providers in COVID-19 Pandemic: A National Veterans Affairs Follow-up Survey Assessing Provider Practice and Views Since June 2020

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To assess the experience, current practices, views and opinions of rheumatology providers at Veterans Affairs (VA) facilities for the care of the patients with rheumatic disease during the COVID-19 pandemic in 2020-21

Methods: We performed an anonymized cross-sectional survey to assess VA rheumatology provider perspective on COVID-19 healthcare issues and resilience, from November 2020 to January 2021, and compare practices to the baseline survey from April-May 2020 (Singh JA, ACR 2020).

Results: Of the 153 eligible VA rheumatologists, 114 (75%) completed the survey. The mean CD-RISC2 score was 6.8 (SD, 1.11; range 0-8; higher=more resilient), higher than the original survey score of 6.35 (SD, 1.26; p=0.004 and p=0.008, respectively). The proportion of rheumatology providers who chose telephone or VVC as the best modality for follow-up of established patients varied widely across rheumatic diseases as follows (Figure 1): (1) gout, osteoporosis, polymyalgia rheumatica, or osteoarthritis (OA), 90-100%; (2) stable rheumatoid arthritis (RA), stable spondyloarthritis (SpA) or stable lupus, scleroderma or vasculitis, 73-88%; (3) local musculoskeletal conditions or tendinitis, 45-46%; (4) lupus, scleroderma, vasculitis, RA or SpA with immunosuppressive, glucocorticoid or disease-modifying antirheumatic disease drug (DMARD)/biologic) changes, 9-20% (Figure 1).

Compared to the original survey, the use of telephone visits was lower by 10-20%, while VVC and in-person were higher by about 10%.

Comfort with Technology: Established Patients. Provider comfort with technology was essentially unchanged compared to the original survey: (1) telephone visits, 82%; (2) VVC visits, 63%. 33% were comfortable with CVT visits, with no previous comparator question (Figure 2). *New patients*. Provider comfort with technology increased compared to the original survey: telephone visits, 40% vs. 25% (p=0.019); VVC visits, 47% vs. 34% (p=0.051; Figure 2).

Comfort with the Quality of Outpatient Visits and Improvement in Comfort Since June 2020 (no previous data/comparator): Providers comfort with the quality of clinical encounter for *established vs. new patients* was as follows (Figure 3): (1) telephone, 63% vs. 27%; (2) VVC, 63% vs. 47%; and (3) CVT 32% vs. 27%. Improvement in comfort with the quality of the clinical encounter since June 2020 for *established vs. new patients* was as follows: telephone, 66% vs. 46%; VVC, 67% vs. 58%; and CVT, 31% vs. 27%.

Adjusted for age, sex, and ethnicity, high provider resilience was significantly associated with a higher odds ratio (OR) of comfort with technology and comfort with the quality of the VVC visit: (1) established patient, 1.71 (95% CI, 0.67-4.40) and 4.13 (95% CI, 1.49-11.44); (2) new patient, 2.79 (95% CI, 1.11-7.05); and 2.69 (95% CI, 1.06-6.82), respectively.

Conclusion: Utilization of and comfort with video visits during the COVID-19 pandemic increased over time among VA rheumatology providers, also associated with provider resilience

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Disclosure: J. Singh, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2, Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4; **J. Richards**, None; **E. Chang**, None; **A. Joseph**, None; **B. Ng**, None.

Abstract Number: 0116

COVID-19 mRNA Vaccine Side Effects Among Individuals with Rheumatic Disease

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Characteristics of vaccinated respondents by side effect experience and vaccine received

	Side Effect Experience			Vaccine Received		
	No Side Effects n=949	Side Effects n=876	*p* value	Pfizer-BioNTech n=990	Moderna n=835	*p* value
Demographics						
Age, years	68.9 (9.4)	65.8 (11.2)	<0.001	67.0 (10.7)	67.9 (10.0)	0.09
Female	76.6	83.9	<0.001	80.1	80.2	0.95
White	94.7	93.7	0.39	93.3	95.4	0.05
Education, years	15.3 (2.1)	15.6 (1.9)	<0.001	15.5 (2.0)	15.4 (2.0)	0.26
Married	69.6	72.9	0.14	70.2	72.2	0.38
Rural	18.3	16.8	0.40	12.7	23.2	<0.001
History of smoking	39.1	35.2	0.09	35.8	39.0	0.17
BMI, kg/m2	27.8 (6.7)	27.4 (6.3)	0.24	27.4 (6.4)	27.9 (6.6)	0.13
Patient-reported outcomes						
Pain (0-10)	3.0 (2.6)	3.2 (2.7)	0.15	3.1 (2.7)	3.0 (2.6)	0.16
Global severity (0-10)	3.1 (2.3)	3.0 (2.3)	0.61	3.1 (2.4)	3.1 (2.3)	0.99
HAQ-II (0-3)	0.7 (0.6)	0.7 (0.6)	0.35	0.7 (0.6)	0.7 (0.6)	0.75
PAS-II (0-10)	2.8 (2.0)	2.8 (2.0)	0.81	2.8 (2.0)	2.7 (2.0)	0.53
Primary diagnosis						
RA	65.4	61.0		63.4	63.3	
OA	16.4	15.9		16.8	15.4	
SLE	4.8	4.4	0.12	3.7	5.6	0.32
FM	2.8	4.8		3.1	4.4	
PsA	3.3	3.9		4.0	3.1	
Other	7.4	10.0		9.0	8.3	
Medications						
csDMARD	47.5	46.7	0.77	46.5	47.9	0.59
bDMARD	33.2	32.6	0.82	33.7	32.0	0.49
tsDMARD	5.7	5.3	0.71	5.4	5.7	0.80
Glucocorticoid	17.1	15.7	0.49	17.2	15.5	0.40
Pandemic-related						
Fully vaccinated	54.8	77.7	<0.001	67.6	63.4	0.06
COVID-19 stress (0-3)	1.5 (0.8)	1.7 (0.7)	<0.001	1.6 (0.8)	1.6 (0.7)	0.86
Sought COVID-19 testing	44.3	48.8	0.08	47.9	44.7	0.21
Tested positive	2.1	4.4	0.02	3.3	3.1	0.84

Values are mean (SD) or %.
Vaccinated = received at least one vaccine dose at the time of the monthly questionnaire response.
HAQ-II=Health Assessment Questionnaire II; PAS-II=Patient Activity Scale II; csDMARD = conventional synthetic DMARD; bDMARD=biologic DMARD; tsDMARD=targeted synthetic DMARD

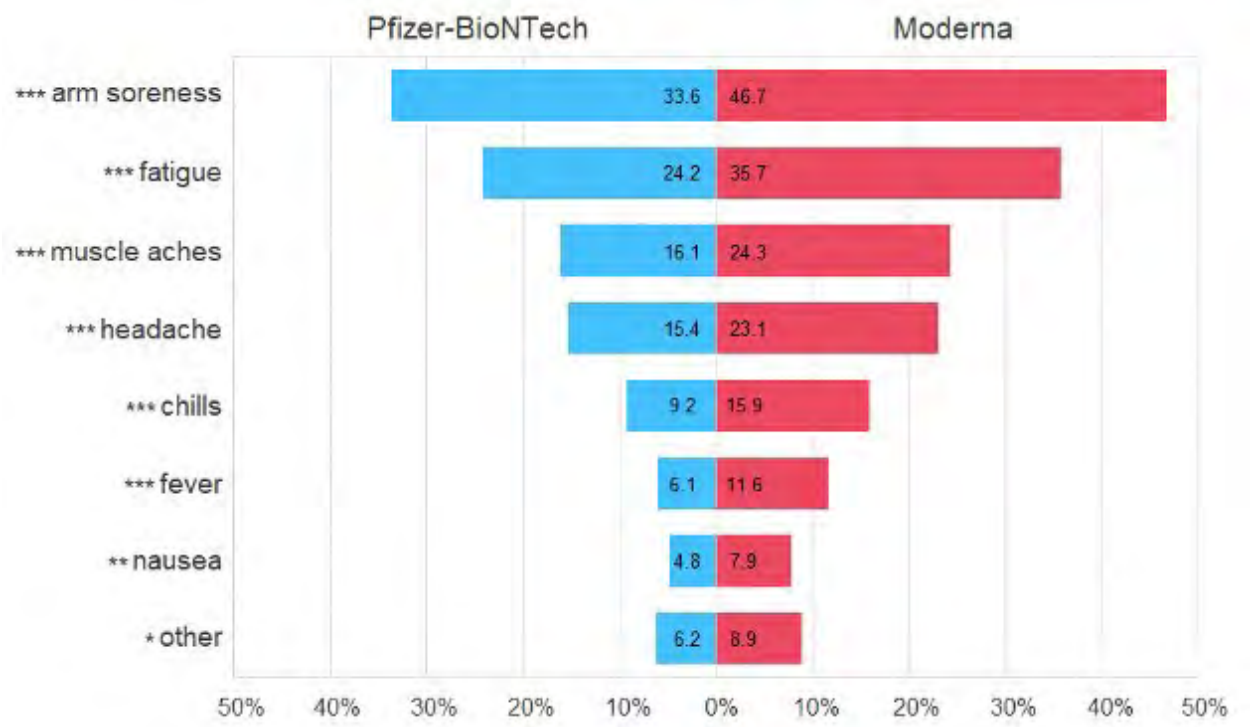

Figure 1. Frequency of side effects by vaccine type. Asterisks indicate statistical significance (*p<0.05, **p<0.01, ***p<0.001).

Background/Purpose: Over 135 million Americans were fully vaccinated to COVID-19 by June 2021, yet there was a paucity of data on side effects for those with autoimmune conditions commonly seen in rheumatology. Side effects can prevent recipients from receiving a second vaccination and can be related to the immunogenicity of the vaccine and/or recipient. The purpose of our study was to characterize the rates and types of COVID-19 vaccine side effects in adults with rheumatic diseases and assess if there were associations with disease treatment, severity, or vaccine type.

Methods: Data were provided by adults enrolled in FORWARD, The National Databank for Rheumatic Diseases. Participants complete comprehensive semiannual questionnaires and were invited to answer supplemental questionnaires focused on COVID-19 vaccination in March and April 2021. Only individuals who received Pfizer-BioNTech or Moderna vaccines were included in this study due to insufficient sample sizes for other vaccines. Vaccinated respondents were compared by whether they reported experiencing side effects following vaccination and by vaccine type, with significance ($p < 0.05$) assessed by Student's t-tests and chi-squared tests, as appropriate. Factors associated with side effects were identified with logistic regression models for the full cohort and for each vaccine type adjusted for age, sex, race, education, rural residency, BMI, physical function (HAQ-II), COVID-19-specific stress (Likert scale), corticosteroid use, hierarchical DMARD group (reference: no DMARD), and diagnosis (reference: OA).

Results: Among 1825 vaccinated respondents, 876 (48%) reported experiencing side effects (Table 1). The most reported side effects included arm soreness (40%), fatigue (30%), muscle aches (20%), and headache (19%). The ranked frequency of each side effect did not differ by vaccine type, though incidence of each side effect was significantly higher among those who received the Moderna vaccine than in those who received the Pfizer-BioNTech vaccine (Figure 1). In the full cohort, younger age, female sex, higher education, full vaccination, and higher COVID-19-related stress were all associated with higher risk of experiencing side effects (Figure 2). Differences by age held true in both the Pfizer-BioNTech (OR 0.96 [0.94, 0.98]) and Moderna (0.97 [0.95, 0.99]) models. Differences by sex (OR 1.83 [1.04, 3.24]) and by COVID-19-related stress (1.5 [1.13, 2.00]) were specific to Moderna vaccine recipients, while differences by education (1.16 [1.04, 1.30]) were specific to Pfizer-BioNTech vaccine recipients.

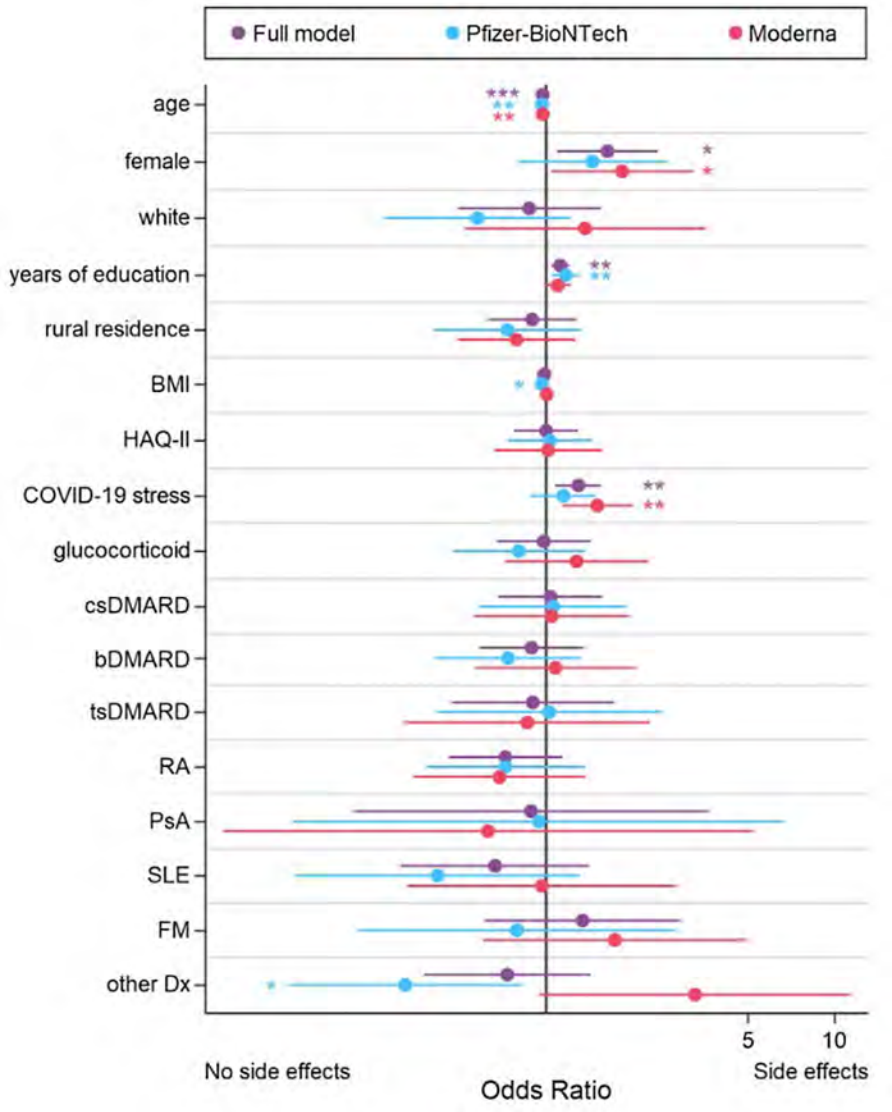

Figure 2. Odds ratios and 95% confidence intervals for factors associated with side effects to COVID-19 vaccine for the full cohort (purple), Pfizer-BioNTech vaccine recipients (blue), and Moderna vaccine recipients (red). Asterisks indicate statistical significance (*$p<0.05$, **$p<0.01$, ***$p<0.001$).

Conclusion: Our findings of increased side effects to Moderna vaccines was consistent with the larger US population, though our side effect rates were comparatively lower and more similar to CDC surveillance[1] after only the first mRNA vaccine even after accounting for our cohorts' older age. A lack of reactogenicity with rheumatic disease, severity, and treatments may be reassuring for the vaccine hesitant, but additional investigation is needed to understand if these lower rates are due to a potentially reduced immune response.

[1]Chapin-Bardales et al. "Reactogenicity Following Receipt of mRNA-Based COVID-19 Vaccines," JAMA, 2021

Disclosure: K. Michaud, None; **A. Cornish**, None; **A. Freifeld**, None; **P. Katz**, None; **K. Wipfler**, None.

Abstract Number: 0117

Flares Following Herpes Zoster Recombinant Zoster Vaccination Among Adults Age ≥50 Years with Immune Mediated Inflammatory Diseases in the United States

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Vaccination (0084–0117)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Although persons with immune mediated inflammatory diseases (IMIDs) are at increased risk of herpes zoster (HZ), there are limited data published on the safety of recombinant zoster vaccine (RZV, Shingrix), or novel vaccine adjuvants, in these populations. We conducted a self-controlled case series analysis (SCCS) to evaluate the risk of possible vaccine-related flares following RZV vaccination in adults with IMIDs.

Methods: We used medical claims data from the 2017–2019 IBM® MarketScan® (persons age 50–64 years) and 2017–2020 Centers for Medicare and Medicaid Services Medicare (persons age ≥65 years) databases to examine flares after RZV vaccination in persons with IMIDs (Rheumatoid Arthritis, RA; Ankylosing Spondylitis, AS; Axial Spondyloarthritis, SpA; Psoriatic Arthritis, PsA; Psoriasis, PsO; Inflammatory Bowel Disease, IBD; Crohn's Disease, CD; Ulcerative Colitis, UD; Systemic lupus erythematosus, SLE). IMIDs were defined using all 3 of the following criteria: (a) ≥2 outpatient visits for their respective conditions, and (b) ≥1 claim for disease-specific medications, and (c) ≥1 visit to a relevant specialist (rheumatologist for RA, AS, SpA, PsA, SLE; gastroenterologist for IBD, CD, UC; dermatologist for PsO). RZV vaccination was defined using NDC and CPT codes. Presumed flares were defined as hospitalization or ER visit for their condition, or treatment with a Medrol Dosepak or steroid injection. We used SCCS methods to compare the rates of flares 1–42 days after (risk window) as compared to 98–140 days prior to RZV vaccination (control window) within individuals.

Results: There were 7,069 50–64-year-olds and 72,434 ≥65-year-olds with both an IMID and ≥1 dose of RZV [Table 1]. Among 50–64-year-olds, 10% developed flares during the control window, and 9% developed flares in the risk window following 1 or 2 doses of RZV. Among ≥65-year-olds, 13% developed flares during the control window, and 11–12% developed flares in the risk window following 1 or 2 doses of RZV. We did not find a statistically significant increase in flares following RZV vaccination for any IMID condition in either age group following either 1 or 2-doses of RZV [Table 2].

Conclusion: This observational study provides new data on the safety of RZV vaccination in adults age ≥50 years with selected IMIDs. Within the limitations of administrative data and our presumed flare definition, we did not find a significant increase in presumed flares for any IMID condition evaluated or by RZV vaccine dose. There were a number of limitations with this study related to distinguishing vaccine-induced flares from reactogenicity and disease worsening. Additional work is ongoing to refine and validate IMID case and flare definitions. Further evaluation of the safety of RZV vaccination in this population is needed to inform vaccine policy recommendations and clinical guidance.

Table 1. Characteristics of Adults Age ≥50 Years with Immune Mediated Inflammatory Diseases (IMIDs) who Received ≥1 Dose of Recombinant Zoster Vaccine (RZV)

	Any IMID	RA	AS	SPA	PsA	PsO	IBD	CD	UC	SLE
MarketScan Patients (Age 50–64 Y)										
No. of Patients	7069	3415	29	37	992	1039	1477	594	916	507
Age in years, Median (IQR)	59 (55-62)	59 (56-62)	55 (53-62)	55 (53-61)	59 (55-62)	59 (56-62)	59 (55-61)	58 (55-61)	59 (55-61)	58 (54-61)
Gender (%)										
Male	31%	21%	76%	62%	42%	42%	45%	43%	46%	8%
Female	69%	79%	24%	38%	58%	58%	55%	57%	54%	92%
RZV Vaccination (#)										
≥1 dose	7069	3415	29	37	992	1039	1477	594	916	507
≥2 doses	4592	2025	18	23	600	613	896	349	571	292
Interval between doses in days (Median, IQR)		89 (69-125)	105 (80-119)	98 (64-119)	85 (68-118)	91 (68-131)	87 (69-122)	85 (68-125)	88 (70-120)	91 (69-135)
Flare (%)										
Control window (15-20 weeks before RZV)	10%	13%	7%	8%	10%	7%	7%	8%	7%	10%
Dose 1 risk (1-42 days after dose 1)	9%	11%	14%	14%	12%	8%	7%	9%	7%	9%
Dose 2 risk window (1-42 days after dose 2)	9%	11%	6%	4%	10%	9%	8%	8%	7%	10%
CMS Medicare Patients (Age ≥65 Y)										
No. of Patients	72434	45851	36	43	6678	5993	12679	5384	7416	4205
Age in years, Median (IQR)	73 (70-78)	74 (70-79)	73 (70-76)	73 (69-75)	72 (69-76)	73 (69-77)	73 (70-77)	73 (70-77)	73 (70-78)	72 (69-77)
Gender										
Male	30%	25%	61%	60%	40%	43%	44%	42%	45%	12%
Female	70%	75%	39%	40%	60%	57%	56%	58%	55%	88%
RZV Vaccination										
≥1 dose	72434	45851	36	43	6678	5993	12679	5384	7416	4205
≥2 doses	62071	35981	31	39	5409	4737	10279	4231	6045	3222
Interval between doses in days (Median, IQR)		96 (71-138)	90 (70-140)	91 (70-135)	96 (71-136)	95 (70-134)	95 (70-135)	96 (71-137)	94 (70-133)	97 (71-138)
Flare										
Control window (15-20 weeks before RZV)	13%	14%	8%	14%	13%	10%	9%	11%	9%	11%
Dose 1 risk (1-42 days after dose 1)	12%	13%	8%	7%	13%	10%	9%	10%	9%	11%
Dose 2 risk window (1-42 days after dose 2)	11%	13%	13%	15%	12%	9%	9%	11%	8%	12%

Table 2. Self-Controlled Case Series Analysis of Flares among Adults Age ≥50 Years with Immune Mediated Inflammatory Diseases (IMIDs) who Received 1 or 2 Doses of Recombinant Zoster Vaccine (RZV)

	Control Window	Risk Window	
	Flares 15–20 weeks before Shingrix (42 d)	Flares 1–42 days after Shingrix	
Group	#	#	Rate Ratio
MarketScan Patients (Age 50–64 Y)			
RA-1 dose	448	364	0.8 (0.7-0.9)
RA-2 dose	253	219	0.9 (0.7-1.0)
AS-1 dose	2	4	2.0 (0.4-10.9)
AS-2 dose	2	1	0.5 (0.0-5.5)
SPA-1 dose	3	5	1.7 (0.4-7.0)
SPA-2 dose	3	1	0.4 (0.0-3.2)
PSA-1 dose	102	116	1.1 (0.9-1.5)
PSA-2 dose	60	56	0.9 (0.6-1.3)
PSO-1 dose	71	87	1.2 (0.9-1.7)
PSO-2 dose	43	52	1.2 (0.8-1.8)
IBD-1 dose	108	110	1.0 (0.8-1.3)
IBD-2 dose	67	66	1.0 (0.7-1.4)
CD-1 dose	50	53	1.1 (0.7-1.6)
CD-2 dose	28	27	1.0(0.6-1.6)
UC-1 dose	60	62	1.0 (0.7-1.5)
UC-2 dose	39	38	1.0 (0.6-1.5)
SLE-1 dose	52	48	0.9 (0.6-1.4)
SLE-2 dose	31	27	0.9 (0.5-1.5)
Any IMID-1 dose	726	671	0.9 (0.8-1.0)
Any IMID-2 dose	422	393	0.9 (0.8-1.1)
CMS Medicare Patients (Age ≥65 Y)			
RA-1 dose	6,362	6,020	0.9 (0.9-1.0)
RA-2 dose	4,879	4,491	0.9 (0.9-1.0)
AS-1 dose	3	3	1.0 (0.2-5.0)
AS-2dose	2	4	1.8 (0.4-8.2)
SPA-1 dose	6	3	0.5 (0.1-2.0)
SPA-2 dose	4	6	1.3 (0.4-4.1)
PSA-1 dose	881	836	0.9 (0.9-1.0)
PSA-2 dose	714	629	0.9 (0.8-1.0)
PSO-1 dose	618	585	0.9 (0.8-1.1)
PSO-2 dose	483	432	0.9 (0.8-1.0)
IBD-1 dose	1,198	1,157	1.0 (0.9-1.0)
IBD-2 dose	968	928	1.0 (0.9-1.1)
CD-1 dose	585	540	0.9 (0.8-1.0)
CD-2 dose	463	458	1.0 (0.9-1.1)
UC-1 dose	635	633	1.0 (0.9-1.1)
UC-2 dose	521	475	0.9 (0.8-1.1)
SLE-1 dose	474	470	1.0 (0.9-1.1)
SLE-2 dose	354	363	1.0 (0.9-1.2)
Any IMID-1 dose	9,073	8,595	0.9 (0.9-1.0)
Any IMID-2 dose	7,029	6,503	0.9 (0.9-1.0)

Disclosure: J. Curtis, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **y. Su**, None; **F. Xie**, None; **c. Clinton**, None.

Abstract Number: 0118

Multidimensional Phenotypes of Sleep Quality Using the Pittsburg Quality Sleep Index and Associations Among Sleep Dimensions and Symptoms in Women Diagnosed with Fibromyalgia

Victoria Menzies, Debra Lynch Kelly and Miichael Weaver, University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: There are over 10 million people in the United States suffering with fibromyalgia syndrome (FMS). Individuals with FMS typically report multiple concurrent symptoms including chronic pain, fatigue, distressed mood and sleep disturbances. Evidence demonstrates that 70%-80% of FMS patients suffer from non-restorative sleep; however, dimensions of sleep disturbance in patients with FMS and associations with symptoms are relatively unexamined in this population but necessary to develop personalized strategies to mitigate symptoms and improve functionality and quality of life for this patient population.

Methods: The objective of this analysis was to phenotype dimensions of sleep in a cohort of 50 women at least 18 years old with a confirmed diagnosis of FMS using previously collected data and to examine associations among sleep dimensions and symptoms (pain, fatigue, depression and anxiety). Sleep dimensions were evaluated using the 19-item self-report Pittsburgh Quality Sleep Index (PQSI) that provides information about multiple dimensions of sleep (quality and patterns). Total PQSI scores over 5 indicate severe sleep disturbance. Well-validated measures were used to assess pain, fatigue, depression and anxiety. R version 4.05 was used for statistical analyses. Descriptive statistics report demographic and clinical characteristics. Distributions for robust correlation coefficients among sleep and symptoms were estimated using a Bayesian approach. Bayes factors (BF) were used as measure of strength of evidence for presence of an association.

Results: The mean age of the sample was 48 (SD=11.8). The majority were white (n=26) and non-Hispanic (n=49). Mean global sleep quality was 11.7 (SD=4.7). Mean pain severity reported was 6.0 (SD=1.7) and pain interference was 6.0 (SD=2.3). Severe fatigue was reported by 50% of the participants. At least moderate depressive symptoms were reported by 56% of study participants, and the mean trait and state anxiety were 48.9 (SD=12.8) and 44.1 (SD=13.5) respectively. Forty-eight (48) bivariate correlations were examined: 19 demonstrated at least moderate evidence supporting an association, with coefficients ranging from .30 to .54: 4 had BF 3-10 (moderate), 7 had BF 10-30 (strong), 1 had a BF 30-100 (very strong), and 7 had a BF >100 (extreme evidence). Associations between sleep dimensions and symptoms with a BF > 100 were noted between depression and sleep quality, sleep meds, days dysfunction, and global sleep quality, and between anxiety trait with sleep quality and sleep medications.

Conclusion: This research provides an in-depth examination of multidimensional sleep phenotypes in a cohort of patients with FMS and punctuates associations among multiple sleep dimensions and symptoms of FMS. Given the severity of sleep disturbance reported in this population, strategies to combat this problem are needed to reduce symptom burden in this vulnerable population. This study provides evidence to prompt the development and testing of personalized interventions to mitigate sleep disturbance and improve functionality and quality of life for individuals with FMS.

Table 1. Correlation coefficient, [95% Credibility Interval], % In ROPE, and Bayes Factor*

	SubjSlpQualPQSI_1	SlpLatency_PQSI_2	SlpDurationPQSI_3	SlpEfficiencyPQSI_4	SlpDisturbPQSI_5	SlpMedsPQSI_6	DayDysfunct_PQSI_7	PQSI_Global_Score
CESD	.54 [0.38, 0.68] 0%, >1000	.16 [-0.06, 0.35] 30.8%, 0.63	.17 [-0.03, 0.38] 26.2%, 0.76	.13 [-0.08, 0.34] 35.1%, 0.53	.34 [0.15, 0.53] 3.0%, 9.0	.54 [0.39, 0.69] 0%, >1000	.48 [0.31, 0.65] 0%, 424	.47 [0.29, 0.63] 0.1%, 253
Trait_ANX	.45 [0.26, 0.61] 0.1%, 119	.09 [-0.12, 0.29] 45.8%, 0.39	.11 [-0.11, 0.31] 40.5%, 0.44	.13 [-0.08, 0.34] 36.9%, 0.50	.27 [0.06, 0.45] 10.9%, 2.2	.45 [0.28, 0.61] 0.1%, 119	.42 [0.22, 0.57] 0.4%, 56.7	.38 [0.20, 0.57] 1.5%, 21.6
State_ANX	.38 [0.18, 0.55] 1.7%, 21.1	.16 [-0.04, 0.37] 29.4%, 0.68	.20 [0.00, 0.40] 20.0%, 1.0	.12 [-0.09, 0.33] 39.5%, 0.48	.20 [-0.01, 0.40] 21.7%, 0.93	.38 [0.18, 0.55] 1.8%, 21.1	.36 [0.18, 0.55] 2.1%, 14.4	.35 [0.16, 0.54] 3.1%, 12.0
BPI_Pain_S	.20 [0.00, 0.41] 20.6%, 1.0	-.09 [-0.29, 0.13] 43.9%, 0.41	.15 [-0.08,0.35] 32.7%, 0.58	.19 [-0.01, 0.40] 23.8%, 0.86	-.03 [-0.24, 0.20] 52.3%, 0.33	.21 [0.00, 0.42] 20.8%, 1.0	.09 [-0.11, 0.31] 44.7%, 0.40	.12 [-0.10, 0.33] 37.9%, 0.50
BPI_Pain_I	.30 [0.12, 0.50] 5.3%, 3.8	.02 [-0.19, 0.23] 55.3%, 0.32	.07 [-0.14]0.28 47.2%, 0.37	.12 [-0.10, 0.32] 38.2%, 0.47	.21 [0.02, 0.42] 19.5%, 1.2	.30 [0.10, 0.48] 6.2%, 3.8	.26 [0.05, 0.45] 11.8%, 2.1	.26 [0.05, 0.45] 10.7%, 2.1
BFI	.38 [0.20, 0.56] 1.5%, 21.5	.03 [-0.17, 0.26] 51.9%, 0.33	0.06 [-0.15, 0.27] 49.9%, 0.36	.10 [-0.11, 0.31] 42.6%, 0.43	.18 [-0.03, 0.38] 24.4%, 0.79	.38 [0.19, 0.55] 1.2%, 21.5	.45 [0.28, 0.63] 0.4%, 152	.32 [0.13, 0.51] 3.9%, 5.9

Note: CESD=Center for Epidemiological Studies-Depression; Trait_Anx=Trait Anxiety; State_Anx=State Anxiety; BPI-S=Brief Pain Inventory-Severity; BPI-I=Brief Pain Inventory-Interference; BFI=Brief Fatigue Inventory; PSQI= Pittsburgh Sleep Quality Index; SubjSlpQual=Subjective Sleep Quality; SlpLatency=Sleep Latency; SlpDuration=Sleep Duration; SlpEfficiency=Sleep Efficiency; SlpDisturb=Sleep Disturbance; SlpMeds=Use of sleeping medications; DayDysfunct=Daytime Dysfunction

*Note: Correlation coefficient: This is the estimated robust bivariate correlation coefficient; Credibility Interval: Provides the values encompassing 95% of the Highest Posterior Density (HPD); ROPE: This is Region of Practical Equivalence, a range of values considered to indicate practically no effect (or, in this case, practically no correlation). For the correlation coefficient, this is the range -0.05, 0.05, which is half the value of a negligible correlation as suggested by Cohen's (1988) rules of thumb. What is provided in the table is the % of estimated correlation values that are contained within that range; Bayes Factor: The Bayes Factor can be thought of as providing a measure of support for the alternate hypothesis (H1) compared to the null hypothesis (H0): >100=Extreme evidence for H1; 30-100=Very strong evidence for H1; 10-30=Strong evidence for H1; 3-10=Moderate evidence for H1; 1-3= Anecdotal evidence for H1; 1= No evidence.

Disclosure: V. Menzies, None; **D. Lynch Kelly**, None; **M. Weaver**, None.

Abstract Number: 0119

Worsened Depression but Improved Fatigue Were the Main Impacts of Severe Lockdown in Non- COVID Infected Australian Fibromyalgia Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To gauge the impact of severe COVID-19 related lockdown restrictions on the mental and physical wellbeing of Australian fibromyalgia patients and their recovery following the conclusion of the lockdown.

Methods: Telephone or online surveys were conducted with sequential patients from a single Australian tertiary centre specialist fibromyalgia clinic during an enforced 100-day stage 4 lockdown in Melbourne in October 2020. Patients were invited to participate if they had been seen in the 12 months prior to lockdown and had recorded illness impact data from that visit. The patients were reassessed 6 months following the end of the lockdown. There was a 73% response rate. Demographic and clinical information was collected. The Fibromyalgia Impact Questionnaire (Revised Version) (FIQR) was used to assess current fibromyalgia illness impact. The Patient Health Questionnaire 9 (PHQ-9) was used to assess depression symptoms.

Table 1. Mean scores (SD) of FIQR, PHQ-9 and selected sub-component scores (n=50/35) (*=p<0.05)

	Pre-lockdown (n=50)	Lockdown (n=50)	t-Test p-value	Post-lockdown (n=35)	t-Test p-value
Mean FIQR Score (SD)	69.61 (16.86)	66.59 (16.13)	0.126	66.41 (15.50)	0.500
Mean PHQ-9 Score (SD)	12.77 (6.74)	14.48 (5.03)	0.01*	13.40 (4.20)	0.041*
Pain (SD)	6.95 (2.16)	6.79 (2.02)	0.598	6.60 (1.50)	0.524
Sleep (SD)	8.33 (1.90)	8.44 (1.59)	0.636	8.06 (0.94)	0.731
Anxiety (SD)	6.53 (3.04)	6.3 (2.71)	0.574	4.43 (2.05)	<0.001*
Depression (SD)	5.28 (3.22)	5.98 (2.63)	0.048*	6.60 (2.14)	0.002*
Fatigue (SD)	8.25 (2.98)	7.29 (2.13)	0.009*	8.29 (1.02)	0.002*

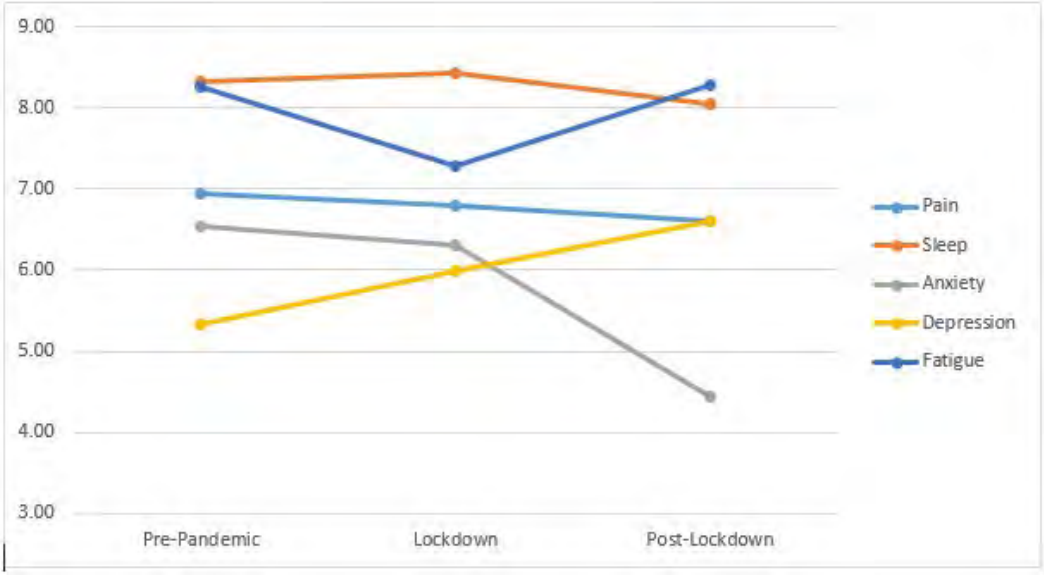

Figure 1. Changes in mean FIQR subdomain scores over time.

Results: Sixty-nine patients were invited to participate, 50 responses were received during the lockdown and 35 responded following the conclusion of the lockdown. No subjects had been diagnosed with COVID infection at any time. Most patients reported increased isolation, decreased exercise, worse sleep and increased use of fibromyalgia-related medications. Twenty-five (50%) of patients had a PHQ-9 score ≥ 15, with 20 patients (40%) reporting moderately-severe and 5 patients (10%) reporting severe depression with an overall mean PHQ9 score of 14.48, this is significantly different to previously collected data from the same cohort where a mean PHQ9 of 12.77 was found (p=0.01). No significant difference was found between pre-lockdown and during lockdown FIQR total score. There was a significant worsening in depression scores and a significant improvement in fatigue subdomain scores. Additionally, there were trends for worse pain, and sleep (table 1).

Six months after the conclusion of the lockdown, surveyed patients self-reported depression had continued to worsen. This seems to contrast with the PHQ-9 scores which show an overall improvement in depression severity compared to the lockdown, resulting in scores not significantly worse than before the lockdown began (Figure 1).

The percentage of patients with mod-severe depression had improved to twelve (34%) patients but this remains higher than previously published data (25%). The observed improvement in fatigue was not sustained with scores returning to pre-pandemic levels. There was a significant improvement in anxiety following the end of the lockdown.

Conclusion: Severe COVID related lockdown restrictions in Melbourne in 2020 resulted in significantly worse reported features of depression and significantly improved fatigue. Other clinical aspects of fibromyalgia were not found to be significantly different from previously reported levels. These changes, other than a continued sense of depression, were not sustained following the conclusion of the lockdown. Whilst the overall mean PHQ-9 score did improve, this remained non-significantly higher than prior to the pandemic. The improvement in fatigue may relate to increased opportunity to rest through the lockdown.

Disclosure: B. Worcester, None; **E. Guymer**, None; **G. Littlejohn**, AstraZeneca, 1, MSD, 1, AbbVie, 1, Janssen, 1, Pfizer, 1, Seqirus, 1.

Abstract Number: 0120

Fibromyalgianess and Glucocorticoid Persistence Among Patients with Rheumatoid Arthritis

Beth Wallace[1], Meriah Moore[2], Andrew Heisler[3], Lutfiyya Muhammad[4], Jing Song[5], Daniel Clauw[2], Clifton Bingham[6], Marcy Bolster[7], Wendy Marder[2], Tuhina Neogi[8], Alyssa Wohlfahrt[9], Dorothy Dunlop[10] and Yvonne Lee[10], [1]Michigan Medicine, VA Ann Arbor Healthcare System, Ann Arbor, MI, [2]University of Michigan, Ann Arbor, MI, [3]Bronson Rheumatology Specialists, Kalamazoo, MI, [4]Northwestern University Feinberg School of Medicine, Chicago, IL, [5]Northwestern University, Worthington, IL, [6]Johns Hopkins University, Baltimore, MD, [7]Massachusetts General Hospital, Boston, MA, [8]Boston University School of Medicine, Boston, MA, [9]Tufts University School of Medicine, Boston, MA, [10]Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Over one-third of patients with rheumatoid arthritis (RA) exhibit evidence of fibromyalgianess, a cluster of somatic symptoms associated with increased sensitivity to painful stimuli. Fibromyalgianess is associated with higher rates of disability among RA patients and inadequate responsiveness to disease-modifying antirheumatic drugs (DMARDs). Up to half of patients with RA often remain on oral glucocorticoids (GCs) for prolonged periods, despite the well-described risk of dose-dependent morbidity and mortality. We know little about how fibromyalgianess might influence GC use in RA. In this study, we examined the longitudinal association between fibromyalgianess and oral GC persistence among RA patients.

Methods: We used data from the Central Pain in Rheumatoid Arthritis (CPIRA) cohort to follow participants with active RA on oral prednisone after they initiated a new DMARD. Fibromyalgianess was measured using the Fibromyalgia Survey Questionnaire (FSQ), previously shown to correlate with key fibromyalgia features often superimposed upon RA. Severity of fibromyalgianess was stratified as follows: FSQ< 8 low, 8-10 moderate, and >10 high/very high. GC persistence was defined as GC use at three-month follow-up visit. The association between baseline fibromyalgianess (exposure) and GC persistence at 3-month follow-up (outcome) was assessed using multiple logistic regression. The analysis was adjusted for baseline demographics, RA duration, serologic status, and inflammatory activity as measured by swollen joint count and C-reactive protein.

Table 1. Baseline characteristics of patients taking glucocorticoids at enrollment (N = 97), stratified by baseline fibromyalgianess severity group

Mean (SD) or %	Fibromyalgianess severity group			
	Low FSQ: 0-7 n = 28	Moderate FSQ: 8-10 n = 26	High FSQ: 11-15 n = 28	Very High FSQ: >15 n = 15
FSQ score (range 0-31)	4.68 (2.04)	9.04 (0.87)	13.21 (1.37)	17.93 (2.49)
WPI score (0-19)	1.86 (1.21)	4.77 (1.61)	6.75 (2.32)	10.60 (1.99)
SSS score (0-12)	2.82 (1.68)	4.27 (1.71)	6.46 (2.40)	7.33 (1.72)
Age (years)	59.85 (14.29)	56.95 (12.08)	52.57 (15.34)	59.75 (12.20)
Female, %	64.3	80.8	82.1	100.0
Caucasian, %	71.4	68.0	74.1	80.0
BMI (kg/m^2)	28.4 (7.67)	28.04 (7.62)	29.31 (8.27)	33.11 (6.05)
Disease duration (years)	9.25 (13.15)	8.99 (11.95)	12.21 (13.68)	10.82 (11.45)
Seropositive, %	92.9	84.0	67.9	73.3
CDAI (range 0-76)	18.98 (11.92)	21.79 (13.89)	22.12 (12.47)	40.95 (15.66)
Patient global (0-10)	2.80 (1.85)	4.07 (2.71)	4.08 (2.02)	4.93 (1.60)
Physician global (0-10)	2.62 (1.39)	3.56 (2.13)	3.31 (2.01)	5.22 (2.39)
Swollen joint count (0-28)	7.96 (8.18)	9.96 (8.97)	10.50 (7.94)	20.20 (8.27)
Tender joint count (0-28)	5.25 (4.99)	5.81 (5.02)	3.64 (3.51)	10.60 (6.93)
CRP (mg/L)	6.29 (6.08)	9.78 (10.18)	7.97 (16.19)	12.16 (12.71)

FSQ: fibromyalgia survey questionnaire; WPI: widespread pain index; SSS: symptom severity score, CDAI: clinical disease activity index

Results: Of 97 participants on prednisone at baseline, 65% were taking prednisone at follow-up. Fifty-seven percent of participants with low baseline fibromyalgianess had persistent GC use, compared to 84% with high or very high fibromyalgianess. After adjustment as outlined above, participants with high/very high baseline fibromyalgianess remained more likely to be on prednisone at follow-up, relative to those with low fibromyalgianess (OR 4.99 [95% CI 1.20 – 20.73]).

Conclusion: In this cohort of patients with active RA, high fibromyalgianess is associated with persistent GC use, independent of inflammatory activity. This finding suggests that non-inflammatory pain related to fibromyalgianess may be misclassified by patients or providers as inflammatory pain related to RA disease activity. Greater insights into clinician and patient perspectives on GC tapering in RA patients with high fibromyalgianess are required to help clinicians distinguish active RA symptoms from manifestations of other chronic pain conditions.

Table 2. Association between A) baseline fibromyalgianess severity group, B) baseline WPI severity group, C) baseline SSS severity group, and persistent use of glucocorticoids at 3 month follow-up (N = 97)

A.	FSQ score category*		
Odds ratio (95% CI) for glucocorticoid persistence	Low (ref) N = 28	Moderate N = 26	High N = 43
Model 1	Reference	0.55 (0.19, 1.62)	**3.86 (1.28, 11.62)**
Model 2	Reference	0.40 (0.11, 1.45)	**5.02 (1.21, 20.84)**
Model 3	Reference	0.32 (0.09, 1.23)	**4.99 (1.20, 20.73)**
B.	**WPI score category****		
Odds ratio (95% CI) for glucocorticoid persistence	Low (ref) N = 30	Moderate N = 25	High N = 42
Model 1	Reference	1.27 (0.44, 3.70)	**4.25 (1.49, 12.16)**
Model 2	Reference	1.72 (0.51, 5.87)	**4.86 (1.39, 16.99)**
Model 3	Reference	1.78 (0.52, 6.14)	**4.60 (1.31, 16.20)**
C.	**SSS score category****		
Odds ratio (95% CI) for glucocorticoid persistence	Low (ref) N = 27	Moderate N = 31	High N = 39
Model 1	Reference	0.69 (0.24, 2.02)	1.13 (0.39, 3.21)
Model 2	Reference	0.67 (0.20, 2.20)	1.11 (0.32, 3.83)
Model 3	Reference	0.57 (0.16, 1.95)	0.99 (0.28, 3.54)

*Based on baseline FSQ stratified as low (0-7), moderate (8-10), high/very high (>=11)
**Based on baseline WPI and SSS stratified as low (0-3), moderate (4-5), high/very high (>5)

Model 1 unadjusted, Model 2 adjusted for baseline non-inflammatory factors (age, gender, enrolling site, BMI, disease duration, and seropositive status), Model 3 adjusted for baseline non-inflammatory and inflammatory factors (swollen joint count and CRP)

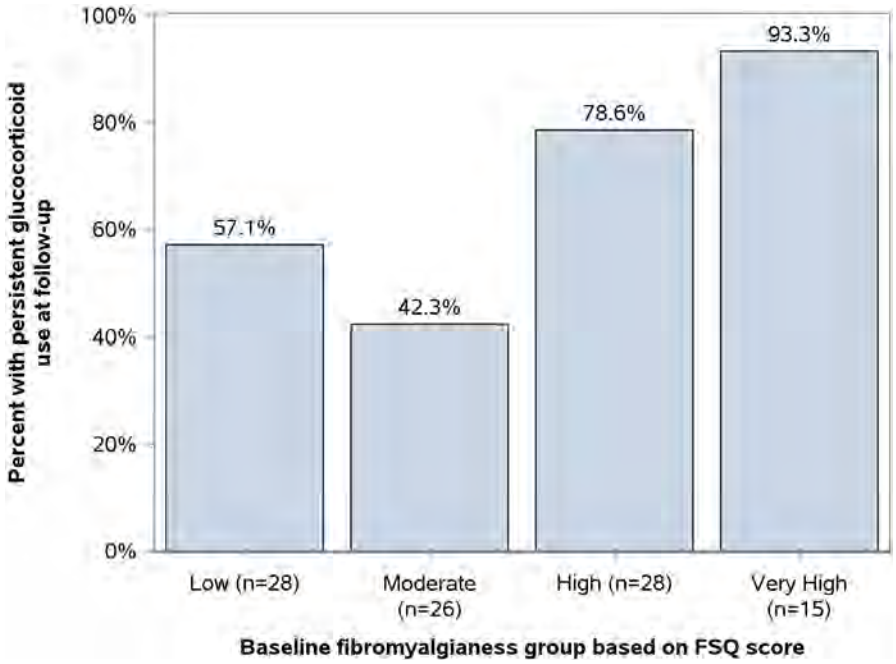

Figure 1. Percentage of patients with persistent use of glucocorticoids at 3-month follow-up, stratified by baseline fibromyalgianess severity group.

Disclosure: B. Wallace, None; **M. Moore**, None; **A. Heisler**, None; **L. Muhammad**, None; **J. Song**, None; **D. Clauw**, Pfizer, 2, 6, Aptinyx, 2, Daiichi, 2, Sankyo, 2, Eli Lilly, 2, 6, Intec Pharma, 2, Samumed, 2, Theravance, 2, Tonix, 2, Zynerba, 2, Nix Patterson LLP, 6, Williams & Connolly LLP, 6; **C. Bingham**, Bristol Myers Squibb, 5, Abbvie, 2, Gilead, 2, Eli Lilly, 2, Janssen, 2, Regeneron, 2, Pfizer, 2, Sanofi, 2; **M. Bolster**, Johnson and Johnson, 11, Genentech, 5, Corbus, 5, Cumberland, 5, PracticeUpdate, 12, Associate Editor, Custom Learning Designs, 2; **W. Marder**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **A. Wohlfahrt**, None; **D. Dunlop**, None; **Y. Lee**, Eli Lilly, 2, 6, Pfizer, 5, Cigna, 11.

Abstract Number: 0121

The Efficacy of Group Behavioral Activation versus Usual Treatment in Patients with Fibromyalgia and Major Depression

Josefina Duran, Alvaro Verges, Ana Rocío Vázquez-Taboada, Matias Gonzalez and Lydia Gomez-Pérez, Pontificia Universidad Católica de Chile, Santiago, Chile

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Fibromyalgia (FM) and major depression frequently coexist. Patients with both conditions have a worse prognosis and higher disability, and their treatment options are scarce. Behavioral activation (BA) is

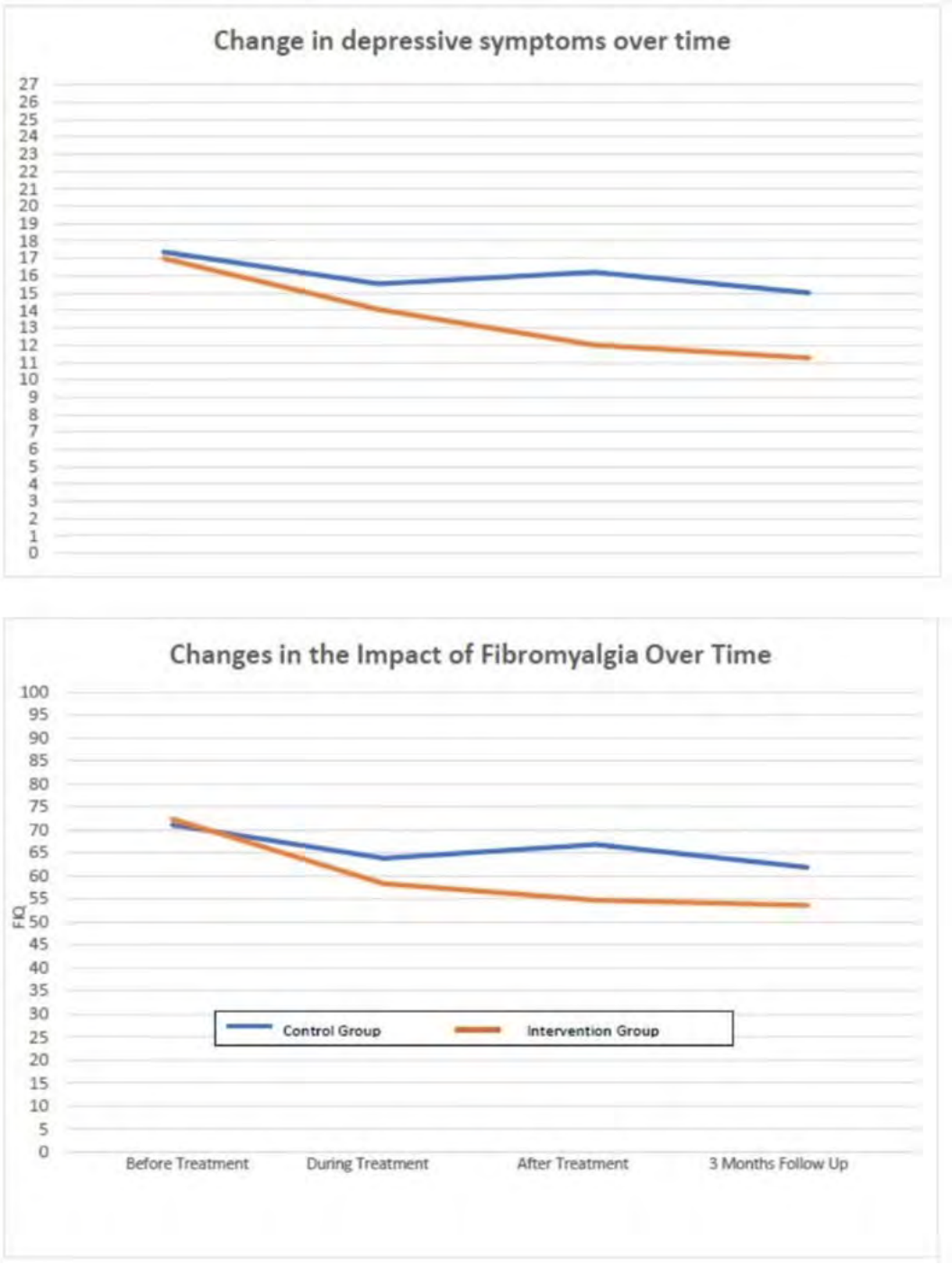

Figure 1. Change in depressive symptoms and in fibromialgia impact (FIQ) at baseline, during the intervention and after follow up.

an evidence-based therapy for depression that is easy to implement and can be implemented as group therapy. Case studies indicate BA may be useful in the management of pain in Fibromyalgia (FM). In this study we aimed to determine the efficacy of group BA for decreasing depressive symptoms and pain intensity in subjects with FM and concomitant depression. This study was funded by a grant from CONICYT (FONIS SA16I0305)

Methods: A randomized controlled trial was performed in which BA in addition to usual care was compared to usual care in women with FM and depression. All subjects included received a stable dose of duloxetine and no other antidepressants. Outcomes were assessed before, during, and after the intervention, as well as at a three months

follow-up using the following instruments: Chilean version of the Patients Health Questionnaire-9 (PHQ-9), Composed Pain Intensity Index, Fibromyalgia Impact Questionnaire Revised (FIQ-R), Pain Catastrophizing Scale (PCS), Pain Vigilance and Awareness Questionnaire (PVAQ), Patients Health Questionnaire (PHQ-15), and Activation subscale of the Behavioral Activation for Depression Scale (BADS). Intent to treat analysis was performed. A Hierarchical Linear Model for repeated measures was performed to determine change in all outcomes described and a Cochran-Mantel-Haenszel test was performed to compare the percentage of subjects that had a reduction in 50% of depressive symptoms. This study was approved by the Medicine Scientific Ethics Committee of the Pontificia Universidad Católica de Chile, Santiago, Chile (N 15-221).

Results: There was a significant improvement in depressive symptoms in the regression model (F 4.71 p=0.03). In addition, the outcome greater than 50% decrease in symptoms also showed a significant improvement both at the end of treatment (χ^2 (1) = 9,43; p = .001) and at the end of follow-up (χ^2 (1) = 3,83; p= .025). Regarding the impact of FM, FIQ showed significant improvement in multiple regression(F 4.22, p=0.006). Finally, catastrophizing decreased (p 0.035) and behavioral activation increased (p =0.003). Pain (p=0.14) and physical symptoms measured by PHQ-15 did not improve (p=0.059).

Conclusion: BA was effective in improving depression, catastrophizing and decreasing FIQ in subjects with depression and FM, making it a potential therapeutic strategy. However no significant change in pain intensity was seen.

Disclosure: J. Duran, None; **A. Verges**, None; **A. Vázquez-Taboada**, None; **M. Gonzalez**, None; **L. Gomez-Pérez**, None.

Abstract Number: 0122

Clinical Impact of a Digital Behavioral Therapy for Fibromyalgia Management: A Randomized Controlled Trial

Stephanie Catella[1], Michael Gendreau[2], Nicolette Vega[1], Allison Kraus[1], Michael Rosenbluth[1], Sherry Soefje[3], Shishuka Malhotra[4] and Lesley Arnold[5], [1]Swing Therapeutics, San Francisco, CA, [2]Gendreau Consulting, LLC, Poway, CA, [3]Excell Research, Oceanside, CA, [4]Neuro-Behavioral Clinical Research, North Canton, OH, [5]University of Cincinnati, Cincinnati, OH

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Recommendations for fibromyalgia management include both pharmacologic and nonpharmacologic treatments. Cognitive behavioral therapy (CBT) has demonstrated level 1A evidence for fibromyalgia management, though access is limited due to few trained clinicians and cost. An at home digital behavioral therapy could significantly increase access.

A smartphone-based Acceptance and Commitment Therapy (ACT) program was developed for fibromyalgia management. ACT is a modern type of CBT increasingly used to manage chronic pain that focuses on acceptance of uncontrollable and untreatable symptoms. A multi-site study is underway to understand the feasibility of a largely virtual study and determine the impact of smartphone-delivered ACT compared to a digital active control.

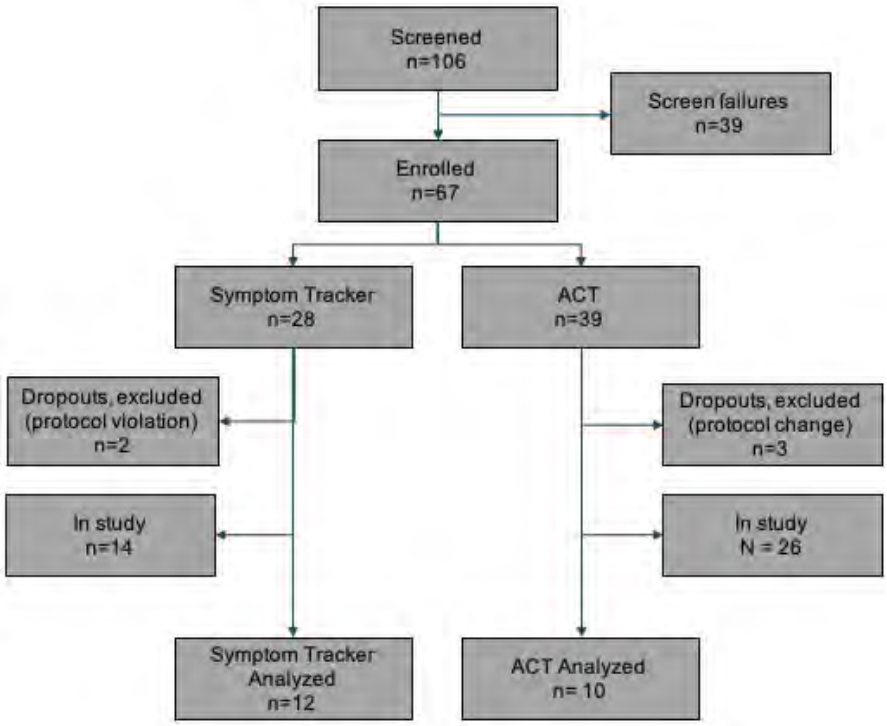

Figure 1. Flow of participants in the SMART-FM study (Consort diagram).

Methods: Participants diagnosed with fibromyalgia using 2016 criteria were randomized to digital ACT or an active control. Participants remained stable on other ongoing fibromyalgia treatment. The digital ACT intervention consists of 41 daily sessions of structured ACT lessons, mindfulness practices, and activities to encourage paced exercise and behavior change. An active control was implemented to account for study engagement and expectation biases. Components of the active control (Symptom Tracker, or ST) include daily symptom tracking and monitoring and access to patient education. During the 12 week study, participants were expected to use the smartphone applications at least 5 days a week.

FIQ-R, the primary outcome, was administered weekly. Secondary outcomes include PGIC, weekly recall pain intensity and interference, and sleep quality (NRS), BDI-II, PROMIS-29, Five Facets of Mindfulness, and Psychological Inflexibility in Pain Scale.

The study has enrolled 67 participants. Twenty-seven participants have completed the study to date and 22 are included in the current analysis set (Figure 1).

Results: The characteristics of the participants are summarized in Table 1. Engagement in both arms is high throughout the study (an average completion of 5 sessions per week in each arm).

Improvement of 20% or greater in total FIQR score was observed in 50% of the ACT group compared to 25% in the ST group. Participants in ACT improved on average 10.5 points (20%) in total FIQR score compared to 4.8 points (9%) in ST. Forty percent of ACT participants reported “much improved” or greater on the PGIC compared to 0% in ST. More improvement was seen in ACT over ST in most other outcome measures. No treatment related adverse events have been observed. This study is ongoing and full results are expected this summer.

Conclusion: A mostly virtual digital therapy study is feasible with high engagement in both ACT and the active control. Participants in the ACT arm achieved greater reductions on FIQ-R and showed greater improvement on PGIC

Table 1. Background characteristics of study participants

Characteristics	Total (N = 67)
Female	66 (99%)
Average age (SD)	52.8 (10.3)
Years since fibromyalgia diagnosis (mean (SD))	12 (9)
Education	
High school	4 (6%)
Some college	24 (36%)
College or higher	39 (58%)
Occupational status	
Working	36 (54%)
Homemaker	3 (4%)
Retired	13 (19%)
Disability	1 (1%)
Other not working	14 (21%)
Fibromyalgia characteristics	
Widespread Pain Index (mean, SD))	13.3 (3.1)
Symptom Severity Score (mean, SD))	8.0 (1.5)
Fatigue (Moderate or greater)	63 (94%)
Waking unrefreshed (Moderate or greater)	60 (90%)
Cognitive symptoms (moderate or greater)	48 (72%)
Concurrent fibromyalgia medications	
Duloxetine	14 (21%)
Gabapentin	12 (18%)
Pregabalin	3 (4%)
Tricyclic antidepressant	9 (13%)
Other antidepressant	8 (12%)
NSAIDs	9 (13%)
Data not available	6 (9%)

compared to ST. Participants in the ACT arm showed greater improvement relative to the ST arm on ACT process measures, suggesting digital ACT is effectively targeting therapeutic processes of change.

The findings suggest that digital ACT may improve fibromyalgia management and appears to be well tolerated.

Disclosure: S. Catella, Swing Therapeutics, 7; **M. Gendreau**, Tonix Pharmaceuticals, 2, Dare Biosciences, 2, Bionomics Limited, 2, Teva Pharmaceuticals, 2, Virios Theraoeutics, 4, 11, Swing Therapeutics, 1, 2, 11; **N. Vega**, Swing Therapeutics, Inc., 3, 11, Stryker Corp, 3; **A. Kraus**, Swing Therapeutics, 3, 11; **M. Rosenbluth**, Swing Therapeutics, 3, 8; **S. Soefje**, Swing Therapeutics, 12, Contracted clinical research site; **S. Malhotra**, None; **L. Arnold**, Pfizer, 2, 5, Teva, 2, 5, Jazz, 2, Lundbeck, 2, Eliem, 2, AbbVie, 5, Tonix, 5, Swing Therapeutics, 5, Aptinyx, 2, 5, Virios Therapeutics, 2, 5, Otsuka, 5.

Abstract Number: 0123

Vestibulocortical Stimulation with Caloric Irrigation Reduces Pain and Improves Subjective Well-Being in Fibromyalgia: An Open-Label Pilot Trial

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SESSION INFORMATION

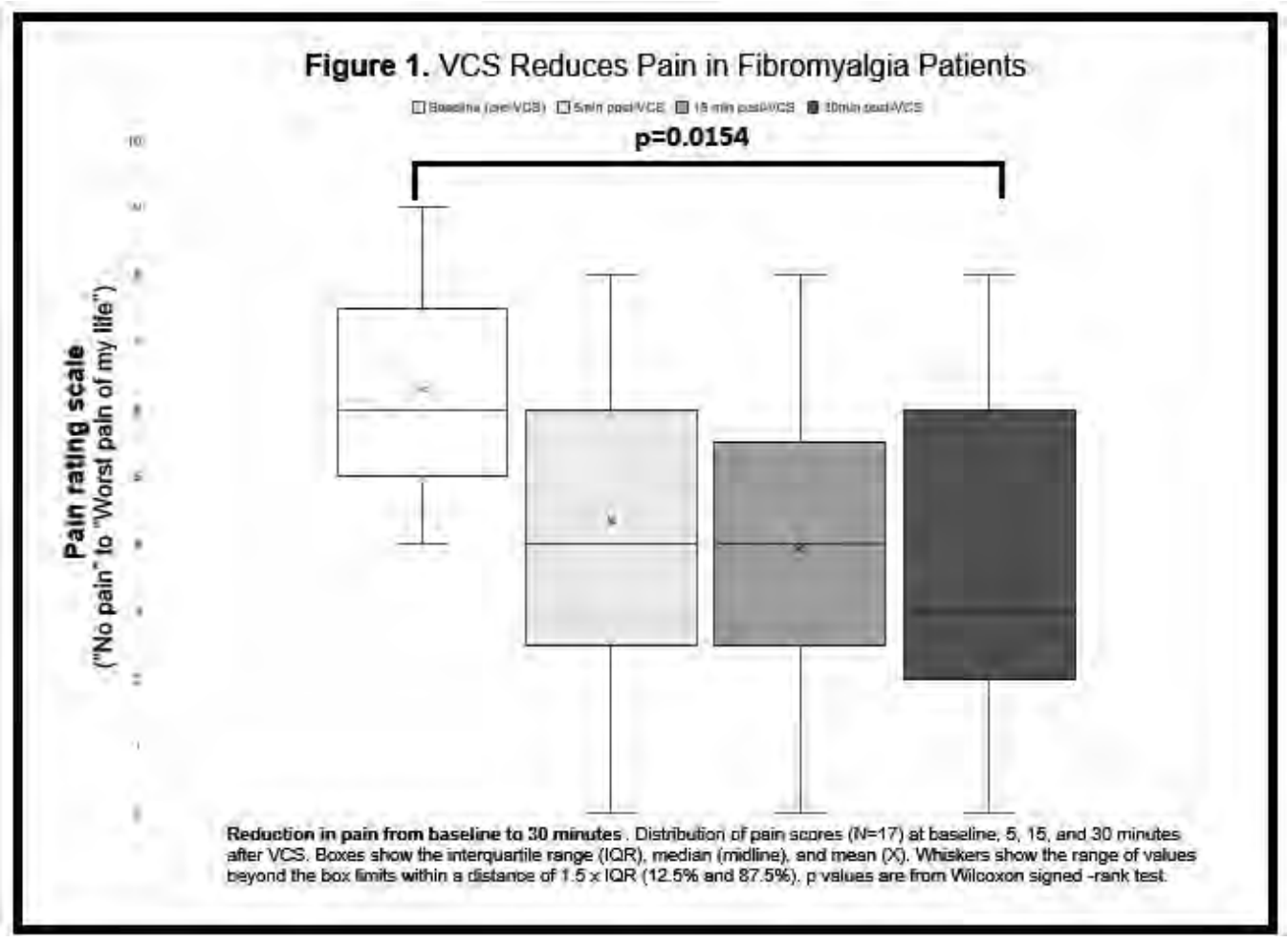
Session Date: Saturday, November 6, 2021

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Safe and effective therapies for fibromyalgia (FM) remain a major unmet clinical need. Vestibulocortical stimulation (VCS) via caloric irrigation is a safe, inexpensive, non-invasive and non-pharmacologic method of brain stimulation with demonstrated analgesic effects in persistent pain syndromes. VCS has also improved mood

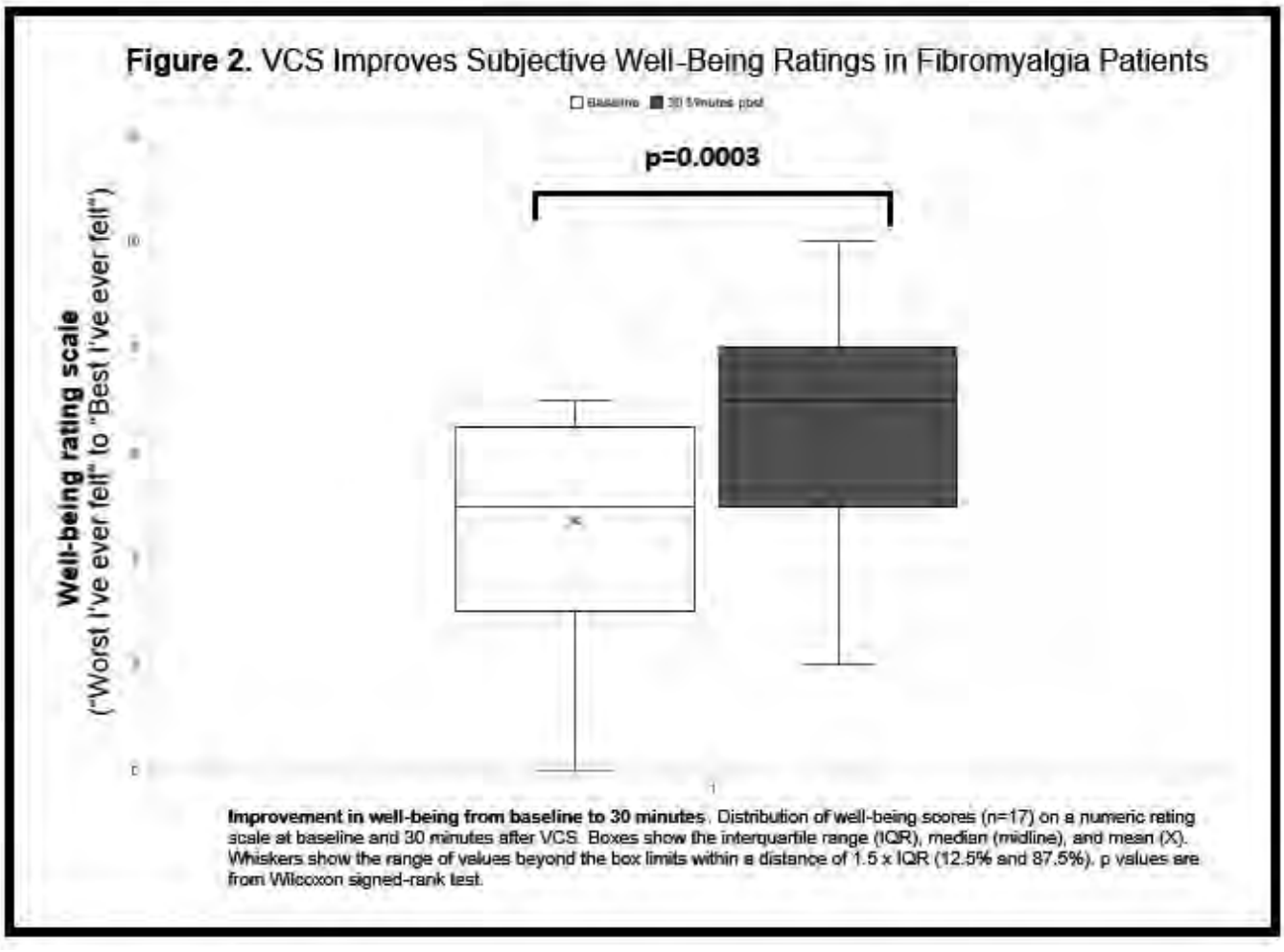


VCS Reduces Pain in Fibromyalgia Patients.

in psychiatric & healthy participants. Here we investigated whether VCS can similarly reduce pain & improve subjective well-being in FM patients.

Methods: We conducted a convenience-based non-randomized open-label pilot trial in 16 FM patients (mean age = 47.1 years; 15 female) recruited from a single rheumatology department. All patients met criteria for FM — defined as ≥7 widespread pain index (WPI) with ≥5 symptom severity score (SSS) or ≥4 WPI with ≥9 SSS. Half of the patient sample had primary FM, while underlying inflammatory disorders were present in 50%. Each participant underwent VCS with 50 cc of cold-water irrigation (4°C) into the right ear at 1–2 cc/second (which induces predominantly left-hemisphere activation). Vestibular stimulation was confirmed by post-procedural nystagmus & subjective vertigo. Pain scores (0–10) were recorded at baseline (before VCS) and at 5min, 15min & 30min after VCS; overall subjective well-being (0–10) was also assessed at baseline & 30min post-procedure. The primary outcome measure was change in mean pain scores collected each day/week following the VCS procedure. There were several secondary outcome measures, including immediate change in pain & subjective well-being after VCS.

Results: Of the outcome measures examined to date, the immediate effects of VCS are most evident. Overall there was a rapid pain reduction at 5 min post-VCS and, at 30 min, pain had decreased in 14/17 (82.4%) participants, increased in 1/17 (6%) and unchanged in 2/17 (12%) (Figure 1; p = .0003—Wilcoxon signed-rank test). In those with pain reductions, half (7/14) showed an improvement of at least 50% from baseline, 1/14 (7%) improved at least 30% and 6/14 (43%) improved < 30%. Subjective well-being ratings had also improved at 30 min post-VCS in 9/17 (53%)



VCS Improves Subjective Well-Being Ratings in Fibromyalgia Patients.

participants, worsened in 3/17 (18%) and were unchanged in 4/17 (24%) (Figure 2; p = .0154—Wilcoxon signed-rank test). While a proportion of participants (8/12 or 67%) reported the procedure was uncomfortable, it was otherwise generally well-tolerated with the large majority (11/12 or 92%) indicating they would have VCS again if it reduced their pain by ≥50% for at least one week — in keeping with recently published VCS tolerability results in a persistent pain cohort (Ngo et al., 2020 *Brain Stimul* 13: 1446–8). There were also no major adverse events in the current trial. Longer-term VCS effects will be reported when primary outcome data collection is completed, however three patients to date have reported sustained & meaningful pain relief for one week after a single VCS administration.

Conclusion: These preliminary results suggest VCS is a safe & well-tolerated procedure with positive effects on pain & subjective well-being in FM. Further investigation is required with repeated VCS (rVCS) in a placebo-controlled randomized trial.

Disclosure: M. Kaplan, None; **C. Zhou**, None; **E. Carroll**, None; **A. Weinberg**, None; **D. Clauw**, Pfizer, 2, 6, Aptinyx, 2, Daiichi, 2, Sankyo, 2, Eli Lilly, 2, 6, Intec Pharma, 2, Samumed, 2, Theravance, 2, Tonix, 2, Zynerba, 2, Nix Patterson LLP, 6, Williams & Connolly LLP, 6; **T. Thanh Ngo**, None; **I. Tassiulas**, None.

Abstract Number: 0124

Nurse-supported Web-based Cognitive Behavioral Therapy for Chronic Musculoskeletal Pain: An Effectiveness Trial

Rami Diab[1], Rebecca Bomar[2], Christina Rinaldi[2], Claudia Campos[2], Sebastian Kaplan[2] and Dennis Ang[3], [1]Wake Forest Baptist Health/Wake Forest School of Medicine, Winston-Salem, NC, [2]Wake Forest School of Medicine / Wake Forest University Baptist Medical Center, Winston-Salem, NC, [3]Wake Forest School of Medicine, Winston-Salem, NC

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Baseline characteristics of study subjects

	Nurse support group (n=30)	Control group (n=30)	P values	All subjects (n=60)
Age in years	52.3 (14.9)	51.8 (20.5)	0.908	52.1 (17.8)
Gender, % female	26 (86.7)	23 (76.7)	0.506	49 (81.7)
Duration of pain ≥ 1 years (%)	29 (96.7)	26 (86.7)	0.353	55 (91.7)
≥3 body sites	28 (93.3)	29 (96.7)	>0.999	57 (95.0)
PHQ-8 depression (score ≥ 10)	5 (16.7)	7 (23.3)	0.748	12 (20.0)
BPI pain intensity (range 0-10)	5.0 (3.8, 6.0)	5.5 (4.8, 6.3)	0.112	5.3 (4.3, 6.1)
BPI pain interference (range 0-10)	4.5 (3.0, 6.1)	5.4 (3.7, 6.6)	0.152	4.9 (3.4, 6.6)
BPI global pain severity (range 0-10)	4.5 (4.3, 5.5)	5.5 (4.6, 6.4)	0.041	5.0 (4.3, 6.1)
Pain Catastrophizing Score total (range 0-52)	15 (8, 24)	16 (9, 25)	0.763	15 (8, 25)

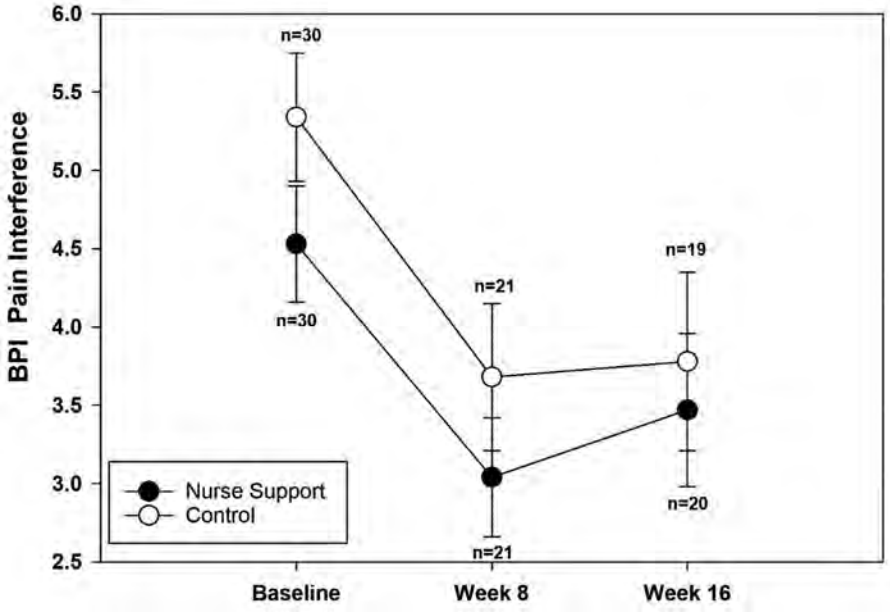


Figure 1. Plot of BPI interference by treatment group over time.

Table 2. Results of primary outcome analysis showing statistically significant improvements from baseline in BPI pain intensity, BPI pain interference, and BPI global pain severity scores between weeks 8 and 16 respectively. Results are given as mean (95% confidence interval) for change from baseline, with * indicating a significant non-zero change

PRIMARY OUTCOMES (Δ from baseline)	Nurse support group (n=30)	Control group (n=30)	P values
BPI global pain severity	3.8 (0.2) -1.2 (-1.7, -0.8)*	3.8 (0.2) -1.5 (-1.9, -1.0)*	0.770
BPI pain intensity	4.0 (0.2) -1.2 (-1.7, -0.6)*	4.2 (0.2) -1.3 (-1.8, -0.8)*	0.542
BPI pain interference	3.5 (0.3) -1.3 (-2.0, -0.7)*	3.5 (0.3) -1.7 (-2.3, -1.0)*	0.924
PROMIS physical function	40.6 (0.7) 3.3 (1.8, 4.7)*	40.1 (0.7) 2.9 (1.4, 4.4)*	0.641

Background/Purpose: Pain accounts for greater than 40% of all symptom-related outpatient visits totaling over 100 million outpatient encounters worth hundreds of billions of dollars annually in the U.S alone. Face-to-face and internet-delivered web-based cognitive behavioral therapy (CBT) have proven safe and effective in managing chronic musculoskeletal pain (CMP), demonstrating clinically significant improvements in pain-related disability and severity. Nonetheless, the effect size for CBT in CMP has been small partly due to low compliance or engagement by study participants. The purpose of this pilot study was to evaluate the effectiveness of nurse-supported web-based CBT in the outpatient setting for management of CMP.

Methods: Sixty subjects with CMP were recruited from the internal medicine and rheumatology clinics at Wake Forest Baptist Medical Center. Subjects were randomized to web-based self-guided CBT with six phone-based nurse support calls (nurse support group, n=30) vs. web-based self-guided CBT alone (control group, n=30). The purpose of the phone calls was to encourage completion of the eight learning modules within the web-based CBT program.

The nurse support calls were made from baseline to week 8. All participants had access to the CBT program from baseline to week 16. Outcome measures were collected at baseline, week 8, and week 16.

Results: Using analysis of covariance (ANCOVA) of week 8 and 16 outcome measures, both nurse support and control groups showed statistically significant improvements from baseline in BPI pain intensity (-1.2 [-1.7, -0.6], P< 0.05; -1.3 [-1.8, -0.8], P< 0.05), BPI pain interference (-1.3 [-2.0, -0.7], P< 0.05; -1.7 [-2.3, -1.0], P< 0.05), and BPI global pain severity (-1.2 [-1.7, -0.8], P< 0.05; -1.5 [-1.9, -1.0], P< 0.05) scores respectively. Amongst all secondary outcome measures, only the PROMIS sleep disturbance showed significant differences between the two groups and favored the nurse support group over the control group (50.5 [1.3] vs. 54.3 [1.3]; P=0.039). All subjects had comparable baseline characteristics including duration of pain ≥ 1 year, number of painful body sites (≥3 vs. < 3), Brief Pain Inventory (BPI) pain intensity, interference, and global pain severity scores (range 0-10), Patient-Reported Outcomes Measurement Information System (PROMIS) measures, Patient Health Questionnaire (PHQ-8) depression scale scores (≥ 10), and pain catastrophizing scores. Twenty (66.7%) of patients in the nurse support group vs. 19 (63.3%) of patients in the control group completed the study. The proportion of subjects who completed ≥ 6 learning modules were 17 (56.7%) in the treatment group vs. 18 (62.1%) in the control group. From baseline to week 8, the median number of completed phone calls made by the nurses were 3.5 calls (Interquartile Range [IQR]: 2, 5) and the median duration of each phone call was about 7 minutes (IQR: 5, 10).

Conclusion: Web-based CBT alone showed similar benefits in pain relief and pain-related disability in comparison to web-based CBT with phone-based nurse support over the short term. If confirmed in a larger study, web-based CBT without phone-based nurse support should be routinely included in any treatment algorithm for CMP.

Disclosure: R. Diab, None; **R. Bomar**, None; **C. Rinaldi**, None; **C. Campos**, None; **S. Kaplan**, None; **D. Ang**, None.

Abstract Number: 0125

Body Mass Composition in Post-menopausal Women with Fibromyalgia: Preliminary Results from a Cross-sectional Monocentric Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Fibromyalgia (FM) is characterized by chronic musculoskeletal widespread pain, fatigue, sleep disturbances and functional symptoms. The primary endpoint of our study aimed to determine whether FM

could affect body composition of post-menopausal women. The secondary objectives investigated potential correlations between disease severity, measured subjectively by patient-compiled questionnaires, with body mass variables.

Methods: Thirty post-menopausal FM female patients (median age 58 years, BMI = 25.8) were diagnosed according to either ACR 1990 fibromyalgia classification criteria or ACR 2010 preliminary diagnostic criteria. They underwent Dual-energy X-ray absorptiometry (DEXA) for clinical purposes (i.e. screening for osteoporosis). The parameters analyzed by a dedicated software (GE Lunar, USA) were the spine and femoral bone mineral density (BMD), the total lean mass and the total body fat (TBF), quantitative variables of bone, muscle and fat composition. Additionally, qualitative analysis of the bone was indexed by the trabecular bone score (TBS). All the variables were compared with the parameters of 30 healthy controls (median age 59 years, BMI = 24.4) matched for sex and age. For each patient, data on disease duration, comorbidities, current treatment and disease severity self-reported scores were collected. The last ones derived from the Italian Fibromyalgia Impact Questionnaire Revised version that each patient independently compiled before the medical visit: widespread pain index (WPI), symptom severity scale (SSS), polysymptomatic distress scale (PDS), modified fibromyalgia assessment status (modFAS) and FIQR total score (FIQ-R).

Results: The clinical features of the patients included in our cohort are reported in table 1. No statistically significant differences were observed between femoral/spine BMD, TBS and muscle mass between patients and controls (p = 0.3, p = 0.06, p = 0.16, p = 0.8 respectively). Conversely, both total and central body fat were significantly higher in patients compared with healthy controls (29.4 kg vs 25.2 kg, 15.7 kg vs 13.2 kg, p = 0.006 and p = 0.01 respectively).

	Patients, N = 30
Age	58.0 [53.8, 69.2]
BMI	25.8 [23.0, 28.4]
Disease duration (years), Median [IQR]	4.5 [2.2, 9.2]
ModFAS, Median [IQR]	24.5 [20.0, 29.2]
PDS, Median [IQR]	17.5 [16.0, 23.2]
SSS, Median [IQR]	8.0 [6.0, 9.0]
WPI, Median [IQR]	12.0 [7.8, 15.0]
FIQ-R, Median [IQR]	57.9 [32.4, 68.8]
Current pharmacological treatment	
Cyclobenzaprine N (%)	24 (80)
Fluoxetine N (%)	5 (16.6)
Duloxetine N (%)	4 (13.3)
Gabapentinoids N (%)	2 (6.6)
Tizanidine N (%)	2 (6.6)
Benzodiazepines N (%)	2 (6.6)
Cannabinoids N (%)	3 (10)
Non-pharmacological treatment	
Aerobic physical activity N (%)	5 (16)
Comorbidities	
Hypertension N (%)	10 (33.3)
Diabetes N (%)	3 (10)
Osteoarthritis N (%)	10 (33.3)
Anxiety/depression N (%)	3 (10)
Psoriasis N (%)	3 (10)

Table 1. Clinical features of FM patients included in our cohort

No significant correlations were observed between body mass composition indexes with scores of disease severity. Body mass composition variables did not statistically differ when patients were sub-analyzed according to pharmacological treatment and comorbidities.

Conclusion: Our preliminary results suggest that FM does not significantly impair bone mass and quality in postmenopausal women, a conclusion in line with the majority of literature evidences [1]. Interestingly, total and central adipose tissue mass resulted higher in our cohort of patients compared with controls despite these findings did not correlate with disease severity. This might be due to a disease-induced sedentary lifestyle and reinforces the concept that physical activity not only should be the mainstay of treatment but also represents the best preventive method of overweight and obesity, one of most reported comorbidities of FM patients.

References: 1. Mateos F, Valero C, Olmos JM, et al. Bone mass and vitamin D levels in women with a diagnosis of fibromyalgia. *Osteoporos Int*. 2014;25(2):525-33.

Disclosure: S. Paolino, None; **E. Hysa**, None; **M. ROSSELLA**, None; **A. Casabella**, None; **L. CARMISCIANO**, None; **E. Gotelli**, None; **C. Pizzorni**, None; **A. Sulli**, Saviopharma, 5, Laboratori Baldacci, 5; **V. Smith**, Boehringer Ingelheim, 2, 6, Janssens, 2, 6; **M. Cutolo**, Bristol Myers Squibb, 5, Boehringer Ingelheim, 5, Celltrion, 6, Janssen, 6.

Abstract Number: 0126

Prevalence of Dyslipidemia in Fibromyalgia: A Single Center Case Control Study from South India

Mithun CB[1], Sandeep Surendran[2], **Sumanth Madan**[2], Arun Tiwari[3], Spoorthy Raj[2], Sekhar Easwar[2] and Greeshma Ravindran[2], [1]Amrita Institute of Medical Sciences, Muvattupuzha, India, [2]Amrita Institute of Medical Sciences, Kochi, India, [3]Amrita Institute of Medical Sciences, Ernakulam, India

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

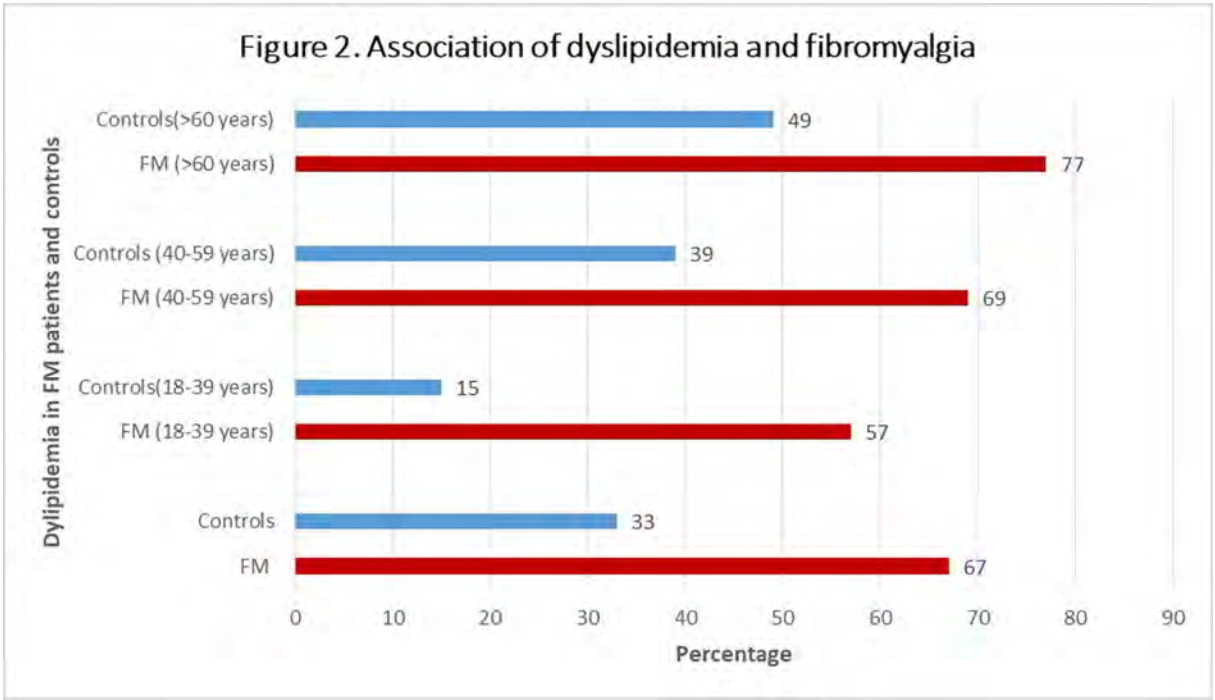
Background/Purpose: Fibromyalgia (FM), a condition characterized by chronic widespread pain, has implications beyond functional disability. FM has been associated with an increased risk of cardiovascular disease in multiple studies, however, there is a paucity of studies looking for dyslipidemia in diagnosed cases of FM. This study sought to explore the association between FM and dyslipidemia.

Methods: This was a case-control study conducted at a tertiary care center in South India from March 2018 to December 2020. FM patients and healthy controls were enrolled in a 1:3 ratio. FM was diagnosed as per the 2016 modified ACR 2010/2011 criteria. Healthy controls who were age, gender, ethnicity and body mass index (BMI) matched were recruited in the study. Fasting lipid profile was obtained from study participants and dyslipidemia was defined by the "Adult treatment panel III criteria". [(1)]The revised fibromyalgia impact questionnaire (FIQR) was used as a tool to ascertain disease severity in FM at diagnosis. The prevalence of dyslipidemia in FM was compared with that of healthy controls and odds ratio was calculated. We also studied the correlation of FIQR with fasting lipid profile. Chi- square test and Pearson correlation coefficient was computed and linear regression t test were applied to test statistical significance. A p value < 0.05 was considered significant.

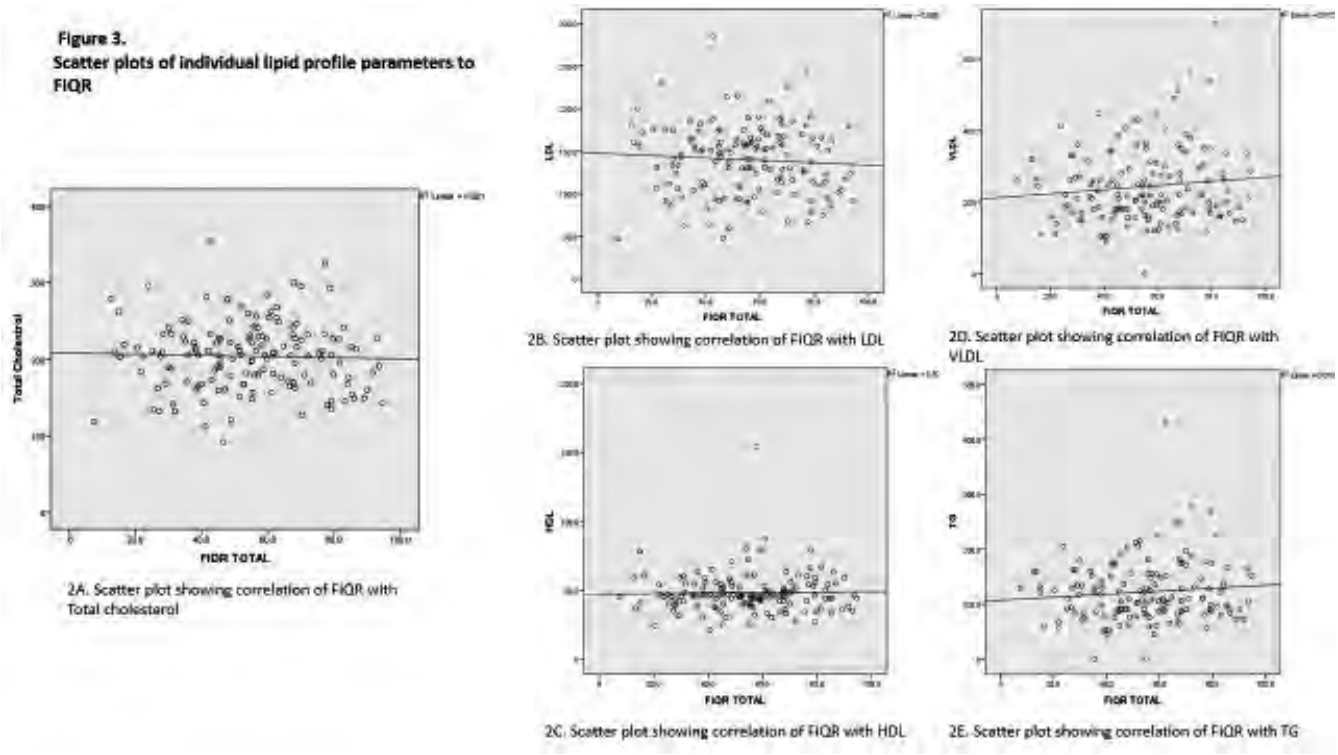
Figure 1: Comparison of presence of dyslipidemia in FM and controls*

	Dyslipidaemia present -no(%)	Dyslipidaemia absent -no (%)	p-value	Odds ratio (95% CI)
FM (n= 149)	100 (67.1%)	49 (32.9%)	<0.001	4.193 (2.826-6.221)
Controls(n=449)	147 (32.7%)	302 (67.3%)		
Age group 18-39 years				
FM (n= 30)	17 (56.7%)	13 (43.3%)	<0.001	7.701 (3.200-18.531)
Controls(n=124)	18 (14.5%)	106 (85.5%)		
Age group 40-59 years				
FM (n= 106)	73 (68.9%)	33 (31.1%)	<0.001	3.539 (2.201-5.692)
Controls(n=286)	110 (38.5%)	176 (61.5%)		
Age group >60 years				
FM (n=13)	10 (76.9%)	3 (23.1%)	0.076	NA
Controls (n=39)	19 (48.7%)	20 (51.3%)		

* FM denotes- fibromyalgia, CI- Confidence interval.



Results: A total of 149 (females- 147) FM cases and 449 healthy controls were enrolled in the study. We noted that dyslipidemia was present in 100 (67%) FM cases and 147 (33%) controls, their difference was statistically significant (p< 0.001; OR 4.193). Subgroup analysis amongst individual age groups showed an increased prevalence of dyslipidemia in the 18-39 years with 17 (57%) amongst FM cases as compared to 18 (15%) in control group (p< 0.001;



OR 7.701). In the 40-59 years age group, 73 (68%) FM patients were dyslipidemic as compared to 110 (39%) of the controls (p< 0.001, OR: 3.539). There was no statistically significant difference in prevalence of dyslipidemia between cases and controls of age greater than 60 years. (Figure 1, Figure 2). There was also no statistically significant correlation between FIQR and individual components of lipid profile (p >0.05). (Figure 3)

Conclusion: In this study, dyslipidemia was more prevalent in FM patients as compared to general population. The findings were consistent in subgroup analysis of age groups 18-39 and 40-59 years. However, FM disease severity did not correlate with individual components of fasting lipid profile in our study. These findings emphasize the need for evaluation of dyslipidemia in fibromyalgia patients.

Reference

1. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III)Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) final report. Circulation 2002; 106:3143–421.

Disclosure: M. CB, None; **S. Surendran**, None; **S. Madan**, None; **A. Tiwari**, None; **S. Raj**, None; **S. Easwar**, None; **G. Ravindran**, None.

Abstract Number: 0127

Interleukin 1 Receptor Antagonist (IL-1Ra) Variable Number of Tandem Repeat (VNTR) Polymorphism in Fibromyalgia Patients in South India

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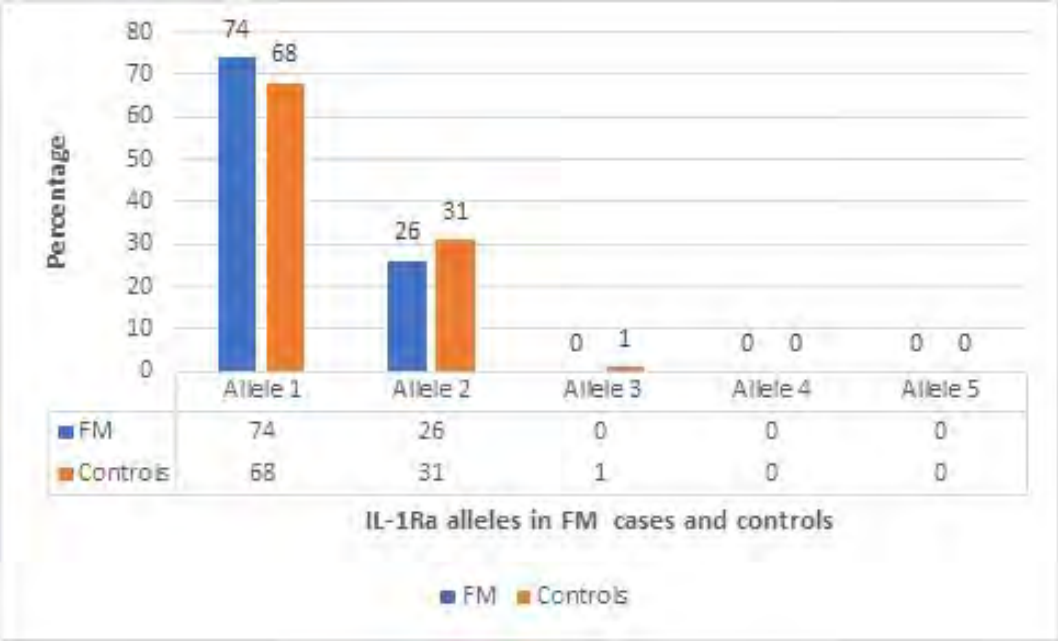
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster (0118–0127)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

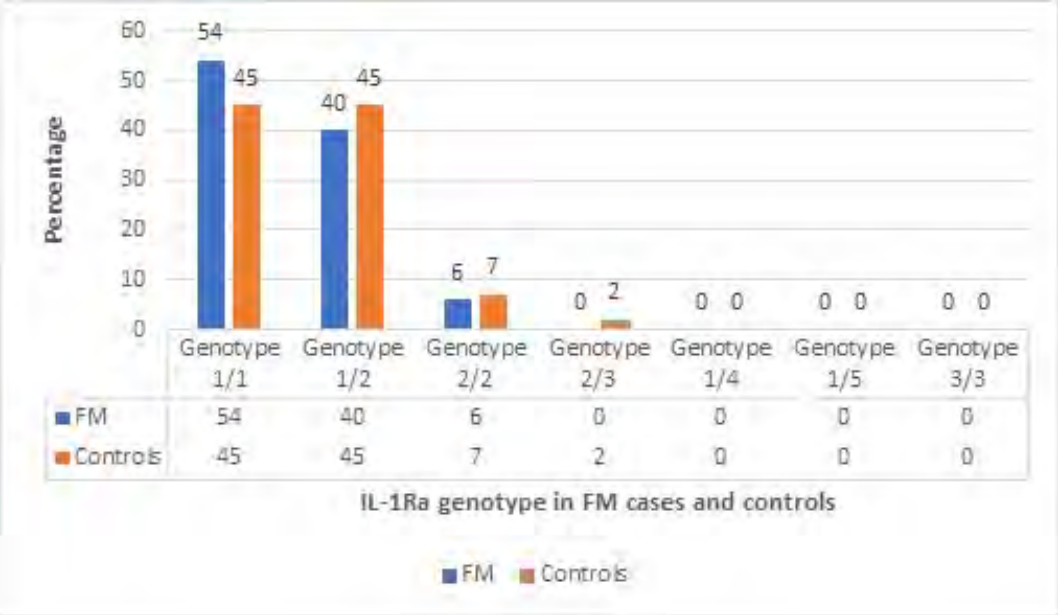
Background/Purpose: Interleukin-1 receptor antagonist (IL-1Ra) variable number of tandem repeats (VNTR) polymorphism is a known to influence the production of IL-1Ra and has been considered as a susceptibility marker for various autoimmune diseases.[1] Serum IL-1Ra levels were found to be low in fibromyalgia (FM) patients in our previous study.[2] Here, we have studied the role of IL-1Ra VNTR polymorphism in influencing disease susceptibility in FM.

Methods: This case-control study was performed at a tertiary care centre in South India from March 2020 to March 2021. FM patients diagnosed as per 2016 modified ACR 2010/2011 criteria and age, gender, and BMI matched healthy controls were included in the study. FM patients with other co-existing rheumatological disease or psychiatric illness were excluded. Genomic DNA was isolated from the peripheral blood of all the enrolled participants and was subjected to polymerase chain reaction to study the frequency of alleles and genotypes of the IL-1Ra gene (IL-1RN) in FM cases and controls. Chi-square and Fisher's exact test were applied to test statistical significance.

Results: A total 79 participants (35 FM cases and 44 matched controls, all females) were enrolled; of the 5 known alleles of IL-1Ra only 3 alleles and out of 8 known genotypes of IL-1Ra only 4 genotypes were detected in our study



Frequency of IL-1 Ra alleles in FM cases and controls.



Frequency of IL-1Ra genotype in FM cases and controls.

Baseline clinical characteristics and disease severity assessment parameters feature of FM patients across the genotypes*

	Genotype 1/1 (n = 19)	Genotype 1/2 (n = 14)	Genotype 2/2 (n = 2)	p-value¶
Age at diagnosis of FM (years)	40.89 ± 10.05	45.71 ± 6.68	46.00 ± 8.48	0.129
BMI (kg/m^2)	24.52 ± 2.75	28.00 ± 3.80	23.00 ± 1.41	**0.012**
WPI	11.26 ± 3.19	10.42 ± 2.73	15.50 ± 2.12	0.437
SSS	7.47 ± 1.57	6.42 ± 1.50	7.50 ± 0.70	0.064
FIQR	48.05 ± 20.67	48.21 ± 19.08	59.50 ± 4.95	0.982
BPI pain	683.94 ± 181.95	637.14 ± 254.52	883.00 ± 165.46	0.542
BPI function	613.52 ± 206	535.42 ± 202.75	450.00 ± 306.88	0.288

* Percentages may not total 100 because of rounding. All the variables are represented in Mean ± Standard deviation. BMI denotes - Body mass index, WPI- Widespread pain index, SSS- Symptom severity score, FIQR- Revised Fibromyalgia Impact Questionnaire, and BPI- Brief pain inventory.

¶ There were only two patients with genotype 2/2 hence it was excluded from this part of statistical analysis and the p-value mentioned here is on comparing various parameters in genotype1/1 and genotype 1/2.

Baseline clinical characteristics and disease severity assessment parameters feature of FM patients across the genotypes.

population. IL-1Ra allele 1 frequency in FM patients was 52 (74%) and 60 (68%) in controls; IL-1Ra allele 2 frequency in FM patients was 18 (36%) and 27 (31%) in controls; IL-1Ra allele 3 was present in only one control; these differences were not significant statistically (p = 0.512) (Figure-1).

IL-1Ra genotype1/1 was present in 19 (54%) FM patients and 20 (45%) controls, genotype 1/2 was present in 14 (40%) FM patients and 20 (45%) controls, genotype 2/2 was present in 2 (6%) of FM patients and 3 (7%) controls, and genotype 2/3 was noted only in one participant of the control group; these differences were not significant statistically (p = 0.753) (Figure-2).

On comparison of baseline characteristics of FM patients with IL-1Ra genotype 1/2 had higher mean BMI- (28.0, SD-3.8 kg/m^2) compared IL-1Ra genotype 1/1 FM patients mean BMI (24.52, SD- 2.75 kg/m^2) and this difference was statistically significant ($p = 0.012$).There was no association of baseline disease severity of FM (assessed by wide spread pain index, symptom severity score, revised fibromyalgia impact questionnaire, brief pain inventory pain and function score) with IL-1Ra genotype and allelic frequency ($p > 0.05$) (Figure-3).

Conclusion: IL-1Ra VNTR polymorphism was not a susceptibility marker for FM in our study population and it did not show any association with FM disease severity parameters. Obesity in FM patients was associated with IL-1Ra genotype 1/2.

References

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2. Surendran S, Mithun CB, P199 Serum cytokines profile in fibromyalgia syndrome and its correlation with disease outcome measures. Rheumatology,2020 April20;59(2).

Disclosure: A. Tiwari, None; **M. CB**, None; **L. Biswas**, None; **S. Surendran**, None; **V. Marwaha**, None; **P. Chickermane**, None; **A. Shahul**, None.

Abstract Number: 0128

Increased Risk of Major Adverse Cardiac Events in Patients with Systemic Lupus Erythematosus After Non-Cardiac Surgery

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The association between systemic lupus erythematosus (SLE) and cardiovascular disease has been well-studied. Cardiovascular disease is a risk factor for major adverse cardiac events (MACE) after surgery. The objective of this study was to estimate the risk of MACE in patients with SLE undergoing moderate to high-risk non-cardiac surgeries compared to control patients with and without diabetes.

Methods: This retrospective, observational study used deidentified administrative data from the Optum Clinformatics Data Mart to identify adult patients who underwent non-cardiac surgery in 2007-2020 via Current Procedural Terminology (CPT) codes. Two independent providers (SB, BB) omitted low risk procedures such as simple skin procedures, endoscopies, ocular surgeries, or orthopedic surgeries that were distal to the elbow or knee joints. From this pool, we defined a SLE cohort (patients who had two or more international classification of diseases (ICD) 9 or 10 codes of 710.0 or M32.xx but not M32.0 within one year before surgery), a diabetic cohort, and a non-diabetic cohort. We matched SLE cases with the diabetic and non-diabetic cohorts by age and gender. Our primary outcome was MACE (including death, myocardial infarction, ischemic stroke, or pulmonary embolism defined by ICD or CPT

Table 1. Multivariable conditional logistic regression model for MACE including death in one month after surgery based on matched cohorts aged 18+.

		Model 1		Model 2		Model 3	
		Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P	Odds Ratio (95% CI)	P
Cohorts							
	Non-DM Control	1		1		1	
	DM control	1.92 (1.72 to 2.14)	<0.001	1.26 (1.12 to 1.41)	<0.001	1.26 (1.12 to 1.41)	<0.001
	SLE	1.51 (1.09 to 2.08)	0.013	0.97 (0.7 to 1.36)	0.88	0.96 (0.69 to 1.34)	0.82
RCRI							
	0			1		1	
	1			2.92 (2.57 to 3.32)	<0.001	2.92 (2.57 to 3.32)	<0.001
	2			8.4 (7.21 to 9.79)	<0.001	8.35 (7.16 to 9.73)	<0.001
	3+			12.72 (10.39 to 15.59)	<0.001	12.68 (10.35 to 15.54)	<0.001
Race							
	White					1	
	Black					1.26 (1.07 to 1.48)	0.005
	Hispanic					0.65 (0.5 to 0.85)	0.002
	Asian					1.3 (0.88 to 1.92)	0.18

codes) within one month post-surgery. We performed a multivariable conditional logistic regression to estimate the odds of MACE within one month of surgery for the three cohorts after adjusting for pre-operative Revised Cardiac Risk Index (RCRI) scores and race (white, black, Hispanic, Asian, and unknown). The RCRI scores include congestive heart failure, coronary artery disease, insulin-dependent diabetes, cerebrovascular disease, and chronic kidney disease (all these variables were defined by claims). Scores greater than one are considered moderate to high risk. We also performed multivariable logistic regression models for MACE amongst SLE patients only that included RCRI scores, age, gender, race, and SLE disease activity (Garris index).

Results: We included 4,750 SLE patients, 484,986 non-diabetes controls, 496,381 diabetes controls and After matching, no significant differences were observed between SLE and diabetic patients in MACE rates. Without adjustment, SLE patients had an increased risk of MACE compared to non-diabetic controls (Table 1, OR 1.51, 95% CI 1.09-2.08); however, the association became nonsignificant after adjusting for RCRI scores (OR 0.97, 95% CI 0.70 – 1.36. Amongst SLE patients, higher RCRI scores, older age, and non-white race were associated with increased risks of MACE, but not gender, pre-operative cardiac testing, or SLE disease activity.

Conclusion: Patients with SLE have an increased risk of MACE within one month after surgery similar to diabetes controls but higher than non-diabetes controls. This risk normalizes after adjusting for pre-operative RCRI scores, suggesting that SLE patients are at an increased risk of MACE because of underlying comorbidities including cardiovascular disease. Our results indicate that SLE confers an increased risk for MACE, independently of disease severity, mediated by pre-existing cardiovascular disease.

Disclosure: S. **Bruera**, None; **X. Lei**, None; **B. Blau**, None; **H. Zhao**, None; **A. Deswal**, None; **J. Yazdany**, Astra Zeneca, 2, 5, Pfizer, 2, 6, Gilead, 5, BMS Foundation, 5; **S. Giordano**, None; **M. Suarez-Almazor**, Gilead, 1, Avenue Therapeutics, 1, ChemoCentryx, 1, Celgene, 1.

Abstract Number: 0129

Real-World Flare Rates and Progression by Treatment Settings Among the Commercially-Insured Systemic Lupus Erythematosus Population in the U.S

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The clinical presentation of systemic lupus erythematosus (SLE) is complicated, as patients cycle through periods of active disease (flares) and remission. To establish the burden of SLE, the heterogenous nature of the population must also be taken into consideration, particularly as it relates to the frequency and nature of flare treatment. The purpose of this study was to assess and characterize the annual rate of SLE flares by the site of care where treated (inpatient hospital [IP], emergency room [ER], and outpatient [OP]), and to observe the progression of specific flare rates and types in a subsequent year.

Methods: SLE patients were selected from IBM MarketScan commercial claims and encounters databases between 1/1/2013–3/31/2019. Inclusion criteria: 1) ≥1 inpatient claim with a diagnosis for SLE, or ≥2 non-diagnostic SLE outpatient claims with at least one rheumatologist or nephrologist specialty designation (index date set to a random SLE service date with ≥12 months of SLE disease history preceding it to create a prevalence cohort), 2) continuous enrollment with medical and pharmacy benefits for 12 months pre- and post-index, and 3) valid steroid Rx claims. SLE flares were defined using a published claims-based algorithm based on presence of SLE-related treatment and diagnosis[1]; results were presented during the 12-month period preceding (year 1) and following index (year 2). Flare

Table 1. Flare Frequency and Severity in Year 2 as a Function of Year 1 Flare Status

	All Patients N = 22,385	
Flare Characteristics in Year 1		
Total flares (Mean, SD)	3.9	2.0
Count of patients with flares (N,%)		
0 flares	1,040	4.6%
1 flare	1,853	8.3%
2 flares	2,892	12.9%
3+ flares	16,600	74.2%
Patients with ≥1 flare treated at IP setting (N, %)	1,163	5.2%
Patients with ≥1 flare treated at ER setting (N, %)	2,395	10.7%
Patients with ≥1 flare treated at OUT setting (N, %)	21,191	94.7%

Table 2. Year 2 Flare Rates by Year 1 Flare Place of Service Among Patients with >=1 Flare

	Patient Cohorts by Flares Treatment Setting in Year 1							
	Patients with 0 Flares in Year 1		Patients with ≥1 Inpatient Flares		Patients with ≥1 ER but No IP flares		Patients with ≥1 OP but No IP/ER flares	
	N = 1,040		N = 1,163		N = 2,072		N = 18,110	
Flare Characteristics in Year 1								
Total flares (Mean, SD)	N/A	N/A	5.2	1.9	4.7	1.8	3.9	1.8
Count of patients with n flares (N,%)								
0 flares	N/A	N/A	0	0.0%	0	0.0%	0	0.0%
1 flare	N/A	N/A	32	2.8%	59	2.8%	1,762	9.7%
2 flares	N/A	N/A	67	5.8%	175	8.4%	2,650	14.6%
3+ flares	N/A	N/A	1,064	91.5%	1,838	88.7%	13,698	75.6%
Patients with ≥1 flare treated at IP setting (N, %)	N/A	N/A	1,163	100.0%	0	0.0%	0	0.0%
Patients with ≥1 flare treated at ER setting (N, %)	N/A	N/A	323	27.8%	2,072	100.0%	0	0.0%
Patients with ≥1 flare treated at OP setting (N, %)	N/A	N/A	1,103	94.8%	1,978	95.5%	18,110	100.0%
Flare Characteristics in Year 2								
Total flares (Mean, SD)	1.3	1.4	4.6	2.0	4.3	2.0	3.9	2.0
Count of patients with n flares (N,%)								
0 flares	364	35.0%	24	2.1%	58	2.8%	838	4.6%
1 flare	285	27.4%	61	5.2%	141	6.8%	1,597	8.8%
2 flares	193	18.6%	93	8.0%	213	10.3%	2,249	12.4%
3+ flares	198	19.0%	985	84.7%	1,660	80.1%	13,426	74.1%
Patients with ≥1 flare treated at IP setting (N, %)	10	1.0%	224	19.3%	166	8.0%	502	2.8%
Patients with ≥1 flare treated at ER setting (N, %)	41	3.9%	290	24.9%	565	27.3%	1,303	7.2%
Patients with ≥1 flare treated at OP setting (N, %)	664	63.8%	1,113	95.7%	1,969	95.0%	17,200	95.0%
Among patients with flares by treatment settings (Mean, SD)								
Number of flares treated at IP (Mean, SD)	1.2	0.4	1.4	0.9	1.2	0.5	1.1	0.4
Average length of stay (in days) per flare treated at IP (Mean, SD)	4.8	5.3	6.3	6.9	5.0	5.0	4.5	5.2
Number of flares treated at ER (Mean, SD)	1.1	0.3	1.7	1.2	1.6	1.0	1.2	0.5
Number of flares treated at OUT (Mean, SD)	2.0	1.2	4.1	1.8	3.9	1.8	4.0	1.9

progression from year 1 to year 2 were observed among four mutually exclusive cohorts of patients who had ≥1 flare treated in IP, ≥1 flare in ER but no IP, ≥1 flare in OP but no IP/ER, and no flares in year 1.

Results: 22,385 SLE patients qualified for the study; 95.4% (N=21,345) presented ≥1 flare in year 1; 5.4% (n=1,163) were treated in the IP, 9.7% (n=2,072) in the ER, and 84.8% (n=18,110) in an OP setting. Nearly 2/3 of patients without a flare in year 1 presented a flare in year 2, with 19.0% presenting ≥3 flares (Table 1). Among patients with a flare in year 1, 75.3% presented ≥3 flares in year 2. Compared to patients without a year 1 flare, those with a prior-year flare were more likely to present year 2 flares in the IP (4.2% vs. 1.0%), ER (10.1% vs. 3.9%), and OP (71.2% vs. 34.6%). Analyses segmented by baseline flare site of care revealed that, among patients with a flare treated in the IP setting, 19.3% presented an IP flare in year 2, and 24.9% presented an ER flare, substantially higher than patients without prior-year flares treated in the IP (Table 2). Compared to patients with baseline flares in the ER or OP settings, those with baseline flares in the IP setting were more likely to present ≥3 flares in that same year (84.7% vs. 80.1% and 74.1%; Figure 1).

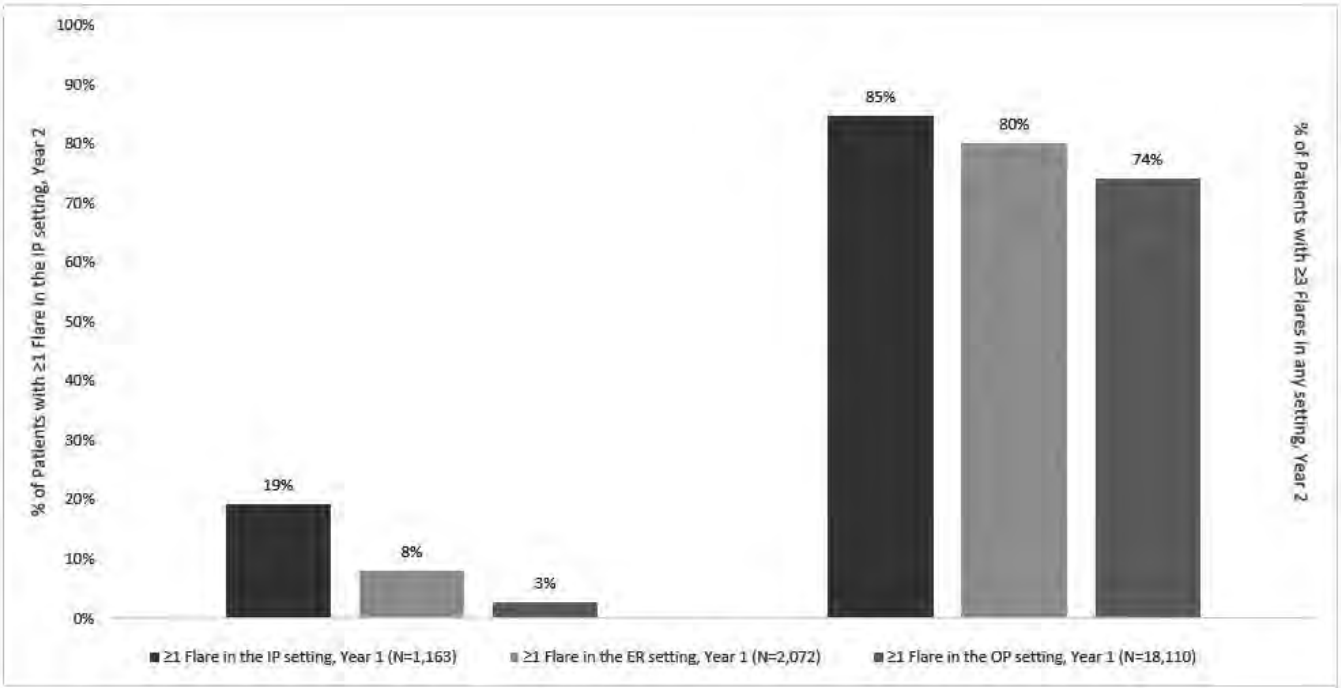

Figure 1. SLE Flare Outcomes in Year 2 as a Function of Prior Year Category.

Conclusion: Rates of SLE flares vary by patient subgroups over time and by flare history. SLE patients with more resource-intensive flares may be more likely to experience additional flares of similar or worse intensity in the future. An accurate assessment of disease flares is critical to quantifying the burden of SLE, and can inform the development of treatment options to control disease and minimize healthcare burden at the population level. Results highlight a potential unmet need in the current treatment landscape.

1. Garris C, et al. J Med Econ. 2013;16(5):667-677.

Disclosure: S. Sze-jung Wu, AstraZeneca, 3; **A. Perry**, AstraZeneca, 2; **H. Varker**, AstraZeneca, 2; **R. Bizier**, AstraZeneca, 2; **J. Tkacz**, AstraZeneca, 2; **R. Ortmann**, AstraZeneca, 3.

Abstract Number: 0130

Clinical and Economic Characterization of Systemic Lupus Erythematosus Patients: Real World Observation Across Disease Severity and Payer Channels in the U.S

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Current literature characterizing the economic and clinical burden of systemic lupus erythematosus (SLE) is outdated and often does not consider SLE disease severity, which is associated with outcomes

Table 1. Patient Characteristics by Baseline Disease Severity and Payer Channel

	Severity of SLE Disease During Baseline											
	Commercial				Medicare				Medicaid			
	Mild N = 5,219	Moderate N = 9,756	Severe N = 7,410	p-value	Mild N = 408	Moderate N = 784	Severe N = 843	p-value	Mild N = 1,190	Moderate N = 2,788	Severe N = 4,213	p-value
Age (Mean, SD)	46.8 (11.3)	46.3 (11.6)	46.5 (11.4)	0.033	71.4 (6.7)	71.2 (7.2)	71.4 (8.0)	0.825	40.2 (12.2)	40.0 (12.5)	41.7 (12.0)	<0.001
Age category (N, %)												
18-34	15.9%	17.5%	17.1%	0.337	0.0%	0.0%	0.0%	0.070	37.2%	36.7%	31.1%	<0.001
35-44	22.7%	22.5%	22.6%		0.0%	0.1%	0.5%		26.5%	26.1%	27.2%	
45-54	31.1%	31.0%	31.1%		0.5%	1.3%	1.5%		20.2%	21.2%	24.5%	
55-64	30.2%	29.1%	29.2%		6.1%	8.2%	9.1%		15.6%	15.4%	16.4%	
65-74	0.0%	0.0%	0.0%		66.9%	60.7%	57.5%		0.5%	0.6%	0.8%	
75+	0.0%	0.0%	0.0%		26.5%	29.7%	31.3%		0.1%	0.1%	0.1%	
Female Sex (N, %)	92.4%	91.1%	92.0%	0.008	90.0%	87.2%	88.3%	0.388	93.5%	93.0%	93.4%	0.832
Elixhauser Comorbidity Index (Mean, SD)	0.5 (3.9)	1.8 (5.8)	2.0 (9.6)	<0.001	1.8 (5.4)	4.7 (8.1)	6.8 (11.0)	<0.001	0.6 (5.6)	2.5 (7.4)	1.6 (11.6)	<0.001
Comorbidities (N, %)												
Cardiovascular Disease	20.7%	35.7%	52.3%	<0.001	43.4%	62.2%	81.3%	<0.001	25.9%	44.3%	63.1%	<0.001
Osteoarthritis	15.6%	20.2%	24.2%	<0.001	46.8%	48.5%	51.1%	0.309	13.6%	22.5%	27.3%	<0.001
Fatigue	12.2%	15.8%	23.0%	<0.001	12.5%	14.0%	20.2%	<0.001	10.7%	17.3%	21.4%	<0.001
Fibromyalgia	10.5%	14.8%	21.8%	<0.001	9.6%	15.3%	16.4%	0.005	16.6%	23.5%	29.0%	<0.001
Kidney Transplant	11.2%	17.3%	25.9%	<0.001	6.4%	10.6%	15.9%	<0.001	21.5%	27.8%	37.9%	<0.001

Table 2. All-Cause Healthcare Resource Utilization and Costs by Baseline Disease Severity and Payer Channel.

	Severity of SLE Disease During Baseline											
	Commercial				Medicare				Medicaid			
	Mild N = 5,219	Moderate N = 9,756	Severe N = 7,410	p-value	Mild N = 408	Moderate N = 784	Severe N = 843	p-value	Mild N = 1,190	Moderate N = 2,788	Severe N = 4,213	p-value
Patients with IP admission (N, %)	4.5%	9.9%	24.2%	<0.001	8.1%	12.6%	37.0%	<0.001	9.2%	17.3%	37.5%	<0.001
# of IP admissions (Mean, SD)	0.1 (0.2)	0.1 (0.4)	0.4 (1.1)	<0.001	0.1 (0.3)	0.2 (0.5)	0.5 (0.8)	<0.001	0.1 (0.4)	0.3 (0.9)	0.9 (1.8)	<0.001
Length of stay (days)/admission among pts with an IP admission (Mean, SD)	3.0 (2.0)	3.6 (3.2)	5.1 (5.4)	<0.001	3.2 (2.3)	4.3 (5.9)	5.4 (5.0)	<0.001	3.3 (3.1)	4.1 (3.5)	5.1 (4.6)	<0.001
Patients with an ER visit (N, %)	19.1%	31.1%	44.4%	<0.001	17.6%	28.6%	45.6%	<0.001	52.3%	66.6%	77.7%	<0.001
# of ER visits (Mean, SD)	0.3 (0.8)	0.6 (1.3)	1.1 (2.3)	<0.001	0.2 (0.6)	0.5 (1.2)	1.1 (1.8)	<0.001	1.4 (2.2)	2.5 (4.1)	4.1 (6.9)	<0.001
Overall Annual Healthcare costs (Mean, SD)	$9,746 (19,332)	$19,567 (37,431)	$63,765 (127,142)	<0.001	$16,273 (28,454)	$28,537 (50,050)	$68,253 (119,932)	<0.001	$5,133 (17,223)	$11,904 (35,241)	$29,354 (75,784)	<0.001

that may vary both within and across sub-populations. The objective of this study was to characterize a prevalence population of SLE and to assess outcomes related to comorbidities, healthcare resource utilization, and flares across disease severity levels and payer channels.

Methods: SLE patients were selected from IBM MarketScan Commercial Claims (COM), Medicare Supplemental (MDCR), and Medicaid (MDCD) Databases from 1/1/2013-3/31/2019. Inclusion criteria were 1) ≥1 inpatient claim with an SLE diagnosis or ≥2 non-diagnostic outpatient SLE claims with ≥1 rheumatologist or nephrologist specialty designation (index date set to random SLE claim with ≥12 months of SLE disease history preceding it), 2) continuous enrollment for 12 months pre-index, and 3) valid steroid Rx claims. SLE disease flares and severity were assessed using a published claims-based algorithm[1]; patient characteristics, healthcare service use/costs, and flare outcomes were assessed during the year prior to index. All results were presented by disease severity and payer channel.

Results: 22,385 COM (23% mild; 44% moderate; 33% severe), 2,035 MDCR (20% mild; 39% moderate; 41% severe), and 8,191 MDCD (15% mild; 34% moderate; 51% severe) patients were included. Mean overall age was 46.5[11.5], 71.3[7.4], 40.9[12.2] years for COM, MDCR, and MDCD, respectively; older age was associated with an increase in disease severity for MDCD patients (p< 0.001). The majority of patients across all subgroups were female (88.2-93.3%) (**Table 1**). The mean Elixhauser Comorbidity Index was 0.5-2.0[3.9-0.6], which increased as SLE disease severity increased (p< 0.001). Common comorbidities included cardiovascular disease (20.7-63.1%), osteoarthritis (13.6-51.1%), and fatigue (10.7-23.0%). Across all payer channels, all-cause inpatient admissions increased significantly with disease severity (4.5%-9.2% mild; 9.9%-17.3% moderate; 24.2%-37.5% severe), with similar trends for emergency room utili-

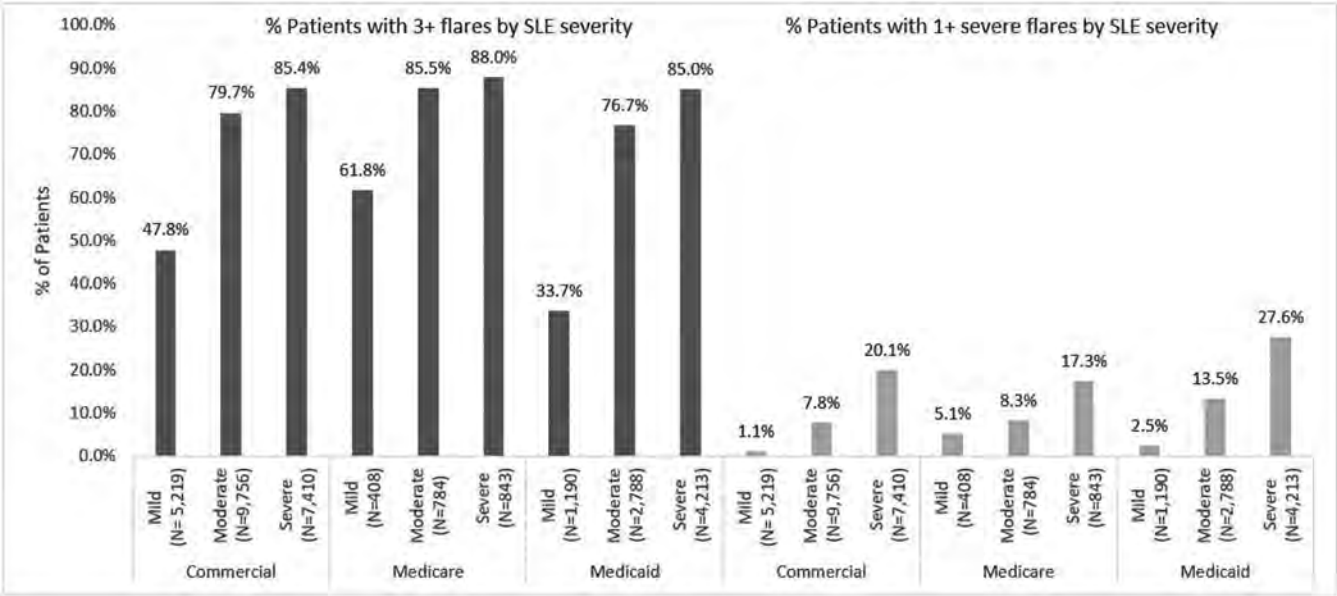

Figure 1. SLE Flare Outcomes by Disease Severity for Each Payer Channel.

zation (17.6%-52.3% mild; 28.6%-66.6% moderate; 44.4%-77.7% severe; all p< 0.001) (**Table 2**). Total healthcare costs were 4-to-6-fold higher among patients with severe vs. mild disease ($29,354-68,253 among severe vs. $5,133-16,273 among mild; p< 0.001). Across all payer groups, the proportion of patients with a severe SLE flare, as well as the proportion of patients with 3+ flares, increased as disease severity also increased (**Figure 1**).

Conclusion: SLE-related comorbidities, disease flares, and healthcare expenditure vary by both disease severity and payer status. SLE patients with more severe SLE disease experience higher rates of comorbidities and SLE flares, which are associated with more intensive resource utilization and costs; Medicaid beneficiaries presented the highest use of ER and IP services. Overall, results demonstrate a potential unmet need in the SLE treatment landscape, especially among patients with more severe disease.

1. Garris C, et al. J Med Econ. 2013;16(5):667-677.

Disclosure: J. Tkacz, AstraZeneca, 2; **A. Perry**, AstraZeneca, 2; **H. Varker**, AstraZeneca, 2; **R. Bizier**, AstraZeneca, 2; **R. Ortmann**, AstraZeneca, 3; **S. Sze-jung Wu**, AstraZeneca, 3.

Abstract Number: 0131

Association of Numeracy with Medication Non-Adherence in Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Over 33% of U.S. adults have limited health literacy or numeracy. Limited health literacy and numeracy have been associated with higher disease activity and worse patient-reported outcomes in systemic lupus erythematosus (SLE). Health literacy involves ability to understand and use health information. A component of health literacy is numeracy, which involves quantitative math skills and is important for understanding and managing complex medication regimens. The objective of this study was to assess the relationship between health numeracy and medication adherence in SLE; we hypothesized that patients with limited numeracy would have higher rates of medication non-adherence.

Methods: SLE patients meeting ACR or SLICC criteria were recruited from a university clinic from March 2019 through January 2021. Numeracy was assessed with the Subjective Numeracy Scale (SNS-3); limited numeracy was defined as SNS-3 $\leq$ 12. Self-reported adherence for SLE medications was obtained using the visual analog scale component of the MASRI (Medication Adherence Self-Report Inventory), a patient-reported percentage of taking medications in the past 1 month (0-100%). In a subset of patients (n=146), objective medication adherence to SLE medications was also determined by Medication Possession Ratio (MPR), the proportion of days with medication supply over a 3-month period, using pharmacy refill data from the electronic health record. Non-adherence was defined as MASRI < 90% and MPR < 80%. We evaluated relationships between numeracy and adherence using descriptive statistics. Logistic regression models estimated the associations of numeracy with non-adherence, adjusting for education level.

Results: The cohort included 218 patients with SLE. The average age was 43, with 94% female and 59% Black race. Mean disease duration was 13 years, with average SLEDAI 3.0 and PGA 0.5; 45% had a history of lupus nephritis.

Compared to patients with adequate numeracy, those with limited numeracy had lower self-reported adherence (54% vs 73%) but paradoxically higher objective adherence (56% vs 44%). In a multivariable logistic regression adjusted for education, patients with low numeracy were twice as likely to self-report non-adherence by MASRI (OR 1.94; 95% CI: 1.07, 3.51) (Table 1).

Conclusion: In our cohort, limited numeracy and non-adherence are common. Although patients with low numeracy filled SLE medications at similar rates to those with adequate numeracy, we found paradoxically they were more likely to report non-adherence. This may reflect true non-adherence but could also be due to difficulty interpreting the adherence question or estimating the percentage they have taken medications. Future studies are needed to further elucidate this relationship.

Adjusted for education, patients with low numeracy were twice as likely to self-report non-adherence by MASRI (OR 1.94; 95% CI: 1.07, 3.51).

Table 1: Logistic Regression of the Associations of Health Numeracy with Adherence

	Adequate Numeracy	Limited Numeracy	p-value	Adjusted OR (95% CI)	p-value
	n=135	n=83			
% Adherent by **Self-Report** (MASRI ≥ 90%)	98 (73%)	45 (54%)	0.008	1.94 (1.07, 3.51)	0.03
	n=89	n=57			
% Adherent by **Objective Adherence** (MPR ≥ 80%)	39 (44%)	32 (56%)	0.2	0.58 (0.29, 1.14)	0.1

*OR adjusted for education

Disclosure: M. Maheswaranathan, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **A. Barr**, None; **C. Howe**, None; **S. Bailey**, Luto, 2, Lundbeck, 2, 5, Merck, 5, Gordon and Betty Moore Foundation, 5, Retirement Research Foundation, 5, Sanofi, 2, National Institutes of Health, 5, Eli lilly, 5, Pfizer, 2, 5, University of Westminster, 2; **S. Hastings**, None; **J. Rogers**, Exagen, 2, 5, Pfizer, 5, Eli Lilly, 2, Immunovant, 2, Northwestern University, 2; **J. Doss**, Pfizer, 5; **L. Criscione-Schreiber**, None; **R. Sadun**, None; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **K. Sun**, None.

Abstract Number: 0132

Hospitalization Rates Among Patients with Systemic Lupus Erythematosus: A Population Based Study

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune multiorgan disease associated with significant morbidity and mortality. Although the survival rate for SLE patients has improved, hospitalization rates and healthcare utilization among SLE patients remain higher than the general population. By using a population-based cohort, we describe hospitalization rates, causes and risk factors among SLE patients compared to non-SLE patients between 2015 and 2020.

Methods: Using an established population-based research infrastructure that links the medical records of all individuals in a geographically well-defined 27-county US population, we identified SLE cases meeting the 2019 ACR/EULAR classification criteria. SLE patients who were residents in the 27-county region on January 1, 2015 were in-

Table 1. Demographic and hospitalization characteristics among SLE patients and comparators

Characteristic	SLE N=479	Comparators N= 479	P-Value
Age, years, Mean (SD)	53.2 (16.2)	53.2 (16.2)	0.99
Female Sex, N (%)	394 (82)	394 (82)	1.00
Race/Ethnicity, N (%)			
White	404 (85%)	412 (86%)	0.93
Asian	15 (3%)	17 (4%)	
other/mixed	8 (2%)	5 (1%)	
Black	18 (4%)	19 (4%)	
American Indian	2 (0%)	2 (0%)	
Hispanic Ethnicity	29 (6%)	24 (5%)	
Length of Stay (days) Median (Range)	4 (0-112)	3 (0-42)	0.001

Table 2. Rate of hospitalization by primary discharge diagnosis using the Clinical Classifications Software among SLE patients and comparators

Grouped primary discharge diagnosis	SLE hospitalization rate/100 person-years	Non-SLE hospitalization rate/100 person-years	Rate Ratio (95% CI)
Overall	26.24	9.27	2.83 (2.43-3.31)
Cardiovascular	4.23	1.57	2.67 (1.86-3.96)
Respiratory	3.40	0.68	4.88 (3.00-8.75)
Musculoskeletal	2.90	0.77	3.72 (2.30-6.50)
Injury/poisoning	2.16	0.47	4.45 (2.48-9.13)
Gastrointestinal	1.99	0.85	2.31 (1.41-4.00)
Infectious	1.70	0.51	3.24 (1.80-6.52)
Genitourinary System	1.29	0.26	4.73 (2.23-12.84)
Mental Illness	0.95	0.77	1.24 (0.68-2.33)
Neoplasm/Oncology	0.91	0.47	1.91 (0.97-4.12)
Pregnancy Morbidity	0.71	0.60	1.18 (0.59-2.43)
Hematologic	0.71	0.04	11.38 (3.24-159.95)
Endocrine/Metabolic	0.66	0.26	2.48 (1.07-6.98)
Dermatological	0.54	0.17	2.93 (1.11-10.50)
Neurological	0.46	0.17	2.49 (0.91-9.03)
Multiorgan/ill defined	0.29	0.13	2.09 (0.63-9.55)

cluded. Patients with SLE were matched by age, sex, race/ethnicity and county of residence to non-SLE patients and were followed until 12/2020. Variables included were age, sex, race/ethnicity, number of hospitalizations, length of stay (LOS) and primary discharge diagnosis. Chi-square and Kruskal-Wallis rank sum tests were used to assess difference in characteristics between cases and controls. Hospitalization data were analyzed using person-year methods and rate ratios were obtained from Poisson models.

Results: We identified 479 SLE patients and 479 comparators. Mean age of SLE patients was 53.2 (SD 16.2) years, 82% were females and 85% were white (Table 1). Between 2015 and 2020, the hospitalization rate of SLE patients was 26.2/100 person-years compared to 9.3/100 person-years among comparators (rate ratio (RR) 2.83; 95% confidence interval (CI) 2.43-3.31; Table 2). LOS was higher among SLE patients (median 4 vs. 3 days; p=0.001). SLE patients were hospitalized at a significantly higher rate than subjects without SLE in 10 of 15 diagnosis categories (Table 2). The highest RR was observed for hematologic diseases (RR 11.38; 95% CI 3.24-159.95) followed by respiratory diseases (RR 4.88; 95% CI 3.00-8.75) and genitourinary diseases (RR 4.73; 95% CI 2.23-12.84). SLE hospitalization rates compared to non-SLE comparators were highest among males (RR 3.18; 95% CI 2.31-4.5), those with SLE duration < 5 years since diagnosis (RR 3.05; 95% CI 2.59-3.62) and age 50-64 years (RR 4.5; 95% CI 3.37-6.2) (Table 3).

Conclusion: SLE patients had nearly 3-fold more hospitalizations than comparators with an increased risk of hospitalization for most diagnosis categories.

Table 3. Rate of hospitalizations among SLE patients and comparators by sex, age and disease duration

Characteristic	SLE hospitalization rate/100 person-years	Non-SLE hospitalization rate/100 person-years	Rate Ratio (95% CI)
Age			
20-49	17.91	5.22	3.4 (2.46-4.86)
50-64	29.54	6.51	4.5 (3.37-6.2)
65+	32.84	16.2	2.02 (1.63-2.52)
Sex			
Female	24.42	8.89	2.74 (2.31-3.27)
Male	35.21	11.01	3.18 (2.31-4.5)
Disease Duration			
<5 years	26.83	8.77	3.05 (2.59-3.62)
5-10 years	22.49	12.82	1.74 (1.19-2.62)

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Abstract Number: 0133

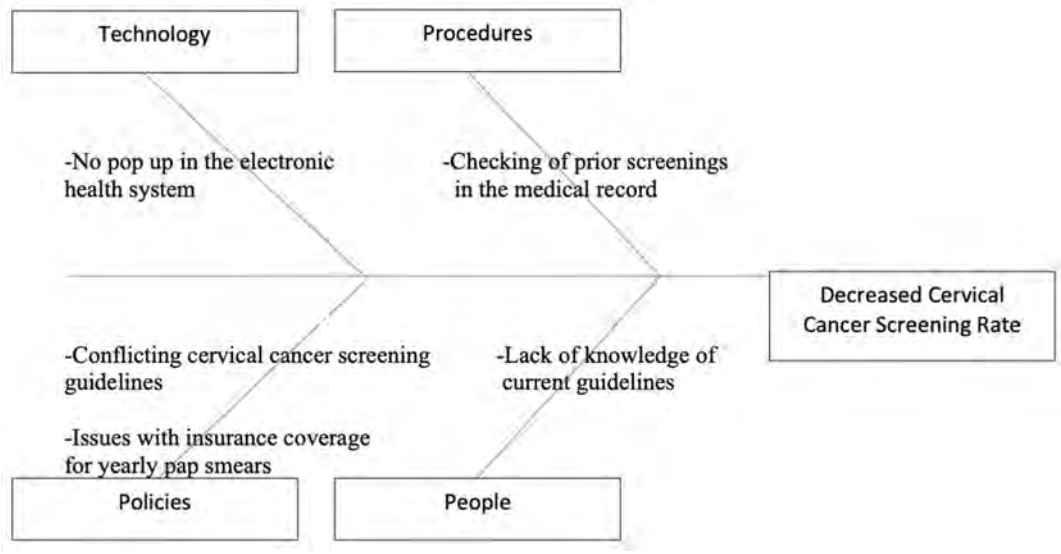
Cervical Cancer Screening Rate in Women with Systemic Lupus Erythematosus

Erica Rosen[1] and Megan Krause[2], [1]University of Kansas, Kansas City, MO, [2]University of Kansas, Kansas City, KS

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Females with systemic lupus erythematosus have increased rates of cervical cancer especially if on immunosuppressive therapy. The American Cancer Society reports the incidence of cervical cancer in the general public to be 7.5/100,000. The incidence has been reported to be significantly higher in females with SLE. Prior studies suggested that women with SLE have lower rates of undergoing timely cervical cancer screenings compared to the general population. The American Cancer Society recommends screening women with SLE at age 21 or 1 year after sexual activity, whichever comes first, with annual pap testing for patients age < 30 and a yearly pap with HPV co-testing if >30. For the general population of women ages 21-65 pap testing every 3 years is recommended for patients < 30 and if >30 cytology is recommended every 3 years or cytology with HPV co-testing every 5 years. This study aimed to determine the rate of cervical cancer screening and incidence of cervical cancer in women with SLE at our single academic institution.



Cause and Effect Diagram.

Methods: A retrospective chart review was conducted at a single tertiary center. Females were included who had the diagnosis of SLE by ICD9/10 codes, had three or more rheumatology visits, and two or more visits with family medicine, internal medicine or OBGYN between the years of 2004-2020. Eligible patients were between 21-65 years of age. The search also included the number of pap smear procedure codes per patient. The rate of cervical cancer screening was estimated for each patient by finding the time difference between the first office visit and last office visit divided by the number of pap smears. A search was also conducted to identify patients who had hysterectomy and only time prior to hysterectomy was included when determining the screening rate. A search was also conducted to identify the incidence of cervical cancer.

Results: 145 patients were identified. 21 patients were found to have had a hysterectomy at some point during the time period and only the time prior to hysterectomy was included. The average time between cervical cancer screenings was found to be 55 months or 4.5 years. Furthermore, increasing age directly correlated with a decrease in screening. The average time between cervical cancer screening for women ages 21-29 was 27 months, women ages 30-39 was 53 months, women ages 40-49 was 50 months, women ages 50-59 was 63 months and women ages >60 was 80 months. Additionally, 4 patients had developed cervical cancer resulting in an incidence of 2.7%. A root cause analysis was preformed to identify causes for decreased cervical cancer screenings.

Conclusion: This chart review identified inadequate cervical cancer screening in women with SLE at this tertiary center. The time between screenings decreased with increasing age. Further research is needed to determine an appropriate screening interval for these patients to avoid unnecessary invasive procedures and increased costs. Future steps are to collaborate with the OBGYN department to provide an interdisciplinary approach in determining appropriate screening intervals and an intervention to improve the overall cervical cancer screening rate in this patient population.

Disclosure: E. Rosen, None; **M. Krause**, None.

Abstract Number: 0134

Systemic Lupus Erythematosus Is a Risk Factor for Mortality in Older Patients with Early-Stage Breast Cancer

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Women with systemic lupus erythematosus (SLE) who develop breast cancer (BC), may receive different therapies (e.g. radiation) than women with BC who do not have SLE. They also have more comorbidities that may affect survival. Our objective was to evaluate survival in women with both SLE and BC, compared with women with BC alone or SLE without cancer.

Methods: We conducted a retrospective observational study using the Surveillance, Epidemiology, and End Results (SEER) and the Texas Cancer Registry (TCR) dataset linked to Medicare claims. We included women aged ≥66 years diagnosed with BC from 2005-2015, and a 5% Medicare non-cancer random sample who resided in the SEER/TCR region. Based on BC and SLE status, we included three groups: 1) BC SLE, 2) BC non-SLE, 3) non-cancer SLE. For women with BC, we collected cancer characteristics (age and year at diagnosis, stage, hormone receptor status) and treatment (chemotherapy, radiation therapy, and surgery type). We matched BC SLE and BC non-SLE with cancer characteristics. We matched non-cancer SLE women with BC SLE with birth year and race and used the matched date of diagnosis as the index date for non-cancer women. SLE was defined with ≥2 international classification of diseases (ICD) 9 or 10 diagnosis codes within 1 year before BC diagnosis (or index date). Overall survival (OS) and breast cancer specific survival (BCSS, only for BC women) were measured from date of diagnosis (or index date). Kaplan-Meier methods and multivariable Cox proportional hazards models were implemented to evaluate the association of survival outcomes with groups adjusting for cancer characteristics and treatment (for BC), comorbidities and the Garris index of SLE disease severity (for SLE only).

Results: We identified 494 BC SLE cases, 145,517 BC non-SLE, and matched 268 non-cancer SLE. The 5-year overall survival for women with early breast cancer (stages 0-II) with and without SLE was 74% (95% confidence interval [CI] 68%-78%) and 86% (95% CI 85%-86%) ($p < 0.001$) respectively. In multivariable models adjusting for cancer characteristics, treatment and comorbidities, BC SLE had increased risks of death (HR 1.65; 95% CI 1.38 to 1.98) compared to the BC non-SLE group but no significant association with BCSS. Comparisons between the SLE groups showed that BC SLE had increased risks of death compared non-cancer SLE after adjusting for SLE disease severity (HR 1.42; 95% CI 1.05 to 1.92).

Conclusion: Our data shows that patients with BC and SLE are at risk of earlier mortality compared to patients with BC alone, even after adjusting for SLE disease activity and comorbidities. Further research is needed to investigate the determinants of these findings and improve survival in this population.

Table 1. Multivariable Cox proportional hazards model of overall survival for matched patients (stage 0-II cohort).

Stage 0-II cohort*	Model 1	Model 2	Model 3	Model 4	Model 5
	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)	HR (95% CI)
SLE status					
Non-SLE	Ref	Ref	Ref	Ref	Ref
SLE	1.98 (1.65-2.36)	1.97 (1.65-2.36)	1.96 (1.64-2.35)	1.95 (1.63-2.34)	1.65 (1.38-1.98)
Age group (years)					
66-70	Ref	Ref	Ref	Ref	Ref
71-75	1.41 (1.23-1.61)	1.42 (1.24-1.63)	1.42 (1.24-1.63)	1.42 (1.24-1.63)	1.36 (1.19-1.56)
76-80	2.23 (1.94-2.57)	2.27 (1.97-2.61)	2.23 (1.94-2.57)	2.2 (1.91-2.54)	2.03 (1.76-2.34)
> 80	4.92 (4.3-5.63)	4.85 (4.24-5.55)	4.76 (4.16-5.45)	4.6 (4.01-5.28)	4 (3.48-4.59)
Race/ethnicity					
White	Ref	Ref	Ref	Ref	Ref
Black	1.07 (0.9-1.26)	1.05 (0.89-1.23)	1.05 (0.89-1.24)	1.05 (0.89-1.24)	0.97 (0.82-1.14)
Hispanic	0.67 (0.53-0.84)	0.63 (0.5-0.8)	0.64 (0.5-0.8)	0.64 (0.51-0.81)	0.62 (0.49-0.79)
Other	0.68 (0.53-0.88)	0.64 (0.49-0.82)	0.63 (0.49-0.81)	0.63 (0.49-0.81)	0.65 (0.51-0.84)
Hormonal receptor status					
Negative	Ref	Ref	Ref	Ref	Ref
Positive	0.75 (0.66-0.86)	0.76 (0.67-0.87)	0.86 (0.75-0.99)	0.85 (0.74-0.98)	0.85 (0.74-0.98)
Surgery					
Breast conserving surgery		Ref	Ref	Ref	Ref
Mastectomy		1.27 (1.15-1.40)	1.28 (1.16-1.42)	1.14 (1.01-1.3)	1.14 (1.00-1.29)
Hormonal therapy (2y)					
No			Ref	Ref	Ref
Yes			0.70 (0.61-0.81)	0.72 (0.63-0.83)	0.70 (0.61-0.81)
Missing			0.90 (0.78-1.03)	0.90 (0.79-1.03)	0.88 (0.77-1.01)
Radiation					
No				Ref	Ref
Yes				0.83 (0.74-0.94)	0.87 (0.77-0.98)
Comorbidity index					
0					Ref
1					1.63 (1.44-1.83)
2+					2.90 (2.59-3.26)

SLE: systemic lupus erythematosus; HR: hazard ratio; CI: confidence interval; Ref: referent.

*Models additionally included adjustment for year of diagnosis, marital status, grade, state buy-in, education quartile and propensity score. Chemotherapy was not significant in the multivariable models 3-5

Disclosure: S. Bruera, None; **X. Lei**, None; **X. Pundole**, Amgen, 3; **H. Zhao**, None; **S. Giordano**, None; **S. Vinod**, None; **M. Suarez-Almazor**, Gilead, 1, Avenue Therapeutics, 1, ChemoCentryx, 1, Celgene, 1.

Abstract Number: 0135

Comparing Rheumatoid Arthritis (RA), Psoriatic Arthritis (PA) and Systemic Lupus Erythematosus (SLE) Total Cost of Care (TCC) in Those with Optimally Managed Depression to Those with Sub-optimally Managed Depression

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatic diseases (RD) are characterized by systemic signs and symptoms, including articular and extra-articular manifestations. Three common forms of RDs are RA, PsA and SLE. RDs are associated with a high risk for psychiatric comorbidities, particularly depression. The impact of comorbid depression on RD patients could substantially impact clinical and economic outcomes. The purpose of this study is to compare the total cost of care (TCC) and medication adherence in RD patients with and without optimally managed depression (OMD).

Methods: This retrospective cohort study identified RD patients with and without depression and patients with depression only, insured by a large Commercial health plan in the United States between January 1, 2017, and December 31, 2017, who were followed up until December 31, 2019. We defined "sub-optimally-managed depression" (SOMD) as having one or more of the following: suboptimal antidepressant adherence (< 80% portion of days covered (PDC)), at least one inpatient admission or emergency room visit with a primary diagnosis of depression or exceeding $5,000 in claims for place of service (POS) 51-58. We defined "OMD" as patients not meeting any of the previously mentioned criteria. Multiple linear regression was used to model the difference between baseline and follow-up for the different cohorts, adjusting for confounders.

Coefficient	Total Cost of Care (TCC) Difference			Medical TCC Difference			Pharmacy TCC Difference		
	Model Estimate	Std. Error	P-Value	Model Estimate	Std. Error	P-Value	Model Estimate	Std. Error	P-Value
Intercept	$10,860	$659	<.001	$8,427	$611	<.001	$6,617	$260	<.001
Depression Only	-$3,191	$475	<.001	-$1,227	$440	0.005	-$5,972	$187	<.001
OMD + RD	$6,884	$1,805	<.001	$6,001	$1,674	<.001	$576	$712	0.418
SOMD + RD	-$2,980	$2,613	0.254	-$2,392	$2,422	0.323	$236	$1,031	0.819
Age	-$20	$10	0.042	-$5	$9	0.610	-$18	$4	<.001
Gender (Male)	-$42	$267	0.874	-$72	$247	0.770	-$2	$105	0.986
LOB = Medicare	$2,209	$735	0.003	$2,402	$681	<.001	-$2,216	$290	<.001
Anxiety Medication	$3,458	$273	<.001	$3,447	$254	<.001	$21	$108	0.844
Diabetes	$4,245	$450	<.001	$3,688	$417	<.001	$453	$177	0.011
Hypertension	-$517	$1,128	0.647	-$205	$1,046	0.844	-$253	$445	0.569
Dylipidemia	-$1,045	$904	0.248	-$674	$838	0.422	-$287	$357	0.420
Depression Only*LOB = Medicare	$2,220	$763	0.004	$567	$707	0.423	$3,732	$301	<.001
OMD + RD*LOB = Medicare	-$2,839	$2,421	0.241	-$2,824	$2,245	0.208	-$256	$955	0.789
SOMD + RD*LOB = Medicare	$2,902	$4,235	0.493	$960	$3,927	0.807	$590	$1,670	0.724

Total Cost Difference Across All Cohorts Adjusted with Multiple Linear Regression.

Coefficient	RD Cost of Care Difference			Medical RD Cost Difference			Pharmacy RD Cost Difference		
	Model Estimate	Std. Error	P-Value	Model Estimate	Std. Error	P-Value	Model Estimate	Std. Error	P-Value
Intercept	$9,275	$1,028	<.001	$1,218	$270	<.001	$8,056	$968	<.001
OMD + RD	$1,063	$1,170	0.363	$1,218	$307	<.001	-$154	$1,101	0.889
SOMD + RD	$648	$1,695	0.702	$155	$445	0.728	$492	$1,595	0.758
Age	-$54	$20	0.007	-$7	$5	0.180	-$47	$19	0.012
Gender (Male)	-$486	$473	0.304	-$190	$124	0.127	-$296	$445	0.506
LOB = Medicare	-$1,947	$627	0.002	$15	$165	0.927	-$1,962	$591	<.001
Anxiety Medication	-$210	$626	0.738	$131	$165	0.426	-$341	$589	0.563
Diabetes	-$775	$751	0.302	-$151	$197	0.445	-$624	$707	0.378
Hypertension	-$600	$1,896	0.752	$274	$498	0.583	-$874	$1,785	0.624
Dylipidemia	$646	$1,763	0.714	-$24	$463	0.959	$670	$1,660	0.687
OMD + RD*LOB = Medicare	-$1,280	$1,559	0.412	-$1,401	$410	<.001	$121	$1,468	0.934
SOMD + RD*LOB = Medicare	-$201	$2,724	0.941	-$341	$716	0.633	$140	$2,565	0.956

RD Cost Difference Across All Cohorts Adjusted with Multiple Linear Regression.

Multiple Linear Regression Coefficient	RD PDC Difference		
	Model Estimate	Std. Error	P-Value
Intercept	-38.30%	3.89%	<.001
OMD + RD	3.54%	4.24%	0.403
SOMD + RD	10.40%	32.26%	0.747
Age	-0.47%	0.07%	<.001
Gender (Male)	0.11%	1.74%	0.949
LOB = Medicare	1.13%	2.52%	0.653
Anxiety Medication	0.19%	2.37%	0.935
Diabetes	-1.53%	3.24%	0.636
Hypertension	1.76%	9.32%	0.851
Dylipidemia	0.60%	7.67%	0.938
Baseline RD	76.03%	1.55%	<.001
Baseline Depression	-2.38%	32.30%	0.941
Baseline Depression 90-day Fill	-5.17%	5.21%	0.320
Baseline RD 90-day Fill	-8.12%	1.65%	<.001
OMD + RD*LOB = Medicare	14.58%	7.38%	0.048
SOMD + RD*LOB = Medicare	-7.33%	9.24%	0.428

Comparing RD Adherence by Cohort Adjusted with Multiple Linear Regression.

Results: This study included 56,156 patients; the majority were female (68.4%); the mean age was 51.7 years (SD = 17.6). After adjustment, the annualized TCC of patients with OMD+RD was $6,884 ($p< 0.001$) more than those with RD alone, a difference that was largely driven by medical benefit spend ($p< 0.001$). Patients with SOMD+RD spent $2,980 ($p=0.254$) less than those with RD alone. When examining RD-related medical cost differences in patients, those with OMD spent $1,218 ($p< 0.001$) more than those with RD alone. During the follow-up period, TCC within patients was largely represented by drug costs, as medical benefit costs excluding RD-medication costs represented, on average, 5% of TCC in the RD alone cohort, 5.5% in the RD cohort and 3.5% in the SOMD+RD cohort. There were no significant differences in RD-medication adherence between groups.

Conclusion: In this study, OMD+RD patients spent significantly more in TCC than SOMD+RD patients. Previous research has shown patients with RDs and comorbid depression have poorer clinical outcomes than patients without comorbid depression. Defining suboptimal treatment of disease through administrative claims has inherent limitations, thus further research is required to understand how closely this definition correlates with clinical outcomes. However, given the dominating expense of targeted immunomodulators in treating RD patients, poorer outcomes in

patients with comorbid depression do not appear to be readily observed when evaluating patient financial outcomes. It is imperative that as alternative payment models are developed for treating RD patients, provider incentives to manage comorbidities effectively are developed beyond TCC related incentives, as these alone could inadvertently disincentivize effective management of depression and other mental health conditions.

Disclosure: J. Couto, CVS Health, 3, 11; **E. Avalos-Reyes**, CVS Health, 3, 11; **A. McCarthy**, CVS Health, 3, 11; **O. Matlin**, CVS Health, 3, 11; **M. Hamburger**, None; **G. Maher**, None; **K. Johnson**, CVS Health, 3, 11.

Abstract Number: 0136

Underutilization of Mental Health Services in a Busy Tertiary Care Rheumatology Facility

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Mental health disorders are prevalent in patients with rheumatic diseases, particularly since many of these diseases present early, have a chronic course, and significantly impact one's daily function. The prevalence of depression and anxiety in SLE is 71-80%.[2] Depression in RA is up to 50%.[1] Some medications (i.e. steroids) also bear potential mental health effects. Rheumatology patients with psychiatric comorbidities use healthcare resources more than their counterparts. While rheumatologists demonstrate awareness of mental health disorders in their patients, utilization of formal screening tools and mental health services is lacking.

Table 1. Patient Demographics, Comorbidities, and Pre-existing Mental Health Disorders, n=63

Age in years (mean)	20-83 (mean=50)
Gender, % (n)	
Male	16% (10)
Female	84% (53)
Comorbidities, % (n)	
Hypertension	40% (25)
Thyroid Disease	24% (15)
Chronic Kidney Disease	16% (10)
Diabetes	14% (9)
Migraine	14% (9)
Hyperlipidemia	13% (8)
Obesity	3% (2)
Pre-existing Mental Health Disorders, % (n)	
General Anxiety Disorder	41% (26)
Major Depressive Disorder	38% (24)
Attention Deficit Hyperactivity Disorder	6% (4)
Bulimia Nervosa	2% (1)

Percentages may not add to one-hundred due to overlap in comorbidities and pre-existing mental health disorders.

Table 2. Underlying Rheumatic Diseases and Reasons for Referral

Reason for Referral to Neuropsychology, n=30, % (n)	
Cognitive Dysfunction	97% (29)
Hallucinations	3% (1)
Reason for Referral to Psychiatry/Psychology, n=33, % (n)	
Pain	37% (12)
Anxiety	30% (10)
Mood Disorder	24% (8)
Schizophrenia	3% (1)
Pseudo-seizures	3% (1)
Cognitive Dysfunction	3% (1)
Underlying Rheumatic Disease(s), % (n)	
Systemic Lupus Erythematosus	40% (25)
Fibromyalgia	32% (20)
Rheumatoid arthritis	14% (9)
Sjogren's Syndrome	10% (6)
Psoriatic Arthritis	8% (5)
Vasculitis	6% (4)
Neuropathy	6% (4)
Raynaud's Syndrome/Phenomenon	5% (3)
Antiphospholipid syndrome	5% (3)
Undifferentiated Connective Tissue Disease	5% (3)
Systemic Sclerosis	3% (2)
Spondyloarthropathy	2% (1)
Gout	2% (1)
Pseudogout	2% (1)
Osteoporosis	2% (1)
Ehlers Danlos Syndrome	2% (1)
Chronic Fatigue Syndrome	2% (1)

Percentages may not add to one-hundred due to overlap in underlying rheumatic disease(s).

Methods: We evaluated all patients referred from the rheumatology clinic at a tertiary care center to mental health providers (psychiatry/psychology/neuropsychology) over a 2-year period (2/2019 – 2/2021). Data collected included age, sex, underlying rheumatic disease, additional medical and psychiatric comorbidities, and reason(s) for referral to mental health services. Subsequent appointments with a mental health provider were noted.

Results: Of 6154 patients seen in the rheumatology clinic over 2 years, only 63 (1%) were referred to mental health providers. Patient demographics and underlying comorbidities are noted in Table 1. The age range of patients was 20-83 years, of whom 84% were female. Reasons for referral are noted in Table 2. 48% of referrals were for neuropsy-

chology, most commonly for evaluation of cognitive dysfunction. 52% of referrals were for psychiatry/psychology, most commonly for evaluation of chronic pain, anxiety, and mood disorders. While most patients had multiple rheumatic diagnoses, SLE was the most common underlying rheumatic disease diagnosis in patients who were referred to mental health (40%), followed by fibromyalgia (32%) and RA (14%). Only 1/3rd of patients originally referred for mental health services were seen by a mental health provider.

Conclusion: Our findings demonstrate a significant underutilization of mental health services by rheumatologists. This is particularly worrisome since our institutional behavioral health and neuropsychology departments offer comprehensive treatment for a variety of mental and behavioral health issues. Although we recognize that the COVID-19 pandemic and limitations of telehealth visits may have contributed to the lower referrals to mental health services, there was, in fact, a greater need for mental health optimization during this time, with anxiety and depression being more prevalent in patients with rheumatic disease during the COVID-19 pandemic. Our study serves as a call for action to appropriately assess and timely refer patients to mental health providers. Further studies on reasons for lack of follow up may provide additional insight for improvement in the care of these patients

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Abstract Number: 0137

Antiviral Use and Healthcare Resource Utilization Among Patients with Rheumatoid Arthritis and Influenza in Three Influenza Seasons, 2016–2019

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Seasonal influenza poses a large burden on the healthcare system. Patients with certain chronic diseases, such as rheumatoid arthritis (RA), are especially vulnerable to developing severe complications due to influenza.

Methods: A retrospective claims analysis to assess whether influenza patients with RA who received antiviral therapy incur lower Healthcare Resource Use (HRU) and costs compared with propensity score matched untreated influenza RA patients by influenza season (October to April of the following year) for three consecutive years (2016–2019). Data from the IBM MarketScan® Commercial US Database for patients diagnosed with RA [1 hospitalization or 2 outpatient claims for RA on separate dates at least 30 days apart] were selected if they contracted influenza (first

instance of an influenza diagnosis), in the outpatient or emergency department (ED) setting each season. HRU (hospitalizations, outpatient visits, or pharmacy fills) and costs were assessed at 14 days & 28 days post-fill date. For the matched untreated group, proxy fill date was determined based on the number of days from index flu diagnosis to first antiviral treatment of matched cases.

Results: From a total of 568,228 patients with a diagnosis of RA, 7743 (1.4%) were diagnosed with influenza during 1 of 3 influenza seasons (2016–2017, 2017–2018, or 2018–2019). Among the 4946 patients with RA meeting the study inclusion criteria (≥18 years old, continuous enrollment) who were diagnosed with influenza from 2016–2019, 3371 (68.2%) received antiviral influenza therapy, 3331 of these were not hospitalized before filling the treatment prescription, and 2638 remained in the sample after propensity score matching. Of 1442 (29.2%) patients with RA and influenza who did not receive antiviral influenza treatment within 30 days after diagnosis, 1348 were not hospitalized and 1319 remained in the sample after matching. At 14 days of follow-up after initiation of antiviral treatment fill, most (>76%) treated and untreated patients had all-cause HRU, and >90% had all-cause HRU after 28 days of follow-up. Outpatient visits were the most common type of HRU and occurred among >70% of treated and untreated patients after 28 days of follow-up. The mean (SD) number of all-cause outpatient visits was 1.21 (1.84) versus 0.96 (1.20) after 14 days ($p < 0.001$) and 2.24 (2.91) versus 1.94 (2.10) after 28 days ($p = 0.0010$), for untreated vs treated, respectively. After 28 days, all-cause ED visits were more common among untreated (8.8%) than treated patients (6.5%) across all influenza seasons; ($p = 0.0118$). Inpatient visits occurred among ~2% of treated and untreated patients during 28 days of follow-up. Mean all-cause HRU-related costs after 28 days of follow-up were >$500 for treated vs $723 for untreated for inpatient stays and >$150 for outpatient visits across both treatment cohorts.

Conclusion: In a large real-world sample of patients with RA and influenza, antiviral treatment was associated with lower healthcare burden compared with no treatment in various categories evaluated.

Disclosure: E. Neuberger, Genentech, Inc., 3, Genentech, Inc., 11; **T. To**, Genentech, Inc., 3, Genentech, Inc., 11; **A. Seetasith**, Genentech, Inc., 3, Genentech, Inc., 11; **S. Arndorfer**, Genentech, Inc., 7; **C. Wallick**, Genentech, Inc., 3, Genentech, Inc., 11.

Abstract Number: 0138

Treatment with Adalimumab in Patients with Chronic Inflammatory Rheumatic Diseases: A Study of Treatment Trajectories on a Patient Level in Clinical Practice

Imke Redeker[1], Stefan Moustakis[2], Styliani Tsiami[2], Xenofon Baraliakos[2], Ioana Andreica[2], Bjoern Buehring[2], Juergen Braun[2] and **Uta Kiltz**[2], [1]German Rheumatism Research Centre (DRFZ), Berlin, Germany, [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table. Patient characteristics at baseline, stratified by treatment trajectory. Table legend on bottom: +values are given as mean (SD)

	Total group N=111 (100%)	Treatment trajectory			
		continued ADA biosimilar therapy N=75 (67.6%)	back-switch to originator ADA therapy N=18 (16.2%)	switch to different bDMARD therapy N=8 (7.2%)	no bDMARD therapy/death/drop out N=10 (9.0%)
Age, y	51.2 (14.5)	51.5 (13.6)	50.6 (16.8)	43.5 (9.5)	56.4 (19.0)
Women, No. (%)	46 (41.4)	27 (36.0)	9 (50.0)	6 (75.0)	4 (40.0)
RA	23 (20.7)	17 (22.7)	2 (11.1)	1 (12.5)	3 (30.0)
axSpA	68 (61.3)	47 (62.7)	11 (61.1)	6 (75.0)	4 (40.0)
PsA	15 (13.5)	7 (9.3)	4 (22.2)	1 (12.5)	3 (30.0)
Other diagnoses	5 (4.5)	4 (5.3)	1 (5.6)	0 (0.0)	0 (0.0)
Disease duration, median (IQR), y	5.0 (2.0-8.0)	5.0 (2.0-9.0)	3.5 (2.0-6.0)	2.0 (1.0-5.5)	4.5 (2.0-8.0)
Duration previous originator ADA therapy	40.7 (27.7)	45.3 (27.8)	35.0 (25.2)	20.3 (24.7)	32.3 (25.1)
DAS28	3.0 (1.0)	2.9 (1.0)	3.4 (1.0)	-	3.3 (1.2)
CRP, median (IQR), mg/L	0.2 (0.1-0.3)	0.1 (0.1-0.2)	0.2 (0.0-0.5)	0.2 (0.2-1.3)	0.3 (0.2-0.4)
HAQ score	1.3 (0.8)	1.1 (0.7)	1.7 (0.8)	-	1.8 (1.0)
ASDAS	2.2 (1.1)	2.0 (1.0)	3.0 (1.2)	2.7 (0.9)	2.3 (0.2)
BASFI	3.5 (2.6)	3.0 (2.5)	5.4 (2.4)	3.4 (1.6)	5.4 (1.6)

+values are given as mean (SD)

Background/Purpose: Adalimumab (ADA) retention rates are impaired in patients (pts.) with chronic inflammatory rheumatic diseases (CIRD) due to loss of efficacy and adverse events, causing ADA discontinuation by 50% of pts. within 5 years (Neovius et al., 2015, Ann Rheum Dis). The introduction of ADA biosimilars has increased non-medical switching from originator to ADA biosimilars in rheumatologic care. This study aims at analysing treatment trajectories over two years in CIRD pts. receiving originator ADA.

Methods: CIRD pts. on originator ADA who switched to ADA biosimilar from 10/2018 onwards were identified and followed until 2020. Disease activity (ASDAS), physical function (HAQ, BASFI), and treatment changes were documented every 3 months. The four predefined treatment trajectories “continued ADA biosimilar therapy”, “back-switch to originator ADA therapy”, “switch to another biological (b) disease modifying anti-rheumatic drug (DMARD) therapy”, and “stopped bDMARD therapy /death /drop out” were used to compare pts. characteristics with different trajectories.

Results: 111 CIRD pts. treated with originator ADA were switched to ADA biosimilar (Table). The majority of pts. (67,6%) continued biosimilar therapy (Figure) while 16% switched back to originator ADA, 7% switched to a different bDMARD, and 9% either stopped treatment (n=9) or died (n=1). Pts. continuing ADA biosimilar were mostly male, older and/or with a longer disease duration than the back switchers to originator ADA and thoseswitching to a different bDMARD (Table). No functional impairment (HAQ, BASFI) and higher disease activity (ASDAS) were observed in switching pts. compared to pts. continuing ADA biosimilar therapy (Table). CsDMARD and glucocorticoid treatment were increased in pts. continuing ADA biosimilar therapy, while pts. switching therapy had more previous bDMARD therapies (Table).

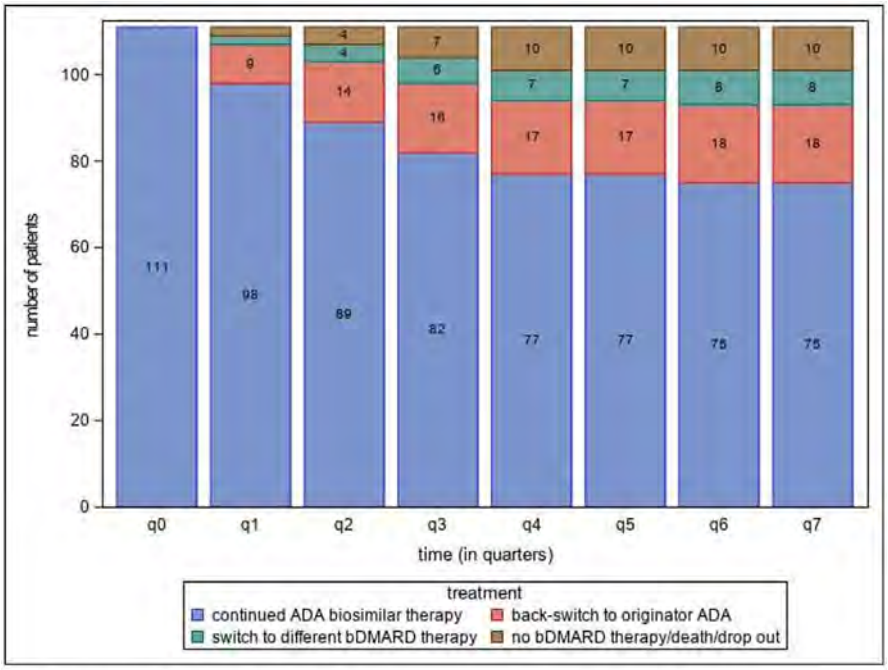

Figure. Treatment trajectories of ADA therapy in patients with CIRD during two years; ADA: adalimumab; bDMARD: biological disease modifying anti-rheumatic drug.

Conclusion: Two thirds of pts. who switched to ADA biosimilar remained on this therapy for 2 years. However, as many as 16% of pts. switched back to ADA originator. Whether or to what degree nocebo effects influenced this needs further study.

Disclosure: I. Redeker, None; **S. Moustakis**, None; **S. Tsiami**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **I. Andreica**, None; **B. Buehring**, None; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5.

Abstract Number: 0139

Treatment of Ankylosing Spondylitis by Primary Care Physicians and Rheumatologists in an Academic Health System: A Retrospective Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: While recommendations for the treatment of ankylosing spondylitis (AS) are largely aligned across various guidelines,[1,2] there remains variability in the treatment. Patients with inflammatory lower back pain, a key symptom of AS, often first visit and receive treatment from their primary care provider (PCP) as opposed to a specialist such as a rheumatologist, which may contribute to this treatment variability. The objective of this analysis was to examine prescribing habits of rheumatologists and PCPs treating AS patients in an academic medical center.

Methods: A retrospective cohort study was performed using the University of Pennsylvania Health System electronic medical record. Patients with a diagnosis of AS (ICD10 M45.X code or M08.1) between January 2017 and September 2020 were included. Baseline characteristics at the time of first diagnosis, visits to rheumatologists and PCPs, and prescribed therapies all within the health system are descriptively reported.

Results: A total of 1,271 patients with a diagnosis code of AS during the study period were identified. The mean age was 51 years, 55% were male, and common comorbidities included hyperlipidemia, hypertension, anemia, and depression (**Table 1**). Nearly 10% of patients had a diagnosis of uveitis prior to or on the date of the AS diagnosis. Within the healthcare system, 49% of patients were seen by both a rheumatologist and PCP on or after their AS diagnosis; 42% saw only a PCP (**Figure 1**). Over a third (36%) of patients followed by a rheumatologist were prescribed a biologic disease-modifying antirheumatic drug (bDMARD) during their follow-up, while only 9% of patients followed

Table 1. Baseline Characteristics in Patients With a Diagnosis of AS

Baseline Characteristics[a]	Patients N = 1,271
Year of first observed diagnosis	
2017	487 (38.3)
2018	302 (23.8)
2019	300 (23.6)
2020	182 (14.3)
Number of diagnosis codes during study, mean (SD)[b]	4.53 (6.74)
1 diagnosis code	528 (41.5)
2 diagnosis codes	227 (17.9)
≥3 diagnosis codes	516 (40.6)
Age at first observed AS diagnostic code, mean (SD)	51.16 (16.88)
Male	698 (54.9)
Relevant Medical History/Comorbidities	
Anemia	263 (20.7)
Anxiety	208 (16.4)
Cancer	119 (9.4)
Chronic pain	175 (13.8)
Depression	211 (16.6)
Diabetes	158 (12.4)
Fatty liver disease	36 (2.8)
Fibromyalgia (ICD-10 codes only)	54 (4.3)
Fibromyalgia (ICD-9 and ICD-10 codes)	126 (9.9)
Hyperlipidemia	391 (30.8)
Hypertension	417 (32.8)
Inflammatory bowel disease	170 (13.4)
Psoriasis	63 (5.0)
Psoriatic arthritis	65 (5.1)
Uveitis	122 (9.6)
Venous thromboembolism	45 (3.5)

[a]n (%) unless otherwise noted. Assessed prior to or on date of diagnosis, and based on a single code
[b]Includes first AS code date

Figure 1. Types of Clinicians Seen Within Healthcare System On or After AS Diagnosis

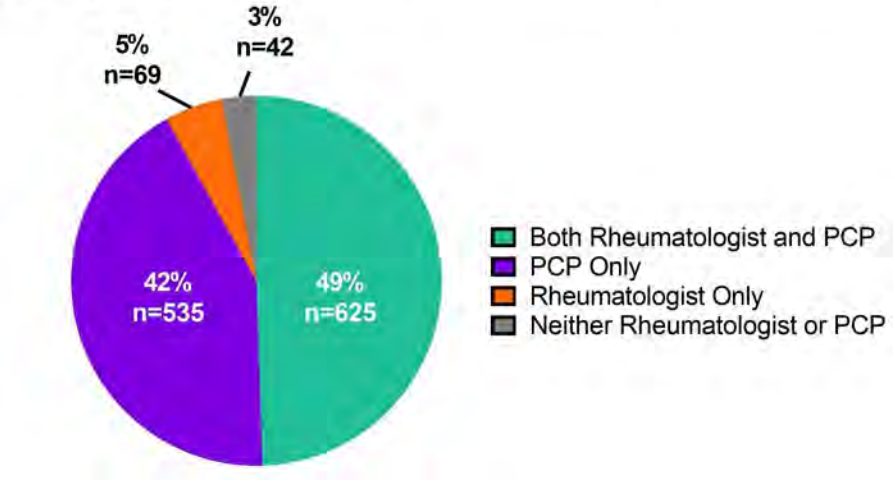
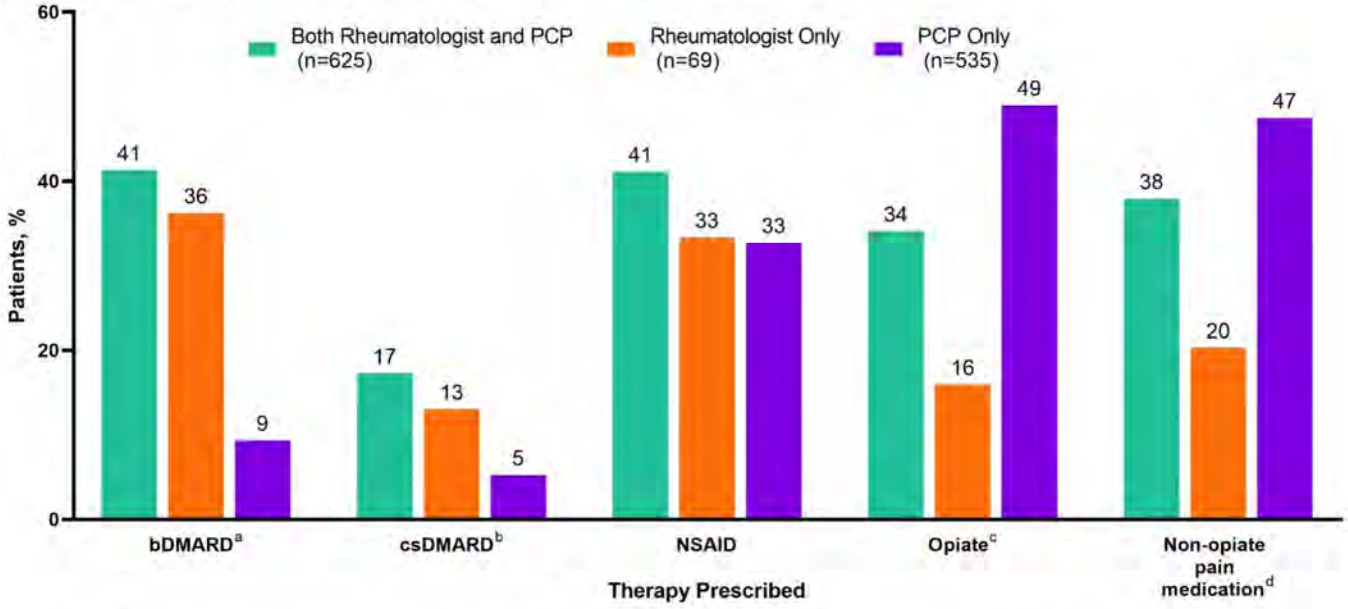


Figure 2. Proportion of Patients Receiving a Prescription for Select Therapies Over the Course of Follow-up by Type of Clinician Seen



bDMARD, biologic disease-modifying antirheumatic drug; csDMARD, conventional synthetic disease-modifying antirhumatic drug; JAKi, Janus kinase inhibitor; NSAID, non-steroidal anti-inflammatory drug; PCP, primary care physician; TIM, targeted immunomodulator.
No patients received a prescription for leflunomide during the course of follow-up.
[a]bDMARD includes tumor necrosis factor (TNF) inhibitor or interleukin-17 (iL-17) inhibitor.
[b]csDMARD includes methotrexate, sulfasalazine, and hydroxychloroquine.
[c]Opiates includes codeine, hydrocodone, morphine, fentanyl, oxycodone, and tramadol.
[d]Non-opiate pain medications includes acetaminophen, duloxetine, aspirin, gabapentin, pregabalin, nortriptyline, and amitriptyline.

by a PCP were prescribed a bDMARD (**Figure 2**). Nearly half of patients followed by only a PCP were prescribed an opiate (49%) or non-opiate (47%) pain medication, while these therapies were prescribed to 16% and 20%, respectively, of patients followed by a rheumatologist without PCP care. Conventional synthetic DMARDs were prescribed to 13% and 5% of patients seen by a rheumatologist only and PCP only, respectively. Among patients followed only by a PCP, opiates (43%), non-opiate pain medication (41%), and NSAIDs (28%) were the most commonly prescribed therapies during the first year after their AS diagnosis. When a patient was followed by both a rheumatologist and

PCP, bDMARDs (31%), NSAIDs (27%), and non-opiate pain medications (27%) were most commonly prescribed in the first year.

Conclusion: In this population of patients with AS followed at an academic medical center, bDMARDs and csDMARDs were more frequently prescribed to patients seen by rheumatologists, while opiate and non-opiate pain medications were more frequently prescribed to patients who saw only a PCP. These findings demonstrate the variability in prescribing patterns between PCPs and rheumatologists and highlight areas for targeted education among non-specialists.

References: 1.Ward MM, et al. *Arthritis Rheumatol*. 2019;71(10):1599-1613.2. van der Heijde D, et al. *Ann Rheum Dis*. 2017;76(6):978-91.

Disclosure: A. Ogdie-Beatty, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2; **M. Magrey**, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5; **R. Fitzsimmons**, None; **S. Abdollahi**, None; **A. Biljan**, AbbVie, 3, 11; **C. Saffore**, AbbVie, 3, 11; **J. Walsh**, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5.

Abstract Number: 0140

Therapeutic Management and Clinical Remission in a Specialized Dermatological-Rheumatological Center for Patients with Psoriasis and Psoriatic Arthritis

Jana Ziob[1], Charlotte Behning[1], Peter Brossart[2], Thomas Bieber[1], Dagmar Wilsmann-Theis[3] and **Valentin Schäfer**[4], [1]University Hospital Bonn, Bonn, Germany, [2]Department of Internal Medicine III, Oncology, Hematology and Rheumatology, University Hospital Bonn, Bonn, Germany, [3]Department for Dermatology and Allery, University Hospital Bonn, Bonn, Germany, [4]Clinic of Internal Medicine III, Oncology, Haematology, Rheumatology and Clinical Immunology, University Hospital Bonn, Bonn, Germany

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: An interdisciplinary approach involving dermatologists and rheumatologists is required for the management of patients with psoriatic arthritis (PsA). The purpose of our study was to examine dermatological-rheumatological therapeutic management of patients with psoriasis and PsA.

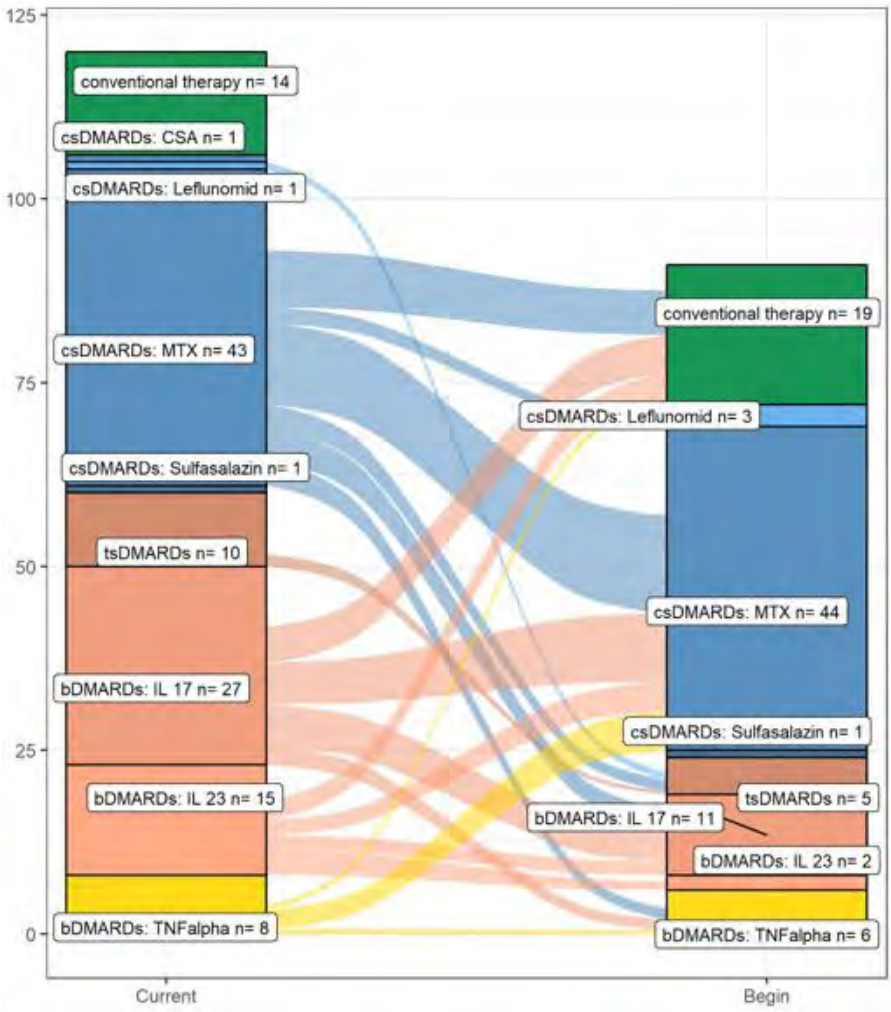
Methods: A retrospective cohort analysis was performed of all dermatology-rheumatology consultations from April 1st, 2016 to January 31st, 2020. From March 1st, 2018 a specialized interdisciplinary PsA center was established. Clinical data including baseline characteristics, treatment status and treatment outcome were collected and analyzed. A follow-up was performed until January 27th, 2021.

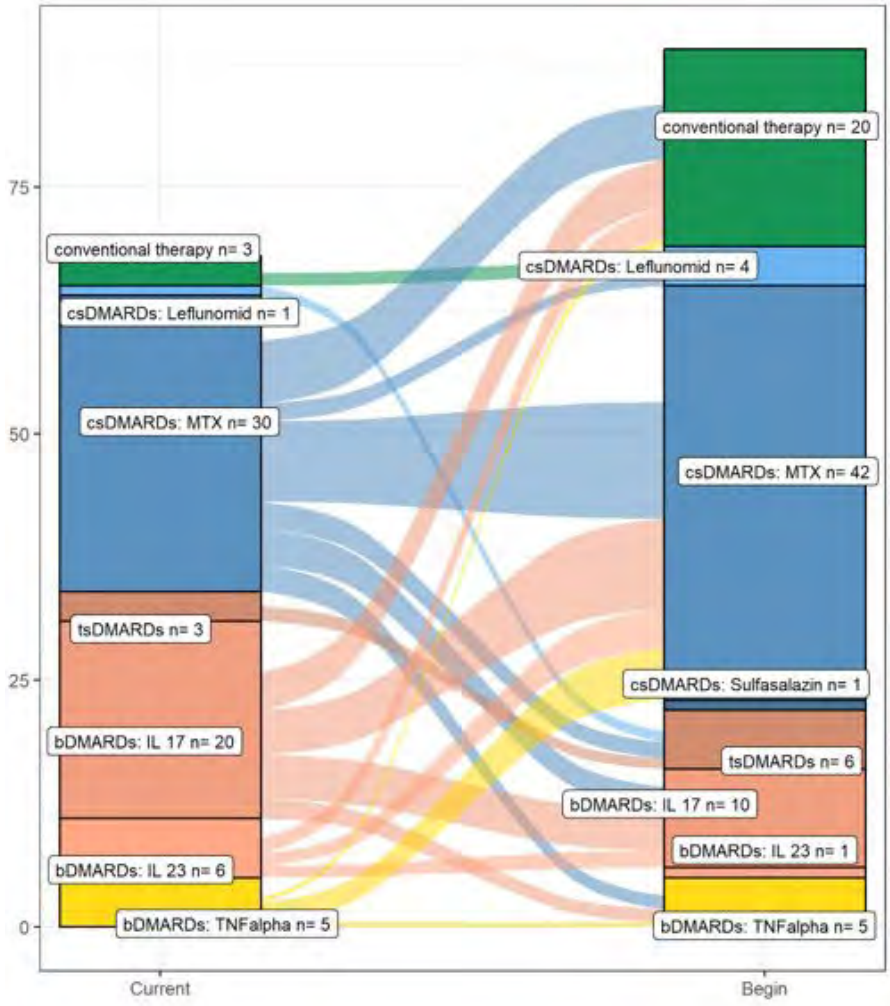
Results: A total of 404 consultations were studied, including 218 psoriasis patients and 103 PsA patients. 34.4 percent of psoriasis patients and 69.9 percent of PsA patients switched systemic medication following consultation.

Most of them began systemic medication, this was twice as common in PsA patients compared to psoriasis patients (Psoriasis: 32.11 %, PsA: 65.05 %). In this context, methotrexate (40.78%), oral glucocorticosteroids (19.42 %), and IL-17 inhibitors (9.71 %) were the most commonly prescribed medications in PsA (Figure 1 and 2). This close collaboration lead to a long-lasting remission time of musculoskeletal complaints (at least 22.5 (IQR:3.0-53.0) median months) and skin lesions (at least 22.0 (IQR:3.0-53.0) median months) in over 60 % of PsA patients (Figure 3).

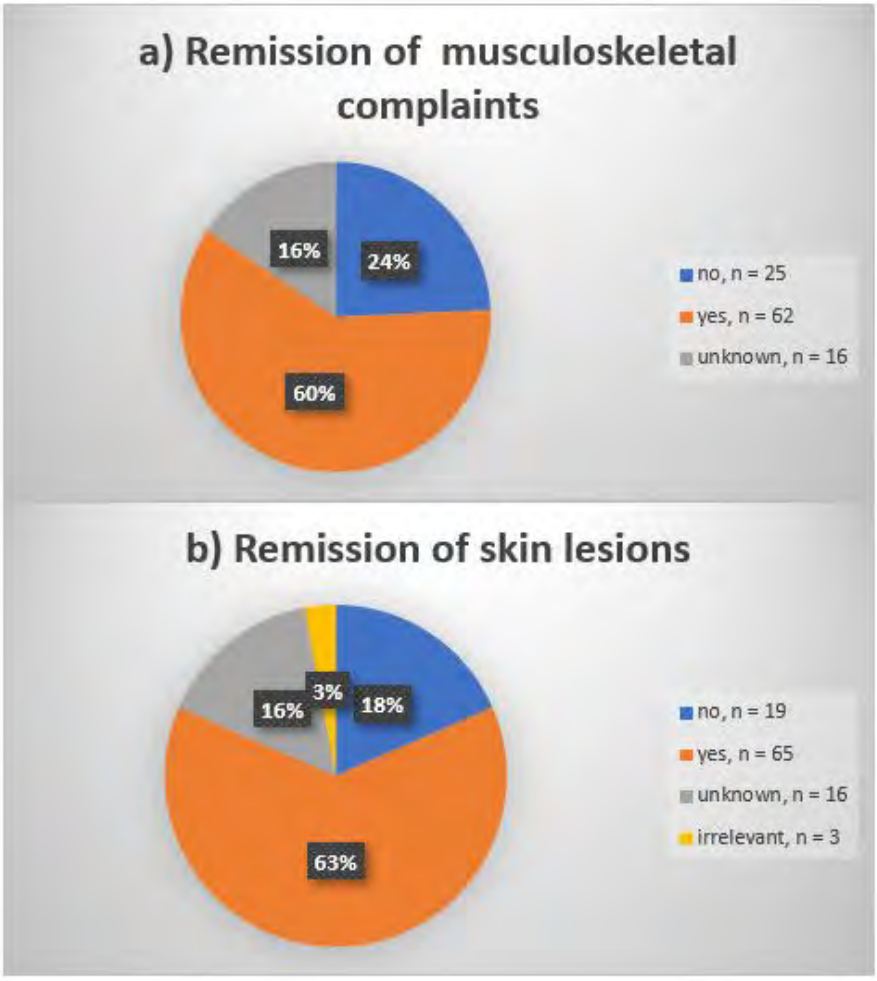
Conclusion: We were able to demonstrate that close collaboration between dermatology and rheumatology can result in improved therapeutic management of psoriasis and PsA patients with a high degree of achieved clinical remission.

Sankey Chart of psoriasis patients illustrating therapeutic management over time in a specialized dermatological-rheumatological center Therapeutic profile of psoriasis patients at time of consultation and initiated systemic therapy divided into conventional therapy, conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), targeted synthetic DMARDs (tsDMARDs), and biologic DMARDs (bDMARDs)





Sankey Chart of psoriatic arthritis patients illustrating therapeutic management over time in a specialized dermatological-rheumatological center Therapeutic profile of psoriatic arthritis patients at time of consultation und initiated systemic therapy divided into conventional therapy, conventional synthetic DMARDs (csDMARDs), targeted synthetic DMARDs (tsDMARDs), and biologic DMARDs (bDMARDs)



Clinical remission in patients with psoriatic arthritis after consultation Abbreviations: n = number

Disclosure: J. Ziob, None; **C. Behning**, None; **P. Brossart**, None; **T. Bieber**, None; **D. Wilsmann-Theis**, None; **V. Schäfer**, None.

Abstract Number: 0141

Who Gets Influenza Vaccinations Prior to and After a Diagnosis of RA? Results from the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Annual influenza vaccination is recommended for adults with RA, but remains low in established RA. We examined influenza vaccination coverage in the year prior to and following RA diagnosis, and individual characteristics including RA medication beliefs associated with vaccination among newly diagnosed participants in the Canadian Early Arthritis Cohort (CATCH).

Methods: The sample included adults enrolled in CATCH between Dec 2017 and Mar 2021 who met 2010 ACR/EULAR criteria, had 1+ year of follow-up, and had completed the Beliefs about Medicines Questionnaire. Vaccinated and non-vaccinated groups were compared using t-tests and chi-square and multivariable logistic regression was used to identify characteristics associated with vaccination in the year prior to (pre-dx) vaccination and the first year of RA (post-dx).

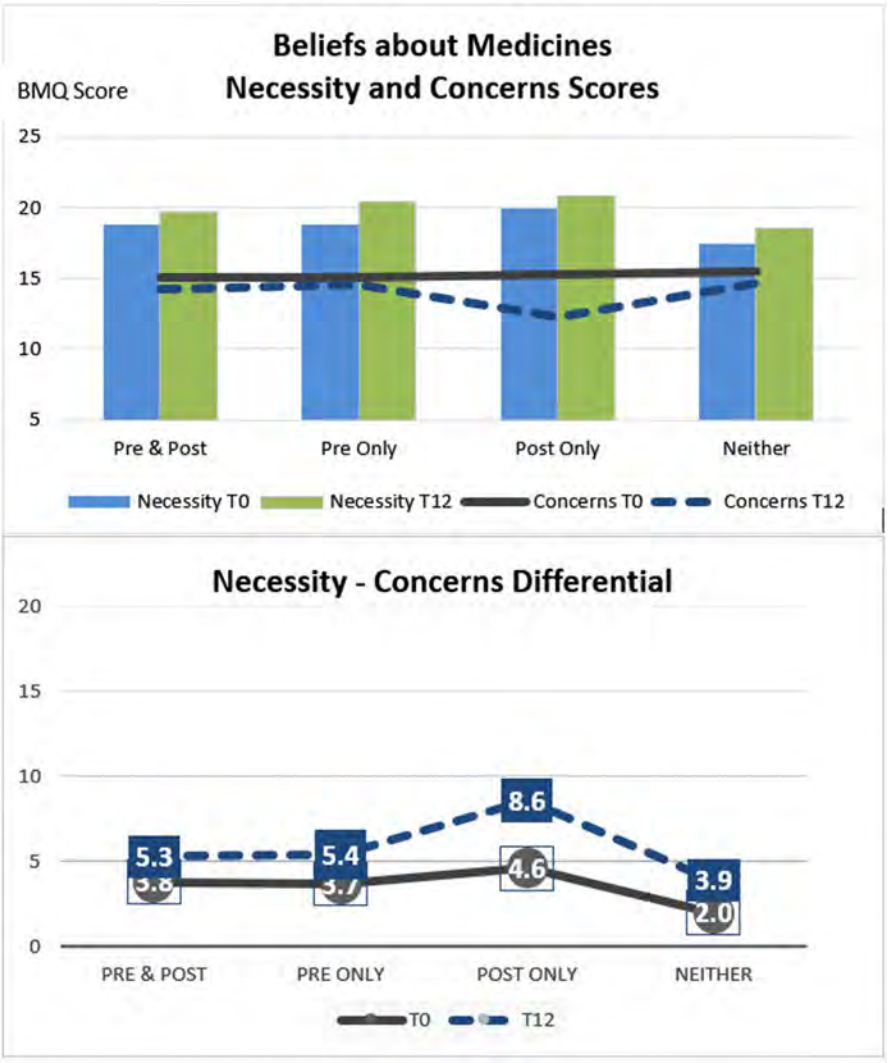
Results: At enrollment, participants (N=405) were mostly white (80%) women (67%) with a mean (SD) age of 56 years and symptom duration of 5 months. Pre-dx, 37% reported being vaccinated, increasing to 42% post-dx. Among 233 patients with vaccination info available post-dx, most (68%) of those vaccinated post-dx reported having been vaccinated pre-dx.

In adjusted analyses, pre-dx influenza vaccination was associated with age ≥65 and having more comorbidities, but not sex, racial background, education, smoking, CDAI, or RA medication beliefs at baseline. Post-dx vaccination was

	Model 1 (n=176)		Model 2 (n=176)		Model 3 (n=176)	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age (years)						
18-64	0.5	0.2 – 1.0	1.1	0.4 – 3.1	1.1	0.4 – 3.2
≥65	1		1		1	
Women	0.6	0.3 – 1.2	**0.3**	**0.1 – 0.8**	**0.2**	**0.1 – 0. 7**
Education						
Up to High School	1		1		1	
Some college/Trade	0.7	0.3 – 1.6	0.6	0.2 – 1.8	0.6	0.2 – 1.7
University	1.6	0.7 – 4.0	2.6	0.9 – 8.0	2.7	0.8 – 8.6
Non-white race	**0.2**	**0.0 – 0.6**	**0.1**	**0.0 – 0.3**	**0.1**	**0.0 – 0.4**
Currently smoking	**0.2**	**0.1 – 0.6**	**0.1**	**0.0 – 0.5**	**0.1**	**0.0 – 0.5**
Comorbidities (RDCI)	1.2	1.0 – 1.6	1.1	0.8 – 1.5	1.1	0.8 – 1.5
CDAI			1.0	0.9 – 1.0	1.0	0.9 – 1.1
RA medications						
Non-MTX DMARDs					1.0	0.4 – 2.7
Advanced therapy*			**5.8**	**1.6 – 21.1**	**6.5**	**1.6 – 26.8**
Corticosteroids (oral)					0. 9	0.3 – 2.7
Necessity – Concerns score					**1.1**	**1.0 – 1.2**
Vaccination previous year			**21.8**	**7.9 – 60.5**	**27.5**	**8.9 – 85.3**

CDAI: Clinical Disease Activity Index; DMARDs: Disease Modifying Antirheumatic Drugs; MTX: Methotrexate; RA: Rheumatoid Arthritis; RDCI: Rheumatic Disease Comorbidity Index. Note: Akaike Information Criterion for Model 1: 218.4; Model 2: 167.6; Model 3: 166.5 *Advanced therapy: Use of biologics or JAKs in the first 12 months.

Multivariable logistic regression models predicting influenza vaccination in the first year after rheumatoid arthritis diagnosis.



RA medication necessity beliefs, concerns and difference score in relation to influenza vaccination in the year prior to (T0) and post (T12) RA diagnosis.

associated with male sex, white racial background, not smoking, biologics/JAK inhibitor use, higher mean Necessity-Concerns differential scores, and pre-dx vaccination (Table). Individuals who were not vaccinated pre-dx but vaccinated post-dx had lower mean Concerns and higher mean Necessity-Concerns differential scores compared to those vaccinated at both timepoints, only pre-diagnosis, or neither timepoints (Figure).

Conclusion: In Canadians with early RA, influenza vaccination coverage remains suboptimal. Certain individual (male sex, non-white race, smoking, medication beliefs/concerns) and treatment characteristics (advanced therapeutics, prior vaccination) were associated with a greater likelihood of vaccination. Higher concerns about RA medications and low necessity beliefs may also predict vaccine hesitancy. Conversations about beliefs and attitudes about RA medications and vaccination history as part of the diagnostic workup may help increase influenza vaccine coverage.

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Abstract Number: 0142

Description of a Scleroderma Cohort and Management of Lung Disease Risk at a Rural Academic Medical Center

Jenna Marinock[1], P. Daniel Nicholas[2], Kirsten Koons[3], Rakesh Kriplani[4], Andrea Berger[4] and David Bulbin[5], [1]Geisinger Commonwealth School of Medicine, Philadelphia, PA, [2]Geisinger Medical Center, Danville, PA, [3]Geisinger Medical Center, Lewisburg, PA, [4]Department of Population Health Sciences, Geisinger Medical Center, Danville, PA, [5]Geisinger Health System, Danville, PA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis interstitial lung disease (SSc-ILD) and pulmonary hypertension (SSc-PH) are leading causes of morbidity and mortality in patients with SSc. Few screening guidelines exist to identify patients early in their disease course. The aim of this study is to characterize a cohort of patients diagnosed with SSc, compare their lung disease risk to that of a subset of the EUSTAR cohort, and better understand screening practices for SSc by rheumatologists in our medical center.

Methods: We conducted a retrospective analysis of patients with SSc at a rural academic medical center. We identified patients 18 years and older with a SSc diagnosis (via ICD-9 and -10 codes) and seen by a rheumatologist between 01/01/2018 and 12/31/2020. We reviewed pulmonary function tests (PFTs) and transthoracic echocardiogram (TTE) orders between 01/01/2017 and 12/31/2020 for monitoring, focusing on diffusion capacity (DLCO) and pulmonary artery systolic pressure (PASP). Patients were defined as having PH if their PASP was >36.0 or if the TTE report stated evidence of PH. We compared the mean DLCO and PASP values to the EUSTAR subset using a two-sample t-test with unequal variance, age using a two-sample t-test with equal variances, and percent female patients using a Pearson's chi-square test. Statistical significance was defined as $p< 0.05$. Rheumatologists were invited to participate in an online, self-administered survey of 15 questions about PFT and TTE ordering practices and physician behaviors regarding abnormal results.

Table 1. Demographics and clinical characteristics of patients with SSc seen between 1/1/2018 and 12/31/2020

Characteristic	N = 244 Patients
Age, mean (SD)	60.3 (13.4)
Female, n (%)	202 (82.8%)
White, n (%)	240 (98.4%)
Year of Most Recent Rheumatology Visit	
2018	22 (8.6%)
2019	36 (14.8%)
2020	187 (76.6%)
Survival Status	
Living	227 (93.0%)
2018 Mortality	2 (0.8%)
2019 Mortality	8 (3.3%)
2020 Mortality	6 (2.5%)
2021 Mortality	1 (0.4%)
DLCO Completed Between 1/1/2017 and 12/31/2020	181 (74.2%)
DLCO, mean (SD)	63.6 (22.0)
DLCO, minimum/maximum	13, 116
Most Recent DLCO Result	
Less than 50	49 (20.1%)
50 or Greater	132 (54.1%)
No PFT Between 1/1/17 and 12/31/20	63 (25.8%)
TTE Order Between 1/1/2017 and 12/31/2020	189 (77.5%)
TTE Completed Between 1/1/2017 and 12/31/2020	186 (76.2%)
PASP, mean (SD) *n = 99*	34.6 (13.7)
PASP, minimum/maximum *n = 99*	12, 112
TTE Interpretation	
Positive for PH	35 (18.8%)
Negative for PH	89 (47.8%)
Inadequate Doppler Signal	48 (25.8%)
No Comment on PH	14 (7.5%)

SSc: systemic sclerosis; SD: standard deviation; DLCO: diffusion capacity; PFT: pulmonary function test; TTE: transthoracic echocardiogram; PASP: pulmonary artery systolic pressure; PH: pulmonary hypertension

Results: A total of 244 patients with a SSc diagnosis were seen in a 3-year period, with 187 (over 75%) patients having a visit in the last year. Please see Table 1 for demographic data. 181 patients (74.2%) had PFTs completed. Of those completed, the average DLCO was 63.6% and 20% of patients had a DLCO less than 50%. For TTEs, 189 patients (77.5%) had TTEs ordered with 3 incomplete tests. Of interest, only 99 (53%) had a reported PASP value, and mean PASP was 34.6mmHg (Table 1). Compared to EUSTAR, patients were older (60.3 vs. 56.3 years; $p< 0.0001$) and mean DLCO values were lower (63.6% vs. 68.7%; $p=0.0031$). Mean PASP comparatively was 34.6 mmHg vs. 29.8 mmHg ($p=0.0009$) (Table 2). The self-administered survey had a completion rate of 84.6% with 11 of 13 physicians electing to participate. Please see Figure 1 for survey results.

Conclusion: We identified an opportunity for early detection of SSc-ILD and SSc-PH in scleroderma patients within our academic health system. This would be achieved by improving ordering practices of PFTs and TTE for scleroderma monitoring. Additionally, we identified our population as, statistically, having potentially more severe disease compared to the EUSTAR cohort. We intend to investigate these findings further and explore clinical and social factors possibly playing a role in disease progression. We are hoping to institute improvements in best practice and develop EHR toolkits to improve monitoring of our SSc patients in the future.

Table 2. Demographics and lung disease risk of rural SSc cohort vs. EUSTAR subset

	EUSTAR n=1476	**Rural cohort n=244**	**p-value**	**Difference in means (95% CI)**
Age, mean (SD)	56.3 (13.5)	60.3 (13.4)	**<0.0001**	4.02 (2.19, 5.85)
Female, n (%)	1280 (86.7%)	202 (82.8%)	0.0992	-
	EUSTAR n=1340	**Rural cohort n=180**	**p-value**	**Difference in means (95% CI)**
DLCO, mean (SD)	68.7 (19.5)	63.6 (22.0)	**0.0031**	-5.15 (-8.55, -1.75)
	EUSTAR n=1476	**Rural cohort n=99**	**p-value**	**Difference in means (95% CI)**
PASP, mean (SD)	29.8 (9.5)	34.6 (13.7)	**0.0009**	4.8 (2.0, 7.6)

SD: standard deviation; CI: confidence interval; DLCO: diffusion capacity; PASP: pulmonary artery systolic pressure. Statistically significant findings are in bold.

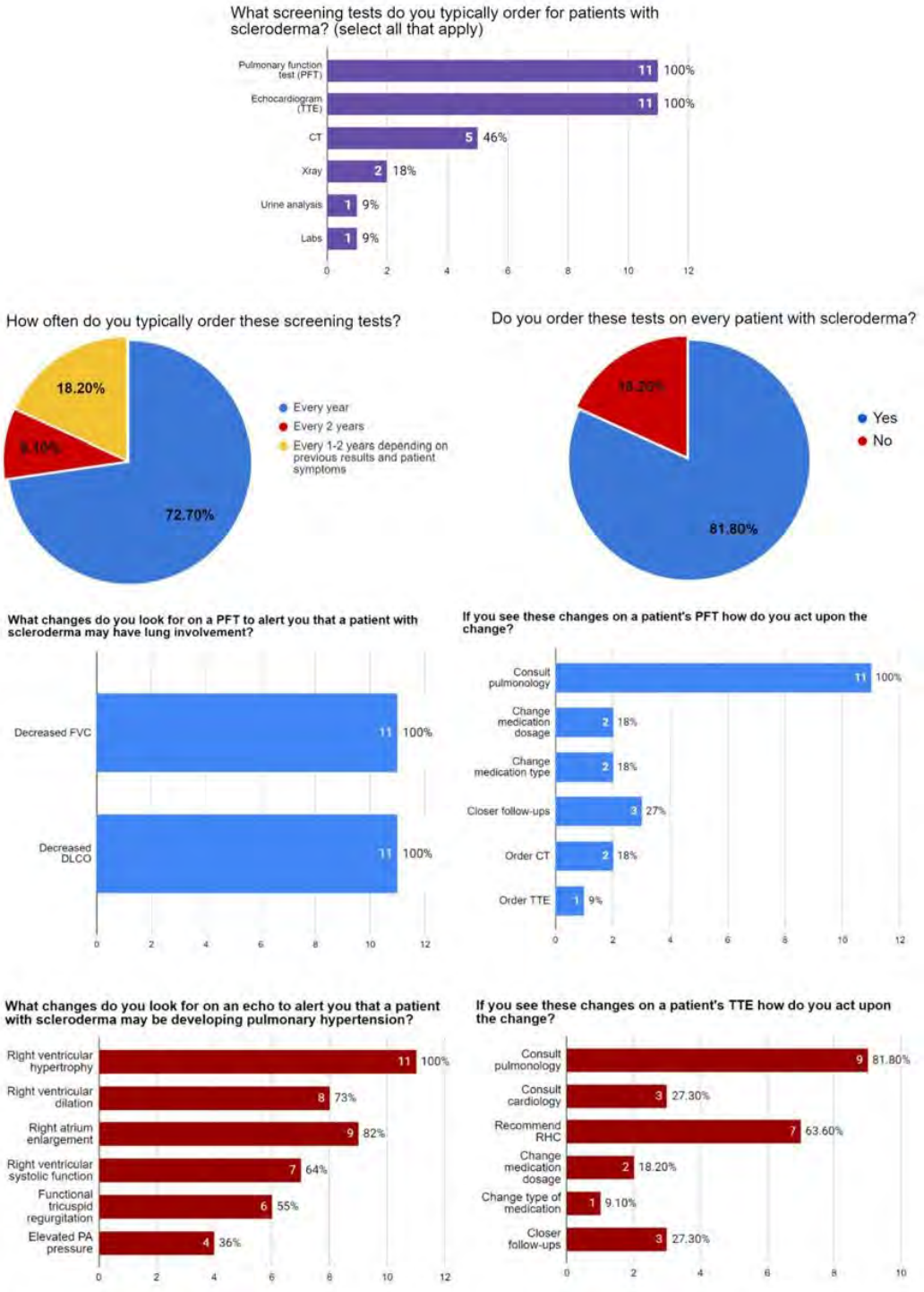

Figure 1. Survey of screening practices of rheumatologists at rural academic medical center

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Abstract Number: 0143

Economic and Healthcare Resource Use Burden of Systemic Sclerosis

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Background/Purpose: The clinical burden of systemic sclerosis (SSc) is substantial and typically characterized by progressive skin, gastrointestinal, pulmonary, and cardiovascular complications and premature death. The objective of this analysis was to describe the healthcare resource use (HCRU) and costs of SSc patients prior to and immediately after diagnosis.

Methods: A retrospective cohort comparison was performed using a claims dataset (IBM® MarketScan® Commercial Database) capturing beneficiary-level claims between 2015-19. SSc patients were identified using diagnosis codes for SSc. Eligible subjects had ≥ 24 months of enrollment without a SSc diagnosis before their first SSc claim ('index date') and ≥ 12 months of enrollment thereafter. Total HCRU and costs, as well as mean cost by care setting for inpatient, outpatient, physician office (PO), and prescription drugs were reported in 2019 USD as mean per member per year (PMPY) amounts for 3 time intervals: 2- and 1-year before and 1-year after index diagnosis. To show the relative cost of SSc, patients with rheumatoid arthritis (RA) but not SSc and a general population ('unaffected') cohort without SSc or RA were matched 1:1 to SSc patients on age and gender.

Results: 902 SSc patients were eligible. Mean age at index SSc diagnosis was 54.3 years old and 84.7% were female. Total mean PMPY cost increased each year from $22,383 to $29,708 to $47,095, 2 years before, 1-year before, and 1-year after index diagnosis, respectively. These costs were higher than the RA (by 17, 27, and 28%) and unaffected (by 119, 208, and 278%) cohorts. Among SSc patients, the outpatient setting represented the largest proportion of cost 1-year after index ($16,392), followed by prescription drugs ($10,692), PO ($10,523), and inpatient ($9,448) settings. PMPY cost for diagnostic imaging services increased each year from $807 to $1,383 to $1,779. 1-year after SSc diagnosis, mean PMPY costs for immunosuppressant, corticosteroid, endothelin receptor antagonist, and proton-pump inhibitor drugs were $4,183, $1,746, $814, and $783, respectively. Among SSc patients, mean

Table. Cost and healthcare resource use among SSc patients by time-interval

Cohort	2 years before Index	1 year before Index	1 year after Index
Systemic sclerosis (N =902)			
Total mean cost (2019, USD)	$22,383	$29,708	$47,095
Inpatient	$3,735	$5,810	$9,488
Outpatient	$7,754	$10,503	$16,392
Physician office	$6,151	$7,456	$10,523
Prescription drug	$4,743	$5,939	$10,692
Mean services per patient	21.9	27.3	36.8

healthcare services per patient increased each year from 22 to 27 to 37 services and were higher as compared to the RA (21, 26, and 32) and unaffected (13, 14, and 15) cohorts.

Conclusion: SSc patients appear to accrue markedly greater healthcare costs and require more services than a matched unaffected general population. Elevated expenditures and HCRU are observed from at least 2 years before a confirmed SSc diagnosis with both increasing over time, a dynamic that likely reflects both the progressive, multisystem nature of SSc and the potential challenges and delays in diagnosis. Additionally, despite no proven disease modifying therapy, SSc patients still accrued substantial drug costs for therapies likely used to suppress emerging sequalae of the underlying disease. Together these findings suggest that SSc patients pose a substantial burden on the US healthcare system and highlights the need for early diagnosis and effective therapies.

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Abstract Number: 0144

Healthcare Utilization and Costs Following Kawasaki Disease in Ontario, Canada

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SESSION INFORMATION
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Background/Purpose: The incidence of Kawasaki Disease (KD) has increased by nearly 50% in Ontario, Canada over the past two decades. Little is known about the long-term burden of illness and healthcare utilization among KD survivors, particularly in a universal healthcare system. The aim of our study was to describe patterns of healthcare utilization and associated costs among KD survivors *vs*. matched controls in Ontario, Canada.

Methods: We used population-based health administrative databases to identify all children (0-18yr) hospitalized for KD in Ontario between 1995-2018. We excluded non-Ontario residents. Each case was matched to 100 non-exposed comparators by age, sex, and index year and follow-up continued until death or March 2019. Our primary outcomes were hospitalization, emergency department and outpatient visits. We evaluated healthcare costs (in Canadian Dollars [CAD], adjusted for inflation to the 2018 year) associated with each event type, as well as composite healthcare costs, including hospitalizations, ED visits and outpatient costs (i.e., lab services, physician billings and capitation payments).

Table 1. Healthcare utilization following Kawasaki disease diagnosis

Type of healthcare utilization		0-1 year following diagnosis		1-5 years following diagnosis		5+ years following diagnosis	
		KD Case	Comparator	KD Case	Comparator	KD Case	Comparator
Hospital admissions	N	N=4,597	N=459,700	N=4,576	N=446,620	N=3,571	N=334,460
	Patients with ≥1 encounter	717 (15.6%)	12,140 (2.6%)	441 (9.6%)	22,418 (5.0%)	463 (13.0%)	33,496 (10.0%)
	Encounter rate (per 1000py)	210.3	35.4	45.4	21.1	28.3	20.7
	Adjusted rate ratio (95% CI)	5.68 (5.57-5.78)	Ref	1.64 (1.52-1.76)	Ref	1.15 (1.04-1.26)	Ref
Outpatient visits	N	N=4,597	N=459,700	N=4,576	N=446,620	N=3,571	N=334,460
	Patients with ≥1 encounter	4,587 (99.8%)	393,683 (85.6%)	4,447 (97.2%)	404,126 (90.5%)	3,389 (94.9%)	296,710 (88.7%)
	Encounter rate (per 1000py)	13,131.5	5,658.7	6,329.3	4,206.0	4,743.6	3,778.4
	Adjusted rate ratio (95% CI)	1.92 (1.89-1.94)	Ref	1.18 (1.16-1.21)	Ref	1.10 (1.06-1.13)	Ref
ED visits	N	N=3,723	N=372,141	N=3,709	N=363,349	N=2,727	N=257,503
	Patients with ≥1 encounter	1,695 (45.5%)	105,297 (28.3%)	2,129 (57.4%)	171,122 (47.1%)	1,668 (61.2%)	139,141 (54.0%)
	Encounter rate (per 1000py)	877.0	486.6	492.1	349.7	358.0	314.3
	Adjusted rate ratio (95% CI)	1.52 (1.46-1.58)	Ref	1.20 (1.16-1.25)	Ref	1.07 (1.01-1.12)	Ref

Table 2. Composite healthcare costs following Kawasaki disease diagnosis

	1 year following diagnosis		1-5 years following diagnosis		5+ years following diagnosis		All Follow-Up	
	Case	Control	Case	Control	Case	Control	Case	Control
N	N=3,723	N=372,141	N=3,709	N=363,349	N=2,741	N=266,295	N=3,723	N=372,141
Total Cost	13,857,768	226,376,416	10,893,549	552,331,449	10,681,631	780,674,171	54,765,907	2,392,490,945
Mean cost per patient ± SD	3,722.20 ± 6,251.58	608.31 ± 5,254.95	2,937.06 ± 9,823.67	1,520.11 ± 7,714.58	3,896.98 ± 11,112.08	2,931.61 ± 12,036.91	14,710.15 ± 28,468.78	6,428.99 ± 24,223.76
Mean cost difference	+ 3113.89	Ref	+ 1416.95	Ref	+ 965.37	Ref	+ 8281.16	Ref
Median cost per patient (IQR)	2,466 (1,888-3,420)	234 (78-521)	1,395 (700-2,523)	689 (239-1,464)	1,566 (519-3,705)	951 (189-2,580)	9,174 (5,100-16,070)	3,148 (1,464-6,115)
Median cost difference	+ 2232	Ref	+ 706	Ref	+ 615	Ref	+ 6026	Ref

Results: We compared 4,597 KD survivors to 459,700 matched comparators. Median follow-up duration was 11.1 years (IQR 5.5-17.0) for KD cases and 10.0 years (IQR 4.5-16.0) for non-exposed children. KD survivors had higher rates of hospitalization (adjusted rate ratio 2.07, 95%CI 2.00-2.15), outpatient visits (1.30, 95%CI 1.28-1.33) and ED visits (1.22, 95%CI 1.18-1.26) throughout follow-up (Table 1). Within 1yr post-discharge, 717 (15.6%) of KD cases were re-hospitalized, 4587 (99.8%) had ≥1 outpatient physician visit and 1695 (45.5%) had ≥1 ED visit. KD survivors had higher composite healthcare costs throughout follow-up (median $9,174 *vs*. $3,148 CAD) (Table 2). Total healthcare costs for KD cases in Ontario were $13.9 million (within one year post-discharge) and $54.8 million (throughout follow-up). Outpatient care was the largest cost driver for both KD (50% of total healthcare costs) and non-exposed cohorts (55%) (Figure 1). However, the proportion of costs attributable to hospitalizations was higher among KD cases (43% *vs*. 36% non-exposed), due to higher hospitalization costs within the first year post-discharge.

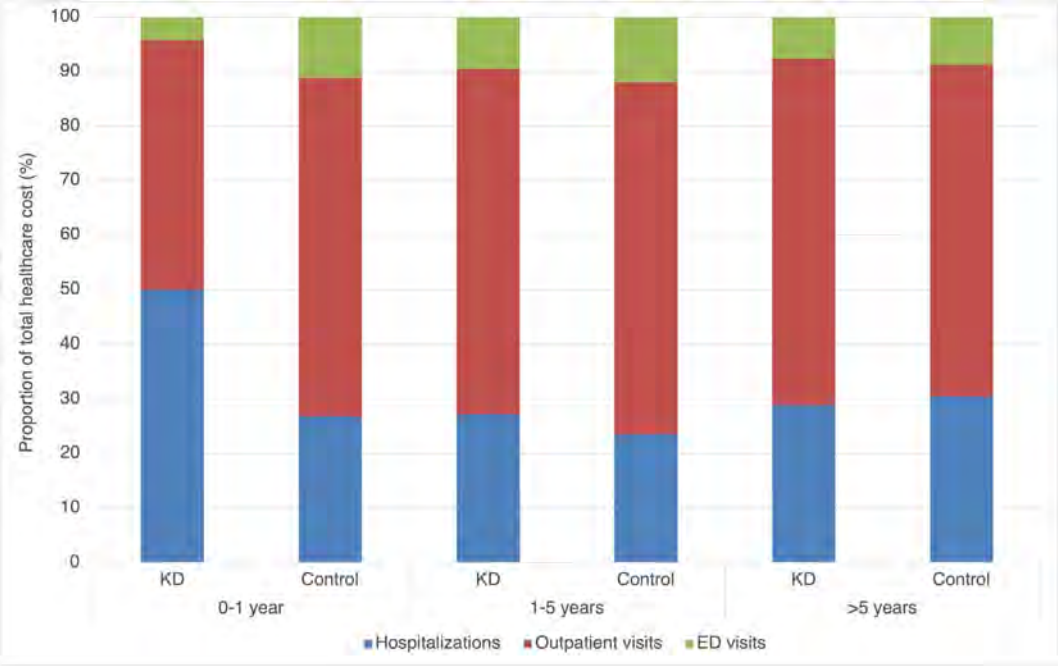

Figure 1. Distribution of healthcare costs following Kawasaki disease diagnosis.

Conclusion: Compared to non-exposed children, KD survivors had significantly higher long-term rates of healthcare utilization and cost. Nearly all KD cases were seen by a pediatrician or primary care physician within one year post-discharge, while less than half were seen by a cardiologist. The rising incidence and attributable costs associated with KD place a significant burden on Ontario's healthcare system.

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Abstract Number: 0145

Rheumatology Provider Perspectives on Using Patient-Reported Outcomes in Clinical Care

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

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Background/Purpose: Patient-reported outcomes (PROs) are surveys completed by patients to provide measurements of health, quality of life, symptoms, and functional status. PROs are useful for documenting changes in patient's health status over time as well as facilitating patient-provider communication about symptoms. Despite the potential benefits for the management of rheumatic diseases, uptake of PROs among rheumatology health care providers has been limited. The authors have been developing methods to promote the integration of specific PROs

(PROMIS® measures for pain intensity, physical function, and sleep disturbance) into rheumatology care at our institution. To inform our future efforts, we conducted a qualitative study to describe rheumatology provider attitudes towards the feasibility and acceptability of reviewing and discussing PROMIS or other PROs in rheumatology practice.

Table 1. Interview participant characteristics (n=8)

Characteristic	Attribute values among interviewees
Type of health care provider	7 physicians, 1 advanced nurse practitioner
Year of health professional degree	Ranged from 1975-2014
% time seeing patients	Ranged from 25-100%
Patient population	Mixed (5), SLE and mixed (1), vasculitis and mixed (1), SLE (1)
Used PROMIS as part of previous study	2 out of 8
Currently uses PROMIS in clinical care	4 out of 8
Currently uses PROMIS/other PROs in clinical care	6 out of 8

Table 2. Perceived benefits/disadvantages of use of patient-reported outcomes in rheumatology care

Perceived benefits	
Theme	**Quote**
Facilitation of patient-provider communication about symptoms	Their numbers [PRO results] don't necessarily match the exam[ination] or my conversation with them, so sometimes, it helps me to clarify what their real pain is and how it's impacting.
Improvement of the patient-provider relationship	Patients like them [PROs], let me tell you one thing, as long as you don't make them fill a million papers. Particularly patients with chronic pain or fatigue, they like it because it's a way for them to express themselves and to perhaps voice those symptoms that are not visible […] If you have swelling, you see it, but the fatigue or the pain, it's not visible.
Informing clinical decisions	I show [the patient their scores], "Your physical function has gone down like this, and your pain score continues to rise. This is all pointing towards somebody who's not in remission. We need to escalate your therapy." The patient gets it.
Documentation/tracking of patient symptoms over time	I think that the greatest benefit [of using PROs] is to understand the current situation. The secondary benefit is to understand the trend.
Supplementing/ complementing physical exam and objective findings	They [PROs] definitely won't replace the physical exam. […] Because actually, I cannot interpret them without the physical exam, right? […] No, they don't replace. They complement if you want something.
Perceived disadvantages	
Theme	**Quote**
Perceived lack of direct positive impact on health outcomes	It's [PROs] helped to explain [things to patients], but I don't know if it necessarily helps with improved outcomes.
PRO information is not always actionable	They're [PROs are] valuable, but they don't allow me to make decisions.
Doubts about the validity of results	[…] patients sometimes use them [PROs] to vent, right, whatever is going on in their life. They will answer bad if they are depressed or if they fight with their husband, so sometimes it's hard to interpret that data objectively for us.
Lack of applicability for certain patients	I think you need to understand which ones [PROs] work for your patient population or for the disease that you are following because they're [PROs are] too broad.

Table 3. Perceived barriers/facilitators for use of patient-reported outcomes in rheumatology care

Barriers	
Theme	**Quote**
Perceived time burden of reviewing and documenting PROs	I would say my initial reaction to it was, this is yet another thing I have to do in a [short clinic visit], and it causes more documentation issues.
Patients not completing PRO questions before the consultation	[…] if you're running 15 minutes behind because you're waiting for someone to finish filling this out, that just doesn't—it's very frustrating at times.
Perception that discussing the scores with patients would be time-consuming/ burdensome	Trying to explain to someone that their PROMIS score going up by one point, 0.1 point—I don't know what the scale is—matters or doesn't matter, especially if it doesn't matter, is disruptive.
Lack of confidence in accessing/ documenting/ interpreting PRO results	I think that a large barrier to feasibility is the provider having to figure out what the result means and then convey it to the patient.
Facilitators	
Theme	**Quote**
Simplicity and ease of reviewing/ documenting/ discussing PRO results with patients	It [reviewing and discussing PROs] is feasible. I think it's very important for the providers to be aware that this is something that doesn't take that much time because we always think of anything else outside of what we need to do with our patients, in terms of clinical matters, is less relevant.
Receipt of training	I think the things that would help me the most would be training so that I can quickly and clearly explain the measure to the patient […] visually, in a way the patient isn't terribly confused and I'm not terribly confused […]
Recommendation by trusted colleagues	When I heard that <Name>, someone who I really respect, who you probably know very well, I bet, has done a lot of work on PROs and the PROMIS scores, I had all intention of—if <Name> doing that and he's spearheading this, then maybe my attitudes on this should change, and I should incorporate these into my note and using the dot phrase he showed me.

Methods: In-depth semi-structured interviews were conducted with health care providers at our institution, who were asked to discuss their experiences and attitudes towards the use of PROs in rheumatology care. We recruited providers who had received training on the use of PROMIS as part of a previous study led by 2 of the authors, as well as providers who had not participated in the previous study. The interviews were conducted via phone or video call and lasted between 30-120 minutes. Written informed consent was obtained from participants before the interviews. The interviews were audio recorded and transcribed for analysis.

Qualitative analysis of the transcripts was conducted using NVivo software. Five of the authors carried out the analysis. We used a combination of inductive and deductive coding. Each transcript was coded independently by at least 2 team members, who met to discuss and reconcile any discrepancies in coding that were >=20% for individual codes. The resulting coded data was reviewed and summarized as themes to describe current uptake, perceived benefits and disadvantages, and perceived barriers and facilitators of using PROMIS/PROs.

Results: The 8 health care providers interviewed included 7 physicians and 1 advanced nurse practitioner; 6 of these currently used PROMIS or other PROs in clinical care (Table 1). Two of the providers were trained in the use of PROMIS as part of our previous study—these providers still used PROMIS in clinical care for their patients. Un-

expectedly, two other providers (1 physician and 1 advanced nurse practitioner) reported routinely using PROMIS in clinical care, although they had not participated in the previous study.

The perceived benefits/disadvantages and barriers/facilitators of using PROs in rheumatology care identified by interviewees are summarized in Tables 2-3.

Conclusion: Rheumatology health care providers had a range of attitudes towards the use of PROMIS/PROs in clinical practice and addressing their concerns will be important for promoting the use of PROMIS and other PROs. Demonstrating the value and ease of using PROs in clinical care is essential for gaining support from health care providers.

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Abstract Number: 0146

Improving Medication Toxicity Lab Monitoring During the COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic led to the rapid implementation of telehealth in rheumatology with unknown implications for medication toxicity lab monitoring. The purpose of this quality improvement (QI) project is to evaluate and improve lab monitoring in patients with rheumatoid arthritis (RA) seen by telehealth. This project was led by adult Rheumatology fellows at a single academic institution as part of our QI curriculum.

Methods: We targeted patients with RA (ICD10 M05/M06), taking methotrexate, sulfasalazine, leflunomide, or azathioprine, seen in a telehealth visit, and no aspartate aminotransferase (AST) in the 2 months before the visit. Our primary aim was to increase the proportion of targeted patients with an AST at our institution in the 2 months after the visit from less than 35% to greater than 50%. A secondary aim was to increase scanned external lab results in the two months after the visit from 7% to greater than 15%. Data were obtained with SlicerDicer, an analytic data tool within our electronic health record and validated by manual review of encounters seen by fellows leading the QI initiative from 7/1/2020 - 10/31/2020. Data were monitored throughout the study period. Providers continuously shared

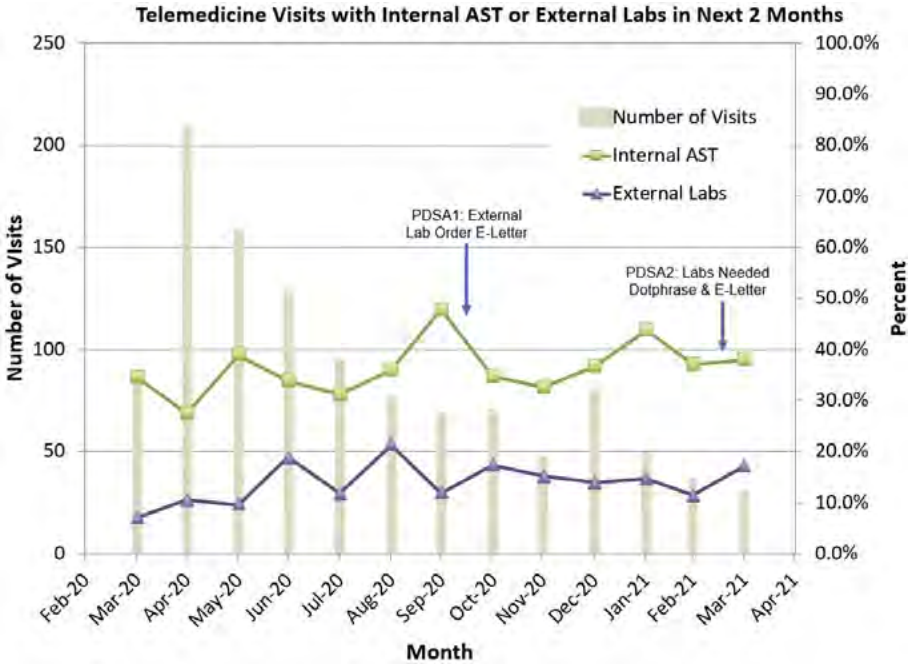

Figure 1. Divisional chart run via SlicerDicer of telemedicine visits with AST at our institution (Internal AST) or External Labs in next 2 months.

resources and best practices. In addition, the following interventions occurred using Plan-Do-Study-Act (PDSA) methodology: (1) standardized process for sending external lab orders to patients electronically (9/15/2020) and (2) letter for patients with detailed instructions on obtaining labs (3/2/2021). Providers in our division were surveyed via Redcap on 2/19/2021 to gather more input on lab monitoring.

Results: There were 1,116 telehealth visits with RA patients targeted by our project from 3/1/2020 – 3/31/2021 (Figure 1). The number of visits declined from a peak of 207 in 4/2020 to 29 in 3/2021. At baseline, patients with an AST performed at our institution in the 2 months after the telehealth visit was 34.5% in 3/2020 and 27.5% in 4/2020. We did not reach our aim of 50% during the study period; the highest proportion was 47.8% in 9/2020. External labs scanned over 2 months at baseline were 7.1% in 3/2020 and 10.6% in 4/2020. Our goal of 15% was reached in half of the months from 6/2020 – 3/2021. PDSA interventions did not substantially impact lab monitoring. The manual chart review included 31 patients; 20 (64.5%) had labs ordered to be done at our institution, 9 (29.0)% externally, and 2 (6.5%) did not have labs ordered. There were 21 (67.7%) without an AST in the preceding two months. Of these, 6/21 (71.4%) had an AST done in the next two months at our institution or externally. The provider survey was sent to 34 providers in our practice; 27 (79.4%) responded. Results are shown in Table 1. Although 23 (85.2%) agreed or strongly agreed that they knew what an “overdue results” in-basket message meant, only 6 (22.2%) “usually” or “always” reacted to these messages. Free text responses on reasons for this discordance are shown in Table 2.

Conclusion: Our study revealed gaps in medication toxicity lab monitoring among RA patients seen via telehealth. Monitoring improved throughout the study period but we have not yet reached our primary aim. An important next step is to develop a standardized process for acting on overdue lab messages.

Table 1. Divisional provider survey responses via RedCap.

I know/understand:	Strongly Disagree n (%)	Disagree n (%)	Agree n (%)	Strongly Agree n (%)
How to instruct patients on obtaining labs at a "lab and leave" location.	1 (3.7%)	4 (14.8%)	14 (51.9%)	8 (29.6%)
How to instruct patients on scheduling a lab appointment at [our clinic] locations.	1 (7.4%)	8 (29.6%)	15 (55.6%)	2 (7.4%)
How to send patients external lab orders electronically through MyChart.	1 (3.7%)	11 (40.7%)	4 (14.8%)	11 (40.7%)
How to mail a letter with external lab orders to a patient's home.	0 (0%)	4 (14.8%)	10 (37%)	13 (48.1%)
What an "overdue results" in-basket message means.	1 (3.7%)	3 (11.1%)	18 (66.7%)	5 (18.5%)
For your telemedicine patients who need lab monitoring for rheumatologic medications, how often do you:	**Never n (%)**	**Sometimes n (%)**	**Usually n (%)**	**Always n (%)**
List an "expected by" date on future lab orders.	4 (14.8%)	2 (11.1%)	5 (18.5%)	15 (55.6%)
Order "standing" labs instead of "future" (one-time) labs.	1 (18.5%)	17 (63%)	2 (7.4%)	3 (11.1%)
React to "overdue results" in-basket messages by reminding the patient they need to get the labs done (or have staff remind them).	11 (40.7%)	10 (37%)	5 (18.5%)	1 (3.7%)

Table 2. Selection of divisional provider survey free responses via RedCap

When you react to "overdue results" in-basket messages by reminding the patient about the labs, what specific actions do you usually take? Please describe.	"Message if needed." "Ask staff/nurse/MA to contact patient." "MyChart message to patient or ask staff assistant to call depending on the urgency." "None. I delete them." "Ask [RNs] to contact patient, find out [if] labs have been drawn, and track down results if they have." "Call patient." "I have a prepped mychart message that I send, but I have not figured out how to do this as a quick action." "I do not have time to address this at all … I am sure that would be helpful, however. I need someone to look through the orders, read my last note and take care of this - not send something else to my in basket." "Scan through them and delete most of them. For some labs, if I recall it as being more important, I will call patient to remind." "Hit 'Done'." "Briefly glance at chart to make sure labs are not up-to-date elsewhere (such as care everywhere or external) … if they have my chart, send a my chart message using a dot phrase … if no my chart, I asked staff to call patient to remind them." "[Forward] to MA." "I do not get these alerts." "Telephone call to staff to call patient to have done."
What major issues have you encountered in ordering and obtaining disease and medication toxicity monitoring labs for telemedicine patients? Please list as many issues as necessary.	"Overdue results coming in incorrectly for external labs." "I don't have time to go through the over due labs. I just won't refill their meds when they ask for refills." "Patients refused to get labs because too scared to go to lab." "The faxed in labs are often lost." "No easy reminder system for people to get standing labs done." "Labs not in system, difficult to find prior outside labs without wasted time searching documents and attachments." "Wasted time going back and forth asking nurses to remind patients to get labs, trying to get results. All the extra time adds up in your day, making it difficult to do other tasks or see more patients." "Lab results getting sent to email without any patient information so impossible to find later." "Even if the lab results get scanned into the [medical record] they are in the [medical record] as a PDF and aren't trendable or meaningfully useful down the road." "Need for [lab] appointment." "Patients don't want to have [labs] done." "Takes months for external labs to get scanned in." "Very cumbersome to order compared to in person lab ordering. Takes multiple extra clicks. Also I have to spend additional time to instruct patient on where to go, perhaps even needing to look up Google Maps on where they live compared to lab facility and verbally tell them phone number. Can take additional 5 minutes." "Patient forgets, disregards instructions to get them done, wants them done externally but for various reasons they are not done or results not received."

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Abstract Number: 0147

A Qualitative Analysis of Methotrexate Self-Injection Education Videos on YouTube: An Update

Amy Semaka, Hillary Wilson and Steven Katz, University of Alberta, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
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Background/Purpose: Patients are turning to the Internet for guidance and information at an increasing rate, requiring clinicians to be aware of the constantly changing resources and quality of information that is available. A previous study demonstrated a minority of YouTube videos were useful for teaching methotrexate self injection.

Methods: Using the search term "Methotrexate injection", two reviewers analyzed the first 75 videos in the YouTube search results. Videos were classified as useful, misleading or a personal patient view. Videos were rated for reliability, comprehensiveness and quality. Discrepancies in ratings were resolved by discussion between the two reviewers.

Results: Out of the 75 videos reviewed, 12 were classified as useful (16%), 47 misleading (63%), and 16 personal patient view (21%). Although this represents a substantial increase from the 2014 study in the proportion of videos that were deemed misleading (63% vs 28%), many of these videos were on methotrexate in general. Mean reliability rating was 4/5 (±0.5) for useful videos, 4/5 (±0.8) for misleading videos, and 3/5 (±0.3) for patient videos ($p < 0.0001$). Mean comprehensiveness was 4/4 (±0.0) for useful videos, 0/4 (±0.0) for misleading videos, and 2/4 (±2) for patient videos ($p < 0.0001$). Mean global quality score was 5/5 (±0.3) for useful videos, 4/5 (±0.7) for misleading videos, and 4/5 (±0.8) for patient videos ($p=0.0002$). Compared to the 2014 study, videos classified as misleading or personal patient view scored significantly higher in the categories of reliability and global quality score ($p < 0.0001$).

Conclusion: While the majority of the videos from the YouTube search were deemed misleading for teaching subcutaneous methotrexate injection, the useful videos were of good quality and had the highest ratings for comprehensiveness. In general, reliability and global quality scores were increased from the previous study, suggesting improvement in overall videos over time. Logistics of the YouTube algorithm may still impede access to the 'best' videos for patient teaching; therefore, clinicians should be prepared to recommend strategies for patients to find high quality videos.

Disclosure: A. Semaka, None; **H. Wilson**, None; **S. Katz**, None.

Abstract Number: 0148

Implementation of an Interprofessional Safety Check to Screen for Latent Tuberculosis at an Academic Tertiary Referral Rheumatology Clinic Increased Screening Rates Compared to Historical Levels

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Health Services Research Poster I: Lupus, Inflammatory Arthritis, & More (0128–0148)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Certain disease-modifying anti-rheumatic drugs (DMARDs) increase the risk of reactivation of latent tuberculosis (TB). While screening for latent TB prior to initiation of these DMARDs is recommended for a most patients, low rates of screening have been reported in national rheumatology registry data[3]. A prior study conducted in our rheumatology clinic at an academic tertiary referral center suggested that only 63% of eligible patients from 2013-2017 were screened for latent TB prior to DMARD initiation. We highlight our approach of implementing a pharmacy-integrated safety check to capture this key safety measure.

Methods: Analysis 1: In October of 2019, we implemented a new pharmacy-integrated workflow in which clinicians prescribe new oral or injectable DMARDs to the university specialty pharmacy which reviews cases for adequate TB screening. DMARD prescriptions were filled or routed to patients' contracted specialty pharmacies only once adequate TB screening was completed unless the clinician specified otherwise. Analysis 2: Using SQL to extract data from the electronic health record (EHR) for the calendar year 2020, we generated a list of patients eligible for TB screening which served as the denominator in calculating our TB screening rate. First, all qualifying DMARD prescriptions were identified. We excluded refills, patients switching between DMARDs, and patients with a history of TB using historic prescription data and information from the past medical history of problem list. Adequately screened cases (numerator) had a result for an interferon gamma release assay or purified protein derivative test within 365 days prior to or 60 days after the DMARD prescription start date We validated all inadequately screened cases by manual chart review.

Results: Analysis 1: In 2020, 97 new qualifying DMARD prescriptions were routed through our workflow. In three cases, the medication was not started due to patient or clinician preference or lack of insurance coverage. These were excluded from the denominator. In two instances, the clinician overrode the requirement for TB screening within 365 days as it had been performed with the prior 18 months. Analysis 2: EHR data extraction identified 159 cases in 2020 eligible for TB screening, and 130 were screened adequately for a TB screening rate of 82%. Differences in numbers of eligible patients in EHR data versus through the workflow were analyzed via manual chart review. Chart review also suggested reasons for inadequate screening including prior TB screening outside of the defined timeframe, treatment hiatus, and prescription of an infusion.

Conclusion: Our intervention was associated with a significant improvement of 19% in our clinic's TB screening rate compared to historic rates. Reviewing EHR data identified additional reasons for missed screening. These reasons for missed screening may inform future process improvement cycles related to capturing this key safety measure.

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Abstract Number: 0149

Development of Joint Effusion, Hyperperfusion and Enthesitis After One Hour of Age-and Gender Adjusted Weight Training

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Ultrasound is an established tool to detect changes of joints, tendons and entheses in rheumatology. However, several studies detected structural and vascular changes in tendons and entheses as well as joint effusion in athletes and physical active individuals (1–3). This evidence may raise the question, whether a patient's ultrasound findings are related to a rheumatic disease or associated with sports activities. The purpose of this study was to evaluate the development of joint effusion, hyperperfusion and enthesitis in large and medium joints of young healthy individuals after one hour of supervised weight training.

Methods: We applied ultrasound to examine the shoulder, elbow, wrist, hip, knee, and ankle joints, as well as associated entheseal sites such as the Achilles tendon and the plantar aponeurosis, in healthy individuals under the age of 30. The ultrasound examination was carried out before, 24h after and 48h after the participants conducted one hour of supervised weight training. Friedman test was applied to determine significant changes of the prevalence of joint effusion and enthesitis within 48h after the physical activity. Bonferroni-corrected p-values are shown for post-hoc tests.

Results: Fifty-one healthy individuals with a mean age of 23.7 years (19;30 ± 2.46) were included, 52.9% were female with a mean BMI of 22.5 kg/m2 (18.6;36.6 ± 3.07). The percentage of individuals with joint effusion in at least one joint increased from 72.55% (n=37) at baseline to 88.24% (n=45) after 24h and to 94.12% (n=48) 48h after the training. The mean number of joints affected by effusion were 1.49 at baseline, 2.82 after 24h and 4.16 after 48h.

Fourteen participants (27.45%) presented with entheseal pathology in at least one enthesis at baseline, 47.06% (n=24) showed pathologies after 24h and in 56.86% (n=29) entheseal pathology was observed 48h after the weight training. The only entheseal pathology observed 24h and 48h after the training was hyperperfusion.

The Friedman test and post-hoc tests revealed a significant increase in joints with effusion within 48 hours of weight training ($Q=-1.255$, $p< 0.0001$). Results also showed a significant increase of detected entheseal pathology from baseline to 48h after the weight training ($Q= -0.588$, $p=0.009$).

Conclusion: Prevalence of joint effusion in large and medium joints as well as the prevalence of entheseal pathology increase significantly within 48h after weight training. Therefore, the patient's sports activities should be taken into account when performing a musculoskeletal ultrasound examination.

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Disclosure: J. Schreiner, None; **D. Scheicht**, None; **P. Karakostas**, None; **J. Ziob**, None; **C. Behning**, None; **P. Preuss**, None; **P. Brossart**, None; **V. Schäfer**, None.

Abstract Number: 0150

Clinical Characteristics and Quantitative CT Findings in Connective Tissue Disease-Associated Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Precapillary Pulmonary Hypertension (PPH) is a known complication of connective tissue disease-associated interstitial lung disease (CTD-ILD) but at present requires right heart catheterization (RHC) for definitive diagnosis. Computed tomography (CT) imaging measures of vascular pruning have been associated with pulmonary vascular disease, but it is unknown whether these CT measures associate with PPH in patients with CTD-ILD. The aims of this study were to 1) compare clinical characteristics of patients with CTD-ILD with and without PPH,

Table 1. Underlying Rheumatic Disease Diagnosis in CTD-ILD Number of patients that met inclusion criteria for each underlying rheumatic disease diagnosis

Rheumatic Disease Diagnosis in CTD-ILD	n
ANCA-associated Vasculitis 2/2 Microscopic Polyangiitis	6
Anti-synthetase Syndrome	13
Diffuse Systemic Sclerosis	9
Limited Systemic Sclerosis	12
Systemic Sclerosis sine Scleroderma	2
Rheumatoid Arthritis	10
Polymyositis	3
Sjogren's Syndrome	1
Systemic Lupus Erythematosus	5
Interstitial Pneumonia with Autoimmune Features (IPAF)	9
Mixed Connective Tissue Disease	11
Total	81

Table 2. Clinical and Imaging Characteristics of CTD-ILD by Presence of Precapillary Pulmonary Hypertension Continuous variables presented as median [interquartile range]. Categorical variables presented as n (%)

Precapillary Pulmonary Hypertension	Precapillary Pulmonary Hypertension (N = 40)	No Pulmonary Hypertension (N = 41)	p-value
Demographics			
Age, years [IQR]	61 [57, 66]	59 [53, 69]	0.43
Male (%)	17 (42.5)	14 (34.1)	0.59
Race (%)			0.66
Asian	1 (2.5)	2 (4.9)	
Black	10 (25.0)	6 (14.6)	
Other	2 (5.0)	2 (4.9)	
White	27 (67.5)	31 (75.6)	
Serologies			
ANA positive (%)	22 (64.7)	21 (53.8)	0.48
SSA positive (%)	5 (12.5)	10 (24.4)	0.28
SSB positive (%)	2 (5.0)	4 (9.8)	0.69
Smooth Ab positive (%)	3 (7.5)	4 (9.8)	1
RNP Ab positive (%)	6 (15.0)	10 (24.4)	0.43
Anti-Jo1 positive (%)	3 (7.5)	5 (12.2)	0.74
Anti-Scl-70 positive (%)	2 (5.0)	3 (7.3)	1
Anti-CCP positive (%)	5 (12.5)	5 (12.2)	1
Rheumatoid Factor positive (%)	10 (25.0)	10 (24.4)	1
RNA Polymerase Ab positive (%)	1 (2.5)	1 (2.4)	1
c-ANCA Ab positive (%)	0 (0.0)	2 (4.9)	0.49
p-ANCA Ab positive (%)	6 (15.0)	2 (4.9)	0.25
Pulmonary Function Testing			
Percentage of Predicted FEV1[IQR]	61 [48, 71]	63 [49, 79]	0.301
Percentage of Predicted FVC [IQR]	59 [48, 69]	60 [46, 80]	0.47
FEV1 to FVC ratio [IQR]	0.82 [0.75, 0.86]	0.81 [0.76, 0.88]	0.87
Percentage of Predicted TLC [IQR]	52 [49, 75]	66 [56, 75]	0.21
Percentage of Predicted DLCO [IQR]	23 [16, 36]	39 [32, 50]	0.002
Right Heart Catheterization Measures			
Precapillary Pulmonary Hypertension	40 (100.0)	0 (0.0)	<0.001
Mean PA Pressure [IQR]	34.0 [26.0, 39.3]	19.5 [16.8, 22.0]	<0.001
Pulmonary Capillary Wedge Pressure [IQR]	7.5 [5.0, 10.5]	9.5 [6.0, 12.0]	0.07
Cardiac Output [IQR]	4.2 [3.7, 5.0]	5.3 [4.7, 6.0]	<0.001
Pulmonary Vascular Resistance dynes sec cm−5 m2 [IQR]	433.8 [304.4, 688.5]	163.2 [129.3, 203.8]	<0.001
Echocardiogram Measures			
Right Ventricular Systolic Function Normal (%)	19 (48.7)	37 (90.2)	<0.001
Right Ventricle Enlarged (%)	23 (62.2)	8 (20.0)	<0.001
Right Ventricular Systolic Pressure [IQR]	56.5 [46.3, 69.5]	38.0 [29.8, 50.0]	<0.001
Quantitative CT Measures (normalized for Total Lung Volume)			
Blood Vessel Volume of all vessels < 5mm2 [IQR]	19.4 [15.2, 23.7]	20.2 [15.6, 23.8]	0.64
Blood Vessel Volume of all vessels < 10mm2 [IQR]	31.9 [28.0, 35.9]	30.5 [26.1, 36.3]	0.55
Blood Vessel Volume of all vessels > 5mm2 [IQR]	45.0 [31.8, 55.2]	37.3 [26.9, 50.8]	0.13
Blood Vessel Volume of all vessels > 10mm2 [IQR]	31.4 [21.4, 41.2]	27.3 [18.4, 36.6]	0.13
Arterial Blood Vessel Volume of all vessels < 5mm2 [IQR]	11.6 [9.1, 14.2]	12.7 [8.2, 14.2]	0.84
Arterial Blood Vessel Volume of all vessels < 10mm2 [IQR]	19.4 [16.7, 21.9]	17.8 [15.2, 19.8]	0.15
Arterial Blood Vessel Volume of all vessels > 5mm2 [IQR]	26.7 [19.5, 35.3]	20.7 [15.3, 28.3]	0.02
Arterial Blood Vessel Volume of all vessels > 10mm2 [IQR]	18.5 [13.1, 24.1]	13.6 [10.1, 19.4]	0.01
Total Arterial Blood Vessel Volume [IQR]	38.1 [30.2, 46.4]	33.6 [27.3, 38.5]	0.01
Total Venous Blood Vessel Volume [IQR]	22.8 [17.6, 30.4]	23.1 [18.7, 30.4]	0.99

2) assess if there are quantitative CT vascular measures that associate with the presence of PPH, and 3) determine if these comparisons differed across various rheumatic diseases.

Methods: We performed a retrospective review of adult patients (>18 years old) with ICD-code diagnoses of ILD and connective tissue disease (CTD) with both a CT chest and RHC within two years of each other in the electronic medical record. Medical charts were reviewed for confirmation of ILD by a pulmonologist, CTD by a rheumatologist, and presence of PPH or absence of pulmonary hypertension by a pulmonologist. CT chest images underwent automated 3D vasculature reconstruction using the Chest Imaging Platform (www.chestimagingplatform.org) with vessel size estimation for calculation of blood vessel volume in arterial, venous, and total blood vessels of size greater than or less than 5 mm^2 and 10 mm^2; these values were divided by CT_{LV} (total lung volume in Liters) to measure blood vessel volume normalized to total lung volume. Descriptive and comparative analyses using Chi-square (categorical variables) and Wilcoxon-ranked sum (continuous variables) tests were performed using R version 4.0.2.

Results: 81 patients met our inclusion criteria (41 without PPH and 40 with PPH; 6 microscopic polyangiitis, 13 antisynthetase syndrome, 9 diffuse systemic sclerosis (SSc), 12 limited SSc, 2 SSc sine scleroderma, 10 rheumatoid arthritis, 3 polymyositis, 1 Sjögren's, 5 systemic lupus erythematosus (SLE), 9 interstitial pneumonia with autoimmune features (IPAF), and 11 mixed CTD). There were no statistical differences in age, sex, race, ethnicity, positive ANA, other autoimmune serologies, spirometry, and TLC measures in patients with PPH and patients without pulmonary hypertension. Predicted carbon monoxide diffusion capacity (DLCO) was significantly reduced in PPH (p=0.002). On quantitative CT compared to patients without pulmonary hypertension, patients with PPH had significantly greater blood vessel volume in arterial vessels (p=0.014), and in arterial vessels greater than 5 mm^2 (p=0.016) and 10 mm^2 (p=0.014), respectively.

Conclusion: Patients with CTD-ILD and precapillary pulmonary hypertension were found on quantitative CT to have greater arterial lung blood volume in vessels of size greater than 5 mm^2 and 10 mm^2. This suggests that distal increases in pulmonary vascular resistance lead to proximal arterial vascular dilation and an increased arterial blood volume on CT scan. Quantitative analysis of CT chest imaging in CTD-ILD may be a useful diagnostic tool for precapillary pulmonary hypertension; however, prospective studies are needed.

Disclosure: S. Jesudasen, None; **B. Patel**, None; **K. D'Silva**, None; **P. Nardelli**, None; **R. San José Estépar**, Quantitative Imaging Solutions, 7; **G. Washko**, None; **R. San José Estépar**, None; **F. Rahaghi**, None; **S. Montesi**, DevPro Biopharma, 2, Wolters Kluwer, 9, Roche, 2, Pliant, 5, United Therapeutics, 5.

Abstract Number: 0151

Usefulness of Ultrasound and (FDG) PET/CT to Detect Cranial and Extracranial Artery Involvement in Patients with Suspected Large Vessel Vasculitis

Juan Molina[1], Isabel Castrejón[2], Javier Rivera[2], Julia Martínez Barrio[2], Juan Carlos Nieto[2], Katerine López[2], Fernando Montero[2], Laura Trives Folguera[2], Carlos González[3] and Jose Maria Alvaro-Gracia[2], [1]Hospital General Universitario Gregorio Maran, Madrid, Spain, [2]Hospital General Universitario Gregorio Marañón, Madrid, Spain, [3]CEIMI, Hospital General Universitario Gregorio Marañón, Madrid, Spain

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultrasound (US) is recommended as the first imaging modality to assess patients presenting with predominantly cranial symptoms of giant cell arteritis (GCA). However, its value in assessing extra-cranial involvement remains unclear, being the ^{8}F-fluorodeoxyglucose (FDG) PET/CT the ancillary study recommended. We aim to compare US versus FDG PET/CT to detect cranial and extra-cranial artery involvement in patients with suspected large vessel vasculitis (LVV).

Methods: Retrospective observational study including patients referred to a GCA fast track pathway (FTP) over a 2-years period. All patients underwent US exam of temporal (TA) and large vessel (LV) (carotid, subclavian and axillary) arteries within 24 hours of referral per protocol. Positive US findings were defined as a halo and/or compression sign in TA and a halo and/or intima media thickness >1mm in LV arteries. FDG PET/CT was performed per clinician criteria and was defined as positive if an artery FDG uptake was higher than liver uptake. The qualitative FDG uptake in the aorta, its aortic branches (carotid, axillary and subclavian), iliac and cranial arteries was also registered. All US

Table 1. Clinical, laboratory and imaging findings of patients included in the fast track pathway with and without LVV. LVV: large vessel vasculitis; PMR: polymyalgia rheumatica; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; US: ultrasound; SD: standard deviation

	Total n=113	Patients with LVV n=37 (32.7%)	Patients without LVV n=76 (67.3%)	p
Demographics				
Age, mean (SD)	74 (11)	74.9 (10.8)	73 (11.2)	0.538
Female, n (%)	84 (74.3%)	27 (73%)	57.6 (75%)	0.817
Laboratory findings				
CRP (mg/dL), mean (SD)	5(6.2)	8.7 (7.4)	3.1 (4.5)	<0.001
ESR (mm/h), mean (SD)	55 (34.6)	70.9 (33.2)	46 (32.3)	0.001
Haemoglobin (g/dL), mean (SD)	12.4 (1.8)	11.7 (1.5)	12.7 (1.8)	0.002
Platelets 10^9/L, mean (SD)	298 (122.3)	354.3 (135.4)	270.2 (105.6)	0.002
Diagnostic criteria				
Fulfilling 1990 GCA criteria, no. of patients	34 (30.1%)	20 (54.1%)	14 (18.4%)	<0.001
Histology				
Temporal artery biopsy positive n=23, no. of patients	8 (34.8%)	8 (40%)	0 (0%)	0.175
Imaging				
^{18}F-FDG-PET/CT positive n=28, no. of patients	12 (42.9%)	11 (61.1%)	1 (10%)	0.009
Aorta uptake n=28, no. of patients	11 (39.3%)	10 (55.6%)	1 (10%)	0.041
Subclavian uptake n=28, no. of patients	8 (28.6%)	8 (44.4%)	0 (0%)	0.025
Axillary uptake n=28, no. of patients	4 (14.3%)	4 (22.2%)	0 (0%)	0.265
Carotid uptake n=28, no. of patients	6 (21.4%)	6 (33.3%)	0 (0%)	0.039
Iliac uptake n=28, no. of patients	6 (21.4%)	5 (27.8%)	1 (10%)	0.375
Cranial arteries uptake n=28, no. of patients	0 (0%)	0 (0%)	0 (0%)	-
Positive US findings, no. of patients	35 (31%)	32 (86.5%)	3 (3.9%)	<0.001
Temporal artery positive, no. of patients	25 (22.1%)	24 (64.9%)	1 (1.3%)	<0.001
Large vessel arteries positive, no. of patients	18 (15.9%)	16 (43.2%)	2 (2.6%)	<0.001
Axillary positive, no. of patients	16 (14.2%)	14 (37.8%)	2 (2.6%)	<0.001
Subclavian positive, no. of patients	11 (9.7%)	11 (29.7%)	0 (0%)	<0.001
Carotid positive, no. of patients	12(10.6%)	12 (32.4%)	0 (0%)	<0.001
Temporal + large vessel arteries positive, no. of patients	8 (7.1%)	8 (21.6%)	0 (0%)	<0.001
Halo sign positive, no. of patients	31 (27.4%)	30 (81.1%)	1 (1.3%)	<0.001
Compression sign positive, no. of patients	19 (16.8%)	18 (48.6%)	1 (1.3%)	<0.001
Stenosis positive, no. of patients	8 (7.1%)	8 (21.6%)	0 (0%)	<0.001

exams were made before the FDG PET/CT evaluation. The external criterion for US and FDG PET/CT comparison was LVV clinical confirmation after 6 months follow-up.

Results: A total of 113 patients were included, 74.3% female with mean age 74 (11) years. After 6 months of follow-up, 37 (32.7%) patients had LVV clinical confirmation (34 GCA and 3 Takayasu). Only 3 (3.9%) patients without LVV versus 32 (86.5%) with LVV had positive US findings (Table 1). Among patients with LVV, 24 (64.9%) had TA involvement and 16 (43.2%) had extra-cranial LVV according to US examination (37.8% axillary, 29.7% subclavian and 32.4% carotid artery involvement). We found a mixed pattern with involvement of both TA and LV arteries in 8 (21.6%) patients. Overall, sensitivity and specificity of US for LVV was 86.5% and 96.1%, respectively, and for exclusively LV involvement was 94.1% and 80.2 %, respectively. A total of 28 patients underwent a FDG-PET/CT, of whom 12 (42.9%) showed positive findings. Taking FDG-PET/CT as the reference, US showed positive extracranial findings in 10 (83.3%) of those 12 patients and was able to detect 2 (12.5%) additional cases of large vessel involvement with negative FDG-PET/CT examination (Table 2). On the other hand, FDG-PET/CT showed LV artery involvement in 2 patients with negative US findings (1 patient with isolated aortitis and 1 patient with aorta and iliac artery involvement) (Table 3). FDG-PET/CT showed cranial arteries uptake in none of patients.

Table 2. Ultrasound findings of patients included in the fast-track pathway taking FDG-PET/CT as the reference for large vessel vasculitis. LVV: large vessel vasculitis; US: ultrasound

	Total n= 28	Patients with positive FDG-PET/CT findings for LLV n=12 (%)	Patients without positive FDG-PET/CT findings for LLV n=16 (%)	p
Positive US findings, no. of patients	16 (57.1%)	10 (83.3%)	6 (37.5%)	0.015
Temporal artery positive, no. of patients	9 (32.1%)	5 (41.7%)	4 (25%)	0.432
Large vessel arteries positive, no. of patients	12 (42.9%)	10 (83.3%)	2 (12.5%)	<0.001
Axillary positive, no. of patients	11 (39.3%)	9 (75%)	2 (12.5%)	0.001
Subclavian positive, no. of patients	9 (32.1%)	8 (66.7%)	1 (6.3%)	0.001
Carotid positive, no. of patients	9(32.1%)	8 (66.7%)	1 (6.3%)	0.001

Table 3. Comparison between US and PET/CT findings in patients with PET/TC proven LVV. TA: temporal artery; CA: carotid artery; AA: axillary artery; SA: subclavian artery, IA: iliac artery

	Ultrasound				FDG-PET/CT					
Patient	TA	CA	SA	AA	TA	CA	SA	AA	Aorta	IA
1	+	+	-	-	-	+	-	-	-	-
2	-	-	-	-	-	-	-	-	+	+
3	+	-	+	+	-	+	+	-	+	+
4	+	-	+	+	-	+	+	+	+	-
5	-	+	+	+	-	-	-	-	+	+
6	+	+	+	+	-	-	+	-	+	+
7	-	+	+	+	-	+	+	+	+	+
8	-	+	+	+	-	+	+	+	+	+
9	-	-	-	-	-	-	-	-	+	-
10	-	+	+	+	-	-	+	-	+	-
11	+	+	+	+	-	+	+	+	+	-
12	+	+	+	+	-	-	+	-	+	-

Conclusion: US is comparable to FDG-PET/CT for LVV diagnosis. Although presence of US extra-cranial artery inflammation is consistent with FDG-PET/CT examination, a negative US scan does not rule out extracranial involvement. FDG-PET/CT is of limited value for assessing cranial arteries. Thus, US may be used as the first line investigation not only in suspected cranial, but also extracranial LVV.

Disclosure: J. Molina, None; **I. Castrejón**, None; **J. Rivera**, None; **J. Martínez Barrio**, None; **J. Nieto**, None; **K. López**, None; **F. Montero**, None; **L. Trives Folguera**, None; **C. González**, None; **J. Alvaro-Gracia**, None.

Abstract Number: 0152

Deep Learning-Derived Chest Radiograph Scores in COVID-19 in Rheumatic Disease Patients versus General Population Comparators

Naomi Patel[1], Kristin D'Silva[1], Matthew Li[1], Tiffany Hsu[2], Michael Di Iorio[3], Xiaoqing Fu[1], Claire Cook[4], Lauren Prisco[5], Lily Martin[6], Kathleen Vanni[6], Alessandra Zaccardelli[6], Yuqing Zhang[7], Jayashree Kalpathy-Cramer[1], Jeffrey Sparks[6] and Zachary Wallace[8], [1]Massachusetts General Hospital, Boston, MA, [2]Brigham and Women's Hospital, Jamaica Plain, MA, [3]Brigham and Women's Hospital, Brookline, MA, [4]Division of Rheumatology, Allergy, and Immunology, Mass General Hospital, Boston, MA, [5]Brigham and Women's Hospital, Pound Ridge, MA, [6]Brigham and Women's Hospital, Boston, MA, [7]Massachusetts General Hospital, Quincy, MA, [8]Massachusetts General Hospital, Newton, MA

SESSION INFORMATION

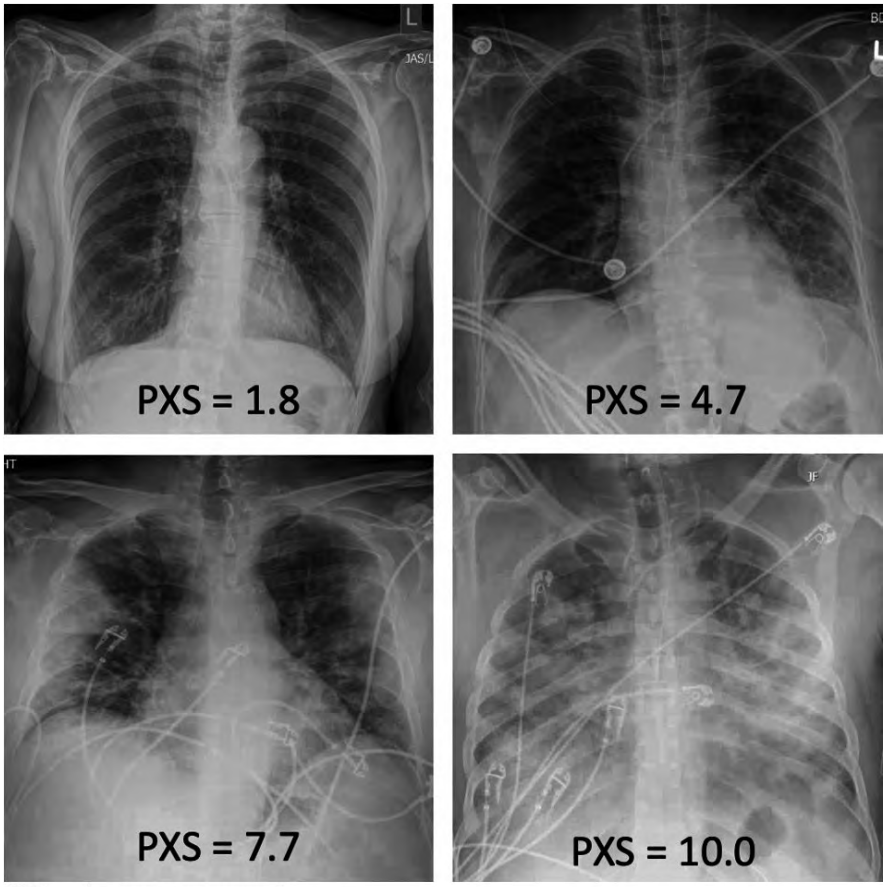
Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatic diseases and COVID-19 may have higher risk of mechanical ventilation than those without rheumatic diseases. We compared COVID-19 lung disease between rheumatic disease



PXS, pulmonary x-ray severity score.

Figure 1. Examples of chest radiographs from patients with COVID-19 and their associated Pulmonary X-ray Severity (PXS) scores.

Table 1. Clinical characteristics of COVID-19 patients with rheumatic disease and comparators without rheumatic disease who had chest radiographs performed

Characteristic	CD20 Inhibitor-Treated Cases (n=114)	Matched Comparators (n=559)	p-value
Age, years, mean ± SD	55 ± 15	54 ± 15	0.44
Female, n (%)	80 (70)	391 (70)	0.96
Race, n (%)			0.43
White	69 (61)	316 (57)	
Black or African American	16 (14)	70 (13)	
Asian	4 (4)	12 (2)	
Other	25 (22)	161 (29)	
Hispanic or Latinx ethnicity, n (%)	6 (5)	46 (8)	0.28
Body mass index, kg/m^2, mean ± SD	28.7 ± 6.2	29.7 ± 6.7	0.16
Smoking status, n (%)			0.06
Never	66 (58)	271 (48)	
Former	29 (25)	126 (23)	
Current	3 (3)	18 (3)	
Unknown	16 (14)	144 (26)	
Charlson Comorbidity Index, median (IQR)	1 (0, 2)	0 (0, 1)	0.001
Comorbidities, n (%)			
Hypertension	45 (39)	120 (21)	<0.0001
Diabetes	13 (11)	56 (10)	0.66
Coronary artery disease	8 (7)	21 (4)	0.12
Heart failure	8 (7)	11 (2)	0.003
Asthma	10 (9)	32 (6)	0.22
Chronic obstructive pulmonary disease	6 (5)	6 (1)	0.002
Obstructive sleep apnea	2 (2)	25 (4)	0.18
Chronic kidney disease	12 (11)	26 (5)	0.01

COVID-19, Coronavirus Disease 2019; SD, standard deviation; IQR, interquartile range.

Table 2. PXS scores from chest radiographs in rheumatic disease patients and matched comparators, using PXS scores from within 2 weeks before or after COVID-19 diagnosis.

	Rheumatic Disease Cases (n=70)	Comparators without Rheumatic Disease (n=463)	p-value
Total number of chest radiographs, N	206	936	
50th percentile PXS score	3.17	3.13	0.13
85th percentile PXS score	9.54	8.02	0.02
PXS score >9, n (%)*	14 (20)	49 (11)	0.02

PXS, pulmonary x-ray severity score.
*Based on the highest PXS score within ±2 weeks of COVID-19 diagnosis.

patients and general population comparators using a deep learning algorithm that extracts a quantitative measure of radiographic lung disease severity.

Methods: We performed a comparative cohort study of patients with rheumatic disease who had confirmed COVID-19 and at least one chest radiograph within ±2 weeks of COVID-19 diagnosis between January 31, 2020 and January 31, 2021 in a large healthcare system and comparators (matched up to 10:1 by age, sex, date of diagnosis, and chest radiograph location). Covariates and COVID-19 outcomes (mechanical ventilation and death) were ex-

tracted from a centralized data warehouse. A previously validated convolutional Siamese neural network algorithm was used to calculate the Pulmonary X-Ray Severity (PXS) score, a quantitative measure of COVID-19 lung severity. Higher scores indicate more severe pulmonary disease (Figure 1). We compared the PXS scores between rheumatic diseases cases and comparators using quantile regression at the 50th and 85th percentiles. We then evaluated the association of severe PXS score (>9) with risk of mechanical ventilation and death among patients with rheumatic diseases using logistic regression.

Results: We identified 70 rheumatic disease patients and 463 general population comparators. Rheumatic disease patients had more comorbidities such as hypertension (54% vs. 32%, p< 0.001), diabetes (31% vs. 15%, p< 0.001), and interstitial lung disease (6% vs. 1%, p< 0.01) (Table 1). The most common rheumatic diseases were rheumatoid arthritis (37%), other inflammatory arthritis (17%), and systemic lupus erythematosus (14%). The maximum PXS score within 2 weeks of COVID-19 diagnosis was similar in the rheumatic disease patients and comparators at the 50th percentile (3.17 vs. 3.13, respectively, p=0.10) but significantly higher among rheumatic disease patients at the 85th percentile (9.54 vs. 8.02, p=0.03) (Table 2). Rheumatic disease patients were more likely to have a maximum PXS score >9 (20% vs. 11%, p=0.02), indicating severe pulmonary disease. Among rheumatic disease patients, those with maximum PXS score >9 more frequently required mechanical ventilation (85% vs. 5%, p< 0.0001) and died (14% vs. 2%, p=0.08) compared to those with PXS score ≤9.

Conclusion: Using a previously validated deep learning algorithm, patients with rheumatic disease and COVID-19 had more severe radiographic lung disease than matched comparators. Among rheumatic disease patients, more severe radiographic disease was associated with higher risk of mechanical ventilation. Future studies are needed to determine if PXS scores may help to risk-stratify patients with rheumatic disease and COVID-19.

Disclosure: N. Patel, None; **K. D'Silva**, None; **M. Li**, None; **T. Hsu**, None; **M. Di Iorio**, None; **X. Fu**, None; **C. Cook**, None; **L. Prisco**, None; **L. Martin**, None; **K. Vanni**, None; **A. Zaccardelli**, None; **Y. Zhang**, None; **J. Kalpathy-Cramer**, GE Healthcare, 5, AWS, 12, Non-financial support, Genentech Foundation, 5; **J. Sparks**, Bristol-Myers Squibb, 2, 5, Amgen, 5, Gilead, 2, Inova, 2, Janssen, 2, Optum, 2, Pfizer, 2; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 0153

Echogenic and Hypervascular Synovium Detected on Ultrasound Are Predictive of a Favorable Response After Intra-articular Corticosteroid Injection in Patients with Knee Osteoarthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Intra-articular corticosteroids (IACS) are commonly used for symptom management in knee osteoarthritis (KOA) patients, despite the fact that many patients do not respond to this treatment. Knee inflammation (synovitis) is increasingly appreciated as an important factor in OA disease progression and pain, yet studies

Table 1. SD. standard deviation; WOMAC- Western Ontario and McMaster Universities Osteoarthritis Index; PGA- Patient Global Assessment rated by visual analogue scale 0-100; KL Grade- Kellgren-Lawrence Grade; ametabolic syndrome defined by the presence of at least 3 of: i) abdominal obesity waist circumference >102 cm in males and >88 cm in females ii) elevated triglycerides >1.7 mmol/L or medication for hypertriglyceridemia iii) Reduced HDL-C <1.0 mmol/L in males and <1.3 mmol/L in females or medication for reduced HDL-C iv) elevated blood pressure >130 mmHg systolic and/or >85mmHg diastolic or antihypertensive drug treatment in a patient with a history of hypertension v) elevated fasting plasma glucose >5.6 mmol/L or medication for hyperglycemia or A1c >6.5%

Table 1- Participant characteristics

Participants (number)	61
Knees (number)	98
Age (years) mean ± SD	63.5 ± 10.1
Male (number, %)	23, 37.7%
Metabolic syndrome[a] (number, %)	21, 34.4%
Baseline WOMAC pain (0-100) mean ± SD	37.3 ± 20.8
Baseline WOMAC function (0-100) mean ± SD	37.6 ± 20.4
Baseline PGA (0-100) mean ± SD	49.4 ± 24.4
KL Grade (number)	
0	11
1	23
2	28
2/osteophyte	3
3	30
4	3
Synovitis Phenotype (number)	
Type A	61
Type B	31
Type C	6

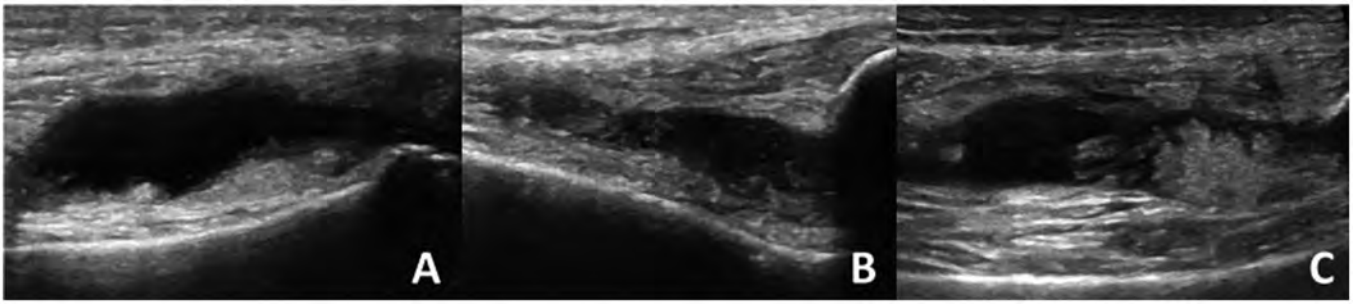

Figure 1. A: Type A synovitis is characterized by a synovial volume predominantly composed of anechoic material (synovial fluid). Little to no circumferential synovial thickening is seen. B: Type B synovitis includes a significant intra-articular abnormal solid component of inflamed synovium which is primarily characterized by low-level echoes. C: In Type C synovitis, inflammation is accompanied by a significant intra-articular solid component of synovium characterized by high level echoes with or without nodular appearance (fronding).

have failed to find any features of inflammation measured by ultrasound (US) that are associated with pain/function response. Our objective is to test whether nuanced features of sonographically-detected inflammation including synovial tissue quality and synovial vascularity are associated with response after IACS.

Methods: KOA patients presenting to a rheumatology center for regular follow up and steroid injection were administered a standardized US and completed patient surveys prior to injection. Using random-effects linear and logistic models, baseline US features were tested for association with improvement in pain, function, patient-reported global assessment (PGA) of disease activity, and OARSI-OMERACT-defined responder status 18-28 days after IACS injection.

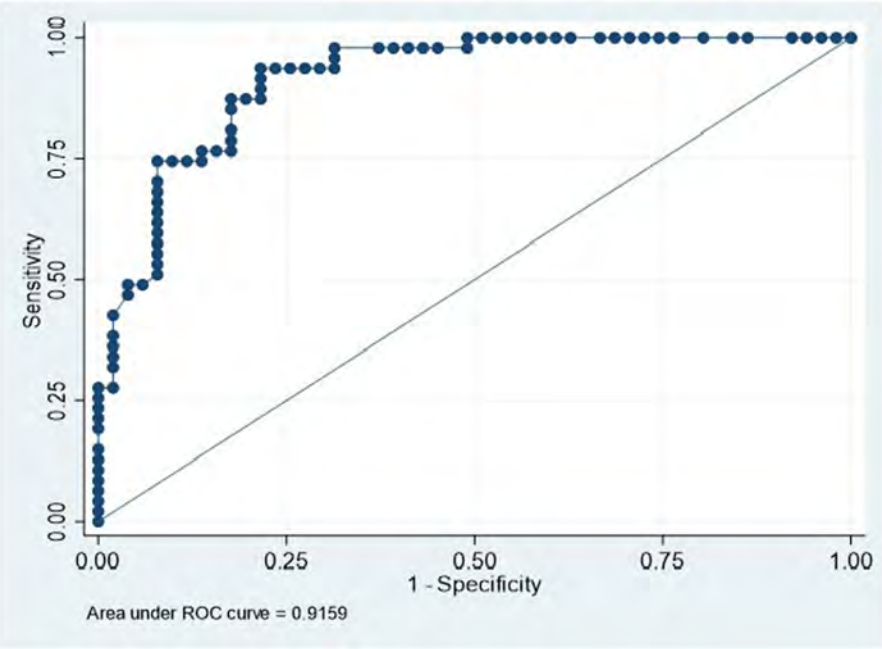

Figure 3. Baseline WOMAC pain and radiographic severity defined as KL grade 3 or 4 (model 1) discriminate between OARSI-OMERACT response with an AUC of 0.9159. With a cut-off probability of P(y)=0.5964, 83.67% of patients are correctly classified into responders or non-responders (sensitivity 74.47% specificity 92.16%).

Results: Individuals with echogenic synovium and positive Power Doppler (PD) signal have an improved response to pain (β= 14.500 & 7.655, respectively) and function (β= 11.677 & β= 7.650, respectively) after IACS. Patients with metabolic syndrome have as much as a 30% reduced response to IACS as measured by PGA of disease activity. Only baseline pain (OR= 1.042) and radiographic severity (OR= 5.282) were associated with OARSI-OMERACT-defined response.

Conclusion: Inflammation is not homogeneous across KOA patients, and response to IACS injections depends on baseline symptoms, the phenotype of synovitis, the presence of blood flow within synovium, and baseline radiographic severity.

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Abstract Number: 0154

Utilization of Magnetic Resonance Imaging in Early Rheumatoid Arthritis: Results from a Population-based Cohort (1999-2014)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
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Background/Purpose: Early diagnosis and treatment initiation improve outcomes for patients with rheumatoid arthritis (RA). Delays to diagnosis and treatment affect patients with seronegative vs seropositive RA disproportionately. Magnetic resonance imaging (MRI) is superior to clinical examination for detecting synovitis in patients with RA and can predict progression to clinical RA from undifferentiated arthritis. We hypothesized that MRI utilization is higher in seronegative vs seropositive patients with early RA, and is increasing over time in recent years.

Methods: A retrospective study was performed of a population-based cohort of patients with incident RA between 1999-2014 who fulfilled either the 1987 or 2010 ACR/EULAR classification criteria. Patients who underwent MRI within (+/-) 1 year of fulfillment of the earlier of either classification criteria for RA were identified using Current Procedural Terminology codes corresponding to MRI studies of the extremities (hand, wrist, elbow, shoulder, foot, ankle, knee, hip). Studies were confirmed via manual chart review. MRIs performed for indications unrelated to arthritis were excluded. MRI utilization was compared between seropositive (RF+ and/or CCP+) and seronegative (RF-, CCP-) patients. Factors associated with undergoing MRI within one year of meeting criteria were analyzed. Comparisons between groups were made using Kruskal-Wallis and Chi-square tests. Utilization of MRI over time was evaluated with a test for trend.

Results: 789 patients with incident RA who fulfilled 1987 and/or 2010 ACR/EULAR classification criteria for RA were included. Of these, 554 (70%) were female, 709 (90%) Caucasian, 534 (68%) RF and/or CCP positive, mean age 55.9 (SD 15.2) at time of meeting criteria. At least one MRI was performed within one year of fulfilling criteria in 165 (21%) of patients over the study interval. Age, sex, race/ethnicity, and smoking status did not differ between groups who did and did not undergo MRI.

RF and CCP autoantibodies were negative in 77 (47%) of those who underwent MRI, versus 178 (29%) who did not ($p< 0.001$). At time of meeting classification criteria, presence of morning stiffness rheumatoid nodules, erosive disease, and abnormal sedimentation rate or C-reactive protein were similar among patients who did and did not undergo MRI. Patients with symptom duration ≥ 6 weeks (64% vs. 46%, $p< 0.001$) and involvement of 4-10 (22% vs. 13%) small joints or >10 (39% vs. 30%) joints ($p< 0.001$) were more likely to have an MRI performed. Prevalence of obesity (BMI ≥ 30 kg/m^2) was similar between MRI (45%) and no MRI (39%) ($p=0.18$) groups.

The median year of fulfilling RA criteria was later in the MRI (2010; IQR 2005-2013) vs no MRI (2008; IQR 2003-2011) ($p< 0.001$) groups. MRI utilization overall increased over time by 9% per calendar year (OR:1.09; 95% CI: 1.05-1.14; $p< 0.001$).

Conclusion: In this population-based cohort of patients with incident RA, MRI was used for evaluation of arthritis within one year of fulfilling classification criteria in 21% of patients. MRI was more commonly used in seronegative than seropositive patients, which may reflect diagnostic uncertainty in the seronegative group. MRI utilization increased over time during the 15-year study interval.

Disclosure: C. Coffey, None; **C. Crowson**, None; **C. Hulshizer**, None; **G. McKenzie**, None; **N. Rhodes**, None; **J. Davis**, Pfizer, 5; **K. Wright**, None.

Abstract Number: 0155

The Additional Value of MRI in Diagnosis of Rheumatoid Arthritis in Undifferentiated Arthritis Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Identifying patients that will develop rheumatoid arthritis (RA) among those presenting with undifferentiated arthritis (UA) remains a clinical dilemma. According to EULAR recommendations magnetic resonance imaging (MRI) is helpful. An important limitation is that UA is not uniformly characterized. UA is formally defined as not fulfilling RA classification criteria (1987- or 2010-criteria). In clinical practice, rheumatologists identify UA based on clinical expertise. The diagnostic value of MRI has only been determined in UA-patients not fulfilling the 1987-criteria. The data on the value of MRI in UA according to the two common and current definitions is lacking. Therefore, we performed a large study to determine this.

Methods: In total 1234 patients, consecutively included in the Leiden early-arthritis cohort (EAC) between august-2010 and march-2020 underwent MRI-scans of hand and foot, that were scored for erosions, bone marrow edema (BME), synovitis (SYN) and tenosynovitis (TS). Two UA-populations were studied: not fulfilling 1987/2010-criteria and having no other diagnosis (criteria-based UA-population, n=405), and expert-opinion of UA (n=564). Patients were followed up for RA-development (fulfilling 1987/2010-criteria) after 1-year. Logistic regression was used, test characteristics and predictive values were determined, also in clinically-relevant subgroups.

Results: Within criteria-based UA-patients, 21% developed RA. Except for BME, all MRI-features were prognostic for RA-development. Only MRI-TS was independently associated with RA-development (OR 2.79, 95% CI: 1.40-5.58), especially within ACPA-negative UA-patients (OR 2.91; 1.42-5.96). Particularly within the oligoarthritis-subgroup, MRI-TS was predictive for RA-development (NPV 93%; PPV 28%; sensitivity 85%; specificity 45%). Compared with oligo-/polyarthritis alone, MRI-TS improved prediction of RA-development within the oligoarthritis-subgroup (Net Reclassification Index 0.28). Similar results were found in the expert opinion UA-population.

Conclusion: This large cohort study showed MRI has additional prognostic value for early identification of RA. The value was highest within ACPA-negative UA-patients with oligoarthritis. Although cost-effectiveness remains to be determined, this shows MRI is useful for early recognition of RA in subgroups of UA-patients.

Disclosure: N. den Hollander, None; **M. Verstappen**, None; **N. Sidhu**, None; **E. van Mulligen**, None; **M. Reijnierse**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0156

Tenosynovitis Detected by Power Doppler Ultrasound: A Differential Feature of Patients with Seronegative Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Background/Purpose: It is known that seronegative rheumatoid arthritis has different characteristics from seropositive RA. Objectives: To estimate the frequency of rheumatoid arthritis (RA) in a cohort of patients who consulted for polyarthralgia, including arthralgia of the hands, and to identify differential features, at diagnosis, between patients with seropositive RA and seronegative RA.

Methods: Prospective cohort study, which included patients over 18 years of age who were admitted for polyarthralgia, including hand arthralgias, to the ¨Reuma-check¨® program from August 2017 to March 2020. In this program, in the first visit (baseline) was performed: laboratory studies (including acute phase reactants, RF and anti-CCP), X-rays of hands and feet, ultrasound of hands with power Doppler technique (22 joints: wrists, MCFs and IFPs bilaterally and 20 tendons: 6 carpal extensor compartments and flexor tendons of 2nd to 5th fingers bilaterally) and interview where sociodemographic data (age, sex), clinical data (time of evolution of arthralgias, comorbidities) and clinimetry

Table 1. Characteristics of patients with a final diagnosis of RA.

	Rheumatoid arthritis, n: 128
Age (years), mean (SD)	56.6 (14.2)
Female, n (%)	90 (70.3)
Smoking, n (%)	54 (42.1)
Patient global VAS (0-100), mean (SD)	55.7 (18.1)
Tender joints (28), mean (SD)	5.3 (3.2)
Swollen joints (28), mean (SD)	1.9 (2.7)
CDAI, mean (SD)	17.7 (8)
DAS28-ERS, mean (SD)	4.2 (1.1)
HAQ, mean (SD)	0.8 (0.4)
RF, n (%)	83 (64.8)
Anti-CCP, n (%)	51 (39.8)
ESR, mean (SD)	29.8 (24.7)
CRP, mean (SD)	9.7 (19.8)
X-ray bone erosions, n (%)	23 (17.9)
Ultrasound tenosynovitis with positive power Doppler signal, n (%)	21 (16.4)
Ultrasound synovitis with positive power Doppler signal, n (%)	37 (28.9)
Median months from symptom onset to diagnosis (IQR)	12 (4,7-36)

Table 2. Comparison of the different features between patients with seropositive RA and seronegative RA.

	Seropositive RA, n: 87	Seronegative RA, n: 41	p value
Age (years), mean (SD)	56.4 (13.7)	57 (15.5)	0.84
Female, n (%)	70.1	70.7	0.94
Smoking, n (%)	54.4	44	0.36
Patient global VAS (0-100), mean (SD)	54.9 (17.4)	58.7 (21.2)	0.54
Tender joints (28), mean (SD)	5 (3.3)	6.3 (2.9)	0.08
Swollen joints (28), mean (SD)	1.9 (2.9)	2.2 (2.1)	0.65
CDAI, mean (SD)	17.1 (8.3)	19.7 (6.8)	0.16
DAS28-ERS, mean (SD)	4.1 (1.1)	4.5 (1.1)	0.16
HAQ, mean (SD)	0.8 (0.4)	0.9 (0.4)	0.23
ESR, mean (SD)	30.8 (25)	26.3 (23.6)	0.41
CRP, mean SD)	9.9 (21)	8.9 (15.5)	0.81
X-ray bone erosions, n (%)	22.7	20	0.77
Ultrasound tenosynovitis with positive power Doppler signal, n (%)	13.7	41.6	0.0028
Ultrasound synovitis with positive power Doppler signal, n (%)	34.9	32	0.78

(Global VAS of the patient, joint count, HAQ); each evaluator (laboratory, imaging and clinical) did not know the data of the other studies carried out. In subsequent visits (only patients who completed at least 2 visits were included), the results were evaluated, and the definitive diagnosis of RA was established or not according to the ACR / EULAR 2010 classification criteria. It was considered as seronegative RA when the patients were negative for both RF and anti-CCP.

Statistical analysis: descriptive statistics, Chi2 test, Fisher's exact test, Student's T-test and Mann Whitney were performed.

Results: A total of 746 (74.4% female and mean age 53.6 years, SD: 14.5) patients with polyarthralgia, including hand arthralgias, were included, of which 128 (17.1%, 95% CI: 14.6- 20) ended with a final diagnosis of RA (Table 1). Of these 128 patients, 87 (67.9%) were seropositive (RF and/or anti-CCP positive), while 41 (32%) were seronegative (RF and anti-CCP negative).

Table 2 shows a comparison of the different features between patients with seropositive RA and seronegative RA. The only feature that showed significant differences was the presence of tenosynovitis detected by ultrasound with a positive power Doppler signal, 13.7% of the patients with seropositive RA vs 41.6% of the patients with seronegative RA ($p = 0.0028$).

Conclusion: The frequency of RA in our cohort of patients with polyarthralgia, including hand arthralgias, was 17.1% and the only differential feature of patients with seronegative RA was the higher proportion of tenosynovitis detected by ultrasound with a positive power Doppler signal in comparison with patients with seropositive RA.

Disclosure: E. Sanchez Prado, None; **S. Ruta**, None; **L. Cuellar**, None; **S. Magri**, None; **R. Garcia Salinas**, None.

Abstract Number: 0157

Development of a Deep Learning Algorithm for the Detection of Sacroiliitis on MRI in Patients with Active Axial Spondyloarthritis

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SESSION INFORMATION

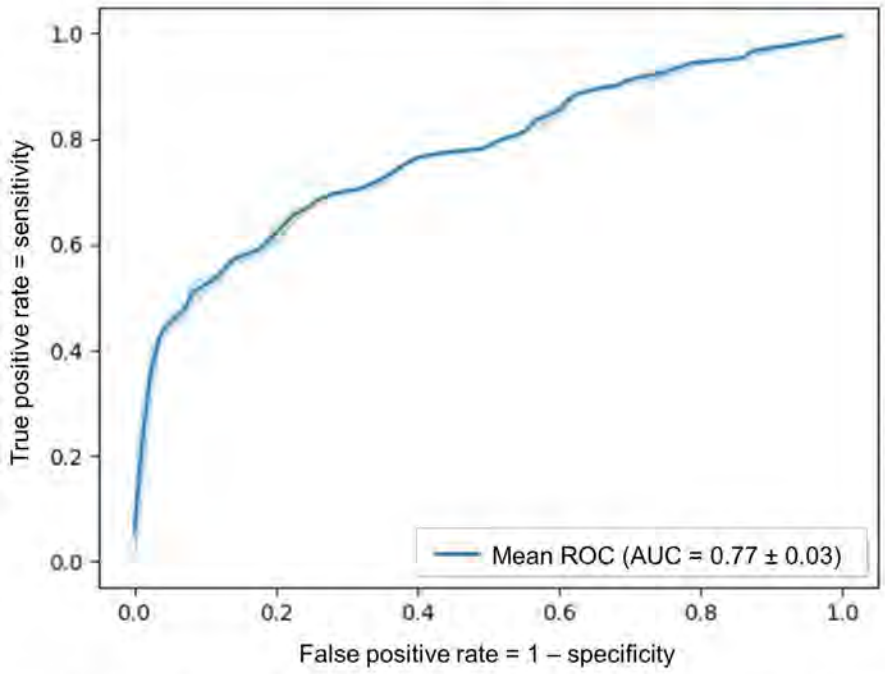
Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Figure 1. Case-level BME lesion detection ROC curve for the 7-fold cross-validation experiment: bootstrapped (n=1000) ROC curve of our method



Mean is shown in dark blue, with ± 1SD shaded in lighter blue. AUC: area under curve; BME: bone marrow edema; ROC: receiver operating characteristic; SD: standard deviation.

Background/Purpose: Magnetic resonance imaging (MRI) plays a critical role in assisting the diagnosis of axial spondyloarthritis (axSpA). There are many characteristic MRI lesions that can be present in patients with axSpA; these have been well characterized in the literature,[1] and, alongside clinical presentation and laboratory features, can be used to assist diagnosis. However, in-depth knowledge of these lesions and their definitions, as well as reliability of identification and scoring, varies amongst general radiologists and rheumatologists.[2] The use of artificial intelligence to develop automated recognition of MRI lesions associated with axSpA has the potential to vastly improve diagnosis of this condition. We present a data-driven approach to automatically detect sacroiliitis on MRI.

Methods: We built a training database of de-identified sacroiliac joint (SIJ) MRI scans containing short tau inversion recovery (STIR) and T1 sequences acquired on 12 scanner models from three vendors (50% Siemens, 46% GE and 4% Philips). This dataset contains baseline MRI images from 202 patients (mean age: 38 years [range: 18–74]; 52% male) scanned at 34 clinical sites in 7 countries (97% from Europe) from interventional studies in patients with axSpA (C-axSpAnd [NCT02552212], BE MOBILE 1 [NCT03928704] and BE MOBILE 2 [NCT03928743]). 85% of the images were from patients with non-radiographic axSpA. Informed consent was collected from all patients for these studies. Three expert readers independently and manually delineated bone marrow edema (BME) lesions in a subset of cases. A positive case was defined as a patient with one or more BME lesions. We developed a two-stage lesion detection pipeline: firstly, a deep learning model binary classified each voxel present in the 3D image as either a normal or BME lesion (mimicking the reader's delineations); secondly, this voxel-level information was aggregated to a binary case-level prediction (positive if one or more BME lesions were predicted). The time to read one patient was < 0.5 min. We then performed a stratified 7-fold cross-validation experiment comparing the automated predictions with ground truth read-outs from the readers.

Results: A total of 280 lesions in 116 BME-positive patients were identified. The presented method achieved case-level BME lesion detection results of 77% area under the receiver operating characteristic (ROC) curve (95% confidence interval [CI]: 71% to 83%; Figure 1), 74% specificity (95% CI: 64% to 83%), 70% sensitivity (95% CI: 62% to 78%) and 79% precision (95% CI: 71% to 86%).

Conclusion: Using MRI images from 202 patients, our automated method achieved robust case-level BME lesion detection results. This methodology has the potential to support radiologists and rheumatologists in detecting BME lesions on MRI scans to aid early and accurate diagnosis of axSpA. Further investigations, including confirmatory analyses and methodological improvements and validation, are warranted.

References: 1.Maksymowych WP. Ann Rheum Dis 2019; 78: 1550–58; 2. Bennett AN. J Rheumatol 2017; 44: 780–5.

Disclosure: J. Nicolaes, UCB Pharma, 3; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **M. Santosh**, UCB Pharma, 3; **A. Carnell**, UCB Pharma, 7; **N. de Peyrecave**, UCB Pharma, 3, 11; **A. Bennett**, None.

Abstract Number: 0158

The Influence of Age on the Prevalence of Inflammatory and Post-inflammatory MRI Lesions in the Sacroiliac Joints of Patients with and Without Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Background/Purpose: Axial spondyloarthritis (axSpA) is clinically characterized by chronic inflammatory back pain and by inflammatory and structural changes in the sacroiliac joint (SIJ) as assessed by magnetic resonance imaging (MRI). Several studies have reported high rates of bone marrow edema (BME) suggestive of inflammatory SIJ changes in up to 20% of individuals in the general population < 45 years. An update of the definition of a positive MRI of the SIJ in axSpA for classification purposes, based on the number of slices or quadrants showing BME or structural changes such as erosions or fat lesions (FL), was recently published by ASAS. The aim of this study is to compare the influence of age on the prevalence of inflammatory and structural MRI changes in the SIJ of patients with chronic low back pain diagnosed with axSpA or non-SpA.

Methods: MRIs of the SIJ of patients referred for differential diagnosis of back pain who were finally diagnosed with axSpA or not by experienced rheumatologists, were evaluated using semi-coronal STIR and T1-weighted MRI sequences. All images were scored blinded to, age, sex and diagnosis for the occurrence of BME, FL, erosions and

Table. Comparison of MRI findings between axSpA and non-SpA patients at different age groups

Age subgroup	Diagnosis	Mean number of SIJ quadrants			Proportion of patients with...		
		BME	FL	Erosion	BME	FL	Erosion
until 29 years	axSpA (n=46)	6.0±3.7	6.8±5.7	4.4±3.8	95.7%	80.4%	89.1%
	non-SpA (n=25)	1.4±1.5	5.4±4.4	0.8±1.5	64,0%	76,0%	48,0%
	p-value	*<0.001*	*0.311*	*<0.001*	*<0.001*	*0.664*	*<0.001*
30-39 years	axSpA (n=50)	5.0±4.1	8.7±5.9	4.6±3.7	92,0%	98,0%	82,0%
	non-SpA (n=26)	1.0±1.3	9.5±6.0	1.1±1.3	46.2%	92.3%	53.8%
	p-value	*<0.001*	*0.485*	*<0.001*	*<0.001*	*0.23*	*0.01*
40-49 years	axSpA (n=47)	4.2±3.7	11.3±6.0	4.6±3.7	85.1%	97.9%	87.2%
	non-SpA (n=35)	1.4±2.9	10.3±5.8	1.6±2.4	34.3%	97.1%	62.9%
	p-value	*<0.001*	*0.413*	*<0.001*	*<0.001*	*0.833*	*0.010*
≥50 years	axSpA (n=32)	5.2±4.9	16.4±5.4	5.5±4.1	87.5%	100,0%	87.5%
	non-SpA (n=48)	1.9±2.1	13.4±4.5	2.0±2.0	66.7%	100%	72.9%
	p-value	*0.001*	*0.006*	*<0.001*	*0.036*	*1,000*	*0.121*

ankylosis on the level of SIJ-quadrants (SIJ-Q). Patient groups were built based on decade of age (until 29, 30-39, 40-49 and ≥50 years).

Results: A total of 309 patients (175 axSpA and 134 non-SpA) with complete MRI sets were included in the analysis. The mean age was 38.5±11.4 and 43.4±13.8, 66.9% and 35.8% were male, the mean CRP was 1.6±2.4 and 1.1±2.1mg/dl and the median back pain symptom duration was 48 and 60 months, respectively. The number of SIJ-Q with BME and erosions was significantly higher in axSpA vs. non-SpA independent of the age group (Table). In comparison, with exception of the patients in the oldest population (≥50 years), the number of SIJ-Q with FL and the number of patients with at least one FL was not different between subgroups, while the number of erosions and FL but not BME was higher in both groups with increasing age. In the univariate analysis, only female sex was significantly associated with higher occurrence of FL.

Conclusion: Despite a relatively high prevalence in non-SpA patients, BME and erosions were significantly more frequent in axSpA independent of age, while the presence of FL was not different between groups. FL and erosions are increasingly found in older age groups independent of diagnosis. These data are relevant for the interpretation of MRI findings in the SIJ of patients suspicious of axSpA.

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Abstract Number: 0159

Structural Damage in Axial Spondyloarthritis: Is There a Preferred Way to Assess Progression over Time?

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Session Time: 8:30AM–10:30AM

Background/Purpose: The aim of this study is to investigate the performance of the modified Stokes Ankylosing Spondylitis Scoring System (mSASSS) in assessing spinal radiographic damage and progression in axial spondyloarthritis (axSpA) using different approaches of radiographs (CR) evaluations.

Methods: Complete sets of cervical and lumbar CRs of patients with axSpA from the German SpA Inception Cohort (GESPIC) at baseline and after 2 years were first blinded to all clinical and demographic characteristics and then

scored using the mSASSS by 5 different experienced readers, 2 blinded and 3 unblinded to the timepoint of CR performance. The final mSASSS score was calculated as a mean of 2 (blinded) or 3 (unblinded exercise) readers. Descriptive statistics, cumulative probability plots and shift analyses *(agreement of 2/2 readers in the blinded group and 2/3 readers in the unblinded group on the level of single vertebral edges)* were performed for each reader group.

Results: A total of 210 patients (mean age 37.3 years, 51% male, 79% HLA-B27 positive) with axSpA (115 radiographic and 95 non-radiographic at baseline) were included. The mean mSASSS score at baseline was 4.3±8.3 vs. 3.4±7.9, while the mean radiographic progression was 0.7±2.3 vs.1.0±1.9 mSASSS units for the blinded vs. the unblinded group, respectively (Figure). On the patient level, progression of ≥2 mSASSS units was found in 30 (14.3%) vs. 37 (17.6%) patients in the blinded vs. the unblinded group, while agreement between both groups was seen in 179 (85.2%) patients, 18 (8.9%) patients for progression and 161 (76.7%) for no progression.

In a more specific analysis of 'definite' CR findings (only scores of 2 for syndesmophytes or 3 for ankylosis), the mean mSASSS score at baseline was 3.3±8.0 vs. 2.6±7.2 and the mean radiographic progression was 0.6±2.4 vs. 0.8±2.1 mSASSS units for the blinded vs. the unblinded group, respectively. On the patient level, progression was found in 37 (17.6%) vs. 33 (15.7%) patients in the blinded vs. the unblinded group, while agreement between groups was seen in 188 (89.5%) patients, 24 (11.3%) for progression and in 164 (78.1%) patients for no progression.

In the shift analysis, mSASSS worsening was found in 35 (0.8%) and mSASSS 'improvement' in only 4 (0.1%) out of the total of 4.373 vertebral edges analyzed in the blinded group and in 109 (2.2%) and 2 (0.04%), respectively, out of the total of 4.914 vertebral edges analyzed in the unblinded group (Table). The majority of progression was found for the development of 'definite' signs of progression (development of syndesmophytes or ankylosis) in both the blinded (25/35, 71.4%) and the unblinded (61/109, 56%) group, while more vertebral edges showing 'minor' signs of progression (no syndesmophytes or ankylosis) were found in the unblinded (48/109, 44%) as compared to the blinded (10/25, 28.6%) group.

Blinded reading						
mSASS Scores		2-year follow-up				Total
		0	1	2	3	
Baseline	0	4.166	10	8	9	4.193
	1	0	29	4	0	33
	2	3	1	48	4	56
	3	0	0	0	92	92
Total		4.169	40	60	105	4.374

Unblinded reading						
mSASS Scores		2-year follow-up				Total
		0	1	2	3	
Baseline	0	4.575	48	14	3	4.640
	1	1	75	16	8	100
	2	0	0	69	20	89
	3	0	1	0	84	85
Total		4.576	124	99	115	4.914

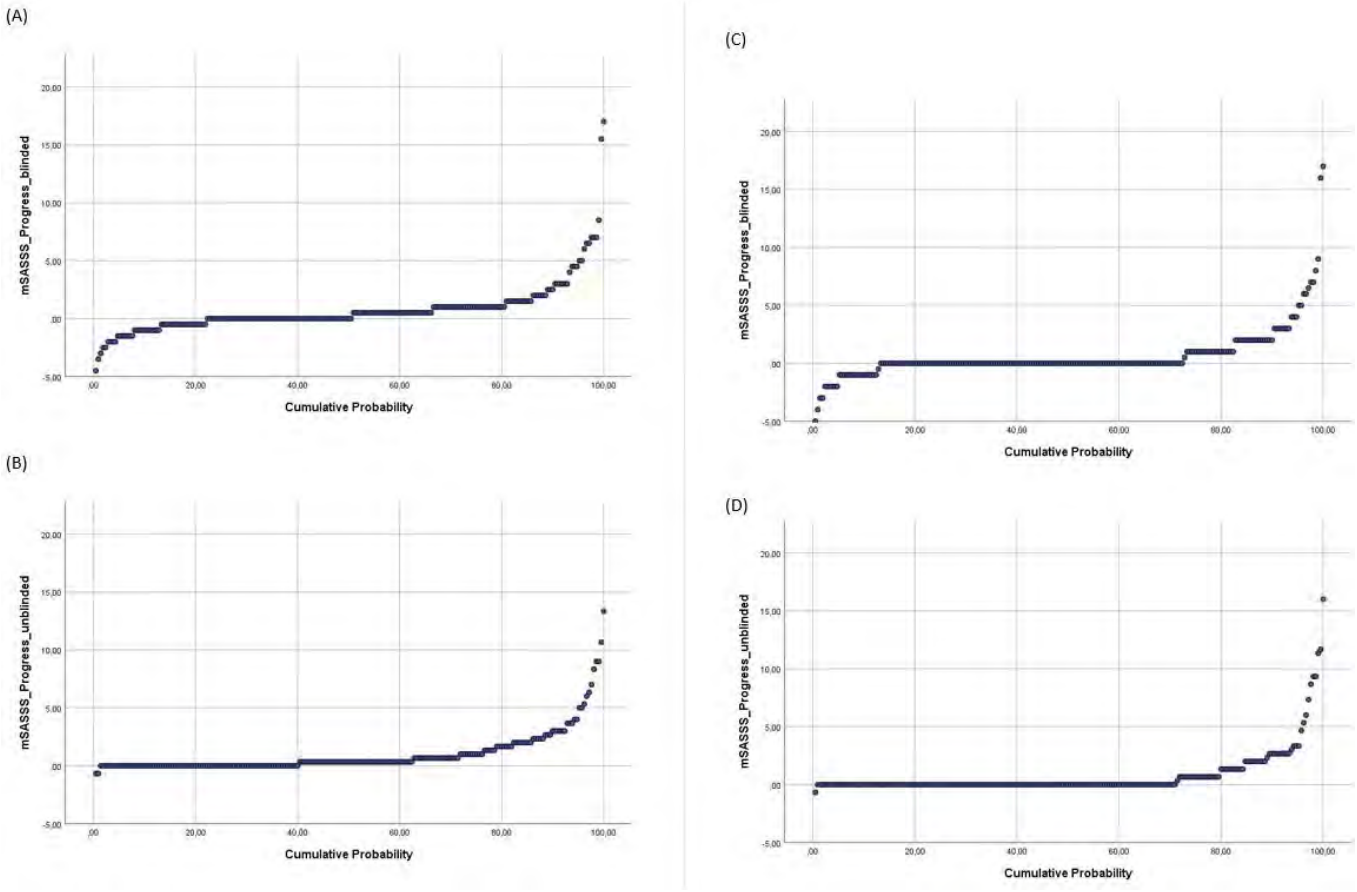

Figure. Cumulative probability plot for mean mSASSS scores for all scores in a blinded (A) and unblinded (B) scoring approach and for 'definite' scores in a blinded (C) and unblinded (D) scoring approach

Conclusion: Despite lower mean mSASSS baseline values, higher mean mSASSS progression was found with the unblinded approach, while in the shift analysis this approach was more specific, confirming the absence of 'improvement' over time.

Disclosure: X. Baraliakos, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **V. Rios Rodriguez**, None; **M. Torgutalp**, None; **A. Dilbaryan**, None; **H. Haibel**, Boehringer, 2, Janssen, 2, 6, MSD, 2, 6, Pfizer, 6, Novartis, 2, Roche, 2, 6, AbbVie, 6; **M. Verba**, None; **J. Sieper**, AbbVie, 2, 5, 6, Merck, 2, 5, 6, Pfizer, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6, Roche, 2, 6; **J. Braun**, Abbvie, 2, 5, 6, Amgen, 2, 5, 6, Celltrion, 2, 5, 6, Chugai, 2, 5, 6, Medac, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, BMS, 2, 5, 6, Boehringer, 2, 5, 6, Celgene, 2, 5, 6, Centocor, 2, 5, 6, Mundipharma, 2, 5, 6, Sanofi-Aventis, 2, 5, 6, Eli Lilly, 2, 5, 6, EBEWE Pharma, 2, 6; **M. Rudwaleit**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, UCB Pharma, 2, AbbVie, 6, Eli Lilly, 6, Novartis, 6, Novartis, 2, UCB Pharma, 6; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6.

Abstract Number: 0160

Identifying Erosive Disease from Radiology Reports of Veterans with Inflammatory Arthritis with Natural Language Processing

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Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The presence of erosive disease influences diagnosis, management, & prognosis in inflammatory arthritis (IA). Inflammatory arthritis research in large datasets is limited by a lack of methods for identifying erosions.

The aim of our project was to develop methods for identifying articular erosions in radiology reports from veterans with IA.

Methods: Included veterans had ≥2 ICD codes for ankylosing spondylitis (AS), psoriatic arthritis (PsA), or rheumatoid arthritis (RA) between 2005- 2019, in Veterans Affairs Corporate Data Warehouse. Chart review & annotation of radiology notes produced the reference standard, & identified erosion terms that informed classification rule development. A rule-based natural language processing (NLP) model was created & revised in training snippets. The NLP method was validated in an independent reference sample of IA patients at the snippet & patient levels.

Results: In 168,667 veterans with inflammatory arthritis, the mean age was 63.1 & 90.3% were male. Method development involved radiology note & erosion term selection, rule development, NLP model building, & method validation. The NLP model accuracy was more than 95% at the snippet level & 90.0% at the patient level, for all IA patients.

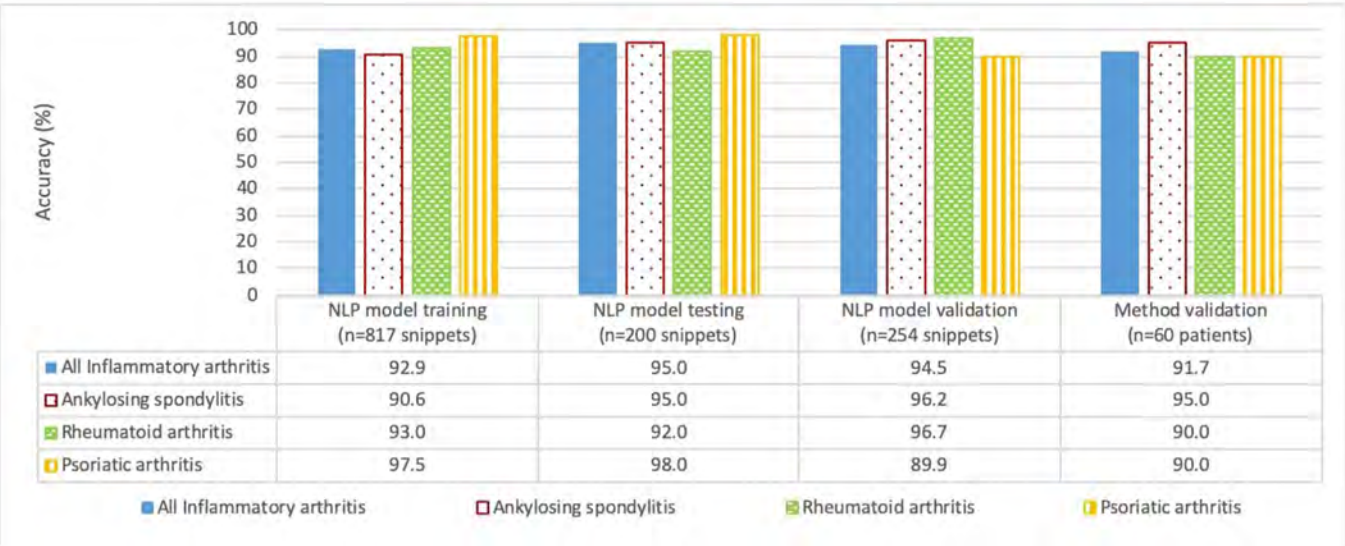
Conclusion: The methods accurately identify erosions from radiology reports of veterans with inflammatory arthritis. They may facilitate a broad range of research involving cohort identification & disease severity stratification.

Step	Description	Number & example
1 Radiology notes	a. Select note titles potentially relevant to IA b. Extract notes with titles potentially related to IA	a. 35,141 notes titles b. 2,926,113 radiology notes
2 Possible meaningful terms	a. Compile list of root terms that may indicate erosion b. Query radiology notes for root term variations c. Select possible meaningful terms	a. 11 root terms (i.e. ero*, pencil*cup, irreg*) b. 1178 variations (i.e. erosion, erotic, erode) c. 179 possible terms (i.e. erosion, erode)
3 Annotation	a. Extract snippets^ containing possible meaningful terms b. Classify snippets according to: 1) Meaningful term, 2) Relevance to joint, 3) Attribution to IA, 4) Affirmation	a. 5000 snippets from radiology notes b. 4068 classifications with 1017 snippets (in rounds of 50-417 snippets for NLP training & testing)
4 Rule development	a. Identify meaningful terms representing erosion b. Exclude erosive processes irrelevant to joint(s) c. Exclude articular erosive processes not attributed to IA d. Classify as affirmed/negated (erosion present/absent)	a. 6 terms (pencil * cup, erosion, erosive, etc.) b. 28 irrelevant processes (i.e. gastric erosion) c. 5 non-IA processes IA (i.e. infection) d. 83 affirmation/negation rules
5 NLP training	Design & revise NLP model until accuracy ≥90%	6 rounds, 817 snippets (AS 417, RA 200, PsA 200)
6 NLP testing	Test NLP model	200 snippets (AS 100, RA 50, PsA 50)
7 Pt classification	a. Develop rules for classifying pts with discordant snippets b. Build reference sample (pts classified as erosive or non-erosive via chart review)	a. 5 rules developed in 368 pts b. 30 IA pts (10 AS, 10 RA, 10 PsA)
8 NLP validation	Validate NLP model in reference sample at snippet level	149 snippets (29 AS, 76 RA, 44 PsA)
9 Method validation	Validate methods (NLP+pt classification) at pt level	30 IA pts (reference sample)

pt= patient. ^Snippets include text containing 30 words before & after meaningful terms

	Training & testing (n=1017 patients)		****Validation in independent population (n=60 patients)**	
	NLP model training (n=817 snippets)	NLP model testing (n=200 snippets)	NLP model validation (n=254 snippets)	Method validation (n=60 patients)
All Inflammatory arthritis	92.9	95.0	94.5	91.7
Ankylosing spondylitis	90.6	95.0	96.2	95.0
Rheumatoid arthritis	93.0	92.0	96.7	90.0
Psoriatic arthritis	97.5	98.0	89.9	90.0

Patient level classifications involve assigning rules for classifying patients with conflicting snippet classifications (in subset of patients with >1 snippet) **Included 20 RA patients, 20 PsA patients, 20 AS patients.



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Psoriatic arthritis	97.5	98.0	89.9	90.0

Accuracy of the NLP methods

Disclosure: G. Penmetsa, None; **J. Walsh**, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5; **S. Pei**, None; **B. Sauer**, Abbvie, 12, I have been an investigator on research contracts supported by Abbvie.; **K. Douglas**, AbbVie, 3, 11; **J. Walker**, Abbvie, 3; **J. Clewell**, Abbvie Inc, 3, 11; **B. Feng**, Ambry Genetics, 9, Pfizer, 5, Regeneron, 5, Astra Zeneca, 5.

Abstract Number: 0161

Does ^{18}F-FDG-PET/MRI Add Metabolic Information to Anatomic Image in Childhood-onset Takayasu's Arteritis Patients? A Multicenter Case Series

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The disease activity assessment in c-TA is a challenge in clinical practice, especially in patients who are under immunosuppression. Our aim was to perform comparison between positron emission tomography (PET) and magnetic resonance angiography (MRA) findings in childhood-onset Takayasu's arteritis (c-TA) patients.

Methods: A three-center cross-sectional study with 17 children and adolescents who fulfilled the EULAR/PRINTO/PReS criteria for c-TA was conducted. The patients underwent ^{18}F-FDG-PET/MRI imaging (SIGMA^{TM} PET/MR, GE Healthcare, Milwakee-MI, USA). Positive MRA consisted of arterial wall thickening with contrast-enhancement, whereas positive PET was defined as arterial wall uptake higher than the normal liver degree of FDG uptake. Patients were divided in three groups according to the different combinations of imaging findings as following: group 1 (PET+MRA+), group 2 (PET+MRA-) and group 3 (PET-MRA+).

Results: Seventeen c-TA patients (65% female) were included. Mean disease duration was nine ±3.6 years. PET identified high-grade ^{18}F-FDG arterial wall uptake in 15 (88.2%) patients and MRA detected thickening with contrast-enhancement in 10 (58.8%). Nine patients were classified as group 1, six as group 2 and 1 as group 3. One patient had no vessel-wall changes in both images. Median of metabolic inflammatory volume (MIV) value was significantly higher in group 1 compared to group 2 (2346 vs. 1177 cm^3; p=0.036) (Table 1). Fifty-four (19%) from 284 available arterial segments presented vessel-wall changes in one or both imaging. Positive PET was found in 35 (12.3%) and positive MRA in 26 (9.2%) vessels (Table 2). Positive findings in vessel-wall were concordant between PET and MRA exams in seven (2.5%) and were not concordant in 47 (16.5%) arterial segments.

Conclusion: Our study demonstrated that ^{18}F-FDG-PET/MRI is a new exam that adds metabolic information to anatomic image in c-TA patients, and may help therapeutic decision, especially for those during immunosuppressive withdrawal.

Table 1. Clinical, laboratorial, treatment data and PET findings in group 1 and 2 in c-TA patients. c-TA: childhood-onset Takayasu's arteritis; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; PET: positron emission tomography; MRA: magnetic resonance angiography; SUVmax: maximum standardized uptake value; MIV: metabolic inflammatory volume. Numerical values are presented in median (IQR). *1 patient had no vessel wall changes in MRA or PET imaging and 1 patient had vessel-wall changes in MRA but no vessel-wall changes in PET

	Group 1: n=9 (PET + MRA +)	Group 2: n=6 (PET + MRA -)	*P value*
Disease duration, years	11.0 (7.1-12.1)	8.1 (3.8-13.5)	0.906
Diagnosis delay, months	11.0 (3.0-27)	20.5 (1.6-41.3)	0.595
ESR, mm in 1st hour	8.0 (4.5-15.5)	4.5 (2.8-13.8)	0.407
CRP, mg/L	2.7 (0.3-15.9)	3.1 (1.6-6.3)	0.859
Angiographic type V, N (%)	5 (55.6)	0	0.044
SUVmax	3.4 (3.1-4.3)	3.1 (2.5-3.9)	0.272
MIV, cm^3	2346 (1438-3304)	1177 (869-1880)	**0.036***
Prednisone, N (%)	4 (44)	1 (16.7)	0.580
Biologics, N (%)	4 (44)	2 (33.3)	1.000

Table 2. PET and MRA findings according to each arterial segment (N=284) in c-TA patients c-TA: childhood-onset Takayasu's arteritis; PET: positron emission tomography; MRA: magnetic resonance angiography; VS: visual score; T+E: thickening + enhancement; RCC: right common carotid; LCC: left common carotid * Vessel-wall changes in PET and MRA that have undergone surgical intervention (5 arterial segments) were not considered

Arterial Segments	PET+ (VS=III)	MRA+ (T+E)	Group 1 PET+MRA+	Group 2 PET+ MRA-	Group 3 PET-MRA+
RCC	2	1	0	2	1
LCC	1	3	0	1	3
Right vertebral	0	0	0	0	0
Left vertebral	0	0	0	0	0
Ascending aorta	11	5	5	6	0
Aortic arch	3	4	1	2	3
Descending aorta	1	5	1	0	4
Innominate	1	1	0	1	1
Right subclavian	1	1	0	1	1
Left subclavian	0	2	0	0	2
Celiac trunk	1	0	0	1	0
Superior mesenteric	0	0	0	0	0
Abdominal aorta	0	4	0	0	4
Right renal	3	0	0	3	0
Left renal	4	0	0	4	0
Right iliac	5	0	0	5	0
Left iliac	2	0	0	2	0
Number of arterial segments	35	26	7	28	19

Disclosure: G. Clemente, None; **A. Souza**, None; **H. Leão Filho**, None; **F. Coelho**, None; **C. Buchpiguel**, None; **M. Lima**, None; **D. Pioto**, None; **M. Fraga**, None; **A. Sakamoto**, None; **C. Carneiro**, None; **R. Pereira**, None; **N. Aikawa**, None; **C. Silva**, None; **L. Campos**, None; **C. Astley**, None; **B. Gualano**, None; **M. Terreri**, Sanofi, 6, Alexion, 6, Pfizer, 6, Novartis, 6, Abbvie, 6, Roche, 6, Biomarin, 6, GSK, 6, Jansen, 12, Clinical studies, UCB, 12, Clinical studies, Bristol, 12, Clinical studies, Lilly, 12, Clinical studies.

Abstract Number: 0162

Cardiac Magnetic Resonance Imaging for Guiding Decision-making on Treatment Duration: Data from RHAPSODY, a Phase 3 Clinical Trial of Rilonacept in Recurrent Pericarditis

Paul Cremer[1], David Lin[2], Alistair Wheeler[3], Antonio Abbate[4], Antonio Brucato[5], Fang Fang[6], Antonella Insalaco[7], Martin LeWinter[8], Basil S. Lewis[9], Sushil A. Luis[10], Stephen J. Nicholls[11], John Petersen[12], Allan Klein[1], Massimo Imazio[13] and John F Paolini[6], [1]Department of Cardiovascular Imaging, Center for the Diagnosis and Treatment of Pericardial Diseases, Heart and Vascular Institute, Cleveland Clinic, Cleveland, OH, [2]Minneapolis Heart Institute at Abbott Northwestern Hospital, Minneapolis, MN, [3]Kiniksa Pharmaceuticals, Ltd., Hamilton, Bermuda, [4]VCU Pauley Heart Center, Virginia Commonwealth University, Richmond, VA, [5]Department of Biomedical and Clinical Science, University of Milano, Fatebenefratelli Hospital, Milan, Italy, [6]Kiniksa Pharmaceuticals Corp., Lexington, MA, [7]Department of Pediatric Medicine, Division of Rheumatology, Bambino Gesù Children's Hospital, Rome, Italy, [8]Cardiology Unit, The University of Vermont Medical Center, The University of Vermont, Burlington, VT, [9]Cardiovascular Clinical Research Institute, Lady Davis Carmel Medical Center, Haifa, Israel, [10]Division of Cardiovascular Ultrasound, Department of Cardiovascular Medicine, Mayo Clinic, Rochester, NY, [11]MonashHeart, Department of Cardiology, Monash University, Clayton, Australia, [12]Swedish Medical Center, Seattle, WA, [13]University Cardiology, Cardiovascular and Thoracic Department, AOU Città della Salute e della Scienza di Torino, Torino, Italy

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The magnitude of pericardial delayed hyperenhancement (DHE) by cardiac magnetic resonance imaging (CMR) illustrates the severity of inflammation in pericarditis. We hypothesized that patients with more severe DHE at baseline may experience earlier recurrence of pericardial disease after interruption of pharmacotherapy that had led to clinical response.

Methods: RHAPSODY is a phase 3 randomized withdrawal (RW) trial of rilonacept, an Interleukin-1α and 1β trap, in patients with recurrent pericarditis (RP) presenting with acute symptoms despite standard of care. Following a run-in period of 12 weeks of rilonacept treatment, clinical responders on rilonacept monotherapy were randomized 1:1 to placebo or continued rilonacept in a double-blind RW period. CMR was collected at baseline prior to rilonacept initiation in 25/86 patients, of whom 14 were later randomized to placebo in the RW period. CMRs were graded (none, trace, mild, moderate, severe, or not measurable) by a central imaging laboratory. We analyzed the baseline CMR data in the context of time to recurrence after randomization.

Results: 25 patients had CMR at baseline: 8% trace, 28% mild, 20% moderate, and 44% severe DHE. In patients randomized to placebo with moderate or severe DHE at baseline, 71.4% experienced a recurrence, with a median time to recurrence of 4.2 weeks. In patients randomized to placebo with trace or mild DHE at baseline, 71.4% experienced a recurrence, but with a longer median time to recurrence of 10.7 weeks after randomization. In patients with CMR at baseline randomized to receive continued rilonacept, none experienced a recurrence during the RW period; 82% had moderate or severe DHE at baseline.

Conclusion: These data support the hypothesis that more severe pericardial DHE at baseline may be associated with shorter time to pericarditis recurrence after interruption of rilonacept therapy. There is growing evidence that the assessment of DHE in the broader context of the evaluation of patients with recurrent pericarditis could be a helpful adjunct for determining treatment duration in affected patients.

Disclosure: P. Cremer, Kiniksa, 5, 12, personal fees, Novartis, 5, Sobi, 12, personal fees; **D. Lin**, Regeneron, 12, fees; **A. Wheeler**, Kiniksa Pharmaceuticals, Ltd., 2; **A. Abbate**, Kiniksa, 5, Olatec, 5, 12, personal fees, Serpin, 5, 12, personal fees, Novartis, 5, 12, personal fees, Novo-Nordisk, 12, personal fees, Cromos Pharma, 12, personal fees, Janssen, 5, 12, personal fees; **A. Brucato**, Kiniksa, 12, My institution received funding from Kiniksa as an investigative site to run the study, Sobi, 5, Acarpia, 5; **F. Fang**, Kiniksa Pharmaceuticals Corp., 3, 11; **A. Insalaco**, None; **M. LeWinter**, Kiniksa, 5, 12, personal fees; **B. Lewis**, Kiniksa, 12, personal fees; **S. Luis**, Kiniksa, 1, Sobi, 1, 2, Medtronic, 2; **S. Nicholls**, Kiniksa, 5, 12, personal fees, AstraZeneca, 2, 5, Amgen, 5, Anthera, 2, 5, Eli Lilly, 2, 5, Esperion, 2, 5, Novartis, 5, Cerenis, 5, The Medicines Company, 5, Resverlogix, 2, 5, InfraReDx, 5, Roche, 5, Sanofi-Regeneron, 2, 5, Liposcience, 5, Akcea, 2, Omthera, 2, Merck, 2, Takeda, 2, CSL Behring, 2, Boehringer Ingelheim, 2; **J. Petersen**, None; **A. Klein**, Kiniksa, 1, 5, Sobi, 1, Pfizer, 1; **M. Imazio**, Kiniksa, 1, Sobi, 1; **J. Paolini**, Kiniksa Pharmaceuticals Corp., 2, 10, 11.

Abstract Number: 0163

Diagnosis of Giant Cell Arteritis in Spain: Data from the ARTESER Registry

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SESSION INFORMATION

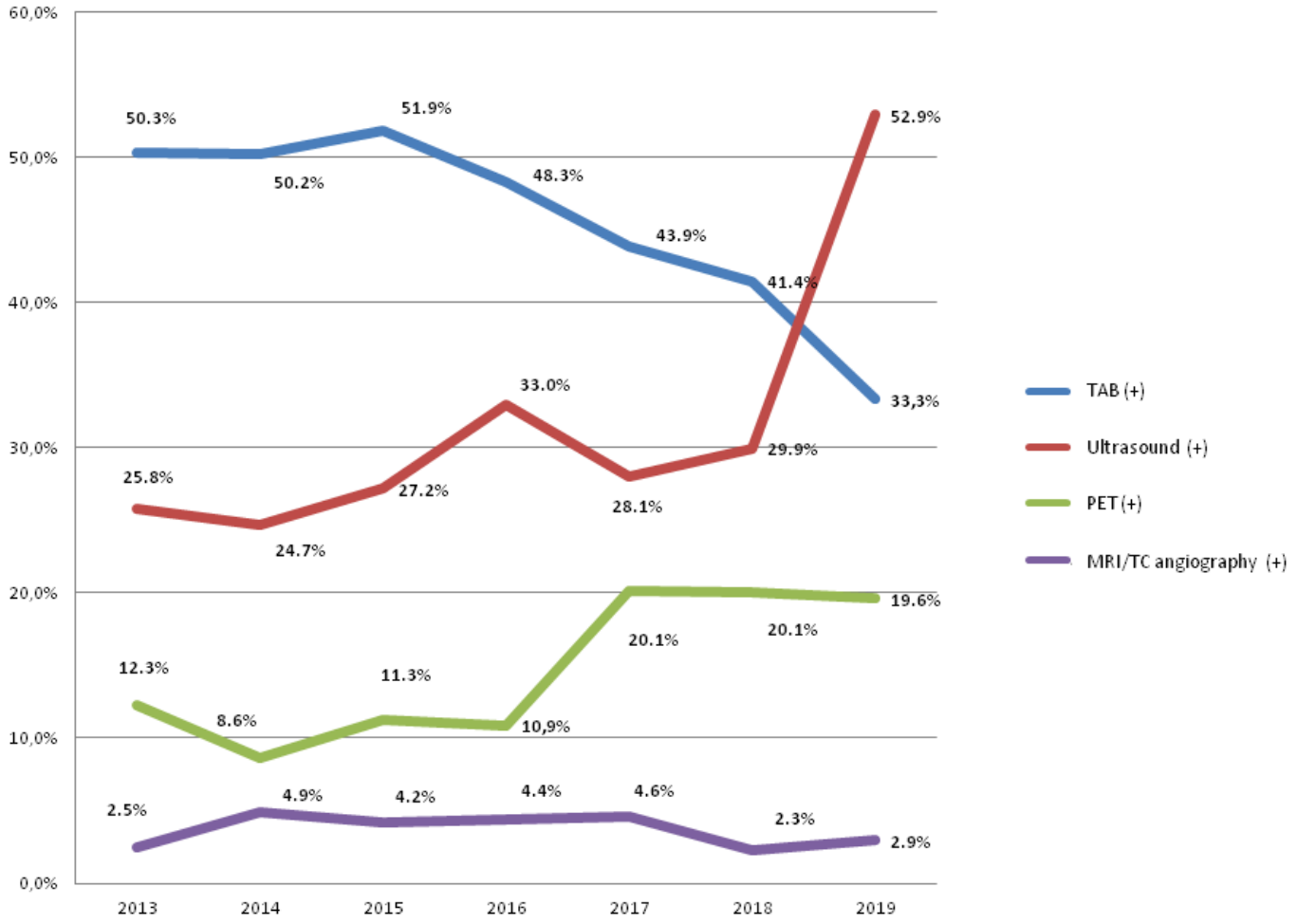
Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: To standardize research studies different classification systems are used. Currently, the ACR Giant Cell Arteritis (GCA) 1990[1] classification criteria is probably the most widely used, but the positive predictive value of these criteria is based on the high specificity of temporal artery biopsy (TAB), but a low sensitivity of TAB has been reported. Therefore, in the last EULAR recommendations for the use of imaging in GCA[2], imaging techniques



were accepted as useful in the diagnosis of GCA. This means that the GCA classification criteria are currently under discussion and evolution. Meanwhile, the diagnosis is based on the experience and judgment of the clinician. Our main objective was to know, how the diagnosis of GCA was made in our country and if the publication of the EULAR recommendations has influenced in the diagnosis of GCA in our clinical practice.

Methods: ARTESER is a multicenter observational retrospective study promoted by the Spanish Society of Rheumatology with 26 participating centers and in which all patients diagnosed with GCA between June 1 2013 and March 29 2019 were included. The gold standard for the diagnosis of the disease was the opinion of the responsible physician according to the clinical, analytical, imaging and TAB data available. This analysis includes the data collected from TAB and imaging (ultrasound, PET, and MRI/CT-angiography).

Results: 1675 patients with GCA were included, mean age ± SD (76.9 ± 8.1) years, 1178 women (70.3%). 776 patients had a positive TAB (46.3%), 503 (30.0%) positive ultrasound, 245 positive PET (14.6%) and 64 positive MRI/CT-angiography (3.8%). Figure 1 shows the temporal evolution of TAB and imaging techniques in the diagnosis of GCA throught the study time.

When the patients who had several of these positive tests were analyzed as support of clinical diagnosis, it was found that TAB was the only specific test performed in 531 patients (31.7%), ultrasound in 257 (15.3%), PET in 135 patients (8.1%) and MRI/CT-angiography in 14 patients (0.8%). Likewise, the data collected showed that the diagnosis based on clinical criteria or physician's opinion without TAB or imaging tests had been made in 417 patients (24.9%).

Conclusion: TAB is the most widely used diagnostic test to confirm GCA. Following the publication of the 2018 EULAR recommendations, ultrasound has displaced TAB as the first diagnostic test. PET is performed in 20% of patients in recent years. There is a wide margin of improvement in the diagnosis of GCA since the clinical diagnosis, without TAB or additional imaging tests, still supports 25% of the diagnoses.

Disclosure: E. De Miguel, Roche, 6, 12, Paid instructor, Abbvie, 2, 5, 6, Novartis, 2, 5, 6, 12, Paid instructor, Pfizer, 2, 5, 6, MSD, 6, BMS, 6, UCB, 6, Grunental, 6, Janssen, 6, 12, Paid instructor, Sanofi, 6, Galapagos, 2; **J. Sánchez-Costa**, None; **J. Narvaez**, None; **M. gonzalez-Gay**, None; **N. Garrido-Puñal**, None; **P. Estrada-Alarcon**, None; **I. Hernández-Rodríguez**, None; **E. Fernández-Fernández**, None; **M. Silva-Diaz**, None; **J. Valero-Jaimes**, None; **I. González-Fernández**, None; **J. Sánchez**, None; **J. Lluch**, None; **E. Galindez-Agirregoikoa**, None; **J. Mendizábal-Mateos**, None; **L. Rodriguez Rodriguez**, None; **J. Loricera García**, None; **A. Muñoz**, None; **S. Castañeda**, None; **P. Moya**, None; **P. Morán-Álvarez**, None; **V. Navarro-Angeles**, None; **J. Calvet-Fontova**, None; **I. Casafont**, None; **F. Ortiz-Sanjuán**, None; **S. Labrada-Arrabal**, None; **C. Campos-Fernández**, None; **M. Alcalde-Villar**, Nordic, 12, Tutor of rheumatology trainee at regional congress; **A. Juan-Mas**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0164

Disrupted Executive Control Network Structural-Functional Integration Is Associated with Inferior Performance of Cognitive Switching Tasks in Patients with Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cognitive flexibility, a process that enables goal-oriented cognitive switching between mental function modes, is central to executive function which is impaired in SLE patients. Multimodal integration of brain network anatomy and functional signals has recently been shown to mediate the cognitive switching process. Specifically, alignment between blood-oxygenation-level-dependent (BOLD) signals and the architecture of the underlying white matter (WM) network is associated with higher cognitive flexibility. In SLE patients, whether WM networks that constrain brain dynamics during cognitive switching is altered remains unknown. Here, brain structural-functional alignment and liberality between SLE patients and healthy controls (HC) were studied by performing the Modified Wisconsin Card Sorting Test (MCST) that probed cognitive flexibility. We hypothesized that the structural-functional integration of the executive control network (ECN) would be disrupted, with behavioral implications in SLE patients.

Methods: We studied 17 SLE patients without neuropsychiatric manifestation (aged 33.3±7.9 years) and 44 HC (aged 28.3±8.2 years). Functional brain magnetic resonance imaging (MRI) during MCST, T1-weighted structural and diffusion MRI were conducted. Region-of-interest (ROI) time series were extracted using a 144-ROI brain functional parcellation scheme. We constructed the anatomical brain network by defining the connectivity between each pair of ROIs as the normalized connection probability derived from probabilistic diffusion tractography. BOLD signals were decomposed into a proportion that aligned with the anatomical network and a proportion that indicated liberality (Fig. 1).

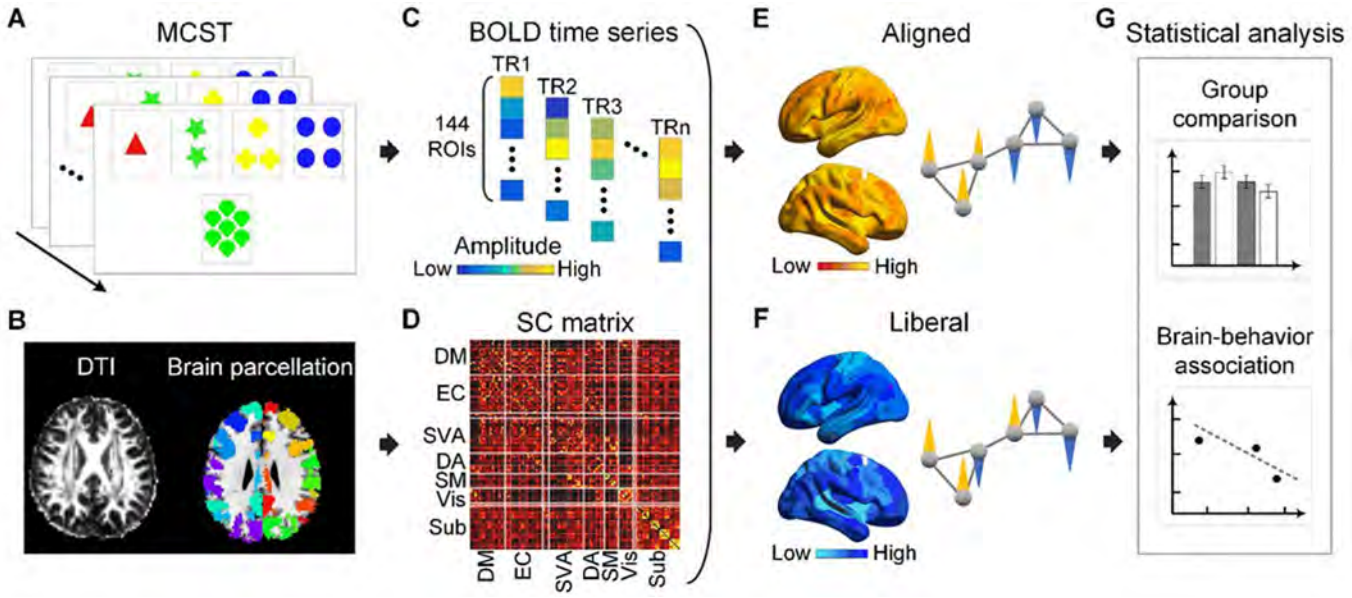

Figure 1. Study design schematic diagram. Subjects performed the Modified Wisconsin Card Sorting Test (MCST) in which they were asked to match the stimulus card at the bottom of the screen to one of the four index cards displayed at top of the screen while undergoing functional MRI scan (A). Structural connectivity (SC) network was constructed using diffusion tensor imaging (DTI) for each individual based on a predefined set of 144 regions of interest (ROIs), which included 114 cortical ROIs and 30 subcortical regions (B & D). ROI blood oxygen level-dependent (BOLD) time series were extracted from fMRI data and decomposed into a proportion which was aligned well with the structural network and a proportion which was liberal from the network (C, D, E & F). We conducted group comparison on functional alignment and liberality between SLE and healthy controls and examined the association of alignment and liberality with task performance (G). Abbreviations: DM: default mode, EC: executive control, SVA: salience/ventral attention, DA: dorsal attention, SM: somatomotor, Vis: visual, Sub: subcortical.

We performed group comparison on alignment and liberality at the global and network levels using two-sample t-tests (a=0.05) and evaluated their relationships with MCST performance.

Results: The two groups did not differ in overall MCST performance. SLE patients showed higher global functional liberality and lower global functional alignment with the structural networks during MCST (p=0.014 and 0.045, respectively) compared to HC. At the network level, SLE patients showed higher liberality in the ECN compared to HC (FDR-corrected, p=0.026). Focusing on the 3 ECN sub-networks (Fig. 2H), the abnormality of functional organization atop the ECN anatomy was driven by the lower alignment in ECN-A and higher liberality in ECN-A and ECN-B in SLE patients (FDR-corrected p=0.007, 0.008 and 0.026, respectively). ECN-A and ECN-B are the typical lateral fronto-parietal executive control regions while ECN-C is near to the default mode network. Higher liberality and lower alignment were correlated with reduced task accuracy ($p< 0.05$). The correlation between ECN liberality and task accuracy remained significant (p=0.023) after controlling for global liberality and alignment.

Conclusion: Our study demonstrated reduced functional-structural alignment of the ECN in SLE patients using a novel graph signal processing method that constrained BOLD signal magnitude to the anatomical network architecture. Reduced functional-structural alignment was associated with poorer cognitive switching performance.

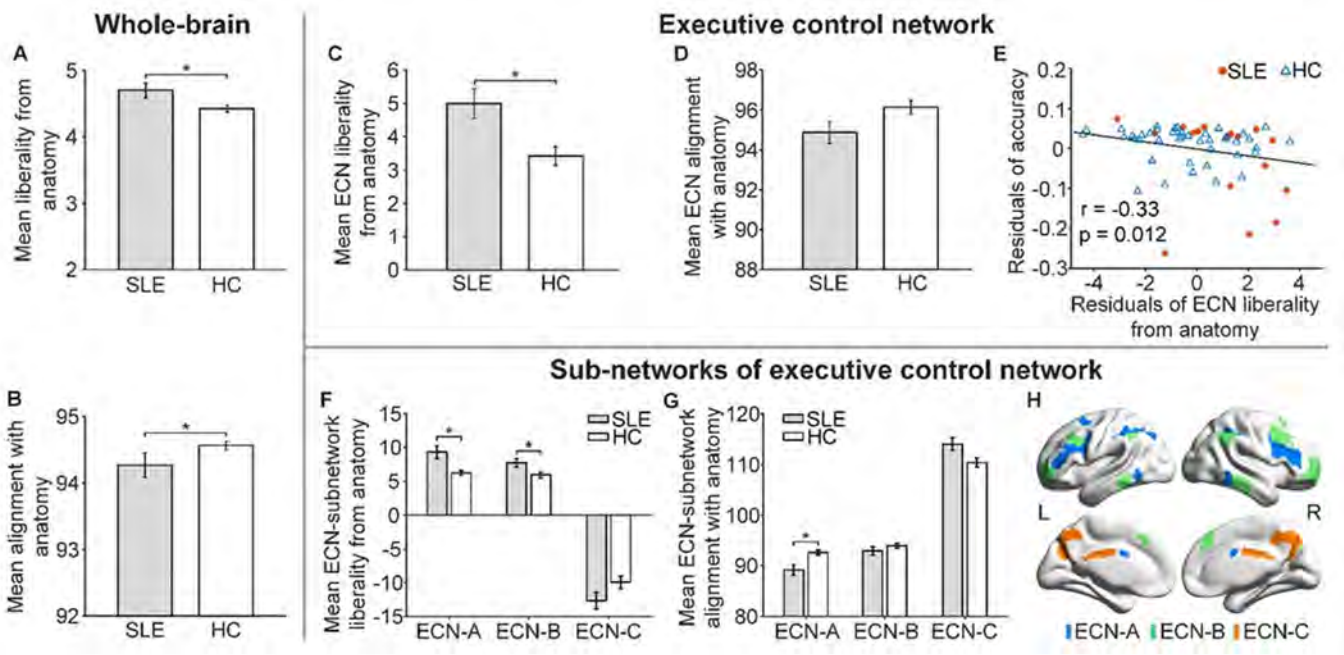

Figure 2. Patients with SLE had higher liberality from anatomy and lower alignment with anatomy related to MCST performance. Patients with SLE showed higher mean liberality from anatomy and lower mean alignment with anatomy during MCST than HC ($p<0.05$, A&B). SLE patients showed higher mean liberality from anatomy in ECN (FDR corrected $p<0.05$) and a trend towards lower mean alignment in ECN during MCST than HC (C&D). Increased mean liberality in ECN was correlated with reduced task accuracy across SLE and HC groups (E). Amongst ECN sub-networks highlighted in the brain surfaces (H), ECN-A and ECN-B showed higher mean liberality from anatomy during MCST in SLE patients than HC, and ECN-A showed lower mean alignment with anatomy during MCST in SLE patients than HC (FDR corrected $p<0.05$, F&G). Error bars represent standard errors. Abbreviations: SLE: systemic lupus erythematosus, HC: healthy control, ECN: executive control network, MCST: Modified Wisconsin Card Sorting Test.

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Abstract Number: 0165

Shear-Wave Elastography Evaluation of Major Salivary Glands and Correlation with B-mode Findings in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Salivary-gland ultrasound has recently shown to help in the diagnosis and monitoring of primary Sjögren's syndrome (pSS)[1]. Shear-wave elastography (SWE) is a promising tool for the quantitative assessment of tissue stiffness[2]. However, studies evaluating its role in ultrasound evaluation of pSS are still limited. This study aimed to investigate the diagnostic performance of SWE in pSS and its correlation with B-mode findings.

Methods: Cross-sectional study including consecutive patients fulfilling the ACR/EULAR 2016 classification criteria for pSS, followed at our Rheumatology clinic, and age and gender-matched healthy controls. A protocolized clinical and ultrasound evaluation was performed for each patient. The four major salivary glands (parotid and submandibular glands, bilaterally) were assessed by SWE and B-mode modalities by 2 and 3 independent operators, respectively, blinded to the diagnosis. B-mode scans were rated using the Hocevar score[3], and mean shear-wave velocity (SWV) values were obtained from 6 different measures for each gland. Student's t-test, chi-square test and Pearson's

Table 1. Patient's clinical characteristics at protocolized evaluation (N=50). SD- standard deviation; ESSDAI – EULAR Sjögren's Syndrome Disease Activity Index; NSAIDs- Nonsteroidal Anti-inflammatory Drugs

	Mean (SD)
Disease duration, years, mean (SD)	12.20 (7.27)
Number of swollen joints, mean (SD)	0.06 (0.42)
Number of tender joints, mean (SD)	0.12 (0.60)
ESSDAI, mean (SD)	0.88 (2.13)
	Positives/Total
Xerostomia	48/50
Xerophthalmia	50/50
Parotid tumefaction	6/50
Fatigue	17/50
History of lymphoma	2/50
Articular involvement	19/50
Pulmonary involvement	5/50
Renal involvement	3/50
Cutaneous involvement	8/50
Hematological involvement	24/50
Peripheral nervous system involvement	2/50
Central nervous system involvement	2/50
Anti-SSA-60 positivity	47/50
Anti-SSB positivity	26/50
Rheumatoid factor positivity	34/49
Cryoglobulins	5/23
Hypocomplementemia (C3 and/or C4)	13/50
Hypergammaglobulinemia	35/50
Minor salivary gland biopsy positivity	16/19
Abnormal salivary gland scintigraphy	22/22
Schirmer's test positivity	42/50
Current medications	
Prednisolone≥1 mg/day	5/50
Immunosuppressives	21/50
NSAIDs	15/50
Pilocarpine	14/50

Table 2. Shear-wave elastography and B-mode findings for the four major salivary glands at protocolized evaluation. pSS- Primary Sjögren's syndrome

	pSS (N=50)	Controls (N=25)	*p* value
Shear-wave velocity (m/s)			
Total, mean (SD)	2.09 (0.32)	1.74 (0.24)	<0.001
Left parotid gland, mean (SD)	2.25 (0.40)	1.83 (0.30)	<0.001
Right parotid gland, mean (SD)	2.25 (0.53)	1.83 (0.31)	<0.001
Left submandibular gland, mean (SD)	1.94 (0.45)	1.70 (0.32)	0.020
Right submandibular gland, mean (SD)	1.90 (0.45)	1.61 (0.32)	0.005
***Hocevar et al.* (range 0-48)**			
Total, mean (SD)	22.2 (8.76)	3.72 (3.46)	<0.001
Left parotid gland, mean (SD)	5.14 (2.45)	0.92 (1.26	<0.001
Right parotid gland, mean (SD)	5.68 (2.43)	0.68 (0.85)	<0.001
Left submandibular gland, mean (SD)	5.68 (2.27)	1.28 (1.31)	<0.001
Right submandibular gland, mean (SD)	5.76 (2.29)	0.84 (1.11)	<0.001

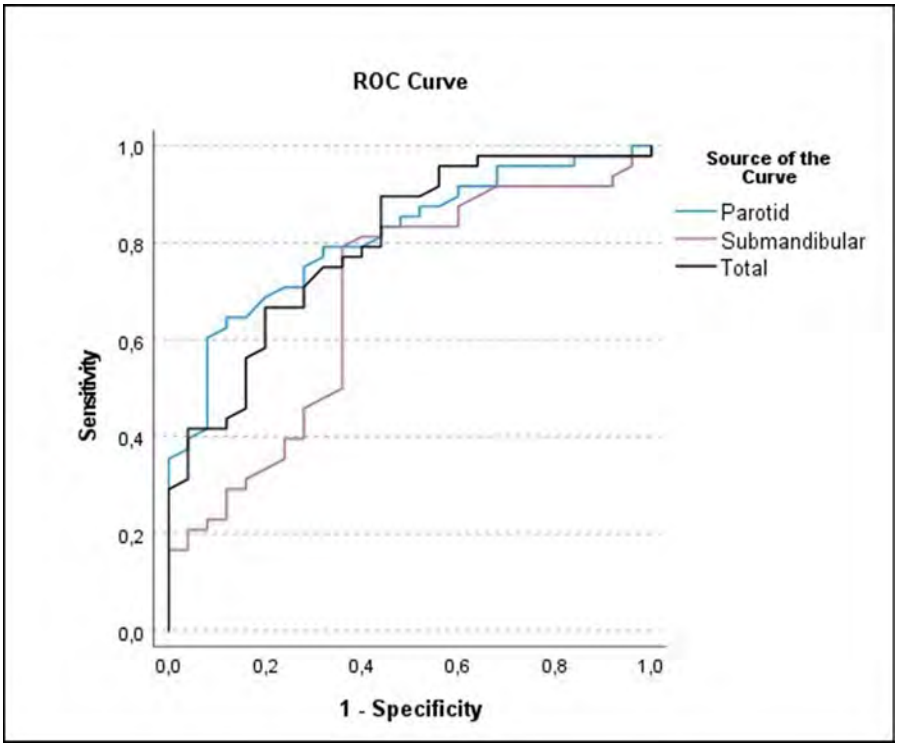

Figure 1. Receiver Operating Characteristics (ROC) analysis for parotid, submandibular and total mean shear wave velocity.

correlation were performed to compare data, as appropriate. Inter and intra-rater reliability were calculated using intraclass-correlation coefficient (ICC). Cut-off values for differentiating pSS patients from controls were calculated using Receiver-Operating Characteristics (ROC) curves.

Results: We included 50 pSS patients (mean (SD) age 56.2 (13.7); 98.0% females) and 25 controls (mean (SD) age 53.5 (9.2); 96.0% females) (Table 1). For SWE and B-mode modalities, inter-rater reliability was moderate to good (ICC: 0.64 and ICC:0.78-0.95, respectively), while intra-rater reliability was good to excellent (ICC:0.74-0.83 and IC-C:0.95-0.98, respectively). Hocevar scores were higher in pSS patients than in controls ($p< 0.001$) in all four glands examined (Table 2). The mean total SWV (2.09 m/s (0.32); $p< 0.001$), mean parotid SWV (2.25 m/s (0.53)) and mean

submandibular SWV values (1.86 m/s (0.36)) were significantly higher in patients than in controls. No significant correlation between Hocevar scores and SWV values was observed. The cut-offs of 1.95 m/s, 1.96 m/s and 1.60 m/s for total, parotid and submandibular SWV values differentiated pSS patients from controls with sensitivity of 65.3%, 77.6% and 79.2% and specificity of 80.0%, 68.0% and 64.0%, respectively. The area under the ROC curve (AUROC) was not significantly different between total SWV (AUROC=0.78) and parotid SWV (AUROC=0.81), p=0.696. Both were significantly greater than AUROC for submandibular SWV (AUROC=0.68), p< 0.05 (Figure 1).

Conclusion: SWE may represent a relevant additional tool for the diagnosis of pSS. SWV values did not correlate with B-mode, probably due to the difficulty in scoring severely fibrotic glands using Hocevar score. Larger studies including patients with pSS and patients with sicca syndrome, as well as standardization of SWE protocols, are warranted to assess the role of SWE in the diagnostic algorithm of pSS.

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Disclosure: A. Prata, None; **J. Freitas**, None; **M. Marques**, None; **F. Costa**, None; **M. Santiago**, None; **S. Serra**, None; **M. Coutinho**, None; **T. Santiago**, None; **J. Lopes Rovisco**, None; **J. Pereira da Silva**, Amgen, 6, Jaba Recordati, 6, Pfizer, 6.

Abstract Number: 0166

Digital Extensor Paratenonitis Is Frequent in Early Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Finger extensor tendon involvement (FEP) or paratenonitis has previously been described by ultrasound (US) in patients suffering from early psoriatic arthritis. Contradictory results were published in patients suffering from rheumatoid arthritis.

We aimed to assess the involvement of FEP in early rheumatoid arthritis (ERA) patients and in asymptomatic subjects.

Methods: Inclusion criteria for ERA patients were: symptom duration < 6 months prior to ERA diagnosis; age >18 years; no DMARD treatment at time of US examination. Inclusion criteria for asymptomatic subjects group were: age >18 years; no other known rheumatic disease (connective tissue diseases, rheumatoid, psoriatic arthritis, spondyloarthritis, hand osteoarthritis, gout, chondrocalcinosis); no psoriasis, no inflammatory bowel diseases. Patients were evaluated clinically (44-tender and 44-swollen joint count), and answered health assessment questionnaires (HAQ). Hand, wrist, feet X-ray and laboratory tests including anti-citrullinated protein antibodies (ACPA), rheumatoid factor (RF) and C-reactive protein (CRP) were performed in all patients. US assessments were performed blinded to clinical and laboratory data. FEP was assessed in longitudinal and in transverse view at all metacarpophalangeal (MCP) joints

and proximal phalangeal joints, both in grey-scale and Doppler mode. FEP was defined as abnormal anechoic and/or hypoechoic (relative to tendon fibers) paratenon widening seen in two perpendiculars planes and was scored as present/absent.

Results: One hundred and four consecutive ERA patients and 44 asymptomatic subjects were included in this study. Mean age and comparable gender distribution were observed between the groups (50.1±1.3 y, ERA *vs*. 45.8±2.0 y, asymptomatic subjects). ACPA were present in 63.5%, RF in 62.5%, tobacco use in 22.1% and x-ray bone erosions in 33.7% of ERA patients. Age, gender, delay between the first symptom and diagnosis, SDAI, CDAI, CRP level, HAQ did not differ significantly between patients with FEP involvement and those without. FEP was present in two-third of ERA patients and absent in asymptomatic subjects (60.6% vs. 0%, p< 0.001). In univariate analysis, the presence of FEP was significantly associated with the presence of MCP erosion (p=0.02), ACPA positivity (p=0.017), rheumatoid factor (p=0.009) and tobacco use (p=0.015). In multivariate analysis, the presence of FEP was significantly associated with the presence of MCP erosions, ACPA positivity and tobacco use (p< 0.01).

Conclusion: FEP is relatively frequent in ERA patients and it is not present in asymptomatic subjects. Our results show that FEP is associated with ACPA positivity and bone erosions, thus identifying patients early with a possibly more aggressive or severe disease.

Disclosure: M. Maruseac, None; **A. NZEUSSEU TOUKAP**, Abbvie, 1, 5, Eli Lilly, 1, 5, Janssen, 1, 5, UCB, 1, 5, Celgene, 1, 5, Pfizer, 1, 5; **M. Stoenoiu**, AbbVie, 2, 5, 6, UCB, 2, 5, 6, Pfizer, 2, 5, 6, MSD, 2, 5, 6, Roche, 2, 5, 6.

Abstract Number: 0167

Reliability of a Novel Pediatric Joint-Specific Scoring System for the Elbow, Wrist and Finger Joints

Patricia Vega-Fernandez[1], Ysabella Esteban[2], Edward Oberle[3], Jean-Philippe Proulx-Gauthier[4], Matthew Clark[5], Hulya Bukulmez[6], Susan Shenoi[7], Akaluck Thatayatikom[8], Heather Benham[9], Emily Brunner[10], Leandra Woolnough[8], Michael Henrickson[1], Laura Ballenger[3], Deidre DeRanieri[11], Sarah Hoffmann[12], Ginger Janow[13], Mekibib Altaye[14], Amy Cassedy[2], Johannes Roth[15] and Tracy Ting[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital and Medical Center, Cincinnati, OH, [3]Nationwide Children's Hospital, Columbus, OH, [4]CHU de Quebec - Universite Laval, Québec City, QC, Canada, [5]Vanderbilt University Medical Center, Nashville, TN, [6]MetroHealth Medical Center, Case Western Reserve, Pepper Pike, OH, [7]Seattle Children's Hospital, Seattle, WA, [8]University of Florida, Gainesville, FL, [9]Scottish RIte Hospital, North Richland Hills, TX, [10]Geisinger, Bloomsburg, PA, [11]Lurie Children's Hospital, Chicago, IL, [12]Children's Hospital of Richmond at VCU, Richmond, VA, [13]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Glen Rock, NJ, [14]Cincinnati Children's Hospital, Cincinnati, OH, [15]University of Ottawa, Ottawa, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The clinical decision-making process in pediatric arthritis lacks an objective, reliable bedside imaging tool. Musculoskeletal ultrasound (MSUS) is increasingly being utilized in children. In order to provide objective assessments of arthritis, reliable scoring systems are needed. Recently, a joint-specific scoring system for the assessment of arthritis of the pediatric elbow, wrist and finger joints were proposed[1]. These scoring systems have excellent reliability when used by experienced ultrasonographers (>7 years of experience). This study aims to assess

Table 1. Inter-rater Reliability Exercise for the Pediatric Elbow, Wrist and Finger Joints

		B-Mode ICC (95% CI)	Power Doppler ICC (95% CI)
Elbow	Anterior recess	0.97 (0.96-0.98)	0.89 (0.84-0.92)
	Posterior Recess	0.96 (0.94-0.97)	0.90 (0.86-0.92)
Wrist	Distal Radioulnar Joint	0.94 (0.92-0.96)	0.96 (0.94-0.97)
	Dorsal Midline Recess	0.93 (0.91-0.94)	0.97 (0.96-0.98)
	Dorsal Ulnar Recess	0.87 (0.81-0.93)	0.83 (0.61-0.91)
	Tendon	0.89 (0.83-0.92)	0.78 (0.66-0.86)
Finger	MCP Dorsal	0.93 (0.91-0.97)	0.97 (0.96-0.98)
	MCP Volar	0.93 (0.91-0.94)	0.85 (0.81-0.88)
	PIP Volar Long	0.96 (0.95-0.97)	0.87 (0.84-0.90)
	PIP Dorsal Long	0.96 (0.94-0.97)	0.95 (0.93-0.97)

Intraclass correlation coefficient (ICC) was based on a two-way random effects model for a single measure. Excellent ICC was defined to be between 0.75-1.00, good 0.60-0.74, fair 0.40-0.59 and poor <0.4. CI: confidence interval. MCP: metacarpophalangeal joint, PIP: proximal interphalangeal joint.

the reliability of a B-Mode and Power Doppler (PD) scoring system for arthritis in the pediatric elbow, wrist and finger when used by sonographers with different levels of expertise.

Methods: As part of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) MSUS workgroup, a 2-hour training session and calibration exercise for each target joint was completed. Subsequently, B-mode and PD scoring exercises of still-images for each targeted joint were performed. Agreement between raters was determined using two-way single score intra-class correlation coefficients (ICC).

Results: 17 pediatric rheumatologists with different levels of ultrasound expertise (1 – 15 years) completed a 2-hour training session and calibration exercise for each targeted joint. Table 1 shows the inter-rater reliability obtained after the scoring exercise was completed for each joint. In general, there was excellent agreement for all B-mode views of the elbow, wrist, and finger joints. The reliability for PD views was excellent for the elbow and finger but was good for the dorsal ulnar recess and tendon views.

Conclusion: This effort identified the need for further training in PD settings and its scoring system(s). A training exercise and calibration exercise addressing the identified needs is ongoing. A novel BM and PD scoring systems for assessing arthritis of the pediatric elbow, wrist and finger joints were shown to have excellent reliability among pediatric MSUS sonographers with different levels of expertise. This reliable joint-specific scoring system for pediatric arthritis could serve as a clinical tool and outcome measure for scientific purposes with further refinement and validation.

1. Vega-Fernandez P, T.T., Oberle E, Figueroa J, McCracken C, Roth J., *Musculoskeletal Ultrasound Study in Childhood Arthritis: A Limited Examination [abstract]*. Arthritis Rheumatol, 2020. 72.

Disclosure: P. Vega-Fernandez, None; **Y. Esteban**, None; **E. Oberle**, None; **J. Proulx-Gauthier**, None; **M. Clark**, None; **H. Bukulmez**, None; **S. Shenoi**, Pfizer, 2; **A. Thatayatikom**, None; **H. Benham**, None; **E. Brunner**, None; **L. Woolnough**, None; **M. Henrickson**, None; **L. Ballenger**, None; **D. DeRanieri**, None; **S. Hoffmann**, None; **G. Janow**, None; **M. Altaye**, None; **A. Cassedy**, None; **J. Roth**, None; **T. Ting**, None.

Abstract Number: 0168

A Crowdsourcing Approach to Develop Machine Learning Models to Quantify Radiographic Joint Damage in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a common chronic autoimmune disease characterized by inflammation of the synovium, leading to joint space narrowing and osseous erosions. The most widely used method for quantifying joint damage is the visual inspection of radiographic images by highly trained readers. This subjective, time-consuming, non-scalable method is an impediment to research on factors associated with RA joint damage and lack of quantitative information on progression of damage may delay appropriate treatment decisions by clinicians. To develop a rapid, automated scoring method and perform a rigorous and unbiased evaluation of method performance, we designed the RA2-DREAM Challenge, a crowdsourced competition to engage the international community of problem solvers (http://www.synapse.org/ra2).

Methods: We provided Challenge participants with 674 sets of radiographic images (hands/wrists and feet) and expert-curated modified Sharp/van der Heijde (SvH) scores on 562 unique patients from two completed NIH supported clinical studies, CLEAR and TETRAD. The data for participants were divided into three subsets: training (367 sets of images and corresponding scores), leaderboard (119 sets of images, no scores), and test datasets (188 sets of images, no scores). Challenge participants submitted containerized methods to automatically score overall RA-related damage (Sub-challenge 1), joint space narrowing (Sub-challenge 2), and erosions (Sub-challenge 3). Participants were allowed multiple submissions during the training phase, up to three submissions during the leaderboard phase, and one final submission. Submitted models were evaluated using a model-to-data framework against the manually curated scores using the weighted root mean square error (RMSE). To determine the overall performance, we ranked each team according to their RMSE, determined the robustness of the ranking by bootstrapping the predictions, and evaluated using the Bayes factor.

Results: We received 189 valid submissions from 26 teams in this open science competition. From the 16 final submissions, four teams were named top performers across the three Sub-challenges. Winning algorithms used various approaches, including joint segmentation annotation, deep learning neural networks (e.g. YOLO, RCNN, ResNet, XGBoost), regression modeling, and ensembled methods. In addition, the submitted models were validated using a set of 50 additional patient images from an independent study, the TEAR Trial. These validation analyses revealed results similar to those of the original Challenge. All submitted models were containerized to aid in the goal of producing a rigorous and reproducible scoring methodology.

Conclusion: After further validation, algorithms from this Challenge may provide feasible, accurate, and quick methods to quantify joint damage in RA. These and other artificial intelligence approaches may be applied to radiographic images from electronic health records to quantitate radiographic damage in RA, providing many datasets for research on factors influencing damage. Automated scoring of damage in RA may also help rheumatology health professionals to make prompt treatment decisions to improve patient outcomes.

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Abstract Number: 0169

Ultrasonography of Auricular Cartilage Is a Useful Tool for Diagnosing and Monitoring Disease Activity in Relapsing Polychondritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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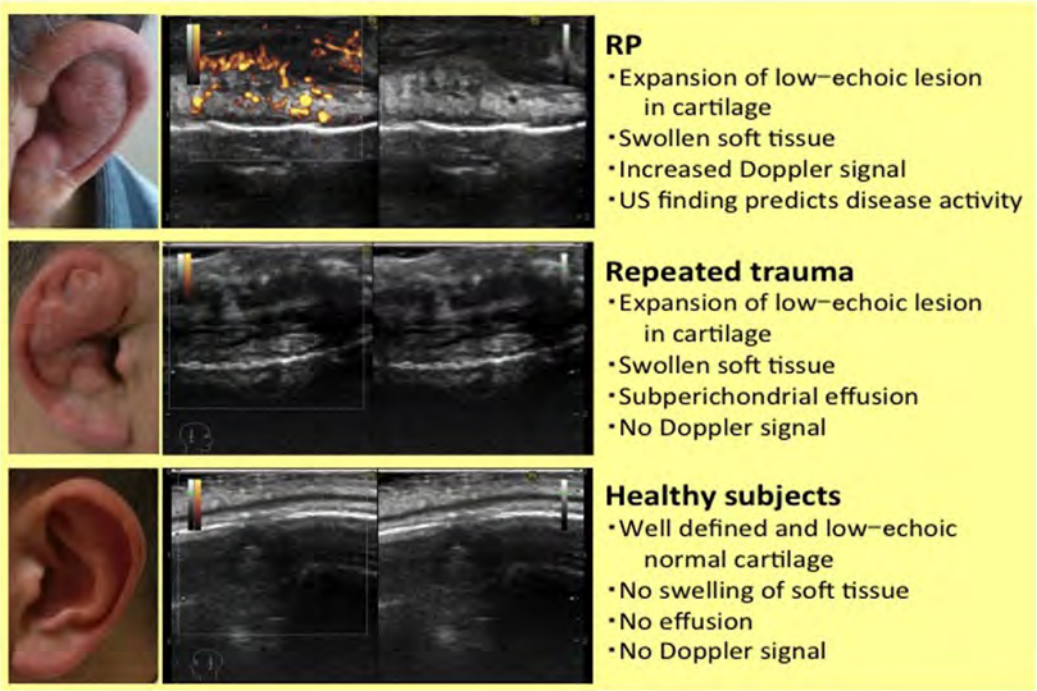
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: In patients with atypical clinical symptoms or imaging findings, because there are no specific and easily measurable markers for RP serologically, it is often difficult to diagnose RP and detect RP flare earlier. Although previous studies have reported the usefulness of imaging tests such as contrast-enhanced CT, MRI, FDG-PET/CT and bone scintigraphy for diagnosis and assessment of disease activity, performing these imaging tests frequently is not realistic without careful consideration of cost, convenience, invasiveness and radiation exposure. Therefore, it is necessary to establish a more convenient and less invasive imaging modality that can be repeatedly used for diagnosis and evaluation of disease activity.

Objective: To assess the clinical utility of ultrasonography (US) in the diagnosis and monitoring of disease activity in relapsing polychondritis (RP).

Methods: Auricular and nasal chondritis of patients with RP (n = 6) were assessed by US before treatment initiation. Changes in the US findings as well as clinical findings and serum inflammatory markers were longitudinally assessed. We also performed US in patients with repeated ear trauma (n = 6), auricular cellulitis (n = 2), and healthy subjects (n = 6) and compared among groups.

Results: In all cases of RP, US finding before treatment showed low-echoic swollen auricular and nasal cartilage with increased Power Doppler signals (PDS), corresponding to biopsy findings. After treatment with prednisolone (PSL) combined with methotrexate, the clinical and serum inflammatory markers were completely resolved. Although perichondrial swelling and PDS on auricular US were also significantly improved, PDS remained in 2 of 6 cases, and these cases showed flare early after tapering PSL. Finally, US findings of RP were substantially differentiated from patients



with repeated trauma and cellulitis and healthy subjects due to the thickness of soft tissue around the cartilage, PDS and subperichondrial serous effusion.

Conclusion: Assessment of RP lesions by US was useful for the evaluation of cartilaginous lesions and monitoring of disease activity, especially when considering the treatment response and the timing of drug tapering.

Disclosure: Y. Taniguchi, None; **H. Nishikawa**, None; **T. Yoshida**, None; **S. Inotani**, None; **Y. Terada**, None.

Abstract Number: 0170

Direct and Conditional Effects of Epicardial Adipose Tissue Volume on Coronary Plaque Progression in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Epicardial adipose tissue volume (EATv) predicts coronary atherosclerosis presence, progression and cardiovascular events in general patients. We recently reported that EATv associated with greater subclinical coronary plaque burden, noncalcified plaque presence and vulnerable plaque characteristics in patients with rheumatoid arthritis (RA). The relationship was stronger in patients without traditional cardiac risk factors, who were not obese and had lower disease duration. We here evaluate the role of EATv on long-term coronary plaque progression and moderators of the association between EATv and plaque formation.

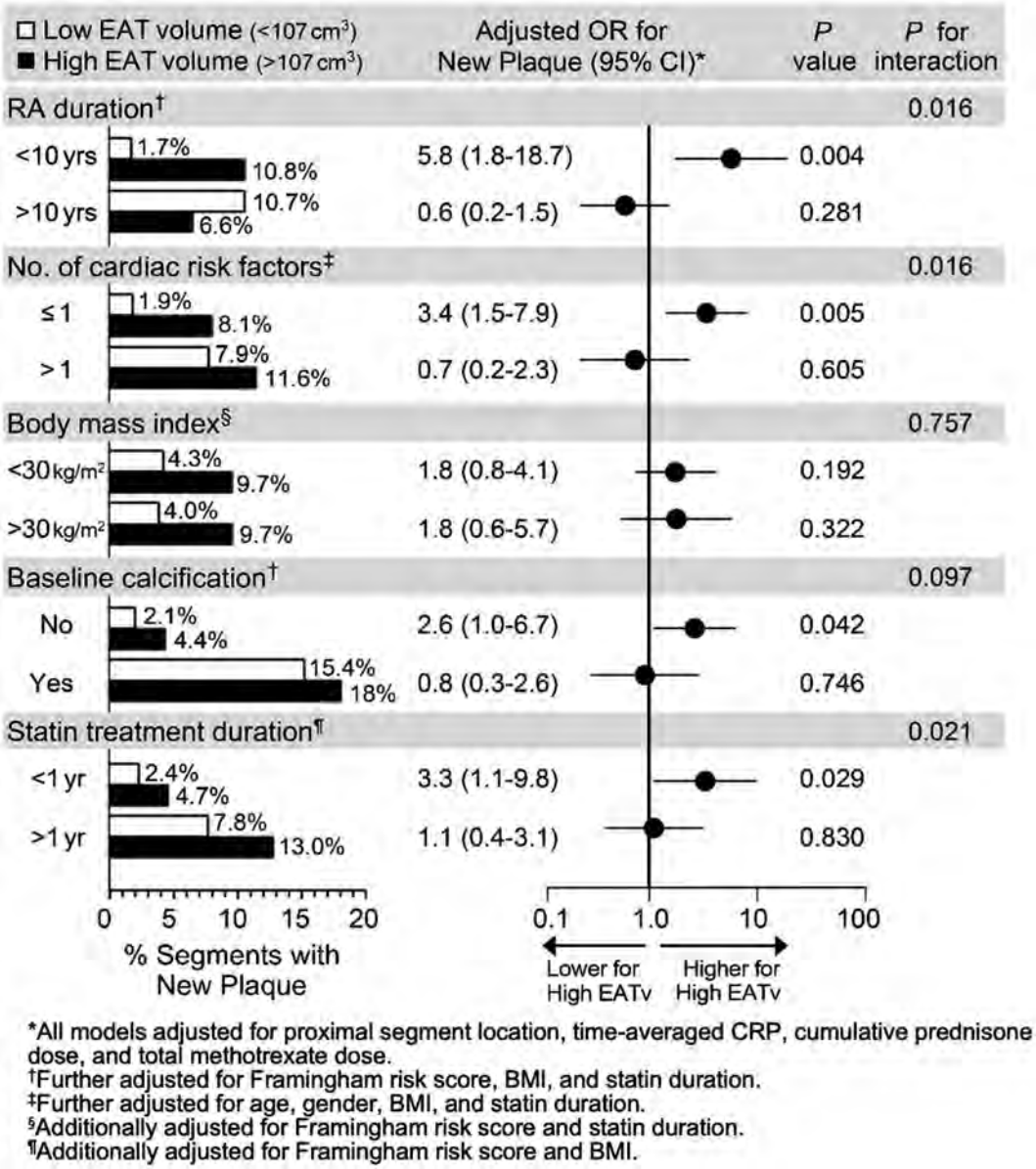

Figure 1. Moderators of influence of EATv on new coronary plaque formation at follow-up.

Methods: This single center observational cohort study included 100 patients without cardiovascular disease who underwent computed tomography angiography for evaluation of EATv and coronary atherosclerosis at baseline and 6.9±0.3 years later, to evaluate plaque progression. New plaque formation in segments without plaque at baseline was the main outcome. Robust multivariable logistic regression evaluated the effect of high versus low EATv (based on median) on likelihood of new plaque formation, accounting for clustering of segments within patients. Potential moderator effects of prespecified predictors were also assessed.

Results: High EATv (>107 cm^3) predicted new plaque formation in segments without baseline plaque (OR 2.77 [95% CI 1.43-5.37], p= 0.003); however, significance was lost in the multivariable model. Importantly, high EATv associated with formation of higher-risk noncalcified and partially calcified plaque after adjusting for Framingham D'Agostino risk score, obesity, segment location, time-averaged CRP, duration of bDMARD and statin treatment and cumulative prednisone dose (adjusted OR 2.57 [95% CI 1.02-6.48], p= 0.045). RA duration (< 10 versus >10 years), cardiac risk factor burden (1 versus >1), presence of partially/ fully calcified plaque in other coronary segments at baseline, and statin exposure (1 versus >1 year, based on median) moderated the effect of EATv on all new plaque formation (all p

for interaction 0.021). Specifically, high EATv predicted new plaque formation in patients with RA duration < 10 years (adjusted OR 5.75 [95% CI 1.77-18.67]), those with 1 cardiac risk factors (adjusted OR 3.40 [95% CI 1.46-7.90]), those without calcification at baseline (adjusted OR 2.65 [95% CI 1.11-6.31]) and those with statin treatment < 1 year (adjusted OR 3.33 [95% CI 1.13-9.77]). This was not the case for patients with RA >10 years, 1 cardiac risk factors, calcification at baseline and statin treatment >1 year (figure 1).

Conclusion: High baseline EATv independently predicted future higher-risk non- and partially calcified coronary plaque in RA. Moreover, it conditionally promoted new plaque formation overall in patients with earlier disease, low cardiac risk factor burden, who had little or no atherosclerosis at baseline and who had limited exposure to statins. These findings indicate the need for a larger prospective evaluation of the role of EATv as a biomarker of coronary atherosclerosis development in RA.

Disclosure: G. Karpouzas, None; **s. ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0171

Bone Erosions and Osteophytes in Premenopausal Women with Long-standing Rheumatoid Arthritis: Association with Systemic Bone Involvement Using HR-pQCT

Mariana Perez[1], Camille Figueiredo[1], Lucas Sales[1], ANA MEDEIROS-RIBEIRO[1], Liliam Takayama[1], Diogo Domiciano[1], Karina Bonfiglioli[1], Valeria Caparbo[1] and Rosa Pereira[2], [1]Rheumatology Division, University of São Paulo, São Paulo, SP, Brazil, [2]Rheumatology Division, University of São Paulo, São Paulo, Brazil

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Two patterns of bone involvement are described in rheumatoid arthritis (RA), systemic and localized. Systemic bone involvement is characterized by loss of generalized bone mass, osteoporosis and risk of fractures, and the localized by periarticular osteopenia, cysts and bone erosions. High-resolution peripheral quantitative computed tomography (HR-pQCT) is an imaging methodology capable of assessing volumetric bone mineral density (vBMD) and bone microarchitecture at the distal tibia and radius, as periarticular bone lesion, catabolic (erosion) and anabolic (osteophytes) in arthropathies inflammatory. The purpose of this study is to evaluate premenopausal women with long-standing RA and to explore the relationship between parameters of systemic and localized bone involvement.

Methods: Eighty consecutive RA premenopausal women were evaluated. Volumetric bone mineral density, microarchitecture and finite element analysis were performed using HR-pQCT at the distal radius and tibia and compared with parameters from 160 female healthy controls matched by age and body mass index. Localized bone involvement was also analyzed using HR-pQCT in the metacarpophalangeal and proximal interphalangeal joints to identify erosions and osteophytes.

Results: The mean age of RA patients was 39.4 ± 6.7 years and disease duration 9.8 ± 5.3 years. RA patients had impaired trabecular, cortical and bone strength parameters, at the distal radius and tibia, compared with healthy controls ($p < 0.05$). Bone erosions and osteophytes were found in 75% and 41.3% of patients, respectively. Comparing patients with and without erosions, at the distal radius and tibia, a lower cortical vBMD (radius: 980 ± 72 versus 1021

± 47mgHA/cm^3, p=0.03; tibia: 979 ± 47 versus 1003 ± 34 mgHA/cm^3, p=0.04) and higher cortical porosity (radius: 2.8 ± 2.5 versus 1.8 ± 1.6%, p=0.04; and tibia: 3.7 ± 1.6 versus 2.7 ± 1.6%, p=0.01) were observed in patients with erosions. At the distal radius, osteophyte volume was positively correlated with trabecular vBMD (0.392, p=0.02), trabecular number (0.381, p=0.03) and stiffness (0.411, p=0.02), and negatively with trabecular separation (-0.364, p=0.04).

Conclusion: This study showed that premenopausal women with long-standing RA had systemic bone fragility at peripheral sites. Moreover, erosions were associated mainly with cortical bone fragility at the distal radius and tibia, and osteophytes correlated with repair of trabecular bone at the radius.

Disclosure: M. Perez, None; **C. Figueiredo**, None; **L. Sales**, None; **A. MEDEIROS-RIBEIRO**, None; **L. Takayama**, None; **D. Domiciano**, None; **K. Bonfiglioli**, None; **V. Caparbo**, None; **R. Pereira**, None.

Abstract Number: 0172

Assessing Relevant Joints for Monitoring CPPD Diseases: A Systematic Literature Review of Imaging Techniques by the OMERACT Ultrasound – CPPD Subgroup

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Imaging has been extensively used for the diagnosis of Calcium Pyrophosphate Deposition Disease (CPPD) but the exact prevalence of joint calcifications at imaging in patients with CPPD has not been thoroughly assessed.

This systematic literature review (SLR) is aimed to estimate the prevalence of calcium crystal deposition in peripheral joints by imaging in suspected or definite CPPD patients to establish relevant joints for CPPD monitoring.

Methods: After defining PICOs, Pubmed and Embase were searched from inception to October 2020 for identifying studies that evaluated the application of Conventional Radiography (CR), Ultrasound (US), Computed Tomography (CT) and Dual Energy Computed Tomography (DECT) in detecting calcifications at peripheral joints in patients with defined or probable CPPD diagnosis. Search strategies based on Mesh terms and free text were applied. Six reviewers independently screened the articles. In a first step, the evaluation was based only on titles and abstracts and

then, the eligible articles were evaluated in full text for inclusion and data extraction. Prespecified criteria were used for including or excluding the articles.

Results: The SLR identified 1826 manuscripts. 543 papers entered in the full text evaluation and 162 articles were finally included. Regarding the first phase, were excluded 954 abstracts, 352 as duplicate, 156 for the language, 47 for the study type, 171 for the population, 171 for the intervention and 57 for the outcome. During the full text evaluation, were excluded 49 for the unavailability of the full text, 18 as duplicate, 8 for the language, 113 for the study type, 48 for the population, 19 for the intervention and 126 for the outcome. Among included, 36 papers considered patients with definite CPPD with a total population of 1530 patients, 977 cases and 533 controls and 126 papers referred to patients with suspected CPPD with a total population of 30569 patients, 3125 affected by CPPD and 27444 controls.

The results about each joint included are summarized in the table attached (since the low number of studies that evaluated CT and DECT, respectively 7 and 1, the data are not shown). In patients with definite diagnosis, knee and wrist are the joints with the higher prevalence of calcifications at both XR and US, followed by the hip, while in patients with suspected CPPD, the knee is the most prevalent followed by the wrist, hip and shoulder (only sites with more than 50 patients assessed considered). The hand joints have the lowest prevalence of CPPD at imaging. The presence of bilateral imaging findings varies depending on the technique used, the site and the type of patient.

Confirmed CPPD Diagnosis

		KNEE	WRIST	HAND	ELBOW	SHOULDER	AC	HIP	ANKLE	FOOT
XR	Imaging positive cases/all cases	383/568 67%	283/411 69%	34/146 23%	53/109 49%	50/144 35%	37/84 44%	115/189 61%	56/209 27%	15/59 25%
	Cases positive bilaterally	59/103 57%	40/79 51%	0/1	3/11 27%	1/6 17%	9/17 53%	33/52 63%	2/36 0,06%	0
US	Imaging positive cases/all cases	265/324 82%	177/211 84%	4/42 9%	1/1 100%	0/30	4/30 13%	47/80 59%	90/209 43%	0
	Cases positive bilaterally	83/96 86%	56/80 70%	1/ 4 25%	0	0	3/ 4 75%	1/2 50%	44/68 65%	0

CPPD Ongoing Diagnosis

		KNEE	WRIST	HAND	ELBOW	SHOULDER	AC	HIP	ANKLE	FOOT
XR	Imaging positive cases/all cases	2453/2829 87%	537/1020 53%	104/617 17%	39/78 50%	85/192 44%	27/31 87%	327/889 37%	25/58 43%	27/51 53%
	Cases positive bilaterally	548/1167 50%	218/339 63%	67/89 75%	27/28 96%	46/52 88%	0/2	101/201 50%	22/22 100%	20/21 95%
US	Imaging positive cases/all cases	241/260 93%	30/84 36%	2/39 5%	1/1 100%	4/12 33%	29/29 100%	1/1 100%	11/49 22%	8/37 22%
	Cases positive bilaterally	1/3 33%	1/2 50%	0	0	0	0	0	0	0

Conclusion: According to the results of this SLR, knees and wrists could be the sentinel joints for CPPD detection by imaging.

For each joint, are illustrated the ratio between positive joints and the overall number of evaluated joints and the ratio between the joints positive bilaterally and the overall number of joints evaluated bilaterally. AC: Acromion-Clavicular

Disclosure: A. Adinolfi, None; **S. Sirotti**, None; **G. Sakellariou**, None; **E. Cipolletta**, None; **E. Filippucci**, None; **F. Porta**, None; **P. Sarzi-Puttini**, None; **C. Scire**, None; **H. Keen**, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **P. Mandl**, MSD, 5, 6, Celgene, 5, 6, Lilly, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6; **C. Pineda**, None; **L. Terslev**, None; **M. D'Agostino**, Sanofi, 2, 6, Novartis, 2, 6, BMS, 2, 6, Janssen, 2, 6, Celgene, 2, 6, Roche, 2, 6, AbbVie, 2, 6, UCB, 2, 6, Eli Lilly, 2, 6; **N. Damjanov**, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Gideon Richter, 2, 6, Merck, 2, 6, Novartis, 2, 6; **A. Iagnocco**, None; **G. Filippou**, None.

Abstract Number: 0173

Greater High-density Lipoprotein Levels over Time Are Linked to Lower Coronary Plaque Formation, Regression and Stabilization of High-risk Lesions in Rheumatoid Arthritis

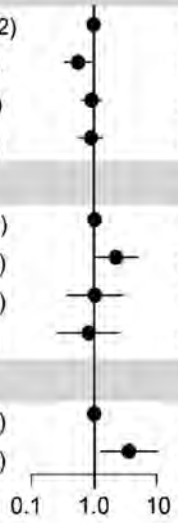
George Karpouzas[1], sarah ormseth[2], Elizabeth Hernandez[2] and Matthew Budoff[3], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]The Lundquist Institute, Harbor-UCLA Medical Center, Torrance, CA, [3]Division of Cardiology, and the Lundquist Institute ay Harbor-UCLA Medical Center, Torrance, CA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The relationship between serum lipoproteins and cardiovascular (CV) disease risk in rheumatoid arthritis (RA) is complex. Their levels and function may vary based on disease activity and medication use. Treatment benefits on high-density lipoprotein (HDL) levels, structure and behavior, in response to treatment have been described. Yet, the impact of HDL-C levels over time on coronary atherosclerosis progression in RA is unknown. We here evaluated the influence of HDL-C levels over time on long-term coronary plaque formation and progression in RA.

Methods: One hundred one patients without CV disease who underwent computed tomography angiography study of coronary atherosclerosis had repeat assessments after 6.9±0.3 years to evaluate plaque progression. Clinical, laboratory and medication data were captured at baseline and throughout follow-up. Robust logistic regression assessed associations between time-averaged HDL-C and likelihood of new plaque formation in segments without plaque at baseline, and transition of partially calcified to fully calcified plaque. Robust multinomial logistic regression evaluated effects of time-averaged HDL-C on likelihood of new noncalcified, partially or fully calcified plaque in segments without plaque (compared to remaining without plaque), and noncalcified plaque regression or transition to partially or fully calcified plaque (compared to remaining noncalcified). Models accounted for clustering of segments within patients and adjusted for Framingham CV risk score, segment location, time-averaged CRP, prednisone dose, bDMARD and statin duration, obesity, and time-averaged triglycerides.

Outcome	No. of coronary segments (%)	Adjusted OR (95% CI) per 1-SD increment in time-averaged HDL*	*P* value
New plaque formation			
None to none	1331 (93.2)	1.00 (reference)	—
None to non-calcified	20 (1.4)	0.56 (0.35-0.92)	0.021
None to mixed	21 (1.5)	0.93 (0.65-1.33)	0.678
None to calcified	56 (3.9)	0.91 (0.59-1.41)	0.673
Non-calcified plaque transition			
Non-calcified to non-calcified	42 (42.9)	1.00 (reference)	—
Non-calcified to none	32 (32.7)	2.21 (1.02-4.83)	0.045
Non-calcified to mixed	16 (16.3)	1.02 (0.37-2.87)	0.961
Non-calcified to calcified	8 (8.2)	0.81 (0.26-2.51)	0.712
Mixed plaque progression			
Mixed to mixed	36 (69.2)	1.00 (reference)	—
Mixed to calcified	16 (30.8)	3.56 (1.25-10.17)	0.018



*Adjusted for Framingham D'Agostino cardiac risk score, proximal segment location, time-averaged CRP, biologic DMARD treatment duration, statin treatment duration, cumulative prednisone dose, waist-to-height ratio, and time-averaged triglycerides.

Figure 1. Impact of HDL-C over time on coronary plaque progression in RA.

Results: Participants were mostly female (n=87, 86.1%), 51.5±10.3 years old and time-averaged HDL-C was 51.7±13.9. Ninety-seven new plaques formed in segments without baseline plaque; 20 were noncalcified, 21 partially, and 56 were fully calcified. Time-averaged HDL-C had no effect on new total plaque formation (adjusted OR 0.88 [95% CI 0.64-1.21]). However, each SD increase in time-averaged HDL-C associated with a 44% lower chance of new noncalcified plaque (adjusted OR 0.56 [95% CI 0.35-0.92], Figure 1); no effect on incident partially or fully calcified plaque was observed. Of 98 noncalcified plaques at baseline, 42 remained unchanged, 32 regressed, 16 transitioned to partially and 8 to fully calcified plaques. Each SD increase in time-averaged HDL-C yielded a 2.2-fold greater chance of noncalcified plaque regression (adjusted OR 2.21 [95% CI 1.02-4.83]). Sixteen of 52 partially calcified plaques transitioned to fully calcified lesions; each SD increment in time-averaged HDL-C) predicted 3.5-fold greater odds of transition of partially to fully calcified plaque (adjusted OR 3.56 [95% CI 1.25-10.17]).

Conclusion: Higher HDL-C over time predicted regression of existing and decreased formation of new higher-risk noncalcified plaque. It also associated with transition of partially calcified to more stable fully calcified plaque. All effects were independent of RA treatment duration, prednisone dose and statin exposure.

Disclosure: G. Karpouzas, None; **s. ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0174

Imaging Neoangiogenesis in Rheumatoid Arthritis II (INIRA II): Whole-body Synovial Uptake of ^{99m}Tc-Maraciclatide Correlates with Power Doppler Ultrasound and Serum Neoangiogenic Biomarkers

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SESSION INFORMATION

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Background/Purpose: ^{99m}Tc-maraciclatide (^{99m}Tc-M) (Serac Healthcare) is a radio-labelled tracer which binds with high affinity to integrin $\alpha_v\beta_3$, a cell-adhesion molecule up-regulated on neoangiogenic blood vessels. It therefore has the potential to image synovial inflammation at the whole-body level.

Our group has previously published interim results showing that ^{99m}Tc-M uptake correlated with power Doppler ultrasound (PDUS) in 25 patients with rheumatoid arthritis (RA)[1]. This study now explores correlation with PDUS and serum biomarkers in a larger group of patients.

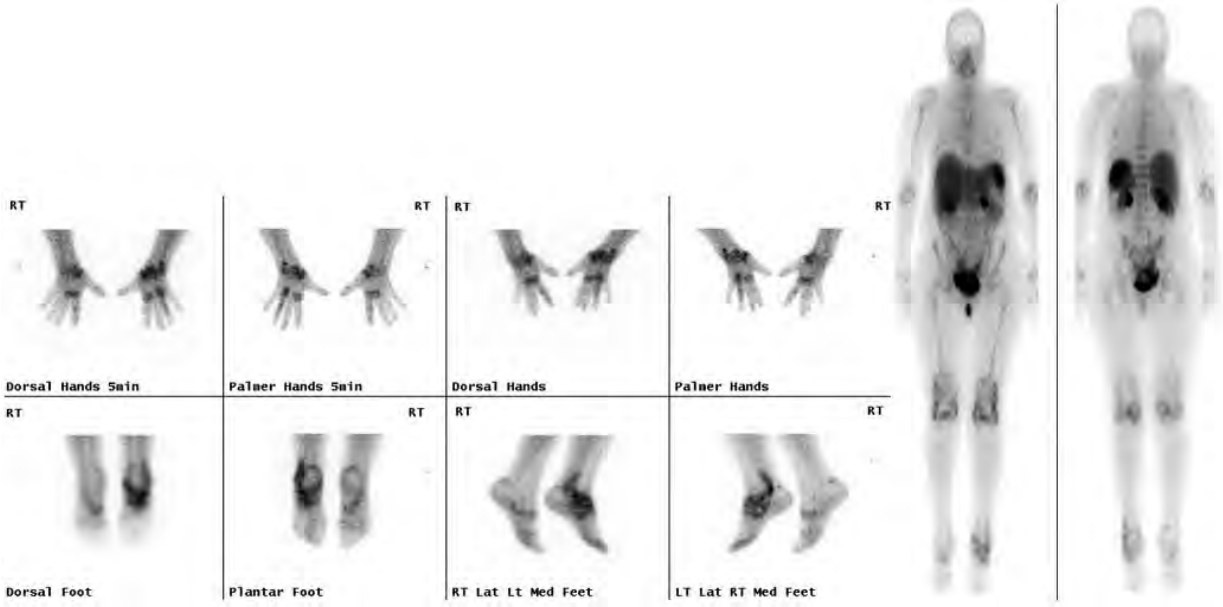

Figure 1: 99mTc-maraciclatide whole body anterior and posterior images; dorsal, palmer, and oblique hand images; and dorsal, plantar, and medial/lateral foot images
Images of a patient with DAS28-CRP of 7.09 showing uptake to the left ring finger flexor and left peroneal tendons, and left PIP4, left MCP2/3, right PIP2, right MCP2/4, bilateral wrist, bilateral elbow, bilateral knee, left ankle, and right mid foot joints

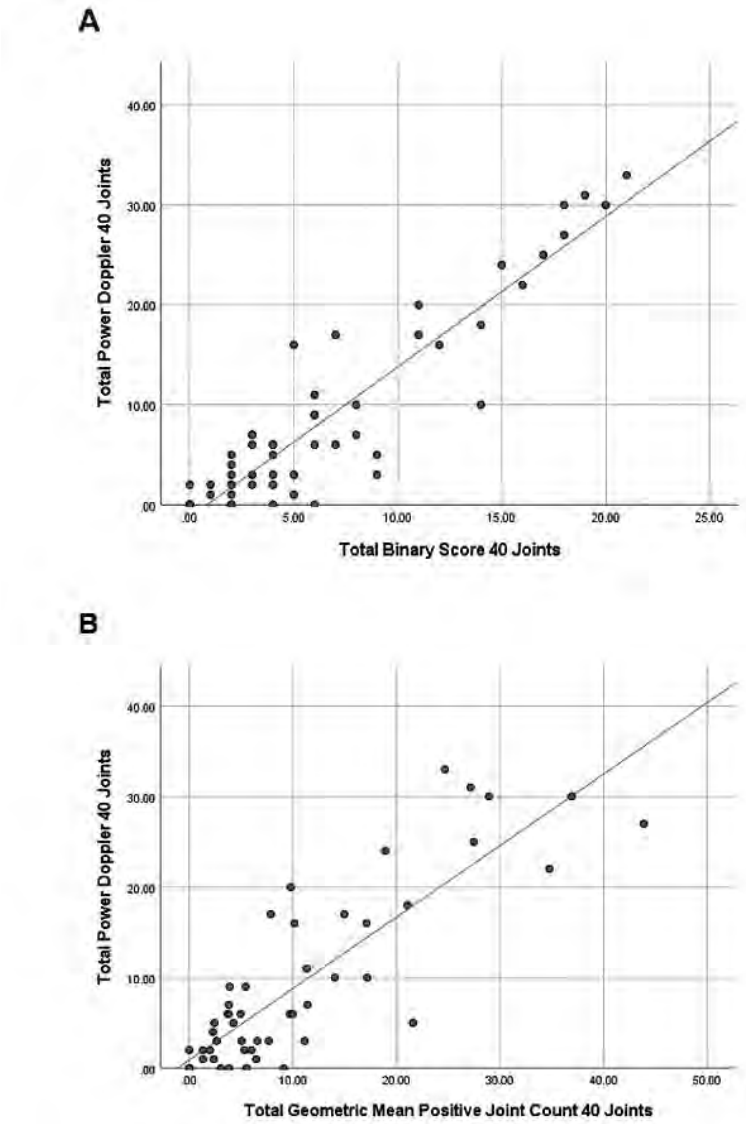

Figure 2 Correlation between Power Doppler Ultrasound and ^{99m}Tc-maraciclatide uptake
A – Total Power Doppler Ultrasound vs Total Binary Score of 40 Joints, r = 0.90, r^2 = 0.82
B – Total Power Doppler Ultrasound vs Total Geometric Mean of 40 Joints, r = 0.85, r^2 = 0.72

Methods: 50 patients with RA (mean disease duration 12.8 (SD 8.2, 1-35 range) years, mean DAS28-CRP 4.8 (1.2, 1.9-7.1)) fulfilling ACR 2010 classification criteria were recruited. Patients had an ultrasound scan of 40 joints. Each joint was scored on a scale of 0-3 for greyscale and PD with a total score calculated per patient.

Within 3 hours patients were injected with 740 MBq of ^{99m}Tc-M. Whole body planar views, and static hand and foot views were taken 2 hours after injection. Acquisition time was 20 minutes for whole body and 20 minutes for hand and foot views. ^{99m}Tc-M images were scored as positive or negative uptake for each joint (binary score). A quantitative (geometric mean, GM) score was calculated for each joint where there was uptake with this corrected for background uptake. Total binary and GM scores per patient were calculated.

Sera was taken from each patient on the day of imaging with analysis of 24 biomarkers via multiplex bead assay.

Total PDUS and ^{99m}Tc-M scores were tested for correlation using Pearson's coefficient of determination (r^2). Spearman's rank correlation (r_s) was used to evaluate correlation between serum biomarkers and imaging modalities. Significance was set at $p< 0.05$.

Results: ^{99m}Tc-M uptake was clear on visual assessment of small and large joints (Figure 1). Strong correlation was observed when total PDUS was compared to total binary ($r^2 = 0.82$, Figure 2) as compared to total GM ^{99m}Tc-M scores ($r^2 = 0.72$). Total GSUS scores also correlated with total binary ($r^2 = 0.74$) and total GM ^{99m}Tc-M scores ($r^2 = 0.60$). p was < 0.001 for all values.

There was substantial inter-assessor agreement with a kappa of 0.79 for PDUS, and 0.82 for ^{99m}Tc-M scan binary scoring respectively. Concordance correlation coefficient was strong at 0.82 for GM scoring.

^{99m}Tc-M uptake at a single joint level had a sensitivity of 78% (95% CI 73-83), specificity of 91% (89-92), positive predictive value (PPV) of 57% (53-61), and negative predictive value (NPV) of 96% (95-97). When assessing small joints alone, sensitivity was 78% (95% CI 72-83), specificity was 94% (93-96), PPV was 72% (67-77), and NPV was 96% (95-97).

There was moderate correlation between MMP3 and total binary ($r_s = 0.44$, $p = 0.002$), and GM ($r_s = 0.52$, $p = 0.001$) scores. There was statistically significant weak correlation between VEGF, IL6, YKL40, IL8 and both imaging modalities (Table 1).

Conclusion: ^{99m}Tc-M uptake is highly correlated with PDUS, and weakly to moderately correlated with serum biomarkers highlighting its potential as an alternative imaging modality that captures total synovial inflammatory load. Recruitment is underway to expand the data to a larger group of patients.

Table 1: Spearman's rank correlation (r_s, p value)

	Power Doppler	Binary Score	Geometric Mean	VEGF	IL-6	MMP-3	YKL-40	IL-8
Power Doppler	X							
Binary Score	0.825 p = 0.001	X						
Geometric Mean	0.734 p = 0.001	0.880 p = 0.001	X					
VEGF	0.368 p = 0.009	0.258 p = 0.074	0.267 p = 0.063	X				
IL-6	0.275 p = 0.05	0.362 p = 0.010	0.390 p = 0.005	0.035 p = 0.809	X			
MMP-3	0.380 p = 0.007	0.439 p = 0.002	0.518 p = 0.001	-0.016 p = 0.916	0.241 p = 0.096	X		
YKL-40	0.064 p = 0.659	0.336 p = 0.017	0.303 p = 0.032	0.022 p = 0.879	0.248 p = 0.082	0.247 p = 0.087	X	
IL-8	0.249 p = 0.082	0.352 p = 0.012	0.236 p = 0.099	-0.006 p = 0.966	0.452 p = 0.001	0.278 p = 0.053	0.0281 p = 0.048	X

Reference 1. Attipoe L, Garrood T, Subesinghe S, et al. Imaging Neoangiogenesis in Rheumatoid Arthritis (INIRA): Whole-Body Synovial Uptake of a 99mTc-Labelled RGD Peptide Is Highly Correlated with Power Doppler Ultrasound - ACR Meeting Abstracts. Arthritis Rheumatol. 2019;71 (suppl. https://acrabstracts.org/abstract/imaging-neoangiogenesis-in-rheumatoid-arthritis-inira-whole-body-synovial-uptake-of-a-99mtc-labelled-rgd-peptide-is-highly-correlated-with-power-doppler-ultrasound/

Disclosure: L. Attipoe, None; **S. Subesinghe**, None; **C. Blanco Gil**, None; **M. Opena**, None; **K. Steel**, None; **S. Ryan**, None; **S. Norton**, None; **M. Rosser**, Serac Healthcare, 3; **G. Cook**, None; **A. Cope**, None; **T. Garrood**, None.

Abstract Number: 0175

Correlation of Subclinical Synovitis with Juvenile Idiopathic Arthritis Outcome Measurements

Patricia Vega-Fernandez[1], Edward Oberle[2], Michael Henrickson[1], Jennifer Huggins[1], Mekibib Altaye[3], Amy Cassedy[4], Johannes Roth[5] and Tracy Ting[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Nationwide Children's Hospital, Columbus, OH, [3]Cincinnati Children's Hospital, Cincinnati, OH, [4]Cincinnati Children's Hospital and Medical Center, Cincinnati, OH, [5]University of Ottawa, Ottawa, ON, Canada

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most common rheumatologic disease of childhood. Active joint count (AJC) is one of the key JIA Core Set variables. However, AJC is a subjective measurement with poor-to-moderate inter-rater agreement. Musculoskeletal Ultrasound (MSUS) is a radiation-free, objective imaging tool currently being used to assess joint inflammation. A novel joint-specific MSUS scoring system for JIA was recently proposed[1]. The aims of this study are: 1. Determine the frequency of subclinical synovitis as per MSUS in all peripheral joints in JIA, 2. Correlate AJC as determined by expert clinician physical examination with moderate to severe MSUS synovitis, 3. Examine the correlation between MSUS synovitis and Juvenile Arthritis Disease Activity Score (JADAS) and patient-reported outcomes

Methods: Data obtained from a previously described study looking to determine the key joints to perform a MSUS examination in JIA[1] was used for the current analysis. Briefly, JIA patients presenting with an AJC >4 and able to perform MSUS within 1 week of starting a Disease-modifying Antirheumatic Drug were eligible for this study. Clinical data including physician global assessment (PhGA), patient global assessment (PGA), patient pain visual analogue scale (VAS) and the Child Health Assessment Questionnaire (CHAQ) were obtained. A comprehensive AJC examination and a 42 joint MSUS examination by an American College of Rheumatology MSUS certified pediatric rheumatologist were performed at baseline and at 3 months. Gray-scale B mode and Power Doppler (PD) images were obtained for each view. Images were scored following a semiquantitative scoring system ranging from 0-normal to 3-severe. Subclinical synovitis was defined as grade 2 and 3 synovitis appreciated by MSUS only. Clinical-JADAS 10 (cJADAS-10) was calculated by the addition of PhGA, PGA, and AJC up to 10 joints. Pearson correlation was used to assess the correlation between AJC and subclinical synovitis. Spearman's correlation coefficients were calculated to determine the association between MSUS synovitis, cJADAS-10 and patient-reported outcomes

Results: A total of 30 patients were enrolled. Table 1 shows the frequency of subclinical synovitis per joint. In general, MSUS detects moderate to severe synovitis in about 25% of the joints determined as normal by physical exam.

Table 1. Frequency of Subclinical Synovitis in Peripheral Joints

Baseline visit *				
	Joint with arthritis by PE *only* (%)	**Joint with arthritis by MSUS *only* (%)**	**Joint with arthritis *on both* PE and MSUS (%)**	**Joint with arthritis by PE *and/or* MSUS (%)**
PIP (n=300)	19 (6.3)	104 (34.7)	75 (25)	198 (66)
MCP (n=300)	20 (6.7)	117 (39)	64 (21.3)	201 (67)
Wrist (n=60)	7 (11.7)	11 (18.3)	32 (53.3)	50 (83.3)
Elbow (n=60)	9 (15)	18 (30)	12 (20)	39 (65)
Shoulder (n=60)	5 (8.3)	13 (21.7)	3 (5)	21 (35)
Hip (n=60)	7 (11.7)	9 (15)	1 (1.7)	17 (28.3)
Knee (n=60)	2 (3.3)	15 (25)	27 (45)	44 (73.3)
Ankle (n=60)	10 (16.7)	16 (26.7)	25 (41.7)	51 (85)
Toes (n=300)	21 (7)	97 (32.3)	10 (3.3)	128 (42.7)
Follow-up visit**				
	Joint with arthritis by PE *only* (%)	**Joint with arthritis by MSUS *only* (%)**	**Joint with arthritis on *both* PE and MSUS (%)**	**Joint with arthritis by PE *and/or* MSUS (%)**
PIP (n=290)	35 (12.1)	67 (23.1)	69 (23.8)	171 (59)
MCP (n=290)	25 (8.6)	73 (25.2)	54 (18.6)	152 (52.4)
Wrist (n=58)	9 (15.5)	13 (22.4)	22 (37.9)	44 (75.9)
Elbow (n=58)	5 (8.6)	20 (34.5)	10 (17.2)	35 (60.3)
Shoulder (n=58)	3 (5.2)	13 (22.4)	2 (3.5)	18 (31)
Hip (n=58)	4 (6.9)	4 (6.9)	0 (0)	8 (13.8)
Knee (n=58)	2 (3.5)	17 (29.3)	12 (20.7)	31 (53.5)
Ankle (n=58)	11 (19)	13 (22.4)	17 (29.3)	41 (70.7)
Toes (n=290)	21 (7.2)	77 (26.6)	11 (3.8)	109 (37.6)

*n = 30 participants ** n= 29 participants. PIP: proximal interphalangeal joint, MCP: metacarpal phalangeal joint. PE: physical examination, MSUS: musculoskeletal ultrasound

Except for the knee where the correlation between MSUS synovitis and AJC was moderate, the correlation between MSUS and AJC for all other peripheral joints was slight to fair (Table 2). MSUS synovitis and patient reported outcomes including CHAQ, patient pain VAS and PGA had slight to fair correlation for B-Mode and moderate correlation for PD. Correlation between MSUS and cJADAS-10 was moderate for both B Mode and PD images. (Table 3)

Conclusion: Subclinical synovitis is commonly observed in a cohort of newly diagnosed JIA patients with greatest differences in digits. The fair to moderate correlation of MSUS synovitis with cJADAS-10 and patient-reported outcomes, suggest that MSUS assesses a different, possibly more objective, domain not determined by traditional JIA outcome measurements. MSUS has the potential to support the diagnosis and assessment of JIA

Table 2. Correlation between MSUS and Physical Exam for each Joint Area

	Baseline		Follow up Visit	
	Pearson Correlation[a]	p Value	Pearson Correlation[a]	p Value
PIPs	0.28	<0.001	0.29	<0.001
MCPs	0.2	0.001	0.3	<0.001
Wrist	0.31	0.015	0.23	0.076
Elbow	0.1	0.417	0.18	0.178
Shoulder	0.1	0.457	0.1	0.45
Hip	0.04	0.734	0.07	0.573
Knee	0.49	<0.001	0.4	0.002
Ankle	0.08	0.542	0.17	0.186
Toes	0.02	0.676	0.03	0.6

PIP: proximal interphalangeal joint, MCP: metacarpal phalangeal joint. [a]Strength of the correlation calculated using Pearson correlation as follows: small: 0 – 0.29, medium: 0.30--0.49, strong 0.5-1.

Table 3. Correlation Between Patient-Reported Outcomes, Disease Activity Measure and MSUS Findings

	Baseline MSUS synovitis		Follow-up MSUS synovitis	
	B-Mode (p-value)	Power-Doppler (p-value)	B-Mode (p-value)	Power-Doppler (p-value)
Patient pain VAS	0.33 (0.079)	0.29 (0.122)	0.01 (0.957)	0.07 (0.735)
PGA	0.37 (0.047)	0.45 (0.012)	0.17 (0.372)	0.12 (0.546)
CHAQ	0.29 (0.126)	0.39 (0.032)	-0.02 (0.915)	0.12 (0.551)
cJADAS-10	0.39 (0.035)	0.57 (0.001)	0.24 (0.205)	0.46 (0.012)

MSUS: musculoskeletal ultrasound, VAS: visual analogue scale, PGA: patient global assessment, CHAQ: Child Health Assessment Questionnaire. clinical Juvenile Arthritis Disease Activity Score in 10 joints (cJADAS-10). Strength of the correlation calculated using Spearman correlation as follows: very weak: 0.0-0.19, weak: 0.2-0.39, moderate 0.4-0.59, strong 0.6-0.79, very strong 0.8-1.0.

Disclosure: P. Vega-Fernandez, None; **E. Oberle**, None; **M. Henrickson**, None; **J. Huggins**, None; **M. Altaye**, None; **A. Cassedy**, None; **J. Roth**, None; **T. Ting**, None.

Abstract Number: 0176

Semi-quantitative Chest Computed Tomography (CT) Analysis in Pediatric Rheumatologic (PR) Patients with Diffuse Lung Disease

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Pediatric Rheumatologic Diffuse Lung Disease Score (PRDLDS)

Pediatric Rheumatologic Diffuse Lung Disease Score (PRDLDS)

I. Component Scores for 1 - 5 (Score 6 lobar Zones [0 – 4]) [120]

(Key: 0 = 0; 1 = 1 - 10%; 2 = 11 - 25%; 3 = 26 - 50%; 4 > 50%)

[1-5] Parenchymal Score		RUL*	RML*	RLL*	LUL*	Ling*	LLL*
1) Pure GGO (pGGO)	[24]						
2) Consolidation (C)	[24]						
3) Pure Fibrosis (PF)	[24]						
4) Honeycomb Cysts (HC)	[24]						
5) Emphysema (E)	[24]						

6) Pulmonary Nodules/Cavitations/Cysts/Masses (Score for R & L Lung & Central vs. Peripheral) [18]
(Small Nodule < 1 cm; Large Nodule = 1 - 3 cm, Mass > 3 cm; Cyst: thin wall

Score		R | L (0 or 1)		R | L [check marks]
1) Small Nodules	[2]	|	Central	|
2) Large Nodules	[2]	|		
3) Cavitary	[2]	|	Peripheral	|
4) Numerous (> 10)	[4]	| (0 or 2)		
5) Cysts	[2]	| (0 or 1)	Upper Predominance	
6) Cysts (> 10)	[4]	| (0 or 2)		
7) Mass/Consolidation	[2]	| (0 or 1)	Lower Predominance	

7) Effusions/PT Score (score R & L lung)

		None/Small R | L (0 or 1)	Moderate/Large R | L (2 or 3)
1) Pleural Effusion	[6]	|	|
2) Pericardial Effusion	[3]	(0 or 1)	(2 or 3)
3) Pleural thickening (PT)	[2]	| (0 or 1)	
4) Other (comments)			

8) Pulmonary Artery Size/Pulmonary Hypertension (Score PA/AA) [11]

(Circle 1 answer)

PA/AA < 1.2	PA/AA > 1.2
0	11

9) Other Comments: _____

II. Total Score: _____ **out of 160 points**

*** RUL = R Upper Lobe, RML = R Middle Lobe, RLL = R Lower Lobe, LUL = L Upper Lobe, Ling = Lingula, LLL = L Lower Lobe.**

Background/Purpose: Spiral chest CT (SCT) is commonly used to evaluate subclinical lung disease in pediatric rheumatology. However, there are no validated scoring tools to objectively evaluate disease severity. The purpose of this study was to determine the feasibility of a semi-quantitative chest CT scoring system (Pediatric Rheumatologic

Table 2. Patient Demographics and Disease

Demographics and Disease	Disease Group (N = 42)	Disease Control Group (N = 34)	Normal Control Group (N = 44)
Mean Age, Yrs (SD)	13.8 ± 3.92	13.6 ± 3.60	10.8 ± 5.08
Gender (Female: Male)	34 F: 8 M	29 F: 5 M	18 F: 26 M
Rheumatologic Disease			
Systemic Sclerosis (SSC)	7	5	
Mixed Connective Tissue Disease (MCTD)	7	5	
Systemic Juvenile Idiopathic Arthritis (sJIA)	4	0	
Juvenile Dermatomyositis (JDM)	1	1	
Anca-Associated Vasculitis (AAV)	11	4	
Systemic Lupus Erythematosus (SLE)	12	19	
Tumor/Malignancy			21
Other			23

Table 3. Scoring Domains and Final Score for Pediatric Rheumatologic Diffuse Lung Disease Score (PRDLDS)

Scoring Domains	Disease Group (N = 42)	Disease Control Group (N=34)	Normal Control Group (N = 44)
Total Parenchymal Score	Median (IQR)	Median(IQR)	(Median: IQR)
S1	7.0 (IQR: 11.50)	0.0 (IQR: 0.00)	0.0 (IQR: 1.00)
S2	2.0 (IQR: 8.25)	2.5 (IQR: 6.00)	2.0 (IQR: 4.00)
S3	3.0 (IQR: 11.25)	1.5 (IQR: 6.25)	1.0 (IQR: 5.00)
Total Pulm Nod/Cav/Cyst/Mass Score			
S1	1.0 (IQR: 2.00)	0.0 (IQR: 0.00)	0.0 (IQR: 0.00)
S2	0.0 (IQR: 1.25)	0.0 (IQR: 0.00)	0.0 (IQR: 0.00)
S3	0.0 (IQR: 1.00)	0.0 (IQR: 0.25)	0.0 (IQR: 0.00)
Total Effusion (Pleural & Pericardial)/Pleural Thick Score			
S1	0.0 (IQR: 2.00)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
S2	0.0 (IQR: 0.00)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
S3	0.0 (IQR: 0.50)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
Pulm HTN Score			
S1	0.00 (IQR: 2.75)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
S2	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
S3	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)	0.00 (IQR: 0.00)
Final Score			
S1	13.5 (IQR: 16.25)	0.0 (IQR: 2.25)*	0.0 (IQR: 2.00)
S2	3.0 (IQR: 14.25)	3.5 (IQR: 8.25)	2.5 (IQR: 6.00)
S3	4.5 (IQR: 12.00)	2.0 (IQR: 9.50)	1.5 (IQR: 6.75)
Final Score-Pulmonary HTN Score			
S1	10.5 (IQR: 13.00)	0.0 (IQR: 0.25)*	0.0 (IQR: 1.00)
S2	2.5 (IQR: 12.50)	2.5 (IQR: 6.25)	2.0 (IQR: 4.75)
S3	4.5 (IQR: 12.00)	2.0 (IQR: 7.50)	1.5 (IQR: 6.75)

Legend: Domain 1 (Total Parenchymal Score); Domain 2 (Total Pulmonary Nodules/Cavitations/Cysts/Masses Score); Domain 3 (Total Pleural and Pericardial Effusions/Pleural Thickness Score); Domain 4 (Pulmonary Hypertension Score); S1 (Radiologist 1); S2(Radiologist 2); S3 (Radiologist 3); IQR (Interquartile Range from 25th to 75th percentile)

Diffuse Lung Disease Score [PRDLDS], Table 1) to assess the prevalence of diffuse lung disease (DLD) assessed by SCT in pediatric rheumatologic patients.

Methods: Three radiologists with varying DLD imaging experience independently scored 1-2 mm inspiratory chest CT scans (96 non-contrast/24 contrast) in 120 pediatric subjects (DG: N=42 PR patients with DLD; DCG: N=34 PR patients without DLD; and NCG: N=44 pediatric normal control subjects with chest CT scans) from 3 medical centers (Children's Hospital of LA, Stanford Children's Health, Mayo Clinic). The SCT scoring system was developed as a modification of the Goldin scoring system[1] for systemic sclerosis adults to account for the full spectrum of DLD findings in PR patients (Table 2). It quantifies the extent of disease for 6 lung zones based on 4 domains: 1) parenchymal domain score (PDS); 2) pulmonary nodule/cavitary/cyst/mass DS; 3) total effusion/pleural thickening DS; and 4) pulmonary hypertension domain score (PHDS).

Results: The overall prevalence of DLD in the disease group based on a cutoff score of ≥ 8 for all lung zones was 68% by the most experienced scorer (S1) in comparison to 41% (S2, S3); the prevalence of total disease was primarily driven by the PDS (74% [S1], 38% [S2, S3] with significant contributions from pure ground glass opacities (GGO) and pure fibrosis (PF) subscores (SS). There was lower disease prevalence noted in domains 2 (7 - 19%), 3 (2 - 5%), and 4 (4 - 23%). Prior DLD scoring experience impacted both the PDS and GGO & PF subscores; radiologist (S1) identified more disease and had greater specificity to discriminate between groups than the more naïve DLD scorers; for S1 scorer: DG - PDS (median 7.0 [IQR:11.5]), GGO SS (median 2.5 [IQR: 5.5]), PF SS (median 4.0 [IQR: 5.00] vs. DCG and NCG both having (median 0.0 [IQR:0.0]). Refer to Table 3.

Conclusion: Semi-quantitative scoring using the PRDLDS is a feasible tool to assess DLD in PR patients. Preliminary data revealed that our PR patients had mild DLD which is primarily contributed by parenchymal disease. Our data demonstrated high inter-rater variability for parenchymal scoring, and problems with PHDS which supports that 1) further training with DLD imaging experts is necessary to improve the reliability and validity of the PRDLDS in quantifying milder lung disease ; 2) non-contrast CTs make it more difficult to evaluate PH accurately; 3) quantitative CT assessment tools are needed to reliably evaluate pulmonary interstitial lung disease in pediatric rheumatologic patients. We are currently evaluating our study cohort with CALIPER (Computer Aided Lung Informatics for Pathology Evaluation and Rating), a quantitative chest CT analyzer that is validated in adults with DLD.

Reference:

1. Goldin JG, Lynch DA, Strollo DC, et al. High-resolution CT scan findings in patients with symptomatic scleroderma-related interstitial lung disease. *Chest*. 2008;134(2):358-367.

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Abstract Number: 0177

Dual-Energy Computed Tomography Three Material Decomposition Improves the Sensitivity of Gout Detection

Justin Tse[1], Douglas Kondro[2], Yves Pauchard[3], Andrea Veljkovic[4], Viviane Frasson[5], David Holdsworth[6], Sarah Manske[7], Paul MacMullan[8] and Peter Salat[7], [1]UNIVERSITY OF CALGARY, Calgary, AB, Canada, [2]STEMCELL Technologies, Cambridge, United Kingdom, [3]Department of Electrical and Software Engineering, Schulich School of Engineering, Calgary, AB, Canada, [4]University of British Columbia, Department of Orthopaedics, Vancouver, BC, Canada, [5]University of Calgary, Human Performance Lab, Calgary, AB, Canada, [6]University of Western Ontario, Department of Surgery, London, ON, Canada, [7]University of Calgary, Department of Radiology, Calgary, AB, Canada, [8]University of Calgary, Department of Rheumatology, Calgary, AB, Canada

SESSION INFORMATION

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Background/Purpose: Gout, a curable musculoskeletal disease, is characterized by the deposition and accumulation of monosodium urate (MSU) crystals within affected joints. Dual-energy computed tomography (DECT), an x-ray-based imaging technique, can non-destructively and non-invasively detect and localize large MSU depositions (*i.e*. tophi). Two recent advancements have made significant contributions to improve DECT's MSU specificity and sensitivity: (1) software generated virtual pseudo-monochromatic images (VMI); and (2) three-material decomposition (3MD) post-processing algorithms. To our knowledge, no studies have examined the effects of combining these two techniques when applied to MSU. Thus, we propose combining VMI and 3MD to improve DECT's sensitivity to MSU.

Methods: A bone (HA) quality phantom (Quality Assurance in Radiology in Medicine) and in-house MSU phantom were scanned together with a fast-kVp switching (80 and 140 kVp) DECT scan (GE Revolution GSI, GE Healthcare). The HA phantom contained rods of 100, 400, and 800 mgHA. The MSU phantom was created by mixing varying concentrations of MSU with 3% agarose to achieve 0, 0.0344, 0.133, 0.283, and 0.652 g/mL. VMIs at 50 and 65 keV were generated (GE Gemstone Spectral Imaging) and decomposed *via* 3MD (Tse *et al*., 2017) into three tissue volumes: soft tissue, bone, and MSU. Results of 3MD + VMI were compared with manufacturer (GE)-based material decomposition (GEMD) and commonly used dual-thresholding.

Additionally, a participant with gout was scanned with above-mentioned DECT protocol, with their foot resting atop both HA and MSU phantoms. Resulting images were decomposed into tissue-specific images *via* 3MD + VMI and GEMD.

Statistical analysis was performed on mean values acquired from 10 × 10 × 10 voxels placed within identical soft tissue (100% agar), bone (HA phantom), and MSU (MSU phantom) regions-of-interest within each decomposed tissue volume. A statistical significance was noted if $p < 0.05$.

Results: The combination of 3MD + VMI performed equally to the manufacturer's in-house material decomposition (GEMD), and both techniques appeared to perform better than common dual-thresholding at all HA and MSU concentrations (Table 1). The only exception between 3MD + VMI and GEMD was the highest MSU concentration (0.652 g/mL), in which 3MD + VMI was slightly significantly different from the standard (p = 0.0479).

Table 1. Mean reported results, and their p-value when compared to the known concentration, of 10 × 10 × 10 voxels placed within ROIs of the HA and MSU phantom under varying decomposition techniques (i.e. 3MD + VMI, GEMD, and Dual-Threshold). * = significant difference (p < 0.05) from standard

Phantom	Concentration	3MD + VMI (*p*-value)	GEMD (*p*-value)	Dual-Threshold (*p*-value)
HA	100 mgHA	89.7 mgHA (0.945)	129.2 mgHA (0.105)	N/A
	400 mgHA	393 mgHA (0.546)	460.1 mgHA (0.475)	N/A
	800 mgHA	796 mgHA (0.196)	904.6 mgHA (0.426)	N/A
MSU	0.0 g/mL	0.0 g/mL (0.223)	0.0 g/mL (>0.999)	N/A
	0.0344 g/mL	0.038 g/mL (0.762)	0.03 g/mL (0.0823)	0.0 g/mL (<0.0001*)
	0.133 g/mL	0.156 g/mL (0.432)	0.09 g/mL (0.345)	0.015 g/mL (<0.0001*)
	0.283 g/mL	0.248 g/mL (0.256)	0.139 g/mL (0.389)	0.390 g/mL (0.252)
	0.652 g/mL	0.650 g/mL (0.0479*)	0.652 g/mL (>0.999)	0.644 g/mL (0.760)

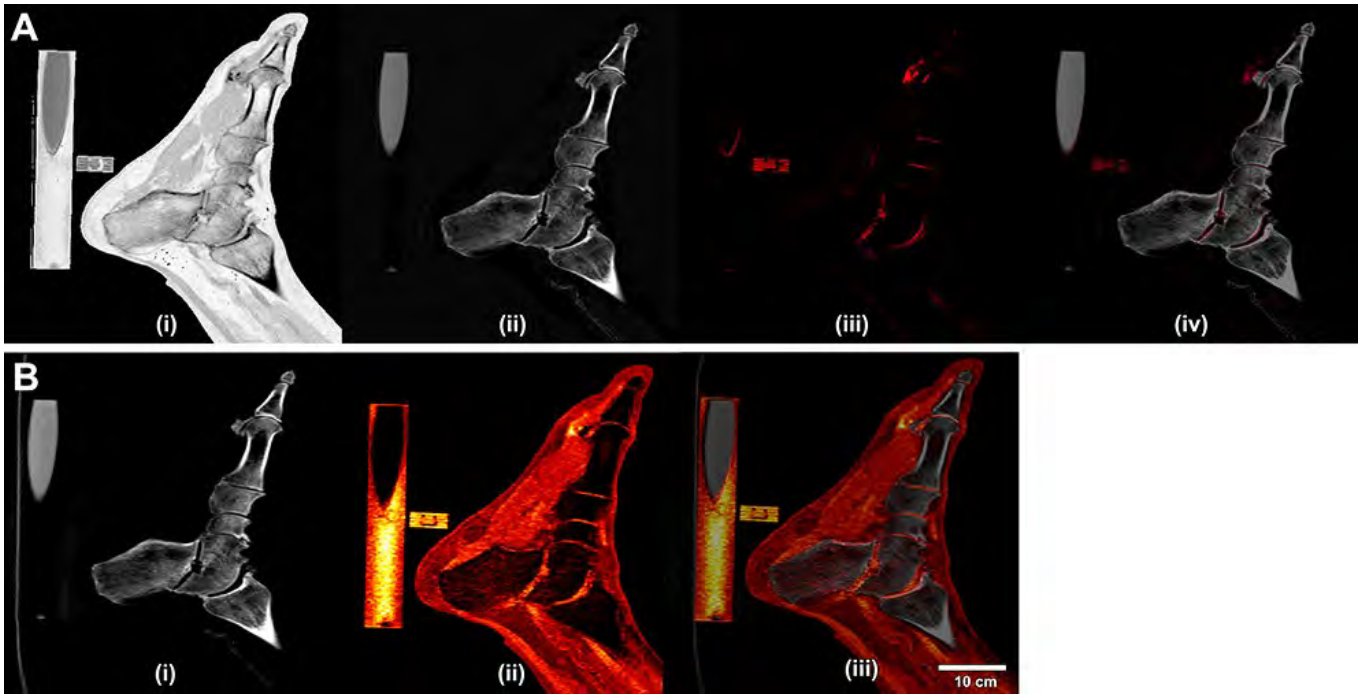

Figure 1. Results of DECT decomposition. (A) The combination of 3MD and VMI results in the distinct and separate visualization of (i) soft tissue, (ii) bone, (iii) MSU, and (iv) an overlay of bone and MSU. (B) GEMD results in the distinct visualization of (i) bone, (ii) MSU deposits, and (iii) an overlay of bone and MSU.

The combination of 3MD + VMI produced clearer depictions MSU deposition (Fig. 1Aiii), when compared to images generated *via* GEMD (Fig. 1Bii), due to the decomposition of a third tissue (*e.g*. soft tissue).

Conclusion: No significant differences between 3MD + VMI *vs* GEMD were observed when measuring HA and MSU concentrations of phantoms being the only objects within the field-of-view (FOV). A preliminary demonstration of 3MD + VMI's enhanced visualization of soft tissue, bone, and MSU was performed (Fig. 1A). Further analysis is required to determine whether the addition of human anatomy may cause artefacts (*e.g*. beam hardening) that will affect measurements of lower MSU concentrations. Additionally, further work can determine whether a better pair of VMIs could further improve the available detection limit by maximizing the DECT decomposition ratio.

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Abstract Number: 0178

Abdominal Obesity May Confound Accuracy of Cardiovascular Risk Prediction in Rheumatoid Arthritis; Can Coronary Atherosclerosis Imaging and Biomarkers Help?

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Accurate cardiovascular risk stratification is essential in rheumatoid arthritis (RA) care. Previous studies evaluated the impact of obesity (defined as body mass index) on all cause and cardiovascular disease (CVD) mortality in RA patients. However, the effect of obesity and particularly abdominal (central) obesity on the predictive ability of cardiovascular risk score models in RA is unclear. We explored the obesity-related predictive value of the Framingham Cardiovascular Risk Score (FRS-CVD) in RA patients without known CVD and interrogated the potential utility of cardiovascular imaging and serum biomarkers to improve risk prediction.

Methods: We evaluated 150 RA patients with coronary CT angiography for atherosclerosis assessment and prospective follow-up for cardiovascular events over 6.0±2.4 years. The 10-year FRS-CVD score was computed at baseline. Abdominal obesity was defined as waist circumference >88 cm in females and >102 cm in males. Extensive plaque was defined as having >5 coronary segments with atherosclerosis. Serum highly-sensitive cardiac troponin I (hscTnI) was measured with Erenna immunoassay. Serum leptin, which is closely related to obesity, was measured with radioimmunoassay. Differences in the predictive value of the FRS-CVD in non-obese versus obese and patients and those with high (>22.1 ng/mL) versus low (< 22.1 ng/mL) leptin were evaluated using area under the curve (AUC) comparisons. The incremental predictive value of extensive plaque and elevated hscTnI (>2.1, highest tertile) beyond the FRS-CVD was explored using change in AUC, continuous net reclassification index (NRI) and integrated discrimination improvement (IDI).

Results: The predictive accuracy of the FRS-CVD was lower in obese patients (AUC 0.660, [95% CI 0.487-0.832] versus non-obese: AUC 0.95 [95% CI 0.897-1.007], *P* for difference = 0.002, Figure 1A) and those with higher leptin (AUC 0.618 [95% CI 0.393-0.842]; versus lower leptin: AUC 0.874 [95% CI 0.772-0.976], *P* for difference = 0.042,

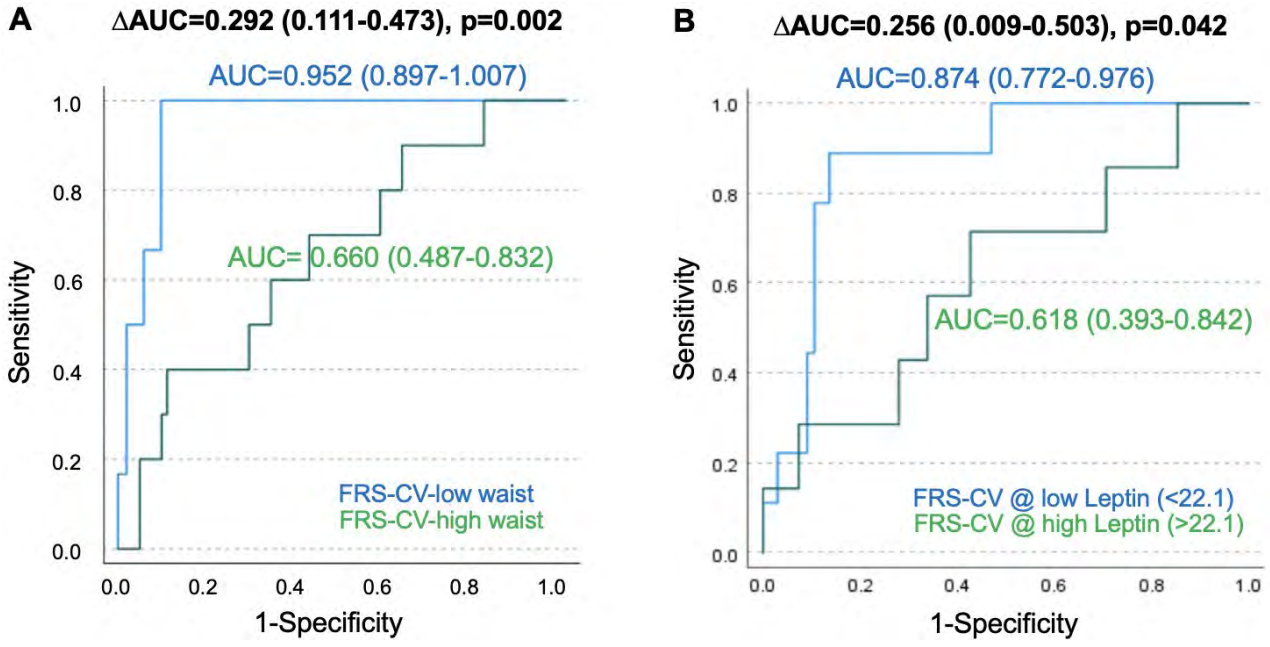


Figure 1. Predictive accuracy of the Framingham cardiovascular risk score according to obesity and leptin levels.

Table 1. Serum hscTnI and extensive coronary plaque increase cardiovascular risk prediction accuracy in obese RA patients

	Obese (High waist circumference)		
CVD Risk Models	**AUC change (95%CI)**	**NRI (95%CI)**	**IDI (95%CI)**
FRS-CV score	referent	referent	referent
FRS-CV score+ hscTnI high1/3 vs. FRS-CV score	**0.123 (0.011-0.274)***	**0.917 (0.309-1.474)***	**0.095 (0.012-0.323)***
FRS-CV score +SIS >5 vs. FRS-CV score	0.082 (-0.009-0.290)	**0.702 (0.098-1.407)***	**0.150 (0.005-0.431)***
FRS-CV score +hscTnI high1/3 +SIS>5 vs. FRS-CV score	**0.179 (0.058-0.378)***	**1.093 (0.517-1.574)***	**0.188 (0.060-0.526)***

AUC: Area under the receiver operator characteristics curve, NRI: Net reclassification index, IDI: Integrated discrimination improvement
*p<0.05

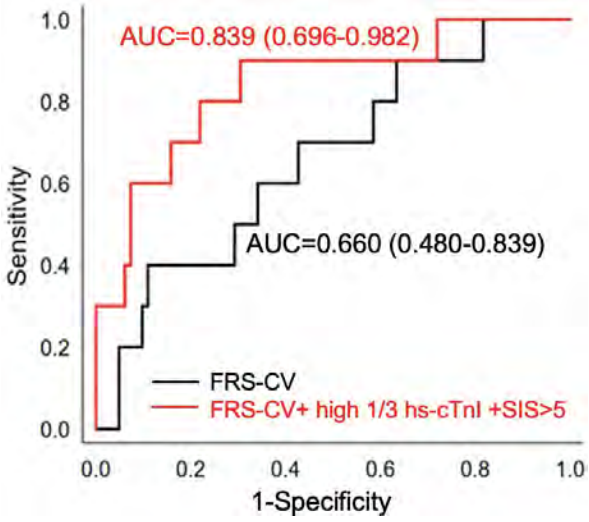


Figure 2. Added predictive accuracy of hscTnI and extensive plaque presence versus Framingham-CVD score alone in obese RA patients.

Figure 1B). The added predictive ability of hscTnI and extensive plaque was evaluated for obese patients given the observed limitations of the FRS-CVD for this subgroup. Sequential addition of elevated hscTnI and extensive plaque presence to the FRS-CVD base model significantly improved risk prediction estimates based on changes in all AUC, NRI and IDI (Table 1). The final model including hscTnI and extensive plaque accurately predicted 83.9% of CVD events in the obese subgroup (Figure 2).

Conclusion: Cardiovascular risk estimate accuracy was significantly lower in RA patients who were obese. The optimization of cardiac risk stratification with the help of non-invasive assessment of coronary atherosclerosis burden and related cardiac damage biomarkers in the serum may warrant further study.

Disclosure: G. Karpouzas, None; **s. ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0179

Impaired Myocardial Flow Reserve on ^{82}Rubidium Positron Emission Tomography Imaging Predicts Adverse Events in Patients with Autoimmune Rheumatic Disease

Attila Feher[1], Nabil Boutagy[1], Evangelos Oikonomou[1], Yi-Hwa Liu[1], Edward Miller[1], Albert Sinusas[1] and Monique Hinchcliff[2], [1]Yale School of Medicine, New Haven, CT, [2]Yale School of Medicine, Westport, CT

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Coronary microvascular dysfunction (CMVD) has been described in patients with autoimmune rheumatic disease (ARD). By noninvasive evaluation of myocardial blood flow (MBF) and myocardial flow reserve (MFR) quantification, positron emission tomography (PET) imaging has emerged as the noninvasive gold standard CMVD assessment. However, to date, no large studies have evaluated PET-derived MFR in ARD patients. It is also unknown whether MFR can predict adverse events in this population.

Methods: Patients with ARD without coronary artery disease who underwent dynamic rest-stress ^{82}Rubidium PET from 05/2012-05/2019 for a clinical indication were retrospectively studied and compared to patients without ARD matched for age, gender and comorbidities. The association between MFR and a composite endpoint of mortality or myocardial infarction (MI) or heart failure (HF) admission was evaluated with time to event and Cox-regression analyses.

Results: In 101 patients with ARD (88% female, age: 62±10 years), stress MBF did not significantly differ between patients with ARD (median with interquartile range [IQR], 1.68 [IQR: 1.39 – 2.07]) compared to those without ARD (1.49 [IQR: 1.26 – 1.93]) (Figure 1A). Conversely, rest MBF was significantly higher in ARD patients (1.00 [IQR: 0.84 – 1.21]) compared to those without an ARD diagnosis (0.80 [IQR: 0.68 – 0.99]) (Figure 1B). Consequently, MFR was significantly reduced in ARD patients compared to patients without ARD (1.68 [IQR: 1.34 – 2.05] vs. 1.86 [IQR: 1.58 – 2.28]) (Figure 1C). MFR did not differ among subtypes of ARDs. During the median follow-up of 3.8 years, there were twelve deaths, two MIs and 18 HF admissions in ARD patients. In survival analysis, patients with ARD and low MFR (MFR< 1.5) had decreased event-free survival for the combined endpoint, when compared to patients with and without ARD and normal MFR (MFR >1.5) and when compared to patients without ARD and low MFR, after adjustment

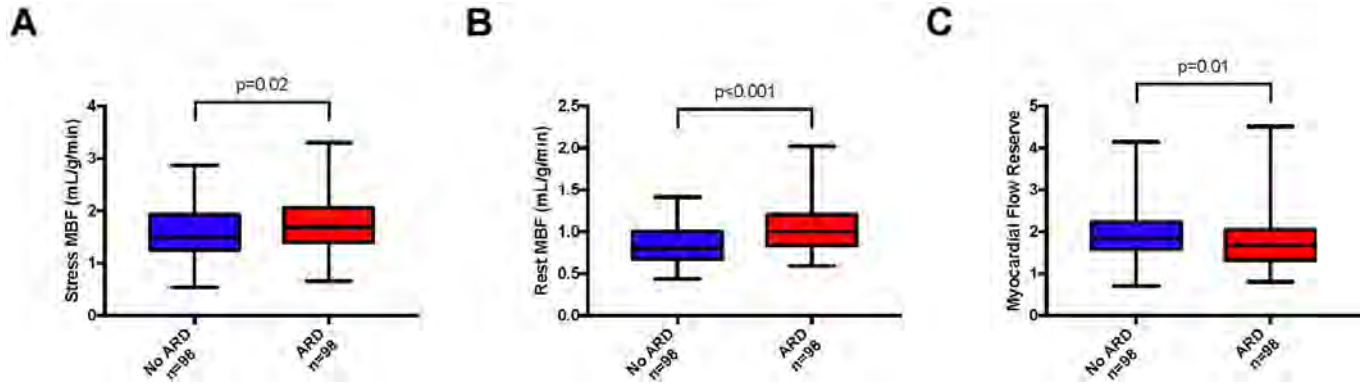


Figure 1. Stress (Panel A) and rest (Panel B) myocardial blood flow (MBF) and myocardial flow reserve values (Panel C) in patients with or without autoimmune rheumatic disease (ARD).

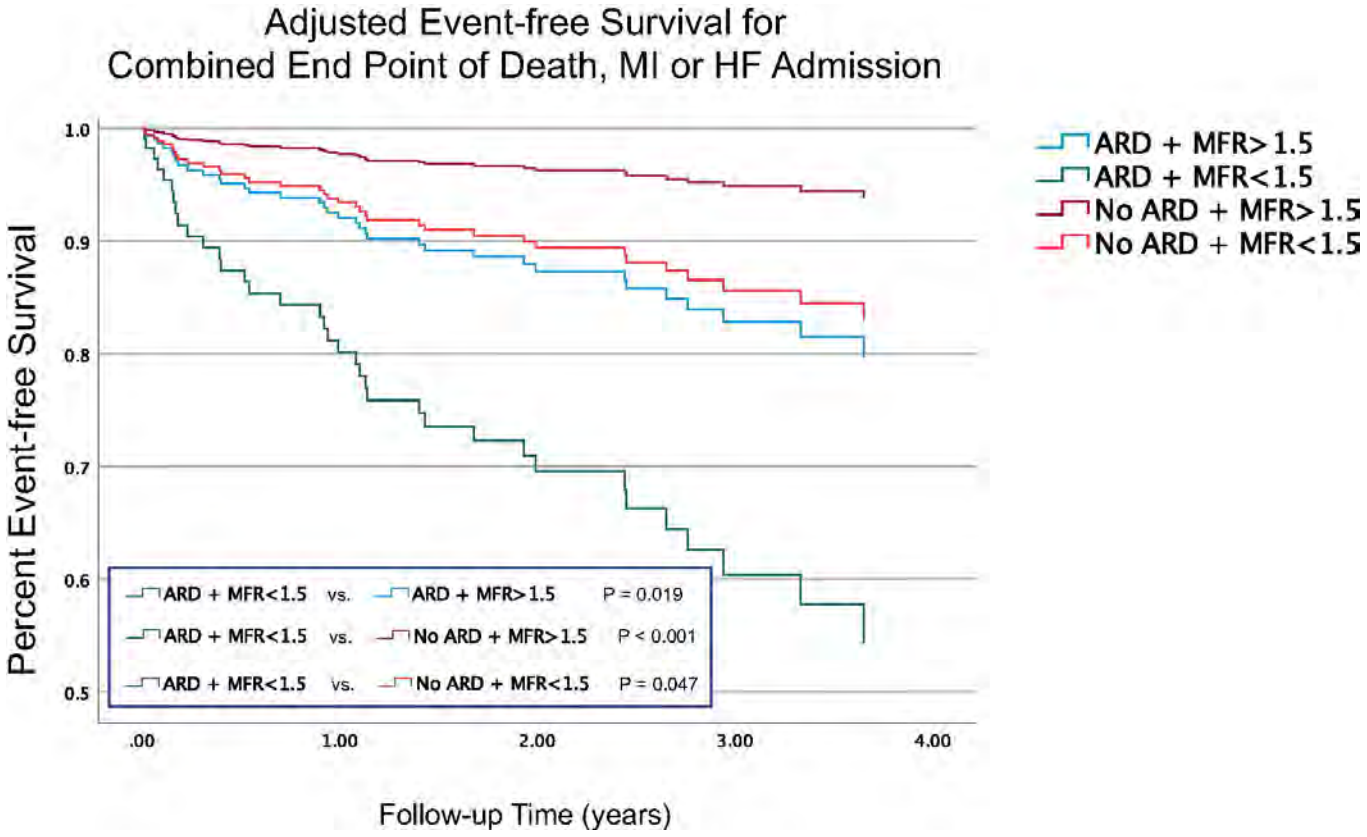


Figure 2. Kaplan Meier plots for event-free survival for the combined end point of death, myocardial infarction (MI) or heart failure (HF) admission in patients with autoimmune rheumatic disease (ARD) based on myocardial flow reserve (MFR).

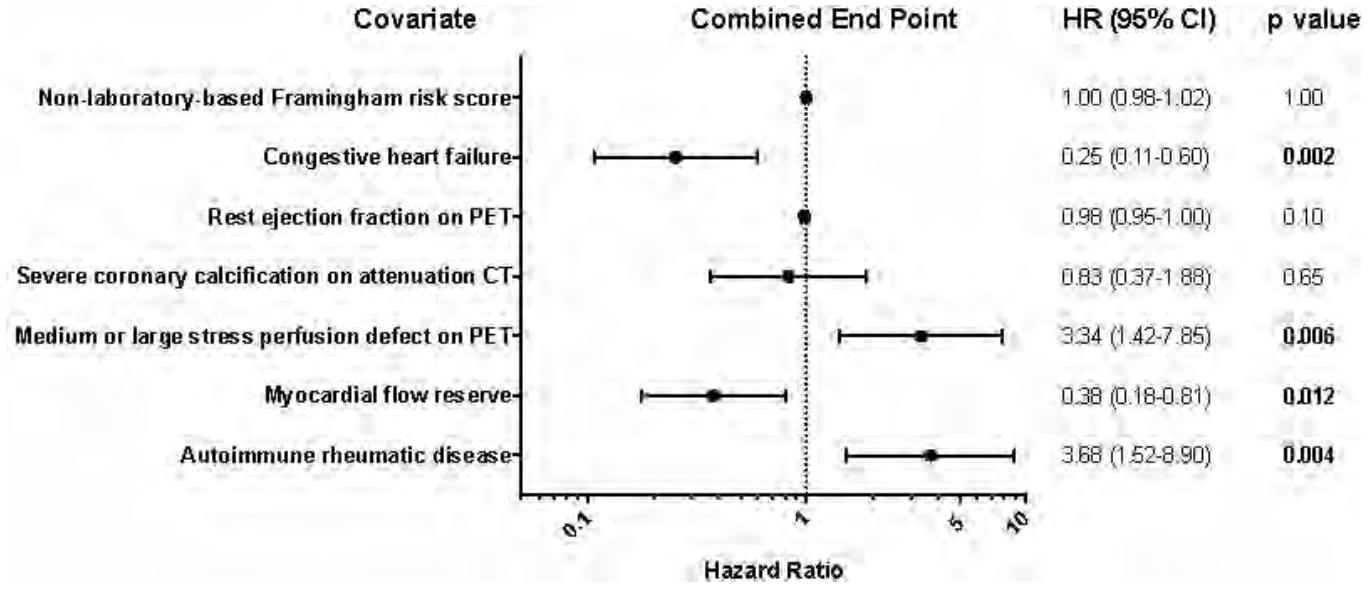


Figure 3. Forest plot of hazard ratios (HR) for the combined end point of death, myocardial infarction or heart failure admission in multivariate Cox proportional hazards regression models in patients with autoimmune rheumatic disease. CT: computed tomography, PET: positron emission tomography.

for the non-laboratory-based Framingham risk score, rest left ventricular ejection fraction, severe coronary calcification, and the presence of medium/large perfusion defects (Figure 2). In Cox-regression analysis, ARD diagnosis and MFR were both independent predictors of adverse events in ARD patients along with congestive HF diagnosis and presence of medium/large stress perfusion defects on PET (Figure 3).

Conclusion: Patients with ARD have significantly reduced PET MFR compared to age-, gender- and comorbidity-matched patients without ARD. Reduced PET MFR and ARD diagnosis are both independent predictors of adverse outcomes.

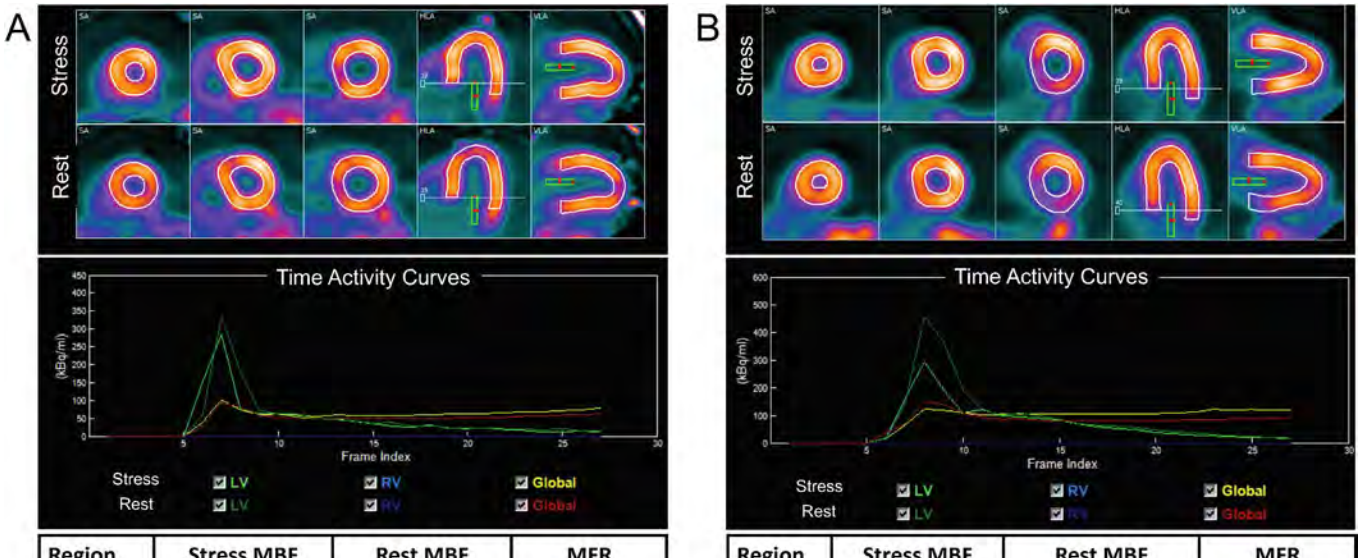
Disclosure: A. Feher, None; **N. Boutagy**, None; **E. Oikonomou**, None; **Y. Liu**, None; **E. Miller**, None; **A. Sinusas**, None; **M. Hinchcliff**, None.

Abstract Number: 0180

Impaired Myocardial Flow Reserve on ^{82}Rubidium Positron Emission Computed Tomography in Patients with Systemic Sclerosis

Attila Feher[1], Nabil Boutagy[1], Evangelos Oikonomou[1], Stephanie Thorn[1], Yi-Hwa Liu[1], Edward Miller[1], Albert Sinusas[1] and Monique Hinchcliff[2], [1]Yale School of Medicine, New Haven, CT, [2]Yale School of Medicine, Westport, CT

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM



Region	Stress MBF (mL/min/g)	Rest MBF (mL/min/g)	MFR
LAD	1.37	1.06	1.28
LCx	1.37	1.24	1.10
RCA	1.22	1.02	1.19
Global	1.32	1.08	1.22

Region	Stress MBF (mL/min/g)	Rest MBF (mL/min/g)	MFR
LAD	2.77	1.11	2.50
LCx	2.58	1.15	2.24
RCA	2.78	0.87	3.20
Global	2.71	1.04	2.60

Figure 1. Representative relative perfusion images, time activity curves and myocardial blood flow (MBF) values obtained at stress (Str) and rest (Rst) for a patient with systemic sclerosis (A) and for a healthy control subject (B). Perfusion imaging showed no perfusion defects, however for the systemic sclerosis patient blood flow quantification revealed global reduction in stress myocardial blood flow and myocardial flow reserve (<2.0) whereas the healthy control subject had normal myocardial blood flow values. SA: short axis, HLA: horizontal long axis, VLA: vertical long axis, LV: left ventricle, RV: right ventricle, LAD: left anterior descending artery, LCX: left circumflex artery, RCA: right coronary artery.

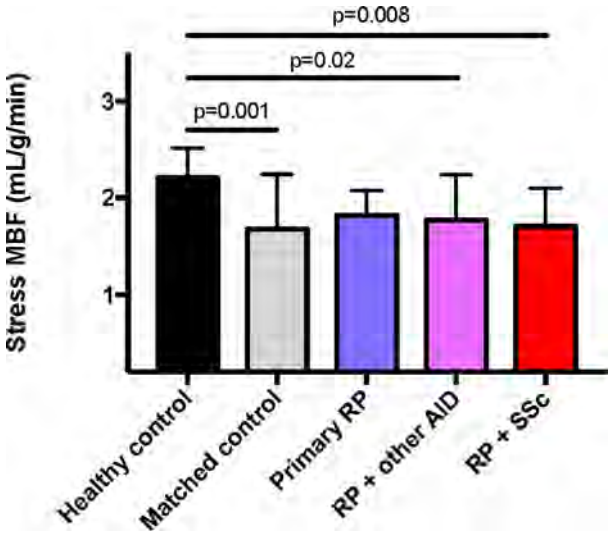


Figure 2. Stress myocardial blood flow (MBF) in healthy controls, matched control patients without Raynaud phenomenon (RP) and in patients with primary RP, secondary RP with autoimmune disease (AID) other than systemic sclerosis (SSc) and in patients with SSc.

Background/Purpose: To investigate the association between Raynaud phenomenon (RP) and coronary microvascular dysfunction, we measured myocardial flow reserve (MFR) using positron emission tomography/computed tomography (PET/CT) in patients with primary and secondary RP and controls.

Methods: Patients with RP and matched controls who underwent dynamic rest-stress 82-Rubidium PET/CT from 09/2012-09/2019 for evaluation of chest pain or dyspnea were studied. Differences in heart rate-blood pressure product corrected MFR and clinical predictors of reduced MFR (< 2.0) were determined (Figure 1.).

Results: 49 patients (80% female, 65 ± 11 years) with RP (11 with primary RP, 18 with systemic sclerosis (SSc) and 20 with other autoimmune diagnoses (AID, n=6 systemic lupus erythematosus, n=6 rheumatoid arthritis, n=4 overlap syndrome, n=2 Sjogren's syndrome, n=2 inflammatory arthritis), 49 patients without RP matched for age, gender and cardiovascular co-morbidities (78% female, 64 ± 13 years) and 14 healthy controls (50% female, 35 ± 5 years) were studied. Primary RP patients, healthy participants and matched control patients had comparable MFR (Figure 2.). In secondary RP patients, only those with underlying SSc had significantly reduced MFR (1.62 ± 0.32) compared to healthy participants (p=0.01, 2.22 ± 0.44) and to matched controls (p=0.03, 2.06 ± 0.61). In univariate (Fig 3A) and multivariable logistic regression (Figure 3B), only SSc was a significant predictor of reduced MFR. We have also identified a correlation between time since autoimmune disease diagnosis and MFR (r= -0.37; 95% CI: -0.61 to -0.09; p=0.01).

Conclusion: Our findings suggest that only secondary, not primary, RP is associated with reduced MFR, and that SSc-RP patients have reduced MFR compared to primary RP and other autoimmune disease patients. Larger prospective studies are warranted to fully elucidate the prognostic value of MFR in patients with secondary RP.

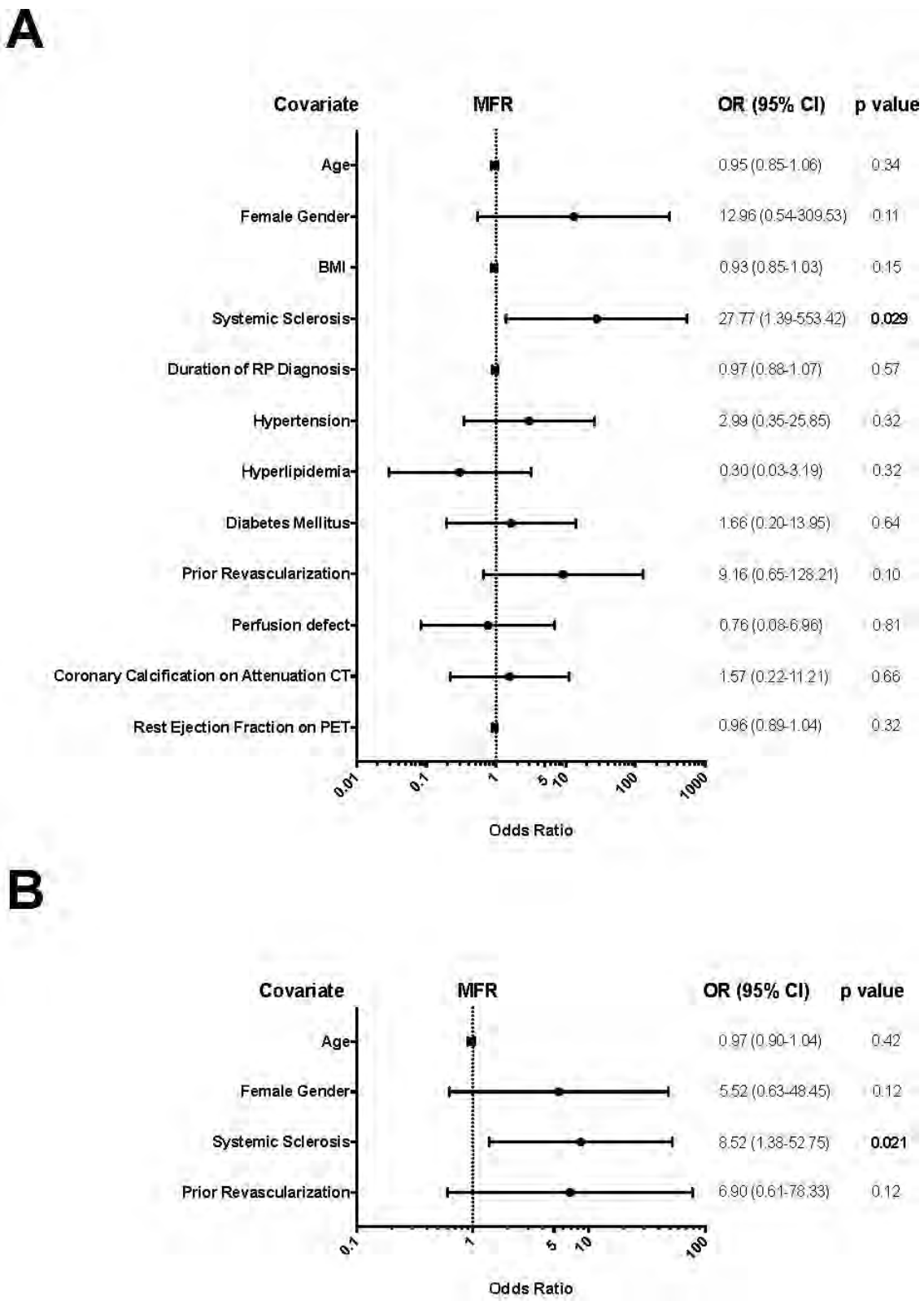


Figure 3. Forest plot of odds ratios (OR) of clinical predictors of reduced myocardial flow reserve (MFR <2.0) in univariate (A) and multivariate (B) regression models. BMI: body mass index, RP: Raynaud phenomenon, CT: computed tomography, PET: positron emission tomography, CI: confidence interval.

Disclosure: A. Feher, None; **N. Boutagy**, None; **E. Oikonomou**, None; **S. Thorn**, None; **Y. Liu**, None; **E. Miller**, None; **A. Sinusas**, None; **M. Hinchcliff**, None.

Abstract Number: 0181

Magnetic Resonance Imaging Findings in Early Rheumatoid Arthritis: Are There Differences Based on Autoantibody Status?

Caitrin Coffey[1], Gavin McKenzie[1], Nicholas Rhodes[1], Cassondra Hulshizer[1], Cynthia Crowson[2], John Davis[1] and Kerry Wright[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Magnetic resonance imaging (MRI) is increasingly used as an adjunct to the physical examination in early rheumatoid arthritis (RA). Characteristic differences in MRI findings between patients with early seropositive and seronegative RA have not previously been described. We aimed to determine whether hand and/or wrist MRI findings differed between patients with incident RA based on autoantibody status.

Methods: Patients with incident RA from a population-based cohort between 1999-2014 who fulfilled either the 1987 or 2010 ACR/EULAR classification criteria for RA were retrospectively reviewed. Patients who underwent MRI of the hand and/or wrist within ± 1 year of fulfillment of the earlier of 1987 or 2010 classification criteria as part of their routine clinical care were identified using Current Procedural Terminology (CPT) codes. Studies were confirmed via manual chart review. MRI images were reviewed and scored according to the Outcome Measures in Rheumatology Clinical Trials (OMERACT) RA MRI scoring system (RAMRIS), by an experienced musculoskeletal radiologist blinded to patients' clinical data. Studies with incomplete images or artifact precluding scoring were excluded at the radiologist's discretion. Serial studies of the ipsilateral hand or wrist were excluded for each patient. RAMRIS scores were compared between seronegative (RF-, CCP-) and seropositive (RF+ and/or CCP+) patients using generalized linear models, with random intercepts to account for multiple studies per patient.

Results: 86 patients with a total of 137 MRI studies of the hand and/or wrist were included for RAMRIS scoring. RF and/or CCP were negative in 53 (62%) of patients. Patients were 71% female, mean age 54.7 (SD 12.5) years, 95% white, 19% current smokers with no significant differences between groups.

57 total hand studies were scored. Mean total hand RAMRIS score was 7.4 (SD 5.1) for seropositive and 8.9 (SD 6.3) for seronegative patients. Mean synovitis, bone erosions, and bone marrow edema scores were comparable between groups (Table).

55 total wrist studies were scored. Mean total wrist RAMRIS score was 9.8 (SD 13.9) for seropositive and 7.8 (SD 6.1) for seronegative patients. Mean total wrist bone marrow edema score was 7.3 (SD 11.3) for seropositive and 2.4 (SD 3.2) for seronegative patients. Mean synovitis and bone erosions scores were comparable between groups (Table).

Estimates using generalized linear models showed that wrist bone marrow edema scores were on average 4.9 RAMRIS units higher in seropositive vs seronegative patients (p=0.014). There was a trend toward higher hand bone marrow edema scores in seronegative vs seropositive patients by 1.07 RAMRIS units that did not reach significance (p=0.067). Other mean RAMRIS scores did not differ significantly between groups.

MRI Site (N)	RF and/or CCP (+)		RF and CCP (-)	
	Mean (SD*)	Median (IQR**)	Mean (SD)	Median (IQR)
Hand				
Total RAMRIS (57)	7.4 (5.1)	6.0 (3.2-10.8)	8.9 (6.3)	8.0 (4.5-11.0)
Synovitis (57)	5.0 (2.4)	4.5 (3.2-6.8)	5.5 (2.7)	5.0 (4.0-8.0)
Erosions (62)	1.5 (2.3)	0 (0-2.5)	1.9 (2.5)	1.0 (0-3.0)
Edema (62)	0.8 (1.2)	0 (0-1.5)	1.5 (2.2)	0 (0.0-2.0)
Wrist				
Total RAMRIS (55)	9.8 (13.9)	4.0 (3.0-9.0)	7.8 (6.1)	5.5 (4.0-10.8)
Synovitis (56)	3.9 (1.8)	3.0 (3.0-5.0)	4.1 (2.1)	4.0 (3.0-6.0)
Erosions (75)	2.5 (3.3)	1.0 (0.0-4.5)	1.5 (2.4)	0.0 (0.0-2.2)
Edema (75)	7.3 (11.3)	1.0 (0.0-7.0)	2.4 (3.2)	1.0 (0.0-4.0)

*SD = standard deviation; **IQR = interquartile range

Conclusion: RAMRIS scores for MRIs of the hands and wrists performed as part of routine clinical care for patients with early, incident RA varied widely. Mean wrist bone marrow edema score was significantly higher in seropositive vs seronegative patients, though mean total RAMRIS scores, synovitis scores, and bone erosions scores did not differ significantly based upon autoantibody status.

Disclosure: C. Coffey, None; **G. McKenzie**, None; **N. Rhodes**, None; **C. Hulshizer**, None; **C. Crowson**, None; **J. Davis**, Pfizer, 5; **K. Wright**, None.

Abstract Number: 0182

Tenderness and Radiographic Progression in Rheumatoid Arthritis and Psoriatic Arthritis

Irina Gessl[1], Mihaela Popescu[2], Gabriela Supp[1], Martina Durechova[1], Michael Zauner[1], Josef Smolen[1], Daniel Aletaha[3] and Peter Mandl[1], [1]Medical University of Vienna, Vienna, Austria, [2]Maisonneuve Rosemont Hospital, Longueuil, QC, Canada, [3]Medical University Vienna, Vienna, Austria

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Imaging of Rheumatic Diseases Poster (0149–0182)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: In rheumatoid arthritis (RA) and psoriatic arthritis (PsA), swelling is regarded as a sign of synovitis and is associated with radiographic progression. However, recent studies show that tenderness might only be a sign of inflammation in early, but not in long-standing disease. Furthermore, the association of tenderness with radiographic progression is not clear. The aim of this study was to assess the predictive value of tenderness in RA and in PsA generally as well as in early and long- standing disease.

Methods: Patients with RA and PsA with at least one tender joint were included. Sonographic (Power Doppler (PD) and gray-scale (GS)) and clinical examination (tenderness and swelling) of 22 joints of the hands as well as x-ray of the hands were performed. Radiographs were scored for erosions and joint space narrowing (JSN) and progression

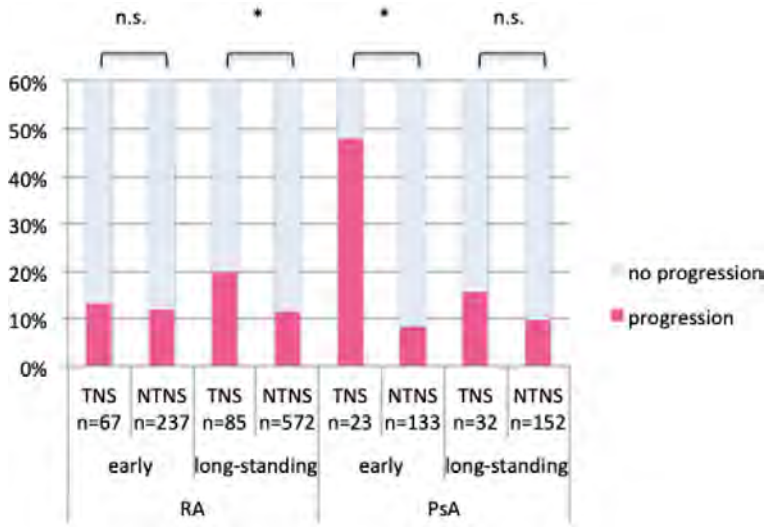


Figure 1. The proportion of joints with progression in tender non-swollen joints (TNS) and non-tender non-swollen joints (NTNS) in patients with early and long-standing rheumatoid arthritis (RA) and psoriatic arthritis (PsA).

in each joint was assessed on a follow-up x-ray after 2 years. Patients were divided into early (≤3 years) and long-standing (≥5 years) disease groups. Logistic regression analyses (forward stepwise conditional approach) including tenderness, GS and PD (model 1) as well as additional factors erosion and JSN at baseline (model 2) in non-swollen joints were calculated for each group.

Results: We included 2.288 joints in RA and 484 joints in PsA. In early RA, only PD remained in model 1 (OR 3.58 95%CI 1.50-8.57, p< 0.01) and only JSN remained in model 2 (OR 1.83, 95%CI 1.26-2.65, p< 0.01). In long-standing RA only PD (OR 2.78, 95%CI 1.53-5.08, p< 0.01) and tenderness (OR 2.00, 95%CI 1.09-3.64, p=0.02) remained in model 1, while only JSN (OR 1.27, 95%CI 1.12-1.44, p< 0.01) and PD (OR 2.19, 95%CI 1.15-4.17, p=0.02) remained in model 2.

In early PsA, only tenderness (OR 6.60, 95%2.04-21.31, p=0< 0.01) remained significant in model 1, while in model 2, only erosions (OR 30.37, 95%CI 5.26-175.37, p< 0.01) remained significant. In model 1 in long-standing PsA, only PD (OR 10.36, 95%CI 3.25-33.03, p< 0.01) remained in the model. In model 2 in long-standing PsA only JSN (OR 2.59, 95%CI 1.59-4.22, p< 0.01) remained significant.

Conclusion: The results of this study show that tenderness in non-swollen joints is not a major risk factor for subsequent radiographic progression in RA and PsA. In all observed groups, tenderness did not remain in the model after adding JSN and erosions suggesting that tenderness might be rather an indicator of structural damage than of current inflammation. Over all groups, PD showed a higher association with radiographic progression than tenderness except for early PsA, where tenderness seems to be a risk factor for subsequent damage.

Disclosure: I. Gessl, Boehringer Ingelheim, 6; **M. Popescu**, None; **G. Supp**, None; **M. Durechova**, None; **M. Zauner**, None; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Aletaha**, AbbVie, 2, 5, Janssen, 2, 5, Medac, 2, 5, Merck, 2, 5, 6, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Novartis, 2, 5, 6, Bristol-Myers Squibb, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6; **P. Mandl**, MSD, 5, 6, Celgene, 5, 6, Lilly, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6.

Abstract Number: 0183

Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 24-Week Results from the Phase 3, Randomized, Double-blind Clinical Trial for CsDMARD-IR and Bio-IR Patients

Merav Lidar[1], Jacob Aelion[2], Gareth Scott Tarr[3], Kim Papp[4], Lisa Barcomb[5], Ahmed M. Soliman[5], Wenjing Lu[6], Ann Eldred[5] and Andrew Ostor[7], [1]Chaim Sheba Medical Center, Ramat Gan, Israel, [2]Arthritis Clinic and West Tennessee Research Institute, Jackson, TN, [3]Winelands Medical Research Centre and the Institute of Orthopaedics and Rheumatology (IOR), Winelands Medi-Clinic Orthopaedic Hospital, Stellenbosch, South Africa, [4]K Papp Clinical Research and Probity Medical Research, Waterloo, ON, Canada, [5]Abbvie Inc., North Chicago, IL, [6]AbbVie Inc., North Chicago, [7]Monash University, Cabrini Hospital, and Emertius Research, Malvern, Australia

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Risankizumab (RZB) is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding to its p19 subunit. RZB is being investigated as a treatment for adults with psoriatic arthritis (PsA).

Methods: KEEPsAKE 2, a double-blind, phase 3 trial, evaluated the safety and efficacy of RZB vs. placebo (PBO) for the treatment of active PsA in patients that had previous inadequate response or intolerance to conventional synthetic disease modifying antirheumatic drug (csDMARD-IR) or 1 or 2 biologic therapies (Bio-IR). The KEEPsAKE 2 trial enrolled adults with a diagnosis of active PsA, active plaque psoriasis or nail psoriasis, ≥ 5 swollen joints, and ≥ 5 tender joints.

Patients were randomized (1:1) to receive blinded subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16. The primary endpoint was the proportion of patients achieving 20% improvement in the American College of Rheumatology score (ACR20) at week 24. Table 1 shows primary and secondary endpoints by prior biologic therapy utilization (0 or ≥ 1). Efficacy was assessed using non-responder imputation incorporating multiple imputations to handle missing data due to COVID-19 (NRI-C) for categorical data and Mixed-Effect Model Repeated Measurement (MMRM) analysis for continuous data. Safety was assessed throughout the study. Results reported here are from the 24-week double-blind period; the open-label period with all patients receiving RZB is ongoing.

Results: A total of 443 patients completed the KEEPsAKE 2 analysis at 24 weeks. Overall, demographics and baseline disease characteristics were similar between the patients receiving RZB and patients receiving PBO; 237 patients were csDMARD-IR (119 RZB and 118 PBO) and 206 patients were Bio-IR (105 RZB and 101 PBO). A numerically higher proportion of patients receiving RZB achieved improvement in disease severity measures compared to those receiving PBO, regardless of prior biologic experience (Table 1). Patients receiving RZB reported numerically greater improvements in patient-reported outcomes compared to those receiving PBO, regardless of prior biologic experience (Table 1). RZB was well tolerated in patients compared to PBO, and no new safety signals were observed.

Conclusion: RZB treatment resulted in improvements in signs and symptoms of PsA compared with PBO in both csDMARD-IR and Bio-IR patients and was well tolerated with no new safety signals.

Table 1. 24 Week Efficacy Results by Prior Biologic Experience

	No Prior Biologic (csDMARD-IR)		Prior Biologic (Bio-IR)	
	RZB 150mg N = 119	PBO N=118	RZB 150 mg N=105	PBO N=101
Primary endpoint				
ACR20, %	56.3	36.6	45.7	14.9
Secondary endpoints				
HAQ-DI, change from baseline	-0.24	-0.12	-0.19	0.04
PASI 90,[a] %	56.5	11.5	53.4	8.8
ACR20 at week 16, %	54.7	27.1	41.0	23.1
MDA, %	31.4	16.1	19.0	5.9
SF-36 PCS score, change from baseline	6.09	3.04	5.58	0.51
FACIT-Fatigue score, change from baseline	5.8	4.1	4.1	1.0
ACR50, %	33.1	13.1	18.5	5.0
ACR70, %	17.6	8.3	5.7	3.0
Resolution of enthesitis,[b] %	40.3	33.7	45.3	26.4
Resolution of dactylitis,[c] %	76.5	46.4	69.6	37.9

ACR20/ACR50/ACR70, ≥ 20/50/70% improvement in American College of Rheumatology score; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASI 90, ≥ 90% reduction in Psoriasis Area Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary,
For all continuous variables, all changes are mean changes from baseline.
Due to COVID-19, between 1 and 4 data points are missing for each endpoint by treatment arm
[a]For patients with involved body surface area ≥ 3% at baseline (RZB no prior biologic N = 65; PBO no prior biologic N = 62; RZB prior biologic N = 58; PBO prior biologic N = 57)
[b]For patients with enthesitis at baseline (RZB no prior biologic N = 72; PBO no prior biologic N = 86; RZB prior biologic N = 75; PBO prior biologic N = 72)
[c]For patients with dactylitis at baseline (RZB no prior biologic N = 17; PBO no prior biologic N = 28; RZB prior biologic N = 23; PBO prior biologic N = 29)

Disclosure: M. Lidar, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Eli Lilly, 2, 5, 6, Galapagos/Gilead, 2, 5, 6, GSK, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6; **J. Aelion**, AbbVie, 5, Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb, 5, Celgene, 5, Eli Lilly, 5, Galapagos/Gilead, 5, Genentech, 5, GlaxoSmithKline,, 5, Horizon, 5, Janssen, 5, Mallinckrodt, 5, Nektar, 5, Nichi-Iko, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Sanofi-Aventis, 5, Selecta, 5, UCB, 5; **G. Tarr**, AbbVie, 1, 6, Cipla, 1, 6, Janssen, 1, 6, Merck, 1, 6, Pfizer, 1, 6; **K. Papp**, AbbVie, 2, 5, 6, Amgen, Astellas, 2, 5, 6, Bausch Health (Valeant), 2, 5, 6, Baxalta, Baxter Takeda, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Dermira, 2, 5, 6, EMD Serono, 2, 5, 6, Forward Pharma, 2, 5, 6, Galderma, 2, 5, 6, GlaxoSmithKline, 2, 5, 6, Janssen, 2, 5, 6, Kyowa Kirin, LEO Pharma, 2, 5, 6, Lilly, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Regeneron, Sanofi Genzyme, 2, 5, 6, Roche,, 2, 5, 6, Stiefel, 2, 5, 6, Sun Pharma, 2, 5, 6, UCB, 2, 5, 6; **L. Barcomb**, AbbVie, 3, 11; **A. Soliman**, AbbVie, 3, 11; **W. Lu**, AbbVie, 3, 11; **A. Eldred**, AbbVie, 3, 11; **A. Ostor**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Janssen, 1, 2, UCB, 1, 2, Paradigm, 1, 2.

Abstract Number: 0184

Phase III, Randomized Trial Comparing Clinical Outcomes Between Patients with Moderate-to-severe Chronic Plaque Psoriasis Receiving Adalimumab Reference Product (RP) Continuously versus Those Who Switched Between BI 695501 and Adalimumab RP

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: BI 695501 is a FDA-approved biosimilar to adalimumab RP (AbbVie), and is approved in seven indications, including rheumatoid arthritis, psoriatic arthritis, juvenile idiopathic arthritis, and ankylosing spondylitis. The objectives of our study were to assess pharmacokinetic similarity, as well as efficacy, immunogenicity, and safety in patients with moderate-to-severe chronic plaque psoriasis receiving adalimumab RP continuously versus those who switched several times between BI 695501 and adalimumab RP.

Methods: Patients with moderate-to-severe chronic plaque psoriasis received adalimumab RP (80 mg Day 1; 40 mg/0.8 mL every other week [EOW] from Weeks 2–12) and were then randomized to 'switching' (BI 695501 40 mg/0.8 mL Weeks 14 and 16; adalimumab RP Weeks 18 and 20; BI 695501 EOW Weeks 22–48) or 'continuous' (adalimumab RP EOW Weeks 14–48) treatment. Primary endpoints were $C_{max,30–32}$ and $AUC_{\tau,30–32}$ (bioequivalence acceptance limits: 80–125%). Secondary endpoints included: PASI75 response, anti-drug antibodies (ADA) and neutralizing ADAs (nAb) at Week 32, and drug-related treatment-emergent adverse events (TEAEs) post-randomization (NCT03210259).

Results: Baseline characteristics were generally balanced between groups (switching, n=118; continuous, n=120). In the analyzable switching (n=104) and continuous groups (n=99), adjusted mean $C_{max,30–32}$ was 7.08 and 7.00 µg/mL, respectively (point estimate for the ratio: 101.14%; 90.2% CI: 93.26, 109.70); adjusted mean $AUC_{\tau,30–32}$ was 2025.83 and 1925.90 µg·h/mL, respectively (105.19%; 90.2% CI: 96.58, 114.64). At Week 32, in the analyzable switching and continuous groups, respectively: 100/118 (85%) and 94/119 (79%) patients had PASI75 response (difference: 5.75%; 90% CI: -2.45, 13.96); 101/112 (90%) and 104/110 (95%) patients were ADA positive; 46/112 (41%) and 46/110 (42%) patients were nAb positive. Post-randomization, 67/118 (57%; switching) and 75/120 (63%; continuous) patients had ≥1 drug-related TEAE.

Conclusion: These data support BI 695501's designation as an interchangeable biosimilar to adalimumab RP, based on similar outcomes between the switching and continuous treatment groups, in terms of pharmacokinetics efficacy, immunogenicity and safety. The results of this study are highly applicable to patients with rheumatoid disease, for which BI 695501 is approved.

Disclosure: A. Menter, Abbott Labs, 1, 2, 5, 6, Amgen, 1, 2, 5, 6, Boehringer Ingelheim, 1, 2, 5, 6, Janssen Biotech, Inc., 1, 2, 5, 6, LEO Pharma, 1, 2, 5, 6, Sienna, 1, 2, 5, 6, Eli-Lilly, 2, 12, Investigator, UCB, 2, 5, 6, Novartis, 6, 12, Investigator, Celgene, 5, 12, Investigator, Merck, 12, Investigator; **D. McCabe**, Boehringer Ingelheim Pharmaceuticals, Inc., 3; **B. Lang**, Boehringer Ingelheim, 3; **J. Schaible**, Boehringer Ingelheim, 3; **S. Kumar Eduru**, Boehringer Ingelheim, 3.

Abstract Number: 0185

Phase 1 Study Results of GS-5718, an Oral IRAK4-Inhibitor: Pharmacodynamics of Single and Multiple Doses of GS-5718 in Healthy Subjects

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Adaptive and innate immune pathways are involved in inflammation and pathogenesis of autoimmune diseases including Rheumatoid Arthritis (RA) and Lupus Erythematosus (LE). Immune complexes found in RA and LE can stimulate production of (pro-) inflammatory cytokines via Toll-like receptor (TLR) activation. Interleukin (IL) receptor-associated kinase 4 (IRAK4) is a key signal transducer downstream of the myddosome-associated TLRs and IL-1 receptors. IRAK4 inhibition blocks (pro-) inflammatory cytokine production and is a potential therapeutic target for RA and LE. This Phase 1 first in human healthy volunteer study evaluated the pharmacodynamics (PD) of GS-5718, a potent and selective IRAK4 inhibitor in clinical development for treatment of RA and LE.

Methods: In this blinded, randomized, placebo-controlled, single and multiple (once daily for 10 days) oral dose Phase 1 study, healthy male and female subjects were enrolled in ascending dose cohorts to receive GS-5718 (15, 50 or 150 mg) or placebo under fasted (single dose cohorts) and fed conditions (multiple dose cohorts). For PD, serial whole blood samples were collected pre-dose and over up to 72 hours after single (Day 1) and multiple dose (Day 1 and 10) administration. A whole blood assay was developed to measure GS-5718 inhibition of ex-vivo (TLR7/8, R848) stimulated secretion of (pro-) inflammatory cytokines. Several (pro-) inflammatory cytokines were evaluated. TNF-α was chosen for the primary PD analysis as it showed the least variability and highest probability to see dose-dependent responses in healthy volunteers in pre-clinical in-vitro studies. The primary PD parameter was percent change of cytokine secretion from baseline (%Δ).

Results: A total of 74 subjects (n = 62 GS-5718; n = 12 placebo) enrolled, completed study drug treatments in this study and were evaluated for PD.

GS-5718 doses ≥ 15 mg significantly decreased ex-vivo stimulated TNF-α compared to placebo in a dose-dependent manner 1 hour until up to 72 hours post single and multiple doses. GS-5718 resulted in sustained >90% inhibition of TNF-α 24 hours after single and multiple doses of 50 mg and 150 mg GS-5718 on day 1 (SAD, MAD) and day 10 after the last dose (MAD), respectively. Administration of 50 mg GS-5718 with food did not result in significantly prolonged time to reach maximal % Δ compared to administration of GS-5718 50 mg under fasting conditions. Percent inhibition of all cytokines measured were highly correlated with each other in all dose cohorts.

Conclusion: GS-5718, administered once daily, resulted in significant and sustained inhibition of ex-vivo stimulated secretion of TNF-α, the main PD biomarker. The PD profile of GS-5718 supports once daily dosing and further development in patients with RA and LE.

Disclosure: S. Roedder, Gilead Sciences, 3; **E. Wendt**, Gilead Sciences, 3; **C. Burris**, Gilead Sciences, 3; **J. Nazareon**, Gilead Sciences, 3; **G. Park**, Gilead Sciences, 3; **P. Pangilinan**, Gilead Sciences, 3; **G. Huang**, Gilead Sciences,

3; **A. Mathur**, Gilead Sciences, 3; **J. Taylor**, Gilead Sciences, 3, 10; **A. Billin**, Gilead Sciences, 3; **F. Matzkies**, Gilead Sciences, 3, 11.

Abstract Number: 0186

Continued Treatment with Nintedanib in Patients with Progressive Fibrosing Autoimmune Disease-Related Interstitial Lung Diseases: Data from INBUILD-ON

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: In the INBUILD trial in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks compared with placebo, with adverse events that were manageable for most patients. The safety and efficacy of nintedanib over longer-term use are being assessed in an open-label extension trial, INBUILD-ON. Here we present the safety and efficacy of nintedanib in patients with autoimmune disease-related ILDs in INBUILD-ON.

Methods: Patients in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted, DLco ≥30%–< 80% predicted, and met criteria for progression of ILD within the 24 months before screening, despite management deemed appropriate in clinical practice. Patients who completed the INBUILD trial on treatment (nintedanib or placebo) were eligible to enter INBUILD-ON. We analyzed adverse events and the change in FVC from baseline to week 60 of INBUILD-ON in the subgroup of patients with autoimmune disease-related ILDs based on a data snapshot taken on 15 October 2020. Analyses were descriptive.

Results: Of the 434 patients treated in INBUILD-ON, 113 had autoimmune disease-related ILDs (52 RA-ILD, 29 SSc-ILD, 13 MCTD-ILD, 19 other autoimmune disease-related ILDs). Of these, 61.9% took ≥1 disease-modifying antirheumatic drug or high-dose glucocorticoid during the trial. Diarrhea was the most frequent adverse event (Table 1). Adverse events led to discontinuation of nintedanib in 11.5% of patients who continued nintedanib in INBUILD-ON (having taken nintedanib in INBUILD) and 29.5% of patients who initiated nintedanib in INBUILD-ON (having taken placebo in INBUILD). The adverse event that most frequently led to discontinuation of nintedanib was diarrhea (Table 2). Mean (SE) changes in FVC from baseline to week 60 of INBUILD-ON were –77.6 (41.1) mL in patients who continued nintedanib (n=32), –32.8 (29.3) mL in patients who initiated nintedanib (n=32) and –55.2 (25.2) mL in all patients (n=64), similar to the change from baseline to week 52 of the INBUILD trial in patients with autoimmune disease-related ILDs who received nintedanib (–78.8 [29.5] mL).

Table 1. Most frequent adverse events in patients with autoimmune disease-related ILDs in INBUILD-ON

	Continued nintedanib (n=52)	Initiated nintedanib (n=61)
Diarrhea	21 (40.4)	33 (54.1)
Nausea	4 (7.7)	10 (16.4)
Aspartate aminotransferase increased	2 (3.8)	11 (18.0)
Alanine aminotransferase increased	1 (1.9)	11 (18.0)
Dyspnea	4 (7.7)	7 (11.5)
Vomiting	3 (5.8)	8 (13.1)
Cough	3 (5.8)	7 (11.5)
Gamma-glutamyltransferase increased	1 (1.9)	8 (13.1)

Data are n (%) of patients with ≥1 such adverse event with onset date between first nintedanib intake and last intake plus 28 days. Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities. Adverse events that were reported in >10% of patients in either the "continued nintedanib" or "initiated nintedanib" group are shown.

Table 2. Most frequent adverse events that led to discontinuation of nintedanib in patients with autoimmune disease-related ILDs in INBUILD-ON

	Continued nintedanib (n=52)	Initiated nintedanib (n=61)
Diarrhea	2 (3.8)	2 (3.3)
Decreased appetite	0	2 (3.3)
Alanine aminotransferase increased	0	2 (3.3)
Aspartate aminotransferase increased	0	2 (3.3)

Data are n (%) of patients with ≥1 such adverse event with onset date between first nintedanib intake and last intake plus 28 days. Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities. Adverse events that led to discontinuation in >2% of patients in either the continued nintedanib or initiated nintedanib group are shown

Conclusion: The adverse event profile of nintedanib in patients with autoimmune disease-related ILDs participating in INBUILD-ON was characterized mainly by gastrointestinal events and was consistent with that reported over 52 weeks in INBUILD. These data support the manageable safety profile of nintedanib over continued use in patients with autoimmune disease-related ILDs.

Disclosure: E. Matteson, Boehringer Ingelheim, 1, 6, Gilead Sciences, 1, 6; **D. Antin-Ozerkis**, Boehringer Ingelheim, 5, FibroGen, 5, Pliant, 5, Galecto, 5, Galapagos, 5, Genentech/Roche, 5; **F. Bonella**, Boehringer Ingelheim, 1, 6, 12, Travel costs, Bristol-Myers Squibb, 1, Fujirebio, 1, 6, Galapagos NV, 1, 6, GlaxoSmithKline, 1, Roche, 1, 6, Roche, 12, Travel costs, Takeda, 1; **N. Chaudhuri**, Boehringer Ingelheim, 1, 6, 12, UK Chief Investigator for the INBUILD study; **V. Cottin**, AstraZeneca, 6, Bayer/Merck Sharp & Dohme, 1, Boehringer Ingelheim, 2, 5, 6, 12, Travel costs for medical meetings, Bristol-Myers Squibb, 1, Celgene, 12, Member of Data Safety Monitoring Board, FibroGen, 12, Member of trial event adjudication committee, Galapagos NV, 1, Galapagos NV, 12, Co-Chair of Data Safety Monitoring Board, Galecto, 12, Member of Data Safety Monitoring Board, Novartis, 1, Novartis, 6, Roche/Promedior, 2, 6, 12, Travel costs for medical meetings and member of steering committee, Roche/Promedior, 12, Chair of Data Safety Monitoring Board, Sanofi, 6, Shionogi, 1; **H. Mueller**, Boehringer Ingelheim, 3; **C. Coeck**, Boehringer Ingelheim, 3; **K. Rohr**, Boehringer Ingelheim, 3; **W. Wuyts**, Boehringer Ingelheim, 5, Roche, 5.

Abstract Number: 0187

Safety and Tolerability of Nintedanib in Patients with Autoimmune Disease-Related Interstitial Lung Diseases: Pooled Data from the SENSCIS and INBUILD Trials

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SESSION INFORMATION

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Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The efficacy and safety of nintedanib have been investigated in patients with systemic sclerosis-associated ILD (SSc-ILD) in the SENSCIS trial and in patients with progressive fibrosing ILDs other than idiopathic pulmonary fibrosis in the INBUILD trial. We used data from these trials to characterize the safety and tolerability of nintedanib in patients with autoimmune disease-related ILDs.

Methods: In both the SENSCIS and INBUILD trials, patients were randomized to receive nintedanib 150 mg bid or placebo. Dose reductions to 100 mg bid and treatment interruptions were permitted to manage adverse events. For this post-hoc analysis, data were pooled from all patients in the SENSCIS trial and patients with autoimmune disease-related ILDs in the INBUILD trial. Adverse events reported by investigators, irrespective of causality, over 52 weeks were analyzed. Analyses were descriptive.

Table. Most frequent adverse events (reported irrespective of causality) in patients with autoimmune disease-related ILDs

	Nintedanib (n=370)	Placebo (n=376)
Diarrhea	271 (73.2)	115 (30.6)
Nausea	113 (30.5)	49 (13.0)
Vomiting	85 (23.0)	36 (9.6)
Skin ulcer	54 (14.6)	50 (13.3)
Nasopharyngitis	46 (12.4)	62 (16.5)
Weight decreased	44 (11.9)	14 (3.7)
Decreased appetite	42 (11.4)	13 (3.5)
Abdominal pain	40 (10.8)	23 (6.1)
Upper respiratory tract infection	39 (10.5)	39 (10.4)
Cough	36 (9.7)	58 (15.4)

Data are n (%) of patients with ≥1 such adverse event over 52 weeks. Adverse events were coded based on preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Adverse events that were reported in >10% of patients in either group based on single MedDRA preferred terms are shown.

Results: The pooled data set comprised 746 patients with autoimmune disease-related ILDs (615 SSc-ILD, 89 RA-ILD, 19 MCTD-ILD, 23 other ILDs), of whom 370 received nintedanib and 376 received placebo. Mean (SD) exposure to trial medication was 10.4 (3.6) months in the nintedanib group and 11.3 (2.6) months in the placebo group. In the nintedanib and placebo groups, respectively, serious adverse events were reported in 26.2% and 23.9% of patients and fatal adverse events in 2.2% and 2.1% of patients. Adverse events led to dose reduction in 32.2% of patients treated with nintedanib and 3.2% of patients in the placebo group. Adverse events led to permanent treatment discontinuation in 16.5% of patients treated with nintedanib and 9.0% of patients in the placebo group. The most frequent adverse event was diarrhea, which was reported in 73.2% of patients treated with nintedanib and 30.6% of patients in the placebo group (Table). Diarrhea led to permanent treatment discontinuation in 6.8% and 0.5% of patients in the nintedanib and placebo groups, respectively. Based on a standardized MedDRA query, liver-related investigations, signs and symptoms were reported in 16.8% of patients in the nintedanib group and 4.5% of patients in the placebo group. In the nintedanib and placebo groups, respectively, major adverse cardiovascular events were reported in 2.7% and 1.9%, myocardial infarction in 0.3% and 0.8%, bleeding in 11.6% and 8.2%, and gastrointestinal perforation in 0% and 0.3% of patients.

Conclusion: In patients with autoimmune-disease related ILDs, the adverse events associated with nintedanib were characterized predominantly by gastrointestinal events and were managed without treatment discontinuation in most patients. The adverse event profile of nintedanib in patients with autoimmune disease-related ILDs was consistent with that observed in patients with other ILDs.

Disclosure: V. Smith, Boehringer Ingelheim, 2, 6, Janssens, 2, 6; **S. Assassi**, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2; **Y. Allanore**, Bayer, 2, Boehringer Ingelheim, 2, 12, Clinical trial investigator, Roche, 2, Chemomab, 2, Curzion, 2, Sanofi, 2, 12, Clinical trial investigator; **L. Loaiza**, Boehringer Ingelheim, 3; **I. Tschoepe**, Boehringer Ingelheim, 7; **M. Kanakapura**, Boehringer Ingelheim, 3; **E. Volkmann**, Boehringer Ingelheim, 2, 6, Corbus, 5, Forbius, 5, Kadmon, 5.

Abstract Number: 0188

Effect of Nintedanib on Categorical Changes in FVC in Patients with Progressive Fibrosing ILDs: Further Analyses of the INBUILD Trial

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SESSION INFORMATION

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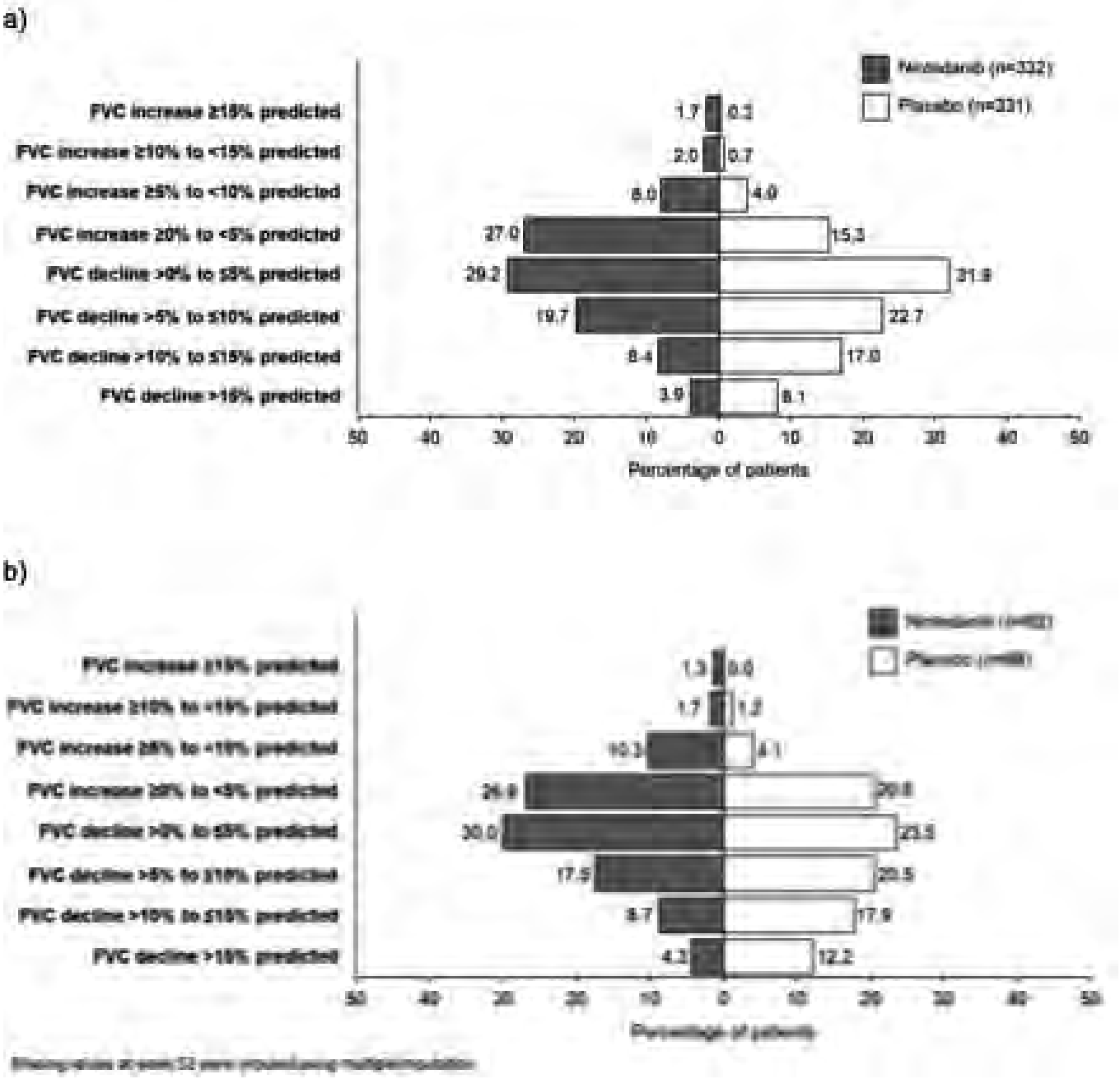
Session Time: 8:30AM–10:30AM

Figure. Proportions of subjects with absolute increases and declines in FVC % predicted at week 52 in a) the overall population, and b) subjects with autoimmune disease-related ILDs.



Background/Purpose: In the INBUILD trial in subjects with progressive fibrosing interstitial lung diseases (ILDs) other than idiopathic pulmonary fibrosis (IPF), nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 57% versus placebo. We assessed the effect of nintedanib on categorical changes in FVC % predicted over 52 weeks.

Methods: Subjects in the INBUILD trial had diffuse fibrosing ILD (reticular abnormality with traction bronchiectasis, with or without honeycombing) of >10% extent on HRCT, FVC ≥45% predicted, DLco ≥30%–< 80% predicted, and

met criteria for progression of ILD within the 24 months before screening, despite management deemed appropriate in clinical practice. In *post-hoc* analyses, we assessed the proportions of subjects with categorical absolute increases or declines in FVC % predicted at week 52. Missing values at week 52 were imputed using multiple imputation. Analyses were descriptive.

Results: Overall, 332 subjects were treated with nintedanib and 331 received placebo. At baseline, mean (SD) FVC was 68.7 (16.0) % predicted in the nintedanib group and 69.3 (15.2) % predicted in the placebo group. In the nintedanib and placebo groups, respectively, 19.7% and 22.7% of subjects had absolute declines in FVC of >5% to ≤10% predicted and 12.3% and 25.1% had absolute declines in FVC >10% predicted, while 11.7% and 5.0% of subjects had absolute increases in FVC of ≥5% predicted (Figure). Similar findings were observed in the subgroup of 170 patients with autoimmune disease related ILDs (Figure).

Conclusion: In the overall population of the INBUILD trial and in the subgroup of subjects with autoimmune disease-related ILDs, the proportions of subjects with clinically relevant declines in FVC over 52 weeks were lower in the nintedanib group than in the placebo group. These results provide further support for the benefit of nintedanib on slowing the progression of ILD in subjects with progressive fibrosing ILD other than IPF.

Disclosure: T. Maher, Apellis, 2, Bayer, 2, Biogen, 2, Blade Therapeutics, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, Galapagos NV, 2, Galecto, 2, GlaxoSmithKline, 2, Indalo, 2, Novartis, 2, Respivent, 2, Roche, 2, Trevi, 2, UCB, 2; **S. Cerri**, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 6, Pfizer, 6; **R. Hallowell**, Boehringer Ingelheim, 2, 5, 6, DynaMed, 2, 6, Galapagos NV, 5, ImpactNetwork, 2, 6, Paradigm Medical, 2, 6, Regeneron, 5, Teladoc, 2, 6, Wolters Kluwer, 2, 6; **D. Koschel**, Boehringer Ingelheim, 2, 6, 12, Financial support for attending meetings, Roche, 2, 6, 12, Financial support for attending meetings; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **L. Tolle**, Boehringer Ingelheim, 6, Genentech, 6; **H. Mueller**, Boehringer Ingelheim, 3; **K. Rohr**, Boehringer Ingelheim, 3; **Y. Inoue**, Boehringer Ingelheim, 1, 6, Roche, 1, Taiho Pharmaceutical Co, Ltd, 1, Savara, 1, Shionogi, 6, Shionogi, 1, Galapagos NV, 1, Japan Agency for Medical Research and Development, 5, Ministry of Health, Labour and Welfare, 5.

Abstract Number: 0189

Tapering and Discontinuation of Background Therapies During the Transition to Rilonacept Monotherapy in RHAPSODY, a Phase 3 Clinical Trial of Rilonacept in Patients with Recurrent Pericarditis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Post-episode tapering of Standard of Care (SoC) medication in patients with recurrent pericarditis (RP) varies considerably. Gradual tapering of corticosteroids (CS) is recommended in ESC guidelines (e.g., decreasing by 1-2.5 mg/day every 2-6 weeks over 1-2 years) to prevent recurrence. We describe successful faster tapering of SoC treatment onto rilonacept monotherapy during RHAPSODY, a Phase 3, placebo-controlled, randomized-withdrawal (RW) trial in RP.

Methods: Patients with acute symptomatic RP despite stable doses of NSAIDs, colchicine, and/or CS in any combination enrolled in a 12-week run-in period in which weekly rilonacept was initiated. After 1-week of stabilization, tapering of CS began at a rate dependent on baseline dose, to be completed by Week 10 for randomization at Week 12 when clinical response was confirmed by reduced pain and normalized CRP levels. Colchicine tapering/discontinuation was initiated no earlier than Week 4. This analysis evaluates time to rilonacept monotherapy in subgroups receiving different combinations of background therapies.

Results: 79 of 86 patients were receiving pharmacotherapy at run-in baseline. Median (95% CI) time to monotherapy (n=79) was 7.9 (7.0-8.1) weeks. Of the patients receiving CS at baseline (41/86 [48%]), 39 (95%) tapered to rilonacept monotherapy, and median time to monotherapy was 7.9 (7.1-8.1) weeks. Of the patients receiving colchicine at baseline (65/86 [76%]), 61 (94%) patients achieved rilonacept monotherapy, and median time to monotherapy was 8.0 (7.1-8.3) weeks. Patients receiving only one SoC therapy achieved rilonacept monotherapy faster (6.1 [0.4-8.1] weeks) than those receiving 2 (8.0 [6.7-9.9] weeks) or 3 (7.7 [7.0-8.3] weeks) therapies. All patients who did not achieve monotherapy had withdrawn from the study for reasons unrelated to pericarditis.

Conclusion: All patients randomized in the RHAPSODY trial discontinued SoC and transitioned to rilonacept monotherapy (median time 7.9 weeks) without a recurrent pericarditis episode during run-in. In patients treated with rilonacept, time to successful discontinuation of SoC, including CS, was substantially shorter than that described in ESC guidelines for pericardial disease (Adler et al. Eur Heart J. 2015;36(42)2921-2964).

Disclosure: A. **Brucato**, Kiniksa, 12, My institution received funding from Kiniksa as an investigative site to run the study, Sobi, 5, Acarpia, 5; **A. Wheeler**, Kiniksa Pharmaceuticals, Ltd., 2; **S. Luis**, Kiniksa, 1, Sobi, 1, 2, Medtronic, 2; **A. Abbate**, Kiniksa, 5, Olatec, 5, 12, personal fees, Serpin, 5, 12, personal fees, Novartis, 5, 12, personal fees, Novo-Nordisk, 12, personal fees, Cromos Pharma, 12, personal fees, Janssen, 5, 12, personal fees; **P. Cremer**, Kiniksa, 5, 12, personal fees, Novartis, 5, Sobi, 12, personal fees; **F. Fang**, Kiniksa Pharmaceuticals Corp., 3, 11; **A. Insalaco**, None; **M. LeWinter**, Kiniksa, 5, 12, personal fees; **B. Lewis**, Kiniksa, 12, personal fees; **D. Lin**, Regeneron, 12, fees; **S. Nicholls**, Kiniksa, 5, 12, personal fees, AstraZeneca, 2, 5, Amgen, 5, Anthera, 2, 5, Eli Lilly, 2, 5, Esperion, 2, 5, Novartis, 5, Cerenis, 5, The Medicines Company, 5, Resverlogix, 2, 5, InfraReDx, 5, Roche, 5, Sanofi-Regeneron, 2, 5, Liposcience, 5, Akcea, 2, Omthera, 2, Merck, 2, Takeda, 2, CSL Behring, 2, Boehringer Ingelheim, 2; **A. Klein**, Kiniksa, 1, 5, Sobi, 1, Pfizer, 1; **M. Imazio**, Kiniksa, 1, Sobi, 1; **J. Paolini**, Kiniksa Pharmaceuticals Corp., 2, 10, 11.

Abstract Number: 0190

Long-term Safety of Canakinumab in Patients with Autoinflammatory Periodic Fever Syndromes - Interim Analysis of the RELIANCE Registry

Jasmin Kuemmerle-Deschner[1], Jorg Henes[2], Birgit Kortus-Goetze[3], Tilmann Kallinich[4], Prasad T. Oommen[5], Juergen Rech[6], Frank Weller-Heinemann[7], Gerd Horneff[8], Ivan Foeldvari[9], Aleš Janda[10], Catharina Schuetz[11], Frank Dressler[12], Michael Borte[13], Markus Hufnagel[14], Axel Braner[15], Florian Meier[16], Michael Fiene[17], Julia Weber-Arden[18] and Norbert Blank[19], [1]Pediatric Rheumatology and Autoinflammatory Reference Center, University Children's Hospital Tuebingen, Tuebingen, Germany, [2]University Hospital Tuebingen, Tuebingen, Germany, [3]Division of Nephrology, University of Marburg, Marburg, Germany, [4]Charité University Medicine, Nuremberg, Germany, [5]Clinic of Pediatric Hematology, Oncology and Clinical Immunology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, [6]Friedrich-Alexander University (FAU) Erlangen-Nuernberg and Universitaetsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Germany, Erlangen, Germany, [7]Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany, [8]Paediatric Rheumatology International Trials Organisation (PRINTO), Sankt Augustin, Germany, [9]Hamburger Zentrum fuer Kinder- und Jugendrheumatologie, Hamburg, Germany, [10]Department of Pediatrics, University Hospital Ulm, Ulm, Germany, [11]Pediatrics, Medizinische Fakultaet Carl Gustav Carus, Technische Universitaet Dresden, Dresden, Germany, [12]Division of Pediatric Pneumology, Allergology and Neonatology, Hannover Medical School, Hannover, Germany, [13]ImmunoDeficiencyCenter Leipzig (IDCL), Hospital St. Georg gGmbH Leipzig, Leipzig, Germany, [14]Division of Pediatric Infectious Diseases and Rheumatology, Department of Pediatrics and Adolescent Medicine, University Hospital Medical Center Freiburg, Medical Faculty, University of Freiburg, Freiburg, Germany, [15]Department of Medicine II, Rheumatology, University Hospital Frankfurt, Germany, Frankfurt a.M., Germany, [16]1 Division of Rheumatology, University Hospital Frankfurt, Goethe University, Frankfurt am Main, Germany 2 Fraunhofer Institute for Molecular Biology and Applied Ecology IME, Project Group Translational Medicine and Pharmacology TMP, Frankfurt am Main, Germany, Frankfurt a.M., Germany, [17]Department of Internal Medicine, District Hospital Demmin, Demmin, Germany, [18]Novartis Pharma GmbH, Nuremberg, Germany, [19]Rheumatology, University Hospital Heidelberg, Eppelheim, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Autoinflammatory periodic fever syndromes (PFS) are characterized by severe systemic and organ inflammation. In clinical trials, successful treatment was achieved with the interleukin-1β inhibitor canakinumab (CAN).

The present study explores the long-term efficacy and safety of CAN in routine clinical practice conditions in pediatric (age ≥2 years) and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

Methods: RELIANCE is a prospective, non-interventional, observational study based in Germany. Patients with clinically confirmed diagnoses of PFS routinely receiving CAN are enrolled. Besides efficacy parameters regarding disease activity and remission, safety parameters were recorded at baseline and assessed at 6-monthly intervals.

Results: Here we present the interim analysis of 168 patients with PFS enrolled in the RELIANCE Registry between October 2017 and December 2020. Mean age in this cohort was 24.7 years (2-79 years) and the proportion of female patients was 51 %. At baseline, median duration of prior CAN treatment was 3 years (0-12 years).

Table. Overview of the CAN safety data of the RELIANCE study across all study indications (N=168 patients). ‡IR, incidence rate per 100 patient years; AE, adverse event; SAE, severe adverse event, SADR, severe adverse drug reaction

Type of event	Number of events	IR‡
AE total	489	173.33
AE non-serious	436	154.33
AE, non-serious, not related	221	78.34
AE, ARI	13	4.61
AE, non-serious adverse drug reaction	215	76.21
SAE, total	53	18.79
SAE, not related	32	11.34
SADR#, total	21	7.44

#Alport's syndrome, appendicitis, blister, cardiovascular disorder, chest pain, circulatory collapse, erythema, febrile convulsion, glomerulonephritis, Hemophilus test positive, pneumonia, premature delivery, skin discoloration, tonsillitis bacterial, tonsillitis streptococcal (each n=1 event, IR 0.35‡), tonsillectomy (2 events, IR 0.71‡), pyrexia (3 events, IR 1.06‡), not yet coded (hospital admission due to exsiccosis upon gastroenteritis, 1 event, IR 0.35‡)

A total of 101 patients (60%) experienced any adverse event (AE) and 22 patients (13%) were affected by severe adverse events (SAE). In 9 patients (5%) SAE were classified as drug related. Of 489 AE, 53 were severe and a total of 21 SAE were classified as treatment-related (table). Overall, 13 AE comprised upper respiratory tract infections (ARI).

Conclusion: The interim data from the RELIANCE study, the longest running real-life canakinumab registry for autoinflammatory periodic fever syndromes, confirm safety of long-term canakinumab treatment across the entire study population.

Disclosure: J. Kuemmerle-Deschner, Novartis, 1, 2, 5, 6, SOBI, 1, 2, 5, 6; **J. Henes**, Roche Pharma, 1, 5, 6, ABBVIE, 6, Novartis, 5, 6, SOBI, 5, 6, LILLY, 6, Pfizer, 5, 6, BMS, 6, Janssen, 6, UCB, 6, Boehringer-Ingelheim, 6; **B. Kortus-Goetze**, Novartis, 2; **T. Kallinich**, None; **P. Oommen**, Novartis, 5; **J. Rech**, Novartis, 2, 5, 6, SOBI, 2, 5, 6, AbbVie, 2, 6, Biogen, 2, 6, BMS, 2, 6, Chugai, 2, 6, GSK, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Mylan, 2, 6, Roche, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **F. Weller-Heinemann**, None; **G. Horneff**, Novartis, 5, 6, Janssen, 5, 6, Roche, 5, Eli-Lilly, 6, Glaxo Smith and Kline, 6, Pfizer, 6, Sobi, 6; **I. Foeldvari**, Novartis, 4; **A. Janda**, None; **C. Schuetz**, None; **F. Dressler**, Novartis, 2, 5, AbbVie, 2, Mylan, 2, Pfizer, 2; **M. Borte**, Shire, 5, Pfizer, 5; **M. Hufnagel**, None; **A. Braner**, Novartis, 2, SOBI, 2; **F. Meier**, Novartis, 6; **M. Fiene**, None; **J. Weber-Arden**, Novartis, 3; **N. Blank**, Novartis, 2, 5, SOBI, 2, 5, Lilly, 2, Pfizer, 2, AbbVie, 2, BMS, 2, MSD, 2, Actelion, 2, UCB, 2, Boehringer Ingelheim, 2, Roche, 2.

Abstract Number: 0191

Influence of Canakinumab Dosing on Long-term Efficacy and Safety in Patients with Cryopyrin-associated Periodic Syndromes (CAPS) - 30-months Interim Analysis of the RELIANCE Registry

Jasmin Kuemmerle-Deschner[1], Birgit Kortus-Goetze[2], Prasad T. Oommen[3], Aleš Janda[4], Juergen Rech[5], Tilmann Kallinich[6], Frank Weller-Heinemann[7], Gerd Horneff[8], Ivan Foeldvari[9], Catharina Schuetz[10], Michael Borte[11], Axel Braner[12], Julia Weber-Arden[13] and Norbert Blank[14], [1]Pediatric Rheumatology and Autoinflammatory Reference Center, University Children's Hospital Tuebingen, Tuebingen, Germany, [2]Division of Nephrology, University of Marburg, Marburg, Germany, [3]Clinic of Pediatric Hematology, Oncology and Clinical Immunology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, [4]Department of Pediatrics, University Hospital Ulm, Ulm, Germany, [5]Friedrich-Alexander University (FAU) Erlangen-Nuernberg and Universitaetsklinikum Erlangen, Department of Internal Medicine 3 - Rheumatology and Immunology, Germany, Erlangen, Germany, [6]Charité University Medicine, Nuremberg, Germany, [7]Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany, [8]Paediatric Rheumatology International Trials Organisation (PRINTO), Sankt Augustin, Germany, [9]Hamburger Zentrum fuer Kinder- und Jugendrheumatologie, Hamburg, Germany, [10]Pediatrics, Medizinische Fakultaet Carl Gustav Carus, Technische Universitaet Dresden, Dresden, Germany, [11]ImmunoDeficiencyCenter Leipzig (IDCL), Hospital St. Georg gGmbH Leipzig, Leipzig, Germany, [12]Department of Medicine II, Rheumatology, University Hospital Frankfurt, Germany, Frankfurt a.M., Germany, [13]Novartis Pharma GmbH, Nuremberg, Germany, [14]Rheumatology, University Hospital Heidelberg, Eppelheim, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The IL-1 inhibitor canakinumab (CAN) induces rapid remission of symptoms of CAPS (Cryopyrin-associated periodic syndromes), a monogenic autoinflammatory disease with severe systemic inflammation, both in clinical trials and in routine practice.The aim of the present study is to investigate the long-term efficacy and safety of CAN in pediatric (≥ 2 years) and adult patients with CAPS (incl. Muckle-Wells syndrome [MWS], familial cold-induced autoinflammatory syndrome [FCAS], and neonatal onset inflammatory systemic disease [NOMID]/chronic infantile neurologic-cutaneous-articular syndrome [CINCA]) in relation to weight-dependent CAN dosing under routine clinical practice conditions.

Methods: The prospective, non-interventional, observational RELIANCE study with 3-year follow-up includes patients with clinically confirmed CAPS diagnosis who routinely receive CAN. Clinical data, physician assessment, and patient-reported outcomes are evaluated at 6-month visits from baseline.

Results: The interim analysis included data from 91 CAPS patients (50% females; 14 [15%] NOMID/CINCA subtypes) enrolled by December 2020. At baseline, median age was 20.5 years and median duration of prior CAN treatment was 6 years. According to physician assessment, 66% of patients achieved disease remission with increasing absence of disease activity according to PGA (physician global assessment, 50-60%). Patients reported stable, low levels of disease activity, fatigue, and Auto-Inflammatory Diseases Activity Index (AIDAI) scores. CAPS affected the social life of 50% of patients and 50% reported days of absence from school/work. At baseline, 2% of patients received less than the standard dose* CAN (SD; < 87.5% of SD), 49% received standard dose CAN (SD CAN; 150 mg and 2mg/kg respectively per 8 weeks) and another 49% received higher than SD CAN (>112.5% of SD). At 30 months, 82% of patients received higher than SD CAN. The laboratory parameters as well as physicians´ and patients´ rating of disease activity remained stable over time, showing sustained remission and disease control in all dosing groups (Table 1).

Table 1. Stratification of efficacy parameters for CAN dosing and weight (N=91)#. *Body weight >40kg: Standard dose is 150 mg per 8 weeks; Body weight ≤40 kg: Standard dose is 2mg per kg per 8 weeks; #Numbers and percentages do not sum up to N=91 or 100%, respectively, due to the number of patients with unknown weight.

		Baseline	12 months	24 months	30 months
% of patients on low/**standard**/high dose CAN, *number of patients analyzed (N)*		2/**49**/49, *N=80*	10/**19**/71, *N=59*	7/**25**/68, *N=28*	0/**18**/82, *N=22*
		PGA absent/mild-moderate/severe			
Physician Global Assessment (PGA), %# of patients	less than CAN SD*	71/14/7	36/64/0	25/63/0	100/0/0
	CAN SD*	19/81/0	22/78/0	50/50/0	0/100/0
	more than CAN SD*	35/57/2	34/54/3	56/39/0	62/38/0
		VAS 0–10, (min; max)			
Patients' assessment of current disease activity (median)	less than CAN SD*	0 (0; 7)	1 (0; 7)	1 (0; 7)	0 (0; 0)
	CAN SD*	2 (0; 6)	2 (0; 4)	3 (2; 4)	2 (1; 3)
	more than CAN SD*	2 (0; 10)	3 (0; 10)	1 (0; 10)	0 (0; 7)

Treatment-related severe adverse events (SAE) occurred in 8 patients, none of them under standard dosing (in 1 patient: less than SD, in 7 patients more than SD).

Conclusion: The 30-month interim analysis of the RELIANCE study shows that long-term treatment with CAN is safe and effective in patients with CAPS. A clear trend towards updosing to more than SD CAN could be observed.

Disclosure: J. Kuemmerle-Deschner, Novartis, 1, 2, 5, 6, SOBI, 1, 2, 5, 6; **B. Kortus-Goetze**, Novartis, 2; **P. Oommen**, Novartis, 5; **A. Janda**, None; **J. Rech**, Novartis, 2, 5, 6, SOBI, 2, 5, 6, AbbVie, 2, 6, Biogen, 2, 6, BMS, 2, 6, Chugai, 2, 6, GSK, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Mylan, 2, 6, Roche, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **T. Kallinich**, None; **F. Weller-Heinemann**, None; **G. Horneff**, Novartis, 5, 6, Janssen, 5, 6, Roche, 5, Eli-Lilly, 6, Glaxo Smith and Kline, 6, Pfizer, 6, Sobi, 6; **I. Foeldvari**, Novartis, 4; **C. Schuetz**, None; **M. Borte**, Shire, 5, Pfizer, 5; **A. Braner**, Novartis, 2, SOBI, 2; **J. Weber-Arden**, Novartis, 3; **N. Blank**, Novartis, 2, 5, SOBI, 2, 5, Lilly, 2, Pfizer, 2, AbbVie, 2, BMS, 2, MSD, 2, Actelion, 2, UCB, 2, Boehringer Ingelheim, 2, Roche, 2.

Abstract Number: 0192

Influence of Canakinumab Dosing on Efficacy and Safety of Long-term Treatment in Patients with Familial Mediterranean Fever - Interim Analysis of the RELIANCE Registry

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Familial Mediterranean Fever (FMF) is characterized by severe systemic and organ inflammation. Successful treatment with rapid remission of symptoms and normalization of laboratory parameters was achieved in most patients with the interleukin-1β inhibitor canakinumab (CAN) in clinical trials. The aim of the present analysis was the evaluation of long-term efficacy and safety of CAN in pediatric (age ≥2 years) and adult patients with FMF with respect to weight-dependent CAN dosing in routine clinical practice.

Methods: RELIANCE is a prospective, non-interventional, observational study based in Germany. Patients with clinically confirmed diagnoses of autoinflammatory periodic fever syndromes routinely receiving CAN are enrolled. Efficacy and safety parameters, CAN dosing as well as weight were recorded at baseline and assessed at 6-monthly intervals within the 3-year observation period of the study.

Results: The interim analysis of the RELIANCE Registry comprises data of 54 FMF patients enrolled by December 2020. Of these, the % of patients reported to receive standard dose CAN (SD CAN; 150 mg or 2mg/kg respectively per 4 weeks) halved from 77% at baseline to 36% at month 18 in favor of less than SD CAN (< 87.5% of SD) and higher than SD CAN (>112.5% of SD). Patients´ and physicians´ rating of disease activity was higher in patients receiving SD CAN and higher (table 1), even though CRP was equally well controlled in all three dosing groups. A total of 11 serious adverse events was reported, of which 1 case of tonsillectomy was classified as drug-related.

Conclusion: The present interim data from the RELIANCE study confirm efficacy and safety of long-term CAN treatment in clinical routine. CRP levels were well controlled in all dosing groups. Remaining disease activity was mainly observed in patients under SD CAN and especially higher than SD CAN.

Table 1. Stratification of efficacy parameters by CAN dose category and weight (N=54)#. *Body weight >40 kg: SD is 150 mg per 4 weeks; Body weight ≤40 kg: SD is 2 mg/kg per 4 weeks #Numbers/percentage do not sum up to N=54/100%, due to unknown weight of some patients

		Baseline	6 months	12 months	18 months
% of patients on low/**standard**/high dose CAN, *number# of patients analysed (N)*		4/**77**/19, *N=47*	31/**41**/28, *N=32*	42/**27**/31, *N=26*	36/**36**/28, *N=14*
		PGA absent/mild-moderate/severe			
Physician Global Assessment (PGA), %# of patients	lower than SD* CAN	54/23/15	80/10/0	78/22/0	80/20/0
	SD* CAN	42/50/0	88/12/0	50/33/0	50/25/0
	higher than SD* CAN	20/60/20	33/67/0	0/67/0	0/100/0
		VAS 0–10, (min; max)			
Patients' assessment of current disease activity (median)	lower than SD* CAN	1 (0; 9)	1 (0; 7)	1 (0; 4)	2 (0; 3)
	SD* CAN	2 (0; 10)	3 (0; 7)	3 (0; 10)	4 (0; 10)
	higher than SD* CAN	4 (1; 5)	3 (0; 6)	3 (1; 5)	4 (1; 6)

Disclosure: J. Henes, Roche Pharma, 1, 5, 6, ABBVIE, 6, Novartis, 5, 6, SOBI, 5, 6, LILLY, 6, Pfizer, 5, 6, BMS, 6, Janssen, 6, UCB, 6, Boehringer-Ingelheim, 6; **N. Blank**, Novartis, 2, 5, SOBI, 2, 5, Lilly, 2, Pfizer, 2, AbbVie, 2, BMS, 2, MSD, 2, Actelion, 2, UCB, 2, Boehringer Ingelheim, 2, Roche, 2; **T. Kallinich**, None; **F. Dressler**, Novartis, 2, 5, AbbVie, 2, Mylan, 2, Pfizer, 2; **G. Horneff**, Novartis, 5, 6, Janssen, 5, 6, Roche, 5, Eli-Lilly, 6, Glaxo Smith and Kline, 6, Pfizer, 6, Sobi, 6; **I. Foeldvari**, Novartis, 4; **M. Hufnagel**, None; **B. Kortus-Goetze**, Novartis, 2; **F. Weller-Heinemann**, None; **F. Meier**, Novartis, 6; **J. Weber-Arden**, Novartis, 3; **J. Kuemmerle-Deschner**, Novartis, 1, 2, 5, 6, SOBI, 1, 2, 5, 6.

Abstract Number: 0193

Tocilizumab for the Treatment of Familial Mediterranean Fever – a Randomized, Double Blind, Placebo-controlled Phase II Study

Jorg Henes[1], Sebastian Saur[2], David Kofler[3], Martin Krusche[4], Theodoros Xenitidis[5], Christoph Meisner[6], Claudia Kedor[7], Ina Koetter[8], Hendrik Schulze-Koops[9] and Eugen Feist[10], [1]University Hospital Tuebingen, Tuebingen, Germany, [2]Universtiy Hostpiatl Tübingen, Tuebingen, Germany, [3]Division of Rheumatology and Clinical Immunology, Department I of Internal Medicine; University Hospital Cologne, Cologne, Germany, [4]Charite Berlin, Berlin, Germany, [5]University Hospital Tuebingen, Rheumatology, Tuebingen, Germany, [6]University Tuebingen, Statistics, Tuebingen, Germany, [7]Charite University Hospital Berlin, Berlin, Germany, [8]University Hospital Hamburg Eppendorf, Hamburg, Germany, [9]Division of Rheumatology and Clinical Immunology, Department of Internal Medicine IV, University of Munich, Munich, Germany, [10]Helios Department of Rheumatology, Vogelsang-Gommern, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Familial Mediterranean Fever (FMF) is the most common auto-inflammatory disease characterized by chronic inflammation, recurrent episodes of fever, abdominal and thoracic pain due to serositis, skin irritations and arthralgia. FMF patients are at risk for severe organ failure due to amyloidosis. Colchicine and IL-1 antagonists are approved therapeutic options but alternative treatment options are still warrant. Tocilizumab (TCZ) is a monoclonal antibody directed against the IL-6 receptor and approved for several other autoimmune diseases that go along with high inflammation markers.

Methods: This was a randomized, blinded, placebo-controlled trial conducted at 5 German centres. Adult patients with FMF, who had at least one known mutation of the MEFV gene and active disease with inadequate response or intolerance to colchicine were included. The physician's global assessment of disease activity (PGA) based on a 5 point-scale was used as a clinical score and had to be >2 at screening. Patients were randomized 1:1 to either receive

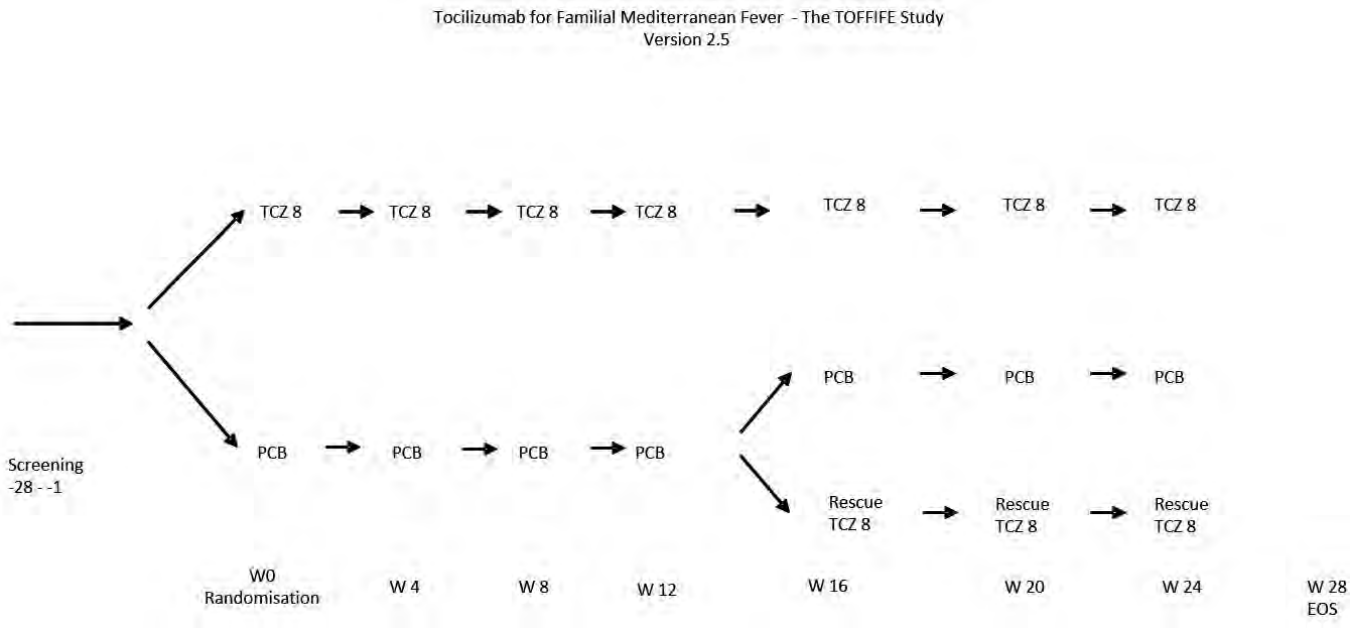

Figure 1. Trial scheme with 1:1 randomization and rescue arm, at week 16.

TCZ intravenously with 8 mg/kg bodyweight or placebo over a period of 24 weeks. Patients with inadequate response after week 12 had the opportunity to receive open label TCZ at week 16. The primary endpoint was the number of patients achieving an adequate response to treatment at week 16, defined as a PGA ≤ 2 + normalized ESR or CRP + normalized SAA. Patients filled out a patient's diary to help the investigators to judge the PGA

Results: Of the 31 included patients, only 25 were randomized, 6 patients dropped out before randomization due to missing data, withdrawal or incompliance. For further evaluation the intention to treat population consisted of 25 patients with a median age of 31 years (range 18 - 53y), of which 14 (56%) were female. In their medical history all were treated with colchicine with inadequate response, whereas in 3 patients anakinra and in 1 patient canakinumab were ineffective. At week 16, the primary endpoint was met by only 2 patients in the TCZ, but none of the patients in the placebo arm (P-value of 0.089). The difference was primarily due to the failed normalization of the laboratory parameters in the placebo group, whereas the difference in PGA was not significant. No new safety aspects occurred.

Conclusion: This is the first randomized, placebo-controlled study on the efficacy of TCZ in patients with active FMF. Our results demonstrate the superiority with regard to our primary endpoint: more patients in the TCZ arm experienced an adequate response to treatment in comparison to placebo. SAA levels only normalized in TCZ treated patients. As TCZ normalizes CRP levels in almost all patients this effectiveness has to be confirmed in a larger trial.

Disclosure: J. Henes, Roche Pharma, 1, 5, 6, ABBVIE, 6, Novartis, 5, 6, SOBI, 5, 6, LILLY, 6, Pfizer, 5, 6, BMS, 6, Janssen, 6, UCB, 6, Boehringer-Ingelheim, 6; **S. Saur**, None; **D. Kofler**, None; **M. Krusche**, Chugai/Roche, 6, Novartis, 5, 6, Sobi, 5, 6, Medac, 6, Gilead, 6, Lilly, 6, Sanofi, 5; **T. Xenitidis**, Novartis, 6, ABBVIE, 6, Pfizer, 5, AMGEN, 6; **C. Meisner**, None; **C. Kedor**, Roche/Chugai, 6; **I. Koetter**, Abbvie, 6, BMS, 6, Chugai, 6, Janssen, 6, Boehringer, 1, 6, Sobi, 1, 6, Amgen, 1, 6, GSK, 1, Lilly, 1, 6, Novartis, 1, 6, Roche, 1, 6, Pfizer, 6; **H. Schulze-Koops**, Roche/Chugai, 2, 5, 6, Sobi, 6, Novartis, 2, 5, 6, AbbVie, 2, 5, 6, Amgen, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Celltrion, 2, 6, Chugai, 2, 6, Gilead Sciences, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Pfizer Inc, 2, 6, Sanofi, 2, 6, Galapagos, 1, 2, UCB, 1, 2; **E. Feist**, R-Pharm, 2, 6, Abbvie, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, AB2Bio, 6, BMS, 6, Celgene, 6, Janssen, 6, Eli Lilly, 2, 5, 6, Medac, 6, MSD, 6, Roche/Chugai, 2, 5, 6, Sanofi, 6, Sobi, 6, UCB, 6.

Abstract Number: 0194

Eye Opening: Use of IL-6 Inhibition in Non-Paraneoplastic Autoimmune Retinopathy

Lisa Carnago[1], Robert Keenan[2], Glenn Jaffe[1], Jordan Deaner[1] and Dilraj Grewal[1], [1]Duke Health, Durham, NC, [2]Florence Rheumatology Center, Articularis Healthcare, Florence, NC

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: There is a lack of robust guidance and consistently effective treatment modalities in non-paraneoplastic autoimmune retinopathy (npAIR) with cystoid macula edema (CME), which is often jointly treated by the Rheumatology provider. This retrospective case series was generated as further evidence is needed to understand options for treatment to include the effect of anti-interleukin-6 (IL-6) receptor monoclonal antibodies Tocilizumab (humanized monoclonal antibody) and Sarilumab (fully humanized monoclonal antibody) in eyes with npAIR with CME.

Table 2. Clinical characteristics of patients who were treated with anti-IL-6 therapy for npAIR with CME

No.	Gender	Age (years)	Eye(s) included in the study	Molecular weights of anti-retinal antibodies (kDa)	Immuno-histochemistry	Duration of follow-up prior to anti-IL-6 therapy (months)	Treatment prior to anti-IL-6 therapy	Concurrent Treatment	Anti-IL-6 therapy			Duration of follow-up on anti-IL-6 therapy (months)	Response
									Agent	Dose (mg/kg)	Route		
1	Female	71	OD	40, 48, 60, 96, 132	Positive	23	MMF, RTX	MMF	Tocilizumab	8.17	IV	24	Improved
			OS				[redacted]	ketorolac OU					Improved
2	Female	72	OD	46	Negative	26	MTX, MMF, RTX		Tocilizumab	7.21	IV	26	Improved
			OS				ketorolac OU	ketorolac OU					Stable
3	Female	46	OD	30, 46	Positive	38	MMF, RTX	MMF	Tocilizumab	7.77	IV	25	Improved
			OS				PA, ketorolac OU	PA, ketorolac OU					Improved
4	Male	70	OD	46, 62, 200	Positive	93	MTX, MMF, RTX		Tocilizumab	7.78	IV	22	Improved
			OS				PA, diclofenac OU	PA, diclofenac OU					Worsened
5	Female	72	OD	40	Positive	32	MMF, ADA		Tocilizumab		SC	11	Improved
			OS				PF, ketorolac OU	FML OU					Stable
6	Female	29	OD	20, 23, 29, 30, 42	Positive	12	ADA, AZA		Sarilumab		SC	25	Improved
			OS	46, 52, 60, 94, 96									Improved
7	Female	35	OD	30, 31, 36, 44, 46, 52, 58	Positive	3		ketorolac OD	Tocilizumab	7.71	IV	34	Stable
			OS										Improved
8	Female	68	OD	30, 36, 40, 46	Negative	30			Tocilizumab	4.12	9	14	Stable
	-												-

IMT = immunosuppressive therapy, Anti-IL-6 = anti-interleukin 6, OD = right eye, OS = left eye, OU = both eyes, MMF = mycophenylate motefil, RTX = rituximab, PA = prednisolone acetate 1.0%, MTX = methotrexate, ADA = adalimumab, AZA = azathioprine. The right eye of patient #6 and the left eye of patient #8 were not included as they had asymmetric disease without CME or ellipsoid loss, they are marked with the placeholder "-"

Table 3. Results of OCT parameters and visual acuity measurements before and after treatment with anti-IL-6 therapy

	Response	Mean baseline prior to anti-IL-6 therapy	Mean at 3 months (n=15)	P-value	Mean at 6 months (n=15)	P-value	Mean at 12 months (n=15)	P-value	Mean at 18 months (n=10)	P-value	Mean at 24 months (n=12)	P-value
CST	Overall	491.9	382.3	***.024**	355.2	***.021**	331.0	***.027**	355.8	***.009**	326.5	***.002**
	Responder	538.8	371.5	***.022**	371.5	***.005**	317.7	***.005**	350.0	***.012**	310.7	***.008**
	Stable	370.0	367.5	.414	379.3	.197	372.3	.109	379.0	.655	277.0	.465
	Failure	511.0	550.0	-	634.0	-	714.0	-				
TMV	Overall	10.26	8.96	***.016**	8.92	***.023**	8.77	***.008**	8.64	***.005**	8.36	***.002**
	Responder	10.75	8.84	***.013**	8.74	***.009**	8.45	***.005**	8.72	***.012**	8.33	***.008**
	Stable	9.28	9.09	.465	9.15	.715	8.99	1.00	8.34	.180	6.24	-
	Failure	9.50	9.63	-	9.77	-	10.03	-				
LogMAR VA	Overall	0.82	0.77	.429	0.80	.553	0.76	.539	0.70	.168	0.73	.306
	Responder	0.97	0.85	.173	0.88	.223	0.81	.104	0.77	.104	0.78	.102
	Stable	0.43	0.49	.465	0.55	.581	0.30	.593	0.25	.317	0.20	-
	Failure	1.00	1.10	-	1.00	-	1.20	-				

Anti-IL-6 = anti-interleukin-6, CST = central subfield thickness (microns), TMV = total macular volume (cubic millimeter)
Statistical analysis could not be performed on subgroups in which n = 1, these P-values are marked with the placeholder "-"

Methods: This retrospective case series included Fourteen eyes from 8 patients with npAIR and CME, all were seropositive for anti-retinal antibodies, treated with anti-IL-6 therapy and had a negative workup for paraneoplastic etiologies. Visual acuity (VA) and central subfield thickness (CST), total macular volume (TMV), and ellipsoid zone integrity change in central 6mm on foveal scan as measured by optical coherence tomography were extracted from charts prior to and at 3, 6, 12, 18, and 24 months after anti-IL-6 therapy was initiated. Eyes that had a >20% reduction in CST were defined as treatment responders, >20% increase in CST as failures, and ≤20% change in CST as stable. The main outcome measures were VA CST, TMV, and ellipsoid zone integrity change.

Results: Eleven eyes of six patients had failed multiple prior immunosuppressive therapies (Table 2). There was a significant reduction (P< .05) in CST at baseline (473.1 mm) after initiation of anti-IL-6 therapy that began at 3 months (389.2 mm) and continued through 24 months (348.7 mm). Similarly, there was a significant reduction (P< .05) in TMV baseline (10.15 mm^3) after initiation of anti-IL-6 therapy that began at 3 months (8.91 mm^3) and continued through 24 months (7.67 mm^3). VA improved from 0.84 to 0.52 at 24-month follow-up but did not reach statistical significance (P=.157). Nine of 14 eyes (64.3%) were treatment responders, 4 eyes (28.6%) were stable, and 1 eye (7.1%) was a treatment failure. After initiation of IL-6 therapy, there was a significant decrease in velocity of EZ change, experiencing an average restoration of 22.7 mm per month (P=.008). At least one eye of all patients responded to anti-IL-6 treatment. No patient experienced adverse effects or required discontinuation of therapy while on anti-IL-6 medication.

Conclusion: In this cohort of patients with npAIR and CME, treatment with anti-IL-6 medications tocilizumab and sarilumab, was associated with reduced CME, partial restoration of the ellipsoid zone, and a trend towards improved VA, while reducing burden of prior immunosuppressive therapies (Table 3). The treatment was well tolerated and

these largely positive and sustained results are important given the limited number of viable treatment options in the management of npAIR.

Disclosure: L. Carnago, None; **R. Keenan**, Sanofi, 6, Abbvie, 6, Horizon Therapeutics, 2, 6, Atom Biosciences, 1, 2, Arthrosi Therapeutics, 2, Selecta Biosciences, 2, 5; **G. Jaffe**, None; **J. Deaner**, Alimeria Sciences, Inc., 1; **D. Grewal**, EyePoint, 2, Genentech, 2.

Abstract Number: 0195

JAK Inhibitors in Refractory Adult and Childhood-Onset Still's Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Excessive and inappropriate production of pro-inflammatory cytokines such as interleukin IL-1, IL-6 or IL-18, is a pathogenic cornerstone in adult and childhood onset Still's disease. Beyond therapies targeting IL-1 or IL-6, Janus kinases (JAK) inhibitors have been proposed for AOSD patients refractory to or intolerant of treatment with biologicals. Recently, it has been suggested that JAK inhibitors might be efficient in refractory AOSD patients.

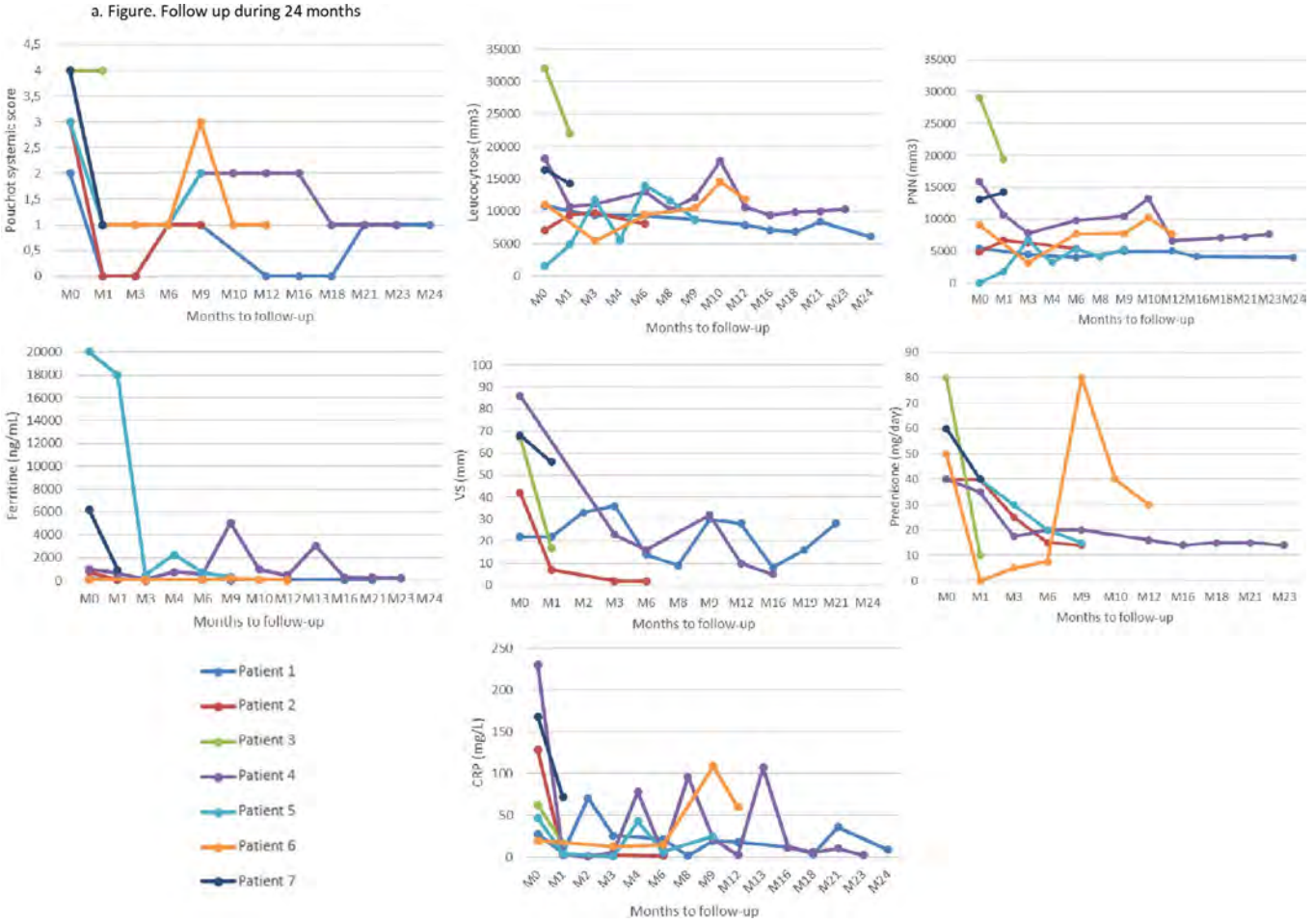
Methods: This retrospective study was based on a national survey of the departments of rheumatology, paediatric rheumatology and internal medicine in all French hospitals from an online call of the "Club Rhumatismes et Inflammation" (www.cri-net.com). The data were collected using a standardized questionnaire, and analyzed at different time points (treatment initiation, M1, M3, M6 and end of the follow-up). The response to JAK inhibitors was categorized as: complete remission (resolution of all clinical and biologic signs), partial remission (clinical improvement with persistence of a few symptoms) or failure (lack of clinical or biological improvement).

Results: 7 patients (5 adults and 2 children) were recruited (Table). Mean age at treatment start was 39.6 +/- 9.6 years for the AOSD patient and 11.0 +/- 7.07 years for the sJIA patients, and mean disease duration was years. The clinical expression was predominantly systemic in 6 patients and chronic articular in one. Response to corticosteroids, conventional synthetic or biological Disease Modifying Anti-Rheumatic Drugs had been considered inadequate in all patients. Baricitinib was used in 4 patients (of whom one was later switched to upadacitinib), ruxolitinib in 2, and tofacitinib in 1. Steroids were concurrently used in all patients, anakinra in one, methotrexate and anakinra in one who was then switched to colchicine and anakinra. At a mean follow-up of 11.3 +/- 9.3 months, partial response was observed in 4 cases (57%) (patients with ruxolitinib, baricitinib or tofacitinib) and failure in 3 (43%) (patients with baricitinib or ruxolitinib). No patient achieved complete remission. At the last visit, steroids could be decreased but not stopped in all patients. Patients with partial response had an average decrease of 63% (40% for tofacitinib and 80% for ruxolitinib between the start and the follow-up end date) and patients with no response were able to reduce steroids by 65% (Table). JAK inhibitors tolerance was excellent in all but one patient who developed organized pneumonia which led to discontinuation of the treatment.

Table. Characteristics of the AOSD patients

No.	Sex	Age (years)	Main symptoms	Treatments before JAKi onset	JAK inhibitors	Steroids at onset (mg/day)	Concomitant treatment	Response at last follow-up	Steroids at the end of follow-up (mg/day)	Follow-up (months)
1	F	6	Fever, polyarthritis, rash	AINS, MTX, ANAKI, TOCI, CANAKI, ADA, THALI	RUXOLITINIB 5mg x 2/day (majoration at 15 mg x 2/day)	3	INDOCID (stop)	Partial Response	1	25
2	F	16	Fever, polyarthritis	ANAKI, MTX, INFLIX, ETANERCEPT, CANAKI, TOCI	BARICITINIB 4 mg/day (majoration at 8 mg/day)	40	APRANAX	Partial Response	14	9
3	M	28	Fever, polyarthritis, rash	ANAKI	BARICITINIB 4mg/day	80	0	**No Response**	10	1
4	M	32	Fever, polyarthritis, rash	TOCI+MTX, ANAKI+MTX, CANAKI+MTX, ADA, CICLO, IgIV	BARICITINIB 4mg/day (stop at M17) UPADACITINIB 15 mg/day	16	MTX 20 mg/week (stop) ANAKINRA 100mg/day COLCHICINE 1.5 mg/day	Partial Response	13	22
5	F	40	Fever, polyarthritis, rash	MTX, IMUREL, CICLO, ETANERCEPT, ANAKI+MTX, TOCI+MTX, IgIV	RUXOLITINIB 15mg x 2/day	60	ANAKI 200mg/day	**No Response**	15	9
6	F	48	Fever, polyarthritis, rash	TOCI, ANAKI, CICLO, CANAKI, IMUREL	TOFACITINIB 5mg x 2/day	50	0	Partial Response	30	12
7	F	50	Fever, polyarthralgia, rash	ANAKI	BARICITINIB 4mg/day	60	0	**No Response**	40	1

Conclusion: JAK inhibitors therapy may be helpful for some patients with refractory Still's disease, but not in monotherapy. However, no complete response was observed in this short series of cases. There might be a difference of response between the molecules, although the number of patients is too low to draw conclusions. Additional information is thus needed to evaluate more precisely the risk-benefit ratio of this treatment, and a possible difference in efficacy among the different groups of JAK inhibitors.



Disclosure: L. GILLARD, None; **S. Mitrovic**, None; **J. Pouchot**, None; **F. Cohen**, None; **M. Michaud**, None; **H. Reumaux**, None; **I. Kone-Paut**, None; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2.

Abstract Number: 0196

A Single Center, Double Blind, Randomized, Placebo-Controlled Trial of Anakinra in Adult Patients with Features of Cytokine Storm Syndrome in COVID-19

Lesley Jackson[1], Randy Cron[1], Nitasha Khullar[2], Christopher Chapleau[3], Dongmei Sun[4] and Winn Chatham[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama Birmingham, Birmingham, AL, [3]UAB Pharmacy, University of Alabama at Birmingham, Birmingham, AL, [4]Division of Clinical Immunology and Rheumatology, The University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Outcomes with anakinra verses placebo, modified intent to treat analysis; N (%) unless otherwise stated. * P values < 0.05

	Anakinra Arm (N = 15)	Placebo Arm (N = 15)	p-value
Primary Outcomes			
Survival Day 10	14 (93.3)	13 (86.7)	1.0
Survived hospitalization	11 (73.3)	11 (73.3)	1.0
Did not require mechanical ventilation	10 (66.7)	10 (66.7)	1.0
Secondary Outcomes			
75% improvement from Day 0 ferritin and CRP elevations by Day 10, N=26	6 (46.2)	7 (53.9)	1.0
75% improvement from Day 0 LDH and D-dimer elevations by Day 10, N=26	0 (0.0)	7 (53.9)	0.005*
Able to maintain oxygen saturation >92% on RA by Day 10, N=27	4 (28.6)	9 (69.2)	0.06

Table 2. Estimation of anakinra effect on the composite of death from any cause or need for invasive mechanical ventilation, after adjustment for potential confounding factors, using a multivariable Cox proportional hazards model.

	Hazard ratio	95% CI	p value
Anakinra group vs Placebo group	1.688	0.354 – 8.048	0.51
Female *vs* Male	0	NA	1
Age ≥65 *vs* <65	2.438	0.0.438 – 13.562	0.31
Number of comorbidities ≥2 *vs* 0-1	0.771	0.054 – 10.93	0.85
Increase in oxygen requirement or oxygen delivery measures to maintain oxygen saturation >90% at Day 2 *vs* no increase in oxygen requirement or oxygen delivery measures to maintain oxygen saturation >90% at Day 2	3.0879E8	NA	1

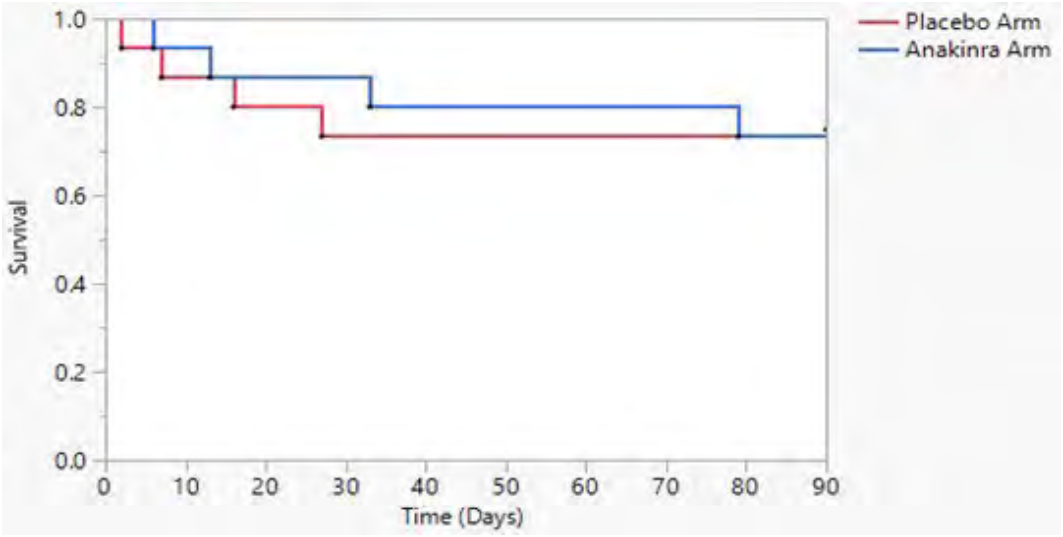


Figure 1. Kaplan Meier Curve demonstrating survival according to treatment with anakinra and placebo groups.

Background/Purpose: Some patients with COVID-19 develop respiratory distress and cytokine storm syndrome (CSS) which is characterized by hyperinflammation and may progress to multi-organ failure. Anakinra is a recombinant interleukin-1 receptor antagonist used to treat some inflammatory disorders and has previously demonstrated mortality benefit in sepsis patients with CSS. Anakinra may play a role in certain patients with COVID-19 to reduce hyperinflammation and improve outcomes. The aim of this study was to assess the efficacy and safety of anakinra when added to standard of care in patients with COVID-19 infection and features of cytokine storm syndrome.

Methods: In this single center, randomized, double-blind, placebo-controlled trial (ClinicalTrials.gov, NCT04362111), adult inpatients were recruited with molecular PCR RNA confirmed SARS-CoV-2 infection, radiographic evidence of COVID-19 pneumonia based on imaging, new or increasing oxygen requirement, ferritin ≥700 ng/ml, and any three of the following: D-dimer ≥500 ng/ml, platelet count < 130,000/mm^3, white blood cell count < 3500/mm^3 or lymphocyte count < 1000/mm^3, AST or ALT >2X the upper limit of normal (ULN), LDH >2X the ULN, C-reactive protein >100 mg/L. Eligible patients were randomly assigned (1:1) to standard of care (SoC) plus anakinra (100 mg subcutaneous every 6 hours for 10 days) or SoC plus placebo. All received dexamethasone. Primary outcome was survival and discharge from the hospital without the need for intubation/mechanical ventilation at day 10. All analyses were done on a modified intention-to-treat basis.

Results: Between August 5, 2020 and January 2, 2021, 32 patients (235 screened) were recruited: 15 assigned to the anakinra group and 17 to placebo group. Two patients in the placebo group withdrew in the initial 48 hours and were excluded from analysis. Mean age was 63 (SD 10.3), 20 (66.7%) participants were men, and 20 (66.7%) were Caucasian. At day 10, 1 (6.7%) patient in the anakinra group had died and 2 (13.3%) patients in the placebo group had died (p=1.0). At hospital discharge, 4 (26.7%) patients in the anakinra group and 4 (26.7%) patients in the usual care group had died. Confirmed microbial infections occurred in 4 patients in the anakinra group and 2 in the placebo group (p=0.7).

Conclusion: Anakinra added to dexamethasone did not significantly impact outcomes in this study of patients with clinical laboratory features of early CSS and mild-to-moderate COVID-19 pneumonia. Additional studies are needed to assess the efficacy and optimal dosing duration of anakinra in patients with more severe COVID-19.

Disclosure: L. Jackson, None; **R. Cron**, SOBI, 1, 2, 5, 6, Pfizer, 1, 5, Novartis, 2, Sironax, 2; **N. Khullar**, None; **C. Chapleau**, None; **D. Sun**, None; **W. Chatham**, None.

Abstract Number: 0197

Successful Treatment of Severe COVID-19 Pneumonia with Simultaneous Tocilizumab and Anakinra - A Case Series

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Session Date: Saturday, November 6, 2021
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Severe and life threating COVID-19 pneumonia is often characterized by local and systemic immune-mediated hyperinflammation At the early disease stage activated monocytes are migrating to the lung and cause the typical opac infiltrates, which lead to an reduction of oxygen uptake. This was the rationale use this combination anti-inflammatory drugs in severe Covid-19 disease. Interleukin (IL)-6 and IL-1 blockade alone, respectively showed contradictory results in severe COVID-19 pneumonia that might be related to the differences is patient populations (early vs. late stage) and to the fact that blockade of just one cytokine might be not sufficient against the cytokine storm. Here we report results of an open-label treatment with a combination of an IL-6 receptor blocker to-

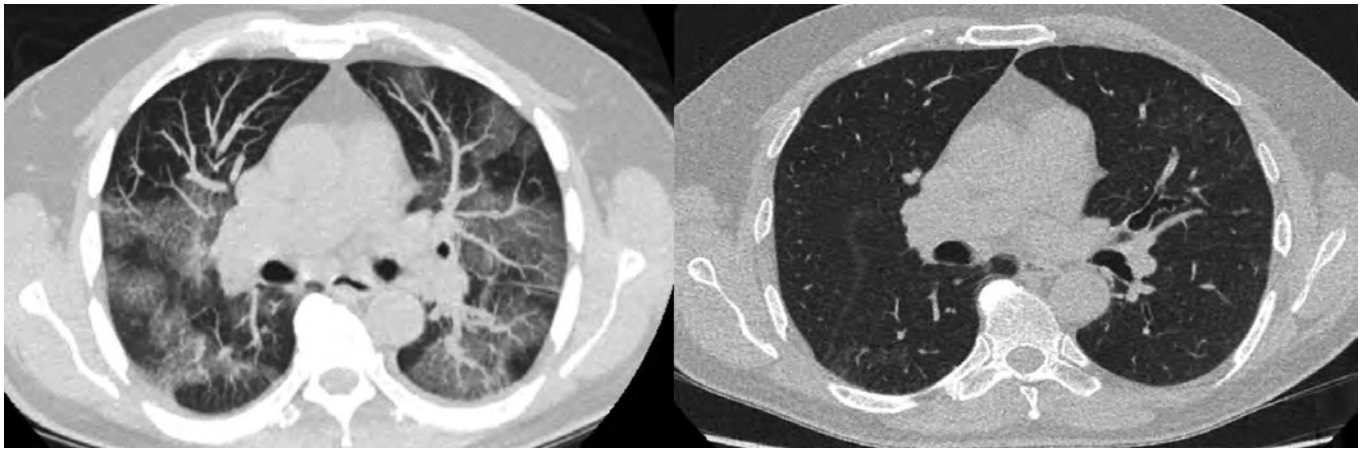

Image 1. CT-Scan of a patient with active COVID-19 infection before and one month after treatment with a combination of tocilizumab and anakinra.

cilizumab and an IL-1 receptor antagonist anakinra in patients with early (up to 10 days since symptom onset) severe COVID-19 pneumonia with evidence of cytokine release.

Methods: Adult patients with, according to WHO criteria, severe to critical COVID-19 infection associated pneumonia and cytokine release, requiring oxygen supplementation and evidence of rapid deterioration and decrease of oxygen saturation to ≤ 95% hospitalized between May 2020 and April 2021 were treated with tocilizumab 8 mg/kg up to 800 mg intravenously and anakinra 100 to 300 mg for 3 to 5 days, starting at the same day. We excluded patients with a symptom duration of > 10 days, patients with evidence of bacterial infection, indicated by an elevated procalcitonin serum level, patients with severe pre-existing lung disease such as severe COPD or heart failure of > II according to the NYHA classification and patients > 80 years. Laboratory parameters and chest CT were performed before and one month after treatment. A semi-quantitative CT score was calculated based on the extent of lobar pneumonia involvement (0:0%; 1, < 5%; 2:5-25%; 3:26-50%; 4:51-75%; 5, > 75%; range 0-5; global score 0-25) for each time point. All patients were informed about the off label use in reference to the statement of the German Robert Koch Institute regarding therapies in “off label use” in COVID-19 patients after carefull consideration of the individual risk-benefit ratio and written individual consents were obtained.

Results: Thirty-one adult patients with severe COVID-19 pneumonia and signs of cytokine release, mean age 54 (30-79) years, 5 female, 26 male, mean symptom duration 6 (3-10) days, were treated. Patients with more than > 10 days of symptoms, evidence of bacterial infection/ elevated procalcitonin and other severe lung diseases were excluded. Computed tomography (CT) scans of the lung were performed initially and after one month; inflammatory activity was assessed on a scale 0 to 25. Twenty-five patients survived without intubation and mechanical lung ventilation, two patients died. C-reactive protein decreased in 19/31 patients to normal ranges. The mean activity CT score decreased from 14 (8-20) to 6 (0-16, n=16).

Conclusion: In conclusion, most of our patients recovered fast and sustained, indicating that early interruption of cytokine release might be very effective in preventing patients from mechanical ventilation, death and long-term damage.

Disclosure: H. Haibel, Boehringer, 2, Janssen, 2, 6, MSD, 2, 6, Pfizer, 6, Novartis, 2, Roche, 2, 6, AbbVie, 6; **S. Angermair**, None; **M. Schumann**, None; **J. Vahldiek**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **T. Schneider**, None.

Abstract Number: 0198

High Dose Intravenous Methylprednisolone Induces Rapid Improvement of Visual Acuity in Non-Infectious Uveitis of Different Immune Mediated Inflammatory Diseases

Nuria Vegas-Revenga[1], José Luis Martin-Varillas[2], Vanesa Calvo-Río[3], Iñigo Gonzalez-Mazon[4], Lara Sánchez-Bilbao[5], Emma Beltrán Catalán[6], Alejandro Fonollosa[7], Ana Blanco[8], Ana Blanco[9], Miguel Cordero Coma[10], Norberto Ortego[11], Ignacio Torre[12], Felix Hernandez[13], Santiago Muñóz-Fernández[14], Maria del Mar Esteban-Ortega[14], Manuel Diaz-Llopis[15], Joaquin Cañal[5], Juan Antonio Ventosa[5], Rosalía Demetrio-Pablo[16], Lucia Cristina Dominguez Casas[17], Santos Castañeda[18], Iván Ferraz-Amaro[19], Miguel Ángel gonzalez-Gay[20] and Ricardo Blanco[3], [1]Hospital Galdakao, Galdakao, Spain, [2]Hospital Sierrallana, Torrelavega, Spain, [3]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [4]H. U. Marques de Valdecilla, Santander, Spain, [5]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [6]Hospital del Mar, Barcelona, Spain, [7]Hospital Universitario de Cruces, Barakaldo, Spain, [8]Hospital Universitario de Donostia, San Sebastián, [9]Hospital Universitario de Donostia, Donostia, Spain, [10]Hospital de León, Leon, Spain, [11]Medicine Department, Universidad de Granada, Granada, Spain, [12]Hospital Universitario de Basurto, Bilbao, Spain, [13]Hospital Doctor Negrín, Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain, [14]Hospital Universitario Infanta Sofia, Madrid, Spain, [15]Hospital Universitario La Fe, Valencia, Spain, [16]Hospital Universitario de Marqués de Valdecilla, Santander, Spain, [17]Hospital Universtario San Agustin, Oviedo, Spain, [18]Hospital Universitario de la Princesa, Madrid, Spain, [19]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [20]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Rapid and effective remission-inducing therapy is mandatory in uveitis to avoid irreversible structural and functional damage. In some severe cases biological agents might be required (1-6). High-dose intravenous methylprednisolone (IVMP) may achieve prompt control of inflammation in most immune mediated inflammatory diseases (IMID), including non-infectious uveitis (NIU). The objective is to evaluate the efficacy and safety of IVMP pulse therapy in NIU of different IMID.

Methods: Multicentre study of 71 patients with severe uveitis who received IVMP. The underlying diseases were: Vogt-Koyanagi-Harada disease (VKHD) (n=24), Behçet disease (BD) (19), Sarcoidosis (5) and idiopathic NIU (23). The main outcome variable was Best-Corrected Visual Acuity (BCVA) estimated using the Snellen chart. BCVA that was assessed at 0 (basal), 2-5, 7, 15 and 30 days after IVMP. The results are expressed as mean ±SD in normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.

Results: We studied 46♀/ 25♂ patients. The main features are shown in TABLE. IVMP dose ranged from 250 to 1000 mg/day administered for 3-5 consecutive days, the dose was established according to the presence or not of other systemic manifestations apart from uveitis. All of them had active intraocular inflammation at the moment of the study. BCVA values improved considerably after 1 month (FIGURE). No major side effects were observed.

Conclusion: High-dose IVMP pulse therapy is useful and safe for a prompt control of BCVA regardless of the underlying IMID.

Table. Main features of 71 patients with NIU. Data are of affected eyes

	VKH (n=24)	Idiophatic (n=23)	Behcet's disease (n=19)	Sarcoidosis (n=5)	Overall (n=71)
Men/Women, n	5/19	9/14	9/10	2/3	71
Mean age (years) ±SD	42 ±11	47 ± 15	33±10	42 ± 22	-
Unilateral/Bilateral NIU, n (%)	2 (8.3)/22(91.7)	10 (43.5)/13(56.5)	4 (21)/15 (79)	3(60)/2(40)	19/52
NIU patterns, n (%)					
Posterior uveitis	6 (25)	9 (39.1)	3 (15.8)	1 (20)	19
Panuveitis	18 (75)	14 (60.9)	16 (84.2)	4 (80)	52
Laboratory data, n (%)					
ANA	2 (8.34)	2 (8.7)	0 (0)	1 (20)	5
HLA B27	0 (0)	4 (17.4)	0 (0)	0 (0)	4
HLA B29	0 (0)	1 (4.3)	0 (0)	0 (0)	1
HLA B51	0 (0)	5 (21.7)	8 (42)	3 (60)	16
Angiotensin Converting Enzyme (ACE)	1 (4.17)	2 (8.7)	0 (0)	1 (20)	4

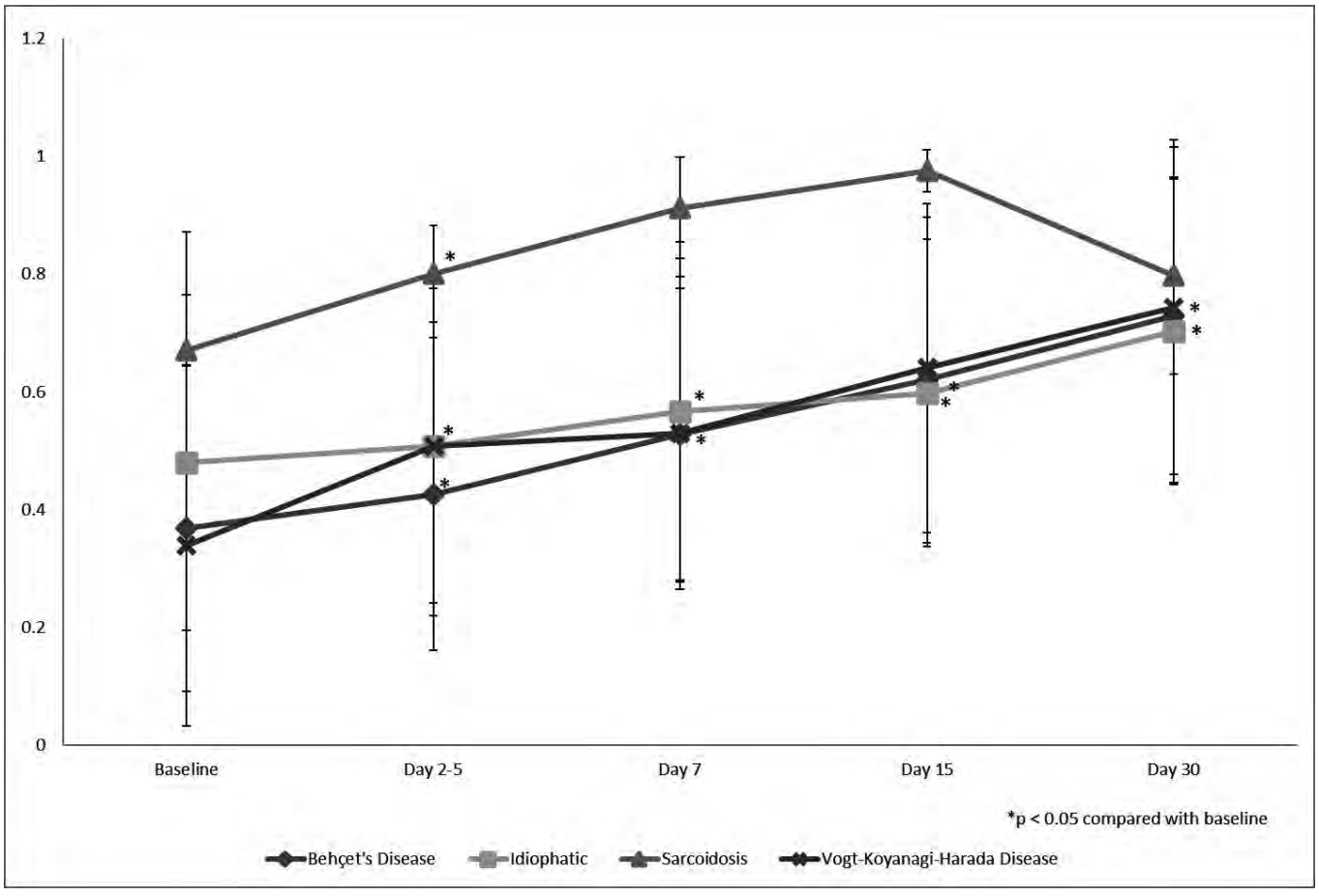

Figure. Improvement of best corrected visual acuity (BCVA).

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Disclosure: N. Vegas-Revenga, None; **J. Martin-Varillas**, None; **V. Calvo-Río**, None; **I. Gonzalez-Mazon**, None; **L. Sánchez-Bilbao**, None; **E. Beltrán Catalán**, None; **A. Fonollosa**, None; **A. Blanco**, None; **A. Blanco**, None; **M. Cordero Coma**, None; **N. Ortego**, None; **I. Torre**, None; **F. Hernandez**, None; **S. Muñóz-Fernández**, None; **M. Esteban-Ortega**, None; **M. Diaz-Llopis**, None; **J. Cañal**, None; **J. Ventosa**, None; **R. Demetrio-Pablo**, None; **L. Dominguez Casas**, None; **S. Castañeda**, None; **I. Ferraz-Amaro**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0199

Rapid Improvement in Cystoid Macular Edema with High Dose Intravenous Methylprednisolone in Non-Infectious Uveitis of Different Immune Mediated Inflammatory Diseases

Nuria Vegas-Revenga[1], José Luis Martin-Varillas[2], Vanesa Calvo-Río[3], Iñigo Gonzalez-Mazon[4], Lara Sánchez-Bilbao[5], Emma Beltrán Catalán[6], Alejandro Fonollosa[7], Ana Blanco[8], Ana Blanco[9], Miguel Cordero Coma[10], Norberto Ortego[11], Ignacio Torre[12], Felix Hernandez[13], Santiago Muñóz-Fernández[14], Maria del Mar Esteban-Ortega[14], Manuel Diaz-Llopis[15], Joaquin Cañal[5], Juan Antonio Ventosa[5], Rosalía Demetrio-Pablo[16], Lucia Cristina Dominguez Casas[17], Santos Castañeda[18], Iván Ferraz-Amaro[19], Miguel Ángel gonzalez-Gay[20] and Ricardo Blanco[3], [1]Hospital Galdakao, Galdakao, Spain, [2]Hospital Sierrallana, Torrelavega, Spain, [3]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [4]H. U. Marques de Valdecilla, Santander, Spain, [5]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [6]Hospital del Mar, Barcelona, Spain, [7]Hospital Universitario de Cruces, Barakaldo, Spain, [8]Hospital Universitario de Donostia, San Sebastián, [9]Hospital Universitario de Donostia, Donostia, Spain, [10]Hospital de León, Leon, Spain, [11]Medicine Department, Universidad de Granada, Granada, Spain, [12]Hospital Universitario de Basurto, Bilbao, Spain, [13]Hospital Doctor Negrín, Las Palmas de Gran Canaria, Las Palmas de Gran Canaria, Spain, [14]Hospital Universitario Infanta Sofia, Madrid, Spain, [15]Hospital Universitario La Fe, Valencia, Spain, [16]Hospital Universitario de Marqués de Valdecilla, Santander, Spain, [17]Hospital Universtario San Agustin, Oviedo, Spain, [18]Hospital Universitario de la Princesa, Madrid, Spain, [19]Hospital Universitario de Canarias, Santa Cruz de Tenerife, Spain, [20]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Cystoid Macular Edema (CME) is the most important cause of blindness in non-infectious uveitis (NIU) (1). Corticosteroids and conventional and/or biological immunosuppressant may be required (1-6). High-dose intravenous methylprednisolone (IVMP) pulse therapy may induce a rapid improvement.

Table. Main features of 66 patients with cystoid macular edema

	VKH (n=24)	Idiophatic (n=23)	Behcet's disease (n=19)	Overall (n=66)
Men/Women, n	5/19	9/14	9/10	66
Mean age (years)	42 ± 11	47 ± 15	33 ± 10	-
Unilateral/Bilateral, n (%)	2 (8.3) /22 (91.7)	10 (43.5) /13 (56.5)	4 (21) /15 (79)	16/50
Inflammatory ocular patterns, n (%)				
Posterior uveitis	6 (25)	9 (39.1)	3 (15.8)	18
Panuveitis	18 (75)	14 (60.9)	16 (84.2)	48
Laboratory data, n (%)				
ANA	2 (8.34)	2 (8.7)	0 (0)	4
HLA B27	0 (0)	4 (17.4)	0 (0)	4
HLA B29	0 (0)	1 (4.3)	0 (0)	1
HLA B51	0 (0)	5 (21.7)	8 (42)	13

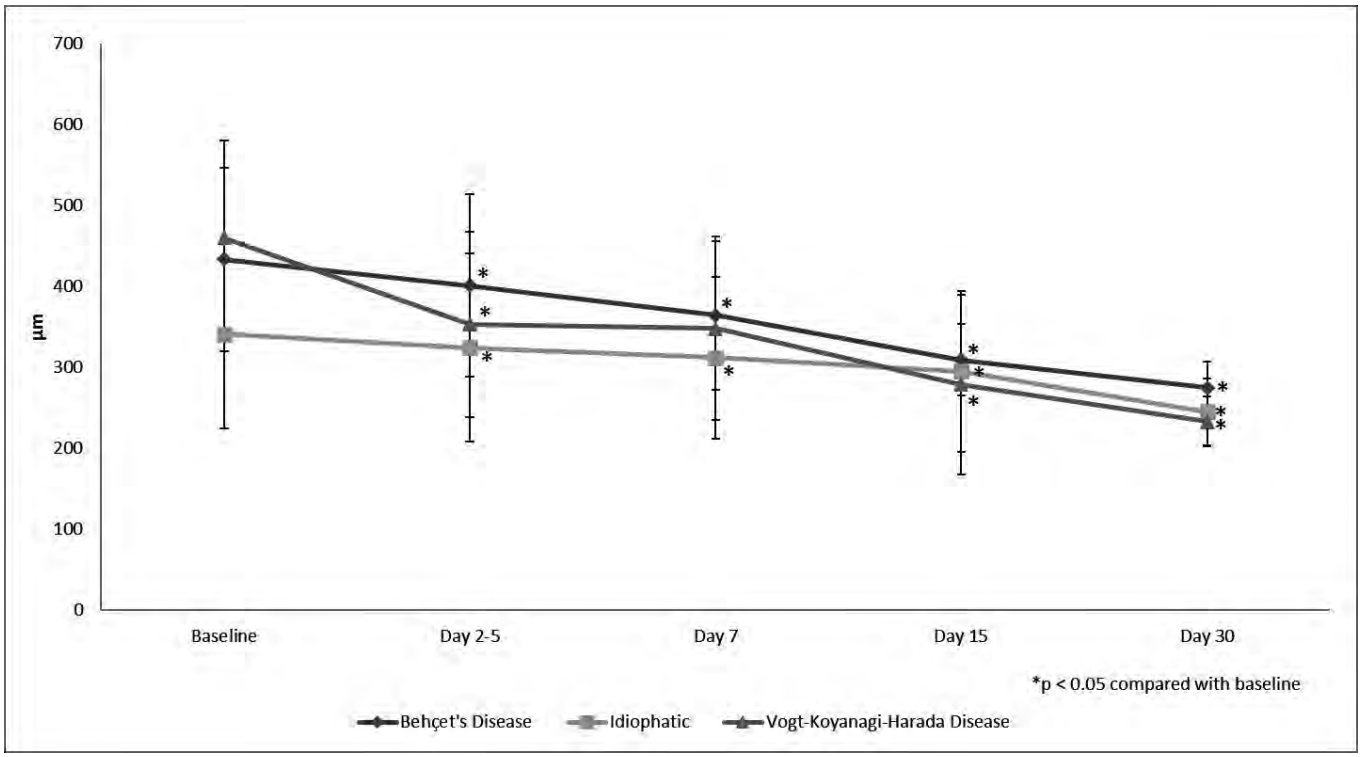

Figure. Improvement of OCT in 66 patients with cystoid macular edema.

The objective is to evaluate the efficacy and safety of IVMP pulse therapy in CME of different immune mediated inflammatory diseases (IMID).

Methods: Multicentre study of 66 patients with severe ocular inflammation who received IVMP. The underlying diseases were: Vogt-Koyanagi-Harada disease (VKHD)(n=24), Behçet's disease (BD) (19) and idiopathic NIU (23). The main outcome variable was macular thickness and macular edema (Optical coherence tomography [OCT] >300 µm); that was assessed at 0 (basal), 2-5, 7, 15 and 30 days after IVMP. The results are expressed as mean ±SD for normally distributed variables, or as median [IQR] when are not. Comparison of continuous variables was performed using the Wilcoxon test.

Results: We studied 43♀/ 23♂ patients. The main features are shown in TABLE. IVMP dose ranged from 250 to 1000 mg/day administered for 3-5 consecutive days, the dose was established according to the presence or not of

other systemic manifestations apart from uveitis. All of them had active intraocular inflammation at the moment of the study. A rapid and maintained statistically improvement was observed in OCT values in all underlying diseases (FIGURE). No major side effects were observed.

Conclusion: High-dose IVMP pulse therapy is useful and safe in the prompt control of CME, regardless of the underlying IMID.

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Disclosure: N. **Vegas-Revenga**, None; **J. Martin-Varillas**, None; **V. Calvo-Río**, None; **I. Gonzalez-Mazon**, None; **L. Sánchez-Bilbao**, None; **E. Beltrán Catalán**, None; **A. Fonollosa**, None; **A. Blanco**, None; **A. Blanco**, None; **M. Cordero Coma**, None; **N. Ortego**, None; **I. Torre**, None; **F. Hernandez**, None; **S. Muñóz-Fernández**, None; **M. Esteban-Ortega**, None; **M. Diaz-Llopis**, None; **J. Cañal**, None; **J. Ventosa**, None; **R. Demetrio-Pablo**, None; **L. Dominguez Casas**, None; **S. Castañeda**, None; **I. Ferraz-Amaro**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0200

In Undifferentiated Arthritis, DMARD-treatment Intensified During the Last Decennia but Did Not Result in Improved Outcomes

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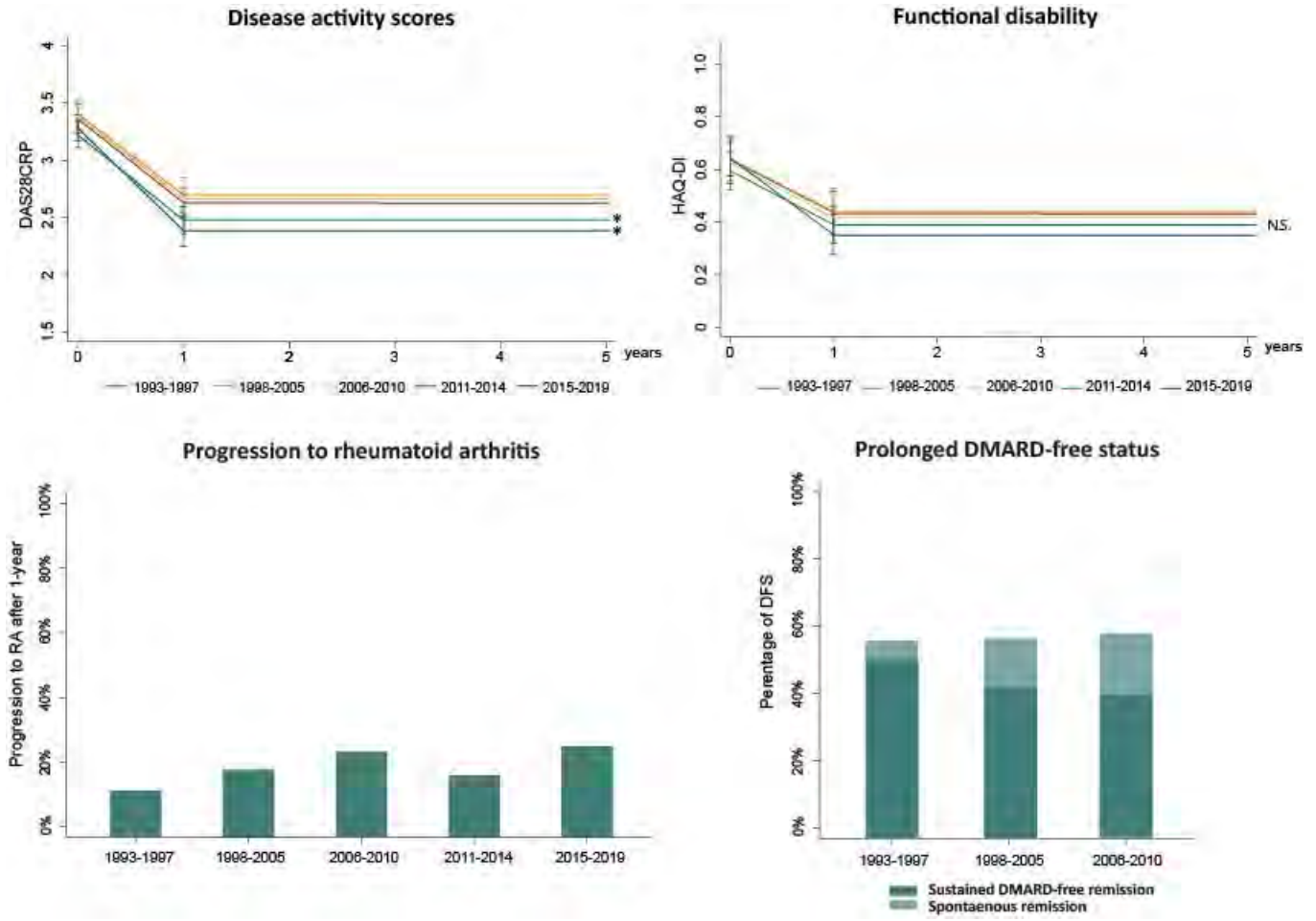
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: International guidelines stress timely DMARD-initiation in early arthritis, also when classification-criteria are not yet fulfilled. Consequently, undifferentiated arthritis (UA)-patients are increasingly treated despite placebo-controlled evidence for DMARD-effectivity in UA. Furthermore, since the introduction of the 2010 classification-criteria, the UA-population changed and trials including UA-patients not fulfilling the 1987- *and* 2010-criteria are absent. With 25-years of observational data, using inclusion-period as instrumental variable for DMARD-treatment, we studied whether enhanced treatment-strategies improved (long-term) outcome in UA.

Methods: UA was defined, in retrospect, as clinical arthritis neither fulfilling the 1987 nor the 2010 criteria for RA, nor any other distinct diagnosis. In total, 1132 UA-patients, consecutively included in the Leiden Early Arthritis Clinic between 1993-2019, were studied, divided into 5 inclusion-periods; 1993-1997, 1998-2005, 2006-2010, 2011-2014, 2015-2019. Frequency of DMARD-initiation was compared between the inclusion-periods as were the following



Legend: Baseline disease activity scores and the decline in the first year did not differ between the inclusion periods. Disease activity after 1-year of follow-up improved from 2011 onwards. HAQ-DI scores at baseline and during follow-up remained similar in all inclusion periods, as did prevalence of DFS (spontaneous remission and sustained remission after DMARD-discontinuation). Also, percentage of patients who progressed to RA after 1-year did not improve. DAS: disease activity score, CRP: C-reactive protein, HAQ-DI: Health Assessment Questionnaire Disability Index, DFS: DMARD-free status, RA: rheumatoid arthritis.

outcomes: DAS28CRP and HAQ-DI during follow-up, prevalence of DMARD-free status (DFS; spontaneous remission or sustained remission after DMARD-stop) and progression to RA (according to the 1987 and/or 2010-criteria).

Results: The current UA-population has relatively mild disease; median SJC 1, TJC 2 and median HAQ 0.6. DMARD-treatment increased from 17% (1993-1997) up-to 52% (2015-2019), in which methotrexate became more common in the last decade. DAS28CRP during follow-up improved from 2011 onwards (range;-0.18,-0.25/p< 0.05). HAQ-scores remained similar (range;-0.00,-0.09/p >0.05), as did DFS-prevalence: 57%, 58%, 59% (1993-1997/1998-2005/2006-2010;p=0.59). Also, the percentage of patients that developed RA did not decrease (14%/21%/26%/18%/27% in the respective inclusion-periods).

Conclusion: Although intensified DMARD-treatment in UA might have led to lower disease activity scores, functionality and long-term outcomes did not improve, indicating potential overtreatment. Stratification methods for the up-to-date UA-population, to identify patients that will develop RA, are warranted.

	Total N = 1132	1993-1997 N = 222	1998-2005 N = 216	2006-2010 N = 214	2011-2015 N = 247	2016-2019 N = 233	*p-value*
Age (years), mean (SD)	52 (17)	49 (17)	49 (18)	52 (17)	53 (16)	56 (16)	*<0.01*
Gender (female), %	59	50	59	62	66	56	*0.01*
Sympt. dur. (wk), median (IQR)	11 (4-26)	10 (3-22)	15 (6-33)	16 (6-31)	8 (3-24)	9 (5-20)	*<0.01*
ACPA-positive, %	5	3	7	3	4	5	*0.28*
RF-positive, %	7	5	7	6	8	10	*0.34*
SJC (0-28), median (IQR)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-3)	1 (1-2)	*0.14*
TJC (0-28), median (IQR)	2 (1-4)	1 (1-3)	2 (1-3)	2 (1-4)	1 (1-4)	2 (1-4)	*0.76*
CRP, median (IQR)	6 (3-17)	9 (4-22)	8 (3-22)	6 (3-21)	4 (3-11)	5 (3-13)	*<0.01*
ESR, median (IQR)	14 (6-33)	18 (9-38)	16 (7-34)	14 (6-33)	11 (6-25)	13 (6-31)	*0.01*
VAS (0-100), median (IQR)	30 (14-50)	30 (14-50)	32 (14-51)	26 (11-50)	30 (18-53)	30 (20-50)	*0.30*
DAS28CRP, median (IQR)	3.29 (2.67-3.93)	3.32 (2.62-3.96)	3.37 (2.69-4.00)	3.34 (2.67-4.08)	3.15 (2.68-3.80)	3.34 (2.67-3.85)	*0.45*
HAQ-DI, median (IQR)	0.50 (0.13-0.91)	0.47 (0.10-0.90)	0.50 (0.14-0.93)	0.51 (0.13-0.93)	0.58 (0.15-0.88)	0.62 (0.13-0.99)	*0.93*

Legend: Baseline characteristics of the total UA-population and per inclusion period. Over time, UA-patients became older and symptom duration declined. Yet, disease activity and functional disability at baseline were comparable between the inclusion periods. Differences between inclusion periods were tested using ANOVA or Kruskal-Wallis test, as appropriate. Missing values were imputed and used for baseline table; values represent mean of the imputed medians calculated using Rubin's rules. ACPA: anticitrullinated protein antibody, CRP: C-reactive protein, DAS: disease activity score, ESR: estimated sedimentation rate, HAQ-DI: health assessment questionnaire disability index, SJC: swollen joint count, TJC: tender joint count, VAS: visual analogue scale.

Disclosure: M. Verstappen, None; **X. Matthijssen**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0201

Australian Psoriatic Arthritis (PsA) Biologic Disease-modifying Antirheumatic Drug (bDMARD) Treatment Pathways Using Sankey Diagrams and Predictive Analysis: A Combined Australian Rheumatology Association Database (ARAD) and Pharmaceutical Benefits Scheme (PBS) Analysis

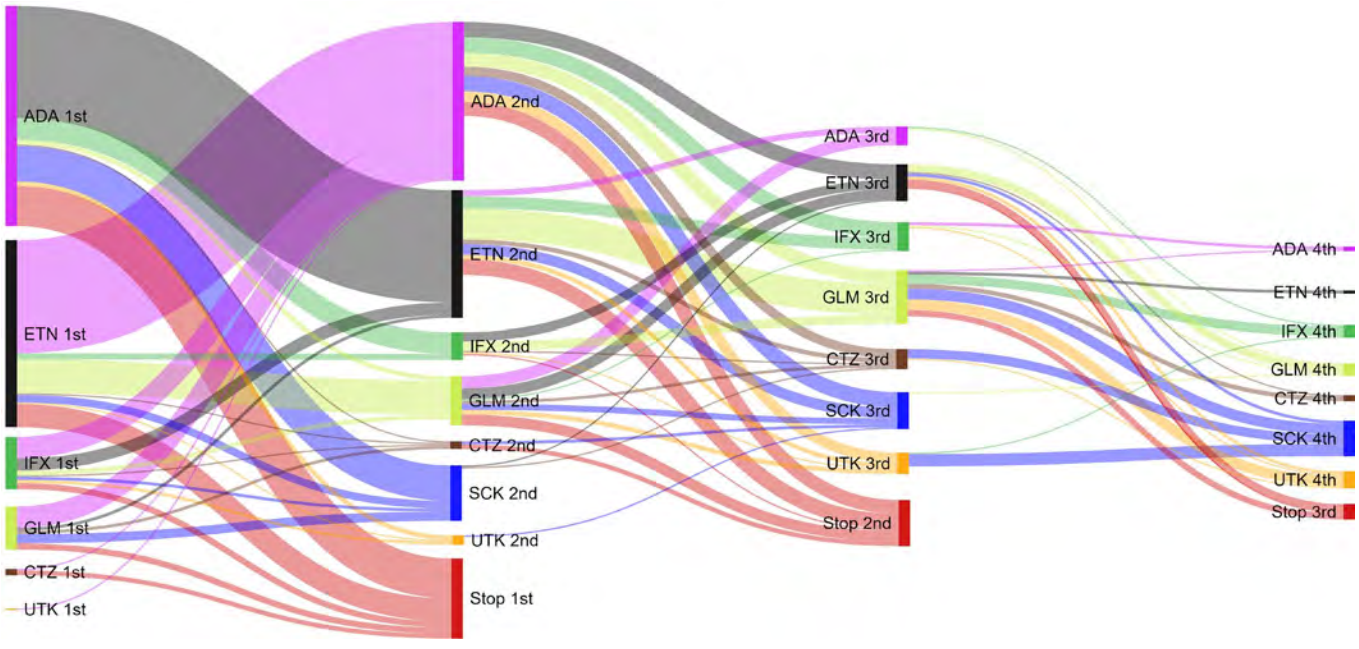
Ashley Fletcher[1], Lyn March[2], Marissa Lassere[3], Catherine Hill[4], Claire Barrett[5], Graeme Carroll[6], Premarani Sinnathurai[7] and Rachelle Buchbinder[8], [1]Cabrini Health, Malvern, Australia, [2]Institute of Bone and Joint Research, Kolling Institute, University of Sydney; Department of Rheumatology, Royal North Shore Hospital, Northern Sydney Local Health District, St Leonards, Sydney, Australia, [3]St George Hospital; School of Population Health, University of New South Wales, Carlton, Australia, [4]Queen Elizabeth Hospital, Woodville, Australia, [5]Redcliffe Hospital, University of Queensland, Margate Beach, Australia, [6]Fiona Stanley Hospital, Perth, Australia, [7]Institute of Bone and Joint Research, Kolling Institute, University of Sydney; Department of Rheumatology, Royal North Shore Hospital, Northern Sydney Local Health District, Sydney, Australia, [8]Cabrini Health/Monash University, Malvern, Australia

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To describe current bDMARD treatment patterns for ARAD participants with PsA, after combining with linked government PBS data.

Methods: ARAD, a voluntary longitudinal observational database established in 2001, collects long-term outcome data for people with inflammatory arthritis in Australia. Participants complete semi-annual, then annual questionnaires. Demographic, clinical, drugs, patient-reported outcome (PRO) measures and reasons for stopping bDMARD therapy, such as inefficacy or side-effects, were extracted from Sept. 2001 to June 2020 for all PsA participants. Socioeconomic status (SES) was derived from the participants address and assigned an Australian Bureau of Statistics (ABS) Socio-Economic Indexes for Areas (SEIFA) score of the Index of Relative Socio-economic Advantage and Disadvantage (IRSAD). PBS is the Australian Government program that subsidises medicines, ARAD participants were linked to PBS data from 2011 to 2018. Logistic regression was used to evaluate baseline characteristics of participants who switched compared to those who did not. Switching patterns determined for each bDMARD and time on first, second and third-line bDMARDs were analysed and reasons for switching in the ARAD data were assessed.

Results: 673 PsA participants were included, 5.4% were excluded as ARAD did not match PBS and 31.3% extended medication records beyond the last ARAD questionnaire. First-line bDMARDs were adalimumab (n=283), etanercept (n=178), golimumab (n=44), infliximab (n=32), secukinumab (n=9), certolizumab (n=6) and ustekinumab (n=4). At 1 year 26.9% starting first-line bDMARD therapy switched to another bDMARD, 37.0% switched from second-line therapies and 31.3% switched from third-line therapies. For First-line bDMARDs, females (OR 1.78; 95%CI: 1.18-2.66), higher SES (lowest vs highest OR 2.47; 95%CI: 1.25-4.87), opioid users (OR 1.64; 95%CI: 1.02-2.63) and worse PRO measures (i.e. EuroQol (EQ-5D) OR 0.28; 95%CI: 0.11-0.69) were more likely to switch. Inefficacy (first-line 50.5%, second-line 65.4%, third-line 62.0%) or side effects (first-line 19.0%, second-line 12.0%, third-line 14.0%) were the most commonly cited reasons for stopping therapy irrespective of line of treatment.



Flow of bDMARD use - switching and stopping from first-line therapy to fourth-line therapy.

Conclusion: Patient self-report medication data in ARAD has a high degree of accuracy when compared with the PBS government database. The treatment pathways for bDMARD use by PsA patients in Australia is complex with 30% switching to another bDMARD therapy after 1 year. Common reasons for switching or stopping were inefficacy and side effects.

Disclosure: A. Fletcher, None; **L. March**, Eli Lilly Australia, 6, 12, ARAD has been supported with unrestricted educational grants administered through the Australian Rheumatology Association, Janssen-Cilag Pty Limited (Janssen) Australia, 12, A3BC receives unrestricted grants from Janssen, Pfizer Australia, 6, 12, ARAD has been supported with unrestricted educational grants administered through the Australian Rheumatology Association, AbbVie Australia, 6, Sandoz Australia, 6, OMERACT (multiple), 12, I am Executive of OMERACT that receives grants from 30 companies; **M. Lassere**, Merck Sharp & Dohme (MSD), 12, This investigator-initiated clinical trial was supported by an unrestricted education grant from Merck Sharp & Dohme (MSD) in 2016-2018, Pfizer Australia, 12, Chair, Steering Committee of the Australian Rheumatology Association Database (ARAD). ARAD has been supported with unrestricted educational grants administered through the Australian Rheumatology Association, Eli Lilly Australia, 12, Chair, Steering Committee of the Australian Rheumatology Association Database (ARAD). ARAD has been supported with unrestricted educational grants administered through the Australian Rheumatology Association, Janssen-Cilag Pty Limited (Janssen) Australia, 12, Chair, Steering Committee of the Australian Rheumatology Association Database (ARAD). ARAD has been supported with unrestricted educational grants administered through the Australian Rheumatology Association; **C. Hill**, None; **C. Barrett**, None; **G. Carroll**, None; **P. Sinnathurai**, None; **R. Buchbinder**, None.

Abstract Number: 0202

Variables Associated with Response to Therapy in Patients with Interstitial Pneumonia with Autoimmune Features

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: We have limited knowledge of the characteristics of patients with interstitial pneumonia with autoimmune features (IPAF) that are associated with response to immunosuppression. Thus, we currently have no data to guide optimal IPAF patient selection for therapy or the optimal immunosuppressive regimen in IPAF. In this study, we use a rigorously phenotyped cohort (based on published IPAF criteria) to characterize features associated with response to immunosuppressive treatment.

Methods: We conducted a retrospective cohort study of 65 IPAF patients to evaluate for serologic, clinical, and radiographic characteristics associated with response to immunosuppression, defined as % relative functional vital capacity (FVC) decline of less than 10%, and absence of death or lung transplant within the first year of continuous immunosuppressive therapy. We used Fisher's exact test, chi-squared test, and Mann Whitney U test, as appropriate, to evaluate for significant differences in characteristics between patients with significant progression and those who did not progress. Multivariate logistic regression was used to further evaluate significant variables while controlling for confounders.

Table 1. Baseline characteristics of the IPAF cohort

	Total (n=65)	Non-progressor (n=51*)	Progressor (n=14*)	p-value
Mean age at diagnosis, years (SD)	58.71 (10.68)	58.15 (10.73)	60.73 (10.60)	0.413
Mean age at continuous immunosuppression initiation, yrs (SD)	60.60 (10.90)	60.01 (10.94)	62.73(10.87)	0.425
Mean duration from diagnosis to start of continuous IS for at least one year, years (SD)	2.05 (2.48)	2.06 (2.55)	2.01 (2.31)	0.786
Gender				0.276
Male	16 (24.62%)	11 (21.57%)	5 (35.71%)	
Female	49 (75.38%)	40 (78.43%)	9 (64.29%)	
Race/Ethnicity				0.188
White, Non-Hispanic	41 (63.08%)	29 (56.86%)	11 (78.57%)	
Black, Non-Hispanic	12 (18.46%)	11 (21.57%)	0 (0%)	
Hispanic	11 (16.92%)	8 (15.69%)	3 (21.43%)	
Asian	3 (4.62%)	3 (5.88%)	0 (0%)	
Smoker (ever)	27 (41.54%)	20 (39.22%)	7 (50.00%)	0.510
Baseline PFTs (prior to initiation of therapy)				
%FVC (SD)	60.30 (15.75)	58.21 (14.48)	67.93 (18.31)	**0.040**
%DLCO (SD)	43.89 (17.37) (n=57)	42.07 (14.58) (n=44)	50.08 (24.35) (n=13)	0.639
UIP radiographic pattern	18 (27.69%)	12 (23.53%)	6 (42.86%)	0.152
Medication use				
Prednisone	55 (84.62%)	45 (88.24%)	10 (71.43%)	0.203
MMF	53 (81.54%)	44 (86.27%)	9 (64.29%)	0.136
Azathioprine	17 (26.15%)	10 (19.61%)	7 (50.00%)	**0.022**
MMF/prednisone	45 (69.23%)	39 (76.47%)	6 (42.86%)	**0.016**
AZA/prednisone	15 (23.08%)	9 (17.65%)	6 (42.86%)	0.072
*Monotherapy***	10 (15.38%)	6 (11.76%)	4 (28.57%)	0.203
*Combination therapy****	55 (84.62%)	45 (88.24%)	10 (71.43%)	0.203

**Unless otherwise indicated*
***Treatment with a single agent during the treatment period*
****Treatment with two or more agents during the treatment period*
Abbreviations: SD – standard deviation; PFT – pulmonary function test, FVC – forced vital capacity; DLCO – diffusing lung capacity for carbon monoxide; MMF – mycophenolate mofetil; AZA – azathioprine.

Results: No baseline features predicted IPAF progression while on treatment, There was a trend of greater progression amongst men, ever smokers, and those with UIP radiographic pattern, although the differences were not statistically significant (Table 1). There was a statistically significant difference in the proportion of patients who were treated with combination therapy of mycophenolate mofetil (MMF) and prednisone whose disease did not progress.

Conclusion: Our study suggests that a combination therapy with MMF and prednisone may be associated with lack of progression in IPAF, including IPAF-UIP, although causality cannot be established. In the future studies, knowledge of cytokine profiles in different IPAF phenotypes may inform management in the early stages of the disease.

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Abstract Number: 0203

Chemoprophylaxis in Latent Tuberculosis Associated with Rheumatic Immune-mediated Diseases. Study of 240 Patients from a Single University Hospital

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Tuberculosis (TB) may be increased with biologic therapy (BT). Diagnosis and treatment of latent TB infection (LTBI) is the best strategy to prevent TB. In Rheumatic Immune-Mediated Diseases (R-IMID) and LTBI, chemoprophylaxis must be used before BT. The drugs more frequently used are Isoniazid (INH), Rifampicin (RIF) and Fluoroquinolones (FQ). These drugs may be associated with side-effects, especially hepatotoxicity.

Our aim was to assess, in a single University Hospital, a) used chemoprophylactic drugs and, b) adverse events with these drugs.

Methods: We included all consecutive patients in the last five years (2016-2020) with a diagnosis of R-IMID and a positive LTBI test (positive tuberculin skin test and/or interferon-γ–release assay), who received chemoprophylaxis prior to BT.

Table. Adverse events with isoniazid at months 1 and 3 and after month 3

	Month 1 (n=232)			Month 3 (n=222)			After month 3 (n=214)		
Adverse events, n (%)	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension	Total	Requiring switching	Requiring suspension
Hepatotoxicity	38 (16.4)	6 (2.6)	0	33 (14.9)	5(2.3)	2 (0.9)	16 (7.5)	2 (0.9)	0
Gastrointestinal side effects	4 (1.3)	3 (1.3)	1 (0.4)	3 (1.5)	0	3 (1.5)	2 (0.9)	0	1 (0.5)
Cutaneous toxicity	2 (0.9)	1 (0.4)	0	0	0	0	0	0	0
Dizziness	1 (0.4)	1 (0.4)	0	0	0	0	0	0	0
Total	44 (19)	11 (4.7)	1 (0.4)	36 (16.2)	5 (2.3)	5(2.2)	18 (8.4)	2 (0.9)	1 (0.5)

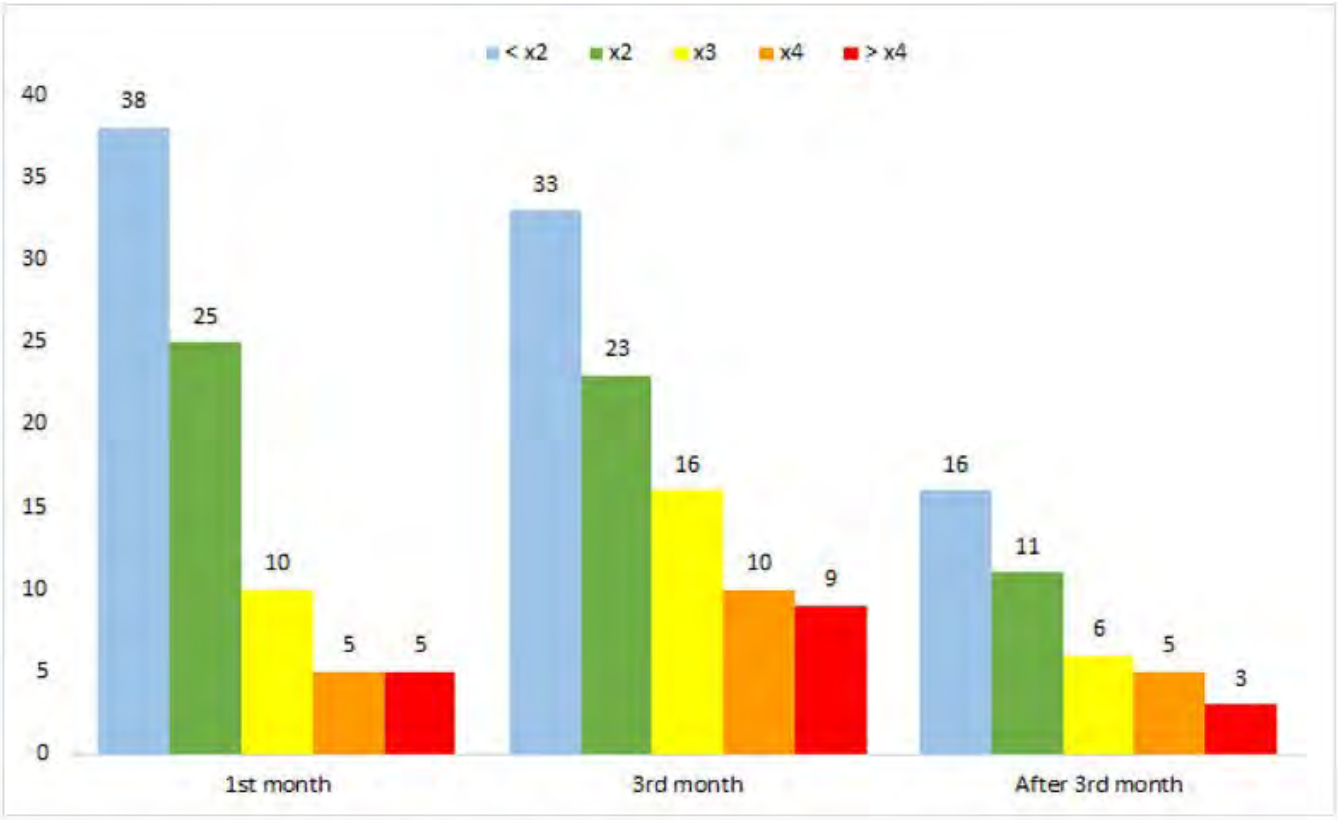


Figure. Liver enzyme elevation over baseline in patients in treatment with isoniazid.

Dose of chemoprophylactic drugs were a) INH (5 mg/kg/d, maximum, 300 mg; for 9 months with vitamin B6), b) RIF (10 mg/kg/d, maximum, 600 mg for 4 months) and c) FQ levofloxacin (500 mg/day for 9 months).

In all patients analytic controls that included liver enzymes were performed at the 1st and 3rd month and then at a variable time.

Results: 240 patients were analyzed (165 women/ 75 men), mean age of 56±11 years. The underlying R-IMID of patients receiving chemoprophylaxis were rheumatoid arthritis (n=74, 30.8%), axial spondyloarthritis (n=59, 24.6%), psoriatic arthritis (n=62, 25.8%), conectivopathies (n=17, 7.1%), vasculitis (n=12, 5%), sarcoidosis (n=2, 0.8%), Behçet's disease (n=1, 0.4%), inflammatory myopathies (n=1, 0.4%) and other (n=12, 5%).

At the onset of chemoprophylaxis they were taking: Prednisone in 61 patients (24 of them above 10 mg/day) and the following conventional DMARD, methotrexate (n=109, 45.4%), hydroxychloroquine (n=20, 8.3%), sulfasalazine (n=11, 4.6%), leflunomide (n=4, 1.7%) and azathioprine (n=2, 0.8%).

The first-line chemoprophylactic drug was INH in 232 (96.7%) patients and RIF in the remaining 8 (3.3%). Due to adverse events, second-line therapy was used in 18 (RIF, n=17 and Levofloxacin, n=1) patients previously treated with INH.

Adverse events were more frequent with INH, being observed in 55 patients (23.7%) out of 232. (TABLE, FIGURE). By contrast, only 1 out of 25 (4%) receiving RIF presented an adverse event, which was hepatotoxicity, requiring suspension of RIF. No adverse events were described in the only patient receiving levofloxacin.

Conclusion: INH is the most used first-line treatment for LTBI. RIF was mainly used as second-line therapy if an adverse event with INH was observed. Treatment was generally well tolerated and most adverse events did not require the withdrawal of the treatment. Hepatotoxicity was the most frequent adverse event with INH and the most frequent cause of treatment withdrawal.

Disclosure: D. Martinez-Lopez, None; **J. Rueda-Gotor**, None; **J. Osorio-Chávez**, None; **C. Álvarez-Reguera**, None; **V. Portilla**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0204

Risk of Hepatitis B Virus Reactivation in Patients with Immune-Mediated Inflammatory Diseases Receiving Biologics: Focus on the Timing of Biologics After Prophylactic Anti-viral Agents

Soo Min Ahn[1], Jonggi Choi[2], Byong Duk Ye[2], Suk-Kyun Yang[2], Ji Seon Oh[3], Yong-Gil Kim[2], Chang-Keun Lee[2], Bin Yoo[1], Sang Hyoung Park[2] and Seokchan Hong[2], [1]ASAN MEDICAL CENTER, Seoul, South Korea, [2]Asan Medical Center, Seoul, Republic of Korea, [3]Asan Medical Center, Ulsan, Republic of Korea

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Clinical characteristics of the study patients.

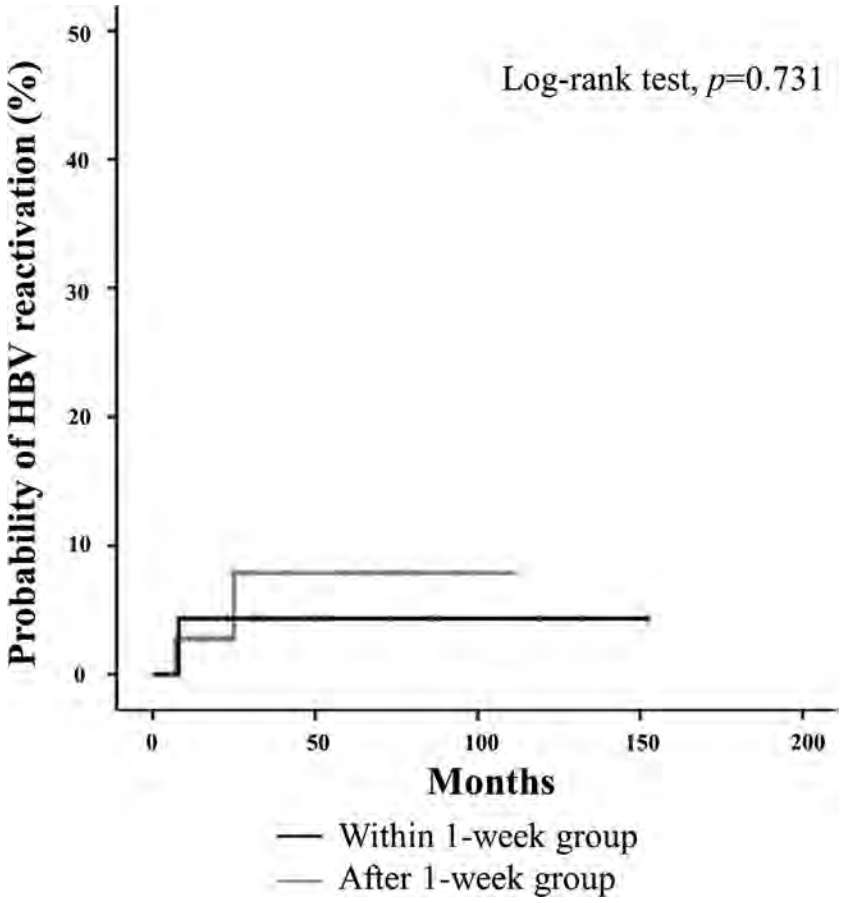
	Total (n = 60)	Within 1-week group (n = 23)	After 1-week group (n = 37)	p-value
Age, years, mean ± SD	47.7 ± 10.4	43.8 ± 10.0	50.1 ± 10.0	0.022
Female, n (%)	32 (53.3)	15 (65.2)	17 (45.9)	0.146
IMIDs, n (%)				0.030
Rheumatoid arthritis	23 (38.3)	9 (39.1)	14 (37.8)	
Ankylosing spondylitis	7 (11.7)	5 (21.7)	2 (5.4)	
Crohn's disease	20 (33.3)	9 (39.1)	11 (29.7)	
Ulcerative colitis	8 (13.3)	0	8 (21.6)	
Others	2 (3.3)	0	2 (5.4)	
Biologics, n (%)				0.593
Anti-TNF-α agents	55 (91.7)	22 (95.7)	33 (89.2)	
Other biologics	5 (8.3)	1 (4.3)	4 (10.8)	
Baseline HBV DNA, IU/ml, median (IQR)	2.1×10^2 (0*–4.6×10^3)	5.4×10^2 (2.0×10^2 –5.6×10^5)	3.7×10^1 (0*–4.3×10^2)	0.001
Anti-viral agents, n (%)				0.222
Entecavir	25 (41.7)	9 (39.1)	16 (43.2)	
Tenofovir	25 (41.7)	8 (34.8)	17 (45.9)	
Lamivudine	9 (15.0)	6 (26.1)	3 (8.1)	
Telbivudine	1 (1.7)	0	1 (2.7)	
Development of HBV reactivation, n (%)	3 (5.0)	1 (4.3)	2 (5.4)	1.000

Background/Purpose: Prophylactic anti-viral therapy is required in patients with hepatitis B virus (HBV) infection receiving biologics because of the high risk of HBV reactivation. However, it is unclear when to start biologics after anti-viral prophylaxis. We investigated the risk of HBV reactivation according to the timing of biologics initiation after anti-HBV prophylaxis in IMID patients with HBV infection.

Methods: We retrospectively evaluated the incidence of HBV reactivation in IMID patients who received biologics between July 2005 and April 2020. The patients were divided into two groups ("within 1-week " vs. "after 1-week") according to the timing of biologics initiation after anti-HBV prophylaxis. The cumulative probabilities and factors associated with HBV reactivation were evaluated.

Results: A total of 60 hepatitis B surface antigen-positive patients with IMID received biologics (within 1-week group, *n* = 23 [38%]; after 1-week group, *n* = 37 [62%]). During a median follow-up of 34 months (interquartile range, 20–74), three (5%) patients developed HBV reactivation. In the univariate analysis, the timing of biologics after HBV prophylaxis was not significantly associated with the risk of HBV reactivation (hazard ratio, 0.657; 95% confidence interval, 0.059–7.327; p = 0.733). The cumulative probabilities of HBV reactivation did not significantly differ according to the timing of biologics as well (p = 0.731).

Conclusion: The risk of HBV reactivation was not significantly associated with the timing of biologics administration after anti-HBV prophylaxis. Thus, biologics may be initiated early in patients with IMID under prophylactic treatment for HBV.



Disclosure: S. Ahn, None; **J. Choi**, None; **B. Ye**, None; **S. Yang**, None; **J. Oh**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None; **S. Park**, None; **S. Hong**, None.

Abstract Number: 0205

An Observational Study from the Perspective of Rheumatology in the Management of Patients with Psoriatic Arthritis in Turkey – LOOP Study

Ediz Dalkilic[1], Dilek Solmaz[2], Orhan Kucuksahin[3], Erhan Capkin[4], Mehmet Emin Derin[5], Didem Arslan[6], Fatih Noyan[7], Nihan Belkis Coskun[1], Sadiye Murat[8], Omer Faruk Sendur[9], Meltem Alkan Melikoglu[10], Savas Gursoy[11], Taciser Kaya[12], Ali Sahin[13], Murat Karkucak[4], Timur Pirildar[14], Mustafa Ender Terzioglu[15], Cemal Bes[16] and Servet Akar[2], [1]Uludag University, School of Medicine – Bursa, Turkey, Bursa, Turkey, [2]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Izmir, Turkey, [3]Ankara State Hospital, School of Medicine, Ankara, Turkey, [4]Karadeniz Technical University, School of Medicine, Trabzon, Turkey, [5]Sivas Numune Hospital, Sivas, Turkey, [6]Cukurova University, School of Medicine – Adana, Turkey, Adana, Turkey, [7]Nazilli State Hospital – Aydın, Turkey, Aydin, Turkey, [8]Istanbul Medeniyet University, Goztepe Training and Research Hospital, İstanbul, Turkey, [9]Adnan Menderes University, School of Medicine, Aydin, Turkey, [10]Ataturk University, School of Medicine, Erzurum, Turkey, [11]Gaziantep University, School of Medicine – Gaziantep, Turkey, Gaziantep, Turkey, [12]Saglik Bilimleri University, Izmır Bozyaka Trainig and Research Hospital – Izmir, Turkey, Izmir, Turkey, [13]Sivas Cumhuriyet University, School of Medicine, Sivas, Turkey, [14]Celal Bayar University, School of Medicine – Manisa, Turkey, Manisa, Turkey, [15]Akdeniz University, School of Medicine, Antalya, Turkey, [16]Saglik Bilimleri University, Basaksehir Cam and Sakura State Hospital – Istanbul, Turkey, Istanbul, Turkey

SESSION INFORMATION

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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Available evidence suggests that timely and effective management of patients with psoriatic arthritis (PsA) can improve long-term outcomes. Current information on the factors which influence the management decisions for PsA is limited in Turkey. The purpose of this study was to evaluate the impact of clinical rheumatology setting on management steps of patients with a confirmed PsA diagnosis from inflammatory musculoskeletal symptom onset to PsA diagnosis.

Methods: All patients were assessed by both rheumatologists and dermatologists across 30 centers in Turkey, and patients with confirmed diagnosis of PsA according to CASPAR criteria were included in the study. Primary outcome of this study was the timeframe from symptom onset to PsA diagnosis; secondary outcomes were time taken from PsA diagnosis to first conventional synthetic disease-modifying antirheumatic drug (csDMARD) and to first biologic DMARD (bDMARD) including switch data for csDMARD and bDMARD.

Results: Of 287 patients enrolled in the study, 243 patients with confirmed diagnosis of PsA were included in this analysis. It was observed that majority of patients were women (n=147, 60.5%). Of 134 patients in rheumatology setting, mean clinical disease activity PsA score (cDAPSA) was 13.42±14.11, demographic and clinical characteristics of patients included in the rheumatology setting are presented in Table 1. In the rheumatology setting the mean time from symptom onset to diagnosis of PsA was 11.12 ± 52.68 months. The mean time from PsA diagnosis to first csDMARD and bDMARD was 2.62 ± 43.10 and 54.61 ± 76.52 months, respectively. Mean time from first csDMARD to first bDMARD was 37.34 ± 46.68 months. In the rheumatology setting patients showed a significantly shorter mean time from symptom onset to diagnosis (11.12 vs. 17.69 months, as compared to dermatologists). The proportion of patients receiving any treatment for PsA was greater in the rheumatology setting (99.3% vs. 82.5%). A higher proportion of patients with PsA in rheumatology setting were treated with csDMARDs (86.5% vs. 62.2%). The first

Table 1. Demographic and clinical characteristics of PsA patients from Rheumatology Setting of the LOOP study

Characteristic	Rheumatology setting (n = 134)	%
Age (years, mean; ±SD)	45.8 (±12.2)	-
Gender (%)		
Female	83	61.9
Male	51	38.1
BMI (kg/m^2, mean; ±SD)	28.3 (±5.9)	-
Skin Symptoms	131	97.8
Dactylitis	78	58.2
Swollen Joints	107	79.9
Family history of psoriasis	50	37.3
Comorbidities		
Any	80	59.7
Depression and/or anxiety	40	29.9
Hypertension	37	27.6
Obesity	32	23.9
Lipid disorder	25	18.7
Diabetes (Type II)	17	12.7
Cardiovascular disease	14	10.4
Osteoporosis	8	6.0

csDMARD in this setting was methotrexate (79.1%) and first bDMARD was a TNF inhibitor (42.5%). Disease activity of 243 patients determined by cDAPSA scores showed 54 (22.2%) of the patients had remission, 73 (30.0%) had low disease activity, 47 (19.3%) had moderate disease activity, 26 (10.7%) had high disease activity and 43 (17.7 %) patients had missing data.

Conclusion: Our study conducted in several regions in Turkey results and obtained from patients with a confirmed PsA diagnosis who were diagnosed and treated by rheumatologists were similar with the globally published data. These results support again significant collaboration of rheumatology and dermatology specialists recommended by well-accepted treatment guidelines and approaches.

Disclosure: E. Dalkilic, AbbVie, 6, MSD, 6, Roche, 6, Pfizer, 6, UCB, 6, Novartis, 6; **D. Solmaz**, Roche, 6, Farmanova, 6, Pfizer, 6, Lilly, 6; **O. Kucuksahin**, None; **E. Capkin**, AbbVie, 2, 6, Roche, 2, 6, MSD, 2, 6, Pfizer, 6; **M. Derin**, None; **D. Arslan**, None; **F. Noyan**, None; **N. Coskun**, None; **S. Murat**, None; **O. Sendur**, None; **M. Melikoglu**, AbbVie, 6, Pfizer, 6, MSD, 6, UCB, 6; **S. Gursoy**, Sanofi, 5, Novartis, 5; **T. Kaya**, None; **A. Sahin**, AbbVie, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6; **M. Karkucak**, AbbVie, 6; **T. Pirildar**, AbbVie, 6; **M. Terzioglu**, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Novartis, 2, 5, 6, Pharmactive, 2, 5, 6, UCB, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6; **C. Bes**, AbbVie, 2, 6; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6.

Abstract Number: 0206

Hydroxycloroquine-Induced Atrioventricular Block in Inmune-Mediated Diseases. Single University Center Study of 293 Patients

Alba Herrero-Morant[1], Adrián Margarida-de Castro[1], Raquel Pérez-Barquín[2], Jon Zubiaur-Zamacola[1], Miguel Ángel gonzalez-Gay[3] and Ricardo Blanco[4], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, [3]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is an extensively used drug in immune-mediated diseases (IMID). Despite its general safety, HCQ can cause serious toxicity such as heart conduction disorders. Atrioventricular block (AVB) is an underrecognized adverse effect that can potentially cause significant morbidity and mortality.

Table. Comparative study between patients with and without AVB

	with AVB *n*= 19	without AVB *n* = 274	*p*
General features at HCQ onset			
Age, years mean±SD	57.4±14.5	46.4±16.8	**0.014**
Female, n (%)	17(89.5)	239(87.4)	0.877
Hypertension, n (%)	14 (73.7)	149 (54.4)	0.118
Dyslipemia, n (%)	11 (58.9)	117 (42.7)	0.265
Diabetes Mellitus, n (%)	5 (26.3)	24 (8.7)	**0.033**
Renal impairment, n (%)	5 (26.3)	29 (10.7)	0.073
Ischemic cardiopathy, n (%)	2 (10.5)	11 (3.9)	0.228
PCR, mg/dL median [IQR]	0.3 [0.1-0.5]	0.4 [0.3-0.8]	0.343
VSG, mg/dL median [IQR]	17.0 [15.0-22.3]	13.0 [7.0-29.5]	0.206
Data at last visit (11.8±8.9 years of follow-up)			
IMID duration, years mean±SD	11.8±8.9	14.3±10.3	0.288
# Use of other cardiotoxic drugs, n (%)	2 (10.5)	11 (4.0)	0.723
HCQ cumulative dose, mg mean±SD	813.2±206.0	996.3±266.9	0.527

(beta blockers, calcium channel blockers, tricyclic drugs, other AVB inducers)

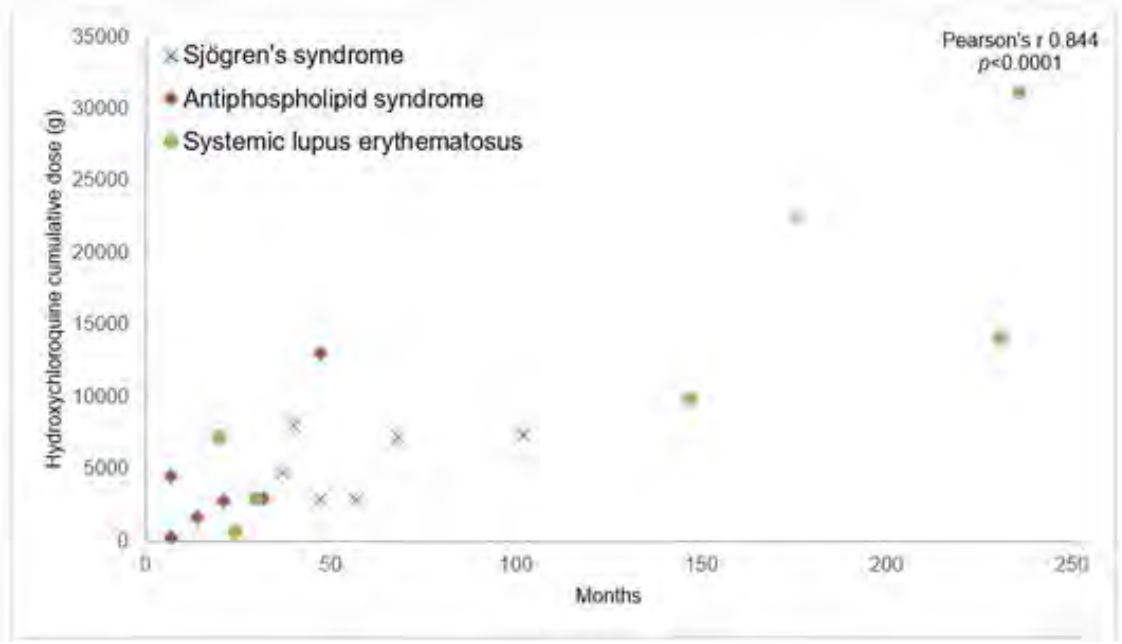


Figure. Presentation of atrioventricular block according to hydroxychloroquine cumulative dose and treatment duration.

The aim of this study was to analyze incidence, presentation, and characteristics of HCQ-induced AVB in IMID.

Methods: Open-label single center study of 293 patients with IMID treated with HCQ for at least 3 months. Electrocardiograms were analyzed at baseline and during HCQ treatment. In addition, a comparative study between patients with and without AVB was conducted.

Results: We studied 293 patients (270 women/23 men; mean age 59.7±14.7 years). Underlying IMID were systemic lupus erythematosus (n=109, 40.6%); undifferentiated connective-tissue disease (n=70, 23.9%), Sjögren's syndrome (n=70, 23.9%), antiphospholipid syndrome (n=31,10.6%) and other IMID (n=13, 4.4%). HCQ was used for 4.1±3.5 years.

After 11.8±8.9 years of follow-up (HCQ mean cumulative dose: 979.7±272.1 g). AVB was observed in 19 out of 293 (6.5%) patients: 16 (84.2%) were first-degree AVB and 3 (15.8%) complete AVB. 4 patients with AVB were treated with a permanent pacemaker.

A comparative study between patients with and without AVB was performed (TABLE). Patients with AVB were older (p=0.014) and had a higher incidence of diabetes mellitus (p=0.033). HCQ cumulative dose and duration of IMID were similar in both groups (p >0.05).

Presentation of atrioventricular block according to hydroxychloroquine cumulative dose and treatment duration is shown in FIGURE. Most of AVB happened in the first 40 months, regardless of HCQ cumulative dose.

Other adverse effects of HCQ were retinopathy (n=16, 5.4%), gastrointestinal alterations (n=14, 4.8%), cutaneous alterations (n=14, 4.8%), allergic reactions (n=4, 1.4%) and myopathy (n=1, 0.3%).

Conclusion: AVB was observed in 6.5% of patients with IMID treated with HCQ. Most AVB were first-degree AVB. HCQ increased the risk of developing an AVB in patients with IMID regardless of HCQ cumulative dose or underlying disease duration. Older patients with diabetes mellitus had a higher risk of developing an AVB.

Disclosure: A. Herrero-Morant, None; **A. Margarida-de Castro**, None; **R. Pérez-Barquín**, None; **J. Zubiaur-Zamacola**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0207

Treatment of Ocular Sarcoidosis: Study of 65 Patients of a Series of 384 Patients from a Single University Hospital

Carmen Álvarez-Reguera[1], Jorge Javier Gaitán-Valdizán[1], Raúl fernández-ramón[1], Rosalia Demetrio-Pablo[1], José Luis Martin-Varillas[2], Lara Sánchez-Bilbao[1], David Martinez-Lopez[1], Iñigo Gonzalez-Mazon[3], Miguel Ángel gonzalez-Gay[4] and Ricardo Blanco[5], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Sierrallana, Torrelavega, Spain, [3]H. U. Marques de Valdecilla, Santander, Spain, [4]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [5]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Ocular involvement is a relatively frequent and potentially severe complication of sarcoidosis. Oral corticosteroids (OCS) are the first-line treatment. Conventional immunosuppressive agents (cIS) and biological therapy (BT) can be used in refractory cases.

The aim of this study was to evaluate the treatment and visual outcomes of a cohort of patients diagnosed with ocular sarcoidosis.

Methods: Study of a large cohort (n=384) of all consecutive patients diagnosed with sarcoidosis from January 1, 1999 to December 31, 2019 at a single University Hospital. Finally, 344 patients were included according the ATS/ERS/WASOG criteria / Different ocular manifestations and the following systemic treatments were assessed: **a)** OCS, **b)** cIS), **c)** monoclonal TNF inhibitors, **d)** Etanercept (ETN), **e)** Tocilizumab (TCZ). Best Corrected Visual Acuity (BCVA) according to different systemic treatments was compared at diagnosis and after one year of follow-up (Kruskall Wallis test).

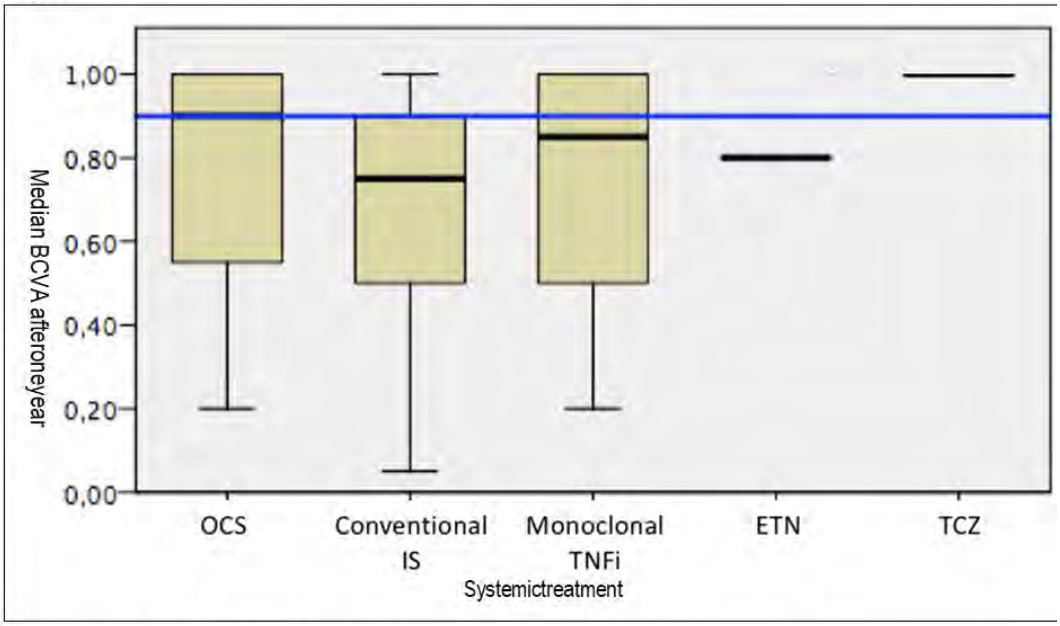
Results: 344 patients were reviewed. From these, 65 (18.9%) presented ocular manifestations as uveitis (83.1%), orbital lesions (7.7%), retinal vasculitis (6.2%), dry eye (6.2%) and scleritis (1.5%). All of them received systemic treatment. BT was particularly used in patients with retinal vasculitis (100%), panuveitis (75%) and orbital lesions (40%). Systemic treatment and BCVA outcome according to ocular manifestations are shown in table. Median BCVA

Table. Median BCVA at onset and after one year according to ocular manifestations and type of systemic therapy.

Type of ocular affectation	*n (%)*	*Median BCVA at onset [IQR]*	*Median BCVA after 1 year [IQR]*	*OCS n (%)*	*cIS n (%)*	*monoclonal TNFi n (%)*	*ETN n (%)*	*TCZ n (%)*
Uveitis	54 (83.1)	0.6 [0.3-0.8]	0.9 [0.6-1]	44 (81.5)	29 (53.7)	16 (29.6)	3 (5.5)	3 (5.5)
- **Anterior**	31 (47.7)	0.7 [0.3-0.8]	0.8 [0.5-1]	22 (70.9)	12 (38.7)	2 (6.5)	2 (6.5)	0
- **Intermediate**	2 (3.1)	0.5	0.7	2 (100)	1 (50)	1 (50)	1 (50)	1 (50)
- **Posterior**	5 (5.2)	0.5 [0.1-0.9]	0.9 [0.9-1]	4 (80)	4 (80)	3 (60)	0	0
- **Panuveitis**	16 (24.6)	0.4 [0.2-0.7]	0.9 [0.5-1]	16 (100)	12 (75)	10 (62.5)	0	2 (12.5)
Orbital lesions	5 (7.7)	0.5 [0.1-0.6]	1 [0.1-1]	4 (80)	2 (40)	2 (40)	0	1 (20)
Retinal vasculitis	4 (6.2)	0.6 [0.5-0.8]	1 [0.6-1]	4 (100)	4 (100)	1 (25)	0	1 (25)
Dry eye	4 (6.2)	1	0.9	2 (50)	1 (25)	0	0	0
Scleritis	1 (1.5)	1	1	1 (100)	0	0	0	0

Abbreviations: BCVA: Best Corrected Visual Acuity; IQR: Interquartile Range; OCS: Oral Corticosteroid; cIS: Conventional Immunosuppressants; Monoclonal TNFi: monoclonal tumour necrosis factor inhibitors; ETN: Etanercept; TCZ: Tocilizumab.

Figure. Median [25,75 IQR] BVCA after one year follow up according to type of systemic treatment in sarcoid uveitis.



Abbreviations: BCVA: BestCorrected Visual Acuity; OCS: Oral Corticosteroid; Conventional IS: Conventional immunosupressants (methotrexate, azathioprine, mycophenolate, cyclophosphamide); Monoclonal TNFi: monoclonal tumour necrosis factor inhibitors (infliximab, adalimumab, golimumab); ETN: Etanercept; TCZ: Tocilizumab.

at onset and after one year was 0.6 [interquartile range (IQR) 0.3-0.8] and 0.9 [0.6-1], respectively. No statistically significant differences were observed between systemic treatments in BCVA of patients with uveitis after 1 year of follow-up **(Figure)**.

Conclusion: Panuveitis, intermediate uveitis and orbital lesions, require a more aggressive treatment than other manifestations of ocular sarcoidosis. In uveitis, an important improvement in BCVA after 1 year of follow-up was observed regardless of the type of treatment used.

Disclosure: C. Álvarez-Reguera, None; **J. Gaitán-Valdizán**, None; **R. fernández-ramón**, None; **R. Demetrio-Pablo**, None; **J. Martin-Varillas**, None; **L. Sánchez-Bilbao**, None; **D. Martinez-Lopez**, None; **I. Gonzalez-Mazon**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 0208

Musculoskeletal Immune-Related Adverse Effects of Immune Checkpoint Inhibitors at a Single Site in a Hispanic Population in Puerto Rico

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICI) belong to a novel group of biologic agents used to treat cancer. ICI increase the immune response to tumor cells by blocking cancer induced immune inhibitory pathways. Immune-related adverse effects (irAE) are a recognized complication of these drugs. Musculoskeletal (MSK) irAE have been described. We studied irAE of ICI in Hispanics at a single site in Puerto Rico, their management and outcome. We report the MSK irAE identified in the population studied.

Methods: A retrospective medical record analysis of 193 patients treated with an ICI was conducted at the Cancer Center of Hospital Auxilio Mutuo in Puerto Rico, beginning from the first therapy with ICI to August 31, 2020. Data abstracted included demographic information, type of cancer, ICI used alone, in combination or sequentially, dose and cycles of ICI, treatment prescribed prior to and during ICI use, comorbidities, development and type of irAE, time to development of irAE from start of ICI, management and outcome of irAE, and autoimmune diseases diagnosed prior to ICI use.

Results: A total of 16 MSK irAE were identified among 14 (7.25%) patients. MSK adverse effects were the third most common irAE identified (8%), following skin (17%) and gastrointestinal involvement (9%). Nine patients were female, and 5 patients were male with a mean age of 63 years (range 34-90).

MSK irAE were observed in 9 of 97 (9.3%) patients that were treated with nivolumab monotherapy and in 3 of 75 (4%) treated with pembrolizumab monotherapy. One in five (20%) patients treated with pembrolizumab followed by nivolumab had a MSK irAE and 1 of 20 (5%) treated with combination ipilimumab and nivolumab experienced a MSK irAE. The most common MSK irAE was arthralgia in 10 patients (71%), polyarticular arthritis in 2 patients (14%), followed by eosinophilic fasciitis, inflammatory myopathy, sicca syndrome, and xerostomia in 7% respectively. The mean time from starting ICI therapy to the development of a MSK irAE was 17 weeks (range 1-111).

***Table 1**: Patient characteristics and musculoskeletal immune-related adverse effects associated to immune checkpoint inhibitors*

Age (years)	Sex	Cancer diagnosis	ICI prescribed	Time in weeks of treatment with ICI	MSK irAE	Time in weeks of irAE after ICI	Other irAE	Time in weeks of irAE after ICI	Other irAE	Time in weeks of irAE after ICI	Treatment	Resolution
63	F	Kidney	Nivolumab	27	Arthralgias	17	Primary Hypothyroidism	14	Bullous rash	35	Analgesics, Synthroid	Partial
68	M	Liver	Nivolumab	104	Arthralgias	12	None	None	None	None	Narcotics	Full
34	F	Hodgkin's	Nivolumab	14	Arthralgias	2	Inflammatory myopathy	2	None	None	Low dose prednisone	Full
36	F	Hodgkin's	Nivolumab	139	Arthralgias	40	New onset pneumonitis	96	None	None	Moderate dose prednisone/ IV steroids	Partial
75	F	NSCLC	Nivolumab	62	Arthralgias	20	None	None	None	None	Low dose prednisone	Partial
75	M	Kidney	Nivolumab	53	Arthralgias	1	Diarrhea	1	None	None	Low dose prednisone	Partial
59	M	Urothelial	Nivolumab	264	Arthralgias	45	Glomerulonephritis	65	Maculopapular rash	29	Moderate dose prednisone/ Topical steroids	Partial
52	F	Non-Hodgkin's lymphoma	Pembrolizumab	72	Arthralgias	5	Polyarticular arthritis	15	None	None	Interval delay of ICI	Partial
90	F	Colorectal	Pembrolizumab	91	Arthralgias	26	None	None	None	None	NSAIDS	Full
57	M	Kidney	Ipilimumab and Nivolumab	9	Arthralgias	2	None	None	None	None	None	Full
72	M	Head/Neck	Pembrolizumab x 6 weeks, Nivolumab x 168 weeks	174	Polyarticular arthritis	111	Nonspecific colitis	140	None	None	Moderate dose prednisone/ Azulfidine	Partial
78	F	NSCLC	Nivolumab	117	Sicca symptoms	20	None	None	None	None	Local oral lubricant	Partial
40	F	Hodgkin's	Pembrolizumab	20	Xerostomia	32	None	None	None	None	Local oral lubricant	Partial
65	M	Head/Neck	Nivolumab	53	Eosinophilic fasciitis	62	None	None	None	None	Moderate dose prednisone/ ICI discontinued	Partial

*Low dose prednisone <20mg/day, †Moderated dose prednisone >20-40mg/day, MSK, musculoskeletal, irAE, immune-related adverse effect, ICI, Immune checkpoint inhibitor

Management of the irAE included prescription of corticosteroids, NSAIDs, sulfasalazine and delay or discontinuation of ICI therapy. Full resolution of the MSK irAE was achieved in 4 patients, while partial resolution was achieved in 10.

Conclusion: ICI MSK irAE were observed in 7.25% of the Hispanic population studied. The most frequent MSK irAE was arthralgias (71%), which was associated with the use of nivolumab as monotherapy in 7 of 10 patients. Two patients (12.5%) experienced more than 1 MSK irAE. However, 5 of 14 patients (35.7%) had an MSK irAE that concurred with a non-MSK irAE. Treatment of the irAE achieved full resolution in 29% of patients. ICI discontinuation or delay in prescription was required in 2 patients and 1 patient required hospitalization. No patients with a prior MSK autoimmune disease had a relapse of their disease on ICI therapy.

Disclosure: A. **Santiago**, None; **S. Vila**, None; **F. Cabanillas**, None.

Abstract Number: 0209

IgG4 Related Disease: Response to Immunosuppressive Therapy - A Single Centre Retrospective Study in the United Kingdom

Shirish Sangle[1], Neil Morton[2], Alina Casian[2], Louise Nel[2], Jennifer Hannah[3] and David D'Cruz[4], [1]Guy's and St Thomas' Hospital NHS Trust, London, United Kingdom, [2]Guys and St Thomas' NHS Trust, London, United Kingdom, [3]Kings College Hospital, London, United Kingdom, [4]Guy's and St Thomas' NHS Foundation Trust, London, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I (0183–0209)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: IgG4 related disease (IgG4-RD) is a rare immune-mediated condition, increasingly being recognised as a multi-organ disorder. It is a relatively new entity and the precise prevalence is not known. It is a chronic fibro-inflammatory condition with raised levels of immunoglobulin G4 and accumulation of plasma cells and fibrosis in the affected tissue. A recent 3-step classification criteria has been developed jointly by ACR/EULAR to help to diagnose IgG4-RD. It includes a variety of exclusion criteria as well as weighted inclusion criteria.

Methods: We present a retrospective observational study of patients seen at Guy's and St Thomas' NHS Foundation Trust Hospitals, London, UK. The data conducted was analysed for clinical presentation, laboratory markers of inflammation, immunoglobulin subsets, autoantibody profiles, imaging and histopathology and compared to the 2019 ACR/EULAR criteria to determine confirmed diagnosis of IgG4-RD. Data was also collected post standard-of-care treatment, including patient clinical outcomes and possible improvement. IgG4 Responder Index was also calculated for each patient before and after treatment.

Results: The study included a multi-ethnic cohort of 83 patients with multi-organ involvement.

Fifty-nine out of eighty-three analysed were classed as confirmed IgG4-RD rather than possible (71%). Seventy-one patients had biopsies of which 49 (91% of confirmed IgG4-RD) were consistent with IgG4-RD. Fifty patients had PET-CT scanning of which uptake was seen in 76% of those with confirmed IgG4-RD (26/34). Immunoglobulin IgG subclass analysis showed significantly higher IgG4 levels in the confirmed IgG4-RD group. Treatments were with corticosteroids and immunosuppressants such as azathioprine, methotrexate, mycophenolate, cyclophosphamide and rituximab.

Post treatment, IgG4-RI was significantly improved. Post-treatment IgG4 levels, as well as inflammatory markers, were significantly reduced in the patients with IgG4-RD disease who had had an initially high IgG4 level (31/43). This was correlated with clinical improvement in twenty-four (77%) of those patients. Fifty-three patients in total showed clinical improvement after treatment (79%). Of the biologics patients (n=15), eleven showed improvement (73%).

Conclusion: IgG4-RD is a fibro-inflammatory disorder involving multiple organs. If not treated adequately patients may develop severe organ damage. It often responds to corticosteroids but may require other immunosuppressive therapy as we have shown, with IgG4 levels and IgG4-RI providing good markers of disease activity. Treatment with biologics such as B cell depletion therapy results are encouraging. It will be interesting to see the outcomes of future biologics controlled trials in IgG4-RD.

Disclosure: S. Sangle, None; **N. Morton**, None; **A. Casian**, None; **L. Nel**, None; **J. Hannah**, None; **D. D'Cruz**, None.

Abstract Number: 0210

Using Machine Learning to Predict Medial Knee Cartilage Worsening over 2 Years Using Gait and Physical Activity: The MOST Study

Kerry Costello[1], David Felson[1], S. Reza Jafarzadeh[2], Neil Segal[3], Cora Lewis[4], Michael Nevitt[5], Cara Lewis[6], Vijay Kolachalama[2] and Deepak Kumar[1], [1]Boston University, Boston, MA, [2]Boston University School of Medicine, Boston, MA, [3]University of Kansas Medical Center, Iowa City, IA, [4]University of Alabama Birmingham, Birmingham, AL, [5]University of California San Francisco, Orinda, CA, [6]Boston University, Brookline, MA

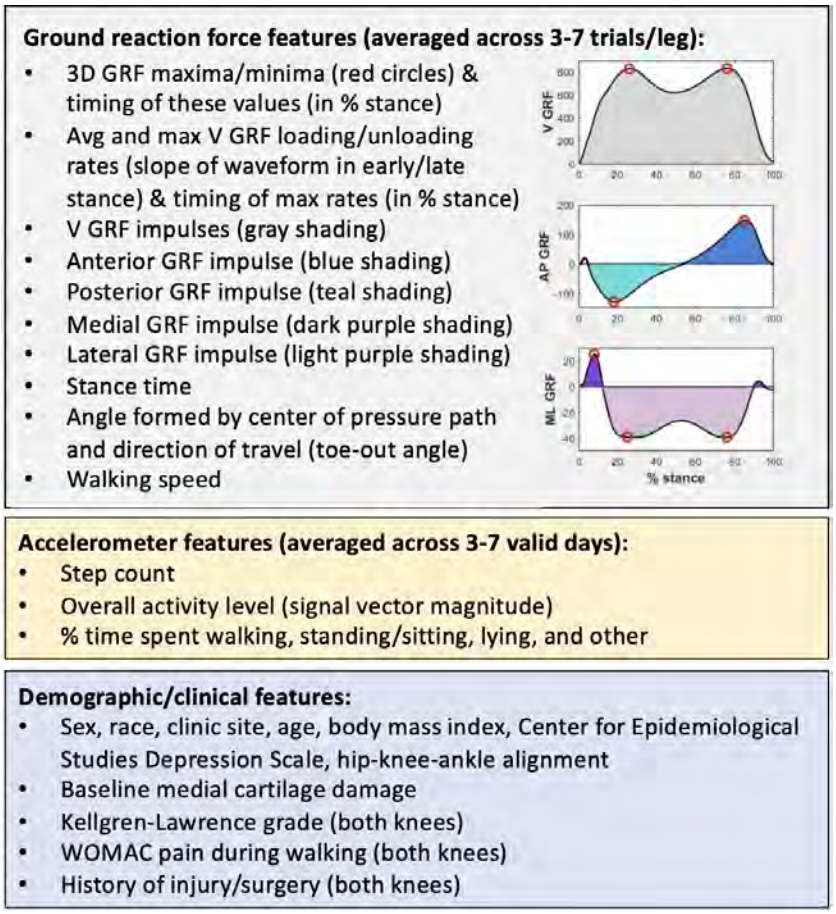


Figure 1. Inputs for Super learning.

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Identifying knees at risk of worsening osteoarthritis (OA) could help to identify individuals in need of interventions. While gait and physical activity are considered important for knee OA pathogenesis, the interrelations between these factors are complex and challenging to specify using traditional statistical models. Machine learning approaches remove the need to pre-specify these underlying relationships among factors when predicting an outcome. Our objective was to investigate the ability of gait and physical activity measures to predict medial tibiofemoral cartilage worsening over 2-years in the Multicenter Osteoarthritis Study (MOST) using machine learning.

Methods: Demographic and clinical data, ground reaction force (GRF) data during self-selected speed walking, and physical activity data from 7 days of accelerometer wear were collected from participants with and without knee pain or radiographic OA at baseline. Cartilage damage was assessed using the MRI Osteoarthritis Knee Score (MOAKS) in one knee per person by two musculoskeletal radiologists in 5 medial tibiofemoral subregions at the baseline and 2-year visits. Progression was defined as worsening cartilage size or depth MOAKS score in any subregion. Knees with Kellgren-Lawrence grades > 2 were excluded to focus on an earlier disease stage. "Super learning" (an ensemble machine learning approach) was used to predict cartilage worsening over 100 random splits into 70% training:30% test data from standardized GRF, accelerometer, and demographic/clinical features (Figure 1). Performance was evaluated using AUC. Important predictors were identified as the 10 features most frequently appearing in the top 10 contributors to prediction (via a variable importance measure statistic) across the 100 data splits. Marginal effects plots were used to determine direction of associations.

Table 1. Baseline sample characteristics

Sample characteristic	n = 1323 participants
Female Sex, n (%)	784 (59.3%)
Race, n participants (%):	
Black or African American	154 (11.6%)
White or Caucasian	1126 (85.1%)
Clinic Site University of Iowa, n (%)	845 (63.9%)
Mean Age in years (s.d.)	58.5 (7.9)
Mean Body Mass Index in kg/m^2 (s.d.)	27.7 (4.9)
Mean Center for Epidemiologic Studies Depression score (s.d.)	5.6 (6.3)
Hip-knee-ankle alignment in degrees (s.d.), negative values indicate varus	-1.3 (2.7)
Baseline medial cartilage damage, n knees (%)	523 (39.5%)
Kellgren-Lawrence Grade, n knees (%):	
KLG = 0	791 (60.1%)
KLG = 1	314 (23.9%)
KLG = 2N (definite osteophyte, no joint space narrowing)	60 (4.6%)
KLG = 2 (definite osteophyte and joint space narrowing)	151 (11.5%)
Previous injury/surgery, n knees (%)	256 (19.3%)
WOMAC pain during walking, n knees (%):	
None	1043 (78.8%)
Mild	241 (18.2%)
Moderate	34 (2.6%)
Severe	4 (0.3%)
Extreme	1 (0.1%)

WOMAC = Western Ontario and McMaster Universities Osteoarthritis Index

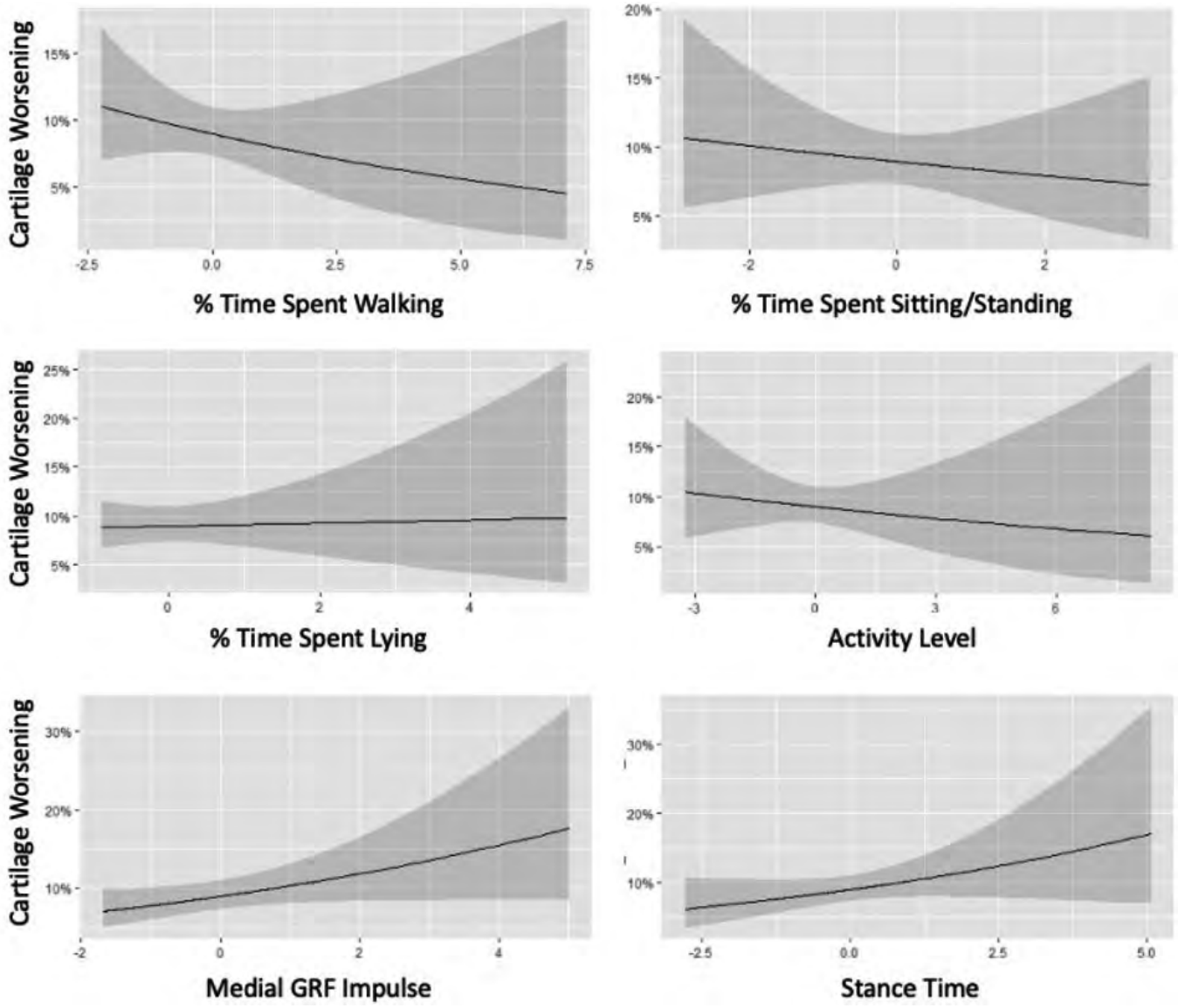


Figure 2. Marginal effects of important physical activity and gait predictors.

Results: Of 1323 legs included in the analysis (Table 1), 14% experienced medial cartilage worsening over 2-years. Across 100 model runs, the median AUC (2.5- and 97.5-th percentiles) on the held-out test sets was 0.78 (0.73-0.85). Important predictors (frequency of appearance in top 10 contributors) included: baseline medial cartilage damage (100), Kellgren-Lawrence grade (83), % time walking (80), % time sitting/standing (65), age (65), % time lying (62), % time in other activities (61), activity level (54), medial GRF impulse (37), and stance time (31). Cartilage worsening was associated with lower % time walking, % time sitting/standing, and activity level, higher % time lying and medial GRF impulse, and longer stance time (Figure 2).

Conclusion: An ensemble machine learning approach incorporating gait, physical activity, and clinical/demographic features showed good performance for predicting cartilage worsening over two years. While determining the relationships among predictors and cartilage loss outcome in the model is not straightforward, this analysis suggests that addressing low time spent walking and overall activity level and/or high medial GRF impulse, among others, may be potential targets to reduce medial tibiofemoral cartilage worsening.

Disclosure: K. Costello, None; **D. Felson**, None; **S. Jafarzadeh**, Pfizer, 5; **N. Segal**, Tenex Health, 2, Pacira CryoHealth, 5, Flexion Therapeutics, 5; **C. Lewis**, None; **M. Nevitt**, None; **C. Lewis**, None; **V. Kolachalama**, None; **D. Kumar**, Pfizer Inc, 5.

Abstract Number: 0211

Unsupervised Machine-learning Algorithms for the Identification of Clinical Phenotypes in the Osteoarthritis Initiative Database

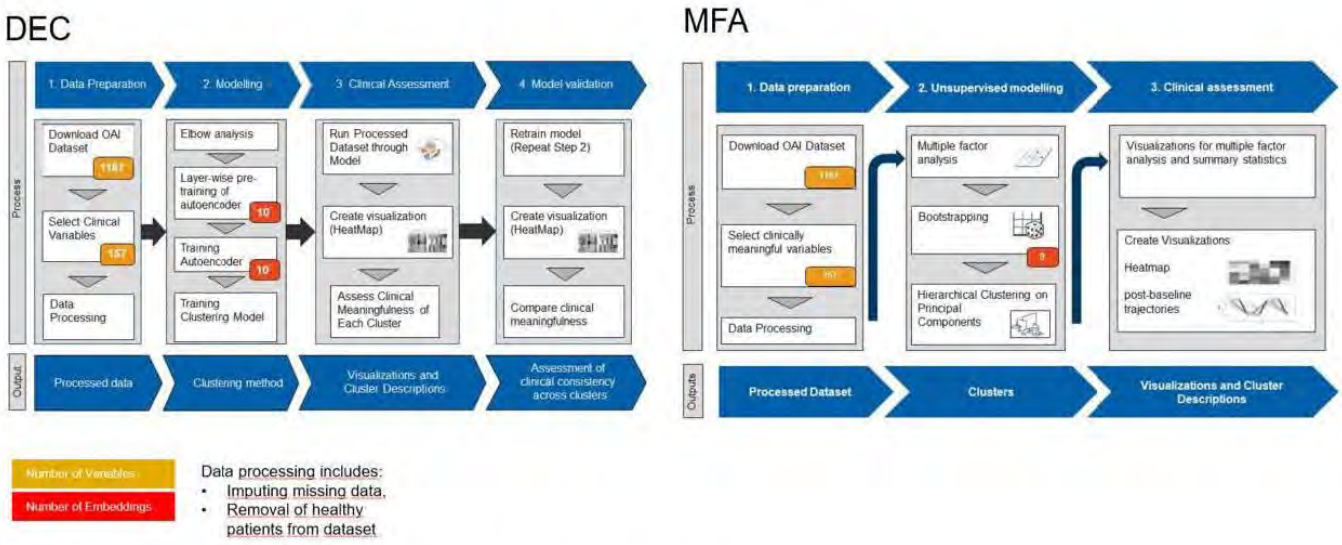
David Demanse[1], László B. Tankó[2], Patrick Lustenberger[3], Philipp Nikolaus[3], Ilja Rasin[3], Damian F. Brennan[3], Franziska Saxer[2], Ronenn Roubenoff[4], Sumehra Premji[1], **Philip Conaghan**[5] and Matthias Schieker[4], [1]Novartis Pharma AG, Basel, Switzerland, [2]Novartis Institutes for Biomedical Research, Basel, Switzerland, [3]IBM Switzerland AG, Zürich, Switzerland, [4]Novartis Institutes for Biomedical Research, Basel, Switzerland, Basel, Switzerland, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis (OA) is a chronic disabling disease, for which there are only limited treatment options. One major challenge in the development of effective treatment strategies for knee OA is the complexity of the underlying pathogenesis. Segmenting patient populations using readily available clinical, radiographic and biological features to define different phenotypes is a prerequisite for personalized patient management. The present study aimed to identify clinical OA phenotypes and their progression based on readily available characteristics using two fundamentally different machine learning algorithms.

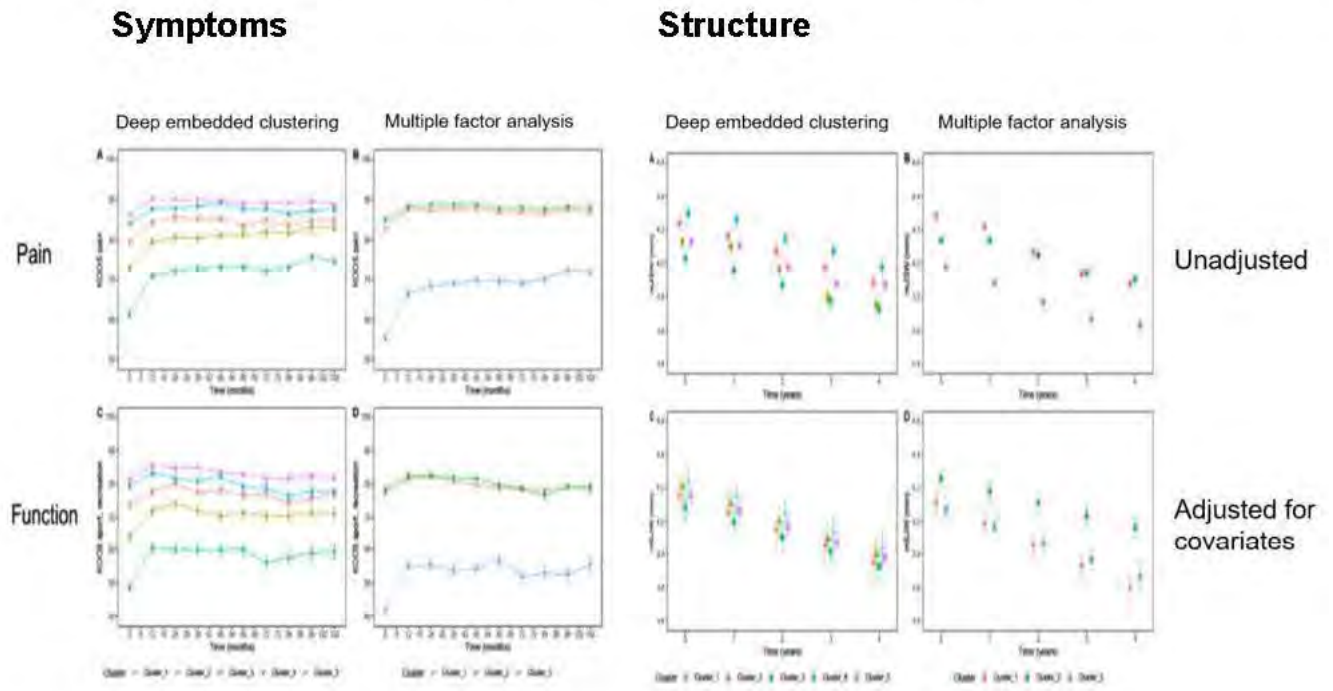
Methods: Clusters were based on 157 easily accessible clinical variables collected from the Osteoarthritis Initiative (OAI) baseline dataset, which included 4,674 participants covering the entire spectrum of knee OA severity. After

Figure 1. Data management from download to analysis



DEC, deep embedded clustering; MFA, multiple factor analysis

Figure 2. Clinical, structural and radiographic progression in the different clusters



KOOS, Knee Injury and Osteoarthritis Outcome Score; mJSW, medial minimum joint space width

reduction of data-dimensionality (i.e., reduction of the complexity without loss of information), the analysis relied on deep embedded clustering (DEC) and multiple factor analysis (MFA), respectively, for the identification of homogenous groups (Figure 1). In addition, radiographic progression of OA was analyzed in the different clusters both clinically (using the Knee Injury and Osteoarthritis Outcome Score, KOOS) over 9 years and structurally (via minimal medial joint space width) over 4 years using a linear mixed effects model.

Results: The analysis yielded 5 clusters in DEC and 3 clusters in MFA with overlap between the two techniques: Both the approaches identified a comorbid cluster which comprised predominantly females with high body mass index (BMI), peri-articular pain, a high burden of comorbidities and depression, low activity levels, pain (KOOS) and functional limitations (cluster 3 in both analyses, Figure 2). Moreover, both approaches identified a cluster of more active participants with low levels of pain measured with the Physical Activity Scale for the Elderly (PASE) and KOOS (cluster 1, Figure 2). This cluster was characterized by a dominance of male patients in MFA analysis. The 3rd MFA cluster was slightly older, relatively lean, with low pain but functional limitations (cluster 2). The three remaining clusters after DEC differed in their levels of pain, waist circumference, activity and/or age. After an initial improvement in all clusters, the intensity of symptoms was stable on cluster-specific level (Figure 2).

Radiographic progression profiles differed only for MFA clusters (Figure 2): the more active (cluster 1), as well as the comorbid cluster (cluster 3) showed faster progression than the older, less active patients (cluster 2). Age, gender, BMI, abdominal obesity, presence of knee pain and malalignment were independent risk factors for structural progression.

Conclusion: We identified differentiated, clinically relevant subpopulations within the OAI data set by using two different machine learning approaches. The cluster-specific baseline characteristics will allow for refinement of inclusion criteria for future interventional clinical trials in specific knee OA phenotypes.

Disclosure: D. Demanse, Novartis, 3, 11; **L. Tankó**, Novartis, 3, 11; **P. Lustenberger**, IBM, 3, Novartis, 11; **P. Nikolaus**, IBM, 3, MSCI Inc., 3; **I. Rasin**, IBM, 3; **D. Brennan**, IBM, 3, Cellen Therapeutics, 1; **F. Saxer**, Novartis, 3, 11; **R. Roubenoff**, Novartis, 3, 11; **S. Premji**, Novartis, 3, 11, Novartis, 2; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **M. Schieker**, Novartis, 3, 11.

Abstract Number: 0212

Unsupervised Clustering of Histology and Ultrasound Scores Identifies Osteoarthritis Subtypes

Maxwell Konnaris[1], Richard Bell[2], Tania Pannellini[3], Edward DiCarlo[2], J. Alex Gibbons[2], O. Kenechi Nwawka[2], Susan Lee[2], Peter Sculco[2], Michael Parks[2], Mark Figgie[2], Laura Donlin[2], Dana Orange[4], Thomas Sculco[2], William Robinson[5], Susan Goodman[2], Miguel Otero[2] and Bella Mehta[6], [1]Hospital or Special Surgery, New York, [2]Hospital for Special Surgery, New York, NY, [3]Research Division and Precision Medicine Laboratory, Hospital for Special Surgery, New York, NY, [4]The Rockefeller University, New York, [5]Stanford University, Palo Alto, CA, [6]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Osteoarthritis – Clinical Poster I (0210–0224)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis (OA) is a prevalent degenerative joint disease and a major cause of pain and disability worldwide. Inflammation of the synovium and surrounding tissues likely contributes to the symptoms and structural progression of OA. The heterogenous nature has posed challenges to the development of disease modifying therapies likely due to different pathogenic mechanisms underlying distinct subtypes of OA. Efforts to subtype the disease have been limited, and integrative approaches are lacking. Here, we applied unsupervised clustering analysis of histology and ultrasound data to identify clinically-relevant knee OA subtypes in patients undergoing total knee arthroplasty (TKA).

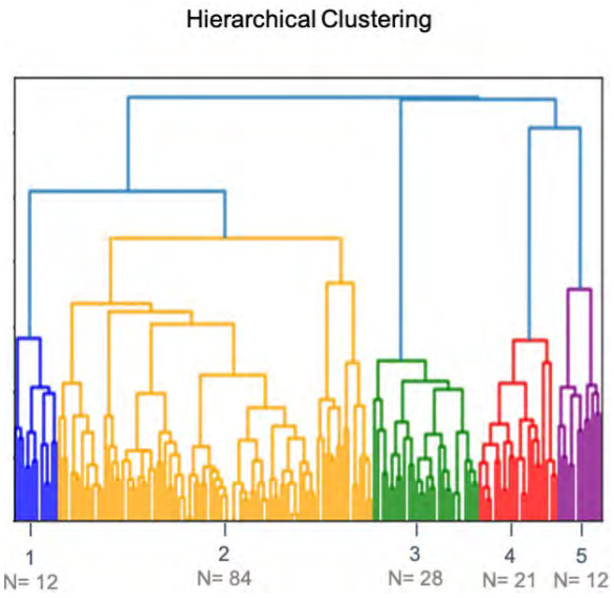


Figure 1. Knee OA subtypes identified by hierarchical clustering. Euclidean Hierarchical clustering revealed 5 knee OA clusters. The number of patients included in each cluster is indicated.

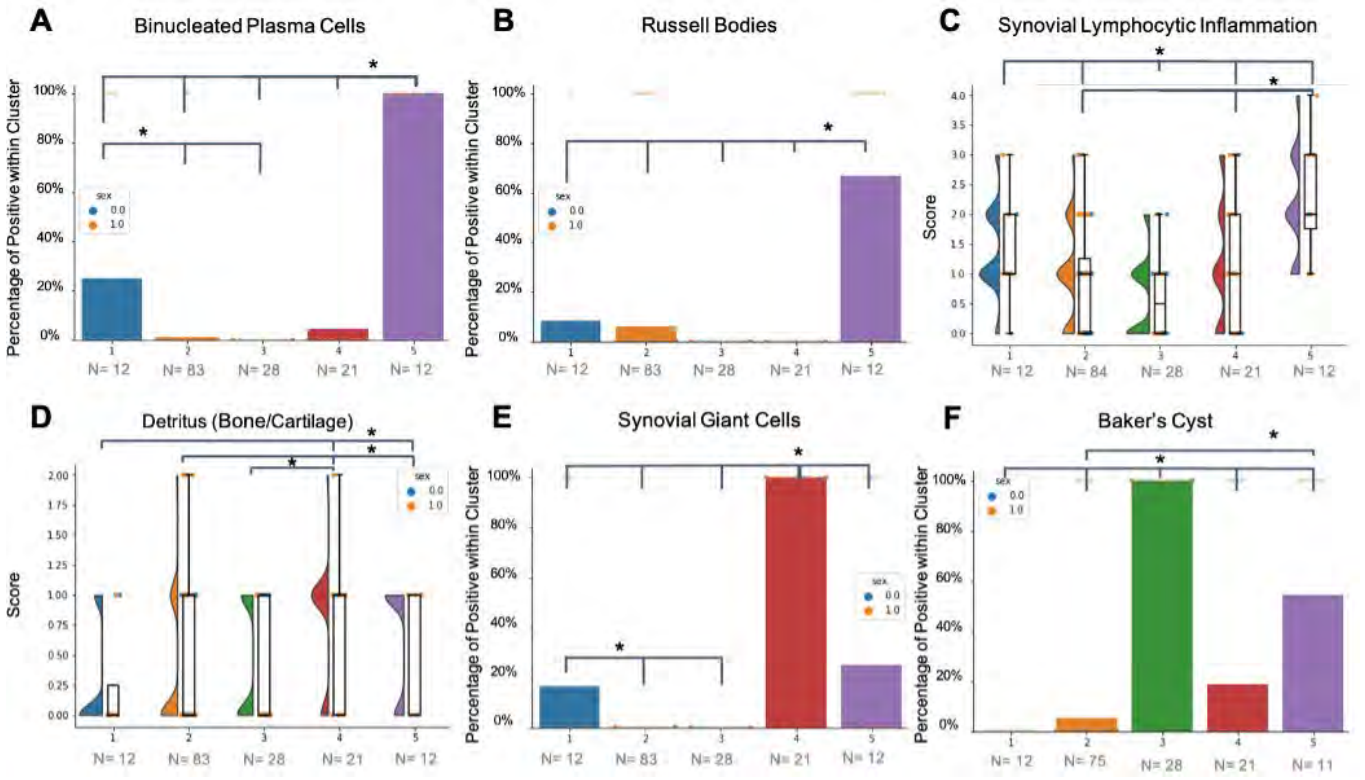


Figure 2. Selected features. Pathology features (A) Binucleated Plasma Cells, (B) Russell Bodies, (C) Synovial Lymphocytic Inflammation, (D) Detritus, and (E) Synovial Giant Cells, and one ultrasound feature (F) Baker's Cyst Presence were important features that determined our cluster separation. Graphs depict a bar plot representing the percentage of patients that had a presence of the indicated variable: Binucleated Plasma Cells, Russell Bodies, Baker's Cyst, and Synovial Giant Cells or a vertical rainbow plot (half violin plot, left, box plot overlaying individual data points, right) representing ordinal variables (Synovial Lymphocytic Inflammation and Detritus) with an increase in score representing worsening pathology. Box plot represents median and interquartile range. Wilcoxon Rank Sum Test was performed, and significance is represented as $P<0.05$ *.

Methods: We prospectively enrolled 160 patients (age 45-75) with end-stage knee OA scheduled for TKA. We collected clinical data, patient-reported data and ultrasounds (43 features, recorded using B-Mode and doppler and evaluated by two radiologists) preoperatively. 21 histologic features were scored by two trained pathologists on hematoxylin and eosin (H&E)-stained synovial biopsies. Histology and ultrasound features with ≥ 5% of variance (n=17) from 157 subjects (with ≤65% missing data) were used for analyses. Min-max scaling was applied, and unsupervised clustering using Euclidean distance and agglomerative hierarchical clustering was conducted. Wilcoxon Rank Sum tests (continuous variables) and Chi squared tests (categorical variables) were performed for statistical comparisons between clusters.

Results: Hierarchical clustering of 12 synovial histology features and 5 ultrasound features revealed 5 OA subtypes (**Figure 1A, B**). These subtypes were defined by the differences in features between subjects and were named accordingly: a *High Inflammatory Subtype* (N=12) with high levels of inflammatory cell infiltrates including plasma cells and lymphocytes, a *Moderate Inflammatory Subtype* (N=12) with moderate levels of the same synovial features, a *Detritic and Synovial Giant Cell Infiltration Subtype* (N=21), *a Minimal Pathology Subtype* (N=28) with presence of Baker's cyst on ultrasound and low levels of synovial inflammation histologic features, and a *Heterogeneous Subtype* (N=84) with little to no findings of inflammation or differences in ultrasound features (**Figure 2A-F**). Both the high and moderate inflammatory subtypes were associated with increased BMI (p=0.048), African American (AA) race (p=0.015), increased levels of ESR (p=0.043) and HS-CRP (p=0.023). The high inflammatory subtype was associated with patient reported major trauma to the affected joint (p=0.025) (**Table 1**).

Table 1. Patient subtypes and demographics. Baseline demographics, clinical features, and blood biomarkers of systemic inflammation were collected at the time of enrollment. Alcohol use is defined as an ordinal variable that represents five categories: 0: No alcohol use, 1: <3 servings per day, 2: 3-5 servings per day, 3: 5-7 servings per day, 4: >7 servings per day. Morning knee stiffness within the week before their pre-surgical screening visit and presence of major trauma to the affected knee are represented as the percentage of patient-reported incidents. Blood Biomarkers were categorized based on subjects that had the presence of levels above normal ranges. Normal ranges for ESR levels differed based on sex and age (females < age 50: 0.0 – 20.0 mm/hr, males < age 50: 0.0 – 15.0 mm/hr, females > age 50: 0.0 – 30.0 mm/hr, males > age 50: 0.0 – 20.0 mm/hr. High sensitivity CRP (HS-CRP) is represented as an ordinal variable that represents patients within normal levels of HS-CRP as 0 and patients outside normal ranges as the deviation from normal ranges. 1 < HS-CRP value < 2 = 1, 2 < HS-CRP value < 3 = 2, 3 < HS-CRP value < 4 = 3, 4 < HS-CRP value < 5 = 4, 5 < HS-CRP value = 5. Data is represented as mean ± SD. Wilcoxon Rank Sum tests were performed for statistical comparisons of continuous variables and Chi Squared tests were performed to compare categorical variables between clusters. Significance is indicated in bold as P<0.05

Cluster Demographics

	All (N = 157)	Cluster 1 (N = 12)	Cluster 2 (N = 84)	Cluster 3 (N = 28)	Cluster 4 (N = 21)	Cluster 5 (N = 12)	P value
Baseline Demographics							
Age	64.9 ± 6.8	63.4 ± 8.6	65.4 ± 6.2	65.5 ± 7.3	62.8 ± 7.2	65.3 ± 7.0	0.578
Sex (Females)	61	4	36	10	8	3	0.772
BMI (kg/m^2)	31.7 ± 6.7	35.4 ± 7.3	31.5 ± 6.5	30.7 ± 5.3	29.7 ± 7.0	35.3 ± 8.3	**0.048**
Race							**0.015**
African American/Black	10.2%	33.3%	2.4%	14.3%	14.3%	25.0%	
Asian	5.1%	8.3%	2.4%	0.0%	14.3%	16.7%	
Alaskan/American Indian	0.6%	0.0%	1.2%	0.0%	0.0%	0.0%	
Caucasian/White	81.5%	58.3%	91.7%	85.7%	66.7%	50.0%	
Native Hawaiian or Pacific Islander	0.6%	0.0%	0.0%	0.0%	4.8%	0.0%	
Other	1.9%	0.0%	2.4%	0.0%	0.0%	8.3%	
Clinical features							
Kellgren-Lawrence Score (Grade 0-4)	3.2 ± 0.8	3.7 ± 0.5	3.2 ± 0.8	3.2 ± 0.7	3.3 ± 0.8	3.1 ± 1.2	0.259
Sum of Comorbidities (0-12)	3.4 ± 2.2	3.4 ± 2.2	3.5 ± 2.2	3.5 ± 2.3	2.5 ± 1.6	4.1 ± 3.0	0.354
Cigarette Pack Years	3.8 ± 7.5	3.8 ± 6.2	3.9 ± 7.5	7.0 ± 10.6	1.1 ± 2.4	0.4 ± 1.0	0.087
Alcohol use (0-4)	1.2 ± 1.3	0.6 ± 1.0	1.5 ± 1.3	1.2 ± 1.4	1.3 ± 1.2	0.5 ± 0.7	0.137
Morning Knee Stiffness Presence	79.0%	67.0%	80.0%	86.0%	76.0%	75.0%	0.730
Major Trauma to Affected Knee	12%	8%	6%	22%	10%	33%	**0.025**
Blood Biomarkers							
Binarized ESR (mm/hr) (0/1)	30.0%	45.0%	21.0%	46.0%	25.0%	50.0%	**0.043**
Ordinal HS-CRP (mg/dL) (0.0 – 1.0 mg/dL) (0-5)	1.7 ± 1.7	2.6 ± 1.9	1.4 ± 1.5	2.2 ± 1.8	1.7 ± 1.7	2.3 ± 2.3	**0.023**

Conclusion: Clustering analysis of synovial histology and ultrasound scoring features identified 5 OA patient subtypes. Two subtypes were associated with AA race, increased BMI, and synovial inflammation, which suggests that demographical factors may play a role in the mechanisms underlying knee OA and warrants further investigation. Our findings suggest that the clinical features and patient reported outcomes represent predictive variables with the potential to be built into algorithms that could be used in the future to guide targeted personalized treatment of these OA subtypes.

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Educaiton Foundation, 4; **W. Robinson**, None; **S. Goodman**, UCB, 1, NOvartis, 5; **M. Otero**, Regeneron Pharmaceuticals, Inc., 2, Tissue Genesis, Inc., 5; **B. Mehta**, Novartis, 1, 6.

Abstract Number: 0213

Quantitative Assessment of Volumetric Change in Hip Effusion Using Artificial Intelligence in Patients with Osteoarthritis of the Hip

Jacob Jaremko[1], Banafshe Felfeliyan[2], Abhilash Hareendranathan[1], Bashiar Thejeel[1], Vanessa Quinn-Laurin[1], Mikkel Ostergaard[3], Philip Conaghan[4], Robert Lambert[1], Janet Ronsky[2] and Walter Maksymowych[1], [1]University of Alberta, Edmonton, AB, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]Copenhagen Center for Arthritis Research, Center for Rheumatology and Spine Diseases, Rigshospitalet, Glostrup, and Department of Clinical Medicine, University of Copenhagen, Glostrup, Denmark, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Accurate quantification of hip effusion volume may aid effective OA management as synovitis of the hip has been associated with pain and structural damage progression. Previous work has shown that volume quantification measures more closely correlate to clinical parameters than conventional measures like femoral neck fluid thickness (FTM). Recently, Artificial Intelligence (AI) based approaches have shown promise in measuring hip effusion volume from MRI sequences. This study examined the feasibility of using AI to quantify the change in effusion volume post intra-articular steroid injection (IASI) using Short-τ Inversion Recovery (STIR) MRI sequences.

Methods: We prospectively collected MRI images from 97 patients who met the ACR clinical classification criteria for hip OA at baseline (before IASI) and at 8 weeks follow-up (after receiving IASI). Two human readers measured the difference in effusion volumes in each image using an interactive tool developed inhouse.

Manually segmented masks of effusion regions from 72 patients were used to train a Mask R-CNN [8] AI model. Changes in effusion volume between baseline and follow-up measured from the remaining 25 patients was used to compare and validate AI measurements vs 2 human readers. The agreement was assessed using the difference in volume (DV), Coefficients of Variation (CoV), and intra-class correlation coefficient (ICC).

Results: The AI model automatically detected effusion regions successfully (Fig 1). Regions of effusion identified by the model both at baseline and follow-up correlated well with human assessment (Fig 2). Agreement in change of effusion volume (DV) measured between human readers was good (ICC=0.80 [0.53, 0.92]). Similarly, ICC between each human reader vs AI predicted ranged between moderate to good (ICC = 0.71-0.76) as summarized in Table 1.

Conclusion: Initial results of automatic quantification of change in effusion volume post -IASI shows moderate to high agreement between AI and human experts. This approach could potentially save expert time in OA MRI assessment resulting in overall improvement in OA care.

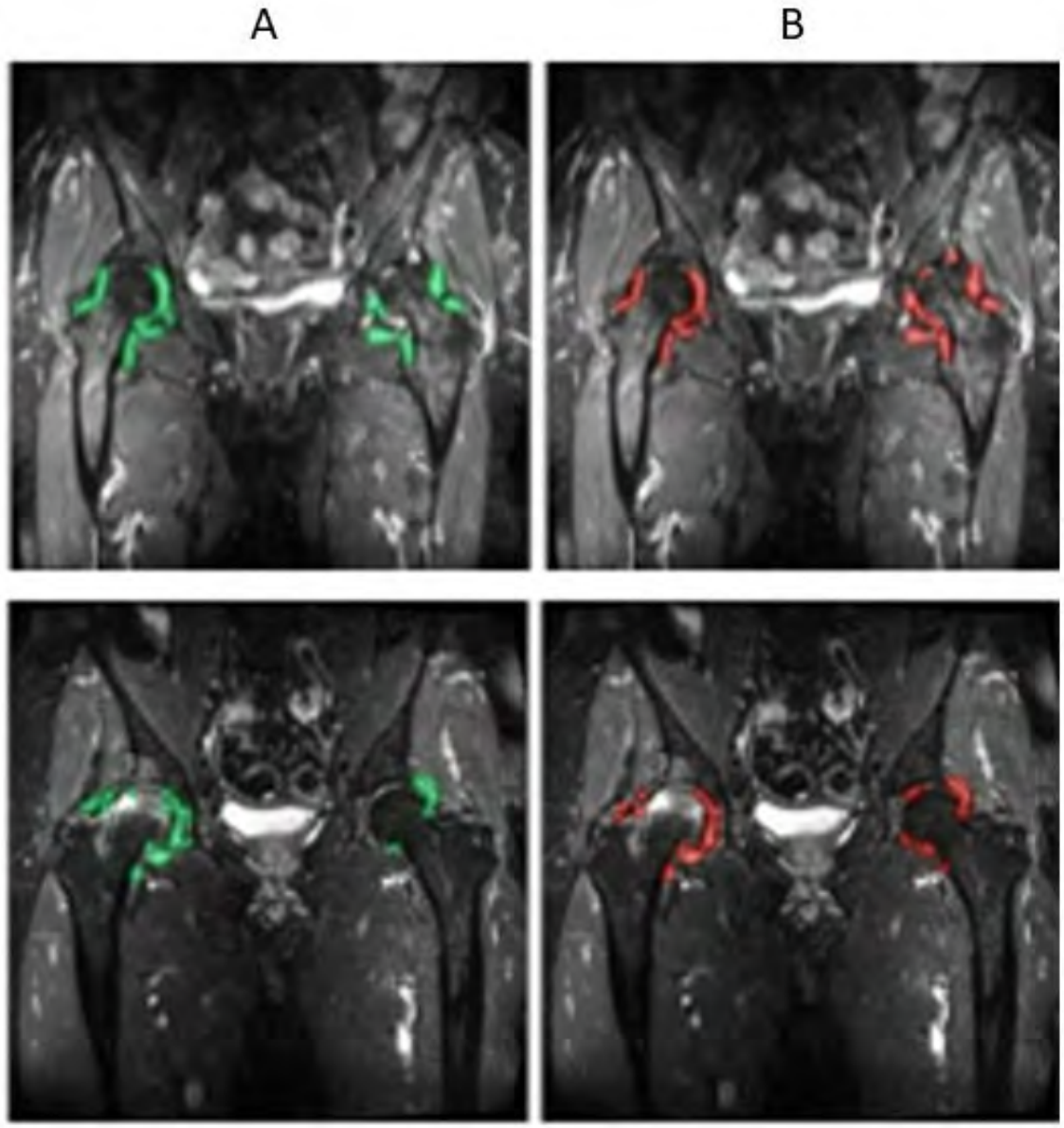

Figure 1. Regions of joint fluid detected by human readers (green, column A) and AI (red, column B) overlain on the original STIR MRI slice from 2 different patients with OA.

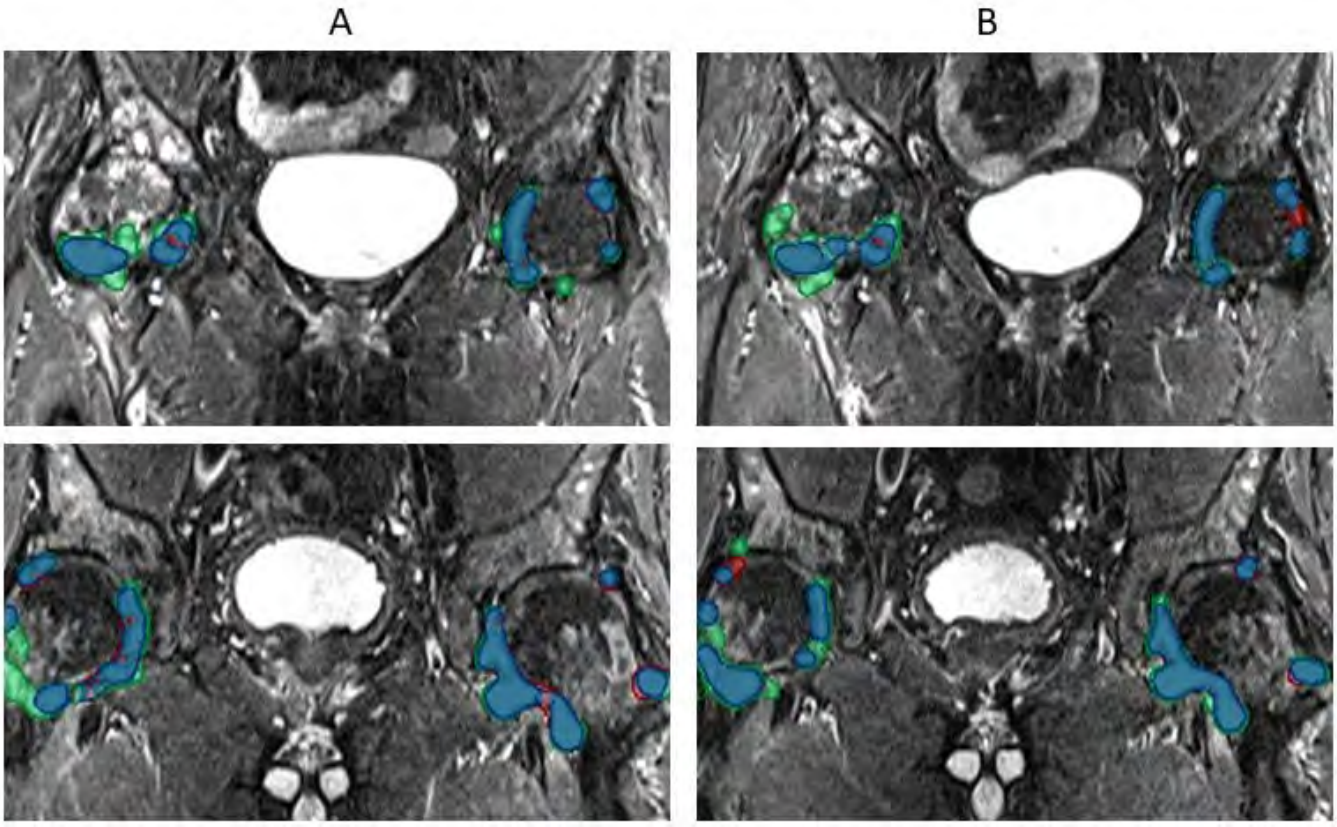

Figure 2. Regions of joint fluid detected by AI on images at baseline (column A) and follow-up (column B) in 2 different patients. Regions of perfect overlap between AI and human readers are shown in blue, segmentation by human readers in green and AI segmentations in red.

Table 1. Agreement in change in effusion volume after IASI measured by human readers and AI assessed using the difference in volume, CoV and ICC

Agreement between reader pairs			
Reader Pair	Difference in Volume Mean ± Standard Deviation	CoV	ICC
Reader 1-2	1130 ± 900	0.21	0.80 [0.53, 0.92]
Reader 1-AI	3060 ±1770	0.33	0.71[0.49,0.87]
Reader 2-AI	2260 ± 1310	0.22	0.76[0.51,0.89]

Disclosure: J. Jaremko, MEDO.ai, 8; **B. Felfeliyan**, None; **A. Hareendranathan**, None; **B. Thejeel**, None; **V. Quinn-Laurin**, None; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **R. Lambert**, Pfizer, 2; **J. Ronsky**, None; **W. Maksymowych**, Abbvie, 2, 5, 6, BMS, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli-Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0214

Baseline Cam or Pincer Morphology Is Associated with Loss of Quantitative Joint Space Width at the Hip: The Johnston County Osteoarthritis Project

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To determine the association between radiographic cam and pincer morphology and loss of hip quantitative joint space width (qJSW) in a community-based cohort.

Methods: Data were from Johnston County OA Project (JoCoOA) participants (>45 years of age) with anteroposterior (AP) pelvis radiographs from baseline and up to 2 follow-up timepoints. A musculoskeletal radiologist assigned all hips a Kellgren-Lawrence grade (KLG). Hip morphology measures were defined on baseline radiographs using OxMorf software (Oxford, UK) by two readers. An independent reader measured qJSW at all timepoints (at 3 locations, Fig 1) using a validated method. All readers were blinded to all other data. Participants self-reported age and race; their height was measured, and body mass index (BMI) calculated at clinic visits. Change in qJSW from baseline to final available follow-up divided by time was modeled by location (10, 30, and 50°) and stratified by sex. Population-averaged linear regression was used to model qJSW change in mm/10 years (mm/10y), accounting for correlation among hips and adjusting for baseline age, race, height, BMI, and qJSW to produce β and 95% confidence intervals [CI]. A sensitivity analysis considered only those hips without baseline rHOA (KLG < 2).

Results: Data from 821 individuals (38% men, 26% Black) with 1619 hips, baseline mean ± SD age 62 ± 9 years, BMI 29 ± 6 kg/m^2 and follow-up (at T1 and/or T2; 9 ± 3 years) were included. At baseline, 9% of women and 26% of men had an AP alpha angle >60° consistent with cam morphology. Acetabular under-coverage (i.e., lateral center edge

Figure 1. Fixed location qJSW measurements

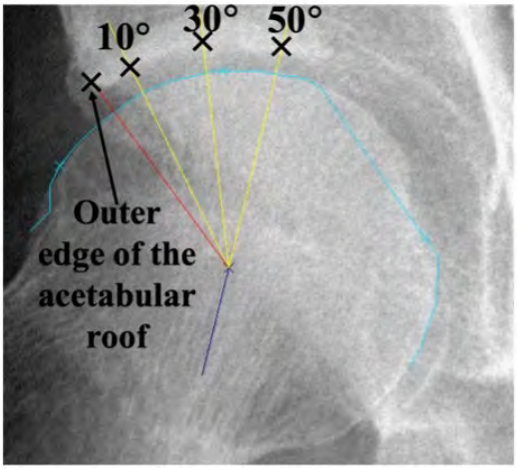

Table 1. Quantitative joint space width (qJSW) at 3 locations over a mean of 9 years of follow-up, overall and by sex

	Overall (N=1619)			Women (n=1006, 62%)			Men (n=613, 38%)		
qJSW at T0-T1 or T0-T2	Total	mean	±SD	Total	mean	±SD	Total	mean	±SD
10-degree location									
Baseline qJSW, mm (range=1.7-9.8)	1596	5.41	±0.96	993	5.21	±0.89	603	5.73	±0.99
Change over follow-up, mm/10y (range: -8.3 to 2.1)	1582	-0.06	±0.69	982	-0.03	±0.67	600	-0.10	±0.72
30-degree location									
Baseline qJSW, mm (range=2.1-9.2)	1551	5.03	±0.95	966	4.86	±0.89	585	5.30	±0.99
Change over follow-up, mm/10y (range: -7.7 to 3.0)	1533	-0.08	±0.67	959	-0.08	±0.62	574	-0.09	±0.74
50-degree location									
Baseline qJSW, mm (range=2.0-8.5)	1547	4.60	±0.88	960	4.45	±0.84	587	4.66	±0.88
Change over follow-up, mm/10y (range: -7.9 to 4.6)	1534	-0.14	±0.67	951	-0.17	±0.64	583	-0.08	±0.72

T0: baseline, 1991-7; T1: 1st follow-up, 1999-2003; T2: 2nd follow up, 2006-11; SD=standard deviation; qJSW changes are per decade

Table 2. Association between radiographic cam and pincer morphologies and qJSW change per year overall and stratified by sex.

	10-degree location		30-degree location		50-degree location	
	Women (n=976)	*Men (n=598)*	*Women (n=954)*	*Men (n=572)*	*Women (n=945)*	*Men (n=581)*
Model by FAI measure	*β (95% CI) mm/10years*	*β (95% CI) mm/10years*	*β (95% CI) mm/10years*	*β (95% CI) mm/10years*	*β (95% CI) mm/10years*	*β (95% CI) mm/10years*
AP alpha angle (per 10° increase)	-0.03 (-0.07, 0.00)	**-0.05 (-0.09, -0.01)**	-0.00 (-0.04, 0.03)	**-0.08 (-0.13, -0.04)**	**-0.07 (-0.11, -0.04)**	-0.04 (-0.08, 0.00)
AP alpha angle > 60°	-0.06 (-0.20, 0.09)	-0.08 (-0.22, 0.05)	0.02 (-0.11, 0.16)	**-0.19 (-0.32, -0.05)**	**-0.25 (-0.39, -0.11)**	-0.05 (-0.18, 0.07)
Triangular index height (per 2mm increase)	-0.03 (-0.06, 0.01)	**-0.11 (-0.16, -0.07)**	0.00 (-0.04, 0.04)	**-0.09 (-0.14, -0.03)**	-0.00 (-0.05, 0.04)	**-0.07 (-0.12, -0.02)**
Triangular index sign	-0.34 (-0.80, 0.13)	**-0.33 (-0.62, -0.03)**	-0.06 (-0.46, 0.34)	-0.09 (-0.39, 0.21)	-0.36 (-0.82, 0.09)	0.03 (-0.24, 0.30)
LCEA (per 5° increase)	0.03 (-0.00, 0.06)	0.00 (-0.05, 0.05)	0.01 (-0.02, 0.04)	0.00 (-0.05, 0.05)	-0.02 (-0.06, 0.01)	0.01 (-0.04, 0.06)
LCEA ≤ 25°	-0.01 (-0.12, 0.09)	-0.04 (-0.17, 0.09)	0.02 (-0.08, 0.12)	-0.01 (-0.14, 0.12)	0.09 (-0.01, 0.19)	0.04 (-0.09, 0.17)
LCEA > 40°	0.00 (-0.15, 0.16)	0.02 (-0.25, 0.29)	0.03 (-0.11, 0.18)	0.12 (-0.15, 0.39)	-0.04 (-0.18, 0.11)	-0.04 (-0.31, 0.23)
Protrusio acetabula	0.12 (-0.05, 0.30)	na	0.04 (-0.13, 0.20)	na	-0.10 (-0.27, 0.06)	na
Cam and Pincer	**0.33 (0.04, 0.61)**	0.07 (-0.38, 0.53)	0.13 (-0.13, 0.39)	0.06 (-0.42, 0.55)	**-0.31 (-0.58, -0.03)**	0.07 (-0.35, 0.48)

Multivariable regression modeling change in qJSW (mm/10y) adjusting for baseline: age, race, height, body mass index, and qJSW; Population-averaged linear models accounting for correlation among hips; Models are stratified by sex to provide adjusted β and 95% confidence intervals and are **bold** when significant at alpha=0.05; na=not applicable; for 3 FAI continuous variables, unit change is chosen to correspond approximately to 1SD

angle [LCEA] £ 25°) was present in about ¼ of the sample and more common in men (31% vs. 22%), while acetabular over-coverage (i.e., LCEA >40° or protrusio) was more common in women (9% vs 5% and 6% vs 0%, respectively). Baseline mean qJSW was around 5mm and decreased by an average of 0.1mm/10y (Table 1).

Among women, AP alpha angle and mixed cam/pincer morphology were significantly associated with loss of qJSW at the 50-degree location (up to 0.31mm/10y). In men, indicators of cam morphology (AP alpha angle and triangular index) were associated with loss of qJSW at all 3 locations (up to 0.33mm/10y). Acetabular under- or over-coverage were not significantly associated with change in qJSW in men or women (Table 2).

When considering only 1303 hips without baseline rHOA (data not shown), AP alpha angle was no longer significantly associated with loss of qJSW in women at the 50-degree location, but acetabular overcoverage became significant (-0.22 [-.40, -0.04]mm/10y), and mixed cam/pincer morphology was strongly associated with qJSW loss (-1.20 [-1.67, -0.73]mm/10y). In men, greater triangular index height remained associated with loss of qJSW at most locations (around 0.1mm/10y) but associations with other cam morphologies were not significant.

Conclusion: These data support a role for cam and pincer morphologies in progression of hip joint space loss. Some of these morphologies increased loss of joint space by more than 3 times (e.g., 0.3mm vs 0.1mm/10y) over the baseline average, suggesting that such measures could be used for risk stratification in clinical studies to identify hips at higher risk for progression.

Disclosure: A. Nelson, Lilly, 1; **C. Alvarez**, None; **Y. Golightly**, None; **J. Stiller**, None; **J. Renner**, None; **N. Arden**, None; **C. Ratzlaff**, None; **J. Duryea**, Biosplice LLC, 5.

Abstract Number: 0215

Ultrasonographic Assessment of Knee Osteoarthritis and Its Agreement with Radiography

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultrasonography (US) has been increasingly utilized for the assessment of various musculoskeletal conditions. However, the value of this tool in diagnosis of osteoarthritis (OA) in clinical practice remains unclear. This study was to 1) to characterize ultrasonographic features of knee OA and their relationship with pain and functional levels and 2) to determine the degree of correlation and agreement between the US and conventional radiography in the assessment of knee OA.

Methods: A cross sectional study was carried out on 145 patients (83.4 % female), aged 40 years or older, with mean age of 61.7 years, and clinically diagnosed with primary knee OA, at the outpatient Rheumatology Clinic, Cho Ray Hospital in the period between August 2018 and August 2019. Patients with concomitant inflammatory joint diseases were excluded. All subjects were clinically assessed for pain using a visual analog scale (VAS) and functional status using the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and underwent knee radiography and US examination. Correlation between ultrasonographic findings and clinical and radiographic features was investigated.

Results: A total of 290 knee joints were evaluated. The most common findings on the US were reduced cartilage thickness (74.5%), osteophytes (66.9%), effusion (55.9%), medial meniscal extrusion (78.6%), lateral meniscal extrusion (39.3%), thickened synovial membrane (17.2%) and Baker's cyst (15.2%). The VAS and WOMAC pain scores correlated positively with the level of effusion and the osteophyte size, and negatively with the medial femoral cartilage thickness measured on the US. There was a positive correlation between the sonographic medial cartilage thickness and the radiographic medial joint space width ($r_s = 0.3$, $p < 0.01$), and between sonographic and radiographic osteophyte grades ($r_s = 0.69$, $p < 0.01$ and $r_s = 0.47$, $p < 0.01$ for medial and lateral joint space, respectively). Osteophytes were found on both US and radiography in 129 (44.5%) knees, only the US in 44 (34.1%) knees, and only radiography in 17 (13.2%) knees (Kappa = 0.58; $p < 0.01$).

Conclusion: These results support the validity of US in the assessment of knee OA lesions in comparison to conventional radiography. Moreover, US appears to be more sensitive than radiophraphy in detecting early changes of knee OA such as cartilage damage and mild osteophytes

Disclosure: K. Nguyen, None; **D. Tran**, None.

Abstract Number: 0216

Distribution of Medial Femur and Tibia Cartilage Volume Change over 48 Months on MRI: Comparison Among Kellgren-Lawrence Grades

Rebecca Amesbury[1], Hedieh Ragati Haghi[1], Todd Laffaye[1], Rebekah Stein[1], Erin Ashbeck[2], C. Kent Kwoh[3], Alexander Mathiessen[1] and Jeffrey Duryea[1], [1]Brigham and Women's Hospital, Boston, MA, [2]University of Arizona Arthritis Center, Tucson, AZ, [3]University of Arizona College of Medicine, Tuscon, AZ

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Semi-automated Local Area Cartilage Segmentation (LACS) software uses two robust coordinate systems to measure cartilage change in focused regions in the femur and tibia. (Figure 1) LACS also offers a topological method to assess change in cartilage volume through the use of responsiveness heat-maps. The purpose of this study was to provide a descriptive assessment of cartilage volume change in the medial femur (MF) and medial tibia (MT) for different (Kellgren-Lawrence) KL grades with the hypothesis that there will be evidence for different patterns of changes in cartilage volume across KL grades 1, 2 and 3.

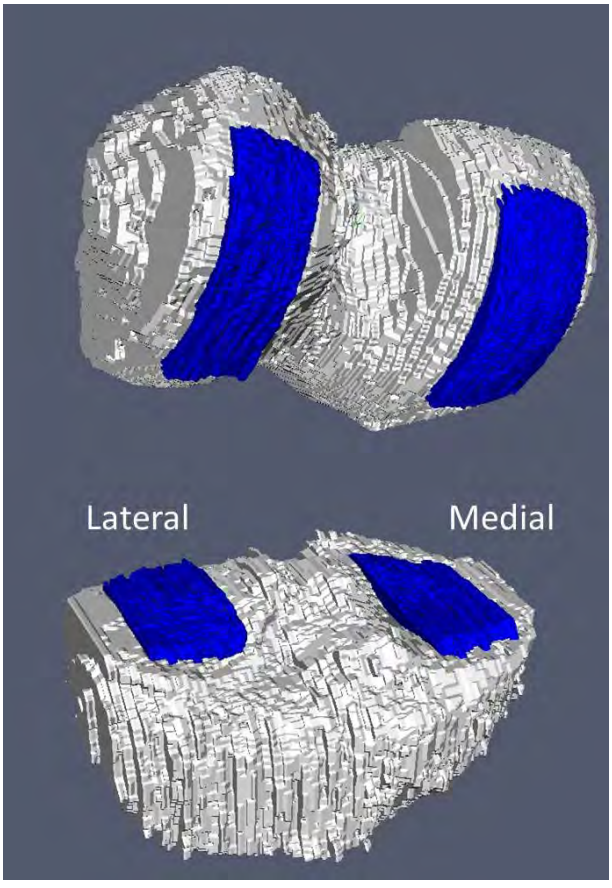

Figure 1. Examples of LACS subregions defined by cylindrical (femur) and Cartesian (tibia) coordinate systems.

Table 1. SRM values for different KL grades

	KL1 (N=160)	KL2 (N=316)	KL3 (N=194)	All (N=670)
MF	-0.32	-0.36	-0.73	-0.46
MT	-0.44	-0.42	-0.61	-0.48

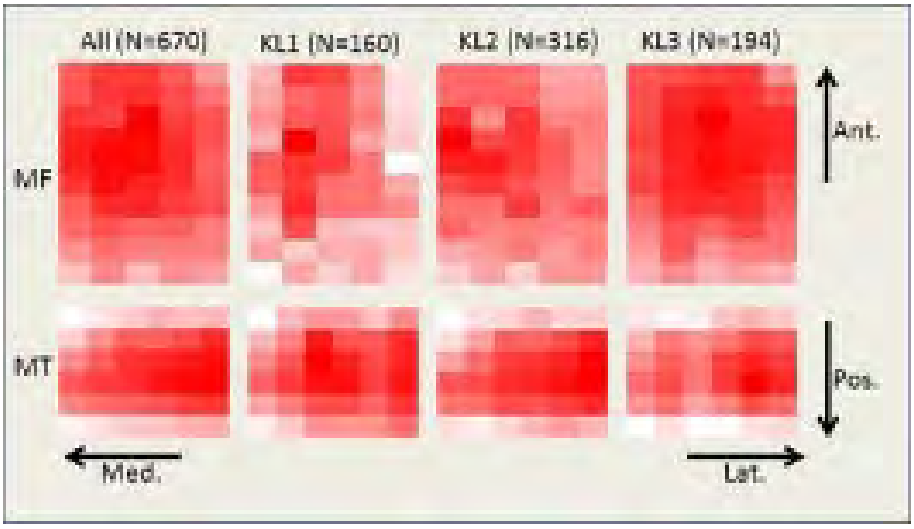

Figure 2. Responsiveness heat-maps for the MF and MT based on the SRM values. Each shaded rectangle represents the sub-regions of cartilage shown in Figure 1. Note, the range of intensities has been renormalized for each condition. Overall magnitude of the change for each category can be appreciated by the values in Table 1.

Methods: Cartilage volume was measured in a central weight-bearing portion of the MF and MT using the LACS method at the baseline (BL) and 48 month visits of 670 participants from the Osteoarthritis Initiative (OAI), a longitudinal observational cohort study. Participants with at least one knee KL 1, 2, or 3 on centrally read baseline posterior-anterior weight-bearing knee radiographs were selected. Participants with a prosthetic knee or KL4 knee at baseline were excluded. One knee per participant was selected, based on maximum KL grade or randomly, if both knees had the same KL grade. Cartilage volume change was calculated as standardized response mean (SRM) for both plates separately. LACS SRM was estimated over grids in the sample and displayed in the form of responsiveness heat-maps, showing topographical change as SRM values over each cartilage plate region. (i.e., blue sub-regions in Figure 1) The mathematical nature of the LACS method permits any grid location to be determined consistently.

Results: At baseline, the participants had a mean age of 61.3 years, a mean BMI of 28.9, and were 41.5% male. The baseline distribution of KL grades was: KL1: 23.9% (N=160), KL2: 47.1% (N=316), KL3: 29.0% (N= 194). SRM values are shown in Table 1. These data indicate that the cartilage volume change is similar between KL1 and KL2 with a substantial increase for KL3. The responsiveness heat-maps are shown in Figure 2. We observed different patterns of change across the heat-maps. With increasing KL grade from 1 to 3, there appeared to be greater amount of change in the lateral portion of both the MF and MT compartments with the MT and MF having similar patterns of change.

Conclusion: As expected, loss of cartilage volume is increased in KL3 knees. But the heat-maps suggest there is more cartilage loss in the inner (lateral) portion of the knee in patients with more advanced OA as seen by a modestly higher intensity in the right-hand side of each heatmap with increasing KL grade. The variation in patterns of change in cartilage volume by KL grade demonstrate that the heat-map approach may offer a way to characterize different disease-related patterns of knee osteoarthritis progression. Additional studies will be necessary to better understand the role of responsiveness heat-maps. In the future, this work will be extended to the lateral compartment, and differences by gender, BMI, age, knee alignment, and other clinical variables will be assessed.

Disclosure: R. Amesbury, None; **H. Ragati Haghi**, None; **T. Laffaye**, None; **R. Stein**, None; **E. Ashbeck**, EMD Serono, 2; **C. Kwoh**, Lilly, 5, Abbvie, 5, Kolon Tissue Gene, 12, DSMB, Regeneron, 1, LG Chem, 1; **A. Mathiessen**, None; **J. Duryea**, Biosplice LLC, 5.

Abstract Number: 0217

The OMERACT Knee Inflammation MRI Scoring System: Validation of Quantitative Methodologies and Tri-compartmental Overlays by Comparison with the MRI Osteoarthritis Knee Score

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Osteoarthritis – Clinical Poster I (0210–0224)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Bone marrow lesions (BML) and synovitis on MRI are independently associated with the severity and progression of osteoarthritis (OA) and randomized controlled trials have targeted reducing the size of BML

Table 1. KIMRISS and MOAKS scores in Two International Multi-reader Exercises

Method	MRI feature	Scores mean (SD)			SDC (% of max)	P value	SRM
		Baseline	One-year Follow up	Change			
EXERCISE A							
MOAKS	BML	3.6 (2.9)	3.4 (2.3)	-0.2 (1.9)	1.0 (2.2%)	0.72	-0.11
	Synovitis-effusion	1.3 (0.8)	1.5 (0.8)	0.2 (0.4)	0.4 (13.3%)	0.017	0.5
KIMRISS	BML	15.7 (13.3)	21.2 (22.5)	5.5 (15.3)	5.6 (1.1%)	0.022	0.36
	Synovitis-effusion	21.8 (12.0)	24.3 (11.9)	2.5 (7.4)	2.8 (2.8%)	0.043	0.34
EXERCISE B							
MOAKS	BML	4.2 (2.6)	3.7 (2.4)	-0.5 (2.1)	1.1 (2.4%)	0.22	-0.24
	Synovitis-effusion	1.2 (0.7)	1.3 (0.8)	0.0 (0.5)	0.4 (13.3%)	0.53	0.0
KIMRISS	BML	22.1 (20.8)	19.1 (17.1)	-3.1 (14.6)	4.3 (0.9%)	0.64	-0.21
	Synovitis-effusion	21.8 (9.3)	22.9 (10.8)	1.1 (7.1)	2.2 (2.2%)	0.46	0.15

Table 2. Intra-class Correlation Coefficients (95%CI)			
Method	**MRI feature**	**Exercise A**	**Exercise B**
KIMRISS status	BML	0.86 (0.78-0.92)	0.91(0.88-0.94)
KIMRISS change		0.88 (0.81-0.93)	0.88 (0.83-0.92)
MOAKS status	BML	0.71 (0.46-0.85)	0.67 (0.56-0.77)
MOAKS change		0.76 (0.64-0.85)	0.69 (0.60-0.78)
KIMRISS status	Synovitis-effusion	0.88 (0.81-0.93)	0.75 (0.52-0.86)
KIMRISS change		0.87 (0.79-0.92)	0.87 (0.82-0.91)
MOAKS status	Synovitis-effusion	0.66 (0.4-0.79)	0.65 (0.52-0.75)
MOAKS change		0.52 (0.36-0.67)	0.48 (0.37-0.60)

Table 3. Correlations with WOMAC pain scores (correlation coefficient, r (p value)) (Exercise B)			
Method	**MRI feature**	**WOMAC status**	**WOMAC change**
KIMRISS status	BML	0.33 (p=0.016)	-0.13 (p=0.35)
MOAKS status		0.27 (p=0.048)	-0.11 (p=0.41)
KIMRISS change	BML	-0.10 (p=0.46)	0.31 (p=0.026)
MOAKS change		-0.017 (p=0.90)	0.30 (p=0.027)
KIMRISS status	Synovitis-effusion	0.37 (p=0.0064)	0.12 (p=0.38)
MOAKS status		0.43 (p=0.0012)	0.10 (p=0.47)
KIMRISS change	Synovitis-effusion	-0.11 (p=0.45)	0.22 (p=0.12)
MOAKS change		-0.14 (p=0.30)	0.27 (p=0.051)

and degree of synovitis for the treatment of OA. We have developed the OMERACT Knee Inflammation MRI Scoring System (KIMRISS) and have recently refined it to maximize reliability and sensitivity to change. Innovations include custom-designed electronic overlays suitable for a touch-screen interface for assessment of BML in 500 subregions on consecutive sagittal slices, a web-based interface with direct online scoring, and real-time iterative calibration (RETIC) prior to formal reading exercises. We aimed to test the feasibility, reliability, and responsiveness of KIMRISS versus an established method, MOAKS, in a multi-reader exercise.

Methods: KIMRISS incorporates web-based graphic overlays for each of femur, tibia, and patella to score BML in 500 subregions on consecutive sagittal slices. S-E is recorded as the largest diameter of the fluid signal on all *consecutive* sagittal slices (scoring range 0-100). All scores are pro-rated for a standardized number of MRI slices. In a pre-reading exercise for KIMRISS, readers scored a RETIC module to attain scoring proficiency, pre-specified as an ICC of ≥0.80 and ≥0.70 for status and change scores of BML and S-E when compared to developer reads. A new web-based scoring platform with overlays designating subregions for scoring BML was developed for MOAKS. We compared reliability for status and change scores of BML and S-E in 2 international multi-reader exercises of baseline and 1-year MRI scans from the Osteoarthritis Initiative: A. 4 expert readers and an OMERACT fellow scored 38 cases selected for MOAKS BML score ≥1. B. 8 expert readers and an OMERACT fellow scored 60 cases selected for MOAKS BML ≥3 and Kellgren-Lawrence (K-L) grade < 3. Reliability was assessed by intra-class correlation coefficient (ICC) and Smallest Detectable Change (SDC), responsiveness by the standardized response mean (SRM), and feasibility using the System Usability Scale (SUS scoring range 0-100).

Results: For exercises A/B, subjects were 55.3%/ 26.7% male, mean(±SD) age 61.7(±9.1)/61.9(8.8) years, and radiographic K-L grade ≤2 in 39.4%/100%. Change was small in both exercises (< 5% of scoring range for KIMRISS and MOAKS BML and S-E) with comparable responsiveness (Table 1). Despite this, ICC for change was consistently good to very good for both BML and S-E and consistently better for KIMRISS with lower SDC as % of scoring range (Table 2). Significant correlations between WOMAC baseline pain scores and KIMRISS and MOAKS baseline BML and S-E scores were observed; significant correlations between WOMAC change and KIMRISS and MOAKS BML change were also noted (Table 3). Mean SUS scores were 88.2 for KIMRISS and 54.3 for MOAKS.

Conclusion: The KIMRISS method for scoring BML and Synovitis-Effusion scores highly for feasibility and demonstrates consistently high reliability when compared to MOAKS. Correlations with WOMAC pain are demonstrable with both methods for both BML and S-E. Further validation for responsiveness is necessary in cases with greater change in MRI features than in the OAI dataset.

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **J. Jaremko**, MEDO.ai, 8; **S. Pedersen**, None; **I. Eshed**, Novartis, 6, Abbvie, 6; **U. Weber**, None; **P. Bird**, Novartis, 1, Pfizer, 1, 6, Eli Lilly, 1, 6, Gilead, 1, 6, Janssen, 1, 6, AbbVie, 6; **A. McReynolds**, None; **S. Wichuk**, None; **J. Paschke**, None; **R. Lambert**, Pfizer, 2.

Abstract Number: 0218

Synovitis Does Not Mediate the Relationship Between Body Mass Index and Progression of Radiographic Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Marina Bañuls[1], Alecio Lombardi[1], Eric Chang[1], Aladdin H Shadyab[1], Nancy Lane[2] and Monica Guma[3], [1]University of California San Diego, San Diego, CA, [2]University of California Davis, Hillsborough, CA, [3]University of California San Diego, La Jolla, CA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Synovial inflammation is associated with knee osteoarthritis (KOA) progression. Body mass index (BMI) has also been associated with KOA progression. Yet, it is unclear whether synovial inflammation mediates the association of BMI with KOA progression. Here, we examined the mediating effect of synovitis in the association between BMI and progression of radiographic KOA in the Osteoarthritis Initiative (OAI) cohort.

Methods: We conducted a case-control study within the OAI. Cases (n = 315) were right knees with an increase of ≥ 1 Kellgren-Lawrence (K-L) from baseline to 48 months of follow-up. Controls (n = 315) were right knees that had no K-L change over 48 months. Cases and controls were matched by age, gender, race and baseline K-L. MRI Osteoarthritis

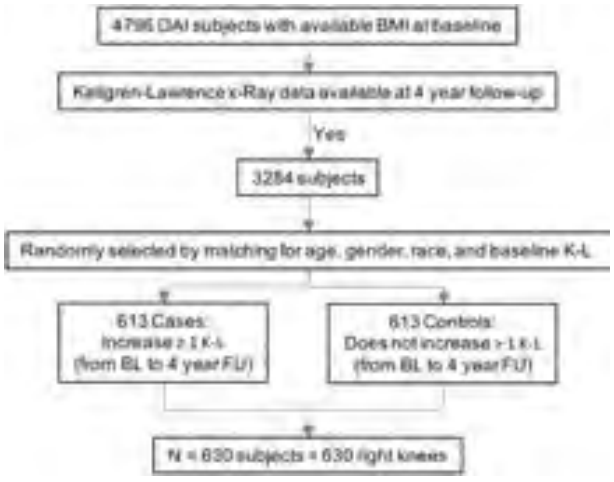

Figure 1. Patient selection from the OAI database.

Table 1. Baseline characteristics of the study participants

Right knees	Total (n = 630)	Cases (n = 315)	Controls (n = 315)
Age (mean ± SD, years)	61 +- 8	61 +- 8	61 +- 8
Female (%)	70.8	70.8	70.8
Racial composition			
White or Caucasian (%)	87	87	87
Black or African American (%)	12.7	12.7	12.7
Other non-white (%)	0.3	0.3	0.3
BMI (mean ± SD, kg/m2)	28.6 +- 4.8	29.1 +- 4.7	28.2 +- 4.9
BMI			
Normal weight (%)	24.9	21.0	28.9
Overweight (%)	37.1	37.5	36.8
Obese (%)	37.0	41.5	34.3
Kellgren-Lawrence			
K-L 0 (%)	36.8	36.8	36.8
K-L 1 (%)	30.2	30.2	30.2
K-L 2 (%)	25.1	25.1	25.1
K-L 3 (%)	7.9	7.9	7.9
Synovitis effusion			
Presence (%)	49.8	59.6	40.1
Score (mean +- SD)	0.56 +- 0.62	0.71 +- 0.67	0.41 +- 0.51
Hoffa synovitis			
Presence (%)	51.9	61.9	42.0
Score (mean +- SD)	0.61 +- 0.66	0.78 +- 0.73	0.44 +- 0.54

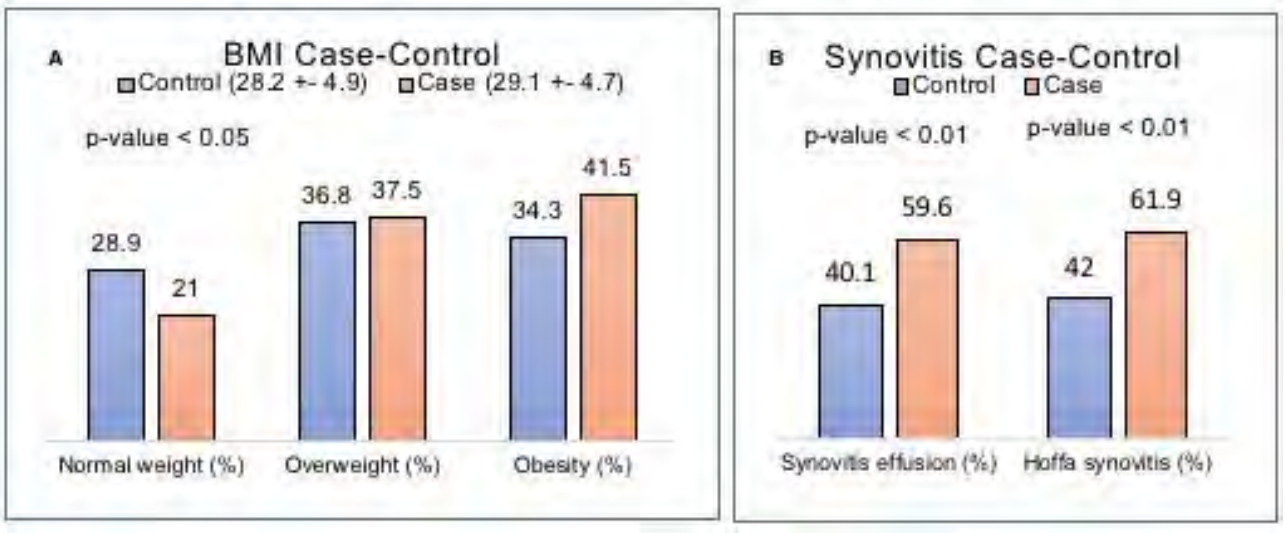

Figure 2. A: Percentage of cases and controls by BMI. P value is overall test of significant for chi square test. B: Percentage of cases and controls with synovitis effusion or Hoffa synovitis. P value is overall test of significant for chi square test.

Knee Score (MOAKS) was used for a semi-quantitative evaluation (0-3) of effusion synovitis and Hoffa-synovitis at baseline. The SPSS PROCESS macro was used to test the mediating effects.

Results: The mean age of participants was 61 years, 70.8% were women, and 87% were white. Baseline knee KL was as follows: 36.8% grade 0, 30.2% grade 1, 25.1% grade 2 and 7.9% grade 3. 24.9% were normal weight (BMI < 24.9 kg/m2), 37.1% were overweight (BMI 25-29.9 kg/m2) and 37.0% were obese (BMI ≥ 30 kg/m2). Average BMI was 28.63 ± 4.8. 49.8% had synovitis effusion with a score of 0.56 ± 0.6, and 51.9% had Hoffa synovitis with a score or 0.61 ± 0.66. Compared with controls, cases had higher BMI (29.1 ± 4.7 vs 28.2 ± 4.9,p< 0.05), and were more likely to be obese (41.5% vs. 34.3%) than controls (p < 0.05). At baseline, cases had higher prevalence of both synovitis

effusion and Hoffa-synovitis than controls (59.6% vs 40.1%, p< 0.01 for synovitis-effusion and 61.9% vs 42%, p< 0.01, for Hoffa synovitis respectively). Yet, in the mediation analysis, neither synovitis effusion nor Hoffa synovitis mediated the relationship between BMI and KOA progression.

Conclusion: Preliminary findings from mediation analysis showed that neither synovitis effusion nor Hoffa synovitis mediated the relationship between BMI and progression of radiographic KOA over a 4-year period. A longer duration of follow-up may be required to determine if synovitis mediates the association between BMI and progression of KOA.

Disclosure: M. Bañuls, None; **A. Lombardi**, None; **E. Chang**, None; **A. H Shadyab**, None; **N. Lane**, Amgen, 2, Pfizer, 2, BriOri Biotech, 4, Makikroft, 2, 6, GSK, 2, UCB, 1; **M. Guma**, Novartis, 5, Pfizer, 5, Gilead, 5, Genentech, 5.

Abstract Number: 0219

Intra-Articular Mineralization on Knee CT and Risk of Cartilage Loss: The Multicenter Osteoarthritis Study

Jean Liew[1], John Lynch[2], Ali Guermazi[1], Mohamed Jarraya[3], David Felson[1], Na Wang[1], Cora Lewis[4], James Torner[5], Michael Nevitt[6] and Tuhina Neogi[7], [1]Boston University, Boston, MA, [2]University of California San Francisco, San Francisco, CA, [3]Massachusetts General Hospital, Boston, MA, [4]University of Alabama Birmingham, Birmingham, AL, [5]University of Iowa, Iowa City, IA, [6]University of California San Francisco, Orinda, CA, [7]Boston University School of Medicine, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Intra-articular (IA) mineralization due to crystal deposition may contribute to OA pathology through inflammation, release of pro-catabolic factors, or altered cartilage biomechanical properties. Prior conflicting studies regarding whether chondrocalcinosis (from IA mineralization) is associated with OA structural progression were limited by the use of insensitive radiographs for visualizing IA mineralization. We studied the relation of IA mineralization on CT (a more sensitive modality) to cartilage loss on knee MRI in older adults, with particular attention to potential joint location- and tissue-specific effects of mineralization on cartilage pathology.

Table. Relationship of IA mineralization to cartilage loss, on knee-level and compartment-specific analyses

	Knee-level	Compartment-specific
IA mineralization	**Risk ratio (95% CI)**	**Risk ratio (95% CI)**
Any mineralization	1.05 (0.90, 1.24)	1.16 (0.88, 1.53)
Any cartilage	1.05 (0.87, 1.27)	**1.40 (1.04, 1.88)**
Any meniscus	1.03 (0.86, 1.24)	1.07 (0.81, 1.42)
Any joint capsule	1.16 (0.95, 1.42)	—

Adjusted for age, sex, race/site, BMI.
Any IA mineralization includes cartilage, meniscus, and joint capsule for knee-level analyses; and cartilage and meniscus for compartment-specific analyses.

Methods: Participants from the Multicenter Osteoarthritis (MOST) study, a longitudinal prospective cohort of older adults, who had knee CTs and MRIs, were included in this longitudinal analysis. IA mineralization was assessed on CT using the Boston University Calcium Knee Score (BUCKS), with semi-quantitative scoring of extent of crystal mineralization 0-3 in WORMS subregions. We categorized presence of mineralization as a BUCKS score >0 in the following tissues: 1) anywhere in the knee; 2) cartilage; 3) meniscus; 4) joint capsule. For cartilage and meniscus, we further classified mineralization as occurring in the medial and/or lateral tibiofemoral compartment. Cartilage worsening on MRI was defined as any increase in the semi-quantitative MOAKS score between baseline and two-year follow-up in a compartment-specific manner and for the whole knee. We evaluated the relation of IA mineralization (defined above) to the presence of MRI cartilage worsening using binomial regression, and with generalized estimating equations for compartment-specific analyses to account for correlations between compartments within a knee. Analyses were performed in a compartment-specific manner for cartilage and meniscus mineralization (i.e., relation of presence of medial mineralization to risk of medial cartilage worsening), and at the whole knee level for capsular mineralization. Analyses were adjusted for age, sex, and body mass index (BMI).

Results: We included 1673 participants (mean age 60.1±9.1, 56% female, mean BMI 28.6±5.0 kg/m^2). Overall, 9.0% had any IA mineralization in the knee; mineralization in the cartilage, meniscus, and joint capsule was present in 6.3%, 7.1%, and 4.0%, respectively. 46.5% had cartilage loss on follow-up anywhere in the knee. In compartment-specific analyses, presence of cartilage mineralization was associated with a 1.40 higher risk of cartilage loss in the same compartment (95% CI, 1.04-1.88); no association was noted for mineralization of the meniscus (Table). Mineralization of any tissue in the knee, regardless of location or tissue type was not associated with cartilage worsening at any location in the knee.

Conclusion: IA mineralization in the cartilage, but not in the meniscus, was associated with higher risk of cartilage loss in the same compartment over two years. Mineralization of the joint capsule was also not associated with cartilage loss anywhere in the knee. These findings suggest potential tissue-specific and localized effects of IA mineralization on cartilage pathology in knee OA.

Disclosure: J. Liew, None; **J. Lynch**, None; **A. Guermazi**, Pfizer, MerckSerono, Regeneron, TissueGene, AstraZeneca, Novartis, 2, BICL, 8; **M. Jarraya**, None; **D. Felson**, None; **N. Wang**, None; **C. Lewis**, None; **J. Torner**, None; **M. Nevitt**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2.

Abstract Number: 0220

Relation of Knee Extensor Power to Worsening Cartilage Damage in the Knee: The MOST Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

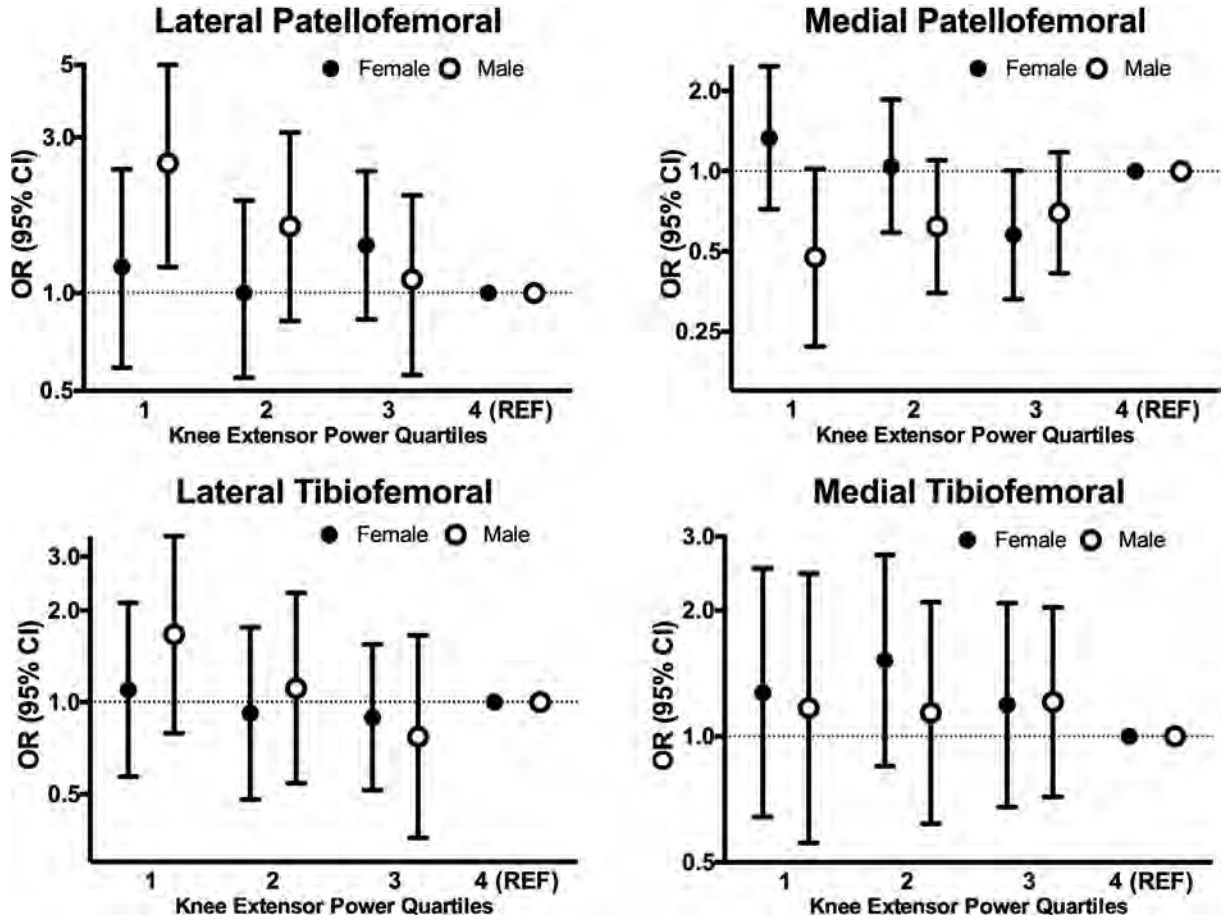

Figure. Relation of quadriceps power quartiles to worsening knee joint cartilage damage in men and women.

Background/Purpose: The relation between knee extensor muscle weakness and osteoarthritis (OA) outcomes has been well-studied. Muscle power, another measure of knee extensor function, however, has been less studied in the context of knee OA. Power is the rate at which a load is moved. Velocity of muscle contraction declines with aging, leading to a more precipitous drop in muscular power than in strength and increases vulnerability to joint injury with minor perturbations. Greater knowledge of the extent to which knee extensor power is a risk factor for worsening structure is clinically important, as muscle power is a potentially modifiable risk factor. Identifying relationships between power and structural change may affect current rehabilitation approaches to manage knee OA by shifting the focus from increasing strength to increasing velocity. Thus, our objective was to determine the relation of knee extensor power to worsening cartilage damage in the knee.

Methods: Knee extensor power was assessed using a HUMAC Norm dynamometer. An isotonic knee extension one repetition maximum (1RM) was first determined. Then participants extended each knee as fast and as hard as they could while moving 40% of the 1RM load. Three trials were performed, and the maximum value in Watts was used in the analyses. Knee extensor power was divided into quartiles. Cartilage damage was assessed using the MRI Osteoarthritis Knee Score (MOAKS) by two musculoskeletal radiologists in 14 subregions of the knee at the 144- and 168-month study visits. Worsening cartilage damage was defined as any increase in score, either in size or depth, over 2 years. Analyses were performed separately for the medial/lateral patellofemoral joints (PFJ) and medial/lateral tibiofemoral joints (TFJ). Our unit of analysis was the subregion (e.g., the lateral patellofemoral joint analyses included the lateral patella and lateral anterior femur subregions). Logistic regression with GEE was used to determine the relation of knee extensor power quartiles to any worsening of cartilage damage adjusting for age, BMI, race, and previous knee injury/surgery. Analyses were performed in women and men separately.

Results: 1547 participants were included in the current analysis; mean age and BMI were 61.0 (9.2) years and 28.6 (4.9) kg/m^2, respectively; 56% were female and 84% white. The mean knee extensor power was 2.8 (1.0) and 3.9 (1.3) Watts in women and men, respectively. Cartilage worsening was present in 7.3, 6.9, 4.9, and 4.6% of subregions in the lateral PFJ, medial PFJ, medial TFJ, and lateral TFJ in women, respectively. In men, cartilage worsening was present in 8.2, 8.5, 7.0, and 2.6% of subregions in the lateral PFJ, medial PFJ, medial TFJ, and lateral TFJ, respectively. There was no relation between knee extensor power and cartilage worsening in any knee compartment in women. In men, compared to those in the highest knee extensor power quartile, those in the lowest quartile had 2.5 (1.2, 5.0) and 0.48 (0.22, 1.0) times the odds (95% CI) of cartilage worsening in the lateral and medial PFJ, respectively.

Conclusion: In men, lower knee extensor power was associated with increased odds of cartilage worsening in the lateral PFJ and decreased the odds of medial PFJ cartilage worsening.

Disclosure: J. Stefanik, None; **D. Felson**, None; **C. Lewis**, None; **G. Rabasa**, None; **A. Guermazi**, Pfizer, MerckSerono, Regeneron, TissueGene, AstraZeneca, Novartis, 2, BICL, 8; **F. Roemer**, None; **M. Nevitt**, None; **C. Lewis**, None; **N. Segal**, Tenex Health, 2, Pacira CryoHealth, 5, Flexion Therapeutics, 5.

Abstract Number: 0221

Trunk Movement Compensation Is Associated with Physical Performance Measures and Fatigue Deficits in Hip Osteoarthritis

Jesse Christensen[1], **David Quammen**[2], Justin Rigby[2], Cory Christiansen[3] and Jennifer Stevens-Lapsley[3], [1]VA Salt Lake City Health Care System, Salt Lake City, UT, [2]University of Utah, Salt Lake City, UT, [3]Department of Physical Medicine and Rehabilitation, University of Colorado Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION
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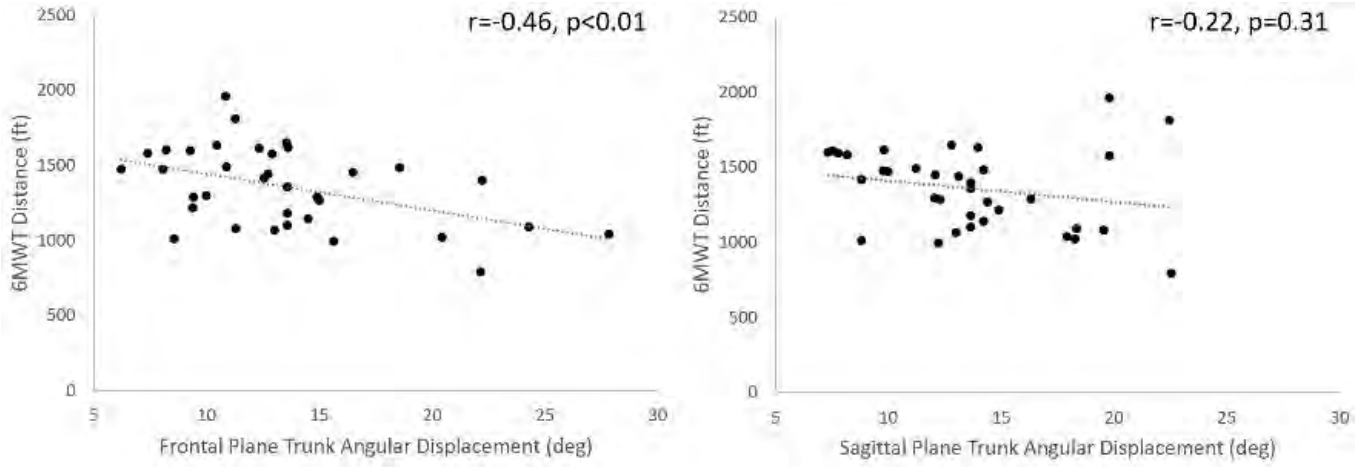
Background/Purpose: Movement compensation is common in people with hip osteoarthritis (HOA) and a biomarker of physical performance and muscle strength deficits in older adults. Inertial measurement units (IMUs) offer novel methods for identifying movement compensation during functional activities. However, the relationship between deficits in physical performance, muscle strength and fatigue on movement compensation is unknown in people with HOA. Therefore, the purpose of this study was to compare the relationship between trunk movement compensation identified by IMUs and physical function assessed by validated physical performance and muscle strength measures.

Methods: Thirty-five participants (63.3±7.4 years, 57% male, 28.6±4.5 kg/m^2) with end-stage HOA who were scheduled to undergo a total hip arthroplasty were enrolled in the study. A cross-sectional study design was used. Two inertial measurement units were used to assess trunk onto pelvis movement compensation during the six-minute walk test (6MWT). Hip abduction, knee extension and knee flexion strength were measured using hand-held dynamometer. General linear regression models were used to regress trunk movement compensation onto 6MWT performance and muscle strength measures. Pairwise t-tests were used to evaluate the influence fatigue has on trunk movement compensation by comparing the first and last minute of the 6MWT.

Results: Greater trunk movement compensation was related to poorer 6MWT ($p< 0.01$; $r=-0.46$). Greater hip abduction weakness was related to increased trunk movement compensation in both the sagittal ($p=0.01$; $r=-0.44$) and



Relationship between trunk angular displacement on six-minute walk test performance.

Table 2. Peak trunk movement compensation during six-minute walk test

Variable	6MWT First Minute			6MWT Last Minute					
	Max	Min	Sum^	Max	Min	Sum^	Mean Diff[d]	SE	p-value[f]
Frontal Plane[a]	0.36 (8.75)	12.24 (9.30)	12.61 (3.70)	0.72 (10.8)	13.95 (12.03)	14.68 (5.32)	2.06	0.66	0.005*
Sagittal Plane[b]	11.70 (6.07)	1.19 (6.41)	13.21 (4.48)	13.80 (6.72)	0.08 (7.15)	13.88 (5.86)	0.67	0.55	0.312

Note: Angular displacement of the trunk during sagittal and frontal plane movement during six-minute walk test. 6MWT, six-minute walk test; Max, maximum; Min, minimum; Diff, difference score between the maximum and minimum peak mean values.

[a] *Values are peak means (standard deviations) from raw data (degrees), positive values indicate angular displacement over the involved limb. Negative values indicate angular displacement over non-involved limb.*

[b] *Values are peak means (standard deviations) from raw data (degrees), positive values indicate angular displacement anteriorly. Negative values indicate angular displacement posteriorly.*

^ *Values are the summation of the magnitude of the maximum and minimum angular displacement.*

[f] *Values are peak mean differences (standard error) from linear regression model*

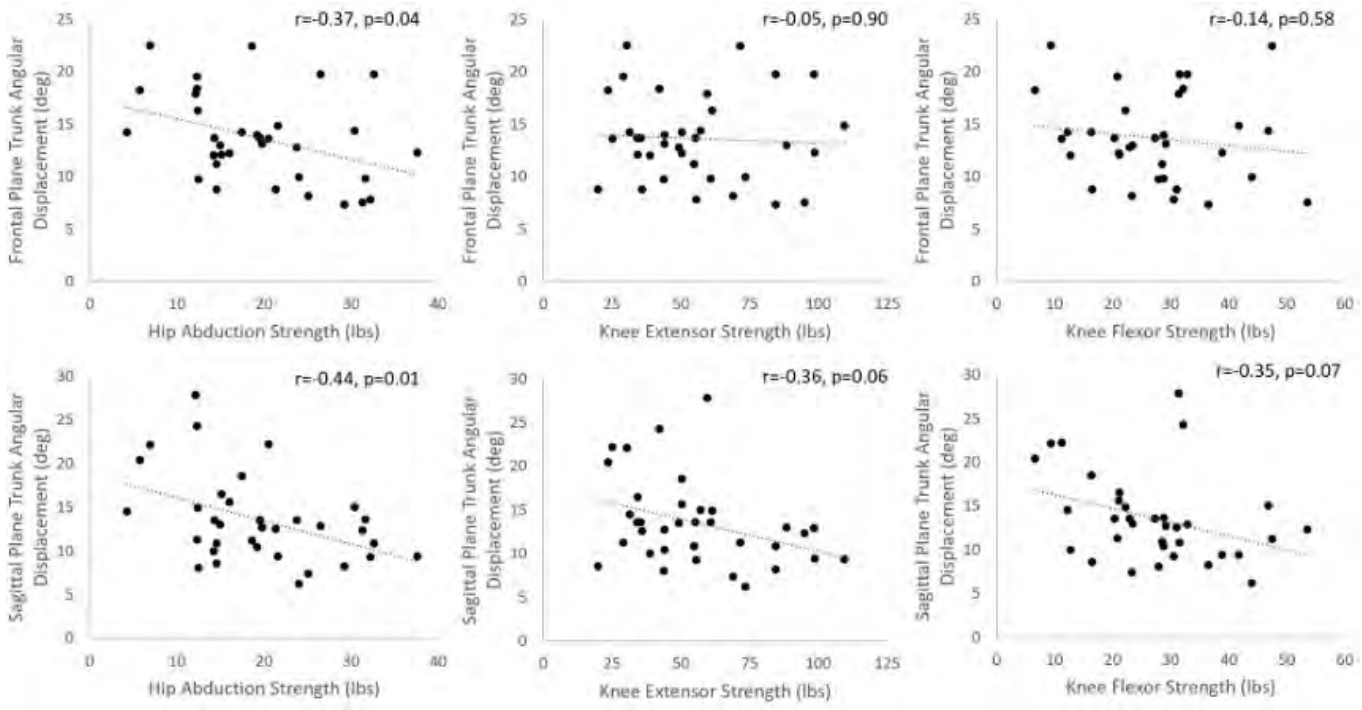
[‡] *p-values adjusted based upon Tukey-Ciminera-Heyse multiple comparison procedure*

* *significant at p<0.05*

Peak trunk movement compensation during the six-minute walk test.

frontal (p=0.04; r=-0.37) planes. Participants demonstrated greater trunk movement compensation during the last minute compared to the first minute (p< 0.01) of 6MWT.

Conclusion: Trunk movement compensation has a negative influence on physical function in people with HOA. Greater trunk movement compensation relates to poorer performance on the six-minute walk test and greater hip



Relationship between muscle weakness on trunk angular displacement during six-minute walk test.

abduction weakness. Prolonged walking leads to a greater increase in trunk movement compensation, which could have future ramifications of accelerated arthritic changes in secondary joints.

Disclosure: J. Christensen, None; **D. Quammen**, None; **J. Rigby**, Azena Medical LLC, 2; **C. Christiansen**, Hanger Clinics, 5; **J. Stevens-Lapsley**, None.

Abstract Number: 0222

Effects of Multi-Joint Osteoarthritis Phenotypes on Self-Reported Physical Function over 3.5 Years: The Johnston County Osteoarthritis Project

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
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Background/Purpose: To determine the differential effects of several literature-based definitions of multi-joint osteoarthritis (MJOA) on change in self-reported physical function in a community-based cohort.

Methods: We previously defined 10 forms of MJOA (Table) based on results from a systematic review of MJOA definitions (PMID 30390991). Here, we focus on the influence of symptomatic MJOA (sxMJOA, i.e., meeting a given MJOA definition with at least one site being symptomatic, see Table) on change in physical function 3.5 years later. The outcome of interest was the change in scores on the Patient Reported Outcomes Measurement Information System

Table. Symptomatic MJOA associations with PROMIS-PF change from baseline (T3) to follow-up (T4)

		Overall	Women	Men	White	Black
MJOA definition (at least one sx joint)	*N*	*β (95% CI)*	*β (95% CI)*	*β (95% CI)*	*β (95% CI)*	*β (95% CI)*
1. ≥1 IP node and ≥2 other sites (hip, knee, spine, ankle, or foot)	582	-0.8 (-1.8, 0.2)	-0.6 (-1.8, 0.6)	-1.3 (-3.1, 0.5)	-1.2 (-2.4, 0.1)	-0.1 (-1.7, 1.6)
2. ≥2 IP, ≥1 CMC and knee or hip	576	**-1.6 (-3.0, -0.1)**	-1.5 (-3.0, 0.1)	-2.0 (-5.5, 1.5)	-1.5 (-3.1, 0.0)	-1.7 (-5.0, 1.5)
3. ≥5 joint sites (DIP, PIP, CMC, hip, knee, spine, ankle, or foot)	582	-0.6 (-2.0, 0.7)	-0.6 (-2.1, 0.9)	-0.8 (-4.1, 2.6)	-0.6 (-2.1, 0.9)	-0.6 (-3.5, 2.2)
4. ≥2 lower body joint sites (hip, knee, spine, ankle, or foot)	582	**-1.2 (-2.2, -0.2)**	**-1.2 (-2.4, -0.0)**	-1.2 (-3.1, 0.7)	**-1.6 (-2.9, -0.4)**	-0.5 (-2.1, 1.2)
5. Knee or hip and 1 other joint site: (spine, ankle, or foot)	580	0.2 (-0.8, 1.1)	-0.1 (-1.3, 1.0)	0.8 (-0.8, 2.7)	-0.1 (-1.3, 1.0)	0.8 (-0.8, 2.3)
6. ≥3 sites (hip, knee, spine, ankle, or foot)	582	-0.8 (-2.2, 0.5)	-0.9 (-2.4, 0.6)	-0.7 (-3.4, 2.0)	-1.6 (-3.1, 0.0)	0.7 (-1.6, 3.0)
7. Bilateral knees and spine	407	**-4.2 (-8.2, -0.1)**	**-4.6 (-8.9, -0.3)**	-1.3 (-12, 9.8)	-4.1 (-8.4, 0.3)	-4.8 (-16, 6.3)
8. ≥3 joint sites (DIP, PIP, CMC, hip, knee, spine, ankle, or foot)	582	-0.7 (-1.8, 0.3)	-0.2 (-1.4, 0.9)	**-2.0 (-3.9, -0.1)**	-0.8 (-2.1, 0.4)	-0.5 (-2.2, 1.1)
9. ≥1 CMC and bilateral nodes	573	-0.2 (-1.8, 1.4)	0.2 (-1.5, 1.8)	-3.9 (-9.0, 1.2)	0.0 (-1.8, 1.8)	-1.2 (-4.8, 2.3)
10. ≥3 IPs or bilateral nodes	581	-1.1 (-2.5, 0.3)	-0.9 (-2.5, 0.6)	-1.6 (-4.5, 1.4)	-0.4 (-2.0, 1.1)*	**-3.5 (-6.5, -0.6)***

*Multivariable regression modeling difference in PROMIS-PF from baseline (T3) to follow-up (T4) adjusting for baseline: cohort, age, sex, race, education, BMI, Charlson Comorbidity Index, PROMIS-PF score, and follow-up time; An interaction term was used to provide adjusted β by sex or race, respectively; *=interaction significant at p-value<0.1; **BOLD**=statistically significant.*

Physical Function Scale, Short Form 10a version 1.0 (PROMIS-PF, PMID 21914216). Data were from participants in the Johnston County OA Project (JoCoOA) who completed the baseline (T3; 2013-15) and follow-up (T4; 2017-18) visits and had data for both baseline sxMJOA and PROMIS-PF scores at baseline and follow-up.

Multivariable linear regression models were performed to assess the association of sxMJOA definitions with PROMIS-PF change from baseline to follow-up, adjusting for baseline: cohort, age, sex, race, education, body mass index (BMI), Charlson Comorbidity Index, PROMIS-PF score, and follow-up time. β and 95% confidence intervals for sx-MJOA are reported, with negative values representing greater reduction in PF in those with sxMJOA. An interaction term was included in the model to provide estimates by sex or race, respectively; as these stratified results were of particular interest, they are reported regardless of statistical significance of this term.

Results: Included individuals (n=586, 71% women, 36% Black) had a mean age of 70 ± 7 years and mean body mass index (BMI) of 32 ± 7 kg/m^2 at baseline. Depending on the definition, the prevalence of sxMJOA ranged from 1 to 51%. Overall PROMIS-PF scores declined (worsened) by about 1 point (mean -1.2 [SD 6.4]) over the 3.5 ± 1 year follow-up, with 53% of individuals experiencing a worsening in score.

Statistically significant decreases in PROMIS-PF scores were seen overall for those with sxMJOA-2, -4, and -7 (Table). The effects of sxMJOA-1, -2, -4 and -5 were similar across sex and race. The largest effect on PROMIS-PF (4–5-point reduction) was from the relatively infrequent sxMJOA-7 (involvement of the bilateral knees and spine), an effect that was strongest in women and Blacks. Men with sxMJOA-8 had reductions in PF not seen in women or by race. sxMJOA-10 (interphalangeal hand OA) was associated with significantly poorer PF scores only in Black participants (3.5-point reduction, p< 0.1 for interaction). sxMJOA-3, -6, and -9 were not associated with PF changes, nor were sums of affected joint sites (data not shown).

Conclusion: Specific subtypes of sxMJOA in which at least one joint site is symptomatic are associated with varying decrements in self-reported physical function, beyond simple summing of affected numbers of joints. In some cases,

important differences by sex and race are observed. These findings suggest the importance of MJOA phenotypes, future work will include other physical function measures, both self-reported and performance-based, and longer follow-up times.

Disclosure: A. Nelson, Lilly, 1; **C. Alvarez**, None; **L. Arbeeva**, None; **J. Renner**, None; **V. Kraus**, Novartis, 2, Paradigm, 2, Gilead, 2, Zimmer, 5; **D. Lascelles**, None; **Y. Golightly**, None.

Abstract Number: 0223

The Association of Clinical and Structural Knee Osteoarthritis with Physical Activity in the Middle-aged Population: The Netherlands Epidemiology of Obesity Study

Sietse Terpstra[1], Jeroen van der Velde[1], Renée de Mutsert[1], Dieuwke Schiphof[2], Monique Reijnierse[1], Frits Rosendaal[1], Lotte van de Stadt[1], Margreet Kloppenburg[1] and Marieke Loef[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Erasmus Medical Center, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Physical activity is a potential target for interventions in knee OA. However, most of the available studies concerning physical activity in individuals with knee OA were performed in relatively old populations with an inactive lifestyle. It is unclear how previous results can be generalized to other populations with different lifestyle and physical activity habits.

Therefore, we investigated if knee OA is associated with lower physical activity in a general middle-aged Dutch population. Furthermore, we investigated the association of physical activity with patient reported outcomes such as knee pain and function, and health-related quality of life in individuals with knee OA.

Methods: We used cross-sectional data from the Netherlands Epidemiology of Obesity (NEO) study, in which participants aged 45-65 years were included. Clinical knee OA was defined using the criteria by Altman et al. Structural knee OA was defined on MRI using the modified criteria by Hunter et al. in a random subset of 1,285 individuals of our study population.

We assessed knee pain and function with the Knee injury and Osteoarthritis Score (KOOS), and health-related quality of life (HRQoL) with the Short Form (SF)-36. Physical activity (in Metabolic Equivalent of Task (MET) hours per week) was assessed using the Short Questionnaire to Assess Health-enhancing physical activity (SQUASH).

We used linear regression analyses to investigate 1) the association of knee OA with physical activity, and 2) of physical activity with knee pain, function, and HRQoL in participants with clinical knee OA. All analyses were adjusted for age, sex, body mass index (BMI), ethnicity, educational level and comorbidities. To account for possible information bias, we performed a sensitivity analysis to assess the association between clinical knee OA and physical activity measured by an accelerometer in a random subset of 15% of the study population.

Table 1. Characteristics of the NEO study population. Numbers represent mean (SD) or percentages. ^median (25th, 75th percentiles). Abbreviations: OA = osteoarthritis. BMI = Body Mass Index. MET = Metabolic Equivalent of Task.

	All	No clinical knee OA	Clinical knee OA
	n = 6,214	86%	14%
General population characteristics			
Age (year)	55.7 (6.0)	55.4 (6.1)	57.5 (5.0)
Sex (% women)	55	54	67
BMI (kg/m^2)	26.3 (4.4)	26.1 (4.3)	27.6 (5.1)
Comorbidities (% present)	24	23	32
Physical activity			
Total^ (MET-hours per week)	118.8 (76.8;155.0)	118.4 (76.6;154.4)	123.5 (77.8;157.2)

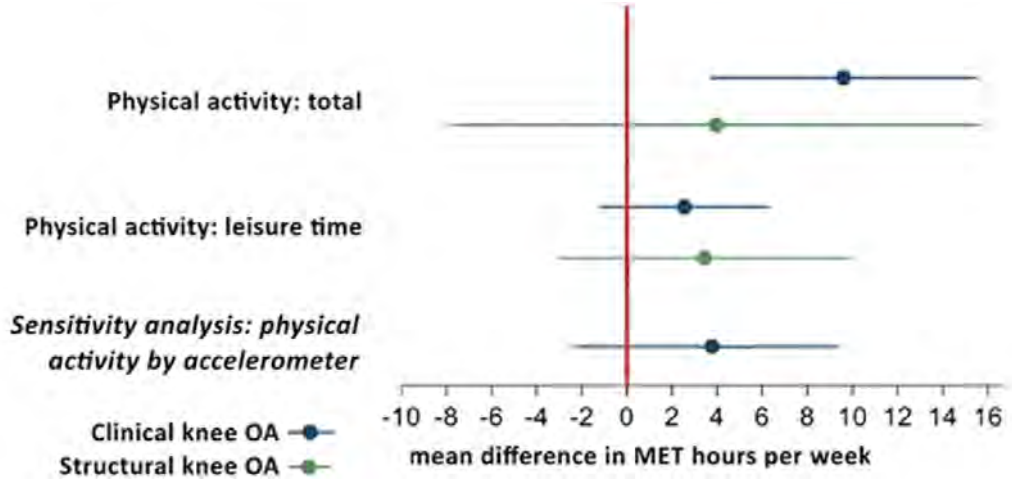

Figure 1. The association of clinical and structural knee osteoarthritis with physical activity adjusted for age, sex, body mass index, ethnicity, educational level and comorbidities. Reference: participants without knee osteoarthritis. MET = Metabolic Equivalent of Task.

Results: Of 6,212 participants, we observed clinical knee OA in 14%, and structural knee OA in 12%. The general population characteristics and median physical activity of our study population are presented in **table 1**. In comparison to participants without knee OA, participants with clinical knee OA had on average 9.60 (95% CI 3.70;15.50) MET hours per week more total physical activity (**figure 1**). Structural knee OA was associated with 3.97 (-7.82; 15.76) MET hours per week more physical activity, compared with no structural knee OA.

Sensitivity analysis showed a weak positive association of clinical knee OA with physical activity measured by an accelerometer: 2.37 (-6.05; 10.80) MET hours per week more physical activity was found in participants with clinical knee OA, compared with participants without clinical knee OA. In the subpopulation of participants with clinical knee OA, physical activity was not associated with knee pain, function or HRQoL.

Conclusion: Knee OA was not associated with lower physical activity in this middle-aged Dutch population. Future research should indicate the optimal treatment advice regarding physical activity for individual knee OA patients.

Disclosure: S. Terpstra, None; **J. van der Velde**, None; **R. de Mutsert**, None; **D. Schiphof**, None; **M. Reijnierse**, None; **F. Rosendaal**, None; **L. van de Stadt**, None; **M. Kloppenburg**, None; **M. Loef**, None.

Abstract Number: 0224

Effects of Kinesiophobia and Physical Function on Physical Activity in Adults with Knee Osteoarthritis

Burcu Aydemir and Kharma Foucher, University of Illinois at Chicago, Chicago, IL

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Osteoarthritis – Clinical Poster I (0210–0224)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Only a small proportion of people with knee osteoarthritis (OA) meet the recommended guidelines for physical activity and it is still unclear why. Lacking regular participation in physical activity is a risk factor for functional limitations in people with knee OA. Psychological factors, such as kinesiophobia (fear of movement), have been linked to activity avoidance behaviors in this population. The purpose of our study was (i) to investigate the effects of selected physical function measures in explaining physical activity, and (ii) to determine whether kinesiophobia may contribute to activity level beyond what is explained by physical function measures.

Methods: Thirty participants (16F | 14M; age, 40-75 y) with doctor diagnosed uni- or bilateral knee OA consented to participate in this cross-sectional study. Physical activity was assessed by self-report using the UCLA activity rating scale (1-10, inactive to regular participation in impact sports). Physical function was assessed using the four square step test (FSST), 30-sec chair stand (CST), timed up and go (TUG), and 40-m fast paced walk (FPWT). These performance-based measures were selected because they assess different domains of physical performance and functional ability. The Tampa Scale for Kinesiophobia (TSK; scale 17-68, no fear to extreme fear of movement) was used to assess the degree of kinesiophobia. We used Spearman correlations and multiple regression analysis to examine the relationships between UCLA activity scores and the predictors. Separate regression models were calculated for each physical function measure, in which TSK score and the covariate sex were the other independent variables, and UCLA score was the dependent variable in all models. Alpha was set at $p < 0.05$ for all analyses. Prior to parametric analysis, data were transformed when necessary, using logarithmic transformations.

Results: Better performance on all physical function measures and lower TSK scores (less fear) were associated with higher self-reported activity levels (Table 1). Regression models significantly accounted for 66.4% to 78.7% of the variance in UCLA scores (Table 2). Better performance on all functional measures predicted higher UCLA scores after controlling for sex and TSK. Lower TSK score (less fear) was a significant predictor of higher UCLA scores in all models after accounting for physical function and sex. Physical function measures were the most important predictors

Table 1. Correlations between UCLA score and predictor variables

	TUG	FPWT	FSST	CST	TSK
Spearman's Rho	-.802*	.758*	-.676*	.663*	-.702*
Mean	9.9	1.4	12.3	9.7	40.2
SD	3.9	0.34	6.4	4.5	7.7

Note: TUG, timed up and go (sec); FPWT, 40-m fast paced walk test (m/sec); FSST, four square step test (sec); CST, 30-sec chair stand test (count); TSK, Tampa Scale for Kinesiophobia. *$p < .01$. Mean UCLA score = 5.13 ± 2.1.

Table 2. Regression parameters from each model predicting UCLA score[a]

	β	t	*p*	R^2	sr^2
Model 1					
Sex	.269	2.85	.008		.067
TUG[a]	-.634	-5.78	<.001	.787	.275
TSK	-.236	-2.09	.047		.036
Model 2					
Sex	.202	1.93	.065		.037
FPWT	.542	4.78	<.001	.740	.228
TSK	-.363	-3.17	.004		.100
Model 3					
Sex	.207	1.88	.071		.039
FSST[a]	-.505	-4.26	<.001	.713	.201
TSK	-.384	-3.21	.004		.114
Model 4					
Sex	.285	2.40	.024		.075
CST	.457	3.42	.002	.664	.151
TSK	-.349	-2.52	.018		.082

Note. [a]Log transformed. β = standardized beta coefficient. sr^2 = the squared semi-partial correlation indicates unique effect of each independent variable. Sex, male = 1. TUG, timed up and go. FPWT, 40-m fast paced walk test. FSST, four square step test. CST, 30-sec chair stand test. TSK, Tampa Scale for Kinesiophobia. All models statistically significant ($p < .001$).

of UCLA scores in each model, uniquely explaining 15.1% to 27.5% of the variation in UCLA scores. However, TSK score uniquely explained 3.6% to 11.4% of the variation seen in UCLA scores.

Conclusion: Physical function measures were associated with UCLA scores, however kinesiophobia also contributed to explaining physical activity level even after accounting for physical function and sex. Assessing both kinesiophobia and physical function could help clinicians better identify knee OA patients that may be prone to avoiding certain activities or exercises.

Disclosure: B. Aydemir, None; **K. Foucher**, None.

Abstract Number: 0225

Prevalence of Sexual Dysfunction and Depression in German Patients with Psoriasis and Psoriatic Arthritis – Results of the PIPPA Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

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Session Time: 8:30AM–10:30AM

Background/Purpose: As known chronic inflammatory diseases have an impact on sexuality. To date, there are only a few studies from North and Latin America which investigated the influence of inflammatory diseases on sexual life

and practically none on patients with psoriasis (Pso) and psoriatic arthritis (PsA) (1-3). Reliable data on the prevalence of sexual dysfunction, quality of life and depression in this population compared to the general population are lacking.

Methods: Patients with psoriasis and psoriatic arthritis in two German tertiary university hospitals were evaluated with a self-designed questionnaire on various sexual and disease specific aspects, a 19-item version of the validated Female Sexual Function Index (FSFI), 15-item version of International Index of Erectile Function (IIEF), Dermatology Life Quality Index (DLQI), the 9-item questionnaire Qualisex, and the Beck's depression inventory (BDI) in a prospective study. The study was approved by our ethics committee and all patients gave written informed consent.

This work was supported by an unrestricted grant by Novartis.

Results: 416 patients were included into the study. Among them 219 suffered from Pso, 94 being females (mean age 45 years) and 125 males (mean age 43 years), as well as 197 PsA patients, 80 being females (mean age 47.5 years) and 117 males (mean age 45 years). The Healthy Control Group (HCG) is composed of 87 women with a median age of 34 years (ranging from 18-64) and 119 men with a median age of 52 years (ranging from 20-69).

The prevalence of sexual dysfunction (SDF) was similarly high in patients with Pso and PsA (82.6 vs. 75.6%) and significantly lower in the HCG (44.8%, p= < 0.0001). Erectile Dysfunction did only differ significantly in younger patients (18-35 years) with moderate-severe manifestation and Pso or PsA (11.8 vs. 9.4%) and no affected men in the HCG (0%, p=0.05).

The prevalence of depression in this cohort was highest in female patients with psoriatic arthritis, with no significant increase compared to female patients with psoriasis (50.1 vs. 34.0%). In comparison, only 3.5% of the women in the healthy control group had depression, which was a highly significant difference (p=0.0001). A similar picture was seen in the male patients with Pso and PsA, with a lower prevalence of depression, especially the severe forms, compared to the female patients (23.2 vs. 29.9%). Here, too, there was a highly significant difference compared to the male control group with a prevalence of 8.5% (p=0.0001).

Conclusion: In this work, for the first time Pso and PsA were studied separately and together with regard to their influence on sexuality and possible depression in men and women and compared with a healthy control group. Our work shows the impact of chronic diseases, such as Pso and PsA, on the sexuality and mood of our patients in a large collective. In patients who suffer from additional articular disease in combination with skin disease, the proportion of erectile dysfunction and depression is particularly high. Physicians should pay more attention to these common comorbidities and consciously address during the medical consultations.

Disclosure: S. Saur, None; **A. Schloegl**, None; **C. Höppner**, None; **A. Gubar**, None; **K. Meier**, AbbVie, 2, 6, Amgen, 2, 6, Biogen, 2, 6, Celgene, 6, Janssen-Cilag, 6, UCB Pharma, 6; **M. Hahn**, Janssen-Cilag, 1, Takeda Pharmaceutical, 6; **J. Henes**, Roche Pharma, 1, 5, 6, ABBVIE, 6, Novartis, 5, 6, SOBI, 5, 6, LILLY, 6, Pfizer, 5, 6, BMS, 6, Janssen, 6, UCB, 6, Boehringer-Ingelheim, 6.

Abstract Number: 0226

High Efficacy, Safety, and Tolerability of Secukinumab Injection with 2 mL Auto-injector (300 Mg) in Adult Patients with Moderate to Severe Plaque Psoriasis: 52-week Results from MATURE, a Randomised, Placebo-controlled Trial

Bardur Sigurgeirsson[1], John Browning[2], Stephen Tyring[3], **Jacek Szepietowski**[4], Raquel Rivera-Díaz[5], Isaak Effendy[6], Deborah Keefe[7], Gerard Bruin[8], Bertrand Paguet[9], Rong Fu[10], Isabelle Hampele[9] and Maximilian Reinhardt[9], [1]University of Iceland, Reykjavík, Iceland, [2]Texas Dermatology and Laser Specialists, Texas, TX, [3]Center for Clinical Studies, Texas, [4]Department of Dermatology, Venereology and Allergology, Wroclaw Medical University, Wroclaw, Poland, [5]Hospital Universitario 12 de Octubre, Madrid, Spain, [6]Departrment of Dermatology and Allergology, University Hospital of Bielefeld, Bielefeld, Germany, [7]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [8]Novartis Institutes for Biomedical Research, Basel, Switzerland, [9]Novartis Pharma AG, Basel, Switzerland, [10]Novartis Institutes of for Biomedical Research, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The MATURE study investigated administration of 300 mg secukinumab (SEC) using a 2 mL autoinjector (AI) device. The objective of this study was to assess efficacy, safety, tolerability, and pharmacokinetics (PK) of the 2 mL AI for SEC 300 mg in patients with moderate to severe plaque psoriasis (PsO).

Methods: MATURE was a multicentre, randomised, double-blind, placebo (PBO)-controlled, parallel-group Phase III trial (NCT03589885) conducted at 22 sites worldwide. The study consisted of 3 periods: screening (screening to baseline [BL]), treatment period 1 (BL to Week 12; pre-dose), and treatment period 2 (Week 12 dose to Week 52). Eligible patients were randomised to receive SEC 300 mg in a 2 mL AI or 2x 1 mL pre-filled syringe (PFS) or PBO. The

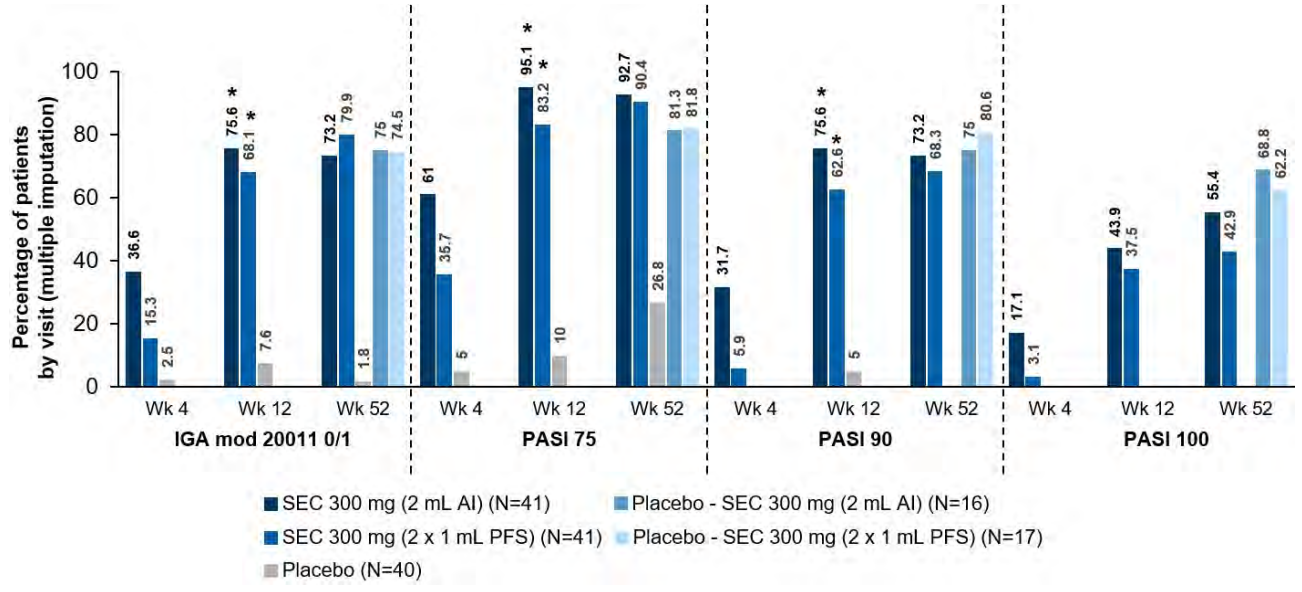

Figure 1. Clinical response rates over time for IGA mod 2011 0/1; PASI 75; PASI 90 and PASI 100. *P<0.0001 vs. placebo at Week 12. AI, autoinjector; IGA mod 2011, investigator's global assessment 2011 modified version; N, number of patients; PASI, Psoriasis Area and Severity Index; PFS, pre-filled syringe.

co-primary endpoints were Psoriasis Area and Severity Index (PASI) 75 and Investigator's Global Assessment (IGA) modified 2011 0/1 responses at Week 12. The key secondary endpoint was PASI 90 response at Week 12. Other secondary endpoints were PK assessments, PASI 75/90/100 responses, DLQI score of 0/1, usability of 2 mL AI (rated through a Self-Injection Assessment Questionnaire [SIAQ]), and safety over a period of 52 weeks.

Results: In total, 122 patients were randomised as follows: SEC 300 mg 2 mL AI (N=41), SEC 300 mg 2x 1 mL PFS (N=41), or PBO (N=40). The study met both co-primary and key secondary endpoints ($p< 0.0001$). At Week 12, SEC 300 mg 2 mL AI and 2x 1 mL PFS showed superior PASI 75 response rates (95.1% and 83.2%, respectively), and IGA mod 2011 0/1 response rates (75.6% and 68.1%, respectively), compared with PBO (10.0% for PASI 75; 7.6% for IGA mod 2011 0/1) (Fig. 1). At Week 12, the PASI 90 response was significantly higher with both SEC groups (2 mL AI [75.6%] and 2x 1 mL PFS [62.6%]) than with PBO (5.0%; $p< 0.0001$ for both) (Fig. 1). Both SEC treatment groups (2 mL AI and 2x 1 mL PFS) showed a similar trend of efficacy to Week 52 (Fig. 1). Similarly, higher DLQI 0/1 response rates were observed in both SEC groups (2 mL AI [71.1%] and 2x 1 mL PFS [72.5%] at Week 12) compared with PBO (8.1%); the trend of high DLQI 0/1 response was sustained up to Week 52 in both SEC groups. The higher mean SEC concentration observed with the 2 ml AI, may explain the slightly faster and numerically higher PASI 90 response. This difference did not affect the incidence of adverse events in either group. SIAQ results showed high usability of self-injection with the 2 mL AI device. In the secukinumab 300 mg (2 mL AI) group, the proportion of "very satisfied" and "satisfied" patients increased substantially from 31.6% before the injection (pre-SIAQ at baseline) to 78.3% (post-SIAQ at baseline) after the first injection and remained above 85% at later visits, reaching 100% at Week 28. Throughout the entire treatment period, only two patients (1.7%) reported one "injection-site reaction" each; both events were attributed to the AI administration (one of them with active drug, the other one with placebo). No new safety signals were observed with the use of the AI over the 52-week period.

Conclusion: SEC 300 mg administered with the 2 mL AI demonstrated superior efficacy over PBO, good tolerability, and convenience of administration in patients with moderate to severe plaque PsO.

Disclosure: B. Sigurgeirsson, Novartis, 2, 6, 12, Advisory board; **J. Browning**, Novartis, 12, Advisory board and investigator, Dermira, 6, 12, Advisory board and investigator, Dermavant, 12, Advisory board, Regeneron, 2, 6, 12, Advisory board and investigator, Leo Pharma, 2, Pfizer, 6, 12, investigator, Amryt, 12, investigator, AnaptysBio, 12, investigator, Arcutis, 12, investigator, Brickell, 12, investigator, Chemocentryx, 12, investigator, Eli Lilly, 12, investigator, Forte, 12, investigator, Galderma, 12, investigator, UCB, 12, investigator, Venthera, 12, investigator; **S. Tyring**, Novartis, 12, Investigator; **J. Szepietowski**, Leo Pharma, 6, 12, advisory board, Novartis, 6, 12, advisory board and investigator, Sanofi-Genzyme, 6, 12, advisory board, Trevi, 12, advisory board and investigator, Viofor, 12, advisory board, Sun Pharma, 6, BMS, 12, investigator, Helm, 12, investigator, Galapagos, 12, investigator, Galderma, 12, investigator, Incyte, 12, investigator, InfaRX, 12, investigator, Janssen-Cilag, 12, investigator, Pfizer, 12, investigator, Regeneron, 12, investigator, UCH, 12, investigator; **R. Rivera-Díaz**, AbbVie Laboratories, 6, 12, advisory board, investigator, travel grant, Janssen Pharmaceuticals Inc, 6, 12, advisory board, investigator, travel grant, Lilly, 12, advisory board, investigator, MSD, 6, 12, travel grant, Leo Pharma, 6, 12, investigator, travel grant, Novartis, 6, 12, investigator, travel grant, Pfizer, 6, 12, advisory board, investigator, travel grant, Celgene, 12, investigator, travel grant; **I. Effendy**, Novartis, 12, Investigator, AbbVie, 12, Investigator, Janssen, 12, Investigator, Leo Pharma, 12, Investigator, Lily, 12, Investigator, Pfizer, 12, Investigator; **D. Keefe**, Novartis Pharmaceuticals Corporation, New Jersey, USA, 3; **G. Bruin**, Novartis Institutes for Biomedical Research, Basel, Switzerland, 3; **B. Paguet**, Novartis Pharma AG, Basel, Switzerland, 3; **R. Fu**, Novartis Institutes of for Biomedical Research, Shanghai, China, 3; **I. Hampele**, Novartis Pharma AG, Basel, Switzerland, 3; **M. Reinhardt**, Novartis Pharma AG, Basel, Switzerland, 3.

Abstract Number: 0227

Work Participation Is Impaired Months Before Clinical Arthritis Is Apparent

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Work participation is still a major issue for patients with rheumatoid arthritis (RA) despite improved management and outcomes. Work loss can be divided into presenteeism (i.e. impaired productivity while at work) and absenteeism (i.e. absence due to illness). Both constitute limitations for the patient as well as an economic burden for society. It is known that in the phase preceding clinical arthritis patients already experience pain and functional limitations. We therefore aimed to investigate how work participation is affected in patients with arthralgia in the 'pre-RA phase' during transition to RA or symptom resolution, and to compare this to the course of the work participation in early RA-patients.

Methods: Three groups of patients were studied; 143 arthralgia-patients converting to clinical arthritis within two years (the Leiden CSA cohort, the SONAR cohort), 617 early RA-patients during 4 years of follow-up (the Leiden EAC) and 57 arthralgia-patients not converting to clinical arthritis with spontaneous resolution of symptoms (Leiden CSA cohort). WPAI and IPCQ were used to measure work-related outcomes. Both presenteeism (impaired productivity at work; scale 0-10 where 0=complete impairment and 10=no impairment) and absenteeism (sick leave and decrease in working hours) were taken into account. Linear Mixed Models and Mixed effect logistic regression models were used to investigate whether the work-related outcomes changed over time. Outcomes were also stratified for ACPA status.

Results: A total of n=103 (72%), n=291 (47%) and n=50 (88%) had paid work at baseline (i.e. the working population). One year prior to the development of clinical arthritis, productivity decreased with 36% (95% CI 24% to 48%), following a downward trend towards the level of RA-patients at diagnosis which was decreased with 50% (95% CI 47% to 53%). Sick leave was reported by 28% (95% CI 20% to 36%) one year prior to the development of clinical arthritis and followed an upward trend towards the level of RA-patients at diagnosis (36% 95% CI 30% to 41%) (Figure1). After treatment start in RA, productivity improved ($p< 0.0001$), and sick leave decreased significantly ($p< 0.0001$. Despite an improvement in productivity and sick leave, working hours significantly decreased over time after being diagnosed with RA($p< 0.0001$). Within the arthralgia-patients with spontaneous symptom relief (n=50), a significant improvement in productivity was observed over time ($p=0.0016$). Stratifying for ACPA showed no difference in work-related outcomes.

Conclusion: Before clinical arthritis is apparent, the productivity level of arthralgia-patients is decreased towards a similarly reduced productivity level in early RA-patients. This underlines the importance of recognizing patients in the pre-arthritis phase, as intervention in this phase could potentially prevent loss in work participation.

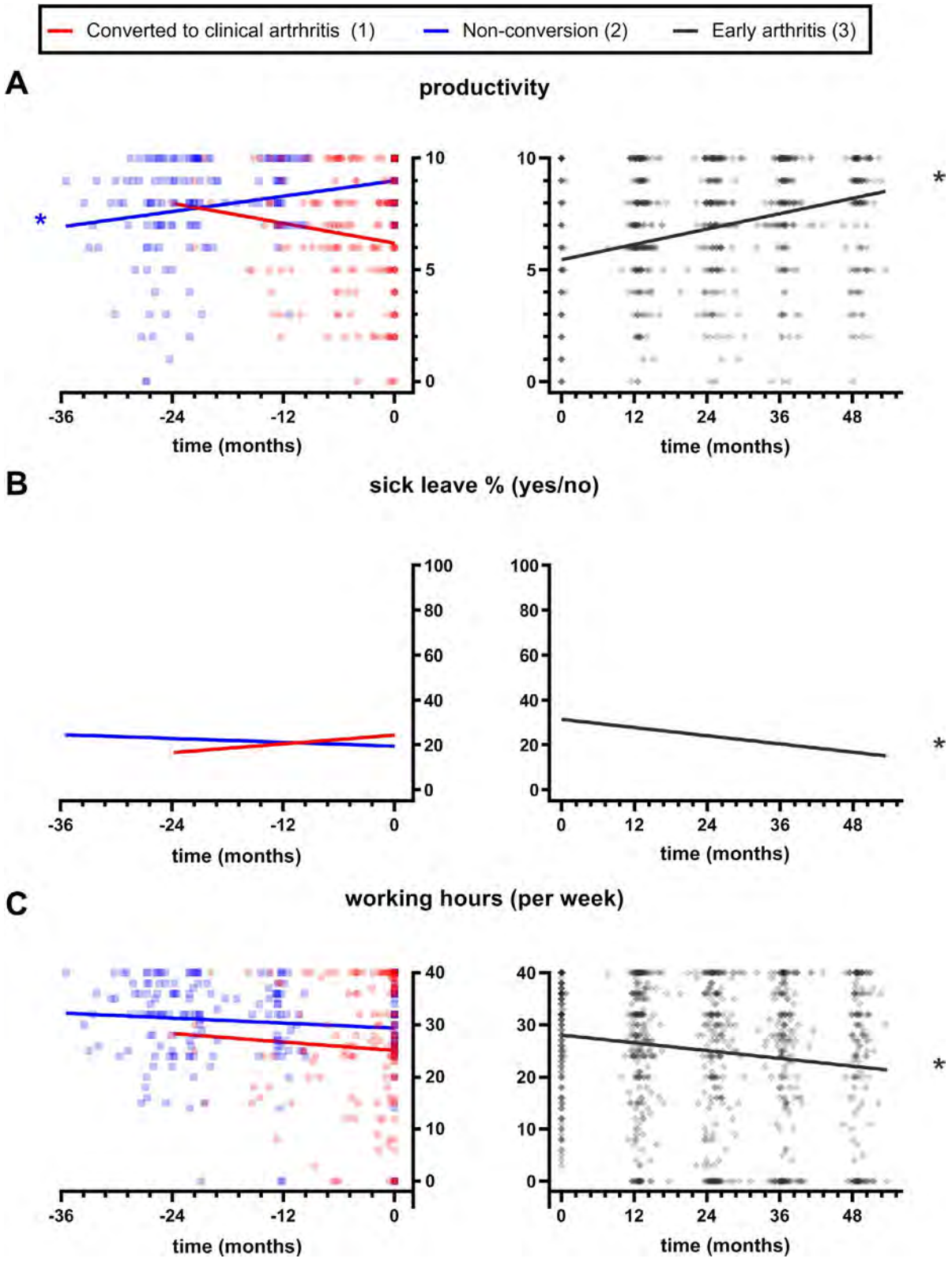

Figure 1. The course of presenteeism and absenteeism over time in; (1) arthralgia-patients converting to clinical arthritis (2) non-converting arthralgia-patients with spontaneous symptom relief and (3) RA-patients. Legend: (1) arthralgia-patients converting to clinical arthritis; 0 at x-axis marks the moment arthritis is diagnosed (2) non-converting arthralgia-patients with spontaneous symptom relief; 0 at x-axis marks the moment patients were symptom free (3) RA-patients; 0 at x-axis marks the moment of diagnosis. Productivity where 0=minimal workplace productivity, 10=maximal workplace productivity. *marks a significant change over time.

Disclosure: C. Rogier, None; **P. de Jong**, None; **A. van der Helm-van Mil**, None; **E. van Mulligen**, None.

Abstract Number: 0228

Optimizing Social Media as a Recruitment Tool for Hard-to-Reach Populations in Rheumatology Clinical Research

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Standard methods of recruitment for clinical research, such as traditional media advertisements, can be inefficient and expensive, especially for underserved communities and asymptomatic individuals. To address this need, we explored the use of online recruitment tools that might improve access to these populations. We evaluated the effectiveness of two online approaches to recruit subjects for an observational study of asymptomatic individuals at risk for developing rheumatoid arthritis (RA): 1) Web-based methods; and 2) Facebook-based advertisements. This strategy focused on asymptomatic first-degree relatives of individuals with RA who self-identify for an observational longitudinal study on transitions to clinical RA.

Methods: A county-wide web-based recruitment campaign was conducted from October through December 2020 consisting of image and text-based ads displayed on various websites and mobile applications. The goal was to identify individuals to participate in screening visit for a study evaluating the evolution of RA with the inclusion of individuals who were CCP3 >2x ULN and no inflammatory arthritis. Ads were targeted to potential subjects using a combination of geofencing (eg, visits to medical centers or rheumatologists), keyword retargeting (eg, “rheumatoid arthritis”), and website remarketing techniques. A Facebook-based recruitment campaign was then conducted from February through April 2021. Facebook users were targeted based on demographics, group membership, and user association. An individual that clicked on an ad was directed to a website containing information about the study, where they could fill out a contact form to provide their information to study staff. Both advertising campaigns were administered by a third-party vendor.

Results: A total of 413,289 ads were displayed during the web campaign and 392,408 ads were displayed during the Facebook campaign. Throughout the duration of the web campaign, there were 428 individual clicks on an ad (0.10% of ads). Only one person contacted the study staff and was screened but did not enroll. Throughout the duration of the Facebook campaign, there were 3649 individual clicks on an ad (0.93% of ads) and 43 people contacted the study staff for screening ($p< 0.0001$ for web-based vs Facebook for clicks). 34 individuals were successfully screened and two were enrolled, with mean age of 52.3±11.3 yrs. In terms of characteristics, 94% of screened individuals were female and 24% were Hispanic. The cost per click for the web campaign was $2.80 and for the Facebook campaign it was $0.71, which corresponded to a cost per self-identifying subject of $1600 for the Web campaign and $60 for the Facebook campaign.

Conclusion: The Facebook recruitment campaign resulted in more screened subjects and was more cost-effective than the web recruitment campaign. A preponderance of women responded to the campaign, and there was excellent representation among the Hispanic population. Facebook ad targeting improved access to individuals who were

closely linked to rheumatoid arthritis patients in their social network and more likely to respond to the ad. The data suggest that social media campaigns can improve outreach to hard-to-reach populations.

Disclosure: V. Tsaltskan, None; **K. Nguyen**, None; **C. Eaglin**, None; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6; **V. Holers**, Jansson, 5; **G. Firestein**, Eli Lilly, 5.

Abstract Number: 0229

The Effects of Self-efficacy on Fatigue and Pain Interference in Black Women with Systemic Lupus Erythematosus: The Role of Depression, Age, and Education

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue and pain are pervasive symptoms that cause escalating distress in patients with SLE, particularly among Black women and other high-risk groups. While these are reportedly amongst the most challenging symptoms to self-manage by SLE patients, self-efficacy can mitigate their negative impact on daily activities. However, older and depressed patients and those with low education may have low self-efficacy. We examined whether self-efficacy affects fatigue and pain interference in Black women with SLE, and whether depression, age, and education alter those relationships.

Methods: Transversal analysis of Black women with a validated diagnosis of SLE, who were enrolled in a population-based cohort called the Georgians Organized Against Lupus (GOAL). PROMIS short forms were used to measure Fatigue, Pain interference, Self-efficacy to manage symptoms (SEMS), Self-efficacy to manage medications and treatment (SEMMT), and Depression. Linear regression analyses were performed to examine the relationship between each outcome (Fatigue and Pain interference) and self-efficacy (SEMS and SEMMT) and the interactions of age, education, and depression with self-efficacy, after adjusting for confounders.

Results: Of 699 participants, 143 (21%) were 18-34, 329 (47%) 35-54, and 227 (33%) ≥55 years old; 261 (37%) attained ≤high school, 226 (32%) some college, and 211 (30 %) ≥bachelor's degree. Table 1 shows an inverse association between Fatigue and SEMS, Fatigue and SEMMT, Pain interference and SEMS, Pain interference and

Table 1: Univariate Linear Regression of Fatigue and Pain interference on Self-efficacy Measures

Factor	Fatigue			Pain interference		
	Slope* (±SE)	P value	MSE	Slope* (±SE)	P value	MSE
SEMS (per 1 point ↑)	-0.556 ± 0.044	<0.001	97.4	-0.394 ± 0.042	<0.001	87.4
SEMMT (per 1 point ↑)	-0.282 ± 0.044	<0.001	113.4	-0.152 ± 0.041	<0.001	96.7

Abbreviations: SE=standard error; MSE=mean squared error; SEMS=self-efficacy to manage symptoms; SEMMT= self-efficacy to manage medications and treatment; *Indicates b regression coefficient.

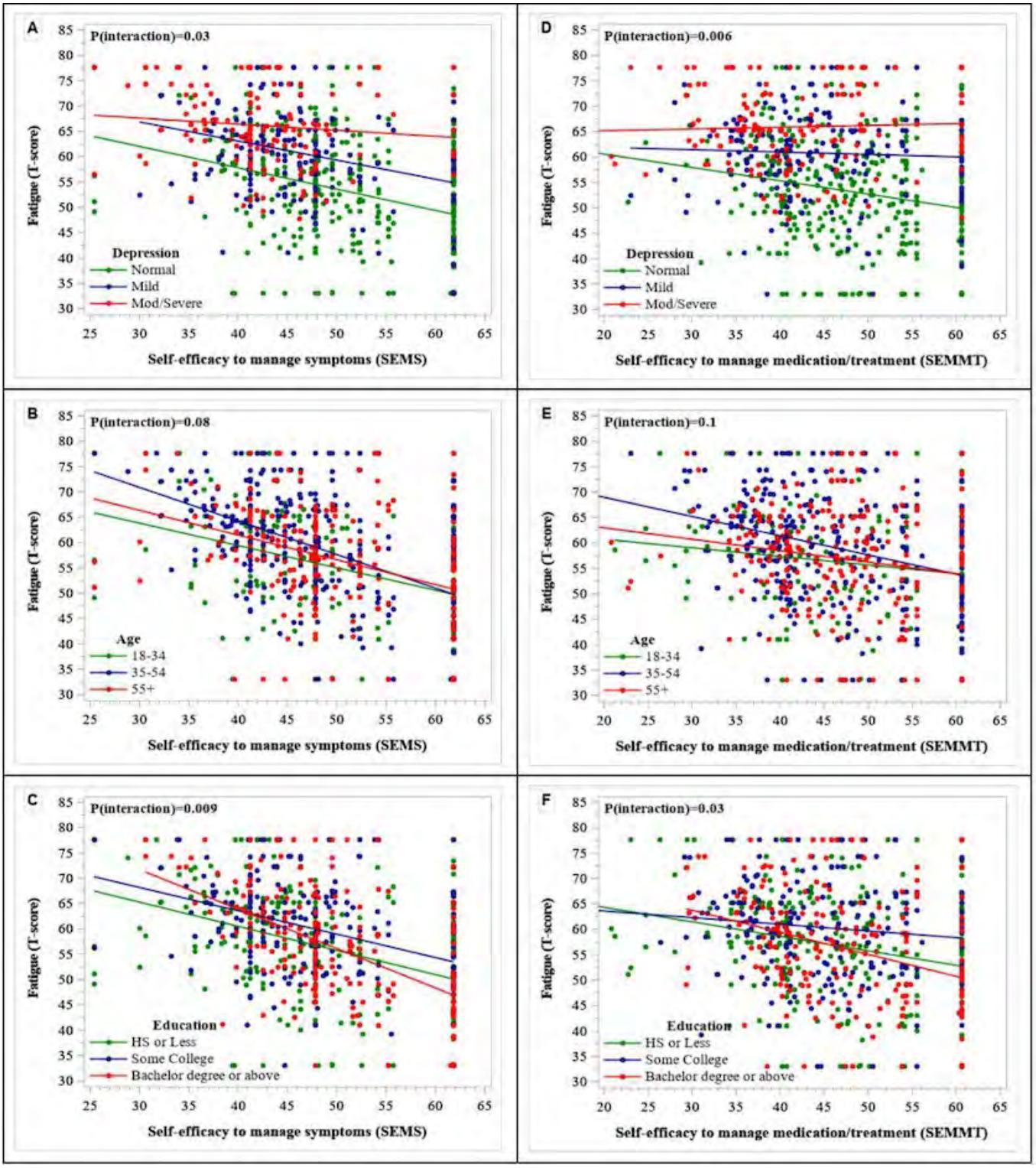

Figure 1. Regression of Fatigue on Self-efficacy to manage symptoms (SEMS) and Self-efficacy to manage medications and treatments (SEMMT) by Depression, Age, and Educational Attainment Categories.

SEMMT. Figure 1 depicts significant interactions between SEMS*Depression (p=0.03), SEMMT*Depression (p=0.006), SEMS*Education (p=0.03) and SEMMT*Education (p=0.009) on Fatigue. Figure 2 shows significant interactions between SEMMT*Depression (p=0.03), SEMS*Age (p=0.03), and SEMS*Education (p=0.0009) on Pain Interference. After adjusting for confounders, SEMS*Depression (p=0.04) and SEMMT*Depression (p=0.009) remained signifi-

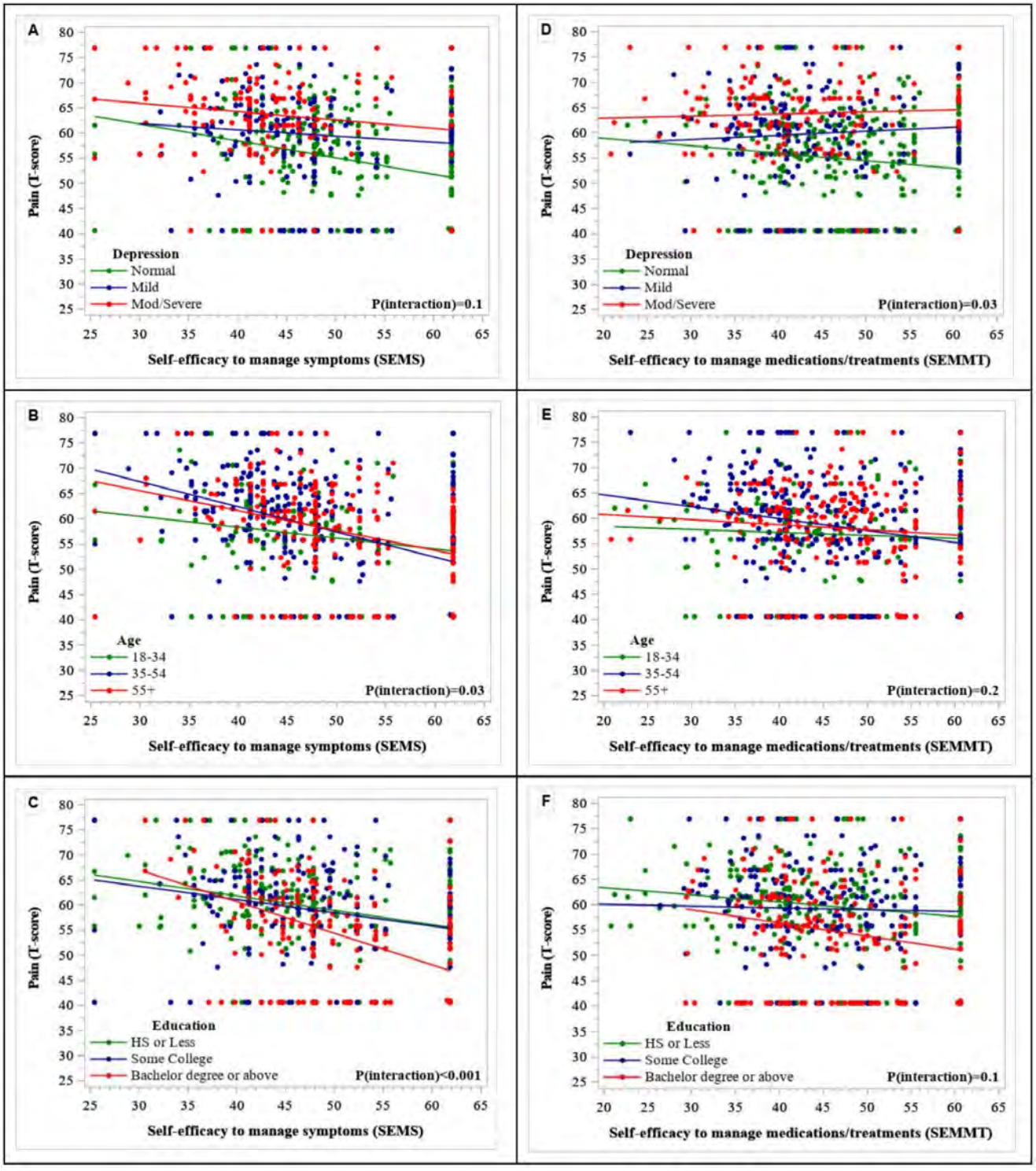

Figure 2. Regression of Pain interference on Self-efficacy to manage symptoms (SEMS) and Self-efficacy to manage medications and treatments (SEMMT) by Depression, Age, and Educational Attainment Categories.

cantly associated with Fatigue, and SEMS*Depression with Pain Interference (p=0.05), with greater adjusted means of each outcome in those with higher depression. SEMS*Education remained significantly associated with Fatigue (p=0.05) and with Pain interference (p=0.04), with lower adjusted means in those with higher education. SEMS*Age was associated with Pain interference (p=0.02), with higher adjusted means of each outcome in older women.

Conclusion: Self-efficacy (to manage symptoms and to manage medications and treatment) were inversely related to both fatigue and pain interference. Depression, age, and education altered those relationships in different ways. These finding may help predict who might benefit most from to efficacy-enhancing interventions.

Disclosure: C. Drenkard, GSK, 1, 5; **K. Easley**, None; **G. Bao**, None; **C. Dunlop-Thomas**, None; **T. Brady**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2.

Abstract Number: 0230

Fatigue and Inflammation in Rheumatoid Arthritis Are Already Disconnected Before Clinical Arthritis Develops

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue is disabling and common in Rheumatoid Arthritis (RA); the causation of fatigue in RA is multidimensional and only partially explained by inflammation. The question arises how fatigue develops in the preclinical phases of RA, and how inflammation is related to fatigue in the pre-arthritis phase. We hypothesized that inflammation explains fatigue to a greater extent at the beginning of developing RA, when processes are not yet chronified. Our aims are therefore (1) to describe the course of fatigue in patients with clinically suspect arthralgia (CSA) towards progression to RA, and (2) to assess the correlation between fatigue and inflammation in CSA patients and compare this to RA at the time of diagnosis.

Methods: 595 CSA patients were included between April 2012 and May 2020 in the Leiden CSA cohort and were followed for the development of RA. Additionally, baseline data of 710 consecutive early RA patients who were included in the Leiden Early Arthritis Cohort between August 2010 and March 2020, were studied. Inflammation was defined by MRI detected inflammation on contrast-enhanced 1.5T-MRI of hand and forefoot (scored according to the RAMRIS-method) and by C reactive protein (CRP) levels, representing local and systemic inflammation, respectively. Fatigue severity was measured on a numerical rating scale (NRS) from 0 (no fatigue) to 10 (extreme fatigue). A linear mixed model was used to analyze whether fatigue increased over time towards the development of RA. Correlations between fatigue and inflammation were studied using Spearman's rank correlation coefficient.

Results: At first presentation, baseline fatigue (mean (SD)) was 4.5 (3) for patients who developed RA. Over time, fatigue severity increased gradually towards 4.7 ± 3.0 at the time of RA development; (β= -0.08 per month away from arthritis development, p=0.07, Figure 1). Assessing the correlation of fatigue with inflammation at CSA onset in patients who later on developed RA, revealed weak correlations with MRI-detected inflammation (*ρ=-0.147,* p=0.25) and with CRP-levels (*ρ=0.165,* p=0.17). For comparison at RA diagnosis, correlations between fatigue severity and

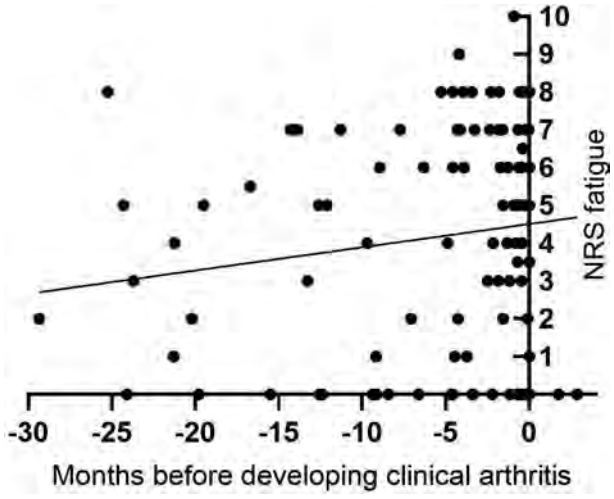

Figure 1. Fatigue in the months preceding development of Rheumatoid Arthritis.

inflammation were *ρ=-0.074*, p=0.09 for MRI-detected inflammation and ρ=*0.023*, p=0.34 for CRP-levels. Hence, although the correlation coefficients were slightly higher at CSA onset than at RA development, the correlations of fatigue with inflammation were weak at both disease phases.

Conclusion: Fatigue increased gradually during progression from arthralgia to RA. The correlation between fatigue with inflammatory measures in pre-RA patients were slightly higher than in early RA patients, but were still weak. This suggests that fatigue symptoms are largely disentangled from inflammation, even in the pre-arthritis phase of RA.

Disclosure: S. Khidir, None; **A. van der Helm-van Mil**, None; **E. van Mulligen**, None.

Abstract Number: 0231

Reducing the Number of Outpatient Clinic Visits by Using the Routine Assessment of Patient Index Data 3 as a Screening Tool

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The long-term and frequent evaluation of disease activity in patients with rheumatoid arthritis (RA) leads to a large burden of planned consultations at outpatient clinics. It might be possible to reduce that burden by prescreening for patients in remission or low disease activity with the electronic Routine Assessment of Patient Index Data 3 (RAPID3). For this purpose, accurate classification of patients in the low or remission category with the RAPID3 is a necessity. The objective is to evaluate the test characteristics and agreement in the low disease activity categories between the Disease Activity Score 28 (DAS28) and the RAPID3 in patients with RA.

Total measurements	4921
Total patients	1630
Female (%)	1234 (76)
Age, mean (SD)	60 (5)
Disease duration, median (IQR)	4,0 (0-7)
Type of RA (%)	
Seropositive	320 (19,6)
Seronegative	132 (8,1)
Unspecified	1178 (72,3)
DAS28, median (IQR)	2,62 (1,78-3,61)
DAS28 per category. (%)	
Remission	2429 (49,4)
Low	819 (16,6)
Medium	1336 (27,1)
High	337 (6,8)
RAPID3, median (IQR)	3,8 (1,8-5,6)
RAPID per category (%)	
Remission	719 (14,6)
Low	669 (13,6)
Medium	1261 (25,6)
High	2272 (46,2)
CRP, median (IQR)	2,5 (0,9-8,0)
BSE, median (IQR)	9 (5,0-24,0)

Table 1: baseline characteristics

Baseline characteristics.

		DAS28		Total
		Low (<3.2)	High (≥3.2)	
RAPID3	Low (≤2.0)	1275 (92,4%)	105 (7,6%)	1380 (28,0%)
	High (>2.0)	1973 (55,7%)	1568 (44,3%)	3533 (72,0%)
Total		3248 (66,0%)	1673 (34,0%)	4921 (100%)
Percentage agreement: 57,8%. Kappa: 0,26				

Table 3: agreement and Cohen's kappa between DAS28 and RAPID3

Agreement and Cohen's kappa between DAS28 and RAPID3.

Methods: We performed a retrospective database study with available clinical data collected as part of usual care from the electronic medical record at Reade Amsterdam. The dataset comprised each completed RAPID3 between June 2014 and March 2021, followed by a DAS28 within 2 weeks in patients with RA. The disease activity categories for both the RAPID3 and DAS28 were dichotomized in low (remission and low disease activity) and high (moderate and high disease activity). Cutoff values were 2.0 for RAPID3 and 3.2 for DAS28. Test characteristics and agreement (Cohen's kappa) were calculated.

Results: A total of 4921 combined RAPID3 and DAS28 measurements were done at Reade in 1630 unique RA patients. The mean age was 60 years and 76% were female with a median disease duration of 4 years. The agreement was considered fair (k=0,260). In total, 1630 (28%) of the RAPID3 measurements were classified as low. The sensitivity to detect low disease activity was 0.39, specificity was 0.94 and the positive predicted value was 0.92.

Conclusion: We showed that when the RAPID3 classifies a patient into the remission or low disease activity state, it is for 92% accurate. Of all consultations, 28% could possibly be postponed following screening with RAPID3. We propose a system where the RAPID3 is one of a few conditions that need to be met before consultations are postponed. Other conditions could include patient-, and physician approval and within-range lab results. Future research needs to focus on the feasibility of this system and finding the proper conditions for it to safely and effectively reduce the number of consultations.

Disclosure: J. Wiegel, None; **B. Seppen**, None; **M. ter wee**, None; **M. Boers**, BMS, 2, Pfizer, 2, GSK, 2, Novartis, 2; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5; **w. Bos**, Abbvie, 5, Pfizer, 5, Novartis, 5.

Abstract Number: 0232

The Impact of Deucravacitinib on Health-Related Quality of Life Measured by the Short Form Health Survey 36-Item Questionnaire: Analysis of a Phase 2 Trial in Patients with Active PsA

Vibeke Strand[1], Philip Mease[2], Atul Deodhar[3], June Ye[4], Miroslawa Nowak[4], Jiyoon Choi[4] and Brandon Becker[4], [1]Stanford University School of Medicine, Portola Valley, CA, [2]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [3]Oregon Health & Science University, Portland, OR, [4]Bristol Myers Squibb, Princeton, NJ

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients (pts) with PsA experience pain, loss of physical function, joint damage, and significant impairments in social and emotional well-being. The Short Form Health Survey 36-item questionnaire (SF-36v2), a generic measure of pt-reported health-related quality of life (HRQOL), includes 36 items and measures 8 domains—physical functioning (PF), role-physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-emotional (RE), and mental health (MH)—that contribute to both physical component summary (PCS) and mental component summary (MCS) scores. Deucravacitinib is a novel, oral selective inhibitor of tyrosine kinase 2 (TYK2), an intracellular kinase that mediates cytokine signaling pathways implicated in the pathogenesis of PsA. In a Phase 2 trial in pts with active PsA, the primary endpoint, ACR 20 response at Week (Wk) 16, was met and deucravacitinib was well tolerated versus placebo (PBO).[1] This analysis further evaluated the effect of deucravacitinib treatment on SF-36 scores.

Methods: This 1-year, randomized, double-blind, placebo-controlled, multicenter Phase 2 trial (NCT03881059) enrolled pts with a PsA diagnosis ≥6 months who fulfilled Classification Criteria for Psoriatic Arthritis at screening and had active joint disease (≥3 tender and ≥3 swollen joints), high-sensitivity CRP ≥3 mg/L, and ≥1 plaque psoriasis lesion (≥2 cm). Pts failed or were intolerant to ≥1 NSAID, conventional synthetic DMARD, and/or 1 TNF inhibitor (TNFi; ≤30%). Pts were randomized 1:1:1 to receive deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. Changes from baseline (BL) in SF-36 PCS and MCS scores at Wk 16 were prespecified key secondary and additional endpoints, respectively. Analyses evaluated the 8 SF-36 domain scores at Wk 16. The proportion of patients who reported improvements ≥2.5 and ≥5-points (the minimum clinically important difference [MCID]) in SF-36 summary and domain scores, respectively, were evaluated.

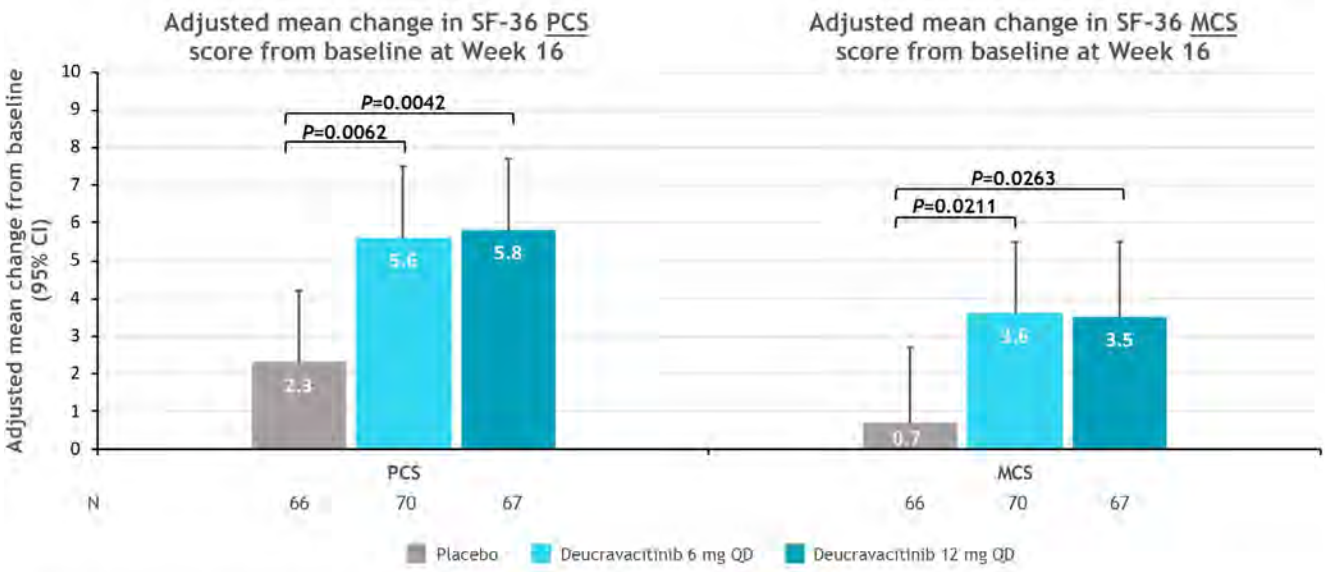
Table. Demographic and Baseline Disease Characteristics

	Placebo n=66	Deucravacitinib 6 mg QD n=70	Deucravacitinib 12 mg QD n=67
Age, years, mean	48.5	50.5	50.5
Gender, female, n (%)	40 (60.6)	30 (42.9)	34 (50.7)
Baseline BMI, kg/m^2, mean	31.2	29.6	30.3
Disease duration since diagnosis, years, median (range)	4.5 (0.6-22.9)	5.3 (0.1-42.8)	3.8 (0.6-27.7)
Tender joint count, mean (SD)	16.9 (9.79)	18.1 (10.33)	19.4 (11.84)
Swollen joint count, mean (SD)	10.5 (7.74)	11.9 (6.99)	11.3 (8.96)
HAQ-DI, mean (SD)	1.3 (0.56)	1.3 (0.59)	1.3 (0.59)
Patients with SPARCC enthesitis score ≥1 at baseline, n (%)	34 (51.5)	43 (61.4)	34 (50.7)
Psoriasis body surface area ≥3% at baseline, n (%)	54 (81.8)	59 (84.3)	52 (77.6)
PASI score at baseline in subjects with ≥3% BSA at baseline, mean (range)	9.09 (1.2-31.4)	8.47 (1.6-33.8)	7.92 (1.4-31.8)
SF-36 PCS score, mean (SD)	33.4 (7.5)	34.0 (8.0)	34.5 (7.0)
SF-36 MCS score, mean (SD)	47.5 (10.9)	45.4 (10.3)	46.9 (10.7)
Oral steroid use at baseline, n (%)	12 (18.2)	7 (10.0)	6 (9.0)
Mean daily dose, mg	4.40	3.71	3.54
Use of csDMARDs at baseline, n (%)	44 (66.7)	45 (64.3)	43 (64.2)
Use of MTX at baseline, n (%)	39 (59.1)	35 (50.0)	37 (55.2)
Mean weekly dose, mg	16.7	16.4	16.5
Prior TNF-inhibitor use, n (%)	11 (16.7)	12 (17.1)	9 (13.4)

BMI, body mass index; BSA, body surface area; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, mental component summary; MTX, methotrexate; PASI, Psoriasis Area and Severity Index; PCS, physical component summary; QD, once daily; SF-36, Short Form Health Survey 36-item questionnaire; SPARCC, Spondyloarthritis Research Consortium of Canada; TNF, tumor necrosis factor.

Results: Of 203 pts randomized, 180 (89%) completed 16 wks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and BL disease characteristics were similar across groups. Mean age was 49.8 years and median PsA duration since diagnosis was 4.5 years. BL mean SF-36 PCS and MCS scores were similar among deucravacitinib 6 mg QD, 12 mg QD, and PBO groups (PCS: 34.0,

Figure 1. Adjusted mean change from baseline in SF-36 scores at Week 16[1]



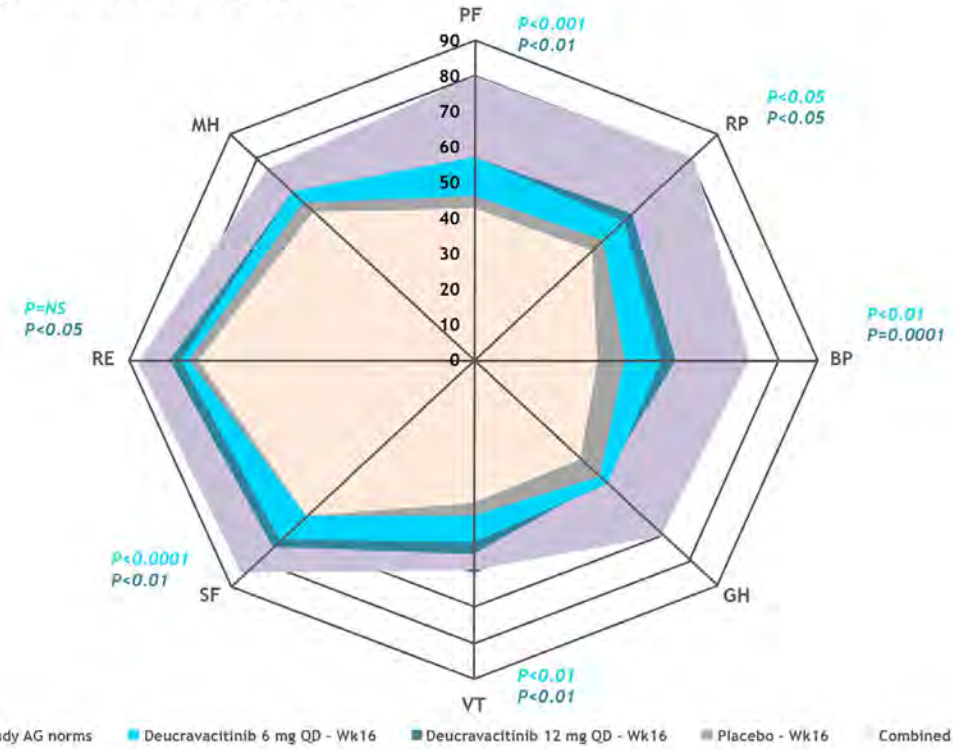
Nominal *P*-values for pairwise comparison vs placebo.
CI, confidence interval; MCS, mental component summary; PCS, physical component summary; QD, once daily; SF-36, Short Form-36.
1. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

34,5, and 33.4; MCS: 45.4, 46.9, and 47.5, respectively; **Table**). At Wk 16, adjusted mean changes from BL in SF-36 PCS and MCS scores were significantly improved ($P< 0.05$) with deucravacitinib 6 and 12 mg QD treatment vs PBO (**Figure 1**). Reported improvements in domain scores with both doses exceeded MCID and were significant in 5 of 8 domains with deucravacitinib 6 mg QD (PF, RP, BP, VT, and SF) and 6 of 8 domains with deucravacitinib 12 mg QD (RE in addition; **Figure 2**).

Conclusion: Pts with PsA receiving deucravacitinib treatment reported clinically meaningful and significant improvements in HRQOL, including fatigue and social functioning in addition to physical functioning and pain, at Wk 16.

Reference: 1. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

Figure 2. Improvements reported in SF-36 domains with deucravacitinib 6 mg QD and 12 mg QD vs PBO at Week 16



	PF	RP	BP	GH	VT	SF	RE	MH
Deucravacitinib 6 mg QD - BL	41.90	42.90	32.50	39.60	39.00	57.00	69.50	58.40
Deucravacitinib 12 mg QD - BL	44.10	46.00	33.40	38.50	43.00	65.50	71.50	59.20
Placebo - BL	42.40	42.80	31.70	40.30	38.80	63.80	75.10	59.90
Deucravacitinib 6 mg QD - Wk16	57.10	55.30	48.90	49.20	51.30	71.40	76.50	66.70
Deucravacitinib 12 mg QD - Wk16	57.50	58.60	53.10	47.50	54.50	73.90	79.50	67.30
Placebo - Wk16	46.30	48.20	39.70	46.40	43.80	62.30	74.40	63.30
Protocol A/G norms	80.32	81.32	71.94	69.76	59.03	84.84	87.74	76.10

Subscale scores for each domain range from 0-100, with higher scores indicating better health status.
BL, baseline; BP, bodily pain; GH, general health; MH, mental health; PBO, placebo; PT, physical functioning; QD, once daily; RE, role-emotional, RP, role-physical; SF, social functioning; SF-36, Short Form-36, VT, vitality; Wk, week.

Disclosure: V. Strand, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **J. Ye**, Bristol Myers Squibb, 3, 11; **M. Nowak**, Bristol Myers Squibb, 3, 11; **J. Choi**, Bristol Myers Squibb, 3, 11; **B. Becker**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0233

Feasibility and Acceptability of an Online Intervention for Lupus Self-Management Based on the Transtheoretical Model of Change

Katherine Carpenter[1], **Melissa French**[1], Sara Balestrieri[2], Sara Johnson[2], Sarah Gilman[3], Cristina Drenkard[4], S Sam Lim[5], Maria Dall'Era[6], Emily Somers[7], Suzanna Zick[8], Victoria Werth[9], Daniel Wallace[10], Melicent Miller[1] and Mary Crimmings[1], [1]Lupus Foundation of America, Washington, DC, [2]Pro-Change Behavior Systems, South Kingstown, RI, [3]Wayfinder Health Strategies, Falls Church, VA, [4]Emory University, Atlanta, GA, [5]Department of Medicine, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, [6]University of California San Francisco, Corte Madera, CA, [7]University of Michigan, Ann Arbor, MI, [8]Department of Family Medicine and Nutritional Sciences, Ann Arbor, MI, [9]Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania and Philadelphia VAMC, Philadelphia, PA, [10]Cedars-Sinai, Los Angeles, CA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The Lupus Foundation of America (LFA) has completed a 5-year cooperative agreement with the CDC to develop and evaluate an online lupus self-management (SM) program based on the Transtheoretical Model of Change. The program, *Strategies to Embrace Living with Lupus Fearlessly* (SELF), is designed to help users adopt 4 key lupus SM behaviors shown to have the highest impact on health and functional status: 1) managing symptoms, 2) managing stress, 3) managing medications, and 4) working with your healthcare team. The pilot was conducted using mixed methods to assess the feasibility and acceptability of SELF.

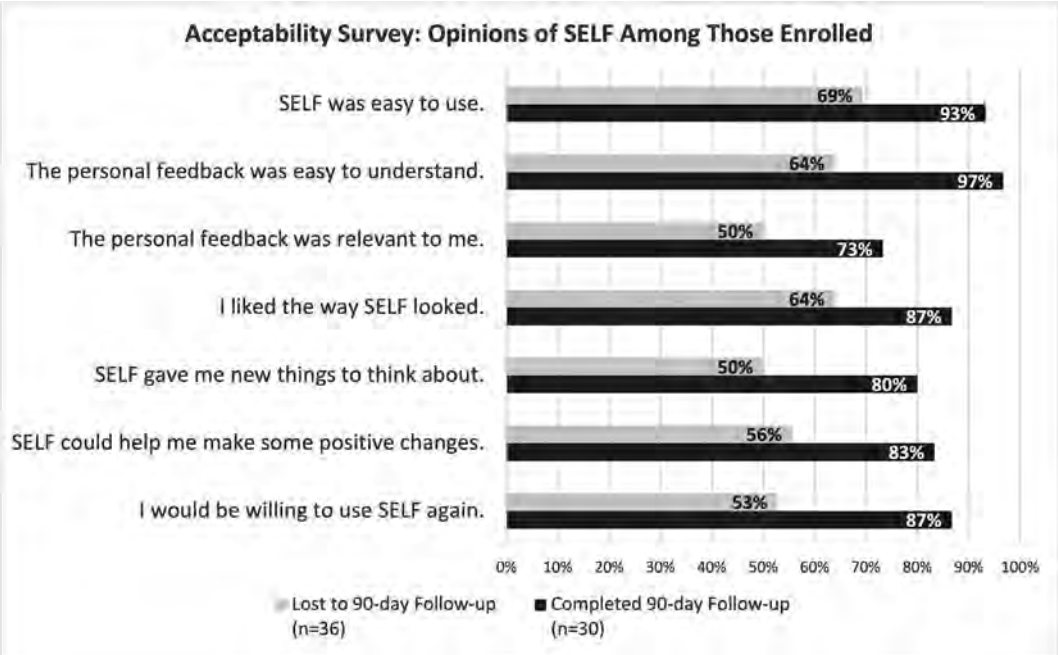


Figure 1. Acceptability surveys were sent to both users who completed 90-day follow-up in SELF and users who disengaged/ were lost to 90-day follow-up in SELF. Most users provided favorable opinions of SELF. Users who completed 90-day follow-up held more favorable opinions than users who were lost to 90-day follow-up.

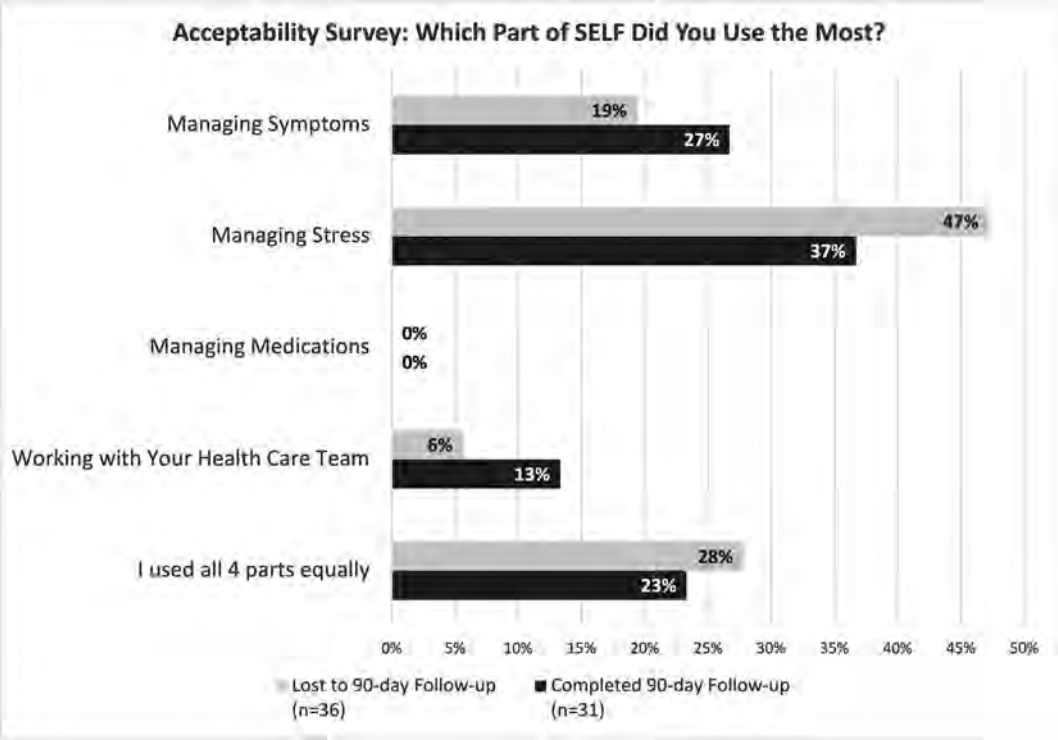


Figure 2. Acceptability surveys were sent to both users who completed 90-day follow-up in SELF and users who disengaged/ were lost to 90-day follow-up in SELF. Managing symptoms and managing stress were the most popular modules.

Methods: SELF consists of an intake assessment, user-tailored SM behavior change guidance/education, and a follow-up assessment every 90 days. At intake, users report their readiness to engage in the 4 SM behaviors consisting of 3-5 skills each. Users select one SM behavior as a focus for a 2-week period and begin the program via a customized web portal. In addition to tailored digital coaching, SELF offers: symptom and medication trackers; a journal; tailored text/email tips; and links to the LFA National Resource Center on Lupus, Health Educators, and LupusConnect™, an online community for peer-to-peer support.

Participants with a lupus diagnosis were recruited from three academic medical centers and the LFA constituency to take part in the 90-day pilot. Program evaluation included intake and follow-up assessments, a follow-up email survey and in-depth interviews. At intake, users were evaluated for their stage of change for each SM skill. They were defined as having a 'skill gap' when staged at one of the building stages. They 'mastered a skill' if they improved from a building stage of change at baseline to a mastery stage at follow-up. Feasibility and acceptability were assessed using enrollment/retention, utilization, readiness for and improvement to SM behaviors, and user feedback.

Results: Of those who registered, 62% (n=150 of 241) completed the intake assessment and 28% (n=42) remained engaged through the 90-day follow-up. Self-reported barriers to engagement included the impact of the COVID-19 pandemic, busy lives, length of intake, and belief that SELF's target audience was newly diagnosed people with lupus (PWL).

Users showed substantial need; 80% had moderate/ high skill gaps in key SM skills. Users who completed the program were successful in building new skills; 57% mastered 1 or more SM skills. Most users provided favorable opinions of SELF (Figure 1) with managing stress and managing symptoms being the most popular modules (Figure 2).

Conclusion: Although the COVID-19 pandemic and other factors impacted participants' time and ability to engage with SELF, this pilot provided valuable insights for optimizing SELF to improve enrollment and retention (e.g., adding

social login and text/email reminders, reducing length of intake). SELF is designed to provide a cohesive, tailored experience to help PWL manage their condition. The pilot showed promising results in meeting user needs and building skills to impact behavior change.

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Abstract Number: 0234

Impact of Early Pain Improvement on Patient-reported Outcomes in Patients with Psoriatic Arthritis: Results from a Phase 3 Trial

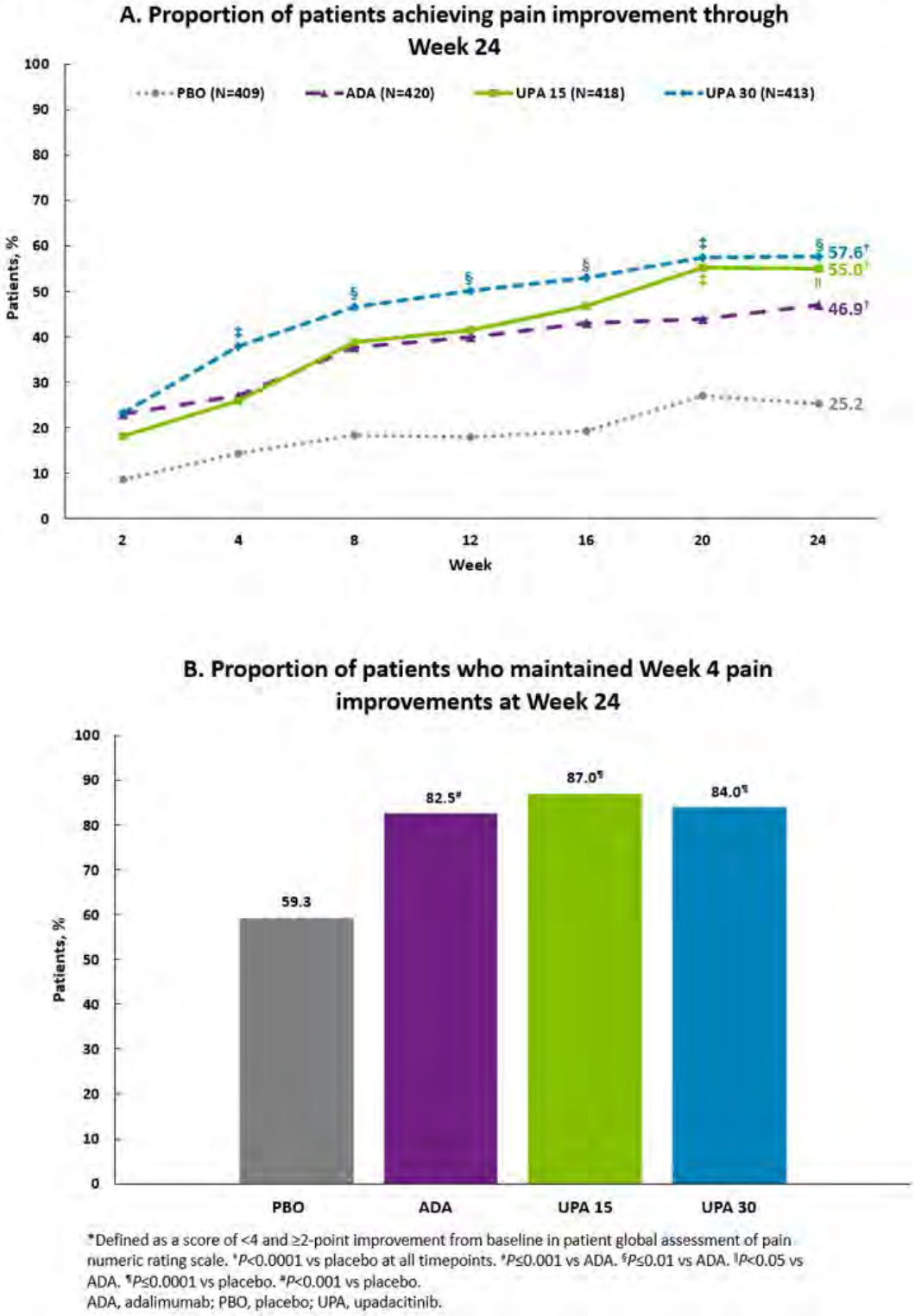
Louis Bessette[1], Beatriz Joven-Ibáñez[2], Carlo Selmi[3], Naijun Chen[4], Koji Kato[5], Ralph Lippe[6], Patrick Zueger[7], Jayeshkumar Patel[4] and Joseph Merola[8], [1]Centre de l'Ostoporose et de Rhumatologie de Qubec, Québec City, QC, Canada, [2]University Hospital 12 de Octubre, Madrid, Spain, [3]Humanitas Research Hospital and Humanitas University, Milan, Italy, [4]AbbVie Inc., North Chicago, IL, [5]AbbVie Inc, Shinagawa- Ku, Japan, [6]AbbVie Deutschland GmbH & Co. KG, Berlin, Germany, [7]AbbVie Inc., Mettawa, IL, [8]Harvard Medical School, Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Pain is a dominant feature of PsA and has been identified by the GRAPPA-OMERACT working group as a core disease domain. Its control is a largely unmet need, especially in patients failing non-biologic DMARDs. The purpose of this study was to evaluate if clinically meaningful improvement in pain, particularly at earlier timepoints after treatment initiation, is associated with greater improvements in other patient reported outcomes (PROs).

Methods: The phase 3 SELECT-PsA1 trial randomized patients with inadequate responses to ≥1 non-biologic DMARDs to receive upadacitinib (UPA) 15 mg once daily (QD), UPA 30 mg QD, adalimumab (ADA) 40 mg every other week, or placebo (PBO) for 24 weeks. Patients with baseline patient global assessment (PGA) of pain numeric rating scale (NRS) score >2 were evaluated. Outcomes assessed included the proportion of patients achieving meaningful pain improvement (defined as achievement of a score of < 4 and ≥2-point decrease from baseline in PGA of pain NRS) through Week 24 and, for those achieving meaningful pain improvement at Weeks 4 (UPA/ADA arms only) or 24, the percentage of patients achieving minimum clinically important differences (MCID) at Week 24 on Health Assessment Questionnaire-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), 36-Item Short-Form Health Survey (SF-36), EuroQoL-5 Dimension, 5 level (EQ-5D-5L), and Work Productivity and Activity Impairment (WPAI). Analyses were performed using the Cochran-Mantel-Haenszel test, adjusting for DMARD use, with non-responder imputation for comparison between treatments, and Chi Square test, with as observed analysis for comparison between responders/nonresponders. *P*-values < 0.05 were nominal.

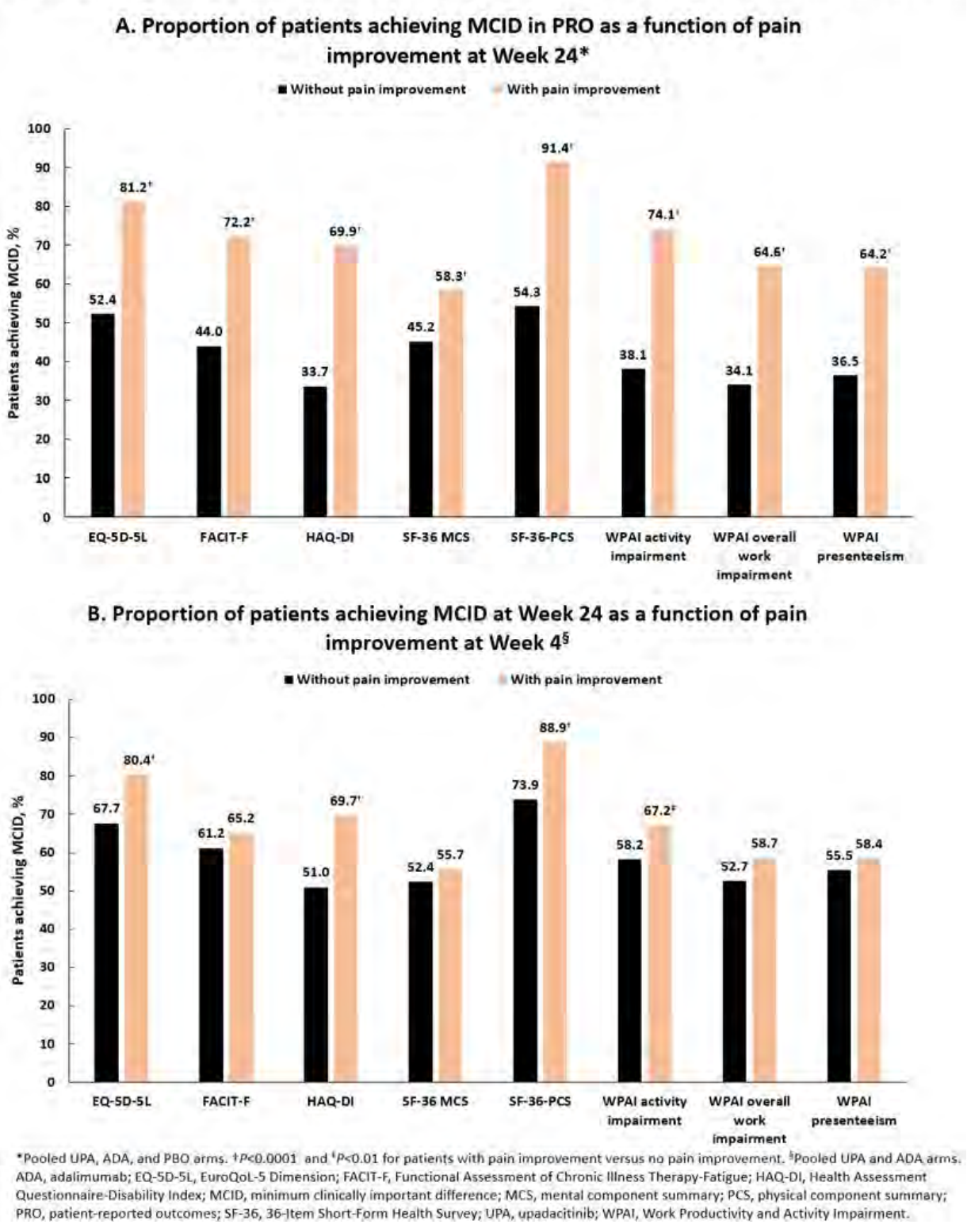
Figure 1. Proportion of patients achieving meaningful pain improvements* with treatment



*Defined as a score of <4 and ≥2-point improvement from baseline in patient global assessment of pain numeric rating scale. †P<0.0001 vs placebo at all timepoints. ‡P≤0.001 vs ADA. §P≤0.01 vs ADA. ‖P<0.05 vs ADA. ¶P≤0.0001 vs placebo. #P<0.001 vs placebo.
ADA, adalimumab; PBO, placebo; UPA, upadacitinib.

Results: A significantly greater proportion of patients with PsA had meaningful pain improvement with UPA 15 mg (N=418), UPA 30 mg (N=413), and ADA (N=420) compared with PBO (N=409) starting as early as Week 2 (P< 0.0001, Figure 1A). Compared with ADA, a significantly greater proportion of patients achieved meaningful pain improvement with UPA 15 mg starting at Week 20 (P< 0.05), and UPA 30 mg starting at Week 4 (P≤0.01). Meaningful pain improve-

Figure 2. Proportion of patients achieving MCID in PRO as a function of pain improvement



*Pooled UPA, ADA, and PBO arms. †$P<0.0001$ and ‡$P<0.01$ for patients with pain improvement versus no pain improvement. §Pooled UPA and ADA arms. ADA, adalimumab; EQ-5D-5L, EuroQoL-5 Dimension; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCID, minimum clinically important difference; MCS, mental component summary; PCS, physical component summary; PRO, patient-reported outcomes; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib; WPAI, Work Productivity and Activity Impairment.

ment was maintained at Week 24 by over 80% of patients on UPA and ADA who had achieved improvement at Week 4 (Figure 1B). For patients who attained meaningful pain improvement at Week 24 vs those who did not, a significantly greater proportion reported values ≥ MCID in all PROs ($P< 0.0001$, Figure 2A). Similarly, for all UPA/ADA patients who

did vs did not attain meaningful pain improvement at Week 4, a significantly greater proportion achieved MCID in EQ-5D-5L, HAQ-DI, SF-36 physical component summary, and WPAI activity impairment at Week 24 ($P < 0.01$, Figure 2B).

Conclusion: A greater proportion of patients achieved meaningful pain improvement with UPA and ADA vs PBO throughout the 24-week treatment period, and with UPA 15 mg vs ADA by Week 20. Meaningful pain improvement by Week 4 was associated with more patients reporting improvements ≥ MCID in several PROs at Week 24. Overall, meaningful pain improvement is closely linked with meaningful improvements in other important outcomes for PsA patients.

Disclosure: L. Bessette, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **B. Joven-Ibáñez**, AbbVie, 6, 12, Participant in clinical trials, Celgene, 2, 6, Janssen, 2, 6, 12, Participant in clinical trials, Novartis, 2, 6, 12, Participant in clinical trials, MSD, 6, Pfizer, 6, UCB, 2, Lilly, 12, Participant in clinical trials; **C. Selmi**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Janssen, 2, 5, 6, Pfizer, 2, 5, 6, Alfa-Wassermann, 2, 6, Biogen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Sanofi-Genzyme, 2, 6; **N. Chen**, AbbVie, 3, 11; **K. Kato**, AbbVie, 3, 11; **R. Lippe**, AbbVie, 3, 11; **P. Zueger**, AbbVie, 3, 11; **J. Patel**, AbbVie, 3; **J. Merola**, AbbVie, 2, Arena, 2, Biogen, 2, Dermavant Sciences, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer Inc, 2, Sun Pharma, 2, UCB Pharma, 2, Avotres Inc, 2, Celgene, 2, EMD Serono, 2, Regeneron, 2, Sanofi, 2, Leo Pharma, 2, Merck, 2, Bristol-Myers Squibb, 2.

Abstract Number: 0235

Are Comorbidities in Patients with Chronic Inflammatory Rheumatic Diseases Associated with Treatment Adherence to Biosimilars in a Non-medical Switch Scenario?

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
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Session Time: 8:30AM–10:30AM

Background/Purpose: The availability of biosimilars has created a financial incentive to encourage non-medical switching if cheaper products are on the market. In patients with chronic inflammatory rheumatic diseases (CIRD), we have previously reported a relatively high retention rate after switching from originator etanercept to its biosimilar. However, this has been different in other studies and the reasons for non-adherence are poorly understood. Comorbidity has recently gained much attention in patients with CIRD and might be a reason for non-adherence.

The aim of this study was to analyse the effectiveness and safety of systematic non-medical switching from originator adalimumab (ADA) to ADA ABP501 biosimilar (ABP) over 6 months in patients with CIRD and to investigate the influence of comorbidities on retention rates.

Methods: Patients with CIRD on originator ADA who switched to ABP subsequently from October 2018 onwards were identified from a large routine database and then followed for 6 months. The presence of comorbidities and

Table 1. Patients and disease characteristics

	Total N=111	RA N=23	axSpA N=68	PsA N=15	Other N=5
Age (years), mean (SD)	51.2 (14.5)	65.1 (12.0)	47.3 (13.1)	51.1 (11.2)	41.8 (14.2)
Women	41.4% (46)	60.9% (14)	32.4% (22)	53.3% (8)	40.0% (2)
Disease duration (years), median (IQR)	5.0 (2.0-8.0)	4.0 (3.0-8.0)	5.0 (2.0-8.0)	4.0 (2.0-13.0)	7.0 (4.0-7.0)
Duration originator ADA therapy (month), mean (SD)	40.7 (27.7)	43.8 (28.6)	39.4 (26.9)	34.7 (29.0)	60.9 (27.7)
Charlson score, mean (SD)	0.8 (1.4)	1.8 (2.1)	0.6 (1.1)	0.7 (1.2)	0.2 (0.4)
Gastroenterological comorbidities	19.8% (22)	26.1% (6)	22.1% (15)	6.7% (1)	0
Hepatic comorbidities	7.2% (8)	17.4% (4)	2.9% (2)	13.3% (2)	0
Hematological conditions	5.4% (6)	8.7% (2)	2.9% (2)	13.3% (2)	0
Cardiovascular comorbidities	39.6% (44)	60.9% (14)	32.4% (22)	33.3% (5)	60.0% (3)
Neurological and psychological comorbidities	17.1% (19)	8.7% (2)	17.6% (12)	33.3% (5)	0
Metabolic comorbidities	14.4% (16)	21.7% (5)	7.4% (5)	26.7% (4)	40.0% (2)
Osteoporosis	18.2% (20)	43.5% (10)	11.9% (8)	6.7% (1)	20.0% (1)
Lung diseases	11.7% (13)	21.7% (5)	8.8% (6)	0	40.0% (2)
Skin diseases	33.3% (37)	26.1% (6)	26.5% (18)	80.0% (12)	20.0% (1)
Eye diseases	19.8% (22)	8.7% (2)	23.5% (16)	6.7% (1)	60.0% (3)
Kidney diseases	10.8% (12)	13.0% (3)	10.3% (7)	0	40.0% (2)
Previous csDMARD therapies, mean (SD)	1.0 (1.0)	1.9 (1.0)	0.6 (0.8)	1.2 (0.7)	1.6 (1.1)
Previous bDMARD therapies, mean (SD)	1.5 (0.8)	1.5 (0.7)	1.4 (0.7)	1.9 (1.2)	1.4 (0.9)
Previous t2sDMARD therapies, mean (SD)	0.0 (0.1)	0.0 (0.2)	0	0	0
csDMARDs	38.7% (43)	69.6% (16)	25.0% (17)	53.3% (8)	40.0% (2)
NSAIDs	14.4% (16)	8.7% (2)	16.2% (11)	20.0% (3)	0
Glucocorticoids	17.1% (19)	43.5% (10)	10.3% (7)	6.7% (1)	20.0% (1)
Glucocorticoids, <5 mg	55.6% (10)	70.0% (7)	33.3% (2)	0	100.0% (1)
Glucocorticoids, 5-10 mg	44.4% (8)	30.0% (3)	66.7% (4)	100.0% (1)	0

Values are shown as % (N) if not stated otherwise.
b/cs/tsDMARD: biological / conventional synthetic / targeted synthetic disease-modifying anti-rheumatic drug; IQR: interquartile range; NSAIDs: non-steroidal anti-inflammatory drugs; SD: standard deviation.

disease characteristics as well as measures of disease activity, physical function and changes in treatment were documented at baseline (the time of switching from originator ADA to ABP), and at months 3 and 6. Longitudinal data including information on the clinical efficacy and safety of ABP, and the reasons for discontinuation were documented.

Results: A total of 111 CIRD patients on treatment with originator ADA were switched to the biosimilar ABP. This comprised 23 patients with rheumatoid arthritis (RA), 68 with axial spondyloarthritis (axSpA), and 15 with psoriatic arthritis (PsA). More than half of the patients (62%) had a Charlson comorbidity score of zero, though there were differences between disease subtypes. RA patients were comparatively older (mean age 65 years) and had the highest mean Charlson score (1.8), see Table 1.

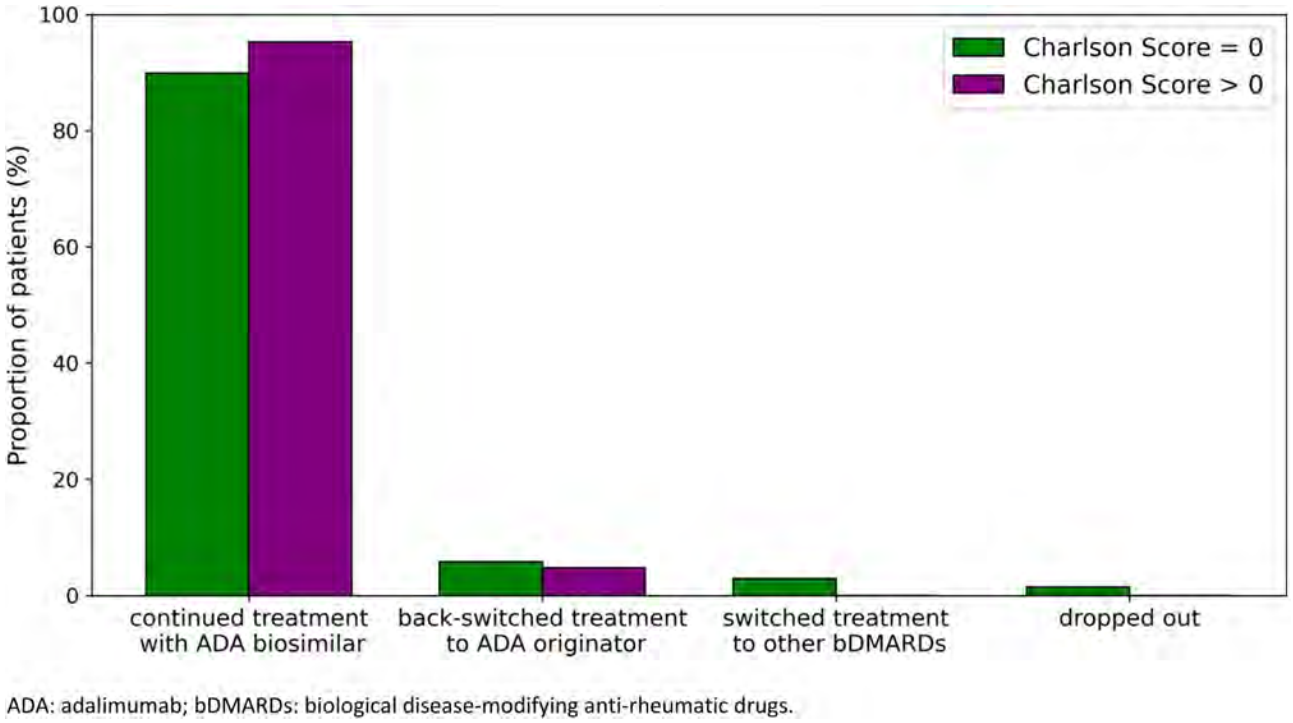
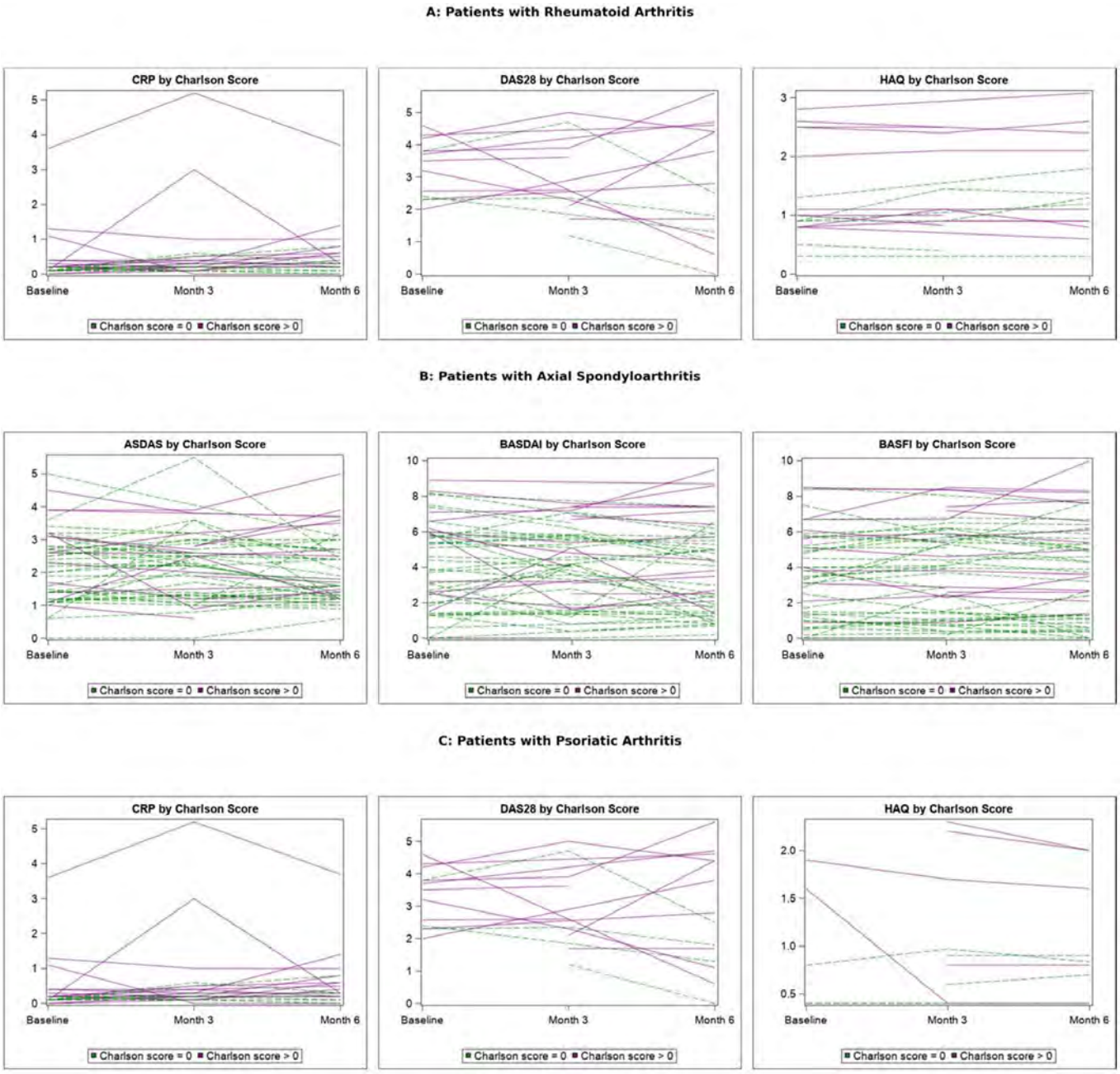


Figure 1. Treatment retention after 6 months stratified by the Charlson comorbidity score.

Treatment retention varied only slightly between patients with a Charlson score of zero and those with a higher score (Figure 1). In both groups, the majority of patients (90% vs 95%) continued therapy with ABP, while only a small proportion either switched back to originator ADA (6% vs 5%), switched to a different biologic (3% vs 0%), or dropped out (1% vs 0%). The main reason for back switch was the occurrence of adverse events, mostly subjective complaints, most frequently pain. Spaghetti plots show the trajectories of scores for disease activity and physical function stratified by disease subtype (Figure 2). Patients with a Charlson comorbidity score > 0 tended to have poorer scores in this regard.

Conclusion: Comorbidity had no influence on the biosimilar retention rate after 6 months in this study but the majority of patients did not have Charlson scores > 0. However, disease activity and physical function tended to be worse among CIRD patients with comorbidity. Cardiovascular disease and osteoporosis were more often present in RA patients than in axSpA or PsA patients, while neurological and psychological comorbidities were more often observed in the latter.



ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; DAS28: Disease Activity Score of 28 joints; HAQ: Health Assessment Questionnaire.

Figure 2. Trajectories of scores for disease activity and physical function stratified by disease subtype and the Charlson comorbidity score.

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Abstract Number: 0236

Maternal Attachment, Anxiety and Depressive Symptoms in Pregnant Women with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Untreated perinatal anxiety symptomatology can be related to symptoms of anxiety and depression during the postpartum. The psychological bond created by the mother between mother and fetus helps to mitigate physical and emotional problems on this stage and in the postpartum. Prenatal maternal attachment acquires special importance because it has been shown that can be a predictor for healthier behavior during pregnancy and better birth outcomes. The aim of this study to correlate the scores between State Trait Anxiety Inventory (STAI), Maternal Antenatal Attachment Scale (MAAS) and Edinburgh Postnatal Depression Scale (EPDS).

Table 1. Demographic characteristics and total scores

	n= 23
Age, mean, years, SD	27.60 (±7.76)
Rheumatic diagnosis, n (%)	
Rheumatoid arthritis	10 (43.47)
Antiphospholipid syndrome	5 (21.73)
Systemic lupus erythematosus	4 (17.39)
Fibromyalgia	2 (8.69)
Dermatomyositis	1 (4.34)
Sjogren's syndrome	1 (4.34)
Questionnaires total score, mean, SD	
State Trait Anxiety Inventory (STAI)	133.82 (±8.46)
Maternal Antenatal Attachment Scale (MAAS)	43.82 (±5.08)
Edinburgh Postnatal Depression Scale (EPDS)	7.65 (±6.0)

SD: standard deviation

Methods: A cross-sectional and descriptive study was conducted from January 2019 to May 2021 at the Pregnancy and Rheumatic Diseases Clinic from the University Hospital "Dr. Jose E. Gonzalez" in Monterrey, Mexico. Pregnant women with ARDs were invited to participate. The STAI is a questionnaire used in clinical settings to diagnose anxiety and to distinguish it from depressive syndromes. It has 20 items for assessing trait anxiety and 20 for state anxiety. All items are rated on a 4-point scale. Higher scores indicate greater anxiety. The MAAS is a 19-item self-report questionnaire which calculates a total attachment score and two subscale scores; one score estimating the quality of the affective attachment and the other that estimates the intensity of concern about the fetus. The EPDS is a set of 10 screening items that can indicate whether a parent has symptoms that are common in women with depression and anxiety during pregnancy and in the year following the birth of a child. The total score is calculated by adding the numbers selected for each of the 10 items, with a cut-off score of 10 points. The validated Spanish version of those instruments were applied during the third trimester. The statistical analysis was performed using the Pearson´s correlation test. Data included descriptive statistics. A p-value < 0.05 was statistically significant. The data were evaluated using the IBM SPSS v24 statistical package (IBM, Armonk, USA).

Results: A total of 23 pregnant women were recruited. A mean age of 27.6 years. The most common diagnosis was rheumatoid arthritis with 10(43.47), followed by antiphospholipid syndrome 5(21.73) and systemic lupus erythematosus 4(17.3), and other diagnosis (fibromyalgia (2), dermatomyositis (1) and Sjogren's syndrome (1)). The STAI mean score was 133.82 points, the MAAS mean score was 43.82 points, and the EPDS mean score was 7.65 points. A negative moderate correlation was found between MAAS and EPDS (-.605, p=0.002) and also a positive moderate correlation between STAI and EPDS (0.442, p=0.034).

Conclusion: The maternal antenatal attachment had a moderate negative correlation with postnatal depression, meaning the less attachment equals a higher frequency of depressive symptoms. Moreover, a positive correlation between anxiety symptoms and depressive symptoms were found. Strategies to enhance the maternal bond must be addressed during all pregnancy stages. Postpartum women should receive psychological support and be screened for depression and anxiety, especially women with preexisting conditions such as ARDs and other chronic diseases.

Disclosure: L. Espinosa-Banuelos, None; **D. Rubio Torres**, None; **M. Corral**, None; **C. Skinner Taylor**, None; **L. Perez-Barbosa**, None; **L. Gutierrez Leal**, None; **A. Lujano-Negrete**, None; **J. Cardenas-de La Garza**, None; **D. Galarza-Delgado**, None.

Abstract Number: 0237

Self-perceived General Health at Start of Anti-TNF Therapy Predicts Therapeutic Response in Patients with Rheumatoid Arthritis: Analysis from the Czech Biologics Registry ATTRA

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 8:30AM–10:30AM

Table 1. Patients' responses and occurrence of DAS28 remission after 12 months
- Univariable logistic regression models (Remission (DAS28-ESR < 2.6) after 12 months (1 – yes vs. 0 – no))

Dataset	D1 (N=1808)		D2 (N=734)	
Parameters (N = 1808)	OR (95% CI)	p	OR (95% CI)	p
Expectation of disease worsening:				
definitely yes / mostly yes (vs. definitely no / mostly no)	1.48 (1.15; 1.91)	0.003	1.66 (1.13; 2.45)	0.010
Not sure (vs. definitely no / mostly no)	0.94 (0.74; 1.21)	0.654	1.11 (0.77; 1.60)	0.587
It seems I become ill more easily than other people:				
definitely yes / mostly yes (vs. definitely no / mostly no)	1.62 (1.27; 2.05)	< 0.001	1.74 (1.20; 2.52)	0.004
Not sure (vs. definitely no / mostly no)	0.96 (0.76; 1.22)	0.753	1.14 (0.80; 1.63)	0.471

Table 2 Patients' responses and occurrence of remission after 12 months - Adjusted odds ratios using logistic regression (OR (odds ratio); CI (confidence interval); logistic regression: 1 – yes; 0 – no)

	D1 (N = 1778)		D2 (n=693)	
Parameters	OR (95% CI)	p	OR (95% CI)	p
Expectation of disease worsening:				
definitely yes / mostly yes (vs. definitely no / mostly no)	1.59 (1.22; 2.08)	< 0.001	1.91 (1.26; 2.88)	0.002
Not sure (vs. definitely no / mostly no)	0.99 (0.76; 1.28)	0.945	1.27 (0.85; 1.88)	0.243
HAQ (at the baseline)	0.63 (0.52; 0.77)	< 0.001	0.46 (0.34; 0.62)	< 0.001
DAS28-ESR (at the baseline)	0.68 (0.60; 0.78)	< 0.001	0.91 (0.77; 1.06)	0.232
Parameters	OR (95% CI)	p	OR (95% CI)	p
It seems I become ill more easily than other people:				
definitely yes / mostly yes (vs. definitely no / mostly no)	2.04 (1.60; 2.61)	< 0.001	2.04 (1.37; 3.03)	< 0.001
Not sure (vs. definitely no / mostly no)	1.09 (0.86; 1.38)	0.466	1.20 (0.82; 1.74)	0.350
HAQ (at the baseline)	0.56 (0.46; 0.67)	< 0.001	0.45 (0.33; 0.62)	< 0.001
DAS28-ESR (at the baseline)	0.72 (0.63; 0.82)	< 0.001	0.89 (0.76; 1.05)	0.165

Background/Purpose: SF-36 and its components, as well as other PROs have been shown to predict various disease outcomes. We hypothesized that positive responses to questions (Q) 11A "I seem to get sick a little easier than other people", and 11C "I expect my health to get worse" from the general health (GH) domain of the SF-36 v1 questionnaire may correspond to a more fragile self-perceived GH status, and thus serve as possible predictors of future disease outcomes in patients with rheumatoid arthritis (RA). We aimed to investigate whether these 2 questions could predict therapeutic response in patients with RA starting their first anti-TNF therapy.

Table 3. Patients' responses and occurrence of remission after 12 months - univariable logistic regression models after PS matching

	D1		D2	
Parameters	OR (95% CI)	p	OR (95% CI)	p
Expectation of disease worsening:	N=845		N=333	
definitely yes / mostly yes (vs. definitely no / mostly no)	1.33 (1.00; 1.77)	0.050	1.51 (0.97; 2.34)	0.066
It seems I become ill more easily than other people:	N=965		N=365	
definitely yes / mostly yes (vs. definitely no / mostly no)	1.56 (1.19; 2.05)	0.001	1.70 (1.12; 2.59)	0.013

Methods: We have used two separate datasets from the Czech biologics registry ATTRA to validate our hypothesis. Dataset D1 included RA patients with at least 1 year follow-up and all relevant data available starting their first-line anti-TNF treatment within period 01/01/2012-31/12/2017 (N=1808), and dataset D2 pts starting in in 01/01/2018–01/01/2020 (N=734). Our primary outcome was DAS28-ESR remission (REM) at 12 months. REM was defined as DAS28< 2.6. Patients were grouped according their response (definitely/mostly yes vs. definitely/mostly no) to Q11A and Q11C at baseline. REM rates after 12 months of 1st-line anti-TNF treatment were compared across patients' groups with Pearson chi-squared test. Firstly, odds ratios (ORs) using logistic regression (univariate, and then adjusted to baseline DAS28 and HAQ) were calculated to predict REM at 12M. Secondly, ORs were calculated after matching pts with positive or negative responses by a propensity score (PS) using sex, age, disease duration, baseline DAS28, calendar year and co-medication to balance baseline differences.

Results: At baseline, 79% and 80% pts were female, mean (SD) age was 52(12) and 54(13) years, DAS28 6.3 (0.9) and 6.2 (1.1), HAQ 1.5(0.6) and 1.5(0.6), 74% and 68% were RF+, 70% and 69% ACPA+ in D1 and D2 resp. In D1 34% and 31% pts, and in D2 32% and 30% responded positively to Q11A and 11C resp. Patients with positive responses to Q11A and 11C tended to have slightly (but statistically significantly) higher DAS28, HAQ, CRP or ESR, and patient- and physician global activity assessment at baseline. At 12 months, 40% (49%), 31% (37%), and 30% (40%) patients with positive, negative and neutral response to Q 11A reached REM; p< 0.001 (p=0.018) in D1 (D2) resp. At 12 months, 42% (51%), 31% (37%), and 30% (40%) patients with positive, negative and neutral response to Q 11C reached REM; p< 0.001 (p=0.04) in D1 (D2) resp. Crude and adjusted ORs for reaching REM according to responses to Q11A and Q11C are shown in tables 1-3.

Conclusion: We provide a robust evidence that self-perceived general health at start of anti-TNF therapy predicts reaching remission at 12 months in pts with RA.

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Disclosure: J. Zavada, None; **L. Nekvindova**, None.

Abstract Number: 0238

The Impact of Preeclampsia on Pregnancies and Infants of Women with Rheumatic Disease

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. *Maternal characteristics of patients with autoimmune disease and comorbid preeclampsia compared to patients with autoimmune disease without preeclampsia*

	Mothers with Preeclampsia			*Mothers without Preeclampsia*			*Total*
Maternal Characteristics	**SLE (N=23)**	**Non-SLE rheumatic disease* (N=15)**	**Total (N=38)**	**SLE (N=63)**	**Non-SLE rheumatic disease* (N=162)**	**Total (N=225)**	**(N=263)**
Maternal Age at Delivery in years. Mean (SD)	30.1 (6)	28.5 (5.8)	29.5 (5.9)	30 (6.2)	32.1 (5.1)	31.5 (5.5)	31.2 (5.6)
Race/Ethnicity							
Non-Hispanic Black	17 (73.9%)	7 (46.7%)	24 (63.2%)	31 (49.2%)	36 (22.2%)	67 (29.8%)	91 (34.6%)
Non-Hispanic White	6 (26.1%)	7 (46.7%)	13 (34.2%)	16 (25.4%)	94 (58.0%)	110 (48.9%)	123 (46.8%)
Hispanic	0	1 (6.7%)	1 (2.6%)	8 (12.7%)	9 (5.6%)	17 (7.6%)	18 (6.8%)
Other	0	0	0	8 (12.7%)	22 (13.6%)	30 (13.3%)	30 (11.4%)
Unknown	0	0	0	0	1 (0.6%)	1 (0.4%)	1 (0.4%)
Insurance							
Private	12 (52.2%)	5 (33.3%)	17 (44.7%)	32 (50.8%)	119 (73.5%)	151 (67.1%)	168 (63.9%)
Public	11 (47.8%)	9 (60%)	20 (52.6%)	30 (47.6%)	36 (22.2%)	66 (29.3%)	86 (32.7%)
Self-Pay	0	1 (6.7%)	1 (2.6%)	1 (1.6%)	7 (4.3%)	8 (3.6%)	9 (3.4%)
Disabled	5 (21.7%)	3 (20.0%)	8 (21.1%)	2 (3.2%)	5 (3.1%)	7 (3.1%)	15 (5.7%)
Postpartum hospital admission in days. Mean (SD)	5.7 (6.5)	4.9 (2.3)	5.4 (5.2)	3.7 (3.1)	3.9 (12.3)	3.9 (10.5)	4.1 (10)
Cesarean section delivery	12 (54.5%)	9 (60.0%)	21 (56.8%)	23 (40.4%)	67 (48.2%)	90 (45.9%)	111 (47.6%)

**Non-SLE rheumatic disease included Mixed Connective Tissue Disease, Undifferentiated Connective Tissue Disease, Sjogren's syndrome, Antiphospholipid Syndrome, Adult Onset Still's Disease, seronegative spondyloarthropathies, juvenile inflammatory arthritis, rheumatoid arthritis, Behcet's disease, Familial Mediterranean Fever, inflammatory eye disease, inflammatory myopathy, sarcoidosis, systemic sclerosis, cutaneous lupus, systemic vaculitides.*

Maternal characteristics of patients with autoimmune disease and comorbid preeclampsia compared to patients with autoimmune disease without preeclampsia.

Background/Purpose: Rheumatic diseases, such as SLE, are associated with serious maternal, pregnancy, and infant complications. The role that preeclampsia plays in these outcomes in women with SLE and other rheumatic disease remains unclear. We compared pregnancy and infant outcomes among women with SLE and other rheumatic diseases with and without preeclampsia in a single academic center.

Methods: Deliveries in women with rheumatic disease were identified from both a prospective cohort of women with rheumatic disease who received care within a university rheumatology clinic and a chart-reviewed list of deliveries to women with an ICD-9/10 code for SLE. Mothers with rheumatic disease were matched with their infants through the electronic medical record (EMR) to allow data extraction. Preeclampsia was determined by the obstetric team at the time of delivery and collected through chart review. Pregnancy and infant outcomes were compared between those with and without preeclampsia.

Results: 263 singleton deliveries were included in the study of whom 14% had preeclampsia. Preeclampsia was significantly more common among women with SLE than with other rheumatic diseases (SLE 27% vs other rheumatic diagnoses 8%, p< 0.001); this pattern persisted among both Black and White women and women with private health insurance. Among women with SLE, however, the rate of preeclampsia was similar between Black and White women

Table 2. *Infant Outcomes of children born to patients with autoimmune disease and comorbid preeclampsia compared to patients with rheumatic disease without preeclampsia*

	Mothers with Preeclampsia			*Mothers without Preeclampsia*			*Total*
Infant Outcomes	**SLE (N=23)**	**Non-SLE rheumatic disease (N=15)**	**Total (N=38)**	**SLE (N=63)**	**Non-SLE rheumatic disease (N=162)**	**Total (N=225)**	**(N=263)**
Average Gestational Age in weeks (SD)	34.7 (4.3)	35.1 (4)	34.9 (4.2)	37.8 (2.5)	38.3 (2.2)	38.2 (2.3)	37.7 (2.9)
Preterm Birth	14 (60.9%)	7 (46.7%)	21 (55.3%)	13 (21.0%)	19 (11.9%)	32 (14.5%)	53 (20.5%)
Very Preterm Birth	3 (13.0%)	1 (6.7%)	4 (10.5%)	1 (1.6%)	2 (1.3%)	3 (1.4%)	7 (2.7%)
NICU Admission	10 (43.5%)	4 (26.7%)	14 (36.8%)	14 (22.2%)	20 (12.3%)	34 (15.1%)	48 (18.3%)
Infant death	1 (4.3%)	0	1 (2.6%)	1 (1.6%)	0	1 (0.4%)	2 (0.8%)
Small for Gestational Age	7 (30.4%)	3 (21.4%)	10 (27.0%)	15 (24.2%)	29 (19.0%)	44 (20.5%)	54 (21.4%)
Adrenal insufficiency	1 (4.3%)	0	1 (2.6%)	0	4 (2.5%)	1 (1.8%)	5 (1.9%)
Hospital admission within first year of life	2 (8.7%)	1 (6.7%)	3 (7.9%)	10 (15.9%)	12 (7.4%)	22 (9.8%)	25 (9.5%)

**Non-SLE rheumatic disease included Mixed Connective Tissue Disease, Undifferentiated Connective Tissue Disease, Sjogren's syndrome, Antiphospholipid Syndrome, Adult Onset Still's Disease, seronegative spondyloarthropathies, juvenile inflammatory arthritis, rheumatoid arthritis, Behcet's disease, Familial Mediterranean Fever, inflammatory eye disease, inflammatory myopathy, sarcoidosis, systemic sclerosis, cutaneous lupus, systemic vaculitides.*

Infant Outcomes of children born to patients with autoimmune disease and comorbid preeclampsia compared to patients with rheumatic disease without preeclampsia.

and those with and without private insurance. Having preeclampsia increased the mother's hospital stay for delivery by an average of 2 days for women with SLE and 1 day for women with other rheumatic diseases.

Infants born to preeclamptic mothers were delivered an average of 3.3-weeks earlier than those without preeclampsia; they were 4-times more likely to be born preterm (55.3% vs 14.5%, p< 0.001), a difference that persisted in mothers with SLE and other rheumatic diagnoses. More than twice as many infants born to preeclamptic mothers were admitted to the neonatal intensive care unit (NICU; 36.8% vs 15.1%, p< 0.0001). While infants born to women with SLE without preeclampsia had modestly higher rates of preterm birth and NICU admission compared to women with other rheumatic diseases, preeclampsia drove these rates significantly higher in all women.

Conclusion: Preeclampsia has important health consequences on mothers with rheumatic disease, including increasing hospitalization at delivery by 1-2 days, and on the infant, increasing the frequency of preterm delivery and NICU admission. Preeclampsia was particularly common among women with SLE in this cohort. These data suggest that preventing preeclampsia could have a dramatic impact on the short- and long-term health of women with rheumatic disease and their children.

Disclosure: M. Milne, None; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **C. Zhao**, None; **B. Goldstein**, None.

Abstract Number: 0239

Work Disability Associated with Fatigue in Patients with Psoriatic Arthritis – a Retrospective Study Using Claims Data, 2009-2019

Elaine Husni[1], Steven Peterson[2], Natalie Dennis[3], Feifei Yang[4], Iris Lin[4], Yiting Wang[5], Soumya Chakravarty[6], Claire Fischer[3], May Shawi[7], Arthur Quenéchdu[3] and Joseph Merola[8], [1]Cleveland Clinic, Cleveland, OH, [2]Janssen Immunology Global Commercial Strategy Organization, Raritan, NJ, [3]Amaris, Health Economics and Market Access, Paris, France, [4]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [5]Janssen R&D, LLC, Titusville, NJ, [6]Janssen Scientific Affairs, LLC and Drexel University College of Medicine, Horsham, PA, [7]Janssen Immunology Global Commercial Strategy Organization, Toronto, ON, Canada, [8]Brigham and Women's Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue is a complex symptom affecting physiological, psychological, and social factors and is commonly seen in psoriatic arthritis (PsA). Fatigue has been shown to be associated with both short-term and long-term work absences. The objective of this study was to evaluate the impact of fatigue on short-term disability among patients with PsA in the United States.

Methods: Adults eligible for short-term disability benefits between 2009 and 2019 were screened in the IBM® MarketScan® Commercial and Health and Productivity Management Databases. Patients with ≥ 2 diagnoses for PsA ≥ 30 days apart were included. Patients with fatigue (i.e., cases) had ≥ 1 fatigue diagnosis after their initial PsA diagnosis, and the first fatigue diagnosis was defined as the index date. Controls were PsA patients who had no fatigue diagnoses during the study period; their index date was defined using the cases' median time from initial PsA to the first fatigue diagnosis. Patients had continuous enrollment from ≥ 6 months before their initial PsA diagnosis (baseline period) to ≥ 12 months after the index date (follow-up period) and had to be eligible for short-term disability benefits

Table 1. Baseline characteristics before and after matching (1) (1) Variables were evaluated during the 6-month baseline period (2) Variables in italic were not included in the matching

	Before matching		After matching	
	Control group	PsA with fatigue	Control group	PsA with fatigue
Number of patients	**3,380**	**1,266**	**1,244**	**1,244**
Age - Mean (SD)	46.4 (9.2)	46.4 (8.8)	46.3 (9.2)	46.4 (8.7)
Female - N (%)	1044 (30.9%)	555 (43.8%)	536 (43.1%)	534 (42.9%)
PsA treatment - N (%)				
NSAIDs (without oral therapy or biologics)	545 (16.1%)	212 (16.7%)	208 (16.7%)	208 (16.7%)
Oral therapy (without biologics)	247 (7.3%)	94 (7.4%)	83 (6.7%)	92 (7.4%)
Biologics	1383 (40.9%)	513 (40.5%)	530 (42.6%)	506 (40.7%)
Systemic steroids	222 (6.6%)	109 (8.6%)	107 (8.6%)	104 (8.4%)
Psoriasis – N (%)[2]	*1683 (49.8%)*	*622 (49.1%)*	*616 (49.5%)*	*613 (49.3%)*
Related conditions - N (%)				
Depression	193 (5.7%)	134 (10.6%)	121 (9.7%)	119 (9.6%)
Anxiety	139 (4.1%)	83 (6.6%)	70 (5.6%)	75 (6.0%)
Sleep disorders	*252 (7.5%)*	*159 (12.6%)*	*130 (10.5%)*	*142 (11.4%)*
Obstructive sleep apnea	171 (5.1%)	96 (7.6%)	79 (6.4%)	88 (7.1%)
Other sleep disorders	110 (3.3%)	91 (7.2%)	77 (6.2%)	75 (6.0%)
Hypothyroidism	196 (5.8%)	107 (8.5%)	106 (8.5%)	98 (7.9%)
Anemia	118 (3.5%)	60 (4.7%)	50 (4.0%)	57 (4.6%)
Fibromyalgia	*111 (3.3%)*	*90 (7.1%)*	*58 (4.7%)*	*83 (6.7%)*
Fibromyalgia or generalized pain	*117 (3.5%)*	*93 (7.3%)*	*59 (4.7%)*	*86 (6.9%)*
Prescription for fibromyalgia treatment	*92 (2.7%)*	*55 (4.3%)*	*43 (3.5%)*	*50 (4.0%)*
Treated patients with fibromyalgia or generalized pain	14 (0.4%)	14 (1.1%)	12 (1.0%)	10 (0.8%)
Charlson Comorbidity Index				
Mean (SD)	0.29 (0.76)	0.38 (0.89)	0.35 (0.85)	0.36 (0.85)
0 - N (%)	*2736 (81.0%)*	*962 (76.0%)*	*970 (78.0%)*	*952 (76.5%)*
1 - N (%)	*449 (13.3%)*	*214 (16.9%)*	*180 (14.5%)*	*207 (16.6%)*
≥ 2 - N (%)	*195 (5.8%)*	*90 (7.1%)*	*94 (7.6%)*	*85 (6.8%)*
Disease severity				
Number of rheumatology visits - Mean (SD)	2.99 (5.79)	3.45 (6.38)	3.44 (6.34)	3.40 (6.35)
Inflammation marker test ordered - N (%)	1743 (51.6%)	726 (57.3%)	703 (56.5%)	706 (56.8%)
Joint pain diagnosis - N (%)	1018 (30.1%)	472 (37.3%)	443 (35.6%)	460 (37.0%)
Number of imaging procedures - Mean (SD)	0.67 (1.03)	0.83 (1.14)	0.82 (1.13)	0.81 (1.08)
Difficulty walking – N (%)	*11 (0.3%)*	*5 (0.4%)*	*2 (0.2%)*	*5 (0.4%)*
Other confounding factors – N (%)				
Vitamin D deficiency	211 (6.2%)	108 (8.5%)	112 (9.0%)	103 (8.3%)
Acute upper respiratory infection	370 (10.9%)	195 (15.4%)	183 (14.7%)	188 (15.1%)

Table 2. Short-term disability outcomes during follow-up.

	Control group	PsA with fatigue	P-value
Number of patients	1,244	1,244	
Patients with short-term disability leave – N (%)	82 (6.6%)	127 (10.2%)	0.0014
Number of short-term disability days – Mean (SD)	3.41 (20.70)	6.92 (32.20)	0.0013
Costs associated with short-term disability – Mean (SD)	$438.09 (2645.63)	$896.54 (4180.10)	0.0011

during the entire follow-up period. Patients with rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, or ulcerative colitis during the study period were excluded from the analyses. Controls were matched 1:1 to cases based on propensity scores that balanced age, gender, year of initial PsA diagnosis, PsA treatment, related conditions, the Charlson Comorbidity Index, variables associated with PsA disease severity, vitamin D deficiency, and common infections (Table 1). Change in short-term disability and associated costs (in 2019 USD) were calculated from baseline through follow-up.

Results: 1,244 patients with fatigue were matched to the control group (Table 1). The average age at baseline was 46.3 years and 43.0% were female. Patients with PsA and fatigue missed an average of 6.9 days due to short-term disability, whereas controls missed an average of 3.4 days (p=0.0013, Table 2). Average costs associated with short-term disability were $438 and $897 for controls and PsA patients with fatigue, respectively (p=0.0011). During follow-up, 6.6% of patients in the control group had at least one short-term disability leave compared to 10.2% of patients with fatigue (p=0.0014).

Conclusion: Higher rates of annual short-term disability were observed among patients with PsA and fatigue than without fatigue. These results highlight the substantial indirect costs and economic burden of fatigue in patients with PsA.

Disclosure: E. Husni, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2; **S. Peterson**, Janssen, 3, 11; **N. Dennis**, None; **F. Yang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **I. Lin**, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 3, 11; **Y. Wang**, Janssen, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Fischer**, None; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Quenéchdu**, None; **J. Merola**, Dermavant, 5, LEO Pharma, 3, Abbvie, 2, Amgen, 2, Bayer, 2, Eli Lilly, 2, Novartis, 2, Janssen, 2, UCB, 2, 5, Celgene, 2, Sanofi-Regeneron, 2, Biogen, 2, Pfizer, 2, BMS, 2.

Abstract Number: 0240

Economic Burden of Fatigue Among Patients with Psoriatic Arthritis – a Retrospective Study Using Claims Data, 2009-2019

Joseph Merola[1], Feifei Yang[2], Natalie Dennis[3], Steven Peterson[4], Iris Lin[2], Yiting Wang[5], Soumya Chakravarty[6], Arthur Quenéchdu[3], May Shawi[7], Claire Fischer[3] and Elaine Husni[8], [1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [2]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [3]Amaris, Health Economics and Market Access, Paris, France, [4]Janssen Immunology Global Commercial Strategy Organization, Raritan, NJ, [5]Janssen R&D, LLC, Titusville, NJ, [6]Janssen Scientific Affairs, LLC and Drexel University College of Medicine, Horsham, PA, [7]Janssen Immunology Global Commercial Strategy Organization, Toronto, ON, Canada, [8]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: Impact (0225–0240)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue is a complex symptom affecting physiological, psychological, and social factors and is commonly seen in psoriatic arthritis (PsA). The objectives of this study were to evaluate healthcare resource utilization and costs associated with fatigue among patients with PsA in the United States.

Methods: The IBM® MarketScan® Commercial Database was used to identify adult patients with PsA between 2009 and 2019. Patients with ≥ 2 diagnoses for PsA ≥ 30 days apart were included. Patients with fatigue (i.e., cases) had ≥ 1 fatigue diagnosis after their initial PsA diagnosis, and the first fatigue diagnosis was defined as the index date. Controls were PsA patients who had no fatigue diagnoses during the study period; their index date was defined using the case's median time from initial PsA to the first fatigue diagnosis. Patients had continuous enrollment from ≥ 6 months before their initial PsA diagnosis (baseline period) to ≥ 12 months after the index date (follow-up period). Patients with comorbid rheumatoid arthritis, ankylosing spondylitis, Crohn's disease, or ulcerative colitis during the study period were excluded from the analyses. Controls were matched 1:1 to patients with PsA and fatigue based on propensity scores that balanced age, gender, year of initial PsA diagnosis, PsA treatment, related conditions, the Charlson Comorbidity Index, variables associated with PsA disease severity, vitamin D deficiency, and respiratory infection (Table 1). Healthcare resource utilization and costs (in 2019 USD) were evaluated during follow-up.

Results: Fatigue was present among 30% of included patients with PsA. 7,350 patients with fatigue were matched to the control group (Table 1). The average age at baseline was 48 years and 59% were female. Average annual all-cause healthcare costs per patient were $26,102 and $34,344 for the control group and patients with fatigue,

Table 1. Baseline characteristics before and after matching (1) (1) Variables were evaluated during the 6-month baseline period (2) Variables in italic were not included in the matching

	Before matching		After matching	
	Control group	PsA with fatigue	Control group	PsA with fatigue
Number of patients	**17,412**	**7,582**	**7,350**	**7,350**
Age - Mean (SD)	47.9 (10.1)	47.9 (9.5)	48.1 (10.1)	47.9 (9.5)
Female - N (%)	7831 (45.0%)	4579 (60.4%)	4385 (59.7%)	4357 (59.3%)
PsA treatment - N (%)				
NSAIDs (without oral therapy or biologics)	2472 (14.2%)	1183 (15.6%)	1117 (15.2%)	1133 (15.4%)
Oral therapy (without biologics)	1166 (6.7%)	574 (7.6%)	539 (7.3%)	552 (7.5%)
Biologics	5937 (34.1%)	2373 (31.3%)	2343 (31.9%)	2312 (31.5%)
Systemic steroids	925 (5.3%)	564 (7.4%)	509 (6.9%)	518 (7.0%)
Psoriasis – N (%)[2]	*8780 (50.4%)*	*3792 (50.0%)*	*3739 (50.9%)*	*3684 (50.1%)*
Related conditions - N (%)				
Depression	1279 (7.3%)	958 (12.6%)	829 (11.3%)	858 (11.7%)
Anxiety	921 (5.3%)	666 (8.8%)	580 (7.9%)	588 (8.0%)
Sleep disorders	*1396 (8.0%)*	*1007 (13.3%)*	*842 (11.5%)*	*882 (12.0%)*
Obstructive sleep apnea	914 (5.2%)	612 (8.1%)	521 (7.1%)	537 (7.3%)
Other sleep disorders	692 (4.0%)	586 (7.7%)	493 (6.7%)	492 (6.7%)
Hypothyroidism	1321 (7.6%)	907 (12.0%)	834 (11.3%)	826 (11.2%)
Anemia	656 (3.8%)	524 (6.9%)	460 (6.3%)	444 (6.0%)
Fibromyalgia	*795 (4.6%)*	*774 (10.2%)*	*488 (6.6%)*	*713 (9.7%)*
Fibromyalgia or generalized pain	*832 (4.8%)*	*805 (10.6%)*	*506 (6.9%)*	*743 (10.1%)*
Prescription for fibromyalgia treatment	*725 (4.2%)*	*535 (7.1%)*	*385 (5.2%)*	*489 (6.7%)*
Treated patients with fibromyalgia or generalized pain	143 (0.8%)	122 (1.6%)	104 (1.4%)	103 (1.4%)
Charlson Comorbidity Index				
Mean (SD)	0.36 (0.88)	0.48 (1.05)	0.45 (1.01)	0.46 (1.03)
0 - N (%)	*13483 (77.4%)*	*5433 (71.7%)*	*5386 (73.3%)*	*5339 (72.6%)*
1 - N (%)	*2648 (15.2%)*	*1381 (18.2%)*	*1272 (17.3%)*	*1316 (17.9%)*
≥ 2 - N (%)	*1281 (7.4%)*	*768 (10.1%)*	*692 (9.4%)*	*695 (9.5%)*
Disease severity				
Number of rheumatology visits - Mean (SD)	2.71 (5.32)	3.40 (6.24)	3.30 (6.26)	3.32 (6.13)
Inflammation marker test ordered - N (%)	8751 (50.3%)	4425 (58.4%)	4193 (57.0%)	4234 (57.6%)
Joint pain diagnosis - N (%)	5392 (31.0%)	3082 (40.6%)	2901 (39.5%)	2905 (39.5%)
Number of imaging procedures - Mean (SD)	0.64 (1.00)	0.84 (1.15)	0.79 (1.13)	0.80 (1.11)
Difficulty walking – N (%)	*73 (0.4%)*	*48 (0.6%)*	*44 (0.6%)*	*43 (0.6%)*
Other confounding factors – N (%)				
Vitamin D deficiency	1259 (7.2%)	861 (11.4%)	783 (10.7%)	774 (10.5%)
Acute upper respiratory infection	2139 (12.3%)	1395 (18.4%)	1286 (17.5%)	1279 (17.4%)

respectively ($p< 0.0001$). The costs were greater among patients with fatigue due to greater inpatient costs (controls: $2,046, fatigue: $3,959), outpatient medical costs (controls: $7,058, fatigue: $11,182), and outpatient pharmacy costs (controls: $16,998, fatigue: $19,203) (Figure 1). Across all categories of healthcare resources, utilization was greater among patients with PsA and fatigue than the control group (Table 2). Patients with PsA and fatigue had significantly more physician office visits than controls during follow-up (average of 11.4 and 8.0, respectively, $p< 0.0001$).

Conclusion: PsA patients with fatigue incurred significantly greater healthcare costs and resource utilization than patients without fatigue. Effective treatments that help reduce fatigue among patients with PsA may improve patient outcomes including decreased healthcare costs. Further research is warranted to better understand what is driving these greater costs.

Table 2. Healthcare resource utilization during follow-up

	Control group	PsA with fatigue	% and mean difference	P-value
Number of patients	7,350	7,350		
Inpatient hospitalizations				
Patients with an admission - N (%)	441 (6.0%)	742 (10.1%)	4.1%	<0.0001
Mean number of hospitalizations (SD)	0.08 (0.35)	0.14 (0.55)	0.06	<0.0001
Hospital outpatient services				
Patients with services - N (%)	4608 (62.7%)	5321 (72.4%)	9.7%	<0.0001
Mean number of services (SD)	12.66 (23.70)	20.02 (36.49)	7.36	<0.0001
Physician office visits				
Patients with visits - N (%)	7150 (97.3%)	7297 (99.3%)	2.0%	<0.0001
Mean number of visits (SD)	8.03 (6.11)	11.37 (7.86)	3.34	<0.0001
Radiology services				
Patients with services - N (%)	4745 (64.6%)	5621 (76.5%)	12.9%	<0.0001
Mean number of services (SD)	3.47 (4.87)	5.16 (7.33)	1.69	<0.0001
Emergency room services				
Patients with services - N (%)	1056 (14.4%)	1710 (23.3%)	8.9%	<0.0001
Mean number of services (SD)	0.90 (4.12)	1.86 (8.03)	0.96	<0.0001
Laboratory services				
Patients with services - N (%)	6754 (91.9%)	7206 (98.0%)	6.1%	<0.0001
Mean number of services (SD)	17.26 (18.55)	27.53 (26.13)	10.27	<0.0001
Outpatient pharmacy services				
Patients with a prescription - N (%)	6213 (84.5%)	6368 (86.6%)	2.1%	0.0056
Mean number of prescriptions (SD)	28.01 (28.24)	35.05 (32.40)	7.04	<0.0001

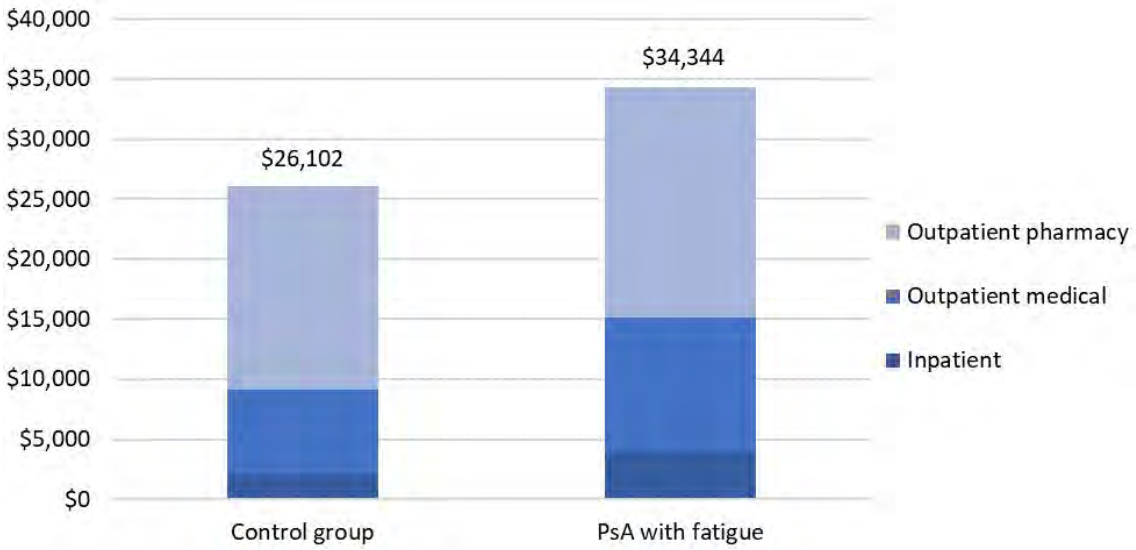

Figure 1. Average healthcare costs per patient during follow-up.

Disclosure: J. Merola, Dermavant, 5, LEO Pharma, 3, Abbvie, 2, Amgen, 2, Bayer, 2, Eli Lilly, 2, Novartis, 2, Janssen, 2, UCB, 2, 5, Celgene, 2, Sanofi-Regeneron, 2, Biogen, 2, Pfizer, 2, BMS, 2; **F. Yang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **N. Dennis**, None; **S. Peterson**, Janssen, 3, 11; **I. Lin**, Janssen Scientific Affairs, LLC, 3, Johnson & Johnson, 3, 11; **Y. Wang**, Janssen, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Quenéchdu**, None; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Fischer**, None; **E. Husni**, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2.

Abstract Number: 0241

Psoriasis Rate Is Increased by the Exposure to TNF Inhibition in Children with JIA

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Paradoxical psoriasis has been increasingly reported in adults after exposure to tumor necrosis factor inhibitors (TNFi). Systematic studies in the pediatric population are lacking. We aimed to investigate the relationship between TNFi therapy and the onset of new psoriasis in children with juvenile idiopathic arthritis (JIA) using Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry data.

Table 1. Baseline Demographics and Summary of Psoriasis Incidence

	Total Population N=8225
Gender (%Male)	2371 (28.8%)
Mean (Std) Age in Years at JIA Diagnosis	7.5 (4.8)
Initial ILAR Category	
Enthesitis related	854 (10.4%)
Oligoarthritis	2937 (35.7%)
Polyarthritis	3177 (38.6%)
Psoriatic	338 (4.1%)
Systemic	711 (8.6%)
Undifferentiaed	208 (2.5%)
Race	
White	6253 (76.0%)
Black	341 (4.2%)
Hispanic	896 (10.9%)
Asian	223 (2.7%)
Other	512 (6.2%)
TNFi Exposure	
Any Use	4437 (53.9%)
Etanercept	2818 (34.3%)
Adalimumab	2516 (30.6%)
Infliximab	590 (7.2%)
First TNFi Prescribed for Use	
Etanercept	2675 (60.3%)
Adalimumab	1527 (34.4%)
Infliximab	207 (4.7%)

Table 2. Association of TNFi Exposure* with New Onset of Psoriasis Among Patients with Juvenile Idiopathic Arthritis

	Unadjusted Hazard Ratio (95% CI)	p-value	Adjusted** Hazard Ratio (95% CI)	p-value
TNFi Ever Exposure				
Never Exposed	ref	-	ref	-
Ever Exposed	3.02 (2.26 to 4.02)	< 0.01	2.93 (2.15 to 3.98)	< 0.01

*TNFi exposure defined as any time observed after initial TNFi prescription, followed until psoriasis or censor

**Adjusted for methotrexate exposure (ever vs. never), gender, race, family hx of psoriasis, and initial ILAR category

Table 3. Summary of Psoriasis Incidence

	Incidence Rate Cases/1,000 Person-years (95%CI)	Median follow-up time (months)	Raw totals
Overall (All Follow-up time)	5.33 (4.67 to 6.07)	46.9	223 cases/41,831 person years
Never exposed to TNFi	3.27 (2.62 to 4.03)	20.4	84 cases/25,700 person years
Ever exposed to TNFi	8.62 (7.27 to 10.14)	33.3	139 cases/16,132 person years
First Exposure to TNFi	8.65 (6.67 to 11.03)	13.5	61 cases/7,056 person years
TNFi Specific exposure			
First Exposure Only			
Etanercept	6.78 (4.69 to 9.50)	15.1	31 cases/4,573 person years
Adalimumab	12.32 (8.22 to 17.8)	11.1	26 cases/2,110 person years
Infliximab	9.04 (2.30 to 24.59)	12.2	3 cases/ 332 person years
Ever Exposure*			
Etanercept	6.97 (4.88 to 9.68)	14.5	33 cases/4,731 person years
Adalimumab	11.98 (8.60 to 16.27)	9.4	38 cases/3,173 person years
Infliximab	6.44 (2.36 to 14.28)	10.4	5 cases/ 776 person years
Total Exposure			
Etanercept	5.46 (3.96 to 7.36)	22.5	40 cases/7,324 person years
Adalimumab	13.41 (10.30 to 17.18)	12.2	59 cases/4,400 person years
Infliximab	8.77 (4.88 to 14.61)	21.8	13 cases/1,483 person years

*With or without other prior TNFi Exposure

Methods: De-identified data were obtained from CARRA registry for patients enrolled in CARRA Registry with a diagnosis of JIA from June 30, 2015 to January 1, 2020 with follow up data available. Patients with Inflammatory Bowel Disease or psoriasis documented on or prior to JIA diagnosis date were excluded, as were patients with incomplete data regarding medication start/stop dates. New onset psoriasis was defined by first recorded instance of psoriasis following JIA diagnosis. Exposure time to TNFi was defined as: 1. Ever Exposure: any time observed after the patient's first exposure to a TNFi until censoring (psoriasis developed, or most recent visit date if continuing TNFi, or 60 days after the discontinuation of the TNFi, whichever was sooner); or 2. Total Exposure: any time observed while actively on TNFi, until censoring; or 3. First Exposure Only: any time observed while actively on the first TNFi, until censoring. Baseline characteristics were analyzed with descriptive statistics. Hazard ratios were calculated between exposed and unexposed groups adjusted for methotrexate exposure, sex, race, family history of psoriasis and initial JIA category.

Results: A total of 8,222 patients were included with a median follow up of 5.3 years. Over half of the patients were prescribed TNFi (n=4,435, 54%; Table 1). The hazard ratio of new onset of psoriasis after Ever Exposure to TNFi was 3.02 (CI 2.26 to 4.02, unadjusted) and 2.93 (2.15 to 3.98, adjusted) ($p< 0.01$) (Table 2). The incidence rate of psoriasis was the highest in children who received adalimumab in Ever Exposure, Total Exposure and First Exposure Only calculations (Table 3). A subanalysis of patients with psoriatic arthritis showed that the risk of new onset TNFi-associated

psoriasis was increased but the increased risk was lower than observed in the other categories combined. The adjusted hazard ratios (95% CI) of psoriasis after TNFi exposure was 1.68 (1.11 to 2.54, adjusted, p=0.01) in psoriatic JIA and 5.60 (3.47 to 9.05, adjusted, p< 0.01) in non-psoriatic JIA.

Conclusion: In a large prospective JIA patient registry, we observed a nearly 3 fold increased risk of psoriasis after TNFi exposure. Increasing awareness of this unwanted side effect in pediatric community is important to ensure timely diagnosis and treatment. Authors include the CARRA Registry Investigators

Disclosure: y. Zhao, Bristol Myers Squibb, 5, Novartis, 2; **E. Sullivan**, None; **M. Son**, None; **T. Beukelman**, UCB, 2, Novartis, 2.

Abstract Number: 0242

FiRst Line Options for Systemic JIA Treatment (FROST): Results from a Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry Consensus Treatment Plan Observational Study

Timothy Beukelman[1], George Tomlinson[2], Peter Nigrovic[3], Anne Dennos[4], Vincent Del Gaizo[5], Mary Ellen Riordan[6], Laura Schanberg[7], Shalini Mohan[8], Erin Pfeifer[9] and Yukiko Kimura[10], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Toronto, Toronto, ON, Canada, [3]Boston Children's Hospital, Brookline, MA, [4]Duke University, Durham, NC, [5]Childhood Arthritis & Rheumatology Research Alliance (CARRA), Whitehouse Station, NJ, [6]Hackensack University Medical Center, Westwood, NJ, [7]Duke University Medical Center, Durham, NC, [8]Genentech, Inc., South San Francisco, CA, [9]Genentech, Inc., Englewood, CO, [10]Hackensack University Medical Center, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The optimal initial treatment for systemic juvenile idiopathic arthritis (sJIA) is unclear. To further study the initial treatment of sJIA, the Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed Consensus Treatment Plans (CTPs) to formalize and standardize current treatment practices into 4 CTPs: initial systemic glucocorticoid (GC) only; initial methotrexate (MTX) +/- GC; initial IL-1 inhibition (IL-1i) +/- GC; and initial IL-6 inhibition (IL-6i) +/- GC. FiRst Line Options for sJIA Treatment (FROST) was a prospective observational study designed to assess the effectiveness and safety of each of the 4 CTPs.

Methods: Patients with recent onset sJIA who were initiating therapy were considered for enrollment in FROST. Key inclusion criteria were fever for ≥2 weeks, arthritis for ≥ 10 days, and at least 1 of the following: evanescent rash, generalized lymphadenopathy, hepatomegaly, splenomegaly, or serositis. Treatment assignment was at the discretion of the treating physician and family. Actual medication usage was captured. The primary study outcome was clinical inactive disease (CID; Wallace ACR provisional criteria) and no current use of GC at 9 months. Selected secondary outcomes included CID irrespective of current GC use and cJADAS-10 without current fever. Because few patients were treated with the GC, MTX, and IL-6i arms, only results for biologic therapy (IL-1i/IL-6i) and non-biologic therapy (GC/MTX) are presented. Results were attributed to the intended CTP, irrespective of treatment actually received (intention to treat). No statistical comparisons were made between treatment arms. Imputation of missing data was not performed.

Table 1. Characteristics of Participants in FROST at study enrollment (N=73)

Characteristic	Overall (N=73)	IL-1i/IL-6i (N=63)	GC/MTX (N=10)
Age (median (IQR))	6.8 (4.1, 11.0)	7.0 (4.0, 11.3)	6.2 (5.6, 7.8)
Male (%)	60%	64%	40%
White Race (%)	63%	67%	40%
Days Since Symptom Onset (mean (sd))	46 (64)	49 (68)	28 (18)
Days Since Diagnosis (median (IQR))	2 (0, 8)	1 (0, 8)	5.5 (0.5, 7)
Physician Global Assessment (mean (sd))	6.0 (2.2)	6.3 (2.1)	4.7 (2.8)
Parent Global Assessment (mean (sd))	5.6 (3.3)	5.7 (3.3)	5.4 (3.6)
Number of Active Joints (mean (sd))	6.6 (7.6)	7.0 (8.0)	4.1 (4.4)
ESR (median (IQR))	73 (57, 97)	71 (54, 97)	88 (76, 90)
C-RP (median (IQR))	15.4 (7.5, 58.1)	16.4 (7.5, 58.1)	13.5 (7.3, 51.4)
Ferritin (median (IQR))	829 (249, 2603)	884 (290, 2652)	363 (81, 779)
Hemoglobin (median (IQR))	10.2 (9.1, 11.4)	10.7 (9.1, 11.5)	9.4 (9.0, 10.2)
CHAQ (mean (sd))	1.3 (1.0)	1.4 (1.0)	1.2 (0.9)
cJADAS-10 (median (IQR))	17.0 (10.5, 21.5)	17.5 (12.0, 21.0)	14.0 (8.0, 23.0)

Table 2. Clinical outcomes at 9 months following enrollment in FROST (N=57)

Outcome	Overall	IL-1i/IL-6i	GC/MTX
CID without current GC use (N (%))	30/53 (57%)	27/47 (57%)	3/6 (50%)
CID irrespective of current GC use (N (%))	32/53 (60%)	29/47 (62%)	3/6 (50%)
cJADAS-10 ≤ 1 + no fever without current GC use (N (%))	32/48 (67%)	29/43 (67%)	3/5 (60%)
cJADAS-10 ≤ 1 + no fever irrespective of current GC use (N (%))	34/48 (71%)	31/43 (72%)	3/5 (60%)
cJADAS-10 ≤ 2.5 + no fever without current GC use (N (%))	36/48 (75%)	33/43 (77%)	3/5 (60%)
cJADAS-10 ≤ 2.5 + no fever irrespective of current GC use (N (%))	38/48 (79%)	35/43 (81%)	3/5 (60%)
cJADAS-10 (mean (SD))	1.5 (3.3)	1.3 (3.0)	3.4 (5.6)
cJADAS-10 (median (IQR))	0 (0, 1.0)	0 (0, 1.0)	0 (0, 4.0)

Results: Overall, 73 patients (characteristics in Table 1) were enrolled in FROST (63 IL-1i/IL-6i and 10 GC/MTX). As intended, all patients in the IL-1i/IL-6i arm started biologic therapy. Initiation of biologic therapy ranged from 7 days prior to enrollment to 61 days after with 75% initiating within 1 day after enrollment. 8/59 (14%) patients who initiated IL-1i subsequently switched to IL-6i, and 0/4 (0%) patients switched from IL-6i to IL-1i. Among patients in the GC/MTX arm, 5 (50%) eventually initiated biologic therapy during the study period (time to initiation 10 to 101 days). The 9-month outcomes are shown in Table 2. 16 patients did not have a 9-month visit recorded. Overall, 57% of patients met the primary outcome of CID without current GC use, and 75% had cJADAS-10 score ≤ 2.5 with no fever and no current GC use. Overall, there were 16 CTCAE grade 3 or higher safety events observed (all in IL1i/IL-6i arm), including 6 episodes of MAS. One patient died of acute liver failure.

Conclusion: Treatment practices have changed tremendously since the CARRA sJIA CTPs were initially developed. Initial biologic therapy is now the most common treatment approach among sJIA patients enrolled in the CARRA Registry. A substantial proportion of patients not initially started on biologics subsequently started a biologic within

the first few months following diagnosis. Excellent treatment outcomes were observed in 57% to 75% of FROST patients overall, depending on the outcome definition.

Disclosure: T. Beukelman, UCB, 2, Novartis, 2; **G. Tomlinson**, None; **P. Nigrovic**, None; **A. Dennos**, None; **V. Del Gaizo**, CARRA, 3; **M. Riordan**, None; **L. Schanberg**, UCB, 12, DSMB member, Sanofi, 12, DSMB member, SOBI, 2, BMS, 5; **S. Mohan**, Genentech, Inc, 3; **E. Pfeifer**, Genentech, Inc., 3; **Y. Kimura**, Genentech, 5, UpToDate, 9, CARRA, 4, 12, Salary support.

Abstract Number: 0243

Effectiveness of Abatacept in Patients with JIA, Classified by Category: Results from the PRCSG/PRINTO JIA Real-World Registry

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Table 1. cJADAS10 scores (mean [median]) by JIA category from baseline to month 60

JIA category	cJADAS10 score	3 months	6 months	9 months	12 months	24 months	36 months	48 months	60 months
Overall	Patient	n = 354 5.8 (4)	n = 336 6.0 (4.3)	n = 321 5.3 (4.0)	n = 328 4.9 (2.5)	n = 214 4.1 (2.5)	n = 135 4.6 (3.0)	n = 85 4.2 (3.0)	n = 46 4.8 (4.3)
	Parent	n = 348 6.1 (4.5)	n = 329 6.0 (3.5)	n = 298 5.4 (4.0)	n = 285 4.6 (2.5)	n = 169 3.9 (2.0)	n = 87 4.4 (3.0)	n = 44 4.3 (3.0)	n = 16 4.4 (3.3)
Polyarticular RF−	Patient	n = 188 5.9 (4.0)	n = 184 6.3 (4.5)	n = 180 5.3 (4.0)	n = 179 5.1 (3.0)	n = 118 3.7 (2.5)	n = 77 4.2 (3.0)	n = 49 4.2 (3.5)	n = 31 5.1 (4.5)
	Parent	n = 186 6.6 (5.0)	n = 178 6.6 (4.0)	n = 166 5.5 (4.0)	n = 149 4.8 (3.0)	n = 95 3.9 (2.5)	n = 46 4.7 (3.3)	n = 24 4.8 (3.8)	n = 10 5.6 (4.8)
Extended oligoarticular	Patient	n = 80 4.6 (2.5)	n = 74 4.9 (3.0)	n = 68 3.6 (2.8)	n = 68 3.6 (1.5)	n = 48 3.7 (1.8)	n = 27 4.0 (3.0)	n = 18 5.1 (3.0)	n = 8 2.6 (2.8)
	Parent	n = 87 4.6 (3.0)	n = 80 4.6 (3.0)	n = 67 3.6 (2.5)	n = 74 3.6 (1.3)	n = 43 2.8 (2.0)	n = 24 4.0 (3.0)	n = 14 4.1 (2.3)	n = 5 2.8 (3.0)
Polyarticular RF+	Patient	n = 34 5.4 (3.0)	n = 33 5.2 (2.5)	n = 31 5.4 (3.5)	n = 33 4.3 (2.0)	n = 20 6.1 (5.3)	n = 14 7.4 (4.8)	n = 7 4.6 (2.0)	–
	Parent	n = 25 5.0 (2.0)	n = 31 5.5 (3.0)	n = 25 5.2 (4.0)	n = 22 3.8 (1.5)	n = 9 4.8 (5.5)	n = 6 3.7 (0.8)	–	–
Psoriatic	Patient	n = 16 5.6 (5.3)	n = 13 4.2 (4.0)	n = 13 4.7 (4.0)	n = 14 4.8 (3.5)	n = 7 2.3 (2.5)	n = 7 3.4 (3.0)	n = 5 3.8 (1.5)	–
	Parent	n = 16 5.7 (4.8)	n = 13 3.7 (3.5)	n = 13 4.9 (3.0)	n = 13 3.9 (2.5)	n = 5 1.1 (1.0)	–	–	–
Enthesitis-related	Patient	n = 14 6.6 (5.5)	n = 13 7.1 (5.5)	n = 13 8.9 (7.5)	n = 13 5.7 (5.0)	n = 6 5.1 (2.8)	–	–	–
	Parent	n = 10 6.6 (5.3)	n = 11 6.9 (6.0)	n = 12 9.7 (8.3)	n = 9 5.9 (5.0)	n = 5 5.9 (2.5)	–	–	–
Undifferentiated	Patient	n = 15 7.8 (7.0)	n = 12 8.1 (7.0)	n = 10 7.2 (6.3)	n = 14 4.8 (1.0)	n = 9 5.9 (1.5)	–	–	–
	Parent	n = 17 8.3 (7.5)	n = 11 8.1 (10.0)	n = 8 6.6 (5.3)	n = 12 7.5 (4.5)	n = 8 7.5 (4.8)	–	–	–
Systemic	Patient	n = 7 12.7 (14.5)	n = 7 11.1 (11.0)	n = 6 14.1 (14.8)	n = 7 12.4 (11.5)	n = 6 6.9 (4.5)	–	–	–
	Parent	n = 7 12.5 (13.0)	n = 5 9.4 (9.5)	n = 7 12.6 (9.5)	n = 6 10.9 (8.0)	–	–	–	–

Blank boxes mean n < 5.
cJADAS10, clinical 10-joint Juvenile Arthritis Disease Activity Score.

SESSION INFORMATION

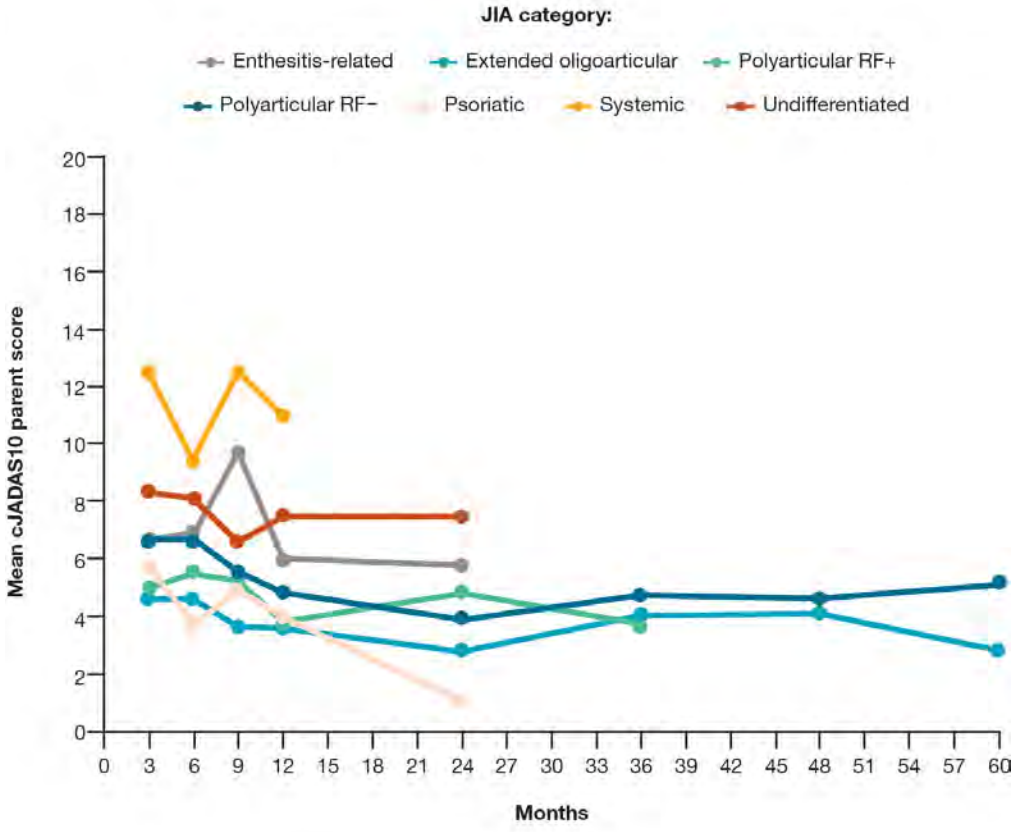
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Long-term treatment with abatacept, a selective T-cell co-stimulation modulator, is effective and well tolerated in patients with JIA.[1–4] The objective of this analysis was to provide real-world data on the longitudinal effectiveness of intravenous (IV) and subcutaneous (SC) abatacept in patients with JIA, classified by category, enrolled in the Pediatric Rheumatology Collaborative Study Group (PRCSG)/Paediatric Rheumatology INternational Trials Organisation (PRINTO) registry.

Methods: Following a standardized protocol and data collection process, clinical sites across 23 countries enrolled patients with JIA receiving/initiating IV or SC abatacept with a planned 10-year duration of follow-up. Treatment response was assessed at 3, 6, 9, 12, 24, 36, 48, and 60 months, and was evaluated in this analysis by clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10). The cJADAS10 used validated cut-offs for low disease activity (LDA; ≤3.8), inactive disease (ID; ≤ 1.0)[5], and remission (ID for ≥ 6 months). An as-observed analysis is presented.

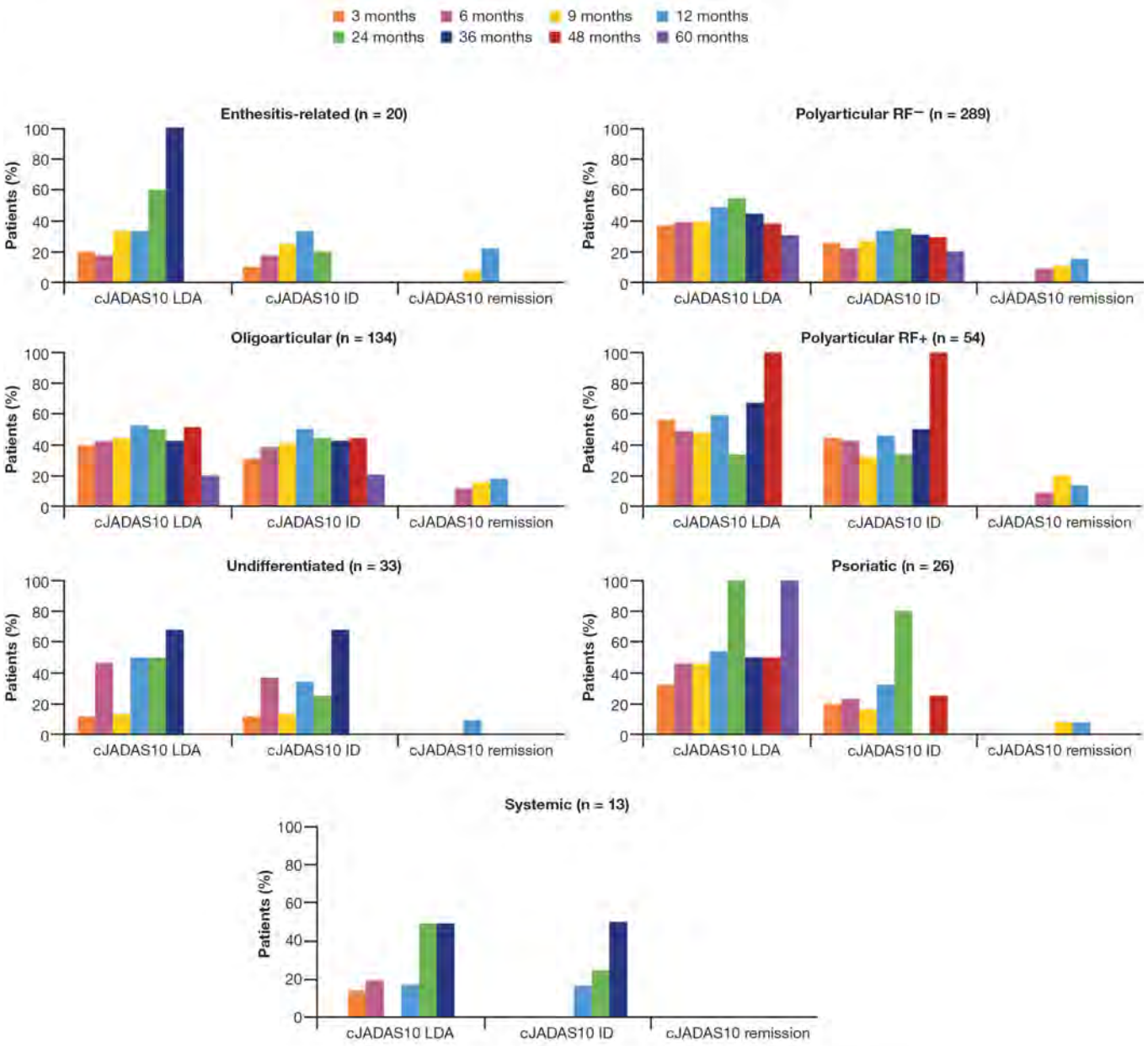
Results: As of March 31, 2020, 569 patients were enrolled in the PRCSG/PRINTO registry; 454 (79.8%) were female. Mean age at enrollment was 13.1 years, mean time since JIA diagnosis was 66.1 months, and mean abatacept treat-

Figure 1. Mean cJADAS10 score (parent) over time by JIA category (as-observed analysis; data for n ≥ 5 shown)



cJADAS10, clinical 10-joint Juvenile Arthritis Disease Activity Score.

Figure 2. Proportions of patients who achieved cJADAS10 (parent) LDA, cJADAS10 (parent) ID, and cJADAS10 (parent) remission over 60 months by JIA category (as-observed analysis)



Validated cJADAS cut-off scores for polyarticular JIA were used: LDA (≤ 3.8), ID (≤ 1.0), and remission (defined as ID for ≥ 6 months).
cJADAS10, clinical 10-joint Juvenile Arthritis Disease Activity Score; ID, inactive disease; LDA, low disease activity.

ment duration was 13.1 months. Half of the patients (n = 289; 50.8%) had polyarticular RF– JIA and a quarter (n = 134; 23.6%) had extended oligoarticular JIA; other enrolled patients had polyarticular RF+ (n = 54; 9.5%), psoriatic (n = 26; 4.6%), enthesitis-related (n = 20; 3.5%), undifferentiated (n = 33; 5.8%), and systemic (n = 13; 2.3%) JIA. The treatment response (patient and parent cJADAS10 score) by JIA category from baseline to month 60 is shown in Table 1. The change in mean cJADAS10 score over time by JIA category (Figure 1) demonstrates a general trend towards reduced score over time. The proportions of patients achieving cJADAS10 LDA and ID by JIA category were generally improved or sustained over time (Figure 2). The low patient numbers in some JIA categories at later time

points were mainly due to patients being lost to follow-up or not having reached those time points due to ongoing enrollment. At 60 months, 30% and 20% of patients with polyarticular RF– JIA (most prevalent category) had achieved and maintained cJADAS10 LDA and ID, respectively. Overall, 14.7% of patients achieved cJADAS10 remission by month 12; similar trends (7–22%) were seen in most JIA categories.

Conclusion: A proportion of patients in each JIA category achieved cJADAS10 LDA and ID. As sample size decreased over time in some JIA categories, these data should be interpreted with caution. Clinically important and sustained responses with abatacept, generally up to 36 and 48 months, were seen in all JIA categories.

References: 1. Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144–1154. 2. Ruperto N, et al. *Lancet* 2008;372:383–391. 3. Lovell DJ, et al. *Arthritis Rheumatol* 2015;67:2759–2770. 4. Ruperto N, et al. *Arthritis Rheumatol* 2010;62:1792–1802. 5. Consolaro A, et al. *Arthritis Care Res (Hoboken)* 2014;66:1703–1709.

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hospital in a fully independent manner without any commitment to third parties, Merck, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Novartis, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Sanofi, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Aurina, 2; **N. Ruperto**, Ablynx, 2, 6, Amgen, 2, 6, Astrazeneca-Medimmune, 2, 6, Aurinia, 2, 6, Bayer, 2, 6, Bristol Myers and Squibb, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Cambridge Healthcare Research (CHR, 2, 6, Celgene, 2, 6, Domain therapeutic, 2, 6, Eli-Lilly, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, EMD Serono, 2, 6, Glaxo Smith and Kline, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Pfizer, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Sobi, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, UCB, 2, 6, F Hoffmann-La Roche, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties.

Abstract Number: 0244

Development of Candidate Criteria for Axial Disease in Juvenile Spondyloarthritis: An International Collaboration

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Central experts' MRI findings
Inflammation
Inflammation in subchondral bone marrow?
Inflammation at site of an erosion cavity?
Inflammation in SIJ capsule?
Joint space enhancement on a contrast enhanced sequence?
Joint fluid?
Enthesitis outside the SI joint?
Structural lesions
Sclerosis?
Erosion?
Fat lesion?
Fat metaplasia in an erosion cavity?
Ankylosis?

Figure 1. Lesions reported by majority of central imaging team as present or absent during the juvenile spondyloarthritis experts' case review that included clinical factors plus central imaging team assessment.

Background/Purpose: As part of a larger study developing classification criteria for axial disease in children with spondyloarthritis (SpA), the objective of this project phase was to identify the strength of association of clinical and imaging features with expert classification.

Methods: We identified key clinical and imaging features to classify children with axial disease through an iterative process that included international Delphi exercise for item generation, systematic literature review, and an item reduction exercise. Case report forms and pelvic imaging (MRI and, if available, radiograph) of children with SpA and suspected axial disease were collected from 14 international centers. All imaging was rated by ≥2 of 7 radiologists from a central imaging team. The central imaging assessment consisted of presence or absence of the lesions shown in Figure 1. Fourteen juvenile SpA experts completed two global assessments using: (1) clinical features and local radiograph report (if available) and (2) clinical factors plus central imaging team assessment (MRI ± radiograph). Each SpA expert rated their confidence that the case was "juvenile SpA with axial disease" on a scale with anchors -3 (very unlikely) to +3 (very likely). High confidence in expert assessment was defined as ≤-2 or ≥+2. Each case was reviewed by 3 experts and consensus was defined as ≥2/3. Strength of association was measured using odds ratios.

Results: Eight domains were chosen for inclusion in the preliminary classification criteria (Table 1). 304 cases were assessed by the experts, of which 208 (68.4%) had findings typical of axial juvenile SpA by the central imaging team. Expert consensus was achieved on 132 (43%) and 202 (66%) of cases with clinical factors (± radiograph) or clinical factors plus central imaging assessment. With central imaging data, the presence of HLA-B27, pain most days, and morning stiffness in the hip/groin were most highly associated with rater confidence in presence of axial disease (Table 1). After the addition of central imaging data, several factors lost their significant association with rater confidence in presence of axial disease, including patient-reported lumbar spinal pain, sacroiliac pain on examination, and nighttime pain. Adding central imaging data affected the consensus assessment of high confidence in the presence/absence of axial disease for 55% (168/304) of cases. The addition of central imaging data facilitated achievement of a majority consensus on an additional 113 cases but lost consensus on 37; of the 113 cases gaining consensus, 43 and 70 reached consensus with high confidence that the case was or was not likely axial disease, respectively. For 18 (5.9%) cases, it changed the directionality of high confidence; 5 cases from axial disease present to axial disease absent and 13 cases from not axial disease to axial disease present.

Conclusion: Imaging significantly impacts the assessment of the presence/absence of axial disease in juvenile SpA and the association of several clinical domains with axial disease. In addition to imaging, HLA-B27 presence, pain

experienced most days, and stiffness in the hip and groin are significantly associated with high rater confidence in axial disease.

Table 1. Features associated with high rater confidence in axial disease with and without central imaging data. Cohort limited to cases where majority raters had high confidence the case was not likely to be axial disease or high confidence the case was likely to be axial disease.

		Clinical data +/- radiograph (N=132)	Clinical plus central imaging data (N=202)
	DOMAIN and Levels	OR (95%CI)	
1	PAIN LOCATION (in groin/hip/buttocks/sacrum/lumbar spine)		
	Lumbar spine pain (patient-reported)	8.82 (4.01-19.43)	1.09 (0.62-1.90)
	Sacroiliac pain with deep palpation/FABER/Mennell/Gaenslen maneuvers	3.19 (1.56-6.51)	1.71 (0.97-2.99)
	Groin/Hip pain (patient-reported)	2.8 (1.38-5.68)	2.83 (1.59-5.03)
	Sacral/Buttock pain (patient-reported)	7.95 (2.81-22.50)	3.49 (1.79-6.82)
2	PAIN CHRONICITY (in groin/hip/ buttocks/sacrum/lumbar spine)		
	Duration		
	≥6 but <12 weeks	0.95 (0.33-2.73)	1.81 (0.52-6.25)
	≥12 weeks	1.2 (0.46-3.13)	2.07 (0.67-6.40)
	Frequency		
	Most days (≥4 days per week)	3.71 (1.19-11.50)	5.5 (1.30-23.32)
	Present every day	2.55 (0.91-7.11)	4.08 (1.07-15.59)
3	PAIN PATTERN (in groin/hip/ buttocks/sacrum/lumbar spine)		
	Nighttime pain	3.17 (1.09-9.17)	1.42 (0.66-3.04)
	Insidious onset	4.71 (1.35-16.50)	3.11 (1.06-9.13)
	Moderate to total relief with nonsteroidal anti-inflammatory medications	4.95 (1.33-18.41)	3.07 (1.12-8.40)
	Improves with activity	13.87 (5.00-38.42)	3.57 (1.83-6.95)
4	STIFFNESS DURATION (in groin/hip/buttocks/sacrum/lumbar spine)		
	≥15 min to <30mins	5.75 (1.00-32.95)	1.36 (0.41-4.47)
	≥30 mins	2.63 (0.53-13.10)	2.07 (0.66-6.54)
5	STIFFNESS PATTERN (in groin/hip/buttocks/sacrum/lumbar spine)		
	Improves with rest	0.47 (0.16-1.41)	1.65 (1.02-2.69)
	Nighttime stiffness	4.71 (0.51-43.36)	2 (0.48-8.41)
	Improves with activity	8.44 (1.50-47.48)	5.09 (1.39-18.60)
	Morning stiffness in buttocks/sacrum/lumbar spine	40.44 (14.52-112.66)	2.46 (1.36-4.46)
	Morning stiffness in hip/groin	6.41 (2.74-14.99)	4.51 (2.24-9.09)

OR = Odds ratio; CI = Confidence interval;

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Long-term Safety and Effectiveness of Abatacept Treatment in Patients with JIA: 5-year Results from the PRCSG/PRINTO JIA Real-World Registry

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Baseline characteristics for the overall JIA population

Characteristic	Patients, N	Value
Age at enrollment, years	569	13.6 (2.9–20.1)
Sex, n (%)		
Female	569	454 (79.8)
Male		115 (20.2)
Months since JIA diagnosis	569	53.7 (0.8–198.5)
Time on abatacept treatment at baseline, months, mean (median)	569	13.1 (6.5)
Physician global disease activity, VAS (0–100)	569	1.0 (0.0–9.5)
JAMAR functionality scale		
Patient	457	3.0 (0.0–36.0)
Parent	482	3.0 (0.0–40.0)
Number of active joints	569	1.0 (0.0–42.0)
Number of joints with LOM	569	1.0 (0.0–65.0)

Data are median (1st–3rd quartiles) unless otherwise stated.

JAMAR, Juvenile Arthritis Multidimensional Assessment Report; LOM, limited range of motion; VAS, visual analog scale.

Table 2. Safety summary for the overall JIA registry population for the total 5-year follow-up period

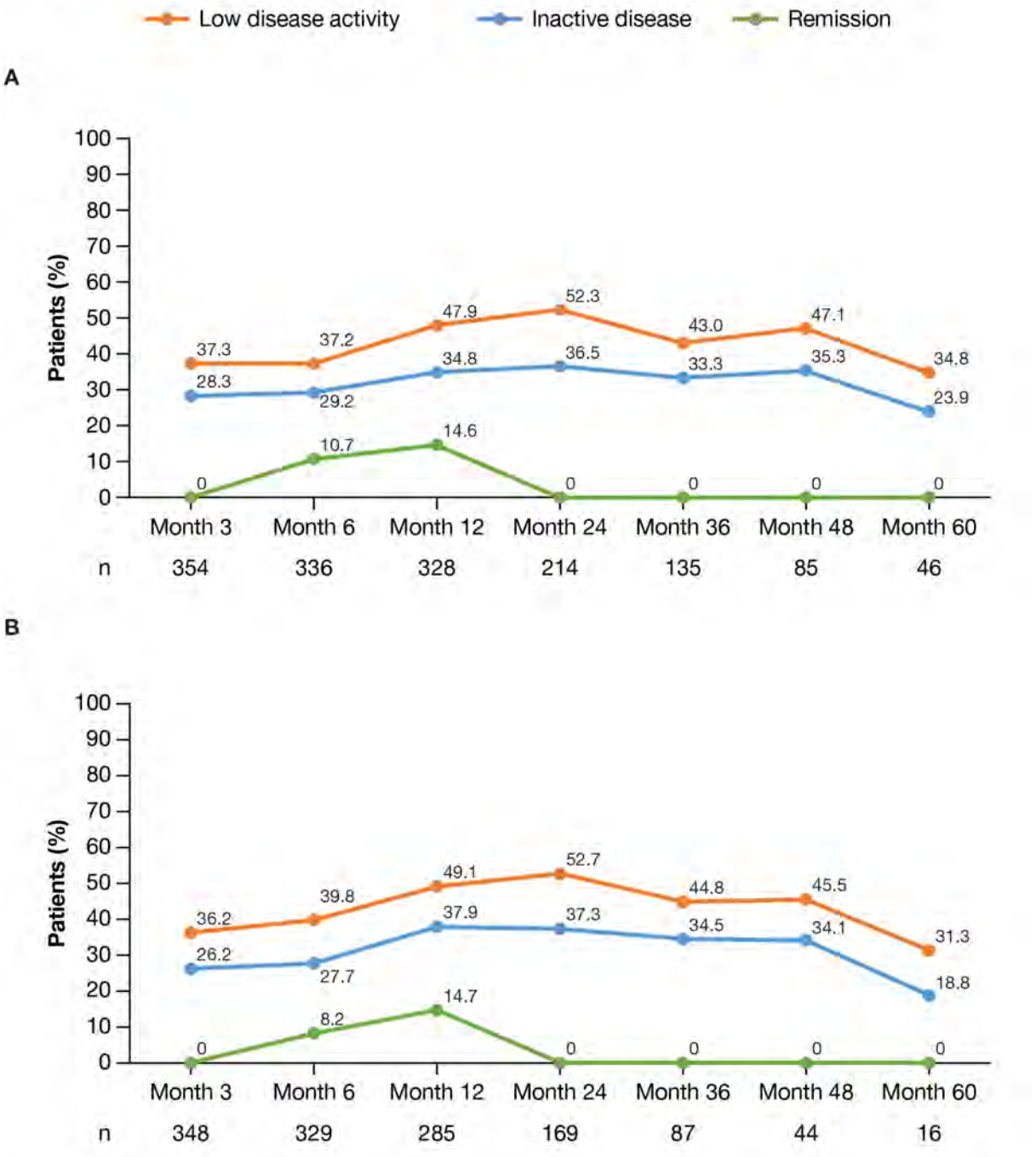
Outcome	Patients, n (%) (N = 569)	Incidence rate[a] (95% CI)
Patients with ≥ 1 AE	95 (16.7)	7.82 (6.33–9.56)
Patients with ≥ 1 SAE	67 (11.8)	5.52 (4.27–7.01)
Patients with ≥ 1 treatment-related SAE	16 (2.8)	1.32 (0.75–2.14)
Patients with ≥ 1 AE causing permanent discontinuation	9 (1.6)	0.74 (0.34–1.41)
Patients with any AE resulting in death[b]	1 (0.2)	0.08 (0.00–0.46)
Patients with ≥ 1 event of special interest	44 (7.7)	3.62 (2.63–4.86)
Serious/targeted infections	18 (3.2)	1.48 (0.88–2.34)
Other autoimmune diseases	8 (1.4)	0.66 (0.28–1.30)
Skin and subcutaneous tissue disorders	8 (1.4)	0.66 (0.28–1.30)
Malignancy	1 (0.2)	0.08 (0.00–0.46)
Antibody testing	**Tests, n (%) (N = 202)**	
Anti-abatacept antibody positive[c]	12 (5.9)	N/A

[a]Incidence rate per 100 patient-years per 569 subjects with 1214.61 person-years of follow up; [b]Due to a cardiovascular event related to pre-existing disease and assessed as unrelated to abatacept treatment; [c]n = 11 specifically for CTLA-4 and possibly for immunoglobulin, and n = 1 specifically for immunoglobulin and/or junction region.

AE, adverse event; CTLA-4, cytotoxic T-lymphocyte associated antigen 4; N/A, not available; SAE, serious AE.

Background/Purpose: Abatacept (ABA) is well tolerated and effective in patients with JIA.[1] The Pediatric Rheumatology Collaborative Study Group (PRCSG)/ Paediatric Rheumatology INternational Trials Organisation (PRINTO) registry monitors long-term safety and efficacy of ABA for JIA treatment.[2] The objective of this analysis was to assess

Figure 1. Proportions of patients achieving cJADAS10 low disease activity, inactive disease, and remission as reported by (A) patients and (B) parents



Remission was defined as inactive disease for ≥ 6 months. Decreasing n over time is due to ongoing enrollment (patients may not have reached later time points at data cut) and loss to follow-up.
cJADAS10, clinical 10-joint Juvenile Arthritis Disease Activity Score.

long-term (5-year) safety and efficacy of ABA in patients with JIA in a real-world setting using data from the PRCSG/PRINTO registry.

Methods: All patients with JIA receiving IV/SC ABA enrolled in the PRCSG/PRINTO registry with ≥ 5 years follow-up were included. Safety and efficacy were assessed at 3, 6, 12, 24, 36, 48, and 60 months. Safety was evaluated by recording serious adverse events (SAEs), events of special interest (ESI; incidence rate [IR]/100 patient-years (py) [95% CI]) and anti-ABA antibody levels. Efficacy outcomes: physician global assessment of disease activity, physician assessment of JIA severity, Juvenile Arthritis Multidimensional Assessment Report (JAMAR) functionality score, overall well-being score, number of active joints, joints with limited range of motion (LOM), clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10), and JIA-ACR30, 50, 70, and 90. cJADAS10 used validated cut-offs for low disease activity (LDA), inactive disease (ID), and remission (ID for ≥ 6 months). As-observed analysis is presented.

Results: Data for 569 patients (1214.61 py of follow-up) were available up to Mar 31, 2020. Baseline characteristics are summarized in Table 1. Over 60 months, IRs/100 py (95% CIs) of patients with ≥ 1 SAE, treatment-related SAE, or ESI were 5.5 (4.3–7.0), 1.3 (0.8–2.1), and 3.6 (2.6–4.9), respectively (Table 2). Overall, 5.9% (12/202) anti-ABA antibody tests were positive. From months 3–60, median physician global disease activity, number of active joints, and joints with LOM were unchanged. The proportion of patients with physician-assessed mild JIA increased from 86% to 96%; corresponding proportions of patients with moderate or severe JIA decreased from 11% to 4% and from 3% to 0%, respectively. Median JAMAR functional scores were 2.0 (patient) and 3.0 (parent) at month 3, and 1.0 each at month 60; a similar pattern was observed for overall well-being scores. Median cJADAS10 scores were 4.0 (patient) and 4.5 (parent) at baseline, and 4.3 (patient) and 3.3 (parent) at month 60. As early as month 3, cJADAS10 LDA and ID were achieved by 37% and 28% of patients, respectively, and sustained over time (Figure 1).

Conclusion: Overall, in patients with JIA, abatacept was well tolerated with no new safety signals. Treatment with abatacept resulted in well-controlled disease activity, with approximately 30% of patients achieving cJADAS10 ID by month 3, which was sustained over 2 years. For the majority of patients, initial improvement on abatacept occurred prior to registry enrollment; therefore the ability to maintain response with ongoing treatment is reflected. These real-world data support the safety and efficacy profile of abatacept as seen in clinical trials.

References

1. Lovell DJ, et al. *Arthritis Rheumatol* 2015;67:2759–2770.
2. Lovell DJ, et al. ACR 2020. Abstract 0714.
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manner without any commitment to third parties, Idorsia, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Cerocor, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, F.Hoffman-La Roche, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Merck, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Novartis, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Sanofi, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Aurina, 2; **D. Lovell**, Bristol Myers Squibb, 12, PI, Abatacept, Juvenile Idiopathic Arthritis, AstraZeneca Pharm, 2, Boehringer Ingleheim, 2, GSK, 2, Hoffman LaRoche, 2, Janssen, 12, Co-PI of overall studies of IV and sub-Q Golimumab in JIA, NIH / NIAMS, 12, R01 AR074098-01A1, NIH / NICHD, 12, NIH / R01 HD 089928-01A1, Novartis, 2, Pfizer, 3, Roche, 12, PI, Tociluzumab, Juvenile Idiopathic Arthritis, UBC, 2; **M. Henrickson**, None; **R. Carrassco**, Novartis, 1; **K. Minden**, Pfizer, 2, 6, Pfizer, 5, Abbvie, 5, 6, Novartis, 2, 6, Novartis, 5, Sanofi, 2, German Arthritis Foundation, 5, Roche, 5, Chugai, 5, GSK, 5, BMS, 5, Biogen, 5; **L. Grebenkina**, None; **J. Nocton**, Bristol Myers Squibb, 5, 12, Site PI for Abatacept Registry research study; **I. Louw**, None; **L. Wagner-Weiner**, Bristol-Myers Squibb, 12, PI / researcher at University of Chicago, Pfizer, 12, PI / researcher at University of Chicago, Abbott, 12, PI / researcher at University of Chicago, UCB, 12, PI / researcher at University of Chicago; **G. Vega Cornejo**, Grin Laboratories, 6, Abbvie, 6, Bayer, 6; **S. Kamphuis**, GlaxoSmithKline, 7, Aurinia, 2; **V. Chasnyk**, Pfizer, 5, Novartis, 5, Amgen, 5, Elli Lilly, 5, Bristol Myers Squibb, 5, GlaxoSmithKline, 5, Roche, 5; **H. Walters**, None; **S. Appenzeller**, None; **J. Anton**, Abbvie, 5, Pfizer, 2, GSK, 2, 5, 6, Roche, 5, Sobi, 2, 5, 6, Novartis, 2, 5, 6, Amgen, 5, Lilly, 5, BMS, 5; **A. Dominique**, Bristol Myers Squibb, 3; **R. Wong**, Bristol Myers Squibb, 3; **L. Dong**, Bristol-Myers Squibb, 3; **T. Kou**, Bristol Myers Squibb, 3; **A. Martini**, Aurinia, 2, 6, Bristol Myers and Squibb, 2, 6, Eli-Lilly, 2, 6, EMD Serono, 2, 6, Janssen, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **N. Ruperto**, Ablynx, 2, 6, Amgen, 2, 6, Astrazeneca-Medimmune, 2, 6, Aurinia, 2, 6, Bayer, 2, 6, Bristol Myers and Squibb, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Cambridge Healthcare Research (CHR, 2, 6, Celgene, 2, 6, Domain therapeutic, 2, 6, Eli-Lilly, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, EMD Serono, 2, 6, Glaxo Smith and Kline, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Pfizer, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Sobi, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, UCB, 2, 6, F Hoffmann-La Roche, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties.

Abstract Number: 0246

Macrophage Activating Syndrome in Patients with Systemic Juvenile Idiopathic Arthritis Treated with Biological Drugs

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) is the most acute and severe form of JIA. Despite the substantial evidence supporting the effectiveness of biologic drugs in the treatment of SJIA, the clinical response has not been largely investigated in Turkey. Macrophage activation syndrome (MAS) is a complication that often occurs during SJIA and associated with mortality.

TURSIS, the 24-month, multi-center, retrospective, non-interventional study aimed to assess the clinical response to biological treatments for SJIA and provide real life data to improve disease outcomes.

Methods: This was a retrospective, multi-center study in patients with SJIA for whom a biological treatment had been initiated. This real-life study is based on secondary data collection from medical records of patients evaluated at the 8 Pediatric Rheumathology Clinics in Turkey (Mar 2013-Dec 2018). Patients' characteristics, clinical inactivity, safety related variables, and ACR70 response were assessed.

Results: The study population (147 patients) consisted of 76 females (51.7%).

During the 2-year study period, 51.0% of patients (n=75) remained on the same biologic. 62 patients (42.2%) had experienced 1 switch in biological drug, and 10 patients (6.8%) switched twice.

32 patients (22.4%) had experienced a MAS attack between the diagnosis of SJIA and baseline (median 5 months). Most of the patients (81.3%) had experienced a single MAS attack; the highest number of MAS attacks per patient was 4. The frequent clinical signs of MAS were persistent fever (93.8%) and rash (81.3%). The frequencies of other clinical findings such as lung and CNS involvement, seizures and encephalopathy were lower during MAS attacks. Available data about the laboratory findings associated with MAS (n=32) revealed that hyperferritinemia was the most observed finding (96.9%) followed by a decrease in Hb level (84.4%) and an increase in LDH level (71.9%). Increased liver function tests (65.6%), hypofibrinogenemia (56.3%), hypoalbuminemia (62.5%), decrease in ESR (59.4%) and hemophagocytosis (53.1%) were the other laboratory findings observed in more than half of the patients with MAS.

Nine patients experienced MAS after baseline during study period. MAS attack was not observed in any patient 12 months after the initiation of biological therapy.

At Month 3, 73.5% of patients were clinically inactive. ACR30, 50 and 70 responses could be achieved in 95.5%, 50% and 45.5% of patients, respectively.

Conclusion: This study described the patient characteristics and the impact of biological drugs on disease activity in a real-life study of patients with SJIA in Turkey. Overall biological therapies resulted in improvement in clinical activity early after initiation. There was a decrease in the frequency of MAS after initiation of biological drugs compared with time to initiation of biologic therapy. Biological drugs were generally well tolerated. Further studies can reveal the differences between the biological drugs on disease outcomes and guide treatment decisions, thereby improving patient management.

Disclosure: B. Sozeri, Novartis, 6; **K. Barut**, Novartis, 6; **E. Atalay**, None; **A. Pac Kisaarslan**, Novartis, 6; **S. Ozdel**, Novartis, 6; **O. Altug**, Novartis, 6; **F. Demir**, None; **B. Makay**, Novartis, 6; **N. Aktay Ayaz**, Novartis, 6; **E. Acar**, Novartis, 3; **F. Haslak**, None; **E. Sag**, Novartis, 6; **M. YILDIZ**, None; **U. Kaya Akca**, None; **A. Adrovic**, Novartis, 6; **Y. Bilginer**, Novartis, 6; **H. Poyrazoglu**, None; **E. Unsal**, Novartis, 6; **O. Kasapcopur**, Novartis, 6, Pfizer, 6, Roche, 6, Abbvie, 6; **S. Ozen**, Novartis, 6.

Abstract Number: 0247

Three-year Effectiveness in Patients with JIA Initiating Abatacept: Results from the PRCSG/PRINTO JIA Real-World Registry

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The ongoing phase 4 Pediatric Rheumatology Collaborative Study Group (PRCSG)/Paediatric Rheumatology INternational Trials Organisation (PRINTO) registry was designed to assess the long-term (up to 10 years) safety and efficacy of abatacept in pediatric patients with all JIA subtypes in a real-world setting.[1] The objective of this analysis was to assess the real-world effectiveness of intravenous and subcutaneous abatacept over 3 years in patients with JIA who initiated treatment with abatacept within 1 month of enrollment in the PRCSG/PRINTO registry.

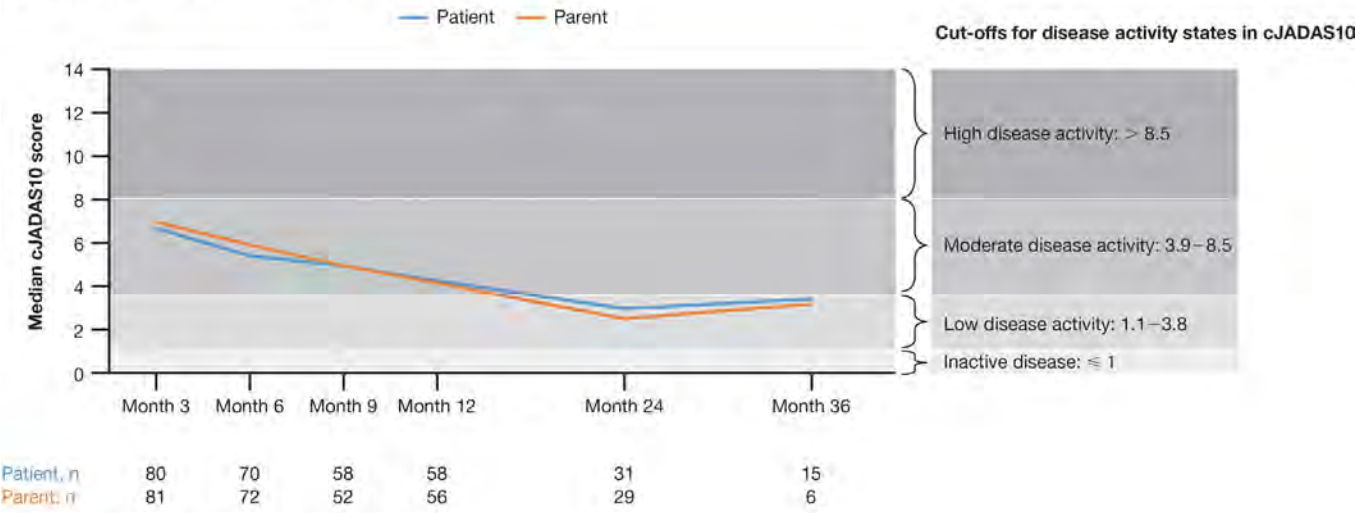
Table 1. Effectiveness outcomes over time in patients with JIA who initiated abatacept within 1 month of enrollment in the PRCSG/PRINTO registry

Outcome	Baseline (N = 134)	Month 3 (N = 134)	Month 6 (N = 134)	Month 9 (N = 134)	Month 12 (N = 134)	Month 24 (N = 134)	Month 36 (N = 134)
Physician global disease activity	3.8 (3.8)	n = 104 2.4 (2.0)	n = 98 2.4 (2.0)	n = 74 1.8 (1.0)	n = 74 1.8 (1.0)	n = 44 1.2 (0.3)	n = 18 1.6 (0.8)
Overall well-being score	4.5 (5.0)	n = 81 3.3 (3.0)	n = 72 3.2 (2.5)	n = 52 2.8 (2.0)	n = 56 2.6 (2.0)	n = 29 2.3 (2.0)	n = 6 1.7 (1.5)
Number of active joints	6.1 (3.0)	n = 104 3.3 (1.0)	n = 98 2.9 (1.0)	n = 74 1.8 (0.0)	n = 74 1.5 (0.0)	n = 44 1.8 (0.0)	n = 18 1.8 (0.0)
Number of joints with limitation in range of motion	6.3 (2.0)	n = 104 3.2 (1.0)	n = 98 2.9 (1.0)	n = 74 2.7 (1.0)	n = 74 1.9 (1.0)	n = 44 3.0 (0.0)	n = 18 3.5 (1.0)
JIA-ACR30, n (%)	N/A	n = 128 39 (30.5)	n = 120 44 (36.7)	n = 110 40 (36.4)	n = 105 45 (42.9)	n = 85 26 (30.6)	n = 71 8 (11.3)
JIA-ACR50, n (%)	N/A	n = 128 32 (25.0)	n = 120 36 (30.0)	n = 110 31 (28.2)	n = 105 42 (40.0)	n = 85 23 (27.1)	n = 71 8 (11.3)
JIA-ACR70, n (%)	N/A	n = 128 18 (14.1)	n = 120 24 (20.0)	n = 110 20 (18.2)	n = 105 28 (26.7)	n = 85 17 (20.0)	n = 71 7 (9.9)
JIA-ACR90, n (%)	N/A	n = 128 8 (6.3)	n = 120 15 (12.5)	n = 110 9 (8.2)	n = 105 15 (14.3)	n = 85 15 (17.6)	n = 71 5 (7.0)

Data are mean (median), unless otherwise stated. As-observed analysis. Outcomes reported by parents.

JIA-ACR30/50/70/90, 30/50/70/90% improvement in JIA-ACR criteria; N/A, not applicable; PRCSG, Pediatric Rheumatology Collaborative Study Group; PRINTO, Paediatric Rheumatology INternational Trials Organisation.

Figure 1. Median cJADAS10 endpoints over time



cJADAS10, clinical 10-joint Juvenile Arthritis Disease Activity Score.

Methods: Using a standardized protocol and data collection process, clinical sites enrolled patients with JIA receiving/starting abatacept. For the current analysis, all patients with JIA who initiated abatacept within 1 month of enrollment in the PRCSG/PRINTO registry were included. Effectiveness was assessed at baseline and at 3, 6, 9, 12, 24, and 36 months. Outcomes include physician global assessment of disease activity, overall well-being score, number of active joints and joints with limited range of motion, the clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10), and JIA-ACR30, 50, 70, and 90. The cJADAS10 used validated cut-offs for low disease activity (LDA; ≤ 3.8), inactive disease (ID; ≤ 1.0), and remission (ID for ≥ 6 months). An as-observed analysis is presented.

Results: As of March 31, 2020, 134 patients who initiated abatacept within 1 month of enrollment in the PRCSG/PRINTO registry were included in this analysis. Of these, 110 (82.1%) were female, the baseline mean (median) age

at enrollment was 12.8 (13.1) years, the time since JIA diagnosis was 60.2 (45.6) months, and the time on abatacept treatment at baseline was 0.28 (0.03) months. Median cJADAS10 scores decreased from month 3 to month 36 and the proportions of patients achieving cJADAS10 LDA and cJADAS10 ID increased over time (**Figure 1**). JIA-ACR 30, 50, 70, and 90 responses were seen as early as month 3 and were sustained over time to month 24; the percentage of patients achieving these responses at month 36 was influenced by the relatively low number of patients (due to ongoing enrollment and loss to follow-up) available for the analysis (**Table 1**). In addition, physician global assessment of disease activity and number of active joints decreased over time (**Table 1**).

Conclusion: In patients with JIA who initiated abatacept within 1 month of joining the PRCSG/PRINTO registry, there were rapid, clinically relevant responses, such as improvement in cJADAS10 scores, number of active joints, number of joints with a limited range of motion and overall well-being. These improvements were sustained over 24 months.

Reference:

1. Lovell DJ, et al. ACR 2020. Abstract 0714.

Medical writing: Claire Line, PhD (Caudex), funded by Bristol Myers Squibb

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Disclosure: N. **Ruperto**, Ablynx, 2, 6, Amgen, 2, 6, Astrazeneca-Medimmune, 2, 6, Aurinia, 2, 6, Bayer, 2, 6, Bristol Myers and Squibb, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Cambridge Healthcare Research (CHR, 2, 6, Celgene, 2, 6, Domain therapeutic, 2, 6, Eli-Lilly, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, EMD Serono, 2, 6, Glaxo Smith and Kline, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Pfizer, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Sobi, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, UCB, 2, 6, F Hoffmann-La Roche, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties; **H. Brunner**, Novartis, 6, Pfizer, 6, Roche, 6, GlaxoSmithKline, 6, Abbvie, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Biogen, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, AstraZeneca-Mediimmune, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Boehringer, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, BMS, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Celgene, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Eli Lilly, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, EMD Serono, 12,

Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Idorsia, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Cerocor, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, F.Hoffman-La Roche, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Merck, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Novartis, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Sanofi, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Aurina, 2; **N. Tzaribachev**, None; **I. Orbán**, None; **V. Staņēviča**, Sandoz, 2, Abbvie, 2, Roche, 2; **A. Quintero del Rio**, Abbott, 2; **P. Quartier**, Abbie, 2, 6, BMS, 2, 6, Chugai-Roche, 2, 6, Lilly, 2, Novartis, 2, 6, Novimmune, 2, Sanofi, 1, 12, Member of a data safety monitoring board, Swedish Orphan Biovitrum, 2, 6; **A. Huber**, None; **D. Kietz**, None; **J. Dare**, Abbvie, 5, Bristol-Myers Squibb, 5, Pfizer, 5, Roche, 5, UCB, 5, Centene Corporation, 3, 11; **D. Kingsbury**, Pfizer, 2; **T. Graham**, None; **I. Foeldvari**, Novartis, 1, Hexal, 1, Pfizer, 1, Lilly, 1, Gilead, 1, Thermo Fischer, 1; **J. Patel**, None; **A. Dominique**, Bristol Myers Squibb, 3; **L. Dong**, Bristol-Myers Squibb, 3; **T. Kou**, Bristol Myers Squibb, 3; **R. Wong**, Bristol Myers Squibb, 3; **A. Martini**, Aurinia, 2, 6, Bristol Myers and Squibb, 2, 6, Eli-Lilly, 2, 6, EMD Serono, 2, 6, Janssen, 2, 6, Pfizer, 2, 6, Roche, 2, 6; **D. Lovell**, Bristol Myers Squibb, 12, PI, Abatacept, Juvenile Idiopathic Arthritis, AstraZeneca Pharm, 2, Boehringer Ingleheim, 2, GSK, 2, Hoffman LaRoche, 2, Janssen, 12, Co-PI of overall studies of IV and sub-Q Golimumab in JIA, NIH / NIAMS, 12, R01 AR074098-01A1, NIH / NICHD, 12, NIH / R01 HD 089928-01A1, Novartis, 2, Pfizer, 3, Roche, 12, PI, Tociluzumab, Juvenile Idiopathic Arthritis, UBC, 2.

Abstract Number: 0248

Proportion of Patients with a Polyphasic Disease Course in Systemic-onset Juvenile Idiopathic Arthritis May Be Higher in the Age of Cytokine Inhibitors

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic-onset juvenile idiopathic arthritis (sJIA) is a pediatric autoinflammatory condition, known for significant variability between patients in its severity and long-term outcomes. The classification of disease course into monophasic, polyphasic (intermittent) and persistent disease has been commonly used, with polyphasic

disease usually recognized in a small portion of patients[1,2] . However, this proportion was established according to data mostly collected before the biologic IL-1 and IL-6 inhibitors were available. It has been recently suggested [3,4] that these medications, now the mainstay of treatment in sJIA, can potentially alter the long-term course of the disease, especially with earlier use.

Methods: A multi-center, retrospective chart review was conducted from 3 hospitals in Israel and 2 in the US, involving patients diagnosed with sJIA between 1998-2019, with a minimum follow-up of 1 year. Disease course classification was done according to previously released definitions.[1] Remission was defined as inactive disease (no active signs or symptoms and no elevation of inflammatory markers) while not receiving any medications for a period of at least 3 months. Polyphasic disease was defined as at least one disease relapse after a period of drug-free remission. Persistent disease was defined as at least 2 years of disease (either active or in remission on immunosuppressive medication) with no drug-free remissions. Monophasic disease was defined as a single episode lasting less than 2 years.

Results: 85 patients met the inclusion criteria (mean follow up 3.6 years, SD ± 2.8). 54 of the patients (63.5%) were female; median age at diagnosis was 5.8 years (IQR = 5.9). 67 (78.9%) were diagnosed in 2012 or later, when IL-1 and IL-6 inhibitors became widely used. 56 (65.9%) were treated with a biologic drug during their disease course. The rates of monophasic, polyphasic and persistent disease were 43.5%, 43.5% and 12.9%, respectively, with a higher-than-expected rate of polyphasic disease and a lower rate of persistent disease than previously published. [1,2,5]

Conclusion: In the age of IL-1 and IL-6 inhibitors, polyphasic sJIA disease course may be more common than previously described, suggesting that cytokine blockers may potentially alter the natural history of this disease.

[1] Singh-Grewal et al, Arthritis Rheum. 2006[2] Barut et al, Int J Rheum Dis. 2019

[3] Henderson LA et al, JCI Insight. 2020 [4]Kessel C et al. (2020) Arthritis Rheumatol

[5] Lomater et al, J Rheumatol. 2000

Disclosure: I. **Marmor**, None; **R. Semo Oz**, None; **A. Hendel**, None; **G. Hazan**, None; **K. Baszis**, None; **A. French**, None; **C. Edens**, None; **i. Tirosh**, None; **Y. Butbul Aviel**, None; **L. Harel**, None; **G. Amarilyo**, None.

Abstract Number: 0249

Open-label, Long-term (10-year) Study of the Safety of Etanercept in Children with Extended Oligoarticular Arthritis, Enthesitis-related Arthritis, or Psoriatic Arthritis

Jelena Vojinović[1], Joke Dehoorne[2], Violeta Panaviene[3], Gordana Susic[4], Gerd Horneff[5], Valda Stanevicha[6], Katarzyna Kobusinska[7], Zbigniew Zuber[8], Bogna Dobrzyniecka[9], Jonathan Akikusa[10], Tadej Avcin[11], Alberto Martini[12], Cecilia Borlenghi[13], Edmund Arthur[14], Svitlana Tatulych[15], Chuanbo Zang[16], Bonnie Vlahos[16] and Nicolino Ruperto[17], [1]Paediatric Rheumatology International Trials Organisation (PRINTO), Nis, Serbia, [2]Paediatric Rheumatology International Trials Organisation (PRINTO), Gent, Belgium, [3]Paediatric Rheumatology International Trials Organisation (PRINTO), Vilnius, Lithuania, [4]Paediatric Rheumatology International Trials Organisation (PRINTO), Belgrade, Serbia, [5]Paediatric Rheumatology International Trials Organisation (PRINTO), Sankt Augustin, Germany, [6]Paediatric Rheumatology International Trials Organisation (PRINTO), Riga, Latvia, [7]Paediatric Rheumatology International Trials Organisation (PRINTO), Bydgoszcz, Poland, [8]Paediatric Rheumatology International Trials Organisation (PRINTO), Lodz, Poland, [9]Paediatric Rheumatology International Trials Organisation (PRINTO), Warsaw, Poland, [10]Paediatric Rheumatology International Trials Organisation (PRINTO), Melbourne, Australia, [11]Paediatric Rheumatology International Trials Organisation (PRINTO), Ljubljana, Slovenia, [12]Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy, [13]Pfizer, Buenos Aires, Argentina, Buenos Aires, Argentina, [14]Pfizer, Peapack, NJ, [15]Pfizer, Groton, CT, [16]Pfizer, Collegeville, PA, [17]IRCCS Istituto Giannina Gaslini; PRINTO, Clinica Pediatrica e Reumatologia, Genova, Italy

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: CLIPPER2 was an 8-year, open-label extension of the phase 3b, multicenter, 2-year CLIPPER study of the safety and efficacy of etanercept (ETN) in the treatment of patients (pts) with juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA). The objective of this analysis was to describe the safety of ETN in this population after 10-years of follow up.

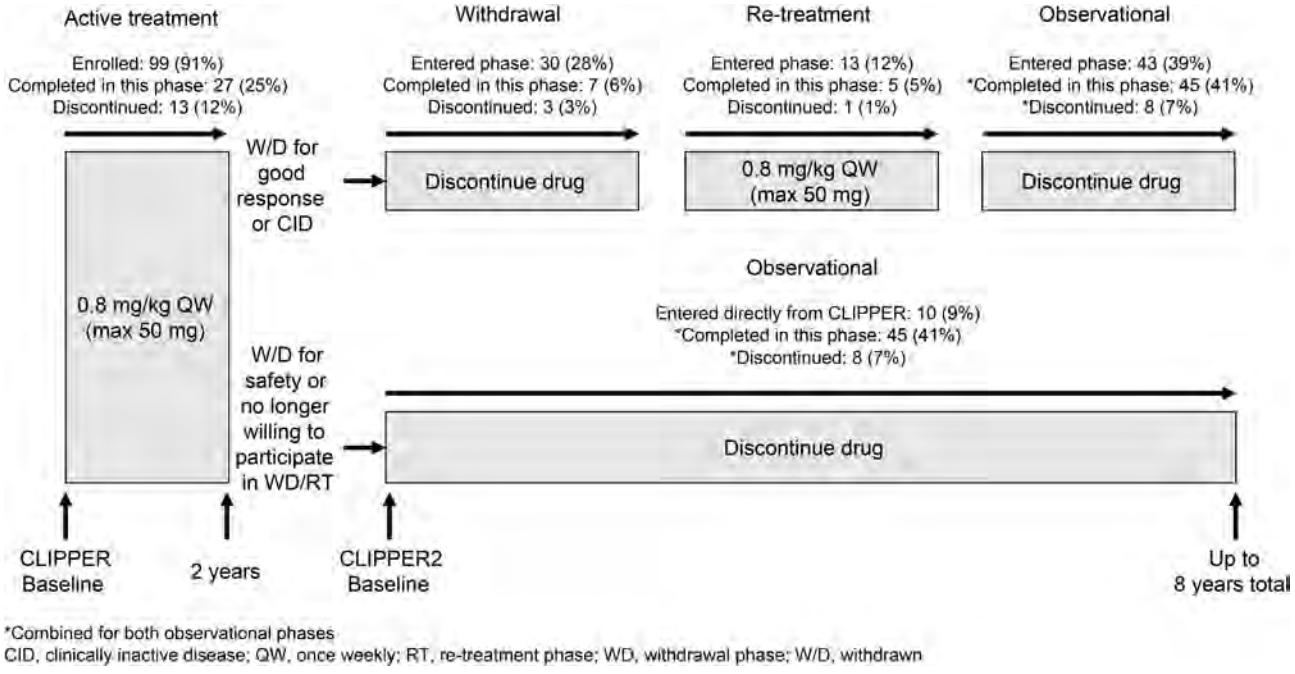


Figure 1. Study Design and Subject Disposition.

Table. ETN Safety Summary (from CLIPPER BL to m120), N (EP100PY) (FAS)*

	eoJIA (EXP = 313.667 PY)	ERA (EXP = 206.971 PY)	PsA (EXP = 162.576 PY)	Total (EXP = 683.214 PY)
TEAEs†	269 (85.76)	176 (85.04)	114 (70.12)	559 (81.82)
Serious TEAEs†	16 (5.10)	17 (8.21)	7 (4.31)	40 (5.85)
TE ISRs	23 (7.33)	29 (14.01)	12 (7.38)	64 (9.37)
TE infections	418 (133.26)	99 (47.83)	155 (95.34)	672 (98.36)
Serious TE infections‡	5 (1.59)	4 (1.93)	5 (3.08)	14 (2.05)
Opportunistic infections§	0	1 (0.48)	1 (0.62)	2 (0.29)
TEAEs causing withdrawal†	7 (2.23)	9 (4.35)	2 (1.23)	18 (2.63)
TE infections causing withdrawal	2 (0.64)	0	1 (0.62)	3 (0.44)

*While on active ETN treatment or within 30 days of last dose

†Excluding infections/ISRs

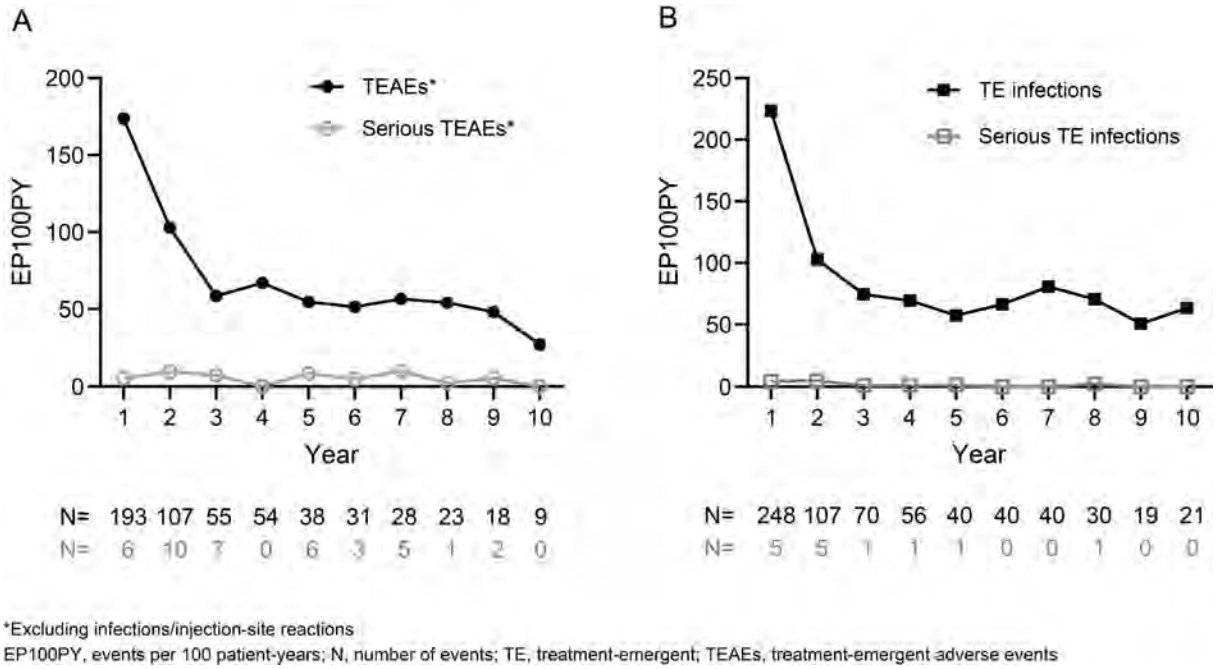
‡Gastroenteritis, 2 (0.29); acute tonsillitis, anal abscess, bronchopneumonia, gastrointestinal infection, helicobacter gastritis, influenza, peritonitis, pharyngitis, pyelocystitis, sepsis, urinary tract infection, viral infection, all 1 (0.15)

§Both herpes zoster

BL, baseline; eoJIA, extended oligoarticular juvenile idiopathic arthritis; EP100PY, events per 100 patient-years; ERA, enthesitis-related arthritis; ETN, etanercept; EXP, exposure to ETN; FAS, full analysis set; ISR, injection-site reaction; m, month; N, number of events; PsA, psoriatic arthritis; PY, patient years; TE, treatment-emergent

Methods: Pts (n=127) with eoJIA (2-17 years), ERA, or PsA (each 12-17 years) who received ≥1 ETN dose (0.8 mg/kg once weekly [max, 50 mg]) in CLIPPER were eligible to enter CLIPPER2. The primary outcome measure was the occurrence of malignancy. Long-term safety was assessed as the total incidence of events from CLIPPER baseline (BL) to month (m) 120, frequency of events per 100 patient-years (EP100PY), and frequency of events in each study year.

Results: A total of 109/127 (86%) pts entered CLIPPER2; 99 (91%) continued in the active treatment period. At m120, 84/109 (77%) pts had completed the study; 27 (25%) while actively taking ETN, 7 (6%) had withdrawn from treatment due to low/inactive disease; 5 (5%) had re-started ETN following an earlier withdrawal from treatment; and 45 (41%) had stopped ETN (but remained under observation) (Figure 1); 25/109 (23%) pts permanently discontinued from the CLIPPER2 study.



*Excluding infections/injection-site reactions
EP100PY, events per 100 patient-years; N, number of events; TE, treatment-emergent; TEAEs, treatment-emergent adverse events

Figure 2. Incidence of TEAEs (A) and TE Infections (B) in CLIPPER/CLIPPER2 by Study Year, N (EP100PY).

In CLIPPER/CLIPPER2, 1 case of malignancy (Hodgkin's disease) was reported (1 pt with eoJIA in year 3). There was 1 case of uveitis (1 pt with eoJIA in year 8) and 3 of Crohn's disease (2 pts with ERA, year 1/year 6; 1 pt with eoJIA, year 5). There were 2 cases of opportunistic infections (both herpes zoster), and no deaths. Overall, there were 559 (81.82 EP100PY) treatment-emergent adverse events (TEAEs) excluding infections and injection-site reactions (ISRs). The overall rate of TE serious infections was low (N=14; 2.05 EP100PY) (Table), with the most common TE serious infection being gastroenteritis (N=2; 0.29 EP100PY). The most frequently reported TEAEs (N [EP100PY]) were headache (28 [4.10]), arthralgia (24 [3.51]), pyrexia (21 [3.07]), diarrhea (14 [2.05]), and leukopenia (12 [1.76]). Overall, 39 patients reported serious TEAEs (excluding infections/ISRs).

The number and frequency (N [EP100PY]) of TEAEs (excluding infections/ISRs) decreased over the 10-year study period from 193 [173.81] in year 1 to 9 [27.15] in year 10. The number and frequency of TE infections and serious TE infections also decreased over the 10-year study period. There was no clear trend of a decrease over time for the incidence of serious TEAEs (Figure 2).

Conclusion: ETN treatment to m120 was well tolerated in this patient population and consistent with the known safety profile. Frequency of TEAEs and TE infections decreased over time. Over 10 years there was I reported event of malignancy and the overall rate of TE serious infections was low.

Trial Registration: NCT00962741/NCT01421069

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full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Cambridge Healthcare Research (CHR, 2, 6, Celgene, 2, 6, Domain therapeutic, 2, 6, Eli-Lilly, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, EMD Serono, 2, 6, Glaxo Smith and Kline, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Pfizer, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Sobi, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, UCB, 2, 6, F Hoffmann-La Roche, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties.

Abstract Number: 0250

Is There a Need for a New Classification Criteria in Juvenile Spondyloarthritis?

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile SpA (JSpA) involve enthesitis related arthritis (ERA), juvenile psoriatic arthritis and undifferentiated arthritis (UA) according to the ILAR criteria. Two different patterns have been found: axial and peripheral. The pediatric form differs from that in adults by a predominant peripheral involvement. The evolution to ankylosis has been reported in one third of all cases after several years. The proposed PRINTO classification criteria for JIA introduced a new approach changing ERA to enthesitis/spondylitis-related JIA (ESRA) resulting in a definition harmonized with that for adults. The purposes were to assess the sensibility and specificity of the provisional new PRINTO JIA classification criteria for ESRA and to compare its performance to others adult´s classification criteria. To identify predictive variables for ankylosis progression.

Methods: Consecutive patients with JSpA (defined as ERA or UA according to ILAR) followed in our center were included. Randomly selected patients with oligoarthritis (23), polyarthritis RF negative (22) and systemic (20) served as controls. Variables recorded included: arthritis, enthesitis, tarsitis, inflammatory back pain (IBP), SI- joint tenderness, presence of HLA-B27 antigen, acute anterior uveitis, history of SpA in a first-degree relative. Imaging on SI-joints (SI joints) on X-ray and/or MRI. Classification criteria for adults were ASAS and Modified New York (NY). Patients with ankylosing progression fulfilled NY criteria. Summary statistics: sensitivity, specificity, positive predictive value (PPV), negative predictive value (NVP), positive Likelihood ratio (+LR) and negative Likelihood ratio (-LR). Univariate and multivariate logistic regression for predictors variables.

Results: 112 patients with JSpA (89 ERA, 23 UA) were included (M: 94), median age at onset: 10 (1-15) years, disease duration at time of first visit 8.5 (1-48) months, follow-up 7 (1-15) years. Controls: 65 JIA (M: 27). At first visit showed: 107 (95%) arthritis, 69 (62%) elevated CRP, 54 (48%) limitation of lumbar spine motion, 56 (50%) HLA-B27, 48(43%) enthesitis, 44 (40%) tarsitis, 42 (37%) IBP, 31 (30%) SI- joint tenderness, 30 (27%) good response to NSAIDS, 26 (23%) positive family history, 12 (10%) dactylitis, 7(6%) uveitis,7(6%) diarrhea, 5(5 %) infectious previous, 2(2%) urethritis, 2(2%) IBD, 2 (2%) buttock pain. Imaging for sacroiliitis: 30 (27%) on X-Ray (23 grade 2 bilateral and 7 grade 3), 26 (23%) on MRI. At first visit (112 patients): 95 (87%) fulfilled ESRA criteria. Disease course (102 patients): 97 (95%). Patients who meet NY criteria: 64 (63%). Table 1 shows the accuracy for classification criteria. The unique predictor variable for ankylosing progression was lumbar limitation (p=0.02). Table 2 shows the accuracy of the selected variables at onset of the disease for predicting the risk of developing JAS.

Conclusion: The new proposed PRINTO criteria was a more sensitive classification criteria than adults' criteria. Lumbar limitation was a predictor variable for ankylosing. The accuracy of each selected variable at onset suggests the probability of a higher suspected index for JSpA.

First Visit	Sensitivity	Specificity	PPV	NPV	+LR	-LR
PRINTO (ESRA)	85%	86%	91%	76%	6.12	0.17
Global ASAS	72%	86%	90%	64%	5.22	0.32
Peripheral ASAS	70%	86%	90%	63%	5.09	0.34
Axial ASAS	23%	96%	92%	42%	7.54	0.79
NY	21%	100%	100%	42%	Infinity	0.78
Disease Course						
PRINTO (ESRA)	95%	86%	91%	92%	6.87	0.05
Global ASAS	96%	86%	91%	93%	6.94	0.04
Peripheral ASAS	96%	86%	91%	93%	6.94	0.04
Axial ASAS	41%	100%	100%	52%	Infinity	0.5 8
NY	63%	100%	100%	63%	Infinity	0. 37

Variable	Sensitivity	Specificity	PPV	NPV	+LR	-LR
Limitation lumbar	68%	100%	100%	66%	Infinity	0.32
HLA-B27	50%	97%	97%	54%	16.39	0.51
Enthesitis	43%	100%	100%	50%	Infinity	0.57
Tarsitis	40%	98%	98%	49%	25.8	0.61
IBP	37%	100%	100%	48%	Infinity	0.62
Sacroiliitis *	27%	100%	100%	44%	Infinity	0.72
Positive family history	23%	89%	78%	40%	2.15	0.86

*on imaging

Disclosure: M. Katsicas, Novartis, 4, Pfizer, 6; **M. Bertinotti**, None; **M. Villarreal**, None.

Abstract Number: 0251

A Comparative Study of the Validity of the DAS28-ESR and JADAS-27 Disease Activity Assessment Indexes for Juvenile Idiopathic Arthritis in Transition and Adults

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The 2020 Rheumatoid Arthritis Clinical Practice Guidelines by the Ministry of Health, Labour, and Welfare Research Group recommends the JADAS27 as a measure of disease activity in transitional and adult JIA, reflecting the characteristics of JIA-affected joint localization, and citing the possibility of underestimation by the DAS28. We compared the validity of DAS28-ESR and JADAS27 in transitional and adult JIA.

Methods: Patients aged 18 years or older at the time of the study with an onset of younger than 18 years were selected from the prospective observational studies of IORRA conducted by the Institute of Rheumatology, Tokyo Women's Medical University.

Results: A total of 3,528 cases (age 39.1(SD 15.1) years at the survey, 13.5 (SD 3.8) years of onset, 25.6 (SD 16.0) years of disease duration) were included in the study. Activity according to both disease activity indices in order of high, medium, low disease activity and remission were DAS28-ESR (mean 2.9, SD 1.3):5.5%, 31.7%, 19.5%, 43.3%, JADAS27 (mean 7.6, SD 6.3): 65.2%, 16.3%, 7.8%, 10.7%, and JADAS 27 and JADAS 27 presented a higher disease activity configuration than DAS28-ESR. The high frequency of active joints was 23.0% in the hands and 12.4% in the elbows. JADAS27-specific joints were active in the ankle (11.3%), neck (2.6%), and hips (1.2%), and in 686 cases (19.4%) with these joints, the DAS28-ESR mean of 2.8 (SD 1.3) and the JADAS27 mean of 7.3 (SD 6.5) was not underestimated by the DAS28-ESR compared to the whole subject.

Conclusion: JADAS27 has been applied to the severity classification of articular JIA as the designated incurable disease in Japan and is socially important in transitional and adult JIA, but it is necessary to recognize the difference between the JADAS27 and the DAS28-ESR in its application.

Disclosure: T. Miyamae, None; **E. Tanaka**, AbbVie Japan GK, 6, Asahi Kasei Corp., 6, Astellas Pharma Inc., 6, Ayumi Pharmaceutical Co., 6, Chugai Pharmaceutical Co., Ltd., 6, Eisai Co., Ltd., 6, Eli Lilly Japan K.K., 6, GlaxoSmithKline K.K., 6, Bristol Myers Squibb, 6, Kyowa Pharma Chemical CO., Ltd., 6, Janssen Pharmaceutical K.K., 6, Mochida Pharmaceutical CO., Ltd., 6, Pfizer Japan Inc., 6, Takeda Pharmaceutical Co., Ltd., 6, Teijin Pharma Ltd., 6; **E. Inoue**, Pfizer, 6, Bristol-Myers Squibb, 6, Nippontect systems, 1; **K. Ikari**, Asahi Kasei Pharma Co., 6, Astellas Pharma Inc., 6, AbbVie Japan GK, 6, Ayumi Pharmaceutical Corporation, 6, Bristol Myers Squibb Co., Ltd., 6, Chugai Pharmaceutical Co., Ltd., 6, Eisai Co., Ltd., 6, Eli Lilly Japan K.K., 6, Janssen Pharmaceutical K.K., 6, Kaken Pharmaceutical Co. Ltd., 6, Mitsubishi Tanabe Pharma Co., 6, Pfizer Japan Inc., 6, Takeda Pharmaceutical Co. Ltd., 6, Teijin Pharma Ltd, 6, UCB Japan Co. Ltd., 6, Ayumi Pharmaceutical Corporation, 5, Chugai Pharmaceutical Co., Ltd., 5, Mitsubishi Tanabe Pharma Co., 5, Mochida Pharmaceutical Co., Ltd., 6, Nippon Kayaku Co., Ltd., 5, Teijin Pharma Ltd., 5; **M. Harigai**, None.

Abstract Number: 0252

Role of Clinical and Laboratory Parameters in Differentiating Infection from Disease Flare in Febrile Patients of Systemic Juvenile Idiopathic Arthritis

Rajesh Kanumuri[1], Suma Balan[2], Vishal Marwaha[2], Sajitha Krishnan[2] and Pranav Chickermane[2], [1]Amrita Institute of Medical Sciences, Guntur, India, [2]Amrita Institute of Medical Sciences, Kochi, India

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Fever is the most common presentation of systemic juvenile idiopathic arthritis (SJIA) and it is difficult to predict whether the fever is due to infection or underlying disease flare. This study has been undertaken to determine the role of clinical and laboratory parameters in differentiating infection and disease flare in febrile patients of SJIA, with particular reference to serum procalcitonin levels.

Methods: In this cross-sectional study, patients diagnosed with SJIA (as per ILAR classification criteria) who presented with fever (temperature ≥38°C) for more than ≥48 hours under the age of 16years between March 2018 to October 2019 were included. Blood samples for hemogram, acute phase reactants (ESR, C- Reactive protein and ferritin) procalcitonin levels were collected along with cultures of the respective body fluids at the time of presentation for the evaluation of fever. Patients were stratified into infection group and disease flare (with or without MAS) group.

Clinical parameter	Yes/No (n)	Infection n (%)	Disease flare n (%)	p value
Quotidian Fever	Yes (23)	2 (8.7)	21 (91.3)	0.046
	No (29)	10 (34.5)	19 (65.5)	
Evanescent Maculopapular rash	Yes (24)	1 (4.2)	23 (95.8)	0.003
	No (28)	11 (39.3)	17 (60.7)	
Joint pains	Yes (19)	0 (0)	19 (100)	0.002
	No (33)	12 (36.4)	21 (63.6)	
Joint swellings	Yes (12)	0 (0)	12 (100)	0.027
	No (40)	12 (30)	28 (70)	

Figure 1. Comparison of clinical manifestations with respect to infection and disease flare groups.

Lab parameter	Group (n)	Mean (SD)	Median (IQR)	p value
Total WBC (count x10^3/μL)	Infection	14.91(6.78)	14.81(8.47)	0.152
	Disease flare	20.67(10.46)	21.02(14.55)	
Hemoglobin (g/dL)	Infection	9.55 (1.77)	10 (2.4)	0.441
	Disease flare	9.85(1.58)	9.8(2.4)	
Platelet (x10^3/μL)	Infection	368.10(202.91)	393 (345)	0.339
	Disease flare	431.97 (214.61)	456 (258)	
ESR (mm/hr)	Infection	41.5 (30.32)	27 (37)	0.253
	Disease flare	55.38 (31.99)	55 (56)	
CRP (mg/dL)	Infection	97.63 (92.55)	72.55 (90.1)	0.15
	Disease flare	135.21 (101.22)	103.51 (119.26)	
Ferritin (ng/ml)	Infection	3650.78 (4237.17)	875.65 (8381)	0.34
	Disease flare	8385.51 (12152.98)	2623 (11376)	
Procalcitonin (ng/ml)	Infection	14.35 (30.42)	1.86 (6.27)	0.38
	Disease flare	5.44 (16.56)	0.38 (2.76)	

Figure 2. Comparison of lab parameters with respect to infection and disease flare groups.

Febrile episodes were categorized as “Infection” based on their clinical profile along with body fluid evaluation & culture or tissue culture or serological assays or any imaging study suggestive of infection and their prompt response to antibiotics without hiking the immunosuppression. “Disease flare” group was defined as those patients with daily fever ≥38°C for ≥2 days in a diagnosed case of SJIA, without any laboratory evidence of infection and the prompt response to hike in immunosuppression. MAS was defined as per the EULAR/ACR 2016 classification criteria. The receiver operating characteristic (ROC) curve analysis was used to find out the respective cut-off values.

Results: A total of 52 visits of 25 patients were included. Twelve (23.1%) were in the infection group and 40 (76.9%) were in the disease flare group (27 were disease flare without MAS and 13 were disease flare with MAS). The mean (SD) & median (IQR) values of laboratory parameters including serum procalcitonin levels did not show any statistical significance in differentiating infection and disease flare groups, whereas clinical parameters like quotidian pattern of fever, evanescent maculopapular rash and joint symptoms showed statistical significance (p value: < 0.05). In patients with disease flare, cut-off values of procalcitonin ≥0.95ng/ml, CRP ≥103mg/L and ferritin ≥ 3842.5 ng/ml predicted MAS with good sensitivity and specificity (p value: < 0.05).

Laboratory parameter	Cut-off value (n)	Disease flare Group		Sensitivity (%)	Specificity (%)	p value	PPV (%)	NPV (%)	Accuracy (%)	PLR	NLR
		With MAS	Without MAS								
Procalcitonin (ng/ml)	≥0.95 (16)	10	6	76.9	77.8	0.002	62.5	87.5	77.5	3.46	0.29
	<0.95 (24)	3	21								
CRP (mg/L)	≥103 (21)	10	11	69.2	63	0.046	47.4	81	65	1.87	0.49
	<103 (19)	3	16								
Ferritin (ng/ml)	≥ 3842.5 (15)	12	3	92.3	88.9	<0.001	80%	96%	90	8.30	0.09
	< 3842.5 (25)	1	24								

MAS: Macrophage activation syndrome, PPV: Positive predictive value, NPV: Negative predictive value, PLR: Positive likelihood ratio, NLR: Negative likelihood ratio.

Figure 3. Cut-off values of Procalcitonin, CRP and Ferritin in differentiating patients of disease flare with MAS and without MAS.

Conclusion: In our study none of the laboratory parameters including serum procalcitonin levels, were useful in differentiating infectious cause of fever from disease flare in febrile patients with SJIA. Serum procalcitonin levels were elevated even in the absence of infection in SJIA disease flare with MAS and a value of ≥0.95ng/ml was found to be a reliable predictor in identifying the MAS complicating SJIA. Presence of classical clinical features of SJIA are helpful in differentiating the disease flare from infection with high accuracy.

Disclosure: R. Kanumuri, None; **S. Balan**, None; **V. Marwaha**, None; **S. Krishnan**, None; **P. Chickermane**, None.

Abstract Number: 0253

Rheumatoid Factor Status as a Predictor of Disease Activity and Disability: An Analysis of the New CARRA Registry Polyarticular Juvenile Idiopathic Arthritis Cohort

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SESSION INFORMATION
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Background/Purpose: Children with rheumatoid factor (RF) positive polyarticular JIA (pJIA) are less likely to go into remission and more likely to develop erosive disease than those with RF negative pJIA. Differences in disease activity and disability over the first year of diagnosis between RF+ versus RF- pJIA have not been described in the new Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry. In this study, we investigate the differences in disease activity and disability by RF status at time of diagnosis and at 12 months among pJIA patients enrolled in the new CARRA Registry.

Methods: We analyzed data from the CARRA Registry collected from July 2015 through February 2020. Inclusion criteria were USA residency and pJIA diagnosis with recorded >4 joints involved in first 6 months of disease, and exclusion criteria was additional diagnosis of other autoimmune disease. Groups were categorized by RF status (positive, negative, or unknown). Duration of morning stiffness was collected and categorized as none, ≤15 minutes, 15-60 minutes, ≥60 minutes, or unknown. Disease activity was assessed with the Clinical Juvenile Arthritis Disease Activity (cJADAS). The Child Health Assessment Questionnaire (CHAQ) scores were collected to assess functional

Table 1. Patient Characteristics and Demographics

	N=1684
Age at Diagnosis	
Median (min, max)	7.0 (3, 11.0)
Sex	
Female	1322 (79%)
Male	362 (21%)
Race and Hispanic Origin	
White	1246 (74%)
Black or African American	63 (3.7%)
Hispanic	167 (9.9%)
Native American, American Indian or Alaskan Native	8 (0.5%)
Asian	53 (3.1%)
Native Hawaiian and other Pacific Islander	5 (0.3%)
Two or more races	100 (5.9%)
Other	14 (0.8%)
Declined Response	42 (2.5%)
Rheumatoid Factor Status	
Negative	1204 (71%)
Positive	309 (18%)
Not Done	190 (11%)

Table 2. Duration of Morning stiffness at diagnosis and 12 months by RF status

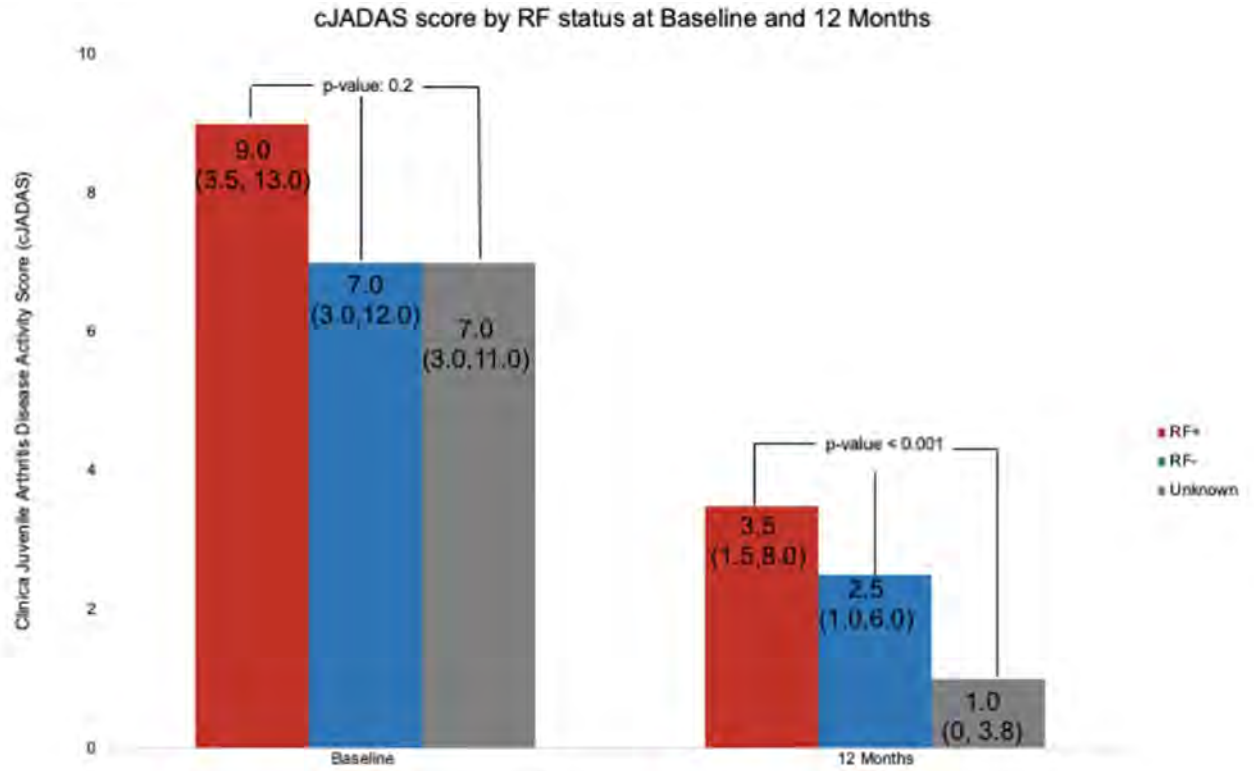
Duration of Morning stiffness at Diagnosis	RF negative N = 1,204[1]	RF Not Done N = 119[1]	RF positive N = 309[1]	p[2]= <0.001
≤15 Minutes	171 (15%)	8 (7.8%)	39 (14%)	
16-60 Minutes	172 (15%)	14 (14%)	46 (16%)	
≥60 Minutes	117 (10%)	14 (14%)	60 (21%)	
None	660 (59%)	66 (65%)	139 (49%)	
Duration of Morning stiffness at 12 months				p[2]= 0.047
≤15 Minutes	127 (11%)	12 (11%)	40 (14%)	
16-60 Minutes	111 (9.8%)	10 (8.9%)	23 (8.0%)	
≥60 Minutes	42 (3.7%)	5 (4.5%)	23 (8.0%)	
None	855 (75%)	85 (76%)	200 (70%)	

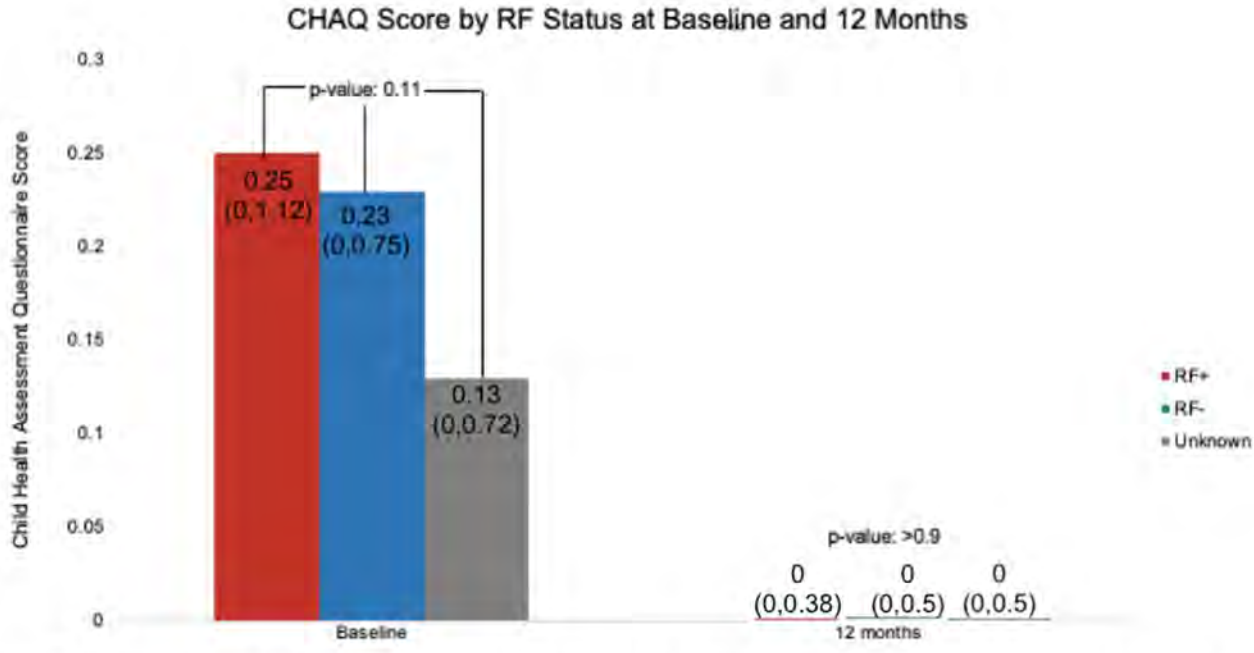
[1] n (%)
[2] Pearson's Chi-squared test

disability. Pearson's chi-squared test used to analyze differences in morning stiffness by RF status at baseline and 12 months. Kruskal- Wallis testing was used to assess differences in disease activity and disability by RF status at baseline and 12 months.

Results: 1684 patients were included in the study. The majority of patients (71%) were RF negative, 18% were RF positive (Table 1). At diagnosis and 12-month visits, RF+ patients had a longer duration of morning stiffness (Table 2,p=< .001, and p< .047, respectively). RF+ pJIA patients had high disease activity (median cJADAS=9, 3.5-13) while RF negative and RF unknown patients had moderate disease activity (Figure 1). There was no statistical difference in cJADAS (p=.2) or CHAQ (p=.11) by RF status at diagnosis. By 12 months, all groups' cJADAS improved, but RF positive patients had a statistically significant higher activity score compared to RF negative or RF unknown patients (p< .001). Despite these clear differences in disease activity, all RF status groups had a CHAQ median score of 0 or no reported disability (p=0.9) at the 12-month visit.

Conclusion: In our unadjusted model, all pJIA patients demonstrated improvement of disease activity as measured by cJADAS and disability as measured by CHAQ during the first year of enrollment in the CARRA registry. However, at the 12-month visit, RF positive patients reported longer duration of morning stiffness duration and a statistically significant higher cJADAS score as compared to other RF groups. Additional studies are needed to assess modifiable factors contributing to this difference in long term disease activity.





cJADAS: Inactive disease ≤1; low disease activity 1.1-2.5; moderate disease activity 2.51-8.5; high disease activity >8.5
CHAQ: No disability = 0; mild disability 0.1 - ≤0.25; mild/moderate disability 0.26 - ≤ 1.25, moderate disability 1.26 - ≤ 2.00; severe disability 2.00 - ≤3.00

Figure 1. Median disease activity (cJADAS) score and functional disability(CHAQ) score among polyarticular JIA patients in the CARRA Registry at baseline and 12 months by rheumatoid factor (RF) status.

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Abstract Number: 0254

Patient and Disease-Level Factors Associated with Sustained Cessation of Medication for Disease Remission in Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The emergence of IL-1 and IL-6 inhibitors (biologics) for the treatment of systemic juvenile idiopathic arthritis (SJIA) has dramatically improved patient outcomes. With higher proportions of patients achieving clinically inactive disease (CID), knowledge gaps exist regarding frequency and predictors of remission off of medications. We leveraged data within the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry to identify demographic, clinical, and laboratory factors associated with sustained cessation (≥6 months) of glucocorticoid, biologic, and non-biologic disease modifying anti-rheumatic drugs (DMARDs) for disease remission in patients with SJIA.

Methods: 766 patients with a diagnosis of SJIA enrolled in the CARRA registry database between August 2015 - July 2020 were evaluated. Patients were excluded if they were diagnosed after enrolment, had missing diagnosis date, had change in diagnosis or unclear diagnosis, was a screen failure, if medication already discontinued prior to enrolment or administered too late after enrolment, if the diagnosis date was after medication start date, or if no exposure to pre-selected medications of interest (glucocorticoids, IL-1 inhibitor, IL-6 inhibitor, methotrexate, and/or tofacitinib). The primary outcome was medication cessation for disease remission for at least 6 month-period. Time-to-event models incorporating left truncation and right censoring with Firth correction were used to assess the association of patient demographics, SJIA disease features, baseline laboratory results, timing of medication start, and macrophage activation syndrome (MAS) with the primary outcome. Variable selection proceeded in two stages. In the first stage, univariable models were constructed. Variables that were significant at the 0.20 significance level in the univariable analysis were candidates for the multivariable model in the second stage. A backward selection approach was used to identify significant factors at the 0.05 level.

Results: A total of 493 SJIA patients met criteria for inclusion in the analysis (Table 1). Eighteen percent (90/493) of SJIA were able to wean off medications for ≥6 months. Table 2 presents the univariate relationships. In the multivariable model, younger age (HR 0.95; 95% CI 0.90-0.99; p=0.02), normal CRP levels defined as < 10 mg/L (>=10 mg/L vs < 10 mg/L HR 0.45; 95% CI 0.26-0.78; p=0.005), and shorter time between diagnosis and start of medications (HR 0.90; 95% CI 0.82-0.995; p=0.04) were associated with successful discontinuation of medications for ≥6 months. A total of 19 (3.9%) patients developed MAS, none of whom were able to discontinue medications for ≥6 months.

Conclusion: In the CARRA SJIA cohort, being younger at enrolment, having a shorter time to start medications after diagnosis, and having a normal CRP were associated with successful medication cessation for disease remission for ≥6 month-period. This study reinforces the existing understanding of a window of opportunity in which earlier initiation of treatment for SJIA patients may lead to better outcomes.

Disclosure: E. Flanagan, None; **R. Peterson**, None; **S. Shenoi**, Pfizer, 2; **H. Chang**, None; **K. Wang**, None; **R. Trachtman**, None; **K. Onel**, None.

Abstract Number: 0255

Identification of Tolerated Disease Activity Level for Individuals with Juvenile Idiopathic Arthritis in the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION
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Background/Purpose: Recent treat to target recommendations for the treatment of juvenile idiopathic arthritis (JIA) recommend frequent evaluation and treatment intensification until the disease activity target (low or inactive disease) is reached. Our objective was to identify the range of disease activity states that was accepted by patients and physicians, using a lack of medication change as a proxy for a sufficiently tolerable disease activity state that did not require JIA treatment change.

Methods: We included all subjects with non-systemic JIA enrolled in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, a clinical registry of >70 North American sites. Tolerated disease activity was determined at the registry visit following no medication change for >180 days prior to the registry visit and 60 days after the visit. Disease activity was assessed by physician global assessment (PGA) (0-10 visual analog scale (VAS), parent/patient global assessment (PtGE) (0-10 VAS), active joint count (AJC), duration of morning stiffness, clinical Juvenile Arthritis Disease Activity Score (cJADAS), American College of Rheumatology (ACR) preliminary criteria for

Table 1. Percentiles for visit disease activity scores at the time of tolerated disease activity (no medication change for >6 months)

	50th percentile	75th percentile	90th percentile	95th percentile	range
PGA (n=14466)	0	1	3	4	0-10
PtGE (n=13167)	0	2	5	6	0-10
AJC (n=15512)	0	1	3	5	0-62
cJADAS (n=12494)	1.5	5	10	13	0-29

PGA – physician global assessment, PtGE – patient/parent global assessment of wellbeing, AJC – active joint count, cJADAS – clinical Juvenile Arthritis Disease Activity Score

Table 2. Logistic regression model results for association of clinical characteristics between disease activity state at the time of tolerated disease activity (no medication change for >6 months)

	cJADAS LDA	cJADAS CID	ACR preliminary criteria for CID	ACR Provisional criteria for CID
Covariate	OR (95% CI)	OR (95% CI)	OR (95% CI)	OR (95% CI)
Age	1.182 (0.939-1.488)	1.024 (0.830-1.265)	0.883 (0.740-1.052)	0.942 (0.786-1.131)
Male (ref female)	1.284 (0.972-1.696)	1.144 (0.889-1.473)	0.954 (0.775-1.174)	0.940 (0.758-1.167)
Race/Ethnicity (ref White)				
Asian	1.132 (0.551-2.326)	0.857 (0.469-1.568)	1.029 (0.617-1.715)	1.079 (0.641-1.814)
Black	0.381 (0.194-0.747)	0.844 (0.413-1.726)	0.494 (0.279-0.877)	0.493 (0.268-0.906)
Hispanic	0.541 (0.345-0.850)	0.613 (0.388-0.968)	0.854 (0.589-1.238)	0.879 (0.598-1.290)
Other	0.651 (0.367-1.155)	0.418 (0.221-0.790)	0.647 (0.398-1.052)	0.663 (0.399-1.101)
JIA subtype (ref oligoarticular)				
RF- polyarticular	0.838 (0.629-1.116)	1.215 (0.943-1.566)	1.377 (1.108-1.711)	1.389 (1.111-1.736)
RF+ polyarticular	1.282 (0.750-2.190)	1.552 (0.945-2.550)	1.806 (1.221-2.671)	1.707 (1.140-2.558)
Psoriatic	0.765 (0.484-1.209)	0.720 (0.456-1.135)	0.788 (0.546-1.136)	0.722 (0.488-1.068)
ERA	0.643 (0.414-0.999)	0.754 (0.481-1.182)	0.972 (0.684-1.381)	0.792 (0.542-1.157)
Undifferentiated	0.653 (0.222-1.920)	1.185 (0.431-3.260)	0.532 (0.231-1.225)	0.671 (0.289-1.555)
Time since diagnosis	0.785 (0.622-0.989)	0.911 (0.737-1.126)	1.034 (0.867-1.233)	0.956 (0.796-1.147)
Age at diagnosis	0.810 (0.643-1.021)	0.926 (0.750-1.143)	1.104 (0.926-1.317)	1.025 (0.855-1.230)
Number of DMARDs	0.923 (0.833-1.022)	0.948 (0.857-1.050)	1.019 (0.937-1.108)	0.966 (0.883-1.056)
PGA at prior visit	1.004 (0.841-1.199)	0.932 (0.759-1.143)	0.970 (0.825-1.139)	1.013 (0.854-1.202)
AJC at prior visit	0.999 (0.931-1.073)	1.004 (0.925-1.089)	0.947 (0.874-1.026)	0.944 (0.865-1.030)
PtGE at prior visit	0.832 (0.731-0.947)	0.758 (0.655-0.878)	0.929 (0.820-1.053)	0.882 (0.771-1.008)
cJADAS at prior visit	0.942 (0.838-1.059)	0.994 (0.872-1.133)	1.057 (0.942-1.187)	1.065 (0.941-1.206)
provCID at prior visit	0.557 (0.295-1.051)	0.572 (0.315-1.038)	0.610 (0.374-0.996)	0.750 (0.450-1.249)
preCID at prior visit	1.584 (0.873-2.872)	1.880 (1.054-3.353)	5.520 (3.435-8.871)	4.508 (2.733-7.433)
Morning stiffness at prior visit (ref none)				
≤15 minutes	0.552 (0.378-0.805)	0.580 (0.386-0.870)	0.875 (0.625-1.225)	0.680 (0.471-0.981)
16-60 minutes	0.647 (0.426-0.981)	0.523 (0.324-0.844)	0.816 (0.565-1.181)	0.512 (0.335-0.780)
>60 minutes	0.454 (0.297-1.002)	0.643 (0.298-1.386)	0.622 (0.345-1.122)	0.587 (0.311-1.107)
Unknown	0.516 (0.308-0.865)	0.670 (0.390-1.151)	0.980 (0.635-1.512)	0.929 (0.592-1.456)

cJADAS LDA – clinical Juvenile Arthritis Disease Activity Score Low Disease Activity, OR – odds ratio, CI – confidence interval, ref – reference, JIA – juvenile idiopathic arthritis, RF – rheumatoid factor, ERA – enthesitis related arthritis, DMARDs – disease modifying anti-rheumatic drug, PGA – physician global assessment, AJC – active joint count, PtGE – patient/parent global assessment of wellbeing, cJADAS – clinical Juvenile Arthritis Disease Activity Score , provCID – ACR provisional criteria for clinical inactive disease, preCID – ACR preliminary criteria for clinical inactive disease

clinical inactive disease (preCID), and the ACR provisional criteria for clinical inactive disease (provCID). Subjects could contribute more than one observation. The association of tolerated inactive or active disease and clinical characteristics were assessed by logistic regression.

Results: There were 8,244 subjects with non-systemic JIA enrolled in the CARRA Registry. No medication change for >180+60 days occurred 16,214 times in 6,235 subjects. Among eligible participants with measurement at the time of the first eligible visit, mean age was 11.7 years, most had oligoarthritis (36%) or rheumatoid factor negative (RF-) polyarthritis (35%), were female (72%), and were white (82%). A physician global score >0 occurred at 45% of tolerated disease activity visits, ≥1 active joints were documented at 29% of visits (Table 1), and 10% patients reported >15 minutes of morning stiffness.

Only 33% (n=6445) of visits met preCID, 29% (n=5753) met provCID, and 25% (n=4815) met cJADAS inactive disease (ID). Black race was associated with decreased likelihood of cJADAS low disease activity (LDA), preCID, and provCID, but not cJADAS ID at the time of tolerated disease activity (Table 2). Polyarticular disease and preCID at the prior visit were associated with increased likelihood of preCID and provCID at tolerated disease activity visit. Enthesitis-related arthritis and time since diagnosis were associated with decreased likelihood of cJADAS LDA and Hispanic ethnicity and PtGE were associated with decreased likelihood of both cJADAS LDA or ID at the tolerated disease activity visit.

Conclusion: In a large North American registry, patients with JIA frequently had episodes of no medication changes for >6 months. At the time of presumed tolerated disease activity, many patients with JIA had active disease by simple and composite measures. Additional studies are needed to investigate the patient characteristics associated with disease activity and to assess the outcomes following maximally tolerated disease activity states.

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Abstract Number: 0256

Consensus Approach to a Treat to Target Strategy in Juvenile Idiopathic Arthritis Care: Report from the 2020 Pediatric Rheumatology Care and Outcomes Improvement Network Consensus Conference

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Table 1. Top ranked answers from second voting rounds for question 1 about key elements in target setting

Table 1 **Question 1: What are the most important elements to consider when setting an individual's target, that considers both the patient/family point of view as well as the point of view of the health care team (i.e., shared decision making)?**
Round 2 results: 140 responses, 20 voters (number of votes received, percent of voters selecting the item)
1. Patient goals (21, 100%) 2. Disease activity score (cJADAS) (18, 80%) 3. Pain domain (16, 70%) 4. Quality of life (12, 60%) 5. Medication domain (12, 60%) 6. Presence of risk factors for poor outcomes (8, 40%) 7. Joint count (7, 25%) 8. Functional ability (6, 30%) 9. Pain interference (6, 25%) 10. Social participation (5, 25%)

Background/Purpose: Treat to target (T2T) is a strategy of adjusting treatment until a therapeutic target is reached. There is growing evidence supporting the use and efficacy of T2T in chronic rheumatic conditions. In 2018, an international task force that did not include parents or patients recommended T2T for juvenile idiopathic arthritis (JIA) treatment. After a successful pilot study, the Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN), a collaborative learning health network of 21 pediatric rheumatology centers across the United States and Canada, has been working together in partnership with patients and families to implement a T2T strategy. For successful implementation in a standard and reliable way in clinical practice, agreement is needed on the following areas: key elements of both (1) target setting and (2) T2T strategy, (3) identifying barriers to implementation and (4) determining eligible patients. In response, a consensus conference was held amongst PR-COIN stakeholders centered around four questions related to the listed areas in order to understand community priorities, to include patient/parent representation, as well as to gain agreement on a statement of understanding regarding the PR-COIN approach.

Table 2. Top ranked answers from second voting rounds for question 2 about key elements in Treat to Target

Table 2 **Question 2: What are the most important elements of a treat to target strategy?**
Round 2 results: 126 responses, 18 voters (number of votes received, percent of voters selecting the item)
1. Shared decision making (19 votes, 100%) 2. Clearly measurable outcomes (17, 89%) 3. Adjustment of treatment to meet goals (12, 83%) 4. Incorporate T2T into clinic workflow (12, 67%) 5. Training of providers and patients on the T2T process (10, 56%) 6. Patient's individual target (9, 50%) 7. Frequent assessment of activity and target status (9, 39%) 8. Provider, patient, and family buy-in (7, 39%) 9. Data collection into registry/EMR and display progress to patients (6, 28%) 10. Use of clinical decision support (5, 28%)

Table 3. Top ranked answers from second voting rounds for question 3 and 4 about important barriers in implementation of Treat to Target and eligible patients

Table 3 **Question 3: What are the most important barriers to implementation of a treat to target strategy?**	**Question 4: Who are the most important patients/patient groups to enroll in a treat to target strategy?**
Round 2: 20 voters, 140 responses (number of votes received, percent of voters selecting the item)	**Round 2: 19 voters, 133 responses** (number of votes received, percent of voters selecting the item)
1. Lack of incorporation of T2T into workflow (21, 90%) 2. Lack of buy-in domain (17, 85%) 3. Lack of resource domain (15, 75%) 4. Clinician time constraints (14, 55%) 5. Virtual care: inability to capture information needed (10, 50%) 6. Patient non-adherence (9, 45%) 7. Change management in providers and staff (9, 45%) 8. Resistance to change by providers and families (6, 30%) 9. Different perceptions and expectations of patients and clinicians (5, 25%) 10. Technical barriers (EMR -PRO measurements) (4, 20%)	1. All JIA patients (27, 58%) 2. Patients with poor prognostic factors (15, 68%) 3. Patient with a high disease burden (13, 63%) 4. Newly diagnosed JIA patients (12, 63%) 5. Diversity (10, 42%) 6. Any condition where disease activity is linked with damage (9, 32%) 7. JIA patient with active disease (8, 42%) 8. JIA patients with a flare (7, 37%) 9. Where targets are defined (6, 37%) 10. Patient seen by multiple providers (6, 26%)

Methods: PR-COIN stakeholders, including health care providers (n=16) and parents (n=4), were invited to form a voting panel. Using nominal group technique, two rounds of voting were held to address the above four areas to select the top 10 responses in rank order. Answers were recorded into an electronic polling software simultaneously by the pollsters and were viewable to the voting members. Each participant placed 7 total votes on answers they thought were of highest significance. Members were allowed to place multiple of their 7 votes on a single answer if desired. Once all votes were recorded, the pollsters revealed the top 10 items for the respective round.

Results: On October 22, 2020, a PR-COIN Consensus Conference was held. (1) Incorporation of patient goals ranked most important when setting a treatment target in both voting rounds. (2) Use of shared decision making (SDM), tracking measurable outcomes, and adjusting treatment to achieve goals were voted as top elements of T2T strategy. (3) Lack of incorporation of T2T into clinic workflow and provider participation in T2T strategy were identified as key barriers to T2T implementation. (4) Patients with JIA with poor prognostic factors and at risk for high disease burden were leading candidates for a T2T approach. Results of the second round of panel voting on the four questions are shown in Tables 1-3.

Conclusion: Thisconsensus conference identified the importance of incorporating patient goals as part of target setting and the influence of patient-stakeholder involvement in drafting treatment recommendations. The PR-COIN approach to T2T will be modified to address the above findings including solicitation of patient goals, optimizing SDM, and better workflow integration. Additional efforts will be required to optimally solicit patient goals and conduct longitudinal monitoring of progress.

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Can We Assess Disability in Juvenile Idiopathic Arthritis with Two Simple Questions? Results from the CAPRI Registry

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SESSION INFORMATION

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Table 1: Performance measures and (95% CI) for three ways of combining the two questions in a FAST index

Measure	HARD+HELP/8	Linear Regression	LASSO
Custom Kappa	0.43 (0.36, 0.51)	0.46 (0.39, 0.54)	0.52 (0.44, 0.60)
Quadratic Kappa	0.62 (0.54, 0.70)	0.65 (0.56, 0.74)	0.69 (0.61, 0.78)
MSPE*	0.31 (0.24, 0.38)	0.16 (0.12, 0.21)	0.14 (0.10, 0.18)
CLOSE**	40% (33, 47)	50% (43, 57)	51% (42, 59)

* MSPE is the mean squared prediction error, the smaller the number the smaller the squared differences between the estimated CHAQ and the measured CHAQ.

** CLOSE is the percent of estimated CHAQ scores that fall within 0.125 units of the measured CHAQ

Background/Purpose: To assess if a combination of two questions (Functional Arthritis Screening with Two Questions - FAST index) can detect and roughly estimate the degree of disability in children with juvenile idiopathic arthritis (JIA) when compared to the 30-item Childhood Health Assessment Questionnaire Disability Index (CHAQ).

Methods: Children newly diagnosed with JIA enrolled in the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) Registry from February 2017 to December 2018 formed a development cohort, while children diagnosed from January 2019 to February 2020 formed a validation cohort. At enrolment and at 1y parents completed the CHAQ. At every clinic visit they answered two questions: 1) Is it hard for your child to run and play because of arthritis? (HARD), 2) Does your child usually need help from you or another person because of arthritis? (HELP). Responses were scored on 21-point horizontal numerical rating scales from 0 to 10 at 0.5 intervals. We explored >20 different models for combining the two questions to estimate CHAQ scores, using cross-validation to measure performance in subjects not used in model development. Model performance was assessed by concordance with measured CHAQ scores (Kappa using quadratic weights or custom weights selected a priori), mean squared prediction error (MSPE), and the proportion of estimated scores within 0.125 units of the measured CHAQ (CLOSE). The selected model will be validated in the validation cohort.

Results: The development cohort included 216 children at enrolment and 159 at 1y. Both questions correlated with the CHAQ at enrolment (Spearman correlation 0.65 for HARD and 0.64 for HELP) and their scores (0 to 10) were stable in patients deemed unchanged by their parents; mean change -0.16 (95%CI -0.5, 0.1) for HARD, -0.3 (-0.5, -0.03) for HELP. Relative to simply adding the two question scores and dividing by 8, a linear regression model including only

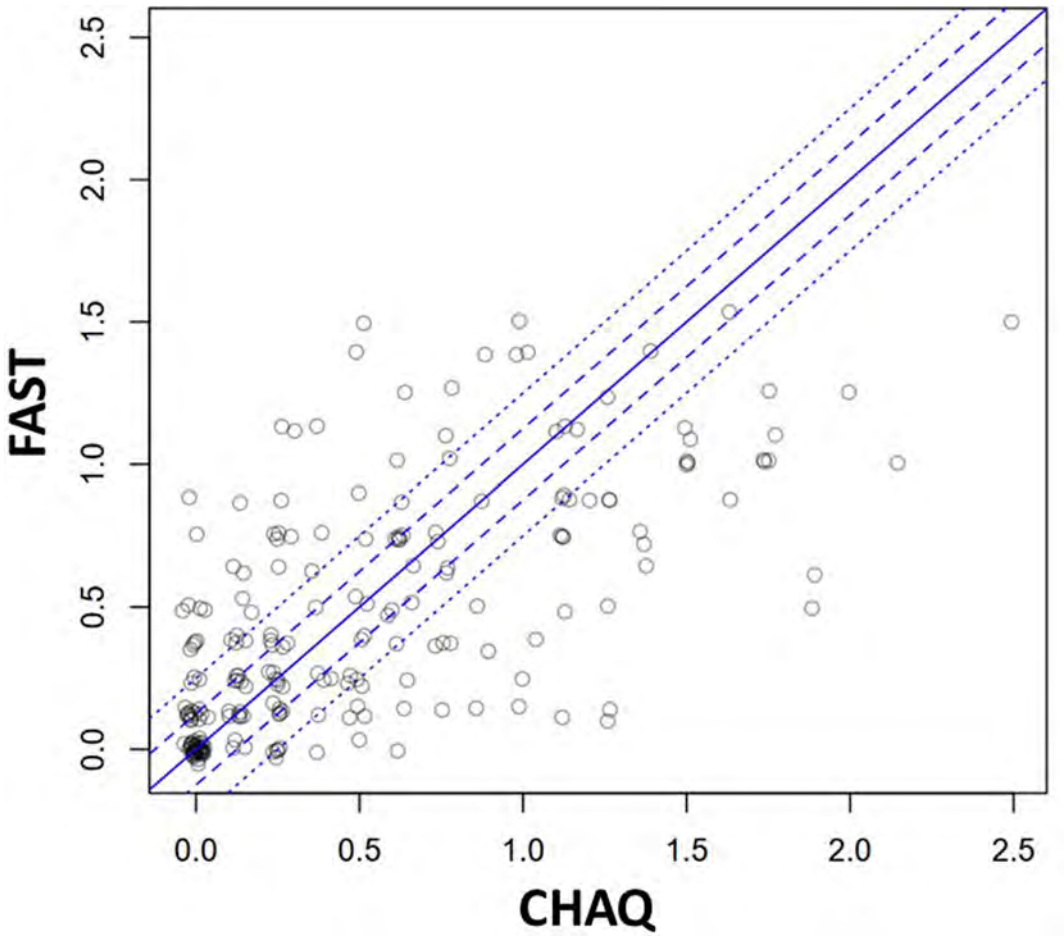

Figure 1. Two-way scatter plot of CHAQ scores estimated with the FAST index and measured CHAQ scores.

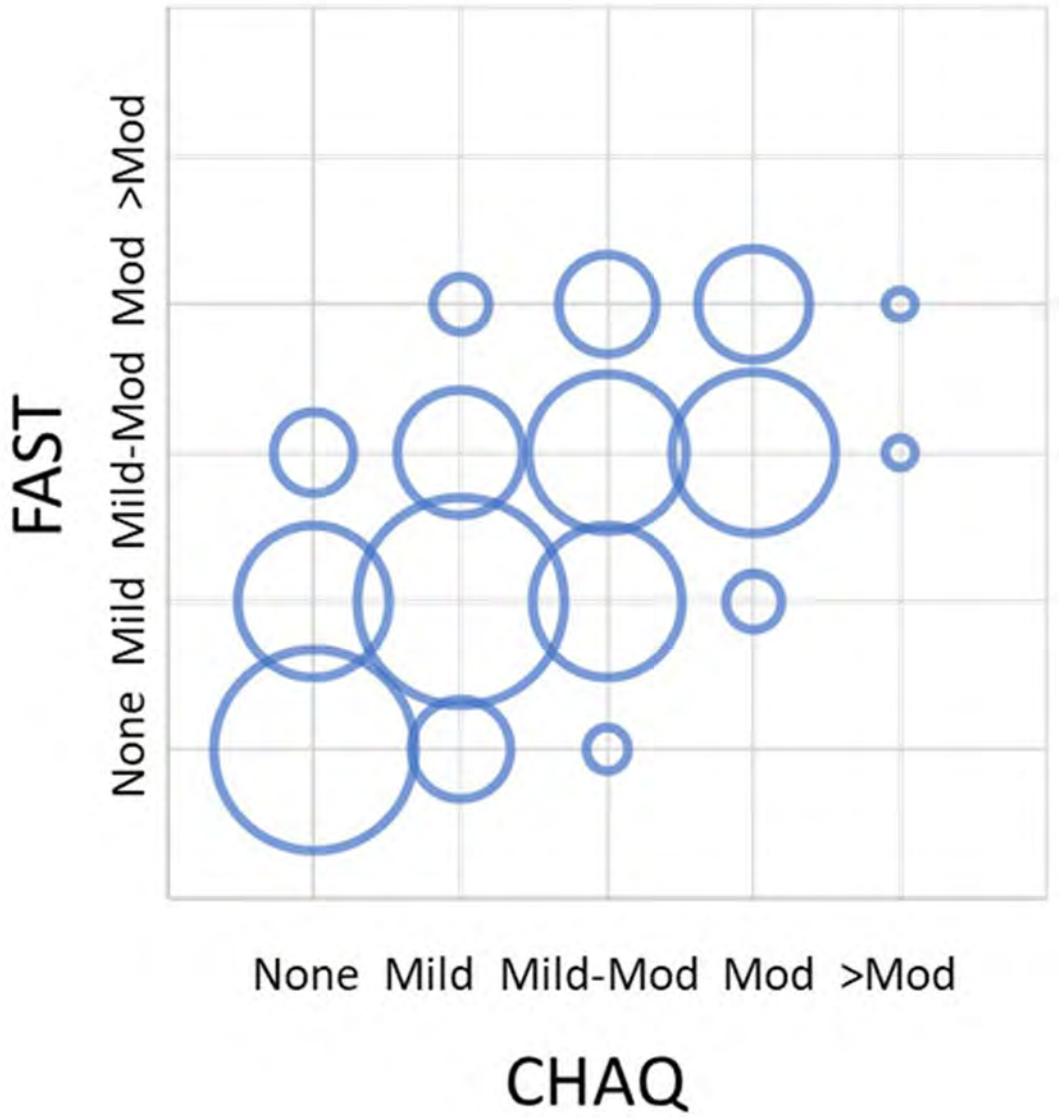

Figure 2. Ability of FAST to detect degrees of disability according to published CHAQ cut-offs (Dempster et al 2001).

HARD and HELP decreased the MSPE by half (Table 1). Using a Least Absolute Shrinkage and Selection Operator (LASSO) to add other patient characteristics led to further improvements. The best LASSO model combined HARD and HELP with age, JIA category, number of active joints and pain intensity to estimate CHAQ scores. We selected the FAST linear regression model for its balance of simplicity and performance. Figure 1 shows the concordance of this model with the measured CHAQ. Sensitivity to detect any disability (CHAQ >0) was 0.94 with a specificity of 0.56. FAST detected some disability in 27/61 (44%) of patients with a CHAQ of zero and often reported higher levels of disability than the CHAQ at lower CHAQ scores (Figure 2). Responsiveness (SRM, mean change from enrolment to 1y divided by the standard deviation) was 0.52 for FAST and 0.40 for CHAQ. Validation cohort analyses are underway.

Conclusion: This FAST index seems highly sensitive to detect disability in children with JIA and often detects unmeasured disability in patients with a CHAQ of zero. It had moderate concordance with levels of disability assessed by CHAQ, but greater sensitivity to change. It could be used as a quick and simple screen for disability at every clinic visit.

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Abstract Number: 0258

Developing Electronic Health Record Algorithms That Accurately Identify Patients with Juvenile Idiopathic Arthritis

Hannah Peterson[1], April Barnado[2] and Anna Patrick[2], [1]Lipscomb University College of Pharmacy, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Electronic Health Records (EHRs) store nearly all clinical data in one central location providing increased accessibility, accuracy, and security. At our institution, the Synthetic Derivative (SD) is a de-identified EHR containing over 3.2 million records that links to a DNA biorepository, BioVU. The objective of this study is to develop an algorithm to detect a highly sensitive and specific cohort of juvenile idiopathic arthritis (JIA) patients in the EHR. Within this cohort, we determine characteristics of the identified JIA patients.

Methods: We developed our cohort by searching International Classification of Diseases, Ninth (ICD-9) and Tenth (ICD-10-CM) Revisions and keywords in the SD. *A priori*, ICD-9 and ICD-10-CM codes and keywords clinically rele-

Table 1. ICD codes and keywords used in JIA algorithms

ICD-9		ICD-10	
714	Disorders of the Musculoskeletal System	M08	Disorders of the Musculoskeletal System
714.3	Juvenile chronic polyarthritis	M08.0	Unspecified juvenile rheumatoid arthritis
714.30	Polyarticular juvenile rheumatoid arthritis, chronic or unspecified	M08.1	Juvenile ankylosing spondylitis
714.31	Polyarticular juvenile rheumatoid arthritis, acute	M08.2	Juvenile rheumatoid arthritis with systemic onset
714.32	Pauciarticular juvenile rheumatoid arthritis	M08.3	Juvenile rheumatoid polyarthritis (seronegative)
714.33	Monoarticular juvenile rheumatoid arthritis	M08.4	Pauciarticular juvenile rheumatoid arthritis
		M08.8	Other juvenile arthritis
		M08.9	Juvenile arthritis, unspecified
		L40	Psoriasis
		L40.54	Psoriatic juvenile arthropathy
Keywords			
"juvenile rheumatoid arthritis" "uveitis"		"juvenile idiopathic arthritis" "enthesitis"	

Table 2. Algorithms with the highest F-scores

Algorithm		PPV	Sensitivity	F-Score
Code Search	Keyword Search			
≥4 counts of any ICD-9 or ICD-10-CM JIA code	juvenile idiopathic arthritis ***OR*** juvenile rheumatoid arthritis ***OR*** uveitis ***OR*** enthesitis	0.865	0.874	0.869
≥3 counts of any ICD-9 or ICD-10-CM JIA code	juvenile idiopathic arthritis ***OR*** juvenile rheumatoid arthritis ***OR*** uveitis ***OR*** enthesitis	0.833	0.895	0.863
≥4 counts of any ICD-9 or ICD-10-CM JIA code	juvenile idiopathic arthritis ***OR*** juvenile rheumatoid arthritis **plus** uveitis ***OR*** enthesitis	0.961	0.768	0.854
≥4 counts of any ICD-9 or ICD-10-CM JIA code	-	0.83	0.874	0.851

vant to juvenile arthritis were selected (Table 1). Keywords were identified by a survey of pediatric rheumatologists at a single site. Keywords selected were included in at least 75% of survey responses and returned less than 3000 cases in individual searches of the SD. Uveitis returned >3000 cases in the SD but was retained due to recurring appearances in confirmed JIA charts. We then combined the ICD codes with the keywords for possible algorithms. Algorithms used varying ICD code counts and searched keywords by "and" or "or" functions. A training set of 200 random charts was identified from a search of ≥1 count of the ICD-9 and ICD-10-CM JIA codes. Case status was determined by a pediatric rheumatologist who required a rheumatology clinic note documenting a JIA diagnosis before age 20. Positive predictive values, sensitivities, and F-scores were calculated for each algorithm. The F-score is the harmonic mean of the PPV and sensitivity and is frequently used in bioinformatics, as it accounts for both PPV and sensitivity.

Results: We analyzed 21 algorithms and ranked them by F-score. Our highest performing algorithm required ≥4 ICD-9 or ICD-10-CM code counts and any of the selected keywords to be present. It identified 1,514 patients and produced an F-score of 0.87. Other high performing algorithms used similar search methods (Table 2). Demographic data and age at first diagnosis in the EHR were analyzed for the cohort with the highest performing algorithm. Our JIA population was 72% female and 81% Caucasian. Approximately 20% of the JIA population had EHR diagnosis in the first 3 years of life, and 84% had EHR diagnosis appearing before 16 years of life. The ICD code that appeared most frequently in our cohort was the ICD-9 code, "Polyarticular juvenile rheumatoid arthritis, chronic or unspecified" (714.30).

Conclusion: We have developed algorithms for accurately identifying JIA patients in the EHR. Combining ICD-9 codes, ICD-10-CM codes and keywords produced a more sensitive and specific cohort than using ICD-9 or ICD-10-CM codes alone. Requiring multiple instances of the ICD-9 or ICD-10-CM codes also improved algorithm performance. Our identified cohort reveals demographic and diagnosis patterns among the JIA patients in our region. Assembling an EHR-based JIA cohort will enable longitudinal, de-identified chart review and linkage to the BioVu DNA repository for future studies.

Disclosure: H. Peterson, None; **A. Barnado**, None; **A. Patrick**, None.

Abstract Number: 0259

JIA Diagnoses and Trends from 2006-2019: Has the U.S. ICD-9-to-ICD-10 Transition Created Coding Artifacts?

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: JIA is the most common rheumatic disease of childhood, but recent data on diagnostic trends in the US are lacking. Furthermore, the impact of the ICD-9/ICD-10 transition on the rates of JIA diagnoses is unclear. We sought to characterize recent trends in JIA claims, including changes related to the US International ICD-9/ICD-10 transition in late 2015.

Methods: We studied JIA diagnoses within administrative claims data on commercially insured children under age 18 from 14 geographically diverse US states in the HealthCore Integrated Research Database (2006-2019). JIA diagnoses were defined by claims with diagnostic codes (ICD-9 696.0, 714, or 720; ICD-10 L40.5, M05, M06, M08, or M45), requiring at least 1 inpatient claim or 2 outpatient claims between 8 and 52 weeks apart. Incident diagnoses were defined as having at least 6 months of baseline data without previous JIA claim; prevalent diagnoses could have occurred at any time. Incidence and prevalence of JIA were calculated quarterly 2006-2019, excluding 6 months before and 6 months after the ICD-9/10 transition to limit transitional coding errors. Trends and changes in level around the

Table. Characteristics of children diagnosed with JIA in commercial administrative claims data, 2006-2019

	Incident JIA Outpatient		Prevalent JIA Outpatient		Incident JIA Inpatient		Prevalent JIA Inpatient	
Characteristics	ICD-9 (n=10,390)	ICD-10 (n=3,830)	ICD-9 (n=14,458)	ICD-10 (n=5,745)	ICD-9 (n=1,118)	ICD-10 (n=511)	ICD-9 (n=1,355)	ICD-10 (n=600)
Age group, %								
0 - 5 years	11.9%	12.7%	15.7%	14.8%	17.5%	14.7%	18.9%	15.1%
6 - 11 years	24.5%	27.6%	29.6%	31.6%	25.1%	25.0%	24.2%	25.4%
12 - 17 years	63.6%	59.7%	54.7%	53.6%	57.3%	60.3%	56.9%	59.4%
Age								
Mean (standard deviation)	12.6 (4.5)	12.2 (4.5)	11.7 (4.6)	11.7 (4.5)	11.7 (4.9)	12.2 (4.8)	11.6 (5.1)	12.2 (4.8)
Sex, %								
Female	63.3%	67.6%	64.5%	69.4%	59.7%	62.0%	59.6%	63.3%
Male	36.7%	32.4%	35.5%	30.6%	40.3%	38.0%	40.4%	36.7%
DMARD dispensed within 6 months after JIA diagnosis, %								
Conventional DMARD	14.7%	27.5%	26.5%	38.8%	18.2%	23.3%	21.2%	25.5%
Biologic DMARD	6.0%	20.6%	17.1%	40.7%	10.9%	30.5%	15.3%	33.5%
Number of medications dispensed within 6 months after JIA diagnosis, mean (standard deviation)								
Number of medication classes	1.9 (2.8)	2.7 (3.0)	2.3 (3.2)	3.4 (3.8)	3.3 (4.1)	4.1 (4.4)	3.8 (4.6)	4.6 (5.0)
Number of medications dispensed	4.6 (7.7)	6.7 (8.9)	6.0 (9.4)	9.0 (11.6)	8.0 (12.0)	10.7 (13.6)	9.5 (13.7)	12.3 (15.4)

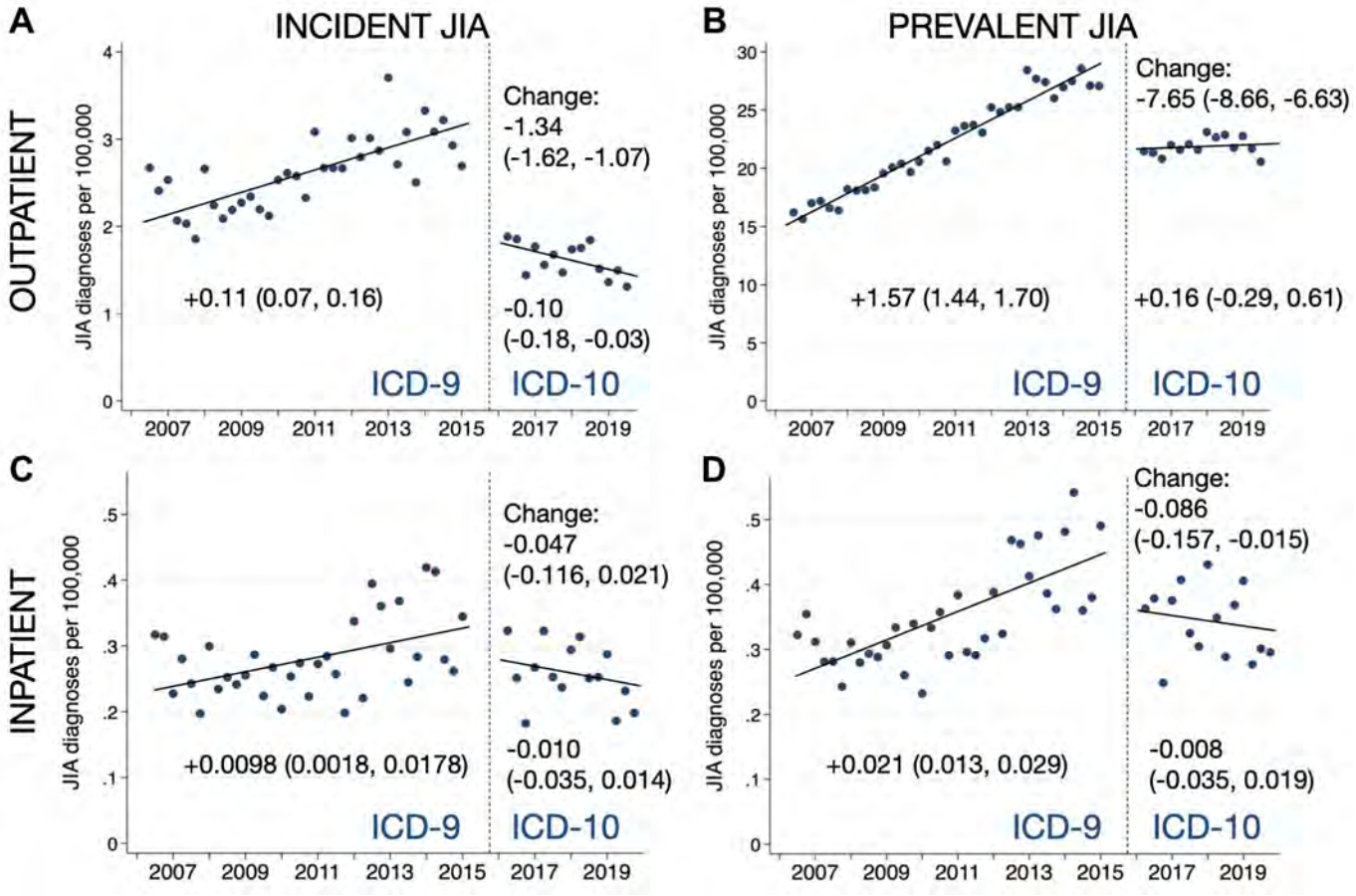

Figure. Trends and changes in ICD-9 and ICD-10 claims for JIA in commercial administrative claims data, 2006-2019. Graphs show yearly rates of JIA diagnoses per 100,000 children in commercial claims data based on ICD-9 codes (2006-2015) or ICD-10 codes (2016-2019). Diagnoses reflected ≥2 outpatient claims 8-52 weeks apart (A and B) or ≥1 inpatient claim (C and D). Incident JIA diagnoses (A and C) required ≥6 months of JIA-free baseline time; prevalent JIA diagnoses (B and D) could have occurred at any time. Trends and changes in level before and after the ICD-9/10 transition were estimated using segmented regression from interrupted time-series.

ICD-9/10 transition were analyzed by single-group interrupted time-series using ordinary least-squares segmented regression.

Results: Of 26.5 million children identified, 22,158 had claims for JIA by ICD-9 or ICD-10 code in any setting (0.084%). Over half of children diagnosed with JIA were 12-17 years old, and approximately 2/3 were female (Table). ICD-9-based incident and prevalent diagnoses of JIA steadily increased in both outpatient and inpatient settings (Figure). Rates of JIA, both incident and prevalent, dropped abruptly in both outpatient and inpatient settings at the time of the ICD-9/10 transition (Figure). In outpatient settings, ICD-10-based incident JIA diagnoses have declined since then, whereas prevalent JIA diagnoses have remained stable (Figure). There have been modest, but not statistically significant, declines in ICD-10-based diagnoses from inpatient settings (Figure). Rates of recorded conventional and biologic DMARD use were higher among children diagnosed by ICD-10 code than children diagnosed by ICD-9 code (Table).

Conclusion: Among commercially insured children, apparent incident and prevalent rates of claims for JIA declined abruptly with the US transition from ICD-9 to ICD-10, likely reflecting an artifact of changes in the sensitivity and specificity of coding practices. The higher prevalence of DMARD use by children diagnosed with JIA in the ICD-10 era could suggest greater diagnostic specificity, but the uncertain validity of both ICD-9 and ICD-10 claims warrants

further research. New JIA diagnoses appeared to rise until 2015 and fall since 2016; more work is needed to establish to what extent these trends reflect temporal changes in coding practices versus true changes in JIA epidemiology.

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Abstract Number: 0260

Impact on Caregivers of Patients with Juvenile Idiopathic Arthritis: A Hospital-based Study from India

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile idiopathic arthritis is a chronic disease that impacts patient's physical and mental health. Caregivers act as a bridge between physicians and patients, by ensuring good adherence to treatment and they also help in assessing the day-to-day life of the patient. The extra burden of caring for a child with JIA and seeing a child with disease can have a significant impact on the caregiver-child or caregiver-family member relations. Data on the impact of JIA on caregivers from South Asia is limited thus, we used a recently described questionnaire.

Methods: Caregivers of patients with JIA who visited the outpatient clinic of the Department of Clinical Immunology and Rheumatology of a tertiary care hospital in North India and consented to participate in the study were included. They were asked to fill out a questionnaire of 28 questions (CAREGIVERS questionnaire described by Torres-Made et al) regarding the emotional, social, financial, labor, family, and relations impact. Information about educational level and relationship to the patient was also collected. Data on disease activity, damage, and medications were collected from patient's hospital records.

Results: Caregivers of 99 patients with JIA were enrolled. 60 of them were fathers and 15 of them mothers, the rest included other relatives Among these 99 patients 59 had enthesitis-related arthritis, 26 had polyarticular JIA, 10 had systemic JIA and 4 had oligoarticular JIA. 40 patients had active disease while the rest were in remission. 12 children had joint damage (JADI score 1-10) and none had any extraarticular damage. 67 patients were on DMARDs, 11 were on NSAIDs alone and 9 were on no treatment. Only 5 patients were on biologicals or tofacitinib.

All of the caregivers had a significant impact on the emotional, social, economic, and labour domains, but spirituality and relations were less affected.

54% of caretakers expressed sadness at the time of diagnosis and 29% expressed denial. This changed to 36 percent showed concern, 24 percent showed sadness and 22 percent of them expressed relief. They were worried about the pain of the patient (34%), the restrictions on mobility (47%) and 10% concerned about the expenses of treatment, and 4%

concerned about the medical appointments. They worried about the future of the child, 39% worried they will have major problems, and 25% worried that child will have some problems in the future. 85% had anxiety and 55 % were sad about sharing the news of child's disease, and 15% didn't want to share it with anyone. Their social life changed a lot for 24% and a little for 31% whereas for 43% it has not changed much. 32% of caretakers neglected their health and 14% became sick. The financial condition worsened for 61% and didn't change for 31%. 54% had to borrow money from others and 6% had to stop buying medicines for their child because of poverty. 28% received financial aids for the treatment.

This impact was equal across all the subtypes of JIA. There was no relationship with the disease activity, damage, or type of medications.

Conclusion: JIA has a significant emotional, social, labor and economic impact on caregivers. Strategies to cope with this impact need to be addressed in the clinic by social workers.

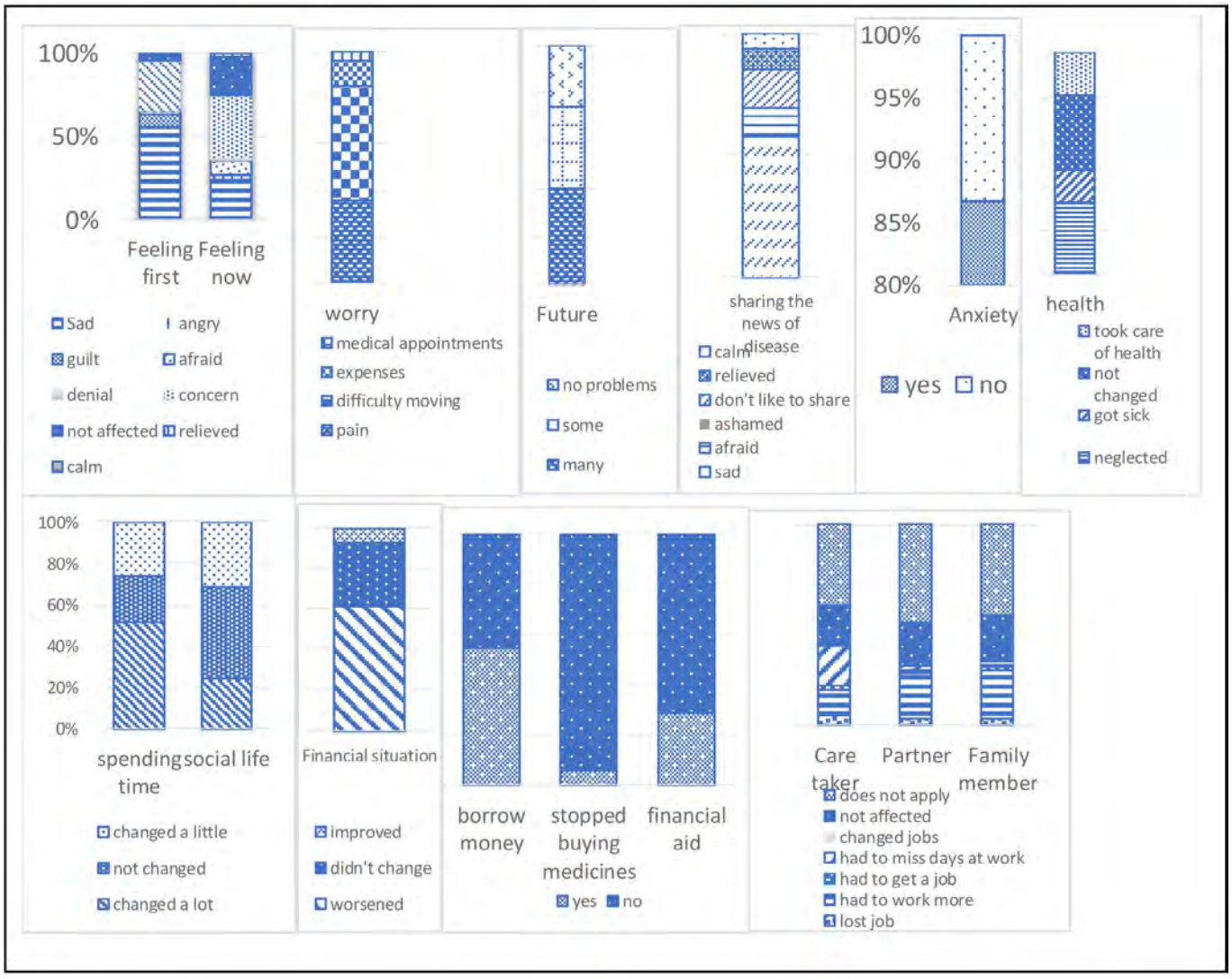

Figure 1. Emotional, social, economic, and labor impact on caregivers of JIA

Domains	Total Score (Min-Max)	Mean	Median (IQR)	Correlation with the total score (r)
Emotional Impact	4-18	13.46±3.89	14(12-15)	0.56(p<0.001)
Social Impact	2-9	5.45±3.82	6(4-7)	0.58(p<0.001)
Economic Impact	0-5	2.33±2.25	2(1-3)	0.38(p<0.001)
Labour Impact	0-15	4.16±8.32	3(0.25-6.75)	0.67(p<0.001)
Family Impact	4-16	6.52±3.26	6(5-8)	0.47(p=0.56)
Relationship Impact	0-8	1.51±2.04	2(1-2)	0.06(p=0.56)
Impact on spirituality	0-5	0.75±1.78	1(0-1)	0.07(p=0.53)
Impact of social networks	0-8	1.48±4.41	0(0-4)	0.34(p=0.01)
Total Score	10-84	35.75±16.68	34(31-40)	1

Caregivers questionnaire-Impact scores

Disclosure: N. Gowda, None; **A. Samuel**, None; **A. Yadav**, None; **A. Aggarwal**, None; **A. Balakrishnan**, None.

Abstract Number: 0261

Methotrexate Withdrawal and Outcomes in Participants with Well-controlled Non-systemic JIA Within the CARRA Registry

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
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Background/Purpose: Methotrexate (MTX) is currently the recommended first-line conventional DMARD for the treatment of JIA with oligo- or polyarthritis. There are limited data on how or when to stop MTX monotherapy for well-controlled JIA. The aims of this study were to 1) describe the MTX withdrawal strategies used for well-controlled JIA in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry, 2) compare time to flare among different MTX withdrawal strategies, and 3) evaluate the duration of disease remission after MTX withdrawal.

Methods: The study population consisted of patients enrolled in the CARRA Registry with a diagnosis of non-systemic JIA on MTX monotherapy for at least 12 months and with 2 consecutive registry visits with no reported disease activity (based on joint count = 0 and no changes in medication). Subjects with systemic JIA, non-JIA rheumatic diseases or inflammatory bowel disease were excluded. Subjects were divided into 3 cohorts: 1) MTX continuation,

Table 1. Selected subject characteristics in the three MTX withdrawal cohorts

Characteristic	Continuing use (N=233)	Tapering (N=90)	Discontinue without taper (N=54)	P-value[1]
DEMOGRAPHICS				
Age in years at diagnosis, median (IQR)	4.04 (2.26, 9.05)	5.12 (2.73, 10.01)	5.75 (2.78, 8.71)	0.21
Female sex	174 (74.68%)	69 (76.67%)	41 (75.93%)	0.93
JIA CHARACTERISTICS				
Years of JIA at baseline, median (IQR)	2.85 (1.52, 6.15)	3.01 (1.80, 5.81)	2.79 (1.80, 5.38)	0.90
JIA Category				0.59
Oligoarthritis	106 (45.69%)	44 (48.89%)	26 (48.15%)	
Polyarthritis (RF -)	90 (38.79%)	37 (41.11%)	19 (35.19%)	
Polyarthritis (RF +)	9 (3.88%)	0 (0.00%)	3 (5.56%)	
Psoriatic arthritis	12 (5.17%)	5 (5.56%)	5 (9.26%)	
Enthesitis related arthritis	8 (3.45%)	2 (2.22%)	1 (1.85%)	
Undifferentiated arthritis	7 (3.02%)	2 (2.22%)	0 (0.00%)	
Prior disease flare	25 (10.73%)	10 (11.11%)	3 (5.56%)	0.49
TREATMENT CHARACTERISTICS				
Months of methotrexate, Median (IQR)	21.70 (17.97, 29.38)	22.03 (18.56, 28.33)	23.20 (16.98, 30.13)	0.97
Any prior TNF inhibitor use	28 (12.02%)	6 (6.67%)	6 (11.11%)	0.37

IQR interquartile range

[1] P-value by Chi-square test, Fisher exact test, or Wilcoxon rank sum test, as appropriate

2) MTX tapering, or 3) MTX discontinuation without taper. Rates of flare (new or increased JIA medication, > 0 joint count) were compared among groups using Kaplan-Meier curves and multivariable Cox regression, adjusted for demographic, disease, and medication history covariates. Rates of remission were also compared between subjects who stopped MTX without taper and subjects who tapered MTX, using descriptive statistics.

Results: Of 9835 persons in the CARRA Registry, 377 fulfilled the study criteria. MTX monotherapy was continued in 233 (61.8%), tapered in 90 (23.9%) and stopped in 54 (14.3%). Of MTX continuers, 25 (10.7%) were subsequently observed to withdraw MTX (2 tapered, 23 stopped). Subject characteristics (Table 1) did not differ significantly among the groups. Most subjects (85%) had oligoarthritis or RF – polyarthritis, consistent with overall JIA enrollment distribution. Prior TNF inhibitor use was less common among those who tapered, while prior flares were less commonly recorded among those who stopped MTX without taper. No association was found between flare of JIA and MTX withdrawal strategy in unadjusted analyses (Figure) or adjusted models (taper vs. continuation: 0.89, 95% CI

Table 2. JIA remission rates after MTX withdrawal

Disease remission	Discontinue without taper[1] (N=58)	All tapers, time from start of taper[1] (N=81)	P-value	Subjects who stopped MTX after taper (N=31)	
				Time from start of taper (N=31)	Time from end of taper (N=24)
@6 months	36 (62.1%)	60 (74.1%)	0.13[2]	28 (90.3%)	15 (62.50%)
@12 months	17 (41.5%)	34 (51.5%)	0.31[2]	14 (60.9%)	7 (43.75%)
Median months in remission (IQR)	6.8 (4.9, 12.9)	10.8 (6.7, 15.6)	0.01[3]	11.9 (7.8, 15.6)	7.4 (4.2, 11.8)

IQR interquartile range; SD standard deviation

[1] Includes some subjects who initially continued MTX before withdrawal

[2] P-value by Chi-square test

[3] P-value by Wilcoxon rank sum test

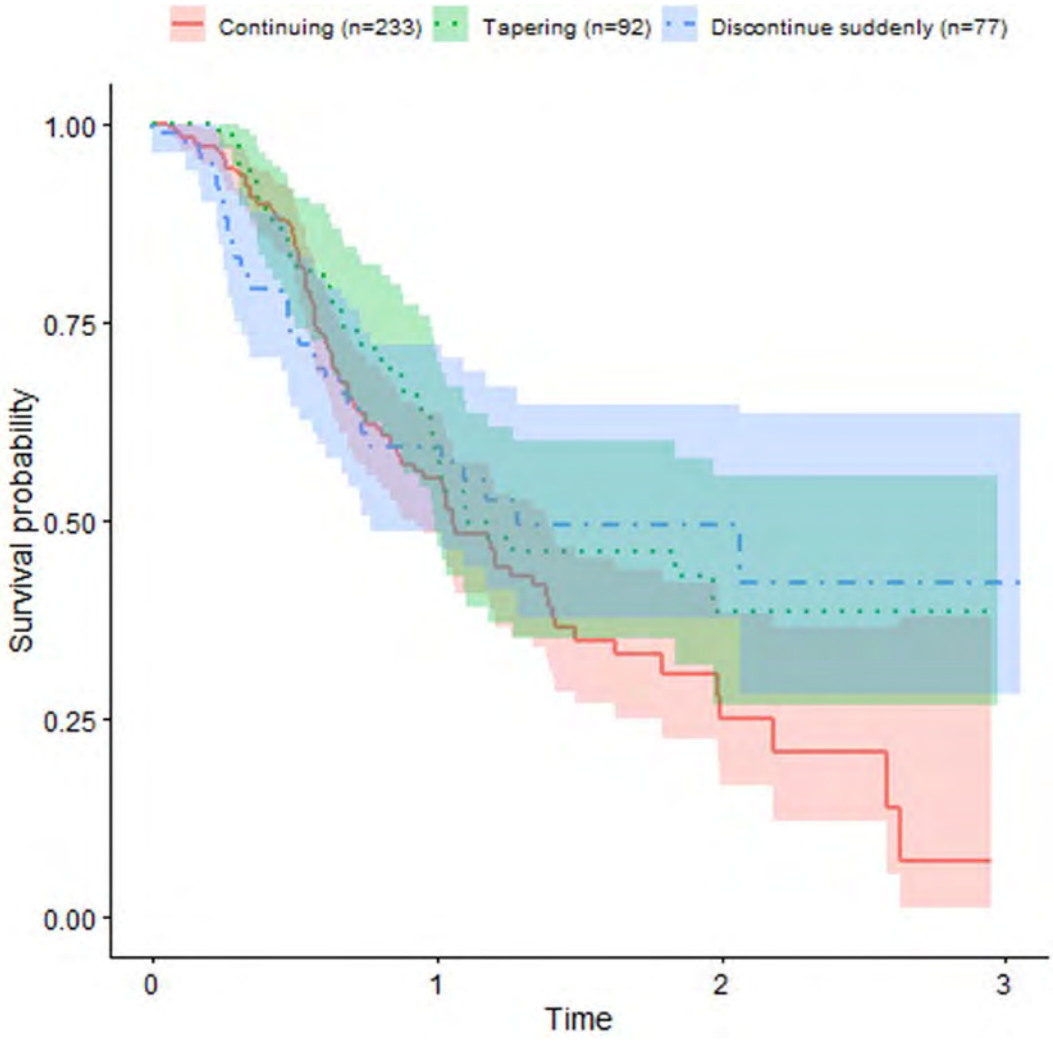

Figure. Kaplan-Meier survival curves comparing risk of flare based on MTX withdrawal strategy.

0.59-1.34; discontinuation vs. continuation: 0.90, 95% CI 0.54-1.48). Rates of sustained remission and median time in remission were modestly higher among those who tapered MTX compared to those who stopped MTX (Table 2). Among those who were in sustained remission after tapering MTX, rates of remission were higher before tapering than afterwards (Table 2).

Conclusion: Within the CARRA Registry, we did not observe significant differences in time to flare between subjects with non-systemic JIA who continued MTX and those who tapered or stopped MTX. This may reflect bias from residual confounding. Rates of sustained remission were modestly higher during times of MTX tapering compared to times after discontinuation.

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Abstract Number: 0262

High Degree of Inter-patient Heterogeneity in Synoviocyte Hyperplasia and Immune Cells Infiltration in the Synovium of Juvenile Idiopathic Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: Increasing evidence indicates that synovial tissue analysis can deliver pathophysiological insights but also individual clinically-relevant information in adult-onset inflammatory arthritides. Little is known about synovial pathology in juvenile idiopathic arthritis, especially regarding inter-patient variability of histopathological features.

To assess the heterogeneity of main synovial features (synoviocyte hyperplasia and immune cells infiltration) in juvenile idiopathic arthritis (JIA) patients and a cohort of young adults (< 30 years old) with early rheumatoid arthritis (RA).

Methods: Synovial biopsies were sampled using needle arthroscopy or ultra-sound (US) guided biopsy during intra-articular joint injection. Tissue was embedded in paraffin then sections were stained with hematoxylin and eosin. Synoviocyte hyperplasia (SH) and immune cells infiltration (ICI) was assessed by an experienced pathologist on a 0 – 3 scale where 0 represents the absence of the feature and 3 the highest level.

Results: 34 JIA patients (age (median ±SD): 15.5±6.47 years, oligo-articular JIA n=28/34, polyarticular JIA n=6/34, ANA-RF-ACPA positivity=56%-10%-3%) and 22 RA (age (median ±SD): 24.3±2.6 years, ANA-RF-ACPA positivity=10%-36%-32%) patients were included. Synovial tissue was obtained from knee (n=49/56), wrist (n=4/56) or metacarpophalangeal/intercarpophalangeal joints (n=3/56), using US guided biopsy in 27% of patients and needle arthroscopy in 73%.

Individual scores of SH and ICI were correlated in both JIA (Spearman's *r*=0.503, p value=0.0024) and RA (Spearman's *r*=0.636, p value=0.0015). There was no significant difference in SH and ICI scores between the 2 groups (SH score (Q25-Q50-Q75) in JIA= 0.5-1.125-2 and in RA = 0.75-2-2 ; ICI score (Q25-Q50-Q75) in JIA= 1-2-2 and in RA = 0.75-2-2.25). Intra-group variability of the two assessed features was comparable between the 2 groups (SH coefficient of variation: 72.2% for JIA and 68.2% for RA ; ICI coefficient of variation: 52.2% for JIA and 71.2% for RA). Within JIA patients, there was no significant difference in SH/ICI scores between groups based on ANA positivity, oligo or polyarticular involvement nor ongoing treatment.

Conclusion: Studying main histological features of synovitis, we found no difference between JIA and young RA patients. Furthermore, we report a similar degree of inter-patient heterogeneity in synovial pathological features of JIA and RA patients. These variations were not explained by common clinical characteristics. Whether they relate to different molecular signatures as suggested in adult RA will be further investigated using bulk tissue RNA sequencing.

Disclosure: C. TRIAILLE, None; **C. BOULANGER**, None; **T. SOKOLOVA**, None; **L. MERIC de BELLEFON**, None; **A. NZEUSSEU TOUKAP**, Abbvie, 1, 5, Eli Lilly, 1, 5, Janssen, 1, 5, UCB, 1, 5, Celgene, 1, 5, Pfizer, 1, 5; **C. GALANT**, None; **N. LIMAYE**, None; **B. LAUWERYS**, UCB Pharma, 3; **P. DUREZ**, Bristol-Myers Squibb, 6, Sanofi, 6, Eli Lilly, 6, Celltrion, 6.

Abstract Number: 0263

Patterns of Medication Switching in Juvenile Idiopathic Arthritis: A Retrospective Analysis of a National Administrative Claims Database

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Although the increasing availability of biologic disease-modifying antirheumatic drugs (bDMARDs) and targeted synthetic DMARDs (tsDMARDs) has significantly improved outcomes for patients with Juvenile Idiopathic Arthritis (JIA), a substantial proportion of patients do not respond to an initial therapy, requiring switching to a second bDMARD/tsDMARD. Subsequent treatment decisions for children with continuing disease activity are haphazard, following a "trial and error approach". The objective of this study is to characterize patterns of bDMARD/tsDMARDswitching among patients with JIA in real-world clinical settings following the initial bDMARD/tsDMARD therapy.

Table 1. Study subjects (n=2,076)

Attribute	
Gender, n (%)	
Female	1346 (64.8)
Male	730 (35.2)
Age, median (IQR)	14 (10 – 18)
Number of switches during the study period, n (%)	
1	644 (31.0)
2	203 (9.8)
3	72 (3.5)
4	19 (0.9)
5	9 (0.4)
6	2 (0.1)
% of early switchers (switching within 180 days of initial therapy)	
Years 2008 to 2010	12.1
Years 2011 to 2013	13.3
Years 2014 to 2016	11.5
Years 2017 to 2020	13.1
First biologic, n (% of total cohort)	
TNFi	1893 (91.2)
Abatacept	45 (2.2)
Tocilizumab	30 (1.4)
Others*	108 (5.2)
Second biologic, n (% of those who received second biologic)	
TNFi	489 (75.9)
Abatacept	32 (5.0)
Tocilizumab	43 (6.7)
Others*	80 (12.4)
Third biologic, n (% of those who received third biologic)	
TNFi	97 (47.8)
Abatacept	23 (11.3)
Tocilizumab	45 (22.2)
Others*	38 (18.7)

*Others include anakinra, canakinumab, rituximab, tofacitinib, ustekinumab, secukinumab

Methods: We conducted a retrospective study of a national administrative claims database in the US (January 2008 to March 2020). Study subjects included children (age < 19 years) who initiated a new bDMARD/tsDMARD therapy, had a medical claim associated with JIA diagnosis, and had been enrolled in the health plans for at least 6 months prior to starting initial bDMARD/tsDMARD therapy. Medications of interest comprised tumor necrosis factor inhibitors (TNFis), abatacept, tocilizumab, anakinra, canakinumab, tofacitinib, ustekinumab, rituximab, and secukinumab.

Results: 2,076 eligible children with JIA were prescribed bDMARD/tsDMARD therapy, most of whom started with TNFis (91%) (Table 1). Median follow-up was 699 days following first reported bDMARD/tsDMARD prescription (IQR

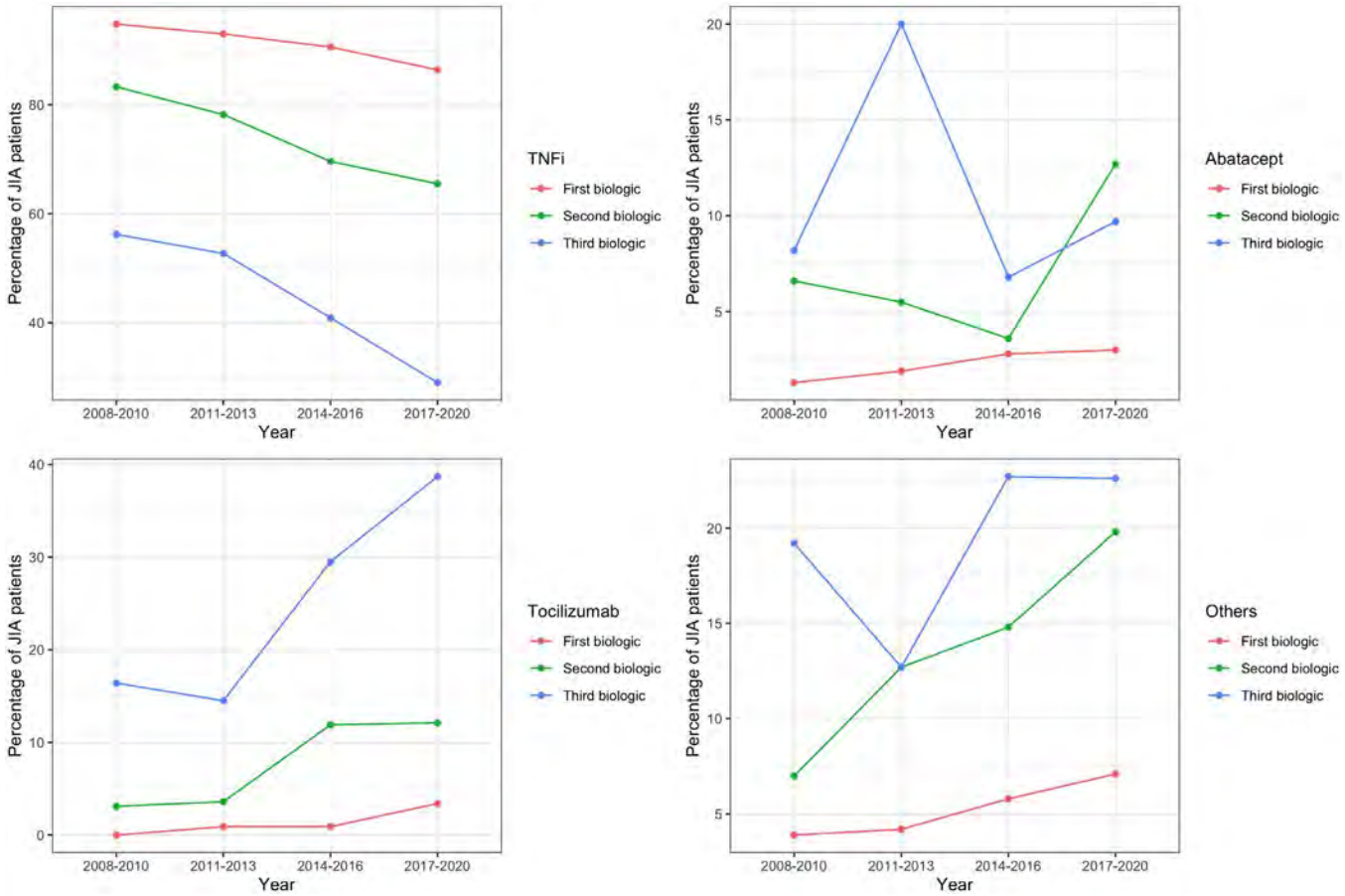

Figure 1. Trends in the use of bDMARD/tsDMARD as initial, second, and third therapy. Others include biologic therapies anakinra, canakinumab, rituximab, ustekinumab, and secukinumab, and the non-biologic therapy tofacitinib. Tocilizumab was FDA approved for use in systemic-onset JIA in 2011.

289-1503). During follow-up, 644 (31%) switched to a second bDMARD/tsDMARD, most commonly to a second TNFi (76%). A further 203 (9.8%) switched to a third bDMARD/tsDMARD and 30 (1.4%) patients received 4 or more bDMARD/tsDMARD therapies. The median time to initiating a second and third bDMARD/tsDMARD were 345 days (IQR 160-835) and 770 days (IQR 395-1435), respectively.

1,745 patients were followed-up for at least 180 days following start of the initial bDMARD/tsDMARD therapy, or switched to a second bDMARD/tsDMARD within 180 days. Among these patients, 193 (11%) started a second bDMARD/tsDMARD within 180 days of the initial therapy (i.e. early switchers). 88% of these patients received TNFi as the initial therapy and 76% switched to another TNFi. Children older than 12 years were more likely to be early switchers, compared with younger children (OR 1.05; 95% CI 1.02-1.08; p< 0.001).

The proportion of early switchers did not vary significantly over the study period. However, changes in the types of bDMARD/tsDMARD used were observed. Notably, there was a significant reduction in the use of TNFi as initial (from 95% in 2008-2010 to 86% in 2017-2020; p< 0.001), second (from 83% in 2008-2010 to 66% in 2017-2020; p< 0.001), and third therapy (from 56% in 2008-2010 to 29% in 2017-2020; p=0.010). There was also a significant trend towards increased use of tocilizumab and other bDMARD/tsDMARD as initial and subsequent therapies (Fig 1).

Conclusion: For many children with JIA, sequential use of bDMARD/tsDMARD is common. One-third of patients in our cohort received a second therapy and one in ten patients switched within 6 months of the initial therapy. More research is needed to evaluate the outcomes and optimal sequence of therapies in this population.

Disclosure: M. Ong, X4 Pharmaceuticals, 5; **S. Ringold**, UpToDate, 9, CARRA, 4, 5, BMS, 12, co-PI on PCORI funded study for which BMS is supplying abatacept; **M. Mannion**, None; **M. Natter**, None; **L. Schanberg**, UCB, 12, DSMB member, Sanofi, 12, DSMB member, SOBI, 2, BMS, 5; **Y. Kimura**, Genentech, 5, UpToDate, 9, CARRA, 4, 12, Salary support.

Abstract Number: 0264

Joint Acoustic Emissions as a Biomarker to Differentiate Between Active and Inactive Juvenile Idiopathic Arthritis via 2-stage Machine Learning Classifier

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) is the most prevalent chronic rheumatic disease and can result in disability in children. JIA most commonly affects the knee. Despite the widespread occurrence of JIA, its heterogeneous presentation and lack of reliable biomarkers make diagnosis and quantifying treatment response challenging. If untreated, the synovitis in JIA can lead to cartilage degeneration and even bone erosion. To evaluate knee health status non-invasively, we can use contact accelerometers that capture the vibrations generated by internal friction of articulating surfaces during movement, also known as joint acoustic emissions (JAE). In this study, we used JAEs to evaluate children's knees and distinguish between healthy, inactive JIA, and active JIA.

Methods: We collected knee JAEs from 51 participants while performing flexion/extensions, including 34 subjects with JIA (23 active/11 inactive) and 17 healthy controls. To these JAE signals, we applied filtering and denoising techniques to extract 15 time-frequency audio features to be used as training data for our Logistic Regression machine learning (ML) classification model. This classifier was implemented in two stages, where at each we obtained a knee health score that indicates the predicted class. The first stage distinguished between healthy and JIA subjects with active and inactive JIA grouped together. The second stage then took only the subjects identified as JIA and classified them as either active or inactive. Hence, our 2-stage classifier was used to evaluate not only presence of, but also severity of JIA.

Results: We validated our 2-stage classifier through leave-one-subject-out cross-validation and obtained an overall 3-class accuracy of 76% when differentiating between healthy, inactive JIA, and active JIA subjects. We obtained a Stage 1 accuracy of 78% and a Stage 2 accuracy of 81%. The least accurate class was inactive JIA, which had both the lower number of sample subjects for training (11) and has the most uncertain label since designation of knee arthritis as "inactive" is primarily clinical and thus is subject to variability. Notice error compounding from both stages results in a lower overall accuracy since second stage depends on first stage predictions, hence, with further ML optimization, we see potential for improved diagnostic accuracy.

Conclusion: These results support the use of JAEs as a novel non-invasive digital biomarker for knee joint health assessment. More accurate characterization of synovitis by magnetic resonance imaging can facilitate improved accuracy of our training dataset which in turn could allow us to differentiate between different levels of synovial inflammation. We have shown that close collaboration between clinicians and bioengineers can result in personalized assessment and thereby improving management of arthritis in children.

Disclosure: L. Rosa, None; **S. Gharehbaghi**, None; **O. Inan**, None; **D. Whittingslow**, None; **L. Ponder**, None; **S. Prahalad**, Novartis, 1.

Abstract Number: 0265

Development and Preliminary Acceptability of JIActiv, a Social Media-Based Program Promoting Engagement in Physical Activity Among Young People Living with Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Pediatric Rheumatology – Clinical Poster I: JIA (0241–0265)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Young people with juvenile idiopathic arthritis (JIA) are at greater risk for adopting chronic sedentary behaviours and not meeting national physical activity guidelines compared to healthy peers, which can have an important impact on their health, daily function and quality of life. Despite the benefits of engaging in an active lifestyle, to our knowledge few appealing, educational and interactive options exist to promote physical activity among young people living with JIA. Our study aimed to develop and explore the preliminary acceptability (i.e. how well the program is received by users, and how it meets their needs) of JIActiv, a 12-week educational and interactive social media-based program promoting physical activity from the perspectives of adolescents and young adults with JIA and parents, and to refine program format and content.

Methods: The JIActiv prototype was developed based on our earlier work which included three systematic reviews, as well as results from our qualitative needs assessment with key stakeholders (young people with JIA, parents, health care professionals and researchers). JIActiv is an educational and interactive program aimed at promoting physical activity in young people with JIA through the delivery of evidence-based information and use of behavior-change strategies via social media. A descriptive qualitative study design was used to assess the acceptability of the JIActiv prototype. Two adolescents 13 to 17 years of age, 13 young adults 18 to 26 years with JIA, and 2 parents were recruited from arthritis patient groups and a Canadian rehabilitation center. Individual audiotaped interviews lasting 60 to 90 minutes were conducted with each participant over Zoom (Enterprise version 5.0.2). Audiotaped findings were transcribed verbatim, sorted, organized and coded using the QDAMiner software. Data was categorised into emerging themes using simple content analysis. Qualitative findings reported on the format, content and potential usefulness of the program.

Results: The vast majority of participants preferred Instagram as the platform for the program and appreciated the presented functionalities. All participants felt that the proposed length of the program and the number of activities per week were appropriate. The informational videos, individual educational and interactive group activities were thought to be pertinent and helpful to motivate young people to engage in physical activity. Participants found that the esthetics of the program could be improved by choosing one color scheme for all postings. None of the participants reported any concerns regarding cyber-bullying. Most participants thought that having a mentor and access to a health care professional would be very helpful to help answer their questions and offer social support. The group format (size and age range of participants) was well accepted by participants.

Conclusion: The JIActiv social media-based program has good preliminary acceptability and is potentially useful for promoting engagement in physical activity among young people with JIA. Participants proposed ideas on how the program could be improved. Additional interview cycles will help to further refine the program.

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Abstract Number: 0266

The Psychosocial Impact of the COVID-19 Pandemic on the Rheumatology Patient Experience

Melissa Flores, Priscilla Toral, Roberta Horton, Adena Batterman, Mavis Seehaus, Juliette Kleinman and Jillian Rose, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Psychology/Social Sciences Poster (0266–0267)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Research shows people with rheumatic conditions may be more susceptible to severe illness from COVID-19 due to their immunocompromised state. The COVID-19 pandemic has been associated with negative impacts on mental health (MH) & there is higher prevalence of depression & anxiety in patients with rheumatic illness. Most studies have focused on the medical impact of COVID-19; however, less is known about the MH impacts in this population. This needs assessment explores the psychosocial impact & needs of rheumatic disease patients during the pandemic.

Methods: A 95-item online survey in English & Spanish with Likert scale & open-ended questions was disseminated nationally from July-Oct. 2020 to rheumatic disease patients age 18+, promoted in NYC hospitals, local/national support programs & social media. The survey assessed physical & mental health, illness management, access to care, social environment & resources. The Patient Health Questionnaire-4 (PHQ-4) & the Hospital Anxiety & Depression Scale (HADS) assessed MH. A comparative analysis was conducted for those who reported a change in emotional health (ECs) vs. those who did not (NECs). Independent samples t-tests & chi-square tests were used to examine differences.

Results: Of the 382 responses received, most were age 35+ (79%), female (91%) & Non-Hispanic (77%). Almost half (46%) were White, 9% Asian, 8% African American & 6% Other. Almost all (96%) had health insurance; 50% were employed.

Most participants had SLE (67%), RA (19%), & Sjogren's syndrome (8%) with a mean of 13 years since diagnosis. Over half (63%) reported a flare since the pandemic & 16% had COVID-19. Only 19% reported no changes to their care during the pandemic; 33% indicated their care switched to telehealth visits or appointments were postponed (19%).

Most (76%) reported a change in their mood and/or emotional health, with 81% indicating that this change was due to the pandemic. The mean PHQ-4 score for all respondents was 4.3 (SD: 3.5) with 31% scoring moderate/severe for psychological distress. The mean HADS Anxiety & HADS Depression scores were 8.2 (SD: 4.9) & 7 (SD: 4.3) with 54% & 43% scoring borderline/abnormal. Most (82%) shared they "feel isolated from others."

Patients who experienced a negative emotional change (ECs) had significantly higher PHQ-4 & HADS scores ($P< 0.001$) than those who did not (NECs). Significant differences were found across these areas: ↑ % switching to telehealth (45% v 23%, $P=0.001$), receiving MH services (31% v 7%, $P< 0.001$), taking medication for their MH (29% v 5%, $P< 0.001$) & starting counseling (14% v 0%, $P=0.001$).

Almost half ECs desired support programs to cope with their condition (49% v 21%, $P< 0.001$), indicating virtual programs on coping with illness, MH resources & virtual support groups would be most helpful.

Conclusion: Despite limitations due to a convenience sample, results contribute to research on the psychosocial impact of the pandemic on rheumatic disease patients—the toll on emotional health & increased isolation. The significant differences found in those who reported an emotional change vs. those who did not support the need for the care team to assess & address MH issues during the pandemic. Further study is needed to assess long-term impacts.

Disclosure: M. Flores, None; **P. Toral**, None; **R. Horton**, None; **A. Batterman**, None; **M. Seehaus**, None; **J. Kleinman**, None; **J. Rose**, None.

Abstract Number: 0267

Psychosocial and Health Measures in Systemic Lupus Erythematosus: Before and During the COVID-19 Pandemic in the Georgian's Organized Against Lupus Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Psychology/Social Sciences Poster (0266–0267)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Disruptions of routines or livelihood and worry during the COVID-19 pandemic may have impacted systemic lupus erythematosus (SLE) patients in multiple ways. We explored pre- and during pandemic changes of SLE disease activity, general health, and psychosocial factors in a large and diverse cohort.

Methods: We examined longitudinal data from Georgians Organized Against Lupus (GOAL), a population-based cohort of adults from Atlanta, Georgia, with a validated diagnosis of SLE. All participants fulfilled 3 or more ACR classification criteria and had a final diagnosis of SLE by a board-certified rheumatologist. Participants responded to validated self-administered instruments on health outcomes at least annually. This study included participants who

Table 1: Characteristics in the GOAL Cohort – Pre-Pandemic and During Pandemic (n=852)

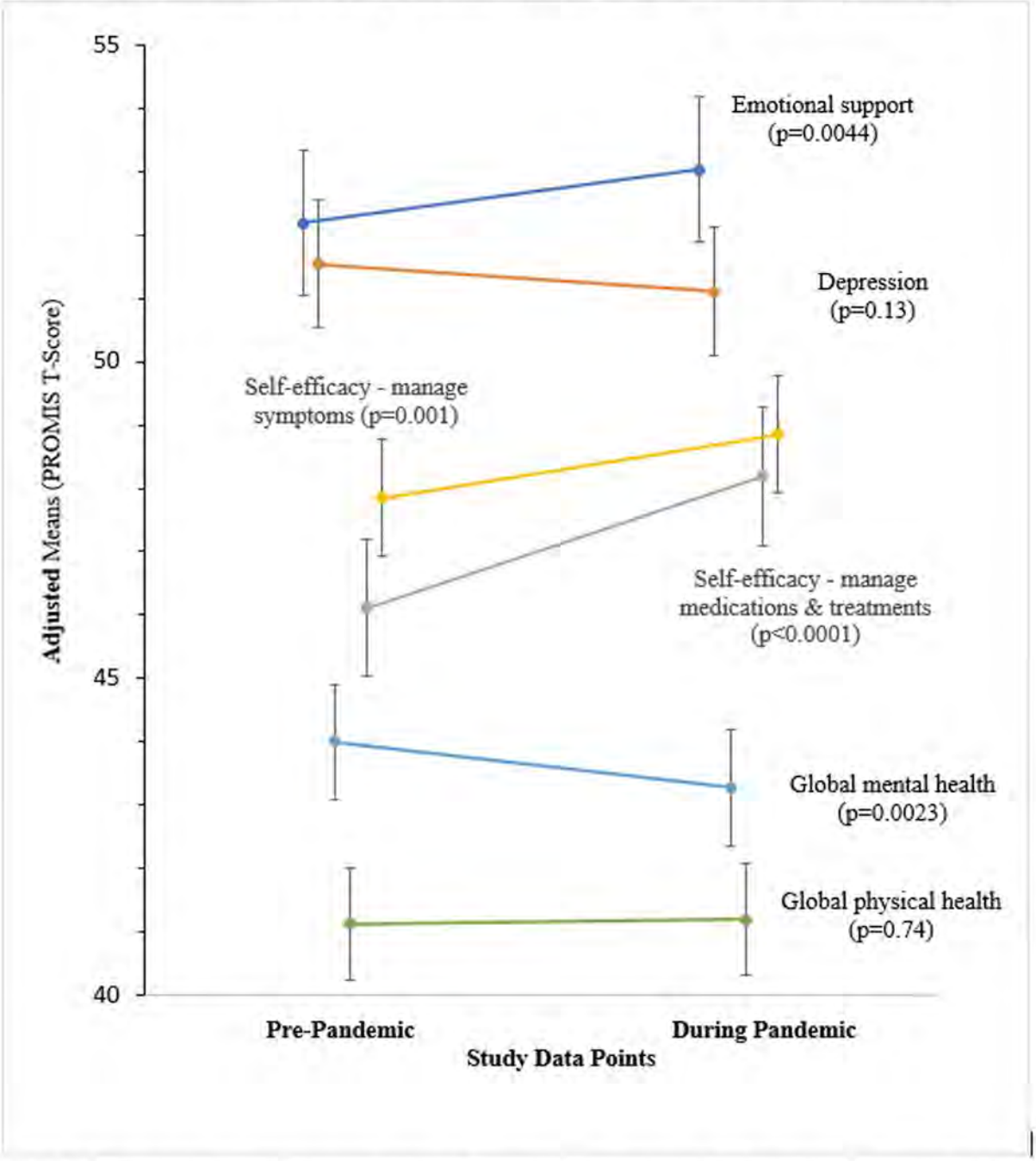
	Pre-Pandemic	During pandemic	P-value (paired)
Health Insurance			
Insurance Type 1) No Insurance	109 (12.8)	86 (10.2)	
2) Private	313 (36.8)	306 (36.2)	
3) Medicare	199 (23.4)	225 (26.6)	0.16**
4) Medicaid	134 (15.7)	131 (15.5)	
5) Medicare and Medicaid	96 (11.3)	97 (11.5)	
SLE Disease Activity			
SLAQ* (disease activity) mean ± SD	15.04 ± 8.69	14.15 ± 8.72	**<0.0001**
Self-reported Health and Psychosocial Factors			
PROMIS Global Physical Health* mean ± SD	40.65 ± 8.84	41.20 ± 8.99	**0.013**
PROMIS Global Mental Health* mean ± SD	43.57 ± 9.34	43.75 ± 9.08	0.46
PROMIS Depression* mean ± SD	51.40 ± 10.65	49.80 ± 9.87	**<0.0001**
PROMIS Emotional Support SF4* mean ± SD	52.05 ± 9.40	53.59 ± 9.16	**<0.0001**
PROMIS Self-Efficacy for Managing Medications and Treatments* mean ± SD	46.51 ± 8.82	49.12 ± 9.64	**<0.0001**
PROMIS Self-Efficacy for Managing Symptoms* mean ± SD	48.37 ± 8.69	50.04 ± 9.10	**<0.0001**
Everyday Discrimination Scale mean ± SD	1.54 ± 0.62	1.44 ± 0.61	**<0.0001**
Cohen's Perceived Stress Scale 10 mean ± SD	17.77 ± 8.08	16.66 ± 7.68	**<0.0001**

Values indicate n (%) unless otherwise specified. PROMIS scores are T scores.
SLAQ - SLE Activity Questionnaire (range 0-47), Everyday Discrimination (range 1-4), PSS10- Cohen's Perceived Stress Scale 10 (range 0-40)
*PROMIS T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation of 10. Higher scores represent more of the concept being measured.
** Symmetry Test.

completed one survey before (2017-2019) and another survey during the pandemic (2020-2021). We explored changes in SLE disease activity, health, and psychosocial elements with the following measures: Systemic Lupus Activity Questionnaire (SLAQ), PROMIS short forms (Global physical and mental health, Depression, Emotional Support, Self-efficacy for managing symptoms, Self-efficacy for managing medications and treatments), Everyday Discrimination Scale, and Cohen's Perceived Stress Scale. Changes in mean scores were assessed using a paired test (univariate analysis). Multivariate regression analysis was performed to further exam differences, with the adjustments for socio-demographics (age, gender, race, education), insurance status, disease damage, stress, and discrimination.

Results: We evaluated 852 participants (94% women, 81% Black, mean age 48). SLE-related characteristics included an average age of diagnosis of 32.2 years (SD ± 11.8), average disease duration of 15.5 years (SD ± 10.2), and

Figure 1: Pre-Pandemic and During Pandemic: Health, Social Support, and Self-Efficacy



PROMIS T-score rescales the raw score into a standardized score with a mean of 50 and a standard deviation of 10. Higher scores indicate more of the domain measured. T-scores adjustments: socio-demographics (age, race, education), insurance, disease severity (SLAQ, SA-BILD), stress, and discrimination.

over 50% with severe disease damage based on the Self-administered Brief Index of Lupus Damage (score ≥ 3). Overall, insurance categories remained without significant changes during the pandemic (Table 1). Except for global mental health, all measures showed significantly better mean scores during the pandemic than pre-pandemic. After adjustments for confounders, mean scores for emotional support and self-efficacy remained markedly better during the pandemic than before the pandemic (Figure 1). The original paired test showed no difference for global mental health; however, mental health was associated with significant worsened change after adjustments.

Conclusion: Our results in a diverse cohort with large numbers of socially vulnerable people show that participants reported improved confidence to manage symptoms, medications, and other treatments in challenging times. Additionally, they received more emotional support during the pandemic. However, global mental health deteriorated. We hypothesize that the stay-at-home pandemic recommendations allowed patients to seek out supportive resources and focus on self-management. Further observations post-pandemic will offer more insight regarding the mental health impact on SLE.

Disclosure: C. Dunlop-Thomas, None; **G. Bao**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **C. Drenkard**, GSK, 1, 5.

Abstract Number: 0268

Effect of Biologic Agents on Lipids and Cardiovascular Risk in Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiovascular disease (CVD) risk scores incorporating measures of inflammation such as the Reynolds risk score (RRS) may be appropriate to predict CVD risk in patients (pts) with rheumatoid arthritis (RA), even though not yet validated for RA pts. The purpose of this analysis was to investigate the effect of biologic DMARDs on lipids and the RRS.

Methods: Pts with at least moderate disease activity (CDAI >10) initiating a biologic DMARD participated in a comparative effectiveness trial (CERTAIN) nested within CorEvitas (formerly known as Corrona) RA registry. Characteristics, including lipid values, hsCRP and RRS in pts initiating a TNF-α inhibitor (TNFi) or non-TNFi (rituximab [RTX], abatacept [ABT] or tocilizumab [TCZ]), were measured at baseline, 3- and 6- months later. Longitudinal mixed models examined the association of individual biologics with changes in lipid levels, hsCRP and RRS after 3- and 6-months of therapy. Log transformations used for skewed distributions (TG, hsCRP, RRS). Generalized structural equation models were estimated to model mediation of CRP, CDAI or swollen joint count on lipid changes when comparing TCZ vs other biologics. TCZ was selected for this comparison given the known - and observed in this analysis (see below) - effects on lipid levels. Patients who interrupted therapy prior to follow up visits or without complete lipid data at all time points were excluded.

Results: 1698 initiations of a biologic were analyzed. Baseline characteristics: 78.7% women, 89.2% Caucasian, 72.3% seropositive. Mean ± SD age was 56.9 ± 12.8, RA disease duration 8.9 ± 9.2 years; CDAI 29.0 ± 12.7. 36.8% of pts were biologic naïve and 24.5% on anti-hyperlipidemic therapy. CVD history (7.9% of patients) did not exclude patients from the analysis. Diabetes mellitus was present in 9.4% of patients and 42.0% were obese (BMI >30). Table 1 shows lipid levels, hsCRP and RRS adjusted changes after 3- and 6-months of therapy. Pts initiating TCZ had a significant increase in total cholesterol, LDL, triglycerides (TG) and a significant decrease in hsCRP compared with patients initiating TNFi. Pts initiating ABT had a significant increase in hsCRP compared with patients initiating TNFi.

Table 1. Baseline lipid levels, log hsCRP and Reynolds Risk Score and adjusted effect of individual biologics at 3 and 6 months after initiating biologic therapya

Change in Lipid Levels, Mean (SE)	TNFi (Ref) N=941	Rituximab N=114	Abatacept N=349	Tocilizumab N=294	P-value[b]
LDL					
Change (3 mon-base)	0.95 (0.92)	0.78 (2.43)	-0.86 (1.4)	9.41 (1.51)**	<0.001
Change (6 mon-base)	-0.14 (0.93)	0.13 (2.45)	0.32 (1.41)	6.91 (1.52)**	<0.001
HDL					
Change (3 mon-base)	-0.14 (0.42)	-0.57 (1.1)	-0.8 (0.64)	1.24 (0.69)*	0.105
Change (6 mon-base)	-0.37 (0.43)	-0.43 (1.11)	-0.44 (0.64)	0.75 (0.69)	0.468
Log Triglyceride					
Change (3 mon-base)	0.01 (0.02)	0.06 (0.04)	0.05 (0.02)	0.04 (0.03)*	0.107
Change (6 mon-base)	0.02 (0.02)	0.04 (0.04)	0.06 (0.02)	0.06 (0.03)**	0.014
Total Cholesterol					
Change (3 mon-base)	0.22 (1.08)	0.99 (2.84)	-0.81 (1.64)	10.57 (1.77)**	<0.001
Change (6 mon-base)	-0.7 (1.09)	-0.33 (2.86)	1.13 (1.65)	8.67 (1.77)**	<0.001
Log hsCRP					
Change (3 mon-base)	-0.29 (0.05)	0.45 (0.12)**	0.18 (0.07)**	-1.37 (0.08)**	<0.001
Change (6 mon-base)	-0.28 (0.05)	0.44 (0.12)**	0.19 (0.07)**	-1.43 (0.08)**	<0.001
Log Reynolds Risk Score					
Change (3 mon-base)	-0.03 (0.02)	0.13 (0.05)*	0.01 (0.03)	-0.14 (0.03)**	<0.001
Change (6 mon-base)	0.01 (0.02)	0.12 (0.05)	0.07 (0.03)	-0.14 (0.03)**	<0.001

* Indicates change from baseline $p < 0.05$
** Indicates change from baseline $p < 0.01$

[a] Mixed Models were fit at 3 and 6 months adjusted for baseline levels and compared among the four drug groups using TNF inhibitors as the reference group. Linear mixed effect regression models are estimated with patient as a random effect. Model adjusted for patient demographics (age, gender, race), behaviors (smoking, drinking), BMI and change in BMI, disease measures including RF+, CCP+,CDAI and HAQ at baseline and change in CDAI and HAQ, prior history of CVD, malignancies, hospitalized infections, and diabetes; use of cholesterol lowering medications, fish oil and flax seed use and any change in cholesterol lowering meds or fish oil. Adjustment was made for patient demographics (age, gender, race), behaviors (smoking, drinking), BMI and change in BMI, disease measures including RF+, CCP+,CDAI and HAQ at baseline and change in CDAI and HAQ, prior history of CVD, malignancies, hospitalized infections, and diabetes; use of cholesterol lowering medications, fish oil and flax seed use and any change in cholesterol lowering meds or fish oil.

[b] *P*-value comparing within row differences between all drug groups (null hypothesis of all means equal)

ABT had significant decreases in log RRS at 3- and 6-month compared to other biologics. Mediator analyses estimated significant effect of hsCRP but not CDAI or swollen joints on lipid changes. Table 2 presents direct, indirect effects, and total effects of TCZ vs other biologics on lipid changes.

Conclusion: The impact of lipid changes on CVD risk must be considered in the context of the burden of inflammation in pts with RA. Lipid increases may not be atherogenic and may occur in the context of the "lipid paradox". In this analysis moderate increases in lipid levels were associated with the therapy initiated and with changes in CRP. Lipid increase did not translate to an increased CVD risk as captured by RRS.

Table 2. Mediator analysis - CRP association with lipid changes for TCZ vs other biologics after 3 and 6 months of therapy[a]

	Lipid change[b]	95% CI	p-value[c]
Combined Effects on LDL at 3 and 6 Months			
Direct Effect of TCZ	7.104	4.527, 9.681	<0.001
Indirect Effect via CRP	1.837	0.853, 2.820	<0.001
Total Effect	8.941	6.554, 11.327	<0.001
Combined Effects on Total Cholesterol at 3 and 6 Months			
Direct Effect of TCZ	7.431	4.498, 10.365	<0.001
Indirect Effect via CRP	4.115	2.911, 5.317	<0.001
Total Effect	11.456	8.818, 14.273	<0.001
Combined effect on log TG at 3 and 6 Months			
Direct Effect of TCZ	0.004	-0.040, 0.047	0.869
Indirect Effect of CRP	0.039	0.022, 0.056	<0.001
Total Effect	0.043	0.004, 0.082	0.033

[a] Generalized structural equations models were used to model the effects of TCZ on lipid levels with CRP as a mediator. Adjustment was made for patient demographics (age, gender, race), behaviors (smoking, drinking), BMI and change in BMI, disease measures including RF+, CCP+,CDAI and HAQ at baseline and change in CDAI and HAQ, prior history of CVD, malignancies, hospitalized infections, and diabetes; use of cholesterol lowering medications, fish oil and flax seed use and any change in cholesterol lowering meds or fish oil.

[b]Difference in change in lipids (LDL, total cholesterol, log triglycerides) between TCZ and other biologics

[c]P-value is the comparison to the null hypothesis that the effect equals zero

Refs: Ridker PM et al. (http://www.ncbi.nlm.nih.gov/pubmed/18997194) C-reactive protein and parental history improve global cardiovascular risk prediction: the Reynolds Risk Score for men.*Circulation*. 2008. 25;118(22):2243-51.

Disclosure: D. Pappas, Sanofi, 1, 6, CorEvitas, 3, 8, 11, Roche Hellas, 2, 6, Abbvie, 2, 6, Novartis, 6, Corrona Research Foundation, 4; **G. Reed**, CorEvitas, LLC, 2, Corrona Research Foundation, 2; **K. Kane**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **J. Kremer**, CoreEvitas, 2, 8, Pfizer, 6, BMS, 2.

Abstract Number: 0269

Autoantibodies and the Risk of Incident Cardiovascular Disease in US Veterans with Rheumatoid Arthritis

Tate Johnson[1], Michael Duryee[2], Carlos Hunter[2], Punyasha Roul[2], Yangyuna Yang[2], Jeremy Sokolove[3], William Robinson[4], Joshua Baker[5], Geoffrey Thiele[2], Ted Mikuls[2] and Bryant England[2], [1]University of Nebraska Medical Center, Elkhorn, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]Stanford University School of Medicine, Berwyn, PA, [4]Stanford University, Stanford, CA, [5]University of Pennsylvania, Philadelphia, PA

Table 1. Associations of RF, anti-CCP, and anti-MAA antibodies with incident cardiovascular disease in US Veterans with rheumatoid arthritis

Autoantibody	MACE aHR (95% CI)	CVD Death aHR (95% CI)
Rheumatoid Factor		
Seropositive (>15 U/mL)	1.28 (0.92-1.78)	**1.72 (1.04-2.86)**
Concentration	**1.15 (1.04-1.27)**	1.16 (0.99-1.34)
Anti-CCP		
Seropositive (>5 U/mL)	0.91 (0.61-1.35)	1.29 (0.78-2.13)
Concentration	1.11 (0.98-1.25)	**1.27 (1.11-1.45)**
Anti-MAA, IgG		
Seropositive*	1.02 (0.83-1.27)	1.38 (0.98-1.95)
Concentration	1.16 (0.99-1.35)	**1.24 (1.06-1.43)**
Anti-MAA, IgM		
Seropositive*	1.20 (0.82-1.75)	1.54 (0.97-2.44)
Concentration	**1.20 (1.03-1.39)**	**1.22 (1.05-1.42)**
Anti-MAA, IgA		
Seropositive*	1.05 (0.67-1.66)	1.20 (0.79-1.82)
Concentration	1.16 (0.93-1.44)	1.14 (0.98-1.33)

Antibodies each assessed in separate models adjusting for age, sex, BMI, current smoking, hypertension, diabetes, lung disease, prior MACE, medications (methotrexate, TNF biologic, prednisone), and DAS28. Values are adjusted hazard ratios per 1 SD change in antibody concentration. Bold values indicate $p<0.05$.

*Anti-MAA antibody status was considered positive if concentrations fell in the top two tertiles among study participants

Abbreviations: CCP = cyclic citrullinated peptide, CI=confidence interval, CVD = cardiovascular disease, aHR=adjusted hazard ratio, MAA = malondialdehyde acetaldehyde, MACE=major adverse cardiovascular event, RF = rheumatoid factor

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Autoantibodies are hypothesized as one of the RA specific factors contributing to a heightened risk of cardiovascular disease (CVD) in this population. However, prior epidemiologic studies of RF and ACPAs with CVD risk in RA are conflicting, and the role of antibodies to other post-translationally modified peptides/proteins

Table 2. Associations of ACPA subtypes with incident cardiovascular disease in US Veterans with rheumatoid arthritis

Autoantibody Antigen	MACE aHR (95% CI)	CVD Death aHR (95% CI)
Apolipoprotein E cit	1.07 (0.97-1.19)	1.09 (0.95-1.26)
Apolipoprotein E (277-296) cit2 cyclic	1.05 (0.99-1.11)	**1.12 (1.02-1.23)**
Biglycan (247-266) cit cyclic	1.06 (0.97-1.17)	**1.16 (1.07-1.25)**
CCP	1.03 (0.93-1.14)	1.12 (0.94-1.34)
Clusterin (221-240) cit cyclic	1.03 (0.90-1.17)	1.08 (0.97-1.21)
Clusterin (231-250) cit cyclic	1.04 (0.92-1.18)	1.10 (0.96-1.26)
Enolase 1A (5-21) cit	1.00 (0.91-1.09)	1.04 (0.86-1.26)
Fibrinogen cit	**1.12 (1.03-1.23)**	**1.20 (1.08-1.33)**
Fibrinogen A (556-575) cit cyclic	1.03 (0.92-1.14)	1.13 (0.99-1.28)
Fibrinogen A (616-635) cit3 cyclic	1.03 (0.93-1.14)	1.11 (0.98-1.26)
Filaggrin (48-65) cit cyclic	1.04 (0.96-1.13)	**1.13 (1.00-1.26)**
Filaggrin (48-65) V1 cit2 cyclic	1.05 (0.94-1.16)	1.13 (0.97-1.31)
Histone 2A cit	1.06 (0.92-1.21)	1.13 (0.95-1.33)
Histone 2A (1-20) cit cyclic	1.05 (0.96-1.15)	1.03 (0.92-1.16)
Histone 2A/a-2 (1-20) cit	1.06 (0.98-1.14)	1.03 (0.91-1.16)
Histone 2B cit	1.05 (0.91-1.20)	1.07 (0.93-1.24)
Histone 2B (62-81) cit cyclic	1.09 (0.93-1.27)	1.11 (0.90-1.37)
Vimentin cit	1.04 (0.88-1.23)	1.06 (0.90-1.25)
Vimentin (58-77) cit3 cyclic	1.02 (0.90-1.17)	1.03 (0.87-1.23)

Antibodies each assessed in separate models adjusting for age, sex, BMI, current smoking, hypertension, diabetes, lung disease, prior MACE, medications (methotrexate, TNF biologic, prednisone), and DAS28. Values are adjusted hazard ratios per 1 SD change in antibody concentration. Bold values indicate $p<0.05$.

Abbreviations: CCP = cyclic citrullinated peptide, CI=confidence interval, cit=citrullinated, CVD = cardiovascular disease, aHR=adjusted hazard ratio, MACE=major adverse cardiovascular event, RF = rheumatoid factor

including malondialdehyde acetaldehyde (anti-MAA) are not well understood. We evaluated the associations of RF, ACPAs, and anti-MAA antibodies with major adverse cardiovascular events (MACE) in RA.

Methods: We studied patients in a multicenter prospective cohort of U.S. veterans with RA. We measured RF by nephelometry, anti-CCP antibody by 2nd generation ELISA, and anti-MAA antibody (IgG, IgM, and IgA) by ELISA on

banked serum from enrollment. In a subset of patients (n=1,422), 19 ACPA subspecificities were measured with a multiplex bead-based assay. Autoantibody concentrations were log-transformed and standardized (per 1 SD). RF and anti-CCP positivity were defined per assay cut-offs while anti-MAA was considered positive if in the upper two tertiles, yielding a similar frequency of positivity. MACE was defined as a composite of myocardial infarction, coronary revascularization, stroke, or CVD-related death identified from VA databases and the National Death Index using a previously validated administrative algorithm. Baseline covariates were obtained from registry and administrative data and included demographics, smoking status, BMI, LDL cholesterol, comorbidities (hypertension, diabetes, lung disease, prior MACE), medications (MTX, TNFi biologics, prednisone), and DAS28. We used multivariable Cox regression to examine the associations of autoantibodies with incident MACE and CVD death.

Results: Among 2,362 RA patients (90% male, mean age 72 years), there were 388 MACE outcomes over 19,868 person-years (PY) of follow-up and 220 CVD deaths. Higher concentrations of RF (aHR per 1 SD 1.15 [1.04-1.27]) and IgM anti-MAA (aHR 1.20 [1.03-1.39]) were associated with risk of MACE (Table 1). Effect sizes were similar for other autoantibodies, though not statistically significant. Similarly, higher concentrations of anti-CCP (aHR 1.27 [1.11-1.45]) and IgG (aHR 1.24 [1.06-1.43]) and IgM (aHR 1.22 [1.05-1.42]) anti-MAA were significantly associated with CVD-death, and non-significant associations were observed for other autoantibodies. When evaluated as seropositivity, estimates were less precise with only RF significantly associated with CVD-death (aHR 1.72 [95% CI 1.04-2.86]). Analyses of ACPA subtypes revealed associations between higher concentrations of anti-cit fibrinogen with MACE (aHR 1.12 [1.03-1.23]) and CVD death (aHR 1.20 [1.08-1.33]) as well as anti-cit apolipoprotein E, biglycan, and filaggrin with CVD death (aHR 1.12 [1.02-1.23], 1.16 [1.07-1.25], and 1.13 [1.00-1.26]).

Conclusion: Higher concentrations of several RA-related autoantibodies were associated with MACE and/or CVD-mortality, providing support to the hypothesis that autoantibodies may directly contribute to excess CVD risk in RA. Additional study is needed to elucidate pathophysiological mechanisms underpinning these epidemiologic associati ons.

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Abstract Number: 0270

Impact of Macrophage Cholesterol Loading Capacity and Interactions with Treatments on Cardiovascular Risk and Coronary Atherosclerosis Burden in Rheumatoid Arthritis

George Karpouzas[1], Bianca Papotti[2], sarah ormseth[3], Marcella Palumbo[4], Elizabeth Hernandez[3], Cinzia Marchi[4], Francesca Zimetti[4], Matthew Budoff[5], Franco Bernini[4] and Nicoletta Ronda[4], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]2. Department of Food and Drug, University of Parma, Italy, Parma, Italy, [3]The Lundquist Institute, Harbor-UCLA Medical Center, Torrance, CA, [4]Department of Food and Drug, University of Parma, Parma, Italy, [5]Division of Cardiology, and the Lundquist Institute ay Harbor-UCLA Medical Center, Torrance, CA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

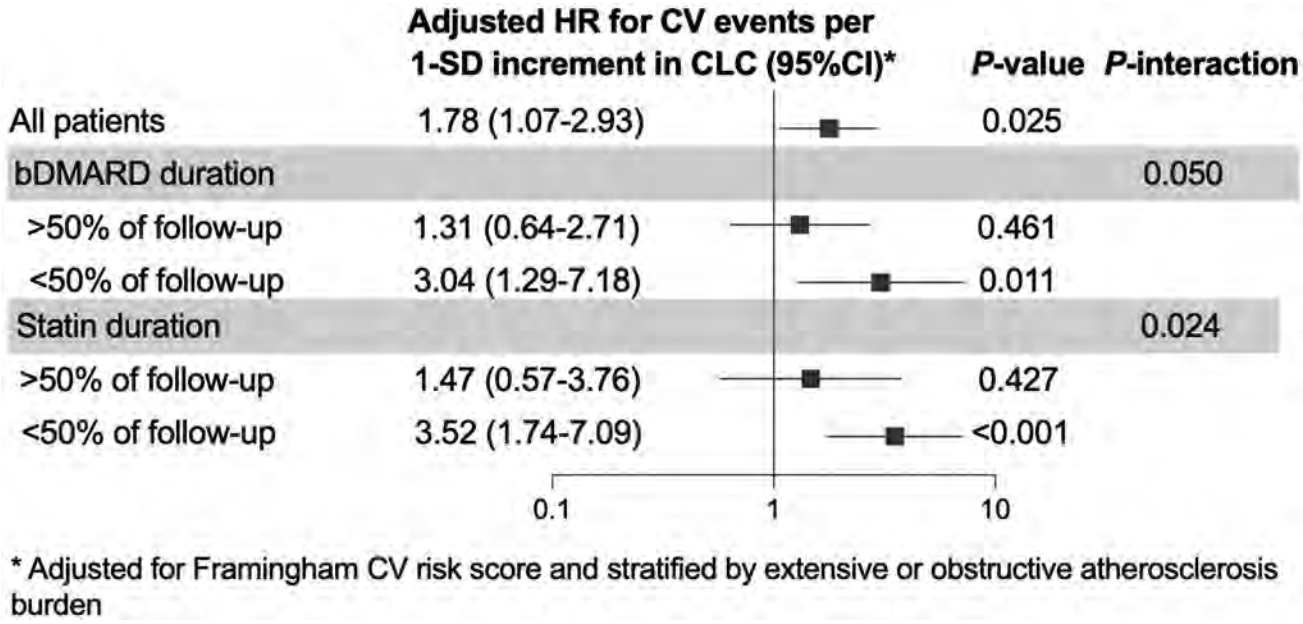

Figure 1. bDMARD and statin therapy condition the impact of CLC on cardiovascular risk in RA.

Background/Purpose: Statins and bDMARDs may decrease cardiovascular risk in RA by lowering coronary plaque formation, promoting regression and altering the composition of atherosclerotic lesions. Macrophage cholesterol loading capacity (CLC) of serum is a functional parameter reflecting both quality and quantity of lipoproteins and is potentially related to foam cell formation. We evaluated the associations between CLC, coronary plaque burden and cardiovascular (CVD) risk in patients with RA. We further explored the moderating effects of RA treatments on these relationships.

Methods: 107 patients with baseline coronary CT angiography for atherosclerosis evaluation and prospective follow-up for cardiovascular events over 6.0±2.4 years were studied. Coronary artery calcium score (CAC), number of segments with plaque and plaque composition were assessed. CLC was the macrophage cholesterol content, measured by fluorometric assay, after a 24 hour incubation with whole serum. Adjusted robust Cox regression evaluated main

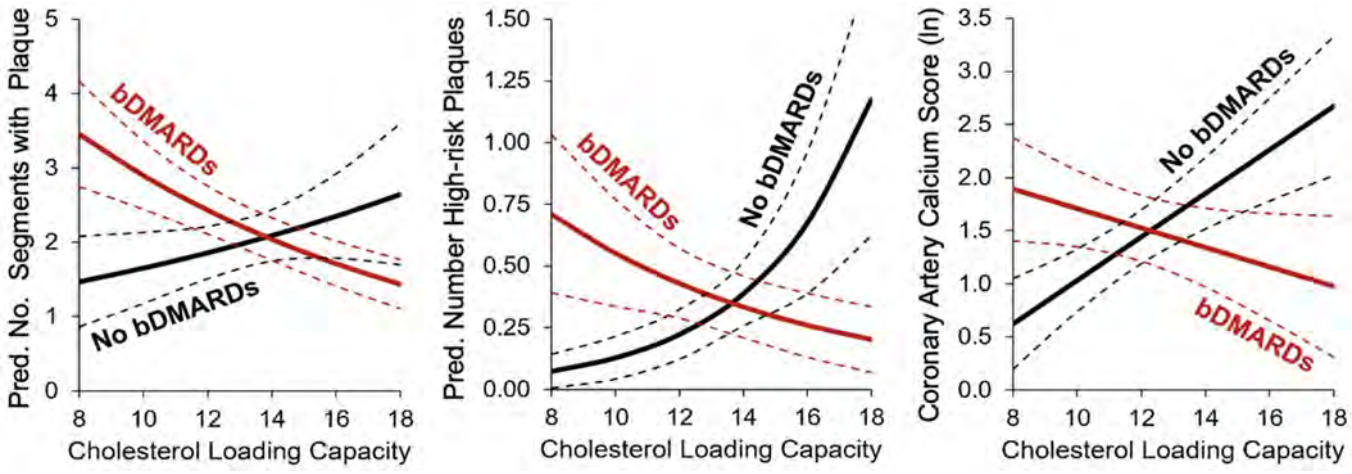

Figure 2. bDMARD therapy conditions the impact of CLC on coronary atherosclerosis burden.

effects and interactions of CLC with bDMARD and statin treatment duration on event risk. Robust linear regression examined the interaction between CLC and bDMARD therapy on CAC burden. Robust negative binomial regressions evaluated interactions between CLC and bDMARD exposure on total and high-risk low-attenuation plaque (LAP) burden.

Results: CLC associated with incident CVD risk (per SD increment; adjusted hazard ratio [aHR] 1.78 [95% CI 1.07-2.93], *P*=0.025), after accounting for Framingham CVD score and baseline atherosclerosis burden. The effect was stronger in patients with less exposure to bDMARDs (< 50% of follow-up: aHR 3.04 [95% CI 1.29-7.18]; versus >50% of follow-up: aHR 1.31 [95% CI 0.64-2.71], Fig. 1) and statins (< 50% of follow-up: aHR 3.52 [95% CI 1.74-7.09]; versus >50% of follow-up: aHR 1.47 [95% CI 0.57-3.76], Fig. 1). In cross-sectional analyses adjusting for Framingham CVD score and DAS28-CRP, CLC (per 1-SD unit) was not related to number of segments with plaque (adjusted rate ratio [aRR] 0.91 [95% CI 0.74-1.13]), number of vulnerable plaques (aRR 1.03 [95% CI 0.64-1.66]) or ln-transformed CAC (β -0.01 [95% CI -0.15-0.14]). However, in analyses stratified by baseline bDMARD use, CLC (per 1-SD unit) was positively related to number of vulnerable plaques (aRR 2.30 [95% CI 1.16-4.57]) and ln-transformed CAC (β 0.27 [95% CI 0.03-0.50]) among bDMARD naïve individuals (Fig. 2). In addition, CLC inversely associated with number of segments with plaque (per SD increment; aRR 0.76 [95% CI 0.61-0.94]) only in bDMARD exposed patients (Fig. 2).Baseline statin use did not significantly modify the effect of CLC on baseline coronary plaque (data not shown).

Conclusion: We showed for the first time that enhanced cholesterol loading onto macrophages (CLC) in RA associated with greater cardiovascular risk; this risk was modified by statin and bDMARD use. CLC further associated with greater CAC score and LAP burden in bDMARD-naïve but not bDMARD-treated patients. The negative association of CLC with total plaque burden in bDMARD-treated patients may reflect lower plaque formation and reduction in atherogenic lipoprotein disposal through vessels.

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Abstract Number: 0271

Higher Prevalence of Subclinical Atherosclerosis in the First Five Years of Rheumatoid Arthritis Diagnosis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have a higher risk of developing a cardiovascular (CV) event than the general population, due to an accelerated process of atherosclerosis, which has been documented to begin in early stages of the disease and is directly associated with systemic inflammation.

The aim of this study was to compare the prevalence of subclinical atherosclerosis detected by carotid ultrasound (US) in patients with RA in the first five years of diagnosis and healthy controls.

Table 1. Demographic and clinical characteristics.

	RA patients (n=53)	Controls (n=53)	*p-value*
Age years, mean ± SD	54.48 ± 9.09	54.86 ± 6.83	NS
Women, n (%)	49 (92.5)	49 (92.5)	NS
T2DM, n (%)	8 (15.1)	7 (13.2)	NS
HTN, n (%)	17 (32.1)	17 (32.1)	NS
Dyslipidemia, n (%)	19 (35.8)	19 (35.8)	NS
Obesity, n (%)	21 (39.6)	20 (37.7)	NS
Active smoking, n (%)	3 (5.7)	4 (7.5)	NS
BMI kg/m^2, median (IQR)	28.78 (25.92-33.21)	27.59 (24.55-33.34)	NS
Disease duration, mean ± SD	2.48 ± 1.31	-	-
DAS28-CRP, median (IQR)	3.21 (1.89-4.12)	-	-
MTX, n (%)	39 (73.6)	-	-
Glucocorticoids, n (%)	29 (54.7)	-	-

NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; DAS28, disease activity score using 28 joints; CPR, C-reactive protein; MTX, methotrexate.

Methods: This was a cross-sectional, observational, and comparative study. A total of 53 patients aged 40-75 years old, with RA diagnosis, in the previous five years, according to the 2010 ACR/EULAR classification criteria, and 53 controls matched by age (±5 years), gender and comorbidities were included in this study. Subjects with a previous CV event were excluded. A carotid US was performed in all study subjects. Subclinical atherosclerosis was evaluated as the presence of carotid plaque (CP) or an increased carotid intima media thickness (cIMT). CP was defined as a cIMT ≥1.2mm or a focal narrowing ≥0.5mm of the surrounding lumen, and an increased cIMT was defined as a value ≥0.8mm. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done with χ^2 test and Fisher's exact test for qualitative variables, and Student's T test and Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

Results: Comparisons of demographic characteristics showed no difference between the RA group and the control group (Table 1). When comparing carotid US findings there was a difference in the presence of CP, being more prevalent in RA patients (26.4% vs 11.3%, p=0.047), in the presence of an increased cIMT, being more prevalent in RA patients (32.1% vs 3.8%, p=< 0.001), in the cIMT as a quantitative variable, being higher in RA patients (0.75mm vs 0.60mm, p=0.001), and in the presence of subclinical atherosclerosis overall, being more prevalent in RA patients (52.8% vs 15.1%, p=< 0.001) (Table 2).

Conclusion: Patients with RA in the first five years of diagnosis have a higher prevalence of subclinical atherosclerosis than the general population. CV evaluation including a carotid US should be done at the time of diagnosis of RA

Table 2. Carotid ultrasound findings.

	RA patients (n=53)	Controls (n=53)	*p-value*
Carotid plaque, n (%)	14 (26.4)	6 (11.3)	**0.047**
Unilateral carotid plaque, n (%)	6 (11.3)	4 (7.5)	NS
Bilateral carotid plaque, n (%)	8 (15.1)	2 (3.8)	**0.046**
cIMT ≥0.8mm, n (%)	17 (32.1)	2 (3.8)	**<0.001**
Unilateral cIMT ≥0.8mm, n (%)	10 (18.9)	2 (3.8)	**0.014**
Bilateral cIMT ≥0.8mm, n (%)	7 (13.2)	0 (0.0)	**0.013**
cIMT mm, median (IQR)	0.75 (0.61-0.97)	0.60 (0.50-0.66)	**0.001**
Subclinical atherosclerosis, n (%)	28 (52.8)	8 (15.1)	**<0.001**

NS, not significant; RA, rheumatoid arthritis; cIMT, carotid intima media thickness.

patients, and subsequently it must be individualized according to the CV risk of each patient, with a maximum of five years to identify those patients who would benefit from an opportune treatment.

Disclosure: N. Guajardo-Jauregui, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **A. Rodriguez-Romero**, None; **J. Loya-Acosta**, None; **A. Meza-Garza**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **J. Castillo-Treviño**, None.

Abstract Number: 0272

RA Disease Activity Is an Independent Predictor of Left Ventricular Mass Changes in an RA Cohort Without Cardiovascular Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) patients have 50% increased risk of heart failure (HF) vs non-RA patients with a distinct phenotype, preserved ejection fraction on transthoracic echocardiography (TTE) and attenuation of classic HF symptoms. Left ventricular (LV) remodeling (abnormal mass and wall thickness) is hypothesized to be an important precursor to clinical HF in the general population. Accordingly, LV structural abnormalities are prevalent in RA patients *without* clinical HF. Specifically, RA patients demonstrate higher mean LV mass index (LVMI) vs non-RA patients in cross-sectional TTE studies, with few correlates to RA associated inflammatory measures. However, pro-

Table 1. Baseline and Follow-up Changes in LV Remodeling Categories

LV Remodeling Categories*	Baseline % (n=164)	Baseline subset % (n=64)	Follow-up subset % (n=64)	Baseline subset (n=64) vs. Follow-up subset (n=64); p-value**
Normal Geometry	65%	65%	45%	***0.03***
Concentric Remodeling	13%	11%	37%	***0.01***
Concentric Hypertrophy	2.2%	1.8%	3.8%	0.32
Eccentric Hypertrophy	19.7%	22%	17%	0.65

* Concentric remodeling: Relative wall thickness (RWT)>0.42 and LVMI<90% tile
Concentric hypertrophy: RWT>0.42 and LVMI>90% tile
Normal geometry: RWT<0.42 and LVMI<90% tile
Eccentric hypertrophy: RWT<0.42 and LVMI>90% tile
**McNemar's Test

Figure 1. Adjusted Annualized Rate of Change in LVMI in Averaged CDAI Groups

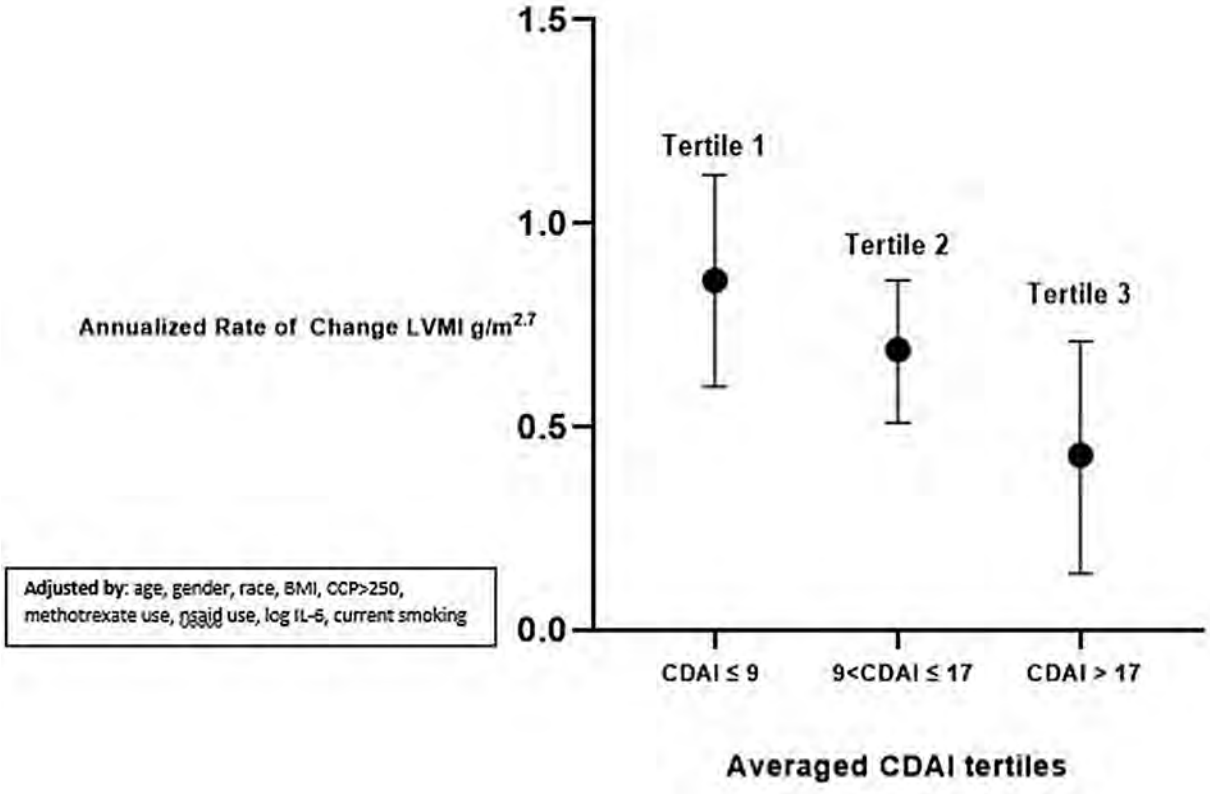


Table 2. Multivariable Associations Between Annualized Rate of Change LVMI and RA and CV Variables

Clinical Covariates	Annualized Rate of ▲LVMI (n=42) Multivariable	
	β	P
Age, per year	-0.0081	0.37
Male versus female	0.077	0.76
Race (binary) white vs non-white	0.16	0.48
BMI, per kg/m²	-0.0016	0.92
Averaged CDAI (baseline + follow-up)	**-0.020**	***0.046***
CCP >250, yes versus no	-0.0039	0.98
Methotrexate use, yes versus no	-0.068	0.72
NSAID use, yes versus no	0.25	0.22
Log IL-6, per mg/liter	0.051	0.58
Current smoker, yes versus no	**0.82**	***0.009***
Prob>F	0.20	
R-Squared	0.32	
Adjusted R-Squared	0.099	

spective changes in LVMI and their significant clinical predictors remain poorly characterized in RA patients without clinical HF. Here we report on the evolution of LVMI in a prospective RA cohort without clinical cardiovascular disease (CVD), as well as its significant RA associated predictors, while adjusting for CV risk factors.

Methods: RA patients (n=164) without CVD underwent RA and CV clinical assessment and TTE at baseline. A subset (n=64) returned for follow-up TTE 3-6 years later. Real-time 3-dimensional (3D) echocardiography was utilized to calculate LV mass (indexed to height ($m^{2.7}$)). LV remodeling categories [concentric remodeling (CRM), concentric hypertrophy (CH), and eccentric hypertrophy (EH)], utilizing the conventional cut-off for relative wall thickness (RWT) >0.42 and LVMI cut-off of >90% tile, were identified in the cohort (Table 1). Multivariable regression models (with LVMI as outcome) were utilized to adjust for biologically plausible confounders identified from univariable regressions.

Results: At baseline, up to 35% demonstrated abnormal LV geometry (CRM, CH, EH) and on follow-up this increased to 55% (Table 1). Specifically, the prevalence of CRM increased significantly from baseline to follow-up (p=0.01) (Table 1). The use of TNF inhibitors (TNFi) was associated (p=0.053) with higher baseline LVMI in multivariable models adjusted for RA and CV factors (no TNFi use vs TNFi use: 28.9 g/$m^{2.7}$ vs 30.5 g/$m^{2.7}$). On follow-up, mean LVMI increased 0.69 g/$m^{2.7}$ per year but this was not statistically significant (p=0.82). The highest tertile of averaged CDAI was associated with the lowest increase in LVMI over time (from 0.86 g/$m^{2.7}$ per year to 0.43 g/$m^{2.7}$ per year) (Figure 1). Averaged CDAI also significantly predicted annualized rate of change in LVMI (p=0.046) (Table 2).

Conclusion: LV remodeling, particularly concentric remodeling, increased over time in RA patients without known CVD. At baseline, the use of TNF inhibitors was significantly associated with higher adjusted LVMI. On follow-up, higher averaged CDAI was associated with the lowest increase in LVMI. Further study is needed to clarify how lowering of RA disease activity through DMARD escalation impacts LVMI, and ultimately the development of clinical HF.

Disclosure: E. Park, None; **K. Ito**, None; **C. Depender**, None; **J. Giles**, AbbVie, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 2, 5, UCB, 2; **J. Bathon**, None.

Abstract Number: 0273

Abnormalities in Left Ventricular Geometry Influenced by Higher Rheumatoid Factor and Anti-Cyclic Citrullinated Peptide Antibody Titers in Rheumatoid Arthritis Patients

Natalia Guajardo-Jauregui, **Dionicio Galarza-Delgado**, Iris Colunga-Pedraza, Jose Azpiri-Lopez, Alejandra Rodriguez-Romero, Alejandro Meza-Garza, Julieta Loya-Acosta, Jesus Cardenas-de La Garza, Salvador Lugo-Perez, Catalina Andrade-Vazquez and Alan De Leon-Yañez, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

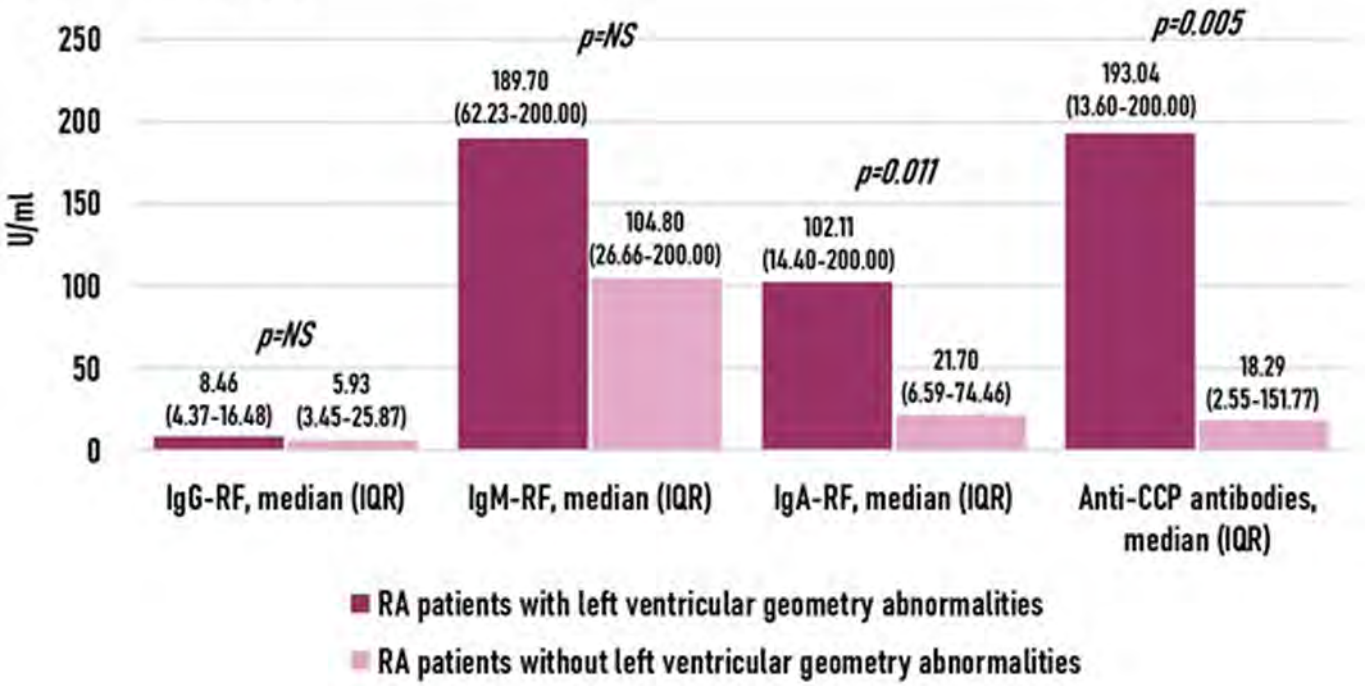
Session Time: 8:30AM–10:30AM

Table 1. Demographic and disease characteristics.

	RA patients with LV geometry abnormalities (n=41)	RA patients without LV geometry abnormalities (n=41)	*p-value*
Age years, mean ± SD	53.12 ± 7.62	52.34 ± 7.74	NS
Women, n (%)	39 (95.1)	39 (95.1)	NS
T2DM, n (%)	7 (17.1)	4 (9.8)	NS
HTN, n (%)	13 (31.7)	10 (24.4)	NS
Dyslipidemia, n (%)	9 (22.0)	11 (26.8)	NS
Active smoking, n (%)	4 (9.8)	3 (7.3)	NS
Obesity, n (%)	11 (26.8)	14 (34.1)	NS
BMI kg/m^2, median (IQR)	27.95 (25.33-31.45)	28.42 (25.84-32.00)	NS
Disease duration years, median (IQR)	10.37 (2.72-17.80)	6.40 (3.43-13.29)	NS
CDAI, median (IQR)	10.00 (3.00-16.50)	14.00 (2.00-22.00)	NS
DAS28-CRP, mean ± SD	3.52 ± 1.42	3.09 ± 1.11	NS
Treatment			
MTX, n (%)	33 (80.5)	34 (82.9)	NS
Glucocorticoids, n (%)	25 (61.0)	23 (56.1)	NS
Antihypertensive, n (%)	13 (31.7)	8 (19.5)	NS
Statins, n (%)	6 (14.6)	4 (9.8)	NS

RA, rheumatoid arthritis; LV, left ventricular; NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; CDAI, clinical disease activity index; DAS28, disease activity score using 28 joints; CPR, C-reactive protein; MTX, methotrexate.

Figure 1. Antibody titers.



Background/Purpose: Rheumatoid arthritis (RA) patients have a higher risk of developing left ventricular (LV) geometry abnormalities which can result in cardiac death. High titers of rheumatoid factor (RF) and anti-cyclic citrullinated peptide (anti-CCP) antibodies are associated with a worse cardiovascular (CV) prognosis in RA patients.

The aim of this study was to assess the association between RF and anti-CCP antibody titers and LV geometry abnormalities detected by a transthoracic echocardiogram.

Methods: This was a cross-sectional, observational, and comparative study. Patients aged 40-75 years who fulfilled the 2010 ACR/EULAR classification criteria underwent a transthoracic echocardiogram. Patients with RA and LV geometry abnormalities were matched to RA-patients without LV geometry abnormalities, by age, gender, comorbidities, and disease characteristics. LV geometry was evaluated with LV mass index and relative wall thickness. A blood sample was taken to measure RF and anti-CCP antibody titers. Comparisons were done with χ^2 test for qualitative variables and Student's t test and Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

Results: A total of 82 RA-patients were included in this study, 41 patients with LV geometry abnormalities and 41 patients without LV geometry abnormalities. Of the 41 patients with LV geometry abnormalities, 37 (90.2%) presented LV concentric remodeling and 4 (9.8%) presented LV concentric hypertrophy. There were no differences in the demographic and clinical characteristics between both groups (Table 1). Patients with altered LV geometry showed higher titers of IgA-RF (102.11 U/mL vs 21.70 U/mL, p=0.011) and anti-CCP antibodies (193.04 U/mL vs 18.29 U/mL, p=0.005). IgG-RF and IgM-RF showed no significant differences between groups (Figure 1).

Conclusion: RA patients with LV geometry abnormalities had higher titers of IgA-RF and anti-CCP antibodies. This suggests an association between antibody titers and CV prognosis in RA patients. Rheumatologists should take these data into account when evaluating CV risk in RA patients, assessing the possibility of performing an echocardiogram for early detection of CV abnormalities and an opportune treatment in this group of patients.

Disclosure: N. Guajardo-Jauregui, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **A. Rodriguez-Romero**, None; **A. Meza-Garza**, None; **J. Loya-Acosta**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **C. Andrade-Vazquez**, None; **A. De Leon-Yañez**, None.

Abstract Number: 0274

Angiopoietin-Like Protein 4, Apolipoprotein C3 and Lipoprotein Lipase Axis in the Abnormal Lipid Profile of Patients with Rheumatoid Arthritis: Relation to Subclinical Atheromatosis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increase in cardiovascular (CV) risk, attributed, among other factors, to the existence of an abnormal lipid profile. The axis made up of angiopoietin-like protein 4 (ANGPTL4), apolipoprotein C3 (ApoC3) and lipoprotein lipase (LPL) has been associated with cardiovascular mortality in healthy population. However, this axis has not been yet characterized in patients with RA. The objective of this study was to evaluate whether there are differences between RA patients and controls in the serum levels of the molecules of this axis, and to analyze their relationship with the activity of the disease or the markers of systemic inflammation as well as with the subclinical atheromatosis that is present in the disease.

Table 1. Multivariable analysis of the differences in lipid profile and angiopoyetin like protein 4, apolipoprotein C3 and lipoprotein lipase serum levels between RA patients and controls

	Controls (n=246)	RA patients (n=323)	Univariable model	Model #1 beta coef (95% CI), p	Model #2 beta coef (95% CI), p
Lipid profile			p		
Cholesterol, mg/dl	198 ± 45	203 ± 38	0.12	5 (-1-12), 0.19	**14 (6-23), 0.001**
Triglycerids, mg/dl	144 ± 68	149 ± 88	0.44		
HDL cholesterol, mg/dl	52 ± 15	56 ± 15	**0.001**	1 (-1-4), 0.35	
LDL cholesterol, mg/dl	117 ± 37	117 ± 33	0.96		
LDL:HDL cholesterol ratio	2.38 ± 0.89	2.25 ± 0.94	0.10	0.01 (-0.15-0.17), 0.91	
Non-HDL cholesterol, mg/dl	146 ± 40	147 ± 38	0.72		
Lipoprotein (a), mg/dl	38 (14-101)	33 (11-111)	0.99		
Apolipoprotein A1, mg/dl	174 ± 39	170 ± 29	0.12	**-10 (-15- -4), 0.001**	**-10 (-16- -3), 0.005**
Apolipoprotein B, mg/dl	104 ± 29	107 ± 47	0.38		
Apo B:Apo A ratio	0.61 ± 0.18	0.64 ± 0.25	0.097	**0.05 (0.02-0.09), 0.006**	-
Atherogenic index	4.01 ± 1.12	3.88 ± 1.33	0.22		
Angiopoyetin like protein 4, ng/ml	73 (47-121)	151 (90-290)	**0.000**	**217 (150-285), 0.000**	**295 (214-376), 0.000**
Apoliprotein C3, mg/dl	62 ± 56	88 ± 52	**0.000**	**30 (20-40), 0.000**	**30 (18-41), 0.000**
Lipoprotein lipase, ng/ml	230 (183-328)	99 (60-156)	**0.000**	**-119 (-158- -80), 0.000**	**-172 (-211- -133), 0.000**

Data represent means ± standard deviation or median (interquartile range) when data were not normally distributed.

HDL: high-density lipoprotein; LDL: low-density lipoprotein.

Model #1: Adjusted for sex, body mass index, abdominal circumference, hypertension, diabetes and statins (variables with a p value < 20 difference between patients and controls).

Model #2: Adjusted for model #1 + rest of lipid molecules (with a p value < 0.20 in the univariate analysis) other than the one that is compared Because collinearity LDL cholesterol, LDL:HDL ratio, non-HDL cholesterol, apoB:apoA, and atherogenic index were excluded of the multivariable analyses in model 2.

Methods: We performed a cross-sectional study that encompassed 569 individuals; 323 patients with RA and 246 controls. Full lipid profile was assessed including serum levels of ANGPTL4, apoC3 and LPL. Carotid intima-media thickness (cIMT) and carotid plaques were assessed in patients. A multivariable analysis, adjusted for standard CV risk factors, was performed to evaluate if there were differences in this axis between patients and controls, and to study the relationship of this axis with data associated with the disease and the presence of subclinical atheromatosis.

Results: After multivariable analysis, adjusted for CV risk factors and for the changes that the disease produces itself over other lipid profile molecules, patients with RA showed higher levels of ANGPTL4 (beta coef. 295 [95% CI 214-376] ng/ml, p=0.000) and ApoC3 (beta coef. 30 [CI95% 18-41] mg / dl, p=0.000), but lower circulating LPL (beta coef. -172 [CI95% -211-133] ng/ml, p=0.000).

Regarding the data related to the disease, an association was found between ESR and ANGPTL4 (beta coef. -3 [CI95% -6--1] ng/ml, p = 0.02), and C-reactive protein and apoC3 (beta coeff. 0.53 [IC95% 0.12-0.95] mg/dl, p=0.01). Likewise, ESR was positively associated with LPL levels (beta coef. 1 [95% CI 0-3] ng/ml, p=0.03). An association was also found between the use of certain treatments and higher serum levels of LPL (hydroxychloroquine, beta coef. 116 [95% CI 30-202] ng/ml, p=0.008; salazopyrin, beta coef. 143 [95% CI 41 -245] ng/ml, p=0.006 and anti-TNF therapy, beta coefficient 101 [95% CI 33-169] ng / ml, p=0.004).

The ANGPTL4-Apoc3-LPL axis did not show a relationship with the presence of carotid plaque in patients with RA. However, while ApoC3 and LPL levels were not associated with cIMT, ANGPTL4 serum levels showed a positive association with it after multivariate analysis (beta coef. 0.06 [95% CI 0.02-0.09] microns, p=0.000).

Conclusion: RA patients have an abnormal ANGPTL4-Apoc3-LPL axis compared to controls. Certain characteristics of the disease related to inflammation justify this alteration. ANGPTL4 serum levels show an independent and significant positive relationship with IMT in patients with RA.

Disclosure: j. Quevedo, None; **L. de Armás-Rillo**, None; **A. de Vera-González**, None; **L. Cáceres**, None; **C. Almeida**, None; **A. González-Delgado**, None; **I. Ferraz-Amaro**, None.

Abstract Number: 0275

Impact of Disease Activity on Left Ventricular Diastolic Dysfunction in Rheumatoid Arthritis Patients

Natalia Guajardo-Jauregui, **Dionicio Galarza-Delgado**, Iris Colunga-Pedraza, Jose Azpiri-Lopez, Alejandra Rodriguez-Romero, Alejandro Meza-Garza, Julieta Loya-Acosta, Jesus Cardenas-de La Garza, Salvador Lugo-Perez, Catalina Andrade-Vazquez and Alan De Leon-Yañez, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

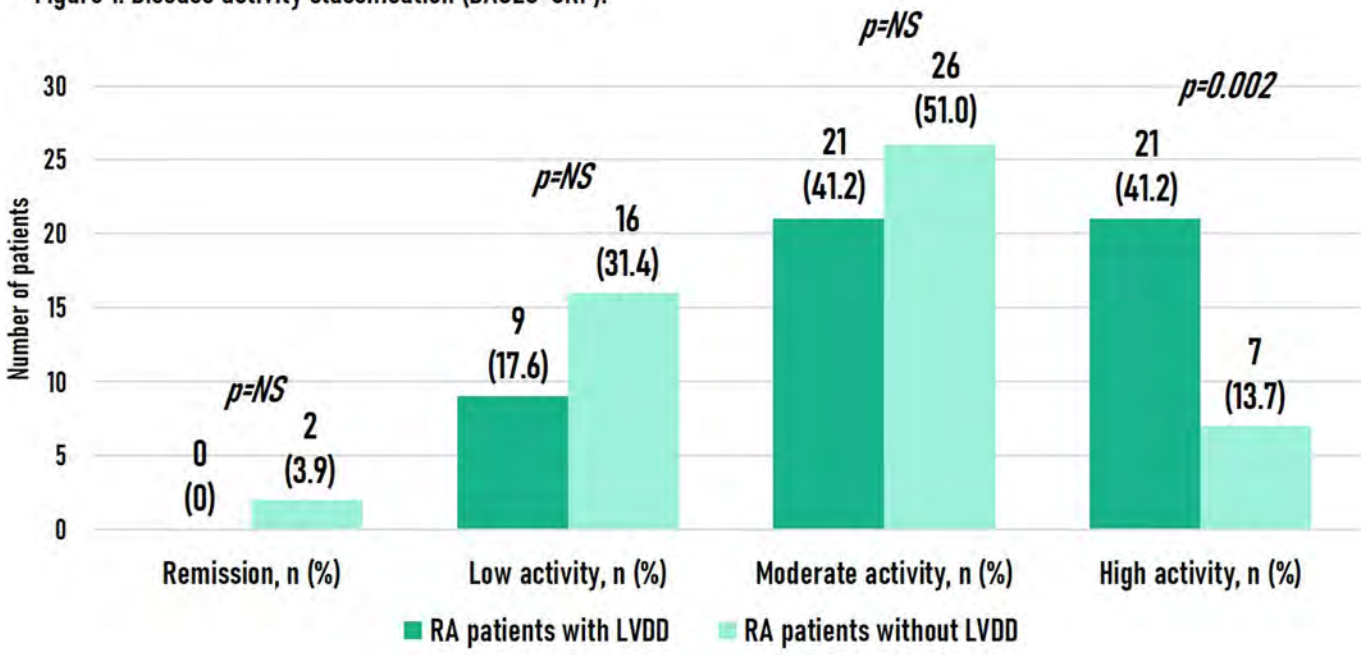
Background/Purpose: Cardiovascular disease (CVD) is the main cause of mortality in patients with rheumatoid arthritis (RA) reflected by a higher prevalence of cardiovascular risk factors (CVRFs), a chronic systemic inflammatory state and heart failure compared to the general population. Left ventricular diastolic dysfunction (LVDD) is attributable to structural abnormalities such as hypertrophy or interstitial fibrosis and impaired myocyte relaxation resulting from ischemia and is frequently asymptomatic. The presence of LVDD could be considered as the first step to development of heart failure.

Table 1. Demographic and disease characteristics

	RA patients with LVDD (n=51)	RA patients without LVDD (n=51)	*p-value*
Women, n (%)	50 (98)	47 (92.2)	NS
Age, years ± SD	56.12 ± 8.76	53.91 ± 5.61	NS
HTN, n (%)	17 (33.3)	13 (25.5)	NS
T2DM, n (%)	6 (11.8)	10 (19.6)	NS
Dyslipidemia, n (%)	17 (33.3)	11 (21.6)	NS
Active smoking, n (%)	5 (9.8)	5 (9.8)	NS
BMI, kg/m² ± SD	28.20 ± 4.89	29.40 ± 5.13	NS
Disease duration, years (IQR)	10.70 (5.16-17.87)	5.66 (2.67-15.64)	**0.033**
DAS28-CRP, median (IQR)	4.88 (3.53-5.45)	3.56 (3.00-4.69)	**0.004**

NS, not significant; HTN, hypertension; T2DM, type 2 diabetes mellitus; BMI, body mass index; DAS28, disease activity score using 28 joints; CPR, C reactive protein.

Figure 1. Disease activity classification (DAS28-CRP).



The aim of the study was to identify the association of disease activity and the presence of LVDD in RA patients.

Methods: This was a cross-sectional, observational, and comparative study of RA subjects that fulfilled the 2010 ACR/EULAR classification criteria, aged 40-75 years. A transthoracic echocardiogram was performed and reviewed by two certified echocardiographers, in all study subjects. A total of fifty-one RA patients diagnosed with LVDD according to the 2016 American Society of Echocardiography (ASE) criteria, and 51 RA patients without LVDD, matched by age, gender, and comorbidities, were included in this study. Disease activity was evaluated with the disease activity score using 28 joints-C reactive protein (DAS28-CRP). Distribution was evaluated with the Kolmogorov-Smirnov test. Chi-square test, Student's t test and Mann-Whitney U test were used for comparations between groups. A p-value < 0.05 was considered statistically significant.

Results: There were no differences between groups regarding age, gender, and comorbidities. Patients with LVDD demonstrated a higher disease activity evaluated by DAS28-CRP (4.88 vs 3.56, $p=0.004$) (Table 1). It was observed that patients with LVDD had a higher prevalence of being classified in the high disease activity category compared to patients without LVDD (41.2% vs. 13.7%, $p=0.002$) (Figure 1). When performing a binary logistic regression, including traditional CVRFs and disease activity, it was found that a high disease activity was the only independent predictor for the presence of LVDD, with an OR 4.70, (95% CI 1.63-13.50, p=0.004).

Conclusion: Patients with RA and LVDD have higher disease activity, so emphasis should be placed on strict antirheumatic treatment to achieve disease control and therefore avoid the risk of developing a CVD and the progression to heart failure.

Disclosure: N. Guajardo-Jauregui, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **A. Rodriguez-Romero**, None; **A. Meza-Garza**, None; **J. Loya-Acosta**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **C. Andrade-Vazquez**, None; **A. De Leon-Yañez**, None.

Abstract Number: 0276

Pulse Pressure as a Predictor of Carotid Plaque in Rheumatoid Arthritis Patients

Natalia Guajardo-Jauregui, **Iris Colunga-Pedraza**, Jose Azpiri-Lopez, Dionicio Galarza-Delgado, Alejandra Rodriguez-Romero, Julieta Loya-Acosta, Alejandro Meza-Garza, Jesus Cardenas-de La Garza, Salvador Lugo-Perez and Jessica Castillo-Treviño, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Pulse pressure (PP) is defined as the difference between systolic and diastolic blood pressure and represents arterial compliance and reflective properties of blood flow. It is well known that gender, age, and ethnicity are intrinsic factors of the patient that influence PP. Brachial PP has recently been associated with subclinical cardiovascular disease after adjustment with traditional cardiovascular risk factors in the general population. However, this relationship has not been studied in patients with rheumatoid arthritis (RA) and its identification would allow earlier adjustments of cardiovascular therapies in this high-risk group.

Table 1. Demographic characteristics.

	RA (n=92)	Controls (n=92)	*p-value*
Women, n (%)	85 (92.4)	85 (92.4)	NS
Age years, mean ± SD	58.0 (55.0-63.0)	56.5 (54.0-61.0)	NS
T2DM, n (%)	17 (18.5)	15 (16.3)	NS
Hypertension, n (%)	33 (35.9)	33 (35.9)	NS
Dyslipidemia, n (%)	30 (32.6)	29 (31.5)	NS
Obesity, n (%)	30 (32.6)	31 (33.7)	NS
Active smoking, n (%)	11 (12.0)	20 (21.7)	NS
	RA patients with CP (n=39)	**RA patients without CP (n=53)**	***p-value***
Women, n (%)	36 (92.3)	49 (92.5)	NS
Age years, mean ± SD	60.13 ± 5.98	58.08 ± 7.00	NS
T2DM, n (%)	9 (23.1)	8 (15.1)	NS
Hypertension, n (%)	16 (41.0)	17 (32.1)	NS
Dyslipidemia, n (%)	13 (33.3)	17 (32.1)	NS
Obesity, n (%)	15 (38.5)	15 (28.3)	NS
Active smoking, n (%)	6 (15.4)	5 (9.4)	NS
Disease duration years median (IQR)	8.44 (3.00-15.50)	12.86 (4.66-19.66)	NS

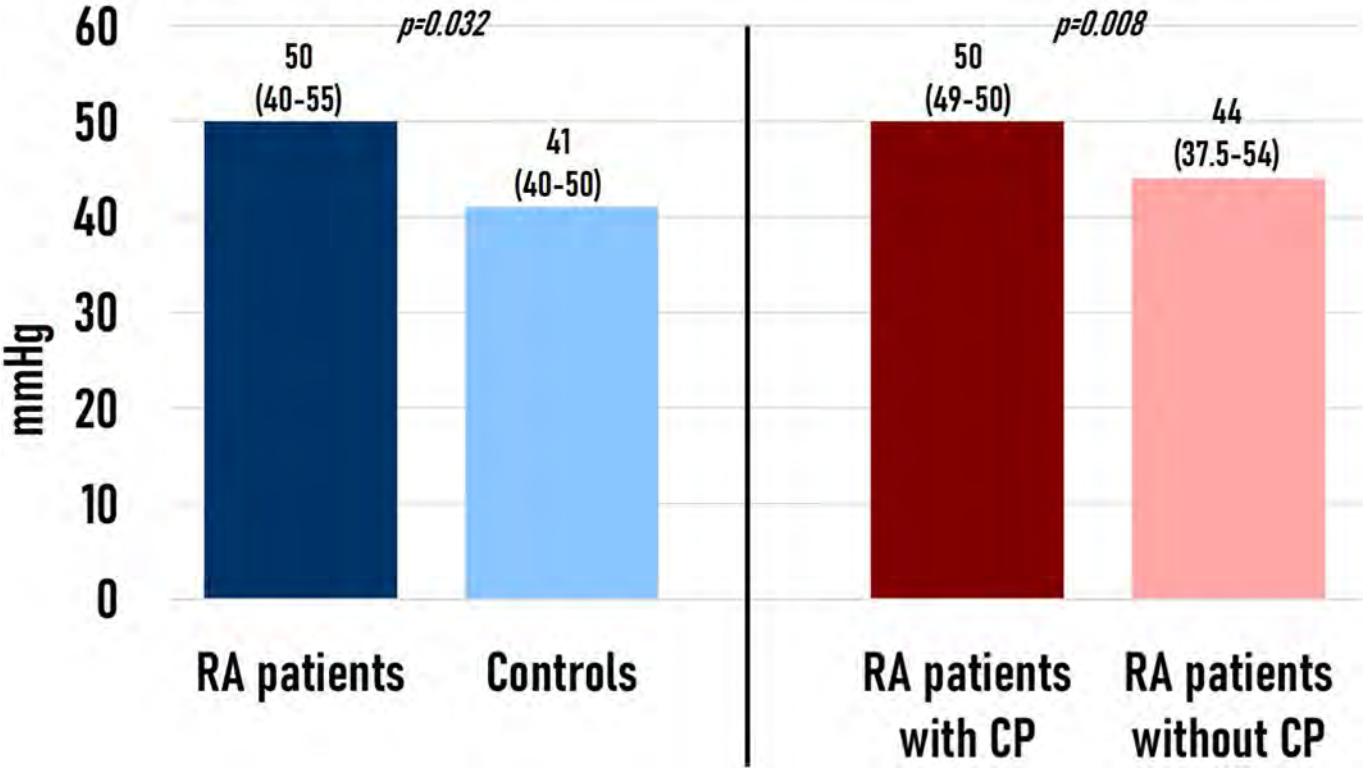
NS, not significant; T2DM, type 2 diabetes mellitus; CP, carotid plaque.

The aim of the study is to analyze the difference of PP between patients with RA and healthy controls. Additionally, to analyze the difference between RA patients with carotid plaque (CP) and without CP.

Methods: This was a cross-sectional, observational, and comparative study of 92 patients with RA aged 40-75 years and who fulfilled the 2010 ACR/EULAR classification criteria. Also, we included 92 controls without RA, matched by gender, age and comorbidities. A carotid ultrasound was performed in RA patients and they were divided into two subgroups, patients with CP and without CP. Blood pressure measurement was taken after 15 minutes of rest on the left arm of all study subjects. Distribution was evaluated with the Kolmogorov-Smirnov test. Descriptive analysis was done using measures of central tendency. Chi-square, Student's t test and Mann-Whitney U test were used for comparations between groups.

Results: We found no differences between groups regarding age, gender, and comorbidities (type 2 diabetes mellitus, hypertension, dyslipidemia, and active smoking) (Table 1). There was a significant difference in PP between patients with RA and controls (50 mmHg vs 41 mmHg respectively, *p=0.032*). When comparing RA patients there was a significant difference in PP of patients with CP and without CP (50 mmHg vs 44 mmHg respectively, *p=0.008*)

Figure 1. Pulse pressure.



(Figure 1). When performing a binary logistic regression, it was found that PP was the only independent risk factor for the presence of CP in patients with RA, OR 1.054 (95% CI 1.008-1.101, *p=0.020*).

Conclusion: Patients with RA had a higher PP than controls. Binary logistic regression showed PP as the only independent risk factor for the presence of subclinical atherosclerosis in RA patients. PP is a parameter that all rheumatologists should consider when evaluating cardiovascular risk in patients with RA.

Disclosure: N. Guajardo-Jauregui, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **D. Galarza-Delgado**, None; **A. Rodriguez-Romero**, None; **J. Loya-Acosta**, None; **A. Meza-Garza**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **J. Castillo-Treviño**, None.

Abstract Number: 0277

Best Cardiovascular Risk Algorithm to Predict Abnormalities in Left Ventricular Geometry in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Discriminatory capacity of the different cardiovascular risk calculators.

Calculators (cut-off point)	AUC	CI 95%		p	Sensitivity	Specificity
		Inferior	Superior			
QRISK3 (≥4.60)	0.646	0.537	0.754	**0.012**	73.8%	54.5%
SCORE	0.591	0.475	0.706	NS	-	-
OMNIBUS (≥3.80)	0.621	0.509	0.734	**0.038**	57.1%	68.2%
FRSL	0.594	0.480	0.707	NS	-	-
FRS-BMI (≥11.02)	0.642	0.530	0.754	**0.015**	61.9%	57.6%
RRS (≥2.25)	0.627	0.514	0.741	**0.029**	47.6%	78.8%

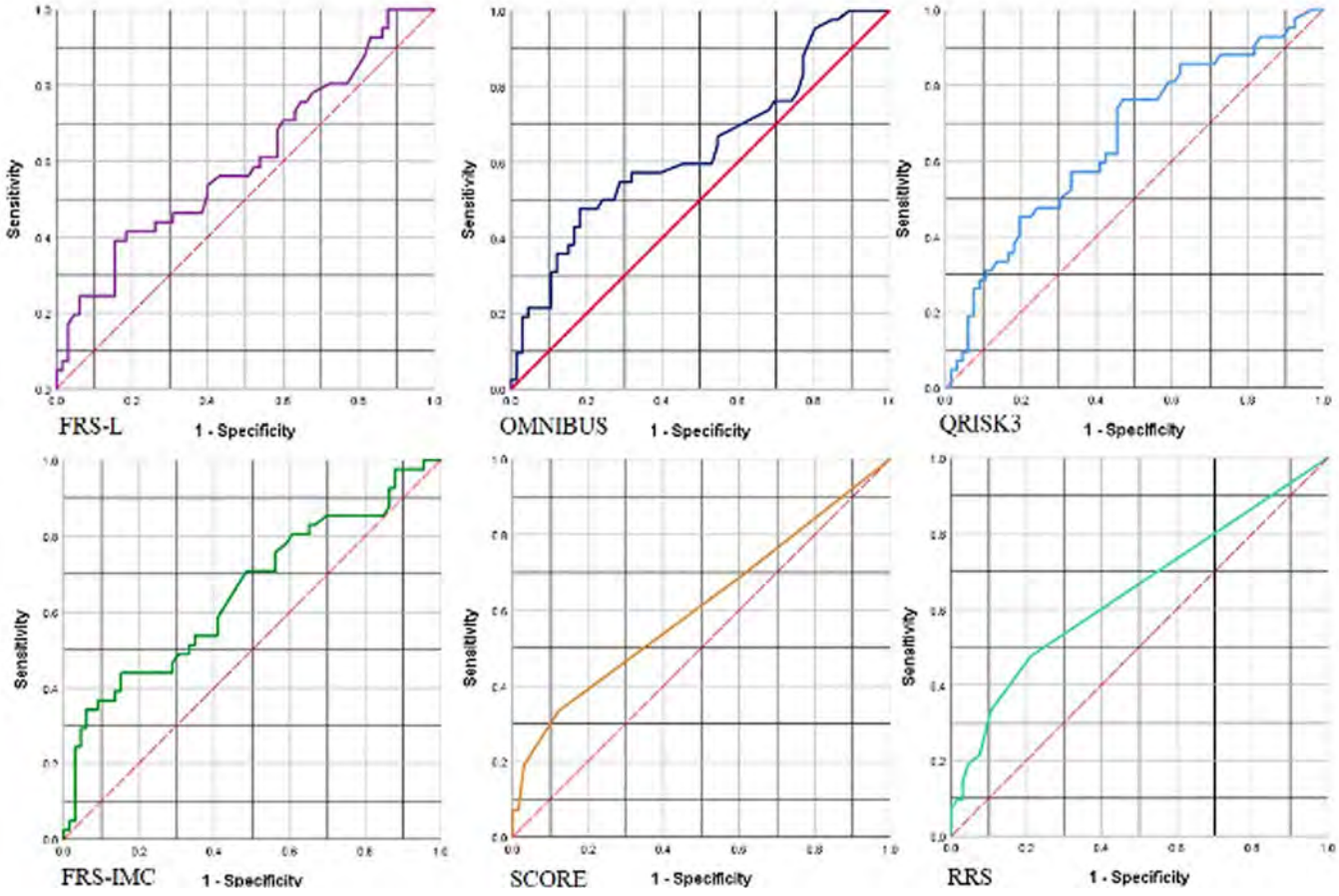
Area Under the Curve, AUC; Framingham Risk Score-Lipids, FRSL; Framingham Risk Score-Body Mass Index, FRS-BMI; Reynolds Risk Score, RRS.

Background/Purpose: A relationship between rheumatoid arthritis (RA) and the presence of abnormalities in left ventricular (LV) geometry such as eccentric remodeling has recently been determined, even in the absence of cardiovascular risk factors and before clinical manifestations. The 2016 EULAR recommendations that cardiovascular (CV) risk prediction models should be adapted by a 1.5 multiplication factor in RA patients. Risk prediction algorithms based on the CV risk factors have been an important tool for adopting preventive measures and intensifying therapies based on the estimated risk but their application in predicting cardiac structural abnormalities has never been studied. The aim of the study is to determine the CV risk calculator that best predicts alterations in ventricular geometry in RA.

Methods: A cross-sectional, observational study of 108 RA patients between 40-75 years, who fulfilled ACR/EULAR 2010 classification criteria. The QRISK3, OMNIBUS, Framingham Risk Score-Lipids, Framingham Risk Score-Body Mass Index (FRS-BMI) and Reynolds Risk Score (RRS) calculators were compared. The diagnostic performance was determined by ROC curves, and the discriminative capacity by the Area Under the Curve (AUC) 95% CI. The echocardiogram was the diagnostic gold standard.

Results: The prevalence of abnormalities in LV geometry was 38.9%. QRISK3 reported AUC of 0.656, 95% CI (0.537-0.754, *p = 0.012*), cut-off point ≥4.6, sensitivity of 73.8% and specificity of 54.5%, and likelihood ratio of +1.62. FRS-BMI showed AUC of 0.642, 95% CI (0.543-0.762, *p = 0.008*), cut-off point ≥11.02, sensitivity and specificity of 61.9% and 57.6% respectively, and likelihood ratio of +1.46. OMNIBUS showed AUC of 0.635, CI 95% (0.525-0.746,

Figure 1. ROC curves of the different cardiovascular risk calculators.



p = 0.018), cut-off point ≥3.8, sensitivity and specificity of 57.1% and 68.2%. While RRS had AUC 0.644, 95% CI (0.534-0.755, *p = 0.012*), cut-off point of 2.25, sensitivity of 47.6% and specificity 78.8%, and likelihood ratio of +2.24 (Figure 1 and Table 1).

Conclusion: The QRISK3 calculator showed the highest discriminative ability and sensitivity to predict abnormalities in LV geometry. However, all calculators demonstrated the need for a lower cut-off point to predict alterations in ventricular geometry. Our findings require adequate reproducibility in other population groups to determine the applicability of CV risk algorithms as predictors of structural alteration of LV.

Disclosure: A. Rodriguez-Romero, None; **J. Azpiri-Lopez**, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **J. Davila-Jimenez**, None; **N. Guajardo-Jauregui**, None; **A. Meza-Garza**, None; **J. Loya-Acosta**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **A. De Leon-Yañez**, None; **C. Andrade-Vazquez**, None.

Abstract Number: 0278

Higher Prevalence of Eccentric Hypertrophy in Rheumatoid Arthritis Patients: A Case-Control Study

Alejandra Rodriguez-Romero, **Jose Azpiri-Lopez**, Dionicio Galarza-Delgado, Iris Colunga-Pedraza, Natalia Guajardo-Jauregui, Julieta Loya-Acosta, Alejandro Meza-Garza, Jesus Cardenas-de La Garza, Salvador Lugo-Perez, Alan De Leon-Yañez and Catalina Andrade-Vazquez, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with Rheumatoid Arthritis (RA) have a higher prevalence of cardiovascular diseases and a strong association with abnormalities in the left ventricular (LV) geometry. Both concentric and eccentric remodeling have been determined as an independent factor for sudden cardiac arrest in the general population with normal or slightly decreased ventricular function but there is still controversy about the factors involved and the pathophysiology in patients with RA. Therefore, the aim of the study is to determine the characteristics of LV geometry and the impact of RA diagnosis.

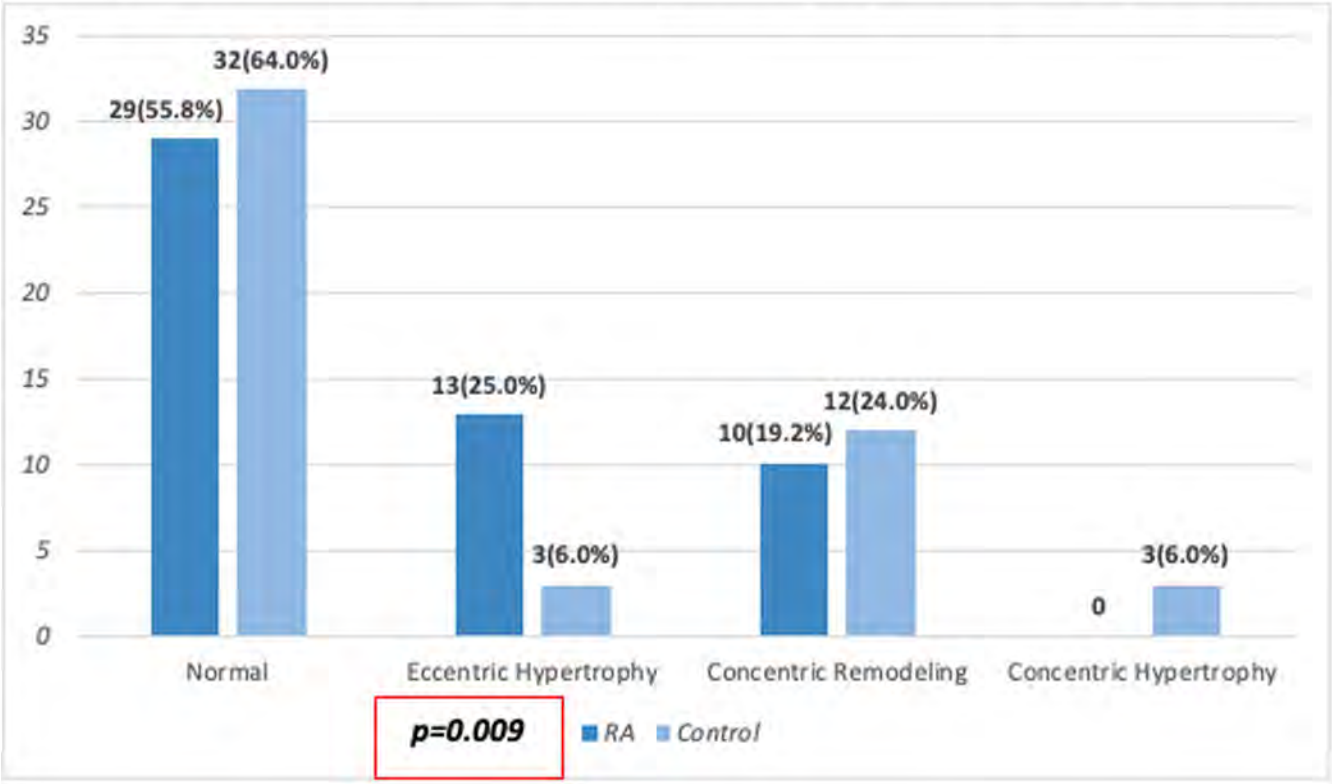
Methods: A case-control study with 52 RA patients that fulfilled ACR/EULAR 2010 classification criteria, aged 40-75 years, and a control group of 50 healthy subjects matched by age, gender, and comorbidities were included for this study. Subjects were evaluated using a transthoracic echocardiogram performed and reviewed by two certified echocardiographers. Ventricular geometry was evaluated with indexed left ventricular mass and relative wall thickness. Descriptive analysis was done using measures of central tendency. Chi-square, Students' T test and Mann-Whitney

Table 1. Demographic characteristics and echocardiographic findings between groups.

	RA (n=52)	Controls (n=50)	*p-value*
Age, years ± SD	51.4 ±6.2	51.1 ± 5.5	NS
Women, n (%)	51 (98.1)	49 (98.0)	NS
Active smoking, n (%)	8 (15.4)	8 (16.0)	NS
Dyslipidemia, n (%)	11 (21.2)	13 (26.0)	NS
Diabetes Mellitus, n (%)	5 (9.6)	5 (10.0)	NS
Hypertension, n (%)	8 (15.4)	10 (20.0)	NS
BMI, kg/m^2 (p25-p75)	27.8 (24.5-31.4)	28.3 (25.4-30.3)	NS
BSA, median (p25-p75)	1.7 (1.6-1.8)	1.8 (1.6-1.9)	**0.003**
Systolic blood pressure, mmHg	119.5 (110.0-127.5)	120.0 (110.7-130.0)	NS
Echocardiographic findings			
LVPWTd, median (p25-p75)	0.9 (0.8-1.0)	0.9 (0.8-1.0)	NS
LVIDd, median (p25-p75)	4.8 (4.3-5.2)	4.6 (4.5-4.9)	NS
LV mass, median (p25-p75)	131.2 (119.5-155.7)	131.2 (113.2-154.3)	NS
LV mass index, median (p25-p75)	78.6 (69.7-95.6)	76.0 (66.7-84.6)	NS
RWT, mean ± SD	0.4 ± 0.09	0.4 ± 0.07	NS

NS, no significant; BMI, body mass index; BSA, body surface area; LVPWTd, left ventricular posterior wall thickness at end-diastole; LVIDd, left ventricular internal dimension at end-diastole; RWT, relative wall thickness.

Figure 1. Abnormalities in left ventricular geometry in patients with RA and controls.



U test were used for comparations between groups. A logistic binary regression was performed with the traditional cardiovascular risk factors (CVRF), age and RA diagnosis.

Results: No significant differences were found in the traditional CVRF (diabetes mellitus, dyslipidemia, active smoking, and hypertension) (Table 1). Most of the subjects reported normal geometry in both groups (55.8% for RA group vs 64.0% for controls). A higher prevalence of eccentric hypertrophy was found in the RA group, 13 (25%) subjects versus 3 (6%) in the control group, *p = 0.009*. The binary regression showed that the diagnosis of RA was the only independent risk factor for the presence of eccentric hypertrophy, OR 7.22 95% CI (1.68-31.02, *p = 0.008*).

Conclusion: There is a higher prevalence of eccentric remodeling in patients with RA independently of traditional CVRF. The diagnosis of RA is an independent risk factor for the presence of eccentric hypertrophy that is associated with higher mortality. Treatment of cardiovascular comorbidities should be intensified in those patients with abnormalities in LV geometry in order to prevent cardiovascular diseases such as heart failure.

Disclosure: A. Rodriguez-Romero, None; **J. Azpiri-Lopez**, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **N. Guajardo-Jauregui**, None; **J. Loya-Acosta**, None; **A. Meza-Garza**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **A. De Leon-Yañez**, None; **C. Andrade-Vazquez**, None.

Abstract Number: 0279

Macrophage Cholesterol Loading Associates with Low-density Lipoprotein Structure, Oxidation, Antibodies Against Oxidized Epitopes and Is Modified by Immunomodulatory Treatments in Patients with Rheumatoid Arthritis

George Karpouzas[1], Bianca Papotti[2], sarah ormseth[3], Marcella Palumbo[4], Elizabeth Hernandez[3], Cinzia Marchi[4], Francesca Zimetti[4], Franco Bernini[4] and Nicoletta Ronda[4], [1]Harbor-UCLA Medical Center, Torrance, CA, [2]2. Department of Food and Drug, University of Parma, Italy, Parma, Italy, [3]The Lundquist Institute, Harbor-UCLA Medical Center, Torrance, CA, [4]Department of Food and Drug, University of Parma, Parma, Italy

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: In Rheumatoid arthritis (RA), immune dysregulation, excess inflammation and oxidative stress may alter lipoprotein level and function and promote LDL oxidation and its uptake by vessel wall macrophages. The cell cholesterol loading capacity of serum (CLC)- as a reflection of both lipoprotein quantity and quality- may be an

Table 1. Multivariable-adjusted β-coefficients for predictors of CLC in the total sample and stratified by bDMARD use and CRP level

	IgG LDL β (95% CI)	IgM LDL β (95% CI)	aCCP+ β (95% CI)	IL-6 β (95% CI)	LDL3+LDL4 β (95% CI)	OxLDL β (95% CI)	Statin use β (95% CI)
Total sample	0.27* (0.06, 0.49)	-0.28** (-0.44, -0.12)	-0.53† (-1.1, 0.04)	0.05 (-0.12, 0.22)	0.18* (0.02, 0.34)	0.21* (0.02, 0.40)	-0.09 (-0.46, 0.29)
bDMARD naïve	0.68*** (0.34, 1.02)	-0.56*** (-0.81, -0.32)	-0.41 (-1.06, 0.25)	0.31* (0.06, 0.57)	0.21† (-0.03, 0.46)	-0.07 (-0.30, 0.16)	-0.78** (-1.28, -0.27)
bDMARD exposed	0.18 (-0.08, 0.44)	-0.26* (-0.5, -0.01)	-0.35 (-1.95, 1.25)	-0.05 (-0.28, 0.18)	0.25* (0.03, 0.48)	0.21 (-0.06, 0.48)	0.2 (-0.4, 0.80)
CRP<4mg/L	0.05 (-0.2, 0.3)	0.03 (-0.27, 0.32)	-0.99* (-1.89, -0.09)	0.24* (0.02, 0.46)	0.17 (-0.05, 0.4o)	-0.22† (-0.46, 0.02)	0.31 (-0.26, 0.88)
CRP>4mg/L	0.25† (-0.02, 0.53)	-0.36*** (-0.53, -0.19)	-0.47 (-1.21, 0.28)	-0.08 (-0.32, 0.16)	0.18† (-0.03, 0.38)	0.45*** (0.23, 0.67)	-0.29 (-0.75, 0.16)

Models adjusted for age, sex, and all other predictors included in this table.

***p<0.001, **p<0.01, *p<0.05, †p<0.10

essential step in foam cell formation, the establishment and progression of atherosclerosis. RA therapies may modify atherosclerosis trajectory by intercepting several of those processes. We evaluated the relationship of inflammation, LDL particle structure, oxidation and immune system recognition of oxidized epitopes with CLC. We next evaluated interactions between RA treatments and these processes on macrophage cholesterol loading.

Methods: 107 RA patients from our previously described PROTECT-RA cohort with coronary atherosclerosis evaluation were studied. Lipoprotein classes and subclasses and their cholesterol content were directly measured using single vertical spin density gradient ultracentrifugation. Oxidized LDL (oxLDL) was measured with monoclonal antibody E06. IgM and IgG antibodies to oxLDL (anti-oxLDL) were assessed with chemiluminescence Elisa. Proinflammatory cytokines were measured with microparticle immunoassay and singe molecule counting (Erenna, Singulex). CLC was measured by fluorometric assay- as macrophage cholesterol content- after a 24-hour incubation with whole serum. Robust, multivariable generalized linear models evaluated associations between inflammation, LDL particle content, LDL oxidation and antibodies against oxLDL with CLC. Similar models explored interactions between RA treatments and markers of inflammation on CLC.

Results: Patients were middle aged (53.9 10.7), mostly female (86%) with seropositive (92%), erosive (66.4%) and well controlled disease (DAS28= 2.49 0.96). Smaller-sized LDL3 and LDL4 levels, oxLDL and anti-oxLDL IgG levels positively associated with CLC (all $p < 0.032$, Table 1); in contrast, anti-oxLDL IgM levels negatively associated with CLC (adjusted β= -0.28 [95% CI -0.44,-0.12], p=0.001). Inflammation modified the effect of LDL oxidation on CLC (p for interaction= 0.001); oxLDL significantly associated with CLC (adjusted β= 0.45 [95% CI 0.23-0.67], p< 0.001) in patients with CRP > 4mg/L (median split), but not those with CRP < 4mg/L. Significant interactions between bDMARD use and Interleukin-6 levels (p= 0.031) and between bDMARD and statin use (p= 0.038) on CLC were also observed. In bDMARD-naïve patients, interleukin-6 positively associated with CLC (adjusted β= 0.31 [95% CI 0.06-0.57], p=0.017) whereas statin use negatively associated with CLC (adjusted β= -0.78 [95% CI -1.28, -0.27], p= 0.003). Neither interleukin-6 nor statin use related to CLC in bDMARD-exposed patients.

Conclusion: Higher content of smaller-sized, readily oxidizable LDL subclasses, greater oxLDL levels -especially in the context of higher inflammation- and greater anti-oxLDL IgG serum concentration associated with greater cholesterol macrophage loading in RA. bDMARD therapies modified the impact of inflammation, lipid particle structure and statin use on CLC.

Disclosure: G. Karpouzas, None; **B. Papotti**, None; **s. ormseth**, None; **M. Palumbo**, None; **E. Hernandez**, None; **C. Marchi**, None; **F. Zimetti**, None; **F. Bernini**, None; **N. Ronda**, None.

Abstract Number: 0280

Mast Cells Contribute to the Development of Lung Fibrosis via Inducing Myofibroblast Differentiation by TGF-β Production

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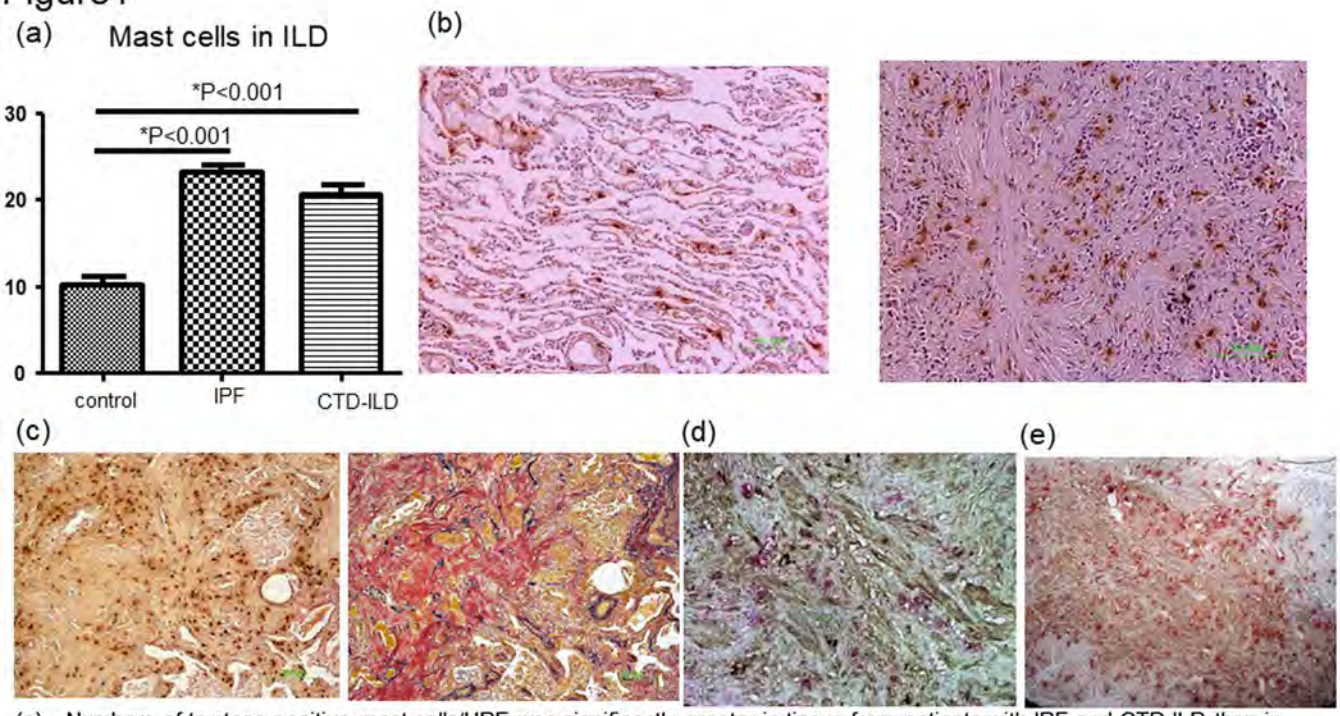
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Figure1



(a) Numbers of tryptase-positive mast cells/HPF was significantly greater in tissue from patients with IPF and CTD-ILD than in tissue from control individuals.

(b) Immunohistochemistry with an anti-tryptase antibody revealed upregulation of mast cells in the lung tissues from patients with IPF(right) compared to that from control individuals(left).

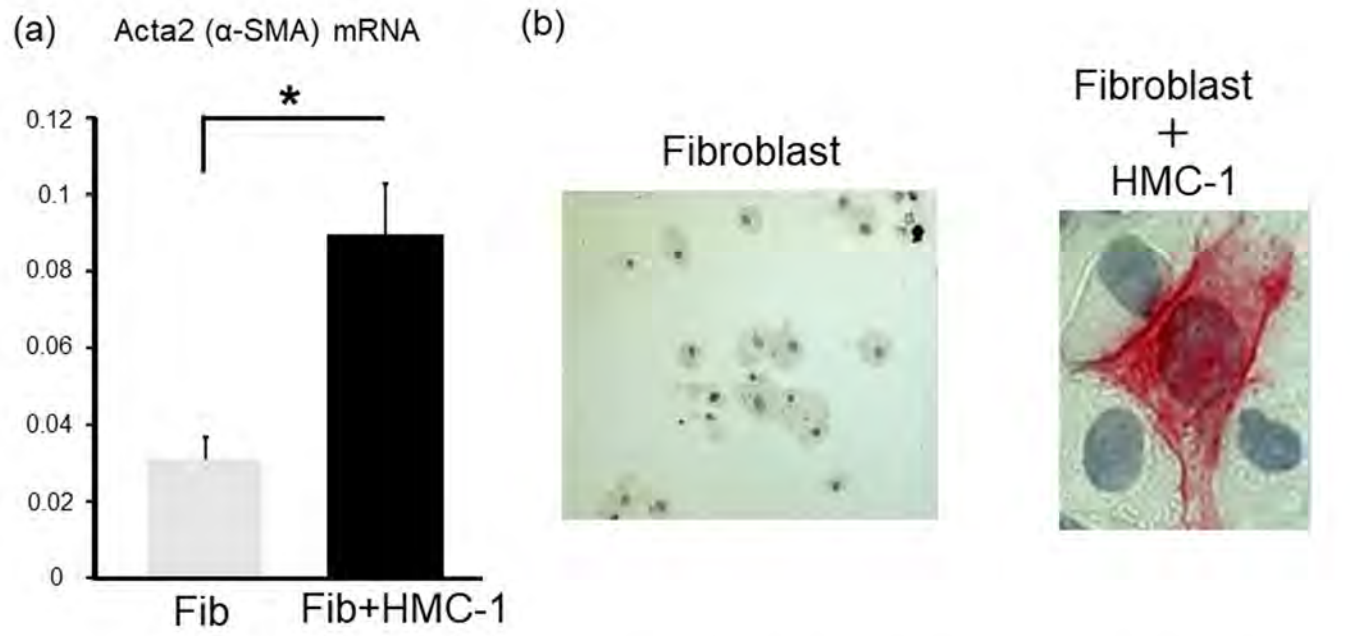
(c) Representative results of tryptase(left) and Verhoeff–Van Gieson staining (right) in serial sections of lung tissue from patients with IPF. Tryptase-positive mast cells (brown cells in the right panel) are frequently in close proximity to Verhoeff–Van Gieson-stained fibroblastic lesions. (left panel).

(d,e) Representative results of double immunohistochemical staining for tryptase and vimentin(d) and tryptase and α-SMA(e) in the lung tissue obtained from patients with IPF. Tryptase-positive mast cells (red cells) were close proximity to vimentin-positive fibroblasts(brown cells) or α-SMA-positive myofibroblasts (brown cells).

Background/Purpose: Idiopathic pulmonary fibrosis is an interstitial lung disease of unknown etiology. The most critical event in the evolution of fibrosis is the appearance of activated myofibroblasts. Mast cells (MC) are reportedly involved in various inflammatory and fibrotic conditions, although little is known about their roles in interstitial lung disease (ILD). Since the pathogenic role of MC in ILD remains unclear, we examined whether MCs play a critical role in the development of pulmonary fibrosis.

Methods: Lung tissue was examined using histology and immunohistochemistry. The samples for biopsy were obtained from the involved lung tissue of 13 patients with idiopathic pulmonary fibrosis (IPF) and 13 patients with connective tissue disease (CTD)-associated-ILD (RA 7 systemic sclerosis 6). As a control, we used noncancerous lung sections of 10 patients who had undergone surgery for lung cancer. We used immunohistochemistry to identify and quantify tryptase-, prolyl-4-hydroxylase β-, and alpha-smooth muscle actin (α-SMA)-positive cells as MCs, fibroblasts, and myofibroblasts, respectively. The co-culture of the human mast cell line (HMC-1) with pulmonary fibroblasts was performed in a Transwell system. Fibroblasts cultured with or without HMC-1 cells were cytospun and the expression of α-SMA, a marker of myofibroblast differentiation, was examined by immunohistochemistry after 7 days of culture. The ACTA2 mRNA synthesis in the fibroblasts was evaluated by RT-qPCR. The conditioned medium for the fibroblast culture was obtained from HMC-1 cells stimulated with recombinant human IL-33 and stem cell factor for 24 hours. Fibroblasts were treated with HMC-1-conditioned medium for 24 hours and the ACTA2 mRNA synthesis in

Figure2



Human pulmonary fibroblasts were cultured with or without human mast cell, HMC-1 for 1 wk in the lower and upper chambers, respectively, of a transwell apparatus. After 1wk co-culture, total RNA was isolated from fibroblasts, followed by qPCR employing primers specific for α-SMA and β-actin.

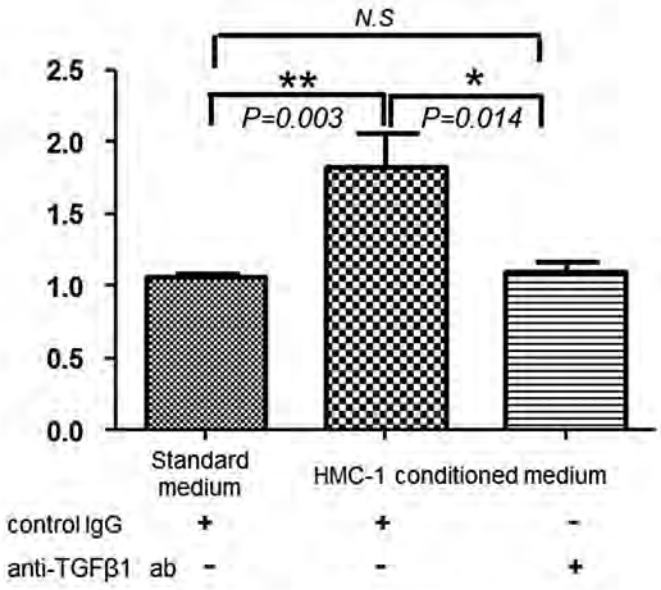
(a) Mast cells promote α- SMA mRNA expression in fibroblasts.
(b) Fibroblasts were detached and placed on glass slides using a standard cytospin approach. Immunocytochemical staining rdetected the positive signal for α-SMA in fibroblasts after coculture with HMC-1.

the fibroblasts was evaluated by RT-qPCR. Neutralization antibodies for human TGF-β1, 2, and 3 were used during the fibroblast culture with HMC-1-conditioned or standard culture media.

Results: MCs were significantly more numerous in the lung samples with IPF and CTD-ILD than in the control (Fig. 1a and b). MCs were proximal to the Elastica van Gieson (EVG)-stained fibrous tissue and pulmonary fibroblasts and myofibroblasts (Fig 1c, d, and e). We examined whether MCs induced pulmonary fibroblasts to differentiate into myofibroblasts. In the co-culture experiment, the ACTA2 mRNA level significantly increased compared to that in the control fibroblast monoculture (Fig. 2a). Consistently with this result, the upregulation of α-SMA in the fibroblasts during the co-culture was confirmed by immunohistochemistry. Furthermore, the ACTA2 mRNA was significantly upregulated in fibroblasts conditioned with the HMC-1 medium compared to that in fibroblasts cultured in a standard medium (Fig. 3). In addition, the neutralization of TGF-β abolished the ACTA2 mRNA upregulation in fibroblasts conditioned in the HMC-1 medium, thereby suggesting that HMC-1-derived TGF-β contributes to myofibroblast differentiation (Fig. 3).

Conclusion: The findings suggest a novel role for MCs in the development of lung fibrosis via TGF-β production-induced myofibroblast differentiation.

Figure3 Mast cell-derived TGFβ induces α-SMA mRNA expression in fibroblast



Fibroblasts cultured in HMC-1 conditioned medium exhibited significant upregulation of α-SMA mRNA. Treatment with neutralizing antibodies specific for TGFβ led to abrogation of this upregulation effect.

Disclosure: S. Kaieda, None; **M. Okamoto**, None; **M. Tominaga**, None; **T. Hoshino**, None.

Abstract Number: 0281

Unsupervised Machine Learning of Expanded Autoantibodies, Cytokines, and Chemokines Improves the Identification of Interstitial Lung Disease in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) frequently complicates the rheumatoid arthritis (RA) disease course, leading to significant morbidity and premature mortality. RA-ILD may be underdiagnosed or detected later in the disease course because of inadequate screening methods. Several peripheral blood biomarkers have been investigated in RA-ILD, but the performance of composite biomarker profiles for identifying RA-ILD in larger RA cohorts is unknown.

Methods: We studied participants in a prospective cohort of U.S. Veterans with RA fulfilling ACR criteria. Demographics, RA history, smoking status, and ACR core measures are collected regularly, complementing a biorepository

Table 1. Association of peripheral biomarkers with prevalent interstitial lung disease in a rheumatoid arthritis cohort

Component (Eigenvalue)	Loading Biomarkers [a]	Adjusted OR (95% CI) for ILD [b]	P value
1 (12.4)	**MCP-4/CCL13, TARC/CCL17, IL-27, MDC/CCL22, IL-6, MCP-1/CCL2**	**0.92 (0.86, 0.98)**	**0.01**
2 (5.1)	IL-4, IL-12p70, IL-1β, IL-2	1.01 (0.93, 1.09)	0.84
3 (2.6)	**IgA anti-MAA-albumin, IgM anti-MAA-albumin, IgG anti-MAA-albumin**	**1.19 (1.03, 1.38)**	**0.02**
4 (2.0)	VEGF, IL-1ra, IL-8	1.16 (0.99, 1.37)	0.07
5 (1.6)	IL-12/23p40, IL-17a	0.91 (0.79, 1.05)	0.18
6 (1.5)	**RF, Anti-CCP, IL-5**	**1.42 (1.21, 1.67)**	**<0.001**
7 (1.2)	IL-15, IL23, IL-3, IL-5	1.00 (0.86, 1.17)	0.97
8 (1.1)	IgA anti-MAA-collagen, IgM anti-MAA-collagen, IgG anti-MAA-collagen	1.11 (0.95, 1.29)	0.20

a. Biomarkers listed are those with principal component loadings >0.3 (in descending order).
b. Model adjusted for age, sex, race, and cigarette smoking history.

of peripheral blood samples obtained at enrollment. We measured 33 cytokines and chemokines (via the MesoScale platform), RF concentration (by nephelometry), anti-CCP concentration (by 2nd generation ELISA), and anti-malondialdehyde acetaldehyde (MAA) antibody concentration (IgA, IgM, and IgG anti-MAA-albumin and anti-MAA-collagen, all by ELISA) from banked serum. Prevalent ILD was determined through validated methods that included detailed, systematic review of medical records for clinical diagnoses, imaging findings, and biopsy reports. The aforementioned biomarkers were log-transformed and standardized. Subsequently, principal component analysis (PCA) was performed, retaining components with eigenvalues >1. The ability of the resultant principal component (PC) scores to improve ILD identification was assessed in multivariable logistic regression models. Receiver operating characteristic curves were generated for clinical (age, sex, race, and cigarette smoking history) and clinical + PC score models.

Results: Among 2,044 RA patients (86% male, mean age 64 years, 79% smoking history), 121 had prevalent ILD. PCA of 33 cytokines/chemokines and 8 RA autoantibodies identified 8 unique biomarker PCs. Biomarkers loading onto each PC after orthogonal rotation are shown in **Table 1**. Kaiser-Meyer-Olkin (KMO) testing showed high adequacy for PCA (KMO=0.93). PC 1 scores (characterized by inflammatory monocyte/macrophage mediators) were negatively associated with the presence of ILD while PC 3 scores (anti-MAA-albumin) and PC 6 scores (RF & anti-CCP) were positively associated with the presence of ILD (**Table 1**). Adding PC scores to a clinical only model improved the discrimination of ILD in the RA cohort, evidenced by an increase in the area under the curve (AUC) from 0.62 to 0.70 (p=0.002; **Figure 1**).

Conclusion: In a large RA cohort with validated ILD diagnoses, we found that unsupervised machine learning of 33 cytokines and chemokines and 8 autoantibodies improved the identification of RA-ILD. RA-related autoantibodies (anti-MAA-albumin, RF, and anti-CCP) were the peripheral biomarkers most closely associated with the presence of RA-ILD, suggesting that serologic antibody responses may have the greatest potential for identifying ILD or at-risk patients. Cohort-wide screening for RA-ILD using peripheral blood biomarkers shows promise as an ILD screening modality and should be further validated in other cohorts.

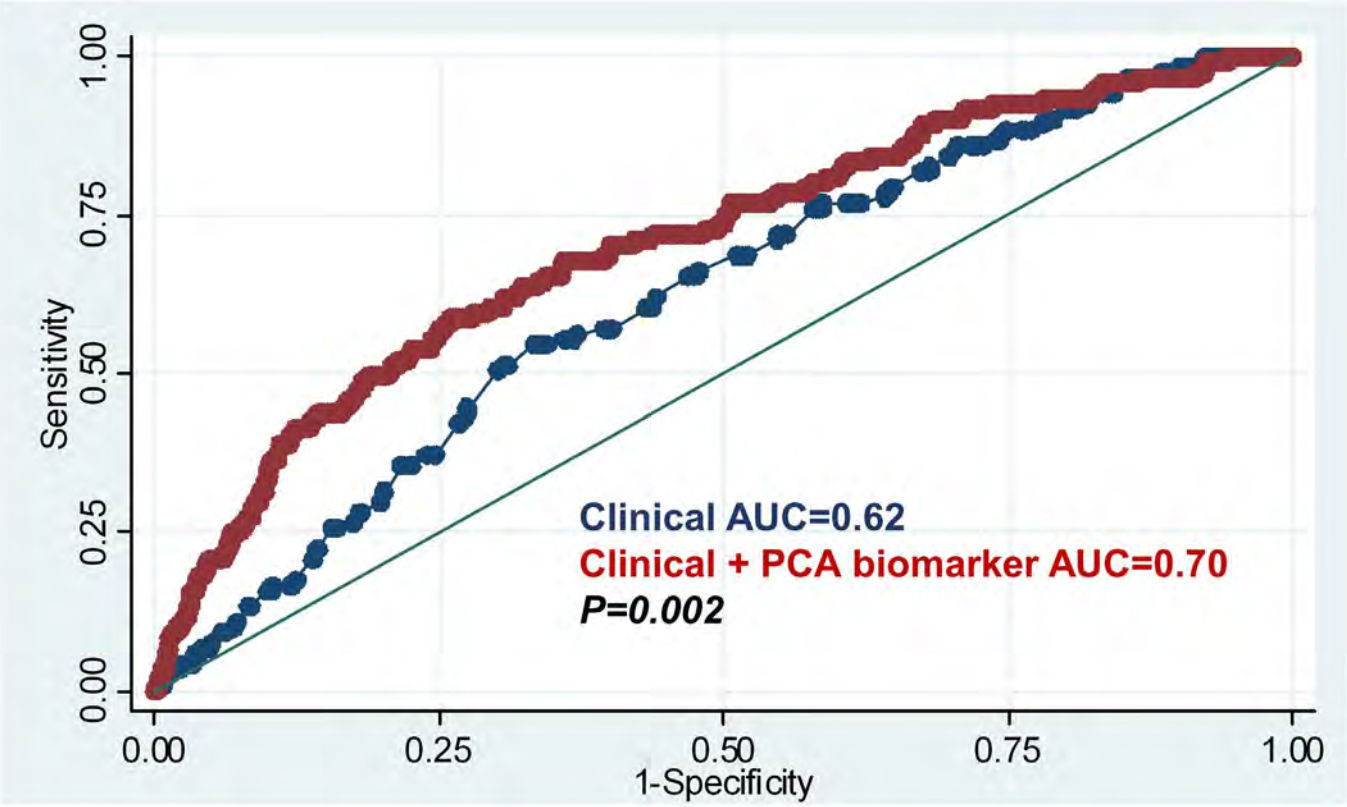

Figure 1. Comparison of the performance of clinical and biomarker models to identify interstitial lung disease in a rheumatoid arthritis cohort.

Disclosure: B. England, Boehringer-Ingelheim, 2; **D. Ascherman**, None; **M. Duryee**, None; **C. Hunter**, None; **Y. Yang**, None; **P. Roul**, None; **H. Sayles**, None; **F. Yu**, None; **J. Poole**, None; **J. Baker**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 0282

5-Year Cardiovascular Event Risk in Early Rheumatoid Arthritis Patients Who Received Treat-to-Target Management: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

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Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Characteristics of ERA subjects and the matched controls

	ERA (n=261)	Controls (n=783)	*p-value*
Age (mean +/- SD)	60.2 +/- 12	60.3 +/- 12	*0.99*
Total cholesterol (mean +/- SD)	4.8 +/- 0.94	4.9 +/- 1.00	*0.34*
High density lipoprotein-cholesterol (median, IQR)	1.4 (1.2-1.6)	1.4 (1.2-1.7)	*0.612*
Low density lipoprotein-cholesterol (mean +/- SD)	2.8 +/- 0.8	2.6 +/- 0.8	*0.27*
Triglyceride (median, IQR)	0.96 (0.7-1.3)	1.2 (0.8-1.7)	*0.00*
Atherogenic index# (mean +/- SD)	-0.07 +/-0.29	-0.15 +/- 0.28	*0.48*
RA disease characteristics	**baseline**	**last visit**	
Seropositivity	89.3%		
Disease duration (median days, IQR)	177 (96-299)	2026 (1818-2126)	
Erythrocyte sedimentation rate (mean +/- SD)	55.7 +/- 34	32.6 +/- 21.3	
C-reactive protein (median, IQR)	7.9 (3.5-22.2)	2.1 (1.0-5.0)	
Swollen joint count (median, IQR)	3 (2-6)	0 (0-1)	
Tender joint count (median, IQR)	6 (3-10)	0 (0-1)	
Patient's global assessment (mean mm +/- SD)	50.7 +/- 26.8	16.0 +/- 18.3	
DAS28-ESR (mean +/- SD)	5.2 +/- 1.3	2.4 +/- 1.8	
DAS28-CRP (mean +/- SD)	4.4 +/- 1.3	1.8 +/- 1.5	
Health assessment questionnaire (mean +/- SD)	0.77 +/- 0.74	0.38 +/- 0.51	

 # Atherogenic index = $\log_{10}$ (triglyceride/HDL-cholesterol)

SD: standard deviation, IQR: interquartile range, DAS28: disease activity score-28

Background/Purpose: Rheumatoid arthritis (RA) is associated with higher cardiovascular disease (CVD) risk due to the underlying inflammation.It is uncertain if the excess CV risk could be reduced by effective suppression of inflammation using the treat-to-target (T2T) approach in patients with early RA (ERA).

Methods: This study compared the 5-year cardiovascular event (CVE) rate among ERA patients managed by a T2T strategy with a CV risk factor-matched non-RA population.

This was an observational study using the Hong Kong Hospital Authority population-based hospital database known as the Clinical Data Analysis and Reporting System (CDARS) and the Clinical Rheumatology Systematic Treat-to-target in Asia Leadership (CRYSTAL) registry. ERA subjects from the registry with baseline disease duration less than 2 years were recruited between 2012-2016. All patients received a tight control, T2T treatment strategy aiming at remission and had been followed for at least 5 years. Each ERA subject was matched to 3 non-RA controls according

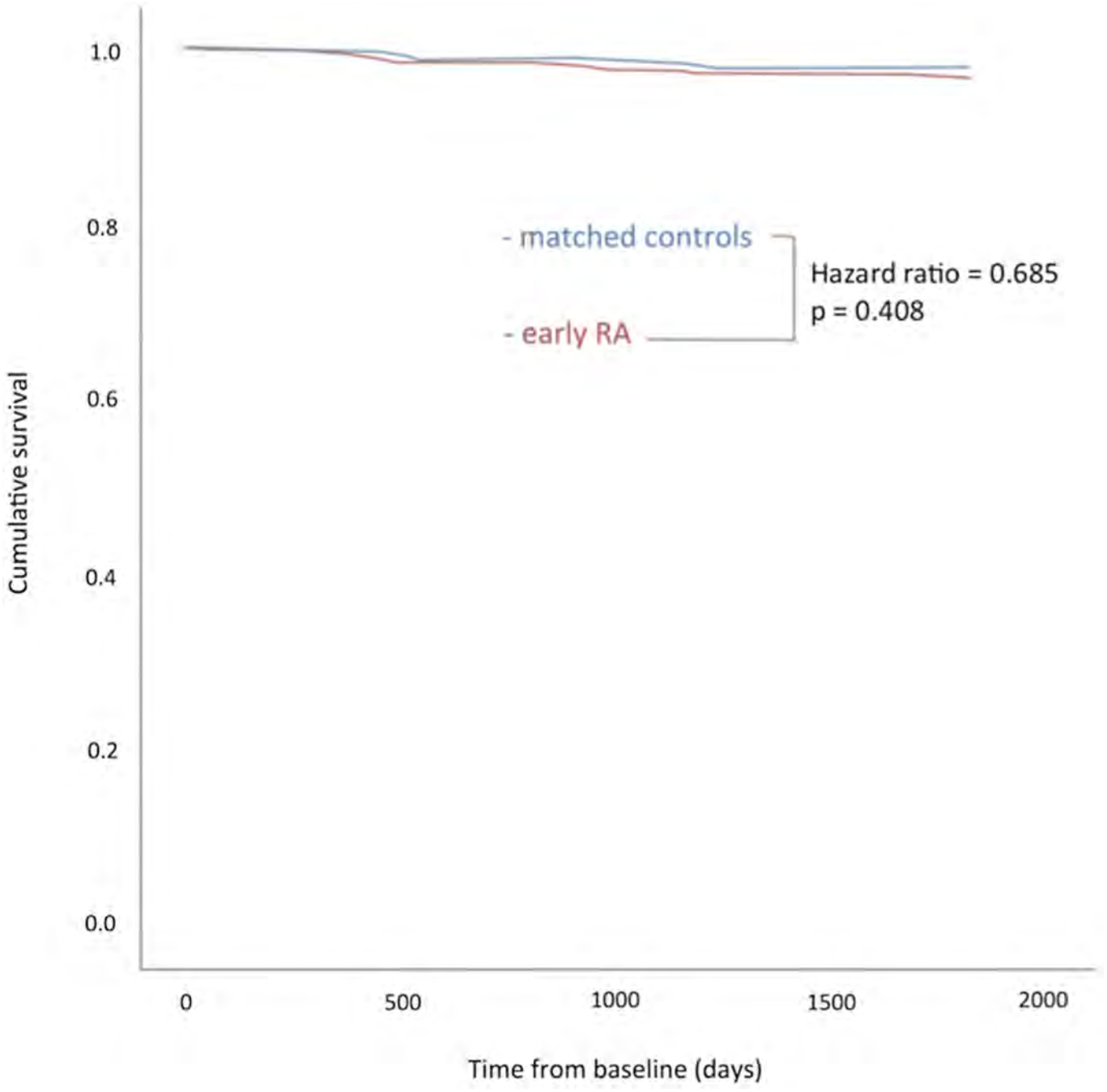

Figure 1. CVE-free survival curves of ERA subjects & matched controls.

to age, gender, smoking status, and the presence of diabetes mellitus (DM), hypertension (HT) and hyperlipidaemia (HL). All subjects on antiplatelet agents, with pre-existing CVD or chronic kidney disease were excluded. All subjects were analysed up to 5 years from baseline. The primary end point was the first occurence of a CVE, namely ischaemic cerebrovascular disease, ischaemic heart disease and heart failure.

Results: The study identified 261 ERA subjects and 783 matched controls. Their characteristics were shown on Table 1. The mean age was 60+/-12 years, 78% were female, 18% were smokers, 8%, 25% and 22% had DM, HT and HL respectively.

CVEs occurred in 2.3% ERA subjects and in 3.3% controls.. The difference was statistically insignificant. The CVE-free survival was shown in Figure 1.

In the ERA cohort, after adjusting for baseline age and atherogenic index, cox-regression analysis showed that i) a longer DAS28 remission duration was protective for CVE with an adjusted hazard ratio (AHR) of 0.46 (95% CI 0.23-0.93), while ii) poor baseline function as reflected by a higher health assessment questionnaire (HAQ) score was predictive of CVE with an AHR of 5.2 (95% CI 1.2-23).

Conclusion: ERA patients treated by a T2T strategy did not develop excess CVE compared to CV risk factor-matched controls over 5 years. A longer disease remission duration was protective while a higher baseline HAQ was associated with a higher CVE risk.

Disclosure: T. Lam, None; **L. Tam**, Janssen, 2, 5, Pfizer, 2, 5, GlaxoSmithKline, 5, AbbVie, 2, Novartis, 5, Amgen, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, Sanofi, 2.

Abstract Number: 0283

Cardiovascular Risk Management in Patients with Rheumatoid Arthritis: A Single-centered Cross-sectional Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiovascular (CV) disease is the leading cause of death in patients with rheumatoid arthritis (RA) and is estimated to be responsible for 29%-32% of all-cause mortality. Meta-analyses of previous cohort studies showed that patients with RA were found to be at 50-60% increased risk of cardiovascular death compared to the general population. Most current American Heart Association (AHA) guidelines place patients with RA as a special population requiring special attention considering it is one of the risk enhancers that prompt physicians to have a lower threshold to initiate statin therapy. The main objective of this study is to evaluate and identify any clinical gaps in the primary prevention of CV risk in patients with RA.

Methods: Data from West Palm Beach VA Medical Center was used to undergo this analysis. All patients from ages 40-79 who had received a diagnosis of RA using the specific ICD09/ICD-10 codes were identified, excluding those with coronary artery disease, cerebrovascular disease or peripheral vascular disease. Data was manually extracted from the Computerized Patient Record System (CPRS), including demographic information (e.g., age, gender and ethnicity), smoking status, vital signs, medical history, active medications, and lipid panel. Patients with an estimated 10-year CV risk of 7.5% or more are determined to be candidates for lipid-lowering therapy.

Results: A total of 317 patients were identified with a mean ± standard deviation (SD) age of 68 ± 8 years, and the majority (77%) were white males. (See Table 1). Three hundred and one (95%) patients had their lipid profile screening

Table 1. Demographic characteristics of the study population and groups based on statin therapy.

Demographic characteristics		Total (n=317)	On statin (n=154)	Not on statin (n=163)	p-value
Age		69 (7)	70 (6)	66 (9)	<0.001*
Male gender		283 (89%)	143 (93%)	140 (86%)	0.04*
Race					0.78
	White	263(83%)	130 (84%)	133 (82%)	
	African American	39 (12%)	16 (10%)	23 (14%)	
	Other	7 (2%)	4 (2.5%)	3 (2%)	
Smoking status					0.33
	Current	64 (20%)	27 (18.5%)	37 (23%)	
	Former	91 (29%)	49 (34%)	42 (27%)	
	Never	149 (47%)	70 (48%)	79 (50%)	
Comorbidities					
	Diabetes mellites	70 (22%)	52 (34%)	18 (11%)	<0.001*
	Hypertension	183 (58%)	109 (71%)	74 (45.5%)	<0.001*
	Coronary artery disease	58 (18%)	43 (28%)	15 (9%)	<0.001*
	Peripheral artery disease	8 (2.5%)	4 (2.5%)	4 (2.5%)	0.93
	Cerebrovascular accident	11 (3.5%)	6 (4%)	5 (3%)	0.68
Antiplatelet use		118 (37%)	84 (45.5%)	34 (20%)	<0.001*
ASCVD risk		23 (14)	28 (14)	19 (13)	<0.001*

Variables are reported as frequency and percentages (%) or median (standard deviation).
ASCVD risk: atherosclerosis and cardiovascular disease risk estimated in 10 years.
*P values < 0.05

test collected in the past 5 years. Out of 165 patients who met the criteria for CVD primary prevention, 68 were on statin therapy (41%). Of which, 48 patients were on a low-intensity statin (71%) despite being candidates for high-intensity statin therapy. Patients on statins were more likely to be older males with diabetes mellites, hypertension, coronary artery disease, or peripheral artery disease, on antiplatelet therapy, and have a higher ASCVD risk score (p-value < 0.05).

Conclusion: Efforts for primary prevention of CV risk in patients with RA are not fully optimized, despite the appropriate screening process for the possible modifiable risk factors. In addition, our study suggests a potential health disparity with regards to prescribing statin in younger and female patients with RA. There is a compelling need for initiating quality improvement projects aimed to improve CV risk control in this particularly vulnerable patient population to improve survival and quality of life.

Disclosure: S. ABOULENAIN, None; **K. Deeb**, None; **M. Abdul Qader**, None; **C. Jones**, None.

Abstract Number: 0284

Risk Factors for Dementia in Patients with Incident Rheumatoid Arthritis: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Growing evidence from observational studies suggests that patients with rheumatoid arthritis (RA) are at increased risk for cognitive impairment and dementia. Longitudinal population-based studies assessing risk factors for Alzheimer's Disease and related dementias (AD/ADRD) in RA are lacking. We aimed to assess risk factors for incident AD/ADRD in a population-based cohort of patients with incident RA.

Methods: This retrospective population-based cohort study included residents of a geographical area who were at least 18 years of age and met 1987 ACR criteria for RA between 1980 and 2014. All individuals were followed until death, migration, or 12/31/2019. Incident dementia was defined as two ICD-9/10 codes for AD/ADRD at least 30 days apart. Patients with AD/ADRD before RA incidence were excluded (n=12). Information on socio-demographics, RA disease characteristics, ever use of antirheumatic medications (i.e. conventional and/or biologic disease-modifying drugs; glucocorticoids), cardiovascular/cerebrovascular disease (CVD) risk factors, and comorbidities was available from medical records. The definition of any CVD included coronary heart disease (i.e., angina pectoris, coronary artery disease, myocardial infarction [MI], and coronary revascularization procedures), cerebral stroke and chronic heart failure. Cox proportional hazards models were used to examine the association between each of these risk factors and incident ADRD, adjusting for age, sex, and calendar year of RA incidence. Time-dependent covariates were used to represent factors that developed during follow-up.

Results: A total of 1,366 patients with RA (mean age 56 years, 69% females, 64% positive for rheumatoid factor and/or cyclic citrullinated peptide antibody) were included. During the median follow-up of 9.4 years, 107 patients (8%) developed AD/ADRD. Older age (hazard ratio [HR] per one year increase 1.15, 95% confidence interval [CI] 1.13-1.17), ever presence of large joint swelling (HR 2.2, 95%CI 1.2-3.9), diabetes mellitus (HR 1.6, 95%CI 1.02-2.5), any CVD (HR 2.4, 95%CI 1.5-4.0), and particularly stroke (HR 3.2, 95%CI 1.9-5.5) and heart failure (HR 1.8, 95%CI 1.1-3.0) were associated with increased risk of AD/ADRD. Use of low-dose aspirin (HR 2.3, 95%CI 1.4-3.8) was associated with increased risk for AD/ADRD, likely due to confounding by indication for CVD. Sex, race, education, smoking, obesity, extraarticular features of RA, antirheumatic medications, hypertension, dyslipidemia, or MI were not associated with risk of AD/ADRD among RA patients.

Conclusion: Apart from age, a universally recognized risk factor for AD/ADRD, clinically active RA manifesting with large joint swelling and the presence of CVD and diabetes mellitus were associated with elevated risk of AD/ADRD among RA patients. Among CVD conditions, cerebral stroke and chronic heart failure were associated with the risk of ADRD. These findings suggest that in addition to aging, the risk of AD/ADRD in RA may be driven by RA disease-related factors while CVD may be partially mediating these associations. Studies are ongoing to further evaluate the role of systemic inflammation and CVD in AD/ADRD overall and by dementia subtype in patients with RA.

Disclosure: E. Myasoedova, None; **M. Mielke**, Biogen, 2; **C. Hulshizer**, None; **J. Davis**, Pfizer, 5; **V. Ramanan**, None; **M. Vassilaki**, Roche, 5, Roche, 2, Biogen, 5, Abbott Laboratories, 12, Equity ownership in Abbott Laboratories, Johnson and Johnson, 12, Equity ownership in Johnson and Johnson, Medtronic, 12, Equity ownership in Medtronic, Amgen, 12, Equity ownership in Amgen; **C. Crowson**, None.

Abstract Number: 0285

Risk of Cardiovascular Disease in Newly Diagnosed Rheumatoid Arthritis: A Current Risk Assessment

Reinder Raadsen[1], Romy Hansildaar[1], Maaike Heslinga[2], Arno van Kuijk[1] and Michael Nurmohamed[3], [1]Reade, Amsterdam, Netherlands, [2]Amsterdam University Medical Center, location VUmc, Amsterdam, Netherlands, [3]Reade and Amsterdam University Medical Center, location VUmc, Amsterdam, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
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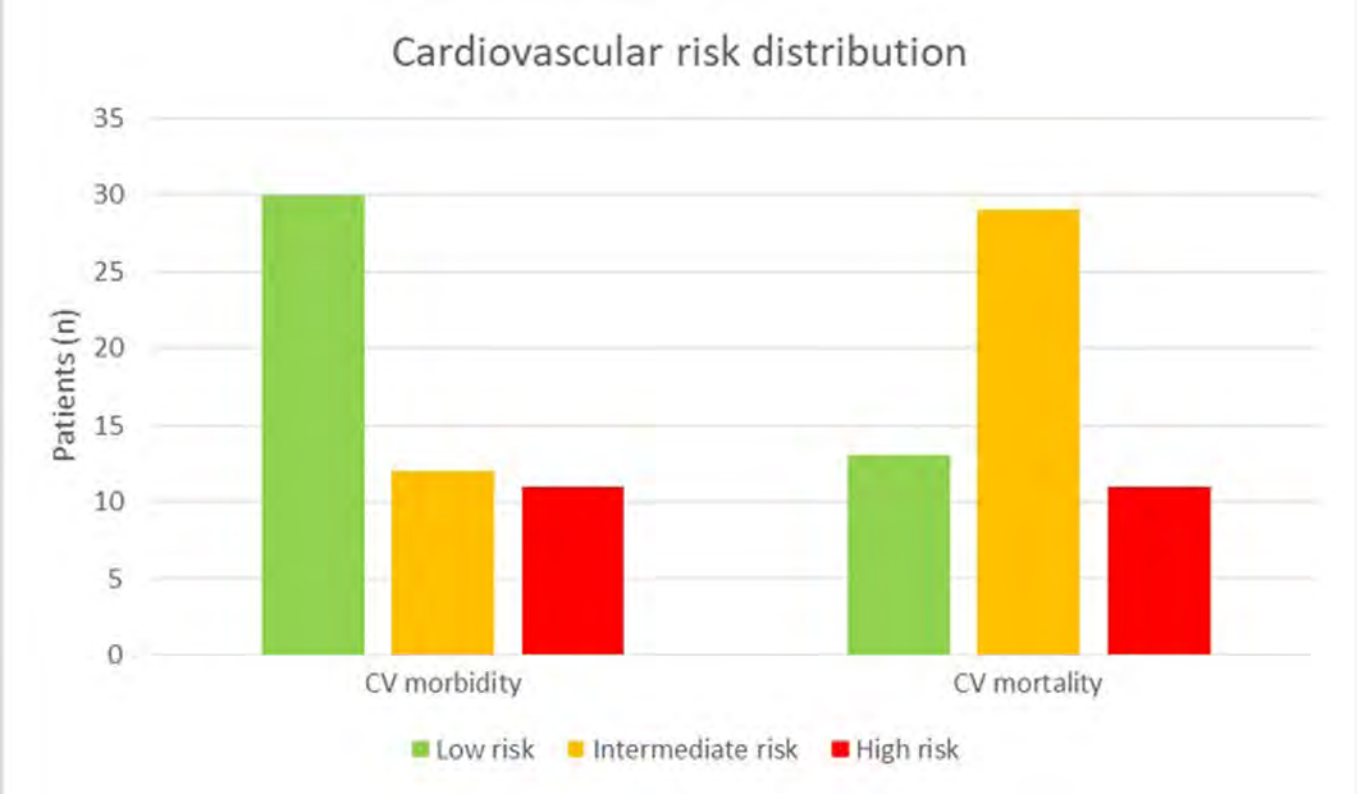
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are known to have an increased risk of developing, mainly ischemic cardiovascular diseases (CVD). This is partly explained by a higher incidence of traditional CV risk factors as hypertension and/or hypercholesterolemia but also due to the systemic inflammation characteristic to RA. RA is considered an independent CV risk by National and International CVD risk management guidelines, and therefore CVD risk screening is recommended. However, the implementation of CV risk management is often poorly performed in daily clinical practice.

The aim of the current study was to investigate the cardiovascular disease risk of newly diagnosed RA patients, and review if and to what extent implementation of CVD risk management had previously taken place.

Methods: Every newly diagnosed RA patient in a large Dutch outpatient rheumatology clinic had CV screening within their first year post-diagnosis during a regularly scheduled visit, where among others smoking habits, blood pressure and lipid profile were measured. A 10-year cardiovascular risk was calculated using a modified SCORE calculator from www.u-prevent.com, which predicts the risk of myocardial infarction, stroke, heart failure, peripheral arterial disease and CV death based on several CV risk factors. To account for RA as a risk factor, the calculator multiplies the risk by 1.5, in accordance with the Dutch CV risk management guideline. The calculated 10-year cardiovascular morbidity risk was categorized in low (< 10%), intermediate (10-19%) and high (≥20%), and the 10-year mortality risk was also categorized in low (< 1%), intermediate (1-4%) and high (≥5%).



Distribution of 10-year cardiovascular risk in rheumatoid arthritis patients. CV = cardiovascular.

Results: A total of 53 patients were included up to this point. Of these, the average age was 57 (±8.5), and 39 (74%) were women. Mean systolic blood pressure was 129 (±17.7) mmHg, with 38 (72%) patients having hypertension. Mean total cholesterol, LDL and HDL were respectively 5.5 (±1.0) mmol, 3.43 (±0.82) mmol and 1.78 (±0.54) mmol, with 30 patients having hypercholesterolemia. The average calculated 10-year morbidity risk of all patients was 13%, and the mortality risk was 3%. Distribution of the 10-year risk in low, intermediate and high is presented in figure 1. Only one patient reported having previous used medication for hypercholesterolemia, but not at the time of enrollment in this study.

Conclusion: 43% of newly diagnosed RA patients had an intermediate or high calculated 10-year CV morbidity risk, and 76% had an intermediate or high mortality risk. Patients with early RA still often have underdiagnosed and severely undertreated risk factors of CVD, such as hypertension and hypercholesterolemia. Early CV risk assessment and management in patients with RA is critical and needs to be implemented as standard care.

Disclosure: R. Raadsen, None; **R. Hansildaar**, None; **M. Heslinga**, None; **A. van Kuijk**, None; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5.

Abstract Number: 0286

Cardiovascular Disease Risk in Inflammatory Arthritis Patients Still Substantially Elevated in 2020

Reinder Raadsen[1], Femke Hooijberg[1], Laura Boekel[1], Erik Vogelzang[2], Gertjan Wolbink[1], Willem Lems[3], Arno van Kuijk[1] and Michael Nurmohamed[4], [1]Reade, Amsterdam, Netherlands, [2]Amsterdam University Medical Center, location VUmc, Amsterdam, Netherlands, [3]VUmc, Amsterdam, Netherlands, [4]Reade and Amsterdam University Medical Center, location VUmc, Amsterdam, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with inflammatory rheumatic diseases such as rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) are at a higher risk for developing cardiovascular diseases (CVD) than the general population. This increased risk is partly due to a higher incidence of traditional cardiovascular (CV) risk factors, such as hypertension and dyslipidemia, and partly due to the underlying systemic inflammation. During the past two decades, the burden of the systemic inflammation has been reduced by more efficacious anti-inflammatory treatment, which somewhat attenuated the increased CV risk of rheumatic patients. However, it remains important to monitor the effects of these new treatment strategies on the prevalence of CVD in patients with a rheumatic disease in systematically controlled cohorts.

The aim of the current report was to evaluate whether the CV risk of patients with inflammatory rheumatic diseases still differs from the general population, despite advances In anti-rheumatic treatment strategies.

Methods: In March 2020, all adult patients with an inflammatory rheumatic disease from the Amsterdam Rheumatology and Immunology Center, location "Reade" were systematically asked to participate in a prospective cohort study. The primary aim of this study was to monitor the impact of the COVID-19 pandemic on patients with inflammatory rheumatic diseases compared to age and sex matched healthy controls. Between April 26, 2020 and May 27, 2020,

Table 1. Values are displayed as mean ± standard deviation (SD), median with interquartile range (IQR) or frequencies with percentages (%). RA = rheumatoid arthritis, PsA = psoriatic arthritis, AS = ankylosing spondylitis, BMI = body mass index, TNF = anti-tumor necrosis factor, IL = interleukin

Table 1. Baseline characteristics

Patient characteristics	All patients (n=1455)	RA (n=979)	PsA (N=261)	AS (n=215)	Controls (n=414)
Mean age - yr	55 ± 13	58 ± 12	55 ± 13	48 ± 13	53 ± 13
Female sex - no (%)	934 (64)	728 (74)	119 (46)	87 (41)	298 (72)
BMI (IQR)	25 (23-28)	25 (22-28)	26 (24-30)	25 (22-28)	24 (22-27)
Smoking - no (%)	178 (12)	126 (13)	17 (7)	35 (16)	34 (8)
Cardiovascular disease – no (%)	157 (11)	107 (11)	28 (11)	22 (10)	30 (7)
Rheumatic medication - no (%)					
csDMARDs	877 (60)	712 (73)	148 (57)	17 (8)	N.A.
Oral glucocorticoids	161 (11)	139 (14)	17 (7)	5 (2)	2 (0.4)
TNF inhibitor	563 (39)	336 (34)	121 (46)	106 (49)	N.A.
IL-6 inhibitor	19 (1)	19 (2)	0	0	N.A.
IL-17 inhibitor	17 (1)	2 (0.2)	7 (3)	8 (4)	N.A.

participants completed the first online questionnaire of the study. Amongst others, information on demographic data, including CV comorbidities and risk factors, and medication use was collected. The baseline characteristics and prevalence of CVD were compared between RA, PsA or AS and healthy controls.

Results: In total, 1455 consecutive patients with an inflammatory rheumatic disease (979 RA patients, 261 PsA patients and 215 AS patients), and 414 healthy controls completed the first questionnaire, as shown in table 1. CV comorbidities were more frequently reported in RA, PsA and AS patients compared to healthy controls; 107 (11%), 28 (11%) and 22 (10%) compared to 30 (7%), respectively. Unadjusted odds ratios with corresponding 95%-confidence intervals for patients with RA, PsA and AS compared to controls were 1.57 (1.03-2.40), 1.54 (0.90-2.64) and 1.46 (0.82-2.60).

Conclusion: We demonstrated that the prevalence of CVD is approximately 1.5 times higher in patients with rheumatic diseases compared to healthy controls (11% vs. 7%, respectively). This corresponds with previous research, although the reported prevalence of CVD in PsA and AS patients is even higher compared to prior studies. This suggests that the CVD risk of patients with rheumatic diseases is still elevated in 2020 compared to the general population, despite the improved management of rheumatic disease activity. Therefore, adequate and timely treatment of CV risk factors remains relevant, not only in patients with RA, but in patients other rheumatic diseases as well.

Disclosure: R. Raadsen, None; **F. Hooijberg**, None; **L. Boekel**, None; **E. Vogelzang**, None; **G. Wolbink**, None; **W. Lems**, Amgen, 6, UCB, 6, Lilly, 6, Merck, 6, Pfizer, 6, Galapagos, 6; **A. van Kuijk**, None; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5.

Abstract Number: 0287

20 Years Follow-up of Cardiovascular Event Risk in Rheumatoid Arthritis Compared to Diabetes

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatoid arthritis have an increased risk for developing cardiovascular diseases (CVD) compared to the general population, similar to the CVD risk in patients with diabetes mellitus (DM). However, there are no controlled studies investigating the incidence of cardiovascular (CV) events in RA patients with follow up of more than 20 years.

The objectives of the current study were to investigate the incidence rates of CV events in a long-term follow up cohort of RA patients, and to compare these to a similar cohort representing the general population, ie. The Hoorn study.

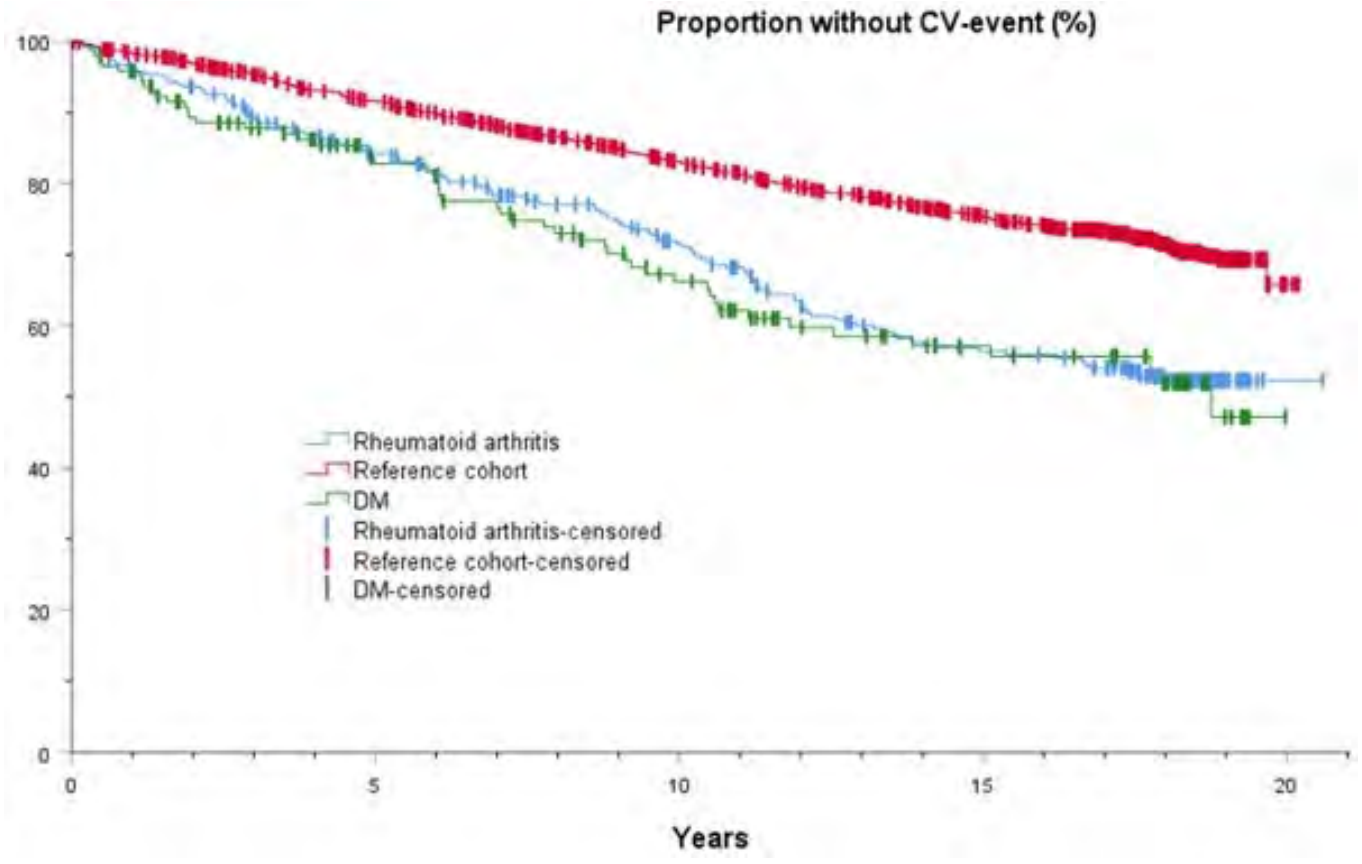

Figure 1. Cardiovascular event-free survival.

Methods: The CARRÉ study is an ongoing prospective cohort study, which started in 2001, investigating CV mortality and morbidity in 353 randomly selected patients with RA. Primary endpoints, i.e. verified medical history of coronary, cerebral or peripheral arterial disease, were determined at baseline, and after three, ten, fifteen and twenty years of follow up. Patients were censored at the date of an experienced CV event or their death. Incidence density rates per 100 patient years were calculated. Data were compared to results from the Hoorn study, a Dutch cohort study of glucose metabolism and other CV risk factors that began in 1989. All participants were subject to an extensive and repeated CV screening program similar to that used in the CARRÉ study. 1.356 nondiabetic controls and 144 patients with DM were used in the comparison.

Results: During follow up, 122 (35%) of RA patients developed a CV event, compared to 353 (26%) of the general population and 53 (37%) of the DM patients. The incidence rate of CV events in RA patients was 3.1 per 100 patient years, with 3.915 years at risk, compared to 1.9 per 100 patient years in the general population and 3.9 per 100 patient years in the DM patients, with 18.791 and 1.374 years at risk, respectively. CV event-free survival is shown in figure 1.

Conclusion: The incidence rate of CV events in RA patients has during 20 years remained consistently higher compared to the general population. The rate of CV events in RA patients has remained the same, despite better control of inflammation, suggesting under-treatment of "traditional" CV risk factors. This again emphasizes the need for timely CVD-risk screening and management

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Disclosure: R. Raadsen, None; **R. Agca**, None; **A. Voskuyl**, Gsk, 1, Boeringher ingelheim, 1, 5; **M. Boers**, BMS, 2, Pfizer, 2, GSK, 2, Novartis, 2; **W. Lems**, Amgen, 6, UCB, 6, Lilly, 6, Merck, 6, Pfizer, 6, Galapagos, 6; **A. van Kuijk**, None; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5.

Abstract Number: 0288

Demographic, Lifestyle, and Clinical Risk Factors for Rheumatoid Arthritis-Associated Bronchiectasis: Role of RA-related Autoantibodies

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Bronchiectasis is a known extra-articular manifestation of rheumatoid arthritis (RA) characterized by bronchial damage and excessive mucus production that predispose patients to risk of serious infection and increased mortality. Traction bronchiectasis is a consequence of architectural distortion from RA-associated interstitial lung disease (RA-ILD), but little is known about risk factors for isolated RA-associated bronchiectasis (RA-BR) that occurs independently of RA-ILD. We investigated factors associated with isolated RA-BR among RA patients.

Table 1: Characteristics of RA bronchiectasis cases and controls

Characteristic	Isolated RA-bronchiectasis cases (n=52)	RA controls without lung disease (n=311)	p-value
Demographics			
Female sex (n, %)	45 (86.5%)	236 (75.9%)	0.09
White (n, %)	46 (88.5%)	269 (86.5%)	0.70
Lifestyle			
Smoking status (n, %)			0.82
Never smoker (n, %)	24 (46.2%)	139 (44.7%)	
Past smoker (n, %)	25 (48.1%)	146 (47.0%)	
Current smoker (n, %)	3 (5.8%)	26 (8.4%)	
Smoking pack-years (median and IQR)	0.0 (0.0, 15.0)	0.5 (0.0, 15.0)	0.60
BMI category (n, %)			**0.02**
Underweight	5 (9.6%)	12 (3.9%)	
Normal	20 (38.5%)	83 (26.7%)	
Overweight	17 (32.7%)	95 (30.6%)	
Obese	10 (19.2%)	121 (38.9%)	
BMI (kg/m^2, median and IQR)	25.2 (22.6, 28.4)	28.1 (24.1, 33.1)	**0.001**
RA clinical factors			
Age at RA diagnosis (years, median and IQR)	53.5 (43.0, 62.5)	52.0 (41.0, 59.0)	0.26
RA duration (years, median (IQR))	11.4 (2.7, 20.3)	6.4 (1.5, 14.8)	0.06
Seropositive RA (n, %)	45 (86.5%)	178 (57.2%)	**<0.0001**
RF+ (n, %)	39 (75.0%)	148 (47.6%)	**0.0001**
RF level (-fold above ULN, median and IQR)	5.3 (1.5, 24.3)	1.0 (1.0, 5.9)	**<0.0001**
CCP+ (n, %)	32 (61.5%)	127 (40.8%)	**0.002**
CCP level (-fold above ULN, median and IQR)	9.3 (0.8, 25.7)	0.78 (0.3, 12.3)	**0.003**

BMI = body mass index; CCP = cyclic citrullinated peptide); IQR = interquartile range; RA = rheumatoid arthritis; RF = rheumatoid factor; ULN = upper limit of normal

Table 2: Associations of demographic, lifestyle, and clinical factors with isolated bronchiectasis in rheumatoid arthritis (n=363)

Characteristic	Multivariable* OR for isolated RA-BR (95%CI)	p-value
Demographics		
Male	1.00	Ref
Female	0.59 (0.24-1.42)	0.24
White	1.00	Ref
Non-White	0.99 (0.37-2.66)	0.99
Lifestyle		
Never smoker	1.00	Ref
Past smoker	0.93 (0.21-4.07)	0.92
Current smoker	0.84 (0.40-1.78)	0.65
Smoking pack-years (per unit)	0.99 (0.97-1.01)	0.44
BMI (per kg/m^2)	**0.93 (0.88-0.99)**	**0.02**
RA clinical factors		
Age at RA diagnosis (per 10 years)	**1.46 (1.07-1.98)**	**0.02**
RA duration (per year)	**1.04 (1.00-1.08)**	**0.04**
Seronegative RA	1.00	Ref
Seropositive RA	**4.40 (1.87-10.35)**	**0.0007**

*Mutually adjusted for all covariates listed.
BMI = body mass index, RA = rheumatoid arthritis

Table 3: Associations of RA-related autoantibodies with isolated bronchiectasis in rheumatoid arthritis (n=363)

RA-related autoantibody status	Multivariable* OR for isolated RA-BR (95%CI)	p-value
RF negative	1.00	Ref
RF positive (>1x ULN)	**4.32 (2.01-9.28)**	**0.0002**
RF negative	1.00	Ref
RF low-positive (>1-3x ULN)	2.02 (0.67-6.06)	0.21
RF high-positive (>3x ULN)	**5.71 (2.59-12.60)**	**<0.0001**
CCP negative	1.00	Ref
CCP positive (>1x ULN)	**3.17 (1.49-6.72)**	**0.003**
CCP negative	1.00	Ref
CCP low-positive (>1-3x ULN)	2.24 (0.52-9.61)	0.28
CCP high-positive (>3x ULN)	**3.21 (1.50-6.88)**	**0.003**

*Adjusted for age, sex, race, RA duration, smoking status, pack-years, and body mass index
BR = bronchiectasis; CCP = cyclic citrullinated peptide; CI = confidence interval; OR = odds ratio; RA = rheumatoid arthritis; RF = rheumatoid factor; ULN = upper limit of normal

Methods: We performed a case-control study using a large institutional biobank and research data repository that recruited patients from clinical sites throughout a multi-hospital healthcare system in New England. Patients with RA were identified using a previously described algorithm and confirmed by medical record review. All patients with RA who had chest computed tomography (CT) imaging, lung biopsy, or autopsy data were reviewed for RA-related lung disease. For each patient, the CT chest imaging performed closest to enrollment was independently reviewed by two expert radiologists and scored for the presence of RA-ILD and interstitial lung abnormalities. Cases of RA-BR were confirmed by review of clinical records and CT scan report, and isolated RA-BR was defined as clinical evidence of bronchiectasis with no evidence of RA-ILD or interstitial lung abnormalities on expert radiology review. Controls had RA but no RA-related lung disease on expert review of CT chest imaging. Covariate data were obtained through survey enrollment and medical record review. The associations between demographic, lifestyle, and clinical factors and RA-BR were examined using multivariable logistic regression.

Results: We identified 52 isolated RA-BR cases and 311 RA controls without RA-related lung disease. There was no significant difference in age between RA-BR cases and controls (median 53.5 vs. 52.0 years, p=0.26); 86.5% of RA-BR cases and 75.9% of controls were female (p=0.09). The median body mass index (BMI) was lower (25.2 kg/m^2, IQR 22.6, 28.4) in RA-BR cases than controls (28.1 kg/m^2, IQR 24.1-33.1; p=0.001). There was a greater proportion of seropositive patients among RA-BR cases (86.5%) than in the control group (57.2%) (p< 0.0001). Seropositive RA had multivariable OR for RA-BR of 4.40 (95%CI 1.87-10.35) compared to seronegative RA. Older age and longer RA duration were each associated with RA-BR (OR 1.46 per decade [95%CI 1.07-1.98], and OR 1.04 per year [95%CI 1.00-1.08], respectively). There was no association of smoking with RA-BR. Patients with high-positive RF had OR for RA-BR of 5.71 (95%CI 2.59-12.60). High-positive CCP was also associated with RA-BR (OR 3.21, 95%CI 1.50-6.88).

Conclusion: We identified seropositivity, older age at RA onset, longer RA duration, and lower BMI as potential novel risk factors for isolated bronchiectasis in RA not due to RA-ILD. High-positive RF and CCP were each strongly associated with RA-BR, suggesting a pathogenic link between RA-related autoantibodies and airway damage in bronchiectasis.

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Abstract Number: 0289

Developing a Score to Predict Preclinical Interstitial Lung Disease in Patients with Rheumatoid Arthritis – a Cross-Sectional Study from the ESPOIR Cohort

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) can be detected in 20% to 60% of patients with rheumatoid arthritis (RA) on high-resolution computed-tomography (HRCT) chest scan and is clinically significant in near 10%. Despite a high morbi-mortality rate, there are no definite strategy for preclinical ILD screening in patients with RA.

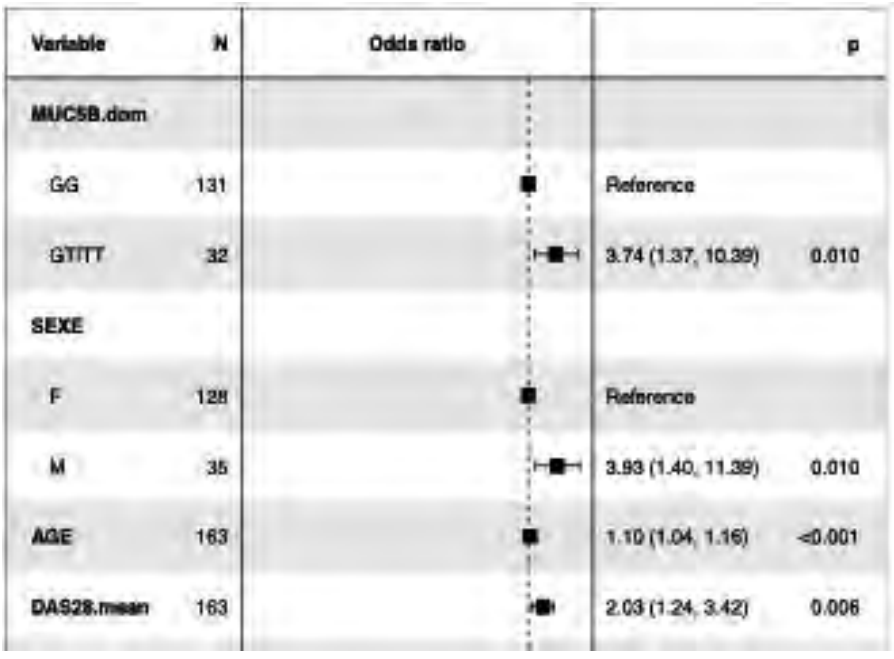

Figure 1. Predictors of ILD occurrence after at least 10 years-follow-up.

To date, several factors have been reported to increase the risk of RA-ILD occurrence (*i.e.* older age at RA onset, ACPA positivity, male sex, RA disease activity, the *MUC5B* rs35705950 promoter variant...). However, none of these risk factors has been validated in a prospective cohort. The ESPOIR prospective cohort includes patients with recent arthritis (less than 6 months) and a definite or probable diagnosis of RA. The objective of our study was to develop and replicate a predictive score that could identify patients with preclinical RA-ILD.

Methods: An ILD detection by chest HRCT scan was systematically offered to every patient with definite RA after at least 10 years-follow-up. Potential predictors of ILD were prospectively collected from baseline to the date of the HRCT scan, and all included patients were genotyped for *MUC5B* rs35705950. A logistic model was used to identify independent predictors for the occurrence of ILD on HRCT scans. A predictive score for preclinical ILD occurrence was developed based on the identified predictors. The score was replicated in an independent population of patients with RA without pulmonary symptoms investigated with chest HRCT.

Results: 163 RA patients according to 2010 ACR/EULAR classification criteria, none of whom had pulmonary symptoms, were investigated with a chest HRCT scan in the ESPOIR cohort (128 women (78.5%), mean RA duration 13.7 ± 1.1 years, age at inclusion 47.6 y/o ± 10.4, mean disease activity score [DAS]-28 during follow up was 3.1 ± 1.0). ILD was detected in 31 patients (19.0%). After logistic regression, independent predictors for preclinical RA-ILD were male sex (OR=3.9 CI $_{95\%}$ [1.4-11.4]), older age at RA onset (OR=1.1 per year CI $_{95\%}$ [1.0-1.2]), mean DAS-28 score during the follow-up (OR=2.0 CI $_{95\%}$ [1.2-3.4]) and *MUC5B* rs35705950 T risk allele (OR=3.7 CI $_{95\%}$ [1.4-10.4]) (Figure 1). The logistic model could predict preclinical ILD occurrence with an AUC=0.82 CI $_{95\%}$ (0.72-0.91). A predictive score for preclinical RA-ILD based on the 4 identified predictive risk factors was developed (Sensitivity [Se] 80%, Specificity [Sp] 56%). The score was replicated in an independent population of 89 RA patients investigated with chest HRCT scan. 15 patients (16.9%) had preclinical RA-ILD. The score could predict RA-ILD in 13 patients (Se 86.7%, Sp 40.5%, negative predictive value 93.8%, positive predictive value 22.3%).

Conclusion: In this study, we developed and replicated a predictive score for preclinical RA-ILD that could help physicians identifying patients with RA in whom a HRCT scan should be performed.

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Abstract Number: 0290

Prevalence and Predictors of Mortality in Rheumatoid Arthritis-Related Lung Disease: Results from a Single Center Study

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SESSION INFORMATION

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Background/Purpose: Rheumatoid arthritis-related lung disease (RA-LD) is a common manifestation of rheumatoid arthritis (RA) and associated with excess mortality. Many studies to date were focused on RA-associated interstitial lung disease (RA-ILD). There are few studies reporting the whole lung manifestations of RA. In this study, we aimed to determine the prevalence of RA-LD and to assess the predictors of mortality in RA-LD patients.

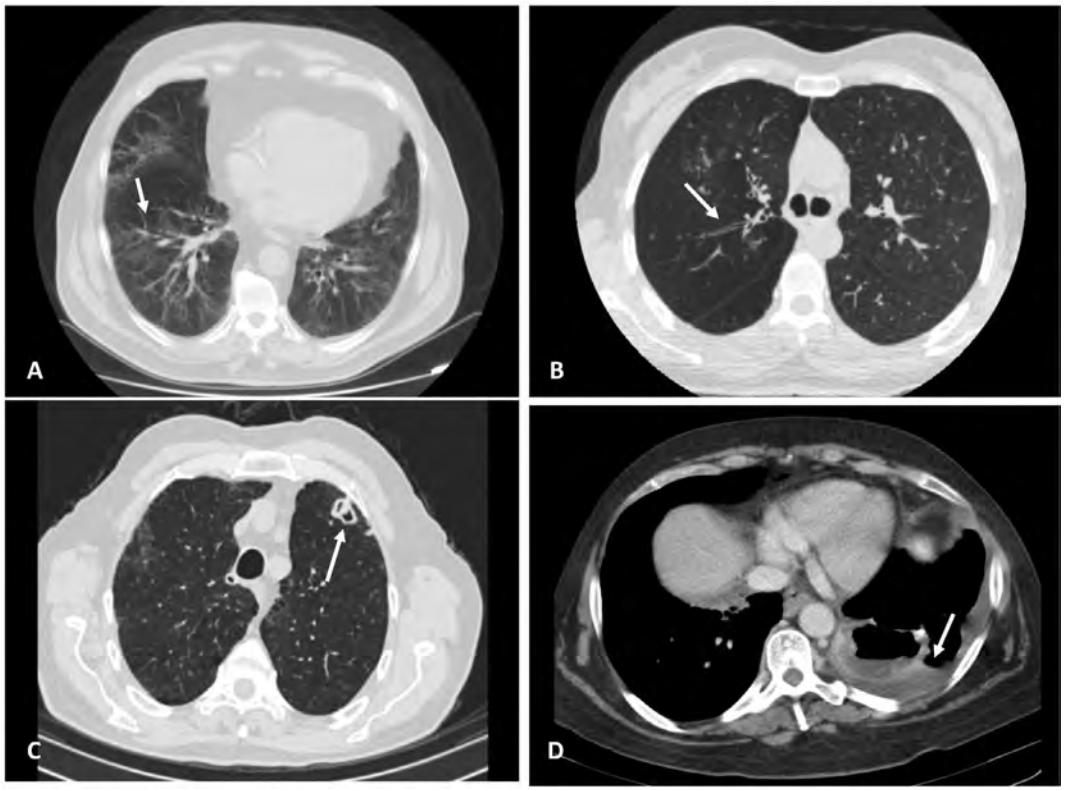

Figure 1. Images of different RA-LD subtypes. Interstitial lung disease with a pattern of nonspecific interstitial pneumonia (A), airway disease presenting with tubular bronchiectasis (B), necrobiotic cavitary rheumatoid nodule (C), pleural effusion (D).

Table 1. Characteristics of patients with different RA-LD subtypes

	RA-ILD (n= 107)	AD (n=119)	RA-PN (n= 70)	RA-PE (n= 31)
Age at RA diagnosis, mean (SD)	54.2 (13.0)	51.9 (12.9)	51.5 (11.4)	49.2 (11.8)
Age at RA-LD diagnosis, mean (SD)	61.6 (10.4)	61.1 (9.7)	59.1 (9.2)	57.0 (10.8)
Male sex, n(%)	54 (50.5)	28 (23.5)	36 (51.4)	20 (64.5)
Smoking, n (%)	52/96 (54.2)	35/96 (36.5)	43/67 (64.2)	21/29 (72.4)
Seropositivity, n (%)	95 (88.8)	103 (86.6)	66 (94.3)	30 (96.8)
CRP (mg/L), median (Q1-Q3)	50.8 (66.5)	41.9 (59.8)	45.3 (52.7)	85.2 (96.3)
High CRP (>5 mg/L), n (%)	99 (92.5)	105 (88.2)	62 (88.6)	29 (93.5)
ESR (mm/h), median (Q1-Q3)	41.9 (26.9)	40.2 (27.5)	42.6 (29.2)	54.3 (37.4)
High ESR (>20 mm/hour), n (%)	84 (78.5)	85 (71.4)	51 (72.9)	25 (80.6)
Antinuclear antibody, n (%)	46/95 (48.4)	57/111(51.4)	26/63 (41.3)	13/30 (43.3)
Erosions on X-ray, n (%)	61 (57.0)	65 (54.6)	37 (52.9)	15 (48.4)
Subcutaneous rheumatoid nodules, n (%)	18 (16.8)	4 (3.4)	10 (14.3)	4 (12.9)
Secondary Sjögren's syndrome, n (%)	8 (7.5)	11 (9.2)	4 (5.7)	1 (3.2)
RA-ILD, n (%)	-	20 (16.8)	28 (40.0)	9 (29.0)
AD, n (%)	20 (18.7)	-	13 (18.6)	5 (16.1)
PN, n (%)	28 (26.2)	13 (10.9)	-	12 (38.7)
RA-PE, n (%)	9 (8.4)	5 (4.2)	12 (17.1)	-
All cause pleural effusion, n (%)	14 (13.1)	16 (13.4)	15 (21.4)	-
2+ subtypes, n (%)	45 (42.1)	28 (23.5)	43 (61.4)	19 (61.3)
Emphysema, n (%)	50 (46.7)	23 (19.3)	30 (42.9)	18 (58.1)
CVD, n (%)	25 (23.4)	21 (17.6)	12 (17.1)	6 (19.4)
Malignancy, n (%)	11 (10.3)	5 (4.2)	4 (5.7)	3 (9.7)
Need for long-term oxygen therapy, n (%)	12 (11.2)	5 (4.2)	2 (2.9)	3 (9.7)
Death, n (%)	30 (28.0)	22 (18.5)	12 (17.1)	8 (25.8)

RA-LD= rheumatoid arthritis-related lung disease, RA-ILD= rheumatoid arthritis-related interstitial lung disease, AD= airway disease, RA-PN= rheumatoid arthritis-related pulmonary nodules, RA-PE= rheumatoid arthritis-related pleural effusion, RA= rheumatoid arthritis, CRP= C reactive protein, ESR= erythrocyte sedimentation rate, CVD= cardiovascular disease

Methods: Patients who attended our rheumatology clinic between January 2010-December 2020 and fulfilled 2010 ACR/EULAR classification criteria for RA were retrospectively evaluated. Among them, patients with abnormal computed tomography of the chest (chest-CT) were scrutinized. RA-LD was defined as the existence of RA-ILD, airway disease (AD), rheumatoid pulmonary nodules (RA-PN) or RA-related pleural effusion (RA-PE). Thoracentesis or lung biopsy results were also used to confirm the existence of RA-LD. The patient data was recorded for each subtype of RA-LD. The date of RA-LD diagnosis was considered the date of the first chest-CT detecting the pathology. To assess the predictors associated with all-cause mortality, logistic regression analysis was performed.

Table 2. Predictors of mortality in RA-LD patients

	Univariate OR (95% CI)	p	Multivariable OR (95% CI)	p
Age at RA-LD diagnosis	1.07 (1.03-1.11)	**<0.001**	1.04 (1.01-1.09)	**0.020**
Male sex	0.92 (0.49-1.71)	0.784	0.72 (0.34-1.52)	0.393
Smoking	0.72 (0.37-1.41)	0.342		
Seropositivity	1.86 (0.62-5.58)	0.267		
RA-ILD (yes vs no)	2.20 (1.18-4.08)	**0.013**	2.28 (1.12-4.64)	**0.023**
All cause pleural effusion	2.22 (1.09-4.53)	**0.028**	3.30 (1.43-7.62)	**0.005**
bDMARDS or tsDMARDs usage	0.42 (0.21-0.84)	**0.015**	0.55 (0.26-1.19)	0.131
Methotrexate usage	0.33 (0.17-0.64)	**0.001**	0.40 (0.19-0.84)	**0.016**
CVD (yes vs no)	2.19 (1.06-4.53)	**0.035**	1.41 (0.61-3.26)	0.420

RA-LD= rheumatoid arthritis-related lung disease, RA-ILD= rheumatoid arthritis-related interstitial lung disease, bDMARDS= biologic disease-modifying anti-rheumatic drugs, tsDMARDs= targeted synthetic disease-modifying anti-rheumatic drugs, CVD= cardiovascular disease

Results: Among 9756 RA patients, 253 (2.6%) patients (38.7% male; mean age at RA and RA-LD diagnoses 52.1 ± 12.4 and 59.9 ± 9.8 years, respectively) had RA-LD. AD was the most common subtype of RA-LD and detected in 119 (47.0%) patients followed by 107 (42.3%) patients with RA-ILD, 70 (27.7%) patients with RA-PN and 31 (12.3%) patients with RA-PE (Figure 1). The characteristics of patients with each subtype are shown in Table 1. Sixty-one (24.1%) patients had 2 or more RA-LD subtypes during their follow-up. After a median of 3.9 years (IQR 5.1), 52 (20.6%) patients died and the 5-year survival rate was 81.8%. In multivariable logistic regression analysis, the existence of RA-ILD, pleural effusion and older age at RA-LD diagnosis were positively associated with higher mortality (odds ratios (OR) were 2.28, 3.30 and 1.04, respectively), whereas methotrexate usage was protective (OR 0.40) (Table 2).

Conclusion: In this single center retrospective study, we showed that the prevalence and mortality of RA-LD was approximately 3% and 20%, respectively. As well as RA-ILD and older age, which are known risk factors, having pleural effusion was also related to mortality. Patients, who received methotrexate, had low mortality rates.

Disclosure: D. Sahin Eroglu, None; **A. Colaklar**, None; **S. Baysal**, None; **M. Torgutalp**, None; **A. Baygul**, None; **S. Sezer**, None; **E. Aydemir Guloksuz**, None; **M. Yuksel**, None; **M. Yayla**, None; **E. Uslu yurteri**, None; **C. Uzun**, None; **O. Ozdemir kumbasar**, None; **M. Turgay**, None; **K. Gulay**, None; **A. Ates**, None.

Abstract Number: 0291

IgA Anti-Cyclic Citrullinated Peptide Antibodies in Bronchoalveolar Lavage Fluid from Patients with Idiopathic Pulmonary Fibrosis Are Associated with Reduced Mortality

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Idiopathic pulmonary fibrosis (IPF) is a form of interstitial lung disease (ILD) that shares many clinical features with rheumatoid arthritis (RA) associated ILD. Our published data found that serum RA-related antibodies, particularly IgA antibodies to CCP, were significantly more prevalent in IPF patients (23%) compared to population controls (6%). However, the mechanisms that lead to anti-CCP generation in IPF are unknown. Of interest, neutrophil extracellular trap (NET) formation externalizes citrullinated proteins and has been implicated in the generation of anti-CCP in RA, including in the lung. The goal of this study was to explore relationships between anti-CCP, markers of NET formation in the lung and outcomes in IPF.

Methods: We included 176 IPF patients from National Jewish Health who had stored bronchoalveolar lavage fluid (BALF). BALF was analyzed for anti-CCP-IgA (in house ELISA), total protein (ELISA) and markers of NETs (neutro-

phil elastase (NE), ELISA, and double stranded (ds)DNA, fluorometric assay). All CCP, NE and dsDNA values were adjusted for total protein level. Date of death was determined by the CDC's National Death Index and mortality was analyzed by Spearman's correlation using days from BALF collection to death within 5 years of BALF collection and cox proportional hazards model. The majority of patients (n=169) also had pulmonary function testing (PFTs), including % predicted forced vital capacity (% FVC) and % predicted diffusion capacity of carbon monoxide (% DLCO), performed within 3 months of BALF collection.

Results: Clinical characteristics of the cohort are listed in Table 1. Overall, we found a significant association between higher levels of BAL anti-CCP and lower 5-year mortality (Figure 1A). In contrast, we found a significant association between higher levels of dsDNA and NE and higher 5-year mortality (Figure 1B-C). Of interest, when IPF patients were stratified by BALF anti-CCP level, the 'Low BALF anti-CCP' group had a significant correlation between markers of NETosis and clinical variables including: 5-year mortality, %FVC and %DLCO while the 'High BALF anti-CCP' group had no association between NETosis markers and these outcomes (Table 2). There was also a significant positive correlation between BALF levels of anti-CCP and markers of NETs (for NE, r=0.20, p=0.010; for dsDNA, r=0.27, p< 0.001).

Conclusion: This is the first study to report anti-CCP-IgA levels in the lung of IPF patients and identify an association with improved mortality. We also found a strong association between anti-CCP and markers of NETs in the lung, suggesting that NETs may lead to anti-CCP generation in the lung in IPF, similar to reports in RA. Based on published studies in IPF that associate BALF neutrophilia with increased mortality, it was not surprising that NET markers in BALF were associated with mortality in our study. However, it was of interest that this association was markedly blunted in IPF patients with the highest BALF anti-CCP levels, suggesting that anti-CCP-IgA may be protective against the detrimental effects of neutrophils in the lung in IPF. Future studies are needed to understand the mechanisms by which such a protective effect in the lung could occur.

Disclosure: S. Matson, None; **C. Cephers**, None; **T. Wilson**, None; **V. Minarchick**, None; **K. Brown**, None; **J. Solomon**, None; **K. Demoruelle**, Pfizer, 5.

Abstract Number: 0292

Suppressed Paraoxonase-1 Activity and Elevated Oxylipins Associate with the Presence of Small Airways Disease in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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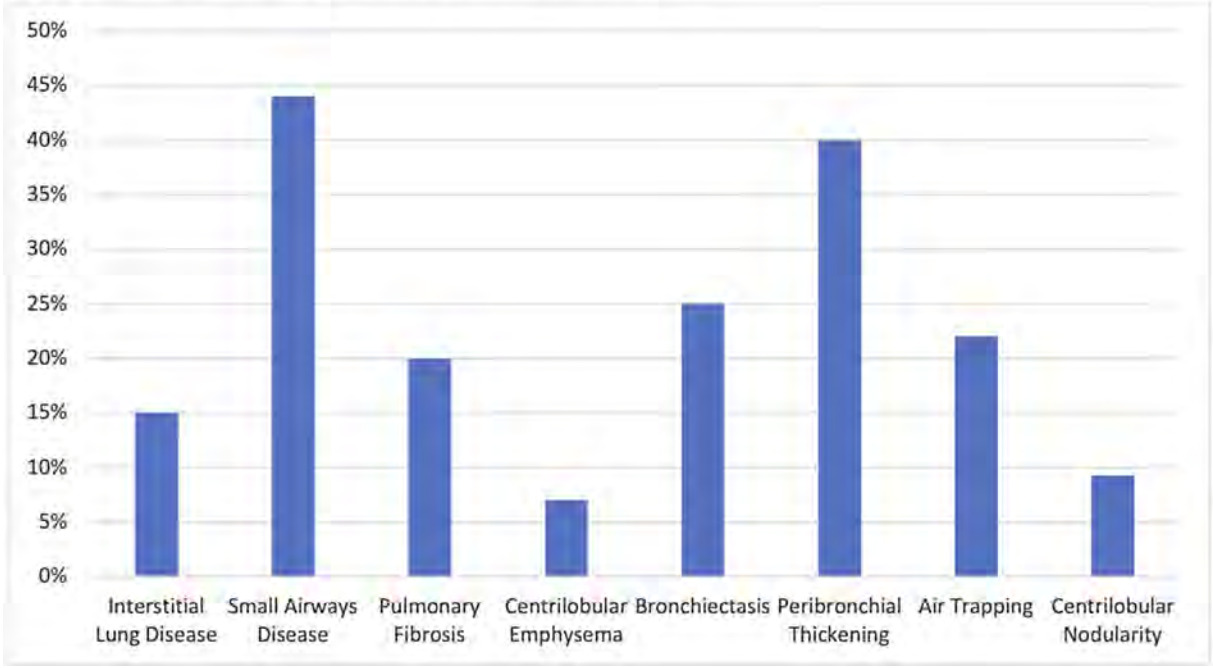
Background/Purpose: Lung disease in patients with rheumatoid arthritis (RA) is common and associates with significantly increased morbidity and mortality. Oxidative stress plays an important role in the inflammatory responses in airway diseases such as asthma and COPD, but has not been fully investigated in RA-associated lung disease (RA-LD). In the current work, we evaluated associations of the biochemical and genetic determinants of the anti-oxidant

Figure 1: Radiographic Lung Disease in an RA Patient Cohort



HDL-associated protein, paraoxonase 1 (PON-1), and measures of systemic oxidative stress with the presence of RA-LD in a longitudinal RA cohort.

Methods: This study was conducted as a retrospective chart review of a longitudinal single-center cohort of 250 RA patients. All RA patients with an available computed tomographic (CT) scan of the chest were included in the analysis. Scans were reviewed by the interpreting radiologist for the presence of interstitial lung disease (ILD), bronchiectasis, pulmonary fibrosis, centrilobular emphysema, and small airways disease (SAD). SAD was defined by the presence of peribronchial thickening, air trapping, or centrilobular nodularity. PON-1 activity was measured by its lactonase, arylesterase, and paraoxonase activities, the PON-1 Q192R polymorphism, and total plasma oxylipins were measured as described previously (Sci Rep2020 Oct 8;10(1):16848, A&R 2013Nov:65(11):2765-72).

Results: Out of 250 RA patients, 108 (43.2%) had CT scans of the chest available for review. The distribution of lung disease involvement in the cohort (figure 1) included 48 patients (44.4%) with SAD and demonstrated peribronchial thickening in 43 (39.8%), air trapping in 24 (22.2%), and centrilobular nodules in 10 (9.3%). Patients with SAD demonstrated significantly lower PON-1 activity as measured by both arylesterase and lactonase activities and higher levels of several oxylipins compared to patients without SAD (Table 2). Lower PON-1 activities correlated with higher levels of 12-HETE, 15-HETE, and 20-OH LTB4 ($r = -0.2$- -0.3, $p < 0.05$). In multivariate logistic regression analyses controlling for known SAD risk factors (RA disease duration, age, sex, smoking, and obesity), lower lactonase and arylesterase activities of PON-1, and higher levels of 12-HETE and 15-HETE remained independently associated with the presence of SAD in RA patients. Such associations were not noted with other types of RA-LD (data not shown).

Conclusion: RA patients with radiographic evidence of SAD demonstrate significantly lower arylesterase and lactonase activities of PON-1 and higher levels of systemic oxidative stress measured by circulating oxylipins, including higher 12-HETE and 15-HETE, which correlated with reduced PON-1 activity. Future studies are warranted to evaluate the relationship of PON-1 and pro-inflammatory oxylipins to the pathogenesis of RA lung disease.

Table 1: Clinical and Laboratory Characteristics of RA Patients with and without Small Airways Disease

	Small Airways Disease Present (n=48, 44.4%)	Small Airways Disease Absent (n=60, 55.6%)
Age (years)	63.3±11.0	62.3±13.4
Female	39(81.3)	53(88.3)
Race- Caucasian	38(79.2)	45(75.0)
Ethnicity- Hispanic	10(20.8)	14(23.3)
BMI (kg/m^2)	29.6±8.3	28.6±6.5
RA disease duration prior to CT (years)	23.0±18.0	16.9±11.1
hsCRP (mg/L)	11.0±17.6	6.4±16.2
ESR (mm/hour)	29.3±22.1	27.0±20.7
Cardiovascular Risk Factors		
H/o Myocardial Infarction	2(5.1)	2(3.5)
H/o Cerebrovascular Accident	2(5.3)	2(3.7)
Hypertension	23(47.9)	29(48.3)
Diabetes	4(8.3)	9(15.0)
Current smoking use	3(8.1)	2(3.9)
Past smoking use	9(27.3)	13(26.5)
Total Cholesterol (mg/dL)	187.2±41.5	199.7±48.4
LDL Cholesterol (mg/dL)	107.5±31.9	108.9±43.4
HDL Cholesterol (mg/dL)	60.9±20.4	65.5±22.1
Triglycerides (mg/dL)	113.4±70.6	136.4±100.6
PON-1 Activity (U/ml)		
Arylesterase activity	**175.8±63.8***	213.4±78.5
Lactonase activity	**18.9±8.5***	23.7±12.4
Paraoxonase activity	470.4±461.5	443.2±303.0
PON-1 Q192R polymorphism		
QQ genotype	16(43.2)	21(56.8)
QR genotype	19(38.8)	30(61.2)
RR genotype	9(45.0)	11(55.0)
Oxylipins (ng/ml)		
20-OH LTB4	0.2±0.2	0.2±0.1
TXB2	21.4±26.7	17.1±20.3
PGE2	1.5±4.2	0.2±0.2
6t12eLTB4	2.6±6.1	1.3±0.2
LTB4	**1.2±3.9***	0.1±0.1
13-HODE	8.0±12.7	5.2±3.2
12-HODE	16.0±25.5	10.4±6.4
9-HODE	16.7±46.5	7.7±5.1
15-HETE	**5.5±10.9***	2.1±1.7
14sHDHA	36.9±34.6	28.8±27.4
11-HETE	4.3±13.8	0.9±0.9
12-HETE	**200.6±208.9***	119.6±117.8
5-HETE	48.5±192.7	1.7±1.2
5 oxo- HETE	2.0±7.2	0.2±0.1

Values are n(%) or mean±SD unless specified
*p<0.05

Table 2: Multivariate Stepwise Logistic Regression Analysis of Predictors of Small Airways Disease

Predictor	Odds Ratio (CI)	P value
Arylesterase Activity Model		
RA Disease Duration	1.03 (0.99-1.08)	0.07
Age (years)	1.01 (0.96-1.06)	0.68
Body Mass Index	1.02 (0.96-1.09)	0.60
Arylesterase Activity of PON1	**0.99 (0.98-0.99)**	**0.03**
Female Gender	0.63 (0.17-2.22)	0.47
Current Smoker	3.36 (0.46-29.65)	0.23
Lactonase Activity Model		
RA Disease Duration	1.03 (0.99-1.07)	0.16
Age (years)	1.01 (0.96-1.06)	0.70
Body Mass Index	1.02 (0.96-1.08)	0.59
Lactonase Activity of PON1	**0.95 (0.90-0.99)**	**0.03**
Female Gender	0.62 (0.18-2.15)	0.45
Current Smoker	3.41 (0.46-25.34)	0.23

CI = Confidence intervals. Note: Model covariates

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Abstract Number: 0293

Increased Prevalence of Scleroderma Specific Autoantibodies in Sero-positive Rheumatoid Arthritis with Lung Involvement

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To evaluate the prevalence of scleroderma (SSc) specific and anti-Ro52 autoantibodies in seropositive rheumatoid arthritis (RA) patients with lung involvement.

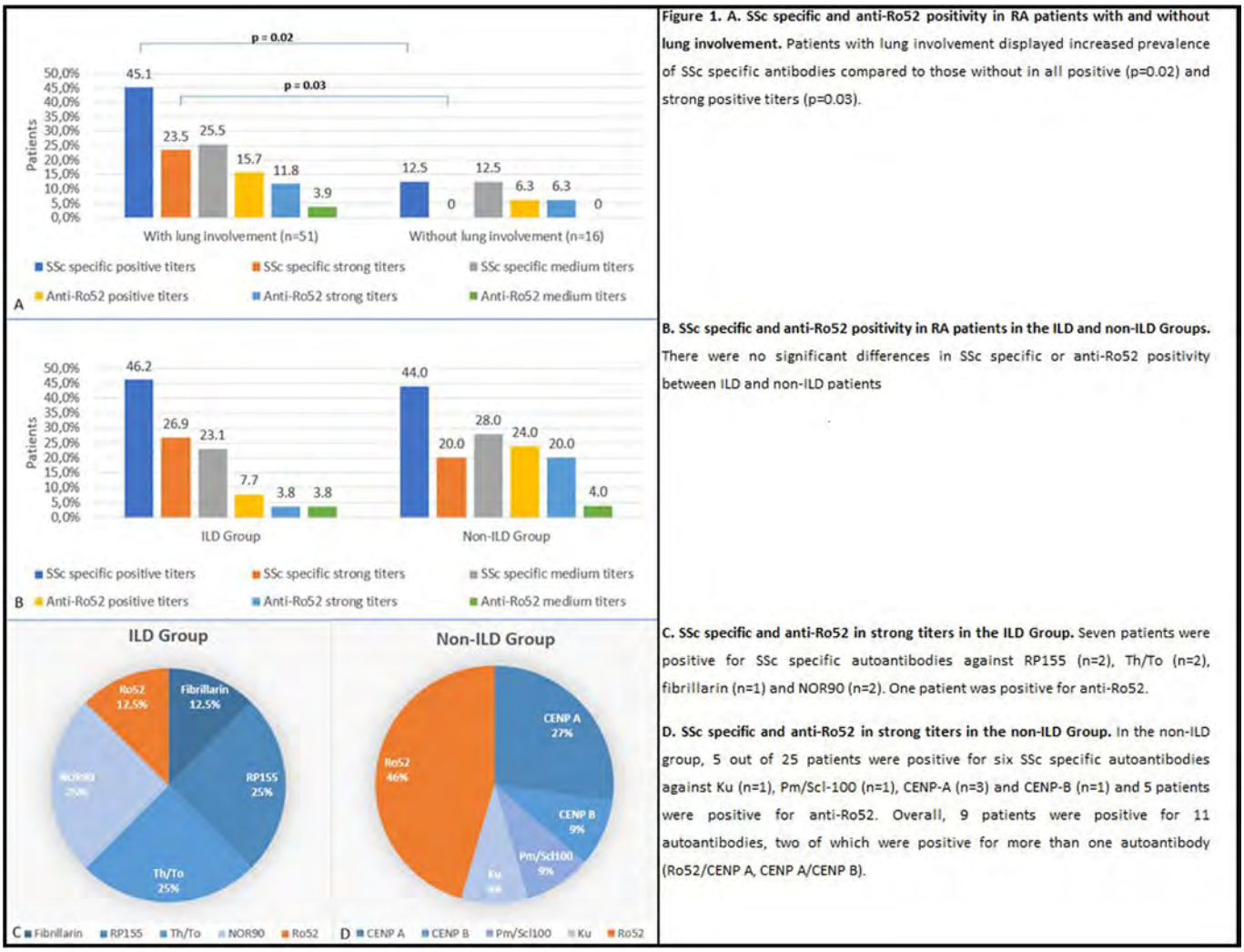

Figure 1. A. SSc specific and anti-Ro52 positivity in RA patients with and without lung involvement. Patients with lung involvement displayed increased prevalence of SSc specific antibodies compared to those without in all positive (p=0.02) and strong positive titers (p=0.03).

B. SSc specific and anti-Ro52 positivity in RA patients in the ILD and non-ILD Groups. There were no significant differences in SSc specific or anti-Ro52 positivity between ILD and non-ILD patients

C. SSc specific and anti-Ro52 in strong titers in the ILD Group. Seven patients were positive for SSc specific autoantibodies against RP155 (n=2), Th/To (n=2), fibrillarin (n=1) and NOR90 (n=2). One patient was positive for anti-Ro52.

D. SSc specific and anti-Ro52 in strong titers in the non-ILD Group. In the non-ILD group, 5 out of 25 patients were positive for six SSc specific autoantibodies against Ku (n=1), Pm/Scl-100 (n=1), CENP-A (n=3) and CENP-B (n=1) and 5 patients were positive for anti-Ro52. Overall, 9 patients were positive for 11 autoantibodies, two of which were positive for more than one autoantibody (Ro52/CENP A, CENP A/CENP B).

Figure 1. SSc-specific and anti-Ro52 antibodies in seropositive RA patients with different types of lung involvement.

Methods: Sera from 67 seropositive RA patients with available high-resolution computed tomography scans (HRCTs) were tested for the presence of SSc-specific and anti-Ro52 antibodies. According to the band intensity, samples were classified in those with medium and strong positive titers. Demographic, clinical, laboratory, imaging and pulmonary function data were recorded. 26 patients suffered from interstitial lung disease (ILD group), 25 had some other type of lung involvement (non-ILD group) and 16 had normal HRCTs (no-lung group).

Results: Autoantibody testing revealed a significantly higher prevalence of positive SSc-specific antibodies in patients with lung involvement compared to the no-lung group (45.1% vs 12.5%, p=0.02) (Figure 1A). Lung involvement was also associated with older age, male sex, heavier smoking, and increased white blood cell counts, CRP and RF values (Table 1). Prevalence of anti-Ro52 positivity was also higher in these patients, but no statistical significance was reached. ILD and non-ILD groups displayed a similar frequency (Figure 1B) but a distinct non-overlapping pattern of SSc-specific antibodies (in strong titers) against RP155, Th/To, fibrillarin and NOR90 autoantigens in the ILD group (Figure 1C) and towards Ku, Pm/Scl100, CENP-A/B in the non-ILD group (Figure 1D)

Table 1. Demographic, clinical, serological and laboratory features of seropositive RA patients with and without lung involvement

	Lung involvement Group (n=51)	No lung Group (n=16)	p value
Demographic Data			
Age of RA diagnosis (years) mean ± SD	52.5 ± 14.7	45.9 ± 14.8	0.16
Age at CT evaluation (years) mean ± SD	64.3 ± 9.7	57.8 ± 11.3	**0.04**
Disease Duration at time of CT evaluation (years) mean ± SD	11.9 ± 12.8	11.9 ± 9.8	0.81
Male Sex %	31.4	6.3	**0.04**
Smoking %	55.1	31.3	0.10
Pack-Years mean ± SD	26.1 ± 34.1	6.2 ± 14.4	**0.03**
Clinical characteristics			
DAS28 at first evaluation mean ± SD	5.4 ± 1.7	4.8 ± 1.4	0.19
DAS28 at CT evaluation mean ± SD	4.0 ± 2.0	3.5 ± 1.8	0.45
Respiratory Abnormalities %	78.7	36.4	**0.005**
Raynaud's Phenomenon %	28.6	28.6	1
Myalgia %	23.3	40	0.28
Muscle Weakness %	11.9	22.2	0.41
Dry Mouth %	39.1	53.8	0.34
Dry Eyes %	32.6	46.2	0.37
Photosensitivity %	7	16.7	0.30
Fever %	26.7	35.7	0.51
Rash %	15.9	7.7	0.45
Dysphagia %	4.8	0	0.48
Digital Ulcers %	2.3	0	0.59
Serological Findings			
RF titers (IU/mL) mean ± SD	314.7 ± 512.5	210.3 ± 477.5	**0.046**
RF positivity %	88.2	75	0.2
Anti-CCP titers (U/mL) mean ± SD	239.0 ± 245.5	173.0 ± 153.4	0.35
Anti-CCP positivity %	94	86.7	0.35
ANA positivity %	61.7	69.2	0.62
Anti-Ro positivity %	11.8	10	0.88
Anti-La positivity %	2.9	0	0.58
ANCA positivity %	5.9	0	0.80
Laboratory values			
WBC (cells/μL) ± SD	8819 ± 2962	7183 ± 1741	**0.04**
CPK (IU/L) ± SD	67 ± 40	84 ± 75	0.82
LDH (IU/L) ± SD	225 ± 74	250 ± 125	0.57
CRP (mg/dL) ± SD	2.0 ± 2.7	0.7 ± 0.7	**0.02**

Conclusion: Seropositive RA patients with lung involvement display several demographic, clinical and laboratory characteristics along with increased rates of SSc-specific autoantibodies. These data imply that seropositive RA patients with lung involvement probably represent a distinct overlap entity, requiring tailored diagnostic and therapeutic approaches.

Disclosure: V. Koulouri, None; **K. Tavernaraki**, None; **M. Giannelou**, None; **C. Mavragani**, None.

Abstract Number: 0294

Comparison of Factors Associated with CT-Scan Progression of Interstitial Lung Disease in Rheumatoid Arthritis and Idiopathic Pulmonary Fibrosis. Retrospective Multicenter Study of 144 Patients

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

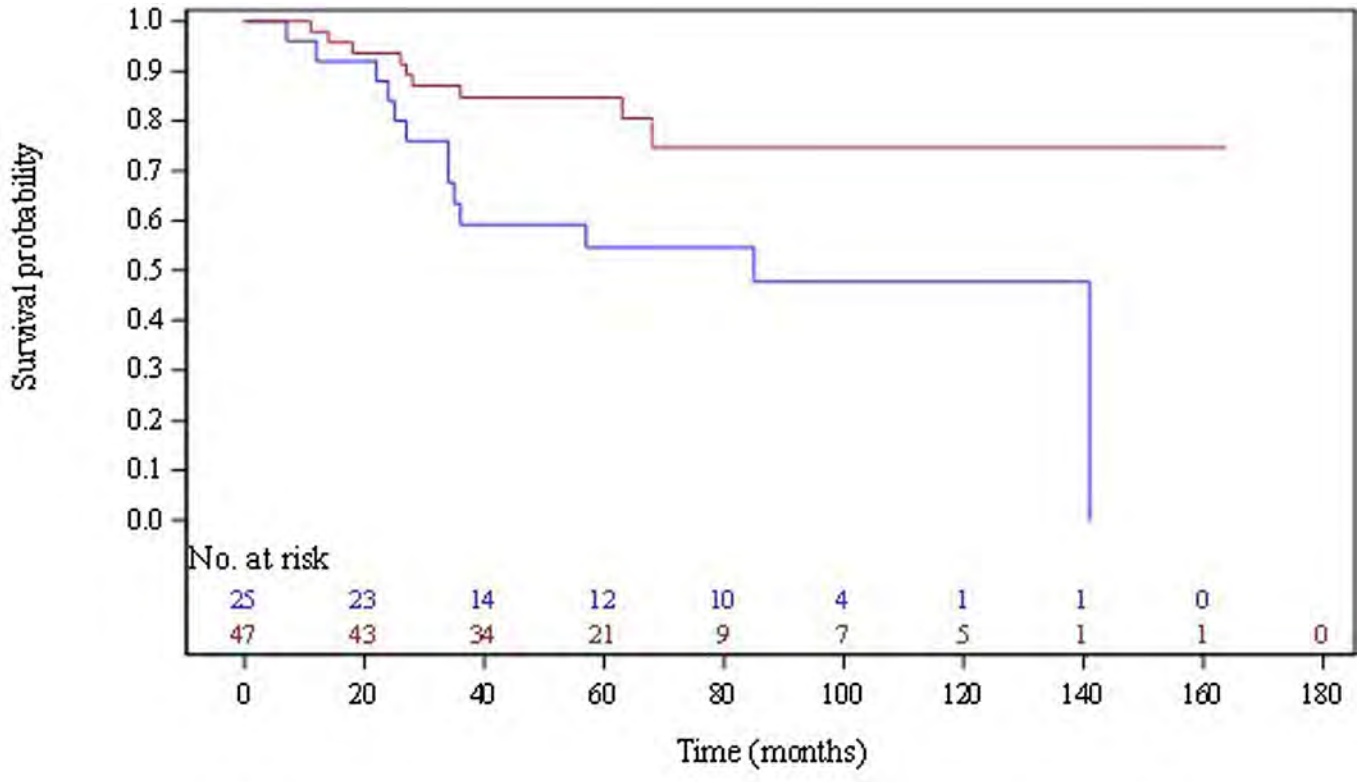
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

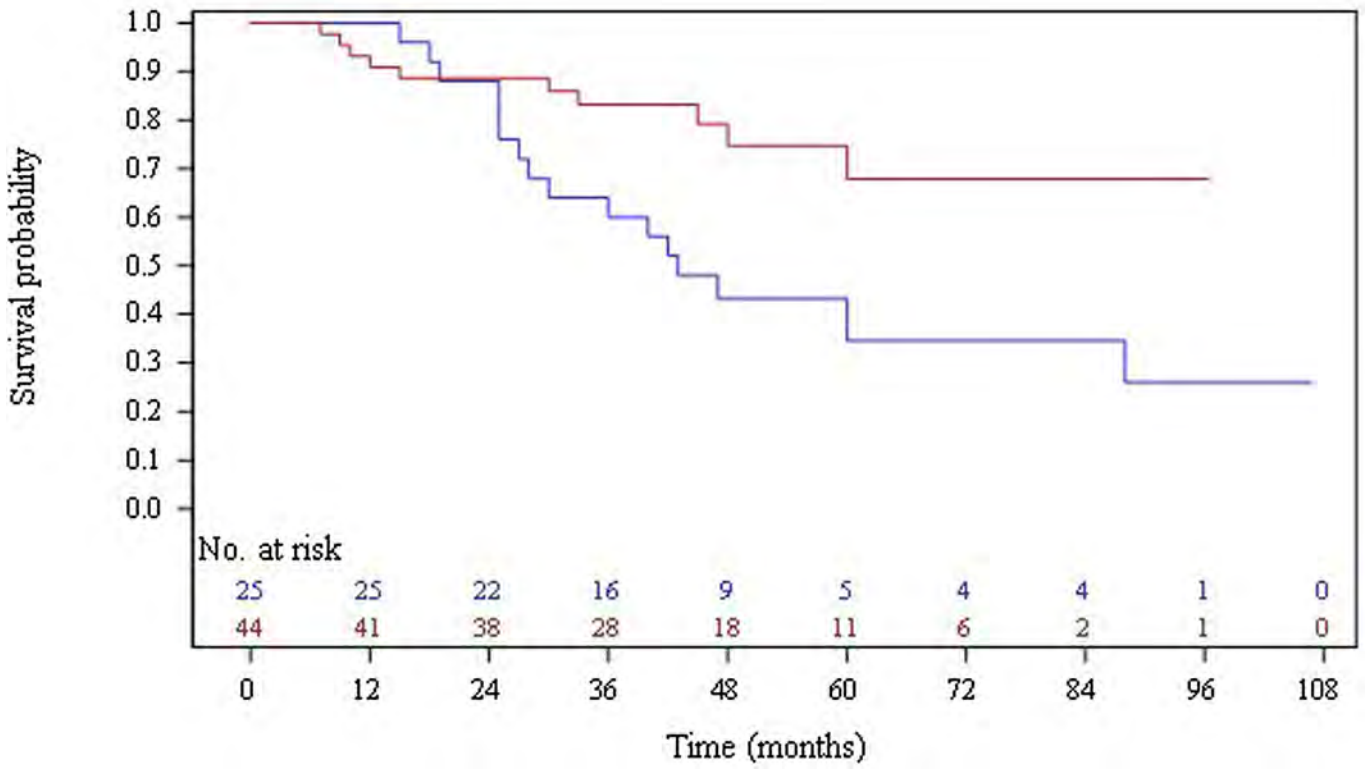
Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Compare factors associated with interstitial lung disease (ILD) progression determined on CT-scan analysis and survival in two distinct populations, patients with rheumatoid arthritis associated interstitial lung disease (RA-ILD) and patients with idiopathic pulmonary fibrosis (IPF).

Methods: RA and IPF patients with ILD confirmed by 2 CT-scans spaced from 6 or more months apart (T0: first CT chest scan describing ILD; Tx: last CT chest scan available) were consecutively included in this retrospective multicenter study from 2010 to 2020. CT-scans were blindly analyzed for each patient at T0 and Tx by 2 independent radiologists to determinate ILD pattern (definite usual interstitial pneumonia (UIP), probable UIP, indeterminate UIP, non-UIP) and progression during the follow-up (progressive or stable ILD) defined by the variation of the fibrosis





score. Characteristics of patients (demographic-clinical-biological findings, pulmonary function tests, and treatments exposure) at T0 and during the follow-up (T0-Tx) were analyzed as potential determinants of ILD progression through multivariable logistic regression analysis. Overall survival was analyzed using Kaplan-Meier method.

Results: 74 RA-ILD patients and 70 IPF patients were included. During a T0-Tx follow-up of 2.8 ± 2 years, ILD progression was identical in the two populations, of 36%. RA-ILD patients and IPF patients were comparable in terms of age, sex, BMI, smoking history, and severity of initial pulmonary function tests, but T0 CRP rate was higher in RA-ILD patients (29 ± 36mg/L vs 9 ± 35mg/L; p< 0.0001) and T0 CT damage was slightly more pronounced in RA-ILD patients (T0 fibrosis score=27% vs 21%; p=0.05). Multivariate analysis identified different risk factors for ILD progression in the 2 populations. A treatment by Methotrexate at ILD diagnosis was associated negatively with ILD progression in RA-ILD patients (OR=0.14 [0.04-0.52]; p=0.0031) while UIP pattern was positively associated with ILD progression (OR=12 [4.38; 39.85], p=0.0001). In IPF patients, pulmonary comorbidities (OR=8.4 [1.4; 51.4], p=0.02) and the need to oxygen therapy during T0-Tx (OR=5.2 [1.2-22.3], p=0.03) were poor prognosis factors. The follow-up to death or end of collection (July 2020) was longer in RA-ILD patients (5.1 years vs 3.8; p=0.001) but survival rate was not significantly different (31% in RA-ILD patients vs 38 % in IFP patients; HR=1.59 [0.89; 2.84], p=0.1) and better for stable ILD than for progressive ILD in both RA-ILD and IPF populations.

Conclusion: We did not identify any common risk factors for ILD progression in RA-ILD and IPF patients, but in both populations, about one third of patients had ILD progression and died.

Survival of RA-ILD population according to ILD progression. Red line represents patients without ILD progression (stable ILD). Blue line represents patients with ILD progression (progressive ILD). HR = 2.73 [1.16;6.42], p = 0.0239.

Survival of IPF population according to ILD progression. Red line represents patients without ILD progression (stable ILD). Blue line represents patients with ILD progression (progressive ILD). HR = 2.73 [1.23;6.06], p = 0.0136.

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Abstract Number: 0295

Weight History and Associations with Cardiovascular Risk in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Cardiovascular Pulmonary Disease (0268–0295)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiovascular disease (CVD) is the leading cause of mortality in rheumatoid arthritis (RA), but traditional CVD risk factors may not accurately characterize risk. For example, RA patients with a high body

Table 1. Patient characteristics at enrollment by weight loss category between age 30 and baseline

	Weight Loss Category (Between Age 30 and Baseline)				*p*-value
	>10% Weight Loss, *n*=903	5-10% Weight Loss, *n*=647	Stable Weight (<5% Weight Gain or Loss), *n*=2627	≥5% Weight Gain, *n*=11,666	
Age (years), mean (SD)	58.3 (11.3)	59.4 (11.5)	58.9 (11.2)	59.3 (9.9)	0.016
Female, %	83	74	76	84	<0.001
White, %	86	89	91	90	0.002
BMI at age 30, mean (SD)	32.0 (10.0)	26.7 (6.4)	24.4 (5.5)	23.9 (4.4)	<0.001
RA duration (years), median (IQR)	9.8 (4.4-18.7)	9.6 (3.9-18.6)	9.6 (3.8-18.5)	8.8 (3.7-17.2)	0.009
History of smoking, %	48	48	44	48	<0.001
Methotrexate use, %	44	44	50	49	0.001
Prednisone use, %	31	31	31	31	0.981
bDMARD, %	30	29	30	31	0.300
NSAIDs, %	43	47	52	53	<0.001
Diabetes, %	15	11	7	9	<0.001
Hypertension, %	44	40	34	46	<0.001
Lung disease, %	24	17	15	21	<0.001
RDCI (0-9), median (IQR)	2 (1-3)	1 (0-2)	1 (0-2)	1 (0-2)	<0.001
HAQ (0-3), median (IQR)	1.3 (0.5-1.8)	0.9 (0.3-1.5)	0.8 (0.1-1.3)	1 (0.4-1.5)	<0.001
Pain Score (0-10), median (IQR)	4.5 (2-7)	3 (1.5-6)	2.5 (1-5)	3.5 (1.5-6.5)	<0.001
Severity Score (0-10), median (IQR)	4 (2-6)	3 (1.5-5)	2.5 (1-5)	3.5 (1.5-5.5)	<0.001

Table 2. Associations between weight change category and CVD events before and after adjustment for factors hypothesized to be mediators in the causal pathway between weight loss and CVD outcomes

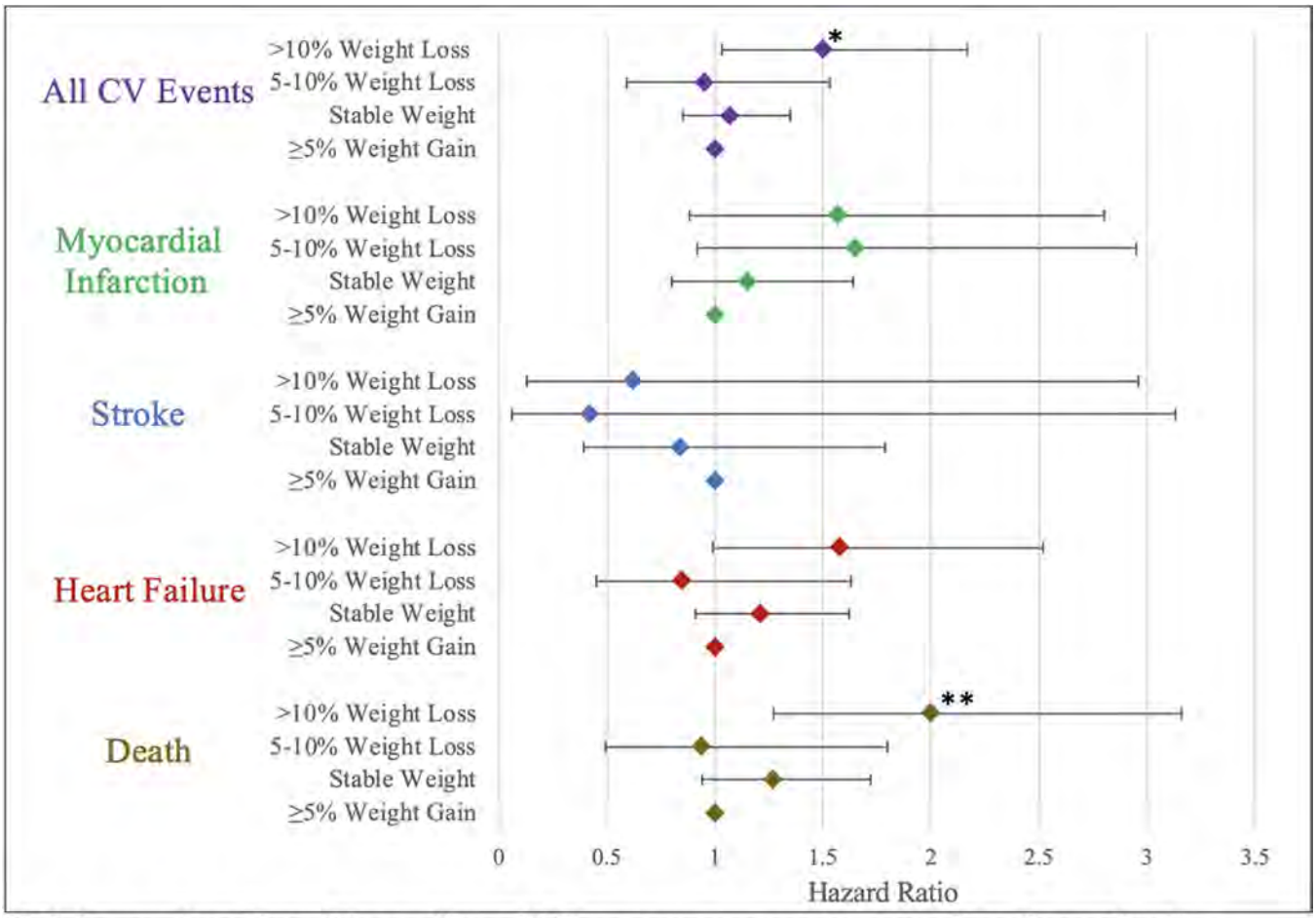
	Model 1: Weight Change Category n=14,012; PY=109,211	Model 2: Weight Change Category + Mediators n=13,771; PY=107,454
	HR (95% CI)	HR (95% CI)
Weight Change Category		
>10% Weight Loss	1.50 (1.03-2.17)*	1.23 (0.83-1.82)
5-10% Weight Loss	0.95 (0.59-1.53)	0.81 (0.50-1.32)
Stable Weight	1.07 (0.85-1.35)	1.09 (0.86-1.38)
≥5% Weight Gain	1 (reference)	1 (reference)
BMI Category		
Underweight (<18.5 kg/m^2)	0.85 (0.43-1.65)	1.01 (0.51-1.98)
Normal Weight (18.5-24.9 kg/m^2)	1 (reference)	1 (reference)
Overweight (25.0-29.9 kg/m^2)	1.36 (1.09-1.70)**	1.20 (0.96-1.50)
Obese (30.0-34.9 kg/m^2)	1.76 (1.35-2.28)***	1.33 (1.02-1.74)*
Very Obese (≥35 kg/m^2)	3.11 (2.35-4.12)***	1.86 (1.37-2.51)***

Models 1 and 2 were also adjusted for age, sex, race, start date, disease duration, smoking history, prednisone use, methotrexate use, and biologic therapy use.
Model 2 was further adjusted for NSAID use, RDCI, HAQ, pain score, severity score, history of diabetes, history of hypertension, and history of lung disease.
PY: person-years; BMI: Body Mass Index. *p<0.05, **p<0.01, ***p<0.001.

mass index (BMI) are not always observed to have higher long-term risks of obesity-related complications, perhaps as the result of long-term pathologic weight loss. Self-report of weight loss may thus serve as a helpful tool in risk-stratification by identifying individuals with adverse metabolic health. In this study, we evaluated the relationship between weight loss since age 30 and CVD along with factors associated with weight loss in patients with RA.

Methods: We studied RA patients (>40 years old, without prior heart disease) enrolled in the FORWARD registry from 1998 to 2021. Weight change from reported weight at age 30 to enrollment was categorized as >10% weight loss, 5-10% weight loss, stable weight, and ≥5% weight gain (reference, due to being the expected change in lifespan). The primary outcome was a composite of nonfatal and fatal CVD since enrollment identified using ICD-9/10 codes (myocardial infarction [MI], stroke, and heart failure [HF]) and validated using hospital/death records. Secondary outcomes were individual CVD events. Multivariable Cox proportional hazards models were used to evaluate associations for weight changes adjusting for confounding variables (age, sex, race, enrollment BMI, year, RA duration, smoking, methotrexate, prednisone, biologic DMARD use). Models were further adjusted for factors that might be influenced by metabolic disturbance and contribute to CVD including the Rheumatic Disease Comorbidity Index (RDCI), Health Assessment Questionnaire Disability Index (HAQ) score, pain score, severity score, diabetes, hypertension, and lung disease.

Results: Among 15,843 participants, 6% had >10% weight loss, 4% had 5-10% weight loss, 17% had a stable weight, and 74% had ≥5% weight gain since age 30. Participant characteristics differed substantially by weight change category (Table 1). There were 579 CVD incidents over 109,211 person-years of follow-up. Weight loss of >10% since age 30 was associated with 50% greater CVD risk independent of baseline BMI category and other baseline characteristics (HR 1.50, 95% CI 1.03-2.17). Weight loss (>10%) was also associated with a 2-fold increase in fatal CVD risk (HR 2.0, 95% CI 1.27-3.16) (Figure 1) and increased MI (HR 1.57, 95% CI 0.88-2.80) and HF risks (HR 1.58, 95% CI 0.99-2.52), although the latter two did not reach statistical significance. Fully adjusted models that



Models were also adjusted for enrollment BMI category, age, sex, race, start date, disease duration, smoking history, prednisone use, methotrexate use, and biologic therapy use.
*p<0.05, **p<0.01 compared to weight gain category.

Figure 1. Associations between weight change category and CVD events by event type in Cox proportional hazards models.

considered metabolic diseases, total comorbidity, disability, and symptoms demonstrated no significant association between weight loss and CVD events (HR: 1.23, 95% CI 0.83-1.82) (Table 2).

Conclusion: Long-term weight loss of >10% body weight is associated with increased CVD risk in RA independent of baseline BMI. The effect is largely explained by a higher prevalence of metabolic risk factors, comorbidity, and disability at enrollment, suggesting that the risk of weight loss in patients with RA is likely explained by worse metabolic health. Historical weight loss may serve as a marker of adverse metabolic health and aid in CVD risk stratification in RA.

Disclosure: L. Federico, None; **K. Michaud**, None; **K. Wipfler**, None; **G. Ozen**, None; **J. Baker**, None.

Abstract Number: 0296

The Impact of Delayed Primary Sjögren's Syndrome Diagnosis on Patient Outcomes: A Real-World Survey in the US

Briana Ndife[1], Sophie Barlow[2], Megan Hughes[2] and Nicola Booth[2], [1]Novartis, East Hanover, NJ, [2]Adelphi Real World, Bollington, United Kingdom

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Diagnosis of primary Sjögren's syndrome (pSS) is challenging due to the disease's phenotypic heterogeneity. pSS patients frequently experience a prolonged period between symptomatic onset and diagnosis, hypothesised to prove detrimental to patient outcomes. The objective of this study was to describe the impact of delayed diagnosis on disease severity and patient outcomes in patients with pSS.

Methods: Data were drawn from the Adelphi Primary Sjögren's Syndrome (pSS) Disease Specific Programme™, a real-world point-in-time survey of rheumatologists and their consulting pSS patients in the United States. Physicians provided data on patient demographics and clinical characteristics. Patients self-completed patient-reported outcome (PRO) tools; including the EuroQol 5-dimension 5-level utility score (EQ-5D), EuroQol visual analogue scale (EQ VAS), Work Productivity and Activity Impairment Index questionnaire (WPAI), and the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) and EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) proxy scores were calculated by assigning scores to physician-perceived severity in each of the associated domains. Patients were compared according to the time between onset of pSS symptoms and diagnosis (< 3 months, 3-6 months, 6-12 months, and >12 months). Analysis of variance and

Table 1. pSS patient demographics and clinical characteristics by time from onset of symptoms to diagnosis

	Overall (n=276)	<3 months (n=81)	3-6 months (n=56)	6-12 months (n=49)	>12 months (n=90)
Age, mean (SD)	52.3 (14.6)	51.7 (17.4)	51.3 (14.3)	51.3 (12.7)	53.9 (12.9)
Female, n (%)	246 (89.1)	73 (90.1)	50 (89.3)	43 (87.8)	80 (88.9)
BMI, mean (SD)	26.3 (5.0)	27.1 (6.5)	26.2 (4.0)	24.8 (3.0)	26.3 (4.8)
Ethnicity, n (%)					
White/Caucasian	233 (80.8)	62 (76.5)	47 (83.9)	41 (83.7)	73 (81.1)
African American	29 (10.5)	10 (12.3)	6 (10.7)	5 (10.2)	8 (8.9)
Other	24 (8.7)	9 (11.2)	3 (5.4)	3 (6.1)	9 (10.0)
Smoking status, n (%)					
Current smoker	16 (6.0)	4 (5.1)	2 (3.6)	2 (4.2)	8 (9.3)
Ex-smoker	62 (23.1)	18 (23.1)	13 (29.2)	14 (29.2)	17 (19.8)
Never smoked	190 (70.9)	56 (71.8)	32 (66.7)	32 (66.7)	61 (70.9)
Employment, n (%)					
Working full time	144 (52.7)	40 (50.0)	34 (60.7)	25 (51.0)	45 (51.1)
Working part time	28 (10.3)	8 (10.0)	4 (7.1)	7 (14.3)	9 (10.2)
Homemaker	33 (12.1)	6 (7.5)	7 (12.5)	5 (10.2)	15 (17.0)
Other	68 (24.9)	26 (32.5)	11 (19.7)	12 (24.5)	19 (21.7)
Months since diagnosis, mean (SD)	51.6 (62.2)	48.1 (55.2)	45.8 (43.6)	40.1 (50.2)	64.5 (80.1)

Table 2. Comparison of patient-reported outcomes, ESSDAI proxy and ESSPRI proxy scores by time from onset of symptoms to diagnosis

	Overall	<3 months	3-6 months	6-12 months	>12 months	p-value
EQ-5D Utility (n=163), mean (SD) [95% CI]	0.79 (0.2) [0.76, 0.82]	0.82 (0.17) [0.77, 0.88]	0.85 (0.18) [0.78, 0.92]	0.8 (0.21) [0.72, 0.87]	0.74 (0.21) [0.68, 0.79]	**0.042**
EQ VAS (n=160), mean (SD) [95% CI]	72.1 (20.3) [68.9, 75.3]	75.2 (20.3) [68.6, 81.8]	77.2 (20) [69.0, 85.5]	76 (22.2) [68.1, 83.8]	66.1 (18.4) [61.5, 70.8]	**0.026**
FACIT-F (n=162), mean (SD) [95% CI]	34.3 (12.4) [32.3, 36.2]	34.3 (11.3) [30.7, 37.9]	38.6 (10.1) [34.5, 42.7]	37.9 (12.3) [33.6, 42.3]	30.5 (13) [27.3, 33.8]	**0.007**
WPAI % overall work impairment (n=82), mean (SD) [95% CI]	24.3 (24.8) [18.9, 29.8]	17.8 (18.5) [7.5, 28.0]	17.2 (20.9) [3.9, 30.5]	21.6 (26.5) [8.4, 34.8]	30.7 (26.6) [21.8, 39.5]	0.197
EDDSAI proxy (n=276), mean (SD) [95% CI]	9.3 (8.9) [8.3, 10.4]	8 (9.1) [6.0, 10.0]	8.1 (8.5) [5.8, 10.4]	9.5 (7.9) [7.2, 11.8]	11.1 (9.2) [9.2, 13.1]	0.083
ESSPRI proxy (n=161), mean (SD) [95% CI]	4 (2.2) [3.6, 4.3]	4.1 (2.2) [3.3, 4.8]	3.1 (1.8) [2.4, 3.8]	3.2 (2.2) [2.4, 4.0]	4.7 (2.1) [4.2, 5.2]	**0.001**
Current physician-reported severity, n (%)						<3months: ref 3-6 months: 1.000 6-12 months: **0.040** >12 months: **0.029**
Mild	164 (59.4)	55 (67.9)	44 (78.6)	22 (44.9)	43 (47.8)	
Moderate	105 (38.0)	26 (32.1)	11 (19.6)	25 (51.0)	43 (47.8)	
Severe	7 (2.5)	0 (0.0)	1 (1.8)	2 (4.1)	4 (4.4)	

Kruskall-Wallis tests were used to examine the impact of delayed diagnosis on ESSDAI, ESSPRI and PRO measures, and Mann-Whitney U-test for physician-perceived current severity using < 3 months as the reference group.

Results: 71 rheumatologists provided information for 276 pSS patients: mean age 52.3 years, 89.1% female and average time since diagnosis 51.6 months (Table 1). Of these patients, 29.3% were diagnosed within 3 months of the onset of pSS symptoms, 20.3% 3-6 months, 17.8% 6-12 months and 32.6% >12 months, with a mean (SD) of 27.5 (68.2) months from the onset of symptoms to diagnosis. Comparative analyses showed that there were significant differences (< 0.05) in EQ-5D utility score, EQ-5D VAS, FACIT-F, proxy ESSPRI scores and physician reported severity between patients with differing time to diagnosis (Table 2), assessed at the time of consultation. Relationships between diagnosis duration and WPAI scores were not statistically significant.

Conclusion: Delayed diagnosis of pSS is associated with poorer patient outcomes; including worsening PRO scores, and ESSPRI scores. pSS diagnosis periods could likely be attenuated by increasing disease awareness amongst physicians; thus improving patient outcomes in pSS.

Disclosure: B. Ndife, Novartis, 3, 11; **S. Barlow**, None; **M. Hughes**, None; **N. Booth**, None.

Abstract Number: 0297

Describing the Disease Burden of Primary Sjögren's Syndrome Patients: Results from a Real-World Survey in the US

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

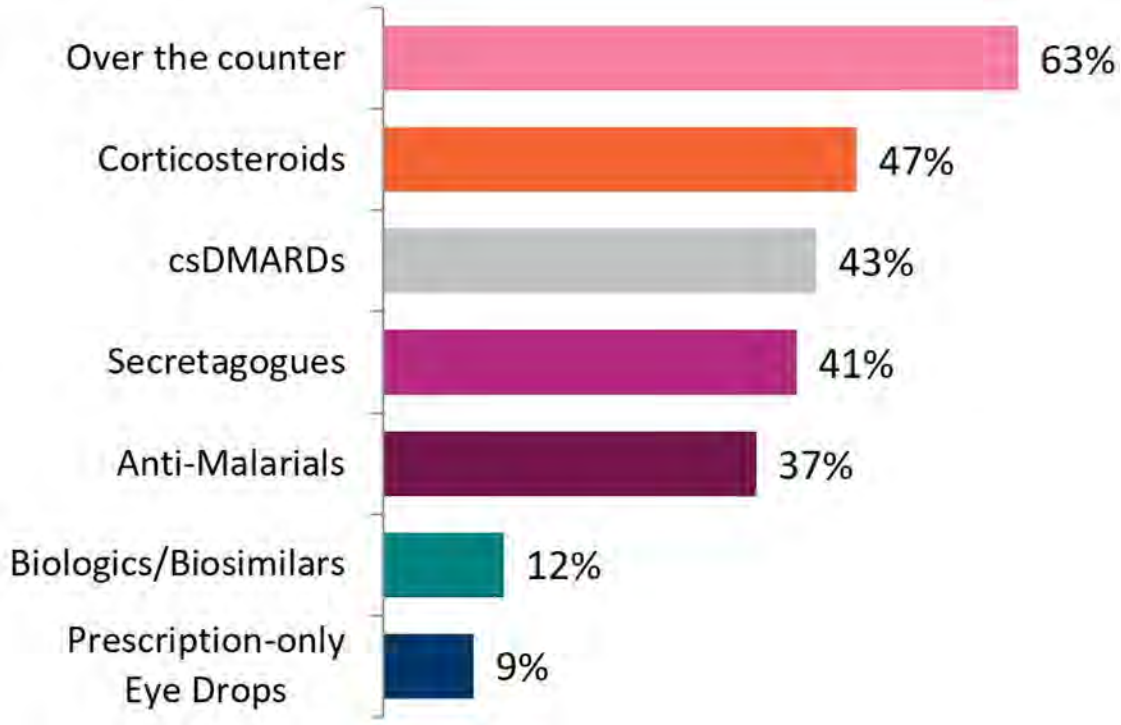

Figure 1. Treatment classes currently received (n=511).

Background/Purpose: Primary Sjogren's syndrome is a highly heterogeneous condition, with limited understanding of the burden of disease. The objective of this study was to describe the patient profile and disease burden of patients with primary Sjogren's syndrome (pSS).

Methods: Data were drawn from the Adelphi primary Sjögren's syndrome Disease Specific Programme™, a real-world point-in-time survey of rheumatologists and their consulting pSS patients in the United States. Rheumatologists provided data about patient demographics and clinical characteristics. Derived EULAR Sjogren's Syndrome Disease Activity Index (ESSDAI) scores were calculated for each patient by assigning a score to the rheumatologists' perception of "not present", "mild", "moderate" or "severe" for each of the twelve domains of the ESSDAI. Patients self-completed patient reported outcome (PRO) tools including the EuroQol 5-Dimension utility score (EQ-5D), Work Productivity and Activity Impairment questionnaire (WPAI) and The Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F). Derived EULAR Sjogren's Syndrome Patient-Reported Index (ESSPRI) scores were calculated using the patients' rating of dryness, fatigue, and pain.

Results: Rheumatologists (n=84) provided data for 511 pSS patients, mean age 53.3 years, 88.5% female, 79.8% white/Caucasian and mean time since diagnosis 4.6 years. Classes of treatment patients were receiving at the time of data collection are shown in Figure 1. Dry eyes and dry mouth were the most prevalent symptoms, present in 86.3% and 62.6% of patients respectively. Almost three quarters of patients (74.8%) experienced physical fatigue and over a third of patients (35.8%) experienced muscle pain at the time of data collection. Most patients experienced articular involvement, with 4.1% of patients experiencing no organ involvement, Table 1. Over half (55.8%) of patients were considered moderate-severe in terms of their derived ESSDAI score at the time of data collection, Table 1. At diagnosis of pSS, 14.9% of patients were considered severe by their physician, 59.7% moderate and 25.4% mild. At the time of consultation 3.9% of patients were severe, 39.9% moderate and 56.2% mild. Scores from PRO tools indicate

Table 1. Organ involvement of pSS patients (n=511)

Organ domains affected, % (n)	
Articular involvement	72.8 (372)
Glandular involvement	35.2 (180)
Hematological involvement	25.4 (130)
Pulmonary involvement	17.0 (87)
Cutaneous involvement	15.3 (78)
Muscular involvement	14.9 (76)
Peripheral nervous system involvement	11.5 (59)
Lymphadenopathy	10.4 (53)
Central nervous system involvement	8.4 (43)
Renal involvement	4.9 (25)
Other	1.2 (6)
None	4.1 (21)
Derived ESSDAI score, mean (SD), *% (n)*	9.5 (9.4)
Mild (0 - <5)	*44.2 (226)*
Moderate (5-13)	*30.9 (158)*
Severe (≥14)	*24.9 (127)*

Table 2. PRO scores by physician-perceived current severity of pSS

	Overall (511)	**Mild (56.2%, 287)**	**Moderate (39.9%, 204)**	**Severe (3.9%, 20)**
EQ5D utility score, mean (SD) [n]	0.79 (0.19) [303]	0.85 (0.16) [152]	0.74 (0.20) [139]	0.66 (0.27) [12]
EQ5D Visual Analogue Scale, mean (SD) [n]	72.1 (20.1) [295]	78.1 (16.5) [145]	67.0 (20.9) [138]	57.4 (26.9) [12]
WPAI, % [n]				
% absenteeism	5.9 [147]	6.0 [68]	5.4 [75]	12.5 [4]
% presenteeism	23.2 [177]	18.4 [89]	27.1 [84]	45.0 [4]
% overall work impairment	24.8 [145]	17.7 [67]	29.7 [74]	51.2 [4]
% activity impairment	30.6 [24.7]	22.7 [143]	37.4 [137]	49.1 [11]
FACIT-fatigue, mean (SD) [n]	34.4 (12.4) [302]	38.0 (11.2) [150]	31.5 (12.7) [140]	24.1 (10.5) [12]
Derived ESSPRI score, mean (SD) [n]	4.0 (2.1) [297]	3.2 (1.9) [146]	4.6 (2.0) [139]	5.9 (2.1) [12]

the impairment that patients experience in everyday life and whilst at work, which worsens with physician-perceived current severity of pSS, Table 2.

Conclusion: Patients experience sicca symptoms and organ involvement, with physical fatigue affecting the majority of patients. Over half of patients are classified moderate-severe in terms of derived ESSDAI scores, despite many patients receiving off-label systemic therapies. PRO scores show patients experience a burden of disease impacting their daily life and work.

Disclosure: B. Ndife, Novartis, 3, 11; **B. Hoskin**, Adelphi Real World, 3; **M. Hughes**, None; **N. Booth**, None.

Abstract Number: 0298

The Clinical Phenotype of Isolated Ocular and Oral Dryness in Sjogren Syndrome, Fulfilling the 2016 ACR-EULAR Classification Criteria

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Dry mouth and eyes are the main clinical features of Sjögren's syndrome (SS), although a minority of patients present without sicca manifestations and isolated cases of oral or ocular dryness are rare. The purpose of this study is to investigate whether isolated mouth or eye dryness constitute distinct clinical phenotypes of SS.

Methods: From a total population of 1765 consecutive patients fulfilling the 2016 ACR-EULAR criteria for SS, who were followed-up in 4 centers from Greece and Italy (Universities of Athens, Pisa, Harokopio and Ioannina) (PAHI group), those with isolated mouth or eye dryness, were identified and matched according to age at SS diagnosis, gender and disease duration from SS diagnosis to last follow up in a 1:2 ratio, with SS patients exhibiting both oral and ocular dryness. The 2 study groups of isolated dryness were defined as follows: a) patients with ocular dryness without oral dryness and b) patients with oral dryness without ocular dryness as documented by the AECG validated questionnaires. Cumulative data regarding glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, lymphadenopathy, arthralgias/arthritis, palpable purpura, liver involvement, kidney involvement, lymphoma), serology (anti Ro/SSA, anti La/SSB, rheumatoid factor, cryoglobulinemia, low C4 complement levels) and histologic features (focus score) were recorded and compared between each study group with their matched SS controls and between the 2 study groups as well. Statistical analysis for categorical data was performed by Fisher exact test or χ^2 square test accordingly and numerical data with Man Whitney test.

Table 1. Comparison of clinical and laboratory features between SS patients with isolated ocular dryness and SS controls with both mouth and eye dryness

DEMOGRAPHICS	DRY EYES n= 72	CONTROLS n= 144	P VALUE
Median age at disease diagnosis, years (range)	46, (21-68)	46, (19-69)	0.89
Median disease duration from SS diagnosis to last follow up, years (range)	3, (0-23)	4, (0-24)	0.98
GLANDULAR AND NON SPECIFIC MANIFESTATIONS			
Salivary gland enlargement	15,4% (11/71)	28,7% (40/139)	**0.05**
Raynaud's phenomenon	26,1% (17/65)	35,2% (43/122)	0.27
Arthralgias	51,3% (37/72)	58,8% (83/141)	0.37
Arthritis	11,6% (7/60)	13,1% (17/129)	0.95
EXTRAEPITHELIAL MANIFESTATIONS			
Glomerulonephritis	1.8% (1/53)	0.9% (1/102)	1
Interstitial Lung Disease	0% (0/68)	3.7% (5/133)	0.17
Autoimmune hepatitis	0% (0/56)	2.6% (3/115)	0.55
Peripheral nervous disease	1.6% (1/61)	1,7% (2/118)	1
Palpable purpura	12.5% (9/72)	12.0% (17/141)	0.89
Persistent lymphadenopathy	20.6% (11/61)	10% (18/118)	0.79
PERIEPITHELIAL MANIFESTATIONS			
Tubulointerstitial nephritis	0% (0/69)	1.4% (2/138)	0.55
Small Airway disease	9.6% (6/62)	5.7% (7/121)	0.50
Primary biliary cholangitis	0% (0/72)	2.1% (3/142)	0.55
Autoimmune thyroiditis	30.0% (12/40)	27.8% (22/79)	0.97
FOCUS SCORE	1,86	1,58	0.47
SEROLOGY			
Rheumatoid Factor	50.7% (33/65)	57.1% (72/126)	0.49
Anti-Ro	86.9% (56/72)	65.7% (105/139)	0.84
Anti-La	31.9% (23/72)	35.9% (50/139)	0.66
LOW C4	40.3% (25/62)	41.3% (50/121)	0.97
Monoclonality	7.8% (5/64)	8.1% (10/122)	0.84
Cryoglobulinemia	8.1% (3/37)	11.5% (9/78)	0.74
ANA antibodies	94.1% (80/85)	84.5% (149/176)	**0.03**
LYMPHOMA	0% (0/72)	11,3% (16/141)	**0.001**

Results: Seventy-two patients with isolated ocular dryness and 74 with isolated oral dryness were identified and compared with 144 and 148 SS controls, respectively. The median disease duration of both study groups was 3 years [range: 0-23 (ocular dryness group) and 0-21 (oral dryness group)] while the median age of SS diagnosis was 46

Table 2. Comparison of clinical and laboratory features between SS patients with isolated ocular and oral dryness

DEMOGRAPHICS	DRY EYES n= 72	DRY MOUTH n= 74	P VALUE
Median age at disease diagnosis, years (range)	46, (21-68)	53.5, (16-79)	**0.005**
Median disease duration from SS diagnosis to last follow up, years (range)	3, (0-23)	3, (0-21)	0.33
GLANDULAR AND NON SPECIFIC MANIFESTATIONS			
Salivary gland enlargement	15,4% (11/71)	29,7% (22/74)	0.06
Raynaud's phenomenon	26,1% (17/65)	23.4% (15/64)	0.87
Arthralgias	51,3% (37/72)	39.1% (29/74)	0.18
Arthritis	11,6% (7/60)	8.6% (6/69)	0.79
EXTRAEPITHELIAL MANIFESTATIONS			
Glomerulonephritis	1.8% (1/53)	0% (0/61)	0.46
Interstitial Lung Disease	0% (0/68)	5.6% (4/71)	0.11
Autoimmune hepatitis	0% (0/56)	0% (0/59)	1
Peripheral nervous disease	1.6% (1/61)	4.8% (3/62)	0.61
Palpable purpura	12.5% (9/72)	4.0% (3/74)	0.07
Persistent lymphadenopathy	20.6% (11/61)	17.7% (11/62)	0.84
PERIEPITHELIAL MANIFESTATIONS			
Tubulointerstitial nephritis	0% (0/69)	5.4% (4/74)	0.12
Small Airway disease	9.6% (6/62)	4.8% (3/62)	0.49
Primary biliary cholangitis	0% (0/72)	0% (0/74)	1
Autoimmune thyroiditis	30.0% (12/40)	37.8% (14/37)	0.62
FOCUS SCORE	1,58	1,87	0.51
SEROLOGY			
Rheumatoid Factor	50.7% (33/65)	54.5% (36/66)	0.79
Anti-Ro	86.9% (56/72)	82.1% (60/73)	0.64
Anti-La	31.9% (23/72)	40.2% (29/72)	0.38
LOW C4	40.3% (25/62)	30.5% (18/59)	0.34
Monoclonality	7.8% (5/64)	8.3% (5/60)	0.82
Cryoglobulinemia	8.1% (3/37)	2.7% (1/36)	0.61
ANA antibodies	94.1% (80/85)	93.0% (67/72)	0.98
LYMPHOMA	0% (0/72)	9.4% (7/74)	**0.01**

years old (range: 21-68) and 53,5 (range: 16-79) respectively. SS patients with isolated eye dryness had statistically significant lower frequency of salivary gland enlargement (35,4% vs 28,7%, p=0,05) and lymphoma (0% vs 11,3%, p=0,001) (Table 1) while in SS patients with isolated oral dryness arthralgias (39,1% vs 65,5%, p= 0,0003) and arthritis (8,6% vs 20,3%, p= 0,05) appeared less frequently, compared to their SS controls, respectively. After comparing the 2 study groups, it was found that SS patients with isolated oral dryness were diagnosed at older age (median: 53,5

vs 46 years old, p=0,005) and were more prone to develop lymphoma (9,4% vs 0%, p=0,01) compared to patients with isolated ocular dryness, without any difference in classical lymphoma predictors, including focus score (Table 2).

Conclusion: Patients with isolated ocular or oral mucosa dryness constitute 8% of total SS population and those with isolated dry eyes display lower frequency of lymphoma.

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Abstract Number: 0299

Sex Hormones and Risk of Sjögren's Syndrome: Hypothesis Generating Findings Implicating Androgen and Estrogen Ratios

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Baseline Demographics by Composite Estrogen Score (Modified from Gatto et al. 2014)

Variable	Total Cohort (n=2183)	CES = 0 (n=698)	CES = 1 (n=918)	CES = 2 (n=449)	CES >= 3 (n=118)	P-value
Age - yr*	55.1 (14.2)	47.3 (12.3)	55.2 (14.2)	64.1 (10.1)	66.5 (9.8)	< 0.001
Age categories						
< 18	1 (0.0%)	0 (0.0%)	1 (0.1%)	0 (0.0%)	0 (0.0%)	
18-39	325 (14.9%)	191 (27.4%)	127 (13.8%)	6 (1.3%)	1 (0.8%)	
40-59	993 (45.5%)	403 (57.7%)	429 (46.7%)	139 (31.0%)	22 (18.6%)	
60-79	794 (36.4%)	103 (14.8%)	331 (36.1%)	275 (61.2%)	85 (72.0%)	
80+	70 (3.2%)	1 (0.1%)	30 (3.3%)	29 (6.5%)	10 (8.5%)	
Race –white	1970 (98.3%)	620 (97.6%)	818 (98.2%)	420 (99.1%)	112 (100.0%)	0.185
Hispanic ethnicity	25 (1.2%)	9 (1.4%)	10 (1.2%)	5 (1.2%)	1 (0.9%)	0.987
Health insurance						< 0.001
Multiple payers	268 (12.3%)	72 (10.3%)	91 (9.9%)	83 (18.5%)	22 (18.6%)	
Private	679 (31.1%)	240 (34.4%)	286 (31.2%)	127 (28.3%)	26 (22.0%)	
Medicaid	232 (10.6%)	99 (14.2%)	101 (11.0%)	22 (4.9%)	10 (8.5%)	
Medicare	225 (10.3%)	16 (2.3%)	94 (10.2%)	86 (19.2%)	29 (24.6%)	
None or unknown	779 (35.7%)	271 (38.8%)	346 (37.7%)	131 (29.2%)	31 (26.3%)	
Tobacco ever	394 (38.7%)	102 (33.1%)	158 (40.5%)	105 (42.5%)	29 (40.3%)	0.104
Alcohol use disorder	195 (8.9%)	65 (9.3%)	79 (8.6%)	42 (9.4%)	9 (7.6%)	0.899

*reported as mean (SD) or N (%)

Table 2. Risk Ratio of Sjögren's Syndrome by Composite Estrogen Score

			Univariate Analysis		Multivariate Analysis*	
Estrogen Score	SS Case (n=546)	Control (n=1637)	RR (95% CI)	P-value	RR (95% CI)	P-value
CES = 0	177 (32.4%)	521 (31.8%)	reference	--	reference	--
CES = 1	200 (36.6%)	718 (43.9%)	0.86 (0.70-1.05)	0.141	0.84 (0.68-1.05)	0.12
CES = 2	136 (24.9%)	313 (19.1%)	1.19 (0.96-1.49)	0.119	1.22 (0.94-1.58)	0.143
CES >= 3	33 (6.0%)	85 (5.2%)	1.10 (0.76-1.60)	0.606	1.18 (0.79-1.77)	0.413

Reported as N (%) or RR (95% CI). *Adjusted for age, race/ethnicity, and health insurance type.

Background/Purpose: Sjögren's syndrome (SS) is the most female predominant systemic autoimmune disease, with peak onset around perimenopause. Estrogen appears to protect against SS, but prior studies lack details on surgical interventions and timing or type of exogenous hormone exposure. The purpose of this study was to determine how specific endogenous and exogenous hormone exposures contribute to SS Risk.

Methods: We performed a retrospective case-control study of adult women, nested within a defined population of Marshfield Clinic Health System (MCHS) patients in north-central Wisconsin. SS cases included patients with one SS diagnosis by a rheumatology provider or two SS diagnoses > 4 weeks apart from a non-rheumatology provider. Those with overlapping autoimmune diseases were excluded. Three controls were included for each SS case and were matched on age. We calculated a composite estrogen score (CES) for each patient, with one point for: 1) body mass index (BMI) ≥30 kg/m^2, 2) menopause ≥55 years, 3) hormone replacement therapy >90 days, and 4) hysterectomy, which was considered a marker of high estrogen because hysterectomy is most often performed for fibroids and

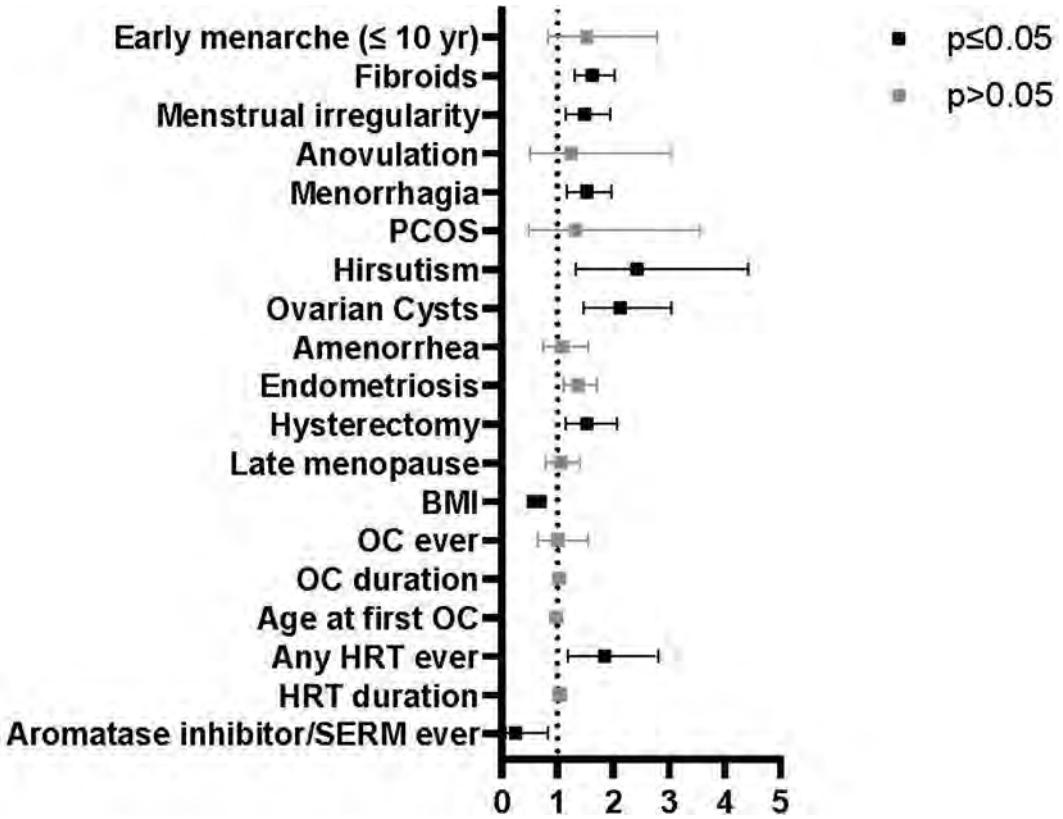

Figure 1. Risk ratios and 95% confidence intervals of individual sex hormone exposure variables controlled for age at index, Caucasian, Ethnicity, and insurance type. Abbreviations: PCOS=polycystic ovarian syndrome; BMI=body mass index; OC=oral contraceptive; HRT=hormone replacement therapy; SERM=selective estrogen receptor modulator.

post-surgical management often includes exogenous hormones. Risk ratios for SS were reported, adjusted for age, race/ethnicity, and health insurance.

Results: There were 546 SS cases and 1,637 age-matched controls. The distribution of CES was 0 (n= 698 (32%)), 1 (n= 918 (42%)), 2 (n= 449 (21%)), and >= 3 (n=118 (5%)) (Table 1). Age, race, and ethnicity were similar between CES groups but health insurance differed. CES was not significantly associated with SS in adjusted models (Table 2). As outlined in Figure 1, the top three individual hormone exposures that were independently associated with SS included hirsutism (RR 2.42 [95% CI 1.32-4.43]), ovarian cysts, (2.12 [1.48-3.04]) and exogenous hormone replacement therapy (1.84 [1.20-2.81]). High BMI (0.62 [0.50-0.77]) and aromatase inhibitor use (0.25 [0.07-0.83]) appeared to be protective against SS.

Conclusion: Higher CES did not result in greater SS risk in this study, but several novel individual SS risk factors were observed, most notably hirsutism and ovarian cysts, which are associated with high androgen and lower estrogen excess. In contrast, high BMI, which is associated with higher levels of peripherally produced estrogen and lower androgen, was associated with lower SS risk. Aromatase inhibitor or SERM use also appeared protective, potentially representing confounding by indication because higher levels of estrogen are associated with breast cancer. These data suggest that the influence of sex hormones on SS pathogenesis may be more complex than prior studies have indicated; SS risk is potentially dependent on androgen-to-estrogen ratios. Further prospective studies are needed to confirm these findings.

Disclosure: S. McCoy, BMS, 2, Novartis, 1, Boehringer Ingelheim, 6; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5; **S. Hetzel**, None; **J. VanWormer**, None.

Abstract Number: 0300

Salivary Gland Epithelial Cells Transcriptomic Analysis Highlight Their Potential Involvement in Extracellular Matrix Modification in Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Salivary gland epithelial cells (SGECs) participate to the hyper activation of the immune system in primary Sjögren's syndrome (pSS). This study aimed to analyze the transcriptomic characteristics of primary cultured SGECs from pSS patients compared to controls, in order to identify pathways involved in pSS pathogenesis.

Methods: Minor salivary gland (MSG) biopsies were obtained from patients referred for suspicion of pSS. pSS was defined according to the 2016 ACR/EULAR criteria. Controls had sicca symptoms without anti-SSA/SSB and with normal MSG. Primary cultures of SGECs were established from MSGs. After 2 to 3 weeks of culture, cells were dissociated and incubated at 37°C for 24h. Total RNA was extracted and reverse-transcribed. Libraries were sequenced

Table 1. Characteristics of the patients included in the study

	RNA-seq experiments on primary cultured SGECs	
	pSS (n=5)	control (n=5)
Median age (min-max)	31 (23-53)	52 (34-56)
Female sex, n (%)	5 (100)	5 (100)
Pathologic Schirmer	2 (50)	2 (50)
Pathologic salivary flow	0 (0)	0 (0)
Focus score ≥ 1, n (%)	5 (100)	0 (0)
SSA, n (%)	5 (100)	0 (0)
Mean ESSDAI (min-max)	4 (2-10)	

on Illumina Nextseq 500. Statistical analyses of the RNA-Seq used DESeq2 package. Absolute FC value >1.5 and p-value< 0.05 was applied to identify up and down-regulated genes.

Results: Patient's characteristics are presented in Table 1. The comparison of gene expression in primary cultured SGECs of pSS compared to controls showed 511 differentially expressed genes: 251 upregulated and 260 down-regulated. Functional enrichment pathway analysis highlighted an over-representation of the Inhibition of Matrix Metalloproteases signaling pathway (Table 2). Among the most upregulated genes, we identified genes involved in extracellular matrix formation, including several collagen genes: *COL3A1* and *COL1A2* with the higher fold-change (FC) (log2FC = 2.40, log2FC = 2.12, respectively). There were also several ADAMDTS genes (A Disintegrin and Metalloproteinases with a Thrombospondin motif) related genes such as *ADAMTS2, ADAMTS16, ADAMTS12* (log2FC = 2.09, log2FC = 1.57, log2FC =1.31, respectively). Other genes that might have a role in saliva secretion such as *CFTR* and *AQP6* were differentially expressed. *CFTR,* which codes for a channel that conducts chloride ions across epithelial membranes, was upregulated (log2FC=1.67), whereas *AQP6* was downregulated (log2FC=-1.44). There was an upregulation of *HLA-C* (log2FC=0.63), as well as *CCR7* (log2FC=1.26). Lastly, we identified an upregulation of the *androgen receptor* (*AR*) gene (log2FC=1.71). A schematic representation of these results is presented in Figure 1.

Conclusion: Differentially expressed genes between pSS and controls SGECs included genes involved in the extracellular matrix formation. This result suggests a role for SGECs in salivary gland fibrosis development. We also

Table 2. Enrichment pathway analysis of primary cultured SGECs from pSS compared to controls in different conditions of stimulation. Selection of the 10 most significant pathways

Ingenuity Canonical Pathways	-log(p-value)
Comparison between unstimulated pSS and controls SGECs	
Inhibition of Matrix Metalloproteases	3.85
Stearate Biosynthesis I (Animals)	3.46
Glycine Biosynthesis I	2.76
Superpathway of Serine and Glycine Biosynthesis I	2.65
γ-linolenate Biosynthesis II (Animals)	2.34
Mitochondrial L-carnitine Shuttle Pathway	2.34
Folate Transformations I	2.3
Glycine Betaine Degradation	2.16
GP6 Signaling Pathway	2.06
Acyl-CoA Hydrolysis	2.03

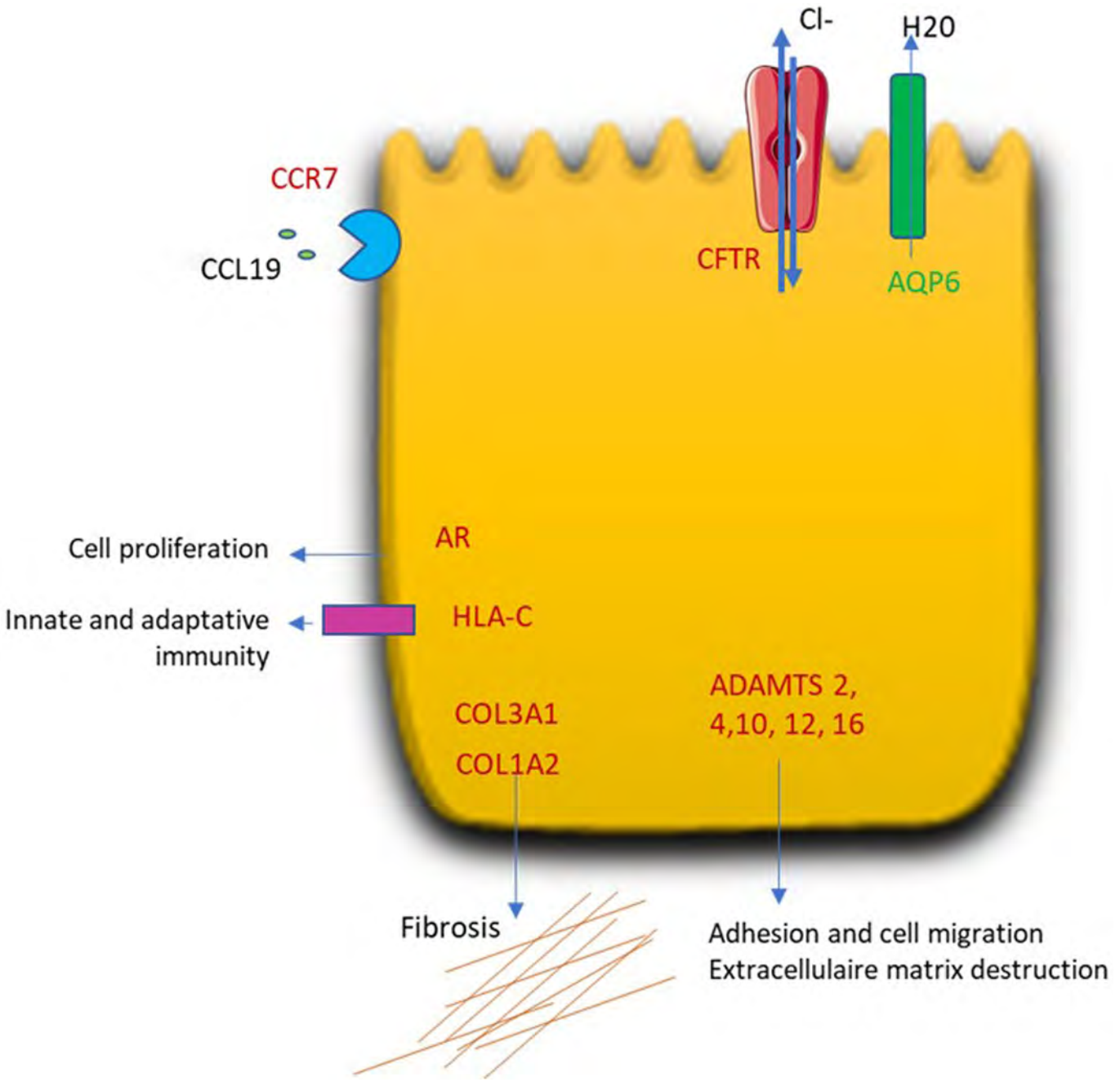

Figure 1. Schematic representation of the differentially expressed genes between pSS and controls in primary cultured SGECs.

observed a downregulation of *AQP6*. A potential role of AQP5 abnormal localization on saliva secretion in pSS has already been described, however, *AQP6* potential involvement in pSS pathophysiology has, to our knowledge, never been described. *CFTR* upregulation in SGECs from pSS compared to controls could be reactive to the salivary gland damage and dysfunction. The differentially expressed genes identified in this RNA-seq analysis need to be confirmed by qPCR.

These results open the perspective of new potential pathogenic pathways involved in pSS, suggesting the involvement of SGECs in extracellular matrix and fibrosis constitution.

Disclosure: E. Rivière, None; **J. Pascaud**, None; **F. Letourneur**, None; **G. Nocturne**, None; **X. Mariette**, GlaxoSmithKline, 2, BMS, 2, Servier, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 0301

Activation of Akt Signaling Pathway in the Minor Salivary Glands of Patients with Primary Sjögren's Syndrome Does Not Relate with Clinical Phenotype

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Akt is a phosphoinositide-dependent serine/threonine kinase with diverse regulatory functions that has been implicated in numerous pathological processes, including oncogenesis and autoimmune diseases. Indirect lines of evidence suggest that this pathway may be implicated in pathogenesis of primary Sjögren's syndrome (pSS). The purpose of this study is to investigate the expression and activation of Akt kinase pathway in different clinical phenotypes of pSS and related lymphomagenesis.

Methods: The expression of the entire protein, the threonine 308-phosphorylated Akt kinase and serine 473-phosphorylated Akt kinase, as well as substrates PRAS40 and FoxO1 (total and phosphorylated forms), which are phosphorylated by Akt, were evaluated by immunohistochemistry in minor salivary glands (MSG) of pSS patients (n=29), non-SS sicca-complaining individuals with negative biopsy (sicca-controls; n=10) and gastric biopsies from patients with MALT lymphoma associated with *Helicobacter pylori* infection (n=5). Sicca-controls and gastric MALT lymphomas served as control goups. The pSS patients group included 10 at low risk for lymphoma development, 10 at high-risk [four of whom, namely pre-lymphoma, developed lymphoma 7.46 years (median time to lymphoma diagnosis, range 2.0-15.5 years) after the MSG biopsy], and 9 with pSS-associated lymphoma.

Results: The phosphorylated forms of Akt, PRAS40 and FoxO1 were strongly detected in the epithelia and all infiltrating mononuclear cells at the MSGs of 27 pSS patients and stomachs of all patients with gastric lymphoma. Low staining was detected in two pSS patients and two sicca-controls. The rest sicca-controls were negative for all molecules. The activation of Akt pathway was not associated with a higher risk for lymphoma development, lymphoma or other disease features.

Conclusion: Our findings disclosed a strong activation of the Akt/mammalian target of rapamycin (mTOR) pathway in MSGs of pSS patients, independently of their clinical phenotype suggesting a role in disease pathogenesis.

Disclosure: I. Stergiou, None; **L. Chatzis**, None; **A. Papanikolaou**, None; **S. Giannouli**, None; **A. Tzioufas**, None; **M. Voulgarelis**, None; **E. Kapsogeorgou**, None.

Abstract Number: 0302

Loss of TAM Receptor Mer Contributes to Sjögren's Syndrome–like Disease in Mice

Richard Witas and Cuong Nguyen, University of Florida, Gainesville, FL

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren's syndrome (SjS) is a chronic autoimmune disease primarily involving the exocrine glands where the involvement of the innate immune system is largely uncharacterized. Mer signaling has been found to be protective in several autoimmune diseases but remains unstudied in SjS. Here, we sought to investigate the protective capacity of Mer signaling in SjS.

Methods: SjS patient sera was evaluated for levels of soluble, inactivated Mer (sMer) via ELISA and sMer levels were correlated to disease manifestations. C57BL/6.NOD-*Aec1Aec2* (SjS^S) mice were assessed for sMer levels, TACE activity, and Mer signaling outcomes. SjS diagnostic criteria were examined in MerKO mice.

Results: sMer levels were elevated in SjS patient sera and positively correlated with focus score, ocular staining scores, rheumatoid factor, and Ro60 autoantibody levels. Increased sMer was also detected in SjS^S mouse sera, coinciding with higher TACE activity, the enzyme responsible for cleavage of Mer, and inactivation of such. Mer signaling outcomes were observed to be diminished in SjS^S mice as evidenced by impaired efferocytosis in SjS^S mouse macrophages and decreased *Socs1* and *Socs3* expression in SjS^S salivary gland (SG). MerKO mice developed SG infiltrates of B and T lymphocytes, SG apoptotic cells, antinuclear antibodies, and reduced saliva flow.

Conclusion: Our data indicate that Mer plays a protective role in SjS, similar to other autoimmune diseases. Furthermore, we suggest a series of events where enhanced ADAM17 activity increases Mer inactivation, depresses Mer signaling, and removes a protection against the loss of self-tolerance and onset of autoimmune disease in SjS^S mice.

Disclosure: R. Witas, None; **C. Nguyen**, None.

Abstract Number: 0303

Extraglandular Manifestations as Initial Presentation in a Cohort of Patients with Primary Sjögren's Syndrome

Lucia Alascio[1], Silvia Papasidero[1], María Alejandra Medina[1], Juan Manuel Bande[1], Silvana Perez[1], Eliana Serrano[1], Diana Klajn[1], Jose Caracciolo[1], Rosella Tralice[2], Erick Rodríguez[2], Felix Romanini[2], Anastasia Secco[2], Sinda Zalles[3], Carolina Segura Escobar[3], Julia Demarchi[3], Geofredo Guillermo Earsman[4], Laura Raiti[5], Sofia Velez[6] and Alejandro Martinez[7], [1]Hospital General de Agudos Dr. Enrique Tornú, Buenos Aires, Argentina, [2]Hospital Rivadavia, Buenos Aires, Buenos Aires, Argentina, [3]Hospital Británico, Buenos Aires, Buenos Aires, Argentina, [4]Hospital Británico, Buenos Aires, La Lucila, Argentina, [5]Clínica Bessone, Buenos Aires, Buenos Aires, Argentina, [6]Consultorio privado de reumatología, Buenos Aires, Argentina, [7]Fundación respirar, Buenos Aires, Mexico City, Mexico

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Primary Sjögren's Syndrome (pSS) is a systemic autoimmune disease which is mostly characterized by the presence of xerophthalmia and xerostomia, caused by the lymphoplasmacytic cell infiltration of the lacrimal and salivary glands. This pathological change can also affect other organs and produce various extraglandular manifestations (EGM), which may precede the typical sicca symptoms. The diversity of clinical presentations may partially explain the delay in diagnosis and determine the prognosis of the disease.

The purpose of this study was to describe the frequency of EGM as initial presentation in a cohort of patients with pSS and to evaluate the delay in diagnosis among patients with EGM versus sicca as initial symptoms. A secondary objective was to correlate disease onset form with age, sex, disease activity, accumulated damage, and other concomitant EGM.

Methods: Multicenter, observational, analytical, cross-sectional study. Consecutive patients ≥ 18 years of age with a diagnosis of pSS were included. Demographic and disease characteristics and clinimetric indices were recorded. EGM were defined by the EULAR-SS disease activity index (ESSDAI). The delay time from the EGM presentation to the diagnosis of the disease, and the time since the pSS diagnosis to the EGM presentation were considered.

Results: One-hundred eleven patients were included, 93% women, mean age 48.7 years (SD 13.2). 97.3% of the patients presented sicca symptoms (being the initial manifestation of the disease in 47% of them) and 90.9% had at least one EGM (being the initial symptom in 53% of the cases). The most frequent initial EGM was joint involvement (70.3%), followed by biological (32.6%) and pulmonary involvement (23.7%). No significant difference was observed in the time from the first manifestation and the diagnosis between the group that started with sicca (92 months [CI95 39.3-134.9] and that with EGM at onset (44.2 months [CI 95 29.2-59.2]); p = 0.063. Patients with EGM as initial symptom were younger at diagnosis compared to those who started with sicca symptoms (46.3 vs 51.4 years, p = 0.042). Mean ESSDAI score was higher in the group with EGM as initial symptom (1.2 vs 0.9; p = 0.002), while mean Sjögren's Syndrome Disease Activity Index (SSDI) score was higher those with initial sicca symptoms (1.3 vs 0.9; p = 0.023). No significant differences were observed in other disease characteristics, or in the distribution of different EGM between the groups with sicca or EGM onset.

Conclusion: More than half of the patients with pSS presented an extraglandular involvement at disease onset. There were no differences in the time from the first manifestation to the diagnosis between the groups with sicca or extranglandular onset.

Disclosure: L. Alascio, None; **S. Papasidero**, None; **M. Medina**, None; **J. Bande**, None; **S. Perez**, None; **E. Serrano**, None; **D. Klajn**, None; **J. Caracciolo**, None; **R. Tralice**, None; **E. Rodríguez**, None; **F. Romanini**, None; **A. Secco**, None; **S. Zalles**, None; **C. Segura Escobar**, None; **J. Demarchi**, None; **G. Earsman**, None; **L. Raiti**, None; **S. Velez**, None; **A. Martinez**, None.

Abstract Number: 0304

Renal Involvement in Sjőgren's Syndrome: Predictors and Impact on Patient Outcome

Rudrarpan Chatterjee[1], Anu Balakrishnan[2], Rajat Kharbanda[1], Upendra Rathore[1], Latika Gupta[1], Durga P Misra[1], Vikas Agarwal[2], Amita Aggarwal[1] and Able Lawrence[2], [1]Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India, [2]Sanjay Gandhi Postgraduate Institute of Medical Sciences, Lucknow, India

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

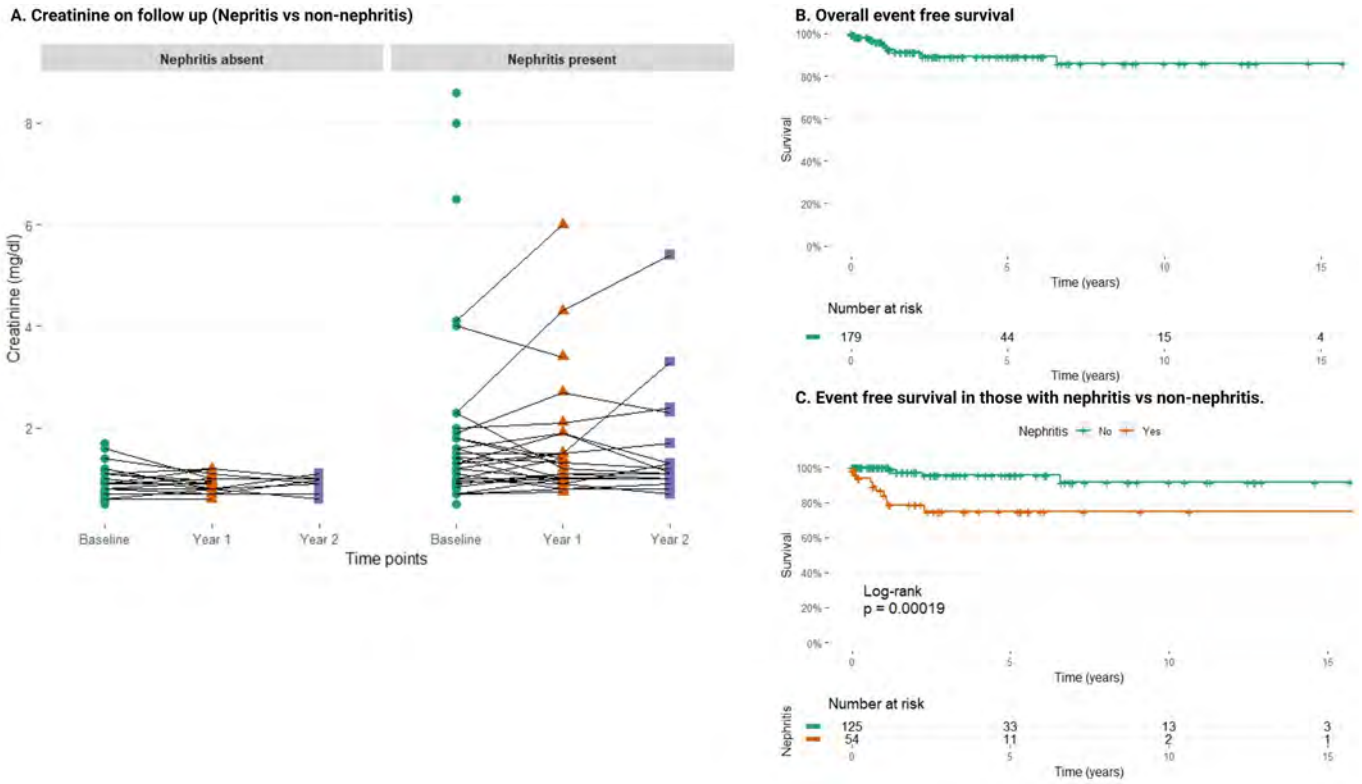
Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Clinical and laboratory features of nephritis in Sjogren's syndrome

	Nephritis (n=54)	Non nephritis (n=125)	Univariate odds ratio (95% CI)
Age (years)	40.19 (13.3)	42.18 (12.9)	-
Female sex	51 (94.4)	115 (92)	1.47(0.39-5.55)
Raynauds	7 (12.9)	11 (8.8)	1.54(0.56-4.22)
Polyarthritis	24 (44.4)	74 (59.7)	0.55(0.29-1.05)
Sicca	40 (74.1)	105 (84)	0.54(0.25-1.18)
Parotitis	6 (11.1)	11 (8.8)	1.30(0.45-3.70)
Vasculitis	13 (24.1)	15 (12)	**2.33(1.02-5.30)***
Photosensitivity	3 (5.6)	11 (8.8)	0.61(0.16-2.88)
Interstitial lung disease	6 (11.1)	25 (20)	0.50(0.19-1.30)
Neuropathy	8 (14.8)	12 (9.6)	1.64(0.63-4.27)
Fatigue***	23 (42.6)	23 (18.4)	**3.29(1.63-6.65)*****
Depression	8 (14.8)	12 (9.6)	1.64(0.63-4.27)
ANA positive*	53 (98.1)	102 (81.6)	**7.79(1.00-60.62)***
Ro52 positive*	45 (83.3)	78 (62.4)	**2.74(1.18-6.39)***
Ro60 positive	43 (79.6)	83 (66.4)	1.71(0.77-3.80)
La*	27 (0.5)	38 (30.4)	**2.13(1.10-4.14)***
Both Ro and La*	27 (0.5)	35 (28)	**2.40(1.23-4.69)***
Lymphopenia*	26 (48.1)	34 (27.2)	**2.27(1.16-4.41)***
Thrombocytopenia	13 (24.1)	29 (23.2)	0.95(0.45-2.02)
Hypergammaglobulinemia	29 (53.7)	42 (33.6)	1.91(0.97-3.78)
C3	118.8 (39.4)	100.99 (27.5)	-
C4	24.94 (14.7)	24.62 (9.9)	-
Rheumatoid factor	223.1 (441.2)	172.8 (301)	-
Baseline creatinine***	1.62(1.65)	0.85(0.2)	-
Creatinine (1 year follow up)***	1.6(1.17)	0.88(0.16)	-
Creatinine (2 year follow up)**	1.62(1.19)	0.88(0.17)	-

Lymphopenia: Absolute lymphocyte count<1500/cumm, thrombocytopenia: platelet count<1.5x10^6/cumm. *: p value<0.05, **: p value<0.01, ***:p value<0.001



Background/Purpose: Renal disease in primary Sjogren's syndrome (pSS) can occur in form of tubulointerstitial nephritis (TIN) or glomerulonephritis (GN). Data from India on pSS is sparse and that on nephritis is even less. Thus, we studied the prevalence and impact of renal disease on patient outcomes.

Methods: Retrospective review of 179 (F:M 12.7:1, age 41.7±12.9 years) patients of pSS (ACR 2016 criteria) was carried out from electronic health records at a single centre from 2000 to 2020. Data on nephritis and other clinical and laboratory variables was collected from baseline visit. Outcomes studied were chronic kidney disease (CKD) and death. Multivariate logistic regression was used to identify predictors. Linear mixed effects models were used to predict rise in creatinine on follow up. Kapan Meier survival analysis was undertaken for a composite outcome of death or CKD.

Results: Among 179 patients with pSS 54 (30.17%) patients had nephritis. Their mean age was 40.19 (13.28) years and they had 157.3 person years follow up. 26 of these 54 patients presented with hypokalemic paralysis (Table 1). Of the 10 renal biopsies, TIN was present in 8 and mesangioproliferative GN in 2.

Vasculitis (OR 2.33), fatigue (OR 3.29), ANA positivity (OR 7.79), anti-Ro52 (OR 2.74), anti-La (OR 2.13), both Ro and La (OR 2.4) and lymphopenia (OR 2.27) were associated with nephritis on univariate analysis. On multivariate analysis, only fatigue (OR 2.83) and an interaction between polyarthritis and vasculitis (OR 9.17) was associated with nephritis.

Creatinine at 1 year (1.6±1.17 vs 0.8±0.2) and 2 years (1.62±1.19 vs 0.8±0.2) follow-up was higher in the nephritis group than those without nephritis (Figure 1a). Adjusted for immunosuppression used, baseline hematuria, leucocyturia, 24 hour urinary protein and thrombocytopenia were independent predictors of rise in creatinine on follow up. Six patients died and 10 patients developed CKD. Event (death or CKD) free survival was 89.1% at 5 years (Figure 1b). Patients with nephritis had worse event free survival as compared to those without nephritis (Figure 1c).

Conclusion: In our cohort almost 1/3rd had nephritis and its presence lead to higher probability of death or CKD.

Disclosure: R. Chatterjee, None; **A. Balakrishnan**, None; **R. Kharbanda**, None; **U. Rathore**, None; **L. Gupta**, None; **D. Misra**, None; **V. Agarwal**, None; **A. Aggarwal**, None; **A. Lawrence**, None.

Abstract Number: 0305

Artificial Neural Networks Approaches to Predict Myocardial Fibrosis in Primary Sjögren Syndrome Patients Without Cardiac Symptoms

Hitomi Kobayashi[1], Yasuyuki Kobayashi[2], Atsuma Nishiwaki[1], Isamu Yokoe[1], Haraoka Masaki[3], Eichi Takaya[3], Yousuke Nagasawa[1], Noboru Kitamura[1], Masami Takei[1] and Hideki Nakamura[1], [1]Nihon University School of Medicine, Itabashi, Japan, [2]St. Marianna University School of Medicine, kowasaki, Japan, [3]St. Marianna University School of Medicine, Kawaski, Japan

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
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Session Time: 8:30AM–10:30AM

Background/Purpose: A recent meta-analysis of cardiovascular diseases demonstrated that the odds of heart failure (HF) was more than 2.54-fold higher in primary Sjögren syndrome (pSS) patients than controls. Cardiac magnetic resonance imaging (CMR) is useful for the early assessment of myocardial abnormalities that precede the development of overt HF. Myocardial dysfunction may arise from a number of distinct processes, including myocardial fibrosis. Global longitudinal strain (GLS), using non-contrast feature tracking cardiac magnetic resonance (FT-CMR), has been reported to be significantly associated with the extent of myocardial fibrosis. Late gadolinium enhancement (LGE) is correspond to myocardial fibrosis. In the last years, artificial neural networks (ANNs) approaches have been shown to be an established method for analyzing large datasets. ANNs could be a useful prediction tool in medical scenarios. This study aimed to predict myocardial fibrosis in pSS assessed by FT-CMR and LGE, by using ANNs models.

Methods: This was a cross-sectional study of patients with pSS registered in our hospital between January 2014 and April 2018. Healthy volunteers were recruited as a control group to be frequency-matched to the age and sex distribution of the pSS patients. pSS patients and controls with no known heart disease or risk factors who underwent CMR. We used a random forest classifier to predict myocardial abnormality in two indices (LGE, GLS). This is an algorithm that uses multiple decision trees for classification. The number of trees in the forest were set as 100. The criteria used to measure the quality of a split was Gini impurity. The classification threshold was set to 0.5. Inputs for the classifier included many valuables including attributes and observed values. The number of variables was finally reduced to 10 (e.g., age, duration, Raynaud phenomenon, body mass index, Framingham score, ESR, rheumatoid factor, IgG, hemoglobin A1c, and N-terminal pro b-type natriuretic peptide) by feature selection based on the trained model.

Results: We evaluated 52 patients with pSS (100% women; mean age, 59.5 ± 9. 0 years) and 20 healthy controls (100% women; mean age, 55.7 ± 4.5 years). All 72 subjects underwent FT-CMR and 52 patients underwent LGE. The pSS patients had significantly lower GLS (p = 0.015) than controls. Abnormal LGE was seen in 10/52 subjects (19%). We created a mathematical model to be able to predict abnormal GLS and LGE with an area under the curve value of 0.72 and 0.79, respectively. The accuracy, sensitivity, specificity, positive predictive value, and negative predictive value for prediction of GLS and abnormal LGE value were 88%, 40%, 100%, 100%, 86%, and 67%, 30%, 88%, 56%, 70%, respectively.

Conclusion: We applied ANNs to identify a prediction model for myocardial fibrosis in pSS patients without cardiac symptoms assessed by CMR. The use of laboratory and clinical items enabled to construct a mathematical model,

potentially identifying pSS patients with myocardial fibrosis. This prediction tool could be used in a clinical practice setting to stratify pSS patients according to myocardial fibrosis.

Disclosure: H. Kobayashi, None; **Y. Kobayashi**, CANON MEDICAL SYSTEMS, 5; **A. Nishiwaki**, None; **I. Yokoe**, None; **H. Masaki**, None; **E. Takaya**, CANON MEDICAL SYSTEMS, 5; **Y. Nagasawa**, None; **N. Kitamura**, None; **M. Takei**, None; **H. Nakamura**, None.

Abstract Number: 0306

Allergic Disorders in Primary Sjögren's Syndrome Compared with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Allergic disorders are occasionally seen in patients with primary Sjögren's syndrome (pSS) [1]. Risk factors are unclear for allergic disorders.

We aimed to compare the prevalence of allergic disorders in pSS and rheumatoid arthritis (RA) ,and to compare the clinical features at diagnosis of pSS with and without drug allergies.

Methods: We retrospectively examined consecutive patients diagnosed with pSS or RA in our hospital from 2010 to 2020. The patients with SS met the criteria of the 1999 revised Japanese Ministry of Health criteria [2]. We included patients with pSS without RA or other rheumatic diseases. The patients with RA met the EULAR/ACR 2010 criteria. We included patients with RA without other rheumatic diseases.

Table 1. Allergic Disorders and Drug Allergies in pSS and RA

	pSS (n = 292)	RA(n= 413)	P
at least one type of allergy, n (%)	160 (54.8)	144 (34.9)	<0.01
food allergy, n (%)	35 (12.0)	27 (6.7)	0.02
drug allergy, n (%)	76 (26.1)	69 (16.7)	<0.01
allergic contact dermatitis, n (%)	10 (3.4)	19 (4.6)	0.6
allergic rhinitis and/or conjunctivitis, n (%)	99 (33.9)	35 (8.5)	<0.01
asthma, n (%)	29 (9.9)	25 (6.1)	0.06

Table 2. Characteristics of patients and prevalence of drug allergy in patients with pSS

	With drug allergy (n = 77)	Without drug allergy (n = 215)	P
Female, n (%)	74 (96.1%)	201 (93.5%)	0.57
Age, year	56.0±15.8	57.8±15.8	0.40
At least one type of allergic diseases, n (%)	77 (100.0%)	84 (26.7%)	<0.01
Food allergy, n (%)	15 (19.5%)	20 (9.3%)	0.02
allergic contact dermatitis, n (%)	4 (5.2%)	6 (2.8%)	0.30
allergic rhinitis and/or conjunctivitis,, n (%)	33 (42.9%)	66 (30.7%)	0.07
Asthma, n (%)	8 (10.4%)	21 (9.8%)	0.83
atopic dermatitis, n (%)	7 (9.1%)	8 (3.7%)	0.08
WBC, /μL	5120.3±1532.2	4996.8±1536.3	0.55
NEUT, %	65.6±73.2	58.7±11.6	0.19
LYMPH, %	31.2±8.5	32.2±0.7	0.44
EOSINO, %	4.1±0.3	2.5±2.1	<0.01
EOSINO, /μL	220.0±247.1	126.4±112.4	<0.01
BASO, %	0.6±0.4	0.7±0.7	0.55
MONO, %	6.9±2.4	6.3±0.1	0.050
RBC, 10^4/μL	417.9±44.0	416.9±62.1	0.90
Hb, g/dL	12.6±0.8	13.1±0.5	0.58
PLT, 10^4/μL	22.9±5.5	22.5±6.2	0.63
ESR, mm/1h	34.7±21.4	31.7±21.4	0.35
TG, mg/dL	99.3±59.1	129.6±86.4	0.24
TP, g/dL	7.7±0.8	7.6±0.6	0.32
Alb, g/dL	4.2±0.3	4.2±0.3	0.91
Cre, mg/dL	0.7±0.1	0.7±0.2	0.39
IgG, mg/dL	2027.9±1408.9	1725.6±586.8	0.01
IgA, mg/dL	262.6±140.8	289.1±142.6	0.18
IgM, mg/dL	117.7±67.7	118.2±75.3	0.97
IgE, IU/mL	283.2±466.2	347.0±588.8	0.74
AST, U/L	24.9±8.7	24.0±9.4	0.51
ALT, U/L	20.4±11.3	20.1±11.7	0.84
CRP, mg/dL	0.17±0.59	0.31±1.5	0.45
Patients with anti-SSA antibody, n (%)	69 (89.6%)	169 (79.2%)	0.06
Patients with anti-SSB antibody, n (%)	37 (48.7%)	80 (40.0%)	0.22

The first analysis was performed on five types of allergic reactions: (1) food allergy (exanthema, angioedema and anaphylaxis after foods exposure), (2) drug allergy (exanthema, angioedema and anaphylaxis after drug exposure), (3) allergic contact dermatitis such as metals, alcohol swab, and other cosmetics, (4) seasonal allergic rhinitis and/or allergic conjunctivitis, and allergic rhinitis and/or allergic conjunctivitis associated with house dust, and (5) asthma.

The secondary analysis was performed on patient baseline laboratory data at diagnosis of pSS and RA patients with or without drug allergies.

Results: In the first analysis, 292 patients with pSS and 413 patients with RA were enrolled (Table 1). The mean ages (pSS, RA) were 57.3±15.8, 66.0±14.6 years old. Females were 94.2% , 78.2%. The mean observation period was 82.7±70.8, 65.6±37.0 months. 54.8% of pSS patients and 34.9% of RA patients presented at least one type of allergic disorders or drug allergies. These included food allergy, drug allergy, allergic rhinitis/conjunctivitis, and asthma. Allergic disorders and drug allergies were more frequent in patients with pSS.

In the second analysis, 77 patients with drug allergies and 215 patients without drug allergies were enrolled (Table 2). The mean ages with drug allergies and without drug allergies were 56.0±15.8 and 57.8±15.8 years old, respectively; females were 96.1% and 93.5%; the mean observation period was 90.9±72.4 and 79.8±70.2 months (Table 2). The pSS patients with drug allergies had higher levels of Immunoglobulin G (IgG) ($p = 0.01$), higher levels of eosinophils ($p< 0.019$), and higher positivity rate of anti–Sjögren's-syndrome-related antigen A autoantibody (anti-SSA antibody) than those without drug allergies ($p = 0.06$) (Table 2).

Conclusion: Patients with pSS had a higher prevalence of allergic disorders and drug allergies than patients with RA. Among patients with pSS, patients with drug allergies had higher levels of IgG, higher levels of eosinophils, and higher positivity rate of anti-SSA antibody than those without drug allergies.

[1] Hama et al. Clinical features of patients with Sjoegren syndrome associated with adult onset Still's disease. Japan College of Rheumatology Annual Congress 2020.

[2] Fujibayashi et al. Revised Japanese criteria for Sjögren's syndrome (1999): availability and validity. Mod Rheumatol. 2004; 14: 425-34 .

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Abstract Number: 0307

Cerebellar Ataxia in Primary Sjogren's Syndrome, Is Gluten Sensitivity the Answer?

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cerebellar ataxia is an uncommon neurological complication of Primary Sjogren's Syndrome (PSS), with case reports being the highest level of evidence available. The underlying disease pathogenesis is unknown, although an immunologically mediated mechanism seems plausible. Gluten sensitivity is common amongst patients with PSS and is a known cause of immune mediated ataxia (gluten ataxia). We aimed to investigate the presence of ataxia in patients with PSS seen in the joint rheumatology-neurology clinics at our institution, and determine if gluten sensitivity is responsible for cerebellar ataxia in some of these patients.

Methods: A retrospective review of all patients who attend the rheumatology and joint rheumatology-neurology clinics was conducted. Patient data including patient demographics, the presence of gluten sensitivity-related antibodies (anti-tissue transglutaminase 2, anti-gliadin IgG and IgA, endomysial antibodies, anti-transglutaminase 6 IgG and IgA), were collected. Patients attending the rheumatology clinics with PSS were asked about the presence of any symptoms of unsteadiness. Such patients underwent MR spectroscopy of the cerebellum looking for any evidence of abnormal cerebellar metabolites (N-acetylaspartate–to-creatine (NAA/Cr) ratio < 1). Electrophysiology results in the form of nerve conduction studies (NCS) or electromyography (EMG) were also collected.

Results: We identified 45 patients with symptoms of impaired balance. Not all of the 236 patients with PSS who regularly attend the rheumatology clinics were assessed for any evidence of loss of balance. Nonetheless, at least 45 out of 236 patients (19.1%) complained of balance problems. The majority of these patients were female (41/45, 91.1%) with a mean age of 64.3 years. Thirty-three out of 45 patients with ataxia (73.3%) tested positive for one or more of gluten sensitivity-related antibodies, with IgA TG6 being the most common (17/33 patients, 51.5%). Out of the 33 gluten sensitive patients, 25 had MR spectroscopy of the cerebellum and 17/25 (68%) had an abnormal NAA/Cr ratio. Twenty-two patients had NCS/EMG studies performed, of which 13 (59.1%) had either a sensory-motor neuropathy or sensory ganglionopathy.

Conclusion: The high prevalence of gluten sensitivity-related autoantibodies, combined with objective evidence of ataxia, suggest that gluten sensitivity may be responsible for the majority of cases of ataxia in PSS. The presence of a neuropathy in some of these patients suggests that sensory ataxia may also be contributing to the impaired balance in some of these patients. There is, however a cohort of patients with ataxia and PSS who are not gluten sensitive. These patients may well have primary autoimmune cerebellar ataxia (PACA). Whilst a therapeutic response to a gluten free diet in patients with gluten ataxia has already been established, it remains to be seen if those patients with PSS and ataxia who have no evidence of gluten sensitivity may benefit from immunosuppression.

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Abstract Number: 0308

Sleep Disorders and Serum Brain-derived Neurotrophic Factor Levels in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: This study aimed to evaluate the sleep quality and its influenced factors in patients with primary Sjögren's syndrome (pSS), and another purpose is to initially explore the clinical significance of serum brain-derived neurotrophic factor (BDNF) in pSS patients.

Methods: A total of 111 pSS patients and 40 age- and sex-matched healthy controls were enrolled in a comparative study of sleep quality using the Pittsburgh Sleep Quality Index(PSQI). Participants completed the following questionnaires including demographic, clinical and laboratory data, assessment of psychological conditions. Serum samples of 63 patients and 25 healthy controls among the all subjects were be collected and serum BDNF levels of them were be detected with ELISA kits.

Results: The frequency of sleep disorder was higher in the pSS patients(68.5%) than in the control subjects(25%). There were positive correlations among age, disease duration, pain, fatigue, anxiety/depression, Xerostomia, and sleep quality in pSS patients. Meanwhile, logistic regression models identified depression, EULAR SS Patient Reported Index (ESSPRI), sweating symptoms were independent risk factors for sleep disorders.

Mean serum levels of BDNF in pSS patients with sleep disorder were significantly higher than in healthy controls and negatively correlated directly with sleep quality in patients with pSS.

Conclusion: The majority of Chinese pSS patients suffered from poor sleep, which significantly impairs their quality of life. The data suggested the need for holistic assessment and management of pSS patients and the importance of objective interventions to improve their sleep quality and finally to lead a better life. BDNF is reduced in pSS patients with sleep disorders, and it may be a biomarker for predicting sleep disorders.

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Abstract Number: 0309

Lymphopenia and Leukopenia in Sjogren Syndrome

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Comparison of clinical and laboratory features between SS leukopenic patients and non leukopenic SS controls

DEMOGRAPHICS	LEUKOPENIA n= 92	CONTROLS n= 184	P VALUE
Median age at disease diagnosis, years (range)	53, (20-79)	54, (18-78)	0.89
Median disease duration from SS diagnosis to last follow up, years (range)	5, (0-22)	4, (0-25)	0.46
GLANDULAR AND NON SPECIFIC MANIFESTATIONS			
Dry mouth	92,1% (82/89)	91,1% (164/180)	0.95
Dry eyes	92,4% (85/92)	91,8% (168/183)	0.94
Salivary gland enlargement	38,4% (35/91)	18,8% (34/181)	**0.0007**
Raynaud's phenomenon	29,8% (53/91)	26,5% (30/180)	0.64
Arthralgias	61,9% (57/92)	71% (130/183)	0.16
Arthritis	14,2% (13/91)	17,2% (30/174)	0.65
Extraepithelial manifestations			
Glomerulonephritis	1% (1/92)	1% (2/183)	1
Interstitial Lung Disease	2.7% (3/92)	3.2% (5/183)	1
Autoimmune hepatitis	0% (0/92)	0.7% (1/138)	1
Peripheral nervous disease	2.1% (2/92)	2,7% (5/183)	1
Palpable purpura	16.3% (15/92)	7.6% (14/183)	**0.04**
Persistent lymphadenopathy	20.6% (19/92)	10% (20/183)	**0.04**
Periepithelial manifestations			
Tubulointerstitial nephritis	1% (1/92)	3.8% (7/183)	0.27
Small Airway disease	4.3% (3/92)	1.6% (4/183)	0.22
Primary biliary cholangitis	0% (0/92)	2.1% (4/183)	0.30
Autoimmune thyroiditis	28.5% (14/49)	43% (35/80)	0.12
SEROLOGY			
Rheumatoid Factor	63.4% (52/82)	58.6% (95/162)	0.56
Anti-Ro	86.9% (80/92)	65.7% (117/178)	**0.0003**
Anti-La	54.9% (50/91)	33.1% (58/175)	**0.0009**
LOW C4	69.4% (58/85)	34.7% (59/167)	**<0.0001**
Monoclonality	14.1% (11/78)	8.8% (15/169)	0.30
Cryoglobulinemia	25.3% (11/63)	13%(16/84)	0.09
ANA antibodies	94.1% (80/85)	84.5% (149/176)	**0.03**
LYMPHOMA	22.8% (21/92)	10% (19/182)	**0.01**

Background/Purpose: Peripheral lymphopenia and leukopenia in Sjögren's syndrome (SS) may suggest systemic disease activity and have been proposed as lymphoma predictors. However, the clinical phenotype of these subsets of SS patients is poorly defined. The objective of the present study is to investigate whether leukopenia and lymphopenia at SS diagnosis interferes with clinical manifestations, serology, disease course and lymphoma development.

Table 2. Comparison of clinical and laboratory features between SS lymphopenic patients and non lymphopenic SS controls

DEMOGRAPHICS	LYMPHOPENIA n= 68	CONTROLS n= 136	P VALUE
Median age at disease diagnosis, years (range)	57, (26-77)	56, (23-77)	0.66
Median disease duration from SS diagnosis to last follow up, years (range)	6, (0-25)	4.5, (0-23)	0.39
GLANDULAR AND NON SPECIFIC MANIFESTATIONS			
Dry mouth	95.5% (65/68)	89.7% (122/136)	**0.04**
Dry eyes	94.1% (64/68)	88.8% (120/135)	0.30
Salivary gland enlargement	45,4% (30/66)	22.3% (30/134)	**0.001**
Raynaud's phenomenon	30.8% (21/68)	28.5% (38/133)	0.85
Arthralgias	58.8% (40/68)	72.7% (99/136)	0.06
Arthritis	20.5% (14/68)	15.2% (19/125)	0.07
Extraepithelial manifestations			
Glomerulonephritis	1.4% (1/68)	1.4% (2/135)	1
Interstitial Lung Disease	5.8% (4/68)	4.4% (6/136)	0.73
Autoimmune hepatitis	1.4% (1/68)	1.9% (2/104)	1
Peripheral nervous disease	4.4% (3/68)	2.2% (3/136)	0.40
Palpable purpura	29.4% (20/68)	8.8% (12/136)	**0.0003**
Persistent lymphadenopathy	22% (15/68)	12.5% (17/136)	0.11
Periepithelial manifestations			
Tubulointerstitial nephritis	0% (0/68)	2.2% (3/136)	0.55
Small Airway disease	4.4% (3/68)	2.2% (3/135)	0.40
Primary biliary cholangitis	0% (0/68)	2.9% (4/136)	0.30
Autoimmune thyroiditis	25% (10/40)	35.4% (22/62)	0.37
SEROLOGY			
Rheumatoid Factor	58.4% (38/65)	57.8% (74/128)	0.94
Anti-Ro	74.2% (49/66)	65.4% (87/133)	0.27
Anti-La	45.4% (30/66)	36.1% (47/130)	0.26
LOW C4	67.1% (43/64)	33% (40/121)	**<0.0001**
Monoclonality	16.3% (10/61)	5.5% (7/127)	**0.03**
Cryoglobulinemia	29.4% (15/51)	11.1%(7/63)	**0.02**
ANA antibodies	95.2% (60/63)	84.6% (110/130)	**0.03**
LYMPHOMA	39.7% (27/68)	13.2% (18/136)	**<0.0001**

Methods: From a total population of 1017 consecutive patients fulfilling the 2016 ACR-EULAR criteria for SS, who were followed-up in 3 centers from Greece (Universities of Athens, Harokopio and Ioannina), those with persistent lymphopenia or leukopenia were identified and matched with non-lymphopenic and non-leukopenic SS controls respectively, according to age at SS diagnosis, gender and disease duration from SS diagnosis to last follow up in a 1:2 ratio. Persistent lymphopenia and leukopenia were defined as an absolute lymphocyte and white blood cell count

< 1000/mm^3 and 4000/mm^3, respectively, detected in at least 3 consecutive visits within 1 year after SS diagnosis. Cumulative data regarding glandular (dry mouth, dry eyes, parotid gland enlargement) and extra-glandular manifestations (Raynaud's phenomenon, lymphadenopathy, arthralgias/arthritis, palpable purpura, liver involvement, kidney involvement, lymphoma), serology (anti Ro/SSA, anti La/SSB, rheumatoid factor, cryoglobulinemia, low C4 complement levels) and histologic features (focus score, presence) were recorded and compared between each study group and their matched SS controls. Statistical analysis for categorical data was performed by Fisher exact test or χ^2 square test accordingly and numerical data with Man Whitney test.

Results: Ninety-two SS patients with leukopenia and 68 with lymphopenia were identified and compared with 184 and 136 non-lymphopenic and non-leukopenic SS controls, respectively. Twenty-four SS patients had both leukopenia and lymphopenia and participated in both study groups. The median disease duration of leukopenic and lymphopenic SS patients was 5 (range: 0 -22) and 6 years (range: 0-25) respectively whereas the median age of SS diagnosis was 53 (range: 20-79) and 57 (range:26-77) years old respectively. SS patients with leukopenia had statistically significant higher frequency of salivary gland enlargement (38,4% vs 18,8%, p=0,0007), palpable purpura (16,3% vs 7,6%, p=0,04), persistent lymphadenopathy (20,6% vs 10%, p=0,04), ANA antibodies (94,1% vs 79,9%, p=0.03), anti SSA/Ro antibodies (86,9% vs 65,7%, p=0,0003), anti SSB/La antibodies (54,9% vs 33,1%, p=0,0007), low C4 serum levels (69,4% vs 34,7%, p=0,007) and lymphoma (22,8% vs 10,4%, p= 0.01) (Table 1). SS patients with lymphopenia had more frequently salivary gland enlargement (45,4% vs 22,3%, p=0.001), palpable purpura (29,4% vs 8,8%, p=0.0003), ANA antibodies (95,2% vs 79,9%, p=0.003)), low C4 serum levels (67,1% vs 33%, p< 0.0001), cryoglobulinemia (29,4% vs 11,1%, p=0.02) and lymphoma (39.7% vs 13.2%, p= < 0.001) (Table 2).

Conclusion: SS patients with leukopenia and lymphopenia constitute specific disease subgroups with distinct clinical phenotypes associated with increased lymphoma prevalence.

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Abstract Number: 0310

Histopathology, Salivary Flow and Ultrasonography of the Parotid Gland: Three Complementary Measurements in Primary Sjögren's Syndrome

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Primary Sjögren's syndrome is a systemic autoimmune disease characterized by dryness of the mouth and eyes. The impact of the disease on salivary glands can be assessed in three different ways: by salivary gland histopathology, measuring salivary flow and salivary gland ultrasonography. To understand the relative value of these different approaches for disease evaluation, it is crucial to understand the relationship between them. As we are in the unique position to explore this relationship in the parotid gland, we aimed to assess construct validity between the three different modalities in the same parotid gland.

Methods: Consecutive patients underwent a diagnostic work-up including a parotid gland biopsy, collection of stimulated parotid gland saliva and parotid ultrasonography. Patients who were classified as primary Sjögren's syndrome according to the ACR-EULAR criteria were included. Construct validity was assessed using Spearman's correlation coefficients.

Results: A total of 41 patients with primary Sjögren's syndrome were included. All patients completed a full work-up within a mean time interval of 2.6 months. Correlations between histopathological items and stimulated parotid salivary flow were poor to fair (ρ=-0.123 for focus score and ρ=-0.259 for percentage of $CD45^+$ infiltrate). Likewise, poor correlations were observed between stimulated parotid salivary flow and parotid ultrasonography (ρ=-0.196). Moderate to good associations were found between histopathological items and parotid ultrasound scores (total ultrasound score: ρ=0.510 for focus score and ρ=0.560 for percentage of $CD45^+$ infiltrate; homogeneity: ρ=0.574 for focus score and ρ=0.633 for percentage of $CD45^+$ infiltrate).

Conclusion: Parotid gland salivary flow was not related to parotid gland histology, nor to parotid gland ultrasonography. Although pSS associated ultrasonographic findings correlated to some extent with the amount of inflammatory infiltrate in the parotid gland biopsy, we conclude that the three modalities that evaluate salivary gland involvement assess different (or at best partly related) constructs. Therefore, histopathology, salivary flow and ultrasonography are complementary measurements and cannot directly replace each other in the work-up of pSS.

Disclosure: M. van Ginkel, None; **E. Mossel**, None; **E. Haacke**, None; **S. Arends**, None; **S. Liefers**, None; **K. Delli**, None; **J. van Nimwegen**, None; **A. Stel**, None; **F. Spijkervet**, None; **A. Vissink**, BMS, 5, Roche, 5; **B. van der vegt**, None; **F. Kroese**, Bristol Myers Squibb, 5, Roche, 5; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2.

Abstract Number: 0311

Ultra High-frequency Ultrasound (UHFUS) of Labial Glands in Primary Sjögren's Syndrome: Serological and Histological Correlations

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Last-generation ultra high-frequency ultrasound (UHFUS) transducers are highly sensitive tools potentially able to open new avenues for the identification of imaging biomarkers. Recently UHFUS has been applied to the study of labial salivary glands (LSG) in patients with suspected primary Sjögren's syndrome (pSS) showing a good diagnostic accuracy in identifying pSS from no-SS sicca. Objective**:**1. to assess the association between UHFUS scoring and LSG histology in patients with established pSS; 2. to explore the association between LSG-UHFUS scoring and anti-Ro antibody specificity (i.e. both anti-Ro60 and Ro52 or isolated anti-Ro52 and anti-Ro60 antibodies).

Methods: Out of a cohort of 207 patients who underwent a UHFUS guided LSG biopsy for suspected pSS (Jan 2018-Apr 2021), we identified 92 patients with an established newly diagnosed pSS (ACR/EULAR 2016 criteria). Patients' clinical, biological and histological features were collected. The anti-Ro antibody specificity and titer were determined by immunoblotting. UHFUS of LSG was performed by using VEVO MD, equipped with a 70 MHz probe, evaluating parenchymal inhomogeneity (score 0-3). For each of the LSG specimens number of foci, focus score (FS) and ectopic lymphoid structures (ELS) were assessed.

Results: We included a total of 92 pSS patients: 41 (44.6%) with anti-Ro60 and anti-Ro52, 6 (6.5%) with anti-Ro60 alone, 25 (27.2%) with anti-Ro52 alone, and 20 (21.7%) with neither antibody. A UHFUS score 1 was observed in 32 (34.8%), a UHFUS score 2 in 47 (51.1%) and a UHFUS score 3 in 13 (14.1%) pSS patients. The UHFUS scoring was equally distributed within the four serotype subgroups; however, we observed a moderate correlation (r=0.300, p=0.01) between the UHFUS scoring and the anti-Ro60 titer. UHFUS score correlated also with IgG levels and with parotid and submandibular US (p< 0.05). No correlation was observed between UHFUS and ESSPRI, salivary flow and ocular tests. Regarding LSG histology, the higher was the UHFUS grading, the higher were: the number of foci (foci, mean (S.D) : 2.6 (2.8) in UHFUS-score 1 vs 5.9 (3.3) in UHFUS-score 3, p=0.001), the FS (FS, mean (S.D): 1.3 (1.2) in UHFUS-score 1 vs 2.1 (0.9) in UHFUS-score 3, p=0.01) and the number of ELS (ELS, mean (S.D): 0.9 (1.1) in UHFUS-score 1 vs 2.5 (1.9) in UHFUS-score 3, p=0.01). Noteworthy, out of the 13 patients with a UHFUS-score 3, 12/13 presented at least one ELS in their biopsies (p=0.01). UHFUS score-3 showed a specificity of 97.1% and a positive predictive value of 92.3% in the evaluation of ELS in LSGs.

Conclusion: UHFUS of LSG appeared significantly associated with serological and histological findings in pSS and may have a role in patients' stratification.

Disclosure: G. Fulvio, None; **F. Ferro**, None; **R. Izzetti**, None; **G. Governato**, None; **S. Fonzetti**, None; **G. La Rocca**, None; **V. Donati**, None; **D. Caramella**, None; **M. Mosca**, None; **C. Baldini**, None.

Abstract Number: 0312

Prognostic Value of Salivary Gland Ultrasonography in Primary Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: In the last decade, salivary gland ultrasonography (SGUS) has appeared as a useful tool for the diagnosis of primary Sjögren's syndrome (pSS) and for the identification of different disease phenotypes. Purpose: To evaluate the usefulness and prognostic value of SGUS in identifying pSS patients at risk of lymphoma

Methods: Sonographic data from a monocentric cohort of pSS patients were collected from 2012 to 2021. Salivary glands were scored using the latest 2019 OMERACT semiquantitative SGUS scoring systems (0-3) based on parenchyma inhomogeneity; SGUS≥2 indicates moderate or severe glandular alterations. For both the parotid glands (PG) and the submandibular glands (SMG), the worse finding of the two sides was used in the analyses. Patients demographics, clinical and histological data were recorded.

Results: We included 137 pSS patients (2 M:135 F, mean age 57±14 yrs) followed for a median follow-up of 43 (22) months. At baseline, 59/137 (43.1%) patients presented a PG-SGUS≥2 and 50/137 (36.5%) a SMG-SGUS≥2. Patients with a SGUS≥2 (either in their PGs or SMGs) presented more frequently hypergammaglobulinemia, Rheumatoid Factor, anti-Ro/SSA positivity and a higher focus score ($p< 0.01$). Patients with a PG-SGUS≥2 presented significantly more often markers of lymphoma development, such as salivary gland swelling, lymphopenia and low complement levels ($p< 0.01$). Over the follow-up, 4/137 patients developed a MALT lymphoma in their PGs. At baseline, all of them had a SGUS grade 3 in their PGs, and two had also a SGUS grade 3 in their SMGs. A significant association emerged between MALT lymphoma and both PG-SGUS≥2 and SMG- SGUS≥2 at baseline ($p< 0.05$). Particularly, PG-SGUS grade 3 was significantly associated with MALT lymphoma development ($p=0.01$).

Conclusion: SGUS may help to identify pSS patients at risk of lymphoma. Patients presenting a PG-SGUS grade 3 deserve a careful assessment to recognize possible lymphoproliferative complications in severely damaged salivary glands.

Disclosure: F. Ferro, None; **G. Governato**, None; **G. Fulvio**, None; **G. La Rocca**, None; **S. Fonzetti**, None; **G. Aringhieri**, None; **V. Donati**, None; **M. Mosca**, None; **C. Baldini**, None.

Abstract Number: 0313

Do Primary Sjögren's Syndrome Patients with Normal Major Salivary Gland Ultrasound Have Less Active Disease?

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultrasonographically depicted morphological changes of major salivary glands (SG) have been recently correlated with the disease activity in primary Sjögren's (pSS)[1]. The aim of our prospective, cross-sectional study was to determine whether pSS patients with normal SG ultrasound indeed have less active disease at baseline.

Methods: We included 129 consecutive adult pSS patients, diagnosed at our secondary - tertiary center between 2017-2019. All patients fulfilled the 2016 ACR/EULAR classification criteria[2] and underwent a routine diagnostic procedure including major SG ultrasound[3] and minor SG biopsy. Disease activity was assessed with ESSDAI[4]. Multivariate logistic regression was used to evaluate factors predicting baseline ESSDAI.

Results: Our pSS cohort consisted of 120 females and 9 males, with a median (IQR) age 62 (51-69) years, and median (IQR) symptom duration of 24 (10-41) months. Among them 95 (73.6 %) had antinuclear antibodies, 98 (76.0%) anti-SSA, 21 (16.3%) had anti-SSB, and 37 (28.6%) had rheumatoid factor (RF), respectively. Four patients had anticentromere antibodies. Twenty-nine (22.5%) patients had 3 or more different autoantibodies. Minor salivary gland biopsy was positive in 83 (64%) patients. Forty-nine patients (38.0%) had a positive major SG ultrasound. Median (IQR) ESSDAI was 2 (0-6), range 0-34 at baseline. Among the ESSDAI components articular and biological component predominated (Figure 1). Using multivariate analysis, we found no association between baseline ESSDAI, and SG US changes, histological focus score, the number of antibodies, patients' age, sex, symptom duration time, inflammatory parameters (ESR and CRP). The single parameter that predicted baseline ESSDAI was the presence of RF ($P < 0.001$). Only anti-SSB ($p=0.004$)) and antinuclear antibodies ($p=0.003$) emerged as predictors of positive SG ultrasound.

Figure 1. ESSDAI by components in our pSS cohort.

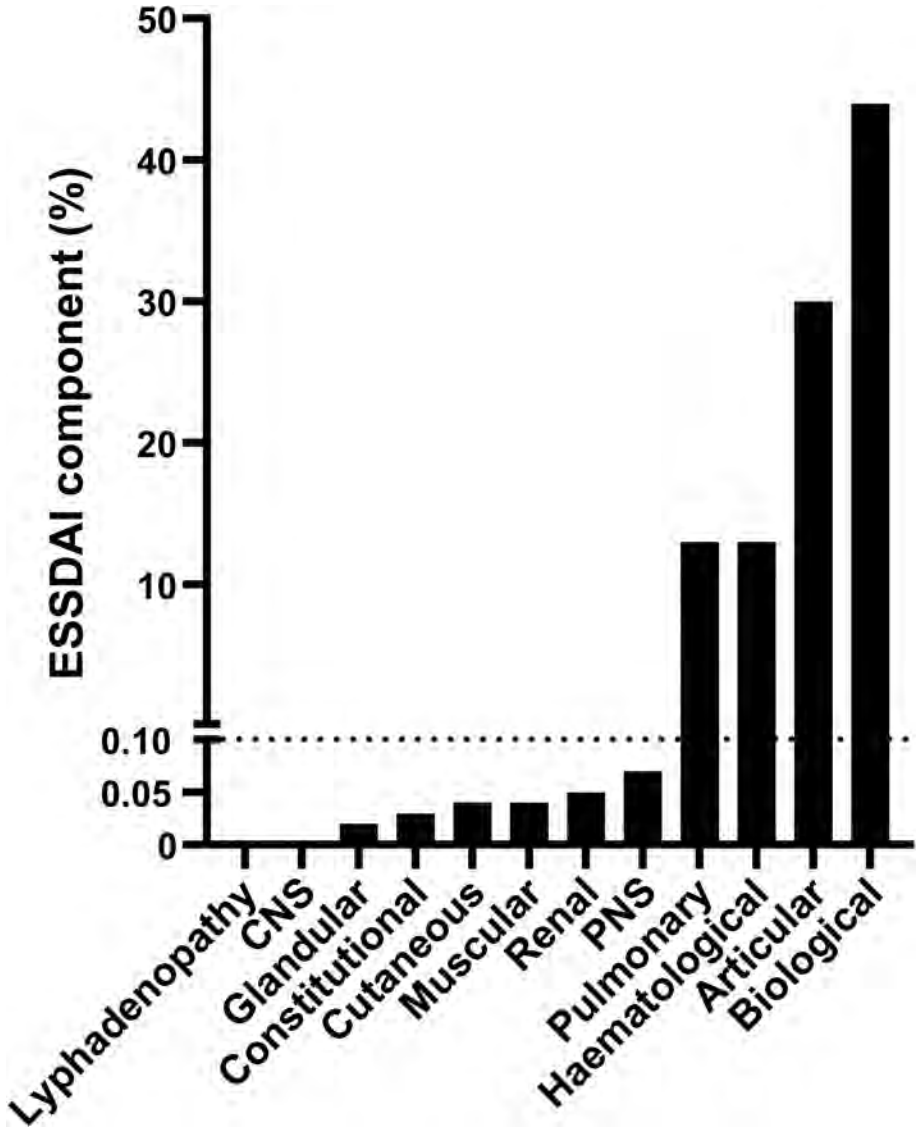

Table 1. Baseline demographic and clinical characteristics of patients who met 2016 ACR/EULAR Classification Criteria for Sjogren's Syndrome compared to those with sicca not otherwise specified (NOS)

Demographic/Clinical Characteristic	Primary Sjogren's Syndrome (n=227)	Sicca NOS (n=85)	*p* value
Age, mean (SD)	57 (14)	54 (12)	**0.030**
Gender, (n, % female)	211 (92%)	78 (92%)	0.92
Race (n, % white)	187 (82%)	69 (81%)	0.94
Ethnicity (n, % non-Hispanic)	220 (97%)	82 (99%)	0.28
Symptom Duration (SD), months	13.4 (9.3)	10.5 (7.9)	**0.013**
Lip Biopsy (n, % positive) *	59/84 (70%)	3/80 (3%)	**<0.001**
Anti-SSA antibodies (n, % positive)	206 (90%)	2 (2.4%)	**<0.001**
Schirmer's test (n, % <5 mm/5 min)	156 (68%)	25 (29%)	**<0.001**
Salivary Flow (n, % <0.1 ml/min)	93 (41%)	18 (21%)	**<0.001**
Current Medication Use:			
Hydroxychloroquine	139 (61%)	32 (38%)	**<0.001**
Methotrexate	25 (11%)	8 (9%)	0.69
Leflunomide	5 (2%)	3 (4%)	0.51
Azathioprine	6 (3%)	1 (1%)	0.44
Rituximab	15 (7%)	2 (2%)	0.14
Anxiolytic	47 (21%)	24 (28%)	0.15
Anti-depressant	54 (24%)	24 (28%)	0.41
ESSPRI (SD)			
Total (0-10)	5.4 (2.2)	5.5 (2.2)	0.73
Pain (0-10)	4.7 (2.9)	5.1 (2.7)	0.36
Dryness (0-10)	6.0 (2.6)	5.7 (2.5)	0.48
Fatigue (0-10)	5.6 (2.7)	5.8 (2.9)	0.59
PROMIS Global Profile Mean T-Score (SD)			
Pain Interference	56.9 (11.0)	60.3 (12.0)	**0.016**
Physical Function	44.2 (9.8)	41.6 (9.0)	0.360
Fatigue	57.2 (10.6)	59.7 (13.2)	0.080
Social Participation	46.9 (10.8)	43.5 (11.7)	**0.015**
Sleep Disturbance	52.2 (10.2)	55.3 (10.6)	**0.020**
Anxiety	52.7 (12.0)	54.7 (12.2)	0.18
Depression	49.1 (11.1)	50.8 (13.3)	0.24

ESSPRI= EULAR's Sjogren's Syndrome Patient Reported Index. *Positive lip biopsy defined as focal lymphocytic sialadenitis; of note, 63% of SS and 11% of sicca NOS patients did not have a completed lip biopsy.

Conclusion: Our results imply that SG US does not predict baseline pSS disease activity, determined by ESSDAI.

References: 1. Milic V, et al. PLoS One 2019. doi: 10.1371/journal.pone.0226498. 2. Shiboski CH et al. Arthritis Rheumatol 2017. doi: 10.1136/annrheumdis-2016-210571.3. Hocevar A et al. Rheumatology (Oxford) 2005. doi: 10.1093/rheumatology/keh588.4. Seror R, et al. ARD 2010. doi: 10.1136/ard.2009.110619corr1.

Table 2. Predictors of fatigue, pain, and Social Participation after controlling for age, gender, race, ethnicity, and symptom duration. *Standardized Beta reported

QoL Domain	Fatigue		Pain		Social Participation	
	β	p value	β	p value	β	p value
Age	-0.112	**0.004**	-0.095	0.051	-0.059	0.103
Gender	-0.005	0.886	-0.032	0.471	0.015	0.637
Race	-0.064	0.091	0.091	0.055	0.008	0.826
Ethnicity	0.010	0.791	-0.042	0.368	-0.011	0.756
Symptom Duration	-0.002	0.957	0.004	0.922	-0.020	0.556
Fatigue	-	-	0.410	**<0.001**	-0.610	**<0.001**
Pain Interference	0.430	**<0.001**	-	-	-0.185	**<0.001**
Sleep Disturbance	0.161	**0.005**	0.147	**0.008**	-0.046	0.251
Anxiety	0.104	0.101	0.044	0.483	-0.013	0.762
Depression	0.042	0.514	0.101	0.107	-0.061	0.172
Physical Function	-0.221	**<0.001**	-0.310	**<0.001**	0.143	**0.001**
Social Participation	-0.864	**<0.001**	-0.342	**<0.001**	-	-
Dryness	0.024	0.624	0.051	0.281	-0.043	0.210

Disclosure: K. Perdan Pirkmajer, None; **M. TOMSIC**, None; **A. Hocevar**, None.

Abstract Number: 0314

PROMIS Provides a Broad Overview of Health-Related Quality of Life in the Evaluation of Sjogren's Syndrome

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjogren's Syndrome (SS) is a systemic autoimmune disease that has considerable impact on health-related quality of life (HRQL). The European League Against Rheumatism (EULAR) Sjogren's Syndrome Patient Reported Index (ESSPRI) is the most widely used questionnaire to evaluate severity of patient-reported symptoms but is limited in scope. We sought to evaluate predictors of pain, fatigue, and social participation in SS using the Patient Reported Outcome Measurement Information System (PROMIS®) HRQL instruments to supplement ESSPRI findings.

Methods: A cross-sectional evaluation was performed on completed questionnaires of consecutive adult patients during visits to a multidisciplinary Sjogren's clinic between March 2018-February 2020. Questionnaires included PROMIS short-forms (depression 4a.v1, anxiety 4a.v1, fatigue 8a.v1, physical function 4a.v2, pain interference 8a.v1

(PI), sleep disturbance 4a.v1, participation in social roles and activities 8a.v1) and the ESSPRI. Patients were either classified as SS by 2016 ACR/EULAR criteria or labeled as "sicca not otherwise specified" (NOS) and used as a comparison group. Descriptive statistics were calculated for disease-related and sociodemographic variables and Pearson correlation was used to evaluate the relationship between subdomains of the ESSPRI and PROMIS. Uni- and multivariable linear regression (MVR) models were used to evaluate predictors of PROMIS PI, fatigue, and social participation after controlling for age, gender, race, ethnicity, and symptom duration.

Results: 227 SS patients and 85 patients with sicca NOS were included. Patients with SS were slightly older (mean (SD) years 57 (14) vs 54 (12), p=0.030) and were mostly female and white (Table 1). Mean (SD) PROMIS T-scores for PI (56.9 (11.0)), fatigue (57.2 (10.6)), and physical function (44.2 (9.8)) were at least ½ SD worse than US population normative values. Among SS patients PROMIS PI (r=0.72) and fatigue (r=0.80) highly correlated with respective ESSPRI pain and fatigue sub-domains. PI, sleep disturbance, poor physical function, and impaired social participation predicted fatigue and similarly fatigue, sleep disturbance, poor physical function, and impaired social participation predicted PI (all p's< 0.01) (Table 2). Fatigue and PI, but not dryness or mood disturbance, were the strongest predictors of social participation in MVR in this SS cohort. Patients with sicca NOS had greater mean T-Scores (SD) for PI (60.3 (12.0)) than the SS cohort in addition to worse social participation (43.5 (11.7)) and SD (55.4 (10.6)) (p's < 0.05). There were no significant differences in ESSPRI domains between patients with SS and sicca NOS.

Conclusion: In our SS cohort, PROMIS PI and fatigue scores correlated highly with respective ESSPRI domains. Fatigue and PI, but not dryness, were found to be the strongest negative predictors of social participation. Given the ability of PROMIS instruments to identify HRQL domains of high impact on SS patients beyond those ascertained through ESSPRI, these questionnaires should be considered as a supplement when evaluating SS patients in clinical care and trials.

Disclosure: D. DiRenzo, None; **S. Robinson**, None; **C. Bingham**, Bristol Myers Squibb, 5, Abbvie, 2, Gilead, 2, Eli Lilly, 2, Janssen, 2, Regeneron, 2, Pfizer, 2, Sanofi, 2; **A. Baer**, Bristol Myers Squibb, 2, UpToDate, 9; **T. Grader-Beck**, Novartis, 2, Abbvie, 5, Eli Lilly, 2, Celgene, 5.

Abstract Number: 0315

Sjögren's Syndrome Symptom Diary (SSSD) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) as Assessments of Symptoms in Sjögren's Syndrome: A Qualitative Exploration of Content Validity and Meaningful Change

Samantha Wratten[1], Natasha Griffiths[2], Carl Cooper[2], Jessica Flynn[2], Rebecca Hall[3], Linda Abetz-Webb[2], Wolfgang Hueber[4], Briana Ndife[5] and Pushpendra Goswami[4], [1]Adelphi Values, Macclesfield, United Kingdom, [2]Adelphi Values, Bollington, United Kingdom, [3]Adelphi Values Ltd, Bollington, United Kingdom, [4]Novartis Pharma AG, Basel, Switzerland, [5]Novartis, East Hanover, NJ

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The aim of this study was to gain qualitative patient feedback on the appropriateness of two Patient Reported Outcome (PRO) measures as assessments of symptoms of Sjögren's. The Sjögren's Syndrome Symptom Diary (SSSD) is a novel daily diary assessing the severity of six core symptoms: eye dryness, mouth dryness, skin dryness, genital dryness (females only), fatigue, and muscle/joint pain. Recently, the SSSD fatigue item wording has been updated to 'tiredness' and two supplementary items have been drafted to capture the most bothersome and most important to improve symptoms from a patient perspective. The Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) is a well-established, 13-item measure of an individual's fatigue and tiredness over the past week, however the content validity of the FACIT-F items has not been confirmed in Sjögren's. In this study the 13-item FACIT-F and new and updated SSSD items were tested with patients with Sjögren's. Patient perceptions of meaningful change on the SSSD were also explored.

Methods: Twelve semi-structured, cognitive telephone interviews were conducted with US adult patients with Sjögren's to cognitively debrief the new SSSD items ('most bothersome' and 'most important to improve'), and the updated SSSD 'tiredness' item. Cognitive debriefing involves actively testing a measure with patients to determine whether each instruction/item is understood as intended and relevant to patient experiences of the condition. In qualitative research a sample of 12 patients is typically considered sufficient to provide a comprehensive assessment of the PRO measure. Meaningful change was explored in relation to the six core SSSD items and for SSSD total average scores. Understanding and relevance of the 13 FACIT-F items were also explored.

Results: The new and updated SSSD items were well-understood by all patients (n=12/12) and all patients selected the same symptom as their most bothersome and the most important to improve from their perspective. The symptom most frequently reported as the most bothersome and important to improve was eye dryness (n=7/12). Meaningful improvement on individual SSSD items varied depending on patients' current Sjögren's severity, and meaningful improvement in relation to the SSSD total score varied from 1-point to 7-points (mean: 2.3 points; mode: 2 points). Such changes were described in relation to improvements in patients' feeling and functioning. FACIT-F items were generally well-understood, although there were some instances of patients not understanding the term 'listless' (n=4/12) in the item 'I feel listless (washed out)'. FACIT-F items were generally relevant; however, there was some variation in patient experiences of fatigue and tiredness related to Sjögren's. The FACIT-F item 'I am too tired to eat' was not relevant to any patients.

Conclusion: These results suggest that the new and updated SSSD items, and FACIT-F items, have good content validity as PRO measures of Sjögren's symptoms. Patient perceptions of meaningful change on the SSSD will be valuable for aiding interpretation of psychometrically-derived responder definitions and informing clinical trial endpoints.

Disclosure: S. Wratten, None; **N. Griffiths**, None; **C. Cooper**, None; **J. Flynn**, None; **R. Hall**, None; **L. Abetz-Webb**, None; **W. Hueber**, Novartis, 3, 11; **B. Ndife**, Novartis, 3, 11; **P. Goswami**, Novartis Pharma AG, 3.

Abstract Number: 0316

Exploring Alternative Responder Definitions for EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) for Use in Sjögren's Clinical Trials

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren's is a chronic autoimmune disease symptomatically characterized by dryness, pain and fatigue, which are typically assessed in clinical trials using EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI). However high placebo response rates are observed when responder definition guidelines (ESSPRI score ≤5 and improvement of ≥1-point or ≥15%) are implemented. The aim of this study was to explore possible options for alternative responder definitions that indicate the optimal balance of sensitivity (the ability to correctly identify improved patients) and specificity (the ability to correctly identify stable patients) to reduce possible misclassification of patients in Sjögren's clinical trial analyses.

Methods: Thresholds for alternative responder definitions were derived using blinded data from a Phase 2b randomized, double-blind, placebo-controlled, multicenter, parallel-group trial (NCT02962895) in primary Sjögren's (n=190 at Week 24) and were validated using blinded pooled data from three Phase 2 randomized, double-blind, placebo-controlled, parallel studies (NCT02775916; NCT02291029; NCT02149420) in primary Sjögren's (n=116 at Week 12; n=68 at Week 24).

Anchor- and distribution-based methods were conducted and triangulated to derive thresholds for an alternative responder definition based on a minimal symptom severity threshold and a more conservative minimal meaningful improvement threshold. A range of anchors were included in the anchor-based analyses based on suitable correlations with ESSPRI (>0.30), including Patient Global Assessment (PaGA), Physician Global Assessment (PhGA), Short Form-36 (SF-36) physical component score (PCS) and mental component score (MCS; validation analyses only), Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F; derivation analyses only), and Multidimensional Fatigue Inventory (MFI; validation analyses only).

Results: Both analysis populations were predominantly female (>90%), white (90%), and with a mean age of 50 years (range: 20-75). A realistic meaningful change threshold range between 1- and 2-points was identified through derivation analysis; ROC estimates and correlation weighted minimal important mean change supported a minimal threshold of 1.5-1.6 for ESSPRI total score. Correlation weighted mean change estimates and upper 95% confidence intervals supported a more conservative value of 2 or more. The minimal symptom severity threshold range was between 3.0 and 5.3, however 3 or less showed the greatest sensitivity and specificity. Validation analyses generally supported the threshold ranges suggested by the derivation analyses, with a meaningful change threshold range of 1.46-2.11 and a minimal symptom severity range of 2.7 to 4.0 based on the most suitable anchors (PaGA and PhGA).

Conclusion: The results of these analyses suggest that an alternative, more conservative composite ESSPRI responder definition could be used in future trials: an ESSPRI score of ≤3 and an improvement in ESSPRI score of 1.5-points or more. Further analysis in unblinded data is warranted to further test the utility of this new endpoint.

Disclosure: S. Wratten, None; **L. Abetz-Webb**, None; **E. Arenson**, None; **M. Greenwood**, Adelphi Group, 3; **R. Hall**, None; **P. Griffiths**, None; **S. Bowman**, Novartis, 1, 2, Astrazeneca, 2, Biogen, 2, BMS, 2, Celgene, 2, Medimmune, 2, MTPharma, 2, Ono, 2, UCB, 2, xtlbio, 2; **W. Hueber**, Novartis, 3, 11; **B. Ndife**, Novartis, 3, 11; **D. Kuessner**, Novartis Pharma AG, 3, 11; **P. Goswami**, Novartis Pharma AG, 3.

Abstract Number: 0317

Patient and Physician Perspectives on EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI) and EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI): A Qualitative Interview Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The aim of this research was to gain qualitative patient and physician feedback on the EULAR Sjögren's syndrome patient reported index (ESSPRI) and the EULAR Sjögren's syndrome disease activity index (ESSDAI). ESSPRI is a 3-item Patient-Reported Outcome measure of Sjögren's symptom severity (dryness, fatigue, joint/muscle pain). ESSDAI is a 12-domain Clinician-Reported Outcome measure of Sjögren's disease activity. Each domain is rated using pre-defined descriptions for each disease activity level (No/Low/Moderate/High). ESSPRI and ESSDAI have been psychometrically validated using data from over 700 patients and with input from over 50 experts (Seror *et al.,* 2016), however qualitative confirmation of the content validity has not been documented.

Methods: Qualitative, semi-structured, cognitive, telephone interviews were conducted with US adult patients with Sjögren's (N=12) and expert Sjögren's physicians in the US, UK and Germany (N=10). These samples are typical of qualitative research and are supplementary to the numerous patients and expert physicians previously involved in the validation of these measures. ESSPRI was tested with patients to explore understanding, relevance, and appropriateness of the 2-week recall period, and obtain patient perspectives of meaningful change in relation to their ESSPRI total score. ESSDAI was tested with physicians to explore the appropriateness of ESSDAI domain weightings, domain-level clinically meaningful improvement, and meaningful change in ESSDAI total scores. Physicians were also asked about the clinical relevance of the ESSPRI 2-week recall period.

Results: ESSPRI items were generally relevant to and well-understood by patients; however, there was some variation in interpretation of the locations of dryness considered when answering the dryness item (most frequent: eye dryness, n=9/12). Most patients (n=11/12) reported that it was easy to remember their symptoms over the past two weeks, as specified by the ESSPRI recall period. Patient-reported meaningful improvement in relation to ESSPRI total scores varied from 1-point to 6-points (mean: 2.4 points; mode: 2 points).

Physicians generally reported that the ESSDAI domain weightings were appropriate. Some physicians suggested that some weightings could be adjusted, with Articular (n=6/10), Haematological (n=5/10), and Biological domains (n=5/10) reported as under-weighted, and Muscular reported as over-weighted by most physicians (n=7/10). Most physicians considered a 1-level change in domain-level disease activity (e.g. from 'High' to 'Moderate') as clinically meaningful for most domains, and improvements of between 2-6 points in total ESSDAI scores were also considered meaningful. Most physicians (n=7/10) reported that the ESSPRI 2-week recall period was appropriate.

Conclusion: These results support the use of ESSPRI and ESSDAI as fit-for-purpose in their current formats, with some suggestions for optimization if desired. Perceptions of meaningful changes on these measures can be useful in interpreting psychometrically-derived responder definitions and informing clinical trial endpoints.

Disclosure: S. Wratten, None; **C. Cooper**, None; **J. Flynn**, None; **N. Griffiths**, None; **R. Hall**, None; **L. Abetz-Webb**, None; **S. Bowman**, Novartis, 1, 2, Astrazeneca, 2, Biogen, 2, BMS, 2, Celgene, 2, Medimmune, 2, MTPharma, 2, Ono, 2, UCB, 2, xtlbio, 2; **W. Hueber**, Novartis, 3, 11; **B. Ndife**, Novartis, 3, 11; **P. Goswami**, Novartis Pharma AG, 3.

Abstract Number: 0318

Correlation Between Prognostic Nutritional Index and Primary Sjögren's Syndrome Disease Activity

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Demographic, clinical, and laboratory features of the patients (n=36)

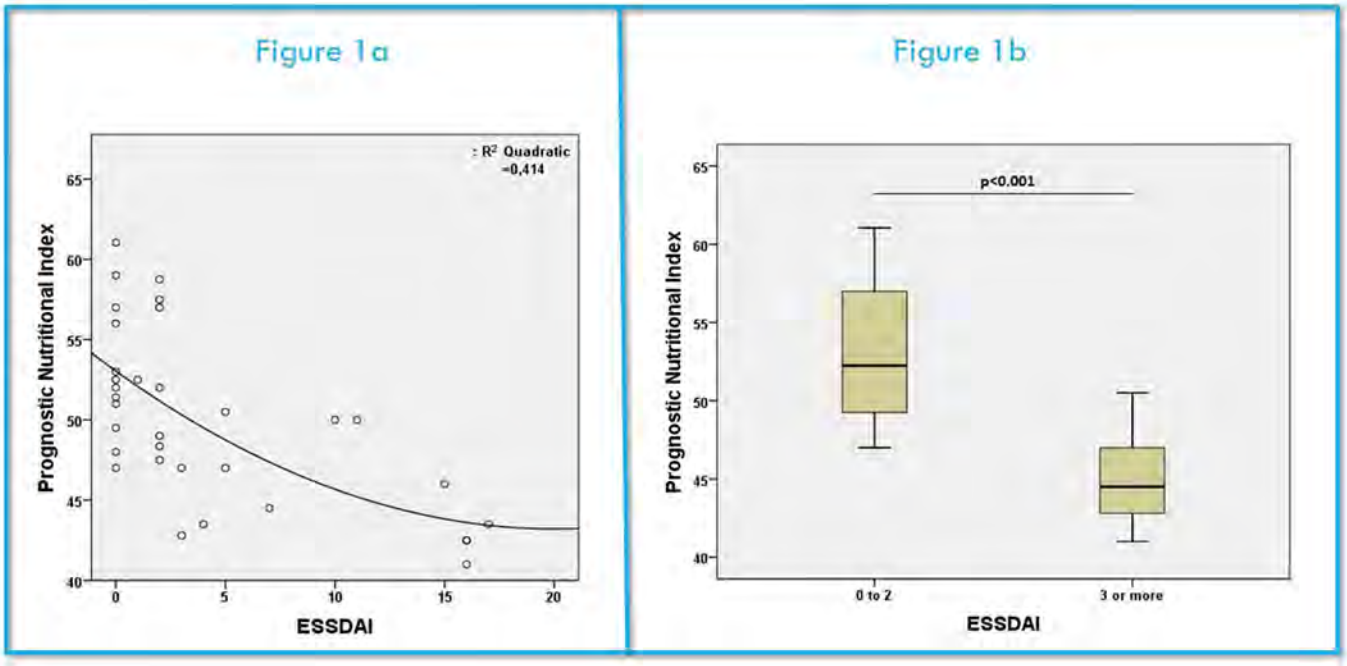
Age, years	57 (IQR: 10)
Disease duration, months	36 (IQR: 45)
Clinical findings, n(%)	
Constitutional symptoms	1 (2.8)
Parotitis	1 (2.8)
Lymphadenopathy	1 (2.8)
Arthritis	9 (25)
Cutaneous involvement	2 (5.6)
Pulmonary involvement	2 (5.6)
Renal involvement	2 (5.6)
Peripheral nervous system involvement	2 (5.6)
Central nervous system involvement	3 (8.4)
Hematological involvement	6 (16.7)
ESSDAI	3 (IQR: 14)
Positive anti-nuclear antibody, n(%)	35 (97.2)
Positive anti-Ro, n(%)	20 (55.6)
Positive anti-La, n(%)	9 (25)
Erythrocyte sedimentation rate, mm/h	18 (IQR: 12)
C-reactive protein, mg/L	4 (IQR: 4.5)
Hemoglobin, g/dL	12.5±1.4
White blood cell count, $x10^9$/L	6.3±2
Lymphocyte count, $x10^9$/L	1.9±0.9
Platelet count, $x10^9$/L	238.2±74.1
Albumin, g/dL	4.1±0.3

n=number, ESSDAI= EULAR Sjögren's Syndrome Disease Activity Index, IQR=interquartile range

Table 2. Correlation matrix for baseline PNI and WBC, PLT, C3, C4, ESR, and CRP

	CRP	ESR	C4	C3	PLT	WBC
PNI	r=0.153 p=0.395	r=-0.143 p=0.435	**r=0.532** **p=0.007**	**r=0.589** **p=0.002**	**r=0.393** **p=0.024**	**r=0.444** **p=0.010**
WBC	r=0.220 p=0.315	r=-0.150 p=0.345	**r=0.420** **p=0.028**	**r=0.430** **p=0.022**	**r=0.428** **p=0.009**	
PLT	r=0.240 p=0.300	r=-0.163 p=0.325	**r=0.530** **p=0.005**	**r=0.534** **p=0.003**		
C3	r=0.220 p=0.153	r=-0.325 p=0.094	**r=0.945** **p<0.001**			
C4	r=0.223 p=0.151	r=-0.305 p=0.120				
ESR	r=0.232 p=0.172					

PNI=Prognostic Nutritional Index, WBC=white blood cell, PLT=platelet, ESR=erythrocyte sedimentation rate, CRP=C-reactive protein



Background/Purpose: Since primary Sjögren's Syndrome (pSS) is a very heterogeneous disease with systemic manifestations, factors influencing the outcome of patients with pSS need to be investigated. Considering previous evidence suggests that markers of serum albumin level and lymphocyte count might be able to predict inflamatory burden, we hypothesised that PNI, calculated from the serum albumin level and total lymphocyte count, could represent convenient and cost-effective biomarker for predicting disease activity in pSS. Therefore, we aimed to investigate the association of PNI with Sjögren disease activity measured by validated EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI).

Methods: In this this cross-sectional study, we included a total of 36 women adult patients with pSS met the 2016 ACR-EULAR Classification Criteria for primary Sjögren's Syndrome which was evaluated in rheumatology clinic from January 2020 to January 2021. We collected laboratory data including erythrocyte sedimentation rate (ESR), C-reactive protein (CRP) level, lymphocyte, and serum albumin levels at diagnosis and last visit. PNI at diagnosis was calculated as (10 × serum albumin [g/dL] + 0.005 × lymphocyte count [/mm^3]). Disease activity was assessed with ESSDAI scores, visual analogue scales (VASs) (global disease, pain, and fatigue) was determinated and compared with PNI.

Results: Median age and disease duration were 57 (IQR: 10) years and 36 (IQR: 45) months, respectively. Demographic, clinical and laboratory features of the patients were provided in Table 1. PNI at the time of diagnosis was 49.9±5.5 and found to be slightly lower in patients with positive anti-Ro antibodies (48.4±5.8 and 52.3±3.7, p=0.023). Baseline PNI also correlated with white blood cell and platelet counts and serum complement levels but not with ESR and CRP (Table 2). Current PNI was 50.1±4.9 and not statistically different from the baseline PNI (p=0.773). It had a moderate negative correlation with ESSDAI (rho=-0.518, p=0.002) but not with the patient global (r=-0.118, p=0.512), physician global (r=-0.134, p=0.456), pain (r=-0.114, p=0.526), and fatigue (r=-0.091, p=0.615) VAS scores. There was a quadratic relationship between the PNI and ESSDAI (Figure 1a). Patients with an ESSDAI of 3 or more had significantly lower PNI compared to those with an ESSDAI of 0 to 2 (45.4±3.2 and 53±4.3, p< 0.001) (Figure 1b).

Conclusion: Our study demonstrates that pSS patients with higher ESSDAI scores had lower values of baseline PNI calculated at the disease diagnosis. In the present study, to the best of our knowledge, we have first evaluated the clinical significance of PNI in patients with pSS. We hypothesize that a lower PNI at diagnosis could indicate a higher inflammatory burden and PNI might be a prognostic tool in pSS however future studies with larger numbers of patients may provide additional information regarding the role of PNI in pSS patients.

Disclosure: K. Kalkan, None; **U. Ilgen**, None; **Z. Ademoğlu**, None; **H. Emmungil**, None.

Abstract Number: 0319

Assessment of EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) Domains in Routine Clinical Practice in an Integrated Delivery Network in the United States

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SESSION INFORMATION
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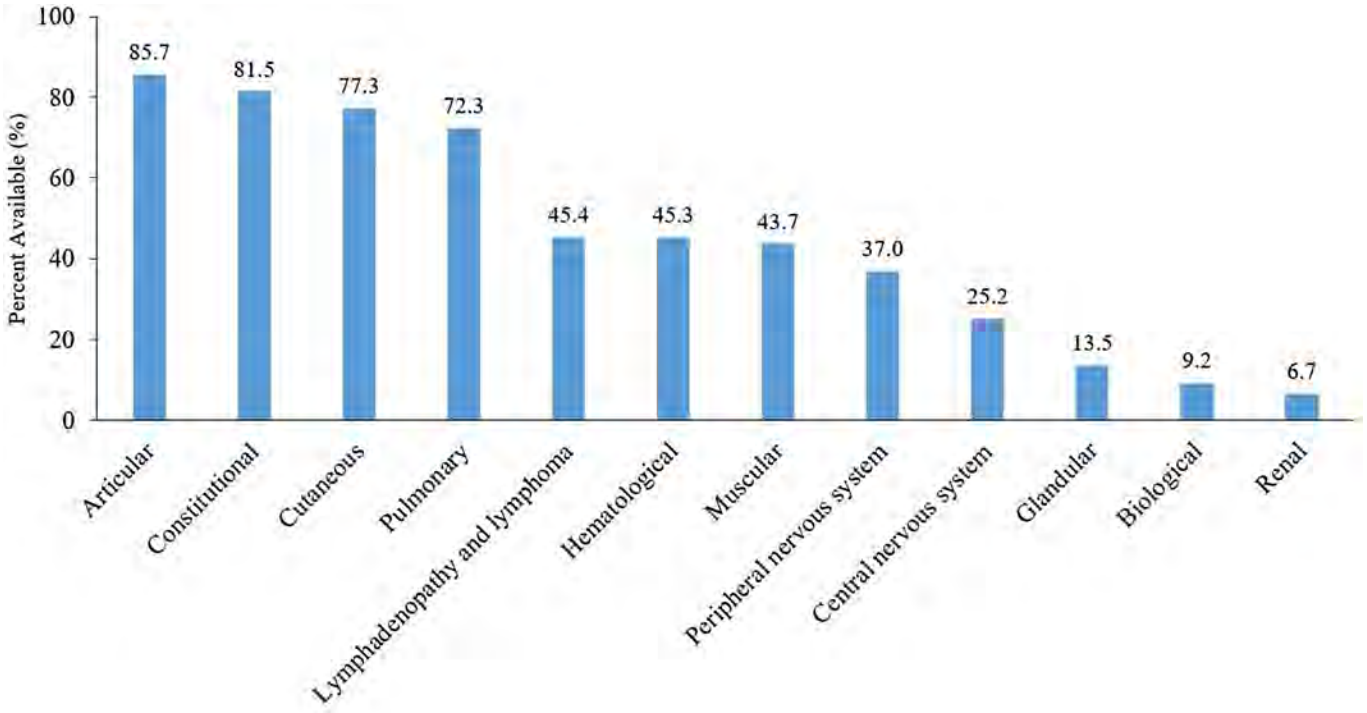

Figure 1. ESSDAI Domains Available for Assessment in Patient Charts.

Background/Purpose: Sjögren's syndrome (SS) is a chronic autoimmune disease associated with diverse phenotypes, which may include systemic disease activity. In real-world practice, the clinical presentation of SS is not well-documented. The purpose of this study was to first assess systemic domain-specific activity using the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI), a validated composite measure of SS severity, and then to describe clinical characteristics and medication use among patients with moderate-to-severe SS and lower severity SS receiving clinical care in the United States (US).

Methods: A retrospective patient chart review was used to identify adult patients with SS receiving care at a major integrated delivery network in Massachusetts. Clinical information needed to assess ESSDAI specific-domain activity was abstracted by research nurses following a review of past rheumatologist visits among patients with SS as part of routine care. Based on the abstracted data from different domains, ESSDAI scores were computed. Patients with ESSDAI scores ≥5 were considered to have moderate-to-severe SS; while those with ESSDAI < 5 would have lower severity SS. Clinical characteristics including comorbidities, medication use, and frequency of specialist visits, were assessed using linked electronic medical records (EMR) and insurance claims 12 months prior to the rheumatologist visit.

Results: As data collection is still ongoing, data from a total of 119 patients with SS collected to date with linked EMR and claims were analyzed. The mean age of patients was 63.6 years, 92.4% were female, and 52.9% experienced SS symptoms for ≥10 years. The three ESSDAI domains with the information available most commonly were articular (85.7%), constitutional (81.5 %), and cutaneous (77.3 %), whereas the least commonly were glandular (13.5%), biological (9.2%), and renal (6.7%, Figure 1). Overall, the most commonly observed comorbidities were rheumatic disease (77.3%), pulmonary disease (28.6%), pain (21.9%), and depression (20.2%, Table 1). Polypharmacy was observed, with DMARDs (37.0%), dermatological (36.1%), and ulcer drugs (36.1%) most frequently reported (Table 2). Specialist visits for internal medicine and rheumatology were most frequently observed, with a mean of 13.1 visits and 4.4 visits per year, respectively (Table 2). Although based on the available information in patient charts, only 3.4% of patients would be classified as having moderate-to-severe SS. Among those potentially classified as having lower severity SS (i.e., ESSDAI < 5), an elevated CCI score and polypharmacy were still observed.

Table 1. Comorbidities

	Overall (N = 119)	Moderate-to-severe SS (N = 4)	Low SS Severity (N = 115)
Medication use, n (%)			
Antianxiety agents	23 (19.3%)	3 (75.0%)	20 (17.4%)
Antiasthmatic	31 (26.1%)	2 (50.0%)	29 (25.2%)
Antidepressants	35 (29.4%)	2 (50.0%)	33 (28.7%)
Anti-infective agents	20 (16.8%)	1 (25.0%)	19 (16.5%)
Anti-inflammatory analgesics	36 (30.3%)	0 (0.0%)	36 (31.3%)
Antimalarials	22 (18.5%)	1 (25.0%)	21 (18.3%)
Corticosteroids	33 (27.7%)	2 (50.0%)	31 (27.0%)
Dermatologicals	43 (36.1%)	3 (75.0%)	40 (34.8%)
DMARDs	44 (37.0%)	3 (75.0%)	41 (35.7%)
Fluoroquinolones	14 (11.8%)	0 (0.0%)	14 (12.2%)
Macrolides	15 (12.6%)	1 (25.0%)	14 (12.2%)
Minerals electrolytes	18 (15.1%)	2 (50.0%)	16 (13.9%)
Multivitamins	12 (10.1%)	1 (25.0%)	11 (9.6%)
Nasal agents	25 (21.0%)	1 (25.0%)	24 (20.9%)
Non-narcotic analgesics	11 (9.2%)	0 (0.0%)	11 (9.6%)
Nonsteroidal anti-inflammatory agents	32 (26.9%)	0 (0.0%)	32 (27.8%)
Ophthalmic agents	37 (31.1%)	3 (75.0%)	34 (29.6%)
Opioid analgesics	36 (30.3%)	2 (50.0%)	34 (29.6%)
Penicillins	20 (16.8%)	1 (25.0%)	19 (16.5%)
Tetracyclines	15 (12.6%)	0 (0.0%)	15 (13.0%)
Ulcer drugs	43 (36.1%)	1 (25.0%)	42 (36.5%)
Vitamins	24 (20.2%)	2 (50.0%)	22 (19.1%)
Specialist visits (PPPY), mean ± SD			
Cardiology	1.2 ± 3.3	4.5 ± 5.8	1.1 ± 3.1
Dermatology	0.7 ± 3.7	0.5 ± 1.0	0.7 ± 3.7
Family practice	1.7 ± 5.1	3.5 ± 7.0	1.7 ± 5.0
Internal medicine	13.1 ± 15.3	22.5 ± 12.1	12.8 ± 15.3
Neurology	0.7 ± 2.1	2.5 ± 5.0	0.6 ± 1.9
Obstetrics and gynecology	0.9 ± 2.7	0.0 ± 0.0	1.0 ± 2.8
Ophthalmology	1.4 ± 2.5	6.0 ± 3.6	1.2 ± 2.3
Psychiatry	1.6 ± 6.5	7.3 ± 13.8	1.4 ± 6.2
Pulmonology	1.4 ± 4.5	3.8 ± 7.5	1.3 ± 4.4
Radiology	1.8 ± 2.3	2.3 ± 1.7	1.7 ± 2.3
Rheumatology	4.4 ± 7.2	2.8 ± 3.4	4.5 ± 7.3

DMARD: Disease-modifying antirheumatic drugs; PPPY: per-patient-per-year

Conclusion: Information needed to fully and reliably assess clinical activity in ESSDAI domains was observed to be frequently incomplete in routine clinical practice, likely underestimating the true number patients with moderate-to-severe SS. A high comorbidity burden and polypharmacy were still observed among these patients, who were mostly classified with lower severity SS, suggesting possible misclassification based on incomplete information in specific ESSDAI domains.

Table 2. Medication use and specialist visits

	Overall (N = 119)	Moderate-to-severe SS (N = 4)	Low SS Severity (N = 115)
Quan-CCI, mean ± SD	1.63 ± 1.37	2.00 ± 1.83	1.62 ± 1.36
CCI comorbidities, n (%)			
Rheumatic disease	92 (77.3%)	2 (50.0%)	90 (78.3%)
Chronic pulmonary disease	34 (28.6%)	3 (75.0%)	31 (27.0%)
Peripheral vascular disease	12 (10.1%)	0 (0.0%)	12 (10.4%)
Renal disease	12 (10.1%)	1 (25.0%)	11 (9.6%)
Mild liver disease	10 (8.4%)	1 (25.0%)	9 (7.8%)
Diabetes without chronic complication	9 (7.6%)	0 (0.0%)	9 (7.8%)
Malignancy	8 (6.7%)	0 (0.0%)	8 (7.0%)
Cerebrovascular disease	7 (5.9%)	1 (25.0%)	6 (5.2%)
Congestive heart failure	4 (3.4%)	0 (0.0%)	4 (3.5%)
Diabetes with chronic complication	4 (3.4%)	0 (0.0%)	4 (3.5%)
Dementia	1 (0.8%)	0 (0.0%)	1 (0.9%)
Myocardial infarction	1 (0.8%)	0 (0.0%)	1 (0. 9%)
Metastatic solid tumor	1 (0.8%)	0 (0.0%)	1 (0. 9%)
Peptic ulcer disease	1 (0.8%)	0 (0.0%)	1 (0. 9%)
AIDS/HIV	0 (0.00%)	0 (0.0%)	0 (0.0%)
Hemiplagia or paraplegia	0 (0.00%)	0 (0.0%)	0 (0.0%)
Moderate or severe liver disease	0 (0.00%)	0 (0.0%)	0 (0.0%)
SS-specific comorbidities, n (%)			
Pain	26 (21.9%)	2 (50.0%)	24 (20.9%)
Depression	24 (20.2%)	2 (50.0%)	22 (19.1%)
Rheumatoid arthritis	24 (20.2%)	2 (50.0%)	22 (19.1%)
Anxiety	20 (16.8%)	2 (50.0%)	18 (15.7%)
Chronic pain	20 (16.8%)	2 (50.0%)	18 (15.7%)
Fatigue	20 (16.8%)	1 (25.0%)	19 (16.5%)
Fibromyalgia	14 (11.8%)	1 (25.0%)	13 (11.3%)
Scleroderma/systemic sclerosis	10 (8.4%)	0 (0.0%)	10 (8.7%)
Systemic lupus erythematosus	9 (7.6%)	0 (0.0%)	9 (7.8%)
Antiphospholipid syndrome	2 (1.7%)	0 (0.0%)	2 (1.7%)
Sign and symptoms involving cognition (e.g., "foggy brain")	2 (1.7%)	0 (0.0%)	2 (1.7%)
Autoimmune hepatitis	1 (0.8%)	0 (0.0%)	1 (0.9%)
Lymphoma	1 (0.8%)	0 (0.0%)	1 (0.9%)
Nephritis	1 (0.8%)	0 (0.0%)	1 (0.9%)
Sialoadenitis	1 (0.8%)	0 (0.0%)	1 (0.9%)

CCI: Charlson Comorbidity Index; SS: Sjögren's syndrome

Disclosure: B. Ndife, Novartis, 3, 11; **I. Pivneva**, Analysis Group, Inc., 3; **C. Rossi**, Analysis Group, Inc., 3; **J. Signorovitch**, Analysis Group, Inc., 3.

Abstract Number: 0320

Performance of the Clinical Trials ESSDAI (ClinTrialsESSDAI), an Adjusted ESSDAI Score, in Two Randomised Clinical Trials in Patients with Primary Sjögren's Syndrome

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SESSION INFORMATION
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Background/Purpose: Recent randomised controlled trials (RCTs) in primary Sjögren's syndrome (pSS) failed to show clinical efficacy.[1-3] Several RCTs used the EULAR Sjögren's Syndrome Disease Activity Index (ESSDAI) as primary endpoint, showing large response rates in active treatment and placebo groups.[1,3] The ESSDAI consists of some domains which are more sensitive to change and easy to score compared to other domains.[4] The objective of this study was to develop the Clinical Trials ESSDAI (ClinTrialsESSDAI), an adjusted ESSDAI score consisting of frequently active and sensitive to change domains, and to compare the performance of the ClinTrialsESSDAI to the Clinical (Clin)ESSDAI and ESSDAI in two RCTs.

Methods: The ASAP-III trial in abatacept (80 pSS patients)[1] and TRACTISS trial in rituximab (133 pSS patients)[2] were used for development and analyses of the ClinTrialsESSDAI. These trials were selected since ASAP-III included only patients with moderate to high disease activity according to ESSDAI, whereas TRACTISS did not apply this inclusion criterion, leading to higher baseline ESSDAI scores in ASAP-III than in TRACTISS (median 13 vs. 4). Activity of ESSDAI domains at baseline was analysed. The six most frequently active domains were selected for the ClinTrialsESSDAI, with exclusion of the biological domain. This is in line with the ClinESSDAI, which does not include the biological domain, to measure a 'true' clinical effect. The ClinTrialsESSDAI score was calculated using existing weights of the ClinESSDAI. Responsiveness of the ClinTrialsESSDAI, ClinESSDAI and ESSDAI was calculated using the standardised response mean (SRM) at the primary endpoint visits: week 24 for ASAP-III, week 48 for TRACTISS. Percentage of patients who reached the minimal clinically important improvement (MCII, decrease of ≥3 points) and low disease activity (LDA, score < 5) was analysed for all three scores.

Results: Besides the biological domain, the six most frequently active domains at baseline in the ASAP-III and TRACTISS trial were the glandular (any activity: 91% and 21%, respectively), articular (58% and 44%), haematological (43% and 24%), constitutional (46% and 15%), lymphadenopathy (29% and 9%) and cutaneous (23% and 11%) domain (Figure 1). These domains were selected for the ClinTrialsESSDAI. Responsiveness was similar using any of the three scores at primary endpoint visits of the ASAP-III and TRACTISS trials (Table 1). Discrimination between active treatment and placebo groups based on MCII and LDA responders was also similar using any of the three scores (Figure 2).

Conclusion: The ClinTrialsESSDAI, consisting of six frequently active and sensitive to change domains of the ESSDAI, shows similar responsiveness and discrimination between treatment groups compared to the ClinESSDAI and ESSDAI in the ASAP-III and TRACTISS RCT. Therefore, this ClinTrialsESSDAI will not solve the problem of discrimination and a composite endpoint combining response at multiple clinically relevant items seems more suitable as primary study endpoint.

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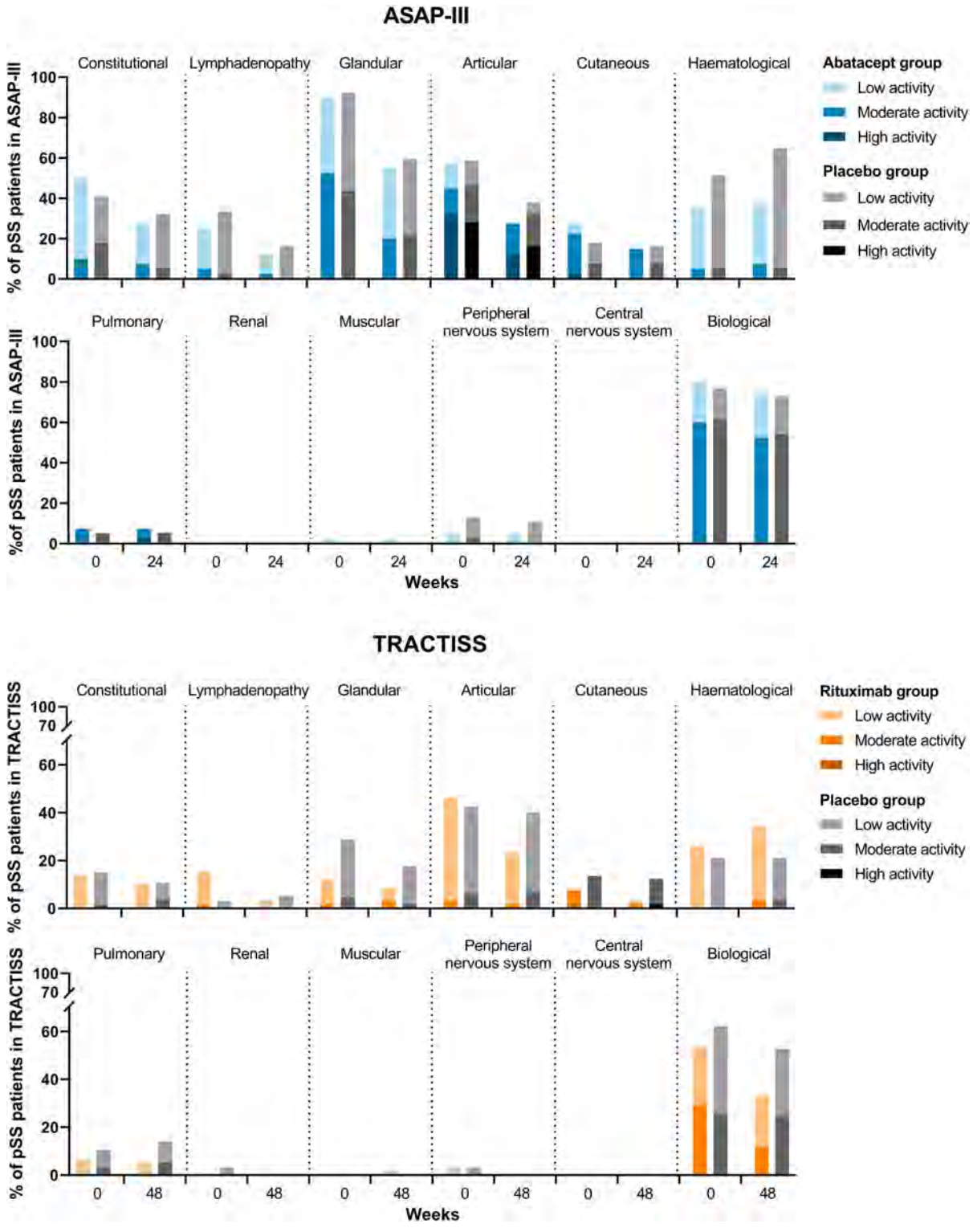

Figure 1. Activity of ESSDAI domains in the ASAP-III and TRACTISS trial.

Table 1 Responsiveness measured with SRM of the ClinTrialsESSDAI, ClinESSDAI and ESSDAI in the ASAP-III and TRACTISS trial

ASAP-III	**ClinTrialsESSDAI**	**ClinESSDAI**	**ESSDAI**
	week 24	*week 24*	*week 24*
Abatacept	-0.65	-0.63	-0.64
Placebo	-0.59	-0.59	-0.61
TRACTISS	**ClinTrialsESSDAI**	**ClinESSDAI**	**ESSDAI**
	week 48	*week 48*	*week 48*
Rituximab	-0.33	-0.34	-0.41
Placebo	-0.13	-0.12	-0.16

Abbreviations: SRM: standardised response mean, ESSDAI: European League Against Rheumatism (EULAR) Sjögren's Syndrome Disease Activity Index, ClinESSDAI: Clinical ESSDAI, ClinTrialsESSDAI: Clinical Trials ESSDAI, ASAP-III: Abatacept Sjögren Active Patients phase III, TRACTISS: Trial of Anti-B cell Therapy in Patients with Primary Sjögren's Syndrome

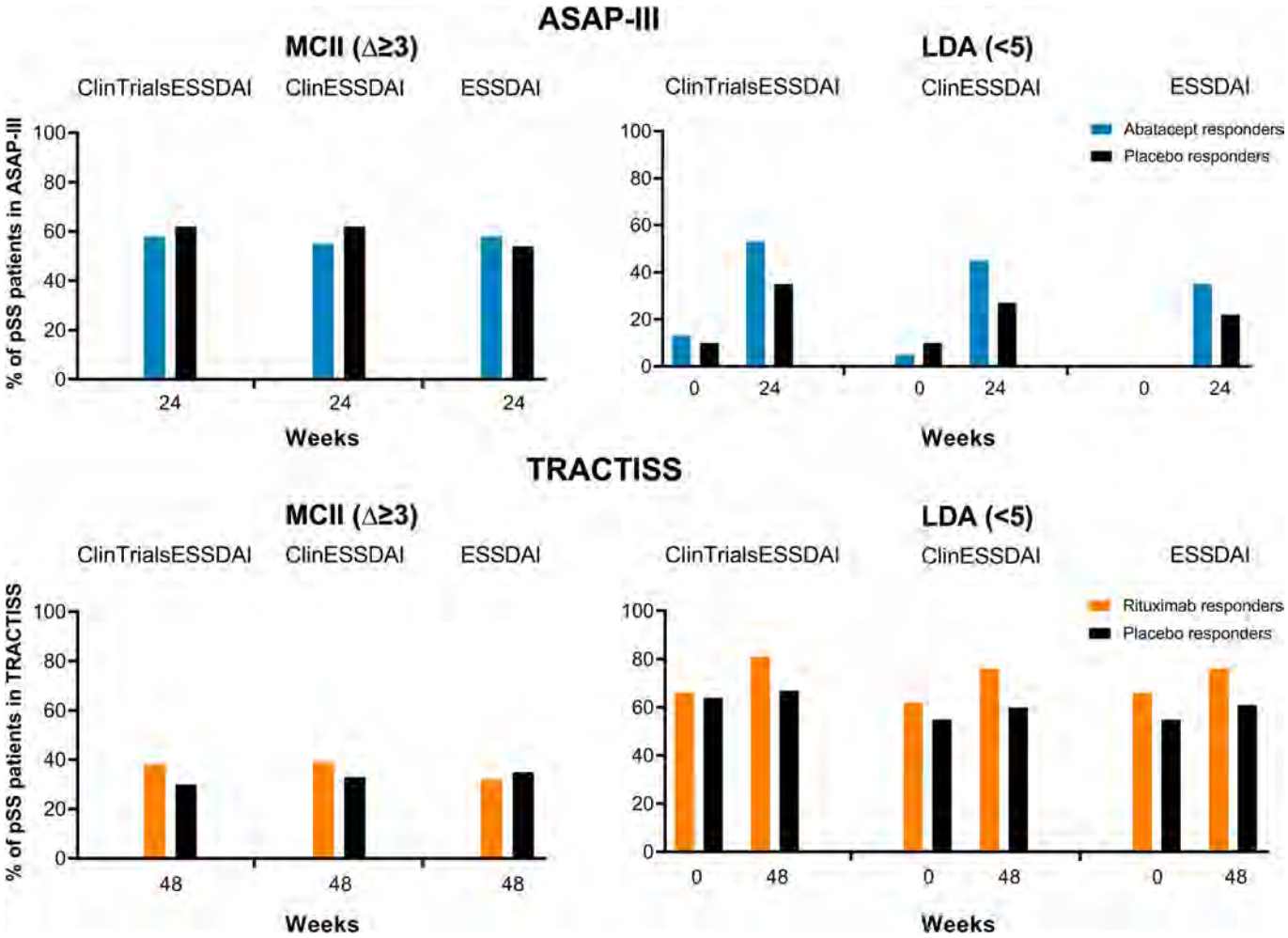

Figure 2. The minimal clinically important improvement (MCII, decrease of ≥3 points) and low disease activity (LDA, score <5) in ESSDAI, ClinESSDAI and ClinTrialsESSDAI (using existing weights of ClinESSDAI) in the ASAP-III and TRACTISS trial.

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Abstract Number: 0321

Sequential Administration of Belimumab and Rituximab in Primary Sjögren's Syndrome Reduces Minor Salivary Gland–Resident B Cells and Delays B-Cell Repopulation in Circulation

André van Maurik[1], David Gardner[2], Saba Nayar[2], Charlotte Smith[2], Kenneth Clark[1], Prafull Mistry[1], Rajesh Punwaney[3], David Roth[3], Robert Henderson[1], Xavier Mariette[4] and **Francesca Barone**[2], [1]GlaxoSmithKline, Stevenage, Hertfordshire, United Kingdom, [2]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom, [3]GlaxoSmithKline, Collegeville, PA, [4]Université Paris- Saclay, Rheumatology, Paris, France

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is characterized by B-cell hyperactivity and elevated serum and saliva B-lymphocyte stimulator (BLyS) levels.[1] Sequential administration of belimumab (BEL; anti-BLyS) and rituximab (RTX; anti-CD20) is a promising strategy to target B cells through distinct but complementary mechanisms.[2] This analysis assesses the changes in minor salivary gland (MSG) and peripheral blood B cells following sequential administration of subcutaneous (SC) BEL and intravenous (IV) RTX (BEL/RTX) in patients with pSS.

Methods: This Phase 2, double-blind study (GSK Study 201842; NCT02631538) randomized 86 adults with active pSS to placebo (PBO; N=13), BEL/RTX (N=24; BEL 200 mg SC weekly to Week [Wk] 24 followed by PBO SC weekly

Table. Key biomarker levels following treatment (completer population)

Biomarker, median (IQR)	PBO (N=8)	BEL/RTX (N=17)	BEL (N=19)	RTX (N=16)
CD20+ B-cell count/mm² (MSG biopsy)				
BL	418.2 (20.7, 763.1)	87.5 (13.3, 252.0)*	65.9 (4.5, 636.3)	106.3 (30.9, 235.1)‡
Wk 24	93.4 (55.2, 518.2)	0.4 (0.0, 1.4)†	60.6 (13.2, 454.5)*	158.3 (2.4, 744.8)§
Plasma cells (CD138+; both CD20+ and CD20-) count/mm² (MSG biopsy)				
BL	90.2 (5.7, 742.9)	33.7 (7.2, 198.0)‖	117.6 (27.3, 199.4)	35.8 (19.3, 226.2)¶
Wk 24	188.0 (22.5, 318.8)	101.6 (15.2, 384.5)§	94.3 (17.0, 204.6)*	93.6 (17.5, 248.6)¶
Memory B cells (CD20+, CD27+) count/mm² (MSG biopsy)				
BL	114.9 (18.3, 388.8)**	14.4 (3.9, 41.3)‖	31.0 (1.4, 141.1)	95.3 (1.9, 219.7)††
Wk 24	57.0 (16.0, 419.6)**	0.8 (0.0, 7.7)†	57.0 (4.4, 437.0)*	2.6 (0.2, 66.8)††
CD19+ B cells/mm³ in circulation				
BL	174.5 (146.0, 231.5)	170.0 (119.0, 281.0)	176.0 (83.0, 203.0)	128.5 (72.0, 238.5)
Wk 1	191.5 (169.0, 224.5)	235.5 (177.5, 405.5)‖	227.0 (133.0, 346.0)‡‡	130.5 (78.5, 265.5)
Wk 12	144.0 (92.0, 189.0)**	2.5 (2.5, 2.5)	79.0 (42.0, 123.0)§§	2.5 (2.5, 2.5)
Wk 24	184.0 (137.0, 218.5)	2.5 (2.5, 2.5)	58.0 (36.0, 90.0)	2.5 (2.5, 25.5)‡
Wk 36	200.5 (174.5, 319.0)	2.5 (2.5, 2.5)‖	47.0 (33.0, 57.0)§§	37.5 (4.3, 81.5)
Wk 44	160.0 (128.0, 248.5)	7.0 (2.5, 27.0)‖	49.0 (34.0, 61.0)‡‡	37.0 (8.3, 112.5)
Wk 52	207.0 (74.0, 278.0)**	47.0 (20.0, 54.0)	38.0 (31.5, 85.5)‖	53.5 (19.0, 169.5)
Wk 68	145.0 (96.0, 289.0)	108.0 (67.0, 149.0)‖	28.0 (18.0, 59.0)‡‡	82.0 (31.5, 171.5)

*n=15; †n=10; ‡n=13; §n=12; ‖n=16; ¶n=14; **n=7; ††n=11; ‡‡n=17; §§n=18

to Wk 52 plus RTX 1000 mg IV, Wk 8 + 10), BEL monotherapy (N=24; BEL 200 mg SC weekly to Wk 52), or RTX monotherapy (N=25; RTX 1000 mg IV, Wk 8 + 10). Primary and secondary endpoints were safety and efficacy.[3] Reported here are the exploratory biomarker endpoints, performed on the completer population (N=60; patients who completed the treatment phase and follow-up). The analyses include CD20+ B-cell, plasma cell and memory B-cell quantification within MSG biopsies (baseline + Wk 24), and changes in peripheral blood B-cell numbers over time to Wk 68.

Results: MSG histology demonstrated that the numbers of infiltrating CD20+ B cells at Wk 24 were lowest in the BEL/RTX arm, with incomplete depletion observed in the monotherapy and PBO arms (Table). Although the levels of MSG memory B cells (CD20+, CD27+) were also lowest in the BEL/RTX and RTX arms, plasma cell numbers were maintained irrespective of treatment. Total peripheral blood CD19+ B cells in circulation were almost completely depleted in the BEL/RTX and RTX arms (Table). In the BEL/RTX arm, after BEL discontinuation at Wk 24, a trend of delayed repopulation of total B cells in circulation was evident relative to RTX. In the BEL/RTX and BEL arms, circulating memory B cells increased initially (baseline [BL]/Wk 1 median [interquartile range, IQR] number of cells/mm^3: BEL/RTX: 28.0 [13.0, 36.0]/47.0 [30.0, 72.5], BEL: 18.0 [14.0, 30.0]/45.0 [19.0, 63.0]), and then returned toward baseline levels over time. However, in the BEL/RTX arm, following the BEL-induced increase, circulating memory B cells reached near complete depletion (Wk 24 median [IQR]: BEL/RTX: 0.2 [0.1, 0.4] cells/mm^3) and remained supressed until Wk 68 (median [IQR]: 3.5 [1.5, 5.0] cells/mm^3).

Conclusion: Relative to BEL or RTX monotherapy, BEL/RTX showed trends for near complete depletion of B cells in MSG, greater depletion of circulating memory B cells, and a longer period of sustained B-cell depletion. Overall, these data support the hypothesis that combined anti-BLyS and anti-CD20 act in a mechanistically complementary manner in pSS. This sequential therapy represents a novel treatment option for patients with pSS with moderate-to-severe disease activity.

Funding: GSK

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Abstract Number: 0322

Histopathological Changes in Parotid and Labial Salivary Gland Tissue in Primary Sjögren's Syndrome Patients After Abatacept Treatment

Uzma Nakshbandi[1], Liseth de Wolff[2], Frans Kroese[1], Silvia Liefers[3], Neelanjana Ray[4], Gwenny Verstappen[1], Fred Spijkervet[3], Marleen Nys[5], Arjan Vissink[6], Robert Wong[7], Bert van der vegt[3] and Hendrika Bootsma[1], [1]University Medical Center Groningen, Groningen, Netherlands, [2]University Medical Centre Groningen, Groningen, Netherlands, [3]University of Groningen, University Medical Center Groningen, Groningen, Netherlands, [4]Bristol-Myers Squibb Company, Lawrenceville, GA, [5]Bristol Myers Squibb, Braine-l'Alleud, Belgium, [6]University of Groningen, University Medical Center Groningen, Leek, Netherlands, [7]Bristol Myers Squibb, Basking Ridge, NJ

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Sjögren's Syndrome – Basic & Clinical Science Poster (0296–0322)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

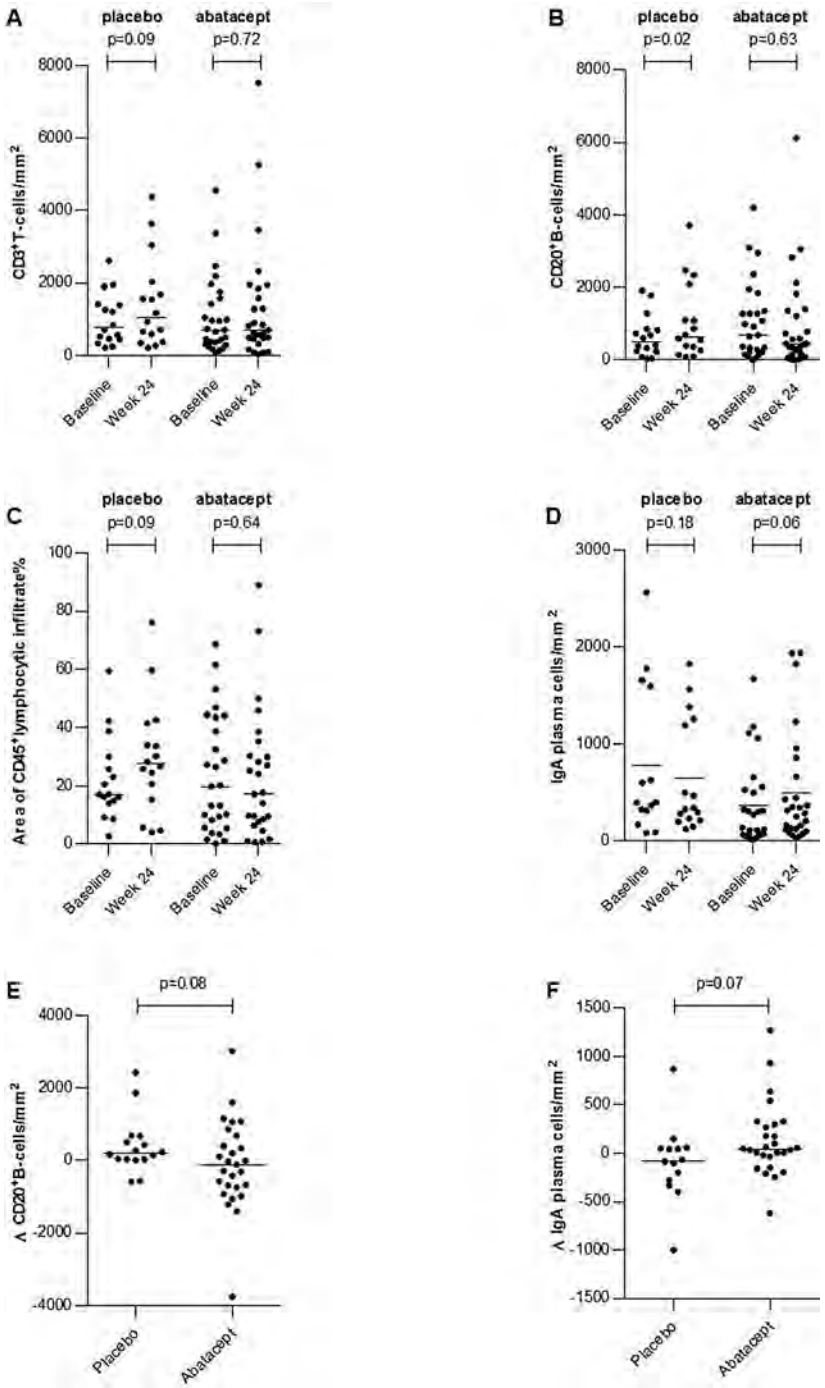

Figure 1. Histological analysis of parotid and labial salivary gland tissue of primary Sjögren's syndrome patients treated with placebo or abatacept. The number of CD3+T-cells (A), CD20+B-cells (B, E) and the relative area of CD45+infiltrates (C) increased in placebo treated patients, while numbers remained stable after treatment with abatacept. In contrast to patients treated with placebo, the number of IgA plasma cells/mm2 in salivary glandular tissue increased after 24 weeks abatacept treatment (D, F). Wilcoxon signed-rank test and McNemar's test were used to compare differences over time within groups. Mann-Whitney U test and Fisher's Exact test were used to compare differences between the abatacept and placebo groups. P-values <0.05 were considered statistically significant.

Table 1. Differences in histopathological characteristics in labial and parotid salivary glandular tissue on baseline in CRESS responders and non-responders

	CRESS responders (n=19)	CRESS non-responders (n=10)	P-value
Area of salivary gland section in mm²	5.00 (2.97-13.38)	4.79 (2.73-7.41)	0.60
Focus score	2.21 (1.44-7.35)	2.56 (1.49-4.94)	1.00
LELs/mm²	0 (0-0.32)	0.19 (0-0.51)	0.46
FDC-networks/mm²	0.35 (0-0.55)	0.20 (0-0.55)	0.80
GCs/mm²	0 (0-0.27)	0 (0-0)	0.29
CD3⁺cells/mm²	500 (296-1432)	745 (420-746)	0.48
CD20⁺cells/mm²	360 (130-1845)	956 (227-1277)	0.80
CD3/CD20 segregation, n(%)	12 (63.0)	5 (50.0)	0.39
CD45⁺cells (%)	13.2 (8.3-44.1)	20.0 (5.2-34.2)	0.95
IgA/IgG plasma cell shift, n(%)	12 (63.0)	9 (90.0)	0.14
IgA plasma cells/mm²	135 (66-661)	306 (64-451)	0.98
IgG plasma cells/mm²	278 (38-723)	156 (81-292)	0.60
IgM plasma cells/mm²	134 (6-155)	117 (3-593)	0.57

Abbreviations: LEL, lymphoepithelial lesion; FDC, follicular dendritic cell; GC, germinal center. Data are presented as median (IQR) or n(%). Mann-Whitney U test and Fisher's Exact test were used to compare differences between CRESS responders and non-responders. P-values <0.05 were considered statistically significant.

Background/Purpose: In a previous open-label phase II study, we showed that abatacept treatment might inhibit local formation of autoreactive memory B cells in parotid glands of primary Sjögren's syndrome (pSS) patients by affecting germinal center (GC) formation, a process dependent on co-stimulation by activated follicular-helper-T-cells[1]. However, limitations of that study were small number of patients, restriction to parotid gland tissue and lack of a placebo group. Therefore the aim of this study was 1) assess the effect of abatacept in pSS patients based on analysis of parotid and labial gland biopsies, and 2) assess the prognostic value of histological characteristics of salivary glandular tissue with regard to responsiveness to abatacept treatment using the newly developed Composite of Relevant Endpoints for Sjogren's Syndrome (CRESS)[2].

Methods: Patients from the Active Sjögren Abatacept Pilot (ASAP II, and ASAP III) and the international (IM101603) trial[3,4] were combined in whom a labial (n=13) or parotid (n=30) salivary gland biopsy was obtained at baseline and after 24 weeks of treatment. Patients received either abatacept (n=27) or placebo (n=16) treatment. After salivary gland biopsies were processed, sections were stained with H&E and immunohistochemically for CD3, CD20, CD45, CD21, Bcl6, IgA/IgG, IgA, IgG and IgM. All sections were evaluated for focus score (FS), GCs, number of lymphoepithelial lesions (LELs) per mm² and their maximal severity, presence of B/T-cell segregation within a focus, follicular dendritic cell (FDC) networks and presence of an IgA/IgG shift. Digital image analysis was used to assess the relative amount of CD45⁺lymphocytic infiltrates and the numbers of CD3⁺T cells, CD20⁺B cells and plasma cell density per mm². Histopathological data at baseline were compared between CRESS responders (n=19) (response to ≥3 of the 5 items) and non-responders (n=10) to abatacept treatment[2].

Results: In parotid and labial glandular sections, the number of $CD20^+$B cells/mm^2 increased significantly in placebo-treated patients (p=0.02), while counts remained stable in patients treated with abatacept. A similar trend was observed in the placebo group for $CD3^+$T cells (p=0.09) and the relative area of $CD45^+$infiltrate (p=0.09). The number of IgA plasma cells/mm^2 increased after 24 weeks of abatacept treatment (p=0.06) (figure 1). No significant decrease in GCs/mm^2 was observed in abatacept-treated pSS patients. Abatacept did not reduce FS, LELs/mm^2, presence of B/T-cell segregation, presence of IgA/IgG shift, nor number of IgG and IgM plasma cells/mm^2. No significant differences in histopathological parameters were found between CRESS responders and non-responders (table 1).

Conclusion: Abatacept potentially inhibits further progression of salivary gland inflammation by preventing further increase in T cell dependent B cell hyperactivity. Salivary gland histopathology could not predict responsiveness to abatacept in pSS patients.

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Disclosure: U. Nakshbandi, None; **L. de Wolff**, None; **F. Kroese**, Bristol Myers Squibb, 5, Roche, 5; **S. Liefers**, None; **N. Ray**, BMS, 3; **G. Verstappen**, None; **F. Spijkervet**, None; **M. Nys**, Bristol Myers Squibb, 3, 11; **A. Vissink**, BMS, 5, Roche, 5; **R. Wong**, Bristol Myers Squibb, 3; **B. van der vegt**, None; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2.

Abstract Number: 0323

Ro Positivity Is an Under-Recognised Poor Prognostic Marker in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antibodies to Ro60 (SSA) or Ro52 (SSB) have been described as one of the defining autoantibodies in Sjogren syndrome but they are also commonly observed in patients with systemic lupus erythematosus (SLE). Sjogren syndrome and SLE frequently coexist and share common pathogenesis and clinical features. We aim to examine the clinical significance of Ro positivity in an Australian SLE cohort.

Methods: Patients from the Australian Lupus Registry and Biobank, all fulfilling SLE classification criteria, were studied according to their baseline anti-Ro positivity status (either Ro60 or Ro52 or both). Comparison between Ro+ve and Ro-ve patients was made using descriptive statistics. Clinical associations of Ro positivity with patient and disease characteristics were studied using logistic regression.

Table 1. Association of anti-Ro positivity with common SLE complications

SLE Complications	Anti-Ro Positivity			Evidence of Association^ OR (95% CI; p-value)
	Total Sample (n = 393)	Ro Negative (n=208)	Ro Positive (n=185)	
Outcomes				
Adjusted mean SLEDAI > 4	113 (28.8%)	46 (22.1%)	67 (36.2%)	**1.95 (1.25 - 3.06; 0.003)**
Annual mild/moderate Flare Rate ≥ 1	86 (21.9%)	40 (19.2%)	46 (24.9%)	1.36 (0.84 - 2.20; 0.216)
Annual severe flare rate ≥ 1	26 (6.6%)	9 (4.3%)	17 (9.2%)	2.19 (0.95 - 5.05; 0.066)
Damage accrual	143 (36.4%)	63 (31.5%)	62 (34.3%)	1.18 (0.78 - 1.78; 0.436)
Manifestations (ever present)				
Arthritis	348 (88.5%)	181 (87.0%)	167 (90.3%)	1.38 (0.74 - 2.60; 0.314)
Malar or discoid rash	317 (80.7%)	160 (76.9%)	157 (84.9%)	**1.68 (1.0 - 2.82; 0.048)**
Presence of any renal manifestation[P]	219 (55.7%)	100 (48.1%)	119 (64.3%)	**1.94 (1.30 - 2.92; 0.001)**
Proteinuria	198 (50.4%)	88 (42.3%)	110 (59.5%)	**1.98 (1.33 - 2.97; 0.001)**
Oral ulcers	197 (50.1%)	98 (47.1%)	99 (53.5%)	1.29 (0.87 - 1.92; 0.206)
Presence of any haematological manifestation	119 (30.3%)	51 (24.5%)	68 (36.8%)	**1.79 (1.16, 2.76; 0.009)**
Lupus nephritis III or IV	110 (28.0%)	53 (25.5%)	57 (30.8%)	0.72 (0.33 - 1.55; 0.399)
Pleural or pericardial effusion	81 (20.6%)	38 (18.3%)	43 (23.2%)	1.35 (0.83 - 2.21; 0.225)
Lupus nephritis II or V	79 (20.1%)	39 (18.8%)	40 (21.6%)	0.76 (0.39 - 1.46; 0.404)
Acute pericarditis	48 (12.2%)	23 (11.1%)	25 (13.5%)	1.26 (0.69 - 2.30; 0.459)
Fever	64 (16.3%)	30 (14.4%)	34 (18.4%)	1.34 (0.78 - 2.29; 0.290)
Seizure	36 (9.2%)	20 (9.6%)	16 (8.6%)	0.89 (0.45 - 1.77; 0.740)
Psychosis	25 (6.4%)	15 (7.2%)	10 (5.4%)	0.74 (0.32 - 1.68; 0.465)
Delirium	19 (4.8%)	11 (5.3%)	8 (4.3%)	0.81 (0.32 - 2.06; 0.657)
Presence of any neurological manifestation[~]	156 (39.7%)	85 (40.9%)	71 (38.4%)	0.90 (0.60 - 1.35; 0.615)
Treatments (ever exposed)				
Hydroxychloroquine	361 (91.9%)	185 (88.9%)	176 (95.1%)	**2.43 (1.09 - 5.40; 0.029)**
Other immunosuppressants[&]	288 (73.3%)	140 (67.3%)	148 (80.0%)	**1.94 (1.22 - 3.08; 0.005)**
Prednisolone	301 (76.6%)	148 (71.2%)	153 (82.7%)	**1.94 (1.19 - 3.15; 0.007)**
Prednisolone ≥ 15mg	191 (48.6%)	87 (41.8%)	104 (56.2%)	**1.79 (1.20 - 2.66; 0.005)**
SSRI[†]	51 (13.0%)	25 (12.0%)	26 (14.1%)	1.20 (0.66 - 2.16; 0.549)
Opioids*	104 (26.5%)	56 (26.9%)	48 (25.9%)	0.95 (0.61 - 1.49; 0.827)

^Reference category is the group of patients not experiencing the SLE complication

[P]Includes exposure to proteinuria, lupus nephritis, urinary casts, haematuria or pyruria convention to use symbols rather than numbers for footnotes

[~]Includes exposure to seizure, psychosis, delirium, peripheral neuropathy, CNS, cranial nerve disorder, lupus headache or stroke

[&]Includes exposure to Azathioprine, Ciclosporin, Cyclophosphamide, Leflunomide, Methotrexate, Mycophenolate, Tacrolimus, Chloroquine, Mercaptopurine, Sulfasalazine, Rituximad or Belimumab

[†]Includes exposure to Citalopram , Desvenlafaxine, Duloxetine, Escitalopram, Fluoxetine, Mirtazapine, Sertraline or Venlafaxine

* Includes exposure to Buprenorphine, Codeine, Fentanyl Patch, Oxycodone, Oxycodone, Naloxone, Paracetamol or Tramadol

Results: 393 patients were studied; 47.1% have positive anti-Ro status. Ro+ patients were more likely to be non-Caucasians (Asian OR 2.92, 95% CI 1.88-4.54, p< 0.001), and have significant association with positive serology other than the well-recognised association with anti-La (SSB) and rheumatoid factor, including positivity to anti-dsDNA and hypocomplementemia. There were no association with positive antiphospholipid antibodies. Ro positive SLE patients were more likely to have High Disease Activity Status (HDAS) (OR 1.68, 95% CI 1.12-2.52, p=0.012) and increased likelihood of high adjusted mean SLEDAI (greater than 4) (OR 1.95, 1.25-3.06, p=0.003). Interestingly there was no difference in damage accrual between the two groups.

25.8% of the Ro positive cohort have associated sicca symptoms that may qualify them for diagnosis of Sjogren syndrome. Consistent with the observation that their overall disease activity is higher, Ro+ SLE patients are more likely to have to have malar or discoid rash (OR 1.68, 95%CI 1- 2.82, p=0.048), haematological manifestation (OR 1.79, 95% CI 1.16-2.76, p=0.009), renal disease (OR for proteinuria was 1.98, 95% CI 1.33-2.97, p=0.0010) (See table 1). Maximum urine proteinuria creatinine ratio was higher in Ro+ve SLE patients (p< 0.001). The minimum lymphocyte and neutrophil counts were also significantly lower in Ro+ve SLE patients (p=0.004 and p=0.001 respectively). Sjogren features such as parotitis, leucocytoclastic vasculitis, interstitial lung disease, and interstitial cystitis were seen in this lupus cohort but did not occur frequently enough to show a difference between Ro+ve and Ro-ve groups. Hypergammaglobulinemia occurred significantly more frequently (OR 1.77, 1.00 -3.16, p-0.05).

Ro+ patients were more likely to be treated with prednisolone (OR 1.94, 1.19-3.15, p=0.007) and immunosuppressants (OR 1.94, 1.22-3.08, p=0.005).

Table 2. Association of patient characteristics with anti-Ro positivity

Patient Characteristics	Anti-Ro Positivity			Evidence of Association^ OR (95% CI; p- value)
	Total Sample (n = 395)	Ro Negative (n=209)	Ro Positive (n=186)	
Female sex	341 (86.8%)	175 (84.1%)	166 (89.7%)	1.65 (0.90 - 3.01; 0.105)
Ethnicity				
Caucasian	191 (48.6%)	124 (59.6%)	67 (36.2%)	1
Asian	152 (38.7%)	59 (28.4%)	93 (50.3%)	**2.92 (1.88 - 4.54; <0.001)**
Other	26 (6.6%)	12 (5.8%)	14 (7.6%)	**2.16 (0.94 - 4.93; 0.068)**
Unknown	24 (6.1%)	13 (6.3%)	11 (5.9%)	
Age at SLE diagnosis				
< 18 years	47 (12.0%)	28 (13.5%)	19 (10.3%)	1
18 - 45 years	265 (67.4%)	136 (65.4%)	129 (69.7%)	1.40 (0.74 - 2.63; 0.298)
> 45 years	81 (20.6%)	44 (21.2%)	37 (20.0%)	1.24 (0.60 - 2.57; 0.564)
Ever achieved HDAS	166 (42.0%)	75 (35.9%)	91 (48.9%)	**1.71 (1.14-2.56; 0.009)**
ANA titre				
ANA titre > 320	328 (83.5%)	168 (80.8%)	160 (86.5%)	1
ANA titre ≤ 320	59 (15.0%)	38 (18.3%)	21 (11.4%)	0.58 (0.33 - 1.03; 0.064)
Serology				
Low C3 or low C4	349 (88.8%)	175 (84.1%)	174 (94.1%)	**3.08 (1.47 - 6.48; 0.003)**
Anti-dsDNA+	314 (79.9%)	158 (76.0%)	156 (84.3%)	**1.83 (1.09 - 3.07; 0.022)**
Anti-phospholipid+	151 (38.4%)	78 (37.5%)	73 (39.5%)	1.09 (0.71 - 1.67; 0.69)
Rheumatoid factor+	112 (28.5%)	46 (22.1%)	66 (35.7%)	**2.11 (1.33 - 3.35; 0.002)**
Anti-RNP+	97 (24.7%)	44 (21.2%)	53 (28.6%)	1.47 (0.93 - 2.33; 0.102)
Anti-La+	72 (18.3%)	1 (0.5%)	71 (38.4%)	**130 (17.83 - 948.61; <0.001)**
Anti-Sm+	67 (17.0%)	29 (13.9%)	38 (20.5%)	1.57 (0.92 - 2.67; 0.096)
Anti-Scl70+	7 (1.8%)	4 (1.9%)	3 (1.6%)	0.85 (0.21 - 3.50; 0.827)
Anti-Jo1+	4 (1.0%)	0 (0.0%)	4 (2.2%)	0.14 (0.54 - 189.64; 0.121)

^Where reference category not specified, the reference category is the absence of the patient characteristic listed in the Table above.

Table 3. Association of anti-Ro positivity with Sjogren syndrome complications

Sjogren Complications	Anti-Ro Positivity			Evidence of Association^ (p- value)
	Total Sample (n = 393)	Ro Negative (n=208)	Ro Positive (n=185)	
Fatigue	119 (30.3%)	61 (29.3%)	58 (31.4%)	0.69
Reflux	90 (22.9%)	46 (22.1%)	44 (23.8%)	0.69
Hypergammaglobulinemia	74 (18.8%)	29 (13.9%)	45 (24.3%)	**0.05**
16 - 20	39 (9.9%)	15 (7.2%)	24 (13.0%)	0.13
> 20	33 (8.4%)	13 (6.3%)	20 (10.8%)	0.22
Fibromyalgia	53 (13.5%)	32 (15.4%)	21 (11.4%)	0.24
Lymphadenopathy	48 (12.2%)	25 (12.0%)	23 (12.4%)	0.90
Autoimmune haemolysis	37 (9.4%)	20 (9.6%)	17 (9.2%)	0.89
Leucocytoclastic vasculitis	27 (6.9%)	13 (6.3%)	14 (7.6%)	0.61
Interstitial lung disease	20 (5.1%)	10 (4.8%)	10 (5.4%)	0.79
Myositis	14 (3.6%)	9 (4.3%)	5 (2.7%)	0.43
Gastrointestinal dysmotility (excluding reflux)	7 (1.8%)	5 (2.4%)	2 (1.1%)	0.45
Parotitis	6 (1.5%)	1 (0.5%)	5 (2.7%)	0.10
B cell lymphoma	5 (1.3%)	3 (1.4%)	2 (1.1%)	1
Renal tubular acidosis	2 (0.5%)	0 (0.0%)	2 (1.1%)	0.22
Interstitial cystitis	1 (0.3%)	0 (0.0%)	1 (0.5%)	0.47

^Where reference category not specified, the reference category is the absence of the patient characteristic listed in the Table above.

Conclusion: Ro positivity is seen frequently in SLE patients. Overlapping lupus and Sjogren features are seen in many patients, and Ro positivity can be used as a biomarker to denote a more severe disease phenotype.

Disclosure: K. Liao, None; **T. De Silva**, None; **J. Bonin**, None; **R. Koelmeyer**, None; **A. Hoi**, AstraZeneca, 2, 5, Janssen, 6, Abbvie, 6.

Abstract Number: 0324

Machine Learning: Identifying Lupus Nephritis Within Systemic Lupus Erythematosus in the Real World

Bruno Teixeira, David Bell, Tim Holbrook and Ben Hoskin, Adelphi Real World, Bollington, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Around 40-70% of patients with systemic lupus erythematosus (SLE) develop lupus nephritis (LN). LN is often underdiagnosed and early diagnosis is crucial for reducing kidney damage. Various tests can diagnose LN including kidney biopsy, but LN symptoms can vary greatly between patients making diagnosis challenging especially in the early stages. We aimed to develop a machine learning (ML)-based approach to classify SLE patients at high risk of LN to assist rheumatologists in their diagnosis.

Methods: Data were drawn from the Adelphi Lupus Disease Specific programme™, a point-in-time survey of rheumatologists and nephrologists and their SLE/LN patients conducted in France, Germany, Italy, Spain, the United Kingdom and the United States of America from Aug–Oct 2015. Rheumatologists and nephrologists each completed record forms for their next 5 consecutive adult SLE and LN patients, respectively, capturing demographic and clinical characteristics. Patients were categorized as LN or non-LN based on physicians' assessment.

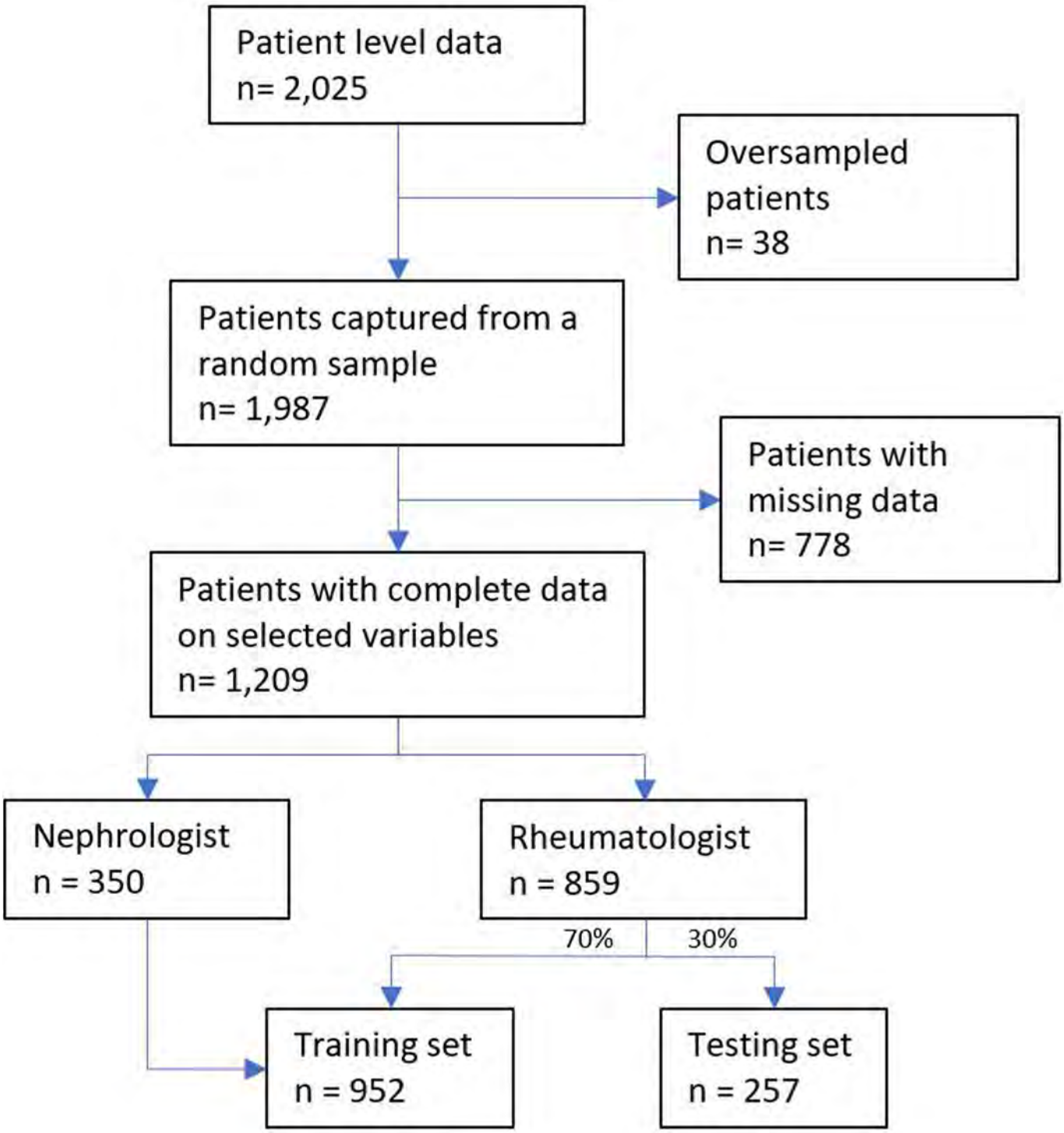
We subset data for training and testing the ML model, selecting 354 variables (from a total of 30 record form questions) based on specialist knowledge of LN pathophysiology. To ensure maximum discriminative power, the training set comprised all nephrologist-diagnosed patient and 70% rheumatologist-diagnosed patient data; the testing set comprised the remaining 30% rheumatologist-diagnosed patient data. Training and hyperparameter tuning were done using 10-fold cross-validation with R and Tidymodels Package. Model predictive performance was assessed by receiver operating characteristic area under the curve (AUC) metric.

Results: The model used data collected by 304 physicians on 1,209 SLE patients including both LN (n=483) and non-LN (n=726) patients (Fig. 1). After testing 2,520 models using the 6 most commonly used classification algorithms we found that the penalized logistic regression (PLR) with elastic net regularization predicted which SLE patients were at highest risk of LN (AUC: 0.91, with negative/positive predictive values of 0.96 and 0.68, respectively) in the testing set. The 3 variables that best predicted LN risk were disease progression, skin problems (both contributing negatively to risk) and musculoskeletal organs affected at diagnosis (with a positive contribution to risk, Fig. 2).

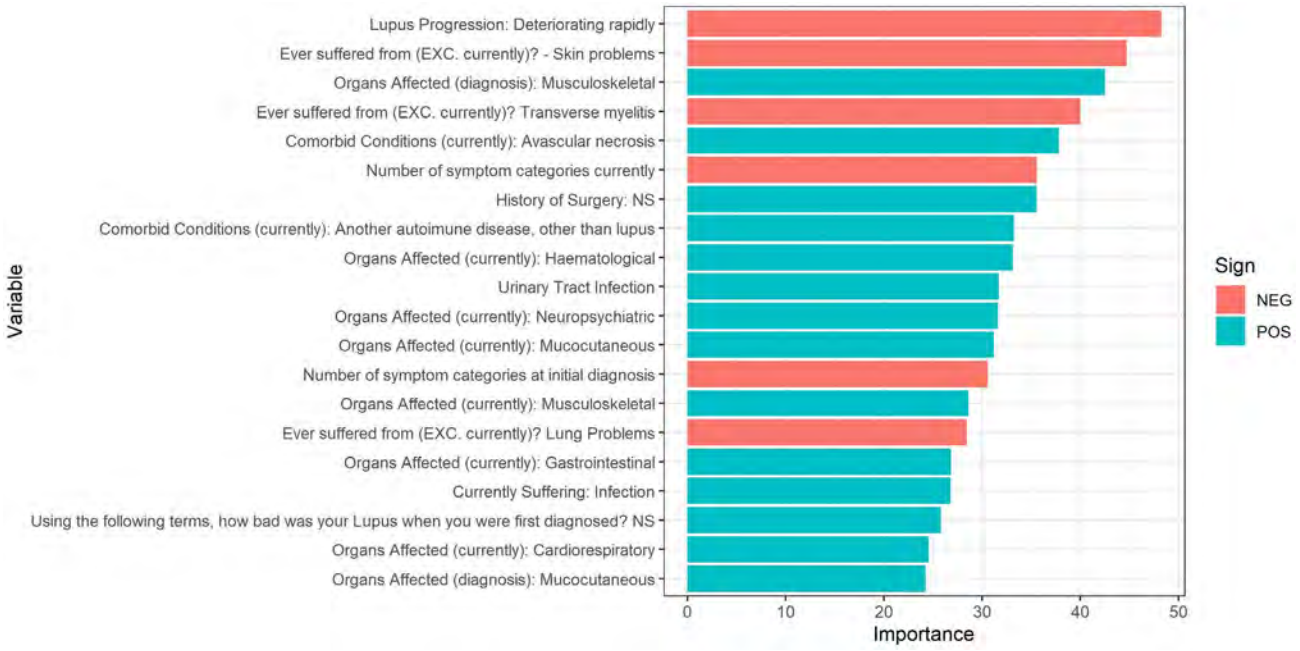
Conclusion: PLR successfully predicted SLE patients' LN risk using real-world data. Although linear discriminant analysis had a slightly better AUC (0.92), PLR results are easier to interpret, making it a suitable model to support rheumatologists identifying LN patients within the SLE population to guide further testing and treatment.

The PLR model had better discriminative power in non-LN vs LN patients. This may have resulted from undiagnosed LN patients remaining within the non-LN patient pool and thus generating false positives, since these high LN risk non-LN patients shared a number of characteristics with LN patients (Fig. 3).

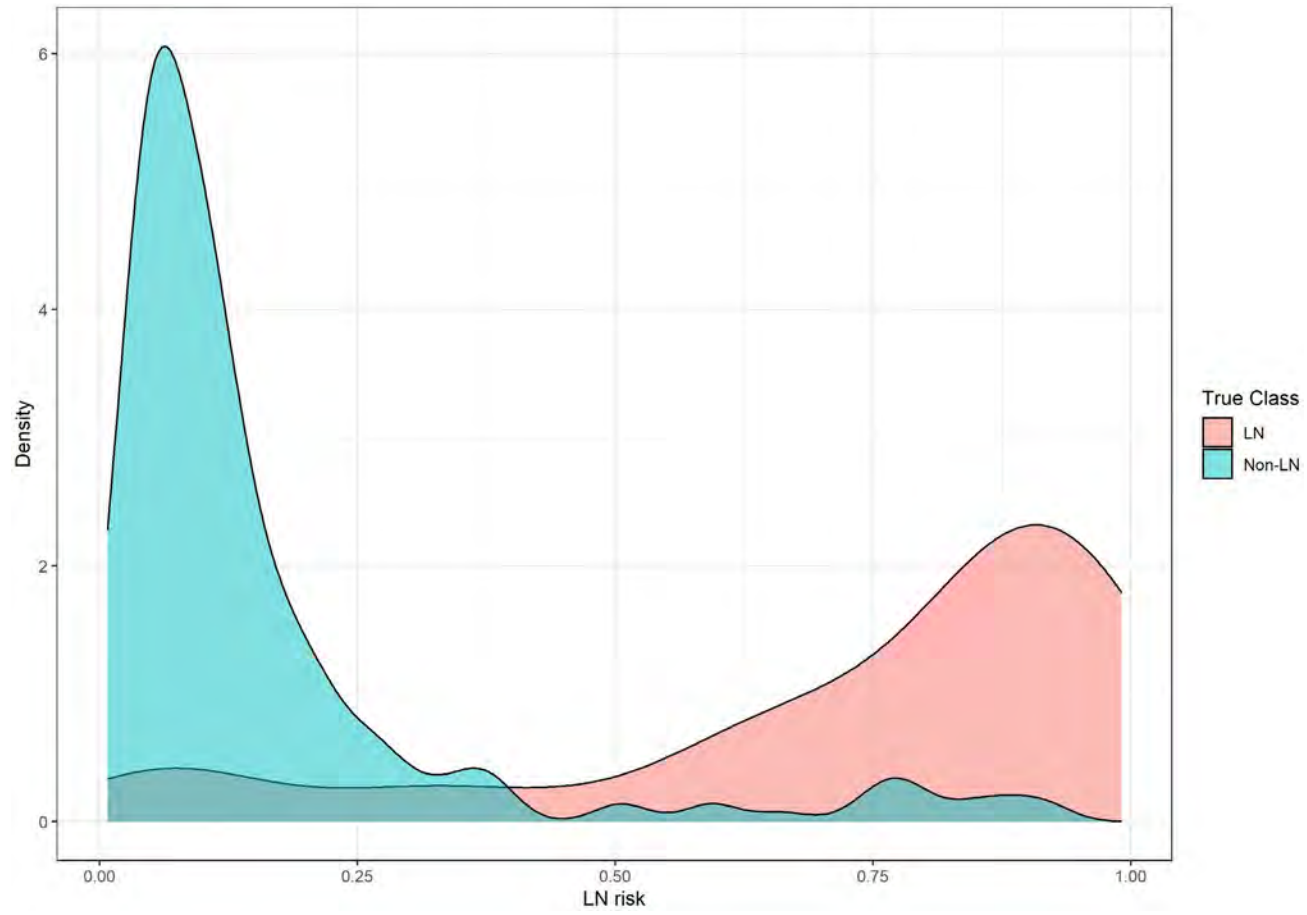
Predictive analysis has shown promising results for LN risk assessment in SLE patients using real-world data, we recommend further prospective validation is required prior to use in a clinical setting.



Patient selection flow



Variable importance plot from the penalized logistic regression model Variables in red contributed negatively to lupus nephritis risk prediction NEG, negative; POS, positive



Density plot for lupus nephritis risk according to the true class in the testing set LN, lupus nephritis

Disclosure: B. Teixeira, Adelphi Real World, 3, Janssen Pharmaceuticals, 3; **D. Bell**, Adelphi Real World, 3; **T. Holbrook**, Adelphi Real World, 3; **B. Hoskin**, Adelphi Real World, 3.

Abstract Number: 0325

A Multianalyte Assay Panel with Cell-bound Complement Activation Products Demonstrates Clinical Utility for the Diagnosis and Treatment of Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The multianalyte assay panel (MAP) consists of cell-bound complement activation products (CB-CAPs) with lupus and non-lupus autoantibodies combined in an algorithm (Dervieux et al., *J Immunol Methods* 2017). The test is intended for patients suspected of systemic lupus erythematosus (SLE) to aid the diagnosis. We demonstrated previously that *t*he MAP has clinical utility, as it facilitates SLE diagnosis and treatment decisions (Wallace *et al., Lupus Sci & Med 2019)*. As the number of patients with a positive MAP in that study was small, the present study was conducted to enrich the population of the MAP positive patients and to generate additional data on the clinical utility of MAP.

Methods: Systematic multicenter retrospective review of medical charts was conducted at 12 rheumatology practices in the United States. Adult patients for chart review were selected by Exagen based on the MAP score. To decrease the risk of bias, sets of 5 possible eligible patients were identified for each site. Each set included 2 negative (< -0.1) and 3 positive (> 0.1): tier-1 positive [MAP(Tier1+)]; tier-2 score > 1 [MAP(High+)]; tier-2 > 0.1 and ≤ 1 [MAP(Low+)]). The cutoff of 1 was based on the likelihood ratio positive of the test. Charts were reviewed at T0 (when the MAP was ordered), T1 (when the results were reviewed) and, if available, T2 (latest visit ≥8 months after T1). Statistical analysis (R) consisted of Kaplan-Meier survival analysis with Cox proportional hazard model and ordered logistic regression, as appropriate.

Results: T0 and T1 were performed for 161 patients. All sites but one reviewed charts as multiples of 5 (5 - 25 patients per site). Charts were reviewed also at T2 for a subset of 90 patients (56%). At T0, physician confidence in SLE diagnosis was low for 93 (58%), moderate for 49 (30%), and high for 19 (12%) patients. Odds of higher confidence in SLE diagnosis increased during the study by 1.74-fold for every unit of increase of the MAP score (p< 0.001). The lupus ICD-10 section (M32) was used as a proxy for diagnosis. Positive MAP led to increased assignment of an SLE code by Cox proportional hazard model (Figure 1). In particular, M32 was assigned to 22 of 65 (34%) MAP positive patients who were anti-dsDNA negative. In addition, MAP negative was superior to anti-dsDNA negative at excluding of an SLE code, as more anti-dsDNA negative than MAP negative patients were at risk of M32 assignment (63% vs 52%) (Figure 1B). Only 3 of the 63 MAP negative patients (5%) were assigned a lupus ICD-10 code during the study, indicating a 95% probability of excluding the SLE diagnosis in MAP negative patients. We also evaluated the use of hydroxychloroquine (HCQ) during the study in the 126 patients who were prescribed HCQ after T0. Kaplan-Meier

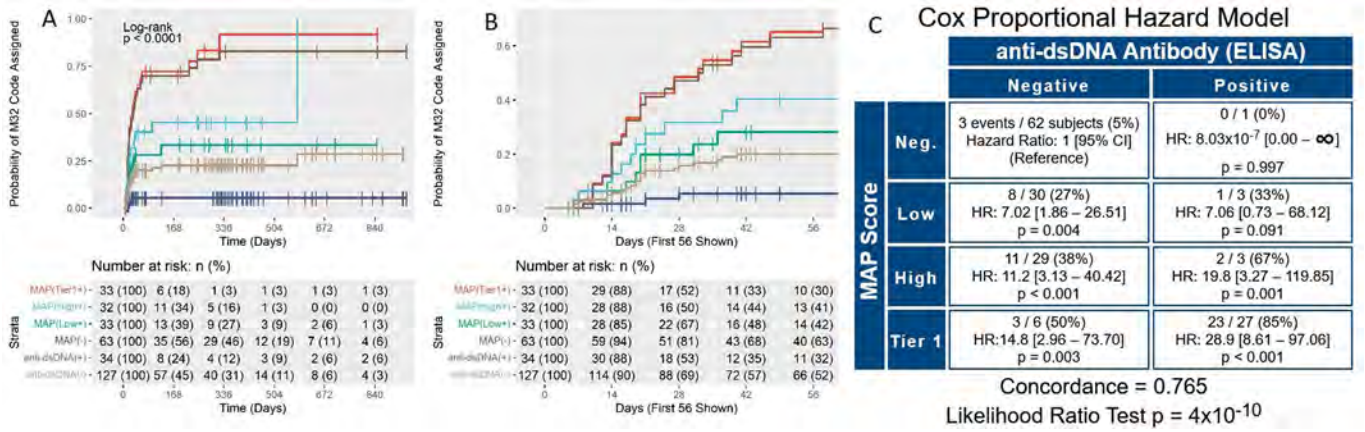

Figure 1. Panels A and B. Kaplan-Meier time-to-event curves for assignment of the M32 ICD-10 section over time. Curves show the percent probability of being assigned the M32 section after T0 for the 4 study groups : tier-1 (MAP(Tier1+)), high tier-2 (MAP(High+)), low tier-2 (MAP(Low+)) negative (MAP(-)), in addition to anti-dsDNA positive (anti-dsDNA(+)) and negative (anti-dsDNA(-)) patients throughout the study. The X-axis reports the number of days since T0. Panels A and B report the same data analysis, with panel B allowing better visualization of the initial portion of the survival curves. Panel C. Cox proportional hazard model comparing the MAP test score (Neg.: negative; Low: low tier-2; High: high tier-2, Tier 1: tier-1 positive) vs. anti-dsDNA antibodies for assignment of the M32 section. In each quadrant, the numerators represent the number of subjects that developed an M32 section after T0 (events, n=51 in total) while the denominators represent all subjects in that quadrant. Concordance and p value of the likelihood ratio test are also reported. For data analysis, we used the date of the visit when the M32 section was recorded in the ICD-10 list.

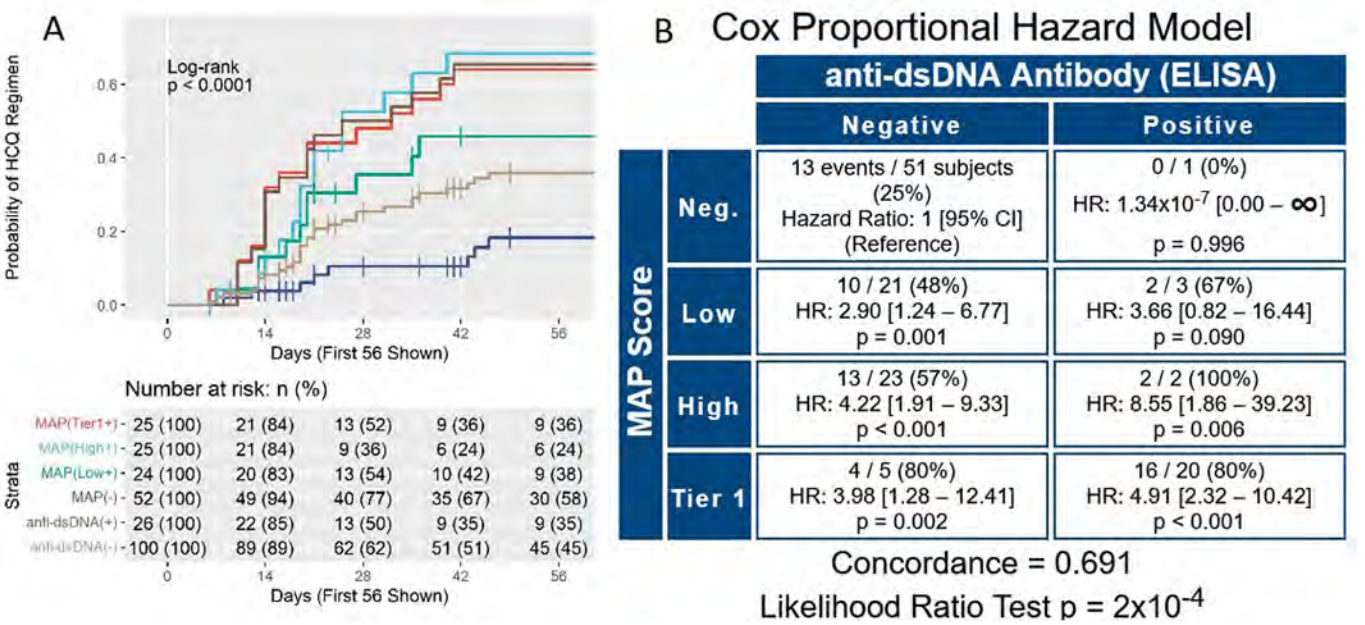

Figure 2. Panel A. Kaplan-Meier time-to-event curves for use of HCQ over time. Curves show the percent probability of using HCQ after T0 for the 4 study groups: tier-1 (MAP(Tier1+)), high tier-2 (MAP(High+)), low tier-2 (MAP(Low+)) negative (MAP(-)), in addition to anti-dsDNA positive (anti-dsDNA(+)) and negative (anti-dsDNA(-)) patients throughout the study. The X-axis reports the number of days since T0 and was truncated at 56 days to allow better visualization of the initial portion of the survival curves. Panel B. Cox proportional hazard model comparing the MAP score (Neg.: negative; Low: low tier-2; High: high tier-2, Tier 1: tier-1 positive) vs. anti-dsDNA antibodies for use of HCQ. In each quadrant, the numerators represent the number of subjects on HCQ after T0 (events, n=60 in total) while the denominators represent all subjects in that quadrant. Concordance and p value of the likelihood ratio test are also reported. For data analysis, we used the date of the visit when HCQ use was recorded in the medication list.

curves and hazard ratios for initiation of HCQ show that MAP positivity led to HCQ treatment, and that MAP negative was superior to anti-dsDNA negative in avoiding HCQ prescription (58% vs. 45%) (Figure 2).

Conclusion: This study demonstrates that the MAP helps to both diagnose and exclude SLE in patients suspected of the disease and, importantly, informs appropriate treatment decisions in this patient population.

Disclosure: R. Alexander, Exagen Inc., 3, 11; **S. Rey**, Exagen Inc., 3; **J. Conklin**, Exagen Inc., 3, 10, 11; **V. Domingues**, exagen, 5, 6, aurinia pharma, 1, 6, abbvie, 1, 2, 6, lilly, 1, 6; **M. Ahmed**, None; **J. Qureshi**, EXAGEN, 7; **A. Weinstein**, Exagen, Inc, 2, 5, 11.

Abstract Number: 0326

Apolipoprotein L1 (APOL1) in African-American SLE: Frequency and Clinical Associations

Michelle Petri[1], Romy Kallas[2], Jessica Li[3], Laurence Magder[4] and Daniel Goldman[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Lankenau Medical Center, Lankenau, PA, [3]Johns Hopkins University, Baltimore, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The APOL1 gene is implicated in induction of TLR3 agonists and interferons as well as in autophagy. Two genetic variants, G1 (2 single nucleotide polymorphisms) and G2 (6 base pair deletion) have been selected evolutionarily as protective against Trypanosoma. These APOL1 high risk allelles are associated with progression to end stage renal disease (ESRD), including lupus nephritis, and in one study with avascular necrosis in SLE. We examined the association of APOL1 in ESRD, avascular necrosis, atherosclerotic events and pulmonary fibrosis in African-American SLE.

Methods: APOL1 G1 (rs73885319 and rs60910145) and G2 (rs71785313) genetic variants were genotyped in 294 SLE African American patients in the Hopkins Cohort using TaqMan assays (Thermofisher Scientific, Waltham MA). APOL1 variants were classified as G1/G1 homozygous (in our dataset, G/G), G2/G2 homozygous (-/-), compound heterozygous G1/G2 (G/T or A/G AND TTATAA/-), G0/G1 heterozygous (G/T or A/G), or G0/G2 heterozygous (TTATAA/-). Based on the variants, patients were stratified into groups with 0, 1, or 2 risk alleles. To address the association between APOL1 group and the three outcomes, we used Kaplan Meier approach to estimate the distribution of time to outcomes from date of birth and log-rank test to compute the p-value. Cox regression was used to estimate the hazard ratio and adjust the relationships. The follow up for each patient ended at the patient's last cohort visit, or at the time of their first event.

Results: 294 African American patients were included in the analysis. 275 (93.5%) were female. The frequency of two copies of the APOL1 risk allele was 12.2% (Table 1). There was a higher proportion of patients with smoking history in the group with 2 risk alleles compared to the low risk groups (Table 2). There was an association with ESRD, but not with AVN, pulmonary fibrosis or cardiovascular events (Table 3).

Conclusion: Our study showed a significantly higher risk of progression to renal failure/ESRD among those with at least one risk allele, with a hazard ratio of 3.50 (p=0.0234 after adjusting for sex, ever smoking and hypertension).

Table 1. Frequency of the alleles and genotypes of APOL1

		Distribution of events	
	n (%)	AVN	Renal failure/ESRD
APOL1 alleles			
0 risk alleles	120 (40.8%)	23 (19.2%)	4 (3.3%)
1 risk allele	138 (46.9%)	25 (18.1%)	17 (12.3%)
2 risk alleles	36 (12.2%)	7 (19.4%)	3 (8.3%)
Genotype			
G0/G0	120 (40.8%)	23 (19.2%)	4 (3.3%)
G0/G1	89 (30.3%)	16 (18.0%)	8 (9.0%)
G0/G2	49 (16.7%)	9 (18.4%)	9 18.4%)
G1/G1	15 (5.1%)	4 (26.7%)	1 (6.7%)
G1/G2	16 (5.4%)	3 (18.8%)	2 (12.5%)
G2/G2	5 (1.7%)	0	0

Table 2. Patient characteristics based on APOL1 genotype

Characteristics	*0 APOL1 risk alleles n=120*	*1 APOL1 risk allele n=138*	*2 APOL1 risk alleles n=36*	*p-value*
Female sex	113 (94.2%)	128 (92.8%)	34 (94.4%)	0.8747
Age at diagnosis	31.6 (10.9)	31.0 (12.6)	28.1 (12.2)	0.3067
Duration of SLE at last follow up	19.8 (8.4)	18.9 (11.8)	21.9 (12.1)	0.3355
Less than or equivalent of high school graduate (<=12yrs)	46 (38.3%)	48 (35%)	15 (41.7%)	0.7233
Family income				
<$30,000	52 (44.8%)	53 (39%)	18 (51.4%)	0.5300
$30,000-<$65,000	32 (27.6%)	42 (30.9%)	11 (31.4%)	
>=$65,000	32 (27.6%)	41 (30.2%)	6 (17.1%)	
Smoking history, ever	39 (32.8%)	38 (27.7%)	18 (51.4%)	0.0285
History of hypertension	76 (63.3%)	93 (67.4%)	24 (66.7%)	0.7836
History of diabetes	16 (13.3%)	10 (7.3%)	4 (11.1%)	0.2682

Table 3. Relationships between events and APOL1 risk alleles (>=1 vs. 0)

	Unadjusted		Adjusted	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Renal insufficiency	1.35 (0.93, 1.96)	0.1166	1.27 (0.87, 1.85)[2]	0.2087[2]
Renal failure/ESRD	3.65 (1.25, 1.069)	0.0181	3.50 (1.19, 10.32)[2]	0.0234[2]
AVN	0.98 (0.57, 1.68)	0.9423	0.80 (0.46, 1.39)[3]	0.4252[3]
Atherosclerotic events	1.17 (0.65, 2.10)	0.6117	1.20 (0.65, 2.20)[4]	0.5598[4]
Pulmonary fibrosis	1.01 (0.56, 1.82)	0.9679	1.05 (0.58, 1.90)[2]	0.8646[2]
[2]adjusted for sex, smoking history and hypertension [3]adjusted for sex, smoking history and highest prednisone dose [4]adjusted for sex, smoking history, hypertension, high cholesterol, obesity				

We did not find an association between APOL1 risk alleles and avascular necrosis/ atherosclerotic events/pulmonary fibrosis. Our analysis included adjustment for smoking, as it is a risk factor for all the outcomes, and included larger numbers of African-American patients and outcomes than previous studies.

Disclosure: M. Petri, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **R. Kallas**, None; **J. Li**, None; **L. Magder**, None; **D. Goldman**, None.

Abstract Number: 0327

Lipoprotein(a) in Systemic Lupus Erythematosus Is Associated with History of Proteinuria and Renal Insufficiency

Caoilfhionn Connolly[1], Jessica Li[2], Daniel Goldman[3], Andrea Fava[2], Laurence Magder[4] and Michelle Petri[3], [1]Johns Hopkins, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Lipoprotein(a) [Lp(a)] is a well-recognized, independent risk factor for atherosclerotic cardiovascular disease. Cardiovascular disease is one of the leading causes of death in patients with systemic lupus erythematosus (SLE). Indeed, women with lupus have 2.66 times increased risk compared to controls, with both

Table 1. Patient characteristics grouped by Lp(a). Lp(a) levels were grouped into <125 and >=125nmol/L

SUBGROUP		Lp(a) level		p-value
		<125 nmol/L (n=279)	>=125 nmol/L (n=96)	
Sex				0.0724
	Female	256 (75.7%)	82 (24.3%)	
	Male	23 (62.2%)	14 (37.8%)	
Ethnicity				<0.0001
	African American	94 (59.5%)	64 (40.5%)	
	Other	36 (85.7%)	6 (14.3%)	
	Caucasian	149 (85.1%)	26 (14.9%)	
Smoking history				0.8892
	Never	209 (74.6%)	71 (25.4%)	
	Ever	68 (73.9%)	24 (26.1%)	
Age at last follow up				0.9106
	<30	15 (71.4%)	6 (28.6%)	
	30-<50	122 (75.3%)	40 (24.7%)	
	>=50+	142 (74%)	50 (26%)	
Age at SLE diagnosis				0.5298
	<30	128 (74.4%)	44 (25.6%)	
	30-<50	120 (72.7%)	45 (27.3%)	
	>=50+	31 (81.6%)	7 (18.4%)	
History of hypertension				0.0009
	Never	145 (82.4%)	31 (17.6%)	
	Ever	134 (67.3%)	65 (32.7%)	
History of cholesterol>=200				0.0094
	Never	147 (80.3%)	36 (19.7%)	
	Ever	131 (68.6%)	60 (31.4%)	
History of diabetes				0.0299
	Never	246 (72.8%)	92 (27.2%)	
	Ever	33 (89.2%)	4 (10.8%)	
History of low C3				0.5270
	Never	119 (76.3%)	37 (23.7%)	
	Ever	160 (73.4%)	58 (26.6%)	
History of Lupus Anticoagulant				0.5312
	Never	194 (73.5%)	70 (26.5%)	
	Ever	85 (76.6%)	26 (23.4%)	

SLE-specific and traditional cardiovascular risk factors playing a role. In this cross-sectional study, we evaluated Lp(a) levels in patients with SLE and evaluated for an association between atherosclerotic events, thrombotic events, renal disease, and disease activity.

Methods: SLE patients fulfilling the revised American College of Rheumatology (ACR) or SLICC classification criteria with a measurement of Lp(a) were included in the analysis. A cutoff of 125 nmol/L was chosen based on expert

Table 2. Associations between events and Lp(a). Lp(a) levels were grouped into <125 and >=125nmol/L

Outcomes	<125 (n=279)	>=125 (n=96)	adjusted estimate (95% CI)[1]	adjusted p-value[1]
Events (ever)				
Any atherosclerotic events	52(18.6%)	13(13.5%)	0.74 (0.37, 1.49)	0.3997
Any cardiovascular events	47(16.8%)	13(13.5%)	0.82 (0.4, 1.66)	0.584
MI	11(3.9%)	3(3.1%)	0.82 (0.21, 3.22)	0.7781
CVA	26(9.3%)	5(5.2%)	0.61 (0.22, 1.7)	0.3462
Angina or Coronary artery bypass grafting	13(4.7%)	6(6.4%)	1.95 (0.65, 5.87)	0.2354
Cardiomyopathy	6(2.2%)	3(3.2%)	1.09 (0.25, 4.68)	0.9072
PAD (claudication, tissue loss)	7(2.5%)	1(1.1%)	0.55 (0.06, 4.8)	0.5856
Any thrombosis (venous or arterial)	73(26.2%)	22(22.9%)	0.75 (0.42, 1.33)	0.3231
Any venous thrombosis	46(16.5%)	16(16.7%)	0.78 (0.4, 1.53)	0.4684
DVT	42(15.1%)	14(14.6%)	0.66 (0.33, 1.36)	0.2619
Proteinuria (history)	126(45.2%)	61(63.5%)	1.78 (1.07, 2.97)	0.0267
Avascular necrosis	21(7.5%)	9(9.4%)	0.84 (0.35, 2.01)	0.6947
Clinical measures at the visit				
PGA, mean (SD)	0.61 (0.62)	0.87 (0.71)	0.19 (0.03, 0.35)[2]	0.0224[2]
UPCR>=500	30 (11.1%)	19 (21.1%)	1.69 (0.84, 3.37)	0.1392
EGFR<60	50 (18.1%)	27 (28.1%)	1.92 (1.05, 3.54)	0.0349

[1]OR (95% CI)/mean estimate (95% CI) and p-values were adjusted for age, sex, and race
[2]mean estimate calculated from linear regression, others are odds ratios
Abbreviations: PGA=physician's global assessment, UPCR=Urine protein to creatinine ratio

opinion. Chi-square test was used to compare the differences between patient characteristics, including traditional and disease specific cardiovascular risk factors, and Lp(a) levels. Logistic regression or linear regression were used, where appropriate, to assess the association between Lp(a) values and the measured outcomes.

Results: 389 measurements of Lp(a), contributed from 375 patients were analyzed; 12 patients had 2 measurements and 1 had 3 measurements. Of these patients, 90% were female, 42% African American, and 47% Caucasian. The distribution of Lp(a) was heavily right skewed; values ranged from 8 to 671 nmol/L with a mean of 94 and median of 47nmol/L. Men, African American patients, patients with history of hypertension and hypercholesterolemia were more likely to have Lp(a) levels >=125 nmol/L. Patients with a history of diabetes were less likely to have levels >=125 nmol/L (Table 1).

In this study, we did not observe an association between Lp(a) and atherosclerotic or thrombotic events. There was an association between elevated Lp(a) level and a history of proteinuria (OR 1.78, p-value=0.026). This association remained significant following adjustment for age, sex, race, low C3, and elevated anti-dsDNA (OR=1.74, p-value=0.0498). There was also an association with eGFR< 60 (p=0.03). Patients with higher Lp(a) levels also had higher physician global activity (p=0.02).

Conclusion: Consistent with the general population, Lp(a) levels skewed toward lower values in patients with SLE. There was not an association between Lp(a) and atherosclerotic or thrombotic events, but this may have been limited due to small sample size. Elevated levels of Lp(a) were associated with proteinuria, reduced eGFR and physician global activity, with an inverse association observed with type 2 diabetes mellitus. An increase in Lp(a) concentrations has previously reported in non-SLE renal disease even prior to reduction in eGFR. The role of Lp(a) as a potential biomarker for early renal disease and poor renal outcomes in SLE warrants further evaluation with consideration for more granular subphenotyping.

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Abstract Number: 0328

Natural Language Processing to Identify Lupus Nephritis Phenotype in Electronic Health Records

Yu Deng[1], Jennifer Pacheco[1], Anh Chung[1], Chengsheng Mao[1], Joshua Smith[2], juan zhao[1], Wei-Qi Wei[2], April Barnado[3], Chunhua Weng[4], Cong Liu[4], Adam Gordon[1], Jingzhi Yu[1], Yacob Tedla[1], Abel Kho[1], Rosalind Ramsey-Goldman[1], Theresa Walunas[1] and Yuan Luo[1], [1]Northwestern University, Chicago, IL, [2]Vanderbilt Universty Medical Center, Nashville, TN, [3]Vanderbilt University Medical Center, Nashville, TN, [4]Columbia University, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is a major disease manifestation of Systemic lupus erythematosus (SLE) leading to organ damage and increased mortality. Accurately identifying lupus nephritis in electronic health records (EHRs), a key component of SLE classification criteria domain, would add value to observational studies and clinical trials. However, information related to LN, e.g., kidney biopsy findings are usually present in clinical notes, not as structured data. In this study, we developed algorithms to identify LN with and without natural language processing (NLP) using EHR data from the Northwestern Medicine Enterprise Data Warehouse (NMEDW). We hypothesize that NLP algorithms including information from the clinical notes will outperform the baseline algorithm using structured data only.

Methods: We identified 472 patients with SLE from the Chicago Lupus Database who also had at least four encounters in the NMEDW. We developed four algorithms: a rule-based algorithm using only structured data and three different NLP algorithms based on L2-regularized logistic regression. In the first NLP algorithm (Full-MetaMap-binary), we used the presence or absence of all the MetaMap extracted concept unique identifiers (CUIs) as features. In the second NLP algorithm (Full-MetaMap-count), we used the same CUIs as features but their number of occurrences as the feature value. In the third NLP algorithm (MetaMap-mixed), we used a mixture of features from structured data, regular expression (regex) concepts, and a curated list of CUIs related to LN. We evaluated all four algorithms in an

internal validation dataset based on F-measure, sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV). We further validated the baseline algorithm and the best performed NLP algorithm on an external dataset from Vanderbilt University Medical Center (VUMC).

Results: In the NMEDW internal validation dataset, the Full-MetaMap-binary, Full-MetaMap-count, and MetaMap mixed model achieved F measures of 0.72, 0.71, 0.79, respectively, compared to the baseline model (F measure, 0.41) (see Table). In the external validation dataset, our best performing NLP model (MetaMap mixed model) improved F measure (0.62 vs 0.96) compared to the structured data only algorithm.

Table 1. Algorithm performance

Dataset	Algorithm	Sensitivity	Specificity	PPV	NPV	F Measure
NMEDW (internal validation)	Baseline	0.43	0.6	0.39	0.64	0.41
NMEDW (internal validation)	Full-MetaMap-binary	0.63	0.93	0.85	0.81	0.72
NMEDW (internal validation)	Full-MetaMap-count	0.6	0.95	0.88	0.8	0.71
NMEDW (internal validation)	MetaMap-mixed	0.74	0.92	0.84	0.86	0.79
VUMC	Baseline	0.92	0.61	0.46	0.96	0.62
VUMC	MetaMap-mixed	1	0.97	0.93	1	0.96

Conclusion: We developed three NLP models and compared them to a structured data only algorithm to identify LN from EHR. The best performing NLP algorithm incorporating structured data, CUIs, and regex concepts improved the F-measure in both internal and external validation datasets. NLP algorithms can serve as powerful tools to accurately identify LN in EHR for clinical research.

Disclosure: Y. Deng, None; **J. Pacheco**, None; **A. Chung**, None; **C. Mao**, None; **J. Smith**, None; **j. zhao**, None; **W. Wei**, None; **A. Barnado**, None; **C. Weng**, None; **C. Liu**, None; **A. Gordon**, None; **J. Yu**, None; **Y. Tedla**, None; **A. Kho**, Datavant, 1, 7, 11; **R. Ramsey-Goldman**, None; **T. Walunas**, None; **Y. Luo**, None.

Abstract Number: 0329

Racial and Ethnic Disparities in Risk of End-Organ Disease Following SLE Diagnosis in a Multi-Ethnic Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Racial and ethnic minorities experience a disproportionate burden of systemic lupus erythematosus (SLE) as well as earlier development of lupus manifestations as compared to White individuals. Data on onset of lupus symptoms across multiple organ domains and in Asian patients in the US is lacking. We analyzed racial/

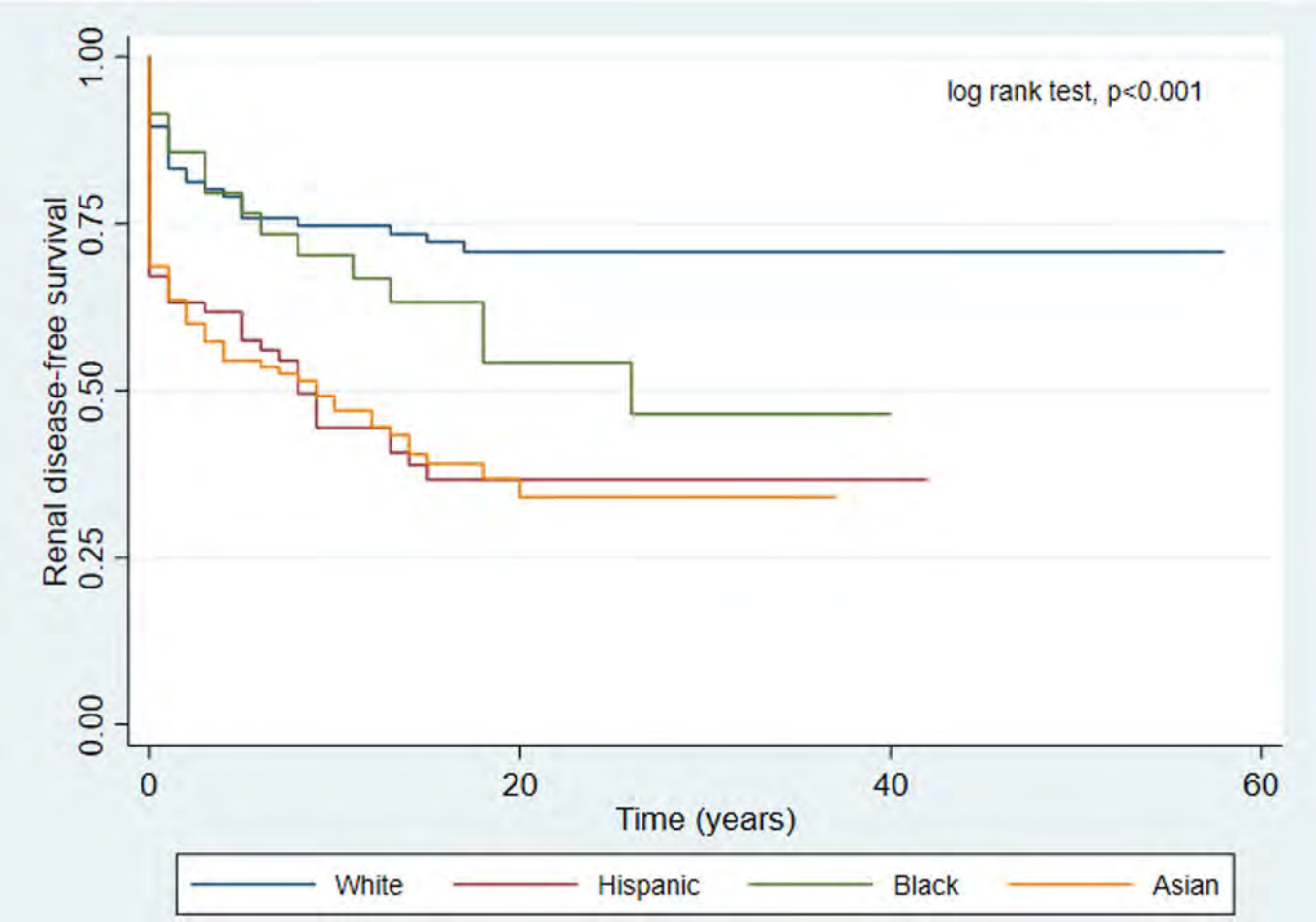

Figure 1. Kaplan-Meier curve depicting time to onset of renal disease by race/ethnicity.

ethnic differences in time to onset of renal, neuropsychiatric, hematologic, cardiovascular, and multiorgan disease following SLE diagnosis in a multi-ethnic cohort of patients.

Methods: The California Lupus Epidemiology Study (CLUES) is a longitudinal cohort of 431 individuals with SLE, of whom 332 participated in a baseline in-person study visit. Data on major end-organ manifestations including dates of onset were collected and confirmed by study rheumatologists. Manifestations of end-organ disease were categorized by organ system: renal (lupus nephritis), neuropsychiatric (seizure, stroke, mononeuritis multiplex, peripheral/cranial neuropathy, myelitis), hematologic (immune thrombocytopenic purpura, autoimmune hemolytic anemia, thrombotic thrombocytopenic purpura), and cardiovascular (heart failure, myocardial ischemia, cardiac arrythmia, Libman-Sacks endocarditis). Multiorgan disease was defined as manifestations in ≥2 of the above organ systems. Self-reported race/ethnicity was categorized as White, Hispanic, Black, and Asian. Kaplan-Meier methods and log-rank tests compared organ system-free survival following SLE diagnosis by race/ethnicity; participants who did not develop outcome of interest were censored at their CLUES study visit. Cox proportional hazard models assessed the risks of end-organ disease by race/ethnicity, with age at diagnosis and female sex as covariates.

Results: CLUES participants are 89% female and have a mean age and age at diagnosis of 45 and 29 years, respectively. The distribution of self-reported race/ethnicity was as follows: 29% White, 23% Hispanic, 11% Black, and 36% Asian. Renal, neuropsychiatric, hematologic, cardiovascular, and multiorgan disease was confirmed in 154 (46%), 53 (16%), 62 (19%), 30 (9%), and 79 (24%) subjects, respectively. The median time to development of multiorgan disease was 9.5, 5, 8, and 3.5 years for White, Hispanic, Black and Asian subjects, respectively. Race/ethnicity

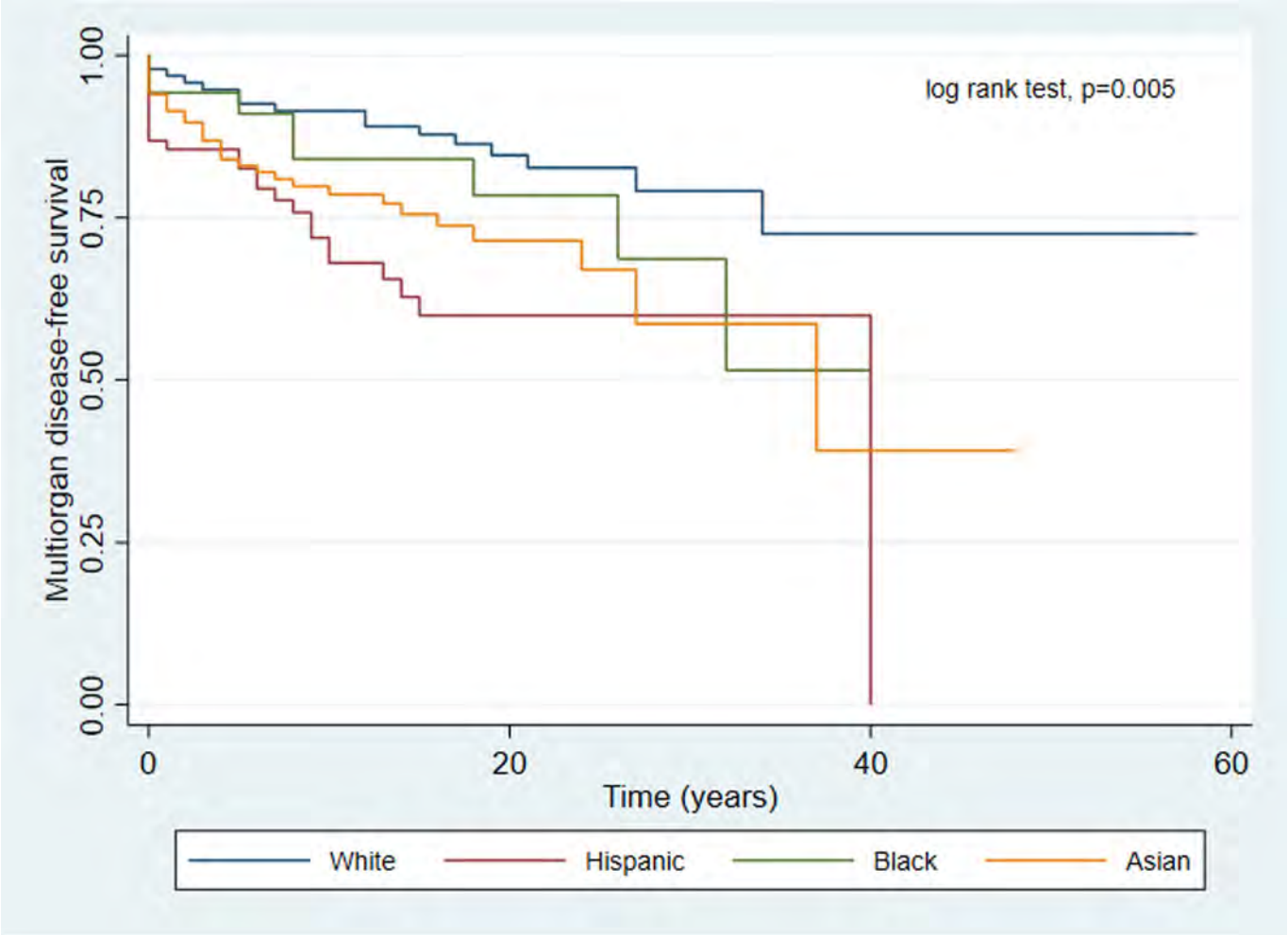

Figure 2. Kaplan-Meier curve depicting time to onset of multiorgan disease by race/ethnicity.

was associated with significant differences in time to onset of renal and multiorgan disease (Figures 1 and 2). Cox regression models showed that non-White racial/ethnic groups experienced greater risks of renal, hematologic, and multiorgan disease as compared to White participants (Table 1).

Table 1. Factors associated with renal, neuropsychiatric, hematologic, cardiovascular, and multiorgan disease following SLE diagnosis in CLUES cohort participants

Variable	Renal*	Neuropsychiatric	Hematologic	Cardiovascular	Multiorgan
Age at diagnosis	0.99 (0.97 - 1.00)	1.02 (1.00 - 1.04)	0.96 (0.94 - 0.99)	1.02 (0.99 - 1.06)	1.01 (0.99 - 1.03)
Female sex	0.40 (0.26 - 0.62)	0.72 (0.32 - 1.62)	0.80 (0.38 - 1.70)	0.62 (0.21 - 1.82)	0.53 (0.28 - 0.99)
Race/ethnicity					
White	*Ref*	*Ref*	*Ref*	*Ref*	*Ref*
Hispanic	2.70 (1.66 - 4.38)	1.23 (0.60 - 2.53)	2.39 (1.16 - 4.92)	1.40 (0.53 - 3.71)	3.02 (1.60 - 5.69)
Black	1.95 (1.03 - 3.71)	1.39 (0.59 - 3.25)	2.11 (0.82 - 5.41)	1.67 (0.56 - 5.02)	1.71 (0.72 - 4.06)
Asian	2.87 (1.82 - 4.51)	0.79 (0.39 - 1.60)	1.70 (0.84 - 3.43)	1.10 (0.43 - 2.82)	2.28 (1.23 - 4.21)

*Hazard ratio (95% confidence interval), estimated using Cox regression models including age at SLE diagnosis and female sex as covariates. Ref, reference category.

Conclusion: Racial/ethnic minorities with lupus are at higher risk for developing end-organ disease as compared to White patients. Black patients experience higher hazards of lupus nephritis compared to White patients, although conclusions in other domains are limited by sample size. Our data highlight the risk of lupus nephritis and multiorgan disease among Hispanic and Asian patients, and hematologic manifestations among Hispanics, who experience these manifestations earlier in their lupus disease course as compared to White patients.

Disclosure: A. Aguirre, None; **A. Seet**, None; **L. Trupin**, None; **P. Katz**, None; **K. Barbour**, None; **C. Lanata**, None; **M. Dall'Era**, AstraZeneca, 2, Aurinia, 2, Biogen, 2, Bristol Myers Squibb, 2, GlaxoSmithKline, 2, Pfizer, 2; **J. Yazdany**, Pfizer, 2, Astra Zeneca, 5, Eli Lilly, 2, University of California, San Francisco, 3.

Abstract Number: 0330

Serologic Phenotypes Distinguish SLE Patients with Myositis And/or Interstitial Lung Disease (ILD)

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Descriptive statistics for SLE patients and differences between groups

Demographics and antibodies variables	Control N=72	ILD and/or Myositis ILD (9), myositis (3), ILD and myositis (2) N=14	Differences (95% CI)[a]
Female sex, N (%)	61 (84.7)	12 (85.7)	0.01 (-0.25, 0.15)
Caucasian race/ethnicity, N (%)	34 (47.2)	5 (35.7)	0.12 (-0.16, 0.34)
Mean age at SLE diagnosis, years (SD)	33.6 (14.2)	29.5 (11.0)	3.83 (-4.15, 11.6)
Mean SLE duration at baseline, years (SD)	2.9 (3.2)	12.7 (13.9)	**4.54 (0.55, 13.23)**
Baseline positive (any titre) for ≥1 test N (%)	63 (87.5)	13 (92.9)	0.05 (-0.2, 0.17)
Positive for ≥1 test (any titre) during follow-up, N (%)	62 (86.1)	14 (100.0)	0.14 (-0.09, 0.24)
Positive for ≥1 test (any titre) baseline/ follow-up, N (%)	67 (93.1)	14 (100.0)	0.07 (-0.15, 0.15)
Baseline positive (med/hi) for ≥1 test N (%)	47 (65.3)	13 (92.9)	**0.28 (0.01, 0.41)**
Positive for ≥1 test (med/hi) during follow-up, N (%)	42 (59.2)	13 (92.9)	0.34 (0.07, 0.47)
Positive for ≥1 test (med/hi) baseline/ follow-up, N (%)	53 (74.6)	14 (100.0)	**0.25 (0.02, 0.37)**

[a] The difference in proportions between groups (Control (n = 72) and cases (n = 14).) as well as their 95% confidence intervals.

Table 2. Descriptive statistics of baseline and follow-up biomarkers between groups

Biomarker variables	Baseline testing		Follow-up testing	
	Control N=72	Myositis and/or ILD N=14	Control N=72	Myositis and/or ILD N=14
KL-6/mucin-1 (MUC-1) >500 U/ml, N (%)	21 (29.2)	7 (50.0)	14 (19.4)	8 (61.5)
Anti Ro52/TRIM21 ≥ 31, Med/High (%)	15 (20.8)	6 (42.9)	14 (19.4)	5 (35.7)
Anti Ku ≥ 31, Med/High (%)	1 (1.4)	3 (21.4)	0 (0.0)	3 (21.4)
Anti TERF1 > 500 U/ml, N (%)	4 (5.6)	1 (7.1)	3 (4.2)	2 (14.3)
Anti NT5c1A/Mup4 ≥ 31, Med/High (%)	5 (6.9)	1 (7.1)	5 (6.9)	1 (7.1)
Anti HMGCR, positive (%)*	0 (0.0)	1 (7.1)	0 (0.0)	1 (7.1)
Anti CENPA ≥ 31, Med/High (%)	5 (6.9)	1 (7.1)	4 (5.6)	1 (7.1)
Anti NOR90 ≥ 31, Med/High (%)	0 (0.0)	1 (7.1)	0 (0.0)	1 (7.1)
Anti CENPB ≥ 31, Med/High (%)	2 (2.8)	2 (14.3)	2 (2.8)	0 (0.0)
Anti Mi2 α ≥ 31, Med/High (%)	2 (2.8)	0 (0.0)	0 (0.0)	1 (7.1)
Anti PMScl _PM75 ≥ 31, Med/High (%)	2 (2.8)	0 (0.0)	3 (4.2)	0 (0.0)
Anti PMScl_PM100 ≥ 31, Med/High (%)	2 (2.8)	0 (0.0)	2 (2.8)	0 (0.0)
Anti PL7≥ 31, Med/High (%)	1 (1.4)	0 (0.0)	2 (2.8)	0 (0.0)
Anti Fibrillarin ≥ 31, Med/High (%)	0 (0.0)	0 (0.0)	2 (2.8)	0 (0.0)
Anti Th/To_hPOP1 ≥ 31, Med/High (%)	0 (0.0)	0 (0.0)	2 (2.8)	0 (0.0)
Anti Scl70 ≥ 31, Med/High (%)	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)
Anti TIF1 γ ≥ 31, Med/High (%)	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)
Anti Mi2 β ≥ 31, Med/High (%)	0 (0.0)	0 (0.0)	1 (1.4)	0 (0.0)

* only one low-positive

Background/Purpose: To determine if a serologic phenotype can be identified in SLE patients with myositis and/or ILD.

Methods: Adult SLE patients (without myositis or ILD at baseline) had annual assessments and provided bio-samples between 2000-2017. Potential new-onset myositis was identified using the SLICC Damage Index (SDI) muscle atrophy/weakness item, the SLEDAI-2K item for myositis, and annual serum creatinine kinase testing. Potential new-onset ILD was identified using the SDI pulmonary fibrosis item. Chart review confirmed cases. Randomly sampled patients from baseline visit (from 2000 onward) became a sub-cohort (N=72). Cases and sub-cohort were compared regarding baseline characteristics. Patients' myositis-related biomarkers were assessed at baseline and one randomly selected follow-up between baseline and end of observation (date of myositis/ILD diagnosis or Dec. 31, 2017).

Table 3. Hazard Ratio for baseline characteristics of SLE patients with myositis and/or ILD (univariate and adjusted models)

Variables	Hazard Ratio for characteristics at baseline	
	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]
Female sex	1.43 (0.32, 6.46)	3.43 (0.36, 32.5)
Caucasian race/ethnicity	0.54 (0.18, 1.62)	0.43 (0.13, 1.48)
Age at SLE diagnosis, years	0.98 (0.93, 1.02)	0.98 (0.93, 1.03)
KL-6/MUC-1 >500 U/ml	**2.87 (1.00, 8.26)**	**4.94 (1.27, 19.2)**
Anti TERF1 > 500 U/ml	1.96 (0.24, 15.7)	1.07 (0.12, 9.80)
Anti Ku ≥31 (Med or High positive)	**4.01 (1.07, 15.1)**	**6.30 (1.01, 39.5)**
Anti Ro52/TRIM21 ≥31 (Med or High positive)	1.74 (0.60, 5.10)	1.16 (0.31, 4.31)
Anti NT5c1A/Mup4 ≥31 (Med or High positive)	1.58 (0.20, 12.3)	2.10 (0.22, 20.0)
Anti CENPA ≥31 (Med or High positive)	1.04 (0.13, 8.00)	0.05 (0.00, 3.15)
Anti CENPB ≥31 (Med or High positive)	3.88 (0.84, 17.8)	**9.36 (1.00, 87.5)**

[a] Adjusted for all variables shown

Line immunoassay (Euroimmun AG, Luebeck, Germany) detected autoantibodies to Mi2-α, Mi2-β, MDA5, NXP2, TIF1γ, PM/Scl75, PM/Scl100, Ku, SRP, Jo-1, EJ, OJ, PL7, PL12, Ro52, HMGCR, NT5c1A/Mup44, CENP-A, -B, Scl70, NOR90, RNAP, and Th/To (hPOP1). An addressable laser bead immunoassay was used to detect antibodies to TERF-1. KL-6 levels were determined by ELISA (R&D Systems). Descriptive analyses and hazards ratios (HRs) were generated for myositis and/or ILD incidence, focusing on baseline serology and adjusting for demographic variables (sex, ethnicity, and age at SLE diagnosis) and positive biomarkers.

Results: The median (IQR) SLE duration at baseline was 1.8 (0.41, 5.6) years. Between 2000-2017, 14 SLE patients (12, 85.7% female) developed myositis and/or ILD over an average follow up of 9.2 years (incidence 17.6 cases per 1000 patient-years). Thirteen of these (92.9%) had at least one medium/high positive biomarker at baseline, versus 47 (65.3%) SLE patients who never developed myositis and/or ILD. The most common baseline biomarkers in patients with myositis and/or ILD were KL-6, anti-Ku, anti-Ro52. In multivariate Cox regression analyses, SLE patients were more likely to develop myositis and/or ILD if they had elevated baseline KL-6, anti-Ku positivity, or anti-CENP-B positivity. Potential limitations include the relatively low number of events.

Conclusion: In this SLE sample, KL-6, anti-Ku, and anti-CENP-B at baseline were highly associated with myositis and/or ILD risk. Ours is the first study of this serologic phenotype, identifying SLE patients most at risk of myositis/ILD.

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Abstract Number: 0331

Urinary MicroRNAs as Systemic Lupus Erythematosus Biomarkers and Its Potential for Accurate Assessment of Disease Severity

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by autoantibody production, immune complex deposition, and heterogeneous clinical manifestations affecting many organs, including the skin, joints, the central nervous system, and the kidneys. Once clinical symptoms have developed, prompt diagnosis and proper management of SLE remain great challenges to physicians. Due to the heterogeneity of immune dysregulation, the severity and progression of the disease largely varies among patients, while no single biomarker has emerged as a surrogate for disease activity or severity of SLE.

Recently, evidence indicates that exosomes play important roles in immune modulation and are associated with the immune pathogenesis of autoimmune diseases, including systemic lupus erythematosus. Exosomes are 20-150 nm-sized vesicles that function as a vital medium for cellular communication. It encapsulates microRNAs (miRNAs), a non-coding RNA, which are known as gene expression modulators, and strongly relates to physiological conditions like disease status. Here, we have developed a mass-producible and sterilizable nanowire-based device (nanowire device) that can extract urinary exosomal microRNAs efficiently. Our objective of the research is to extract urinal exosomes and detect microRNAs using nanowire devices, and identify biomarkers which could support SLE diagnosis and identify its status and severity.

Methods: Exosomes were extracted by nanowire device and miRNA expression was measured from urine samples of 30 SLE patients and 30 non-SLE donors using a microarray to yield comprehensive microRNA expression profiles.

Results: Differential expression analysis revealed 242 biomarker miRNAs candidates,160 up-regulated and 82 down-regulated in SLE patients compared with healthy individuals. Down-regulation patterns were related to the severity of the disease, revealing severity-specific miRNAs.Pathway analyses revealed the candidate miRNAs showed relation with genes strongly related to SLE including JAK-STAT and BCL pathways. Moreover, we adopted a support vector machine model and successfully developed a classifier to detect SLE based on these miRNA expression patterns, which showed remarkably high sensitivity (0.89) and specificity (0.82).

Conclusion: These findings show that urinary miRNAs may provide insights into SLE pathogenesis, and could be a potential biomarker of disease activity, paving the way to a liquid biopsy for individualized SLE treatment.

Disclosure: H. Yamaguchi, Craif Inc., 3; **Y. Ando**, Craif inc., 3; **M. Mizunuma**, Craif.inc, 3, 4; **M. Inami**, Astellas Pharma Inc., 3; **K. Suzumura**, Astellas Pharma Inc., 3; **Y. Ichikawa**, Craif inc., 4.

Abstract Number: 0332

Prevalence of Systemic Lupus Erythematosus in the United States: Updated Population Representative Estimates from the Medical Expenditure Panel Survey (MEPS) 2016-2018

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Figure 1. US Annual SLE Prevalence Across Diagnostic Definitions (2016-2018)

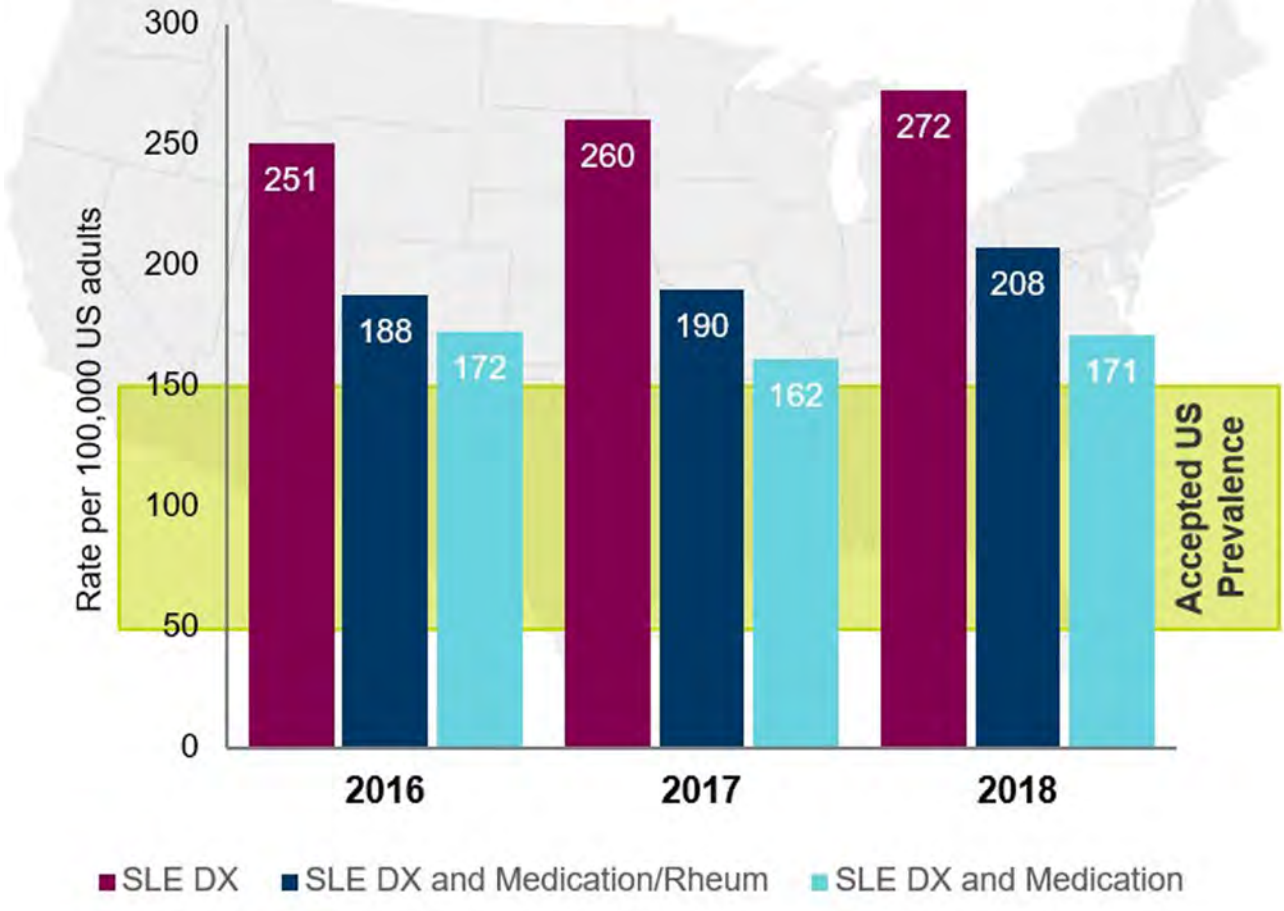

Table 1. SLE prevalence per 100,000 total US adults and 95 % confidence interval (CI) stratified by key demographic characteristics. (2016-2018 Pooled)

	SLE DX Only	[Default SLE criteria] SLE Diagnosis + Medication/ Rheumatologist	SLE Diagnosis + Medication
Overall	261 (203, 319)	195 (149, 242)	168 (130, 206)
Age subgroup			
<45	247 (160, 333)	177 (107, 246)	139 (84, 193)
45+	274 (203, 344)	211 (154, 268)	193 (142, 245)
Gender, n(%)			
Male	41 (11, 72)	37 (7, 68)	34 (6, 61)
Female	467 (362, 572)	343 (260, 427)	295 (224, 365)
Geographic Region, n(%)			
Northeast	235 (107, 364)	179 (58, 299)	153 (58, 249)
Midwest	300 (168, 432)	205 (112, 298)	197 (105, 289)
South	310 (199, 421)	244 (153, 336)	196 (129, 264)
West	180 (92, 267)	130 (68, 192)	117 (60, 174)
Health Insurance Coverage Indicator, n(%)			
Any Private	211 (152, 270)	168 (115, 220)	143 (98, 188)
Public Only	435 (293, 577)	311 (202, 421)	270 (175, 366)
Uninsured	219 (21, 417)	116 (19, 213)	112 (15, 208)
Race, n(%)			
White - no other race reported	245 (181, 310)	187 (133, 241)	158 (114, 201)
Black - no other race reported	366 (231, 502)	287 (162, 412)	252 (145, 358)
Other single race	92 (11, 173)	80 (2, 159)	80 (2, 159)
Multiple Races Reported	680 (35, 1326)	323 (0, 690)	323 (0, 690)
Ethnicity, n(%)			
Mexican/Mex American/Chicano	157 (71, 244)	136.9 (61, 213)	111.5 (41, 182)
Non-Mexican Hispanic	437 (215, 659)	319 (125, 513)	288 (119, 456)
Non-Hispanic	259 (195, 324)	192 (142, 243)	166 (122, 209)
Education Completed, n(%)			
<= Grade 12	216 (142, 289)	157 (97, 217)	142 (86, 199)
1-2 years college	261 (140, 381)	180 (92, 269)	165 (81, 248)
3-4 years college	311 (183, 438)	233 (128, 339)	204 (109, 298)
5+ years college	341 (137, 545)	293 (94, 491)	208 (87, 329)

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, multi-organ, autoimmune disease whose prevalence in the US has not been recently updated in real-world studies. Prevalence estimates range from 50-150 per 100,000 adults in the US, but these estimates are due to be refreshed. In addition, the heterogeneity of the clinical manifestations of SLE and lack of a diagnostic test make SLE prevalence challenging to quantify. Therefore, our study sought to utilize recent nationally representative population data to estimate prevalence estimates of SLE in the US.

Methods: We analyzed data from the 2016 - 2018 Medical Expenditure Panel Surveys (MEPS), an annual survey using a complex sampling strategy to represent the US civilian non-institutionalized population. Prevalence was defined as self-reported SLE diagnosis with additional SLE-related medication use and/or any rheumatologist visit during the calendar year. Two other SLE diagnostic criteria were used as a sensitivity analysis (sensitive: SLE diagnosis only; restrictive: SLE diagnosed and currently treated). Self-reported SLE was linked to a specific visit to a healthcare professional (outpatient or inpatient). The annual prevalence was reported per 100,000 US adults and 95 % confidence interval (CI) stratified by key demographic characteristics.

Results: From 2016-2018, 96,996 adults reported annual data in MEPS, of which 199 (0.20%) reported SLE diagnosis, 154 (0.16%) respondents report SLE with either SLE-related medication and/or rheumatologist visit, and 139 (0.14%) respondents reported SLE with SLE-related medication. The pooled weighted annual prevalence of SLE using each respective SLE-definition was 261 (95% CI: 203, 319); 195 (95% CI: 149, 242) and 168 (95% CI: 130, 206) per 100,000 adults. From 2016 to 2018, the prevalence of SLE appeared to increase slightly. The prevalence of SLE was about 9 times higher in females compared to males (343 vs. 37 per 100,000 adults). Individuals who reported Black or multiple races and Mexican Hispanic ethnicity appeared to have a higher prevalence of SLE compared to white or non-Hispanic adults, respectively. Respondents with public insurance (Medicare or Medicaid) were twice as likely to report SLE than those privately insured (311 vs. 168 per 100,000 adults). Respondents in the Southern region of the US had a slightly higher prevalence of SLE compared to other regions (North, West, or East). The 95% confidence intervals were relatively wide across most stratified analyses, limiting the ability to detect population differences.

Conclusion: The self-reported SLE prevalence in the US was higher across all three disease definitions in MEPS than the currently accepted estimate of 50 to 150 per 100,000 adults. Similar to other studies, females, Black, and Hispanic respondents were found to have a higher prevalence of SLE compared to males and white or non-Hispanic individuals. While many real-world studies include only single-payer populations, we demonstrate a more diverse payer patient-population and a higher burden of SLE. SLE prevalence is challenging to quantify; however, this study suggests that the actual US of SLE prevalence may be higher than reported.

Disclosure: M. Pollack, AstraZeneca, LP., 3; **S. Sze-jung Wu**, AstraZeneca, 3; **E. Farrelly**, AstraZeneca, 2; **S. Grabich**, AstraZeneca, 2; **R. Ortmann**, AstraZeneca, 3.

Abstract Number: 0333

Validation of the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) Classification Criteria for Systemic Lupus Erythematosus (SLE) in Hong Kong Chinese

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1

Classification criteria	Sensitivity	Specificity	AUC of ROC curve
1997 ACR	85.9%	94.3%	0.948
2012 SLICC	97.7%	86.3%	0.980
2019 EULAR/ACR with 10 points as cut-off	96.1%	85.8%	0.979
2019 EULAR/ACR with 9 points as cut-off	97.5%	65.8%	
2019 EULAR/ACR with 11 points as cut-off	95.0%	88.0%	
2019 EULAR/ACR with 10 points as cut-off (men)	94.4%	93.1%	
2019 EULAR/ACR with 10 points as cut-off (women)	96.2%	84.5%	
a2019 EULAR/ACR with 10 points as cut-off (age >50 years)	93.4%	91.1%	
2019 EULAR/ACR with 10 points as cut-off (age ≤50 years)	96.7%	79.2%	

Background/Purpose: To validate the 2019 EULAR/ACR classification criteria for SLE in Hong Kong Chinese patients and compare its performance with the 2012 Systemic Lupus International Collaborating Clinics (SLICC) and 1997 American college of rheumatology (ACR) criteria

Methods: We retrospectively reviewed the medical records of consecutive patients who attended the Rheumatology clinics in Tuen Mun and Pok Oi hospitals between May and September 2019. Patients with anti-nuclear antibody (ANA) ≥1:80 were included and patients with ANA < 1:80 or no ANA results were excluded. Patients were evaluated and cross-checked for the fulfilment of the 1997 ACR, 2012 SLICC and 2019 EULAR/ACR criteria by two investigators (YKC,CL). Medical records were then reviewed by an expert panel consisting of 3 senior rheumatologists, who were blinded for the results of the criteria evaluation, for a diagnosis of SLE based on the clinical judgement and therapeutic decisions. Teleconferences were arranged by the panel to discuss the discrepancies of the final diagnosis and agreement was made by voting. The three SLE criteria were evaluated against the clinical diagnosis of SLE as judged by the expert panel on the sensitivity and specificity, which was calculated by 2x2 contingency tables ("condition positive" = clinical diagnosis of SLE; "test positive" = criteria positive for SLE) with standard formulas (sensitivity = true positive/[true positive + false negative]; specificity = true negative / [true negative + false positive]). Receiver operating characteristic (ROC) curve was used to study the optimal cut-off points from the EULAR/ACR criteria for the highest summation of specificity and sensitivity.

Results: 3967 patients were screened; 1533 patients who were positive for ANA (≥1:80) were included (88.2% women). The mean age of these patients at first rheumatology clinic attendance was 45.6±15.6 years and the duration of follow-up was 8.3±6.4 years. A total of 562 patients were judged to have SLE by the expert panel (discrepancy of clinical diagnosis in 135 patients resolved with voting). The sensitivity and specificity of the three SLE classification criteria in our patients are listed in Table 1. ROC analysis showed that the best cut-off for a clinical diagnosis of SLE using the EULAR/ACR criteria was 10 points (area under the curve [AUC] 0.979; sensitivity 96.1% and specificity 85.8%). Similar figures were obtained for subgroups of patients stratified by gender and different age ranges.

Conclusion: In our cohort of Hong Kong Chinese patients, the 2019 EULAR/ACR criteria is more sensitive but less specific when compared with 1997 ACR criteria for classifying SLE. On the other hand, the EULAR/ACR criteria is less sensitive but more specific than the 2012 SLICC criteria. The specificity of the EULAR/ACR criteria for SLE is higher in male than female patients. In our patients older than 50 years, the EULAR/ACR criteria is less sensitive but more specific for a classification of SLE. Overall, the performance of the EULAR/ACR criteria for a diagnosis of SLE in our study is similar to that reported in recent Asian studies although the sensitivity is lower, which may be related to the inclusion of ANA+ patients only.

Disclosure: C. Mok, None; **Y. Chung**, None; **C. Lee**, None; **L. Ho**, None; **C. To**, None.

Abstract Number: 0334

Association Between Systemic Lupus Erythematosus and Myasthenia Gravis: A Population-Based National Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) and myasthenia gravis (MG) are two autoimmune disorders that have a young female preponderance, relapsing-remitting course, and positive antinuclear antibodies. The coexistence of SLE and MG has been reported in the literature with the majority of cases MG preceding SLE diagnosis[1]. There has been no controlled epidemiological study to prove a real association between these two diseases.

This study aims to estimate the prevalence of SLE among MG patients compared to non-MG patients and to study the demographics of the MG patients who developed SLE preceding or following MG diagnosis.

Methods: This is a retrospective observational study using the IBM Explorys database, a pooled de-identified clinical database of > 60 million unique patients in the US with patient-level data. The Explorys collects aggregated, standardized, and normalized clinical data from different electronic health records automatically updated in near real-time. International Classification of Diseases – 9 (ICD-9) diagnosis codes were used to define SLE and MG patients. For SLE patients, the ICD code was used along with at least two rheumatologist visits for patients ≥ 18 years of age. The control group included adults ≥ 18 years of age with the exclusion of MG diagnosis. We further stratified the cohorts by adding the following variables to the search tool: age, race, gender, smoking status, thymectomy, autoimmune

Table 1. Demographics and clinical characteristics of MG patients and controls with SLE

Variables	MG with SLE n=370 n (%)	Controls with SLE n=65,000 n (%)
Age		
> 65 years	130 (35.14)	19,740 (30.37)
18-65 years	230 (62.16)	45,470 (69.95)
Gender		
Male	30 (8.11)	6,110 (9.4)
Female	330 (89.19)	58,900 (90.61)
Race		
African American	70 (18.92)	15,680 (24.12)
Caucasian	270 (72.97)	43,370 (66.72)
Smoking status		
Never smoked	50 (13.51)	8,050 (12.38)
Active smoker	90 (24.32)	15,570 (23.95)
Ex-smoker	120 (32.43)	17,590 (27.06)
Autoimmune comorbidities		
Autoimmune thyroiditis	40 (10.81)	2,510 (3.86)
Pernicious anemia	20 (5.4)	840 (1.29)
Psoriasis	30 (8.11)	2,660 (4.09)
Systemic vasculitis	10 (2.7)	650 (1)
Rheumatoid arthritis	110 (29.73)	16,500 (25.38)
Miscellaneous comorbidities		
Diabetes Mellitus		
Type 1	30 (8.11)	2,770 (4.26)
Type2	100 (27.03)	12,800 (19.69)
Kidney Disease		
CKD	90 (24.32)	11,010 (16.94)
ESRD	10 (2.7)	2390 (3.68)
Thyroid Disease		
Hypothyroidism	160 (43.34)	18,320 (28.18)
Hyperthyroidism	50 (13.51)	3,850 (5.92)
Essential hypertension	220 (59.46)	35,970 (55.34)
Metabolic syndrome	10 (2.7)	1,100 (1.69)
Coronary artery disease	80 (21.62)	9,660 (14.86)
Cerebral infarction	60 (16.22)	4,870 (7.49)
Chronic obstructive lung disease	90 (24.32)	9,560 (14.71)

Table 2. Risk factors for increased SLE prevalence among MG patients

Variables	MG with SLE n=370 n (%)	MG without SLE n=25,380 n (%)	P value
Age			
> 65 years	130 (35.14)	15,760 (62.1)	<0.0001
18-65 years	230 (62.16)	9,730 (38.34)	<0.0001
Gender			
Male	30 (8.11)	11,450 (45.11)	<0.0001
Female	330 (89.19)	13,840 (54.53)	<0.0001
Race			
African American	70 (18.92)	2,730 (10.76)	<0.0001
Caucasian	270 (72.97)	18,810 (74.11)	0.61
Thymectomy			
Total thymectomy	30 (8.11)	670 (2.64)	<0.0001
Partial thymectomy	20 (5.4)	480 (1.89)	<0.0001
Autoimmune comorbidities			
Autoimmune thyroiditis	40 (10.81)	530 (2.09)	<0.0001
Pernicious anemia	20 (5.4)	310 (1.22)	<0.0001
Psoriasis	30 (8.11)	470 (1.85)	<0.0001
Systemic vasculitis	10 (2.7)	60 (0.24)	<0.0001
Rheumatoid arthritis	110 (29.73)	1,040 (4.1)	<0.0001
Miscellaneous comorbidities			
Diabetes Mellites			
Type 1	30 (8.11)	810 (3.19)	<0.0001
Type2	100 (27.03)	7,090 (27.93)	0.7
Kidney Disease			
Chronic kidney disease	90 (24.32)	3,230 (12.73)	<0.0001
End stage renal disease	10 (2.7)	380 (1.5)	0.06
Thyroid Disease			
Hypothyroidism	160 (43.34)	6,100 (24.03)	<0.0001
Hyperthyroidism	50 (13.51)	1,340 (5.28)	<0.0001
Essential hypertension	220 (59.46)	14,890 (58.69)	0.76
Metabolic syndrome	10 (2.7)	330 (1.3)	0.02
Coronary artery disease	80 (21.62)	5,070 (19.98)	0.43
Cerebral infarction	60 (16.22)	2,080 (8.19)	<0.0001
Chronic obstructive lung disease	90 (24.32)	3,580 (14.1)	<0.0001

and miscellaneous comorbidities. The index date was defined as the date of the SLE diagnosis occurring in the MG patients. A chi-square test of association was performed along with the odds ratio (OR), its standard error, and the 95% confidence interval (CI).

Results: Prevalence rates of SLE and MG among total active patients of 59,896,040 were found to match the reported rates in the literature (0.1% and 0.04% subsequently)[2,3].

Of the 26,110 patients with MG, 370 had a diagnosis of SLE (1.42%) compared to 65,000 of 59,869,730 controls (0.11%). MG patients found to have increased odds of SLE compared to control group (OR 13.38, 95% CI: 2.08 to 14.84, P < 0.0001).

Demographics and clinical characteristics of MG patients and controls with SLE are shown in table 1. Risk factors for increased SLE risk among MG patients are shown in table 2. Female sex, African American race, thymectomy, autoimmune diseases, and miscellaneous comorbidities such as thyroid disease were significantly more common in MG patients who developed lupus.

The MG cohort who underwent thymectomy (n = 730) had an increased risk of SLE (30 out of 730) compared to MG patients who didn't undergo thymectomy (340 out of 25,380), (OR 3.11, 95% CI: 2.12 to 4.55, P < 0.0001).

Conclusion: Our study strongly supports the higher prevalence of SLE in MG patients and highlights the risk factors of the development of lupus in MG patients. MG patients should be evaluated for the coexistence of SLE especially in post-thymectomy patients and the young African American women with a history of other autoimmune diseases. Additionally, assessment for MG is suggested in lupus patients with unexplained muscular weakness.

References:

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Disclosure: S. Merjanah, None; **A. Igoe**, None; **D. Kaelber**, None; **R. Scofield**, None.

Abstract Number: 0335

Performances of Different Classification Criteria for Systemic Lupus Erythematosus in a Single Center Cohort from Turkey

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Recently developed EULAR/ACR classification criteria for systemic lupus erythematosus (SLE) has important differences compared to the 2012 Systemic Lupus International Collaborating Clinics (SLICC) SLE classification criteria and the revised 1997 American College of Rheumatology (ACR) crite-

Table 1- Sensitivity, positive predictive value, specificity and negative predictive value of 1997 ACR, 2012 SLICC and 2019 EULAR/ACR classification criteria

	SLE (+)	SLE (-)	Sensitivity (%)	Positive Predictive Value (%)	Specificity (%)	Negative Predictive Value (%)
1997 ACR	(+) 306 (-) 86	15 279	78.1	95.3	94.9	76.4
2012 SLICC	(+) 356 (-) 36	26 268	90.8	93.2	91.2	88.1
2019 EULAR/ACR	(+) 368 (-) 24	28 266	93.8	92.9	90.5	91.7

ria:The obligatory entry criterion of antinuclear antibody (ANA) positivity is introduced and a "weighted" approach is used.Sensitivity and specificity of these three criteria have been debated and may vary in different populations and clinical settings. We aim to compare the performances of three criteria sets/rules in a large cohort of patients and relevant diseased controls from a reference center with dedicated clinics for SLE and other autoimmune/inflammatory connective tissue diseases from Turkey.

Methods: We reviewed the medical records of SLE patients and diseased controls for clinical and laboratory features relevant to all sets of criteria. Criteria sets/rules were analysed based on sensitivity, positive predictive value, specificity and negative predictive value, using clinical diagnosis with at least 6 months of follow-up as the gold standard. A subgroup analysis was performed in ANA positive patients for both SLE group and control group. SLE patients that did not fulfil 2012 SLICC criteria and 2019 EULAR/ACR criteria and diseased controls that fulfilled these criteria were evaluated.

Results: A total of 392 SLE patients and 294 non-SLE diseased controls (48 undifferentiated connective tissue disease, 51 Sjögren's syndrome, 43 idiopathic inflammatory myopathy, 50 systemic sclerosis, 52 primary antiphospholipid syndrome (APS), 15 rheumatoid arthritis, 15 psoriatic arthritis and 20 ANCA associated vasculitis) were included in the study. Hundred and fourteen patients (16.6%) were ANA negative.

Sensitivity was more than 90% for both 2012 SLICC criteria and 2019 EULAR/ACR criteria and positive predictive value was more than 90% for all three criteria (Table 1). Specificity was the highest for 1997 ACR criteria. Negative predictive value was 76.4% for ACR criteria, 88.1% for SLICC criteria and 91.7% for EULAR/ACR criteria.

In ANA positive patients, sensitivity was 79.1% for 1997 ACR criteria, 91.9% for 2012 SLICC criteria and 96.1% for 2019 EULAR/ACR criteria. Specificity was 92.6% for ACR criteria, 87.8% for SLICC criteria and 85.1% for EULAR/ACR criteria.

Eleven clinically diagnosed SLE patients had insufficient number of items for both 2012 SLICC and 2019 EULAR/ACR criteria. Both criteria were fulfilled by 16 diseased controls: 9 with Sjögren's syndrome, 5 with APS, one with dermatomyositis and one with systemic sclerosis.

Conclusion: In this cohort, although all three criteria have sufficient specificity, the sensitivity and negative predictive value of 1997 ACR criteria are the lowest. Overall, 2019 EULAR/ACR and 2012 SLICC criteria have a comparable performance, but if only ANA positive cases and controls are analysed, the specificity of both criteria decrease to less than 90%. Some SLE patients with a clinical diagnosis lacked sufficient number of criteria. Mostly, patients with Sjögren's syndrome or antiphospholipid syndrome are prone to misclassification by both recent criteria.

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Abstract Number: 0336

The Incremental Clinical Utility of a Multianalyte Assay Panel with Cell-Bound Complement Activation Products versus a Traditional ANA Testing Strategy for the Diagnosis and Treatment of SLE

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The comparative clinical utility of various diagnostic tests to aid the differential diagnosis of SLE is unclear. We compare the outcomes of testing with a multianalyte assay panel (MAP) with cell-bound complement activation products vs. standard of care lab testing in patients suspected of having SLE.

Methods: We used data from the electronic health record (EHR)-based Columbus registry from 1/2016 to 12/2020 for analysis and linked Healthcore medical, pharmacy, and claims data. We established two cohorts for comparison, the MAP testing strategy cohort and the traditional ANA testing strategy cohort (tANA), with or without anti-dsDNA or anti-Smith. All lab results from the MAP cohort were obtained directly from the lab vendor. Results from the tANA cohort were available from within the EHR. Baseline data was collected for both cohorts at 12 months (or more) before first testing. Using this data, we characterized the demographics, comorbidities, other autoimmune diagnoses, and medications (including SLE treatments and glucocorticoids). Except for SLE (which might have been only a working diagnosis), patients with pre-existing rheumatology conditions already identified at time of testing were excluded. Descriptive statistics compared the characteristics of MAP and tANA testing episodes. Logistic regression was used to estimate odds ratios (OR) comparing the likelihood of SLE medication initiation and SLE diagnosis between the MAP and tANA cohorts. Multivariable adjustment was performed and included all imbalanced covariates described in table 1 with standardized mean difference (SMD) >0.10. A subgroup analysis was conducted in patients new to the practice in the preceding 12 months

Results: The MAP and tANA cohorts consisted of 21,827 and 22,778 testing episodes, respectively. Patients in both cohorts were of similar age, mean 51 and 54 years, respectively for MAP and tANA, predominantly female (85 and 81%), and majority white (57 and 64%). Approximately 4-5% of MAP and tANA patients already had a SLE diagnosis ICD-10 code prior to testing. A total of 2,437 (11.17%) patients tested positive by MAP compared to 5,364 (23.55%) of patients who tested positive by tANA.

Among patients with no baseline prescription for a SLE medication, MAP positive patients were more likely to initiate SLE medications compared to tANA positive patients (43% vs. 32%, adjusted OR = 2.13, 95% CI 1.85-2.44). Effects were stronger in the subgroup of patients new to the practice, 55% vs. 33% (adjusted OR = 2.77, 95% CI 2.31-3.32). MAP positive patients were approximately fivefold more likely to be diagnosed with SLE as compared to the tANA positive patients, 31 vs. 8% (adjusted OR = 4.78, 95% CI 4.04-5.65); similar results were observed in the subgroup

of new patients (adjusted OR = 6.34, 95% CI 5.12-7.86). Among MAP algorithm negative patients, 96% were not diagnosed with SLE compared to 99% of tANA negative patients.

Table 1: Baseline* Characteristics of patients undergoing AVISE and tANA (tANA) tests without pre-existing (non-SLE) autoimmune diagnoses

	AVISE	tANA	SMD
N (testing episodes)	21,827	22,778	
Age	50.9 (15.5)	53.8 (15.8)	0.19
Sex (Female)	18525 (84.9)	18,551 (81.4)	0.14
Race/ethnicity			0.19
White	12,406 (56.8)	14,589 (64.0)	
Black	1,937 (8.9)	2,386 (10.5)	
Other	7,484 (34.3)	5,803 (25.5)	
Pre-existing diagnoses, %			
Fibromyalgia	1,766 (8.1)	4,125 (18.1)	0.30
UCTD (i.e., M359 Systemic involvement of connective tissue, unspecified)	901 (4.1)	1,624 (7.1)	0.01
SLE (i.e., M32. *, ignoring M32.0)	947 (4.3)	1,017 (4.5)	0.13
SLE Medications			
HCQ	1,342 (6.1)	2,261 (9.9)	0.14
MMF	159 (0.7)	301 (1.3)	0.06
MTX	246 (1.1)	560 (2.5)	0.10
AZA	148 (0.7)	226 (1.0)	0.03
LEF	69 (0.3)	90 (0.4)	0.02
RTX	11 (0.1)	34 (0.1)	0.03
BEL	52 (0.2)	77 (0.3)	0.02
Prednisone	1,818 (8.3)	3,952 (17.4)	0.27
Pain and depression medications			
Oral NSAIDs	2,880 (13.2)	7,138 (31.3)	0.45
Opioids	821 (3.8)	1,938 (8.5)	0.20
SNRIs (duloxetine, venlafaxine)	1054 (4.8)	2278 (10.0)	0.20
SSRIs	1228 (5.6)	2530 (11.1)	0.20
Neuropathic pain medications (gabapentin, pregabalin)	1548 (7.1)	3776 (16.6)	0.30
Healthcare utilization			
Number of prior physician visits, mean (SD)	0.71 (1.50)	1.31 (1.70)	0.37
Prior other test**	0.08 (0.38)	0.03 (0.19)	
Gap from new patient/consultation 99XXX*** visit			
Days, mean (SD),	38.3 (155.4)	28.6 (120.8)	0.07
Missing, %	12,842 (58.8)	4,641 (20.4)	0.86

*baseline refers to all available data before the AVISE and tANA test result was reported †For AVISE group is the tANA, for tANA is the AVISE ‡New patient ambulatory codes: 99201-5; new consultation codes: 99241-5 tANA – traditional antinuclear antibody; SLE – systemic lupus erythematosus; UCTD – undifferentiated connective tissue disease; HCQ – hydroxychloroquine; MMF – mycophenolate; MTX – methotrexate; AZA – Azathioprine; LEF – leflunomide; RTX – rituximab; BEL – Belimumab; NSAID – non-steroidal anti-inflammatory; SNRI – serotonin-norephinephrine reuptake inhibitors; SSRI - selective serotonin reuptake inhibitor; SMD = standardized mean difference (SMDs > 0.10 are considered potentially clinically important).

Table 2. Diagnostic and SLE treatment outcomes among all patients testing MAP positive as described previously (Dervieux et al., *J Immunol Methods* 2017) vs. tANA positive patients (defined as an ANA ≥ 1:160 and/or positive anti-dsDNA and/or positive anti-Smith based on laboratory cutoffs). SLE medication initiation was defined as a new (post-test) prescription for hydroxychloroquine, methotrexate, mycophenolate, azathioprine, leflunomide, rituximab, or belimumab.

Outcome	Adjusted* Odds Ratio (95% CI)
SLE Medication initiation MAP vs. tANA (referent)	2.13 (1.85-2.44)
Diagnosis (M32 ICD 10 code) MAP vs. tANA (referent)	4.78 (4.04-5.65)

*adjusted for imbalanced covariates described in table 1 with SMD >0.10

Table 3. Subgroup analysis of diagnostic and SLE treatment outcomes among newly referred (<12 months) patients testing MAP positive vs. tANA positive.

Outcome	Adjusted* Odds Ratio (95% CI)
SLE Medication initiation MAP vs. tANA (referent)	2.77 (2.31-3.32)
Diagnosis (M32 ICD 10 code) MAP vs. tANA (referent)	6.34 (5.12-7.86)

*adjusted for imbalanced covariates described in table 1 with SMD >0.10

Conclusion: Positive MAP results associated with a greater likelihood to initiate SLE medications and to receive a SLE diagnosis compared to tANA while maintaining comparable negative predictive value. The findings highlight the superior actionability of MAP results vs. tANA.

Disclosure: T. O'Malley, Exagen, 3, 11; **F. Xie**, None; **y. Su**, None; **c. Clinton**, None; **D. Zack**, Exagen Inc, 3, 4, 11, Xencor, 2, 11; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **J. Wegener**, Exagen, 3, 11.

Abstract Number: 0337

Rarity of Pneumocystis Jirovecii Pneumonia in Patients with Systemic Lupus Erythematosus Using a Real-world, Electronic Health Record

Ben Boone and April Barnado, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Infection is the leading cause of mortality and one of the most common causes of hospitalization in patients with systemic lupus erythematosus (SLE). *Pneumocystis jirovecii* pneumonia (PJP) is a highly morbid but preventable opportunistic infection in SLE patients. Prior studies have not investigated patient factors associated

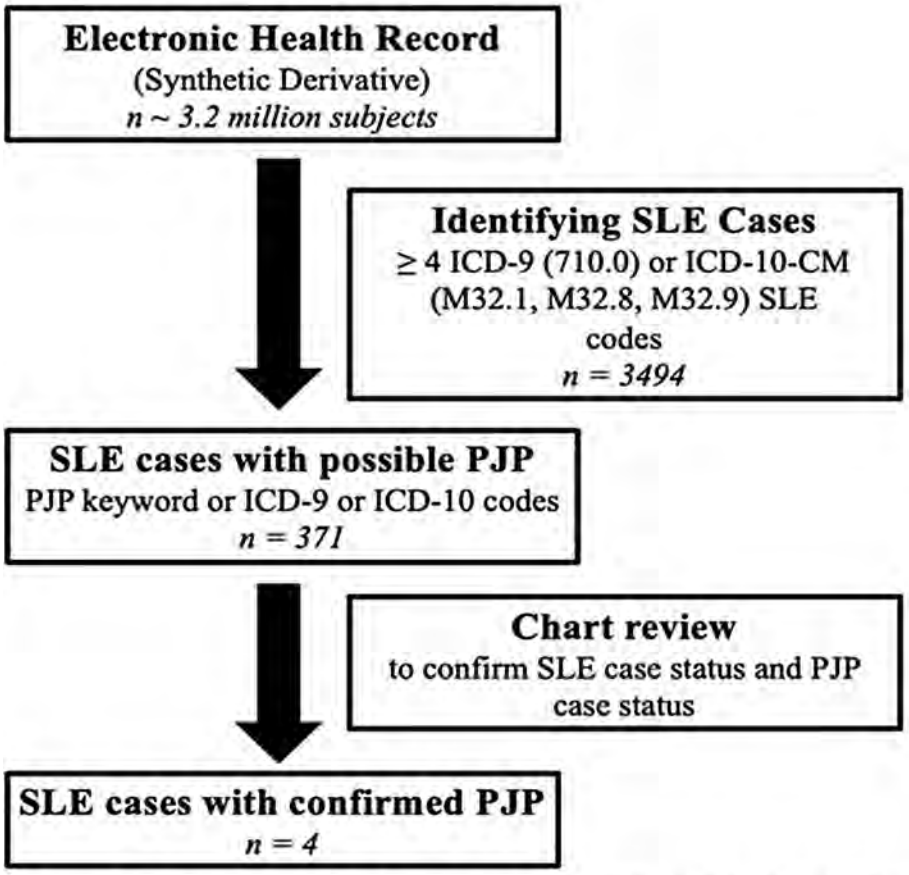

Figure 1. Flow chart of cohort selection. Potential SLE patients with PJP were selected from a de-identified EHR by first applying ≥ 4 SLE ICD-9 or ICD-10-CM codes and then applying PJP keywords and ICD-9 and ICD-10-CM codes. These patients were then all chart reviewed to determine if a PJP case.

with PJP infection in SLE using an electronic health record (EHR) cohort. Using a real-world, EHR cohort, we assessed the frequency of PJP infection in SLE patients and patient factors associated with infection.

Methods: We identified potential SLE cases from a de-identified EHR called the Synthetic Derivative with over 3.2 million subjects with over 30 years of follow-up using a previously validated algorithm of 4 or more SLE ICD-9 or ICD-10 CM codes with a positive predictive value of 90%. Within this set, we then required either a PJP ICD-9 or ICD-10 CM code or PJP keywords. PJP keywords included "PJP", "*Pneumocystis jirovecii*", "Pneumocystis", "PJP pneumonia", or "pneumocystis pneumonia". The cohort selection is summarized in Figure 1. Confirmed PJP infection was defined by positive immunofluorescence, polymerase chain reaction, or Gömöri methenamine silver staining on sputum or bronchoalveolar lavage specimen. We reviewed charts to collect data on demographics, SLE disease manifestations, medication exposure, laboratory values, and PJP prophylaxis use. We assessed for current and preceding 90-day cumulative dosing of corticosteroids at time of diagnosis from notes, inpatient and outpatient electronic prescribing systems, and phone messages. The current and recent use of non-steroid immunosuppressants over 90 days was recorded, as well as any co-morbid immunodeficiency.

Results: We conducted chart review on 371 SLE patients with any mention of PJP from 1989 to 2020. A total of 119 patients underwent bronchoscopy for PJP testing, 16 underwent sputum sampling, and 10 underwent testing from

Table 1. Characteristics of Patients with SLE Diagnosed with PJP.

Age	Sex	Race	*Pneumocystis jirovecii* testing Modality	Current daily prednisone dose (mg)[1]	Cumulative prednisone dose in previous 90 days (mg)[1]	Non-steroid immuno-suppressants in previous 90 days[1]	HIV/ AIDS[1]	WBC[1] (cells/μL)	Lymphocytes[1] (cells/μL)	CD4 count[1] (cells/μL)
28	F	African-American	PCR[2]	15	1,120	Azathioprine	No	6300	310	N/A[4]
31	F	Caucasian	GMS[3]	30	3,250	None	No	2800	120	N/A[4]
43	F	Caucasian	GMS[3]	0	0	None	Yes	1100	N/A[4]	17
44	F	African-American	GMS[3]	0	0	None	Yes	3300	550	104

[1]Timing in relation to *Pneumocystis jirovecii* pneumonia diagnosis; [2] Polymerase chain reaction; [3] Gömöri methenamine silver; [4] Not available

other sites. We confirmed PJP infection in 4 of these patients. The characteristics of these patients, including relevant therapies and laboratory evaluation, are summarized in Table 1. Two of the 4 patients were infected with human immunodeficiency virus (HIV) and acquired immunodeficiency syndrome (AIDS) with CD4 lymphocyte counts less than 200 cells/mL. Neither of these patients had been exposed to any steroids or non-steroid immunosuppressive therapy in the 90 days preceding PJP diagnosis. Of the 2 SLE patients without HIV/AIDS, both had significant lymphopenia in addition to significant recent steroid exposure. None of the 4 patients were on PJP prophylaxis.

Conclusion: Using a large EHR cohort, 2 SLE patients without co-morbid HIV/AIDS were identified as having PJP. Both patients were on moderate doses of corticosteroids, with one on a non-steroid immunosuppressant, and neither on PJP antimicrobial prophylaxis. With 2 confirmed cases of PJP in non-HIV/AIDS SLE patients in over 30 years at a large academic institution, PJP seems to be a rare complication in SLE. This rarity may contribute to lack of well-defined risk factors for PJP infection or formal recommendations for PJP prophylaxis in SLE patients.

Disclosure: B. Boone, None; **A. Barnado**, None.

Abstract Number: 0338

Serum and Urine Galectin-9, IP-10 and SIGLEC-1 as Biomarkers of Disease Activity in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Galectin-9, interferon-inducible protein-10 (IP-10) and sialoadhesin (SIGLEC-1) are proteins associated with interferon signature, and considered as potential biomarkers reflecting disease activity in patients with systemic lupus erythematosus (SLE). In this study, we aimed to investigate the association of serum and urine levels of galectin-9, IP-10 and SIGLEC-1 with disease activity in patients with SLE.

Table 1. Serum and urine levels of biomarkers across study groups.

Biomarker	Active SLE (n=63)	Inactive SLE (n=30)	Healthy Control (n=32)
sGalectin-9 (ng/ml)	11.73 (7.52-14.15)	8.66 (7.51-10.02)	5.61 (4.56-6.6)
sIP-10 (pg/ml)	279.4 (147.5-430.3)	173.4 (142.2-247.9)	74.3 (58.8-103)
sSIGLEC-1 (pg/ml)	181.2 (157.8-213.9)	182.5 (169.9-203.1)	258.3 (179-602)
uGalectin-9 (ng/ml)	8.83 (4.07-18.11)	11.54 (7.03-15.07)	10.63 (5.55-17.4)
uIP-10 (pg/ml)	34.4 (15.9-73,9)	20.8 (9.9-53.3)	12.2 (1.8-25.7)
uSIGLEC-1 (pg/ml)	321 (236.3-370.9)	297.6 (247.7-371)	290 (205.1-323.5)
uGalectin-9 (ng/mgCre)	15.50 (9.60-32.05)	11.41 (8.78-19.54)	13.57 (11.27-22.08)
uIP-10 (pg/mgCre)	73.4 (40.9-136.9)	26.1 (18.1-55.1)	16.4 (5-32.5)
uSIGLEC-1 (pg/mgCre)	619.6 (389.4-1056.5)	393.2 (248.6-715.8)	425.6 (264.7-925.9)

Methods: Sixty-three patients with active SLE (31 renal and 32 extrarenal) were included in the study. Thirty inactive patients with SLE (15 renal and 15 extrarenal) and 32 healthy volunteers were selected as control groups. Serum (s) and urine (u) levels of galectin-9, IP-10 and SIGLEC-1 were tested using ELISA. Urine levels of biomarkers were normalized by urine creatinine.

Results: Groups were comparable with regard to sex and age distribution. Of 125 participants, 102 (81.6%) were female and median age was 33 (28-44.5) years. Proliferative lupus nephritis (LN) (class III/III+V and IV/IV+V) were found

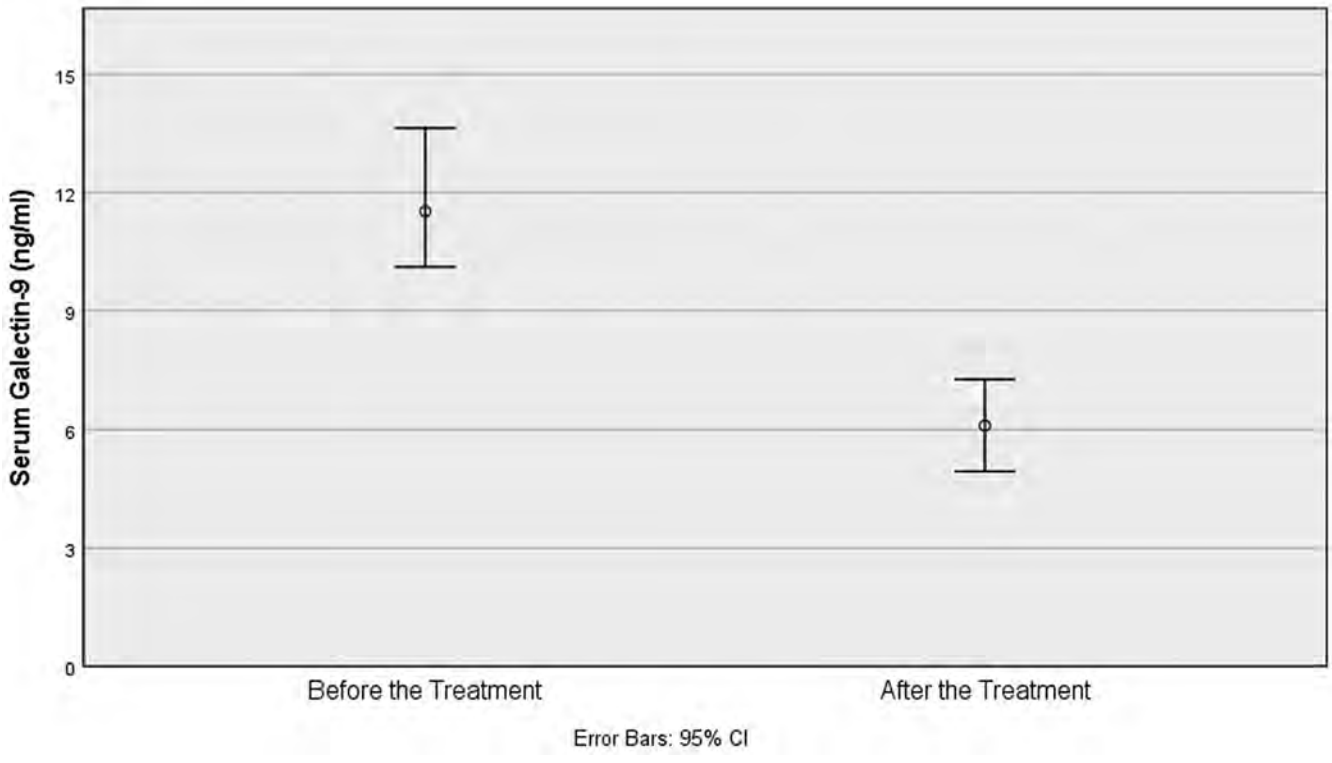

Figure 1. Serum levels of galectin-9 before and after the treatment in 41 patients with active SLE.

in 22 patients with active renal SLE (70.9%), while 6 patients (19.3%) had pure class V and 3 (9.7%) had class II LN. Levels of sIP-10, uIP-10, sGalectin-9 and uSIGLEC-1 were significantly higher in the active SLE group compared to the inactive SLE group (sIP-10 p=0.046, uIP-10 p< 0.001, sGalectin-9 p=0.031 and uSIGLEC-1 p=0.006); however, no differences were detected in the comparison of uGalectin-9 and sSIGLEC-1 between the groups (uGalectin-9 p=0.180 and sSIGLEC-1 p=0.699) (Table 1). Serum and urine levels of galectin-9, IP-10 and SIGLEC-1 did not differ between patients with active renal and extrarenal SLE. Levels of sIP-10, uIP-10 and uSIGLEC-1 were correlated with SLE Disease Activity Index (SLEDAI). Serum and urine levels of all biomarkers were re-tested in 41 of 63 patients (65%) with active SLE after a median treatment of 8 (5-22.5) months. At the time of the second tests, there was a significant decrease in disease activity as measured by SLEDAI [2 (0-4)] compared to the time of the first tests [10 (6-15.5)]. Comparison of sGalectin-9 levels between the serum at the time of active disease and remission showed a very significant decline (p< 0.001) as shown in Figure 1. uGalectin-9, sIP-10 and uSIGLEC-1 also decreased after treatment; however, the difference was not statistically significant.

Conclusion: sIP-10, uIP-10, sGalectin-9 and uSIGLEC-1 are associated with disease activity in SLE. None is able to discriminate active renal from active extrarenal disease. sGalectin-9 may be a valuable biomarker to monitor response after treatment for active disease (Funded by Scientific Research Projects Coordination Unit of Istanbul University. Project number: TSA-2019-34218).

Disclosure: S. Mirioglu, None; **S. Cinar**, None; **O. Uludag**, None; **E. Gurel**, None; **S. Varelci**, None; **Y. Ozluk**, None; **I. Kilicaslan**, None; **Y. Yalcinkaya**, None; **H. Yazici**, None; **A. Gül**, None; **M. Inanc**, None; **B. Esen**, None.

Abstract Number: 0339

Trends in Disparity by Age, Sex and Race for Systemic Lupus Erythematosus Patients

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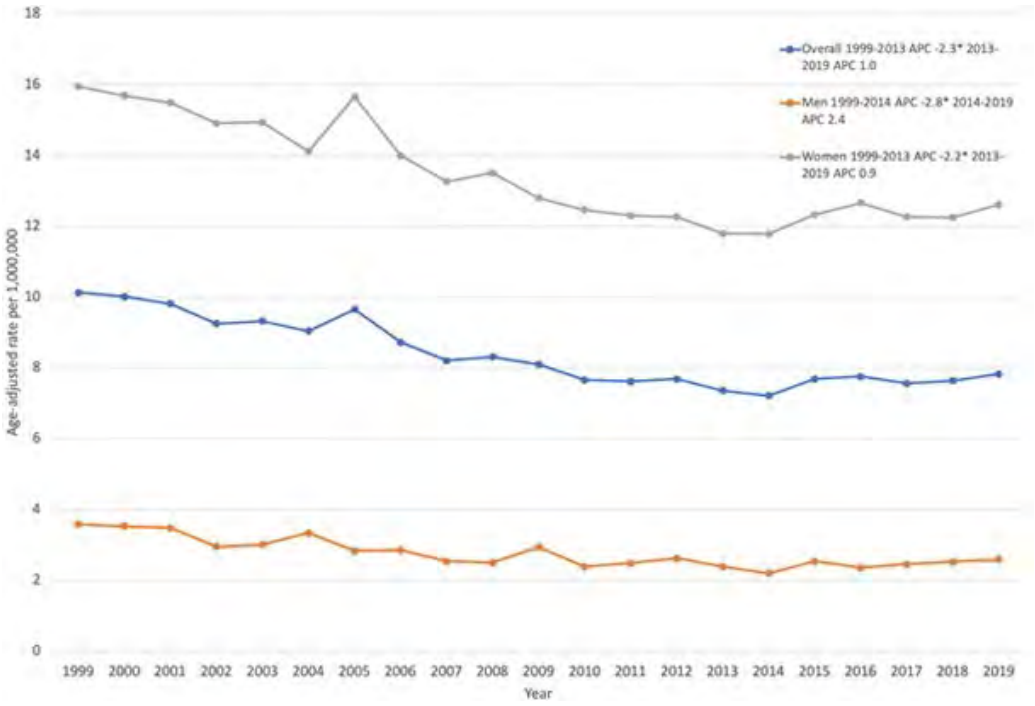
SESSION INFORMATION

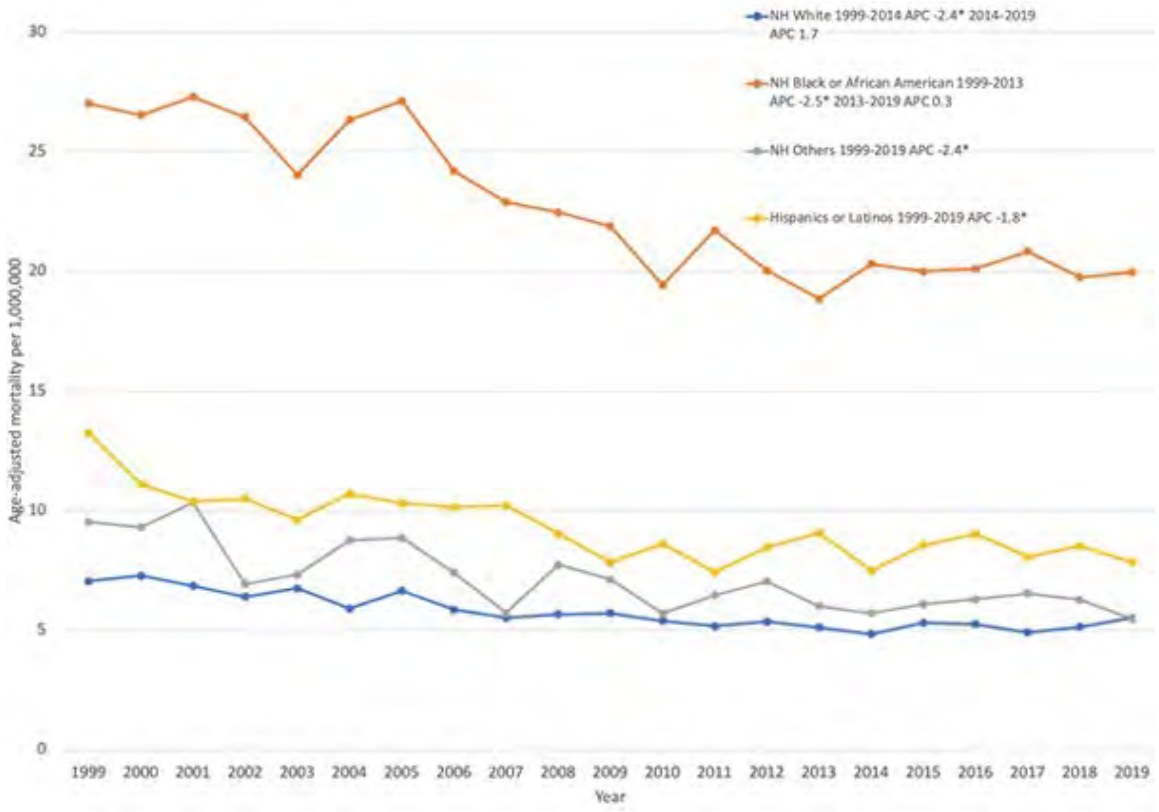
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Important disparities in SLE patients persist based on their sex and racial/ethnic status. The aim of this study is to examine the trends in SLE-related deaths stratified on age, sex, and race/ethnicity in the United States from 1999 to 2019.

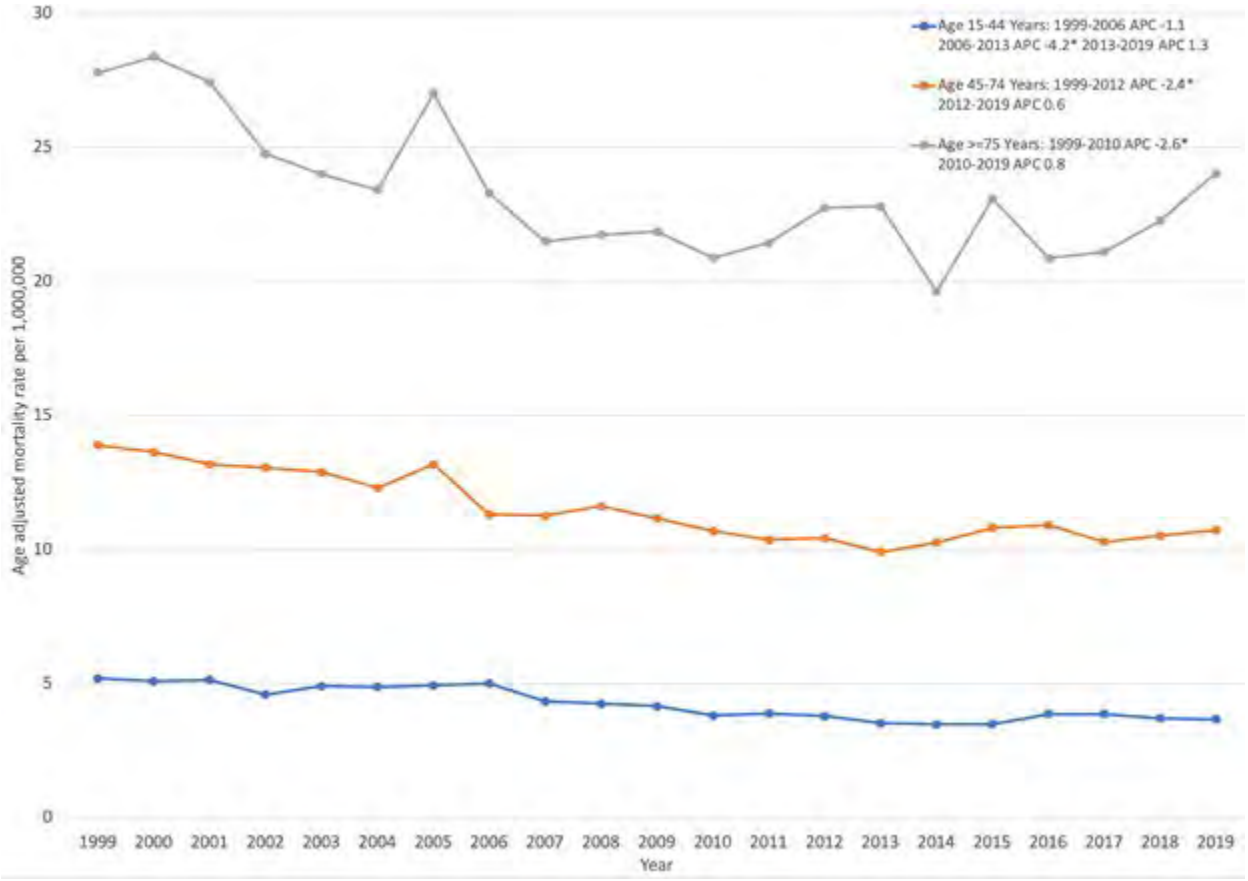
Methods: We used CDC Wide-ranging Online Data for Epidemiologic Research (CDC WONDER) to access National Vital Statistics System data from 1999 to 2019. SLE-related deaths (age >/= 15 years) were identified using the International Classification of Diseases, Tenth Revision, codes M32.x from multiple causes of death and were represented as age-adjusted mortality rates (AAMR) per 1,000,000 population. Joinpoint regression was used to examine changes in trend and annual percentage change (APC) in SLE related deaths overall and stratified by age groups (15-44 years [young], 45-74 years [midlife], and >/=75 years [old]), sex, racial/ethnic groups (non-Hispanic whites [NHWs], non-Hispanic blacks [NHBs], Hispanics, non-Hispanic Others [NH Others] (includes Asian or Pacific Islanders, and American Indian or Alaska Natives)).



Overall and sex-stratified SLE–related mortality rates in the United States, 1999 to 2019. *Indicates that the APC is significantly different from zero at α=0.05.



SLE–related mortality rates stratified by race/ethnicity in the United States, 1999 to 2019. *Indicates that the APC is significantly different from zero at α=0.05.



SLE–related mortality rates stratified by age groups in the United States, 1999 to 2019. *Indicates that the APC is significantly different from zero at α=0.05.

Results: AAMR related to SLE decreased from 10.13 to 7.36 in 2013 (APC -2.3[95% CI, –2.7 to –1.9]) and then remained stable (7.83) after that till 2019 (APC 1.0[95% CI, 1.1 to [95% CI, –0.5 to –2.5]). AAMR was higher in women (13.41) than men (2.73) in all years. Among the racial/ethnic groups, AAMR was highest in NHBs (22.51), followed by Hispanics (9.07), NH-Others (6.93), and lastly, NHWs (5.76) in all years. AAMR was highest in old (23.24) followed by midlife (11.46) and young (4.28). APC in AAMR decreased in men (-2.8) till 2014 and women (-2.2) till 2013 and remained stable after that. APC in AAMR decreased in NHWs (-2.4) until 2014 and NHBs (-2.5) until 2013 and remained stable after that. APC in AAMR decreased throughout the study period in NH Others (-2.4) and Hispanics (-1.8). APC in AAMR decreased from 2006-2013 in young (-4.2) and remained stable after that. APC in AAMR decreased in midlife (-2.4) until 2012 and old (-2.6) until 2010 and remained stable after that.

Conclusion: After the initial decline, SLE-related mortality has remained stable since 2013. Stratification by racial/ethnic status reveals significant disparities, which calls for further research to understand the underlying factors to help develop preventative strategies.

Disclosure: A. Akhlaq, None; **A. Mannan Khan Minhas**, None.

Abstract Number: 0340

Urinary L-selectin Predicts Disease Activity and Histological Changes in Lupus Nephritis

Huihua Ding[1], Yiwei Shen[1], Min Dai[1], Chandra Mohan[2] and Nan Shen[3], [1]Shanghai JiaoTong University School of Medicine, Shanghai, China (People's Republic), [2]University of Houston, Houston, TX, [3]Shanghai Jiang Tong University School of Medicine, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: There remains unmet needs of non-invasive markers of disease activity, damage, prognosis, and treatment response in lupus nephritis patients. Here, we aim to validate urinary L-selectin (CD62L) as a novel biomarker of disease activity and histological changes of LN in a Chinese SLE cohort.

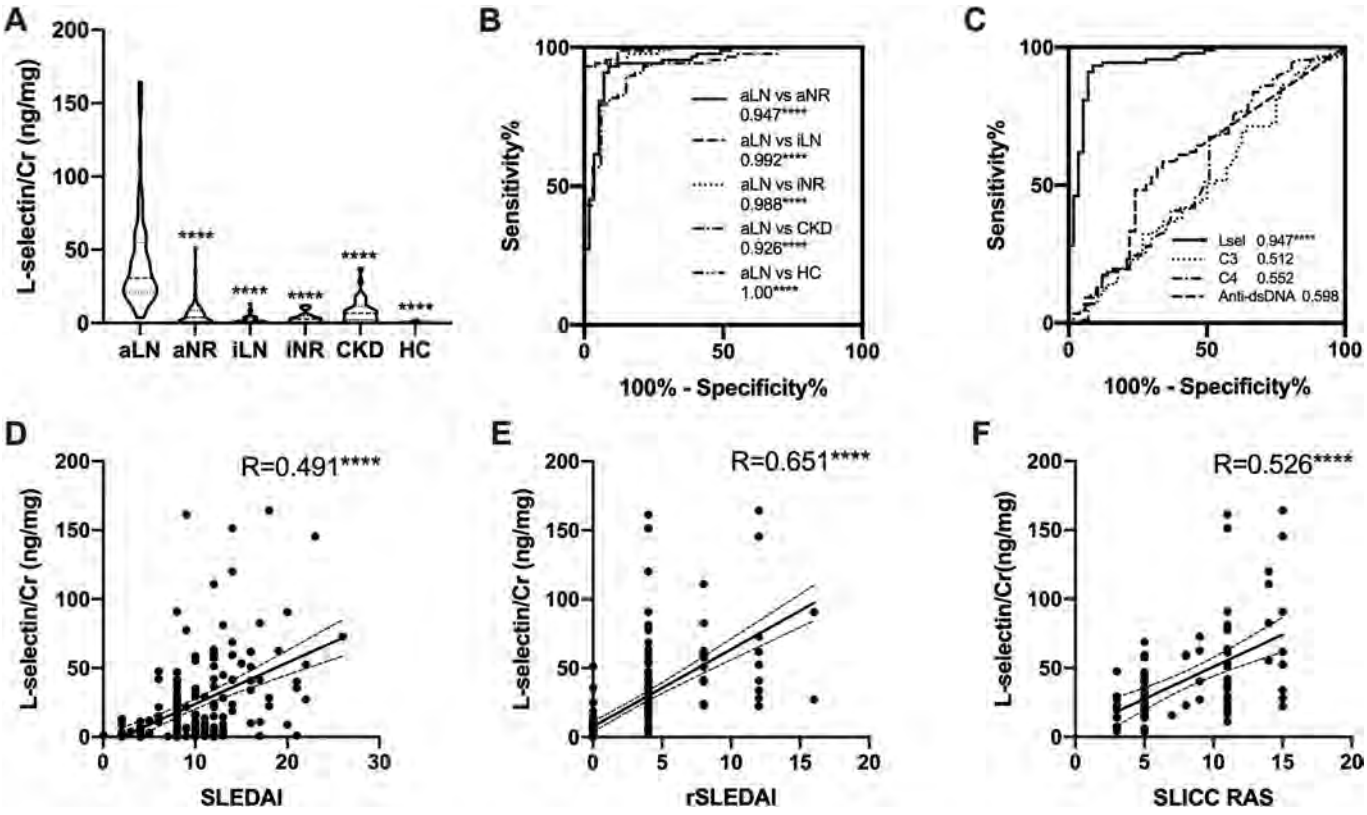


Figure 1. Urine L-selectin levels and its correlation with clinical indices. (A) Urine L-selectin was significantly elevated exclusively in aLN patients when compared with HC (ng/mg), or aNR, iLN, iNR patients, or even CKD patients. (B) Receiver operating characteristic curve analysis (ROC) showed urine L-selectin significantly discriminated aLN patients from aNR, iLN, iNR, CKD and HC. Values in the plot indicate areas under curve. (C) ROC analysis showed urine L-selectin outperformed C3, C4 or anti-dsDNA antibody in discriminating active lupus nephritis (aLN) from active non-renal SLE (aNR). Values in the plot indicate areas under curve (AUC). (D, E, F) Urine L-selectin was correlated significantly with SLEDAI, rSLEDAI and SLICC RAS. aLN, active lupus nephritis; HC, health control; aNR, active non-renal; iLN, inactive lupus nephritis; iNR, inactive non-renal; CKD, chronic kidney disease; C3, complement 3; C4, complement 4; R, Spearman's correlation coefficient; SLEDAI, Systemic Lupus Erythematosus Disease Activity Index; rSLEDAI, renal SLEDAI; SLICC RAS, SLICC renal activity score; ****P<0.0001.

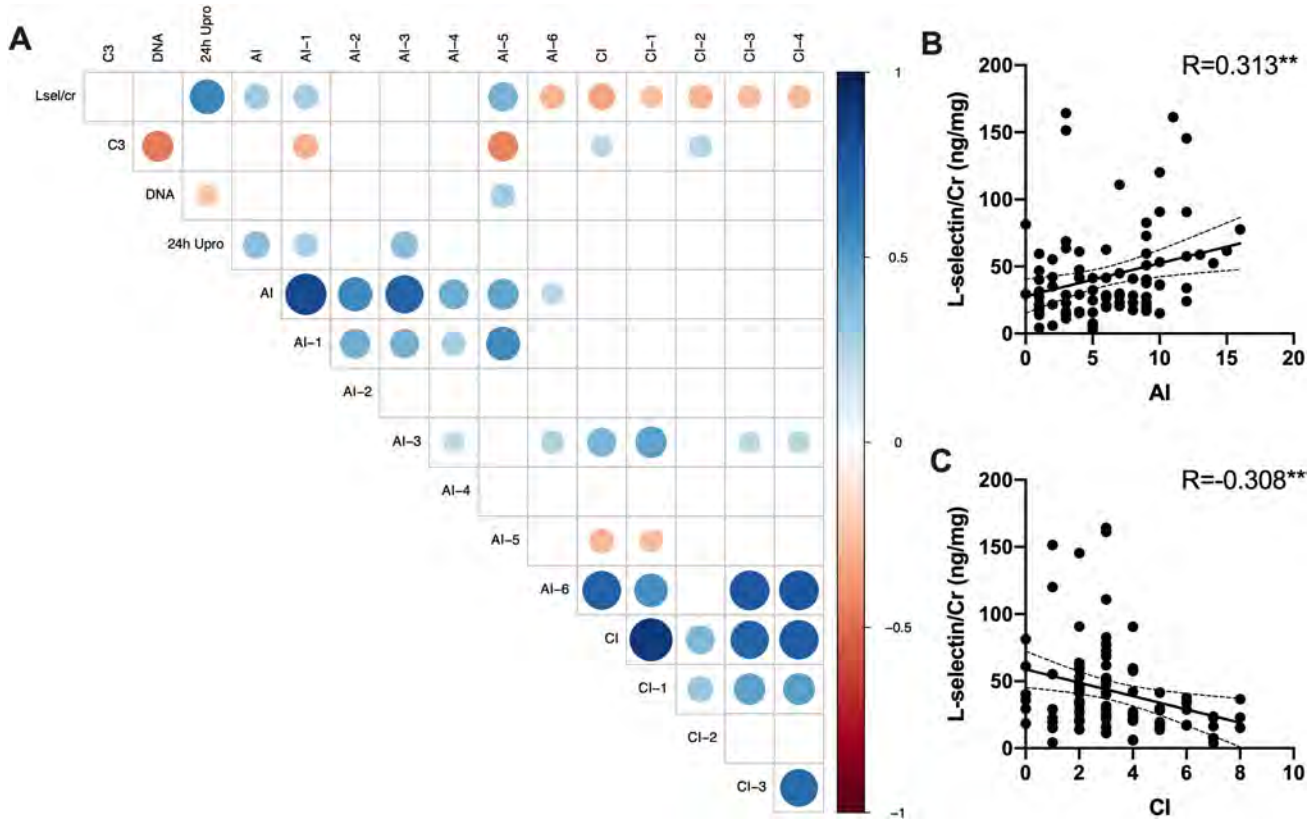


Figure 2. Correlation analysis between urine L-selectin and renal histopathology. (A) Correlation heatmap analysis for comparison of L-selectin and conventional metrics (C3, anti-dsDNA and 24h Upro) in AI, CI and their component attributes. The size and color of circles reflected the corresponding correlation coefficient values (R) of correlation analysis. The larger the circle, the bigger the value. Circles in which the corresponding R values were over 0.05 were removed off the squares. (B, C) Correlation analysis between urine L-selectin and AI, CI in renal histopathology. AI, activity index; CI, chronicity index; DNA, anti-dsDNA antibody; 24h Upro, 24-hour urine protein quantity; AI-1, Endocapillary hypercellularity; AI-2, Glomerular leukocyte infiltration; AI-3, Cellular and/or fibrocellular crescents; AI-4, Fibrinoid necrosis and/or karyorrhexis; AI-5, Wire loop deposits; AI-6, Interstitial inflammation; CI-1, Glomerulosclerosis; CI-2, Fibrous crescents; CI-3, Interstitial fibrosis; CI-4, Tubular atrophy; R, Spearman's correlation coefficient; **P<0.01.

Methods: In a single center Chinese lupus cohort, a total of 197 SLE patients were recruited. 33 chronic kidney disease (CKD) patients and 27 health volunteers were also included as controls. Urine L-selective levels were tested using ELISA. Clinical characteristics and laboratory tests were collected at baseline. Renal histopathology was viewed by an experienced renal pathologist for paired urine-kidney biopsy samples from active LN patients. Furthermore, 18 patients with active LN were followed up for a minimum of 6 months, and we valuated their clinical outcomes and, simultaneously, retested their urine L-selective levels at the end of follow up.

Results: In the cross-sectional cohort, urine L-selectin was significantly increased in active lupus nephritis (aLN) patients (n=89) exclusively compared with active SLE patients without renal involvement (aNR) (n=57) ($p < 0.0001$), inactive LN patients (iLN) (n=25) ($p < 0.0001$), inactive SLE patients without renal involvement (n=26) ($p < 0.0001$), chronic kidney disease (CKD) patients (n=33) ($p < 0.0001$), and health controls (n=27) ($p < 0.0001$) **(Fig.1A)**. ROC analysis further confirmed that urine L-selectin had the better capacity to discriminate aLN patients from other groups, especially from aNR patients **(Fig.1B)**, outperforming conventional indices (C3, C4 and anti-dsDNA) **(Fig.1C)**. Correlation analysis exhibited urine L-selectin correlated well with the SLEDAI score ($r = 0.491$, $p < 0.0001$), renal SLEDAI (rSLEDAI) score ($r = 0.651$, $p < 0.0001$), and SLICC renal activity score (SLICC RAS) ($r = 0.526$, $p < 0.0001$) **(Fig.1D-1F)**. Moreover, urine L-selectin positively correlated with activity index (AI) ($r = 0.313$, $p < 0.01$) and negatively correlated with chronicity index (CI) ($r = -0.308$, $p < 0.01$) of renal pathology. It also strongly correlated with their related pathological attributes (endocapillary hypercellularity, fibrinoid necrosis and/or karyorrhexis, wire loop deposits, interstitial inflammation; glomerulosclerosis, fibrous crescents, interstitial fibrosis and tubular atrophy) (all $p < 0.05$) **(Fig.2A-2C)**. In the follow-up cohort, 12 patients

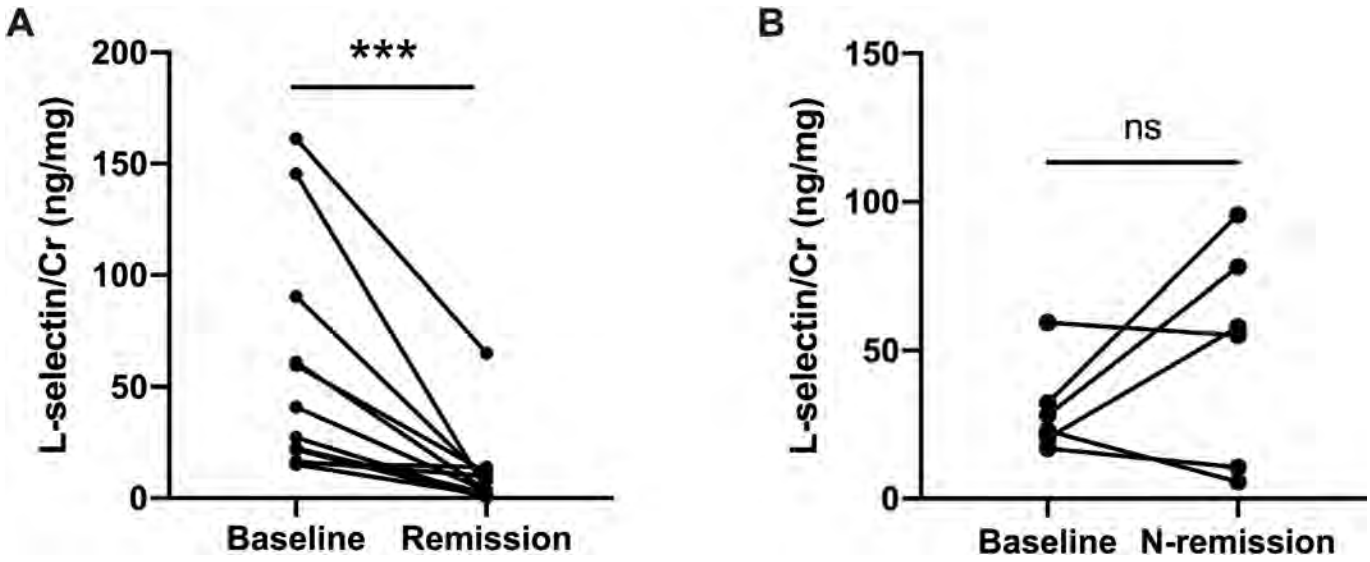


Figure 3. Urine L-selectin may reflect treatment response in clinical situation. The urine L-selectin levels (A) decreased in remission group (CR+PR) (n=12), while (B) remained stable in non-remission group (NR) (n=6). Mann-Whitney U test. N-remission, non-remission. *** P<0.001.

achieved complete remission or partial remission, while 6 patients still maintained no remission. In remission group, urine L-selectin levels at the end of follow up were lower than those at baseline ($p < 0.01$) **(Fig.3A)**. While in non-remission group, urine L-selectin levels showed no differences between the baseline and the end of follow up ($p = 0.44$) **(Fig.3B)**.

Conclusion: Urine L-selectin is a novel biomarker of lupus nephritis disease activity and potential to predict renal histopathology. Besides, it may reflect treatment response of patients in clinical situation.

Disclosure: H. Ding, None; **Y. Shen**, None; **M. Dai**, None; **C. Mohan**, None; **N. Shen**, None.

Abstract Number: 0341

Addition of Narrative Text Abstraction to ICD-Based Abstraction Significantly Improves Identification of Lupus Nephritis in Real-World Data

Meghan Tierney and Chris Rowe, PicnicHealth, San Francisco, CA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is often underrecognized and difficult to identify retrospectively, presenting challenges for clinicians and researchers hoping to explore this condition using real-world data (RWD). Common abstraction techniques use ICD codes to pull diagnoses from electronic health records (EHR). However, documentation of LN as a specific diagnosis is an inconsistent practice across providers, leading to underrepresented LN prevalence. Adding abstraction of unstructured narrative text may improve RWD for LN research.

Methods: We retrieved medical records for patients with lupus across the U.S. To be included in the study, patients were required to have a lupus diagnosis documented in their medical record. Natural language processing and

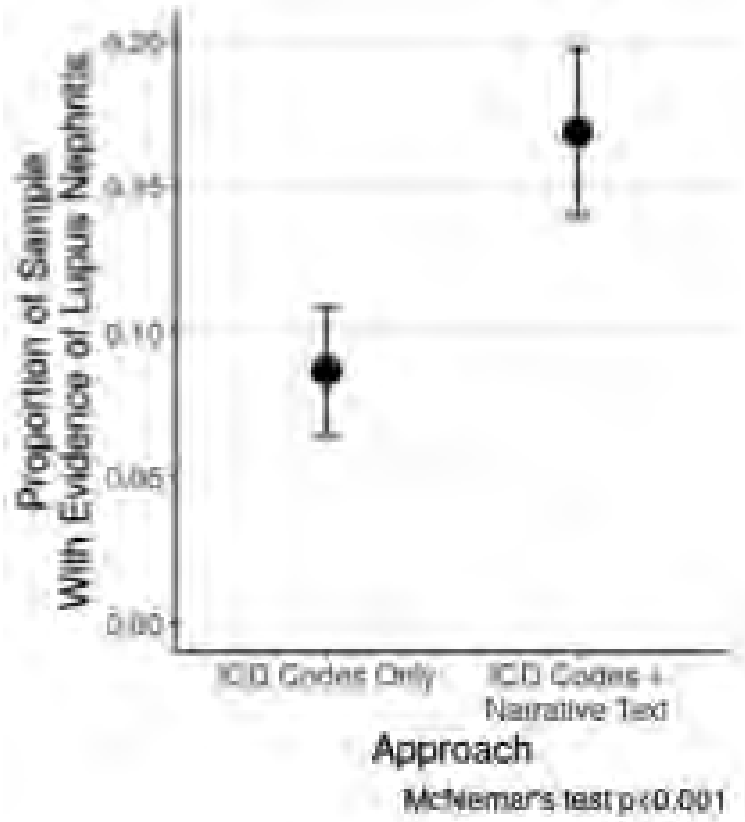


Figure 1. Comparison of the performance of ICD code-only abstraction to ICD code + narrative text abstraction of lupus nephritis from electronic health records.

human-reviewed machine learning were used to abstract and structure the data. We compared 2 approaches to identifying LN in EHR: 1) Query structured sections of the EHR using an ICD-based case definition* (ICD-only); 2) Employ the first approach but also query all unstructured narrative text for LN-related terms (ICD + narrative text). All terms identified using either approach were manually reviewed for validity. For each approach, we calculated the proportion of the sample with evidence of LN (percent, 95% CI) and compared performance using McNemar's test.

Results: Our sample of 635 patients with a diagnosis of lupus in their medical record was 95% female, had a median age of 47 years (IQR=39-56), and resided in 46 U.S. states and Washington D.C. Records spanned a median of 5.4 years (IQR=2.4-10.2), including a median of 6 (IQR=3-13) providers and 3 (IQR=1-5) care sites. The ICD-only approach identified evidence of LN in 55 (8.7%, 95%CI = 6.5-10.8%) patients and the ICD + narrative text approach identified 107 (16.9%, 13.9-19.8%) patients ($p < 0.001$, Figure 1). Leveraging unstructured narrative text identified 95% more patients with LN than only using ICD codes in structured sections of the EHR.

Conclusion: Narrative text abstraction significantly increased capture of LN in this sample of patients with lupus, demonstrating that use of ICD codes alone is not sufficient. An ICD + narrative text has the potential to improve the quality of RWD and better facilitate the generation of RWD for lupus research. Future research should investigate the remaining gap between the rates of LN identified in this manner and the prevalence expected from clinical practice.

*Adapted from Li T. et al, 2021 and Chibnik LB et. al, 2010 (Table 1).

Table 1. Criteria[a] used to identify patients with lupus nephritis (LN) based on ICD codes found in structured sections of electronic health records. Patients were required to have either presence of the specific ICD-10 code for LN (M32.14) *or* presence of ≥2 of the following ICD-9 codes for clinical indicators of nephritis:

ICD-9 Code	Associated Diagnosis
583.81	Nephritis or nephropathy, not specified as acute or chronic, in diseases classified elsewhere
791.0	Proteinuria
581.9	Nephrotic syndrome with unspecified pathological lesion in kidney
580.0	Acute glomerulonephritis with lesion of proliferative glomerulonephritis
582[b]	Chronic glomerulonephritis
583[b]	Nephritis and nephropathy, not specified as acute or chronic
584[b]	Acute kidney failure
585.5	Chronic kidney disease, stage V
585.9	Chronic kidney disease, unspecified
586[b]	Renal failure, unspecified
585.6	End stage renal disease
V56[b]	Renal dialysis encounter

a. Adapted from *Li T. et al, 2021* and *Chibnik LB et. al, 2010*.
b. All ICD-9 codes with this root were included.

References:

1. Li T, Lee, I Jayakumar D, et al. Development and validation of lupus nephritis case definitions using United States veterans affairs electronic health records. Lupus 2021; 30: 518-526.
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Disclosure: M. Tierney, PicnicHealth, 3, 11; **C. Rowe**, PicnicHealth, 3, 11.

Abstract Number: 0342

RAIL Distinguishes Responder and Non-Responder in Pediatric Lupus Nephritis

Ellen Cody[1], Scott Wenderfer[2], Qing Ma[1], Angela Merritt[1], Prasad Devarajan[1] and Hermine Brunner[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Baylor College of Medicine, Houston, TX

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a diagnostic and therapeutic challenge, particularly lupus nephritis (LN). We described a composite score, the Renal Activity Index for Lupus (RAIL), consisting of neutrophil gelatinase-associated lipocalin (NGAL), kidney injury molecule-1 (KIM-1), monocyte chemotactic protein 1 (MCP-1), adiponectin, hemopexin and ceruloplasmin, where higher scores reflect more active inflammation on biopsy. We hypothesize that when followed longitudinally during induction therapy, a change in RAIL score distinguishes clinical responders from non-responders.

Methods: Pediatric patients (< 18 years) diagnosed with LN were included (IRB #2008-0635), N=15. Diagnosis was made according to ACR criteria for SLE with renal biopsy confirmation of LN. Urine was collected at diagnosis and end of induction. Responders were defined by urine protein to creatinine ratio < 0.2 mg/mg, absence of hematuria, and normal glomerular filtration rate. Response also defined as improved activity index on follow up biopsy. There were 10 responders, 5 non-responders. Analysis by T-test, as well as sensitivity and specificity for no change in RAIL score.

Results: RAIL score in the responder group pre and post therapy was significantly different, p-value 0.015. T-Test between non-responder and responder difference scores showed trend towards significance, p-value 0.081 (Fig 1).

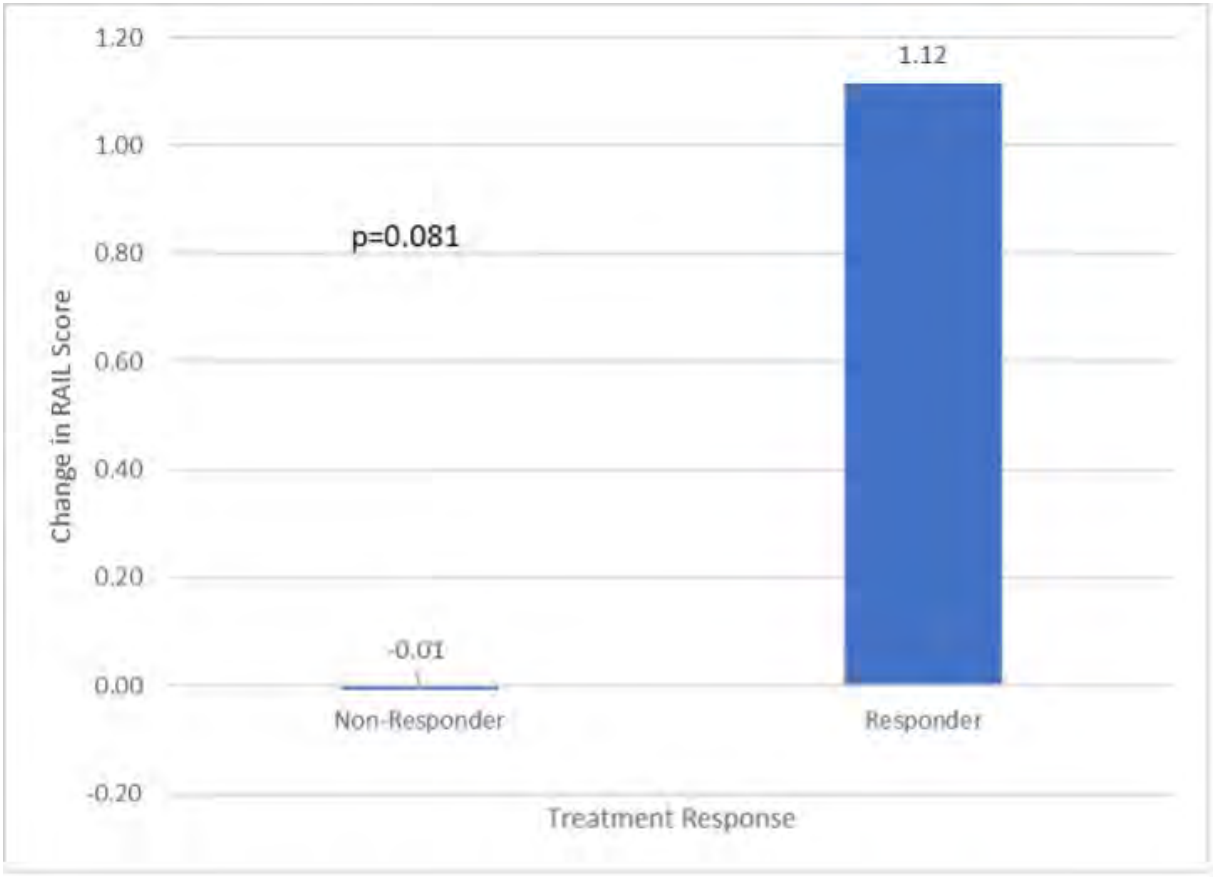


Figure 1. Change in RAIL Score in Clinical Non-Responders vs Responders.

Most responders had a difference of at least 0.5 during induction, whereas most non-responder had no difference or an increase in RAIL score, and a change score >0 identified responders with 90% sensitivity.

Conclusion: A change in RAIL during induction therapy is promising for predicting responders vs non-responders, with average decrease of 1 compared to no change. To further evaluate, more samples are needed, which is on-going.

Disclosure: E. Cody, None; **S. Wenderfer**, Bristol-Myers Squibb, 2; **Q. Ma**, None; **A. Merritt**, None; **P. Devarajan**, BioPorto Inc, 1; **H. Brunner**, Novartis, 6, Pfizer, 6, Roche, 6, GlaxoSmithKline, 6, Abbvie, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Biogen, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, AstraZeneca-Mediimmune, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Boehringer, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, BMS, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Celgene, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Eli Lilly, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, EMD Serono, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Idorsia, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Cerocor, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, F.Hoffman-La Roche, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Merck, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Novartis, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Sanofi, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Aurina, 2.

Abstract Number: 0343

Overview of the Childhood Systemic Lupus Erythematosus (cSLE) Cohort in the CARRA Registry

Christine Bacha[1], Anne Dennos[2], Andrea Knight[3], Laura Schanberg[4], Mary Beth Son[5], Emily von Scheven[6], Shahla Amin[7], Charles Helmick[8] and Aimee Hersh[9], [1]Nationwide Children's Hospital, Grandview Heights, OH, [2]Duke University, Durham, NC, [3]Hospital for Sick Children, Toronto, ON, Canada, [4]Duke University Medical Center, Durham, NC, [5]Boston Children's Hospital, Brookline, MA, [6]University of California San Francisco, San Francisco, CA, [7]CARRA, Durham, NC, [8]Centers for Disease Control and Prevention, Atlanta, GA, [9]University of Utah, Salt Lake City, UT

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry is a multicenter, observational registry that collects demographic, clinical, and provider- and patient-reported data from pa-

Table 1. Sociodemographic characteristics of the CARRA cSLE Registry Cohort at enrollment

Characteristics	N=671
Gender, n (%)	
Male	99 (14.8)
Female	572 (85.3)
Age at enrollment (years)	
Median	15
Mean (SD)	14.3 (2.9)
IQR	11-15
Race/ethnicity (self-reported), n (%)	
White	175 (26.1)
Black	199 (29.7)
Hispanic	155 (23.1)
American Indian/Alaskan native	8 (1.2)
Asian	99 (14.8)
Middle Eastern/North African	7 (1)
Native Hawaiian/Pacific Islander	3 (0.5)
Other	12 (1.8)
Prefer not to answer/Missing	13 (1.9)
Insurance, n (%)	
Private	312 (46.5)
Public insurance	277 (41.3)
Uninsured	17 (2.5)
Other	65 (9.7)
Income, n (%)	
<25,000	84 (12.5)
25,000-49,999	108 (16.1)
50,000-74,999	62 (9.2)
75,000-99,999	60 (8.9)
100,000-150,000	61 (9.1)
≥ 150,000	64 (9.5)
Prefer not to answer/Unknown	232 (34.6)

IQR, interquartile range

Table 2. Prevalence of the American College of Rheumatology (ACR) Classification Criteria and SLICC Classification Criteria in a cSLE cohort (N= 671)[1]

	No (%) of patients fulfilling each criterion at:		
Characteristic	Time of diagnosis	Enrollment	Last follow-up
	N (%)	N (%)	N (%)
ACR and SLICC Criteria			
Oral or nasal ulcers	159 (23.8)	190 (28.4)	206 (30.8)
Cutaneous			
Malar rash (ACR)	241 (36.1)	276 (41.3)	306 (45.6)
Discoid rash (ACR)	63 (9.4)	76 (11.4)	87 (13)
Photosensitivity (ACR)	88 (13.2)	101 (15.1)	117 (17.4)
Acute cutaneous lupus (SLICC)	292 (43.7)	334 (50)	367 (54.9)
Chronic cutaneous lupus (SLICC)	99 (14.8)	118 (17.7)	138 (20.7)
Nonscarring alopecia (SLICC)*	94 (78.3)	120 (18)	136 (20.4)
Arthritis	337 (50.5)	375 (56.1)	395 (59.1)
Serositis			
ACR	94 (14.1)	122 (18.3)	126 (18.8)
Pleuritis	74 (11.1)	96 (14.4)	100 (14.9)
Pericarditis	42 (6.3)	51 (7.6)	53 (7.9)
SLICC	101 (15.1)	132 (19.8)	137 (20.5)
Nephritis*			
ACR	185 (62.5)	259 (87.5)	287 (62.1)
SLICC[2]	230 (69.7)	289 (88.1)	321 (65.6)
Neurologic disorder			
ACR[3]	32 (4.9)	36 (5.4)	41 (6.1)
SLICC[4]	47 (7)	55 (8.2)	67 (10)
Cytopenias			
Leukopenia	268 (40.1)	310 (46.4)	342 (51.2)
Thrombocytopenia	144 (21.6)	154 (23.1)	166 (24.9)
Hemolytic anemia	223 (33.2)	245 (36.7)	252 (37.6)
Lymphopenia (ACR)*	19 (40.4)	23 (46.9)	79 (21.4)
Lymphopenia (SLICC)*	13 (28.3)	16 (34.8)	54 (15.4)
Antinuclear antibody*	585 (90.6)	636 (98.3)	647 (98.5)
Anti-dsDNA*	437 (69.4)	504 (80)	510 (80.8)
Anti-Smith*	293 (51.9)	321 (56.7)	326 (57.5)
Low complement*(SLICC)	25 (3.7)	28 (80.9)	136 (88.8)
Direct Coombs' test*(SLICC)*	209 (53.3)	232 (59.2)	232 (59.2)

* Incomplete data, does not include all 671 patients

1. Does not include numbers for antiphospholipid antibodies as associated dates in the current data harvest were unavailable
2. Defined by renal biopsy showing ISN class II, III, IV, or V OR urine protein/creatinine (or 24h urine) for protein representing 500 mg of protein/ 24h OR red blood cell casts
3. Defined as seizures or psychosis
4. Defined as seizures, psychosis, mononeuritis multiplex, myelitis, peripheral/cranial neuropathy or acute confusional state
5. Includes low C3, low C4, low CH50
6. In the absence of hemolytic anemia

tients with pediatric-onset rheumatic diseases in North America, Israel and Italy. This study aimed to describe the demographic features, cumulative clinical manifestations, and treatments of the childhood systemic lupus erythematosus (cSLE) cohort within the CARRA Registry.

Methods: Since 2015, the CARRA Registry has enrolled 10,411 patients at 70 centers. Childhood-onset SLE enrollment began in March 2017. We performed a retrospective cohort study of patients with cSLE enrolled in the US between March 2017 to December 2020. Inclusion criteria for participants in the CARRA cSLE Registry include: 1) diagnosis of cSLE at < 18 years based on American College of Rheumatology (ACR) or Systemic Lupus Erythema-

Table 3. Immunosuppressive treatment in the CARRA cSLE Registry Cohort (N=671).

Medication	Ever Prescribed N (%)	Currently prescribed N (%)
Steroids	614 (83.7)	308 (42)
Oral	569 (77.5)	305 (41.6)
Intravenous	319 (43.5)	15 (2)
Hydroxychloroquine	631 (94)	598 (89.1)
Mycophenolate Mofetil	373 (55.6)	295 (44)
Cyclophosphamide	97 (14.5)	22 (3.3)
Azathioprine	131 (19.5)	81 (12.1)
Rituximab	131 (16.7)	28 (4.1)
Belimumab	32 (4.9)	28 (4.2)
Other[1]	113 (16.8)	60 (8.9)

1. Leflunomide, Methotrexate

tosus International Collaborating Clinics (SLICC) criteria; 2) enrollment within two years of cSLE diagnosis or at the time of a flare of lupus nephritis; and 3) enrollment prior to 21 years of age. Sociodemographic and clinical data were summarized using descriptive statistics.

Results: The current registry cohort includes 671 participants with cSLE. The majority are female (85%) with mean age at enrollment of 14.3 (SD 2.9) years. The cohort is both ethnically and racially diverse (Table 1). Socioeconomic status varies widely, noting 12.5% having a household income below $25,000/year. The median time from symptom onset to diagnosis was two months (interquartile range (IQR) 25 days to 6 months), from diagnosis to enrollment was 5 (IQR 1-15) months, and from enrollment to end of follow up was 14 (IQR 6 to 23) months. At the end of the follow-up period, more than 60% of participants developed nephritis as defined by ACR or SLICC criteria. 6.1% and 10% had neurological manifestations per ACR and SLICC criteria, respectively (Table 2). Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) at enrollment was a median of 4 (IQR 2-10). Most patients were prescribed hydroxychloroquine. In the first 2-3 years of disease, participants received a variety of immunosuppressive therapies including Mycophenolate Mofetil, Cyclophosphamide, Azathioprine, Rituximab, Belimumab and disease modifying anti-rheumatic drugs such as Leflunomide and Methotrexate. 84% of patients were prescribed either oral or intravenous glucocorticoids during their disease course (Table 3).

Conclusion: The CARRA Registry has enrolled a racially and ethnically diverse cohort of cSLE patients in the early course of their disease. These participants exhibit moderate disease activity and although the use of hydroxychloroquine in this cohort is high, a significant proportion of patients are utilizing glucocorticoids at the last study visit. We anticipate enrolling a minimum of 1000 participants with more than ten years of follow-up. This cohort, which is one of the Centers for Disease Control (CDC) funded SLE registries, provides a unique opportunity to describe the natural history, treatments, and outcomes in patients with cSLE.

Disclosure: C. Bacha, None; **A. Dennos**, None; **A. Knight**, None; **L. Schanberg**, UCB, 12, DSMB member, Sanofi, 12, DSMB member, SOBI, 2, BMS, 5; **M. Son**, None; **E. von Scheven**, None; **S. Amin**, None; **C. Helmick**, None; **A. Hersh**, None.

Abstract Number: 0344

Anti-gAChR Antibody as a Novel Biomarker for Lupus Enteritis in Systemic Lupus Erythematosus

Kuniyuki Aso[1], Michihito Kono[1], Keita Ninagawa[1], Nobuya Abe[1], Yuichiro Fujieda[1], Masaru Kato[1], Olga Amengual[1], Kenji Oku[1] and Tatsuya Atsumi[2], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, [2]Hokkaido University, Sapporo, Japan

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-ganglionic nicotinic acetylcholine receptor (gAChR) antibody (Ab) is associated with widespread autonomic dysfunction in autoimmune autonomic ganglionopathy. Although it is also detected in several autoimmune diseases, including systemic lupus erythematosus (SLE), the clinical significance of anti-gAChR Ab remains unclear. The aim of this study was to compare the clinical manifestation of lupus patients with anti-gAChR Ab.

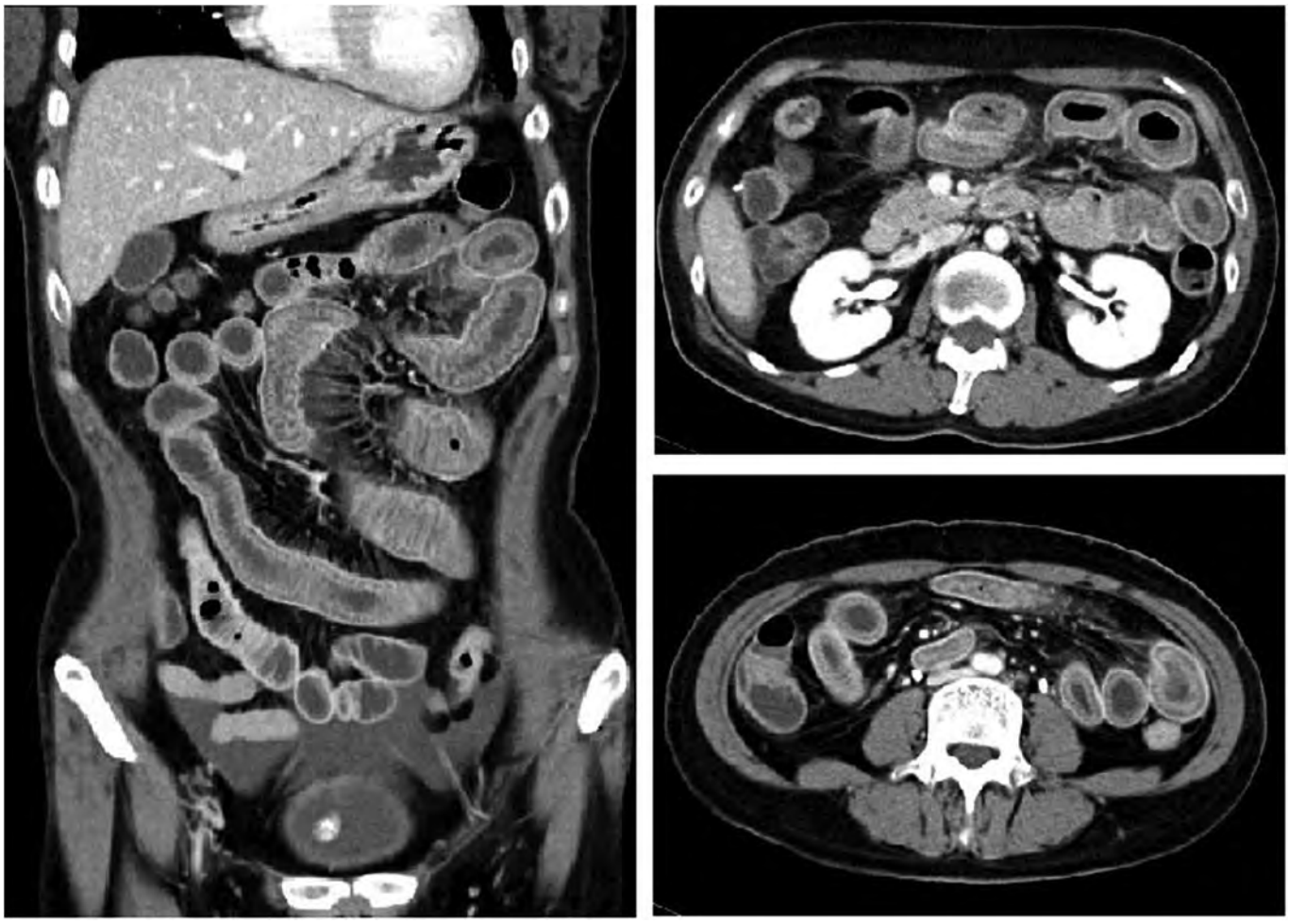


Figure. Lupus enteritis.

Methods: This retrospective study comprised adult patients with SLE who visited Hokkaido University Hospital from 2007 through 2019. A luciferase immunoprecipitation assay was performed to measure anti-gAChRα3 and β4 subunits Ab in the sera of these patients. The effect of immunosuppressants on anti-gAChR Ab levels was also evaluated. The Mann-Whitney U test was used for comparison of continuous data, while the Fisher's exact test was used for comparison of categorical variables. Predictors affecting clinical manifestations were assessed by logistic regression analysis. The cumulative recurrence rate was estimated by Kaplan-Meier analysis.

Results: Overall, 144 patients with SLE were enrolled in this study. The clinical manifestations of these patients included lupus nephritis (45.8%), neuropsychiatric SLE (31.9%), antiphospholipid syndrome (22.2%), pericarditis and/or pleuritis (18.8%), and lupus enteritis (LE, 14.6%, Figure). Among these patients, anti-gAChRα3 and β4 subunit Ab were positive for 29 (20.1%) and 8 (5.6%), respectively. The patients with anti-gAChRα3 Ab had LE more frequently than those without (37.9 vs. 8.7%, $p< 0.001$). The levels of anti-gAChRα3 Ab were significantly reduced ($p = 0.001$) after immunosuppressive treatment in the patients with LE. Logistic regression analysis revealed that anti-gAChRα3 Ab (odds ratio [OR] 11.1, 95% Confidence Interval [95%CI] 3.4-36.2, $p< 0.001$)and lupus cystitis (OR 16.3, 95%CI 2.07-127.8, $p=0.006$) were independent predictors for having LE. The ten-year cumulative LE relapse rate from the date of sera collection was significantly high in the patients with anti-gAChRα3 Ab compared to those without (27.0% vs. 2.3%, $p< 0.001$).

Conclusion: Anti-gAChRα3 Ab would be a new biomarker for the development and recurrence of LE in patients with SLE.

Disclosure: K. Aso, None; **M. Kono**, GlaxoSmithKline plc, 5, Mitsubishi Tanabe, 5, Astellas, 5, Sanofi, 5, Taisho Pharmaceutical, 5, NIPPON SHINYAKU CO., LTD., 5, Taiju Life Social Welfare Foundation, 5, Kowa Company. Ltd., 5, Terumo Corporation, 5; **K. Ninagawa**, None; **N. Abe**, None; **Y. Fujieda**, None; **M. Kato**, GSK, 5, Actelion, 5; **O. Amengual**, None; **K. Oku**, None; **T. Atsumi**, AbbVie Japan GK, 2, 6, Astellas Pharma Inc., 5, 6, Bristol-Myers Squibb Co. Ltd, 6, Chugai Pharmaceutical Co. Ltd, 5, 6, Daiichi Sankyo Co. Ltd, 5, 6, Eisai Co. Ltd., 6, Eli Lilly Japan K.K, 6, Mitsubishi Tanabe Pharma Co.;, 5, 6, Pfizer Japan Inc, 2, 5, 6, Takeda Pharmaceutical Co. Ltd, 5, 6, UCB Japan Co. Ltd, 6, AstraZeneca plc, 2, Boehringer Ingelheim Co. Ltd, 2, Medical & Biological Laboratories Co. Ltd, 2, Novartis Pharma K.K, 2, Ono Pharmaceutical Co. Ltd, 2, Alexion Inc, 5, Otsuka Pharmaceutical Co., Ltd, 5, Gilead Sciences, Inc., 5, 6.

Abstract Number: 0345

Anti-MPP-1 Autoantibodies in Systemic Lupus Erythematosus: A Potential Biomarker for Neuropsychiatric Manifestations

Eugene Krustev[1], Katherine Buhler[1], Francesca Cardwell[2], Marvin Fritzler[1], Ann Clarke[1] and May Choi[3], [1]University of Calgary, Calgary, AB, Canada, [2]University of Waterloo, Burlington, ON, Canada, [3]Brigham and Women's Hospital | University of Calgary, Calgary, AB, Canada

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Neuropsychiatric systemic lupus erythematosus (NPSLE) can involve the central (CNS) and peripheral nervous system (PNS). Several autoantibodies have been associated with CNS NPSLE including anti-phospholipid, anti-ribosomal P and anti-NMDA receptor 2; however, there are no known autoantibodies specifically

Table 1. Baseline demographic and clinical characteristics of SLE patients who were ever anti-MPP1 positive (MPP1+) vs those who were not (MPP1-)

	Entire Cohort (n=301)	MPP1- (n=241)	MPP1+ (n=60)	Odds Ratio (95% CI)	P value
Sex, % Female	**92.4%**	**94.6%**	**83.3%**	**0.3 (0.1, 0.7)**	**0.003**
Ethnicity, % white	61.1%	60.8%	65.2%	1.1 (0.6, 2.1)	0.824
Age of SLE Onset - years, mean ± SD	35.8 ± 15.3	36.2 ±15.2	34.5 ±16.0	--	0.452
Age at Enrollment - years, mean ± SD	**47.5 ± 15.5**	**48.4 ± 15.6**	**43.9 ± 15.0**	**--**	**0.044**
Disease Duration - years, mean ± SD	11.4 ± 11.5	11.9 ± 11.8	9.4 ± 10.0	--	0.127
Number of Follow up visits – mean ± SD	1.8 ± 0.8	1.7 ± 0.8	1.9 ± 0.8	--	0.115
SLEDAI-2K at Enrollment – mean ± SD	3.7 ± 3.8	3.4 ± 3.4	4.5 ± 5.0	--	0.059
SLICC Criteria[1]					
Lupus Nephritis[2]	20.4%	19.5%	24.1%	1.3 (0.6, 2.7)	0.460
Acute Cutaneous Lupus	58.4%	60.9%	48.1%	0.6 (0.3, 1.1)	0.088
Chronic Cutaneous Lupus	10.6%	11.4%	7.4%	0.6 (0.2, 1.9)	0.397
Oral ulcers	48.2%	48.6%	46.3%	0.9 (0.5, 1.7)	0.758
Nonscarring alopecia	40.9%	39.5%	46.3%	1.3 (0.7, 2.4)	0.366
Nonerosive arthritis	78.1%	77.7%	79.6%	1.1 (0.5, 2.3)	0.762
Serositis	32.5%	30.9%	38.9%	1.4 (0.8, 2.6)	0.262
Renal	29.9%	28.6%	35.2%	1.3 (0.7, 2.5)	0.346
Hemolytic anemia	7.3%	7.3%	7.4%	1.0 (0.3, 3.2)	0.973
Leukopenia	**44.9%**	**40.5%**	**63.0%**	**2.5 (1.4, 4.6)**	**0.003**
Lymphopenia	**31.0%**	**27.3%**	**46.3%**	**2.3 (1.3, 4.2)**	**0.007**
Thrombocytopenia	17.9%	19.1%	13.0%	0.6 (0.3, 1.5)	0.292
ANA	97.4%	96.8%	100.0%	3.8 (0.2, 68.1)	0.184
Anti-dsDNA	68.2%	65.9%	77.8%	1.8 (0.9, 3.6)	0.093
Anti-Sm	**24.8%**	**19.5%**	**46.3%**	**3.6 (1.9, 6.7)**	**<0.001**
Lupus Anticoagulant	15.7%	15.5%	16.7%	1.1 (0.5, 2.4)	0.826
Anti-cardiolipin	16.1%	14.1%	24.1%	1.9 (0.9, 4.0)	0.073
Anti-ß2 glycoprotein 1	13.9%	13.6%	14.8%	1.1 (0.5, 2.6)	0.822
Hypocomplementemia	**42.3%**	**35.9%**	**68.5%**	**3.9 (2.1, 7.3)**	**<0.001**
Direct Coombs'[3]	5.8%	4.5%	11.1%	2.6 (0.9, 7.6)	0.065

Bold indicates statistically significant result (p<0.05). Abbreviations: ANA, antinuclear antibody; Anti-dsDNA, anti-double-stranded DNA; Anti-Sm, anti-Smith; MPP1, M-phase phosphoprotein 1; SD, standard deviation; SLE, systemic lupus erythematosus; SLEDAI-2K, SLE disease activity index. 1. Excluding neurologic criteria, see **Table 2**. 2. Lupus nephritis defined by renal biopsy showing ISN class 2, 3, 4, or 5 and autoantibody (ANA or anti-dsDNA) and exclusion of other causes including viral (HIV, hepatitis B, hepatitis C) and malignancy. 3. Direct Coombs' test in absence of hemolytic anemia.

associated with PNS involvement. M-Phase Phosphoprotein 1 (MPP1; also known as kinesin family member 20B, KIF20B) is a protein involved in cytokinesis and anti-MPP1 autoantibodies have been associated with idiopathic ataxia. We examined the frequency of anti-MPP1 and its demographic and clinical associations including CNS and PNS NPSLE in our local SLE cohort.

Methods: Patients fulfilled the ACR or SLICC classification criteria (CC) for SLE. Age, sex, race, SLEDAI-2K, SLICC CC, and sera were collected at the time of enrolment and up to two follow up visits. NPSLE events fulfilling the ACR case definitions were identified from date of SLE diagnosis by medical record review. Anti-MPP1 titers were determined by an addressable laser bead immunoassay (ALBIA) utilizing a purified recombinant protein. ALBIA results were expressed as median florescence units (MFU). A dilution of ≥1:500 MFU was considered positive. Chi-squared and t-tests were performed to compare demographic and clinical characteristics, including NPSLE manifestations, between patients who were ever anti-MPP1 positive (MPP1+) vs those who were never positive (MPP1-). Multivariable logistic regression analysis was used to determine associations between MPP1+ and variables that were statistically significant in the univariable analysis ($p < 0.05$).

Results: Of the 301 SLE patients studied (mean disease duration 11.4 ± 11.5 years), 19.9% were MPP1+. When compared to MPP1- patients, MPP1+ patients had a lower proportion of females (OR 0.3, 95% CI 0.1-0.7), were younger at enrolment (43.9 ± 15.0 years vs 48.4 ± 15.6 years; p=0.04), had more leukopenia (OR 2.5, 95% CI 1.4-4.6), lymphopenia (OR 2.3, 95% CI 1.3-4.2), anti-Sm antibodies (OR 3.6, 95% CI 1.9-6.7) and hypocomplementemia (OR

Table 2. Neuropsychiatric SLE manifestations according to the American College of Rheumatology case definitions in patients who were ever anti-MPP1 positive (MPP1+) vs those who were not (MPP1-)

Neuropsychiatric SLE Manifestations	Entire Cohort (n=293)	MPP1- (n=234)	MPP1+ (n=59)	Odds Ratio (95%CI)	P value
Any Neurological Manifestation	72.4%	72.3%	72.9%	1.0 (0.5, 2.0)	0.934
Any Central Neurologic Manifestation	69.0%	70.2%	64.4%	0.8 (0.4, 1.4)	0.388
Headache	45.1%	45.3%	44.1%	1.0 (0.5, 1.7)	0.865
Mood Disorder	24.1%	25.1%	20.3%	0.8 (0.4, 1.5)	0.444
Seizures and/or Seizure Disorder	8.2%	9.4%	3.4%	0.3 (0.1, 1.5)	0.132
Cognitive Dysfunction	13.0%	12.8%	13.6%	1.1 (0.5, 2.5)	0.880
Anxiety Disorder	14.0%	13.7%	15.3%	1.1 (0.5, 2.5)	0.755
Cerebrovascular Disease	12.3%	12.4%	11.9%	1.0 (0.4, 2.3)	0.912
Acute Confusional State	4.8%	5.6%	1.7%	0.3 (0.0, 2.3)	0.214
Psychosis	1.7%	1.7%	1.7%	1.0 (0.1, 9.1)	0.997
Myelopathy	0.7%	0.4%	1.7%	4.0 (0.2, 65.2)	0.291
Movement Disorder	0.3%	0.4%	0.0%	1.3 (0.1, 32.6)	0.615
Aseptic Meningitis	0.3%	0.4%	0.0%	1.3 (0.1, 32.6)	0.615
Demyelinating Syndrome	0.3%	0.4%	0.0%	1.3 (0.1, 32.6)	0.615
Any Peripheral Neurologic Manifestation	**17.7%**	**13.7%**	**33.9%**	**3.2 (1.7, 6.2)**	**<0.001**
Polyneuropathy	8.5%	8.5%	8.5%	1.0 (0.4, 2.8)	0.986
Mononeuropathy	**3.1%**	**1.3%**	**10.2%**	**8.7 (2.1, 36.0)**	**<0.001**
Cranial Neuropathy	**6.5%**	**3.4%**	**18.6%**	**6.5 (2.5, 17.0)**	**<0.001**
Acute Inflammatory Demyelinating Polyneuropathy	0.3%	0.0%	1.7%	12.0 (0.5, 299.0)	0.05
Autonomic Disorder	1.4%	1.3%	1.7%	1.3 (0.1, 13.0)	0.807
Plexopathy	0.0%	0.0%	0.0%	–	--
Myasthenia Gravis	0.7%	0.9%	0.0%	0.7 (0.0, 16.5)	0.476

Bold indicates statistically significant result (p<0.05). Abbreviations: MPP1, M-phase phosphoprotein 1.

3.9, 95% CI 2.1-7.3) (Table 1). 72.4% of patients met criteria for any NPSLE manifestation with no difference between MPP1+ and MPP1- patients (Table 2). When PNS NPSLE manifestations were examined, patients with any peripheral neuropathy (OR 3.2, 95% CI 1.7-6.2), mononeuropathy (OR 8.7, 95% CI 2.1-36.0), and cranial neuropathy (OR 6.5,

Table 3. Multivariable analysis for demographic and clinical associations of anti-MPP1 antibodies

Demographic and Clinical Characteristics	Model 1[1]	Model 2 [1]
Any Peripheral Neuropathy	**4.8 (2.2-10.8)**	--
Mononeuropathy	--	5.9 (1.0-36.7)
Cranial Neuropathy	--	**9.7 (2.9-32.2)**
Female	0.4 (0.1-1.1)	0.4 (0.1-1.1)
Age at Enrollment	1.0 (1.0-1.0)	1.0 (1.0-1.0)
Leukopenia	**2.3 (1.1-4.6)**	1.9 (0.9-3.9)
Lymphopenia	2.0 (1.0-4.0)	1.9 (0.9-4.0)
Anti-Sm	**3.3 (1.6-6.9)**	**3.4 (1.6-7.0)**
Hypocomplementemia	**2.7 (1.3-5.5)**	**3.1 (1.4-6.7)**

Results are expressed as odds ratios (95% CI) for the association between the corresponding variable and MPP1+. Covariables included significant variables from univariable analysis (p<0.05). 1. Model 1 includes any peripheral neurologic manifestation while in model 2 the specific subtypes mononeuropathy and cranial neuropathy were analyzed. Bold indicates statistically significant result (p<0.05). Abbreviations: Anti-Sm, anti-Smith.

95% CI 2.5-17.0) were more likely to be MPP1+. Multivariable analysis demonstrated that any peripheral neuropathy (OR 4.8, 95% CI 2.2-10.8) and cranial neuropathies remained significantly associated with MPP1+ (OR 9.7, 95% CI 2.9-32.2) (Table 3).

Conclusion: Anti-MPP1 may be an important biomarker for peripheral neuropathies, in particular, cranial neuropathies in SLE. These findings are being validated in a larger, multicentre SLE cohort.

Disclosure: E. Krustev, Intercept Pharmaceuticals Inc, 11, Mountain Valley MD Holdings INC, 11, Gilead Sciences INC, 11; **K. Buhler**, None; **F. Cardwell**, None; **M. Fritzler**, Inova Diagnostics Inc., 2, 6, Werfen International, 2, Alexion Canada, 6, Mitogen Diagnostics Corp., 3, 8, 9, 10; **A. Clarke**, AstraZeneca, 2, GSK, 6, BMS, 2, Exagen Diagnostics, 2; **M. Choi**, MitogenDx, 1, 2.

Abstract Number: 0346

The CB-CAPillary™ Test Kit: A Tool for Point-of-Care Assays to Measure Cell-Bound Complement Activation Products

Joseph Ahearn[1], Susan Manzi[1] and Chau-Ching Liu[2], [1]Allegheny Health Network, Wexford, PA, [2]Allegheny Health Network, Pittsburgh, PA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Cell-bound complement activation products (CB-CAPs) have been validated as biomarkers for systemic lupus erythematosus (SLE) diagnosis, monitoring and stratification, and for identification of patients with pre-lupus. However, CB-CAP assays currently require live cells, are time and temperature sensitive, and must be performed by a dedicated technician with a flow cytometer. We have developed a CB-CAP assay that eliminates the need for live cells and a flow cytometer and can yield results in minutes.

Methods: Four different methods have been developed to measure CB-CAPs without the need for a flow cytometer. One method, described here, utilizes a CB-CAPillary™ Test Kit (patent pending), analogous to a urine dipstick, to rapidly measure levels of CB-CAPs in body fluids. Erythrocyte C4d (EC4d) levels determined by a traditional flow-cytometric assay were compared with those determined using the novel CB-CAPillary™ assay device. Assays were performed using fresh erythrocytes, freeze-thawed erythrocytes, and erythrocyte lysates. Blood samples were obtained from patients with SLE and from non-lupus subjects. Correlations between results obtained by flow cytometry and those generated by the CB-CAPillary™ assay device were analyzed by Pearson correlation.

Results: EC4d levels determined by FACS ranged from 2.93-70.42. The correlation between EC4d in erythrocyte lysates determined using a FACs cytometer and EC4d determined using a CB-CAPillary™ test kit was R^2=0.89. The correlation between EC4d in erythrocyte freeze-thawed samples determined using a FACs cytometer and EC4d determined using a CB-CAPillary™ test kit was R^2=0.99. TC4d/BC4d were also successfully detected in buffy coat lysates.

Conclusion: This proof-of-concept study demonstrates that CB-CAP assays can be performed within minutes, and without the need for flow cytometry, live cells, or a dedicated technician. The CB-CAPillary™ test kit enables a rapid

and inexpensive method for determining cell-bound complement activation levels for lupus diagnosis, monitoring and stratification and for identification of patients with pre-lupus. As a point-of-care test kit, it could be available to patients and physicians globally. CB-CAPillary™ test kits for measurement of BC4d, TC4d, PC4d and RC4d are also being developed with the methods described here.

Disclosure: J. Ahearn, Exagen, 2, 10; **S. Manzi**, Astra Zenecs, 2, 5, Cugene, 2, Eli Lilly, 2, Exagen, 2, 5, 10, UCB, 2, GSK, 2; **C. Liu**, None.

Abstract Number: 0347

Longitudinal ANA Titers in SLE and ANA+ Controls

Emily Littlejohn[1], Lingxuan Kong[2], Kelly Speth[2], Lu Wang[2] and Emily Somers[2], [1]Cleveland Clinic, Cleveland, OH, [2]University of Michigan, Ann Arbor, MI

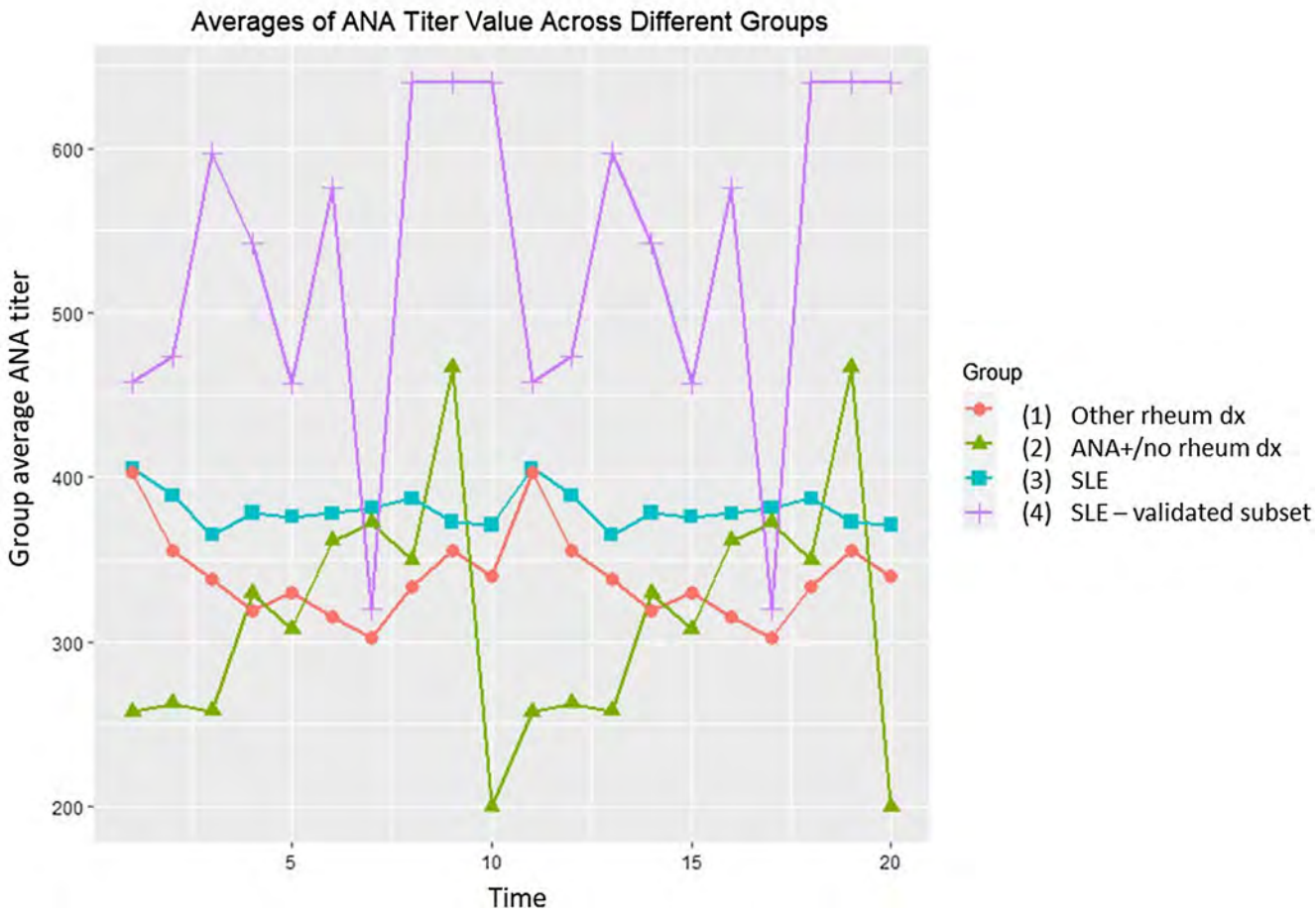
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antinuclear or anticellular antibodies (ANAs), are a hallmark of systemic lupus erythematosus (SLE). ANAs are also a marker of subclinical autoimmunity, with ~13% of the general adult population ANA+. Risk factors for developing subclinical autoimmunity are poorly understood. An important step is to understand trajectories of ANA positivity and titers within individuals over time. We performed an exploratory analysis of electronic health record (EHR) data to assess intraindividual variation in ANAs longitudinally.

Methods: Utilizing our academic health center's EHR we formed a sub-cohort of all patients with at least 2 ANA tests (by immunofluorescence, IFA). A titer of ≥1:80 was considered positive. We evaluated the effect of time on the titer value using a longitudinal random effect model comparing across different patient groups defined by ICD codes: (1) ANA-associated rheumatic diseases (Sjogren's Syndrome, dermatomyositis, polymyositis, scleroderma, undifferentiated connective tissue disease, mixed connective tissue disease); (2) ANA+ controls without rheumatic disease; (3) SLE. A subset of SLE was validated by a rheumatologist and fulfilled ACR/SLICC criteria (4).

Results: 7226 patients had at least two valid ANA-IFA lab results (SLE by ICD n=1706, validated SLE n=54, alternate rheumatic diagnosis n=1644, ANA+/no rheumatic diagnosis n=3822). Of 5603 patients with a positive ANA at the first observation, 4 (7%) of SLE and 953 (17.2%) of non-SLE and had a subsequent negative ANA. Longitudinally, the strength of ANA titer changed over time ($p< 0.001$) among both SLE and non-SLE patients. Controlling for time, SLE patients had a higher odds of a positive ANA titer on average vs non-SLE [OR 1.44, 95% CI (1.19, 1.75)]. SLE patients also had a higher odds ratio on average of a positive ANA titer associated with time change compared to non-SLE [ratio of OR overtime 1.09, 95% CI (1.02, 1.17), $p< 0.001$].

Conclusion: While previous cross-sectional data have shown that ANAs tend to increase with age, longitudinal data of intra-individual patterns are lacking. Our data provide initial evidence of intra-individual variability over time, with SLE patients having increasing titers over time. Future work includes investigating demographic and other covariates to discern titers in SLE and non-SLE ANA+ clinical phenotypes. We seek to determine if pre-clinical (or subclinical) periods are opportunities for intervention to modify the course of autoimmunity and clinical progression.



Longitudinal trajectory of average ANA titers over the order of measurement across 4 different groups of patients.

Disclosure: E. Littlejohn, Aurinia Pharmaceuticals, 6; **L. Kong**, None; **K. Speth**, None; **L. Wang**, None; **E. Somers**, None.

Abstract Number: 0348

The New EULAR/ ACR 2019 SLE Classification Criteria: A Predictor of Long-term Outcomes

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Demographic characteristics in our cohort at baseline. Values are expressed as mean ± SD or n (%).

Variables	EULAR/ACR Score < 20 N = 415	EULAR/ACR Score ≥ 20 N = 452	P value
Race			
Caucasian	316 (76.1)	262 (58.0)	**<0.001**
Black	42 (10.1)	81 (17.9)	**0.002**
Chinese	20 (4.8)	52 (11.5)	**<0.001**
Age, years	38.1 ± 15.1	34.5 ± 13.1	**<0.001**
Disease duration, years	0.2 ± 0.3	0.2 ± 0.3	0.86
SLEDAI-2K score	6.3 ± 5.4	12.2 ± 8.9	**<0.001**
SDI[a] score	0.1 ± 0.4	0.1 ± 0.4	0.13
SDI[a] > 0	23 (5.5)	34 (7.5)	0.24
Treatment			
GC[b] use	241 (58.1)	374 (82.7)	**<0.001**
Immunosuppressive use	83 (20.0)	166 (36.7)	**<0.001**
Antimalarial use	222 (53.5)	247 (54.6)	0.73

[a]SLICC/ACR Damage Index
[b] Glucocorticoid.

Background/Purpose: We recently demonstrated that a EULAR/ACR classification Criteria score ≥ 20 predicts a higher disease activity throughout the first 5 years after diagnosis. Given that disease activity is associated with damage accrual and mortality, we aimed to determine the ability of a EULAR/ACR score ≥20 to predict these long-term outcomes.

Methods: Inception SLE patients recruited in the first 12 months after diagnosis were included.

For each patient a EULAR/ACR score was calculated based on the baseline clinical and laboratory information. The baseline information was obtained from the first 2 visits.

Patients were divided into 2 groups depending on their EULAR/ACR score < 20 or ≥20. In order to determine the ability of a EULAR/ACR ≥20 to predict damage accrual and mortality the following outcomes were assessed:

1. Time to first damage accrual, defined as any increase in the SLICC/ACR Damage Index (SDI) and time to death within the first 10 years after SLE diagnosis, analyzed using Kaplan Meier survival curves. For damage accrual, death within the 10 years was used as competing risk. Multivariable Cox Proportional regressions was performed to calculate the risk.

Table 2. Outcomes within 10 years of follow-up. Values are expressed as mean ± SD or n (%).			
Outcomes	**EULAR/ACR score < 20 N=415**	**EULAR/ACR score ≥ 20 N=452**	**P value**
Death	24 (5.8)	44 (9.7)	**0.03**
Time to death, years	5.0±2.9	3.6±3.1	0.07
Increase in SDI[a]	167 (40)	210 (46)	**0.02**
Time to SDI[a] increase, years	2.9±2.7	3.0±2.9	0.52
SDI[a] score[#]	0.97±1.42	1.28±1.47	**0.03**
SDI[a] Domains[#]			
Ocular	20 (10.26)	34 (15.96)	0.08
Neurologic	19 (9.74)	28 (13.15)	0.28
Renal	5 (2.56)	19 (8.92)	**0.006**
Pulmonary	3 (1.54)	9 (4.23)	0.10
Cardiovascular	22 (11.28)	14 (6.57)	0.09
Vascular	6 (3.08)	8 (3.76)	0.70
Gastrointestinal	5 (2.56)	6 (2.82)	0.87
Muskuloeskeletal	38 (19.49)	54 (25.35)	0.15
Skin	18 (9.23)	21 (9.86)	0.82
Gonadal	1 (0.51)	3 (1.41)	0.35
Diabetes	3 (1.54)	14 (6.57)	**0.01**
Malignancy	5 (2.56)	3 (1.41)	0.40
[#] At 10 years of follow-up, N = 190 and 206 in the low and high score groups respectively. [a] SLICC/ACR Damage Index			

2. Mean SDI score at the 10th year of follow-up was calculated.

Results: A total of 867 inception patients were included. **Table 1** shows baseline clinical characteristics of the cohort.

The proportion of patients who accrued damage within the first 10 years and the mean SDI at 10 years were significantly higher in the group of ≥ 20**.** When looking at the specific domains in SDI, the group with a score ≥ 20 at 10 years of follow-up had significantly more renal damage and a higher percentage of diabetes (**Table 2)**.

On multivariable regression analysis, after adjusting for age and ethnicity, a score ≥ 20 continued to significantly predict damage accrual, HR 1.28 (1.04-1.57), p=0.02. When we excluded patients who had damage at enrollment the results were similar (**Table 3**).

Sixty-eight (7.8%) of patients died within the first 10 years of follow-up, the percent of deaths was higher in the group with a score ≥ 20, (**Table 2**). Individuals in the ≥ 20 group had twice the probability of dying compared to patients with the lower score, the hazard ratios with significant p values confirmed this finding (**Table 3**).

Conclusion: A EULAR/ACR score ≥20 is an indicator of damage accrual and mortality in SLE.

Table 3: Univariate and Multivariable Cox Regression analysis. Factors associated with damage accrual and death within 10 years of follow-up.				
	Univariate Cox Regression		Multivariable Cox Regression	
First damage accrued (any increase in SDI[a])				
VARIABLE	Hazard Ratio (95% CI)	P value	Hazard Ratio (95% CI)	P value
Age at first visit	1.02 (1.01-1.03)	**<0.001**	1.02 (1.01-1.03)	**<0.001**
Caucasian vs non-caucasian	0.88 (0.71-1.08)	0.22	0.89 (0.72-1.11)	0.31
EULAR/ACR score < or ≥20	1.21 (0.98-1.48)	**0.07**	1.3 (1.04-1.57)	**0.02**
First damage accrued (Initial SDI[a] >0)[#]				
Age at first visit	1.02 (1.01-1.03)	**<0.001**	1.02 (1.02-1.03)	**<0.001**
Caucasian vs non-caucasian	0.88 (0.71-1.10)	0.27	0.91 (0.73-1.14)	0.42
EULAR/ACR score < or ≥20	1.25 (1.01-1.54)	**0.04**	1.33 (1.07-1.64)	**0.009**
Mortality				
Age at first visit	1.05 (1.03-1.06)	**<0.001**	1.05 (1.03-1.07)	**<0.001**
Caucasian vs non-caucasian	1.46 (0.84-2.57)	0.17	1.48 (0.84-2.62)	0.17
EULAR/ACR score < or ≥20	1.66 (1.01-2.73)	**0.04**	2.13 (1.28-3.54)	**0.003**
[#] 57 patients who had damage at entry were excluded for the analysis [a] SLICC/ACR Damage Index				

Disclosure: L. Whittall-Garcia, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **M. Urowitz**, GlaxoSmithKline, 2, 5, 6, UCB, 2, Lilly, 6, AstraZeneca, 2; **J. Su**, None; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6; **S. Johnson**, None.

Abstract Number: 0349

Performance of the 2019 EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus in a Predominantly African American Cohort

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Classification criteria for systemic lupus erythematosus (SLE) were recently published by the European League Against Rheumatism (EULAR) and American College of Rheumatology (ACR) to reflect current diagnostic approaches and improve statistical performance with addition of entry criterion and item weighting. The

Table 1. Comparison of Clinical Characteristics Between Patients Fulfilling and Patients Not Fulfilling the EULAR/ACR Criteria for SLE

Characteristics	Fulfills 2019 EULAR/ACR Criteria – No (n=61, 8.9%)	Fulfills 2019 EULAR/ACR Criteria – Yes (n=621, 91.1%)	P-value
African American %	37 (60.7%)	487 (78.4%)	<0.01
Hispanic %	0 (0%)	20 (3.2%)	0.24 (NS)
Female %	55 (90.2%)	563 (90.7%)	0.90 (NS)
Age at diagnosis	38.2 ± 15.7 yrs	30.1 ± 13.4 yrs	<0.01
Smoking history	15 (24.6%)	150 (25.3%)	0.90 (NS)
Insured	43 (95.6%)	483 (94.0%)	0.67 (NS)
High school graduate	42 (93.3%)	430 (83.3%)	0.09 (NS)
Disease duration	17.6 ± 9.3 yrs	19.0 ± 9.0 yrs	0.88 (NS)
Childhood onset SLE (≤18)	4 (6.6%)	121 (19.5%)	0.01
Overlap syndrome	13 (27.1%)	153 (31.1%)	0.57 (NS)
SLICC Damage Index: Any damage*	28 (45.9%)	406 (65.4%)	<0.01
SLICC Damage Index: High damage**	16 (26.2%)	274 (44.1%)	0.01
Fulfilling ACR 1997 Criteria	34 (55.7%)	582 (93.7%)	<0.01
Not fulfilling ACR 1997 criteria	27 (44.2%)	39 (6.3%)	<0.01

*Any damage defined as a SLICC Damage index score of ≥1
**High damage defined as a SLICC Damage index score of ≥2

validation cohort included a small proportion of African American patients, a population disproportionately affected by early and severe SLE. We evaluated the performance of the EULAR/ACR 2019 criteria within a predominantly African American well-characterized cohort of patients with SLE.

Methods: Patients enrolled in a single center longitudinal prospective study of SLE were included, excluding patients without a confirmed expert clinical rheumatologist diagnosis of SLE. Demographic, clinical, and immunologic features were compared between the EULAR/ACR Classification Criteria for SLE and the 1997 ACR criteria. Chart review was completed for missing values. Fulfilling criteria for SLE was defined as the presence ≥4 ACR criteria or ≥10 points for the EULAR/ACR criteria. ”Any damage” on the Systemic Lupus International Collaborating Clinics (SLICC) Damage Index is a score ≥1 and “high damage” is a score ≥2.

Results: A total of 682 patients with SLE were included. Of the 682 patients, 524 identified as black (76.3%), 20 as non-black Hispanic (2.9%), and 90.6% female. Patients with childhood onset SLE (diagnosed at ≤ 18 years) comprised 18.3% of the cohort. A proportion of the SLE patients have an additional overlapping autoimmune disease (n=166, 30.7%) most commonly Sjogren’s, RA, or autoimmune thyroid disease. SLICC damage was present in 63.6% of patients (n=434), with 42.5% (n=290) having high damage. The mean 1997 ACR criteria score was 5.6 (median 5) out of 11 possible. The mean EULAR/ACR criteria score was 20.6 (median 20) out of 51 possible.

Table 1 compares patients fulfilling EULAR/ACR criteria to the 8.9% who did not. Table 2 compares patients fulfilling ACR criteria to those fulfilling EULAR/ACR criteria. Of patients who meet ACR criteria, blacks were more likely to meet EULAR/ACR criteria compared to whites (96.4% vs 87.9%, respectively, p< 0.01). EULAR/ACR criteria had

Table 2. Comparison of Clinical Characteristics Between Patients Fulfilling the 1997 ACR Criteria and Patients Fulfilling the EULAR/ACR Criteria for SLE

Characteristics	Fulfills 1997 ACR Criteria	Fulfills 2019 EULAR/ACR Criteria	p-value
Number of patients *n* (%)	616 (90.3%)	621 (91.1%)	<0.01
African American	476 (77.3%)	487 (78.4%)	0.21 (NS)
Hispanic	16 (2.6%)	20 (3.2%)	0.11 (NS)
Female %	559 (90.5%)	563 (90.7%)	0.69 (NS)
Age at diagnosis	30.4 ± 13.4 yrs	30.1 ± 13.4 yrs	0.35 (NS)
Smoking history	148 (25.0%)	150 (25.3%)	0.71 (NS)
Insured	482 (94.0%)	483 (94.0%)	0.91 (NS)
High school graduate	435 (84.1%)	430 (83.3%)	0.56 (NS)
Disease duration	19.3 ± 9.0 yrs	19.0 ± 9.0 yrs	0.28 (NS)
Childhood onset SLE (≤18)	114 (18.5%)	121 (19.5%)	0.06 (NS)
Overlap syndrome	151 (91%)	153 (31.1%)	0.69 (NS)
SLICC Damage Index: Any damage*	400 (64.9%)	406 (65.4%)	0.43 (NS)
SLICC Damage Index: High damage**	273 (44.3%)	274 (44.1%)	0.86 (NS)

*Any damage defined as a SLICC Damage index score of ≥1

**High damage defined as a SLICC Damage index score of ≥2

a sensitivity of 91.1% overall (92.9% among black patients, p< 0.01) and the ACR criteria had sensitivity of 90.3% overall (90.8% among black patients, p< 0.01). Contributing to this gap were differences in ANA positivity (99.0% of blacks compared to 96.2% of non-blacks, p=0.01) and lupus nephritis, especially Class III and IV by biopsy (59.5 % of blacks compared to 33.5% of non-blacks, p< 0.01).

Conclusion: In this cohort of predominately African American patients with SLE, the sensitivities of the ACR 1997 criteria and EULAR/ACR 2019 criteria differed significantly by race. ANA positivity as an entry criterion, in addition to higher weighting for renal disease, accounts for some of the higher sensitivity of the EULAR/ACR criteria among African Americans. The importance of knowing the performance characteristics of these criteria, particularly for African American patients, cannot be understated, as the need for identifying patients for early intervention is critical.

Disclosure: J. English, None; **D. Wilson**, None; **G. Gilkeson**, None; **J. Oates**, None; **D. Kamen**, None.

Abstract Number: 0350

EPI-SIGN: Epigenetic SLE Indicators of Glomerular Nephritis

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SESSION INFORMATION

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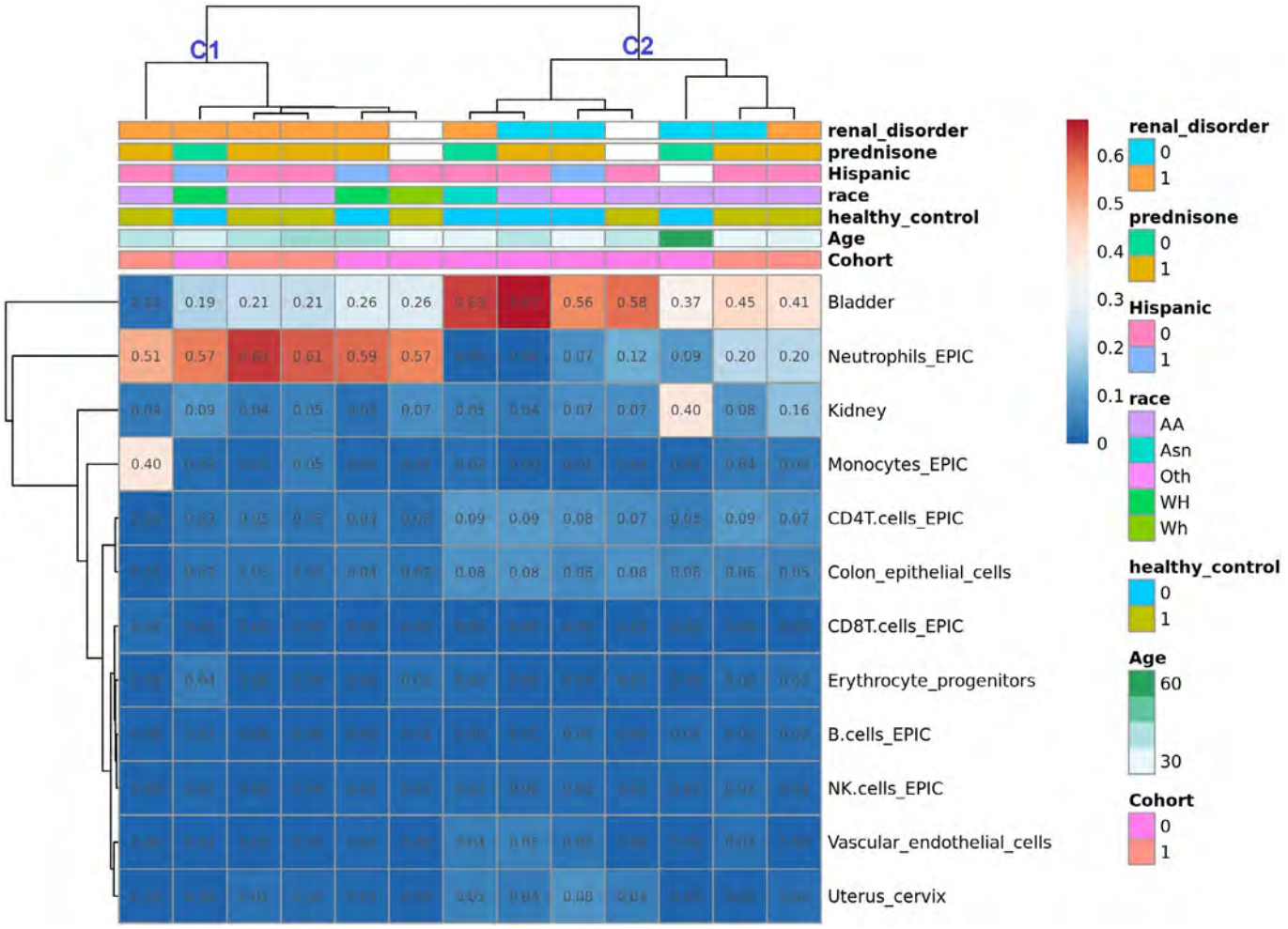
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is more common and severe in those of African Ancestry (AA) who, relative to Europeans, are twice as likely to develop lupus nephritis (LN)[1]. Early nephritis detection can improve outcomes; however, current strategies rely on clinically apparent kidney injury and invasive biopsies, representing a barrier to care in socioeconomically marginalized patients[2]. Urine sediment epigenetics, which contains invading immune cells, offers a conveniently accessible window into the SLE kidney[3, 4].

Methods: This pilot study tested the feasibility of urine epigenetic signature to identify LN in 14 SLE patients in the USA and Nigeria and 2 healthy controls (HC). Consenting participants provided up to 10mL of urine, which was processed fresh (n=4) or treated with 40mM EDTA and 20µl Penicillin/Streptomycin before freezing at -80°C. Samples from Nigeria were shipped on dry ice for processing at the USA site. Urine was centrifuged, and DNA extracted from sediment with the Zymo Research Quick-DNA Urine kit. Methylation of purified DNA was assessed with the Illumina Methylation EPIC BeadChip. Data was analyzed in R using the minfi v1.32.0 software suite. Probe intensities were background corrected and annotated with the IlluminaHumanMethylationEPICanno.ilm10b5.hg38 package. Clus-

Table 1 Stratified by Cohort

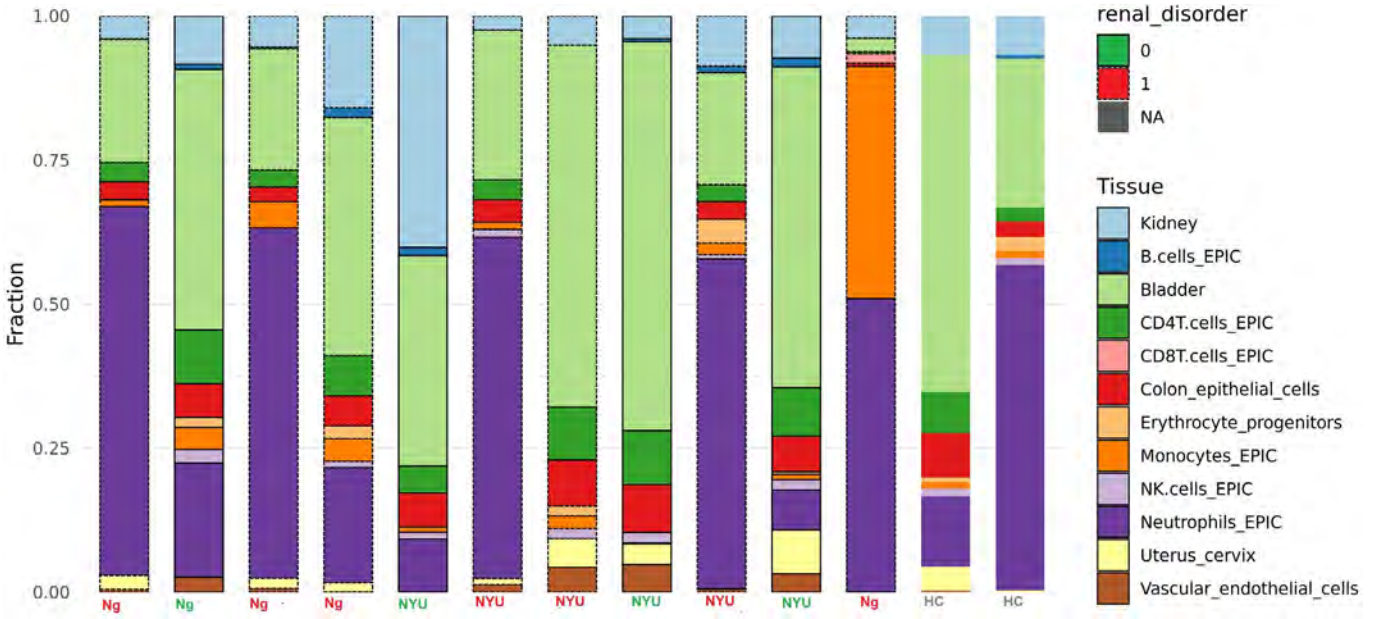
n	NYU 6	Nigeria 8	P value
Demographics			
Age (SD)	38.8 (15.7)	37.3 (8.3)	0.8
Female (%)	6 (100.0)	8 (100.0)	NA
SLE Duration (SD)	15.0 (12.3)	6.6 (3.9)	0.1
SLEDAI score (SD)	4.2 (4.2)	4.8 (6.1)	0.8
Proteinuria (%)	1 (16.7)	4 (50.0)	0.5
Medications			
Hydroxychloroquine (%)	6 (100.0)	8 (100.0)	NA
Dose (SD)	316.7 (98.3)	200.0 (0.0)	0.005
Prednisone (%)	3 (50.0)	8 (100.0)	0.1
Dose (SD)	12.1 (18.1)	11.9 (4.6)	0.9
Mycophenolate (%)	4 (66.7)	0 (0.0)	0.03
Dose (SD)	1250.0 (1172.6)	0.0 (0.0)	0.01
Azathioprine (%)	0 (0.0)	6 (75.0)	0.02
Dose (SD)	0.00 (0.0)	43.8 (32.0)	0.006
Rituximab (%)	1 (16.7)	0 (0.0)	0.9
Tacrolimus (%)	1 (16.7)	0 (0.0)	0.9
SLE ACR Criteria			
ANA (%)	6 (100.0)	8 (100.0)	NA
Malar (%)	2 (33.3)	5 (62.5)	0.6
Discoid (%)	1 (16.7)	1 (12.5)	1.0
Photosensitivity (%)	0 (0.0)	3 (37.5)	0.3
Oral Ulcers (%)	1 (16.7)	3 (37.5)	0.8
Arthritis (%)	4 (66.7)	7 (87.5)	0.8
Serositis (%)	2 (33.3)	2 (25.0)	1.0
Lupus nephritis (%)	3 (50.0)	5 (62.5)	1.0
Neurologic (%)	0 (0.0)	1 (12.5)	1.0
Hematologic (%)	5 (83.3)	4 (50.0)	0.5
Immunologic (%)	5 (83.3)	8 (100.0)	0.9



Heatmap showing participants (Y axis) clustered by identified urinary cell types (X axis). Metadata including renal disorder are annotated on the upper X axis. Two clusters, C1 and C2 differentiate renal disorder as defined by ACR criteria.

tering was performed with principal component analysis (PCA) or multidimensional scaling (MDS) with the top 1000 most variable CpG probes or the 59 control SNP probes on-board the EPIC BeadChip. Intra-sample cell heterogeneity was deconvolved using EpiDISH v2.2.2[5]. Associations between nephritis and differential proportions of each reference cell methylome were tested using a Mann Whitney test.

Results: Participant demographics by cohort (USA=6, Nigeria=8) and clinical features are shown in Table 1. In the NYU cohort (and HC), 3 participants were Hispanic, 2 were Asian, and 3 were AA. LN was present in 50% and 62% of the NYU and Nigerian cohorts respectively. At least 100ng of DNA was extracted from 13/16 samples. Fresh, frozen, and shipped-frozen samples produced similar quality DNA; beta distributions and probe intensities were sufficient for CpG calling. PCA analysis of the top 1000 differentially methylated CpG sites revealed clusters by ancestry. Cell type deconvolution revealed that bladder, neutrophils, kidney epithelial, monocytes, CD4 T cells, CD8T Cells, erythrocyte progenitors, B cells, and NK cells were among the most highly represented. A dendrogram of cell type reference fractions produced two major clusters (C1 and C2) which differentiated LN from non-nephritis with 6/7 in C1 and 2/7 in C2 having LN (OR: 12.5, p=0.06; Figure 1). In C2, one LN participant was in complete remission, and the other had predominantly proteinuric disease without active sediment. LN samples were characterized by higher relative fractions of neutrophils and monocytes, and lower fractions of CD4T cells and NK cells compared to non-nephritis samples (Figure 2).



Stacked bar chart showing estimated urinary sediment cell proportion by participant donor. The cohort is indicated along the X axis: Ng=Nigeria cohort; NYU= USA cohort. The label color indicates the presence or absence of renal disorder with green labels indicating non-nephritis and red labels indicating nephritis participants.

Conclusion: These preliminary data support the feasibility of bulk urine sediment as an epigenetic biomarker of LN, and further analysis looking at pathways and genes within cell proportions associated with LN in larger studies.

Values are expressed as N (%) for categorical variables and mean± standard deviation (SD) for continuous variables. Categorical variables compared using Fischer's exact test; continuous variables compared using the two-sample T-test or Mann Whitney U Test.

Disclosure: A. Blazer, Glaxo Smith Kline, 1, 2, Novartis, 1; **O. Ayanlowo**, None; **W. Liao**, None; **D. Dey**, None; **J. Divers**, None; **U. Ima-Edomwonyin**, None; **H. Olaosebikan**, None; **C. Lanata**, None; **G. Nadkarni**, Astrazeneca, 2, Reata, 2, BioVie, 2; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **P. Izmirly**, Momenta/Janssen, 1; **T. Niewold**, None.

Abstract Number: 0351

Gene Signature Fingerprints Divide SLE Patients in Subgroups with Similar Biological Disease Profiles: A Multicenter Longitudinal Study

Javad Wahadat[1], Dieneke Schonenberg-Meinema[2], Cornelia van Helden-Meeuwsen[1], Sander van Tilburg[1], Noortje Groot[3], Ellen Schatorjé[4], Esther Hoppenreijs[4], Petra Hissink Muller[5], Danielle Brinkman[6], Denis Dvorak[7], Marleen Verkaaik[3], Katerina Bouchalova[8], Merlijn van den Berg[2], Sylvia Kamphuis[9] and Marjan Versnel[1], [1]Erasmus University Medical Center, Rotterdam, Netherlands, [2]Emma Children's Hospital, Amsterdam University Medical Center, Amsterdam, Netherlands, [3]Sophia Children's Hospital, Erasmus University Medical Center, Rotterdam, Netherlands, [4]Amalia Children's Hospital, Nijmegen, Netherlands, [5]Willem Alexander Children's Hospital, Leiden University Medical Center, Leiden, Netherlands, [6]Willem Alexander Children's Hospital, Leiden University Medical Center, Leiderdorp, Netherlands, [7]Faculty of Medicine and Dentistry, Palacky University Olomouc and University Hospital, Olomouc, Czech Republic, [8]Department of Pediatrics, Faculty of Medicine and Dentistry, Palacky University and University Hospital, Olomouc, Czech Republic, [9]Sophia Children's Hospital, Erasmus University Medical Center, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Clinical phenotyping and predicting treatment responses in Systemic Lupus Erythematosus (SLE) patients is challenging. Extensive blood transcriptional profiling has identified various gene modules that seem promising for stratification of SLE patients. This study was undertaken to translate transcriptomic data into gene signatures suitable for introduction into clinical practice and to associate these signatures with disease activity.

Methods: RT-PCR of multiple genes from the Interferon M1.2, Interferon M5.12, neutrophil (NPh)- and plasma cell (PLC) modules followed by a principle component analysis was used to identify indicator genes per gene signature. Gene signatures were measured in longitudinal samples from two childhood onset SLE cohorts (n=101 and n=34, respectively) and associated with clinical features. Disease activity was measured using SELENA-SLEDAI. Cluster analysis subdivided patients into three fingerprint groups termed 1) all-signatures-low, 2) only IFN high (M1.2 and/or M5.12) and 3) high NPh and/or PLC.

Results: All gene signatures were significantly associated with disease activity in cross-sectionally collected samples. The PLC signature showed the highest association with disease activity. Also, in longitudinally collected samples, the PLC signature was associated with disease activity and showed a decrease over time. When patients were divided into fingerprints, the highest disease activity was observed in the high NPh and/or PLC group. The lowest disease activity was observed in the all-signatures-low group. The same distribution could be reproduced in samples from an independent SLE cohort.

Conclusion: Gene signatures are associated with disease activity and can be suitable tools to sub-classify SLE patients into groups with similar pathogenically activated immunological pathways.

Disclosure: J. Wahadat, None; **D. Schonenberg-Meinema**, None; **C. van Helden-Meeuwsen**, None; **S. van Tilburg**, None; **N. Groot**, None; **E. Schatorjé**, None; **E. Hoppenreijs**, None; **P. Hissink Muller**, None; **D. Brinkman**, None; **D. Dvorak**, None; **M. Verkaaik**, None; **K. Bouchalova**, None; **M. van den Berg**, None; **S. Kamphuis**, GlaxoSmithKline, 7, Aurinia, 2; **M. Versnel**, None.

Abstract Number: 0352

Native American and African American Rheumatic Disease Patients Exhibit Accelerated Biological Aging Compared to European Americans

Joseph Kheir, Carla Guthridge, Nicolas Dominguez, Wade DeJager, Sarah Cooper, Joel Guthridge and Judith James, Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The universal process of aging is associated with increased risk of disease and death as a result of changing physiologic and molecular processes. In autoimmune patients, the process of aging can be exac-

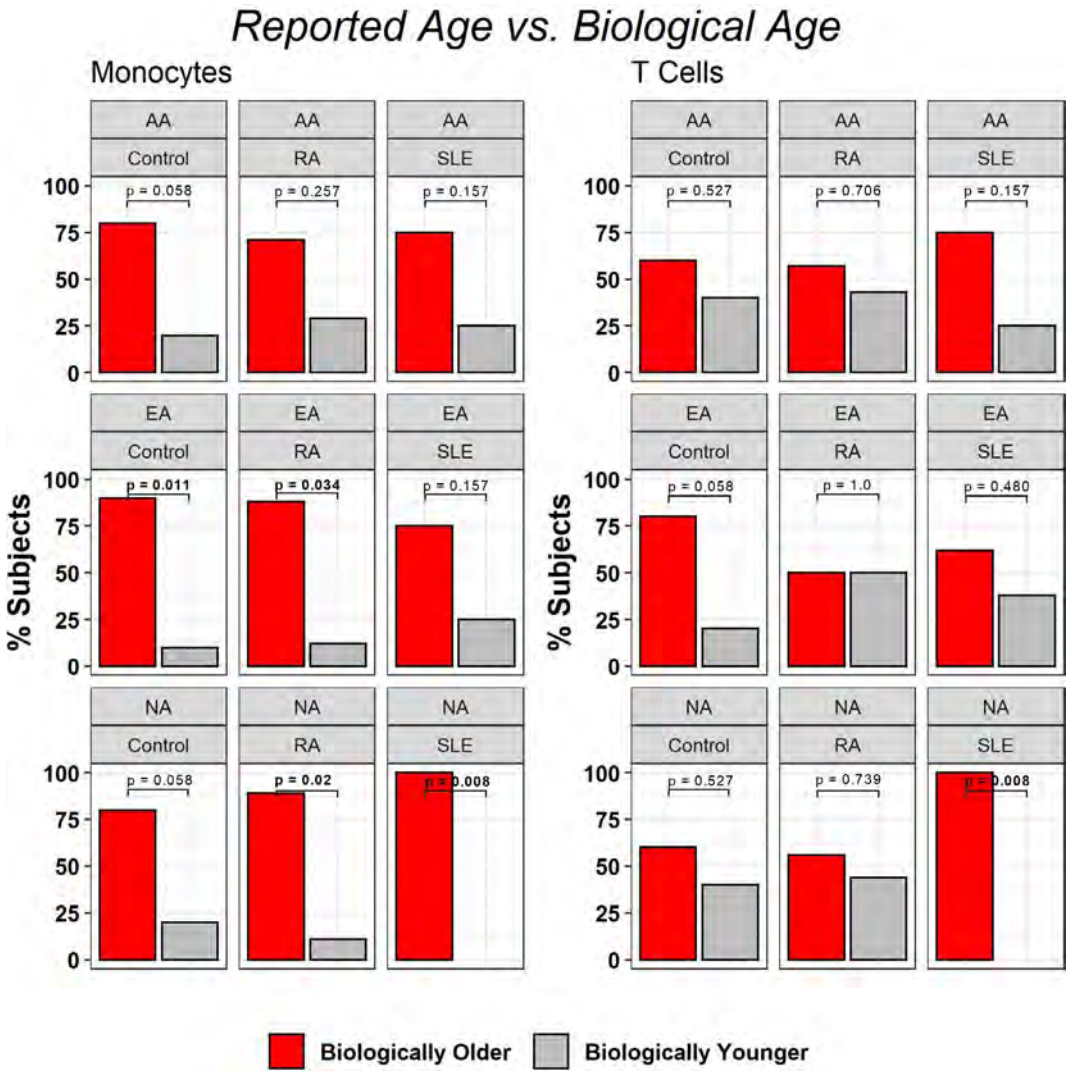


Figure 1. Biologically older versus younger patients by DNA methylation age.

erbated by chronic low-grade inflammation and the accumulation of biologic damage. We have previously demonstrated that Native American rheumatic disease patients present unique clinical and serological phenotypes with regards to systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). Because of such unique presentations of autoimmune disease, we hypothesize that Native American RA and SLE patients will exhibit an older biological age compared to chronological age relative to other racial groups.

Methods: Age matched (+/- 8 years) SLE, RA and control patients were selected across three racial groups, Native American (NA, n = 26), African American (AA, n = 25) and European American (EA, n = 26). T cells, B cells and Monocytes were isolated from PBMCs and DNA extracted. DNA was used for whole methylome analysis using the Illumina Infinium Human MethylationEpic BeadChip microarray. DNAm age, an indicator of biological age, was calculated using the Grimage algorithm leveraging differences in methylation at key CpG sites. Telomere length and mitochondrial DNA copy number were assayed using the absolute human telomere length and mitochondrial DNA copy number dual quantification qPCR (AHDQ) assay from ScienCell Research Laboratories.

Results: All NA SLE patients (n = 7) exhibited a biologically older age for T cells and monocytes compared to reported age (p = 0.008). Although not significant, a similar trend was observer for AA (75%, n = 6) SLE patients. EA SLE patients had similar biologic and stated ages. 89% of NA RA patients (n = 8, p = 0.02) exhibited a biologically older age in monocytes but not in T cells (p = 0.739). Similarly, 88% of EA RA patients (n = 7, p = 0.034) exhibited a biologically

older age in monocytes but not in T cells (p = 1.0) relative to reported age. AA RA patients had similar biologic and stated ages. The difference in biological age and reported age for NA SLE patients ranged from 1.2 years to 13 years with an average age difference of 7.1 years for monocytes and 3.5 years to 10.5 years with an average difference of 7.2 years for T cells. Interestingly, the age difference in biologically older NA RA patients ranged from 0.7 to 7.2 with an average of 3.7 years and 5.6 to 15 with an average of 7.9 years for monocytes and T Cells respectively. No statistical differences were observed in telomere length or mitochondrial DNA copy number.

Conclusion: Aging and the accumulation of low-grade chronic inflammation can lead to an increased susceptibility to disease and death. Our study demonstrated that 100% of Native American SLE patients in our cohort were biologically older than their reported age. This stark difference between biological and reported age coupled with unique clinical and laboratory phenotypes underscores the importance of further multi-omic investigation of Native American rheumatic diseases in order to elucidate causal biological pathways.

Disclosure: J. Kheir, None; **C. Guthridge**, None; **N. Dominguez**, None; **W. DeJager**, None; **S. Cooper**, None; **J. Guthridge**, None; **J. James**, Progentec Diagnostics, Inc., 2.

Abstract Number: 0353

Soluble Urine ALCAM Reflects Renal Disease Activity in Lupus Nephritis

Dalena Chu[1], Noa Schwartz[2], Jeanette Ampudia[1], Joel Guthridge[3], Judith James[3], Jill Buyon[4], Stephen Connelly[1], Maple Fung[5], Cherie Ng[1], Chandra Mohan[6] and Chaim Putterman[7], [1]Equillium, Inc., La Jolla, CA, [2]Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK, [4]NYU School of Medicine, New York, NY, [5]Equillium, Inc., San Diego, CA, [6]University of Houston, Houston, TX, [7]Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is a leading cause of morbidity and mortality in systemic lupus erythematosus (SLE) patients. While LN pathogenesis has yet to be fully elucidated, T cells have been strongly implicated in mechanisms of disease. CD6 is a co-stimulatory receptor on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen presenting cells and epithelial and endothelial tissues. The CD6-ALCAM pathway plays an integral role in modulating T cell activation and trafficking and is central to immune-mediated inflammation. Previously, we reported that soluble urine ALCAM is a potential biomarker of disease in LN. Here, we evaluated the correlation of serum and urine ALCAM and CD6 with disease activity over time.

Methods: Patient samples were acquired through the Accelerating Medicines Partnership (AMP), a public-private partnership to accelerate development of therapeutics for diseases such as LN. Serum and urine samples were obtained from patients with biopsy proven LN (n=345) and living kidney donor controls (n=68). Follow-up longitudinal sampling (3, 6, and 12 months) was available for 143 LN patients. ALCAM levels were quantified by ELISA, while CD6 levels were quantified by an electrochemiluminescent assay. Levels were analyzed cross-sectionally (first visit) and longitudinally against disease measures that included proteinuria, SLEDAI, the renal components of the SLEDAI score (R-SLEDAI), ISN-RPS histological class of the lesion, serological parameters, and patient characteristics.

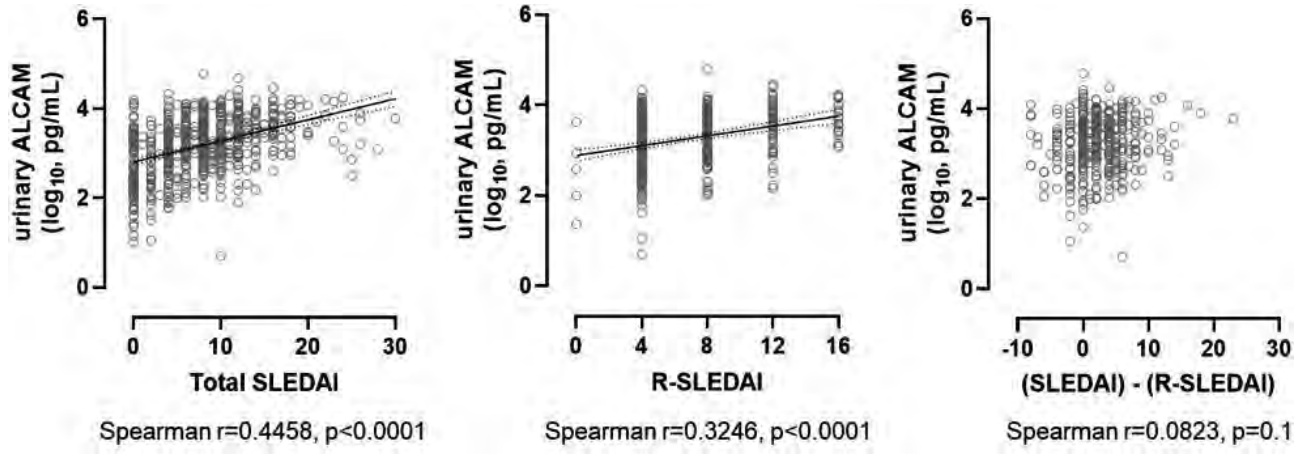

Figure 1. Urinary ALCAM correlates with renal but not non-renal SLEDAI scores. Correlation of urinary ALCAM with SLEDAI (left panel), R-SLEDAI (middle panel), and the non-renal portion of SLEDAI (calculated by subtracting R-SLEDAI from the total SLEDAI; right panel).

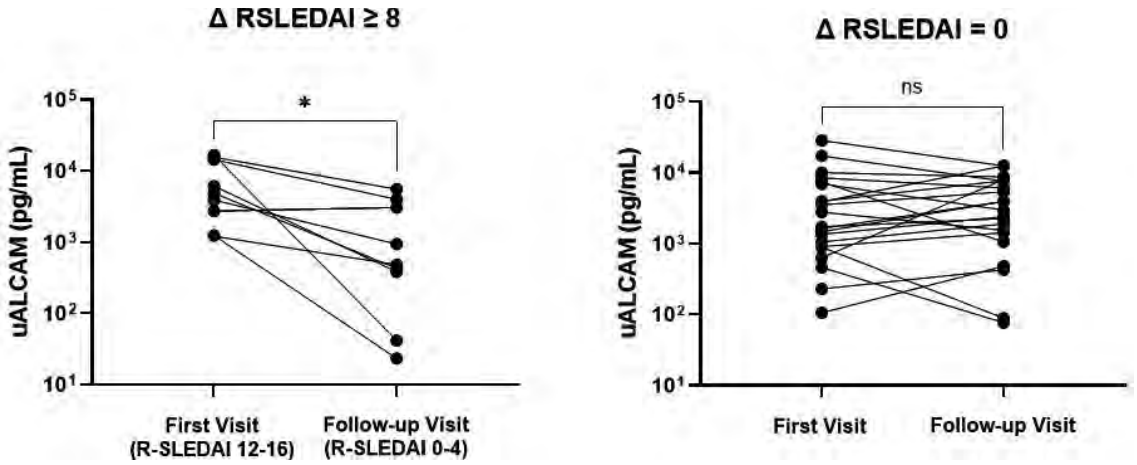

Figure 2. Urinary ALCAM decreases with decreased R-SLEDAI score over time. (Left panel) Urinary ALCAM levels in patients (n=10) with a decrease in R-SLEDAI ≥ 8 over a 6-12 month period were compared at the two timepoints. ALCAM levels decreased at the subsequent visit consistent with change in R-SLEDAI. No patients were available to analyze with an increase in R-SLEDAI. (Right panel) In comparison, subjects with no change in R-SLEDAI over the 12 months did not exhibit significant decreases in urinary ALCAM. Paired t-test, *p<0.05.

Results: Consistent with our previous findings, cross-sectional analysis showed that urinary ALCAM was significantly elevated in LN patients (mean 4333.5 pg/mL, 95% CI [3614.0, 5053.0]) compared to control subjects (mean 214.4 pg/mL, 95% CI [152.9, 276.0]) (*p< 0.001*), but that there were no differences in serum ALCAM levels. Urinary ALCAM levels significantly correlated with SLEDAI and R-SLEDAI scores (but did not correlate to the non-renal portion of SLEDAI (SLEDAI – R-SLEDAI) (Figure 1), suggesting that ALCAM level is associated with the renal activity. This was supported by near-significant correlations with C3 (*p=0.07*) and C4 levels (*p=0.05*). Serum and urine levels of CD6 were similar between cases and control subjects and did not change with disease activity, suggesting that the differences observed in urinary ALCAM levels are not due to hemodynamic changes or non-specific loss of glomerular permeability. In patients followed with longitudinal sampling, urinary ALCAM reflected changes in SLEDAI and R-SLEDAI. Furthermore, in preliminary analysis of a subset of patients who exhibited significant changes in R-SLEDAI across visits, intra-patient comparison of the respective timepoints reflected concomitant significant changes in urinary ALCAM levels (Figure 2).

Conclusion: Here, we expand upon previous studies and provide additional support in a large multi-center cohort, by showing that urinary ALCAM levels are elevated in SLE patients with active LN and decline with clinical improvement. Studies in progress are evaluating the implications of these findings in predicting therapeutic responses in LN, as well as longer term disease outcomes and prognosis.

Disclosure: D. Chu, Equillium, Inc., 3, 10, 11; **N. Schwartz**, None; **J. Ampudia**, None; **J. Guthridge**, None; **J. James**, Progentec Diagnostics, Inc., 2; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **S. Connelly**, None; **M. Fung**, Equillium Inc, 3, Arena Pharmaceuticals, 3; **C. Ng**, Equillium, Inc, 3, 11; **C. Mohan**, None; **C. Putterman**, equllium, 2, 5, Progentec, 2, Kidneycure, 2.

Abstract Number: 0354

A Cross-Sectional Study of Rheumatoid Arthritis Diagnoses in Patients with Systemic Lupus Erythematosus

Kathryn Starzyk[1], Gary Curhan[2] and Julia Brault[2], [1]OM1, Inc, Boston, MA, [2]OM1, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Features of autoimmune conditions may coexist in individual patients, which may represent an overlapping single disease with features of both (i.e., 'rhupus'), or the presence of two distinct diseases. Rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) share some genetic etiologies and distinguishing between lupus arthropathy and RA features poses clinical challenges. Given the potential for drug-induced or exacerbation of SLE with some of the available biologic treatment options, understanding the benefit-risk scenarios in the context of real-world phenotypes is important.

Methods: The OM1 SLE Registry (OM1, Inc; Boston, MA) follows more than 46,900 SLE patients in the U.S. managed by rheumatologists longitudinally with deep clinical data, including laboratory, patient-reported and disease activity information, and linked administrative claims starting from 2013. Index date was set by the first registry encounter with an SLE diagnosis code and ≥18 months of baseline available. Potential RA comorbidity was defined as at least 2 outpatient RA diagnosis codes ≥365 days apart or inpatient RA codes. Other comorbidities were defined by the pres-

Table 1. Patient Characteristics at Index

	SLE Registry Patients (N=44,186)	SLE Registry Patients with RA diagnosis codes (N=2,096)
Mean age (SD)	51 (15)	56 (14)
Female, n (%)	40,507 (92)	1,930 (92)
Race, n (%)		
White	24,542 (56)	1267 (60)
Black	8,318 (19)	349 (17)
Asian	858 (2)	26 (1)
Other	428 (1)	28 (1)
Unknown	10,040 (23)	426 (20)
Ethnicity, n (%)		
Hispanic	2,933 (7)	127 (6)
Non-Hispanic	28,212 (64)	1480 (71)
Unknown	13,041 (30)	489 (23)

Table 2. Other Autoimmune Comorbidities & Recent Treatment History

	All SLE Registry Patients (N=44,186)	SLE Registry Patients with RA (N=2,096)
Other comorbid autoimmune conditions, n (%)		
Sjögrens	9,355 (21)	560 (27)
Autoimmune thyroiditis	1,910 (4)	96 (5)
Scleroderma	1,578 (4)	106 (5)
Dermatopolymyositis	843 (2)	40 (2)
Other comorbidities		
Hypertension	24,517 (55)	1,402 (67)
Obesity	17,508 (40)	917 (44)
Osteoporosis	9,078 (21)	744 (35)
T2DM	8,287 (19)	563 (27)
Cardiac arrhythmia	6,142 (14)	376 (18)
Recent treatment history (past 18 months), n (%)		
Systemic corticosteroids	22,158 (50)	1,377 (66)
Hydroxychloroquine	18,396 (42)	837 (40)
Methotrexate	2,885 (7)	460 (22)
Mycophenolate mofetil	2,567 (6)	86 (4)
Azathioprine	2,327 (5)	132 (6)
TNF-alpha inhibitors	1,194 (3)	450 (21)
Belimumab	1,203 (3)	45 (2)
Leflunomide	905 (2)	205 (10)
Rituximab	481 (1)	168 (8)
Sulfasalazine	447 (1)	75 (4)
Abatacept	342 (1)	159 (8)
JAK inhibitors	171 (<1)	79 (4)
Cyclophosphamide	124 (<1)	5 (<1)
Patient-reported RAPID3 (Routine Assessment of Patient Index Data 3, range 0-10)*		
Result available, n (%)	16,524 (37)	1,012 (48)
Mean score closest to index (SD)	4.0 (2.0)	4.0 (2.0)

ence of at least 2 outpatient diagnosis codes ≥30 days apart or one inpatient diagnosis code prior to index. Obesity was defined as BMI ≥30 kg/m2. Medications were identified by prescriptions, administrations and/or fills. RAPID3 (Routine Assessment of Patient Index Data 3) at index date was also explored.

Results: The study included 44,186 patients (92% female) from the OM1 SLE Registry, 2096 (4.7%) of whom met RA code criteria (Table 1). Over 46% of SLE-RA cohort patients had ≥1 RA diagnosis codes in at least 3 calendar years during follow-up. The SLE-RA cohort was older (56 versus 51 years), with a higher proportion of white and non-hispanic patients than the SLE patients overall. Mean patient-reported joint-related disease activity was moderate (mean RAPID-3 = 4) across all patients. Autoimmune (e.g., Sjögren's) and other comorbidities were more common in the SLE-RA cohort (Table 2). Recent treatment with systemic steroids, methotrexate, leflunomide and biologic DMARDs was more commonly seen in SLE-RA patients (Table 2).

Conclusion: RA diagnoses in patients within the SLE Registry was higher than expected based on the literature. Classification for this study was based upon clinical diagnosis in routine practice by a rheumatologist and ACR diagnostic criteria may or may not have been applied. Further research is needed to better understand the chronologic path of these conditions (or their features) and implications for treatment.

Disclosure: K. Starzyk, None; **G. Curhan**, None; **J. Brault**, None.

Abstract Number: 0355

Utilization of a Clinical Data Research Network to Assess Systemic Lupus International Collaborating Clinics Classification Criteria Attributes in Patients with Systemic Lupus Erythematosus

Noah Forrest[1], Kathryn Jackson[2], Al'ona Furmanchuk[2], Anika Ghosh[2], Jennifer Pacheco[2], Vesna Mitrovic[2], Abel Kho[2], Rosalind Ramsey-Goldman[2] and Theresa Walunas[2], [1]Feinberg School of Medicine, Chicago, [2]Northwestern University, Chicago, IL

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by a heterogenous clinical phenotype that may present differently over time and between patients, which can create challenges for identification and treatment of individuals being seen at multiple care centers. Clinical data research networks (CDRN) aim to pool electronic health records (EHR) to provide more complete clinical information for patients shared across care centers. We sought to determine whether algorithms to identify Systemic Lupus International Coordinating Clinics (SLICC) classification criteria attributes, using structured EHR data, could be applied to a CDRN to describe people with SLE.

Methods: The attribute identification frequency of SLICC criteria are represented in Table 1. We identified 6,488 persons ≥ 3 SLE diagnoses and 1,201,999 persons with no diagnosis codes for SLE. The following SLICC attributes were identified from each group and identified at the following rates (No diagnosis vs. ≥3 diagnoses): Oral Ulcers: 2.1% vs. 3.5%, Alopecia: 2.5% vs. 5%, Neurological: 18% vs. 23%, Arthritis: 2.5% vs. 6.8%, Serositis: 7.1% vs. 17%, Acute Cutaneous: 0.17% vs. 19%, Chronic Cutaneous: 0.1% vs. 18%, Renal: 10% vs. 29%, Thrombocytopenia: 6.3% vs. 14%, Leukopenia: 67% vs. 77%, Hemolytic Anemia: 1.4% vs. 4.8, Antinuclear Antibodies: 2.2% vs. 26%, Anti-dsDNA Antibodies: 1.6% vs. 42%, Anti-Sm Antibodies: 0.078% vs. 6%, Antiphospholipid Antibodies: 0.26 % vs. 7.1%, Low complement: 0.56% vs. 37%, Direct Coombs Test: 0.057% vs. 1.4%. The percent of patients satisfying the SLICC definition of SLE 0.81% among those without a SLE diagnosis and 43% among those with ≥3 SLE diagnoses.

Table 1. SLICC Classification Criteria Attribute Identification Rates

Criterion	All Patients N (%)	No SLE Diagnoses N (%)	≥ 3 SLE Diagnoses N (%)	P-Value No SLE vs. ≥ 3 Diagnoses
Total (N)	**1213130**	**1201999**	**6488**	
Oral Ulcers	26079 (2.1%)	25760 (2.1%)	227 (3.5%)	8.45E-14*
Alopecia	30092 (2.5%)	29598 (2.5%)	327 (5%)	4.03E-40*
Neurological	214984 (18%)	212624 (18%)	1462 (23%)	2.78E-24*
Arthritis	30693 (2.5%)	29949 (2.5%)	442 (6.8%)	1.82E-107*
Serositis	87479 (7.2%)	85870 (7.1%)	1133 (17%)	8.83E-225*
Acute Cutaneous Lupus	3644 (0.3%)	2062 (0.17%)	1256 (19%)	<2.23e-308*†
Chronic Cutaneous Lupus	2704 (0.22%)	1221 (0.1%)	1141 (18%)	<2.23e-308*
Renal Disease	127890 (11%)	125377 (10%)	1866 (29%)	<2.23e-308*
Thrombocytopenia	77681 (6.4%)	76313 (6.3%)	928 (14%)	1.02E-149*
Leukopenia	808840 (67%)	800966 (67%)	4989 (77%)	1.56E-68*
Hemolytic Anemia	17123 (1.4%)	16672 (1.4%)	314 (4.8%)	1.71E-121*
Anti-Nuclear Antibodies	28842 (2.4%)	26257 (2.2%)	1715 (26%)	<2.23e-308*
Anti-dsDNA Antibodies	22867 (1.9%)	19136 (1.6%)	2706 (42%)	<2.23e-308*
Anti-Smith Antibodies	1473 (0.12%)	936 (0.078%)	388 (6%)	<2.23e-308*
Anti-Phospholipid Antibodies	3774 (0.31%)	3139 (0.26%)	458 (7.1%)	<2.23e-308*
Direct Coombs Test	809 (0.067%)	691 (0.057%)	91 (1.4%)	<2.23e-308*
Low Complement	9696 (0.8%)	6707 (0.56%)	2401 (37%)	<2.23e-308*

* Significant with $\alpha = 0.05$; Bonferroni Corrected with n comparisons = 17

† Lower limit of reporting numeric class double in R software environment

Results: The attribute identification frequency of SLICC criteria are represented in Table 1. We identified 6,488 persons ≥ 3 SLE diagnoses and 1,201,999 persons with no diagnosis codes for SLE. The following SLICC attributes were identified from each group and identified at the following rates (No diagnosis vs. ≥3 diagnoses): Oral Ulcers: 2.1% vs. 3.5%, Alopecia: 2.5% vs. 5%, Neurological: 18% vs. 23%, Arthritis: 2.5% vs. 6.8%, Serositis: 7.1% vs. 17%, Acute Cutaneous: 0.17% vs. 19%, Chronic Cutaneous: 0.1% vs. 18%, Renal: 10% vs. 29%, Thrombocytopenia: 6.3% vs. 14%, Leukopenia: 67% vs. 77%, Hemolytic Anemia: 1.4% vs. 4.8, Antinuclear Antibodies: 2.2% vs. 26%, Anti-dsDNA Antibodies: 1.6% vs. 42%, Anti-Sm Antibodies: 0.078% vs. 6%, Antiphospholipid Antibodies: 0.26 % vs. 7.1%, Low complement: 0.56% vs. 37%, Direct Coombs Test: 0.057% vs. 1.4%. The number of patients satisfying the SLICC definition of "Definite SLE" was 7684 persons (0.64%) among those without a SLE diagnosis and 2487 persons (38%) among those with ≥3 SLE diagnoses.

Conclusion: The results demonstrate that we can identify all SLICC classification criteria attributes in the CAPriCORN data set. We observed an increased rate of attribute identification for all SLICC criteria and an increased rate of definite SLE classification via SLICC in patients with ≥3 SLE diagnoses when compared with patients without any SLE diagnoses, consistent with an expected higher occurrence rate for persons with SLE. This suggests that SLE presentation can be characterized in CDRN data.

Disclosure: N. Forrest, None; **K. Jackson**, None; **A. Furmanchuk**, None; **A. Ghosh**, None; **J. Pacheco**, None; **V. Mitrovic**, None; **A. Kho**, Datavant, 1; **R. Ramsey-Goldman**, None; **T. Walunas**, None.

Abstract Number: 0356

The Role of Neutrophils in the Clinical Severity of Lupus Nephritis Patients with Concurrent Skin Disease

Lais Osmani, Sicong Shan, Zoe Chafouleas, Jason Pettus and Sladjana Skopelja-Gardner, Dartmouth Hitchcock Medical Center, Lebanon, NH

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Diagnosis (0323–0356)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Skin disease affects >80% of lupus patients and has been linked to lupus nephritis (LN) flares. We recently found that skin inflammation caused by UV light can trigger both local and systemic immune responses, in the blood and the kidney. This inflammation also led to kidney injury, associated with increased expression of renal inflammatory and injury markers and proteinuria. The observed renal injury was mediated by neutrophils, which migrated from the inflamed skin to the kidneys, localizing predominantly to the tubulointerstitial areas. These data prompted the hypothesis that presence of concurrent skin disease in lupus patients leads to worse nephritis mediated by neutrophils.

Methods: Kidney biopsies from 43 LN patients (2005-2020, IRB# 02000844) were retrieved from the Dartmouth Hitchcock Medical Center tissue bank and grouped into: i) LN with concurrent skin rash (malar, subacute, or discoid n =15) and ii) LN without skin rash (EMR review and/or skin biopsy, n=6) at the time of LN diagnosis (class IV). Patients with inconclusive or incomplete skin findings were excluded. The study included only female patients. Clinical and laboratory data (absolute neutrophil (ANC) and lymphocyte (ALC) counts, serum creatinine, estimated glomerular filtration rate (GFR), autoantibody titers, and complement levels) were collected by retrospective chart review. Histologic and immunofluorescence data were extracted from kidney biopsy reports. Student's t-test was performed to detect statistically significant differences between patient groups.

Results: Presence of skin rash at the time of LN flare was indicative of more active disease, reflected by higher ANA and anti-dsDNA IgG titers, and low complement C3 and C4 levels. Of interest, LN patients with concurrent skin disease had higher absolute neutrophil counts ($p < 0.05$) and neutrophil-lymphocyte ratio ($p< 0.01$), but not lymphocyte absolute counts, compared to LN patients without a concurrent skin rash. High neutrophil counts in the presence of skin disease associated with lower glomerular filtration rate (GFR < 60; $p< 0.01$). This association was not seen in the absence of concurrent skin disease and rash alone did not predict GFR. Analysis of kidney immunofluorescence revealed that concurrent skin disease at the time of LN flare associated with greater IgA deposition. In particular, increased renal IgA levels associated with higher neutrophil but not lymphocyte counts ($p < 0.01$). This was specific to IgA as no associations with IgG or IgM deposition were detected.

Conclusion: Our study provides several novel findings that suggest neutrophils may be the pathogenic link between skin inflammation and lupus nephritis flares: i) higher neutrophil counts are found in the presence of a skin rash at the time of LN flare, ii) neutrophilia but not lymphocytosis in the presence of a skin rash associates with worse kidney function (low GFR), and iii) high neutrophil levels in the presence of skin rash associate with increased renal IgA deposition. The newly identified relationship between neutrophil levels and kidney IgA provides a novel model of IgA-driven activation of neutrophils leading to kidney injury initiated by skin inflammation.

Disclosure: L. Osmani, None; **S. Shan**, None; **Z. Chafouleas**, None; **J. Pettus**, None; **S. Skopelja-Gardner**, None.

Abstract Number: 0357

Identifying Predictors of Unemployment in Axial Spondyloarthropathy: Data from the Ankylosing Spondylitis Registry of Ireland

Sinead Maguire[1], Wilson Fiona[2], Phil Gallagher[3] and Finbar (Barry) O'Shea[1], [1]St James's Hospital, Dublin, Ireland, [2]Discipline of Physiotherapy, Trinity College Dublin, Dublin, Ireland, [3]St Vincent's Hospital, Dublin, Ireland

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthropathy (axSpA) is an inflammatory arthritis of the axial skeleton. Persistent disease activity can result in significant disability and affect ability to maintain employment. The Ankylosing

Table 1. Characteristics of the employed versus unemployed cohort in the ASRI

	Unemployed n (%)	Employed n (%)	*p value*
n	189 (21.6%)	687 (78.4%)	
Males	155 (82%)	489 (71.2%)	***0.01***
Females	34 (18%)	198 (28.8%)	
Age	45.66	45.95	*0.79*
Disease duration	18.9	19.6	*0.51*
Delay to diagnosis	7.39	8.14	*0.28*
Age at Symptom onset	26.76	26.37	*0.66*
Caucasian	177 (93.7%)	622 (90.5%)	*0.1*
HLA-B27 +	130 *of 145* (89.7%)	472 *of 480* (98.3%)	*0.98*
Radiographic sacroiliitis	154 (81.5%)	529 (77%)	*0.41*
MRI sacroiliitis	72 (38.1%)	317 (46.1%)	*0.13*
Arthritis	60 (31.7%)	206 (30%)	*0.89*
Enthesitis	41 (21.7%)	111 (16.2%)	*0.15*
Dactylitis	13 (6.9%)	42 (6.1%)	*0.49*
Psoriasis	32 (16.9%)	112 (16.3%)	*0.87*
Uveitis	64 (33.9%)	233 (33.9%)	*0.29*
Colitis	12 (6.3%)	79 (11.5%)	*0.07*
NSAIDs	98 (51.9%)	349 (50.8%)	*0.59*
DMARDs	45 (23.8%)	153 (22.3%)	*0.46*
Biologic	141 (74.6%)	453 (65.9%)	*0.07*

Abbreviations: HLA-B27 -human leukocyte antigen B27; MRI -magnetic resonance imaging; NSAIDs -non-steroidal anti-inflammatory medications; DMARDs -disease modifying anti-rheumatic drugs

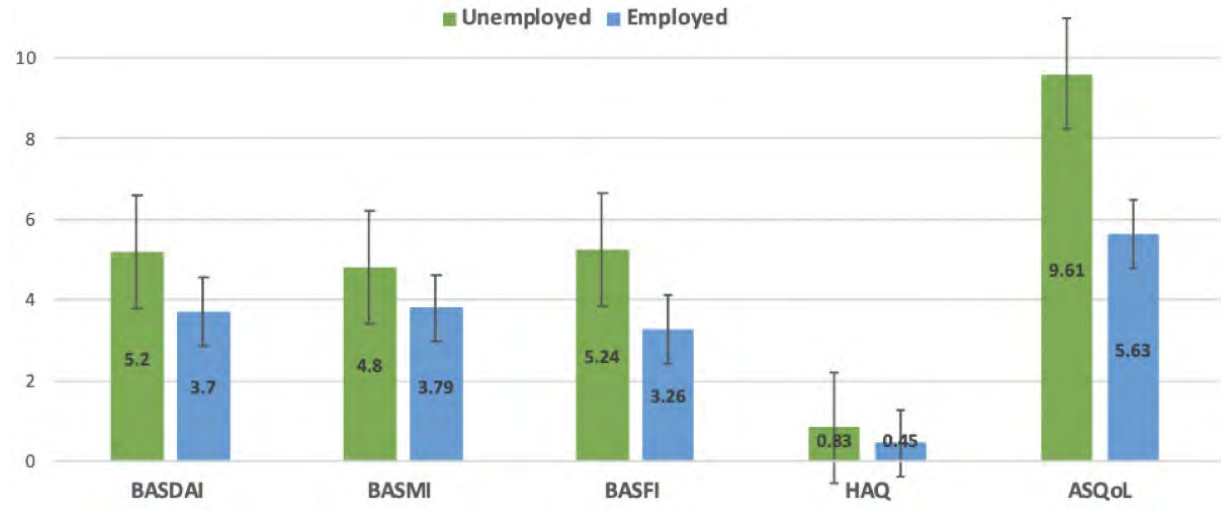

Figure 1. Comparison of mean outcomes on the basis of employment, all differences were statistically significant at the p<0.01 level.

Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data on axSpA in Ireland. The aim of this study was to examine the prevalence of unemployment in axSpA and quantify the impact on burden of disease, level of function and quality of life.

Methods: For the purposes of this analysis data was extracted from the ASRI on participants with employment data recorded. Patients were analysed on the basis of employment and categorised as employed or unemployed. A two tailed t-test was used to test for statistical significance in mean continuous variables between groups. For categorical variables, an independent chi-squared test of independence determined statistical significance. An alpha level of p< 0.05 was deemed significant. IBM SPSS v.26 was used for data and statistical analysis.

Results: Employment status was available for 876 patients enrolled in the ASRI. Overall 21.6% (189) of the population was unemployed, which is considerably higher than national averages of 6.2-13.1% during the same period. In addition, 24% (213) reported axSpA as a limitation in work ability. Unemployed patients reported significantly worse BASDAI (5.2 vs 3.7, p< 0.01), BASMI (4.8 vs 3.79, p< 0.01), BASFI (5.24 vs 3.26, p< 0.01), HAQ (0.83 vs 0.45, p< 0.01), and ASQoL scores (9.61 vs 5.63, p< 0.01) compared to employed axSpA patients(figure 1). A higher proportion of males were unemployed as compared to females (table 1). No significant differences were noted in pattern of disease, medication usage or baseline demographics. Male sex (OR 2.31, 95% CI 1.32-4.04), worse BASMI (OR 1.19,

Table 2. Prediction model for risk of unemployment in AxSpA

	Odds Ratio	95% CI	*p value*
Gender	2.31	1.32 - 4.04	**<0.01**
Age	0.98	0.95 - 0.99	**0.02**
Delay to diagnosis	0.99	0.96 - 1.02	0.51
Disease duration	1.00	0.98 - 1.02	0.81
BASDAI	1.09	0.96 - 1.23	0.19
BASMI	1.19	1.05 - 1.35	**0.01**
BASFI	1.02	0.93 - 1.13	0.68
HAQ	1.48	0.84 - 2.16	0.18
ASQoL	1.07	1.01 - 1.14	**0.02**

95% CI 1.05-1.35) and worse ASQoL scores (OR 1.07, 95% CI 1.01-1.14) were found to be significant predictors of unemployment (table 2).

Conclusion: Prevalence of unemployment in axSpA is notably higher than nationally reported averages from the general population. Despite a high uptake of biologic therapy in this group, these patients have higher levels of disease activity, poorer levels of function and worse quality of life compared to employed axSpA patients. Predictors of unemployment were male sex, worse spinal mobility and poorer quality of life. In males, higher average BASMI scores were a significant contributing factor to the higher rates of unemployment observed. Prompt intervention for patients with worsening outcome measures, in particular spinal restriction, would provide an opportunity for occupational supports and prevent progression to unemployment.

Disclosure: S. Maguire, Gilead, 5; **W. Fiona**, None; **P. Gallagher**, None; **F. O'Shea**, None.

Abstract Number: 0358

Work Participation in Patients with Axial Spondyloarthritis in Germany: Results from a Multicenter, Observational Survey

Uta Kiltz[1], Kirsten Hoeper[2], Ludwig Hammel[3], Sebastian Lieb[4], Andreas Haehle[4] and Dirk Meyer-Olson[5], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany, [2]Regionales Kooperatives Rheumazentrum Niedersachsen e. V.; Medizinische Hochschule Hannover, Department of Rheumatology and Immunology, Hannover, Germany,, Hannover, Germany, [3]Deutsche Vereinigung Morbus Bechterew e.V.,, Schweinfurt, Germany, [4]Novartis Pharma GmbH, Immunology, Hepatology and Dermatology, Nürnberg, Germany, [5]m&i Fachklinik Bad Pyrmont, Hannover, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory condition often associated with impaired working participation[1] not only translating to devastating outcomes for patients (pts) but also increased economic and social burden due to a significant amount of indirect costs. Data on the different work participation domains in axSpA pts with access to biologic therapies are limited. The objective of this survey is to characterise the different domains of work participation [presenteeism, absenteeism, sick leave, unemployment, disability pensions] in axSpA pts and their associations with demographic and clinical confounders.

Methods: Pts with confirmed clinical diagnosis of axSpA were enrolled in a multicenter, observational ATTENTUS survey conducted across Germany (Nov-2019 to Jul-2020). To ensure high data quality, inclusion criteria was verified by external monitoring, followed by evaluation of the domains of impaired work participation, including absenteeism and presenteeism (WPAI). Demographics, clinical parameters and patient related outcomes (PROs) were collected via tablet This analysis included all working patients ≥18 years.; and excluded students and retired pts. Pts without absenteeism (value=0) and presenteeism ≤20% were defined as no impairment at work.

Results: A total of 787 axSpA pts were enrolled in the survey. Seven students, 68 retired pts and 17 pts not fulfilling the inclusion criteria were excluded from this analysis, leaving 695 pts with complete data sets. Baseline data are outlined in **Table**. 50 pts received disability pensions, 29 pts received unemployment benefits, 590 (84.9%) pts reported

Table 1. Descriptive characteristics of the study population				
Mean (SD), if not otherwise specified	Impaired WP(n=453)	Full WP(n=242)	p-value	Total (n=695)
Age (yrs)	46.7 (11.1)	42.8 (10.1)	**<0.001**	45.3 (10.9)
BMI	28.5 (14.0)	27.0 (6.8)	0.146	28.0 (12.0)
Male, n(%)	246 (54)	177 (73)	**<0.001**	423 (61)
Disease duration (yrs)	12.7 (11.3)	12.4 (10.2)	0.813	12.6 (11.0)
Level of education attained, n(%), university degree	104 (23.0)	82 (33.9)	**0.001**	186 (26.8)
In a committed relation, n(%)	310 (68.4)	159 (65.7)	0.464	469 (67.5)
ASAS-HI	8.0 (3.3)	3.7 (3.0)	**<0.001**	6.5 (3.8)
BASDAI	4.8 (1.9)	2.1 (1.6)	**<0.001**	3.9 (2.2)
BASDAI > 4, n(%)	286 (63.1)	28 (11.6)	**<0.001**	314 (45.2)
BASDAI ≥ 4, n(%)	296 (65.3)	28 (11.6)	**<0.001**	324 (46.6)
Fatigue [BASDAI #1]	5.8 (2.1)	2.8 (2.1)	**<0.001**	4.7 (2.5)
Duration morning stiffness [BASDAI #6]	3.5 (2.4)	1.6 (1.8)	**<0.001**	2.8 (2.4)
BASFI	4.2 (2.3)	1.5 (1.5)	**<0.001**	3.3 (2.4)
Biologic treatment, n(%)	230 (50.8)	134 (55.4)	0.390	364 (52.4)
Full time employment, n(%)	256 (56.5)	202 (83.5)	**<0.001**	458 (65.9)
Absenteeism	17.9 (32.1)	0	-	10.6 (26.2)
Presenteeism	48.6 (21.00)	9.8 (8.3)	-	32.6 (25.6)
Overall work impairment score	55.5 (24.0)	9.8 (8.3)	**<0.001**	37.2 (29.6)
Activity impairment	53.9 (21.2)	17.6 (17.1)	**<0.001**	41.2 (26.4)
ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, basal metabolic index; n, number of pts; SD, standard deviation; WP, work productivity; years, yrs				

paid work [part-time: n=132 (22.4%); full-time: n=458 (65.9%)], with 242 (41.0%) pts having no impairments at work. 379 (64.2%) employed pts took sick leave within the previous 12 months (mo) (< 3 mo: n=351; 3–6 mo: n=17; >6 mo: n=11). Absenteeism and presenteeism occurred in 140 (23.7%) and 496 (84.1%) pts, respectively. Pts without impairments were mostly of young age, male sex, well-educated, with low disease activity, less fatigue and shorter duration of morning stiffness, and preserved global and physical functioning. No apparent differences between pts with and without impairment of work participation were observed in terms of biologic treatment, disease duration and BMI.

Conclusion: There was a substantial impact on work participation for axSpA pts. Despite numerous available therapeutic options physical function was still impaired and lead to high rates of impairment of work participation. Pts with impaired work participation compared to pts with no impairment, reported increased fatigue, longer duration of morning stiffness, decreased functional capacity, female sex and a lower level of education.

References:

1. Ramoda R et al. *Arthritis Res Ther*. 2016;78

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **K. Hoeper**, Abbvie, 2, 6, Chugai, 2, 6, Gilead, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Sandoz Hexal, 2, 6, Sanofi, 2, 6; **L. Hammel**, None; **S. Lieb**, Novartis, 3; **A. Haehle**, Novartis, 3; **D. Meyer-Olson**, Abbvie, 2, 6, Amgen, 2, 6, Berlin Chemie, 2, 6, Bristol Myers Squibb, 2, 6, Cellgene, 2, 6, Chugai, 2, 6, Fresenius Kabi, 2, 6, GSK, 2, 6, Jansen Cilag, 2, 6, Eli Lilly, 2, 6, Medac, 2, 6, Merck Sharp & Dome, 2, 6, Mylan, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sandoz Hexal, 2, 6, Sanofi, 2, 6, UCB, 2, 6.

Abstract Number: 0359

Patient Journey with Axial Spondyloarthritis: Critical Issues from the Patient Perspective. Results from the European Map of Axial Spondyloarthritis (EMAS)

Marco Garrido-Cumbrera[1], Denis Poddubnyy[2], Christine Bundy[3], Laura Christen[4], Raj Mahapatra[5], Souzi Makri[6], Carlos Jesús Delgado-Domínguez[7], Sergio Sanz-Gomez[7], Pedro Plazuelo-Ramos[8] and Victoria Navarro-Compán[9], [1]Health & Territory Research (HTR), University of Seville, Sevilla, Spain, [2]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [3]Cardiff University, Cardiff, Wales, United Kingdom, [4]Novartis Pharma AG, Basel, Switzerland, [5]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [6]Cyprus League Against Rheumatism (CYPLAR), Limassol, Cyprus, [7]Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain, [8]Spanish Federation of Spondyloarthritis Associations (CEADE), Madrid, Spain, [9]Rheumatology service, Hospital Universitario La Paz-IdiPaz, Madrid, Spain

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: The journey of axial spondyloarthritis (axSpA) for most patients is slow and arduous. The goal of this analysis is to assess the journey to diagnosis and further management in axSpA patients.

Methods: Data from 2,846 unselected patients from EMAS, generated through an online survey (2017-2018) across 13 European countries were analysed. Descriptive analysis of sociodemographic factors, insurance scheme, diagnostic journey and post diagnosis healthcare utilization was performed. The Mann-Whitey test was used to analyse possible differences between BASDAI and the number of visits to healthcare professionals and followup tests undertaken.

Results: The mean age was 43.9 years, 61.3% were female, 48.1% university educated, 67.9% married, 53.9% employed and 81.7% had public health insurance. Mean age at symptoms onset was 26.6 (11.1), while mean age at diagnosis was 33.7 (11.5) and mean diagnostic delay was 7.4 years. Over 50% had a diagnostic delay of >4 years. Prior to receiving a diagnosis, patients visited on average 2.6 specialists. The most commonly performed diagnostic

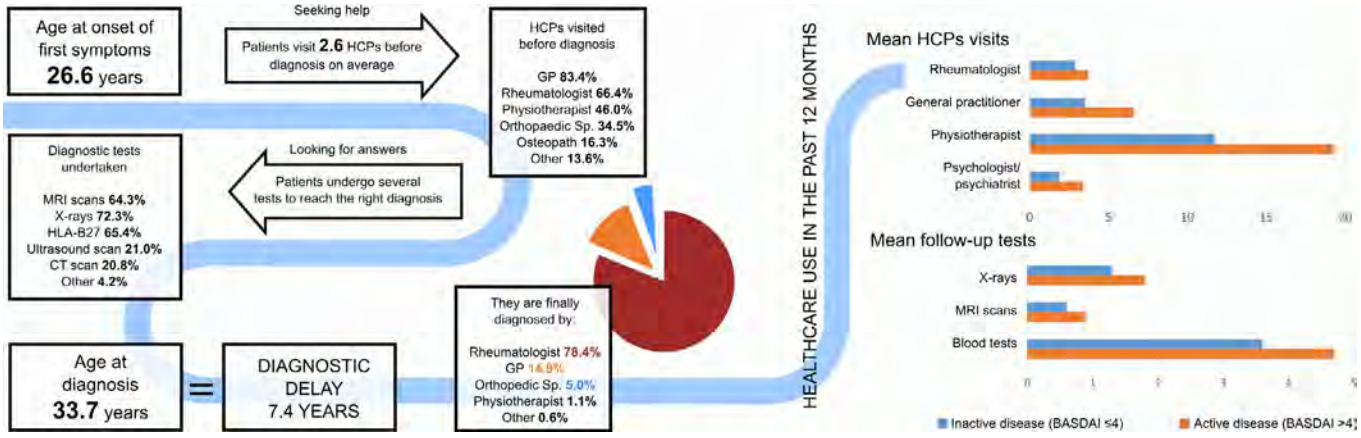

Figure 1. Diagnostic pathway of EMAS axSpA patients.

tests were x-rays (72.3%), HLA B27 tests (65.4%) and MRIs (64.3%). 78.4% were diagnosed by a rheumatologist while 14.9% received their diagnosis by a General Practitioner (GP). Patients who experienced a diagnostic delay of more than a year (n=2,208) undertook a considerable number of visits to specialists and medical tests in the year prior to participating in EMAS, which increased with disease activity. Patients with active disease (BASDAI >4) reported a higher number of visits to rheumatologists (3.7±3.5 vs 2.9±2.6), general practitioners (6.6±10.0 vs 3.5±4.1), physiotherapists (19.3±25.0 vs 11.7±17.0), and psychologists/psychiatrists (3.4±10.7 vs 1.9±7.7). Regarding follow-up tests, they also undertook more x-rays (1.8 ± 2.8 vs. 1.3 ± 1.9), MRI scans (0.9 ± 1.2 vs. 0.6 ± 1.1), and blood tests (4.7 ± 4.4 vs 3.6 ± 3.2) compared to patients with inactive disease (Figure 1). However, one in five patients visited the rheumatologist only once in the year prior to EMAS (21.1%).

Conclusion: Diagnostic delay continues to be a key challenge in the axSpA patient journey, with patients waiting an average of 7.4 years and visiting multiple doctors and undertaking a significant number of medical tests prior to diagnosis. Once diagnosed, disease management presents a further challenge, as patients with higher disease activity reported more healthcare professional visits as well as medical tests. Safeguarding health and controlling healthcare utilization requires effective disease management, greater education for non-specialists, rapid referral routes for diagnosis and collaborative care between specialists and nonspecialists.

Disclosure: M. Garrido-Cumbrera, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **C. Bundy**, Abbvie, 2, Celgene, 2, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2; **L. Christen**, Novartis, 3; **R. Mahapatra**, None; **S. Makri**, None; **C. Delgado-Domínguez**, None; **S. Sanz-Gomez**, None; **P. Plazuelo-Ramos**, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5.

Abstract Number: 0360

Factors Associated with Pain Intensity in Axial Spondyloarthritis. Results from the EuropeanMap of Axial Spondyloarthritis (EMAS)

Marco Garrido-Cumbrera[1], Victoria Navarro-Compán[2], Christine Bundy[3], Laura Christen[4], Raj Mahapatra[5], Souzi Makri[6], Carlos Jesús Delgado-Domínguez[7], José Correa-Fernández[7], Pedro Plazuelo-Ramos[8] and Denis Poddubnyy[9], [1]Health & Territory Research (HTR), University of Seville, Sevilla, Spain, [2]Rheumatology service, Hospital Universitario La Paz-IdiPaz, Madrid, Spain, [3]Cardiff University, Cardiff, Wales, United Kingdom, [4]Novartis Pharma AG, Basel, Switzerland, [5]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [6]Cyprus League Against Rheumatism (CYPLAR), Limassol, Cyprus, [7]Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain, [8]Spanish Federation of Spondyloarthritis Associations (CEADE), Madrid, Spain, [9]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Pain is a hallmark of axial spondyloarthritis (axSpA) and can significantly deteriorate patients' health status. This analysis aims to investigate factors associated with pain intensity in a large sample of European axSpA patients.

Methods: 2,846 unselected patients participated in EMAS, an online survey (2017-2018) across 13 European countries. Data from 2,636 participants who reported pain were analysed. Pain was measured by the mean of two BASDAI

Table 1. Regression analysis of the association of pain intensity (0-10 NRS) with demographic, socioeconomic and axSpA-related factors (N = 850)

	Univariable		Multivariable	
	B	95% CI	B	95% CI
Gender. Female[1]	0.604	**0.432, 0.775**	0.260	**0.003, 0.517**
Educational level. No University[2]	0.671	**0.504, 0.838**	0.376	**0.118,0.634**
Marital Status. Divorced/Separated[3]	0.495	**0.209, 0.780**	-0.044	-0.468, 0.380
Body Mass Index. Obese[4]	0.362	-0.097, 0.821	NA	NA
GHQ-12 (0-12)	0.182	**0.163, 0.201**	0.100	**0.064, 0.137**
Functional Limitation (0-54)	0.036	**0.030, 0.041**	0.009	-0.001, 0.018
Spinal Stiffness (3-12)	0.357	**0.326, 0.388**	0.288	**0.234, 0.342**
Diagnostic Delay, years	0.020	**0.010, 0.030**	-0.015	-0.032, 0.002
Work-Related Issues. Yes	1.338	**1.095, 1.582**	0.654	**0.338, 0.970**
Difficulty finding job due to axSpA. Yes	1.568	**1.362, 1.774**	0.476	**0.176, 0.776**
Work choice determinate by axSpA. Yes	0.808	**0.633, 0.983**	0.199	-0.069, 0.467
Physical activity. No	0.494	**0.263, 0.725**	-0.128	-0.497, 0.242
Anxiety diagnosis. Yes	0.935	**0.753, 1.117**	-0.047	-0.416, 0.321
Depression diagnosis. Yes	1.107	**0.919, 1.295**	0.115	-0.270, 0.500
Sleep disorder diagnosis. Yes	1.042	**0.871, 1.213**	-0.091	-0.392, 0.211

[1]Female vs Male; [2]No university studies (no schooling, primary and high school) vs University studies; [3]Divorced/separated vs single, married and widow; [4]Obese vs not obese (underweight, normal and overweight).

questions (range 0 “no pain” to 10 “most severe pain”): "How would you describe the overall level of AS neck, back or hip pain you have had?” and “How would you describe the overall level of pain/swelling in joints other than neck, back, hips you have had?”. Linear regression analysis was applied to identify associations between pain intensity and sociodemographic factors, patient-reported outcomes [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), mental health using the 12-item General Health Questionnaire GHQ-12 (0-12)], work life, physical activity and comorbidities (N= 850).

Results: The mean age of the sample was 44 years, 61.4% were female, 49.4% had a university degree and 67.7% were married. The average reported pain intensity was 5.3 (±2.2); 76.2% reported pain intensity ≥4, with the greatest intensity reported by women (5.5 vs 4.9, p< 0.001), those not university educated (5.6 vs 5.0, p< 0.001), separated or divorced compared to singles (5.8 vs 5.2, p=0.004), and not physically active (5.7 vs 5.2, p< 0.001). In addition, employed patients who experienced work-related issues reported greater pain (5.2 vs 3.9) as did those who experienced/ believed they would face difficulties finding work due to axSpA (5.9 vs 4.3), and those whose employment choice was determined by axSpA (5.7 vs 4.9; all p< 0.001). Moreover, associations with anxiety (5.9 vs 5.0), depression (6.1 vs 5.0) and sleep disorders (5.9 vs 4.9; all p< 0.001) were also found. The multiple linear regression model showed that those with higher pain intensity reported at least one work-related issue (B= 0.65), difficulties finding work due to axSpA (B= 0.48), not having attended university (B=0.38), greater spinal stiffness (B= 0.29), being female (B= 0.26) and poorer mental health (GHQ-12; B= 0.10; Table 1).

Conclusion: Pain was most strongly associated with working life impairment, as well as with spinal stiffness. Pain was also associated with suffering from depression, anxiety and sleep disorders. Understanding how pain affects individuals and shared-decision making between rheumatologists and patients are essential for long-term disease management and preserving quality of life of axSpA patients.

Disclosure: M. Garrido-Cumbrera, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5; **C. Bundy**, Abbvie, 2, Celgene, 2, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2; **L. Christen**, Novartis, 3; **R. Mahapatra**, None; **S. Makri**, None; **C. Delgado-Domínguez**, None; **J. Correa-Fernández**, None; **P. Plazuelo-Ramos**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6.

Abstract Number: 0361

Factors Associated with Engaging in Physical Activity in Axial Spondyloarthritis. Results from the European Map of Axial Spondyloarthritis (EMAS)

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Physical activity is an essential component in axial spondyloarthritis (axSpA) care, improving physical and mental wellbeing. This analysis aims to identify factors associated with engaging in physical activity among axSpA patients.

Methods: Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were analysed. Engaging in physical activity was assessed by the following item: "Do you do any physical or sporting activity?" for which participants could report at least 1 physical activity or that they did not do any physical activity. BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and mental health using General Health Questionnaire GHQ-12 (0-12) were assessed. Mann-Whitney and Pearson's $\chi 2$ tests were used to analyse

Table 1. Regression analysis. Dependent variable: physical activity (n= 2,424)

	Univariable logistic analysis		Multivariable logistic analysis	
Qualitative variables	**OR**	**p[7]**	**OR**	**p[7]**
Gender. Male[1]	1.478	**<0.001**	1.388	**0.018**
Educational level. University[2]	1.732	**<0.001**	1.535	**0.001**
Marital Status. Married[3]	1.732	**<0.001**	1.181	0.219
Patient organization. Member[4]	1.707	**<0.001**	1.910	**<0.001**
Body Mass Index. Not Obese[5]	1.692	**<0.001**	1.577	**0.003**
Employment status. Employed[6]	1.284	**0.013**	1.001	0.993
Quantitative variables	**B**	**p[8]**	**B**	**p[8]**
Age	0.011	**0.007**	0.017	**0.006**
BASDAI (0-10)	-0.149	**<0.001**	-0.039	0.351
GHQ-12 (0-12)	-0.064	**<0.001**	-0.042	**0.013**
Functional Limitation (0-54)	-0.005	0.090	0.002	0.606
Spinal Stiffness (3-12)	-0.105	**<0.001**	-0.110	**<0.001**
Proportion of life with axSpA (0-1)	1.041	**0.001**	0.694	0.083

[1]Male vs Female; [2]University vs no university (no schooling, primary, high school); [3]Married vs single, separated/divorced and widow;[4] Member vs not; [5]Not obese (underweight, normal and overweight) vs obese; [6]Employed vs not (unemployed, sick leave, early retirement/retirement, housework and student).[7]p-value for test H_0: OR = 1 [8]p-value for test H_0 B = 0.

relationships between engaging in physical activity and sociodemographic factors, patient-reported outcomes, employment, lifestyle and comorbidities. Univariable and multivariable binary logistic regression were used to analyse variables possibly explaining engagement in physical activity (N= 2,424).

Results: Mean age of the sample was 43.9±12.3 years, 61.3% were female, 48.1% had a university degree and 67.9% were married. 81.8% (n= 2,329) engaged in at least one kind of physical activity. Those physically active were typically male (85.3% vs 79.7% female, p< 0.001), university educated (86.0% vs 78.0%, p< 0.001), married (83.1% vs 79.2%, p=0.046), and members of a patient organisation (86.4% vs 78.9%, p< 0.001). 25.1% of obese patients (n=533) did not engage in physical exercise (v. 16.6%, p< 0.001). Those who did not engage in physical activity reported greater disease activity (6.0±1.9 vs 5.4±2.0 BASDAI, p< 0.001), functional limitation (21.6±15.0 vs 20.2±16.5, p=0.010), spinal stiffness (8.3±2.6 vs 7.6±2.5, p< 0.001), and poorer mental health (5.9±4.2 vs 4.8±4.1 GHQ-12, p< 0.001). Furthermore, 83.9% of those employed (n=1,457) were physically active, versus 73.7% of unemployed (n=205; p< 0.001). In the multivariable binary logistic regression, the qualitative variables associated with engaging in physical activity were belonging to a patient organisation (OR=1.91), not being obese (OR= 1.58), being university educated (OR= 1.54), and being male (OR= 1.39). The quantitative variables associated were lower spinal stiffness (B= -0.110), better mental health (B= -0.042), and one year age increase (B= 0.017; Table 1).

Conclusion: These results show that increasing age, being male, university educated, member of a patient organisation, not obese, having lower spinal stiffness, and better mental health increase the probability of engaging in physical activity. Physical activity is an important part of axSpA care and patient organizations play a critical role in enhancing access to and participation in physical activity.

Disclosure: M. Garrido-Cumbrera, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5; **C. Bundy**, Abbvie, 2, Celgene, 2, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2; **L. Christen**, Novartis, 3; **R. Mahapatra**, None; **S. Makri**, None; **C. Delgado-Domínguez**, None; **D. Gálvez-Ruiz**, None; **P. Plazuelo-Ramos**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6.

Abstract Number: 0362

Achievement of Stringent Thresholds of Disease Control Is Associated with Reduced Burden on Work and Household Productivity in Patients with Axial Spondyloarthritis

Martin Rudwaleit[1], Pedro Machado[2], Lianne Gensler[3], Vanessa Taieb[4], Natasha de Peyrecave[5], Bengt Hoepken[6] and Désirée van der Heijde[7], [1]University of Bielefeld, Klinikum Bielefeld, Bielefeld, Germany, [2]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [3]Department of Rheumatology, University of California San Francisco, San Francisco, CA, [4]UCB Pharma, Slough, United Kingdom, [5]UCB Pharma, Brussels, Belgium, [6]UCB Pharma, Monheim am Rhein, Germany, [7]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

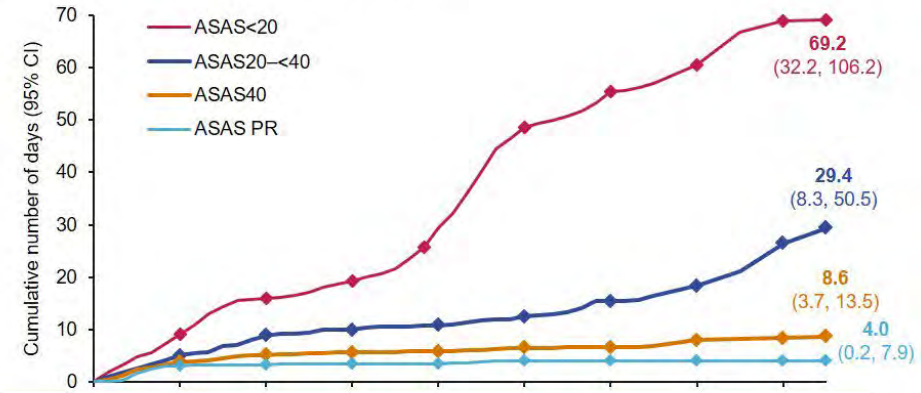
Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is associated with increased absence from work and reduced work productivity, which can impact employment status.[1] TNF inhibitors such as certolizumab pegol (CZP) have been shown to improve work productivity in patients (pts) with axSpA.[2,3] However, the association between the extent of clinical improvement and work/household productivity over long-term CZP treatment has not been evaluated. The objective of this study was to evaluate the association between the extent of improvement in clinical outcomes and burden on paid work and household productivity in pts with axSpA over 4 years' CZP treatment.

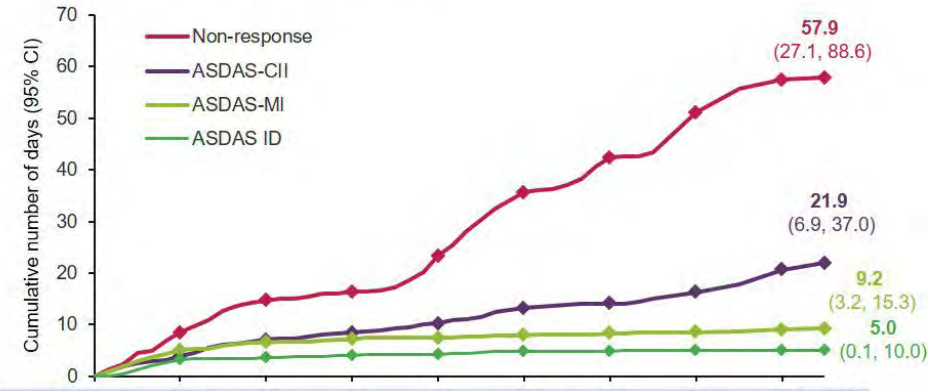
Figure 1. Paid work absenteeism by (A) ASAS response and (B) ASDAS response

A) Paid work absenteeism by ASAS response



Weighted n	Week	24	48	72	96	120	144	168	192	204
	ASAS<20	56	38	34	32	31	33	26	23	21
	ASAS20–<40	37	31	25	29	23	18	23	25	22
	ASAS40	111	124	116	109	111	108	106	98	92
	ASAS PR	66	64	63	63	61	64	59	53	52

B) Paid work absenteeism by ASDAS response

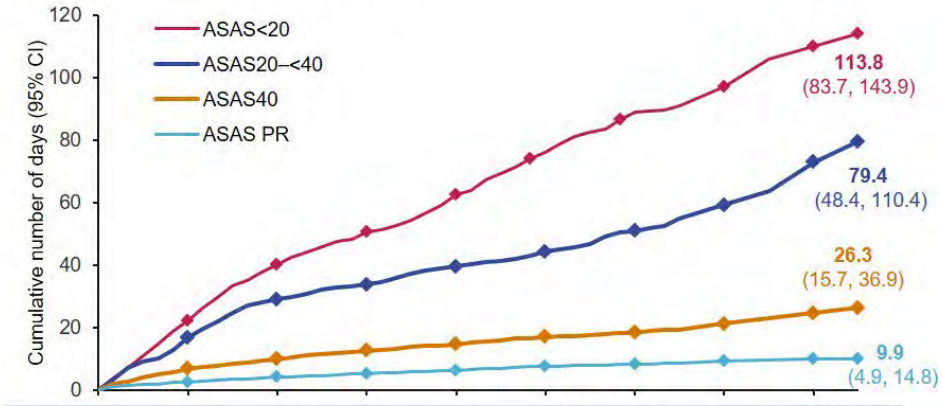


Weighted n	Week	24	48	72	96	120	144	168	192	204
	Non-response	58	45	39	42	34	33	32	27	25
	ASDAS-CII	57	50	44	38	43	47	41	47	47
	ASDAS-MI	92	101	97	95	92	83	86	74	69
	ASDAS ID	65	62	53	59	59	56	54	54	45

Paid work absenteeism refers to missed work because of arthritis (Q2 of WPS). Reported estimates are from a weighted generalized estimating equations model and the inverse probability of study discontinuation was used as the weight. The estimates are cumulative mean numbers from baseline (Day 1) through each time point. ASAS<20: <20% improvement; ASAS20–<40: ≥20–<40% improvement; ASAS40: ≥40% improvement; ASAS PR: a score of ≤2 in all 4 ASAS domains; ASDAS-CII: change ≥1.1–≤2.0 units; ASDAS-MI: change >2.0 units; ASDAS non-response: change ≤1.1 unit; ASDAS ID: ASDAS <1.3. ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; CII: clinically important improvement; CI: confidence interval; ID: inactive disease; MI: major improvement; PR: partial remission; WPS: Work Productivity Survey.

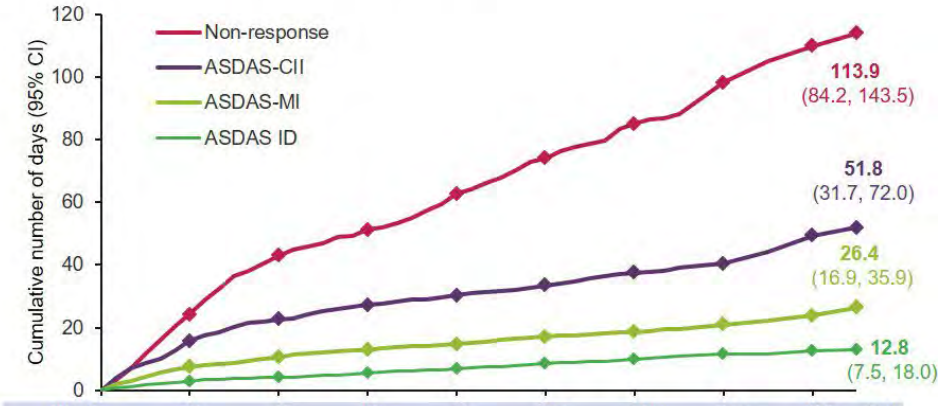
Figure 2. Paid work presenteeism by (A) ASAS response and (B) ASDAS response

A) Paid work presenteeism by ASAS response



Weighted n	Week	24	48	72	96	120	144	168	192	204
	ASAS<20	56	38	34	32	31	33	26	23	21
	ASAS20–<40	37	31	25	29	23	18	23	25	22
	ASAS40	111	124	116	109	111	108	106	98	92
	ASAS PR	66	64	63	63	61	64	59	53	52

B) Paid work presenteeism by ASDAS response



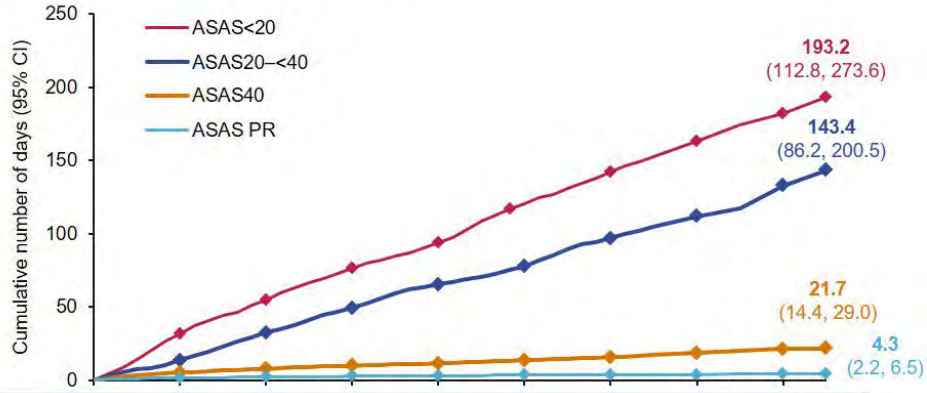
Weighted n	Week	24	48	72	96	120	144	168	192	204
	Non-response	58	45	39	42	34	33	32	27	25
	ASDAS-CII	57	50	44	38	43	47	41	47	47
	ASDAS-MI	92	101	97	95	92	83	86	74	69
	ASDAS ID	65	62	53	59	59	56	54	54	45

Paid work presenteeism refers to reduced productivity at work (WPS Q3). Reported estimates are from a weighted generalized estimating equations model and the inverse probability of study discontinuation was used as the weight. The estimates are cumulative mean numbers from baseline (Day 1) through each time point. ASAS<20: <20% improvement; ASAS20–<40: ≥20–<40% improvement; ASAS40: ≥40% improvement; ASAS PR: a score of ≤2 in all 4 ASAS domains; ASDAS-CII: change ≥1.1–≤2.0 units; ASDAS-MI: change >2.0 units; ASDAS non-response: change ≤1.1 unit; ASDAS ID: ASDAS <1.3. ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; CII: clinically important improvement; CI: confidence interval; ID: inactive disease; MI: major improvement; PR: partial remission; WPS: Work Productivity Survey.

Methods: These analyses use observed data from pts originally randomized to CZP in the phase 3 RAPID-axSpA study (NCT01087762).[4] Paid work absenteeism and presenteeism, and household work productivity, assessed using the validated arthritis-specific Work Productivity Survey (WPS),[5] are reported for pts who had: ASAS< 20, ASAS20–< 40, ASAS40 and ASAS partial remission (PR); ASDAS clinically important improvement (CII), major improvement (MI)

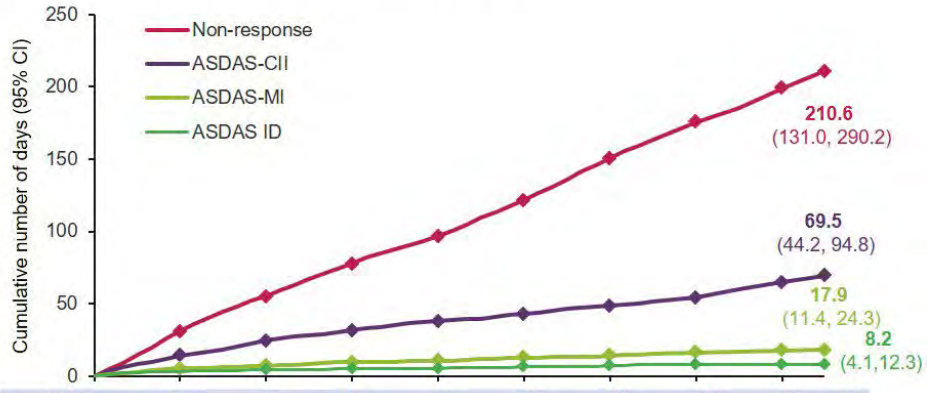
Figure 3. Household work absenteeism by (A) ASAS response and (B) ASDAS response

A) Household work absenteeism by ASAS response



Weighted n	Week	24	48	72	96	120	144	168	192	204
	ASAS<20	56	38	34	32	31	33	26	23	21
	ASAS20–<40	37	31	25	29	23	18	23	25	22
	ASAS40	111	124	116	109	111	108	106	98	92
	ASAS PR	66	64	63	63	61	64	59	53	52

B) Household work absenteeism by ASDAS response



Weighted n	Week	24	48	72	96	120	144	168	192	204
	Non-response	58	45	39	42	34	33	32	27	25
	ASDAS-CII	57	50	44	38	43	47	41	47	47
	ASDAS-MI	92	101	97	95	92	83	86	74	69
	ASDAS ID	65	62	53	59	59	56	54	54	45

Household work absenteeism refers to days not performing household work (WPS Q5). Reported estimates are from a weighted generalized estimating equations model and the inverse probability of study discontinuation was used as the weight. The estimates are cumulative mean numbers from baseline (Day 1) through each time point. ASAS<20: <20% improvement; ASAS20–<40: ≥20–<40% improvement; ASAS40: ≥40% improvement; ASAS PR: a score of ≤2 in all 4 ASAS domains; ASDAS-CII: change ≥1.1–≤2.0 units; ASDAS-MI: change >2.0 units; ASDAS non-response: change ≤1.1 unit; ASDAS ID: ASDAS <1.3. ASAS: Assessment of SpondyloArthritis international Society; ASDAS: Ankylosing Spondylitis Disease Activity Score; CII: clinically important improvement; CI: confidence interval; ID: inactive disease; MI: major improvement; PR: partial remission; WPS: Work Productivity Survey.

or non-response; and ASDAS inactive disease (ID). Mean number of days missed or days with reduced productivity each month was calculated by concurrent disease activity/response level and summarized across months to estimate cumulative burden over 204 weeks (wks) using a weighted generalized estimating equations model. An inverse probability-weighted (IPW) model was used to account for predictors of dropout which assigned greater weight to pts who remained in the study vs similar pts who dropped out.

Results: Of 218 CZP-randomized pts, 203, 191 and 142 completed Wks 24, 48 and 204, respectively; at baseline, 157 (72%) were employed outside the home. At Wk 204, 15.8% of pts had ASAS< 20, 16.4% ASAS20–< 40, 67.8% ASAS40 and 37.9% ASAS PR. Up to Wk 204, achievement of the more stringent ASAS PR and ASAS40 was associated with fewer days (4.0 and 8.6, respectively) of paid work absenteeism compared to pts who achieved ASAS< 20 or ASAS20–< 40 (69.2 and 29.4, respectively) (Figure 1A). At Wk 204, 49.0% and 33.1% of pts achieved ASDAS-MI and ASDAS-CII, and 31.8% reached ASDAS ID. ASDAS ID was associated with fewer days of paid work absenteeism over 204 wks (5.0) compared to ASDAS-MI (9.2), ASDAS-CII (21.9) or non-response (57.9) (Figure 1B). Similar findings were observed for paid work presenteeism and household work productivity (Figures 2 and 3), with achievement of more stringent responses associated with fewer days of work presenteeism or days unable to perform housework.

Conclusion: Achievement of optimal thresholds of clinical response in pts with axSpA after 4 years' treatment was associated with reduced burden on paid work and household productivity, indicating the importance of targeting stringent thresholds of disease control to limit the impact of axSpA on pts' daily lives.

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Abstract Number: 0363

Disease Course and Disease Burden in Patients with Axial Spondyloarthritis: Results from 5-year Multicountry Prospective Observational Study

Denis Poddubnyy[1], Joachim Sieper[2], Servet Akar[3], Santiago Muñoz-Fernández[4], Hildrun Haibel[2], Fabiana Ganz[5] and Robert Inman[6], [1]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [2]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [3]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Izmir, Turkey, [4]Servicio de Reumatología, Hospital Universitario Infanta Sofía, Madrid, Spain, [5]Abbvie Inc., North Chicago, IL, [6]University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

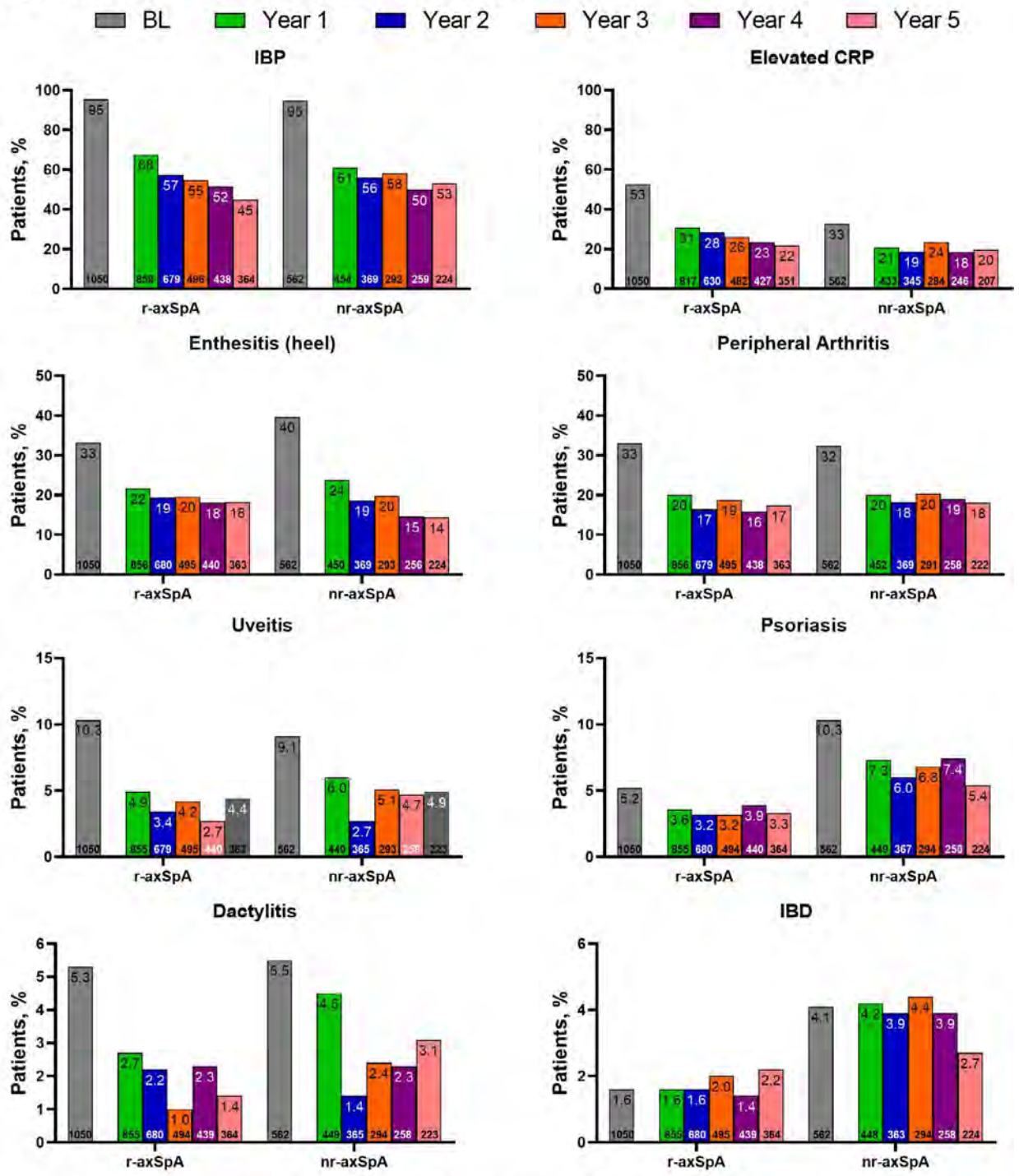
Table 1. Baseline Demographics and Disease Characteristics		
	r-axSpA n=1050	nr-axSpA n=562
Age, y, mean (SD)	34.4 (11.0)	35.3 (9.6)
Men, n (%)	744 (71)	271 (48)
Symptom duration, month, mean (SD)	61.0 (88.0) n=1040	47.7 (66.4) n=555
HLA-B27 (positive), n (%)	604 (69) n=870	273 (57) n=476
Number of SpA features, mean (SD)	2.4 (1.1)	2.3 (1.2)
Inflammatory back pain, n (%)	1002 (95)	533 (95)
Peripheral arthritis, n (%)	347 (33)	182 (32)
Enthesitis (heel), n (%)	349 (33)	223 (40)
Dactylitis, n (%)	56 (5)	31 (6)
Uveitis, n (%)	108 (10)	51 (9)
Psoriasis, n (%)	55 (5)	58 (10)
IBD, n (%)	17 (2)	23 (4)
Good response to NSAIDs, n (%)	640 (61)	337 (60)
Family history of SpA, n (%)	197 (19)	104 (19)
Elevated CRP, n (%)	553 (53)	183 (33)
Active sacroiliitis on MRI, n (%)	279 (27)	298 (53)
Coronary artery disease, n (%)	9 (1) n=980	3 (1) n=526
Current Treatment, n (%)		
NSAIDs	810 (77)	437 (78)
Methotrexate	62 (6)	43 (8)
Sulfasalazine	256 (24)	118 (21)
DMARDs, other	56 (5)	17 (3)
Systemic corticosteroids	81 (8)	41 (7)
Analgesics	146 (14)	101 (18)
TNF inhibitors	181 (17)	60 (11)
axSpA, axial spondyloarthritis; HLA-B27, human leukocyte antigen B27; IBD, inflammatory bowel disease; nr, non-radiographic; r, radiographic.		

Background/Purpose: Patients (pts) with axial SpA (axSpA) can be classified into radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA) based on the presence or absence of radiographic sacroiliitis. The PROOF study evaluated disease course and disease burden of pts with nr-axSpA and r-axSpA over 5 years.

Methods: PROOF was a real-world, prospective, observational study conducted in rheumatology clinical practices in 29 countries in 6 geographic regions. The study enrolled adults with current/past chronic back pain for ≥3 months and onset before 45 years of age. Study visits occurred at baseline (BL) and yearly thereafter. Clinical characteristics and disease burden of axSpA over 5 years were evaluated. Flares of SpA features (mean number over the previous year) were also assessed.

Results: Of 2633 enrolled pts, 2165 (82%) were diagnosed with axSpA and fulfilled the Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA. Among these, 1612 (74%) were classified as having r-axSpA (1050 [65%]) or nr-axSpA (562 [35%]) based on fulfilling ASAS criteria by central reading; 27% and 53%, respectively, had active sacroiliitis on MRI (Table 1). Compared with r-axSpA, higher proportion of nr-axSpA pts had enthesitis (40% vs 33%), psoriasis (10% vs 5%), and inflammatory bowel disease (IBD, 4% vs 2%) at BL. Consistent with previous studies,[1] higher proportions of r-axSpA vs nr-axSpA pts were men (71% vs 48%) and had elevated CRP (53% vs 33%; Table 1). A similar trend was observed over 5 years: higher proportion of pts with r-axSpA had elevated CRP, whereas psoriasis and IBD were more common among pts with nr-axSpA; occurrence of enthesitis was similar between r-axSpA and nr-axSpA on subsequent visits (Figure 1). The use of medications was similar between r-axSpA and nr-axSpA pts at BL (Table 1) and changes in treatment patterns (eg, reduced use of NSAIDs, corticosteroids,

Figure 1. Proportion of Patients With SpA Features Over Time*

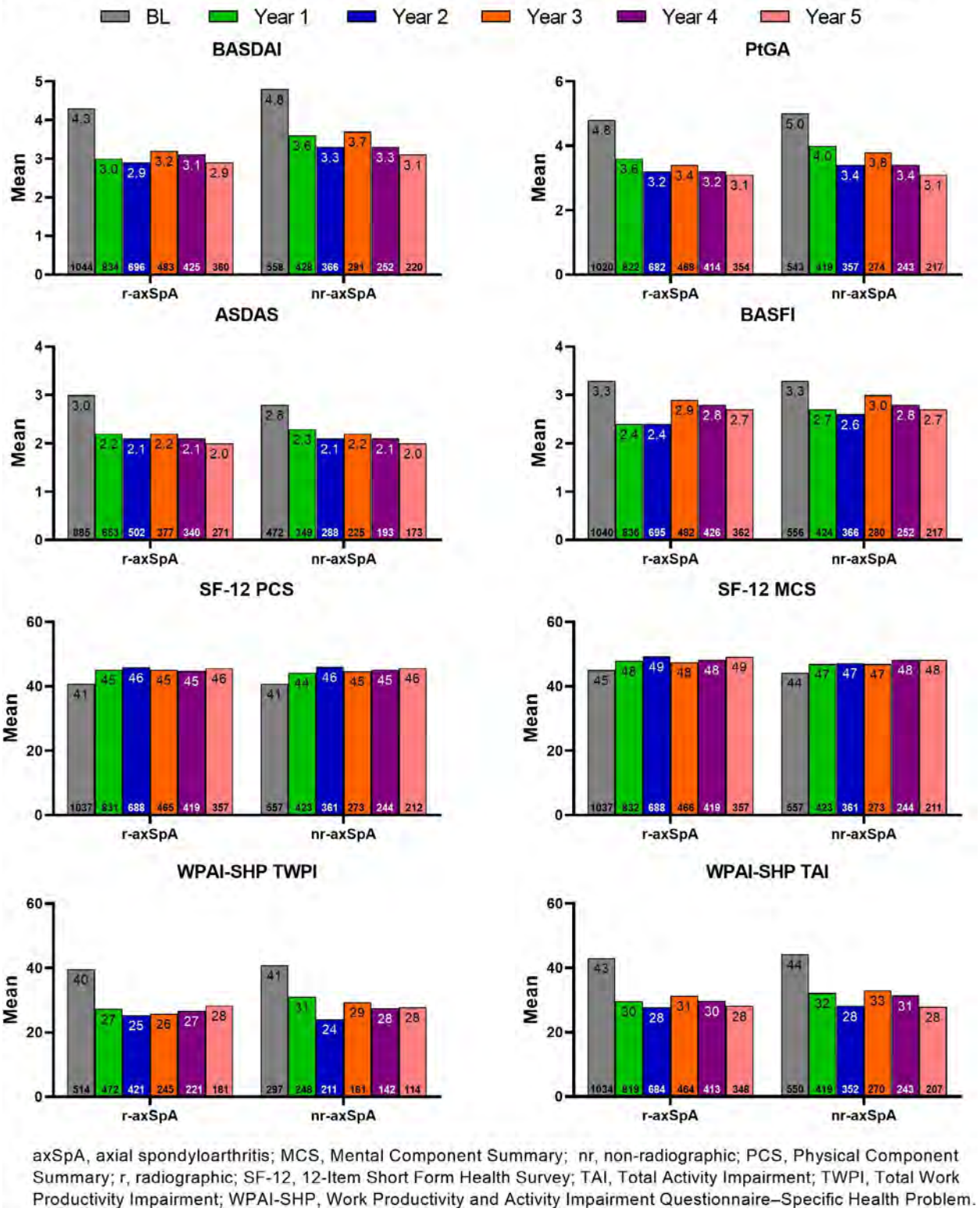


axSpA, axial spondyloarthritis; IBD, inflammatory bowel disease; IBP, inflammatory back pain; nr, non-radiographic; r, radiographic.

*Values at baseline are for proportions of patients with ever presence of the SpA feature, and values at yearly visits are proportions of patients with presence of the SpA feature since last visit.

sulfasalazine, and other DMARDs and increased use of TNF inhibitors) were similar between populations over time. Pts with r-axSpA had a higher mean frequency of inflammatory back pain (IBP) flares per year at years 1 and 2 (22.2 and 17.4, respectively [vs 13.8 and 5.3 with nr-axSpA]) and peripheral arthritis flares per year at years 1 and 2 (8.9 and

Figure 2. Disease Activity, Quality of Life, and Work Impairment Outcomes Over Time



axSpA, axial spondyloarthritis; MCS, Mental Component Summary; nr, non-radiographic; PCS, Physical Component Summary; r, radiographic; SF-12, 12-Item Short Form Health Survey; TAI, Total Activity Impairment; TWPI, Total Work Productivity Impairment; WPAI-SHP, Work Productivity and Activity Impairment Questionnaire–Specific Health Problem.

19.0 [vs 4.2 and 4.5 with nr-axSpA]); however, no differences were observed throughout the rest of the study. Mean number of IBD (0.8–9.0 vs 0.5–0.9) and psoriasis (2.2–4.2 vs 1.1–1.5) flares was higher among pts with nr-axSpA vs r-axSpA, respectively, at each study visit. Disease activity decreased in both r-axSpA and nr-axSpA populations over

time; results on physical function, pt global assessment of disease activity, quality of life, and work impairment were similar between populations through 5 years (Figure 2).

Conclusion: In this study, a higher proportion of pts were diagnosed with r-axSpA at baseline. Patients with r-axSpA and nr-axSpA share a similar clinical presentation, except for certain extra-articular manifestations (eg, psoriasis and IBD), which were more prevalent among nr-axSpA pts. Both groups showed a comparable burden of disease and treatment over 5 years.

1. López-Medina C, *et al*. *RMD Open,* 2019;5:e001108

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Abstract Number: 0364

Dose Tapering of TNF Inhibitors in Patients with Axial Spondyloarthritis in Routine Care – 2-year Clinical and MRI Outcomes and Predictors of Successful Tapering

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SESSION INFORMATION

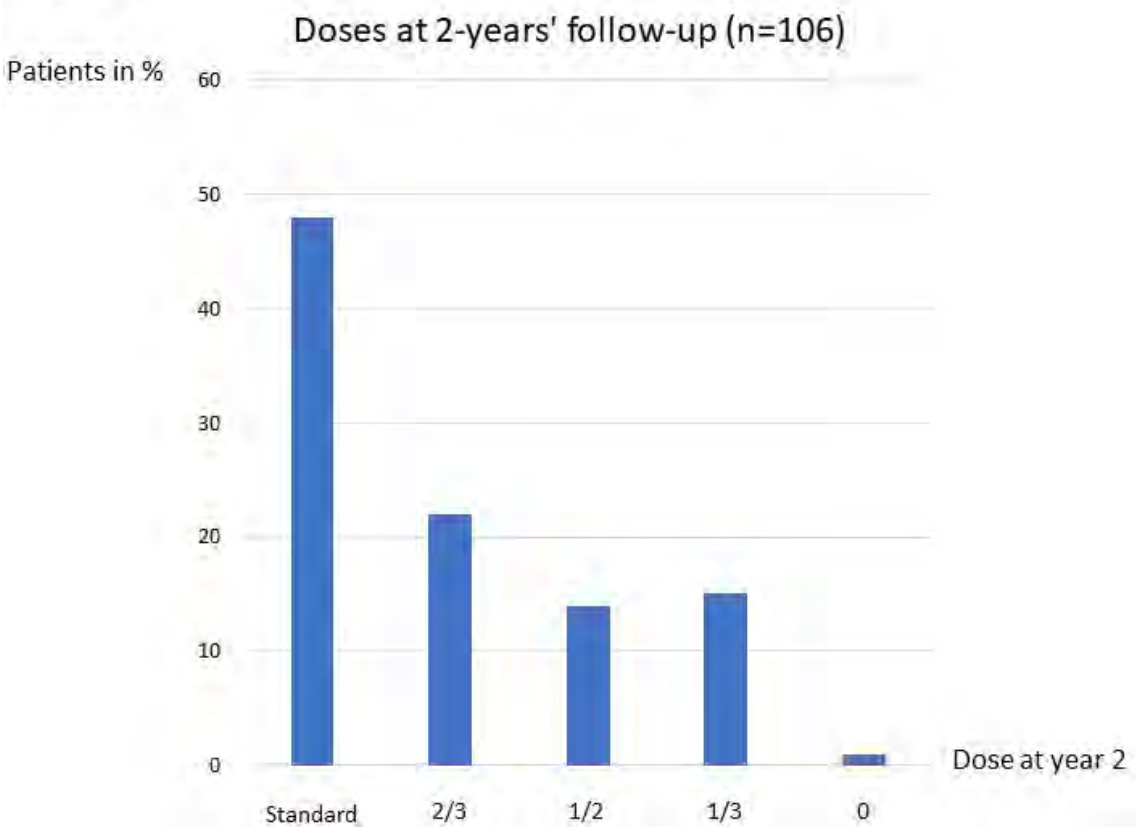
Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Figure 1



Background/Purpose: In a 2-year follow-up study of patients with axial spondyloarthritis (axSpA) in clinical remission who tapered Tumor Necrosis Factor inhibitor (TNFi) treatment according to a clinical guideline, we aimed to investigate 1) the proportion who successfully tapered/discontinued therapy, 2) baseline predictors of successful tapering/discontinuation, 3) the proportion regaining clinical remission after flare and 4) the progression on magnetic resonance imaging (MRI) and radiography.

Methods: One-hundred-and-nine patients (78 (72%) on standard, 31 (28%) on reduced dose) in clinical remission with Bath ankylosing spondylitis disease activity index (BASDAI)< 40, physician global score< 40 and no signs of disease activity the previous year tapered TNFi to 2/3 of standard dose at baseline, 1/2 at week 16, 1/3 at week 32 and withdrew at week 48. Patients who experienced clinical, BASDAI or MRI flare stopped tapering and escalated to the previous dose. Prediction analyses were done by multivariable regression.

Results: Of the 106 patients who completed 2-year follow-up, 55 patients (52%) had successfully tapered (Table 1): 23 patients (22%) receiving 2/3, 15 (14%) 1/2, 16 (15%) 1/3 dose and 1 (1%) discontinued (Figure 1). In the entire patient group (all doses patients) lower physician global score (Odds ratio (OR)=0.86 (95% Confidence Interval=0.75-0.98); p=0.017), lower Spondyloarthritis Research Consortium of Canada Sacroiliac Joint Erosion score (OR=0.78 (0.57-0.98); p=0.029) and current smoking (OR=3.28 (1.15-10.57); p=0.026) were independent predictors for successful tapering. In patients at standard dose at baseline (standard dose patients) lower physician score was the only independent predictor of successful tapering (OR=0.79 (0.64-0.93); p=0.003) (Table 2). At 2 years, 97% of patients were in clinical remission. Minimal changes in imaging variables were observed.

Table 1. Baseline characteristics at 2 years, stratified by successful tapering in All Doses Cohort (109 patients) and Standard Dose Cohort (78 patients)

	All Doses Cohort				Standard Dose Cohort			
	All (n=109)	No successful tapering (n=51)	Successful tapering (n=55)	p-value	All (n=78)	No successful tapering (n=45)	Successful tapering (n=31)	p-value
Baseline demographics								
Male gender, n (%)	92 (84%)	43 (84%)	47 (85%)	1	66 (85%)	38 (84%)	27 (87%)	1
Age, years	44 (36-52)	44 (38-54)	44 (33-51)	0.409	43 (34-53)	44 (38-53)	37 (32-52)	0.199
Time since diagnosis, years	10 (6-15)	10 (5-15)	9 (6-18)	0.977	8 (5-14)	9 (5-14)	6 (4-10)	0.152
Current smoker, n (%)	23 (21%)	7 (14%)	16 (30%)	0.092	15 (20%)	6 (14%)	9 (30%)	0.154
HLA-B27 positivity, n (%)	91 (87%)	39 (81%)	49 (91%)	0.249	63 (85%)	33 (79%)	28 (93%)	0.107
Disease characteristics at baseline								
TNF inhibitor, n (%)				0.196				0.120
Adalimumab	38 (35%)	20 (39%)	18 (33%)		24 (31%)	18 (40%)	6 (19%)	
Etanercept	13 (12%)	7 (14%)	4 (7%)		7 (9%)	4 (9%)	2 (6%)	
Certolizumab pegol	3 (3%)	0 (0%)	3 (5%)		3 (4%)	0 (0%)	3 (10%)	
Golimumab	27 (25%)	14 (27%)	12 (22%)		26 (33%)	14 (31%)	11 (35%)	
Infliximab	28 (26%)	10 (20%)	18 (33%)		18 (23%)	9 (20%)	9 (29%)	
CRP >3 mg/l, n (%)	19 (17%)	9 (18%)	9 (16%)	1	11 (14%)	8 (18%)	2 (6%)	0.185
BASMI (0-100)	10 (0-30)	10 (0-30)	10 (0-28)	0.540	10 (0-30)	10 (0-30)	10 (0-20)	0.464
Back pain (yes), n (%)	12 (11%)	11 (22%)	1 (2%)	**0.002**	11 (14%)	10 (22%)	1 (3%)	**0.042**
Inflammatory back pain (yes), n (%)	1 (1%)	1 (2%)	0 (0%)	0.495	0 (0%)	0 (0%)	0 (0%)	-
Physician global VAS (0-100)	5 (3-7)	5 (4-8)	4 (3-6)	0.087	4 (3-6)	5 (4-7)	4 (2-5)	**0.009**
Physician global VAS <40, n (%)	109 (100%)	51 (100%)	55 (100%)	-	78 (100%)	45 (100%)	31 (100%)	-
ASDAS	1.0 (0.6-1.3)	1.1 (0.9-1.4)	0.9 (0.6-1.3)	0.109	1.1 (0.7-1.4)	1.2 (0.9-1.4)	0.9 (0.6-1.4)	0.089
ASDAS <1.3, n (%)	77 (71%)	35 (69%)	40 (73%)	0.803	52 (67%)	30 (67%)	21 (68%)	1
ASDAS <2.1, n (%)	101 (93%)	50 (98%)	49 (89%)	0.114	73 (94%)	44 (98%)	28 (90%)	0.298
VAS physician confidence to taper (0-100)	72 (63-78)	71 (62-79)	73 (67-78)	0.362	73 (67-81)	71 (63-80)	74 (70-81)	**0.041**
VAS patient confidence to taper (0-100)	61 (48-89)	50 (48-82)	77 (48-92)	0.104	64 (49-88)	50 (47-86)	79 (50-91)	**0.025**
PROs at baseline								
BASDAI (0-100)	10.8 (4.8-21.2)	15.8 (6.6-22.0)	8.2 (4.0-19.6)	**0.034**	12.0 (5.7-22.1)	15.8 (6.6-22.0)	10.8 (4.0-21.1)	0.192
BASDAI<40, n (%)	108 (99%)	51 (100%)	55 (100%)	-	77 (99%)	45 (100%)	31 (100%)	-
BASFI (0-100)	10.2 (3.6-21.7)	10.7 (5.3-21.6)	7.6 (2.5-20.1)	0.483	11.0 (3.8-21.6)	11.0 (5.3-21.7)	11.0 (3.8-18.1)	0.627
Patient pain VAS (0-100)	8 (2-17)	10 (3-20)	6 (2-14)	0.064	8 (3-19)	10 (5-21)	5 (0-14)	0.073
Patient fatigue VAS (0-100)	15 (6-30)	16 (7-39)	12 (6-26)	0.076	16 (8-32)	17 (8-39)	15 (8-28)	0.290
Patient global VAS (0-100)	9 (4-18)	11 (6-17)	8 (2-22)	0.153	10 (5-20)	11 (7-19)	8 (2-24)	0.228
HAQ-S (0-3)	0.2 (0.1-0.4)	0.2 (0.1-0.4)	0.1 (0.0-0.4)	0.101	0.2 (0.1-0.4)	0.2 (0.1-0.4)	0.1 (0.0-0.2)	0.066
EQ-5D (0-1)	0.9 (0.8-1.0)	0.9 (0.8-0.9)	0.9 (0.8-1.0)	0.155	0.9 (0.8-1.0)	0.9 (0.8-0.9)	0.9 (0.8-1.0)	0.300
ASAS Health index (0-17)	2.0 (0.8-4.4)	3.0 (1.0-5.0)	2.0 (0.0-4.0)	0.095	2.0 (1.0-4.0)	3.0 (1.0-5.0)	2.0 (0.0-3.6)	0.128
Imaging variables at baseline								
mNYc positive, n (%)	71 (68%)	31 (65%)	38 (70%)	0.681	50 (67%)	28 (65%)	20 (67%)	1
mSASSS (0-72)	1 (0-18)	1 (0-18)	1 (0-12)	0.828	0 (0-12)	0 (0-18)	0 (0-10)	0.519
SPARCC SIJ Inflammation index (0-72)	0 (0-0)	0 (0-0)	0 (0-0)	0.104	0 (0-0)	0 (0-0)	0 (0-0)	0.104
SPARCC spine total inflammation (0-108)	0 (0-3)	0 (0-2)	0 (0-4)	0.841	0 (0-2)	0 (0-2)	0 (0-2)	0.741
CANDEN MRI spine inflammation score (0-614)	0 (0-2)	0 (0-2)	0 (0-2)	0.977	0 (0-2)	0 (0-2)	0 (0-2)	0.551
SPARCC SSS Fat (0-40)	11 (3-25)	10 (2-19)	16 (4-27)	0.219	10 (3-24)	10 (2-22)	9 (3-24)	0.697
SPARCC SSS Erosion (0-40)	0 (0-1)	0 (0-1)	0 (0-0)	0.231	0 (0-1)	0 (0-1)	0 (0-0)	0.514
SPARCC SSS Backfill (0-20)	0 (0-6)	1 (0-6)	0 (0-5)	0.400	1 (0-8)	0 (0-6)	2 (0-10)	0.592
SPARCC SSS Ankylosis (0-20)	1 (0-12)	0 (0-12)	1 (0-12)	0.795	0 (0-12)	0 (0-12)	1 (0-10)	0.930
CANDEN MRI spine fat score (510)	3 (0-11)	2 (0-9)	3 (0-14)	0.197	2 (0-11)	1 (0-10)	2 (0-12)	0.488
CANDEN MRI spine bone erosion score (208)	0 (0-0)	0 (0-0)	0 (0-0)	0.877	0 (0-0)	0 (0-0)	0 (0-0)	0.891
CANDEN MRI spine NBF score (0-460)	8 (0-32)	8 (0-32)	12 (2-30)	0.784	6 (0-24)	6 (0-30)	4 (0-18)	0.713

Conclusion: Fifty-two % of patients with axSpA in clinical remission could successfully taper TNFi by following a clinical guideline and maintain remission at 2-years' follow-up, while only 1% discontinued. Baseline physician global score was an independent predictor of successful tapering.

Table 2. Univariate and multivariable logistic regression analyses for prediction of successful tapering at 2-year follow-up in Standard Dose Prediction Cohort (75 patients) and All Doses Prediction Cohort (101 patients)

All Doses Prediction Cohort (n=101)						
	Univariate analyses			Final multivariable analyses*		
Predictor	OR	95% CI	p-value	OR	95% CI	p-value
Male gender	1.20	(0.39 - 3.74)	0.750			
Age	0.98	(0.95 - 1.02)	0.296			
Time since diagnosis	0.99	(0.94 - 1.03)	0.527			
Current smoker	2.54	(0.96 - 7.27)	**0.061**	3.28	(1.15 - 10.57)	0.026
HLA-B27 positive	2.10	(0.68 - 7.18)	0.197			
previous bDMARDs	0.82	(0.47 - 1.40)	0.459			
Patient pain VAS	0.98	(0.94 - 1.01)	0.195			
Physician global VAS	0.88	(0.77 - 0.99)	**0.029**	0.86	(0.75 - 0.98)	0.017
ASDAS	0.66	(0.31 - 1.36)	0.262			
mNYc positive	1.23	(0.54 - 2.83)	0.616			
SPARCC SIJ Inflammation Index	0.79	(0.53 - 1.05)	0.108			
CANDEN Total inflammation	0.97	(0.87 - 1.07)	0.557			
SPARCC SSS Erosion	0.82	(0.62 - 1.01)	**0.066**	0.78	(0.57 - 0.98)	0.029
CANDEN Fat	1.02	(1.00 - 1.05)	**0.074**			
AUC (95% CI)#				0.66 (0.54 - 0.76)		
Standard Dose Prediction Cohort (n=75)						
	Univariate analyses			Final multivariable analyses**		
Predictor	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Male gender	1.28	(0.34 - 5.36)	0.718			
Age	0.98	(0.93 - 1.02)	0.260			
Time since diagnosis	0.98	(0.92 - 1.03)	0.429			
Current smoker	2.60	(0.83 - 8.67)	0.100			
HLA-B27 positive	3.62	(0.89 - 22.43)	**0.074**			
previous bDMARDs	0.72	(0.34 - 1.40)	0.344			
Patient pain VAS	0.98	(0.93 - 1.02)	0.240			
Physician global VAS	0.79	(0.64 - 0.93)	**0.004**	0.79	(0.64 - 0.93)	0.003
ASDAS	0.50	(0.19 - 1.19)	0.118			
mNYc positive	1.11	(0.42 - 2.96)	0.833			
SPARCC SIJ Inflammation Index	0.70	(0.34 - 1.05)	**0.097**			
CANDEN Total inflammation	0.97	(0.86 - 1.08)	0.604			
SPARCC SSS Erosion	0.84	(0.61 - 1.05)	0.137			
CANDEN Fat	1.02	(0.99 - 1.06)	0.200			
AUC (95% CI)#				0.68 (0.57 - 0.80)		

Values are median (IQR) unless otherwise stated. Mann Whitney U test, chi-square test or Fisher's exact test (as appropriate) was used for analysing between-group differences; bold indicates statistically significant p-values; P<0.05 was considered statistically significant. "-" indicates that p-value could not be calculated.

Predictors were selected by applying backward selection in stacked data. p-values by likelihood ratio tests. Bold indicates p-values<0.1 in univariate analyses. *Results were derived in all imputed datasets (missing values in selected predictors), where model estimates are pooled based on Rubin's rules. Profile likelihood CIs were calculated according to the Pseudo-Variance modification of Rubin's rule (PVR). AUC was estimated based on internal validation by bootstrapping with 100 samples per imputed dataset. **Results were derived in non-imputed data (no missing values in selected predictors). CIs given as profile likelihood CIs. AUC was estimated based on internal validation by bootstrapping with 1000 samples. #The bootstrap 0.632+ estimate was calculated to correct for optimism.

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Abstract Number: 0365

A Cluster Analysis in Patients with Axial Spondyloarthritis Using TNFi Based on Clinical Characteristics

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies using cluster analysis technique in axial spondyloarthritis (axSpA) patients have consistently identified distinct groups of patients in terms of their clinical characteristics: those with pure axial symptoms and those with a high frequency of peripheral manifestations. Due to the cross-sectional nature of these studies, however, prognostic information such as drug survival of anti-TNF agents in these group were not provided.

Methods: Clinical characteristics and demographic data of axSpA patients in KOBIO registry were analyzed using hierarchical clustering analysis. After clustering, drug survivals of anti-TNF agents were compared between these groups.

Results: 1,042 patients were included in the study with no missing data. The hierarchical cluster analysis classified patients in two groups; one with predominant isolated axial manifestations (axial group, n=828) and the other with more frequent extra-axial symptoms (extra-axial group, n=214). Almost all extra-axial symptoms (peripheral arthritis, enthesitis, uveitis, and psoriasis) were more frequently observed in extra-axial group than axial group. In addition,

Table 1. Clinical characteristics of divided groups

Group	Axial group (n = 828)	Extra-axial group (n = 214)	*p*-value
Age at starting TNFi (years, %)	38.18 (12.76)	38.85 (14.28)	0.618
Sex (male, %)	651 (78.6)	142 (66.4)	0.001
Late onset (age ≥ 40 years, %)	247 (29.8)	82 (38.3)	0.034
Long disease duration (≥ 2 years, %)	380 (45.9)	46 (21.5)	< 0.001
HLA-B27 positivity (%)	740 (89.4)	189 (88.3)	0.782
Inflammatory back pain (%)	704 (85.0)	183 (85.5)	0.943
Radiographic sacroiliitis (%)	745 (90.0)	189 (88.3)	0.618
Peripheral arthritis (%)	203 (24.5)	185 (86.4)	< 0.001
Enthesitis (%)	68 (8.2)	150 (70.1)	< 0.001
Uveitis (%)	168 (20.3)	54 (25.2)	0.197
Psoriasis (%)	16 (1.9)	11 (5.1)	0.029
IBD (%)	9 (1.1)	4 (1.9)	0.618
Good response to NSAIDs (%)	212 (25.6)	146 (68.2)	< 0.001
csDMARD use (%)	75 (9.1)	32 (15.0)	0.029
NSAID use (%)	714 (86.2)	190 (88.8)	0.486
SJC	0.50 (2.37)	1.21 (1.80)	< 0.001
TJC	0.71 (2.67)	2.32 (4.00)	< 0.001
BASDAI	5.94 (1.92)	6.37 (1.81)	0.005
BASFI	3.42 (2.56)	3.66 (2.56)	0.305
ASDAS-ESR	3.65 (1.00)	4.05 (1.08)	< 0.001
ASDAS-CRP	3.61 (1.00)	3.87 (1.07)	0.003
ESR (mm/h)	35.65 (28.76)	46.46 (33.21)	< 0.001
CRP (mg/dL)	2.11 (2.74)	2.89 (3.60)	0.006

patients with shorter disease duration, late disease onset, and high disease activity were classified in extra-axial group (Table 1). Interestingly, the extra-axial group had lower drug survival probability than the axial group (p=0.001, Figure 1).

Conclusion: Cluster analysis of AS patients using anti-TNF agents classified two distinct groups of patients in terms of their clinical phenotypes and revealed that the patients with prominent extra-axial manifestations had lower drug survival with anti-TNF agents.

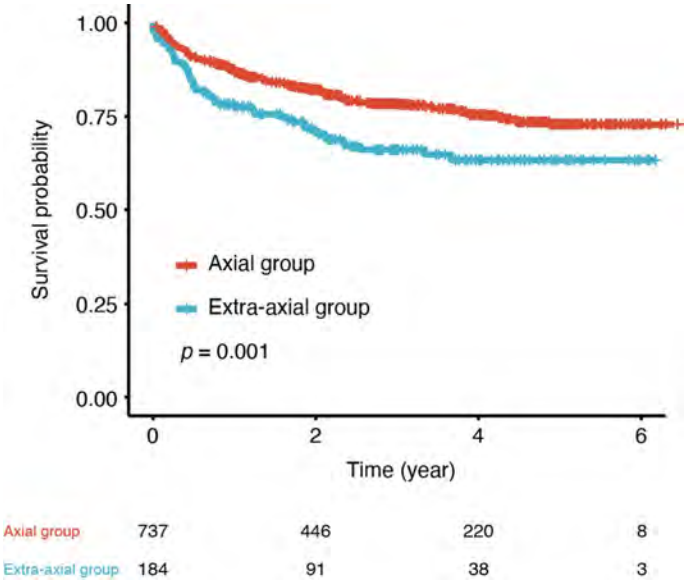

Figure 1. Drug survival probabilities of TNFi compared by Kaplan-Meier survival analysis between axial and extra-axial groups.

Disclosure: S. Lee, None; **S. Kang**, None; **Y. Eun**, None; **H. Kim**, None; **H. Cha**, None; **E. Koh**, None; **J. Lee**, None.

Abstract Number: 0366

Why Is It so Difficult for AxSpA Patients to Find a Job? Results from the European Map of Axial Spondyloarthritis (EMAS)

Marco Garrido-Cumbrera[1], Victoria Navarro-Compán[2], Christine Bundy[3], Souzi Makri[4], Laura Christen[5], José Correa-Fernández[6], Sergio Sanz-Gomez[6], Raj Mahapatra[7], Carlos Jesús Delgado-Domínguez[6] and Denis Poddubnyy[8], [1]Health & Territory Research (HTR), University of Seville, Sevilla, Spain, [2]Rheumatology service, Hospital Universitario La Paz-IdiPaz, Madrid, Spain, [3]Cardiff University, Cardiff, Wales, United Kingdom, [4]Cyprus League Against Rheumatism (CYPLAR), Limassol, Cyprus, [5]Novartis Pharma AG, Basel, Switzerland, [6]Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain, [7]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [8]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: AxSpA is associated with substantial negative consequences regarding work status and career prospects. The aim is to identify factors associated with barriers to job access among European axSpA patients.

Methods: Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were analyzed. Difficulties in finding a job was assessed by the following item: "Do you think it is or it would be difficult for you to find a job because of your Spondylitis/Spondyloarthritis? (Yes/No)". Differences in sociodemographic factors, patient-reported outcomes [BASDAI (0-10), spinal stiffness (3-12), functional limitation (0-54), and mental health status using the 12-item General Health Questionnaire (0-12)], employment, lifestyle habits, and comorbidities were assessed through Mann-Whitney and $\chi 2$ tests. Univariable and multivariable binary logistic regression were used to identify variables possibly explaining difficulties/perceived difficulties finding a job due to axSpA.

	Mean ± SD or n (%)		p-value
	Difficulties finding a job due to axSpA		
	Yes 1,357 (74.4%)	No 466 (25.6%)	
Sociodemographic			
Gender. Female	850 (62.6)	291 (62.4)	0.941
Marital status. Separated/divorced	155 (11.4)	24 (5.2)	**0.001**
Educational level. University	614 (45.2)	310 (66.5)	**<0.001**
Overweight/Obesity	686 (50.6)	209 (44.8)	**0.034**
Restriction and adaption due to axSpA			
Restriction driving. High, n= 1,024	320 (37.0)	21 (13.3)	**<0.001**
Restriction using public transportation. High, n= 872	306 (40.2)	12 (10.9)	**<0.001**
Adaption in workplace (ever). Yes, n= 1,769	620 (47.6)	207 (44.4)	0.240
Moved to another job (ever). Yes, n= 1,772	466 (35.7)	101 (21.7)	**<0.001**
Adapting car. Yes, n= 1,790	348 (26.3)	80 (17.2)	**<0.001**
Use of customized shoes. Yes, n= 1,807	806 (60.1)	189 (40.6)	**<0.001**
PROs			
BASDAI (0-10), n= 1,734	6.0 ± 1.8	4.4 ± 2.0	**<0.001**
GHQ-12 (0-12), n= 1,751	6.0 ± 4.2	3.1 ±3.4	**<0.001**
Functional Limitation Index (0-54), n= 1,814	22.8 ± 16.6	9.2 ±10.0	**<0.001**
Spinal Stiffness (3-12), n= 1,767	8.2 ± 2.4	6.4 ± 2.2	**<0.001**
Diagnostic delay, n= 1,743	7.7 ± 8.2	5.8 ± 7.7	**<0.001**
Comorbidities			
Anxiety. Yes, n= 1,743	507 (38.8)	82 (18.8)	**<0.001**
Depression. Yes, n= 1,736	458 (35.2)	68 (15.6)	**<0.001**
Sleep disorder. Yes, n= 1,737	612 (47.0)	116 (26.6)	**<0.001**

Table 2. Logistic regression analysis for variables associated with difficulty finding a job due to axSpA (N=1,502)

	Univariable analysis		Multivariable analysis	
Qualitative factors	**OR**	**95% CI**	**OR**	**95% CI**
Marital status. Separated/divorced	2.38	**1.52, 3.70**	1.60	0.94, 2.70
Educational level. University	0.42	**0.33, 0.52**	0.53	**0.40, 0.70**
BMI. Overweight/Obesity	1.26	**1.02, 1.55**	1.07	0.81, 1.40
Restriction driving. High	6.60	**4.18, 10.40**	1.10	0.60, 2.02
Restriction using public transportation. High	11.11	**6.18, 19.99**	2.22	**1.07, 4.63**
Moved to another job (ever). Yes	2.01	**1.57, 2.57**	1.44	**1.06, 1.96**
Adapting car. Yes	1.72	**1.31, 2.25**	1.21	0.85, 1.71
Use of customized shoes. Yes	2.21	**1.78, 2.74**	1.58	**1.20, 2.08**
Anxiety. Yes	2.74	**2.10, 3.57**	1.12	0.75, 1.69
Depression. Yes	2.93	**2.21, 3.89**	1.32	0.86, 2.02
Sleep disorder. Yes	2.45	**1.93, 3.11**	1.23	0.90, 1.69
Quantitative factors	**B**	**95% CI**	**B**	**95% CI**
BASDAI (0-10)	1.55	**1.46, 1.64**	1.18	**1.09, 1.28**
GHQ-12 (0-12)	1.21	**1.18, 1.25**	1.09	**1.05, 1.14**
Functional Limitation Index (0-54)	1.08	**1.07, 1.09**	1.04	**1.02, 1.06**
Spinal Stiffness (3-12)	1.35	**1.29, 1.41**	1.13	**1.06, 1.21**
Diagnostic delay, years	1.04	**1.02, 1.05**	1.00	0.99, 1.02

Results: Among the 1,823 patients who responded to difficulties/perceived difficulties in finding a job due to axSpA, mean age was 41.4±10.7 years, 62.6% female, 50.7% had a university degree, and 65.6% were married. 56.8% were employed, 8.4% unemployed, and 28.2% on sick leave. 1,357 (74.4%) reported they had or would have difficulties finding a job. Compared to those without difficulties, patients with difficulties were typically separated/divorced (11.4% vs 5.2%, p=0.001), less university educated (45.2% vs 66.5%, p< 0.001), and overweight/obese (50.6% vs

44.8%, p=0.034). Those with difficulties had increased restrictions when driving (37.0% vs 13.3%), or when using public transportation (40.2% vs 10.9%), had previously changed jobs because of axSpA (35.7% vs 21.7%), required adaptions to their car (26.3% vs 17.2%) or shoes (60.1% vs 40.6%), had longer diagnostic delay (7.7 vs 5.8 years), higher disease activity (BASDAI 6.0 vs 4.4), poorer mental health through GHQ-12 (6.0 vs 3.1), greater functional limitation (22.8 vs 9.2), and spinal stiffness (8.2 vs 6.4), as well as higher rates of anxiety (38.8% vs 18.8%), depression (35.2% vs 15.6%), and sleep disorders (47.0% vs 26.6%, all p< 0.001). In the logistic regression analysis, the qualitative factors associated with difficulties finding a job were restrictions using public transportation (OR=2.22), use of customized shoes (OR=1.58), not having university education (OR=0.53) and having had previously changed jobs due to barriers created by axSpA (OR=1.44). The quantitative factors associated were disease activity (OR=1.18), spinal stiffness (OR=1.13), poorer mental health (OR=1.09), and functional limitation (OR=1.04).

Conclusion: Three out of four axSpA patients had, or perceived they would have, difficulties in finding a job. Poor physical and mental health, together with the need for mobility adaptations, lower educational level, having changed job due to axSpA were factors associated with difficulties/perceived difficulties in finding a job. Early diagnosis, effective treatment and greater advocacy in the workplace are needed to enable axSpA patients to search for and remain in employment.

Disclosure: M. Garrido-Cumbrera, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5; **C. Bundy**, Abbvie, 2, Celgene, 2, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2; **S. Makri**, None; **L. Christen**, Novartis, 3; **J. Correa-Fernández**, None; **S. Sanz-Gomez**, None; **R. Mahapatra**, None; **C. Delgado-Domínguez**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6.

Abstract Number: 0367

Can Belonging to an AxSpA Patient Organization Be Associated with Benefits to Its Members? Results from the European Map of Axial Spondyloarthritis (EMAS)

Marco Garrido-Cumbrera[1], Souzi Makri[2], Denis Poddubnyy[3], Christine Bundy[4], Laura Christen[5], Sergio Sanz-Gomez[6], José Correa-Fernández[6], Raj Mahapatra[7], Carlos Jesús Delgado-Domínguez[6] and Victoria Navarro-Compán[8], [1]Health & Territory Research (HTR), University of Seville, Sevilla, Spain, [2]Cyprus League Against Rheumatism (CYPLAR), Limassol, Cyprus, [3]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [4]Cardiff University, Cardiff, Wales, United Kingdom, [5]Novartis Pharma AG, Basel, Switzerland, [6]Health & Territory Research (HTR), Universidad de Sevilla, Seville, Spain, [7]Axial Spondyloarthritis International Federation (ASIF), London, United Kingdom, [8]Rheumatology service, Hospital Universitario La Paz-IdiPaz, Madrid, Spain

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Patient organizations (POs) provide education and support services aimed to improve the quality of life of axSpA patients. This analysis aims to identify factors associated with PO membership among European axSpA patients.

Methods: Data from 2,846 unselected patients participating in EMAS, an online survey (2017-2018) across 13 European countries, were collected. Membership of patient organizations was assessed by the following item: “Are you a member of any Spondylitis Support Group or Association? (Yes/No)”. Differences in sociodemographics, patient-

Table 1. Bivariate analysis between members and non-members of POs (N= 2,846 unless specified)

	Mean ± SD or n (%)		p-value
	Member 1,107 (38.9%)	Non-member 1,739 (61.1%)	
Sociodemographic			
Gender. Male	459 (41.5)	641 (36.9)	**0.014**
Marital status. Married	811 (73.3)	1,122 (64.5)	**<0.001**
Educational level. University	559 (50.9)	811 (46.6)	0.195
BMI. Overweight/Obesity	616 (55.6)	870 (50.0)	**0.003**
Life habits			
Physical activity. Yes	957 (86.4)	1,372 (78.9)	**<0.001**
Smoking. Yes, n= 2,751	333 (31.1)	567 (33.7)	0.155
Patient history			
Family affected by axSpA. Yes, n= 2,244	425 (48.1)	450 (33.1)	**<0.001**
Years living with axSpA, n= 2,716	21.0 ± 13.2	14.8 ± 11.2	**<0.001**
Diagnostic delay, n= 2,652	8.6 ± 8.9	6.7 ± 8.1	**<0.001**
PROs			
BASDAI (0-10), n= 2,584	5.4 ± 2.0	5.5 ± 2.0	0.064
GHQ-12, n= 2,640	4.7 ± 4.0	5.1 ± 4.2	**0.036**
Spinal Stiffness (3-12), n= 2,660	8.0 ± 2.4	7.6 ± 2.5	**<0.001**
Comorbidities			
Anxiety. Yes, n= 2,718	299 (27.8)	510 (31.1)	0.068
Depression. Yes, n= 2,714	277 (25.7)	433 (26.5)	0.672
Sleep disorder. Yes, n= 2,713	413 (38.8)	645 (39.1)	0.876
Treatments			
Biologics (ever). Yes, n= 2,316	392 (49.1)	561 (37.0)	**<0.001**

Table 2. Logistic regression analysis for variables associated with PO membership (N=1,654)

	Univariable analysis		Multivariable analysis	
	OR	95% CI	OR	95% CI
Gender. Male	1.21	**1.04, 1.42**	1.10	0.88, 1.38
Marital status. Married	1.51	**1.28, 1.79**	1.25	0.99, 1.57
Overweight/Obesity	1.25	**1.08, 1.46**	0.95	0.77, 1.19
Physical activity. Yes	1.71	**1.39, 2.10**	1.43	**1.07, 1.92**
Family affected by axSpA. Yes	1.87	**1.57, 2.23**	1.34	**1.07, 1.68**
Years living with axSpA	1.04	**1.04, 1.05**	1.03	**1.02, 1.05**
GHQ-12 (0-12)	0.98	**0.96, 0.99**	0.99	0.96, 1.01
Spinal Stiffness (3-12)	1.07	**1.04, 1.10**	1.01	0.97, 1.06
Diagnostic delay, years	1.03	**1.02, 1.04**	0.99	0.98, 1.01
Biologics (ever). Yes	1.64	**1.38, 1.95**	1.87	**1.50, 2.32**

reported outcomes [BASDAI (0-10), spinal stiffness (3-12), and mental health through GHQ-12 (0-12)], employment, lifestyle habits, comorbidities, and treatments between PO members/non-members were assessed through Mann-Whitney and Pearson's χ^2 tests. Univariable and multivariable binary logistic regression were used to identify variables possibly explaining PO membership.

Results: 1,654 patients were included. Mean age was 43.0 (±12.3) years, 59.6% were female, 46.8% had a university degree, and 66.5% were married. 1,107 patients (38.9%) were members of a PO. Compared to non-members, members were more frequently male (41.5% vs 36.9%, p=0.014), married (73.3% vs 64.5%, p< 0.001), more overweight/obese (55.6% vs 50.0%, p=0.003), physically active (86.4% vs 78.9%, p< 0.001), had relatives affected by axSpA (48.1% vs 33.1%), longer disease duration (21.0 vs 14.8 years, p< 0.001), better mental health (4.7 vs 5.1, p=0.036), longer diagnostic delay (8.6 vs 6.7, p< 0.001), and were more likely to have ever taken biologics (49.1% vs 37.0%, p< 0.001). In the multivariable logistic regression analysis, the variables associated with PO membership were having ever taken biologics (OR= 1.87), being physically active (OR= 1.43), having relatives affected by axSpA (OR= 1.34), and disease duration (OR= 1.03).

Conclusion: PO members were more likely to have advanced disease, as suggested by the disease duration. Greater experience with biologics among PO members could be attributed to higher disease severity but also to having access to lay-level information on treatment options. Notably, members were also more likely to engage in physical activity, a complementary treatment strongly promoted by POs and recommended by ASAS/EULAR. Engaging patients earlier and throughout their disease journey is likely to improve long-term health and quality of life.

Disclosure: M. Garrido-Cumbrera, None; **S. Makri**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **C. Bundy**, Abbvie, 2, Celgene, 2, Janssen, 2, Lilly, 2, Novartis, 2, Pfizer, 2; **L. Christen**, Novartis, 3; **S. Sanz-Gomez**, None; **J. Correa-Fernández**, None; **R. Mahapatra**, None; **C. Delgado-Domínguez**, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5.

Abstract Number: 0368

Geographical Prevalence of Family History in Patients with Axial SpA and Its Association with HLA-B27: Data from the Worldwide ASAS-perSpA Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Research has shown that in patients with axial spondyloarthritis (axSpA), the most common form of spondyloarthritis (SpA) in a family history is axSpA. Moreover, the association between a positive family history of spondyloarthritis (PFH) and HLA-B27 carriership is driven by a PFH of axSpA and possibly acute anterior uveitis (AAU), but not by other forms of SpA. However, this research was limited to mostly Western European patients and it is unknown if this holds true in axSpA patients in other parts of the world. Therefore, we aimed to investigate the impact of geographical region on family history and its association with HLA-B27 carriership in patients with axSpA around the world.

Methods: Data from the Assessment in SpondyloArthritis international Society (ASAS) peripheral involvement in Spondyloarthritis (ASAS-perSpA) study was used. Analyses were restricted to patients with an axSpA diagnosis who had information available on HLA-B27 status and family history. The frequencies of any PFH, as well as a PFH for axSpA, psoriasis, AAU, inflammatory bowel disease (IBD) and reactive arthritis (ReA), were determined per geographical region. Logistic regression models were built to assess the effect of HLA-B27 status on the occurrence of any PFH and occurrence of each disease in a PFH in the total population and also stratified per geographical region.

Results: In total, 2,048 patients were included from 4 regions: Asia (n=545), Europe & North America (n=840), Latin America (n=202), and Middle East & North Africa (n=461). Patients had a median age (IQR) of 40 (31-50) years, 31% were female, and had a disease duration of 11 (5-20) years.

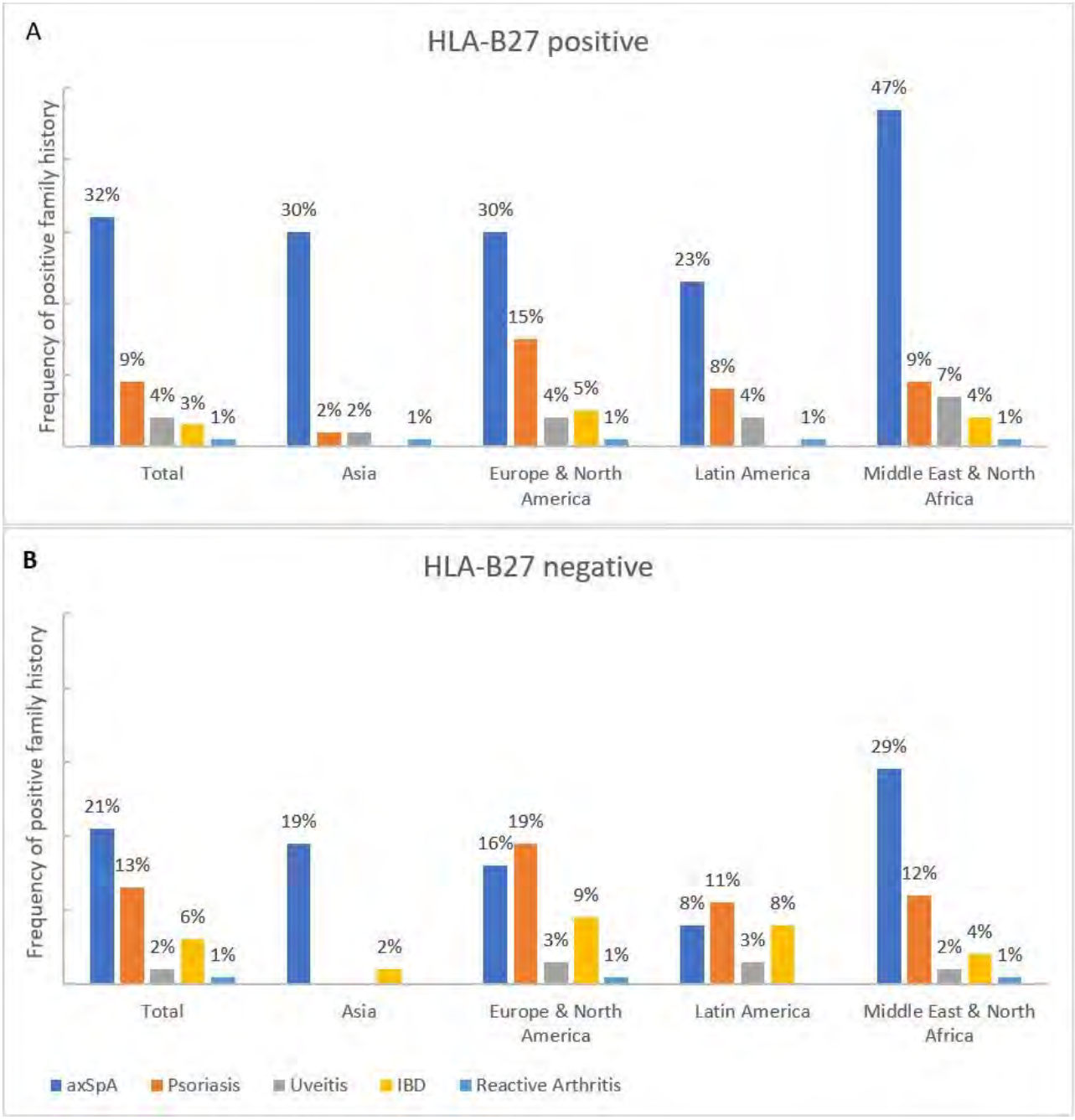

Figure. Frequency of positive family history per disease split per region for HLA-B27 positive patients (A) and HLA-B27 negative patients (B).

A PFH of axSpA was the most common in all geographical regions, regardless of HLA-B27 carriership. A PFH of psoriasis and IBD appeared to be more common in HLA-B27 negative patients, and a PFH of ReA was rare in all patients (Figure).

Univariable logistic regression models showed an association between a PFH and HLA-B27 carriership in the Asian population, but this association does not seem apparent in the other geographical regions (Table). Contrary, a PFH of axSpA was associated with HLA-B27 carriership in all geographical regions except the Middle East & North Africa (Table). An association between HLA-B27 carriership and a PFH of psoriasis was solely present in Middle East & North Africa (OR=0.4, 95% CI 0.2-0.7), and an association with a PFH of IBD was solely present in Europe & North America (OR=0.5, 95% CI 0.3-0.9). No associations were found for HLA-B27 carriership and a PFH of AAU and ReA in any geographical region.

Table Univariable associations between HLA-B27 carriership and a positive family history of axSpA patients in the ASAS-perSpA cohort stratified per geographical region

	HLA-B27+ n=1,609	HLA-B27- n=439	OR (95% CI)	p-value
Any positive family history				
Total population				
Yes	**631**	**149**	**1.26 (1.01-1.57)**	**0.044**
No	978	290	Ref.	
Per geographical region				
Asia	**157/487**	**11/58**	**4.23 (2.26-7.91)**	**<0.001**
Europe & North America	270/658	67/182	1.19 (0.89-1.61)	0.241
Latin America	50/164	9/38	1.65 (0.80-3.39)	0.175
Middle East & North Africa	154/300	62/161	0.74 (0.53-1.02)	0.063
Positive family history for axSpA				
Total population				
Yes	**518**	**90**	**1.84 (1.43-2.38)**	**<0.001**
No	1,087	348	Ref.	
Per geographical region				
Asia	**144/487**	**11/58**	**4.19 (2.24-7.83)**	**<0.001**
Europe & North America	**196/658**	**30/182**	**2.09 (1.40-3.13)**	**<0.001**
Latin America	**37/164**	**3/38**	**3.95 (1.21-12.89)**	**0.023**
Middle East & North Africa	141/300	46/161	0.98 (0.69-1.40)	0.917

axSpA, axial spondyloarthritis; **CI,** confidence interval; **HLA-B27,** human leucocyte antigen B27; **OR,** odds ratio

Conclusion: Throughout the world, axSpA was the most common form of SpA in a family history. In all regions except one, a PFH of axSpA was associated with HLA-B27 carriership in axSpA patients. These results suggest that the current expert definition of a PFH of SpA should be revaluated.

Disclosure: M. van Lunteren, None; **A. Boel**, None; **C. López Medina**, None; **J. Sieper**, AbbVie, 2, 5, 6, Merck, 2, 5, 6, Pfizer, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6, Roche, 2, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **F. van Gaalen**, Stichting ASAS, 5, Stichting vrienden van Sole Mio, 5, Jacobus stichting, 5, Novartis, 5, UCB, 5, Abb Vie, 12, personal fees, MSD, 12, personal fees, Bristol Myers Squibb, 12, personal fees, ASAS EC, 2, ASAS treasurer, 2.

Abstract Number: 0369

High Frequency of Complications in Axial Spondyloarthropathy Pregnancies: Emerging Data from the Ankylosing Spondylitis Registry of Ireland

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: National registries are excellent sources of data to allow analysis of inflammatory arthritis such as axial spondyloarthropathy (axSpA). Our understanding of axSpA has evolved rapidly over time resulting in improved recognition of the disease. Unfortunately, for women with axSpA there is limited data on pregnancy outcomes in this population. To address this issue, data was collected on pregnancy within the Ankylosing Spondylitis Registry of Ireland (ASRI), which is a source of epidemiological data on axSpA in Ireland. The aim of this study is to examine the prevalence of pregnancy and fetal complications in females with axSpA.

Methods: The ASRI records information on baseline demographics, imaging, medications, patient outcomes and comorbidities. To be considered for enrolment patients must have been diagnosed with axSpA by a Rheumatologist and meet the ASAS criteria for axSpA. Informed consent was obtained from all patients by a trained investigator, with ethical approval obtained from local hospital ethics committees. A dedicated section within the ASRI collects data on pregnancy, fertility and breastfeeding. Data on these outcomes was then recorded retrospectively for axSpA females enrolled in the ASRI.

Results: At the time of analysis 220 females were enrolled in the ASRI, representing 24.3% of the total population of the registry. Mean age of females was 43.9 years, with a mean disease duration of 18 years and mean delay to diagnosis 7.86 years. 68.6% (151) had radiographic sacoiliitis, while 49.5% (109) had sacroiliitis on MRI. Mean scores for females in the ASRI were: BASDAI 4.6, BASFI 3.82, BASMI, HAQ 0.6, and ASQoL 7.65.

Data on pregnancy was available in 76 women, with 61 women reporting a total of 210 pregnancies resulting in 166 live births. Of these pregnancies 58.1% (122) were uncomplicated and 41.9% (88) were complicated, with 11.4% (24) of pregnancies encountering multiple complications (figure 1).

The frequency of miscarriage was high affecting 20.5% (43) of pregnancies overall in 37.7% (23) of women with a history of pregnancy. Of the pregnancies resulting in live births, the most common pregnancy complication was caesarean section in 10.8% (18) followed by preterm delivery in 11.4% (15), while the most common fetal complication was NICU admission in 11.4% (19) (figure 2). Only 4 women (5.3%) reported difficult conceiving and need for fertility specialist referral, but none underwent assisted reproductive therapy. Prevalence of breastfeeding was low, reported in 33.7% (56) of live births.

Conclusion: Data from the ASRI indicates a high frequency of pregnancy and fetal complications in women with axSpA. These results represent a preliminary analysis of pregnancy outcomes in axSpA pregnancies collected via a

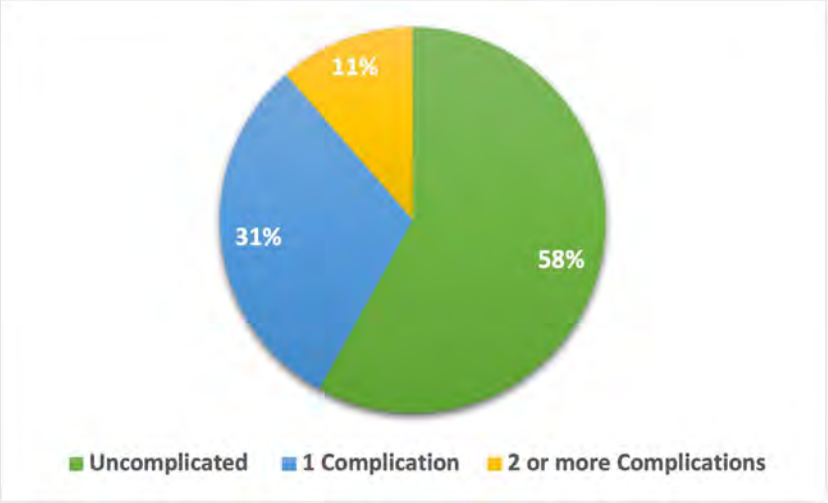

Figure 1. Frequency of Complications per Pregnancy.

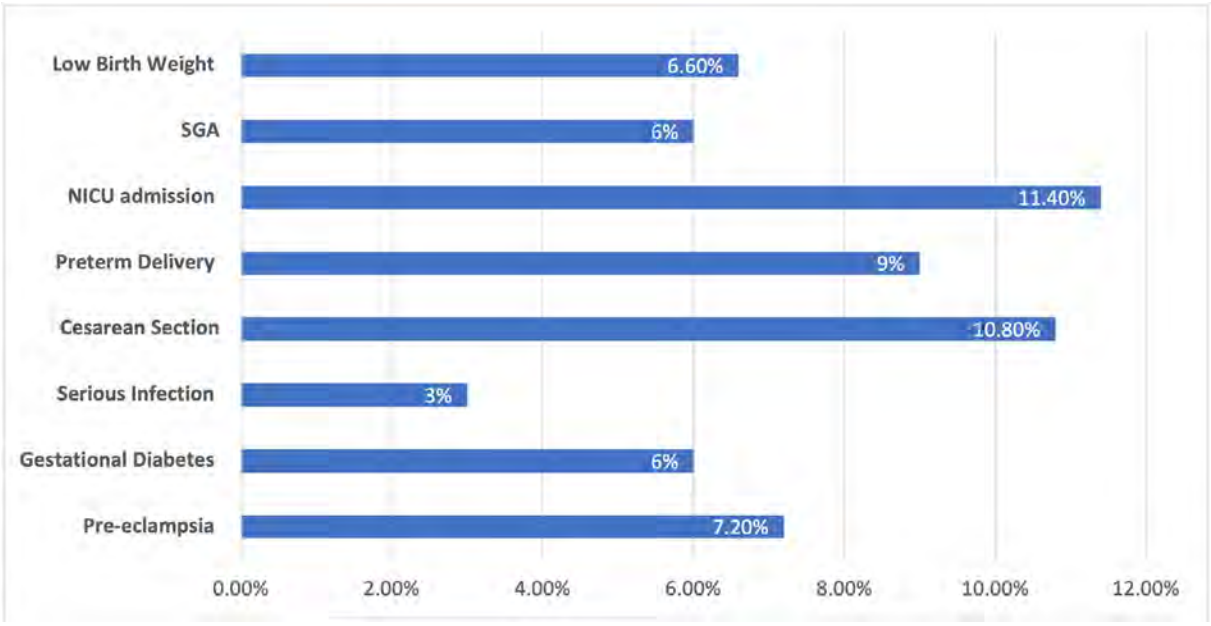

Figure 2. Prevalence of Pregnancy & Fetal Complications in Pregnancies resulting in Live Births.

large national registry. Ongoing data collection will allow comparison to national averages. This provides much needed insight into the impact of axSpA on pregnancy, which can be used to improve monitoring and management of axSpA women during their pregnancies. Furthermore, data on prevalence of breastfeeding can be used to encourage discussion of benefits and safety while on medication of breastfeeding between Rheumatologists and axSpA women.

Disclosure: S. Maguire, Gilead, 5; **P. Gallagher**, None; **F. O'Shea**, None.

Abstract Number: 0370

Awareness and Attitudes Regarding Axial Spondyloarthritis Among Primary Care Providers

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: There is significant discrepancy between population and diagnostic prevalence of axial spondyloarthritis (axSpA) and ankylosing spondylitis (AS) in the US. Delayed and missed diagnosis of axSpA in clinical practice may result from lack of timely referral by non-rheumatologists. Primary care providers (PCPs) are the main source for referral of back pain patients to rheumatologists in the US. In this study, we aim to assess knowledge, awareness and attitudes about axSpA among PCPs to identify gaps in knowledge and devise strategies for early referral.

Methods: In this ongoing study, we distributed a HIPAA compliant secure electronic survey created through Yale Qualtrics Survey tool to select PCPs within several academic institutions and affiliated practices. Our survey includes questions on demographics, practice setting, practice patterns and knowledge assessment surrounding axSpA.

Results: One hundred and thirty-eight providers completed the survey, with response rate of 40%. Among respondents, 68% were female, 76% MDs and 24% advanced practioners. Practice setting included 21% in academic practice and 46% in multi-specialty group. PCPs at different stages in their careers were surveyed. Twenty two percent saw < 30 patients/week, 55% saw 30-60 patients/week and 22% saw 61-90 patients/week. Ninety six percent were at least somewhat familiar with the term inflammatory back pain (IBP). Fifty eight percent reported that they never or rarely assess for IBP; 40% reported that they are not comfortable with making the diagnosis of IBP. Majority (83%) never or rarely ordered HLA B27, and 65% never or rarely ordered CRP for young patients with chronic back pain. Seventy six percent ordered X-ray lumbar spine at least often, and 54% rarely or never ordered MRI lumbar spine in chronic back pain patients. Seventy two percent rarely or never ordered X-ray sacroiliac joint and 97% rarely or never ordered MRI sacroiliac joint. At least fifty percent reported that they never or rarely asked about peripheral arthritis, psoriasis or inflammatory back pain, and at least 75% reported that they rarely or never asked about uveitis or enthesitis. Fifty percent of the providers reported that they never or rarely asked about family history of spondyloarthritis. Forty six percent were not familiar with the change in nomenclature around the terms axSpA and AS. Forty percent were not comfortable with making diagnosis of AS, and seventy percent were not comfortable with making diagnosis of AxSpA.

Conclusion: Our preliminary results confirm lack of knowledge and awareness regarding IBP and changed nomenclature of axSpA among PCPs. PCPs may not be evaluating chronic back pain patients for axSpA, which can contribute to lack of referral and delay in diagnosis.

Disclosure: Y. Afinogenova, None; **S. Alexander**, None; **N. Maheshwari**, None; **S. Kiwalkar**, None; **A. Danve**, Abbvie, 1, Novartis, 5, 6.

Abstract Number: 0371

Self-referral Strategy for Early Diagnosis of Axial Spondyloarthritis- Preliminary Analysis from Finding Axial Spondyloarthritis Study

Yuliya Afinogenova[1], Swetha Ann Alexander[2], Andrew Haims[3] and Abhijeet Danve[4], [1]Yale School of Medicine, Hamden, CT, [2]University of Connecticut, Hartford, CT, [3]Yale School of Medicine, New Haven, CT, [4]Yale University, Rocky Hill, CT

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

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Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Patient Flow Chart

	Total	MyChart	Facebook
Total number of survey responses	634	332	302
Mean age (years)	44.3±13.4	44.2±13.7	44.5±12.9
Positive pre-screen (out of total survey responses)	428	206 (62%)	222 (74%)
Positive A-tool (out of total survey responses)	268	132 (40%)	136 (45%)
Seen for a visit (out of positive A-tool)	51	31 (23.5%)	20 (14.7%)

Background/Purpose: Lack of timely rheumatology referral for suspected axial spondyloarthritis (axSpA) is a major contributor to delayed diagnosis in patients with chronic back pain (CBP). Poor disease awareness among non-rheumatologists and busy practice patterns adversely affect referral process. In ongoing Finding Axial Sponyloarthri-

Table 2. Patient Characteristics of Those with AxSpA and without AxSpA Diagnosis following Physician Visit, Labs and Imaging

	AxSpA (n=15)	No AxSpA (n=28)	Total (n=43)
Age, years, mean±SD	47.47±8.77	38.54±10.13	41.65±10.49
Gender (%Female)	11 (73.30%)	20 (71.40%)	31 (72.10%)
Ethnicity (%Non-Hispanic)	14 (93.30%)	22 (78.60%)	36 (83.70%)
Age at onset of back pain, mean±SD	33.73±6.03	24.89±7.0	27.98±7.86
Clinically Inflammatory back pain	13 (86.7%)	16 (61.5%)	29 (70.7%)
Peripheral arthritis (past or present)	8 (53.3%)	10 (35.7%)	18 (41.9%)
Enthesitis (past or present)	8 (53.3%)	17 (60.7%)	25 (58.1%)
Dactylitis (past or present)	3 (20.0%)	0 (0.0%)	3 (7.1%)
Psoriasis	1 (6.7%)	3 (10.7%)	4 (9.3%)
Uveitis	0 (0.0%)	0 (0.0%)	0 (0.0%)
UC/CD	1 (6.7%)	0 (0.0%)	1 (2.3%)
Family history of psoriasis, IBD or AS)	7 (46.7%)	14 (50.0%)	21 (48.8%)
Positive HLA B27	3 (20.0%)	0 (0.0%)	3 (7.0%)
CRP, mean±SD	5.27±6.54	3.98±4.36	4.44±5.2
BASDAI, mean±SD	5.30±2.38	5.77±2.23	5.61±2.27
BASFI, mean±SD	3.33±2.21	4.15±1.81	3.86±1.97
BASMI, mean±SD	2.33±0.91	2.21±0.84	2.26±0.85
RAPID3 total score, mean±SD	11.85±5.61	14.09±4.85	13.31±5.17
Fulfilled ASAS inflammatory back pain criteria	14 (93.3%)	21 (80.8%)	35 (85.40%)

tis (FaxSpA) study, we are evaluating the effectiveness of a self-referral strategy where the screening tool is directly distributed to at risk patients using electronic medical record and social media.

Methods: In a prospective single center study, we developed a screening tool (A-tool) that consists of 3 question prescreen and 8 question screening questionnaire (SQ). Patients who pass all questions in prescreen can access the SQ. A-tool is considered positive in case of 3 or more positive responses to SQ. A-tool is distributed online via patient portal (Mychart) to those age 18 to 65 yr with CBP listed on the problem list. A-tool is also distributed via Facebook to those in our geographical area. Patients with positive A-tool are contacted to confirm eligibility and are invited for a visit. Patients with known diagnosis of axSpA, age >65 yr and previous spine surgery are excluded. Patients undergo history and physical, labs (CRP and HLA-B27) and imaging studies (X-ray and MRI of pelvis). Clinician's judgement is considered gold standard for diagnosis of axSpA. DNA and plasma samples are stored for biomarker research. Statistical analysis was done with descriptive statistics, T-test and chi-square tests.

Results: Total 634 patients took the survey through MyChart (52%) or Facebook (48%) from April 2019 to March 2020 (Table 1). Among the responders, 428 (68%) had positive pre-screen and 268 (42%) had positive A-tool. We were unable to reach 90 subjects. Sixty-seven were ineligible after a phone interview (11 had confirmed axSpA, 15 had previous surgery, 18 changed answers to A-tool). Another 38 were unable to come or were no longer interested. As of November 2020, 51 patients came for study visit and 43 completed labs and imaging. Out of 43 patients, 15 (34.9%) were diagnosed with axSpA (6 with AS and 9 with nr-axSpA) (Table 2). There was a trend suggesting that as the number of positive responses on SQ increases, likelihood of axSpA diagnosis was greater.

Conclusion: Our preliminary findings suggest that A-tool based self-referral strategy for early diagnosis of axSpA among patients with CBP is practical and feasible approach. We need larger prospective study to validate our findings and confirm the effectiveness of the A-tool based referral strategy.

Disclosure: Y. Afinogenova, None; **S. Alexander**, None; **A. Haims**, None; **A. Danve**, Abbvie, 1, Novartis, 5, 6.

Abstract Number: 0372

Impact of Gender and Age on Ankylosing Spondylitis Patient Profiles at Golimumab Initiation and 12-Month Outcomes

Ariel Masetto[1], Proton Rahman[2], Michelle Teo[3], Pauline Boulos[4], Emmanouil Rampakakis[5], Meagan Rachich[6], Allen Lehman[6], Francois Nantel[7] and Odalis Asin-Milan[6], [1]Universite de Sherbrooke, Sherbrooke, QC, Canada, [2]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [3]Penticton Regional Hospital, Penticton, BC, Canada, [4]., Hamilton, ON, Canada, [5]JSS Medical Research, Montréal, QC, Canada, [6]Janssen Inc., Toronto, ON, Canada, [7]., Montréal, QC, Canada

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

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Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Gender and age have been previously identified as independent predictors of response to anti-TNFs. The aim of this analysis was to compare, between genders and age groups, the profile and outcomes of ankylosing spondylitis (AS) patients treated with golimumab during routine Canadian care.

Methods: This is a post-hoc analysis of data from the Biologic Treatment Registry Across Canada (BioTRAC). Patients with AS who initiated treatment with subcutaneous golimumab were included. Patients were grouped into age tertiles (Young: 18.5–39.1 years; Middle: 39.2–51.2; Old: 51.3–90.2) and further stratified by gender. The impact of age and gender on outcomes (ASDAS clinically important improvement [CII; $\Delta \geq 1.1$], major improvement [MI; $\Delta \geq 2.0$], and HAQ< 0.5) and treatment retention were assessed with multivariate logistic and cox regressions, respectively, adjusting for age tertile, gender, HLA-B27 and respective outcome at baseline.

Results: 421 patients were included with a mean (SD) age of 45.7 (13.3) years and disease duration of 6.0 (10.1) years. Across age tertiles, significant differences ($p < 0.05$) were observed at baseline in disease duration, employment status, insurance coverage, previous smoking status, number of previous DMARDs, previous use of NSAIDs or MTX, concomitant use of DMARDs or oral steroids, and BASFI. Gender, RF status, anti-CPP status, family history, current smoking status, previous use of DMARDs or oral steroids, experience with biologics, concomitant NSAIDs or MTX, ASDAS, BASDAI, HAQ, enthesitis, and dactylitis were comparable. Between genders, significant differences were observed in weight, current/previous smoking status, and BASDAI.

Based on multivariate regression, patients in Young age tertile vs. Old were more likely to achieve ASDAS-MI at 12 months (OR [95% CI]: 3.53 [1.00–12.41]) and HAQ< 0.5 at both 6 (2.84 [1.37–5.89]) and 12 (2.63 [1.22–5.70]) months. Achievement of ASDAS-MI at 12 months was also more likely among male patients (4.16 [1.31–13.23]). There was no impact of gender or age tertiles on ASDAS-CII achievement.

With respect to treatment retention, male patients were more likely to stay on golimumab treatment (HR [95%]: 2.32 [1.11-4.76]). However, age tertile was not associated with retention.

Across age tertiles, AE incidence was comparable; however, SAE incidence was substantially higher among older patients. Between genders, AE incidence was lower among males, with no differences in SAE incidence.

Conclusion: Significant variations in baseline characteristics, treatment outcomes, and safety profile exist across age groups and gender.

Disclosure: A. Masetto, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Amgen, 5, Merck, 5, Teva, 5; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **M. Teo**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 5, Eli Lilly, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 2, 5; **P. Boulos**, Janssen, 1, 6; **E. Rampakakis**, None; **M. Rachich**, Janssen, 3, 11; **A. Lehman**, Janssen Inc., 3; **F. Nantel**, None; **O. Asin-Milan**, Janssen, 3.

Abstract Number: 0373

Self-monitoring of Disease Activity with a Smartphone App Is Feasible in Routine Clinical Management of Patients with Axial Spondyloarthritis – a Proof of Concept Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Assessment and monitoring of disease activity and functioning is of major importance for qualified management of patients with axial spondyloarthritis (axSpA). This includes tight control strategies with strict monitoring and adaptation of therapy. Although closer monitoring is superior to routine care, more intensive treatment schedules can often not be realized because of time constraints and shortage of personal resources. Using a health app for the recording of patient reported outcomes (PRO) in clinical routine may facilitate patient monitoring but there is a lack of data on this strategy.

The aim of this study was to investigate the practical use and the adherence to a commercialised health app by axSpA patients with respect to usability, feasibility, and equivalence of data in clinical management.

Table 1. Demographic data of the studied group at baseline and characteristics of app-adherent and non-app-adherent patients Table legend on the bottom: * Values given as mean (SD) otherwise indicated

	Patients (n=69)	adherent (n=20)	non-adherent (n=49)	Significance
Age, years	41.5 (11.3) *	46.1 (10.6)	39.6 (11.2)	**0.040**
Male, n (%)	40 (58%)	12 (60%)	28 (57%)	0.827
Symptom duration, years	16.7 (11.6)	17.8 (12.9)	16.3 (11.2)	0.686
Diagnosis since, years	11.2 (9.8)	12.9 (10.5)	10.5 (9.3)	0.542
University education, n (%)	15 (22%)	4 (20%)	11 (22%)	0.823
Employed, n (%)	49 (71%)	39 (77.6%)	11 (55 %)	0.061
Frequent use of electronic media, n (%)	62 (89.9%)	19 (95%)	43 (87.8%)	0.366
Current use of health apps, n (%)	35 (50.7%)	10 (50%)	25 (51%)	0.939
Biologic DMARD therapy, n (%)	53 (76.8%)	11 (55%)	42 (85.7%)	**0.006**
Patients starting a new therapy at baseline, n (%)	16 (23.2%)	6 (30%)	10 (20.4%)	0.392
ASDAS > 2,1 at Baseline, n (%)	44 (63.8%)	17 (85%)	27 (55.1%)	**0.019**
Elevated CRP at Baseline, n (%)	24 (34.8%)	11 (55%)	13 (26%)	**0.024**

Table 2. Clinical data on face-to-face visits. Table legend on the bottom: * Values given as mean (SD) otherwise indicated. a Due to the COVID-19 pandemic, a part of the visits had to be made by telephone and mail. Thus, for V2 (n=57) and V3 (n=56), CRP and ASDAS values are not available for all patients.

	V1 (n=69)	V2 (n=67)	V3 (n=64)
Pain level (NRS 0-10)	5.0 (2.5) *	4.0 (2.3)	4.3 (2.4)
BASDAI	4.3 (2.0)	3.7 (2.0)	4.1 (2.3)
CRP (mg/dl)	0.7 (1.6)	0.7 (1.9) (n=57)[a]	0.5 (0.8) (n=56)[a]
ASDAS	2.5 (1.0)	2.1 (0.8) (n=57)[a]	2.4 (1.0) (n=56)[a]
NSAID-Score	33.6 (33.4)	37.6 (32.3)	38.4 (31.0)

Methods: Consecutively included patients with a clinical diagnosis of axSpA were asked to submit electronic patient-reported outcomes (ePROs) such as pain and BASDAI scores regularly but at least every 2 weeks over a period of 6 months. All patients were instructed to handle the free of charge AxSpA Live App, a Class I certified medical device, that was available for Android and iOS operating systems. In addition to patient and disease characteristics, information on previous experience with health apps was collected. The first clinical visit was followed by two face-to-face visits, each 3 months apart, in which patients completed BASFI, pain (NRS 0-10), ASDAS, and the Mobile App Rating Scale (MARS) and the System Usability Scale (SUS) to assess the quality and usability of the app.

Results: Out of 103 axSpA patients asked, 69 agreed to use the AxSpA Live App (67%) on a regular basis. Five patients did not have a smartphone, one was unable to download the app for technical reasons, and 28 had other personal reasons (Tables 1 and 2). Among the participating patients 62 reported to use electronic media frequently (89.9%), and they had previously used health apps (mean number of apps used 1.0 ± 1.3). The majority (64 (92.8%))

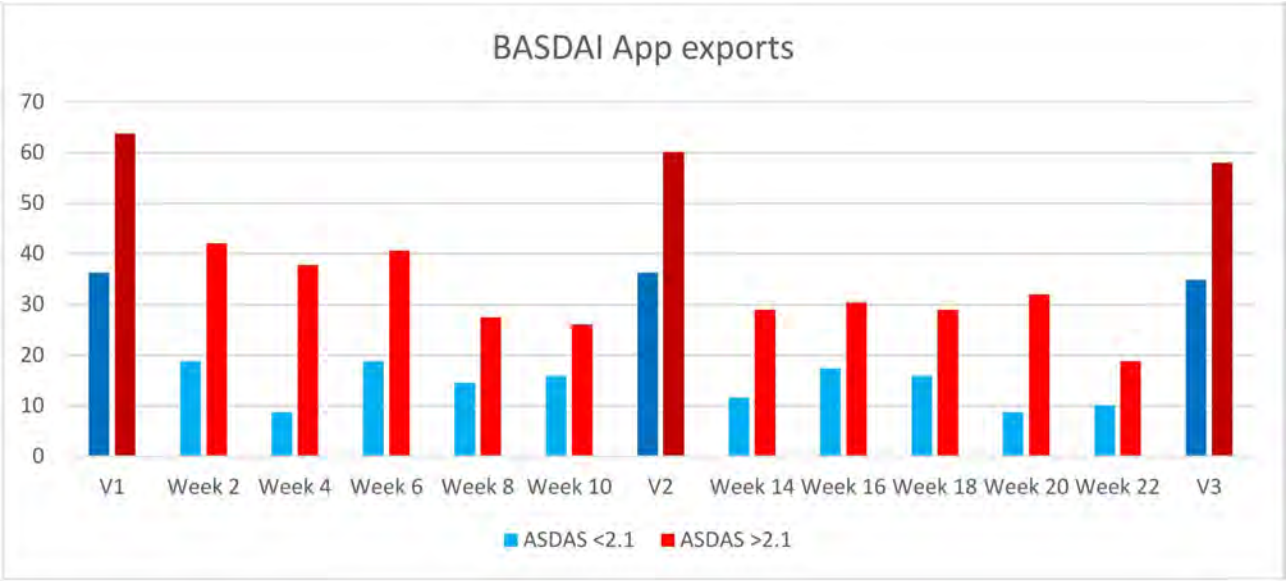

Figure 1. Number of patients with export of electronic BASDAI scores (light colour) and BASDAI scores at face-to-face visit (dark colour) stratified by disease activity.

of patients completed 6 months (92.8%). Patients' adherence for app transmissions every 2 weeks was low, with 29% and 28.6% after 3 and 6 months, respectively. Significant predictors for a good adherence were high disease activity as assessed by ASDAS (P = 0.019) and older age (P = 0.04). There were no systematic differences between BASDAI scores documented on paper or by app (ICC 0.99 (95%CI 0.98 – 0.99). The quality and usability of the app was rated with a mean MARS and SUS scores of 3.6 and 71.2, respectively, which corresponds to a good to acceptable rating.

Conclusion: The majority of patients with axSpA was able to use the AxSpA Live App but adherence over 6 months was poor. Poor adherence rate can possibly be explained by the high number of required transfers. High disease activity and older age had a positive influence on the frequency of reporting. Our data suggest that the use of apps should focus on more severely affected patients. Interventions with use of a digital application seems feasible for axSpA patients with high disease activity who are in need for intensified treatment.

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **R. Kempin**, None; **J. Richter**, Abbvie, 2, Lilly, 2, 6, Pfizer, 6, Sanofi, 2, 6; **A. Schlegel**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **S. Tsiami**, None; **B. Buehring**, None; **D. Kiefer**, None; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5.

Abstract Number: 0374

Validation of the Ankylosing Spondylitis Disease Activity Score with a Quick Quantitative Creactiveprotein Assay (ASDAS-qCRP) in Patients with Axial Spondyloarthritis (axSpA): Aprospective, National, Multi-center Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Disease activity categories by ASDAS-qCRP vs. ASDASCRP

		ASDAS-qCRP (n = 251)			
		Inactive Disease (< 1.3)	Low Disease Activity (1.3 - < 2.1)	High Disease Activity (2.1 - 3.5)	Very high Disease Activity (> 3.5)
ASDAS-CRP	Inactive Disease (< 1.3)	56 (22.3%)	2 (0.8%)		
	Low Disease Activity (1.3 - < 2.1)		62 (24.7%)	7 (2.8%)	
	High Disease Activity (2.1 - 3.5)			97 (38.6%)	
	Very high Disease Activity (> 3.5)				27 (10.8%)

The fields highlighted in red indicate that disease activity categories do not match.
ASDAS = Ankylosing Spondylitis Disease Activity Score, CRP = C-reactive protein, qCRP = quick quantitative CRP

Background/Purpose: According to international recommendations, the Ankylosing Spondylitis Disease Activity Score (ASDAS) is the preferred score for assessing disease activity in axial spondyloarthritis (axSpA) [1]. However, routine determination of C-reactive protein (CRP) to calculate ASDAS values takes hours to days. This limits the use of ASDAS in clinical routine and clinical trials and hinders the implementation of treat-to-target approaches in axSpA.

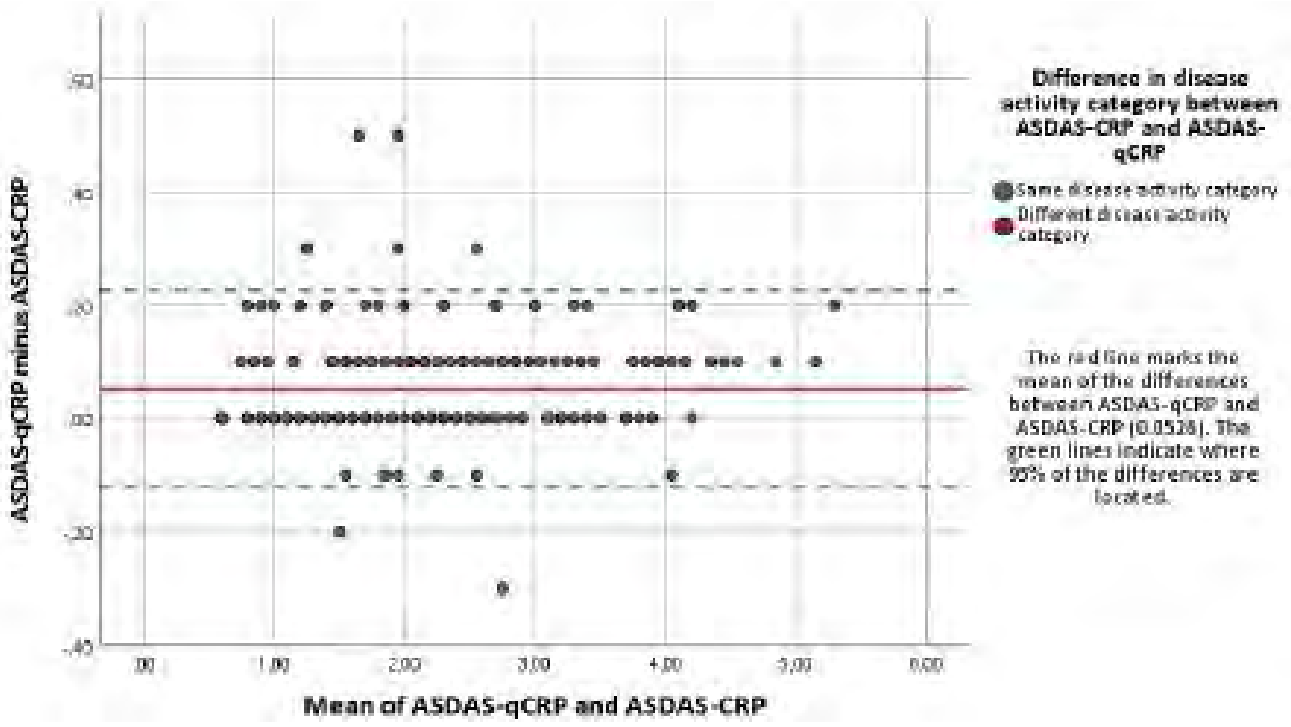

Figure 1. Bland-Altman plot for ASDAS-qCRP and ASDAS-CRP.

Whereas quick quantitative CRP (qCRP) tests allow CRP assessment within a few minutes. In a pilot project the performance of qCRP-based ASDAS assessment (ASDAS-qCRP) was already investigated in a single center study of 50 newly diagnosed, bDMARD-naïve axSpA patients with promising results [2]. Therefore, the objective of our study was to validate the ASDAS-qCRP in a prospective, multicenter study of axSpA patients in a typical axSpA cohort with an appropriate sample size.

Methods: The study was conducted in five centers in Germany. Consecutive adult (≥ 18 years) axSpA patients were included. In addition to a rheumatological assessment, including patient reported outcomes (PROs), routine CRP and erythrocyte sedimentation rate (ESR) were measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument“ (Aidian Oy, Finland) was performed at the study center (measurement range 0.5 - 200 mg/l for hematocrit concentrations of 40 – 45%). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for ASDAS-CRP and ASDAS-qCRP.

Results: In this study 251 axSpA patients were included between January and September 2020 (mean age: 38.4 years; mean disease duration: 6.2 years, 159 patients (63.3%) were male, 211 (84.1%) HLA-B27 positive and 195 (77.7%) were classified as radiographic axSpA). 143 patients (57.0%) were treated with bDMARDs. CRP and qCRP showed mean values of 2.12 and 2.17 mg/l, respectively. With the ASDAS-qCRP, 242 patients (96.4%) were assigned to the same disease activity category as compared to the ASDAS based on the conventional lab CRP measurement (Table 1). Weighted Cohen´s kappa was 0.966 (95%CI: 0.943; 0.988). ICC for ASDAS-CRP- and ASDAS-qCRP-values was 0.997 (95%CI: 0.994; 0.999). The agreement of ASDAS-qCRP and ASDAS-CRP is shown in a Bland-Altman plot (Figure 1).

Conclusion: The ASDAS-qCRP and ASDAS-CRP showed an almost perfect agreement on the assignment to disease activity categories (96%) with the important advantage of time. With ASDAS-qCRP, rheumatologists could base their clinical decision-making on a disease activity measurement by using a composite score immediately. ASDAS-qCRP, therefore, can be integrated in clinical routine and clinical trials in the future and may facilitate implementation of the treat-to-target concept in axial SpA.

References:

1. Smolen JS, et al. Ann Rheum Dis. 2018 Jan; 77(1):3-17.
2. Proft F, et al. Joint Bone Spine. 2019 Jul 29.

Acknowledgements: The authors would like to deeply thank Braun T, Doerwald C, Deter N, Höppner C, Lackinger J, Lorenz C, Lunkwitz K, Mandt B, Sron S and Zernicke J for their practical support and coordinating the study.

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Abstract Number: 0375

Optimizing a Referral Strategy for Patients with a High Probability of Axial Spondyloarthritis: The Role of Age and Symptom Duration

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: One of the most important prerequisites for a timely diagnosis of axial spondyloarthritis (axSpA) is the early referral of a patient with back pain to a rheumatologist. In the past years a number of referral strategies has been proposed, most of them in line with the ASAS referral recommendations [1] and with a similar performance – about 30-40% of the referred patients can be diagnosed with axSpA after examination by a rheumatologist. In addition to physicianbased strategies, an online self-referral (OSR) strategy has been recently proposed and evaluated about 20% of the patients being diagnosed with axSpA after rheumatologic evaluation [2]. The objective of the current analysis was to investigate the role of age and symptom duration for the optimization of a physician-based and an OSR strategy for axSpA.

Methods: In the OptiRef study, patients with chronic back pain and suspicion of axSpA either referred by primary care physicians /orthopedists using the Berlin referral tool (=physician based) or based on a referral recommendation of an OSR were evaluated by rheumatologists in a specialized center [2]. All patients underwent a structured examination including imaging that resulted into the final diagnosis of axSpA or no axSpA. The relationship between age, symptom duration and the likelihood of axSpA diagnosis was evaluated in this analysis.

Table 1. Patient characteristics: Total

	Total N=360	Berlin tool N=180	Self-referral N=180	p-value
Diagnosis of axial SpA, n (%)	106 (29.4%)	71 (39.4%)	35 (19.4%)	<0.0001
Age, years, mean (SD)	36.9 (10.4)	37.2 (11.5)	36.6 (9.2)	>0.99
Male sex, n (%)	177 (49.2%)	100 (55.6%)	77 (42.8%)	0.02
Back pain duration, years, mean (SD)	7.9 (7.6)	6.5 (6.9)	9.2 (8.1)	<0.0001
HLA-B27 positive, n (%)	141 (40.9%)	104 (59.8%)	37 (21.6%)	<0.0001
CRP elevation, n (%)	52 (14.8%)	34 (19.4%)	18 (10.2%)	0.02
Inflammatory back pain, n (%)	204 (56.7%)	103 (57.2%)	101 (56.1%)	0.92

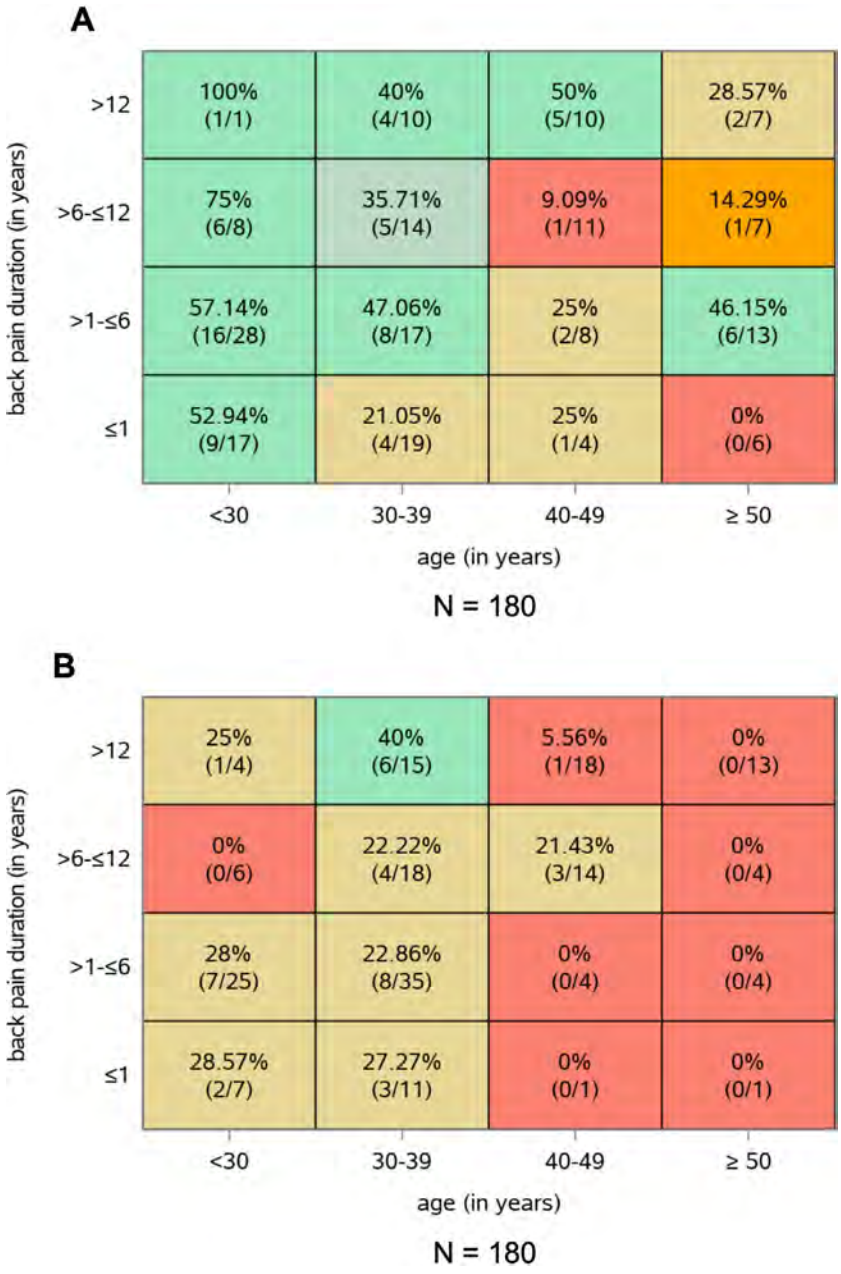

Figure 1. Heatmaps depicting the proportions of patients diagnosed with axSpA in relation to age and symptom duration in the physician-based (A) and OSR (B) groups.

Results: A total of 360 patients (180 presented via the OSR and 180 referred by the physician based referral strategy) were included in this analysis. Patient's characteristics are shown in Table 1. A total of 71 patients (39.4%) in the physician-based group and 35 patients (19.4%) in the OSR group were finally diagnosed with axSpA. The heatmaps depicting the relationship between the proportions of patients diagnosed with axSpA and age plus symptom duration (Figure 1) showed a clear decline of the axSpA probability with increasing age. In the physician-referred group, however, axSpA was diagnosed even in patients who were above 50 years at the timepoint of the examination, while there were only few patients with axSpA in the self-referred group aged 40-49 years, and none in the age group ≥50 years. Interestingly, there was no clear relationship between symptom duration and probability of the diagnosis: axSpA was diagnosed in a substantial proportion of patients even with a long history of back pain (>12 years) in both subgroups.

Conclusion: The probability of axSpA is high in patients suffering from back pain and aged < 40 years with a substantial decline thereafter. Therefore, a referral strategy based on self-evaluation of symptoms should be more focused on a younger patient population, while physician-based strategies do not require such a restriction.

References:

1. Poddubnyy D, et al. Ann Rheum Dis 2015 Aug; 74(8):1483-1487.
2. Proft F, et al. Semin Arthritis Rheum. 2020; 50(5):1015-1021.

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Abstract Number: 0376

Impact of Patient and Disease Characteristics on Global Functioning and Health in Patients with Axial Spondyloarthritis: A Bayesian Network Analysis of Data from an Early axSpA Cohort

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Current knowledge on the health status of patients (pts.) with axial spondyloarthritis (axSpA) mainly focusses on physical function and disease activity. Using a generic measure for physical- or mental health (SF36), a hierarchical relationship between disease activity, spinal damage, spinal mobility, physical function and overall health has been demonstrated in pts. with radiographic axSpA (r-axSpA) [1]. Disease-specific global functioning and health can be assessed in pts. with axSpA using the ASAS Health Index (ASAS HI), which encompasses physical function, as well as aspects of emotional and social functioning and aspects of activity and participation. To build a structural model that visualizes interrelationships of different patient- and disease characteristics with global functioning and health in pts. with early axSpA.

Table 1. Patient and disease characteristics at month 72

	N = 398
Gender (male), N (%)	181 (45%)
Age (years)	40.7 (8.7)
Symptom duration (years)	7.5 (0.9)
BMI (kg/m²)	25.0 (4.6)
ASDAS	2.0 (1.0)
BASFI (0–10)	2.3 (2.1)
BASMI (0–10)	2.5 (1.0)
mSASSS (0-72)	1.0 (3.6)
ASAS HI (0-17)	5.7 (3.9)
good global functioning: ASAS HI ≤5, N (%)	201 (51%)
moderate global functioning: 5< ASAS HI <12, N (%)	160 (40%)
bad global functioning: ASAS HI ≥12, N (%)	37 (9%)
Comorbidity count	1.4 (0.7)

Methods: Data of pts. with axSpA from the DESIR cohort was analyzed, which included information on socio-demographics (age, BMI), disease activity (ASDAS), physical function (BASFI), spinal mobility (BASMI), structural damage (mSASSS), disease-specific global functioning (ASAS HI), and comorbidity count. Information on patient- and disease characteristics was retrieved from the visit performed 72 months after inclusion, which was the first time point of ASAS HI collection. A Bayesian network (BN) was used to obtain insight of the underlying structural model. BNs are probabilistic graphical models consisting of "nodes" (representing specific variables) joined by "edges" (lines

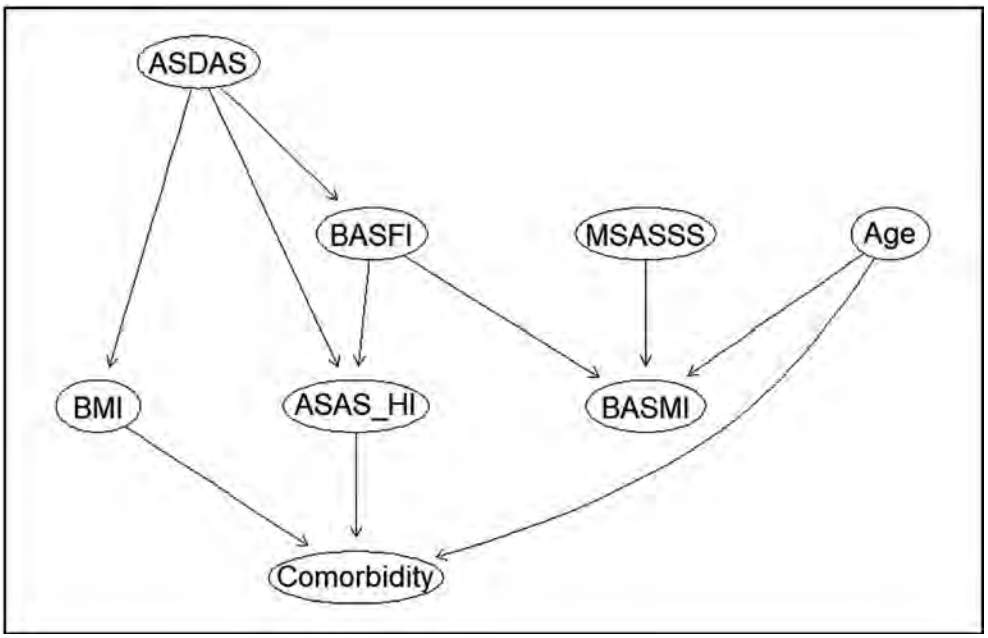

Figure 1. Structural model on interrelationships of different patient- and disease characteristics with global functioning and health (ASAS HI) in patients with early axSpA.

representing directions of effects). They are capable of capturing complex relationships between variables and allow the incorporation of existing (prior) knowledge from previous studies.

Results: The DESIR cohort contained data from 582 pts. at month 72, of whom 398 had data for ASAS HI. Descriptive information of these pts. is shown in Table 1. The mean ASAS HI was 5.7 (range: 0 - 16). Applying existing cut-offs for ASAS HI, 51% had 'good' global functioning (ASAS HI ≥5), 40% had 'moderate' global functioning (5< ASAS HI < 12) and 9% had 'bad' global functioning (ASAS HI ≥12). The structural model that was constructed from combining data and prior expert knowledge is visualized in Figure 1. It suggests that ASDAS and BASFI have a direct effect on ASAS HI as well that ASDAS has an indirect effect via BASFI. Moreover, the model suggests that BMI is also determined by ASDAS, and that BASFI determines BASMI, which is in turn also influenced by age and mSASSS. In addition, it suggests a direct effect of age, BMI and ASAS HI on the comorbidity count. The model denies a relationship between BASMI or mSASSS and ASAS HI.

Conclusion: The BN-analysis approach, that combines prior knowledge and measured data, serves to better understand the construct of global functioning and health in pts. with early axSpA. Our model shows that global functioning (ASAS-HI) is determined both by patient reported physical function (BASFI) and by disease activity (ASDAS), which confirms the hierarchical model once proposed by Machado et al. The observed directional relationship between ASAS HI and comorbidity count is counterintuitive and requires further investigation.

Reference: Machado P, ARD 2011.

Disclosure: I. Redeker, None; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **S. Ramiro**, AbbVie, 2, Eli Lilly, 2, MSD, 2, Novartis, 2, Sanofi, 2, UCB, 2, MSD, 5; **A. Boonen**, None; **M. Dougados**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5.

Abstract Number: 0377

The Prevalence of Inflammatory Back Pain and HLA-B27 in a Large Population-Based Cohort in the Netherlands

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic low back pain (CLBP; back pain >3 months) with onset at age < 45 and inflammatory back pain (IBP) are regarded as early presenting and key features of axial spondyloarthritis (axSpA), and HLA-B27 as its most important genetic risk factor. Despite increasing familiarity with non-radiographic axSpA and the advent of Magnetic Resonance Imaging in demonstrating sacroiliitis, the long delay in axSpA diagnosis has not improved. The objective of this study was to explore the prevalence of CLBP and IBP in combination with HLA-B27 in the general population.

Methods: Participants of the Lifelines cohort, a large population-based cohort of the northern region of the Netherlands, filled out a questionnaire on chronic low back pain and IBP. Chronic low back pain was defined as an affirmative answer to the question 'Did you suffer from low back pain for ≥3 months?'. IBP was questioned based on the validated European Spondyloarthropathy Study Group (ESSG) IBP criteria and was confirmed if at least 4 out of the following 5 criteria were present: (a) onset before age 45, (b) insidious onset, (c) improvement with exercise, (d) associated with morning stiffness, (e) at least 3 months duration. Participants reporting to have been diagnosed with axSpA were identified using variations of the search terms "Bechterew", "spondyloarthritis" and "ankylosing spondylitis". The Illumina global screening array (GSA) beadchip-24 v1.0 was used to genotype genome-wide SNPs in a subset of Lifelines participants. HLA-B haplotypes were imputed using neighboring SNPs with HIBAG, which is an R-package, using published parameter estimates. The predicted HLA-B haplotype was considered valid if the posterior probability was >80%.

Results: 94.277 participants answered the question about CLBP, of which 22.804 (24.2%) participants reported CLBP. CLBP before the age of 45 could be identified in 17.481 (18.6%) participants. Of the 93.665 participants with ESSG questionnaire data available, 13.514 (14.4%) fulfilled the IBP criteria. HLA-B haplotype was determined with high prediction accuracy (posterior probability >0.8) in 29.399 Lifelines participants of which 2.279 (7.8%) were HLA-B27+. In the group of HLA-B27+ participants with CLBP (n=373; 23.2%), 238 (14.8%) also fulfilled the ESSG IBP criteria. Only 11 (4.6%) of these participants reported a previous axSpA diagnosis.

Conclusion: In this large Dutch population-based cohort, 7.8% were HLA-B27 positive, similar to earlier studies. Considerable underdiagnosis of axSpA may be expected since only a minor proportion of HLA-B27+ participants with CLBP fulfilling the ESSG IBP criteria reported to have been diagnosed with axSpA.

Disclosure: S. Kieskamp, Novartis, 5; **S. Arends**, None; **E. Brouwer**, Roche, 2, 6; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2; **I. Nolte**, None; **A. Spoorenberg**, Novartis, 5, Abbvie, 2, Novartis, 2, Pfizer, 2, MSD, 2, UCB, 2, 5.

Abstract Number: 0378

Comparison of Demographic, Clinic and Radiological Features of Axial Spondyloarthritis Patients with and Without Accompanying Familial Mediterranean Fever

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The co-existence rate of Familial Mediterranean Fever (FMF) and axial spondyloarthritis (axSpA) in adults is ranging from 0.5% to 7.5%. Clinical implications of this association in the course of FMF is still a research question. Compared to axSpA, FMF+axSpA tends to have more peripheral joint involvement and start at an earlier age, but may have similar prevalence of psoriasis and inflammatory bowel disease. The aim of this study was to compare of demographic, clinic and radiological features of patients with axSpA and FMF+axSpA.

Methods: A total of 9630 FMF patients was detected according to the ICD-10 code (E85.0) of FMF in Hacettepe University Hospital database. 241 of these patients also had axSpA according to the ICD-10 code (M45). FMF diagnosis was confirmed by Tel- Hashomer criteria. AxSpA diagnosis was confirmed by either presence of sacroiliitis on sacroiliac radiography according to the Modified New York (mNY) Criteria or presence of active sacroiliitis according to ASAS criteria on magnetic resonance imaging. 136 patients were confirmed according to these criterias as having FMF+axSpA. 107 of these patients were previously treated with any biological drugs. As a control group, 102 consequent axSpA patients without FMF previously treated with any biological drugs recorded on the TReasure database, age and sex matched with other group and followed up at our center were included in the analysis. Demographic, clinic and radiological features of those patients in both groups were compared. $p < 0.05$ was considered as statistically significant, correction for multiple comparisons was not performed.

Results: 107 patients (54 (50.5%) female) were included in FMF+axSpA group and 102 patients (50 (49.0%) female) were included in axSpA group. Age at axSpA symptom onset and diagnosis were earlier, disease durations were longer in FMF+axSpA group in our study cohort (Table 1). Frequency of axSpA signs and symptoms were comparable. Amyloidosis was more prevalent in FMF+axSpA group (7.5% vs. 1%, p=0.04). 94 (87.9%) patients in FMF+axSpA group and 98 (96.1%) patients in axSpA group had radiographic sacroiliitis according to mNY criteria (p=0.03). Lumbar mSASSS score was higher and lumbar syndesmophyte frequency were higher in FMF+axSpA group. Severe spinal involvement (BASRI≥4 and total ankylosis) is similar in both groups. Radiologically documented moderate to severe hip disease and total hip replacement were more prevalent in FMF+axSpA group (respectively; 23.4% vs. 4.7%, p< 0.001; 11.2% vs. 2.8%, p=0.016).

Conclusion: Co-existence of FMF and axSpA significantly brought the age of axSpA onset earlier. Radiographic characteristics in FMF+axSpA were found to point a more advanced disease, however a possible bias related to high disease duration of FMF+axSpA. As expected, rate of amyloidosis and hip involvement were higher in FMF+axSpA group.

Table 1. Comparison of demographic, clinic and radiological features of two groups

Demographic, Clinic and Radiological Features	FMF+axSpA (n=107)	axSpA (n=102)	p value
Age [year, median (25-75)]	38 (32-48)	39 (32-48)	0.98
Sex (female) n (%)	54 (50.5)	50 (49.0)	0.84
Age at axSpA symptom onset [year, median (25-75)]	21 (16-29)	27 (21-37)	**<0.001**
Age at axSpA diagnosis [year, median (25-75)]	27 (21-36)	32 (24-43)	**0.001**
Duration after axSpA symptom onset [year,median (25-75)]	15 (10-21)	9 (5-14)	**<0.001**
AxSpA signs and symptoms n (%)			
Enthesitis	30/107 (28.0)	16/66 (24.2)	0.58
Dactylitis	5/107 (4.7)	9/91 (9.9)	0.15
Uveitis	15/107 (14.0)	8/102 (7.8)	0.15
Inflammatory bowel disease	6/107 (5.6)	3/99 (2.9)	0.34
Psoriasis	7/107 (6.5)	15/102 (14.7)	0.055
Amyloidosis n (%)	8 (7.5)	1 (1.0)	**0.04**
AxSpA family history n (%)	24/107 (22.4)	27/101 (26.7)	0.47
HLA B27 (+) n (%)	17/56 (30.4)	41/93 (44.1)	0.09
Sacroiliac radiography n (%)			
mNY criteria positivity	94 (87.9)	98 (96.1)	**0.03**
Bilateral grade 3 and higher	55 (51.9)	28 (27.5)	**<0.001**
mSASSS median (25-75)	6 (2-20) (n=22)	0 (0-9) (n=16)	0.15
Cervical	1 (0-8) (n=42)	0 (0) (n=19)	0.13
Lumbar	3 (0-7) (n=97)	0 (0-4) (n=77)	**0.01**
Syndesmophyte n (%)			
Cervical	19/42 (45.2)	4/19 (21.1)	0.07
Lumbar	20/96 (20.8)	7/77 (9.1)	**0.03**
Bridging syndesmophyte n (%)	18/97 (18.6)	17/92 (18.5)	0.99
BASRI-spinal score ≥4 n (%)	11/97 (11.3)	9/92 (9.8)	0.73
Total ankylosis n (%)	5/97 (5.2)	3/92 (3.3)	0.52
BASRI-hip score median (25-75)	0 (0-3)	0 (0-0)	**<0.001**
Moderate to severe hip disease n (%)	25 (23,4)	5 (4.7)	**<0.001**
Total hip replacement n (%)	12 (11.2)	3 (2.8)	**0.016**

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Abstract Number: 0379

Pain Sensitivity in Axial Spondyloarthritis – Comparisons Between Patients and Controls, Women and Men, and Between Different Pain Groups

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic widespread pain (CWP) is common in axial spondyloarthritis (axSpA). For ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) patients, no differences were found in pain measures, including algometry-assessed pain sensitivity (1), while comparisons versus controls and regarding sex were not reported. The current study aimed to assess differences in pain sensitivity in patients and controls, women and men, and between patients with and without CWP, using different CWP definitions.

Methods: We studied 172 patients with AS/radiographic axSpA and 84 patients with nr-axSpA (modified New York/ASAS criteria) from a well-characterized cohort (2), and 44 controls, frequency-matched for age and sex. All subjects were assessed for pain sensitivity (pain threshold, pain tolerance and temporal summation of pain) by computerized cuff pressure algometry (3), and reported pain intensity, duration, and distribution. The participants were categorized by a mannequin (18 pain sites) (4) into CWP, chronic regional pain or no chronic pain according to the CWP assessment of the 1990 fibromyalgia criteria (CWP1990) and with the novel 2019 CWP criteria (CWP2019) mannequin adopted to 15 pain sites by excluding the chest and adding knees to upper legs (5). Comparisons between patients and controls, women and men, and pain groups defined by CWP1990 and CWP2019 using Student's t-test/Chi-square test, as appropriate.

Results: Characteristics for patients and controls are presented in the Table. Comparisons between patients and controls showed no differences in pain sensitivity measures except a trend ($p=0.056$) towards lower pain threshold for axSpA patients. The patients reported significantly higher pain intensity and more painful sites than controls (≤ 0.001).

Women with axSpA, reported lower pain threshold and tolerance, higher pain intensity, and more painful sites than men (all $p \leq 0.01$). More women also reported CWP than men (CWP1990; 52% vs. 29%/CWP2019; 31% vs. 15%) (Figure 1), but with no difference in pain sensitivity for men and women who reported CWP, irrespective of CWP definition.

A larger group of the axSpA patients reported CWP according to CWP1990 than controls (40% vs. 5%) while 22% of the axSpA patients and none of the controls reported CWP according to CWP2019 (Figure 1). Patients with CWP2019

Table; Characteristics of the study population

	AxSpA patients			Controls
	All n=256	Women n=119	Men n=137	n=44
Male sex, n (%)	137 (54)			24 (54)
Age, years	51 (13)	49 (14)	52 (13)	50 (13)
Symptom duration, years	25 (14)	23 (14)	27 (13)	
ASDAS-CRP	1.8 (0.9)	2.0 (0.9)	1.6 (0.9)	
BASDAI	3.0 (2.2)	3.6 (2.1)	2.4 (2.1)	
BASFI	2.0 (2.2)	2.4 (2.2)	1.7 (2.1)	
BASMI	3.0 (1.6)	2.6 (1.3)	3.3 (1.8)	
EQ-5D	0.73 (0.24)	0.67 (0.26)	0.77 (0.22)	0.92 (0.12)
NRS global, cm (0-10)	3.1 (2.5)	3.8 (2.5)	2.5 (2.4)	1.0 (1.0)
NRS fatigue, cm (0-10)	3.4 (2.8)	4.2 (2.8)	2.8 (2.6)	2.1 (1.8)
NRS pain, cm (0-10)	3.1 (2.6)	3.9 (2.6)	2.5 (2.3)	1.4 (1.6)
Pain sites (0-18)	4.1 (4.1)	5.5 (4.2)	2.9 (3.6)	1.1 (2.1)
Paingroup 1/2/3 (CWP1990), %	31/29/40	17/31/52	44/27/29	65/30/5
Paingroup 1/2/3 (CWP2019), %	31/46/23	17/52/31	44/41/15	65/35/0
Leg PDT, kPa	31.5 (15.1)	28.6 (14.2)	34.3 (15.6)	36.8 (18.3)
Leg PTT, kPa	64.8 (27.2)	57.5 (24.9)	71.8 (27.6)	71.4 (22.9)
TSI	0.62 (0.55)	0.58 (0.62)	0.66 (0.49)	0.49 (0.43)
Ongoing csDMARD, n (%)	54 (21)	31 (26)	23 (17)	
Ongoing bDMARD, n (%)	110 (43)	47 (39)	63 (46)	
Ongoing tsDMARD n (%)	1 (0.4)	1 (0.8)	0	

Mean (S.D.) if not otherwise stated. Missing data, n (%): Symptom duration 1 (0.4%); ASDAS-CRP 10 (4%); BASDAI 11 (4%), BASFI 13 (5%); BASMI 2 (0.8%); NRS Global 6 (2%); NRS Fatigue 6 (2%); NRS pain 6 (2%); Painsites 3 (1%); Paingroup 1990 3 (1%). Paingroup 2019 3 (1%); LegPDT 50 (17%); Leg PTT 50 (17%); TSI 55 (18%). Patients on anticoagulant therapy did not perform the algometry pain sensitivity assessment. AxSpA, axial spondyloarthritis; ASDAS-CRP, ankylosing spondylitis disease activity score using CRP; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; BASMI, Bath ankylosing spondylitis metrology index; EQ-5D, EuroQol 5-Dimensions (British preference set); NRS, Numeric rating scale; Paingroup 1, no chronic pain; Paingroup 2, chronic regional pain; Paingroup 3, chronic widespread pain; CWP, Chronic widespread pain; PDT, pain threshold; PTT, pain tolerance; TSI, temporal summation index; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; bDMARD biologic disease-modifying anti-rheumatic drug; tsDMARD, targeted synthetic disease-modifying anti-rheumatic drug.

had lower pain threshold and tolerance, while patients with CWP1990 only had lower pain tolerance than patients without chronic pain (Figure 2). For temporal summation no differences between any of the groups were found.

Conclusion: Chronic widespread pain is more common in axSpA patients than controls and in women compared to men, irrespective of CWP definition. Despite this, men and women with axSpA and concomitant CWP express similar levels of pain sensitivity. The CWP2019 definition identified a smaller group of patients with high pain sensitivity than CWP1990. CWP2019 may therefore be more accurate in identifying patients with more severe chronic pain.

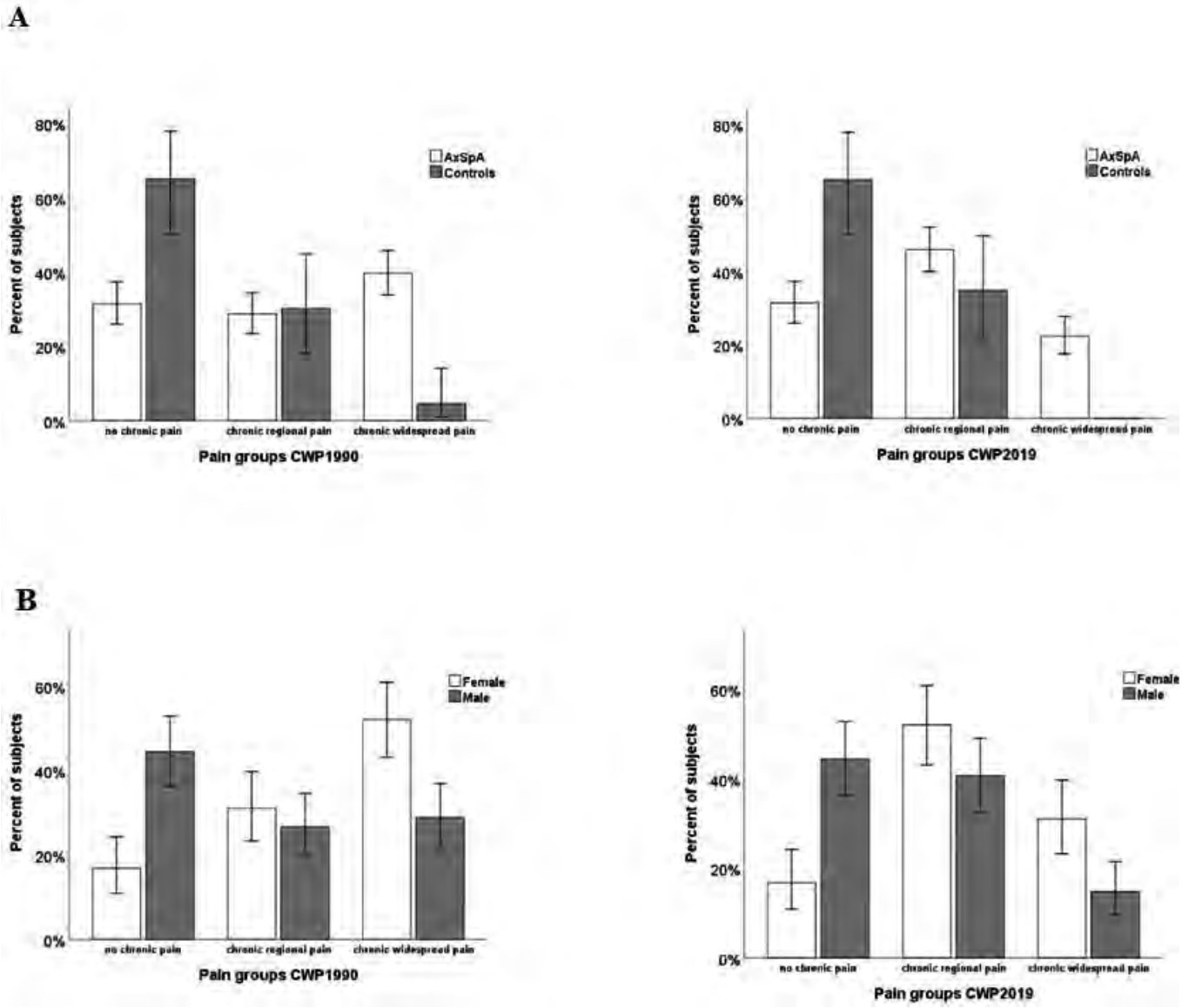

Figure 1. Bar charts showing the distribution in pain groups according to CWP1990 and CWP2019 for A) axSpA patients (AS/radiographic and nr-axSpA combined) and controls, and B) for men and women with axSpA. Error bars with 95% CI (all p≤0.001).

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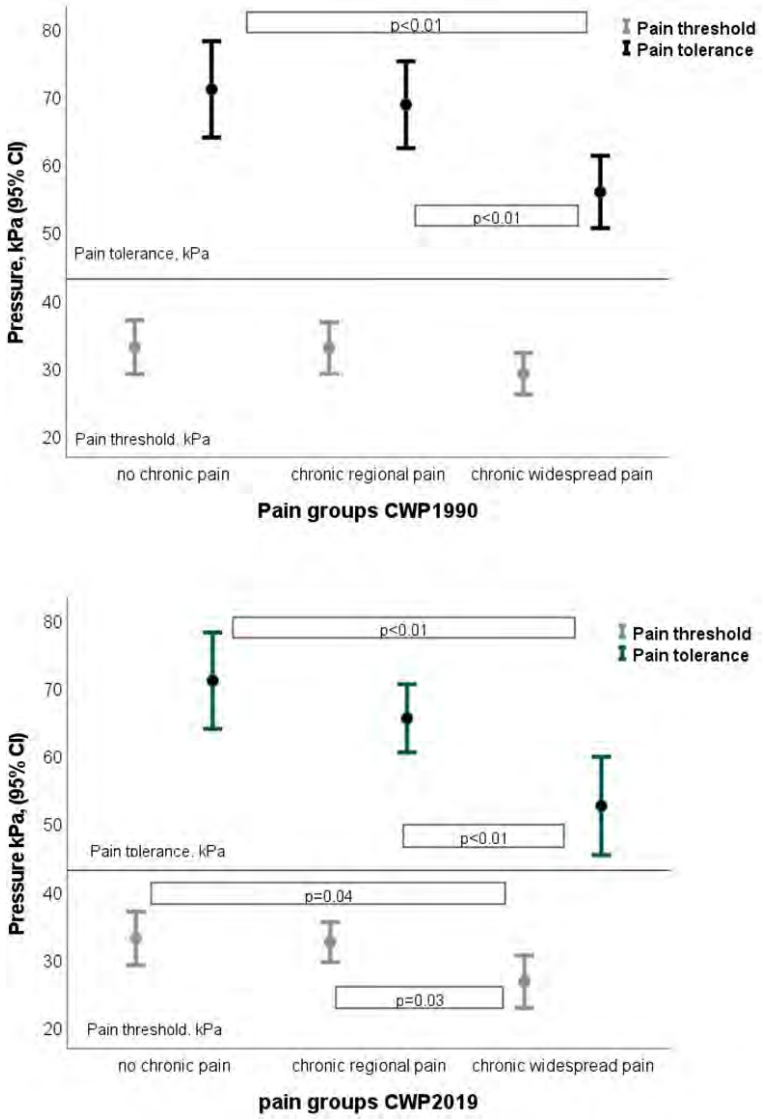

Figure 2. Pain sensitivity (pain threshold and pain tolerance) in patients with AxSpA and chronic widespread pain according to CWP1990 and CWP2019 respectively. Error bars with 95% CI.

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Abstract Number: 0380

Sick Leave and Its Predictors in Early Axial Spondyloarthritis: The Role of Clinical and Socioeconomic Factors. Five-year Data from the DESIR Cohort

Elena Nikiphorou[1], Annelies Boonen[2], PEDRO CARVALHO[3], Bruno Fautrel[4], Pascal Richette[5], Pedro Machado[6], Désirée van der Heijde[7], Robert Landewé[8] and Sofia Ramiro[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Centre+ (MUMC+), Maastricht, Limburg, Netherlands, [3]hospital de Faro, LISBON, Portugal, [4]Pitié Salpêtrière Hospital, APHP, Sorbonne Université, Paris, France, [5]Lariboisiere Hospital, Paris, France, [6]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [7]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands, [8]Amsterdam Rheumatology & Clinical Immunology Center, Amsterdam, Netherlands; Zuyderland MC, Heerlen, Netherlands

SESSION INFORMATION

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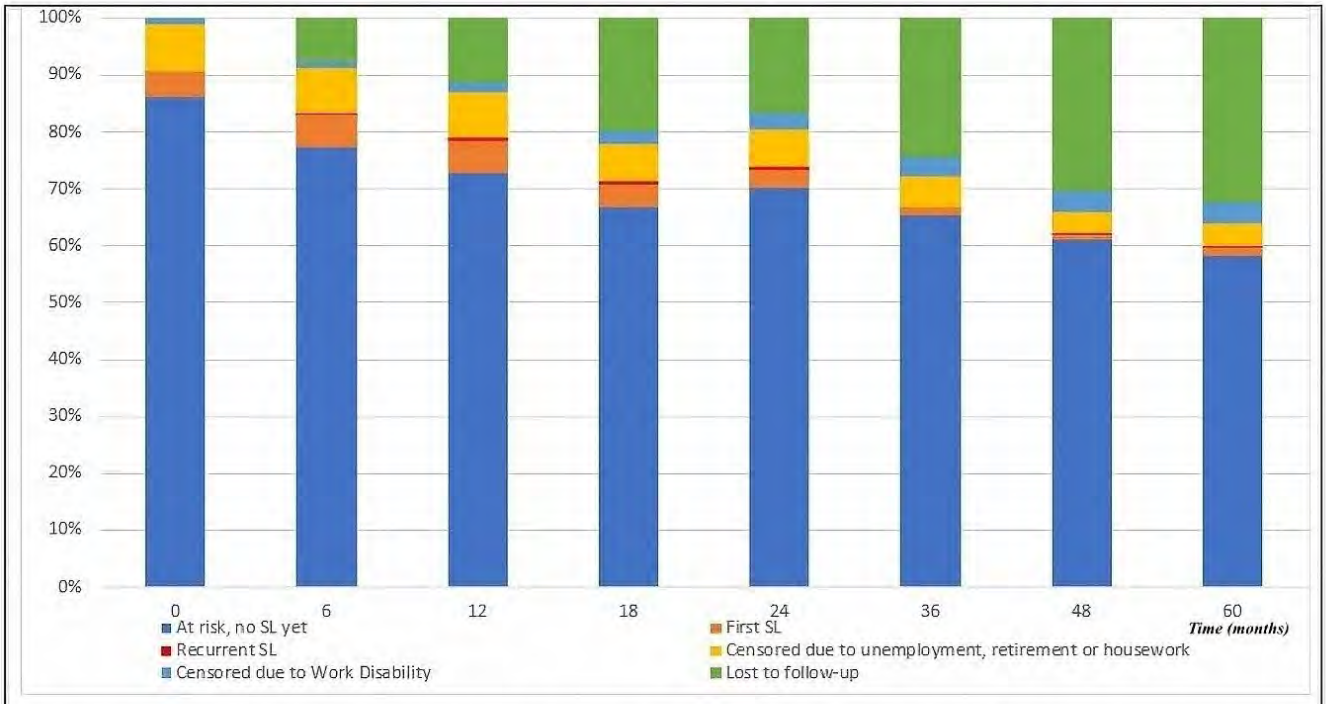
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM



Time (months)	0		6		12		18		24		36		48		60	
Frequency	n	%	n	%	n	%	n	%	N	%	n	%	n	%	n	%
At risk, no SL yet	606	86%	533	77%	502	73%	461	67%	485	70%	461	65%	423	61%	404	58%
First SL	32	5%	40	6%	41	6%	26	4%	21	3%	11	2%	7	1%	10	1%
Recurrent SL	0	0%	2	0%	4	0%	4	0%	5	0%	0	0%	1	0%	2	0%
Censored[1]	59	8%	55	8%	55	8%	45	7%	45	7%	37	5%	26	4%	28	4%
Censored[2]	7	1%	7	1%	10	1%	16	2%	20	3%	25	4%	26	4%	25	4%
Lost to follow-up	0	0%	53	8%	79	11%	137	20%	115	17%	172	24%	211	30%	224	32%
Total	704		690		691		689		691		706		694		693	

SL=Sick Leave; [1]Censored due to unemployment/ retirement/ housework; [2]Censored due to work disability.

Background/Purpose: Sick leave (SL) represents an often poorly studied adverse work outcome especially in early axSpA, with speculation around the potential role of clinical and socioeconomic (SE) factors.

Methods: Patients with a clinical diagnosis of axSpA from the DESIR cohort with work-related data and up to five-year follow-up were studied. Incidence, time to first SL and potential baseline and time-varying predictors were analysed, with a focus on socioeconomic variables (age, gender, ethnicity, education, job-type, marital and parental status). Univariable analyses, followed by collinearity and interaction tests, guided subsequent multivariable time-varying Cox survival model building.

Results: In total, 704 axSpA patients were included (mean (SD) age 33.8 (8.6); 46% male). At baseline, 80% of patients were employed; of these, 5.7% reported being on SL. The distribution of first and recurrent SL episodes over time is shown in Figure 1. The incidence of SL amongst those at risk during the study-period (n=620, 88%) was 0.05 (95% CI 0.03-0.06) per 1000 days of follow-up. Mean (SD) time to first SL was 806 (595) days (range:175-2021 days). In multivariable models, male gender (HR 0.41 (95%CI 0.20-0.86)) and higher education (HR 0.48 (95%CI 0.24-0.95)) were associated with lower hazard of SL, while higher disease activity (HR 1.49 (95%CI 1.04-2.13)), older age, smoking and use of TNFi were associated with higher hazard of SL.

Conclusion: In this early axSpA cohort of young, working-age individuals, male gender and higher education were independently associated with a lower hazard of SL, whereas older age and higher disease activity were associated with higher hazard of SL. The findings suggest a role of socioeconomic factors in adverse work outcomes, alongside active disease.

Disclosure: E. Nikiphorou, Celltrion, 1, Pfizer, 1, 6, Sanofi, 1, Gilead, 1, AbbVie, 1, 6, Lilly, 1, 6, Galapagos, 6; **A. Boonen**, None; **P. CARVALHO**, None; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **P. Richette**, AbbVie, 1, 6, Amgen, 1, 6, Celgene, 1, 6, Janssen, 1, 6, Eli Lilly, 1, 6, MSD, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, AstraZeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **S. Ramiro**, AbbVie, 2, Eli Lilly, 2, MSD, 2, Novartis, 2, Sanofi, 2, UCB, 2, MSD, 5.

Abstract Number: 0381

How Do Clinical and Socioeconomic Factors Impact on Work Disability in Early Axial Spondyloarthritis? Five-year Data from the DESIR Cohort

Elena Nikiphorou[1], Annelies Boonen[2], Bruno Fautrel[3], Pascal Richette[4], Robert Landewé[5], Désirée van der Heijde[6] and Sofia Ramiro[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Centre+ (MUMC+), Maastricht, Limburg, Netherlands, [3]Pitié Salpêtrière Hospital, APHP, Sorbonne Université, Paris, France, [4]Lariboisiere Hospital, Paris, France, [5]Amsterdam Rheumatology & Clinical Immunology Center, Amsterdam, Netherlands; Zuyderland MC, Heerlen, Netherlands, [6]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands

SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: There remains substantial unmet need to study work disability (WD) in early axSpA. Previous studies suggest that treatment interventions alone do not improve work outcomes and that socioeconomic (SE) as well as clinical factors may play an important role.

Methods: Patients from the DESIR cohort with a clinical diagnosis of axSpA were studied over 5 years. Time to WD and potential baseline and time-varying predictors were explored, with a focus on socioeconomic (including ethnicity, education, job-type, marital/parental status) and clinical (including disease activity, function, mobility) factors. Univariable analyses, collinearity, and interaction tests guided subsequent multivariable time-varying Cox survival analyses.

Results: From 704 patients eligible for this study, the estimated incidence of WD amongst those identified at-risk (n=663, 94%) and across the five-years of DESIR, was 0.05 (95% CI 0.03-0.06) per 1000 days. Significant differences in baseline socioeconomic factors, including lower educational status and clinical measures, including worse disease activity, were seen in patients developing WD over follow-up, compared to those who never did. In the main multivariable model, educational status was no longer predictive of WD, whereas the Ankylosing Spondylitis (AS) disease activity score (ASDAS) and the Bath AS functional index (BASFI) were significantly and independently associated with a higher hazard of WD (HR[95%CI] 1.79[1.27-2.54] and 1.42[1.22-1.65], respectively).

Conclusion: WD was an infrequent event in this early axSpA cohort. Nevertheless, clinical factors were amongst the strongest predictors of WD, over socioeconomic factors, with worse disease activity and function independently associated with a higher hazard of WD. Disease severity remains a strong predictor of adverse work outcome even in early disease, despite substantial advances in therapeutic strategies in axSpA.

Disclosure: E. Nikiphorou, Celltrion, 1, Pfizer, 1, 6, Sanofi, 1, Gilead, 1, AbbVie, 1, 6, Lilly, 1, 6, Galapagos, 6; **A. Boonen**, None; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **P. Richette**, AbbVie, 1, 6, Amgen, 1, 6, Celgene, 1, 6, Janssen, 1, 6, Eli Lilly, 1, 6, MSD, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **S. Ramiro**, AbbVie, 2, Eli Lilly, 2, MSD, 2, Novartis, 2, Sanofi, 2, UCB, 2, MSD, 5.

Abstract Number: 0382

Six-year Results from the Esperanza Cohort: Evaluation of Clinical Features, Disease Activity Measures and Treatment Aspects in Axial and Peripheral Early Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Esperanza was a multicenter national health program developed to facilitate an early diagnosis of patients with Spondyloarthritis (SpA) in Spain. The main objective of this study is to compare the clinical evolution of patients with axial SpA (axSpA) and peripheral SpA (pSpA) included in this program.

Methods: Patients from the Esperanza cohort fulfilling ASAS criteria for axSpA or pSpA and completed the 6-year follow-up were included. Patients were classified a cording to the predominant symptom. In case of having axSpA and pSpA, they were classified as axSpA. Clinical features, disease activity and treatment aspects at baseline and 6-year visit were evaluated.

Results: Six-year follow-up data from 178 (83.5%) fulfilling ASAS criteria at the final visit were available: 133 (74.7%) for axSpA and 45 for pSpA (25.3%). 118 (66.3%) were males (50.6% with axSpA and 62.2%, pSpA, p=0.4). Patients with axSpA had more frequently positive HLA-B27 (90.5%) vs. (9.5%), p< 0.001. Follow-up clinical features are shown in table 1. At the final visit, both axSpA and pSpA presented an improvement in clinical symptoms, disease activity (CRP, BASDAI, BASDAS and VAS-pt) and quality of life (ASQoL). A worsening of mobility (BASMI) was observed in both groups. The prevalence of uveitis, psoriasis and inflammatory bowel disease (IBD) at baseline was 10.7%, 18% and 5.6%, respectively. At the 6-year visit, the cumulative prevalence (CP) was 14% for uveitis (16.5% in axSpA and 6.7% in pSpA), 22.5% for psoriasis (12.8% in axSpA and 51.1% in pSpA) and 7.9% for IBD (5.3% in axSpA and 15.6% in pSpA). Most of the patients were prescribed NSAIDS at baseline and more patients maintained this treatment at the 6-year visit in axSpA compared with pSpA (96.9% vs 87.5%, p=0.02). At the final visit, a higher percentage with pSpA received csDMARDs in comparison with axSpA (81% vs. 35.7%, p< 0.001). Sixty (44.4%) patients received biologic therapy at the final visit and no differences were observed in their prescription: 43% in axSpA and 48.6% in pSpA(p=0.6).

	Baseline visit			Six-year visit				
Characteristics	1 AxSpA n=133	2 pSpA n=45	P value 1-2	3 AxSpA n=133	4 pSpA n=45	P value 3-4	P value 1-3	P value 2-4
Age (years), mean ± SD	33.2 ± 7.5	35.3 ± 7	0.09	39.6 ± 9.6	40.9 ± 6.9	0.107	<0.001	<0.001
Back pain, n (%)	125 (94%)	21 (46.7%)	<0.001	40 (30%)	6 (13.3%)	0.083	<0.001	0.002
Morning stiffness n (%)	106 (80%)	18 (40%)	<0.001	20 (15%)	5 (11.1%)	0.746	<0.001	<0.001
Impr. exercise n (%)	93 (70%)	10 (22%)	<0.001	19 (14%)	3 (6.7%)	0.375	<0.001	<0.001
Night awakening n (%)	88 (66.2%)	12 (26.7%)	<0.001	11 (8.3%)	3 (6.7%)	0.94	<0.001	<0.001
Arthritis, n (%)	32 (24.1%)	40 (89%)	<0.001	8 (6%)	10 (22.2%)	0.006	<0.001	0.061
Enthesitis, n (%)	46 (34.6%)	23 (51.1%)	0.11	10 (7.5%)	1 (2.2%)	0.39	<0.001	<0.001
Dactylitis, n (%)	13 (9.8%)	15 (33.3%)	0.01	1 (0.8%)	2 (4.4%)	0.24	<0.001	<0.001
CP of uveitis, n (%)	17 (12.8%)	2 (4.4%)	0.28	22(16.5%)	3 (6.7%)	0.5	<0.001	<0.001
CP of Psoriasis, n (%)	11 (8.3%)	21 (46.7%)	<0.001	17(12.8%)	23(51.1%)	0.02	<0.001	<0.001
CP of IBD, n (%)	4 (3%)	6 (13,3%)	0,029	7 (5.3%)	7 (15.6%)	0,69	<0.001	<0.001
SJC (0-68), mean ± SD	0.2 ± 0.9	2.1 ± 2.8	<0,001	0.2 ± 1.1	0.5 ± 1.1	0.11	0.62	<0.001
CRP (mg/L), mean ± SD	8.3 ± 11.6	8.9 ± 12.7	0.77	3.6 ± 4.9	5.1 ± 7.7	0.26	<0.001	0.045
BASDAI (0-10), mean ± SD	4 ± 2.2	4.2 ±2.4	0.59	2.4 ± 2.1	2.3 ± 2.1	0.67	<0.001	0.001
BASFI (0-10), mean ± SD	2.4 ± 2.2	2.4 ± 2.4	0.94	2.1 ± 2.2	1.6 ± 1.9	0.2	0.17	0.289
BASDAS, mean ± SD	2.3 ± 1.1	2.5 ± 1.3	0.264	1.6 ± 1.4	1.6 ± 0.9	0.690	<0.001	0.001
BASMI, mean ± SD	1.4 ± 1.3	1.2 ± 0.9	0.43	1.9 ± 1	1.6 ± 0.7	0.19	<0.001	0.002
VAS (0-10) physician, mean ± SD	3.1 ± 2.4	2.9 ± 2.4	0.61	1.8 ± 1.8	1.8 ± 1.6	0.92	<0.001	0.04
VAS (0-10) patient, mean ± SD	4.1 ± 2.7	4.8 ± 3	0.23	2.8 ± 2.3	2.4 ± 2.2	0.32	<0.001	0.03
ASQoL, mean ± SD	5.9 ± 4.7	6.4 ± 5.6	0.6	2.9 ± 3.8	3.9 ± 4.9	0.38	<0.001	0.006

Conclusion: The early diagnosis of recent-onset SpA achieves a significant improvement in clinical features, disease activity and quality of life in patients with axSpA and pSpA after 6 years of follow-up. Although previous publications revealed a low radiographic progression in this cohort[1], the worsening of BASMI must aware clinicians of possible evolutive structural damage.

Reference: 1. Fernández-Carballido et al. RMD Open. 2020 Sep;6(2):e001345

Disclosure: C. Tornero, None; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5; **r. almodovar**, None; **C. fernández-Carballido**, None; **A. Hernández**, None; **B. Joven-Ibáñez**, AbbVie, 6, 12, Participant in clinical trials, Celgene, 2, 6, Janssen, 2, 6, 12, Participant in clinical trials, Novartis, 2, 6, 12, Participant in clinical trials, MSD, 6, Pfizer, 6, UCB, 2, Lilly, 12, Participant in clinical trials; **X. Juanola**, None; **M. Ladehesa-Pineda**, None; **J. maneiro**, None; **A. Mas**, None; **c. Montilla**, None; **M. Moreno**, None; **M. moreno**, UCB, 6, Abbvie, 2, 6, Novartis, 2, 6; **J. pinto**, None; **j. Quevedo**, None; **J. Rosas**, None; **T. Ruiz**, None; **J. Sanz**, None; **E. De Miguel**, Roche, 6, 12, Paid instructor, Abbvie, 2, 5, 6, Novartis, 2, 5, 6, 12, Paid instructor, Pfizer, 2, 5, 6, MSD, 6, BMS, 6, UCB, 6, Grunental, 6, Janssen, 6, 12, Paid instructor, Sanofi, 6, Galapagos, 2.

Abstract Number: 0383

Differences Between Male vs. Female Presenting with Back Pain in an Integrated Delivery System

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Back pain exerts significant economic burden and in its inflammatory form is the main clinical symptom of axial spondylarthritis. We evaluated differences in patient history between males and females presenting with back pain. We also evaluated the association between sex and axial spondylarthritis (axSpA).

Methods: A retrospective study was conducted in adult (age 21 & up) members belonging to Kaiser Permanente Southern California health plan. Between 01/2009-12/2013, we included patients who presented with either a diagnosis or chief compliant of back pain during a face-to-face encounter with a provider. Patients were followed until 12/2020 to see if they subsequently developed axSpA. We evaluated differences between male and female patient's history (in the 3 years prior to back-pain diagnosis) of: pain medication use (non-steroidal anti-inflammatory drugs (NSAIDs), opioid drugs, non-opioid drugs, corticosteroids, biologic and synthetic disease-modifying antirheumatic drugs (DMARDs)); imaging tests (X-ray, computed tomography, magnetic resonance imaging, ultrasound etc.); and laboratory tests for inflammation (erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)). Differences between sex in patient history were evaluated by multivariable logistic regression model adjusting for socio-demographic factors (age, race, ethnicity, insurance type, education, and income), modifiable risk factors (smoking status and obesity) and prevalence of Elixhauser comorbidity conditions. A proportional hazards model adjusting for socio-demographic factors, modifiable risk factors and comorbid conditions was used to evaluate the association between sex and axSpA. Loss to follow-up due to death or health plan disenrollment was right censored in the proportional hazards model.

Results: The sample (N= 107,598) was predominantly made up of females (52%). The majority (36%) age category was 21-45 years, while the majority (45%) of patients had 2 or more Elixhauser comorbidity conditions. Female sex was associated with significantly (all $P< 0.001$) higher odds of history of pain medication use [NSAIDs (odds ratio (OR) 1.40 (95% CI 1.36-1.44)), opioids (OR 1.25 (1.22-1.29)), non-opioids (OR 1.49 (1.38-1.60)), corticosteroids (OR 1.11 (1.07-1.15)) and synthetic DMARDs (OR 1.65 (1.48-1.83))]. Female sex was also associated with nearly 4-fold higher odds of history of imaging test orders (OR 3.81 (3.68-3.93)) and 38% higher odds of history of inflammation detection laboratory test orders (OR 1.38 (1.34-1.42)). Lastly, female sex was associated with 36% higher hazard of future axSpA diagnosis (hazard ratio 1.36 (1.20 -1.54))).

Conclusion: In this retrospective study, female sex was found to be disproportionately associated with higher odds of pain medication use, history of imaging tests and laboratory tests for inflammation, observed prior to back pain. We also observed higher hazard of future axSpA diagnosis in females presenting with back pain. More studies are needed to better understand the natural history of back pain and if it predominantly relates to non-radiographic axSpA in females.

Disclosure: A. Kawatkar, Novartis Pharmaceuticals Corporation, 5; **E. Yi**, Novartis, 3; **E. Estrada**, Novartis Pharmaceuticals Corporation, 5; **J. Pio**, Novartis Pharmaceuticals Corporation, 5; **C. Portugal**, Novartis Pharmaceuticals Corporation, 5; **D. Yi**, Novartis Pharmaceuticals Corporation, 5; **S. Lee**, Novartis Pharmaceuticals Corporation, 5, 6.

Abstract Number: 0384

A Tough Cell: The Argument for a Biomarker of Clinical and Imaging Outcomes in Spondyloarthritis: The Neutrophil Lymphocyte Ratio and the Platelet Lymphocyte Ratio

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Biomarkers of disease activity/severity and imaging outcomes in axial spondyloarthritis (axSpA) remain a challenge. The most common relevant biomarker is the C-Reactive Protein (CRP), but it is elevated in only 60% of clinically active axSpA patients and demonstrates low specificity. Several epidemiologic studies have identified the neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) as useful tools in the characterization of inflammatory disease. In this study, we explored the utility of the NLR and PLR in axSpA and their associations with patient reported outcomes (PROs), CRP and the erythrocyte sedimentation ratio (ESR), and sacroiliac joint (SIJ) radiograph damage scores.

Methods: The study population consisted of US veterans with a clinical diagnosis of axSpA enrolled in the Program to Understand Long-term Outcomes of Spondylarthritis (PULSAR) registry. Included data were sociodemographics, PROs, and pharmacologic variables. Absolute neutrophil, platelet, and lymphocyte counts were extracted from the VA Corporate Data Warehouse (CDW). To moderate the effect of medications on lab values, analyses were restricted to encounters in which patients were not taking disease modifying anti-rheumatic drugs. SIJ 3-view radiographs (Ferguson and obliques) were evaluated by three blinded readers using the scoring from the modified New York (mNY) criteria. Associations between NLR and PLR and the CRP, PROs (BASDAI and BASFI), and radiograph scores were calculated using linear regression and plotted with a superimposed regression line (including 95% CIs). Cell count data were used only if they were same day as clinical data (apart from radiographs within 90 days of labs). Statistical analysis was performed using STATA/MP v15 software.

Results: In the PULSAR registry, a majority were white males, HLAB27 positive, and reported current or former tobacco use (Table 1). Of 254 patients with a diagnosis of axSpA, the NLR and PLR were both associated the CRP with $p < 0.001$ (Figure 1). The CRP however, was not significantly associated with BASDAI or BASFI. In contrast, the ESR

Table 1. Demographic information of patients enrolled in PULSAR registry	
Variable	
Age, years	53.4
Gender, %male	92
Race/Ethnicity	
White, %	70
Black, %	14
Hispanic, %	7
American-Indian, %	14
Asian, %	10
Other, %	12
Unknown, %	5
HLA B27, % positive	82
Tobacco use	
Never user, %	34
Former user, %	43
Current user, %	24
Baseline BASDAI, mean (standard deviation)	3.95 (2.32)
Baseline BASFI, mean (standard deviation)	3.86 (2.51)
TNFi use	
Infliximab, %	26
Adalimumab, %	18
Etanercept, %	11
Certolizumab, %	2
Golimumab, %	3

BASDAI = Bath Ankylosing Spondylitis Disease Activity Index
BASFI = Bath Ankylosing Spondylitis Functional Index
TNFi = Tumor Necrosis Factor inhibitor

Figure 1. Linear regression of NLR and CRP (*left*) and PLR and CRP (*right*) in patients with axSpA

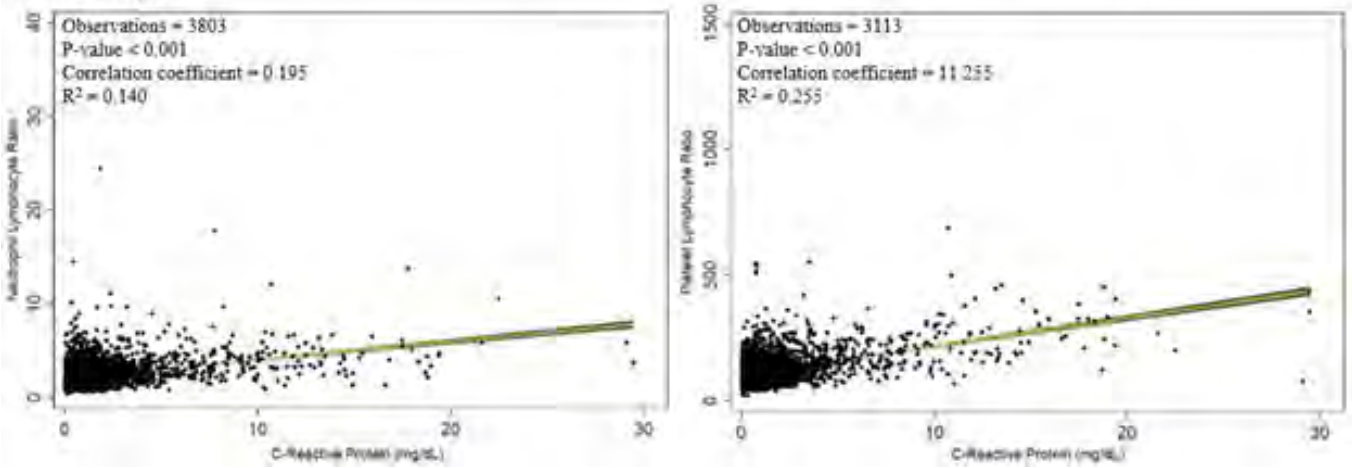

Table 2. Correlation of selected lab data (CRP, ESR, NLR, PLR) and PROs in patients with axSpA

Lab	PRO	Observations	*p*-value	Correlation Coefficient (95% CI)	R^2
CRP	BASDAI	275	0.102	0.037 (-0.007 – 0.082)	0.0098
	BASFI	237	0.211	0.034 (-0.096 – 0.089)	0.0067
ESR	BASDAI	155	0.026	0.013 (0.002 – 0.023)	0.0322
	BASFI	120	<0.001	0.031 (0.018 – 0.045)	0.1506
NLR	BASDAI	194	0.628	0.056 (-0.172 – 0.285)	0.0012
	BASFI	157	0.038	0.292 (0.016 – 0.567)	0.0274
PLR	BASDAI	141	0.028	0.006 (0.001 – 0.011)	0.0343
	BASFI	105	0.128	0.006 (-0.002 – 0.015)	0.0224

was the only inflammatory marker with significant associations to both BASDAI ($p = 0.026$) and BASFI ($p < 0.001$). The NLR had statistically significant correlation with BASFI ($p = 0.038$) while the PLR had statistically significant correlation with BASDAI ($p = 0.028$) (Table 2). There was no significant correlation between radiographic scores by mNY criteria and CRP, ESR, NLR, or PLR.

Conclusion: In our cohort, axSpA patients were found to have specific correlations between the NLR, PLR and PROs, suggesting additional parameters for disease assessment in clinical practice. Radiographs however did not correlate with selected laboratory data, perhaps reflecting poor correlation of accumulative damage with the transient nature of inflammatory, NLR and PLR indices. Additional variables in larger numbers of axSpA patients may provide further guidance of the utility of these biomarkers.

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Abstract Number: 0385

The Diagnostic Utility of Serum interleukin-22 in Patients with Suspected Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: There is an unmet need for a reliable biomarker for the diagnosis and differentiation of AxSpA from its multiple mimickers. Serum levels of IL-22, which is tightly involved in the pathogenesis of AxSpA, have been previously found significantly elevated in patients with AxSpA, when compared to healthy individuals or persons with osteoarthritis.

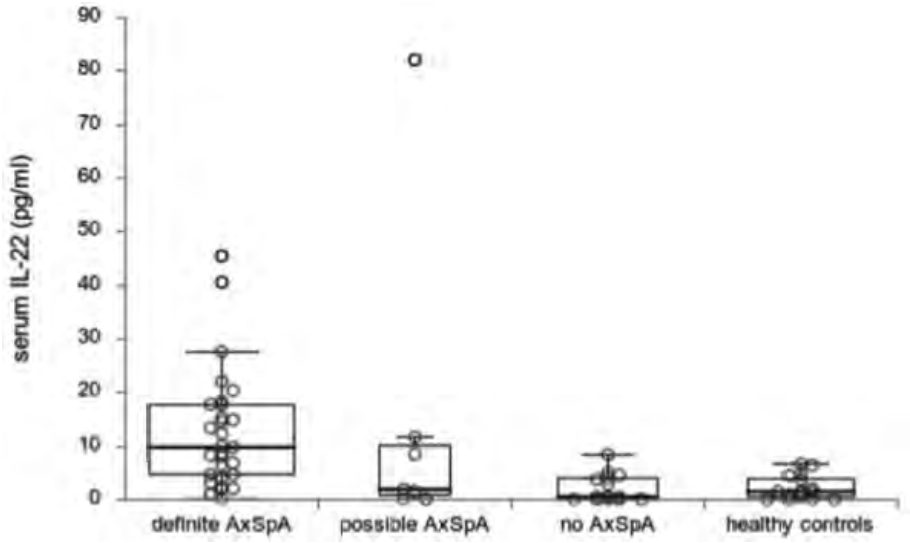

Figure 1. Serum levels of IL-22 in study participants.

Methods: Consecutive patients with established or suspected AxSpA, followed in the outpatient clinic of Bnai Zion Medical Center, Haifa, were enrolled. The demographic and anamnestic data, as well as results of laboratory and imaging studies and estimates of disease activity were acquired from patients' charts. The final diagnosis of definite or probable SpA, or alternative diagnoses, based on the existing medical data, was determined by the joint opinion of the treating rheumatologist and a senior author (GS), blinded to the estimates of the serum IL-22, which were examined by Quantikine ELISA Human IL-22 Immunoassay.

Results: Serum levels of IL-22 were significantly higher in patients with definite AxSpA (29 patients) compared to patients with alternative diagnoses (14 patients) and healthy volunteers (16 individuals) ($p< 0.001$ for both comparisons). Patients with possible AxSpA (7 patients) had a wide range of data distribution, probably reflecting its heterogeneity. The sensitivity and specificity of the serum levels of IL-22 for the AxSpA diagnosis were 0.68 (95% CI 0.49-0.84) and 0.86 (95% CI 0.68-0.95), respectively, for the cut-off of 5 pg/ml, and 0.48 (95% CI 0.29-0.67) and 1 (95% CI 0.85-1) for the cut-off of 10 pg/ml. In patients with AxSpA, serum IL-22 levels did not correlate with mSASSS, BASDAI, ASDAS indices or serum CRP levels, with all results far away from the level of statistical significance.

Conclusion: Serum IL-22 leves are elevated in patients with AxSpA and can serve as an independent biomarker for the differentiation of AxSpA from its non-inflammatory mimickers.

Disclosure: M. Sagiv, None; **A. Awisat**, None; **A. Shouval**, None; **R. Peri**, None; **M. Adawi**, None; **F. Sabbah**, None; **I. Rosner**, None; **A. Kessel**, None; **G. Slobodin**, None.

Abstract Number: 0386

Delay to Diagnosis in Axial Spondyloarthritis: The Gap Is Closing, but Persistent Association with Severe Disease

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Aspects of Axial Spondyloarthritis (0357–0386)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Diagnostic delay in axial spondyloarthritis (axSpA) presents a challenge in the management of the condition, despite increased awareness. Reducing the gap between symptom onset and time of diagnosis is needed to limit associated morbidity and mortality. We aimed to examine delay to diagnosis in a large cohort of well characterised individuals with axSpA, with the specific objectives of:

1. Assessing if delay to diagnosis has reduced in individuals with more recent onset of disease

2. Identifying clinical and demographic characteristics associated with delayed diagnosis

3. Determining whether sex has an impact on delay to diagnosis

4. Assessing the association between delay to diagnosis and disease severity.

Methods: The Ankylosing Spondylitis Registry of Ireland (ASRI) provided the cohort for this study. The objectives of ASRI are to provide descriptive epidemiological data on the Irish axSpA population. A standardised clinical assessment is performed on each patient. Structured interviews provide patient-reported data. Delay to diagnosis was calculated as age at diagnosis minus age at symptom onset. Validated outcome measures were collected: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath AS Functional Index (BASFI), Health Assessment Questionnaire (HAQ), AS Quality of Life (ASQoL), and Bath AS Metrology Index (BASMI).

Results: Eight hundred and eighty-six patients were included, 644 of whom were male (73%), mean age 46 years (SD 13) and 76% (n=667) fulfilled modified New York (mNY) criteria. Detailed baseline clinical and demographic characteristics are outlined in Table 1.

Table 1. Baseline demographic and clinical characteristics

Variable	
Age, mean (SD)	45.9 (12.6)
Female, n (%)	232 (26.2)
Smoker, n (%)	503 (56.8)
HLA-B27 positive, n (%)	602 (67.9)
Disease duration, median (25^{th},75^{th})	17.1 (9.5, 27.8)
Delay to diagnosis, median (25^{th},75^{th})	5 (2.0, 11.0)
• 0-5 years, n (%)	• 444 (50.1)
• 5-10 years, n (%)	• 192 (21.7)
• >10 years, n (%)	• 232 (26.2)
AAU, n (%)	297 (33.5)
PsO, n (%)	144 (16.3)
IBD, n (%)	91 (10.3)
BASMI, mean (SD)	4.0 (2.1)
BASFI, mean (SD)	3.7 (2.9)
BASDAI, mean (SD)	4.0 (2.4)
HAQ, median (25^{th}, 75^{th})	0.38 (0.0, 0.8)
ASQoL, mean (SD)	6.5 (5.5)

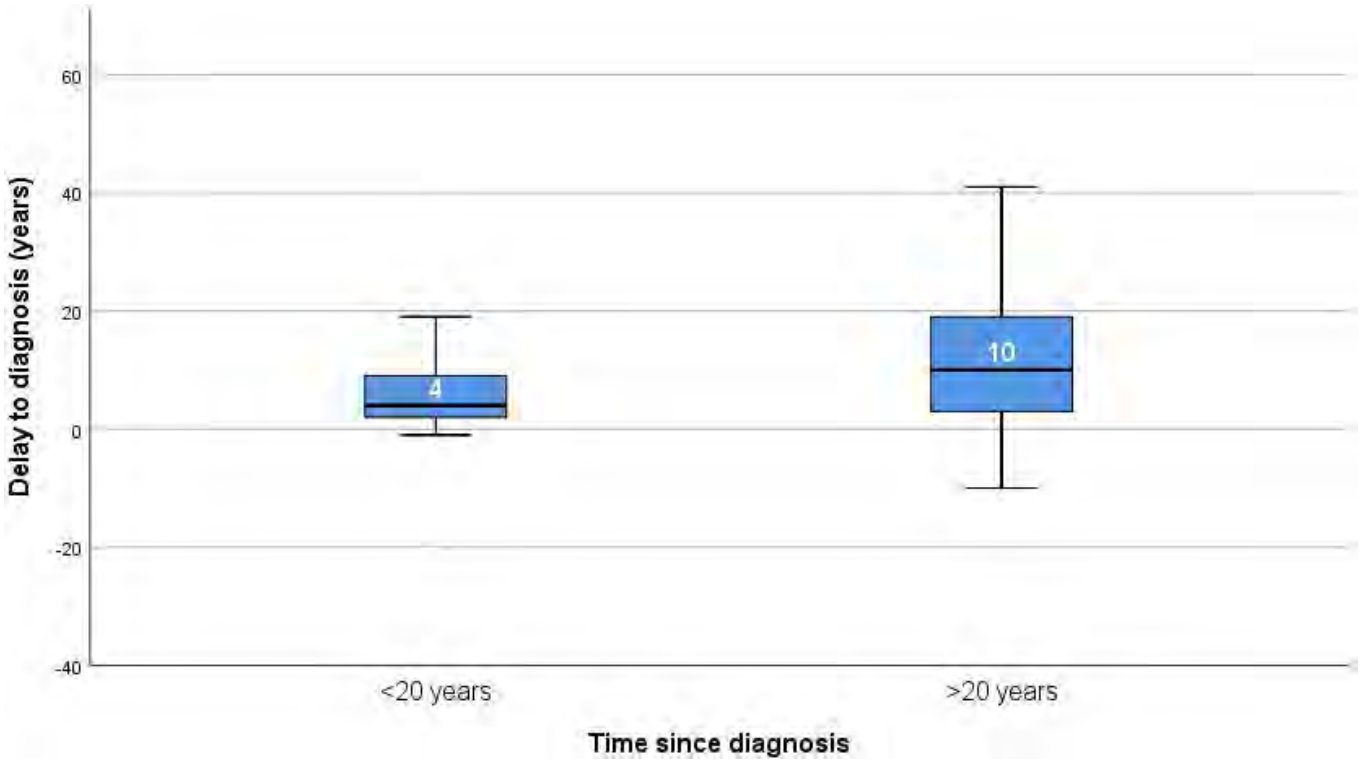

Figure 1. Boxplot demonstrating median delay to diagnosis according to time since diagnosis.

The mean (SD) disease duration was 19 (12) years, with 27% having a duration of less than 10 years, 32% having duration of 10-20 years and 42% with a duration of >20 years. The median delay to diagnosis in the whole cohort was 5 years (2, 11), with 51% (n=444) of the cohort diagnosed within 5 years, 22% (n=192) diagnosed between 5-10 years and 27% (n=232) diagnosed more than ten years from symptom onset. The median delay to diagnosis has reduced significantly (< 0.01) in recent years (see Figure 1).

Factors associated with a shorter delay to diagnosis include smoking (6.7 vs 8.9 years, p< 0.01), peripheral arthritis (7.0 vs 8.4 years, p=0.02) and absence of sacroiliitis on x-rays (6.5 vs 8.4 years, p=0.03). HLA-B27 status had no impact on delay to diagnosis and there was no difference between sexes. The presence of EAM did not influence the delay to diagnosis.

When compared to a delay of < 5 years, individuals with a delay to diagnosis > 10 years had significantly higher BASMI (4.7 vs 4.0, p=0.01) and BASFI (4.8 vs 3.8, p=0.02) scores, with no difference in BASDAI (4.1 vs 3.9, p=0.6).

Conclusion: Although still present, delay to diagnosis has reduced in individuals with a more recent diagnosis of axSpA, with no sex effect seen. Longer delays to diagnosis are associated with more severe disease in this cohort, indicating a significant unmet need in the management of axSpA.

Disclosure: M. McWalter, None; **C. MacGearailt**, None; **S. Maguire**, Gilead, 5; **F. O'Shea**, None; **G. Fitzgerald**, AbbVie Pharmaceuticals, 1.

Abstract Number: 0387

Predictors for Progressive Fibrosis in Patients with Connective Tissue Disease Associated Interstitial Lung Diseases

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Connective tissue disease associated interstitial lung disease (CTD-ILD) is associated with decreased quality of life and high mortality risk. Outcome and treatment response is unpredictable. This study aimed to identify clinical predictors for CTD-ILD with poor outcome.

Methods: We performed a retrospective single center cohort study in outpatients with CTD-ILD seen between 2004 and 2018. Clinical, biochemical data as well as pulmonary function test (PFT) and high-resolution computed tomography (HRCT) results were recorded. The ILD patterns were classified according to the classification for idiopathic interstitial pneumonia and categorised into fibrotic or inflammatory. Overall survival and progressive fibrosing ILD (PF-ILD, defined as ≥ 10% decline in FVC, ≥ 15% decline in DLCO, or progression of the fibrosis on HRCT within two years) were assessed.

Results: In total, 150 patients with CTD-ILD were included. Table 1 shows the baseline patient characteristics. Thirty (20%) deaths occurred during a median follow-up of 40 months (IQR 27.3–60.8), which were attributed to pulmonary infection in six (4%), respiratory failure due to PF-ILD in ten (7%) and due to other causes in fourteen patients. PF-ILD occurred in 74 (49.3%) patients and was associated with poor overall survival. (Figure 1) Age, smoking, C-reactive protein, and steroid-use were independently associated with increased mortality risk as well. (Table 2) Furthermore, patients with diabetes mellitus (adjusted OR 4.2, 95%CI 1.05–16.78), steroid-use (adjusted OR 2.38, 95%CI 1.09–5.18), and a fibrotic HRCT pattern at baseline (adjusted OR 3.02, 95%CI 1.11–8.24) had a higher risk of PF-ILD.

Conclusion: PF-ILD is associated with increased mortality in patients with CTD-ILD. Patients with a fibrotic HRCT pattern at baseline, diabetes mellitus and steroid-use have a higher risk of developing PF-ILD.

Table 1. Baseline patient characteristics. Abbreviations: CTD, connective tissue disease; MCTD, mixed connective tissue disease; SLE, systemic lupus erythematosus; UCTD, undifferentiated connective tissue disease; IVIG, intravenous immunoglobulin; HSCT, Hematopoietic stem-cell transplantation; TNFi, tumor necrosis factor alfa inhibitor; UIP, usual interstitial pneumonia; NSIP, non-specific interstitial pneumonia; PPFE, pleuroparenchymal fibro-elastosis; OP, organising pneumonia; LIP, lymphocytic interstitial pneumonia

Characteristic	Patients N=150
Female, n(%)	95 (63.3)
Age (years), median (IQR)	57 (48–68)
Disease Duration of CTD (months), median (IQR)	14 (2–73)
Systemic sclerosis, n(%)	53(35.3)
Sjögren's syndrome, n(%)	19(12.7)
Myositis, n(%)	29(19.3)
Rheumatoid arthritis, n(%)	24(16)
SLE, n(%)	5(3.3)
MCTD, n(%)	4(2.7)
UCTD, n(%)	16(10.7)
Comorbidities, n(%)	
Coronary artery disease	18 (12.0)
Congestive heart failure	15 (10)
Pulmonary hypertension	17 (11.3)
Diabetes mellitus	15 (10.0)
Cerebrovascular event	5 (3.3)
Obesity (BMI > 35)	11 (7.3)
Smoking status, n(%)	
Current	9 (6.0)
Former	69 (46)
Never	71(47.3)
Immunosuppression, n(%)	
azathioprine	12 (8)
mycophenolate mofetil	48 (32)
cyclophosphamide	1 (0.7)
rituximab	20 (13.3)
IVIG	2 (1.3)
HSCT	3 (2)
methotrexate	16 (10.7)
hydroxychloroquine	22 (14.7)
cyclosporine	5 (3.3)
tacrolimus	1 (0.7)
leflunomide	4 (2.7)
adalimumab	3 (2)
etanercept	1 (0.7)
infliximab	1 (0.7)
belimumab	1 (0.7)
tocilizumab	1 (0.7)
prednisolone	78 (52)
Fibrotic CT patterns, n(%)	
UIP	12 (8)
Fibrotic NSIP	18 (12)
PPFE	1 (0.7)
OP/UIP	1 (0.7)
LIP/UIP	1 (0.7)
Inflammatory CT patterns, n(%)	
Cellular NSIP	55 (36.7)
Mix NSIP	36 (24)
OP	6 (4)
LIP	6 (4)
NSIP/OP	12 (8)
LIP/NSIP	2 (1.3)

Table 2. Predictors of mortality with multivariable adjustment in Cox regression. MMF, mycophenolate mofetil; HR, hazard ratio; 95%CI, 95% confidence interval; CRP, c-reactive protein; PF-ILD, progressive fibrosing interstitial lung diseases; AMA, Anti-mitochondrial antibody

Risk factor	Crud HR (95%CI)	P-value	Adjusted HR (95%CI)	P-value
Age	1.11 (1.06–1.15)	<0.001	1.08 (1.02–1.15)	0.007
Smoking	1.64 (0.79–3.43)	0.187	7.02 (1.99–24.77)	0.002
Congestive heart failure	1.86 (0.75–4.58)	0.179	0.57 (0.16–2.05)	0.385
MMF-use	0.55 (0.23–1.35)	0.195	0.95 (0.25–3.66)	0.938
Steroid-use	4.37 (1.67–11.45)	0.003	5.11 (1.01–25.84)	0.049
CRP	1.01 (1.00–1.02)	0.028	1.01 (1.00–1.02)	0.022
PF-ILD	3.71 (1.40–9.82)	0.008	5.85 (1.19–28.77)	0.03
Anti-centromere	3.34 (1.14–9.79)	0.028	3.60 (0.84–15.39)	0.084
Anti-Ro	2.98 (1.42–6.23)	0.004	2.78 (0.77–10.01)	0.118
AMA	12.14 (2.69–54.89)	0.001	13.33 (0.63–281.90)	0.096

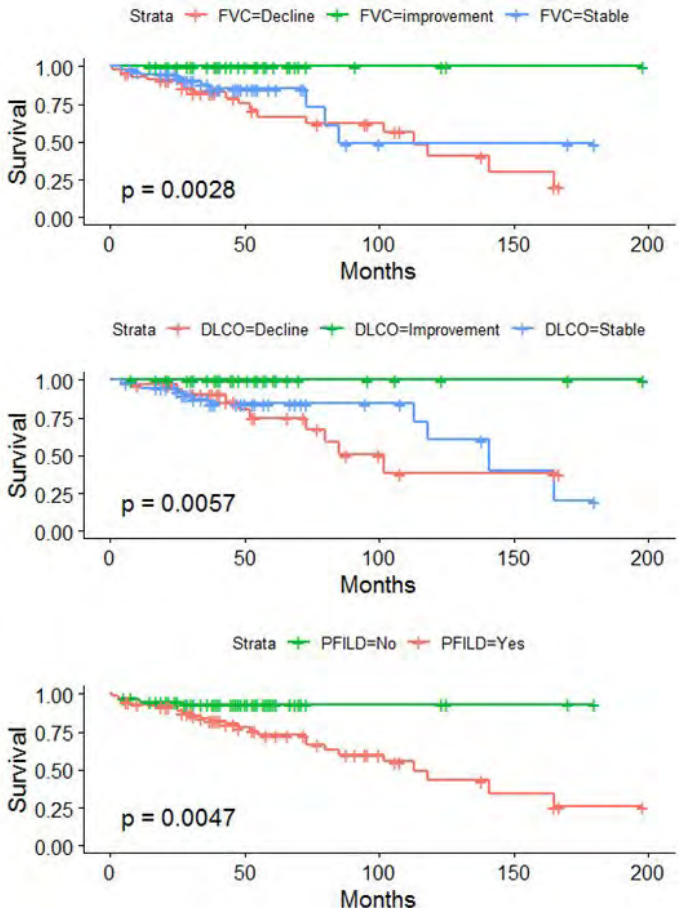

Figure 1. The Kaplan-Meier plots for survival analysis among predicted forced vital capacity (FVC), predicted single-breath diffusing capacity for carbon monoxide (DLCO), and progressive fibrosing interstitial lung diseases (PFILD).

Disclosure: Y. Chiu, None; **J. Spierings**, Boehringer Ingelheim, 5, Miltenyi, 5; **P. de Jong**, Sanifit, 2, Inozyme, 2; **F. Mohamed Hoesein**, None; **J. Grutters**, None; **J. van Laar**, Abbvie, 6, Arxx Tx, 6, Galapagos, 6, Gesyntha, 6, Leadiant, 6, Roche, 6, Boehringer Ingelheim, 5, Astra Zeneca, 5, MSD, 5, Roche, 5; **M. Voortman**, None.

Abstract Number: 0388

Prediction Tool for Damage Accrual Trajectory in Incident Systemic Sclerosis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a systemic autoimmune disease associated with the accrual of organ damage over time, which can be measured using the Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI). The natural history of SSc is heterogenous ranging from benign to severe with the latter associated with high mortality. The aim of this study was to build a prediction model that could identify newly diagnosed SSc patients at higher risk of accruing damage quickly.

Methods: Incident adult SSc cases (disease duration < 2 years) were identified in the Australian Scleroderma Interest Group (ASIG) and Canadian Scleroderma Research Group (CSRG) registries. Patients meeting 2013 ACR-EULAR Scleroderma classification criteria were included. Using a combination of group-based trajectory modelling and substantive knowledge, we identified two trajectories of damage accrual (fast, slow) for each of diffuse and limited patients. Baseline variables associated with trajectory membership were entered into logistic regression models. Using backward selection, prediction models for the two cutaneous SSc subset groups were built independently since the actual DI trajectories for the two subsets were very different from one another. ROC curves were analyzed to

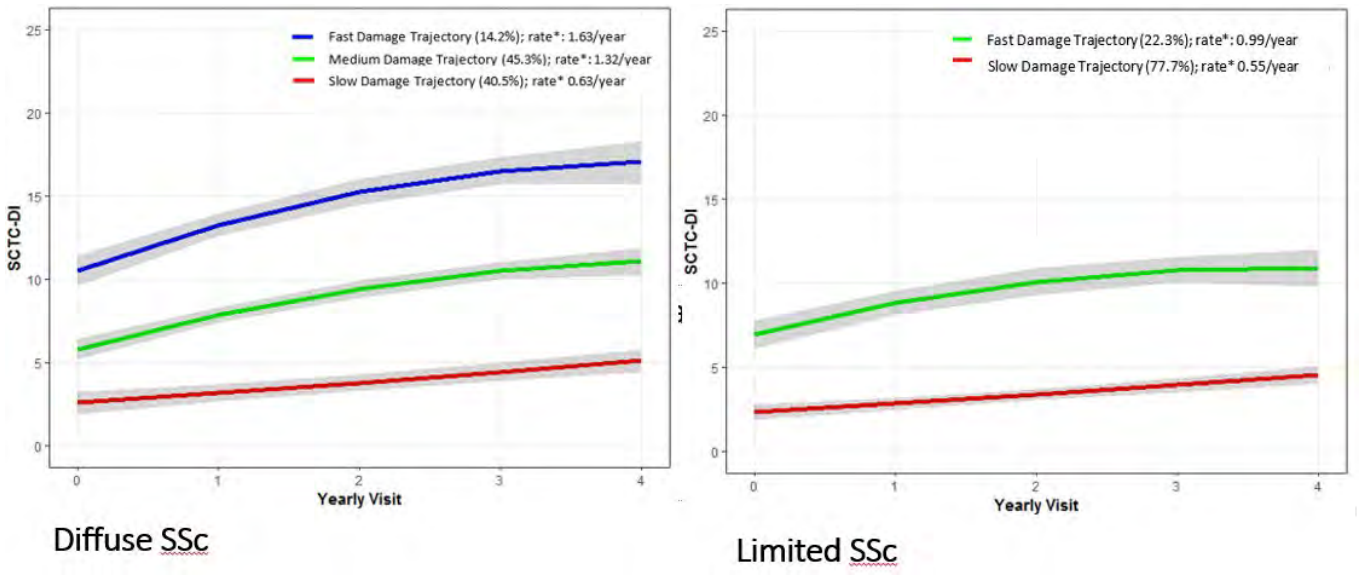

Figure 1. Incident Systemic Sclerosis Damage Trajectories.

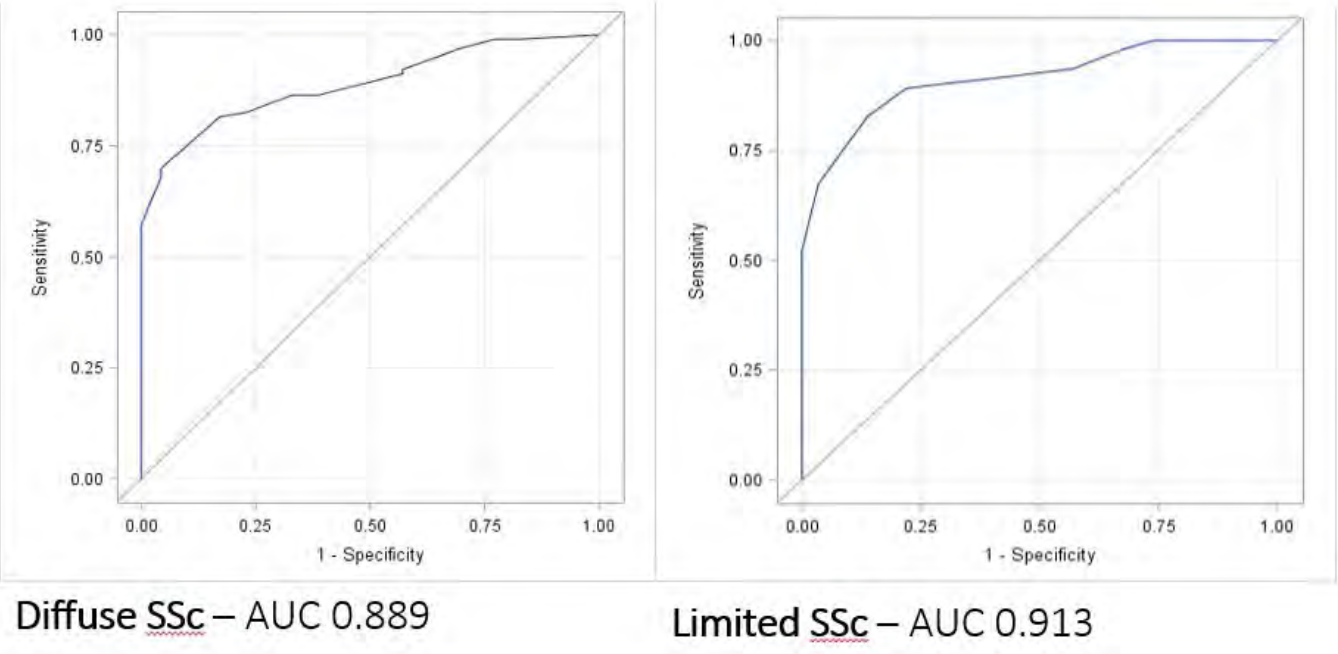

Figure 2. ROC Curves for the Prediction Models

Table 1. Variable Selection for Final Prediction Models

	Diffuse (n=192)				Limited (n=210)			
	Full model		Selected model		Full model		Selected model	
	OR (95% CI)	P values	OR (95% CI)	P values	OR (95% CI)	P values	OR (95% CI)	P values
Age	1.02 (0.98, 1.06)	0.377			1.03 (0.99, 1.07)	0.115		
Male	3.23 (1.02, 10.21)	0.046	3.29 (1.17, 9.25)	0.024	0.73 (0.15, 3.52)	0.699		
Caucasian	0.46 (0.10, 2.07)	0.312						
CRP (log)	1.18 (0.82, 1.69)	0.364			0.96 (0.68, 1.35)	0.806		
ESR (log)	0.90 (0.58, 1.39)	0.629			1.37 (0.86, 2.19)	0.181		
TFRs	1.18 (0.38, 3.72)	0.776						
Baseline SCTC-DI	2.05 (1.61, 2.63)	<.001	2.07 (1.65, 2.58)	<.001	3.09 (2.09, 4.57)	<.001	2.79 (2.02, 3.84)	<.001

determine the optimal cut-offs for the predictive variables. The Hosmer–Lemeshow Goodness-of-Fit test was used to determine prediction accuracy.

Results: 402 patients were included. The mean age was 53 years, 20% were men, 85% were Caucasian, and 47% had diffuse disease. For the diffuse subset, the mean length of follow up was 3.0 years (SD ± 1.2) and 60% were in the fast trajectory, whereas the mean length of follow up was 3.1 years (SD ± 1.1) and 23% were in the fast trajectory in the limited subset (Figure 1). The final prediction model included male sex and baseline SCTC-DI for the diffuse subset, and only baseline SCTC-DI for limited (Table 1). The ROC curves for the limited and diffuse prediction models showed good discriminative abilities (AUC 0.91 and 0.89, respectively) (Figure 2). In limited patients, a baseline DI ≥ 5 predicts a fast damage trajectory with a sensitivity of 0.70 and specificity of 0.96. In diffuse patients, a baseline DI ≥ 4 in men and ≥ 6 in women, predicts a fast damage trajectory with a sensitivity of 0.83 and specificity of 0.86. The

Hosmer-Lemeshow Goodness-of-Fit test confirmed the prediction accuracy of both models (p = 0.77 for diffuse and p = 0.33 for limited).

Conclusion: Baseline disease damage as gauged by the SCTC-DI, and sex can be used as predictors of future damage trajectories. These prediction models may be useful in the clinical or trial design setting.

Disclosure: A. Barbacki, None; **A. Man**, Abbvie, 2, Boehringer Ingelheim, 2; **M. Wang**, None; **D. Johnson**, None; **Y. Zhang**, None; **M. Nikpour**, None; **M. Baron**, None.

Abstract Number: 0389

Use of Nintedanib for the Treatment of Systemic Sclerosis-associated Interstitial Lung Disease at Expert Scleroderma Centers in the United States

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) affects 40-60% of adults with systemic sclerosis (SSc) and is the leading cause of death in this population. Nintedanib, a tyrosine kinase inhibitor, was the first medication to receive Food & Drug Administration approval for the treatment of SSc-ILD, in September 2019, based on the results of the SENSCIS trial. The most common adverse event (AE) associated with nintedanib is gastrointestinal distress. Of the 288 participants who received nintedanib in the SENSCIS trial, 75.7% experienced diarrhea, 31.6% nausea, and 24.7% vomiting. Moreover, 16% of participants discontinued nintedanib due to an AE.[1] It is unknown how nintedanib is being used in clinical practice. The aims of this study were to describe the nintedanib prescribing practices at expert SSc centers in the US.

Methods: We performed a prospective cohort study of patients enrolled in the Collaborative National Quality and Efficacy Registry (CONQUER) at 13 sites in the US between June 6, 2018, and March 1, 2021. CONQUER is a US-based, prospective, multicenter cohort of adults with SSc who met 2013 ACR/EULAR Classification Criteria and had a disease duration ≤ 5 years from the 1st non-Raynaud's symptom at enrollment. We compared baseline characteristics between participants with SSc-ILD who did and did not receive nintedanib. Descriptive data are presented due to the small sample size of subjects who received nintedanib.

Results: 459 SSc patients were enrolled in CONQUER, of whom 202 (44%) had ILD. Of the 202 participants with SSc-ILD, 14 (6.9%) had taken nintedanib at some point during their SSc-ILD disease course. Among those who received nintedanib compared to those who did not, a greater proportion were male (42.9% vs. 19.1%), Hispan-

Table 1. Baseline Characteristics by Nintedanib Status

	Overall (N = 202)	Ever on Nintedanib: Yes (N = 14)	Ever on Nintedanib: No (N = 188)
Age (years) at baseline visit	53.5 (42.3, 63.6)	48.1 (38.8, 59.0)	53.5 (42.9, 63.7)
Sex			
Male	42 (20.8%)	6 (42.9%)	36 (19.1%)
Female	160 (79.2%)	8 (57.1%)	152 (80.9%)
Race			
White	156 (79.6%)	12 (85.7%)	144 (79.1%)
Black or African American	24 (12.2%)	2 (14.3%)	22 (12.1%)
Other	16 (8.2%)	0 (0.0%)	16 (8.8%)
Ethnicity			
Hispanic or Latino	23 (11.6%)	3 (21.4%)	20 (10.8%)
Not Hispanic or Latino	176 (88.4%)	11 (78.6%)	165 (89.2%)
Smoking status			
Never	137 (67.8%)	11 (78.6%)	126 (67.0%)
Former	59 (29.2%)	3 (21.4%)	56 (29.8%)
Current	6 (3.0%)	0 (0.0%)	6 (3.2%)
Disease duration (years) from date of first non-Raynaud's symptom to baseline visit	2.7 (1.4, 3.8)	3.0 (1.5, 3.8)	2.7 (1.4, 3.9)
SSc subtype			
Limited cutaneous	75 (37.1%)	5 (35.7%)	70 (37.2%)
Diffuse cutaneous	127 (62.9%)	9 (64.3%)	118 (62.8%)
ANA positive	183 (90.6%)	13 (92.9%)	170 (90.4%)
Anti-Scl-70 positive	74 (36.6%)	7 (50.0%)	67 (35.6%)
Anti-centromere positive	19 (9.4%)	0 (0.0%)	19 (10.1%)
Anti-RNA Polymerase III positive	44 (21.8%)	1 (7.1%)	43 (22.9%)
Baseline supplemental oxygen use	13 (6.5%)	3 (21.4%)	10 (5.3%)
Crackles on exam	71 (35.3%)	10 (71.4%)	61 (32.6%)
Modified Rodnan Skin Score (mRSS)	10.0 (5.0, 19.0)	14.0 (7.0, 24.0)	10.0 (5.0, 18.0)
UCLA SCTC GIT 2.0 score Overall	0.3 (0.1, 0.6)	0.2 (0.1, 0.7)	0.3 (0.1, 0.6)
Reflux	0.4 (0.0, 1.0)	0.4 (0.1, 0.9)	0.4 (0.0, 1.0)
Distension/Bloating	0.8 (0.0, 1.3)	0.5 (0.0, 0.5)	0.8 (0.0, 1.3)
Fecal Soilage	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)	0.0 (0.0, 0.0)
Diarrhea	0.0 (0.0, 0.5)	0.5 (0.0, 1.0)	0.0 (0.0, 0.5)
Social Functioning	0.0 (0.0, 0.3)	0.2 (0.0, 0.2)	0.0 (0.0, 0.3)
Emotional Well-Being	0.0 (0.0, 0.3)	0.0 (0.0, 0.1)	0.0 (0.0, 0.3)
Constipation	0.0 (0.0, 0.5)	0.0 (0.0, 0.5)	0.0 (0.0, 0.6)

All variables are baseline characteristics except autoantibodies which are positive if any visit contained a positive. Continuous variables are summarized using median (interquartile range) and categorical variables are summarized using counts (percentages).
The numbers of missing values are as follows: ethnicity 3, supplemental oxygen 1, crackles 1, GIT total 17, reflux 17, distension/bloating 18, fecal soilage 21, diarrhea 18, social functioning 18, emotional well-being 18, constipation 17

ic (21.4% vs. 10.8%), never smokers (78.6% vs. 67.0%), Scl-70 positive (50.0% vs. 35.6%), and had crackles on exam (71.4% vs. 32.6%), while a smaller percentage were centromere positive (0% vs. 10.1%) or RNA polymerase 3 positive (7.1% vs. 22.9%) (Table 1). The median baseline diarrhea scale score of the UCLA SCTC GIT 2.0 was in

Table 2. Baseline Pulmonary Function Test Results by Nintedanib Status

	Overall (N = 202)	Ever on Nintedanib: Yes (N = 14)	Ever on Nintedanib: No (N = 188)
FVC (L)	2.8 (2.2, 3.4)	2.5 (2.2, 3.3)	2.8 (2.2, 3.4)
FVC % predicted	79.0 (67.0, 90.0)	70.0 (62.0, 78.0)	80.5 (67.0, 91.0)
FVC % predicted category			
<80%	95 (47.0%)	10 (71.4%)	85 (45.2%)
≥80%	90 (44.6%)	3 (21.4%)	87 (46.3%)
Missing	17 (8.4%)	1 (7.1%)	16 (8.5%)
FEV1 (L)	2.3 (1.8, 2.7)	2.0 (1.9, 2.6)	2.3 (1.8, 2.7)
FEV1 % predicted	83.0 (69.0, 92.0)	76.0 (67.0, 85.0)	84.0 (70.0, 93.0)
FEV1 % predicted category			
<80%	81 (40.1%)	9 (64.3%)	72 (38.3%)
≥80%	101 (50.0%)	4 (28.6%)	97 (51.6%)
Missing	20 (9.9%)	1 (7.1%)	19 (10.1%)
FEV1/FVC (actual)	83.0 (78.0, 88.0)	84.0 (84.0, 89.0)	82.0 (78.0, 88.0)
TLC (L)	4.4 (3.7, 5.1)	3.5 (2.9, 6.7)	4.4 (3.8, 5.1)
TLC % predicted	80.0 (66.7, 92.0)	66.4 (55.0, 85.0)	81.0 (69.0, 93.0)
TLC % predicted category			
<80%	57 (28.2%)	5 (35.7%)	52 (27.7%)
≥80%	63 (31.2%)	2 (14.3%)	61 (32.4%)
Missing	82 (40.6%)	7 (50.0%)	75 (39.9%)
DLCO (mL/min/mmHg)	15.8 (11.8, 20.2)	14.5 (7.6, 17.7)	15.9 (11.8, 20.2)
DLCO % predicted	66.0 (49.0, 80.0)	55.0 (29.0, 68.0)	67.0 (50.0, 80.0)
DLCO % predicted category			
<80%	125 (61.9%)	9 (64.3%)	116 (61.7%)
≥80%	44 (21.8%)	2 (14.3%)	42 (22.3%)
Missing	33 (16.3%)	3 (21.4%)	30 (16.0%)

Continuous variables are summarized using median (interquartile range) and categorical variables are summarized using counts (percentages).
FEV1/FVC had 21 missing values

the “moderate” range for those who received nintedanib and in the “none-to-mild” range for those who did not. SSc patients who received nintedanib had lower baseline forced vital capacity, total lung capacity, and diffusion capacity for carbon monoxide than those who did not (Table 2). Of the 14 patients who received nintedanib, 10 (71.4%) have remained on it, 2 (14.3%) stopped and then restarted it, and 2 (14.3%) discontinued it. Twelve of the 14 (85.7%) patients who received nintedanib were concurrently receiving mycophenolate mofetil (MMF).

Conclusion: A relatively small percentage of patients with SSc-ILD enrolled in CONQUER have received nintedanib. The majority of patients who received nintedanib did so in combination with MMF. Most patients who received nintedanib were able to remain on this therapy. Future research should explore the tolerability of nintedanib in clinical practice, including reasons for discontinuation. Longitudinal registries such as CONQUER are critical for understanding SSc care in the US.

Reference:

1. Distler O, Highland KB, Gahlemann M, et al. Nintedanib for systemic sclerosis-associated interstitial lung disease. N Engl J Med 2019;380:2518-28.

Disclosure: E. Bernstein, Boehringer Ingelheim, 1, 2, 5, Pfizer, 5, Kadmon, 5, Eicos Sciences, Inc., 5, Corbus, 5; **J. VanBuren**, None; **S. Assassi**, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2; **F. Castelino**, Boehringer Ingelheim, 2, Kadmon, 5; **L. Chung**, Boerhinger Ingelheim, 1, 5, 6, Genentech, 2, Eicos, 1, Reata, 1; **C. Correia**, Boehringer Ingelheim, 2, 6; **L. Evnin**, Boehringer Ingelheim, 5, Actelion (a Janssen company), 5; **T. Frech**, None; **E. Startup**, None; **J. Gordon**, Cumberland Pharmaceuticals, 5, EICOS Sciences, 5; **F. Hant**, None; **L. Hummers**, Boerhinger Ingelheim, 1, 5, Corbus Pharmaceuticals, 1, 5, Cumberland Pharmaceuticals, 5, Kadmon Corporation, 5, Medpace, 5; **N. Sandorfi**, None; **A. Shah**, None; **V. Shanmugam**, None; **V. Steen**, Boehringer Ingelheim, 1, 2, 5, 6, Corbus, 5, Corbus, 1, Eicos Sciences, Inc, 2, 5, CSL Behring, 5, CSL Behring, 2; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2.

Abstract Number: 0390

Vaccination Against COVID-19: Self-Reported Experiences of Patients with Systemic Sclerosis in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort

Kimberly Showalter[1], Jessica Gordon[1], Yin Wu[2], Linda Kwakkenbos[3], Marie-Eve Carrier[4], Richard Henry[2], Nora Østbø[2], Julia Nordlund[2], Angelica Bourgeault[2], Mara Canedo Ayala[2], Marie-Nicole Discepola[2], Andrea Carboni Jiménez[2], Christopher Denton[5], Luc Mouthon[6], Brett Thombs[7] and Robert Spiera[1], [1]Hospital for Special Surgery, New York, NY, [2]Lady Davis Institute of the Jewish General Hospital, Montréal, QC, Canada, [3]Department of Clinical Psychology, Radboud University Behavioural Science Institute, Nijmegen, Netherlands, [4]Lady Davis Institute for Medical Research, Jewish General Hospital, Montréal, QC, Canada, [5]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom, [6]Centre de Référence Maladies Autoimmunes Systémiques Rares d'Ile de France, Hôpital Cochin, Assistance Publique-Hôpitaux de Paris, Paris, France, [7]Lady Davis Institute for Medical Research, Jewish General Hospital; Department of Psychiatry, McGill University, Montréal, QC, Canada

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 vaccination is recommended for individuals with rheumatic diseases, yet data are limited regarding vaccine safety in this population, particularly among those with rare autoimmune conditions such as systemic sclerosis (SSc; scleroderma). The purpose of this cross-sectional, observational study was to evaluate the self-reported experiences of individuals with SSc who have received at least one dose of a COVID-19 vaccine.

Methods: Participants were adults with physician-verified SSc enrolled in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort. SPIN includes 47 international centers and has approximately 1600 active participants. From April 9 to May 15, 2021, participants from the SPIN Cohort were invited by email and popups during regular SPIN Cohort assessments to participate in a COVID-19 vaccine survey, which was conducted in English and French. The survey inquired about whether participants had received the COVID-19 vaccine and their experience with vaccination. Frequencies and means (standard deviation (SD)) are reported. Characteristics are compared between

Table 1. Characteristics of responders within the Scleroderma Patient-centered Intervention Network (SPIN) Cohort who have received at least one dose of a COVID-19 vaccine

Clinical Variable	Total Vaccinated (N=699)
Age, years, mean (SD)	62 (11)
Female, n (%)	616 (88%)
Race/ethnicity, n (%)[a]	
White	597 (86%)
Black	32 (5%)
Other	61 (9%)
Location, n (%)[b]	
Canada	181 (26%)
United States of America	249 (36%)
United Kingdom	83 (12%)
France	181 (26%)
Mexico	1 (<1%)
Australia	4 (1%)
Scleroderma subtype, n (%)	
Limited	423 (61%)
Diffuse	251 (36%)
Sine	21 (3%)
Not defined	4 (1%)
Disease duration*, years, mean (SD)[c]	15 (9)
Medication, any immunosuppressive+, n (%)	397 (43%)
Steroid	150 (22%)
Hydroxychloroquine	103 (15%)
Methotrexate	64 (9%)
Azathioprine	15 (2%)
Mycophenolate	158 (23%)
Tocilizumab	14 (2%)
Abatacept	5 (1%)
Tofacitinib	7 (1%)
Cyclophosphamide	11 (2%)
Rituximab	19 (3%)
History of stem cell transplant	18 (3%)
History of ILD, n (%)	207 (30%)
History of PH, n (%)	121 (17%)
Tobacco use, current, n (%)	20 (3%)
History of COVID-19 infection, n (%)	48 (7%)

Legend: ILD=interstitial lung disease; PH=pulmonary hypertension; *Time since first non-Raynaud's Phenomenon symptom; +Includes all listed except hydroxychloroquine; [a]N=690; [b]N=678; [c]N=671

those with and without self-reported adverse reactions using chi-square or t-test. Logistic regression was used to compare likelihood of self-reported adverse reactions by vaccine type.

Results: Among 932 responders, 699 (75%) had received at least one dose of a COVID-19 vaccine, and 358 (51%) had also received a second dose. The majority of participants received the Pfizer vaccine (63%). Demographic data are presented in Table 1. Most responders did not make changes to their SSc medications for the first (94%) or second (92%) vaccine dose. Adverse reactions were self-reported in 270 individuals (39%) after the first vaccine dose and 209 individuals (58%) after the second vaccine dose (Table 2). The three most common symptoms after the first and second vaccine dose were sore arm (30% and 45%, respectively), fatigue (23% and 40%, respectively), and muscle aches (9% and 22%, respectively). No serious allergic reactions were reported. Self-reported flares of SSc symptoms were rare after the first (6%) and second vaccine dose (10%), and most common symptoms were fatigue and muscle weakness (Table 2). Those with (vs. without) self-reported adverse reactions (any) to the COVID-19

Table 2. Patient-reported adverse reactions following COVID-19 vaccination among individuals with systemic sclerosis (N=699)		
Post-vaccine outcome reported, n (%)	**First vaccine (N=699)**	**Second vaccine (N=358)**
No symptoms	429 (61%)	149 (42%)
Sore arm	211 (30%)	161 (45%)
Fatigue	157 (23%)	143 (40%)
Muscle aches	60 (9%)	80 (22%)
Joint pain	42 (6%)	41 (12%)
Flu-like symptoms	46 (7%)	50 (14%)
Fever	42 (6%)	49 (14%)
Chills	42 (6%)	59 (17%)
Shortness of breath	15 (2%)	9 (3%)
Rash	13 (1%)	10 (3%)
Severe allergy	0 (0%)	0 (0%)
Hives	0 (0%)	1 (1%)
Systemic sclerosis symptom worsening*	41 (6%)	37 (10%)
Legend: *Most common SSc symptom worsening (first dose): fatigue (n=23), muscle weakness (n=13), shortness of breath (n=12), Raynaud's (n=11), arthritis (n=11). +Most common SSc symptom worsening (second dose): fatigue (n=19), muscle weakness (n=11), gastrointestinal symptoms (n=11), arthritis (n=11), Raynaud's (n=8), shortness of breath (n=8).		

Table 3. Adverse reactions (including systemic sclerosis-related symptoms) reported among individuals with systemic sclerosis who received COVID-19 vaccination (first dose only)			
Clinical Variable	**Adverse Reaction Reported (n=270)**	**No Adverse Reaction Reported (n=429)**	**p-value / Odds Ratio (95% CI)**
Age, years, mean (SD)	60 (10)	63 (12)	0.001
Female, n (%)	254 (94%)	362 (84%)	<0.001
History of COVID infection, n (%)	27 (10%)	21 (5%)	0.009
Vaccine, n (%)			
Pfizer/BioNTech	144 (53%)	293 (68%)	Reference
Moderna	66 (24%)	76 (18%)	1.77 (1.20, 2.60)
University of Oxford /AstraZeneca	54 (20%)	50 (12%)	2.20 (1.23, 3.39)
Other/Unsure*	6 (2%)	10 (2%)	1.22 (0.44, 3.43)
Legend: *Includes Johnson and Johnson, Sputnik V, Convidicea (Ad5-nCoV) CanSino Biologics (China), Novavax, other, and unsure			

vaccine were younger (60 vs. 63, p=0.001), more often female (94% vs. 84%, p< 0.001), and more often had a prior history of COVID-19 (10% vs. 5%, p=0.009) (Table 3). Compared to those who received the Pfizer vaccine, the odds of a self-reported adverse reaction were higher for those who received Moderna (OR 1.77, 95% CI 1.20, 2.60) or AstraZeneca (OR 2.20, 95% CI 1.43, 3.39) vaccines.

Conclusion: The rate and types of self-reported adverse reactions to the COVID-19 vaccine among individuals with SSc were similar to those observed in the general population. Few individuals altered their medication regimen for the vaccine, and self-reported worsening of SSc symptoms was rare.

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Abstract Number: 0391

High Frequency Ultrasound Imaging of Skin Thickness in Patients with Early Diffuse Cutaneous Systemic Sclerosis: An Objective Outcome Measure to Track Change over Time

Elizabeth Marjanovic[1], Calvin Heal[1], Tonia Moore[1], Joanne Manning[2], Sarah Wilkinson[1], Graham Dinsdale[2], Mark Dickinson[1], Jack Wilkinson[1], Ariane Herrick[3] and **Andrea Murray**[1], [1]University of Manchester, Manchester, United Kingdom, [2]Salford Royal NHS Foundation Trust, Manchester, United Kingdom, [3]University of Manchester, Salford, United Kingdom

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: There are currently no validated objective measures of systemic sclerosis (SSc)-related skin thickening and this hampers clinical trials of potential new treatments. The modified Rodnan skin score (mRSS, the current gold standard) has limitations including concerns about inter-rater reliability. The aim of this study was to test the hypothesis that high frequency ultrasound (HFUS), which measures skin thickness is (a) sensitive to change and (b) correlates with local 'skin score' (criterion validity), both OMERACT criteria for validation.

Methods: In this prospective study, patients with early diffuse cutaneous SSc (dcSSc; duration of first non-Raynaud's clinical manifestation < 5 years) underwent HFUS at each visit. Imaging was carried out at nine sites (most corresponding to sites assessed for mRSS; non-dominant ring finger, dorsum of hand, forearm, upper arm, forehead, anterior chest, abdomen, leg and dorsum of foot. Local skin score (0-3; 0 normal, 3 unable to move) was also assessed at each site. Images were assessed by one observer; skin thickness was measured as the distance from the surface of the skin to the base of the dermis (i.e. epidermis and dermis). The average thickness was taken of 3 measures made on each image at the left, centre and right in order to take into account any differences in thickness across the image (Figure 1). Longitudinal data underwent linear mixed effects modelling; a random intercept model with a Holm- Bonferroni correction applied.

Table 1. Imaging site, local skin (palpation) score co-efficient indicative of relationship between local palpation and HFUS (increase in coefficient indicative of positive relationship), confidence intervals and adjusted p value (p'); *p'<0.05

Site	Local palpation score co-eff	Confidence intervals	p'
Non-dominant ring finger	0.029	(-0.169 to 0.227)	0.464
Dorsum of hand	0.303	(0.119 to 0.488)	0.024*
Forearm	0.296	(0.127 to 0.465)	0.014*
Upper arm	0.134	(-0.010 to 0.278)	0.464
Forehead	0.035	(-0.167 to 0.237)	0.464
Chest	0.241	(0.102 to 0.379)	0.014*
Abdomen	0.125	(-0.038 to 0.287)	0.261
Leg	0.346	(0.197 to 0.495)	0.044*
Dorsum of the foot	0.134	(-0.007 to 0.276)	0.210

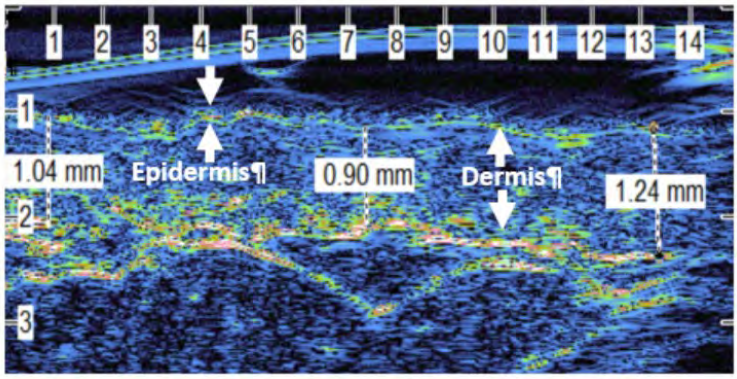
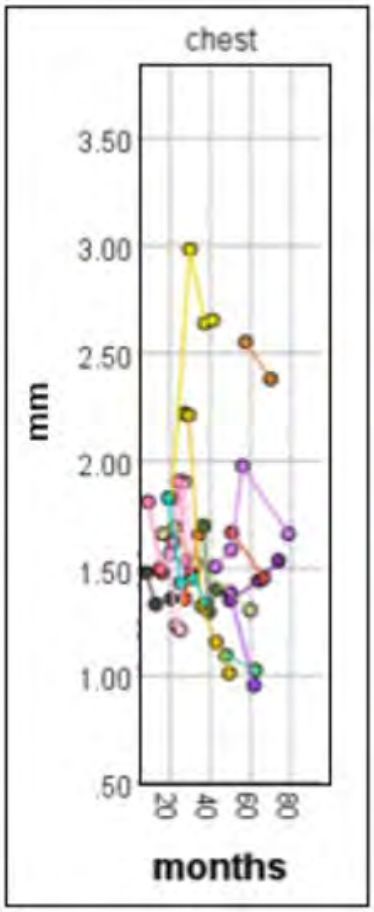


Figure 1. Example of an HFUS image of the chest showing mark-ups on the left, centre and right. Numbers in white boxes along the top and side of the image represent mm.



Graph of skin thickness (mm) as measured by HFUS with time (months); each colour represents a patient.

Results: Seventeen patients with dcSSc were recruited (10 F:7M), median age 54 (range 42 to 61) years, median duration of Raynaud's 2 (IQR 2- 5) years and duration of first non-Raynaud's clinical manifestation 2 (1- 4) years. Three patients had 5 sets of measures, four had 4, four had 3, six had 2; median duration of follow-up of 16 months (range 7-43 months). Although patients did not follow a set pattern of change (i.e. skin thickness increased for some patients and sites and decreased for others) HFUS was sensitive to changes in thickness (example in Figure 2). Modelling indicated that changes in local skin score tracked well with changes in HFUS thickness measures at the dorsum of the hand, forearm, chest and leg (indicated by the local skin score coefficent in Table 1, p'< 0.05).

Conclusion: Conclusions

In patients with early dcSSc HFUS was able to determine differences in skin thickness with time, indicative of sensitivity to change.

Changes in skin thickness as measured by HFUS mirrored changes assessed by local palpation scores at several sites.

Patients at first visit had different levels of skin thickening due to the different durations and

severities of disease, this heterogeneity makes identifying patterns of change over time in patients difficult.

These findings support the hypothesis that HFUS is sensitive to change and shows criterion validity, showing promise for future validation of HFUS as an outcome measure in clinical trials.

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Abstract Number: 0392

Faecal Incontinence in Scleroderma: Prevalence, Impact and Response to Sacral Neuromodulation in an Single Centre Observational Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Scleroderma (SSc) is a chronic autoimmune disorder involving multiple organs, the gastrointestinal system (GI) commonly involved in up to 90% of the sufferers. Faecal incontinence (FI) is frequent manifestation of SSc but data on prevalence of FI are lacking. Treatment options are limited. This study aims to estimate the prevalence of FI in patients with SSc managed at a tertiary referral centre and to determine the efficacy of sacral neuromodulation (SNS) in cases of failed medical management.

Methods: Data was extracted from the STRIKE observational cohort database (Stratification for risk of progression in scleroderma) between 2015 and 2020. Collected data included Patient Reported Outcomes included gastrointestinal VAS scores. Data were categorised into 2 groups based on GI involvement using descriptive statistics, including uni- and multii-variate analysis were applicable. SHAQ-DI indices were calculated for the 2 groups. Faecal incontinence was defined as the inability to control bowel movements causing passive leakage of faeces from the rectum. Prevalence of FI was estimated in this cohort. Anorectal involvement was identified using anorectal manometry and endoanal ultrasound. A positive response to SNS was defined as a >50% improvement in continence score leading

to insertion of a permanent SNS implant. Improvements were measured based on improvements FIQL scores and reduction in the frequencies of bowel movements on follow up.

Results: 539 patients were available in the dataset of which 300 had all follow up information available to be included in the study. Among the 300 patients analysed 26 patients had FI (8.66%). 25 were females (96%). Mean age was 62.4 years, 17 (65.38%) patients had limited SSc and 4 (15.38%) with diffuse SSc. Mean disease duration of 14 years. 70.2% were ANA positive, 50% were ACA, and 19.23% were SCL70 positive. Median (IQR) GI VAS for patients with FI was 60 (40-85) as compared to 10 (0-50) for patients without FI. Median HAQ-DI for FI was 2.75 (0-5.25) as compared to 3.06 (0.6-5.65) for patients without FI. In patients with FI, internal anal sphincter (IAS) atrophy was found in 42.23%, anterior sphincter defect was seen 23.07%. Pudendal neuropathy was observed in 21.73% patients with FI. Anorectal intussusception with perianal descent was seen in 15.38% patients with FI. Pelvic physiotherapy did not benefit any patients. 34.61% patients received a permanent SNS of which 88.5% had a good treatment effect.

Conclusion: The prevalence of FI in our cohort of patients with SSc was 8.6% but is probably underestimated given the reservations that patients feel in declaring FI as a symptom. Patients with FI had higher GI VAS whereas higher overall HAQ scores in non FI patients. FI does affects the quality of life considerably. The finding of sphincter atrophy and pudendal neuropathy warrant further investigation and comparison with non SSc FI cohorts. Despite the need of large controlled studies, the high response to SNS supports its potential role for treating FI in SSc patients. However, reasons for failure of SNS need to be investigated further.

Disclosure: N. Suresh, None; **R. Karanth**, None; **D. Jayne**, None; **G. Abignano**, None; **F. Del Galdo**, Boehringer-Ingelheim, 1, 2, 5, 6, Astra-Zeneca, 1, 2, 5, 6, Jannsenn, 6, Chemomab, 2, 5, Capella Biosciences, 2, 5, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 0393

Severity and Impact of Gastrointestinal Symptoms in Patients with SSc-ILD Treated with Nintedanib: Data from SENSCIS-ON

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

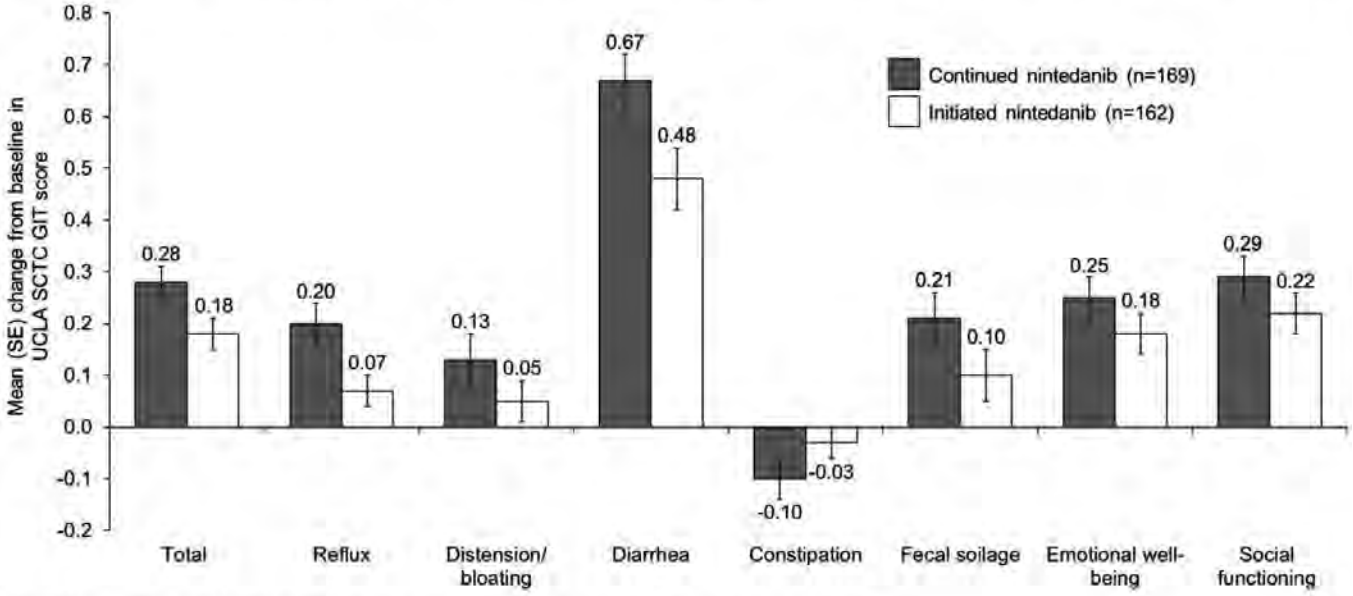
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Gastrointestinal (GI) involvement is a common manifestation of systemic sclerosis (SSc) and a frequent side-effect of drugs used to treat SSc. In the SENSCIS trial, nintedanib reduced the rate of decline in forced vital capacity (FVC) in patients with SSc-associated interstitial lung disease (SSc-ILD), with an adverse

Figure. Changes in UCLA SCTC GIT scores from baseline to week 52 of SENSCIS-ON



n=168 for changes in UCLA SCTC GIT total score and diarrhea scale score in the continued nintedanib group.

Table 1. Changes in severity and impact of gastrointestinal symptoms based on UCLA SCTC GIT total score between baseline and week 52 of SENSCIS-ON

		Baseline				
		None or mild	Moderate	Severe or very severe	Missing	Total
Week 52	**Continued nintedanib**					
	None or mild	81 (41.1)	5 (2.5)	0	4 (2.0)	90 (45.7)
	Moderate	38 (19.3)	10 (5.1)	0	1 (0.5)	49 (24.9)
	Severe or very severe	13 (6.6)	14 (7.1)	7 (3.6)	1 (0.5)	35 (17.8)
	Missing	6 (3.0)	3 (1.5)	1 (0.5)	13 (6.6)	23 (11.7)
	Total	138 (70.1)	32 (16.2)	8 (4.1)	19 (9.6)	197 (100)
	Initiated nintedanib					
	None or mild	87 (35.2)	6 (2.4)	1 (0.4)	4 (1.6)	98 (39.7)
	Moderate	35 (14.2)	12 (4.9)	2 (0.8)	3 (1.2)	52 (21.1)
	Severe or very severe	8 (3.2)	7 (2.8)	4 (1.6)	1 (0.4)	20 (8.1)
	Missing	37 (15.0)	15 (6.1)	4 (1.6)	21 (8.5)	77 (31.2)
	Total	167 (67.6)	40 (16.2)	11 (4.5)	29 (11.7)	247 (100)

Data are n (%) of patients. None or mild=scores of 0 to 0.49; moderate=scores of 0.5 to 1; severe or very severe=scores of 1.01 to 3.

event profile characterized predominantly by GI events. We assessed the severity and impact of GI symptoms on quality of life in patients treated with nintedanib in the open-label extension of the SENSCIS trial, SENSCIS-ON.

Table 2. Changes in severity of diarrhea symptoms based on UCLA SCTC GIT diarrhea scale score between baseline and week 52 of SENSCIS-ON

		Baseline				
		None or mild	Moderate	Severe or very severe	Missing	Total
Week 52	**Continued nintedanib**					
	None or mild	35 (17.8)	6 (3.0)	0	1 (0.5)	42 (21.3)
	Moderate	50 (25.4)	17 (8.6)	2 (1.0)	4 (2.0)	73 (37.1)
	Severe or very severe	34 (17.3)	22 11.2	2 (1.0)	1 (0.5)	59 (29.9)
	Missing	6 (3.0)	2 (1.0)	2 (1.0)	13 (6.6)	23 (11.7)
	Total	125 (63.5)	47 (23.9)	6 (3.0)	19 (9.6)	197 (100)
	Initiated nintedanib					
	None or mild	31 (12.6)	15 (6.1)	2 (0.8)	3 (1.2)	51 (20.6)
	Moderate	39 (15.8)	22 (8.9)	3 (1.2)	3 (1.2)	67 (27.1)
	Severe or very severe	23 (9.3)	21 (8.5)	6 (2.4)	2 (0.8)	52 (21.1)
	Missing	32 (13.0)	19 (7.7)	5 (2.0)	21 (8.5)	77 (31.2)
	Total	125 (50.6)	77 (31.2)	16 (6.5)	29 (11.7)	247 (100)

Data are n (%) of patients. None or mild=scores of 0 to 0.49; moderate=scores of 0.5 to 1; severe or very severe=scores of 1.01 to 2.

Methods: Patients with SSc-ILD who completed the SENSCIS trial or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive were eligible to enter SENSCIS-ON. Patients who received nintedanib in SENSCIS (up to 100 weeks) and continued nintedanib in SENSCIS-ON comprised the "continued nintedanib" group. Patients who received placebo in SENSCIS and initiated nintedanib in SENSCIS-ON, or who received nintedanib for a short time in the DDI study, comprised the "initiated nintedanib" group. There was a maximum interruption of 12 weeks between the last dose of nintedanib in SENSCIS and the first dose in SENSCIS-ON. We assessed changes in scores on the UCLA Scleroderma Clinical Trial Consortium Gastrointestinal Tract (UCLA SCTC GIT) questionnaire v2.0 from baseline to week 52. This questionnaire comprises 7 scales measuring the severity and impact of GI symptoms: reflux, distension or bloating, fecal soilage, diarrhea, constipation, emotional well-being, social functioning. Each scale is scored from 0 to 3 except for the diarrhea scale (0 to 2) and constipation scale (0 to 2.5). The total score, derived as the mean of the scores for the scales except constipation, ranges from 0 to 2.83, with higher scores indicating worse symptoms.

Results: The "continued nintedanib" group comprised 197 patients and the "initiated nintedanib" group comprised 247 patients (231 from SENSCIS). Of these, 178 and 218 patients, respectively, provided a total UCLA SCTC GIT score at baseline. At baseline, mean (SD) total scores were 0.33 (0.33) and 0.33 (0.34) in the continued nintedanib and initiated nintedanib groups, respectively. Mean (SD) scores on the 7 scales ranged from 0.16 (0.52) to 0.70 (0.73) in the continued nintedanib group and from 0.13 (0.43) to 0.64 (0.68) in the initiated nintedanib group. Increases (worsening) in scores were observed in both groups from baseline to week 52, except for on the constipation scale (Figure). Based on the total score, between baseline and week 52, the proportion of patients with moderate or severe

or very severe GI symptoms increased, but 45.7% and 39.7% of patients in the continued nintedanib and initiated nintedanib groups, respectively, had no or mild GI symptoms at week 52 (Table 1). Changes in the diarrhea scale score are shown in Table 2.

Conclusion: In the SENSCIS-ON trial, the majority of patients with SSc-ILD treated with nintedanib had no or mild GI symptoms at baseline. A small worsening in GI symptoms was observed over 52 weeks. Diarrhea had the greatest impact, reflecting the adverse event profile of nintedanib. Recommendations for the management of diarrhea in patients treated with nintedanib should be implemented in clinical practice.

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Abstract Number: 0394

Hyperspectral Imaging in Systemic Sclerosis-Raynaud Phenomenon

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SESSION INFORMATION
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Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Raynaud phenomenon (RP), a microcirculatory, vasospastic disorder, may be primary or secondary to an autoimmune disease [e.g., an early indicator of systemic sclerosis (SSc)]. Raynaud phenomenon clinical trials have been hampered by the lack of a robust, feasible, and quantitative methodology for assessing change over time. Hyperspectral imaging (HSI) noninvasively measures oxygenated hemoglobin (oxyHb) and deoxygenated he-

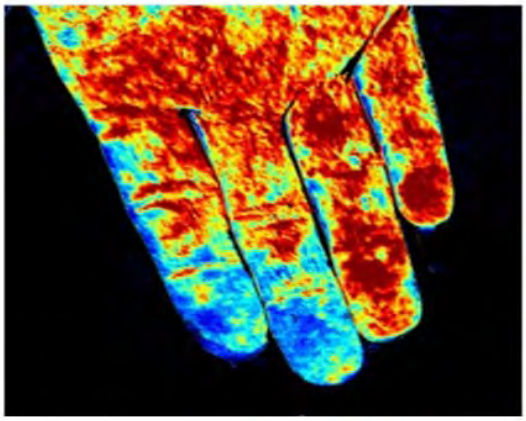

Figure 1. Hyperspectral Imaging Heatmap. A representative HSI OxyHb image. Red: higher OxyHb [arbitrary units (AU)]; Blue: lower OxyHb (AU). In this patient, only the left two fingers demonstrated RP color changes.

moglobin (deoxyHb) concentrations, and oxygen saturation (O2 sat) in the skin microcirculation by visible spectroscopy (a spectrometer quantifies hemoglobin light absorption). Data are depicted as an oxygenation heatmap (Fig. 1). The study goal is to explore the potential role of HSI in quantifying SSc-RP hand microcirculation.

Methods: The Yale University Human Investigation Committee approved this prospective study (HIC# 2000026608) of Yale Scleroderma Program patients and healthy control participants (HC). Patients with SSc completed two patient-reported outcome (PRO) instruments: the Raynaud Condition Score (RCS) and the Cochin Hand Function Scale (CHFS) to assess symptom burden. Then, bilateral palmar HSI (HyperMed™, Waltham, MA) was obtained in a temperature-controlled room (22°C). OxyHb, deoxyHb and O2 sat values were calculated using a default region of interest (ROI) measuring 78 mm^2 on the palmar side of the fingertips and palm (for normalization) (Fig. 2). Subjects then underwent a cold provocation challenge whereby hands were submerged in 15°C for one minute, and HSI was subsequently repeated at 0, 10, and 20 minutes (min.). Statistical analysis was performed using the mixed effects model (Stata, College Station, TX).

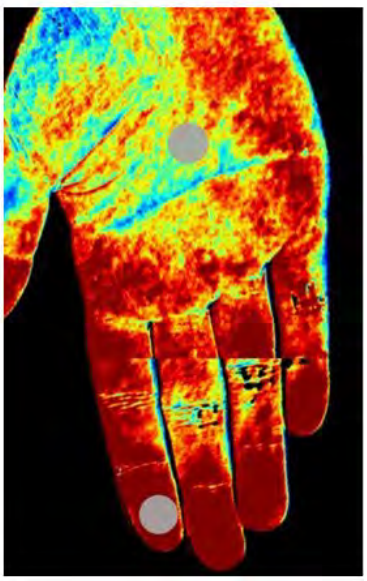

Figure 2. Region of interest (ROI) on the palmar side of palm (used for normalization) and fingertips.

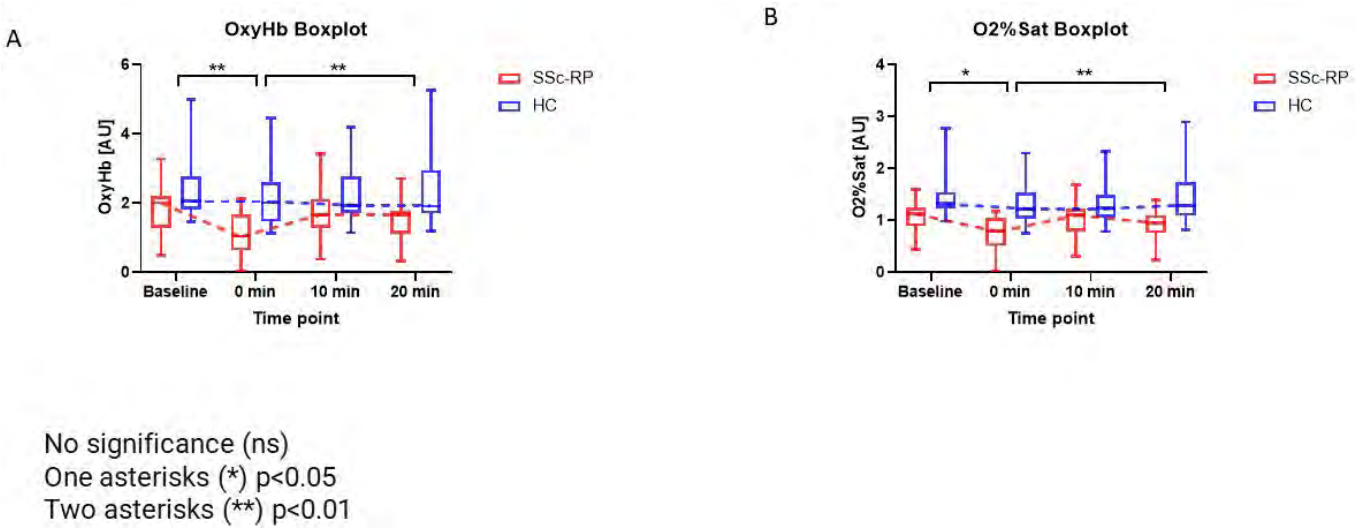

Figure 3. A. Box plot of oxyHb over time in systemic sclerosis (SSc) and healthy control participants (HC) between baseline and during cold provocation challenge and B. Box plot of O2 sat over time in systemic sclerosis (SSc) and healthy control participants (HC) between baseline and during cold provocation challenge.

Results: The mean and standard deviation (SD) age and % female for SSc (n=13) and HC (n=13) participants were 49±22 and 40±13 years (y), and 92% and 94% female, respectively. The mean (SD) SSc duration was 10.9 ± 10.4 y with 69% having limited cutaneous SSc. Thirty eight percent of SSc subjects had prior digital ulcers; none were current. Sixty-two% and 38% of SSc patients were prescribed a calcium channel blocker and statin, respectively. Baseline oxyHb, deoxyHb and O2 sat maps did not significantly differ between SSc and HC participants. However, after cold provocation, images from baseline to 0 min revealed significant reductions in mean slopes of oxyHb and O2 sat for SSc (-0.71, -0.33) compared to HC (-0.22, -0.11; p=0.005, 0.014, respectively). There were no differences in deoxyHb maps between SSc patients and HC immediately post cold challenge. From 0 to 20 min, SSc subjects had more change in oxyHb (p=0.001), deoxyHb (p=0.003), and O2 sat (p< 0.001) compared to HC (Fig. 3).

Conclusion: We showed that HSI is a feasible approach for microcirculation measurement in the hands of SSc patients and HC participants. SSc subjects had a greater decline in oxyHb and O2 sat images from baseline to time 0 (after cold provocation) with significant change in oxyHb, O2 sat, and deoxyHb compared to HC subjects thereafter. These data suggest that HSI technology to assess RP vascular dysfunction is a potential quantitative measure for SSc-RP severity and activity in clinical trials.

Disclosure: A. Gupta, None; **S. Teaw**, None; **A. Williams**, None; **F. Wilson**, None; **B. Sumpio**, None; **B. Sumpio**, None; **M. Hinchcliff**, None.

Abstract Number: 0395

RNA Polymerase III Autoantibody Levels and Risk of Systemic Sclerosis in Patients with Raynaud Phenomenon

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Table 1. Demographics and Clinical Characteristics at Index Date (initial anti-RNAP III test)

	anti-RNAP III status			p value
	Weak (n=44)	Moderate (n=23)	Strong (n=51)	
Demographics				
Mean age (years)	51.25	55.30	62.22	0.0022
Female, n (%)	88.64	82.61	78.43	0.4196
White, n (%)	83.33	81.82	86.27	0.8692
Laboratory data				
Scl-70 antibody level by category				
Not sent (%)	2.27	0.00	3.92	0.2005
Negative (%)	90.70	95.65	97.96	
Equivocal (%)	0.00	2.04	0.00	
Positive (%)	9.30	4.35	0.00	
Centromere antibody level by category				
Not sent (%)	9.09	4.35	3.92	0.0059
Negative(%)	82.50	95.45	100.00	
Positive (%)	17.50	4.55	0.00	
ANA pattern				
Centromere	7.14	4.35	0.00	0.1114
Nucleolar	16.67	13.04	4.26	
Other*	76.19	82.61	95.74	
ANA titer				
Not sent	4.55	0.00	5.88	0.0157
Negative	9.09	4.35	3.92	
1:40	14.29	13.04	6.25	
1:80-1:160	14.29	13.04	14.58	
1:320-1:1280	26.19	39.13	66.67	
>1:1280	35.71	30.43	8.33	
ESR, mean +/- SD mm/hour	35.59	28.00	17.83	0.0061
CRP mean +/- SD mg/liter	10.81	15.61	7.48	0.3237
Lifestyle and family history				
Smoking history				
Former	18.18	30.43	41.18	0.0227
Current	9.09	21.74	3.92	
Never	72.73	47.83	54.90	
BMI				
<25	45.45	43.48	50.98	0.3989
25 to <30	20.45	39.13	23.53	
>30	34.09	17.39	25.49	
Family history of SSc	2.27	4.35	0.00	0.3824
Family history of Raynaud	4.65	13.04	5.88	0.4125
Family history of rheumatic disease	22.73	8.70	23.53	0.3043
Co-morbidities				
Thyroid disease	20.45	13.04	19.61	0.742
HTN	22.73	21.74	25.49	0.9228
Other CTD**	43.18	8.70	3.92	<.0001
Clinical presentation				
Digital pitting	4.65	4.35	5.88	0.9476
Digital ulcers	9.30	13.04	15.69	0.6555
GAVE	2.27	4.35	9.80	0.2854
Interstitial lung disease	25.00	47.83	39.22	0.1413
Malignancy	13.64	8.70	31.37	0.0315
Nailfold capillary changes	58.33	61.90	72.73	0.3808
Puffy hands	36.36	39.13	66.67	0.0069
Pulmonary hypertension	6.82	13.04	13.73	0.5330
Reflux	54.55	73.91	72.55	0.1250
Scleroderma renal crisis	2.27	13.04	11.76	0.1753
Skin thickening	32.56	73.91	94.12	<.0001
Telangiectasias	25.58	26.09	33.33	0.6717

*cytoplasmic, diffuse, homogeneous, speckled, oligo dots

**inflammatory myopathy, mixed connective tissue disease, systemic lupus erythematosus

Table 2. Association between anti-RNAP III levels and risk of SSc

anti-RNAP III level	No. patients	P-years	No. SSc	Rate of SSc (1/100 PYs)	Crude HR (95% CI)	Adj. HR* (95% CI)
Weak	44	150	14	9.3	1.0 (reference)	1.0 (reference)
Moderate	23	186	16	8.6	1.50 (0.78, 2.88)	1.49 (0.74, 3.01)
Strong	51	268	49	18.3	2.57 (1.43, 4.61)	2.88 (1.53, 5.41)
P for trend					0.0023	0.0028

*Potential confounders: age, gender, tobacco use, malignancy, other connective tissue disease, renal crisis, nailfold capillary changes, ANA pattern, +anti-centromere antibody, +anti-Scl-70 antibody

Background/Purpose: Raynaud phenomenon is often the initial manifestation in systemic sclerosis (SSc) and can precede other SSc symptoms by years (1). Several SSc-specific autoantibodies are useful to identify patients with isolated Raynaud phenomenon (RP) at risk of progression to SSc (2). Anti-RNA polymerase III (anti-RNAP III) is associated with diffuse skin thickening, risk for renal crisis, and malignancy (3,4). The level of anti-RNAP III in patients with RP and the risk of progression to SSc has not previously been evaluated. We examined the relationship between anti-RNAP III levels and SSc risk among patients with RP.

Methods: We performed a retrospective cohort analysis of anti-RNAP III positive patients with RP seen at a US tertiary hospital system between January 1, 2010 and December 31, 2020. SSc diagnosis was determined through medical record review utilizing the 2013 ACR-EULAR classification criteria. Anti-RNAP III levels were classified into three categories: weak (20-39 units), moderate (40-80 units), and strong positive (> 80 units). We estimated the rate of developing SSc for each anti-RNAP III category and examined their relation using a cause-specific Cox-proportional hazard model accounting for competing risk of death. In the multivariable regression model, we adjusted for socio-demographic and lifestyle factors, family history of rheumatic disease, comorbidities, and several laboratory results.

Results: We identified 118 patients with anti-RNAP III and RP. Patients with strong positive anti-RNAP III levels were more likely to be older, have negative centromere antibodies, a smoking history, a malignancy history, puffy hands, and skin thickening (Table 1). During 604 person-years of follow up, 79 patients developed SSc. The rate of SSc development was 9.3, 8.6, and 18.3 per 100-person-years among patients with weak, moderate, and strong positive anti-RNAP III levels, respectively (Table 2). Compared with those with weak anti-RNAP III levels, adjusted hazard ratios for patients with moderate and strong positive anti-RNAP III levels were 1.49 (95% CI: 0.74-3.01) and 2.88 (95% CI: 1.53-5.41), respectively (P for trend < 0.003).

Conclusion: Patients with high levels of anti-RNAP III had a much higher risk of progression to SSc than those with moderate and weak levels. Our findings suggest the level of anti-RNAP III is a strong predictor for the risk of SSc among patients with RP and those with high levels of anti-RNAP III should be closely monitored for development of SSc.

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Abstract Number: 0396

Esophageal Involvement and Gastroesophageal Reflux Disease in Patients with SSc-ILD: Data from a Sub-Study of the SENSCIS Trial

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SESSION INFORMATION

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Background/Purpose: Upper gastrointestinal involvement such as esophageal dilation is frequently observed in patients with SSc-ILD and may be associated with the presence or severity of SSc-ILD. We assessed the characteristics of patients with SSc-ILD based on the presence of esophageal distension and gastroesophageal reflux disease (GERD), and based on widest esophageal diameter, using data from the SENSCIS trial.

Table 1. Characteristics of patients with esophageal distension with and without GERD* at baseline in the HRCT sub-study of the SENSCIS trial

	Esophageal distension and GERD (n=85)	Esophageal distension and no GERD (n=25)
Female	65.9	76.0
Age, years	53.7 (12.5)	58.2 (11.8)
Race		
White	69.4	44.0
Asian	20.0	56.0
Black or African-American	8.2	0
Other	1.2	0
Body mass index, kg/m^2	26.0 (4.8)	25.7 (4.5)
Time since onset of first non-Raynaud symptom, years	3.2 (1.5)	2.3 (1.2)
Diffuse cutaneous SSc	47.1	24.0
mRSS	9.0 (8.0)	7.1 (5.3)
Extent of fibrotic ILD on HRCT, %†	36.9 (19.4)	34.8 (24.0)
FVC % predicted	73.9 (16.0)	80.6 (16.5)
DLco % predicted	51.2 (13.7)	59.3 (17.4)
SGRQ total score	39.0 (20.6)	29.3 (17.0)

Data are mean (SD) or % of patients. Seven patients had GERD and no esophageal distension.

*Presence of GERD was based on "esophageal (dysphagia, reflux)" reported as SSc-related medical history.

†Assessed visually in the whole lung to the nearest 5%. Pure (non-fibrotic) ground-glass opacity was not included.

Table 2. Characteristics of patients by widest esophageal diameter at baseline in the HRCT sub-study of the SENSCIS trial

	Widest esophageal diameter at baseline ≤15mm (n=41)	Widest esophageal diameter at baseline >15mm (n=75)
Female	82.9	60.0
Age, years	56.3 (11.6)	54.0 (12.8)
Race		
White	65.9	64.0
Asian	26.8	26.7
Black or African-American	4.9	6.7
Other	0	1.3
Body mass index, kg/m^2	26.9 (5.9)	25.8 (4.3)
Time since onset of first non-Raynaud symptom, years	2.9 (1.4)	3.1 (1.5)
Diffuse cutaneous SSc	22.0	52.0
mRSS	6.1 (6.9)	9.6 (7.6)
GERD*	68.3	84.0
Extent of fibrotic ILD on HRCT, %†	29.1 (18.5)	39.1 (20.7)
FVC % predicted	78.0 (15.6)	73.7 (16.5)
DLco % predicted	56.0 (17.3)	51.7 (13.7)
SGRQ total score	33.7 (20.4)	39.0 (19.7)

Data are mean (SD) or % of patients. *Presence of GERD was based on "esophageal (dysphagia, reflux)" reported as SSc-related medical history. †Assessed visually in the whole lung to the nearest 5%. Pure (non-fibrotic) ground-glass opacity was not included.

Methods: Patients in the SENSCIS trial had SSc with first non-Raynaud symptom ≤7 years before screening and an extent of fibrotic ILD on HRCT (based on visual assessment of the whole lung) ≥10%. In a sub-study, the presence of esophageal distension and the widest esophageal diameter (i.e. the largest distance between internal esophageal mucosal limits for three diameter measurements) were assessed at baseline using high-resolution computed tomography (HRCT). In descriptive analyses, we assessed the characteristics of patients in subgroups by the presence (yes/no) of esophageal distension and GERD, and by widest esophageal diameter ≤15mm vs >15mm at baseline.

Results: Of 576 patients in the SENSCIS trial, 150 participated in the HRCT sub-study, of whom 117 had data available on esophageal distension at baseline. Of these, 85 (72.6%) had both esophageal distension and GERD, 25 (21.4%) had esophageal distension and no GERD, and 7 (6.0%) had GERD and no esophageal distension. Compared with patients with esophageal distension but no GERD, the subgroup of patients with both esophageal distension and GERD had a greater proportion of patients with diffuse cutaneous SSc, worse modified Rodnan skin scores, greater extent of fibrotic ILD on HRCT, worse lung function, and worse quality of life based on the St George's Respiratory Questionnaire (SGRQ) total score (Table 1). Of 116 patients with data available on esophageal diameter at baseline, 75 (64.7%) had a widest esophageal diameter >15mm. Compared with patients with a smaller esophageal diameter, the subgroup of patients with a widest esophageal diameter >15mm had a greater proportion of patients with GERD, greater proportion of patients with diffuse cutaneous SSc, worse modified Rodnan skin scores, greater extent of fibrotic ILD on HRCT, worse lung function, and worse quality of life based on the SGRQ total score (Table 2).

Conclusion: Exploratory analyses of data from a sub-study of the SENSCIS trial suggest that the combination of esophageal involvement and GERD, and a widest esophageal diameter >15 mm, were associated with worse disease severity in patients with SSc-ILD.

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Safety and Persistence of Monthly Intravenous Iloprost in Systemic Sclerosis

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Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Vasculopathy is a crucial feature of systemic sclerosis (SSc). Raynaud's phenomenon (RP) and digital ulcers (DU) greatly impact the patients' quality of life. Intravenous (IV) iloprost is broadly used to treat RP and DU secondary to SSc. However, no internationally accepted standardised protocol on iloprost use is currently available.

Methods: We reviewed the clinical records of patients with SSc-related DU and/or moderate-to-severe RP (more than two attacks/day with at least moderate pain) not responsive to calcium channel blockers (CCB), receiving or that have received IV iloprost infusions from January 1st 2011 to March 31st 2021. There were no restrictions concerning combination treatments or comorbidities. Our protocol for IV iloprost consists of an initial ten-hour infusion of iloprost 200ng/mL (0.05 mg in 250 ml of 0.9% saline solution) on five consecutive days, followed by a single-day infusion every month. Over the ten hours of infusion, there is a progressive increase of the dose, up to the patient's maximum tolerated dose, ranging from 0.5 to 1.5 ng/kg/min. The infusion rate starts at 4 ml/h and is increased according to the following scheme: 4 mL/h (1st hour), 8 mL/h (2nd hour), 12 mL/h (3rdhour), and then 16 mL/h if tolerated by the patient, until the end of the infusion. Adverse events were assessed by consulting clinical records.

Demographic data	
Female, n (%)	47 (95.9)
Mean age, years ± SD	56.7 ± 18.1
Mean age at diagnosis, years ± SD	47.9 ± 18
Median disease duration, years (range)	13.9 (1-55)
Median disease duration at the beginning of the treatment, years (range)	2.4 (0.3-6)
Clinical subtypes	
dcSSc, n (%)	12 (24.5)
lcSSc, n (%)	27 (55.1)
Sine scleroderma, n (%)	1 (2)
VEDOSS, n (%)	1 (2)
Overlap syndrome, n (%)	8 (16.3)
Auto-antibody	
Anti-Scl 70, n (%)	19 (38.8)
ACA, n (%)	24 (49)
Pm/Scl, n (%)	6 (12.2)
Clinical manifestations	
R, n (%)	49 (100)
Digital ulcers (active/history) , n (%)	42 (85.7)
Telangiectasia, n (%)	28 (57.1)
Calcinosis, n (%)	7 (14.3)
Dysphagia, n (%)	8 (16.3)
Reflux, n (%)	16 (32.7)
ILD, n (%)	18 (36.7)
PAH, n (%)	3 (6.1)
Arthritis/arthralgia, n (%)	18 (36.7)
Concomitant treatment for RP/DU	
Nifedipine/amlodipine, n (%)	45 (91.8)
Bosentan, n (%)	14 (28.6)
Sildenafil, n (%)	5 (10.2)

Table 1. Demographic and clinical data of SSc patients. ACA – anticentromere antibodies; *dcSSc* - diffuse cutaneous systemic sclerosis; DU - digital ulcers; ILD – interstitial lung disease; lcSSc. - limited cutaneous SSc; PAH – pulmonary arterial hypertension; RP - Raynaud's phenomenon; SD - standard deviation; VEDOSS - very early diagnosis of systemic sclerosis.

Results: Forty-nine patients with SSc have been treated with IV iloprost according to our treatment protocol. Patients' characteristics and clinical features are presented in Table 1. Thirty patients initiated iloprost to treat DUs, 14 to treat RP and 5 to treat both. Sixty per cent of patients in the DU group resolved the DUs within the first month of therapy. RP significantly improved in 64% of patients in the RP group within a month. In the RP+DU group, 60% of patients resolved the DUs and significantly improved RP after three months. Currently, 36 patients are actively undergoing treatment. The reasons for discontinuation in the remaining 13 patients included clinical improvement (N=5), switch to treatment with ambulatory elastomeric pump (N=4), death (N=3) or change of follow-up to another hospital (N=1). Iloprost persistence at two and five years after treatment onset was 95.9% and 83.7% (Figure 1), respectively. Nine adverse events were recorded (18.4% of patients): headache was reported in four patients, hypotension in three patients, tachycardia in one patient and generalised erythroderma in one patient.

Conclusion: SSc patients achieved clinical improvement with a good tolerability profile, leading to a high drug persistence rate. Side effects were managed by adapting the infusion rate. Our data support that monthly single iloprostinfusions can be effective, safely administered and adjusted according to the drug tolerance.

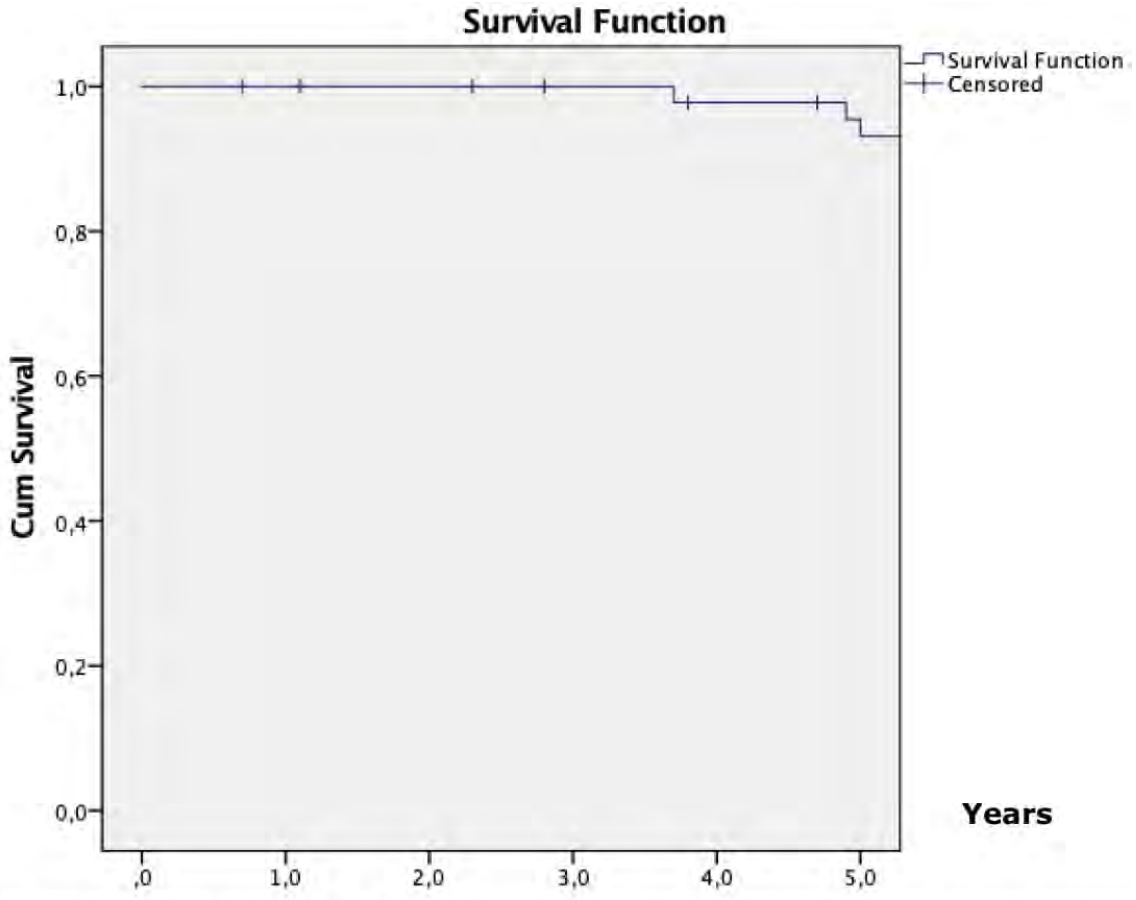

Fig. 1 Kaplan-Meier analysis of the treatment persistence of Iloprost up to five years after treatment onset.

Disclosure: P. Martins, None; **E. Dourado**, None; **J. Fonseca**, None; **V. Romão**, None; **C. Resende**, None.

Abstract Number: 0398

Performance of ACR CRISS Score and Revised ACR CRISS Response in a Phase 3 Trial of Lenabasum in Diffuse Cutaneous Systemic Sclerosis (dcSSc) in Which Background Immunosuppressive Therapies (bIST) Were Allowed

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: ACR CRISS score is the probability of improvement from baseline in each participant (pt) ranging from 0 to 1 (no to high probability), based change in 5 core items: mRSS, FVC%, PtGA, MDGA, and HAQ-DI. Development of this score was done by experts who assessed profiles of dcSSc pts who were recruited in clinical practice on bIST, so its performance and reflection of pt opinion of improvement is unknown in clinical trials in which

Table 1. ACR CRISS Scores by Background Immunosuppressive Therapies and Participant-reported Category of Improvement, at 1 Year

Background immunosuppressive therapies (bIST)	n, % N = 325	ACR CRISS score, median, by participant-reported category of improvement from baseline, range 0 – 1		
		All	Moderate	Major
MMF	171 (53%)	0.937	0.954	0.990
Non-MMF bIST	105 (32%)	0.810	0.962	0.981
All treatments	325 (100%)	0.853	0.951	0.983

Table 2. Revised ACR CRISS Responses, by Background Immunosuppressive Therapies and Participant-reported Category of Improvement, at 1 Year

Background immunosuppressive therapies (bIST)	rCRISS response	% participants achieving rCRISS responses, by participant-reported category of improvement at 1 year		
		All	Moderate	Major
MMF All, n = 171 Moderate improvement, n = 45 Major improvement n = 37	20/5	56%	67%	65%
	25/5	49%	60%	57%
	30/5	42%	**47%**	**54%**
	35/5	36%	**38%**	**51%**
	40/5	33%	**33%**	**46%**
Non-MMF bIST All, n = 105 Moderate improvement, n = 26 Major improvement n = 9	20/5	40%	50%	67%
	25/5	35%	42%	67%
	30/5	28%	**35%**	**56%**
	35/5	20%	**19%**	**44%**
	40/5	20%	**19%**	**44%**
All treatments All, n = 325 Moderate improvement, n = 83 Major improvement n = 48	20/5	47%	57%	63%
	25/5	41%	51%	56%
	30/5	34%	**41%**	**52%**
	35/5	27%	**29%**	**48%**
	40/5	25%	**27%**	**44%**

bIST such as mycophenolate (MMF) are widely used. Revised ACR CRISS (rCRISS) responses are the proportion of pts who improve in ≥ 3/5 core items by certain percentages, for example, 30% (except ≥ 5% in FVC%). Performances were assessed of ACR CRISS score (prospectively as primary endpoint) and rCRISS responses (retrospectively) in a Phase 3 trial in which bIST were allowed.

Methods: Data were analyzed from a 1-year Phase 3 double-blind, placebo-controlled study of lenabasum in pts with dcSSc ≤ 6 years duration, with stable doses of bIST allowed. Pts completed a Patient Global Assessment of Change to categorize their improvement as None, Slight, Moderate, or Major. All cohorts were combined for analyses as the primary endpoint was not meet. Pre-specified analyses had identified a statistically significant effect of MMF on ACR CRISS score in this study, so analyses were done first in pts on MMF, then results validated in other patients.

Results: 276/325 (85%) pts were on bIST. Among 171 pts on MMF, 65% of pts reported improvement at 1 year, which was moderate or major in 48%. ACR CRISS score had a ceiling effect (median = 0.937), with similar scores in pts reporting moderate and major improvement (Table 1). rCRISS responses were examined for potential to distinguish between higher levels of treatment effect, reported by pt opinion. Pts on MMF who reported moderate or major improvement had ~3 core items that improved by ≥ 20% vs. ~2 core items in pts reporting no improvement, supporting requirement for ≥ 3 core items to improve when defining rCRISS responses. rCRISS responses of at

least 30/5 (≥ 3 core items improved by ≥ 30%, except ≥ 5% for FVC%) were numerically greater in pts on MMF who reported major vs. moderate improvement (Table 2), with greater discrimination using 35/5 and 40/5 than 30/5 responses. The rCRISS 30/5, 35/5, and 40/5 responses were 52%, 48%, and 44%, respectively, in pts reporting major improvement on background MMF (Table 2). All these findings were directionally confirmed in pts on non-MMF bIST.

Conclusion: In this Phase 3 trial, bIST provided treatment effect, with about half the pts on background MMF reporting moderate or major improvement at 1 year. Use of the ACR CRISS score to prove efficacy on top of bIST was constrained by its ceiling effect. rCRISS 30/5 or greater responses may help distinguish high level treatment effects on top of bIST. rCRISS responses may be ~ 50% in pts given placebo on top of bIST, setting a high bar for proving additional treatment effect. Use of rCRISS responses to improve the ACR CRISS score may decrease the ceiling effect, provide an equal weight for 5 core items, and improve the interpretation of data (similar to ACR 20% response in RA). These findings should be confirmed in other trials in which pts receive current standard treatment with bIST.

Disclosure: D. Khanna, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **R. Spiera**, GSK, 2, 5, Boehringer Ingelheim Pharmaceuticals, 5, Chemocentryx, 2, 5, Corbus Pharmaceutical, 5, Formation Biologics, 2, 5, InflaRx, 5, Kadmon, 5, Astra Zeneca, 5, Abbvie, 2, CSL Behring, 2, Sanofi, 2, Janssen Pharmaceuticals, 2, Genentech/Roche, 2, 5; **B. White**, Corbus Pharmaceuticals Inc., 3, 8.

Abstract Number: 0399

Nailfold Videocapillaroscopy Findings and Associations with Organ Involvement in Mixed Connective Tissue Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Mixed connective tissue disease (MCTD) is a rare autoimmune condition characterized by Raynaud's phenomenon, positivity of antibodies targeting the U1 small nuclear ribonucleoprotein particle (U1 snRNP), various clinical features and potential risk of severe cardio-pulmonary involvement (interstitial lung disease, ILD, and pulmonary hypertension, PH).

Nailfold videocapillaroscopy (NVC) is a simple, non-invasive and inexpensive imaging technique that allows a detailed assessment of skin microcirculation. NVC abnormalities have been barely described in MCTD and associations between NVC features and MCTD disease characteristics have only been partially investigated. Our objective was to describe the NVC patterns observed in MCTD and assess their potential association with disease characteristics.

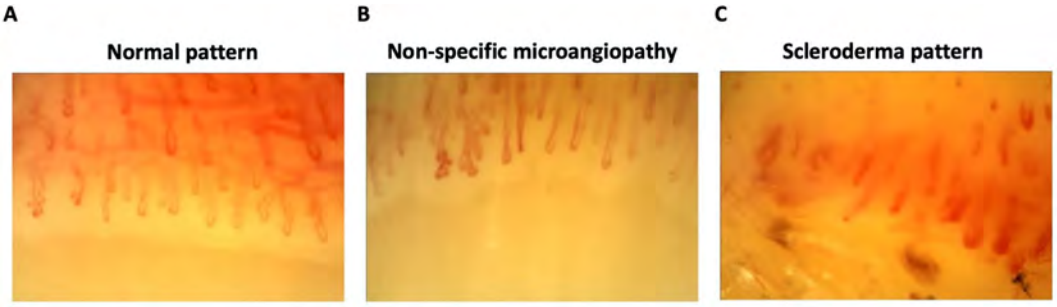


Figure 1. Representative nailfold videocapillaroscopy (NVC) patterns; A, normal NVC pattern; B, non-specific organic microangiopathy; C, Scleroderma pattern.

Methods: Cross-sectional study based on the retrospective analysis of patients hospitalized in the department of Rheumatology, Cochin Hospital, Paris France. To be included, patients were required to fulfill at least one classification criteria used in MCTD. The following data were collected: demographics, clinical features, para-clinical and laboratory data, treatment, and NVC findings.

Results: 51 patients met the inclusion criteria. Mean age was 51±12 years, 44 (86%) were women, mean disease duration was 13.8±11.1 years and 16 patients (31%) had ILD. Three different NVC patterns have been identified in our cohort: a) normal findings in 6 patients (11,7 %) (Figure 1A); b) non-specific organic microangiopathy in 16 patients (31,4%) (Figure 1B) and c) scleroderma pattern in 18 patients (35.3%) (Figure 1C), defined by the presence of at least 3 of the 4 following features: at least 1 giant capillary, decreased capillary density (< 7/mm), avascular areas and disorganization of capillary bed architecture (4). Scleroderma pattern was associated with clinical features of systemic sclerosis: skin sclerosis (9/18 vs. 5/33; p=0.008) and digital ulcers (6/18 vs. 2/31; p=0.017). Conversely, no association was observed between the normal or the non-specific NVC pattern and disease specific characteristics. Interestingly, we observed a significant reduction in the number of capillaries in patients with ILD (4.80±1.87 vs. 6.03±1.47; p=0.039), and patients with severe reduction of capillary density (≤4/mm) were more likely to have ILD (5/7 vs. 5/33; p=0.002). Neoangiogenesis was also more frequent in patients with ILD (6/13 vs. 4/27; p=0.034). Multivariate logistic regression analysis showed that the association between severe reduction of capillary density and ILD was observed independently of the presence of a scleroderma NVC pattern and skin fibrosis.

Conclusion: We identified three main NVC patterns in MCTD patients. The scleroderma NVC pattern was associated with clinical scleroderma characteristics whereas non-specific microangiopathy and normal NVC were not associated with a specific phenotype. Moreover, severe capillary loss was independently associated with the presence of ILD. These data suggest that NVC may be helpful for disease risk stratification in MCTD, and that NVC findings, and particularly severe capillary loss, may be a warning for the presence of ILD.

Disclosure: C. Kasser, None; **G. Boleto**, None; **Y. Allanore**, None; **J. Avouac**, None.

Abstract Number: 0400

Item Development for the Assessment of Systemic Sclerosis-associated Raynaud's Phenomenon (ASRAP) Questionnaire

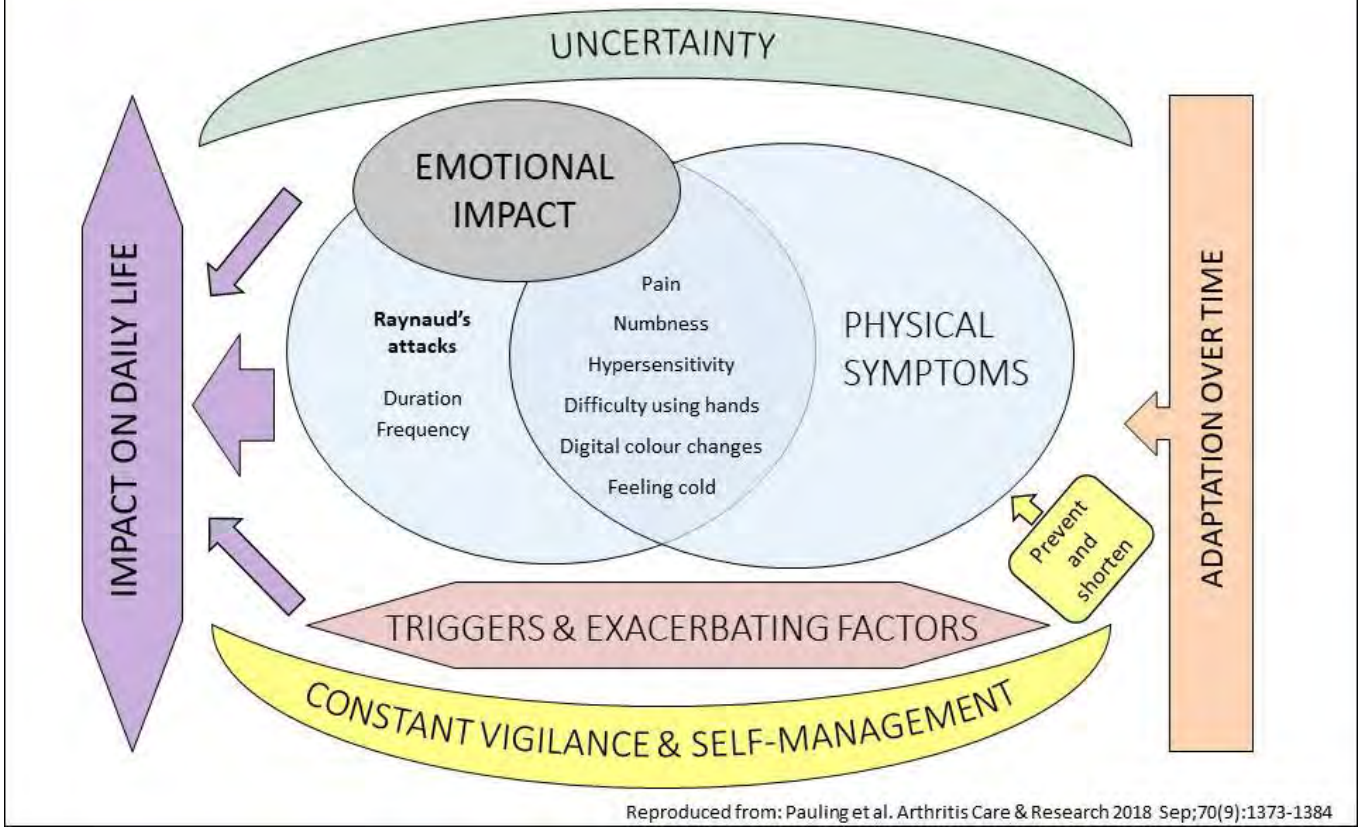
John Pauling[1], Lesley Ann Saketkoo[2], Dinesh Khanna[3], Christopher Denton[4], Tracy Frech[5], Ariane Herrick[6], Laura Hummers[7], Ami Shah[8] and Robyn Domsic[9], [1]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]University Medical Center - Comprehensive Pulmonary Hypertension Center, New Orleans, LA, [3]University of Michigan, Ann Arbor, MI, [4]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom, [5]University of Utah, Salt Lake City, UT, [6]University of Manchester, Salford, United Kingdom, [7]Johns Hopkins Univerisity, Baltimore, MD, [8]Johns Hopkins Rheumatology, Baltimore, MD, [9]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The episodic and uniquely personalised nature of Raynaud's phenomenon (RP) has led to reliance upon self-report to capture how patients 'feel' and 'function'. Existing diary-based patient-reported outcome (PRO) instruments have not supported marketing authorisation of promising therapeutic interventions for RP in patients with systemic sclerosis (SSc). We report item development for the novel Assessment of Systemic sclerosis-associated RAynaud's Phenomenon (ASRAP) questionnaire.

Methods: The conceptual framework for the ASRAP questionnaire was to devise a novel PRO instrument that captured the severity and impact of SSc-RP. A provisional item bank was developed with input from patient insight partners with candidate items grounded in the themes and sub-themes identified in an earlier international multicentre qualitative research study of SSc-RP (Figure 1). Iterative modification of the items was undertaken with input from 4 SSc experts and a patient research partner to ensure item wording, recall period and response options were simple, understandable, relevant to specific domain concepts and conformed to internationally agreed standards. Linguistic evaluation was assessed using the Simple Measure of Gobbledygook (SMOG) with modification to achieve a readability age of < 14 years. Cognitive de-briefing interviews were held with English-speaking

Figure 1. Conceptual map of the patient experience of Systemic sclerosis-associated Raynaud's phenomenon



Reproduced from: Pauling et al. Arthritis Care & Research 2018 Sep;70(9):1373-1384

Figure 2. Linguistic evaluation of provisional ASRAP items using Simple Measure of Gobbledygook (SMOG) calculator

Original item wording (# item)	SMOG analysis	Revised Item wording (# item)	Revised SMOG analysis
#8. Raynaud's symptoms have interfered with my ability to use my fingers	SMOG index: 16.2 Total words: 11 Polysyllabic words: 2	#8. Raynaud's symptoms have made it difficult to use my fingers	SMOG index: 13.8 Total words: 10. Polysyllabic words: 1
#9. How frequently have you been experiencing attacks of Raynaud's symptoms?	SMOG index: 16.2 Total words: 10 Polysyllabic words: 2	#9. How often have you experienced attacks of Raynaud's symptoms?	SMOG index: 8.1 Total words: 10 Polysyllabic words: 0
#19. Raynaud's symptoms have bothered me due to inability to do my usual things	SMOG index: 16.2 Total words: 13 Polysyllabic words: 2	#19. Being unable to do normal things because of Raynaud's symptoms has bothered me	SMOG index: 13.8 Total words: 13 Polysyllabic words: 1
#21. Raynaud's symptoms have interfered with my ability to go shopping	SMOG index: 16.2 Total words: 10 Polysyllabic words: 2	#21. Raynaud's symptoms have made it difficult when I have been shopping	SMOG index: 13.8 Total words: 11 Polysyllabic words: 1
#22. Raynaud's symptoms have interfered with my ability to do housework/ gardening	SMOG index: 18 Total words: 9 Polysyllabic words: 3	#22. Raynaud's symptoms have made it difficult to do work around the house	SMOG index: 13.8 Total words: 12 Polysyllabic words: 1
#23. Raynaud's symptoms have interfered with my ability to socialise	SMOG index: 18 Total words: 9 Polysyllabic words: 3	#23. Raynaud's symptoms have made social events/doing sport difficult	SMOG index: 13.8 Total words: 10 Polysyllabic words: 1
#24. Raynaud's symptoms have interfered with my ability to do my job (paid or unpaid)	SMOG index: 16.2 Total words: 14 Polysyllabic words: 2	#24. Raynaud's symptoms have made it difficult to do my job (paid or unpaid)	SMOG index: 13.8 Total words: 13 Polysyllabic words: 1
#25. Raynaud's symptoms have interfered with my home/family life	SMOG index: 16.2 Total words: 8 Polysyllabic words: 2	#25. Raynaud's symptoms have had an effect on my home / family life	SMOG index: 13.8 Total words: 12 Polysyllabic words: 1
#26. Raynaud's symptoms have interfered with personal relationships	SMOG index: 18 Total words: 7 Polysyllabic words: 3	#26. Raynaud's symptoms have had an effect on my personal / private life	SMOG index: 13.8 Total words: 12 Polysyllabic words: 1
#28. Visiting a grocery store /supermarket has caused Raynaud's symptoms	SMOG index: 18 Total words: 9 Polysyllabic words: 3	#28. Going inside a grocery store / supermarket has caused Raynaud's symptoms	SMOG index: 13.8 Total words: 12 Polysyllabic words: 1
#35. I have limited my activities (going outside/doing things I enjoy) to avoid worsening Raynaud's symptoms	SMOG index: 19.6 Total words: 15 Polysyllabic words: 4	#35. I have avoided doing things (e.g. going outside / doing things I enjoy) to avoid making my Raynaud's symptoms worse	SMOG index: 11.4 Total words: 21 Polysyllabic words: 1

patients at US and UK sites. An item tracking matrix was devised to document modifications throughout the item development process.

Results: A provisional item-bank of 37 candidate items was devised to capture the patient experience of SSc-RP with respect to physical symptoms (n=10), emotional distress (n=7), impact on daily life (n=6), exacerbating factors (n=6), self-management (n=4), adaptation (n=3) and uncertainty (n=2). An additional 2 items were proposed following expert review. Item recall period and response options were optimised for item response theory. Modification to 11 items to improve readability ensure a SMOG index < 14.0 for all items (Figure 2). Cognitive de-briefing interviews were held with 7 patients and led to modification to 11 items, alongside changes to format and structure of the ASRAP questionnaire (Figure 3). No new items were proposed during cognitive de-briefing.

Conclusion: The ASRAP questionnaire item bank has been devised and tested with direct input from an international consortium of SSc experts and patients. The items have been tested to ensure they reflect the intended conceptual framework and fully capture the lived experience of SSc-RP in wording that is comprehensible, minimizes ambiguity

Figure 3. Item Tracking Matrix detailing changes to format and item wording following cognitive de-briefing interviews

Item number or general change	Original item wording/formatting	New item wording/format change
Strengthen focus on 7-day recall period	Considering your Raynaud's attacks over the last 7 days [presented in lower case bold)	In the **PAST 7 DAYS**... [shortened with 'past 7 days' presented in capital letters, in bold and underlined using largest font possible]
9	How often have you experienced attacks of Raynaud's symptoms?	On average, how often have you experienced attacks of Raynaud's symptoms?
10	On average, how much total time have you spent each day experiencing attacks of Raynaud's symptoms?	On average, how much total time per day have you experienced attacks of Raynaud's symptoms?
11	Response option 4: '10-20 minutes' Response option 5: 'Over 30 minutes'	Change response option 4 to '10-25 minutes' Change response option 5 to 'over 25 minutes'
12	Raynaud's symptoms have made me upset/tearful	Raynaud's symptoms have made me tearful
14	Raynaud's symptoms have made me Annoyed/frustrated	Raynaud's symptoms have made me frustrated
18	Raynaud's symptoms have caused low mood / made me depressed	Raynaud's symptoms have made me sad/depressed
23	Raynaud's symptoms have made social events / doing sport difficult	Raynaud's symptoms have made social events / doing exercise difficult
27	I have been able to reduce (control) the intensity my Raynaud's symptoms?	I have been able to reduce (control) the intensity of my Raynaud's symptoms?
28-32	'This activity not undertaken' currently on far left of response options	Move 'This activity not undertaken' response option column to the far right
28	Going inside a grocery store / super-market has caused Raynaud's symptoms	Being inside a grocery store / super-market has caused Raynaud's symptoms
31 and 32	Inadvertent consideration of being indoors by one subject	Switch positions of items 31 and 32
34	I have used hand warmers/put my hands in warm water to control/ manage Raynaud's symptoms	I have used techniques (e.g. hand warmers/putting hands in warm water/sitting on hands) to control/ manage Raynaud's symptoms'
39	Changes to my normal routine have caused me to worry about possible worsening of Raynaud's symptoms	A change in my normal routine has caused me to worry about possible worsening of my Raynaud's symptoms

and meets accepted criteria for optimal translatability into non-English languages. The provisional 39-item ASRAP questionnaire shall progress to formal validation.

Disclosure: J. Pauling, None; **L. Saketkoo**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/ Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **T. Frech**, None; **A. Herrick**, None; **L. Hummers**, Boerhinger Ingelheim, 1, 5, Corbus Pharmaceuticals, 1, 5, Cumberland Pharmaceuticals, 5, Kadmon Corporation, 5, Medpace, 5; **A. Shah**, None; **R. Domsic**, None.

Abstract Number: 0401

Item Reduction for the Assessment of Systemic Sclerosis-associated RAynaud's Phenomenon (ASRAP) Questionnaire Using Data from the International Multicentre ASRAP Validation Study

John Pauling[1], Lan Yu[2], Christopher Denton[3], Tracy Frech[4], Ariane Herrick[5], Laura Hummers[6], Lesley Ann Saketkoo[7], Ami Shah[8], Dinesh Khanna[9] and Robyn Domsic[2], [1]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]University of Pittsburgh, Pittsburgh, PA, [3]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom, [4]University of Utah, Salt Lake City, UT, [5]University of Manchester, Salford, United Kingdom, [6]Johns Hopkins Univerisity, Baltimore, MD, [7]University Medical Center - Comprehensive Pulmonary Hypertension Center, New Orleans, LA, [8]Johns Hopkins Rheumatology, Baltimore, MD, [9]University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: The Assessment of Systemic sclerosis-associated RAynaud's Phenomenon (ASRAP) questionnaire is a novel patient-reported outcome (PRO) instrument devised to assess the severity and impact of SSc-RP. We report a data driven approach to item reduction of the preliminary 39-item questionnaire.

Methods: The international multicentre ASRAP validation study enrolled SSc patients with RP from English speaking UK (n=3) and US (n=4) SSc centres during 2 consecutive winters (2019-2021). All participants completed a 39-item ASRAP questionnaire. Pooled data was used to assess dimensionality, before splitting the cohort to facilitate exploratory and confirmatory factor analyses (CFA). Items with low factor loadings < 0.5 and/or low item discrimination parameter estimates (α< 1.5) were considered for removal. Local dependency (LD) marginal Chi square analyses identified redundant items. Goodness-of-fitness testing examined the extent to which observed data fitted the item response model. Finally, differential item functioning (DIF) explored extent to which each item may measuredifferent concepts according to geographic enrolment (UK versus US sites). At each step, items were retained if content validity considered them essential.

Results: A total of 438 SSc subjects were enrolled at UK (n=238) and US (n=200) sites, with adequate data for analysis on 421 subjects. Eigenvalues for uni- and bi-dimensional options were 21.577 and 3.08 respectively. A single

Figure 1. Example Item Discrimination Parameter estimates for ASRAP Items 1 & 2 (α values >1.0 satisfactory)

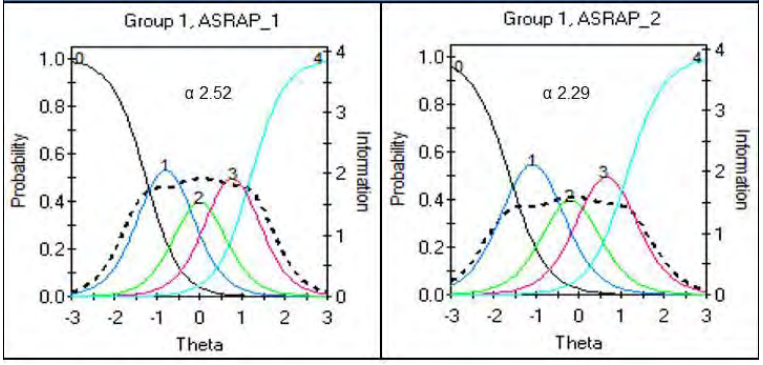

Figure 2. Local Dependency Marginal Chi Square analysis for redundancy (LD Chi Square values <10 desirable and higher values indicate greater redundancy)

Item Pairing		LD Chi-Square	Decision
ASRAP_1	ASRAP_2	12.3	Remove item 2
ASRAP_1	ASRAP_3	10.3	
ASRAP_2	ASRAP_3	26.9	
ASRAP_3	ASRAP_5	12.6	Remove item 5
ASRAP_3	ASRAP_6	10.2	
ASRAP_4	ASRAP_5	11.7	
ASRAP_6	ASRAP_7	19.8	Retain both
ASRAP_9	ASRAP_10	27.4	Remove item 10 Retain item 9
ASRAP_9	ASRAP_11	12.1	
ASRAP_10	ASRAP_11	39.6	
ASRAP_25	ASRAP_26	25.7	Remove item 25
ASRAP_28	ASRAP_29	17.3	Remove item 29
ASRAP_33	ASRAP_37	11.1	Retain both
ASRAP_35	ASRAP_38	19.3	Remove item 38

Figure 3. Summary of item reduction for ASRAP questionnaire

Item	Factor Analysis		IRT Analysis				Content Review
	Exploratory	Confirmatory	*a* parameter	Local Dependency	Model Fit	DIF-Location	
Item 1							
Item 2				X		X	REMOVE
Item 3							
Item 4							
Item 5				X		X	REMOVE
Item 6-8							
Item 9					X		KEEP
Item 10				X	X		REMOVE
Item 11-24							
Item 25				X			REMOVE
Item 26							
Item 27					X		REMOVE
Item 28							
Item 29				X			REMOVE
Item 30	X	X	X				REMOVE
Item 31	X	X					REMOVE
Item 32							
Item 33	X	X	X				REMOVE
Item 34			X				REMOVE
Item 35						X	REMOVE
Item 36-37							
Item 38				X	X		REMOVE
Item 39							

factor solution provided the best-fitting model with factor loadings for the majority of factors ~0.8. Three items were removed owing to lower factor loadings (0.415-0.443). CFA revealed a Root Mean Square Error of Approximation of 0.114, a Standardized Root Mean Square Residual of 0.083 and a Confirmatory Factor Index of 0.917; each indicating excellent fit. Four low scoring Item Discrimination Parameter estimates (Figure 1) were identified (alpha scores of 1.04-1.25), leading to removal of one item (the remainder having already been removed). Only 14 potentially redundant pairings were identified using LD marginal chi square (>10 indicates redundancy), which led to the removal of a further 6 items (Figure 2). Model fit analyses identified 3 problematic items; one of which was removed, one retained due to content validity and the other already removed). Finally, DIF identified 3 items which differed due to geographic location (2 already removed) and led to removal of an item (Figure 3).

Conclusion: We report a data driven approach (focussed on item response theory) to removing problematic or redundant items from the provisional ASRAP item bank. This has facilitated item reduction to a 27-item PRO instrument that will undergo psychometric testing and other tests of reliability and construct validity.

Disclosure: J. Pauling, None; **L. Yu**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **T. Frech**, None; **A. Herrick**, None; **L. Hummers**, Boerhinger Ingelheim, 1, 5, Corbus Pharmaceuticals, 1, 5, Cumberland Pharmaceuticals, 5, Kadmon Corporation, 5, Medpace, 5; **L. Saketkoo**, None; **A. Shah**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **R. Domsic**, None.

Abstract Number: 0402

What Is the Patient's Perspective on Symptoms Experience in Limited Cutaneous Systemic Sclerosis?

Alain Lescoat[1], Susan Murphy[2], Yen Chen[3], Nadia Vann[1], David Cella[4] and Dinesh Khanna[3], [1]Michigan Scleroderma Program, University of Michigan, Ann Arbor, MI, [2]University of Michigan, Grosse Ile, MI, [3]University of Michigan, Ann Arbor, MI, [4]Department of Medical Social Sciences, Northwestern University Feinberg School of Medicine, Chicago, IL

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Limited cutaneous SSc (lcSSc) affects approximately 60-70% of SSc patients but drug development and therapeutic research has largely focused on the more severe diffuse SSc. As a result, lcSSc has been rather neglected with respect to development of relevant outcome measures. To identify relevant candidate items (outcome measures) to include in a future combined response index for clinical trial assessment of lcSSc patients (the CRISTAL index: Combined Response Index for Scleroderma Trials Assessing Limited SSc), this qualitative study aimed to identify the most salient domains affecting everyday life from the patients' perspective and to capture the overall symptom experience of lcSSc.

Table 1: Domains and outcomes reported as bothersome or impacting by patients with lcSSc

Domains mentioned (22) *=mentioned in all focus groups	Symptoms and/or outcomes mentioned (93)	
Fatigue*	-Tiredness -Exhaustion / Lack of endurance	-Mental fatigue -Running out of energy
Cognition	-Brain fog / memory loss	
Digital Ulcers*	-Sores / open digital wounds -Foot hole / digital ulcers on the toes -New DU onset -Number of DUs / recurrent DUs -DU healing-time /time to heal	-DU-related pain -DU-related Neuropathic pain -Auto-amputation / Acro-osteolysis -Surgical amputation -infected DU
Gastro-Intestinal*	-GERD -Heartburns -Dysphagia -Throwing up -Failed swallowing -cough -Sore Throat	-Odynophagia -gastroparesis -early satiety -stomach pain -Diarrhea -Weight loss -malabsorption
Raynaud's*	-Attacks or episodes -Lack of circulation -Finger pain / Fingertip pain -Numbness/loss of feeling -Ischemia-reperfusion	-Finger/hand stiffness -Color change -Acrocyanosis -Chilblains -cold extremities
Calcinosis	-Onset of calcinosis -Calcinosis-related pain -pseudo-tumoral calcinosis	-affecting different body parts -flares/episodes of calcinosis
Pulmonary*	-Dyspnea / shortness of breath -Evolution of PFT parameters	-CT scan evolution / Lung fibrosis
Sicca syndrome	-dry eyes -dry mouse	-Tongue burn / sensitive oral mucosa
Musculoskeletal*	-joint pain -synovitis / tenosynovitis -morning stiffness -Joint tenderness	-Diminished range of motion -Muscle pain -Strength loss -cramps
Pain	-Neuropathic pain -Soft tissue pain	-Indescribable pain -Fibromyalgia-like or fibromyalgia-related pain
Skin*	-Hand/finger/feet puffiness or swelling -Itching/pruritus -skin thickening -skin tightening -hypertrophic cuticles / cuticles splitting	-extent of skin involvement / mRSS -skin cracks -Aspect/appearance of the hands / Overall skin appearance -Finger and hand deformity
Vasculopathy other than DU and/or Raynaud	-Widespread vasculopathy -telangiectasia	-obliterative vascular disease
Cardiac*	-Shortness of breath -Left ventricular heart failure -Right heart catheterization parameters	-PH/PAH -Diastolic dysfunction / Myocardial fibrosis
Sleep	-difficulties in staying asleep/night awakenings	-difficulties in falling asleep
Sexual Health	-Dyspareunia	-Erectile dysfunction
Renal	-Renal insufficiency / need for dialysis	
Dental Health	-Teeth loss / Tooth decay	
Mental Health	- Low moral/ Negative ideas	-Depression
Global Health	-General looking -General shape	-General feeling
Quality of Life	-Altered quality of life	
Survival	-Shorter life expectancy	
Biomarkers	-Acute phase reactants	

Methods: A participatory action research approach facilitated collaboration between patients and researchers in the identification of domains and candidate items that lcSSc patients consider most important (i.e., symptoms that are most bothersome and affect daily life). Focus groups with lcSSc were conducted using a predefined guide with 10 open-ended questions. The number of focus groups was determined by data saturation. Focus groups were

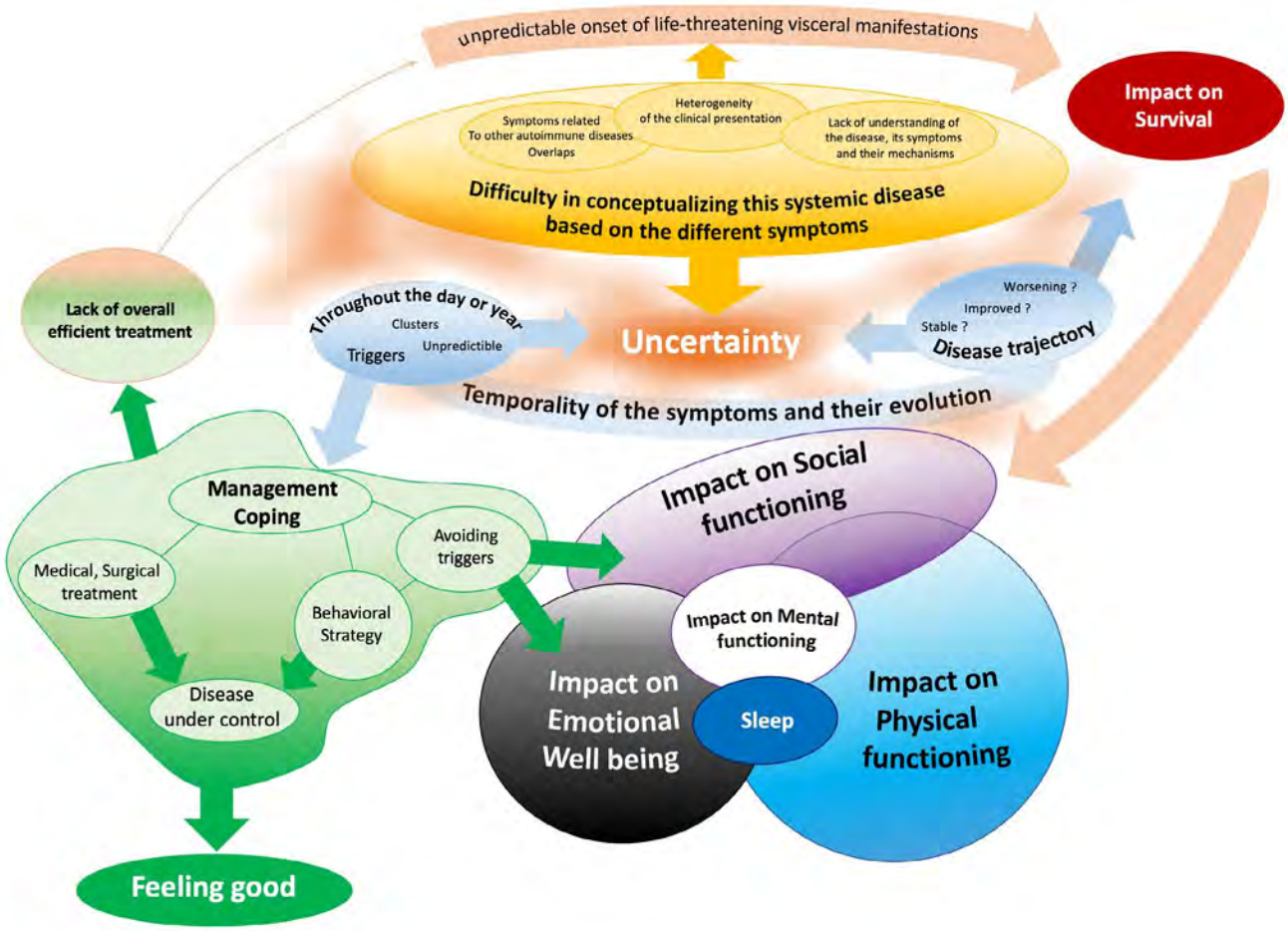

Figure 1 : Preliminary conceptual model of symptom experience in patients with lcSSc

recorded, transcribed verbatim, and de-identified. A hierarchical taxonomy of domains/outcomes and experience-related themes was developed using an iterative, deductive and inductive approach with two independent coders. Throughout the coding process, the codebook was revised and edited in a collaborative process that included a patient partner as co-investigator.

Results: Twenty-six patients with lcSSc (median age 56 yo (25-77yo); 42% with early disease< 5 years, 15.4% >20 years) from the University of Michigan were included in 4 focus groups lasting 2-hours each. One group included only men; two were only women; and one was with both sexes. Twenty-two domains were identified, comprising 93 symptoms and/or outcomes. Eight domains were reported in all four focus groups: fatigue, digital ulcers, gastro-intestinal involvement, Raynaud's phenomenon, pulmonary involvement, cardiac involvement, musculoskeletal manifestations and skin involvement (**Table 1**). The 14 remaining domains notably included calcinosis, sicca syndrome, sexual health and survival. In terms of symptom experience, 6 themes were identified: difficulty in conceptualizing the disease, experiencing the temporality of SSc-related symptoms, uncertainty, need for coping and better management, impact of the symptoms on functioning (comprising social, mental and physical functioning) and impact of the symptoms on emotional well-being. The connections between these themes are represented in a preliminary conceptual map (**Figure 1**).

Conclusion: This qualitative study based on a participatory action research approach allowed a comprehensive identification of key domains and related-outcomes in lcSSc and provide in depth analysis on symptoms experience

in this neglected but frequent subset of the disease. These results paved the way for the selection of candidate items (outcome measures) to include in a future patient-centered, combined response index for clinical trial assessment of lcSSc.

Disclosure: A. Lescoat, None; **S. Murphy**, None; **Y. Chen**, None; **N. Vann**, None; **D. Cella**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2.

Abstract Number: 0403

Effect of Nintedanib on KL-6 in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease

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SESSION INFORMATION
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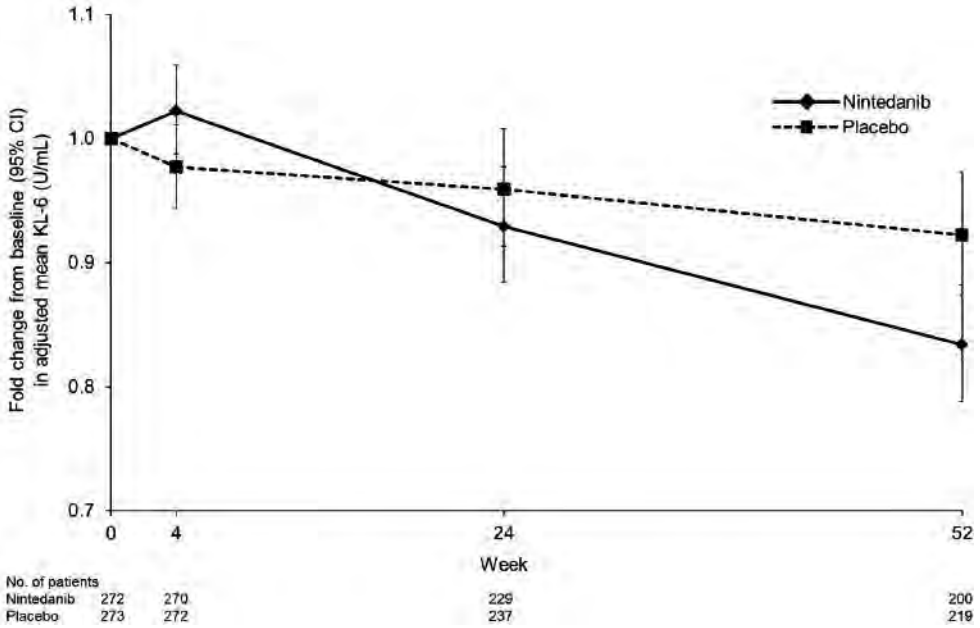
Session Time: 8:30AM–10:30AM

Background/Purpose: Krebs von den Lungen-6 (KL-6), a marker of lung epithelial and endothelial injury, has been associated with progression of interstitial lung disease associated with systemic sclerosis (SSc-ILD). In the SENSCIS trial, nintedanib, an intracellular inhibitor of tyrosine kinases, slowed the rate of decline in forced vital capacity (FVC) in patients with SSc-ILD compared with placebo. We assessed the associations between levels of KL-6 and clinical variables, and the effect of nintedanib on changes in KL-6 in the SENSCIS trial.

Methods: Patients in the SENSCIS trial had SSc with first non-Raynaud symptom ≤7 years before screening and an extent of fibrotic ILD on HRCT ≥10%. Blood samples for biomarker analysis were taken at baseline and at weeks 4, 24 and 52. Absolute changes from baseline in KL-6 over 52 weeks were analyzed using a mixed model for repeated measures and restricted maximum likelihood approach. Data were $\log_{10}$ transformed prior to analysis and estimates of change from baseline were back-transformed to provide fold changes. Associations between KL-6 levels and age, FVC, DLco, SpO_2, modified Rodnan skin score, St George's Respiratory Questionnaire total score, and digital ulcer net burden at baseline, and between changes from baseline in KL-6 and each clinical variable over 52 weeks, were assessed using Spearman's correlation coefficients (rho). Correlations with a coefficient ≥0.25 and a p-value < 0.05 were considered notable.

Results: Of 576 treated patients, 559 (97.0%) had data on KL-6 levels at baseline. At baseline, there was a weak negative correlation between KL-6 levels and DLco % predicted (rho: –0.38 [95% CI: –0.45, –0.31]; nominal p< 0.0001).

Figure. Fold changes from baseline in KL-6 over 52 weeks based on a mixed model for repeated measures with fixed categorical effects of treatment at each visit, anti-topoisomerase I antibody status, sex, SSc subtype (limited cutaneous SSc or diffuse cutaneous SSc), mycophenolate use at baseline, methotrexate use at baseline, and fixed continuous effects of baseline KL-6 value at each visit, body mass index and age.



No notable correlations were observed between KL-6 and other clinical variables at baseline. No notable correlations were observed between changes in KL-6 and changes in other clinical variables over 52 weeks. Fold changes from baseline in adjusted mean KL-6 at week 52 were 0.83 (95% CI: 0.79, 0.88) in the nintedanib group and 0.92 (95% CI: 0.87, 0.97) in the placebo group (ratio of 0.91 [95% CI: 0.84, 0.98]; nominal p=0.01) (Figure). Mean (SE) absolute changes from baseline in KL-6 at week 52 were –202.2 (47.5) U/mL in the nintedanib group and –124.5 (54.8) U/mL in the placebo group. There was no significant difference between the nintedanib and placebo groups in fold change from baseline in adjusted mean KL-6 at week 24.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, higher KL-6 levels at baseline were associated with lower DLco % predicted. KL-6 levels decreased over 52 weeks both in the nintedanib and placebo group, with a larger decrease in the nintedanib group. These data suggest that KL-6 demonstrates a pharmacodynamic response to nintedanib in patients with SSc-ILD over 52 weeks of treatment.

Disclosure: S. Assassi, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **M. Cutolo**, Bristol Myers Squibb, 5, Boehringer Ingelheim, 5, Celltrion, 6, Janssen, 6; **T. Luckhardt**, Boehringer Ingelheim, 6, Boehringer Ingelheim, 12, Registry Committee Member; **C. Diefenbach**, Boehringer Ingelheim, 3; **C. Ittrich**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **M. Kuwana**, Boehringer Ingelheim, 5, 6, One Pharmaceuticals, 5, 6, Chugai, 6, Janssen, 6, Astellas, 6, Tanabe Mitsubishi, 6, Pfizer, 6, Nippon Shinyaku, 6, Corbus, 2, Mochida, 2, Kissei, 2, MBL, 9.

Abstract Number: 0404

Perifollicular Hypopigmentation in Systemic Sclerosis: Associations with Clinical Features and Internal Organ Involvement

Melody Chung[1], Jamie Perin[1], Carrie Richardson[2], Christopher Mecoli[3], Fred Wigley[1] and Zsuzsanna McMahan[4], [1]Johns Hopkins University, Baltimore, MD, [2]Rush University Medical Center, Chicago, IL, [3]Johns Hopkins University School of Medicine, Baltimore, MD, [4]Johns Hopkins Rheumatology, Baltimore, MD

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Background/Purpose: Among the autoimmune rheumatic diseases, there is precedent for utilizing cutaneous manifestations of systemic disease as clues to clinical phenotype and disease prognosis. Though skin thickening affects >90% of patients with SSc, perifollicular hypopigmentation is observed less frequently. We sought to determine whether perifollicular hypopigmentation is associated with demographics, clinical features, and autoantibody profiles.

Methods: Data from SSc patients were prospectively collected from a single tertiary academic medical center. Patients were consecutively recruited, with additional targeted recruitment to enrich for patients with hypopigmentation. A standardized data collection form was completed on each patient including anatomic distribution of hypopigmentation. Autoantibody screens were performed using the commercially available Euroline immunoblot assay [Scleroderma Nucleoli Profile Uroline (IgG); Euroimmun, Lubeck, Germany]. Associations between perifollicular hypopigmentation and distinct features of SSc were assessed using logistic regression.

Results: Of the 179 adult SSc patients enrolled (Table 1), 36 (20%) SSc patients had perifollicular hypopigmentation. Among patients with perifollicular hypopigmentation, 94% (n=34) were female and 33% (n=12) had limited cutaneous SSc. Significant heterogeneity in the distribution of perifollicular hypopigmentation was observed, with dominant patterns involving the face/scalp (n=19), posterior neck (n=14), chest/back/leg (n=12/region), and dorsum hand (n=11) (Table 1). In univariable logistic regression analyses, black race (OR 15.63, 95% CI 6.6-37.20, p< 0.001), diffuse cutaneous disease (OR 4.62, 95% CI 2.11-10.09, p< 0.001), a higher maximum MRSS (OR 1.05, 95% CI 1.02-1.08, p=0.003), myopathy (OR 3.92, 95% CI 1.80-8.57, p< 0.001), a lower minimum FVC % predicted (OR 0.96, 95% CI 0.94-0.99, p=0.001), and a lower minimum DLCO % predicted (OR 0.97, 95% CI 0.95-0.99, p=0.009) were associated with perifollicular hypopigmentation (Table 2). An association with severe GI involvement (OR 2.77, 95% CI 0.85-9.07, p=0.09) trended towards significance. Anti-centromere antibodies inversely associated with perifollicular hypopigmentation (OR 0.24, 95% CI 0.07-0.86, p=0.028). In multivariable logistic regression analyses, diffuse cutaneous subtype (OR 4.28, 95% CI 1.46-12.53, p=0.008) was significantly associated with perifollicular hypopigmentation, even after adjusting for age, race, and disease duration. An association between perifollicular hypopigmentation and the presence of myopathy trended towards significance (OR 2.30, 95% CI 0.87-6.10, p=0.09).

Conclusion: Perifollicular hypopigmentation is observed in a subset of patients with SSc, and associates with diffuse cutaneous disease, black race, and myopathy. The distribution of perifollicular hypopigmentation is variable, with distinct patterns observed across patients. Larger longitudinal studies exploring whether specific patterns of perifollicular hypopigmentation associate with the development of internal organ complications may provide insight into patient risk stratification.

Table 1. Characteristics of the SSc patients with and without perifollicular hypopigmentation in the Scleroderma Center cohort

Clinical and demographic features	Hypopigmentation (n=36)	No hypopigmentation (n=143)	p-value
Age at first symptom, mean (SD)	57 (14)	60 (13)	0.230
Disease duration from first SSc-associated symptom, years, median (IQR)	9 (5-14)	13 (8-22)	0.070
Female sex, % (n)	94 (34)	87 (123)	0.375
Race/Ethnicity, % (n)			
White	19 (7)	85 (120)	**<0.001**
Black	60 (24)	11 (16)	
Asian	8 (3)	1 (2)	
Other Missing	6 (2) 0	2 (3) 1 (2)	
Ever smoker, % (n)	19 (7/36)	39 (53/136)	**<0.001**
SSc Type, % (n)			
Limited cutaneous disease Diffuse cutaneous disease Missing	33 (12) 67 (24) 0	67 (97) 30 (42) 3 (4)	**<0.001**
Maximum MRSS, median (IQR)	17 (11-21)	5 (2-15)	**<0.001**
Severe GI involvement, (≥3)*, % (n)	14 (5/35)	6 (8/141)	0.081
Cardiac involvement (≥3)*, % (n)	17 (5/30)	9 (11/124)	0.209
Myopathy, % (n)	47 (17)	19 (26/140)	**<0.001**
Raynaud's severity (≥3)*, % (n)	28 (10)	19 (27/141)	0.256
Lung involvement (≥3)*, % (n)	41 (13/32)	31 (37/121)	0.281
Cancer, % (n)	6 (2)	16 (23)	0.175
Telangiectasia, % (n)	80 (28/35)	91 (129/141)	0.066
Calcinosis, % (n)	49 (17/35)	44 (62/140)	0.649
Pulmonary function parameters			
FVC % predicted, mean (SD)	59 (± 14) (n=29)	73 (± 20) (n=114)	**<0.001**
DLCO % predicted, mean (n)	53 (± 12) (n=29)	66 (± 25) (n=112)	**0.007**
RVSP by echo (mmHg), median (IQR)	42 (30-49) (n=36)	31 (28-43) (n=143)	0.154
Antibodies, % (n)			
Scl-70 (i.e. Topoisomerase-1)	19 (5/27)	15 (16/109)	0.567
Centromere (CENP)	11 (3/27)	34 (37/109)	**0.020**
RNA polymerase III	15 (4/27)	15 (16/109)	1.000
U3RNP	7 (2/27)	3 (3/109)	0.258
PM/Scl	4 (1/27)	11 (11/109)	0.459
Ku	0 (0/27)	3 (3/109)	1.000
Th/To	7 (2/27)	3 (3/109)	0.258

*Based on Medsger severity scale.
Abbreviations: MRSS=modified Rodnan skin score; GI=gastrointestinal; FVC=forced vital capacity (% predicted); DLCO=diffusing capacity (% predicted); RVSP=right ventricular systolic pressure. Significant p values in bold.

Table 2. Univariable and multivariable logistic regression analysis evaluating the association between perifollicular hypopigmentation and clinical and serological factors associated with systemic sclerosis

Variable	Unadjusted OR	95% CI	p-value	Adjusted OR*	95% CI	p-value
Disease duration from first SSc-associated symptom (n=176)	0.97	0.92-1.00	0.075	—	—	—
Black/African-American (n=177)	15.63	6.6-37.20	**<0.001**	—	—	—
Diffuse cutaneous subtype (n=175)	4.62	2.11-10.09	**<0.001**	4.28	1.46-12.53	**0.008**
Modified Rodnan skin score (n=170)	1.05	1.02-1.08	**0.003**	1.07	1.02-1.12	**0.009**
Myopathy (n=176)	3.92	1.80-8.57	**<0.001**	2.30	0.87-6.10	0.09
Minimum FVC (n=143)	0.96	0.94-0.99	**0.001**	0.99	0.95-1.02	0.36
Minimum DLCO (n=141)	0.97	0.95-0.99	**0.009**	0.99	0.97-1.02	0.45
Anti-centromere antibody (n=136)	0.24	0.07-0.86	**0.028**	0.75	0.17-3.28	0.70
*Separate logistic regression analyses were conducted relating each variable with perifollicular hypopigmentation, adjusted for age, race, and disease duration.						

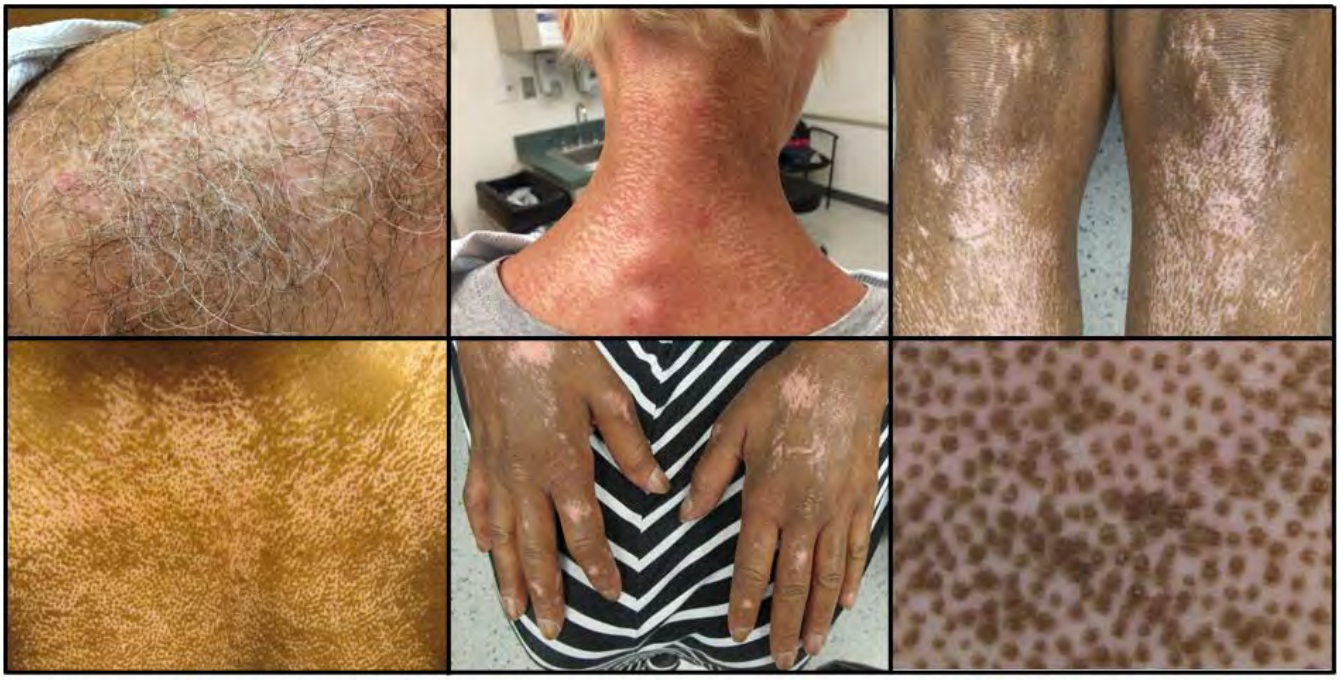

Figure 1. Various distributions of perifollicular hypopigmentation were observed, such as (starting from top left rotating in clockwise order): scalp, neck, legs, back (zoomed in), hands, and chest.

Disclosure: M. Chung, None; **J. Perin**, None; **C. Richardson**, None; **C. Mecoli**, None; **F. Wigley**, None; **Z. McMahan**, None.

Abstract Number: 0405

Retrospective Study on the Prognostic Value of Cardiac Magnetic Resonance Imaging Abnormalities in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiac involvement is a leading cause of death in systemic sclerosis (SSc). Cardiac MRI (CMR) is useful in the early assessment of cardiac disease. Our aim was to describe the characteristics of patients with inflammatory and/or fibrotic abnormalities on CMR and their clinical outcomes in a large retrospective SSc cohort.

Methods: We identified SSc patients with CMR done from 2010 to 2020 by searching the electronic database of a tertiary-care university center. CMR abnormalities of interest were edema (T2 hyperintensity) and fibrosis (late gadolinium enhancement, LGE). Outcomes included heart failure, atrial and ventricular arrhythmias, need for pacemaker or defibrillator and cardiac death (not attributable to other causes). Student's, Mann-Whitney U and chi-square tests were used to compare patient characteristics.

Results: A total of 114 CMRs performed in 99 patients were identified (95% met ACR-EULAR criteria). Mean (SD) age was 57.8 (11.7) years and median (IQR) disease duration was 5.9 (2.6-12.8) years. Patients were mostly female (80%) and white (92%). Half of CMRs were performed as screening tests (asymptomatic), 25% were done to investigate cardiac symptoms and 25% were done following abnormal cardiac investigations.

After excluding two patients with coronary artery disease-related changes, 12 (12%) patients had inflammatory and/or fibrotic CMR abnormalities (LGE, n=11; T2 hyperintensity, n=5), of whom 4 were asymptomatic. LGE was most often described as heterogeneous, linear or focal/nodular areas of enhancement affecting the left ventricular mid-wall and/or subendocardial layers of the basal and/or mid-cavity segments, in non-ischemic distributions involving the antero-septal (n=5), inferior (n=5), infero-lateral (n=5), anterior (n=3), antero-lateral (n=3) and/or infero-septal (n=2) segments.

Baseline characteristics are presented in Table 1. Patients with abnormal CMR more often had cardiac symptoms/signs or abnormal investigations (80% vs 44%, p=0.02), lower left ventricular ejection fractions (p=0.007) and higher troponin levels (p=0.013). They were also numerically more often males (40% vs 18%) with hypertension (50% vs

Table 1. Baseline characteristics, stratified by the presence of CMR abnormalities

	No CMR abnormalities (n=97)	CMR abnormalities (n=15)	P-values
Age at time of CMR, years (mean, SD)	57.4 (11.4)	60.2 (15.7)	0.478
Female sex	71 (82%)	6 (60%)	0.235
White race	80 (92%)	9 (90%)	1.000
Smoking (ever)	30 (38%)	3 (33%)	1.000
Hypertension	23 (27%)	5 (50%)	0.255
Diabetes mellitus II	8 (9%)	0 (0%)	0.680
Obesity (BMI >30)	15 (18%)	1 (10%)	0.869
Disease duration at time of CMR, years (median, IQR)	5.9 [2.7, 13.1]	6.8 [1.7, 12.5]	0.674
Diffuse subtype	35 (40%)	4 (40%)	1.000
Anti-centromere	20 (25%)	3 (33%)	0.872
Anti-topoisomerase I	15 (18%)	3 (30%)	0.632
Myositis	9 (11%)	2 (20%)	0.731
Arthritis	24 (28%)	1 (10%)	0.390
Digital ulcers/scars	28 (34%)	5 (50%)	0.506
Interstitial lung disease	46 (54%)	8 (80%)	0.207
Pulmonary arterial hypertension	26 (31%)	3 (30%)	1.000
Cardiac symptoms/signs or abnormal investigations at time of CMR	43 (44%)	12 (80%)	0.022
Left ventricular ejection fraction, % (median, IQR)	60 [57, 64]	56 [46, 58]	0.007
Troponin, ng/L (median, IQR)	7 [5, 14]	20 [10, 32]	0.013
NT-proBNP, ng/L (median, IQR)	40 [19, 67]	52 [23, 60]	0.702
Follow-up time, years (mean, SD)	4.4 (2.9)	3.6 (3.4)	0.457

CMR= Cardiac Magnetic Resonance Imaging

27%), myositis (20% vs 11%), digital ulcers/scars (50% vs 34%), interstitial lung disease (80% vs 54%) and anti-topoisomerase I antibodies (30% vs 18%).

Over a mean (SD) follow-up of 4.3 (2.9) years, no patient developed new-onset heart failure. One patient with normal CMR developed syncope with frequent premature ventricular contractions (6% of QRS complexes) on Holter and inflammation/fibrosis on follow-up CMR, leading to implantable defibrillator placement 3 years after the initial CMR. Two patients with symptomatic myocarditis died from sudden death within one year of the initial abnormal CMR. None of the four asymptomatic patients with CMR abnormalities developed clinically apparent cardiac complications.

Conclusion: In this real-world SSc cohort, CMR abnormalities were found in 12% of patients, most of whom had clinically apparent cardiac disease. Abnormalities in asymptomatic patients were infrequent. Further study is required to determine the value of CMR screening in asymptomatic SSc patients.

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Abstract Number: 0406

Gender Differences in Clinical Features and Outcomes of Systemic Sclerosis: Analysis of Reuma.pt/SSc Registry

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a rare connective tissue disease of unknown etiology, with a broad spectrum of clinical and laboratory features. Evidence for the role of sex in the clinical manifestations of SSc patients is emerging. Some multicenter cohorts have shown that male SSc patients have more severe disease [Freire M, et al. Clin Exp Rheumatol 2017; Peoples C, et al. J Scleroderma Relat Disord 2016].

Our objective was to assess the clinical manifestations and survival in the cohort of Portuguese SSc patients according to gender.

Methods: Data from adult SSc patients included in Reuma.pt database was analyzed. Demographic features, SSc subsets, main clinical and immunological features, treatments used and survival data were evaluated and compared between genders. Survival was calculated for patients included in Reuma.pt within the first two years of diagnosis. Of the 1054 patients included, 716 (68%) fulfilled ACR/EULAR 2013 criteria.

Results: In total, 1054 adult patients with SSc were included, 132 (12.5%) males. No differences in demographic features and comorbidities were found between women and men, except for a higher rate of smokers among men (64.5% vs 19.2%; p< 0.01). Diffuse cutaneous SSc subtype and anti-topoisomerase antibodies were more prevalent in males (Table 1). Raynaud's phenomenon (RP) and skin thickening were the most frequently observed clinical manifestations, RP being more prevalent in females (84.1% vs 94%, p=0.04) and skin thickening proximal to metacarpophalangeal and metatarsophalangeal joints in males (83.2% vs 75%, p=0.03). Additionally, male patients presented significantly more myositis (13.3% vs 4.6%, p< 0.01), interstitial lung disease (38.9% vs 27.1%, p=0.03) and gastric involvement (20.4% vs 11.3%, p< 0.01). One-third of patients were treated with immunomodulators, with

Table 1. Cumulative clinical and immunologic features and treatments used. MCF - metacarpophalageal joints; MTF – metatarsophalangeal joints. Pulmonary arterial hypertension confirmed by right heart catheterization. Immunomodulators include Methotrexate, Leflunomide, Hydroxychloroquine; Immunosuppressants include Azathioprine, Mycophenolate Mofetil and Cyclophosphamide. P-value comparing female and male

	Whole cohort N=1054	Female N= 922 (87.5%)	Male N=132 (12.5%)	P-value
Limited cutaneous SSc - N (%)	579 (56.3)	525 (58.3)	54 (42.2)	
Diffuse cutaneous SSc – N(%)	180 (17.5)	136 (15.1)	44 (34.4)	
Preclinic SSc – N(%)	134 (13)	121 (13.4)	13 (10.2)	**<0.01**
SSc sine scleroderma – N(%)	34 (3.3)	31 (3.4)	3 (2.3)	
Overlap syndrome – N(%)	101 (9.8)	87 (9.7)	14 (10.9)	
Skin thickening proximal do MCF/MTF joints– N (%) no= 962	734 (76.3)	634 (75)	147 (83.2)	**0.03**
Sclerodactyly – N (%) no= 855	547 (64)	473 (63.1)	74 (70.5)	0.14
Raynaud's Phenomenon – N (%) no=1010	943 (93.4)	828 (94)	115 (89.1)	**0.04**
Musculoskeletal involvement – N(%) no=972	479 (45.4)	410 (45.4)	69 (52.3)	0.09
Myositis – N (%) no=943	54 (5.7)	38 (4.6)	16 (13.3)	**<0.01**
Cardiac involvement – N (%) no=924	71 (7.7)	65 (8)	6 (5.4)	0.34
Renal involvement – N (%) no= 917	17 (1.9)	13 (1.6)	4 (3.5)	0.17
Gastrointestinal involvement - N(%) no=972	425 (43.7)	362 (42.6)	63 (51.6)	0.06
Gastric involvement – N(%) no=916	114 (12.4)	91 (11.3)	23 (20.4)	**<0.01**
Pulmonary involvement – N(%) no=915	261 (28.5)	218 (27.2)	43 (37.7)	**0.02**
Pulmonar arterial hypertension – N(%) no= 871	14 (1.6)	13 (1.7)	1 (0.9)	0.56
Interstitial lung disease – N(%) no=765	218 (28.5)	183 (27.1)	35 (38.9)	**0.03**
Antinuclear antibodies - N (%) no=1040	934 (89.8)	827 (90.9)	107 (82.3)	**0.01**
Anti-centromere – N(%) no= 1027	540 (52.6)	509 (56.6)	31 (24.4)	**<0.01**
Anti-topoisomerase I – N(%) no=1020	214 (21)	174 (19.6)	40 (30.8)	**0.01**
Anti-RNA polymerase III – N(%) no=710	25 (3.5)	20 (3.3)	5 (5.2)	0.58
Immunomodulators/ Immunossupressants – N(%)	420 (39.8)	363 (39.4)	57 (43.2)	0.40
Calcium channel blockers – N(%)	527 (50)	459 (49.8)	68 (51.5)	0.71
PPIs/Ranitidine/Prokinetics – N(%)	353 (33.5)	309 (33.5)	44 (33.3)	0.97

no differences in the pattern of drugs used between genders. During follow-up, more deaths were reported in men (12.1% vs 7.3%, p=0.04). However, the overall 1-, 3- and 5-year survival was not significantly different between men and women (96.4% vs 98.2%, 93% vs 95.9% and 83.4% vs 93.2%, p=0.08, Figure 1).

Conclusion: This study confirms the existence of gender differences in clinical and immunologic features of SSc patients. Although SSc is less common in men, they have a more severe expression of internal organ involvement. Nevertheless, no statistically significant differences were found in survival rates.

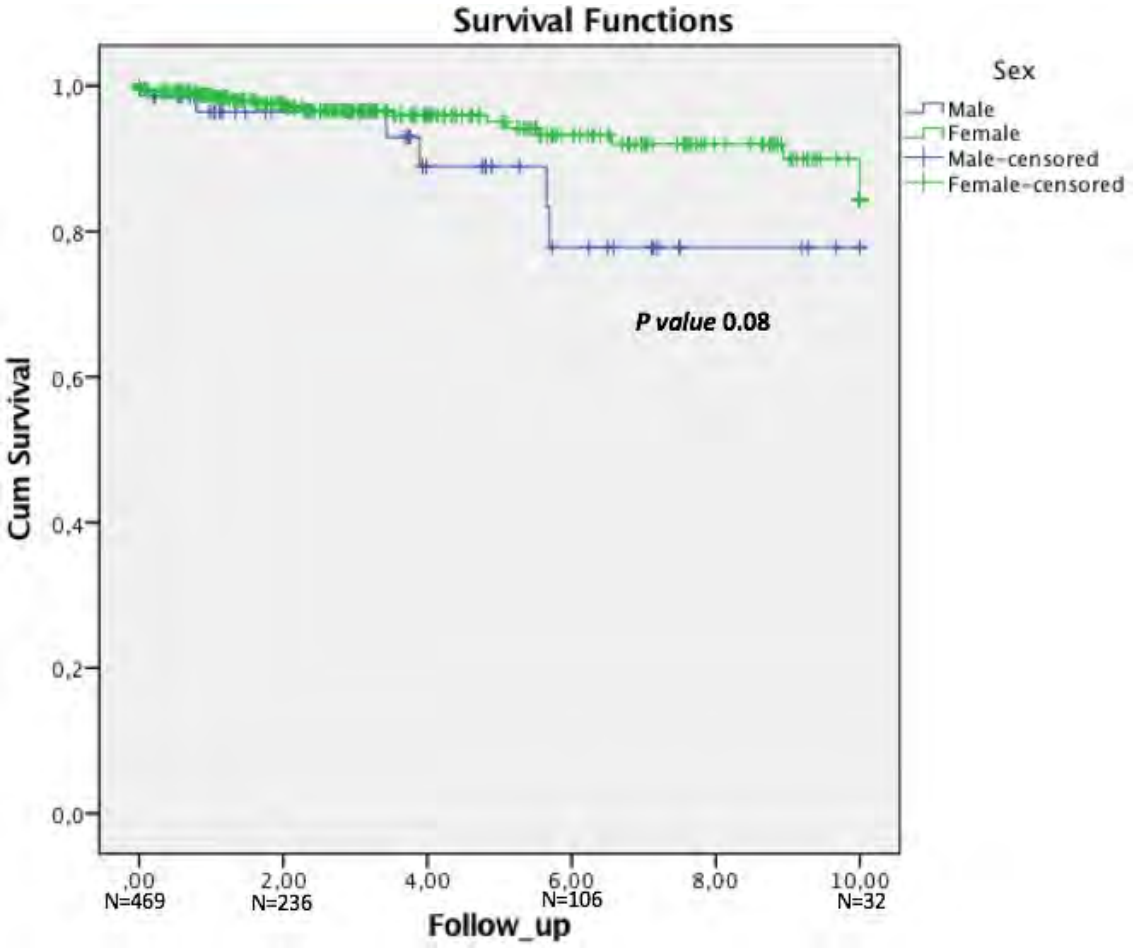

Figure 1. Survival from diagnosis of patients with SSc included in the cohort in the first two years of disease (N=469). The X and Y axes represent follow-up time in years and the proportion of patients still on follow-up, respectively.

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Abstract Number: 0407

The Clinical Role of T1 Mapping Cardiac Magnetic Resonance Imaging for Detecting Cardiac Involvement in the Early Stage of Systemic Sclerosis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is characterized by skin and internal organs tissue fibrosis including the myocardium. Cardiovascular magnetic resonance (CMR) parametric mapping is a promising modality to detect diffuse myocardial fibrosis.

The study aims to detect early-stage cardiac involvement in SSc using CMR parametric mapping and evaluate the associations with clinical and laboratory findings.

Methods: 24 controls (12 female, 58.0±18.9 years) and 57 SSc patients (51 female, 59.4±12.9 years) underwent CMR at 3.0T and analyzed myocardial damage using parametric mapping and compared with clinical data.

Results: The mean disease duration in the SSc group was 3.9±7.4 years, and four patients had pulmonary hypertension. The mean left ventricular (LV) ejection fraction was 58.3±8.1 in the SSc group and 56.9±7.0 in the control group. LV global longitudinal and circumferential strain evaluated by CMR feature tracking showed no significant differences between the two groups. Focal fibrosis on late gadolinium enhancement was found in 9 SSc patients (15.7%) but none of the controls. Mid-ventricular native T1 and extracellular volume fraction were significantly higher in SSc patients compared with the control group (1331.2±65.4mesc vs. 1253.6±44.1msec, p< 0.0001 and 32.4±4.1% vs. 28.3±3.3%, p< 0.0001, respectively). There was a significant correlation between native T1 and BNP levels (r=0.353,

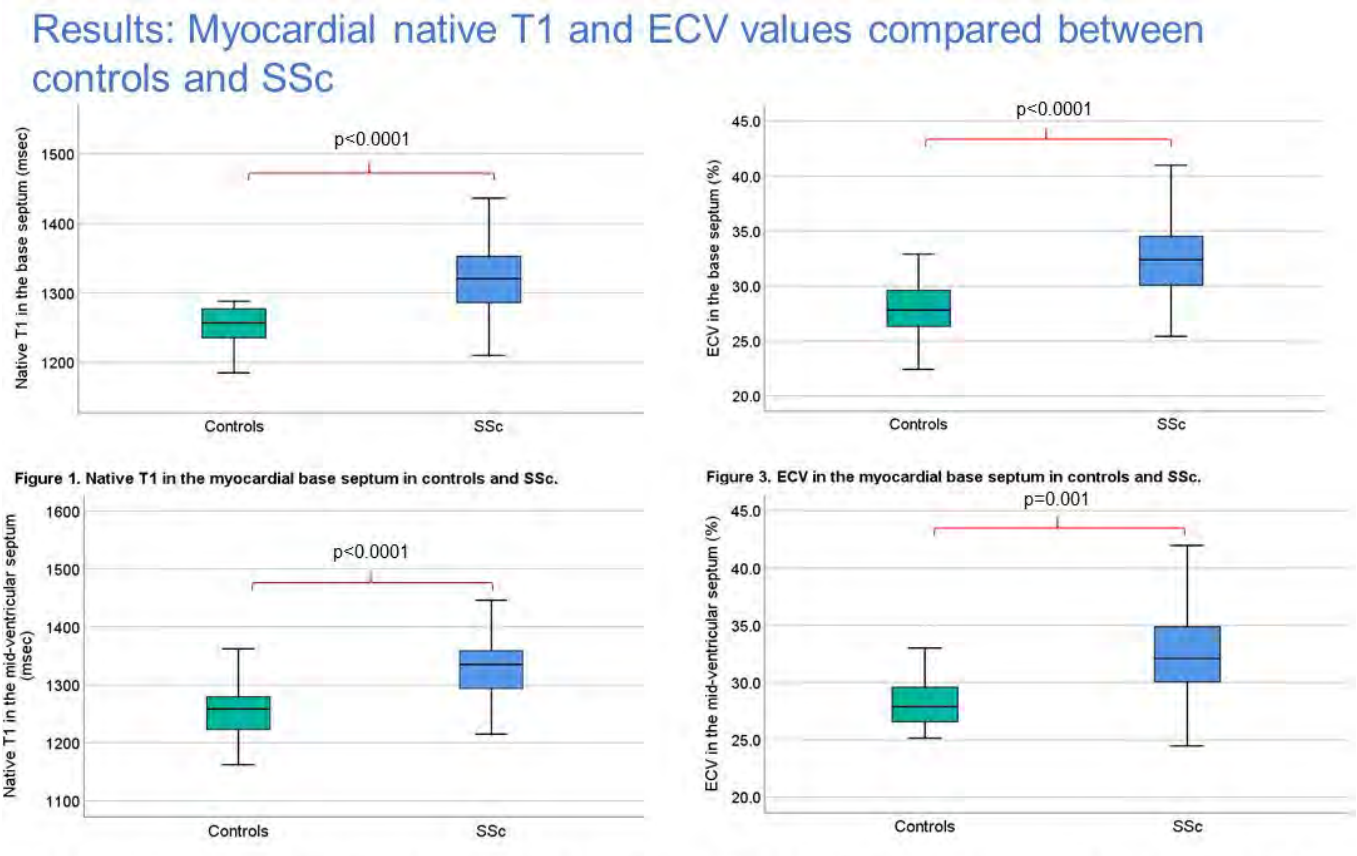

Figure 1. Native T1 in the myocardial base septum in controls and SSc.

Figure 3. ECV in the myocardial base septum in controls and SSc.

Figure 2. Native T1 in the myocardial mid-ventricular septum in controls and SSc.

Figure 4. ECV in the myocardial mid-ventricular septum in controls and SSc.

Results: Myocardial native T1 and ECV values compared between controls and SSc

Results: Baseline characteristics of patients with SSc

	Low and medium native T1 SSc group (n=37)	High native T1 SSc group (n=19)	p value
Antinuclear antibody specificity			
Scl70, n (%)	5 (13.5%)	5 (26.3%)	0.205
Anti-centromere antibody, n (%)	23 (62.1%)	6 (31.5%)	0.030
RNA polymerase III, n (%)	2 (5.4%)	1 (5.2%)	0.737
Cutaneous vascular symptoms			
Raynaud syndrome, n (%)	33 (91.6%)	18 (94.7%)	0.570
Raynaud disease duration (years), mean ± SD	5.9 ± 7.9	7.7 ± 8.0	0.433
Digital ulcer, n (%)	1 (2.7%)	6 (31.5%)	0.005
Sclerodactuly, n (%)	28 (75.6%)	12 (63.1%)	0.326
Pitting scars, n (%)	6 (16.2%)	4 (21.0%)	0.458
Telangiectasia, n (%)	4 (10.8%)	7 (36.8%)	0.027
Nailfold bleeding, n (%)	22 (59.4%)	15 (78.9%)	0.145
Puffy fingers, n (%)	23 (41.0%)	11 (57.8%)	0.757

Results: Baseline characteristics of patients with SSc

p=0.008) in the SSc group. SSc patients were divided into two groups, low and medium native T1 group (n=37) and high native T1 group (n=19). Cutaneous vascular symptoms including digital ulcer and telangiectasia were significantly higher in the high native T1 SSc group compared with the low and medium native T1 SSc group (6 (31.5%) vs. 1 (2.7%), p=0.005 and 7 (36.8%) vs. 4 (10.8%), p=0.027). There were no differences in biventricular volume and contraction, but the left and right atrial volume index were significantly larger in the high native T1 SSc group than the low and medium native T1 SSc group (all p< 0.05). In univariate logistic regression analysis revealed that diffuse cutaneous SSc, the coexistence of digital ulcer, telangiectasia, albumin, hemoglobin, and erythrocyte sedimentation rate were independent predictors of mid-ventricular high native T1 values. In multivariate logistic regression analysis, the coexistence of digital ulcers was the only independent predictor of mid-ventricular high native T1 values in the SSc group (p=0.013 odds ratio=12, CI 1.1-138.9).

Results: Univariate and multivariate logistic regression analysis for predicting mid-ventricular septum high native T1

Predictors of high native T1	Univariate logistic regression analysis			Multivariate logistic regression analysis		
	Odds ratio	95% CI	p value	Odds ratio	95% CI	p value
Age	0.993	0.951-1.036	0.743			
Disease duration	1.000	1.000-1.000	0.433			
Diffuse cutaneous SSc	3.560	1.101-11.509	0.034	2.636	0.466-14.896	0.273
Digital ulcer	16.615	1.823-151.454	0.013	12.393	1.105-138.967	0.041
Telangiectasia	4.812	1.193-19.416	0.027	1.760	0.223-13.865	0.591
Interstitial lung disease	3.300	0.941-11.575	0.062			
Brain natriuretic peptide	1.006	1.000-1.013	0.069			
Albumin	0.187	0.049-0.723	0.015	2.089	0.211-20.678	0.529
Hemoglobin	0.543	0.339-0.868	0.011	0.664	0.349-1.265	0.213
Erythrocyte sedimentation rate	1.042	1.005-1.079	0.024	1.030	0.985-1.078	0.199

Results: Univariate and multivariate logistic regression analysis for predicting mid-ventricular septum high native T1

Conclusion: Native T1 mapping is a useful method to detect early myocardial damage in SSc patients. The clinician should take notice of cardiac involvement in SSc patients with progressed skin lesions even without cardiac symptoms.

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A Histogram-based Densitometry Index to Support the Identification and the Assessment of Severity of Interstitial Lung Disease in Systemic Sclerosis: Applicability in Conventional and Low-dose Computed Tomography

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SESSION INFORMATION

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Background/Purpose: High resolution computed tomography (conventional CT) represents the diagnostic gold standard for systemic sclerosis-related interstitial lung disease (SSc-ILD). A low-dose 9-slices (reduced) CT protocol was previously shown to be a highly sensitive tool to screen for ILD and to classify it into limited or extensive according to the Goh et al visual staging system (1). Histogram-based densitometry analysis is an automated quantitative evaluation of SSc-ILD, with mean lung attenuation, skewness, and kurtosis as main variables, recently merged into a Computerized Integrated Index (CII) (2). CII has shown good discrimination of SSc-ILD presence and association with the Goh et al staging on conventional CT. We aimed at testing the CII in reduced CT, in comparison to conventional CT, in discriminating for the presence and severity of SSc-ILD.

Methods: We analyzed prospectively collected conventional and reduced CT images of SSc patients followed at our tertiary referral center. The Goh et al staging (limited vs extensive ILD) was applied by an experienced radiologist. Conventional and reduced CT images were analyzed using the free-source software Horos to obtain the CII, named conventional and reduced CII respectively. We measured the association between CIIs and categories using generalized estimating equations (GEE). The predictive ability of CIIs was assessed in a ROC analysis.

Results: We enrolled 468 SSc patients, further described in the table 1: 427 had undergone at least one conventional CT (total 719 CTs), 345 at least one reduced CT (total 814 reduced CTs). Both CT and reduced CT images were available at the same visits for 243 patients (total 294 conventional + reduced CTs). The three groups were comparable

Table 1. Characteristics of the study population

Parameters	Distribution among the whole cohort (n=468)
Age [years, mean ± SD]	57 ± 14
Disease duration [years, mean ± SD]	9 ± 11
Female sex [n (%)]	381 (81.4)
Diffuse cutaneous subset [n (%)]	112 (24)
Anti-Centromere antibody positive [n (%)]	212 (45)
Anti-Topoisomerase I antibody positive [n (%)]	126 (27)
Anti-RNA polymerase III antibody positive [n (%)]	50 (11)
Anti-PM/Scl antibody positive [n (%)]	55 (12)
Digital ulcers [ever, n (%)]	98 (21)
Arthritis [ever, n (%)]	83 (18)
Pulmonary arterial hypertension [n (%)]	21 (4)
Scleroderma Renal Crisis [n (%)]	9 (2)
Interstitial lung disease on HRCT [n (%)]	212 (45)
Extensive ILD on HRCT [n (% of ILD positive patients)]	54 (26)
FVC% [mean ± SD]	96 ± 20
DLCO% [mean ± SD]	75 ± 22
NYHA functional class ≥ 2 [n (%)]	177 (38)
Ongoing immunosuppressive medication [n (%)]	93 (20)

in terms of ILD prevalence and extensive ILD (48% vs 45% vs 48% and 25% vs 21% vs 20%, in conventional CT, reduced CT and conventional + reduced CTs groups, respectively).

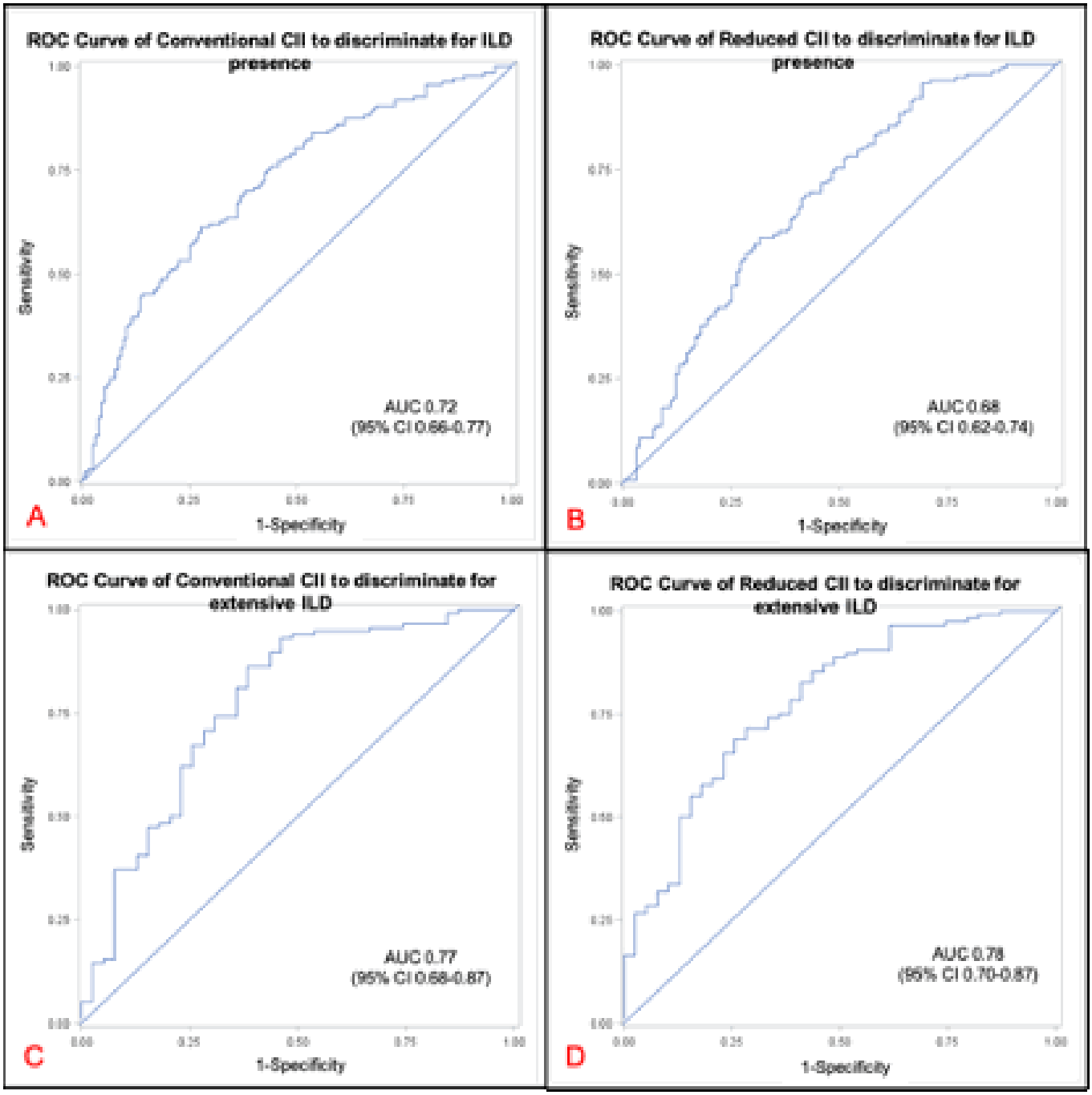
Both conventional and reduced CII significantly differentiated ILD vs non-ILD (mean conventional CII-0.46±0.15vs 0.67±0.09, p< 0.001 and mean reduced CII -0.50±0.17 vs 0.48±0.11, p< 0.001, respectively). Similarly, they separated limited vs extensive ILD (mean conventional CII -0.12±0.14 vs -1.48±0.21, p< 0.001, and mean reduced CII -0.25±0.13 vs -1.71±0.20, p< 0.001, respectively).

The two CIIs similarly predicted the presence of ILD [conventional CII AUC 0.72 (95% CI 0.66-0.77) vs reduced CII AUC 0.68 (95% CI 0.62-0.74); p=0.28, Figure 1A-B]. A similar performance was shown for extensive vs limited ILD [conventional CII AUC 0.77 (95% CI 0.68-0.87) vs reduced CII AUC 0.78 (95% CI 0.70-0.87), p=0.86, Figure 1C-D].

A cut-off for conventional CII< -0.96 (85% sensitivity, 62% specificity) or a reduced CII< -1.85 (85% sensitivity, 54% specificity) was chosen for an optimal sensitivity to detect extensive ILD.

Conclusion: We validated the ability of the CII to detect the presence of ILD and identified cut-offs for both conventional and reduced CII to discriminate between extensive versus limited ILD. Further validation of the proposed cut-offs is ongoing to further support its use in clinical practice and research.

References: 1) Goh et al, Am J Respir Crit Care Med 2008; 2)Bocchino et al, Sci Rep 2019



ROC curve analysis for conventional and reduced CII for discrimination of ILD presence and extensive ILD.

Disclosure: C. BRUNI, Boehringer-Ingelheim, 1, 2; **A. Garaiman**, None; **L. Tofani**, None; **S. Jordan**, None; **C. Mihai**, Roche, 6, Boehringer-Ingelheim, 2, 6, Mepha Pharma, 6, MEDtalks Switzerland, 6; **R. Dobrota**, None; **M. ELHAI**, Gilead, 12, Travel Support for ACR 2019, BMS, 6, Roche, 12, Travel Support for Congress; **M. Becker**, None; **M. Matucci-Cerinic**, Merck, 5, 6, Actelion, 5, 6, Janssen, 6, Eli Lilly and Company, 6, Biogen, 6; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2.

Abstract Number: 0409

Factors Predicting Mortality in an Indian Cohort of Systemic Sclerosis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis is characterised by high morbidity and mortality due to disease-related or treatment-related complications.

Methods: Data of patients of systemic sclerosis between 1990 and March 2020 was retrieved from case files and electronic health records (EHR). We determined the number of deaths in our cohort of 789 patients with systemic sclerosis from EHR and teleconsultation, and their causes. Kaplan-Meier curve was used to calculate survival at 1, 2, 5 and 10 years of follow-up duration We evaluated baseline characteristics of patients of systemic sclerosis who experienced mortality and compared them with live controls, after matching for age, sex and duration of follow-up, in a case-control design.

Results: There were a total of 90 deaths. The causes were 32 due to Interstitial lung disease (ILD) related deaths, 7 Gastrointestinal (GI) related, 6 malignancies, 5 Scleroderma renal crisis (SRC), and 3 Pulmonary arterial hypertension (PAH). Most of these patients (19 out of 32, 59.4%) had infection as the cause of death; 5 had pulmonary tuberculosis. Twenty four patients died in a non-hospital setting. Mean age at death was 38 years (Standard error [SE]- 1.24), and median duration of follow-up was 338 days (95% CI- 27-1619). Male- female ration was 8:82. Kaplan-Meier curve showed survival rate at 1, 2, 5 and 10 years of follow-up was 93.7%, 89.5%, 78.9% and 72.1% respectively. On univariable analysis, patients who died had greater number of hospital admissions, higher modified Rodnan skin score (mRSS), a higher frequency of ILD, PAH, cardiac involvement, SRC and history of infections. Using multivariable adjusted analysis, only mRSS, number of admissions and infections were significantly higher compared to live controls.

Conclusion: Interstitial lung disease and related lower respiratory tract infections were the most common cause of mortality in systemic sclerosis. Infections accounted for 32.22% of the deaths. Higher skin score, infections and number of admissions were identified as significant risk factors for mortality in multivariable adjusted analysis.

Disclosure: T. Sundaram, None; **D. Misra**, None; **R. Chatterjee**, None; **S. Ahmed**, None; **V. Agarwal**, None.

Abstract Number: 0410

Long-term Outcomes of Vascular Grafting of Medium Sized Vessels of the Wrist and Hand in Patients with Medication Refractory Systemic Sclerosis Related Raynaud's Phenomenon at the University of Pennsylvania from 2009-2019

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Raynaud's phenomenon (RP) seen in patients with an underlying autoimmune rheumatic disorder have both functional and structural dysfunction at the microvascular level and in more severe forms at the macrovascular level; leading to the characteristic clinical picture. In most cases, preventive actions and pharmacotherapy can be of help. However, a more severe subgroup of patients may develop painful ulcerations, gangrene and digital amputations that are difficult to control. In medication refractory RP, and when medium vessel involvement is identified, surgical revascularization has been attempted. Previous studies have examined the short-term results of revascularization; however long-term outcomes in autoimmune medication refractory RP patients are limited.

Methods: Following Institutional Review Board approval, patients at the University of Pennsylvania between 2009-2019 were identified based on ICD-9 and 10 diagnosis codes for systemic sclerosis (Ssc), Raynaud's and vascular grafting. The patients within the study fulfilled the ACR/EULAR 2013 classification criteria for SSc. Retrospective chart review for pre and postoperative patient reported symptoms, clinical exam findings, and imaging results were collected. Long-term results for digital ulcers, pain, color change and occlusion were compared.

Results: Nine patients, 10 hands (with no prior revascularization), were identified to meet the inclusion criteria. The majority of the patients were female and older than 45 years at surgery. Complete occlusion was noted in all hands at surgery, with revascularization occurring almost exclusively in the ulnar artery, and venous graft most often obtained from the lower extremity. There were no surgical complications and Doppler ultrasound was used to confirm pulsatile blood flow through graft and digits prior to closing. Patients were followed for an average of 24 months with 3 patient deaths within the first two years and one patient who transferred medical care. All other patients are still being followed for symptoms. Ongoing and unremitting digital ulcers, pain and color change were noted in 2 patients, both who had medication mal-adherence. The other patients had subjective and objective resolution, or decrease in digital ulcers, pain, color change (inconsistently noted) and no occlusions.

Conclusion: This is the first long term study to follow patients and attempt to measure the benefits of arterial revascularization in medication refractory SSc -RP patients through digital ulcer, pain, color change and occlusion occurrence. At follow-up, the majority of the hands showed improvement or resolution of Raynaud's symptoms even months - years later.

Disclosure: N. Sandorfi, None; **C. Derk**, None; **N. Hajnoczky**, None.

Abstract Number: 0411

Pharmacokinetics, Safety, and Efficacy of Subcutaneous Brodalumab for Systemic Sclerosis with Moderate-to-severe Skin Thickening: A Single-arm, Open-label, Multi-dose, Phase 1 Trial

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: The exact role of interleukin-17 in systemic sclerosis (SSc) has not been established. This trial assessed the pharmacokinetics (PK), safety, and efficacy of multiple subcutaneous doses of brodalumab 210 mg administered every 2 weeks in Japanese SSc patients with moderate-to-severe skin thickening.

Methods: In this open-label, multiple-dose, phase 1 study, eligible patients received 52-week treatment. Primary endpoints were PK and safety. Secondary endpoints included change from baseline in the modified Rodnan Skin Score (mRSS) and Composite Response Index in Systemic Sclerosis (CRISS) score. Exploratory endpoints included lymphocyte subset testing.

Results: Eight patients were enrolled. Mean (SD) age was 53.6 (10.6) years, total mRSS was 23.1 (5.1), and SSc disease duration was 2.2 (1.9) years. Mean (SD) serum brodalumab trough concentration increased to 21.8 (16.7) μg/mL at week 2 and remained almost constant at week 52. Drug-related treatment-emergent adverse events were observed in three patients: oral candidiasis (n=3), vulvovaginal candidiasis (n=1), and arthralgia (n=1). A rapid and significant decrease in mRSS was observed as early as week 4 ($p< 0.005$), which continued until week 52 ($p< 0.0001$). At week 52, all patients achieved a CRISS score ≥0.6. The Th17/Treg balance showed a significant sustained Treg dominance over 52 weeks ($p< 0.05$). The significant decrease in the number of immunoglobulin G^+ class-switched memory B cells and plasmablasts ($p< 0.01$) was accompanied by a significant increase in the number of transitional B cells ($p< 0.05$) by week 52.

Conclusion: Brodalumab demonstrated a rapid, sustained, and significant decrease in mRSS over 52 weeks in Japanese SSc patients with moderate-to-severe skin thickening, which could be attributed to its direct effects on fibroblasts and indirect effects via impacts on B and T cell subsets.

Disclosure: T. Fukasawa, None; **A. Yoshizaki**, None; **S. Ebata**, None; **S. Sato**, None.

Abstract Number: 0412

Prevalence, Distribution, Clinical Correlates and Outcomes of Upper Extremity Macrovascular Disease in Systemic Sclerosis: Results from a Single Center Referral Cohort (2001-2018)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: To study the prevalence, anatomical distribution, clinical correlates and outcomes of macrovascular disease (MVD) on duplex ultrasound (US) of the upper extremity in Systemic sclerosis (SSc) patients evaluated at a single tertiary referral center.

Table 1. Clinical characteristics of 269 Systemic sclerosis (SSc) patients that underwent duplex US between 2001-2018, overall and by presence or absence of macrovascular disease (MVD)

	Overall (N=269)	MVD (N=74)	No MVD (N=195)	p-value
Demographics				
Age at procedure(y); mean (SD)	57.4 (13.3)	61.7 (10.7)	55.7 (13.8)	**0.002**
Sex (Female)	217 (81%)	61 (82%)	156 (80%)	0.65
Race (White)	249 (93%)	71 (96%)	178 (91%)	0.21
BMI (kg/m^2) at study	26.5 (6.1)	25.0 (5.3)	27.0 (6.3)	**0.02**
Smoking status				0.42
Never	152 (57%)	40 (54%)	112 (57%)	
Former	100 (37%)	27 (36%)	73 (37%)	
Current	17 (6%)	7 (9%)	10 (5%)	
Disease characteristics				
SSc subtype:				0.29
Limited	210 (78%)	61 (82%)	149 (76%)	
Diffuse	59 (22%)	13 (18%)	46 (24%)	
Time from SSc diagnosis to duplex US (months)	58.2 (86)	80.9 (127.3)	49.5 (62)	0.59
Raynaud's phenomenon	264 (98%)	74 (100%)	190 (97%)	0.16
Digital occlusive arterial disease	223 (82.9%)	66 (89.2%)	157 (80.5%)	0.09
Telangiectasias	236 (88%)	70 (96%)	166 (86%)	**0.02**
Calcinosis	101 (43%)	41 (57%)	60 (37%)	**0.005**
Abnormal nailfold capillaries*	133 (73%)	28 (67%)	105 (74%)	0.32
Interstitial lung disease	105 (39%)	30 (41%)	75 (38%)	0. 75
Pulmonary hypertension	50 (19%)	16 (22%)	34 (17%)	0.43
Gastrointestinal dysmotility	192 (71%)	61 (82%)	131 (67%)	**0.01**
Renal crisis	17 (6%)	7 (9%)	10 (5%)	0.19
SSc specific antibodies:	175 (68%)	52 (78%)	123 (65%)	**0.05**
Centromere	115 (64%)	43 (86%)	72 (55%)	**<0.001**
Scl-70	48 (19%)	7 (11%)	41 (22%)	0.07
RNA-Polymerase	19 (20%)	2 (11%)	17 (22%)	0.29
Medications				
Calcium channel blockers	135 (50%)	41 (55%)	94 (48%)	0.29
Phosphodiesterase inhibitors	31 (12%)	7 (9%)	24 (12%)	0.51
Endothelin receptor antagonists	7 (3%)	1 (1%)	6 (3%)	0.42
Prostacyclin/Prostaglandin-I_2	3 (1%)	0 (0%)	3 (2%)	0.28
Aspirin	104 (39%)	26 (35%)	78 (40%)	0.46
Alpha-blockers	55 (20%)	20 (27%)	35 (18%)	0.10
Statins	48 (18%)	15 (20%)	33 (17%)	0.52
Fluoxetine	10 (4%)	1 (1%)	9 (5%)	0.21
Pentoxifylline (Trental)	13 (5%)	7 (9%)	6 (3%)	**0.03**
Angiotensin receptor blockers	27 (10%)	11 (15%)	16 (8%)	0.11
Topical nitroglycerine	18 (7%)	7 (9%)	11 (6%)	0.26
Botox injections	3 (1%)	2 (3%)	1 (1%)	0.13
Sympathectomy	14 (5%)	6 (8%)	8 (4%)	0.19
Disease comorbidities				
Hypertension	107 (40%)	34 (46%)	73 (37%)	0.20
Hypercholesterolemia	114 (42%)	37 (50%)	77 (40%)	0.12
Diabetes mellitus	20 (7%)	7 (9%)	13 (7%)	0.44
Coronary artery disease	28 (10%)	8 (11%)	20 (10%)	0.89
Digital ischemic complications				
Digital ulcer	203 (75.4%)	66 (89.2%)	137 (70.3%)	**0.001**
Digital tip pitting/scars	138 (51.3%)	43 (58.1%)	95 (48.7%)	0.17
Digital gangrene/amputation	76 (28.3%)	35 (47.3%)	41 (21%)	**<0.001**
Any digital ischemic complication	217 (80.7%)	69 (93.2%)	148 (75.9%)	**0.001**

Baseline characteristics were compared using Chi square, Fisher exact or Rank sum tests
*86 of 269 SSc patients did not have a nailfold capillary exam documented.

Methods: Medical records of SSc patients meeting ACR/EULAR 2013 classification criteria that underwent upper extremity duplex US with laser doppler flowmetry between Jan 2001-Dec 2018 at our institution were retrospectively reviewed to abstract the presence or absence of MVD (stenosis/occlusion involving the palmar arch, ulnar, radial,

Table 2. Association between macrovascular disease and digital ischemic complications in 269 patients with Systemic sclerosis. Logistic regression models were adjusted for age at duplex US and gender

Digital Ischemic Complication	Macrovascular disease	OR	95% CI	P value
Digital Ulcers	Any MVD vs. None	3.95	1.85-9.51	<0.001
	Unilateral vs. None	4.29	1.6-14.96	0.009
	Bilateral vs None	3.62	1.33-12.69	0.02
Digital Tip pitting/Scars	Any MVD vs. None	1.57	0.90-2.76	0.081
	Unilateral vs. None	1.10	0.55-2.22	0.78
	Bilateral vs None	2.44	1.13-5.55	0.03
Digital Gangrene/Amputation	Any MVD vs. None	3.36	1.87-6.06	<0.001
	Unilateral vs. None	3.40	1.65-7.02	< 0.001
	Bilateral vs None	3.31	1.52-7.16	0.002
Any Digital Involvement	Any MVD vs. None	4.99	2.05-15.0	<0.001
	Unilateral vs. None	4.41	1.48-19.01	0.02
	Bilateral vs None	5.87	1.67-37.29	0.02

brachial, axillary and/or subclavian arteries). Demographics, clinical characteristics, and outcomes were abstracted to evaluate risk factors associated with MVD in SSc and its association with digital ischemic complications. Logistic regression models were adjusted for age at vascular study and gender.

Results: 269 SSc patients (mean age 57.4 ± 13.3 y, 81% female, 93% Caucasian) underwent upper extremity duplex US during the study period. Mean disease duration was 4.8 ± 7.2 y. The majority had limited cutaneous SSc (lcSSc) (78%) and 68% had a positive SSc specific antibody. Cohort characteristics are described in Table 1.

Macrovascular arterial disease was prevalent at the time of duplex US in 74 patients (28%; bilateral in 13%): Ulnar occlusive disease was the most common, noted in 68 patients (25%; bilateral in 11%) followed by radial in 14 (5%), palmar arch in 6 (2%) and subclavian in 4 (1%). No patients had brachial or axillary artery involvement.

SSc patients with MVD were compared to those without MVD, and were noted to have a significantly higher prevalence of centromere pattern-ANA (86% vs 55%, $p < 0.001$), older age (61.7 vs 55.7 y, p=0.002), calcinosis (57% vs 37%, p= 0.005), telangiectasias (96% vs 85%, p=0.02) and GI dysmotility (82% vs 67%, p=0.01). Mean BMI was lower among those with MVD (25 vs 27, p=0.02). Digital occlusive arterial disease (defined as pre- and post-warming blood flow of ≤206 arbitrary units on laser doppler flowmetry) was higher among those with MVD (89.2% vs 80.5%, p=0.09), but did not reach significance. There was no difference in skin sclerosis, nailfold capillary abnormalities, ILD, PAH, renal crisis, cardiac involvement, inflammatory arthritis and myositis among SSc patients with and without MVD.

Patients with MVD had a significantly higher odds of having any digital ischemic complications (digital ulcers, pitting scars, gangrene, amputation) than those without MVD (93.2% vs 75.9%, OR 4.99, p =0.001) (Table 2). The odds of certain digital ischemic complications were even higher among those with bilateral MVD than unilateral or no MVD as shown.

Conclusion: In this largest single center cohort of SSc patients assessed with duplex US, more than 1 in 4 patients had MVD. Ulnar occlusive disease was most common, followed by radial arterial disease. Presence of MVD increased the odds of developing digital ischemic complications 4 to 5-fold among patients with SSc. This study highlights the

high prevalence of MVD in SSc, and need to consider aggressive therapeutic intervention in those with MVD to prevent digital ischemic complications.

Disclosure: A. Makol, None; **C. Coffey**, None; **T. Gunderson**, None; **A. Hinze**, None; **Y. Radwan**, None; **C. Crowson**, None; **D. Liedl**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **P. Wennberg**, None.

Abstract Number: 0413

Predictors of ILD Development and Timing of Onset in Systemic Sclerosis: A Canadian Cohort

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I (0387–0413)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

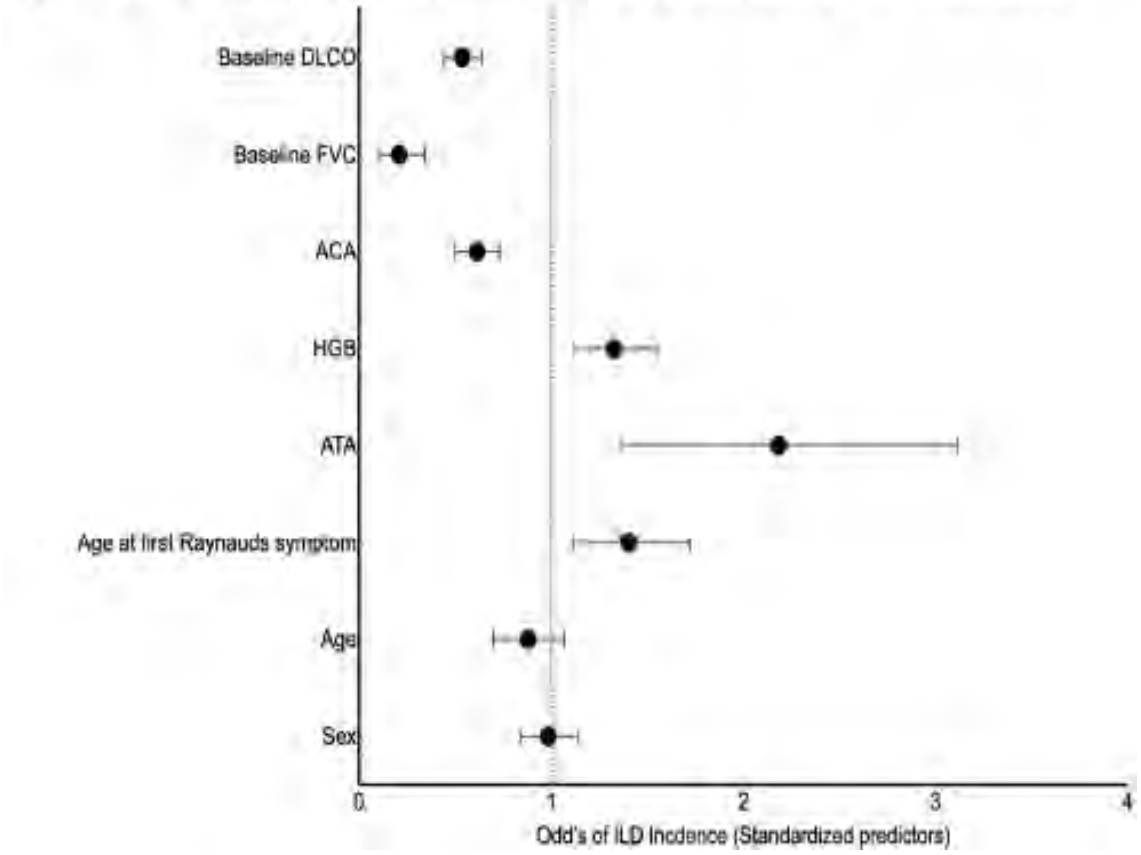
Background/Purpose: In patients with SSc, interstitial lung disease (SSc-ILD) and pulmonary hypertension affect 50-70% of patients and are the leading cause of death. Recent trials in anti-fibrotic medications have shown promise in reducing rates of lung function decline in patients with SSc-ILD. Identifying SSc-ILD development and initiating therapy early is essential to optimizing therapeutic benefit. We aimed to identify predictors of SSc-ILD and compared early (< 5 years from SSc diagnosis) versus late onset to aid in optimizing targeted screening for SSc-ILD.

Methods: We analyzed data from the Canadian Scleroderma Research Group (CSRG) patient registry. Patients ≥18 years with follow-up until July 2019 were included. Logistic regression modelling by ordinary least squares and forward stepwise regression were run to identify patient factors associated with SSc-ILD development as well as its early onset (< 5 years from SSc diagnosis). Factors associated with incident ILD were determined as were factors associated with early versus late onset using all patients who developed SSc-ILD during follow-up. Bonferroni correction was utilized to limit Type 1 errors.

Table 1: Significant logistic regressions between predictors and ILD incidence

	Univariate	
Predictor	**Odd's Ratio (95%CI)**	**P value**
Baseline DLCO predicted	0.96 (0.95, 0.96)	1.37E-24
Baseline FVC	0.35 (0.28, 0.43)	2.82E-21
Cyclophosphamide (never/unknown)	0.16 (0.10, 0.26)	3.39E-14
ATA	3.85 (2.70, 5.48)	8.62E-14
ACA	0.28 (0.20, 0.40)	1.62E-12
NYHA Level	2.04 (1.67, 2.49)	3.19E-12
Diffuse Subset	2.11 (1.58, 2.81)	3.45E-07
ESR	1.02 (1.01, 1.02)	1.30E-05
Pneumotoxic Rx	1.76 (1.31, 2.35)	1.45E-04
Azathioprine (never/unknown)	0.39 (0.24, 0.64)	2.06E-04
Immune Modulator	1.69 (1.27, 2.24)	3.41E-04
PAH	1.95 (1.34, 2.83)	4.69E-04

Figure 1. Stepwise (forward) selection for predictors of ILD Incidence



Results: Of 1695 patients followed between August 2004 and July 2019, 417 developed SSc-ILD; 227 were incident diagnoses after registry entry. Patients were predominantly middle-aged Caucasian females. General risk factors for ILD including family history, environmental exposures and smoking histories were overall low prevalence in the population and similar between those that did and did not develop SSc-ILD.

Logistic regression identified 12 patient factors associated with increased or decreased odds of developing ILD independent of age and sex (Table 1). Forward stepwise selection revealed 6 significant predictors of SSc-ILD development (Figure 1). Age at SSc diagnosis was the only predictor of early-onset SSc-ILD with older age at SSc diagnosis being associated with increased odds of SSc-ILD onset before 5 years (Table 2).

Conclusion: In a large Canadian cohort we identified 6 factors significantly associated with risk of developing SSc-ILD: baseline pulmonary function (with higher baseline DLCO and FVC reducing risk), antibody status (ATA positivity increasing risk, ACA positivity decreasing risk), elevated hemoglobin and older age at Raynaud's onset. Only older age at SSc diagnosis was predictive of early-onset SSc-ILD .

Table 2: Stepwise selection for early versus late incident ILD

	Final Model	
Predictor	**Odd's Ratio (95%CI)**	**Pvalue**
Age at SSc Dx	2.66 (2.15, 3.47)	9.05E-16
Age at ILD Dx	0.38 (0.26, 0.51)	1.22E-08
Age	1.01 (0.77, 1.34)	0.96
Sex	0.97 (0.29, 2.98)	0.96

Disclosure: J. Kapralik, None; **R. Morton**, None; **M. Farooqi**, None; **K. Beattie**, None; **N. Hambly**, None; **M. Larche**, Adiga Life Science Inc, 10.

Abstract Number: 0414

Effect of Induction Therapies on Ear, Nose and Throat Involvement in Anti-neutrophil Cytoplasmic Antibody Associated Vasculitis: Results from a Multi-center Cohort Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Up to 87% of patients with anti-neutrophil cytoplasmic antibody (ANCA)- associated vasculitis (AAV) have ear, nose and throat (ENT) involvement, which can lead to permanent damage and negatively impacts quality of life. Unfortunately guidelines on the optimal management of ENT symptoms are currently lacking and only few studies, mostly with small patient numbers, evaluated the effect of systemic therapies on ENT disease activity. The aim of this study was therefore to compare the impact of induction therapies on ENT symptoms in patients with AAV.

Methods: In this retrospective study, AAV patients with ENT involvement treated at one of the two Dutch centers between January 2010 and April 2020 were included. Clinical, histological and laboratory data were collected from electronic patient records. ENT involvement was defined as 1) at least one ENT symptom according to the Birmingham vasculitis activity score (BVAS) and/or 2) presence of saddle nose deformity. Regression analyses were used to identify associations between the induction agents cyclophosphamide (CYC) and rituximab (RTX) and disease activity while correcting for confounders (follow-up time, age, sex, renal and pulmonary involvement). Some patients (N=41) had a period of treatment with CYC and a treatment period with RTX over the follow-up period. This dependency was taken into account using Generalized Estimating Equation.

Results: In our centers, 213 (67.8%) of 320 AAV patients had ENT involvement. In these 213 patients, median age at disease onset was 52.5 years (IQR 22) and 45.5% was male (N=97). Median BVAS was 12 (IQR 12) at diagnosis and 0 (IQR 2) at last visit. Relapse rate was 0.06 per year (IQR 0.17). At relapse 49.7% (N=78) had ENT involvement and 29.0% (N=60) had ENT activity at last visit (Table 1).

Male patients had a lower risk of ENT activity at last follow-up (OR 0.31 (CI 0.16-0.62), p=0.001) compared to females, as did patients with a lower age at disease onset (OR 0.98 (CI 0.95-0.99), p=0.020). Renal and pulmonary involvement, biopsy results, and ANCA titer, ESR and CRP at diagnosis were not significantly associated with ENT activity at last visit.

In total 140 (65.7%) patients were treated with CYC and 57 (26.8%) with RTX. No statistically significant difference in ENT activity at last visit was observed between patients treated with oral or intravenous CYC compared to RTX (adjusted OR 0.61 (95% CI 0.34-1.09), p=0.093). Furthermore, there was no significant difference in the number of

Table 1. Patient characteristics

		All patients N=213	Patients treated with CYC N=140 (65.7%)	Patients treated with RTX N=57 (26.8%)	p-value*
Age at disease onset, median (IQR)		52.5 (22)	53.0 (19)	49.0 (20)	0.232
Follow-up time in years, median (IQR)		8.4 (13.6)	11.1 (15.1)	9.0 (12.9)	0.101
Male sex, N (%)		97 (45.5%)	73 (52.1%)	24 (42.1%)	0.213
Deceased, N (%)		32 (15.5%)	28 (20.3%)	4 (7.1%)	0.032
AAV Type, N (%)	GPA	178 (83.6%)	126 (91.3%)	50 (92.6%)	0.619
	EGPA	24 (11.3%)	9 (6.5%)	2 (3.7%)	0.516
	MPA	4 (1.9%)	3 (2.2%)	2 (3.7%)	0.628
	Unknown	7 (3.3%)	2 (1.4%)	3 (5.3%)	0.147
ANCA MPO positivity, N (%)		32 (16.5%)	19 (14.8%)	8 (14.3%)	1.000
ANCA PR3 positivity, N (%)		127 (65.5%)	100 (78.1%)	44 (78.6%)	1.000
Renal involvement		88 (41.9%)	78 (56.9%)	29 (50.9%)	0.621
Pulmonary involvement		101 (47.6%)	78 (56.1%)	30 (52.6%)	0.695
Saddle nose deformity	at diagnosis	11 (6.8%)	5 (5.1%)	6 (14.0%)	0.091
	developed during follow-up	9 (3.5%)	6 (5.2%)	2 (3.9%)	1.000
BVAS at diagnosis, median (IQR)		12.0 (12)	15.5 (11)	12.0 (10)	0.014
BVAS at last visit, median (IQR)		0.0 (2)	0.0 (2)	0.0 (4)	0.324
Total number of relapses, median (IQR)		1.0 (2)	1.0 (2)	2.0 (3)	0.046

AAV: ANCA-associated vasculitis; ANCA: anti-neutrophil cytoplasmic antibody; BVAS: Birmingham vasculitis activity score; CYC: cyclophosphamide; EGPA: eosinophilic granulomatosis with polyangiitis; GPA: granulomatosis with polyangiitis; IQR: interquartile range; MPA: microscopic polyangiitis; MPO: myeloperoxidase; N; number; PR3: proteinase 3, RTX: rituximab.

*p-values were calculated using chi-square tests for categorical data. For continuous variables, p-values were calculated using the Mann-Whitney U test.

patients with at least one ENT relapse between the RTX and CYC group (adjusted OR 0.61 (CI 0.30-1.28), p=0.192). Eight (3.8%) patients received methotrexate as induction therapy. In these patients median age at disease onset was 45.5 years (IQR 30) and 75.0% (N=6) was female. These eight patients had a median relapse rate of < 0.01 per year (IQR 0.16) and three (37.5%) patients had ENT activity at last follow-up.

Conclusion: We found no significant difference in ENT activity at last visit or history of ENT relapse between CYC and RTX treated patients. Importantly, persistent ENT symptoms during flares were observed in a considerable number of patients, which emphasizes the need for further research on optimal management of ENT symptoms in AAV.

Disclosure: R. Krol, None; **C. Schaap**, None; **P. Welsing**, None; **R. Klaasen**, None; **H. Remmelts**, None; **C. Hagen**, None; **F. van Reekum**, None; **M. Heijstek**, ROCHE, 6; **J. Spierings**, Boehringer Ingelheim, 5, Miltenyi, 5.

Abstract Number: 0415

Utility of the 22-Item Sinonasal Outcome Test Patient-Reported Outcome Instrument in ANCA-Associated Vasculitis

Ellen Romich, Sherry Chou and Rennie Rhee, University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: ANCA-associated vasculitis (AAV) causes sinus symptoms that impact quality of life. The 22-item Sinonasal Outcome Test (SNOT-22) is a patient-reported outcome measure to assess symptoms and quality of life in chronic rhinosinusitis but has not been well-studied in AAV. We compared SNOT-22 scores during remission and active disease in AAV patients with and without sinus involvement and investigated if SNOT-22 scores can predict subsequent relapse.

Methods: Subjects with AAV (granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), eosinophilic granulomatosis with polyangiitis (EGPA) based on 1990 ACR classification criteria or Chapel Hill Consensus Conference nomenclature) and healthy controls were followed longitudinally with measures of disease activity [BVAS/WG, physician global assessment (PGA)], SNOT-22, and treatment. SNOT-22 questions are scored on a 0-5 scale with higher scores for worse symptoms and include 5 subdomains (rhinologic, extra-nasal rhinologic, ear/facial, psycho-

Table 1. Demographics and disease characteristics

	All AAV Subjects (GPA, MPA, EGPA)	GPA	MPA	EGPA	Healthy controls
	n=159	n=106	n=21	n=32	n=70
Demographics					
Age, mean (SD)	55 (15.7)	53 (16.3)	60 (16.3)	56 (12.4)	58 (13.6)
Sex, n (% female sex)	91 (57%)	59 (56%)	11 (52%)	21 (66%)	42 (60%)
Number of visits per subject, mean (SD)	4.8 (2.7)	5.0 (2.5)	3.9 (2.7)	5.0 (3.3)	1.9 (1.2)
Disease characteristics at enrollment					
Duration of diagnosis (years), median [IQR]	3.3 [1.0, 6.4]	3.5 [1.0, 6.4]	3.5 [1.3, 7.0]	2.7 [1.0, 5.2]	
Positive ANCA ELISA					
PR3-ANCA	76 (48%)	73 (69%)	3 (14%)	0	
MPO-ANCA	58 (36%)	29 (27%)	18 (86%)	11 (34%)	
History of flare, n (%)	87 (55%)	57 (54%)	10 (48%)	20 (63%)	
Flare involving sino-nasal area	50/87 (57%)	39/57 (68%)	0/10	11/20 (55%)	
History of rhinosinusitis from AAV, n (%)	122 (78%)	89 (84%)	3 (16%)	30 (94%)	
Study visits					
Number of visits	n=747	n=509	n=79	n=159	
Visits with active disease since last visit, n (% of total visits)	110 (15%)	78 (15%)	11 (14%)	21 (13%)	
Visits with active sinonasal disease since last visit, n (% of active visits)	69 (63%)	53 (68%)	0 (0%)	16 (76%)	
Time between visits (months), mean (SD)	3.5 (3.3)	3.6 (3.3)	3.3 (3.8)	3.3 (3.2)	
Active disease visits					
Birmingham Vasculitis Activity Score, median [IQR]	3 [2, 4]	3 [2, 4]	3 [1, 6]	2 [1, 3]	
Physician global assessment, median [IQR]	6 [4, 7]	6 [4, 7]	7 [5, 8]	5 [4, 7]	
Glucocorticoid use, n (%)	54 (50%)	36 (47%)	7 (73%)	11 (52%)	
Any non-glucocorticoid immunosuppressive, n (%)[a]	50 (46%)	32 (42%)	6 (55%)	12 (57%)	
Rituximab, within prior 6 months	37 (34%)	27 (35%)	3 (27%)	7 (33%)	
Antibiotic use, n (%)	2 (2%)	1 (1%)	1 (9%)	0	
Nasal therapies, n (%)					
Nasal steroid or irrigation	14 (13%)	8 (10%)	0	6 (29%)	
Mupirocin	10 (9%)	8 (10%)	0	2 (10%)	
Any nasal antibiotic	11 (10%)	9 (12%)	0	2 (10%)	
Current allergies, n (%)	43 (49%)	27 (35%)	3 (27%)	13 (62%)	

Abbreviations: ANCA, anti-neutrophil cytoplasmic antibodies; IQR, interquartile range; PR3, proteinase-3; MPO, myeloperoxidase; [a]Non-glucocorticoid immunosuppressives include: azathioprine, cyclophosphamide, methotrexate, mycophenolate, mepolizumab

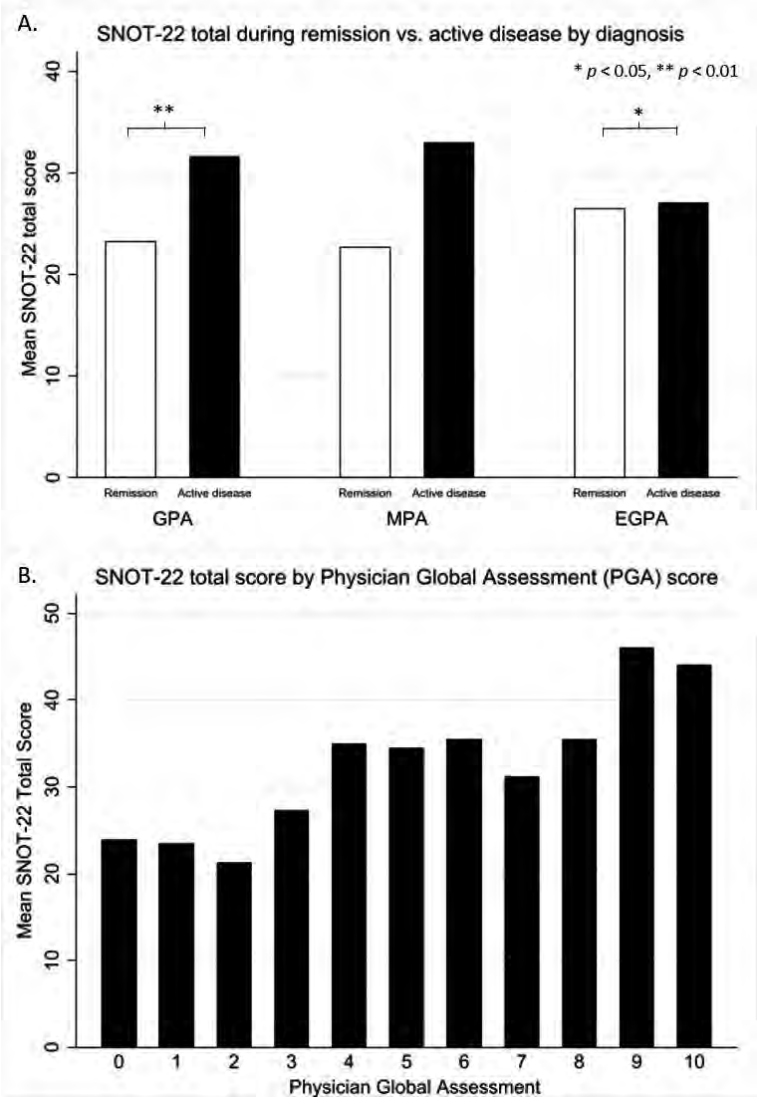

Figure 1. A) SNOT-22 total score at remission and active disease visits according to diagnosis. Asterisks indicate significant differences in adjusted model. B) SNOT-22 total score for all AAV subject visits plotted against Physician Global Assessment showing higher disease activity measure corresponds with higher SNOT-22 total score (p<0.001 in adjusted model).

logical, sleep). Generalized estimating equations evaluated the association between SNOT-22 scores and disease activity. Models were adjusted for concomitant seasonal allergies and use of antibiotics, immunosuppressive drugs, and sinus rinses.

Results: 159 AAV subjects (106 GPA, 21 MPA, 32 EGPA) with 747 visits (110 active disease visits, mean interval 3.5 months) and 70 controls were included (Table 1). Baseline SNOT-22 total scores were higher in AAV vs. controls (mean (SD): 27.5 (1.6) vs. 15.4 (2.1), $p< 0.01$) and higher for AAV subjects with vs. without sinus involvement (mean (SD): 30.3 (20.5) vs. 17.8 (13.2), $p< 0.01$). Adjusted SNOT-22 total scores were significantly higher during active disease vs. remission for GPA and EGPA but not MPA (Figure 1A). Subgroup analyses demonstrated similar results among subjects with a history of sinonasal involvement but not among subjects without baseline sinonasal disease (p=0.3). For all AAV, higher PGA was associated with higher SNOT-22 total (Figure 1B). In GPA, active disease was associated with higher scores in each SNOT-22 subdomain except sleep. Compared to remission visits, active disease was associated with worse scores occurred in the psychological and sleep subdomains for MPA and in the rhinologic subdomain for EGPA (Figure 2). Prior SNOT-22 total scores were not associated with subsequent relapse among all

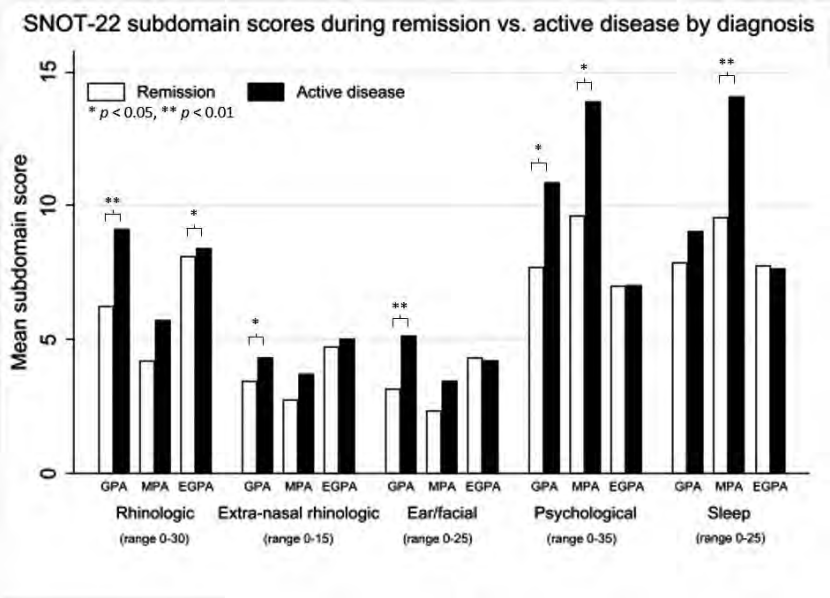

Figure 2. SNOT-22 subdomain scores during remission and active disease. Results demonstrate higher scores during active disease with larger effect on certain subdomains according to diagnosis. Asterisks indicate significant differences in adjusted model.

visits, but when limiting visits to those 2 months apart, increase in SNOT-22 score at prior visits was associated with subsequent relapse (adj OR 1.15 per score change of 5, 95% CI: 1.0-1.3, p=0.03).

Conclusion: In AAV, SNOT-22 scores are higher during active disease vs. remission particularly among patients with previous sinus involvement. The subdomains impacted most by disease activity differ by disease type. When measured within 2 months, change in SNOT-22 scores at remission are associated with subsequent relapse. SNOT-22 may be an informative patient-reported outcome measure to monitor disease activity in AAV patients.

Disclosure: E. Romich, None; **S. Chou**, None; **R. Rhee**, None.

Abstract Number: 0416

Pharmacological Response of Rituximab Based on Dose Intensity in Maintenance Therapy of ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Rituximab (RTX) has demonstrated efficacy in maintenance therapy in ANCA-associated vasculitis. However, different dosing protocols have been used in clinical trials and there is no consensus regarding the optimal regiment. The purpose of this work is to evaluate the variability of RTX dosing in a real-world cohort of ANCA-associated vasculitis patients and the relationship with pharmacological response.

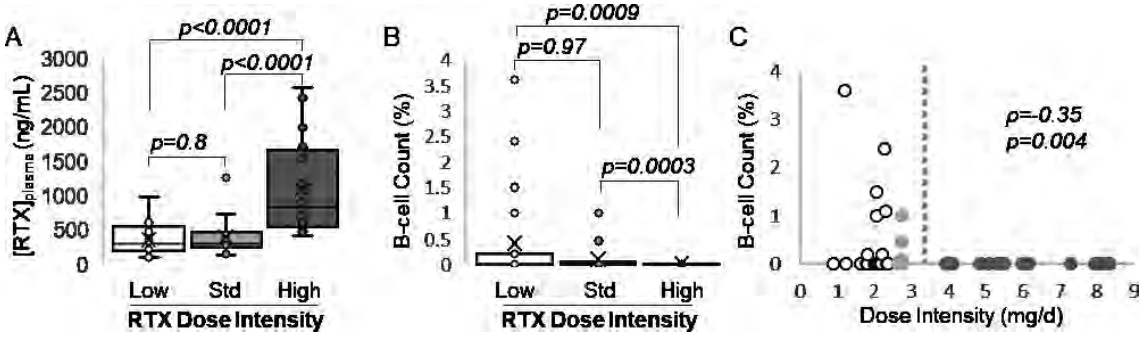

Figure 1

Methods: Patients with a diagnosis of either granulomatosis with polyangiitis (GPA, n=23) or microscopic polyangiitis (MPA, n=5) from a single tertiary care academic medical center were followed prospectively for over 2 years during remission therapy with RTX. All patients met either the 1990 ACR criteria for GPA or the 2012 Chapel Hill Consensus Conference definition for MPA. Dosing of RTX was at the discretion of the treating physician, based on clinical factors and not ANCA titers or B-cell counts. Peripheral blood samples were collected just prior to RTX infusions (i.e. trough of therapy). Demographics, RTX dosing information and laboratory measure of pharmacologic response, including B-cell counts and ANCA titers, were collected throughout the follow-up period. RTX dose intensity was calculated as the RTX dose normalized to dosing interval (mg/d). Stratification of dose intensity was based on a 'standard' dosing regimen of 500mg every 5-7 months with others classified as 'low' or 'high' dosing. Spearman's rank correlations, unpaired T-tests and Wilcoxon rank-sum testing were used as appropriate.

Results: Mean age at enrollment was 60 ± 14 years, with 68% being female. At baseline, 13 patients were positive for PR3-ANCA, 14 MPO-ANCA and 1 ANCA-negative. The mean dose of RTX infusions was 640 ± 221 mg with a mean interval of 210 ± 88 days. The mean peripheral trough concentration of RTX was 622 ± 548 ng/ml. Peripheral RTX concentrations were significantly associated with dose intensity ($p < 0.0001$) (figure 1A). Patients with undetectable B-cells had a significantly higher RTX dose intensity compared patients with detectable B-cells (4.1±2.6 vs 2.7±1.2 mg/d, $p< 0.0001$). Patients with both undetectable B-cells and negative ANCA titers tended to have higher RTX dose intensities (4.4±2.5 vs 2.3±0.5 mg/d, p=0.06). Patients receiving 'standard' dosing regimens (2.4-3.3 mg/d, equivalent to 500mg every 5-7 months) had a significantly higher percentage of B-cells compared to higher dose intensities (p=0.0003) (figure 1B). All patients treated with a dose intensity greater than 3.3 mg/d had undetectable B-cells (figure 1C). In the high intensity group 100% of patients had undetectable B-cells versus 69% and 60% for low and standard dosing (p=0.03) (figure 2A). There were no differences in the groups regarding ANCA negativity (figure 2B). While not significant, there was a dose-dependent relationship between dose intensity and the combination of undetectable B-cells and ANCA negativity (p=0.21) (figure 2C).

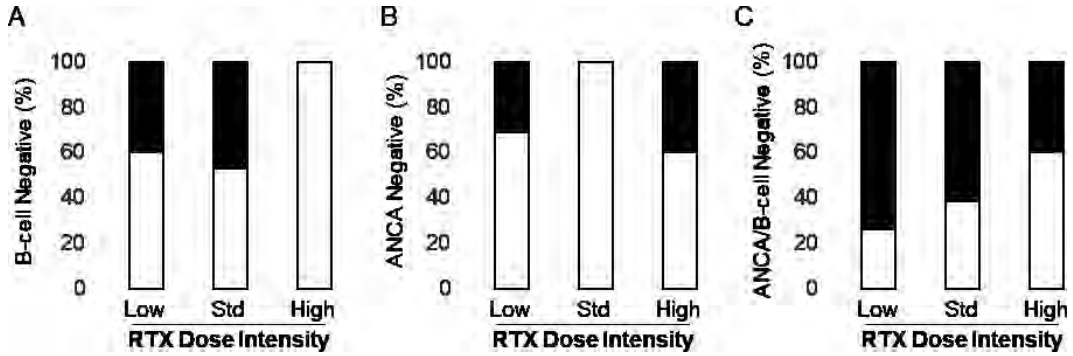

Figure 2

Conclusion: Standard RTX maintenance dosing intensity of 500 mg every 6 months may be inadequate to maintain B cell depletion in a significant number of patients. A target RTX dose intensity of greater than 3.3 mg/d is required to maintain B-cell depletion.

Disclosure: J. Springer, None; **R. Funk**, None.

Abstract Number: 0417

Neurologic Involvement in ANCA-associated Vasculitis: Data from Multicenter Longitudinal Observational Study

Rula Hajj-Ali[1], Robert Butler[2], Carol Langford[3], Leonard Calabrese[2], David Cuthbertson[4], Nader Khalidi[5], Curry Lee Md Koening[6], Carol McAlear[7], Paul Monach[8], Larry Moreland[9], Christian Pagnoux[10], Philip Seo[11], Ulrich Specks[12], Antoine Sreih[7], Kenneth Warrington[13] and Peter Merkel[7], [1]Cleveland Clinic, Hunting Valley, OH, [2]Cleveland Clinic, Cleveland, OH, [3]Cleveland Clinic, Moreland Hills, OH, [4]University of South Florida, Tampa, FL, [5]McMaster University, Hamilton, ON, Canada, [6]LIMITED TO OFFICIAL UNIVERSITY DUTIES ONLY, Salt Lake City, UT, [7]University of Pennsylvania, Philadelphia, PA, [8]Brigham and Women's Hospital, Boston, MA, [9]University of Colorado, Denver, CO, [10]Mount Sinai Hospital, Toronto, ON, Canada, [11]Johns Hopkins University, Baltimore, MD, [12]Mayo Clinic, Rochester, MN, [13]Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

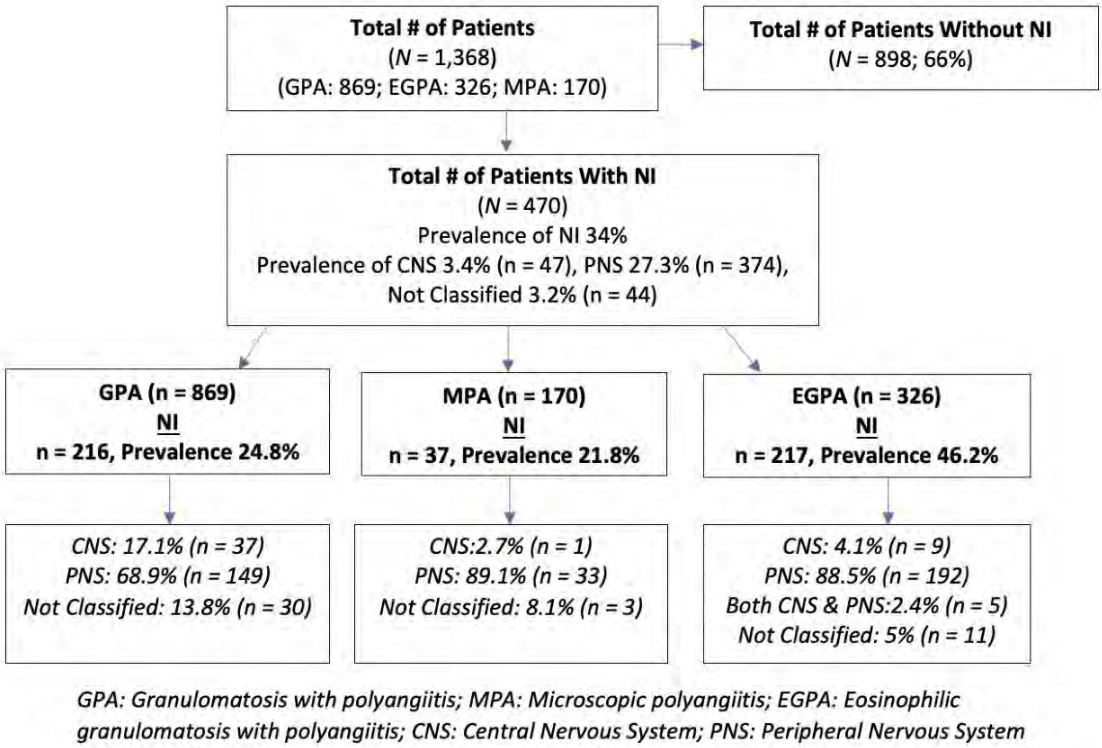

Figure 1. Prevalence of neurologic involvement (NI) in patients with ANCA-associated vasculitis.

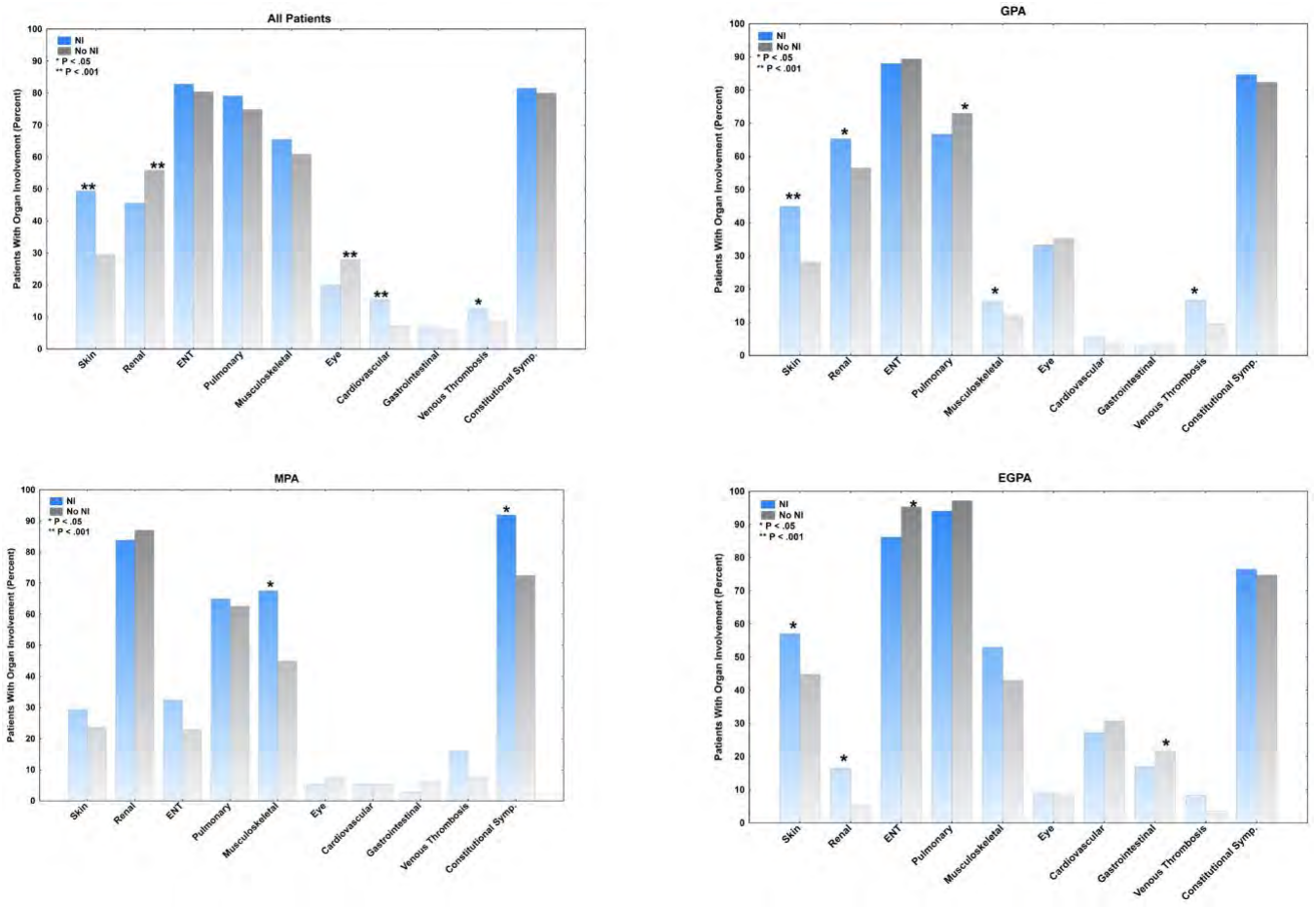

Figure 2. Organ involvement with patient with ANCA-associated vasculitis with and without neurologic involvement (NI) by disease.

Background/Purpose: The prevalence of neurologic involvement (NI) in ANCA-associated vasculitis (AAV), especially central nervous system (CNS) involvement, is not well characterized. This project aimed to describe the prevalence and types of peripheral nervous system (PNS) NI and CNS NI in AAV, and associations of NI with other manifestation of vasculitis.

Methods: Analysis of patients with AAV [granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), or eosinophilic granulomatosis with polyangiitis (EGPA)] participating in a multicenter longitudinal observational study. Data were from 2006-2021 from patients at least 18 years old at enrollment. Standardized forms were used to document patient demographics, disease type, organ involvement, and ANCA status. Patient subsets were compared according to presence or absence of NI.

Results: Data from 1368 patients were available: 470 (34%) had NI (Figure 1) of whom 216 (46%) had GPA, 37 (7.8%) had MPA, and 217 (46.2%) had EGPA. The prevalence of NI was 24.8% (216/869) in GPA, 22% (37/170) in MPA, and 67% (217/326) in EGPA. The prevalence of CNS NI in the total cohort was 47/1368 (3.4%) and the prevalence of PNS NI was 374/1368 (27.3%), with 44 patients (3.2%) having NI that was not classified. GPA was the most common diagnosis in patients with CNS NI (78% compared to 2% in MPA and 19% in EGPA). For PNS NI, EGPA was the most common diagnosis (51% compared to 40% in GPA and 8.8% in MPA).

Patient sex and race did not differ between patients with or without NI. Patients with NI were 53% female and 47% male, 88.7% were White, 1.5 % Black, 3.2% Hispanic, and 4.8% Asian. Mean age at diagnosis of patients with NI

was higher than patients without NI (51.4 vs 47.0 years, p <0.001). NI was associated with skin (49.4% vs. 29.5%, p < 0.001), venous thrombosis (12.8% vs. 8.6%, p= 0.016), and cardiovascular (15.5% vs. 7.2%, p < 0.001) involvement. Patients with NI were less likely to have renal (45.6% vs. 55.9%, p < 0.001), and eye (20 % vs. 28%, p < 0.001) involvement. NI was associated with skin and kidney involvement in EGPA, musculoskeletal, skin, kidney, venous thromboses in GPA and constitutional and musculoskeletal symptoms in MPA (Figure 2).

Patients with NI were more likely to have P-ANCA pattern (43.1 % vs 31.2 % p =0008) and anti-MPO (44.4% vs 30% p < .0001) than patients with no NI.

Conclusion: NI in AAV is common, occurring in approximately one-third of patients, and was most common in EGPA, compared to GPA or MPA. CNS NI occurs more commonly in GPA. NI is associated with various specific organ systems and P-ANCA/anti MPO positivity. These data are informative for clinicians and patients with AAV, and should raise the awareness of this common manifestation of vasculitis. The relationships of NI with other specific manifestations of disease warrants additional study.

Disclosure: R. Hajj-Ali, Novartis, 6, Rockpointe, INC., 6, Projects In Knowledge, 6, UpToDate, 9; **R. Butler**, None; **C. Langford**, None; **L. Calabrese**, Lilly, 2, BMS, 2, Genentech, 2; **D. Cuthbertson**, None; **N. Khalidi**, Roche, 12, Advisory Board for GCA CME November 2020, BMS, 12, Clinical Trial (Investigator Initiated- BMS supplied drug only, no fees received from BMS), Sanofi, 12, Clinical Trial 2020 GCA and PMR, Abbvie, 12, Clinical Trial 2020-2021 GCA; **C. KOENING**, None; **C. McAlear**, None; **P. Monach**, Kiniksa, 1, Celgene, 2, Chemocentryx, 1; **L. Moreland**, None; **C. Pagnoux**, Gsk, 2, 5, 6, Roche, 2, 5, 6, Otuska, 2, Pfizer, 5, 6, Chemocentryx, 2, Astrazeneca, 1; **P. Seo**, Amgen, 1, Janssen, 1; **U. Specks**, ChemoCentryx, 2, 5, Genentech, 5, Bristo-Myer Squibb, 5, InflxRX, 5, Astra Zeneca, 1, 5, GSK, 5; **A. Sreih**, Bristol Myers Squibb, 3, Alexion, 11; **H. Alessi**, Eli Lilly, 5, Kiniksa, 5; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9.

Abstract Number: 0418

Longitudinal Patterns of Renal Function in ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Renal involvement is common in ANCA-associated vasculitis (AAV). Prior analyses show that end stage renal disease (ESRD) in AAV may be multifactorial. Little is known about the longitudinal course of renal dysfunction in contemporary AAV cohorts. We aimed to identify renal function trajectories using an unbiased approach, and to assess the baseline comorbidities and outcomes associated with these trajectories.

Methods: Patients with a baseline creatinine (30-365 days before treatment initiation) were included from the Mass General Brigham AAV Cohort, a consecutive inception cohort (2002-2017). Follow-up began 1 year before and was

Table: Characteristics of the Study Cohort, N(%)

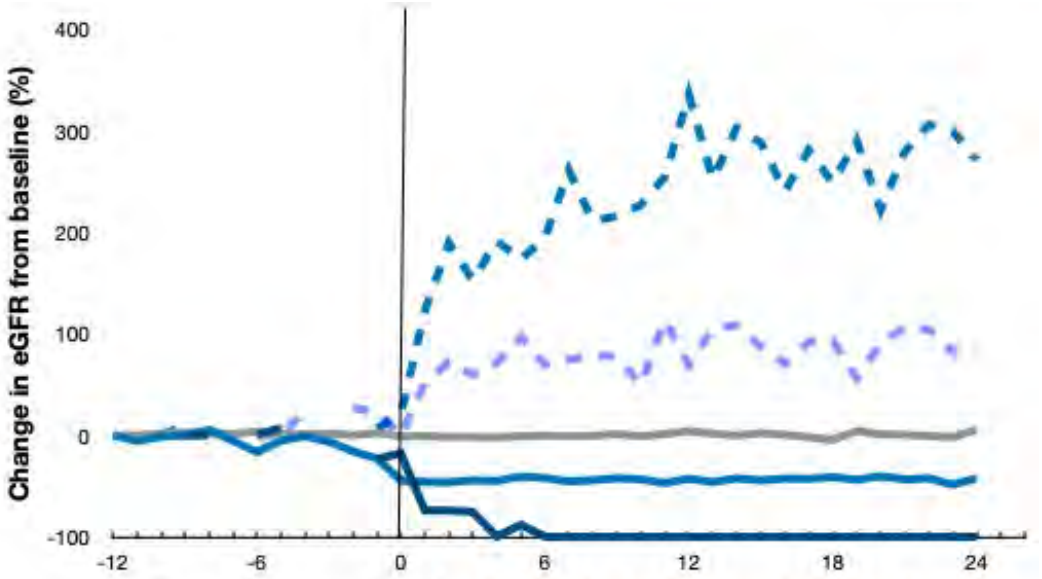
		Overall	Rapid decline	Slow decline	Stable	Recovery	Marked recovery	p-value
N		430	30	37	316	35	12	
Age at diagnosis		59 ± 18	62 ± 16	66 ± 15	58 ± 18	60 ± 18	54 ± 21	0.06
Male sex (%)		180 (42)	15 (50)	17 (46)	128 (41)	15 (43)	5 (42)	0.86
Race/ethnicity								
	White	357 (86)	24 (86)	30 (81)	263 (86)	30 (86)	10 (83)	0.33
	Black	10 (2)	2 (7)	3 (8)	3 (1)	1 (3)	1 (8)	
	Hispanic	13 (3)	0 (0)	3 (8)	10 (3)	0 (0)	0 (0)	
	Asian	7 (2)	1 (4)	0 (0)	6 (2)	0 (0)	0 (0)	
	Other	6 (1)	0 (0)	0 (0)	4 (1)	2 (6)	0 (0)	
	Native American	1 (0.2)	0 (0)	0 (0)	1 (0.3)	0 (0)	0 (0)	
	Not recorded	23 (6)	11 (4)	1 (3)	18 (6)	2 (6)	1 (8)	
Probability of group membership			0.99 (0.32-1.0)	0.99 (0.99-1.0)	0.98 (0.89-0.99)	0.99 (0.99-1.0)	1.0 (1.0-1.0)	
DM at baseline		65 (15)	3 (10)	9 (24)	49 (16)	2 (6)	2 (16)	0.19
HTN at baseline		205 (48)	22 (74)	24 (65)	138 (44)	16 (46)	5 (41)	<0.01
MPO serology		280 (65)	22 (73)	31 (84)	198 (63)	24 (69)	5 (42)	0.03
Baseline eGFR prior to AAV		67 (38-82)	39 (35-88)	52 (27-79)	70 (50-83)	75 (34-87)	40 (11-75)	0.10
Baseline eGFR during AAV		45 (13-77)	4 (2-6)	20 (8-35)	60 (30-85)	14 (5-29)	5 (3-11)	<0.0001
BVAS at baseline		4 (3-6)	5 (4-7)	5 (4-6)	4 (3-5.5)	6 (4-7)	5.5 (4-6)	<0.0001
RBC casts or glomerulonephritis		217 (50)	29 (97)	25 (68)	123 (39)	29 (83)	11 (92)	<0.0001
Biopsy category	N	97	12	17	52	11	5	0.60
	Focal	20 (21)	0 (0)	6 (35)	13 (25)	1 (9)	0 (0)	
	Crescentic	24 (25)	4 (33)	2 (12)	12 (23)	3 (27)	3 (60)	
	Mixed	19 (20)	2 (17)	3 (18)	10 (19)	3 (27)	1 (20)	
	Sclerotic	27 (28)	5 (42)	5 (29)	14 (27)	2 (18)	1 (20)	
Treatment resistance *		64 (33)	18 (86)	13 (43)	25 (24)	4 (14)	4 (33)	<0.0001
Any dialysis		75 (17)	23 (77)	13 (35)	33 (10)	4 (11)	2 (17)	<0.0001
Transplant		12 (3)	5 (17)	2 (5)	5 (2)	0 (0)	0 (0)	<0.0001
ESRD		64 (15)	30 (100)	10 (27)	22 (7)	2 (6)	0 (0)	<0.0001
Death		115 (27)	17 (57)	14 (38)	75 (24)	5 (14)	4 (33)	<0.01
eGFR at 1 year (mL/min/1.73m^2)		49 (25-79)	2.4 (0.8-4.9)	31 (22-45)	66 (40-87)	29 (22-43)	26 (18-46)	<0.0001
eGFR at 2 years (mL/min/1.73m^2)		58 (35-79)	0 (0-0)	32 (23-50)	68 (45-85)	50 (47-66)	58 (41-95)	<0.0001
eGFR at 5 years (mL/min/1.73m^2)		62 (34-81)	0 (0-0)	33 (14-41)	69 (49-86)	54 (32-70)	68 (45-85)	<0.0001

Values reported as N(%), mean ± standard deviation or median (25%-75%)). AAV: ANCA-associated vasculitis. BVAS: Birmingham vasculitis activity score. ESRD: end stage renal disease. eGFR: estimated glomerular filtration rate. Treatment resistance is reported only among those with renal involvement.

truncated 10 years after treatment initiation. Treatment resistance was defined as lack of remission following the first course of therapy; remission was defined by stabilization or improvement of estimated glomerular filtration rate (eGFR) without hematuria for ≥1 month. In patients without repeat urinalysis, stabilization or improvement of eGFR was considered evidence of remission.

We calculated eGFR using CKD-EPI without race multiplier. We used trajectory analysis to identify groups with similar longitudinal change in renal function, defined as percentage of pre-AAV eGFR over the first 24 months of follow up. Final models were selected by fit statistics and face validity.

ESRD was defined as (1) need for dialysis for >60 days, (2) dialysis until death if the patient died between 14-60 days of follow up, or (3) renal transplant, as identified by chart review and United States Renal Data System records.



Number at Risk

Months	-12	-6	0	6	12	18	24
Rapid decline	30	30	29	5	4	4	3
Slow decline	35	35	35	35	35	30	29
Stable	314	314	309	294	291	288	259
Recovery	35	35	35	33	33	33	33
Marked recov.	12	12	12	11	11	11	11

Logistic regression was used to evaluate risk factors for trajectory group membership, and Cox proportional hazards models were used to estimate risk of ESRD in each trajectory group, accounting for competing risk of death.

Results: Of 484 patients in the cohort, 430 were included. We identified 5 groups (Figure): rapid decline (RD) (N=30), slow decline (SD) (N=37), stable (N=316), recovery (N=35) and marked recovery (N=12). The median posterior probability of group membership was >0.98 in all groups, indicating excellent fit.

Age, sex, race and biopsy class were overall similar between groups; however, RD and SD groups tended to be older than those with a stable course, and sclerotic biopsy classification was most common among RD. MPO serology and hypertension (HTN), but not diabetes (DM), were more common in RD and SD than other groups (Table). Treatment resistance was more common in RD than SD (86% vs 43%, $p< 0.001$), and more common in these groups than in the stable and recovery groups.

In a logistic model adjusted for age and ANCA type, baseline HTN (OR 2.3, 95% CI 1.3-4.4) but not DM (OR 0.9, 95%CI 0.4-1.8) was associated with odds of membership in RD or SD groups versus any other group. In an age-adjusted model, the RD and SD groups had a higher risk of ESRD compared to the stable group (HR 647, 95%CI 128-377 and HR 14, 95%CI 4-46, respectively).

Conclusion: In a large AAV cohort, we identified distinct patterns of change in renal function. Baseline HTN was associated with a worse trajectory and treatment resistance was more common among those with a worse trajectory. Both RD and SD groups were associated with higher risk of ESRD.

Disclosure: J. Hanberg, None; **X. Fu**, None; **C. Cook**, None; **J. Stone**, Principia Biopharma Inc, a Sanofi Company, 5, 12, personal fees; **H. Choi**, None; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 0419

Post-induction ANCA Titer Does Not Predict Mortality or Renal Outcomes: A Target Trial Emulation Study

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

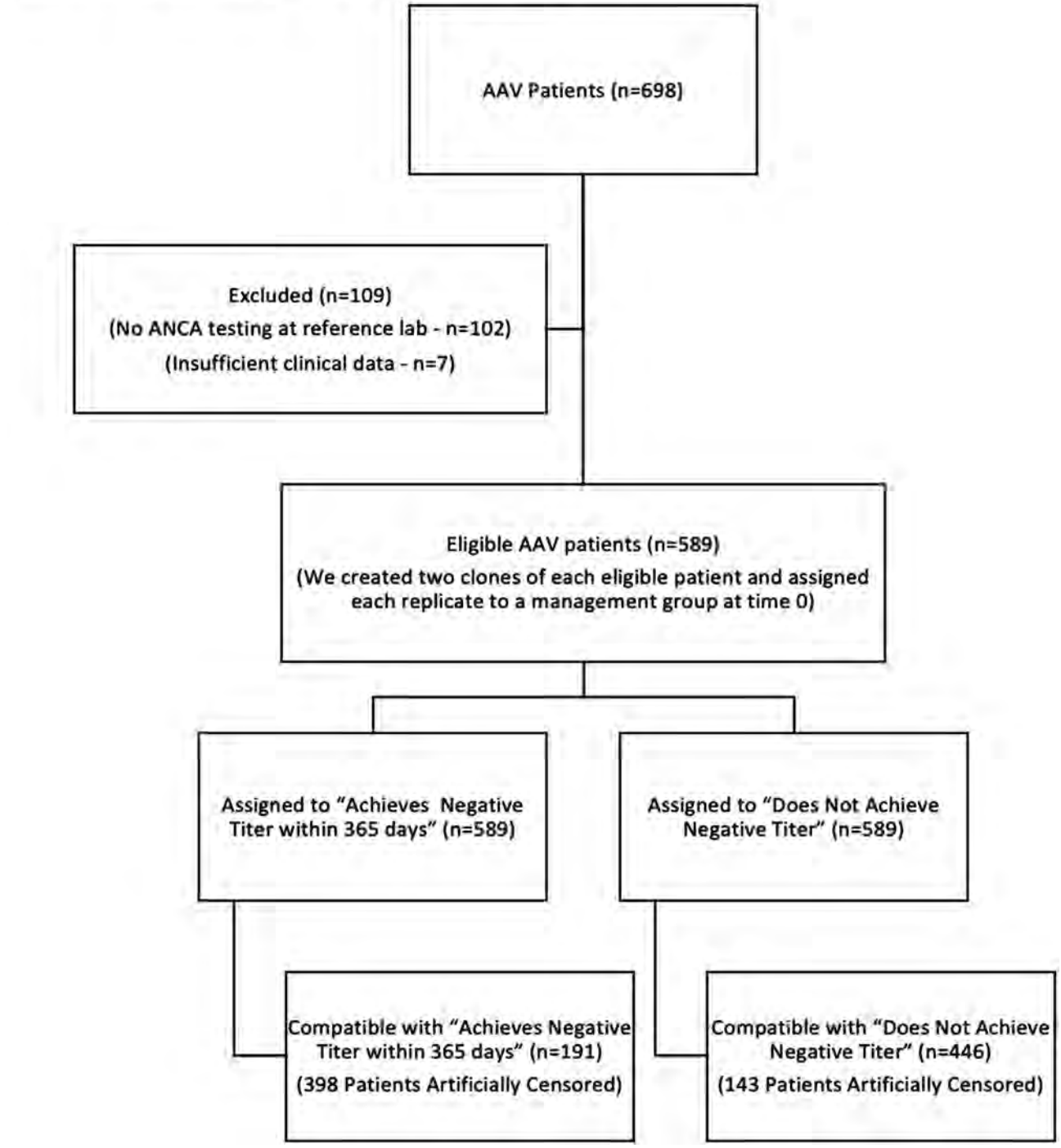
Session Time: 8:30AM–10:30AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is associated with increased risk of end-stage renal disease (ESRD) and death. In most cases, circulating ANCA targeting proteinase-3 (PR3) or myeloperoxidase (MPO) are present and may be pathogenic. Studies of the association of post-treatment ANCA titers with future outcomes have yielded conflicting results. We evaluated the association of achieving a negative ANCA titer during the first year of treatment with ESRD and death.

Methods: Cases were obtained from a consecutive inception cohort of AAV patients who received care at a large multi-hospital system between 2002-2019. All cases were PR3- or MPO-ANCA+. ANCA titers were obtained from a single reference laboratory. Mortality data were obtained from the National Death Index and ESRD status from the United States Renal Data System. To address confounding and immortal-time bias, we performed a target trial emulation study to examine the association of post-induction ANCA titer with risk of ESRD or death using a previously described cloning, censoring and weighting approach. We designed a hypothetical trial with two management strategies: "achieve a negative titer" or "do not achieve negative titer" within 365 days of induction. "Clones" of each patient were included in each hypothetical management arm and censored when they violated the assigned strategy. The composite outcome – risk of ESRD or death within five years – was estimated using Cox models after accounting for informative censoring using inverse-probability-of-censoring weighting and adjusting for baseline covariates.

Results: The study included 589 patients (mean age: 60 years; 58% female; 88% white) with 24.4 ± 24.6 months of mean follow up (Table 1). The majority were MPO-ANCA+ (70%) and had renal manifestations (65%). Rituximab (RTX)-based induction strategies were used in 48%. 32% achieved a negative titer within one year of induction. In the target trial, the HR for the primary outcome of ESRD or death was 1.02 (95%CI 0.84-1.24) in the group that achieved a negative titer compared to the group that did not (Table 2). In analyses stratified by remission induction strategy, the HR for ESRD or death was 0.95 (95%CI 0.72-1.26) in RTX-based and 1.11 (95%CI 0.83-1.48) in cyclophosphamide (CYC)-based regimen users when comparing those who achieved a negative titer vs those who did not. The HR for ESRD or death was 0.85 (95%CI 0.56-1.27) in the PR3-ANCA+ and 1.12 (95%CI 0.90-1.40) in the MPO-ANCA+ groups that achieved a negative titer. There was a trend toward lower risk of death among PR3-ANCA+ patients who achieved a negative titer (HR 0.58 [95%CI 0.33-1.02]).

Figure 1: Flow Chart of Eligible Patients and Target Trial Design



Conclusion: In this target trial using a large cohort of AAV patients, achieving a negative ANCA titer within one year of induction was not associated with improved renal or mortality outcomes. This finding was seen in both RTX- and CYC-treated patients. There was a trend towards decreased risk of death in the PR3-ANCA+ patients who achieved a negative titer, although this did not reach statistical significance. These findings suggest that post-induction ANCA titers have limited ability to predict mortality and ESRD outcomes in AAV.

Table 1: Baseline Characteristics of Participants (n=589)

Characteristic	Total (n=589, %)
Age (years mean, SD)	60 +/- 18
Male	249 (42%)
Race	
White	516 (88%)
Black	11 (2%)
Asian	9 (2%)
Other	53 (9%)
ANCA status	
PR3-ANCA+	179 (30%)
MPO-ANCA+	410 (70%)
Organ Involvement	
Any major	454 (77%)
Renal	380 (65%)
Pulmonary	284 (48%)
Head and neck	256 (43%)
Other	230 (39%)
Disease activity at diagnosis (BVAS/WG mean, SD)	5.0 +/- 2.2
Induction treatment	
Included RTX	281 (48%)
Included CYC	201 (34%)
Other (no RTX or CYC)	107 (18%)
Follow up	
Time (months, mean, SD)	24.4 (24.6)
ANCA measurements during follow up* (mean, SD)	9.7 (8.8)
ANCA measurements in first year after induction (mean, SD)	4.9 (2.9)
Labs (median, IQR)	
Cr (mg/dL)	1.6 (1.0, 3.6)
eGFR (mL/min/1.72m^2)	35.5 (13.5, 71.4)
ESR (mm/hr)	17.0 (8.0, 36.0)
CRP (mg/L)	4.6 (1.4, 15.5)
Death or ESRD within 5 years**	157 (27%)
ESRD within 5 years	77 (13%)
Death within 5 years	97 (17%)

* within five years of induction or from induction to primary outcome if <5 years

** composite primary outcome

ANCA = antineutrophil cytoplasmic antibody, BVAS/WG = Birmingham Vasculitis Activity Score for Wegener's Granulomatosis, Cr = creatinine, CRP = C-reactive protein, CYC = cyclophosphamide, dL = deciliter, eGFR = estimated glomerular filtration rate, ESR = erythrocyte sedimentation rate, IQR = interquartile range, mg = milligram, mL = milliliter, mm = millimeter, L = liter, RTX = rituximab, SD = standard deviation

Table 2: The Association of Achieving a Negative ANCA Titer with ESRD and Death

	Achieve Negative Titer HR (95%CI)	Does Not Achieve Negative Titer
All Patients		
Risk of ESRD or Death	1.02 (0.84, 1.24)	Ref
Risk of ESRD	0.99 (0.76, 1.30)	Ref
Risk of Death	0.88 (0.68, 1.14)	Ref
PR3-ANCA+		
Risk of ESRD or Death	0.85 (0.56, 1.27)	Ref
Risk of ESRD	0.87 (0.53, 1.42)	Ref
Risk of Death	0.58 (0.33, 1.02)	Ref
MPO-ANCA+		
Risk of ESRD or Death	1.12 (0.9, 1.40)	Ref
Risk of ESRD	1.07 (0.78, 1.47)	Ref
Risk of Death	1.03 (0.77, 1.37)	Ref
RTX or RTX/CYC Treated		
Risk of ESRD or Death	0.95 (0.72, 1.26)	Ref
Risk of ESRD	0.84 (0.6, 1.33)	Ref
Risk of Death	0.84 (0.60, 1.19)	Ref
CYC Only Treated		
Risk of ESRD or Death	1.11 (0.83, 1.48)	Ref
Risk of ESRD	1.03 (0.70, 1.50	Ref
Risk of Death	1.05 (0.67, 1.63)	Ref

ANCA = antineutrophil cytoplasmic antibody, CYC = cyclophosphamide, ESRD = end-stage renal disease, MPO = myeloperoxidase, PR3 = proteinase-3, RTX = rituximab

Disclosure: G. McDermott, None; **X. Fu**, None; **C. Cook**, None; **J. Stone**, Principia Biopharma Inc, a Sanofi Company, 5, 12, personal fees; **Y. Zhang**, None; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 0420

Development and Validation of a Simulation Model for Maintenance Treatment in ANCA-Associated Vasculitis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: ANCA-associated vasculitis (AAV) care has evolved over the last two decades with several approaches to remission maintenance. However, these approaches have trade-offs regarding the risk of flare, infection, end-stage renal disease (ESRD), and other outcomes which impact morbidity, mortality, and costs. We developed a simulation model to project clinical outcomes in individuals with specific disease features, which can be used to inform clinical decision-making and identify uncertainties that strongly affect outcomes.

Methods: We developed a state-transition, microsimulation model of people with AAV (TreeAge Pro Healthcare 2020). Figure 1 displays the health states; individuals remain in or transition between health states monthly. At model start, individuals draw for demographic and disease-specific characteristics and then transition between the active AAV or inactive states (i.e., relapse/remission, stratified by major/minor severity) and are at risk for severe infection, ESRD, or death. Transition rates are stratified by demographic and disease-specific characteristics. Table 1 shows

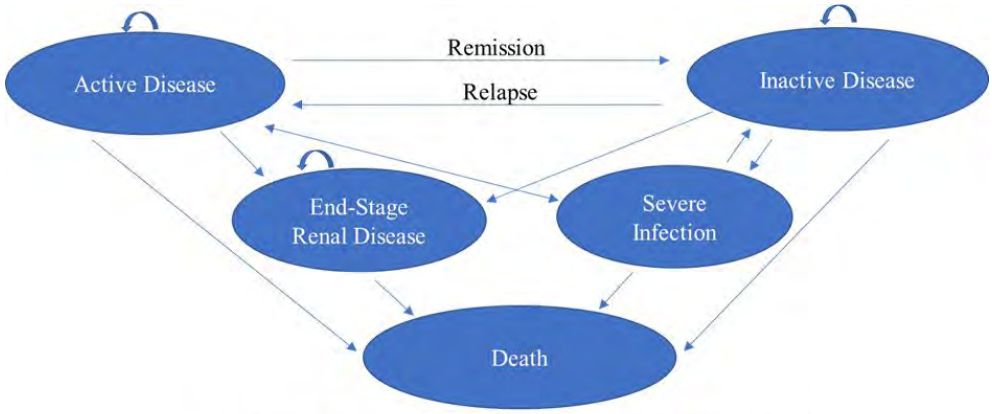

Figure 1. AAV State-Transition Model.

Table 1. Model Input Parameters

Input Parameter	Base Case Value (Ref)	
Baseline Cohort Characteristics[1]		
Age (mean [SD], years)	60.6 (13.0)	
Male (%)	58.2%	
PR3-ANCA (N, %)	58.0%	
Renal Involvement (N, %)	71.1%	
Relapse (monthly probability)[1-6]	**Tailored Treatment**	**Fixed Schedule**
PR3-ANCA Major Relapse	0.00351	0.00171
PR3-ANCA Minor Relapse	0.00477	0.00292
MPO-ANCA Major Relapse	0.00171	0.00085
MPO-ANCA Minor Relapse	0.00231	0.00143
Severe Infection (monthly probability)[1, 2]		
Active Disease	0.00944	0.00944
Inactive Disease	0.00419	0.00785
End-Stage Renal Disease (monthly probability)		
Active Disease		
History of Renal Involvement	0.00966[7]	
No History of Renal Involvement	*Age- and sex-stratified*[8]	
Inactive Disease		
History of Renal Involvement	*2.0 * Age- and sex-stratified*[8]	
No History of Renal Involvement	*Age- and sex-stratified*[8]	
Mortality (monthly probability)		
Active Disease	*SMR of 2.5 * age- and sex-stratified*[9]	
Inactive Disease	*SMR of 1.5 * age- and sex-stratified*[9]	
ESRD	*Age- and sex-stratified*[8]	
Severe Infection	*Age- and sex-stratified*[10]	

CDC: Centers for Disease Control and Prevention; USRDS: United States Renal Data System; HCUP: Healthcare Cost and Utilization Project; SMR, standardized mortality ratio; References:

1. Charles P, et al. Ann Rheum Dis. 2018;77(8):1143-9. 2. Smith RM, et al. Ann Rheum Dis. 2020;79(9):1243-9.
3. Guillevin L, et al. N Engl J Med. 2014;371(19):1771-80. 4. Lionaki S, et al. Arthritis Rheum. 2012;64(10):3452-62. 5. Hogan SL, et al. Ann Intern Med. 2005;143(9):621-31. 6. Walsh M, et al. Arthritis Rheum. 2012;64(2):542-8. 7. Rhee RL, et al. Arthritis Rheumatol. 2016;68(7):1711-20. 8. United States Renal Data System. 2020 USRDS Annual Data Report, 2020. 9. Arias E, Xu J. United States Life Tables, 2017.

model input parameters. The distribution of baseline demographics (i.e., age, sex, ANCA type, renal involvement) are from the MAINRITSAN 2 trial, which compared fixed-schedule rituximab (RTX) to a tailored approach based on rising ANCA or B cell titers for remission maintenance. We obtained probabilities of relapse, severe infection, and ESRD from MAINRITSAN 2, and other clinical trials, cohort studies, and national registries. We estimated mortality based

Table 2. Comparison of AAV Model Projected Outcomes with MAINRITSAN 2 Outcomes Over 28 Months

	Fixed Treatment		Tailored Treatment	
	AAV Model	MAINRITSAN 2	AAV Model	MAINRITSAN 2
Number	10,000	81	10,000	81
Minor Relapse	7.4% (6.9%-7.9%)	6.2% (1.0%-11.4%)	10.1% (9.5%-10.7%)	8.6% (2.5%-14.8%)
Major Relapse	4.3% (3.9%-4.7%)	3.7% (0.0%-7.8%)	7.0% (6.5%-7.5%)	7.4% (1.7%-13.1%)
≥ 1 Severe Infection	19.1% (18.2%-20.0%)	19.8% (11.1%-28.4%)	10.9% (10.3%-11.6%)	10.2% (3.4%-16.4%)
ESRD	0.5% (0.4%-0.6%)	1.2% (0.0%-3.6%)	0.6% (0.5%-0.8%)	0% (0%-0%)
Death	5.9% (5.4%-6.4%)	3.7% (0.0%-7.8%)	5.4% (5.0%-5.8%)	1.2% (0.0%-3.6%)

on disease-specific features and background age- and sex-adjusted rates derived from US life tables. We then used the AAV model to project outcomes with tailored vs fixed-schedule RTX among people in remission at baseline over 28 months, as studied in MAINRITSAN 2. We performed face validity assessment with experts in the field. We used mean average percent error (MAPE) to assess how the model-projected outcomes compared to those observed in MAINRITSAN 2.

Results: Over 28 months, the AAV model projected fewer minor and major relapses with fixed vs tailored RTX (7.4% [95% CI 6.9%-7.9%] vs 10.1% [9.5%-10.7%] and 4.3% [3.9% vs 4.7%] vs 7.0% [6.5%-7.5%]). More patients had at least one severe infection in the fixed vs tailored group (19.1% [18.2%-20.0%] vs 10.9% [10.3%-11.6%]). ESRD was uncommon in both groups (0.5% [0.4%-0.6%] vs 0.6% [0.5%-0.8%]). The mean survival was the same in both strategies (27.0 ± 3.9 vs 27.0 ± 3.8 months). Compared to the MAINRITSAN 2 trials results (Table 2), the projected rates of relapse, severe infection, ESRD, and death in the AAV model were similar (MAPE, 1.5%, range 0.4%-4.3%). Limitations include that we made assumptions regarding differences in mortality rates during active vs inactive disease states.

Conclusion: We established the face validity and internal validation of a novel AAV state-transition model that projects key outcomes, including minor and major relapse, severe infection, ESRD, and death. This model can be adapted to compare other strategies (e.g., azathioprine) and incorporate other health states (e.g., steroid toxicity), quality of life, and costs.

Disclosure: Z. Wallace, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2; **J. Stone**, Principia Biopharma Inc, a Sanofi Company, 5, 12, personal fees; **H. Choi**, None; **E. Hyle**, None.

Abstract Number: 0421

Negative vs. Positive Antineutrophil Cytoplasmic Antibody Granulomatosis with Polyangiitis, a Case-control Study

Marta Casal Moura, Samuel D. Falde, Ulrich Specks and Misbah Baqir, Mayo Clinic, Rochester, MN

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA) negative granulomatosis with polyangiitis (GPA) is a challenging diagnosis. There is paucity of literature regarding the clinical course of ANCA-negative GPA especially when comparing that of ANCA-positive GPA.

Methods: We conducted a single-center, sex and age matched case-control and case-crossover study of ANCA-negative GPA vs. ANCA-positive GPA patients evaluated at our institution from January 1, 1996 to December 31, 2015. Clinical features, outcomes and correlation with ANCA status were characterized.

Results: We identified 110 patients with ANCA-negative GPA, mostly females (72, 65.5%) with median age of 55 (IQR 39-65) years at the time of diagnosis. Disease severity was milder in ANCA-negative GPA (BVAS/WG = 1 vs. 6 points, p< 0.0001). Mucous membranous/eye manifestations were more frequent in ANCA-negative GPA, whereas general symptoms (fever, weight loss, arthralgia, myalgia), pulmonary and renal involvement were more frequent in ANCA-positive GPA. Time to remission was longer in ANCA-negative GPA (27.7 vs. 18.8 months, p=0.004). Greater number of ANCA-positive GPA patients relapsed at 60 months (21.8% vs. 9.1%, p=0.009) compared to ANCA-negative GPA and time to relapse was shorter (49.8 vs. 54.8 months, p=0.043) in ANCA-positive GPA. Patients with general manifestations, BMI > 30 kg/m^2 and necrotizing granulomatous inflammation were more likely to relapse. ANCA seroconversion from negative to positive was observed in 16 patients. After seroconversion, patients had higher mean BVAS/WG score (p< 0.0001) and increased incidence of relapses (p=0.004) in comparison with the time before ANCA seroconversion. Necrotizing granulomatous inflammation and vasculitis on biopsy at the time of ANCA-negative GPA diagnosis were identified as risk factors for ANCA-positive seroconversion.

Conclusion: ANCA-negative GPA patients have milder disease (BVAS/WG) and are less likely to relapse when compared with patients with ANCA-positive GPA. ANCA seroconversion portends higher disease severity and an increased frequency of relapse.

Disclosure: M. Casal Moura, None; **S. Falde**, None; **U. Specks**, ChemoCentryx, 2, 5, Genentech, 5, Bristo-Myer Squibb, 5, InflxRX, 5, Astra Zeneca, 1, 5, GSK, 5; **M. Baqir**, None.

Abstract Number: 0422

Cancer in Patients with ANCA-associated Vasculitis: Which Came First, the Chicken or the Egg?

Elif Ediboglu[1], Riza Can Kardas[2], Ertugrul Cagri bolek[3], Resit Yildirim[4], DenizCan Guven[5], Saadettin Kilickap[5], Omer Dizdar[5], Melek Yalcin Mutlu[6], Ozan Cemal Icacan[7], Gizem Ayan[8], Emre Bilgin[8], Nazife Sule Yasar Bilge[9], Levent Kilic[8], Timucin Kasifoglu[4], Cemal Bes[10], Servet Akar[11] and **Omer Karadag**[12], [1]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, İzmir, Turkey, [2]Hacettepe University Faculty of Medicine, Department of Internal Medicine, Ankara, Turkey, [3]Vasculitis Translational Research Program, NIAMS, NIH, US, Lanham, MD, [4]Eskisehir Osmangazi University, Department of Internal Medicine, Division of Rheumatology, Eskisehir, Turkey, [5]Hacettepe University Medical Faculty, Department of Medical Oncology, Ankara, Turkey, [6]University of Health Sciences, Istanbul, [7]University of Health Sciences, Istanbul, Turkey, [8]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [9]Eskisehir Osmangazi University Medical Faculty, Eskisehir, Turkey, [10]Saglik Bilimleri University, Basaksehir Cam and Sakura State Hospital – Istanbul, Turkey, Istanbul, Turkey, [11]Izmir Katip Celebi University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Izmir, Turkey, [12]Hacettepe University, Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Ankara, Turkey

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Distribution and characteristics of of AAV patients with cancer history

Case No	AAV subgroup	Age/ Gender	Smoking Status (Ever)	Cyclophosphamide	Diagnosis of Cancer	Cancer Extent	Timing	Time to cancer from vasculitis (Months)	Survival Status
1	GPA	67, M	No	N/A	Colon	Localized	Before AAV	-102.28	Exitus (not related to cancer)
2	GPA	44, F	No	N/A	Endometrium	Localized	Before AAV	-47.51	Alive
3	GPA	69, M	Yes	N/A	Bladder	Localized	Before AAV	-46.55	Exitus (not related to cancer)
4	uAAV	61, M	Yes	N/A	Lung (SCC)	Localized	Before AAV	-23.08	Alive
5	GPA	69, M	No	N/A	Lip SCC	Localized	Before AAV	-21.67	Exitus (not related to cancer)
6	GPA	43, M	No	N/A	Malign mesenchymal tumor	Localized	Before AAV	-18.71	Alive
7	EGPA	69, M	Yes	Yes	Lung (SCC)	Localized	**After AAV**	6.21	Exitus (unknown)
8	GPA	69, M	Yes	No	Larynx	Localized	**After AAV**	7.04	Alive
9	EGPA	52, M	Yes	Yes	Lip SCC	Localized	**After AAV**	11.15	Alive
10	GPA	58, M	Yes	Yes	Basal Cell Carcinoma	Localized	**After AAV**	13.91	Alive
11	MPA	67, M	Yes	Yes	Bladder	Localized	**After AAV**	24.00	Alive
12	GPA	73, M	Yes	No	Lung (Adenocarcinoma)	Locally advanced or Metastatic	**After AAV**	33.93	Exitus (related to cancer)
13	GPA	64, M	No	Yes	Colon	Localized	**After AAV**	59.57	Exitus (Unknown)
14	GPA	66, F	Yes	Yes	Thyroid	Localized	**After AAV**	84.00	Alive
15	GPA	53, M	Yes	No	Marginal Zone Lymphoma	Localized	**After AAV**	109.25	Alive
16	GPA	73, M	Yes	No	Bladder	Localized	**After AAV**	323.90	Alive

Background/Purpose: Many studies linking vasculitis to the development of malignancy based on chronic inflammation, cytotoxicity, emergence of vasculitis as a paraneoplastic disease. Even previous studies emphasize the role of cyclophosphamide, recent AAV cohort studies, where cumulative cyclophosphamide is lower than the historical cohorts, do not show such associations with cancer. The objective was to identify characteristics of adult AAV patients having a history of cancer and compare with AAV patients with no history of cancer.

Methods: In this nationwide study we used Turkish Vasculitis Study Group Registry (TRVaS)-a newly established, multicenter, and e-database of Turkey. Among 517 AAV patients, data regarding cancer was available in 373 (72%) patients. Demographics, clinical characteristics, medications, smoking data were analyzed. Retrospective analysis of patients that presented cancer before AAV diagnosis or after AAV diagnosıs was done. Regarding malignancies, type of cancer, clinical or pathological stage, treatment response were also recorded. AAV patients were groupped according to having cancer after AAV diagnosis or no cancer history. Groups were compared in terms of demographic, clinical features, and medications. Relative risk was measured using the standardized incidence ratio (SIR), which was calculated by the ratio of cancer cases except non-melanoma skin cancer among AAV patients to the expected cases for the background population. The expected number of cases was calculated by multiplying the measured person-years by the incidence rate of cancer in Turkey. Cancer data were obtained from the GLOBOCAN 2020 estimates of new cases in Turkey.

Results: Totally 16 patients had ever cancer history before AAV diagnosis in 6 and after AAV diagnosis in 10 patients. Distribution of cancer diagnosis were lung cancer (n=3), bladder (n=3), skin (n=3), colon (n=2), endometrium, lymphoma, thyroid, larynx, and malign mesenchymal tumor (Table 1). Patients with cancer history were older and male predominant (Table 2). Smoking history was present in 90% of the patients with cancer. In the comparison of AAV patients with cancer after AAV diagnosis with AAV patients with no cancer history, no difference was found in terms of clinical features of AAV except for pulmonary involvement(Table-2). Cyclophosphamide usage and dosages were similar between groups. Cancer risk was found to be over 2 times higher than the general population for the analysis of AAV patients who developed cancer after the diagnosis (SIR: 2.3, 95% CI: 1.2-4.1, P=0.02).

Table 2. Comparison of Cancer (+)AAV patients with AAV patients no cancer history

	Cancer (+) AAV (n=10)	Cancer (-) AAV (n=357)	p
ANCA Clinical Subtypes			
EGPA, n (%)	2 (20)	52 (14.5)	0.59
GPA, n (%)	7 (70)	208 (27.9)	
MPA, n (%)	0 (0)	48 (13.4)	
Unclassified AAV, n (%)	1 (10)	51 (14.2)	
IFA Test at diagnosis			
IFA Not Tested	0 (0)	9/224 (4)	0.79
IFA Negative	3/8 (37.5)	69/224 (30.8)	
pANCA pattern	3/8 (37.5)	62/224 (27.7)	
cANCA pattern	2/8 (25)	84 (37.5)	
ELISA Test at diagnosis			
ELISA Not Tested	1/4 (25)	18/145 (12.4)	0.02
ELISA Negative	0(0)	4/145 (2.8)	
Anti-MPO	1/4 (25))	50/145 (34.5)	
Anti-PR3	1/4 (25)	71/145 (49.0)	
Others	1/4 (25)	2/145 (1.4)	
Male gender, n (%)	9 (90)	185 (51.8)	**0.02**
Age at diagnosis, years mean ± SD	62.4 ± 9.6	49.4 ± 17.1	**0.008**
Age at last visit, years mean ± SD	64.4 ± 7.6	53.4 ± 16.2	**0.03**
Follow-up time, months median (IQR)	8 (26)	36 (100.15)	**0.046**
Death, n (%)	2 (20)	49/353 (13.9)	0.64
Constitutional Symptoms	7 (70)	274/354 (77.4)	0.43
Mucocutaneous Findings	3 (30)	81/354 (22.9)	0.71
Musculoskeletal Findings	2 (20)	97/354 (27.4)	0.73
Eye Findings	2 (20)	54/351 (15.4)	0.66
ENT Findings	6 (60)	175 /353 (49.6)	0.75
Pulmonary Involvement	10 (100)	220/354 (62.2)	**0.02**
Cardiovascular Involvement	0 (0)	7/347 (2)	1
Gastrointestinal Involvement	0 (0)	16/352 (4.6)	1
Nephrological and/or Genitourinary Involvement	7(70)	220/354 (62.1)	0.75
Central Nervous System Involvement	0 (0)	13/353 (3.7)	1
Peripheral Nervous System Involvement	2 (20)	35/352 (9.9)	0.24
Cyclophosphamide	6 (60)	226 (63.0)	1
Rituximab	3 (30)	106 (19.5)	1

Conclusion: It seems AAV patients have an increased risk for overall malignancies as in European cohorts (1). Smoking was the most seen and preventable risk factor. Cyclophosphamide usage with lower doses in recent years decrease the importance of cyclophosphamide-related cancer. Cancer was more seen in AAV patients not only after AAV diagnosis but also before AAV diagnosis. Further studies required to better understand of which came first, the chicken or the egg?

Reference: 1. Heijl C, Westman K, Höglund P, et al. Malignancies in Patients with Antineutrophil Cytoplasmic Antibody-associated Vasculitis: A Population-based Cohort Study. J Rheumatol. 2020 Aug 1;47(8):1229-1237.

Disclosure: E. Ediboglu, None; **R. Kardas**, None; **E. bolek**, None; **R. Yildirim**, None; **D. Guven**, None; **S. Kilickap**, None; **O. Dizdar**, None; **M. Yalcin Mutlu**, None; **O. Icacan**, None; **G. Ayan**, None; **E. Bilgin**, None; **N. Yasar Bilge**, None; **L. Kilic**, None; **T. Kasifoglu**, None; **C. Bes**, AbbVie, 2, 6; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6; **O. Karadag**, Omer Karadag has received research grants from Roche, Pfzer as study investigator and received consulting fees from Celltrion., 6.

Abstract Number: 0423

Urine and Plasma Complement Ba Levels During Flares of Nephritis in Patients with ANCA-Associated Vasculitis

Salem Almaani[1], Huijuan Song[2], Meshora Sthanithra[2], Christopher Toy[2], Anna Levesque[2], Lynn Fussner[3], Alexa Meara[3], Haikady Nagaraja[2], David Cuthbertson[4], Nader Khalidi[5], CURRY LEE MD KOENING[6], Carol Langford[7], Carol McAlear[8], Larry Moreland[9], Christian Pagnoux[10], Philip Seo[11], Antoine Sreih[12], Kenneth Warrington[13], Paul Monach[14], Peter Merkel[8], Brad Rovin[3] and Dan Birmingham[2], [1]Ohio State University Medical Center, Columbus, OH, [2]Ohio State university, Columbus, OH, [3]Ohio State University Wexner Medical Center, Columbus, OH, [4]University of South Florida, Tampa, FL, [5]McMaster University, Hamilton, ON, Canada, [6]LIMITED TO OFFICIAL UNIVERSITY DUTIES ONLY, Salt Lake City, UT, [7]Cleveland Clinic, Moreland Hills, OH, [8]University of Pennsylvania, Philadelphia, PA, [9]University of Colorado, Denver, CO, [10]Mount Sinai Hospital, Toronto, ON, Canada, [11]Johns Hopkins University, Baltimore, MD, [12]Univeristy of Pennsylvania, Philadelphia, PA, [13]NIH/NIAMS, Bethesda, MD, [14]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

	Long-Term Remission (n=20)	Non-Renal Flare (n=19)	Renal Flare (n=21)	p-value
Male	8 (40%)	8 (42%)	16 (76%)	0.03
White	18 (90%)	19 (100%)	19 (90%)	NS
Non-Hispanic	18 (90%)	19 (100%)	17 (81%)	NS
Age (years)	52 ± 15	54 ± 20	55 ± 13	NS
Disease duration at visit 1 (years)	11.1 ± 8.6	7.3 ± 5.9	4.9 ± 3.8	0.02
Granulomatosis with polyangiitis	14	14	16	
Microscopic polyangiitis	4	1	3	
Eosinophilic granulomatosis with polyangiitis	2	4	2	
ANCA Type				
cANCA/pANCA/unmeasured	10/2/8	9/4/6	12/4/5	
PR3/MPO/unmeasured	12/3/5	8/5/6	14/4/3	
BVAS	0	8 (5-10)	14 (12-18)	
rBVAS	0	0	10 (6-12)	
eGFR	74 (61-101)	83 (74-104)	50 (38-59)	

Figure 1. Patient demographics and disease characteristics.
Data depicted n (%); mean ± standard deviation; median (inter-quartile range) as appropriate.
Fisher's exact test used to compare group memberships and ANOVA used to compare continuous variables. Data obtained at flare visits for the non-renal flare and renal flare groups; and at the last visit for the long-term remission group.
ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cyctoplasmic ANCA; pANCA: perinuclear ANCA; PR3: proteinase 3; MPO: myeloperoxidase; BVAS: Birmingham Vasculitis Activity Score; rBVAS: active renal disease per BVAS; eGFR: estimated glomerular filtration rate.

	Long-Term Remission (n=20)	Non-Renal Flare (n=19)	Renal Flare (n=21)	p-value
Male	8 (40%)	8 (42%)	16 (76%)	0.03
White	18 (90%)	19 (100%)	19 (90%)	NS
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Age (years)	52 ± 15	54 ± 20	55 ± 13	NS
Disease duration at visit 1 (years)	11.1 ± 8.6	7.3 ± 5.9	4.9 ± 3.8	0.02
Granulomatosis with polyangiitis	14	14	16	
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ANCA Type				
cANCA/pANCA/unmeasured	10/2/8	9/4/6	12/4/5	
PR3/MPO/unmeasured	12/3/5	8/5/6	14/4/3	
BVAS	0	8 (5-10)	14 (12-18)	
rBVAS	0	0	10 (6-12)	
eGFR	74 (61-101)	83 (74-104)	50 (38-59)	

Figure 1. Patient demographics and disease characteristics.
Data depicted n (%); mean ± standard deviation; median (inter-quartile range) as appropriate.
Fisher's exact test used to compare group memberships and ANOVA used to compare continuous variables. Data obtained at flare visits for the non-renal flare and renal flare groups; and at the last visit for the long-term remission group.
ANCA: anti-neutrophil cytoplasmic antibody; cANCA: cytoplasmic ANCA; pANCA: perinuclear ANCA; PR3: proteinase 3; MPO: myeloperoxidase; BVAS: Birmingham Vasculitis Activity Score;
rBVAS: active renal disease per BVAS; eGFR: estimated glomerular filtration rate.

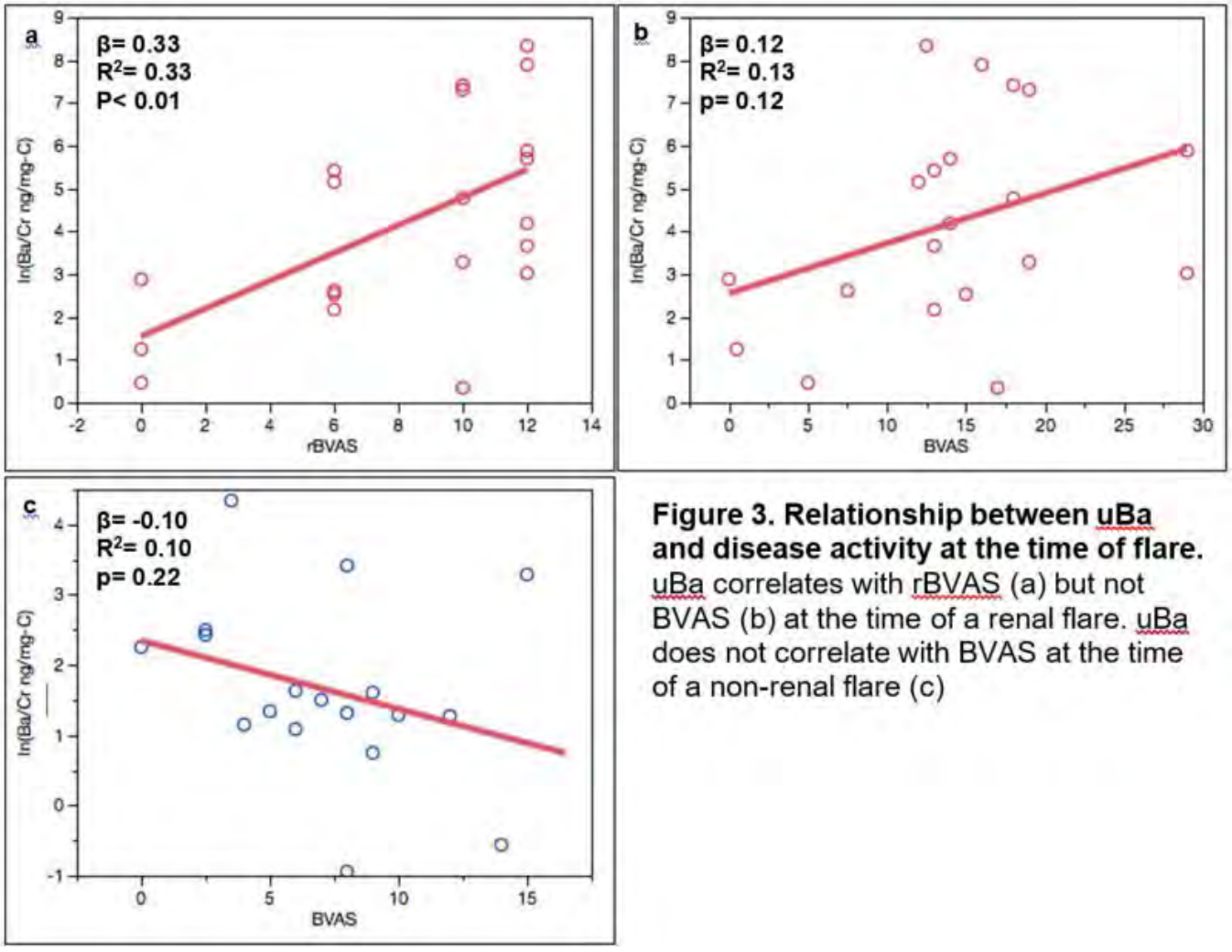

Figure 3. Relationship between uBa and disease activity at the time of flare. uBa correlates with rBVAS (a) but not BVAS (b) at the time of a renal flare. uBa does not correlate with BVAS at the time of a non-renal flare (c)

Background/Purpose: The alternative complement pathway has been implicated in the pathogenesis of ANCA-associated vasculitis (AAV), however it is not clear whether activation of complement occurs systemically or in affected organs such as the kidney. This study measured levels of urinary and plasma complement fragment Ba (uBa and pBa respectively) at multiple timepoints in patients with AAV.

Methods: Ba was measured by ELISA in serial samples of urine (uBa) and plasma (pBa) from 20 AAV patients who developed a renal flare, 20 who developed a non-renal flare, and 20 in long-term remission. Changes in Ba levels were modeled using linear mixed effect models.

Results: Cohort characteristics are given in **Figure.1**. uBa levels increased at renal flare, but did not increase at non-renal flare, and remained stable in long-term remission (**Figure 2a**). pBa levels were stable over time in all groups (**Figure 2b**). uBa correlated with renal AAV activity measured as the renal component of the BVAS score (R^2= 0.33, p< 0.01) (**Figure 3a**), but did not correlate with the overall BVAS score during renal flare (R^2= 0.13, p=0.12) or non-renal flare (R^2= 0.10, p=0.22) (**Figure 3b,c**).

Conclusion: Urine, but not plasma, Ba levels increase at the time of a flare of renal disease in AAV, suggesting intra-renal alternative complement pathway activation. uBa has the potential for use as a surveillance biomarker of renal vasculitis.

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Abstract Number: 0424

Incremental Healthcare Costs of Eosinophilic Granulomatosis with Polyangiitis (EGPA) Compared to Asthma: Retrospective Analysis of Commercial Claims Data in the United States (US)

Christopher Bell[1], Juliana Meyers[2] and Mayank Ajmera[2], [1]GlaxoSmithKline, Research Triangle Park, NC, [2]RTI-Health Solutions, Research Triangle Park, NC

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Eosinophilic granulomatosis with polyangiitis (EGPA), formerly Churg-Strauss Syndrome, is a rare, complex multisystem disorder, characterized by vascular inflammation and multisystem organ damage. EGPA manifests as asthma, chronic rhinosinusitis, blood/tissue eosinophilia, and vasculitis. In part due to its rare nature, there is an absence of real-world data quantifying the healthcare cost of EGPA. This study aims to quantify the incremental healthcare resource utilization (HRU) and costs associated with EGPA as compared to asthma using commercial insurance claims data in the United States (US).

Table 1. Study Results			
Variables	EGPA	Asthma	p-value
N	7,183	35,915	
Age, mean (SD)	51.0 (13.9)	51.2 (14.0)	N/A[a]
Female, N (%)	5,294 (73.7)	26,470 (73.7)	N/A[a]
Charlson Comorbidity Index, mean (SD)	2.8 (2.7)	2.8 (2.7)	N/A[a]
≥1 Prescription 12-Month Post-Index, N (%)			
SABA	3,157 (44.0)	16,078 (44.8)	0.204
ICS	2,960 (41.2)	12,290 (34.2)	<0.001
ICS/LABA	1,724 (24.0)	6,789 (18.9)	<0.001
Leukotriene modifiers	1,277 (17.8)	4,859 (13.5)	<0.001
Oral corticosteroids	4,452 (62.0)	13,704 (38.2)	<0.001
≥1 Healthcare Claim 12-Month Post-Index, N (%)			
Inpatient visit	2,580 (35.9)	9,066 (25.2)	<0.001
Emergency department visit	3,076 (42.8)	13,307 (37.)	<0.001
Outpatient hospital visit	6,294 (87.6)	27,738 (77.2)	<0.001
Physician office visit	7,110 (99.0)	35,095 (97.7)	<0.001
Other outpatient care[b]	5,558 (77.4)	25,326 (70.5)	<0.001
Pharmacy claim	6,300 (87.7)	31,390 (87.4)	0.474
12-Month Post-Index Cost (US$2018), mean (SD)			
Inpatient	$17,342 (56,188)	$8,764 (36,869)	<0.001
Emergency department	$1,054 (4,103)	$791 (3,418)	<0.001
Outpatient hospital visit	$10,498 (30,198)	$5,526 (19,898)	<0.001
Physician office visit	$6,009 (14,183)	$3,081 (7,748)	<0.001
Other outpatient care[b]	$3,596 (21,969)	$2,205 (14,894)	<0.001
Pharmacy claim	$5,906 (12,008)	$4,120 (9,300)	<0.001
Total Cost	$44,405 (82,061)	$24,487 (54,691)	<0.001

EGPA: eosinophilic granulomatosis with polyangiitis; ICS: inhaled corticosteroid; LABA: long-acting beta-agonist; N: number; N/A: not available; SABA: short-acting beta-agonist; SD: standard deviation.
[a]Not available due to variable used in matching criteria.
[b]Home health care, laboratory, etc.

Methods: A retrospective analysis was conducted using the IQVIA PharMetrics Plus Database identifying patients (pts) diagnosed with EGPA between 30 September 2008 and 01 October 2018. Prior to the implementation of ICD-10, EGPA diagnosis was based on published ICD-9-based algorithms.[1,2] Post October 2015, EGPA diagnosis was based on ICD-10 code M30.1 (polyarteritis with lung involvement [Churg-Strauss]). The first observed ICD-9/10 claim for EGPA was the index date. An asthma control cohort (ICD-9: 493.X; ICD-10: J45.X) was also identified (date of first asthma claim = index date). Pts in both cohorts were ≥18 years of age with continuous health plan enrollment (6-months pre- and 12-months post-index). Pts in the EGPA cohort were matched to pts in the asthma cohort (matching ratio 1:5) using direct covariate matching (age at index, year of index, gender, geographic region, and Charlson-Comorbidity Index [CCI] score). Results are reported as counts, percentages and means (standard deviation [SD]). Multivariable analysis was conducted to estimate adjusted total, all-cause costs using a generalized linear model (GLM). Statistical comparisons were evaluated at α=0.05 level.

Results: After matching, the EGPA and asthma cohorts consisted of 7,183 and 35,915 pts, respectively. Based on covariate matching, the cohorts were similar in terms of baseline characteristics (mean age: 51 years; 73% female; mean CCI score: 2.8) (Table 1). In the 12-month post-index period, significant differences between the EGPA and asthma cohorts were observed (Table 1) for the following: (1) proportion of pts with asthma-related medication (with exception of short-acting beta-agonists), (2) proportion of pts with ≥1 HRU claim by setting of care (with exception of pharmacy claims); and (3) mean total costs and costs by setting of care. Unadjusted total costs in the 12-month post-index period were $44,404 (82,060) and $24,487 (54,691) in the EGPA and asthma cohorts, respectively ($p< 0.001$). Adjusted total costs in the 12-month post-index period were $34,004 in the EGPA cohort and $19,552 in the asthma cohort (rate ratio: 1.74; 95% confidence internal: 1.68, 1.79; $p< 0.001$).

Conclusion: In the 12-month post-index period, HRU and costs were significantly higher for EGPA patients than asthma pts. This study demonstrates the incremental burden of EGPA and highlights the need for effective treatments that reduce the burden of disease and improve patient outcomes.

[1]Sreih et al. *Pharmacoepidemiol Drug Saf* 2016;25:1368-74.
[2]Harrold et al. *Pharmacoepidemiol Drug Saf* 2004;13:661-7.

Disclosure: C. Bell, GlaxoSmithKline, 3, 11; **J. Meyers**, None; **M. Ajmera**, None.

Abstract Number: 0425

Diagnostic Accuracy of Muscle MRI for Muscular Vasculitis in Anti-neutrophil Cytoplasmic Antibody-associated Vasculitis: A Pilot Study

Ryuta Inaba, Daisuke Waki, Keisuke Nishimura, Tomohiro Yoshida, Kaoru Mizukawa, Shintaro Yamamoto, Osamu Iri, Kohei Yo and Hiroyuki Murabe, Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Japan

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Histopathologic confirmation is the golden standard for diagnosis of anti-neutrophil cytoplasmic antibody-associated vasculitis (AAV), but sometimes can be difficult because of its invasion (e.g. renal biopsy) or low diagnostic yield (e.g. otorhinolaryngological biopsy). Some studies suggest that muscle biopsy (MB) is a useful tool for diagnosis of AAV owing to its safety and high diagnostic yield and muscle MRI could guide the site of MB [1]. However, there are no previous studies focusing on diagnostic yield of muscle MRI for systemic vasculitis. We aimed to assess the positive predictive value (PPV) of a muscle MRI for MB and describe the muscle MRI features of systemic vasculitis.

Methods: We included all AAV patients who performed muscle MRI at diagnosis or recurrence in our center between 2009 and 2020. The proof of muscular vasculitis was based on the presence of necrotizing vasculitis on MB. As previously reported in polyarteritis nodosa, MRI findings are evaluated with a focus on muscle and fascial lesions. Muscle MRI findings were classified into the following four categories: "diffuse", "patchy", "perivascular", and “myofasciitis” [2]. Duplication of MRI findings was allowed and counted in each category. We calculated PPV of muscle MRI for muscular vasculitis and compared characteristics of the patients with MB positive and those with MB negative.

Results: Among 68 AAV patients with a muscle MRI performed, 62 patients had a positive finding of muscle MRI. Of the positive MRI results, 35 patients (56.5%) presented diffuse pattern, 21 (33.9%) patients presented patchy pattern, and 6 patients (9.8%) presented perivascular pattern, and 39 patients (62.9%) had myofasciitis pattern. Among 39 patients with myofasciitis, there were 29 patients with diffuse pattern, 8 with patchy pattern, 2 with perivascular pattern, and none with myofasciitis alone. Open biopsy was performed in 36 patients (85.7%), and needle biopsy was performed in 6 patients. 31 patients were positive for MB, 10 patients were negative for MB. Among the patients underwent MB, PPV of a muscle MRI for muscular vasculitis was 75.6% (31/41). Comparing MB positive patients and MB negative patients, the clinical diagnosis of MPA (93.8% vs 63.6%), receiving open biopsy (93.5% vs 63.9%), and the diffuse pattern (75.0% vs 9.1%) and myofasciitis pattern (65.6% vs 18.2%) were significantly higher in MB

Table 1 Baseline clinical and biological characteristics in patients with MB positive and MB negative. MB Muscle biopsy, MPO Myeloperoxidase, PR3 Proteinase 3, ANCA Anti-neutrophil cytoplasmic antibody, MPA Microscopic polyangiitis, EGPA Eosinophilic granulomatosis with polyangiitis, GPA Granulomatosis with polyangiitis, BVAS the Birmingham Vasculitis Activity Score, CK serum Creatine kinase, Cre Creatinine, CRP C-reactive protein, Hb hemoglobin. †Comparison between patients with MB positive and MB negative (<0.05 is considered to be statistically significant)

Characteristics	All (n = 68)	MB negative (n = 11)	MB positive (n =31)	P-value †
Sex, male, n (%)	26(38.2)	2(7.7)	12(37.5)	0.283
Age, years, median (IQR)	77(69-80.3)	74.0(74.0-84.5)	77.0(71.5-80.0)	0.197
MPO, n (%)	65(95.6)	10(90.9)	31(96.9)	0.262
PR3, n (%)	2(2.9)	1(9.1)	0(0)	0.262
ANCA negative, n (%)	1(1.5)	0(0.0)	0(0)	-
Diagnosis, n (%)				
MPA	54(79.4)	7(63.6)	29(93.8)	0.0321
EGPA	7(10.3)	1(9.1)	1(3.1)	0.460
GPA	7(10.3)	3(27.3)	1(3.1)	0.0486
open biospy, n (%)	36(85.7)	7(63.6)	29(93.5)	0.0321
needle biopsy, n (%)	6(8.8)	4(36.4)	2(6.5)	0.0321
MRI positive, n (%)	62(91.2)	10(90.9)	31(96.9)	0.262
diffuse, n (%)	35(56.5)	1(9.1)	24(75.0)	0.000116
patchy, n (%)	21(33.9)	9(81.8)	5(15.6)	0.000183
perivascular, n (%)	6(9.8)	0(0.0)	2(6.3)	1.000
myofasciitis, n (%)	39(62.9)	2(18.2)	21(65.6)	0.0114
BVAS, median (IQR)	15(8-19)	11(5-14)	14(8-21)	0.112
Clinical features, n (%)				
Fever	37(54.4)	5(45.5)	21(65.6)	0.281
Weight_loss	28(41.2)	5(45.5)	15(46.9)	0.696
Grap pain	49(72.1)	8(72.7)	27(84.4)	0.353
Myaglia	39(57.4)	8(72.7)	18(56.3)	0.485
Arthralgia	15(22.1)	1(9.1)	10(31.3)	0.234
Lung	42(61.8)	5(45.5)	21(65.6)	0.281
Peri_Nerve	14(20.6)	0(0.0)	8(25.0)	0.086
Renal	39(57.4)	6(54.5)	15(46.9)	1.000
Biologic features, median (IQR)				
CK (U/L)	26(17-60)	25(17-38)	21(13-38)	0.753
Lymphocytes (/μL)	1061(808-1545)	1061(885-1222)	1077(933-1722)	0.301
Neutrophils (/μL)	8797(6623-20839)	9050(7903-10500)	8854(6786-13169)	1.000
Cre (mg/dL)	0.82(0.59-1.51)	0.69(0.57-1.17)	0.67(0.54-1.36)	0.841
CRP (mg/L)	9.2(5.2-13.0)	10.5(6.6-12.3)	9.7(6.9-14.0)	0.756
Hb (g/dL)	10.2(8.7-11.3)	9.8(8.5-11.5)	10.1(8.9-11.0)	0.797

positive patients. There was no significant difference in clinical and laboratory features including vascular disease activity between the two groups.

Conclusion: Muscle MRI can predict the positivity of MB and muscular vasculitis with a high probability. In addition, specific MRI findings (diffuse and myofasciitis patterns) can predict a positive muscle biopsy with high probability.

[1] Mathieu L *et al*. Muscle biopsy in anti-neutrophil cytoplasmic antibody-associated vasculitis: diagnostic yield depends on anti-neutrophil cytoplasmic antibody type, sex and neutrophil count. Rheumatology 2021; 60:699-707.

[2] Yusuhn K *et al*. Muscle involvement in polyarteritis nodosa: report of eight cases with characteristic contrast enhancement pattern on MRI. AJR2016; 206:378-384.

Table 2. The positive predictive value of muscle MRI for muscle biopsy is 75.6% (31/41)

	biopsy positive, n	biopsy negative, n	SUM, n
MRI positive, n	31	10	41
MRI negative, n	0	1	1

Positive Predictive Value : 75.6%

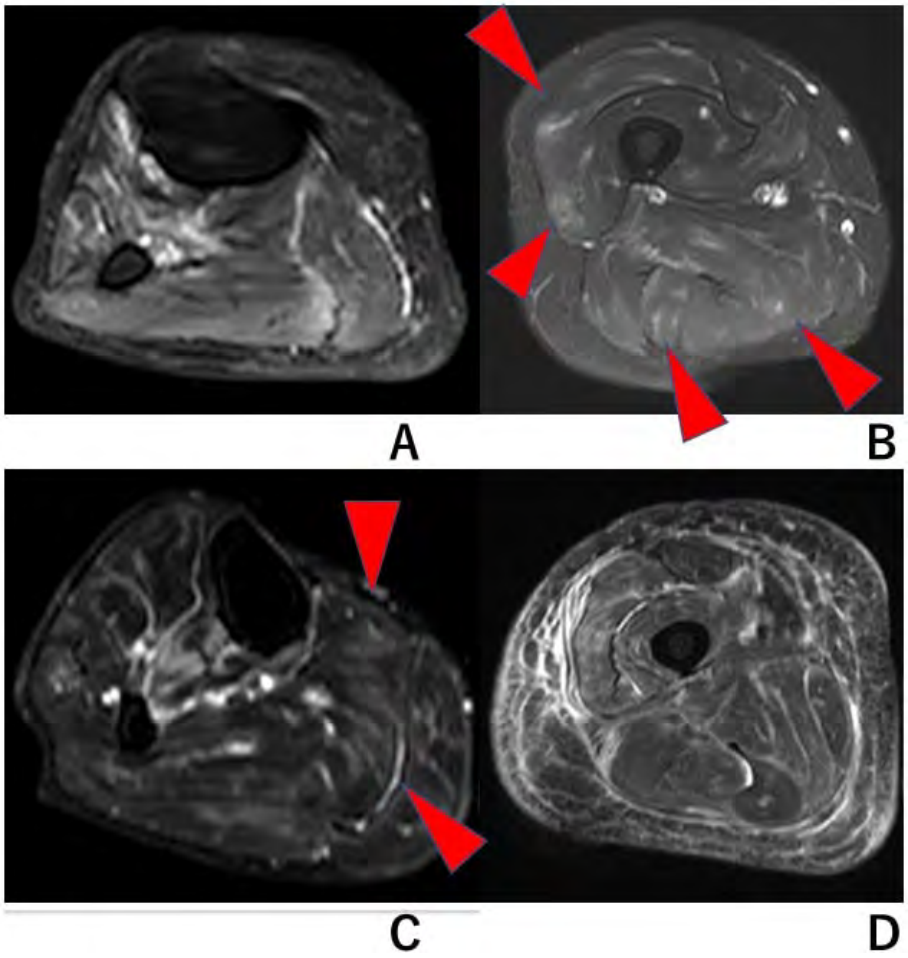

Figure 2. Muscle MRI of patterns of muscle signal alterations. MRIs show (A) “diffuse” (most area of the involved muscle show a high signal), (B) “perivascular” (a small area centered on blood vessels show a high signal), (C) “patchy” (geographic area of the involved muscle show a high signal), (D) “fascial lesion” (a high signal is seen in the fascia).

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Abstract Number: 0426

Ocular Manifestations of ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Background/Purpose: ANCA-associated vasculitides (AAV) are multisystem diseases that can have multiple ophthalmic manifestations. Although there are some data on ocular disease in granulomatosis with polyangiitis (GPA), even less are available for microscopic polyangiitis (MPA) and eosinophilic granulomatosis with polyangiitis (EGPA). Further, there also few reports differentiating symptoms seen at disease onset compared to later in the course of the illness, or whether ophthalmic manifestations are related to other anatomically local disease or systemic manifestations in general.

Methods: Patients with GPA, MPA, or EGPA enrolled in a longitudinal study between April 2006 and April 2021 were included in this study. Data concerning diagnosis, demographics, cranial disease manifestations and their time of onset, treatment, and ocular complications were extracted. Prevalence of ophthalmic manifestations at disease onset and incidence of manifestations over the course of follow up, median time to onset of new manifestations and complications, and correlations with otolaryngologic and neurologic manifestations of disease were calculated.

Results: Data from 1389 patients were included for analysis which included 6392.8 patient-years of follow up. There were 852 cases of GPA, 165 cases of MPA, and 372 cases of EGPA; with 258 (30.3%), 7 (4.2%), and 13 (3.5%) ocular manifestations present at baseline, respectively (Table 1). The most common manifestations seen were conjunctivitis/episcleritis and scleritis, though 38.5% of the ocular manifestations in EGPA were retinal vasculitis. Multiple ophthalmic manifestations were seen in 79 (9.3%) of patients with GPA, and in none with EGPA. In GPA, the prevalence of

Table 1. Number and type of ocular manifestations of vasculitis at disease onset in ANCA-associated vasculitis

Baseline Manifestations	GPA	MPA	EGPA
Total number of patients	852	165	372
Any ocular manifestations	258 (30.3%)	7 (4.2%)	13 (3.5%)
>1 ocular manifestations	79 (9.3%)	3 (1.8%)	0 (0.0%)
Conjunctivitis or episcleritis	111 (13.0%)	3 (1.8%)	3 (0.8%)
Scleritis	61 (7.2%)	3 (1.8%)	1 (0.3%)
Uveitis	22 (2.6%)	0 (0.0%)	2 (0.5%)
Dacrocystitis and/or lacrimal duct obstruction	36 (4.2%)	0 (0.0%)	0 (0.0%)
Orbital Mass or proptosis	26 (3.1%)	0 (0.0%)	0 (0.0%)
Peripheral ulcerative keratitis	9 (1.1%)	1 (0.6%)	0 (0.0%)
Retinal exudates or hemorrhage	3 (0.4%)	2 (1.2%)	0 (0.0%)
Retinal vasculitis	7 (0.8%)	1 (0.6%)	5 (1.3%)

Table 2. Number of ocular manifestations during disease follow up and median time to onset in patients with ANCA-associated vasculitis

	GPA n=852	Time from disease onset [years (IQR)]	MPA n=165	Time from disease onset [years (IQR)]	EGPA n=372	Time from disease onset [years (IQR)]
Specific manifestation: n (%)						
Any ocular manifestation	56 (6.6)	-	1 (0.6)	-	2 (0.5)	-
***De novo* ophthalmic manifestations**	30 (3.5)	-	0	-	2 (0.5)	-
Conjunctivitis or episcleritis	22 (2.6)	5.2 (3.3-10.9)	1 (0.6)	4.4*	1 (0.3)	4.5*
Scleritis	13 (1.5)	3.4 (1.6-5.9)	0	-	0	-
Uveitis	7 (0.8)	3.9 (1.8-15.2)	0	-	0	-
Dacrocystitis and/or lacrimal duct obstruction	21 (2.5)	8.6 (4.0-11.7)	0	-	0	-
Orbital mass or proptosis	9 (1.1)	12.6 (6.8-15.4)	0	-	0	-
Peripheral ulcerative keratitis	2 (0.2)	7.9 (1.1-14.7)	0	-	0	-
Retinal exudates or hemorrhage	0	-	0	-	0	-
Retinal vasculitis	0	-	0	-	1 (0.3)	7.8*

IQR: inter-quartile range; *denotes a single patient

manifestations was similar when stratified by c-ANCA/PR3 positivity, except for conjunctivitis/episcleritis ($p< 0.01$). Inflammatory ocular manifestations presented earlier in the disease course (Table 2). During follow up, 6.6% patients with GPA had incident ocular manifestations, while such events were rare in MPA (0.6%) and EGPA (0.5%). There were no significant correlations seen between ophthalmic, otolaryngologic, and neurologic manifestations of disease. The most common complication seen across all 3 diseases was cataracts, seen in 9.1-15.3% of patients. Non-cataract complications followed a similar pattern to other manifestations: 67 (7.9%) patients with GPA experienced such complications followed by 10 (2.7%) of those with EGPA, and 7 (4.2%) of those with MPA (Table 3).

Conclusion: Among patients with AAV, ophthalmic manifestations and complications are common in GPA, but rare in MPA and EGPA. Inflammatory eye conditions are the most common ophthalmic manifestation seen, and cataracts

Table 3. Ophthalmic complications of disease in patients with ANCA-associated vasculitis

Complication: n (%)	GPA n=852	MPA n=165	EGPA n=372
Any ocular complication	154 (18.1)	19 (11.5)	65 (17.5)
Any non-cataract complication	67 (7.9)	7 (4.2)	10 (2.7)
>1 ocular complication	32 (3.8)	3 (1.8)	2 (0.5)
Visual impairment or diplopia	23 (2.7)	2 (1.2)	1 (0.3)
Blindness in one eye	8 (0.9)	1 (0.6)	0
Cataracts	112 (13.1)	15 (9.1)	57 (15.3)
Optic atrophy	6 (0.7)	0	0
Optic neuritis	8 (0.9)	0	0
Retinal changes	4 (0.5)	1 (0.6)	2 (0.5)
Peripheral vascular retinal changes	27 (3.2)	3 (1.8)	7 (1.9)
Orbital wall destruction	12 (1.4)	0	0

are the most common complication. New ophthalmic manifestations after disease onset are rare. These data are informative for clinicians caring for patients with AAV and investigators studying this spectrum of vasculitis.

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Abstract Number: 0427

Increased Risk of Severe Infections and Mortality in Patients with Newly Diagnosed Anti-neutrophil Cytoplasmic Antibody–associated Vasculitis: A Population-based Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antineutrophil cytoplasm antibody (ANCA)-associated vasculitides (AAV) are a group of multisystem inflammatory diseases of the small blood vessels. Infections are serious complications in AAV and often associated with premature mortality. Existing studies on the risk of infection in AAV patients and relative risk when compared to the general population suffer from small sample sizes, selected hospitalized samples and lack of control of potential confounders. To evaluate the independent effect of AAV on the risk of severe infection and infection-related mortality.

Methods: Using administrative data from British Columbia, Canada and a previously validated AAV case definition, we conducted an age- and gender- matched cohort study of all patients with incident AAV between January 1, 1997 and March 31, 2015. The non-AAV individuals were randomly selected from the general population and 10:1 matched to the AAV patients on age, sex and AAV index year. Primary outcome was the first severe infection after AAV onset necessitating hospitalization or occurring during hospitalization. Secondary outcomes were infection-related mortality and total number of severe infections. To evaluate the relative risk of severe infection outcomes for AAV patients relative to general controls, we used: 1) Cox proportional hazard models to compute hazard ratios for the first severe infection as well as for the infection-related mortality; 2) Poisson regression to compute the rate ratios for total counts of infections. These analyses were controlled for the baseline variables listed in Table 1 to assess independent effects of AAV on infection outcomes.

Results: We identified 559 AAV patients and matched them with 5,590 non-AAV individuals from the general population (57% females, mean age 54), yielding 187 and 510 first severe infections (Table 2) during 2,603 and 36,111 person-years follow-up, respectively. The crude incidence rate ratios were 4.85, 3.72 and 5.08 for first severe infec-

Variable *	AAV cohort N=559	Non-AAV cohort N=5,590
Demographics		
Age, mean (median)	53.6 (55)	53.9 (55)
Female, n (%)	320 (57.3%)	3,200 (57.3%)
Rural, n (%)	72 (12.9%)	765 (13.7%)
Neighborhood income quintile,		
1 (Lowest)	103 (18.4%)	1,092 (19.5%)
2	120 (21.5%)	1,106 (19.8%)
3	112 (20.0%)	1,135 (20.3%)
4	105 (18.8%)	1,132 (20.3%)
5 (Highest)	119 (21.3%)	1,125 (20.1%)
Health Resource Utilization *, mean (median)		
Number of outpatient visits	23.6 (20.0)	8.3 (5.0)
Number of hospitalizations	0.9 (0.0)	0.2 (0.0)
Comorbidities *, n (%)		
Alcoholism	1 (0.2%)	35 (0.6%)
Hypertension	131 (23.4%)	1,134(20.3%)
Cerebrovascular accidents	23 (4.1%)	73 (1.3%)
Ischemic heart disease	51 (9.1%)	282 (5.0%)
Myocardial infarction	5 (0.9%)	19 (0.3%)
Congestive heart failure	30 (5.4%)	76 (1.4%)
COPD-related diseases	126 (22.5%)	376 (6.7%)
Depression	40 (7.2%)	449 (8.0%)
Malignancy (Cancer)	120 (21.5%)	550 (9.8%)
Charlson comorbidity index, mean (median)	1.0 (0.0)	0.3 (0.0)
Medications *, n (%)		
NSAIDs	145 (25.9%)	722 (12.9%)
HRT	25 (4.5%)	209 (3.7%)
Glucocorticoids	283 (50.6%)	213 (3.8%)
CVD drugs	156 (27.9%)	1220 (21.8%)
Fibrates/statins	1 (0.2%)	36 (0.6%)
Anti-diabetic medications	41 (7.3%)	357 (6.4%)
Rituximab	3 (0.5%)	1 (0.0%)
History of Infection *		
Prior hospitalized infection	61 (10.9%)	65 (1.2%)

tion, infection-related mortality and total counts of infections, respectively. After adjusting for all confounders, the independent effect of AAV on the risk of for first severe infection, infection-related mortality and total number of severe infections was 3.77, 3.84 and 3.29, respectively.

Conclusion: In this population-based study, we found AAV was associated with increased risks of first severe infection (3.8-fold), infection-related mortality (3.8-fold) and a greater total number of severe infections (3.3-fold). This highlights the higher risks of infection in AAV patients.

Baseline characteristics of individuals with AAV and without AAV. Abbreviations: AAV, Antineutrophil cytoplasm antibody-associated vasculitides; SD, standard deviation; COPD, chronic obstructive pulmonary disease; NSAIDs, non-steroidal anti-inflammatory drugs including cyclooxygenase-2 inhibitors; HRT, hormone replacement therapy; CVD, cardiovascular diseases. *All baseline characteristics were measured over one year prior to the start of follow-up except that age was measured at the start date of the follow-up.

Risk of severe infection in AAV relative to non-AAV during follow-up. Abbreviations: AAV, Antineutrophil cytoplasm antibody-associated vasculitides; IR, incidence rate; IRR, incidence rate ratio; HR, hazard ratio; CI, confidence interval. *Adjusted for covariates listed in Table 1.

Post-AAV diagnosis first severe infection		
	AAV cohort N=559	Non-AAV cohort N=5,590
No. of events	187	510
IR per 1,000 person-years	71.84	14.12
IRR (95% CI)	4.85 (4.10-5.74)	1
Age and gender adjusted HR (95% CI)	5.35 (4.49-6.38)	1
All but GC adjusted HR (95% CI)	3.33 (2.67-4.14)	1
Fully adjusted HR* (95% CI)	3.77 (2.94-4.85)	1
Post-AAV total number of severe infections		
Infection episodes	403	864
IR per 1,000 person-years	115.71	22.77
IRR (95% CI)	5.08 (4.52-5.72)	1
Age and gender adjusted rate ratio (95% CI)	5.37 (4.77-6.05)	1
All but GC adjusted rate ratio (95% CI)	3.18 (2.77-3.66)	1
Fully adjusted rate ratio* (95% CI)	3.29 (2.82-3.85)	1
Infection-related mortality		
No. of infection-related death events	29	85
IR per 1,000 person-years	8.33	2.24
IRR (95% CI)	3.72 (2.44-5.67)	1
Age and gender adjusted HR (95% CI)	4.43 (2.89-6.79)	1
All but GC adjusted HR (95% CI)	3.67 (2.14-6.31)	1
Fully adjusted HR* (95% CI)	3.84 (2.13-6.91)	1

Disclosure: K. Zhao, None; **H. Xie**, None; **J. Esdaile**, None; **J. Avina-Zubieta**, None.

Abstract Number: 0428

ANCA Positivity and ANCA Associated Vasculitis in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-neutrophil cytoplasmic antibody (ANCA) associated vasculitis (AAV) with rheumatoid arthritis (RA) has been reported rarely, and, studies have found ANCA positivity in RA. The objective of the study was to describe a cohort of patients with RA and AAV and to compare patients with RA+AAV to those with RA+ANCA positivity without AAV.

Methods: In this retrospective study, a cohort of patients with RA+ANCA positivity evaluated at an academic center were included. Data abstracted included demographics, seropositivity, ANCA specificity, clinical characteristics of RA, diagnosis of AAV and clinical features of AAV.

Results: The study included 77 patients, mean (±SD) age 60.2 (17.2) years, 78% female. ANCA serologies included perinuclear (p)-ANCA in 58%, cytoplasmic (c)-ANCA in 26%, myeloperoxidase (MPO) in 43% and proteinase 3 (PR3) in 26%. Twenty patients (26%) were p-ANCA/MPO positive, 3 patients (4%) c-ANCA/PR3 positive, 7 patients (9%) were p-ANCA/PR3 positive and 1 patient (1%) was c-ANCA/MPO positive.

Twenty-five patients (32%) had a diagnosis of AAV; 9 (36%) microscopic polyangiitis (MPA), 8 (32%) granulomatosis with polyangiitis (GPA), 1 (4%) eosinophilic granulomatosis with polangiitis (EGPA), 1 (4%) GPA versus rheumatoid vasculitis (peripheral ulcerative keratitis, scleritis, sudden hearing loss, MPO positive). In 6 patients (24%) diagnosis was unclassifiable (1 interstitial lung disease attributed to vasculitis, 3 cutaneous vasculitis with ulcerations, 1 case of multiple digital infarctions from vasculitis, 1 leukocytoclastic vasculitis). Diagnosis of RA preceded vasculitis in 92% cases, was concurrent in 4% and followed vasculitis in 4%. Clinical manifestations of AAV are in Table 1. Among patients with RA+ANCA positivity but no diagnosis of AAV, 1 patient had nasal septal perforation with polyposis, 1 patient had vasculitic rashes and neuropathy attributed to vasculitis from RA, 2 patients had retinal vasculitis.

A comparison of patients with RA+AAV, and, patients with RA+ANCA without AAV is in Table 2. A higher proportion of patients with ANCA positivity via indirect immunofluorescence (IIF) along with antibody specificity to MPO or PR3 had a clinical diagnosis of AAV. These findings remained significant even if the 6 patients with unclassifiable disease were excluded (data not shown).

Table 1: Clinical manifestations of ANCA-associated vasculitis in patients with concurrent diagnosis of Rheumatoid Arthritis.

Clinical Manifestation	N (%)
Cutaneous	7 (28)
Isolated cutaneous	6 (24)
Paucimmune glomerulonephritis	10 (40)
Mononeuritis multiplex	3 (12)
Pulmonary	
Interstitial lung disease	4 (16)
Pulmonary nodules	4 (16)
Diffuse alveolar hemorrhage	1 (4)
Ear, nose, throat	
Sinusitis, nasal septal perforation, hearing loss or polychondritis	6 (24)
Tracheal stenosis	2 (8)
Ocular (scleritis, peripheral ulcerative keratitis)	3 (12)
Pachymeningitis with optic nerve involvement	1 (4)

N = number

Table 2: Comparison of patients with rheumatoid arthritis (RA) and diagnosis of anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) to patients with RA with positive ANCA but no evidence of AAV

Variable	RA+AAV N=25	RA+ANCA without AAV N=52	p-value
Mean (±SD) age, years	59.3 (17.3)	60.6 (17.3)	0.69
Female sex, N (%)	20 (80)	40 (77)	1
Race, N (%)			0.17
Caucasian	15 (60)	17 (33)	
Black	2 (8)	2 (4)	
Asian	2 (8)	8 (15)	
Other	4 (16)	17 (31)	
Unknown or Declined	2 (8)	8 (15)	
Ethnicity, N (%)			
Hispanic/Latino	12 (48)	10 (19)	0.01
Seropositivity, N (%)	16 (64)	28 (54)	0.45
RhF positive	13 (56)	21 (41)	0.31
CCP positive	7 (32)	20 (43)	0.44
RhF and CCP positive, N (%)	4 (18)	13 (27)	0.56
p-ANCA	18 (72)	27 (52)	0.14
c-ANCA	8 (32)	12 (23)	0.42
MPO	15 (60)	18 (35)	0.05
PR3	8 (32)	12 (23)	0.42
p-ANCA/MPO or c-ANCA/PR3	16 (64)	7 (14)	<0.001
Any positive ANCA on IIF and positive ELISA	20 (80)	11 (21)	<0.001
Joint erosions on x-ray	7/19 (37)	11/42 (26)	0.55

SD = standard deviation, N= number, RhF = rheumatoid factor, CCP = cyclic citrullinated peptide, p-ANCA = perinuclear ANCA, c-ANCA = cytoplasmic ANCA, MPO = myeloperoxidase, PR3 = proteinase 3, IIF = indirect immunofluorescence, ELISA = enzyme linked immunosorbent assay

Conclusion: AAV in RA included an even number of cases of GPA and MPA. The diagnosis of RA almost always preceded the diagnosis of AAV and renal involvement was the most commonly present manifestation of AAV. There was uncertainty regarding attribution of isolated cutaneous vasculitis to RA or AAV and 24% of this cohort diagnosed as AAV had isolated skin disease. Many patients without vasculitis had positive MPO or PR3 antibodies. The presence of ANCA via IIF with MPO or PR3, even if discordant, separated patients with RA+AAV from those without vasculitis highlighting the need for clinical vigilance in this subset of patients with RA. The immune mechanisms underlying this rare overlap need to be elucidated.

Disclosure: C. O'Brien, None; **V. Ranganath**, None; **T. Kermani**, None.

Abstract Number: 0429

Causes and Characteristics of Death in ANCA-Associated Vasculitis - A Large, Real-Life, Contemporary Cohort Analysis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Demographics. Reported as n (%) unless otherwise specified. SD: standard deviation; IQR: interquartile range; PR3: proteinase-3; MPO: myeloperoxidase; BVAS/WG: Birmingham Vasculitis Activity Score for Wegener's Granulomatosis; ESRD: end-stage renal disease; RTX: rituximab; CYC: cyclophosphamide. *Death certificates were not available for 14 patients

	Entire Cohort (n=484)	All Deceased (n=130)	Deceased with Death Information (n=72)
Mean age at diagnosis, years (SD)	58.2 (17.3)	71.4 (10.6)	71.4 (10.7)
Mean age at death, years (SD)	N/A	77.2 (10.2)	76.9 (10.1)
Year of diagnosis			
2002-2005	102 (21)	42 (32)	23 (32)
2006-2009	130 (27)	41 (32)	20 (28)
2010-2013	177 (37)	33 (25)	20 (28)
2014-2017	75 (15)	14 (11)	9 (13)
Years from diagnosis to death, median (IQR)	N/A	4.4 (1.6, 7.5)	3.2 (0.6, 6.6)
Sex			
Male	196 (40)	67 (52)	43 (60)
Race			
White	395 (82)	104 (80)	57 (79)
Asian	10 (2)	2 (2)	2 (3)
Black	12 (2)	4 (3)	2 (3)
Other	25 (5)	5 (4)	2 (3)
Unknown	42 (9)	15 (12)	9 (13)
ANCA			
PR3-ANCA+	171 (35)	29 (22)	17 (24)
MPO-ANCA+	313 (65)	101 (78)	55 (76)
Baseline BVAS/WG, mean (SD)	4.7 (2.1)	4.5 (1.8)	4.9 (1.9)
Any Renal Involvement at baseline	315 (65)	98 (75)	56 (78)
ESRD at any time	76 (16)	42 (32)	30 (42)
Initial Treatment Strategy			
RTX-Based	189 (39)	38 (29)	25 (35)
CYC-Based	223 (46)	78 (60)	38 (53)
Other	72 (15)	14 (11)	9 (13)
AAV ICD-10 code included in death certificate	N/A	24/116* (21)	15/63* (24)

Background/Purpose: Despite improvements, patients with ANCA-associated vasculitis (AAV) have a higher risk of death than the general population. Contemporary treatment is associated with high remission rates, but infection, end-stage renal disease (ESRD), and other complications remain common. To identify research priorities, guide study

Table 2. Conditions of Death. Total N=72 AAV patients for whom death information was available in chart review. ICD: International Classification of Diseases. *Treatment with rituximab within the last 6 months or documented B cell depletion at the time of death was considered immunosuppression; other treatments included glucocorticoids and other disease-modifying anti-rheumatic drugs (DMARDs). **Death certificates were available for 116 patients of total 130 AAV deaths

	N (%)
Location of death	
Acute care hospital	47 (65)
Rehabilitation/Nursing facility	6 (8.3)
Hospice	13 (18)
Home	5 (7)
Unknown	1 (1)
On immunosuppression*	53 (73.6)
Disease Activity	
Induction	21 (29)
Flare	5 (7)
Remission	42 (64)
AAV ICD-10 code included in death certificate	24/116** (21)

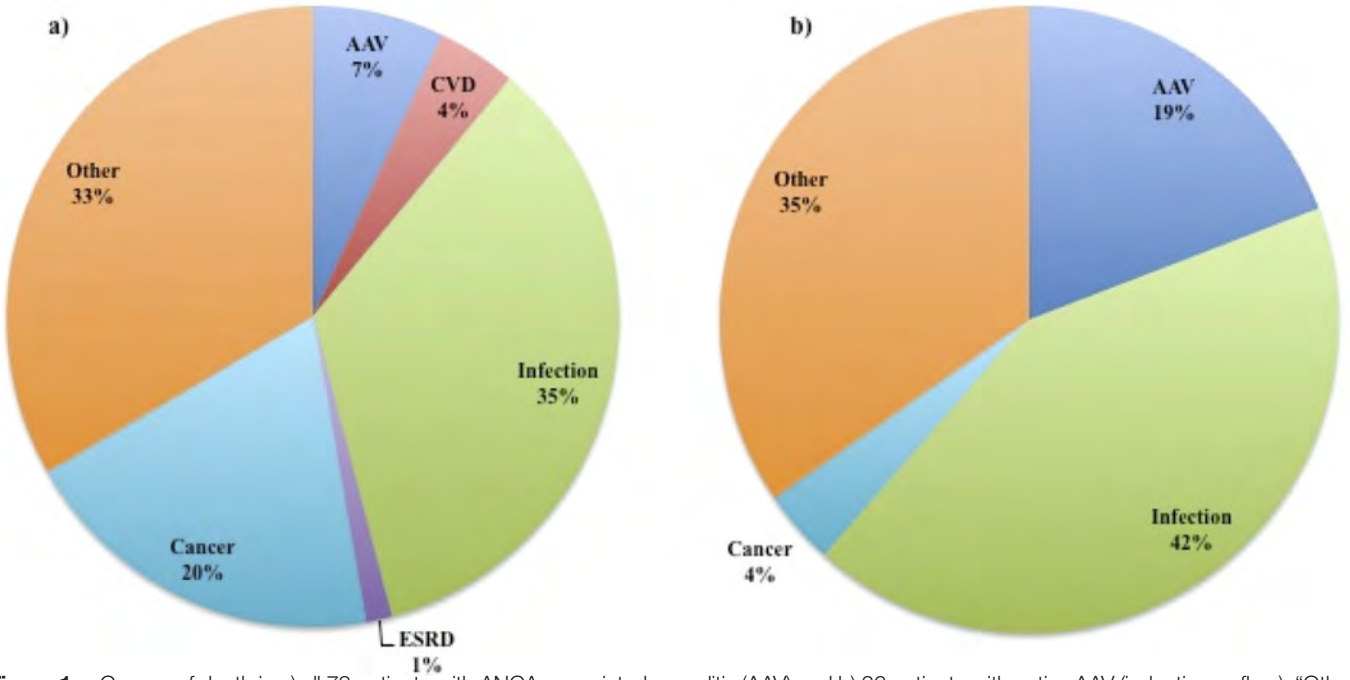

Figure 1. Causes of death in a) all 72 patients with ANCA-associated vasculitis (AAV) and b) 26 patients with active AAV (induction or flare). "Other" deaths included conditions unrelated to AAV such as surgical complications, valvular heart disease, dementia, and cardiac arrest of unknown etiology. CVD: cardiovascular disease (defined as acute ischemic CV event); ESRD: end-stage renal disease.

design, and develop interventions to improve survival, comprehensive data on causes and characteristics of death in a real-world, contemporary AAV cohort are needed.

Methods: We identified patients from a multi-center consecutive inception AAV cohort who were diagnosed and died between 2002-2017. Death was ascertained by linkage to the electronic health record and the National Death Index; death certificates were obtained. Two rheumatologists independently reviewed each chart to extract death details; differences were resolved by consensus. Each death was categorized as resulting from active vasculitis, acute ischemic cardiovascular (CV) event, infection, ESRD, cancer, or other. AAV disease status at the time of death was categorized as "induction" (≤ 6 months since treatment initiation), "flare" (increased disease activity within 6 months), or "remission." We extracted details regarding treatment and place of death. We also determined the sensitivity of a diagnosis of AAV on a death certificate by tabulating the presence of AAV ICD-10 codes (M31.3, M31.7) on any line.

Results: Of 484 patients in the AAV cohort, 130 (27%) died and 72 had records from the time of death available for review. Characteristics of the cohort are included in Table 1. The mean age at death was 71 years, and the median time from diagnosis to death was 4.4 years. 67 out of 130 (52%) were male. Of deaths with EHR data available at the time of death (n=72), 42 (64%) occurred during periods of remission, 21 (29%) during induction, and 5 (7%) during flare. The majority occurred while on immunosuppression (53, 74%), and 47 (65%) occurred in acute care hospitals (Table 2). The most common cause of death was infection (25, 35%), followed by cancer (14, 20%), AAV (5, 7%), acute ischemic CV events (3, 4%), ESRD (1, 1%), and other (24, 33%), which included cardiac arrest of uncertain cause (Figure 1). Deaths from active AAV were rare (5, 7%): cerebral vasculitis (n=1), pulmonary disease (n=3), and multi-organ failure (n=1). Among those with active AAV (induction or flare), infection remained the most common cause (11, 42%). The sensitivity of death certificates for identifying patients with AAV was 21% (24 of 116 certificates); in 3 cases, AAV was misclassified as other vasculitis.

Conclusion: In a contemporary AAV cohort, most deaths were infectious and occurred in remission on maintenance immunosuppression; deaths from active AAV were rare, and some of cardiac etiology were difficult to classify. These results highlight the need for personalized strategies that reduce infection risk during remission maintenance without

sacrificing disease control. Additional studies are needed to understand the burden of CV disease in AAV. The use of national death certificate data to estimate the burden of death due to AAV will underestimate the impact of AAV on death.

Disclosure: G. Katz, None; **C. Cook**, None; **X. Fu**, None; **H. Choi**, None; **Z. Wallace**, BMS, 5, Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 0430

Interstitial Lung Disease in ANCA-Associated Vasculitis: Associated Factors and Outcomes

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)

Session Type: Poster Session A

Session Time: 8:30AM–10:30AM

Table 1. Characteristics of Patients with AAV-ILD and AAV Comparators

Characteristic*	AAV (n=587)	AAV-ILD (n=97)	p-value
Demographics			
Age, mean (SD)^	58 (18)	67 (12)	< 0.001
Age at ILD, mean (SD)	N/A	66 (12)	
ILD at or prior to AAV diagnosis	N/A	85 (88)	
Male	236 (40)	44 (45)	0.3
Race			0.4
White	508 (87)	83 (86)	
Black	11 (2)	3 (3)	
Asian	11 (2)	0 (0)	
Other	15 (3)	2 (2)	
Ever Smoker	292 (50)	58 (60)	0.069
ANCA status			< 0.001
MPO-ANCA +	376 (64)	94 (97)	
PR3-ANCA +	211 (36)	3 (3)	
Organ involvement			
Head and neck	264 (45)	30 (31)	0.01
Pulmonary	261 (44)	68 (70)	< 0.001
Renal	388 (66)	54 (56)	0.047
Neurologic	56 (10)	7 (7)	0.5
AAV disease activity score			
BVAS/WG, mean (SD)	5 (2)	5 (2)	0.009
Comorbidities			
COPD	N/A	25 (26)	
GERD	N/A	21 (22)	
RA/CTD Serologies	N/A	23 (24)	
PH	N/A	64 (66)	
Charlson Comorbidity Index, mean (SD)	2 (2)	2 (3)	0.3
PFTs			
FVC, mean (SD)	N/A	3 (2)	
FVC % predicted, mean (SD)	N/A	79 (20)	
DLCO corrected Hb, mean (SD)	N/A	13 (5)	
DLCO % predicted, mean (SD)	N/A	53 (22)	
ILD Pattern			
UIP	N/A	29 (30)	
Non-UIP	N/A	68 (70)	
Mortality	148 (25)	39 (40)	0.002
*N(%) unless otherwise noted; ^Age at AAV Diagnosis			

Table 2. The Association of ILD with All-Cause Mortality in ANCA-Associated Vasculitis

Model*	AAV-ILD (HR, 95% CI)	No ILD
Unadjusted	1.54 (1.07, 2.21)	1.0 (Ref)
Sex-adjusted	1.54 (1.07, 2.21)	1.0 (Ref)
Sex and ANCA-type adjusted	1.52 (1.05, 2.20)	1.0 (Ref)
Sex, ANCA-type, and BVAS-adjusted	1.53 (1.05, 2.21)	1.0 (Ref)
*Age as time scale		

Background/Purpose: Despite treatment advances, ANCA-associated vasculitis (AAV) remains associated with excess morbidity and mortality. Interstitial lung disease (ILD) is an increasingly recognized manifestation of AAV but its prevalence, characteristics, and outcomes remain poorly defined. Additionally, most studies of AAV-ILD have been performed in AAV cohorts assembled in Asia where MPO-ANCA+ disease is highly prevalent. We sought to characterize factors associated with AAV-ILD and mortality in AAV-ILD in a large North-American-based AAV cohort.

Methods: AAV-ILD cases were identified by screening a consecutive inception PR3- or MPO-ANCA+ AAV multicenter cohort assembled between 2002 and 2019 for ICD-9/10 codes relevant to the diagnosis of ILD. Each case identified by this screen then underwent a manual review of the electronic health record (EHR) and available chest imaging. Two board-certified radiologists reviewed all available computer tomography (CT) scans of the chest for each patient to assess for interstitial lung disease and classify the type of ILD (UIP vs non-UIP). Patients with uncertain radiographic features were considered to not have ILD. Demographics, AAV disease features, results of pulmonary function tests, and comorbidities were extracted from the EHR. The baseline Birmingham Vasculitis Activity Score/Wegener's Granulomatosis (BVAS/WG) was determined for each patient. All-cause mortality was assessed by linkage to the National Death Index. Univariate analyses were used to assess the association of demographic- and disease-specific factors with AAV-ILD. Unadjusted and adjusted Cox proportional hazard models with age as the time scale were used to assess the association of AAV-ILD with death among patients with AAV.

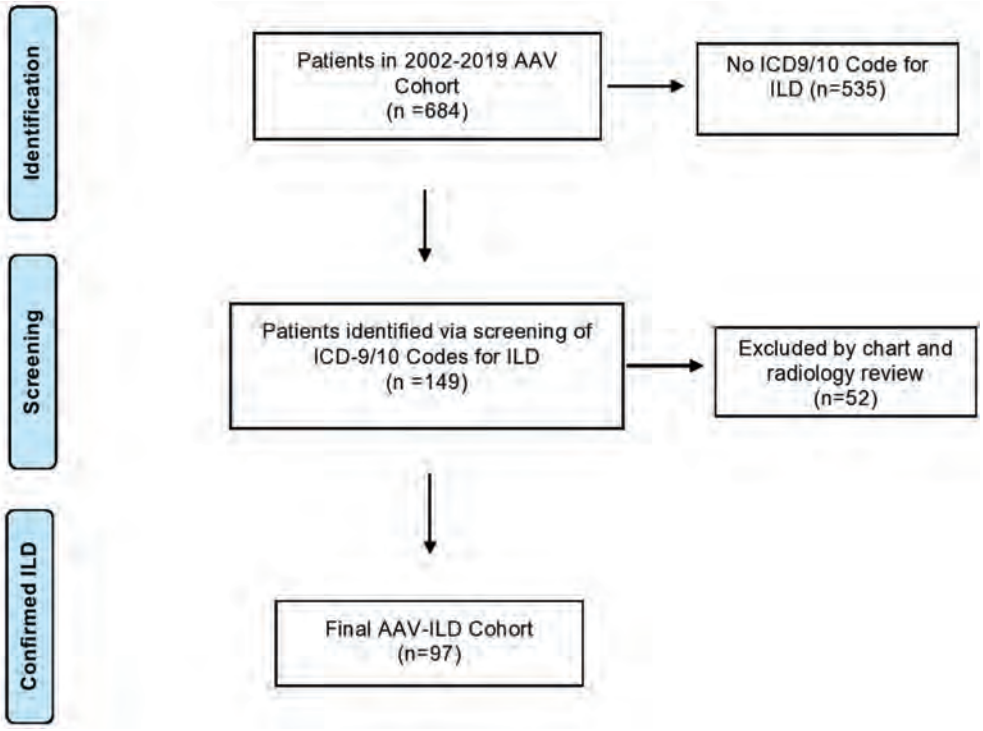

Figure 1. Patient Identification and Screening for ILD Inclusion.

Results: Of 698 patients from the cohort, 14 were excluded because of insufficient records and 684 were screened (Figure 1). Of those screened, 97 (14.2%) had AAV-ILD. Patients with AAV-ILD were older (67±12yrs vs 58±18yrs, p< 0.001) than those with AAV-non-ILD; sex distribution was similar (55% vs 60% female, p=0.7) (Table 1). Compared to AAV-non-ILD, AAV-ILD patients were more often MPO-ANCA+ (97% vs. 64%, p< 0.001) and less often had head and neck involvement (31% vs 45%, p=0.01). The diagnosis of ILD preceded or occurred concurrently with the diagnosis of AAV in 85 (88%) patients. The ILD pattern was classified as UIP in 29 (30%) patients with AAV-ILD. The mean (SD) FVC % predicted among AAV-ILD patients was 79±20% and adjusted DLCO % predicted was 53±22% (Table 1). AAV-ILD was associated with a 53% higher risk of death than AAV-non-ILD in analyses adjusted for age, sex, baseline BVAS/WG, and ANCA type (HR=1.53, 95% CI 1.05, 2.21) (Table 2).

Conclusion: In a large North American cohort of AAV patients, we estimated the prevalence of AAV-ILD as 14% and observed strong associations with MPO-ANCA positive disease. In the vast majority of cases, AAV-ILD was present prior to or at the time of AAV diagnosis, highlighting that it is a feature that may precede other manifestations of AAV. Compared with AAV patients without ILD, those with ILD have a higher risk of all-cause mortality. Additional studies are needed to understand the response of ILD in AAV to conventional AAV treatment regimens.

Disclosure: B. Doliner, None; **K. Rodriguez**, None; **S. Montesi**, None; **X. Fu**, None; **A. Sharma**, Hummingbird Diagnostics Inc., 5, Parexel, 12, trial reader for hospital contracted clinical research trial programs, Bioclinica, 12, trial reader for hospital contracted clinical research trial programs, ImagingEndpoints, 12, trial reader for hospital contracted clinical research trial programs, ERT, 12, trial reader for hospital contracted clinical research trial programs, Elsevier, 9; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 0431

Clinical Characteristics and Outcomes of ANCA-Associated and Non Immune-Mediated Hypertrophic Pachymeningitis: A Comparative Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Hypertrophic pachymeningitis (HP) is an infrequent manifestation in autoimmune and non-autoimmune conditions. The differences in clinical characteristics and outcomes of ANCA-associated and non-immune-mediated HP have not been thoroughly explored.

We aimed to explore the clinical characteristics and outcomes of patients with ANCA-associated HP (ANCA-HP) in comparison to non-immuno-mediated HP (NIM-HP) from a single center.

Methods: We performed a retrospective single center study. We included patients with a diagnosis of HP that were followed from 2003 to 2020 in a referral center. HP was defined as focal or diffuse thickening with or without enhancement visualized on magnetic resonance imaging of the brain or spine. ANCA-associated-vasculitis were diagnosed according with the 1990 American College of Rheumatology Classification Criteria, 2012 Chapel Hill Consensus nomenclature and/

Table 1. Etiologies of non-immune-mediated hypertrophic pachymeningitis

Etiology	N = 33 n (%)
Infectious HP	10 (30.3)
Tuberculosis	6 (18.2)
Micobacterium bovis	1 (3%)
Mucormicosis	1 (3%)
Bacterial abscess	1 (3%)
Syphilis/HSV-1	1 (3%)
Neoplastic HP	23 (69.7)
Non Hodgkin lymphoma	6 (18.2)
Meningioma	4 (12.1)
Meningeal carcinomatosis	3 (9.1)
Multiple myeloma/Plasmocytoma	3 (9.1)
Erdheim-Chester disease	2 (6)
Acute lymphocytic leukemia	2 (6)
Chronic myeloid leukemia	1 (3)
Rosai-Dorfman disease	1 (3)
Hodgkin lymphoma	1 (3)
HP: hypertrophic pachymeningitis; HSV-1: herpes simplex virus-1	

or the European Medicines Agency Consensus algorithm for the classification of vasculitis. The underlying disease in NIM-HP patients was diagnosed by using international accepted criteria as appropriate. NIM-HP were further subclassified in infectious HP and neoplastic HP. We performed a comparison between the ANCA-HP and the NIM-HP group using Student t-test or Mann-Whitney U test for continuous variables, and Chi-square or Fisher's exact test for categorical variables.

Results: We included 52 patients with HP. Nineteen (36.5%) were ANCA-HP and 33 (63.5%) NIM-HP. All ANCA-HP patients had diagnosis of granulomatosis with polyangiitis; 11 (57.9%) were PR3-ANCA positive, 3 (15.8%) MPO-ANCA positive, 2 (10.5%) double positive, 2 (10.5%) C-ANCA positive, and 1 (5.2%) P-ANCA positive. Thirty-three were NIM-HP (63.5%); of them, 10 (19.2%) were infectious HP and 23 (44.2%) neoplastic HP (Table 1). Forty-nine (94.2%) patients had cranial, 2 (3.8) spinal, and 1 (1.9%) cranial/spinal HP. In 24 (46.2%) patients HP presented after, in 10 (19.2%) before, and in 18 (34.6%) concomitant to the underlying disease diagnosis. Forty (76.9%) patients had associated comorbidities.

The clinical presentation, laboratory findings and outcomes of our cohort are shown in Table 2. Patients with ANCA-HP presented more frequently with headache, papilledema, ataxia, and cranial neuropathy (especially VII, VIII, IX, X and XII nerves), extra-neurological involvement, leukocytosis, and less frequently with altered mental status and hypoglycorrhachia. Furthermore, ANCA-HP presented more commonly remission ever, however, relapses were more frequent. In both groups, at a median follow-up time of 40 (IQR 17.5-72) months, 6 (11.5%) patients with neoplastic HP died.

Conclusion: ANCA-HP and NIM-HP had specific differences in clinical presentation and laboratory findings that may allow clinicians to suspect one cause over the other in clinical practice. The disparities in outcomes reflect the relapsing-remitting nature of ANCA-associated vasculitis.

Table 2. Characteristics of patients with hypertrophic pachymeningitis

	Total	ANCA-HP (n=19)	NIM-HP (n=33)	p
Female, n (%)	26 (56)	8 (42.1)	18 (54.5)	0.56
Age, mean ± SD, years	43.7 ± 14.1	42.3 ± 13.9	44.4 ± 14.4	0.61
Craneal, n (%)	49 (96.1)	17 (94.4)	32 (97)	1.0
Time to diagnosis, median (IQR), days	30 (10-120)	26.5 (3-120)	37 (10-210)	0.40
Comorbidities, n (%)	40 (76.9)	14 (73.7)	26 (78.8)	0.67
Acute, n (%)	20 (38.5)	9 (47.4)	11 (33.3)	0.31
Subacute, n (%)	13 (25)	2 (10.5)	11 (33.3)	0.06
Chronic, n (%)	16 (30.8)	8 (42.1)	8 (24.2)	0.17
Asymptomatic, n (%)	3 (5.8)	0	3 (9.1)	0.17
Headache, n (%)	28 (53.8)	14 (73.7)	14 (42.4)	0.02
Visual loss, n (%)	7 (13.5)	4 (21.1)	3 (9.1)	0.40
Diplopia, n (%)	7 (13.5)	4 (21.2)	3 (9.1)	0.40
Papilledema, n (%)	5 (9.6)	4 (21.1)	1 (3)	0.05
Altered mental status, n (%)	6 (11.6)	0	6 (18.2)	0.07
Seizures, n (%)	11 (21.2)	5 (26.3)	6 (18.2)	0.48
Fever, n (%)	11 (21.2)	4 (21.1)	7 (21.2)	1.01
Ataxia, n (%)	3 (5.8)	3 (5.8)	0	0.04
Craneal neuropathy, n (%)	19(36.5)	10 (52.6)	9 (27.3)	0.08
VII nerve, n (%)	7 (13.5)	6 (31.6)	1 (3)	0.007
VIII nerve, n (%)	7 (13.5)	7 (36.8)	0	<0.001
IX nerve, n (%)	6 (11.5)	5 (26.3)	1 (3)	0.02
X nerve, n (%)	5 (9.6)	4 (21.2)	1 (3)	0.05
XII, nerve, n (%)	3 (5.8)	3 (15.8)	0	0.04
Extraneurological involvement, n (%)	36 (69.2)	19 (100)	17 (51.5)	<0.001
Leucocytosis, n (%)	15 (28.8)	9 (47.4)	6 (18.2)	0.02
High CRP, n (%)	17 (65.4)	11 (64.7)	6 (66.7)	1.0
High ESD, n (%)	20 (71.4)	12 (63.2)	8 (88.9)	0.21
High CSF protein, n (%)	16 (64)	6 (46.2)	10 (83.3)	0.09
Low CSF glucose, n (%)	7 (28)	0	7 (58.3)	0.002
Remission (ever), n (%)	32 (72.7)	15 (93.8)	17 (60.7)	0.02
Complete, n (%)	23 (59)	9 (60)	14 (58.3)	1.0
Partial, n (%)	9 (23.1)	6 (40)	3 (12.5)	0.04
Relapses, n (%)	7 (17.5)	7 (43.8)	0	0.001
Death, n (%)	6 (13.6)	0	6 (28)	0.07

ANCA-HP: ANCA-associated hypertrophic pachymeningitis; CRP: C-reactive protein; CSF: cerebrospinal fluid; ESD: erythrocyte sedimentation rate; NIM-HP: non-immuno-mediated hypertrophic pachymeningitis

Disclosure: E. Martin-Nares, None; **L. Cano Cruz**, None; **A. Hinojosa-Azaola**, None.

Abstract Number: 0432

Anti-IL5 Therapy in Eosinophilic Granulomatosis with Polyangiitis (EGPA): A Longitudinal Follow-up Study ≥ 24months

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: In the randomized, placebo-controlled MIRRA trial for relapsing and refractory eosinophilic granulomatosis with polyangiitis (EGPA), adjuvant therapy with 300mg anti-IL5 mAB Mepolizumab [MEPO] for 12 months (M), accrued longer times in remission, reduced steroid exposure and reduced relapse rates[2]. The aim of this study is to analyze the outcome of 100mg MEPO monthly s/c for a minimum of 24M in EGPA. Changes to adjuvant immunosuppression and indications for anti-IL5 class switch from MEPO 100mg s/c to Benralizumab (BRZ) or Reslizumab (Res) were assessed.

Methods: In this retrospective descriptive study, 20 EGPA patients received 100mg s/c MEPO every 4 weeks for a minimum of 24M (maximum duration 43M). Anti-IL5 therapy was switched between agents for poor response or intolerance. Time points of assessment included MEPO commencement, 6, 12, 18 and 24 months.

Results: Overall, there was a 50% reduction in steroid usage by 12 months. This continued to fall out to 24M. All 20 EGPA patients receiving anti -IL5 therapy, ranging from 24-43 months remain on therapy. 50% have remained on 100mg s/c MEPO and 50% have switched to an altenative anti-IL5 agent - 9 switched to benralizumab, 1 initially on benralizumab to reslizumab. All remain on anti-IL5 therapy after switch. Three patients had a break of therapy, but all resumed anti-IL5 treatment. 8 have anti-IL5 monotherapy as their maintenace regimen, an additional 6 weaned off conventional immunosuppressants. 6 continued or commenced conventional immunotherapy therapy which is well tolerated. ANCA serology normalized in all four positive patients by 12 months.

Conclusion: The relapsing nature of EGPA places a potential dependency of therapy on steroids, underscoring the importance of pathway specific biologics to minimize exposure, prevent tissue damage and ensure early response to therapy. There was a 50% reduction in steroid dosage in this study by 12 months and steroid requirements continue to decrease to 24 M. Longer-term anti-IL5 therapy is continuing in all 20 patients due to clinical benefits achieved.

Table 1. EGPA patients commenced on Mepolizumab [100mg s/c]

Demographics	All [n=20]	
Gender ratio M/F	7 M: 13 F	
ANCA positive/ negative	3 Anti-MPO, 1Anti-PR3 positive/ 16 ANCA negative	
Median Age of diagnosis of EGPA	50.5 years [IQR 44.75-5] *	
Median age	54 years [IQR 50-61.25] *	
EGPA disease characteristics	N=20 [%]	
Asthma	20[100%]	
Serum eosinophilia or biopsy evidence [N=19]	19 [100%]	
Pulmonary infiltrates, non-fixed	13[65%]	
Neuropathy, mono/poly	5 [25%]	
Sino-nasal abnormality	19[95%]	
Glomerulonephritis	4[20%]	
Cardiomyopathy	6[30%]	
Immunosuppressants	From diagnosis to anti-IL5 commencement	Anti-IL5 start-point
Steroids	20[100 %]	20[100%]
Cyclophosphamide	7 [35 %]	0[0%]
Rituximab	8 [40 %]	2[10%]
Azathioprine	13[40 %]	3[10%]
Mycophenolate mofetil	11[55 %]	3[10%]
Methotrexate	4[20%]	1[5%]
Omalizumab	1[5%]	0[0%]
Campath	1[5%]	0[0%]

Abbreviations: IQR* = interquartile range, M=male, F =female.

Table 2: Anti-IL5 agent over course of treatment and adjuvant conventional immunosuppression

Case	Months	Continue	Agent	MEPO (M)	BEN (M)	Adjuvant therapy
1	43	Switched	BRZ	22	21	MMF started, IVIG [-]
2	43	Restart/Switch	BRZ	12	8	MTX stopped
3	40	Continue	MEPO	40		MMF stopped
4	37	Continue	MEPO	37		
5	37	Continue	MEPO	37		MMF started
6	36	Continue	MEPO	36		MTX started
7	36	Switched	BRZ	31	5	MMF started
8	35	Restart/Switch	BRZ/RES	13	1BRZ/ 15 RES	
9	34	Continue	MEPO	34		AZA continued
10	34	Continue	MEPO	34		
11	34	Switched	BRZ	21	13	MMF stopped
12	33	Continue	MEPO	33		
13	32	Continue	MEPO	32		AZA stopped
14	32	Switched	BRZ	22	10	Rituximab
15	31	Continue	MEPO	31		
16	31	Restart/Switch	BRZ	12	8	
17	26	Continue	MEPO	26		
18	26	Switched	BRZ	12	14	MMF stopped
19	24	Switched	BRZ	21	3	
20	24	Switched	BRZ	12	12	AZA stopped

Response to therapy

Prednisolone dose [N= 20]	**M0**	**M6**	**M12**	**M18**	**M24**
Mean ±SD	18 mg ± 10.31	12.26 mg ±6.8	9.37mg ± 5.3	9.71mg ± 8.1	7.7 mg ±7.08

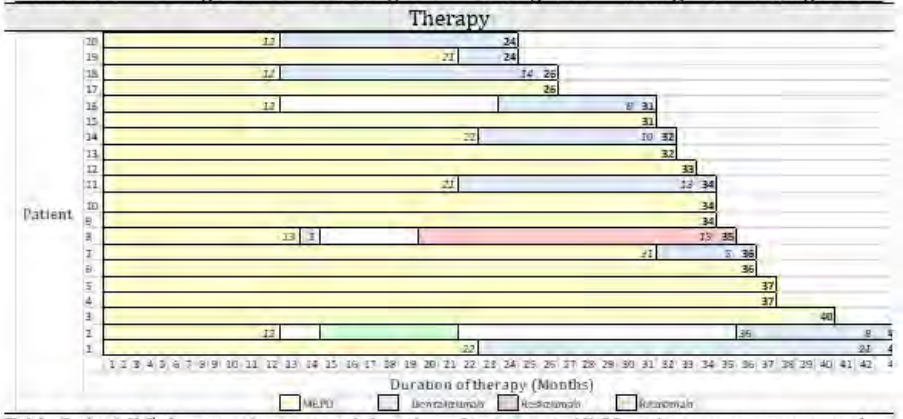

Table 3: Anti-IL5 therapeutic agent and duration of treatment. All 20 patients were commenced on MEPO 100mg s/c. 50% (N=10) remain on MEPO, whilst 10 switched to Benralizumab (BRZ). One subsequently converted to Reslizumab (RES). Three had a break from anti-IL5 therapy but returned to treatment with good response including steroid reduction. one had rituximab between anti-IL5 courses.

Anti-IL5 therapeutic agent, duration of treatment and adjuvant therapy.

Anti-IL5 monotherapy is effective in some cases. Adjuvant immunotherapy is well tolerated and reduced in some cases. This study demonstrates that anti-IL5 therapy serves as a favorable model for steroid minimization in EGPA.

Disclosure: A. Egan, None; **P. Sivasothy**, None; **L. Willcocks**, None; **R. Jones**, GSK, 1; **M. Martinez Del Pero**, None; **D. Jayne**, ChemoCentryx, 2, 5, GSK, 2, 5, Roche/Genentech, 5, Sanofi-Genzyme, 5, AstraZeneca, 2, Boehringer-Ingelheim, 2, Celgene, 2, InflaRx, 2.

Abstract Number: 0433

Use of 2-Mercaptoethane Sodium Sulfonate Prophylaxis in Cyclophosphamide-Treated Patients with ANCA-Associated Vasculitis: Results of an Electronic Survey

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Co-prescribing mesna with CYC for AAV aims to prevent the potential urotoxic effects of CYC. We investigated current clinical practice related to prescribing mesna prophylaxis or not for CYC-treated patients with AAV.

Methods: We searched MEDLINE for publications with the MeSH term "ANCA-associated vasculitis" over a 10-year period. Email addresses of authors were extracted from the online information. These authors were invited by email to participate in an online SurveyMonkey® survey asking about the characteristics of the respondent, their experience with AAV, and their practice in using CYC to treat AAV and in using mesna in CYC-treated patients with AAV and the underlying rationale. We compared 15 response variables to identify factors associated with the use of mesna. Response variables with multiple categories were first analyzed across all categories; if the omnibus test result was significant, additional analyses were used to identify the categories, which were the sources of group separation. Statistical analyses involved Pearson's chi-square test or Fisher's exact test. For multiple-response variables, the Rao-Scott correction was applied.

Results: The 139 participants were from 34 countries and were essentially MDs (98%) who mainly worked in rheumatology (50%), nephrology (25%) or internal medicine/immunology (18%). Mesna was given with CYC systematically, never, or on a case-by-case basis by 68%, 19% and 13% of respondents, respectively. As compared with systematic mesna-prescribers, never/occasional mesna-prescribers reported a longer time since receiving their degree (≥ 15 years: 80% vs 50%, P< 0.001), were more frequently based in England/United States (than in France/Germany/Italy) (78% vs 21%, P< 0.001), had longer involvement in care of patients with AAV (≥15 years: 62% vs 37%, P=0.006), had less practice in using intermittent pulse therapy as the exclusive/predominant CYC administration scheme (62% vs 89%, P< 0.001), and, as a rationale underpinning their mesna practice, had less adherence to local operational procedures (47% vs 73%, P=0.002) or (inter)national management guidelines for AAV (16% vs 49%, P< 0.001).

Conclusion: Practice with regard to prescribing mesna in conjunction with CYC to treat AAV is heterogeneous. Systematic mesna use prevailed over never or occasional use. The decision to prescribe mesna may be based more on circumstantial than structural reasons.

Disclosure: L. Joos, None; **S. Gonzalez Chiappe**, None; **T. Neumann**, None; **A. Mahr**, Celgene, 2, Chugai, 2, 6, Roche, 6, Amgen, 1, 6.

Abstract Number: 0434

Protein Profiling in Pre-dating Samples Separate MPO-ANCA Vasculitis from PR3-ANCA Vasculitis

Mikael Brink[1], Ewa Berglin[1], Aladdin Mohammad[2], Andrey Alexeyenko[3], Kristina Lejon[1] and Solbritt Rantapaa-Dahlqvist[4], [1]Umeå Universitet, Umeå, Sweden, [2]Lund University, Lund, Sweden, [3]Karolinska Institutet, Stockholm, Sweden, [4]Ume University, Umea, Sweden

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is considered a chronic relapsing condition, with unknown etiology. This study was undertaken to gain insight to the molecular processes and potential biomarkers in blood samples collected prior to the onset of symptoms

Methods: The National Patient Register and Cause of Death register were searched for AAV-ICD codes and linked to the registers of five biobanks and eighty-five AAV cases were identified (34 males, 51 females) with samples >1month< 10years from AAV symptom onset. For each case two controls matched for sex, age, and sampling date were included. Samples were analyzed using ELISAs for PR3- or MPO-ANCA specificities. Ninety-two protein markers were analyzed using Olink Inflammation panel, (OLINK, Uppsala, Sweden) with 73 eligible after quality control.

Results: Eight protein markers were significantly altered between pre-AAV and controls, with higher levels of CCL23, CXCL5 ($p< 0.01$-0.05) and lower levels of Flt3L, STAMBP, ADA, TNFB, CX3CL1 and IL-15RA ($p< 0.01$-0.05) in the pre-AAV individuals. Nine protein markers were found significantly associated with time to symptom onset; CXCL9, CD244, VEGFA, CXCL1, TNFSF9, OPG, CSF-1, IFN-gamma and CD40 ($p< 0.01$-0.05). In pre-AAV individuals, six proteins were associated with MPO-ANCA-positivity compared with the MPO-ANCA-negative pre-AAV individuals which showed no overlap with the seven proteins related to PR3-ANCA-positivity.

Conclusion: To our knowledge our study is the first to analyze for and identify protein markers before symptom onset in AAV. This allowed for further studies of underlying cellular and molecular mechanisms in AAV pathogenesis as well as the diversification into PR3-ANCA and MPO-ANCA subphenotypes.

Disclosure: M. Brink, None; **E. Berglin**, None; **A. Mohammad**, Roche, 6, Amgen, 1, Vifor, 6, Lilly, 6; **A. Alexeyenko**, None; **K. Lejon**, None; **S. Rantapaa-Dahlqvist**, None.

Abstract Number: 0435

Myeloperoxidase Activity in Individuals with Antineutrophil Cytoplasmic Antibodies (ANCA) Can Be Inhibited by RLS-0071

Parvathi Kumar[1], Pamela Hair[1], Ulrich Thienel[1], Kenji Cunnion[1], Neel Krishna[2] and Christos Gabriel[3], [1]ReAlta Life Sciences Inc, Norfolk, VA, [2]ReAlta Life Sciences Inc., Norfolk, VA, [3]Children's Hospital of The King's Daughters, Norfolk

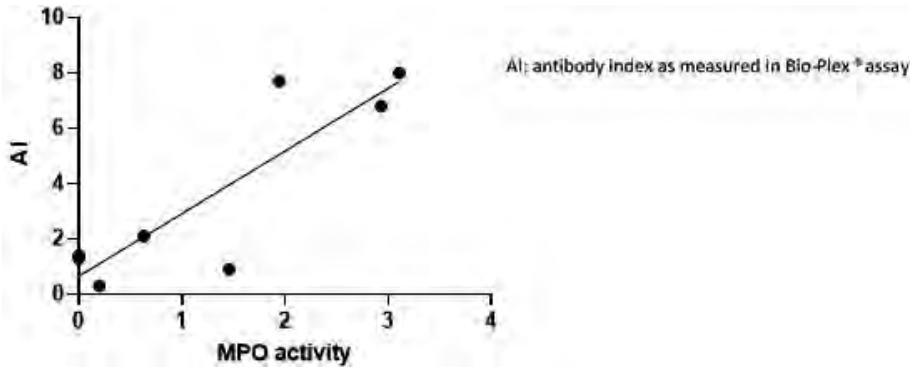
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-neutrophil cytoplasm antibodies (ANCA) are immunoglobulin G (IgG) autoantibodies directed against constituents of primary neutrophil granules (Davies, Moran et al. 1982). There is strong clinical, in vitro and in vivo evidence to suggest that ANCAs are pathogenic (Jennette and Falk 2014) causing pauci-immune necrotizing and crescentic glomerulonephritis (NCGN) and systemic small vessel vasculitis. One of the major target antigens for ANCA is myeloperoxidase (MPO) (Schreiber, Xiao et al. 2006). Both MPO and the reactive oxidants it generates have been implicated as participating in tissue injury in a large number of inflammatory conditions (Nicholls and Hazen 2005). There is no available information as to activity of circulating MPO in individuals with AAV although there is limited evidence that MPO-ANCAs, extracellular MPO, and in situ immune complexes composed of MPO and anti-MPO antibodies may have an important role in the pathogenesis of glomerular capillary injury in MPO-ANCA associated vasculitis (Arimura, Kawashima et al. 2013). Additionally, MPO can stimulate Neutrophil Extracellular Trap (NET) formation which exacerbate inflammation contributing to the dysfunction in AAV as evidenced by NETs found on kidney biopsy specimens from patients with small vessel vasculitis (Kessenbrock, Krumbholz et al. 2009). ReAlta's lead compound, RLS-0071, is a PEGylated peptide which has exhibits inhibition of MPO activity in animal models and ex vivo and demonstrates inhibition of MPO activity on an equimolar basis to the prototypical MPO inhibitor ABAH (4-aminobenzoic acid hydride). RLS-0071 also inhibits neutrophil mediated NETosis in vitro and in vivo (Hair, Enos et al. 2019, Enos, Hair et al. 2020).

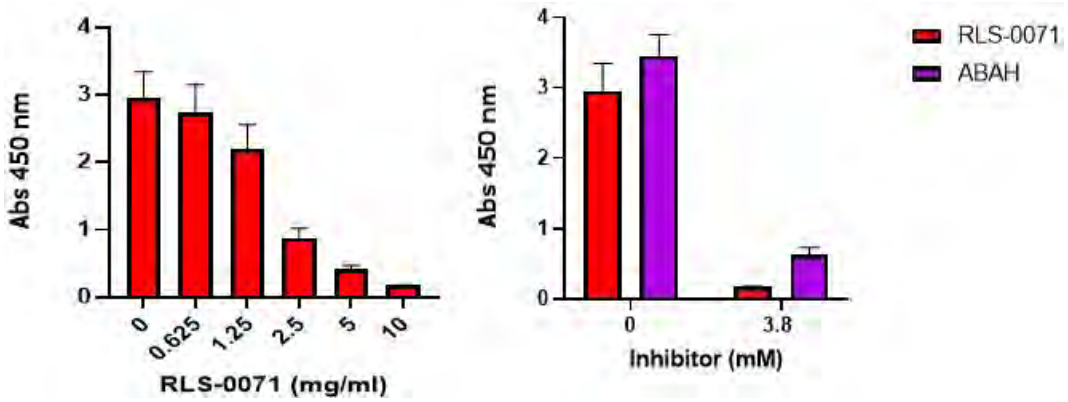
Methods: To better understand the role of MPO in ANCA associated pathophysiology, we conducted pilot analyses measuring MPO activity in plasma samples acquired commercially from individuals with known ANCA. AI (Antibody Index) units were available for each sample which represents a composite score of anti- MPO, anti- PR3 and anti-GBM antibody titers. MPO activity was measured using a TMB oxidation assay in which absorbance was measured a 450nm in a plate reader. The efficacy of RLS-0071 to inhibit MPO activity was evaluated in this assay.

Results: MPO activity as measured at 450nm absorbance ranged from 0 to 3.105. A positive correlation between MPO activity with the AI units in patient samples was observed (R^2= 0.76; p=0.0046). Addition of increasing concentrations of RLS-0071 to the patient samples showed a dose dependent decrease in MPO activity to a similar level as that observed with the MPO inhibitor ABAH.

Conclusion: In this pilot study, plasma from patients with ANCA demonstrated a wide range of MPO activity with the AI units trending with plasma MPO activity. Additionally, RLS-0071 inhibited MPO activity in plasma acquired from individuals with ANCA associated pathophysiology. Future studies will focus on elucidating relationships between MPO activity, MPO quantity, free plasma DNA as a surrogate measurement of NETs and anti-MPO titers.



Positive correlation between MPO activity with AI (composite score of anti- MPO, anti- PR3 and anti- GBM antibody titers)



Dose responsive decrease in MPO activity by RLS-0071 comparable to prototypical MPO inhibitor ABAH

Disclosure: P. Kumar, ReAlta Life Sciences Inc, 3, ReAlta Life Sciences Inc, 2; **P. Hair**, ReAlta Life Sciences Inc, 3; **U. Thienel**, ReAlta Life Sciences Inc, 3; **K. Cunnion**, ReAlta Life Sciences Inc, 3, 4; **N. Krishna**, ReAlta Life Sciences Inc, 3; **C. Gabriel**, None.

Abstract Number: 0436

Ocular and Orbital Manifestations of Granulomatosis with Polyangiitis: A Systematic Review of Published Cases

Madeleine Yeakle[1], **Allen Tsiyer**[1], Daniel Bishev[1], Kayvon Moin[1], Victoria Garofalo[1], Allison Parrill[1], Alexander Hatsis[2], Tyler Wickas[2] and Prachi Anand[3], [1]American University of the Caribbean School of Medicine, Cupecoy, Netherlands Antilles, [2]Department of Ophthalmology, Nassau University Medical Center, East Meadow, NY, [3]Department of Rheumatology, Nassau University Medical Center, East Meadow, NY

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Vasculitis – ANCA-Associated Poster (0414–0436)
Session Type: Poster Session A
Session Time: 8:30AM–10:30AM

Background/Purpose: Granulomatosis with polyangiitis (GPA), formerly known as Wegener's Granulomatosis, is a systemic autoimmune condition caused by granulomatous inflammation of small and medium arteries, arterioles and venules (1). While GPA most commonly affects the upper respiratory tract, lungs and kidneys; ophthalmologic symptoms including orbital and ocular manifestations contribute to morbidity in GPA patients. Ophthalmic manifestations of GPA occur in up to 58% (2) of patients involving the optic nerve, eyelid and orbital structures (3). Diagnoses recorded in current literature include scleritis, episcleritis, keratitis, proptosis, sclerochoroidal granulomas (4), ptosis, uveitis, sclerouveitis, and retinal vein occlusion (5). We aim to systematically analyze published cases of orbital and ocular GPA to characterize symptoms, complications, and outcomes. This may increase provider awareness to prevent misdiagnoses and complications, and lessen patient disease burden.

Methods: On March 21st, 2021, a literary search was conducted from the following electronic databases: PubMed, Web of Science, and Scopus using the MeSH terms "(Orbital OR Ocular) AND (Wegener's OR Wegener OR polyangiitis OR granulomatosis) following PRISMA guidelines (#CRD42021244745). The search included case reports and series discussing patients diagnosed with GPA confirmed ocular or orbital symptoms. We restricted our search to articles published or translated articles in the English language. All articles were included regardless of patient age, gender, sex, ethnicity, or country of origin.

Results: The literature search returned 2,579 articles with 372 meeting inclusion criteria representing 158 (54.1%) female and 134 (45.9%) male patients. The mean age of ocular or orbital symptom presentation and GPA diagnosis were 47.99 and 45.81 years of age, respectively. Fifty percent were not previously diagnosed with GPA prior to presenting with ocular or orbital symptoms. The most common presenting symptom was vision impairment (54.5%) followed by orbital mass (43.8%), proptosis (40.4%), eye pain (39.7%), and extraocular muscle limitation (33.9%). Histopathological examination of orbital/ocular biopsy identified granulomas in 48.5% of patients. Proteinase 3 anti-neutrophil cytoplasmic antibody (c-ANCA) and perinuclear anti-neutrophil cytoplasmic antibody (p-ANCA) positivity was found in 60.4% and 9.9% of patients, respectively. Systemic manifestations of GPA included pulmonary (34.6%), genitourinary (21.9%) and central nervous system (6.5%) among patients. Overall, 18.9% patients relapsed, 11.9% suffered blindness and 3.4% were treated with enucleation. Death was reported in 3.8% of cases. Patient outcomes encompassed full resolution (30.1%), partial resolution (47.3%), and unknown (21.6%).

Conclusion: Our review found that half of patients without prior GPA diagnosis presented with ocular and orbital symptoms. Clinical awareness and early diagnosis of ophthalmological GPA may prevent disease-related complications and improve patient outcomes.

Disclosure: M. Yeakle, None; **A. Tsiyer**, None; **D. Bishev**, None; **K. Moin**, None; **V. Garofalo**, None; **A. Parrill**, None; **A. Hatsis**, None; **T. Wickas**, None; **P. Anand**, None.

Abstract Number: 0437

Factors Associated with Reduced Immunogenicity of the BNT162b2 mRNA COVID-19 Vaccine in Patients with Autoimmune Inflammatory Rheumatic Diseases (AIIRD) Treated with Rituximab

Victoria Furer[1], Tali Eviatar[2], Devy Zisman[3], Hagit Peleg[4], Daphna Paran[5], David Levartovsky[1], Ilana Kaufman[6], Michael Zisapel[1], Ofir Elalouf[7], Roni Meidan[1], Adi Broyde[8], Ari Polachek[9], Jonathan Wollman[7], Katya Meridor[10], Hila Nochomovitz[1], Adi Silberman[1], Dana Rosenberg[1], Joy Feld[11], Amir Haddad[12], Tal Gazitt[13], Muna Elias[3], Nizar Hijaze[14], Fadi Kharouf[4], Gabi Shefer[1], Orly Sharon[1], Sara Pel[1], Sharon Nevo[1] and Ori Elkayam[15], [1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [2]Tel Aviv Sourasky Medical Center, Givataim, Israel, [3]Carmel Medical Center, Haifa, Israel, [4]Hadassah Medical Center, Jerusalem, Israel, [5]Tel Aviv Sourasky Medical Center-Ichilov Hospital, Even Yehuda, Israel, [6]Tel Aviv Sourasky Medical Center, Petach Tiqwa, Israel, [7]Tel Aviv Medical Center, Herzliya, Israel, [8]Tel Aviv Sourasky Medical Center, KIBBUTZ GIVAT HAIM I, Israel, [9]Sourasky Medical Center, Petah-Tikva, Israel, [10]Tel Aviv Sourasky Medical Center, Kfar Saba, Israel, [11]Carmel and Zvulun Medical Centre, Haifa, Israel, [12]Carmel Medical Centre, Haifa, Israel, [13]Carmel Hospital, Haifa, Israel, [14]Carmel medical centre, Tamra, Israel, [15]Tel Aviv Medical Center, Tel Aviv, Israel

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Immunological Complications of Therapy (0437–0440)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Rituximab (RTX) has been associated with impaired humoral response to vaccination. This study aim was to identify the predictors for a lack of humoral response to the BNT162b2 mRNA vaccine in patients with autoimmune inflammatory rheumatic diseases (AIIRD) treated with RTX.

Methods: We conducted a sub-analysis of the prospective multicenter study investigating immunogenicity of the two-dose regimen BNT162b2 mRNA vaccine in adult AIIRD patients, including rheumatoid arthritis (RA), systemic lupus erythematosus, systemic vasculitis, and inflammatory myositis treated with RTX compared to controls with-

Table 1. demographic and clinical characteristics of AIIRD patients treated with rituximab (RTX) and controls

	AIIRD patients treated with RTX n=98	Controls n=122	P value
Age, years median, range	66 (23-88)	50.5 (18-90)	<0.0001
Gender, female, n (%)	74 (75.51)	79 (64.75)	0.105
AIIRD data			
RA, n (%)	47 (47.96)	NA	
SLE, n (%)	8 (8.16)	NA	
ANCA-associated vasculitis, n (%)	22 (22.45)	NA	
Other systemic vasculitis, n (%)	6 (6.12)	NA	
IIM, n (%)	15 (15.31)	NA	
Concomitant IgG4 disease, n (%)	2 (2.5)	NA	
Concomitant lymphoma, n (%)	4 (5)	NA	
AIIRD duration, years, mean±SD	12.3±10.26	NA	
Rituximab data			
Serum IgG level (prior the last RTX course (mg/dL), mean±SD	1010.7±479.21	NA	
Hypogammaglobulinemia<500 (prior the last RTX course, n (%)	6 (6.52)	NA	
RTX cumulative dose (mg), mean±SD	8654.7±7020.27	NA	
RTX dose of the last course prior vaccination (mg), mean±SD	1637.9±592.93	NA	
Total RTX courses, mean±SD	5.1±3.84	NA	
Time interval between last RTX course and BNT162b2 vaccine, days, mean±SD	256.1±333.21	NA	
Concomitant immunosuppressants			
Methotrexate, n (%)	15 (15.31)	NA	
Methotrexate dose, mg/week, mean±SD	13.3±5.47	NA	
Prednisone, n (%)	46 (46.94)	NA	
Prednisone dose, mg/d, mean±SD	5.8±3.47	NA	
Leflunomide, n (%) Mycophenolate mofetil, n (%) IVIG, n (%)	2 (2.04) 5 (5.1) 7 (7.14)		

AIIRD, autoimmune inflammatory rheumatic disease; n, number; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; ANCA, antineutrophil cytoplasmic antibody; IIM, idiopathic inflammatory myopathies; IgG, immune globulin G; SD, standard deviation; DAS28, disease activity score 28; SLEDAI, systemic lupus erythematosus disease activity index; PGA, patient global assessment; PhGA, physician global assessment; VAS, visual analogue scale; RTX, rituximab; IVIG, intravenous immune globulin.

Table 2. Comparison between AIIRD patients treated with rituximab according to seropositive and seronegative response to vaccination.

	Seropositive patients, n=38	Seronegative patients, n=60	P value
Age, years median, range	66 (30-88)	67 (23-87)	0.388
Gender, female, n (%)	31 (81.58)	43 (71.67)	0.338
AIIRD diagnosis			
RA, n (%)	21 (55.26)	26 (43.33)	0.302*
SLE, n (%)	6 (15.79)	2 (3.33)	0.052*
ANCA-associated vasculitis, n (%)	5 (13.16)	17 (28.33)	0.089*
Other systemic vasculitis, n (%)	2 (5.26)	4 (6.67)	1*
IIM, n (%), n (%)	4 (10.53)	11 (18.33)	0.393*
Disease duration, years, mean SD	14.05±11.01	11.23±9.69	0.188
History of lymphoma, n (%)	3 (9.09)	1 (2.13)	0.301
Rituximab data			
Serum IgG level (prior the RTX last course), mean±SD	1232.98±624.45	880.44±306.82	0.004
Hypogammaglobulinemia<500 (prior the last RTX course), n (%)	1 (2.94)	5 (8.62)	0.407
Rituximab cumulative dose (mg) mean±SD	7077.89±6145.63	9653.33±7397.67	0.077
Rituximab dose of the last course prior vaccination (mg), mean±SD	1776.58±570.85	1550±594.47	0.065
Total RTX courses, mean±SD	3.92±3.18	5.9±4.04	0.012
Time interval between last RTX course and BNT162b2 vaccine, days, mean±SD	410.63±459.66	158.27±157.89	0.002
Up to 180 days	11 (28.95)	47 (78.33)	<0.0001
181-365 days	13 (34.21)	11 (18.33)	
Over 365 days	14 (36.84)	2 (3.33)	
Concomitant immunosuppressants			
Methotrexate, n (%)	5 (13.16)	10 (16.67)	0.777
Methotrexate dose, mg/week, mean±SD	10.83±5.2	14.17±5.59	0.386
Prednisone, n (%)	16 (42.11)	30 (50)	0.535
Prednisone dose, mg/d, mean±SD	5.4±3.42	5.92±3.53	0.633
Leflunomide, n (%)	1 (2.63)	1 (1.67)	1
Mycophenolate mofetil, n (%)	1 (2.63)	4 (6.67)	0.646
IVIG, n (%)	3 (7.89)	4 (6.67)	1

* Fisher exact test p-value for the comparison between the relevant diagnosis (RA, SLE, etc.) and all other diagnoses AIIRD, autoimmune inflammatory rheumatic disease; n, number; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; ANCA, antineutrophil cytoplasmic antibody; IIM, idiopathic inflammatory myopathies; IgG, immune globulin G; SD, standard deviation; RTX, rituximab; IVIG, intravenous immune globulin.

Table 3. Stepwise backward model logistic regressions predicting seropositive result*.

Variable	OR	95% CI	p-value
RA	0.04	0.003-0.621	REF
SLE	0.536	0.033-8.784	0.662
ANCA-associated vasculitis	0.223	0.047-1.057	0.059
Other systemic vasculitis	0.476	0.038-5.98	0.566
IIM	0.333	0.057-1.956	0.223
Serum IgG level (prior the last RTX course)	1.002	1-1.004	**0.013**
Total RTX courses	0.875	0.744-1.03	0.108
Time interval between last RTX course and BNT162b2 vaccine	1.007	1.003-1.011	**0.002**

* Original model included SLE, ANCA associated vasculitis, other systemic vasculitis, IIM, disease duration, serum IgG levels, cumulative rituximab dose, rituximab last course dose, total rituximab courses, and time interval between the last rituximab course and BNT162b2 vaccine. Including and staying criterion was $p < 0.2$. RA was considered as a reference for diagnosis. RA, rheumatoid arthritis; SLE, systemic lupus erythematosus; ANCA, antineutrophil cytoplasmic antibody; IIM, idiopathic inflammatory myopathies; IgG, immune globulin G; RTX, rituximab.

out rheumatic diseases or immunosuppressants use. Data on the serum IgG level prior to administration of the last course of RTX were collected. Post-vaccination serum IgG levels against SARS-CoV-2 spike S1/S2 proteins were measured 2 - 6 weeks after the 2nd vaccine dose. Seropositivity was defined as IgG ³15 binding antibody units (BAU)/ml.

Statistical analysis included a stepwise backward multiple logistic regression for predicting a seropositive result on AIIRD patients with all data available (n=92), starting with all individual variables showing the significance level < 0.2 between seropositive and seronegative result.

Results: A total of 98 AIIRD patients (75.5% females) and 122 controls (64.8% females) were included in the study (table 1). AIIRD patients were significantly older vs controls, mean±standard deviation (SD) 62.3±14.6 vs 50.8±14.6 years, p>0.0001, respectively. Among AIIRD patients, 4 had a past history of lymphoma. Following vaccination, the seropositivity rate and S1/S2 IgG levels (mean±SD) were significantly lower among AIIRD patients vs controls, 38.8% (n=38) vs 100%, $p < 0.0001$ and 49.9±81 vs 218.4±81.2 BAU/ml, $p < 0.0001$, respectively.

Seronegative and seropositive AIIRD patients treated with RTX significantly differed by the total number of RTX courses, mean 5.9±4.0 vs 3.9±3.2, p=0.012; IgG levels prior to administration of the last course of RTX, 880.4±306.8 vs 1233±624 mg/dl, p=0.0036 and the interval between the last RTX course and vaccination, 158.3±157.9 vs 410.6±459.7 days, p=0.0019 (table 2). Multivariate logistic regression predicting a seropositive response to vaccination in patients treated with RTX showed that RA conferred the highest probability for a positive response, while ANCA-associated vasculitis conferred the lowest probability for a positive response. The odds ratio (OR) of ANCA associated vasculitis

was marginally significant (OR = 0.223, p=0.059). Two other variables –IgG level prior the last course of RTX and interval (days) between the last RTX course and vaccination – were associated with a seropositive response: for every 1 mg/dl IgG increment - OR 1.002, 95%CI 1-1.004, p=0.013, and for every day increment - OR 1.007, 95%CI 1.003-1.001, p=0.002, respectively. (table 3)

Conclusion: In AIIRD patients treated with RTX, high exposure to RTX over time, low IgG levels prior to the last RTX course, and a short interval between the last RTX course and BNT162b2 vaccination predicted the absence of a humoral response to vaccination. These data should guide the optimal timing of vaccination in patients treated with RTX.

Disclosure: V. Furer, None; **T. Eviatar**, None; **D. Zisman**, None; **H. Peleg**, None; **D. Paran**, None; **D. Levartovsky**, None; **I. Kaufman**, None; **M. Zisapel**, None; **O. Elalouf**, None; **R. Meidan**, None; **A. Broyde**, None; **A. Polachek**, None; **J. Wollman**, None; **K. Meridor**, None; **H. Nochomovitz**, None; **A. Silberman**, None; **D. Rosenberg**, None; **J. Feld**, None; **A. Haddad**, None; **T. Gazitt**, None; **M. Elias**, None; **N. Hijaze**, None; **F. Kharouf**, None; **G. Shefer**, None; **O. Sharon**, None; **S. Pel**, None; **S. Nevo**, None; **O. Elkayam**, NOVARTIS, 1, 2, 6, Pfizer, 1, 2, 5, 6, Lilly, 1, 2, 6, Abbvie, 1, 6, BI, 1, 6.

Abstract Number: 0438

Rheumatological Immune-Related Adverse Events of Immune Checkpoint Inhibitors Based on the FDA Adverse Event Reporting System

Alicia Rodriguez-Pla, Mayo Clinic Arizona, Scottsdale, AZ

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Immunological Complications of Therapy (0437–0440)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) provide effective treatment for many cancers but, presumably due to persistent activation of the immune system, they cause a variety of immune-related adverse events (irAEs) in almost every organ. Rheumatological manifestations have been reported in ~5-10% of patients treated with ICIs. We aimed to analyze the rheumatological irAEs (rh-irAEs) reported to the FDA Adverse Event Reporting System (FAERS) from October 2012 through March 2021.

Methods: From October 1st, 2012, to March 31st, 2021, we studied all case reports found on the FAERS database when any of the following seven FDA-approved ICIs, nivolumab, pembrolizumab, ipilimumab, atezolizumab, durvalumab, avelumab, or cemiplimab, was the primary suspect of the reported adverse events (AEs).

Of the 6,090 different AEs reported for the ICIs, we selected 186 irAEs, which were rheumatological manifestations, or were associated with rheumatological conditions. We calculated the frequencies of rh-irAEs for each ICI. RStudio v1.4.1106 was used for general data analysis and the R package openEBGM v0.8.3 was used for the calculation of disproportionality scores such as the Empirical Bayes Geometric Mean (EBGM) with its 90% two-sided credibility interval, frequently used in safety signal detection models. Drug-event combinations with an EBGM 5% lower limit credibility interval ≥ 1 were considered significant.

Results: During the study period, 90,974 individual case safety reports (ICSR) included 236,239 AEs with one ICI as the primary suspect of the AE. The highest frequency of AEs was reported for nivolumab (49.6%), followed by pembrolizumab (23.4%), ipilimumab (12.6%), atezolizumab (8.6%), durvalumab (4.6%), avelumab (0.9%), and cemi-

Table 1. The 5 most frequent rheumatological immune-related adverse events by checkpoint inhibitor

ICI	Rheumatological irAEs	N	%
Nivolumab	Arthralgia	755	12.8
	Back pain	581	9.8
	Myalgia	381	6.4
	Arthritis	346	5.9
	Muscular weakness	333	5.6
Pembrolizumab	Arthralgia	390	12.7
	Myalgia	225	7.3
	Neuropathy peripheral	184	6
	Muscular weakness	171	5.6
	Pain in extremity	168	5.5
Ipilimumab	Arthralgia	113	11.8
	Back pain	97	10.1
	Muscular weakness	95	9.9
	Neuropathy peripheral	85	8.8
	Myalgia	53	5.5
Durvalumab	Arthralgia	55	14
	Muscular weakness	34	8.7
	Myalgia	28	7.1
	Back pain	27	6.9
	Myositis	25	6.4
Avelumab	Neuropathy peripheral	10	14.9
	Back pain	9	13.4
	Sjogren's syndrome	7	10.4
	Myositis	6	9
	Sarcoidosis	4	6
Atezolimumab	Neuropathy peripheral	10	14.9
	Back pain	9	13.4
	Sjogren's syndrome	7	10.4
	Myositis	6	9
	Sarcoidosis	4	6
Cemiplimab	Back pain	7	11.9
	Myositis	6	10.2
	Myalgia	6	10.2
	Arthralgia	6	10.2
	Muscular weakness	4	6.8

ICI: Immune checkpoint inhibitor. IrAEs: Immune-related adverse events.

Table 2. Statistically Significant Drug-Event Combination of Rheumatological Immune-Related Adverse Events by Immune Checkpoint InhibitorsTable 2. Statistically Significant Drug-Event Combination of Rheumatological Immune-Related Adverse Events by Immune Checkpoint Inhibitors

ICI	IrAEs	N	EBGM 05	EBGM	EBGM 95
Pembrolizumab	Immune-mediated arthritis	35	1.95	2.66	3.51
Pembrolizumab	Immune-mediated myositis	38	1.46	2.11	2.85
Pembrolizumab	Polymyalgia rheumatica	73	1.44	1.82	2.28
Ipilimumab	Neuropathy peripheral	84	1.21	1.45	1.74
Atezolimumab	Muscular weakness	70	1.11	1.33	1.6
Atezolimumab	Myositis	63	1.11	1.35	1.64
Ipilimumab	Muscular weakness	95	1.11	1.3	1.52
Nivolumab	Back pain	581	1.1	1.17	1.25
Ipilimumab	Erythema nodosum	9	1.09	2.47	4.85
Atezolimumab	Neuropathy peripheral	55	1.08	1.32	1.63
Avelumab	Sjogren's syndrome	7	1.07	2.78	5.85
Nivolumab	Joint swelling	130	1.07	1.22	1.4
Pembrolizumab	Neuropathy peripheral	184	1.07	1.2	1.35
Nivolumab	Arthritis	346	1.06	1.16	1.26
Nivolumab	Musculoskeletal pain	184	1.06	1.19	1.33
Nivolumab	Polyarthritis	124	1.06	1.22	1.4
Atezolimumab	Sarcoidosis	17	1.04	1.61	2.76
Nivolumab	Musculoskeletal stiffness	94	1.04	1.22	1.43
Nivolumab	Rheumatic disorder	40	1	1.26	1.58
Pembrolizumab	Myalgia	225	1	1.11	1.23
Pembrolizumab	Pain in extremity	168	1	1.13	1.27

ICI: Immune checkpoint inhibitor. IrAEs: Immune-related adverse events. N: number of drug-even combination. EBGM: Empirical Bayes Geometric Mean. EBGM 05: Lower limit of the 90% credibility interval of EBGM. EBGM 95: Upper limit of the 90% credibility internal of EBGM. The table is sorted in decreasing order of EGBM 05.

plimab (0.3%). The AEs were more frequent in males (62.7%) than in females (37.3%). Of the total ICSRs, 84.2% were expedited because they reported serious, unexpected irAEs.

Rh-irAEs were 11,203 (4.7%) out of the 236,239 AEs reported. These rh-irAEs were reported in 3,898 (4.3%) out of the 90,974 ICSRs. For the ICSRs containing rh-irAEs, 78.5% were expedited. Unspecific complains, such as arthralgia, myalgia or muscle weakness were among the most frequent rh-irAEs. Avelumab and atezolizumab were associated with Sjogren's syndrome and sarcoidosis. Durvalumab, avelumab, atezolimumab and cemiplimab were all associated with myositis (Table 1). Twenty-one drug-event combinations were significant for EBGM (Table 2). Of those, nivolumab and pembrolizumab were the two most frequent ICI, with 7 and 6 significant drug-event combinations, respectively.

Conclusion: Approximately 5% of the reported ICIs-associated AEs were rh-irAEs. The most frequent complaints were unspecific, such as arthralgia, myalgia, or muscle weakness. Arthritis, myositis, Sjogren's syndrome, and sarcoidosis were also relatively frequent. The improved understanding of the mechanism of action of the ICIs and the characteristics of the rh-irAEs may help to elucidate the pathogenesis of the autoimmune disorders that they trigger.

Disclosure: A. Rodriguez-Pla, None.

Abstract Number: 0439

Predictors of Rheumatic Immune-related Adverse Events and *de Novo* Inflammatory Arthritis After Immune Checkpoint Inhibitor-treatment for Cancer

Amy Cunningham-Bussel[1], Jiaqi Wang[2], Lauren Prisco[3], Lily Martin[2], Kathleen Vanni[2], Alessandra Zaccardelli[2], Mazen Nasrallah[4], Lydia Gedmintas[2], Lindsey MacFarlane[5], Nancy Shadick[6], Mark M. Awad[7], Osama E. Rahma[7], Nicole LeBoeuf[8], Ellen Gravallese[9] and Jeffrey Sparks[2], [1]Brigham and Women's, Brookline, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Pound Ridge, MA, [4]MGH, Somerville, MA, [5]Brigham and Women's Hospital, Brookline, MA, [6]Brigham & Women's Hospital, Boston, MA, [7]Dana-Farber Cancer Institute, Boston, [8]Brigham and Women's Hospital, Department of Dermatology, Boston, MA, [9]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Immunological Complications of Therapy (0437–0440)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Immune-related adverse events (irAEs) are a frequent and serious complication of immune checkpoint inhibitor (ICI) treatment for cancer, which can resemble primary rheumatic diseases. Predictors associated with development of rheumatic irAEs have not been well characterized in previous studies due to lack of a comparator group and sample size limitations. The aim of this study was to identify predictors at time of ICI initiation associated with rheumatic irAEs as well as *de novo* inflammatory arthritis, the most common type of rheumatic irAE.

Methods: We performed a case-control study of all cancer patients initiating an ICI at a large tertiary academic health care system and cancer center (2011-2020). We screened for rheumatic irAEs through a comprehensive medical record review of all patients evaluated by a rheumatologist or prescribed an immunomodulator (IM) after initial ICI prescription (baseline), using electronic query. IMs are one of 55 medications used to treat irAEs based on published guidelines. Two board-certified rheumatologists confirmed the presence and type of rheumatic irAE case by independent medical record review. Controls had no pre-existing rheumatic disease, did not receive glucocorticoids, had no IM or rheumatologic evaluation after ICI, and survived at least 6 months after initial ICI (since patients with

early demise may not have an opportunity to develop a rheumatic irAE). We found no patients with rheumatic irAEs on medical record review of 100 random controls (negative predictive value 100%). Predictors at the initiation of ICI included: cancer type (the most prevalent cancer, lung cancer was the reference group), ICI regimen, pre-existing autoimmune disease, and glucocorticoid use. Multivariable logistic regression estimated odds ratios (ORs) for rheumatic irAE case status. A similar analysis was performed to find predictors of *de novo* inflammatory arthritis.

Results: We found 8,028 ICI recipients (mean age 65.5 years, 43.1% female, and 31.8% with lung cancer). We identified 226 (2.8%) confirmed rheumatic irAE cases and 118 (1.5%) with *de novo* inflammatory arthritis. There were 2,312 controls without rheumatic irAEs included in analyses. Baseline predictors of rheumatic irAE case status were: melanoma (OR 4.01, 2.51-6.40) or genitourinary (GU) cancer (OR 2.19, 1.37-3.48, ref=lung cancer), combination ICI (OR 2.35, 1.48-3.74, ref=PD-1), pre-existing autoimmune disease (OR 2.04, 1.46-2.86), and glucocorticoid use within one year prior to ICI (OR 2.13, 1.51-2.98, ref=non-use) (**Figure 1**). Baseline predictors of *de novo* inflammatory arthritis were similar: melanoma (OR 2.95, 1.60-5.43) or GU cancer (OR 2.39, 1.34-4.26, ref=lung cancer), combination ICI (OR 2.31, 1.26-4.26, ref=PD-1), pre-existing autoimmune disease (OR 2.74, 1.79-4.19), and glucocorticoid use one year prior to ICI (OR 1.96, 1.26-3.06, ref=non-use) (**Figure 2**).

Conclusion: In this large study of patients who received an ICI, we found melanoma, GU cancer, pre-existing autoimmune disease, and glucocorticoid use within 1 year of ICI may be novel predictors of rheumatic irAEs. The possible biologic basis of these associations should be the subject of future research.

Figure 1. Multivariable odds ratios (OR) for development of rheumatic irAEs (n=226 cases), compared to 2,312 controls*

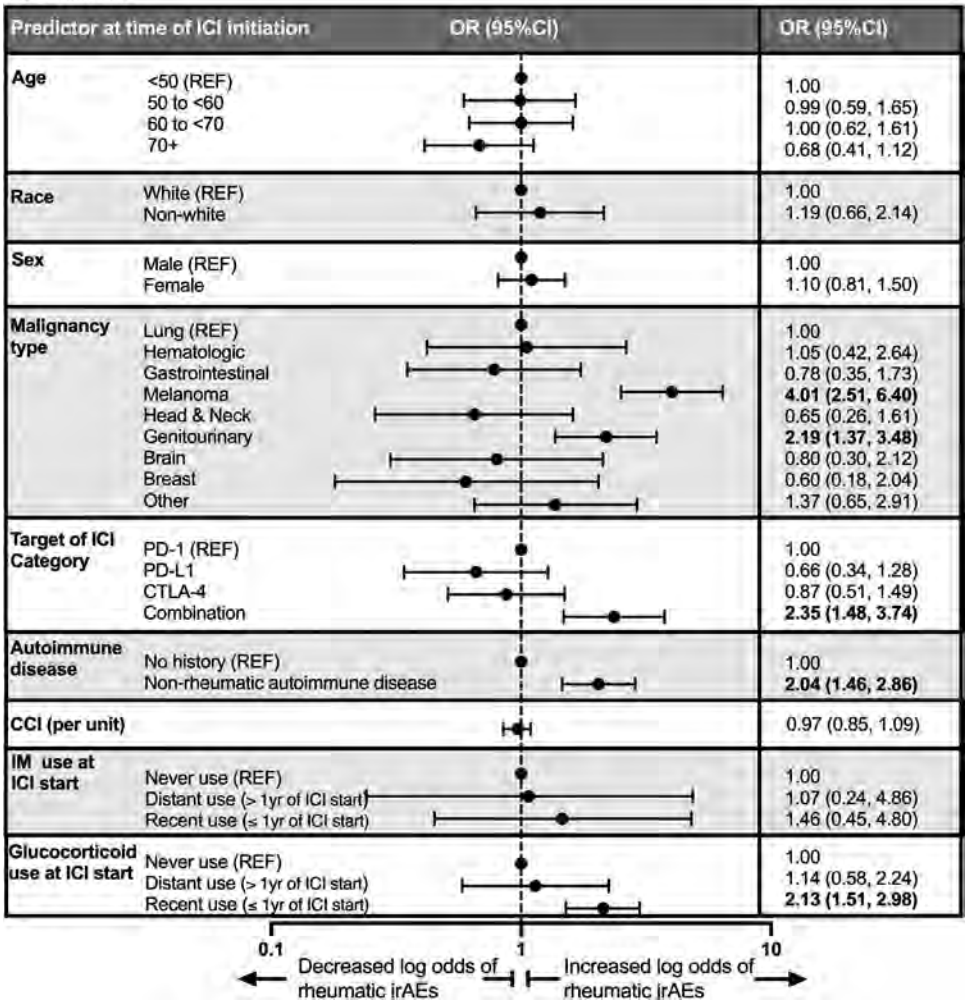
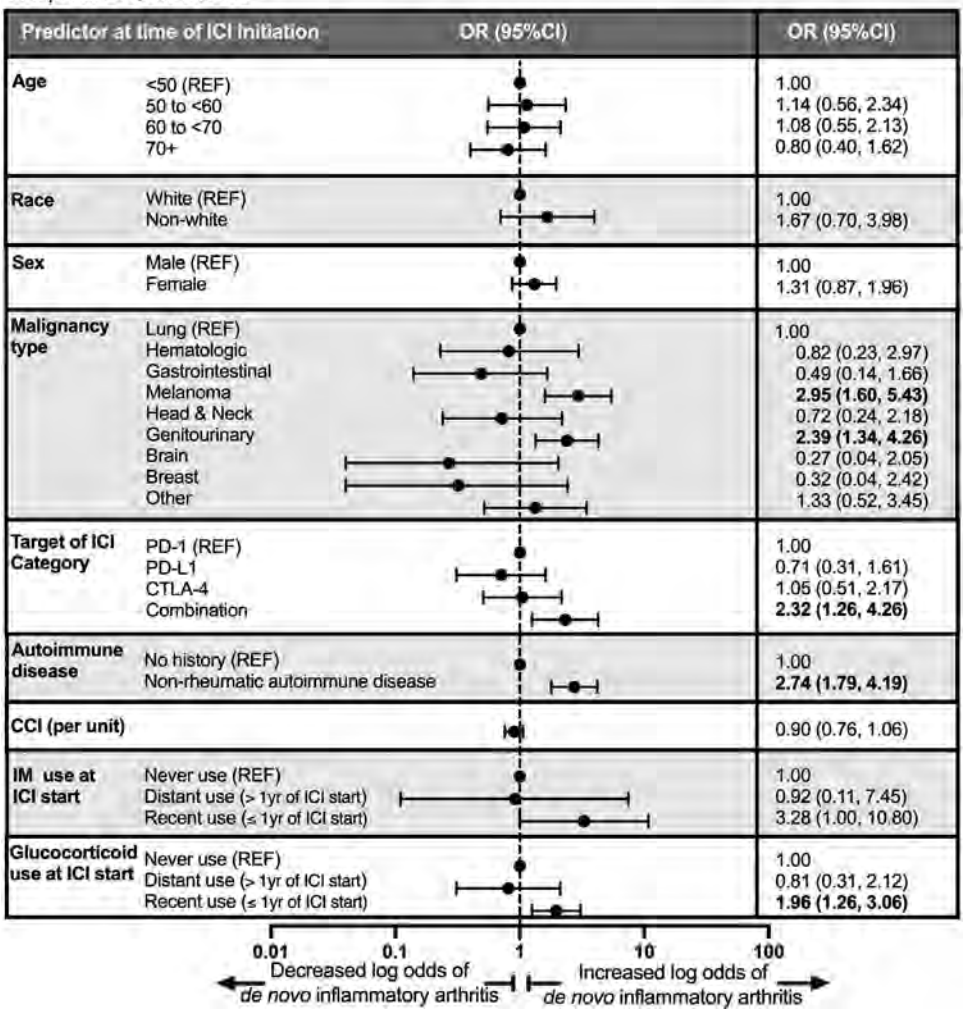


Figure 2. Multivariable odds ratios (OR) for development of *de novo* inflammatory arthritis (n=118 cases), compared to 2,312 controls*



Bolded values have p<0.05. *Controls were patients without rheumatic disease at baseline, used no glucocorticoid or immunomodulator after baseline, and had no rheumatologic evaluation after baseline. Multivariable models were mutually adjusted for all covariates listed in the column. CCI, Charlson Comorbidity Index; CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; ICI, immune checkpoint inhibitors; IM, immunomodulator; irAE, immune-related adverse event; OR, odds ratio; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; REF, Reference.

Bolded values have p<0.05. *Controls were patients without rheumatic disease at baseline, used no glucocorticoid or immunomodulator after baseline, and had no rheumatologic evaluation after baseline. Multivariable models were mutually adjusted for all covariates listed in the column. CCI, Charlson Comorbidity Index; CI, confidence interval; CTLA-4, cytotoxic T-lymphocyte-associated protein 4; ICI, immune checkpoint inhibitors; IM, immunomodulator; irAE, immune-related adverse event; OR, odds ratio; PD-1, programmed cell death protein 1; PD-L1, programmed death ligand 1; REF, Reference.

Disclosure: A. Cunningham-Bussel, None; **J. Wang**, None; **L. Prisco**, None; **L. Martin**, None; **K. Vanni**, None; **A. Zaccardelli**, None; **M. Nasrallah**, None; **L. Gedmintas**, Bristol-Myers Squibb, 5, Amgen, 5, Eli Lilly, 5, Crescendo Biosciences, 5, Sanofi, 5, Mallinckrodt, 5, Bristol-Myers Squibb, 2; **L. MacFarlane**, None; **N. Shadick**, Amgen, 5, BMS, 2, 5, Eli Lilly, 5, Sanofi, 5, Mallinckrodt, 5; **M. Awad**, Genentech, 12, Bristol-Myers Squibb, 12, Merck, 12, AstraZeneca, 5, AstraZeneca, 12, Eli Lilly, 5, Maverick, 12, Blueprint Medicine, 12, Syndax, 12, Ariad, 12, Nektar, 12, Gritstone, 12, ArcherDX, 12, Mirati, 12, NextCure, 12, Novartis, 12, EMD Serono, 12, Panvaxal/NovaRx, 12; **O. Rahma**, Merck, 5, Merck, 2, BMS, 6, Celgene, 2, Five Prime, 2, GSK, 2, Bayer, 2, Puretech, 12, Roche/Genentech, 2, Puretech, 2,

Imvax, 2, Sobi, 2; **N. LeBoeuf**, Bayer, 2, Seattle Genetics, 2, Sanofi, 2, Silverback, 2, Synox Therapeutics, 2; **E. Gravallese**, None; **J. Sparks**, Bristol-Myers Squibb, 2, 5, Amgen, 5, Gilead, 2, Inova, 2, Janssen, 2, Optum, 2, Pfizer, 2.

Abstract Number: 0440

Association Between Rheumatic Autoantibody Positivity and Immune-related Adverse Events

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Immunological Complications of Therapy (0437–0440)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: The advent of immune checkpoint inhibitors (ICIs) has revolutionized cancer therapy; however, their use can lead to off-target toxicities called immune-related adverse events (irAEs) that closely resemble

Table 1: Study Characteristics

Gender	
Female	79 (52%)
Male	73 (48%)
Total	152
Age at cancer diagnosis, Mean (Range, Std Dev)	59 (15-94, 15)
Race	
White	97 (64%)
Black/African American	40 (26%)
Asian/Mideast Indian	5 (3%)
Hispanic	2 (1%)
American Indian/Alaskan Native	1 (1%)
More than one race	6 (4%)
Patient declined	1 (1%)
Primary malignancy	
Melanoma	34 (22%)
Non-small Cell Lung Cancer	33 (22%)
Genitourinary Cancers	18 (12%)
Small Cell Lung Cancer	13 (9%)
Hepatocellular Carcinoma	7 (5%)
Head and Neck SqCC	9 (6%)
Other	38 (25%)
Immunotherapy	
CTLA4i	14 (9%)
PD1/PDL1i	114 (75%)
Combination	24 (16%)
Immune-related adverse events	
irAE development	90 (59%)
No irAE development	62 (41%)
Severity (Based on CTCAE Scale)	
Grade 1	10 (11%)
Grade 2	28 (31%)
Grade 3	35 (39%)
Grade 4	14 (16%)
Grade 5	2 (2%)
Autoantibody positivity (positive/checked)	
Any type autoantibody	96/152
ANA	84/138
RF	18/88
CCP	6/54

primary autoimmune disease. Our study aimed to better understand the association between autoantibody positivity and irAE development.

Methods: Patients with cancer who were treated with ICIs from 1/1/2011 to 12/21/2020 and had a rheumatic autoantibody checked were retrospectively identified. Rheumatic autoantibodies evaluation in our study focused on the following serologies: Antinuclear antibody (ANA), Rheumatoid factor (RF), Cyclic citrullinated protein (CCP), but also included analysis of other serologies (anti–Sjögren's-syndrome-related antigen A and B autoantibodies (SSA, SSB), double-stranded DNA, antineutrophil cytoplastic antibodies, angiotensin converting enzyme). Logistic regression model was used to evaluate the relationship between autoantibody analysis and irAE development as well as cancer outcome. Specificity, sensitivity and predictive values were also estimated. Cancer outcome was defined by objective response rate (ORR).

Results: 152 total patients were identified for review. Demographics are as noted in table 1. Of the patients who had rheumatic autoantibodies ordered, 90 (59%) were found to have irAE development. After adjusting for age at cancer diagnosis, sex, race, diagnosis of malignancy, and ICI group, patients with pre-ICI autoantibody positivity had greater odds of irAE development (OR 17.5, 95% CI 1.76-174.10, p=0.015). Development of irAE was associated with a 3.43 greater odds of an ORR for primary malignancy (95%CI: 1.35-8.72, p=0.01). There was no significant association with post-ICI autoantibody testing and any-type irAEs and the sensitivity, specificity, positive predictive value, and negative predictive value of any autoantibody positivity in development of irAEs were as follows: 63%, 30%, 56%, and 37% respectively. Subgroup analysis of rheumatic irAEs revealed a strong association between RF and CCP; for ICI-arthritis, RF showed sensitivity=0.24 and specificity=0.90 while CCP showed sensitivity=0.10 and specificity=0.98. Negative predictive values of RF and CCP for development of ICI-arthritis were 0.84 and 0.82 respectively.

Conclusion: Our results demonstrate strong association with pre-ICI autoantibody positivity and any-type irAE development as well as high specificity of RF and CCP for ICI-arthritis. Our findings justify prospective evaluation of rheumatic serologies and association with irAE development.

Disclosure: K. Mathias, None; **M. Lopez Velazquez**, None; **P. Reid**, Co-inventor of a filed patent covering the use of low-dose tocilizumab in viral infections., 10.

Abstract Number: 0441

A Randomized, Double-blind, Placebo-controlled Study of Arimoclomol in Patients with Inclusion Body Myositis

Pedro Machado[1], Richard Barohn[2], Michael McDermott[3], Thomas Blaetter[4], Tom Lloyd[5], Aziz Shaibani[6], Miriam Freimer[7], Anthony Amato[8], Emma Ciafaloni[3], Sarah Jones[9], Tahseen Mozaffar[10], Summer Gibson[11], Matthew Wicklund[12], Todd Levine[13], Claus Sundgreen[4], Tim Carstensen[4], Karen Bonefeld[4], Anders Jørgensen[4], Karina Phonekeo[4], Andrew Heim[14], Laura Herbelin[14], Michael Hanna[15] and Mazen Dimachkie[14], [1]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [2]University of Missouri - Columbia, Columbia, MO, [3]University of Rochester, Rochester, NY, [4]Orphazyme A/S, Copenhagen, Denmark, [5]Johns Hopkins University, Baltimore, MD, [6]Nerve and Musle Center, Houston, TX, [7]Ohio State University, Columbus, OH, [8]Brigham and Women's Hospital, Boston, MA, [9]University of Virginia, Charlottesville, VA, [10]University of California Irvine, Irvine, CA, [11]University of Utah, Salt Lake City, UT, [12]University of Colorado, Denver, CO, [13]Phoenix Neurological Associates, Phoenix, AZ, [14]University of Kansas Medical Center, Kansas City, KS, [15]University College London, London, United Kingdom

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies (0441–0444)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Inclusion body myositis (IBM) is the most common idiopathic inflammatory myopathy occurring in patients over the age of 45 years. Since immune suppression has not been effective, modulating the cytoprotective "heat shock response" (HSR) represents a candidate therapeutic approach targeting both inflammation and degeneration. In a pilot study, arimoclomol, an amplifier of the HSR, was safe and well tolerated with some trends suggesting efficacy at 8 months in subjects with IBM. Our aim is to present the efficacy and safety/tolerability data from a phase 2/3 randomized controlled trial of arimoclomol in IBM (NCT02753530).

Methods: In this international multicenter, double-blind, placebo-controlled trial, subjects were randomized (1:1) to receive either arimoclomol citrate 400 mg or matching placebo capsules three times a day (1,200 mg/day) for 20 months. The primary outcome measure was the change from baseline to Month 20 in the IBM Functional Rating Scale (IBMFRS) total score. Hierarchically ordered key secondary outcome measures included hand grip strength (strongest hand), Modified Time Up and Go, Manual Muscle Testing (24 muscles), 6-minute walk test distance, and the Short-Form 36 health survey. Other outcome measures included patient and clinician impressions, and other measures of muscle strength and function. Drug safety and tolerability were evaluated.

Results: One hundred fifty-two IBM subjects fulfilling ENMC 2011 criteria were randomized with mean age 67.2 years (SD 8.1), mostly men (76%), mean disease duration 98 months (SD 58), and mean baseline IBMFRS of 27.4 (SD 4.6). The IBMFRS declined by a mean of 3.25 points with arimoclomol vs. 2.26 points with placebo over 20 months (p=0.11). Secondary efficacy outcome measures did not show any statistically significant treatment group differences. Most frequently reported AEs observed with higher incidence in arimoclomol group were gastrointestinal disorders (54.8% vs. 39.7%). Patients receiving arimoclomol were more likely to discontinue treatment due to AEs (17.8% vs. 5.1%). The relative frequency of serious AEs was comparable in the two treatment arms (arimoclomol 15.1% vs. placebo 23.1%). Elevated transaminases were reported in the first three months and were more frequently observed with arimoclomol than with placebo (15.4% vs. 6.4%).

Conclusion: This trial did not demonstrate a benefit of arimoclomol in IBM with respect to its primary and secondary efficacy endpoints.

Disclosure: P. Machado, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **R. Barohn**, Orphazyme, 2, Orphazyme, 5; **M. McDermott**, Orphazyme, 5; **T. Blaetter**, Orphazyme, 3; **T. Lloyd**, Orphazyme, 5; **A. Shaibani**, Orphazyme, 5; **M. Freimer**, Orphazyme, 5; **A. Amato**, Orphazyme, 5; **E. Ciafaloni**, Orphazyme, 5; **S. Jones**, Orphazyme, 5; **T. Mozaffar**, None; **S. Gibson**, Orphazyme, 5; **M. Wicklund**, Orphazyme, 5; **T. Levine**, None; **C. Sundgreen**, Orphazyme, 3; **T. Carstensen**, Orphazyme, 3; **K. Bonefeld**, Orphazyme, 3; **A. Jørgensen**, Orphazyme, 3; **K. Phonekeo**, Orphazyme, 3; **A. Heim**, Orphazyme, 5; **L. Herbelin**, Orphazyme, 2, 5; **M. Hanna**, Orphazyme, 2, 5; **M. Dimachkie**, Octapharma, 2, 5, CSL-Behring, 2, 5, Orphazyme, 2, 5, Kezar, 1, 2, 5, UCB, 1, 2, 5, Shire Takeda, 2, 5, Bristol-Myers Squibb, 5, Corbus, 5, FDA/OOPD, 5, IMACS, 4.

Abstract Number: 0442

Identification of Plexin D1 on Circulating Extracellular Vesicles as a Potential Biomarker of Polymyositis and Dermatomyositis

Kenichi Uto[1], Koji Ueda[2], Takaichi Okano[1], Kengo Akashi[1], Soshi Takahashi[3], Yuji Nakamachi[4], Takamitsu Imanishi[1], Seiji Kawano[1], Yoshihiko Yano[5] and Jun Saegusa[6], [1]Kobe University Hospital, Kobe, Japan, [2]Japanese Foundation for Cancer Research, Tokyo, Japan, [3]Shinko Hospital, Kobe, Japan, [4]Kobe University School of Medicine, Kobe, Japan, [5]Department of Clinical Laboratory, Kobe University Hospital, Kobe, Japan, [6]Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan

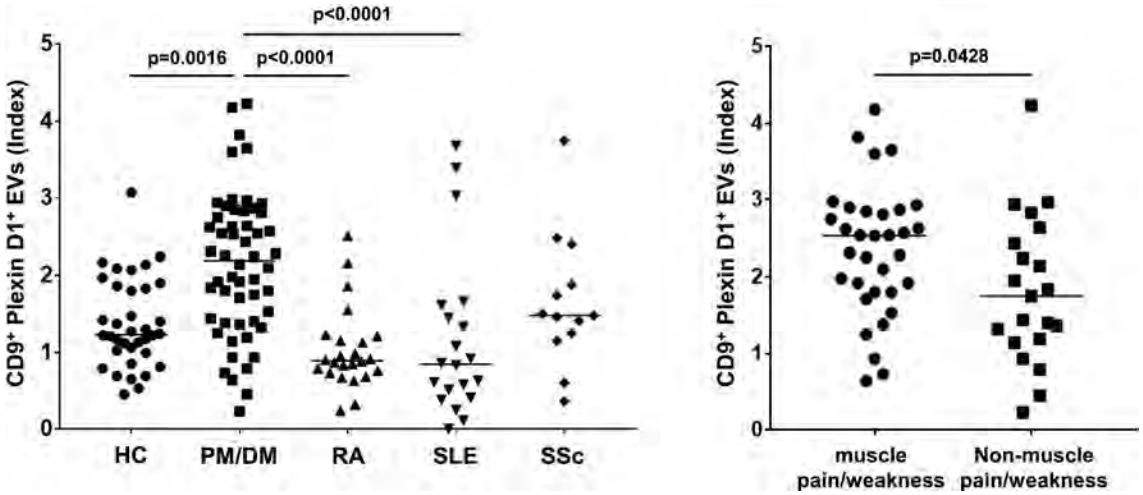
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies (0441–0444)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Extracellular vesicles (EVs), including exosomes and microvesicles, are small membrane vesicles released by almost all cell types and are found circulating in blood and other body fluids. Circulating EVs are promising as a novel type of systemic biomarker for various different diseases because their cargoes (miRNAs, mRNAs, and proteins) reflect their cellular origin and function. Increasing evidence suggests that surface proteins (e.g. membrane proteins) on EVs, especially exosomes, are altered in pathological conditions and useful as non-invasive biomarkers for cancer diagnosis and prognosis. However, they have rarely been employed as serum biomarkers for autoimmune diseases. The aim of this study is to identify disease-specific surface proteins on EVs as novel serum biomarkers of polymyositis and dermatomyositis (PM/DM).

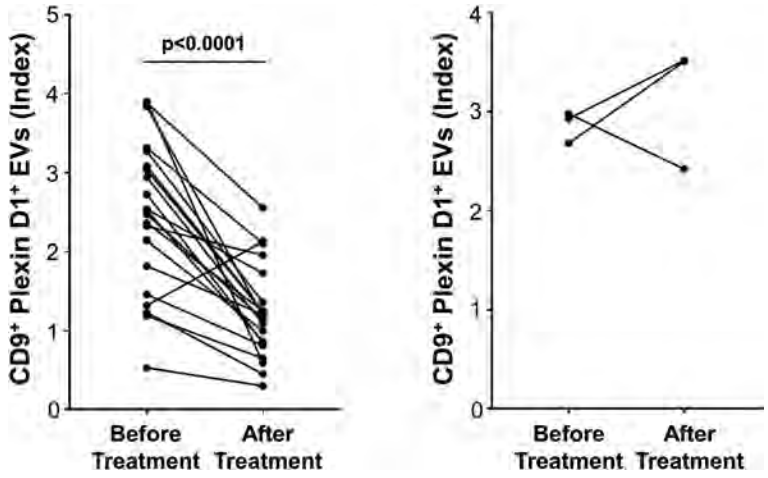
Methods: Serum EVs were purified by size exclusion chromatography using sera of 10 PM/DM, 23 patients with other autoimmune diseases and 10 healthy controls (HC). Comprehensive proteomic analysis of serum EVs was performed by liquid chromatography-tandem mass spectrometry (LC/MS). We identified membrane proteins preferentially present in serum EVs of PM/DM patients by bioinformatics and biostatistical analyses. We developed sandwich ELISA for directly detecting serum EVs expressing disease-specific membrane proteins and measured their expression levels using sera of 54 PM/DM, 24 rheumatoid arthritis (RA), 20 systemic lupus erythematosus (SLE), 13 systemic sclerosis patients, and 36 HC.

Results: LC/MS analysis identified 1,220 proteins in serum EVs. From the volcano plots combining different bioinformatics analyses (DAVID gene ontology and UniProtKB/Swiss-prot), we identified 5 membrane proteins as significantly upregulated in serum EVs of PM/DM patients. Of these, Plexin D1 was enriched in those from PM/DM patients relative to HC (p=0.0237) or patients without PM/DM (p=0.0593). Using our sandwich ELISA, we found that levels of Plexin D1-positive EVs (Plexin D1$^+$ EVs) in serum were significantly greater in PM/DM patients than in HC (p=0.0016), RA (p< 0.0001) or SLE patients (p< 0.0001). Serum levels of Plexin D1$^+$ EVs were greater in those PM/DM patients with muscle pain or weakness (p=0.0428). Serum levels of Plexin D1$^+$ EVs were correlated with levels of aldolase (r_s=0.481, p=0.027), total blood cells (r_s=0.381, p=0.046), neutrophils (r_s=0.450, p=0.019), and platelets (r_s=0.408, p=0.031) in PM/DM patients. Finally, serum levels of Plexin D1$^+$ EVs decreased significantly in patients with PM/DM in clinical remission after treatment (p< 0.0001).

Conclusion: We have identified levels of circulating Plexin D1$^+$ EVs as a novel serum biomarker for PM/DM.



Serum levels of Plexin D1-positive EVs are higher in PM/DM patients with associated muscle pain or weakness



Serum levels of Plexin D1-positive EVs are decreased in PM/DM patients after treatment. Change of serum levels of CD9+ Plexin D1+ EVs in PM/DM patients after treatment in 21 PM/DM patients who achieved clinical remission (left) and 3 PM/DM patients who did not (right).

Disclosure: K. Uto, None; **K. Ueda**, None; **T. Okano**, None; **K. Akashi**, None; **S. Takahashi**, None; **Y. Nakamachi**, None; **T. Imanishi**, None; **S. Kawano**, None; **Y. Yano**, None; **J. Saegusa**, None.

Abstract Number: 0443

Safety and Efficacy of Belimumab in the Treatment of Adult Idiopathic Inflammatory Myositis (Polymyositis and Dermatomyositis)

Priyal Chadha[1], Sonali Narain[2], Preeya Nandkumar[3], Cristine Sison[4], Elena Schiopu[5], Todd Levine[6], James Tsang[7] and **Galina Marder**[8], [1]SUNY Upstate Medical University, Syracuse, NY, [2]Northwell Health, Great Neck, NY, [3]Division of Rheumatology, Department of Medicine, Northwell, Great Neck, NY, [4]Biostatistics Unit , Department of Molecular Medicine, Feinstein Institutes for Medical Research at Northwell Health, Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [5]University of Michigan, Ann Arbor, MI, [6]Phoenix Neurological Associates, Phoenix, AZ, [7]Center for Research Informatics & Innovation (CRII), Feinstein Institute for Medical Research at Northwell Health, Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [8]Division of Rheumatology, Department of Medicine, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Muscle Biology, Myositis & Myopathies (0441–0444)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Treatment of Idiopathic Inflammatory Myositis (IIM) includes steroids and immunosuppressive agents. Targeting IL6, IL1, TNF for treatment of IIM has not been successful, and the role of B-cell depleting therapy remains uncertain. This study was designed to assess the safety and efficacy of belimumab for IIM patients.

Methods: We conducted a 40-week multicenter randomized, double blind, placebo controlled clinical trial with a 24-week open label extension of intravenous (IV) belimumab for adult patients with refractory IIM. All patients met Peter and Bohan criteria and ACR 2017 classification criteria of polymyositis / dermatomyositis (PM/DM) with PM diagnosis adjudication. Refractory IIM was defined as inadequate response/ intolerance to 3 months of glucocorticoids and/or at least one immunosuppressive agent (IS). Standard Core Set Measures (CSM) with MMT8 < 125/150 were used to define active disease. Patients on standard of care (SoC) therapy were randomized 1:1 to IV belimumab 10mg/kg or placebo for 40 weeks followed

	Belimumab N= 9	SoC N= 6
Age (years)		
Mean (SD)	58.7 (14)	47 (11.5)
Median (range)	46 (28-64)	47 (31-65)
Gender (n)		
Male	3 (33.3%)	1 (16.7 %)
Female	6 (66.7 %)	5 (83.3%)
Race		
African American	6 (66.7 %)	0
White	3 (33.3%)	3 (50%)
Asian - Central/South Asian Heritage	0	2 (33.3%)
White - Arabic/North African	0	1(16.7 %)
Subtype of IIM %		
DM	2 (22.2%)	2 (33.3 %)
PM	7 (77.8%)	4 (66.7%)
Disease duration (years)		
Mean (SD)	2.6 (3.3)	5.3 (4.4)
Median (range)	1.5 (0-9)	4.5 (1-13)
Serological profile		
ANA and other MAA*	5 (55.6%)	5 (83.3 %)
SSA/SSB	4 (44.4%)	2 (33.3%)
MSA ** (Anti-Jo-1, Anti-PL-7, Anti-PL-12, Anti-EJ, Anti-OJ, Anti-KS, Anti-SPR, Anti-Mi-2, NXP2 ab, anti HMGCR)	3 (33.3%)	1(16.7 %)
% double positive	5 (55.6%)	3 (50.0 %)
Clinical characteristics		
Failed <1 IS	6 (66.7%)	1 (16.7 %)
Failed > 1 IS	3 (33.3%)	5(83.3%)
Baseline prednisone dose		
Mean dose (mg)(SD)	9.58 (4.76)	5.67 (4.71)
Concurrent immunosuppressive agents		
% Prednisone	6 (66.7 %)	3 (50.0%)
% MTX^, MMF^^ or AZA^^^	7 (77.8 %)	4 (66.7%)
% IVIG	5 (55.6 %)	5 (83.3 %)
% on ≥2 (including IVIG)	3 (33.3%)	3 (50.0%)
CSM (mean (SD)) by MDAAT***		
Patient global VAS**** (0-10)	5.3 (1.6)	6.5 (3.2)
MD global VAS (0-10)	4.1 (1.9)	5.4 (0.7)
MMT (0-150)	118.9 (5.8)	113.7 (8.2)
Muscle enzyme - CPK (U/L)	2043.8 (1933)	515 (623.8)
Muscle activity score VAS (0-10)	4.456 (1.182)	5.483 (0.494)
Extra-muscular disease activity VAS (0-10)	0.68 (1.4)	1.37 (1.4)
Cutaneous VAS (0-10)	0.278 (0.359)	1.867 (1.897)
Pulmonary VAS (0-10)	0.400 (0.050)	0.917 (0.050)
HAQ***** (0-3)	1.38 (0.72)	1.15(0.50)
MDI ******(0-10)	0.911(1.036)	1.900 (1.719)

* MAA – Myositis associated antibodies ,** MSA- Myositis specific antibodies,*** MDAAT -Myositis Disease Activity Assessment Tool, **** VAS- visual analogue score, ***** HAQ – Health Assessment Questionnaire, ******MDI - Muscle damage index HAQ
^ MTX-Methotrexate, ^^ MMF – Mycophenolate Mofetil, ^^^AZA- Azathioprine

Baseline demographics and clinical characteristics of Beliumumab and SoC

by 24 weeks belimumab 10mg/kg in open label phase. The primary outcomes were the proportions of patients reaching a Definition of Improvement (DOI) and Total Improvement Score (TIS) at week 40 in belimumab arm vs. SoC alone arm. Secondary endpoints included DOI, TIS at week 64, CSM changes, prednisone dose change, safety profiles at 40 and 64

Time point	Response instruments	Belimumab	SOC	P value
Definition of improvement DOI (%)		**N 8**	**N 6**	
40 weeks (n / %)	*DOI w 40*	3 /8 (37.5%)	1 /6 (16.7%)	0.60 (NS)
		N 7	**N 5**	
64 weeks (n / %)	*DOI w 64*	3 /7 (42.9 %)	0 / 0%	0.23 (NS)
Total improvement score (TIS)*				
40 weeks (score)		**N 8**	**N 6**	
	Mean TIS (SD)	38.8 (24.9)	37.9 (5.8)	
	Median TIS (range)	41.25 (5-72.5)	35 (32.5-47.5)	0.89 (NS)
64 weeks (score)		**N 7**	**N 5**	
	Mean TIS (SD)	41.1(25.3)	36.01 (13.1)	
	Median TIS (range)	40 (5-72.5)	33.75	0.76 (NS)
% of patient reaching TIS				
40 weeks (n / %)		**N 8**	**N 6**	
	None or minimal	3/8 (37.5%)	4/6 (66.7%)	
	Moderate + major	5/8 (62.5%)	2/6 (33.3%)	0.59 (NS)
64 weeks (n / %)		**N 7**	**N 5**	
	None or minimal	3/7 (42.9 %)	3/5 (60%)	
	Moderate + major	4/7 (57.1 %)	2/5 (40%)	0.99 (NS)
* 2016 ACR/EULAR Clinical Response Criteria (no response, minor, major, and moderate response)				

Disease response indexes (DOI and TIS)

	Belimumab	SoC
SAE	1 perforated appendicitis *	0
Infections		
Upper respiratory infection	3	5
Infection after urethroplasty	1	0
Urinary Tract Infection	0	1
Adjustment disorder	1***	0
Transaminitis	1	0
Other	2 arthralgia/myalgia 1 rash 4 gout flare ** 2 leg swelling 1 fracture 1 actinic keratosis 1 hypertension 1 hyperglycemia 1 hyperlipidemia 1 GERD 1 stye	1 arthralgia 1 rash 2 lightheadedness ** 1 migraine 3 sleepiness ** 1 UC flare 1 candida esophagitis 1 cough 1 pulmonary consolidation 1 shoulder dislocation 1 GERD 1 cataract
* the patient received only 3 doses of belimumab and was not included in efficacy analysis ** including multiple events per patient *** not related to treatment arm assignment- belimumab was continued		

Incidence of Serious Adverse Events (SAE) and Adverse Events

weeks. Descriptive statistics (means, SDs, medians, ranges, frequencies, proportions) are presented. The Mann-Whitney test and Fisher's exact test were used to analyze continuous and categorical variables, respectively.

Results: 16 patients were randomized, 15 received at least 4 doses of belimumab or placebo to be included in the analysis (9 belimumab; 6 placebo) (Baseline characteristics are in Table 1).

The proportion of patients reaching DOI by week 40 was numerically higher in belimumab arm (belimumab 37.5% / SoC 16.7 %). The mean TIS was similar between 2 groups (mean (SD) belimumab 38.8 (24.9)/ SoC 37.9 (5.8). At week 64, 42.9 % of patients on belimumab achieved DOI, while no patients in the original SoC arm did. Numerically more patients on belimumab had moderate or major improvement than on SoC (belimumab 62.5%/ SoC 33.3%) at week 40, and (belimumab 57.1% /SoC 40.0 %) at week 64. Of 15 patients only 2 had a major response at week 40 (TIS= 72.5) that sustained to week 64; both had received belimumab. Infections were evenly distributed between two arms. One patient in the belimumab arm had an adjustment disorder exacerbation, determined not to be belimumab related and the drug was continued with no interruption (Table 3).

Conclusion: In this 40-week multicenter randomized, double blind placebo-controlled trial with 24 weeks open label phase, we observed numerically higher proportion of patients on belimumab reaching DOI vs. on SoC only arm. A higher proportion of patients on Belimumab achieved sustained moderate or major TIS at 40 and 64 weeks compared to SOC. Detected differences were not statistically significant, however the sample size was small.

Disclosure: P. Chadha, None; **S. Narain**, None; **P. Nandkumar**, None; **C. Sison**, None; **E. Schiopu**, Octapharma, 2, 5; **T. Levine**, None; **J. Tsang**, None; **G. Marder**, GlaxoSmithKline, 5.

Abstract Number: 0444

COVID-19 Vaccination in Autoimmune Disease (CoVAD) Study: Interim Analysis of Safety in Idiopathic Inflammatory Myopathies from a Large Multicentre Global Survey

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Muscle Biology, Myositis & Myopathies (0441–0444)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

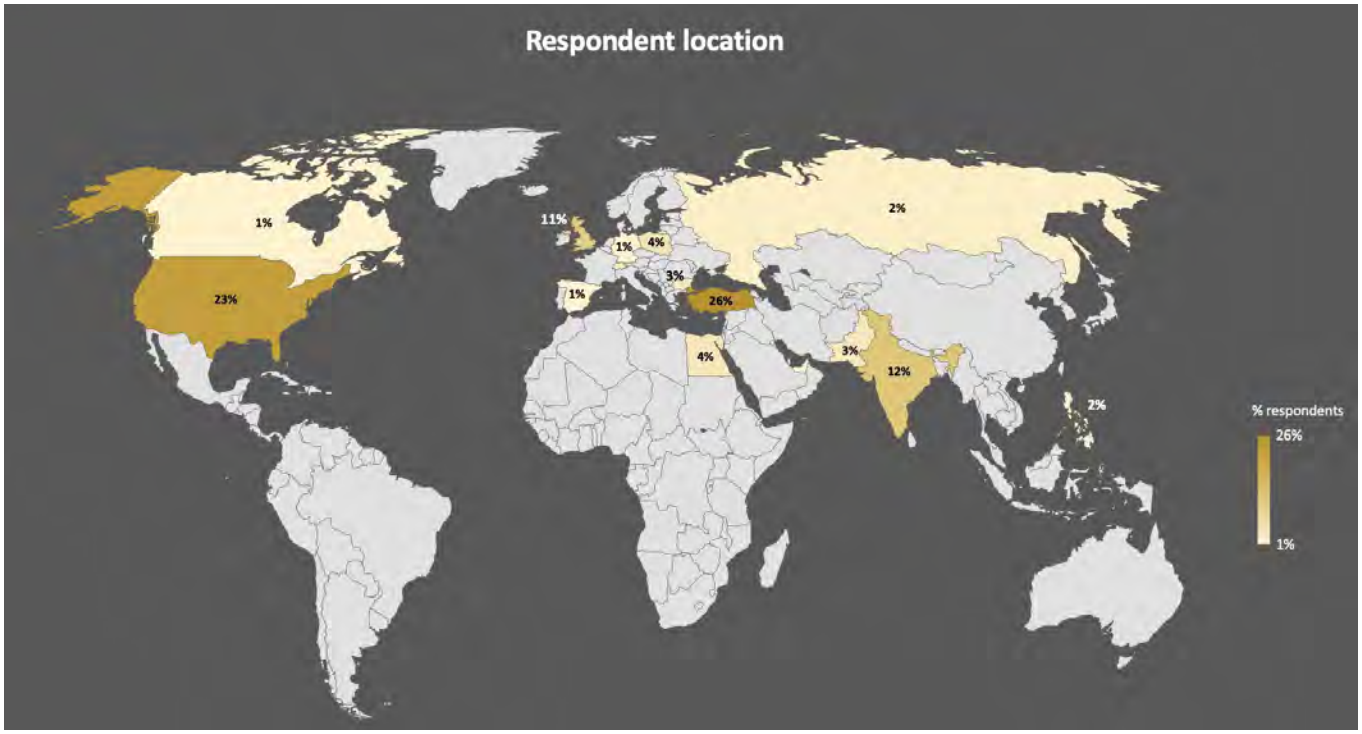
Background/Purpose: Numerous Covid-19 vaccines have demonstrated efficacy and safety against SARS-CoV-2 in general population. Despite favorable adverse effect (ADRs) profile of vaccines, there have been concerns regarding activation of aberrant immune responses. Moreover, vaccine safety data in idiopathic inflammatory myopathies (IIM)

Table 1. Population characteristics

Variable	Total N 5927 (%)	IIM 979 (%)	Other AID 2566 (%)	Healthy controls 2382
Age (mean)	42.6 years	60.0	44.6	34.7
Gender				
M:F	0.4:1	0.3:1	0.24:1	0.56:1
Ethnicity (n=4009)				
Caucasian (White)	2441 (60.89%)	747 (76.3)	731 (28.5%)	1049 (44.0%)
African American or of African origin (Black)	45 (1.12%)	37 (3.8%)	8 (0.31%)	9 (0.38%)
Asian	982 (24.49%)	43 (4.4%)	276 (10.8%)	669 (28.1%)
Hispanic	42 (1.05%)	33 (3.4%)	7 (0.27%)	11 (0.46%)
Native American/Indigenous/Pacific Islander	4 (0.10%)	0 (0%)	1 (0.04%)	3 (0.13%)
Do not wish to disclose	304 (7.58%)	11 (1.1%)	108 (4.2%)	186 (7.8%)
Other	191 (4.76%)	14 (1.4%)	42 (1.6%)	138 (5.8%)
Vaccine taken (n=4693)				
Pfizer-BioNTech	1370 (29.19%)	480 (49.0%)	515 (20.1%)	437 (18.3%)
Oxford/Astra Zeneca	421 (8.97%)	81 (8.3%)	180 (7.0%)	173 (7.3%)
Johnson & Johnson (J&J)	18 (0.38%)	10 (1.0%)	5 (0.19%)	5 (0.21%)
Moderna	590 (12.57%)	360 (36.8%)	170 (6.6%)	102 (4.3%)
Novavax	3 (0.06%)	0 (0%)	178 (6.9%)	0 (0%)
Covishield	576 (12.27%)	29 (3.0%)	3 (0.12%)	373 (15.7%)
Covaxin (Bharat Biotech)	80 (1.70%)	10 (1.0%)	30 (1.2%)	41 (1.7%)
Sputnik	115 (2.45%)	4 (0.41%)	25 (0.97%)	86 (3.6%)
Sinopharm	1399 (29.81%)	4 (0.41%)	263 (10.2%)	1132 (47.5%)
I am not sure	28 (0.60%)	0 (0%)	25 (0.97%)	15 (0.63%)
Other	93 (1.98%)	0(0%)	52 (2.0%)	41 (1.7%)
Diagnosis (n=4693)				
No autoimmune disease	2382 (40.1%)	Figure 1	NA	NA
Dermatomyositis	341 (7.27%)	341 (34.8%)		
Polymyositis	185 (3.94%)	185 (18.8%)		
Inclusion Body Myositis	259 (5.52%)	259 (26.4%)		
Anti-synthetase syndrome	91 (1.94%)	91 (9.2%)		
Necrotizing myositis	44 (0.94%)	44 (4.4%)		
Juvenile dermatomyositis	11 (0.23%)	11 (1.1%)		
Overlap Myositis with lupus or Sjogren or Systemic sclerosis or Rheumatoid arthritis	48 (1.02%)	48 (4.9%)		
Mixed Connective Tissue Disease	73 (1.56%,)		73 (2.84%)	
Systemic Sclerosis	97 (2.07%)		97 (3.78%)	
Sjogren syndrome	104 (2.22%)		104 (4.05%)	
Rheumatoid Arthritis	369 (7.86%)		369 (14.4%)	
Vasculitis	53 (1.13%)		53 (2.07%)	
Systemic lupus erythematosus	147 (3.13%)		147 (5.73%)	
Ankylosing Spondylitis or Psoriatic arthritis	149 (3.17%)		149 (5.81%)	
Inflammatory bowel disease	159 (3.39%)		159 (6.20%)	
Multiple sclerosis	20 (0.43%)		20 (0.78%)	
Myasthenia gravis	36 (0.77%)		36 (1.40%)	
Pernicious anemia	8 (0.17%)		8 (0.31%)	
Hemolytic anemia / idiopathic thrombocytopenic purpura (ITP)	7 (0.15%)		7 (0.27%)	
Thyroid	467 (9.95%)		467 (18.2%)	
Type 1 Diabetes	71 (1.51%)		71 (2.77%)	
Polymyalgia Rheumatica (PMR)	20 (0.21%)		20 (0.78%)	
Other autoimmune disease	483 (10.29%)		786 (29.5%)	
Discontinued medicines before vaccination		**125**	157	
Duration of discontinuing medicines (mean)		**17.9 days**	26.8 days	

and other systemic autoimmune diseases (AID) is rather limited. We aimed to evaluate safety of Covid-19 vaccines in IIMs patients in comparison with other AIDs and non-autoimmune disease controls using a patient reported world-wide electronic survey by an international CoVAD study group.

Methods: We developed an extensive self-report e-survey to assess safety of the COVID-19 vaccine in IIMs and other AIDs and non-autoimmune controls. The questionnaire was pilot tested, validated and translated into 15 languages on surveymonkey.com, and vetted by international experts. The survey questions were designed to evaluate previous COVID infection, current vaccination status, as well as short term (within one week) as well as long term (1-12 months) adverse drug reactions (ADRs) following vaccine administration. Rheumatologists from >50 centers conducted the e-survey to their patients as well as their non-autoimmune family members. In addition, the survey was floated on social



Respondent location

media platforms and online patient support group members across the world. We analyzed the data from baseline survey (Feb – May 2021, 7-day ADRs) for descriptive statistics as well as inter-group comparison using chi-square or t-test.

Results: A total of 7467 subjects attempted the survey with mean age of 42.6 years, 71.4% female, 60.9% Caucasians with most patients from US, European Union and India (table 1, figure 1). Among these 5219 (69.9% of respondents) were fully vaccinated and 1540 (20.2%) were not vaccinated with vaccine hesitancy (657,42.7%) and non-availability (534, 34.7%) being the most common reasons. Among 5927 vaccinated respondents, 979 (16.5%) had IIM, 2566 (43.3%) other AIDs, and 2382 (40.1%) were controls.

Respondents with IIM were elder (60 years) than other AIDs and controls (42.6 and 34.7 year respectively) (Table 1, Figure 1). A total of 875 (15.3%) respondents got Covid-19 infection, with significantly lower proportion of IIM patients (76, 2.2%) as compared to AIDs (403, 15.7%) and controls (404, 16.9%), $p < 0.0001$. Notably IIM patients were also less likely to be symptomatic than AIDs and controls when they got infected [RR 0.6 (0.4-1.0), 0.4 (0.3-0.7)].

Overall, 51.0% IIM had some symptoms (minor ADRs) after vaccination with only 6.0% being severe ADRs. IIM patients were equally prone to minor reactions as compared to controls (Table 2). However, they were more prone to anaphylaxis, marked dyspnea, and severe rashes. Overall, IIM exhibited higher prevalence of severe ADRs as compared with other AIDs. However, there was no difference in hospitalization among the groups.

Conclusion: IIMs patients had a modest increase in severe ADRs 7-day post vaccination as compared to controls as well as other autoimmune diseases, although not contributing to increased hospitalization. The survey in ongoing and will have much larger patient population and longitudinal results in future.

Disclosure: L. Gupta, None; **J. Lilleker**, Orhce, 1, Biogen, 6; **V. Agarwal**, None; **S. Kardes**, None; **M. Milchert**, None; **T. Gheita**, None; **B. Salim**, None; **T. Velikova**, None; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2; **H. Chinoy**, None; **V. Aggarwal**, None; **R. Aggarwal**, Mallinckrodt,

Table 2: COVID infection and effects of COVID-19 vaccination in IIM versus Controls and other AIDs

	IIM n=979, %	Controls n=2382	Other AID 2566	RR, CI (IIM versus Controls and Other AID)
COVID infection	76 (2.2%)	404 (16.9%)****	403 (15.7%) ****	0.5 (0.4-0.6), 0.5 (0.4-0.7)
Symptoms	89 (9.1%)	377 (15.8%)*	387 (15.1%)****	0.6 (0.4-1.0), 0.4 (0.3-0.7)
Injection site pain	658 (67.2%)	1415 (59.4%)****	953 (37.1%)****	1.3 (1.1-1.5), 2.5 (2.1-2.8)
Minor adverse reaction to vaccine	500 (51.0%)	1183 (49.7%)	852 (33.2%)****	NS, 1.7 (1.5-1.9)
Myalgia	114 (11.6%)	307 (12.9%)	223 (8.7%)**	NS, 1.3 (1.1-1.5)
Body ache	195 (19.9%)	473 (19.9%)	346 (13.5%)****	NS, 1.4 (1.2-1.6)
Fever	114 (11.6%)	428 (18.0%)****	254 (9.9%)	0.7 (0.6-0.8), NS
Chills	155 (15.8%)	271 (11.4%)***	209 (8.1%)****	1.3 (1.2-1.5), 1.6 (1.4-1.9)
Nausea and Vomiting	269 (27.5%)	109 (4.6%)****	90 (3.5%)****	3.0 (2.7-3.3), 3.4 (3.1-3.7)
Headache	234 (23.9%)	467 (19.6%)**	354 (13.8%)****	1.2 (1.1-1.3), 1.6 (1.4-1.8)
Rashes	24 (2.5%)	18 (0.76%)***	27 (1.1%)**	1.9 (1.5-2.5), 1.7 (1.2-2.2)
Fatigue	295 (30.1%)	572 (24.0%)***	423 (16.5%)****	1.3 (1.1-1.3), 1.3 (1.2-1.3)
Diarrhoea	18 (1.8%)	43 (1.8%)	46 (1.8%)	NS
Abdominal pain	24 (2.5%)	27 (1.1%)**	39 (1.5%)	1.6 (1.2-2.1), NS
High pulse rate or palpitations	20 (2.0%)	53 (2.2%)	52 (2.0%)	NS
Rise in Blood pressure	1 (0.10%)	18 (0.76%)*	20 (0.78%)*	0.2 (0.03-0.9), 0.2 (0.0-0.8)
Fainting	2 (0.20%)	7 (0.29%)	8 (0.31%)	NS
Difficulty in breathing	6 (0.61%)	19 (0.80%)	15 (0.58%)	NS
Dizziness	51 (5.2%)	92 (3.9%)	81 (3.2%)**	NS, 1.4 (1.1-1.8)
Chest pain	12 (1.2%)	26 (1.1%)	23 (0.905)	NS
Other	63 (6.4%)	112 (4.7%)*	114 (4.4%)	1.3 (1.0-1.5)
Major ADRs	59 (6.0%)	39 (1.6%)****	61 (2.3%)****	2.1 (1.8-2.5), 1.8 (1.4-2.1)
Anaphylaxis	7 (0.72%)	4 (0.17%)*	4 (0.16%)****	2.2 (1.2-2.9), 2.3 (1.3-3.1)
Marked difficulty in breathing	13 (1.3%)	14 (0.59%)*	11 (0.43%)**	1.7 (1.1-2.3), 2.0 (1.3-2.7)
Throat closure	7 (0.72%)	4 (0.17%)*	10 (0.40%)	2.2 (1.2-2.9), NS
Severe rashes	7 (0.72%)	6 (0.25%)*	7 (0.27%)	1.9 (1.0-2.6), NS
Other	40 (4.1%)	22 (0.92%)****	33 (1.3%)****	2.3 (1.8-2.7), 2.0 (1.6-2.5)
Hospitalization	7 (0.72%)	7 (0.29%)	11 (0.43%)	NS

*P<0.05, **p<0.01, **p<0.001, p<0.0001

1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2.

Abstract Number: 0445

Safety and Efficacy of Denosumab vs Risedronate in Patients with Glucocorticoid-Induced Osteoporosis and Rheumatoid Arthritis

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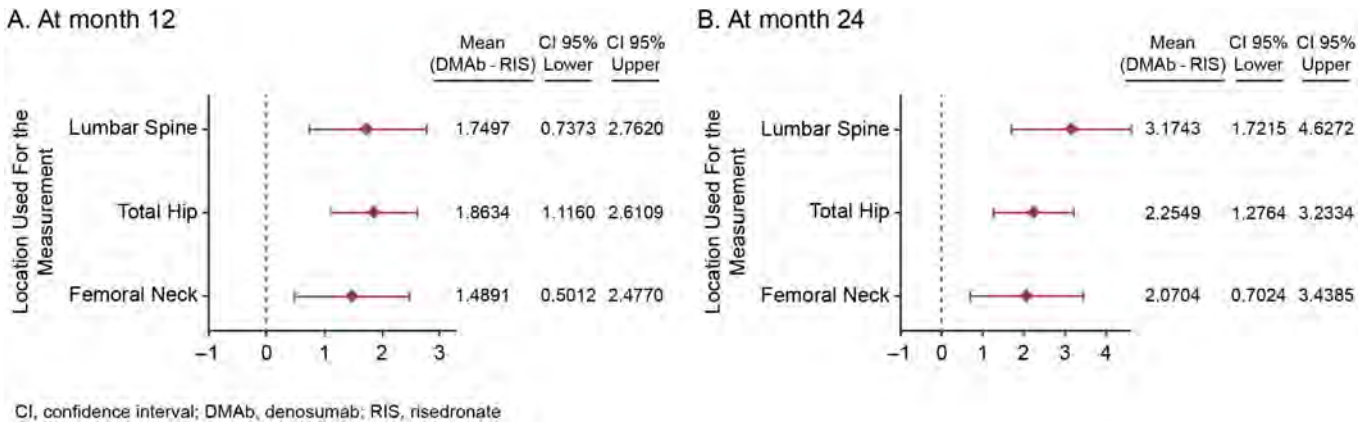
SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (0445–0448)

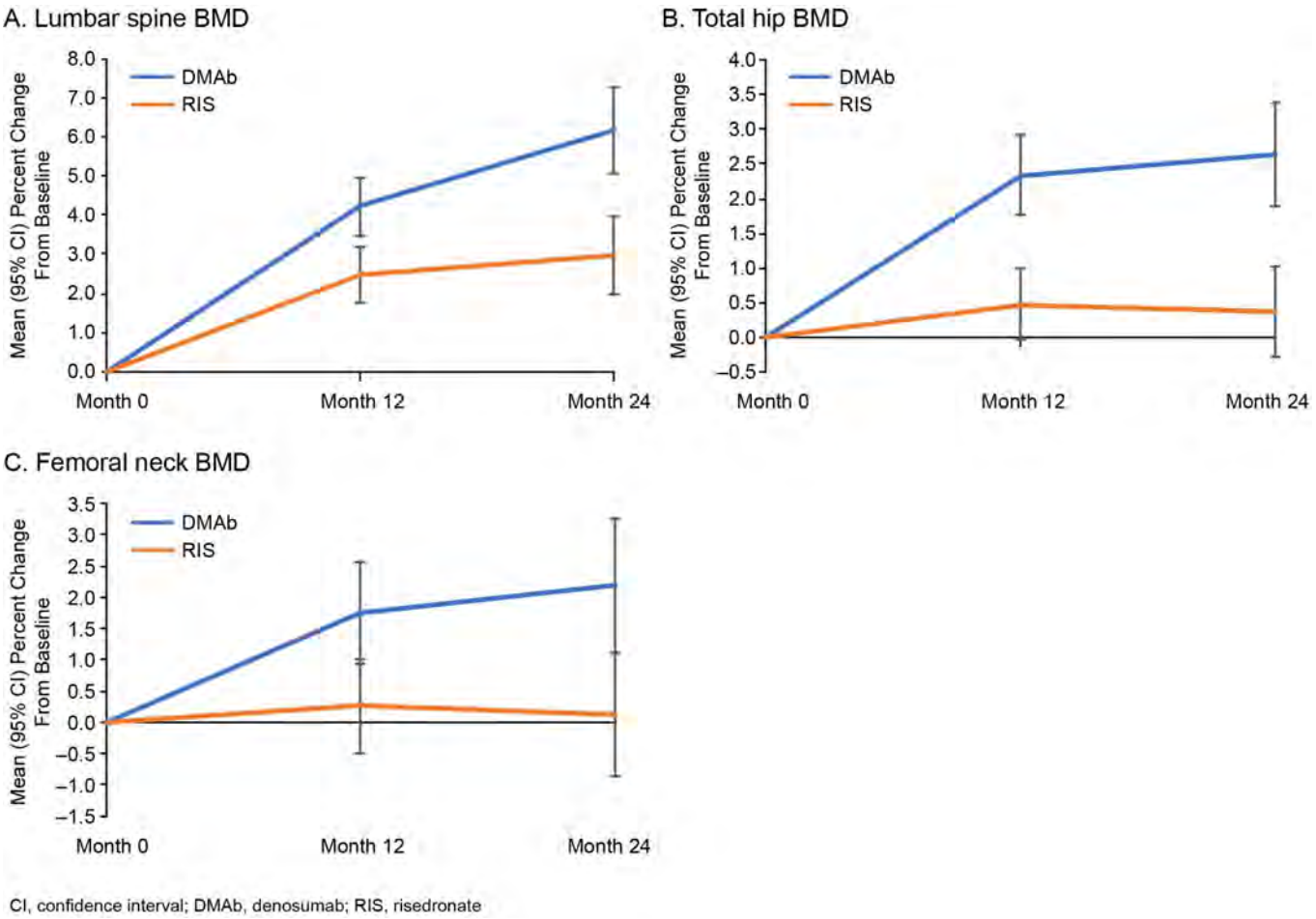
Session Type: Abstract Session

Session Time: 9:30AM–10:30AM



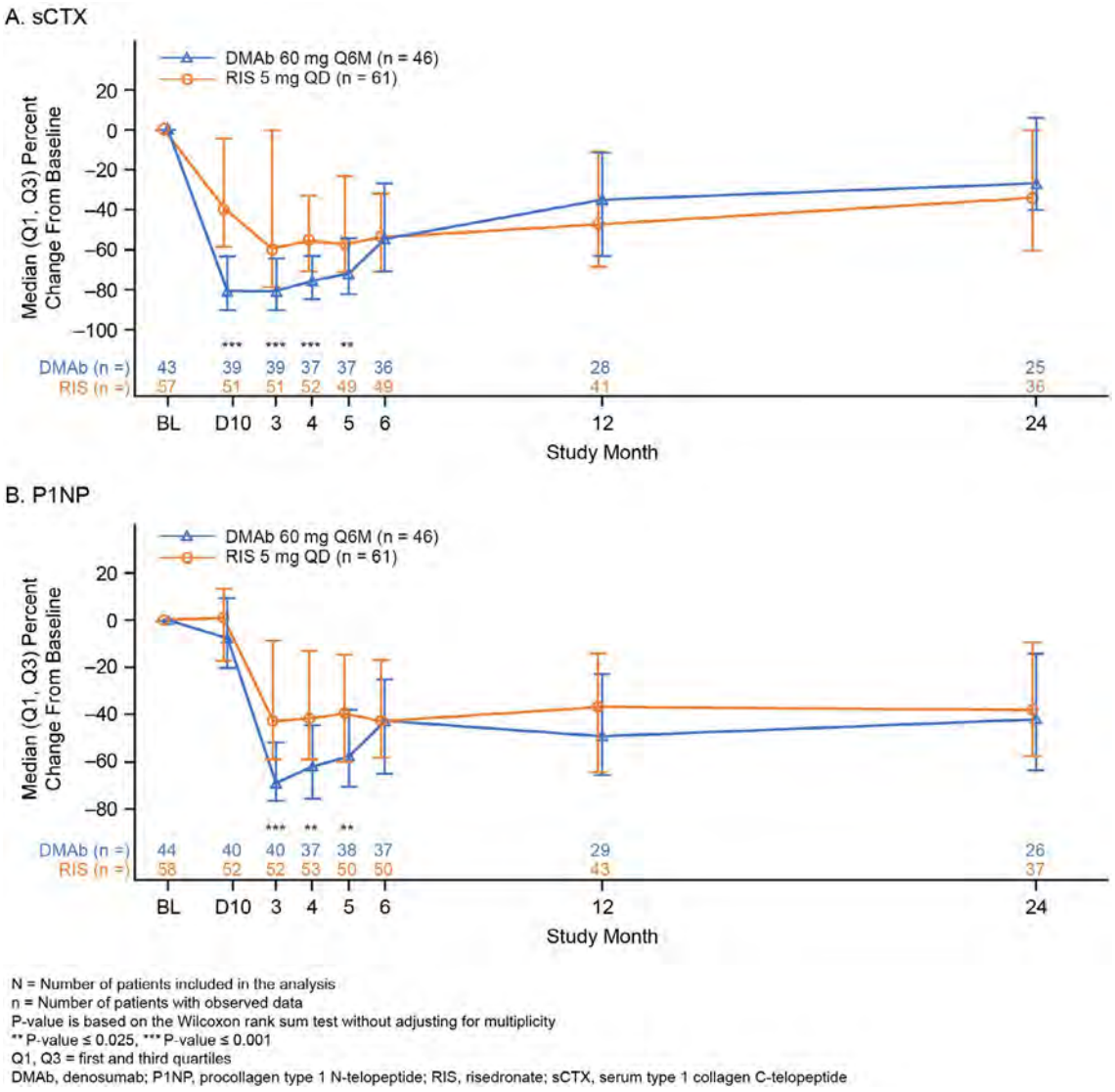
CI, confidence interval; DMAb, denosumab; RIS, risedronate

Figure 1. Mean difference in percent change from baseline in BMD between DMAb and RIS.



CI, confidence interval; DMAb, denosumab; RIS, risedronate

Figure 2. Percent change from baseline in BMD.



N = Number of patients included in the analysis
n = Number of patients with observed data
P-value is based on the Wilcoxon rank sum test without adjusting for multiplicity
** P-value ≤ 0.025, *** P-value ≤ 0.001
Q1, Q3 = first and third quartiles
DMAb, denosumab; P1NP, procollagen type 1 N-telopeptide; RIS, risedronate; sCTX, serum type 1 collagen C-telopeptide

Figure 3. Percent change from baseline in bone turnover markers

Background/Purpose: Denosumab (DMAb) is approved for the treatment of glucocorticoid (GC)–induced osteoporosis (GiOP). In a phase 3, international, active-controlled, double-blind, double-dummy study, treatment with DMAb was superior to treatment with risedronate (RIS) in terms of increase in BMD at both lumbar spine (LS) and total hip (TH) in GC-treated patients with osteoporosis (Saag KG et al *Arthritis Rheumatol*. 2019;71:1174–1184). In this post hoc subgroup analysis, we evaluated the efficacy of DMAb vs RIS in patients with GiOP and RA.

Methods: This post hoc subgroup analysis included both GC-initiating and GC-continuing patients (≥ 7.5 mg daily prednisone or equivalent for < 3 and ≥ 3 months before screening, respectively) with GiOP and RA who were randomized 1:1 to receive DMAb (60 mg every 6 months) or RIS (5 mg once daily) for 24 months. All patients received daily calcium (≥ 1,000 mg) and vitamin D (≥ 800 IU). The primary objective of this analysis was to test if increases in LS BMD by DXA at month 12 were greater with DMAb vs RIS based on the mean difference in percent change from baseline. Secondary objectives included between-group comparisons of the mean percent change from baseline in LS, TH, and femoral neck (FN) BMD and in serum type 1 collagen C-telopeptide (sCTX) and procollagen type 1 N-telopeptide (P1NP) at months 12 and 24; safety was assessed through the incidence of treatment-emergent adverse

events (TEAEs). BMD changes were analyzed using repeated measures analysis of covariance (ANCOVA). Serum CTX and P1NP were reported as median and interquartile ranges.

Results: A total of 300 patients (DMAb = 143; RIS = 157) were included in this analysis. Mean (SD) prednisone-equivalent doses at baseline for the DMAb and RIS groups were 10.5 (4.2) mg and 10.3 (4.6) mg, respectively. The mean difference (95% CI) in percent change from baseline in BMD between the DMAb and RIS groups was significant at LS, TH, and FN at both timepoints assessed (month 12 LS: 1.8% [0.7–2.8]; Figure 1). The mean percent change from baseline in BMD at month 24 was significant at LS, TH, and FN with DMAb and only at LS with RIS (Figure 2). A significant decrease in the sCTX and P1NP levels was observed in DMAb vs RIS patients during the first 5 months; however, the percent changes from baseline for both sCTX and P1NP were not significantly different between the DMAb and RIS groups at months 12 and 24 (Figure 3). The overall incidence of TEAEs was similar between the 2 groups (DMAb: 78.3%; RIS: 75.8%), including that of TEAEs of interest—infections (DMAb: 30.8% vs RIS: 34.4%) and cardiac disorders (DMAb: 4.9% vs RIS: 6.4%). The incidence of osteoporotic fractures was numerically lower in the DMAb (n = 9; 6.3%) vs RIS (n = 15; 9.6%) group.

Conclusion: Compared with RIS, treatment with DMAb showed significantly larger gains in BMD in patients with GiOP and RA receiving GC treatment. The overall safety profile was similar for both treatments.

Disclosure: J. Adachi, Amgen, 2, 5, 6, Lilly, 2; **A. Chines**, Amgen, 3, 11; **S. Huang**, Amgen, 3, 11; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5; **W. Lems**, Amgen, 6, UCB, 6, Lilly, 6, Merck, 6, Pfizer, 6, Galapagos, 6; **P. Geusens**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Lilly, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB Pharma, 2, 5, 6, Will, 2, 5, 6.

Abstract Number: 0446

Clinical Characteristics, Including History of Myocardial Infarction and Stroke, Among US PMO Women Initiating Treatment with Romosozumab and Other Anti-osteoporosis Therapies

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (0445–0448)
Session Type: Abstract Session
Session Time: 9:30AM–10:30AM

Background/Purpose: This study is an ongoing USFDA post-marketing requirement (2020-2024) to assess the impact of boxed warning on romosozumab (romo) treatment and the feasibility of future comparative safety analysis using real-world data. As of March 2021, about 14,958 person-years of exposure to romo have been reported in US. Results from the first interim report utilized Optum claims and supplemental EHR data covering the period between April 2019–March 2020.

Methods: This is a retrospective, repeated analysis within five 1-year (yr) blocks of calendar time following marketing approval of romo in 2019. Women at least 55 yrs old who had newly initiated romo, denosumab (dmab), zolendronate (zol), PTH analogues, or oral bisphosphonates (BPs) were included. We describe the proportion of women who experienced a myocardial infarction (MI) or stroke in the year before drug initiation, as well as history of cardiovascular

Table 1. Selected baseline demographics and health care utilization among new users of romo and other OP treatments

	Romosozumab (N = 1946)	Denosumab (N = 16 279)	Zoledronate (N = 6292)	PTH Analogs* (N = 1517)	Oral BPs (N = 38 544)
Mean age (SD) (years)	74.8 (8.8)	74.6 (8.1) SMD 0.02	72.9 (7.9) **SMD 0.18**	70.7 (8.7) **SMD 0.38**	72.1 (7.7) **SMD 0.26**
55-64 years, N (%)	266 (13.7)	1718 (10.6) SMD 0.08	896 (14.2) SMD -0.01	405 (26.7) **SMD -0.28**	5683 (14.7) SMD -0.03
65-74 years, N (%)	686 (35.3)	6532 (40.1) SMD -0.08	2784 (44.2) **SMD -0.15**	596 (39.3) SMD -0.07	19126 (49.6) SMD -0.24
≥ 75 years, N (%)	994 (51.1)	8029 (49.3) SMD 0.03	2612 (41.5) **SMD 0.16**	516 (34.0) **SMD 0.28**	13735 (35.6) **SMD 0.26**
Mean health resource utilization					
Inpatient hospitalizations	0.6	0.3 **SMD 0.21**	0.3 **SMD 0.23**	0.6 SMD 0.01	0.2 **SMD 0.30**
Outpatient visits	44.4	34.9 **SMD 0.22**	34.7 **SMD 0.23**	42.4 SMD 0.05	25.0 **SMD 0.46**
Emergency room visits	1.5	0.7 **SMD 0.28**	0.7 **SMD 0.30**	1.1 **SMD 0.14**	0.5 **SMD 0.35**
Cardiology visits	1.7	0.9 **SMD 0.19**	0.9 **SMD 0.21**	1.1 **SMD 0.15**	0.6 **SMD 0.29**
Electrocardiograms	2.0	1.2 **SMD 0.27**	1.1 **SMD 0.29**	1.4 **SMD 0.21**	0.9 **SMD 0.36**

Abbreviations: PTH: parathyroid hormone; **BP**: bisphosphonates; **SD**: standard deviation; **SMD** = standardized mean difference

*Includes teriparatide and abaloparatide

(CV) diseases, osteoporosis, other comorbidities and concomitant medications, and healthcare utilization using all available historical data up to 19 years. Four pairwise comparisons were conducted to describe the differences in the above histories compared with romo, before and after propensity score (PS) matching. Standardized mean differences (SMD) >0.1 indicated imbalance between groups.

Results: Patients newly initiating romo (N=1,946; mean age 74.8 yr) were older than zol (N=6,292; 72.9 yr), PTH (N=1,517; 70.7 yr), and oral BPs (N=38,544; 72.1 yr). Romo patients had increased prevalence of chronic diseases (eg, hypertension, hyperlipidemia, type II DM) and healthcare utilization, and had more prior fractures and OP treatments (**Table 1-3**). Using all available historical data, the proportion of patients with MI/stroke history was higher in romo patients (9%/11.5%) than dmab (6.8%/8.6%), PTH (7.4%/9.0%), zol (5.9%/7.0%) and oral BPs (5.4%/6.0%) (**Table 2**). When limited to 1 yr before treatment initiation, the proportions of patients with MI/stroke in romo were very low (MI: 0.4%, N=8; stroke: 0.5%, N=9) and similar to other OP treatments (all SMDs< 0.1). All baseline characteristics were balanced after PS matching.

Conclusion: Patients who initiated romo were a high OP-risk population and generally had more comorbidities including CV risk factors. Nevertheless, the low proportion of patients who had a MI/stroke within 1-yr prior to treatment initiation suggests the label boxed warning language may have had the intended effect on patient selection.

Table 2. History of MI, stroke, other cardiovascular diseases and selected comorbidity

	Romosozumab (N = 1946)	Denosumab (N = 16279)	Zoledronate (N = 6292)	PTH Analogs** (N = 1517)	Oral BPs (N = 38544)
MI (recent)[a]	8 (0.4)	48 (0.3)	18 (0.3)	3 (0.2)	89 (0.2)
Stroke (recent)[a]	9 (0.5)	53 (0.3)	23 (0.4)	3 (0.2)	87 (0.2)
MI (past)[b]	176 (9.0)	1,112 (6.8)	369 (5.9)*	113 (7.4)	2,098 (5.4)*
Stroke (past)[b]	223 (11.5)	1,398 (8.6)	440 (7.0)*	136 (9.0)	2,301 (6.0)*
Type II diabetes mellitus	544 (28.0)	3678 (22.6)	1272 (20.2)*	346 (22.8)	9315 (24.2)
Hypertension	1466 (75.3)	11614 (71.3)	4224 (67.1)*	990 (65.3)*	25484 (66.1)*
Hyperlipidemia	1336 (68.7)	11200 (68.8)	4026 (64.0)	928 (61.2)*	24266 (63.0)
Arrhythmia	491 (25.2)	2858 (17.6)*	1012 (16.1)*	274 (18.1)*	4647 (12.1)*
COPD	595 (30.6)	3723 (22.9)*	1308 (20.8)*	377 (24.9)	7265 (18.8)*
Asthma	345 (17.7)	2146 (13.2)	914 (14.5)	255 (16.8)	4210 (10.9)*
Dementia	219 (11.3)	1116 (6.9)*	388 (6.2)*	87 (5.7)*	1776 (4.6)*
Depression	702 (36.1)	4890 (30.0)	1970 (31.3)	597 (39.4)	10048 (26.1)*
Smoking	759 (39.0)	4940 (30.3)*	1919 (30.5)*	515 (33.9)*	10974 (28.5)*

* Signals prematching imbalance, based on SMD > 0.10 with romosozumab > comparator

** Includes teriparatide and abaloparatide

Abbreviations: **BP** = bisphosphonates; **MI** = myocardial infarction; **PTH** = parathyroid hormone; **SMD** = standardized mean difference; **COPD** = chronic obstructive pulmonary disease

[a] within 1 year before treatment initiation; [b] using all available historical data

Table 3. Osteoporosis Related History and Treatments Among Patients Exposed to Romosozumab and other OP Meds

	Romosozumab (N = 1946)	Denosumab (N = 16279)	Zoledronate (N = 6292)	PTH Analogs (N = 1517)	Oral BPs (N = 38544)
Osteoporosis diagnosis,N (%)	1,732 (89.0)	15,066 (92.6)	5,497 (87.4)	1,462 (96.4)	26,095 (67.7)*
Hip fracture,N (%)	185 (9.5)	1,127 (6.9)	332 (5.3)*	204 (13.5)	1,491 (3.9)*
Vertebral fracture,N (%)	417 (21.4)	2,491 (15.3)*	775 (12.3)*	480 (31.6)**	2,533 (6.6)*
Other fractures,N (%)	392 (20.1)	2,668 (16.4)	847 (13.5)*	423 (27.9)**	4,168 (10.8)*
Mean number of fracture related hospitalizations (SD)	0.1 (0.4)	0.1 (0.3)	0.1 (0.3)*	0.2 (0.5)**	<0.1 (0.2)*
Oral BPs,N (%)	643 (33.0)	6599 (40.5)**	2043 (32.5)	654 (43.1)**	-
IV BPs,N (%)	150 (7.7)	1142 (7.0)	29 (0.5)*	93 (6.1)	293 (0.8)*
Denosumab,N (%)	356 (18.3)	-	684 (10.9)*	259 (17.1)	1058 (2.7)*
PTH analogs,N (%)	80 (4.1)	614 (3.8)	189 (3.0)	-	185 (0.5)*

* Signals prematching imbalance, based on SMD > 0.10 with romosozumab > comparator

** SMD < -0.10 signalling prematching imbalance with romosozumab < comparator

BP = bisphosphonates; **IV** = intravenous; **PTH** = parathyroid hormone; **SMD** = standardized mean difference

Disclosure: J. Lin, Amgen Inc, 3, 11; **C. Nielson**, Amgen Inc, 3, 11; **M. Oates**, Amgen Inc, 3, 11; **C. Deignan**, Amgen Inc, 3, 11, Amgen Inc, 3, 11; **Z. Yu**, Amgen Inc, 3, 11.

Abstract Number: 0447

Bone Anabolic Effects of a Novel Orally-Available Small Molecule SIK2/SIK3 Inhibitor

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (0445–0448)

Session Type: Abstract Session

Session Time: 9:30AM–10:30AM

Background/Purpose: Orally-available bone anabolic agents represent a major unmet medical need for patients with osteoporosis. Widespread use of parathyroid hormone (PTH)-based osteo-anabolic therapies is limited by the need for daily injections. PTH stimulates bone formation via activating a signaling cascade in osteocytes that inhibits salt inducible kinases (SIK) 2 and 3. The purpose of this study is to test a novel, orally-available SIK2/SIK3 inhibitor (SIK2/SIK3i) in preclinical osteoporosis models.

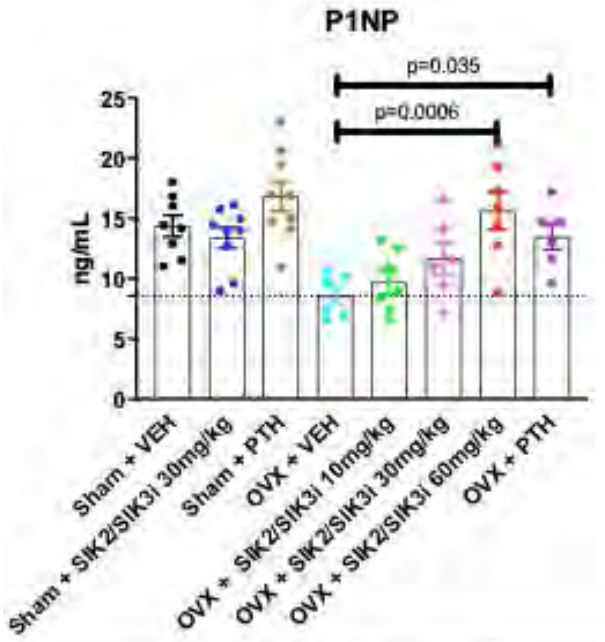

Figure 1. Fasting serum was collected in OVX mice after 6 weeks of drug treatment. In OVX animals, SIK2/SIK3i treatment led to dose dependent increases in the bone formation marker P1NP.

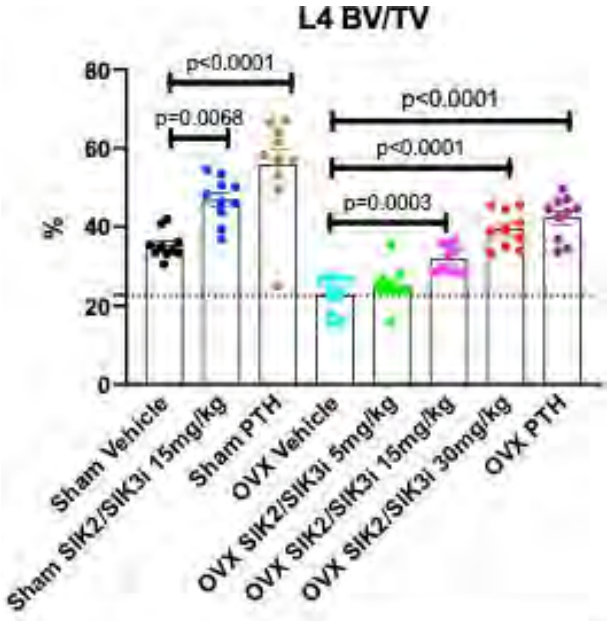

Figure 2. L4 vertebral bodies were analyzed by µCT to measure bone volume fractions in OVX rats. 8 weeks of SIK2/SIK3i treatment led to dose dependent increases in L4 trabecular bone mass.

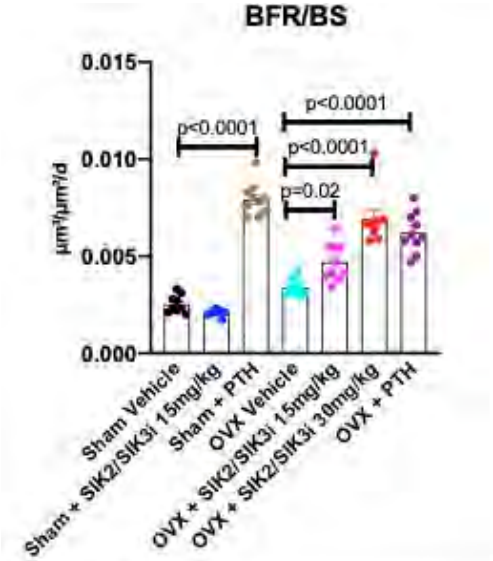

Figure 3. Dynamic histomorphometry was performed in OVX rats following dual calcein labeling to measure the bone formation rate. SIK2/SIK3i treatment led to dose dependent increases in bone formation in OVX animals.

Methods: An osteocyte-like cell line was treated with PTH and SIK2/SIK3i. Cells were treated for 60 minutes followed by immunoblotting for phosphorylated forms of SIK2/SIK3 substrates HDAC4/5. Cells were treated for 4 hours followed RT-qPCR to measure gene expression.

A SIK2/SIK3 inhibitor was tested in two models of post-menopausal bone loss: oophorectomized (OVX) mice and rats. Direct comparison was made to treatment with intermittent PTH. 64 twelve-week-old Balb/c mice were subjected to sham (n=26) or OVX (n=38) surgery. 5 weeks later, mice were treated for 6 weeks with vehicle (n=15), SIK2/SIK3i 10 mg/kg PO BID (n=8), SIK2/SIK3i 30 mg/kg PO BID (n=17), SIK2/SIK3i 60 mg/kg PO BID (n=8), or PTH 1-34 100 mcg/kg SC (n=16). Upon sacrifice, fasting serum was collected to measure bone turnover markers P1NP and CTX, along with femur and L5 vertebrae for μCT, and femurs for histomorphometry.

Next, 80 twelve-week-old Sprague-Dawley rats were subjected to sham (n=30) or OVX (n=50) surgery. 8 weeks later, rats were treated for 8 weeks with vehicle (n=20), SIK2/SIK3i 5 mg/kg PO BID (n=10), SIK2/SIK3i 15 mg/kg PO BID (n=20), SIK2/SIK3i 30 mg/kg PO BID (n=10), and PTH 1-34 40 mcg/kg SC (n=20). Fasting serum was collected at 1, 4, and 8 weeks. At sacrifice, femur and L4 vertebral bodies were collected for μCT, histomorphometry, and biomechanical testing. Two-way ANOVA followed by Tukey post-hoc tests were performed.

Results: In Ocy454 cells, SIK2/SIK3i treatment led to dose-dependent reductions in SIK2/SIK3 substrate HDAC4/5 phosphorylation. SIK2/SIK3i treatment suppressed SOST mRNA expression (EC_{50} = 310 nM).

In OVX mice, SIK2/SIK3i led to dose-dependent increases in the bone formation marker P1NP (p=0.0006) (Figure 1). In OVX mice, SIK2/SIK3i increased L5 bone mass (p=0.0001) and femur cortical thickness (p=0.038) by μCT. Histomorphometry showed that SIK2/SIK3i increased mineralizing surface (p=0.0142) and bone formation rate (p=0.009).

Increased bone anabolism was also observed in OVX rats treated with SIK2/SIK3i, which also led to initial increases in serum P1NP, followed by increased levels of both P1NP and CTX at later time points. SIK2/SIK3i increased trabecular bone mass in OVX rats in femur (p< 0.001) and L4 vertebrae (p< 0.001) (Figure 2). Mechanical testing of L4 vertebrae demonstrated proportionate increases in bone strength and bone mass. Finally, SIK2/SIK3i increased bone formation rate in a dose-dependent manner (p< 0.001) to a degree similar to that of PTH (Figure 3).

Conclusion: SIK2/SIK3i increases trabecular bone formation and bone mass in OVX rodents. Orally-available small molecule SIK2/SIK3 inhibitors may represent a promising new treatment strategy for post-menopausal osteoporosis.

Disclosure: C. Tang, None; **S. Verma**, None; **S. De Vos**, Galapagos NV, 3; **D. Amantini**, Galapagos NV, 3; **P. Clement-Lacroix**, Galapagos SASU, 3; **N. Desroy**, Galapagos NV, 3; **A. Speziale**, Galapagos GmbH, 3; **D. Brooks**, None; **M. Bouxsein**, None; **J. da Silva Martins**, None; **Y. Zhao**, None; **H. Kronenberg**, Galapagos NV, 5; **M. Wein**, Galapagos NV, 5.

Abstract Number: 0448

Bone Microarchitecture Assessed by 3D High-resolution Peripheral Quantitative Computed Tomography (HR-pQCT) as Predictor of Incident Fracture in Rheumatic Disease Patients on Long-term Glucocorticoid- a Five-year Longitudinal Study

ho SO[1], Xerox Lau[1], Vivian Hung[1], Steve Pang[2], Shirley Ying[3], Kitty Kwok[4], Ka Lai Lee[5], Jolly Lee[6], Jack Lee[1], James Griffith[1], Ling Qin[1] and Lai-Shan Tam[7], [1]The Chinese University of Hong Kong, Hong Kong, Hong Kong, [2]Kwong Wah Hospital, Hong Kong, Hong Kong, [3]Prince Margaret Hospital, Hong Kong, Hong Kong, [4]Queen Elizabeth Hospital, Hong Kong, Hong Kong, [5]Pamela Youde Nethersole Eastern Hospital, Hong Kong, Hong Kong, [6]Tai Po Hospital, Hong Kong, Hong Kong, [7]Department of Medicine & Therapeutics, The Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong, China (People's Republic)

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science (0445–0448)

Session Type: Abstract Session

Session Time: 9:30AM–10:30AM

Background/Purpose: Impaired bone quality and strength estimated by high resolution peripheral quantitative computer tomography (HR-pQCT) in patients with rheumatic diseases on long-term glucocorticoid (LTGC) therapy could discriminate patients with and without fragility fracture, independent of areal bone mineral density (aBMD) (1). The aim of this study was to ascertain whether compromised vBMD, bone microarchitecture and estimated bone strength at baseline in rheumatic disease patients on LTGC therapy could predict incident fragility fracture.

Methods: Two hundred and twenty rheumatological patients on LTGC with (n=110) or without (n=110) fragility fracture who participated in a cross-sectional study with dual-energy X-ray absorptiometry (DXA) and HR-pQCT done

Table 1. Baseline demographic and clinical characteristics

	Control group (n=74)	Incident fracture group (n=35)	p
Age (years)	55.9 ± 13.2	59.1 ± 9.7	0.200
Female (%)	60 (81.1%)	29 (82.9%)	0.823
Disease Type (%)			0.297
SLE	35 (55.2%)	20 (66.7%)	
RA	15 (20.3%)	8 (22.9%)	
Polymyositis	4 (5.4%)	2 (5.7%)	
Dermatomyositis	0 (0%)	1 (2.9%)	
Others	19 (25.7%)	4 (11.4%)	
Smoking (%)	11 (14.9%)	5 (14.3%)	0.792
Drinking (%)	23 (31.0%)	8 (22.9%)	0.506
Family history of fracture (%)	12 (16.2%)	7 (20%)	0.627
Prevalent fracture (%)	8 (10.8%)	9 (25.7%)	**0.045**
Mobility class (%)			0.134
Unaided	66 (89.2%)	26 (74.3%)	
Stick-walking	7 (9.5%)	8 (22.9%)	
Wheelchair	1 (1.4%)	1 (2.9%)	
Cumulative GC dose (mg)	33436.4 ± 21518.3	34827.0 ± 17002.6	0.739
Anti-osteoporotic treatment (%)			0.206
Current	12 (16.2%)	7 (20%)	
Ever	10 (13.5%)	9 (25.7%)	
Never	52 (70.3%)	19 (54.3%)	
Baseline osteoporosis status according to aBMD			**0.031**
Osteoporosis	18 (24.3%)	17 (48.6%)	
Osteopenia	40 (54.1%)	11 (31.4%)	
Normal	16 (21.6%)	7 (20%)	
FRAX score (%)			
Major Osteoporotic Fracture	10.61 ± 11.68	16.43 ± 15.19	**0.053** 0.096
Hip Fracture	4.40 ± 7.75	7.93 ± 10.92	
aBMD (g/cm²) at:			
Femoral neck	0.654 ± 0.120	0.622 ± 0.128	0.206
Hip	0.789 ± 0.140	0.764 ± 0.142	0.402
Lumbar spine	0.849 ± 0.142	0.810 ± 0.170	0.211

GC: glucocorticoid; FRAX: fracture risk assessment score; aBMD: areal bone mineral density.

Table 2. Baseline vBMD and microstructure of the distal radius/tibia in patients with and without incident fracture

	Distal radius			Distal tibia		
	Control group	Incident fracture group	*P*	Control group	Incident fracture group	*P*
Ct. area (mm2)	51.38 ± 14.6	48.95 ± 15.74	0.434	100.13 ± 30.37	89.36 ± 23.42	0.050
Tb. area (mm2)	174.80 ± 46.13	171.54 ± 42.85	0.727	520.44 ± 111.97	536.16 ± 125.11	0.520
Average vBMD (mgHA/cm3)	315.50 ± 82.09	298.37 ± 81.42	0.312	259.88 ± 69.41	237.52 ± 64.72	0.120
Ct. vBMD (mgHA/cm3)	885.46 ± 82.45	873.68 ± 73.84	0.475	849.73 ± 71.39	829.44 ± 82.50	0.200
Ct. thickness (mm)	0.811 ± 0.221	0.782 ± 0.234	0.530	1.03 ± 0.318	0.920 ± 0.269	0.097
Ct. perimeter (cm)	63.75 ± 7.26	62.79 ± 7.10	0.518	98.19 ± 8.55	98.63 ± 9.86	0.818
Tb. vBMD (mgHA/cm3)	120.93 ± 43.81	109.64 ± 38.71	0.197	132.4 ± 38.00	122.11 ± 32.21	0.179
pTb. vBMD (mgHA/cm3)	180.63 ± 42.52	173.16 ± 39.44	0.385	198.10 ± 42.30	186.25 ± 35.31	0.164
mTb.vBMD (mgHA/cm3)	79.47 ± 46.56	65.57 ± 40.85	0.135	87.75 ± 36.96	78.49 ± 32.59	0.219
meta/inn.vBMD	5.67 ± 2.14	2.98 ± 1.96	0.399	2.53 ± 1.06	2.64 ± 1.26	0.616
Tb. BV/TV	0.101 ± 0.037	0.091 ± 0.032	0.200	0.110 ± 0.017	0.102 ± 0.027	0.179
Tb. number (1/mm)	1.360 ± 0.365	1.345 ± 0.364	0.841	1.463 ± 0.280	1.425 ± 0.283	0.522
Tb. thickness (mm)	0.075 ± 0.024	0.068 ± 0.022	0.140	0.075 ± 0.016	0.072 ± 0.015	0.251
Tb. separation (mm)	0.776 ± 0.545	0.774 ± 0.415	0.979	0.639 ± 0.182	0.659 ± 0.157	0.586
Tb. inhomogeneity (mm)	0.401 ± 0.476	0.396 ± 0.331	0.948	0.340 ± 0.215	0.329 ± 0.111	0.792
Stiffness (kN/mm)	64657.0 ± 18693.0	60036.3 ± 19182.5	0.237	161948.2 ± 42652.2	142411.2 ± 35028.6	**0.020**
Est. failure load (N)	-3207.9 ± 932.6	-2977.9 ± 157.1	0.234	-8163.2 ± 2078.6	-7217.8 ± 1737.2	**0.022**

vBMD: volumetric bone mineral density; Ct.: cortical; Tb: trabecular; pTb: peripheral region adjacent to the cortex; mTb: the central medullary region; BV/TV: bone volume fraction; Est: estimated.

between 2014-2016 were invited to have a 5th year follow-up assessment. All patients had a repeat assessment with 1) aBMD and 2) HR-pQCT 3) spine radiographs. The occurrence of new fragility fracture after 5 years was documented. The baseline clinical characteristics, aBMD, FRAX and HR-pQCT parameters in patients who experienced a new fragility fracture during the 5-year follow-up period (incident fracture group) were compared with patients who did not (control group).

Results: In this interim analysis, a total of 109 patients were recruited. The mean age of the patients at the 5th year visit was 61.9 ± 12.2 years and there was a female predominance of 81.7%. Systemic lupus erythematosus (50.9%) and rheumatoid arthritis (21.3%) were the commonest rheumatological diagnoses. At baseline, 46.8% and 32.1% of the patients were osteopenic and osteoporotic respectively, 15.6% had a prevalent fracture. The baseline 10-year major osteoporotic and hip fracture risks by fracture risk assessment tool (FRAX) were 14.5 ± 13.7 and 6.5 ± 9.8 respectively. After 5 years, 35 (32.1%) of the patients developed new fractures (24 vertebral, 11 non-vertebral). The clinical characteristics of the incident facture group and the control group are shown in table 1. There was no difference in the aBMD and FRAX scores between the two groups. When comparing the HR-pQCT parameters, the incident fracture group had significantly lower tibial stiffness and failure load than the control group (table 2). Multivariate logistic regression confirmed that baseline bone stiffness (p=0.024) and failure load (p=0.026) over tibia were independent predictors of new fractures after adjusting for age, gender, prevalent fracture and osteoporosis status.

Conclusion: We conclude that impairment of bone strength over distal tibia on HR-pQCT predicts the occurrence of incident fracture in rheumatic disease patients on LTGC.

Disclosure: h. SO, None; **X. Lau**, None; **V. Hung**, None; **S. Pang**, None; **S. Ying**, None; **K. Kwok**, None; **K. Lee**, None; **J. Lee**, None; **J. Lee**, None; **J. Griffith**, None; **L. Qin**, None; **L. Tam**, Janssen, 2, 5, Pfizer, 2, 5, GlaxoSmith-Kline, 5, AbbVie, 2, Novartis, 5, Amgen, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, Sanofi, 2.

Abstract Number: 0449

Identification of Serum Protein Biomarkers at Baseline to Distinguish Radiographic Progressors from Non-Progressors in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes I (0449–0452)

Session Type: Abstract Session

Session Time: 9:30AM–10:30AM

Background/Purpose: A delay in diagnosis and management of patients with PsA leads to poor radiographic and functional outcomes [1]. The need to identify which patients might progress radiographically has been recognised by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) as a key area of unmet need within PsA [2]. It is anticipated that biomarkers for radiographic joint damage will help in patient stratification so those with greater likelihood of poor outcome may be treated more timely and aggressively. The identification of such biomarkers would also be useful in clinical research to evaluate novel treatment efficacy in selected subjects at higher risk of rapid progression. The SPIRIT-P1 (NCT01695239) Phase 3 randomized controlled trial (RCT) of ixekizumab, a high-affinity IL-17A antagonist antibody, in active PsA patients resulted in reduced progression of structural damage [3], however 5-10% of patients who progressed may have benefitted from an earlier or more aggressive treatment if identified using biomarkers at the outset. The aim of this study was to use mass spectrometry-based proteomics to identify protein biomarkers which might distinguish at baseline those patients who progress to joint damage from those who will not. Top-ranking protein biomarkers were then combined with key clinical parameters to try to improve the discrimination of progressors (P) from non-progressors (NP) to joint damage.

Methods: Baseline serum samples from 83 PsA patients (28 P and 55 NP) were obtained from the SPIRIT-P1 RCT. Radiographic P showed a >0.5 change from baseline modified total Sharp score at week 24 or 52. Two proteomic analyses were performed: 1) unbiased discovery using mass spectrometry of the 83 baseline samples; and 2) targeted analysis of in-house panel of 206 proteins originally developed to distinguish between arthropathies. Univariate and multivariate machine learning random forest modelling was undertaken on the 2 proteomic datasets.

Results: Unbiased discovery proteomics resulted in the identification of 74 unique peptides which were significantly differentially expressed (ANOVA $p < 0.01$). Random forest modelling identified 15 top-ranking peptides which could distinguish NP from P with a ROC AUC of 0.94. Univariate analysis of the 206 proteins measured by targeted proteomics revealed 4 differentially expressed peptides (ANOVA $p < 0.01$) and random forest modelling revealed the top 15 candidate peptides could distinguish P from NP with a ROC AUC of 0.85. The baseline clinical data was combined with candidate peptides biomarkers in additional random forest models and this revealed improved model performance.

Conclusion: Data from 2 complimentary proteomic approaches was subjected to univariate and multivariate machine learning statistical analysis which revealed a total of 103 candidate biomarker peptides corresponding with 69 proteins that can potentially discriminate PsA patients who will progress to radiographic damage from those who will not. Random forest models produced convincing ROC AUCs which were improved by inclusion of patient clinical baseline data. The data, whilst promising, requires further validation using separate cohorts of similar patient samples.

[1] V. Ocampo D and D. Gladman, "Psoriatic arthritis," *F1000Research*, vol. 8, p. 1665, Sep. 2019, doi: 10.12688/f1000research.19144.1.

[2] C. T. Ritchlin *et al.*, "Biomarkers in psoriasis and psoriatic arthritis: GRAPPA 2008," *J. Rheumatol.*, vol. 37, no. 2, pp. 462–467, Feb. 2010, doi: 10.3899/jrheum.090957.

[3] P. J. Mease *et al.*, "Ixekizumab, an interleukin-17A specific monoclonal antibody, for the treatment of biologic-naive patients with active psoriatic arthritis: results from the 24-week randomised, double-blind, placebocontrolled and active (adalimumab)-controlled period of th," *Ann. Rheum. Dis.*, vol. 76, no. 1, pp. 79–87, Jan. 2017, doi: 10.1136/annrheumdis-2016-209709.

Disclosure: O. Coleman, Atturos, 3; **B. Wundervald**, Atturos, 7; **R. Zhou**, Atturos, 3; **J. Waddington**, Atturos Ltd, 3; **R. Graham**, None; **C. Graham**, None; **G. McMullan**, None; **A. Parnell**, Atturos, 11; **V. Chandran**, Abbvie, 1, 2, 5, Amgen, 1, 2, 5, Eli Lilly, 1, 2, 5, BMS, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, AstraZeneca, 12, Spousal employment, Celgene, 2, 5, UCB Pharma, 2, 5; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **G. Gallo**, Eli Lilly and Company, 3; **V. Krishnan**, Eli Lilly and Company, 3, 11; **S. Pennington**, Atturos, 4, 8, 10, 11; **O. FitzGerald**, Novartis, 5, 6, UCB, 5, 6, Pfizer, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Lilly, 5, 6, Biogen, 6, Eli Lilly, 5, 6.

Abstract Number: 0450

Identifying Trajectories of Radiographic Spinal Disease in Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes I (0449–0452)

Session Type: Abstract Session

Session Time: 9:30AM–10:30AM

Background/Purpose: Little is known about the natural history of spinal disease in Ankylosing Spondylitis (AS). Our objective was to identify distinct patterns of change in vertebral involvement over time and to study associated clinical factors.

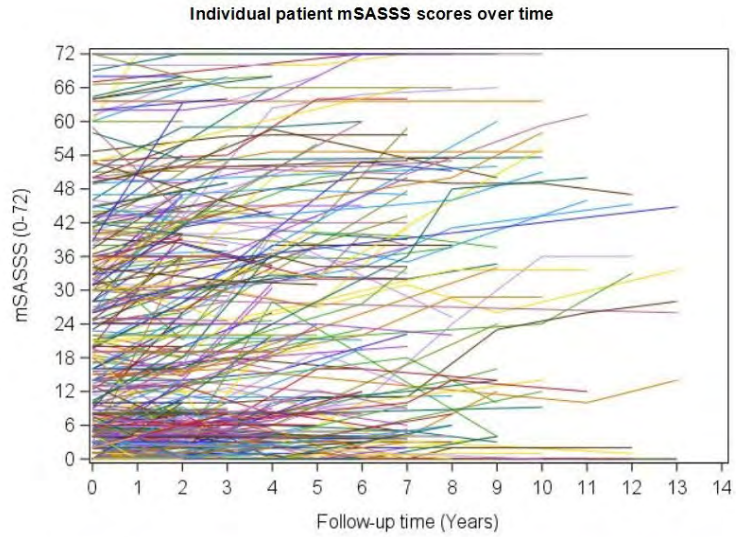

Figure 1. Time in years is along the X-axis and total Modified Stokes Ankylosing Spinal Score is along the Y-axis. Each individual line (n=561) represents a patient in the PSOAS cohort from time in cohort entry with all complete mSASSS scores included with at least 2 sets of radiographs.

Methods: Data were analyzed from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS) cohort. All patients met modified New York Criteria for AS, and had ≥2 sets of radiographs scored by modified Stoke Ankylosing Spondylitis Spinal Score (mSASSS) read by local-rheumatologist and central-radiologist between 2002-2017.

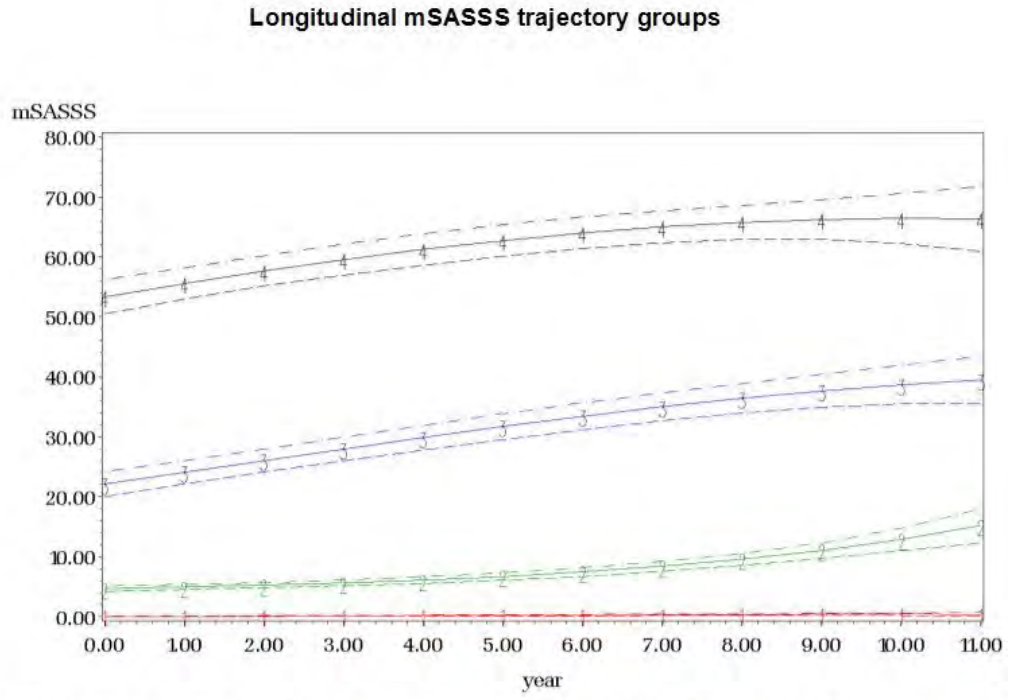

Figure 2. Time in years is along the X-axis and total Modified Stokes Ankylosing Spinal Score is along the Y-axis. The solid line represents the estimated mean with dotted lines representing the 95% confidence Interval. Trajectory groups from this patient cohort (n=561) include are: 1(Red Line) Non-Progressors, Group 2(Green Line) Late Progressors, Group 3 (Blue Line) - Early progressors and Group 4 (Black Line) Rapid Progressors. Including adjustments included: time-variant (Tumor necrosis factor inhibitor use and abnormal C-reactive protein) and time-invariant risk-factors (e.g. gender, smoking, and disease duration).

Table 1. Baseline Predictors of Trajectory group membership in the 4-group mSASSS model (non-progressor group is the reference group)

Variable	Coefficient Estimate	p-value
Late Progressors		
Baseline mSASSS*	-2.09	<0.001
Gender (Male vs. Female)*	0.58	0.02
Disease duration (≥20 years vs. <20 years)*	0.01	<0.001
Smoking history (Yes vs. No)	0.19	0.63
Hx of TNFi (Yes vs. No)	0.09	0.72
C-reactive protein (Elevated vs. Non-elevated)	0.04	0.70
BASDAI (≥4 vs. <4)	0.003	0.95
Early Progressors		
Baseline mSASSS*	-4.24	<0.001
Gender (Male vs. Female)*	1.40	<0.001
Disease duration (≥20 years vs. <20 years)*	0.13	<0.001
Smoking history (Yes vs. No)	0.65	0.14
Hx of TNFi (Yes vs. No)	0.51	0.11
C-reactive protein (elevated vs. non-elevated)	0.28	0.01
BASDAI (≥4 vs. <4)	-0.02	0.66
Rapid Progressors		
Baseline mSASSS*	-5.87	<0.001
Gender (Male vs. Female)*	2.46	<0.001
Disease duration (≥20 years vs. <20 years)*	0.15	<0.001
Smoking history (Yes vs. No)*	0.91	0.04
Hx of TNFi (Yes vs. No)	0.11	0.74
C-reactive protein (Elevated vs. Non-elevated)*	0.30	0.01
BASDAI (≥4 vs. <4)	0.04	0.52

*p<0.05

Group-based trajectory modeling (GBTM) was used to classify patients into distinct groups of longitudinal mSASSS considering sociodemographic and clinical covariables. The optimal trajectory model and number of trajectories was selected using Nagin's Bayesian information Criteria (BIC) (1).

Results: A total of 561 patients with 1618 radiographs was analyzed (Figure 1). The optimum number of trajectory groups identified was four (BIC -4062). These groups were subsequently categorized as: Non-progressors (204 patients, 37% of total), late-progressors (147, 26%), early-progressors (107, 19%) and rapid-progressors (103, 18%) (Figure 2). Baseline predictors associated with higher spinal disease burden groups included: male, gender, longer disease duration, and smoking history (Table 1.). In addition, elevated time-varying C-reactive protein (eCRP) levels were positively associated with higher disease progression groups and time-varying anti-TNF use was associated with decreased mSASSS progression in the rapid-progressor group.

Conclusion: GBTM identified 4 major patterns of spinal disease progression in the PSOAS cohort. Male gender, longer disease duration, eCRP and smoking were associated with higher spinal disease groups. Independent confirmation in other AS cohorts is needed to confirm these radiographic patterns.

Reference:

1. Nagin, D. *Group-Based Modeling of Development*. Cambridge: Harvard University Press; 2005

Time in years is along the X-axis and total Modified Stokes Ankylosing Spinal Score is along the Y-axis. Each individual line (n=561) represents a patient in the PSOAS cohort from time in cohort entry with all complete mSASSS scores included with at least 2 sets of radiographs.
Time in years is along the X-axis and total Modified Stokes Ankylosing Spinal Score is along the Y-axis. The solid line represents the estimated mean with dotted lines representing the 95% confidence Interval. Trajectory groups from this patient cohort (n=561) include are: 1(Red Line) Non-Progressors, Group 2(Green Line) Late Progressors, Group 3 (Blue Line) -Early progressors and Group 4 (Black Line) Rapid Progressors. Including adjustments included: time-variant (Tumor necrosis factor inhibitor use and abnormal C-reactive protein) and time-invariant risk-factors (e.g. gender, smoking, and disease duration).

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Abstract Number: 0451

Tumor Necrosis Factor Inhibitors Show a Delayed Effect on Radiographic Sacroiliitis Progression in Patients with Early Axial Spondyloarthritis: 10-Year Results from the German Spondyloarthritis Inception Cohort

Murat Torgutalp[1], Valeria Rios Rodriguez[1], Maryna Verba[2], Mikhail Protopopov[3], Fabian Proft[1], Judith Rademacher[1], Hildrun Haibel[3], Martin Rudwaleit[4], Joachim Sieper[3] and Denis Poddubnyy[5], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Berlin, Germany, [3]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [4]University of Bielefeld, Klinikum Bielefeld, Bielefeld, Germany, [5]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes I (0449–0452)
Session Type: Abstract Session
Session Time: 9:30AM–10:30AM

Background/Purpose: Observational cohort studies have shown that there is low, but still detectable progression level in radiographic sacroiliitis, which might also have an impact on the function in patients with axial spondyloarthritis (axSpA). Recent data showed that tumor necrosis factor inhibitors (TNFi) might retard spinal progression when initiated earlier and taken longer in patients with axSpA. However, the question of whether they also have such an effect on radiographic progression in sacroiliac joints (SIJs) is still unclear.

In this study, we aimed to investigate the longitudinal association between radiographic sacroiliitis progression and treatment with TNFi in patients with early axial SpA in a long-term inception cohort.

Methods: Based on the availability of at least two sets of SIJ radiographs, 301 patients (166 with nr-axSpA, symptom duration ≤5 years and 135 with r-axSpA, symptom duration ≤10 years) from the German Spondyloarthritis Inception Cohort (GESPIC) were included in this analysis. These patients contributed with a total of 737 2-year radiographic

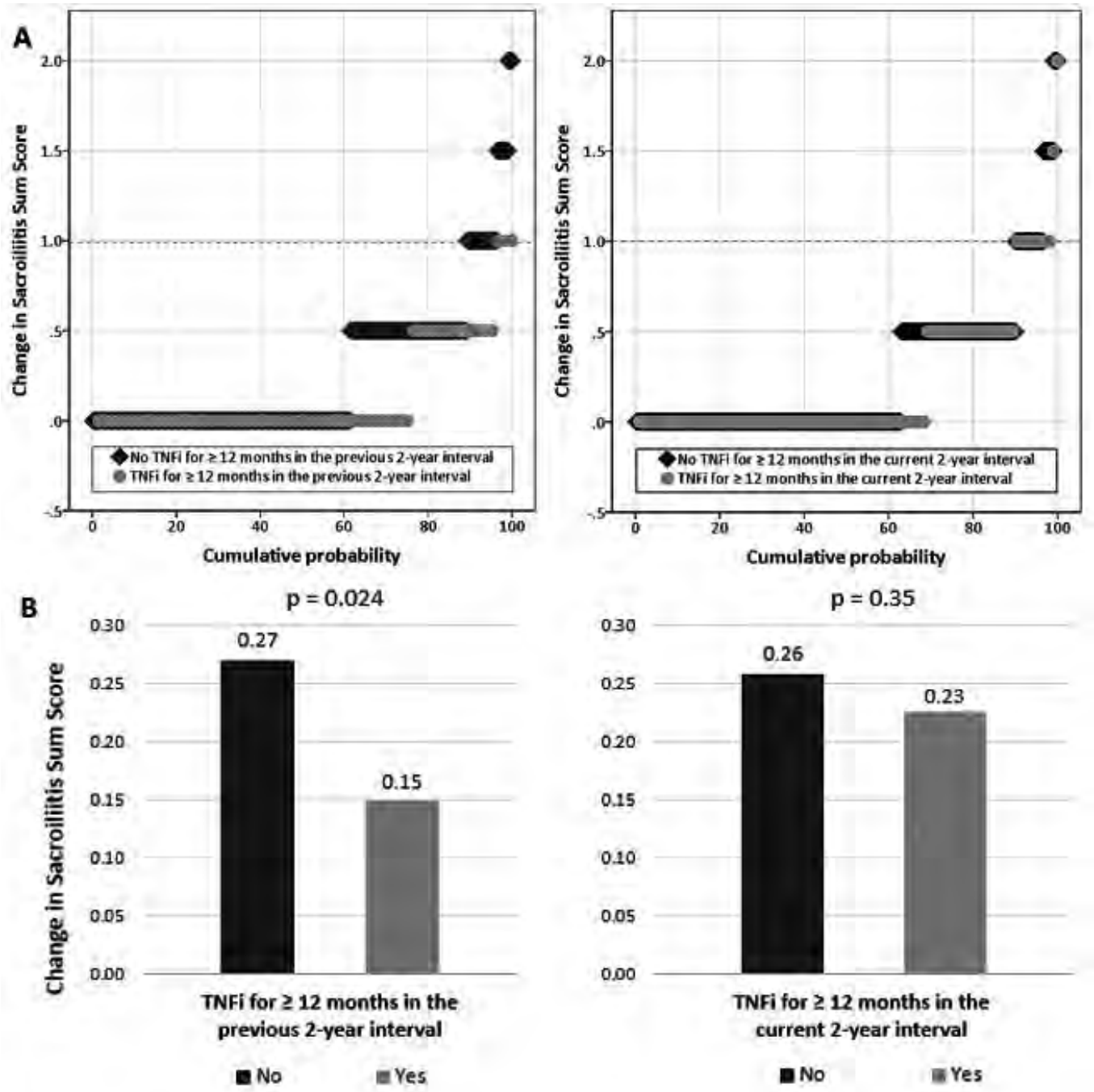

Figure. A). Cumulative probability plot of the 2-year progression in the sacroiliitis sum score, stratified by receiving at least 12 months TNFi in the previous and current 2-year radiographic intervals. B) The change in sacroiliitis sum scores over two years in patients with axial spondyloarthritis treated vs non-treated with TNFi at least 12 months in the previous and current 2-year radiographic intervals.

intervals. Two trained and calibrated central readers scored the radiographs according to the modified New York criteria. If both scored an image as definite radiographic sacroiliitis, the patient was classified as having r-axSpA. The sacroiliac sum score was calculated as a mean of both readers. The association between previous as well as current TNFi use and radiographic sacroiliitis progression, which was defined as the change in the sacroiliitis sum score over 2 years, was analysed using longitudinal generalized estimating equations (GEE) analysis.

Results: At baseline, 9 (3.0%) patients were treated with a TNFi, and 87 (28.9%) patients received at least one TNFi during the entire follow-up period. A total of 141 of the radiographic intervals were covered with TNFi of any duration, while 109

Table. The longitudinal GEE analysis of the association between progression in the sacroiliitis sum score and TNFi use

TNFi treatment definition	Reference	β* (95% CI)
TNFi for ≥ 12 months in the previous 2-year interval	No TNFi for ≥ 12 months in the previous 2-year interval	**-0.09 (-0.18, -0.003)**
Any TNFi use in the previous 2-year interval	No TNFi use in the previous 2-year interval	-0.09 (-0.17, 0.002)
TNFi for ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the current 2-year interval	-0.03 (-0.11, 0.06)
Any TNFi use in the current 2-year interval	No TNFi use in the current 2-year interval	0.05 (-0.05, 0.14)
TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	No TNFi for ≥ 12 months in the previous and ≥ 12 months in the current 2-year interval	-0.08 (-0.17, 0.004)

* Parameter estimates from the multivariable models adjusted for **sex**, **age** at the beginning of the current 2-year interval, **HLA-B27** positivity, **symptom duration** at the beginning of the current 2-year interval, time-averaged elevated **CRP**, time-averaged **BASDAI**, and time-averaged **NSAID intake score** in the current 2-year interval.

of them were covered with a TNFi of at least 12 months. While receiving ≥12 months TNFi in the previous interval was associated with a lower progression of the sacroiliitis sum score compared to not receiving TNFi in the previous interval, this was not the case in patients who received TNFi ≥12 months in the current 2-year interval (Figure 1). The significant association between TNF ≥12 months in the previous interval and progression in the sacroiliitis sum score were confirmed in the adjusted multivariable longitudinal GEE analysis. In addition, a similar trend for the beneficial effects was observed in different models, which included other treatment definitions with TNFi in the previous 2-year interval (Table).

Conclusion: Treatment with TNFi was associated with retardation of radiographic

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Abstract Number: 0452

Total-Body ^{18}F-FDG PET/CT Imaging: A Tool for Diagnosis and Quantifying Inflammatory Burden of Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes I (0449–0452)

Session Type: Abstract Session

Session Time: 9:30AM–10:30AM

Background/Purpose: The underlying pathology in psoriatic arthritis (PsA) is systemic inflammation. The Total Body (TB)-PET/CT with the ^{18}F-FDG radiotracer captures glucose metabolism across the entire body, and provides standardized measures as surrogates for degree of inflammation such as SUVmax. So, we predicted that these TB-PET/CT indices will correlate with the existing outcome measures of the 5 clinical domains of PsA (DAPSA, Leeds Enthesitis Index, Leeds Dactylitis Index, BASDAI and NAPSI). The objective of this study is to validate TB-PET/CT imaging as a diagnostic tool and for describing systemic disease activity of PsA.

Methods: We have prospectively recruited 40 participants (30 male, 10 female), with PsA (n=15), RA (n=10), and OA (n=15). All subjects underwent a single-timepoint TB-PET/CT scan on the uEXPLORER scanner using the PET radiotracer ^{18}F-FDG. Qualitative findings and different patterns for these 3 conditions were evaluated. We quantified the degree of inflammation (SUVmax) and determined pathologic predilection for anatomical domains of bones/ligaments of in PsA, RA and OA.

Results: In PsA patients, large number of joints showed positive findings in all participants. Multiple sites of enthesitis were visualized in the majority of scans (n=14/15). Furthermore, nail matrix showed increased uptake in 9/15 participants. Less frequent features included spine involvement of the supra/interspinous ligaments/bursae (n=6), sacroiliac joint (n=2), and dactylitis (n=2).

The uptake patterns and intensity were significantly different in patients with PsA compared to those with OA and RA (Fig 1 A and 1B). Fig 1 A, shows in PsA, joints were affected asymmetrically. In the Fig 1 B PET-CT imaging of the hands in PsA compared to RA clearly had: (a) asymmetry (b) also other characteristic pathologies such as in PsA there is inflammation of the extensor tendon and DIP in the left index along with marked nail matrix inflammation. The relative maximum standardized uptake value (rSUV$_{max}$) was significantly higher in participants with PsA compared to OA. There was a fair (68%) agreement between the DAPSA score and the PET averaged SUV$_{max}$. Figure 2 demonstrates the significance of a single TB-PET/CT scan in identifying the extent and the nature of joint, entheses, and nail involvement in PsA.

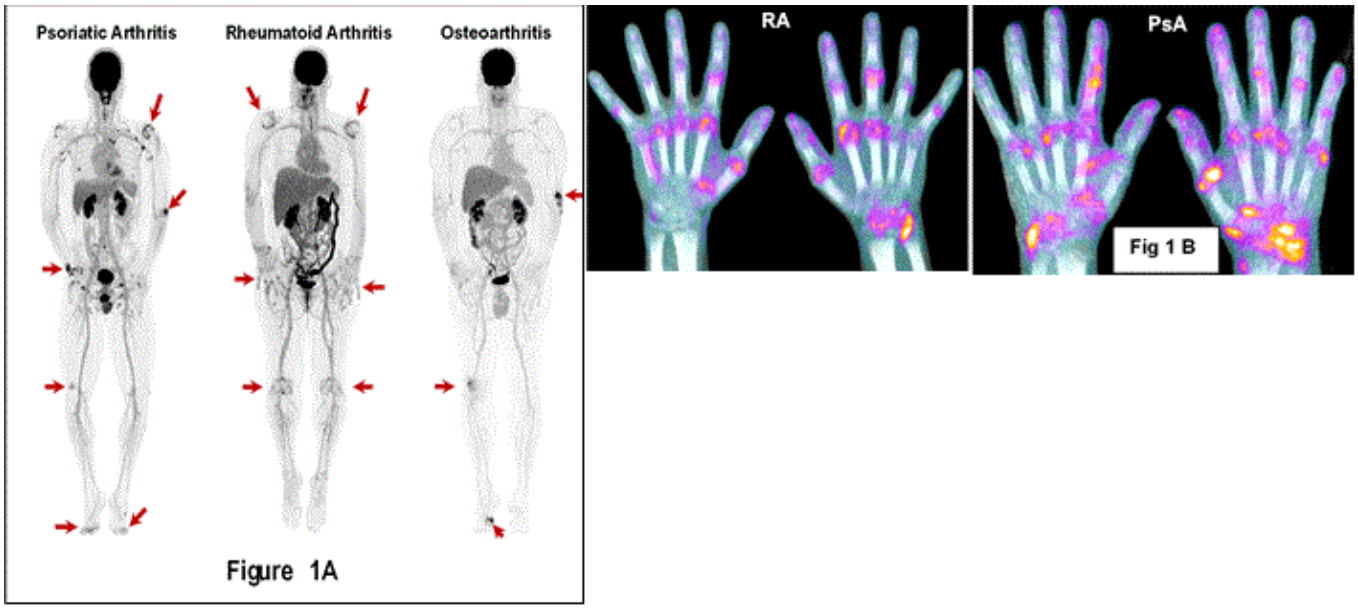

Figure 1. A. TB-PET/CT scans: Left: In PsA, showing multiple joints affected asymmetrically. Center: In RA: multiple joints affected, symmetric; including the shoulders, PIP joints of the hands and knees. Right: In OA, with few affected joints left elbow, right knee and right big toe. Figure 1: B. Compared to RA in PsA: (i) arthritis of small joints is asymmetric; evidenced by sparing of PIP/DIP of 3rd,4th,5th digits in the left hand (ii) there is inflammation of the extensor tendon and DIP in the left index finger and marked nail matrix inflammation in several fingers in both hands.

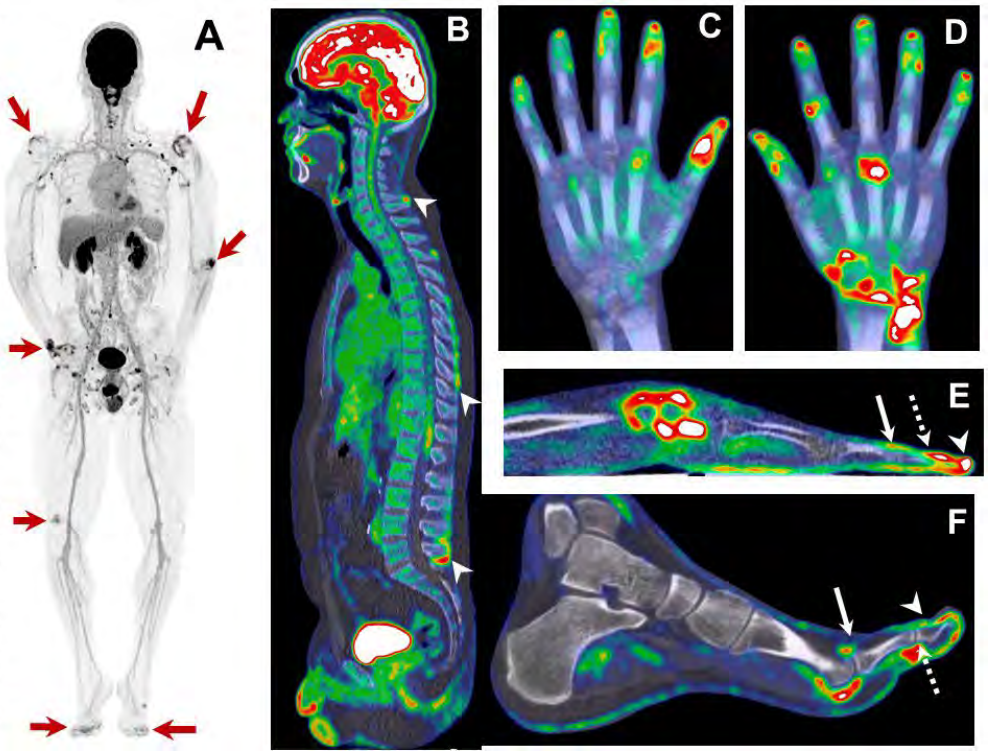

Fig 2: Total-Body evaluation of PsA:

(A) Maximum-intensity projection (MIP) of a Total-Body PET scan in a 40 y/o male demonstrating multiple asymmetric affection of the large and small joints (arrows).

(B) The spine entheses are involved at multiple levels and are well-visualized in the fused sagittal PET/CT image (arrowheads, B).

(C) and (D) Fused PET/CT images of the right and left hands demonstrating classic asymmetric arthritis of wrists, PIP and MCP joints and bilateral inflammation of the nail matrix.

E. Magnified fused sagittal view of the index finger (D), demonstrating nail matrix (arrowhead), DIP (dashed arrow) and PIP (solid arrow).

F. Magnified fused sagittal view of the right foot (F), demonstrating sausage digit of the right great toe along with inflammation of nail matrix (arrowhead), IP (dashed arrow) and MTP joints (solid arrow)

Figure 2. A single Total Body-PET/CT scan can identify the extent and the nature of joint, spine, entheses, and nail involvement in PsA.

Conclusion: Our results indicates that TB-PET/CT measures can identify unique pathologies of PsA (Fig 1 and Fig 2) compared to RA and OA such as (i) asymmetric synovitis of large and small joints, (ii) systemic generalized enthesitis (iii) DIP inflammation, (iv) inflammation of the extensor tendons of fingers and its association with its enthesitis and adjacent nail matrix inflammation, (v) nail matrix inflammation, (vi) dactylitis, (vii) spondyloarthritis with sacroiliitis and diffuse enthesitis of the spine.

These observations substantiate our proposal that TB-PET/CT identifies the pathologies unique for 5 clinical domains of PsA, differentiates from RA/PsA, provides a diagnosis, extent/severity of the disease with a quantitative measure of total inflammatory burden and identifies subclinical developing pathologies of PsA. Thus, a diagnostic tool for early disease at the point of transition from psoriasis.

Disclosure: S. Raychaudhuri, Johnson & Johnson, 1, Abbvie, 5, 6, Sun Pharma, 5, UCB company, 1, Novartis, 1, Pfizer, 5; **Y. Abdelhafez**, None; **S. Kundu-Raychaudhuri**, Sun Pharma, 5; **A. Chaudhari**, None.

Abstract Number: 0453

Efficacy and Safety of Risankizumab for Active Psoriatic Arthritis: 24-Week Integrated Results from 2 Phase 3, Randomized, Double-blind Clinical Trials for CsDMARD-IR and Bio-IR Patients

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Plenary I (0453–0457)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: Risankizumab (RZB) is a humanized immunoglobulin G1 monoclonal antibody that specifically inhibits interleukin 23 by binding to its p19 subunit. RZB is being investigated as a treatment for adults with psoriatic arthritis (PsA).

Methods: KEEPsAKE 1 and 2, double-blind, phase 3 trials, evaluated the efficacy and safety of RZB vs. placebo (PBO) for the treatment of active PsA. The trials enrolled adults with a diagnosis of active PsA, active plaque psoriasis or nail psoriasis, and ≥ 5 swollen joints and ≥ 5 tender joints. Both studies enrolled patients that had previously had an inadequate response or intolerance to ≥ 1 conventional synthetic disease modifying antirheumatic drug (csDMARD-IR). The KEEPsAKE 2 trial also enrolled patients that previously had an inadequate response or intolerance to 1 or 2 biologic therapies (Bio-IR).

In both trials, patients were randomized (1:1) to receive blinded subcutaneous RZB 150 mg or PBO at weeks 0, 4, and 16. The primary endpoint for this pooled analysis was the proportion of patients achieving 20% improvement

Table 1. Efficacy at Week 24

	RZB 150 mg N = 707	PBO N=700	Difference (95% CI)
Primary endpoint			
ACR20, %	55.5	31.3	24.0 (19.0, 29.0)***
Secondary endpoints			
HAQ-DI[a], change from baseline	-0.27	-0.08	-0.19 (-0.24, -0.14)***
PASI 90,[c] %	53.2	10.0	43.1 (37.3, 48.8)***
ACR20 at week 16, %	53.7	31.1	22.4 (17.0, 27.8)***
MDA, %	25.2	10.6	14.6 (10.6, 18.5)***
SF-36 PCS score,[b] change from baseline	6.09	2.62	3.47 (2.70, 4.23)***
FACIT-Fatigue score,[b] change from baseline	5.4	3.0	2.5 (1.5, 3.4)***
ACR50, %	31.2	10.6	20.6 (16.5, 24.7)***
ACR70, %	14.1	5.0	9.0 (6.0, 12.1)***
Resolution of enthesitis,[d] %	48.4	34.8	13.9 (7.6, 20.2)***
Resolution of dactylitis,[e] %	68.1	51.0	16.9 (7.5, 26.4)***

ACR20/ACR50/ACR70, ≥ 20/50/70% improvement in American College of Rheumatology score; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASI 90, ≥ 90% reduction in Psoriasis Area Severity Index; PBO, placebo; RZB, risankizumab; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary
Due to COVID-19, between 1 and 15 data points are missing for each endpoint per treatment arm
*** P-value <0.001
[a] Non-missing data at baseline RZB N = 706; PBO N = 698
[b] Non-missing data at baseline RZB N = 706; PBO N = 696
[c] For patients with involved body surface area ≥ 3% at baseline (RZB N = 396; PBO N = 391)
[d] For patients with enthesitis at baseline (RZB N = 444; PBO N = 448)
[e] For patients with dactylitis at baseline (RZB N = 188; PBO N = 204)

Table 2: Safety

	RZB 150 mg N=707 N (%)	PBO N=700 N (%)
Any AE	322 (45.5)	307 (43.9)
Serious AE	21 (3.0)	31 (4.4)
AE leading to discontinuation of study drug	6 (0.8)	10 (1.4)
Adjudicated MACE	1 (0.1)	0 (0.0)
Serious infections	7 (1.0)	11 (1.6)
Malignant tumors (including NMSC)	1 (0.1)	3 (0.4)
Excluding NMSC	0 (0.0)	2 (0.3)
Any COVID-19 Related AE	2 (0.3)	2 (0.3)
Deaths[a]	1 (0.1)	0 (0.0)

AE, adverse event; MACE, major adverse cardiac events; NMSC, nonmelanoma skin cancer

[a] Due to urosepsis in 81-year-old patient with dementia

in American College of Rheumatology score (ACR20) at week 24. Non-responder imputation incorporating multiple imputations to handle missing data due to COVID-19 (NRI-C) was used for categorical efficacy data and Mixed-Effect Model Repeated Measurement (MMRM) analysis was used for continuous efficacy data. Safety was assessed throughout the study. Results reported here are from the 24-week double-blind period; the open-label period with all patients receiving RZB is ongoing.

Results: A total of 1407 patients (RZB, N = 707; PBO, N = 700) were initially enrolled and 1354 (RZB, N = 688; PBO, N = 666) completed the 24-week assessments. Demographics and baseline disease characteristics were similar between the two groups. Patients receiving RZB achieved higher rates of ACR20 than patients receiving PBO at Week 24 (**Table 1**, 55.5% vs 31.3%, $P < 0.001$). Patients receiving RZB showed greater improvements than patients receiving PBO in all secondary clinical and patient-reported outcome endpoints **(Table 1)**. RZB was well tolerated, and no new safety signals were observed **(Table 2)**.**Conclusion:** RZB resulted in statistically greater improvements in signs and symptoms of PsA compared with PBO and was well tolerated with no new safety signals.

Disclosure: A. Ostor, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6; **K. Papp**, AbbVie, 2, 5, 6, Amgen, Astellas, 2, 5, 6, Bausch Health (Valeant), 2, 5, 6, Baxalta, Baxter Takeda, 2, 5, 6, Boehringer Ingelheim, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Dermira, 2, 5, 6, EMD Serono, 2, 5, 6, Forward Pharma, 2, 5, 6, Galderma, 2, 5, 6, GlaxoSmithKline, 2, 5, 6, Janssen, 2, 5, 6, Kyowa Kirin, LEO Pharma, 2, 5, 6, Lilly, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Regeneron, Sanofi Genzyme, 2, 5, 6, Roche,, 2, 5, 6, Stiefel, 2, 5, 6, Sun Pharma, 2, 5, 6, UCB, 2, 5, 6; **M. Moreno**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Merck, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Boehringer Ingelheim, and GlaxoSmithKline, 2, 5, 6; **C. Spargo**, AbbVie, 2, 6, EliLilly, 2, 6, Janssen, 2, 6, Pfizer, 2, 6, Novartis, 2, 6, Roche, 2, 6, Mundipharma, 2, 6; **L. Barcomb**, AbbVie, 3, 11; **A. Soliman**, AbbVie, 3, 11; **W. Lu**, AbbVie, 3, 11; **A. Eldred**, AbbVie, 3, 11; **L. Kristensen**, AbbVie, 2, 6, Amgen, 2, 6, Biogen, Bristol-Myers Squibb, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Lilly, 2, 6, Merck, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6.

Abstract Number: 0454

Lupus Nephritis Mortality in the United States, 1999-2019: Profound Disparities by Race/Ethnicity and Place of Residence and a Recent Worsening Trend

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Plenary I (0453–0457)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: Mortality from SLE has improved over the last two decades, but remains disproportionately high relative to general population mortality. Lupus nephritis (LN) occurs in 50-80% of childhood-onset and over 40% of adult-onset SLE patients. End-stage renal disease (ESRD) due to LN portends a high premature death burden compared to other manifestations of SLE – up to 26-times higher – and double the risk for hospital mortality compared with patients with all-cause ESRD. However, there have been no major population-based studies on mortality trends in LN over time across the U.S. We aimed to analyze mortality trends across the United States (U.S.) over two decades, 1999-2019, and to identify population characteristics associated with LN mortality.

Methods: We utilized the CDC's WONDER database that compiles mortality data from death certificates in all 50 states and District of Columbia. We obtained death counts attributed to SLE and LN, overall and by race/ethnicity and urbanization. Data on race/ethnicity were obtained for Hispanic, non-Hispanic (NH) White, NH Black, NH American-India/Alaska Native, and NH Asian/Pacific Islander. Urbanization was based off the 2006 urbanization data and is categorized based on population size – large central metropolitan (metro), large fringe metro, medium metro, small metro, micropolitan, and nonmetropolitan. Using these data, we calculated age-standardized mortality rate (ASMR) per 100,000 persons for LN deaths for each year from 1999 to 2019. We used joinpoint regression to fit piecewise-linear trends to yearly LN-ASMR, and for SLE-ASMR for comparison.

Results: From 1999 to 2019, there were 8,899 deaths attributed to LN and 25,973 deaths due to SLE. Overall, LN-ASMR decreased by 26.1% in 21 years. Joinpoint trend analysis showed that LN-ASMR decreased from 1999 to 2009, plateaued between 2009 and 2012, decreased again from 2012 to 2015, but significantly increased from 2015 to 2019. Such decrease-and-increase trend was not seen in all SLE-ASMR that continuously decreased from 1999 through 2019. Black persons were profoundly overrepresented in LN deaths (38%), while they account for only 12.8% of US population. On the other hand, white persons that represent 65.4% of US population accounted for 41.5% of all LN deaths. LN-ASMR in black persons was 6-fold higher than in white persons and >2-fold higher than in all other race/ethnic groups. LN-ASMR was also significantly higher in Hispanics, American-Indian/Alaska Natives, and Asian/Pacific Islanders than in white persons. Whereas 29.6% of US population lived in large central metro area, they accounted for 35.1% of LN deaths. LN-ASMR was highest in large central metro ($p < 0.05$ relative to all other areas), followed by medium metro that had higher LN-ASMR than in large fringe metro, small metro, micropolitan and nonmetro areas.

Conclusion: LN mortality rate has decreased since 1999, however, it showed an increasing trend from 2015 to 2019. LN mortality exhibited profound disparities by race/ethnicity and place of residence, with higher mortality in non-white persons and in those living in large central and medium metro. Studies are urgently needed to understand reasons underlying these disparities and the recent worsening trend.

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Abstract Number: 0455

Abatacept Reverses Subclinical Arthritis in Patients with High-risk to Develop Rheumatoid Arthritis -results from the Randomized, Placebo-controlled ARIAA Study in RA-at Risk Patients

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Plenary I (0453–0457)

Session Type: Plenary Session

Session Time: 10:30AM–12:00PM

Table 1:
Demographics

			Group		
	Statistic		Abatacept	Placebo	Z: Total
Age(years)		N	49	49	98
		MEAN	51.29	48.55	49.92
Sex	Female	N (%)	31 (63.3)	39 (79.6)	70 (71.4)
	Male	N (%)	18 (36.7)	10 (20.4)	28 (28.6)
Arthralgia		N (%)	49 (100.0)	49 (100.0)	98 (100.0)
Days from diagnosis		N	48	47	95
		MEAN	882.58	387.34	637.57
		P			0.2307
Pain at baseline (VAS 0-100)		N	49	49	98
		MEAN	42.22	42.84	42.53
		P			0.9717
Disease activity at baseline (VAS 0-100)		N	49	49	98
		MEAN	42.16	43.04	42.60
		P			0.9066

P(numeric): Wilcoxon rank sum test (k=2 groups)

Background/Purpose: Rheumatoid arthritis (RA) has a preclinical phase that is characterized by the presence of antibodies against citrullinated proteins (ACPA), subclinical arthritis and pain. ACPA emerge years before the clinical onset of RA. In a subset of such individuals with ACPA (but not yet RA) imaging studies have revealed the presence of inflammatory and structural lesions. This subset of patients is at increased risk for the development of RA. As T cell mediated B cell activation is a key step for triggering the onset of autoimmune inflammatory diseases, such as RA, interventions that target this process may be useful for very early interventions, ultimately preventing the onset of RA. Abatacept appears to be an attractive approach in such task, as it interrupts the activation of T cells and has a well-known favourable safety profile in the treatment of RA.

To test whether abatacept, compared to placebo, reverses subclinical arthritis in patients with ACPA and MRI signs of inflammation, who have not yet developed RA.

Table 2

Primary Endpoint Analysis (Improvement in Inflammation Score) -ITT

			Treatment		
			Abatacept	Placebo	Z: Total
		Statistic			
PRIM_RESP3 *)	No	N (%)	19 (38.8)	34 (69.4)	53 (54.1)
	Yes	N (%)	30 (61.2)	15 (30.6)	45 (45.9)
		P			0.0043

P(numeric): Wilcoxon rank sum test (k=2 groups)
P(categorial): Fishers exact test (2x2tables)

Primary Endpoint Analysis (Improvement in Inflammation Score) -ITT
*) composite of synovitis, tenosynovitis, and osteitis

Methods: ARIAA is a randomized double-blinded placebo-controlled multi-center study in RA-at risk individuals that ACPA positive and show MRI signs of inflammation. The study is composed by a 6 months treatment phase with either abatacept s.c. 125 mg weekly or placebo and 12 months follow up with no treatment. The primary analysis is done on the ITT population and missing values were rated as treatment failures. The primary endpoint was defined as an improvement in at least one of the MRI inflammation parameters (any change from baseline > 0 assessing synovitis, tenosynovitis and osteitis) according to the RAMRIS score.

Results: Between November 2014 and December 2019 a total of 139 patients were included into ARIAA by 14 study sites (11 in Germany, 1 in the Czech Republic and 2 in Spain). Of them, 100 patients were randomized to receive either abatacept or placebo. Two patients were excluded from the ITT population. As a result, 98 patients could be evaluated for efficacy and safety. The primary endpoint of ARIAA was reached: 61% of the patients in the abatacept group improved in at least one of the MRI parameters (synovitis, tenosynovitis, and osteitis) compared to only 31% in the placebo group (p=0.0043). Moreover, arthritis developed in 17 patients in the placebo group (34.7%) but only 4 patients (8.2%) in the abatacept group (p= 0.0025).

12 serious adverse events (1 gastritis, 1 cellulitis, 1 pneumonia, 1 tendinitis calcificans, 1 Rotator cuff syndrome, 1 Cholelithiasis, 1 x peripheral arterial occlusive disease, 1 x chronic idiopathic pain syndrom, 1 prostate cancer, 1 penile neoplasm; 1 trabeculectomy, 1 cataract operation) have been reported between 2014 - 2021, with only one (pneumonia) was assessed to have a causal relationship to study treatment.

Conclusion: These data show that abatacept significantly improves subclinical arthritis in patients at high risk to develop RA. In addition, the data also support the concept that early intervention may prevent or at least delay the development of RA.

Disclosure: J. Rech, Novartis, 2, 5, 6, SOBI, 2, 5, 6, AbbVie, 2, 6, Biogen, 2, 6, BMS, 2, 6, Chugai, 2, 6, GSK, 2, 6, Janssen, 2, 6, Lilly, 2, 6, MSD, 2, 6, Mylan, 2, 6, Roche, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **K. Tascilar**, None; **M. Hagen**, None; **L. Valor Mendez**, None; **A. Kleyer**, None; **G. Kroenke**, None; **D. Simon**, None; **V. Schoenau**, None; **A. Hueber**, None; **S. Kleinert**, Novartis, 5, Abbvie, 1, Siemens Healthineers, 1, Sanofi, 11; **X. Baraliakos**, None; **M. Fleck**, None; **A. Rubbert-Roth**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 2, 6, Roche, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sanofi, 2, 6, Amgen, 2, 6, Novartis, 2, 6; **F. Behrens**, Chugai, 5, 6, AbbVie, 6, Amgen, 6, GlaxoSmithKline, 5, Janssen, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Boehringer Ingelheim, 6, Celgene, 6, Eli Lilly, 6, Merck, 6, Novartis, 6, Sanofi, 6, UCB, 6; **D. Kofler**, None; **M. Feuchtenberger**, None; **M. Zaenker**, None; **R. Voll**, None; **C. Glaser**, None; **E. Feist**, R-Pharm, 2, 6, Abbvie, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, AB2Bio, 6, BMS, 6, Celgene, 6, Janssen, 6, Eli Lilly, 2, 5, 6, Medac, 6, MSD, 6, Roche/Chugai, 2, 5, 6, Sanofi, 6, Sobi, 6, UCB, 6; **G. Burmester**, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6; **K. Karberg**, None; **J. Strunk**, None; **J. Cañete**, Abbvie, 6, Pfizer, 6, Janssen, 6; **E. Naredo**, AbbVie, 6, Roche, 6, BMS, 6, Pfizer, 6, UCB, 6, Lilly, 5, 6, Novartis, 6, Janssen, 6, Celgene GmbH, 6; **M. Filkova**, None; **L. Senolt**, None; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6.

Abstract Number: 0456

Functional Connectivity, Enhanced Blood-Brain Barrier Leakage and Cognitive Impairment in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Plenary I (0453–0457)

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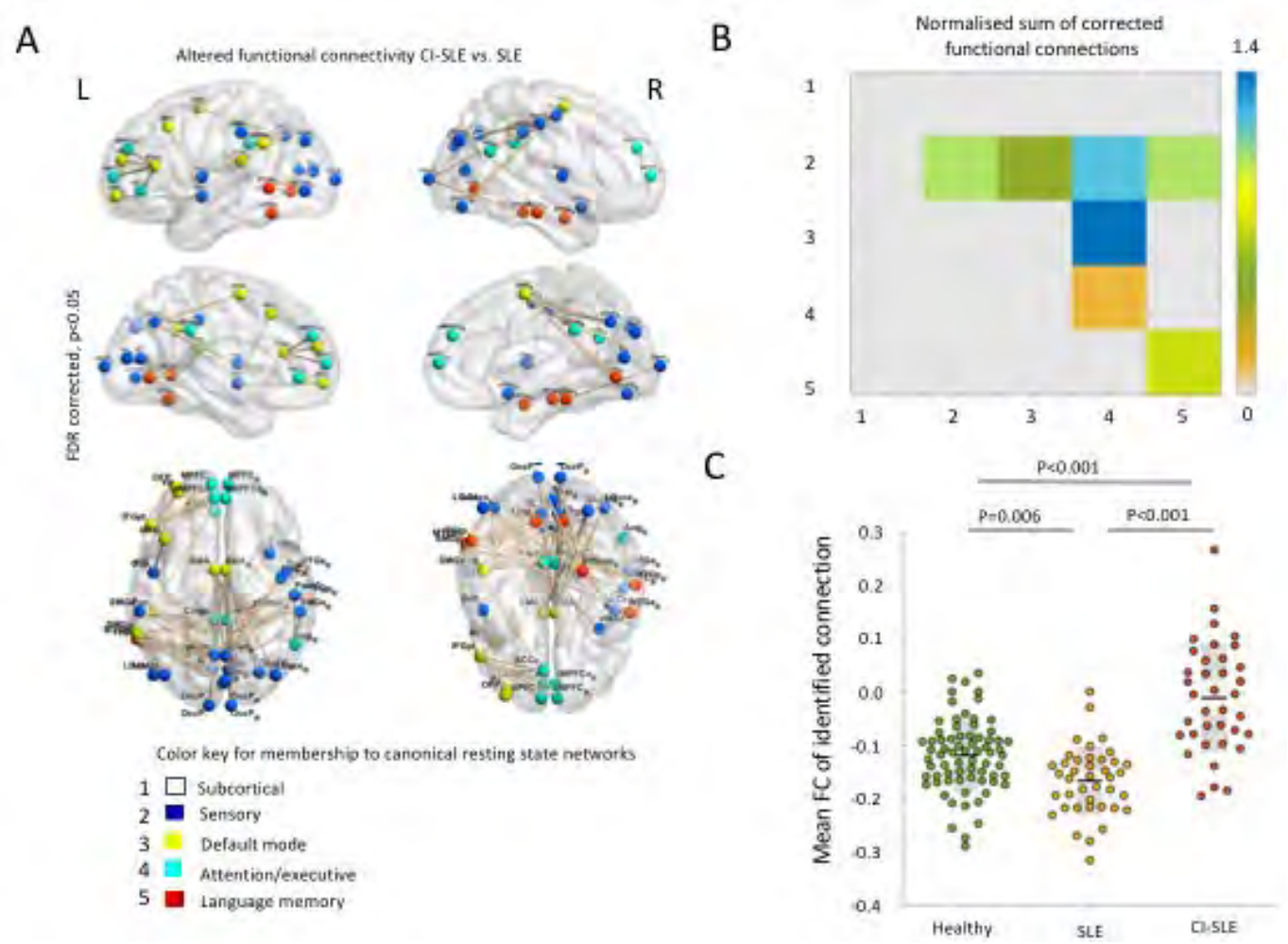

Figure 1. The association between resting state functional connectivity (rsFC) and cognitive impairment (CI) in patients with SLE. A. Contrast maps showing brain regions (colored nodes) with significant reductions in functional connections (yellow edges) in patients with SLE and CI (CI-SLE) compared to patients with SLE and normal cognition. Multiple comparisons were corrected using False Discovery Rate (FDR) at 0.05. Node colors represent membership in each of the five canonical resting state networks (color key legend at the left lower corner). B. Summed and normalized rsFC contrast matrix depicting the sum of corrected significant functional connections (CI-SLE < SLE). Color heat map (right) represents range of values; numbers represent resting-state networks as defined in the key below Panel A. C. Pearson correlation r-values reflecting the associations of all significant connections identified in Panels A & B were averaged and compared between patients with SLE and CI, patients with SLE and normal cognition, and healthy controls (see text for details). Data is presented as a scatter plot over a boxplot; the mean is shown as a black line.

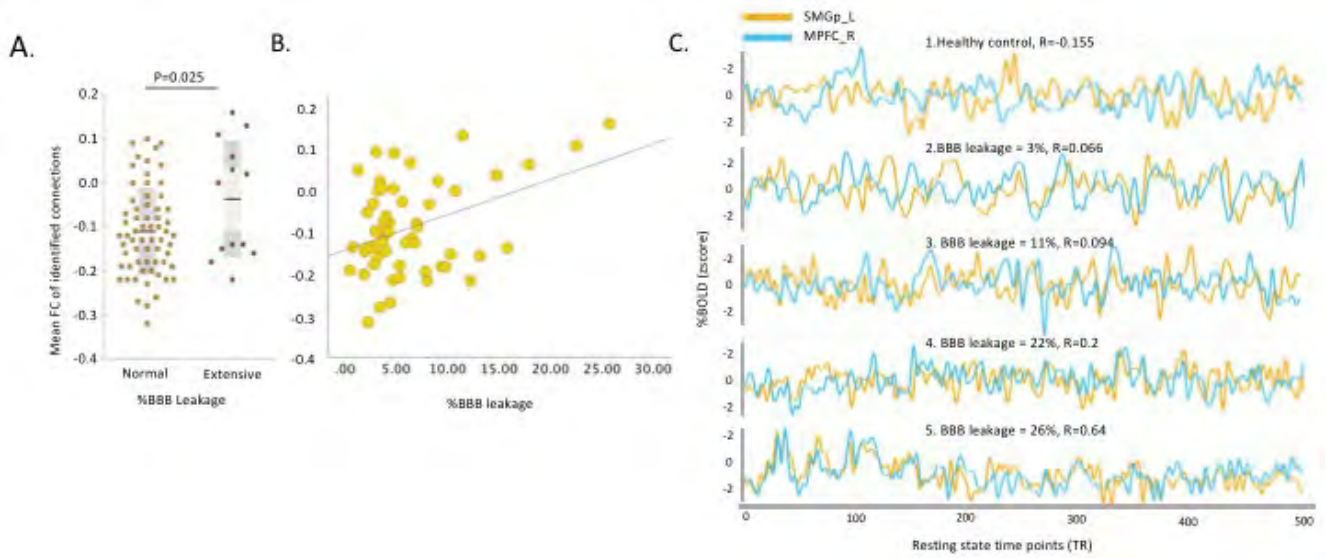

Figure 2. Altered rsFC in patients with SLE is associated with extensive blood-brain barrier leakage (BBB). A. In individual patients with SLE, the mean R-value of all significant functional connections was significantly higher in those with extensive BBB leakage. Data is presented as a scatter plot over a boxplot; the mean is shown as a black line. Significance is derived from the Spearman t-test. B. In individual patients with SLE, there was a trend in the association between the mean of all significant functional connections with %BBB disruption at p=0.082 (Kendal's Tau). C. %BOLD signal (z-scored) for two representative nodes are plotted for five different study participants in order of increasing %BBB disruption (#1 healthy control; #2 SLE with normal cognitive testing; #3-5 SLE with cognitive impairment). The plots show a shift from negative (#1) or no connectivity (#2) to positive connectivity (#3-5) between the two nodes with increase in %BBB leakage. SMGp_L (orange line): left supramarginal gyrus posterior; MPFC_R (blue line): right medial prefrontal cortex.

Background/Purpose: Cognitive impairment is the most frequent manifestation of neuropsychiatric systemic lupus erythematosus (NPSLE), yet the mechanisms underlying it remain poorly understood. We have previously reported an association between enhanced permeability of the blood-brain barrier (BBB), loss of grey matter volume and cognitive impairment in SLE patients. To further explore these associations and identify pathogenetic mechanisms the current study examined non-task based functional connectivity between brain regions using resting state functional magnetic resonance imaging (rsfMRI).

Methods: Adult patients with SLE (n=78, age 49.4 ± 14.3 years, 89.7% female) and healthy controls (n=71, age 38.9 ± 12.9 years, 69.0% female) were recruited at a single academic medical center. To identify cognitive impairment (CI) in SLE patients, global cognitive function and performance in five individual cognitive domains were assessed using standard neuropsychological tests. Quantitative assessment of BBB permeability was measured in SLE patients by dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI). All study participants underwent rsfMRI, in which blood oxygen level dependent (BOLD) signals were collected as a proxy for neural activation. Mean BOLD signals were extracted from 131 regions across five canonical resting-state brain networks to analyze the resting-state functional connectivity (rsFC) between brain regions. The rsFC values were then compared between healthy controls, SLE patients with and without CI and between SLE patients with and without extensive BBB permeability.

Results: Fifty-one connections between functional brain regions were found to differ between SLE patients with CI and those without CI (P< 0.05, FDR corrected). Multivariate analysis of variance demonstrated differences between SLE patients with CI and healthy controls (P=0.006) (Figure 1A & 1C). In SLE patients with CI, within-network connectivity was significantly different for the sensory, attention/executive, and language memory networks (Figure 1B). The between-network connectivity differences occurred primarily between the sensory and attention/executive networks and between the default-mode and language-memory networks (Figure 1B). Mean functional connectivity of affect-

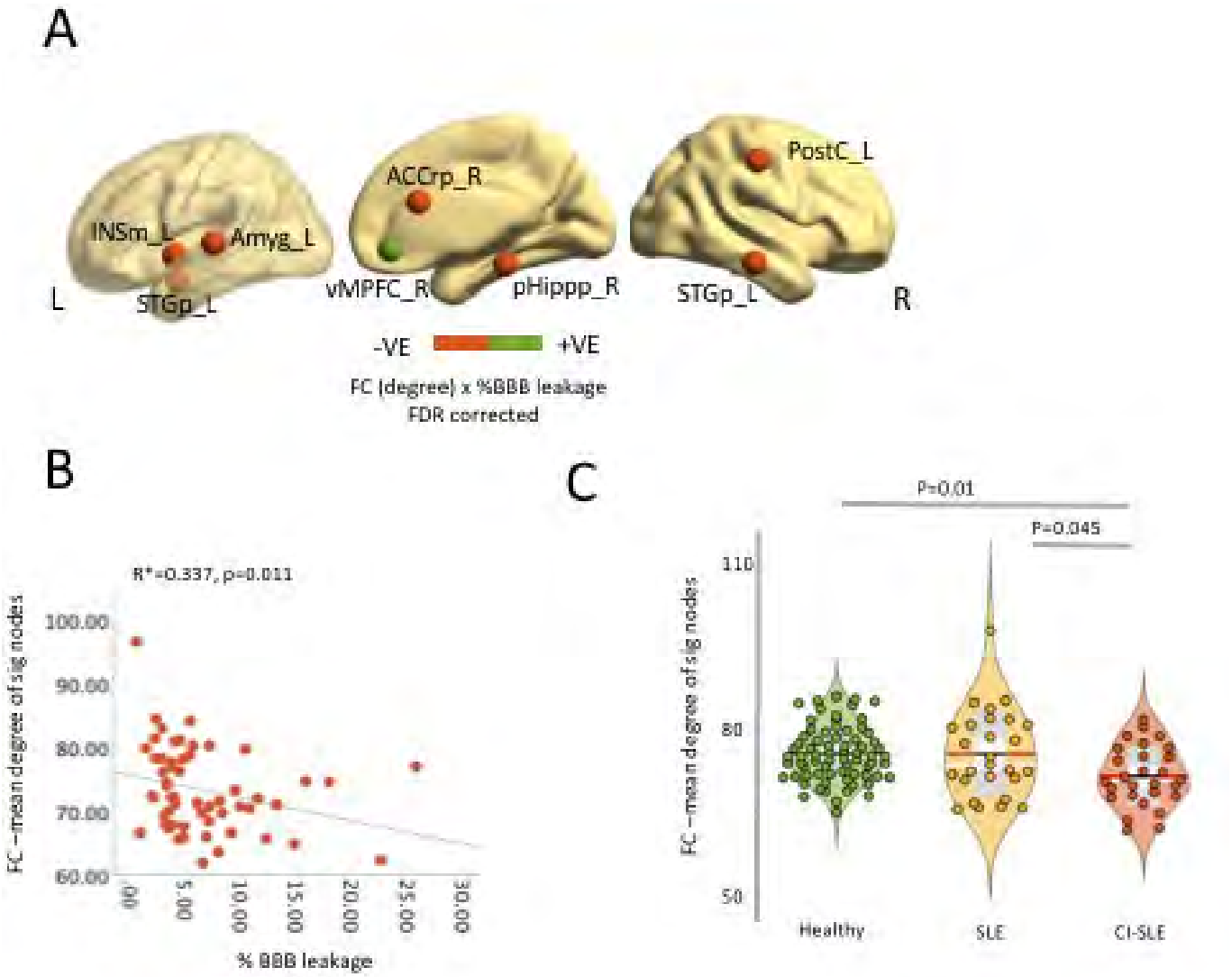

Figure 3. The total number of connections of specific brain regions (or nodal degree) is linked with %BBB leakage and cognitive impairment. A. Nodes in brain regions with decreased (red) or increased (green) connections (degree) were correlated with %BBB leakage (Spearman , corrected for multiple comparisons using False Discovery Rate). Abbreviations: INSm_L, left middle insula; STGp_L, left superior temporal gyrus; Amyg_L, left amygdala, ACCrp_R, right anterior cingulate cortex rostral posterior; pHippp_R, right parahippocampal gyrus posterior; PostC_L, left post central gyrus (S1); vMPFC_R, right ventral medial prefrontal cortex. B. Higher %BBB leakage is associated with lower average degree of the negatively affected nodes (Spearman). C. The average degree of affected nodes is significantly lower in patients with SLE and CI (CI-SLE) compared to patients with SLE with normal cognition (SLE) and healthy controls. Violin plot with scatter box plot with mean shown in red and median in white horizontal lines; p values computed with Kruskal Wallis test.

ed regions was different between SLE patients with normal BBB permeability and SLE patients with extensive BBB leakage (P=0.025) (Figure 2A & 2B). SLE patients with CI (Figure 1C) and those with extensive BBB leakage (Figure 2) had more positive functional connections compared to the other groups. Finally, the total number of brain-wide connections of specific brain regions decreased with higher BBB permeability (P=0.011) and was lower in SLE patients with CI than in SLE patients without CI (P=0.01, Figure 3).

Conclusion: SLE patients with CI demonstrated distinct differences in brain functional connectivity relative to SLE patients without CI and healthy controls. Within the SLE sample, these functional connectivity differences were also seen in those with extensive BBB leakage, suggesting an association between BBB leakage and neural pathology underlying CI in SLE patients.

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Abstract Number: 0457

Immunosuppression Attenuates Antibody and Neutralization Titers in Patients with Chronic Inflammatory Disease Following SARS-CoV-2 Vaccination

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Plenary I (0453–0457)

Session Type: Plenary Session

Session Time: 10:30AM–12:00PM

Background/Purpose: Individuals with chronic inflammatory diseases (CID) are frequently treated with immunosuppressive medications that can increase their risk of severe COVID-19. While novel mRNA-based SARS-CoV-2 vaccination platforms provide robust protection in immunocompetent individuals, the immunogenicity in CID patients. Therefore, determining the effectiveness of SARS-CoV-2 vaccines in these patients is essential to risk-stratify them with impaired protection and provide clinical guidance regarding medication management.

Methods: We initiated the COVID-19 Vaccine Responses in Patients with Autoimmune Disease (COVaRiPAD) study, a prospective assessment of mRNA-based vaccine immunogenicity and reactogenicity in patients with CID. We collected blood from 197 adults with CIDs and 53 immunocompetent controls before initial immunization and 1-2 weeks after the second immunization. Serum anti-SARS-CoV-2 spike (S) IgG+ binding and neutralizing antibody titers were quantified to assess the magnitude and quality of the humoral response following vaccination.

Results: Compared to immunocompetent controls, a three-fold reduction in anti-S IgG titers (P=0.0046) and SARS-CoV-2 neutralization (P< 0.0001) to the D614G common variant were observed in CID patients. B cell depletion and glucocorticoids exerted the strongest effect with a 36- and 13-fold reduction in humoral responses, respectively (p< 0.0001). Janus kinase inhibitors and antimetabolites, including methotrexate, also blunted antibody titers in multivariate regression analyses (P< 0.0001, P=0.0023, respectively). Other targeted therapies, such as TNF inhibitors, IL-12/23 inhibitors, and integrin inhibitors, had only modest impacts on antibody formation and neutralization.

Conclusion: CID patients treated with immunosuppressive therapies exhibit impaired SARS-CoV-2 vaccine-induced immunity, with glucocorticoids and B cell depletion therapy more severely impeding optimal responses. We are currently determining cross-variant neutralization, long-term antibody and neutralization titers, and T cell responses in this cohort.

Table 1. Demographic and Clinical Characteristics of Participants with Chronic Inflammatory Diseases

Characteristics	Control (N=63)	CID (N=197)
Age, years		
Mean ± SD	43.4 ± 14.1	48.2 ± 16.1
Age category — no. of participants (%)		
<65yr	48 (86.8)	158 (80.2)
≥65yr	7 (13.2)	39 (19.8)
Gender — no. of participants (%)[‡]		
Female	29 (54.7)	145 (73.6)
Male	24 (45.3)	52 (26.4)
Hispanic or Latinx ethnicity – no. of participants (%)[‡]		
Hispanic or Latinx	5 (7.5)	8 (4.1)
Not Hispanic or Latinx	49 (92.6)	189 (95.9)
Race or ethnic group — no. of participants (%)[‡]		
White	42 (79.2)	176 (89.3)
Asian	7 13.2)	9 (4.6)
Black or African American	1 (1.9)	9 (4.6)
Other	3 (5.7)	3 (1.5)
BMI (kg/m2), mean ± SD		26.6 ± 6.3
Days after 2nd immunization for blood sample, mean ± SD		8.5 ± 2.8
Immunologic Diagnosis - no. of participants (%)[§]		
Inflammatory Bowel Disease		70 (33.5)
Crohn's Disease		43 (21.8)
Ulcerative Colitis		22 (11.2)
Other		5 (2.5)
Rheumatoid Arthritis		45 (22.8)
Spondyloarthritis		23 (11.7)
Axial Spondyloarthritis		8 (4.1)
Psoriatic Arthritis/Psoriasis		10 (5.1)
IBD Arthritis		5 (2.5)
Uveitis		8 (4.1)
Systemic Lupus Erythematosus		22 (11.2)
Other Connective Tissue Disease[¶]		13 (6.6)
Sjögren's Syndrome		14 (7.1)
Vasculitis		5 (2.5)
Autoinflammatory Syndrome		2 (1.0)
Multiple Sclerosis		16 (8.1)
Neuromyelitis Optica		1 (0.5)
IgG4-Related Disease		2 (1.0)
Hidradenitis Suppurativa		1 (0.5)
Human Immunodeficiency Virus		1 (0.5)
Anti-phospholipid Syndrome		1 (0.5)
Psoriasis		9 (4.6)
Alopecia areata		1 (0.5)
Medication exposure - no. of participants (%)		
Prednisone		21 (10.7)
Mean mg/day ± SD		6.5 ± 6.8
Range, mg/day		1 - 20
Disease Modifying Antirheumatic Drug (DMARD)		
Methotrexate		40 (20.3)
Mean mg/week ± SD		17.1 ± 5.4
Range, mg/day		7.5 - 25
Hydroxychloroquine		41 (20.8)
Mycophenolate Mofetil		10 (5.1)
Mycophenolic acid		1 (0.5)
Azathioprine		10 (5.1)
Leflunomide		7 (3.6)
Sulfasalazine		11 (5.6)
6-mercaptopurine		5 (2.5)
Tofacitinib		1 (0.5)
Janus Kinase inhibitors		
Tofacitinib		12 (6.1)
Upadacitinib		1 (0.5)
Biological therapies		
Tumor Necrosis Factor inhibitors[§]		56 (28.4)
B cell depleting therapies[†]		19 (9.6)
Belimumab		4 (2.0)
Vedolizumab		12 (9.0)
Natalizumab		1 (0.5)
Interleukin 12/23 or 23 inhibitors[*]		15 (7.6)
Abatacept		4 (2.0)
Tocilizumab		1 (0.5)
Ixekizumab		1 (0.5)
Canakinumab		1 (0.5)
Colchicine		3 (1.5)
Intravenous immunoglobulin		3 (1.5)
Fingolimod		1 (0.5)
Siponimod		1 (0.5)
Ibrutinib		1 (0.5)
Dimethyl Fumarate		1 (0.5)
Nonsteroidal Anti-inflammatory Drugs (NSAIDs)		27 (20.3)
No DMARDs or biologics		5 (2.5)

[§]Patients could be diagnosed with more than 1 condition, such that the sum of diagnoses is greater than the number of participants.

[‡]Gender, Race or ethnic group was reported by the participant.

[¶]Other Connective Tissue Disease includes undifferentiated connective tissue disease, mixed connective tissue disease, dermatomyositis, polymyositis, and scleroderma

[§]Tumor Necrosis Factor inhibitors includes adalimumab (n=20), certolizumab pegol (n=5), etanercept (n=14), golimumab (n=23 and infliximab (n=14).

[†]B cell depleting therapies include rituximab (n=13), ocrelizumab (n=5), and obinutuzumab (n=1).

[*]Interleukin 12/23 inhibitors include ustekinumab (n=14) and interleukin 23 inhibitors include guselkumab (n=1)

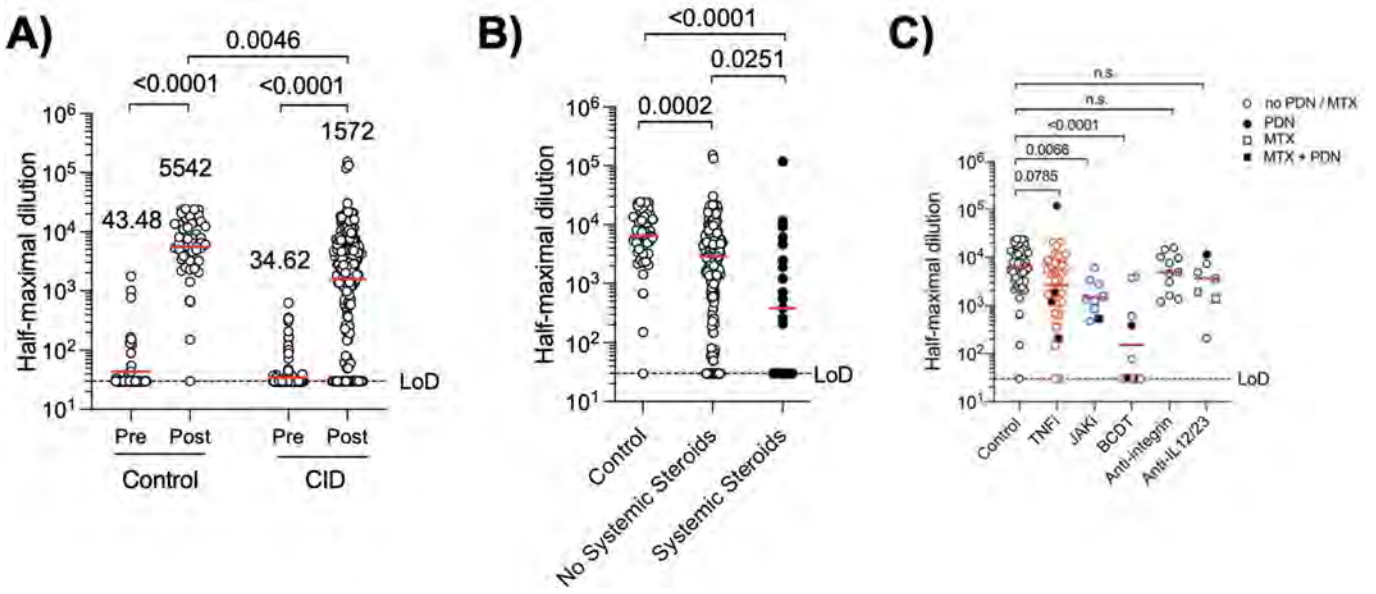

Figure 1

Disclosure: M. Paley, None; **P. Deepak**, Abbvie, 1, Takeda Pharmaceuticals LLC, 5, Janssen Pharrmaceuticals, 1, Pfizer, 1, Prometheus Biosciences, 1, Boehringer Ingelheim, 1, 5, Arena Pharmaceuticals, 1, 5, Bristol-Myers Squibb-Celgene, 5; **W. Kim**, None; **M. Yang**, None; **A. Carividi**, None; **E. Demissie**, None; **A. El-Qunni,**, None; **A. Haile**, None; **K. Huang**, None; **B. Kinnett**, None; **M. Liebeskind**, None; **Z. Liu**, None; **L. McMorrow**, None; **D. Paez**, None; **N. Pawar**, None; **D. Perantie**, None; **R. Schriefer**, None; **S. Sides**, None; **M. Thapa**, None; **S. Akuse**, None; **S. Burdess**, None; **A. Rose**, None; **L. Mitchell**, None; **S. Chahin**, None; **M. Ciorba**, Abbvie, 2, Pfizer, 2, 5, BMS, 2, Theravance, 2, Incyte, 5, Janssen, 5; **J. Graf**, None; **P. Katz**, None; **M. Matloubian**, Virtuoso Therapeutics Inc., 2; **J. O'Halloran**, None; **R. Presti**, None; **G. Wu**, Novartis, 2, Genentech, 2, Biogen, 5, EMD Serono, 5, Roche, 5; **S. Whelan**, Vit Biotechnology, 5, Abbvie, 5, SAb Therapeutics, 5; **W. Buchser**, None; **L. Gensler**, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2; **M. Nakamura**, None; **A. Ellebedy**, Emergent BioSolutions, 5, Abbvie, 5; **A. Kim**, Kypha, Inc., 5, GlaxoSmith-Kline, 2, 5, 6, Alexion Pharmaceuticals, 2, Annexon Biosciences, 2, Aurinia Pharmaceuticals, 2, 6.

Abstract Number: 0458

Single Cell Profiling Reveals a Wnt-mediated Transcriptional Gradient That Drives Inflammation in Rheumatoid Arthritis Synovial Fibroblast Pathology

Alisa Mueller[1], Angela Zou[1], Emily Taylor[2], Triin Major[2], David Gardner[3], Adam Croft[4], Roche Fibroblast Network Consortium[5], Andrew Filer[2], Christopher Buckley[6], Kevin Wei[1], Ilya Korsunsky[1], Soumya Raychaudhuri[1] and Michael Brenner[7], [1]Brigham and Women's Hospital, Boston, MA, [2]University of Birmingham, Birmingham, United Kingdom, [3]University of Birmingham, College of Medical and Dental Sciences, Birmingham, United Kingdom, [4]University of Birmingham, Halesowen, United Kingdom, [5]Roche Innovation Center Basel, Basel, Switzerland, [6]University of Oxford, Oxford, United Kingdom, [7]Brigham and Women's Hospital, Harvard Medical School, Newton, MA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: RA – Etiology & Pathogenesis (0458–0461)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Synovial fibroblasts are key inflammatory aggressors in rheumatoid arthritis (RA) that mediate cartilage and bone destruction, yet therapies directly targeting these cells are lacking. Our previous single cell analy-

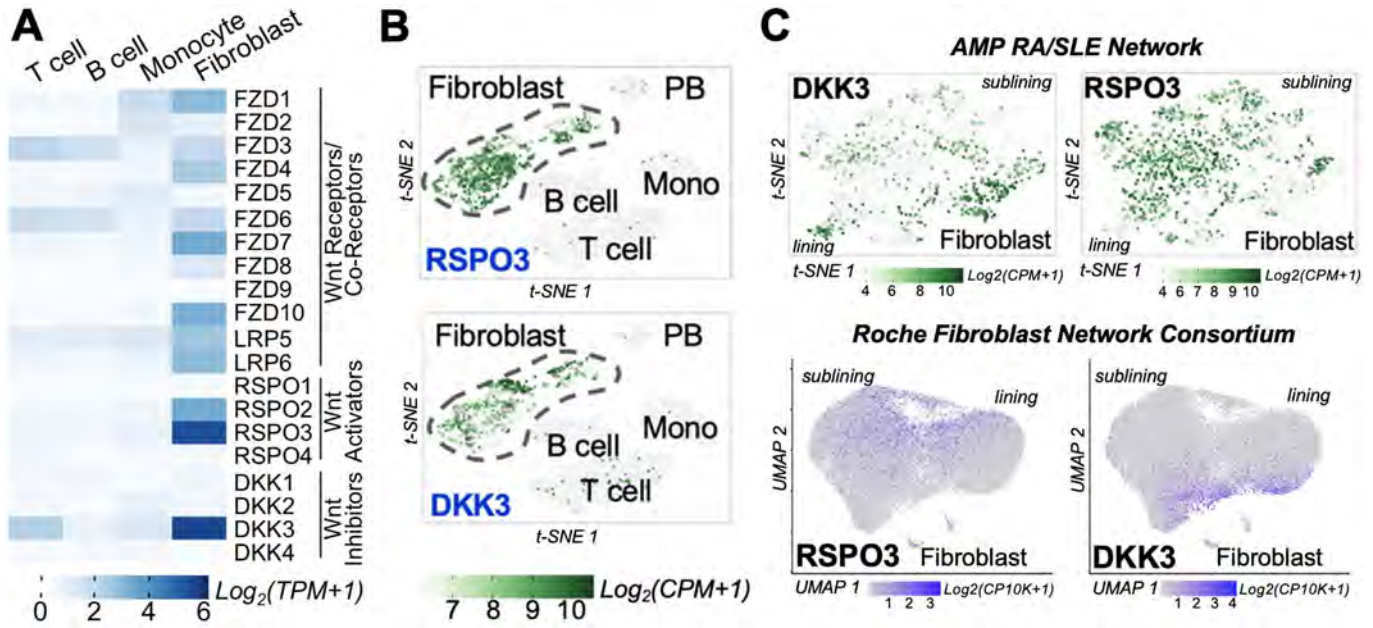

Figure 1. Synovial fibroblasts are poised for Wnt signaling, and expression of Wnt agonist RSPO3 is inversely correlated with Wnt antagonist DKK3 among fibroblast subpopulations. A) Expression of Wnt receptors, co-receptors, activators, and inhibitors from bulk RNA sequencing of synovial populations in OA and RA patients are predominantly expressed in fibroblasts. (B) Single-cell sequencing analyses of synovial cells from OA and RA patients confirms fibroblast-specific expression of a number of Wnt pathway members including DKK3 and RSPO3. (C) DKK3 and RSPO3 exhibit reciprocal patterns of expression within synovial fibroblast subpopulations in independent studies.

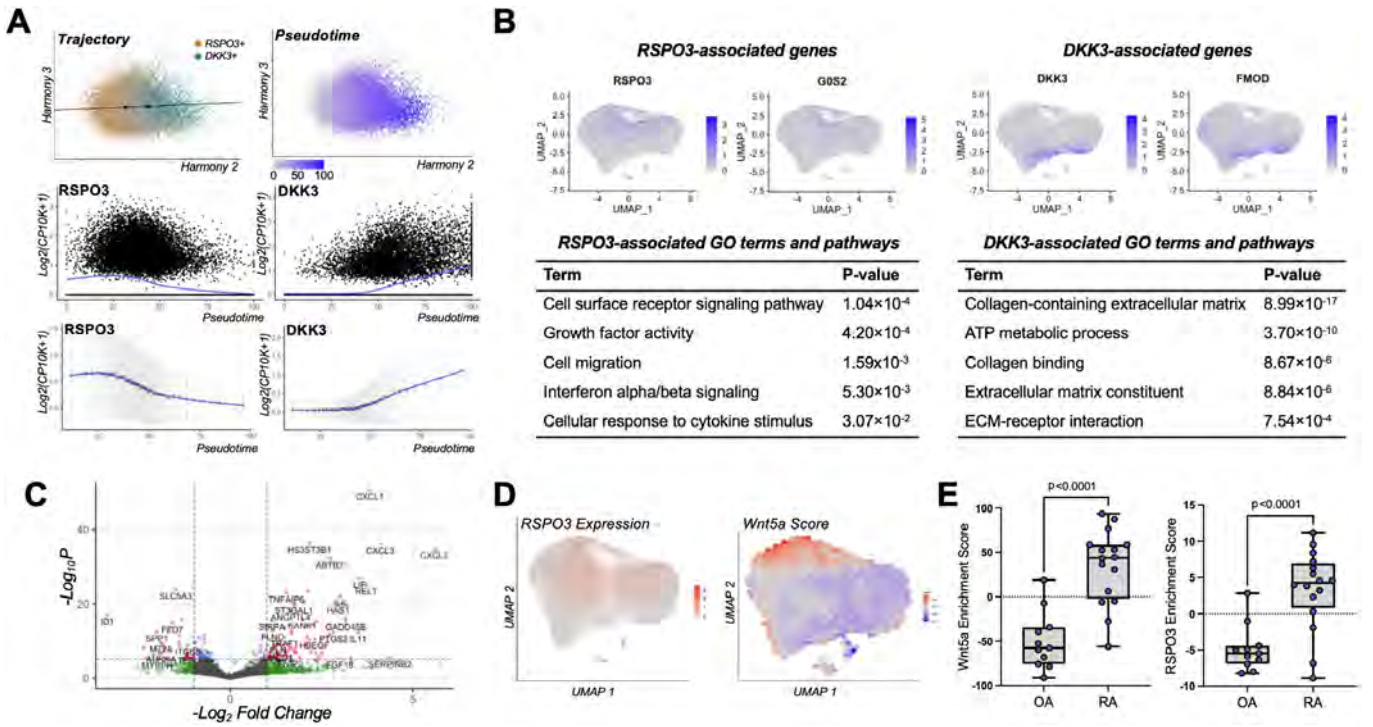

Figure 2. RSPO3 and DKK3 define a transcriptional gradient that is correlated with Wnt activity and inflammation. A) Trajectory analysis identifies genes that follow expression patterns that are similar to RSPO3 and DKK3 (B) Genes associated with RSPO3 show enrichment for cell growth, migration, and cytokine signaling while genes associated with DKK3 are linked to structural collagen components and extracellular matrix. (C) Differential expression analysis of synovial fibroblasts treated with Wnt5a compared with controls reveals that non-canonical Wnt signaling is associated with genes that drive inflammatory pathways. (D) RSPO3 expression is correlated with higher non-canonical Wnt activity. (E) Human fibroblasts isolated from leukocyte-rich RA synovial tissue show enhanced Wnt activity scores and RSPO3 enrichment scores compared with synovial fibroblasts isolated from OA samples.

ses revealed multiple clusters including a fibroblast subpopulation characterized by high expression of DKK3, a Wnt-associated gene. Wnt activation can promote cell proliferation, invasion, and differentiation, making it an attractive, potentially targetable pathway in RA. Here, we report that non-canonical Wnt signaling drives a strong inflammatory gene expression signature among synovial fibroblasts.

Methods: Bulk and single cell RNA sequencing data from the Accelerating Medicines Partnership (AMP) RA/SLE Network were used to analyze expression of Wnt pathway members among synovial populations in osteoarthritis (OA) and RA. To delineate fibroblast-specific patterns of Wnt signaling, we further utilized a comprehensive stromal cell-selected single cell dataset from the Roche Fibroblast Network Consortium that includes over 73,000 fibroblasts derived from OA and RA synovium as well as other chronic inflammatory diseases. Trajectory analysis was employed to identify a gradient of Wnt expression across fibroblast populations. We developed Wnt activation signatures using in vitro stimulation of human RA-derived synovial fibroblast lines treated with canonical and non-canonical Wnt ligands.

Results: Among all synovial cell populations, Wnt pathway members are predominantly expressed in fibroblast subsets. These molecules include Frizzed receptors, LRP5/6 co-receptors, R-spondin (RSPO) Wnt agonists, and Dickkopf (DKK) Wnt antagonists. Interestingly, non-canonical Wnt ligands dominate in expression as do RSPO3 and DKK3 (Figure 1A and 1B). Strikingly, RSPO3 and DKK3 are expressed reciprocally in distinct populations. Instead of being cluster-specific, RSPO3 and DKK3 form a strong gradient along both lining and sublining fibroblasts (Figure 1C). Using trajectory analysis, we demonstrate that RSPO3 and DKK3 correlate with genes that are differentially associated with inflammation and tissue repair, respectively (Figure 2A and 2B). To explore Wnt pathway activity along this gradient, we generated a non-canonical Wnt activation signature using synovial fibroblasts stimulated with Wnt5a. This signature reveals that non-canonical Wnt signaling drives fibroblast inflammation (Figure 2C) and is particularly active among cells expressing Wnt agonist RSPO3 (Figure 2D). The Wnt5a and RSPO3 gene signatures are also enhanced in fibroblasts derived from inflamed RA synovial tissue compared with those from OA synovial tissue while the DKK3 signature is reduced, suggesting increased Wnt activity in inflammatory RA (Figure 2E). Moreover, analyses show comparable Wnt-mediated gradients in Sjogren's syndrome and interstitial lung disease, indicating broader disease applicability.

Conclusion: We identify non-canonical Wnt signaling as a novel mechanism contributing to RA synovial fibroblast heterogeneity and inflammatory phenotype. This work provides a foundation for the development of Wnt-modulating pharmacologic strategies targeting synovial fibroblasts in RA.

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Abstract Number: 0459

CCN1: An Angiogenic Actor Implicated in the Structural Damages of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Abstracts: RA – Etiology & Pathogenesis (0458–0461)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: We have previously shown that decreased expression of the deacetylase sirtuin-1 (SIRT1) contributes to the proliferative, activated and proangiogenic profile of endothelial cells (EC) in rheumatoid arthritis (RA). The matricellular protein CCN1, characterized by proangiogenic and immunomodulatory properties, may be directly implicated in these processes, since its expression is negatively regulated by SIRT1.Our objective was to study the implication of CCN1 in RA pathogenesis.

Methods: CCN1 expression was assessed in ECs (25 RA and 10 controls) by quantitative RT-PCR, western blot and ELISA, in the synovial tissue (5 RA and 5 controls) by immunohistochemistry and immunofluorescence, and in the serum (205 RA and 20 controls) by ELISA. Invalidation of CCN1 in RA ECs was achieved through the use of shRNA and neutralizing monoclonal antibodies. The functional consequences of CCN1 invalidation in RA ECs were studied i) *in vitro* by the analysis of proliferation (cell impedance), tube formation in Matrigel and migration in Boyden chambers; and ii) *in vivo*in the murine model of tumor neoangiogenesis. Conditional invalidation of CCN1 in ECs was analyzed in the mouse model of methyl-BSA-induced arthritis.

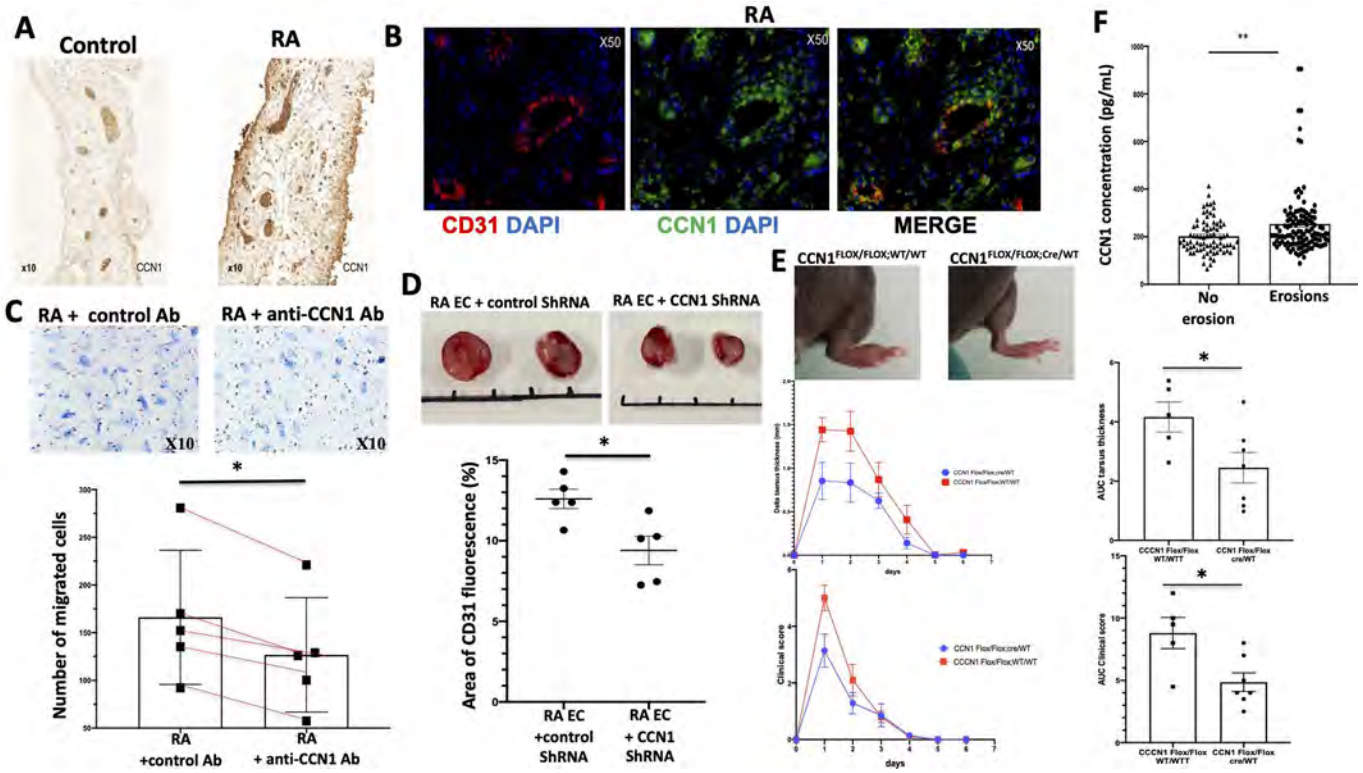

Figure 1. Implication of CCN1 in the pathogenesis of rheumatoid arthritis (RA). A, Representative immunohistochemistry staining for CCN1. B, Representative confocal microscopy analyses. p<0.01. C, Representative images of RA endothelial cell (EC) migration; Y-axis shows the number of migrated cells, statistical test: Wilcoxon test, * p<0.05. D, Representative subcutaneous tumors, Y-axis shows the fluorescence area in %, statistical test: Wilcoxon test, * p<0.05. E, mBSA-induced arthritis in littermates of CCN1 Flox/Flox; WT/WT mice (n=5) and SCCN1 Flox/Flox; Cre/WT mice (n=7); Y-axis shows tarsus thickness and clinical score, as well as the area under the curve (AUC) of tarsus thickness (C) and the clinical score (D). statistical test: Student t test, * p<0.05. F, CCN1 serum concentrations; statistical test: Student t test, ** p<0.01.

Results: CCN1 mRNA and protein expression were increased by 1.72- (p = 0.012) and 7.2-fold (p=0.008) in RA ECs compared to controls, respectively. CCN1 concentrations were significantly increased in RA EC culture supernatants (930±153 vs. 359±199 pg/mL, p=0.007). CCN1 was overexpressed in the synovial tissue of RA patients (Figure 1A) and confocal microscopy analyses revealed a prominent CCN1 expression in the vascular endothelium (CD31 +) and T cells (CD3 +) (Figure 1B). *In vitro*, recombinant TNF-α and IL-17 induced the mRNA and protein expression of CCN1 in RA ECs. CCN1 invalidation was associated with reduced proliferative capacities, delayed capillary tube formation, and decreased migration (Figure 1C) of RA ECs. *In vivo*, subcutaneous transplantation of CT26 tumor cells combined with RA ECs transfected with CCN1 shRNA to CB17 SCID mice was associated with a 51% reduction in tumor volume (p=0.008) and a 27% reduction in tumoral vascular density (p=0.032) compared with mice transplanted with MOCK transfected RA-ECs (Figure 1D). Conditional deletion of CCN1 in ECs through a Cre-LoxP recombination system alleviated signs of methyl-BSA-induced arthritis (Figure 1E). Serum CCN1 concentrations were significantly higher in the presence of bone erosions (253±139 vs. 202±7 pg/mL, p=0.002) (Figure 1F) and correlated with radiographic Larsen score (r=0.3, p=0.001) and HAQ (r=0.25, p=0.012).

Conclusion: CCN1 is overexpressed in ECs and the synovial tissue of patients with RA. CCN1 also regulate the functional properties of RA ECs and their angiogenic potential *in vivo.* Moreover, endothelial inactivation of CCN1 alleviate experimental arthritis. CCN1 could represent a new therapeutic target, which is being evaluated in experimental models of erosive arthritis. CCN1 may also be a reliable biomarker of structural damages given the association between its serum concentrations and the extent of radiographic lesions. The performance of CCN1 serum levels to predict structural progression is under investigation.

Disclosure: J. Avouac, None; **A. Steelandt**, None; **O. Amiar**, None; **A. Leblond**, None; **C. Orvain**, None; **A. Cauvet**, None; **V. Gonzalez**, None; **Y. Allanore**, None.

Abstract Number: 0460

Single-cell Profiling of B and T Cell Repertoire and Gene Expression in the RA Synovium Reveals Tissue Specific Clonal Expansion

Nida Meednu[1], Aaron Wagner[2], Garett Dunlap[3], Fan Zhang[4], Anna Helena Jonsson[5], Kevin Wei[5], Paul Utz[6], William Robinson[7], Holden Maecker[7], Judith James[8], Joel Guthridge[8], S. Louis Bridges, Jr.[9], Vivian Bykerk[9], Laura Donlin[9], Susan Goodman[9], Edward DiCarlo[9], Christopher Ritchlin[10], Darren Tabechian[2], James Lederer[11], Ellen Gravallese[12], Mandy McGeachy[13], Gary Firestein[14], David Boyle[15], Peter Gregersen[16], Diane Horowitz[17], Harris Perlman[18], Arthur Mandelin[18], Joan Bathon[19], Laura Geraldino-Pardilla[19], Laura Hughes[20], V. Michael Holers[21], Kevin Deane[22], Larry Moreland[21], Andrew Filer[23], Costantino Pitzalis[24], Lindsy Forbess[25], Ami Ben-artzi[26], Karen Salomon-Escoto[27], Soumya Raychaudhuri[5], Michael Brenner[28], Deepak Rao[5], Andrew McDavid[2], Jennifer Anolik[1] and Accelerating Medicines Partership (AMP) RA/SLE Network[29], [1]University of Rochester Medical center, Rochester, NY, [2]University of Rochester, Rochester, NY, [3]Harvard University, Somerville, MA, [4]Harvard Medical School, Boston, MA, [5]Brigham and Women's Hospital, Boston, MA, [6]Stanford University, Stanford, CA, [7]Stanford University, Palo Alto, CA, [8]Oklahoma Medical Research Foundation, Oklahoma City, OK, [9]Hospital for Special Surgery, New York, NY, [10]Division of Allergy, Immunology, and Rheumatology, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY, [11]Brigham and Women's Hospital and Harvard Medical School, Millis, MA, [12]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA, [13]University of Pittsburgh, Pittsburgh, PA, [14]University of California San Diego, San Diego, CA, [15]University of California San Diego, La Jolla, CA, [16]The Feinstein Institute for Medical Research, Larchmont, NY, [17]Northwell Health, Jericho, NY, [18]Northwestern University, Chicago, IL, [19]Columbia University, New York, NY, [20]University of Alabama at Birmingham, Birmingham, AL, [21]University of Colorado, Denver, CO, [22]University of Colorado Denver, Denver, CO, [23]University of Birmingham, Birmingham, United Kingdom, [24]Queen Mary University of London, London, United Kingdom, [25]Cedars-Sinai Medical Center, Los Angeles, CA, [26]Cedars-Sinai Medical Center, Beverly Hills, CA, [27]University of Massachusetts Medical School, Shrewsbury, MA, [28]Brigham and Women's Hospital, Harvard Medical School, Newton, MA, [29]Brigham and Women's Hospital, Everett, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: RA – Etiology & Pathogenesis (0458–0461)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: B cell and T cell activation pathways in the synovium are an incompletely understood feature of rheumatoid arthritis. In this study, utilizing single cell RNA sequencing coupled with B and T cell repertoire sequencing to characterize B and T cell states that may play a role in immune activation within the synovium, we define potential developmental relationships and identify key signaling pathways that support local immune cell activation and development of autoreactive plasma cells.

Methods: B and T cells were sorted by flow cytometry from RA synovial tissue (n=13) and matched peripheral blood (PBL) (n=10) as part of the AMP Network Phase 2. Single cell RNA sequencing was performed on the 10x Genomics platform with poly-A selected, 5' initiated expression and BCR or TCR libraries generated from each single cell. Quality control criteria (# of genes detected and % mitochondria gene) were applied to the sequencing data. Clustering analysis using gene expression was performed to identify B cell and T cell subsets. In B cells, we analyzed somatic hypermutation (SHM), immunoglobulin isotype and clonality. Diversity was assessed by looking at V(D)J segment usage frequencies and CDR3 properties. In T cells, we assessed the extent of oligoclonality in different T cell subsets and the overlap in repertoires across T cell subsets.

Results: After applying QC, over 50,000 lymphocytes were available for downstream analysis (36,000 from PBL and 20,600 cells from synovial tissue). Clustering identified various naive and activated B cell populations, plasma cells, and naive CD4 and CD8, Treg and effector T cell states. We observed synovial enrichment of clusters including activated B cells, Tph cells, and granzyme K-expressing CD8 T cells. Activated synovial B cells had significantly higher SHM compared to PBL. In every subject, we observed substantial clonal expansion in both the synovium and peripheral blood, as well as clones shared between these tissues. Naïve B and T cells exhibited fewer expanded clonotypes than non-naïve populations. In both B cells and T cells, there was clonal sharing across synovial sub-populations, including between IgG and IgA plasma cells, activated B cell and plasma cells, and between memory and effector T cells. Together, our findings suggest in situ differentiation of selected B and T cell clones and trafficking of these expanded clones between blood and synovium.

Conclusion: Our data demonstrate the value of integrating gene expression and repertoire data for the study of T and B cell responses in RA synovial tissue and provide evidence of in situ selection.

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2, 4FO Ventures, 2, Mestag Therapeutics, 2, 11; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6; **A. McDavid**, None; **J. Anolik**, None; **A. (AMP) RA/SLE Network**, None.

Abstract Number: 0461

Plasmablast-derived Autoantibodies from Individuals At-risk for RA That Target RA-relevant Antigens Are Polyreactive with Arthritogenic Bacteria

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: RA – Etiology & Pathogenesis (0458–0461)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Circulating autoantibodies like ACPA frequently develop years before symptoms of RA, during which the individual is at-risk for disease. Several lines of evidence suggest that these autoantibodies may be driven by microbial-mucosal interactions. We hypothesized that discrete gut-derived bacteria drive autoantibody generation.

Methods: Dual IgA/IgG family plasmablasts (n=94) were isolated from 4 individuals at-risk for RA, defined as serum anti-CCP+ (75%) and/or RF+ (75%), and from 2 anti-CCP+ individuals with early RA. Fab domains from the plasmablast-derived mAbs (PB-mAbs), selected for binding of RA-relevant antigens on a protein microarray, were expressed in a mouse IgG2a scaffold. The PB-mAbs were used to identify targeted fecal bacteria, and *Ruminococcaceae(Rumino)* strains were isolated from the feces of a human at-risk for RA. 16S sequencing identified seven *Rumino* family strains of interest, and through whole genome sequencing we identified an as yet unnamed species within genus *Subdoligranulum (Sbg)*. Human PBMC were isolated and exposed to individual strains of *Sbg* to gauge memory responses by assessing *in vitro* CD154+ upregulation on CD4+ T cells. Germ free DBA/1 mice were colonized with each *Sbg* strain, as well as *Prevotella copri* and PBS as controls, and were monitored for stable colonization, autoantibody development, and joint swelling. Serum collected from arthritogenic *Sbg* monocolonized mice was injected into naive germ-free DBA/1 mice, and mice were monitored for joint swelling.

Results: All PB-mAbs bound RA-relevant antigens and 58/94 (62%) targeted families *Lachno(spiraceae)/Rumino* from a pool of fecal bacteria (derived from 5 healthy controls, 8 at-risk individuals, and 5 RA cases) at a disproportionately elevated level (56.31 ± 12.85% of all bacteria bound) compared to other taxa, suggesting cross-reactivity between bacterial and host antigens. We verified PB-mAb binding of *Lachno/Rumino* using our generated *Sbg* strains. We then observed an MHC class II-dependent memory T cell response in PBMCs against a subset of the *Sbg* strains in individuals with RA that was nearly absent in controls. To determine if *Sbg* could induce autoantibodies *in vivo*, germ-free mice were stably colonized with the *Sbg* strains, *P. copri*, or sterile PBS; within 14 days, joint swelling was observed only in mice monocolonized with a subset of the *Sbg* strains. Joint swelling was associated with an expansion of

antibodies to RA-relevant antigens. Transfer of serum from affected *Sbg* strain colonized mice, but not *P. copri* or PBS controls, to naïve mice resulted in joint swelling.

Conclusion: A subset of circulating dual IgA/IgG PB-mAbs isolated from individuals at-risk for RA target both RA-relevant antigens and bacteria within families *Lachno/Rumino*. A specific strain from the genus *Sbg* established from an at-risk individual were recognized by T cells from RA cases. When germ-free mice were monocolonized with the specific *Sbg* strain, they developed joint swelling and serum autoantibodies capable of transferring the joint swelling phenotype. Our data suggests one model in which a strain of bacteria is capable of stimulating the development of pathogenic autoantibodies.

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Abstract Number: 0462

Remotely Delivered Cognitive Behavioural and Personalised Exercise Interventions Reduce Fatigue Severity and Impact in Inflammatory Rheumatic Diseases: Results from a Multi-centre Randomised Controlled Parallel Group Trial

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Inflammatory rheumatic disease (IRD) related fatigue is pervasive and disabling, even in otherwise stable disease. Although cognitive-behavioural approaches (CBAs) and personalised exercise programmes (PEP) are considered effective treatments, rheumatology services encounter significant implementation barriers: 1) existing interventions have not been standardised and tested across the range of IRDs managed by rheumatology 2) the requisite specialist expertise does not commonly exist within rheumatology multi-disciplinary teams (MDT) 3) regular face to face sessions are often undesirable for patients, especially during a pandemic.

This is the first study to test remotely delivered CBA and PEP, by the rheumatology MDT, across IRDs.

Table 1 Baseline characteristics of study participants

Variable	PEP (n 124)	CBA (n 121)	Usual Care (n 122)
Age [years]#	56.4 (12.3)	59.3 (13.0)	56.8 (12.7)
Missing	1 (0.8)	0 (0)	0 (0)
Gender†			
Female	97 (78.2)	84 (69.4)	93 (76.2)
Male	26 (21.0)	37 (30.6)	29 (23.8)
Missing			
Employment Group†			
Working full-time (30+hrs /week)	35 (28.2)	36 (29.8)	38 (31.1)
Working part-time (<30+hrs /week)	16 (12.9)	16 (13.2)	23 (18.9)
Unemployed and looking for work	2 (1.6)	1 (0.8)	1 (0.8)
Unable to work because of illness or disability	20 (16.1)	14 (11.6)	16 (13.1)
At home and not looking for paid employment	4 (3.2)	2 (1.7)	3 (2.5)
Student	2 (1.6)	2 (1.7)	1 (0.8)
Retired	42 (33.9)	46 (38.0)	36 (29.5)
Other	2 (1.6)	3 (2.5)	2 (1.6)
Missing	1 (0.8)	1 (0.8)	2 (1.6)
Disease duration [years]#	11.9 (11.3)	10.7 (9.1)	11.8 (10.1)
Missing	33 (26.6)	24 (19.8)	31 (25.5)
Other co-morbidities (Charlson Index)#	1.5 (0.9)	1.8 (1.2)	1.6 (1.1)
Missing	1 (0.8)	0 (0)	0 (0)
Erythrocyte Sedimentation Rate [mm]#	17 (15)	18 (19)	14 (14)
Missing	3 (2.4)	4 (3.3)	1 (0.8)
Disease Activity self-report (NRS 0-10)#	5.6 (2.4)	5.7 (2.2)	5.6 (2.2)
Missing	1 (0.8)	1 (0.8)	1 (0.8)

#Continuous data: mean (sd) †Ordinal data: N n(%)

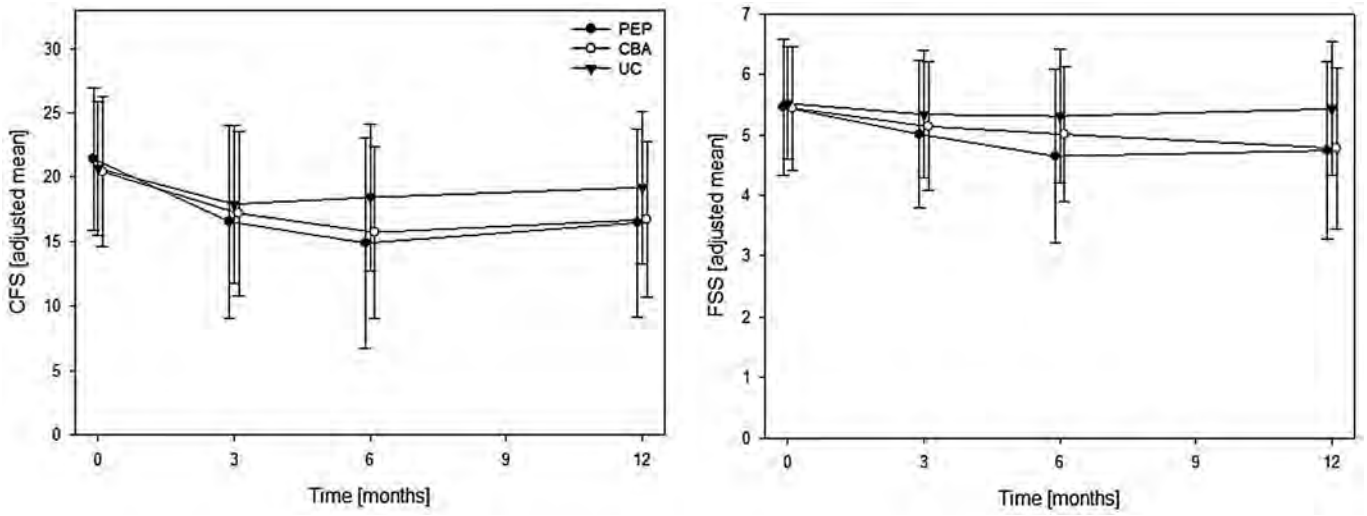

Figure 1. Fatigue severity (CFS) and fatigue impact (FSS) over time by treatment group Data are shown as adjusted means (sd). All models adjusted for their baseline outcome measure, HADS depression subscale >10 at baseline as fixed effects fixed effect with Centre clustering and individuals nested within Centre's as random effects. PEP, personalised exercise programme; CBA, cognitive-behavioural approach; UC, usual care; HADS, Hospital Anxiety and Depression Scale.

Table 2 Secondary outcomes at 12 months

Outcome	PEP	CBA	UC	PEP vs UC	CBA vs UC
HADS Anxiety	7.8 (4.9); 73	7.8 (4.4); 86	7.8 (4.6); 85	-0.7 [-1.6, 0.1]; 0.100	-0.4 [-1.3, 0.5]; 0.358
HADS Depression	5.4 (3.6); 75	6.0 (3.4); 88	6.3 (3.5); 85	-1.0 [-1.7, -0.2]; 0.009	-0.4 [-1.1, 0.3]; 0.303
Pain	5.2 (2.7); 79	5.3 (2.4); 93	5.3 (2.7); 92	-0.3 [-0.9, 0.3]; 0.401	0.1 [-0.4, 0.7]; 0.630
Sleep	11.6 (5.9); 75	10.8 (5.8); 89	12.9 (5.7); 81	-1.3 [-2.6, -0.1]; 0.033	-1.8 [-3.0, -0.6]; 0.003
Work (WPAI)	31.0 (21.6); 21	42.7 (23.9); 29	49.0 (25.6); 31	-14.1 [-26.7, -1.4]; 0.029	-6.3 [-17.8, 5.3]; 0.287

Methods: A multicentre, three-arm randomised controlled trial of usual care (UC) alongside telephone delivered CBA or PEP were tested against UC alone. UC typically comprised a fatigue self-management education booklet. Patients with any stable (unaltered immunomodulatory therapy for ≥3 months), physician diagnosed IRD were considered eligible if they reported significant (≥6 on numeric rating 0-10 scale, NRS) and persisting (≥3 months) fatigue. CBA and PEP was delivered by members of the rheumatology MDT, who received specialist training and supervision. Patients received up to 7 sessions across 14 weeks with a booster session at 6 months. Primary outcomes were fatigue severity (Chalder Fatigue Scale, CFS) and impact (Fatigue Severity Scale, FSS) at 12 months. Secondary outcomes included depression (Hospital Anxiety and Depression Scale), pain (NRS), sleep disturbance (Jenkins) and Work Productivity and Activity Impairment (WPA-I), also at 12 months. Generalized linear mixed models were used to compare the effectiveness of active therapies versus UC following an Intention-To-Treat approach. Results are expressed as mean difference (md) with 95% confidence intervals (95% CI).

Results: 368 IRD patients (55% rheumatoid arthritis, 21% connective tissue disease, 19% spondyloarthritis, 5% other IRD) were randomised. Baseline characteristics were similarly distributed across the trial arms (table 1). 73% and 85% completed PEP and CBA respectively and primary outcome data was available for 77% of all patients. PEP and CBA significantly improved fatigue severity (CFS md -2.9, 95% CI [-4.6, -1.2], p=0.001 and md -2.5, 95% CI [-4.01, -0.8], p=0.003, respectively) and fatigue impact (FSS md -0.6, 95% CI [-0.9, -0.3], p< 0.001 and md -0.6, 95% CI [-0.8, -0.3], p< 0.001, respectively) compared to UC alone at 12 months (figure 1). Both PEP and CBA also improved sleep (Jenkins md -1.3, 95% CI [-2.56, -0.1] and -1.8, 95% CI [-3.0, -0.6], respectively), while PEP further improved depression (HADS md -1.0, 95% CI [-1.7, -0.2]) and overall work impairment (WPAI md -14.1, 95% CI [-26.7, -1.4]) (table 2).

Conclusion: Telephone delivered CBA and PEP provided statistically and clinically significant reductions in fatigue severity and impact for a wide range of stable IRD patients. The benefit was maintained for 6 months following treatment completion and was successfully delivered by members of the rheumatology MDT after specialist training.

Data are shown as adjusted means (sd); n. Results are expressed as mean difference (md) with 95% confidence intervals (95% CI) and p-value. All models adjusted for their baseline outcome measure, HADS depression subscale >10 at baseline as fixed effects fixed effect with Centre clustering and individuals nested within Centre's as random effects. PEP, personalised exercise programme; CBA, cognitive-behavioural approach; UC, usual care; HADS, Hospital Anxiety and Depression Scale; WPAI, Work Productivity and Activity Impairment (overall work impairment domain);

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to support scientific meeting, Celgene, 12, Grant to institution to support scientific meeting, Consilient Health, 12, Grant to institution to support scientific meeting, Eli Lilly, 5, 12, Grant to institution to support scientific meeting, Novartis, 12, Grant to institution to support scientific meeting, Roche, 12, Grant to institution to support scientific meeting, Sandoz, 12, Grant to institution to support scientific meeting, Sanofi-Genzyme, 12, Grant to institution to support scientific meeting, Thornton & Ross, 12, Grant to institution to support scientific meeting, UCB, 12, Grant to institution to support scientific meeting, Astra-Zeneca, 5, Kyowa Kirin, 5; **S. Siebert**, AbbVie, 5, 6, Biogen, 6, Amgen (previously Celgene), 5, 6, Bristol Myers Squibb, 5, Boehringer-Ingelheim, 5, Novartis, 5, 6, UCB, 5, 6, Janssen, 1, 5, 6, GlaxoSmithKline, 5; **A. Wearden**, None; **G. Macfarlane**, GSK, 5, AMGEN, 5; **N. Basu**, Vifor, 2, 6, Lilly, 1, 5, 6, GSK, 1, Gilead, 1, Vorso, 5.

Abstract Number: 0463

Treatment Persistence Among Medicare Beneficiaries with Seropositive Rheumatoid Arthritis Initiating Biologic or Targeted Synthetic DMARDs

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Health Services Research (0462–0465)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Recent exploratory clinical trial and retrospective studies[1] suggest that patients with seropositive RA (rheumatoid factor [RF]+ and/or anti-cyclic citrullinated peptide [anti-CCP]+) treated with abatacept experience increased clinical efficacy compared to those treated with other biologic or targeted synthetic (b/ts) DMARDs. This biomarker-defined patient group may also demonstrate increased treatment durability. The objective of this study was to describe treatment persistence to abatacept and 2 comparison treatment groups (tumor necrosis factor inhibitors [TNFi] and Janus kinase inhibitors [JAKi]) among Medicare patients with seropositive RA.

Figure 1. Time to Treatment Discontinuation

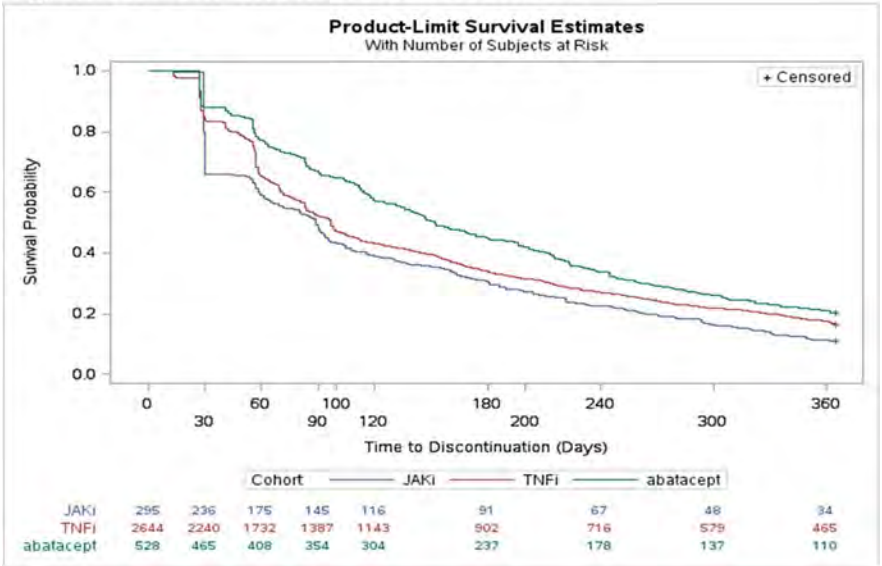

Table 1. Cox Proportional Hazards Model for Time to Treatment Discontinuation

Covariate	DF	Coefficient	SE	P-value	HR	95% CI	
						Lower	Upper
Abatacept vs. TNFi	1	0.183	0.049	0.000	1.201	1.091	1.322
Abatacept vs. JAKi	1	0.309	0.075	0.000	1.362	1.175	1.578

SE = standard error; HR = hazard ratio; CI = confidence interval; TNFi = tumor necrosis factor inhibitors; JAKi = Janus kinase inhibitors

Covariates also included age, gender, race/ethnicity, region, dual Medicare/Medicaid eligibility, low income subsidy status, baseline Charlson Comorbidity Index score, glucocorticoid use at baseline, serious infection at baseline, prior csDMARD at baseline, and prior biologic use at baseline

Methods: This retrospective cohort study utilized 100% Medicare Fee-for-Service Parts A/B/D claims linked to Prognos laboratory data January 1, 2012-December 31, 2019. Patients included had ≥2 claims in any setting, on separate days, ≥7 days apart, with an ICD-9-CM or ICD-10-CM diagnosis code for RA and RF+ and anti-CCP+ test results. The index date was the date of RA treatment initiation. Patients were placed into 3 mutually exclusive treatment groups based on index treatment: 1) abatacept, 2) a TNFi, or 3) a JAKi. Other treatment classes were excluded due to low sample size. Patients were required to have 1 year of continuous pre- and post-index enrollment. Baseline demographic and clinical characteristics were reported and persistence during follow up was evaluated. Treatment persistence was calculated for each patient from the index date until the earliest of treatment gap >15 days, switch in therapy, or end of follow up. Risk of time to treatment discontinuation over 1 year by index treatment was estimated using Kaplan Meier curves and Cox proportional hazard model, adjusting for baseline patient characteristics.

Results: A total of 3,468 seropositive RA patients (abatacept: 528 [15.2%]; TNFi: 2,654 [76.5%); JAKi: 295 [8.5%]) were included in the study sample. The population had mean (SD) age of 66.4 (10.0) years, was 78.3% female, and 73.9% White. Approximately 90% of patients were biologic naïve prior to index. Within each index treatment group, 21.4%, 18.2%, and 12.5% of patients utilizing abatacept, TNFi, and JAKi, respectively, had persistence to the index medication for 1 year. After drug initiation, patients spent a median (IQR) of 269 (140-332) days on abatacept, 206 (111-322) days on a TNFi, and 218 (90-316) days on a JAKi. Patients on abatacept had longer time to treatment discontinuation (median 152 days) compared to patients on TNFi (97) and JAKi (89), before adjustment (Figure 1) and after adjustment (HR vs. TNFi: 1.3; 95% CI: 1.1–1.4; HR vs. JAKi: 1.4; 95% CI: 1.2–1.7; Table 1).

Conclusion: Among Medicare beneficiaries with seropositive RA, those on abatacept were more often persistent to their index treatment and had longer time to treatment discontinuation at 1 year compared to patients on TNFi or JAKi which may be reflective of treatment efficacy.

References:

1. Han X, Lobo F, Broder MS, et al. Persistence with Early-Line Abatacept versus Tumor Necrosis Factor-Inhibitors for Rheumatoid Arthritis Complicated by Poor Prognostic Factors. *JHEOR*. 2021;8(1):71-78. doi:10.36469/jheor.2021.23684

Disclosure: S. Park, Bristol Myers Squibb, 3; **T. Schwartz**, Bristol Myers Squibb, 2, 5, Life Sciences Companies, 12, I am employee of Avalere health which provides consulting and advisory services to life sciences companies; **X. Han**, Bristol Myers Squibb, 3; **S. Robinson**, None; **S. Kakehi**, Bristol Myers Squibb, 3; **K. Wittstock**, Bristol Myers Squibb, 3, 11; **K. Norris**, None; **A. Murunga**, None; **A. Silverstein**, Bristol Myers Squibb, 5, 12, Employee of Avalere Health, which received funding from Bristol-Myers Squibb for the research; **J. Sparks**, Bristol-Myers Squibb, 2, Gilead, 2, Inova Diagnostics, 2, Optum, 2, Pfizer, 2.

Abstract Number: 0464

The Impact of Timely Post-Discharge Follow-up on Readmission Risk Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Health Services Research (0462–0465)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) has the 6th highest hospital readmission rate of all US chronic diseases with significant health disparities and costs. Transitional care management with higher reimbursement for post-discharge care within 14 days has been shown to decrease 30-day hospital readmissions in other chronic diseases. However, the impact of timely follow-up care (within 14 days) on readmission has not been evaluated among SLE patients. Our objectives were to (1) examine predictors of timely post-discharge follow-up and (2) compare all-cause 30-day readmissions after hospitalization with and without timely ambulatory follow-up among SLE patients.

Methods: We conducted a retrospective cohort study using a 20% random sample of all US Medicare hospitalizations in 2014. Hospitalized patients in the study had an SLE diagnosis code, age ≥18 years, alive at discharge, discharged to home, and not receiving hospice. Baseline characteristics of patients with inpatient stays with and without follow-up with a primary care provider or rheumatologist within 14 days of index hospital discharge were compared. Multivariate general estimating equation (GEE) models clustered by patient were used to determine the predictors and the effects of timely follow-up on 30-day rehospitalization risk.

Results: Compared to SLE admissions with timely (within 14 days) post-hospitalization follow-up (n=3118, 36%), those without timely follow-up (n=5530, 64%) were more likely to be younger, non-White, and living in the most disadvantaged neighborhoods (Table 1). Patients without timely follow-up were more likely to have comorbidities such as renal failure, depression, and tobacco, drug, or opioid use disorders. Observed thirty-day readmission rates were higher among those without timely follow-up (26% vs 20%), and only 11% of follow-up within 14 days was with rheumatology. Young adults had 10% lower timely follow-up (27 vs 37%) and 15% higher readmissions (37 vs 22%; Tables 2 & 3). Multivariable predictors of timely follow-up showed higher odds per year of age (aOR 1.01 (1.01,1.02); Table 2), but lower odds for those with renal failure (aOR 0.74 (0.65,0.84)), and those residing in the most disadvantaged neighborhoods (aOR 0.87 (0.76,0.99)) and rural areas (aOR 0.72 (0.58,0.88)). Timely post-discharge follow-up predicted 21% lower odds of readmission (aOR 0.79 (0.70,0.89); Table 3). Unlike younger age, race/ethnicity, rurality, and neighborhood disadvantage did not predict readmission risk after considering timely follow-up.

Conclusion: Hospitalized Medicare beneficiaries with SLE were 20% less likely to be readmitted within 30 days if they received post discharge follow-up within 14 days with either rheumatology or primary care, even after adjusting for comorbidities. Adjusted risk factors for lack of timely follow-up care included younger age, living in the most disadvantaged neighborhoods or in a rural area, and renal failure. To overcome limitations in this study our next analysis will explore whether immortal time bias influences outcomes. Other future studies should investigate targeted interventions to increase timely post-discharge follow-up care to reduce SLE readmissions and health disparities.

Table 1. Baseline characteristics of SLE hospitalizations by receipt of timely post-discharge follow-up

		Overall n= 8648 n(%)	Follow-up w/in 14 days n= 3118 n(%)	No timely follow-up n= 5530 n(%)	p value
Age group	18-35	1107 (12.8)	303 (9.7)	804 (14.5)	<0.01
	36-64	4267 (49.3)	1484 (47.6)	2783 (50.3)	
	65+	3274 (37.9)	1331 (42.7)	1943 (35.1)	
Sex	Female	7688 (88.9)	2768 (88.8)	4920 (89)	
Race/ethnicity	White	4705 (54.4)	1799 (57.7)	2906 (52.6)	<0.01
	Asian/Pacific Islander	117 (1.4)	34 (1.1)	83 (1.5)	
	Black	2703 (31.3)	910 (29.2)	1793 (32.4)	
	Hispanic	902 (10.4)	313 (10.0)	589 (10.7)	
	North American Native	104 (1.2)	33 (1.1)	71 (1.3)	
	Other/Unknown	117 (1.4)	29 (0.9)	88 (1.6)	
ADI disadvantage (mean, [SD])	Most Disadvantaged Quintile	2102 (25.3)	669 (22.5)	1433 (26.9)	<0.01
RUCA	Urban	6309 (73.2)	2326 (74.7)	3983 (72.3)	<0.01
	Suburban	745 (8.6)	269 (8.6)	476 (8.6)	
	Large rural	923 (10.7)	323 (10.4)	600 (10.9)	
	Small town/rural	648 (7.5)	196 (6.3)	452 (8.2)	
Receipt of Medicaid		4237 (49.0)	1417 (45.5)	2820 (51.0)	<0.01
Disability as Medicare reason		6022 (69.6)	2112 (67.7)	3910 (70.7)	<0.01
HCC score (mean, [SD])		3.6 [2.4]	3.5 [2.3]	3.7 [2.5]	<0.01
Renal failure		3520 (40.7)	1089 (34.9)	2431 (44.0)	<0.01
Congestive heart failure		2366 (27.4)	849 (27.2)	1517 (27.4)	0.84
Chronic lung disease		3533 (40.9)	1300 (41.7)	2233 (40.4)	
Diabetes		2754 (31.9)	998 (32.0)	1756 (31.8)	0.81
Liver disease		718 (8.3)	272 (8.7)	446 (8.1)	0.29
Obesity		2039 (23.6)	743 (23.8)	1296 (23.4)	0.68
Valvular disease		1452 (16.8)	501 (16.1)	951 (17.2)	0.18
Anxiety		4352 (50.3)	1570 (50.4)	2782 (50.3)	0.97
Depression		2805 (32.4)	953 (11.0)	1852 (21.4)	<0.01
Tobacco use disorder		2694 (31.2)	912 (29.3)	1782 (32.2)	<0.01
Alcohol use disorder		223 (2.6)	65 (2.1)	158 (1.8)	0.03
Opioid/Drug use disorder		1285 (14.9)	427 (13.7)	858 (15.5)	0.02
30-Day Outcomes	Observation stays	433 (5.0)	155 (5.0)	278 (5.0)	0.91
	ED visits	3027 (35.0)	1019 (32.7)	2008 (36.3)	<0.01
	Readmissions	1975 (23.7)	614 (20.1)	1361 (25.8)	<0.01
	Deaths	115 (1.3)	27 (0.9)	88 (1.6)	<0.01
Primary Care timely follow-up		—	2637 (84.6)	—	
Rheumatology timely follow-up		—	340 (10.9)	—	

Table 2. Observed rates and adjusted odds ratios of timely post-discharge follow-up visit after SLE hospitalization

		Observed Rates (%)	Adjusted odds ratio	Adjusted 95% CI
Age at admission (years)		—	**1.01**	**1.01-1.02**
	Age 18-35	27.4	—	—
	Age >35	37.3	—	—
Sex	Female	36.0	0.98	0.82-1.16
Race/ethnicity	White	38.2	Ref	Ref
	Asian/Pacific Islander	29.1	0.78	0.50-1.21
	Black	33.7	1.03	0.89-1.19
	Hispanic	34.7	1.04	0.85-1.26
	North American Native	31.7	1.07	0.67-1.73
	Other/Unknown	24.8	0.63	0.39-1.03
Receipt of Medicaid		33.4	1.03	0.90-1.17
Disability as Medicare reason		35.1	1.10	0.96-1.26
ADI disadvantage	Most Disadvantaged Quintile	31.8	**0.87**	**0.76-0.99**
RUCA	Urban	36.8	Ref	Ref
	Suburban	36.1	0.90	0.75-1.09
	Large rural	35.0	0.93	0.78-1.11
	Small town/rural	30.3	**0.72**	**0.58-0.88**
HCC score		—	1.00	0.97-1.02
Renal failure		30.9	**0.74**	**0.65-0.84**
Tobacco use disorder		33.9	0.92	0.82-1.05
Opioid/Drug use disorder		33.2	1.03	0.87-1.22
Alcohol use disorder		29.2	0.78	0.55-1.11

GEE Multivariable model clustered by patient used n=8291 hospitalizations with full data, representing n=5352 patients. In a separate model, statistically significant discharge codes as predictors for timely follow-up included infectious diseases and parasites (aOR 1.80), skin diseases (aOR 1.51), respiratory system diseases (aOR 1.49) and circulatory system diseases (aOR 1.37); Abbreviations: ADI=Area Deprivation Index, RUCA=Rural Urban Commuting Area, HCC=Hierarchical Condition Category.

Table 3. Observed rates and adjusted odds ratios for 30-day readmission after SLE hospitalization

		Observed Rates (%)	Adjusted odds ratio	Adjusted 95% CI
Timely discharge follow-up		20.1	**0.79**	**0.70-0.89**
Age at admission (years)		—	**0.99**	**0.98-0.99**
	Age 18-35	36.6	—	—
	Age >35	21.8	—	—
Sex	Female	23.7	0.91	0.75-1.11
Race/ethnicity	White	20.2	Ref	Ref
	Asian/Pacific Islander	17.3	0.70	0.43-1.14
	Black	29.5	1.05	0.89-1.24
	Hispanic	23.7	0.85	0.68-1.06
	North American Native	33.7	1.37	0.86-2.20
	Other/Unknown	26.8	0.99	0.60-1.65
Receipt of Medicaid		28.2	1.03	0.89-1.20
Disability		24.4	**0.77**	**0.66-0.91**
ADI disadvantage	Most Disadvantaged Quintile	26.0	0.97	0.83-1.14
RUCA	Urban	24.7	Ref	Ref
	Suburban	18.1	0.81	0.64-1.02
	Large rural	24.0	1.01	0.82-1.25
	Small town/rural	20.1	0.95	0.73-1.23
Tertiary discharge volume	Highest	24.3	Ref	Ref
	Middle	24.4	0.93	0.79-1.09
	Lowest	21.9	1.02	0.89-1.17
HCC score		—	**1.21**	**1.17-1.25**
Opioid/Drug use disorder		39.2	**1.39**	**1.16-1.67**
Alcohol use disorder		37.4	**1.52**	**1.08-2.16**
Congestive heart failure		35.8	**1.35**	**1.15-1.58**
Pulmonary circulatory disease		38.4	**1.26**	**1.04-1.54**

GEE Multivariable model clustered by patient used n=7989 hospitalizations with full data, representing n=5352 patients. Other comorbidities (anxiety, chronic lung disease, depression, diabetes, neoplasms, neurological disorders, obesity, peripheral vascular disease, tobacco use, and valvular disease) were also adjusted for in the model, but were not significant. Abbreviations: ADI=Area Deprivation Index, RUCA=Rural Urban Commuting Area, HCC=Hierarchical Condition Category.

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Abstract Number: 0465

Cost-effectiveness of Treatment Strategies Involving Arthroscopic Partial Meniscectomy and Physical Therapy for Degenerative Meniscal Tear

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Health Services Research (0462–0465)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Knee osteoarthritis (KOA) and meniscal tear (MT) are highly prevalent and often concomitant. Treatments for MT in the presence of KOA include physical therapy (PT; non-surgical) and arthroscopic partial meniscectomy (APM; surgical). Several randomized controlled trials (RCTs) suggest APM yields similar or only slightly better outcomes than PT for MT patients, but many of these trials have ~30% crossover from PT to APM, limiting their ability to isolate treatment benefits. Whether APM is cost-effective for those with KOA and MT has received little study.

Methods: We evaluated quality-adjusted life-years (QALYs), cumulative medical costs over five and 10 years, and incremental cost-effectiveness ratios (ICERs) of three treatment strategies: (1) PT Only, (2) PT + Optional APM, for those whose pain persists after a 3-month PT program, and (3) APM Only. Subjects whose pain persisted were offered total knee replacement (TKR) as a final treatment. We used the OAPol Model, a validated Monte Carlo state-transition simulation of KOA. We used a cohort with baseline KOA, MT, and demographics derived from the Meniscal Tear in Osteoarthritis Research (MeTeOR) RCT of APM vs. PT (mean age: 58; KOOS pain: 47 (0-100); KL1: 45%, KL2: 26%, KL3: 29%). We used previously published estimates of quality-of-life utilities and background medical costs based on pain, comorbidities, age, and BMI. Using published data, we estimated the risks and costs of APM complications and modeled KOA progression, with heightened progression among subjects treated with APM (relative risk: 1.62). We used MeTeOR data to estimate mean reductions in pain for subjects with low or high baseline pain (PT, low pain: 8 points; PT, high pain: 17; APM, low pain: 15; APM, high pain: 30), treatment costs (PT: $804; APM: $4,301), and utilization rates of Optional APM over one year (35%) and TKR over five years (2% for subjects treated non-surgically; 10% for those treated surgically). In sensitivity analyses we varied: indirect costs from productivity losses, Optional APM and TKR uptake rates, baseline pain, relative risk of KOA progression post-APM, duration of crossover period when subjects who failed PT are eligible for Optional APM, and efficacy of Optional APM. We discounted costs and QALYs at 3%/year and calculated ICERs as ratios of change in medical costs (2019 USD) to change in QALYs between strategies.

Table. Cost-effectiveness of treatment strategies involving APM and PT in patients with KOA and MT over a five-year time frame

Strategy	Cost	QALY	ICER
PT Only	$31,279	3.4044	--
PT + Optional APM	$33,280	3.4694	$30,800/QALY
APM Only	$36,351	3.4760	$465,300/QALY

Results: Relative to PT Only, PT + Optional APM added 0.065 QALYs and $2,001 in costs over five years (ICER: $30,800/QALY). Relative to PT + Optional APM, APM Only added 0.0066 QALYs and $3,071 (ICER: $465,300/QALY). The 10-year analysis produced similar ICERs. Results were sensitive to reducing the efficacy of APM in the PT + Optional APM strategy compared to the APM Only strategy.

Conclusion: At a willingness-to-pay threshold of $50,000/QALY, PT followed by APM, if pain persists post-PT, is a cost-effective treatment for those with KOA and MT. Immediate APM is not cost-effective. These findings are robust despite base case assumptions that favor non-surgical approaches but are sensitive to reductions in Optional APM efficacy.

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Abstract Number: 0466

Subclinical Large Vessel Vasculitis in Polymyalgia Rheumatica

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Imaging of Rheumatic Diseases (0466–0469)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Polymyalgia rheumatica (PMR) and giant cell arteritis (GCA) are closely related diseases. PMR occurs in approximately 50 % of GCA patients[1], however the frequency of subclinical GCA in PMR has not been widely studied. Furthermore risk factors for the clinical expression of GCA in PMR have not been clearly established. The aim of our multicenter, prospective study was to determine the prevalence of subclinical GCA in newly diagnosed PMR, using vascular ultrasound (US) as a diagnostic modality.

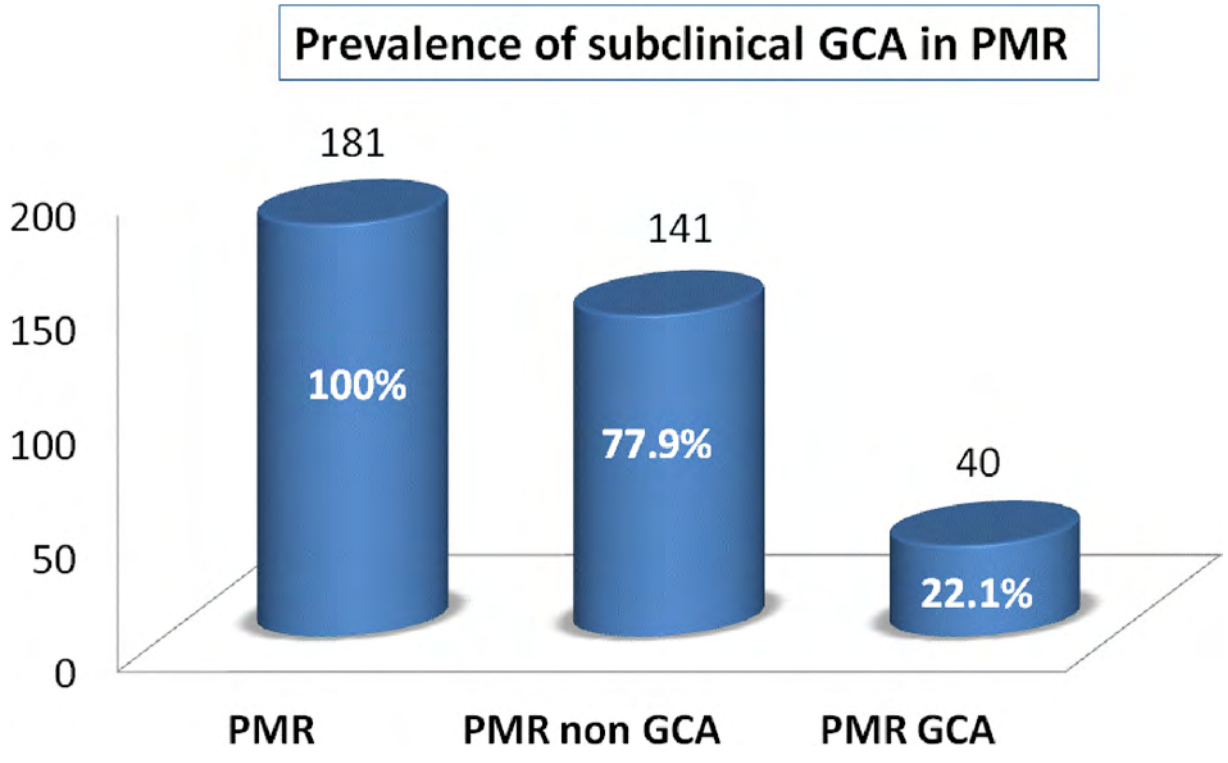
Methods: Six rheumatology centers participated in the study. The studied cohort represented consecutive newly diagnosed PMR patients who fulfilled 2012 EULAR/ACR Provisional Classification Criteria for Polymyalgia Rheumatica[2] and had no symptoms or signs suggestive for GCA. Besides hip and shoulder ultrasound all studied patients underwent detailed US examination of 5 vessel territories, bilaterally (i.e. temporal, carotid, subclavian, axillary and femoral arteries). The halo sing was considered as positive US finding[3]. In addition intima-media thickness of arteries was measured, with a cut-off of 0.34 mm for temporal arteries (TA) frontal and parietal, 0.42mm for common TA, and 1 mm for common carotid, axillary and subclavian arteries for positive result. Clinical characteristics of PMR patients were recorded and the frequency of subclinical GCA determined.

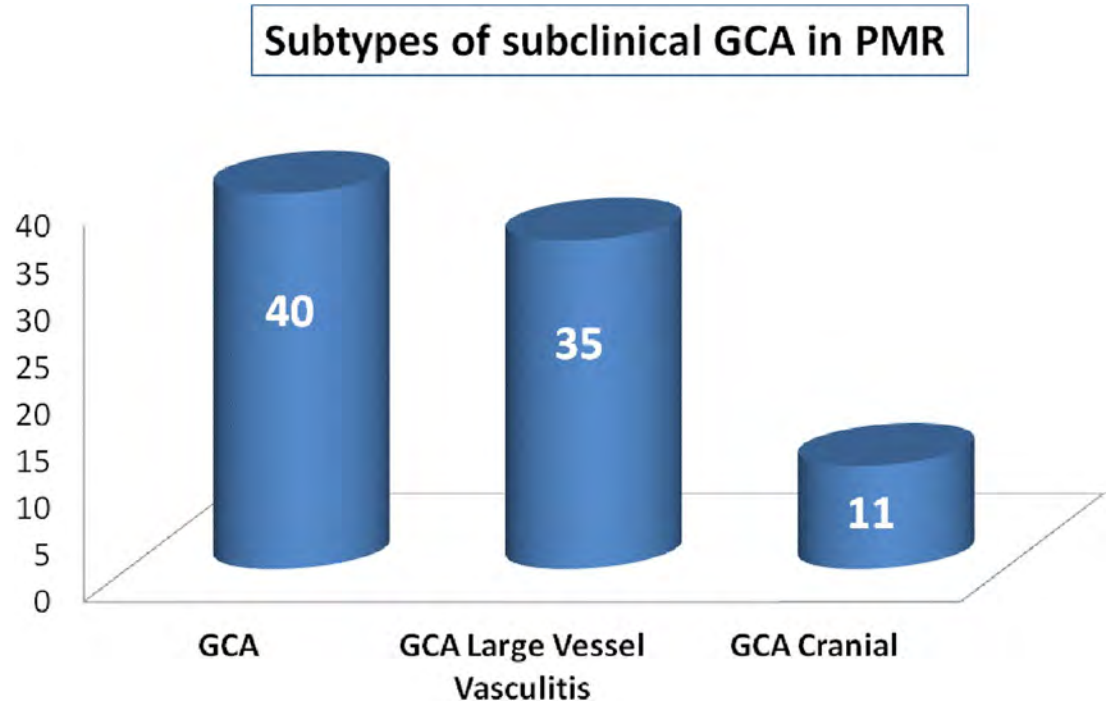
Results: US examinations were performed in 181 patients, 97 (53.6%) females with a mean age of 72.63±7.99 years. A halo sign was found on at least one of the examined arteries in 40 patients (22.1%). Cranial artery involvement was found in 11/120 patients, and 35/181 patients (19.3%) had extracranial large artery involvement (Figure 1 and 2). Table 1 shows the characteristics of studied population. Except of patient age that was significantly higher in PMR with GCA, there were no other specific PMR signs or symptoms predictive for subclinical US proven vasculitis.

Clinical and demographic characteristics

	PMR study n=181	PMR without GCA n=141	PMR with GCA n=40
Age (mean±SD)*	72.63±7.99	71.82±7.94	75.63±7.03
Sex (female/male)	97/84	74/67	23/17
Shoulder pain	173	135 (95.7%)	38 (95.0%)
Hip pain	145	113 (80.1%)	32 (80.0%)
Neck pain	99	76 (53.9%)	23 (57.5%)
Morning stiffness	153	122 (86.5%)	31 (77.5%)
Weight loss	43	34 (24.1)	9 (22.5%)
Fever	20	17 (12.1%)	3 (7.5%)
Peripheral arthritis	42	36 (25.5%)	8 (20%)
Pitting edema	22	18 (12.8%)	4 (10%)
Headache	20	13 (9.2%)	7 ((17.5%)
Duration symptoms (weeks)	8.82±6.76	8.70±6.91	9.37±6.07
CRP mg/l	55.62±45.77	58.00±47.64	43.85±33.57
ESR mm/h	59±27	59 ±28	61±27

PMR= Polymyalgia rheumatica; GCA= giant cell arteritis; SD= standard deviation.
*p<0.01 between PMR with and without GCA





Conclusion: The prevalence of subclinical GCA in patients with PMR was 22.1%. Increasing age emerged as a risk factor for subclinical GCA .

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Abstract Number: 0467

Assessing the Extent of Lumbosacral Spinal Urate Deposition in Patients with Tophaceous and Nontophaceous Gout Compared with Non-gout Controls Using Dual-Energy CT (DECT)

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Axial gout involvement was first reported in 1950 (1). Over 100 cases have subsequently been published. Reported cases have presented as acute back pain, cord compression, and/or neurologic symptoms, with diagnosis made by invasive procedure (surgical excision or biopsy). However, the true extent of MSU deposition in the spine of gout patients, including asymptomatic patients or those with non-specific symptoms, is unknown and likely higher. *We used DECT to determine the extent of MSU deposition in the lumbosacral spines of patients with gout, with and without tophi, compared to controls without gout*.

Methods: We recruited controls, nontophaceous, and tophaceous gout patients, age 45-80. Individuals with CPPD disease, RA, spondyloarthropathy, active spinal malignancy, or on urate lowering treatment (ULT) ≥ 6 months were excluded. Gout subjects met 2015 ACR gout classification criteria, with entry serum urate (sU) of >6.8 mg/dL (>6.0 mg/dL if on ULT for < 6 months). Demographics, gout history, Aberdeen back pain scale, sU, ESR, and CRP were collected. Subjects underwent DECT of the lumbosacral spine (LS) to assess for MSU deposition.

Results: 75 subjects were enrolled, and 72 completed the study (1 nontophaceous gout patient lost to follow-up prior to DECT, 2 tophaceous excluded after sU at time of DECT found to be < 6.0mg/dL). All groups were similar in age in years (controls 61.8±3.8, nontophaceous 64.0±6.1, tophaceous 60.4±11.0, p=0.81) but differed in BMI (controls 28.3±6.5 kg/m^2, nontophaceous 34.1±7.2 kg/m^2, tophaceous 29.5±4.5 kg/m^2, p=0.03) and creatinine (controls 1.0±0.2 mg/dL, nontophaceous 1.4±0.7 mg/dL, tophaceous 1.4±0.6 mg/dL, p< 0.05). Mean sU and ESR were higher in gout subjects (sU-controls 5.3±1 mg/dL, nontophaceous 8.5±1.7 mg/dL, tophaceous 8.5±1.6 mg/dL, p< 0.05; ESR-controls 13.7±13.8 mm/h, nontophaceous 26.5±19.4 mm/h, tophaceous 25.1±15.7 mm/h, p< 0.05). Using standard DECT settings for MSU visualization, gout patients had larger MSU volumes than controls (controls 2.2±1.2 cm^3, all gout 5.23±6.9 cm^3; p =0.03). Tophaceous patients had numerically greater MSU deposition compared with nontophaceous (6.0±8.9 cm^{3,} vs 4.4±4.3 cm^3, ns). Reanalysis of a subset of scans using highly specific settings to eliminate artifact reduced the number of subjects with MSU signal but confirmed greater prevalence of deposition among gout patients (n=29; controls with deposition 0/9, nontophaceous with deposition 1/11, tophaceous with deposition 2/9). Back pain was also more common among gout patients. No subject had frank tophi on spinal DECT.

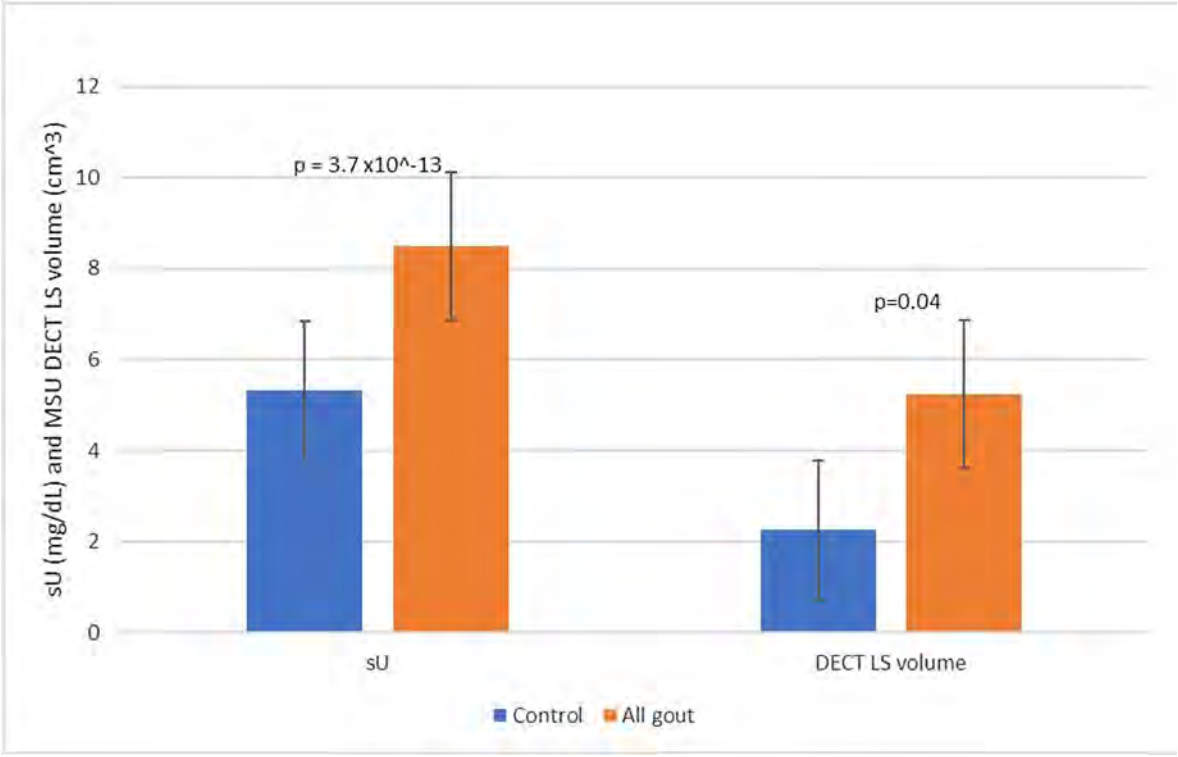

Figure 1. Mean sU and DECT LS volume (control vs all gout).

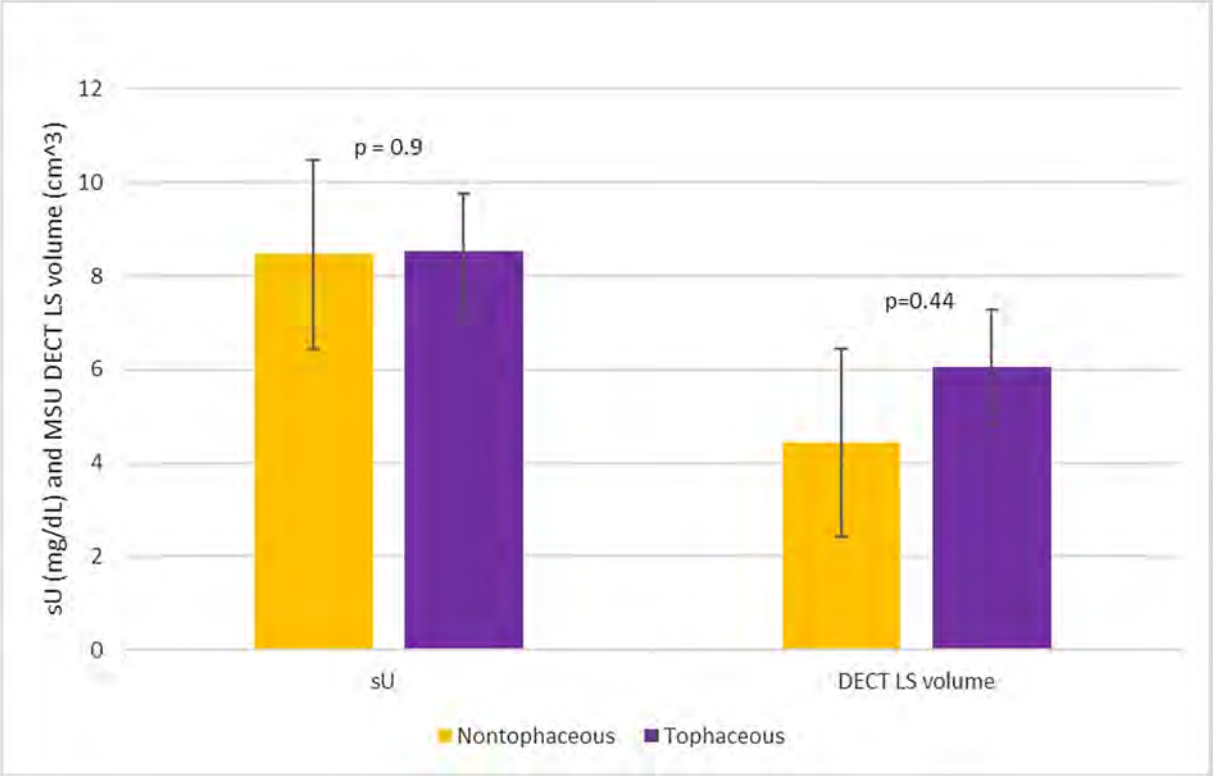

Figure 2. Mean sU and DECT LS volume (nontophaceous gout vs tophaceous gout).

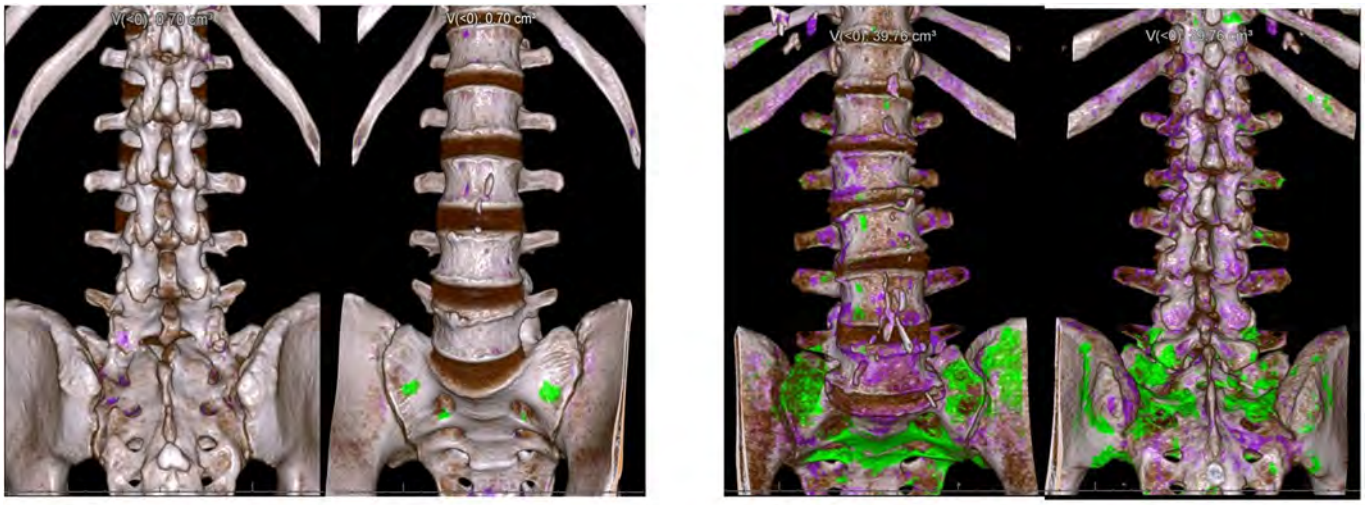

Figure 3. Comparison of Control vs Tophaceous Gout Patient LS DECT, green represents MSU deposition.

Conclusion: Gout patients have significantly greater intercritical inflammation and LS MSU deposition than controls, and trend toward greater deposition among patients with tophi. Preliminary results using the most stringent DECT threshold settings suggests MSU differences are not artifact. The complete data set is currently undergoing evaluation and the full results will be presented.

Supported by an investigator-initiated grant from Horizon Pharma.

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1. Toprover M, Krasnokutsky S, Pillinger MH. Gout in the Spine: Imaging, Diagnosis, and Outcomes. Curr Rheumatol Rep. 2015;17(12):70.

Disclosure: M. Toprover, Horizon Pharma, 2; **M. Mechlin**, Siemens, 6; **A. Slobodnick**, None; **V. Pike**, None; **C. Oh**, None; **C. Davis**, None; **T. Fields**, Horizon Pharmaceuticals, 1, Avion Pharmaceuticals, 1; **F. Becce**, Horizon, 2, Siemens Healthineers, 5; **M. Pillinger**, Horizon Therapeutics, 1, 5, Hikma Pharmaceuticals, 5.

Abstract Number: 0468

During Development of Rheumatoid Arthritis, Intermetatarsal Bursitis May Occur Before Clinical Joint Swelling: A Large MRI Study in Patients with Clinically Suspect Arthralgia

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Imaging of Rheumatic Diseases (0466–0469)
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Background/Purpose: Inflammation of the synovial lining is a hallmark of rheumatoid arthritis (RA). A synovial lining is not only present at synovial joints and tendon sheaths but also at bursae. Inflammation of the synovium-lined intermetatarsal bursae in the forefoot, intermetatarsal bursitis (IMB), was recently identified with MRI. It is specific for early RA and present in 69% of RA patients at diagnosis. During development of RA, MRI-detectable subclinical synovitis and tenosynovitis often occur before clinical arthritis presents. Whether IMB is also present in a pre-arthritis stage is unknown. Therefore, a large MRI-study in patients with clinically suspect arthralgia (CSA) was performed to assess the occurrence of IMB and its association with progression to clinical arthritis.

Methods: We studied 577 consecutive patients presenting with CSA. CSA was defined as recent-onset arthralgia of small joints that is likely to progress to RA based on the clinical expertise of the rheumatologist. Participants underwent unilateral contrast-enhanced 1.5T MRI of the forefoot, metacarpophalangeal (MCP) joints and wrist at baseline. Thereafter patients were followed for detection of clinical arthritis, as identified at physical joint examination by the rheumatologist. Baseline MRIs were evaluated for IMB-presence and -size in dorsoplantar direction at all 4 intermetatarsal spaces. Also synovitis, tenosynovitis and osteitis were assessed in line with the RA MRI scoring system (summed as RAMRIS-inflammation). IMB and RAMRIS-inflammation features were considered positive if uncommon in the general population (i.e. scored above the 95th-percentile of age-matched symptom-free controls). Cox regression analysed the association of IMB with progression to clinical arthritis; multivariable analyses adjusted for RAMRIS-inflammation which is known to associate with progression to clinical arthritis. Analyses were repeated stratified for ACPA-status, since ACPA-positive and ACPA-negative RA harbor differences in pathophysiology.

Results: 23% of CSA-patients had IMB (i.e., dorsoplantar size above the reference in symptom-free controls). IMB was more frequent in ACPA-positive than ACPA-negative CSA-patients (56% versus 19%, $p< 0.001$). Patients with IMB were more likely to also have subclinical synovitis (OR 2.4 (95%CI 1.2–4.8)) and tenosynovitis (11.5 (5.1–26.2)) on forefoot MRI, but not osteitis (0.8 (0.4–1.7)). Median follow-up was 25 months. Patients with IMB developed clinical arthritis more

often than patients without IMB (HR 3.3 (2.1-5.1)). This association was independent of synovitis-, tenosynovitis- and osteitis-presence at the forefoot, MCPs or wrist (adjusted HR 1.7 (1.03–2.7)). IMB predicted clinical arthritis development in ACPA-positive CSA (adjusted HR 2.2 (1.0–5.0)) but not in ACPA-negative CSA patients (0.8 (0.4–1.6)).

Conclusion: A quarter of CSA patients have IMB, which is frequently accompanied by subclinical synovitis and tenosynovitis. IMB precedes the development of clinical arthritis, and in particular the development of ACPA-positive RA. These results reinforce the notion that not only intra- but also juxta-articular synovial inflammation is involved in the development of RA.

Disclosure: B. van Dijk, None; **F. Wouters**, None; **E. van Mulligen**, None; **M. Reijnierse**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0469

Imaging Characteristics in Patients with Spondyloarthritis Using a Novel Heel Enthesitis Magnetic Resonance Imaging Scoring (HEMRIS) System: Post-hoc Analysis of a Phase 3 Secukinumab Trial

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SESSION INFORMATION
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Session Title: Abstracts: Imaging of Rheumatic Diseases (0466–0469)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: The heel is a frequently affected anatomical site for enthesitis in spondyloarthritis (SpA).[1] Recently, the Outcome Measures in Rheumatology (OMERACT) group developed and validated the Heel Enthesitis MRI Scoring system (HEMRIS) that takes both inflammatory and structural features of enthesitis into account.[2] ACHILLES (NCT02771210) is a prospective randomized controlled trial, investigating both clinical and imaging endpoints in patients (pts) with SpA and heel enthesitis.[3] Here, we report a post hoc analysis applying HEMRIS system in blinded and centrally read MRI data of the heel from the ACHILLES trial (N=204).

Methods: ACHILLES included pts (≥18 years) with active psoriatic arthritis or axial SpA, with clinical and MRI-positive heel enthesitis, refractory to standard treatment (either Non-steroidal anti-inflammatory drugs or Tumor necrosis factor-inhibitors). Pts were randomized to receive s.c. secukinumab (SEC) 150 mg, 300 mg or placebo (PBO) at baseline, Weeks (Wks) 1, 2, 3, and 4, followed by once every 4 wks. At Wk 24, pts on PBO were switched to SEC 150 or 300 mg. MRI-positive heel enthesitis was confirmed in all pts by local investigators and was defined as tendinitis and/or bone marrow edema (BME) in the area of the Achilles' tendon and/or the plantar aponeurosis. MRIs were performed at three time points: screening (SCR), Wks 24, and 52. In the present analysis, all MRIs were re-evaluated by two blinded central readers in a consensus read fashion for a priori defined MRI parameters based on HEMRIS system.

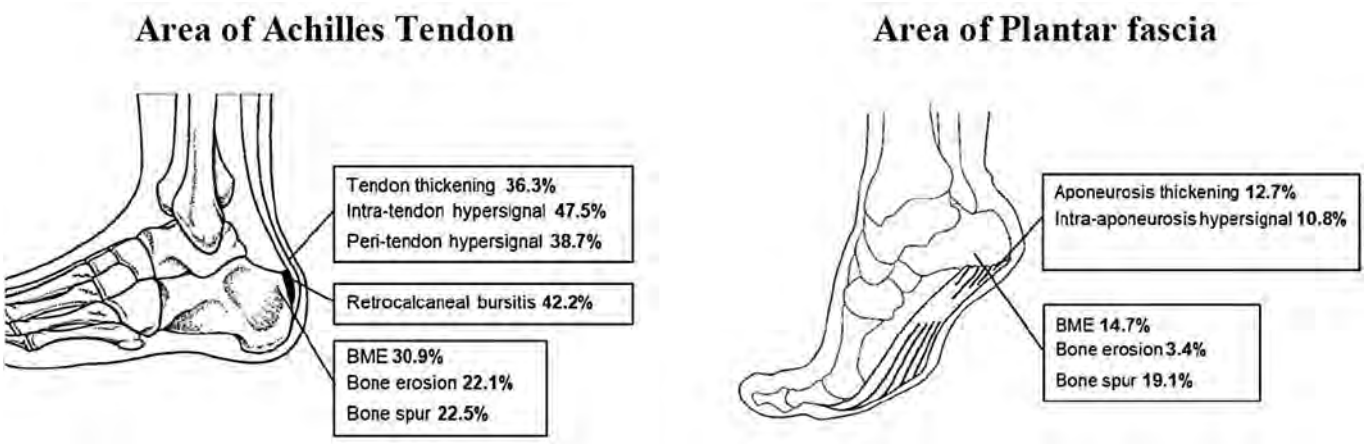

Figure. Inflammatory and structural pathologies at screening.

Results: Structural and inflammatory parameters at SCR are shown in **Figure**. At SCR, 156/204 (76.5%) pts presented with total entheseal inflammation score >0, 131/204 (64.2%) with total structural damage score >0, and 171/204 (83.8 %) with any entheseal inflammation and/or structural damage, considering both Achilles tendon and plantar fascia. The mean total entheseal inflammation score at SCR was 3.58 (N=204) and the mean change (SD) from SCR to Wk 24 and to Wk 52 was -1.05 (2.11) and -1.26 (2.28) in the SEC group vs -0.74 (2.21) and -1.17 (2.73) in the placebo group, respectively. The mean total structural damage score at SCR was 1.85 (N=204) and the mean change (SD) from SCR to Wk 24 and to Wk 52 was -0.01 (0.71) and -0.09 (0.66) in the SEC group vs 0.12 (0.56) and 0.06 (0.83) in the PBO-SEC group, respectively. Mean scores at SCR and mean change over time for individual parameters are given in **Table 1 and Table 2**, respectively.

Table 1. Inflammatory and structural pathologies – Mean score at screening

Mean score (SD)	Secukinumab N = 102	Placebo N = 102
Intra-tendon/aponeurosis hypersignal	0.90 (1.09)	0.96 (1.18)
Peri-tendon/aponeurosis hypersignal	0.86 (1.13)	0.96 (1.27)
Retro calcaneal bursitis at Achilles tendon	0.90 (1.19)	0.84 (1.14)
BME	0.92 (1.38)	0.80 (1.26)
Tendon/aponeurosis thickening	0.85 (1.16)	0.89 (1.13)
Bone erosion	0.37 (0.70)	0.25 (0.57)
Bone spur	0.70 (1.19)	0.63 (1.19)
Data presented are as observed. Pathologies reported for the area of Achilles tendon and plantar fascia, except bursitis (Achilles tendon only). N represents number of patients included in the analysis at screening.		

Table 2. Inflammatory and structural pathologies – Mean change from screening to Wk 24

Mean change (SD); 95% CI	Secukinumab N = 91	Placebo N = 90
Intra-tendon/aponeurosis hypersignal	–0.12 (–0.03); –0.11, –0.13	–0.20 (–0.17); –0.16, –0.24
Peri-tendon/aponeurosis hypersignal	–0.32 (–0.27); –0.26, –0.37	–0.19 (–0.20); –0.15, –0.23
Retro calcaneal bursitis at Achilles tendon	–0.35 (–0.22); –0.31, –0.40	–0.08 (–0.16); –0.04, –0.11
BME	–0.26 (–0.26); –0.21, –0.32	–0.28 (–0.16); –0.24, –0.31
Tendon/aponeurosis thickening	–0.01 (–0.01); –0.01, –0.01	0.02 (–0.01); 0.02, 0.02
Bone erosion	–0.02 (0); –0.02, –0.02	0.08 (0.10); 0.06, 0.10
Bone spur	0.02 (0.04); 0.01, 0.03	0.02 (–0.01); 0.02, 0.02
Data presented are as observed. Pathologies reported for the area of Achilles tendon and plantar fascia, except bursitis (Achilles tendon only). N represents number of patients included in the analysis at Wk 24.		

Conclusion: Based on the newly developed HEMRIS system, entheseal inflammation and/or structural damage was not confirmed for 16.2% of pts with SpA enrolled in the ACHILLES trial. The mean improvements in total inflammation and total structural damage scores were higher in the SEC-treated pts compared to placebo. The observed magnitude of improvement for the SEC-treated pts was more pronounced for the peri-tendon/aponeurosis hypersignal, bursitis and bone erosion.

References:

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2. Mathew AJ, et al. *J Rheumatol*. 2019;46:1232–8.
3. Behrens F, et al. *Arthritis Rheumatol*. 2019;71 (suppl 10). Abstract 2503.

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Abstract Number: 0470

Inhibition of Toll-Like Receptor 7 (TLR7) with the Potent and Selective Inhibitor of Human TLR7 and TLR8 BMS-986256 Provides Robust Efficacy in Murine Lupus Models, Reversing Established Disease

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
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Session Time: 11:00AM–12:00PM

Background/Purpose: TLR7, a member of the Toll-Like Receptor family, recognizes ssRNA and is primarily expressed in plasmacytoid dendritic cells and B cells. TLR7 has been implicated in systemic lupus erythematosus (SLE) in knockout mouse studies, but effects of inhibition at disease onset or in established disease are not well understood. Mouse TLR7 carries out human TLR7 functions, whereas mouse TLR8 does not carry out human TLR8 responses. BMS-986256 is a potent and selective inhibitor of TLR7 and TLR8 currently in clinical development for immune-mediated diseases. BMS-986256 has similar human and mouse TLR7 potency and was used in murine lupus models to investigate the role of TLR7 in disease onset and in established disease.

Methods: MRL/lpr mice and NZB/W mice were treated orally, once daily with vehicle or selected doses of BMS-986256 and/or prednisolone after anti-dsDNA antibodies developed but before onset of proteinuria. Alternatively, NZB/W mice were treated therapeutically in established disease (proteinuria at levels of 60–100 mg/dL) or advanced disease (proteinuria >100 mg/dL). Human blood was treated with BMS-986256 and prednisolone, stimulated with the TLR7 agonist gardiquimod or the TLR8 agonist TL8-506, and IL-6 production was measured to determine synergy.

Results: BMS-986256 treatment for 8 weeks in the MRL/lpr model provided robust inhibition of proteinuria onset and inhibition of IgG deposition in the kidney, with inhibition of autoantibody production. BMS-986256 treatment for 24 weeks in the NZB/W model resulted in nearly complete inhibition of proteinuria onset and IgG deposition in the kidney. Treatment of NZB/W mice with proteinuria of 60–100 mg/dL for 14 weeks and mice with proteinuria of >100 mg/dL for 10 weeks resulted in reversal of proteinuria, IgG deposition in the kidney, and kidney tissue damage, while markedly increasing survival in both established and advanced disease models. Production of anti-dsDNA, anti-SmRNP and anti-Ro autoantibody titers and cytokine production were inhibited in preventative, therapeutic and established models. BMS-986256 displayed steroid-sparing activity in all the disease models, when single agent and combination treatments with prednisolone were compared. BMS-986256 acted synergistically with steroid treatment to inhibit TLR7 and 8 responses in human blood.

Conclusion: The potent and selective TLR7/8 inhibitor BMS-986256 displayed robust efficacy in the MRL/lpr and NZB/W models of lupus. Therapeutic treatment with BMS-986256 reversed proteinuria, immune complex deposition, and kidney tissue damage in established and advanced disease NZB/W models. Treatment reduced titers of autoantibodies implicated in lupus as well as cytokine responses. BMS-986256 displayed steroid-sparing activity in the disease models and acted synergistically with steroid treatment in human blood. These results indicate that TLR7 plays an important role in both the initiation and progression of disease and support the potential of BMS-986256 in

the treatment of SLE. Given the robust pharmacological efficacy observed in this study, BMS-986256, currently under investigation in patients with cutaneous lupus (CLE), was advanced to a Phase 2 trial in SLE patients.

Disclosure: S. Dudhgaonkar, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3, Bristol Myers Squibb, 2; **A. Rudra**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **S. Ranade**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **S. Subramani**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **J. Nagar**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **P. Karunanithi**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **P. Bhutani**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **V. Kurawattimath**, Biocon Bristol Myers Squibb Research Center, Syngene International Ltd, 3; **R. Zhang**, Bristol Myers Squibb, 3; **H. Qiu**, Bristol Myers Squibb, 3; **A. DYCKMAN**, Bristol Myers Squibb, 3; **G. Schieven**, Bristol Myers Squibb, 3, Genesis Biotechnology Group, 3.

Abstract Number: 0471

Therapeutic Efficacy of BT-104, an Oral LANCL2 Agonist, for the Treatment of Systemic Lupus Erythematosus

Andrew Leber, Raquel Hontecillas, Nuria Tubau-Juni, Sarah Fitch, Jyoti Chauhan and Josep Bassaganya-Riera, Landos Biopharma, Blacksburg, VA

SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

Background/Purpose: Systemic lupus erythematosus is a complex disease in which the immune system is dysfunctional at multiple levels including impaired regulatory responses, altered self-antigen processing and increased autoantibody production. LANCL2 is a novel anti-inflammatory target that has been first targeted by a gut-restricted compound, omilancor (BT-11), currently in Phase II/III clinical development for inflammatory bowel diseases. BT-104 functions through similar immunometabolic mechanisms, increasing the suppressive capacity and stability of regulatory CD4+ T cells while also supporting the metabolic demands of autophagy in phagocytes.

Methods: Based on these immunological effects, we evaluated oral BT-104 in three mouse models of lupus: the NZB/W F1 model, the MRL/lpr model and the bm12 adoptive transfer model. Mice were treated daily with oral BT-104 from ages 24 to 36 wk in the NZB/W F1 model, from ages 12 to 18 wk in the MRL/lpr model and from 1 to 2 wk post-transfer in the bm12 model. Therapeutic efficacy was evaluated by proteinuria, anti-nuclear antibody titers, immune cell changes in the blood and spleen, and histological inflammatory changes in the kidney. Further, the MRL/lpr model was used to identify global transcriptional signatures of BT-104 in blood and spleen after oral treatment. The translational efficacy of BT-104 was evaluated in PBMCs from SLE patients *in vitro*.

Results: In the NZB/W F1 and MRL/lpr models, BT-104 protected against worsening from baseline in proteinuria grade in greater than 90% of mice, improved proteinuria grade in roughly half of mice, and reduced anti-nuclear antibody levels by three-fold. BT-104 reduced overall histological score in the kidneys, including improvement in interstitial inflammation, glomerular proliferation, and cellular crescents. Immunologically, across all three models, BT-104 significantly reduced IL17+ and IL21+ CD4+ T cells in the spleen while significantly increasing CD25+ FOXP3+ regulatory CD4+ T cells (Treg). BT-104 significantly reduces the production of interferon alpha in human PBMCs from SLE patients in response to general (PMA and ionomycin), TLR7 (gardiquimod) and CpG oligonucleotide (ODN2395) stimuli.

Conclusion: Based on the preclinical data generated, BT-104 is a promising therapeutic for systemic lupus erythematosus and other rheumatic conditions. BT-104 is expected to enter Phase I clinical testing in normal healthy volunteers in Q4 2021.

Disclosure: A. Leber, Landos Biopharma, 3; **R. Hontecillas**, Landos Biopharma, 3, 4, 11; **N. Tubau-Juni**, Landos Biopharma, Inc., 3, 11; **S. Fitch**, Landos Biopharma, 3; **J. Chauhan**, None; **J. Bassaganya-Riera**, Landos Biopharma, 3, 4, 8, 11.

Abstract Number: 0472

An Atlas of Human and Mouse Intrarenal Immune Cells in Lupus Nephritis Reveals Homologous Immune Populations Across Common Mouse Strains and Species

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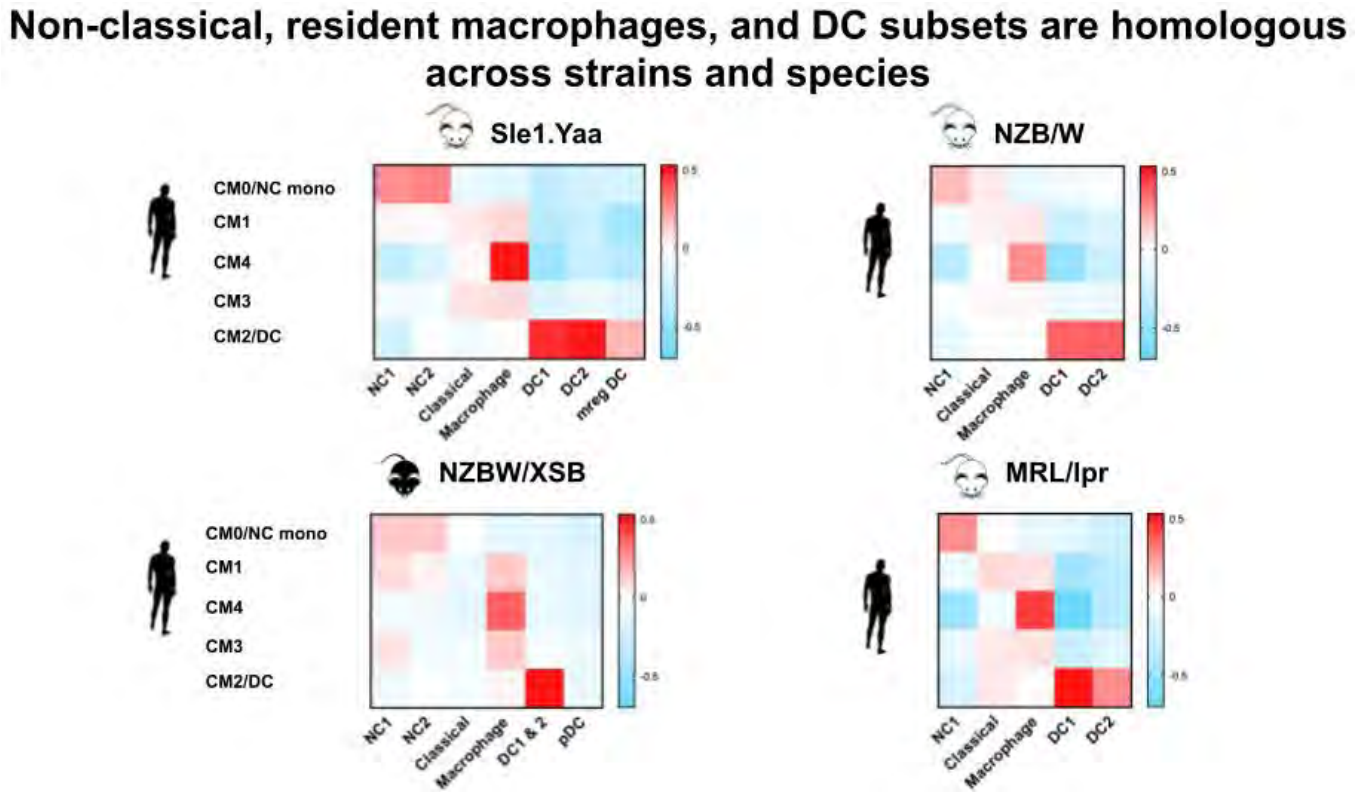
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: SLE – Animal Models (0470–0473)
Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

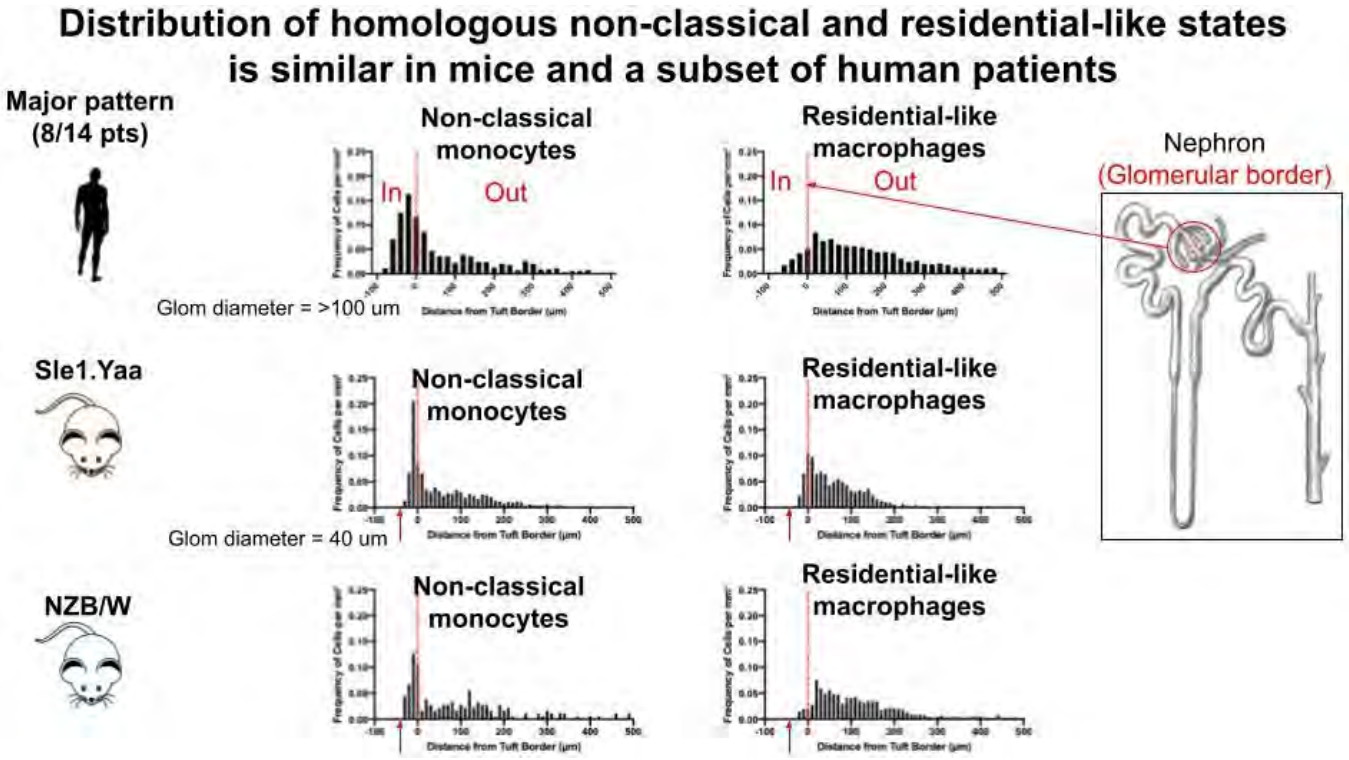
Background/Purpose: We discovered 21 immune cell-types in lupus nephritis kidney biopsies as part of the Accelerating Medicines Partnership (AMP) consortium. These immune cells are the basis of new hypotheses about the drivers of disease. However, we cannot feasibly collect immune cells from human kidney biopsies for mechanistic testing. Mouse lupus models and humans share important clinical features including autoantibody development and kidney injury that progresses to failure. How mice recapitulate human lupus nephritis remains an open question. Here, we used single cell RNA sequencing to identify homologous intrarenal immune cell subsets and conserved gene programs from humans and four common lupus strains.

Methods: Using AMP protocols we sorted CD45+ cells from dissociated mouse kidneys with spontaneous adaptive-driven autoimmunity (NZB/W and MRL/lpr) and TLR7-overexpression innate-driven autoimmunity (Sle1.Yaa and NZW/BXSB) in early and nephritic disease. We profiled single cell transcriptomes using 10x Genomics and analyzed droplets that contained >500 genes and UMIs after doublet removal using Seurat 3.0. We analyzed the top 2000 variable genes for clustering and differential gene expression. We compared transcriptomes of intrarenal immune cells collected from mice at early and peak clinical disease to those from humans at peak clinical disease.

Results: We identified intrarenal myeloid, T-, and B-cell subsets from >75,000 cells passing QC. Many subsets were shared among strains and homologous to human subsets. In particular, the myeloid compartment in mice and humans contained: i) non-classical monocytes that expressed TNF and fate related transcription factors (Spi1, Nr4a1); ii) a novel Fcrl5+ non-classical monocyte unique to TLR7-overexpression strains that emerged in nephritic mouse kidneys and expressed Nr1h3 known to regulate lipids and inflammation; iii) resident-like macrophages that expressed genes for tissue repair (Igf1, Pdgfrb), immunomodulation (Creb5, Dab2), and phagocytosis (Mertk, Gas6); resident-like macrophages in adaptive-driven lupus strains shifted gene expression from anti-fibrotic to remodeling that correlated with proteinuria. We spatially mapped these homologous cells in kidney sections and found they localized to similar compartments in mice and in most human patients.



Conclusion: Most intrarenal myeloid, T-, and B-cell subsets in early and nephritic disease were common to mouse strains; unique subsets correlated with genetic susceptibility. TLR7-overexpression strains contained a novel and unique Fcrl5+ non-classical monocyte. Spontaneous strains contained a population of residential-like macrophages that shifted gene expression from anti-fibrotic to remodeling in nephritic mice. Both non-classical and residential-



like macrophages in mice and humans shared genes critical for tissue repair, immunomodulation, and immune cell recruitment. Further, each of these cell-types localized to similar locations in kidney sections in mice and a subset of human patients. These findings support shared roles of these cells in lupus nephritis. We hope our work opens a new path using mouse models to more precisely study aspects of human disease.

Heatmaps representing how well intrarenal mouse myeloid clusters from each lupus strain expressed gene signatures from human myeloid subsets from lupus nephritis biopsies. The warmer colors represent higher expression of human signatures in corresponding mouse clusters. Mouse NC1 and NC2 (non-classical 1 and 2) highly expressed the signature from human CM0/NC1 (non-classical); mouse macrophage expressed the signature from human CM4; mouse DC1 and DC2 (dendritic cell 1 and 2) expressed the signature from human CM2/DC2.

Homologous subsets were spatially mapped across kidney sections and plotted as function of distance relative to the glomerular border. This location was chosen because significant histopathologic tissue changes occur here that influence disease classification. Homologous human and mouse non-classical monocytes (left panel of histograms) are both enriched inside glomerular structures and form a gradient toward the borders outside the glomerulus. Homologous human and mouse residential-like macrophages (right panel) both localize to the glomerulus to a lesser extent, and form a gradient toward the glomerular edge. This spatial phenotype is conserved in mice and in the majority but not all of the patients we interrogated. Thus, the distribution of these homologous cells is similar in mice and a subset of human patients. These data suggest homologous cells carry out conserved effector functions in the same anatomic compartments in mice and a subset of humans.

Disclosure: P. Hoover, None; **M. Peters**, None; **D. Lieb**, None; **R. Wang**, None; **G. Dunlap**, None; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6; **N. Hacohen**, None; **A. Davidson**, None.

Abstract Number: 0473

Disease-Associated Microglia Are Implicated in Neuropsychiatric Manifestations of Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Title: Abstracts: SLE – Animal Models (0470–0473)
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Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune syndrome affecting multiple organs, including the brain. Though 50% of patients may experience neuropsychiatric symptoms (NPSLE), underlying disease mechanisms remain largely unknown. Microglia, the tissue-resident macrophage of the brain, are heterogenous and may be associated with a homeostatic microglia ($CD11c^{lo}$) or disease-associated microglia (DAM; $CD11c^{hi}$) state, a subset common to Alzheimer's disease (AD). In AD, DAM co-localize with amyloid-b (Ab) plaques, are enriched for genes involved in lysosomal, lipid metabolism and phagocytic pathways and may play a protective role in the early stages of AD by reducing Ab plaque burden. Our group was the first to show that expression of DAM-associated genes correlates with the severity of hippocampal- and cerebellar-associated behavioral deficits in microglia isolated from two NP-SLE models prior to overt systemic disease. While DAM have been extensively studied in AD, to date no studies have specifically examined DAM in NPSLE.

Methods: FACS-purified CD45$^{dim/+}$CD11b^{+} cells from whole brain of 11-12-month-old female WT and NPSLE-prone CReCOM mice (n=1) were analyzed by single-cell RNA-seq (scRNA-seq; 10X Genomics 3' v3.0). NPSLE-prone MRL$^{lpr/lpr}$ female mice were intraperitoneally injected at 10 weeks of age with fingolimod, a sphingosine-1-phosphate receptor modulator that reduces microglia activation and improves blood brain barrier integrity, or vehicle control 3 times/week for 4 weeks and underwent behavioral testing. FACSorted bulk CD11c^{lo} homeostatic microglia and DAM were subjected to the Quantseq 3' RNA-seq. GO analysis (GOrilla) of treatment-unique genes determined enriched processes.

Results: SingleR designated microglia from merged scRNA-seq data, with cluster-specific genes identifying DAM and a CD11c^{lo} homeostatic subset in control and CReCOM mice. CReCOM DAM are enriched for genes associated with antigen presentation but depleted for genes associated with phagocytosis, which is in contrast to DAM in AD that are critical for phagocytic functions. Moreover, CReCOM CD11c^{lo} microglia upregulate genes linked to synapse pruning and phagocytosis, consistent with exacerbated synaptic pruning by microglia in NPSLE models. Fingolimod treatment improved depression and spatial memory issues in MRL$^{lpr/lpr}$ mice. DAM transition from a CD11c^{lo} homeostatic microglia state; thus, MRL$^{lpr/lpr}$ DAM are enriched for DAM-associated genes compared to CD11c^{lo} microglial counterparts. However, fingolimod treatment restricted expression of DAM-associated genes in DAM and induced a unique signature in DAM enriched for genes linked to behavior- and synapse-related processes.

Conclusion: We find that DAM appear to lack typical functions in NPSLE-like disease and restricted expression of the DAM transcriptional program in NPSLE DAM corresponds to improved behavioral outcomes. Together, these discoveries mark the first to implicate DAM as a potentially pathogenic microglia subset in NPSLE. In future studies, we will explore whether DAM actively participate in the initiation of NPSLE-like disease.

Disclosure: H. Makinde, None; **S. Chen**, None; **E. Mike**, None; **C. Putterman**, equllium, 2, 5, Progentec, 2, Kidneycure, 2; **D. Winter**, None; **C. Cuda**, None.

Abstract Number: 0474

Correlation of Fibromyalgia Survey Questionnaire and Quantitative Sensory Testing Among Patients with Active Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes (0474–0477)
Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

Background/Purpose: Patients with rheumatoid arthritis (RA) commonly demonstrate disordered pain processing, termed central sensitization (CS). CS is typically measured using quantitative sensory testing (QST), which is burdensome to patients. The self-administered fibromyalgia survey questionnaire (FSQ) has been proposed as a low-burden surrogate measure of CS. We examine the correlation between FSQ and QST in a population with active RA.

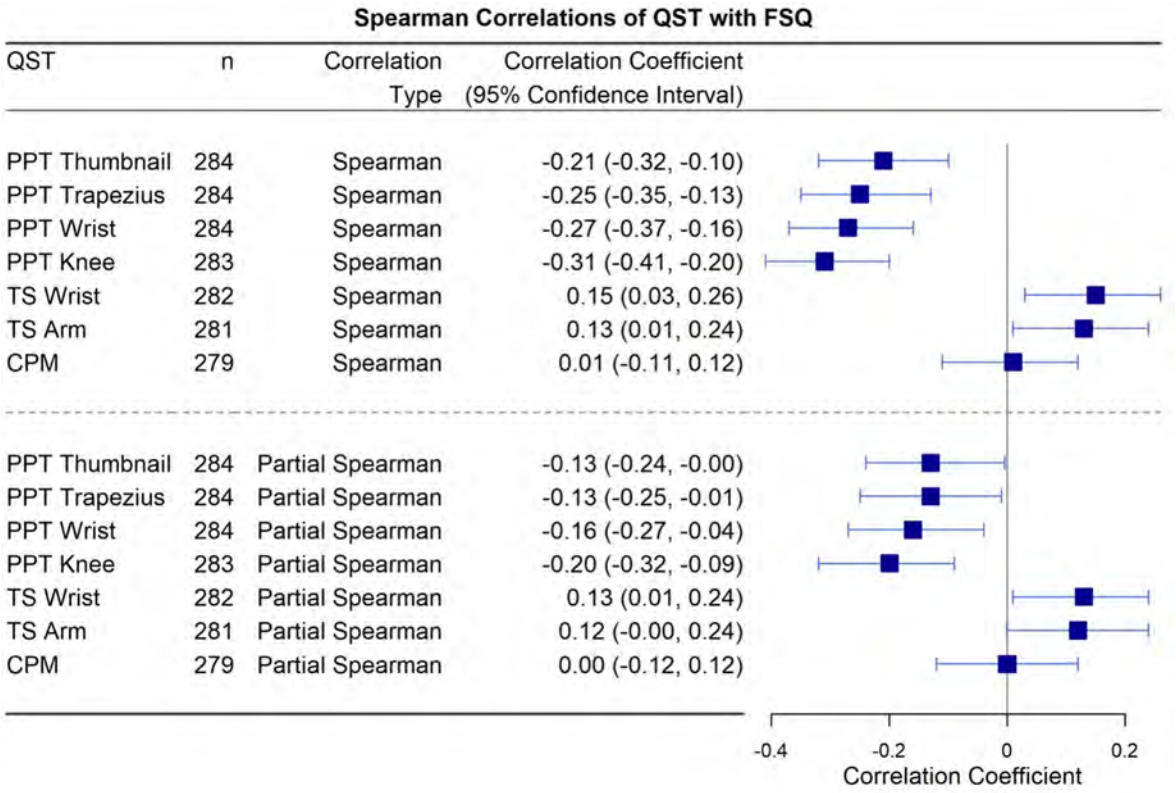

Figure 1. Unadjusted and adjusted correlations between QST measures and FSQ. Adjusted for age, sex, race, BMI, seropositivity, swollen joint count, CRP, pain catastrophizing, and site. PPT = pressure pain threshold; TS = temporal summation; CPM = conditioned pain modulation.

Methods: RA patients in the multicenter Central Pain in Rheumatoid Arthritis cohort underwent FSQ and QST evaluation at enrollment. QST measures included pressure pain threshold (PPT) at thumb, trapezius, wrist and knee, temporal summation (TS) at wrist and arm, and conditioned pain modulation (CPM). Spearman correlation was assessed between FSQ and each QST measure, adjusted for age, sex, race, body mass index, sero-status, swollen joint count, C-reactive protein, pain catastrophizing, and study site. We performed sensitivity analyses stratified by a) patient sex and b) sub-components of the FSQ (widespread pain index [WPI], and symptom severity scale [SSS]).

Results: Among 285 RA patients with high RA activity (mean baseline Clinical Disease Activity Index score of 24.56), FSQ was weakly but statistically significantly correlated with PPT (r = -0.21 to -0.31), and TS (r = 0.13 to 0.15) at all sites in unadjusted analyses (Figure 1). After adjustment for the covariates above, statistically significant correlations persisted for PPT at all sites except the thumb, and for TS at the wrist. Sensitivity analyses did not identify any differences in association based on sex or differences in associations with the components of the FSQ (WPI or SSS).

Conclusion: FSQ and QST were correlated among patients with active RA, but the strength of association was weak. These results do not support the use of FSQ as a proxy measurement for QST-assessed central sensitization among patients with active RA.

Disclosure: M. Moore, None; **B. Wallace**, None; **J. Song**, None; **L. Muhammad**, None; **A. Heisler**, None; **D. Clauw**, Pfizer, 2, 6, Aptinyx, 2, Daiichi, 2, Sankyo, 2, Eli Lilly, 2, 6, Intec Pharma, 2, Samumed, 2, Theravance, 2, Tonix, 2, Zynerba, 2, Nix Patterson LLP, 6, Williams & Connolly LLP, 6; **M. Bolster**, Johnson and Johnson, 11, Genentech, 5, Corbus, 5, Cumberland, 5, PracticeUpdate, 12, Associate Editor, Custom Learning Designs, 2; **W. Marder**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **A. Wohlfahrt**, None; **D. Dunlop**, None; **Y. Lee**, Eli Lilly, 2, 6, Pfizer, 5, Cigna, 11.

Abstract Number: 0475

Quantitative Analysis of Gender and Racial Disparities in Randomized Controlled Trials of Fibromyalgia

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes (0474–0477)
Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

Background/Purpose: Fibromyalgia is a chronic pain syndrome characterized by widespread musculoskeletal pain, mood disorders, fatigue, and cognitive and sleep disturbance. Mainstay treatments include tricyclic antidepressants, selective serotonin/serotonin norepinephrine reuptake inhibitors, and antiepileptic drugs. The purpose of this study was to examine whether or not gender and racial disparities exist in the context of research subjects recruited for clinical studies performed on the only three FDA approved medications for fibromyalgia.

Methods: The PubMed database was searched for clinical trials studying duloxetine (DLX), milnacipran (MLN), or pregabalin (PRG) for the treatment of fibromyalgia. Studies with randomized, double blind, placebo controlled design involving any of the above medications as monotherapy and reporting on gender and ethnic demographic parameters published over the last 10 years were included. Ethnic backgrounds were grouped into Caucasian or White, African American, Hispanic, Asian, and Other respectively.

Results: A total of 28 studies met inclusion criteria. Paired t-tests demonstrated a female gender preponderance of research participants for all of the DLX, MLN, and PRG treatment groups analyzed separately ($p < 0.05$ each) and collectively ($p < 0.001$). White or Caucasian was the predominant ethnic group across all treatment groups analyzed

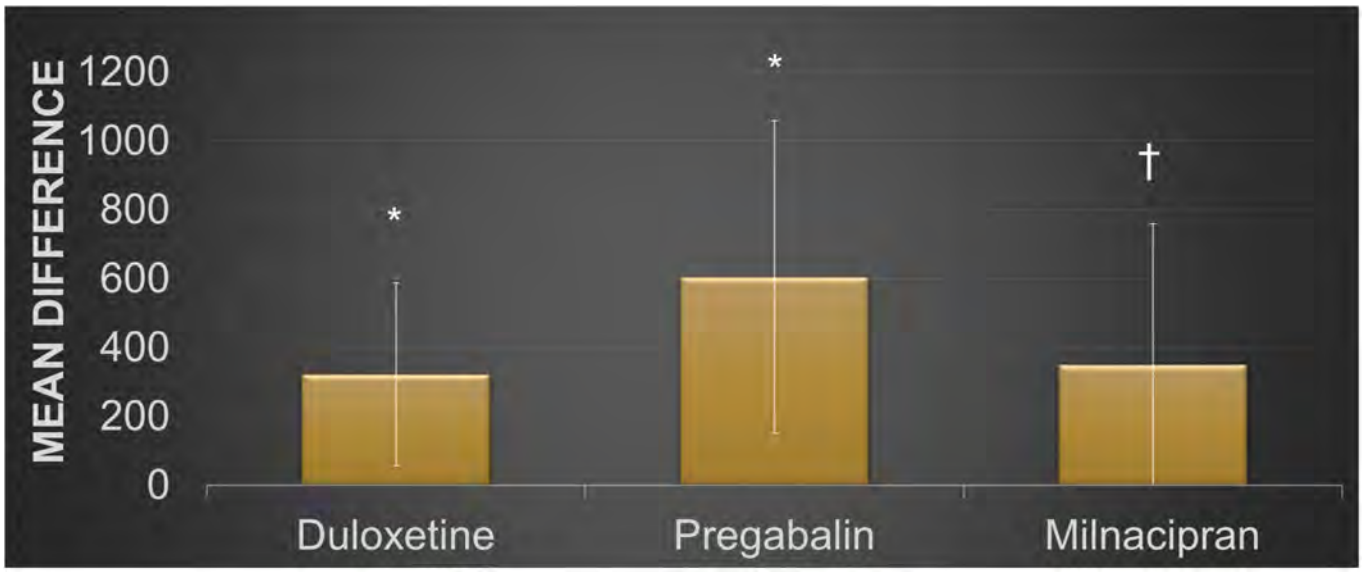

Figure 1. Statistically significant overrepresentation of Caucasian or White research subjects in comparison to all other ethnic groups as determined by paired t-tests (* denotes $p<0.005$, † denotes $p<0.05$).

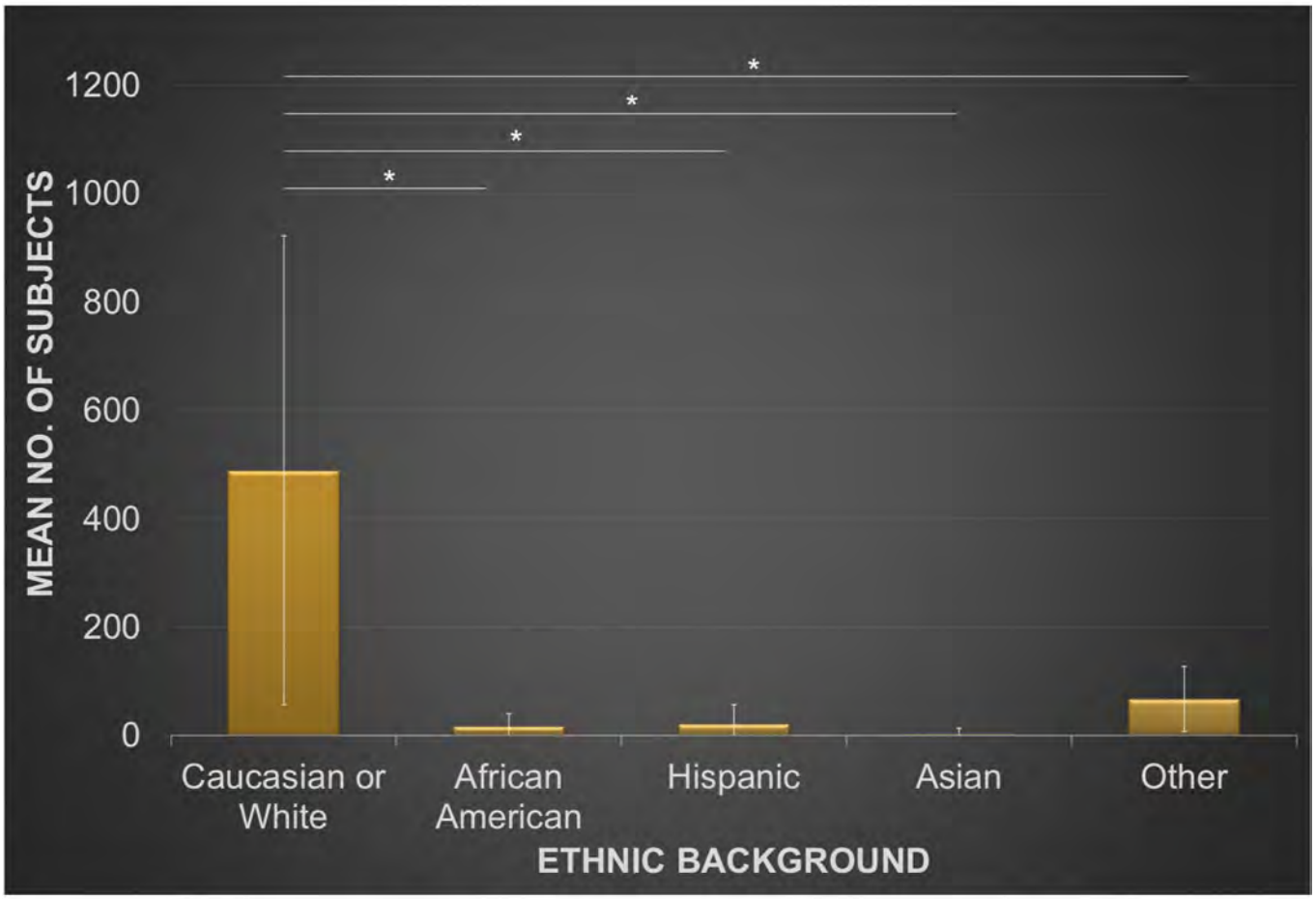

Figure 2. Statistically significant overrepresentation of Caucasian or White research subjects in comparison to African American, Hispanic, Asian, and all other ethnic groups remaining as determined by paired t-tests (* denotes p<0.001).

separately (86.4±6.1% DLX, 89.2±6.2% PRG, and 87.3±8.1% MLN) or collectively (87.6±6.7%). There were no statistically significant differences between group means across all treatment groups as determined by one-way ANOVA for White or Caucasian (F(2,25)=1.57, p=0.23), African American (F(2,25)=2.71, p=0.09), Asian (F(2,25)=0.64, p=0.54), or all ethnic groups combined (F(2,25)=1.6, p=0.22); as was the case for studies conducted within (F(2,22)=1.79, p=0.19) or outside (F(1,3)=0.1, p=0.77) the USA. Nonetheless, a statistically significant difference was observed by

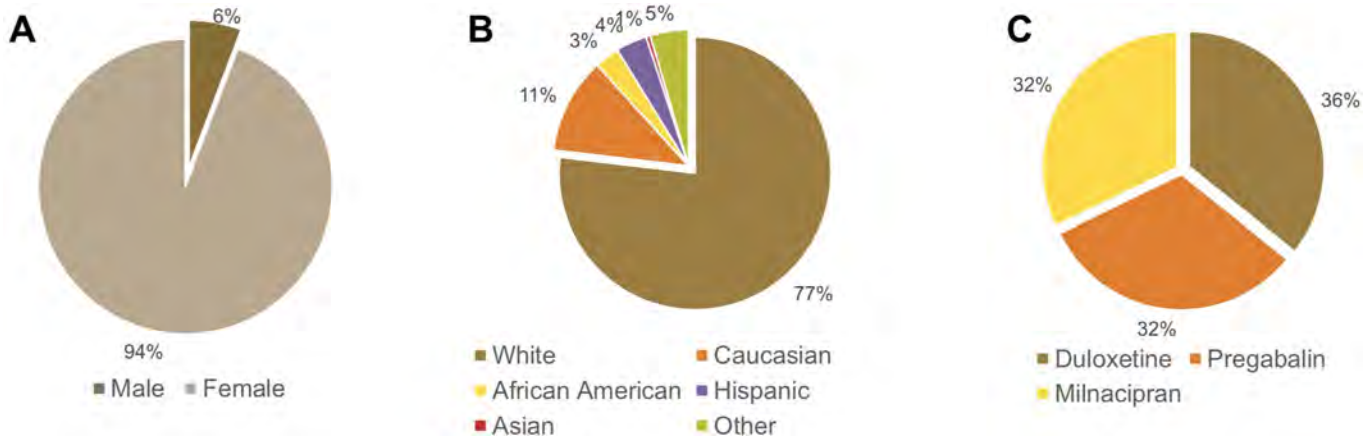

Figure 3. Demographic representation of research participants by gender (A) and ethnic background (B); and classification of included studies by medication.

one-way ANOVA for the Hispanic ethnic group ($F(2,25)=5.19$, $p< 0.05$). Paired t-tests revealed a statistically significant overrepresentation of Caucasian or White research subjects (489.25±432.70) in comparison to African American (17±23.39, $t(27)=6.06$, $p< 0.001$), Hispanic (21.29±35.43, $t(27)=5.78$, $p< 0.001$), Asian (2.93±10.51, $t(27)=5.95$, $p< 0.001$), or all other ethnic groups examined (67.32±60.03, $t(27)=5.76$, $p< 0.001$). A similar pattern of Caucasian or White subject overrepresentation in comparison to all other ethnic groups was found on subgroup analysis for all of the DLX (mean(diff)=322.20±265.27, $t(9)=3.83$, $p< 0.005$), PRG (mean(diff)=604.56±453.60, $t(8)=3.40$, $p< 0.005$), and MLN (mean(diff)=350.11±408.85, $t(8)=2.57$, $p< 0.05$) treatment groups respectively.

Conclusion: Evidence of widespread gender and racial disparities amongst subjects recruited for clinical trials of various pharmacologic agents for fibromyalgia exist. Whereas female preponderance for fibromyalgia is believed to reflect a true gender predilection of this disorder more research is needed to determine whether or not racial disparities observed indeed reflect on the nature of the disease.

Disclosure: R. Diab, None; **A. Malik**, None; **M. Al Rifai**, None; **D. Ang**, None.

Abstract Number: 0476

Factors Associated with Pain Reduction and Improved Well-Being Among Fibromyalgia Patients Using Medical Cannabis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes (0474–0477)
Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

Background/Purpose: Fibromyalgia (FM) is characterized by a constellation of symptoms that are often poorly responsive to current treatments, and patients are increasingly turning to medical cannabis (MC) as a strategy to improve pain and well-being. To date, little is known about the factors that may contribute to the perceived benefits of medical cannabis in patients with FM. Given that negative affect (i.e., anxiety, depression) and sleep problems contribute to heightened pain intensity and poor well-being, improvements in these variables might indirectly contribute to MC treatment benefits. Factors contributing to continuation of MC treatment, a surrogate for treatment satisfaction, are also largely unknown. The objectives of the present analyses were: 1) to examine whether changes in negative affect and sleep problems contributed to changes in pain intensity and well-being following initiation of MC; 2) to examine the factors contributing to MC treatment continuation.

Methods: Patients included in this study were part of a prospective, observational, non-comparative registry of adult patients who initiated MC under the supervision of a physician between 2015 and 2018 in Quebec, Canada. Sociodemographic and clinical characteristics were recorded at baseline. MC treatment characteristics (MC products, routes, doses) and symptom variables were assessed during in-clinic visits at baseline and every three months for a period of one year.

Results: Of the 2068 chronic non-cancer pain patients enrolled in this registry, 308 (14.9 %) had FM. The FM sample included 87 % women (mean age: 52.3 ± 12.9 years) and most patients (54.3 %) were using a combination of THC

and CBD. Results revealed significant improvements in pain intensity and well-being following initiation of MC (both ps < .05). A multilevel mediation analysis subsequently revealed that reductions in pain intensity were mediated by reductions in negative affect (p < .001) and sleep problems (p < .001). Improvements in well-being were mediated by reductions in negative affect (p < .001) and pain intensity (p < .05). MC was continued by 74%, 58.8%, 39.6%, and 23.1% of FM patients at the 3, 6, 9, and 12-month time points, respectively. The likelihood of treatment discontinuation was higher among patients with higher levels of pain and negative affect (both ps < .05), but was unrelated to the degree of improvement in these symptoms over the course of MC treatment (all ps > .05).

Conclusion: Our findings suggest that reductions in negative affect and sleep problems are important contributors to improvements in pain intensity and well-being among FM patients using MC. Discontinuation of MC was more common among those with higher levels of pain and negative affect but was not related to symptom improvement. These findings are a move towards precision medicine in MC recommendations for treatment of FM.

Disclosure: M. Martel, None; **L. Waldman**, None; **R. Sotoodeh**, None; **A. Vigano**, Canopy Growth, 2, 5, 6, Tilray, 2, 5, 6, Syqe, 1; **Y. Moride**, Many companies (15+), 1, 2; **M. Canac-Marquis**, None; **R. Gamaoun**, None; **M. Kalaba**, Canopy Growth Corporation, 3; **P. Beaulieu**, None; **J. Desroches**, None; **M. Ware**, Canopy Growth Corporation, 3; **J. Perez**, Spectrum Therapeutics, 6; **Y. Shir**, None; **M. Fitzcharles**, None.

Abstract Number: 0477

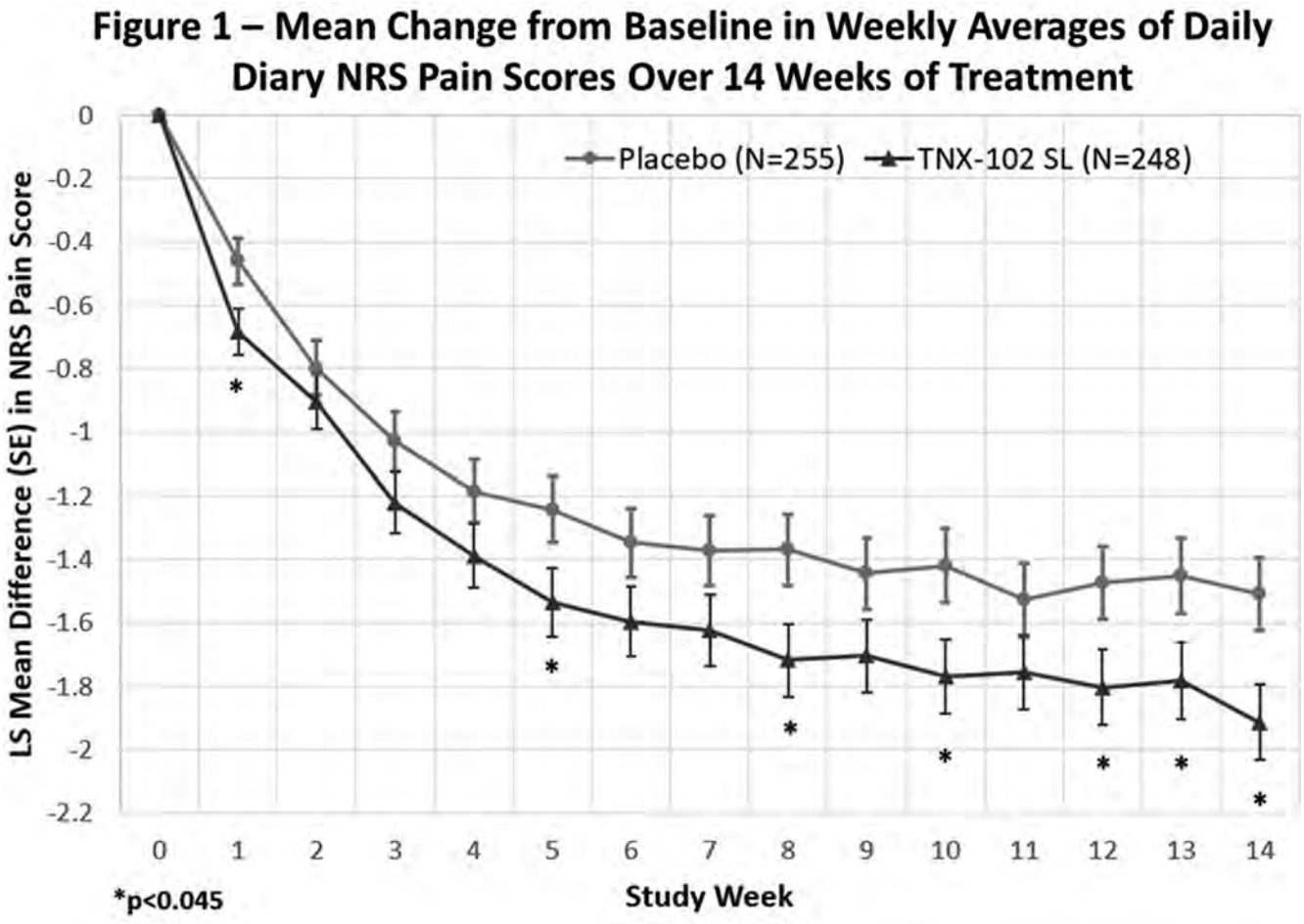
TNX-102 SL (Sublingual Cyclobenzaprine) for the Treatment of Fibromyalgia in the RELIEF Study: Positive Results of a Phase 3 Randomized, Double-Blind, Placebo-Controlled Multicenter Efficacy and Safety Trial

Gregory Sullivan[1], Mary Kelley[2], Annabelle Iserson[1], Perry Peters[2], Ashild Peters[2], Candace Flint[1], Judy Gendreau[3], Herb Harris[1], Ben Vaughn[4] and Seth Lederman[5], [1]Tonix Pharmaceuticals, Inc., Chatham, NJ, [2]Tonix Pharmaceuticals, Inc., San Diego, CA, [3]Gendreau Consulting, LLC, Poway, CA, [4]Rho, Inc., Cary, NC, [5]Tonix Pharmaceuticals, Inc., South Dartmouth, MA

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Fibromyalgia & Other Clinical Pain Syndromes (0474–0477)
Session Type: Abstract Session
Session Time: 11:00AM–12:00PM

Background/Purpose: Fibromyalgia (FM) is characterized by chronic widespread pain, fatigue, and nonrestorative sleep, a symptom constellation suggestive of a pathological disturbance in central pain processing known as central sensitization. TNX-102 SL* (cyclobenzaprine HCl sublingual tablets, 'TNX') targets improvement in sleep quality in order to reverse central sensitization. Prior studies of TNX at a 2.8 mg dose in FM showed signals for broad efficacy but narrowly missed significance on primary outcome of daily diary pain reduction. This Phase 3 trial ('RELIEF'#) evaluated efficacy and safety of TNX for FM at twice the dose, 5.6 mg.

Methods: The Intent-to-treat sample of 503 patients meeting 2016 FM diagnostic criteria were enrolled at 39 U.S. sites and received TNX 2.8 mg or placebo for 2 weeks followed by TNX 5.6 mg or placebo for 12 weeks. Primary outcome measure was change from baseline in weekly average of daily diary pain scores (0-10 NRS) at Week 14, analyzed by mixed model repeated measures with multiple imputation (MMRM-MI). The 1st key secondary analysis was Patient Global Impression of Change (PGIC) responders by logistic regression. Remaining key secondaries (by



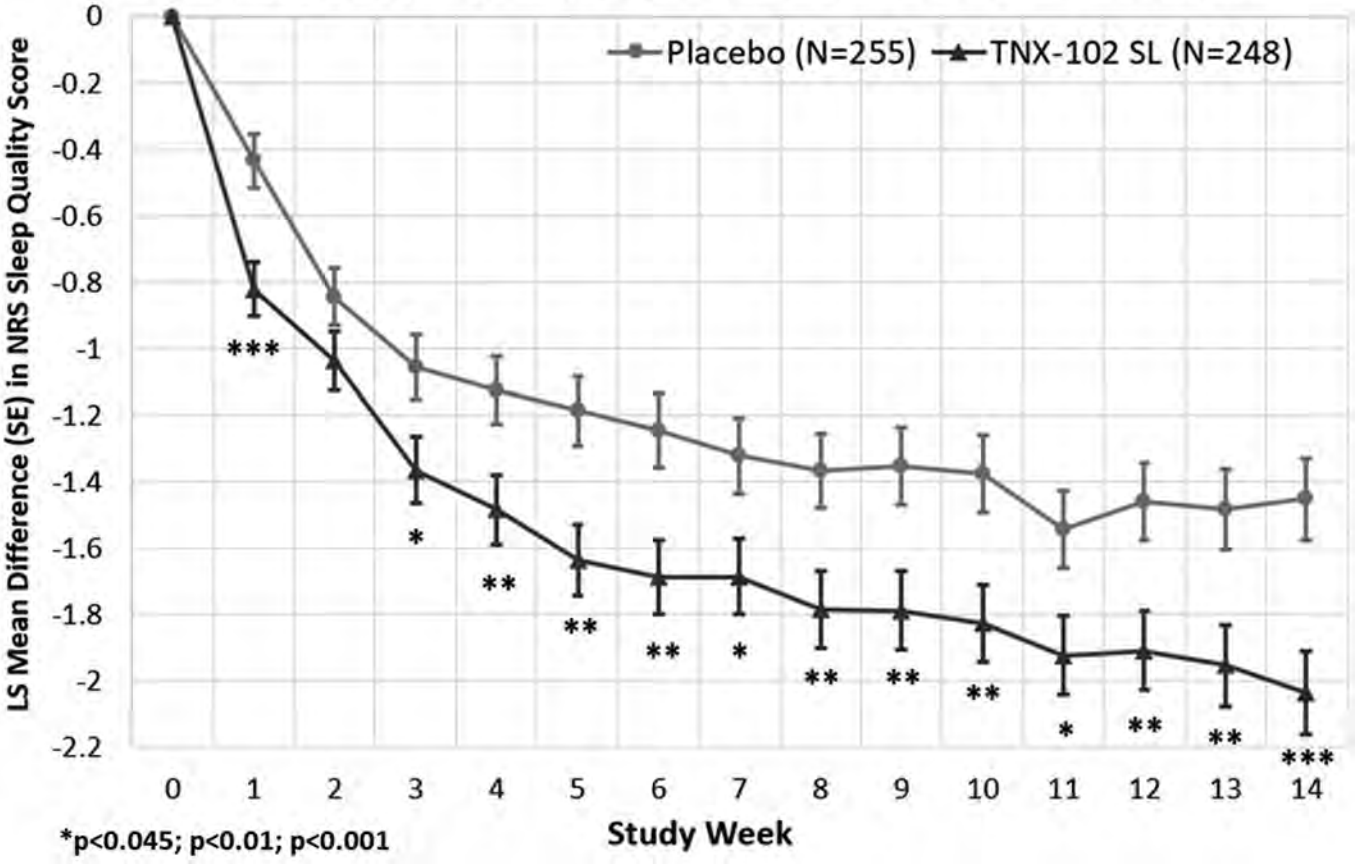
MMRM-MI) included: Fibromyalgia Impact Questionnaire-Revised (FIQ-R) symptom domain; FIQ-R function domain; Patient Reported Outcomes Measurement Information System (PROMIS) Sleep Disturbance; PROMIS Fatigue; and daily diary NRS of sleep quality. To adjust for multiplicity, a sequential, ordered test procedure was applied to each (at $p < 0.045$ to account for an interim analysis α-spend).

Results: TNX was effective in decreasing daily diary pain compared to placebo (p=0.010; **Fig. 1**). A ≥30% pain reduction responder analysis indicated 46.8% TNX responders vs. 34.9% on placebo (p=0.006). By PGIC, 37.5% on TNX were responders, which was numerically but not significantly greater than 29.4% on placebo (p=0.058). TNX also provided greater separation from placebo on: FIQ-R Symptoms (p=0.007), Function (p=0.009); PROMIS Sleep Disturbance ($p < 0.001$) and Fatigue (p=0.018); and daily diary sleep quality ($p < 0.001$; **Fig. 2**).

In the TNX group, 82.3% completed vs. 83.5% on placebo. Systemic adverse events (AEs) were infrequent, with somnolence/sedation the only category at a rate of ≥ 5% on TNX (5.6% TNX; 1.2% placebo). The most common local administration site reaction was oral numbness (17.3% TNX; 0.8% placebo) which was episodic and typically temporally related to dosing, resolving in < 60 min in most occurrences. AEs led to premature study discontinuation in 8.9% on TNX vs. 3.9% on placebo.

Conclusion: Bedtime TNX at the 5.6 mg dose significantly reduced daily pain, provided a larger rate of ≥30% pain responders. It showed activity in improving sleep, fatigue, and other FM symptoms and measures of function. In addition, nightly TNX 5.6 mg was well tolerated. Taken together, these findings indicate TNX-102 SL primarily targets sleep quality and may thereby reduce central sensitization, leading to improvement at the syndromal level, manifesting as broad-spectrum activity across symptoms of FM.

Figure 2 – Mean Change from Baseline in Weekly Averages of Daily Diary NRS Sleep Quality Scores Over 14 Weeks of Treatment



Disclosure: G. Sullivan, Tonix Pharmaceuticals Inc, 3, 4, 10, 11; **M. Kelley**, Tonix Pharmaceuticals Inc, 3, 11; **A. Iserson**, Tonix Pharmaceuticals, 3; **P. Peters**, Tonix Pharmaceuticals Inc, 3, 11; **A. Peters**, Tonix Pharmaceuticals Inc, 3, 11; **C. Flint**, Tonix Pharmaceuticals Inc, 3, 11; **J. Gendreau**, Tonix Pharmaceuticals Inc, 2, Virios Therapeutics, 2, Dare Bioscience, Inc., 2; **H. Harris**, Tonix Pharmaceuticals Inc, 3, 11; **B. Vaughn**, Tonix Pharmaceuticals, 2; **S. Lederman**, Tonix Pharmaceuticals Inc, 3, 4, 11.

Abstract Number: 0478

Identification of Clinical Phenotypes of Hand Osteoarthritis Using Hierarchical Clustering Method

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Hand osteoarthritis (OA) is an heterogenous disease in terms of risk factors, localization and severity. This heterogeneity also applies to the clinical presentation and to the symptoms and is still poorly investigated. Our objective was to delineate the symptom-based phenotypes in a hand OA population using integrative analyses based on the cardinal symptoms of hand OA (pain, functional limitation, stiffness, esthetic discomfort).

Methods: We used the baseline data from the hospital-based hand OA cohort DIGICOD (PMID: 33689840). Clustering segregation was performed on AUSCAN subscores (0-100) of pain, function, stiffness separately, and the visual analog scale (0-100 mm) of esthetic discomfort. Hierarchical agglomerative clustering analyses were performed on 389 patients based on the Euclidean distance and the Ward D2 agglomeration method. Differences between cluster's characteristics were assessed by Kruskal-Wallis, Wilcoxon and Fisher exact tests. The Bonferroni method was applied on adjusted p-values to correct for multiple testing.

Results: Among the 389 patients analyzed, the AUSCAN subscores and the visual analog scale of esthetic discomfort enabled to identify 5 distinct clinical clusters by hierarchical clustering (Figure 1). We further characterized the composition of these clusters (Figure 2). Cluster 1 (N=88) is mainly composed of low symptomatic patients, cluster 2 (N = 91) of patients with mild symptoms (pain, stiffness and functional limitation), cluster 3 (N=80) of patients displaying esthetic discomfort mainly (without pain), cluster 4 (N =42) of high level of pain, stiffness and functional disability but without esthetic discomfort and cluster 5 (N=88) of the combined features of cluster 4 plus high level of esthetic discomfort. Age and hand OA duration were significantly different amongst clusters and higher in clusters 4 and 5 (p=0.06 and p=0.0002). Men were mostly present in low and mild-symptomatic cluster 1 and 2 (p=0.002). The clusters did not differ significantly for BMI, metabolic syndrome and CRP level, although metabolic syndrome represented 45.4 % of the highly symptomatic cluster 5 vs 26.1 % of low symptomatic cluster 1 (p= 0.01). The esthetic discomfort (corresponding to clusters 3 and 4) was associated with higher number of articular nodes (p=0.0003) and with radiographic erosive hand OA (p=0.04). Clusters 3, 4 and 5 were composed with patients more severe joint structure

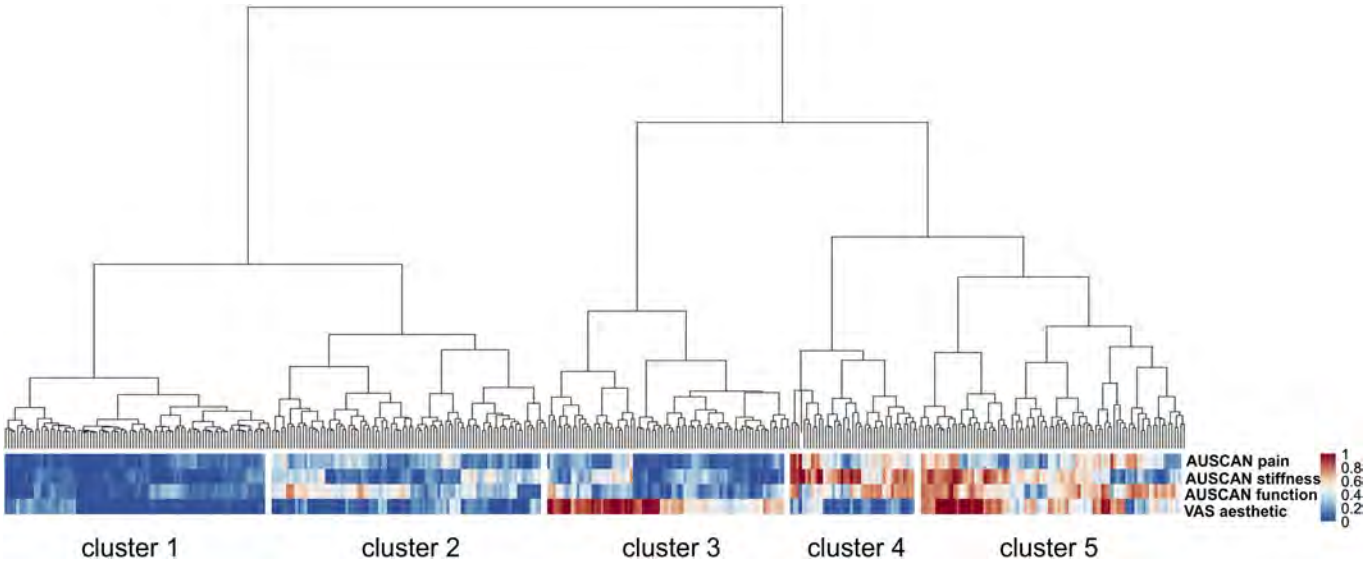

Figure 1. identification by clusters of hand OA phenotypes. The heatmap represents the results of hierarchical agglomerative clustering performed on AUSCAN pain, function and stiffness, and VAS esthetic data collected on 389 patients from the DIGICOD cohort.

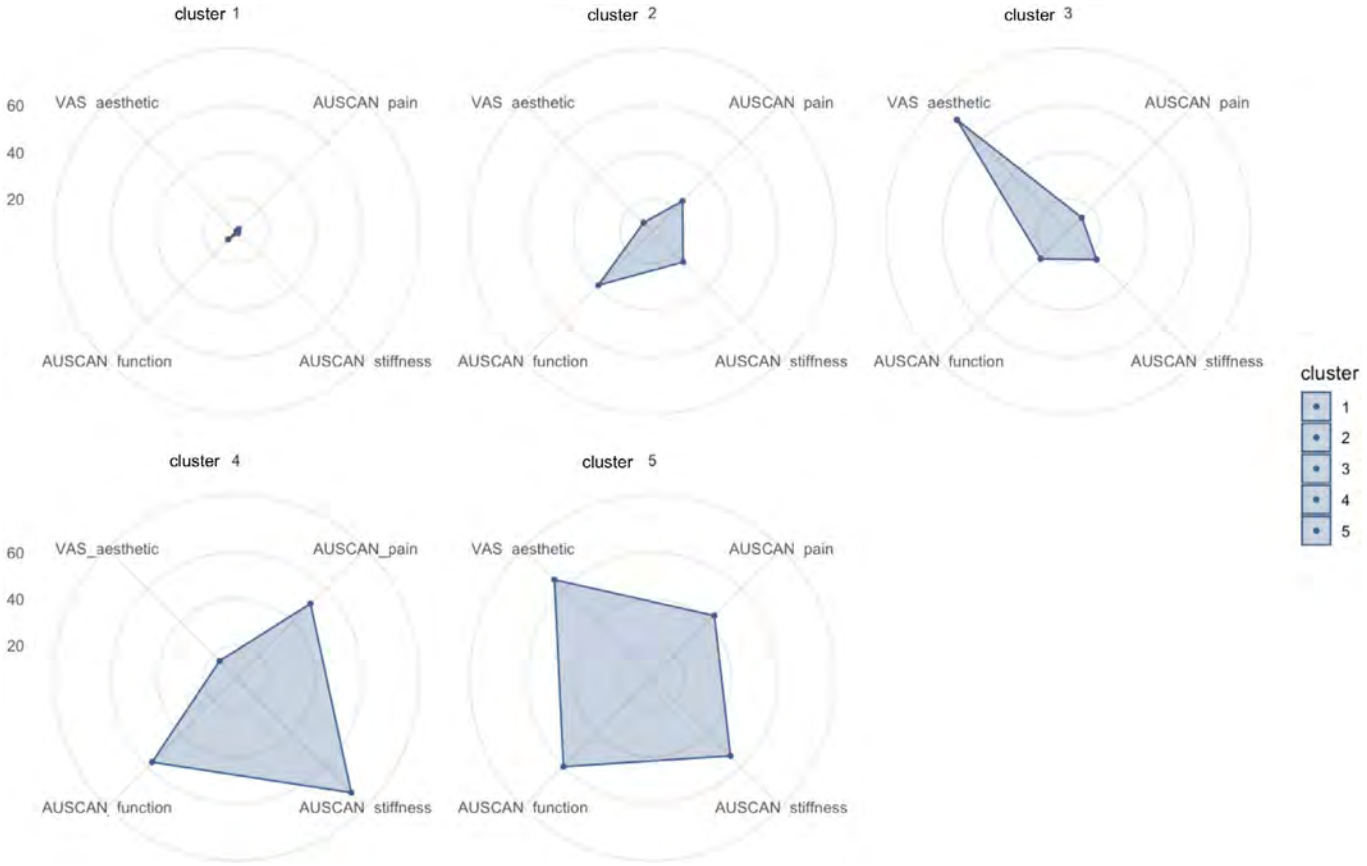

Figure 2. Contribution of the different symptoms to hand OA clusters. Radar plots represent for each cluster the contribution of each symptom based on the AUSCAN pain, function and stiffness, and the VAS esthetic. The values correspond to the mean of the 4 values expressed in each cluster.

alteration since they displayed higher sum of the Kellgren Lawrence score for all hand joints (p< 0.00001) compared to cluster 1. Clusters 4 and 5 have also a higher Hospital Anxiety and Depression score (p=0.0004). Patients' main

Table 1 Descriptive variables of the DIGICOD Cohort according to each cluster

		Overall (N= 389)	Cluster 1 (N = 88)	Cluster 2 (N = 91)	Cluster 3 (N = 80)	Cluster 4 (N= 42)	Cluster 5 (N= 88)					
demographic criteria								p.value	p.adj		SMD	Missing (%)
age (mean (SD))		66.50 (7.41)	64.89 (8.99)	65.72 (7.15)	65.92 (6.27)	68.28 (7.33)	68.58 (6.40)	0.004	0.066	NS	0.273	0
sex (%)	Femme	329 (84.6)	62 (70.5)	72 (79.1)	74 (92.5)	37 (88.1)	84 (95.5)	<0.0001	0.0002	***	0.363	0
	Homme	60 (15.4)	26 (29.5)	19 (20.9)	6 (7.5)	5 (11.9)	4 (4.5)					
metabolism												
BMI (mean (SD))		25.09 (4.36)	24.79 (3.85)	25.96 (5.26)	24.37 (3.59)	26.02 (3.58)	24.71 (4.64)	0.072	1	NS	0.218	1.3
metabolic syndrom (%)	0	243 (62.5)	62 (70.5)	57 (62.6)	51 (63.7)	27 (64.3)	46 (52.3)	0.243	1	NS	0.261	2.6
	1	136 (35.0)	23 (26.1)	30 (33.0)	28 (35.0)	15 (35.7)	40 (45.5)					
CRP (%)	0	289 (74.3)	67 (76.1)	69 (75.8)	52 (65.0)	32 (76.2)	69 (78.4)	0.182	1	NS	0.247	17
	1	34 (8.7)	4 (4.5)	8 (8.8)	8 (10.0)	3 (7.1)	11 (12.5)					
OA histor												
HOA_duration (mean (SD))		12.83 (9.66)	8.25 (6.62)	12.70 (9.72)	13.64 (9.49)	13.98 (9.42)	16.29 (10.82)	<0.0001	<0.0001	****	0.8	3.1
HOA familial history (%)	0	114 (29.3)	20 (22.7)	27 (29.7)	22 (27.5)	17 (40.5)	28 (31.8)	0.343	1	NS	0.245	3.1
	1	263 (67.6)	65 (73.9)	62 (68.1)	57 (71.2)	22 (52.4)	57 (64.8)					
radiographic OA												
erosive HOA (%)	0	255 (65.6)	69 (78.4)	61 (67.0)	49 (61.3)	31 (73.8)	45 (51.1)	0.002	0.036	*	0.29	0.3
	1	134 (34.4)	19 (21.6)	30 (33.0)	31 (38.8)	11 (26.2)	43 (48.9)					
KL_score_sum (mean (SD))		46.14 (17.73)	37.87 (17.47)	43.24 (18.23)	48.04 (17.15)	48.92 (16.04)	54.64 (14.30)	<0.0001	<0.0001	****	0.474	4.1
clinical examination												
main expectation (%)	aesthetitic	30 (7.7)	7 (8.0)	0 (0.0)	18 (22.5)	0 (0.0)	5 (5.7)	<0.0001	0.0003	***	0.473	0
	function	194 (49.9)	48 (54.5)	48 (52.7)	32 (40.0)	26 (61.9)	40 (45.5)					
	pain	164 (42.2)	32 (36.4)	43 (47.3)	30 (37.5)	16 (38.1)	43 (48.9)					
prehension strong hand (mean (SD))		26.06 (12.58)	31.84 (14.81)	28.26 (12.01)	24.02 (9.33)	21.90 (10.61)	21.84 (11.67)	<0.0001	<0.0001	****	0.434	0
Number of swollen joints 30 (mean (SD))		1.21 (2.13)	0.83 (1.78)	1.12 (2.25)	1.39 (2.73)	0.93 (1.67)	1.68 (1.81)	0.075	1	NS	0.215	0.3
Number of pressure pain joint 30 (mean (SD))		4.60 (4.49)	2.55 (3.35)	3.97 (3.50)	3.92 (3.62)	7.24 (6.04)	6.65 (4.91)	<0.0001	<0.0001	****	0.546	0
Number of nodosity 30 (mean (SD))		12.26 (7.47)	10.11 (6.78)	10.97 (7.98)	13.07 (6.78)	12.74 (6.71)	14.80 (7.79)	0.0002	0.003	**	0.316	0

expectation of improvement in all clusters was function, except pain for the highly symptomatic cluster 5. Only cluster 4 and 5 which represented one third of our cohort (N=130) had a mean AUSCAN pain score ≥ 40 mm.

Conclusion: The identification of these 5 clinical symptomatic phenotypes through hierarchical clustering illustrates the heterogeneity of the clinical presentation of hand OA. This opens toward a tailored therapeutic management according to each cluster and may help rationalizing patient recruitment in clinical trials evaluating symptomatic drugs.

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Abstract Number: 0479

A Novel Semi-automated Classifier of Radiographic Hip Osteoarthritis on DXA Scans Is Strongly Predictive of Pain, Clinical Diagnosis and Joint Replacement: Findings from 40,000 Participants in UK Biobank

Benjamin Faber[1], Raja Ebsim[2], Fiona Saunders[3], Monika Frysz[1], Claudia Lindner[2], Jennifer Gregory[3], Richard Aspden[3], Nicholas Harvey[4], George Davey Smith[1], Timothy Cootes[2] and Jon Tobias[1], [1]University of Bristol, Bristol, United Kingdom, [2]University of Manchester, Manchester, United Kingdom, [3]University of Aberdeen, Aberdeen, United Kingdom, [4]University of Southampton, Southampton, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Radiographic hip osteoarthritis (rHOA) is traditionally defined on hip or pelvic radiographs, using subjective methods such as Kellgren-Lawrence scoring. Associations between subjective rHOA measures and clinical outcomes such as hip pain are inconsistent. Applying digital analytical tools to high-resolution dual-energy X-ray absorptiometry (DXA) scans, we aimed to (1) develop a novel semi-automated classifier for rHOA, (2) apply this to available hip DXAs from UK Biobank (UKB), and (3) evaluate face validity of the classifier based on prevalence data and relationships with hip pain, hospital diagnosed OA, and risk of total hip replacement (THR).

Methods: Osteophyte area was manually measured (in mm^2) at the lateral acetabulum, superior-lateral and inferior-medial femoral head on left hip DXAs obtained from individuals in UKB (Figure 1). Osteophyte area thresholds were defined and subsequently applied to categorise each osteophyte into grades 0-3. Minimum joint space width (mJSW) was automatically measured (in mm) over the superior joint space using outline points placed by a machine learning based approach. Thresholds of mJSW were used to categorise individuals into joint space narrowing (JSN) grades 0-3. Osteophyte and JSN grades were summated for each individual to give a rHOA score of 0-12. Hips were then categorised into rHOA grades 0-4 based on rHOA score. Logistic regression was used to examine associations between rHOA grade and hip pain derived from a questionnaire, and hospital diagnosed OA and THR from electronic health record national linkage (HES). Our adjusted model included age, sex, height and weight as covariates.

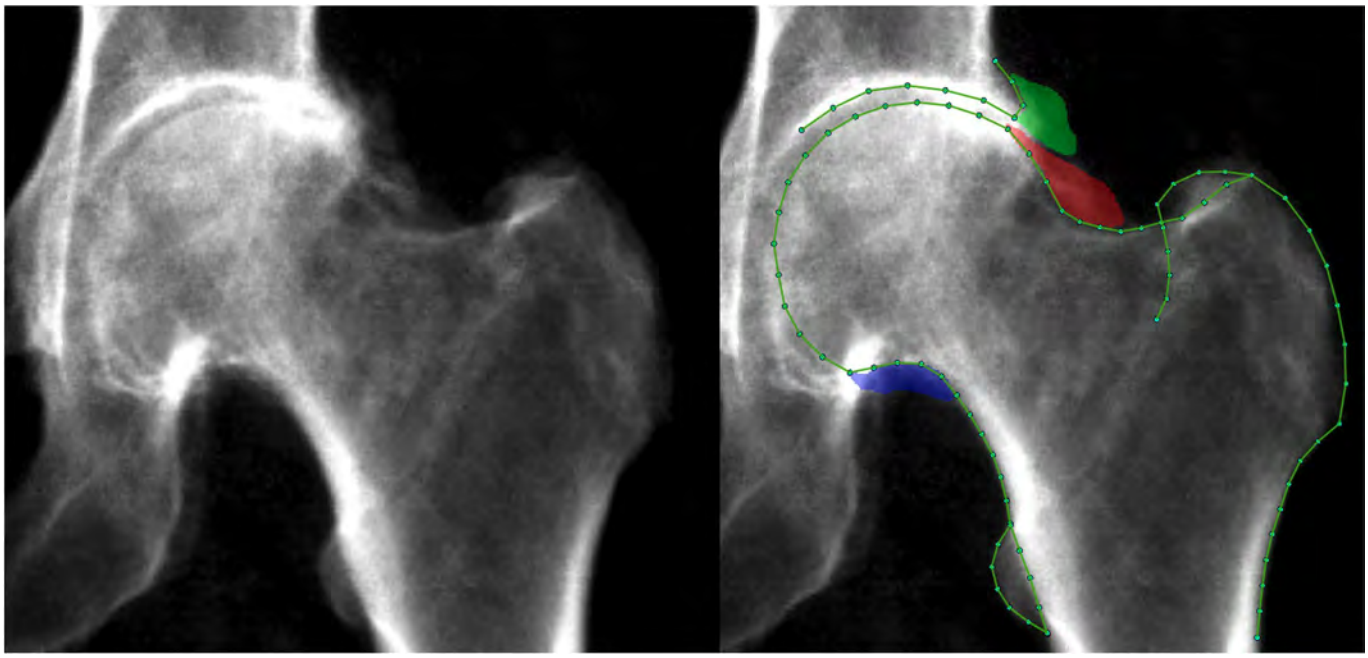

Figure 1. The left image shows a DXA scan from UK Biobank. The right image shows the same DXA scan with osteophytes and outline points marked.

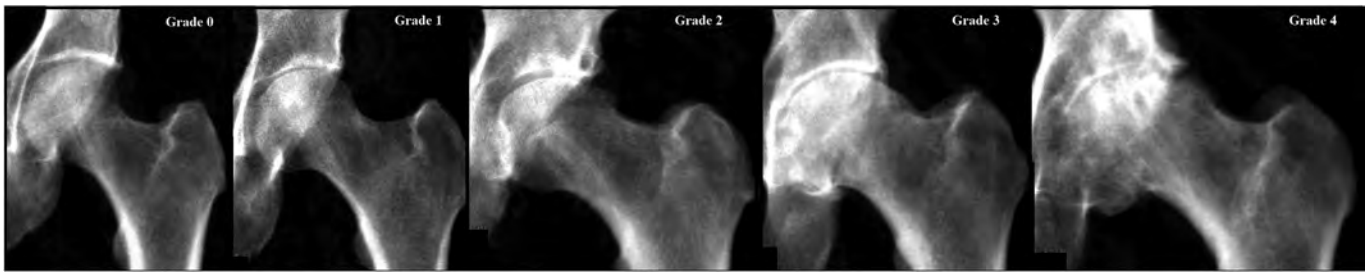

Figure 2. Example DXAs of each rHOA grade.

Results: 40,340 individuals were included in the study [mean age 63.7 (range 44-82), 19294/21046 male/female]. 32758 (81.2%) had rHOA grade 0, 4565 (11.3%) grade 1, 2317 (5.7%) grade 2, 543 (1.3%) grade 3, 157 (0.4%) grade 4 (Figure 2), with all features of rHOA being more common in males than females. rHOA grades ≥2 were associated with all three clinical outcomes in both unadjusted and adjusted models, a clear dose-response relationship was seen with each increase in grade showing a large rise in odds ratio (Figure 3).

Conclusion: Having developed a semi-automated classifier for rHOA on hip DXA scans, we successfully applied this to over 40,000 individuals from UKB, yielding expected findings for OA prevalence including higher rates in males compared with females. The validity of our classifier was further supported by the strong and progressive relationships observed between rHOA and hip pain, and risks of hospital diagnosed hip OA and THR. We conclude that hip DXA scans provide a promising means of objectively defining rHOA, with potential application in the clinic and as a research tool.

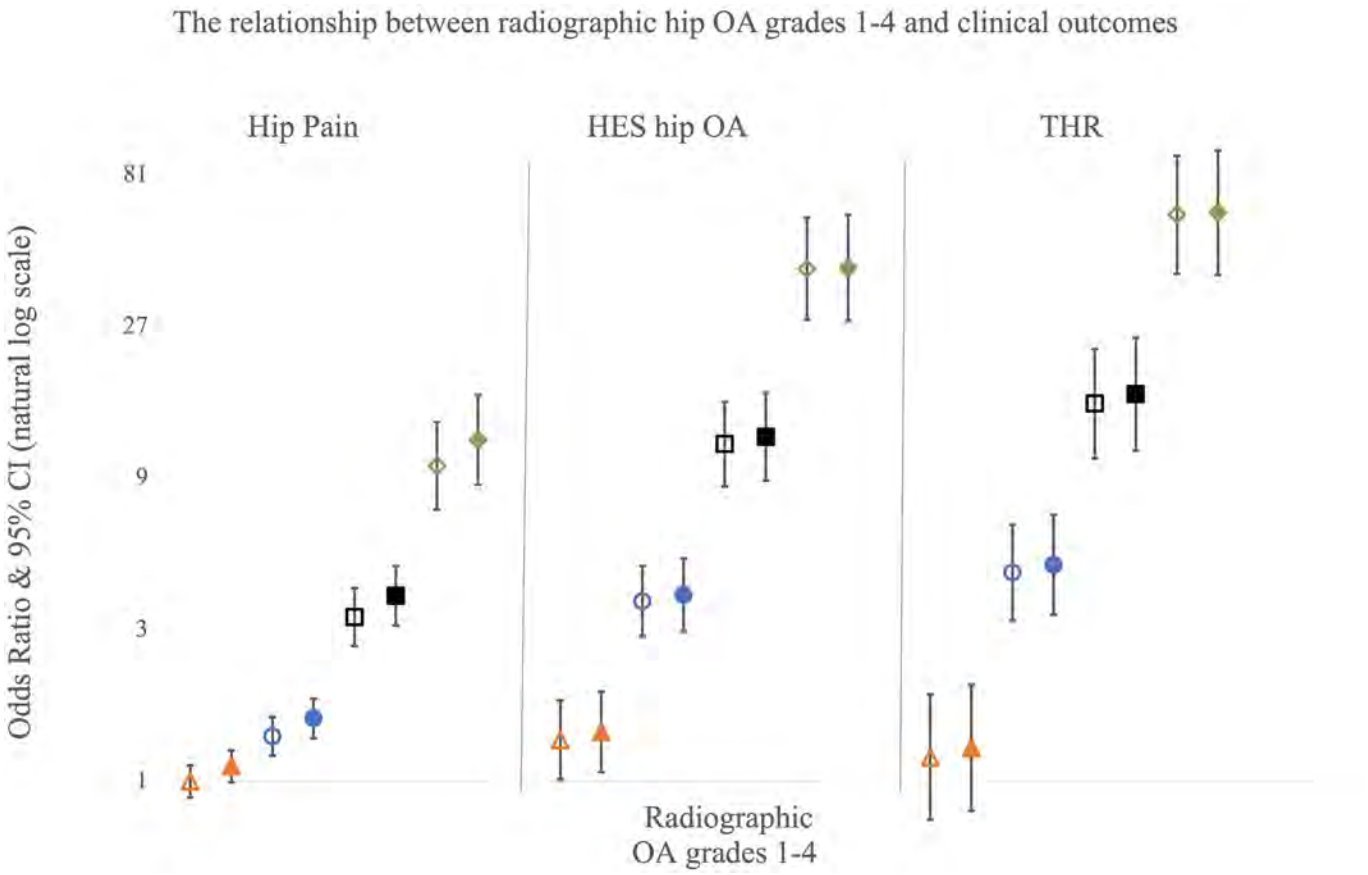

Figure 3. The associations between rHOA grades (1-4) and clinical outcomes. Odds ratios are plotted with 95% confidence intervals either side. Triangles = grade 1, circles = grade 2, squares = grade 3, and diamonds = grade 4. Unadjusted results = hollow shapes, and adjusted results = filled shapes. The Y-axis scale is natural log based.

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Abstract Number: 0480

Signs of Regression to the Mean in Observational Data from a Nation-Wide Exercise and Education Intervention for Osteoarthritis

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Patients who enroll in interventions are likely to do so when they experience a flare-up in symptoms. This may create issues in interpretation of effectiveness due to regression to the mean (RTM). We evaluated signs of RTM in patients from a first-line intervention for knee osteoarthritis (OA).

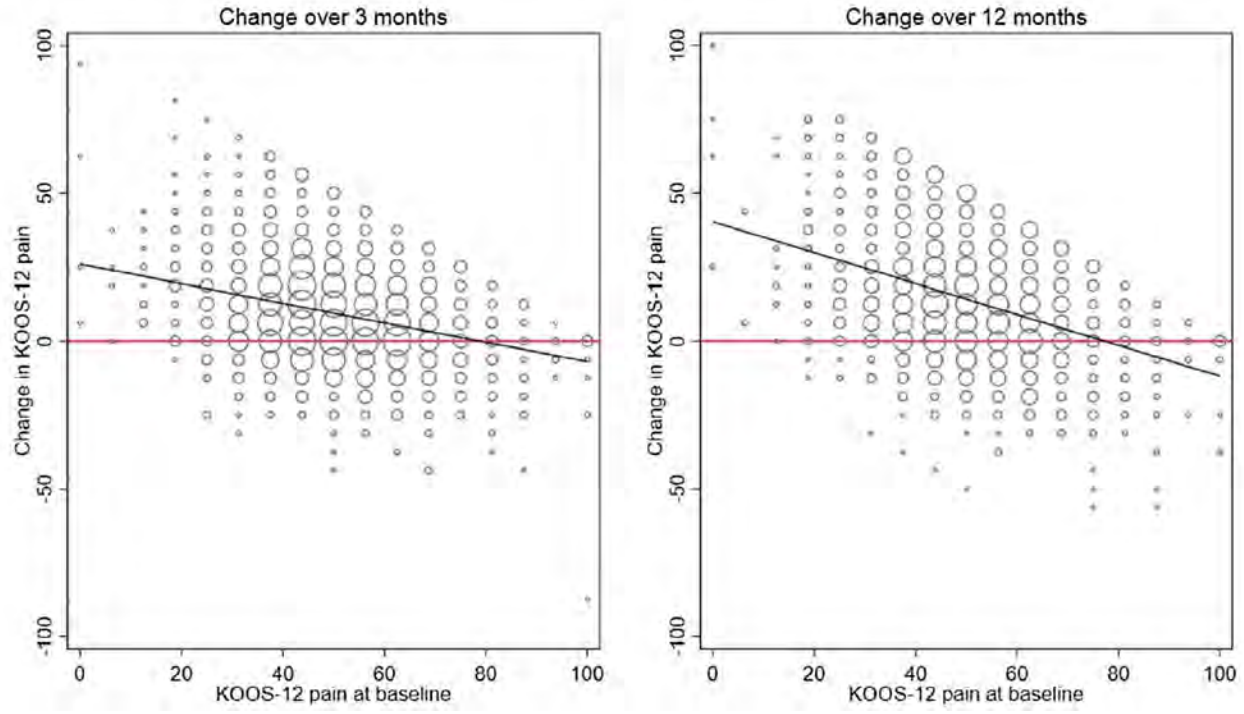
Table 1. Key descriptive statistics for the study cohorts.

		Age, mean yrs (SD)	% women	Body mass index, mean (SD)	KOOS-12 pain, mean (SD)
GLA:D® knee OA participants at baseline	n=4717	66 (9)	69	29 (5)	50 (16)
Persons with knee OA in observational cohorts	OAI, 12 months, n=1085	61 (9)	56	30 (5)	68 (21)
	OAI, 24 months, n=1044	61 (9)	56	30 (5)	69 (21)
	MOA, n=486	73 (7)	65	29 (6)	66 (22)

Methods: We used data from the Good Life with osteoArthritis in Denmark (GLA:D®) program of knee OA patients enrolled from July, 2018 until January, 2019 and included data on knee pain measured with KOOS-12 pain subscale (0-100, worst to best) at baseline, 3 and 12 months. GLA:D® is an 8-week exercise and education program for OA. Radiographic OA is not required, but 86% of the knee OA patients reported that they had knee X-rays taken prior to commencing the program, and more than 90% of those stated that the images showed signs of OA.

To estimate mean levels of pain in a population of persons with knee OA we used cohort data from the Osteoarthritis Initiative (OAI), USA and the Malmö Osteoarthritis study (MOA), Sweden. From OAI we included subjects with radio-

Figure 1. Plot of change in KOOS-12 pain from baseline to 3 months (n=3384) and 12 months (n=2833) vs the baseline pain level; GLA:D® participants with non-missing data. The black line shows linear fit. Size of circles is proportional to the number of persons.



graphic knee OA (KL grade ≥2) at baseline, 12 or 24 months and reporting knee pain, aching or stiffness on most days of at least one month the past 12 months at the baseline visit. We report KOOS-12 values at 12 and 24 months. MOA consisted of two parts – first, persons responded to a postal questionnaire, later they had a clinical visit when knee X-rays were taken. From MOA, we included subjects who had both signs of OA on X-rays and reported knee pain in the postal questionnaire. Thus, taking the fluctuation of OA symptoms into account, we identified the underlying population of persons with knee OA in both OAI and MOA using data collected at one time point (requiring presence of knee pain). We then evaluated their KOOS-12 pain value at *another* time point. This means, that although the persons suffer from OA pain, we do not select them by conditioning on current knee pain.

We evaluated two key signs of potential for RTM: 1) worse pain levels in those enrolled in the first-line intervention than in the underlying population with the disease, and 2) negative correlation between baseline values and change as well as greater/lower average improvement among participants with worse/less pain levels compared to the mean baseline value.

Results: The mean KOOS-12 pain level reported at baseline when enrolling in GLA:D® were worse than in persons with knee OA from OAI and MOA by 16 to 19 points (Table 1). Further, in GLA:D® we found a negative correlation between KOOS-12 pain at baseline and its change of -0.31 (95%CI -0.33, -0.27) at 3 months and -0.39 (95%CI -0.42,-0.35) at the 12 months follow-up (Fig 1). At 12 months, the persons with baseline KOOS pain ≤50 had improved on average by 19 points, while those with baseline pain >50 had improved on average by 6 points. Corresponding data for change from baseline to 3 months were 13 and 4 points, respectively.

Conclusion: Data from a first-line intervention for knee OA display key signs of RTM. As RTM represents no true improvement, but only reflects natural fluctuations of the symptoms, there is a need to determine its magnitude to better understand the true effectiveness of OA interventions in uncontrolled study designs.

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Abstract Number: 0481

The Day-to-day Variability of Pain and the Relationship with Physical Activity in People with Knee Osteoarthritis: A Longitudinal, Observational Feasibility Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Pain is a cardinal symptom in people with knee osteoarthritis (OA). However, pain in knee OA is often infrequently measured both in clinical practice and research studies, meaning little is known about the day-to-day variability of it. Although physical activity is recognised to affect pain, it has been hard to measure both concurrently and study this relationship. In this study we aimed to assess the use of smartwatches to describe the day-to-day variability of pain and assess how this compares to the current standardised assessments of pain at less frequent time points. We also aimed to assess whether the use of a smartwatch can help us to explore the relationship between pain and physical activity levels in people with knee OA.

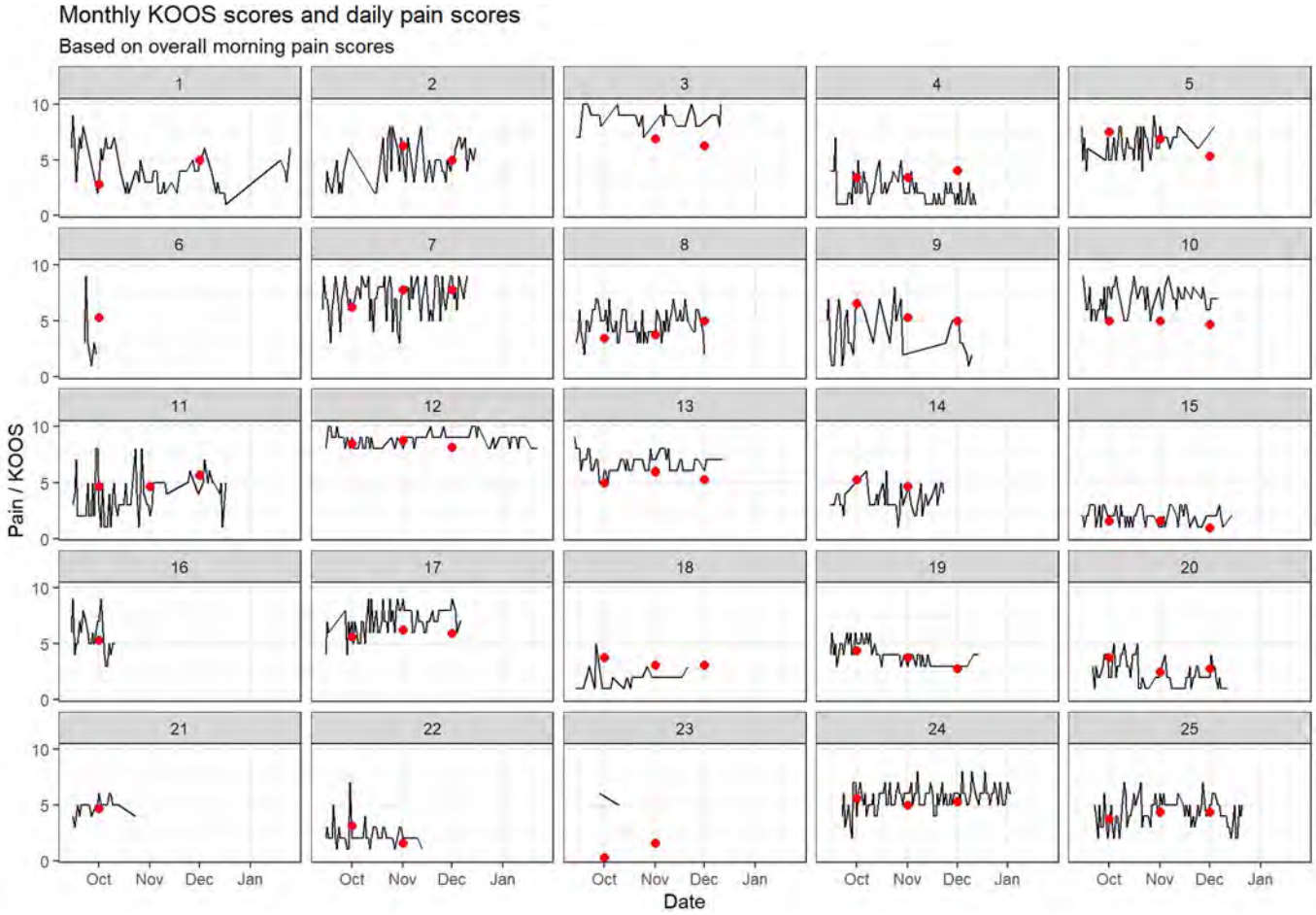

Figure 1. Daily morning pain scores for the 25 participants throughout the three-month study period. The red dots are the respective Knee Injury and Osteoarthritis Outcome Score (KOOS) for each month.

Methods: We performed a longitudinal, observational feasibility smartwatch study in participants with self-diagnosed knee OA over a three-month period. Participants were provided with a consumer cellular smartwatch with a bespoke app that collected patient-reported outcomes via questionnaires. The app triggered questions about daily level of knee pain twice a day and 17 questions from the Knee Injury and Osteoarthritis Outcome Score once a month. Physical activity was measured in the form of daily step counts.

Results: 26 participants were recruited; one left the study early and so was excluded from subsequent analyses. The mean age of participants was 65 years, with a standard deviation of 8 years, 13 were male and the median (IQR) BMI was 27 (25, 35) kg/m^2.

The use of the consumer cellular smartwatch app was successful in assessing and recording data on patient reported outcomes and continuous sensor data simultaneously. We found that pain in knee OA fell into three main categories (sustained high levels of pain, sustained low levels of pain and fluctuating pain) but there was considerable day-to-day variation in pain levels within these categories. Furthermore, as illustrated in Figure 1, we also found that participants with stable monthly KOOS scores had a lot of day-to-day variability in pain levels in between their monthly scores, raising doubt as to whether patients with stable monthly KOOS scores truly represent stable knee OA and whether this is an accurate method for monitoring OA. Interestingly, we also found that those with high/ low levels of pain have a similar step count average but those with fluctuating pain have much lower levels of activity. This may indicate that fluctuating pain (i.e., pain that is unpredictable/ always changing) may be more troublesome to knee OA patients than those with consistently high levels of pain.

Conclusion: This study provides important insights related to the day-to-day variability of pain in knee OA and its links to physical activity. The results from this can help us start to understand pain in people with knee OA. In the

future, larger studies may inform the development of personalized physical activity recommendations for people with knee OA, based on their optimal level of physical activity in relation to their pain.

Disclosure: A. Vivekanantham, None; **D. Selby**, None; **M. Lunt**, None; **T. O'Neill**, None; **W. Dixon**, Google, 2, Bayer, 2, Abbvie, 2.

Abstract Number: 0482

Metformin Use Reduces the Risk of Developing Osteoarthritis: A Propensity Score Matching Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Preclinical and observational data suggest a protective effect of metformin against developing osteoarthritis (OA).[1,2] In this retrospective cohort study, we evaluated the time to developing osteoarthritis and time to joint replacement in patients with diabetes mellitus (DM) treated with metformin compared to patients with DM who did not receive metformin or any other DM treatment.

Methods: This was a retrospective cohort study using claims data from the Optum Clinformatics™ Data Mart between 2003 and 2019. We identified patients aged 40 years or older with more than two years of continuous enrollment and at least two ICD-9 or ICD-10 codes for DM separated by 14 days or more. Patients were excluded if they had type I DM, if they received any DM medication other than metformin, or if they had a prior diagnosis of OA, inflammatory arthritis, or joint replacement. The exposed group included patients treated with metformin, and the control group included patients with DM who were not treated with any medications for DM. We conducted 1:1 propensity score matching and used Cox proportional hazard models to calculate the adjusted hazard ratio (HR) of 1.) developing OA and 2.) undergoing hip or knee joint replacement. Kaplan-Meier curves were created to report the time to diagnosis of OA.

Results: A total of 384,146 patients met study inclusion and exclusion criteria, of which 104,652 were treated with metformin and 274,494 were not. After propensity score matching, both groups had a mean age of 59.4 years and were 43.2% female (**Table 1**). In a multivariable analysis, after adjusting for age, gender, race/ethnicity, and Charlson comorbidity score, the risk of developing OA was reduced by 21% for patients who had been treated with metformin compared to those who had not (adjusted HR 0.79; 95% confidence interval (CI) 0.77-81; p< 0.001), and the adjusted HR for time to joint replacement was 0.90 (95% CI, 0.83-0.98; p=0.01). After propensity score matching, the adjusted HR for developing OA was 0.77 (95% CI, 0.74-0.81; p< .001) and the adjusted HR for time to joint replacement was 0.86 (95% CI, 0.75-0.99; p=0.038) (**Table 2**). Survival analysis demonstrates separation of the Kaplan-Meier curves by 24 months after treatment initiation (**Figure**).

Conclusion: This study demonstrates a significant reduction in the risk of developing OA and in the need for joint replacement in DM patients treated with metformin compared to DM patients who did not receive metformin. Results from this study further support the preclinical and observational data that metformin may have a protective effect against the development of OA. Future interventional studies with metformin for the treatment or prevention of OA could be considered.

Table 1. Baseline characteristics of patients before and after 1:1 propensity score matching

	Before PS-matching			After PS-matching		
	Metformin (*n* = 104652)	**Control (*n* = 274494)**	**SMD**	**Metformin (*n* = 104652)**	**Control (*n* = 104652)**	**SMD**
Age in years, mean (SD)	59.4 (11.1)	64.6 (12.4)	0.439	59.4 (11.1)	59.4 (11.1)	<0.001
Gender, n (%)			0.093			0.015
Female	45191 (43.2)	133647 (47.8)		45191 (43.2)	45193 (43.2)	
Male	59444 (56.8)	145809 (52.2)		59444 (56.8)	59457 (56.8)	
Unknown	17 (0.0)	38 (0.0)		17 (0.0)	2 (0.0)	
Race, n (%)			0.032			<0.001
White	63869 (61.0)	169770 (60.7)		63869 (61.0)	63868 (61.0)	
Black	11749 (11.2)	30193 (10.8)		11749 (11.2)	11756 (11.2)	
Asian	5723 (5.5)	15757 (5.6)		5723 (5.5)	5716 (5.5)	
Hispanic	15184 (14.5)	39874 (14.3)		15184 (14.5)	15180 (14.5)	
Unknown	8127 (7.8)	23900 (8.6)		8127 (7.8)	8132 (7.8)	
Education, n (%)			0.061			0.075
Less than 12th grade	877 (0.8)	2450 (0.9)		877 (0.8)	829 (0.8)	
High school diploma	30091 (28.8)	74605 (26.7)		30091 (28.8)	27595 (26.4)	
Less than bachelor's degree	53841 (51.4)	143573 (51.4)		53841 (51.4)	54151 (51.7)	
Bachelor's degree or higher	13896 (13.3)	41171 (14.7)		13896 (13.3)	16255 (15.5)	
Unknown	5947 (5.7)	17695 (6.3)		5947 (5.7)	5822 (5.6)	
Charlson comorbidity score, n (%)			0.326			0.002
0	70467 (67.3)	152865 (54.6)		70467 (67.3)	70479 (67.3)	
1-2	27150 (25.9)	83713 (30.0)		27150 (25.9)	27153 (25.9)	
3-4	5081 (4.9)	27718 (9.9)		5081 (4.9)	5091 (4.9)	
5-6	1008 (1.0)	9228 (3.3)		1008 (1.0)	996 (1.0)	
> 6	946 (0.9)	6150 (2.2)		946 (0.9)	933 (0.9)	

PS = propensity score; SMD = standardized mean difference; SD = standard deviation.

Table 2. Risk of developing osteoarthritis or undergoing joint replacement after propensity score matching

		Propensity score matched	
Outcome	**Variable**	**aHR (95% CI)**	**p value**
Time to OA diagnosis	Metformin vs. Control	0.77 (0.74-0.81)	<0.001
Time to joint replacement	Metformin vs. Control	0.86 (0.75-0.99)	0.038

aHR = adjusted hazard ratio; 95% CI = 95% confidence interval; OA = osteoarthritis.

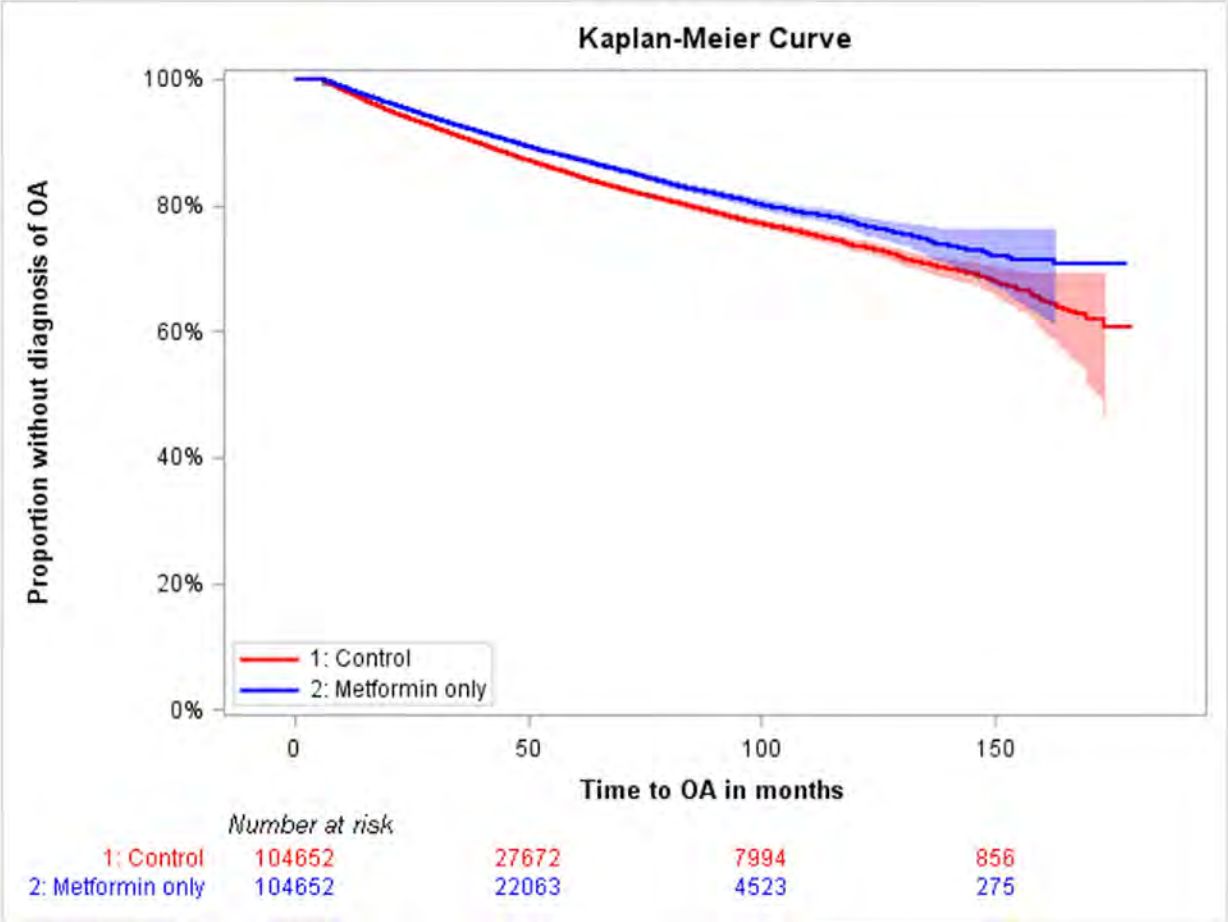

Figure. Kaplan-Meier curve of time to osteoarthritis diagnosis in metformin treated patients compared to controls after propensity score matching.

References:

1. Wang Y, Hussain SM, Wluka AE, et al., Arthritis Res Ther 21, 127 (2019).
2. Li J, Zhang B, Liu WX, et al., Ann Rheum Dis 79, 635-645 (2020).

Disclosure: K. Sheth, None; **D. Lu**, None; **R. Lu**, None; **W. Robinson**, None; **M. Baker**, Vorso Corp, 2.

Abstract Number: 0483

Frequent Use of Prescription Oral NSAIDs Among People with Knee or Hip Osteoarthritis Despite Contraindications to or Precautions with NSAIDs

Tuhina Neogi[1], Andrea Dell'isola[2], Martin Englund[2] and Aleksandra Turkiewicz[2], [1]Boston University School of Medicine, Boston, MA, [2]Lund University, Lund, Sweden

SESSION INFORMATION

Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Osteoarthritis – Clinical (0478–0483)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Table 1. Descriptive data on the study sample.

	Without contraindications N=27 558	With contraindications N=2762	Without precautions N=20992	With precautions N=6566
Age (years), mean (SD)	67.12 (12.26)	71.62 (11.83)	65.26 (11.87)	73.07 (11.59)
Male, n (%)	11352 (41)	1177 (43)	8479 (40)	2873 (44)
Income, annual, per 100 000 SEK, mean (SD)	2.22 (3.13)	1.98 (4.15)	2.32 (3.36)	1.93 (2.24)
Education 15+ years, n (%)	3617 (13)	237 (9)	3052 (15)	565 (9)
Contraindications:				
GI bleed, n (%)	0 (0)	2238 (81)	0 (0)	0 (0)
Chronic kidney disease, stage 3-5, n (%)	0 (0)	486 (18)	0 (0)	0 (0)
Acute kidney disease, n (%)	0 (0)	223 (8)	0 (0)	0 (0)
Precautions:				
Ischeamic heart disease, n (%)	3509 (13)	820 (30)	0 (0)	3509 (53)
Heart failure, n (%)	1589 (6)	452 (16)	0 (0)	1589 (24)
Gastroesophageal reflux disease, n (%)	1918 (7)	653 (24)	0 (0)	1918 (29)
Crohn's disease or Ulcerative colitis, n (%)	362 (1)	70 (3)	0 (0)	362 (6)
Chronic kidney disease, stage 1-2, n (%)	993 (4)	442 (16)	0 (0)	993 (15)

Background/Purpose: Oral NSAIDs are recommended for OA management. However, many patients with OA have contraindications to NSAIDs or have comorbidities that warrant precaution. Because few other oral therapies are available, such patients may still receive NSAIDs or may instead receive opioids, which are not recommended and have numerous concerning adverse effects. They may also receive physical therapy (PT), an effective option, as a safe alternative. We evaluated the patterns of NSAID, opioid, and PT use among persons with newly diagnosed knee or hip OA with and without NSAID contraindications or precautions using population-based Swedish register data.

Methods: We used register data on healthcare use and dispensed drugs, and population register to identify adults aged ≥35 as of Jan 1, 2010 residing in Skåne region in Sweden, between 1998-2009 and without a knee or hip OA diagnosis during this time. Among this cohort, we identified people with incident knee or hip OA using ICD-10 codes between 2010- 2015. We identified contraindications to or precautions for oral NSAIDs based on ICD-10 codes prior to or at the time of OA diagnosis. Contraindications included gastrointestinal bleed/ ulcer, chronic kidney disease (CKD) stage ≥3 (dialysis, transplant), acute renal failure. Precautions included coronary artery disease, heart failure, gastroesophageal reflux disease, inflammatory bowel disease, CKD stage 1 or 2, other kidney diseases. During the first year after a new OA diagnosis among those with vs. without contraindications or precautions, we evaluated the prevalence and relative risk of: 1) regular oral NSAID use (see **Figure 1** for definition); 2) regular opioid use (see **Fig 1**); 3) physical therapy visit descriptively and in confounder-adjusted logistic regression models with standardization to compute risk ratios.

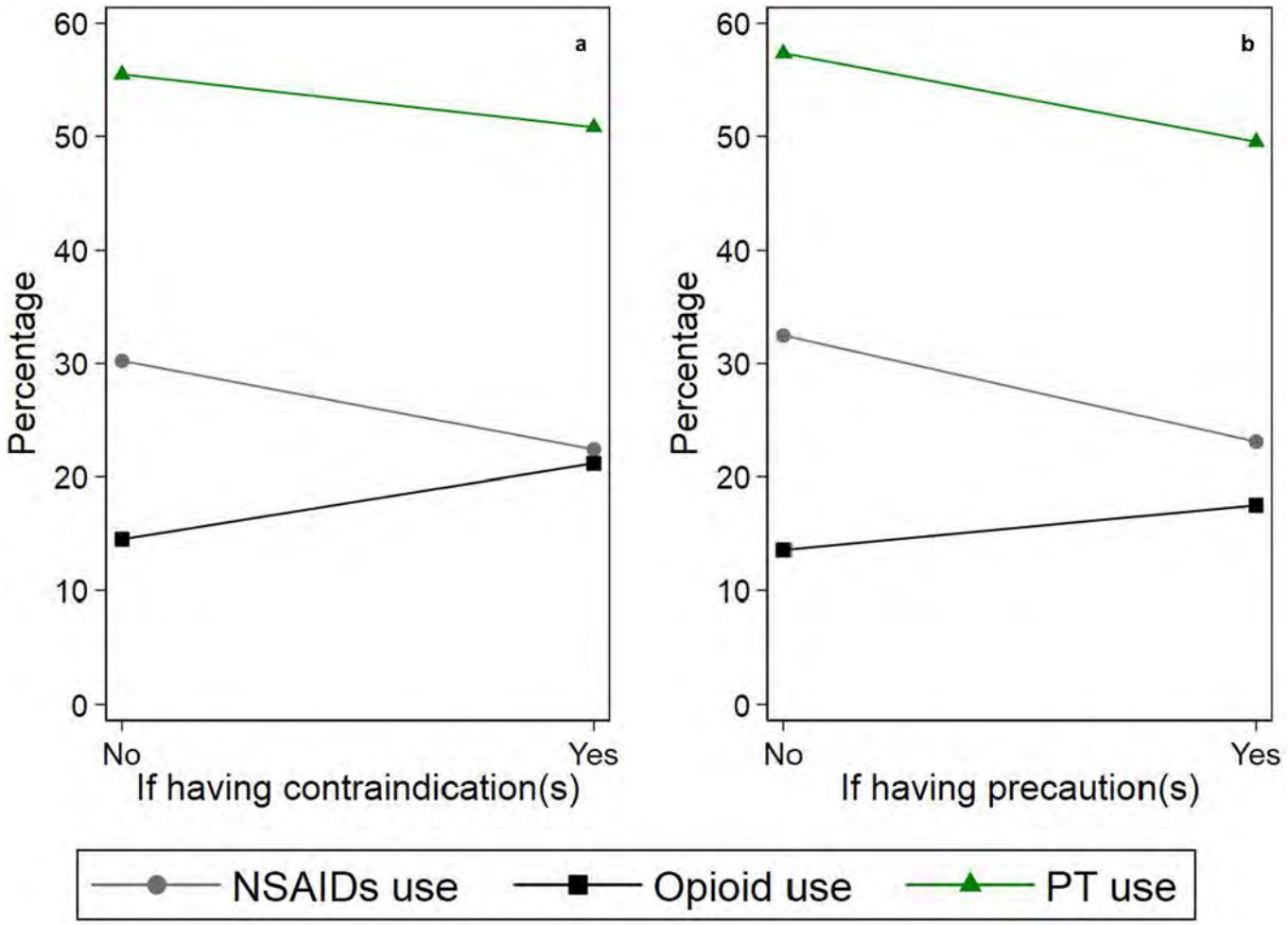

Figure 1. Crude prevalence of NSAIDs, opioid and physical therapy (PT) in persons with newly diagnosed knee or hip OA during the first year after diagnosis, by presence of contraindications or precautions for NSAIDs use. Regular use of NSAIDs or opioids were defined as ≥30 total daily doses prescribed within 90 days from first prescription to ensure regular use for something other than an acute problem.

Results: We included 30,320 persons (21,682 knee OA; 9124 hip OA; 486 were diagnosed with both on the same date; mean age 67, ~41% male, **Table 1**). Overall, 9.1% had contraindications to NSAIDs, and 21.7% had at least one precaution. There was lower prevalence of regular NSAID use among those with vs. without contraindication to NSAIDs (22% vs. 30%), but higher prevalence of regular opioid use (21% vs. 15%) (**Figure 1a**); a similar pattern was seen for those with vs. without precautions for NSAIDs (NSAID use: 23% vs. 32%; (opioid use: 18% vs. 14%) (**Figure 1b**). The lowest prevalence of regular NSAID use was among those with CKD stage ≥3 (10%); they also had highest prevalence of regular opioid use (25%). Prevalence of PT was slightly lower among those with contraindications (51%) or precautions (50%) than those without (55% and 57%, respectively). In adjusted analyses, those with contraindications or precautions were at 1.2 to 1.5 times higher risk of regular opioid prescriptions than those without, while use of PT was not increased for any group (**Figure 2**).

Conclusion: People with knee or hip OA who have contraindications to or precautions for NSAIDs had higher risk of regular opioid use, but not PT, within the first year of their OA diagnosis. These data highlight the negative impact of having a paucity of treatment options for people with OA who are unable to safely use NSAIDs, and lack of sufficient use of PT for these at-risk patients.

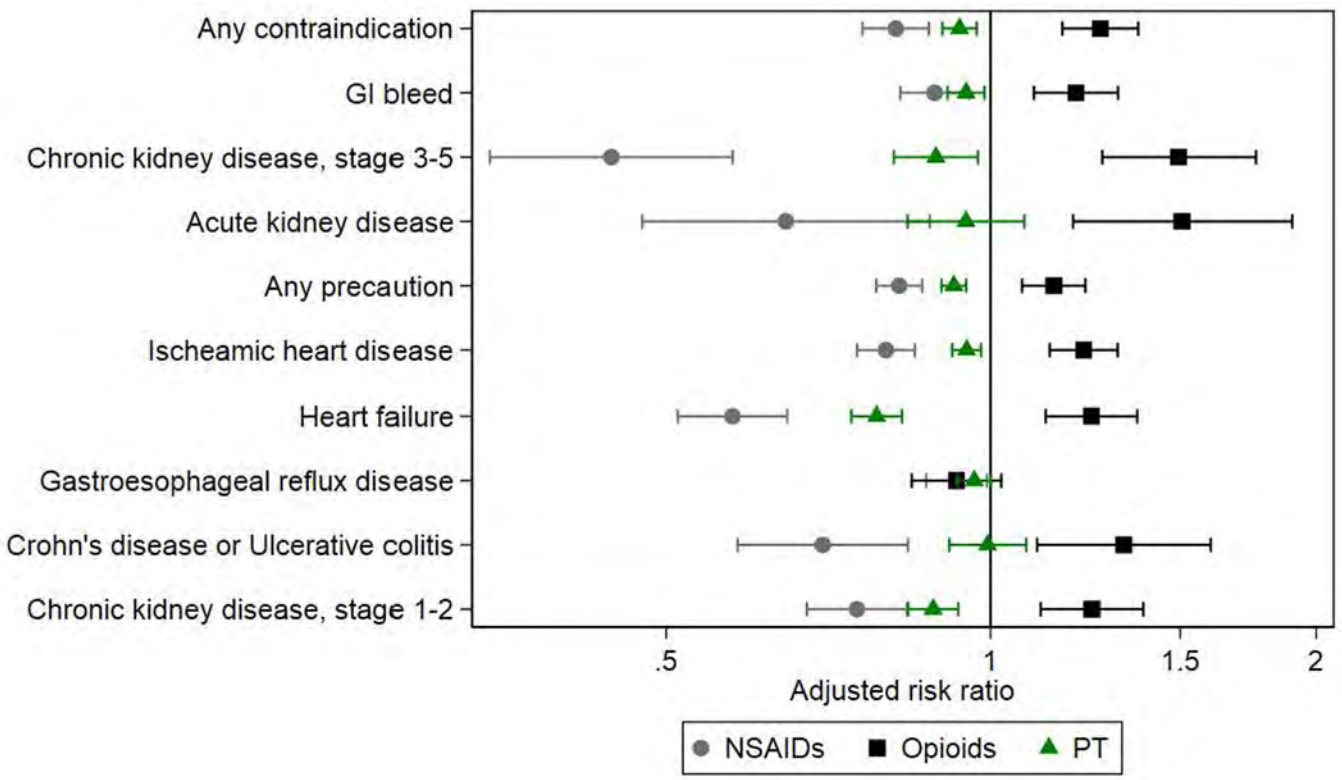

Figure 2. Adjusted risk ratios of NSAIDs, opioid and physical therapy (PT) use in persons with newly diagnosed knee or hip OA during the first year after diagnosis, comparing those with and without contraindications and precautions of NSAIDs use. The logistic regression model was adjusted for age-group, sex, marital status, if born outside Sweden, income group, education level, year of OA diagnosis, healthcare use (operationalized in 5 variables, if inpatient visit, if specialist contact with psychiatry, categorized number of specialist visits in somatic care, primary care and with other healthcare professionals [not physicians]). Risk ratios were derived using method of standardization.

Disclosure: T. Neogi, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **A. Dell'isola**, None; **M. Englund**, None; **A. Turkiewicz**, None.

Abstract Number: 0484

RheumMadness: Creating an Online Community of Inquiry

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Professional Education (0484–0487)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: RheumMadness is an online collaborative learning experience in which rheumatology concepts compete as teams in a tournament. The Community of Inquiry (CoI) framework describes the cognitive, social, and teaching "presences" in a social constructivist learning activity. This study analyzes participant engagement and the CoI presences in the first year of RheumMadness.

Table 1. Post-survey results: demographics and engagement with RheumMadness

	All Respondents n (%)	Full Participants n = 19 (%)	Partial Participants n = 39 (%)
Total Respondents	58 (100%)	19 (100%)	39 (100%)
Position / Training Level			
Attending physician	31 (53.4%)	11 (57.9%)	20 (51.3%)
Fellow	19 (32.8%)	6 (31.6%)	13 (33.3%)
Resident	4 (6.9%)	2 (10.5%)	2 (5.1%)
Other*	4 (6.9%)	0 (0.0%)	4 (10.2%)
Country of Residence			
USA	50 (86.2%)	16 (84.2%)	34 (87.2%)
Non-USA†	8 (13.8%)	3 (15.8%)	5 (12.8%)
Unique Roles in RheumMadness			
Participated in scouting report creation	14 (24.1%)	4 (21.1%)	10 (25.6%)
Blue Ribbon Panel member	7 (12.1%)	4 (21.1%)	3 (7.7%)
Podcast Episodes Listened to			
None	22 (37.9%)	0 (0.0%)	22 (56.4%)
Some	14 (24.1%)	0 (0.0%)	14 (35.9%)
About half	9 (15.5%)	6 (31.6%)	3 (7.7%)
Many	9 (15.5%)	9 (47.4%)	0 (0.0%)
All	4 (6.9%)	4 (21.1%)	0 (0.0%)
Scouting Reports Reviewed			
None	7 (12.1%)	0 (0.0%)	7 (17.9%)
Some	15 (25.9%)	0 (0.0%)	15 (38.5%)
About half	5 (8.6%)	3 (15.8%)	2 (5.1%)
Many	13 (22.4%)	6 (31.6%)	7 (17.9%)
All	18 (31.0%)	10 (52.6%)	8 (20.5%)
Social Media - Frequency of Reading Posts			
Never	9 (15.5%)	0 (0.0%)	9 (23.1%)
Rarely (just once or twice)	7 (12.1%)	0 (0.0%)	7 (17.9%)
Occasionally (about once per week)	11 (19.0%)	4 (21.1%)	7 (17.9%)
A moderate amount (several times per week)	19 (32.8%)	10 (52.6%)	9 (23.1%)
A great deal (about every day)	12 (20.7%)	5 (26.3%)	7 (17.9%)
Social Media - Frequency of Writing Posts			
Never	29 (50.0%)	3 (15.8%)	26 (66.7%)
Rarely (just once or twice)	6 (10.3%)	2 (10.5%)	4 (10.3%)
Occasionally (about once per week)	10 (17.2%)	5 (26.3%)	5 (12.8%)
A moderate amount (several times per week)	12 (20.7%)	9 (47.4%)	3 (7.7%)
A great deal (about every day)	1 (1.7%)	0 (0.0%)	1 (2.6%)
Table Notes			
*Other participants included 1 APP trainee, 1 medical student, and 2 patients			
† Non-USA countries of residence included Canada (2), Denmark (1), India (2), Ireland (2), and the Philippines (1)			

Methods: RheumMadness 2021 included 16 concepts in a single-elimination bracket, scouting reports reviewing each concept created by >40 fellows from 14 fellowship programs, and a podcast (15 episodes). Participants completed brackets predicting the outcome of tournament matchups (decided by 7 judges) and discussed RheumMadness on social media (Facebook/Twitter). Web-based analytics tracked engagement with each element in RheumMadness. A Qualtrics survey was emailed to participants and shared on social media to assess engagement with RheumMadness and perceptions of the CoI presences. CoI questions were adapted from a validated 34-item CoI survey. Respondents were categorized as "full participants" if they listened to at least half the podcast episodes, read at least half the scouting reports and read social media posts at least once per week; the remainder were "partial participants." Survey data were analyzed with Fisher's exact test and Pearson's correlation for linear relationships.

Table 2. Community of Inquiry (CoI) survey results for full and partial participants

	Full Participants Number of responses (%)			Partial Participants Number of responses (%)		
	Disagree or Strongly Disagree	Neutral	Agree or Strongly Agree	Disagree or Strongly Disagree	Neutral	Agree or Strongly Agree
Cognitive Presence						
Triggering	0 (0%)	0 (0%)	57 (100%)	1 (0.9%)	17 (14.5%)	99 (84.6%)
Exploration	6 (10.5%)	11 (19.3%)	40 (70.2%)	16 (13.7%)	44 (37.6%)	57 (48.7%)
Integration	3 (5.3%)	9 (15.8%)	45 (78.8%)	4 (3.4%)	41 (35.0%)	72 (61.5%)
Resolution	0 (0%)	9 (15.8%)	48 (84.2%)	15 (12.9%)	31 (26.5%)	71 (60.7%)
Overall cognitive presence	9 (3.9%)	29 (12.7%)	190 (83.3%)	36 (7.7%)	133 (28.4%)	299 (63.9%)
Social Presence						
Affective expression	0 (0%)	8 (14.0%)	49 (86.0%)	15 (12.8%)	30 (25.6%)	72 (61.5%)
Open communication	0 (0%)	10 (17.5%)	47 (82.5%)	8 (6.8%)	48 (41.0%)	61 (52.1%)
Group cohesion	3 (5.3%)	13 (22.8%)	41 (71.9%)	5 (4.3%)	60 (51.3%)	52 (44.4%)
Overall social presence	3 (1.8%)	18.1%)	137 (80.1%)	28 (8.0%)	138 (39.3%)	185 (52.7%)
Teaching Presence						
Design & organization	0 (0%)	2 (2.6%)	74 (97.4%)	3 (1.9%)	17 (10.9%)	136 (87.2%)
Facilitation	0 (0%)	4 (3.5%)	110 (96.5%)	1 (0.4%)	56 (23.9%)	177 (75.6%)
Direct instruction	0 (0%)	4 (7.0%)	53 (93.0%)	2 (1.7%)	25 (21.4%)	90 (76.9%)
Overall teaching presence	0 (0%)	10 (4.0%)	237 (96.0%)	6 (1.2%)	98 (19.3%)	403 (79.5%)

Table Notes

- Rows highlighted in yellow were tested for difference in response frequency between full and partial participants; all showed $p < 0.001$
- 8 out of 1,972 potential responses were left blank. These all occurred in the partial participant group. Blank responses were considered "neutral."

Results: 105 brackets were submitted in the tournament. There were 1,542 scouting report page views (96 per report) and 2,449 podcast downloads (163 per episode). The Facebook group accrued 81 members. On Twitter, there were 486 tweets from 105 users, generating 2,312,386 potential Twitter impressions.

	Overall CoI Score§ r coefficient (p value)¶	Cognitive Presence r coefficient (p value)¶	Social Presence r coefficient (p value)¶	Teaching Presence r coefficient (p value)¶
Overall Engagement*	0.72 ($p < 0.001$)	0.57 ($p < 0.001$)	0.64 ($p < 0.001$)	0.59 ($p < 0.001$)
Podcast Engagement	0.54 ($p < 0.001$)	0.48 ($p < 0.001$)	0.45 ($p < 0.001$)	0.43 ($p < 0.001$)
Scouting Report Engagement	0.49 ($p < 0.001$)	0.49 ($p < 0.001$)	0.31 ($p = 0.016$)	0.46 ($p < 0.001$)
Social Media Engagement†	0.65 ($p < 0.001$)	0.33 ($p = 0.011$)	0.78 ($p < 0.001$)	0.50 ($p < 0.001$)

Table Notes

Correlation strength highlighting key:
green = strong ($r > 0.6$)
yellow = moderate (r of 0.4 - 0.59)
orange = weak (r of 0.2 - 0.39)

*Overall Engagement is the average of podcast, scouting report, and social media engagement ratings

†Social Media Engagement is the average ratings for frequency of social media reading and posting

§ Overall Community of Inquiry Score is the weighted average of the cognitive, social, and teaching presence ratings

¶ p value for significance set at 0.003125 after Bonferroni correction for 16 tests, non-significant values in orange

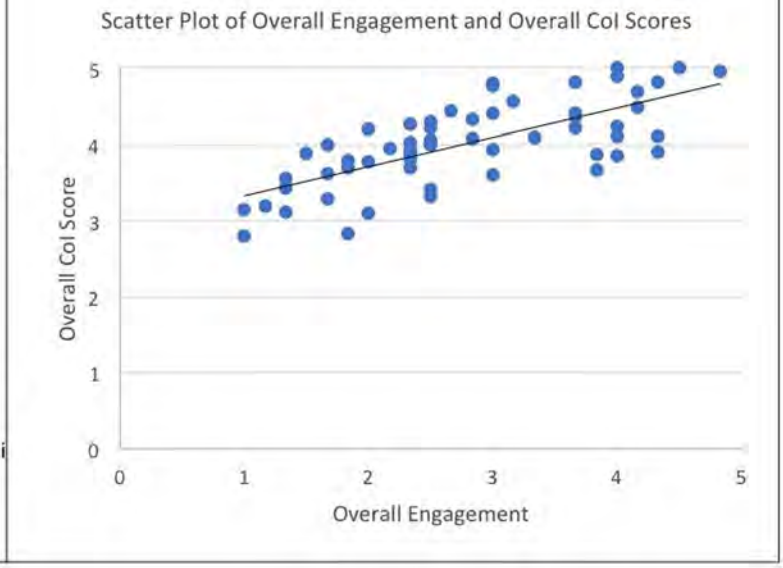

Figure 1. Correlation between Community of Inquiry (CoI) scores and RheumMadness engagement.

The post-survey was sent to 100 participants who submitted a bracket; the remaining 5 brackets were from the study team. Of recipients, 58/100 (58%) responded; 19 (32.8%) were full and 39 (67.2%) partial participants. Demographics and reported engagement are shown in Table 1. CoI results are shown in Table 2. The majority of full and partial participants indicated agreement with prompts relating to the cognitive, social, and teaching presence; agreement was more frequent among full participants in each presence ($p< 0.001$).

Correlation analyses are shown in Figure 1. There was a significant, strongly positive correlation between overall engagement with RheumMadness and overall CoI survey scores ($r=0.72$, $p< 0.001$). The cognitive presence showed a moderate correlation with scouting report and podcast engagement but no significant correlation with social media. The social presence correlated strongly with social media and moderately with podcast engagement but no significant correlation with scouting reports. The teaching presence correlated moderately with all components.

Conclusion: RheumMadness successfully engaged learners in an online learning community. Most participants agreed that RheumMadness fostered meaningful cognitive, social, and teaching presences, especially among full participants. The cognitive presence was fostered primarily by didactic elements – the scouting reports and podcast. The social presence was fostered by social media and, to a lesser extent, the podcast. All elements contributed to the teaching presence.

Disclosure: D. Leverenz, Pfizer, 5; **A. Udupa**, None; **D. Saygin**, None; **G. Katz**, None; **C. Witt**, None; **L. Criscione-Schreiber**, GlaxoSmithKline, 5; **M. Sparks**, National Kidney Foundation, 6.

Abstract Number: 0485

The Impact of COVID-19 on Rheumatology Trainee Health and Wellbeing: Results from the COVID-19 Global Rheumatology Alliance Trainee Survey

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Professional Education (0484–0487)

Session Type: Abstract Session

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Background/Purpose: The COVID-19 pandemic has disrupted healthcare delivery and education of physicians, including rheumatology trainees. Our objective was to assess the impact of the COVID-19 pandemic on rheumatology trainee health, well-being, and features of burnout.

Table 1. Characteristics of US respondents

	n (%)
US Geographic Region	
New England	16 (14)
Mid East	36 (31)
Great Lakes	13 (11)
Plains	8 (7)
Pacific region and Southeast	13 (11)
Southwest	7 (6)
Rocky Mountains	5 (4)
Far West	18 (16)
Post graduate training year	
1	37 (32)
2	40 (35)
3	20 (17)
4 or higher	5 (4)
Completed training in 2020	14 (12.1)
Program type	
Adult	86 (74)
Pediatric	26 (22)
Combined adult/pediatric	4 (3)

Table 2. Rheumatology trainees reporting health vulnerabilities or having acquired COVID-19

	United States n = 116	Rest of the World (ROW) n = 186	Combined n = 302
Disability, n (%)	1 (0.1)	9 (4)	10 (3)
High risk, n (%)	11 (10)	19 (10)	30 (10)
Pregnant, n (%)	10 (9)	9 (4)	19 (6)
Quarantining, n (%)	44 (38)	38 (20)	82 (27)
Acquired COVID-19, n (%)	8 (7)	33 (18)	41 (14)

Methods: A voluntary, anonymous, web-based survey was administered in English, Spanish, or French from 8/19/20 to 10/5/20. Adult and pediatric rheumatology trainees worldwide who were in training in 2020 were invited to participate via social media and email. Using multiple choice questions and Likert scales, we assessed the impact of COVID-19 on trainee well-being.

Results: The 302 rheumatology trainees who responded were from 33 countries, 116 (38%) from the United States (US); rest of the world (ROW) data includes trainees from Europe (87), Asia (50), South America (21), Canada (12),

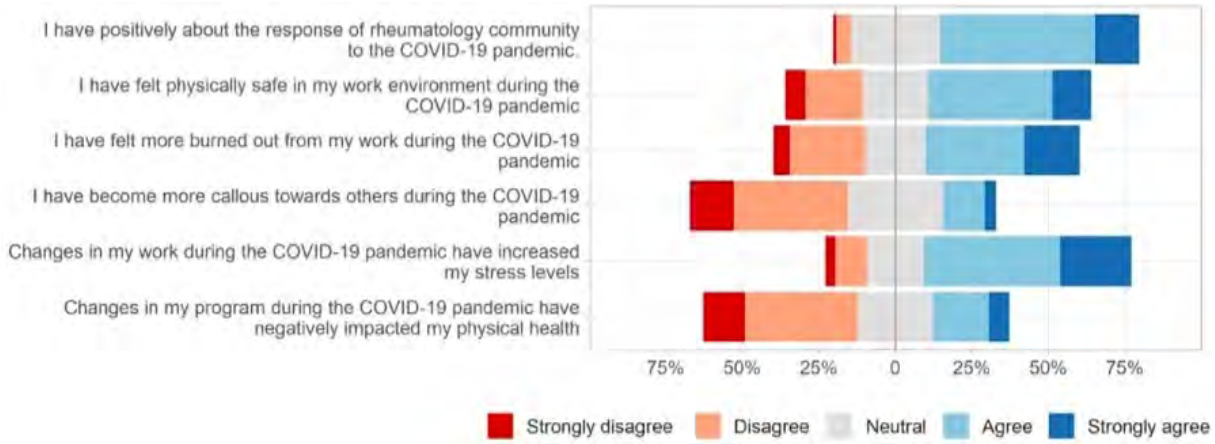

Figure 1. Rheumatology trainee perceptions of pandemic impact.

Australia (8), and Africa (4). The regional distribution of the US trainees is shown in Table 1. The majority of both US and ROW respondents were adult rheumatology trainees (74% and 89%, respectively).

Globally, 30 respondents (10%) reported having health condition(s) putting them at perceived high risk for severe COVID-19; 41 trainees (14%) reported having COVID-19 (Table 2). Seventy-five trainees (25%) reported a negative impact of work changes on their physical health, while 68% (204) reported an increase in stress levels and 50% (151) reported feeling burned out (Figure 1). Less than 20% (52, 17%) reported feeling more callous towards others, a feature of burnout. Compared to US trainees, trainees in ROW more frequently reported that the pandemic negatively impacted their physical health (10% of US vs 34% of ROW trainees, $p < 0.05$). No significant differences were observed between US trainees and ROW in burnout, stress, or feeling more callous towards others.

Trainees globally reported their perceptions of their programs and rheumatology as positive: 66% (198) reported feeling supported by their training program, 72% (212) felt positive about their career choice, and 65% (190) felt positive about the response of the rheumatology community.

Conclusion: We previously reported several negative impacts of the COVID-19 pandemic on rheumatology education and clinical training. The pandemic has also negatively affected rheumatology trainees' physical health, stress levels, and burnout, which should be recognized when supporting trainees post-pandemic. A higher proportion of ROW trainees reported a negative impact of the pandemic on their physical health compared to US trainees, perhaps due to COVID hotspot areas or differences in redeployment requirements. Our survey demonstrates that a large number of trainees feel burned out (52%), compared to 28% of trainees reported feeling burned out in a survey performed before the pandemic[1]. Reassuringly, the majority feel supported by their training program and their perceptions of their choice of career remain positive.

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gen, 2, Pfizer, 2; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **P. Robinson**, Abbvie, 1, Novartis, 1, 5, 6, Atom Biosciences, 1, Janssen, 5, 6, Eli Lilly, 1, 2, 6, Gilead, 6, UCB Pharma, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 6; **E. Sirotich**, None; **P. Sufka**, Wiley Publishing, 6; **J. Yazdany**, Astra Zeneca, 2, 5, Pfizer, 2, 6, Gilead, 5, BMS Foundation, 5; **J. Liew**, Pfizer, 5; **R. Grainger**, Pfizer New Zealand, 6, 12, support to travel to conference, Jansenn Autralia, 6, 12, travel to symposia, AbbVie New Zealand, 6, Cornerstones, 6, novartis, 1; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2; **A. Jayatilleke**, None.

Abstract Number: 0486

A Practical Approach to Competency-based Evaluations and Milestone Mapping for Adult Rheumatology Fellowship Programs

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SESSION INFORMATION
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Background/Purpose: The American College of Rheumatology has developed 14 Entrustable Professional Activities (EPAs) for Adult Rheumatology that define broad clinical competency goals for fellowship. At the same time, the Accreditation Council for Graduate Medical Education (ACGME) requires programs to assess and report fellow progress toward a set of comprehensive training Milestones. While these tools provide a helpful framework for guiding and monitoring fellow progress, they are either too general (EPAs) or too comprehensive (Milestones) to serve as ready-made assessment tools for individual clinical rotations. Here, we describe a strategy for creating practical rotation-specific assessment tools that reflect EPAs and produce useful Milestone data.

Methods: In academic year (AY) 18/19, clinician-educator faculty/senior fellows and site directors from each of 3 training hospitals at a large, urban, university-based adult rheumatology program were asked to craft evaluation objectives for continuity clinic and inpatient consult rotations. Objectives were 1) EPA-representing, 2) task-oriented, 3) readily observable, and 4) frequently or uniquely observed during the rotation. Teams also mapped each objective to Internal Medicine Subspecialty Milestones. A Milestone was mapped to an objective if it met 2 or more of the following: 1) it covered all/most task activities; 2) was critical to task; 3) was unique to task; or 4) was not better represented by another objective (for any rotation). Objectives and mapping were reviewed and approved by the Program Evaluation Committee. Using these objectives, fellows were evaluated every 1 – 2 months using a 5-point competency-based scale. Evaluations (scores + comments) were made available to fellows in real time. For semi-annual reviews, each Milestone level was calculated from the average of scores of all mapped objectives and verified/adjusted by the Clinical Competency Committee (CCC). Fellow perception of evaluation process was assessed via anonymous internal and ACGME surveys of our program.

Results: We developed 9 – 13 objectives for each of six core clinical rotations (Table 1) and mapped them to Milestones. The new evaluation objectives and mapping algorithm were introduced in AY 19/20. Based on internal anonymous surveys, fellow satisfaction with the evaluation process increased from 4.0±0.8 out of 5.0 to 4.8±0.4 out of 5.0. On anonymous ACGME surveys, fellow perception of evaluation processes in general rose from 78.6% compliant in AY 18/19 to 95.8% compliant in AY 20/21. Analysis of Milestone maps and Milestone performance trends over

Table 1. Example of EPA-reflecting, task-oriented evaluation objectives for a continuity clinic rotation (county hospital). For select objectives, evaluator prompts are shown in italics. Dates in parentheses indicate expected time to achieve competence

Accurately diagnose a patient presenting with systemic inflammatory disease. *In this context, consider the fellow's ability to gather and interpret relevant primary medical data; acquire an accurate and appropriately detailed history; perform an appropriately detailed physical exam; demonstrate effective diagnostic reasoning (e.g., framing of problem, assembling an appropriately broad and prioritized differential diagnosis, avoidance of diagnostic pitfalls); and recommend/order appropriate diagnostic tests. (12 months)*
Accurately diagnose a patient presenting with inflammatory arthritis. *(prompt not shown)*
Manage the care of a patient with SLE or other systemic inflammatory disease. *In this context, consider the fellow's ability to gather and interpret relevant primary medical data; effectively acquire an interim history and synthesize information; perform an appropriately detailed physical examination; recognize and address co-morbidities; choose appropriate diagnostic and monitoring tests; formulate an appropriate and evidence-based therapeutic plan; effectively communicate assessment and recommendations to patient; address patient's concerns; effectively educate patient/family; recognize and address barriers to therapeutic relationship; ensure appropriate follow-up; and communicate effectively with primary care provider and relevant specialists. (18 months)*
Manage the care of a patient with rheumatoid arthritis or chronic inflammatory arthritis syndrome. *(prompt not shown)*
Perform a procedure (e.g., arthrocentesis, or injection of tendon, joint, or bursa) and analyze synovial/bursal fluid. *(prompt not shown)*
Prescribe immunosuppressive therapy/chemotherapy for a patient with chronic autoimmune/inflammatory disease. *(prompt not shown)*
Effectively utilize interpreters and cultural liaisons to perform a clinic visit. *(prompt not shown)*
For an individual patient, identify and facilitate solutions for financial, social, cultural, or physical barriers to receiving rheumatology care. *(prompt not shown)*
Perform pre- and post-visit (non-visit) components of an outpatient consultation. *(prompt not shown)*
Accurately diagnose and treat a patient with regional/focal musculoskeletal pain. *(prompt not shown)*
Effectively manage rheumatology care of continuity clinic patients while not in clinic. *In this context, consider the fellow's ability to assume professional responsibility for all assigned patients; arrange for timely and appropriate patient follow-up; develop and utilize a system for obtaining, reviewing, and responding to test results between visits; communicate with patients, staff, and other care providers in a timely and effective fashion when not in clinic; appropriately sign out care of continuity clinic patients when transitioning off-duty (e.g., weekends, leave) (6 months); appropriately document and bill for prolonged services and telephone encounters before/after visits (24 months).*
Practice preventive medicine in a patient with chronic rheumatic disease. *(prompt not shown)*
Improve clinical performance based on feedback, evaluation, and practice data. *(prompt not shown)*

time identified some gaps in overall assessment and areas of curricular strength/weakness (not shown). We are now mapping objectives to the new ACGME Milestones for adult rheumatology (Table 2).

Conclusion: We describe a practical approach for developing rotation-specific, task-oriented evaluation objectives that can generate Milestone data useful for tracking progress of individual trainees as well as curriculum effectiveness. In addition, fellow satisfaction with the evaluation process appeared to improve. We believe our approach is highly adaptable and could be useful to a wide range of training programs.

Table 2. Proposed Rheumatology Milestone mapping of evaluation objectives from Table 1 (continuity clinic, county hospital). Note that some Milestones did not meet mapping criteria with any objective. PC = patient care; MK = medical knowledge; SBP = systems-based practice; PBLI = practice-based learning and improvement; P = professionalism; ICS = interpersonal and communication skills

	Gathers an Essential and Accurate Patient History	Physical Examination	Comprehensive Management Plan Development	Therapeutics, Including Immunomodulatory Agents	Procedures	Provides Consultative Care	Possesses Clinical Knowledge	Knowledge of Diagnostic Testing	Scholarly Activity	Patient Safety and Quality Improvement (QI)	System Navigation for Patient-Centered Care	Physician Role in Health Care Systems	Evidence-Based and Informed Practice	Commitment to Reflective Practice and Personal Growth	Professional Behavior	Ethical Principles	Accountability/Conscientiousness	Self-Awareness and Help-Seeking	Patient- and Family-Centered Communication	Interprofessional and Team Communication	Patient-Centered Interprofessional Communication within Health Care Systems
	PC1	PC2	PC3	PC4	PC5	PC6	MK1	MK2	MK3	SBP1	SBP2	SBP3	PBLI1	PBL2	P1	P2	P3	P4	ICS1	ICS2	ICS3
1. Accurately diagnose a patient presenting with systemic inflammatory disease.	X	X					X	X													
2. Accurately diagnose a patient presenting with inflammatory arthritis.	X	X					X	X													
3. Manage the care of a patient with SLE or other systemic inflammatory disease.			X								X		X								
4. Manage the care of a patient with rheumatoid arthritis or chronic inflammatory arthritis syndrome.			X																		
5. Perform a procedure (e.g., arthrocentesis, or injection of tendon, joint, or bursa) and analyze synovial/bursal fluid.					X																
6. Prescribe immunosuppressive therapy/chemotherapy for a patient with chronic autoimmune/inflammatory disease.				X						X			X								
7. Effectively utilize interpreters and cultural liaisons to perform a clinic visit.																			X		
8. For an individual patient, identify and facilitate solutions for financial, social, cultural, or physical barriers to receiving rheumatology care.											X	X				X					
9. Perform pre- and post-visit (non-visit) components of an outpatient consultation.						X						X									X
10. Accurately diagnose and treat a patient with regional/focal musculoskeletal pain.		X		X			X	X					X								
11. Effectively manage rheumatology care of continuity clinic patients while not in clinic.											X				X	X	X				
12. Practice preventive medicine in a patient with chronic rheumatic disease.										X											
13. Improve clinical performance based on feedback, evaluation, and practice data.														X				X			

Disclosure: G. hughes, None; **S. Chung**, None; **E. Wahl**, None; **J. Thomason**, None; **B. Ng**, None; **I. Sacksen**, None; **A. Bays**, Genentech, 5, Abbvie, 5.

Abstract Number: 0487

A Needs Assessment for the Transition into a Rheumatology Program Director Role: Survey of Current and Former Rheumatology Program Directors

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Professional Education (0484–0487)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: Clinical educators taking on the new role as program director (PD) must have the time and resources to learn about all the processes (e.g., accreditation, assessment) that are essential to the effective management of a fellowship training program. Lack of preparation can lead to inadequate performance and dissatisfaction with the role. We conducted a needs assessment of current and former rheumatology PDs to determine the type of

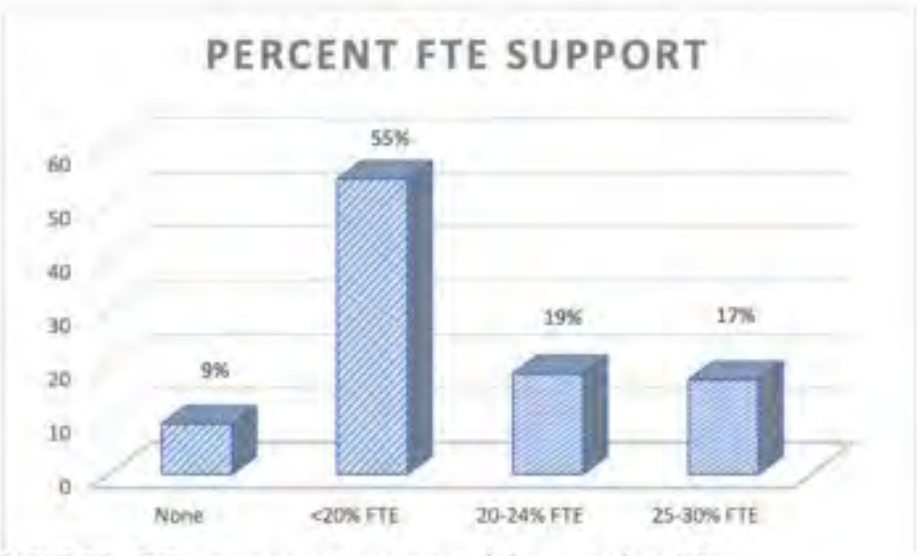

FIGURE 1. FTE support among surveyed rheumatology PDs.

support needed to become an effective rheumatology PD. The survey asked variables that might affect their transition to a leadership role (such as previous experience, fiscal and mentor support), the enthusiasm for rheumatology-specific PD mentorship, overall satisfaction with the transition, and specific resources that would have eased the transition.

Methods: An electronic survey was emailed to 186 current and former rheumatology program directors currently on the American College of Rheumatology's Committee on Training and Workforce listserv. Survey question types included single response, multi-select and free response.

Results: Ninety (48.4%) current or former rheumatology PDs responded to the survey. Of the 90 responses, 86 (46.2%) were completed beyond the demographics questions. Respondents to the survey were evenly split between

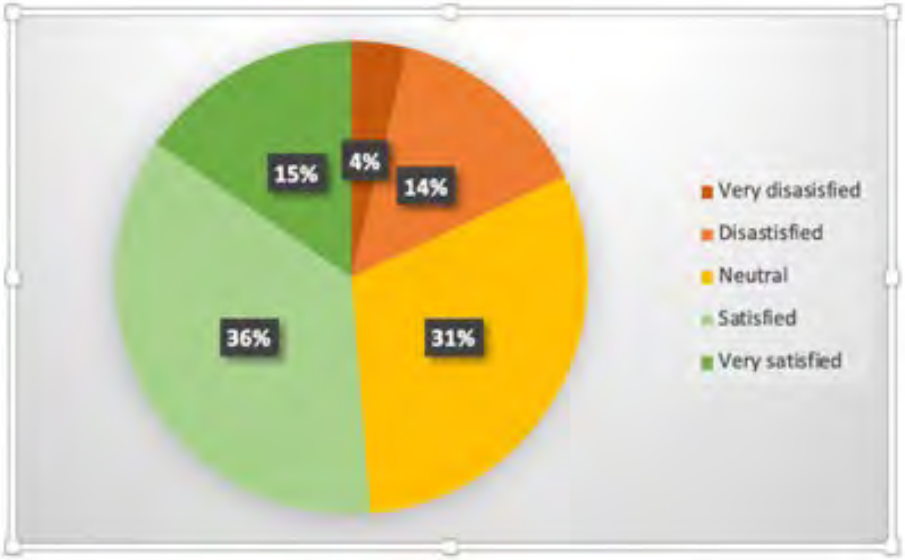

Figure 2.
Satisfaction with process of transitioning to PD role (78 total respondents)

newer and more experienced PDs; 50% of respondents had been a rheumatology PD for 5 years or less in the rheumatology PD role whereas 50% of respondents had been in this role for more than 5 years. Full-time equivalent (FTE) support for PDs varied considerably, with the majority of PDs (64%) receiving less than 20% FTE for their role as program director. Eight (9 %) respondents did not receive any support for their role as PD. Of those who completed a question on their satisfaction with the transition process, only 12 (15.7%) respondents were very satisfied with their transition to becoming a PD whereas 49% (38 out of 78) where neutral, dissatisfied or very dissatisfied with the transition (Fig. 1). There was overwhelming support (88%) for a transition mentorship program for new PDs. Program directors were most interested in a curriculum that included a practical discussion of how to run a program (86.9%), developing core curriculum (46.5%) and assessment of fellows (46.5%).

Conclusion: Based on our survey of PDs, we identified several areas suitable for innovation. A mentor program for new PDs was desired by most, indicating the need for additional support and training during the PD transition period. Furthermore, FTE support was found to be less than that outlined in the Accreditation Council for Graduate Medical Education (ACGME) common program requirements (at least 20%) for the majority of the rheumatology PDs. These results should inform key stakeholders on the need for more support for PDs to include mentorship, educational content and fiscal support.

Disclosure: R. Wolfe, None; **F. Koumpouras**, GSK, 1, 2, 5, BMS, 5, Astra Zeneca, 1, Aurinia, 5, 6, UCB, 5, ABBvie, 5, Janssen, 5; **A. Dua**, Abbvie, 1, 2, 6, Novartis, 2, Chemocentryx, 2; **P. Seo**, Amgen, 1, Janssen, 1; **S. Helfgott**, None; **B. Jonas**, None.

Abstract Number: 0488

Efficacy and Safety of Brepocitinib (Tyrosine Kinase 2/Janus Kinase 1 Inhibitor) for the Treatment of Active Psoriatic Arthritis: Results from a Phase 2b Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment I: Emerging Therapies (0488–0491)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: Brepocitinib is a small-molecule tyrosine kinase 2/Janus kinase 1 inhibitor that has shown promising results in an oral formulation for plaque psoriasis and alopecia areata and is under investigation for PsA.

Methods: This Phase 2b, randomized placebo (PBO)-controlled trial compared the efficacy and safety of once-daily (QD) oral doses of brepocitinib (10, 30, and 60 mg) vs PBO in patients (pts) with active PsA (NCT03963401). Eligible pts were aged 18–75, met CASPAR (ClASsification criteria for Psoriatic ARthritis), and had active PsA despite treatment or intolerance to NSAIDs/DMARDs; stable doses of conventional synthetic DMARDs were allowed, and up to 30% of pts with prior use of one TNF inhibitor were allowed. Pts were randomized (2:2:1:2) to receive brepocitinib 60

Table 1. ACR20/50/70, MDA, and PASI75/90 response rates at Week 16 and Week 52

	Week 16 (initial dose)				Week 52	
	PBO (N=67)	Brepocitinib 10 mg QD (N=31)	Brepocitinib 30 mg QD (N=60)	Brepocitinib 60 mg QD (N=59)[a]	Brepocitinib 30 mg QD (N=108)	Brepocitinib 60 mg QD (N=110)
Primary endpoint (at Week 16)						
ACR20 response, % (n)	43.3 (29)	64.5 (20)	66.7 (40)*,**	74.6 (44)*,**	67.6 (73)	60.9 (67)
Selected binary secondary endpoints						
ACR50 response, % (n)	10.4 (7)	32.3 (10)*	48.3 (29)*,**	44.1 (26)*,**	54.6 (59)	44.6 (49)
ACR70 response, % (n)	0.7% (0)[b]	9.7 (3)*	26.7 (16)*	23.7 (14)*	41.7 (45)	36.4 (40)
MDA response, % (n)	3.0 (2)	19.4 (6)*	35.0 (21)*	35.6 (21)*	46.3 (50)	42.7 (47)
Pts evaluable for PASI, n[c]	**41**	**21**	**39**	**39**	**67**	**74**
PASI75 response, % (n)	24.4 (10)	57.1 (12)*	59.0 (23)*,**	69.2 (27)*,**	64.2 (43)	60.8 (45)
PASI90 response, % (n)	12.2 (5)	33.3 (7)*	33.3 (13)*,**	53.9 (21)*,**	53.7 (36)	46.0 (34)

Missing data were treated as non-responses.

[a]One pt was excluded because they missed their Week 16 visit due to COVID-19.

[b]Continuity correction was applied for an observed 0 response rate.

[c]Analysis population of PASI endpoints consisted of a subgroup of pts with baseline BSA ≥3% and PASI >0 (65% of the total population).

*The 1-sided raw p-value for the treatment comparison vs PBO was <0.05.

**The treatment group showed statistically significant treatment effect vs PBO under the pre-specified study testing procedure.

Per pre-specified study testing procedure, the primary endpoint (ACR20 at Week 16) was tested based on the Dunnett's method, with an adjusted one-sided p-value <0.05 defined as a statistically significant treatment effect vs PBO. Other endpoints of interest were tested in the order of PASI75 → ACR50 → PASI90 → PASI100 → HAQ-DI hierarchically under the significance level of 5% (1-sided) only if a dose group was tested significantly for the primary endpoint.

HAQ-DI, HAQ – Disability Index; MDA, minimal disease activity; PASI75/90/100, Psoriasis Area and Severity Index 75/90/100; PBO, placebo; pt, patient; QD, once daily.

mg QD, 30 mg QD, 10 mg QD, or PBO for 16 weeks, advancing to brepocitinib 30 or 60 mg QD from Week 16 to 52. Primary endpoint: pts meeting ACR20 response at Week 16. Selected secondary, exploratory, and safety endpoints are reported.

Results: A total of 218 pts were randomized and treated. Demographics and baseline disease characteristics were generally similar across groups, and the majority of pts (93.1%) completed the Week 16 visit. At Week 16, significantly higher proportions of pts in the brepocitinib 30 and 60 mg QD groups achieved an ACR20 response vs PBO (Table 1). Brepocitinib 30 and 60 mg QD groups achieved significantly higher response rates vs PBO, starting as early as Week 4, and response rates continued to increase to Week 16 for ACR20/50/70, Minimal Disease Activity, and Pso-

Table 2. CFB in selected continuous secondary endpoints at Week 16

	Week 16 (initial dose)			
Endpoint, CFB, LS mean (95% CI)	**PBO (N=62)**	**Brepocitinib 10 mg QD (N=27)**	**Brepocitinib 30 mg QD (N=57)**	**Brepocitinib 60 mg QD (N=57)**
PASDAS	-0.90 (-1.18, -0.63)	-1.86 (-2.27, -1.45)*	-2.20 (-2.49, -1.91)*	-2.35 (-2.64, -2.06)*
HAQ-DI	-0.18 (-0.28, -0.08)	-0.32 (-0.47, -0.17)	-0.50 (-0.61, -0.39)*	-0.50 (-0.61, -0.40)*
SF-36 PCS	1.73 (0.06, 3.40)	5.04 (2.56, 7.52)*	6.76 (4.99, 8.53)*	6.57 (4.80, 8.34)*
FACIT-F	3.84 (2.02, 5.65)	4.60 (1.89, 7.31)	7.13 (5.23, 9.04)*	5.89 (3.99, 7.79)

N values may be less than stated in some categories due to missing data or disease characteristics at baseline.

Baseline was defined as the measurements at Day 1. Data from the screening period was used if Day 1 data were missing.

MMRM contained fixed factors of treatment, visit (discrete variable, up to Week 16), treatment by visit interaction, and baseline value. An unstructured variance–covariance matrix was fitted. If there was a convergence issue with an unstructured matrix, the model was fit with a heterogeneous compound symmetry matrix.

*Statistically significant from PBO using MMRM, 1-sided raw p-value <0.05.

CFB, change from baseline; CI, confidence interval; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI, HAQ – Disability Index; LS, least squares; MMRM, mixed model for repeated measures; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; QD, once daily; SF-36 PCS, Short Form-36 Health Survey Physical Component Summary.

Table 3. Treatment-emergent AEs and AEs of special interest up to and after Week 16 (up to Week 52)

Number (%) of pts	Up to Week 16 (initial dose)					After Week 16	
	PBO (n=67)	Brepocitinib				Brepocitinib	
		10 mg QD (n=31)	30 mg QD (n=60)	60 mg QD (n=60)	Total (n=151)	30 mg QD (n=108)	60 mg QD (n=110)
Any AE	32 (47.8)	14 (45.2)	33 (55.0)	40 (66.7)	87 (57.6)	50 (46.3)	55 (50.0)
SAE	1 (1.5)	0 (0.0)	3 (5.0)	1 (1.7)	4 (2.6)	7 (6.5)	1 (0.9)
AE leading to discontinuation of study drug	3 (4.5)	0 (0.0)	2 (3.3)	3 (5.0)	5 (3.3)	5 (4.6)	10 (9.1)
Deaths	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Infections and infestations (SOC)	16 (23.9)	9 (29.0)	21 (33.0)	21 (35.0)	51 (33.8)	19 (17.6)	27 (24.6)
Serious infections	0 (0.0)	0 (0.0)	2 (3.3)	0 (0.0)	2 (1.3)	3 (2.8)	1 (0.9)
Adjudicated opportunistic infections	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.9)	1 (0.9)
Herpes zoster/varicella	0 (0.0)	1 (3.2)	1 (1.7)	0 (0.0)	2 (1.3)	1 (0.9)	1 (0.9)
Active tuberculosis	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
COVID-19 infections	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	6 (5.6)	8 (7.3)
Neoplasms, benign, malignant, and unspecified (SOC)	0 (0.0)	0 (0.0)	0 (0.0)	2 (3.3)	2 (1.3)	1 (0.9)	0 (0.0)
Embolic and thrombotic events	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

Both adjudicated opportunistic infections were herpes zoster

AE, adverse event; PBO, placebo; pt, patient; QD, once daily; SAE, serious adverse event; SOC, system organ class.

riasis Activity and Severity Index 75/90. Responses were maintained to Week 52 (Table 1). Brepocitinib 30 and 60 mg QD were associated with significant improvements in disease activity and quality of life outcomes (e.g. fatigue, functioning) at Week 16 vs PBO (Table 2). Improvements in dactylitis and Spondyloarthritis Research Consortium of Canada enthesitis resolution were observed at Week 16 in the brepocitinib 60 mg group vs PBO; resolution continued to improve or remain steady through Week 52 in the 30 mg and 60 mg groups, respectively. In the 16-week treatment period, there were more pts with adverse events (AEs) in the brepocitinib 30 mg (n=33) and 60 mg (n=40) QD groups vs PBO (n=32). Most AEs were mild in severity (165/250 [66%]) at Week 16. Key safety findings are shown in Table 3. There were 17 serious AEs (SAEs) in 12 pts during this study, including 7 SAEs in 6 pts through Week 16. The overall safety profile over 52 weeks was consistent with approved Janus kinase inhibitors, including cases of serious herpes zoster infections and changes in select lab parameters. There were no major adverse cardiovascular events, venous thromboembolic events, or deaths.

Conclusion: Brepocitinib demonstrated superior efficacy vs PBO across numerous PsA disease domains in pts with active PsA at Week 16, with improvements in more refractory domains continuing over 52 weeks. There were more AEs in the brepocitinib groups vs PBO over 16 weeks. The overall safety of brepocitinib was consistent with other approved Janus kinase inhibitors.

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Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **P. Silwinska-Stanczyk**, Pfizer Inc, 2; **M. Miakisz**, None; **A. Ostor**, AbbVie, 1, 2, 12, Bristol Myers Squibb, 1, 2, 12, Roche, 1, 2, 12, Janssen, 1, 2, 12, Eli Lilly, 1, 2, 12, Novartis, 1, 2, 12, Pifzer Inc, 1, 2, 12, UCB, 1, 2, 12, Gilead, 1, 2, 12, Paradigm, 1, 2, 12; **E. Peeva**, Pfizer Inc, 3, 11; **M. Vincent**, Pfizer Inc, 3, 11; **V. Sikirica**, Pfizer Inc, 3, 11; **R. Winnette**, Pfizer Inc, 3, 11; **R. Qiu**, Pfizer Inc, 3, 11; **G. Li**, Pfizer Inc, 3, Alexion Pharmaceuticals, 3; **G. Feng**, Pfizer Inc, 3, 11; **J. Beebe**, Pfizer Inc, 3, 11; **D. Martin**, Pfizer Inc, 3, 11.

Abstract Number: 0489

CC-99677: A Novel, Oral, Selective MK2 Inhibitor with Sustainable Multi-Cytokine Inhibition for the Treatment of Ankylosing Spondylitis and Other Inflammatory Diseases

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment I: Emerging Therapies (0488–0491)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Inhibitors of p38 are associated with tachyphylaxis in patients with RA and other inflammatory diseases, where early reduction in ex vivo production of cytokines, such as TNF-α, or endogenous inflammatory markers, such as CRP, did not persist despite continued treatment. Thus, p38 inhibitors have not advanced in clinical development. Targets downstream of p38 have been identified to avoid these limitations. The mitogen-activated protein kinase-activated protein kinase-2 (MK2) pathway is activated downstream of p38, and activation of MK2 increases the stability and translation of mRNA of proinflammatory factors (e.g., TNF-α, IL-17, IL-6). CC-99677 is a novel, irreversible, covalent MK2 inhibitor. Here, we report data from the first-in-human multiple ascending-dose study to characterize the safety, pharmacokinetics (PK), and pharmacodynamics (PD) in healthy volunteers dosed with CC-99677.

Methods: A phase 1, randomized, double-blind, placebo-controlled study (NCT03554993) was performed involving 37 healthy adult volunteers who were enrolled into 5 dose-level cohorts ranging from 10 to 150 mg of CC-99677 or placebo with 3:1 randomization. Participants were dosed daily for 14 days. The primary outcome of this study was safety and tolerability of multiple daily doses of CC-99677. Secondary and exploratory outcomes included assessment of the plasma CC-99677 PK profile and evaluation of the PD effects of CC-99677 as measured by MK2 target occupancy and ex vivo inhibition of inflammatory cytokines in participant whole blood.

Results: Multiple doses of CC-99677 up to 150 mg for 14 days were safe and well tolerated by the healthy adult subjects in this study. The multiple-dose PK characteristics of CC-99677 showed a linear, dose-proportional increase in exposure from 10 to 150 mg with a once-daily dosing schedule over 14 days. CC-99677 peak concentration (C_{max}), time to reach C_{max} (T_{max}), and area under the curve from time 0 to the time of last measurement (AUC_{0-t}) were similar on day 1 and day 14 (last day of dosing) across the dose range of 10 to 150 mg, suggesting limited or no accumulation of CC-99677 with repeat once-daily dosing. There was a cumulative increase in target engagement with once-daily administration of CC-99677 for 14 days, reaching steady-state levels by day 8. Daily treatment resulted in dose-dependent increases in target engagement between 10 and 120 mg and plateauing at the 120- and 150-mg dose levels. Sustained reduction during the dosing period in TNF-α and other cytokine and chemokine production was observed in ex vivo stimulated blood from subjects who received once-daily doses >10 mg CC-99677 for 14 days.

Conclusion: Administration of CC-99677 was safe and well tolerated, resulted in linear PK, and demonstrated sustained reduction of ex vivo whole blood TNF-α, IL-6, and chemokine synthesis. The lack of tachyphylaxis in human cells exposed to CC-99677, compared with previous disappointing results targeting the p38 axis, is encouraging. Thus, CC-99677 inhibition of MK2 is a promising approach for the treatment of inflammatory diseases. Phase 2 studies of CC-99677 in patients with spondyloarthritis are planned.

Disclosure: K. Mensah, Bristol Myers Squibb, 3, 11; **R. Gaur**, Bristol Myers Squibb, 3, 11; **J. Connarn**, Bristol Myers Squibb, 3, 11; **M. Thomas**, Bristol Myers Squibb, 3, 11; **L. Liu**, Bristol Myers Squibb, 3, 11; **S. Mair**, Quotient Sciences, 3, 11; **F. Ramírez-Valle**, Bristol Myers Squibb, 3, 11; **M. Palmisano**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0490

Biomarker Changes with Selective Tyrosine Kinase 2 Inhibitor, Deucravacitinib, in PsA: Effects on Disease Markers and Tyrosine Kinase 2− versus Janus Kinase 1/2/3−mediated Pathways

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment I: Emerging Therapies (0488–0491)

Session Type: Abstract Session

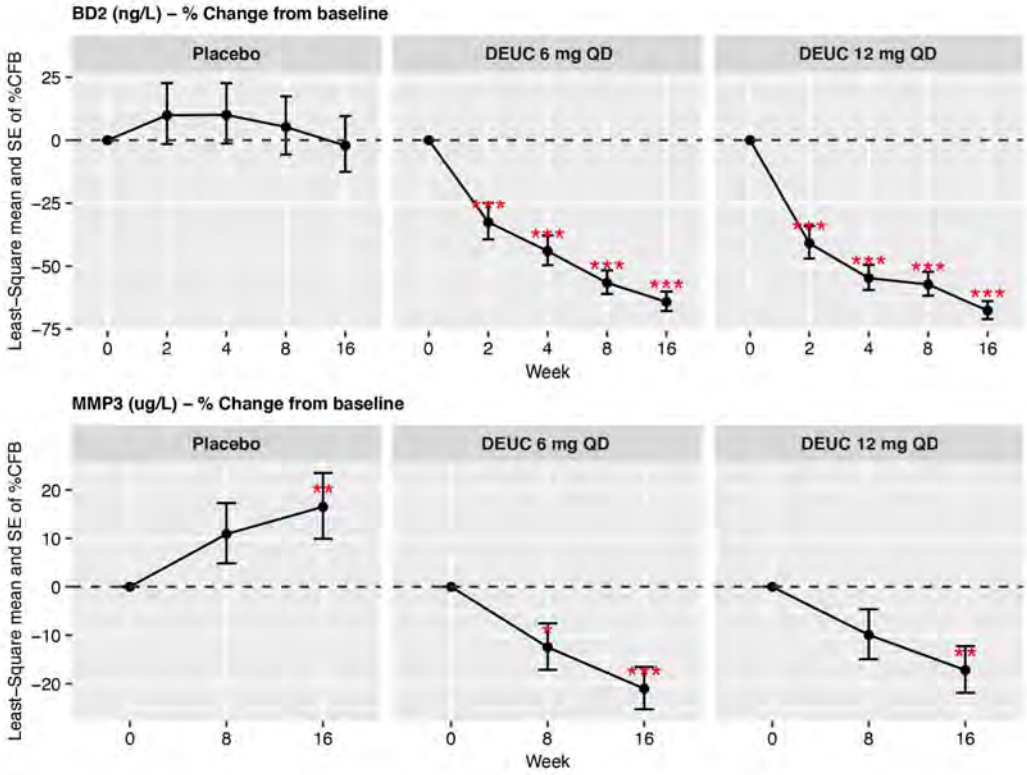
Session Time: 2:00PM–3:00PM

Background/Purpose: Deucravacitinib is a novel, oral, selective tyrosine kinase 2 (TYK2) inhibitor with a unique mechanism of action that has demonstrated efficacy in patients (pts) with psoriasis and PsA. TYK2 selectively mediates cytokine signaling restricted to specific inflammatory pathways (eg, IL-23, IL-12, and Type I interferons), whereas Janus kinase (JAK) 1/2/3 signaling is involved in broader immune responses, as well as in hematopoietic pathways and in lipid metabolism. Use of JAK1/2/3 inhibitors is associated with signature changes in laboratory variables in the blood. The current study assessed the effects of deucravacitinib on biomarkers of TYK2- vs JAK1/2/3–mediated pathways, as well as of joint disease, in patients with PsA.

Methods: A double-blind Phase 2 trial (NCT03881059) enrolled 203 pts with PsA randomized 1:1:1 to deucravacitinib 6 mg once daily (QD), 12 mg QD, or placebo (PBO).[1] Levels of biomarkers of interest and lymphocyte subsets in the blood were measured by immunoassays, flow cytometry, and standard methods from baseline (BL) through Week 16.

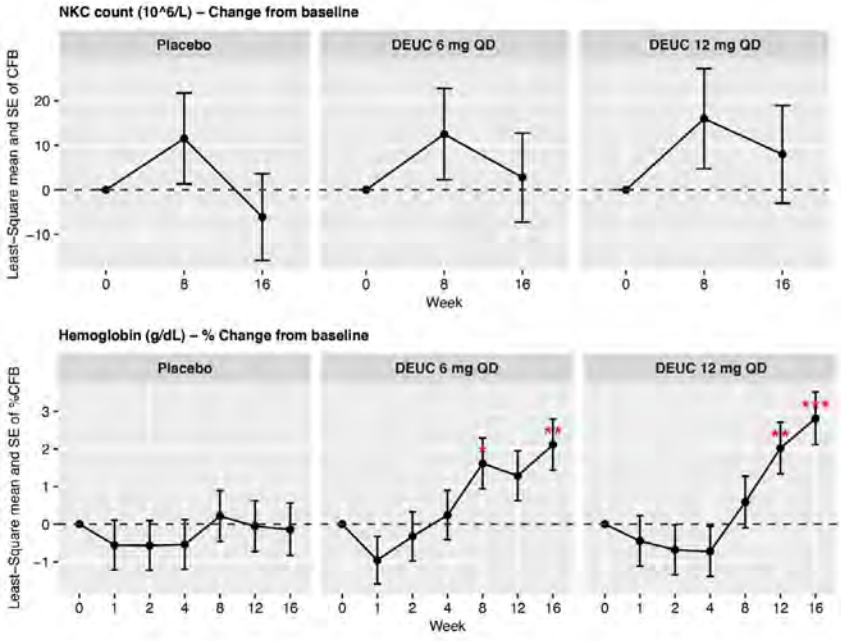
Results: BL serum concentrations of IL-23−driven IL-17A and IL-17−induced β-defensin 2 and IL-19 were elevated and significantly correlated with severity of skin involvement by Psoriasis Area and Severity Index scores ($\rho \geq 0.4$; $P < 0.0001$). Both deucravacitinib doses, but not PBO, reduced IL-17A, β-defensin 2 (Figure 1), and IL-19 over time. Serum levels of IFN-I−driven chemokine ligand 9 (CXCL9) and CXCL10, and Type I/II IFN-inducible proteins, either remained stable or decreased after deucravacitinib treatment vs PBO. TNF-α levels remained stable in deucravacitinib-treated pts but increased in the PBO group. At BL, the neoepitope marker of Type IV collagen degradation mediated by MMPs (C4M) was positively associated with Psoriatic Arthritis Disease Activity Score (PASDAS; $\rho=0.29$; $P < 0.0001$). BL MMP3 concentrations showed modest and positive correlations with swollen joint count ($\rho=0.24$; $P < 0.001$), PASDAS ($\rho=0.21$; $P < 0.01$), and Disease Activity Index in Psoriatic Arthritis ($\rho=0.19$; $P < 0.01$). MMP3 (Figure 1) and C4M were suppressed in deucravacitinib- but not PBO-treated pts. NK cell counts remained stable and small increases in hemoglobin were observed after treatment with deucravacitinib (Figure 2). There were no clinically meaningful changes in mean levels of serum cholesterol, creatinine, neutrophils, and platelets over time with deucravacitinib treatment.

Figure 1. Effects on levels of BD2 and MMP3 by deucravacitinib and placebo



*P<0.05; **P<0.01; ***P<0.001. BD2, β-defensin 2. CFB, change from baseline; DEUC, deucravacitinib.

Figure 2. NK cell counts and hemoglobin profiles in deucravacitinib- and placebo-treated patients



*P<0.05; **P<0.01; ***P<0.001. CFB, change from baseline; DEUC, deucravacitinib.

Conclusion: Deucravacitinib suppressed biomarkers of IL-23/IL-17 and IFN-I pathways concomitant with clinical symptom improvements in deucravacitinib-treated PsA pts. Joint damage is associated with an increase in MMP3, and suppression of C4M and MMP3 by deucravacitinib suggested an improvement in extracellular matrix turnover upon TYK2 pathway inhibition. Differentiation of deucravacitinib from JAK1/2/3 inhibitors was evidenced by the lack of adverse effects of deucravacitinib on hematologic and serum chemistry variables that are known to change with JAK1/2/3 inhibitors.

Reference: 1. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

Disclosure: O. FitzGerald, Novartis, 5, 6, UCB, 5, 6, Pfizer, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Lilly, 5, 6, Biogen, 6, Eli Lilly, 5, 6; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **L. Gao**, Bristol Myers Squibb, 3, 11; **S. Hu**, Bristol Myers Squibb, 3, 11; **M. Nowak**, Bristol Myers Squibb, 3, 11; **S. Banerjee**, Bristol Myers Squibb, 3, 11; **I. Catlett**, Bristol Myers Squibb, 3, 11; **X. Guo**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0491

Bimekizumab Long-Term Safety and Efficacy in Patients with Ankylosing Spondylitis: Interim Results After 3 Years of Treatment in an Ongoing Phase 2b Study

Lianne Gensler[1], Atul Deodhar[2], Désirée van der Heijde[3], Denis Poddubnyy[4], Alan Kivitz[5], Maxime Dougados[6], Natasha de Peyrecave[7], Marga Oortgiesen[8], Thomas Vaux[9], Carmen Fleurinck[7] and Xenofon Baraliakos[10], [1]Department of Rheumatology, University of California San Francisco, San Francisco, CA, [2]Oregon Health & Science University, Portland, OR, [3]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands, [4]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [5]Altoona Center for Clinical Research, Duncansville, PA, [6]Université de Paris . Department of Rheumatology - Hôpital Cochin. Assistance Publique - Hôpitaux de Paris . INSERM (U1153): Clinical epidemiology and biostatistics, PRES Sorbonne Paris-Cité. Paris, France., Paris, France, [7]UCB Pharma, Brussels, Belgium, [8]UCB Pharma, Raleigh, NC, [9]UCB Pharma, Slough, United Kingdom, [10]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment I: Emerging Therapies (0488–0491)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits both interleukin (IL)-17F and IL-17A, has been demonstrated to be efficacious and well tolerated in patients (pts) with ankylosing spondylitis (AS) treated for up to 156 weeks (wks).[1–3] We report 3-year (yr) interim safety and efficacy of BKZ in pts with active AS from a 1-yr phase 2b study (BE AGILE; NCT02963506) and its ongoing 4-yr open-label extension (OLE; NCT03355573).

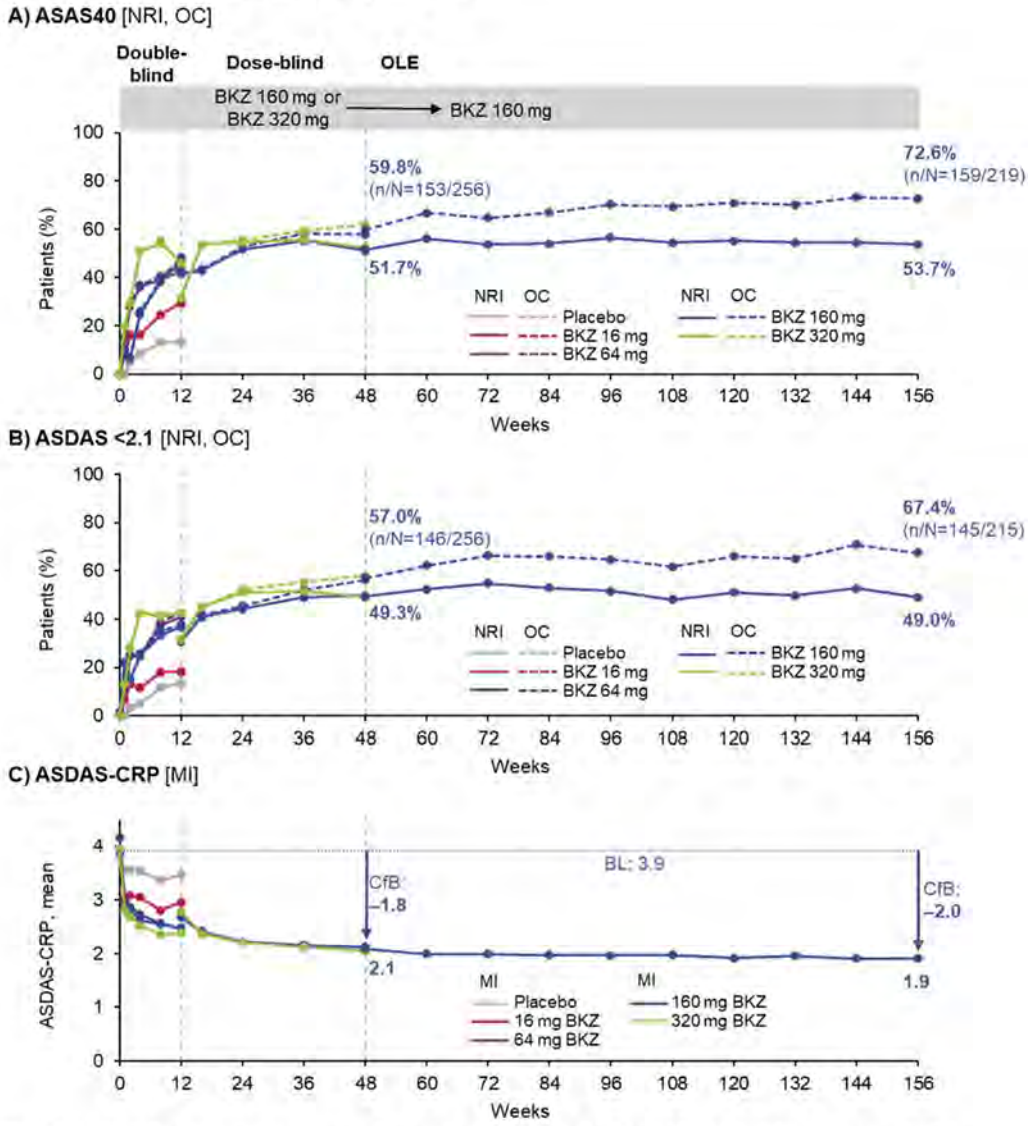
Table. Safety for exposure to bimekizumab in BE AGILE and the OLE

	BE AGILE Weeks 0–48			OLE Weeks 48–156
n (%) [EAIR/100 PY]	BKZ 160 mg [a] (n=149; 114.2 PY)	BKZ 320 mg [a] (n=150; 119.6 PY)	Total (N=303; 261.3 PY)	Total (N=255; 554.7 PY)
Any TEAE	103 (69.1) [168.7]	122 (81.3) [221.1]	235 (77.6) [186.2]	215 (84.3) [110.8]
Serious TEAEs	5 (3.4) [4.4]	6 (4.0) [5.1]	13 (4.3) [5.1]	31 (12.2) [5.9]
Study discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)	14 (5.5)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)	90 (35.3)
Deaths	1 (0.7)	0	1 (0.3)	1 (0.4)
Key TEAEs of special monitoring				
Serious infections	3 (2.0) [2.7]	1 (0.7) [0.8]	4 (1.3) [1.5]	6 (2.4) [1.1]
Candida infections [b]	10 (6.7) [9.1]	9 (6.0) [7.9]	19 (6.3) [7.5]	15 (5.9) [2.8]
Oral candidiasis	8 (5.4) [7.2]	8 (5.3) [7.0]	16 (5.3) [6.3]	13 (5.1) [2.4]
Neutropenia	1 (0.7) [0.9]	0	1 (0.3) [0.4]	1 (0.4) [0.2]
Adjudicated SIB	0	0	0	1 (0.4) [0.2]
Depression	0	0	1 (0.3) [0.4]	1 (0.4) [0.2]
IBD	1 (0.7) [0.9]	2 (1.3) [1.7]	4 (1.3) [1.5]	6 (2.4) [1.1]
Injection site reactions	0	3 (2.0) [2.6]	3 (1.0) [1.2]	1 (0.4) [0.2]
Anterior uveitis [c]	1 (0.7) [0.9]	1 (0.7) [0.8]	2 (0.7) [0.8]	4 (1.6) [0.7]

BE AGILE (N=303) and OLE (N=255) safety sets (patients who received ≥1 dose of BKZ during the relevant study period). All patients received BKZ 160 mg Q4W during the OLE (Wks 48–156) after completing BKZ 160 mg or 320 mg Q4W at Wk 48 in BE AGILE. [a] Data are shown for Wks 0–48 by dose-blind treatment group (i.e. patients received the indicated dose during the dose-blind period [Wks 12–48]); [b] All *Candida* infections were mild to moderate, none were systemic; [c] Anterior uveitis was not a TEAE of special monitoring in this study and is included as an extra-musculoskeletal manifestation. There was one death in BE AGILE (cardiac arrest) and one in the OLE (road traffic accident); neither was considered treatment-related. AS: ankylosing spondylitis; BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; OLE: open-label extension; PY: patient-years; Q4W: every 4 wks; SIB: suicidal ideation and behavior; TEAE: treatment-emergent adverse event; wk: week.

Methods: The BE AGILE study design has been described previously.[1] Following the 12-wk double-blind, placebo-controlled dose-ranging period, pts received BKZ 160 mg or 320 mg every 4 wks (Q4W) in the dose-blind period to Wk 48. Pts completing Wk 48 were eligible to enter the OLE where all pts received BKZ 160 mg Q4W. We report results following a total of 3 yrs of treatment. Treatment-emergent adverse events (TEAEs) are reported separately for BKZ exposure in BE AGILE and the OLE (safety sets). Efficacy outcomes are reported primarily for the dose-blind set.

Figure 1. Efficacy responses to Week 156

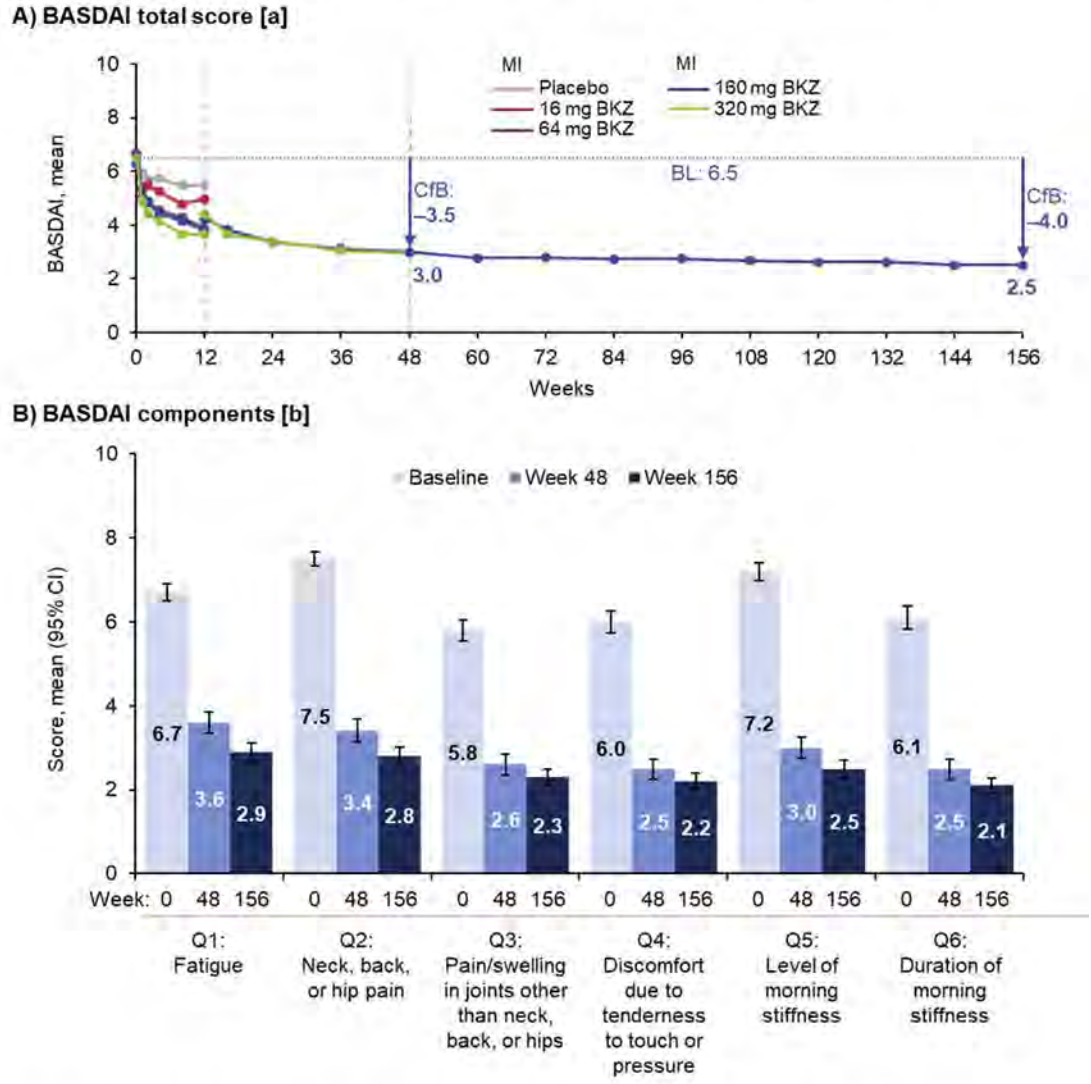


BE AGILE FAS (all randomized patients who received ≥1 dose of BKZ and had a valid measurement of the ASAS components at baseline; N=303) for Wks 0–12; dose-blind set (patients who started the dose-blind period at Wk 12 and received ≥1 dose of BKZ during the dose-blind period, including the dose at Wk 12; N=296) for Wks 12–156. Data (reported as NRI and OC, or MI) are shown for all timepoints from BE AGILE baseline to Wk 156; in the NRI analyses, patients who did not enter the OLE were considered non-responders from Wk 48 onwards. Patients randomized to placebo, BKZ 16 mg or BKZ 64 mg are shown through the dose-blind period following re-randomization at Wk 12 to either BKZ 160 mg or 320 mg. For Wks 48–156, data are shown for all patients entering the OLE; these patients received BKZ 160 mg after completing BKZ 160 mg or 320 mg in Wks 12–48 of BE AGILE. For ASDAS-CRP, baseline mean score (blue dotted line) is shown for the dose-blind set. ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; CRP: C-reactive protein; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; wk: week.

Analyses utilized non-responder imputation (NRI) and observed case (OC) methodology, or multiple imputation (MI); for NRI, pts who did not enter the OLE were considered non-responders from Wk 48 onwards.

Results: 296/303 (97.7%) pts randomized at BE AGILE study baseline (BL) entered the dose-blind period at Wk 12; 262/303 (86.5%) pts completed Wk 48 on BKZ. At Wk 48, 256/303 (84.5%) pts entered the OLE, of whom 255 received BKZ 160 mg Q4W; 224/303 (73.9%) pts completed Wk 156. For Wks 0–48 (and the OLE), exposure-adjusted

Figure 2. BASDAI scores from baseline to Week 156 (multiple imputation)



[a] BE AGILE FAS (N=303) for Wks 0–12 and dose-blind set (N=296) for Wks 12–156; [b] Dose-blind set (N=296) for all timepoints; data pooled across all treatment groups. All data reported for MI analyses. 256 patients had a BASDAI efficacy assessment on entering the OLE at Wk 48 and 217 patients had a BASDAI efficacy assessment at Wk 156. For BASDAI total score, patients randomized to placebo, BKZ 16 mg or BKZ 64 mg are shown through the dose-blind period following re-randomization at Wk 12 to either BKZ 160 mg or 320 mg. For Wks 48–156, data are shown for all patients entering the OLE; these patients received BKZ 160 mg after completing BKZ 160 mg or 320 mg in Wks 12–48 of BE AGILE. For BASDAI components, black bars show 95% CI. For BASDAI total score, baseline mean (blue dotted line) is shown for the dose-blind set. It is noted that, as components of the total BASDAI score, the BASDAI component scores are not independent secondary outcomes. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; BL: baseline; CfB: change from baseline; CI: confidence interval; MI: multiple imputation; OLE: open-label extension; wk: week.

incidence rates (EAIRs) per 100 pt-yrs were 186.2 (OLE: 110.8) for any TEAE, 5.1 (OLE: 5.9) for serious TEAEs, 1.5 (OLE: 1.1) for serious infections, and 7.5 (OLE: 2.8) for Candida infections (Table). Overall, EAIRs of TEAEs in the OLE remained stable or were lower than in Wks 0–48. The majority of Candida infections were oral candidiasis; all Candida infections were mild or moderate. EAIRs of inflammatory bowel disease, anterior uveitis, and injection site reactions were low across BE AGILE and the OLE (Table). In the NRI analyses, the percentage of pts achieving ASAS40 response or ASDAS < 2.1 was sustained from Wk 48 to Wk 156 (Figure 1A–B). Following substantial improvements from BL to Wk 48 in mean ASDAS-CRP (3.9 to 2.1) and BASDAI total score (6.5 to 3.0), responses were sustained

over a further 2 yrs of BKZ treatment to 1.9 and 2.5, respectively, at Wk 156 (Figure 1D & 2A). All BASDAI components demonstrated continued improvements in pt-reported fatigue, spinal pain, joint pain and swelling, discomfort due to tenderness to touch or pressure, and intensity and duration of morning stiffness (Figure 2B).

Conclusion: The long-term safety profile of BKZ in pts with AS was in line with previous observations, with no new safety signals identified after 3-yr BKZ exposure.[1–3] Efficacy was maintained and consistent over 3 yrs of BKZ treatment, highlighting the potential of dual inhibition of IL-17F and IL-17A in the treatment of AS.

References: 1. van der Heijde D. Ann Rheum Dis 2020;79:595–604; 2. Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10):1364;3. van der Heijde D. Ann Rheum Dis 2021;80 (suppl 1):332–3.

Disclosure: L. Gensler, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **A. Kivitz**, Pfizer, 2, 6, 11, 12, Sanofi, 2, 6, 11, 12, GlaxoSmithKline, 11, Gilead Sciences, Inc.,, 2, 11, Novartis, 2, 6, 12, AbbVie, 2, 6, 11, Boehringer Ingelheim, 2, Janssen, 2, Regeneron, 2, 6, 12, SUN Pharma Advanced Research, 2, Amgen, 11, Lilly, 6, Celgene, 6, 12, Flexion, 2, 6, Genzyme, 2, 6, 12, Merck, 6, 12, UCB, 6, Horizon, 6, 12; **M. Dougados**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **N. de Peyrecave**, UCB Pharma, 3, 11; **M. Oortgiesen**, UCB Pharma, 3; **T. Vaux**, UCB Pharma, 3; **C. Fleurinck**, UCB Pharma, 3; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2.

Abstract Number: 0492

Racial Differences in Glucocorticoid Use Among Medicaid Beneficiaries with Incident Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Healthcare Disparities in Rheumatology (0492–0495)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Glucocorticoids (GCs) are an integral part of systemic lupus erythematosus (SLE) treatment. Long-term use of GCs is associated with adverse effects. This study evaluated racial differences in GC use among individuals within the first year of SLE diagnosis.

Methods: Using Medicaid claims data (2000-2010) from 27 states, we identified individuals aged 18-65 years with incident SLE (≥3 SLE ICD-9 codes separated by ≥30 days with no SLE codes in the 24 months before the first code [index date]). We required 1 year of continuous enrollment following the index date and ≥1 prescription for oral or intravenous GCs during that year. We calculated the prednisone-equivalent glucocorticoid dose (GD) for each 30-day period for 1

Table 1. Baseline Characteristics of Medicaid Beneficiaries with Incident SLE and Glucocorticoid Use within the First Year Stratified by Trajectory

Characteristics	Overall Cohort at Baseline (N=6,323)	Overall Cohort (0- 6 Months)	Overall Cohort (6- 12 Months)	High Dose Trajectory (N=628)	Low Dose Trajectory (N=3593)	Uptrending Trajectory (N=1060)	Downtrending Trajectory (N=1042)
Male sex – N (%)	314 (5.0)	--	--	48 (7.6)	145 (4.0)	61 (5.8)	60 (5.8)
Mean (SD) Age	37.2 (11.8)	--	--	35.8 (12.2)	38.3 (11.5)	37.5 (12.2)	34.1 (11.6)
Age Category – N (%)							
18 -34 years	2759 (43.6)	--	--	318 (50.6)	1408 (39.2)	450 (42.5)	583 (55.6)
35-50 years	2552 (40.4)	--	--	217 (34.6)	1569 (43.7)	418 (39.4)	348 (33.4)
51-65 years	1012 (16.0)	--	--	93 (14.8)	616 (17.1)	192 (18.1)	111 (10.7)
Geographic Region – N (%)							
Northeast	1505 (23.8)	--	--	192 (30.6)	791 (22.0)	270 (25.5)	252 (24.2)
South	2504 (39.6)	--	--	209 (33.3)	1501 (41.8)	403 (38.0)	391 (37.5)
West	1482 (23.4)	--	--	139 (22.0)	827 (23.0)	267 (25.2)	250 (24.0)
Midwest	832 (13.2)	--	--	89 (14.2)	474 (13.2)	120 (11.3)	149 (1.3)
Race – N (%)							
Black	2843 (45.0)	--	--	322 (51.3)	1494 (41.6)	496 (46.8)	531 (51.0)
White	1883 (29.8)	--	--	127 (20.2)	1251 (34.8)	271 (25.6)	234 (22.5)
Hispanic	1147 (18.1)	--	--	126 (20.1)	611 (17.0)	208 (19.6)	202 (19.4)
Asian	245 (3.9)	--	--	31 (4.9)	115 (3.2)	46 (4.3)	53 (5.1)
Other	205 (3.2)	--	--	22 (3.5)	122 (3.4)	39 (3.7)	22 (2.1)
Area Median Income – mean (SD)	44343.04 (16269.10)	--	--	44932.67 (17718.29)	44542.09 (16159.05)	44128.57 (16054.54)	43563.48 (15935.43)
Mean SLE Risk Adjustment Index (SD)	1.2 (2.3)	1.9 (3.0)	1.3 (2.6)	1.7 (2.7)	1.1 (2.2)	1.2 (2.3)	1.5 (2.5)
Comorbidities- N (%)							
Cardiovascular disease	2153 (34.1)	2693 (42.6)	2245 (35.5)	245 (39.0)	1186 (33.0)	345 (32.6)	377 (36.2)
Renal Disease*	18 (0.3)	575 (9.1)	540 (8.5)	NR	NR	NR	NR
Diabetes	629 (10.0)	804 (12.7)	792 (12.5)	59 (9.39)	385 (10.7)	102 (9.6)	83 (8.0)
Pregnancy	603 (9.5)	432 (6.8)	320 (5.1)	65 (10.4)	318 (8.9)	75 (7.2)	145 (13.9)
Hydroxychloroquine – N (%)	1093 (17.3)	2415 (38.2)	1931 (30.5)	94 (15.0)	619 (17.2)	217 (20.5)	163 (15.6)
Immunosuppressive Use – N. (%)	681 (10.8)	1273 (20.1)	1156 (18.3)	89 (14.2)	312 (8.7)	164 (15.5)	116 (11.1)
Mean Outpatient Visits – mean (SD)	6.9 (8.2)	6.8 (6.0)	5.5 (5.6)	6.6 (8.3)	7.4 (8.7)	6.0 (7.2)	6.5 (7.4)
ED Visits – mean (SD)	2.2 (4.8)	1.9 (3.6)	1.6 (3.6)	2.1 (3.8)	2.3 (5.3)	1.9 (4.4)	2.3 (4.0)
Hospitalizations – mean (SD)	1.9 (5.6)	4.1 (9.8)	2.3 (7.4)	3.1 (9.2)	1.6 (5.0)	1.7 (4.7)	2.3 (5.0)
Receipt of vaccinations – N (%)	443 (7.0)	432 (6.8)	417 (6.6)	35 (5.6)	284 (7.9)	67 (6.3)	57 (5.5)
ED=Emergency Department; * Includes lupus nephritis, NR = Not reported (cell size <11); Characteristics stratified by trajectory are for the baseline period 12 months prior to the index date.							

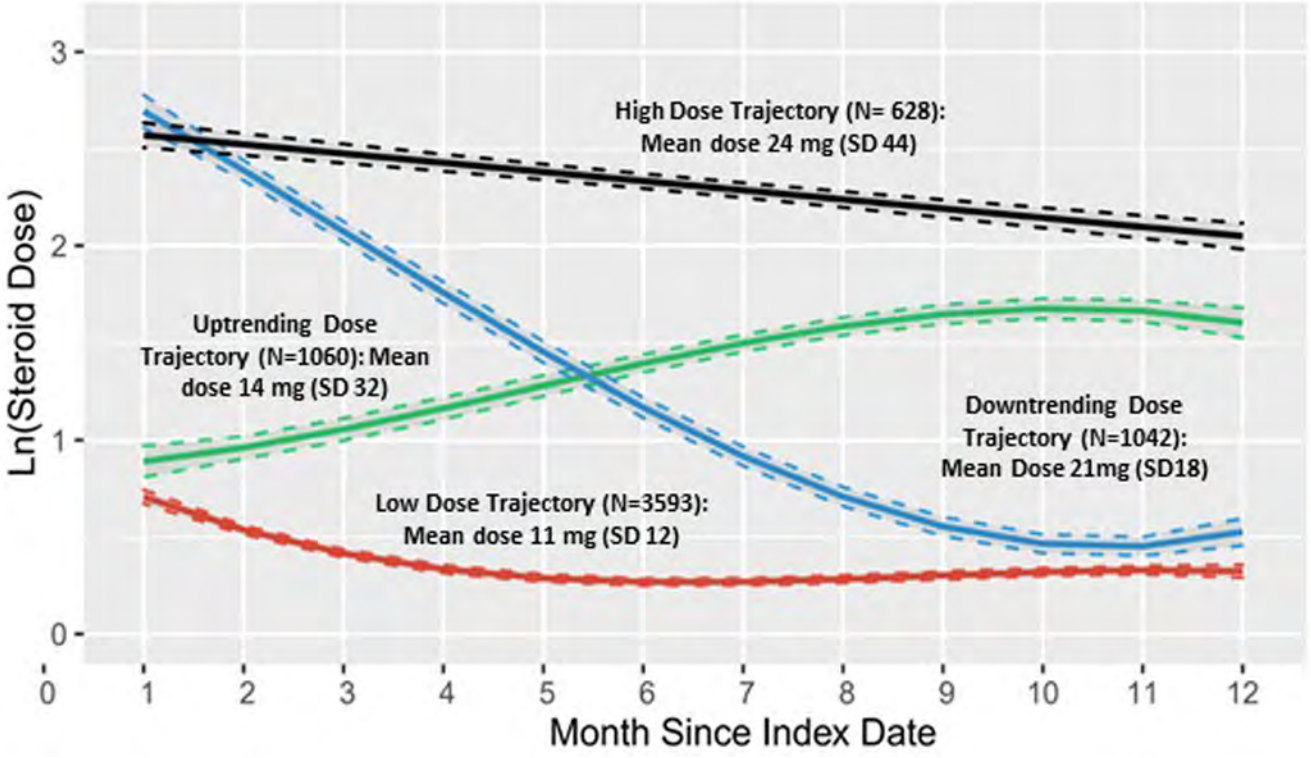

Figure 1. Trajectories of Glucocorticoid Use for Medicaid Beneficiaries with Incident SLE (N=6323).

year following the index date. We constructed group-based trajectory models (GBTMs) to identify dynamic patterns of GC use. We examined baseline demographics, medications, comorbidities, and SLE-related clinical manifestations (SLE risk adjustment index, Ward, MM. J Rheum, 2001), in the 1 year prior to the index date. We used multinomial logistic regression to estimate the odds of being in the highest vs. lowest trajectory (OR, 95% CI). We estimated GBTMs stratified by race/ethnicity and updated covariates at 6 and 12 months to understand differences in GC patterns.

Results: Among 11,280 adults with incident SLE, 6,323 (53%) received ≥1 prescription for GC during the 1-year follow-up period. The mean (SD) age was 37 (12), 5% were male, 30% identified as White, 45% Black, 18% Hispanic, and 4% Asian (**Table 1**). The overall mean (SD) daily prednisone-equivalent GD was 18 mg (33) for Black patients, 17 mg (39) for Hispanic, 17 mg (17) for Asian, and 14 mg (14) for White. A four-group trajectory model for GC use and dose provided the best fit for the data (**Fig 1**). The highest trajectory of persistent moderate-to-high dose GC users included 628 individuals (10%); the mean (SD) GD was 24 mg (44). The lowest trajectory included 3593 individuals (57%); mean (SD) GD 11 mg (12). Multinomial models adjusted for demographics demonstrated greater odds of belonging to the highest vs. lowest steroid trajectory for Black (OR 2.23, 95% CI 1.77-2.80), Hispanic (OR 1.95, 95% CI 1.48-2.56), and Asian (OR 2.56, 95% CI 1.63-4.02) individuals vs. White; after adjusting for comorbidities, medications, healthcare use, and the SLE risk adjustment index, the ORs remained similar. In GBTMs stratified by race/ethnicity, Black, Hispanic and Asian individuals vs. White had more individuals in the highest GD and use trajectories. Comparing the highest GD utilizers by race/ethnicity during 0-6 month and 6-12 month intervals post-index date, there were no differences in immunosuppressive use. Black individuals had fewer outpatient visits and received fewer vaccinations than White individuals.

Conclusion: In this population of Medicaid beneficiaries with incident SLE, >50% received GC, and of those, 26% received at least moderate GC doses during the first year. While Black, Hispanic and Asian individuals had more SLE-related manifestations, this alone may not explain these differences. Access to high-quality outpatient care may be a modifiable factor that could address high dose GC use across racial/ethnic groups.

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Abstract Number: 0493

Hospitalization for SLE Flare Has Reduced over Two Decades in the United States: A Longitudinal Population-based Study

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Healthcare Disparities in Rheumatology (0492–0495)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Longitudinal data are limited on SLE flare hospitalizations. This study aims to study longitudinal trends of SLE flare hospitalizations in the last 2 decades in the United States (U.S) using national population data.

Table 1. Characteristics and longitudinal trends of hospitalizations for Systemic Lupus Erythematosus flare from 1998 to 2018 Abbreviations: SLE, Systemic Lupus Erythematosus; USD, United States Dollars, I: Incidence per 100,000 persons, CCI, Charleston comorbidity index. p<0.005 was statistically significant. * We included hospitalizations for patients aged ≥18 years with a principal diagnosis of SLE * The incidence of SLE flare hospitalizations was calculated by dividing the number of SLE hospitalizations in the NIS by the population estimate of the U.S on July 1 of the corresponding year. The population estimates were obtained from the U.S Census Bureau Website *** All hospital charges were adjusted for inflation by using the medical expenditure panel survey-based factor for hospital care and were presented in 2018 United States dollars (USD)

Variables	1998	2003	2008	2013	2018	Adjusted p trend
*SLE flare hospitalizations **						
n	11,221	12,651	12,553	11,170	10,350	<0.0001
*I, 100,000***	4.1	4.4	4.1	3.5	3.2	
Female, %	87.4	87.6	85.6	86.6	86.7	0.451
Mean Age, years	41.5	39.1	38.6	38.2	38.3	<0.0001
Race						
White, %	44.9	31.1	31.7	26.4	23.2	0.904
Black, %	37.7	43.5	40.6	46.3	44.7	<0.0001
Hispanic, %	11.4	18	17.6	18.4	22.6	<0.0001
Asian, %	2.7	4.7	5	4.5	5.6	<0.0001
CCI score						<0.0001
0-2, %	83.3	81	67	65.2	59.9	
≥3, %	16.7	19	33	34.8	40.1	
Deceased						<0.0001
n	220	265	160	160	120	
%	2	2.1	1.3	1.4	1.2	
Mean Length of stay, days	6.9	6.8	6.7	6.6	6.6	<0.0001
*Mean total Charge, USD ****	28,765	48,163	55,805	66,192	76,171	<0.0001
All adult hospitalization (control population)						
n, million	28	30.7	32.1	30	30.3	
Female %	61	61.3	60.4	59	57.4	<0.0001
Mean Age, years	57	56.8	57.2	57.4	58.2	<0.0001
Race, %						
White	74.7	69.1	70.7	68.7	66.9	<0.0001
Black	13.5	13.8	12.9	14.7	15.1	0.06
Hispanic	8	11.8	10	10.6	11.5	<0.0001
Asian	1.7	2.4	2.6	2.5	2.8	<0.0001
CCI score						<0.0001
0-2	86.7	86.7	80.8	76.2	68.6	
≥3	13.3	13.3	19.2	23.8	31.4	
Deceased						*<0.0001*
n	826,044	790,407	746,564	652,360	679,740	
%	2.9	2.6	2.3	2.2	2.2	
Mean Length of stay, days	5.1	4.8	4.7	4.7	4.8	<0.0001
*Mean total Charge, USD ****	22,727	32,172	38,628	45,994	56,706	<0.0001

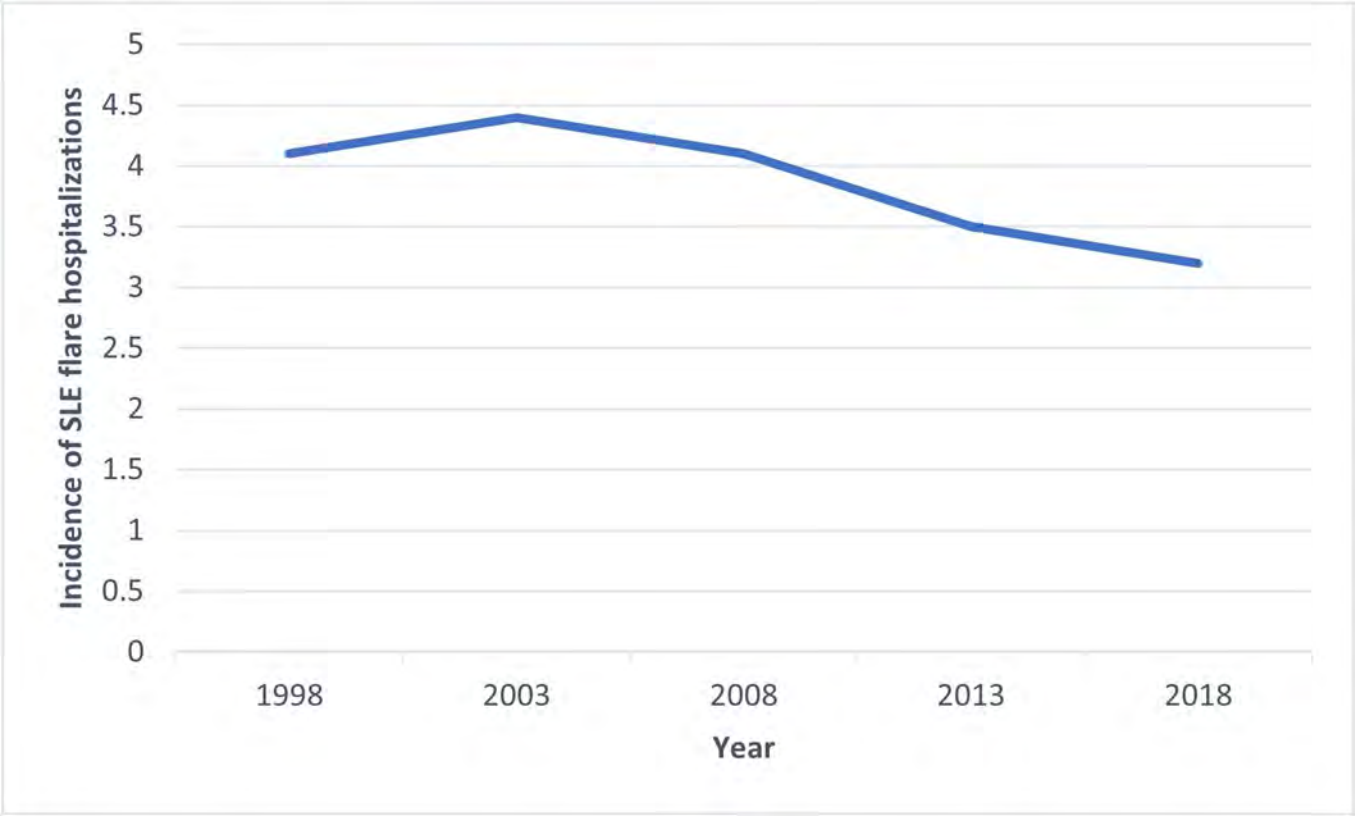

Figure 1. Incidence of Systemic Lupus Erythematosus flare hospitalizations from 1998 to 2018.

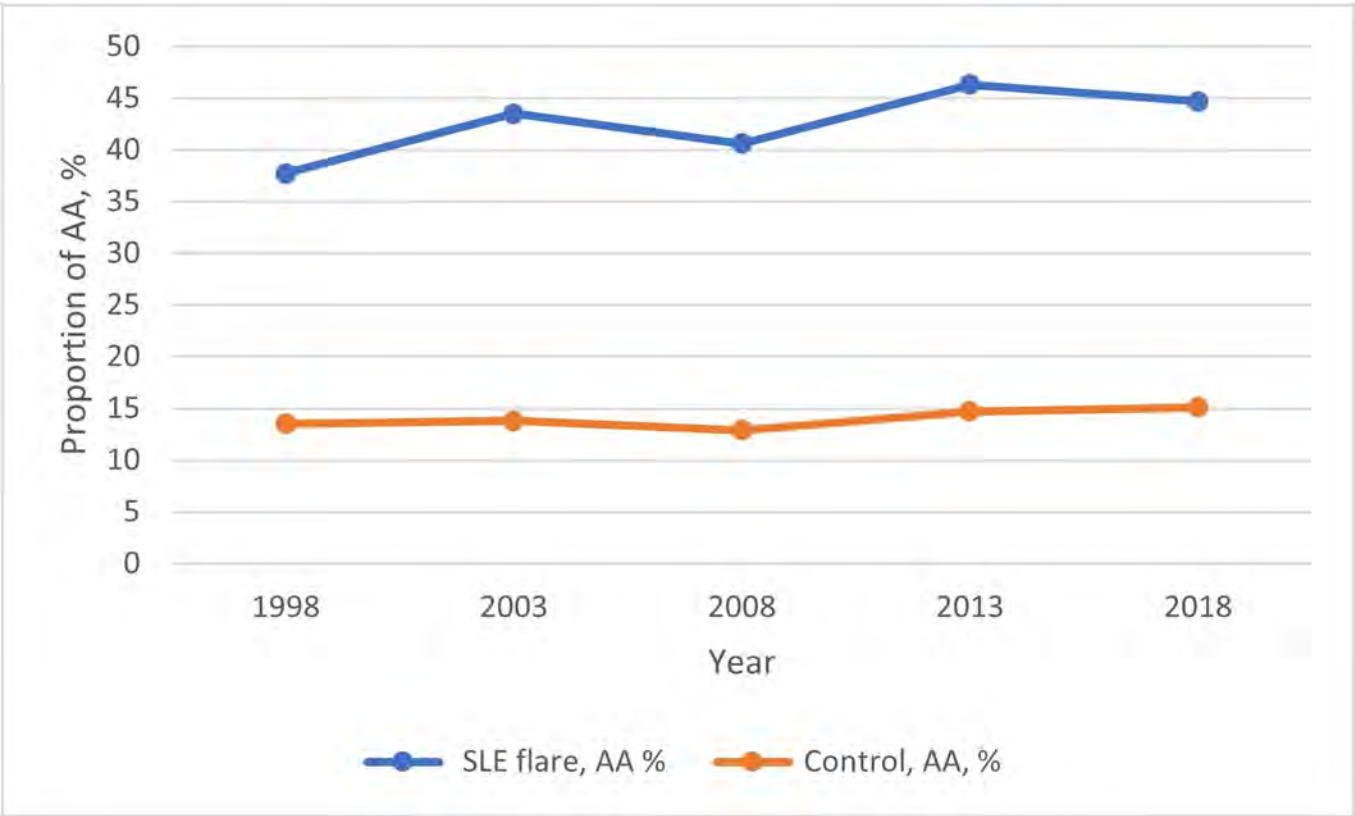

Figure 2. Proportion of African Americans in Systemic Lupus Erythematosus flare hospitalizations and control population from 1998 to 2018. All adult hospitalizations aged ≥ 18 years was used as the control population.

Methods: Data were obtained from the National Inpatient Sample database (NIS), the largest hospitalization database in the U.S. We performed a 21-year longitudinal trend analysis of NIS 1998-2018. Every 5th year of the NIS during this study period was sampled. We obtained data from NIS 1998, 2003, 2008, 2013, and 2018 databases. We searched for hospitalizations for patients aged≥ 18 years with "principal" diagnosis of SLE using ICD 9 code "7100" or ICD 10 code "M32". We defined an SLE flare hospitalization as one with a "principal" diagnosis of SLE. The "principal" diagnosis is the main reason for hospitalization. All hospitalizations for patients aged≥ 18 years were used as the control population. NIS underwent a redesign in 2012, hence revised trend weights were used to make estimates comparable across the years. Multivariable logistic and linear regression was used to calculate adjusted p-trend for categorical and continuous outcomes, respectively. We adjusted for changes in demographics and charlson comorbidity index (CCI) score over time. STATA version 16 was used for analysis.

Results: Incidence of SLE flare hospitalization reduced from 4.1 per 100,000 in 1998 to 3.2 per 100,000 in 2018 (adjusted p-trend < 0.0001). See Figure 1. Proportion of hospitalized African American (AA) SLE flare hospitalizations increased from 37.7% in 1998 to 44.7% in 2018 (adjusted p-trend < 0.0001), while hospitalized AA in the control increased from 13.5% in 1998 to 15.1% in 2018 (adjusted p-trend=0.06). See Figure 2. Racial trends of other ethnic groups were similar between SLE flare and the control population. Hospital length of stay (LOS) reduced and total hospital charges and CCI score increased for both the SLE flare and control groups during our study period (Table 1).

Conclusion: The incidence of hospitalization for SLE flare has reduced in the last two decades in the U.S. This may reflect improving outpatient SLE flare recognition and management. Although AA makes up only 13-15% of the general adult hospitalized population, they constitute the majority of SLE flare hospitalizations (38-46%). The burden of SLE flare hospitalizations among AA has increased over the last 2 decades. This may reflect a lack of access to primary and specialist care among AA. More studies on racial disparities in SLE flare hospitalizations are needed.

Disclosure: E. Edigin, None; **P. Eseaton**, None; **C. Osuorji**, None; **N. Chukwu**, None; **O. Amoda**, None; **K. Olabode**, None; **A. Manadan**, None.

Abstract Number: 0494

The Distribution of Social Deprivation, Distance to Care and Disease Burden in Rheumatoid Arthritis Patients in the United States

Sharon Dowell[1], Huifeng Yun[2], Jeffrey Curtis[3], Lang Chen[4], Manuela Pedra-Nobre[5], Dianne Wollaston[6], SAWSAN NAJMEY[7], Cynthia Lawrence-Elliott[8], Theresa Lawrence-Ford[9], Heather North[10], Robin Dore[11], Soha Dolatabadi[12], Thaila Ramanujam[13], Anne Winkler[14], Stacy Kennedy[15], Stephanie Ott[16], Stephanie Ledbetter[17], Grace Wright[18] and **Gail Kerr**[19], [1]Howard University College of Medicine, Washington, DC, [2]University of Alabama Birmingham, Birmingham, AL, [3]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, [4]University of Alabama, Birmingham, AL, [5]North Jersey Rheum. Center, Westfield, NJ, [6]Memorial Advanced Rheumatology, Houston, TX, [7]Midstate Rheumatology Center, PA, Freehold, NJ, [8]North Georgia Rheum Group, Atlanta, GA, [9]North Georgia Rheum Group, Atlanta, MD, [10]Pardee UNC, Hendersonville, NC, [11]Robin K. Dore, MD Inc, Tustin, CA, [12]Soha Dolatabadi, MD, Los Angeles, CA, [13]Santa Cruz Rheumatology, Inc., Santa Cruz, CA, [14]Winkler Medical Practice, Springfield, MO, [15]Rowan Diagnostic Clinic, Concord, NC, [16]Fairfield Medical Center, Carroll, OH, [17]University of Alabama at Birmingham, Birmingham, AL, [18]Grace C Wright MD PC, and Association of Women in Rheumatology, New York, NY, [19]Washington D.C., Veterans Affairs Medical Center (VAMC)/Georgetown and Howard Universities, Washington, DC

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Healthcare Disparities in Rheumatology (0492–0495)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Table. Clinical Characteristics, Insurance, Area Deprivation Index, and Distance to Care of RISE cohort

	Mid-West	West	Northeast	South
N	41,364	21,111	19,983	101,425
Age, mean (SD)	63.51 (13.79)	63.28 (14.25)	63.92 (13.85)	63.75 (13.79)
Sex, n (%)	31,278 (75.6%)	16,393 (77.7%)	15,221 (76.2%)	79,052 (77.9%)
Race, n (%)				
White	28,425 (68.7%)	14,435 (68.4%)	15,544 (77.8%)	69,102 (68.1%)
African American	1,809 (4.4%)	547 (2.6%)	1,132 (5.7%)	12,317 (12.1%)
Other/unknown	11,130 (26.9%)	6129 (36.0)	3,307 (16.5)	20,006 (19.6)
Seropositive (n/miss,%)	24,453/867(59.1%)	13,953/150 (66.1%)	9,462/437 (47.4%)	61,520/4166(60.7%)
Insurance, n (%)				
Medicaid	912 (2.2%)	1,158 (5.5%)	466 (2.3%)	1,798 (1.8%)
Medicare	11,850 (28.6%)	6,364 (30.1%)	5,399 (27.0%)	26,375 (26.0%)
Private	12,138 (29.3%)	6,651 (31.5%)	5,418 (27.1%)	25,251 (24.9%)
Other/unknown	16,464 (39.8)	6,938 (32.8)	8700 (43.5)	48001 (47.4)
CDAI				
remission	3,921 (9.5%)	3,808 (18.0%)	2,820 (14.1%)	9,249 (9.1%)
low	7,098 (17.2%)	5,372 (25.4%)	2,356 (11.8%)	16,228 (16.0%)
moderate	4,266 (10.3%)	2,884 (13.7%)	1,324 (6.6%)	9,660 (9.5%)
high	1,694 (4.1%)	1,023 (4.8%)	540 (2.7%)	4,205 (4.1%)
miss	24,385 (59.0%)	8,024 (38.0%)	12,943 (64.8%)	62,083 (61.2%)
RAPID3				
Remission	9,521 (23.0%)	2,152 (10.2%)	2,200 (11.0%)	13,871 (13.7%)
Low	6,462 (15.6%)	960 (4.5%)	1,098 (5.5%)	8,475 (8.4%)
Moderate	7,764 (18.8%)	1,697 (8.0%)	1,950 (9.8%)	16,276 (16.0%)
High	8,521 (20.6%)	1,936 (9.2%)	2,490 (12.5%)	24,906 (24.6%)
Miss	9,096 (22.0%)	14,366 (68.0%)	12,245 (61.3%)	37,897 (37.4%)
RxRisk Score, Median (25%, 75%)	3.00 (2.00, 7.00)	3.00 (1.00, 5.00)	3.00 (1.00, 5.00)	4.00 (2.00, 7.00)
ADI >80%	3,930 (9.5%)	886 (4.2%)	977 (4.9%)	15,854 (15.6%)
Distance to care (n, miles)	41358,28.5[77.4]	21080.35.5[156]	10078,3.6[102]	101385,37[85.3]

Background/Purpose: The overall success of RA therapy is dependent on access to specialty care, insurance coverage and effective management of associated comorbidities. Whether RA disease burden, disease status and care differs amongst patients in various regions of the US, requires further delineation.

Methods: RA patients enrolled in the Rheumatology Informatics System for Effectiveness (RISE) registry with at least two ambulatory visits between 01/2018 and 03/2020 and ≥ 1 prescription for RA medication, were evaluated. Last ambulatory visit was defined as the index date; baseline defined as 18 months prior to index date. Seropositivity was evaluated using all available data, whereas RA disease activity (CDAI, RAPID3), comorbidity burden, sociodemographic status (SES), geographic region (West, Midwest, South, Northeast), health insurance type (Medicare, Medicaid, Private), were baseline. Comorbidity burden was evaluated using treatment risk (Rxrisk-no. of conditions treated out of 46 disease entities). Based on zip codes, we obtained area deprivation index (ADI= national/regional) to define low SES (i.e. ADI > 80 = high deprivation). Median travel distance between patients' and practice sites zip codes, was calculated. A linear regression model was used to analyze associations between RA disease activity (CDAI/RAPID3) and comorbidity (# of RxRisk categories) adjusting for age, sex, geographic region, race and insurance type.

Results: Enrollment data for 184,722 RA patients (mean age 64 years [13.85], 77.2% female) from 182 RISE sites was analyzed (Table 1). Disease activity was higher in blacks, and in patients from South regions and with Medicaid/Medicare coverage. Mean ADI was 45.56 [25.85] with 12% of sites in high deprivation areas (ADI >80), which was particularly relevant to practice sites in the South, and with higher frequencies in rural vs urban areas (Figure 1). Patients with ADI >80 received primarily Medicaid coverage, the majority of whom were seen by a minority of providers; >60% of socially deprived patients were cared for by only 22% of RISE practices. Overall, the median percentage Medicaid participants for sites was 0.16%, with fewer than 20 rheumatology practices caring for 50%

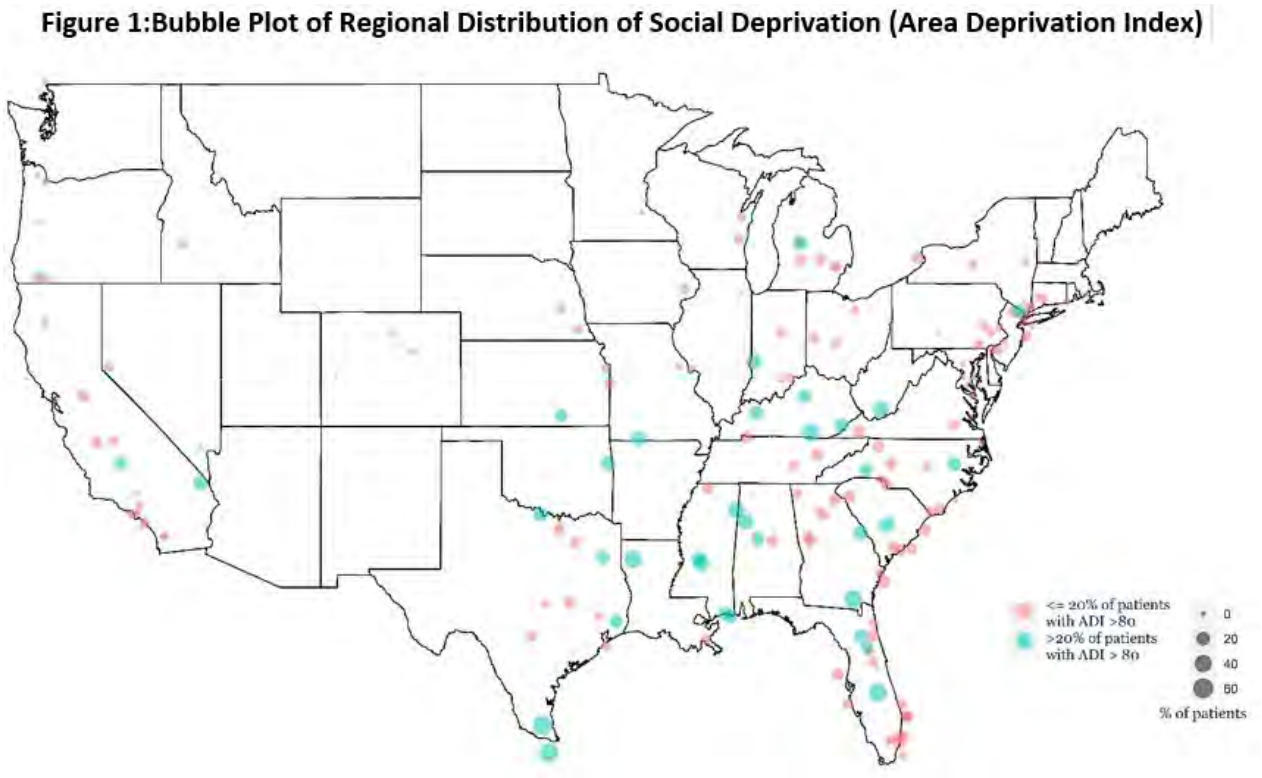

Figure 1 Bubble plot.

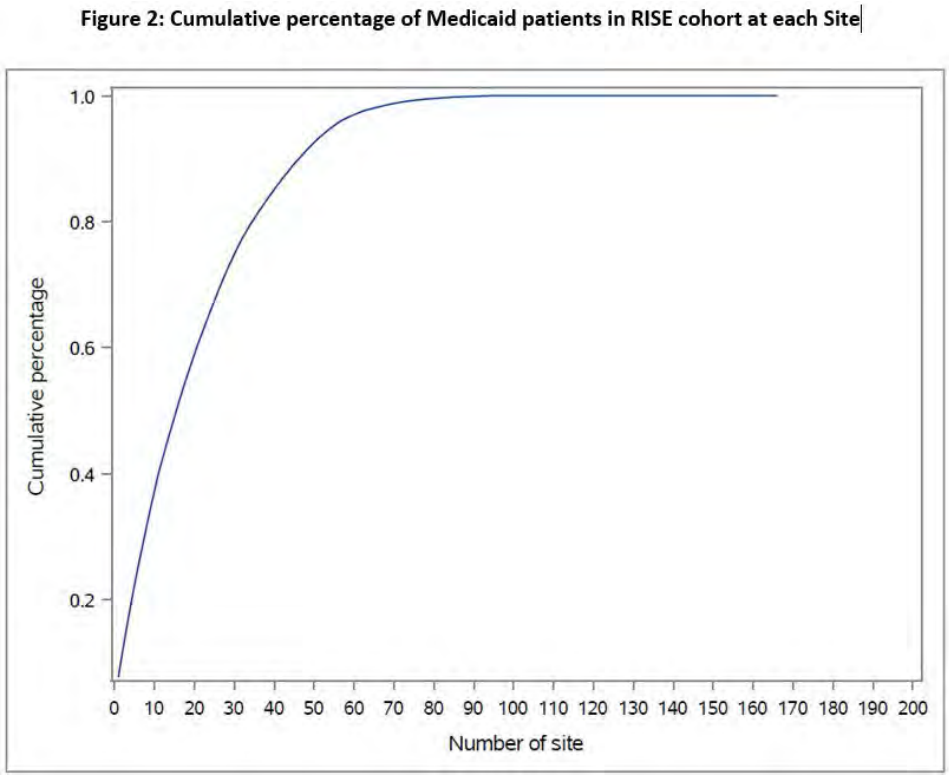

Figure 2 Cumulative percentage.

of all RA patients (Figure 2). Most patients resided within 50 miles of their provider, but 2.9% of patients were >200 miles away from specialist care, mainly in South and West regions. Like disease activity, higher category RxRisk patients had predominant Southern regional distribution and Medicare/Medicaid coverage, but < 200 miles to access care. There was significant correlation between RxRisk and disease activity (Pearson coefficient: RAPID3 0.28, CDAI 0.15).

Conclusion: Type of insurance, not race or distance to specialty care, was associated with overall RA disease activity and burden). A disproportionately large fraction of socially deprived, rural, high comorbidity, and Medicaid-covered RA patients were cared for by a minority of rheumatology practices. Studies are needed in high deprivation areas to determine the impact of interventions targeting more equitable distribution of specialty care, enhanced reimbursement and access to advanced therapies, so as to improve RA patient outcomes in vulnerable patients.

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Abstract Number: 0495

Racial/Ethnic Differences in Multimorbidity Between Patients with Systemic Lupus Erythematosus and Comparators in a Large Nationwide US Study

Ali Duarte-Garcia[1], Herbert Heien[1], Nilay Shah[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Healthcare Disparities in Rheumatology (0492–0495)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased burden of multimorbidity. Racial/ethnic disparities have also been associated with an increased burden of multimorbidity. We aimed to compare racial/ethnic difference in multimorbidity between patients with SLE and non-SLE comparators.

Methods: We used the OptumLabs Data Warehouse (OLDW), a longitudinal, real-world data asset with de-identified administrative claims for commercial and Medicare Advantage enrollees, to identify cases of SLE and matched comparators. Cases were defined as patients with ≥3 diagnoses of SLE between January 2006 and September 2015. Controls were persons without SLE matched 1:1 to SLE cases on age, sex, race/ethnicity, and enrollment date. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), non-Hispanic Asian (Asian), Hispanic, based on derived rule sets. Multimorbidity (2 or more comorbidities) was defined using 172 chronic comorbidities from the chronic condition indicator of the clinical classification software (healthcare cost and utilization project). SLE,

Table. Comparison of multimorbidity prevalence between race/ethnicity among patients without SLE and patients with SLE.		
	Multimorbidity (2+ conditions) Odds ratio*	Multimorbidity (5+ conditions) odds ratio*
Non SLE		
White	Ref.	Ref.
Asian	0.66 (0.55-0.78)	0.67 (0.48-0.93)
Black	1.15 (1.07-1.23)	1.3 (1.17-1.46)
Hispanic	1.0 (0.91-1.09)	1.05 (0.9-1.23)
SLE		
White	Ref.	Ref.
Asian	0.8 (0.7-0.9)	0.72 (0.61-0.87)
Black	1.05 (1.0-1.12)	1.15 (1.07-1.23)
Hispanic	1.08 (1.0-1.16)	1.04 (0.95-1.14)
*Adjusted for age, sex, and region		

cutaneous lupus, and rheumatoid arthritis ICD-9 codes were excluded from the analysis. Two or more ICD-9 codes at least 30 days apart were used to define a comorbidity. A secondary analysis was performed including those with 5 or more comorbidities (substantial multimorbidity). Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI) adjusted for age, sex, and region.

Results: The study included 34,869 cases with SLE and 34,869 matched non-SLE comparators. The mean age was 48 (SD 14.2) years, and 90.6% were female for both cohorts. 66.4% of the patients in both cohorts were White, 18.4% Black, 3.4% Asian and 18.4% Hispanic. Patients with SLE had more multimorbidity than non-SLE subjects (58.1% vs 26.3%). Among the non-SLE patients 26.7% of Whites experienced multimorbidity, compared to 16% of Asians, 22.6% of Hispanics, and 29.2% of Blacks. After adjustment for age, sex and geographic region, Blacks had higher multimorbidity (OR 1.15; 95%CI 1.07-1.23), Asians had lower multimorbidity (OR 0.66; 95%CI 0.55-0.78) while Hispanics (OR 1.0; 95%CI 0.91-1.09) had no difference in multimorbidity compared to Whites. Among the SLE patients, 58.6% of Whites experienced multimorbidity, compared to 47.2% of Asians, 56.0% of Hispanics, and 59.5% of Blacks. Adjusted analyses showed less pronounced decrease in multimorbidity for Asians (OR: 0.80; 95%CI: 0.70-0.90) and a less pronounced increase in Blacks (OR: 1.05; 95%CI: 0.99-1.12) and a similar increase in multimorbidity among Hispanics (OR: 1.07; 95%CI: 1.00-1.15) compared to Whites in the SLE cohort. Similar findings were observed in secondary analysis of those with 5 or more comorbidities (Table)

Conclusion: This large nationwide study showed increased occurrence of multimorbidity in SLE versus non-SLE patients across racial/ethnic groups. Racial/ethnic disparities in multimorbidity were more pronounced among patients without SLE compared to SLE patients. These findings suggest that the effects of race/ethnicity and SLE are not cumulative.

Disclosure: A. Duarte-Garcia, None; **H. Heien**, None; **N. Shah**, None; **C. Crowson**, None.

Abstract Number: 0496

Safety and Efficacy of Rituximab for Systemic Sclerosis: A Double-Blind, Parallel-Group Comparison, Investigators Initiated Confirmatory Randomized Clinical Trial (DESIRES Study)

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SESSION INFORMATION

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Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)

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Session Time: 3:30PM–5:00PM

Background/Purpose: Systemic sclerosis (SSc) is a systemic autoimmune disease belonging to collagen diseases, characterized by fibrosis of various organs including the skin and lungs, and vascular damage. SSc is considered to have a high unmet medical need because of its poor prognosis in severe cases and the lack of satisfactory and effective treatments. Previous studies have shown that B cells play a major role in the development of SSc. In fact, several clinical studies have suggested that B cell depletion therapy with rituximab, anti-CD20 antibody, is effective. However, no randomized, placebo-controlled trial has been able to confirm the efficacy of rituximab in SSc, which implies that there has been no high-quality evidence to date.

Methods: In this study, a multicenter, double-blind, placebo-controlled, parallel-group comparison, investigator-initiated clinical trial was conducted to evaluate the safety and efficacy of rituximab for SSc. Patients were randomized 1:1 to rituximab (375 mg/m^2) or placebo and received the study drug intravenously once a week for 4 weeks. The primary endpoint was the change in the modified Rodnan total skin thickness score, a semiquantitative measure of the degree of skin sclerosis, 24 weeks after the start of the intervention. The main secondary endpoint was the change in %forced vital capacity (%FVC) at 24 weeks. This trial had been registered with ClinicalTrials.gov (NCT04274257) and UMIN-CTR (UMIN000030139).

Results: A total of 56 patients participated in the study, 54 of whom received rituximab or placebo. Twenty-four weeks after the start of the intervention, the modified Rodnan total skin thickness score was significantly improved in the rituximab group compared to the placebo group (6.30 decrease in the rituximab group vs. 2.14 increase in the placebo group; difference 8.44 [95% confidence interval -11.00 to -5.88]; $P < 0.0001$). In addition, the %FVC of 48 patients with interstitial lung disease was significantly improved in the rituximab group than in the placebo group at 24 weeks (0.09% improvement in the rituximab group vs. 2.87% deterioration in the placebo group; difference 2.96% [95% confidence interval 0.08 to 5.84]; $P = 0.04$). The incidence of adverse events was comparable between the two groups, and there were no significantly increased adverse events in either group. There were no deaths during the trial.

Conclusion: This study was the first to validate the efficacy and safety of rituximab for skin sclerosis in SSc. Moreover, this clinical trial suggested the efficacy of rituximab for SSc-associated interstitial lung disease. Therefore, it is promising that rituximab becomes a new standard therapy for SSc.

Disclosure: S. Ebata, None; **A. Yoshizaki**, None; **K. Oba**, None; **K. Kashiwabara**, None; **K. Ueda**, None; **Y. Umemura**, None; **T. Watadani**, None; **T. Fukasawa**, None; **S. Miura**, None; **A. Yoshizaki-Ogawa**, None; **Y. Asano**, None; **N. Okiyama**, None; **M. Kodera**, None; **M. Hasegawa**, None; **S. Sato**, None.

Abstract Number: 0497

Efficacy in Patient Subgroups in the INCREASE Trial, a Phase III Trial to Evaluate Inhaled Treprostinil in Patients with Pulmonary Hypertension Due to Parenchymal Lung Disease

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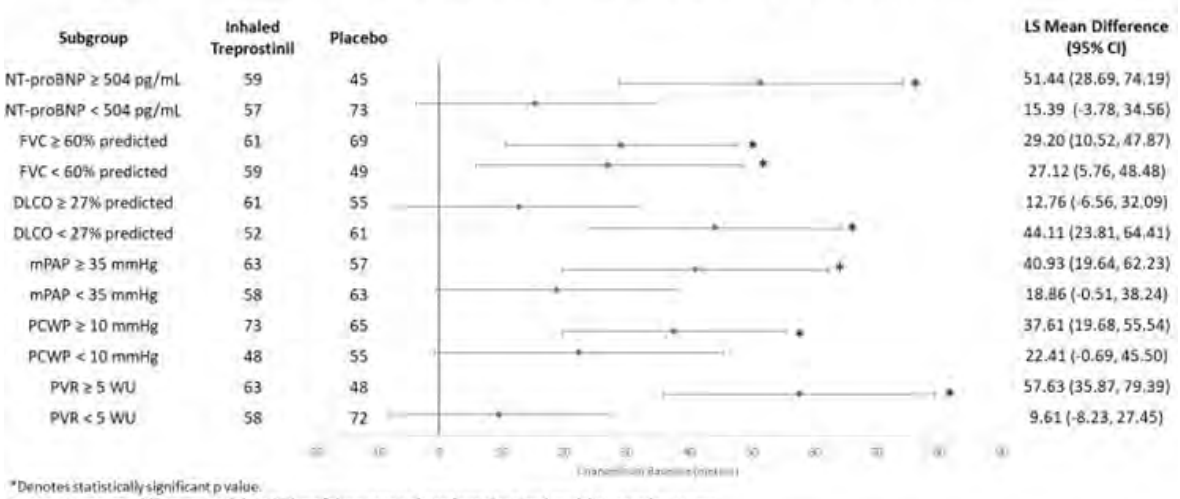
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: INCREASE was a 16-week trial evaluating the safety and efficacy of inhaled treprostinil (iTRE) in patients with pulmonary hypertension associated with interstitial lung disease (PH-ILD). The study met its primary efficacy endpoint of change in 6-minute walking distance (6MWD), demonstrated by a 31m improvement from baseline (260m). Secondary endpoints, including change in N-terminal pro b-type natriuretic peptide (NT-proBNP) and

Figure 1: Treatment Effect of iTRE on Change in 6MWD



*Denotes statistically significant p value.
Least squares mean differences and their 95% confidence intervals are from the mixed model repeated measures
6MWD: six-minute walk distance; FVC: forced vital capacity; CI: confidence interval; DLCO: diffusing capacity for carbon monoxide; LS: least squares; mPAP: mean pulmonary arterial pressure; NT-proBNP: N-terminal pro hormone B-type natriuretic peptide; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance

Figure 2: Treatment Effect of iTRE on Change in NT-proBNP*

Subgroup	Inhaled Treprostinil	Placebo	LS Mean Difference (95% CI)
NT-proBNP ≥ 504 pg/mL	64	49	0.64 (0.49, 0.84)
NT-proBNP < 504 pg/mL	59	78	0.52 (0.37, 0.72)
FVC ≥ 60% predicted	67	72	0.58 (0.45, 0.74)
FVC < 60% predicted	56	53	0.65 (0.46, 0.92)
DLCO ≥ 27% predicted	67	60	0.70 (0.54, 0.92)
DLCO < 27% predicted	52	63	0.54 (0.38 0.75)
mPAP ≥ 35 mmHg	63	63	0.49 (0.36, 0.65)
mPAP < 35 mmHg	60	64	0.71 (0.52, 0.95)
PCWP ≥ 10 mmHg	72	72	0.54 (0.42, 0.69)
PCWP < 10 mmHg	51	55	0.66 (0.46, 0.96)
PVR ≥ 5 WU	61	52	0.62 (0.50, 0.83)
PVR < 5 WU	62	75	0.51 (0.36, 0.72)

*Denotes statistically significant p value for all values
Least squares mean differences and their 95% confidence intervals are from the mixed model repeated measures
6MWD: six-minute walk distance; FVC: forced vital capacity; CI: confidence interval; DLCO: diffusing capacity for carbon monoxide; LS: least squares; mPAP: mean pulmonary arterial pressure; NT-proBNP: N-terminal pro hormone B-type natriuretic peptide; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance

time to clinical worsening, were also met. Post-hoc analyses were conducted to investigate clinical endpoints within patient subgroups.

Methods: All 326 patients randomized in INCREASE were included in the present analyses, of which 72 patients (iTre 40, placebo 32) had connective tissue disease as the cause of their underlying lung disease. Patient subgroups were delineated by median values of the following baseline characteristics: PVR (< 5 WU, ≥5WU), PCWP (< 10 mmHg, ≥10 mmHg), mPAP (< 35 mmHg, ≥35 mmHg), DLCO (< 27% predicted, ≥27% predicted), FVC (< 60% predicted, ≥60% predicted) and NT-proBNP (< 504 pg/mL, ≥504 pg/mL). Clinical worsening was defined as any of the following: cardiopulmonary hospitalization, decrease in 6MWD >15% from baseline, all-cause death, or lung transplantation.

Results: 6MWD improvements were demonstrated in all subgroups. Statistically significant improvements occurred in patients with above median PVR, PCWP, mPAP; lower than median DLCO; and in both above median and below

Figure 3: Treatment Effect of iTRE on Time to Clinical Worsening

Subgroup	Inhaled Treprostinil	Placebo	HR (95% CI)
NT-proBNP ≥ 504 pg/mL	83	75	0.57 (0.33, 0.98)
NT-proBNP < 504 pg/mL	73	85	0.81 (0.42, 1.56)
FVC ≥ 60% predicted	84	89	0.64 (0.35, 1.16)
FVC < 60% predicted	78	72	0.70 (0.39, 1.27)
DLCO ≥ 27% predicted	87	71	1.01 (0.48, 2.12)
DLCO < 27% predicted	65	82	0.66 (0.38, 1.15)
mPAP ≥ 35 mmHg	89	83	0.57 (0.32, 1.01)
mPAP < 35 mmHg	74	80	0.76 (0.41, 1.42)
PCWP ≥ 10 mmHg	95	91	0.86 (0.50, 1.48)
PCWP < 10 mmHg	68	72	0.46 (0.23, 0.90)
PVR ≥ 5 WU	90	73	0.57 (0.33, 0.98)
PVR < 5 WU	73	90	0.70 (0.36, 1.35)

Treprostinil better
Placebo better
*Denotes statistically significant p value
Hazard ratio and 95% confidence interval were calculated with proportional hazards model
FVC: forced vital capacity; CI: confidence interval; DLCO: diffusing capacity for carbon monoxide; HR: hazard ratio; mPAP: mean pulmonary arterial pressure; NT-proBNP: N-terminal pro hormone B-type natriuretic peptide; PCWP: pulmonary capillary wedge pressure; PVR: pulmonary vascular resistance

median FVC and NT-proBNP cohorts (p≤0.013 for all). Statistically significant reductions in NT-proBNP were demonstrated in all subgroups (p≤0.028 for all). Statistically significant benefit in time to clinical worsening with iTRE was observed in above median PVR, mPAP, and NT-proBNP; and lower PCWP (p≤0.0493 for all). Overall, response separation in clinical endpoints indicated greater improvement for patients with above median NT-proBNP and PVR. A similar trend of benefit was observed in lower DLCO and higher mPAP subgroups.

Conclusion: These analyses demonstrate improvements in clinical endpoints with inhaled treprostinil across patient subgroups. Patients with more advanced pulmonary vascular disease stand to gain the most benefit with inhaled treprostinil therapy.

Disclosure: V. Tapson, Bayer, 1, Janssen / johnson & Johnson, 1, 5, 6, United Therapeutics, 1, 5, 6; **S. Nathan**, United Therapeutics, 1, 2, 6; **R. Girgis**, United Therapeutics, 5; **J. Runo**, None; **R. Bag**, None; **A. Talwar**, None; **P. Smith**, United Therapeutics, 3; **L. Edwards**, United Therapeutics Corporation, 3, 11; **C. Park**, United Therapeutics, 3; **A. Waxman**, United Therapeutics, 1, Acceleron, 1, ARIA CV, 1, Gossamer, 5, INSMED, 1.

Abstract Number: 0498

Background Mycophenolate (MMF) Treatment Is Associated with Improved Outcomes in a Phase 3 Trial of Lenabasum in Diffuse Cutaneous Systemic Sclerosis (dcSSc)

Robert Spiera[1], Dan Furst[2], Tracy Frech[3], Masataka Kuwana[4], Laura Hummers[5], Wendy Stevens[6], Suzanne Kafaja[7], Eun bong Lee[8], Scott Constantine[9], Nancy Dgetluck[9], Barbara White[10] and Christopher Denton[11], [1]Hospital for Special Surgery, New York, NY, [2]University of California Los Angeles, Los Angeles, CA, [3]University of Utah, Salt Lake City, UT, [4]Department of Allergy and Rheumatology, Nippon Medical School Graduate School of Medicine, Tokyo, Japan, [5]Johns Hopkins Univerisity, Baltimore, MD, [6]St Vincent's Hospital, Melbourne, Australia, [7]University of California Los Angeles Division of Rheumatology, Los Angeles, CA, [8]Seoul National University Hospital, Seoul, Republic of Korea, [9]Corbus Pharmaceuticals, Inc., Norwood, MA, [10]Corbus Pharmaceuticals, Norwood, MA, [11]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Treatment of dcSSc is evolving, with limited information on relative efficacies of different immunosuppressive therapies (IST). Our hypothesis was that patients on MMF have better efficacy outcomes than patients on other IST or no IST, in a clinical trial context.

Methods: Data were analyzed from a 1-year Phase 3 double-blind, placebo-controlled study of lenabasum in subjects with dcSSc ≤ 6 years duration. Background IST (bIST) were allowed in doses that were stable for ≥ 8 weeks before Screening. Enrolling sites were mostly academic specialty clinics for patients with SSc. All cohorts were combined for analyses, because the primary efficacy endpoint (ACR CRISS score) was not met. Subjects were categorized by bIST use: None, MMF, Steroids (≤ 10 mg/day oral prednisone or equivalent), Methotrexate (MTX), and All Other IST. Baseline demographics, disease characteristics, and efficacy outcomes were determined and impact of MMF on certain outcomes was determined in mixed model repeated measures analyses (MMRM) with visit, MMF

Table 1. Baseline demographics and baseline immunosuppressive therapies (bIST)

Baseline Demographics or IST	Subjects by Baseline Immunosuppressive Therapies (bIST) n, mean (SD) or % bIST group. N = 325 total subjects					
	All subjects	No bIST	MMF	Steroids	MTX	All Other IST
	325	49 (15%)	171 (53%)	90 (28%)	62 (19%)	77 (24%)
Age, years	50.5 (12.9)	54.6 (11.1)	51.0 (12.9)	47.9 (13.0)	46.4 (13.2)	50.0 (13.2)
Female	244 (75%)	34 (67%)	133 (78%)	71 (79%)	42 (68%)	60 (78%)
Region: US/ Asia/ Other Countries[1]	36%/18%/45%	24%/31%/45%[2]	53%/8%/38%[3]	28%/32%/40%[2]	19%/18%/63%[2]	27%/14%/45%
Race: White/ Asian /Other	68%/21%/10%	53%/31%/16%[4]	75%/13%/11%	52%/37%/11%[3]	73%/18%/10%	75%/17%/8%
Monotherapy bIST	169 (52%)	-	95 (56%)	18 (20%)	32 (52%)	18 (23%)
Combination bIST	107 (33%)	-	76 (44%)	72 (80%)	30 (48%)	59 (77%)
bIST treatment duration						
• ≤ 1 year			94 (55%)	52 (57%)	29 (47%)	31(40%)
• < 1 to ≤ 2 years			20 (12%)	10 (11%)	14 (23%)	15 (19%)
• > 2 years			57 (33%)	28 (31%)	19 (31%)	31 (40%)

[1]Asia indicates Japan and South Korea in this study; Other Countries are Australia, Canada, Germany, Great Britain, Israel, Italy, Netherlands, Poland, Spain, as per randomization. [2]P ≤ 0.05, [3]P ≤ 0.01, [4]P ≤ 0.001 compared to all subjects

use, MMF-by-visit interaction, baseline mRSS score, disease duration, region, lenabasum treatment, and lenabasum treatment-by-visit interaction as fixed effects.

Results: 276/325 (85%) subjects used bIST (Table 1). MMF was used in about twice as many subjects as Steroids (53% vs. 28%), followed in descending order by: MTX (19%); and All Other bIST, comprised of hydroxychloroquine (11%); tocilizumab, immunoglobulins, and azathioprine (4% each); and chloroquine, cyclophosphamide, abatacept, tacrolimus, and cyclosporine (≤ 1% each). Subjects treated with different bIST had similar age and sex. Treatment with MMF was more common in the US and White subjects, whereas treatment with Steroids or No bIST was more common in Asia and Asian subjects. Treatment with MTX was more common in Other Countries (mostly Europe).

Table 2. Baseline disease characteristics and outcomes, by use of baseline immunosuppressive therapies (bIST)

Baseline Disease Characteristic or Outcome	Subjects by Baseline IST n, mean (SD) or % IST group. N = 325 total subjects					
	All	None	MMF	Steroids	MTX	Others
	325	49	171	90	62	77
Dis. duration, mon	32 (17.5)	29 (17.9)	30 (17.5)	31 (16.0)	30 (15.7)	36 (17.2)
Anti-Scl-70 antibody	127 (39%)	13 (27%)	60 (35%)	42 (47%)	29 (47%)	36 (47%)
Anti-RNAP antibody	115 (35%)	13 (27%)	76 (44%)	34 (38%)	19 (31%)	26 (34%)
ILD	248 (76%)	35 (71%)	133 (78%)	76 (84%)	42 (68%)	65 (84%)
mRSS	22.4 (8.21)	21.4 (7.70)	23.2 (8.15)	22.4 (8.12)	22.0 (8.37)	24.2 (8.26)
MDGA	5.4 (1.56)	5.1 (1.58)	5.4 (1.59)	5.4 (1.27)	5.6 (1.48)	5.8 (1.62)[1]
HAQ-DI	1.113 (0.7561)	0.921 (0.6407)	1.178 (0.7317)	1.134 (0.7702)	1.101 (0.7777)	1.338 (0.7626)[1]
PtGA	4.9 (2.14)	5.0 (2.56)	4.7 (2.07)	5.0 (1.96)	5.1 (1.95)	5.1 (1.89)
FVC %	80.2 (15.93)	83.0 (11.77)	78.4 (16.06)	78.8 (18.12)	81.6 (16.44)	78.5 (16.14)
Outcomes at 1 year						
ACR CRISS score (1st, 3rd quartiles)	0.853 (0.070, 0.997)	0.352 (0.001, 0.919)	0.936 (0.316, 0.999)	0.790 (0.325, 0.995)	0.527 (0.011, 0.982)	0.950 (0.232, 0.999)
Δ mRSS	-7.3 (6.90)	-4.5 (6.75)	-8.6 (7.15)	-6.9 (6.75)	-5.0 (6.34)	-8.6 (6.52)
Δ MDGA	-1.8 (1.75)	-1.2 (1.89)	-2.0 (1.74)	-1.8 (1.50)	-1.9 (1.85)	-2.0 (1.52)
Δ HAQ-DI	-0.107 (0.4316)	0.011 (0.3753)	-0.161 (0.4444)	-0.146 (0.4283)	-0.082 (0.4644)	-0.201 (0.4266)
Δ PtGA	-0.9 (2.47)	-1.0 (2.85)	-1.1 (2.40)	-1.1 (2.27)	-0.7 (2.46)	-0.8 (1.94)
Δ FVC, %	-1.6 (16.66)	-3.9 (6.90)	-0.4 (6.89)	-0.9 (8.54)	-2.5 (7.66)	-1.41 (8.77)

[1] P ≤ 0.05 compared to all subjects

Table 3. Type 3 Tests of Fixed Effects

Effect	ACR CRISS Score Pr > F	FVC, % predicted Pr > F
Visit	< 0.0001	< 0.0001
MMF	0.0002	0.0526
MMF-by-visit interaction	0.0290	0.0530
Baseline FVC	-	< 0.0001
Baseline mRSS	0.4699	-
Region	0.5342	0.2259
Disease duration	0.4074	0.4229
Lenabasum treatment	0.8590	0.9294
Lenabasum treatment-by-visit interaction	0.9980	0.6687

MMF and MTX were used more commonly as monotherapy (56% and 52%), respectively, than Steroids (20%). Treatment duration of bIST (≤ 1 year, >1 – ≤ 2years, > 2 years) did not differ significantly among bIST groups.

Subjects treated with MMF had greater improvement in most efficacy outcomes than subjects treated with MTX or steroids without MMF (Table 2). Visit, use of MMF, and MMF-by-visit interaction had significant effects on ACR CRISS score, whereas baseline mRSS, region, disease duration, lenabasum treatment, and lenabasum treatment-by-visit interaction did not (Table 3). Use of MMF, visit, MMF-by-visit interaction, and baseline FVC % also influenced change in FVC%, whereas the other fixed effects did not.

Conclusion: MMF was the most commonly used bIST in this Phase 3 study of dcSSc subjects. Treatment with MMF during the trial was associated with better outcomes than treatment with MTX or Steroids without MMF. In future dcSSc trials that enroll subjects on bIST, statistical analyses should consider that subjects on placebo added to bIST are, in fact, receiving active concomitant treatment that will confound trial results over time. Differences in proportion of subjects on MMF, other IST, and no IST may also influence results. Efficacy outcomes will need to detect improvement beyond the substantial efficacy already provided by bIST over time.

Disclosure: R. Spiera, GSK, 2, 5, Boehringer Ingelheim Pharmaceuticals, 5, Chemocentryx, 2, 5, Corbus Pharmaceutical, 5, Formation Biologics, 2, 5, InflaRx, 5, Kadmon, 5, Astra Zeneca, 5, Abbvie, 2, CSL Behring, 2, Sanofi, 2, Janssen Pharmaceuticals, 2, Genentech/Roche, 2, 5; **D. Furst**, Actelion, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corbus, 2, 6, Galapagos, 2, 5, GSK, 6, Sanofi, 2, 5, 6, Roche/Genentech, 5, National Institutes of Health, 5, Novartis, 2, 5, Pfizer, 2, 5; **T. Frech**, None; **M. Kuwana**, Boehringer Ingelheim, 5, 6, One Pharmaceuticals, 5, 6, Chugai, 6, Janssen, 6, Astellas, 6, Tanabe Mitsubishi, 6, Pfizer, 6, Nippon Shinyaku, 6, Corbus, 2, Mochida, 2, Kissei, 2, MBL, 9; **L. Hummers**, Boerhinger Ingelheim, 1, 5, Corbus Pharmaceuticals, 1, 5, Cumberland Pharmaceuticals, 5, Kadmon Corporation, 5, Medpace, 5; **W. Stevens**, Corbus Pharmaceuticals, Inc., 5, janssen, 1, 5, 6, GSK, 5, Boehringer Ingelheim, 1, 5, Arena Pharmacueticals, 5, Gossamer, 1; **S. Kafaja**, Eicos, 2, 5, Corbus, 2, Galapagos, 5, Cumberland, 5, Novartis, 5; **E. Lee**, None; **S. Constantine**, Corbus Pharmaceuticals, Inc, 3; **N. Dgetluck**, Corbus Pharmaceuticals, Inc., 3; **B. White**, Corbus Pharmaceuticals Inc., 3, 8; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 0499

Preliminary Assessment of Internal Reliability and Construct Validity of Long and Short-form Assessment of Systemic Sclerosis-associated RAynaud's Phenomenon (ASRAP) Questionnaires

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: The Assessment of Systemic sclerosis-associated RAynaud's Phenomenon (ASRAP) questionnaire is a novel patient-reported outcome instrument devised to assess the severity and impact of SSc-RP. The

Figure 1. Psychometric testing of long and short-form ASRAP questionnaires. Correlation with legacy instruments for assessing RP severity, cold sensitivity, functional capacity, pain and global health

Domains		RP severity & impact global assessments		Cold sensitivity	Function		Pain	Global health assessment
Instruments		Scleroderma HAQ-RP VAS	RP- global severity VAS	CSS total	HAQ-DI	DHI total	Pain Intensity VAS	Global VAS
27-item long form ASRAP questionnaire	Pearson Correlation	0.723**	0.665**	0.512**	0.449**	0.507**	0.559**	0.436**
	Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	N	402	407	380	396	391	347	407
10-item short form ASRAP questionnaire	Pearson Correlation	0.727**	0.647**	0.488**	0.497**	0.533**	0.576**	0.449**
	Sig. (2-tailed)	0.000	0.000	0.000	0.000	0.000	0.000	0.000
	N	382	387	361	376	373	330	387

RP, Raynaud's phenomenon; HAQ-DI, health assessment questionnaire-disability index; VAS, visual analogue scale; DHI, Duruoz Hand Index; CSS, cold sensitivity scale

ASRAP items are grounded in the patient experience of SSc-RP. We report the development and subsequent assessment of internal reliability and preliminary construct validity testing of long and short-form versions of the ASRAP questionnaire.

Methods: The international multicentre ASRAP validation study enrolled English speaking SSc-RP patients from UK and US scleroderma centres during 2 consecutive winters 2019-2021. All participants completed a 39-item ASRAP questionnaire. Item reduction, scale scoring and derivation of a short-form ASRAP were based upon item response theory (IRT) assumptions and calibrated using the graded response model. The final 27-item long-form scores were correlated with a 10-item short form scores using Pearson's correlation. Once scales were devised, preliminary assessment of construct validity was determined by Pearson's correlation between long and short-form ASRAP scores and a range of concurrent disease specific and legacy instruments capturing SSc-RP patient measures of disease activity/impact and relevant domains including cold sensitivity, pain, function and patient global health.

Results: A total of 438 SSc patients were enrolled at UK (n=238) and US (n=200) sites. A data driven approach with expert opinion was used to devise a 27-item long-form and 10-item short-form. Internal reliability between long and short form ASRAP questionnaires was excellent with Pearson correlation coefficient values of 0.976 ($p< 0.0001$). Evidence of construct validity of the long and short form ASRAP was indicated by strong agreement with existing global assessments of RP severity and impact (Scleroderma Health Assessment Questionnaire RP VAS and Patient RP global VAS (Figure 1). The short and long-form ASRAP questionnaire also had statistically significant correlations (in anticipated direction) with legacy instruments for assessing disability, hand function, pain and global health assessment (Figure 1).

Conclusion: Our preliminary analysis from the ASRAP validation study indicates strong internal reliability between long and putative short form ASRAP questionnaires. Cross-sectional psychometric analyses have indicated encouraging agreement with both global assessments of RP impact/severity and legacy instruments for assessing other relevant aspects of health pertinent to SSc. Further work to assess longitudinal reliability and sensitivity of change of the ASRAP questionnaire is planned.

Disclosure: J. Pauling, None; **L. Yu**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **T. Frech**, None; **A. Herrick**, None; **L. Hummers**, Boerhinger Ingelheim, 1, 5, Corbus Pharmaceuticals, 1, 5, Cumberland Pharmaceuticals, 5, Kadmon Corporation, 5, Medpace, 5; **L. Saketkoo**, None; **A. Shah**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **R. Domsic**, None.

Abstract Number: 0500

Clinical Phenotypes of Patients with Systemic Sclerosis with Distinct Molecular Signatures in the Skin

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: Although two subsets in systemic sclerosis (SSc) have been identified based on degree of skin disease, the current classification system, limited vs. diffuse cutaneous, does not reliably predict which patients will develop progressive skin fibrosis and internal organ involvement. Genome-wide analysis of gene expression in the skin has been used to classify patients with SSc into four intrinsic gene expression subsets: fibroproliferative, inflammatory, limited, and normal-like. The objective of this study was to characterize and define the clinical characteristics and markers of disease severity based upon intrinsic subset.

Methods: Subject-level data were prospectively obtained for SSc patients and healthy controls who underwent skin biopsies. Patients fulfilled the ACR/EULAR 2013 classification criteria and had clinically active disease determined by one treating physician. Paired skin biopsies of the forearm were performed: one for histology and one for DNA microarray analyses to measure gene expression. Intrinsic subsets were assigned using a trained Glmnet machine learning classifier. Clinical information including laboratory, pulmonary function test, chest high-resolution computer tomography (HRCT), echocardiography and patient-reported outcomes (PROs) were collected at baseline and longitudinally. Statistical analysis was performed to compare clinical characteristics and markers of disease severity between intrinsic subset groups (SAS, town and state).

Results: 223 participants (165 SSc and 58 control) were categorized by intrinsic subtypes (Figure 1). Demographic and clinical characteristics of SSc patients by intrinsic subset are shown in Table 1. Normal-like subset had signif-

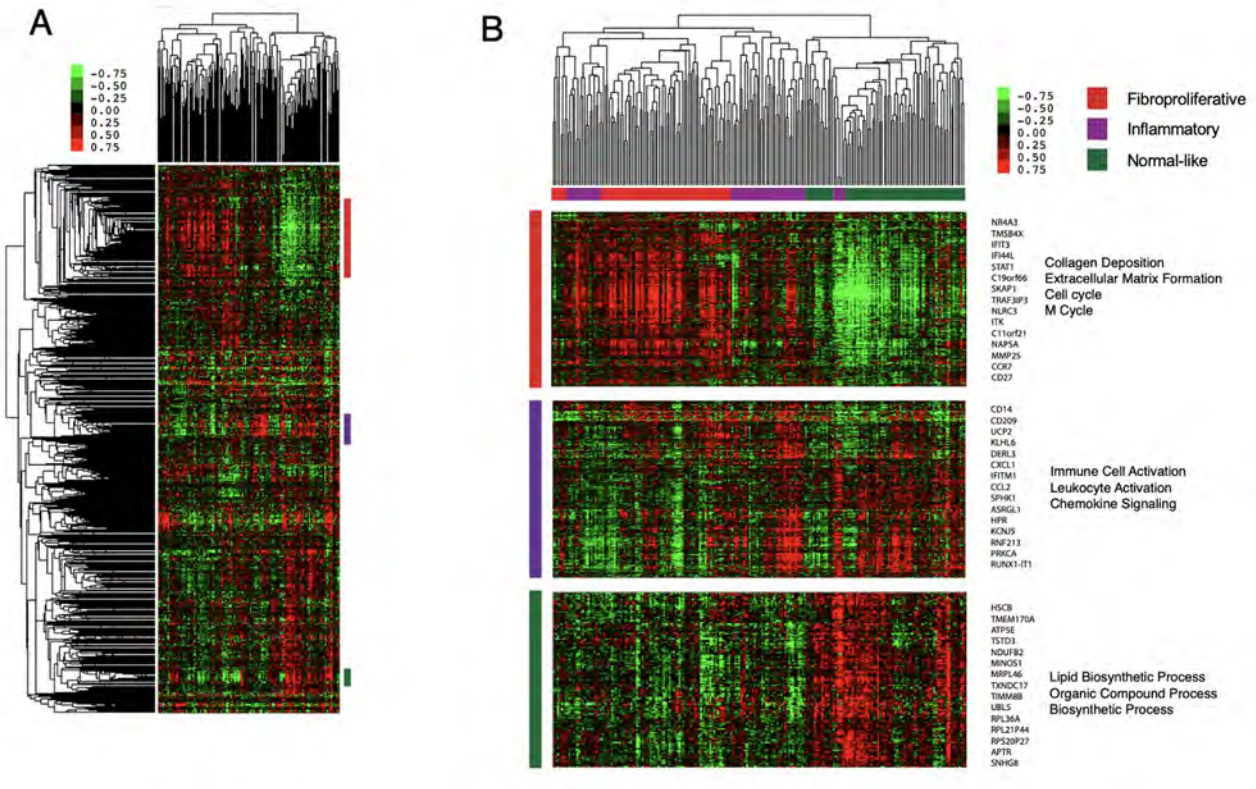

Figure 1. Gene expression signatures and cluster analysis of intrinsic subsets in patients with SSc.

Table 1. Demographic and clinical characteristics of SSc patients by intrinsic subset

Characteristics	Intrinsic Subset, n=165 (n=115 diffuse, n=50 limited cutaneous SSc)				
	Normal-like n=58	Limited n=2	Inflammatory n=72	Fibroproliferative n=33	P-value
Age, years (mean ± SD)	49.5 ± 11.8	56.5 ± 2.1	52.7 ± 9.8	47.3 ± 12.9	0.09
Sex, female, n (%)	51 (88)	2 (100)	56 (78)	28 (85)	0.45
Race, n (%)					0.22
White	47 (81.0)	2 (100.0)	52 (72.2)	24 (72.7)	
Black	6 (10.3)	0 (0.0)	7 (9.7)	8 (24.2)	
Asian	2 (3.5)	0 (0.0)	3 (4.2)	0 (0.0)	
Hispanic	1 (1.7)	0 (0.0)	9 (12.5)	1 (3.0)	
SSc subtype, %					
Limited	64.0	4.0	14.0	18.0	<.0001
Diffuse	22.6	0.0	56.5	20.9	
Disease Duration, month (mean ± SD)	69 ± 73	121 ± 5	29 ± 33	39± 50	<.0001
ANA, positive, n (%)	54 (93)	2 (100)	68 (94)	29 (88)	0.54
ANA pattern, n (%)					0.10
Centromere	9 (19)	1 (0)	3 (5)	2 (7)	
Speckled	20 (42)	2 (50)	28 (48)	8 (29)	
Homogenous	15 (31)	2 (50)	14 (24)	10 (37)	
Nucleolar	4 (8)	0 (0)	14(24)	7 (26)	
Antibodies, positive, n (%)					
Scl-70	15 (27)	9 (0.0)	14 (19)	15 (46)	0.04
ACA	11 (19)	0 (0.0)	3 (4)	2 (6)	0.04
RNA pol III	8 (14)	0 (0.0)	38 (53)	4 (12)	<.0001
Platelets, median [IQR], n	287 [89]	217 [24]	326 [132]	275.5 [76]	<.0001
ESR, median [IQR], n	18 [31]	30 [4]	19.5 [39]	14 [23]	0.82
CRP, median [IQR], n	0.5 [0.6]	0.25 [0]	0.6 [0.8]	0.5 [0.5]	0.20

icantly more limited cutaneous patients (p< 0.001) and longer disease duration (p< 0.001). SSc antibodies differed by subsets with ACA, Scl70 and RNA poly III associated with normal-like (p=0.04), fibroproliferative (p=0.04) and inflammatory (p< 0.001) subsets respectively. Pulmonary, cardiac and PROs by intrinsic subset are shown in Table 2. Inflammatory subset had significantly higher modified Rodnan skin scores (p< 0.001). Fibroproliferative subset had a trend toward worse lung fibrosis scores and significantly more ILD present on HRCT (p=0.04). For PROs, inflammatory and fibroproliferative subsets scored worse in fatigue, sleep disturbance, social participation and pain domains (p< 0.04) compared to patients in limited or normal-like subsets.

Conclusion: This study utilized molecular signatures in the skin to classify SSc patients into distinct subsets that had significantly different clinical characteristics. Patients in the normal-like subset were more likely to have limited cutaneous disease and longer disease duration, suggesting milder disease. The inflammatory subset had more severe skin disease and the fibroproliferative subset had more significant fibrotic lung disease. Both inflammatory and fibroproliferative patients endorsed worse PROs than their normal-like counterparts. This study elucidates the clinical relevance of distinct molecular subsets in the skin and contributes to the growing effort to better define and characterize the vast heterogenicity in SSc.

Table 2. Skin, pulmonary, cardiac and patient reported outcome by intrinsic subset

Mean ± SD or n (%)	Intrinsic Subset				
	Normal-like	Limited	Inflammatory	Fibro-Proliferative	p-value
Skin Score					
mRSS	8.6 ± 5.9	5.0 ± 2.8	22.1 ± 9.9	12.3 ± 7.1	<.0001
Pulmonary function tests					
FVC % Predicted	82 ± 18	77 ± 46	79 ± 18	75 ± 16	0.406
FEV1 % Predicted	82 ± 17	86 ± 16	82 ± 14	76 ± 16	0.407
TLC % Predicted	89 ± 19	94 ± 51	88 ± 17	82 ± 18	0.346
DLCO % Predicted	69 ± 20	50 ± 35	72 ± 20	63 ± 22	0.154
Chest HRCT					
Fibrosis Score	3.6 ± 4.1	6.5 ± 4.9	2.2 ± 2.9	4.3 ± 4.6	0.078
GGO Score	6.2 ± 5.4	5.5 ± 2.1	4.3 ± 4.4	7.4 ± 5.4	0.085
Total lung score	9.2 ± 8.6	12.0 ± 7.1	6.5 ± 6.4	11.7 ± 9.2	0.063
ILD present, n (%)	21 (62)	2 (100)	31 (65)	21 (91)	0.038
Echocardiogram					
LVEF %	63 ± 7	60 ± 3	62 ± 5	62 ± 5	0.846
LV mass (g/m^2)	76.6 ± 18.2	62.5 ± 1.9	80.6 ± 24.9	79.2 ± 18.4	0.602
TAPSE (cm)	2.2 ± 0.4	2.0 ± 0.1	2.2 ± 0.4	2.1 ± 0.4	0.680
RV FAC	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.4 ± 0.1	0.991
PASP (mm Hg)	32.4 ± 9.2	41.4 ± 15.9	30.9 ± 9.8	28.2 ± 7.8	0.151
Diastolic dysfunction, n (%)	23 (55)	0 (0.0)	19 (39)	9 (35)	0.195
PROMIS29					
Anxiety	52.8 ± 9.4	44.2 ± 5.5	52.0 ± 9.5	54.4 ± 8.8	0.469
Depression score	49.3 ± 8.1	44.9 ± 5.6	51.9 ± 10.1	52.7 ± 9.4	0.337
Fatigue	52.9 ± 11.1	38.4 ± 6.7	57.4 ± 8.9	57.3 ± 9.6	0.020
Physical Function	45.8 ± 9.4	46.6 ± 2.3	42.8 ± 9.4	44.1 ± 9.9	0.568
Sleep Disturbance	50.3 ± 8.4	48.5 ±10.3	55.9 ± 9.2	53.6 ± 7.1	0.037
Satisfaction with Social Participation	48.9 ± 10.1	54.6 ± 1.3	41.7 ± 11.1	42.7 ± 11.2	0.013
Pain Interference	53.7 ± 9.7	41.6 ± 0.0	58.4 ± 9.3	59.4 ± 9.4	0.011
Pain (10-point scale)	3.0 ± 2.2	0.5 ± 0.7	4.5 ± 2.4	4.5 ± 2.4	0.002

mRSS = modified Rodnan skin score, FVC=forced vital capacity, FEV1=forced expiratory volume in one second, TLC=total lung capacity DLCO=diffusion for carbon monoxide, HRCT=high-resolution computed tomography of the thorax. LVEF=left ventricular ejection fraction, LV=left ventricle, TAPSE=tricuspid annular plane systolic excursion, RV FAC=right ventricular fractional area change, PASP=pulmonary artery systolic pressure.

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Abstract Number: 0501

Immunogenicity of a Single Dose of Covid-19 Vaccination in Patients with Systemic Sclerosis with or Without Immunosupression

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Clinical (0496–0501)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Systemic Sclerosis (SSc) is a rare connective tissue disease with multi-systemic involvement, which at times requires the use of immunosuppressive medication. None of the currently approved vaccines for COVID-19 have been tested for efficacy in Immunocompromised individuals. As no data were available on the potential blunting of the immune response against the vaccine caused by immunosuppressant administration, neither on the potential effects of the vaccines on disease activity or progression, we set out to measure serum markers of disease activity and the immune response of the first dose of Oxford/AstraZeneca and Pfizer vaccine in patients with Systemic Sclerosis with or without immunosuppression.

Methods: Forty patients with SSc from our observational study were invited to participate in this study. At the time of abstract submission full data were available for twenty-two patients. Sera samples were tested before and 4 weeks after (± 7 days) the patients' first Covid vaccine using two Luminex xMAP based assays. The first (LABScreen COVID plus [CE-IVD]) that measures levels of IgG against SARS-CoV-2 spike protein subunits S1 and S2, the spike receptor-binding domain, and nucleocapsid protein [NP]. The second, a custom made multiplex assay to measure the concentration of 6 chemokines (ccl2, ccl8, ccl19, cxcl9, cxcl10, cxcl11) to determine the IFN score, as previously described (Carriero A et al 2019). Patients with known COVID-19 infection were not invited to take part in the study.

Results: Seven patients were found to have evidence of antibodies on the sample prior to vaccination and excluded from seroconversion analysis. None of the patients reported any serious adverse reaction to the vaccine, or any immediate complications, including the ones with previous signs of infection. 88% of patients on immunosuppression (Mycophenalate Mofetil [MMF] or Methotrexate [MTX]) showed no seroconversion, whereas all patients on either Hydroxychloroquine or no immunosuppression seroconverted after the first dose. None of the participants had a positive result for NP in the second sample, testifying no actual infection within the duration of the study. Regardless of immunosuppression, none of the twenty-two patients showed a significant change of serum IFN score at 4 weeks following vaccination.

Conclusion: Within the limitations of our small sample size, our data has shown that there is a clear reduction in the Covid-19 vaccines ability to produce antibodies in patients on standard immunosuppression such as MMF or MTX. On the other hand, the vaccination was safe and did not cause an increase in the serum IFN score of the patients, nor

any immediate complication, regardless of their immunosuppressive treatments. The study is currently analysing the response rate to the second dose. If results are confirmed, a booster third dose preceded by suspension of immunosuppressive therapy should be considered in this patient cohort.

Disclosure: V. Kakkar, None; **R. Ross**, None; **R. Karanth**, None; **S. Lahiri**, None; **P. Mulipa**, None; **P. Hughes**, None; **B. Clarke**, None; **C. Carter**, None; **M. Lobb**, None; **S. Savic**, None; **F. Del Galdo**, Boehringer-Ingelheim, 1, 2, 5, 6, Astra-Zeneca, 1, 2, 5, 6, Jannsenn, 6, Chemomab, 2, 5, Capella Biosciences, 2, 5, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 0502

Global Transcriptomic Profiling Identifies Differential Gene Expression Signatures Between Inflammatory and Non-inflammatory Aortic Aneurysms

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SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders (0502–0507)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Table 1. Demographic characteristics of study participants.

	Aortitis (n = 25)	Control (n = 25)
Sex (female/male)	15/10	17/8
Age (years)		
Mean±SD	74.5±5.8	72.2±6.2
Range (min–max)	61.1–84.3	54.5–83.5
ESR (mm/hr)		
Mean±SD	10.1±8.1	16.6±12.6
Range (min–max)	0–25	2–43
N/A (n)	11	15
CRP (mg/L)		
Mean±SD	5.3±3.2	10.7±20.2
Range (min–max)	2.90–14.1	2.0–64.1
N/A (n)	11	157
Treatment		
Prednisone use (n, %)	1 (4.0%)	0 (0.0 %)
Aspirin use (n, %)	15 (60.0%)	12 (48.0%)
Statin use (n, %)	9 (36.0%)	15 (60.0%)
ACE/ARB use (n, %)	11 (44.0%)	18 (72.0%)
Smoking History (n)		
Current	6	3
Former	9	8
Never	10	14
History of other rheumatic diseases		
GCA[α]	8	0
Others (Iritis, Psoriasis, gout)	0	3
None	17	22

[α]Giant cell arteritis

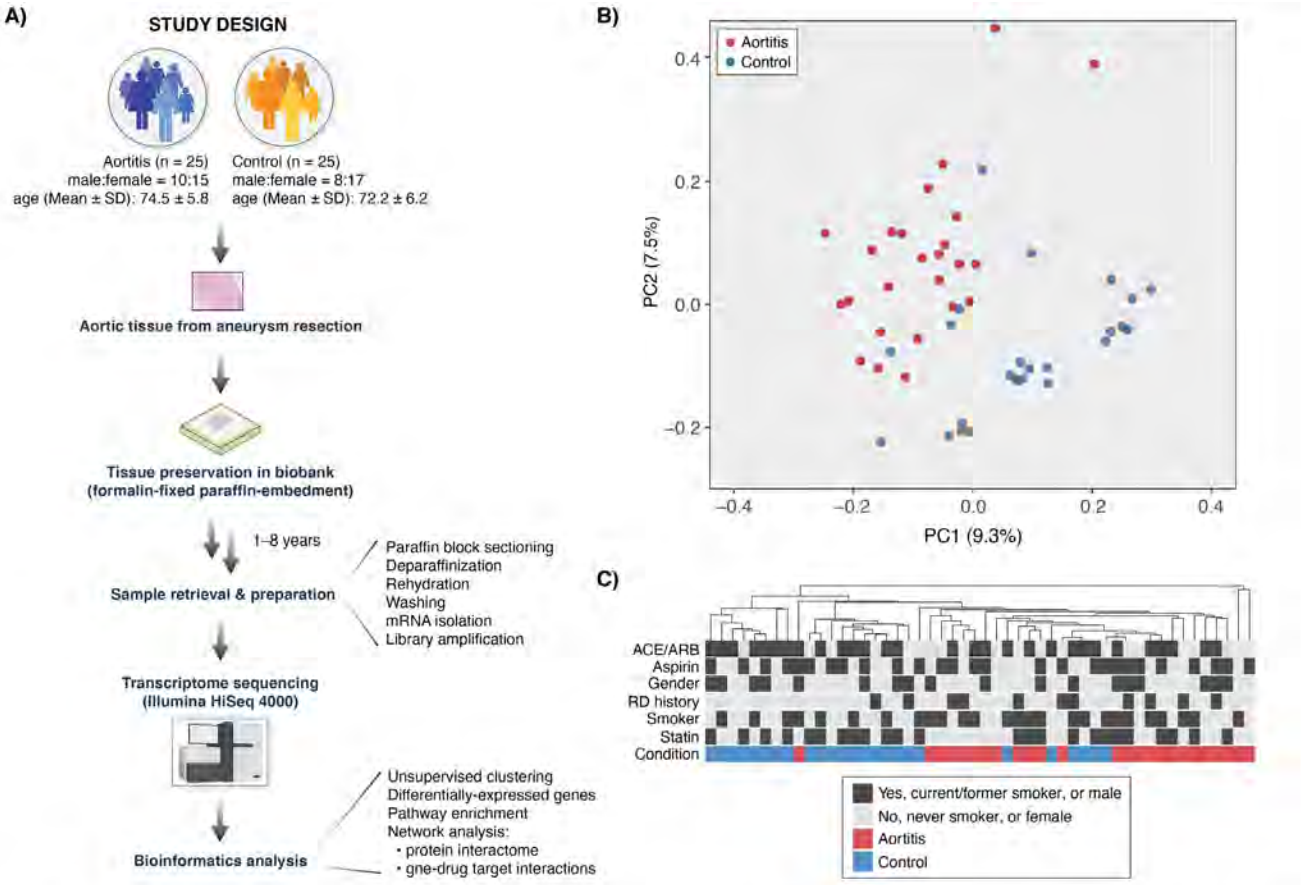

Figure 1. Study design and data analysis pipeline on genome-wide expression (transcriptome) profiles of inflammatory and non-inflammatory aortic aneurysms.
(A) Study design to investigate transcriptomic differences between inflammatory and non-inflammatory aortic aneurysm.
(B) PCA on gene expression profiles (26,475 total genes) from 50 temporal artery tissue samples across two patient groups (Aortitis = 25; Non-inflammatory aneurysm control = 25).
(C) Hierarchical clustering on all 50 gene expression profiles shows that samples group together mostly by disease condition (aortitis/control) rather than by clinical characteristics (i.e., ACE/ARB use, aspirin use, gender, RD history, smoking status, and statin use).
PCA: principal component analysis; ACE/ARB: angiotensin converting enzyme inhibitors/angiotensin receptor blockers; RD history: history of other rheumatic diseases.

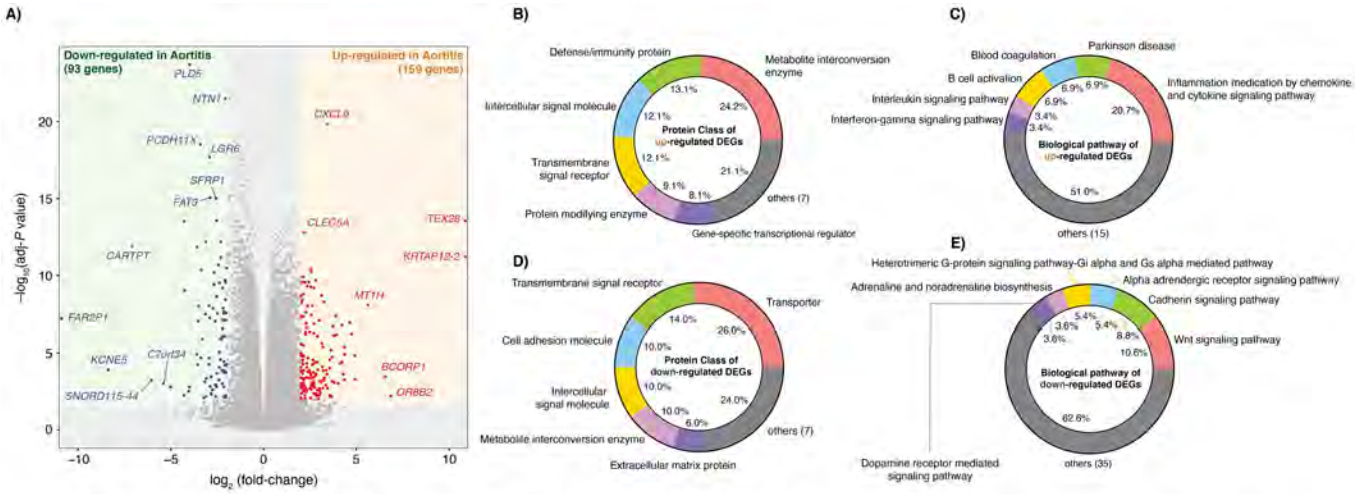

Figure 2. Differentially-expressed genes (DEGs) and their functional categories reveal transcriptomic signatures of aortitis.
(A) A total of 159 and 93 genes were identified to be significantly up-regulated and down-regulated, respectively, in aortitis (Benjamini-Hochberg adjusted P-value < 0.01 and |log2(fold-change in mean expression values)| > 2).
(B) Functional annotations (protein class) of the up-regulated differentially expressed genes (DEGs).
(C) Functional annotations (biological pathway) of the up-regulated DEGs.
(D) Functional annotations (protein class) of the down-regulated DEGs.
(E) Functional annotations (biological pathway) of the down-regulated DEGs.
DEGs and fold-changes were calculated by DEseq2 (v1.30.0) while controlling for clincial covariates (i.e., ACE/ARB, statin, history of RD).
Functional classifications were performed using the PANTHER Database (v16.0).

Background/Purpose: Non-infectious aortitis may be a manifestation of systemic large vessel vasculitis such as giant cell arteritis (GCA) or may be a form of single organ vasculitis termed 'clinically isolated aortitis' (CIA). Aortitis is generally diagnosed after aortic aneurysm surgery and histopathologic examination of resected aortic tissue. At current, there is no specific biomarker that assists physicians in their diagnostic and treatment decisions for aortitis. Moreover, a genome-wide expression analysis to detect differences in transcriptomic signatures between inflammatory and non-inflammatory aortic aneurysms has not been conducted to date. To this end, we used global transcriptome profiling (RNA-seq) to provide novel insights into the biomolecular processes underlying inflammatory aortic aneurysms. We also compared the transcriptomic signature of aortic tissue from patients with CIA and GCA.

Methods: RNA-seq (HiSeq 4000) was performed on formalin-fixed paraffin-embedded (FFPE) resected aortic tissue from 25 aortitis and 25 non-inflammatory aneurysm control patients undergoing surgical aortic repair (Table 1, Fig. 1). Differentially expressed genes (DEGs) between the two groups were identified while controlling for the potentially confounding effects (i.e., use of Statin, use of angiotensin converting enzyme inhibitors or angiotensin receptor blockers, and history of other rheumatic diseases). Protein-protein interactions from STRING and drug-gene pharmacological interaction information from DBIdb were used to construct DEG interactome and pharmacogenomic networks, respectively. In addition, DAVID was used to identify enriched biomolecular functions (Gene Ontology) for the gene sets from the DEGs, the DEG interactome network, and the pharmacogenomic network.

Results: We identified 159 and 93 genes to be significantly up-regulated and down-regulated, respectively, in aortitis (adj-$P < 0.01$, $|\log2(FC)| > 2$) compared to non-inflammatory aortic tissue (Fig. 2). Up-regulated genes were enriched with functions related to immune response and inflammation, defense against bacteria, and interferon response pathways; while the down-regulated genes were enriched with plasma membrane and neuronal processes. Of note, the gene expression profiles of aortic tissue from patients with aortitis related to GCA (n=8) was no different than those of aortic tissue from patients with CIA (n=17). In aortitis, 30 out of 36 genes from the hub of the DEG interactome network were enriched with immune-related functions. Finally, our pharmacogenomic network analysis identified 16 genes that could be targeted with FDA-approved drugs.

Conclusion: Global transcriptome profiling on FFPE aortic specimens from patients with aortitis identified upregulated genes related to immune response and inflammation. Interestingly, we demonstrate for the first time that the transcriptomic signature of CIA is similar to that of GCA, suggesting that CIA may be a limited presentation of GCA. This study also facilitates the characterization of dysregulated molecular pathways in aortitis, and could provide a promising direction for biomarker discovery and treatment.

Disclosure: B. Hur, None; **M. Koster**, None; **J. Jang**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **J. Sung**, None.

Abstract Number: 0503

18F-fluorodeoxyglucose Positron Emission Tomography as a Predictor of Angiographic Progression of Disease in Large-vessel Vasculitis

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SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders (0502–0507)
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Background/Purpose: There is limited prospective data characterizing arterial lesions over time in giant cell arteritis (GCA) and Takayasu's arteritis (TAK), the two main forms of large-vessel vasculitis (LVV). FDG-PET can detect vascular inflammation. Whether vascular PET findings predict angiographic change is unknown.

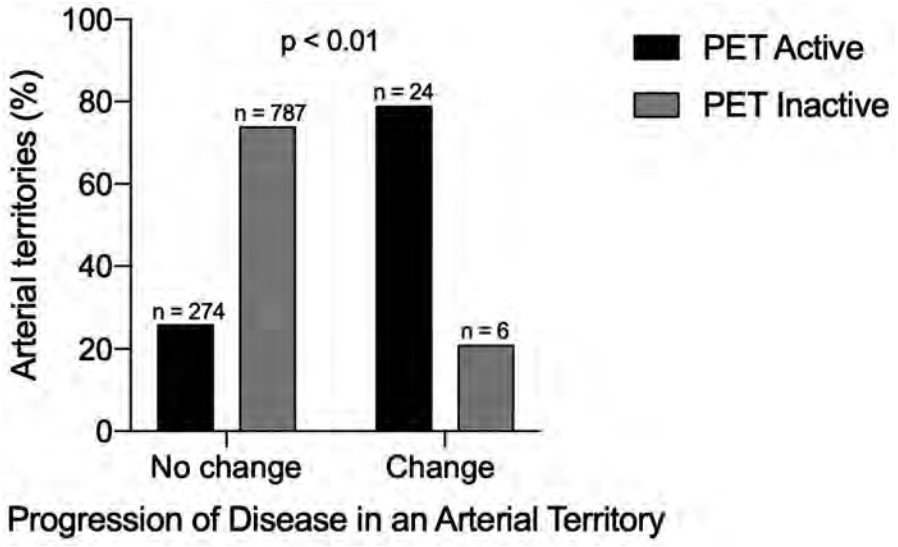
Methods: Patients with GCA or TAK were recruited into a prospective, observational cohort. All patients underwent magnetic resonance (MR) or computed tomography (CT) angiography and a follow-up study ≥6 months after baseline per a standardized imaging protocol. Arterial lesions, defined as stenosis, occlusion, or aneurysm, were evaluated in 4 segments of the aorta and 13 branch arteries by a central reader blinded to clinical status. Development of new lesions in these same territories was recorded, and existing lesions were characterized as improved, worsened, or unchanged over time.

All patients underwent FDG-PET on the same date as angiography. Qualitative assessment of FDG uptake was performed in each corresponding arterial territory evaluated by angiography. Active vasculitis was defined as greater FDG uptake in the arterial wall compared to the liver by visual inspection.

Conditional logistic regression using a within-person matched design selecting for cases of asymmetric angiographic progression in paired arterial territories (e.g. bilateral subclavian arteries) was performed to evaluate whether FDG-PET activity was independently associated with angiographic progression, controlling for all person-level confounders.

Results: 1162 arterial territories were evaluated from 70 patients with LVV (TAK=38; GCA=32). Over 1.6 years of median follow-up, new lesions developed only in 8 arterial territories, exclusively in 5 patients with TAK. Arterial lesions improved in 16 territories (GCA = 7, TAK = 9) and worsened in 6 territories (GCA = 1, TAK = 5). Typically, angiographic change was asymmetric in paired arteries (26/30 territories).

FDG-PET activity was evaluated in 1091/1162 (94%) of corresponding arterial territories. PET activity in an arterial territory at baseline was significantly associated with change in that arterial territory on follow-up angiography



($p < 0.01$), with a sensitivity of 80% and specificity of 74% **(FIGURE)**. Most arterial territories without PET activity at baseline remained unchanged over time by angiography, yielding a negative predictive value of 99%. Most territories with PET activity also did not show change over time, but of the territories with angiographic change, the majority had PET activity (24/30 territories). Using conditional logistic regression, an arterial territory with baseline PET activity had a 3-fold increased risk for angiographic progression of disease compared to the paired arterial territory without PET activity ($p < 0.01$).

Conclusion: Development of angiographic change was infrequent in this cohort of patients with LVV. Lack of PET activity was strongly associated with stable angiographic disease. Most cases of angiographic change were asymmetric in paired arterial territories with PET activity present only in the affected side at baseline. These data may inform recommendations for imaging monitoring in LVV.

Disclosure: K. Quinn, None; **M. Ahlman**, None; **H. Alessi**, None; **A. Malayeri**, None; **J. Marko**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 0504

Longitudinal Patterns of Vascular Inflammation in Large-vessel Vasculitis

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SESSION INFORMATION
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Session Type: Abstract Session
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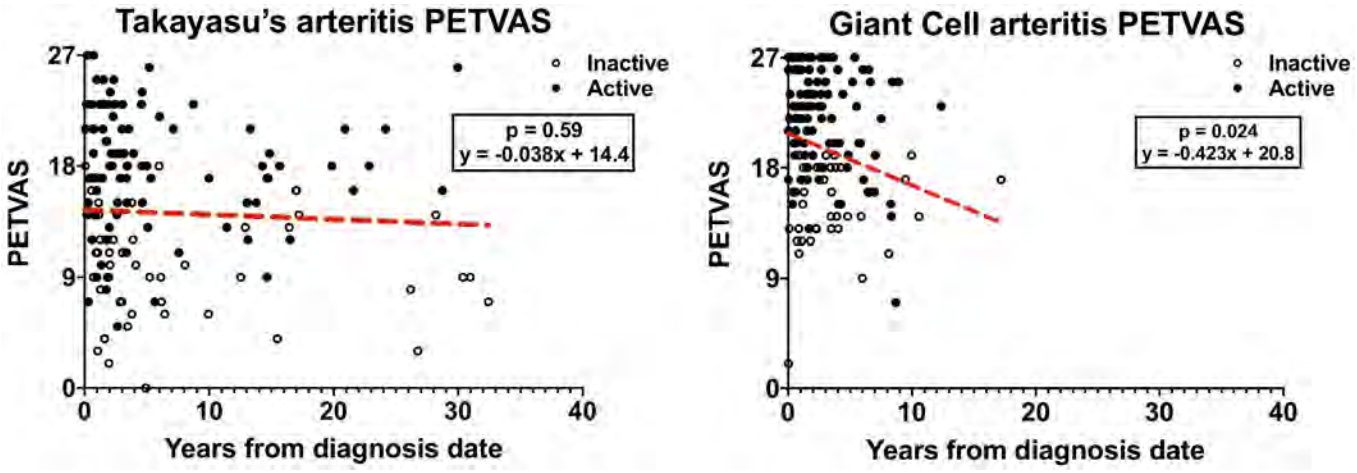
Background/Purpose: The two main forms of large vessel vasculitis (LVV), giant cell arteritis (GCA) and Takayasu's arteritis (TAK), are clinically heterogenous diseases with variable disease courses. Although ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) can be used to detect vascular inflammation, there is little data detailing PET activity over time in LVV.

Methods: Patients with TAK or GCA who fulfilled existing classification criteria were recruited into a single-center prospective, observational cohort. Patients could be enrolled at any point in the disease course. All patients underwent FDG-PET at recruitment per a standardized imaging protocol with follow up imaging at ≥6-month intervals whenever possible. Qualitative assessment of FDG uptake was performed via visual assessment of 9 arterial territories each scored on a scale from 0-3, yielding a summary score ranging from 0-27, PETVAS (PET Vascular Activity Score). Higher scores indicate greater global burden of vascular inflammation. Each study was subjectively interpreted by a central reader, blinded to clinical status, as active or inactive vasculitis. Fisher exact and Mann-Whitney *U* tests were used to compare variables. Linear regression was used to study trends in PETVAS over time.

Results: A total of 322 FDG-PET scans were examined in 121 LVV patients (TAK = 66; GCA = 55). There were 160 FDG-PET scans from TAK patients and 162 scans from GCA patients.



In the first year after diagnosis, 48 patients (TAK = 21; GCA = 27) had at least one PET at a mean disease duration of 175 days (TAK = 146 days; GCA = 197 days). Of these, 37 patients (77%, TAK = 17; GCA = 20) had an active FDG-PET scan. Median PETVAS in the first year after diagnosis was significantly greater in GCA than TAK (22 vs. 17, $p < 0.01$), but median daily steroid dose at time of imaging was not significantly different between GCA and TAK (10 vs. 7.5mg/day, $p = 0.32$). One to five years after diagnosis, 68 patients (TAK = 34; GCA = 34) contributed 152 scans (TAK = 68, GCA = 84), and 105 (69%, TAK = 44; GCA = 61) showed active disease. Beyond 5 years, 38 patients (TAK = 27; GCA = 11) contributed 77 scans (TAK = 49, GCA = 28), and 45 (58%, TAK = 27; GCA = 18) showed active disease.

PETVAS scores significantly decreased at a rate of -0.42 PETVAS/year over a mean disease duration of 2.9 years for GCA patients. PETVAS scores did not significantly decrease for TAK patients over a mean disease duration of 6.3 years (FIGURE).

Of 36 patients with ≥3 FDG-PET scans performed >1 year after diagnosis, scans from 13 patients (TAK = 6; GCA = 7) always showed active disease, scans from 3 patients never showed active disease (TAK = 3; GCA = 0), and scans from 20 patients (TAK = 8; GCA = 12) showed active or inactive disease on serial imaging.

Conclusion: Longitudinal patterns of vascular PET activity are different between TAK and GCA. Patients with GCA have a higher burden of vascular inflammation on FDG-PET during the first year of disease compared to TAK. On average, vascular PET activity significantly decreases over time only in GCA. Most patients with LVV continue to have active vasculitis on PET years after diagnosis despite treatment. Changes in PET activity are dynamic, even in later phases of disease, suggesting LVV is a chronic, inflammatory and relapsing disease.

Disclosure: H. Alessi, None; **K. Quinn**, None; **M. Ahlman**, None; **Y. Luo**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 0505

Risk of Venous and Arterial Thromboembolism in Patients with Giant Cell Arteritis And/or Polymyalgia Rheumatica: A Veterans Health Administration Population-Based Study in the United States

Despina Michailidou[1], Tianyu Zhang[2], Pavlos Stamatis[3] and Bernard Ng[4], [1]Division of Rheumatology, University of Washington, Seattle, WA, [2]Department of Biostatistics, University of Washington, Seattle, WA, [3]Lund University, Lund, Sweden, [4]Rheumatology Section, VA Puget Sound HCS, University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Saturday, November 6, 2021

Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders (0502–0507)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are two chronic systemic inflammatory diseases that primarily affect elderly women. Both diseases can be complicated by inflammatory induced thrombosis, however the risk of thromboembolism among male patients with GCA and/or PMR is yet unknown. Due to the tight relationship between inflammation and thrombosis contributing to increased morbidity and mortality, we sought to determine the incidence rate of venous and arterial thrombotic events in patients with GCA and/or PMR among Veterans of the US. The objective of this study was to evaluate the risk of thromboembolism and retinal vascular events in GCA, PMR, and/or overlap of GCA with PMR compared to osteoarthritis (OA) in a Veteran's based population.

Methods: 1,581 patients with GCA, 10,940 with PMR, and 1,230 with GCA and PMR as well as 120,708 age- and sex-matched patients with OA, were identified in this retrospective study. Incidence rate ratios (IRR) of pulmonary embolism (PE), deep venous thrombosis (DVT), arterial thromboembolism of extremities (ATE), central retinal artery and vein occlusion (CRAO and CRVO) were calculated. We also calculated hazard ratios (HRs) of thromboembolic events in study groups, adjusting for independent risk factors of thromboembolism.

Results: Patients with GCA, PMR and GCA with PMR had higher IRs of all thromboembolic events as compared to patients with OA (Table 1). Patients with overlap of GCA and PMR had a lower risk of deep venous thrombosis (HR: 2.13, 95%CI:1.53-2.97, p< 0.001) and retinal vascular events (HR: 4.46, 95%CI:2.49-7.96, p< 0.001) as compared to patients with GCA (HR: 4.17, 95%CI:3.38-5.15, p< 0.001, and HR: 10.60, 95%CI: 7.56-14.86, p< 0.001, respectively), but a higher risk of retinal vascular events as compared to patients with PMR (HR: 2.33, 95%CI:1.75-3.11, p< 0.001) (Table 2).

Table 1. Risk of Incident PE, DVT, ATE, and combined CRAO/ CRVO among patients with GCA, PMR, GCA&PMR and OA

	GCA N=1,581	PMR N=10,490	GCA&PMR N=1,230	OA N=120,708
PE				
Cases, n	32	130	22	596
Crude incidence (%)	2	1.2	1.8	0.5
Incidence Rate/1000 Person-years	3.68	2.04	3.73	0.58
Incidence Rate Ratio (95% CI)	6.26 (4.30-8.78)	3.47 (2.89-4.18)	6.34 (4.02-9.45)	1
DVT				
Cases, n	69	217	25	1240
Crude incidence (%)	4	2	2	1
Incidence Rate/1000 Person-years	8.10	3.43	4.25	1.23
Incidence Rate Ratio (95% CI)	6.58 (5.12-8.32)	2.79 (2.41-3.22)	3.46 (2.26-5.02)	1
ATE				
Cases, n	10	23	6	176
Crude incidence (%)	0.6	0.2	0.5	0.1
Incidence Rate/1000 Person-years	1.13	0.35	1.00	0.17
Incidence Rate Ratio (95% CI)	6.57 (3.24-11.77)	2.07 (1.30-3.12)	5.81 (2.28 -11.98)	1
Combined CRAO/CRVO				
Cases, n	24	53	13	285
Crude incidence (%)	1.5	0.5	1	0.2
Incidence Rate/1000 Person-years	2.76	0.82	2.19	0.28
Incidence Rate Ratio (95% CI)	9.84 (6.32-14.59)	2.94(2.17 -3.91)	7.82 (4.26 -13.06)	1

Table 2. Hazard Ratios (HRs) of PE, DVT, ATE, and combined CRAO/CRVO associated with GCA, PMR, and GCA&PMR compared to OA

	GCA	PMR	GCA&PMR
PE (HR, 95%CI, p-value)	4.29 (3.15-5.85), <0.001	3.03 (2.57-3.57), <0.001	3.42 (2.29-5.10), <0.001
DVT (HR, 95%CI, p-value)	4.17 (3.38-5.14), <0.001	2.25 (1. 99-2.54), <0.001	2.13 (1.53-2.97), <0.001
ATE (HR, 95%CI, p-value)	3.25 (1.82-5.82), <0.001	1.80 (1.27-2.55), <0.001	3.10 (1.53-6.29), <0.001
CRAO /CRVO (HR, 95%CI, p-value)	10.60 (7.56-14.86), <0.001	2.33 (1.75-3.11), <0.001	4.46 (2.49-7.96), <0.001

Conclusion: The risk of thromboembolic events was higher in patients with GCA, PMR, and GCA with PMR compared to referenced population, and differed based on disease diagnosis. These findings may alert providers to be mindful of the importance for close monitoring of these patients for thromboembolic risk factors and may emphasize the need for a risk stratification strategy that would allow identification of high-risk patients.

Disclosure: D. **Michailidou**, None; **T. Zhang**, None; **P. Stamatis**, None; **B. Ng**, None.

Abstract Number: 0506

Transcriptomic Changes Induced by Mavrilimumab versus Tocilizumab in ex-vivo Cultured Arteries from Patients with Giant-cell Arteritis

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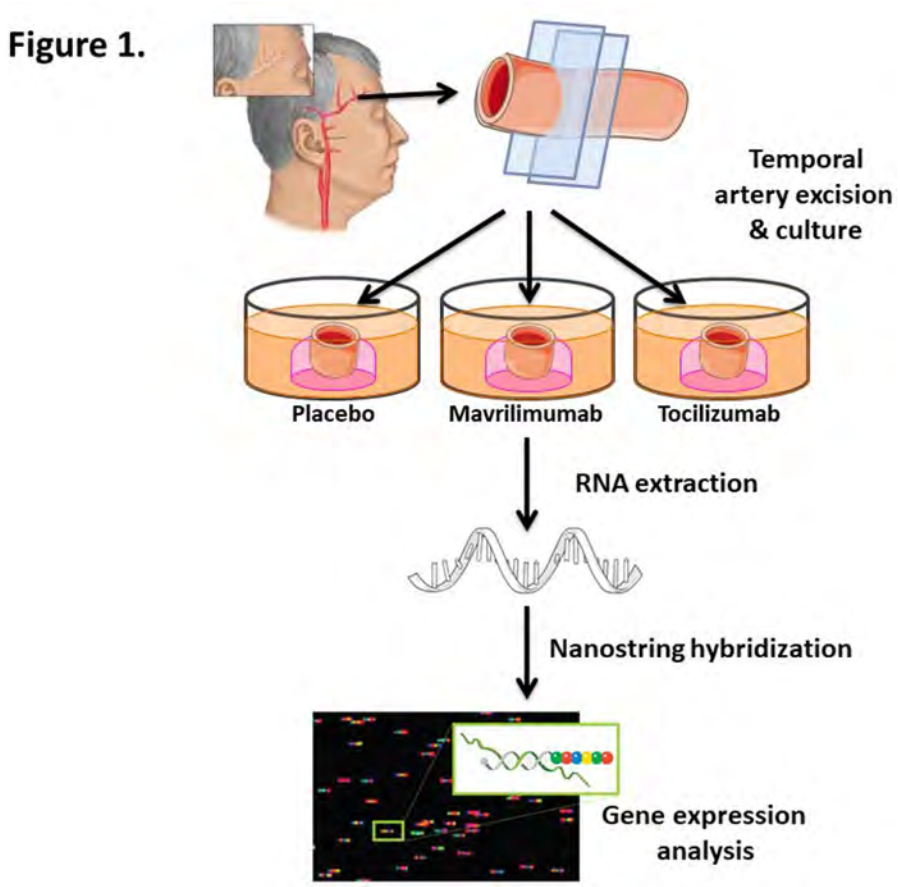
SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders (0502–0507)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Giant cell arteritis (GCA) is a chronic disease, and affected patients suffer from relapses and glucocorticoid (GC)-related toxicity. Targeted therapies are emerging with the aim of achieving better disease control and reducing GC exposure. Blocking IL-6 receptor with tocilizumab has been a major advance in the treatment of GCA. However, approximately 40% of patients treated with tocilizumab in combination with GCs experience a flare or tocilizumab-related adverse event. Blocking GM-CSF receptor a with mavrilimumab significantly reduced risk of relapse and improved sustained remission at week 26 vs placebo in a Phase 2 trial. Not all patients satisfactorily respond to any therapy, indicating heterogeneity in leading pathogenic pathways among patients. For these reasons, it is crucial to understand the specific impact of targeted therapies on vascular lesions.

In this study we investigated transcriptomic changes induced by tocilizumab or mavrilimumab in *ex-vivo* cultured arteries from patients with GCA.

Methods: Temporal artery sections obtained for diagnostic purposes from 11 patients with histopathologically-confirmed GCA and 3 controls were cultured *ex-vivo* and exposed to placebo, mavrilimumab, or tocilizumab (both at 20 µg/mL) for 5 days (Fig 1). Of 11 GCA donors, 2 had received no treatment prior to biopsy, 2 had received a single prednisone (60 mg) dose, 1 had received 2 daily doses, and the remaining 6 had extended treatment; in prednisone-



treated patients, mean (SEM) treatment duration was 17.9 ±8.7 days. Samples were homogenized, and total RNA was extracted with TRIzol reagent. 100 ng of RNA per sample were processed with Nanostring Inflammation gene expression assay (256 transcripts) and hybridized using nCounter Prep Station. Barcode counts from nCounter Digital Analyzer were processed with nSolver 4.0 Software. Normalised data were analyzed using R Studio 4.0.5 and IBM SPSS 22.0, and paired Wilcoxon tests were applied individually to each treatment comparison group for each analysed gene.

Results: 67 out of 250 transcripts were differentially expressed between arteries from GCA patients and arteries from control patients (all placebo-treated). Of those, only 9 transcripts remained significant after correction for multiple comparisons, with a false discovery rate ≤0.05. 81 transcripts were differentially expressed in at least one comparison across groups (Fig 2). 15 transcripts were lower, and 6 were higher in the mavrilimumab group vs placebo; 3 transcripts were lower, and 2 were higher in the tocilizumab group vs placebo (Fig 3A-3B). Most changes elicited between treatments were unique, but CXCL-1 was common (Fig 3C). None remained significant after correction for multiple comparisons.

Conclusion: Mavrilimumab and tocilizumab have a different transcriptomic impact on cultured arteries from patients with GCA, with some overlapping effects, although differential effects may have been attenuated by prior GC use. A better understanding of the impact of targeted therapies on vascular inflammation is needed to improve treatment options for patients with GCA.

Figure 2.

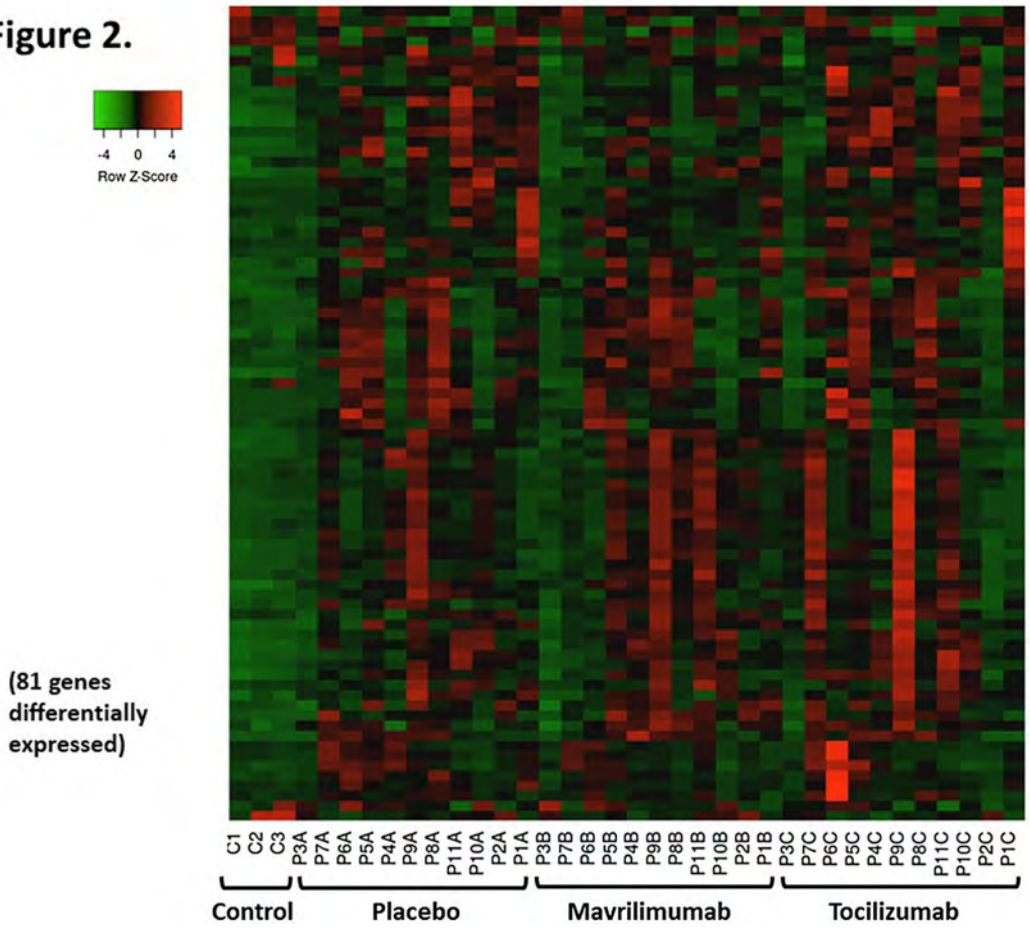
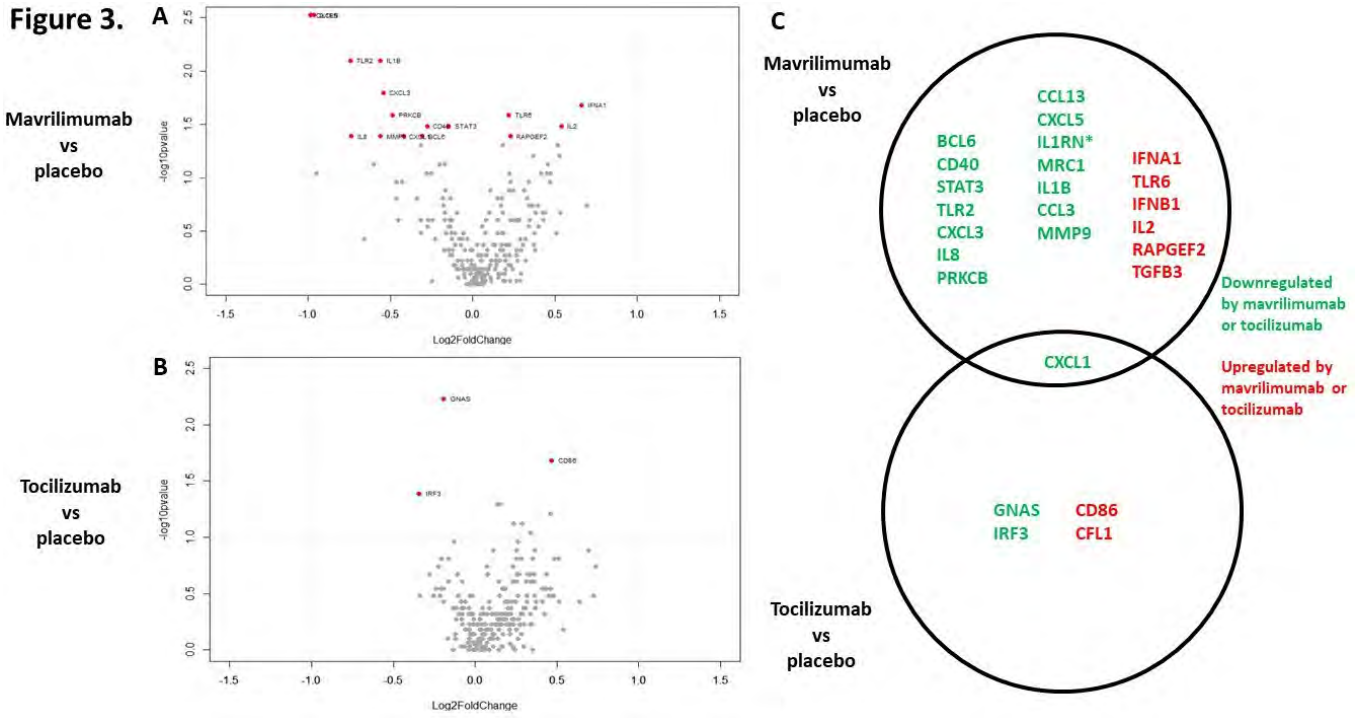


Figure 3.



Disclosure: M. Corbera- Bellalta, Agencia Estatal de Investigación (PID2020-114909RB-I00), 12, funding, Vasculitis Foundation, 12, funding; **F. Kamberovic**, ITN-HELICAL (MSC actions), 12, funding; **F. Araujo**, None; **R. Alba-Rovira**, Instituto de Salud Carlos IIII (Río Hortega), 12, Instituto de Salud Carlos IIII (Río Hortega); **G. Espigol-Frigolé**, None; **M. Alba**, BITRECS program, 12, funding; **S. Prieto-Gonzalez**, None; **J. Hernández-Rodríguez**, None; **P. Pérez-Galán**, None; **A. Joseph**, Kiniksa Pharmaceuticals Corp., 3, 11; **J. Paolini**, Kiniksa Pharmaceuticals Corp., 2, 10, 11; **M. Cid**, Kiniksa, 5, 12, meeting attendance support, Janssen, 2, GlaxoSmithKline, 2, 12, educational support, AbbVie, 2, Vifor, 12, educational support, Roche, 12, meeting attendance support.

Abstract Number: 0507

Tocilizumab in Patients with New Onset Polymyalgia Rheumatica (PMR-SPARE) – a Phase 2/3 Randomized Controlled Trial

Michael Bonelli[1], Helga Radner[1], Josef Smolen[1], Martina Durechova[1], Jutta Stieger[2], Rusmir Husic[3], Andreas Kerschbaumer[1], Christian Dejaco[4] and Daniel Aletaha[5], [1]Medical University of Vienna, Vienna, Austria, [2]2nd Department of Medicine, Hietzing Hospital, Vienna, Austria, [3]Medical University of Graz, Graz, Austria, [4]Rheumatology, Hospital of Brunico (SABES-ASDAA), Brunico, Italy, Brunico, Italy, [5]Medical University Vienna, Vienna, Austria

SESSION INFORMATION
Session Date: Saturday, November 6, 2021
Session Title: Abstracts: Vasculitis – Non-ANCA-Associated & Related Disorders (0502–0507)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: PMR is the second most common inflammatory rheumatic disease of people aged 50 years or older. Glucocorticoid therapy is highly effective, but many patients require treatment for several years with significant risk of adverse events. Therefore, effective glucocorticoid sparing agents are needed. Here we investigate the efficacy and safety of tocilizumab versus placebo on background treatment with glucocorticoids in patients with new onset PMR.

Methods: In this double-blind, multi-center phase 2/3 clinical trial, we randomly assigned patients from three centers with new onset PMR in a 1:1 ratio to receive subcutaneous tocilizumab at 162mg weekly or matching placebo for 16 weeks, with 8 weeks of follow-up. All patients received oral prednisone at a starting dose of 20mg, but were rapidly tapered to nil over eleven weeks. The primary endpoint was the proportion of patients in glucocorticoid-free remission at week 16; key secondary endpoints, including time to first relapse and cumulative glucocorticoid dose at weeks 16 and 24, were evaluated. This study is registered with clinicaltrials.gov (NCT03263715).

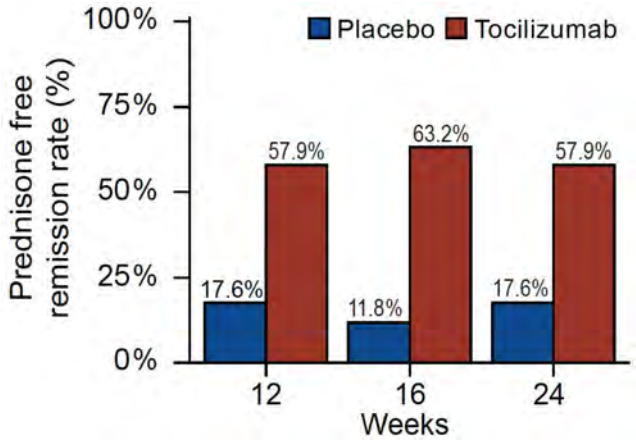


Figure 1. GC-free remission in PMR patients treated with TCZ vs Placebo.

Results: In accordance with the power calculation informed by previous open studies, 36 patients were randomly assigned to tocilizumab (n=19) or placebo (n=17). Glucocorticoid-free remission at week 16 was achieved in 12/19 patients treated with tocilizumab (63.2%) vs 2/17 patients treated with placebo (11.8%), corresponding to an odds ratio of 12.9 (95 % confidence interval: 2.2 to 73.6) in favor of tocilizumab (p=0.002 by Fisher's exact test). Mean (±SD) time to first relapse was 130±13 and 82±11 days (p=0.007), and the median (interquartile range) cumulative glucocorticoid dose was 727 (721;842) and 935 (861;1244) mg (p=0.003), respectively (Figure 1).

In hierarchical analyses, statistical significance was reached for many secondary outcomes including cumulative prednisone dose at week 24 **(Table 1)**.

Serious adverse events were observed in five patients receiving placebo and in one patient receiving tocilizumab.

Conclusion: In this first randomized controlled trial of tocilizumab in PMR, patients with new onset PMR undergoing rapid glucocorticoid tapering, tocilizumab was superior to placebo regarding sustained glucocorticoid-free remission, time to relapse, and cumulative glucocorticoid dose.

Table 1. Secondary endpoints in the intention to treat population

Testing hierarchy	Secondary endpoints*	Tocilizumab	Placebo	p-value
1	Proportion of patients in glucocorticoid-free remission at week 12	57.9%	17.6%	0.02
2	Proportion of patients in glucocorticoid-free remission at week 24	57.9%	17.6%	0.02
3	Time to first relapse (days; mean±SE)	130 (±13)	82 (±11)	0.007
4	Cumulative prednisone dose at week 16 (mg)	727 (721-842)	935 (861 - 1244)	0.003
5	Cumulative prednisone dose at week 24 (mg)	781 (721-972)	1290 (1106 - 1809)	0.001
6	Proportion of subjects with increased ESR (>20mm/h) at week 24 **or** Proportion of subjects with increased CRP (> 5mg/L) at week 24	21.1% 42.1%	47.1% 52.9%	n.r. n.r.
7	Pain by visual analogue scale (mm) at week 16	12.0 (4.0-29.0)	15.0 (1.5 - 45.5)	n.d.
8	Patient global assessment of disease activity by visual analogue scale (mm) at week 16	8.0 (3.0-25.0)	16.0 (3.0 - 50.0)	n.d.
9	Evaluator global assessment by visual analogue scale (mm) at week 16	2.0 (0-6.0)	5.0 (1.0 - 30.0)	n.d.
10	Short Form-36 (Physical Component Score) at week 16	56.3 (48.8-61.0)	46.9 (42.2 - 49.8)	n.d.
11	Health Assessment Questionnaire (0-3) at week 16	0.0 (0.0-0.5)	0.88 (0.13 - 1.13)	n.d.

* Data shown are medians and interquartile ranges, unless stated otherwise n.d., not done (given the hierarchical testing rule); n.r., not reported (first non-significant value in the hierarchical testing)

Disclosure: M. Bonelli, None; **H. Radner**, None; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **M. Durechova**, None; **J. Stieger**, None; **R. Husic**, None; **A. Kerschbaumer**, ABBVIE, 2, bristol-meyers squibb, 2, celgene, 2, Eli Lilly, 2, gilead, 2, Merck Sharp and Dohme, 2, Novartis, 2, Pfizer, 2; **C. Dejaco**, None; **D. Aletaha**, AbbVie, 2, 5, Janssen, 2, 5, Medac, 2, 5, Merck, 2, 5, 6, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Novartis, 2, 5, 6, Bristol-Myers Squibb, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6.

Abstract Number: 0508

The Impact of Macrophages Stimulated with Malondialdehyde-Acetaldehyde And/or Citrulline Modified Proteins on Fibroblasts Activation

Nozima Aripova, Michael Duryee, Evan Ryan, Peter Maloley, Bryant England, James O'Dell, Ted Mikuls and Geoffrey Thiele, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In rheumatoid arthritis (RA), chronic synovial inflammation is accompanied by fibrotic responses that together lead to pannus formation and progressive joint damage. Exposure to malondialdehyde-acetaldehyde adducts (MAA) and/or citrullinated (CIT) proteins in isolation or in combination significantly influence in vitro inflammatory and fibrotic responses in macrophage and fibroblast cell lines in isolation. However, the potential interaction between these two cell types in the context of exposure to different post-translationally (co-)modified proteins has not been well delineated. The purpose of this study was to evaluate whether soluble factors secreted by macrophages (U937 cells) in response to MAA and/or CIT modified proteins affect the inflammatory and/or fibrotic responses by human fibroblast-like synoviocytes derived from RA synovium (HFLS-RA).

Methods: PMA-treated U937 cells were stimulated with MAA, CIT, or MAA-CIT modified human serum albumin (HSA) or fibrinogen (FIB) for 24 hours. Cell supernatants were collected and analyzed for the following cytokines: MIP-1α, IL-1β, and IL-18 using Meso Scale Discovery (MSD) platform. In a separate experiment, HFLS-RA cells were co-incubated with previously collected U937 supernatants (following antigen stimulation as above) and mRNA was isolated to evaluate fibrotic markers with PCR: type II collagen (COL2A1), MMP9, and vimentin (VIM). To account for the fact that increased mRNA expression could derive from modified antigens in the supernatant, we set a control following direct stimulation of HFLS-RA cells with MAA and/or CIT modified antigen in the absence of supernatants. One-way ANOVA was used to compare cytokine and mRNA levels across groups.

Results: Stimulation of U937 cells with MAA, CIT, or MAA-CIT modified HSA demonstrated a significant increase in MIP-1α and IL-1β release (**Fig.1A, C**). In contrast, MIP-1α and IL-1β release were the greatest with FIB-CIT stimulation, followed by FIB-MAA-CIT (**Fig.1B, D**). IL-18 concentrations were increased significantly with HSA-MAA, HSA-MAA-CIT, and FIB-MAA-CIT stimulation (**Fig.1E, F**). When HFLS-RA cells were stimulated with HSA-MAA treated U937 supernatants, mRNA levels of COL2A1 and MMP9 increased 3 and 4-fold, respectively, compared to HSA-MAA stimulation without U937 supernatants (**Fig.2A**). Dually modified (MAA-CIT) HSA and FIB treated U937 supernatants increased HFLS-RA mRNA levels for VIM (**Fig.2A, B**). FIB-CIT and FIB-MAA-CIT treated U937 supernatants

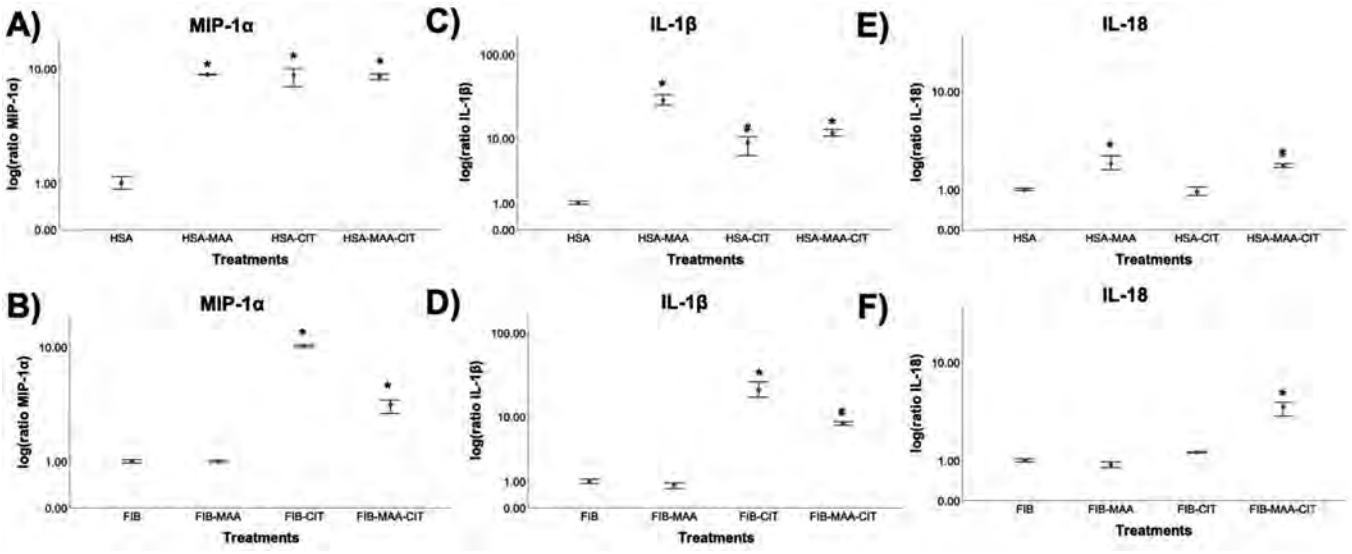


Figure 1. Cytokine release from stimulated U937 cells. U937 cells were incubated with HSA (A,C, and E) and FIB (B,D and F) modified antigens. Afterwards, the supernatants were collected for analysis of; MIP-1**α** (A,B), IL-1**β** (C,D), and IL-18 (E,F) release using Mesoscale Discovery assay kit. The concentration of all cytokines were measured in pg/mL and normalized to native protein. Log based 10 ratio of modified protein to native protein is represented on y-axis (HSA and FIB respectively). #p<0.05, *p<0.001, n=3.

increased HFLS-RA mRNA levels for both COL2A1 and MMP9 as compared to direct stimulation of HFLS-RA with FIB-CIT and FIB-MAA-CIT antigens without U937 supernatants (**Fig.2B**).

Conclusion: These results suggest a disease model whereby MAA and/or CIT modified proteins stimulate macrophages to release a unique combination of soluble mediators (such as MIP-1α, IL-1β or IL-18) that activate HFLSs and upregulate protein expression driving tissue fibrosis, in an antigen-specific manner (**Fig. 3**). Together with prior studies demonstrating MAA and CIT co-localization in RA synovium, these results indicate that MAA and/or CIT modified antigens may play a direct role in the development of fibrosis that has been observed in RA joint pathogenesis.

A)

	With supernatants from U937 cells				*Without supernatants from U937 cells*			
	HSA	**HSA-MAA**	**HSA-CIT**	**HSA-MAA-CIT**	**HSA**	**HSA-MAA**	**HSA-CIT**	**HSA-MAA-CIT**
COL2A1	1.07	**3.61(*)**	1.31	**2.58(*)**	1.00	1.29	0.60	**0.68(*)**
MMP9	1.00	**11.27(*)**	1.98	0.47	1.00	**3.16(*)**	1.61	1.39
VIM	1.22	**0.36(*)**	**0.61(*)**	**2.42(*)**	1.03	**0.12(*)**	1.35	1.12

B)

	With supernatants from U937 cells				*Without supernatants from U937 cells*			
	FIB	**FIB-MAA**	**FIB-CIT**	**FIB-MAA-CIT**	**FIB**	**FIB-MAA**	**FIB-CIT**	**FIB-MAA-CIT**
COL2A1	0.99	0.59	**4.05(*)**	**5.58(*)**	0.95	1.11	1.31	**0.32(*)**
MMP9	0.95	1.31	**9.75(*)**	**6.62(*)**	1.12	0.73	2.75	**3.75(*)**
VIM	1.02	1.07	**0.17(*)**	**2.35(*)**	1.02	**0.60(#)**	**0.20(*)**	**2.45(*)**

Figure 2. PCR for mRNA levels of fibrosis markers from stimulated HFLS-RA cells. HFLS-RA cells were stimulated with either supernatants from modified antigens treated U937 cells or with directly modified antigens. RNA was collected from HFLS-RA cells and categorized as incubation with HSA (A) or FIB (B) modified antigens. The data is represented as relative quantity (Rq) of fibrosis markers. #p<0.05, *p<0.001, n=3.

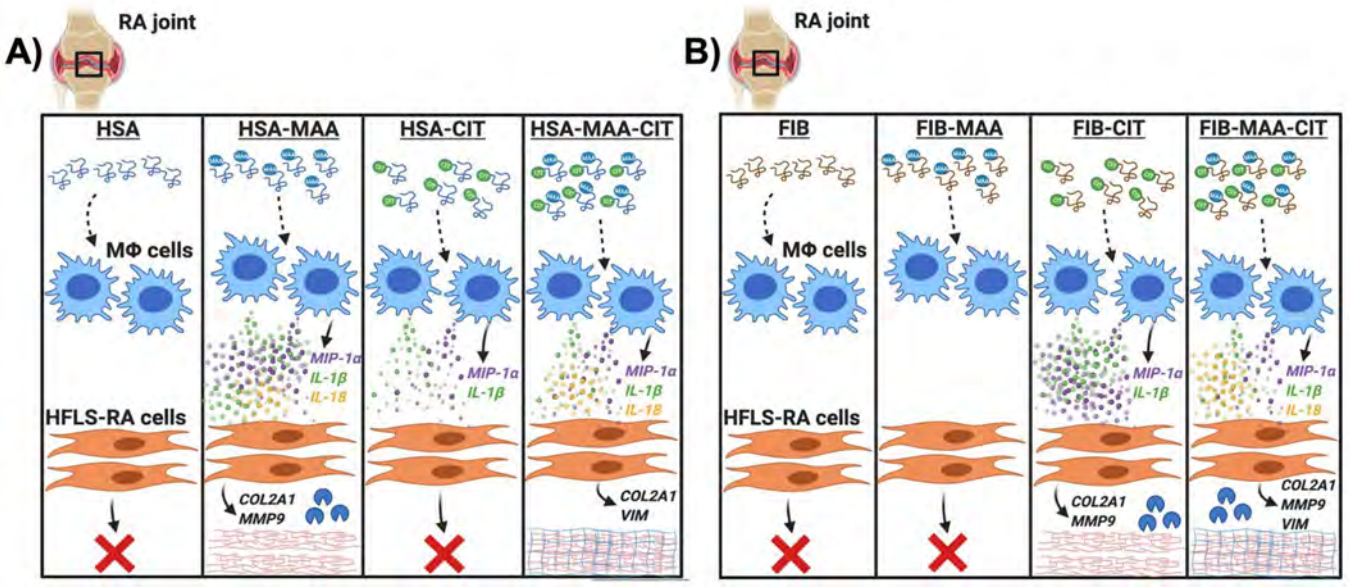


Figure 3. Summary of the experiment and results evaluating the effects of U937 macrophage soluble factor release on stimulation of HFLS-RA cell extracellular matrix expression. U937 macrophage stimulation with HSA (A) and FIB (B) modified antigens.

Disclosure: N. Aripova, None; **M. Duryee**, None; **E. Ryan**, None; **P. Maloley**, None; **B. England**, Boehringer-Ingelheim, 2; **J. O'Dell**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6.

Abstract Number: 0509

Selective Inhibition of Tyrosine Kinase 2 with Deucravacitinib Compared with Janus Kinase 1/2/3 Inhibitors

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Deucravacitinib is a novel, oral, allosteric agent that selectively inhibits intracellular signaling by binding to the tyrosine kinase 2 (TYK2) pseudokinase domain rather than to the conserved active site in the kinase domain. The high functional selectivity for TYK2 versus other signaling tyrosine kinases has been confirmed in cell- and whole blood–based assays.[1] Kinase selectivity should provide a differentiated risk/benefit profile due to potent TYK2 inhibition and minimal activity against other kinases. In a 1-year, double-blind, Phase 2 trial (NCT03881059), deucravacitinib was efficacious and well tolerated versus placebo in patients with active PsA.[2] The objective of this analysis was to understand the selectivity profile of deucravacitinib for TYK2 versus Janus kinase (JAK) 1/2/3, compared with the approved JAK inhibitors tofacitinib (Tofa), upadacitinib (Upa), and baricitinib (Bari), at clinically relevant doses and plasma concentrations.

Methods: In vitro whole-blood assays were established to measure the activity of common intracellular pairings of signaling tyrosine kinases (JAK1/3, JAK2/2, and TYK2/JAK2). Deucravacitinib, Tofa, Upa, and Bari concentrations providing half-maximal inhibition (IC_{50}) of relevant signaling readouts were determined. Whole-blood IC_{50} values were plotted against known pharmacokinetic profiles of these agents at doses evaluated in Phase 3 trials, including approved doses. Time durations when concentrations were greater than IC_{50} and projected average daily inhibition were evaluated.

Results: At clinically relevant doses and exposures, deucravacitinib steady-state plasma concentrations were higher than the TYK2 whole-blood IC_{50} for a considerable part (9–18 hours) of the day. The maximal plasma concentration (C_{max}) of deucravacitinib was 8- to 17-fold lower than the JAK1/3 whole-blood IC_{50} and >48- to >102-fold lower than the JAK2/2 whole-blood IC_{50}, indicating lack of meaningful inhibition of JAK1/2/3 by deucravacitinib at clinically relevant doses. Average daily inhibition of TYK2 by deucravacitinib ranged from 50% to 69%. Tofa, Upa, and Bari exhibited varying degrees of daily average inhibition at steady-state against JAK1/3 (70%–94%) and JAK2/2 (23%–67%). Projected C_{max} values of Tofa, Upa, and Bari were 17- to 33-fold lower than TYK2 IC_{50}, indicating minimal or no meaningful inhibition of TYK2.

Conclusion: Deucravacitinib has high functional selectivity for TYK2 at clinically relevant doses and plasma concentrations. In contrast, Tofa, Upa, and Bari inhibit JAK1/2/3 to varying degrees but do not inhibit TYK2 at clinically relevant concentrations. These results indicate that deucravacitinib is a distinct class of signaling kinase inhibitor compared with JAK1/2/3 inhibitors. Studies in multiple immune-mediated inflammatory diseases including plaque psoriasis, psoriatic arthritis, lupus, and inflammatory bowel disease will further assess the safety and efficacy of deucravacitinib.

References

1. Burke JR et al. *Sci Transl Med*. 2019;11:1-16.
2. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

Disclosure: A. Chimalakonda, Bristol Myers Squibb, 3, 11; **J. Burke**, Bristol Myers Squibb, 3, 11; **L. Cheng**, Bristol Myers Squibb, 3, 11; **I. Catlett**, Bristol Myers Squibb, 3, 11; **M. Tagen**, Bristol Myers Squibb, 3, 11; **Q. Zhao**, Bristol Myers Squibb, 3, 11; **A. Patel**, Bristol Myers Squibb, 3, 11; **J. Shen**, Bristol Myers Squibb, 3, 11; **I. Girgis**, Bristol Myers Squibb, 3, 11; **S. Banerjee**, Bristol Myers Squibb, 3, 11; **J. Throup**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0510

Fibrinogen Modified with Malondialdehyde-Acetaldehyde Adduct (MAA) And/or Citrulline (CIT) Induces Unique Cellular Responses in Human RA Synoviocytes

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
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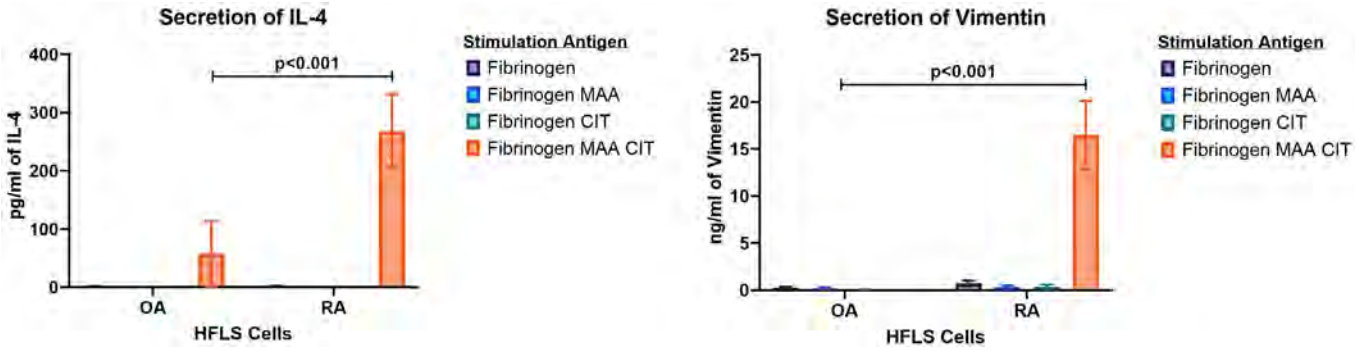

Figure 1. Pro-fibrotic factors release from stimulated HFLS-RA cells. HFLS-RA cells were incubated with Fibrinogen modified antigens. Afterwards, the supernatants were collected for analysis of: IL-4 (A) and vimentin (B) release using Mesoscale Discovery assay kit. The concentration of all cytokines was measured in ng/mL. p<0.001 significantly different from all OA cell antigen treatments. n=4.

Background/Purpose: Malondialdehyde (MDA) is produced in response to oxidative stress and is associated with inflammation and disease pathogenesis. MDA can break down and form acetaldehyde (AA). Together MDA and AA can non-enzymatically combine to create a stable protein adduct termed malondialdehyde-acetaldehyde adduct (MAA), which is strongly immunogenic, even in the absence adjuvant. Our group showed that MAA modified proteins are present in Rheumatoid Arthritis (RA) synovium and co-localize with citrullinated (CIT) antigens known to be strongly associated with the pathogenesis of RA. RA synovium is characterized by a combination of pro-inflammatory and pro-fibrotic signals secreted by immune cells and resident human fibroblast-like synoviocytes (HFLS). The purpose of this study is to evaluate pro-inflammatory and pro-fibrotic signals released by HFLS from patients with RA (HFLS-RA) vs. HFLS from patients with osteoarthritis (HFLS-OA) when stimulated with an extracellular matrix protein fibrinogen (Fib) modified with MAA, CIT, or the combination of MAA-CIT.

Methods: The HFLS-RA and HFLS-OA cell lines were cultured for 24 hours in the presence of 25 µg/mL of; unmodified Fib or Fib modified with MAA, CIT, or MAA-CIT. Supernatants were collected and analyzed by ELISA using the Meso Scale Diagnostics (MSD) platform for the release of pro-inflammatory and pro-fibrotic markers.

Results: Compared to HFLS-OA cells, HFLS-RA cells stimulated with Fib-MAA-CIT (Figures 1 and 2) significantly increased the secretion of vimentin and IL-4 (pro-fibrotic markers), and IL-6, IL-8, and MCP-1 (pro-inflammatory markers). HFLS-RA cells stimulated with Fib-CIT showed significantly increased levels of only the pro-inflammatory markers; IL-6 and MCP-1 (**Figure 2**) as compared to HFLS-OA cells. Additionally, HFLS-RA cells stimulated with Fib-MAA showed significantly increased secretions of the pro-inflammatory marker IL-8 (Figure 2B) compared to HFLS-OA cells.

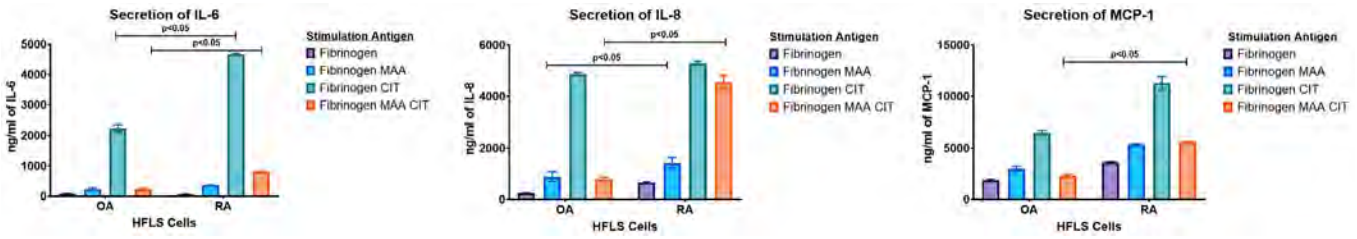

Figure 2. Pro-inflammatory cytokines release from stimulated HFLS-RA cells. HFLS-RA cells were incubated with Fibrinogen modified antigens. Afterwards, the supernatants were collected for analysis of: IL-6 (A), IL-8 (B), and MCP-1 (C) release using Mesoscale Discovery assay kit. The concentration of all cytokines was measured in ng/mL. p<0.05 significantly different from OA cells treated with Fib-Cit. p<0.05 significantly different from OA cells treated with Fib-MAA-CIT. n=4.

Conclusion: These studies demonstrate that HFLS-RA cells secreted significantly increased pro-inflammatory and/or pro-fibrotic markers when compared to HFLS-OA cells depending on whether fibrinogen was modified with MAA, CIT or MAA-CIT. Additionally, these data also suggest that the HFLS-RA cells developed unique cellular responses compared to OA cells, making them useful in understanding how these modified proteins affect HFLS cells. Thus, further studies will evaluate the effects of other extracellular proteins that have been implicated in the pathogenesis of RA, and modified with MAA, CIT or MAA-CIT on the expression of pro-inflammatory and pro-fibrotic markers.

Disclosure: B. **Wordekemper**, None; **N. Aripova**, None; **M. Duryee**, None; **E. Daubach**, None; **B. England**, Boehringer-Ingelheim, 2; **J. O'Dell**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6.

Abstract Number: 0511

Tumor Necrosis Factor-α Modulates Endothelial-to-mesenchymal Transition and Increases Protein Tyrosine Phosphatase 1B

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Endothelial dysfunction is a hallmark in the pathogenesis of many inflammatory diseases. The endothelial-to-mesenchymal transition (EndoMT) is a process where endothelial cells lose their endothelial features and acquire fibroblast-like phenotype. EndoMT has been associated with vasculopathy, atherogenesis, and it is promoted by several proinflammatory cytokines, such as tumor necrosis factor α (TNF-α). Protein tyrosine phosphatase 1B (PTP1B) modulates many signaling pathways associated with inflammatory mediators and has been associated with endothelial dysfunction and cardiovascular disturbances. However, it remains unclear the role of PTP1B in TNFα-induced EndoMT.

Objective. To characterize EndoMT promoted by TNF-α in human endothelial cells (ECs) and the putative role of PTP1B in this process.

Methods: Human aortic endothelial cells (HAECs) were used as model for *in vitro* induction of EndoMT. These ECs were incubated with human recombinant TNF-α (25 ng/mL) for 2 and 4 days. Expression of endothelial markers (eNOS, CD31, VE-cadherin) and mesenchymal marker (N-cadherin), and the transcription factors SNAI1, TWIST1 and ZEB1 along with PTP1B during EndoMT were evaluated by Western blot (WB). Canonical NF-κB pathway activation in EndoMT was assessed by phosphorylation of p65-Ser536, degradation of IkB-α and nuclear translocation of p65 by WB and immunofluorescence (IF). Inhibition of NF-kB pathway was assessed by using the IKK-β specific inhibitor BMS-345531 (5 μM).

Results: HAECs underwent EndoMT after 2- and 4-days TNF-α treatment. Expression of eNOS, CD31 and VE-cadherin were downregulated, and N-cadherin was upregulated as well as the transcription factors SNAI1, TWIST1

and ZEB1. Concomitant with this process, PTP1B increased its expression levels. TNF-α induced phosphorylation of NF-κB (p65-Ser 536) and degradation of IκB-α. Nuclear translocation of p65 was more evident 15 min after treatment. ECs pre-treated with BMS-345531 before TNF-α addition decreased TNF-α-induced phosphorylation of NF-κB (p65-Ser 536) and nuclear translocation of p65, and prevented degradation of IκB-α. Furthermore, decreased expression of N-cadherin, SNAI1 and TWIST1 was observed after 2 days of treatment with BMS-345531 + TNF-α.

Conclusion: TNF-α promotes EndoMT in human ECs by activating canonical NF-κB pathway. During this process PTP1B increases its expression levels. Pharmacological inhibition of IKK-β attenuated TNF-α-induced NF-kB activation with concomitant inhibition of EndoMT. These findings unveil an important pathway in endothelial dysfunction and vasculopathy associated with inflammatory conditions and suggest novel avenues for intervention.

Disclosure: J. Romo-Tena, None; **J. Esparza-Lopez**, None; **C. Carmona-Rivera**, None; **L. blanco**, None; **M. Kaplan**, None; **M. Ibarra-Sánchez**, None.

Abstract Number: 0512

Peficitinib and Filgotinib Inhibit Angiogenesis via Suppression of VEGF Production in Rheumatoid Arthritis Fibroblast-like Synoviocytes

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SESSION INFORMATION
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Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Peficitinib and filgotinib are novel Janus kinase (JAK) inhibitors developed for the treatment of rheumatoid arthritis (RA). Peficitinib inhibits all JAKs, especially JAK3. Filgotinib, on the other hand, is a JAK1 selective inhibitor. In this study, to clarify the effect of different JAK inhibition selectivity on angiogenesis in RA fibroblasts, we examined the role of peficitinib and filgotinib in RA angiogenesis.

Methods: In order to confirm if the effect of peficitinib and filgotinib on IL-6 and IL-6R responses in RA fibroblast-like synoviocytes (FLS) and human umbilical vein endothelial cells (HUVECs), western blot analysis was performed. RA FLS and HUVECs were stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) after treated peficitinib (0.1, 1, 5μM) or filgotinib (0.1, 1, 5μM) for 24 h. Next, to evaluate the effects of peficitinib and filgotinib on RA angiogenesis, we performed in vitro Matrigel tube formation assays using HUVECs. In addition, HUVECs were co-cultured in peficitinib (5 μM) or filgotinib (5 μM) treated RA FLS supernatant, and added on Matrigel. Furthermore, to confirm the direct effects of peficitinib and filgotinib on HUVECs, peficitinib or filgotinib was added to HUVECs supernatant. Finally, to measure the cytokines and chemokines in RA FLS supernatant, RA FLS supernatant was obtained from RA FLS-conditioned medium stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) with or without adding peficitinib (5 μM) or filgotinib (5 μM). The amount of VEGF, RANTES/CCL5, MCP-1/CCL2, MMP-3, fractalkine/CX3CL1, ENA78/CXCL5 and IL-8 in RA FLS conditioned medium was determined using ELISA.

Results: We found phosphorylation of STAT1, STAT3 and STAT5 in RA FLS was suppressed by peficitinib and filgotinib. However, phosphorylation of STAT3 in HUVEC was not suppressed by filgotinib. Next, peficitinib or filgotinib treated RA FLS conditioned medium reduced HUVEC tube formation compared to nontreated RA FLS conditioned

medium (number of endothelial cell tubes formed ± SEM; Control 13.8 ± 1.23, peficitinib 8.5 ± 1.12, filgotinib 8.33 ± 0.73). Filgotinib directry reduced HUVEC tube formation compared to nontreated HUVECs supernatant (Control 7.41 ± 1.04, peficitinib 7.5 ± 0.95, filgotinib 4.58 ± 0.73). Furthermore, we found peficitinib and filgotinib suppress the secretion of VEGF in RA FLS (mean ± SEM; Control: 72.2 ± 1.17, Peficitinib: 42.6 ± 0.26, Filgotinib: 57.35 ± 0.41 pg/ml). Peficitinib significantly suppressed the secretion of VEGF in RA FLS than filgotinib.

Conclusion: Peficitinib and filgotinib suppressed the secretion of VEGF in RA FLS and RA angiogenesis through inhibition of VEGF. Differences in JAK inhibition selectivity of peficitinib and filgotinib affect the suppression of RA angiogenesis.

Disclosure: Y. Ikari, None; **T. Isozaki**, None; **K. Wakabayashi**, None; **T. Kasama**, None.

Abstract Number: 0513

Spirulina Activates IFNγ via TLR4 in Dermatomyositis Skin and Peripheral Blood

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SESSION INFORMATION
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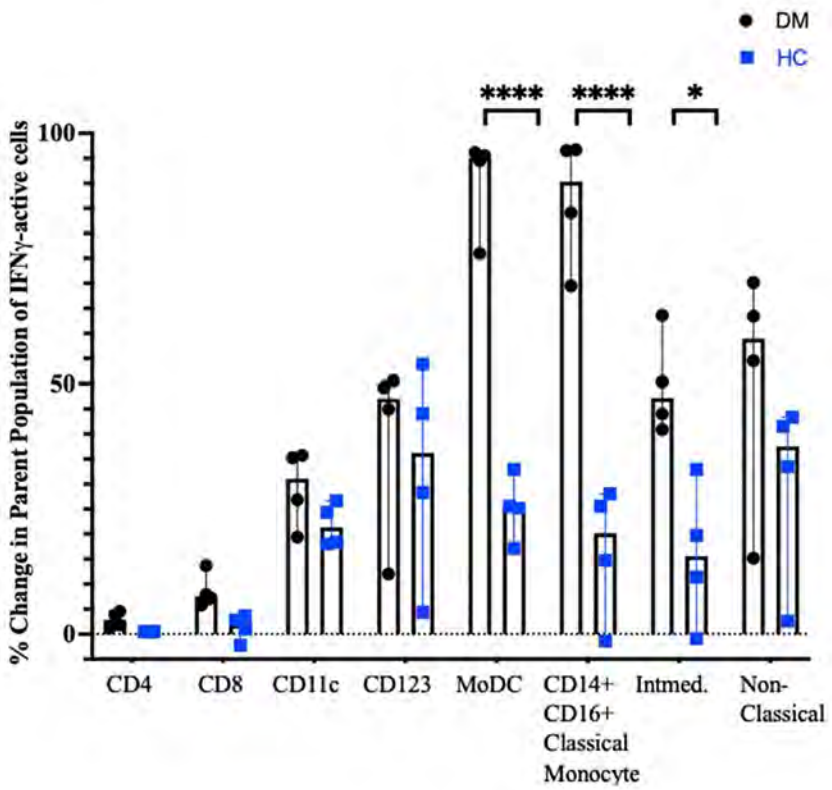
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Our group has previously shown that Spirulina, a popular herbal supplement with purported immune boosting effects, is temporally associated with dermatomyositis (DM) onset and flare. We have previously shown *in vitro* that Spirulina induces IFNγ.

Methods: Here, we sought to identify which cells and inflammatory pathways are activated as a result of Spirulina stimulation in DM patients. Given the important differences between the blood and end organ immune compartments, we sought to interrogate the effects of Spirulina in both blood and skin. We utilized multiplexed flow cytometry on DM patient PBMCs stimulated with 0.3mg/mL of Spirulina. Using GraphPad prism V8.4.3, comparisons between healthy controls and DM were made with Students t-test and comparison of multiple groups were made by one way ANOVA with a post hoc Tukey test. Correlations were analyzed with Pearson's r. With flow cytometry, we investigated Spirulina's immunostimulatory effects at the cellular level. Eight cell lineages were evaluated in PBMCs using FACS Symphony A3 Lite and analyzed with FlowJo V10.7.1.

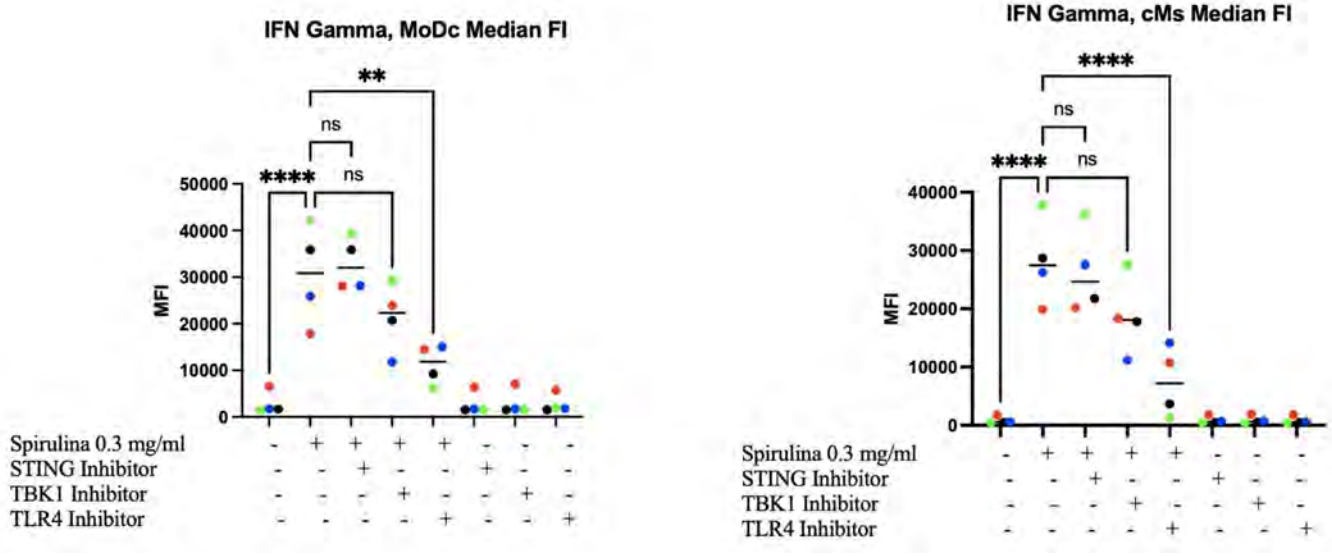
Results: When evaluating % change in activation with 0.3 mg/ml of Spirulina in DM and HC for IFNγ, monocyte-derived DCs (moDCs) and classical monocytes (CMs) had a significantly greater % increase in CMs and moDCs in DM compared to HC (Figure 1). With stimulation at 0.3 mg/mL of Spirulina, the IFNγ+ moDCs MFI increased by 11.7 fold relative to no stimulation ($p < 0.0001$). The MFI of CMs secreting IFNγ increased 32.0 fold with 0.3 mg/mL when compared to no added Spirulina ($p < 0.0001$) (Figure 2a and 2b). Pre-treatment with TLR4 inhibitor prior to Spirulina 0.3mg/ml of stimulation suppressed the MFI of IFNγ activation by 63.07% in moDCs, and by 73.4% in CMs ($p < 0.05$

Figure 1

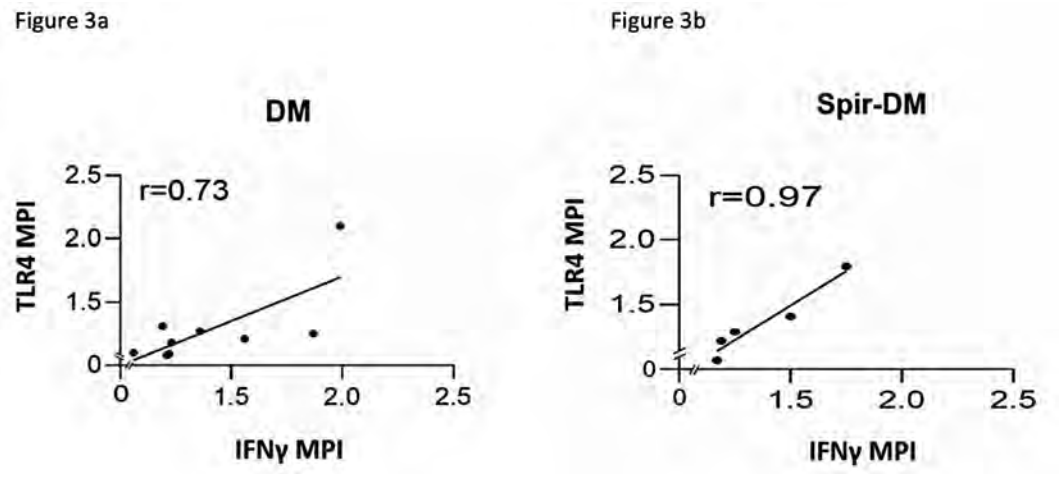


Cell specific production of IFNγ as a percent change of parent population with 0.3 mg/ml of Spirulina in dermatomyositis and healthy control patients measured by multiplexed flow cytometry.

and p< 0.001, respectively). We then performed imaging mass cytometry on lesional DM skin from patients with new-onset DM and a clear history of novel Spirulina consumption in the immediately preceding period (Spir-DM). Unsupervised clustering of dermal cells using the Phenograph algorithm yielded 14 unique cell types. MoDCs were



IFNγ production is stimulated by 0.3mg/mL of Spirulina in moDCs and CMs and is suppressed by inhibition of TLR4.



TLR4 expression is positively correlated with IFNγ production in DM (r=0.73) and Spir-DM (r=0.97) skin.

manually gated on CD14 and CD11c. CMs, were the predominant cell type (16.1%), followed by CD4 T cells (14.6%), CD163+ macrophages (9.6%), and moDCs (9.3%). There was overlap of CD14, CD11c, and IFNγ in Spir-DM skin, supporting an important role for moDCs and CM in the production of IFNγ. We then compared IFNγ and TLR4 expression in DM (Figure 3a) and Spir-DM (Figure 3b), finding a stronger positive correlation in Spir-DM (r=0.97) than in DM alone (r=0.73).

Conclusion: These results further implicate Spirulina as a likely culprit in the development of DM in some patients. Our data suggest that Spirulina may promote autoimmunity via production of IFNγ in CMs and moDCs in both the blood and skin, thereby implicating Spirulina in the development of DM in some susceptible patients.

Disclosure: D. Diaz, None; **T. Vazquez**, None; **C. Bax**, None; **J. Patel**, None; **M. Grinnell**, None; **E. Keyes**, None; **Y. Li**, None; **V. Werth**, None.

Abstract Number: 0514

Extracellular Sulfatase-2 Mediates TNF-α Inflammatory Signaling in Human Rheumatoid Arthritis Synovial Fibroblasts

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: TNF-α drives RA synovial fibroblast (RASF)-mediated hyperplasia and joint tissue destruction. Extracellular sulfatase-2 (Sulf-2) influences receptor/ligand binding and subsequent signaling of chemokines, cytokines, and growth factors, however, the potential role of Sulf-2 in TNF-α signaling has remained unexplored. Our

study compared Sulf-2 expression in synovial tissues and serum from hTNFtg mice and human RA patients vs. non-diseased controls and determined effects of Sulf-2 on TNF-α signaling and inflammation in human RASFs.

Methods: Sulf-2 expression was measured in human non-diseased vs. RA synovial tissues (NLSTs vs. RASTs) by qRT-PCR and Western blotting. Sulf-2 expression in wild-type C57BL/6 vs. hTNFtg mouse ankle sections was compared by fluorescence IHC. Soluble Sulf-2 in mouse and human serum was measured by ELISA. Global effects of Sulf-2 gene knockdown by siRNA on TNF-α-induced gene expression were studied using an RNA sequencing (RNA-seq) array. Differentially expressed genes (DEGs) were analyzed using edgeR package of R software. Selected gene targets were validated by qRT-PCR and Western blotting/ELISA. TNF-α signaling pathways affected by Sulf-2 knockdown were analyzed.

Results: Sulf-2 mRNA was 3-fold higher (n=6 each; $p< 0.001$) and protein 5-fold higher (n=5 each; $p< 0.01$) in RAST vs. NLST. Soluble Sulf-2 in human serum was ~2-fold higher in RA (n=48) over non-diseased (NL, n=50; $p< 0.001$). Sulf-2 expression was elevated in the inflamed synovium of hTNFtg mice over wild-type (n=3 each). Soluble Sulf-2 was elevated ~20% in hTNFtg male mice (n=3, n.s.) and 2-fold in females (n=3, $p< 0.05$) over wild-type. In the RNA-seq array of TNF-α-activated RASFs, Sulf-2 siRNA modulated ~2,500 DEG vs. NC siRNA (FDR< 0.05). Gene ontology showed Sulf-2 significantly altered expression of genes in the canonical pathway *role of macrophages, fibroblasts and endothelial cells in RA*. qRT-PCR confirmed that Sulf-2 knockdown reduced TNF-α-induced ICAM1 (-58%), VCAM1 (-50%), CAD11 (-45%), PDPN (-34%), CCL5 (-55%), CX3CL1 (-59%), CXCL10 (-65%), CXCL11 (-63%) compared to NC siRNA (n=4-6, $p< 0.01$). Signaling studies identified PKC-δ as a key intermediate in TNF-α induced adhesion proteins. Sulf-2 knockdown suppressed TNF-α-induced p-PKC-δ (Thr^{505})(-52%) and p-JNK(Thr^{183}/Tyr^{185}) (-36%)(n=6; $p< 0.05$) and nuclear translocation of inflammatory transcription factors including NFkB p65 and c-Rel.

Conclusion: Our results provide novel evidence of the role of Sulf-2 in TNF-α activated signaling pathways in human RASFs. Further studies may decipher the therapeutic value of targeting Sulf-2 in the treatment of RA.

Disclosure: R. Siegel, None; **A. singh**, None; **J. Vinh**, None; **H. Kenney**, None; **E. Schwarz**, Janssen, Johnson & Johnson, 12, Anti-TNF and placebo antibodies were a gift from Janssen, J&J; **D. Fox**, None; **S. Khuder**, None; **S. Ahmed**, None.

Abstract Number: 0515

The Extracellular Sulfatase-2 Inhibitor OKN-007 Abrogates TNF-α-induced Inflammatory Mediators in Human Rheumatoid Arthritis Synovial Fibroblasts

Ruby Siegel, Sang Han and Salah-uddin Ahmed, Washington State University, Spokane, WA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Cytokines & Cell Trafficking Poster (0508–0516)
Session Type: Poster Session B
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Background/Purpose: Recent unpublished findings from our lab show that the extracellular enzyme sulfatase-2 (Sulf-2) facilitates pro-inflammatory TNF-α signaling which activates rheumatoid arthritis synovial fibroblasts (RASFs). The small molecule drug OKN-007 has been reported to inhibit Sulf-2 activity. OKN-007 demonstrated safety in hu-

man clinical trials at sustained plasma concentrations averaging 300 micromolar. In this study, we tested the efficacy of OKN-007 in reducing TNF-α-induced adhesion molecule and chemokine production by RASFs.

Methods: Experiments utilized primary human RASFs (n=5; age 30-61) from de-identified synovial tissues obtained under an IRB-approved protocol, from patients who met the ACR criteria for RA and were not treated with biologics. MTT viability assay was used to measure potential toxicity of OKN-007 [0-1000 μM] alone or with TNF-α for 24 h. To test effect of Sulf-2 inhibition on TNF-α induced proteins, RASFs were pre-treated with OKN-007 (0-1000 μM) for 12 h followed by TNF-α (20 ng/mL) stimulation for 24 h. RASFs not stimulated with TNF-α served as a negative control. Concentration of CCL2, CXCL5, CCL5, CXCL10, CXCL11 in cell supernatants were measured by ELISA. Expression of MAPK/NF-κB signaling and adhesion molecules (ICAM-1 and VCAM-1) were measured by densitometry on Western blots. The Sulf-2-inhibitory effects of OKN-007 were further validated by Sulf-2 small-interfering RNA (siRNA) method. Statistical value $p< 0.05$ was considered significant.

Results: OKN-007 alone at a dose range of 0-1000 μM did not significantly affect RASF viability (n=4). When combined with TNF-α, OKN-007 [500, 1000 μM] reduced the RASF viability by 22% and 29%, respectively (n=4; $p< 0.05$), suggesting sensitization of RASFs to TNF-α-induced apoptosis. Adhesion molecule expression was normalized to β-actin, accounting for any cell loss. OKN-007 [500, 1000 μM] decreased TNF-α-induced ICAM-1 by 20% and 36% and VCAM-1 by 23% and 35%, respectively (n=4; $p< 0.05$). OKN-007 (500-1000 μM) inhibited TNF-α-induced CCL2 (23-28%), CXCL5 (66-75%), CCL5 (~65%), CXCL10 (80-95%), and CXCL11 (43-65%) (n=4; $p< 0.05$). Further validation of the pharmacologic inhibition using Sulf-2-directed siRNA showed similar inhibition of TNF-α-induced chemokine production and adhesion molecule expression by human RASFs (n=4; $p< 0.05$). Evaluation of the signaling molecules suggest that OKN-007 suppressed TNF-α-induced signaling pathways to elicit its anti-inflammatory activity.

Conclusion: Our study in human RASFs suggests that pharmacologic inhibition of Sulf-2 with a safe, non-immunosuppressive compound may provide an adjunct therapeutic value with anti-TNF therapy for the treatment of RA.

Disclosure: R. Siegel, None; **S. Han**, None; **S. Ahmed**, None.

Abstract Number: 0516

Dual Fibroblast Transdifferentiation Mediated by Type I Interferon: Application to Anti-Ro Mediated Congenital Heart Block

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SESSION INFORMATION
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Background/Purpose: Linking inflammation to fibrosis, a common end stage feature of many autoantibody mediated rheumatic diseases, remains a challenge. Indeed the signature hallmark of anti-Ro associated congenital heart block (CHB) is rapid replacement of the AV node by fibrosis during the late 2nd trimester. Previously reported in vitro coculture experiments and transcriptomic analysis position type I Interferons in the pathogenesis of conduction disease, but it remains to be identified how IFNa contributes to a pathological cardiac fibroblast. By focusing solely

on smooth muscle actin (SMAc), heterogeneity in myofibroblasts has been underappreciated. The current study was initiated to evaluate Fibroblast-Specific Protein 1 (FSP1), a fibroblast marker with demonstrated responsiveness to the Wnt/β-catenin pathway, and its contribution, in concert with interferon alpha (IFNa), to cardiac injury propagated by maternal anti-Ro.

Methods: An in vitro model of anti-Ro mediated CHB employed co-culture of supernatants by hY3 (a noncoding ssRNA, anti-Ro proxy)-treated human macrophages (THP1 cells) with human cardiac fetal fibroblasts. In addition, fibroblasts were treated with IFNa or recombinant Wnt3A with and without their respective inhibitors (neutralizing IFNa antibody (NIFNa), ICG-001). Using standard techniques, assessments included transcriptomics (qPCR, IFNa stimulated genes (ISG)), immunofluorescence (IF) and flow cytometry (FC).

Results: Use of derivative of hY3-transfected THP1 cells (hY3 supernatants) markedly upregulated the fibroblast expression of ISGs, IFIT-1 and SIGLEC-1 supporting the secretion of IFNa by the THP-1 cells. After exposure to IFNa, SMAc and FSP1 expression in fibroblasts were significantly increased compared to untreated cells (SMAc: 23,347±2077 vs. 89.5±21, p< 0.01; FSP1: 2282.7±293 vs. 70.1±3, N=3, p< 0.01). As predicted, fibroblasts treated with hY3 supernatants also significantly promoted SMAc and FSP1 myofibroblast subtypes compared to untreated fibroblasts using IF (**Figure 1**) and FC (SMAc: 6463.7±593 vs. 89.5±21, N=3, p< 0.01; FSP: 1339.0±154 vs. 70.1±3, N=3, p< 0.02) but to a lesser degree than observed with IFNa . There was a gap in SMAc and FSP1 expression between IFNa and hY3 treatments, however, it was mitigated when fibroblasts were co-treated with hY3 supernatants and Wnt3a. hY3 supernatants/Wnt3a co-treatment showed remarkable synergy, unexplained by either treatment alone (hY3 supernatant + Wnt3a vs IFNa-induced expression (SMAc: 20,526.3±2617 vs. 23,346.7±2077, N=3, n.s., FSP1: 2118.7±193 vs. 2282.7±293, N=3, n.s.)., a phenotype that was attenuated by cotreatment with NIFNa, a result implicating IFNa as an autacoid factor of dual fibroblast transdifferentiation (IF, **Figure 1,** lower right panel). In parallel, the contribution of Wnt3a to IFNa a-induced FSP1 and SMAc expression was supported by their reduced expression when IFNa -treated fibroblasts were exposed to ICG-001.

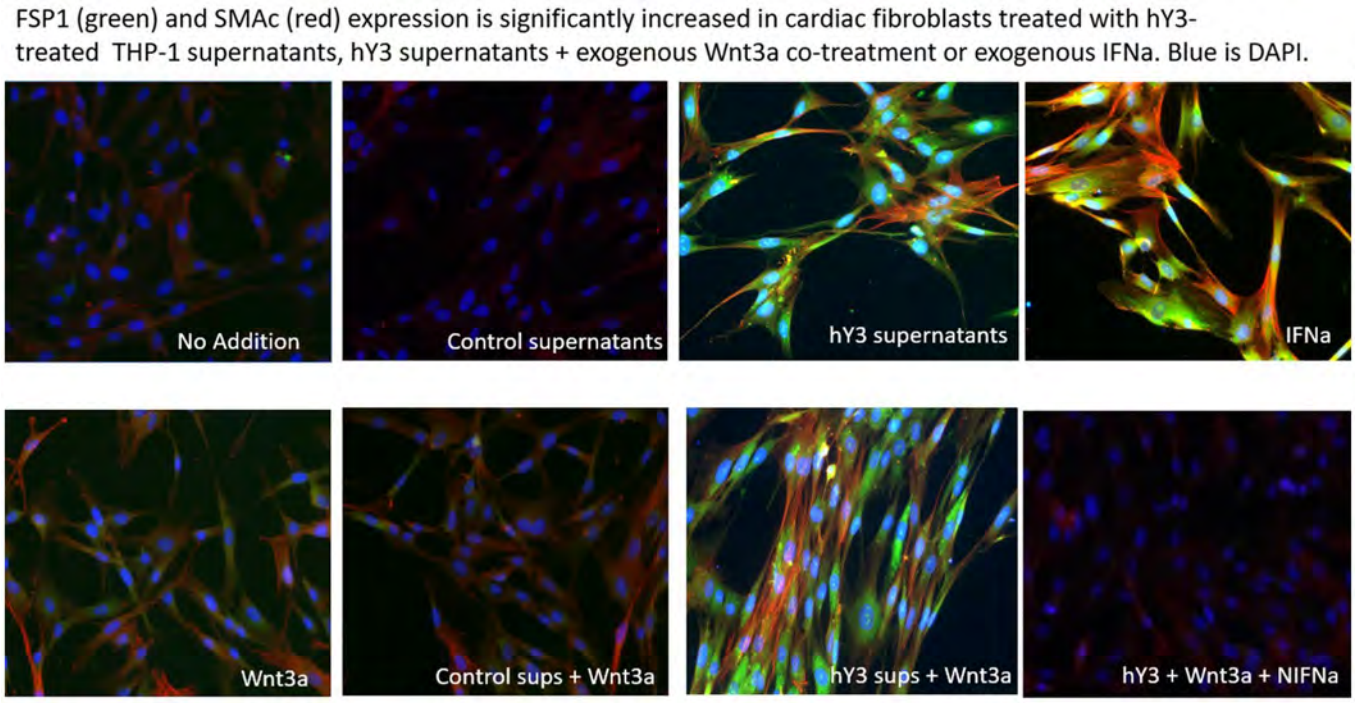

Figure 1. Condition hY3 sups/Wnt3a co-treatment of human fetal cardiac fibroblast result in the extreme phenotype extending to every fibroblast within the culture. Lower right panel shows attenuation of phenotype by neutralizing antibody to IFNa (NIFNa), a result implicating IFNa as an autacoid factor of dual fibroblast transdifferentiation.

Conclusion: These data support that an important component of anti-Ro mediated injury involves pathological activated fibroblast phenotypes reflecting dual transdifferentiation mediated by type I Interferon and disorders of the Wnt/β-catenin pathway.

Disclosure: C. Firl, None; **M. Chang**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **R. Clancy**, None.

Abstract Number: 0517

TPMT and *NUDT15* Genotype and Azathioprine Myelotoxicity in Patients with Inflammatory Conditions: Results from Real-World Clinical Practice

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SESSION INFORMATION
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Background/Purpose: Azathioprine is frequently used for the treatment of several inflammatory conditions. However, treatment is often limited by adverse events, in particular myelotoxicity. Both thiopurine-S-methyltransferase (TPMT) and nudix hydrolase-15 (NUDT15) are enzymes involved in the metabolism of azathioprine; variants in the genes encoding these enzymes contribute to an increased risk for azathioprine myelotoxicity. Recently, the Clinical Pharmacogenetics Implementation Consortium (CPIC) provided information on how to interpret *TPMT* and *NUDT15* genotype data to guide azathioprine use and to decrease the risk of azathioprine-related myelotoxicity. However, despite these recommendations, little is known about the role of this genetic information in routine clinical care of patients with inflammatory conditions treated with azathioprine. We hypothesized that *TPMT* and *NUDT15* genotype information predicts azathioprine discontinuation due to myelotoxicity.

Methods: We performed a retrospective cohort study in new azathioprine users. All patients were prescribed azathioprine to treat rheumatological and inflammatory conditions (e.g, vasculitis, systemic lupus erythematosus, rheu-

Table. Baseline Characteristics by TPMT or NUDT15 phenotype

	NUDT15 or TPMT poor or intermediate metabolizers n=123	NUDT15 or TPMT normal or indeterminate metabolizers n=1425	p-value
Age in years, mean±SD	42.1±17.0	43.4±17.6	0.72
Female sex, n (%)	80 (65.0%)	963 (67.6%)	0.62
White, n (%)	99 (81.8%)	1234 (87.4%)	0.21
Indications, n (%)			0.24
Systemic lupus erythematosus	17 (13.8%)	162 (11.4%)	
Inflammatory bowel disease	33 (26.8%)	484 (34.0%)	
Autoimmune disease other than lupus	73 (59.4%)	779 (54.7%)	
Azathioprine initial dose (mg/day), mean±SD	67.8±38.3	79.1±47.9	0.02

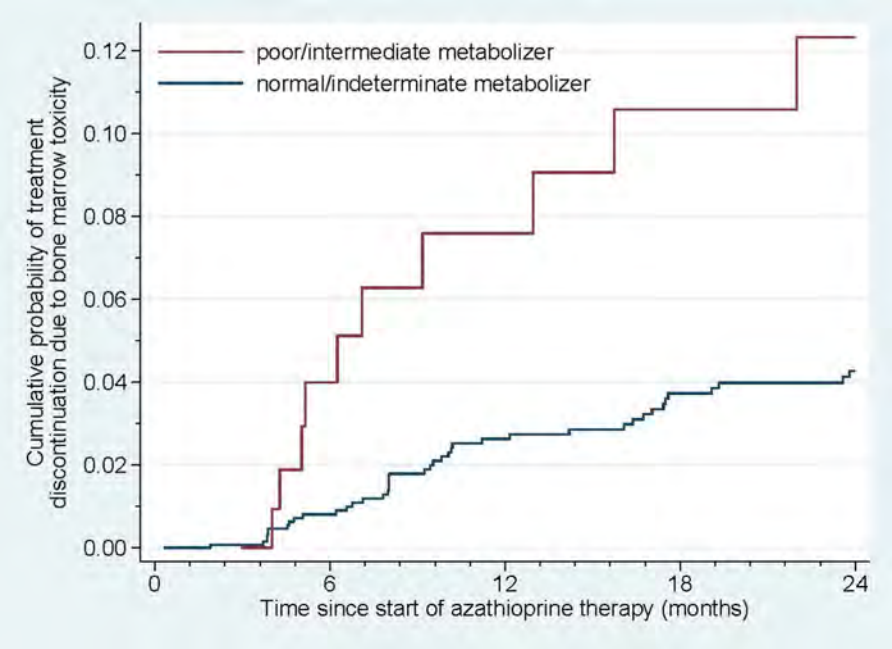

Figure. Probability of azathioprine discontinuation through 24 months by TPMT or NUDT15 phenotype.

matoid arthritis, autoimmune hepatitis and inflammatory bowel disease). Using BioVU, a clinical practice-based biobank at a tertiary medical center, we first identified new users for the conditions listed above and then reviewed de-identified clinical records, collected variables (age, sex, clinical indication for azathioprine use, and azathioprine daily dose); for those who discontinued azathioprine, we adjudicated the attributed reason blinded to genotypes. Genotyping was performed on the MEGAchip. Following quality control and imputation, we used CPIC guidelines to determine TPMT and NUDT15 metabolizer status; patients were classified based on the poorer of the two as either: (1) poor/intermediate (PM/IM); or (2) normal/indeterminate metabolizers (NM/ID).

Results: We studied 1548 new users of azathioprine followed over a median of 1.9 years. Their median age was 43.4±17.5 years, 67% were female, and 87% were white. A total of 123 patients were classified as PM/IM, and 1425 patients as NM/ID; 75 patients stopped azathioprine treatment due to myelotoxicity (13 among PM/IM and 62 among NM/ID)(Table). PM/IM metabolizer status was associated with a 2.56 times higher risk of stopping azathioprine due to myelotoxicity compared to NM/ID (HR=2.56, 95% CI:1.41-4.67, p=0.002)(Figure). This association remained significant after adjustment for race, age at baseline, sex, primary indication, and initial dose of azathioprine (aHR=2.48, 95% CI: 1.35-4.56, p=0.003) as well as when restricted to whites (aHR2=2.16, p=0.04). A sensitivity analysis, excluding patients who were classified as indeterminate metabolizers (n=8), showed similar results (HR=2.60, p=0.002 and aHR=2.50, p=0.003). The cumulative hazard for discontinuation due to myelotoxicity at two years was 12.3% (95% CI: 6.6-23.2%) in PM/IM, compared to 4.3% (95% CI: 3.1-5.8%) in NM/ID.

Conclusion: TPMT and NUDT15 phenotype metabolizer status predicts an increased risk for myelotoxicity in patients who received azathioprine for inflammatory conditions.

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Abstract Number: 0518

Predicted Expression of Genes Involved in the Thiopurine Metabolic Pathway Is Associated with Azathioprine Discontinuation Due to Bone Marrow Toxicity

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

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Background/Purpose: Azathioprine is a thiopurine used to treat inflammatory conditions; however, it is often discontinued due to dose-dependent bone marrow toxicity. The Pharmacogenomics Knowledgebase (PharmGKB) lists 25 genes in the metabolic pathway, therefore, small effect changes caused by variants in these genes may combine to large effect. Only two of these genes (*TPMT* and *NUDT15*) are in clinical guidelines for thiopurine use and only explain less than 25% of azathioprine-induced bone marrow toxicity. We hypothesize that a risk score that combines the expression of other genes in the thiopurine metabolic pathway would be associated with azathioprine discontinuation due to bone marrow toxicity among TPMT and NUDT15 normal metabolizers.

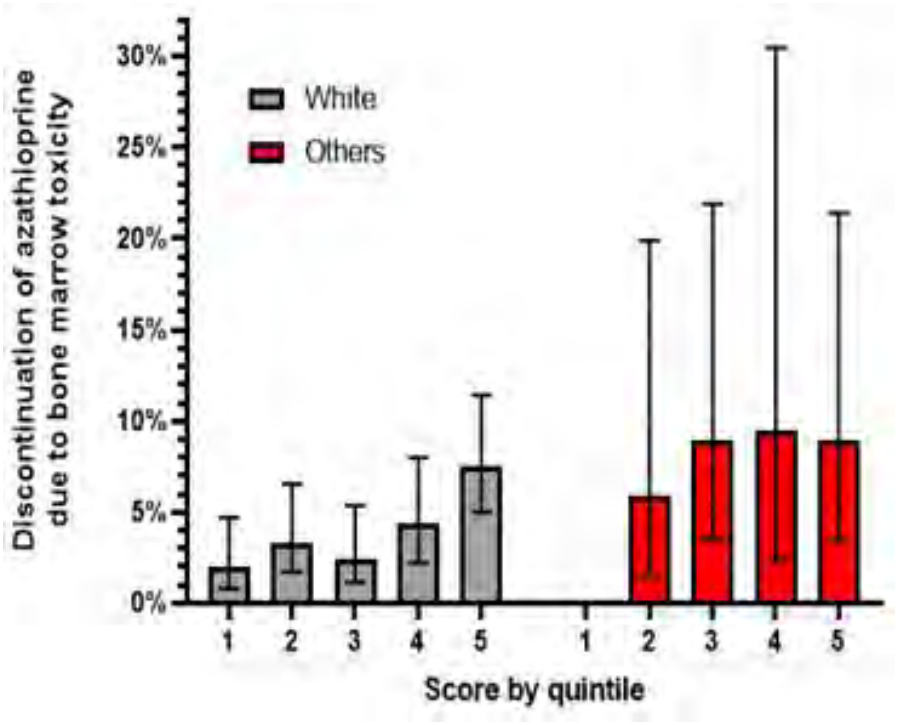

Figure: Association between discontinuing azathioprine and risk score by quintile. Vertical axis is percent discontinued azathioprine due to possible bone marrow toxicity with 95% confidence interval. The horizontal axis separates each quantile by White and non-White.

Methods: In a retrospective cohort of patients with vasculitis, SLE, RA, or other inflammatory conditions (e.g., autoimmune hepatitis, IBD) we identified new users of azathioprine who were TPMT and NUDT15 normal metabolizers and collected information from their clinical records. The outcome was possible bone marrow toxicity—defined as discontinuing azathioprine due to any cytopenia. Genotyping was performed using the MEGAchip and, following imputation and quality control, we used PrediXcan (GTEx version 8 MASHR-based eQTL models) to estimate the genetically regulated expression of 13 genes involved in azathioprine metabolism (*ADK*, *AOX1*, *GDA*, *GMPS, GSTA1, GSTM1, IMPDH1, ITPA, NME1, NME2, NT5C2, PPAT, RMM2*), and 4 involved in azathioprine transport (*ABCC4, SLC29A1, SLC29A1*, and *SCL29A2*). As most drug metabolism occurs in the liver, we selected liver-specific estimations. We used Lasso regression that included all 17 predicted gene expressions and 5 principal components for model selection (i.e. relaxed Lasso). We built a score based upon the resulting coefficients of selected variables. Based on score quintiles, we used cox hazard models to test whether scores were associated with azathioprine discontinuation due to cytopenia among Whites and whether the same score showed similar trends in those who reported other races or race unknown.

Results: We studied 1417 patients followed over a median of 1.9 years. Mean age was 43.6±17.6 years, 959 (67.7%) were female, initial daily dose 78.9± 47.8, and 1230 (87%) were White; 61 discontinued azathioprine due to cytopenia. The risk score included the predicted expression of the two genes (*AOX1* and *NME1*) that had non-zero coefficients from the lasso regression. White patients with the highest score quintile had a significantly higher risk of discontinuing azathioprine due to cytopenia compared to those in the lowest quintile [HR=3.65 (95% C.I. 1.37-9.73, p=0.010]. Results remained significant after adjustment for age, sex, azathioprine indication, and azathioprine initial daily dose [HR=3.77 (95% C.I. 1.41-10.06), p=0.008]. A similar association was observed among 187 patients who either reported other races or race unknown ($p< 0.001$).

Conclusion: Among patients who were TPMT and NUDT15 normal metabolizers, a score combining AOX1 and NME1 expression was associated with discontinuation of azathioprine due to bone marrow toxicity. Further studies are needed to replicate these findings in different cohorts.

Disclosure: L. Daniel, None; **A. Dickson**, None; **J. Zanussi**, None; **T. Miller-Fleming**, None; **P. Straub**, None; **W. Wei**, None; **D. Plummer**, None; **W. Dupont**, None; **G. Liu**, None; **P. Anandi**, None; **T. Reese**, None; **K. Birdwell**, None; **V. Kawai**, None; **A. Hung**, None; **N. Cox**, None; **Q. Feng**, None; **C. Stein**, None; **C. Chung**, NIH/NIGMS: R01GM126535 (This Research), 5, NCATS/NIH: UL1 TR002243 (Vanderbilt National Center for Advancing Translational Science), 5, NIGMS/OD: RC2GM092618 (BioVU), 5, NHGRI/NIGMS: U01HG004603 (BioVU), 5.

Abstract Number: 0519

The Relationship of Genetics and Clinically Suspect Arthralgia in RA Development Assessed Using HC, CSA and RA Patients

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Time: 8:30AM–10:30AM

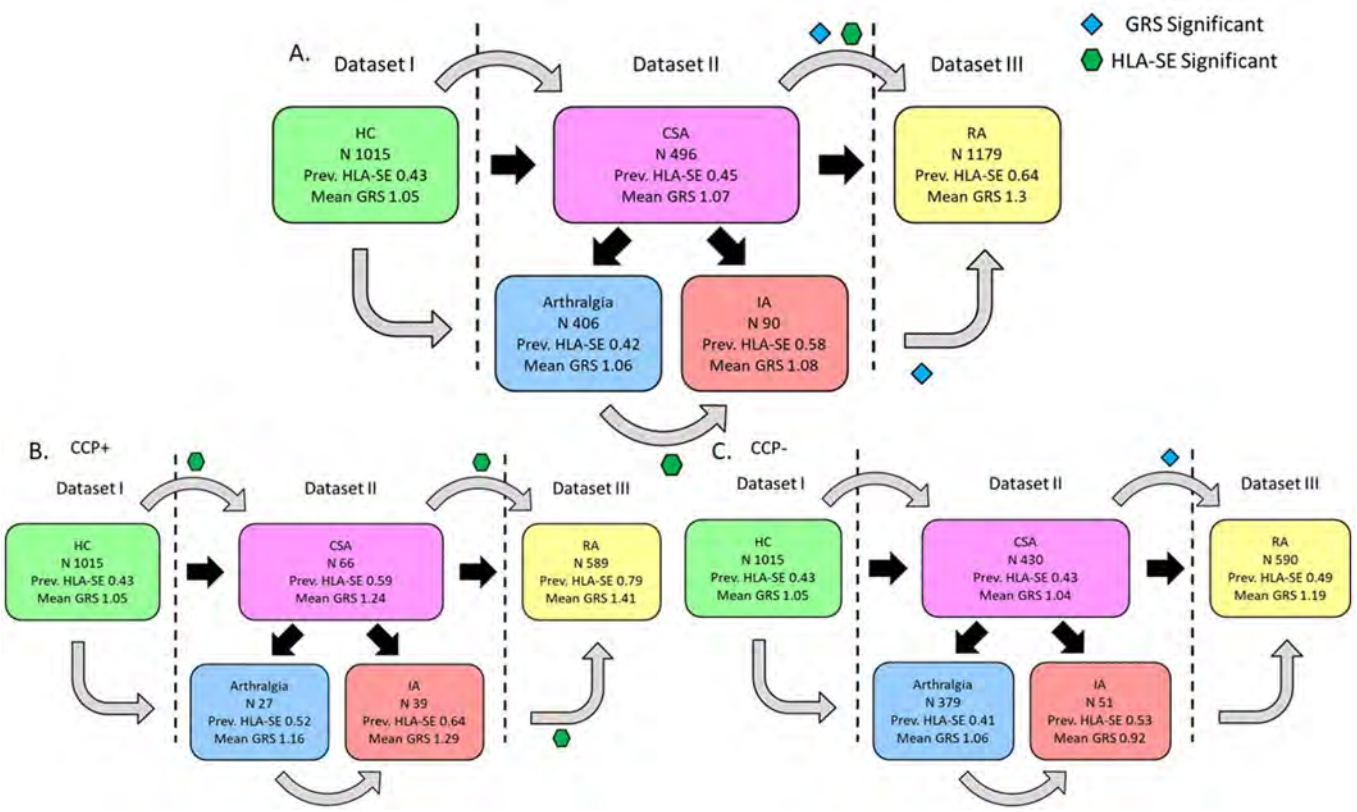

Figure 1. Distribution of HLA-SE and RA Genetic Risk Score (GRS) across Healthy Controls (HC), CSA (converters to Inflammatory Arthritis (IA) and non converters (Arthralgia)) and established RA. Blue diamonds (GRS) and green hexagons (SE) indicate logistic regression significance. Both full datasets (A) and CCP+ (B) and CCP- (C) strata of CSA and RA are shown.

Background/Purpose: The identification of a pre-RA stage of patients with clinically suspect arthralgia (CSA) has proven to be beneficial in the early detection of Rheumatoid disease. Similarly, genetic susceptibility studies have identified important genetic risk factors for the development of (CCP positive) RA.[1] The question that arises is whether these findings represent independent etiological pathways and could therefore be complimentary in the early diagnosis of RA. We therefore aimed to corroborate the knowledge of genetic differences between HC and RA patients and extend it to include the CSA stage of disease.

Methods: We used three datasets sampled from the same region: 1,085 healthy controls (HC), 530 CSA and 1,277 RA patients. CSA patients were monitored for a median of 2 years for conversion into clinically apparent inflammatory arthritis (CSAc) or not (CSAnc).[2] Genotype data of all individuals was identically processed, including separate imputation of the HLA region using SNP2HLA with the T1DGC panel. A Genetic Risk Score (GRS) consisting of 85 RA risk SNP's derived from literature was calculated for all samples.[3] HLA-SE positivity was defined as the presence of at least 1 of the HLA-DRB1 alleles.

We assessed the association of the GRS and HLA-SE with disease stage using logistic regression in the full data and in the CCP+ and CCP- strata of the CSA and RA populations.

Results: The GRS increased with disease stage, from 1.05 in HC to 1.3 in established RA cases. This was significant between CSA and RA (OR: 1.36, 95%CI: 1.21 – 1.53, P-value: < .001), and CSAc and RA (OR: 1.29, 95%CI: 1.02 – 1.64, P-value: .037). HLA-SE prevalence also differed significantly between CSA and RA (OR: 2.59, 95%CI: 2.07 – 3.24, P-value: < .001), which could be attributed to the difference between CSAnc and CSAc (OR: 1.88, 95%CI: 1.18 – 2.99, P-value: .007). (Fig. 1A) In CCP+ patients only the differences in SE between HC and CSA (OR: 1.89, 95%CI:

1.14 – 3.13, P-value: .014), CSA and RA (OR: 2.6, 95%CI: 1.53 – 4.41, P-value: < .001) and CSAc and RA (OR: 2.1, 95%CI: 1.06 – 4.16, P-value: .033) were significant. (Fig. 1B) The increase in GRS from CSA to RA, observed in the full datasets, remained significant in the CCP- strata (OR: 1.21, 95%CI: 1.04 – 1.42, P-value: .013). (Fig. 1C).

Conclusion: The current results seem to indicate a role for HLA-SE in the development of arthritis, whereas the GRS more specifically associates with the development of RA. This latter association was also observed in the CCP- CSA and established RA populations. We can conclude that known RA genetics distinguish progressed disease from earlier stages independently of CCP, even when taking the at-risk stage of CSA into consideration.

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Disclosure: M. Maurits, None; **F. Wouters**, None; **E. Niemantsverdriet**, None; **T. Huizinga**, None; **A. van der Helm-van Mil**, None; **R. Knevel**, Pfizer, 5.

Abstract Number: 0520

Leukocyte Immunoglobulin-like Receptor A3 Facilitates Neutrophil Extracellular Trap Formation in TLR7-induced Lupus Mice

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SESSION INFORMATION
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Background/Purpose: Leukocyte immunoglobulin-like receptor A3 (LILRA3) is a secreted protein belongs to LILR family. Our research group previously reported that the functional *LILRA3* is a novel genetic risk for multiple autoimmune diseases including systemic lupus erythematosus (SLE). However, the function of LILRA3 in development of lupus is unclear. Dysfunctional neutrophils play a pathogenic role in SLE, particularly through the release of neutrophil extracellular traps (NETs). The aim of this study was to functionally characterize the role of LILRA3 in NET formation in the TLR7-induced lupus-like model.

Methods: To functionally study the role of LILRA3 in autoimmune diseases, we constructed the *LILRA3* knock-in (KI) mice. The lupus-like disease was induced by the epicutaneous application of the TLR7 agonist imiquimod (IMQ) three times a week. The C57BL/6 wild-type and *LILRA3*-KI mice were sacrificed on day 14, 28, and 56 after treatment of IMQ. Flow cytometry was used to evaluate the proportions of neutrophils in peripheral blood (PB), spleen, and bone marrow (BW), respectively. To assess NETosis (NETs release), complementary approaches were utilized. The total extracellular DNA was quantified as relative fluorescence units upon the addition of Sytox Green by using the SYTOX Green assay. Immunofluorescence staining was applied to label the neutrophil elastase and citrullinated Histone H3(Cit-H3). Enzyme-linked immunosorbent assay was applied to detect antibodies in serum.

Results: he proportions of $CD11b^+ly6G^+$ neutrophils were significantly increased in PB, spleen and BM from IMQ-treated *LILRA3*-KI (KI-IMQ) mice, compared to IMQ-treated WT (WT-IMQ) mice and WT control mice on day 14 and 28 ($P < 0.01$). After 56 days of IMQ treatment, there was no significant difference in the proportion of PB and BM $CD11b^+ly6G^+$ neutrophils across the 3 groups, but the splenic $CD11b^+ly6G^+$ neutrophils were remarkably increased from KI-IMQ mice, compared to WT-IMQ and WT control mice ($P < 0.01$). Furthermore, BM neutrophils from KI-IMQ mice displayed an enhanced release of NETs as compared to that from WT-IMQ and WT control mice at three time points ($P < 0.01$). After phorbol myristate acetate (PMA) or Calcimycin (A23187) stimulation, a similar phenomenon was also observed for BM neutrophils from KI-IMQ mice. Concentration of serum anti-dsDNA IgG was significantly elevated in KI-IMQ mice as compared to WT-IMQ and WT control mice ($P < 0.001$).

Conclusion: Our data suggest that LILRA3 may promote lupus-like disease through excessive neutrophil activation and NET formation in TLR7-induced lupus mice.

Disclosure: H. Liu, None; **Y. Tang**, None; **C. Chen**, None; **J. Guo**, None.

Abstract Number: 0521

Genome-Wide DNA Methylation and Gene Expression Signatures in Classical Monocytes from African Ancestry Patients with Systemic Sclerosis

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Background/Purpose: Systemic sclerosis (SSc) is a multisystem autoimmune disorder that has an unclear etiology and disproportionately affects individuals of African ancestry (AA). Despite this, AA individuals are dramatically underrepresented in SSc research. Additionally, monocytes show heightened activation in SSc, and in AA relative to European ancestry (EA) individuals. Monocytes are thus a good target tissue for elucidating disease mechanisms. In this study, we sought to identify changes in genome-wide DNA methylation and gene expression levels in classical monocytes from AA SSc patients and unaffected AA controls.

Methods: Classical monocytes (CD14++CD16-) were FACS-isolated from 17 SSc cases and 18 controls. All patients met the 2013 ACR/EULAR classification criteria for SSc. All participants were self-reported AA female. DNA methylation was profiled using Illumina's MethylationEPIC BeadChip to identify differentially methylated CpGs. RNA-seq was performed to identify differentially expressed genes. Expression quantitative trait methylation (eQTM) analysis was computed to identify CpGs associated with changes in gene expression.

Results: Many of the top differentially methylated CpGs map to genes with roles in immune pathways, including T-cell surface glycoprotein *CD5,* oligoadenylate synthetase *OAS3*, and DNA repair *FANCC*. The SSc monocyte transcriptome showed an enrichment of genes in the AMPK signaling pathway, genes involved in chromatin organization, transcription factor binding, and glycogen storage diseases. The top differentially expressed genes include hepara-

nase *HPSE*, collagen *COL9A2*, and chromatin regulator *SMARCA4*. The top eQTM genes included transcriptional repressor homolog *PCGF1*, RNA helicase *DDX27*, transcription factor *E2F4*, and hydrolase *KYNU*.

Conclusion: To the best of our knowledge, this is the first study to investigate DNA methylation and gene expression signatures in classical monocytes from SSc patients of African ancestry. The relatively modest differences in DNA methylation and gene expression observed between patients and controls is consistent with prior evidence of stronger inflammatory signatures in AA relative to EA individuals. These data support a possible role for DNA methylation and gene expression differences in mediating sustained monocyte activation and susceptibility to SSc in AA individuals.

Disclosure: S. Smith, None; **P. Allen**, None; **R. Wilson**, None; **J. Wirth**, None; **D. Baker Frost**, boehringer ingelheim, 1, Atheneum Partners, 2; **G. Gilkeson**, None; **M. Cunningham**, None; **D. Absher**, None; **P. Ramos**, None.

Abstract Number: 0522

Genetics of Rheumatoid Arthritis Remission; HLA-SE Associated with Remission in Anti-CCP Positive Patients

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SESSION INFORMATION

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Background/Purpose: Rheumatoid Arthritis (RA) patients capable of reaching clinical remission potentially have a specific genetic profile that allows them to regain immune tolerance. The identification of these genes could provide insights into the etiology of RA, as well as immunological pathways which could serve as novel drug targets.

We set out to test the association between established RA genetic risk variants and achieving remission at 6 months.

Methods: We computed genetic risk scores (GRS) comprised of RA susceptibility variants[1] and HLA-shared epitope (SE) allele status separately in 3,984 DMARD naïve patients across 9 datasets from inception cohorts. Remission was assessed at 6 months and defined as DAS28CRP values below 2.6. Values were imputed where necessary using predictive mean matching by MICE. We first tested whether baseline DAS28CRP changed with increasing GRS using

Table 1. Summary of the data separated by disease activity after 6 months.

	All	Remission at 6 months	No remission at 6 months
N	3,984	1,577	2,407
Age, *mean (sd)*	55.25 (13.75)	55.21 (14.12)	55.27 (13.51)
Female *%*	64.61%	62.59 %	65.93 %
ACPA+ *%*	56.00%	55.61 %	56.25 %
Baseline DAS28, *mean (sd)*	4.29 (1.43)	3.74 (1.54)	4.65 (1.23)

linear regression. Next, we used logistic regression to determine the relationship between the GRS and HLA-SE alleles and 6 month DAS28CRP remission in all cohorts independently. Using inverse variance weighted meta-analysis we concatenated these results into a singular effect estimate.

Due to the known differences in genetic background of anti-CCP positive and negative RA, we also repeated the analyses in only anti-CCP positive patients.

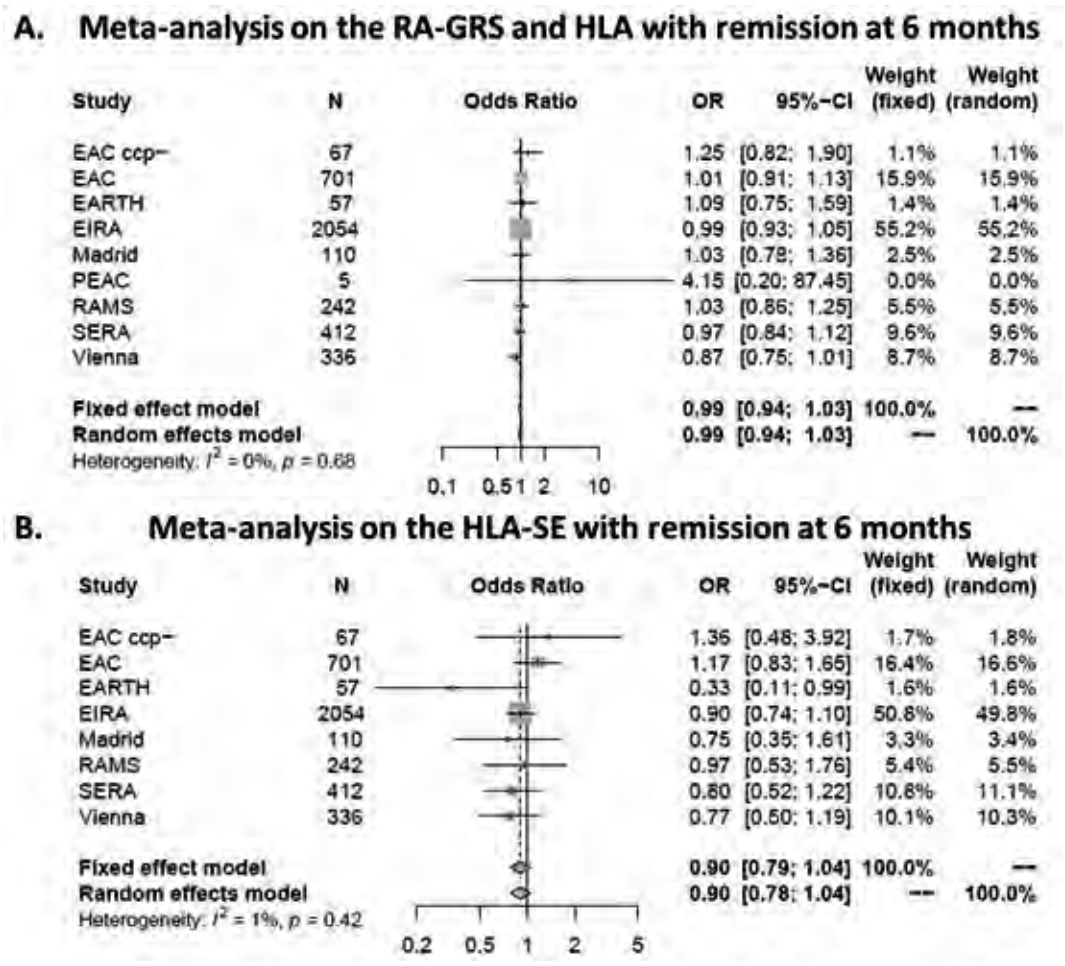

Figure 1. Inverse weighted meta-analysis of (A) the GRS + HLA and (B) the HLA-SE. Includes the dataset name (Study), sample size (N), odds ratio (OR), 95% confidence intervals (95%-CI) and the weights of the fixed and random effect models. I2 = percentage of variation across studies due to heterogeneity.

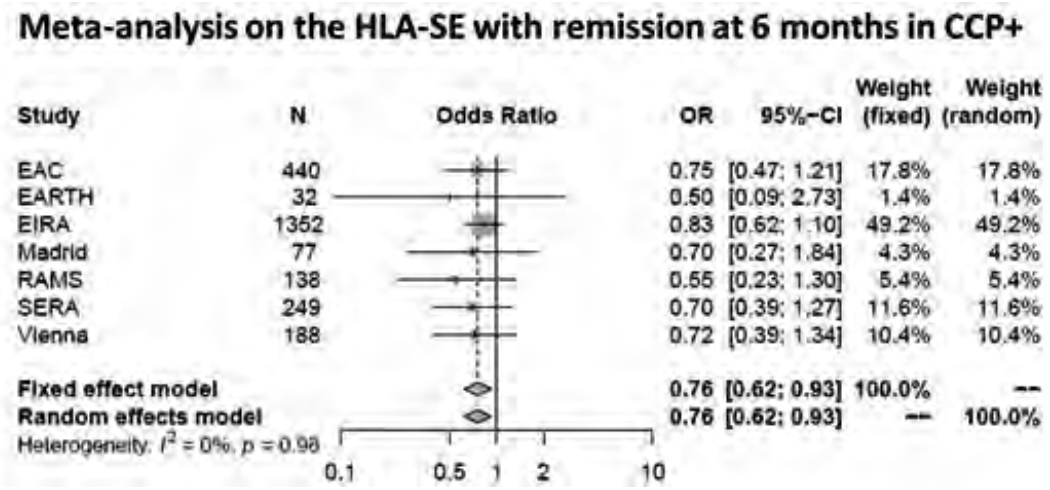

Figure 2. Inverse weighted meta-analysis of the HLA-SE in CCP positive patients. Includes the dataset name (Study), sample size (N), odds ratio (OR), 95% confidence intervals (95%-CI) and the weights of the fixed and random effect models. I2 = percentage of variation across studies due to heterogeneity.

Results: Baseline clinical variables did not differ between patients who achieved remission and those who did not (**Table 1**). Distribution of the GRS was consistent between datasets. Neither GRS nor HLA-SE alleles were associated with baseline DAS28CRP (OR 1.01; 95% CI 0.99 - 1.04). A fixed effect meta-analysis showed no significant effect of the GRS (OR 0.99; 95% CI 0.94 - 1.03) or HLA-SE alleles (OR 0.90; 95% CI 0.79 - 1.04) on remission at 6 months (**Figure 1**). In the seropositive analyses we did observe one significant association; HLA-SE alleles positivity reduced the likelihood of 6 months DAS28CRP remission in the anti-CCP positive stratum (OR 0.79; 95% CI 0.62 – 93) (**Figure 2**).

Conclusion: Of the known RA genetic risk variants only HLA-SE alleles are associated with a decreased chance of obtaining remission in the anti-CCP positive population in these combined cohorts. Studies encompassing broader genetic profiles are needed to further elucidate the genetics of RA remission.

References

1). Knevel R et al. Sci Transl Med. 2020;12(545):eaay1548.

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Abstract Number: 0523

Transcriptional Subsetting of SLE Patient Cohorts Based on Metabolic Pathway Activity

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus is a highly complex, heterogeneous, autoimmune disorder, with diverse clinical presentation and innate and adaptive immune system involvement. There is a need to better understand the molecular basis for dysregulated immune system function and disease pathophysiology in SLE in order to assign individuals to more homogeneous mechanistic subsets, enabling the identification of targets for more effective, cohort-specific, therapies with a higher impact in clinical improvement. Previous studies have used whole transcriptome data to identify key molecular features in order to achieve meaningful assignment of SLE patients into subsets defined to a large extent by predominate immune cell types in peripheral blood. These studies have allowed us to make inferences as to the contribution of specific immune cells to disease in different patient groups.

Methods: As metabolic regulation of innate and adaptive immune cells is increasingly appreciated as a driver of disease phenotypes, we sought to investigate if patient heterogeneity could be revealed by focusing solely on metabolic pathways relevant to the activation state of immune cells found in the peripheral blood. We collected a set of 84 metabolic pathways and gene sets, comprised of a total of 1,692 genes, and calculated the pathway eigengenes as described elsewhere (1). We applied our methodology to the ILLUMINATE-1 clinical trial cohort transcriptomics data set (2), generated from whole blood samples collected from 879 patients. After calculating the pathway eigengenes for the patient cohort, we performed unsupervised clustering using 30 different algorithms, in order to determine the optimal number of clusters in these data (Fig 1.) Additionally, we calculated the predicted immune cell population for each patient as described elsewhere (3), enabling us to ascribe biological significance to the identified clusters. Our results show that, when comparing the patient clusters on whole transcriptome data versus on pathway eigengenes,

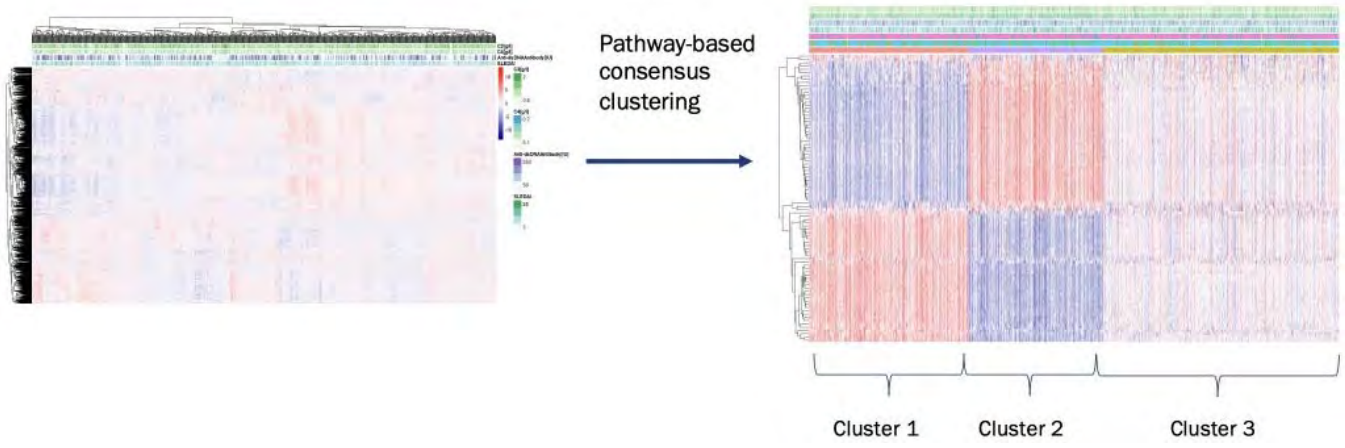

Figure 1. Metabolism-based patient sub-setting. Our approach introduces higher resolution in the understanding of patient data, allowing for a clearer definition of biologically-relevant clusters.

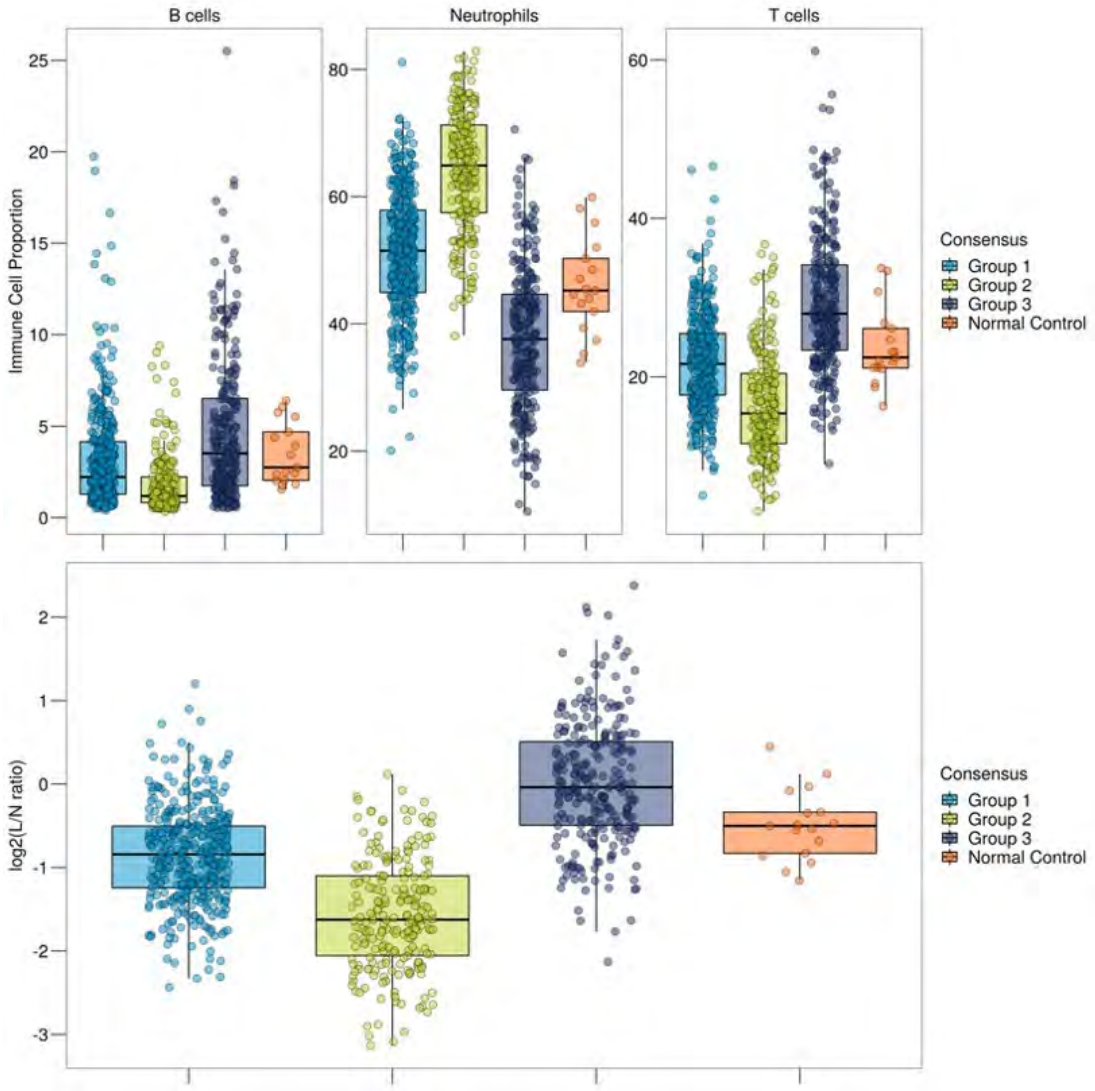

Figure 2. Immune cell population inference based on the ABIS algorithm. Using our metabolism-based patient sub-setting strategy we can clearly defined, in an unbiased manner, biologically relevant patient groups.

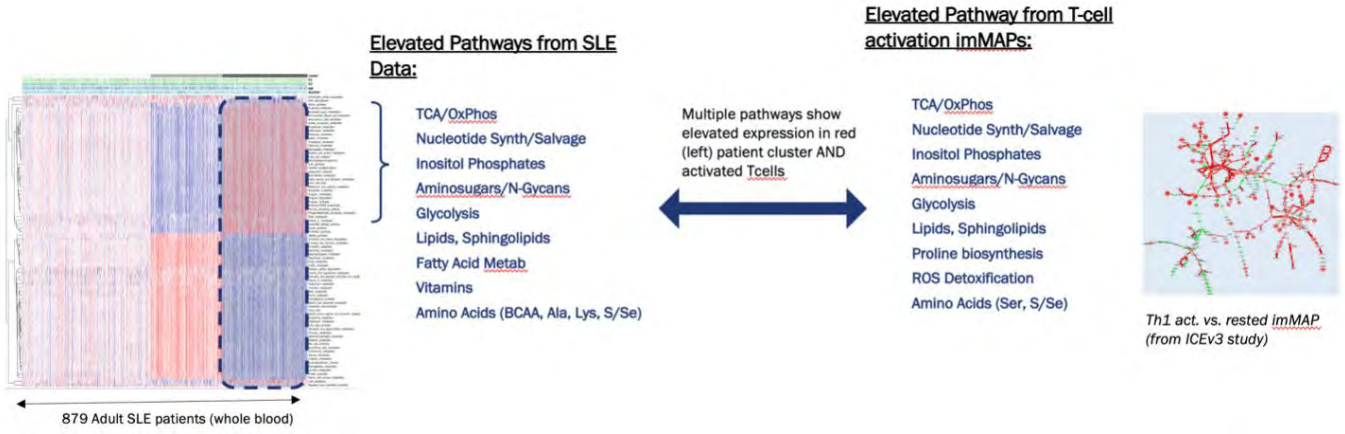

Figure 3. Patient subsets and imMAPs. We compared our unbiased clustering approach to data generated using our imMAP algorithm and we found a strong overlap between the lymphocytic cluster and the T cell activation imMAP, given further credence to our metabolism-based approach for patient subsetting.

there is an enrichment in the immune cell populations in the latter (Fig 2), reflecting not only their proportion but also their activation or effector state. Furthermore, we compared the clustering results based on the pathway eigengenes with our immunometabolism map (imMAP), an algorithm for the integration of transcriptional and metabolic profiles, run on data from primary human effector memory peripheral blood T cells activated by anti-CD3/CD28/CD2, highlighting how the high lymphocytic cluster preserves features captured by our imMAP (Fig 3.)

Results: Our results indicate that SLE patients can be differentiated based upon metabolic features with potential important biological and clinical significance, given the increasing appreciation for disease-associated immune cell metabolic reprogramming in autoimmune diseases (4, 5).

Conclusion: Insights from these studies will facilitate discovery of novel targets that impact the disease-associated metabolic programming of immune cell drivers of SLE and provide a framework for precision medicine approaches to assign individual patients to disease subgroups that would best benefit from drugs modulating those targets.

Disclosure: D. **Camacho**, Rheos Medicines, 3; **J. Swantek**, Rheos Medicines, 3; **K. Soh**, Rheos Medicines, 3; **J. Kamphorst**, Rheos Medicines, 3, 8; **V. Kaimal**, Rheos Medicines, 3; **J. Monroe**, Rheos Medicines, 2, Rubius Therapeutics, 2, AnaptysBio, 2; **E. Driggers**, Rheos Medicines, 3, 8.

Abstract Number: 0524

Development of Biomarker Models to Identify HLA-related Microbiome Associations in Anti-Ro+ Mothers of Children with Neonatal Lupus

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-Ro autoantibody production often precedes the development of Systemic Lupus Erythematosus (SLE) or Sjogren's syndrome (SS) by years. For anti-Ro+ mothers enrolled in the Research Registry for Neonatal Lupus (RRNL), progression to SS or SLE occurs in about a quarter, while most remain asymptomatic or develop only minor rheumatic symptoms (Asym/UAS). Thus, RRNL mothers uniquely offer a promise to identify genotype-phenotype relationships that are important to preclinical autoimmunity. Since multiple SLE risk alleles from Class II HLA genes are present in anti-Ro+ mothers, we examined interactions of specific microbiome taxa with Class II HLA by independent analytic paths with the goal to identify HLA-related microbiome associations in Anti-Ro+ Mothers of Children with Neonatal Lupus.

Cluster	Asvm/UAS	SS/SLE	Total
1	4	10	14
2	9	19	28
3	8	8	16
4	2	19	21
5	4	8	12
6	2	0	2

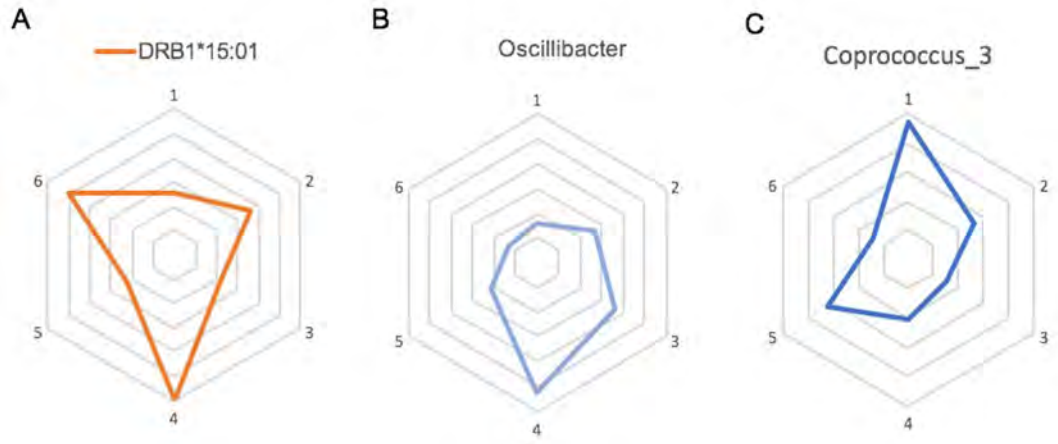

Figure 1. Distribution of subjects (anti-Ro+ mothers), HLA DRB1*15:01 and taxa of interest at clusters 1=6.

Methods: Subjects included 125 RRNL mothers and 23 healthy controls. Stool microbiomes of anti-Ro+ women in RRNL (Asym/UAS, SS/SLE), and healthy controls (HC) were processed using 16S ribosomal RNA sequencing. Sera/plasma were evaluated for cytokines and autoantibody levels. Alleles from HLA Class II genes were genotyped using NextGen sequencing of HLA region or imputed (HIBAG) from GWAS data. Independent analytic paths sought to explore associations of specific taxa and class II HLA included: 1) use of a cumulative logit model to test interactions between FDR significant genera and HLA alleles and 2) assignment of SLE, SS, UAS patients and HC to molecular phenotype clusters by Random Forest (RF), an unsupervised machine learning tool using Z-score transformed cytokine soluble mediators and autoantibody values with settings and the gap statistic that were used to estimate the

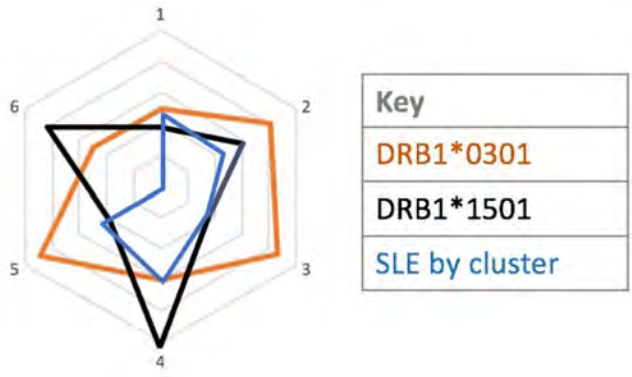

Figure 2. The distribution of DRB1*1501, DRB1*0301, and SS/SLE disease classification at cluster profiles representing evaluations of RRNL mothers.

optimal number of patients and HC within clusters. The overlapping distribution of SS/SLE, HLA alleles and taxa at clusters were then examined.

Results: Findings related to DRB1*15:01 and an interaction with genera of the *Ruminococcaceae* family were tested. *Oscillibacter*, with FDR-adjusted significance was shown to exhibit evidence of an interaction (P=0.033 (OR=0.60 (0.37-0.96)). In order to authenticate that SLE HLA risk alleles modify the strength of the association, we examined the molecular phenotype clusters from RF clustering. Radar plots were used to visualize the distribution HLA alleles and the enrichment of microbiome taxa within these clinically relevant phenotypic clusters (**Figure 1**). DRB1*1501 shows enrichment at cluster 4. Interestingly, the distribution of *Oscillibacter*, but not *Coprococcus 3* was nearly superimposable with the Class II HLA allele with enrichment at cluster 4. However, the distribution of DRB1*1501 was not enriched at cluster profiles representing evaluations of DRB1*0301 and SS/SLE disease classification (**Figure 2**) demonstrating a limitation of DRB1*1501 to predict risk for transition from benign to pathologic autoimmunity in anti-Ro+ mothers of children with neonatal lupus.

Conclusion: These data support the use of molecular phenotypes that are linked to genetic-environmental interactions to identify HLA-related microbiome associations.

Disclosure: R. Clancy, None; **M. Marion**, None; **H. Ainsworth**, None; **M. Beel**, None; **M. Chang**, None; **C. Guthridge**, None; **J. Guthridge**, None; **T. Howard**, None; **P. Izmirly**, Momenta/Janssen, 1; **J. Kheir**, None; **M. Masson**, None; **M. Smith**, None; **J. James**, Progentec Diagnostics, Inc., 2; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **C. Langefeld**, None.

Abstract Number: 0525

STEAP3, FZD2 and EGFLAM Are Novel Genetic Risk Loci for Granulomatosis with Polyangitis: A Genome Wide Association Study from UK Biobank

Mehmet Hocaoglu[1], Jamal Mikdashi[2], Yi-Ju Chen[2], James Perry[2] and Charles Hong[2], [1]University of Maryland Medical Center, Midtown Campus, Baltimore, MD, [2]University of Maryland School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
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Background/Purpose: Granulomatosis with Polyangitis (GPA) is a systemic ANCA associated small vessel vasculitis. Prior genetic studies demonstrated a strong association of HLA Class II region with GPA. The literature on the non-HLA risk loci is limited as only the minority of the multiple candidate risk loci were able to be replicated in subsequent studies. The aim of this study is to examine the role of non-HLA genetic risk factors for GPA using the genomic data from UK Biobank cohort.

Methods: Our study utilized the UK Biobank database which has over 820,000 genotyped SNPs with up to 90 million imputed variants for 500,000 volunteers from the general population in the United Kingdom (UK). The genetic information of each participant is linked with their International Classification of Diseases (ICD)-10, procedure and treatment codes. 175 patients with ICD-10 code M31.3 Granulomatosis with polyangitis were included in our study as cases. >95% of the cases had at least one other supporting clinical, treatment or procedural codes related to

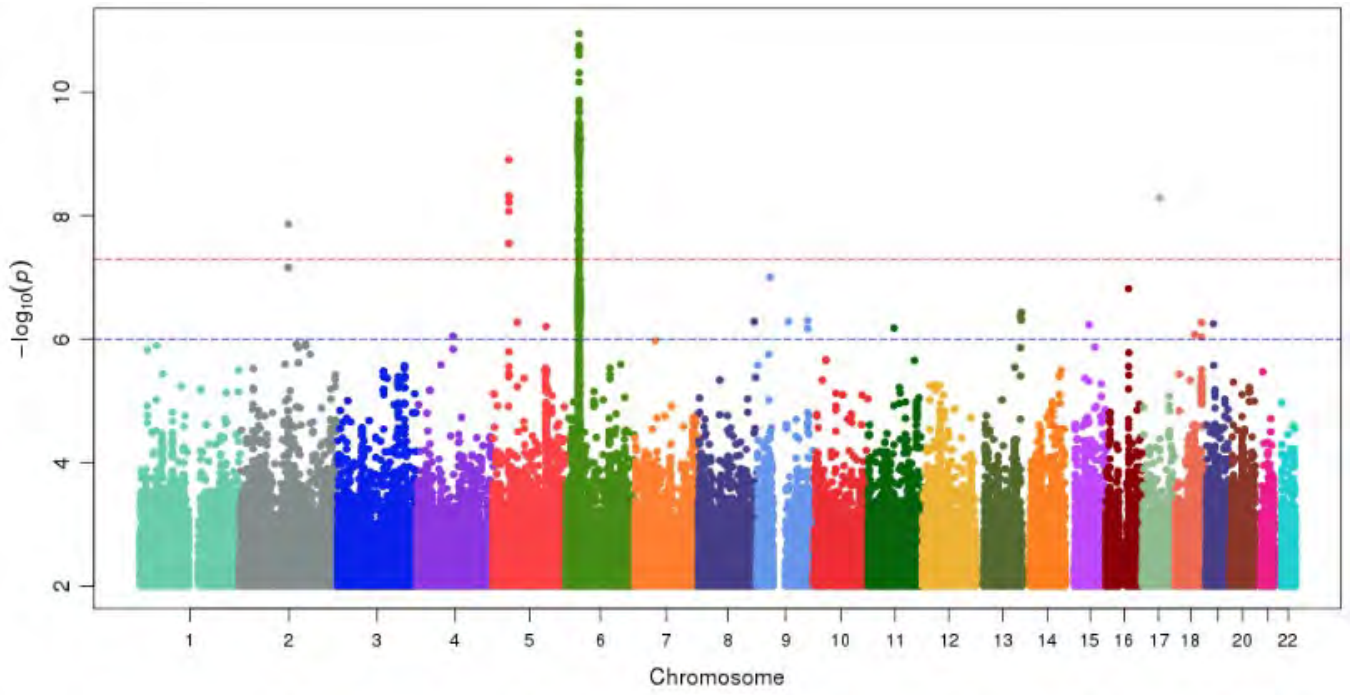

Figure 1. Manhattan plot of Genome-wide association study results for Single Nucleotide Polymorphisms with a MAF> 0.5% for Granulomatosis with polyangitis (GPA).

SNP	Chromosome	Type	Gene	P value	MAF	OR
rs6723312	2	intergenic	'STEAP3	$1.3*10^{-8}$	%10.4	2.2
rs2561807	5	intronic	'EGFLAM	$1.2*10^{-9}$	%9.23	2.4
rs13184051	5	intronic	'EGFLAM	$6.1*10^{-9}$	%10.2	2.3
rs2731965	5	intronic	'EGFLAM	$8.4*10^{-9}$	%8.8	2.3
rs2561824	5	intronic	'EGFLAM	$2.8*10^{-8}$	%8.6	2.3
rs2561823	5	intronic	'EGFLAM	$2.8*10^{-8}$	%8.6	2.3
rs60174623	5	intronic	'EGFLAM	$4.8*10^{-9}$	%10	2.3
rs34201149	5	intronic	'EGFLAM	$4.8*10^{-9}$	%10.3	2.3
rs568915088	17	intergenic	'FZD2	$5.1*10^{-9}$	%0.5	9.5

Table 1. Variants outside of the MHC class II region that are associated with Granulomatosis with polyangitis (GPA).

GPA. Sex, age and ancestry matched control subjects were assigned for each case from the same cohort in a 1:20 case: control study design. Related individuals and individuals with autoimmune diseases associated with secondary vasculitis were excluded. The genome wide association analysis was performed using Plink2 methodology.

Results: We identified a total of 338 SNPs with a genome wide significance level of $< 5x10^{-8}$ and minor allele frequency of >0.5%. (Figure 1) 329 of the significant variants were located at the MHC Class II region in chromosome 6. Within the MHC Class II locus, the SNP with strongest association was rs1042169, an exonic missense variant found in *HLA-DPB1* gene. Multiple other SNPs in strong LD with our top hit were identified in *HLADPB2, RING1, MIR219A1, RXRB, RING1* and *HSD17B8* loci. Independent SNPs were also identified in the *HLADPA1 and COL11A2* loci. Outside of the MHC region, nine SNPs exceeded the threshold for genome wide significance. 7 of those were found in *EGFLAM* locus in strong linkage disequilibrium with our top hit rs2561807, an intronic variant. Two intergenic SNPs with genome wide significance level were identified in *STEAP3* and *FZD2* loci, rs6723312 and rs568915088 respectively. (Table 1) Both rs2561807 and rs6723312 demonstrated dose dependence with significantly higher prevalence in homozygotes compared to heterozygotes. (Figure 2)

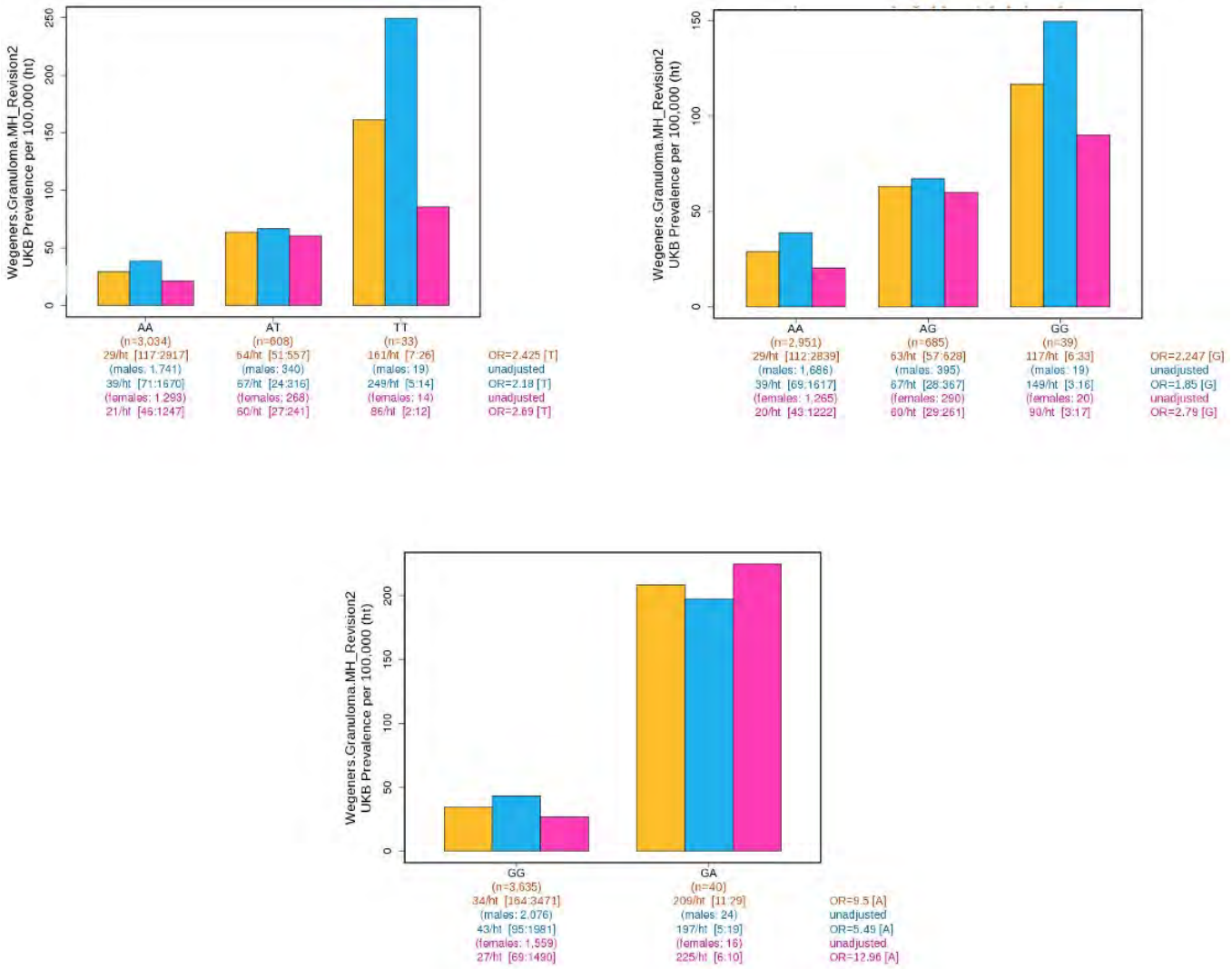

Figure 2. Prevalence of Granulomatosis with Polyangiitis (GPA) per 100,000 participants per genotype in the UK Biobank for rs6723312, rs2561807 and rs568915088 variants.

Conclusion: In this genome wide association study, we confirmed the previously reported association of HLA-DP with GPA and identified EGFLAM, STEAP3 and FZD2 as new genetic risk loci. Further research on the role of non HLA region for genetic susceptibility of GPA is warranted.

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

Abstract Number: 0526

Transcriptional Factor Profiling Denotes Specific Synovial Macrophage Heterogeneity

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Macrophages are critical to the pathogenesis of rheumatoid arthritis(RA), but several distinct macrophage subpopulations co-exist in the synovium of joints. In steady-state, tissue-resident macrophages maintain joint integrity and are required for tissue homeostasis. On the other hand, macrophages contribute to inflammation through the production of cytokines, release of degradative enzymes, and recruitment of other immune cells. However, we currently lack specific targets to regulate macrophage function at the molecular level in the context of developing and relapsing disease.

Methods: We utilized functional genomic analysis of murine and human synovium including single cell-CITE and ATAC seq.

Results: Based on our analysis of gene expression, we characterized the 4 synovial macrophage populations as follows: MA=CX3CR1+MHCII- tissue-resident synovial lining, MB=CX3CR1+MHCII+ newly infiltrating cells; MC=CX3CR1-MHCII- tissue-resident interstitial, MD=CX3CR1-MHCII+ monocyte-derived interstitial. We then characterized the 4 subpopulations of synovial macrophages at days 0, 3, 7, 13 and 21 post serum transfer induced arthritis (STIA). We clustered the genes that were differentially expressed over the course of STIA in any subpopulation into 6 clusters (STIA I-VI). STIA I-III represent an increase in expression of inflammation and immune response genes that is most prominent in infiltrating MB. In contrast, STIA IV-VI represent a decrease in expression of homeostatic (largely interstitial MC and MD), cell cycle (MB), and tissue-resident genes (preferentially MA), respectively. To achieve better resolution on the transcriptional profile of synovial macrophages, we performed bulk RNA-seq on each subpopulation as well as classical and non-classical monocytes. We defined 5 clusters of genes that vary in expression across macrophages: c1=MA-specific; c2=tissue-resident-specific (MA and MC), c3=monocyte-derived-specific (MB and MD), c4=tissue-resident and monocyte; c5=MB and monocyte. To identify TFs that regulate each cluster, we performed motif-finding using the HOMER package. We identified that the MAFB sequence motif was associated with c3 and increased in expression from monocytes to tissue-resident macrophages supporting its role in monocyte-macrophage transition. On the other hand, the MEF2C sequence motif and gene expression suggested it played a role in tissue-residency. By performing a similar analysis on STIA time course clusters, we found that MAFB is associated with increased expression of inflammatory genes, whereas MEF2C is linked with decreased expression of homeostatic and tissue-resident genes. We also determined that macrophage sub-populations identified in mice were recapitulated in human patients from the synovial tissue of 7 RA patients. We found that patients exhibited varying macrophage composition, specifically, the proportion of MA and MC tended to be negatively correlated with disease severity, while MB and MD exhibited the opposite trend.

Conclusion: These studies established the dynamics and transcriptional regulation of monocyte-derived macrophages in inflammatory arthritis from mice and human synovium.

Disclosure: D. Winter, None; **C. Cuda**, None; **S. Chen**, None; **A. Montgomery**, None; **S. Dominguez**, None; **G. Gadhvi**, None; **H. Perlman**, Kiniksa, 1, 2.

Abstract Number: 0527

Role of Terminal Uridylyl Transferase 7 in TNF-α-Induced Inflammation in Rheumatoid Arthritis Synovial Fibroblasts *In Vitro*

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Terminal uridylyl transferase 7 (TUT7), also known as Zcchc6, is a zinc finger domain-containing protein responsible for terminal uridylation of miRNA, implicated in pre-miRNA maturation and mature miRNA degradation. Dysregulated microRNA (miRNA) expression in human rheumatoid arthritis synovial fibroblast (RASFs) has been observed when compared to non-diseased SFs (NLSFs). Differential expression of miRNA is found to be associated with dysregulated miRNA biogenesis and degrading enzyme activity or stoichiometric differences in the amount of these proteins inside the cells. However, the role of TUT7 remains unexplored in RASFs.

Methods: Protein levels of miRNA biogenesis and degrading enzymes were compared by Western blotting in whole cell extracts prepared from RASFs and NLSFs. RASFs were treated with TNF-α for 24 h were used to evaluate changes in gene expression of miRNA biogenesis and degrading enzymes. RNA sequencing was performed in RASFs transfected with TUT7 siRNA or negative control (NC) siRNA in presence or absence of TNF-α (20 ng/ml) using an Ion Proton™ System. Effects of the loss of TUT7 were examined by gene enrichment of differentially expressed genes (DEGs) in presence or absence of TNF-α, followed by Gene Ontology analysis to determine key pathways modulated. Culture supernatants from siRNA-transfected samples were tested by ELISA to determine cytokine or chemokine production. Statistical value of $p < 0.05$ was considered significant.

Results: Western blot analysis of miRNA biogenesis machinery confirmed increased expression of Ago1 and Ago2 and decreased expression of TUT7 in RASFs compared to NLSFs (N=3 $p< 0.05$). We assessed the effects of TUT7 ablation by siRNA on TNF-α-induced synovial inflammation in human RASFs by RNA sequencing. RNA Sequencing analysis revealed that, out of 20,814 genes in the array, 218 DEGs were statistically qualified candidates altered in the absence of TUT7. Gene ontology study of DEGs revealed significant effects of TUT7 knockdown on cellular response to starvation, protein processing in ER, skeletal system development, heart development, and spliceosomal tri-snRNP complex assembly. Validation of RNA-seq data by quantitative RT-PCR analysis of response to TNF-α during transient knockdown of TUT7 confirmed the upregulated expression of matrix metalloproteinases (MMP1, MMP3), chemokines (CXCL5, IL-8) and cytokine (IL-6) transcripts in human RASFs. In corroboration of the mRNA data, ELISA results from TUT7 siRNA-transfected RASFs supernatants showed the significant upregulation of TNF-α-induced IL-6, IL-8, CXCL5, MMP-1, and MMP-3 production (N=4; $p< 0.05$).

Conclusion: This study provides novel evidence showing that loss of endogenous TUT7 in RASFs may exacerbate their hyper-responsiveness to inflammatory cytokines such as TNF-α by modulating the miRNA degradation pathway.

Disclosure: A. singh, None; **f. Shaikh**, None; **S. Ahmed**, None.

Abstract Number: 0528

Interferon Pathway Lupus Risk Alleles Modulate Risk of Death from Acute COVID-19

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Type I interferon (IFN) is critical in our defense against viral infections. Increased type I IFN pathway activation is a genetic risk factor for systemic lupus erythematosus (SLE), and a number of common alleles contribute to the genetic high IFN trait. In this study, we examine whether these common gain-of-function alleles in the type I IFN pathway are associated with protection from mortality in acute COVID-19.

Methods: We studied IFN pathway SLE risk genes in patients with acute COVID-19 admitted to NYU Langone hospitals (751 European-American and 398 African-American ancestry). The samples were genotyped using low depth sequencing and imputation, and we analyzed data from the following SNPs: IRF5 (rs2004640, rs3807306, rs10488631, rs2280714), IRF7/PHRF (rs1131665, rs4963128), IRF8 (rs17445836, rs12444486), and PRKG1 (rs7897633). Ancestral backgrounds were analyzed separately, and mortality after acute COVID-19 was the primary outcome.

Results: We observed specific IRF5 haplotypes that are protective against SLE risk were associated with increased risk of mortality in acute COVID-19 patients in European-American ancestry (OR=3.74, p=0.015). Alleles of PRKG1 were also associated with mortality from COVID-19 in the European-American ancestry cohort (OR=1.80, p=0.0057), and this risk factor was particularly strong in younger patients (OR=29.2, p=0.01 in ages 45-54). IRF8 genotype at rs1244486 was associated with protection from mortality in COVID-19 in African-American subjects aged 65 and older (OR=0.34, p=0.04).

Conclusion: We find that a number of type I IFN pathway genes associated with risk of SLE also modulate risk of death during acute COVID-19. Similar to their associations with SLE, these alleles are variably associated with COVID-19 mortality across ancestral backgrounds, suggesting ancestral differences in the genetic regulation of the IFN pathway. These data confirm the critical role of the IFN pathway in our defense against viral infections, and support the idea that some common SLE risk alleles exert protective effects in anti-viral immunity.

Disclosure: I. **Nln**, None; **R. Fernandez Ruiz**, None; **T. Wampler Muskardin**, None; **S. Tuminello**, None; **M. Attur**, None; **E. Itturate**, None; **C. Petrilli**, None; **S. Abramson**, None; **A. Chakravarti**, None; **T. Niewold**, None.

Abstract Number: 0529

COPA Syndrome-associated Mutations in Lung Transplant Recipients for Interstitial Lung Disease

Sarah Beshay[1], Isabella Osuna[2], Jessica Smith[1], Justin Branch[3], Laura Muruato[3], Marietta DeGuzman[3], Pamela McShane[1], Yuelan Ren[1], Rajeev Singh[1], Manuel Silva Carmona[3], Sandeep Sahay[1] and **Tiphanie Vogel**[3], [1]Houston Methodist, Houston, [2]Rice University, Houston, TX, [3]Baylor College of Medicine, Houston, TX

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: COPA syndrome is a rare monogenic cause of immune-mediated lung disease, and it can mimic rheumatic diseases including rheumatoid arthritis (RA) with ILD, lupus and vasculitis. Like most genetic disease, COPA syndrome typically develops in childhood, but adult-onset cases have been reported. We recently established that a 77-year-old female who is 14 years out from double lung transplantation for a diagnosis of idiopathic pulmonary fibrosis (IPF) onset at age 60 years, her son with RA-ILD, and her granddaughter with juvenile arthritis complicated by ILD all have COPA syndrome. We then decided to determine the prevalence of COPA syndrome-associated mutations in patients with ILD who received lung transplantation.

Methods: We retrospectively reviewed 10 years of lung transplant recipients for ILD at a large transplant center

and identified patients with pulmonary fibrosis with or without a rheumatologic diagnosis. Targeted Sanger sequencing of the COPA syndrome hotspot (exons 8 and 9 of the *COPA* gene) was performed on amplified DNA extracted from explanted lung tissue.

Results: 427 transplant patients were identified; 66% were men and the mean age was 61 years. 55% received bilateral lung transplant. 62% had a diagnosis of idiopathic pulmonary fibrosis, 28% had a comorbid autoimmune condition, and 10% had other ILDs. To date, *COPA* sequencing has been completed for 147 patients and we have identified 4 patients with *COPA* mutations (2.7%), 3 with the most commonly reported variant (c.698G >A, p.R233H) and 1 with a novel variant (c.716C >T, p.A239V). The 1 female and 3 male patients had been diagnosed with RA-ILD, IPF, IPF and combined pulmonary fibrosis and edema (CPFE) as adults. All received bilateral lung transplant at an average age of 61 years (range 55-66 years). The 3 surviving patients are 11, 11 and 5 years out from transplant, however, the female patient with RA-ILD died 2 years post-transplantation secondary to chronic allograft rejection.

Conclusion: COPA syndrome is a rare entity and gaps exist in its recognition, diagnosis and management. We found that mutations in the *COPA* gene underlie some cases of severe pulmonary fibrosis labeled as other forms of adult-onset ILD. Identification and characterization of patients with such mutations will better define this rare disorder and serves as a step toward devising effective therapeutic strategies for patients with COPA syndrome.

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Abstract Number: 0530

Dysregulation of IGFI/IGF1R Pathway and IGF1R+3179A/G Polymorphism in Pathogenesis of Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren's syndrome (SS) is an autoimmune exocrinopathy characterized by chronic salivary and lacrimal gland dysfunction. Alterations of Insulin-like growth factor (IGF) pathway has been recently linked to the development of systemic autoimmune diseases possibly through induction of apoptotic pathways and genetic variants of the IGF1 receptor (IGF1R) gene, has been shown to increase systemic lupus erythematosus (SLE) susceptibility. The aim of this study was to investigate whether genetic variations of the IGF1R contribute to SS pathogenesis and inflammasome activation, previously shown to be a contributor in SS related lymphomagenesis.

Methods: DNA was extracted from whole peripheral blood derived from 200 SS patients fulfilling the 2016 ACR/EULAR criteria and 336 HC and genotyped for the rs2229765 IGF1R polymorphism by RFLP-PCR assay. To explore potential functional implications of the IGF1R rs2229765, total RNA was extracted from minor salivary glands bi-

Table 1. Frequency of rs2229765 variant in SS patients and healthy controls

SNP rs2229765	Model	Genotype	HC (n=219) n (%)	SS (n=200) n (%)	OR [95%CI]	p-value
	Codominant	G/G	112 (33.3%)	66 (33%)	1.00	
		G/A	188 (56%)	90 (45 %)	0.82 (0.55-1.21)	**0.0013**
		A/A	36 (10.7%)	44 (22%)	**2.07 (1.21-3.54)**	
	Dominant	G/G	112 (33.3%)	66 (33%)	1.00	0.94
		A/G-A/A	224 (66.7%)	134 (67%)	1.02 (0.70-1.47)	
	Recessive	G/G-G/A	300 (89.3%)	156 (78%)	1.00	**<0.001**
		A/A	36 (10.7%)	44 (22%)	**2.35 (1.45-3.80)**	
	Overdominant	G/G-A/A	148 (44%)	110 (55%)	1.00	**0.014**
		G/A	188 (56%)	90 (45%)	**0.64 (0.45-0.92)**	
	Log-additive				1.30 (1.00-1.69)	0.26

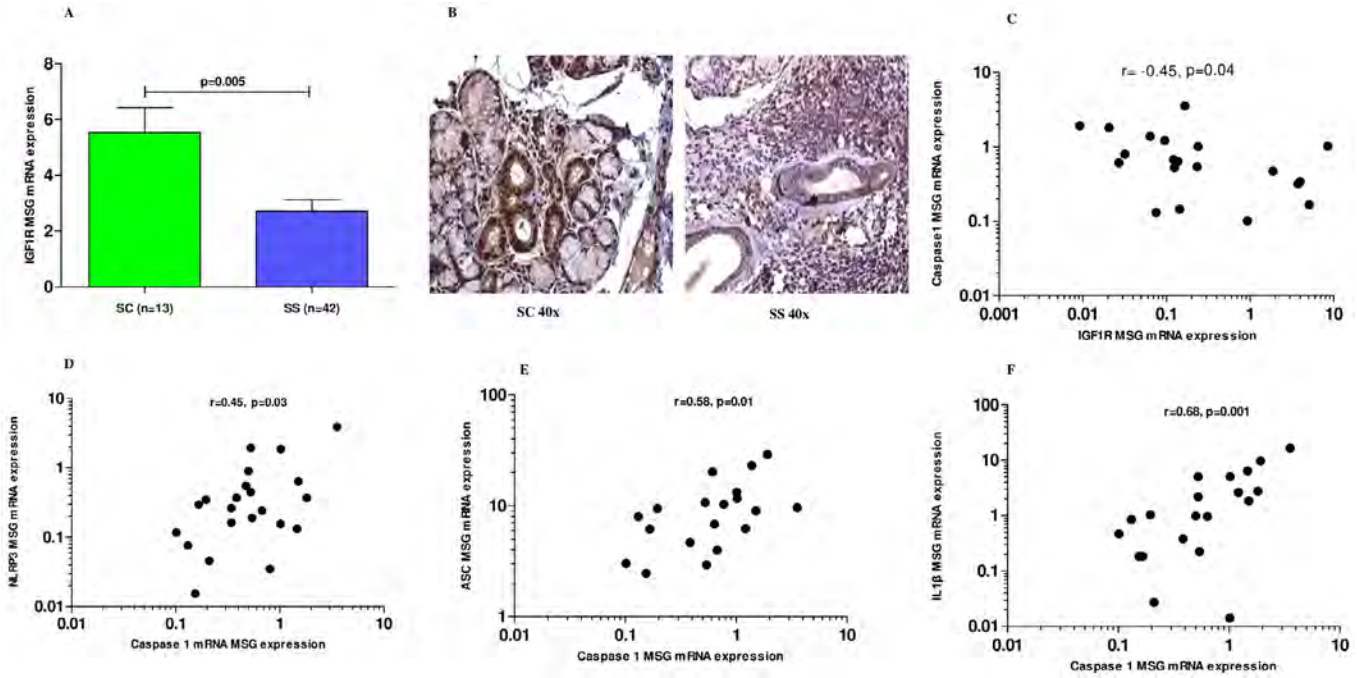

Figure 1. IGF1R mRNA and immunohistochemical expression in MSG tissues and gene expression correlations.

opsies (MSG) of 50 SS patients and 13 sicca controls (SC, presenting with ocular and /or oral dryness) and mRNA expression of IGF1R, as well as downstream inflammatory apoptotic mediators including caspases 1, 4, 5 and inflammasome components NLRP3, ASC, IL-1β, IL-18 was quantitated by RT-PCR. IGF1R immunohistochemical (IHC) expression was also assessed in formalin-fixed, paraffin-embedded MSG tissue sections derived from 5 SS patients and 5 SC. Statistical analysis was performed with GraphPad and SNPstats software. All subjects gave informed consent in accordance with the Declaration of Helsinki.

Results: Increased frequency of the AA genotype was detected in primary SS patients compared to HC (22% vs 10.7%, OR: 2.35 [1.45-3.80, 95% CI], p<0.001) (Table 1). SS patients displayed reduced IGF1R at both mRNA and protein level in MSG tissues (mainly in ductal cells) compared to SC (mean±SD=2.97±2.62 vs mean±SD=5.53±3.23, p=0.009) (Figs 1 and 2). Of interest, IGF-1R expression was negatively associated with caspase-1 transcripts (r= -0.45, p=0.04), which in turn were positively correlated with NLRP3 (p=0.45, p=0.03), ASC (r=0.58, p=0.01) and IL1β (r=0.68, p=0.001).

Conclusion: In the present study, rs2229765 IGF1R variant has been shown to increase susceptibility for primary SS. Decreased trophic signals in salivary gland epithelial cells as a result of dampened IGF1R mRNA and protein expression in salivary gland tissues could be related to increased apoptosis and subsequently to activation of inflammasome pathways in the setting of primary SS.

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Abstract Number: 0531

Molecular Heterogeneity Between Different Classes of Lupus Nephritis as Revealed by Kidney Biopsy Proteomics

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Genetics, Genomics & Proteomics Poster (0517–0533)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) causes substantial morbidity and mortality. LN is histopathologically divided into six classes, which currently serves as the basis for making treatment decisions. Pathogenesis underlying different classes of LN is unclear. To identify the molecular differences, we studied the quantitative protein changes across all six LN classes using tandem mass spectrometry proteomics analyses of kidney biopsies from patients.

Methods: Kidney biopsies from 48 subjects, including 10 normal donor kidneys and 38 LN kidneys, were obtained from UCLA Pathology. All biopsies were reviewed independently by two pathologists. Protein was extracted from biopsy tissues and subjected to tandem mass spectrometry proteomics analyses. We measured the peptides expression quantitatively using Orbitrap LC-MS/MS system. Peptides were annotated and the abundance of peptides was normalized. The data were presented as mean ± SD and median with range (minimum–maximum), and categorical data were presented as frequencies and proportions. Wilcoxon rank-sum test with two-tailed distribution was used in the statistical comparisons between groups unless otherwise indicated. The p-values were adjusted for multiple testing with p.adjust in R using false discovery rate. The principal component analysis based on Spearman's rank correlation coefficients between samples was performed using R. We employed a machine learning analysis with random forest classification to build a probabilistic-based prediction model of LN disease vs. healthy controls. Pathway analyses of differentially expressed peptides with absolute log2 fold change greater than one was completed with Ingenuity Pathway Analysis.

Results: Proteomics analysis identified 2190 peptides quantifiable in all 48 kidney biopsies. Of these, 655 peptides were significantly differentially expressed, including 304 upregulated peptides and 351 downregulated peptides ($p < 0.05$). In principal component analyses, all class VI biopsies clustered with the control specimens, and when class VI biopsies were excluded controls neatly separated from LN (classes I-V). Through random forest classification, we built a probabilistic-based prediction model that can discriminate LN disease (class I-V) vs. healthy controls utilizing 273 of the 655 peptides differentially expressed between the groups, which maintained a receiver operating characteristic area under the curve accuracy of 87.5% with 95% CI (0.7131, 0.9985), and an out-of-bag error rate of 3.7%. Of these 273, peptides representing VIM, ETFB, SERPINA1, BHMT, IGHG1, and MDH2 had the highest mean decrease accuracy and Gini. Next, we utilized Ingenuity pathway analysis (IPA) to seek differentially expressed proteins and pathways in individual LN classes compared to controls. While a set of proteins and pathways were significantly differentially expressed across LN classes, certain proteins and pathways discriminated individual LN classes.

Conclusion: Our data indicate the unique molecular signatures that differentiate LN classes and pave the way for defining the unique molecular pathogenesis of individual LN classes, thus introducing the basis for designing class-specific treatment in LN.

Disclosure: A. AbuMaziad, None; **A. Amarnani**, None; **R. Singh**, None.

Abstract Number: 0532

Development of a Predictive Tool for the Rapid Progressive Knee Osteoarthritis Phenotype: Data from the Osteoarthritis Initiative

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: There is a pressing need of identifying patients suffering the rapid progressive phenotype of Osteoarthritis (RPOA) to implement prevention strategies and to include them in clinical trials. Both nuclear and mitochondrial DNA (mtDNA) polymorphisms have been associated with susceptibility and incidence/progression of the disease. Preliminary analyses by our group showed the nuclear single nucleotide polymorphism (nSNP) rs12107036 at TP63 as a potential risk factor for RPOA of the knee.

Our objectives in the present work are:

- To analyze the influence of the interactions between mtDNA haplogroups and the nSNP rs12107036
- To apply Next Generation Sequencing (NGS) techniques to discover novel mitochondrial genetic variants to construct predictive models of RPOA of the knee.

Methods: 1102 Caucasian subjects from the Osteoarthritis Initiative (OAI) were classified into two groups:

- Rapid progressors (N=255), baseline KL grade 0-1 in at least one knee, that increases up to KL≥ 3 during 48-month follow-up; or baseline KL grade 2 in at least one knee that increases up to KL grade 4 during the follow-up.
- Non-rapid progressors (N=847), with the same baseline characteristics as rapid progressors, but with a slower or no evolution over time.

mtDNA haplogroups and rs12107036 were assigned by mini-sequencing techniques. Novel mtDNA variants were analyzed by NGS. Statistical analyses included chi-square tests followed by generalized estimating equations. Relative excess risk due to interaction (RERI) and attributable proportion (AP) was evaluated for the additive interaction between mtDNA clusters and nSNP rs12107036. Confounder variables, including gender, age, BMI, previous injury, contralateral OA and WOMAC pain, were taken into account. All the analyses were performed using SPSS Statistics v24 and epi.R package included in R software v3.6.3.

Table 1. Predictive model for the risk of RPOA phenotype of the knee. $mtDNA Clusters: group of haplogroups with a common phylogenetic origin BMI: Body Mass Index; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; OR: Odds Ratio; CI: confidence interval; #: statistical significance declared at P < 0.05, in bold.

Variable	p-value	OR	95% CI lower	95% CI upper
Clinical variables				
Age	**<0,001#**	1,056	1,039	1,075
Sex (Female)	0,179	1,235	0,908	1,68
BMI	**<0,001#**	1,065	1,031	1,101
Contralateral knee OA (Yes)	**<0,001#**	1,993	1,465	2,71
Previous Injury (Yes)	**<0,001#**	1,803	1,320	2,462
WOMAC pain	**0,002#**	1,090	1,032	1,152
Genetic variables				
rs12107036 G	0,144	1,241	0,929	1,659
mt16519C	**0,004#**	1,632	1,166	2,284
mtDNA Clusters				
Others	0,758	0,903	0,473	1,724
TJ	0,333	1,296	0,766	2,192
UK	0,107	0,679	0,423	1,088
HV	Reference			
rs12107036 G * mtDNA Cluster interactions				
rs12107036 G * Others	0,483	0,781	0,392	1,556
rs12107036 G * TJ	0,136	0,636	0,351	1,152
rs12107036 G * UK	**0,041#**	1,703	1,022	2,836
rs12107036 G * HV	Reference			

Results: Chi-square analyses revealed that patients carrying the allele G of rs12107036 and mtDNA cluster UK have an increased risk of developing RPOA of the knee (OR 2,013; p=0,001 vs OR 1,221; p=0,049). An excess of 70,3% of the RERI between nSNP rs12107036 and mtDNA cluster UK was detected, indicating that 47,1% (AP=0,471) of the risk is attributable to this interaction, meaning that harboring both genetic factors increase 4,7 times the risk of RPOA compared to having just one. On the other hand, the in-depth sequencing of mtDNA revealed the mt16519C variant as significantly overrepresented in the rapid-progressors group (OR 1,620; p=0,002).

In the predictive model, the interaction between rs12107036 and mtDNA cluster UK (p=0,041, OR=1,703), as well as the mitochondrial variant 16519C (p=0,004,OR=1,632), showed a significant association with RPOA of the knee, in addition to age (p= < 0,001, OR=1,056), BMI (p= < 0,001, OR=1,065), contralateral OA (p= < 0,001, OR=1,993), previous injury in the target knee (p= < 0,001, OR=1,803) and WOMAC pain (p=0,002, OR=1,090) (Table 1).

Conclusion: Our predictive model indicates that mtDNA genetic variants are useful, not only as modulators of the influence of specific nuclear polymorphisms on the risk of developing RPOA, but also as candidate genetic biomarkers of this phenotype.

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Abstract Number: 0533

Identification of a Novel Susceptibility Locus for Small Vessel Vasculitis with Autoantibodies Against Myeloperoxidase

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: ANCA-associated vasculitides (AAV) are rare but aggressive autoimmune disorders. The pathogenesis of the disorders is complex and still poorly understood; only a few genetic loci have been associated with AAV. The aim of this project was to identify and characterize novel susceptibility loci for AAV positive for myeloperoxidase (MPO) or proteinase 3 (PR3) ANCA.

Methods: Genetic association analyses were performed after Illumina sequencing of 1853 genes and subsequent replication with genotyping of candidate single-nucleotide polymorphisms (SNPs) in a total cohort of 1110 Scandinavian cases with granulomatosis with polyangiitis (GPA) or microscopic polyangiitis (MPA) and 1589 controls. A novel AAV-associated SNP was analyzed for allele-specific effects on gene expression using luciferase reporter assay.

Results: Associations between PR3-ANCA positive AAV and the *HLA-DPB1*, *HLA-DPA1* and *SERPINA1* genes and between MPO-ANCA positive AAV and the *HLA-DQB1* locus identified in previous genome-wide studies were confirmed in the present study. In addition, a novel locus on chromosome 6 was identified as associated with MPO-ANCA positive AAV. The rare allele of the novel disease-associated SNP affected downstream gene expression in a cell type specific manner.

Conclusion: This study confirms previous findings of genetic associations specific for PR3-ANCA positive and MPO-ANCA positive AAV, respectively. A novel susceptibility locus for MPO-ANCA positive AAV was identified, where the disease-associated SNP may facilitate the development of autoimmunity through a negative effect on the expression of the closest gene in specific cell types.

Disclosure: J. Dahlqvist, None; **D. Ekman**, None; **B. Sennblad**, None; **S. Kozyrev**, None; **J. Nordin**, None; . **Karlsson**, None; **J. Meadows**, None; **E. Hellbacher**, None; **S. Rantapaa-Dahlqvist**, None; **E. Berglin**, None; **B. Stegmayr**, None; **B. Baslund**, None; . **Palm**, None; **H. Haukeland**, None; **I. Gunnarsson**, None; **A. Bruchfeld**, None; **M. Segelmark**, None; **S. Ohlsson**, None; **A. Mohammad**, Roche, 6, Amgen, 1, Vifor, 6, Lilly, 6; **A. Svärd**, None; **R. Pullerits**, None; **H. Herlitz**, None; **A. Söderbergh**, Roche, 6; **G. Rosengren Pielberg**, None; **F. Farias**, None; **L. Hultin Rosenberg**, None; **M. Bianchi**, None; **E. Muren**, None; **R. Omdal**, None; **R. Jonsson**, None; **M. Eloranta**, None; **L. Ronnblom**, None; **P. Söderkvist**, None; **A. Knight**, None; **P. Eriksson**, None; **K. Lindblad-Toh**, None.

Abstract Number: 0534

Lymphatic Dysfunction in Murine Lupus Photosensitivity

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SESSION INFORMATION
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Background/Purpose: The lymphatic system is composed of vessels which carry fluid, soluble molecules, and cells from peripheral tissue to draining lymph nodes. Photosensitivity, an exaggerated inflammatory response in response to ultraviolet radiation (UVR), is present in most patients with Systemic Lupus Erythematosus (SLE). Lymphatic dysfunction has been shown to induce photosensitivity in wild-type models, thus we hypothesized that lymphatic dysfunction could contribute to photosensitivity in SLE.

Methods: We examined MRL/lpr lupus prone mice for lymphatic function by injecting Evan's Blue into the ear and measuring retention. Ear thickness and flow cytometric analysis were used to assess photosensitivity. This was similarly done in an inducible lupus model using chronic epicutaneous application of imiquimod on B6 mice. We then investigated the utility of improving lymphatic drainage using two approaches. First, we used manual lymphatic drainage (MLD) in the MRL/lpr mice. Second, we used the imiquimod inducible lupus phenotype in a novel mouse model with enhanced lymphatic function (inducible lymphatic endothelial cell specific PTEN KO).

Results: MRL/lpr mice had greater Evan's blue retention compared to controls suggesting lupus prone mice have impaired lymphatic drainage. MLD improved lymphatic drainage and reduced photosensitivity. Imiquimod treated PTEN KO mice had reduced photosensitivity and reduced systemic immune activation compared with imiquimod treated controls.

Conclusion: This data suggests that lymphatic dysfunction contributes to photosensitivity in murine lupus and improving lymphatic flow, even with simple MLD, can ameliorate photosensitivity. Future studies will determine the etiology of lymphatic dysfunction in murine lupus and the mechanism of lessened photosensitivity with improved lymphatic drainage. If similar immune circuitry defects are present in patients with SLE, altering lymphatics could be a novel target for new therapeutics.

Disclosure: W. Ambler, None; **N. Schwartz**, None; **J. Shin**, None; **R. Kataru**, None; **C. Carballo**, None; **S. Rodeo**, None; **B. Mehrara**, Puretech corp, 2, Regeneron, 12, Investigator initiated research award; **T. Lu**, None.

Abstract Number: 0535

Therapeutic Efficacy of a Biomimetic ALXR Agonist in Murine Systemic Lupus Erythematosus (SLE)

Priyal Dave[1], Tiange Dong[1], Andrew Mead[1], Isaac Asante[1], Brandon Ebright[1], Eugene Zhou[1], RIta Li[1], Nicos Petasis[1], William Stohl[2] and Stan Louie[1], [1]University of Southern California, Los Angeles, CA, [2]University of Southern California Keck School of Medicine, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Animal Models Poster (0534–0540)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Neutrophils are key initiators and promoters of autoimmunity, including SLE, via the elaboration of neutrophil extracellular traps (NETs). We tested the efficacy of the biolipid mimetic, NAP1051 that has transcellular activity in the inflammatory process. NAP1051 is a lipid-based agonist of FPR2/ALXR that inhibits neutrophil migration and promotes macrophage mediated efferocytosis in SLE-prone NZM 2328 mice.

Methods: Female NZM mice 4-5 months of age (when serologic autoimmune and renal glomerulonephritis have developed) were gavaged with graded doses of NAP1051 (2.5, 5.0, 10 mg/kg/day and vehicle; n=5 per group) for 28 consecutive days and monitored for proteinuria. At study termination, blood chemistry, CBC, and immune profiles were determined. Kidneys were harvested for expression of inflammatory cytokines and markers of NETosis. The kidneys were also assessed by H&E staining and T-cell infiltration, IgG and C3 complex depositions by immunofluorescence staining.

Results: NAP1051 dramatically attenuated nephritis in a dose-dependent manner, as evidenced by reduced proteinuria, serum BUN levels, expression of inflammatory cytokines (IL-1β, TNF- α), and expression of biomarkers of NETosis (NOX-2, PAD4 and NE) in the kidney (Figure 1). Infiltrating T-cells and glomerular deposition of C3 and IgG in

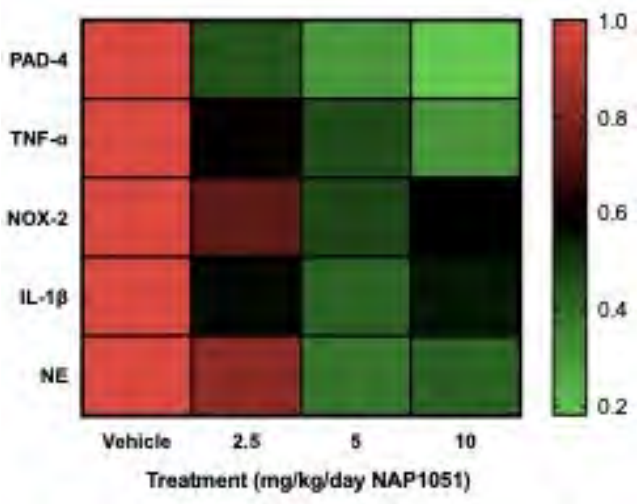

Figure 1. Heat map of gene expression of NETosis and inflammatory markers.

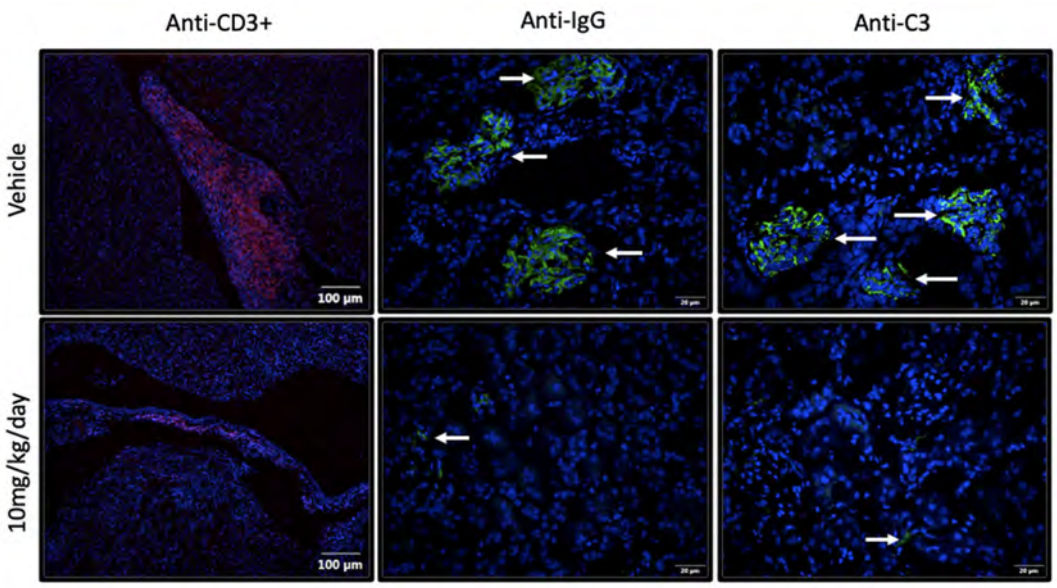

Figure 2. Immunofluorescence staining for CD3+ cells, IgG, and C3 in kidney sections from NZM 2328 mice. Top Left: Infiltrating T-cells are greater in number in the vehicle group than in the treatment group. Blue: DAPI, Red: Anti-CD3+ staining. Bottom Right: Considerably greater IgG and C3 deposition is appreciated in vehicle-treated mice than in NAP1051-treated mice. Blue: DAPI, Green: Anti-IgG staining/Anti-C3 staining. The white arrows indicate deposition of IgG and C3 complexes. Pictures for the anti-CD3+ were taken with a 10X objective and the anti-IgG/anti-C3 were taken with a 40X objective.

the kidney were also greatly reduced by NAP1051 treatment (Figure 2). Perhaps most strikingly, vehicle-treated mice developed glomerular crescents, consistent with rapidly progressive glomerulonephritis, whereas glomerular pathology was completely absent at the higher doses of NAP1051 (Figure 3). Importantly, there were no biochemical or

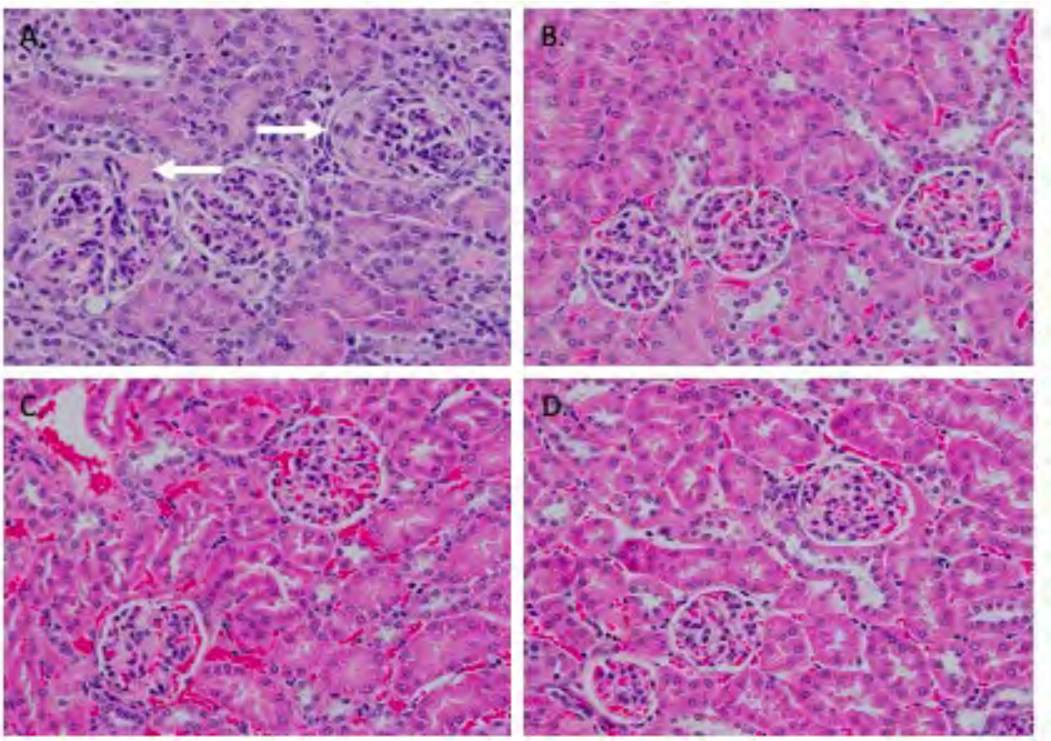

Figure 3. Kidney sections from A: Vehicle, B: 2.5 mg/kg/day, C: 5 mg/kg/day and D: 10 mg/kg/day. The white arrows point to glomerular crescents. Pictures were taken with a 40X objective.

histological signs of drug-related toxicities at any tested dose. Serological testing showed no changes in anti-dsDNA and anti-IgG levels between treatment groups.

Conclusion: NAP1051 demonstrated dose-dependent efficacy clinically and pathologically in NZM mice. NAP1051 prevented chronic glomerulonephritis, damage to the kidney tissues and reduced the expression of inflammatory markers without signs of toxicity. Interestingly, NAP1051 reduced T-cell infiltration into the kidney without affecting circulating autoantibody levels, suggesting that this compound exerts its therapeutic effect in a manner that is independent of autoantibody production. NAP1051 was also able to reduce NETosis biomarker expression in a dosage-dependent manner, suggesting that it is able to reduce PAD4 and neutrophil elastase expression. Taken together, NAP1051 exerts its activity through modulating NETosis for the treatment of SLE. Additional studies are currently underway to confirm these initial results and, if confirmed, would set the stage for evaluation in human SLE.

Disclosure: P. Dave, None; **T. Dong**, None; **A. Mead**, None; **I. Asante**, None; **B. Ebright**, None; **E. Zhou**, None; **R. Li**, None; **N. Petasis**, None; **W. Stohl**, Gilead, 5, Pfizer, 5, GlaxoSmithKline, 2, 5; **S. Louie**, None.

Abstract Number: 0536

The EIF4 Translational Inhibitor Pateamine a Improves Immunological and Neurological Functions in *BXSB.yaa* Lupus Mice

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Animal Models Poster (0534–0540)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease characterized by loss of tolerance and activation of the immune response. Clinical manifestations are heterogeneous and several organs can be affected including skin, joints, central nervous system and kidney. Traditional treatments include the use of hydroxychloroquine, glucocorticosteroids, immunosuppressive and more recently, biological drugs such as belimumab or rituximab. In the last decade new alternatives have been proposed based on targeting interferon and cytokines. Mouse models have been extremely helpful to test the efficacy of new SLE therapies. In this work we analyze the therapeutic potential of a natural compound, Patemina A (PatA) to treat SLE. Pat A is an inhibitor of the translation initiation process with immunosuppressive properties that has been tested successfully in cancer mouse models.

Methods: To test Pat A efficiency in SLE we used the BXSB.Yaa lupus model. Animals were treated for 8 weeks starting at the initial stages of disease (12 weeks). Sera was collected every three weeks and disease signs were followed. At the final point we performed serological analyses (cytokines and autoantibodies), flow cytometry on spleen to evaluate different cell populations, kidney histological and functional assays and behavioral tests to evaluate neuropsychiatric changes.

Results: Our data shows that Pat A treatment increases the survival rate and is able to reduce circulating levels of proinflammatory cytokines and autoantibodies. We also observed improvement of cognitive functions (learning/memory, and depression behavioral tests) together with a reduction of proinflammatory cytokines locally in the hippocampus.

Conclusion: These data suggests that translation inhibition improves lupus disease signs at the immunological and neurological levels opening a new line of research based on translation inhibition to treat lupus and other autoimmune diseases.

Disclosure: G. Gómez-Hernández, None; **N. Varela**, None; **H. Bagavant**, None; **G. Barturen**, None; **M. Alarcon-Riquelme**, None; **M. Morell**, None.

Abstract Number: 0537

The Clinical, Oral Small Molecule IRAK4 Inhibitor, GS-5718, Improves Survival and Reduces Disease Pathologies by Modulating Multiple Inflammatory Endpoints in the Murine NZB/W Model of Spontaneous Lupus

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Animal Models Poster (0534–0540)
Session Type: Poster Session B
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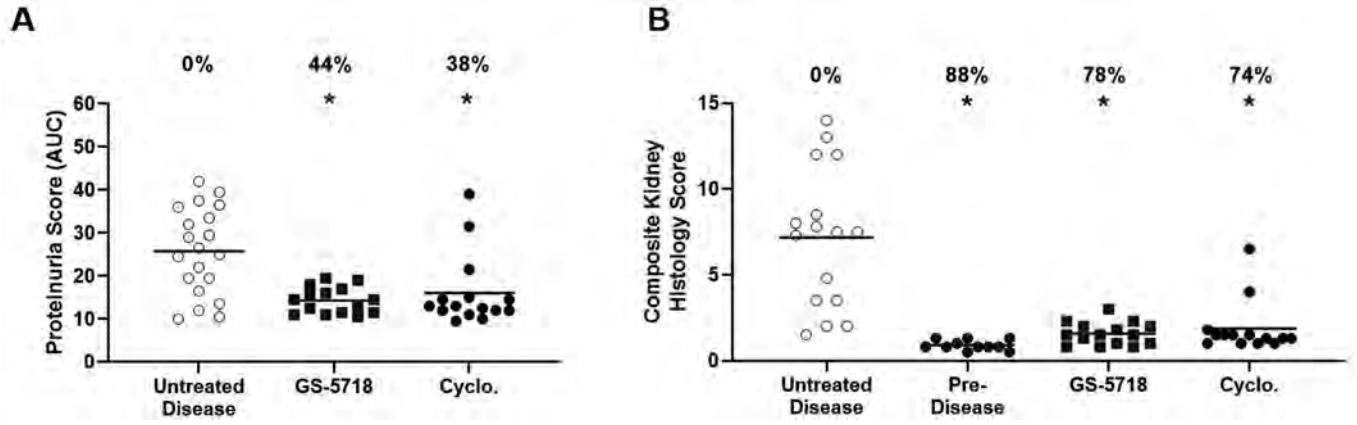
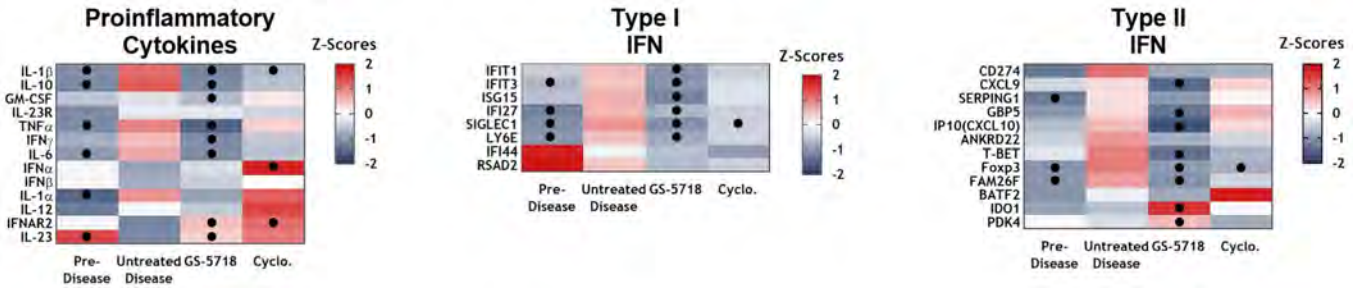
Background/Purpose: Lupus is a heterogenous autoimmune disease characterized by loss of immune tolerance, production of nucleic acid:autoantibody immune complexes, immune cell hyperactivation, and increased proinflammatory cytokine and interferon production. Interleukin receptor associated kinase 4 (IRAK4) is a serine/threonine kinase that modulates proinflammatory cytokine and type I interferon production downstream of toll-like receptors (TLRs) and IL-1 receptors (IL-1Rs) in immune cells. It is well established that TLR signaling (predominately TLR7 and TLR9) plays a key role in the pathogenesis of lupus[1] and thus inhibition of IRAK4 represents a promising target for the therapeutic treatment of lupus.

The murine NZB/W model recapitulates many lupus-like disease pathologies including proteinuria, hyperactive B and T cells, high titers of autoantibodies, and splenic and kidney abnormalities[2,3]. Current standard of care treatments,



(A) Total proteinuria score (area under curve, AUC, weeks 28 to 38). (B) Composite kidney score (glomerulus, crescent, protein cast, interstitial inflammation, and vasculitis score). Cyclo., Cyclophosphamide; %, Percent change from untreated disease; *, p-value < 0.05 Kruskal-Wallis (Dunn's post-hoc) vs. untreated disease.



(A-C) Z-scores of gene expression changes (fold-change relative to untreated disease) for proinflammatory cytokines (A), type I IFNs (B), and type II IFNs (C) genes. Cyclo., Cyclophosphamide; *, p-value < 0.05 Kruskal-Wallis (Dunn's post-hoc) vs. untreated disease.

including methotrexate, cyclophosphamide, mycophenolate mofetil, and blockers of B-cell activating factor (BAFF) have demonstrated efficacy (e.g. improved survival and/or clinical pathologies) in this model[2,3]. Demonstrating beneficial effects of IRAK4 inhibition in this model would support clinical evaluation in lupus.

Methods: In this study we investigated the efficacy of GS-5718, a highly selective, competitive inhibitor of IRAK4, to improve survival and attenuate disease pathology in the murine NZB/W model of spontaneous lupus.

Results: GS-5718 treated animals displayed improved in-life disease outcomes, histological measures, and pharmacodynamically reduced multiple inflammatory endpoints. Administration of GS-5718 showed statistically significant improvements in survival and reduced proteinuria, splenomegaly, and serum cholesterol levels compared to control animals. Kidney histology revealed GS-5718 treatment decreased swelling, crescent formation and periodic acid-Schiff (PAS) staining in glomeruli, protein casts in the cortex, and perivascular infiltration. These improvements in disease pathologies were accompanied by statistically significant reductions in peripheral cytokine production, kidney cytokine and interferon gene expression, and splenic immune cell infiltration.

Conclusion: GS-5718 treatment showed statistically significant improvements in survival and disease progression in a murine NZB/W spontaneous lupus model accompanied by improvements in pharmacodynamic inflammatory endpoints. These results suggest a pathological role for IRAK4 signaling in a pre-clinical mouse lupus model and supports further evaluation of GS-5718 for therapeutic intervention in lupus patients.

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Disclosure: A. Yadon, Gilead Sciences, Inc., 3; **V. Gorney**, Gilead Sciences, Inc., 3; **A. Hammond**, Gilead Sciences, Inc., 3; **E. Grant**, Gilead Sciences, Inc., 3; **A. Clarke**, Gilead Sciences, Inc., 3.

Abstract Number: 0538

Strengthening Nuclear Envelope Ameliorates UVB-triggered Skin Inflammation and Kidney Damage in Lupus Mice

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Animal Models Poster (0534–0540)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultraviolet B (UVB) exposure triggers lupus flare by worsening skin lesions and systemic symptoms such as lupus nephritis. The effects of UVB-induced skin inflammation on kidney activity have not been well understood. NETosis has been implicated in lupus. We have seen that UVB induces neutrophil recruitment to skin with NET formation and exhibition of NET-associated proinflammatory cytokines. Our mechanistic studies revealed that nuclear envelope rupture and NET formation are driven by PKCα-mediated lamin B (lmnb) disassembly. Strengthening nuclear envelope by lamin B overexpression decreases NETosis and exhibition of NET-associated cytokines in the skin of UVB-irradiated lmnb1$^{Tg/+}$ mice. Furthermore, other studies reported that UVB can trigger an IFNα signature both in skin and kidneys, and neutrophils in the inflamed skin can migrate back to the circulation through reverse transmigration, then be recruited to the kidneys, resulting in transient proteinuria in wildtype mice. However, the involvement of NETosis in UVB-mediated lupus flare in skin and kidneys has not been studied.

Methods: We generated lupus-prone mice with lamin B overexpression by backcrossing lmnb1$^{Tg/+}$ mice with MRL/lpr (lpr) mice for 10 generations. Female MRL/lpr-lmnb1$^{Tg/+}$ mice and their MRL/lpr littermates (8-week-old) were exposed to UVB at 150 mJ/cm^2/day for 5 consecutive days. We examined skin lesions, proteinuria, infiltrates, and NET formation in the skin and kidneys of these mice.

Results: Our data show that UVB exposure induces inflammatory responses with increased skin thickness, more infiltrates and NET formation in the skin, proteinuria and increased NET formation, NET-associated IFNα, IgG deposition, and hypercellularity in the kidneys of UVB-irradiated MRL/lpr mice. In addition, our data demonstrate decreased NET formation and less skin inflammation with attenuated skin thickness and infiltrates ($p< 0.01$) in the skin, decreased proteinuria, and reduced NET formation, NET-associated IFNα, IgG deposition, and hypercellularity in the kidneys of MRL/lpr-lmnb1$^{Tg/+}$ mice as compared to those in control MRL/lpr mice after UVB exposure. Interestingly, the skin infiltrates ($r=0.57$, $p< 0.05$) or NET formation in skin ($r=0.54$, $p< 0.05$) were positively correlated with proteinuria. Importantly, NET formation ($r=0.56$, $p< 0.05$), NET-associated IFNα ($r=0.60$, $p< 0.05$), IgG deposition ($r=0.7$, $p< 0.01$), or hypercellularity ($r=0.65$, $p< 0.01$) in glomeruli were also positively correlated with proteinuria.

Conclusion: We conclude that inhibition of NET formation by strengthening the nuclear envelope integrity can ameliorate UVB-triggered skin inflammation, proteinuria, and kidney damage in young lupus-prone mice. Therefore, our results provide insights into novel therapeutics into UVB-induced lupus flare.

Disclosure: X. Lyu, None; **M. Li**, None; **P. Zhang**, None; **V. Werth**, None; **M. Liu**, None.

Abstract Number: 0539

Vgll3-transgenic Autoimmune Mice Display Features of Cutaneous Fibrosis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Animal Models Poster (0534–0540)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Fibrosis is characterized by collagen deposition, fibro/myofibroblast accumulation, and extracellular matrix remodeling and can lead to disfiguring skin changes. In cutaneous lupus, scar formation after discoid lesion eruption may evolve from enhanced fibrotic phenotypes. Thus, understanding how fibrosis evolves in discoid lupus lesions is important to prevent morbidity and low quality of life for patients with cutaneous lupus. Recent work from our laboratory has shown that epidermal-directed overexpression of murine *Vgll3* causes severe lupus-like skin lesions reminiscent of discoid lupus erythematosus (DLE), as well as systemic autoimmune disease with end-organ damage. Given the apparent fibrotic nature of the skin lesions in transgenic (TG) *Vgll3* mice, we wanted to determine whether *Vgll3* induced fibrosis.

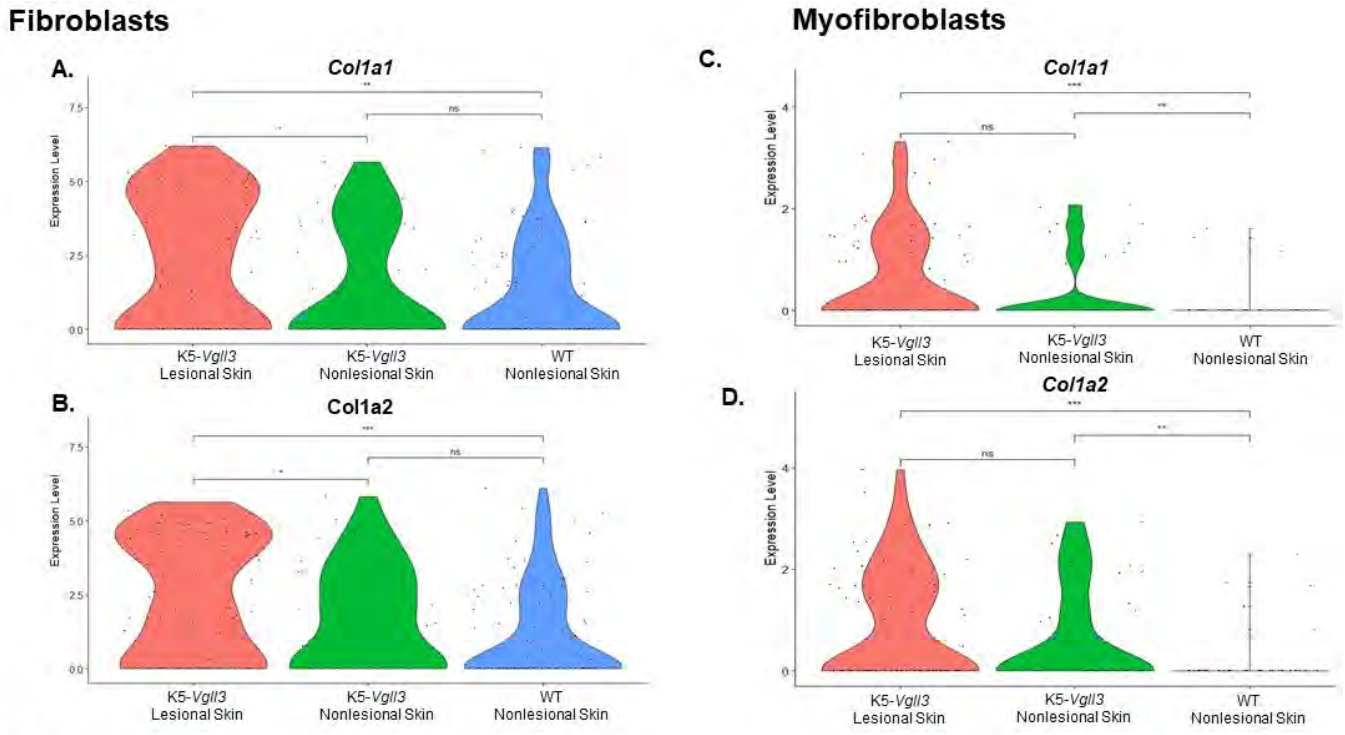

Fig. 1

A. *Col1a1* Gene expression in fibroblasts from lesional and nonlesional skin in K5-*Vgll3* mice and nonlesional skin in WT.
B. *Col1a2* expression in fibroblasts.
C. *Col1a1* Gene expression in myofibroblasts from lesional and nonlesional skin in K5-*Vgll3* mice and nonlesional skin in WT.
D. *Col1a2* expression in myofibroblasts.

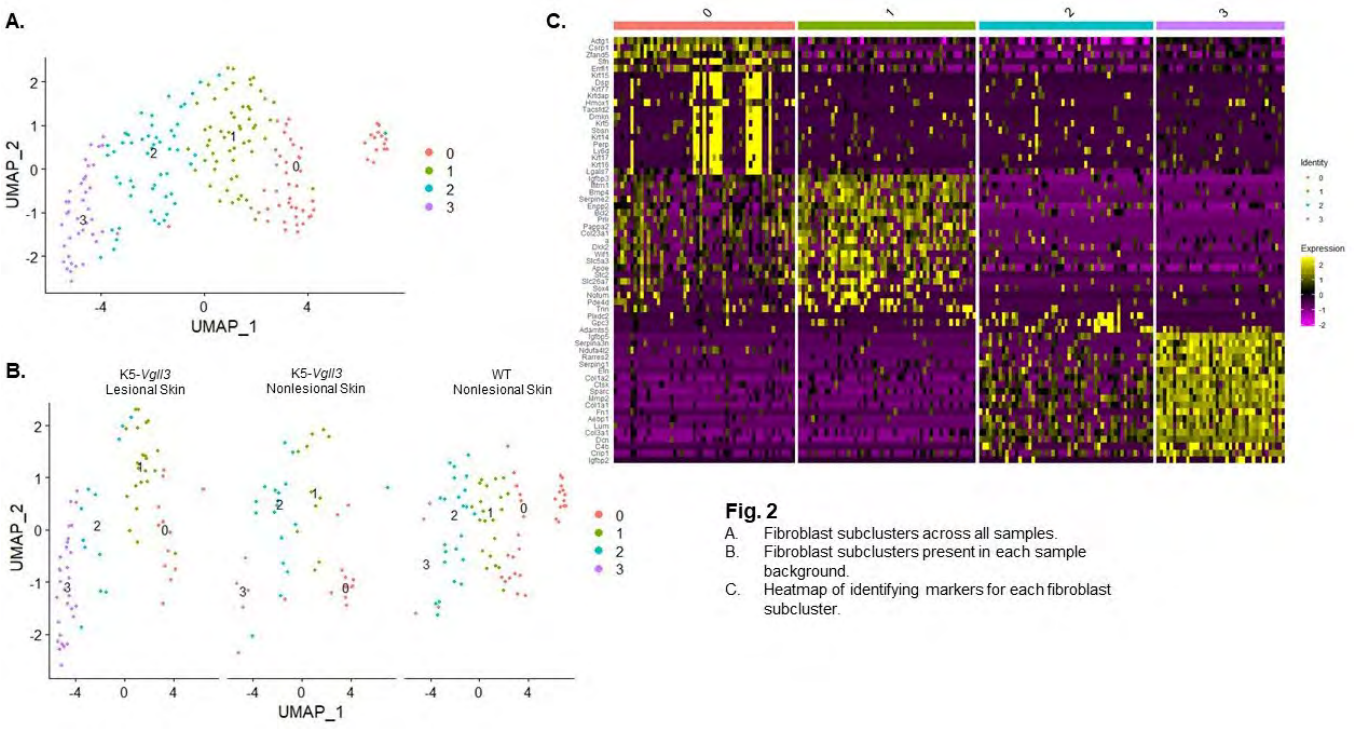

Fig. 2
A. Fibroblast subclusters across all samples.
B. Fibroblast subclusters present in each sample background.
C. Heatmap of identifying markers for each fibroblast subcluster.

Methods: 2-3 month old male and female transgenic (TG) mice overexpressing *Vgll3* in the epidermis under the K5 promoter were compared to male and female TG wild type (WT) C57Bl/6 mice (n= 3-5 per group). Fibrotic biomarkers of human DLE and scleroderma were compared via immunohistochemistry. In addition, we used single-cell RNA-sequencing (scRNA-seq) via 10x platform and bulk RNA-seq of lesional and nonlesional skin to investigate the transcriptomes of the potential cellular fibrotic players such as fibroblasts (FBs) and myofibroblasts (MYOFBs). ScRNA-seq data were analyzed using Seurat. Several subclusters of FBs, MYOFBs, and T cells were identified and fibrotic markers for each FBs subcluster were analyzed. Gene expression of fibrosis-associated genes in FBs/MYOFBs from lesional and nonlesional skin in K5-*Vgll3* mice as well as WT were identified.

Results: Epidermal *Vgll3* overexpression resulted in development of not only cutaneous inflammation but also severe fibrosis, as evidenced by trichrome staining. Immunohistochemistry identified increased infiltration of granulocytes/monocytes accompanied by significant expression of fibrotic biomarkers (*Acta2*, *Col1*, *Tgfb1*, *Ctgf)* and pro-fibrotic cytokines (*Il4* and *Il13*) in TG mice. These same markers were also seen in human DLE and scleroderma lesions compared to healthy human skin. Overall, lesional *Vgll3* TG skin exhibited higher expression of *Col1a1 and Col1a2*. ScRNA-seq of *Vgll3* TG lesional skin vs. WT skin demonstrated that the increased expression of these collagen genes was localized to fibroblast and myofibroblast populations. (**Fig. 1**). Four FBs subclusters were identified across all samples, and a unique FB subcluster (cluster 3, **Fig. 2**) in *Vgll3* TG mice was noted that uniquely exhibited higher expression of *Col1a1 and Col1a2* compared to WT mice.

Conclusion: The detection of high expression of *Ctgf* and *Tgfb1* as well as *Col1* mRNA and protein in the skin of TG mice suggests that skin-directed overexpression of *Vgll3* may impact fibrosis development. The changes in *Vgll3* TG mice are reflected in human scleroderma and DLE lesional samples, suggesting that pathways and inflammatory responses regulated by *Vgll3* may contribute to fibrosis. Further studies will elucidate the specific mechanisms that may be targetable in this pathway to better treat and prevent fibrosis in autoimmune disease patients.

Disclosure: M. Gharaee-Kermani, None; **A. Billi**, None; **M. Hildebrandt**, None; **J. Martens**, None; **R. Wasikowski**, None; **J. Kahlenberg**, astra zeneca, 1, 2, ventus therapeutics, 1, Bristol Myers Squibb, 1, 5, Janssen, 5, q32 bio, 5, GlaxoSmithKlein, 1, Eli Lilly, 1; **J. Gudjonsson**, Almirall, 5, Eli Lilly, 5, BMS, 5.

Abstract Number: 0540

Behavioral Deficits May Precede Influx of Brain-Infiltrating Macrophages in Neuropsychiatric Symptoms of Systemic Lupus Erythematosus

Hadijat Makinde, Miranda Gurra, Yidan Wang, Sara Radecki and **Carla Cuda**, Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Animal Models Poster (0534–0540)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex autoimmune disease that affects many end organs including the brain. Despite a prevalence of over 50% in SLE patients depending on the attribution model, neuropsychiatric symptoms of SLE (NPSLE), including anxiety and movement disorders, are among the least understood complications. Notwithstanding the paucity of data examining underlying mechanisms, accumulating evidence points to microglia, the resident innate immune cells in the brain, as a driver of disease. The cross-talk between infiltrating monocyte-derived macrophages and microglia plays a critical role in directing microglial responses. However, the question remains whether macrophage infiltration precedes NPSLE manifestations. Here, we longitudinally investigate macrophage infiltration into the brain in two models of SLE.

Methods: B6 and SLE-prone B6.*Sle1Sle2Sle3* (B6.TC; Jackson #007228) mice underwent a battery of behavioral tasks at 2 months of age. Spleen and cervical lymph nodes were weighed as an indicator of systemic disease from female B6 and B6.TC mice spanning disease progression (n=3-5/timepoint; 2, 5, 8, 11 months of age). At each timepoint, brains were perfused and extracted, meninges were removed and live $CD45^{+}CD11b^{+}$ cells were FACSorted from pooled cell suspensions (n=3/strain/timepoint to account for biological variability) for single-cell RNA-seq (10X Genomics 3' v3.1) in conjunction with cellular indexing of transcriptomes and epitopes by sequencing (CITE-seq); analysis pending. Two additional cohorts of B6 and B6.TC mice were evaluated for brain microglia infiltration and microglial distribution via flow cytometry at 11 months of age. NPSLE-prone CReCOM mice showed behavioral deficits at 3 months of age and underwent longitudinal analyses described above.

Results: Similar to patients with NPSLE, B6.TC mice exhibited heightened anxiety, impaired motor coordination and locomotive deficits compared to control mice, suggesting B6.TC mice are a valid model for NPSLE-associated symptoms. NPSLE-prone mice showed an age-dependent increase in splenomegaly and lymphadenopathy. At 11 months of age, microglia were expanded in NPSLE-prone mice compared to their respective controls, including the recently discovered disease-associated microglia subset associated with neurodegenerative disease. Further, there was an age-dependent increase in the number of brain-infiltrating macrophages in NPSLE-prone mice. However, levels of brain-infiltrating macrophages were comparable to levels in control mice at 2 months of age, indicating that macrophage infiltration occurs between 2 and 5 months of age in NPSLE-prone mice.

Conclusion: As macrophage levels in the brains of NPSLE-prone mice are comparable to control levels at 2 months of age but behavioral deficits occur at 2-3 months of age in NPSLE-prone mice, we provide the first evidence that

macrophage infiltration may be a response to NPSLE-like disease incited by brain-intrinsic mechanisms rather than a cause. Future studies will identify the exact timing of macrophage infiltration to define their role as either disease initiators or responders and dissect macrophage heterogeneity during NPSLE progression.

Disclosure: H. Makinde, None; **M. Gurra**, None; **Y. Wang**, None; **S. Radecki**, None; **C. Cuda**, None.

Abstract Number: 0541

N-formyl Methionine Peptide-mediated Neutrophil Activation in Systemic Sclerosis

Runa Kuley[1], Ryan Stultz[2], Bhargavi Duvvuri[2], Roger Hesselstrand[3], J Lee Nelson[4] and Christian Lood[2], [1]Division of Rheumatology, University of Washington, Seattle, WA, [2]University of Washington, Seattle, WA, [3]Lund University, Lund, Sweden, [4]Fred Hutchinson Cancer Research Center, University of Washington, Seattle, WA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a complex systemic autoimmune disease, and its etiology is unknown. Exaggerated neutrophil activation and formation of neutrophil extracellular traps (NETs) are reported in SSc, but its involvement in SSc pathogenesis is not clear. In the present study we assessed markers of neutrophil activation and NET formation in plasma samples from SSc patients (n=101), investigating their association with markers of inflammation and disease phenotype in SSc. Additionally, factors contributing to neutrophil-mediated inflammation in SSc remains largely unknown. Among the neutrophil activating factors, extracellular mitochondrial components have been reported in several autoinflammatory conditions, supporting inflammation and recruitment of neutrophils through among others mitochondrial-derived N-formyl methionine (fMet). The aim of the current study is to assess whether SSc patients have elevated levels of extracellular mitochondrial components and their role in neutrophil-mediated inflammation in SSc pathogenesis.

Methods: Markers of neutrophil activation (calprotectin), cell death (NETs, measured as myeloperoxidase-DNA complexes) and levels of fMet were analyzed in plasma obtained from two SSc patient cohorts (Cohort I: 81 SSc and 40 healthy controls, Cohort II: 20 SSc and 24 healthy controls) using ELISA. Neutrophil activation assays were performed in presence or absence of formyl peptide receptor 1 (FPR1) inhibitor cyclosporin H.

Results: Elevated levels of neutrophil activation markers, calprotectin and NETs were observed in SSc patients as compared to healthy controls ($P < 0.0001$) associating with a severe disease phenotype. Further, SSc patients had elevated levels of fMet in circulation as compared to healthy controls ($P < 0.0001$). Of note, levels of fMet were significantly higher in patients with diffuse versus limited SSc patients ($p< 0.04$). Consistent with a role for fMet in promoting neutrophil activation, fMet levels correlated with neutrophil activation markers calprotectin and NETs ($r=0.34$, $p=0.002$; $r=0.29$, $p< 0.01$ respectively). Additionally, plasma samples from a subset of SSc patients with high levels of fMet in circulation induced *de novo* neutrophil activation through FPR1-dependent mechanisms.

Conclusion: Our data for the first time implicates an important role for the mitochondrial component fMet in promoting neutrophil-mediated inflammation in SSc. We propose, targeting fMet-mediated inflammation pathways may provide opportunities to treat SSc patients, which is in need of novel therapeutics. Finally, our neutrophil and mitochondrial-derived biomarkers may provide for opportunities to better stratify patients and in patient management.

Disclosure: R. Kuley, None; **R. Stultz**, None; **B. Duvvuri**, None; **R. Hesselstrand**, None; **J. Nelson**, None; **C. Lood**, Exagen Diagnostic, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 5, Horizon Diagnostic, 5.

Abstract Number: 0542

Functional Characterization of Glycoprotein Nonmetastatic Melanoma Protein B in Scleroderma Fibrosis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Glycoprotein nonmetastatic melanoma protein B (GPNMB) is widely expressed on stromal cells and immune cells. It is involved in various cell functions such as cell adhesion, migration, proliferation, and differentiation, and has been implicated in various pathological conditions including cancer and neurodegenerative diseases. This membrane bound protein can be cleaved into a soluble form by ADAM10. By interacting with various cell surface receptors including CD44, soluble (s)GPNMB has the ability to activate various cell types, including fibroblasts. In this study, we set forth to determine the role of sGPNMB in fibroblast functions in systemic sclerosis (SSc).

Methods: Dermal fibroblasts were isolated from skin biopsies from healthy subjects and patients with diffuse cutaneous (dc)SSc. GPNMB expression was analyzed by qPCR, Western blotting, and immunofluorescence. sGPNMB was measured using ELISA. The effects of sGPNMB (0.01-100ng/ml) on fibroblast function were analyzed using Western blotting, proliferation, migration, and gel contraction assays. To induce a myofibroblast phenotype, normal fibroblasts were incubated with TGFβ for 72 hours. To determine the differences between groups, Mann–Whitney U test, Wilcoxon test, Kruskal–Wallis test, or two-way ANOVA were performed. P values of less than 0.05 were considered statistically significant.

Results: In dcSSc fibroblasts, *GPNMB* was upregulated compared to normal fibroblasts. In addition, dcSSc fibroblasts secreted higher levels of sGPNMB (147.4 ± 50.2 pg/ml vs. 84.8 ± 14.8 pg/ml, $p < 0.05$), partly due to increased ADAM10. sGPNMB (1 and 10 ng/ml) downregulated profibrotic genes, including collagen I and α-smooth muscle actin in dcSSc fibroblasts. In addition, it inhibited cell proliferation and gel contraction, while it had minimal effect on fibroblast migration. The anti-fibrotic effect of sGPNMB is, at least in part, mediated through CD44, as CD44 knockdown inhibits response to sGPNMB. GPNMB is regulated by its own soluble form and also through epigenetic mechanisms. TGFβ downregulated GPNMB and decreased the release of its soluble form in normal fibroblasts. We also confirmed the role of ADAM10 as the sheddase for GPNMB in dermal fibroblasts, as inhibition of ADAM10 decreased sGPNMB levels significantly after concomitant TGFβ treatment.

Conclusion: We showed for the first time, an anti-fibrotic role of sGPNMB in dcSSc fibroblasts. We also established the ADAM10-sGPNMB-CD44 axis in dermal fibroblasts; ADAM10 cleaves off the soluble form of GPNMB, which mediates its effect through CD44 in both paracrine and autocrine fashions. The futile anti-fibrotic effect in dcSSc fibroblasts might be due to the low levels of sGPNMB released from these cells (pg/ml range) vs. the dose needed (ng/ml range) for the anti-fibrotic effect. We also revealed a complex regulatory network for GPNMB in dcSSc fibroblasts, as it appears to be suppressed by TGFβ.

Disclosure: P. Palisoc, None; **L. Vaikutis**, None; **E. Model**, None; **M. Omara**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **E. Tsou**, None; **A. Sawalha**, None.

Abstract Number: 0543

Novel Insights into Systemic Sclerosis Using a Sensitive Computational Method to Analyze Whole-genome Bisulfite Sequencing Data

Jeffrey Yu[1], Tianyuan Lu[1], Kaiqiong Zhao[1], Kathleen Oros Klein[1], Maximilien Lora[2], Ines Colmegna[3], Celia MT Greenwood[4] and Marie Hudson[2], [1]Lady Davis Institute for Medical Research, Jewish General Hospital, Montréal, QC, Canada, [2]McGill University, Montréal, QC, Canada, [3]The Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [4]Epidemiology, Biostatistics and Occupational Health / Faculty of Medicine and Health Sciences / McGill University, Montréal, QC, Canada

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: While the etiology of systemic sclerosis (SSc) remains largely unknown, epigenetic dysregulation including abnormal DNA methylation is thought to contribute to its onset and progression. Currently, the most comprehensive assay for profiling DNA methylation is whole-genome bisulfite sequencing (WGBS), but its precision depends on read depth and it may be subject to sequencing errors. SOMNiBUS (Zhao et al. 2020) was developed to overcome some of these limitations. This one-stage method infers smooth covariate effects across regions while accounting for variable read depth, missing data patterns, sequencing errors, and confounders such as age. Using SOMNiBUS, we reanalyzed WGBS data on SSc patients and controls initially analyzed using

Figure 1. Manhattan plot of DMRs (starting position) with nCpG ≥ 60 detected by SOMNiBUS

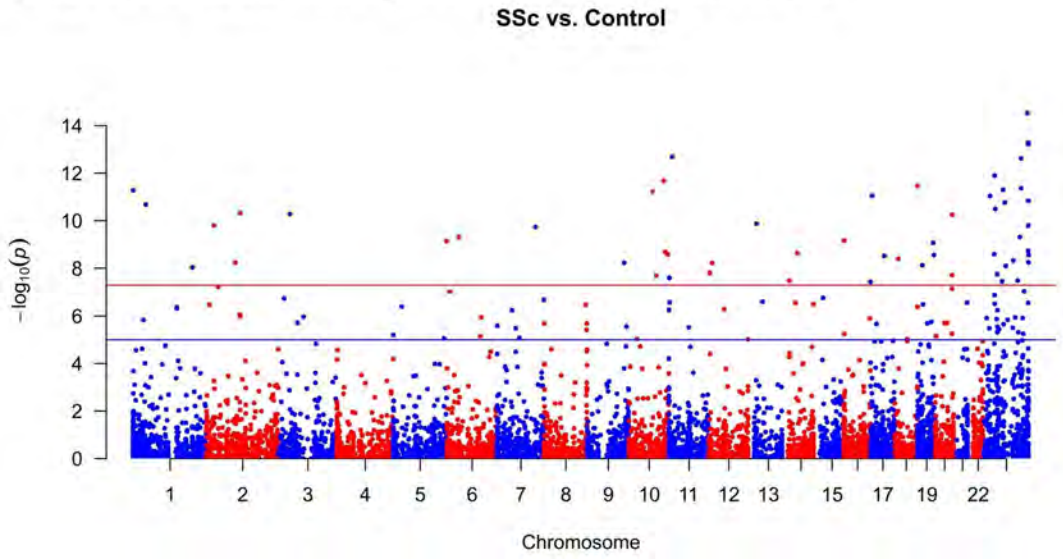

Table 1: Comparison of methods for DMR detection

Method Used	Number of DMRs		Number of Genes with DMRs within a gene's DRR	
	α = 1e-5	α = 5e-2	α = 1e-5 for DMRs	α = 5e-2 for DMRs
SOMNiBUS (p-value < α)	139	1228	161 (see Table 2)	1440
Bumphunter (q-value < α)	0	599	0	340 (34 for DMRs with > 60 CpGs)

Table 2. Genes identified by SOMNiBUS (DMR of p-value ≤ 1e-5 within the gene's DRR)

Range	Genes	Count
Chromosome	*(ordered by significance)*	
1-22 (Autosomal)	FLT4, SLC6A12, WDR97, SDHAP3, SH3BP2, VPS26C, ARL4C, RIBC2, GALNT18, GFRA1, NOC2L, KLHL17, PLEKHN1, ZMIZ1, ZNF232, USP6, MPL, CDC20, PAX8-AS1, PAX8, MOBP, URAD, POMC, MEST, NFYA, ADCY10P1, PRR25, DUSP22, ZNF808, FGFR2, ABHD12B, GLRX3, EPS8L1, PPP1R12C, HOXB3, PTPN2, ANKRD23, ANKRD39, PTGS1, LINC01252, KLF2, NAV1, PARP11, LINC00865, H19, DHRS4L1, RPH3AL, MAP4K3, TMEM14C, OTUD7A, EFHB, WDR60, PARD6G-AS1, KCNQ1OT1, GATD3A, C14orf28, TMEM121, SSBP4, ISYNA1, ELL, IAH1, TRAPPC9, LSP1P3, PPIAL4F, RB1, FIGNL2, IFITM1, IFITM3, GRB10, RGPD8, PSD4, CADM2, DCBLD1, GOPC, SLC7A5, CA5A, TFAP2E, GNAS, SIX5, DMPK, PTPRT, MAGI1, NECAB3, E2F1, RGS9BP, NUDT19, ERICH1, FAM83H, FAM83H-AS1, CCDC144NL, ADAP1, IFT140, NCS1, UNC93B1, LINC01005, GLI4, ZNF696, GNAS-AS1, SLC9A3, CENPB, CDC25B, MARCKS, LINC01268, HSPB1, YWHAG, NEURL1B, LRRC37A6P, SIGLEC15, FBRSL1	109
X	CHST7, ZXDA, PDK3, HMGB3, TMEM187, MIR3202-1, HCFC1, MIR3202-2, PLXNA3, RAB33A, EFNB1, EMD, EIF2S3, FLNA, NEXMIF, CASK, IKBKG, G6PD, DUSP9, DCAF12L2, SLC6A8, RPGR, CMC4, MTCP1, BRCC3, BEX2, SNORA36A, SNORA56, DKC1, PGK1, PORCN, EBP, DOCK11, MSN, CCNQ, OTUD5, KCND1, AMMECR1, SMIM10L2B, PRPS2, CDK16, USP11, RPS6KA6, DLG3, PLP2, MAGIX, ZMAT1, MBTPS2, FGD1, CCDC120, C1GALT1C1, WAS	52
Top 5 Pathways (Chr. 1-22)	*(alphabetical)*	
Cell Cycle, Cellular Development, Cellular Growth and Proliferation	ARL4C, Cdc2, CDC20, CDC25B, Cdk, CDK4/6, CG, Cyclin A, Cyclin B, Cyclin E, DUSP22, E2f, E2F1, ERK1/2, FGFR2, FSH, Gamma tubulin, H19, Histone h2a, Lh, MAGI1, MEST, NAV1, NFYA, Osteocalcin, PAX8, phosphatase, PPP1R12C, PTGS1, PTPase, PTPN2, PTPRT, Rb, RB1, SH3BP2	18
Cell Morphology, Cellular Assembly and Organization, Cellular Function and Maintenance	26s Proteasome, Actin, Ap1, caspase, CD3, CENPB, Ck2, ELL, EPS8L1, estrogen receptor, F Actin, GLRX3, GNAS, GOPC, Histone h3, Histone h4, HSPB1, MAP4K3, Mapk, MARCKS, NFkB (complex), NOC2L, Pde, Pka, Pkc(s), POMC, RNA polymerase II, Sapk, SLC9A3, TCR, TMEM14C, TRAPPC9, Ubiquitin, USP6, YWHAG	16
Cell-To-Cell Signaling and Interaction, Cellular Assembly and Organization, Infectious Diseases	ADAP1, Akt, Alp, Creb, FLT4, GALNT18, GFRA1, GRB10, IFITM1, IFITM3, IFN Beta, IgG, Igm, IL1, Immunoglobulin, Insulin, Interferon alpha, KLF2, MAP2K1/2, Mek, MPL, Notch, PARP11, PI3K (complex), PI3K (family), PP2A, RPH3AL, SIGLEC15, SLC7A5, SRC (family), STAT, STAT5a/b, SYK/ZAP, TMEM121, UNC93B1	15
Drug Metabolism, Neurological Disease, Tissue Morphology	ALB, ARTN, beta-estradiol, CADM2, calpain, EFHB, ERICH1, ERK, GNAS-AS1, GRIN3A, IFT140, Jnk, JOSD2, KCNQ1OT1, KLHL29, MYC, NCS1, NRTN, P38 MAPK, RGPD4 (includes others), RGS9, RGS9BP, SLC6A12, SNCA, SOD2, STUB1, taurine, TFAP2E, THBS1, TNF, TP53I3, Vegf, VPS26C, ZNF232, ZNF696	14
Cell Cycle, Hereditary Disorder, Neurological Disease	ANKRD23, ARID5A, ATXN1, BRWD3, DCBLD1, DMPK, EEF1B2, EEF1D, EPN2, HOXB3, HRAS, HSPA1L, ISYNA1, MTF1, NOC2L, NPM1, OTUD7A, PLEKHN1, PLEKHO1, PPIAL4G (includes others), PRDX4, PSD4, RIBC2, RNH1, RPL18A, RRP8, SAE1, SDHA, SIX5, taurine, TRAF6, UBE2M, VARS1, ZNF808, ZRANB1	13
Pathways (Chr. X)	*(alphabetical)*	
Antigen Presentation, Hereditary Disorder, Organismal Injury and Abnormalities	Actin, AMPK, BRCC3, C1GALT1C1, Calmodulin, CASK, CD3, CDK16, DLG3, DUSP9, EBP, EFNB1, EMD, ERK, ERK1/2, F Actin, FLNA, FSH, G6PD, Hsp90, IKBKG, Immunoglobulin, Lh, MSN, OTUD5, Pak, PDK3, PGK1, PLP2, PRPS2, SLC6A8, TCR, Ubiquitin, USP11, WAS	21
Cancer, Gastrointestinal Disease, Organismal Injury and Abnormalities	ADNP2, ADRB2, ANKS1B, ARHGEF26, DRD3, EGFR, ELMO2, EPHB1, FIGN, GALNT10, GRB2, HMGB3, IL16, KCND1, KIF26A, MADD, MAGIX, MAPK1, MBTPS2, Nrp-PlexinA, PHF20, PLXNA3, RAPGEF1, RPS6KA6, SEMA6D, SHB, SHC1, SPATS2L, SRGAP3, TMEM187, TRAPPC11, VIRMA, ZMAT1, ZXDA, ZXDC	9
Cell Death and Survival, Cellular Development, Skeletal and Muscular System Development and Function	AKT1, AMMECR1, BANK1, CADM1, CCDC120, CCNA2, CCND1, CCNQ, CDK4/6, CMC4, COPS6, CTNNAL1, CTNNB1, DCAF12L2, EPHB3, FAT10 Cancer Signaling Pathway, FOXO1, GOLM2, GSK3B, HCN1, JMJD8, MSP-RON Signaling In Cancer Cells Pathway, MTCP1, NPDC1, NRCAM, NRP2, OTUD7B, PORCN, RAB33A, RPGR, RUFY3, SEMA6D, TCF7L2, TET1, WDFY2	9
Developmental Disorder, Hereditary Disorder, Neurological Disease	Akt, BANK1, BEX2, CHST7, cytokine, DDAH2, DKC1, DPF1, Eif2, EIF2S3, FASTKD1, FGD1, FOXN2, HCFC1, Insulin, Jnk, MAPKAPK5, NFkB (complex), NLRP12, NPHS1, NR2C1, NTN4, NYAP1, OTUD7B, P38 MAPK, PELI3, Ras homolog, Rnr, SMARCA4, SMIM10L2B, urea, UTP, UTP18, Vegf, ZKSCAN3	7
Developmental Disorder, Hereditary Disorder, Neurological Disease	AHNAK, ARHGAP5, DOCK11, EPB41L2, NEXMIF, RNF123	2

bumphunter (Jaffe et al. 2012, Aryee et al. 2014, Lu et al., 2019), a less sensitive two-stage approach that fits single CpG associations first, followed by separate coefficient smoothing based on the fitted associations. We aimed to identify novel regions of dysregulated DNA methylation, thus providing a more comprehensive understanding of SSc pathogenesis.

Methods: Purified CD4+ T lymphocytes for 9 SSc and 4 control females were sequenced using WGBS. We separated the resulting sequence into regions with cuts made when adjacent CpG sites were spaced more than 200 bp apart. 8268 regions containing ≥ 60 CpGs were retained for analysis. DMRs were inferred with SOMNiBUS region-level test, adjusted for age. Pathway enrichment analysis was performed with Ingenuity Pathway Analysis (IPA) for genes with DMRs located on the gene body or within regulatory regions. We compared the results to those obtained by bumphunter in terms of plausibility of enriched pathways and agreement in genes detected.

Results: We identified more DMRs with SOMNIBUS compared to bumphunter for both significance levels tested (Fig. 1 & Table 1). We selected all DMRs with a suggestive association defined by regional significance ≤ 1e-5 that overlapped either with a gene body or with the region 10,000 bp upstream of its transcription start site, allowing us to annotate DMRs up to the distal regulatory region (DRR), resulting in 161 differentially methylated genes (DMGs; Table 2). Changing the regional significance threshold to ≤ 0.05 for DMRs, we obtained 1,440 DMGs for SOMNiBUS compared to 340 DMGs for bumphunter (Table 1), 77 of which were identified by both methods. SOMNiBUS detected 29% of bumphunter's DMGs with DMRs of < 60 CpGs, along with 22% of bumphunter's other DMGs. In analyses stratified by autosomal and X chromosomes, the top-ranked autosomal gene was FLT4, a lymphangiogenic orchestrator previously associated with SSc (Manetti et al., 2019); 52 genes were identified on the X-chromosome (Table 2). IPA identified 10 enriched pathways for autosomal chromosomes with cell cycling as the top-ranked pathway and 5 enriched pathways for chromosomes X with antigen presentation as the top-ranked pathway (Table 2).

Conclusion: Using a novel and more powerful computational approach, we identified new and biologically plausible regions of the genome associated with SSc. These findings deepen biological insights into SSc and provide novel avenues of investigation into its pathogenesis.

Disclosure: J. Yu, None; **T. Lu**, None; **K. Zhao**, None; **K. Klein**, None; **M. Lora**, None; **I. Colmegna**, None; **C. Greenwood**, None; **M. Hudson**, None.

Abstract Number: 0544

Targeting CD13/aminopeptidase N as a Novel Therapeutic Approach for Scleroderma Fibrosis

Eliza Pei-Suen Tsou, M.Asif Amin, Phillip Campbell, Mikel Gurrea-Rubio, Morgan Omara, Ellen Model, Pamela Palisoc, Mustafa Ali, Sirapa Vichaikul, Jonatan Hervoso, Jeffrey Ruth, Dinesh Khanna and David Fox, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Aminopeptidase N, also known as CD13, is a Zn^{2+}-dependent membrane bound ectopeptidase widely expressed in mammalian cells including rheumatoid arthritis (RA) fibroblast-like synoviocytes (FLS), myeloid cells, and endothelial cells. CD13 exists in two forms, the membrane-binding and the MMP14 cleaved-soluble form. We previously showed that CD13 is shed from FLS. In addition, soluble (s)CD13 induces EC angiogenesis, FLS proliferation, and acute inflammatory arthritis in mice. In earlier studies we showed that sCD13 induces immune cell migration by binding to G-protein-coupled receptors. Recently we have identified bradykinin receptor B1 (B1R) as the previously unknown receptor for sCD13. We propose that CD13 is a compelling new target for scleroderma (SSc), as it induces immune cell migration and promotes fibroblast activation.

Methods: Dermal fibroblasts were isolated from skin biopsies from healthy subjects and patients with diffuse cutaneous (dc)SSc. Gene expression was analyzed by qPCR and Western blotting. sCD13 was measured using ELISA. The effects of sCD13 and B1R inhibitor on fibroblast function were analyzed using Western blotting, proliferation, migration, and gel contraction assays. To induce a myofibroblast phenotype, normal fibroblasts were incubated with TGFβ for 72 hours. The bleomycin-induced skin fibrosis mouse model was used to determine the effect of CD13 or B1R inhibition *in vivo*. To determine the differences between groups, Students t-test, Mann–Whitney U test, and Kruskal–Wallis test were performed. P values of less than 0.05 were considered statistically significant.

Results: CD13 knockout mice are resistant to bleomycin-induced skin fibrosis, as shown by significant reduction in skin thickness and hydroxyproline content after bleomycin injection compared to wild type mice. Dermal fibroblasts from SSc patients showed increased B1R expression and released significantly higher amount of sCD13 compared to healthy controls. In normal fibroblasts, *BDKRB1* (gene encoding B1R) and *MMP14* were induced by TGFβ, while *ANPEP* (gene encoding CD13) was downregulated. sCD13 induced pro-fibrotic gene expression, proliferation, migration, and gel contraction in SSc fibroblasts, and these effects were blocked by a B1R antagonist. Inhibition of B1R also prevented bleomycin-induced skin fibrosis in wild type mice.

Conclusion: We've established the pro-fibrotic properties of sCD13 in SSc fibroblasts and in an animal model of fibrosis. sCD13 exerts its pro-fibrotic effect by acting on B1R, and this in turn reinforces a myofibroblast phenotype in SSc fibroblasts. The elevated levels of B1R and sCD13 in SSc fibroblasts are mediated by TGFβ, since TGFβ increased *BDKRB1* as well as MMP14 expression, which in turn cleaves CD13 into its soluble form. Targeting the sCD13-B1R axis appears to be a promising therapeutic approach for SSc.

Disclosure: E. Tsou, None; **M. Amin**, None; **P. Campbell**, None; **M. Gurrea-Rubio**, None; **M. Omara**, None; **E. Model**, None; **P. Palisoc**, None; **M. Ali**, None; **S. Vichaikul**, None; **J. Hervoso**, None; **J. Ruth**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **D. Fox**, None.

Abstract Number: 0545

SIRT1 Modulates the Senescent Phenotype in Scleroderma Endothelial Cells

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Vascular abnormalities in systemic sclerosis (SSc) are characterized by injury to vascular wall and extensive damage of the microvessels. It has been shown that the endothelial cells (ECs) isolated from patient skin biopsies show dysregulated phenotypes including impaired angiogenesis, increased oxidative stress, barrier dysfunction, and endothelial-to-mesenchymal transition (Endo-MT). Interestingly, all the above-mentioned events are characteristics of the endothelial phenotype of sirtuin 1 (SIRT1)-deficient ECs. SIRT1 is a class III NAD-dependent histone deacetylase that maintains EC function by deacetylating both histones or non-histone proteins. SIRT1-deficient ECs show impaired angiogenesis, eNOS inactivation, increased oxidative stress, and accelerated senescence. It is possible that endothelial SIRT1 deficiency plays a fundamental role in endothelial dysfunction in SSc. In this study, the impact of SIRT1 on SSc EC is determined.

Methods: Dermal ECs were isolated from skin biopsies from healthy subjects and patients with diffuse cutaneous (dc)SSc. Senescence was measured by immunofluorescence, β-galactosidase assay, and senescence-associated secretory phenotype (SASP). EC functions were determined by Matrigel tube formation assay and proliferation assays. SIRT1 activators, including resveratrol, sodium hydrosulfide, or nicotinamide mononucleotide, or SIRT1 inhibitor EX527 were used to treat ECs. SIRT1 expression in ECs were modulated by siRNA knockdown or overexpression. P values of less than 0.05 were considered statistically significant.

Results: We first showed that endothelial SIRT1 was essential for normal endothelial function in human dermal microvascular ECs (HMVECs), as knockdown or inactivation of SIRT1 inhibited cell proliferation and angiogenesis while increased Endo-MT and senescence. In contrast, overexpression or activation of SIRT1 in HMVECs led to opposite observations. We found that *SIRT1* was significantly downregulated in SSc ECs. This was accompanied with increased acetylation of SIRT1-target proteins including eNOS, p53, and NF-kB p65. SSc ECs also showed increased senescence, determined by increased senescent markers and SASP, and reduced eNOS activity. Enhanced staining of senescent markers was co-localized with blood vessels in SSc skin. Overexpression or activation of SIRT1 in SSc ECs significantly enhanced cell proliferation and angiogenesis, while decreased senescence. To determine the mechanism for SIRT1 downregulation in SSc ECs, we uncovered the p53-miR34a-SIRT1 axis in these cells. We found significantly elevated levels of *TP53*, acetylated-p53, and miR34a in SSc ECs, which are key members of the regulatory loop for SIRT1 that leads to downregulation of SIRT1 and elevated levels of p21.

Conclusion: In this study, we provided a link between epigenetic regulation and endothelial senescence in SSc, and presented a novel mechanism for the dysregulated endothelial phenotype that characterizes this disease. Class III histone deacetylases also show potent anti-fibrotic effects in the skin and lungs. Our results offer a strong scientific framework for repurposing SIRT1 activators as targeted therapeutics to treat SSc patients.

Disclosure: E. Model, None; **M. Omara**, None; **P. Palisoc**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **E. Tsou**, None.

Abstract Number: 0546

Integrated Analysis of Dermal Blister Fluid Proteomics and Genome-wide Skin Gene Expression Gives New Insight into Pathogenesis of Systemic Sclerosis

Kristina Clark[1], Eszter Csomor[2], Corrado Campochiaro[3], Adam Taylor[4], Yee Voan Teo[2], Katherine Nevin[2], Mary Morse[2], Voon Ong[5], Emma Derrett-Smith[6], Nicolas Wisniacki[2], Shaun Flint[2] and Christopher Denton[7], [1]University College London, London, United Kingdom, [2]GlaxoSmithKline, Stevenage, Hertfordshire, United Kingdom, [3]Royal Free Hospital London, London, United Kingdom, [4]GlaxoSmithKline, London, United Kingdom, [5]University College London Medical School Royal Free Campus, London, United Kingdom, [6]University College London Division of Medicine, London, United Kingdom, [7]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

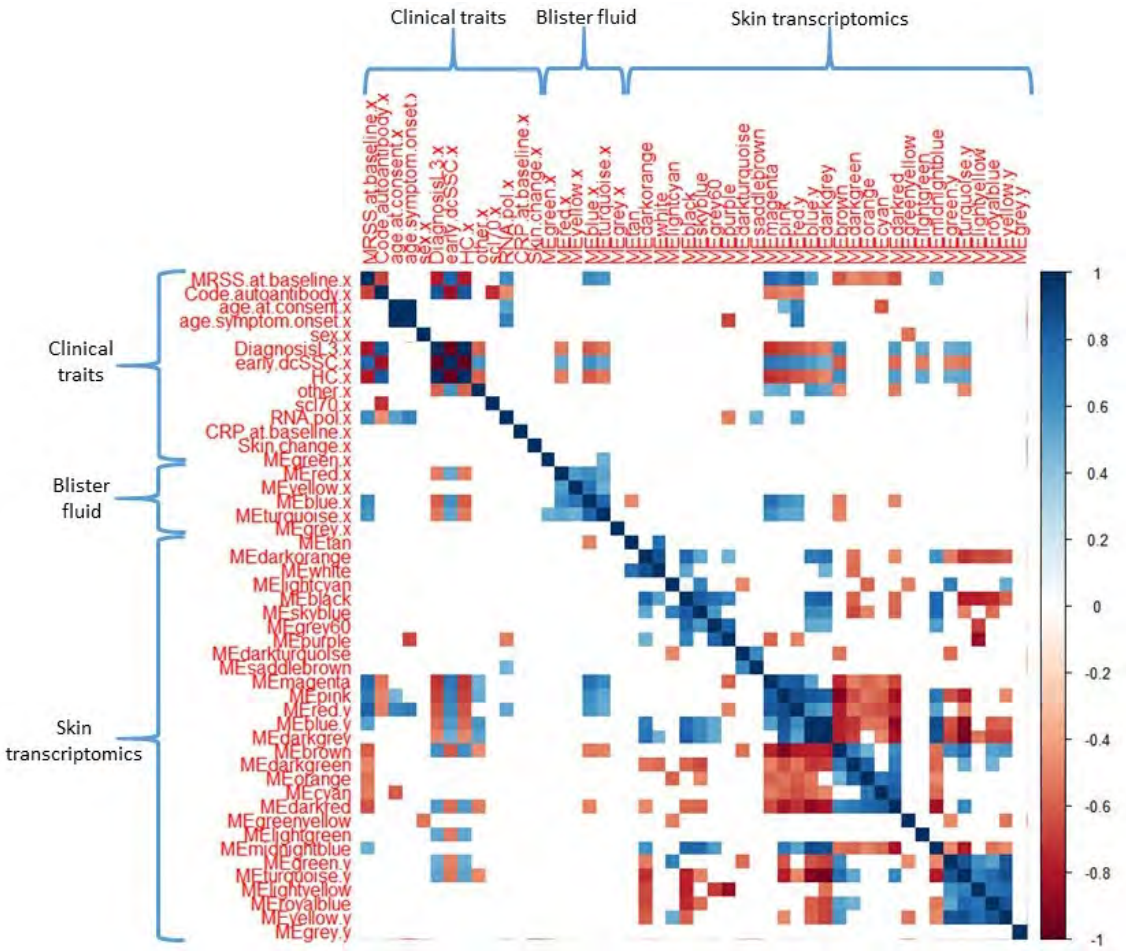


Figure 1. Correlation matrix highlighting only significant correlations between blister modules, skin transcriptomic modules and clinical traits.

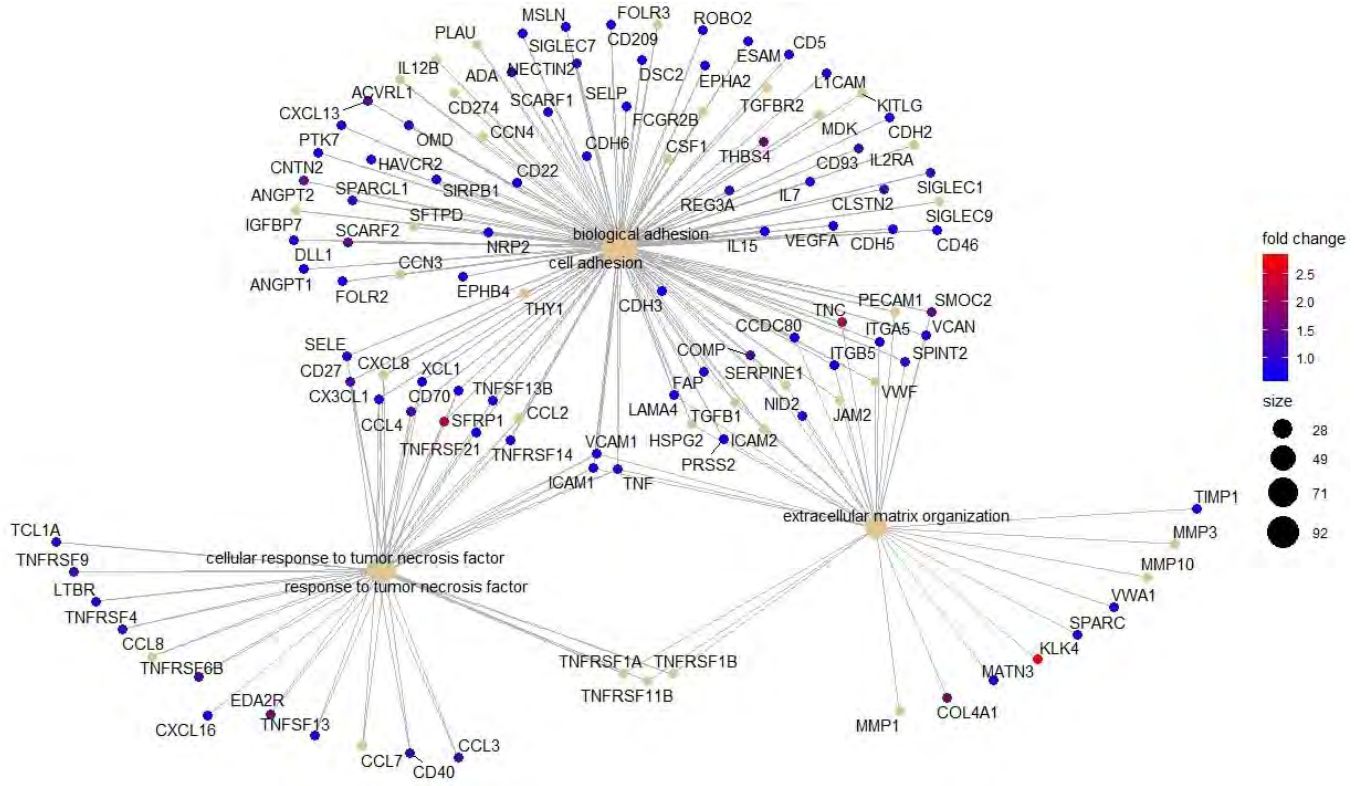


Figure 2 Network plot for skin blister "blue" module.

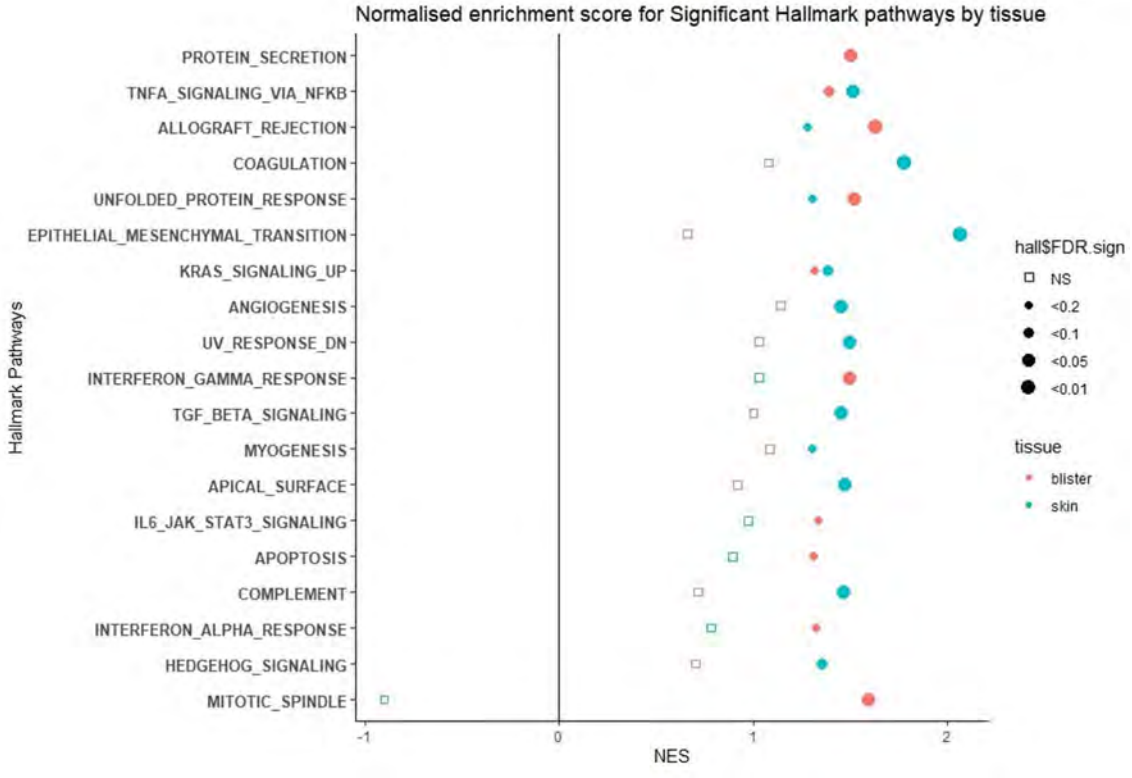


Figure 3 Cleveland plot of Hallmark pathways enriched in "blue" and "magenta" modules.

Background/Purpose: Suction blister fluid provides a unique opportunity to analyse the dermal microenvironment of SSc. We report an integrated analysis of proteomic data from dermal interstitial fluid in early dcSSc patients compared with healthy controls (HC), and genome-wide transcriptomic analysis of concurrently taken skin biopsies. Interpreting differential protein expression in the context of RNA sequencing (RNAseq) provides unique insight into potential mediators and pathways relevant to SSc.

Methods: The BIOPSY cohort recruited 21 early dcSSc patients with mean skin score (MRSS) of 21 (sd 11) and 16 HCs. Forearm skin blister fluid was obtained using the dermal suction blister method and assayed using the Olink platform (www.olink.com) (1192 proteins). Simultaneous 4mm punch biopsies were taken from all subjects, for genome-wide transcriptomic profiling by RNAseq. Integrated analysis of gene and protein expression data, together with SSc clinical and laboratory characteristics was conducted using WGCNA and clusterProfiler in R. This method clusters individual analytes into modules sharing similar expression patterns. Each module has been arbitrarily assigned as a colour. Modules with significant correlation to early dcSSc diagnosis, and with each other, were identified. Significant genes or proteins within a module were identified by a fold change of at least 1.5 compared to HCs.

Results: WGCNA identified 6 modules in blister fluid, and 30 modules from skin RNAseq data (Figure 1). The magenta module (385 genes) in the skin correlated most significantly with early dcSSc ($r=0.74$, $p< 0.001$), and MRSS at baseline ($r=0.82$, $p< 0.001$). The blue module (450 proteins) in the blister fluid correlated most strongly with early dcSSc disease ($r=0.6$, $p< 0.001$), MRSS at baseline ($r=0.63$, $p< 0.001$), and skin progression ($r=0.54$, $p=0.002$). Both modules significantly correlated with each other ($r=0.6$, $p< 0.05$).

Consistent with current concepts of SSc pathogenesis, key biological processes identified in the magenta module were angiogenesis, extracellular matrix (ECM) structure, and endothelial cell proliferation, with COMP, COL4A4, COL11A1 having the highest fold change compared to HC. The blue module consisted of proteins centred around ECM organisation, cell adhesion, and response to TNF, with upregulation of SFRP1, TNC and KLK4 in early dcSSc compared to HC (Figure 2).

Significant Hallmark pathways were compared between the two modules in each tissue modality and HCs (Figure 3). Notably, some pathways were upregulated in both skin gene expression (magenta) and blister fluid (blue) modules including NFKB signalling, allograft rejection, and KRAS signalling. Significantly activated pathways in magenta (skin gene) but not the blue module (blister fluid protein) included angiogenesis, Hedgehog and TGFβ signalling. Conversely, protein secretion, IFNγ response and mitotic spindle pathways were significantly increased only in the blue module.

Conclusion: the molecular pathology of SSc. Correlation with skin severity or progression suggests potential for developing a novel composite biomarker for skin.

Disclosure: K. **Clark**, None; **E. Csomor**, GlaxoSmithKline, 3; **C. Campochiaro**, None; **A. Taylor**, GlaxoSmithKline, 3; **Y. Teo**, GlaxoSmithKline, 3; **K. Nevin**, GlaxoSmithKline, 3; **M. Morse**, GlaxoSmithKline, 3; **V. Ong**, None; **E. Derrett-Smith**, None; **N. Wisniacki**, GlaxoSmithKline, 3; **S. Flint**, GlaxoSmithKline, 3; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 0547

Autologous Haematopoietic Stem Cell Transplantation for Systemic Sclerosis Results in Sustained Changes in Immunoregulatory T and NK Cells

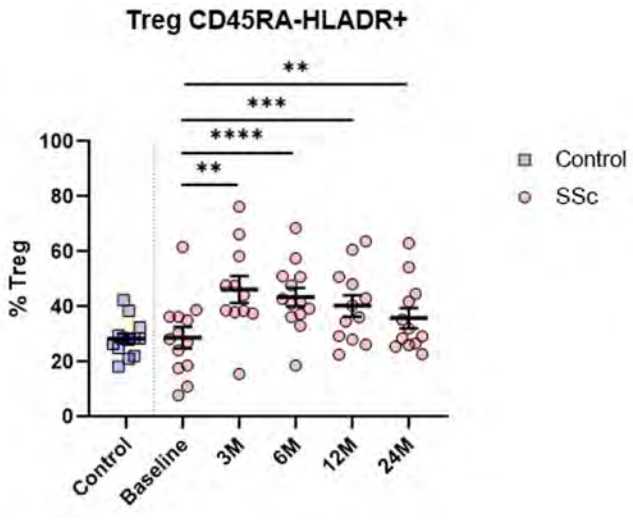
Ross Penglase, Malini Visweswaran, John Zaunders, Laila Girgis, David Ma and John Moore, St Vincent's Hospital, Sydney, Australia

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Autologous Haematopoietic Stem Cell Transplantation (AHSCT) is an effective treatment for severe systemic sclerosis (SSc). To date, mechanistic studies have indicated possible pro-regulatory and tolerogenic shifts in adaptive immunity. This study aims to describe the changes in key adaptive and innate immune cell populations following AHSCT, with a focus on previously undescribed T cell subpopulations in the transplant setting.

Methods: High-dimensional immunophenotyping of cryopreserved peripheral blood mononuclear cells (PBMCs) from severe SSc patients (n=13) was performed at baseline and 3, 6, 12 and 24 month timepoints post-AHSCT using two custom-designed 18-colour flow cytometry panels. Key adaptive and innate immune populations were examined along with specific subsets within the $CD4^+$ population, including markers for recent thymic egress (CD31) and potential skin-homing (cutaneous lymphocyte antigen, CLA). Data were analysed by one-way ANOVA.

Results: Following AHSCT, there was a decrease in the absolute CD4 count until 12 months, with a sustained increase in the absolute CD8 count and reversal of the CD4/CD8 ratio. $CD4^+$ conventional (Tconv) and $CD25^+CD127^-$ regulatory (Treg) cells exhibited an early proportional shift from a naïve to memory phenotype. While the percentage and absolute counts of Tregs did not change, there was early and sustained expansion of the highly suppressive $CD45RA^-HLADR^+$ Treg subset (% Treg, pre 29.8% vs 24 months 35.88% p=0.008). Furthermore, there was an early and sustained expansion of circulating skin-homing CLA^+ Tregs (% Treg, pre 28.4% vs 6 months 39.8% p< 0.001).



CD45RA-HLADR+ Tregs as a percentage of total Tregs (CD4+CD25+CD127-).

Recent thymic emigrant ($CD45RA^+CD31^+$) $CD4^+$ Tconvs and Tregs recovered by 24 months, indicative of resumed thymic output of both populations. The percentage of $CD19^+$ B cells increased significantly by 6 months (pre 3.3% vs 6 months 5.9% p=0.02). There was an early and sustained increase in the percentage of NK cells to 12 months, particularly the putatively immunosuppressive $CD56^{hi}$ subpopulation (pre 0.5% vs 12 months 1.1% p=0.005). There was no change in circulating basophils or the proportions of activated, intermediate or classical monocytes.

Conclusion: AHSCT results in both early and long term kinetic shifts in adaptive and innate immune cell populations in SSc patients. Although the overall proportion of circulating Tregs does not change, the early and sustained expansion of Tregs with a highly-suppressive phenotype and skin-homing potential may contribute to the clinical remission following AHSCT. In the long term, there is resumption of thymic output of $CD4^+$ Tregs. Harnessing these mechanistic data may inform future targeted therapies for SSc.

Disclosure: R. Penglase, Janssen, 12; **M. Visweswaran**, None; **J. Zaunders**, None; **L. Girgis**, Janssen, 12, Sponsorship for Conference Attendance, UCB, 12, Sponsorship for Conference Attendance; **D. Ma**, Phebra, 5; **J. Moore**, None.

Abstract Number: 0548

Rapamycin Blocks the Profibrotic Effects of Fli1 Downregulation in Scleroderma Myeloid Cells

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune fibrotic disease with unclear pathogenesis and no effective therapies. Increased proportion of CD163-positive, profibrotic macrophages has been described in SSc, but its contribution to SSc pathogenesis is unclear. Activation of the mammalian target of Rapamycin (mTOR) pathway has been linked to SSc fibrosis, and was also previously shown to induce a profibrotic phenotype in macrophages. We have recently demonstrated that Fli1, a member of the Ets family of transcription factors, is underexpressed in SSc myeloid cells. Co-culture of human dermal fibroblasts and Fli1 depleted myeloid cells resulted in potent induction of CD163 and other profibrotic genes in myeloid cells, and abundant collagen deposition by fibroblasts, which

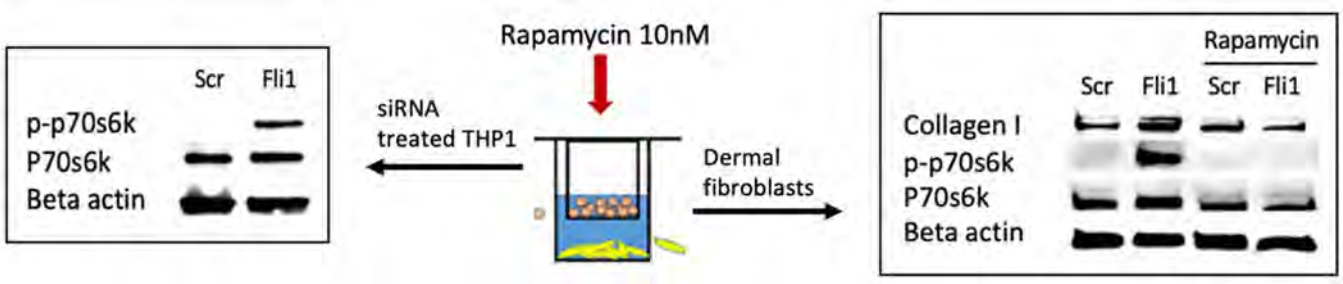

Figure.1. Myeloid cells with low Fli1 induce mTORC1 activation. Western blot analysis of protein extracts from Thp1 (left) and fibroblasts (right) after 48 h of coculture with siRNA treated THP1 cells in the presence and absence of Rapamycin. n>3 each, representative data shown.

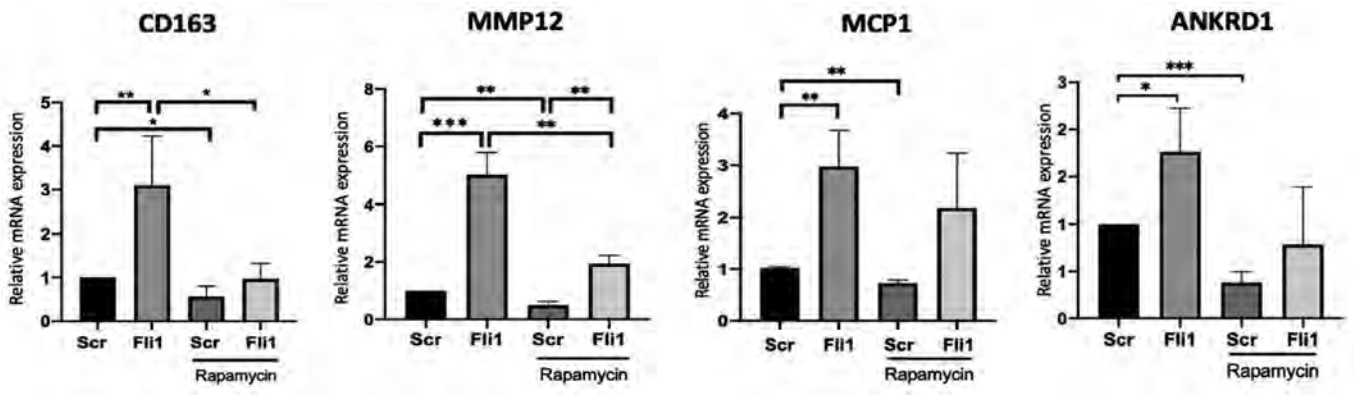

Figure 2. Inhibition of the mTOR signaling via Rapamycin blocks the elevation in CD163, MMP12, MCP1 and ANKRD1 in myeloid cells with low Fli1. n= 3 each * P ≤ 0.05, ** P ≤0 .01, *** p ≤ 0.001

was independent of TGFβ pathway activation.[1] The aim of our study was to evaluate the mechanism by which deletion of Fli1 in myeloid cells exerts its profibrotic effects.

Methods: Primary human dermal fibroblasts were isolated from skin biopsies and were co-cultured with THP1 cells using inserts. Fli1 was depleted via siRNA in THP1 cells using Lipofectamine, and Rapamycin (10nM) was used to treat the co-cultures. Western blot was used to assess the protein levels of collagen and P-p70S6K (Thr^{389}), and qRT-PCR was used to measure mRNA expression of CD163, MCP1, MMP12 and ANKRD1.

Results: Co-culture of human dermal fibroblasts and Fli1 depleted macrophages resulted in activation of the mTOR pathway, with increased phosphorylation of p70S6K (Thr^{389}) in THP1 cells and dermal fibroblasts. Rapamycin treatment blocked the increase in collagen deposition by fibroblasts cocultured with Fli1 depleted myeloid cells (Fig.1). Furthermore, blockade of the mTOR pathway using Rapamycin in THP1 cells alone, in the presence or absence of siRNA against Fli1, reversed the effects of Fli1 inhibition on the mRNA levels of CD163, MCP1, MMP12 and ANKRD1 in these cells (Fig.2).

Conclusion: Fli1 deletion in myeloid cells triggers activation of a profibrotic phenotype, with increased fibroblast collagen deposition, via activation of the mTOR signaling pathway. Myeloid Fli1 deficiency may contribute to SSc pathogenesis, and Rapamycin may be a potential therapeutic option for SSc fibrosis.

Disclosure: F. El-adili, None; **G. Marden**, None; **M. Trojanowska**, None; **A. Bujor**, None.

Abstract Number: 0549

Upregulation of Prostanoid EP2 Receptors and Meditation of Treprostinil Anti-Proliferative Effects in Scleroderma Smooth Muscle Cells

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Progressive functional and structural vascular disorder is one of the hallmark features of Systemic Sclerosis (Scleroderma, SSc). Vascular dysfunction leads to dysregulated vascular tone control and activation of vascular smooth muscle cells (vSMCs) resulting in enhanced vasospasm and intimal hyperplasia. We previously reported downregulation of the prostacyclin receptor (IP) in SSc skin and vSMCs. In this study we examined IP signaling in SSc and control vSMCs using an IP-specific agonist. Also, it is now clear that in conditions where IP expression is repressed, as in Pulmonary Arterial Hypertension (PAH) or in experimental IP knockdown, the prostacyclin analog treprostinil may engage other receptors including PPARs, EP1, EP2, EP4, or DP1 to mediate its effects. Thus, we examined the role of these receptors in mediating treprostinil effects.

Methods: vSMCs were isolated from involved SSc skin (no=5) matched healthy subjects. cAMP levels were measured by ELISA after the addition of treprostinil or the specific IP agonist MRE 269, before and after the addition of the epigenetic inhibitors 5-Aza 2 deoxycytidine (Aza) and trichostatin (TSA). Cell proliferation was measured by MTT assay. Treprostinil inhibition of proliferation was tested after the addition of specific antagonists to EP1, EP2, EP4, DP1, PPAR α, δ, and ɣ.

Results: Treprostinil stimulated cAMP expression in SSc and control cells to the same degree, while MRE 269 stimulated cAMP in control cells but failed to stimulate SSc cells. The addition of epigenetic inhibitors Aza and TSA restored MRE 269 ability to stimulate cAMP in SSc cells to a level equal to control values. Treprostinil inhibited vSMCs proliferation in a dose-dependent fashion. The addition of the specific antagonist to EP1, EP4, DP1, PPAR α, and δ to SSc and control vSMCs did not influence the degree of treprostinil mediated inhibition of vSMCs proliferation. The addition of PPAR ɣ antagonist had modest effects on treprostinil mediated inhibition of SSc vSMCs proliferation, while the addition of EP2 antagonist significantly diminished treprostinil inhibition of SSc vSMCs proliferation. The expression levels of EP2 were upregulated 9 folds in SSc vSMCs and PPARɣ 3 folds over levels in control cells. There was no difference in the expression levels of PPAR α, β/ δ, EP1, and EP4 between SSc and control vSMCs and DP1 expression level was significantly repressed in SSc cells.

Conclusion: We identified defective IP receptor signaling in SSc cells that were reversed by the addition of the epigenetic inhibitors confirming the involvement of epigenetics in the repression of IP expression in SSc cells. Moreover, treprostinil stimulated cAMP in SSc and normal cells equally suggesting that treprostinil uses other receptors to mediate its effects. Using specific antagonists, we show that treprostinil engages mainly EP2 in it is effects and to a much less extent PPARɣ. mRNA expression data showed a significant increase expression of EP4 and PPAR- γ in SSc cells when compared to normal cells.

Disclosure: Y. **Wang**, None; **N. Altorok**, None; **B. Kahaleh**, None.

Abstract Number: 0550

Treatment Regimens and Outcomes in Systemic Sclerosis-associated Pulmonary Arterial Hypertension

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SESSION INFORMATION

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Background/Purpose: Pulmonary arterial hypertension (PAH) is a major clinical challenge in systemic sclerosis (SSc). It is associated with impaired quality of life and high mortality. In 2015, the treatment recommendations changed, recommending upfront combination therapy from the time of diagnosis. The objective of this study was to assess the impact of upfront dual combination therapy versus monotherapy on PAH progression and mortality.

Methods: We included all patients with SSc who had right heart catheterization (RHC) between 2005 and 2018 at Oslo University Hospital, and who were diagnosed with PAH, defined as a mean pulmonary arterial pressure (mPAP) ≥ 25 mmHg and a pulmonary artery wedge pressure ≤ 15mmHg in the absence of interstitial lung disease (ILD). Longitudinal clinical characteristics including treatment were assessed; vital status were available in all patients. To study treatment regimens over time, patients were categorized into three subgroups in regard to diagnostic periods. To secure that all patients had at least 3 years of follow up, group 1 consisted of patients diagnosed between 2005 and 2009, group 2 of patients diagnosed between 2010 and 2014, and group 3 of patients diagnosed between 2015 and 2018. Treatment was initiated as soon as PAH had been confirmed, and included (1) an endothelin-1 receptor antagonist (ERA) and/or (2) a phosphodiesterase-5 inhibitor (PDE5 inhibitor). To assess the impact of treatment regimens on mortality and PAH progression, two outcomes were assessed, including (1) death and (2) PAH-progression defined as a) intensified PAH treatment, b) increasing respiratory symptoms and/or c) hemodynamic progression defined as reduction in the cardiac index (CI) to less than 2.5 l/min/m^2, or mixed venous oxygen saturation (SVO2) < 65%. We constructed Kaplan-Meier plots and performed time-to-event analyses.

Table 1. SSc: systemic sclerosis; PAH: pulmonary arterial hypertension; lcSSc: limited cutaneous systemic sclerosis; ACA: anti-centromere antibodies; NYHA: New York Heart Functional Classification; mPAP: mean pulmonary arterial pressure; PVR: pulmonary vascular resistance; PAWP: pulmonary artery wedge pressure; SvO2: mixed venous oxygen saturation; ERA: Endothelin-1-inhibitor; PDE5 inhibitor: Phosphodiesterase-5-inhibitor

	All patients N= 56	Group 1 N= 13	Group 2 N= 25	Group 3 N= 18
Age at SSc onset, mean years (SD)	59 (±14)	60 (±11)	59 (±16)	58 (±12)
Age at PAH diagnosis, mean years (SD)	66 (±11)	64 (±8)	68 (±13)	64 (±10)
Female sex, n (%)	45 (80 %)	9 (70 %)	22 (88 %)	14 (78 %)
lcSSc, n (%)	52 (93 %)	12 (92 %)	23 (92 %)	17 (94 %)
ACA, n (%)	42 (75 %)	11 (85 %)	21 (84 %)	10 (56 %)
NYHA 3 or 4 at PAH diagnosis, n (%)	39 (70%)	11 (85%)	16 (64%)	12 (67%)
NT-proBNP at PAH-diagnosis, pmol/l (SD)	317 (±556)	283 (±294)	350 (±577)	294 (±674)
Right heart catheterization				
mPAP, mmHg (SD)	36.6 (±9.7)	40.5 (±9.8)	36.6 (±10.5)	33.8 (±8.0)
Cardiac index, l/min/m^2 (SD)	2.8 (±0.8)	2.6 (±0.9)	2.9 (±0.8)	2.9 (±0.7)
PVR, Wood units (SD)	6.3 (±3.9)	8.0 (±5.8)	6.0 (±3.3)	5.4 (±2.5)
PAWP, mmHg (SD)	8.3 (±3.3)	7.4 (±3.5)	8.1 (±3.4)	9.1 (±3.0)
SvO2, % (SD)	65.2 (±10.1)	62.6 (±8.8)	63.8 (±12.8)	68.7 (±4.8)
Upfront monotherapy, n (%)	37 (67 %)	11 (85 %)	20 (80 %)	6 (35 %)
ERA, n (%)	32 (87 %)	8 (73 %)	19 (95 %)	5 (83 %)
PDE5 inhibitor, n (%)	5 (14 %)	3 (27 %)	1 (5 %)	1 (17 %)
Upfront combination therapy, n (%)	11 (20 %)	0 (0 %)	2 (8 %)	9 (53 %)
Death 1 year follow up, n (%)	12 (21 %)	1 (8 %)	9 (36 %)	2 (11 %)
Death 3 year follow up, n (%)	25 (45 %)	8 (62 %)	11 (44 %)	6 (33 %)
PAH progression 1 year follow up, n (%)	24 (47 %)	8 (67 %)	10 (44 %)	6 (38 %)
PAH progression 3 year follow up, n (%)	31 (61 %)	10 (83 %)	14 (61 %)	7 (44 %)

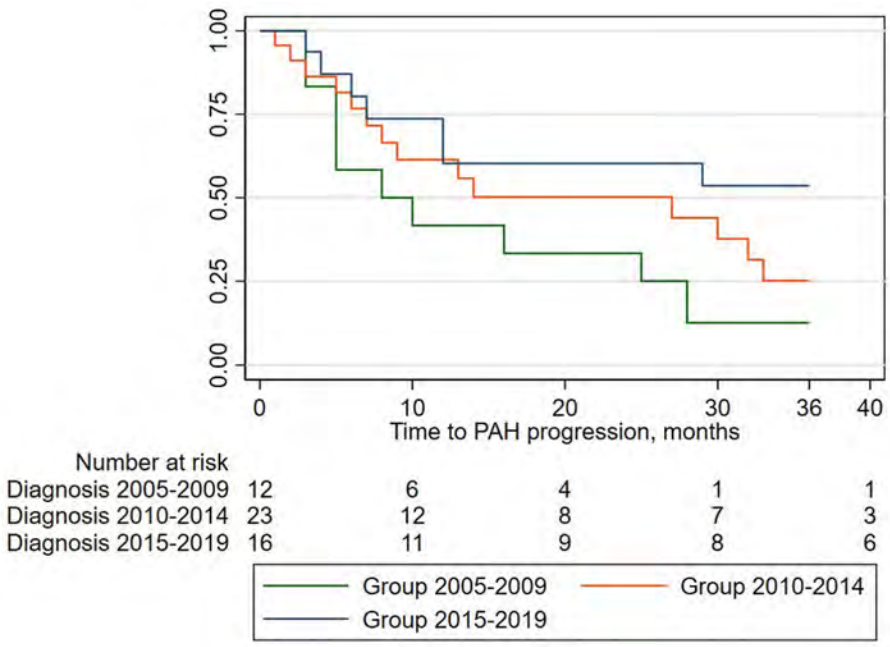

Figure 1. Kaplan Meier curve showing time to PAH progression in SSc-PAH patients segregated by the time of PAH diagnosis.

Results: In total, 191 patients had RHC in the study period, whereof 56 (29 %) SSc patients had a PAH diagnosis. Mean age at SSc-diagnosis was 59 years, mean age at PAH-diagnosis 66 years; 80 % were female and 93 % had limited cutaneous SSc (table 1). None of the patients in group 1 started upfront combination therapy compared to 53 % of patients in group 3. Event-free survival was better in group 3 compared to groups 1 and 2 as shown in the table and figure (p=0.05). 3-year survival increased numerically across groups 1 through 3, from 54% via 62% to 78% (p= 0.148).

Conclusion: We show that upfront dual combination therapy for SSc-PAH has been used more frequently after 2015 in Norway. This shift is associated with less progression of PAH and increased survival in patients with SSc-PAH. This may indicate that there is a benefit of upfront dual combination therapy in SSc-PAH patients in addition to higher awareness and better monitoring strategies.

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Abstract Number: 0551

Metabolic Intermediate Dimethyl-Alpha-Ketoglutarate Is a Novel Repressor of Pathogenic Myofibroblast Reprogramming and Skin Fibrosis in Systemic Sclerosis

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SESSION INFORMATION

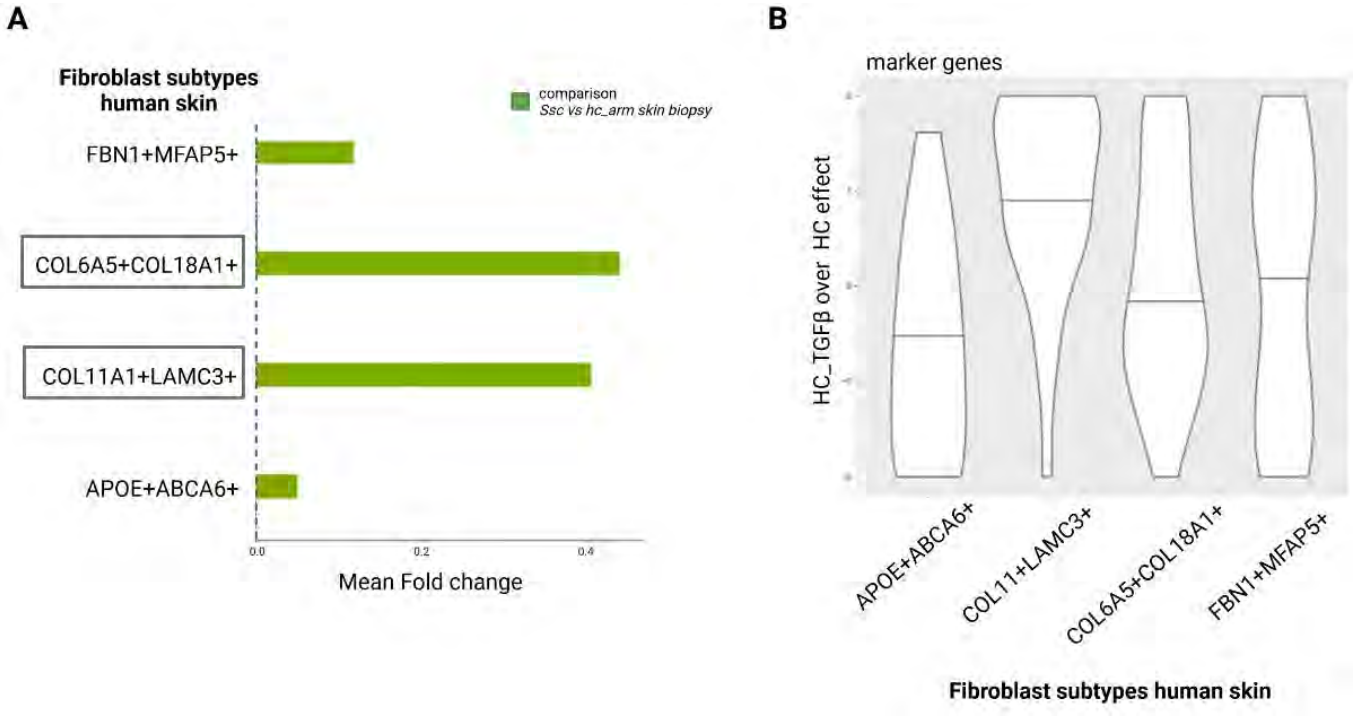
Session Date: Sunday, November 7, 2021

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Metabolic perturbations drive fibroblast-to-myofibroblast reprogramming and tissue fibrosis. Restoring perturbed metabolism might represent a new antifibrotic strategy. Here we explored the capacity of



(A) Expanded inflammatory fibroblasts and myofibroblasts in SSc skin. (B) TGFβ upregulates COL11+LAMC3+ myofibroblast marker genes in DF.

dimethyl-alpha-ketoglutarate (dm-aKG), a core cell metabolite, to regulate myofibroblast function and skin fibrosis in SSc.

Methods: To discover dysregulated genes, pathways, and cell types in SSc skin, we integrated skin transcriptomes of 76 SSc patients and 26 healthy controls (HC) from three different cohorts (GSE:45485, 59785, 9285/32413) using limma and GSEA. We deconvoluted cell types in bulk skin transcriptomes using human skin single-cell RNA-seq data[1]. We compared the dysregulated genes in SSc skin with RNA-seq data from cultured TGFβ-treated healthy human dermal fibroblasts (DF) and validated gene dysregulations with RNA-seq data from skin biopsies of the PRESS cohort with 48 early diffuse SSc patients and 33 HC. We studied the effects of dm-aKG on myofibroblast differentiation and pro-fibrotic activation in 2D and 3D cultures of SSc and HC DF treated or not with TGFβ. We analyzed gene (RNA-seq, qPCR) and protein (Western blot, ELISA) expression and contractile (collagen gel contraction), migratory (wound scratch assay, DF spheroids) and invasive (collagen gel invasion in DF spheroids) cell functions. Statistical significance was set at $p< 0.05$.

Results: Our deconvolution of skin transcriptomes demonstrated an enrichment of specific fibroblast populations in SSc vs. HC skin: COL6A5+COL18A1+ inflammatory fibroblasts and COL11+LAMC3+ myofibroblasts were highly abundant in SSc skin (Fig. 1A). TGFβ increased the expression of several marker genes of the COL11+LAMC3+ myofibroblasts (Fig. 1B). Meanwhile, dm-aKG decreased the TGFβ-induced *LAMC3* and *COL11* mRNA expression in cultured DF, suggesting that TGFβ might facilitate, while dm-aKG could repress the COL11+LAMC3+ myofibroblast expansion in SSc skin. We uncovered dysregulation of several aKG-associated metabolic pathways in SSc skin transcriptomes, such as mitochondrial respiration and oxidoreductase activity. Dm-aKG repressed the TGFβ-regulated pro-fibrotic responses and myofibroblast differentiation of DF as measured by procollagen-1, fibronectin and aSMA protein reduction. Furthermore, dm-aKG reversed the TGFβ-induced increase of genes regulating cytoskeleton organization (*NEXN, CAP2, ANTXR1, LIMCH1, TGM2)*, cell contraction *(ANKRD1, OXTR, FZD2, DYSF, CSRP2)* and extracellular matrix dynamics (*COL10A1, COL11A1, MMP14, MMP3, ADAMTS4, MATN3, SULF1, HAPLN1)*. These genes were all upregulated in skin from early diffuse SSc patients (PRESS cohort). Most importantly, functional experiments confirmed the core role of dm-aKG in suppressing contractile, migratory and invasive properties of TGFβ-activated DF.

Conclusion: Dm-aKG reverses the dysregulated expression of myofibroblast-linked gene signatures of the SSc skin and potently represses core myofibroblast functions. Thus, dm-aKG could represent a new therapy to combat skin fibrosis in SSc.

[1]*He H et al. J Allergy Clin Immunol 2020*

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Abstract Number: 0552

Long Non-coding RNA H19X as a Regulator of Endothelial Adhesion Molecules in Systemic Sclerosis

Francesca Tirelli[1], Elena Pachera[1], Robert Lafyatis[2], Menqi Huang[3], Francesco Zulian[4], Gabriela Kania[1] and Oliver Distler[5], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [2]University of Pittsburgh, Pittsburgh, PA, [3]Division of Rheumatology and Clinical Immunology, Department of Medicine, University of Pittsburgh, Pittsburgh, PA, [4]Rheumatology Unit, Department of Woman and Child Health - University of Padova, Padova, Italy, [5]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich/University of Zurich, Zurich, Switzerland

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Long non-coding RNAs (lncRNAs) are non-coding transcripts involved in the regulation of gene expression; their role in disease development, to date, remains largely under investigation. Recently, we showed that lncRNA H19X is pivotal in the regulation of TGFβ driven fibrosis in SSc. Here, we aimed to characterize the functional relevance of H19X in endothelial cell (EC) activation, a crucial mechanism in SSc vasculopathy.

Methods: Single-cell RNA-sequencing (scRNA-seq) was performed on 27 dcSSc and 10 healthy controls (HC) skin biopsies. After library preparation (10X Genomics protocol) and sequencing (Illumina NextSeq-500 platform), the reads were examined by quality metrics and transcripts mapped to reference human genome (GRCh38). Data analysis was performed using Seurat package in R (v. 3.0). A total of 4981 EC (1583 from HC and 3398 from SSc patients, 59-342 EC per subject), characterized by enrichment of EC markers of *CLDN5*, *VWF* and *PECAM1,* were identified and analyzed for the expression of H19X and specific EC activation markers. The function of H19X was analyzed in Human Dermal Microvascular EC (HDMEC). H19X expression was analyzed by qPCR after HDMEC stimulation with different proinflammatory cytokines at biologically relevant concentrations. HDMEC were transfected using locked nucleic acid antisense oligonucleotides (LNA GapmeRs). Western Blot (WB) and qPCR were used to analyze the effects of H19X silencing on endothelial adhesion molecules.

Results: scRNA-seq data from skin biopsies showed a significant upregulation of H19X in SSc compared to healthy EC (p=0.0095), which was observed also for various EC subclusters. Identified subclusters included arterial (characterized by *SEMA3G*, *HEY1*), capillary (*CA4*, *RGCC*), venous (*ACKR1*, *VCAM1*) and lymphatic (*PROX1*, *LYVE1*) EC. Two additional clusters, proliferating (*TOP2A*, *MKI67*) and injured (*HSGP2*, *APLNR*) EC, were represented almost exclusively in SSc ECs. Specifically, the highest expression of H19X was found in injured SSc EC and capillary SSc EC. Overall, 1.5% of the SSc EC, about 51 cells, expressed detectable levels of H19X. In HDMEC (n=3), H19X was consistently induced by IFNα, IFNβ and IFNγ as well as by different IFN combination stimulations (IFNα+β+γ and α+γ). Time curve analysis demonstrated that the strongest induction was observed between 48h and 72h. Importantly, H19X knockdown lead to a consistent and significant decrease of mRNAs of the adhesion molecule VCAM1, both in untreated HDMEC (n=4, p=0.006) as well as after IFN stimulation. A decrease of VCAM1 could be also demonstrated by WB analysis (untreated, n=4, p=0.01, semiquantitative analysis). Furthermore, co-expression analysis of the scRNA-seq data from skin biopsies confirmed a higher expression of several adhesion molecules in EC expressing H19X, including ICAM, VCAM1 and JAM3.

Conclusion: H19X is overexpressed in SSc endothelium and is stimulated by IFNs. Our results point to a role of H19X as a regulator of adhesion molecules in EC, thus suggesting its potential involvement in the pathogenesis of SSc vasculopathy.

Disclosure: F. Tirelli, None; **E. Pachera**, None; **R. Lafyatis**, Bristol Meyers Squibb, 2, 5, Formation, 2, 5, Corbus, 5, Moderna, 5, Regeneron, 5, Pfizer, 5, Kiniksa, 5, Sanofi, 2, Merck, 2, Genentech/Roche, 2, Acceleron, 2, Boehringer-Ingelheim, 2; **M. Huang**, None; **F. Zulian**, None; **G. Kania**, None; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2.

Abstract Number: 0553

IgG from Systemic Sclerosis Patients Induce a Profibrosing and Serotype-dependent Phenotype in Normal Dermal Fibroblast: A Multi-omics Study

Aurélien Chepy[1], Solange Vivier[2], Fabrice Bray[3], Martin Figeac[4], Jean-Pascal Meneboo[4], Camille Ternynck[5], Lucile Guilbert[2], Manel Jendoubi[2], Christian Rolando[3], David Launay[1], Sylvain Dubucquoi[6], Guillemette Marot[5] and Vincent Sobanski[1], [1]Univ. Lille, Inserm, CHU Lille, Service de Médecine Interne, U1286 - INFINITE - Institute for Translational Research in Inflammation, F-59000 Lille, France, Lille, France, [2]Univ. Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, F59000 Lille, France, Lille, France, [3]Univ. Lille, CNRS, USR 3290 - MSAP - Miniaturisation pour la Synthèse, l'Analyse et la Protéomique, F-59000 Lille, France, Lille, France, [4]Université de Lille, Functional Genomics Platform, Lille, France., Lille, France, [5]ULR 2694 – METRICS : évaluation des technologies de santé et des pratiques médicales, université de Lille, CHU de Lille, 59000 Lille, France, Lille, France, [6]Univ. Lille, U1286 – INFINITE – Institute for Translational Research in Inflammation, F59000 Lille, France, Lille

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Antinuclear antibodies are frequent in systemic sclerosis (SSc). While recognized as potent biomarkers, their pathogenic role is much more debated. This study explored the effect of purified IgG from SSc patients on the phenotype and function of healthy dermal fibroblast (FB) using an innovative and unbiased multi-omics approach.

Methods: Normal dermal FB were cultured in the presence of purified IgG from patients with diffuse cutaneous SSc (dcSSc), limited cutaneous SSc or healthy controls (HC). FB proteome and transcriptome were explored using mass spectrometry coupled with liquid chromatography (LC-MS/MS) and microarray assays, respectively.

Results: Proteomic analysis identified 3310 differentially expressed proteins (DEP). SSc sera and purified IgG induced singular modifications FB protein profiles. These FB proteome changes were dependent of SSc serotype, especially pronounced with purified IgG from anti-topoisomerase I antibodies (ATA) positive patients (**Figure 1**). The enriched Gene Ontology (GO) terms upregulated in IgG purified SSc were involved in macroautophagy, positive regulation of protein transport and cell adhesion molecule transport. Transcriptomic analysis distinguished 764 differentially expressed genes and confirmed that IgG from dcSSc can induce profibrotic changes in genes profiles of FB. IgG from ATA positive patients induced singular changes: 629 DEP were identified in dcSSc ATA+ purified IgG and GO terms analysis showed enrichment in focal adhesion, cadherin binding, cytosolic part or lytic vacuole. Filamin A was the most strongly overexpressed protein in the presence of purified IgG compared to HC (**Figure 2**).

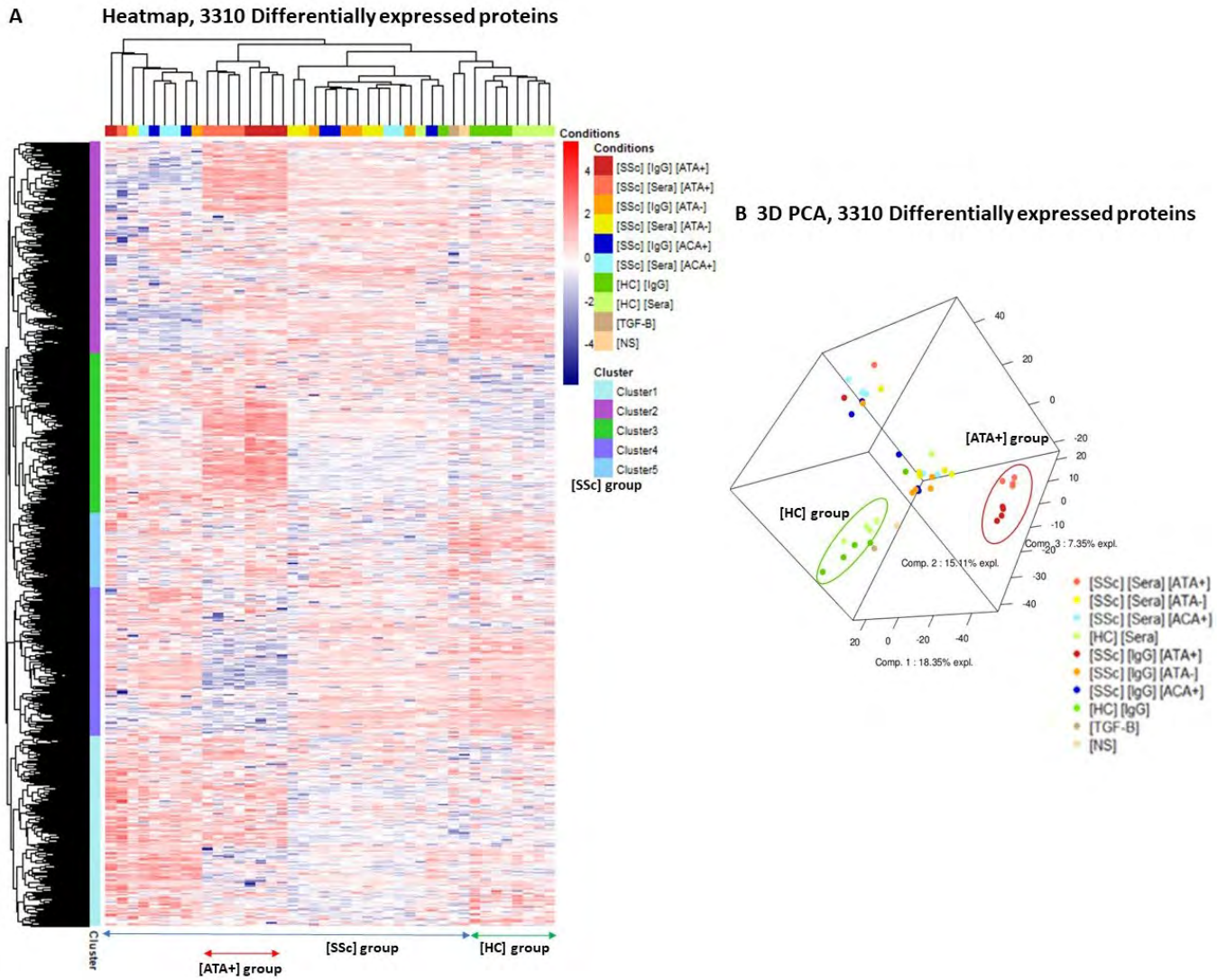

Figure 1 legend: 1.A: heatmap representing 3310 differentially expressed proteins in proteomic analysis by Liquid chromatography–mass spectrometry (LC-MS/MS). Supervised clustering identified 5 different cluster of protein expression profile. 803, 894, 673, 626, 314 proteins were respectively found in cluster1, 2, 3, 4 and 5. 1.B: PCA of differentially expressed proteins. PCA highlights proteins expression by the FB according to SSc serotype. [ATA+] seemed to induce a singular protein expression profile compared to others SSc and SSc. PCA: principal component analysis. [HC] [Sera]: sera from healthy control; [HC] [IgG]: IgG from healthy control; [SSc] [Sera] [ATA+]: Sera from diffuse systemic sclerosis anti-Topoisomerase-I positive antibodies; [SSc] [IgG] [ATA+]: IgG from diffuse systemic sclerosis anti-Topoisomerase-I positive antibodies; [SSc] [Sera] [ATA-]: Sera from diffuse systemic sclerosis anti-Topoisomerase-I negative antibodies; [SSc] [IgG] [ATA-]: IgG from diffuse systemic sclerosis anti-Topoisomerase-I negative antibodies; [SSc] [Sera] [ACA+]: Sera from limited systemic sclerosis anti-centromere positive antibodies; [SSc] [IgG] [ACA+]: IgG from limited systemic sclerosis anti-centromere positive antibodies; [TGF-B]: fibroblast stimulated in the presence of TGF-**β**; [NS]: non stimulated fibroblast.

Conclusion: We identified that purified IgG from SSc can modify the phenotype of normal dermal FB. This effect seems dependent of the serotype. Purified IgG from dcSSc exhibited profibrotic properties with a singular profile of proteins expression and mRNA in patients with ATA.

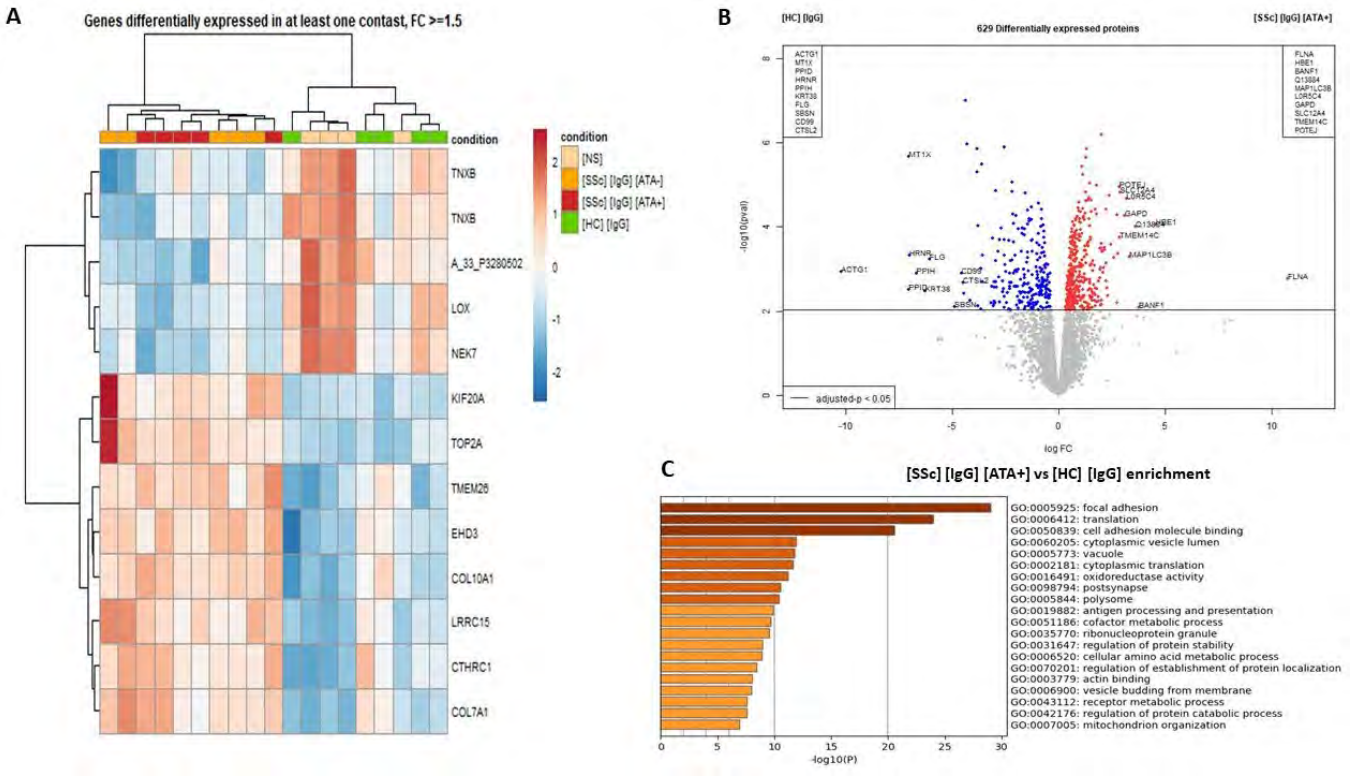

Figure 2 legend: A: heatmap (transcriptomic analysis) represented genes dysregulated in at least one contrast with FC>1.5 in the DNA probes dysregulated in proteomic analysis; B: Volcanoplot (proteomic analysis) represented the comparison [SSc] [IgG] [ATA+] vs [HC] [IgG]; proteins with adjust p-value <0.05 and Log Fold Change >1.4 or <-1.4 were considered; C: Enriched clusters GO terms in the comparison [SSc] [IgG] [ATA+] vs [HC] [IgG] according to upregulated proteins, analysis done with Metascape; [HC] [IgG]: IgG from healthy control; [SSc] [IgG] [ATA+]: IgG from diffuse systemic sclerosis anti-Topoisomerase-I positive antibodies; [SSc] [IgG] [ATA-]: IgG from diffuse systemic sclerosis anti-Topoisomerase-I negative antibodies; [SSc] [IgG]: IgG from systemic sclerosis patients; [NS]: non stimulated fibroblast.

Disclosure: A. Chepy, CSL Behring, 5; **S. Vivier**, None; **F. Bray**, None; **M. Figeac**, None; **J. Meneboo**, None; **C. Ternynck**, None; **L. Guilbert**, None; **M. Jendoubi**, None; **C. Rolando**, None; **D. Launay**, None; **S. Dubucquoi**, None; **G. Marot**, None; **V. Sobanski**, None.

Abstract Number: 0554

Reverse Signaling Through PD-L1 Plays a Central Role in Extracellular Matrix Protein Secretion from Cutaneous Myofibroblasts in Systemic Sclerosis

Maithri Aspari[1], Stinne Greisen[1], Malene Hvid[1], Klaus Sondergaard[2], Voon Ong[3], Christopher Denton[4], David Abraham[5] and Bent Deleuran[1], [1]Aarhus University, Aarhus, Denmark, [2]Aarhus University Hospital, Aarhus, Denmark, [3]University College London Medical School Royal Free Campus, London, United Kingdom, [4]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom, [5]University College London, London, United Kingdom

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster (0541–0559)

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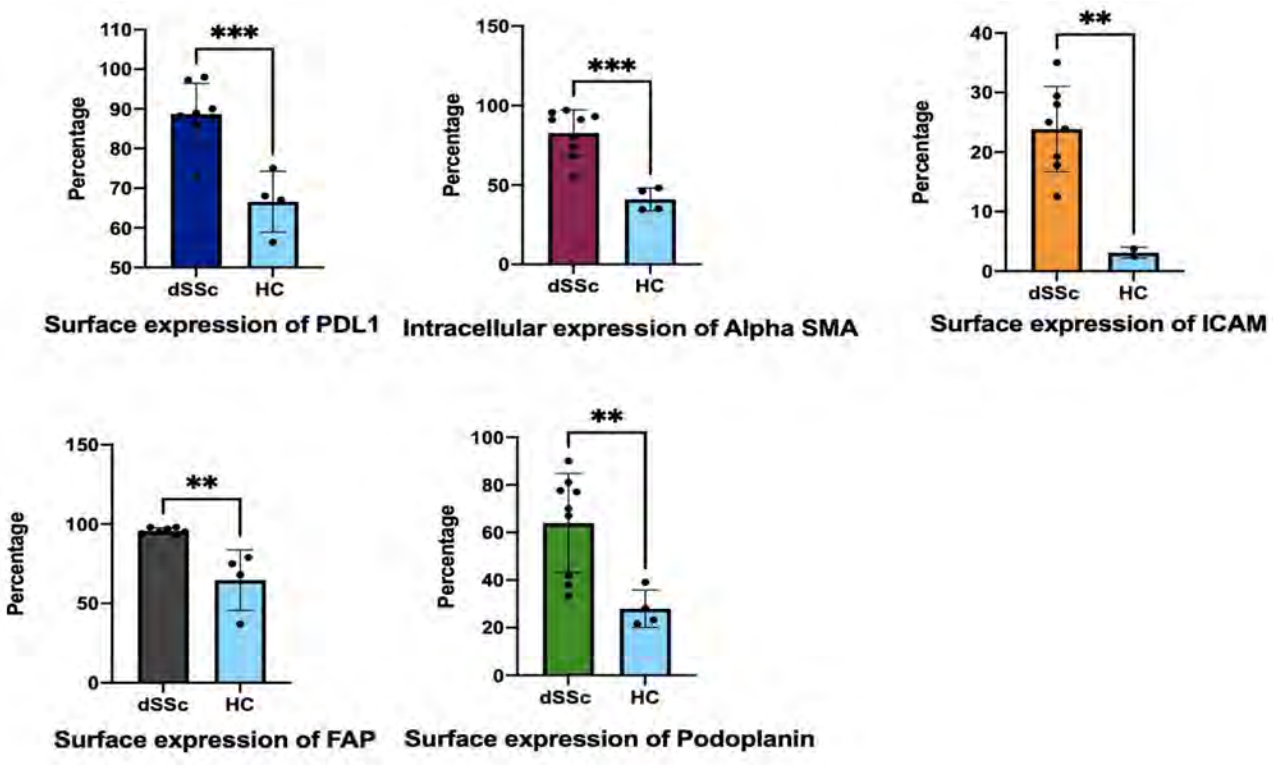

Figure 1. Fibroblast from dSSc fibroblasts increased PD-L1, a-SMA, ICAM-1, FAP and PDPN compared with HC after stimulation with TGFb for 48h.

Background/Purpose: The PD-1/PD-L1 pathway has been implicated in Systemic Sclerosis (dSSc). This disease is dominated by increased extracellular matrix deposition initiated by myofibroblasts. We therefore examined the PD-1/PD-L1 pathway in dSSc myofibroblasts and its influence on fibrosis.

Methods: Dermal fibroblasts were isolated from the skin from patients with dSSc (n=9) and compared with dermal fibroblasts from healthy controls (HC)(n=4). Cells were stimulated with TGF β for 48 hours and analyzed by flow cytometry for expression of the surface proteins CD45, Thymocyte differentiation antigen-1 /(CD90 Thy-1), podoplanin (PDPN), Programmed Death Protein Ligand-1(PD-L1), Fibroblast activation Protein (FAP),and Intercellular adhesion molecule-1 (ICAM-1) and alpha smooth muscle actin (α- SMA). Supernatants were analyzed for the production of Type 1 Procollagen and IL-6. Parallel to this, dcSSc fibroblasts, were stimulated with IFNγ (10ng/ml) for 48 hours followed by addition of anti-PD-L1 antibody (atrezolizumab, 5ug/ml) and soluble, recombinant PD-1 (RPD-1;1ug/ml). Supernatants were harvested after 48 hours and analyzed for production of Type 1 Procollagen and Fibronectin.

Results: $CD45^{neg}$ fibroblasts, from both dSSc as well as HC could be identified by their expression of Thy-1 and Podoplanin. Upon stimulation with TGFβ, fibroblasts from dSSc patients increased the percentages of myofibroblasts expressing PD-L1, α- SMA, ICAM-1, FAP and Podoplanin when compared to HC fibroblasts.(Figure 1) All $p < 0.05$, Figure 1. Upon concatenating and analyzing this data by tSNE, we could demarcate a distinct populations of the myofibroblasts that had a high expression of PD-L1 together with ICAM-1 (Figure 2). Compared with HC, dcSSc fibroblasts were characterized by an increased production of Type 1 Procollagen and IL -6, this was highly increased by stimulation with TGFβ, still most pronounced in dSSc (Figure 3a). To explore the role of PD-L1 in fibrosis, we added an anti-PD-L1 monoclonal antibody, or rPD-1 to fibroblasts. Both increased the production of Type 1 Pro-collagen, whereas fibronectin was only increased by adding the anti-PD-L1 antibody(Figure 3b).

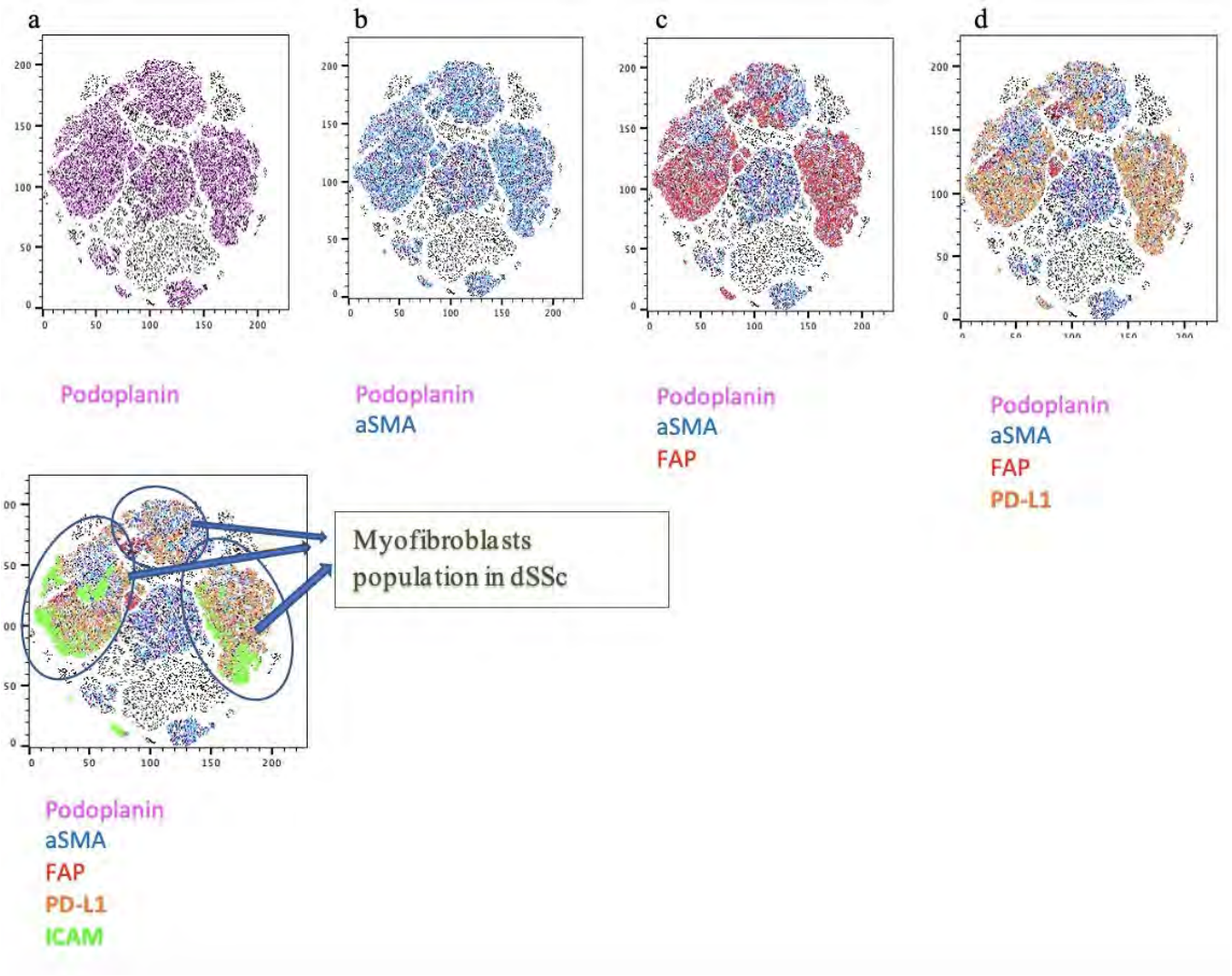

Figure 2. A t-SNE analysis of concatenated dSSc fibroblasts populations that were CD90 positive with overlay of markers of fibroblast activation such as Podoplanin, FAP and intracellular expression of Alpha SMA. A distinct myofibroblast population could be identified that express the above markers together with PD-L1 and ICAM-1.

Conclusion: dSSc fibroblasts are distinct from dermal fibroblasts from HC, both in their phenotype and functionality. The myofibroblast population can thus be defined as a subset within the dSSc fibroblasts with high and co-expression of PD-L1, FAP, Podoplanin, and ICAM. PD-L1 plays an important role in regulating fibrosis, and inflammation in dSSc and our results supports the notion that PD-L1 does this through reverse signaling.

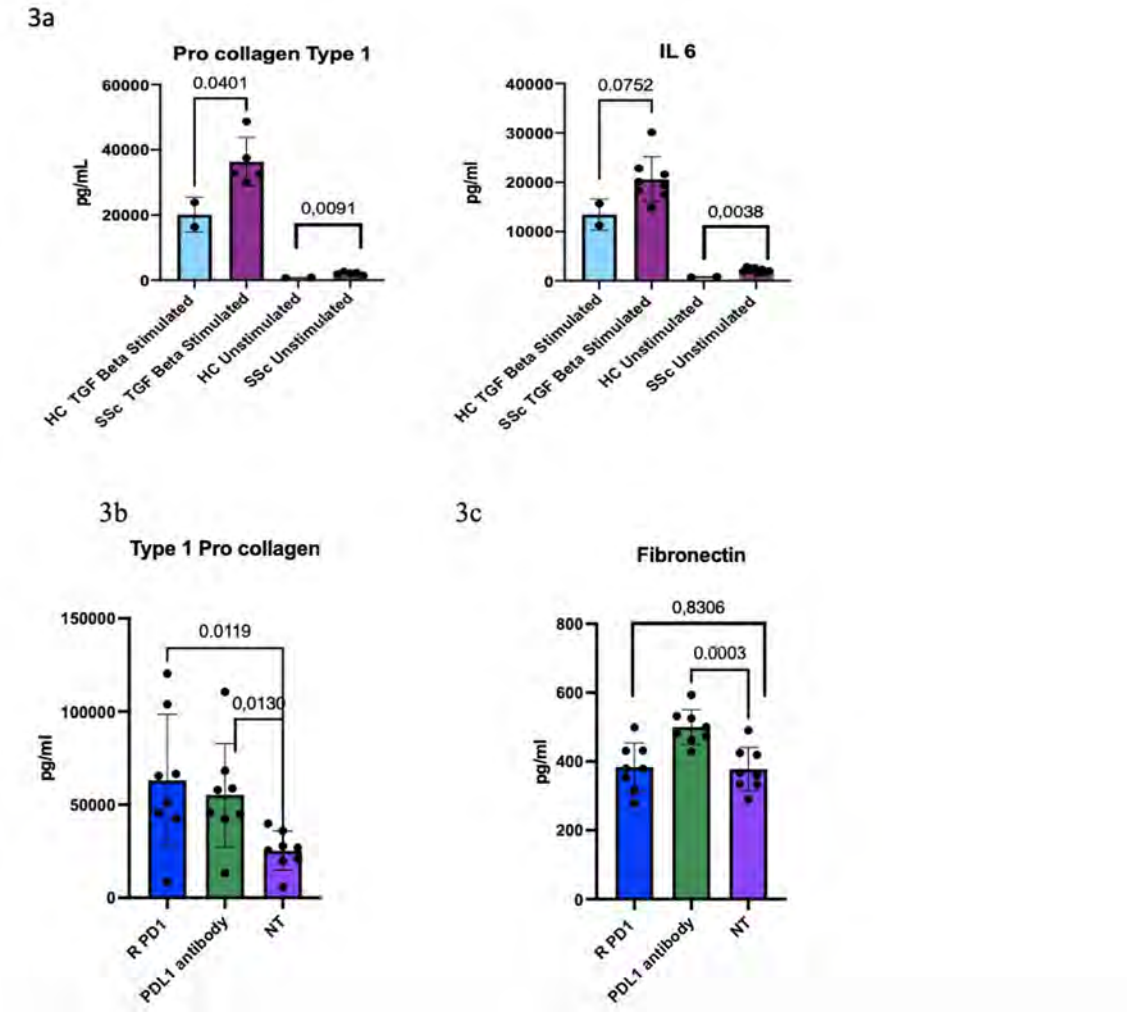

Figure 3. Increased type 1 collagen production (a) and IL-6 (b) by dSSc fibroblasts when compared with healthy controls (HC), with or without stimulation by TGFb. Type 1 procollagen (c) and fibronectin (d) production after addition of an anti-PD-L1 antibody or sPD-1 in dSSc fibroblasts.

Disclosure: M. Aspari, None; **S. Greisen**, None; **M. Hvid**, None; **K. Sondergaard**, None; **V. Ong**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **D. Abraham**, None; **B. Deleuran**, None.

Abstract Number: 0555

Pathway-Driven Drug Repositioning in Systemic Sclerosis from Omics Data

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SESSION INFORMATION

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Background/Purpose: Omic analyses of systemic sclerosis (SSc) skin biopsy datasets identified distinct sets of patients that respond differently to treatment. The goal of this study was to use the Connectivity Map (CMAP) library of gene expression profiles from drug treatments of cell lines to identify pathways and small molecules (perturbagens) that would normalize the aberrant gene expression profiles in SSc patients back to that of healthy controls.

Methods: CMAP 2.0 data was processed with RMA, quantile normalized, and fit to a multichip linear model. Probes were collapsed as average intensity and formatted for gene fold-change as the ratio of treatment to control intensities. DNA microarray data from SSc patient skin were obtained from Milano et al (GSE9285) and Pendergrass et al (GSE32413) then analyzed by Gene Set Variation Analysis (GSVA) in R for single-sample enrichment scores. Enrichment scores significant for each intrinsic subset of SSc patients were determined and perturbagens that have potential to regulate these pathways were chosen for further study. 3D skin-like tissues were constructed with dermal fibroblasts from ATCC, treated with selected perturbagens, and analyzed with H&E or Sirius Red for visualization.

Results: We focused on analyses on the inflammatory and fibroproliferative pathogenic subsets. Pathways specific to these two subsets were selected from publicly available gene expression data from SSc and control skin through single-sample GSVA. We identified 608 pathways enriched for upregulation in the inflammatory subset and 667 pathways enriched for upregulation in the fibroproliferative subset. Using single sample GSVA, we identified all CMAP perturbagens predicted to modulate the pathways in the inflammatory or fibroproliferative subsets. A parallel analysis using the BASE algorithm was also performed and perturbagens identified in both analyses were chosen for further study. EGFR inhibitors were shown to regulate gene set pathways from the inflammatory subset of SSc patients. We determined that PI3K inhibitors modulated gene set pathways from the fibroproliferative subset of SSc patients. Experimental validation of the PI3K inhibitor decreased collagen 1 expression of fibroblasts grown in 2D cell culture. Inhibitors were also analyzed in self-assembled (SA) 3D skin-like tissues containing only normal dermal fibroblasts, with and without TGFB stimulation. The PI3K inhibitor showed decreased extracellular matrix deposition, likely as a result of reduced collagen expression within the tissue environment. The EGFR inhibitor showed less significant changes in either tissue thickness or collagen deposition.

Conclusion: Multiple small molecule inhibitors have been identified that regulate gene set pathways that are specific to two molecular subsets of SSc patients determined by gene expression profiling. Testing these perturbagens within cell culture and 3D skin like tissues showed that PI3K inhibitors may inhibit multiple aspects of SSc disease progression in dermal fibroblasts.

Disclosure: D. **Popovich**, None; **T. Abel**, None; **N. Kosarek**, None; **M. Espinoza**, None; **R. Parvizi**, None; **J. Garlick**, None; **M. Whitfield**, Celdara Medical, LLC, 2, 5, 8, 12, Scientific Founder, Bristol Myers Squibb, 2, 5, 6, Acceleron, 2, Corbus Pharmaceuticals, 2, 6, Abbvie, 6, Kadmon, 6.

Abstract Number: 0556

Investigating the Heterogeneity of Skin Macrophages in Systemic Scleroderma

Hadijat Makinde[1], Salina Dominguez[1], Monique Hinchcliff[2], Deborah Winter[3] and Harris Perlman[1], [1]Northwestern University, Chicago, IL, [2]Yale School of Medicine, Westport, CT, [3]Northwestern University Division of Rheumatology, Chicago, IL

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Background/Purpose: The etiology and pathogenesis of systemic sclerosis (SSc) are poorly understood; however, an increasing body of evidence supports an early inflammatory phase that precedes fibrosis. Macrophages have been implicated in the inflammatory process that leads to the reorganization of the extracellular matrix (ECM) leading to the development of end-organ fibrosis. Macrophages also contribute to disease progression by production of reactive oxygen species, matrix-degrading enzymes, as well as by antigen presentation. However, macrophages are heterogeneous thus individual subsets may have differential functions in a tissue- and disease-specific context. Here we evaluate the transcriptional heterogeneity of macrophages present in the skin of SSc patients.

Methods: $CD45^+$ immune cells were sorted from skin biopsies using multiparameter fluorescence-activated cell sorting (FACS) from early diffuse cutaneous (dc) SSc patients (630 cells from 5 patients). Cellular Indexing of Transcriptomes and Epitopes by Sequencing (CITE-Seq) was performed, and samples were processed using the 10X Genomics 3' v3.0 pipeline and analyzed using the Seurat package with modifications when needed.

Results: Six individual clusters were resolved from immune cells isolated from SSc skin. Differentially expressed genes between clusters identified at least two distinct macrophage subsets that comprise one-third of all immune cells, including a monocyte-derived macrophage subset (LYV^+ $CD68^+$; 20% of all cells) and Langerhans cells ($CD1a^+$ $CD207^+$; 13% of all cells) that are associated with distinct pathways. Macrophage subsets identified by RNA expression were confirmed via antibody-derived tags and show heterogeneity in their gene and protein expression of CD11b, CD11c, and CCR2, among other key identifying features, that directly relate to their functional capabilities. These macrophage subsets also displayed differences in their expression of HLA-antigens, indicating distinct antigen presentation capabilities.

Conclusion: These data show for the first time that macrophages within fibrotic skin of patients with SSc come in many flavors corresponding to distinct functions. This highlights the importance of precisely identifying immune cells within an affected organ and their corresponding mechanisms contributing to the pathogenesis of SSc. Only then can we target specific immune cell populations that drive the inflammatory process, which may be more beneficial than the current approach of broadly targeting immune cells during disease progression. Future directions include interrogating how these macrophage subsets differ compared to those found in the skin of control patients as well as delving into potentially pathogenic lymphocytic populations.

Disclosure: H. Makinde, None; **S. Dominguez**, None; **M. Hinchcliff**, None; **D. Winter**, None; **H. Perlman**, Kiniksa, 1, 2.

Abstract Number: 0557

The Beta Secretase BACE1 Induces Systemic Sclerosis (SSc) Fibroblast Activation Through the Regulation of the Pro-Fibrotic Notch Signalling Pathway

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Background/Purpose: Extensive work in the Alzheimer's field has shown BACE1 plays an important role in amyloid beta processing. Additionally, there is evidence showing BACE1 regulating Notch signalling and disrupting angiogenesis in the context of Alzheimer's. Given the known role of Notch signalling and disrupted angiogenesis in Systemic Sclerosis (SSc), in this study we investigated the role of BACE1 in the profibrotic phenotype of dermal fibroblasts from SSc skin.

Methods: Dermal fibroblasts were obtained from full thickness skin biopsies from early-diffuse cutaneous SSc patients. Protein was collected from the fibroblasts and BACE1 protein levels were assessed by western blot. SSc patient fibroblasts were treated with the BACE1 inhibitor M3.

Results: BACE1 protein levels were found to be expressed at significantly higher levels in SSc patient fibroblasts compared to healthy controls (1.9-Fold). Inhibition of BACE1 with the specific small molecule inhibitor led to reduced myofibroblast marker (Collagen type 1, alpha smooth muscle actin and CTGF) expression in SSc fibroblasts. Further analysis found inhibition of BACE1 could block the morphogen (TGF-b, Sonic hedgehog and Wnt-3a) mediated fibroblast activation. The BACE1 inhibitor reduced alpha smooth muscle actin expression in TGF-b stimulated fibroblasts by 50%, in sonic hedgehog stimulated cells by 65% and in Wnt-3a stimulated cells by 35%. Finally, treatment of SSc fibroblasts with the BACE1 small molecule inhibitor resulted in reduced expression of the active form of Notch1 and downstream targets Hes1 and GLI2, suggesting BACE1 contributes to SSc fibroblast phenotype through the activation of Notch signalling pathway.

Conclusion: We have identified a novel role for BACE1 in SSc myofibroblast activation through Notch1. This further strengthen the important role Notch signalling plays in SSc. Furthermore, this study highlights BACE1 as a potential novel antifibrotic target for therapeutic intervention which could be investigated with a number of BACE1 inhibitors currently in clinical trials for Alzheimer's.

Disclosure: C. Wasson, None; **E. Clavane**, None; **R. Ross**, None; **P. Meakin**, None; **F. Del Galdo**, Boehringer-Ingelheim, 1, 2, 5, 6, Astra-Zeneca, 1, 2, 5, 6, Jannsenn, 6, Chemomab, 2, 5, Capella Biosciences, 2, 5, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 0558

The Systemic Sclerosis (SSc) Risk Gene A20 (TNFAIP3) and Its Repressor DREAM Determine Susceptibility to Fibrosis

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SESSION INFORMATION

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Background/Purpose: The ubiquitin-editing enzyme A20, encoded by TNFAIP3, is genetically implicated in autoimmune and inflammatory diseases. A20 plays a pivotal role in regulating inflammatory cellular pathways, and is tightly regulated by the downstream regulatory element antagonist modulator (DREAM) and other factors. Variants of TNFAIP3 are also associated with SSc and lung fibrosis in multi-ethnic cohorts. However, it remains unclear how genetic factors contribute to pathogenesis, and which cell types drive pathology due to SSc-specific genetic alterations. We therefore characterized the expression, function and role of A20 and DREAM in SSc and disease models

Methods: A20 and DREAM were measured in transcriptome datasets, skin and lung biopsies, and skin fibroblasts from SSc patients and healthy controls. The hypothesis that loss of A20 might play a direct pathogenic role in fibrosis was tested in A20 haploinsufficient mice that have reduced A20 comparable to humans harboring A20 risk alleles; and in mice with fibroblasts-specific deletion of A20 or DREAM. The role of A20 in myofibroblast transition was directly examined in skin and lung fibroblasts, dermal vascular endothelial cells (DMVE), adipose-derived stem cells (ADSC) and preadipocytes. A selective AdipoR1/R2 agonist was used to modulate A20 expression in skin fibroblasts and *in vivo* models of dermal fibrosis

Results: Unbiased transcriptome analysis of skin and lung biopsies indicated decreased A20 in SSc, whereas the negative A20 regulator DREAM was significantly elevated and anti-correlated with A20. In a variety of human and mouse mesenchymal cells, A20 potently inhibited profibrotic gene expression, myofibroblast transition and other fibrotic responses via blocking multiple SSc-linked signaling pathways. Mice haploinsufficient for A20, or harboring fibroblasts-specific A20 deletion, recapitulated major pathological and genomic features of SSc. In contrast, mice lacking DREAM (and showing elevated A20 expression) were protected from fibrosis. AdipoRon, an orally active small molecule targeting cellular adiponectin receptors, stimulated A20 expression *in vitro* in wild type but not in A20-deficient fibroblasts, potentially accounting for its anti-fibrotic activity

Conclusion: We provide first evidence that in addition to its well-established role in regulating inflammatory responses, A20 has a novel function in mitigating fibroblast activation. Together with DREAM, A20 thus constitutes a critical cell-intrinsic regulatory circuit governing fibrotic processes. Dysregulation of this circuit might be implicated in SSc pathogenesis, and represents a druggable target for fibrosis therapy

Disclosure: S. Bale, None; **W. Wang**, None; **R. Marangoni**, None; **E. Herzog**, None; **B. Schock**, None; **S. Bhattacharyya**, None; **V. John**, None.

Abstract Number: 0559

Targeting NNMT as a Novel Metabolic Approach to Treat Systemic Sclerosis

M.Asif Amin[1], Bo Shi[2], Pei-Suen Tsou[1], Swarna Bale[1], Phillip Campbell[1], Mikel Gurrea-Rubio[1], Mark Eckert[3], Ernst Lengyel[3], Johann Gudjonsson[4] and Varga John[1], [1]University of Michigan, Ann Arbor, MI, [2]Nothwestern university, Chicago, IL, [3]University of chicago, Chicago, IL, [4]Department of Dermatology, University of Michigan, Ann Arbor, MI

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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Fibrosis, the hallmark of systemic sclerosis (SSc), is associated with metabolic and epigenetic alterations that are incompletely characterized. Our laboratory had previously implicated dysregulated nicotinamide adenine dinucleotide (NAD) metabolism associated with upregulation of the NAD hydrolase CD38 in SSc *pathogenesis*. Nicotinamide N-methyl transferase (NNMT) is a cellular enzyme with key roles in NAD homeostasis via de novo NAD generation through the salvage pathway. By irreversibly methylating the NAD precursor nicotinamide (NAM) and reducing its availability for NAD salvage synthesis while also depleting the universal methyl donor S-adenosylmethionine, NNMT uniquely links cellular energy consumption and epigenetic modifications. Moreover, NNMT promotes stromal cancer-associated fibroblast differentiation, and elevated NNMT is implicated in metastasis. In this study, we sought to examine the expression and role of NNMT in SSc fibrosis.

Methods: Gene expression in SSc skin biopsies was determined by bulk and single cell RNA-Seq and immunolabelling. To investigate the impact of NNMT, human skin fibroblasts in cultures were incubated with transforming forming growth factor (TGF-β) and NNMT inhibitors followed by PCR, immunolabelling, immunofluorescence (IF), NAD assays and migration assays using Incucyte™ Live Cell Imaging. Genomewide transcript level changes and chromatin remodeling were determined.

Results: NNMT expression is significantly elevated in SSc skin biopsies, and in explanted skin fibroblasts. NNMT mRNA levels in the skin are positively associated with TGF-β activity in multiple SSc datasets. Moreover, NNMT levels are strongly associated with CD38 levels in SSc skin biopsies, and a combined gene score for NNMT plus CD38 robustly correlated with the skin score (MRSS). The number of NNMT-immunopositive interstitial cells was elevated in both papillary and reticular dermis from SSc patients. TGF-β strongly increased the expression of NNMT in normal fibroblasts. Targeted pharmacological inhibition of NNMT markedly attenuated TGF-β-induced cellular fibrotic responses.

Conclusion: NNMT, which represents a nexus linking cellular energy metabolism and epigenetic chromosome modeling, is highly expressed in explanted SSc fibroblasts and SSc skin biopsies. NNMT is inducible by TGF-β and directly contributes to the induction of fibrotic cellular responses, while its pharmacological blockade mitigates fibrosis *in vitro*. The profibrotic effects of NNMT potentially implicate altered NAD metabolism as well as changes in DNA methylation and related epigenetic mechanisms. Targeting NNMT with selective inhibitors therefore represents a novel therapeutic approach for fibrotic diseases such as SSc.

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Abstract Number: 0560

Effectiveness, Safety, Quality of Life and Patient Satisfaction with Tofacitinib Treatment in Adult Patients with Rheumatoid Arthritis Under Routine Clinical Care: Second Interim Analysis of a German Non-Interventional, Prospective, Multi-Center Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Tofacitinib is a Janus kinase inhibitor, which is orally applied and is approved for rheumatoid arthritis among other indications. ESCALATE-RA is the first prospective, non-interventional study with tofacitinib in Germany. The first patient was enrolled end of 2017 and results of the first interim analysis were published in 2020.

Table. 1. Demographics, Clinical Data at Baseline and Tofacitinib Treatment Persistence (M12- and M24-population).

	M12 (N=862)	M24 (N=466)
	n/n_{tot} (%)	n/n_{tot} (%)
Gender		
Female	656/862 (76.1%)	360/466 (77.3%)
Smoking status		
Smoker	197/840 (23.5%)	98/448 (21.9%)
Ex-smoker	165/840 (19.6%)	82/448 (18.3%)
Non-smoker	478/840 (56.9%)	268/448 (59.8%)
Prognostic factors		
Moderate to severe RA	816/861 (94.8%)	448/466 (96.1%)
ACPA positive	460/856 (53.7%)	252/465 (54.2%)
Rheumatoid factor positive	539/861 (62.6%)	286/466 (61.4%)
Treatment persistence after 1 year (M12), after 2 years (M24) respectively (Kaplan-Meier 95% CI)	56% (53%;59%)	53% (48%;57%)
Time to 1st Treatment Escalation (days)	303	526

ACPA, Anti-citrullinated protein antibodies; CI, confidence interval; N, Number of patients with M12-/M24-visit; n_{tot}, Number of patients with available data; RA, rheumatoid arthritis

Table. 2. Disease Activity, Functional Ability, Health-related Quality of Life, Patient Satisfaction and Safety (M12- and M24-population).

	M12 (N=862)	M24 (N=466)
Disease Activity		
DAS28-4 (ESR)		
BL Mean (SD), (n_{tot})	4.71 (1.31), (492)	4.64 (1.28), (253)
M12 / M24 Mean (SD), (n_{tot})	2.94 (1.17), (467)	3.01 (1.14), (202)
Mean change BL to M12 / M24 (SD), (n_{tot})	-1.70 (1.48), (398)	-1.55 (1.48), (163)
DAS28-4 (CRP)		
BL Mean (SD), (n_{tot})	4.36 (1.23), (484)	4.29 (1.16), (252)
M12 / M24 Mean (SD), (n_{tot})	2.58 (1.03), (456)	2.61 (1.00), (187)
Mean change BL to M12 / M24 (SD), (n_{tot})	-1.78 (1.42), (403)	-1.62 (1.36), (158)
Functional Ability		
Morning Stiffness (min)		
BL Mean (SD), (n_{tot})	72.57 (70.70), (506)	67.59 (66.67), (275)
M12 / M24 Mean (SD), (n_{tot})	42.85 (38.97), (297)	36.40 (35.65), (125)
Mean change BL to M12 / M24 (SD), (n_{tot})	-38.56 (132.06), (268)	-23.59 (62.07), (116)
Functional Ability Questionnaire Hannover (FFbH)		
BL Mean (SD), (n_{tot})	61.81 (22.99), (620)	62.93 (21.72), (337)
M12 / M24 Mean (SD), (n_{tot})	70.80 (22.99), (523)	72.61 (22.90), (220)
Mean change BL to M12 / M24 (SD), (n_{tot})	8.10 (15.96), (521)	7.55 (17.03), (219)
FFbH Remission Rate (FFbH >83%) to M12 / M24 n/n_{tot} (%)	185/523 (35.4%)	89/220 (40.5%)
Health-related Quality of Life		
EuroQoL EQ-5D-3L Total Score		
BL Mean (SD), (n_{tot})	0.56 (0.21), (811)	0.59 (0.19), (331)
M12 / M24 Mean (SD), (n_{tot})	0.69 (0.17), (517)	0.71 (0.19), (216)
Mean change BL to M12 / M24 (SD), (n_{tot})	0.13 (0.21), (515)	0.12 (0.19), (215)
FACIT Fatigue Scale		
BL Mean (SD), (n_{tot})	29.70 (11.27), (603)	30.22 (10.68), (330)
M12 / M24 Mean (SD), (n_{tot})	35.78 (10.97), (506)	37.19 (11.16), (216)
Mean change BL to M12 / M24 (SD), (n_{tot})	5.78 (10.21), (504)	5.75 (8.76), (215)
Patient Satisfaction at M12 / M24, n/n_{tot} (%)		
Extremely dissatisfied	35/523 (6.7%)	10/219 (4.6%)
Dissatisfied	17/523 (3.3%)	6/219 (2.7%)
Neither satisfied nor dissatisfied	52/523 (9.9%)	18/219 (8.2%)
Satisfied	293/523 (56.0%)	112/219 (51.1%)
Extremely Satisfied	126/523 (24.1%)	73/219 (33.3%)
Safety	**SAS M12 (N=865) n/N (%)**	**SAS M24 (N=466) n/N (%)**
Adverse Events* (Patients)		
with AEs	579/865 (66.9%)	344/466 (73.8%)
with tofacitinib related AE	389/865 (45.0%)	237/466 (50.9%)
discontinued study drug due to AE but continued study	244/865 (28.2%)	154/466 (33.0%)
with dose reduction or temporary discontinuation due to AE	138/865 (16.0%)	86/466 (18.5%)
Most common AEs related to Tofacitinib (Patients)		
with insufficient efficacy/lack of efficacy/loss of efficacy	192/865 (22.2%)	117/466 (25.1%)
with nausea	26/865 (3.0%)	16/466 (3.4%)
with herpes zoster infection	18/865 (2.1%)	17/466 (3.6%)
with headache	16/865 (1.8%)	7/466 (1.5%)
Deaths		
All causalities	2/865 (0.2%)	0/466 (0.0%)
Treatment related according to the assessment of the HCP	0/865 (0.0%)	0/466 (0.0%)

*An AE is any untoward medical occurrence in a patient administered a medicinal product
AE, adverse event; BL, baseline; CRP, C-reactive protein; DAS28-4, disease activity score in 28 joints based on 4 variables; ESR, erythrocyte sedimentation rate; FACIT, Functional Assessment of Chronic Illness Therapy; FFbH, Functional Ability Questionnaire Hannover; M12/M24, visit after 12/24 months of treatment; HCP, healthcare professional; N, Number of patients with M12/M24 visit; n_{tot}, Number of patients with available data; SAS, Safety Analysis Set; SD, standard deviation

Methods: The enrollment of the planned 1500 patients takes place Germany-wide (87 recruiting sites as of 08 May 2021). Adult patients eligible for tofacitinib therapy are documented quarterly in a standardized manner from the first tofacitinib intake up to 24 months and remain within the study even after switching to another DMARD or combination of DMARDs. This second interim analysis (cut-off date 29 Jan 2021) describes patients, who reached visit M12 after 12 months as well as patients who reached the final visit M24 after 24 months. Missing observations were not taken into account. Since this is an ongoing study, small changes in numbers may occur after the final data quality checks.

Results: At data cut-off, 1227 patients were enrolled, 862 (70.3%) patients reached M12 and 466 (38.0%) patients reached M24. In both populations mean age was 59 years, approx. three quarters of patients were female and over 60% were seropositive. 52.5% of M12- and 54.7% of M24-population were treated with a bDMARD immediately prior to enrollment. Tofacitinib treatment persistence was 56% after 1 year in M12-population and 53% after 2 years in M24-population (Table 1).

A reduction of disease activity and morning stiffness was observed in both populations over time while functional ability according to FFbH (Functional Ability Questionnaire Hannover, German short questionnaire for the assessment of patient functional capacity in the context of basic everyday activities (range: 0-100% functional capacity) [1]) increased in both populations. The mean change from BL of disease activity and morning stiffness as well as functional ability was somewhat more pronounced in M12- than in M24-population. Functional remission was achieved by more patients in the M24- (40.5%) than in M12-population (35.4%). Furthermore, patients in both populations showed a comparable improvement in self-reported quality of life and the majority of patients in both populations were satisfied or extremely satisfied with tofacitinib treatment (Table 2).

AEs occurred in 66.9% (M12-population), and 73.8% (M24-population) of patients, respectively. Approx. half of the M12- as well as the M24-population had AEs related to tofacitinib, less than one-third of patients in both populations discontinued study drug due to AE but remained in the study. Two deaths were reported in M12-population (Table 2).

Conclusion: This second interim analysis shows a good effectiveness and an increased quality of life with tofacitinib therapy. Safety results were consistent with the known safety profile of tofacitinib. These results are in line with those of the first interim analysis.

[1] Lautenschläger J, Mau W, Kohlmann T, Raspe HH, Struve F, Brückle W, et al. [Comparative evaluation of a German version of the Health Assessment Questionnaire and the Hannover Functional Capacity Questionnaire]. [Article in German] Z Rheumatol 1997;56:144–55

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Abstract Number: 0561

Enhancing the Identification of Rheumatoid Arthritis-Associated Interstitial Lung Disease in Electronic Health Records Through Text Mining of Computerized Tomography Reports

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) is an extraarticular manifestation of RA that leads to increased morbidity and mortality. Algorithms incorporating multiple diagnostic and procedure codes as well as treating provider specialty have been developed to identify RA-ILD patients in administrative data sources. Positive predictive values (PPV) for such algorithms range between 70-85%. In this study, we adapted these RA-ILD algorithms to electronic health record (EHR) data and used text mining to capture ILD terms within chest CT reports.

Methods: We identified possible RA-ILD cases at a large academic medical center by searching the EHR for patients with at least one ICD-9/10 or SNOMED Clinical Terms code for both RA and ILD. Detailed medical record review was performed to validate RA-ILD diagnoses (reference standard). When available, chest CT images were separately reviewed by an expert in ILD for the presence/absence of ILD, blinded to the clinical data. We applied previously validated RA-ILD administrative algorithms with various combinations of ICD-9/10 codes for ILD, CPT codes for chest CT or lung biopsy, and provider specialty (pulmonology or rheumatology). Subsequently, we used text mining by automated regular expressions to identify ILD related terms (e.g. ground glass, honeycombing) and variations of these terms in chest CT reports within the EHR. We tested the performance of the aforementioned algorithms with/without these ILD terms.

Results: Of the 114 possible RA-ILD cases, 77 were validated by record review (**Table 1)**. Patients were on average 67.4 years old and most commonly white (82.3%), female (66.7%), and seropositive (82.6%). Among the validated

Table 1. Patient characteristics

	Overall cohort*	Validated RA-ILD cases
Number	114	77
Age, years	67.4	68.7
Female sex	76/114 (66.7%)	46/77 (59.7%)
White race	93/113 (82.3%)	61/77 (79.2%)
Seropositive[x]	81/98 (82.6%)	60/70 (85.7%)
Current/former smoker	54/97 (55.7%)	38/66 (57.6%)

Values mean (SD) or n (%) of non-missing
** patients with ≥1 ICD-9/10 code for both RA and ILD*
[x] As determined by lab values when available, or provider documentation when labs not available

Table 2. Performance of RA-ILD algorithms with and without text mining for ILD terms from CT reports

	Algorithm search criteria*	PPV (95% CI)	RA-ILD cases identified, n (% referent to algorithm 1)	Change in PPV with text phrase searching
Administrative RA-ILD algorithms				
Algorithm 1	≥ 1 ICD for ILD	70.6 (61.1, 79.0)	77 (100)	n/a
Algorithm 2	≥ 1 ICD for ILD plus specialty code	83.3 (72.7, 91.1)	60 (77.9)	n/a
Algorithm 3	≥ 1 ICD for ILD plus specialty code or CT/biopsy	78.1 (68.5, 85.9)	75 (97.4)	n/a
Algorithm 4	≥ 2 ICD for ILD	85.5 (75.6, 92.5)	65 (84.4)	n/a
Algorithm 5	≥ 2 ICD for ILD plus specialty code	90.5 (80.4, 96.4)	57 (74.0)	n/a
Algorithm 6	≥ 2 ICD for ILD plus specialty code or CT/biopsy	87.7 (77.9, 94.2)	64 (83.1)	n/a
Algorithms plus ILD term searching of CT reports				
Algorithm 1T	Algorithm 1 plus ILD term search^T	84.2 (68.7, 94.0)	32 (41.6)	13.6
Algorithm 2T	Algorithm 2 plus ILD term search^T	95.8 (78.9, 99.9)	23 (29.9)	12.5
Algorithm 3T	Algorithm 3 plus ILD term search^T	88.9 (73.9, 96.9)	32 (41.6)	10.8
Algorithm 4T	Algorithm 4 plus ILD term search^T	96.3 (81.0, 99.9)	26 (33.8)	10.8
Algorithm 5T	Algorithm 5 plus ILD term search^T	95.8 (78.9, 99.9)	23 (29.9)	5.3
Algorithm 6T	Algorithm 6 plus ILD term search^T	96.3 (81.0, 99.9)	26 (33.8)	8.6

** All algorithms additionally required ≥1 ICD or SNOMED CT code for rheumatoid arthritis*
T: search of CT reports for ≥1 of the following: 'honeycomb', 'honey comb', 'interstitial lung disease', 'pulmonary fibrosis', 'ground glass opacit', 'groundglass', 'reticular opacit', 'reticulation', 'rheumatoid lung'
Abbreviations: ICD = International Classification of Diseases; ILD = interstitial lung disease; CT = computed tomography; PPV = positive predictive value; 95% CI = 95% confidence interval; n/a = not applicable

RA-ILD cases, 56 had CT images available with 50 expertly read as RA-ILD (5 indeterminate). Administrative algorithms (Algorithms 1-6) had positive predictive values (PPVs) for RA-ILD ranging from 70.6 to 90.5% (**Table 2**). Algorithm 5 (≥2 ICD for ILD plus specialty code) had the highest PPV, but identified fewer RA-ILD cases (57/77). The addition of ILD terms extracted through text mining increased the PPV compared to similar administrative algorithms by 5-13%. Notably, adding an ILD term from chest CT to the simplest administrative algorithm (Algorithm 1T) yielded a PPV similar to the most complex administrative algorithms (Algorithms 5 and 6). Fewer RA-ILD cases were identified with ILD term searching (range 23 to 32), since many patients did not have available CT reports. Findings were similar in sensitivity analyses that considered expert read of available CTs the reference standard.

Conclusion: An ILD algorithm initially derived and validated in administrative claims data had similarly high validity when applied to EHR data. Incorporating ILD related terms from chest CT reports substantially increased the PPV, but reduced sensitivity. Declines in sensitivity due to the unavailability of CT reports may be attenuated in integrated health care systems and as data sharing across EHRs improves. Our findings demonstrate how existing administrative algorithms can be improved to better identify RA-ILD for comparative effectiveness and outcomes research that utilizes EHRs.

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Abstract Number: 0562

Inpatient Epidemiology and Resource Utilization of Ankylosing Spondylitis: National Inpatient Sample 2018

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Little is known about inpatient epidemiology, economic burden and resource utilization of patients with ankylosing spondylitis (AS). The current study aims to describe those characteristics using a nationwide database.

Methods: Patients with AS were identified from the National Inpatient Sample (NIS), the largest inpatient database in the United States (US) consisting of over 4,000 non-federal acute care hospitals, using ICD-10 CM codes. The rest of patients in the database without diagnostic codes for AS were used as comparators. Data on demographics, reasons for hospitalization, length of stay, mortality, morbidity and total hospitalization charges were extracted and compared between patients with and without AS. A multivariate logistic regression model was constructed to adjust for confounders. All analyzed data was extracted from the database of the year 2018.

Results: A total of 19,130 admissions with AS were identified. The inpatient prevalence of AS was 53.9 cases per 100,000 admissions. Sepsis (27.4%), hip and knee arthroplasty (18.8%), pneumonia (7.5%), acute kidney injury (6.8%) and non-ST elevated myocardial infarction (6.2%) were the most common reasons for hospitalization. After adjusting for potential confounders, hospitalizations among patients with AS were significantly associated with longer length of stay (0.37 more days; 95% confidence interval (CI), 0.44 – 0.89) and risk for admission to intensive care unit with adjusted odds ratio (aOR) of 1.23 (95% CI, 1.11 – 1.37). Other inpatient outcomes, including inpatient mortality, shock and multiorgan failure were not significantly different between patients with and without AS. Hospitalizations of patients with AS were associated with higher cost as demonstrated by an adjusted additional mean of $4,685 (95% CI, $3,715 - $5,655) for total hospital cost and an adjusted additional mean of $19,097 (95% CI, $12,675 – $25,519) for total hospitalization charges when compared to patients without AS.

Conclusion: Inpatient prevalence of AS was higher than what would be expected from prevalence in general population. Infection and arthroplasty were the main reasons for the need for inpatient care. Hospitalizations of patients with AS were associated with longer length of stay, need for admission to ICU and cost.

Disclosure: P. Ungprasert, None; **T. Chaikijurajai**, None; **K. Wijarnpreecha**, None; **P. Kroner**, None.

Abstract Number: 0563

Validating the FRAX Score in a US Population-Based Study of Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Background/Purpose: The FRAX tool, launched by the World Health Organization Collaborating Centre at the University of Sheffield in 2008 (https://www.sheffield.ac.uk/FRAX/), is widely used to quickly and reliably estimate an individual's fracture risk, outputting the ten-year probability of major osteoporotic fracture (thoracic/lumbar vertebra, proximal femur, distal forearm, or proximal humerus) and the ten-year probability of hip fracture. The FRAX algorithm accounts for the influence of several risk factors, including rheumatoid arthritis (RA), as individuals with RA are known have an excess burden of fractures. However, the use of FRAX specifically within RA populations to estimate fracture risk has not been widely studied. Therefore, the purpose of this study was to determine the accuracy of FRAX risk predictions for US individuals with RA.

Methods: In this retrospective cohort study, all patients aged 40-90 years within a geographically defined region who fulfilled the 1987 American College of Rheumatology criteria for RA from 1980 to 2007 were identified and followed until death, migration, or last medical record review. Each RA patient was matched 1:1 on age and sex to a patient of the same region without RA. The date of RA criteria fulfillment served as the baseline date for RA patients and matched subjects. Ten-year predictions for major osteoporotic and hip fractures were estimated using the FRAX tool.

Table 1. Comparison of observed and predicted fracture risk in RA and non-RA patients

Subgroup	N		Fractures*		SIR (95% CI)
			Observed	Predicted	
RA	662	*Osteoporotic:*	76	67.0	1.13 (0.91-1.42)
		Hip:	21	23.3	0.90 (0.59-1.38)
Males	220	*Osteoporotic:*	20	15.8	1.27 (0.82-1.97)
		Hip:	4	5.0	0.80 (0.30-2.12)
Females	442	*Osteoporotic:*	56	51.3	1.09 (0.84-1.42)
		Hip:	17	18.2	0.93 (0.58-1.50)
Age 40-59	334	*Osteoporotic:*	20	17.2	1.16 (0.75-1.80)
		Hip:	2	2.0	1.01 (0.25-4.02)
Age 60-79	270	*Osteoporotic:*	44	37.2	1.18 (0.88-1.59)
		Hip:	14	13.8	1.01 (0.60-1.71)
Age 80+	58	*Osteoporotic:*	12	12.6	0.95 (0.54-1.67)
		Hip:	5	7.5	0.67 (0.28-1.61)
Non-RA	658	*Osteoporotic:*	46	40.5	1.14 (0.85-1.52)
		Hip:	10	10.1	0.99 (0.53-1.84)
Males	218	*Osteoporotic:*	6	8.8	0.68 (0.31-1.52)
		Hip:	1	1.9	0.54 (0.08-3.82)
Females	440	*Osteoporotic:*	40	31.7	1.26 (0.92-1.72)
		Hip:	9	8.2	1.09 (0.57-2.10)
Age 40-59	339	*Osteoporotic:*	9	10.6	0.85 (0.44-1.63)
		Hip:	1	0.8	1.26 (0.18-8.92)
Age 60-79	265	*Osteoporotic:*	25	22.8	1.10 (0.74-1.62)
		Hip:	6	5.9	1.01 (0.45-2.25)
Age 80+	54	*Osteoporotic:*	12	7.0	1.70 (0.97-3.00)
		Hip:	3	3.4	0.89 (0.29-2.76)

*Number of patients with a fracture

FRAX prediction scores (without bone mineral density) were calculated from patient age, sex, body mass index, and the following dichotomous risk factors: RA, previous fracture, secondary osteoporosis, glucocorticoid use, smoking status, and alcohol use. Fractures were ascertained through follow-up, truncated at 10 years. Standardized incidence ratios (SIR) and 95% confidence intervals (CI) were calculated to compare observed and predicted fractures.

Results: The study included 662 RA patients and 658 non-RA comparators. RA and non-RA subjects were predominantly white females (67% female; RA: 95% white, non-RA: 94% white) with a mean age of 60.6 and 60.5 years at baseline, respectively. Individuals with RA had increased occurrence of all other dichotomous risk factors compared to non-RA comparators, with the exception of previous fractures, which was similar between RA and non-RA groups. Among RA patients, 76 major osteoporotic and 21 hip fractures were observed during follow-up (median follow-up: 9.7 years, IQR: 5.7, 10.0 years) compared to the predicted 67.0 major osteoporotic fractures (SIR: 1.13, 95% CI: 0.91-1.42) and 23.3 hip fractures (SIR: 0.90, 95% CI: 0.59-1.38). The observed and predicted major osteoporotic and hip fracture risks were similar for RA and non-RA patients, with no significant differences among sex and age subgroups. For non-RA patients over the age of 80 years, the observed risk for major osteoporotic fracture was slightly elevated (SIR: 1.70, 95% CI: 0.97-3.00), but this difference did not reach significance.

Conclusion: The findings of this study support that the FRAX tool is an accurate method for estimating major osteoporotic and hip fracture risk in individuals with RA.

Disclosure: M. Peterson, None; **C. Crowson**, None; **E. Myasoedova**, None; **S. Amin**, None; **J. Davis**, Pfizer, 5; **S. Achenbach**, None; **S. Kholsa**, None; **E. Atkinson**, None.

Abstract Number: 0564

Associations of Sinusitis, Pharyngitis, and Respiratory Tract Disease Burden with Incident Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Increasing evidence implicates respiratory mucosa in the pathogenesis of rheumatoid arthritis (RA). However, individual respiratory tract diseases, especially of the upper airways, sinuses, and pharynx, have remained relatively understudied for RA risk. We aimed to determine whether specific respiratory tract diseases are associated with rheumatoid arthritis RA development.

Methods: This case-control study was performed within a large, single center biobank. We matched newly diagnosed RA cases to three controls on age, sex, and electronic health record (EHR) history. We identified RA using a validated algorithm incorporating diagnosis codes, medications, and natural language processing, and then confirmed cases by medical record review. We confirmed date of RA diagnosis by medical record review and obtained RA serostatus from clinical laboratory results. "Seropositive" RA included positivity for rheumatoid factor and/or anti-citrullinated protein antibodies. Respiratory tract disease exposure required one inpatient or two outpatient codes two years before index date of RA or matched date (mean positive predictive value 86%). We obtained covariates including

Table 1. Associations between preceding respiratory tract diseases (at least two years before index date) and incident RA

	Number (%)		Adjusted* Odds Ratio for RA (95% CI)		
Respiratory tract disease	RA cases (n=741)	Controls (n=2,223)	All RA cases (n=741)	Seropositive RA cases (n=426)**	Seronegative RA cases (n=303)
Any respiratory tract disease	346 (47)	931 (42)	1.16 (0.95,1.42)	1.14 (0.87,1.50)	1.24 (0.92,1.69)
Acute upper	171 (23)	432 (19)	1.25 (0.98,1.60)	1.24 (0.88,1.74)	1.36 (0.94,1.97)
Acute sinusitis	45 (6)	86 (4)	**1.61 (1.05,2.45)**	**1.89 (1.03,3.49)**	1.43 (0.77,2.64)
Acute pharyngitis	80 (11)	192 (9)	1.34 (0.97,1.85)	1.18 (0.75,1.85)	**1.68 (1.02,2.74)**
Chronic upper	104 (14)	286 (13)	1.18 (0.89,1.56)	1.12 (0.76,1.65)	1.30 (0.85,2.00)
Chronic sinusitis	42 (6)	68 (3)	**2.16 (1.39,3.35)**	1.55 (0.83,2.88)	**3.23 (1.65,6.32)**
Chronic rhinitis/pharyngitis	17 (2)	33 (1)	1.77 (0.95,3.27)	**2.46 (1.01,5.99)**	1.56 (0.63,3.88)
Acute lower	78 (11)	153 (7)	1.37 (0.98,1.91)	1.46 (0.94,2.28)	1.30 (0.76,2.20)
Pneumonia	38 (5)	87 (4)	1.17 (0.76,1.81)	1.00 (0.54,1.87)	1.53 (0.81,2.86)
Chronic lower	121 (16)	263 (12)	**1.32 (1.01,1.74)**	1.24 (0.85,1.81)	1.49 (0.99,2.23)
Asthma	93 (13)	193 (9)	**1.39 (1.03,1.87)**	1.35 (0.89,2.05)	1.49 (0.96,2.31)
COPD	43 (6)	83 (4)	1.35 (0.88,2.06)	1.20 (0.67,2.15)	1.55 (0.82,2.93)

BMI = body mass index, CI = confidence interval, COPD = chronic obstructive pulmonary disease, RA = rheumatoid arthritis
*Reference group was individuals with no respiratory tract disease codes prior to index date. Adjusting for age, sex, EHR history, enrollment year, race/ethnicity, education, BMI, smoking status, and pack-years. Bold values are statistically significant.
**RA cases without RA-related autoantibody test results (n=12) could not be classified by serostatus. Their n=36 matched controls were also removed from these analyses.

smoking status and pack-years from the biobank survey, supplemented by electronic health record data. Conditional logistic regression models calculated odds ratios (OR) for RA with 95% confidence intervals (CI), adjusting for potential confounders including age, sex, length of EHR history, biobank enrollment year, race/ethnicity, education, body mass index, smoking status, and smoking pack-years. We then stratified by serostatus and smoking.

Results: We identified 741 newly diagnosed RA cases and 2,223 controls (both median age 55, 76% female). In the pre-index exposure period, any respiratory tract disease was present in 47% of cases and 42% of controls. Acute sinusitis (OR 1.61, 95% CI:1.05,2.45), chronic sinusitis (OR 2.16, 95% CI:1.39,3.35), and asthma (OR 1.39, 95%

Table 2. Associations between preceding respiratory tract diseases (at least two years before index date) and incident RA, stratified by smoking pack-years

Respiratory tract disease	Nonsmokers (n=1,606)	>0 to 10 Pack-years (n=757)	>10 Pack-years (n=601)
Any respiratory tract disease	1.02 (0.77,1.34)	0.81 (0.55,1.19)	**1.52 (1.02,2.27)**
Acute upper	0.97 (0.69,1.36)	0.85 (0.53,1.37)	**1.80 (1.08,2.97)**
Acute sinusitis	1.35 (0.74,2.44)	1.19 (0.55,2.61)	1.94 (0.89,4.25)
Acute pharyngitis	0.87 (0.56,1.36)	1.04 (0.57,1.91)	**2.22 (1.10,4.50)**
Chronic upper	1.01 (0.69,1.47)	0.67 (0.37,1.23)	1.69 (0.94,3.02)
Chronic sinusitis	**1.86 (1.05, 3.29)**	0.54 (0.18,1.64)	**4.90 (1.93,12.42)**
Chronic rhinitis/pharyngitis	1.71 (0.79,3.72)	0.25 (0.03,1.95)	**
Acute lower	1.20 (0.75,1.93)	0.62 (0.30,1.32)	**2.49 (1.37,4.53)**
Pneumonia	1.07 (0.57,2.03)	0.68 (0.28,1.69)	2.14 (0.99,4.64)
Chronic lower	1.18 (0.81,1.73)	0.97 (0.56,1.69)	1.71 (0.99,2.94)
Asthma	1.23 (0.82,1.84)	1.12 (0.62,2.02)	1.54 (0.80,2.96)
COPD	1.53 (0.77,3.04)	0.55 (0.19,1.55)	**2.00 (1.06,3.77)**

BMI = body mass index, CI = confidence interval, COPD = chronic obstructive pulmonary disease, RA = rheumatoid arthritis
*Reference was individuals with no respiratory tract disease codes prior to index date. Adjusting for age, sex, EHR history, enrollment year, race/ethnicity, education, BMI. Bold values are statistically significant.
**Model did not converge due to few outcomes in the reference group

CI:1.03,1.87) were associated with increased risk of RA diagnosis (Table 1). Acute respiratory tract disease burden during the pre-index exposure period was also associated with increased RA risk (OR 1.30 per 10 diagnosis codes, 95% CI:1.08,1.55). Acute pharyngitis was associated with seronegative RA (OR 1.68, 95% CI:1.02,2.74) but not seropositive RA; chronic rhinitis/pharyngitis was associated with seropositive RA (OR 2.46, 95% CI:1.01,5.99) but not seronegative RA. Respiratory tract diseases tended towards higher associations with RA in smokers, especially >10 pack-years (OR 1.52, 95% CI:1.02,2.27; p 0.10 for interaction; Table 2).

Conclusion: We identified novel associations of acute/chronic sinusitis, pharyngitis, and acute respiratory tract disease burden with RA risk. These results suggest that the mucosal paradigm of RA pathogenesis may not only involve the lower respiratory tract, but also the upper respiratory tract.

Disclosure: V. Kronzer, None; **W. Huang**, None; **A. Zaccardelli**, None; **C. Crowson**, None; **J. Davis**, Pfizer, 5; **R. Vassallo**, Pfizer, 5, Bristol Myers Sqibb, 5, Sun Pharma, 5, Genentech, 5; **T. Doyle**, Bristol Myers Sqibb, 5, Boehringer Ingelheim, 2, Genentech, 5; **E. Losina**, None; **J. Sparks**, Bristol-Myers Squibb, 2, 5, Amgen, 5, Gilead, 2, Inova, 2, Janssen, 2, Optum, 2, Pfizer, 2.

Abstract Number: 0565

Increased Risk for Inflammatory Arthritis in Veterans with Depression or Anxiety

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Depression and anxiety are common in patients with inflammatory arthritis (IA), and have been reported as risk factors for various inflammatory diseases. The study objective was to estimate the risk of IA in patients with newly diagnosed depression or anxiety (mental health disorders [MHD]), relative to matched controls.

Methods: The MHD population consisted of veterans with ≥2 International Classification of Diseases (ICD) codes for a MHD between 1/1/2007-12/31/2019, with at least 2 years of active VA system use prior to date of their initial MHD ICD code (index date). Control group patients had no MHD ICD codes and were matched to the MHD patients on gender, age, and date of VA enrollment. Control group patients were assigned the same index date as their corresponding match. Patients were excluded if they had an ICD code for IA (rheumatoid arthritis, psoriatic arthritis, or ankylosing spondylitis) prior to their index date. The cumulative IA incidence was depicted with Kaplan-Meier analysis. Hazard ratios (HR) were adjusted by race, ethnicity, body mass index, smoking status, Charlson Comorbidity Index, and socioeconomic status.

Results: The population consisted of 1,378,462 veterans (689,231 MHD & 689,231 controls). The mean age was 61.1, and 92.5% were male. The cumulative incidence of IA increased linearly for up to 13 years after the initial MHD diagnosis (Figure). The incident rate per 1000 patient years was higher in the MHD group than the control group for all IA (2.74 vs. 1.71) and for subsets with RA (2.09 vs 1.32), PsA (0.35 vs 0.22), and AS (0.29 vs 0.16) (Table 1). The

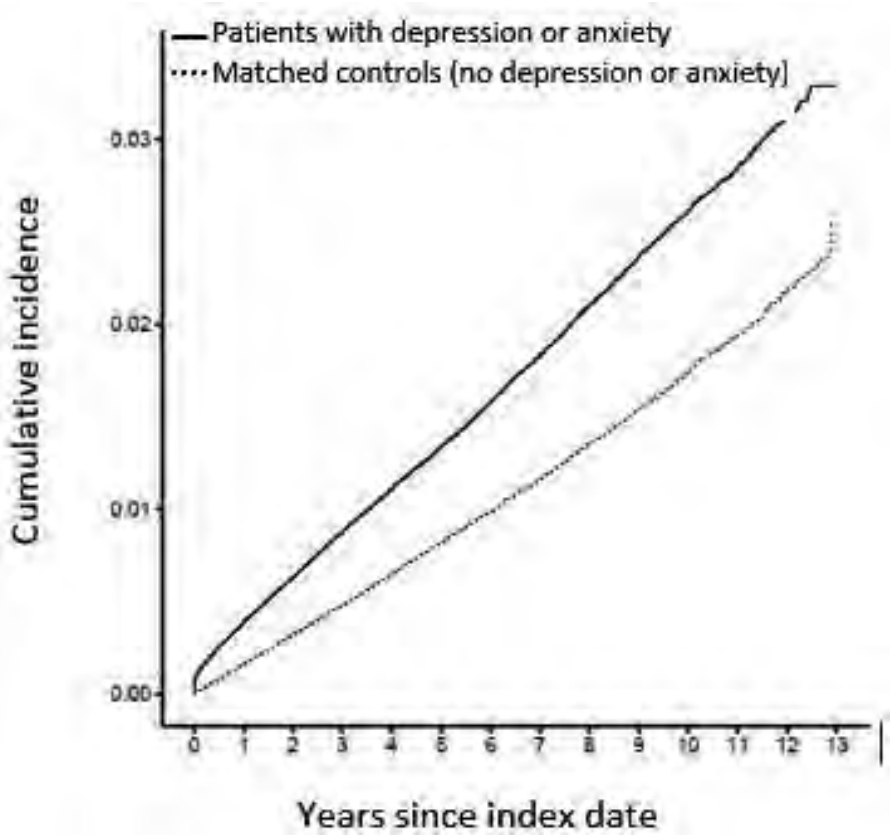

Table. Incident inflammatory arthritis in patients with and without a mental health disorder (depression or anxiety)

	MHD n=689,231	No MHD* n=689,231	MHD n=689,231	No MHD* n=689,231	MHD n=689,231	No MHD* n=689,231	MHD n=689,231	No MHD* n=689,231
Outcome	**Inflammatory arthritis****	**Inflammatory arthritis****	**Rheumatoid arthritis**	**Rheumatoid arthritis**	**Psoriatic arthritis**	**Psoriatic arthritis**	**Ankylosing spondylitis**	**Ankylosing spondylitis**
# Patients with outcome	9754	5491	7459	4247	1255	713	1040	531
Time to outcome & IR								
Mean follow-up, years (95% CIs)	5.16 (5.15, 5.17)	4.67 (4.66, 4.68)	5.17 (5.17, 5.18)	4.67 (4.67, 4.68)	5.21 (5.20, 5.21)	4.69 (4.69, 4.70)	5.21 (5.21, 5.21)	4.69 (4.69, 4.70)
Mean # years to outcome (95% CI)	3.51 (3.45, 3.57)	4.01 (3.93, 4.09)	3.49 (3.42, 3.56)	4.00 (3.91, 4.09)	3.45 (3.29, 3.62)	3.88 (3.67, 4.09)	3.76 (3.57, 3.96)	4.29 (4.02, 4.56)
Follow-up time, person-years	3,556,559	3,216,704	3,564,970	3,221,197	3,589,496	3,233,878	3,590,997	3,234,918
IR per 1000 person-years (95% CIs)	2.74 (2.69, 2.80)	1.71 (1.66, 1.75)	2.09 (2.05, 2.14)	1.32 (1.28, 1.36)	0.35 (0.33, 0.37)	0.22 (0.20, 0.24)	0.29 (0.27,0.31)	0.16 (0.15, 0.18)
HR for outcome (95% CIs)								
Unadjusted	1.61 (1.56, 1.67)	Reference	1.59 (1.54,1.66)	Reference	1.59 (1.45,1.75)	Reference	1.77 (1.60, 1.97)	Reference
+race-adjusted	1.61 (1.56, 1.67)	Reference	1.59 (1.53, 1.65)	Reference	1.62 (1.48, 1.77)	Reference	1.78 (1.60, 1.97)	Reference
+ethnicity-adjusted	1.61 (1.56, 1.67)	Reference	1.59 (1.53, 1.65)	Reference	1.61 (1.47, 1.77)	Reference	1.75 (1.58, 1.95)	Reference
+BMI-adjusted	1.61 (1.56, 1.67)	Reference	1.59 (1.53, 1.65)	Reference	1.61 (1.47, 1.77	Reference	1.76 (1.58, 1.95)	Reference
+smoking-adjusted	1.60 (1.55, 1.65)	Reference	1.58 (1.52, 1.64)	Reference	1.58 (1.44, 1.74)	Reference	1.78 (1.60, 1.98)	Reference
+CCI-adjusted	1.59 (1.54, 1.65)	Reference	1.56 (1.51, 1.63)	Reference	1.60 (1.46, 1.75	Reference	1.77 (1.60, 1.97)	Reference
+SES-adjusted	1.59 (1.54, 1.65)	Reference	1.56 (1.51, 1.63)	Reference	1.60 (1.46, 1.76)	Reference	1.77 (1.60, 1.97)	Reference

MHD = mental health disorders.*Patients without a MHD were matched to MHD patients on gender, age, and date of enrollment into the VA.
**Inflammatory arthritis includes subtypes of rheumatoid arthritis, psoriatic arthritis, and ankylosing spondylitis. IR= incident rate. HR= hazard ratio.
CCI = Charleson Comorbidity Index. SES = socioeconomic status as measure by the Area Deprivation Index

adjusted HR for IA in veterans with vs. without a MHD was 1.59 for all IA, 1.56 for RA, 1.60 for PsA, and 1.77 for AS. All comparisons between MHD and control groups yielded a p-value < 0.001.

Conclusion: Veterans with depression or anxiety have an elevated risk for developing IA. These finding may inform future efforts to identify shared risk factors and characterize the mechanistic relationships between MHD and IA.

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Abstract Number: 0566

Natural Language Processing of Electronic Health Record Notes Captures Forced Vital Capacity in Rheumatoid Arthritis-Associated Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis-interstitial lung disease (RA-ILD) has a poor long-term prognosis, including premature mortality. Longitudinal monitoring of patients in clinical and clinical trial settings includes the routine measurement of forced vital capacity (FVC) from pulmonary function tests (PFT). However, the availability of PFT data in real-world datasets is highly variable, limiting examination of this key outcome in long-term observational studies. Natural Language Processing (NLP), an artificial intelligence method, has been used to transform unstructured text from the electronic health record (EHR) to structured clinical data. We aimed to develop a NLP program to capture FVC values from EHR notes.

Methods: We identified patients in the Veterans Health Administration (VA) with RA-ILD between 2000 and 2020 by ICD-9/10 codes for RA and ILD, based on previously validated RA-ILD algorithms. We developed a NLP program to capture FVC values from all available notes from the EHR using MS SQLServer, based on a program for FEV1 values (Akgun et al. *PLoS ONE*, 2020). We identified FVC string patterns and extracted numeric values in proximity to these strings. Subsequently, we performed several processing steps to account for variability in note type and structure, related PFT output (e.g. FEV1/FVC ratio), and values copied across multiple notes. Dates were assigned to FVC values by cross referencing EHR note dates with the most recent date accompanying CPT codes for PFTs. FVC values derived by the NLP program were compared to observed FVC values recorded directly from PFT equipment and available as structured data in the VA Corporate Data Warehouse (CDW). These represent a subset of all PFTs completed in the VA due to PFT compatibility.

Results: We developed and tested the NLP program in a cohort of 7,485 patients with RA-ILD. In the VA CDW, there were 6,002 FVC values for 1,843 unique patients. The NLP program increased the yield of FVC values by >2.6-fold, extracting 15,983 FVC values for 4,849 patients. Among 3,037 date matched FVC values from NLP and CDW, mean

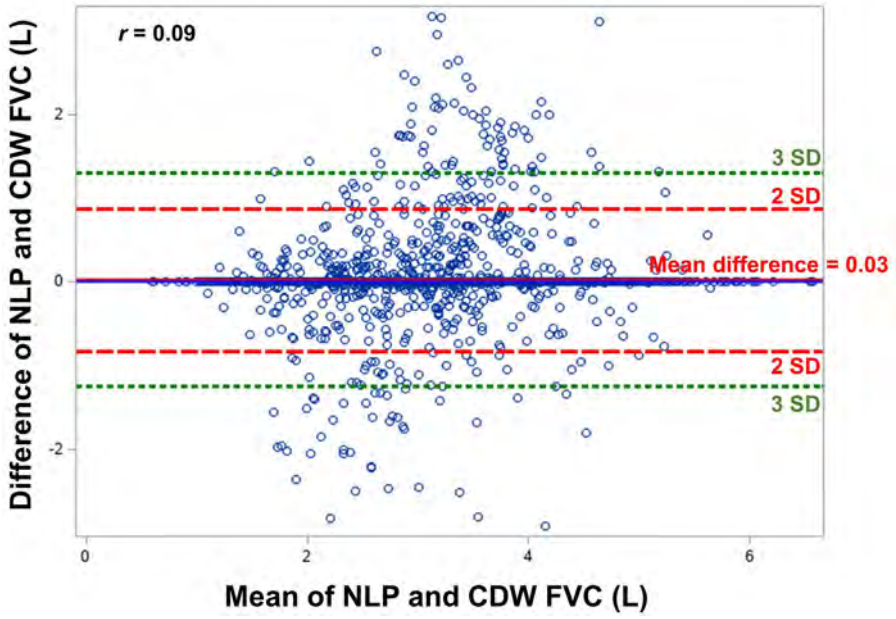

Figure 1. Bland-Altman plot comparing absolute differences in FVC values with mean FVC values. Abbreviations: CDW, Corporate Data Warehouse; FVC, forced vital capacity; NLP, natural language processing; SD, standard deviation

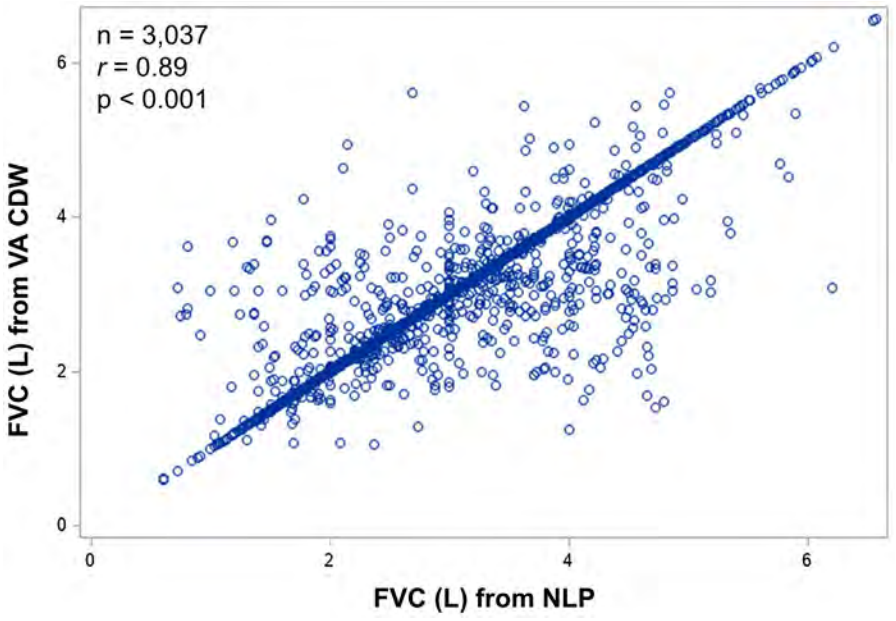

Figure 2. Scatter plot demonstrating the correlation of forced vital capacity values obtained from the natural language processing program (NLP) to values obtained from pulmonary function test equipment (VA CDW). Abbreviations: CDW, Corporate Data Warehouse; FVC, forced vital capacity; NLP, natural language processing

Table 1. Change in forced vital capacity over time in RA-ILD using data from natural language processing and PFT equipment (VA CDW).

	First FVC, L	Last FVC, L	Change in FVC, L	P value
NLP program *(n=3,325)*	3.26 (0.94)	2.96 (0.93)	-0.30 (0.86)	<0.001
VA CDW *(n=1,181)*	3.22 (0.89)	2.92 (0.89)	-0.29 (0.66)	<0.001

Values mean (SD), P value by paired t-test

Mean 5.2 years between FVC measurements in NLP and 4.8 years in CDW

Abbreviations: CDW, Corporate Data Warehouse; FVC, forced vital capacity; NLP, natural language processing; PFT; pulmonary function test; RA-ILD, rheumatoid arthritis-interstitial lung disease; VA, Veterans Affairs

(SD) FVC was 3.0 (0.9) L from both sources, and 80% of NLP values were within 0.1L of CDW values. The mean difference in FVC between NLP and CDW values was 0.03L with no systematic bias in NLP derived FVC values seen on Bland-Altman plot (**Figure 1**). NLP and CDW FVC values strongly correlated (**Figure 2**, r=0.89, p< 0.001). A total of 3,325 RA-ILD patients had at least two FVC values captured by NLP. Comparing the first and last FVC values, there was a mean decline in FVC of -0.30 (SD 0.86) L over a mean follow-up of 5.2 (SD 4.6) years (p< 0.001 by paired t-test) (**Table 1**). Similar changes in FVC (mean -0.29 [SD 0.66] L) were observed using CDW data, but this data source captured fewer RA-ILD patients (n=1,181).

Conclusion: NLP of EHR notes substantially increases the capture of longitudinal FVC values among patients with RA-ILD. These values are highly accurate compared to the gold standard of direct output from PFT equipment which may not always be available in structured format. Use of this NLP program can facilitate clinical and epidemiologic research studies in RA-ILD by capturing longitudinal changes among one of the most critical outcomes measures in RA-ILD.

Disclosure: P. **Roul**, None; **Y. Yang**, None; **D. Hershberger**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **J. Rojas**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **B. Sauer**, None; **B. England**, Boehringer-Ingelheim, 2.

Abstract Number: 0567

Determinants of Health-Related Quality of Life in Spondyloarthritis and Comparison with Chronic Low Back Pain – Results from a Nation-Wide Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Spondyloarthritis (SpA) causes pain, fatigue, stiffness, loss of physical function and impaired health-related quality of life (HRQoL).

This study aims to: 1) to compare HRQoL in patients with SpA, chronic low back pain (CLBP) and subjects with no rheumatic disease (noRMD), and 2) to evaluate determinants of HRQoL in SpA patients, in a population-based setting.

Methods: Data from EpiReumaPt, a national health survey with 10 661 adult participants, randomly selected, that were screened for rheumatic and musculoskeletal diseases (RMDs) was used. Subjects were asked about socio-demographic data, lifestyle habits, chronic non-communicable diseases and HRQoL. SpA diagnosis was based on a positive expert opinion (rheumatologist) combined with predefined criteria; SpA disease activity was also collected. CLBP was established by predefined criteria and noRMD by expert opinion. Univariate and multivariate linear regressions were performed to explore factors associated with QoL assessed by EuroQoL- 5 Dimensions 3L (EQ-5D).

Results: We included 92 SpA, 1376 CLBP and 679 with noRMD. The mean age was 48.4 years (SD=13.7) for SpA, 58.8 years (SD=14.6) for CLBP and 45.9 years (SD=15.6) for noRMD. The 3 groups had a female predominance (64.1%, 70.3% and 53.9%, respectively). SpA and CLBP had similar HRQoL reflected by EQ5D-3L index (ß=-0.03, p-value=0.33), much lower when compared to subjects noRMD (ß=-0.14, p-value< 0.001) (table I), Patients with SpA had lower scores in all EQ-5D dimensions, similar in patients with CLBP, but much higher than in participants noRMD. Pain, was reported in almost 60% of SpA adults, followed by limitations in mobility. In our cohort, SpA adults showed similar individual perception of health than adults with CLBP by EuroQoL visual analogue scale (ß=0.03, p-value=0.989), that was much lower (higher score=better health) when compared to adults noRMD (ß=-7.49, p-value=<

Table I - Comparison of quality of life and physical function between subjects with Spondyloarthritis and chronic low back pain and between subjects with Spondyloarthritis and without rheumatic diseases

	SpA n=92	CLBP n=1376	noRMD n=679	Crude OR SpA/CLBP [95% CI]	Crude p-value SpA/CLBP	Adjusted OR SpA/CLBP[a] [95% CI]	Adjusted p-value SpA/CLBP[a]	Crude OR SpA/noRMD [95% CI]	Crude p-value SpA/noRMD	Adjusted OR SpA/noRMD[b] [95% CI]	Adjusted p-value SpA/noRMD
EQ-5D											
Mobility				0.742 [0.465; 1.155]	0.196	1.371 [0.812; 2.275]	0.229	4.34 [2.588; 7.183]	**<<0.001**	4.54 [2.5; 8.212]	**<<0.001**
No problems	63 (68.48%)	849 (61.7%)	613 (90.41%)								
Some or extreme problems	29 (31.52%)	527 (38.3%)	65 (9.59%)								
Self-care				0.647 [0.31; 1.208]	0.204	1.374 [0.626; 2.758]	0.397	4.23 [1.833;9.231]	**<<0.001**	4.856 [1.849; 1.257]	**0.001**
No problems	82 (89.13%)	1156 (84.13%)	659 (97.2%)								
Some or extreme problems	10 (10.87%)	218 (15.87%)	19 (2.8%)								
Usual activities				0.957 [0.6; 1.492]	0.849	1.592 [0.943; 2.641]	0.075	4.423 [2.635;7.326]	**<<0.001**	4.65 [2.56;8.44]	**<<0.001**
No problems	63 (68.48%)	927 (67.52%)	615 (90.56%)								
Some or extreme problems	29 (31.52%)	446 (32.48%)	64 (9.43%)								
Pain/discomfort				1.074 [0.699; 1.672]	0.748	1.351 [0.845;2.187]	0.213	5.15 [3.284; 8.2]	**<<0.001**	4.726 [2.937; 7.703]	**<<0.001**
No pain/discomfort	35 (38.04%)	546 (39.74%)	516 (75.99%)								
Moderate or extreme pain /discomfort	57 (61.96%)	828 (60.26%)	163 (24.01%)								
Anxiety/depression				0.973 [0.603; 1.529]	0.908	1.143 [0.681; 1.877]	0.604	1.961 [1.185; 3.173]	**0.007**	1.499 [0.871; 2.488]	0.135
Not anxious/depressed	65 (70.65%)	958 (70.08%)	557 (82.52%)								
Moderately or extremely anxious/depressed	27 (29.35%)	409 (29.92%)	118 (17.48%)								
Quality of life EQ5D score (mean ± sd)	0.69 ± 0.25	0.66 ± 0.27	0.86 ± 0.21	0.03 [-0.03; 0.086]	0.3	-0.03 [-0.08; 0.03]	0.33	-0.167 [-0.213;-0.121]	**<<0.001**	-0.141 [-0.186; -0.1]	**<<0.001**
EQ VAS (mean ± sd)	65.28 ± 18.1	60.92 ± 19.86	75.69 ± 17.64	4.36 [0.108; 8.6]	**0.04**	0.03 [-4.06; 4.12]	0.989	-10.414 [-14.34;6.49]	**<<0.001**	-7.488 [-11.2; -3.78]	**<<0.001**

EQ-5D: EuroQoL- 5 Dimensions 3L; EQ VAS: EuroQoL visual analogue scale; HAQ:
SpA- Spondyloarthritis; CLBP- Chronic low back pain; noRMD- No Rheumatic diseases; [a]OR adjusted for: gender, age-group, NUTII, education level, employment status, BMI and number of noncommunicable Diseases; [b]OR adjusted for: gender, age-group, NUTII, marital status and number of noncommunicable Diseases
Sample size is not constant due to missing data: **SpA** - Mobility (n=92); Self-care (n=92); Usual activities (n=92); Pain/discomfort (n=92); Anxiety/depression (n=92); Quality of life EQ5D score (n=91); HAQ score (n=92). **CLBP** - Mobility (n=1376); Self-care (n=1374); Usual activities (n=1373); Pain/discomfort (n=1374); Anxiety/depression (n=1367); Quality of life EQ5D score (n=1362); HAQ score (n=1376). **NoRMD** - Mobility (n=678); Self-care (n=678); Usual activities (n=679); Pain/discomfort (n=679); Anxiety/depression (n=675); Quality of life EQ5D score (n=675); HAQ score (n=679).

Table II- Factors associated with health-related quality of life (EQ-5D) in Spondyloarthritis subjects (Multivariate model).

Variable		β	Std.Error	p-value	CI 95%
Regular physical Exercise					
	No	Ref			
	Yes	0.18	0.05	**<0.001**	[0.1; 0.3]
Number of chronic non-communicable diseases					
	0-2	Ref			
	≥ 3	-0.18	0.05	**<0.001**	[-0.24; -0.03]
Disease activity	Inactive	Ref			
	Active	-0.13	0.06	**0.036**	[-0.29; -0.05]

Std. error: Standard error; CI: Confidance Interval
Residual standard error: 0.2033 on 79 degrees of freedom
Multiple R-squared: 0.3543, Adjusted R-squared: 0.3298
F-statistic: 14.45 on 3 and 79 DF, p-value: 1.362e-07

0.001) (table I). Considering the factors associated with HRQoL in SpA, multimorbidity (³3 chronic non-communicable diseases) (ß=-0.18; p-value< 0.001) and an active disease (ß=-0.13; p-value=0.036), were associated with worse HRQoL; on the other hand, regular physical exercise was significantly associated with better HRQoL (ß=0.18; p-value< 0.001) (table II). Our model can explain 35.43% of the variance of HRQoL in SpA subjects.

Conclusion: In this nation-wide study, SpA showed a similar impact in HRQoL than CLBP. An active disease, multimorbidity and regular physical exercise are largely responsible for HRQoL in SpA.

Disclosure: H. Santos, None; **A. Henriques**, None; **A. Rodrigues**, None; **J. Branco**, None; **H. Canhao**, None.

Abstract Number: 0568

Construction of the Veterans Affairs National Rheumatoid Arthritis Database (VANRAD)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The Department of Veterans Affairs (DVA) provides comprehensive medical care at minimal or no cost to 9 million veterans annually through 170 medical centers and 1074 outpatient clinics across the United States. In 1999, the DVA established a national, fully integrated electronic health record (EHR), which now includes approximately 24 million veterans. However, few studies have used Veterans Affairs (VA) EHR data to examine the validity of diagnoses of RA. We developed a validated, national database of patients with RA who received VA care

Table 1: Proportion of patients with a valid RA diagnosis[1] as a function of RF and aCCP laboratory results

Test Result		aCCP							
		Not Available (0)[2]		Negative (-)		Positive (+)		Total	
RF	Not Available (0)	(N = 1253)[3]		N RA[4] Poss[5] RA	427 89.7% 5.9%	N RA Poss RA	1,159 98.2% 0.0%	N RA Poss RA	1,586 93.5% 3.2%
	Negative (-)	N RA Poss RA	810 86.3% 3.9%	N RA Poss RA	5,308 65.3% 11.9%	N RA Poss RA	2,005 94.5% 0.0%	N RA Poss RA	8,123 80.7% 5.8%
	Positive (+)	N RA Poss RA	2,229 94.6% 0.0%	N RA Poss RA	2,566 78.0% 8.5%	N RA Poss RA	12,978 95.8% 2.1%	N RA Poss RA	17,773 87.6% 4.3%
	Total	N RA Poss RA	3,039 90.7% 1.9%	N RA Poss RA	8.301 76.1% 9.2%	N RA Poss RA	16,142 95.9% 0.5%	N RA Poss RA	27,482 85.9% 4.7%

[1]Diagnosis given by the treating rheumatologist.
[2]No test results available or test results available but without normal range values.
[3]1,253 patients without available or interpretable RF or aCCP excluded from initial cohort.
[4]Percentage of 553 charts reviewed confirmed as RA.
[5]Poss RA = Possible RA. Patients met our inclusion criteria but the treating rheumatologist never made a definitive diagnosis of RA or alternative diagnosis (from 553 charts reviewed).

since the introduction of International Classification of Diseases, tenth revision (ICD-10) coding in 2015. This Veterans Affairs National Rheumatoid Arthritis Database (VANRAD) will provide infrastructure for retrospective and prospective research to address the 'real-world' care of patients with RA.

Methods: Patients with the following criteria were identified from the VA EHR as of October 2, 2020: (a) ≥1 ICD-10 diagnosis code of RA; (b) treatment with ≥1 DMARD; (c) ≥2 VA rheumatology clinic visits; and (d) ≥1 RF and/or anti-CCP (aCCP) antibody test result. From this group, 553 EHRs were randomly selected for review. The 'gold standard' for the diagnosis of RA was the treating rheumatologist's diagnosis, documented in the EHR.

Results: A total of 27,482 patients met eligibility criteria. Sociodemographic characteristics were: 85.6% male; mean age of 69.7 years (y) (standard deviation [SD]=10.9 y; range=21.9 y to 100.5 y); 76.4% white, 17.0% African American; and mean VA care for 14.1 y (SD=5.3 y, range=0.04 y to 20.0 y).

For patients with ≥1 RF or aCCP test, the positive predictive value (PPV) for RA ranged from 65.3% (RF-/aCCP-) to 95.8% (RF+/aCCP+); rheumatologists' likelihood of a 'possible' diagnosis was higher if the aCCP test result was negative or not available (Table 1). Excluding patients with a second rheumatologic diagnosis did not improve PPV results (data not shown).

The percentage of RA-confirmed patients with 1 test not available, and whose complementary test was negative (RF0/aCCP- or RF-/aCCP0), was greater than the percentage of patients for whom both tests were negative (RF-/aCCP-). This suggests our data extraction methods may have been incomplete or that unidentified bias may have been present, and warrants further study.

Conclusion: Our methodology for constructing an RA database by selecting patients with ≥2 rheumatology clinic visits, an ICD-10 diagnosis of RA, treatment with ≥1 DMARD, and a minimum of 1 RF or aCCP test result has high positive predictive value for RA. Positive RF and aCCP test results were strong predictors of rheumatologists' diagnostic certainty for an RA diagnosis. Thus, the VANRAD and the associated EHR provide opportunity for a wide range of retrospective observational and prospective longitudinal studies based on 'real-world' patient care.

References: Ng B, et al. *Arthritis Care Res* 2012;64:1490-6; Hanly JG, et al. *Open Access Rheumatol* 2015;7:69-75.

Disclosure: A. Joseph, Bristol Myers Squibb, 5; **J. Yanagida**, None; **X. Huang**, Washington University in St. Louis, 3; **P. Ranganathan**, None; **M. Laurie**, Bristol Myers Squibb, 3, 11; **H. Xian**, Bristol Myers Squibb, 5; **S. Eisen**, Bristol Myers Squibb, 7.

Abstract Number: 0569

All-Cause and Cause-Specific Mortality in Spondyloarthritis: A Systematic Review and Meta-Analysis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

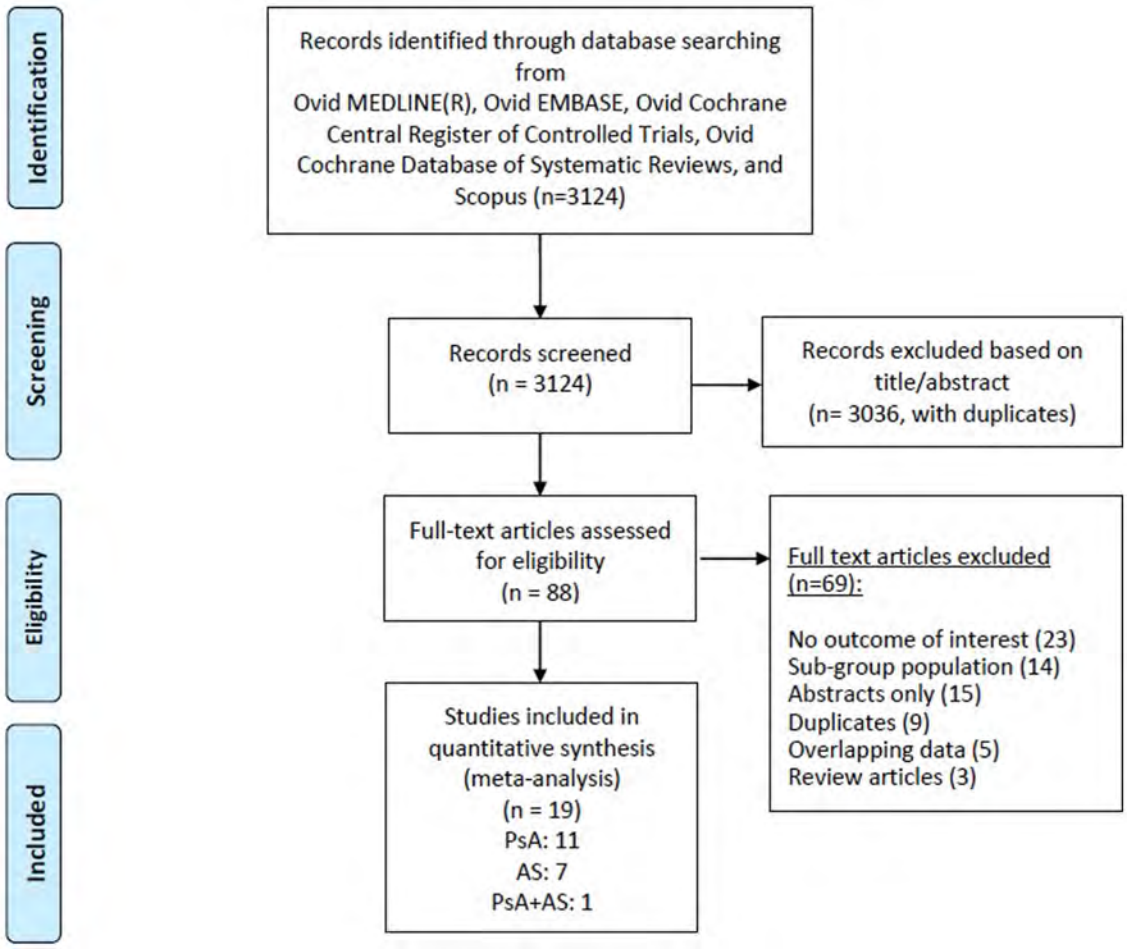

Figure 1. Prisma Flow Diagram

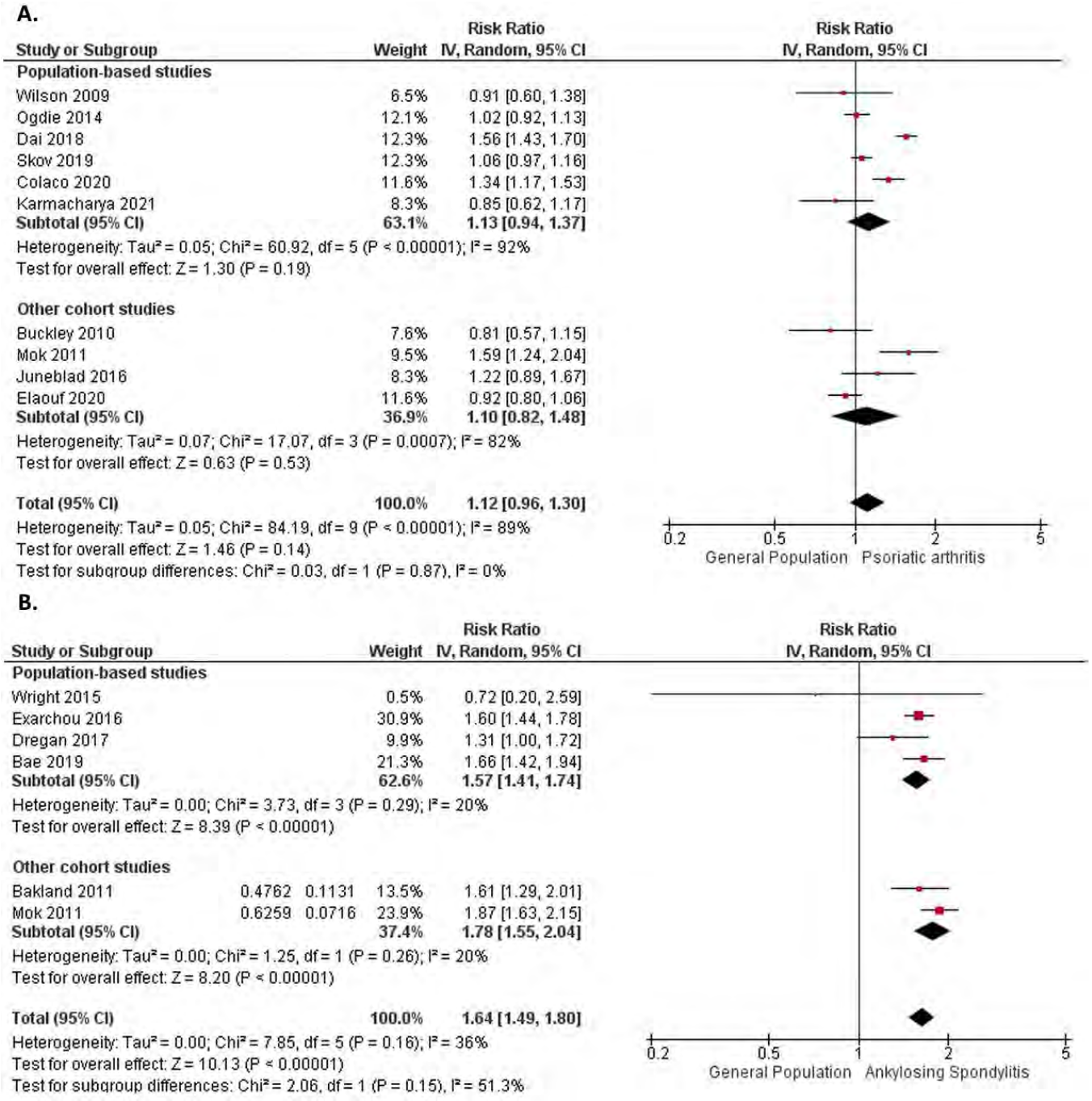

Figure 2. Forrest Plot for All-cause mortality in A)Psoriatic Arthritis B)Ankylosing Spondylitis

Background/Purpose: Spondyloarthritides (SpA) represent a group of chronic inflammatory diseases associated with a higher risk of cardio-metabolic comorbidities compared to the general population. It is unclear how these comorbidities are associated with mortality in SpA, and studies on mortality in SpA have shown inconsistent results. We performed a systematic review and meta-analysis of all-cause and cause-specific mortality in psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Methods: A comprehensive database search was performed for studies reporting all-cause or cause-specific mortality in patients with PsA and AS compared with the general population. Pooled relative risks (RRs) were calculated using random-effects model.

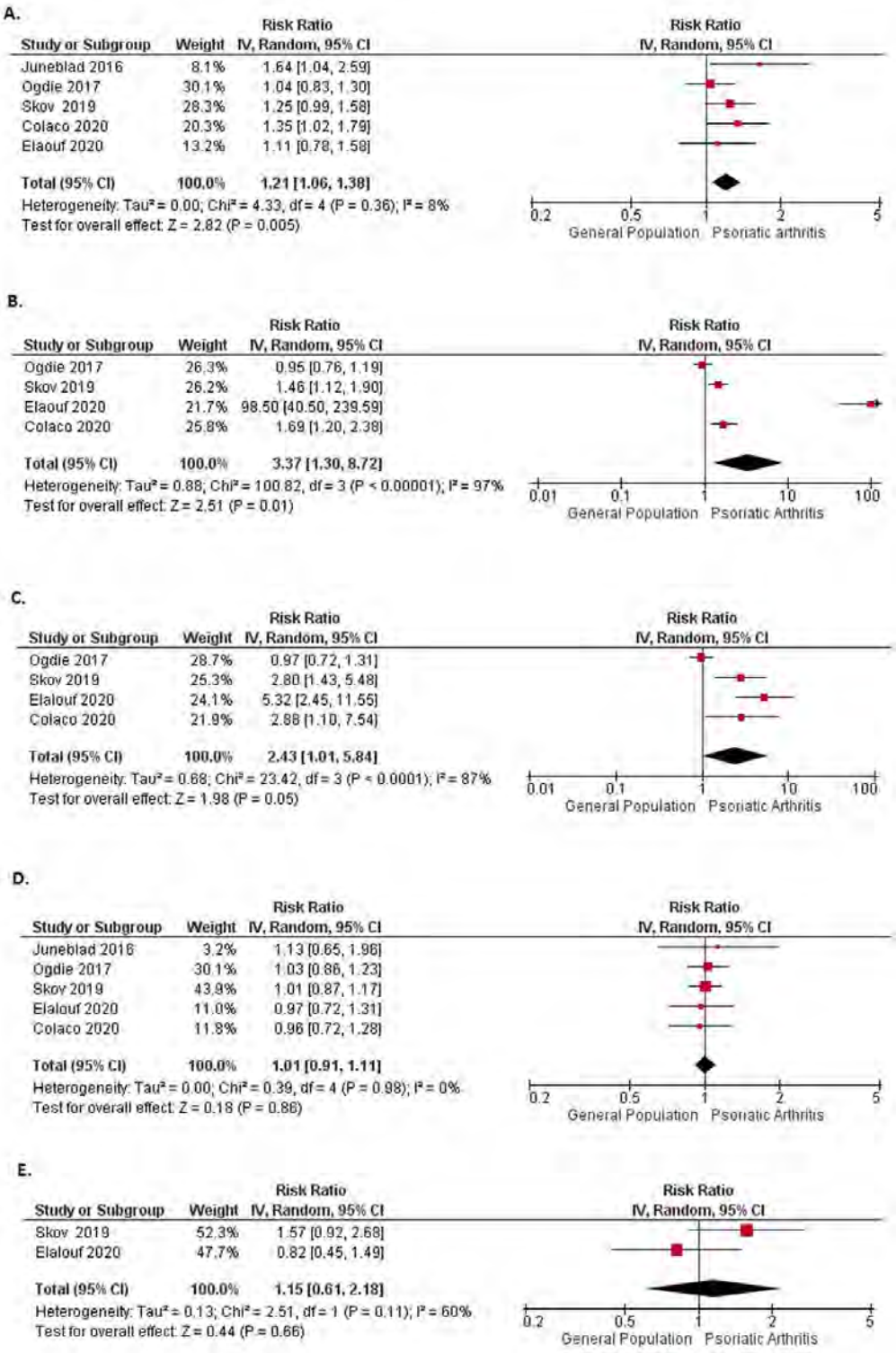

Figure 3. Forrest plot for cause-specific mortality in psoriatic arthritis A) cardiovascular B) respiratory C) infections D) malignancy E) Injury and poisoning

Results: We included 19 studies (eleven for PsA, seven for AS, one for both). In PsA studies, there was no increased mortality compared to the general population (RR: 1.12, 95% CI: 0.96-1.30, 10 studies). Cardiovascular, respiratory, and infection specific mortality risks were significantly higher for PsA patients (RR: 1.21, 95% CI: 1.06-1.38; RR: 3.37, 95% CI: 1.30-8.72; and 2.43, 95% CI: 1.01-5.84, respectively). Cancer related mortality in PsA was not higher

than the general population (RR: 1.01, 95% CI: 0.91-1.11). In AS, we found a higher risk of death from all causes (RR 1.64, 95% CI: 1.49-1.80, 6 studies) and cardiovascular causes compared to the general population (RR 1.35, 95% CI: 1.01-1.81, 3 studies).

Conclusion: This systematic review and meta-analysis showed a significantly increased risk of overall mortality in AS, but not PsA. Cardiovascular-specific mortality was higher for both PsA and AS, which emphasizes the importance of early screening and management of comorbidities to mitigate mortality risk.

Disclosure: H. Chaudhary, None; **N. Bohra**, None; **K. Syed**, None; **A. Donato**, None; **M. Murad**, None; **P. Karmacharya**, None.

Abstract Number: 0570

A Narrowed, but Persistent Mortality Gap: A National, Matched Cohort Study in U.S. Veterans with Rheumatoid Arthritis from 2000-2017

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Unadjusted all-cause mortality rates and major causes of death in Veterans with and without RA.

	RA (n=69,433)	Non-RA (n=612,230)
Follow-up time (person-years)	500,762	4,861,490
Total deaths (N)	24,214	173,234
Incidence rate (95% CI), all-cause mortality (per 1000 person-years)	48.4 (47.7-49.0)	35.6 (35.5-35.8)
Causes of death (N)		
Cardiovascular	7,784	57,436
Cancer	5,653	44,589
Respiratory	3,776	21,408
External causes	975	7,908
Endocrine	918	8,017
Infection	861	4,734
Gastrointestinal	850	6,610
Nervous system	728	8,431
Mental health	622	6,211
Genitourinary	590	4,692
Blood disorders	143	573
Skin	66	236

Table 1. Unadjusted all-cause mortality rates and major causes of death in Veterans with and without RA

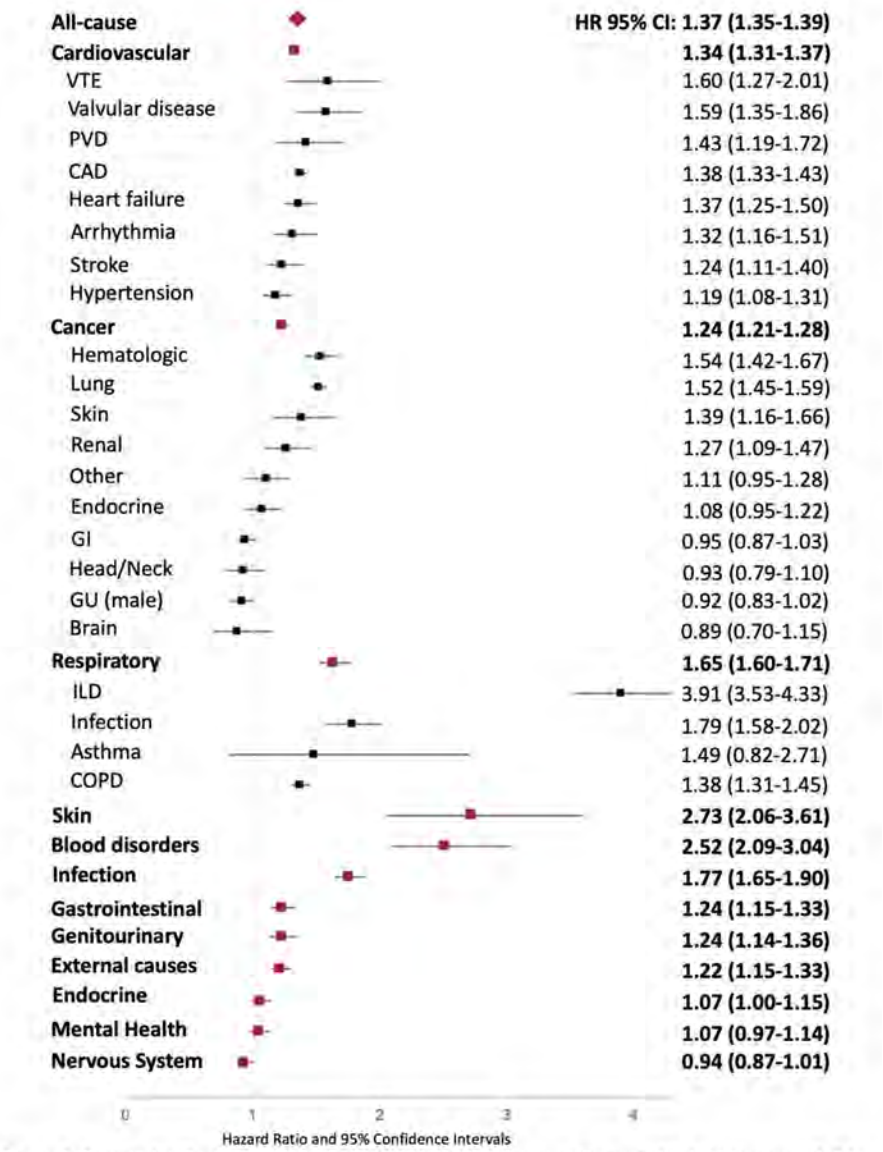

Figure 1. Forest plot illustrating the risk of all-cause and cause-specific mortality in Veterans with RA

Abbreviations: CAD=coronary artery disease, CI=Confidence interval, COPD=chronic obstructive pulmonary disease GI=gastrointestinal, GU=genitourinary HR=hazard ratio, ILD=interstitial lung disease, PVD=peripheral vascular disease, VTE=venous thromboembolism

Figure 1. Forest plot illustrating the risk of all-cause and cause-specific mortality in Veterans with RA

Background/Purpose: Rheumatoid arthritis (RA) is recognized to increase the risk of premature death. The impact of RA on survival varies across causes of death, though few studies have precisely estimated mortality risk for specific causes. While all-cause mortality appears to be improving, perhaps due to advances in care, it remains unclear how these advances have impacted cause-specific mortality, particularly relative to the non-RA population. We examined risk and temporal trends in all-cause and cause-specific mortality in RA in the Veterans Health Administration (VHA), the largest integrated healthcare system in the U.S.

Methods: We conducted a retrospective, matched cohort study in the VHA from 1/1/2000-12/31/2017. RA patients (≥2 ICD codes for RA, rheumatologist diagnosis, and a positive autoantibody or DMARD fill) were matched up to 1:10 on age, sex, and year of VHA enrollment to non-RA patients. RA was considered incident if they received care in the VHA for ≥365 days without a RA diagnostic code or DMARD fill. Patients were followed from fulfillment of the RA algorithm (corresponding calendar date for non-RA) until death or end of study period. Vital status and cause of death

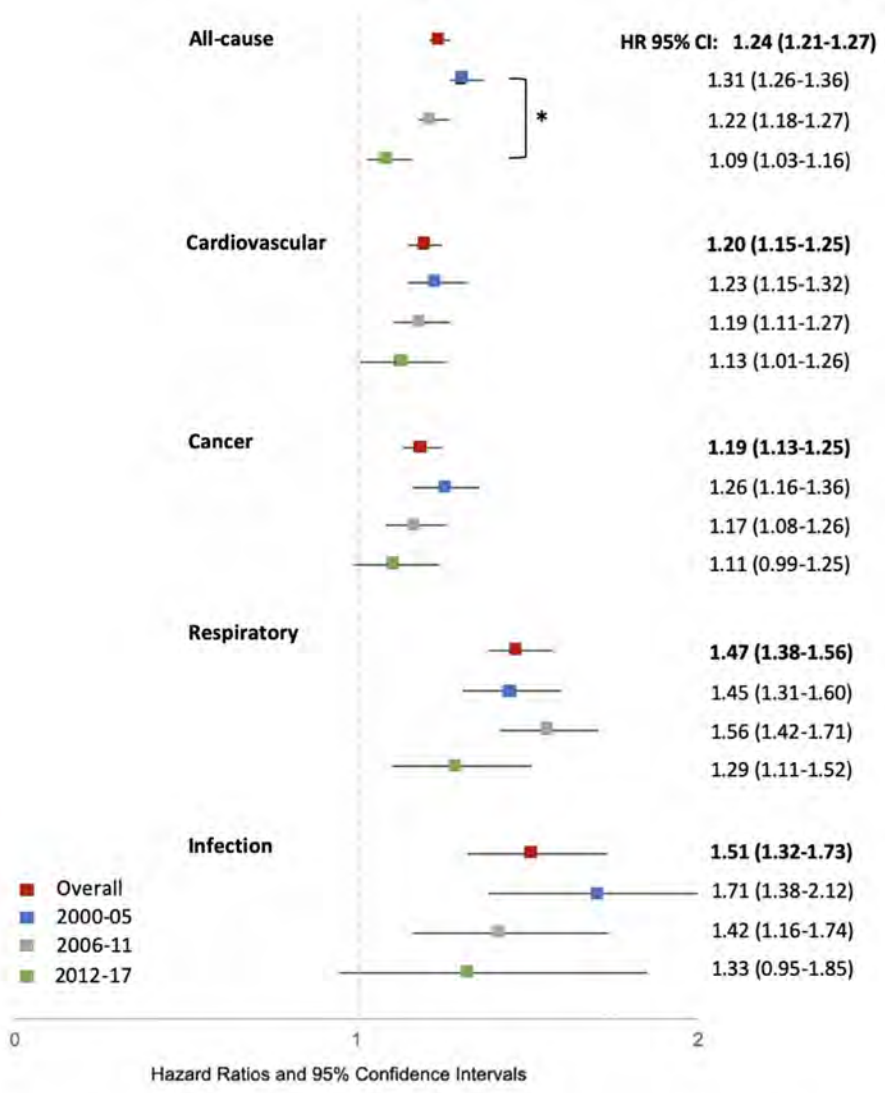

Figure 2. Forest plot illustrating overall risk and temporal trends of all-cause mortality and select causes of death in Veterans with incident RA.

*Interaction between RA status and 2012-17 vs 2000-05 time period, p = 0.02

Abbreviations: CI=confidence interval, HR=hazard ratio

Figure 2. Forest plot illustrating overall risk and temporal trends of all-cause mortality and select causes of death in Veterans with incident RA

were obtained from the National Death Index. Baseline covariates were obtained from national VHA databases and included demographics, smoking status, BMI, Rheumatic Disease Comorbidity Index, and health care utilization. Cox regression was used to examine the association of RA with all-cause and cause-specific mortality.

Results: We matched 69,433 RA patients (n=48,828 incident RA) to 612,230 non-RA patients. RA patients in this study were predominantly male (88.0%), had a mean age of 63 years, and were more frequently current smokers with greater comorbidity compared to non-RA. Crude incidence rates and causes of death are detailed in **Table 1**. After multivariable adjustment, RA patients were at increased risk of all-cause (HR 1.37 [95% CI 1.35-1.39]), cardiovascular (HR 1.34 [1.31-1.37]), cancer (HR 1.24 [1.21-1.28]), respiratory (HR 1.65 [1.60-1.71]), and infection-related mortality (HR 1.77, 1.65-1.90), as well as other less frequent causes **(Figure 1)**. Within these major causes of death, interstitial lung disease (ILD)-related deaths were most closely associated with RA (HR 3.91 [3.53-4.33]). Results were similar

in the incident RA cohort. In the incident cohort, all-cause mortality risk related to RA was significantly lower during 2012-2017 compared to 2000-2005 **(Figure 2)**, but still higher compared to non-RA. RA-associated risk for cardiovascular, cancer, respiratory, and infectious mortality were also numerically lowest in 2012-2017 but remained higher compared to non-RA.

Conclusion: In a national study of US veterans with and without RA from 2000-2017, we estimated a 37% increased risk of all-cause mortality in RA. Excess mortality was driven by cardiovascular, cancer, and respiratory causes, particularly ILD which was the most overrepresented cause of death in RA. Though our findings provide further support that RA-related mortality risk is improving over time, a mortality gap remains for all-cause and cause-specific mortality in RA suggesting continued efforts are needed to improve longevity.

Disclosure: T. Johnson, None; **Y. Yang**, None; **P. Roul**, None; **B. Sauer**, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **B. England**, Boehringer-Ingelheim, 2.

Abstract Number: 0571

The National Incidence of Clinically Diagnosed Psoriatic Arthritis in Sweden 2014-2016

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

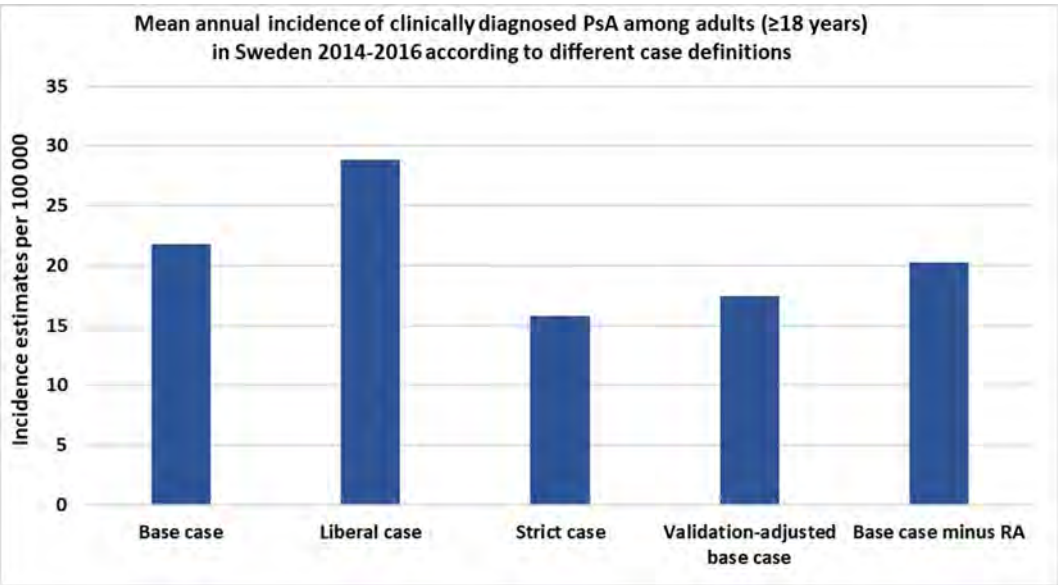
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

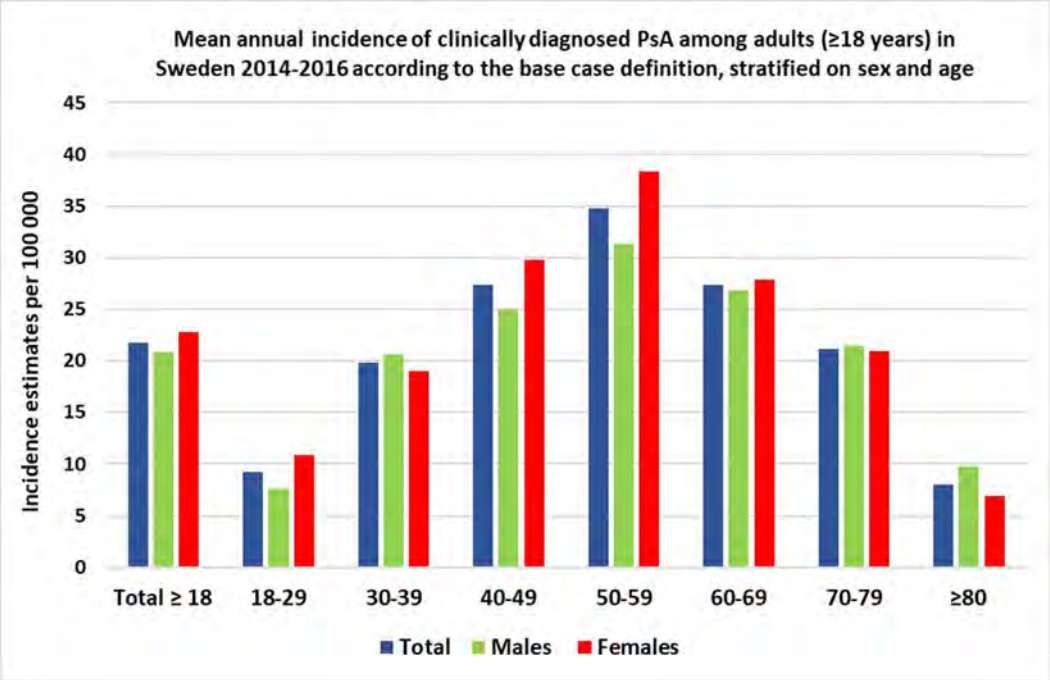
Background/Purpose: Psoriatic arthritis (PsA) incidence estimates vary considerably, and nationwide estimates are sparse. In Sweden, PsA is typically diagnosed in specialized care, although a limited subset with very mild disease may never be referred from primary care. The objectives of the current study were to estimate the mean annual incidence of PsA, diagnosed in specialized care, among adults in Sweden 2014-2016, overall and stratified by sex/age/education, and to describe the use of disease modifying anti-rheumatic drugs (DMARDs) among such cases.

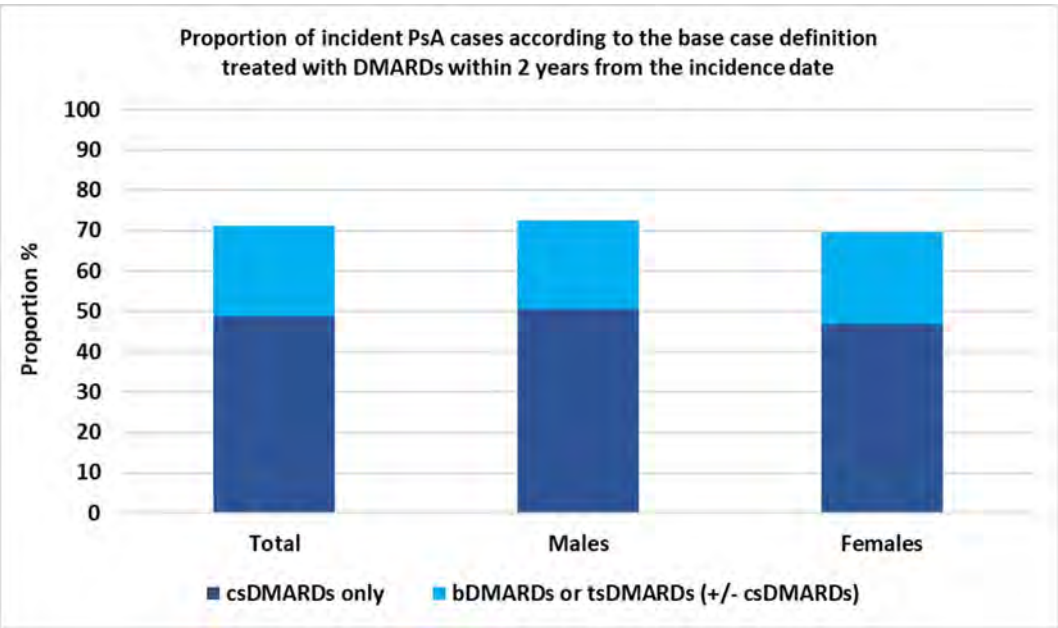
Methods: Incident PsA cases ≥18 years (y) 2014-2016 were identified from the Swedish National Patient Register (NPR) and/or the Swedish Rheumatology Quality register (SRQ), based on five different definitions; A) Base case (BC): ≥1 ICD-10 code for PsA (L40.5/M07.0-M07.3) as main diagnosis from rheumatology or internal medicine (IM) in NPR or PsA diagnosis registered in SRQ during the relevant year, and no prior such diagnoses; B) Liberal: ≥1 ICD code for PsA as main or secondary diagnosis from any department in NPR or PsA diagnosis in SRQ during the relevant year, and no prior such diagnoses; C) Strict: ≥1 ICD code for PsA as main diagnosis from rheumatology/IM during the relevant year and no prior such ICD registration or PsA diagnosis in SRQ, plus ≥1 additional PsA ICD code (main or secondary from any department) within 2 years of the first in NPR; D) As BC, but reducing the number of PsA cases in line with a prior validation study in which 80% of 200 incident cases fulfilled PsA classification criteria; E) As BC,



but excluding cases with ≥1 main diagnosis of rheumatoid arthritis from rheumatology/IM in NPR before or during 2 years after the incidence date. Irrespective of definition, cases < 18y at the incidence date or with a diagnosis of juvenile idiopathic arthritis (main/secondary) from any department in NPR or in SRQ ever, were excluded. Furthermore, DMARD use among cases within 2 years from the incidence date was assessed. The Swedish population the relevant years, demographics, education and treatments were retrieved from other national registers.

Results: The national, mean annual incidence of PsA, diagnosed in specialized care 2014-2016, in the population ≥18y was estimated at 21.8/100 000. Corresponding sensitivity analysis estimates ranged from 15.8 to 28.8/100 000 (Figure 1). The highest incidence was observed in the age-group 50-59y, followed by the age-groups 40-49 and 60-69y, regardless of sex (Figure 2). Irrespective of definition, the PsA incidence was numerically higher among females (Figure 2). Higher education was associated with lower age-/sex-standardized PsA incidence (>12y, 10-12y, ≤9y education: 21.1 vs 28.9 vs 25.1/100 000, respectively, in adults ≥30y by the BC definition). Among incident PsA cases





(BC definition), 22% received biologic or targeted synthetic DMARDs within two years of the incidence date, while an additional 49% received conventional synthetic DMARDs only (Figure 3).

Conclusion: The incidence of PsA, diagnosed in specialized care, in the adult Swedish population 2014-2016 was estimated at around 20/100 000. Almost 3/4 of cases received DMARD therapy within 2 years of the incidence date.

csDMARDs: Sulfasalazine, Leflunomide, Ciclosporine, Azathioprine, Methotrexate, Sodium aurothiomalate, Auranofin, Chloroquine, Hydroxychloroquine bDMARDs: Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab, Abatacept, Ixekizumab, Secukinumab, Ustekinumab tsDMARDs: Apremilast, Tofacitinib

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Disclosure: S. Exarchou, Novartis, 2, Janssen-Cilag AB, 2, AbbVie, 2; **D. Di Giuseppe**, None; **G. Alenius**, None; **E. Klingberg**, Eli Lilly, 6, Novartis, 2, Roche, 5; **V. Sigurdardottir**, Novartis, 2; **S. Wedrén**, None; **U. Lindström**, None; **C. Turesson**, Bristol-Myers Squibb, 5, Roche, 2, Abbvie, 6, Bristol-Myers Squibb, 6, Nordic Drugs, 6, Pfizer, 6, Roche, 6; **L. Jacobsson**, AbbVie, 2, Eli Lilly, 2, Janssen-Cilag AB, 2, Novartis, 2, Pfizer, 2; **J. Askling**, AbbVie, 5, BMS, 5, Eli Lilly, 5, Merck, 5, Pfizer, 5, Roche, 5, Samsung Bioepis, 5, Sanofi, 5, UCB Pharma, 5; **J. Karlsson Wallman**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Novartis, 2, UCB Pharma, 2.

Abstract Number: 0572

Circulating Cytokines and Chemokines Are Associated with the Risk of Incident Cardiovascular Disease in Rheumatoid Arthritis Independent of Conventional Disease Activity Measures

Tate Johnson[1], Michael Duryee[2], Carlos Hunter[2], Punyasha Roul[2], Yangyuna Yang[2], Joshua Baker[3], Geoffrey Thiele[2], Ted Mikuls[2] and Bryant England[2], [1]University of Nebraska Medical Center, Elkhorn, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Cardiovascular disease (CVD) is the leading cause of death in rheumatoid arthritis (RA). While chronic inflammation contributes to CVD pathogenesis, the role of specific circulating inflammatory mediators with CVD risk in RA is unclear. Because existing risk calculators underestimate CVD risk in RA patients, additional biomarkers to prognosticate CVD risk are needed. We evaluated the associations of serum cytokines and chemokines with incident major adverse cardiovascular events (MACE) and whether subclinical inflammation as assessed by these mediators predicts future CVD.

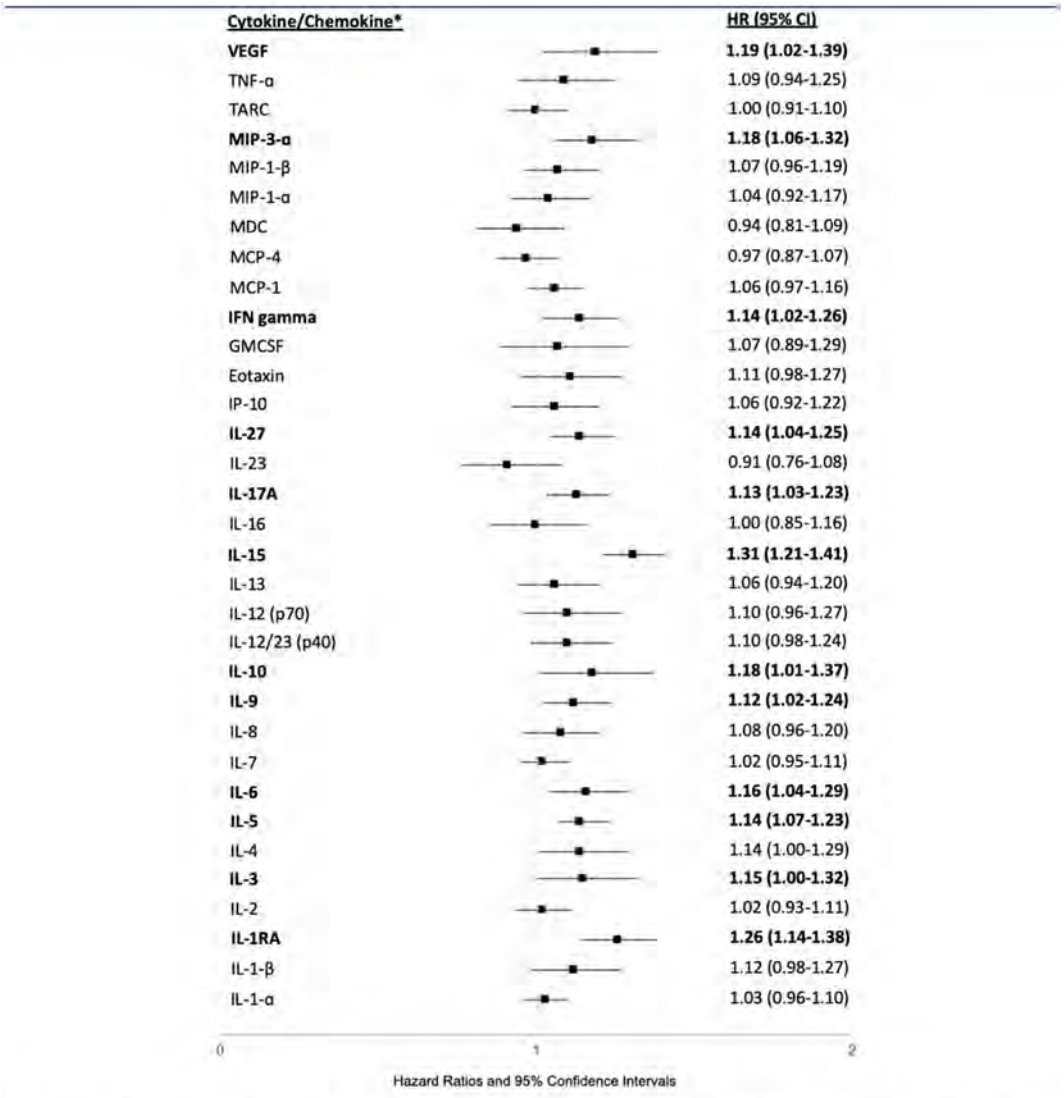

Figure 1. Association of circulating cytokine and chemokine concentrations with incident major adverse cardiovascular events in rheumatoid arthritis. Cytokines and chemokines each assessed in separate models adjusting for age, sex, BMI, current smoking, hypertension, diabetes, lung disease, prior MACE, medications (methotrexate, TNF biologic, prednisone), and DAS28. Values are hazard ratios per 1 SD change in analyte concentration.

*Analytes in bold indicate p<0.05

Abbreviations: CI=confidence interval, HF=hazard ratio, IL=interleukin, MDC=macrophage derived chemokine, MIP=macrophage inflammatory protein, TARC=thymus- and activation-regulated chemokine, TNF=tumor necrosis factor VEGF = vascular endothelial growth factor

Figure 1. Association of circulating cytokine and chemokine concentrations with incident major adverse cardiovascular events in rheumatoid arthritis

Methods: We included patients from a prospective, multicenter cohort of US Veterans with RA between 2003-2020 and followed them from enrollment to incident MACE, death, or end of follow-up. MACE was defined as a composite of myocardial infarction, coronary revascularization, stroke, or CVD-related death and identified with previously validated algorithms using ICD codes and the National Death Index. A multiplex assay was used to measure cytokines and chemokines (n=33) using serum banked at study enrollment. Values were log-transformed, standardized, and considered elevated if >2 SD above the mean. Covariates included demographics, smoking status, BMI, comorbidities (hypertension, diabetes, lung disease, prior MACE), LDL cholesterol, DAS28, and medications (methotrexate, TNFi, prednisone) at enrollment. Associations between individual analytes with incident MACE were estimated using multivariable Cox regression. In secondary analyses, we additionally adjusted for DAS28 and restricted the cohort to patients in remission or low disease activity (LDA).

Results: We studied 2,712 RA patients (mean age 72 years, 90% male, mean DAS28 of 3.7). We identified 406 MACE outcomes over 22,216 person-years of follow-up (19.3 events per 1,000 PY, mean time to event 4.9 years). After multivariable adjustment including traditional CVD risk factors, 12 of 33 analytes were significantly associated with an increased risk of MACE (HR per 1 SD range 1.11-1.22). Associations between cytokines / chemokines and incident MACE persisted after further adjusting for baseline DAS28 (Figure 1). Among 683 patients in remission/LDA at enrollment, 97 MACE outcomes occurred in follow-up. Five analytes (IL-6, IL-15, IL-17A, IFN-g, and macrophage inflammatory protein-3-α) remained associated with incident MACE (HR range 1.19-1.50) in these patients. The number of elevated cytokines was associated with an increased risk of MACE in the overall (HR 1.06 [95% CI 1.01-1.10]) and LDA / remission cohort (HR 1.11 [1.06-1.11]).

Conclusion: In a prospective, multicenter RA cohort, several circulating cytokines and chemokines were associated with a heighted risk of incident MACE, independent of traditional CVD risk factors and clinical RA disease activity. Elevated concentrations of these pro-inflammatory mediators similarly predicted MACE even in those in LDA or remission. Together, these findings suggest that measuring pro-inflammatory mediators in RA patients may aid in CVD risk stratification and prevention beyond existing traditional and RA-related CVD risk factors.

Disclosure: T. Johnson, None; **M. Duryee**, None; **C. Hunter**, None; **P. Roul**, None; **Y. Yang**, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **B. England**, Boehringer-Ingelheim, 2.

Abstract Number: 0573

Biosimilar to Biosimilar Infliximab Switching in Real-world Patients with Inflammatory Arthritis Followed in the Danish DANBIO Registry: Switch from Originator Infliximab to CT-P13 and Then to GP1111

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table. Baseline characteristics at time of 1st and 2nd biosimilar switch, overall and stratified by treatment status after 1 year

	1st switch: originator infliximab -> biosimilar CT-P13				2nd switch: biosimilar CT-P13 -> GP1111			
	Overall	Treatment status 1-year		P value for difference	Overall	Treatment status 1-year		P value for difference
		On drug	Withdrawn*			On drug	Withdrawn**	
Number, N (%)	**780**	**651 (83)**	**129 (17)**		**407**	**371 (91)**	**36 (9)**	
RA/PsA/AxSpA, %	50/15/35	49/15/36	56/16/28		45/16/39	44/17/40	60/9/31	
Female, %	52	**50**	**62**	**0.02**	47	46	61	0.1
Age, years	56 (46-67)	56 (45-67)	57 (47-68)	0.5	57 (48-68)	57 (48-68)	62 (51-68)	0.3
Concomitant MTX (RA) %	90	92	84	0.1	92	**94**	**44**	**0.02**
In remission (yes), %	325 (42)	273 (42)	52 (40)	0.4	204 (50)	**193 (52)**	**11 (31)**	**0.04**
CRP, mg/L	4 (2-8)	4 (2-8)	4 (2-7)	0.9	2 (1-4)	2 (1-3)	3 (1-5)	0.2
Physician global VAS, mm	5 (2-11)	5 (2-11)	6 (2-13)	0.4	5 (1-10)	4 (1-10)	8 (2-21)	0.05
VAS pain, mm	23 (9-46)	**22 (8-42)**	**34 (13-61)**	**<0.001**	**20 (7-40)**	**18 (7-36)**	**45 (29-67)**	**<0.001**
VAS fatigue, mm	36 (15-64)	**34 (14-58)**	**50 (21-74)**	**0.002**	**29 (12-56)**	**27 (11-54)**	**58 (36-78)**	**<0.001**
Patient global VAS, mm	27 (12-55)	**26 (12-52)**	**39 (17-68)**	**<0.001**	**21 (9-47)**	**21 (8-44)**	**52 (25-81)**	**<0.001**
HAQ	0.63 (0.13-1.3)	0.63 (0.13-1.0)	0.88 (0.13-1.25)	0.1	0.38 (0-0.9)	0.38 (0-0.9)	0.9 (0.5-1.4)	<0.001
PASS yes, n (%)	363 (47)	**309 (48)**	**54 (42)**	**0.01**	**273 (67)**	**255 (69)**	**18 (50)**	**0.06**
Comorbidities¶ ≥1	277 (36)	**221 (34)**	**52 (40)**	**0.03**	138 (34)	123 (33)	15 (42)	0.8

Numbers are median (interquartile ranges), unless otherwise stated. Remission: DAS28 <2.6 (RA, PsA), ASDAS <1.3 (AxSpA).

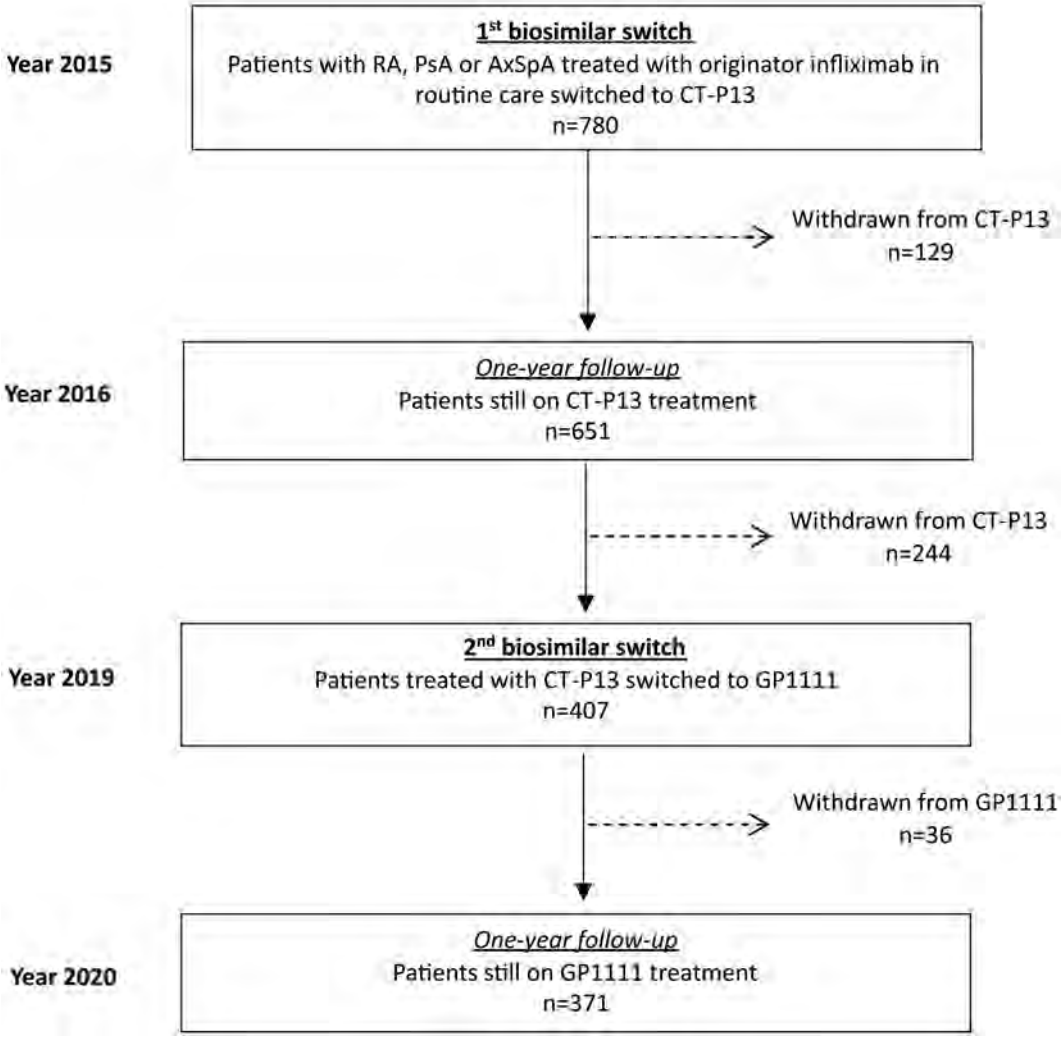
*Withdrawals n (%): Lack of effect (LOE) 65 (50), Adverse events (AE) 26 (20), Several/Other 21(16)

**Withdrawals: LOE 9 (25), AE 8 (22), Several/Other 6 (17)

¶ 0-10 years prior to baseline

AxSpA: Axial Spondyloarthritis, CRP: C-reactive protein; DAS-28: Disease activity score (4 variables); HAQ: Functional status (Health assessment Questionnaire) 0-3; MTX: Methotrexate; PASS: Patient Acceptable Symptom State (yes/no); Patient pain (VAS 0-100), Fatigue (VAS 0-100), Patient global assessment (VAS 0-100), Physician global VAS (visual analog scale [VAS], 0-100), PsA: Psoriatic Arthritis and RA: Rheumatoid Arthritis.

Figure Flowchart of patient inclusion and follow-up



Background/Purpose: In routine care, biosimilar to biosimilar infliximab switching may occur to save costs (=non-medical switching). Previous studies have investigated the efficacy and safety of a switch from originator infliximab to one of its biosimilars, whereas evidence regarding biosimilar to biosimilar switching is non-existing. Thus, robust, well-designed studies are needed to investigate the consequences of multiple switches on treatment effectiveness, drug safety and patient-reported outcomes.

In this real-life study, we aimed to explore baseline clinical characteristics and one-year treatment status in patients with inflammatory arthritis, who underwent mandatory multiple infliximab biosimilar switches (from originator infliximab to CT-P13 and subsequently to GP1111).

Methods: Observational cohort study based on DANBIO registry (clinical data) linked with national patient registries (prior comorbidities). For each switch, main outcomes were one-year treatment status (withdrawn yes/no), reasons for withdrawal, and baseline characteristics associated with withdrawal (Mann-Whitney, χ^2 test).

Results: In 2015, 780 patients switched from originator infliximab to biosimilar CT-P13 in accordance with a national guideline (366 RA/113 PsA/256 AxSpA; 51% women; median age 56 years; disease duration 14 years, infliximab treatment 7 years), **Table**. At baseline, 42% was in remission. At 1 year, 83% maintained CT-P13 treatment.

In 2019, 52% of the 780 patients were still receiving treatment with CT-P13 and performed a 2nd biosimilar switch to GP1111 due to change of guideline. After 1 year, 91% maintained GP1111, **Figure**.

For both rounds of switching, withdrawal during follow-up was associated with higher baseline patient-reported outcomes (PROs), higher HAQ and less frequent acceptable symptom state (PASS=yes) whereas objective markers (CRP, physician global) were similar.

Conclusion: Multiple biosimilar infliximab switches were well tolerated in patients who were long-term users of the originator. Risk of withdrawal was associated with higher baseline PROs, suggesting that outcomes were more affected by patient-related than drug-related factors.

Acknowledgements: We thank departments reporting to the DANBIO registry. Partly sponsored by Sandoz, who had no influence on the analysis, interpretation and presentation of data.

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Abstract Number: 0574

Prevalence and Early Progression of Lung Diseases in Patients with Recently-Diagnosed Rheumatoid Arthritis: A Prospective Cohort Study

Tina Mahajan[1], Daniel Hershberger[1], Matt Devries[2], Punyasha Roul[1], Yangyuna Yang[1], Sherrie Edwards[1], Geoffrey Thiele[1], Ted Mikuls[1], James O'Dell[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Medical Center, Omaha

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Several types of lung diseases complicate the rheumatoid arthritis (RA) disease course such as interstitial lung disease (ILD) and obstructive lung diseases. The prevalence of lung diseases varies substantially across studies, and there remains a poor understanding of the progression of lung diseases early in the RA disease course. We aimed to identify the prevalence and early progression of lung diseases in patients with recently diagnosed RA.

Methods: We performed a prospective cohort study of lung diseases in recently-diagnosed RA patients at an academic center from 2017-2021. Patients fulfilled the 2010 ACR criteria for RA and were diagnosed within the prior two years. At baseline and 1-year follow-up visits, patient-reported outcomes measures (e.g. Modified Research Council [MRC] dyspnea scale and Health Assessment Questionnaire), clinical assessments (e.g. DAS28-ESR), and complete

Table 1. Prevalence and Radiographic Severity of Lung Abnormalities on High-Resolution CT in Early RA Patients (n=37)

	Prevalence, N (%)	Severity of Lung Abnormalities*, Median (range)
Any Airway disease	21 (59.5%)	-
Bronchial wall thickening	2 (5.4%)	4, 7**
Bronchiectasis	3 (8.1%)	2 (1-6)
Air trapping	17 (45.9%)	6 (2-16)
Centrilobular opacities	1 (2.7%)	4**
Emphysema	5 (13.5%)	3 (2-10)
Any Parenchymal disease	11 (29.7%)	-
Ground glass opacities	7 (18.9%)	4 (2-7)
Honeycombing	1 (2.7%)	2**
Fibrosis/Reticulation	7 (18.9%)	4 (2-6)
Pulmonary nodules	23 (62.2%)	-
Pleural disease	2 (5.4%)	-

Categories not mutually exclusive
*Abnormalities scored 0-4 by % involvement in 6 lung regions; score range 0-24; adapted from Goldin et al. *Chest* 134(2):358-367, 2008. Demoruelle et al. *Arth Rheum* 64(6):1756-1761, 2012.
**individual severity scores listed

Prevalence and Radiographic Severity of Lung Abnormalities on High-Resolution CT

pulmonary function tests (PFTs) were collected. At the initial visit, a high-resolution computed tomography (HRCT) scan of the lungs was completed with thin (1.25 mm) slices with prone and supine imaging. HRCTs were scored semi-quantitatively in 6 lung regions by an expert chest radiologist blinded to clinical data.

Results: Among 37 recently-diagnosed RA patients, mean age was 57.2 (SD 11.9) years, and the majority were female (81.1%), white (81.1%), seropositive (83.8% RF, 86.5% anti-CCP), and MTX treated (81.1%). Cigarette smoking history was present in 59.5%, but a minority of patients had clinically-diagnosed lung disease (5.4% COPD, 10.8% asthma, 2.7% ILD). Despite 86.5% of subjects reporting no or only slight dyspnea (MRC grade 0 or 1), 29.7% had evidence of parenchymal disease, 59.5% had evidence of airway disease, and 62.2% had pulmonary nodules on HRCT (**Table 1)**. Semiquantitative HRCT scoring revealed most airway and parenchymal abnormalities to be mild in severity. Similarly, physiologic impairment on PFTs was infrequent with 16.2% demonstrating restrictive and 18.9% obstructive spirometry. Among patients who have completed 1-year of follow-up (n=27), there was no significant change in PFT parameters (FEV1, FVC, TLC, DLCO) or MRC score (**Table 2**). Stability in PFTs was present even among RA patients with detectable lung disease on HRCT. Baseline DAS28-ESR was negatively correlated with FVC (r = -0.42, p = 0.01) and positively correlated with MRC scores (r=0.57, p< 0.001), but not with other PFT parameters or with HRCT findings. Seropositivity for RF or anti-CCP antibody was not associated with an increase in airway or parenchymal abnormalities.

Conclusion: In this prospective cohort of patients with recently-diagnosed RA who underwent systematic evaluation for lung disease, airway and parenchymal abnormalities were commonly detected on HRCT but mild in severity. Pulmonary nodules were the most detected HRCT finding. Physiologic impairment was infrequent, and the stability of PFTs and dyspnea symptoms early after RA diagnosis is reassuring and may suggest that patients with asymptomatic imaging findings do not require treatment modifications, though longer follow-up periods are needed.

Table 2. Changes in PFT Parameters and MRC Dyspnea Scores over 1-Year of Follow-Up

	Baseline visit	1-Year Follow-Up Visit	P value*
Overall cohort (n=27)			
FVC % predicted	97.2 (18.8)	97.1 (18.8)	0.12
FEV1 % predicted	91.7 (21.2)	94.6 (22.4)	0.13
TLC % predicted	99.1(13.9)	100.6 (16.2)	0.47
DLCO % predicted	80.2 (13.6)	79.4 (14.9)	0.56
MRC dyspnea score (n=26)	0.7 (0.8)	0.7 (0.6)	0.63
Any airway or parenchymal disease (n=15)			
FVC % predicted	88.2 (16.4)	92.7 (20.7)	0.12
FEV1 % predicted	86.3 (21.2)	90.0 (24.4)	0.23
TLC % predicted	93.4 (13.1)	96.2 (15.5)	0.39
DLCO % predicted	80.3 (13.5)	80.1 (14.2)	0.88
MRC dyspnea score	0.9 (0.8)	0.8 (0.7)	0.77
Any airway disease (n=11)			
FVC % predicted	85.4 (15.9)	91.0 (15.5)	0.10
FEV1 % predicted	84.4 (21.8)	89.0 (20.6)	0.12
TLC % predicted	94.9 (13.4)	96.0 (16.1)	0.70
DLCO % predicted	80.9 (14.9)	80.8 (15.3)	0.96
MRC dyspnea score	1.1 (0.8)	0.7 (0.6)	0.10
Any parenchymal disease (n=4)			
FVC % predicted*	93.0 (19.1)	97.4 (34.1)	n/a
FEV1 % predicted*	91.7 (21.6)	92.7 (36.8)	n/a
TLC % predicted*	89.3 (13.1)	96.8 (15.9)	n/a
DLCO % predicted*	78.8 (10.7)	78.2 (12.6)	n/a
MRC dyspnea score	0.25 (0.5)	1.0 (0.8)	n/a

Values are mean (SD)
P value from t-test of individuals with baseline and 1-year follow-up PFTs
*n=4 with baseline and follow-up PFTs
Abbreviations: MRC, Medical Research Council; FVC, forced vital capacity; FEV1, forced expiratory volume in one second; TLC, total lung capacity; DLCO, diffusion capacity of the lung for carbon monoxide

Disclosure: T. Mahajan, None; **D. Hershberger**, None; **M. Devries**, None; **P. Roul**, None; **Y. Yang**, None; **S. Edwards**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **J. O'Dell**, None; **B. England**, Boehringer-Ingelheim, 2.

Abstract Number: 0575

World Mortality of Spondyloarthritis and Inflammatory Bowel Diseases in 2015 and Its Evolution Between 2001 and 2015

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: There is little epidemiological data on mortality in spondyloarthritis (SpA). This study aimed to determine countries' mortality rates of ankylosing spondylitis (AS) and psoriatic arthritis (PsA), as well as chronic inflammatory bowel diseases (IBDs), which are related to SpA, and to describe their evolution between 2001 and 2015.

Methods: We used mortality data from the World Health Organisation (WHO), freely available on its website, which shows the number of deaths classified by age, sex, and cause of death coded by ICD-10. The code M45 was used for AS, L405 for PsA, K50 for Crohn's disease (CD), and K51 for ulcerative colitis (UC). Age-standardized mortality rates (ASMR) were constructed using the 2015 WHO reference population and are expressed as deaths per million inhabitants. Temporal trend analyses of ASMR were performed between 2001 and 2015, considering only countries with up to 3 years of missing data, using joinpoint regression.

Results: In 2015, the global ASMR of AS was 0.13 (0.11-0.14), ranging from 0.02 in Japan to 2.00 in Iceland (Figure 1A). The ASMR was 0.20 (0.18-0.23) for men and 0.07 (0.06-0.09) for women ($p < 0.0001$). The trend analysis did not show any significant variation between 2001 and 2015 (Figure 2A). The ASMR in Europe (0.17 (0.15-0.20)) was significantly higher than in North America (0.12 (0.09-0.14)) ($p=0.008$), South America (0.09 (0.06-0.12)) ($p=0.0001$) and Asia (0.08 (0.05-0.10)) ($p < 0.0001$).

For PsA, the global ASMR in 2015 was 0.04 (0.03-0.05), ranging from 0.01 in Mexico to 0.13 in Greece (Figure 1B). The ASMR was 0.06 (0.04-0.07) for men and 0.03 (0.02-0.04) for women ($p=0.01$). The trend analysis showed a signif-

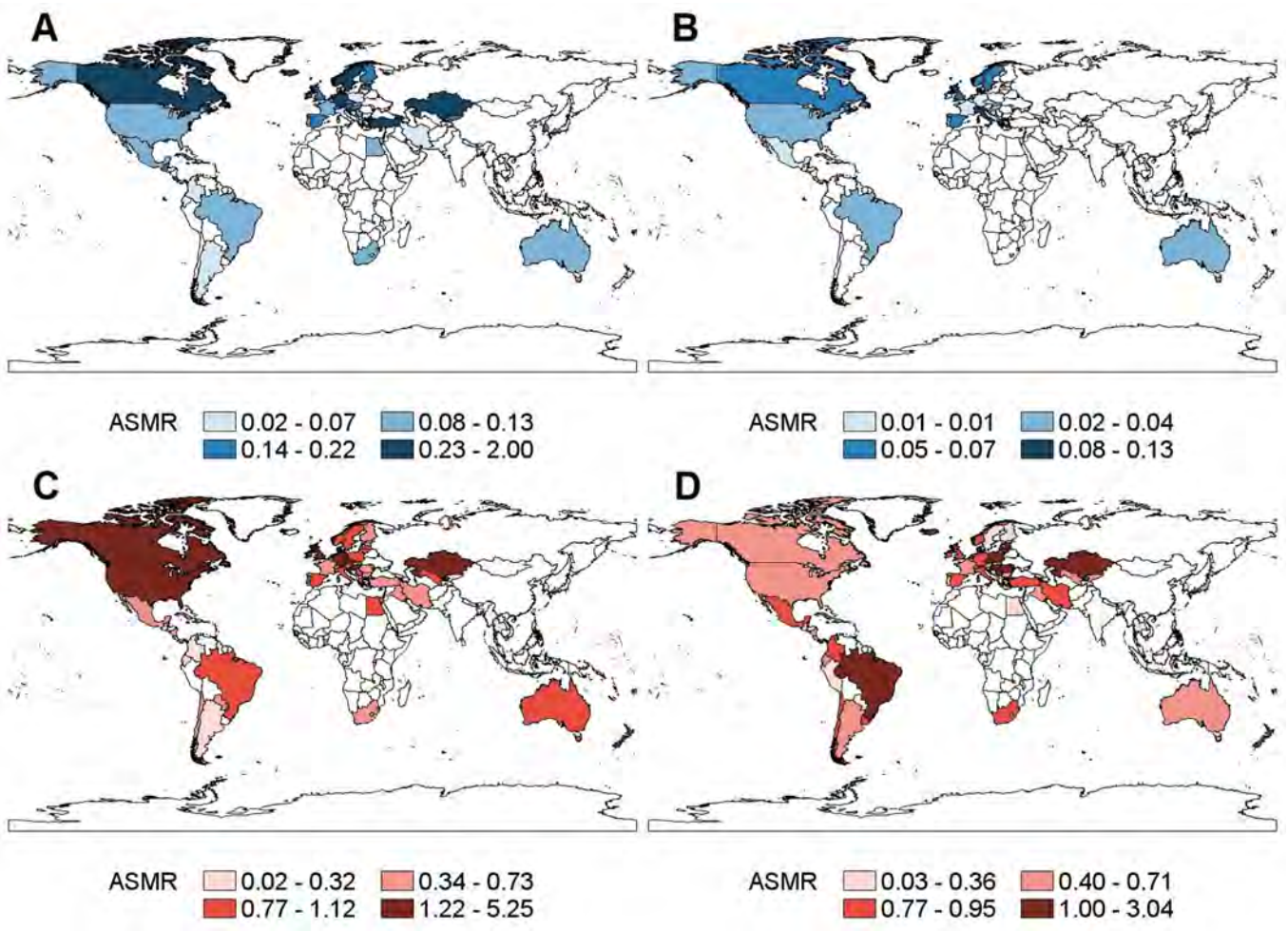

Figure 1. 2015 ASMR by country for ankylosing spondylitis (A), psoriatic arthritis (B), Crohn's disease (C) and ulcerative colitis (D).

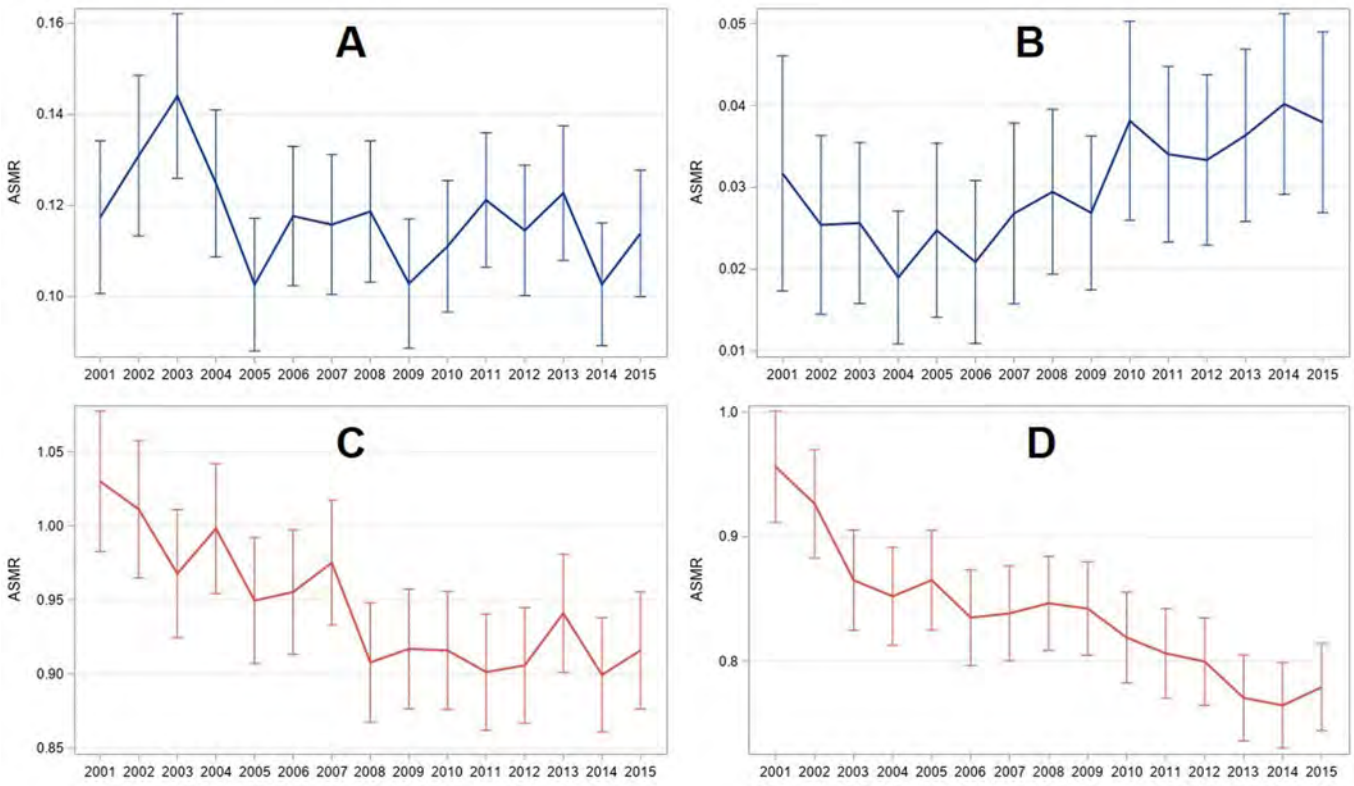

Figure 2. Evolution of the global ASMR with its 95% confidence interval from 2001 to 2015 for ankylosing spondylitis (A), psoriatic arthritis (B), Crohn's disease (C) and ulcerative colitis (D).

icant increase from 2004 to 2015 with a mean annual percent change (APC) of 5.94% (p=0.02) (Figure 2B). The ASMR in Europe (0.05 (0.03-0.06)) was significantly higher than in South America (0.02 (0.00-0.03)) (p=0.02).

For CD, the global ASMR in 2015 was 0.86 (0.82-0.89), ranging from 0.02 in Thailand to 5.25 in Luxembourg (Figure 1C). The ASMR was 0.41 (0.38-0.43) for men and 0.38 (0.36-0.41) for women (p=0.17). The trend analysis showed a significant decrease from 2001 to 2015 with a mean APC of -0.82% (p=0.048) (Figure 2C). The ASMR in Europe (1.12 (1.05-1.19)) was significantly lower than in North America (1.31 (1.21-1.41)) (p=0.001), but significantly higher than in South America (0.57 (0.51-0.64)) ($p < 0.0001$) and Asia (0.27 (0.23-0.32)) ($p < 0.0001$).

For UC, the global ASMR in 2015 was 0.76 (0.73-0.79), ranging from 0.03 in Thailand to 5.48 in Saint Lucia (Figure 1D). The ASMR was 0.37 (0.35-0.39) for men and 0.23 (0.21-0.24) for women ($p < 0.0001$). The trend analysis showed a significant decrease from 2001 to 2015 with a mean APC of -1.29% (p=0.01) (Figure 2D). The ASMR in Europe (1.00 (0.93-1.06)) was significantly higher than in North America (0.64 (0.57-0.71)) ($p < 0.0001$), Africa (0.57 (0.41-0.72)) ($p < 0.0001$), South America (0.84 (0.76-0.91)) (p=0.003)), Asia (0.47 (0.93-1.06)) and Oceania (0.58 (0.38-0.79)) (p=0.003).

Conclusion: ASMR for IBD are higher than those for SpA and are decreasing over time, in contrast to SpA where they remain essentially stable. There are geographical disparities which must be interpreted with caution due to the declarative nature of the data.

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Abstract Number: 0576

Associations of the *MUC5B* Promoter Variant with Timing of Articular Diagnosis and Interstitial Lung Disease in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The common promoter variant of *MUC5B* (G >T, rs35705950) is associated with increased mucin 5B production in lung parenchyma and is an established genetic risk factor for rheumatoid arthritis-associated interstitial lung disease (RA-ILD). The associations of this genetic polymorphism with features of the articular RA disease course and RA-ILD onset have not been previously studied. We investigated the association of the *MUC5B* promoter variant with age of RA onset and timing of RA-ILD within the RA disease course.

Methods: Patients with RA were identified from a large, multi-hospital biospecimen and clinical data collection study using a previously described algorithm and confirmed by medical record review. All patients with RA who had computed tomography (CT) imaging of the chest, lung biopsy, or autopsy were identified and screened for RA-ILD. RA-ILD was confirmed based on imaging findings, pulmonary function testing, and pathologic information using accepted criteria. We analyzed RA patients with available genotype information on

Table 1: Characteristics of patients with rheumatoid arthritis at enrollment (n=1,005).

Characteristic	*MUC5B* promoter variant (n=155)	No *MUC5B* promoter variant (n=850)	p-value
Demographics			
Female sex (n, %)	119 (76.7%)	676 (67.3%)	0.44
White (n, %)	139 (89.7%)	695 (81.8%)	**0.005**
Smoking			
Smoking status, n (%)			0.09
Never	67 (43.2%)	444 (52.3%)	
Past	72 (46.5%)	342 (40.3%)	
Current	16 (10.3%)	63 (7.4%)	
Smoking pack-years (median, IQR)	2.5 (0-17)	0 (0-8.8)	**0.007**
RA clinical features			
Age at articular RA diagnosis (years, median, IQR)	50.1 (36.1-60.0)	45.7 (32.9-56.6)	**0.045**
Articular RA diagnosis at age >55 years (n, %)	61 (39.4%)	242 (28.5%)	**0.008**
Seropositive RA (n, %)	85 (54.8%)	520 (61.2%)	0.33
RF-positive RA (n, %)	69 (44.5%)	463 (54.5%)	0.07
CCP-positive RA (n, %)	62 (40.0%)	376 (44.2%)	0.52
Shared epitope present (n, %)	75 (48.4%)	375 (44.1%)	0.29
RA-ILD (n, %)	20 (12.9%)	32 (3.8%)	**<0.0001**

CCP = cyclic citrullinated peptide; IQR = interquartile range; RA = rheumatoid arthritis; RF = rheumatoid factor; ULN = upper limit of normal

Table 2: Associations of the *MUC5B* promoter variant with RA and RA-ILD characteristics

Outcomes	*MUC5B* promoter variant (n=155)	No *MUC5B* promoter variant (n=850)
RA-ILD (n, %)	20 (12.9%)	32 (3.8%)
Unadjusted OR (95%CI)	**3.79 (2.10-6.82)**	Ref
Model 1 (main) OR (95%CI)	**3.59 (1.97-6.55)**	Ref
Model 2 (main + smoking) OR (95%CI)	**3.65 (2.00-6.68)**	Ref
RA-ILD in pre-RA or early RA* (n, %)	10 (6.5%)	10 (1.2%)
Unadjusted OR (95%CI)	**5.79 (2.37-14.16)**	Ref
Model 1 (main) OR (95%CI)	**5.84 (2.29-14.89)**	Ref
Multivariable model 2 (main + smoking) OR (95%CI)	**5.97 (2.35-15.13)**	Ref
Articular RA diagnosis at age >55 years (n, %)	61 (39.4%)	242 (28.5%)
Unadjusted OR (95%CI)	**1.63 (1.14-2.33)**	Ref
Model 1 (main) OR (95%CI)	**1.58 (1.10-2.27)**	Ref
Model 2 (main + smoking) OR (95%CI)	**1.56 (1.08-2.26)**	Ref

Model 1 = adjusted for age at RA diagnosis, sex, race
Model 2 = adjusted for age at RA diagnosis, sex, race, smoking status, and continuous smoking pack-years
* within five years of RA diagnosis
CI = confidence interval; OR = odds ratio; RA = rheumatoid arthritis; RA-ILD = rheumatoid arthritis-associated interstitial lung disease

rs35705950. Dates of RA and RA-ILD onset were determined by medical record review. Smoking and other covariate data were obtained by health questionnaire survey at enrollment and supplemented by electronic query and medical record review. We compared continuous variables using Wilcoxon rank sum tests and categorical variables using chi-squared tests. We examined the associations between *MUC5B* promoter variant status and features of RA including age of RA onset and RA-ILD onset relative to articular RA-onset using multivariable logistic regression.

Results: We identified 1,005 RA patients with available genotype data for rs35705950 (mean age 45 years; 79% women; 83% White). The *MUC5B* promoter variant was present in 155 RA patients (15.4%). A greater proportion of patients with the variant developed RA-ILD (12.9% vs. 3.8%, multivariable odds ratio (OR) 3.59 [95%CI 1.97-6.55]. Patients with the *MUC5B* promoter variant had increased odds of RA-ILD in the early RA period (prior to or within 5 years of articular RA diagnosis; OR 5.84, 95%CI 2.29-14.89). The *MUC5B* promoter variant was associated with older age of articular RA onset (50.1 vs 45.7 years, p=0.045) and increased odds of articular disease onset after age 55 (OR 1.58, 95%CI 1.10-2.27. The proportion with seropositive RA was similar by *MUC5B* status (54.8% vs. 61.2%, p=0.33).

Conclusion: We found that the *MUC5B* promoter variant may influence both older-onset RA and RA-ILD development in preclinical or early RA. *MUC5B* may impact RA-ILD risk early in the disease course of RA, particularly in those with older-onset RA, regardless of serostatus. These findings may lead to the identification of RA patients amenable to screening or prevention strategies for RA-ILD.

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Comorbidity Burden as Scored Using the Rheumatic Disease Comorbidity Index (RDCI) Is Associated with Varying Treatment Patterns in Patients with Inflammatory Arthritis – a Study Using the EHR-Derived Rheumatic and Arthritis Disease Information Registry (RADIR)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Higher comorbidity burden (CB) has been associated with treatment choices in RA, but not assessed in populations including multiple forms of inflammatory arthritis (IA) in routine practice settings. The Rheumatic Disease Comorbidity Index (RDCI), scored 0-9, is a validated method of quantifying CB in RA patients, but is infrequently reported in USA-based electronic health record (EHR)-derived cohort studies. The objective of this study is to examine if a higher CB is associated with differential prescribing and reported use (Rx) of oral glucocorticoids (GC) and TNF inhibitors (TNFi), therapies both commonly used to treat many forms of IA, using data from a new EHR-derived 'Rheumatic and Arthritic Diseases Information Registry' (RADIR) of patients with systemic rheumatic diseases (SRDs).

Methods: We constructed RADIR to include adults aged ≥ 18 years seen at least twice by a rheumatologist from 3/1/2018-2/28/2021 at a tertiary academic center in New York City. Eligible patients had ≥ 2 ICD-10-CM codes entered ≥7 days apart for a SRD which can present with IA. Patient data included demographics, labs, medications, and comorbid conditions (reported by ≥ 2 ICD-10-CM codes) to score the RDCI. Of 12,216 patients entered into RADIR, we included patients with forms of IA commonly treated with TNFi. IA patients included in this retrospective cohort study had ≥ 2 ICD-10-CM codes for RA, PsA, AS, SpA, JRA, JIA, Auto Inflammatory Syndromes, Enteric or Reactive Arthritis, Sarcoidosis, or Behcet's Disease. Rx of GC and TNFi, demographics, and comorbidities were compared in IA patients with a low CB (RDCI ≤ 2) and high CB (RDCI > 2) by Pearson's chi-squared tests. Two multivariable logistic regression models were used to assess for independent associations (odds ratio (OR), 95% CI) between RDCI score and Rx of GC and TNFi in IA, using age, gender, race, ethnicity, obese BMI and smoking as covariates.

Results: Patients with 11 types of IA (n= 6,587) were mostly white (74%), female (72%), and without exposure to tobacco (67%) (Table 1). Most frequent forms of IA were RA (65%) and PSA (22%) (Table 1). Patients with a high CB (RDCI >2) were older and more often Black, Hispanic/Latinx, and with a BMI ≥ 30 (Table 2). Patients with a high CB had more Rx of GC and less Rx of TNFi (Table 2). Regression analyses revealed that for every 1 point increase in the RDCI, there was a 0.09 decrease in the odds of Rx of TNFi (OR 0.91, 95%CI [0.85, 0.98]) and a 0.26 increase in the odds (OR 1.26, 95%CI [1.19, 1.33]) of Rx of GC, while controlling for age, sex, race, ethnicity, obesity and smoking status (Table 3).

Table 1. Patient Characteristics	
	Total Cohort (N=6,574)
Age in years, mean (SD)	58.7 (16.3)
Male Sex	1824 (27.7%)
Race	
White	4874 (74.1%)
Black	513 (7.8%)
Other	953 (14.5%)
Ethnicity	
Hispanic/Latinx	709 (10.8%)
Smoking Status	
Never	4404 (67.0%)
Ever (Former, Current, Passive)	2161 (32.9%)
Obese (BMI≥30)	2055 (31.3%)
Rheumatic Diseases	
RA	4287 (65.2%)
PsA	1436 (21.8%)
Other	979 (14.9%)
Comorbidity	
Lung Disease	435 (6.6%)
Myocardial Infarction	20 (0.3%)
Other Cardiovascular Disease	347(5.3%)
Stroke	46 (0.7%)
Hypertension	751 (11.4%)
Fracture	380 (5.8%)
Depression	250 (3.8%)
Diabetes mellitus	242 (3.7%)
Cancer	206 (3.1%)
Ulcer/Other Stomach Problem	72 (1.1%)
Current Medication Use	
Oral Steroids	1497 (22.8%)
csDMARDs	1774 (27.0%)
TNFi bDMARDs	1623 (24.7%)
Note: All results are reported as n (%) unless otherwise noted. Comorbid conditions were used to calculate the RDCI and were determined using ICD-10 codes. Some pts had more than one IA diagnosis.	

Conclusion: This analysis of a large sample of IA patients cared for in practice included in a new EHR-derived registry of SRDs indicates more patients will be prescribed GCs and fewer prescribed TNFi as CB progressively increases, a relationship previously only described in RA. These data suggest that IA patients with a high CB may be receiving suboptimal treatment. These findings may have implications regarding safety, effectiveness and health disparities of Rx patterns that warrant further investigation.

Table 2. Comparison of Demographics, Comorbidities and Medication in IA Patients with High vs. Low Comorbidity Burden Estimated using the Rheumatic Disease Comorbidity Index (RDCI)

Variable	Low Comorbidity Burden (RDCI≤2)	High Comorbidity Burden (RDCI>2)	P-Value
N = 6574	6215	359	<0.01
Age in years, mean (SD)	58.1 (16.4)	68.1 (12.9)	<0.01
Male Sex	1718 (27.6%)	106 (29.5%)	0.44
Race			
White	4617 (74.3%)	257 (71.6%)	<0.01
Black	468 (7.5%)	45 (12.5%)	
Other	905 (14.6%)	48 (13.4%)	
Ethnicity			
Hispanic/Latinx	676 (10.9%)	33 (9.2%)	0.030
Smoking Status			
Ever Smoker	1996 (32.1%)	165 (46.0%)	<0.01
Obese (BMI≥30)	1890 (30.4%)	165 (46.0%)	<0.01
Comorbidity			
Lung Disease	216 (3.5%)	219 (61.0%)	<0.01
Myocardial Infarction	6 (0.1%)	14 (3.9%)	<0.01
Other Cardiovascular Disease	167 (2.7%)	180 (50.1%)	<0.01
Stroke	24 (0.4%)	22 (6.1%)	<0.01
Hypertension	537 (8.6%)	214 (59.6%)	<0.01
Fracture	271 (4.4%)	109 (30.4%)	<0.01
Depression	151 (2.4%)	99 (27.6%)	<0.01
Diabetes mellitus	159 (2.6%)	83 (23.1%)	<0.01
Cancer	153 (2.5%)	53 (14.8%)	<0.01
Ulcer or Other Stomach Problem	51 (0.8%)	21 (5.8%)	<0.01
RDCI, Median (IQR)	0 (0,1)	3 (3,4)	<0.01
Prescribed/Reported Medication			
Oral Glucocorticoids	1364 (21.9%)	133 (37.0%)	<0.01
csDMARDs	1657 (26.7%)	117 (32.6%)	0.017
TNFi bDMARDs	1574 (25.3%)	49 (13.6%)	<0.01
Non-TNFi bDMARDs	768 (12.4%)	49 (13.6%)	0.46

Values are reported as n (%) unless noted; Ever smoker = former, current, or passive smoker

Table 3: The Odds of being prescribed or reporting use of TNFi or GC in patients with IA with an increasing Comorbidity Burden as scored by RDCI

	Model 1 – TNF inhibitors		Model 2 – Glucocorticoids	
Model Co-Variates	OR (95% CI)	p-value	OR (95% CI)	p-value
Per 1 Unit of RDCI	0.91 (0.86, 0.98)	0.01	1.26 (1.19, 1.33)	<0.01
Age	0.98 (0.97,0.98)	<0.01	1.01 (1.01,1.01)	<0.01
Male Sex	1.32 (1.16,1.50)	<0.01	0.77 (0.67, 0.89)	<0.01
Black	0.87 (0.69,1.09)	0.21	1.36 (1.11,1.68)	<0.01
Hispanic or Latinx	0.90 (0.73,1.10)	0.29	1.38 (1.14, 1.68)	<0.01
Obese BMI (≥30)	1.15 (1.01,1.31)	0.03	1.04 (0.91, 1.19)	0.55
Ever Smoker	0.92 (0.81, 1.05)	0.24	1.01 (0.89, 1.15)	0.90

RDCI Rheumatic Diseases Comorbidity Index (0-9); Data are from 2 independent regression models

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Abstract Number: 0578

Hyperinsulinemic Diet and Increased Risk of Female Gout: 2 Prospective Cohort Studies of US Women over 30 Years

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SESSION INFORMATION
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Background/Purpose: Gout and the metabolic (insulin resistance) syndrome frequently coexist. Intravenous insulin has been shown to raise serum urate (SU) levels in physiologic studies[1] and a Mendelian Randomization study[2] showed a causal role of fasting insulin on the risk of hyperuricemia and gout. However, it is unknown whether habitual hyperinsulinemic dietary intake confers gout risk, especially in women, a pertinent subgroup given the rising global burden of female gout,[3] and higher prevalence of obesity and type II diabetes in female gout patients compared to males. We prospectively examined the relation between two distinct insulin-related dietary indices and risk of incident gout in two large cohorts of US women over 30 years.

Methods: We studied 170,699 women from the Nurses Health Study I (1986-2016) & II (1989-2017) free of gout at baseline. Dietary intake and covariates were ascertained by validated questionnaires every 2-4 years, along with new cases of physician-diagnosed gout every 2 years. Insulinemic potential of diet was evaluated using: 1) a food-based

Table 1. Hazard Ratio (HR) of Incident Gout According to Quintiles of Insulin-Related Dietary Index

	Q1: Least insulinemic	Q2	Q3	Q4	Q5: Most insulinemic	P for trend
EDIH (dietary hyperinsulinemic potential): measure of insulin resistance						
N cases	681	804	991	1216	1591	
Person-years	864,128	864,106	864,051	863,383	861,601	
Incidence rate (per 1000 person-years)	79	93	115	141	185	
Incidence rate ratio	1.00 (Ref)	1.21	1.50	1.84	2.41	
Age-adjusted HR (95% CI)	1.00 (Ref)	1.20 (1.08 to 1.32)	1.50 (1.36 to 1.66)	1.91 (1.74 to 2.10)	2.64 (2.41 to 2.89)	<0.001
Multivariable HR (95% CI)*	1.00 (Ref)	1.10 (0.99 to 1.22)	1.30 (1.18 to 1.43)	1.54 (1.40 to 1.70)	1.91 (1.74 to 2.09)	<0.001
Multivariable HR (95% CI) (+ BMI)**	1.00 (Ref)	1.03 (0.93 to 1.14)	1.16 (1.05 to 1.28)	1.30 (1.18 to 1.43)	1.49 (1.35 to 1.63)	<0.001
Dietary Insulin Index (DII): measure of transient, post-prandial insulin secretion and sensitivity						
	Q1: Lowest Insulin Sensitivity	Q2	Q3	Q4	Q5: Greatest Insulin Sensitivity	P for trend
N cases	1293	1095	1044	948	903	
Person-years	863,311	863,854	863,656	863,791	862,656	
Incidence rate (per 1000 person-years)	150	127	121	110	105	
Incidence rate ratio	1.00 (Ref)	0.85	0.81	0.73	0.70	
Age-adjusted HR (95% CI)	1.00 (Ref)	0.86 (0.79 to 0.93)	0.82 (0.76 to 0.89)	0.75 (0.69 to 0.81)	0.69 (0.64 to 0.76)	<0.001
Multivariable HR (95% CI)*	1.00 (Ref)	0.82 (0.76 to 0.89)	0.79 (0.73 to 0.86)	0.73 (0.67 to 0.80)	0.74 (0.68 to 0.80)	<0.001
Multivariable HR (95% CI) (+ BMI)**	1.00 (Ref)	0.88 (0.81 to 0.95)	0.85 (0.78 to 0.92)	0.77 (0.71 to 0.84)	0.74 (0.68 to 0.81)	<0.001

*Multivariable (MV) models adjusted for age (month), White race, smoking, menopause, hormone use, physical activity (MET h/week), history of hypertension, and diuretic use. **MV + BMI models additionally adjusted for body mass index (BMI), a likely causal intermediate.

empirical dietary index for hyperinsulinemia (EDIH) score that was pre-defined based on circulating C-peptide levels,[4] and reflects *insulin resistance*;[5] and 2) dietary insulin index (DII), which reflects *transient, postprandial insulin secretion*.[5] We assigned EDIH and DII scores for each woman, adjusted for total energy intake, and used Cox proportional hazard models to prospectively examine the relation between cumulative average scores and incident gout, adjusting for potential confounders.

Results: We ascertained 5,283 cases of incident gout over 4,317,270 person-years: 3,670 cases in the NHS and 1,613 in the NHS II. In pooled multivariable-adjusted (MV) analyses, women in highest EDIH quintile (i.e., higher insulin resistance) had 1.9-times (95% CI 1.7 to 2.1) greater gout risk, compared to the lowest (**Table 1**). This attenuated with further adjustment for BMI, a likely causal intermediate, but remained positive (MV HR 1.5, 95% CI 1.4 to 1.7). DII scores were inversely associated with gout risk (HR 0.74, 95% CI 0.68 to 0.80) (**Table 1)**.

Table 2. Hazard Ratio (HR) of Incident Gout According to Quintiles of Hyperinsulinemic Diet (EDIH) Score, by subgroups

	Q1: Least insulinemic	Q2	Q3	Q4	Q5: Most insulinemic	P for interaction
Age, years						
< 60	1.00 (Ref)	1.20 (1.00 to 1.44)	1.39 (1.17 to 1.66)	1.73 (1.47 to 2.05)	2.06 (1.75 to 2.42)	0.24
≥ 60	1.00 (Ref)	1.06 (0.94 to 1.20)	1.25 (1.11 to 1.41)	1.45 (1.29 to 1.62)	1.82 (1.63 to 2.04)	
Body mass index, kg/m^2						
< 25	1.00 (Ref)	1.15 (0.97 to 1.35)	1.30 (1.11 to 1.54)	1.35 (1.14 to 1.60)	1.70 (1.43 to 2.02)	0.82
25-29.9	1.00 (Ref)	0.86 (0.72 to 1.02)	1.02 (0.86 to 1.20)	1.08 (0.91 to 1.28)	1.46 (1.24 to 1.71)	
≥ 30	1.00 (Ref)	1.13 (0.92 to 1.38)	1.22 (1.01 to 1.47)	1.51 (1.26 to 1.80)	1.59 (1.34 to 1.89)	
Physical activity, MET h/week						
< 25	1.00 (Ref)	1.12 (0.99 to 1.25)	1.31 (1.17 to 1.47)	1.54 (1.38 to 1.71)	1.90 (1.72 to 2.11)	0.69
≥ 25	1.00 (Ref)	1.06 (0.85 to 1.32)	1.24 (1.00 to 1.55)	1.56 (1.26 to 1.94)	1.99 (1.61 to 2.46)	
Alcohol use						
No	1.00 (Ref)	1.20 (0.94 to 1.54)	1.10 (0.87 to 1.40)	1.47 (1.17 to 1.85)	1.95 (1.56 to 2.43)	0.34
Yes	1.00 (Ref)	1.07 (0.96 to 1.20)	1.35 (1.21 to 1.50)	1.54 (1.39 to 1.72)	1.84 (1.66 to 2.04)	

EDIH effects were similar across subgroups (**Table 2**) and cohorts, with HRs of 1.8 (1.7 to 2.1) in the NHS I (mean age of 50 years at baseline; 49% post-menopausal) and 2.1 (1.7 to 2.4) in the NHS II (mean age 36 years at baseline; 3.6% post-menopausal).

Conclusion: EDIH scores, reflecting chronic hyperinsulinemia (i.e., greater insulin resistance with reduced clearance), were positively associated with the risk of incident gout in these large prospective cohorts of US women, even beyond the pathway through adiposity. Conversely, higher DII scores, which reflect short-term, postprandial elevations in insulin levels (i.e., higher insulin sensitivity) conferred a lower risk. This corroborates human physiologic experiments[1] and Mendelian Randomization studies[2] showing insulin resistance can increase SU levels by decreasing renal excretion of urate and supports lowering insulinemic potential of diet as a strategy to reduce gout risk, especially in women.

[1]Facchini *JAMA* (1991); PMID 1820474
[2]McCormick *Arthrit Rheum* (2021); PMID 33982892
[3]Xia; *Rheumatology* (2020); PMID 31624843
[4]Tabung; PMID 27821188
[5]Lee; PMID 32618519

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Abstract Number: 0579

Predicting Treatment Change in Rheumatoid Arthritis Patients Treated with TNF Inhibitors as First-Line Biologic Agent

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patient characteristics including serostatus, body mass index (BMI), and smoking are considered to be associated with their response to disease-modifying anti-rheumatic drugs (DMARD) treatment for rheumatoid arthritis (RA); however, previous real-world studies using claims data failed to identify factors strongly related to biologic DMARD treatment patterns. We utilized a linked database of claims and electronic health records (EHR) to explore how additional factors derived from the clinically rich EHR data may play a role in predicting

Methods: We used Optum Market Clarity database which linked pharmacy and medical claims with continuous, longitudinal EHR data from 01/01/2011 to 09/30/2019. We identified adults with RA who initiated a TNFi from prescription or procedure records. The first TNFi prescription date was defined as index date. Patients were required to have at least two RA diagnosis codes without any biologic or targeted synthetic (ts) DMARDs during 365-day pre-index baseline period. One-year continuous clinical activity were required before and after the index date. Outcomes were assessed during one-year post-index period. The primary outcome was any treatment change defined as having a different TNFi or switching to non-TNFi biologic or tsDMARDs. The secondary outcomes were the individual components of the primary outcome and non-persistence. Treatment non-persistence was defined as having no subsequent refill of the index TNFi or other biologics/tsDMARDs. Multivariable logistic regression with pre-defined variables and least absolute shrinkage and selection operator (LASSO) regression model were used as prediction models. C-statistics of each model and odds ratios (OR) with 95% confidence intervals of predictors were reported.

Results: We identified 24,871 RA cohort who initiated TNFi: 10,471 adalimumab, 1,166 certolizumab pegol, 9,391 etanercept, 1,037 golimumab, and 2,806 infliximab initiators. The mean age was 55.5 (±13.7) years and 77.2% were female. 83% were White, and 53.3% were covered by commercial insurances. 30.9% of the study patients were seropositive (**Table 1**). During the one-year after index TNFi initiation, 5,527 (22.2%) patients had either TNFi cycling or switching to non-TNFi/tsDMARDs. Specifically, 3,870 (15.6%) had TNFi cycling, 1,646 (6.6%) switched to non-TNFi biologics, and 780 (3.1%) switched to tsDMARDs. 5,157 (20.7%) were non-persistent users. In multivariable logistic regression models, index TNFi, gender, race, and insurance types were predictors of the treatment changes (**Table 2**). Model performance was similar between the regular and LASSO regression models. Adding EHR-specific factors, including BMI, smoking status, and serology tests improved the prediction models to some extent but the model performance was still suboptimal (c-statistics 0.64).

Conclusion: Predicting treatment change in RA patients with both claims and clinically rich EHR data still remains challenging. It could be due to unmeasured factors such as prescriber's preference or patient's belief in the medication which may play an important role in the treatment patterns.

Table 1. Selected baseline characteristics of study population

N	**24871**
Age on the index date, years, mean (SD)	55.5 (13.7)
Female sex, n (%)	19194 (77.2%)
RACE, n (%)	
African American	2324 (9.3%)
Asian	297 (1.2%)
White	20636 (83.0%)
Other/Unknown	1614 (6.5%)
Ethnicity, n (%)	
Hispanic	1506 (6.1%)
Not Hispanic	21736 (87.4%)
Unknown	1629 (6.6%)
Insurance type, n (%)	
Commercial	13260 (53.3%)
Medicaid	1845 (7.4%)
Medicare	4246 (17.1%)
Other Payor Type	696 (2.8%)
Uninsured	1035 (4.2%)
Unknown	3789 (15.2%)
Frailty score, n (%)	
Robust	15016 (60.4%)
Prefrail	8823 (35.5%)
Mildly frail	995 (4.0%)
Moderate to severe frail	37 (0.15%)
Combined comorbidity score, mean (SD)	0.73 (1.6)
Comorbidities and medication, n (%)	
Heart failure	629 (2.5%)
Interstitial lung disease	1029 (4.1%)
Inflammatory bowel disease	583 (2.3%)
Malignancy	2049 (8.2%)
Systemic lupus erythematosus	413 (1.7%)
Type 2 diabetes	3296 (13.3%)
NSAIDs	11354 (45.7%)
Selective cox-2 inhibitors	7302 (29.4%)
Opioids	9867 (39.7%)
Systemic glucocorticoids	11716 (47.1%)
Serostatus, n (%)	
Positive	7690 (30.9%)
Negative	4759 (19.1%)
Missing	12422 (49.9%)

*Adjusted for index drug (ref = adalimumab), age, female sex, race, ethnicity, region, insurance type, index calendar year, BMI categories, smoking status, diabetes, heart failure, venous thromboembolism, psoriasis, systemic lupus erythematosus, inflammatory bowel disease, malignancy, interstitial lung disease, combined comorbidity score, frailty score, NSAIDs, Coxib-2 inhibitors, systemic glucocorticoids, opioids, CRP/hsCRP test results, serostatus.

Table 2. Adjusted* OR (95% CI) and performance of regular multivariable prediction models

	Any treatment change	Non-persistence
N (%) of outcome	*5527 (22.2) %*	*5157 (20.7%)*
C-stat	*0.640*	*0.630*
Index TNFi		
Certolizumab	1.61 (1.40, 1.85)	0.73 (0.62, 0.85)
Etanercept	1.08 (1.01, 1.16)	0.99 (0.92, 1.06)
Golimumab	1.30 (1.12, 1.51)	0.61 (0.51, 0.73)
Infliximab	0.72 (0.64, 0.82)	0.49 (0.43, 0.55)
Adalimumab	ref	ref
Age (yr)	0.99 (0.99, 0.99)	1.01 (1.01, 1.01)
Gender		
Female	1.30 (1.21, 1.41)	1.01 (0.94, 1.09)
Male	ref	ref
Race		
African American	0.70 (0.62, 0.78)	1.09 (0.98, 1.22)
Other	0.99 (0.87, 1.12)	1.05 (0.92, 1.20)
White	ref	ref
Ethnicity		
Hispanic	0.80 (0.69, 0.93)	1.19 (1.03, 1.37)
Non-Hispanic	ref	ref
Insurance type		
Medicaid vs. commercial	1.02 (0.90, 1.14)	0.97 (0.85, 1.10)
Medicare vs. commercial	1.00 (0.90, 1.10)	1.01 (0.92, 1.11)
Other payer type vs. commercial	0.89 (0.74, 1.07)	1.11 (0.92, 1.34)
Uninsured vs. commercial	0.67 (0.57, 0.79)	1.56 (1.35, 1.81)
Commercial	ref	ref
BMI		
Underweight	0.94 (0.71, 1.26)	1.12 (0.85, 1.47)
Overweight	1.03 (0.94, 1.13)	1.04 (0.95, 1.14)
Obese	1.12 (1.03, 1.22)	1.01 (0.93, 1.10)
Normal	ref	Ref
Smoking status		
Current smoker	0.98 (0.89, 1.07)	1.21 (1.10, 1.33)
Past smoker	1.04 (0.97, 1.12)	1.05 (0.97, 1.14)
Never smoker	ref	ref
Combined comorbidity score	0.97 (0.94, 0.99)	1.05 (1.03, 1.08)
Serostatus		
Negative	1.10 (1.02, 1.19)	1.06 (0.97, 1.16)
Positive	ref	ref

*Adjusted for index drug (ref = adalimumab), age, female sex, race, ethnicity, region, insurance type, index calendar year, BMI categories, smoking status, diabetes, heart failure, venous thromboembolism, psoriasis, systemic lupus erythematosus, inflammatory bowel disease, malignancy, interstitial lung disease, combined comorbidity score, frailty score, NSAIDs, Coxib-2 inhibitors, systemic glucocorticoids, opioids, CRP/hsCRP test results, serostatus.

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Abstract Number: 0580

Association Between Female Reproductive Factors and Gout: A Nationwide Population-based Cohort Study of 1 Million Postmenopausal Women

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

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Background/Purpose: Previous studies have shown that the incidence and risk factors of gout differs according to sex. However, little research has been done on the association between reproductive factors and gout. We conducted an analysis of a large nationwide population-based cohort of postmenopausal women to determine whether there is an association between reproductive factors and the incidence of gout.

Methods: A total of 1,076,378 postmenopausal women aged 40–69 years who participated in national health screenings in 2009 were included in the study. The outcome was the occurrence of incident gout, which was defined using the ICD-10 code of gout (M10) in the claim database. Cox proportional hazard models were used for the analyses and stratified analyses according to body mass index (BMI) and the presence/absence of chronic kidney disease (CKD) were performed.

Results: The mean follow-up duration was 8.1 years, and incident cases of gout were 64,052 (incidence rate, 7.31 per 1,000 person-years). Later menarche, earlier menopause, and a shorter reproductive span were associated with a high risk of gout. No association between parity and gout incidence was observed. Use of oral contraceptives (OC) and hormone replacement therapy (HRT) were associated with an increased risk of gout. The association between reproductive factors and gout was not statistical significant in the high BMI group. The effects of OC and HRT usage on gout were not significant in the CKD group.

Conclusion: Shorter exposure to endogenous estrogen was associated with a high risk of gout. Conversely, exposure to exogenous estrogen such as OC and HRT was associated with an increased risk of gout.

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Rheumatoid Arthritis Treatment Patterns in Massachusetts: Informative Findings from Insurance Claims Data

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Background/Purpose: A real-world current state of RA patients in Massachusetts (MA) is analyzed to provide a novel assessment of demographics, treatment patterns, and clinical settings of care, with particular focus on initial and subsequent prescribing patterns of DMARDs.

Methods: This was a retrospective cohort analysis of the MA Center for Health Information and Analysis all-payers claims database from 2013-2017, which aggregates claims data covering ~70% of the population, excluding traditional (fee-for-service) Medicare. The analytic cohort included all adults (18+ years) with ³2 RA-related claims on different dates. The treated cohort required ³1 claim for a conventional synthetic, biologic, or targeted synthetic DMARD (csDMARD, bDMARD, or tsDMARD, respectively). Further analysis included treatment patterns by year, demographics, medication, and specialization level (non-rheumatology (i.e. PCP and other specialty), general rheumatology, or a designated RA Center of Excellence).

Table 1 shows the baseline and demographic characteristics of the RA analysis cohort and treated RA cohort, including gender, age, index year, number of patients, insurance type, specialization level and duration data

Variable	RA Analysis Cohort N=70,613	Treated RA Cohort N=39,062
Gender		
Male	17,290 (24.5)	9,332 (23.9)
Female	52,735 (74.7)	29,350 (75.1)
Other/Unknown	588 (0.8)	380 (1.0)
Age Category, years (Prevalent)		
RA Patient Age Observations		
2013-2017[1], N	246,014	145,095
18-24	3,613 (1.5)	2,562 (1.8)
25-34	9,879 (4.0)	6,768 (4.7)
35-44	19,591 (8.0)	13,079 (9.0)
45-54	44,982 (18.3)	30,227 (20.8)
55-64	62,750 (25.5)	40,974 (28.2)
65-74	52,820 (21.5)	30,362 (20.9)
75+	52,379 (21.3)	21,123 (14.6)
Index Year		
2013	38,589 (54.6)	23,327 (59.7)
2014	11,412 (16.2)	5,375 (13.8)
2015	9,535 (13.5)	4,654 (11.9)
2016	6,451 (9.1)	3,414 (8.7)
2017	4,626 (6.5)	2,292 (5.9)
RA Treatment Index Year		
2013		11,510 (55.1)
2014		5,265 (13.5)
2015		4,456 (11.4)
2016		4,397 (11.3)
2017		3,434 (8.8)
RA Patients "Present"[2]		
2013	38,589 (54.6)	23,258 (59.5)
2014	48,316 (68.4)	28,011 (71.7)
2015	54,976 (77.9)	31,500 (80.6)
2016	53,555 (75.8)	32,045 (82.0)
2017	50,719 (71.8)	30,296 (77.6)
Insurance Type[3]		
PPO	12,904 (18.3)	7,178 (18.4)
HMO	19,041 (27.0)	13,437 (34.4)
Medicaid	15,221 (21.6)	8,287 (21.2)
Medicare (Part A or B)	9,166 (13.0)	3,964 (10.1)
Other	14,811 (21.0)	6,195 (15.9)
Specialization level[4]		
Rheumatology at COE	10,756 (15.2)	7,895 (20.2)
General rheumatology	17,953 (25.4)	11,886 (30.4)
Non-rheumatology	41,904 (59.3)	19,281 (49.4)
Duration Data[5]		
0-6 months	1,212 (1.7)	375 (1.0)
6-12 months	2,013 (2.9)	886 (2.3)
12-24 months	4,603 (6.5)	2,066 (5.3)
24-36 months	9,793 (13.9)	4,129 (10.6)
36-48 months	7,885 (11.2)	4,553 (11.7)
>48 months	45,107 (63.9)	27,053 (69.3)

RA: Rheumatoid arthritis; PPO: Preferred provider organization; HMO: Health maintenance organization; COE: Center of excellence

[*]Values are the number (%) unless indicated otherwise. Results are based all patients in each cohort unless otherwise stated.

[1] Age category is summarized for patients who have been diagnosed with RA (i.e., index year and later) who are "Present" (have at least one claim) in data set for year of observation. Table presents aggregate of age observations across 2013-2017, therefore patients contribute for each year of observation. Patient count reflects sum of years of observation (with non-missing age) for RA population.

[2] RA Patients "Present" by year summarizes the size of the RA cohort by year. To be counted, patients must have been diagnosed with RA (i.e., index year and later) and have at least one claim in data set for year of observation.

[3] Table includes all observed insurance types; therefore, categories will add to more than 100%.

[4] Specialization level was the most specialized care setting at which a patient had at least 2 encounters according to the hierarchy: rheumatology at center of excellence, general rheumatology, non- rheumatology.

[5] Duration data is a claims-based proxy for patient-level observation time and is calculated as the duration between a patient's first (earliest date) medical or pharmacy claim and last (latest date) medical or pharmacy claim.

Results: The analytic cohort comprised 70,613 patients. The majority were female (74.7%), age ³45 years (86.6%), index date in 2013 (54.6%), the latter suggesting established RA diagnoses. (Table 1) The treated cohort included 39,062 patients (55.3%), of which 13,149 (33.7%) received only a single csDMARD, predominately HCQ (46.4%) or MTX (44.9%). HCQ as a single agent was more common in female patients of childbearing age, with HCQ use falling

Table 2 shows RA treatment groups and patterns by DMARD type

Treatment Groups 2013-2017	Treated RA Cohort N=39,062	
Any csDMARD	***18,670 (47.8)***	
1 csDMARD only	13,149 (33.7)	
>1 csDMARD	5,521 (14.1)	
Any TNFi/other bDMARD/tsDMARD (+/- csDMARD)	***20,392 (52.2)***	
Single TNFi/other bDMARD/tsDMARD (+/- csDMARD)	***11,145 (28.5)***	
1 TNFi only	2,888 (7.4)	
1 TNFi and 1+ csDMARD	5,502 (14.1)	
1 other bDMARD only	1,357 (3.5)	
1 other bDMARD and 1+ csDMARD	1,095 (2.8)	
1 tsDMARD only	59 (0.2)	
1 tsDMARD and 1+ csDMARD	244 (0.6)	
Multiple TNFi/other bDMARD/tsDMARD (+/- csDMARD)	***9,247 (23.7)***	
> 1 other bDMARD	2,495 (6.4)	
Other bDMARD, TNFi, and 1+ csDMARD	1,800 (4.6)	
> 1 other bDMARD and 1+ csDMARD	1,576 (4.0)	
> 1 TNFi and 1+ csDMARD	1,379 (3.5)	
Other bDMARD and TNFi	681 (1.7)	
Other bDMARD, TNFi, tsDMARD, and 1+ csDMARD	354 (0.9)	
> 1TNFi	320 (0.8)	
TNFi, tsDMARD, and 1+ csDMARD	318 (0.8)	
Other bDMARD, tsDMARD, and 1+ csDMARD	175 (0.4)	
Other bDMARD and tsDMARD	56 (0.1)	
TNFi and tsDMARD	52 (0.1)	
1 csDMARD only 2013-2017, N	**13,149**	
Hydroxychloroquine	6,107 (46.4)	
Methotrexate	5,901 (44.9)	
Sulfasalazine	648 (4.9)	
Leflunomide	493 (3.7)	
Multiple csDMARDs 2013-2017, N	**5,521**	
csDMARD regimen (15+ days overlap)	4,953 (89.7)	
Combination csDMARD Therapy 2013-2017		
Number patients with a multiple csDMARD regimen, N₂	***4,953 (% N₂[1])***	
Number of multiple csDMARD regimens observed, N₂	***7,938***	***(% N₂[2])***
Methotrexate, hydroxychloroquine	4,202 (84.8)	(52.9)
Hydroxychloroquine, sulfasalazine	1,287 (26.0)	(16.2)
Methotrexate, sulfasalazine	809 (16.3)	(10.2)
Hydroxychloroquine, leflunomide	656 (13.2)	(8.3)
Methotrexate, leflunomide	550 (11.1)	(6.9)
Methotrexate, hydroxychloroquine, sulfasalazine	176 (3.6)	(2.2)
Leflunomide, sulfasalazine	169 (3.4)	(2.1)
Hydroxychloroquine, leflunomide, methotrexate	56 (1.1)	(0.7)
Hydroxychloroquine, leflunomide, sulfasalazine	24 (0.5)	(0.3)

csDMARD: conventional synthetic disease modifying anti-rheumatic drug; TNFi: tumor necrosis factor inhibitor; bDMARD: biologic disease modifying anti-rheumatic drug; tsDMARD: targeted synthetic disease modifying anti-rheumatic drug

[1] Values are the number (%).

[2] Patients can add to multiple categories, therefore categories will add up to more than 100%.

[3] Excludes combinations with <11 patients, therefore categories will not add up to 100%.

Note: Treatment groupings represent all RA drug observations (all claims for RA drugs) for the specified time period (2013-2017) and do not differentiate sequential versus concomitant use, except where noted for combination csDMARD therapy.

steadily with increasing age, opposite that of MTX. An additional 14.1% received >1 csDMARD, either sequentially (1.4%) or in combination (12.7%). MTX plus HCQ was the most common regimen in 84.8% of patients on combination therapy. Triple therapy (MTX, HCQ, and SSZ) was taken by 3.6% of patients receiving combination csDMARD-only therapy. (Table 2)

A bDMARD and/or tsDMARD was taken by 20,392 patients (52.2%), of which 9,247 (45.3%) had claims for >1 bDMARD or tsDMARD, suggesting a regimen change. (Table 2) Among a subcohort of 3,495 patients who took ³1 bDMARD or tsDMARD with ³6 months of prescribing data prior to the first prescription, etanercept (ETN) and

Table 3 shows a subcohort analysis of patients who took more than one biologic and targeted synthetic DMARD with at least 6 months of prescribing data prior to the first prescription, demonstrating initial and subsequent biologic or targeted synthetic DMARD with duration between 1st and 2nd drug

		Specialization Level		
	Overall	Rheumatology COE	General Rheumatology	Non-Rheumatology
Initial b/tsDMARD Sub-cohort, N	**3,495**			
	3,495 (100)	1,365 (39.1)	1,351 (38.7)	779 (22.3)
1st b/tsDMARD, N[1]	**3,495**	**1,365**	**1,351**	**779**
Etanercept	1,222 (35.0)	448 (32.8)	486 (36.0)	288 (37.0)
Adalimumab	1,093 (31.3)	433 (31.7)	418 (30.9)	242 (31.1)
Abatacept	289 (8.3)	147 (10.8)	93 (6.9)	49 (6.3)
Rituximab	235 (6.7)	92 (6.7)	81 (6.0)	62 (8.0)
Tofacitinib	208 (6.0)	91 (6.7)	86 (6.4)	31 (4.0)
Infliximab	199 (5.7)	57 (4.2)	89 (6.6)	53 (6.8)
Golimumab	129 (3.7)	42 (3.1)	55 (4.1)	32 (4.1)
Tocilizumab	62 (1.8)	25 (1.8)	25 (1.9)	12 (1.5)
Certolizumab Pegol	46 (1.3)	23 (1.7)	** **	** **
Other[2]	** **	** **	** **	** **
2nd b/tsDMARD Users	**998** (28.6)			
Duration Between 1st, 2nd b/tsDMARD, N	**998**			
0-3 months	663 (66.4)			
3-6 months	128 (12.8)			
6-12 months	118 (11.8)			
12+ months	89 (8.9)			
2nd b/tsDMARD, N[1]	**998**			
Adalimumab	287 (28.8)			
Etanercept	186 (18.6)			
Tofacitinib	117 (11.7)			
Abatacept	105 (10.5)			
Tocilizumab	96 (9.6)			
Infliximab	69 (6.9)			
Golimumab	57 (5.7)			
Rituximab	45 (4.5)			

COE: center of excellence, b/tsDMARD: biologic disease modifying anti-rheumatic drug/targeted synthetic disease modifying anti-rheumatic drug

*Values are the number (%).
**Individual cell counts <11 and cell counts from which individual cell counts <11 could be calculated are suppressed.
[1] Excludes cells of <11 patients, therefore categories will not add up to 100%.
[2] Other includes Anakinra and Sarilumab

adalimumab (ADA) were the most common initial agents (66.3%). Of those, 998 patients (28.6%) had claims for a second bDMARD or tsDMARD. Of 998, a TNF-inhibitor (TNFi) was the first agent in 818 (82.0%), and the second agent for the majority was another TNFi (70.3%), followed by other bDMARD (20.5%) and tsDMARD (9.2%). (Table 3)

Specialization level was rheumatology for 40.7% of the analysis cohort, 50.6% of the treated cohort, and 77.7% of those initiating a bDMARD or tsDMARD. (Table 1). Drug selection varied by specialization level. Among the 8,390 (21.5%) patients receiving a single TNFi agent (+/- csDMARD), more patients received ETN and ADA in rheumatology settings and infliximab in non-rheumatology settings.

Conclusion: Overall, DMARD prescribing was low, and there was a high level of HCQ monotherapy and TNFi use. An unexpectedly high number of RA patients in MA were treated in non-rheumatology settings. This first state-wide current state analysis of RA in MA elucidates treatment patterns for RA in the United States, highlighting opportunities for practice improvement and helping to direct treatments in a timely and patient-centered fashion.

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Abstract Number: 0582

Altered Risk of Gout According to Change of Metabolic Parameters in Young Adults

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Background/Purpose: Previous studies have shown a link between gout and metabolic syndrome (MetS). It is well known that lifestyle modifications such as weight reduction and abstinence from alcohol are effective in the treatment of gout, but data are lacking on how exactly the change of metabolic parameters affects gout. The purpose of this study was to investigate the relationship between gout risk and metabolic parameters in a nationwide population based young adult cohort, and to determine whether changes in metabolic parameters affect gout risk changes.

Methods: Among adults aged 20-39 years who participated in the national health checkup program from 2009 to 2012, 2,598,905 subjects who participated in the health checkup again two years later were included in the analysis to evaluate the effect of changes in metabolic parameters on the occurrence of gout. Outcome was defined as the occurrence of gout, where the ICD-10 code M10 was registered twice in the claim database. Cox proportional hazard model and Kaplan Meier curve were used for analysis.

Results: The mean age of the study population was 32.7 years, and 62.4% were male. The mean follow-up duration was 5.71 years, and 71,245 subjects were newly diagnosed with gout (incidence rate 4.80 per 1,000 person-years). Compared to those who did not have MetS at two health screenings, the risk of gout was 2.5 times higher in those who had MetS consistently (adjusted HR 2.54; 95% CI 2.48, 2.60). The adjusted HR of gout of those who did not have MetS at the first checkup but developed MetS at the second checkup was 1.88, and the adjusted HR of gout of those who had MetS at the first checkup but did not have MetS at the second checkup was 1.76. Each component of MetS was also associated with an increase in the risk of gout, and hypertriglyceridemia and abdominal obesity showed the greatest association.

Conclusion: In young adults, the risk of gout was highest in those with persistent MetS compared to those who did not. Among the components of MetS, hypertriglyceridemia and abdominal obesity had the greatest association with the risk of gout. Management of MetS in young adults is helpful in reducing the risk of gout.

Disclosure: Y. Eun, None; **I. Kim**, None; **K. Han**, None; **S. Kang**, None; **S. Lee**, None; **H. Cha**, None; **E. Koh**, None; **H. Kim**, None; **J. Lee**, None.

Abstract Number: 0583

Obesity and Lower Socioeconomic Position Are Independently Associated with Incident Osteoarthritis and Rheumatoid Arthritis: Results from the English Longitudinal Study of Ageing

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1: Weighted Cox proportional hazards regression for the associations between different definitions of obesity and SEP indicators and OA and RA

Predictors	OA		RA	
	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI)	Unadjusted HR (95% CI)	Fully adjusted HR (95% CI)
Total obesity (BMI≥30kg/m²)				
Non-obesity	ref	ref	ref	ref
Obesity	1.54 (1.39, 1.71)	1.47 (1.33, 1.64)	1.63 (1.42, 1.87)	1.50 (1.31, 1.73)
Central obesity (WC≥102 cm for men and ≥88 cm for women)				
Non-central obesity	ref	ref	ref	ref
Central obesity	1.46 (1.33, 1.62)	1.34 (1.21, 1.48)	1.54 (1.34, 1.77)	1.37 (1.19, 1.58)
Education				
Less than O-level	ref	ref		
O-level or equivalent	0.76 (0.68, 0.85)	0.88 (0.78, 0.99)	0.62 (0.53, 0.73)	0.78 (0.66, 0.92)
Higher than O-level	0.64 (0.57, 0.72)	0.81 (0.71, 0.92)	0.51 (0.44, 0.61)	0.70 (0.58, 0.83)
Occupation (NS-SEC3)				
Routine / manual	ref	ref	ref	ref
Intermediate	0.85 (0.75, 0.96)	0.88 (0.78, 0.99)	0.76 (0.65, 0.90)	0.83 (0.70, 0.99)
Managerial / professional	0.70 (0.62, 0.78)	0.81 (0.72, 0.92)	0.54 (0.46, 0.64)	0.65 (0.55, 0.77)
Wealth (1=least amount of wealth, 5= most amount of wealth)				
Quintile 1	ref	ref	ref	ref
Quintile 2	0.82 (0.70, 0.97)	0.89 (0.75, 1.05)	0.78 (0.63, 0.96)	0.90 (0.72, 1.12)
Quintile 3	0.76 (0.65, 0.89)	0.82 (0.70, 0.97)	0.65 (0.53, 0.80)	0.78 (0.63, 0.97)
Quintile 4	0.66 (0.56, 0.77)	0.73 (0.62, 0.87)	0.57 (0.46, 0.71)	0.73 (0.58, 0.91)
Quintile 5	0.55 (0.47, 0.64)	0.65 (0.55, 0.77)	0.38 (0.31, 0.48)	0.53 (0.41, 0.67)
Index of Multiple Deprivation (1= most deprived, 5= least deprived)				
Quintile 1	ref	ref	ref	ref
Quintile 2	0.76 (0.63, 0.90)	0.79 (0.66, 0.94)	0.77 (0.61, 0.96)	0.81 (0.65, 1.02)
Quintile 3	0.75 (0.63, 0.88)	0.78 (0.66, 0.93)	0.61 (0.49, 0.77)	0.68 (0.54, 0.86)
Quintile 4	0.66 (0.56, 0.77)	0.69 (0.58, 0.82)	0.54 (0.44, 0.68)	0.60 (0.48, 0.76)
Quintile 5	0.64 (0.54, 0.75)	0.71 (0.59, 0.84)	0.45 (0.36, 0.57)	0.54 (0.43, 0.68)

HR, hazard ratio; CI, confidence interval; ref, reference category; WC, waist circumference; NS-SEC, national statistic socio-economic classification. Fully adjusted model for obesity/central obesity: adjusted for gender, age, ethnicity, alcohol, smoking, education, occupation, wealth and index of multiple deprivation. Fully adjusted model for socioeconomic indicators: adjusted for age, gender, alcohol, smoking, BMI and WC. There was no indication of moderation between obesity and SEP indicators and incident OA/RA. Overall p-values for interaction OA: obesity*education=0.691, obesity*occupation=0.890, obesity*wealth = 0.882, obesity*IMD=0.252. Overall p-values for interaction RA: obesity*education=0.409, obesity*occupation=0.138, obesity*wealth=0.759, obesity*IMD=0.422.

Background/Purpose: Obesity is a known risk factor for OA and hypothesised as a risk factor for RA, although due to different underlying mechanisms. Lower socioeconomic position (SEP) has also been associated with both OA and RA. Given the well-established links between SEP and obesity, there may be interactions between these two risk factors in the development of OA and RA. This study investigated obesity and SEP in relation to incident OA and RA including potential interactions between obesity and SEP.

Methods: The English Longitudinal Study of Ageing (ELSA) is a nationally representative panel study of adults aged ≥50 years, with biannual waves of data collection (2002–2019). Participants with at least one nurse visit measuring height, weight and waist circumference (WC) and one follow-up assessment were included in this study. BMI of ≥30kg/m^2 and WC ≥102 cm for men and ≥88 cm for women defined total and central obesity, respectively. Level of education, occupation (current or last occupation if retired), wealth quintiles and index of multiple deprivation (IMD) quintiles were used as SEP indicators. Outcomes were self-reported incident OA and RA during follow-up. Prevalent OA and RA cases at baseline were excluded for the two different samples; however, people with OA could be included in the RA analyses and vice versa. Weighted Cox proportional hazards models were used to investigate the associations of obesity and SEP indicators with incident OA and RA separately, controlling for baseline covariates. Effect modification of each SEP indicator and obesity was tested by including interaction terms between them. Multiple imputation using chained equations was used to impute missing data on predictors and covariates.

Results: The OA and RA analyses included 9,281 (51.3% female; mean age 63.6 (SD 9.6); mean follow-up 7.8 (SD 4.2) years; and 2,369 incident cases of OA) and 10,931 (54.1% female; mean age 64.0 (standard deviation (SD) 9.6); mean follow-up 8.8 (SD 4.2) years; and 1,216 incident cases of RA) participants, respectively. In both samples, more women than men had total and central obesity. Total and central obesity were both associated with incident OA and RA and these associations were maintained after adjustment for covariates, including SEP indicators (Table 1). Those with the lowest education, who are/were employed in manual/routine occupations, who have lower wealth status and were from the most deprived areas were more likely to develop OA and RA; this is seen in basic models and maintained after adjustments for covariates including BMI and WC (Table 1). There was no evidence of effect modification/interactions between obesity and SEP indicators.

Conclusion: Obesity and SEP are both associated with incident OA and RA among adults aged 50 years and older in England and there was no evidence of an interaction between obesity and SEP indicators for incident OA and RA. Although obesity is a known risk factor for OA, the results show that SEP is independently associated with incident OA. Educating rheumatologists and public health experts about the importance of both of these factors, may result in better prevention strategies. To understand underlying mechanisms, further research should investigate the mediators of these associations.

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Abstract Number: 0584

High Number of Comorbidities and Concomitant Medications at Baseline in the Glucocorticoid Low-dose Outcome in Rheumatoid Arthritis (GLORIA) Study: An Older Population with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Older people are often underrepresented in trials because the generally high number of comorbid conditions (1). The objective of this abstract is to document the baseline status and frequency of comorbid conditions and concomitant medications in the GLORIA study population which consists of older rheumatoid arthritis (RA) patients.

Methods: This double-blind, randomized, placebo-controlled, multicenter trial (2) was open for patients with RA according to the 1987 or 2010 criteria, age ≥65 years, and disease activity score of 28 joints (DAS28) of ≥2.6. Its pragmatic design featured minimal exclusion criteria tailored to seniors. Patients were recruited from rheumatology clinics in 7 European countries. Eligible patients were randomized to two years of treatment with daily 5 mg prednisolone or matching placebo. All other medication was allowed, except for glucocorticoids.

Results: The population consists of 451 patients with mean disease duration 10.6 (Q1-Q3: 3-15) years. The majority (70%) is female, mean age is 72.5 (Q1-Q3: 68-76, range: 65-88) years, 66% were positive for rheumatoid factor and 56% for ACPA. Patients had a median of 6 comorbidities besides RA (4 active) and therefore used multiple medications (median 7, max 19 for all indications) (Table 1). The most common comorbidities in this older population are, by system organ class: cardiac and vascular disorders (17%), musculoskeletal and connective tissue disorders excl. RA (16%), and metabolism and nutrition disorders (9%). At baseline, patients were most frequently on medication for gastroprotection or hypertension (both 51%). Most patients also have an extensive history of anti-rheumatic treatment. At the start of the trial most patients (79%) were on cDMARD treatment; 14% were on bDMARDs/tsDMARDs. Almost half of the patients previously had been treated with glucocorticoids, with a mean duration of 3.4 years and a mean last dose of 4.6 mg/day.

Conclusion: Our data show the medical reality of a study population aged 65+ when minimal eligibility criteria are applied. These patients with multiple comorbidities next to RA and concomitant treatment are similar to patients seen

Table 1. Reported comorbidities and concomitant medications at baseline in the safety population of the GLORIA trial (n=449; total number of comorbidities: 2752).

Comorbidities, (median, range per patient)	**6**	**0-26**
Active	4	0-15
Past	1	0-14
By System Organ Class (%)		
Cardiac and Vascular Disorders	17	
Hypertension	9	
Musculoskeletal (excl RA)	16	
Osteoarthritis	4	
Osteoporosis	4	
Metabolism	9	
Lipid/cholesterol	5	
Diabetes	2	
Concomitant medications (median, range)	**7**	**0-19**
By indication (%)		
Osteoporosis (excl Ca/D)	13	
Anticoagulation	22	
Gastroprotection	51	
Hypertension	51	
Hypercholesterolemia	28	
Diabetes	7	
RA disease features (mean, SD)		
DAS28 (as observed), mean (SD)	4.5	1.0
DAS28CRP (as observed), mean (SD)	4.1	1.0
HAQ (0-3), mean (SD)	1.2	0.7
RA treatment (patient count, %)	**Current**	**Previous**
cDMARD	356 (79)	133 (30)
bDMARD/tsDMARD	65 (14)	47 (10)
NSAID	111 (25)	326 (72)
Glucocorticoids	xxx	210 (47)

in routine care. This increases generalizability and relevance of the trial results. At the same time, interpretation of those results, especially those regarding safety of the intervention, will need to take comorbidity into account.

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Abstract Number: 0585

Predictors of Health-Related Quality of Life in Rheumatoid Arthritis Patients

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

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Background/Purpose: Health-related quality of life (HRQoL) is lower in rheumatoid arthritis (RA) patients compared to the general population, yet a comprehensive study evaluating predictors and the relative contribution of sociodemographic, RA-related, comorbidities, and lifestyle factors is lacking. Our study's objectives were to identify factors that predict 1) HRQoL one year after baseline assessment; and 2) change in HRQoL over 12 months.

Methods: Survey data from a longitudinal quality of care study of RA patients recruited from a population-based cohort identified using administrative data were analysed. Participants who completed a questionnaire in 2015 and 2016 assessing sociodemographic, health status (RA-related and comorbidities), and lifestyle variables were included. The dependent variable HRQoL was measured using EQ5D-VAS. Three model selection procedures for multivariable linear regression models – stepwise selection (p-entry< 0.05;p-exit≥0.15), all-possible selection, and LASSO method – were used to select important HRQoL predictors. Models were compared using cross-validation (CV) and the model with smallest CV error was selected. Model selections without and with 2015 EQ5D-VAS, in separate analyses, were conducted to determine best models for absolute value-, and change in HRQoL, respectively. We used R^2 to assess the variance explained by each model and to determine the relative contributions of sociodemographic, RA-related, comorbidities, and lifestyle factors (sum of R^2 values for each domain). Data analyses were conducted using RStudio 1.3.1093.

Results: Our sample included 168 individuals with RA (72% women, mean age 70.7 ± 10.6 years, mean disease duration 24.3 ± 11.9 years). EQ5D-VAS in 2016 was 67.5/100 ± 19.4. Significant predictors and variance explained

Table 1. Model excluding 2015 HRQoL

Variable	Coefficient (95%CI)	p-value	R^2
Age >65yo (yes vs. no)	7.37 (1.94, 12.80)	<0.01	0.025
Alcohol consumption (yes vs. no)	7.75 (2.20, 13.31)	<0.01	0.061
Depression score (0-27)	-1.44 (-2.01, -0.86)	<0.01	0.143
HAQII (0-3)	-8.04 (-12.23, -3.86)	<0.01	0.100
Smoking (yes vs. no)	9.80 (0.42, 19.18)	0.041	0.008
Total model AIC=1416.93, R^2=0.34			

*Variables evaluated for inclusion in the multivariable model included Sociodemographic factors (age, sex, ethnicity, marital status, rural vs. urban residence, education, employment, income), health status factors (RA-related measures [physical function (HAQII), disease activity (RADAI), pain, fatigue], and comorbidities, including depression (PHQ9), obesity), and lifestyle factors (physical activity, smoking, alcohol consumption).

Table 2. Model including 2015 HRQoL			
Variable	**Coefficient (95%CI)**	**p-value**	**R^2**
Age >65yo (yes vs. no)	5.61 (0.42, 10.81)	0.034	0.019
Alcohol consumption (yes vs. no)	7.14 (1.88, 12.39)	<0.01	0.052
Depression score (0-27)	-0.71 (-1.35, -0.07)	0.030	0.086
RADAI (0-10)	-0.06 (-0.12, 0.00)	0.058	0.073
Sex (male)	4.74 (-0.64, 10.12)	0.084	0.010
2015 HRQoL (0-100)	0.39 (0.23, 0.55)	<0.01	0.162
Total model AIC=1401.85, R^2=0.40			
*Variables evaluated for inclusion in the multivariable model included Sociodemographic factors (age, sex, ethnicity, marital status, rural vs. urban residence, education, employment, income), health status factors (RA-related measures [physical function (HAQII), disease activity (RADAI), pain, fatigue), and comorbidities, including depression (PHQ9), obesity), and lifestyle factors (physical activity, smoking, alcohol consumption).			

by models without, and with, 2015 HRQoL are presented in Tables 1 and 2, respectively. The model controlling for baseline 2015 HRQoL had a lower AIC and better predictive ability (R^2 value) for 2016 HRQoL. HRQoL in the previous year contributed most to predicting HRQoL. Of the RA-related factors, only disease activity and physical function (in models with, and without, 2015-HRQoL) were significant predictors. Both variables were highly correlated (r=0.69) and likely capture similar disease effects. Of the comorbidities evaluated, only depression predicted HRQoL, and it had a greater contribution to HRQoL than RA-related factors. Lifestyle and sociodemographic factors evaluated in our study contributed little to HRQoL.

Our study limitations include potential respondent bias and a predominantly White and older sample with longstanding disease. Our findings may not be generalizable to samples with different characteristics.

Conclusion: HRQoL in our RA sample was multifactorial. Predictors from different domains contributed to HRQoL. HRQoL in the previous year contributed most to predicting future HRQoL. Depression was the second most important predictor. Early identification and management of depression may improve overall HRQoL in RA patients.

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Abstract Number: 0586

Recommended Fiber Intake, but Not Overall Dietary Quality, Is Associated with Reduced Risk of Rheumatoid Arthritis – Results from a Nested Case-control Study

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1.

Table 1. Cut-off values for dietary components included in the Diet Quality Index (DQI).

DQI components	Recommendation
Fibre (g/MJ)	≥2.4
Vegetables and fruits (g/day)	≥400
Fish (g/week)	≥300
Sucrose (E%)	<10
Saturated fatty acid (E%)	≤14
Polyunsaturated fatty acid (E%)	5–10

Background/Purpose: Diet has received attention as a factor possibly contributing to development of rheumatoid arthritis (RA). The aim of this study was to investigate the relation between overall diet quality, diet components, and the risk of RA.

Methods: Participants in a population-based cohort established in 1991-1996 who were subsequently diagnosed with RA were identified through register linkage and validated in a structured process. Four controls for each case, matched for sex, year of birth, and year of inclusion, were selected from the study cohort. The controls were alive

Table 2.

Table 2. Odds ratios (ORs) describing the relation between Diet Quality Index (DQI) and its components and the risk of developing rheumatoid arthritis. Conditional logistic regression analysis.

	Adjusted for total energy intake*		Adjusted for total energy intake, smoking, alcohol (quintiles), leisure time physical activity*	
	OR	95% CI	OR	95% CI
DQI components				
Compliant with recommendation				
Fiber	**0.48**	**0.28–0.82**	**0.51**	**0.29–0.90**
Vegetables and fruits	**0.52**	**0.31–0.88**	**0.55**	**0.32–0.95**
Fish	1.13	0.70–1.81	1.25	0.76–2.05
Sucrose	0.84	0.51–1.40	0.90	0.53–1.55
Saturated fatty acids (SFA)	0.81	0.46–1.41	0.86	0.48–1.52
Polyunsaturated fatty acids (PUFA)	1.63	0.96–2.76	1.66	0.97–2.85
DQI-score				
0–1	1.00	(Ref)	1.00	(Ref)
2–4	1.27	0.75–2.18	1.53	0.87–2.68
5–6	0.79	0.37–1.72	0.94	0.41–2.12
Total	0.89	0.75–1.05	0.93	0.78–1.11
Continuous variables per SD				
Fiber	**0.71**	**0.53–0.94**	**0.73**	**0.54–0.98**
Vegetables and fruits	0.76	0.57–1.00	0.78	0.59–1.03
Fish	1.07	0.85–1.35	1.16	0.90–1.49
Sucrose	1.06	0.84–1.35	1.03	0.80–1.32
Saturated fatty acids	0.98	0.76–1.27	0.95	0.73–1.24
Polyunsaturated fatty acids	1.10	0.86–1.40	1.11	0.86–1.43

Standard deviation (SD), Percent of total energy intake (E%), Confidence interval (CI), Reference (Ref)
* All energy misreporters excluded

and RA-free when the index person was diagnosed with RA. At inclusion, diet was assessed using a seven-day food diary, a diet history questionnaire, and a complementary diet interview.

The validated Diet Quality Index (DQI) has been developed for distinguishing high-quality and low-quality diets by assessing adherence to the Swedish nutrition recommendations from 2005 and the Swedish dietary guidelines. The DQI score ranges from 0 to 6. A score of 1 is assigned to each component where the individual is compliant with the recommendation, i.e. fiber, fruit and vegetables, fish and shellfish, saturated fat, polyunsaturated fat, and sucrose (Table 1).

We applied conditional logistic regression analysis to study the relation between DQI, its components, and RA. The DQI was divided into categories, defined as low (0–1) (reference), moderate (2–4) and high (5–6), the category "low" was set as the reference. All models were adjusted for reported total energy intake, and potential misreporters of total energy intake were excluded.

We designed multivariable models in which we included covariates that have been associated with diet and RA (smoking, alcohol and leisure time physical activity). Interrelationships between dietary variables were assessed using Spearman's correlation test.

Results: In the study population, 172 RA cases were identified. Greater fiber intake was associated with decreased risk of RA both as dichotomous (i.e. compliant with recommendation or not) and continuous variables, with adjusted odds ratios (ORs) 0.48 (95% CI 0.28–0.82) and 0.71 per SD (95% CI 0.53–0.94), respectively. Furthermore, intake of vegetables and fruit >400 g/day was associated with decreased risk of RA, OR 0.52 (95% CI 0.31–0.88). The DQI was not associated with RA in these models (Table 2).

In multivariable models, associations for fiber and vegetables and fruits remained significant. There were strong correlations between intakes of vegetables and fruits and fiber (r=0.67 for continuous variables and r=0.50 for dichotomous variables). In the final multivariable model, compliance with the recommendation for intake of fibre was associated with lower risk of RA (OR 0.51; 95% CI 0.29–0.90).

Conclusion: In conclusion, fiber intake was independently associated with decreased risk of RA. Fiber intake was highly correlated with intake of vegetables and fruits, which was also associated with decreased risk of RA in multivariable models. No statistically significant associations were seen for DQI with the development of RA. Our results indicate that individual foods, rather than overall diet quality, associate with RA.

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Abstract Number: 0587

DMARD Use in Medicare Patients with Rheumatoid Arthritis and Risk of Long-Term Opioid Use

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Table 1. Risk of Long-Term Opioid Use Based on DMARD Regimen

	DMARD Regimen	Adjusted OR (95% CI)
Drug Group	No DMARD	1.00 (Reference)
	Single DMARD*	0.91 (0.85, 0.97)
	DMARD Combination*	0.86 (0.78, 0.94)
	Non-TNF Biologic‡ without Methotrexate	0.88 (0.79, 0.97)
	Non-TNF Biologic‡ + Methotrexate	0.87 (0.77, 0.98)
	TNF without Methotrexate	0.88 (0.79, 0.97)
	TNF + Methotrexate	0.83 (0.75, 0.91)

* Includes Methotrexate, Leflunomide, Sulfasalazine, Hydroxychloroquine
‡ Includes Rituximab, Abatacept, IL-6 inhibitors, and JAK Inhibitors

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk for opioid use. Disease-modifying antirheumatic drugs (DMARDs) have led to better control of disease activity. Whether this has led to decreased opioid use in RA patients for pain control is unclear. We thus conducted a cross-sectional study examining different types of DMARD use in patients with rheumatoid arthritis (RA) and its association with long-term opioid use using national Medicare database.

Methods: We identified a cohort of RA patients enlisted in Medicare database for the year 2017-18 who were receiving at least 30-day prescription of opioids. We evaluated the long-term opioid use in this cohort. Long-term opioid use was defined as receiving opioid prescription for at least 90 consecutive days. The risk of long-term opioid use was compared between DMARD users and non-DMARD users. Patients on DMARDs were further subclassified into regimens set forth by American College of Rheumatology (ACR) for treatment of RA. Demographics and risk factors including depression, anxiety, drug use, and opioid use disorder were also obtained.

Results: The study was composed of 27, 028 RA patients receiving opioid prescription for at least 30 days. The mean age was 69.7 years, 80% were female, 76.8% were Caucasian, and 11.7% were African American. Seventy percent of patients were on DMARDs. Long-term opioid use was lower among DMARD users compared to non-DMARD users (37.4% vs 43.3%). Risk factors for long-term opioid use were common in both groups but higher in non-DMARD users (anxiety 42.8% vs 31.9%, depression 43.6% vs 36.6%, previous drug abuse 18.6% vs 12.2%, and previous opioid use disorder 17.0% vs 11.0%). After adjusting for these factors, the odds of long-term opioid use was significantly lower among DMARD users compared to non-DMARD users (OR 0.89, 95% CI 0.84-0.93). The odds remained low irrespective of DMARD regimen (Table 1).

Conclusion: DMARD use in RA patients was associated with decreased risk of long-term opioid use. These agents represent a possible opportunity to lower the risk of long-term opioid use in an especially vulnerable population. Appropriate use of DMARDs in RA patients may result in decreased dependence on opioids for chronic pain.

Disclosure: A. Sood, None; **Y. Kuo**, None; **J. Westra**, None; **M. Raji**, None.

Abstract Number: 0588

Effectiveness of TNFi versus Non-TNFi Biologics on Disease Activity in Obese Patients with Rheumatoid Arthritis: Data from the ACR's RISE Registry

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Our understanding of how medications such as biologic disease modifying anti-rheumatic drugs and targeted small molecules (b/tsDMARDs) influence disease activity in RA is based largely on randomized controlled trials (RCTs). However, most U.S. trials in RA are limited by small sample sizes and have often excluded patients who are older, male, racial/ethnic minorities and across the spectrum of body mass index (BMI). Whether effectiveness of b/tsDMARDs varies in real-world populations has largely been unexplored. We aimed to examine differences in longitudinal RA disease activity by demographic and clinical characteristics using the RISE registry. We simulated various treatment assignments of b/tsDMARDs that have been examined in RCTs: namely, TNF-inhibitors (TNFi) and non-TNFi.

Methods: We included 16,448 individuals from the ACR's RISE registry with > 2 RA diagnoses (ICD-9: 714.0, ICD-10: M06.9) > 30 days apart, who had at least 2 recorded clinical disease activity index (CDAI) scores and no historical b/tsDMARD use documented in RISE. b/tsDMARD use and CDAI scores were assessed at each quarter; covariates included sex, race (white, Black, Asian, other), ethnicity (Hispanic/non-Hispanic), age, smoking, obesity (BMI > 30 mg/kg2), area deprivation index, other DMARD use, RF status, anti-CCP status, and practice type. Longitudinal targeted maximum likelihood estimation estimated the average treatment effect (ATE) of cumulative TNFi vs. non-TNFi use over a 12-month period on CDAI score among the entire population and across various subgroups based on demographic and clinical characteristics, accounting for censoring.

Results: Approximately 75% of patients were female with a mean age of 65.1 (+/- 13.7) years. Sixty percent of patients were white, 8% black, 2% Asian, and 30% other/mixed or unknown race; 6% were Hispanic, and 42% obese.

Table 1. Average treatment effect (ATE) of cumulative TNFi vs. non-TNFi use at 12-months on CDAI score in obese patients with RA

	TNFi vs. Non-TNFi ATE (95% CI)	TNFi vs. Abatacept ATE (95% CI)	TNFi vs. Rituximab ATE (95% CI)	TNFi vs. Tocilizumab ATE (95% CI)	TNFi vs. Tofacitinib ATE (95% CI)
Overall (n=16,448)	0.85 (-0.26, 1.96)	2.37 (1.38, 3.35)*	2.12 (1.21, 3.02)*	2.71 (1.79, 3.64)*	0.44 (-0.45, 1.34)
Obese					
Yes (n=6,832)	0.63 (-1.08, 2.34)	3.29 (1.96, 4.61)*	-1.06 (-2.36, 0.23)	0.68 (-0.55, 1.92)	1.08 (-0.07, 2.23)
No (n=9,616)	0.64 (-0.71, 1.99	0.63 (-0.56, 1.81)	1.84 (0.83, 2.84)	4.00 (2.97, 5.03)*	-0.60 (-1.74, 0.54)

*$P<0.05$

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

The mean CDAI score at baseline was 11.3 (+/- 10.7). For the overall population, there was no significant difference in disease activity between TNFi and non-TNFi at 12 months (ATE= 0.85, 95% CI -0.26, 1.96; Table 1). Similarly, there was no significant difference in disease activity between TNFi and non-TNFi in obese and non-obese individuals. However, analyses by specific non-TNFi medications demonstrated higher disease activity associated with TNFi use compared to abatacept in obese patients (ATE=3.29, 95% CI 1.96, 4.61), but not non-obese patients. Contrastingly, TNFi use was associated with higher disease activity compared to tocilizumab in non-obese patients (ATE=4.00, 95% CI 2.97, 5.03), but not obese patients. In analyses comparing TNFi use and rituximab, and TNFi and tofacitinib, there were no differences in disease activity scores at 12 months for obese and non-obese patients.

Conclusion: Results from this RCT simulation study suggest that specific non-TNFi may have differential effects for obese and non-obese individuals with rheumatic disease, even though some medications are adjusted for weight. These novel findings fill gaps where RCTs have not been conducted, highlight the need for inclusion of diverse populations in future trials, and have the potential to lead to a more personalized approach to rheumatologic care.

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Abstract Number: 0589

Circulating Adipokines and Risk of Rheumatoid Arthritis in Women

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Adipokines secreted by adipose tissues thought to be involved in RA pathogenesis by stimulating systematic inflammation. We examined the association between circulating adipokines (leptin, visfatin and resistin) and risk of developing RA in women.

Methods: We conducted a nested case-control study within the Nurses' Health Study and Nurses' Health Study II among 202 incident RA cases with a preclinical blood sample and 399 controls (~1:2) who were free of RA at the time of diagnosis of index case, and matched on age, ethnicity, fasting status, time of day of blood draw, and menopausal status /hormone use. All covariates were measured before blood draw. Adipokine biomarkers were log-transformed to improve normality. Multivariable linear regression models adjusted for matching factors and other potential confounders were used to examine the differences in adjusted means of circulating leptin, visfatin, and resistin between pre-clinical RA cases and controls. We examined strata defined by age at RA diagnosis, BMI, time between blood draw and RA (0-3.9, 4-< 7.9 and >8 years), and RA seropositivity (rheumatoid factor and/or anti-cyclic citrullinated peptide).

Results: Characteristics of the pre-RA cases and controls are shown in Table 1. After adjusting for matching factors and other risk factors, pre-clinical RA cases had a significantly higher level of leptin compared with controls (p=0.002) (Table 2). No significant differences were observed in levels of visfatin and resistin between all pre-clinical RA cases and controls. In stratified analyses for leptin, significant associations were found among women aged 55 years or

Table 1. Age-standardized characteristics of study participants at one questionnaire cycle prior to blood draw in the NHS and NHS II

	NHS		NHS II	
	Pre-RA Cases (n=75)	Controls (n=148)	Pre-RA Cases (n=127)	Controls (n=251)
Age, years, mean (SD) [a]	51.5 (5.5)	51.5 (5.6)	44.4 (5.6)	44.6 (5.7)
Census annual income, dollar, mean (SD)	51417.8 (21273.6)	52189.1 (19663.2)	47685.8 (17957.1)	48635.2 (21157.2)
BMI, kg/m^2, mean (SD)	25.4 (4.1)	24.9 (4.1)	27 (5.3)	25.7 (5.6)
Smoking packyears, %				
Never smoker	50.6	43.9	56.3	67.0
<10	14.7	23.0	10.8	14.4
10-20	10.8	9.5	16.2	9.4
20+	23.9	23.0	16.7	8.3
Missing	0.0	0.7	0.0	0.8
Smoking status, %				
Never	50.6	43.9	56.3	67.0
Past	40.2	43.9	27.6	20.4
Current	9.2	12.2	16.1	11.8
Alcohol intake, g/day, mean (SD)	5.6(7.1)	6.8(9.5)	3.9 (6.8)	3.8 (6.4)
AHEI, mean (SD)	50.1 (8.5)	50.1 (10.5)	49.5 (10)	48.9 (10.4)
METs per week, mean (SD)	14.7(12.3)	15.9(27.1)	19.1 (21)	20.1 (20.5)
Menopausal and hormone use, %				
Premenopausal	33.3	29.2	74.4	74.8
Postmenopausal, no use	18.5	26.3	6.5	4.8
Postmenopausal, any use	48.2	44.5	19.1	20.4
Oral contraceptive use, %				
Never	28.2	31.0	15.9	13.2
Past	71.8	69.0	83.2	85.1
Current	0	0	0.9	1.6
Parity and breastfeeding, %				
Nulliparous	6.6	2.7	13.5	18.6
Parous, None/<1months	29.3	35.1	14.2	14.8
Parous, 1-3months	16.0	10.1	9.3	4.7
Parous, 4-11months	32.1	26.3	22.8	16.3
Parous, 12+months	14.6	24.3	39.3	44.4

Abbreviation: AHEI, alternative healthy eating index; MET, metabolic equivalent of task.
[a] All values other than age were directly standardized to age distribution (in 10-year intervals) of all participants.

less, women who had BMI < 25 kg/m^2 at the date of blood draw, and those who underwent blood draw 4-7.9 years before RA diagnosis or matched controls. Similarly, seropositive cases but not seronegative cases, had a higher level of leptin compared to controls. A significant difference in resistin level was also observed among women with BMI< 25 kg/m^2 and who underwent blood draw < 4 years before diagnosis vs. controls. In exploratory analyses, among both cases and controls, a higher level of leptin was significantly associated with higher levels of inflammatory markers [*monocyte chemoattractant protein-1 (*MCP-1), IL6, and tumor necrosis factor receptor *2 (*TNFR2)] (Table 3).

Conclusion: Circulating level of leptin was higher in women with preclinical RA than in controls. These results indicated that adipokines secreted by adipose tissues may be involved in RA pathogenesis. The screening for leptin could be used to identify high risk groups to prevent RA.

Table 2. Adjusted means (Least square means) of log-transformed biomarkers in the pooled data from NHS and NHS II*

	Leptin (log(ng/ml))			Resistin (log(ng/ml))			Visfatin (log(ng/ml))		
	Pre-RA Cases	Controls	P for difference	Pre-RA Cases	Controls	P for difference	Pre-RA Cases	Controls	P for difference
All women	**3.10(0.06)**	**2.90(0.05)**	**0.002**	2.34(0.04)	2.31(0.03)	0.42	2.17(0.12)	2.21(0.10)	0.78
Stratified analyses:									
Age									
<=55 years (n=502)	**3.14(0.07)**	**2.88(0.06)**	**<0.001**	2.32(0.04)	2.33(0.04)	0.95	2.16(0.14)	2.24(0.12)	0.60
>55 years (n=99)	2.99(0.25)	2.93(0.25)	0.74	2.51(0.14)	2.43(0.14)	0.40	2.50(0.53)	2.13(0.55)	0.32
BMI category									
<25 kg/m^2(n=320)	**2.70(0.08)**	**2.47(0.07)**	**0.005**	**2.40(0.06)**	**2.27(0.05)**	**0.02**	2.43(0.19)	2.29(0.15)	0.45
25-29.9 kg/m^2(n=172)	3.13(0.07)	3.08(0.06)	0.50	2.27(0.07)	2.34(0.06)	0.28	1.71(0.23)	1.92(0.21)	0.39
30+ kg/m^2(n=109)	3.68(0.12)	3.85(0.10)	0.21	2.34(0.08)	2.40(0.07)	0.49	2.15(0.27)	2.37(0.23)	0.46
Time from blood draw									
<4 years (n=174)	3.10(0.11)	2.90(0.10)	0.10	**2.43(0.07)**	**2.23(0.06)**	**0.01**	2.24(0.22)	1.94(0.19)	0.23
4-7.9 years (n=143)	**3.26(0.15)**	**2.90(0.12)**	**0.01**	2.26(0.08)	2.29(0.06)	0.73	2.46(0.32)	2.36(0.25)	0.74
8+ years (n=284)	3.01(0.11)	2.86(0.09)	0.14	2.34(0.06)	2.35(0.05)	0.76	2.17(0.19)	2.39(0.16)	0.21
Type									
Seropositive (n=385)	**3.12(0.08)**	**2.86(0.07)**	**0.002**	2.35(0.05)	2.32(0.04)	0.44	2.18(0.15)	2.25(0.13)	0.67
Seronegative (n=196)	3.01(0.11)	2.92(0.09)	0.42	2.36(0.08)	2.33(0.06)	0.68	2.35(0.23)	2.30(0.18)	0.84

* Multivariable linear regression adjusting for cohort, age at blood draw, menopausal status, census median income, smoking packyears, Alternate Heathy Eating Index, physical activity, and parity and breastfeeding.

Table 3. Circulating adipokine levels and inflammatory biomarkers by case/control status (a subsample exploratory analysis)

	Pre-RA Cases						Controls					
	Leptin		Resistin		Visfatin		Leptin		Resistin		Visfatin	
	Beta (SE)*	p	Beta (SE)	p	Beta (SE)*	p	Beta (SE)*	p	Beta (SE)*	p	Beta (SE)*	p
MCP-1 †	0.003 (0.001)	**0.04**	0.001 (0.004)	0.75	0.0002 (0.0008)	0.79	0.003 (0.001)	**0.002**	-0.001 (0.003)	0.73	-0.00007 (0.0007)	0.93
IL-6 ‡	0.008 (0.004)	**0.07**	0.013 (0.019)	0.51	-0.005 (0.008)	0.52	0.009 (0.003)	**0.007**	0.03 (0.017)	**0.07**	-0.002 (0.003)	0.54
TNFR2 §	7.80 (3.58)	**0.04**	19.08 (15.49)	0.23	0.24 (6.54)	0.97	7.54 (2.66)	**0.006**	53.48 (14.83)	**0.001**	1.67 (2.65)	0.53

* Linear regression models with log-transformed markers of inflammation.
† Mcp-1: monocyte chemoattractant protein-1; 150 pre-RA cases, 296 controls.
‡ IL-6: Interleukin 6; 36 pre-RA cases, 71 controls TNFR2.
§ Tumor necrosis factor receptor 2; 36 pre-RA cases, 71 controls.

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Association of Lipid Mediator Profiles and Development of Future Incident Inflammatory Arthritis in a High Risk, Anti-citrullinated Protein Antibody Positive Population

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SESSION INFORMATION

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Background/Purpose: Lipid mediators are endogenously derived from the metabolism of omega-3 and omega-6 polyunsaturated fatty acids (PUFAs) and have important roles in promoting and resolving inflammation. As such PUFAs have been implicated in the pathogenesis of systemic inflammatory and autoimmune diseases including rheumatoid arthritis (RA). As lipid mediators share common pathways and enzymes, individual lipid mediators do not act in isolation and therefore must be analyzed in combination as a profile. The goal of this study was to determine the association of polyunsaturated fatty acid (PUFA)-derived lipid mediator profiles with progression from pre-diagnosis RA-related autoimmunity to clinically apparent inflammatory arthritis (IA).

Methods: Using the Studies of the Etiologies of Rheumatoid Arthritis (SERA), we examined a prospective cohort that includes first-degree relatives (FDRs) of individuals with RA (FDR cohort) and individuals who screened positive for RA-related autoantibodies at health fairs (screened cohort). We followed 133 anti-CCP3.1 positive participants, of which 29 participants subsequently developed IA during follow-up (mean time to IA development = 1.15 years). Exposures

Table 1. Characteristics of the ACPA-positive study participants (n = 133) at baseline visit. Except where indicated otherwise, values are the number (%); IA = inflammatory arthritis

Characteristic	IA Control (n = 104)	IA Case (n=29)	p-value
Age, mean (SD)	54.3 (13.5)	49.9 (14.7)	0.152
Gender, Female	73 (70.2%)	18 (62.1%)	0.544
Race, non-Hispanic White	87 (83.7%)	21 (72.4%)	0.271
Education, high school or higher	82 (78.8%)	25 (86.2%)	0.536
Shared epitope (SE), present	47 (45.2%)	20 (69.0%)	0.040
Smoker†, non-smoker	61 (58.7%)	18 (62.1%)	0.836
Recruitment Group, FDR	69 (66.3%)	11 (37.9%)	0.0108

Except where indicated otherwise, values are the number (%); IA = inflammatory arthritis.
† Data were missing for 1 participant.

Average of 3.74 years of follow-up

Table 2. PC Factor Loadings. Factor loadings are shown for each lipid mediator for the 5 profiles of interest. Lipid mediators with large impact loadings are highlighted either red (negative loading) or green (positive loading). Negative loadings means the individual lipid mediator is negatively correlated with the PC, while positive loadings means the individual lipid mediator is positively correlated. The precursor fatty acid and omega fatty acid type (either omega3 or omega6) are shown for each lipid mediator

Lipid Mediator	*Precursor Fatty Acid*	*Omega Type*	*PC1*	*PC2*	*PC3*	*PC4*	*PC5*
9-HOTrE	ALA	omega3	-0.08	**-0.36**	-0.01	**0.19**	-0.15
19,20-DiHDPE	DHA	omega3	-0.09	**-0.36**	0.04	0.14	-0.06
13-HOTrE	ALA	omega3	-0.10	**-0.35**	-0.07	**0.18**	**-0.18**
13-OxoODE	LA	omega6	**-0.19**	**-0.21**	-0.14	0.12	-0.08
9,10-EpOME	LA	omega6	-0.09	**-0.21**	-0.01	**0.31**	-0.08
9-OxoODE	LA	omega6	**-0.16**	**-0.19**	-0.11	0.06	-0.04
14,15-DiHETrE	ARA	omega6	-0.14	**-0.18**	**0.33**	-0.09	**0.28**
12-HETE	ARA	omega6	-0.14	-0.16	**-0.28**	**-0.25**	0.03
5,6-DiHETrE	ARA	omega6	**-0.18**	-0.16	-0.01	0.00	0.00
EKODE	LA	omega6	-0.12	-0.15	0.02	0.11	0.16
17,18-DiHETE	EPA	omega3	-0.11	-0.13	**0.24**	0.02	**-0.18**
11,12-DiHETrE	ARA	omega6	-0.12	-0.13	**0.33**	-0.13	**0.32**
12-HHTrE	ARA	omega6	-0.14	-0.12	**-0.27**	**-0.22**	-0.02
KOTrE	ALA	omega3	-0.02	-0.12	-0.07	**-0.24**	0.01
8,9-DiHETrE	ARA	omega6	**-0.17**	-0.11	**0.29**	-0.05	**0.27**
11,12-EET	ARA	omega6	-0.03	-0.09	-0.11	0.02	-0.03
15-HETE	ARA	omega6	**-0.24**	-0.09	-0.09	-0.16	0.15
19,20-EpDPE	DHA	omega3	-0.02	-0.08	0.11	**-0.16**	**-0.20**
15-HEPE	EPA	omega3	-0.02	-0.06	0.09	**-0.34**	-0.09
11-HDoHE	DHA	omega3	**-0.20**	-0.05	**-0.25**	-0.15	-0.04
TXB2	ARA	omega6	-0.01	-0.04	**-0.22**	-0.05	0.14
20-HETE	ARA	omega6	-0.01	-0.04	-0.13	**-0.34**	0.04
14-HDHA	DHA	omega3	0.00	-0.03	-0.11	**-0.35**	-0.15
8s-HETE	ARA	omega6	**-0.24**	-0.02	0.11	-0.04	0.13
8-HEPE	EPA	omega3	-0.07	-0.01	**0.19**	**-0.23**	**-0.29**
17-HDHA	DHA	omega3	0.01	0.00	0.05	**-0.18**	**-0.17**
17,18-EpETE	EPA	omega3	**-0.17**	0.04	**0.18**	0.01	**-0.37**
15-HETrE	DGLA	omega6	**-0.25**	0.12	-0.02	0.00	0.13
5-HETrE	DGLA	omega6	**-0.22**	0.12	**0.19**	-0.03	0.08
11-HETE	ARA	omega6	**-0.26**	0.13	-0.15	0.00	0.10
5-HEPE	EPA	omega3	**-0.19**	0.14	**0.18**	-0.02	**-0.34**
8-HETrE	DGLA	omega6	**-0.24**	0.14	-0.02	0.07	0.08
LXA4	ARA	omega6	-0.16	0.14	-0.13	0.07	0.01
8-HDoHE	DHA	omega3	**-0.19**	**0.16**	**0.16**	-0.07	**-0.26**
9-HETE	ARA	omega6	**-0.25**	**0.18**	0.03	0.00	0.03
5-KETE	ARA	omega6	**-0.21**	**0.19**	-0.14	0.16	-0.05
14,15-EET	ARA	omega6	**-0.24**	**0.20**	-0.09	0.10	-0.04
5-HETE	ARA	omega6	**-0.24**	**0.20**	-0.10	0.12	-0.02

Table 3. Cox proportional hazard results for the outcome of Inflammatory Arthritis (IA) for each lipid mediator profile (PC). All models were adjusted for age at baseline and recruitment type (FDR or health fair). For total population models, SE status was adjusted for as well

Lipid Mediator Profile	Population	Hazard Ratio	95% Confidence Interval	p-value
PC1	Total	0.97	(0.83, 1.13)	0.675
PC2	**Total**	**0.79**	**(0.66, 0.96)**	**0.018**
PC3	Total	1.01	(0.75, 1.36)	0.938
PC4*	SE Negative	0.99	(0.56, 1.77)	0.981
PC4*	**SE Positive**	**0.53**	**(0.32, 0.87)**	**0.012**
PC5	Total	0.86	(0.64, 1.17)	0.340

*PC4 had a significant interaction effect with SE (p-value = 0.048) and therefore reporting the stratified results for this profile.

included concentrations (pg/ml) of lipid mediators quantified from baseline plasma samples via liquid chromatography tandem mass spectrometry with profiles identified via principal component analysis (PCA). Multivariable Cox proportional hazard models were then developed for each lipid mediator profile, either stratified by or adjusted for HLA-DRB1 shared epitope status (dependent on presence of effect modification between lipid mediator profile and shared epitope).

Results: Baseline characteristics of the study population is shown in Table 1. The top 5 PCA components (PC) explained >50% of all variance among the lipid mediators, with the factor loadings of each lipid mediator shown in Table 2. Of these lipid mediator profiles, PC2 had a significant protective effect on IA risk (HR 0.79, 95% CI: 0.66-0.96, p-value = 0.018) in the total study population (Table 3). For profile PC2, the important lipid mediators had a mix of positive and negative loadings for lipid mediators in the cytochrome P450 soluble epoxide hydrolase (CYP sEH) and 15-lipoxygenase (15-LOX) enzymatic pathways. PC4 also demonstrated a significant protective effect on IA risk, but only within the shared epitope positive study population (HR 0.53, 95% CI: 0.32-0.87, p-value = 0.012). For profile PC4, the vast majority of important lipid mediators had negative loading factors and are downstream products from omega-3 parent fatty acids. Other lipid profiles identified showed no association with the risk of IA.

Conclusion: Our study revealed two lipid mediator profiles to be significantly associated with incident IA in a high-risk pre-diagnosis cohort characterized by ACPA positivity. These findings suggest specific PUFA metabolite profiles impact on the early evolution of RA and ultimately the development of IA, some working solely within the SE positive population.

Disclosure: L. Vanderlinden, None; **E. Bemis**, None; **K. Polinski**, None; **K. Demoruelle**, Pfizer, 5; **M. Feser**, None; **J. Seifert**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **M. Weisman**, Novartis, 2, Gilead, 2, GSK, 2, UCB, 2; **J. Buckner**, Janssen R&D, 5; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6; **M. Clare-Salzler**, None; **V. Holers**, Jansson, 5; **J. Norris**, None.

Abstract Number: 0591

The Temporal Association Between Hospital Admissions, Disease-modifying Anti-rheumatic Drugs Usage and Direct Health Care Costs in Rheumatoid Arthritis Patients

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) carries a substantial burden for patients and society in terms of morbidity, disability, and medical expenses. The Australian Pharmaceutical Benefits Scheme (PBS) subsidised biological disease-modifying anti-rheumatic drugs (bDMARD) since 2003. We investigated the association between subsidised bDMARD therapy for RA in 2003 hospitalisation rates and health care costs.

Methods: Hospital admissions for RA patients between 1995 and 2014 were identified in the Western Australia (WA) Hospital Morbidity Data Collection (ICD codes 714 and M05.00–M06.99). State-specific dispensing data for conventional

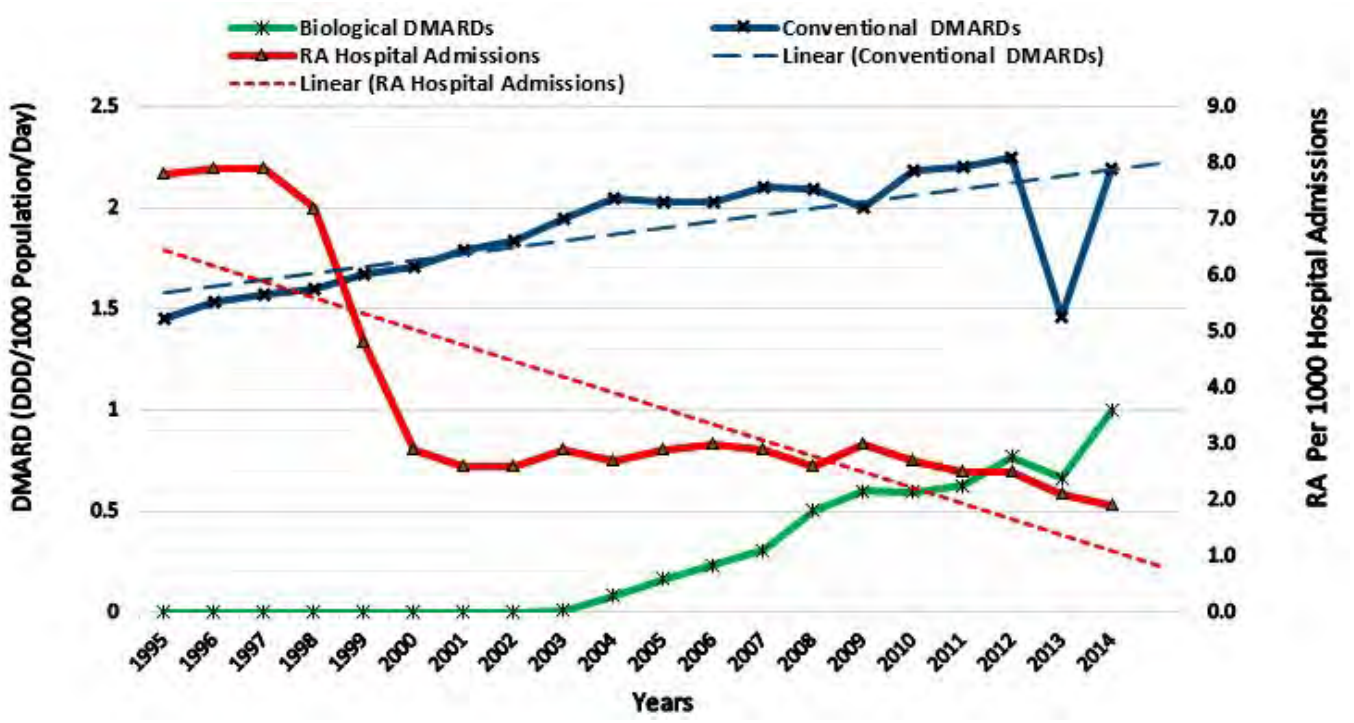

Figure 1. Conventional and biological DMARD trends and hospital admission for rheumatoid arthritis, 1995–2014, Western Australia. DDD, defined daily doses; DMARD, disease-modifying anti-rheumatic drugs; RA, Rheumatoid Arthritis.

DMARD (cDMARD) and bDMARD for RA was obtained from Statistics Australia and expressed as defined daily doses /1000 population/day (DDD) using the WA population census. Principal component analysis (PCA) was applied to determine the relationship between DMARD use and hospital admission rates. Total expenditure for DMARD and RA hospital admissions were obtained from the PBS domain and Australia's health care expenditure report.

Results: A total of 17,125 patients had 50,353 admissions with a diagnostic code for RA. Between 1995 and 2002, the number of RA admissions fell from 7.9 to 2.6/1,000 admissions, while cDMARD use rose from 1.45 to 1.84 DDD. Between 2003–2014, RA admissions decreased further to 1.9/1,000 hospital admissions, while cDMARD use increased to 2.19 DDD and bDMARDs from 0.01 to 1.0 DDD. In PCA analysis, cDMARD (methotrexate and leflunomide) and bDMARD use had an inverse relationship with hospital admission rates. The annual costs of bDMARD utilisation was 22.5 million in 2003–2014, while annual cost savings of RA hospital admissions was 9.2 million.

Conclusion: The increased use of cDMARD use for RA has coincided with a significant decline in hospital admissions for RA patients in WA, while a more modest further decline followed bDMARD introduction. BDMARD therapy was not as cost-effective as cDMARD in relation to RA hospital admissions costs.

Disclosure: K. Almutairi, None; **J. Nossent**, None; **D. Preen**, None; **H. Keen**, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **C. Inderjeeth**, None.

Abstract Number: 0592

Gender Modifies the Effect of Rheumatoid Arthritis on All-Cause Mortality

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic and systemic autoimmune disease which predominantly affects joints with varying severity. While RA has been found to be more prevalent in women, there is conflicting information about gender-specific mortality rate as it relates to RA. In this study, we explored the relationship between RA and all-cause mortality and if gender modifies this effect.

Methods: The study was conducted on participants aged 20 years or older in the United States living. We assessed RA status by using the arthritis screening in the NHANES survey for the years 1999 to 2010 with mortality follow-up through December 31, 2015. Prospective analysis was performed using complex samples Cox Regression with adjustment for known confounders to determine the relationship of RA and mortality, especially as it pertains to gender.

Results: Prevalence of RA in this population (N=27,371) was 1.9% among males and 2.8% among females. The mean follow-up was 11.1 years. For all-cause mortality, the overall unadjusted hazard ratio (HR) of rheumatoid arthritis to no rheumatoid arthritis was 2.89 (95% confidence interval [CI], 2.48-3.37, $p < 0.001$). Adjusted HR was elevated, 1.34 (CI 1.04-1.73, $p < 0.05$), among female participants with RA but closer to 1.0 (1.02 CI 0.83-1.25, $p > 0.05$) among male participants with RA, after controlling for medical (obesity, diabetes, CKD, and CVD) and demographic risk factors (age, education, and food insecurity).

Table 1. Multivariable Cox Hazard Model for Rheumatoid Arthritis and all-cause mortality after controlling for demographic and medical risk factors stratified by gender

	Male All Cause-Mortality (n=15,878)			Female All Cause-Mortality (n=8,173)		
Variable	**HR**	**95% CI**	**P-value**	**HR**	**95% CI**	**P-value**
Rheumatoid Arthritis	1.02	0.83-1.25	0.86	1.34	1.04-1.73	0.03
Cardiovascular Disease[a]	1.44	1.23-1.69	<0.001	1.69	1.39-2.04	<0.001
Obesity (Reference: BMI < 30)	1.30	1.10-1.55	0.004	0.99	0.81-1.22	0.93
Diabetes	1.56	1.28-1.90	<0.001	1.55	1.23-1.96	<0.001
Chronic Kidney Disease[b]	1.56	1.35-1.79	<0.001	1.63	1.34-1.98	<0.001
Education						
Some High School	1.69	1.41-2.04	<0.001	1.37	1.11-1.67	0.003
High School Grad	1.47	1.28-1.69	<0.001	1.14	0.92-1.42	0.22
Some College	Reference	Reference	Reference	Reference	Reference	Reference
Age	1.08	1.07-1.08	<0.001	1.08	1.08-1.09	<0.001
Ethnicity						
Non-Hispanic White	Reference	Reference	Reference	Reference	Reference	Reference
Non-Hispanic Black	1.26	1.01-1.59	<0.001	1.19	0.97-1.47	0.09
Hispanic	0.98	0.78-1.23	0.68	1.07	0.78-1.45	0.68
Other	0.75	0.44-1.28	0.29	1.24	0.80-1.90	0.33

[a]Cardiovascular disease was defined by self-reported positive response to congestive heart failure, stroke, angina, coronary heart disease, or heart attack.
[b]Chronic Kidney Disease was ascertained through the classification of Glomerular Filtration Rate determined by the Cockcroft-Gault equation.

Conclusion: RA was found to cause three times higher mortality rate than the general population, which is higher than previous estimates. The findings also show that RA disproportionately affects females and also leads to worse outcome than in males. Risk scoring and social policy, when addressing RA, should address gender disparities related to outcomes.

Disclosure: S. Banerjee, None; **S. Falls**, None.

Abstract Number: 0593

Labour Force Participation Among Individuals with Osteoarthritis, Rheumatoid Arthritis/Other Arthritis Types, or with Joint Symptoms but Without a Diagnosis: An Age-Stratified Population-Based Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Epidemiology & Public Health Poster II: Inflammatory Arthritis – RA, SpA, & Gout (0560–0593)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Having arthritis is known to affect labour force participation. Most research has focused on individuals with doctor-diagnosed rheumatoid arthritis (RA) and, to a lesser extent, doctor-diagnosed osteoarthritis (OA). However, for younger working-age adults in particular, OA is often underdiagnosed and underreported. Using a national population-based sample and with a focus on age-specific associations, we compared labour force participation among individuals with doctor diagnosed OA, RA or other arthritis types, and those with joint symptoms but no diagnosis.

Methods: Data are from the Canadian Longitudinal Study on Aging (Cycle 1), a national study with sociodemographic, economic and health data from Canadians aged 45-85. All data were self-reported and include questions on labour force participation, and if respondents had doctor-diagnosed RA/other type of arthritis, or OA (hands, hips or knees). Respondents also reported on joint symptoms in these joints. Five mutually exclusive groups were derived:

Table 1. Characteristics of the Canadian Longitudinal Study on Aging sample.

	Overall (n = 24, 813)	45-54 years of age (n = 7,595)	55-65 years of age (n = 9,856)	65-74 years of age (n = 7,362)
		%		
Controls (no arthritis/no joint symptoms)	43.6	55.3	41.4	34.6
RA or other arthritis type	12.4	9.8	12.6	14.7
Osteoarthritis	19.9	10.2	21.3	28.1
1 joint site symptom (no arthritis diagnosis)	18.6	19.6	19.2	16.8
2-3 joint site symptom (no arthritis diagnosis)	5.5	5.1	5.5	5.9
Female	51.2	51.7	51.6	50.1
Has dependents ≤18 years old at home	18.5	45.9	9.0	2.9
< Post secondary education	13.0	9.4	12.6	17.3
Comorbid conditions 0-1	28.8	42.3	28.1	15.8
2-3	43.6	43.2	44.6	42.8
4+	27.6	14.6	27.3	41.4
Out of the labour force	39.3	9.9	37.1	72.7

Table 2. Results from age-stratified log-binomial regression analyses assessing associations (reported as prevalence ratios) between arthritis groups and labour force participation (out vs. in labour force), Canadian Longitudinal Study on Aging.

	Age stratified models* Prevalence Ratio ((95% CI))		
	45-54	55-64	65-74
RA or other arthritis type	**1.30 (1.06, 1.60)**	**1.09 (1.01, 1.19)**	0.99 (0.95, 1.03)
Osteoarthritis	**1.31 (1.08, 1.60)**	**1.12 (1.05, 1.20)**	1.02 (0.98, 1.05)
1 joint site symptom (no arthritis)	1.04 (0.87, 1.25)	1.05 (0.98, 1.13)	0.99 (0.95, 1.03)
2-3 joint site symptom (no arthritis)	**1.33 (1.04, 1.70)**	1.02 (0.91, 1.15)	1.02 (0.97, 1.08)

Bolded estimates indicate statistical significance at p<0.05

*adjusted for sex, education, if respondent had a dependent (≤18 years of age) living at home, and comorbidities

controls (no arthritis/no joint symptoms), RA/other, OA, and for those with no arthritis diagnosis but with symptoms, single joint site and 2-3 joint site symptoms.

Age-stratified (45-54/55-64/64-74) log-binomial regressions were used to examine the association (reported as prevalence ratios) between labour force participation and group membership. Analyses were adjusted for sex, education, dependent (≤18 years of age) living at home and comorbidities.

Results: From a sample of 24,813, 20% had OA, 12% RA/other types of arthritis, and 19% and 6% had 1 joint site symptoms and 2-3 joint site symptoms, respectively, without an arthritis diagnosis (Table 1).

In the youngest age group (45-54) individuals with OA, RA/other, and those with 2-3 joint symptoms but without a diagnosis were equally likely to be out of the labour force (Table 2). Among those aged 54-64, those with OA and RA/other types were equally likely to have an increased likelihood of being out of the labour force. No differences in labour force participation were found between the groups in the older age group.

Conclusion: OA and RA/other arthritis types were similarly associated with being out of the labour force for working age adults. Importantly, among individuals in the youngest age group, individuals with symptoms at 2-3 joint sites but without a diagnosis were as likely to be out of the labour force as those with OA and RA/other arthritis types. Younger individuals may be less likely to make a physician visit for joint symptoms or to receive an arthritis diagnosis. An exclusive focus on diagnosed arthritis may miss an important segment of the population to target with interventions to positively impact labour force participation.

Disclosure: S. Zahid, None; **E. Badley**, None; **A. Perruccio**, None.

Abstract Number: 0594

The Burden of Systemic Lupus in Five Distinct Racial and Ethnic Groups in Israel: A Population-based Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Misclassification of race and ethnicity in data can impact how disparities in prevalence, incidence, severity, and complications of systemic lupus erythematosus (SLE) are interpreted. Categorizing and labeling individuals' race/ethnicity is often limited to preset options. Consequently, in many regions, people of Middle Eastern descent are asked to choose between "White" and "Other." Our objective was to use population-based data from Israel to characterize the burden of SLE in the population by infrequently examined race/ethnic groups (i.e. Sephardi, Ashkenazi, Ethiopian, Arab/Bedouin, and Mixed ancestry).

Methods: A cohort of patients with SLE was identified using electronic health record data between 2010 and 2017 from Clalit Health Services (CHS), the largest healthcare provider in Israel comprising 53% of the adult population (4.7 million patients). SLE prevalence was estimated on January 1, 2017 and annual incidence was examined over time for several SLE definitions by sex, age, and ethnicity. Ethnicity (Sephardi, Ashkenazi, Ethiopian, Arab/Bedouin, Mixed

	SLE Case Definitions
Most Sensitive	*Definition 1*. At least one visit with the relevant ICD9 code (710.0 or other based on findings from the Clalit database and accompanying free text) for SLE. Defined as present with the first of these codes (N=6,267).
	Definition 2. At least one visit with the relevant ICD9 code (710.0 or other based on findings from the Clalit database) and accompanying free text for SLE, and at least one ANA positive test result (N=3,493).
	Definition 3. At least one visit with the relevant ICD9 code (710.0 or other based on findings from the Clalit database) for SLE in inpatient setting, or at least two visits coded for SLE in outpatient setting (N=3,637).
	Definition 4. At least two visits with the relevant ICD9 code (inpatient or outpatient setting) plus at least one positive ANA test result (N=2,418).
	Definition 5. At least two visits with the relevant ICD9 code for SLE in inpatient or outpatient setting (or both), with at least one SLE-coded visit from a specialist (including nephrology, rheumatology, immunology, dermatology or internal medicine) (N=2,243).
Most Specific	*Definition 6*. At least two visits with the relevant ICD9 code for SLE in inpatient or outpatient setting (or both), with at least one SLE-coded visit from a specialist (nephrology, rheumatology, immunology, dermatology or internal medicine), plus at least one related lab finding, including positive ANA, positive anti-dsDNA, low C3, low C4 (N=1,967).

*Prevalence estimates as of January 1, 2017

Figure 1. SLE Case Definition Classifications from most sensitive to most specific. *

Table 1. Characteristics of prevalent SLE cases in Clalit Health Services (CHS) vs random sample of general CHS membership during follow-up

	Definition 2 SLE Cases n=3,493	Definition 5 SLE Cases n=2,243	Random Clalit Sample n=404,853
Demographics			
Age (mean±SD)	50.5±16.1	50.4±15.8	35.5±23.7
Sex (% female)	88.0	87.0	51.0
Racial/Ethnic group			
Arab/Bedouin	23.0	23.0	27.0
Ashkenazi	20.0	17.0	20.0
Ethiopian	1.0	1.0	3.0
Sephardi	33.0	35.0	26.0
Mixed	2.0	2.0	4.0
Unknown	21.0	21.0	20.0
Socio-economic status			
Low	30.0	30.0	34.0
Medium	36.0	38.0	35.0
High	34.0	32.0	31.0
Clinical Factors			
Smoking status			
Current smoker	14.0	17.0	13.0
Non-smoker	69.0	66.0	66.0
Past smoker	17.0	18.0	21.0
Diabetes	16.0	19.0	10.0
Hypertension	38.0	44.0	18.0

shown as % yes unless otherwise specified

Jews, Unknown) was defined using data on four grandparents; and categorized those with more than one noted ethnicity among grandparents as "mixed", while those missing 2 or more grandparents was "unknown". We used SLE definitions from the existing literature and added serologic testing to generate six definitions varying in sensitivity and specificity (Fig 1). These definitions incorporated ICD9 coded inpatient and outpatient visits, provider type/specialty, number of SLE-coded visits, and serologic testing (including antinuclear antibody positivity, anti-double stranded DNA antibodies, and low C3 and C4).

Results: In total, our study population included up to 6,267 potential SLE cases and 404,838 comparators from the CHS membership. The distribution of sociodemographic factors varied little between case Definitions 2 and 5 (Table 1). The prevalent cases, regardless of definition, were older and more likely to be female, have hypertension, diabetes, and kidney disease than the general CHS comparator group. Overall prevalence on January 1, 2017 ranged from 155 cases per 100,000 to 49 cases per 100,000 depending on the sensitivity vs specificity of the definition. Women comprised the majority of prevalent and incident cases across all age groups, and prevalence increased with age. Among

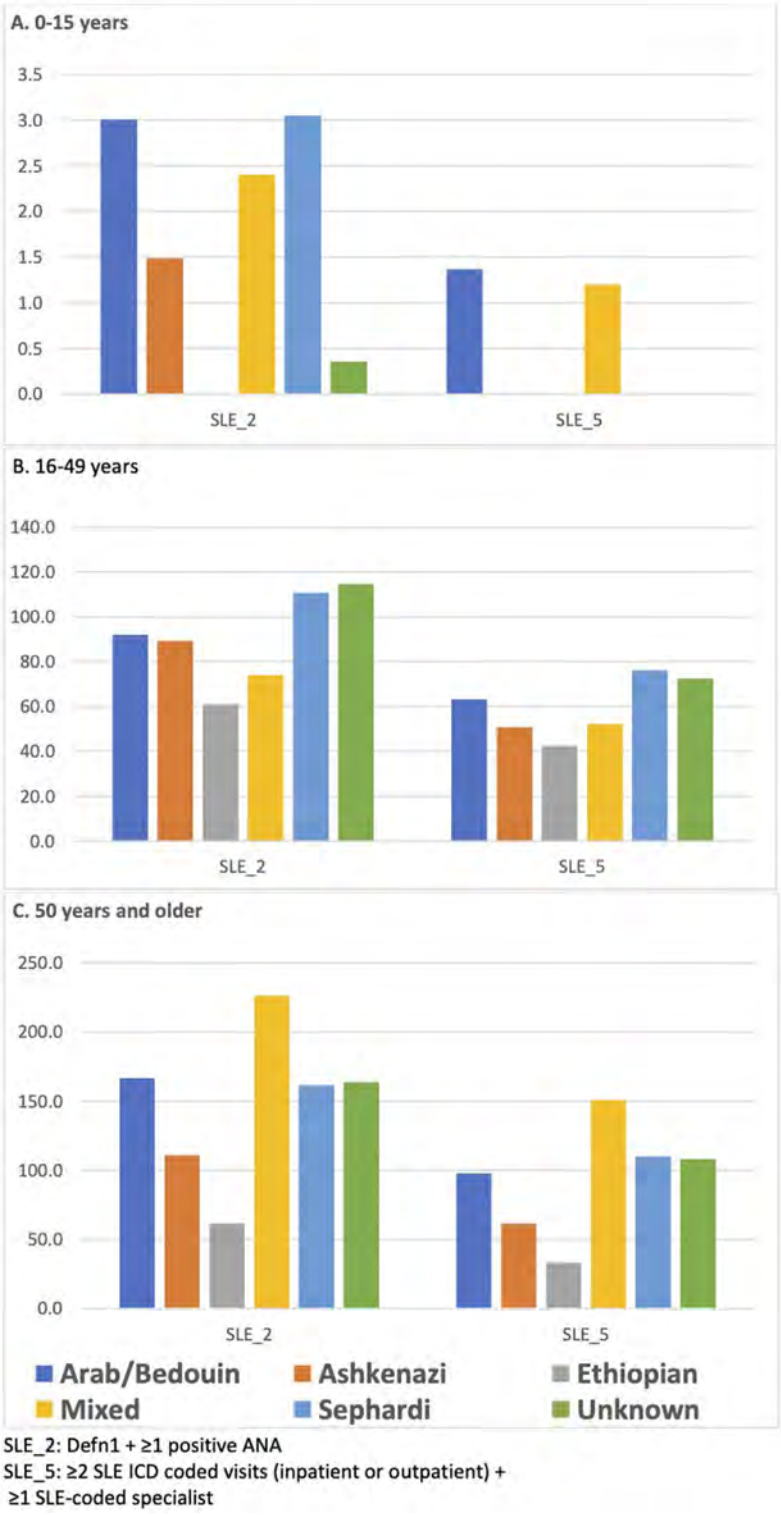

Figure 2. SLE Prevalence (per 100,000) by age and race/ethnicity in Clalit Health Services, Jan 1, 2017

children (0-15y) prevalence was highest among Arab/Bedouin and Sephardic groups (Figure 2). Among 16-49 year-olds, prevalence was highest among Sephardi and those of unknown ethnicity. Among those 50+ years, prevalence was highest among those of mixed ancestry. Individuals with Ethiopian ancestry had the lowest prevalence in all age groups. Overall incidence was highest in Sephardi and Arab/Bedouin groups (data not shown).

Conclusion: In our retrospective study, the burden of SLE in Israel appeared to vary by race/ethnicity and age. Notably, differences in SLE prevalence and incidence became apparent when groups that are typically misclassified as "White" or "Other" were further stratified into their racial and ethnic groups.

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Abstract Number: 0595

Lupus Nephritis Disparities Amongst Hospitalizations in the United States: A National Inpatient Sample Study

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SESSION INFORMATION
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Background/Purpose: Black, Hispanic, and Native American populations in the US experience increased morbidity and mortality from systemic lupus erythematosus (SLE), with higher rates and worse outcomes for lupus nephritis (LN). The purpose of our study was to identify socio-demographic indicators and outcomes of lupus nephritis on a national level in order to identify disparities and potential areas for intervention.

Methods: Our study utilizes the National Inpatient Sample (NIS), which is an all-payer national database. We used the NIS to identify inpatient hospitalizations between October 2015 and December 2017 with an ICD-10 diagnosis of SLE stratified by the additional diagnosis of lupus nephritis (LN) in patients 18 or older. We calculated the rate of lupus nephritis during hospitalizations, organized by patient and facility demographics. In addition, we examined dialysis, death, and cost of care for SLE and LN hospitalizations.

Results: We identified 333,020 hospitalizations with SLE, of which 8,575 (2.6%) included an LN diagnosis. The median age was lower LN group compare to SLE patients without LN (37 vs 55 years, $p < .001$) (Table 1). SLE disproportionately affects females, however, the lupus nephritis rate was higher in males than females (3.8 vs. 2.4). Hospitalizations with SLE were disproportionately higher in the White population, Black cohort (28.1%) and relatively lower in the Hispanic cohort (11.6%) Rates of LN were higher for Blacks (4.6%), Hispanics (4.0%) and Other races (3.7%) compared to Whites (1.1%, all $p < .001$). The lowest income quartile had the highest rate of LN (3.0%) and the upper quartile the lowest (2.1%, $p < .001$). Discharge with dialysis- dependence occurred in 29% of hospitalizations with LN diagnoses (Table 2). Cost of hospitalization was significantly higher with LN than without LN ($11,200 vs. $9,109, $p < .001$) (Table 3).

Table 1. Patient demographic characteristics stratified by lupus nephritis

	SLE without LN (n = 324,445)	SLE with LN (n = 8,575)	Rate of Lupus Nephritis (%)	p
Age at admission	54.6 [41.5- 66.0]	36.6 [24.2- 50.4]		<.001
Age				<.001
18-24	3.3	14.3	10.4	
25-34	10.7	29.9	6.8	
35-44	15.0	20.8	3.5	
45-54	19.8	15.5	2.0	
55-64	22.4	11.8	1.4	
65-74	17.6	5.3	0.8	
75+	11.2	2.3	0.6	
Sex				
Male	10.5	15.9	3.8	<.001
Female	89.5	84.1	2.4	
Race				
White	55.1	22.7	1.1	<.001
Black	28.1	51.4	4.6	
Hispanic	11.6	18.3	4.0	
Other	5.2	7.6	3.7	
Income Quartile				
0 to 25th	34.7	40.3	3.0	<.001
26th to 50th	24.8	24.1	2.5	
51st to 75th	22.4	20.8	2.4	
76th to 100th	18.1	14.8	2.1	

Conclusion: From the NIS hospitalizations, the presence of LN among hospitalizations with SLE is disproportionately associated with younger populations, Black and Hispanic populations and lowest income quartile. These hospitalizations primarily occur at urban teaching hospitals. There was a significant increase in cost associated with these hospitalizations. The rate of LN and dialysis is particularly concerning given the younger age of these hospitalizations. Further investigation is essential for identifying the structural causes that leads to these disparities and informing equitable care for patients with SLE and LN.

Table 2. Clinical characteristics stratified by lupus nephritis

	SLE without LN (n = 324,445)	SLE with LN (n = 8,575)	Rate of Lupus Nephritis (%)
Dependence on Dialysis	5.7	29.2	11.9

Table 3. In-hospital outcomes stratified by lupus nephritis

	SLE without LN (*n* = 324,445)	SLE with LN (*n* = 8,575)	*P value*
Hospital Cost, 2017 $	9,109 (9,012-9,207)	11,200 (10,721-11,742)	<.001

Disclosure: S. Gupta, None; **K. Willer**, None; **A. Begovic**, None; **M. Waters**, None; **L. Tarantino**, None; **O. Badejo**, None; **R. Walters**, None; **T. Townley**, None.

Abstract Number: 0596

Racial Disparities in US Adults with Systemic Lupus Erythematosus: Prevalence, Quality of Life, Comorbidities and Healthcare Costs

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SESSION INFORMATION
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Background/Purpose: SLE is a chronic, multisystem autoimmune disease characterized by reoccurring flares and remissions. It is more common among Asian, Black, and Hispanic populations. Racial disparity in SLE disease burden, including socioeconomic status (SES), and quality of life (QOL), is not well described in SLE patients. Our study sought to characterize the prevalence of SLE, demographic characteristics, SES, QOL, and health care resource utilization between Black vs. White adults in the US.

Methods: We analyzed 2016 - 2018 Medical Expenditure Panel Surveys (MEPS). MEPS is an annual survey designed to represent the US civilian non-institutionalized population. MEPS oversamples specific racial minority groups to

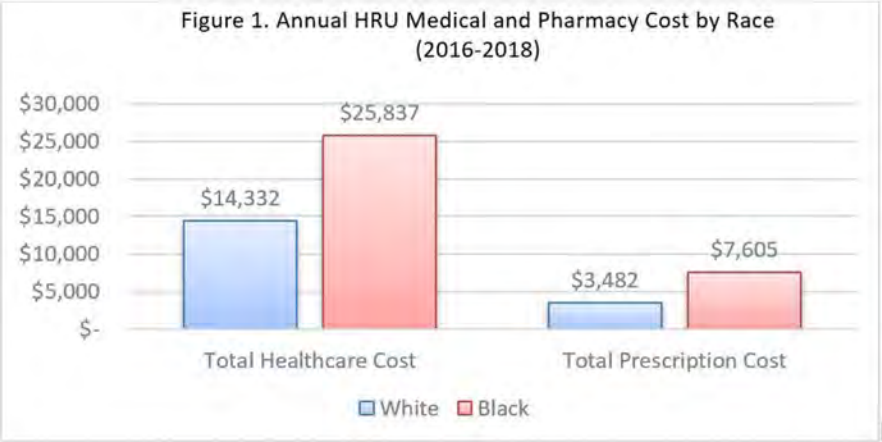

Table 1. Key SLE Respondent Characteristics by Race in MEPS (2016-2018)	White	Black
Demographic/Cohort Characteristics		
Married	**63%**	15%
Private insurance	**67%**	37%
Public Insurance	28%	**59%**
Employed	**53%**	39%
College education (3+ years)	**55%**	25%
Socio-economic status		
Food stamps	14%	**36%**
Problem paying bills	20%	**43%**
Income *(mean (sd))*	$41,251 (SD:$4,323)	**$21,811 (SD:$6,200)**
Poverty status (poor)	12%	**45%**

[a]Insurance types are independent; therefore, respondents could have had more than 1 type in a year

ensure adequate representation. Annual SLE respondents were identified using ICD-10 **M32 and had to have either SLE-related medication or at least 1 rheumatologist visit during the calendar year to be included for analysis. Descriptive** comparisons were pooled across all three years and stratified by Black, White or Other races, with results focusing on Black vs. White comparison.

Results: The prevalence of SLE was higher in Black adults 287 (95% CI: 162, 412) per 100,000 compared to White adults 187 (95% CI: 133, 241) per 100,000. Black SLE respondents were younger (46.8 vs. 50.1 years old), less likely to be married (15% vs. 63%), less likely to have 3+ years of college education (24% vs. 55%), less likely to be

Table 2. Key SLE Respondent Comorbidities and QOL Measures by Race in MEPS (2016-2018)	White	Black
Comorbidities		
Arthritis	54%	**86%**
Type 2 Diabetes	6%	**30%**
Heart disease	19%	**27%**
Stroke	5%	**17%**
Myocardial infarction (MI)	1%	**10%**
Respondent with >2 comorbidities	19%	**39%**
Respondent rated QOL		
Respondent-rated health (good or excellent)	**54%**	25%
Health limits activity a lot	19%	**36%**
Completely unable to do activity	14%	**52%**
Not depressed in the last 2 weeks	**59%**	34%
Limitation in physical functioning[a]	39%	**61%**
A lot of difficulties or unable to…..		
Lift 10 lbs	27%	**44%**
Walk up 10 steps	23%	**64%**
Walk 3 blocks	52%	**81%**
Walk a mile	65%	**89%**
Using fingers to grasp	8%	**21%**

[a]All adults who responded "Yes" to "Limitation in physical functioning were asked the subsequent questions

employed (39% vs. 53%), and less likely be privately insured (37% vs. 67%) (Table 1). Black SLE respondents had a significantly higher prevalence of select comorbidities including arthritis (86% vs. 54%), diabetes (30% vs. 6%) , stroke (17% vs. 5%). MI (10% vs. 1%),and heart disease (27% vs. 19%). Black adults reported poorer overall health and health-limited activity, including the ability to work (Table 2). 52% Black adults (vs. 14% White) reported "completely unable to do activities." White SLE respondents were 2–3 times less likely to report difficulty with physical limitations—including standing, walking, bending, and reaching. More Black respondents reported using antimalarial medication than White (80% vs. 57%), with no other differences in SLE-related medications. Overall, Black SLE respondents had higher annual healthcare expenses ($25,837 (95% CI 16,318 - $34,972) vs $14,332 (95% CI 9,551 - $19,112)) which were driven by higher costs within office visits and emergency room events. Prescription costs were also higher in Black compared to White respondents, although not statistically different.

Conclusion: In this survey population, when compared with White SLE adults, Black SLE adults were younger, presented with more comorbidities, reported more physical limitations, and higher expenses in emergency room visits and overall healthcare spending. These differences may adversely affect long-term outcomes, suggesting there is a continuing need to further assess racial disparities in SLE to improve outcomes for this population.

Disclosure: S. Grabich, AstraZeneca, 2; **C. Seal**, Amerisourcebergen, 3; **R. Ortmann**, AstraZeneca, 3; **S. Sze-jung Wu**, AstraZeneca, 3.

Abstract Number: 0597

Sex Differences in Multimorbidity Between Patients with Systemic Lupus Erythematosus and Comparators in a Large Nationwide US Study

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Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased burden of multimorbidity. Although many comorbidities may vary by sex and men with lupus may have more severe disease than women, sex differences in multimorbidity among SLE patients have not been examined.

Table. Comparison of multimorbidity prevalence between females and males among patients without SLE and patients with SLE.

	Multimorbidity (2+ conditions) Odds ratio*	Multimorbidity (5+ conditions) odds ratio*
Non SLE		
Women	Ref.	Ref.
Men	0.91 (0.83-0.99)	0.93 (0.80-1.08)
SLE		
Women	Ref.	Ref.
Men	1.09 (1.01-1.18)	1.15(1.05-1.25)
*Adjusted for age, race/ethnicity, and region		

Methods: We used the OptumLabs Data Warehouse (OLDW), a longitudinal, real-world data asset with de-identified administrative claims for commercial and Medicare Advantage enrollees, to identify cases of SLE and matched comparators. Cases were defined as patients with ≥3 diagnoses of SLE between January 2006 and September 2015. Controls were persons without SLE matched 1:1 to SLE cases on age, sex, race/ethnicity, and enrollment date. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), Asian, Hispanic, based on self-report or derived rule sets. Multimorbidity (2 or more comorbidities) was defined using 172 chronic comorbidities from the chronic condition indicator of the clinical classification software (healthcare cost and utilization project). SLE, cutaneous lupus, and rheumatoid arthritis ICD-9 codes were excluded from the analysis. Two or more ICD-9 codes at least 30 days apart were used to define a comorbidity. A secondary analysis was performed including those with 5 or more comorbidities. Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI) adjusted for age, race/ethnicity, and region.

Results: The study included 34,752 cases with SLE and 34,752 matched non-SLE comparators. The mean age was 48 years (SD 14.2), and 90.6% were female for both cohorts in both cohorts, women were slightly younger (mean age 48 vs. 50 years). In both cohorts, women were more racially/ethnically diverse than men, with 66.2% of women (69.4% men) being White, 11.8% (12.3%) Hispanic, 18.7% (14.8%) Black, 3.4% (3.5%) Asian.

Patients with SLE had more multimorbidity than non-SLE subjects (58.1% vs 26.3%). Observed rates of multimorbidity were higher in men than women with SLE (57.8% women vs 60.9% men, p=0.0006), but similar non-SLE patients, (26.3% women vs 26.1% men, p=0.74). Following adjustment for age, race/ethnicity, and geographic region, multimorbidity among SLE patients remained higher in men (OR: 1.09; 95% CI: 1.01-1.18) compared to women and but lower for non-SLE men than women (OR: 0.91; 95% CI: 0.83-0.99). Secondary analysis in those with 5 or more comorbidities also demonstrated higher multimorbidity in men with SLE compared to women (OR: 1.15; 95%CI: 1.05-1.25), but similar in those without SLE (OR:0.93, 95% CI: 0.93 (0.8-1.08) (Table).

Conclusion: This large, nationwide claims study showed increased occurrence of multimorbidity in men with SLE compared to women with SLE, but similar to men and women without SLE. These differences may reflect the long-term effects of more severe disease in men with SLE than women.

Disclosure: A. Duarte-Garcia, None; **H. Heien**, None; **N. Shah**, None; **C. Crowson**, None.

Abstract Number: 0598

Differences in Discoid Lupus Erythematosus Skin Lesion Distribution and Characteristics in Black and Non-Black Patients: A Retrospective Cohort Study

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Background/Purpose: Epidemiological studies have shown that discoid lupus erythematosus (DLE) has a higher incidence and prevalence in minorities, particularly Black individuals. Racial differences in clinical features amongst

Table 1. Demographics and clinical characteristics of 112 Black and 71 non-Black DLE patients

Demographics and Clinical Characteristics	Black (N=112)	Non-Black[a] (N=71)	P-Value
Age at Initial Visit (Yr), Median (IQR)	50.0 (39.2-56.9)	46.0 (35.5-54.3)	0.041[c]
Age at Diagnosis (Yr), Median (IQR)	40.0 (30.0-49.0)	36.0 (27.0-47.0)	0.266[c]
Gender, n (%)			0.716[d]
Male	18 (16%)	10 (14%)	
Female	94 (84%)	61 (86%)	
Disease Duration at Initial Visit (Yr), Median (IQR)	4.4 (0.9-12.4)	3.5 (1.0-10.2)	0.964[c]
Follow up Duration (Yr), Median (IQR)	0.4 (0.0-2.9)	0.4 (0.0-2.9)	0.967[c]
SLE Diagnosis, n (%)			0.222[d]
Yes	48 (43%)	24 (34%)	
No	64 (57%)	47 (66%)	
Smoking Status n (%)[b]			0.451[d]
Current Smoker	42 (38%)	25 (39%)	
Past Smoker	25 (23%)	10 (16%)	
Never Smoked	43 (39%)	30 (46%)	
Baseline CLASI Activity Score, Median (IQR)	4.5 (2.0-9.0)	5.0 (2.0-10.0)	0.912[c]
Baseline CLASI Damage Score, Median (IQR)	10.0 (6.0-14.5)	6.0 (3.0-10.0)	**<0.001[c]**

[a] Non-Black patients consisted of 45 Caucasians, 18 Hispanics, 5 Asians, 2 Mixed patients and 1 Middle Eastern patient with DLE.
[b] Smoking status is missing for 8 patients.
[c] P-values were calculated with Mann Whitney U test.
[d] P-values were calculated with Chi-Square test.
Abbreviations: CLASI – Cutaneous Lupus Erythematosus Disease Activity and Severity Index, DLE – Discoid Lupus Erythematosus, IQR – Interquartile Range, Yr - Year

DLE patients are not well understood. The objective of this retrospective cohort study was to examine the differences in DLE lesion distribution and characteristics of Black individuals compared to non-Black individuals.

Methods: Patients were recruited from the University of Texas Southwestern cutaneous lupus erythematosus (CLE) registry from January 2009 to June 2020. Adult DLE patients with a reported race/ethnicity and Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) scores were included in this study. Patients were excluded if they had an additional CLE subtype, or if they were < 18 years old. DLE lesion locations and characteristics based on CLASI scores were the primary outcome variables. The primary predictor variable was race, which was categorized into Blacks and non-Blacks. Additional predictor variables included age at initial visit, gender, disease duration at initial visit, follow up duration, smoking status and presence or absence of SLE. SKINDEX-29+3 qualify of life scores were secondary outcome measures. Univariate analyses were performed to determine demographic differences and to compare lesion location, lesion characteristics, and quality of life scores between Black and non-Black patients. Multivariable logistic regression was performed to determine significant predictors of DLE lesion location.

Results: 183 DLE patients (112 Black and 71 non-Black) were included in this study. Black DLE patients had worse baseline CLASI damage scores compared to non-Black DLE patients (median: 10.0 (IQR: 6.0-14.5) vs. 6.0 (3.0-10.0), p< 0.001) (**Table 1**) and were more likely to have. In univariate analysis, Black patients were more likely to have scalp involvement [OR (95% CI): 2.54 (1.12-5.79), p=0.013] (**Table 2**). In multivariable analysis, Black patients had 2.54 (1.20-5.37) greater odds of having scalp involvement (p=0.015) and 1.97 (1.06-3.68) greater odds of having ear

Table 2. Univariate analyses of DLE lesion distribution based on CLASI scores in 112 Black and 71 non-Black patients

Anatomical Location	Black (N, %)	Non-Black (N, %)	OR (95% CI)	P-Value[a]
Scalp	97 (87%)	51 (72%)	2.54 (1.12-5.79)	**0.013**
Ears	66 (59%)	32 (45%)	0.92 (0.92-3.33)	0.067
Nose/Malar Area	60 (59%)	40 (56%)	0.89 (0.47-1.70)	0.714
Rest of Face	63 (56%)	37 (53%)	1.18 (0.62-2.24)	0.584
V-Area of Neck (Front)	22 (20%)	19 (27%)	0.67 (0.31-1.44)	0.260
Posterior Neck/Shoulders	22 (20%)	20 (28%)	0.62 (0.29-1.33)	0.181
Chest	20 (18%)	18 (25%)	0.64 (0.29-1.41)	0.223
Abdomen	10 (9%)	1 (1%)	N/A[b]	0.053[c]
Back and Buttocks	27 (24%)	18 (25%)	0.94 (0.44-1.99)	0.849
Arms	40 (36%)	25 (35%)	1.02 (0.53-2.00)	0.945
Hands	19 (17%)	9 (13%)	1.41 (0.56-3.77)	0.432
Legs	23 (21%)	18 (25%)	0.76 (0.36-1.65)	0.446
Feet	20 (18%)	8 (11%)	1.71 (0.67-4.77)	0.228
Mucous Membrane	15 (13%)	9 (13%)	1.07 (0.41-2.94)	0.889

[a] P-values were calculated with Chi-square test unless otherwise specified.
[b] OR not calculated due to low numbers of patients with abdomen involvement in the non-Black patient group.
[c] P-values were calculated with Fisher's exact test.
Abbreviations: CLASI - Cutaneous Lupus Erythematosus Disease Area and Severity Index, DLE – Discoid lupus erythematous

Table 3. Univariate analyses of DLE lesion characteristics based on CLASI scores in 112 Black and 71 Non-Black patients

Anatomical Location and Lesion Characteristics	Black (N, %)	Non-Black (N, %)	P-Value[a]
Erythema in Any Location	99 (88%)	63 (89%)	0.944
Scale in Any Location	78 (69%)	53 (75%)	0.464
Dyspigmentation in Any Location	111 (99%)	56 (79%)	**<0.001**
Scarring in Any Location	100 (89%)	55 (77%)	0.030
Scalp			
Erythema	75 (59%)	42 (67%)	0.284
Scale/Hypertrophy	58 (52%)	34 (48%)	0.607
Dyspigmentation	92 (82%)	32 (48%)	**<0.001**
Scarring Alopecia	89 (79%)	40 (56%)	**0.001**
Non-Scarring Alopecia	49 (44%)	29 (41%)	0.699
Ears			
Erythema	36 (32%)	20 (28%)	0.570
Scale/Hypertrophy	34 (30%)	22 (31%)	0.928
Dyspigmentation	63 (56%)	25 (35%)	**0.006**
Scarring	31 (28%)	14 (20%)	0.223

[a] P-Values were calculated with Chi-Square test.
Abbreviations: CLASI - Cutaneous Lupus Erythematosus Disease Area and Severity Index, DLE – Discoid lupus erythematous

involvement (p=0.032) compared to non-Blacks. Black patients were more likely to have dyspigmentation (99% vs. 79%, p< 0.001) in any anatomical location), scalp (82% vs. 48%, p< 0.001), and ear (56% vs. 35%, p=0.006). They were also more likely to have scarring alopecia (79% vs. 56%, p=0.001) than non-Blacks (**Table 3**). No significant differences in SKINDEX-29+3 scores were seen between Black and non-Black patients with DLE.

Conclusion: Black DLE patients have important lesion location and characteristic differences compared to non-Black DLE patients. Signs of disease damage, particularly ear dyspigmentation, scalp dyspigmentation and scarring alopecia, can more frequently affect Black DLE patients and can help assist diagnosis and treatment plans. Our findings will help clinicians better understand racial differences in DLE presentation, which may lead to proper diagnosis and treatment initiation.

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Abstract Number: 0599

Effectiveness of a Provider Led Intervention on Medication Adherence in an Urban Lupus Clinic

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Background/Purpose: Medication adherence is a difficult charge in SLE. Up to 75% of lupus patients are non-adherent with hydroxychloroquine (HCQ). Pharmacy refill data measured by percent days covered (PDC) and HCQ levels are the main adherence measures used in SLE. Health literacy is an important culprit in non-adherence. Social cognitive behavior theories have been applied to understand the link between medication adherence and health literacy. Health literacy universal precautions refers to the steps that providers should take assuming all patients have difficulty comprehending health information. This study aimed to evaluate the effect of a provider led universal precautions intervention on medication adherence using indirect (PDC) and direct (HCQ blood level) measures of medication adherence and disease activity measures in a predominantly Hispanic, low SES, low health literacy, SLE population.

Methods: Data collected during a 6-month prospective intervention was compared with data from the 6-month pre-intervention period. Interventions based on the Agency for Healthcare Research and Quality universal health literacy precautions kit included 1) encouraging questions, 2) teach-back communication, and 3) brown-bag medication review. Analysis was performed using paired t-tests, comparing PDC (for HCQ, corticosteroids, immunosuppres-

Table 1, Demographics

Total	**N=28**
Sex	Female, 100%
Age, years	41.5 ± 15.4
Race, n (%)	10 (36%) Black 8 (29%) White 7 (25%) Other 2 (7%) Declined 1 (3%) Asian
Ethnicity, n (%)	20 (71%) Hispanic 8 (29%) non-Hispanic
Preferred Language, n (%)	14 (50%) Spanish 14 (50%) English
Insurance, n (%)	24 (86%) Medicaid 4 (14%) Medicare
Disease Duration, years	10.02± 8.9
Average HCQ dose, mg/day	407 ± 37.8
Average time between visit 1 and 2, days	113.8 ± 72.6
Average HCQ level, ng/mL Pre-Intervention, n=10 Post-Intervention, n=10	 1129 ± 504 ng/mL 1056 ±496 ng/mL
Active SLE Manifestations	**N (%)**
Arthritis	15 (54%)
Nephritis	10 (36%)
Rash	7 (25%)
Alopecia	6 (21%)
Hypocomplementemia	6 (21%)
Leukopenia	5 (33%)
SLE Medications	**N (%)**
Corticosteroids	7 (25%)
Mycophenolate Mofetil Azathioprine Methotrexate	8 (29%) 2 (7%) 2 (7%)
Rituximab Belimumab, subcutaneous	2 (7%) 1 (4%)

sants, and biologics), HCQ levels, and the hybrid SLEDAI (SLE disease activity index) scores from the pre- and post-intervention period. 60% of our cohort has limited health literacy.

Results: The study included 28 women with SLE, mean age 43.1± 15.4 years, 71% Hispanic. 50% reported Spanish as preferred language, disease duration 10± 9 years. All patients had state funded health insurance (86% Medicaid, 14% Medicare) consistent with low SES. Patients reported taking 407 ± 37.8 mg of HCQ/day. Additionally, 25% of

Table 2, Percent Days Covered (PDC)

	N=	**Mean Pre-Implementation**	**SD**	**Mean Post-Implementation**	**SD**	**p-value**
PDC, Hydroxychloroquine	28	0.61	0.39	0.53	0.39	0.58
PDC, Corticosteroids	7	0.6	0.34	0.67	0.23	0.67
PDC, Immunosuppressants*	11	0.57	0.41	0.57	0.42	0.99
PDC, Biologics**	3	0.83	0.29	0.83	0.29	0.99

*Immunosupressants: Methotrexate, Azathioprine, Mycophenolate Mofetil

**Biologics: Rituximab, subcutaneous Belimumab

patients were prescribed corticosteroids, 11% biologics, and 43% immunosuppressants. During the intervention period, physicians completed 56 patient visits, 2 visits/patient, 113 ± 72 days apart. Median toolkit administration time was < 5 minutes. HCQ PDC decreased from 0.61 pre- to 0.53 post- intervention (p=NS); non-adherent < 0.80. HCQ blood levels were >1000 ng/mL both pre- and post-intervention, therapeutic HCQ > 500ng/ml. On an individual level, PDCs and blood levels were discordant. Two patients had high post intervention PDC (>0.8) and sub-therapeutic blood levels. Prednisone adherence based on PDC increased from 0.6 to 0.67 (p=NS). Immunosuppressants PDC remained the same, 0.57. Biologics PDC was >0.8. SLEDAI decreased from 4.02 ± 4.31 to 2.88 ± 2.67 ($p < 0.05$).

Conclusion: In a population of predominantly Hispanic patients with SLE, low health literacy, and low SES, non-adherence was high across all medications except for biologics. The application of health literacy interventions provided conflicting results. This discordance could be due to differences in the recall periods; the recall period for PDC is 6 months, while HCQ levels only reflect weeks of adherence. The reasons for this discordance and non-adherence need to be further investigated and improved interventions to increase adherence should be sought.

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Abstract Number: 0600

A Cohort Study of Retention in Ambulatory Lupus Care Among Medicare Patients with SLE-related Hospitalizations

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Background/Purpose: In other conditions that require chronic management, poor retention in ambulatory care is associated with adverse outcomes. We previously identified that living in the most disadvantaged neighborhoods was the greatest predictor of poor care retention among lupus patients in one urban cohort. Given high hospitalization and rehospitalization rates among lupus patients, this study aims to measure rates and predictors of retention in lupus care prior to hospitalization. Results will inform efforts to improve care retention, health disparities, and outcomes for patients with lupus.

Methods: This retrospective cohort study used a 20% random Medicare sample of adult hospitalizations with an SLE diagnosis code from 2013-2014. Inclusion required at least one year of continuous Medicare AB coverage before hospitalization.

Retention in lupus care was measured in the 12 months prior to hospitalization. Visit-based retention in care used an established threshold of at least two ambulatory rheumatologist visits >= 90 days apart. Rates of visit-defined care retention were calculated by sociodemographic and comorbidity groups. Generalized logistic regression, clustered by patient, was performed to identify predictors of care retention.

Table 1. Care retention status by baseline characteristics of Medicare admissions with SLE

		SLE n = 11,296 n (cohort %)	Visit retention n = 4,149 n (row %)	No visit retention n = 7,147 n (row %)	p value*
Patient Variables					
Age group	18-35	1,175 (10.4)	388 (33.0)	787 (67.0)	0.002
	36-64	5,034 (44.6)	1,818 (36.1)	3,216 (63.9)	
	65+	5,087 (45.0)	1,943 (38.2)	3,144 (61.8)	
Sex	Female	10,086 (89.3)	3,791 (37.6)	6,295 (62.4)	<0.001
Race/Ethnicity	Asian/Pacific Islander	152 (1.4)	66 (43.4)	86 (56.6)	0.020
	Black	3,264 (28.9)	1,132 (34.7)	2,132 (65.3)	
	Hispanic	1,077 (9.5)	388 (36.0)	689 (64.0)	
	Native American	130 (1.2)	43 (33.1)	87 (66.9)	
	White	6,546 (58.0)	2,468 (37.7)	4,078 (62.3)	
	Other/Unknown	127 (1.1)	52 (40.9)	75 (59.1)	
Medicaid		5,230 (46.3)	1,695 (32.4)	3,535 (67.6)	<0.001
Disability		7,336 (64.9)	2,723 (37.1)	4,613 (62.9)	0.244
RUCA	Urban Core	8,176 (72.5)	3,061 (37.4)	5,115 (62.6)	<0.001
	Suburban	961 (8.5)	373 (38.8)	588 (61.2)	
	Large rural	1,219 (10.8)	441 (36.2)	778 (63.8)	
	Small town/ Rural	916 (8.1)	270 (29.5)	646 (70.5)	
ADI Quintile	Most Disadvantaged	2,631 (24.2)	861 (32.7)	1,770 (67.3)	<0.001
HCC Score (mean, [SD])		3.8 [2.5]	3.6 [2.4]	3.9 [2.6]	<0.001
Comorbidities	Anxiety	5,752 (50.9)	1,971 (34.3)	3,781 (65.7)	<0.001
	Alcohol use disorder	286 (2.5)	58 (20.3)	228 (79.7)	<0.001
	CHF	3,227 (28.6)	998 (30.9)	2,229 (69.1)	<0.001
	Chronic lung disease	4,663 (41.3)	1,634 (35.0)	3,029 (65.0)	0.002
	Diabetes mellitus	3,698 (32.7)	1,222 (33.0)	2,476 (67.0)	<0.001
	Depression	3,693 (32.7)	1,306 (35.4)	2,387 (64.6)	0.036
	Renal failure	4516 (40.0)	1,371 (30.4)	3,145 (69.6)	<0.001
	Liver disease	911 (8.1)	326 (35.8)	585 (64.2)	0.537
	Obesity	2,655 (23.5)	1,022 (38.5)	1,633 (61.5)	0.031
	Opioid/drug use disorder	1,570 (13.9)	479 (30.5)	1,091 (69.5)	<0.001
	Tobacco use disorder	3,347 (29.6)	1,008 (30.1)	2,339 (69.9)	<0.001
	Valvular disease	1,915 (17.0)	675 (35.3)	1,240 (64.7)	0.139
30-Day Readmission (n [column %])		2,601 (24.0)	891 [21.5]	1,710 [23.9]	0.001

**p values calculated using ANOVA for numeric variables and chi-square for categorical comparisons.*
Abbreviations: RUCA = rural urban commuting area, ADI = area deprivation index, HCC= Hierarchical Classification Code, CHF = congestive heart failure.

Results: Among 11,296 SLE-related hospitalizations, the overall observed rate of visit-defined care retention in the year prior to hospitalization was just 36.7%. White, Black, and Hispanic patients had lower rates of retention when compared to Asian/Pacific Islander patients (37.7%, 34.7%, 36.0% vs. 43.4% p=0.02, Table 1). Retention rates for rural-residing patients were significantly lower than suburban (29.5% vs 38.8%, $p < 0.001$). Hospitalizations associated with the most disadvantaged neighborhood ADI quintile had lower rates of patient retention (32.7% vs 38.5%, $p < 0.001$). Thirty-day rehospitalization rates were 21.5% among those with baseline retention compared to 23.9% without.

Multivariable analysis showed that women were more often retained (aOR 1.41, 95% CI 1.15-1.73) (Table 2). Rural residents had 26% lower odds of being retained in care when compared to urban residents (0.74, 0.59-0.94). History

Table 2. Odds Ratios for Predictors of Visit-Defined Care Retention

		Adjusted Odds Ratio	Adjusted 95% CI
Age at admission (yrs)		**0.99**	**0.98-0.99**
Sex	Female	**1.41**	**1.15-1.73**
Race/ethnicity	White	Ref	Ref
	Asian/Pacific Islander	1.29	0.82-2.02
	Black	1.02	0.86-1.22
	Hispanic	1.02	0.80-1.30
	North American Native	1.23	0.63-2.42
	Other/Unknown	1.27	0.69-2.34
Medicaid		**0.73**	**0.63-0.85**
Disability		1.12	0.95-1.31
ADI Disadvantage	Most Disadvantaged Quintile	0.88	0.75-1.03
RUCA	Urban	Ref	Ref
	Suburban	1.03	0.83-1.28
	Large Rural	0.99	0.80-1.22
	Small town/ Rural	**0.74**	**0.59-0.94**
HCC score		1.03	0.99-1.08
Comorbidities	Anxiety	**0.83**	**0.73-0.95**
	Alcohol use disorder	**0.54**	**0.35-0.84**
	Diabetes mellitus	**0.84**	**0.73-0.97**
	Fluid & electrolyte disorders	**0.79**	**0.70-0.90**
	Obesity	**1.23**	**1.05-1.44**
	Peripheral vascular disease	**0.83**	**0.70-0.99**
	Renal failure	**0.64**	**0.56-0.75**
	Tobacco use disorder	**0.75**	**0.64-0.88**

The model also adjusted for additional comorbidities (chronic lung disease, coagulopathy, congestive heart failure, depression, liver disease, neoplasms, neurological disease, opioid or drug use disorder, pulmonary circulatory disease, valvular disease, weight loss) which were not significant predictors.

of Medicaid enrollment, a proxy of low SES, was significantly associated with decreased odds of retention in care (0.73, 0.63-0.85). Similarly, alcohol use (0.54, 0.35-0.84), tobacco use disorders (0.75, 0.64-0.88), and renal failure (0.64, 0.56-0.75) were associated with lower odds of retention in care. Obesity predicted 23% greater odds of retention (1.23, 1.05-1.44). Race/ethnicity and ADI quintile were not significant in the full model. Limitations include potential misclassification of NP/PA visits.

Conclusion: Rural residence and lower SES, indicated by Medicaid eligibility, predicted lower likelihood of retention in ambulatory lupus care prior to hospitalization. Several comorbid conditions, including renal failure, also predicted lower retention. Those retained in care had lower rates of 30-day readmission. Findings highlight the importance of addressing ambulatory access and outreach to retain and re-engage lupus patients in rheumatology care. Results can aid patient-provider communication on the importance of continuity of lupus care.

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Abstract Number: 0601

Racial Differences in Medication Beliefs Among SLE Patients

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Medication adherence is essential to establishing and maintaining disease remission among SLE patients. Patients' beliefs about treatment influence engagement and adherence to therapy. We previously found racial disparities in medication adherence between White and non-White SLE patients, but racial differences in beliefs about medications have not been well explored. In this study, we investigated differences in medication beliefs and their association with medication adherence between White and non-White SLE patients.

Methods: Patients meeting ACR or SLICC SLE criteria completed the 18-item Beliefs about Medicines Questionnaire (BMQ), which measures four belief domains: disease-specific medication necessity, disease-specific medication concern, general medication overuse, and general medication harm. Adherence was measured using the Domains of Subjective Extent of Nonadherence (DOSE- nonadherence) questionnaire. Due to small numbers of patients who identified as Asian and Hispanic, they were grouped with Black patients and analyzed as non-White. We compared median BMQ scores between White and non-White patients, and explored differences in BMQ scores between adherent and non-adherent patients by race.

Results: This analysis included 102 patients (48 White, 48 Black, 5 Asian, 1 Hispanic, mean age 50, 96% female, 33% < college education, 54% private insurance). For the 18 individual questions, 11 produced answers that were statistically different between the White and non-White patients. Compared to Whites, non-White patients had more general beliefs that medications are harmful (8.5 [interquartile range (IQR) 7-10] vs 7 [IQR 5-9], p=0.005) and overused (11 [IQR 9-12] vs 8.5 [IQR 8-10], p=0.003).

Table 1. comparing BMQ domains between adherent and non-adherent patients by race

	White			Non-white		
	Adherent (n=32)	Nonadherent (n=15)	p-value	Adherent (n=24)	Nonadherent (n=29)	p-value
BMQ specific necessity[1]	20[18-23.5]	19[17-22]	0.5	20[17.5-21.5]	17[15-20]	0.06
BMQ specific concern[1]	**11[7-13]**	**13.5[12-19]**	**0.03**	12[10-16]	15.5[13-17]	0.1
BMQ general overuse[2]	8[7-10]	9[8-10]	0.3	**9.5[8-12]**	**11[10-13]**	**0.04**
BMQ general harm[2]	7[5-8]	8[5-9]	0.4	**8[6-10]**	**9.5[8-11]**	**0.008**

[1] score range 5-25, [2] score range 4-20; BMQ = Beliefs in Medicines Questionnaire

While 71% of White patients reported adherence, only 44% of non-White patients reported adherence. Among White patients, those who were nonadherent reported more SLE-specific medication concerns. In contrast, among non-White patients, those who were non-adherent reported more general beliefs that medications are harmful and overused (Table 1).

Conclusion: We found significant differences in medication beliefs between White and non-White SLE patients with the greatest difference in general beliefs about medications. These racial differences in medication beliefs were also present in adherence data, with non-adherence in the White group being driven by specific concerns about SLE medications while non-adherence in the non-White group was driven by general concerns about medications. These results suggest adherence interventions tailored to race may be more effective, with a focus on building trust in the non-White community. Future studies should investigate the relationship between medication beliefs and SLE outcomes. The extent to which racial differences in medication beliefs may be driven by mistrust in the medical system and systemic racism also deserves further study.

Disclosure: D. **Anderson**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **R. Sadun**, None; **J. Rogers**, Exagen, 2, 5, Pfizer, 5, Eli Lilly, 2, Immunovant, 2, Northwestern University, 2; **L. Criscione-Schreiber**, GlaxoSmithKline, 5; **J. Doss**, Pfizer, 5; **C. Volis**, None; **T. Coles**, Merck, 5; **K. Sun**, None.

Abstract Number: 0602

Use of a Popular Opinion Leader Model to Disseminate Information Virtually About Clinical Trial Enrollment to People of Color with Lupus

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SESSION INFORMATION
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Background/Purpose: Despite a disproportionate burden of systemic lupus erythematosus (SLE) and disparities in adverse outcomes among Black compared to white individuals, people of color are underrepresented in SLE clinical trials. Our aims were: 1) to leverage a community-academic partnership in Boston and Chicago to develop clinical trial education modules for individuals who self-identify as Black with SLE and 2) to recruit and train trusted Popular Opinion Leaders (POLs) with robust social networks to disseminate this information in their communities. Due to COVID-19, we adapted the traditional, in-person, community-based POL model to a virtual platform and assessed the feasibility of this approach.

Methods: Rheumatologists and public health experts from two academic institutions developed training modules in partnership with community leaders and SLE advocates in Boston and Chicago. POLs age ≥18 years old with and without SLE were recruited through community- and hospital-based networks from Boston and Chicago neighborhoods with high proportions of Black individuals. To train the POLs, five presentations were delivered using an interactive, virtual platform. Modules included: 1) Description of the POL Model, 2-3) Introduction to Clinical Trials, I/II, 4) History of Racism and Clinical Trials, and 5) Clinical Trials: Barriers, Facilitators, and Mediators. POLs completed

Table. Characteristics of Popular Opinion Leaders (POLs) in Boston and Chicago			
Site		Boston	Chicago
Number of POLs		19	17
Mean (SD) Age		55.6 (11.4)	52.8 (18.2)
Sex – N (%)	Female	18 (95)	14 (82)
	Male	1 (5)	3 (18)
Self-identified Race/Ethnicity- N (%)	Black/African American	13 (68)	16 (94)
	White	3 (16)	0
	Other	2 (11)	0
	Hispanic	1 (5)	1 (6)
Educational Attainment* – N (%)	High School	6 (32)	1 (6)
	Technical School/GED	3 (16)	2 (13)
	Bachelor's Degree	4 (21)	6 (38)
	Master's Degree	6 (32)	3 (19)
Mean Years of Work Experience (SD)		28.8 (13)	27.4 (10)
Marital Status- N (%)	Single	11 (58)	7 (41)
	Married	4 (21)	6 (35)
	Divorced	3 (16)	2 (12)
	Widowed	1 (5)	2 (12)
Housing – N (%)	Live with spouse, blood relatives and family	10 (53)	10 (59)
	Live alone	9 (47)	7 (41)
Self-Reported Health Conditions – N (%)	Diagnosed with lupus	12 (63)	13 (77)
	Diabetes	1 (5)	0
	Hypertension	7 (37)	9 (53)
	Arthritis	12 (63)	12 (71)
	Obesity	9 (47)	4 (24)
Relative with Lupus – N (%)		8 (42)	11 (65)
Previous Community Experience- N (%)	Previous training as a health promoter	8 (42)	3 (18)
	Participated in previous lupus educational training	13 (68)	13 (77)
	Hosted presentations or community-based events	11 (58)	9 (53)
	Gave testimony	10 (53)	5 (56)
	Presented at health fairs	8 (42)	8 (89)
	Distributed educational materials	10 (53)	8 (89)
	Contacted stakeholders	6 (32)	3 (33)
	Participated in patient advocacy	9 (47)	4 (44)
	Collected information from community members (surveys or other)	6 (32)	3 (33)
	Patient navigation	5 (26)	3 (33)
Social Network- N (%)	Member of a gym/sports club	7 (37)	8 (47)
	Member of a faith-based organization such as a church or ministry	11 (58)	13 (77)
	Have meeting places with social network members	10 (53)	8 (47)
Abbreviations: POL, Popular Opinion Leader; GED, General Educational Development; *5 not reported in Chicago cohort			

pre and post tests for the modules, which were compared using paired t-tests. POLs were also taught to use virtual platforms to share information learned with their social networks. POLs reported their dissemination data.

Results: Nineteen POLs were recruited in Boston and 17 in Chicago (**Table)**. In Boston, 18 (95%) were female, 13 (68%) self-identified as Black, and mean age was 55.6 years. In Chicago, 14 (82%) were female, 16 (94%) self-identified as Black, and mean age was 52.8 years. Retention of POLs throughout the training was 82% both in Boston and Chicago. For the two-part clinical trials module, POLs' knowledge of clinical trials improved significantly overall (mean difference of 3.92 points, 95% CI 3.35-5.89), and separately in Boston (mean difference of 2.80 points, 95% CI 3.33-7.18,) and Chicago (mean difference of 5.45 points, 95% CI 2.42-6.10). As of May 2021, 7 POLs documented 36 encounters and reached 1,023 total individuals; dissemination is ongoing. Boston POLs reached 233 people, including 122 individuals through a sorority newsletter, 104 through Zoom, 6 through phone calls, and 1 in person. Chicago POLs personally reached 240 individuals, including 163 people in a social media group for SLE patients and families, as well as 550 individuals through email interactions.

Conclusion: The POL model was effectively adapted to a virtual program in the context of the COVID-19 pandemic. Modules developed jointly by academic and community partners were implemented and successfully improved knowledge regarding clinical trials. POL retention was high, possibly due to the convenience of virtual trainings and the sense of community developed through the training sessions. POLs successfully disseminated information virtually about clinical trials. Further studies are needed to determine impact on the diversity of SLE trial enrollment.

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Abstract Number: 0603

Barriers and Potential Solutions in the Recruitment and Retention of Older Patients in Clinical Trials – Lessons Learned from Six Large Multi-center Randomized Controlled Trials

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SESSION INFORMATION

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Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Older people remain underrepresented in clinical trials, and evidence generated in younger populations cannot always be generalized to older patients.

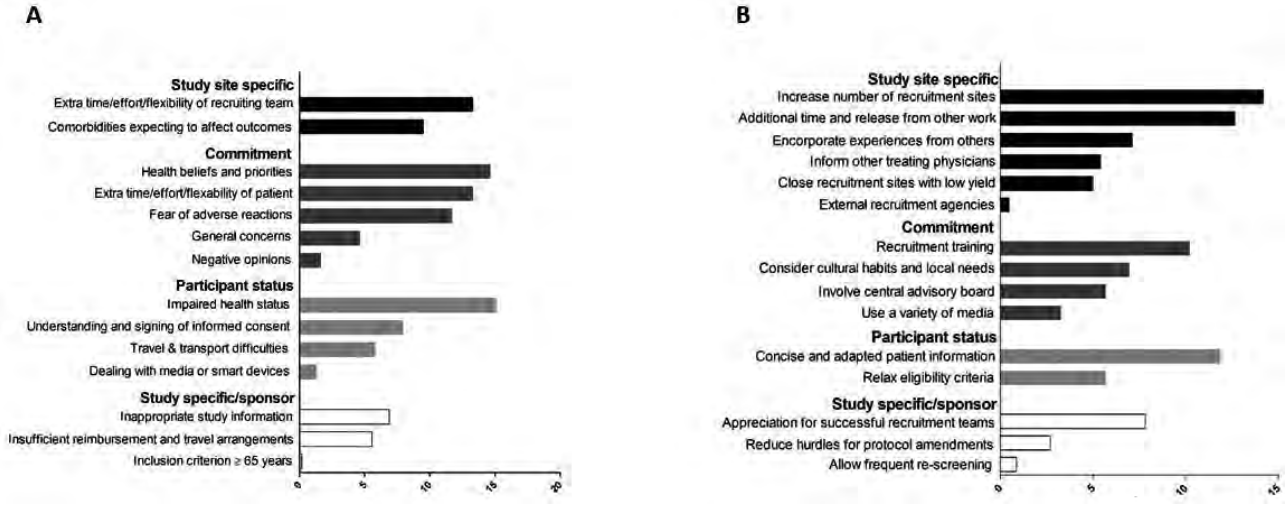
We aimed to identify key barriers and to discuss solutions to specific issues affecting recruitment and retention of older participants in clinical trials based on experience gained from six current European randomized controlled trials (RCTs) focusing on older People (Table 1).

Methods: A multidisciplinary group of experts including representatives of the six RCTs held two networking conferences and compiled lists of potential barriers and solutions. Every item was subsequently allocated points by each study team according to how important it was perceived to be for their RCTs.

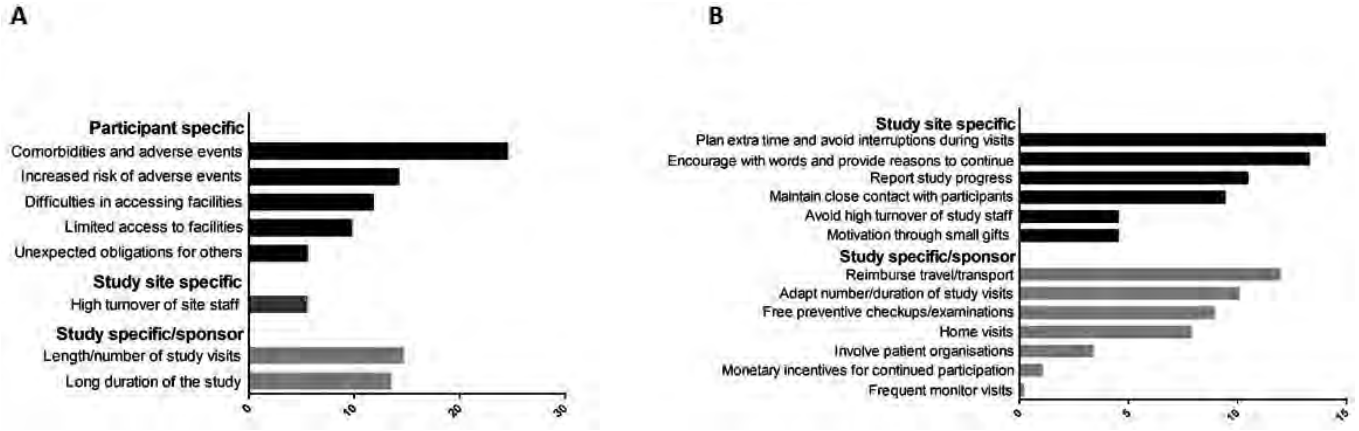
Results: The six RCTs enrolled 7612 older patients (Table 1). Key barriers to recruitment were impaired health status, comorbidities and diverse health beliefs including priorities within different cultural Systems (Figure 1A). All trials had to increase the number of recruitment sites. Other measures felt to be effective included the provision of extra time, communication training for the study staff and a re-design of patient Information (Figure 1B). Key barriers for retention included the presence of severe comorbidities and the occurrence of adverse events. Long study duration, frequent study visits and difficulties accessing the study site were also mentioned (Figure 2A). Solutions felt to be effective included spending more time maintaining close contact with the participants, appropriate measures to show appreciation and reimbursement of travel Arrangements (Figure 2B).

Six international multi-center randomized controlled trials (RCTs), designed for patients aged ≥ 65 years and supported by the European Commission Horizon 2020 research and innovation programme

Trial Acronym	Participants enrolled	Countries	Short description
GLORIA	451	Portugal, Germany, Italy, Slovakia, Hungary, Romania, The Netherlands,	Comparing the cost-effectiveness and safety of additional low-dose glucocorticoid in treatment strategies for elderly patients with rheumatoid arthritis
SECURE	2499	Spain, Italy, Germany, France, Poland, Hungary, Czech Republic	Secondary prevention of cardiovascular disease in the elderly
SITLESS	1369	Spain, France, United Kingdom, Germany, Denmark	Exercise referral schemes enhanced by self-management strategies to battle sedentary behaviour in the elderly
OPERAM	2008	Switzerland, Belgium, The Netherlands, Ireland	Optimising therapy to prevent avoidable hospital admissions in the multimorbid elderly
EU-CaRE	179 (RCT part)	Denmark, Spain, The Netherlands, France, Switzerland	The European study on effectiveness and sustainability of current cardiac rehabilitation programmes in the elderly RCT: effectiveness of tele-rehabilitation in patients not (willing to) taking part in regular rehabilitation
PRECIOUS	Currently 1106	United Kingdom, Norway, Italy, Hungary, The Netherlands, Poland, Estonia, Germany, Greece	Prevention of complications to Improve outcome in elderly patients with acute Stroke



A: Challenges in retention. Mean number of points awarded per item (standard error range: 1,92 – 4,84). The more points an item got, the more relevant it was perceived to be for the respective trial. B: Solutions in retention. Mean number of points awarded per item (standard error range: 0,21 – 4,47). The more points an item got, the more relevant it was perceived to be for the respective trial.



A: Challenges in retention. Mean number of points awarded per item (standard error range: 1,92 – 4,84). The more points an item got, the more relevant it was perceived to be for the respective trial. B: Solutions in retention. Mean number of points awarded per item (standard error range: 0,21 – 4,47). The more points an item got, the more relevant it was perceived to be for the respective trial.

Conclusion: Recruitment and retention of older patients in trials requires special recognition and a targeted approach. Our results provide scientifically-based practical recommendations for optimizing future studies in this population.

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Abstract Number: 0604

Disparities in Burden of Disease in Patients with RA Across Racial and Ethnic Groups

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Prior research has shown that differences exist in disease activity and clinical outcomes for RA across racial and ethnic groups in the US.[1] This study provides an updated analysis examining differences in disease burden and change in clinical outcomes over time across racial and ethnic groups.

Methods: This study used data from CorEvitas' RA Registry, which consists of over 56,000 RA patients across 42 US states. We included patients with a visit during two time periods (visit 1: 2013–2015; visit 2: 2018–2020) and selected the first visit in the first time period and the last visit in the second time period for each patient. Patients self-reported race and ethnicity at enrollment; Clinical Disease Activity Index (CDAI) score was obtained at both visits.

Table 1. Demographic and clinical characteristics of study population by race/ethnicity

	Visit 1 (2013–2015)				Visit 2 (2018–2020)			
	White	Black	Hispanic	Asian	White	Black	Hispanic	Asian
Total n	8142	527	545	149	8142	527	545	149
Patient demographics								
Age, years, mean (SD)	60.7 (11.6)	59.5 (11.7)	55.1 (13.0)	57.2 (12.3)	66.7 (11.6)	65.4 (11.7)	61.1 (13.1)	63.2 (12.5)
Female	6181 (75.9)	449 (85.2)	452 (82.9)	127 (85.2)	6181 (75.9)	449 (85.2)	452 (82.9)	127 (85.2)
Private insurance	6034 (74.1)	325 (61.7)	398 (73.0)	122 (81.9)	4768 (58.6)	272 (51.6)	315 (57.8)	100 (67.1)
Medicare insurance	3061 (37.6)	214 (40.6)	150 (27.5)	33 (22.1)	4495 (55.2)	283 (53.7)	230 (42.2)	56 (37.6)
Markers of RA severity								
Seropositivity[a]	n = 5309	n = 310	n = 384	n = 100	n = 5720	n = 328	n = 409	n = 110
	4018 (75.7)	262 (84.5)	314 (81.8)	85 (85.0)	4351 (76.1)	275 (83.8)	337 (82.4)	90 (81.8)
Duration of disease, years, mean (SD)	11.8 (9.8)	9.8 (8.7)	11.1 (9.6)	10.6 (8.4)	17.9 (10.0)	15.8 (8.9)	17.1 (9.8)	16.6 (8.5)
Number of prior DMARDs, mean (SD)	1.5 (1.8)	1.3 (1.6)	1.6 (1.9)	1.5 (1.7)	2.7 (2.4)	2.4 (2.2)	2.9 (2.4)	2.5 (2.3)
Disabled	n = 7996	n = 518	n = 531	n = 145	n = 7938	n = 514	n = 531	n = 141
	881 (11.0)	97 (18.7)	85 (16.0)	11 (7.6)	896 (11.3)	93 (18.1)	92 (17.3)	6 (4.3)
Current RA treatment								
MTX use	5010 (61.5)	360 (68.3)	318 (58.3)	91 (61.1)	3852 (47.3)	275 (52.2)	256 (47.0)	72 (48.3)
Non-MTX csDMARD use	2373 (29.1)	151 (28.7)	141 (25.9)	36 (24.2)	2261 (27.8)	169 (32.1)	125 (22.9)	37 (24.8)
b/tsDMARD use	4626 (56.8)	280 (53.1)	338 (62.0)	89 (59.7)	4914 (60.4)	314 (59.6)	361 (66.2)	93 (62.4)
Prednisone use	1778 (21.8)	137 (26.0)	120 (22.0)	23 (15.4)	1449 (17.8)	113 (21.4)	85 (15.6)	16 (10.7)
History of comorbidities								
Cardiovascular disease	909 (11.2)	54 (10.2)	42 (7.7)	6 (4.0)	1488 (18.3)	77 (14.6)	63 (11.6)	16 (10.7)
Cancer	649 (8.0)	34 (6.5)	30 (5.5)	9 (6.0)	981 (12.0)	54 (10.2)	44 (8.1)	12 (8.1)
Hypertension	2640 (32.4)	217 (41.2)	146 (26.8)	32 (21.5)	2805 (34.5)	228 (43.3)	153 (28.1)	35 (23.5)
Diabetes	626 (7.7)	77 (14.6)	60 (11.0)	10 (6.7)	709 (8.7)	83 (15.7)	64 (11.7)	12 (8.1)
Anxiety/depression	1310 (16.1)	86 (16.3)	101 (18.5)	16 (10.7)	1479 (18.2)	102 (19.4)	122 (22.4)	16 (10.7)
Serious infections	4924 (60.5)	256 (48.6)	296 (54.3)	75 (50.3)	6000 (73.7)	320 (60.7)	372 (68.3)	93 (62.4)

Data are n (%) unless otherwise specified.

[a]Seropositivity defined as RF+ or ACPA+.

b/tsDMARD, biologic/targeted synthetic DMARD; csDMARD, conventional synthetic DMARD; SD, standard deviation.

Table 2. Adjusted marginal mean (95% CI) for each outcome measure by race/ethnicity

	Visit 1 (2013–2015)				Visit 2 (2018–2020)			
	Mean	95% CI	Pairwise *P*[a]	Overall *P*[a]	Mean	95% CI	Pairwise *P*[a]	Overall *P*[a]
CDAI score								
White	9.9	(8.7–11.1)	Reference	0.058	8.0	(7.0–8.9)	Reference	0.027
Black	10.2	(8.6–11.8)	0.632		8.3	(7.0–9.6)	0.491	
Hispanic	11.1	(9.5–12.6)	0.033		9.2	(8.0–10.4)	0.005	
Asian	11.7	(9.5–14.0)	0.069		9.0	(7.2–10.8)	0.225	
Proportion of patients in LDA								
White	68.8	(63.5–73.6)	Reference	0.364	78.8	(73.8–83.1)	Reference	0.048
Black	64.2	(56.0–71.7)	0.146		76.3	(68.6–82.5)	0.324	
Hispanic	67.1	(59.5–74.0)	0.546		72.4	(64.5–79.1)	0.007	
Asian	63.2	(50.3–74.5)	0.313		76.1	(63.7–85.3)	0.575	
Proportion of patients in remission								
White	27.2	(22.9–31.8)	Reference	0.379	31.2	(26.8–36.0)	Reference	0.052
Black	24.8	(18.7–32.2)	0.440		26.5	(20.4–33.6)	0.114	
Hispanic	26.1	(20.0–33.3)	0.718		25.1	(19.5–31.8)	0.028	
Asian	20.0	(12.8–29.8)	0.110		26.1	(17.8–36.6)	0.281	
HAQ-DI score								
White	0.68	(0.65–0.71)	Reference	0.009	0.76	(0.73–0.80)	Reference	0.002
Black	0.75	(0.67–0.82)	0.063		0.84	(0.77–0.92)	0.027	
Hispanic	0.78	(0.71–0.85)	0.003		0.87	(0.80–0.94)	0.001	
Asian	0.71	(0.59–0.83)	0.596		0.78	(0.66–0.90)	0.833	

[a]Pairwise *P* is used to determine if there is a difference between means in patients in a specific race/ethnicity group compared with White patients; overall *P* is used to assess the differences in means across all race/ethnicity groups.

CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; LDA, low disease activity.

Table 3. Adjusted marginal mean change (95% CI) for each outcome measures over seven-year period by race/ethnicity

	Mean change	95% CI	Pairwise *P*[a]	Overall *P*[a]
Change in CDAI score from visit 1 to visit 2				
White	−2.01	(−2.73 to −1.28)	Reference	0.077
Black	−2.08	(−3.21 to −0.96)	0.873	
Hispanic	−0.88	(−1.95 to 0.18)	0.010	
Asian	−2.01	(−3.73 to −0.30)	0.995	
Achievement of LDA (%)[b]				
White	54.7	(49.0 to 60.2)	Reference	0.474
Black	50.3	(39.6 to 60.9)	0.397	
Hispanic	49.2	(38.9 to 59.5)	0.255	
Asian	61.2	(41.6 to 77.8)	0.498	
Achievement of remission (%)[b]				
White	19.2	(16.3 to 22.5)	Reference	0.905
Black	17.9	(12.7 to 24.6)	0.662	
Hispanic	19.2	(14.0 to 25.8)	0.994	
Asian	21.9	(13.5 to 33.6)	0.560	
Change in HAQ-DI score from visit 1 to visit 2				
White	0.07	(0.04 to 0.09)	Reference	0.145
Black	0.08	(0.02 to 0.14)	0.660	
Hispanic	0.10	(0.04 to 0.16)	0.218	
Asian	−0.03	(−0.13 to 0.07)	0.063	

[a]Pairwise *P* is used to determine if there is a difference between means in patients in a specific race/ethnicity group compared with White patients; overall *P* is used to assess the differences in means across all race/ethnicity groups; [b]Only performed for those not in the disease state at visit 1 (patients not in LDA at visit 1: White, n = 2871; Black, n = 231; Hispanic, n = 235; Asian, n = 48; patients not in remission at visit 1: White, n = 5698; Black, n = 401; Hispanic, n = 409; Asian, n = 102).
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; LDA, low disease activity.

Patient characteristics at visits 1 and 2 by race/ethnicity (white [non-Hispanic], Black [non-Hispanic], Hispanic, or Asian) are summarized. The primary outcome was CDAI at visits 1 and 2. Secondary outcomes included the proportion of patients in low disease activity (LDA; CDAI ≤ 10) or remission (CDAI ≤ 2.8), and HAQ-disability index (DI) at each visit. We evaluated mean change in CDAI and HAQ-DI from visit 1 to 2 and probability of achieving LDA and remission at visit 2.

Linear regression models were adjusted for demographics, clinical characteristics, and site as a random effect variable. From these models, marginal means or mean change for each outcome were computed; overall and pairwise tests were used to detect differences in outcomes between races.

Results: Of 9363 eligible patients (8142 White, 527 Black, 545 Hispanic, 149 Asian), a majority (76–85%) were female. Mean age at visit 1 ranged from 55.1 to 60.7 years, and mean disease duration ranged from 9.8 to 11.8 years (**Table 1**). Many patients had history of serious infections (50–61%) and hypertension (22–41%).

In adjusted analyses, we estimated higher CDAI scores for Hispanic vs White patients at both visits 1 and 2 (**Table 2**). Proportions of patients in LDA and remission were similar across groups at visit 1; at visit 2, a significantly lower proportion of Hispanic patients were in LDA and remission compared with White patients.

Functional status declined over time for all groups, indicated by greater mean HAQ-DI scores at visit 2 vs visit 1. Compared with White patients, Hispanic patients had significantly higher mean HAQ-DI scores at visit 1, and both Black and Hispanic patients had significantly higher mean HAQ-DI scores at visit 2 (**Table 2**).

Longitudinally, CDAI scores improved for all groups from visit 1 to 2, though Hispanic patients improved significantly less than White patients (**Table 3**). There were no statistically significant differences in achievement of LDA or remission or change in HAQ-DI over time across groups.

Conclusion: Disease activity improved over the 7-year time period across all racial and ethnic groups. However, disparities between racial and ethnic groups in disease activity and functional status did persist over time, suggesting that further effort is needed to understand the drivers of these discrepancies and close this racial gap.

Reference

1. Greenberg JD, et al. *Am J Med* 2013;126:1089–1098.
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Abstract Number: 0605

Impact of Area of Residence on Perceptions of Health and Disease Activity in Ethnic Minorities with Rheumatoid Arthritis in an Urban Setting

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Health care disparities in hypertension and other chronic disease are well established. Ethnic minority residents of Washington DC, particularly Wards 7 and 8, have higher rates of chronic disease and shortened lifespans, but little is known about the impact on rheumatoid arthritis (RA) in these areas. The Ethnic Minority Rheumatoid Arthritis Consortium (Howard University Hospital –[HUH]) comprised of 9 sites nationwide, reported more severe RA disease, worse outcomes, and less use of biologic therapy. Further, socioeconomic factors were linked to delayed diagnosis, worse prognosticators/seropositivity and functional outcomes. Patient assessment of overall health and disease activity have been shown to correlate positively with RA outcomes, but may be influenced by non-RA factors such as comorbidities. HUH serves a primarily DC residential African American population. We evaluated the association of area of residence on perceptions of health and RA disease status.

Methods: EMRAC participants seen at HUH and with at least one follow-up visit were evaluated. The associations of sociodemographic factors and RA disease status with Wards/Area of residence, perception of health (poor, fair, good, excellent) and physical activity (seldom, monthly, weekly) were evaluated. Logistic regression models were used to estimate associations of patients' perception of health and RA disease activity (RAPID3) within non-DC and DC regions, adjusting for gender, age, race, physical activity and comorbidities.

Results: An enrollment cohort of 96 EMRAC subjects (females 83%, mean age 55 years (SD 15.5) was available for analysis (Table 1.). Wards 4-8 corresponded to the NE, SE areas of DC and comprised of younger patients with more frequent seropositivity and higher disease activity compared to Wards 1-3 (NW, SW DC). Sixty-four percent (56/87)

Table 1: Baseline Characteristics of Cohort in Relation to Area of Residence

	Non-DC	Wards 1-3	Wards 4-8	p-value**
Region		**NW**	**NE/SE**	
N = 96	27	18	51	
Age (mean (SD))	61.04 (9.74)	61.11 (16.73)	52.96 (16.70)	**0.04**
Male Gender	5 (18.5)	2 (11.1)	9 (17.6)	0.78
Physical Activity				0.78
Almost never	12 (44.4)	10 (55.6)	25 (49.0)	
Monthly	2 (7.4)	0 (0.0)	2 (3.9)	
Weekly	13 (48.1)	8 (44.4)	24 (47.1)	
Tobacco Use				0.13
None	20 (74.1)	12 (66.7)	26 (51.0)	
Current	1 (3.7)	1 (5.6)	11 (21.6)	
Past	6 (22.2)	5 (27.8)	14 (27.5)	
Race				0.08
Black	23 (85.2)	11 (61.1)	46 (90.2)	
Latino	3 (11.1)	6 (33.3)	4 (7.8)	
Other	1 (3.7)	1 (5.6)	1 (2.0)	
Education level (n = 89)				0.01
Less than High School	1 (4.2)	6 (35.3)	3 (6.2)	
Greater than High School	14 (58.3)	5 (29.4)	23 (47.9)	
High School	9 (37.5)	6 (35.3)	22 (45.8)	
Insurance (n = 86)				**0.005**
Medicaid	0 (0)	5 (33.3)	22 (45.8)	
Medicare	5 (21.7)	4 (26.7)	7 (14.6)	
Private	18(78.3)	6 (40.0)	19 (39.6)	
Perception of health is Poor to Fair (n = 69)	3 (15.8)	6 (46.2)	14 (37.8)	0.14
Rapid3 at enrollment in remission/LDA (n = 87)	13 (56.5)	6 (40.0)	12 (24.5)	**0.03**
Rapid3 at follow-up in remission/LDA (n = 66)	11 (84.6)	5 (41.7)	17 (41.5)	**0.02**
Serological status (n = 90)				**0.03**
CCP Ab Positive	2 (8.0)	0 (0.0)	1 (2.1)	
RF positive	1 (4.0)	4 (23.5)	8 (16.7)	
Both	20 (80.0)	9 (52.9)	38 (79.2)	
Negative	2 (8.0)	4 (23.5)	1 (2.1)	

**N(column%) and Chi-square reported

had moderate to high disease activity; of whom, 66% of whom were from Wards 4-8. More non-DC patients were in remission/low disease activity at baseline and at 18 months – 13/23 (56.5%) and 11/13 (84.6%) respectively. Of 69 DC residents, 46 patients reported good to excellent perception of health (7 NW, 13 NE, and 10 SE). Of the remaining 23 DC residents (who reported fair to poor health), 70% resided in NE, SE areas. Non-DC residents (84%) were more likely to have a good to excellent perception of health compared to DC residents. Insurance data were available for 86 patients, 5 (6%) had non-DC Medicare/Medicaid, 38 (44%) had DC Medicare/Medicaid, and 43 (50%) were privately insured. Weekly physical activity was positively associated with perception of good health, regardless of area of residence (p-value: 0.02). Logistic regression (Table 2), controlling for demographic factors, found low disease activity and a non-DC domicile was significant (p-value: 0.05).

Table 2: Linear Regression Model for dependent variable Moderate to high disease activity

Observations: 48
Dependent Variable: Moderate to high disease activity on follow-up
Type: Generalized linear model
MODEL FIT:
$X^2(11) = 16.19$, $p = 0.13$
Standard errors: MLE

	exp (Est.)	2.5%	97.5%	z val.	p
(Intercept)	2.07	0.06	66.61	0.41	0.68
Non-DC Region	0.15	0.02	0.94	-2.03	0.04
NW DC Region	2.67	0.38	18.70	0.99	0.32
SE DC Region	1.16	0.26	5.13	0.20	0.84
Age	1.01	0.96	1.05	0.32	0.75
Male Gender	0.80	0.13	5.11	-0.23	0.81
Latino	0.31	0.04	2.13	-1.19	0.23
Poor to Fair Perception of Health	2.38	0.57	9.91	1.19	0.24
RF & CCP Positive	0.32	0.03	4.00	-0.88	0.38
RF & CCP Negative	4.25	0.12	148.82	0.80	0.42
RF positive	0.39	0.03	5.14	-0.72	0.47
Comorbidities present	1.45	0.31	6.86	0.47	0.64

Conclusion: RA patients in an urban region served by a single institution demonstrated differences in disease activity and perceptions of health based on area of residence. While physical activity may play a role in the perception of health it may not be solely explained by RA disease activity. Evaluation of the role of insurance coverage and physical activity in improving RA outcomes is a priority in this vulnerable population

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Abstract Number: 0606

How Might We Care for Rheumatoid Arthritis (RA) Patients Unable to See a Rheumatologist And/or Use Certain of Our Medications? Proposed Preliminary Recommendations for RA Patients Who Don't Meet Our Established Guidelines

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Physicians share responsibilities to promote social justice and assure equitable healthcare for all. Street medicine (SM) is a field dedicated to address the need of homeless patients, often by visiting them in the street or anywhere they reside to deliver care. We, rheumatologists and SM providers, have been interested in identifying and improving the management and outcomes of our homeless RA patients. They do not fit available

Table 1. Key Principles, Key Terms, and Drug Categories for the Proposed Rheumatoid Arthritis Guidelines

Key Principles	
1. Focus on common barriers to access to medical care including homelessness. 2. Cost, distance, transportation and access to medications are important priorities. 3. Disease activity measurement using an ACR-recommended measure should be performed if possible but may not be feasible and providers must use best clinical judgement. 4. Functional status assessment should be performed when possible and services including PT, OT and assistance devices are important tools. 5. Patients with low RA disease activity or is in clinical remission should generally be maintained and treatment changes should be made when disease activity is moderate to high. 6. Treatment recommendations of one medication over another means does not imply that the non-favored medication is contraindicated, and use may be considered per provider preference. 7. In making treatment decisions, priority should be made on maximizing functionality and minimizing suffering. Lab work, subspecialty appointments, and monitoring may be obtained as possible.	
Key Term	**Definition**
Homeless RA Patient	Adults, >18 years, meeting the ACR RA classification criteria and experiencing housing insecurity
Disease activity	Low, moderate, or high as per validated scales, ideally CDAI or RAPID-3 given minimal reliance on labs
Optimal dosing of RA treatments	1) Medication dosing to achieve benefit given consideration of patient priorities 2) ideally taken at least 3 months before therapy escalation or switching
Drug category	**Description**
Disease Modifying Anti-rheumatic Drugs (DMARDs)	Leflunomide (10 mg PO uptitrate to 20 mg daily), sulfasalazine (500 mg PO BID uptitrate to 1,000 mg BID), hydroxychloroquine (5 mg/kg PO), methotrexate (10 mg PO or SQ), uptitrate to 20-25 mg weekly), tofacitinib (5 mg PO BID), minocycline (100 mg PO BID), auranofin (6 mg PO daily)
Glucocorticoids	Low dose <10 mg daily, high dose >10 mg daily, short term <3 months
TNFα inhibitor (TNFi)	Adalimumab (40 mg SQ every other week), certolizumab pegol (400 mg SQ week 0, 2, 4 then 200 mg every other week), etanercept (50 mg SQ weekly), golimumab (2 mg/kg SQ week 0, 4, then every 8 weeks), infliximab (3 mg/kg SQ week 0, 2, 6 then every 8 weeks)
Rituximab	1,000 mg IV day 1, day 15
Other biologics	Those that could be administered SQ (i.e., abatacept, tocilizumab, anakinra) may be considered

treatment guidelines or recommendations. Nor do many patients worldwide who, for challenges including distance, transportation, disabilities, income, and insurance, have limited access to care and medications. Therefore, with the encouragement of the SM Institute, we propose guidelines for rheumatologists and non-rheumatologists seeing these patients.

Methods: We adapted procedures for guidelines development from the ACR. A leadership team, of senior rheumatology faculty with extensive experience, including with guidelines, in RA (RSP) and SM (CF, BF), examined the available evidence. A research team critically reviewed the pertinent literature, synthesized the discussion, and formulated

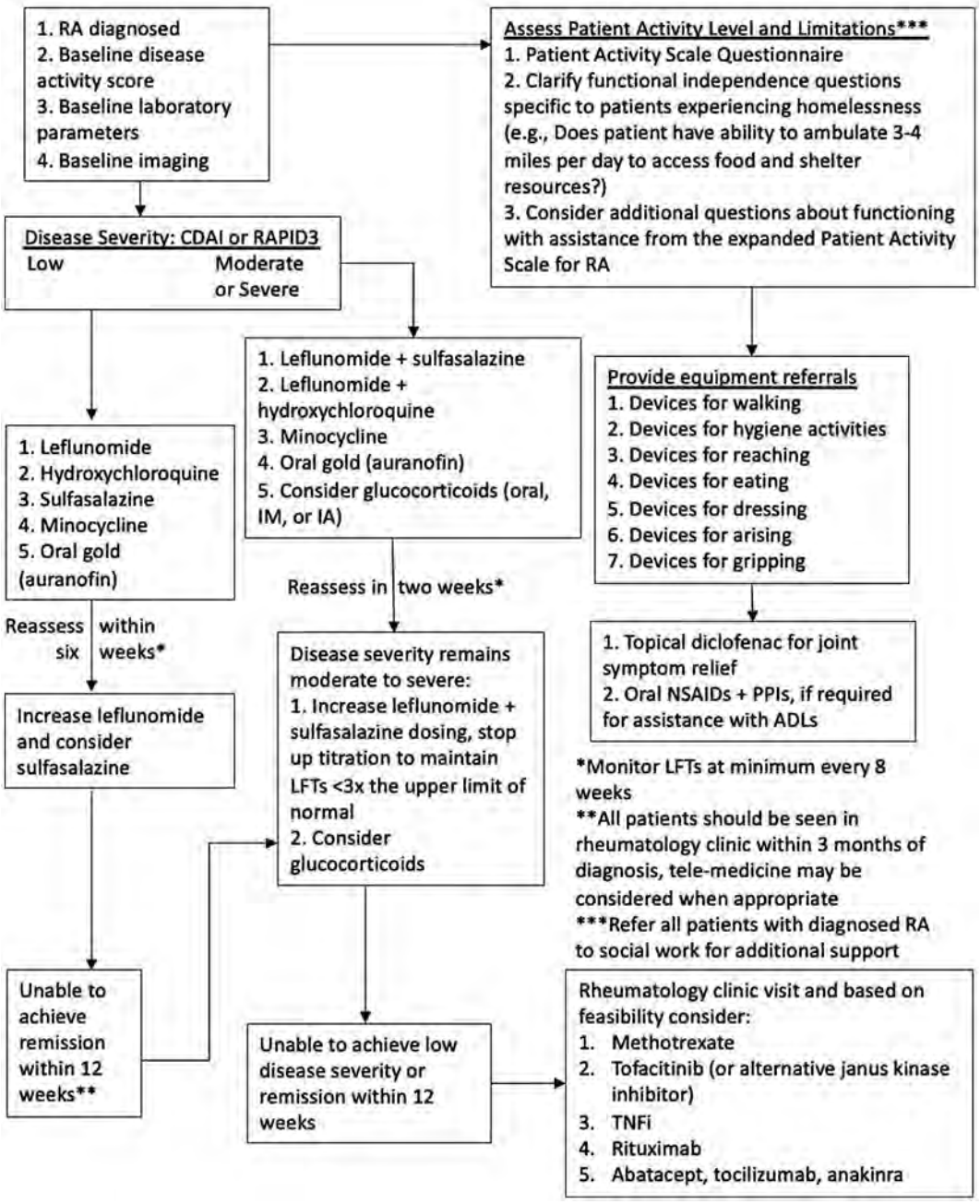

Figure 1. Proposed Rheumatoid Arthritis Treatment Algorithm.

guiding principles and PICO (population, intervention, comparator, and outcome) for possible regimens (NZW, AA, BR, SH). For each PICO question, the panel reviewed evidence and provided recommendations. Also assessed were data about therapies' efficacy, potential toxicities, ease of administration and monitoring, cost, and likely availability. The authors communicated through a series of questions focused on describing their approaches to affected patients.

Results: The Table summarizes key principles, terms, descriptions, and drug categories. We developed the principles outlined in Figure 1, which are based on patients' inability to consistently access rheumatologists; obtain, take, and store medications reliably; or get routine laboratory (or other) studies. Initial treatment regimens include leflunomide

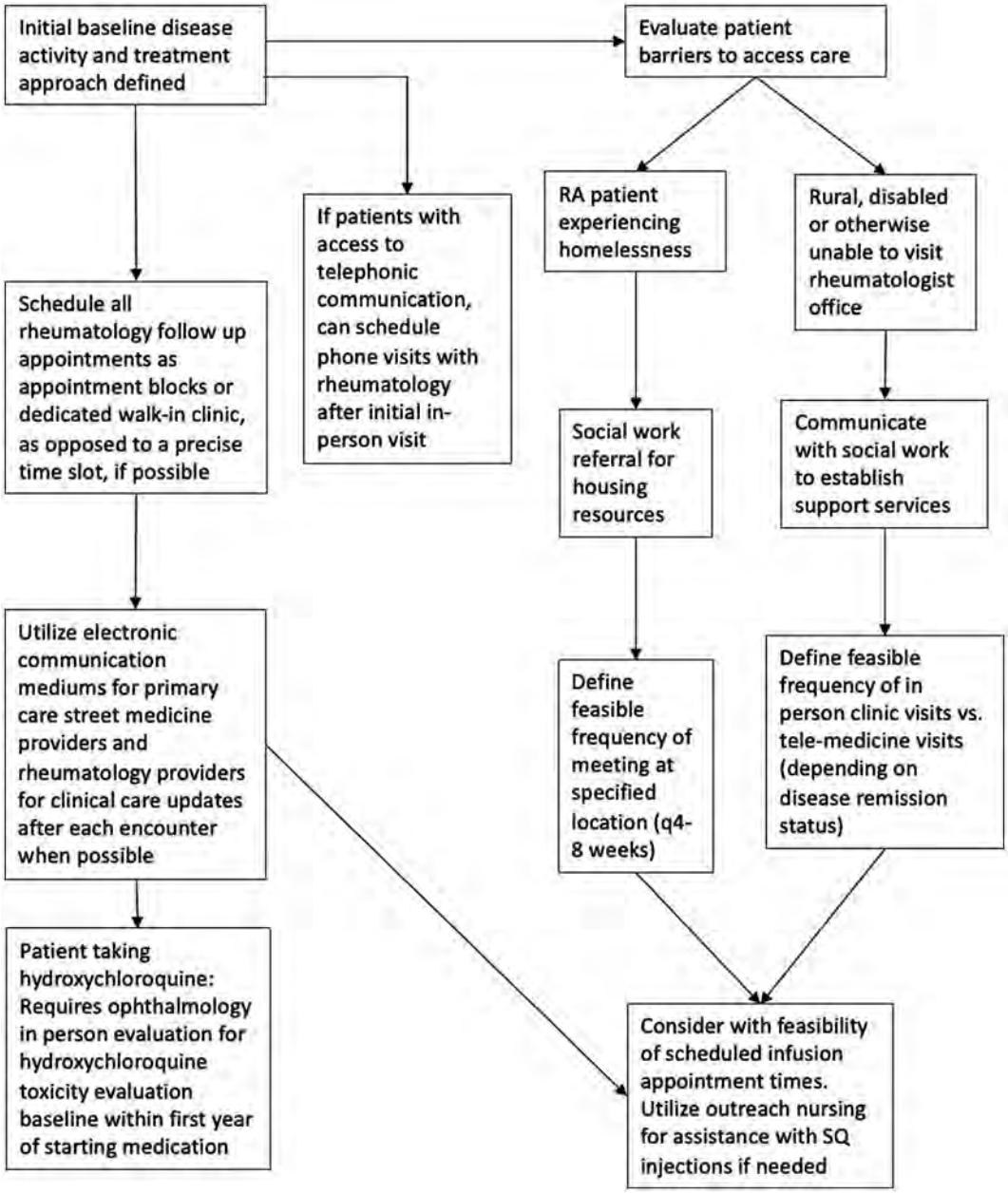

Figure 2. Proposed Rheumatoid Arthritis Continued Care Guideline

and sulfasalazine; alternatives are hydroxychloroquine, minocycline, methotrexate, auranofin, steroids (intermittently, low dose, or IA/IM), janus kinase inhibitors, and, for some, rituximab or other biologics. Figure 2 presents a proposed algorithm for continuity of care, individualized to patients' contexts. Referrals for certain adjunctive/assistance equipment are included.

Conclusion: Our efforts to care for our homeless patients led us to consider what is minimally adequate or acceptable rheumatologic care, how is it defined and quantified, and how might we conceive more innovative ways to provide/deliver it or its equivalent (i.e., SM, tele-medicine, or other). We propose guidelines for providers caring for those vulnerable patients unable to see rheumatologists or follow current treatment regimens, those for whom available guidelines do not apply or are not realistic. SM practice and limited experience with homeless patients suggest that

our proposed approach could be salutary for those patients worldwide who are challenged to see a rheumatologist or use (some of) our medications.

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Abstract Number: 0607

Validation Studies of Rheumatoid Arthritis Patient-Reported Outcome Measures in Diverse Populations at Risk for Inequity: A Systematic Review

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SESSION INFORMATION
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Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Existing patient-reported outcome measures (PROMs) in rheumatoid arthritis (RA) may be limited in their applicability to populations that experience inequities. We conducted a systematic review to identify validation studies for PROMs in populations at risk for inequity.

Methods: A systematic review of MEDLINE and EMBASE was completed. The search strategy was developed to identify measurement property studies for PROMs of interest (selected pain, disease activity, global evaluation and quality of life scales) in patients with RA. We identified experimental, observational, and qualitative studies reporting analysis of feasibility, construct validity and discriminant ability metrics for populations at risk for inequity by various factors including race, ethnicity, culture or language; employment status; gender and sex identity; education level; socioeconomic status; social support; age; health literacy and disability. A narrative synthesis was conducted.

Results: From 19,786 titles and abstracts screened, we identified 14 unique studies reporting validation metrics for pain (n=3), DAS28-ESR or DAS28-CRP (n=2), ACR20 (n=1), patient global assessment (n=2), EQ5D (n=4), and PROMIS® (n=3) by race (n=10 studies), age (n=6 studies), sex and gender identity (n=5 studies), education level (n=2 studies), and disability, literacy, employment status, social support level and socioeconomic status (n=1 study each). Most studies reported construct validity metrics (n=13), with 5 studies reporting on feasibility and 3 studies reporting on discriminant validity metrics. A visual summary of results is presented in the OMERACT Summary of Measurement Properties (SOMP)-Equity Extension table (Table 1). Overall, studies by culture or language demonstrated good measurement property metrics. There was significantly limited assessment of measurement property metrics for other populations at risk for inequity.

Conclusion: Our study highlights important gaps in patient representation in rheumatology research for accepted patient-reported outcome measures. New PROMs being developed for research and clinical practice should ensure

Progress-Plus Disparity Domain	Feasibility	Construct Validity	Discriminant Ability
Place of Residence	*no studies*	*no studies*	*no studies*
Race, Ethnicity, Culture, Language	Pain VAS (Japanese[1], Columbian[2]) PGA (Columbian[2]) PROMIS® Physical Function Item Bank (Dutch[3])	Pain VAS (Spanish[4], Japanese[1]) DAS28-CRP (Korean[5]) PGA (Columbian[2]) $EQ5D_{utility}$ (Portuguese[6]) $EQ5D_{utility}$ (Thai[7]) PROMIS® Physical Function Item Bank (Arabic[8]) PROMIS® Pain Interference Item Bank (Arabic[8]) PROMIS® Pain Intensity Item Bank (Arabic[8]) PROMIS® Fatigue Item Bank (Arabic[8]) PROMIS® Sleep Item Bank (Arabic[8]) PROMIS® Anxiety Item Bank (Arabic[8]) PROMIS® Depression Item Bank (Arabic[8]) PROMIS® Pain Interference Item Bank (Dutch-Flemish[9]) PROMIS® Pain Behaviour Item Bank (Dutch-Flemish[9])	Pain VAS (Spanish[4], Japanese[1]) DAS28-CRP (Korean[5]) ACR20 (White, Black, Hispanic[10])
		Pain VAS (Columbian[2])	
Occupation		$EQ5D_{utility}$[11] $EQ5D_{vas}$[11]	
Gender/Sex Identity		PROMIS® Pain Behaviour Item Bank (Dutch-Flemish[9])	
			ACR20[10]
		DAS28-ESR[12] $EQ5D_{utility}$ (Thai[7])	
Religion	*no studies*	*no studies*	*no studies*
Education Level		$EQ5D_{profile}$[13] $EQ5D_{utility}$[11] $EQ5D_{vas}$[11]	
Socioeconomic status		$EQ5D_{utility}$[11] $EQ5D_{vas}$[11]	
Social support level		$EQ5D_{utility}$[11] $EQ5D_{vas}$[11]	
Age		$EQ5D_{profile}$[13] $EQ5D_{utility}$[11] $EQ5D_{vas}$[11]	
		DAS28-ESR[12]	ACR20[10]
		$EQ5D_{utility}$ (Thai[7]) PROMIS® Pain Behaviour Item Bank (Dutch-Flemish[9])	
Health literacy	PGA[14]	PGA[14]	
Disability		$EQ5D_{profile}$[11]	$EQ5D_{utility}$[11]
			$EQ5D_{vas}$[11]

Legend VAS visual analogue scale; PGA patient global assessment; DAS28 disease activity score based on 28 joint counts; CRP C-reactive protein. items in green are those where the primary study concluded that the instrument met feasibility, construct validity or discriminant ability requirements for the construct tested. Items in amber are those where the measurement properties were potentially valid or had discriminant ability however with remaining uncertainty. Items in red indicate did not have construct validity or discriminant ability in the population it was tested in.

OMERACT Summary of Measurement Properties (SOMP)-Equity Extension for Patient-Reported Outcome Measures

and report representation of patients from populations facing inequities in the testing of metrics of feasibility, construct validity and discriminant ability.

Disclosure: C. Barnabe, Pfizer, 1, Gilead, 1, Novartis, 6, Sanofi, 6, Celltrion, 1; **A. Wattiaux**, None; **J. Petkovic**, None; **D. Beaton**, None; **B. Shea**, None; **R. Greer-Smith**, None; **J. Humphreys**, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5; **P. Tugwell**, None; **V. Umaefulam**, None.

Abstract Number: 0608

Adaptation of a Shared Decision-Making Tool for Early Rheumatoid Arthritis Treatment Decisions with Indigenous Patients

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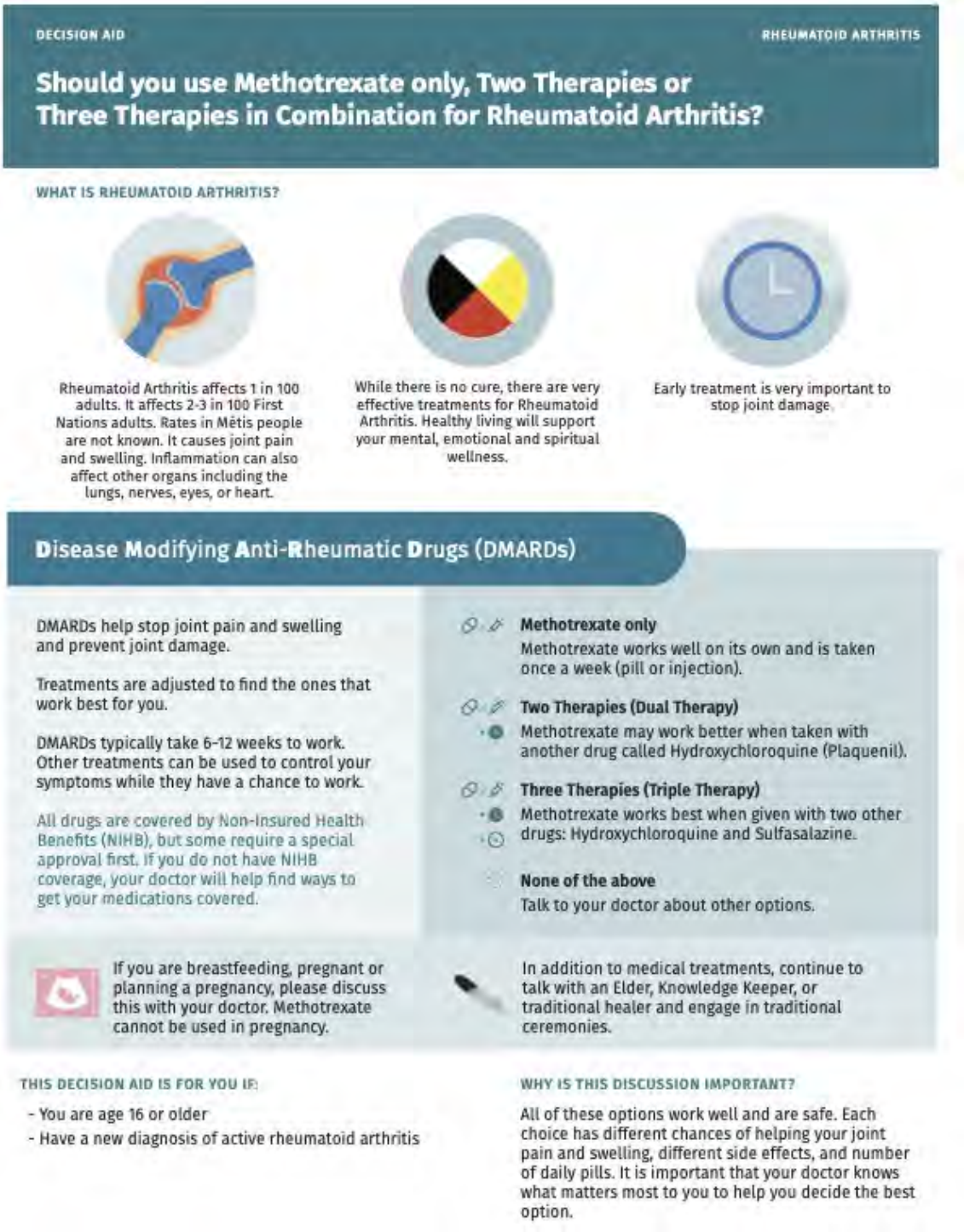
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patient decision aids (PtDA) can enable shared decision-making between patients and healthcare providers. We have previously developed a PtDA for first-line methotrexate-based treatment options in rheumatoid arthritis (RA). Adaptations to PtDAs for use with populations facing inequities in healthcare can improve the relevancy of information presented, incorporate appropriate cultural context, and address health literacy concerns. Our objective was to adapt the Early RA PtDA for use with Canadian Indigenous patients making initial disease-modifying treatment choices.

Methods: The Early RA PtDA was modified through an iterative process using data obtained from semi-structured interviews with Indigenous patients with RA using an interview guide. A thematic analysis of interview transcriptions was completed using NVivo 12 software. Initial modifications were made based on the input of a first cohort of patients, with the revised Early RA PtDA verified by a second cohort of patients.

Results: The initial directions for modification were provided by 7 participants, while 9 participants were recruited for the verification cohort. All participants were women living with RA and self-identified as First Nations, Plains Cree, or Indigenous. In the first iteration, the revisions made were to 1) clarify medication names and routes of administration; 2) include Indigenous traditional healing practice options; 3) provide information on formulary coverage for Indigenous patients; 4) simplify text; and 5) include Indigenous images, and use colors aligned with Canadian Indigenous community representation. The second cohort perceived the revised Early RA PtDA to be acceptable for layout and information content, with appreciation expressed by participants for including Indigenous traditional healing practices as adjuncts to treatment, which was seen as beneficial for advancing communication and relationship building with health practitioners. Additional revisions were requested to increase text legibility, insert more Indigenous images, make further changes in colors, address formulary coverage for non-status First Nations patients, and include information on lifestyle factors in managing RA. Indigenous patient-specific evidence on the efficacy and safety of medication options should be included in future iterations if data available, and translation of key words into the end-users' Indigenous languages should be included for implementation of the PtDA.

Conclusion: Incorporating Indigenous-specific adaptations in the design of PtDAs may increase use and relevancy to support patient focused care and engagement in treatment decisions, thereby supporting health-equity oriented health service interventions.



DECISION AID

RHEUMATOID ARTHRITIS

Should you use Methotrexate only, Two Therapies or Three Therapies in Combination for Rheumatoid Arthritis?

WHAT IS RHEUMATOID ARTHRITIS?

Rheumatoid Arthritis affects 1 in 100 adults. It affects 2-3 in 100 First Nations adults. Rates in Métis people are not known. It causes joint pain and swelling. Inflammation can also affect other organs including the lungs, nerves, eyes, or heart.

While there is no cure, there are very effective treatments for Rheumatoid Arthritis. Healthy living will support your mental, emotional and spiritual wellness.

Early treatment is very important to stop joint damage.

Disease Modifying Anti-Rheumatic Drugs (DMARDs)

DMARDs help stop joint pain and swelling and prevent joint damage.

Treatments are adjusted to find the ones that work best for you.

DMARDs typically take 6-12 weeks to work. Other treatments can be used to control your symptoms while they have a chance to work.

All drugs are covered by Non-Insured Health Benefits (NIHB), but some require a special approval first. If you do not have NIHB coverage, your doctor will help find ways to get your medications covered.

Methotrexate only
Methotrexate works well on its own and is taken once a week (pill or injection).

Two Therapies (Dual Therapy)
- Methotrexate may work better when taken with another drug called Hydroxychloroquine (Plaquenil).

Three Therapies (Triple Therapy)
- Methotrexate works best when given with two other drugs: Hydroxychloroquine and Sulfasalazine.

None of the above
Talk to your doctor about other options.

If you are breastfeeding, pregnant or planning a pregnancy, please discuss this with your doctor. Methotrexate cannot be used in pregnancy.

In addition to medical treatments, continue to talk with an Elder, Knowledge Keeper, or traditional healer and engage in traditional ceremonies.

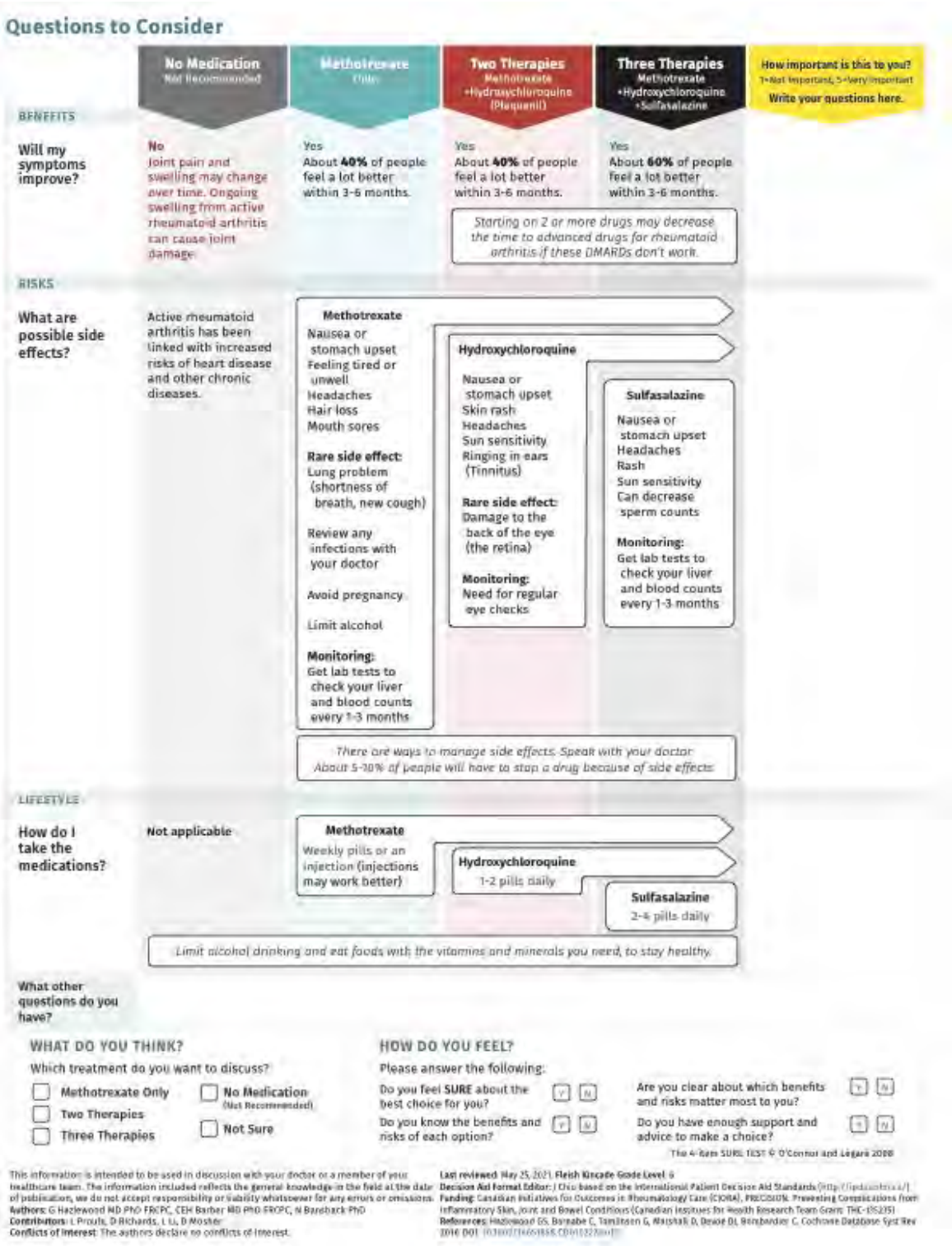
THIS DECISION AID IS FOR YOU IF:

- You are age 16 or older
- Have a new diagnosis of active rheumatoid arthritis

WHY IS THIS DISCUSSION IMPORTANT?

All of these options work well and are safe. Each choice has different chances of helping your joint pain and swelling, different side effects, and number of daily pills. It is important that your doctor knows what matters most to you to help you decide the best option.

Adapted Early RA Decision Aid for Indigenous Patient Use (Page 1)



Adapted Early RA Decision Aid for Indigenous Patient Use (Page 2)

Disclosure: V. Umaefulam, None; **T. Fox**, None; **G. Hazlewood**, None; **N. Bansback**, None; **C. Barber**, None; **C. Barnabe**, Pfizer, 1, Gilead, 1, Novartis, 6, Sanofi, 6, Celltrion, 1.

Abstract Number: 0609

Challenges of Caring for Patients with Inflammatory Arthritis Experiencing Homelessness: Preliminary (12- Month) Follow-up Observations and Identification of Certain Barriers to Care

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Homelessness is a public health crisis. Those with housing insecurity have unique barriers to healthcare that confound their outcomes. Because of the paucity of data about rheumatic disease patients (pts) with housing insecurity, we sought to better understand these challenges and develop approaches to improve their care.

As rheumatologists and "street medicine" providers, we identified homeless pts with rheumatic diseases to improve management and outcomes, reflecting responsibilities to promote social justice and equitable healthcare. We previously reported observations on 17 pts with inflammatory arthritis (15 rheumatoid arthritis [RA], 2 psoriatic arthritis [PsA]) (Clin Rheum 40:413-20, 2021). Here, we provide follow up on our pts and their perspectives on barriers to care.

Methods: We obtained follow-up clinical information from our original 17 pts and compared this to data summarized and published about them from 12 months previously. We also created a 100-question survey to assess pts' challenges and needs.

Results: Follow-up 12-month clinical information was available from 13/17 homeless (H) and 13/17 randomized, non-homeless (NH), controls. H were 54% and NH 92% female; H mean age was 57 (±9) and NH 61 (±8) years old; H 38% and NH 31% African American; H 38% and NH 23% Latino; and H 15% and NH 8% Caucasian.

H remained less well with more disease than NH-- poorer clinic appointment compliance (80% vs 91%, $p< 0.05$), more emergency services use (20 vs 5 ED visits), less use of DMARDs (43% vs 100%, $p< 0.01$), more steroid use (29% vs 0%, $p< 0.01$), and higher inflammatory markers (ESR 32 vs 26 mm/hr and CRP 17 vs 5 mg/L). 78% of H were assessed as stable, 14% improved, and 7% worse; 21% had stable controlled and 57% stable active disease vs 62% and 0% in NH ($p< 0.01$).

Among the H, 6 (4 RA, 2 PsA) completed the survey, 2 declined, and 9 could not to be reached. All 6 had found housing although all still had housing insecurity; 4 (67%) were homeless in the past. 3/6 (50%) obtained housing from social assistance during hospitalization following disease exacerbation while homeless. Average monthly income was $873. 5/6 (83.3%) were unable to work due to health and were in considerable pain that adversely impacted their physical and mental health and ability to perform ADLs. Their perceived "greatest need" included dental care, physical therapy, knee surgery, employment, socialization secondary to isolation, and stable housing.

Conclusion: These observations, while limited to modest numbers of pts and difficulties sustaining contact, add to our understanding of the unique challenges of homeless pts and provide a framework for strengthening collaboration between "street medicine" and rheumatology care providers to improve treatment and outcomes. This is supported

by the fact that half of surveyed pts obtained housing following hospitalization while homeless. Moreover, pts' perceived "greatest needs" went beyond housing and rheumatological care and indicate the importance of access to social and specialty services (ie, mental health, physical therapy, dental care, and employment). Collectively, these data suggest exciting opportunities to offer our homeless pts better quality and more equitable care.

Disclosure: B. Rai, None; **N. Zagelbaum Ward**, None; **A. Amarnani**, None; **C. Feldman**, None; **B. Feldman**, None; **R. Panush**, None.

Abstract Number: 0610

Evaluating Patient No Show Rates to Rheumatology Appointments Across a Regional Healthcare System

Osman Bhatty[1], Rebecca Schorr[2], Tarun Sharma[1] and Mary Chester Wasko[1], [1]Allegheny Health Network, Pittsburgh, PA, [2]Highmark Health, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: No-show visits in various clinical settings are costly to providers and to health care systems, potentially representing between 3-14% of a clinic's yearly income. This revenue challenge is compounded in rheumatology, as barriers to care delivery include socioeconomic factors for patients and prolonged wait times for appointments due to a growing shortage of rheumatologists nationwide. If patients at high risk for missing a referral appointment can be prospectively identified, then a strategic intervention to reduce the likelihood of a missed appointment will be fiscally advantageous and more effectively deliver rheumatic disease care to those in need. This study aims to characterize "no show" patients referred for outpatient rheumatology evaluation so that such a strategic intervention ultimately can follow.

Methods: Our electronic health record was queried for all patients who received ambulatory care referrals to a rheumatology provider within our healthcare system from January to December 2019. Basic demographic information, appointment characteristics and appointment outcomes were collected. Two patient groups were created based on their appointment outcomes; the first was comprised of all referred patients that no-showed, and the second included cancellations and completions. Patient and appointment characteristics were then compared between groups. Descriptive data is presented as mean (standard deviation) or median (interquartile range) for continuous variables and frequency (percentage) for categorical variables. Continuous variables were compared using a t-test or Mann-

Total Patients	2167
No Show	186 (8.6%)
Age	53.5 (16)
Female	1592 (73%)
African American	216 (10%)
Payer, Highmark BCBS	1001 (46%)
Appointment Made to Appointment Date, days	70 (22-98)
Referral Generated to Appointment Made, days	10 (2-76)

Patients Referred to Rheumatology within Allegheny Health Network in 2019

Variable	No Show	Completed & Cancelled	P-Value
Age	50.7 (15)	53.7 (16)	0.009
Female	135 (73%)	1457 (74%)	0.775
Appointment Made to Appointment Date, days	74 (30096)	70 (21-99)	0.337
Referral Generated to Appointment Made, days	33.4 (4-109)	9 (2-71)	0.0002
African American	43 (24%)	173 (9.1%)	<0.0001
Month			
Jan	13 (7%)	157 (7.9%)	0.65
Feb	11 (5.9%)	138 (7%)	0.588
Mar	13 (7%)	143 (7.2%)	0.908
Apr	17 (9.1%)	197 (9.9%)	0.725
May	15 (8.1%)	162 (8.2%)	0.957
June	16 (8.6%)	161 (8.1%)	0.821
Jul	11 (5.9%)	165 (8.3%)	0.249
Aug	16 (8.6%)	167 (8.4%)	0.936
Sep	13 (7%)	170 (8.6%)	0.455
Oct	22 (12%)	208 (11%)	0.574
Nov	22 (12%)	163 (8.2%)	0.09
Dec	17 (9.1%)	150 (7.6%)	0.443

Characteristics of Patients that No Showed and those that Cancelled/Completed

Variables	OR [95% CI]	P-Value
Age (with every 1 year)	0.984 [0.974, 0.99]	0.0019
Sex	0.871 [0.62, 1.2]	0.437
African American	2.352 [1.7, 3.3]	<0.001
Appointment Made to Appointment Date, days	1 [0.998, 1.0]	0.073
Referral Generated to Appointment Made, days	1.00 [1,1]	<0.0001
Month	1.0 [0.97, 1.1]	0.476

Multivariable Analysis to Determine Odds of Patient No Show

Whitney U test, as appropriate. Categorical data were analyzed using a chi-squared test or Fisher's exact test, as appropriate. A multivariable regression model finally was constructed to determine odds of no-show using those variables that statistically differed between groups.

Results: Across Allegheny Health Network, 2167 unique patients received ambulatory referrals to rheumatology in 2019 [Table 1]; 186 were no-shows. The month of the appointment nor the time between the date the appointment was made and the actual appointment date reached significance in regards to higher risk of no showing, although November did have the highest rates (12% vs. 8.2%, p=0.09) [Table 2]. In multivariable analysis, younger age (50.7 y vs 53.7 y, p=0.009) and African American race (24% vs. 9.15%, $p < 0.0001$) increased the odds of no-showing to an appointment [Table 3]. Longer duration from when the referral was generated by the physician to when the patient called to make the appointment was noted in the group of patients that no showed (33.4 days vs 9 days, p=0.0002) [Table 2].

Conclusion: Demographic (younger age, African American race) and appointment features (delay in patients calling for an appointment) characterized practitioner-referred rheumatology patients at high risk for no-showing for a new patient appointment. Future strategies to reduce no-show rates should address socioeconomic barriers to health care in high-risk individuals and improve access to new patient appointments.

Disclosure: O. **Bhatty**, None; **R. Schorr**, None; **T. Sharma**, None; **M. Wasko**, None.

Abstract Number: 0611

Association of Area Deprivation Index and Practice Patterns of Medicare Part D Rheumatologists

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Geographic disparities in the distribution and practice patterns of rheumatology providers may negatively impact patients with rheumatic diseases. The objective of this study was to describe the distribution of rheumatologists with respect to the area deprivation index (ADI) and to identify differences in practice patterns among Medicare Part D rheumatologist prescribers.

Methods: Prescriber data from the Medicare Part D Prescriber Public Use Files from 2013-2018 were downloaded. These data were joined to zip code level area deprivation index (ADI) data from the University of Wisconsin-Madison Neighborhood Atlas and presented as means and standard deviations (SDs). The ADI per zip code and number of rheumatologists per zip code were analyzed using Pearson's correlation. The average number of rheumatologists

	Observations (n = 31,034)
Beneficiary Count	302.91 ± 223.78
Total Drug Cost per Beneficiary	$2,208.54 ± $2,115.87
Medicare Part D Claims per Beneficiary	8.21 ± 3.42
Low-Income Subsidy Claims	0.35 ± 0.20
Average Age of Beneficiaries	69.49 ± 3.59
Number of Female Beneficiaries	239.24 ± 163.47
Risk Score of Beneficiaries	1.43 ± 0.22
Prescriptions per 100 beneficiaries bDMARD csDMARD Gabapentinoid NSAID Opioid Steroid	 41.93 ± 38.39 249.23 ± 138.53 46.21 ± 45.14 73.96 ± 65.14 94.81 ± 98.88 122.92 ± 70.32
30 Day Fills per Beneficiary	0.34 ± 0.52
Day Supply per Beneficiary	9.14 ± 14.65

Mean and Standard Deviation of Clinician Level Data Across Rheumatologists from 2013 to 2018

	2013	2014	2015	2016	2017	2018	p-value
Average Number of Rheumatologists per Zip Code	1.59 ± 1.52	1.60 ± 1.51	1.60 ± 1.49	1.60 ± 1.50	1.58 ± 1.56	1.56 ± 1.43	0.313
Average ADI	40.31 ± 27.34	40.39 ± 27.28	40.53 ± 27.20	40.42 ± 27.19	40.56 ± 27.19	40.70 ± 26.97	0.621

Descriptives of ADI and Rheumatologists by Year

	ADI Quintile 1	ADI Quintile 2	ADI Quintile 3	ADI Quintile 4	ADI Quintile 5	p-value
Beneficiary Count	254.18 ± 183.90	313.19 ± 198.61	332.09 ± 229.96	360.20 ± 228.3	387.63 ± 257.52	< 0.001
Age of Beneficiary	70.79 ± 3.55	69.80 ± 3.31	69.58 ± 3.01	68.87 ± 3.27	68.62 ± 3.23	< 0.001
Total Drug Cost per Beneficiary	$2,914.09 ± $2,368.53	$2,722.58 ± $1,951.13	$2,585.90 ± $2,037.56	$2,783.52 ± $1,894.13	$2,581.10 ± $1,581.27	< 0.001
Low-Income Subsidy Claims	0.34 ± 0.23	0.33 ± 0.19	0.32 ± 0.17	0.36 ± 0.18	0.37 ± 0.19	< 0.001
Risk Score of Beneficiaries	1.43 ± 0.23	1.41 ± 0.21	1.40 ± 0.18	1.43 ± 0.19	1.44 ± 0.19	< 0.001
Prescriptions						
bDMARD	42.78 ± 47.02	41.18 ± 37.94	39.80 ± 31.44	44.58 ± 34.12	42.02 ± 29.22	< 0.001
csDMARD	220.10 ± 125.40	247.99 ± 142.40	262.51 ± 134.35	272.10 ± 139.69	278.18 ± 154.92	< 0.001
Gabapentinoid	41.14 ± 41.40	43.51 ± 36.07	47.21 ± 48.75	50.45 ± 44.88	58.76 ± 61.88	< 0.001
NSAID	75.20 ± 66.19	73.12 ± 59.33	69.28 ± 71.71	75.50 ± 61.31	79.95 ± 66.90	< 0.001
Opioid	77.02 ± 82.07	96.74 ± 98.73	97.60 ± 96.37	108.99 ± 121.69	115.08 ± 104.19	< 0.001
Steroid	116.05 ± 66.43	123.63 ± 68.43	126.24 ± 73.32	128.31 ± 68.18	126.79 ± 80.63	< 0.001

Comparison Practice Patterns by ADI Quintile

and the average ADI values for each zip code were stratified by year and analyzed using one-way ANOVAs. Prescribing rates per 100 beneficiaries were calculated for corticosteroids, non-steroidal anti-inflammatory drugs (NSAIDs), gabapentinoids, opioids, conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs), and targeted synthetic or biological (ts/bDMARDs) and analyzed using one-way ANOVAs.

Results: This study identified 5,642 rheumatologists who participated in the Medicare Part D program from 2013 to 2018. These rheumatologists served an average of 302.9 +/- 223.8 beneficiaries with an average age of 69.5 +/- 3.6 years (Table 1). In an unadjusted linear model of the number of rheumatologists per zip code, there was no significant relationship with ADI ($p = 0.159$). In two one-way ANOVA models, there was no relationship between year and the average number of rheumatologists per zip code ($p = 0.313$) or the average ADI ($p = 0.621$) (Table 2). Per 100 beneficiaries, providers who practiced in a higher ADI quintiles cared for significantly more patients and prescribed more conventional synthetic disease modifying anti-rheumatic drugs, more gabapentinoids, and more opioids ($p < 0.001$ for all comparisons) (Table 3).

Conclusion: There was no significant association between the number of rheumatologists per zip code and the ADI per zip code. Rheumatologists who practice in zip codes with higher deprivation indexes saw more patients and prescribed more csDMARDS, more gabapentinoids, and more opioids. Prescribing rates for biologic and targeted synthetic DMARDs did not vary substantially, suggesting that access to health insurance may mitigate geographical disparities.

Disclosure: S. Tai, None; **I. Mbonu**, None; **M. Putman**, None.

Abstract Number: 0612

Rheumatology Care for the Underserved in Central Texas

Veena Patel, Rajvi Patel and Kevin Hackshaw, Dell Medical School - UT Health Austin, Austin, TX

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
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Background/Purpose: Health disparities exist among the uninsured and access to rheumatology is incredibly limited to this patient population. We reside in a state without Medicaid expansion and more than 19% of residents in our county are uninsured. In an effort to improve access, our clinic opened in a federally qualified health center in

Table 1. Demographic information. MAP: medical access program. SFS: sliding fee schedule (health care coverage offered to those who are uninsured and ineligible for MAP).CCHC: another type of healthcare coverage offered to those that do not qualify for MAP

		n (%)
Age	49yo (18-86)	
Sex	F	546 (80)
	M	136 (20)
Race	Hispanic	458 (67)
	White	159 (23)
	Black	62 (9)
	Middle Eastern	18 (3)
	South Asian	9 (1)
	East Asian	6 (1)
	Hawaiian/PI	1 (0.1)
	Deferred	13 (2)
Language	English	355 (52)
	Spanish	306 (45)
	Arabic	7 (1)
	Hindi	3 (0.4)
	Vietnamese	2 (0.3)
	Chinese	1 (0.1)
	Other	8 (1)
Insurance/ Health Care Coverage	MAP	363 (53)
	Private	86 (13)
	Medicaid	62 (9)
	SFS	59 (9)
	CCHC	39 (6)
	No Coverage	38 (6)
	Medicare	35 (5)
Travis County Resident	Yes	595 (87)

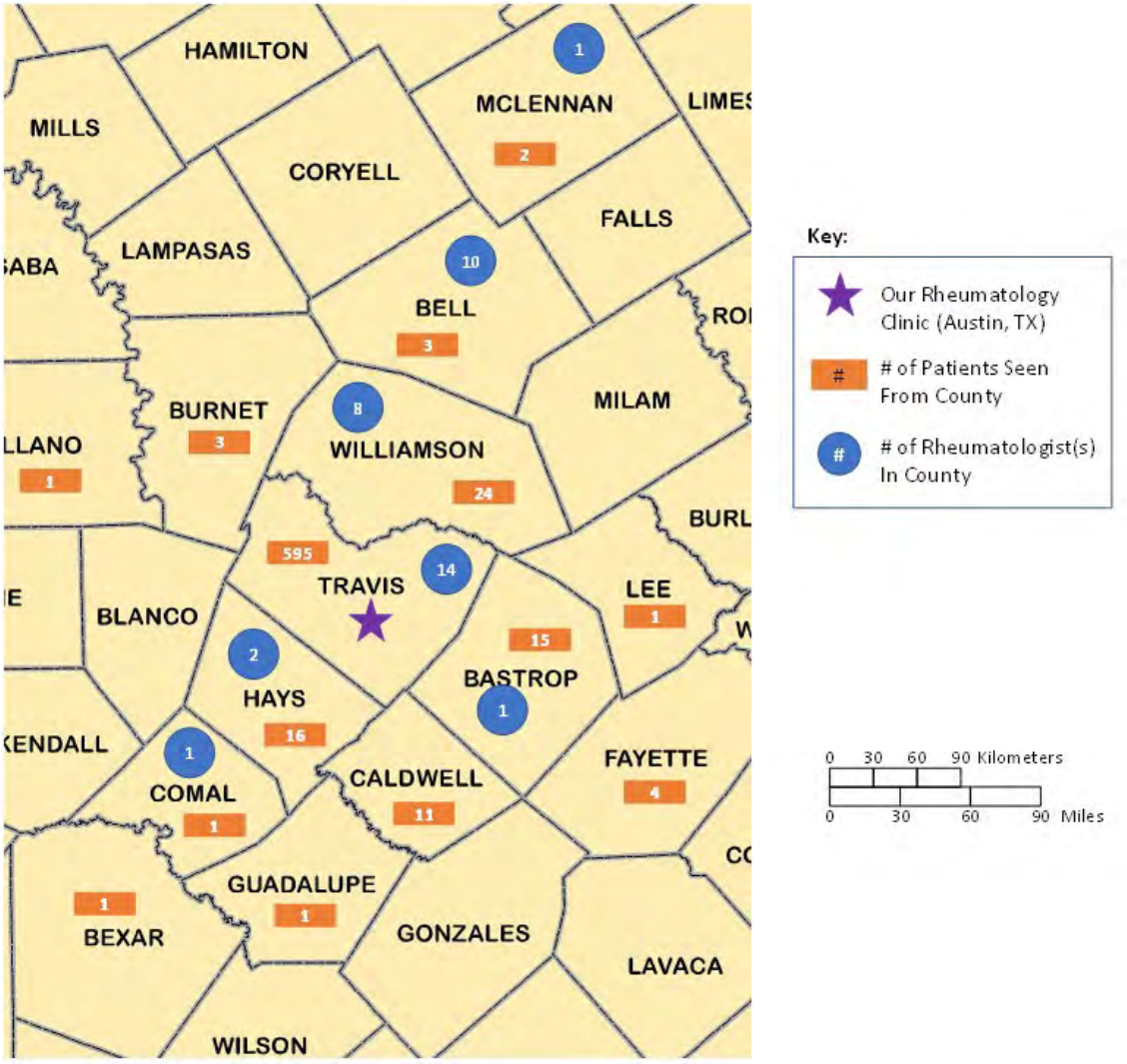
Table 2. Referral and patient information. This table lists the reasons for referral and outcomes of initial visit. Of patients confirmed or newly diagnosed with rheumatic disease, prior rheumatology evaluation was recorded and if disease was active on presentation. For rheumatoid arthritis patients, presence of erosive disease was noted and number of swollen/tender joints as recorded. Of note, those marked "N/A" were telehealth visits and physical exams were not performed

		n (%)
Reason for Referral (n = 682)	Joint pain	147 (22)
	Positive ANA	99 (15)
	Positive other labs	34 (5)
	Estb care RA	185 (27)
	Estb care SLE	63 (9)
	Estb care other rheum dz	108 (16)
	Other	46 (7)
Outcome of initial visit (n = 682)	Agree with diagnosis, continue treatment	65 (10)
	Agree with diagnosis, change/restart treatment	190 (28)
	Diagnosed with rheum dz	42 (6)
	Ongoing workup for possible rheum dz	93 (14)
	Started on tx for rheum dz	130 (19)
	Appropriate referral, no rheum dz	129 (19)
	Inappropriate referral	29 (4)
	Emergent	2 (0.3)
	Found another rheum	2 (0.3)
Patients with rheumatic disease (n = 426)	New diagnosis	106 /308 (34)
	Confirmed prior diagnosis	320/374 (86)
	Has seen a rheumatologist before:	165
	> 2 years ago	97
	< 2 years ago	68
	Active disease at initial visit:	351
	Yes	275
	No	76
	N/A	8
Rheumatoid arthritis patients (n = 182)	Erosive disease present at initial visit	71(39)
	Swollen/Tender Joint count:	
	<3	37
	3 through 10	63
	11 through 20	45
	>20	22
	N/A	15
	On DMARDs at 1st visit	100 (55)
	Therapy escalated or started on 1st visit	111 (61)

September 2018. In Travis County, uninsured low-income residents can apply for health care coverage through the medical access program (MAP), funded by tax payer dollars. Our division of 3 rheumatologists are the only caregivers in the area who accept MAP patients.

The purpose of this project was to gather baseline data by reviewing referrals and recognize characteristics of this underserved population. Our ultimate goal is to use this information to create future improvements in our clinic to promote health equity.

Table 1. Locations of patients seen by county in relation to our clinic (in Austin,Texas). The majority of patients seen at our clinic reside in Travis county, but there are a number of patients traveling from surrounding counties (many of which have rheumatologists) that travel to see us. *Note: There are 5 patients from counties not shown ranging 170-385 miles from our clinic



Methods: Chart review was done of all rheumatology referrals from 9/2018 – 11/2020. Using REDcap, we collected demographic data, referral information, patient characteristics and visit outcomes. For patients exhibiting active symptoms related to rheumatic disease, we used information noted in the "physical exam" of clinic notes to record the number of swollen/tender joints and disease activity. Using Google, we recorded the number of rheumatologists in each surrounding county and categorized them by main practice location.

Results: There were 1245 referrals by 11/2020 and 682 patients were seen in rheumatology clinic. Fifty-three patients declined appointment, 148 were no-shows, 178 were not able to be reached to schedule, 71 were incomplete and 113 had unknown referral status.

Table 1 reports demographic data. Five hundred forty-six patients (80%) were female, 458 (67.2%) Hispanic, 355 (52%) spoke English and 306 (44.9%) were Spanish speakers. The majority had health care coverage through MAP (53.2%).

Table 2 shows referral and patient information. The majority of patients were referred to establish care for a previously diagnosed rheumatic condition (320/682, 47%). Sixteen percent of referrals led to a new rheumatology diagnosis. Of

patients with rheumatic disease, 78% (275/351) had active disease at initial visit. The majority of RA patients had >3 swollen/tender joints and had therapy started or escalated at first visit. Seventy-one RA patients (39%) had erosive disease at initial visit.

Thirteen percent of patients travelled from outside of Travis county for an appointment. Image 1 shows that many passed other rheumatologists in surrounding counties. The furthest patient travelled from Lubbock county 375 miles away.

Conclusion: This study showed our clinic provided access to a diverse underserved population in need of rheumatologic care. A large portion already held a rheumatic diagnosis and unfortunately many had active, and even erosive disease, at the time of initial visit. While the majority are Travis county residents with MAP coverage, there were many who travelled out of county to see us. To continue to promote health equity, areas identified for improvement include understanding why many patients did not come to their initial visit, accurate referral tracking, learning surrounding county charitable care options, and engaging local rheumatologists in this process.

Disclosure: V. Patel, None; **R. Patel**, None; **K. Hackshaw**, None.

Abstract Number: 0613

Racial/Ethnic Disparities in Prescription Medications in a Large Urban Medical Center

J. Thomas Berry, William Galanter, Alia Welsh, Sandra Folarin, Reginald Woods and Huan Chang, UIC Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: African Americans and Hispanics with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) continue to have worse disease-related health outcomes relative to Whites. This pilot study investigates the relationship between living in a disadvantaged neighborhood and the frequency of being prescribed a biologic agent or a conventional disease modifying rheumatic drug (DMARD). The objective of this study was to determine if a relationship exists between race/ethnicity, living in a disadvantaged neighborhood, and the frequency of being prescribed disease-specific treatment for RA or SLE.

Methods: Data from the electronic medical record (EMR) of a large urban hospital were analyzed for the period from January 1, 2020 through September 30, 2020. Independent variables included age, insurance information, address with zip code, race/ethnicity, and sex. The area deprivation index score was calculated using the neighborhood atlas website mapping tool. Rheumatologic medications were the dependent variables. Prescribed biologic agents or conventional DMARDs were compared between racial/ethnic groups. Prescriptions of steroids, non-steroidal medications, and opiates were also compared.

Results: Altogether there were 1326 unique patients with RA (n=859) or SLE (n=457). There were 181 non-Hispanic Whites, 671 non-Hispanic Blacks, and 347 Hispanic patients.

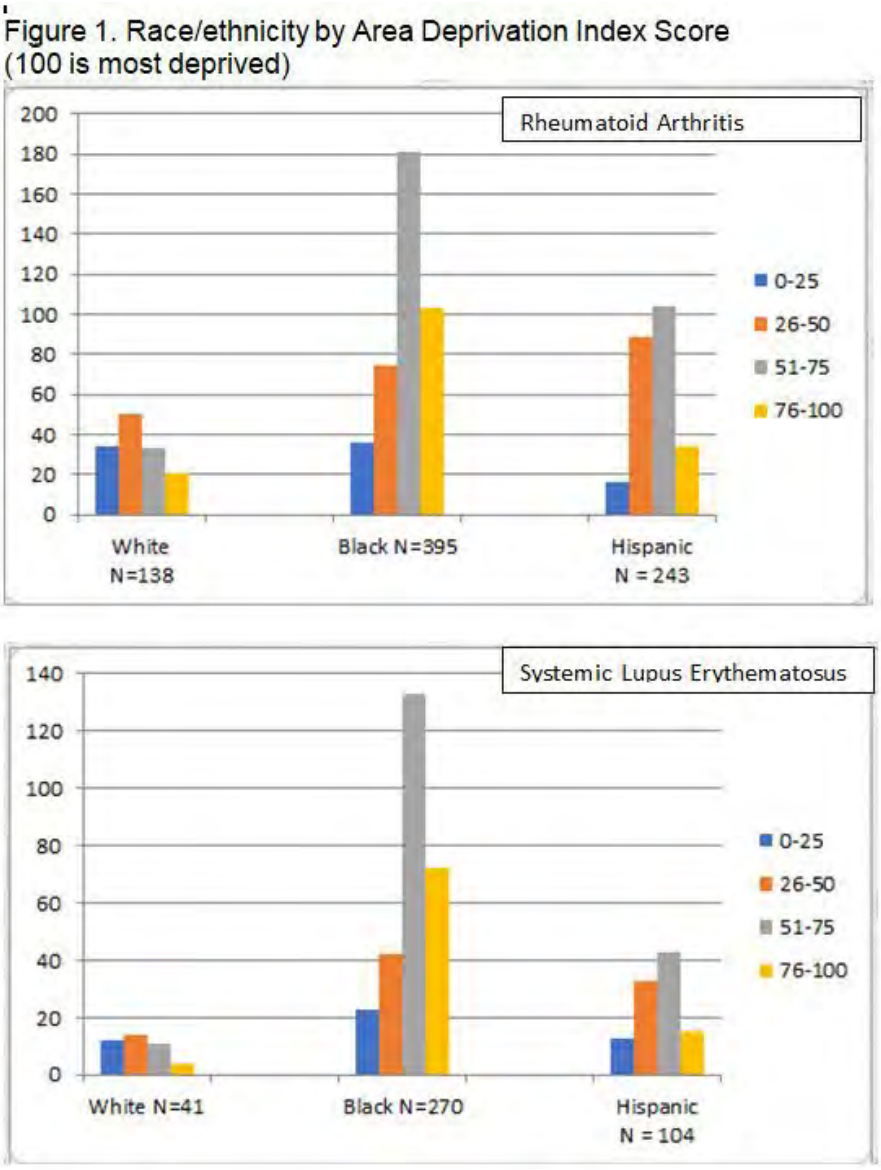


Figure 1. Race/ethnicity by area deprivation index score.

Area deprivation index scores were higher among Black and Hispanic patients compared to White patients for both RA and SLE patients ($p < 0.00001$ RA and SLE) . Minorities with RA were also more likely to have Medicaid health insurance than Whites ($p < 0.00005$ RA; $p < 0.59$ SLE). Results showed that physician prescribing patterns did not vary with area deprivation index scores ($p< 0.878$ RA; $p < 0.08$ SLE).

Conclusion: Among patients with RA and SLE, Blacks and Hispanics are more likely to live in an area with a higher area deprivation index score. Black RA patients were more likely to have Medicaid as their insurance. Physician prescribing patterns did not vary with area deprivation scores. Future studies with larger sample sizes are needed to help quantify the relationships between area deprivation scores and insurance in order to better understand physician prescribing patterns in patients, particularly among minority groups living in these areas, and to understand how these factors may influence disease-related health outcomes in RA and SLE.

Disclosure: J. Berry, None; **W. Galanter**, None; **A. Welsh**, None; **S. Folarin**, None; **R. Woods**, None; **H. Chang**, None.

Abstract Number: 0614

Sex and Race Based Utilization of Healthcare for Ocular Inflammation and Infection: Comparing the Results from the Medicare and the IRIS Data

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Health care utilization has an impact on disease progression and outcome in rheumatologic care. Disparities based on race, sex, education and income level affect care of our patients. Ocular inflammatory diseases increase disease burden in many rheumatologic conditions. We have compared Medicare and Intelligent Research in Sight (IRIS) data to identify similarities and differences in healthcare utilization for ocular inflammatory and infectious diseases. IRIS is a clinical registry, assembled by the American Academy of Ophthalmology. Registry

Annual utilization for infectious and inflammatory eye diseases: Medicare: By Race: 2016-2017

	2016		2017	
Race	%	(95% CI)	%	(95% CI)
All Races	10.98%	(10.97 - 10.99)	11.33%	(11.32 - 11.34)
Asian	15.33%	(15.25 - 15.41)	15.60%	(15.52 - 15.68)
Black	8.74%	(8.71 - 8.77)	8.94%	(8.91 - 8.97)
Hispanic	11.51%	(11.46 - 11.56)	11.60%	(11.55 - 11.64)
North American	10.05%	(9.91 - 10.20)	10.21%	(10.07 - 10.35)
White	11.07%	(11.06 - 11.08)	11.44%	(11.43 - 11.46)
Other	12.08%	(11.95 - 12.22)	12.61%	(12.48 - 12.75)

Annual utilization for infectious and inflammatory eye diseases by Race: IRIS: 2016-2017

	2016		2017	
Race	%	(95% CI)	%	(95% CI)
All Races	42.49	(42.47 - 42.50)	41.83	(41.81 - 41.84)
Asian	46.32	(46.22 - 46.43)	46.61	(46.50 - 46.71)
Black	44.11	(44.04 - 44.18)	42.74	(42.68 - 42.81)
Hispanic	44.89	(44.82 - 44.96)	44.06	(44.00 - 44.13)
North American	48.53	(48.07 - 49.00)	48.08	(47.62 - 48.53)
White	42.78	(42.76 - 42.80)	42.02	(42.00 - 42.04)
Other	34.98	(34.68 - 35.28)	34.74	(34.44 - 35.04)
Unknown	38.65	(38.61 - 38.70)	39.12	(39.08 - 39.16)

% Number or person with the condition per 100 in the dataset

Annual utilization for infectious and inflammatory eye diseases by race and sex: Medicare: 2016.

2016					
Male and Race	**%**	**(95 % CI)**	**Female and Race**	**%**	**(95 % CI)**
Male Asian	13.34	(13.22 - 13.46)	**Female Asian**	16.80	(16.69 - 16.92)
Male Black	6.46	(6.42 - 6.50)	Female Black	10.52	(10.47 - 10.57)
Male Hispanic	9.33	(9.27 - 9.40)	**Female Hispanic**	13.41	(13.34 - 13.48)
Male North American	8.07	(7.88 - 8.26)	Female North American	11.63	(11.43 - 11.83)
Male White	9.20	(9.18 - 9.22)	Female White	12.57	(12.55 - 12.59)
Male Other	10.06	(9.89 - 10.24)	**Female Other**	13.94	(13.75 - 14.14)

Annual utilization for infectious and inflammatory eye diseases: IRIS: By Race and Sex: 2016

2016					
	%	**(95 % CI)**		**%**	**(95 % CI)**
Male and Race			**Female and Race**		
Male Asian	45.58	(45.42 - 45.75)	**Female Asian**	46.84	(46.70 - 46.97)
Male Black	43.39	(43.28 - 43.50)	Female Black	44.52	(44.43 - 44.60)
Male Hispanic	44.29	(44.19 - 44.39)	Female Hispanic	45.17	(45.08 - 45.26)
Male North American	48.14	(47.42 - 48.86)	**Female North American**	48.84	(48.23 - 49.46)
Male White	42.06	(42.03 - 42.10)	Female White	43.29	(43.26 - 43.31)
Male Other	34.76	(34.29 - 35.22)	Female Other	35.14	(34.75 - 35.54)
Male Unknown	38.20	(38.14 - 38.27)	Female Unknown	39.09	(39.03 - 39.15)

%: Number or person with the condition per 100 in the dataset

Medicare and IRIS Utilization by Race and Sex: 2016

uses Health Insurance Portability and Accountability Act (HIPAA) compliant methods to collect data directly from participating Ophthalmology practices' individual electronic medical record (EMR) systems. In 2018, the registry collected data from more than 90% of ophthalmologists nationally

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

VEHSS uses ICD-10 codes to identify ocular disorders and organizes them into two level categorization, which are category and subgroup. Each code is categorized in one subgroup and multiple subgroups are combined to form a category. The inflammatory and infectious eye disease category includes subgroups of ocular inflammatory conditions, lacrimal system and orbital inflammation, keratitis, conjunctivitis, eyelid inflammation and infection and endophthalmitis.

Annual utilization for infectious and inflammatory eye diseases by Race and Sex: Medicare: 2017.

2017					
Male and Race	**%**	**(95 % CI)**	**Female and Race**	**%**	**(95 % CI)**
Male Asian	13.48	(13.37 - 13.60)	**Female Asian**	17.15	(17.04 - 17.26)
Male Black	6.53	(6.48 - 6.57)	Female Black	10.85	(10.80 - 10.90)
Male Hispanic	9.33	(9.27 - 9.39)	**Female Hispanic**	13.58	(13.51 - 13.65)
Male North American	8.22	(8.03 - 8.42)	Female North American	11.78	(11.58 - 11.99)
Male White	9.39	(9.37 - 9.41)	Female White	13.10	(13.09 - 13.12)
Male Other	10.43	(10.25 - 10.61)	**Female Other**	14.59	(14.39 - 14.79)

Annual utilization for infectious and inflammatory eye diseases: By Race and Sex: IRIS: 2017

2017					
Male and Race	**%**	(95 % CI)	**Female and Race**	**%**	(95 % CI)
Male Asian	45.77%	(45.61 - 45.93)	**Female Asian**	47.19	(47.06 - 47.33)
Male Black	41.91%	(41.80 - 42.01)	Female Black	43.22	(43.14 - 43.31)
Male Hispanic	43.35%	(43.24 - 43.45)	Female Hispanic	44.45	(44.37 - 44.54)
Male North American	47.35%	(46.65 - 48.06)	**Female North American**	48.63	(48.03 - 49.23)
Male White	41.18%	(41.14 - 41.21)	Female White	42.61	(42.58 - 42.64)
Male Other	34.02%	(33.56 - 34.48)	Female Other	35.25	(34.86 - 35.65)
Male Unknown	38.53%	(38.46 - 38.59)	Female Unknown	39.72	(39.67 - 39.78)

% Number or person with the condition per 100 in the dataset

Medicare and IRIS Utilization by Race and Sex 2017

Utilization for the the Medicare and IRIS data was compared for the years 2016-2017. We have identified the impact of utilization for both the databases when stratified by sex and race alone and when stratified by race and sex together.

Results: Females have higher utilization across all races for the inflammatory and infectious eye diseases for both Medicare and IRIS data, for both 2016 and 2017. Asians have higher utilization for both males and females in both the databases. Whereas Hispanics have second highest utilization for Medicare data and North American Natives have second highest utilization for the IRIS data for both the years 2016-2017.

When the Medicare and IRIS databases are stratified by both race and sex, Asian females have the highest utilization, followed by Asian males for both the databases for both the years.

For the IRIS database, North American females have the second highest utilization followed by the North American males for both the years. For Medicare database, other females and other males have the second highest utilization followed by the Hispanic females and Hispanic males.

Conclusion: Comparing the Medicare and the IRIS data provides significant complimentary information on eye care utilization for inflammatory and infectious eye diseases. Females, Asians, Hispanics and Native Americans having

higher utilization for both the years 2016-2017. This may be due to higher disease prevalence or higher service utilization. Further studies are needed to clarify this and to help in making informed policy decisions.

Disclosure: K. Chauhan, None; **J. Rosenbaum**, AbbVie, 2, UCB, 2, Novartis, 2, Gilead, 2, Corvus, 2, Roivant, 2, Revolo, 2, Neoleukin, 2, Affibody, 2, Santen, 2, Celgene, 2, Bristol Myers, 2, Pfizer, 5, Horizon, 5, UpToDate, 9.

Abstract Number: 0615

Socioeconomic Characteristics Associated with Electronic Health Care Utilization in an Urban Rheumatology Clinic During the COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In the US, the COVID-19 pandemic has prompted increased utilization of telemedicine (TM), electronic patient portals (EPPs), and other electronic modalities of health care delivery. Here, we assessed for socioeconomic inequities in TM and EPP utilization in an urban county hospital rheumatology clinic during COVID-19.

Methods: Using the electronic health record (EHR), demographic features (age, sex, race, ethnicity, language, distance from hospital, payor) on all patients completing visits between 3/1/2019 and 2/28/2020 (pre-COVID period) and 4/1/2020 and 3/31/2021 (COVID period) were analyzed. Bivariate logistic regression analysis was performed to obtain adjusted odds ratios (aORs) for primary outcome (completion of ≥ 1 TM visit during COVID) and secondary outcome (any utilization of the EPP from its inception in 2013 through date of data pull, 4/1/2021).

Results: 1,503 patients completed 3,837 visits in the pre-COVID period (all in-person visits). During COVID, 1,442 patients completed 3,406 visits (40.6% in-person, 20.4% TM, 29.1% telephone visits). 864 patients were seen in both periods. Demographic and visit characteristics are shown in Table 1. During COVID, younger age, farther distance from hospital, female sex, English language preference, White race identity, and commercial payor were associated with TM use (Table 2). White-identifying patients were 2.1x and 2.3x more likely than Black/African-American and American Indian/Alaska Native patients, respectively, to use TM. English-preferring patients were 3.8x and 3.0x more likely than Spanish-preferring and other non-English-preferring patients to use TM, respectively. Among patients seen during COVID, EPP use was associated with younger age, female sex, non-Hispanic/Latinx ethnicity, White race identity, English language preference, and commercial payor (Table 3). White-identifying patients were 3.5x and 3.7x more likely than Black/African-American and American Indian/Alaska Native patients, respectively, to use EPP. English-preferring patients were 14.1x and 4.7x more likely than Spanish-preferring and other non-English-preferring patients to use EPP.

Conclusion: We observed significant age-, sex-, race-, and language-related inequities in TM and EPP use during COVID-19 among patients in an urban county hospital rheumatology clinic. The strongest single predictor of both TM and EPP use was English language preference. Given the growing importance electronic health care delivery, it is

Table 1. Demographic Features and Visit Utilization for Patients from Pre-COVID and COVID Periods

	pre-COVID (n = 1,503)	**COVID** (n = 1,442)	
	Patients, No. (%), except where indicated		Value
Age, y, mean (SE)	50.51 (0.4065)	50.00 (0.4159)	0.3472[a]
< 55	843 (56.1)	850 (58.9)	0.2026[b]
55 – 64	363 (24.2)	310 (21.5)	
65 – 74	216 (14.4)	193 (13.4)	
≥ 75	81 (5.4)	89 (6.2)	
Sex			
Female	1011 (67.3)	968 (67.1)	0.9693[c]
Male	491 (32.7)	473 (32.8)	
Distance from Hospital, mi., median (SE)	14.00 (5.435)	12.00 (4.785)	0.0762[a]
< 10	596 (39.7)	606 (42.0)	0.4599[b]
10—24	498 (33.1)	485 (33.6)	
25 – 49	200 (13.3)	172 (11.9)	
50 – 99	98 (6.5)	86 (6.0)	
≥ 100	111 (7.4)	92 (6.4)	
Visits/individual, mean (SE)			
Total	2.553 (0.04859)	2.362 (0.04663)	**< 0.0001[a]**
In-person	2.553 (0.04859)	0.9584 (0.03197)	**< 0.0001[a]**
Telemedicine	n/a	0.7184 (0.02987)	n/a
Phone	n/a	0.6852 (0.03077)	n/a
Established Patients			
No	922 (61.3)	956 (66.3)	**0.0058[c]**
Yes	581 (38.7)	486 (33.7)	
EPP Login			
No	533 (35.5)	455 (31.6)	**0.0273[b]**
Yes	970 (64.5)	987 (68.4)	
Ethnicity			
Not Hispanic or Latinx	1117 (74.3)	1042 (72.3)	0.4482[b]
Hispanic or Latinx	232 (15.4)	242 (16.8)	
Missing (declined to answer, unknown, unavailable)	154 (10.2)	158 (11.0)	
Race			
White	850 (56.6)	802 (55.6)	0.4203[b]
American Indian or Alaska Native	45 (3.0)	40 (2.8)	
Asian	184 (12.2)	167 (11.6)	
Black or African American	238 (15.8)	217 (15.0)	
Native Hawaiian or Other Pacific Islander	23 (1.5)	32 (2.2)	
Missing (Declined to Answer/Unknown/Unavailable)	163 (10.8)	184 (12.8)	
Language			
English	1187 (79.0)	1121 (77.7)	0.4774[b]
Spanish	160 (10.6)	174 (12.1)	
Non-English/Non-Spanish	156 (10.4)	147 (10.2)	
Payor Group			
Commercial (incl. Blue Shield)	439 (29.2)	423 (29.3)	0.2071[b]
Self-pay	59 (3.9)	77 (5.3)	
Medicaid (incl. pending Medicaid)	354 (23.6)	340 (23.6)	
Medicare (incl. MedAdvantage)	336 (22.4)	285 (19.8)	
Other (unknown, Worker's Comp, Tricare, Group Health, Case Rate, other)	315 (21.0)	317 (22.0)	

EPP, Electronic patient portal
[a]Mann Whitney test, two-sided
[b]Chi-square test, two-sided
[c]Fisher's exact test, two-sided

critical to identify and address language and socioeconomic barriers to TM and EPP access in order to provide just and equitable rheumatology care.

Table 2. Adjusted Odds Ratios for Telemedicine Utilization

			95% C.I.		
	B	**OR**	**Lower**	**Upper**	**Sig.**
Age, y (vs. < 55)					**0.000**
55 – 64	-0.880	0.415	0.307	0.560	**0.000**
65 – 74	-0.842	0.431	0.284	0.654	**0.000**
≥ 75	-0.627	0.534	0.303	0.942	**0.030**
Sex (vs. female)	-0.371	0.690	0.539	0.883	**0.003**
Distance from Hospital, mi. (vs. < 10)					**0.003**
10—24	0.377	1.457	1.113	1.908	**0.006**
25 – 49	0.582	1.789	1.235	2.592	**0.002**
50 – 99	0.644	1.904	1.164	3.113	**0.010**
≥ 100	0.447	1.564	0.972	2.516	0.065
Ethnicity (vs. not Hispanic or Lantinx)					0.642
Hispanic or Latinx	-0.166	0.847	0.530	1.355	0.489
Missing (declined to answer, unknown, unavailable)	0.106	1.112	0.667	1.855	0.685
Race (vs. White)					**0.002**
American Indian or Alaska Native	-0.843	0.431	0.200	0.929	**0.032**
Asian	-0.170	0.844	0.557	1.278	0.423
Black or African American	-0.733	0.480	0.334	0.692	**0.000**
Native Hawaiian or Other Pacific Islander	0.113	1.120	0.519	2.417	0.774
Missing (Declined to Answer/Unknown/Unavailable)	-0.102	0.903	0.557	1.463	0.677
Language (vs. English)					**0.000**
Spanish	-1.341	0.262	0.149	0.460	**0.000**
Non-English/Non-Spanish	-1.112	0.329	0.201	0.537	**0.000**
Payor (vs. Commercial)					**0.005**
Self-pay	-0.487	0.615	0.316	1.194	0.151
Medicaid	-0.514	0.598	0.435	0.823	**0.002**
Medicare (Includes MedAdvantage)	-0.374	0.688	0.462	1.026	0.067
Other (unknown, L&I, other)	-0.004	0.996	0.725	1.371	0.983

EPP, Electronic patient portal
All variables included in analysis are shown

Table 3. Adjusted Odds Ratios for EPP Utilization During COVID Period

			95% C.I.		
	B	**OR**	**Lower**	**Upper**	**Sig.**
Age, y (vs. < 55)					**0.000**
55 – 64	-0.818	0.442	0.317	0.615	**0.000**
65 – 74	-0.579	0.561	0.356	0.883	**0.012**
≥ 75	-0.351	0.704	0.376	1.319	0.274
Sex (vs. female)	-0.525	0.591	0.446	0.784	**0.000**
Distance from Hospital, mi. (vs. < 10)					0.109
10—24	0.400	1.491	1.092	2.036	**0.012**
25 – 49	0.067	1.069	0.688	1.662	0.767
50 – 99	0.454	1.575	0.824	3.010	0.169
≥ 100	0.109	1.115	0.622	1.998	0.714
Ethnicity (vs. not Hispanic or Latinx)					**0.002**
Hispanic or Latinx	-0.725	0.484	0.282	0.831	**0.008**
Missing (declined to answer, unknown, unavailable)	-0.926	0.396	0.222	0.707	**0.002**
Race (vs. White)					**0.000**
American Indian or Alaska Native	-1.321	0.267	0.126	0.564	**0.001**
Asian	-0.226	0.797	0.485	1.312	0.373
Black or African American	-1.262	0.283	0.194	0.413	**0.000**
Native Hawaiian or Other Pacific Islander	-0.117	0.889	0.334	2.364	0.814
Other (Declined to Answer/Unknown/Unavailable)	-0.095	0.910	0.529	1.564	0.732
Language (vs. English)					**0.000**
Spanish	-2.646	0.071	0.038	0.132	**0.000**
Non-English/Non-Spanish	-1.557	0.211	0.135	0.329	**0.000**
Payor (vs. Commercial)					**0.000**
Self-pay	-0.362	0.696	0.357	1.357	0.288
Medicaid	-1.080	0.340	0.229	0.503	**0.000**
Medicare (Includes MedAdvantage)	-0.797	0.451	0.281	0.721	**0.001**
Other (unknown, L&I, other)	-0.729	0.483	0.320	0.729	**0.001**
All variables included in analysis are shown					

Disclosure: J. Thomason, None; **B. Mantilla**, None; **A. Bays**, Genentech, 5, Abbvie, 5; **I. Huang**, None; **G. hughes**, None.

Abstract Number: 0616

Race and Socioeconomic Status and COVID-19 Outcomes in Patients with Rheumatic Diseases: Findings from a Tertiary Care Center in the Deep South

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The southern United States is home to a large proportion of non-Hispanic Black Americans, a group which has historically been disproportionately affected by healthcare disparities. Alabama in particular stands

Table 1. Characteristics of Rheumatology Patients by Race

	White race (n=152)	Black race (n=104)	P value
Age (median [IQR])	59.00 [50.25, 71.00]	54.00 [46.75, 63.00]	0.01
Sex, Female (%)	113 (74.0)	91 (87.5)	0.01
BMI (median [IQR])	31.14 [25.48, 36.26]	33.80 [29.74, 39.80]	<0.01
Charlson Comorbidity Index (median [IQR])	2.00 [1.00, 4.00]	3.00 [1.00, 4.00]	<0.01
Smoking (%)			NS
ever	47 (30.9)	31 (29.8)	
never	105 (69.1)	73 (70.2)	
ADI-State (median [IQR])	2.00 [1.00, 4.00]	6.00 [3.00, 9.00]	<0.0001
ADI-Nation (median [IQR])	46.00 [29.00, 65.75]	76.00 [55.50, 91.00]	<0.0001
ADI Group (%)			<0.0001
ADI-Nation ≤ Q25	55 (36.2)	9 (8.7)	
Q25 < ADI-Nation ≤ Q75	76 (50.0)	49 (47.1)	
ADI-Nation > Q75	21 (13.8)	46 (44.2)	
Rheumatic diagnosis (%)			n/a
Crystalline	14 (9.2)	8 (7.7)	
Lupus	21 (13.8)	34 (32.7)	
Myositis	1 (0.7)	4 (3.8)	
Noninflammatory	36 (23.7)	19 (18.3)	
Other	28 (18.4)	18 (17.3)	
Rheumatoid arthritis	24 (15.8)	16 (15.4)	
Spondyloarthropathies	18 (11.8)	4 (3.8)	
Vasculitis	10 (6.6)	1 (1.0)	
Prednisone use (%)	30 (19.7)	32 (30.8)	0.05
Medication (%)			0.01
No DMARD	53 (35.3)	32 (30.8)	
csDMARD only	17 (11.3)	8 (7.7)	
bDMARD only	46 (30.7)	53 (51.0)	
csDMARD and bDMARD	34 (22.7)	11 (10.6)	
Hospitalization (%)	47 (30.9)	42 (40.4)	0.14
Ventilation status (%)			
Not hospitalized/no supplemental oxygen	115 (78.8)	69 (67.6)	
Supplemental oxygen	27 (18.6)	24 (23.5)	NS
Mechanical ventilation	4 (2.7)	9 (8.8)	NS
Need for Intensive Care (%)			NS
No/Not Hospitalized	134 (92.4)	89 (87.3)	
Yes	11 (7.6)	13 (22.7)	
Death (%)	5 (3.3)	3 (2.9)	NS

[1] BMI = Body Mass Index. ADI = Area Deprivation Index. csDMARD = conventional/synthetic DMARD. bDMARD = biologic DMARD. NS = Not significant. n/a = not applicable or not calculated

in the top quintile for both percentage of African American population and poverty rates. The COVID-19 pandemic has highlighted the impact of these disparities, particularly in those with rheumatic disease who, on average, already have a high utilization of healthcare services. A study nested within a voluntary U.S. physician registry showed poorer outcomes in racial/ethnic minority patients. However, data on socioeconomic status for registry patients was not

Table 2. Association of Race/Ethnicity and Census-tract Socioeconomic Status with Hospitalization due to COVID-19 Among Rheumatology Patients at a Tertiary Care Center in the Deep South

	OR	95% CI	P value
Hospitalized (n=256)			
Race (Black vs White)	1.15	0.59-2.24	0.68
Gender (F vs M)	1.29	0.61-2.74	0.51
Age	1.03	1.00-1.05	0.03
Charlson Score	1.45	1.26-1.65	<0.0001
BMI	1.04	1.00-1.08	0.05
ADI-Nation Q25-Q75 vs < Q25	1.37	0.64-2.95	0.56
ADI-Nation >Q75 vs <Q25	1.33	0.53-3.32	0.79

reported. Our study examined the impact of race and socioeconomic status on COVID-19 outcomes in patients with rheumatic disease from a large tertiary care rheumatology practice in the Deep South.

Methods: We systematically identified rheumatology patients established at our medical center with a history of COVID-19 infection, confirmed by PCR. A retrospective medical record review was conducted to extract demographic characteristics, rheumatic disease type and treatment, comorbidities, and COVID-19 outcomes. COVID-19 outcomes studied included hospitalization, need for supplemental oxygen, need for mechanical ventilation, and death. Race/ethnicity was categorized as white, Black, or other. Census-tract socioeconomic status using area deprivation index (ADI) was calculated. Multivariate logistic regression was performed adjusting for the effect of age, sex, body mass index (BMI), comorbidities (by Charlson Comorbidity index), rheumatic disease type, rheumatic disease medications taken prior to COVID-19 infection, prednisone use prior to infection, and ADI.

Results: A total of 256 rheumatology patients who had tested positive for COVID-19 at our institution were included, of whom 104 (40.6%) were Black and 152 (59.4%) were white (Table 1). Eight patients identified as "other" race were excluded from this analysis. Mean national area deprivation index for white patients was 46, while Black patients were more disadvantaged with a mean ADI of 76. Black patients also had higher baseline comorbidities and had a higher rate of hospitalization. However, after multivariate adjustment, Black race and ADI were not associated with hospitalization, need for supplemental oxygen, or need for mechanical ventilation. Variables noted to be significantly associated with hospitalization in multivariate analysis included age, BMI, and comorbidities (Table 2).

Conclusion: Although Black patients had a higher rate of hospitalization compared to white patients, race and census-tract socioeconomic status were not associated with significantly worse COVID-19 outcomes after accounting for confounders in this analysis. Possible explanations for these findings are lack of patient-level socioeconomic data, small sample size, and unmeasured confounding. Further investigation is needed to address this complex relationship between race and socioeconomic status and COVID-19 outcomes.

Disclosure: A. Taylor, None; **D. Sun**, None; **J. Foster**, None; **M. Danila**, Pfizer, 5, Pfizer, 11, AbbVie, 1, Amgen, 5, Amgen, 1, Boehringer Ingelheim, 5, Horizon, 5, WebMD, 12, writer, Novartis, 1.

Abstract Number: 0617

Concerns and Beliefs About COVID-19 Vaccination Among Racial and Ethnic Minority Patients with Rheumatic Disease

Maria I. Danila, Lesley Jackson, Amy Mudano, Giovanna Rosas, Jeanne Merchant, Jeffrey Foster and Kenneth Saag, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Alabama lags behind many other states in COVID-19 vaccination uptake and racial/ethnic minority groups face COVID-19 vaccine access disparities. Moreover, lack of vaccination access and medical mistrust among Alabama's large African American population, a vestige of the devastating Tuskegee Syphilis study, further perpetuate health care disparities. We examined concerns and beliefs about COVID-19 vaccination among racial and ethnic minority patients receiving rheumatology care at a large academic medical center in the Deep South and factors associated with COVID-19 vaccine receipt.

Table 1: Characteristics of Rheumatology Clinic Patients from Racial and Ethnic Minority Groups.

Variable	N=150
Female, yes	130 (86.7%)
Age, years, mean (SD)	54 (15.9)
Black or African American	141 (94.0%)
Education, some college or more	103 (68.7%)
Flu vaccine ever, yes	121 (80.7%)
Flu vaccine 2020 - 2021, yes	91 (60.7%)
Medical mistrust, no	75 (50%)
Vaccine confidence, mean (SD)	3.9 (0.95)
Received COVID-19 vaccination	100 (66.7%)
No COVID-19 vaccine receipt	
Did not plan to get vaccinated	16 (32%)
Common reasons for not getting vaccinated	
Side effects of the vaccine	19 (55.9%)
Disease flare	18 (52.9%)
Know someone who had side effects	11 (32.4%)
Vaccine will give me COVID-19	7 (20.6%)
Will modify my DNA	6 (17.6%)
Reactions to other vaccines	5 (14.7%)
Key information needed during COVID-19 vaccine deliberation	
Long term efficacy	18 (52.9%)
Desire to talk to my doctor	17 (50.0%)
Side effects in people with my health condition	15 (44.1%)
Efficacy in people with my health condition	14 (41.2%)

Frequency (%) or mean (standard deviation) shown. Vaccine confidence scale ranges from 1 (strongly disagree to 7 strongly agree); higher scores are better.

Table 2. Factors Associated with Receipt of COVID-19 Vaccine Among Racial and Ethnic Minority Patients in Rheumatology Clinic.

	Model 1			
Variable	Odds Ratio	95% Confidence Interval		P value
Age, years				
<45	Ref.			
45 - 64	2.84	1.06	7.58	0.04
65+	3.95	1.05	14.91	0.04
Sex, women	3.16	0.82	12.18	0.09
COVID-19 vaccine safety concerns, yes	0.27	0.09	0.83	0.03
Past influenza vaccination, yes	3.47	1.20	10.00	0.02
Vaccine confidence	3.71	2.07	6.66	<0.0001
Medical mistrust, no	0.56	0.17	1.82	0.33

Methods: In April 2021, we invited racial and ethnic minority patients to complete a survey on a tablet computer during an in-person visit to the rheumatology clinics at our center. Vaccination confidence was assessed using the confidence scale from the validated 5C psychological antecedents of vaccination. Descriptive statistics summarized attitudes and beliefs about COVID-19 vaccination and multivariable logistic regression determined factors associated with receipt of a COVID-19 vaccine. The following factors were examined: age, sex, education, vaccine confidence, safety concerns, medical mistrust, past flu vaccine receipt.

Results: Of the 156 racial and ethnic minority patients approached between April 19 and May 6, 2021, 150 agreed to complete the survey. Mean (standard deviation) for age was 54 (15.9) years, 86.9% were women, 94% identified themselves as Black or African American, 69% had at least some college, and 22% said they believed they would have gotten better medical care if they belonged to a different race or ethnic group (**Table 1**). Although 81% of respondents reported prior receipt of flu vaccine, only two thirds reported having had the COVID-19 vaccine. Of those who were not yet vaccinated (N=50), half had been offered the vaccine and a third said they did not plan were to be vaccinated. The most common reasons for not getting vaccinated included concerns about side effects (56%), fear of disease flare (53%), knowing someone who had a bad experience with the vaccine (32%), concern of getting COVID-19 from the vaccine (21%), and concern that the vaccine would "modify my DNA" (18%). Those not yet vaccinated expressed a need to obtain information about the efficacy and safety of this vaccination in people with rheumatic disease. After multivariable adjustment, older age, not having safety concerns about COVID-19 vaccine, past flu vaccine receipt, and higher vaccine confidence were associated with COVID-19 vaccination (**Table 2**). There was no association between reporting medical mistrust and COVID-19 vaccine receipt.

Conclusion: During the COVID-19 vaccine roll out in Alabama, one in ten racial and ethnic minority patients in a large academic rheumatology clinic said they were unlikely to get vaccinated. Older age, past flu vaccine receipt, higher confidence in and lack of safety concerns about the COVID-19 vaccine were associated with COVID-19 vaccination. Our findings highlight the need for tailored COVID-19 vaccination programs for individuals with rheumatic diseases in these subpopulations susceptible to health disparities to help ensure individual and societal protection against COVID-19.

Disclosure: M. Danila, Pfizer, 5, Pfizer, 11, AbbVie, 1, Amgen, 5, Amgen, 1, Boehringer Ingelheim, 5, Horizon, 5, WebMD, 12, writer, Novartis, 1; **L. Jackson**, None; **A. Mudano**, None; **G. Rosas**, None; **J. Merchant**, None; **J. Foster**, None; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5.

Abstract Number: 0618

Post-acute Sequelae of SARS-CoV-2 and Serological Response in a Cohort of Patients with Rheumatic Diseases

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The longitudinal experience of COVID-19 illness in patients with rheumatic diseases is emerging. Reports from the general population have described post-acute sequelae of SARS-CoV-2 (PASC) including de novo autoimmunity but evidence in patients with pre-existing rheumatic diseases is limited. We sought to characterize PASC in patients with rheumatic diseases in our majority Latino patient cohort. Further, we investigated the relationship between COVID-19 illness, the subsequent development of new autoantibodies, and increased rheumatic disease activity.

Methods: This is a retrospective study of patients with rheumatic diseases from an existing observational cohort, comprising of 72.4% Latino patients. Patients seen between April 1, 2020 to May 15, 2021 were included in analyses. We reviewed demographics, rheumatic disease, immunomodulatory therapies, and PASC symptoms. Antibodies to SARS-CoV-2 were measured for patients reporting infection. Antibodies to extractable nuclear antigens and anti-phospholipid antibodies were repeated once in the post-acute period when feasible. Data for continuous variables were expressed as the mean ± SD and categorical variables were summarized by computing counts of patients (%). Fisher's exact test was used, and significance threshold was 0.05.

Results: During the study period, 54 patients reported COVID-19 illness, representing 17.5% of our cohort of 307 active patients (Table 1); 53 were Latino patients. Most patients had mild illness with 8 patients (14.8%) requiring inpatient management. There were no COVID-19 related deaths. SARS-CoV-2 IgG was assessed in sera in 52 individuals, and 5 patients (9.6%) were found to have negative titers while 83.3% of initially positive patients maintained their antibodies 9 months post infection. Of 47 patients assessed, 27 (57.4%) reported PASC symptoms and 24 of those patients (37.5%) had persistent PASC six months post infection. Autoantibody tests were performed in 39 patients after acute COVID-19 infection and a new autoantibody was detected in 8 patients (18.6%). Anti-RNP developed in 5 patients, anti-Scl70 in one patient, and anti-phospholipid antibodies in 2 patients. Subgroup analysis revealed a significantly higher frequency of autoantibody development in patients with RA when compared to other patients with COVID-19 (7/18 vs 1/21, p=0.01). This autoantibody development was higher than RA patients without COVID-19. The frequency of self-reported worsened rheumatic symptoms was higher among patients who developed a new autoantibody in the post-COVID-19 period than in other patients (6 of 8 vs 8 of 37, p=0.006).

Conclusion: Latino patients not only have an increased rate of COVID-19 infection but also shoulder an outsized burden of its post-acute sequelae. The finding of de novo autoantibody production in 18.6% of patients, post-COVID-19, could foretell the development of a new autoimmune phenomenon. Patients in high-risk groups for COVID-19, particularly marginalized groups, will require closer monitoring, early identification, and therapeutic intervention for detecting this new autoimmune phenotype. This likely will be an ongoing, long term effort.

Table 1. Demographic and clinical profile of rheumatology patients with COVID-19 illness

	COVID-19 Illness (n= 54)
Demographic	
Age, mean ± SD	47.1 ± 8.5
Sex	
Female	49 (90.7)
Male	5 (9.2)
Latino/Hispanic ethnicity	53 (98.1)
BMI, mean ± SD, kg/m^2	31.2± 5.9
Comorbidities	19 (35.2)
Hypertension	11 (20.3)
Diabetes mellitus	5 (9.2)
Previous lung disease	4 (7.4)
Ever tobacco use	6 (11.1)
Rheumatic Disease	
Rheumatoid Arthritis	25 (46.2)
Systemic Lupus Erythematosus	15 (27.7)
Overlap/MCTD	3 (5.5)
Other inflammatory /autoimmune (AAV, PsA, pSS, AS, SSc, AOSD, IIM)	11 (20.3)
Medications, baseline	
Glucocorticoids	16 (29.6)
Average daily dose, mean ± SD mg	7.1 (4.6)
cDMARDs	44 (81.4)
Biologic/Small Molecule	22 (40.7)
Post COVID-19 & Rheumatic Disease Courses	
Positive SARS-CoV-2 Serology*	46 (90.1)
Positive SARS-CoV-2 Serology >9 months post infection#	15 (83.3)
Post-Acute Sequelae of SARS-CoV-2 infection¶	27 (57.4)
PASC present >6 months post infection‡	9 (37.5)
De novo autoantibody detected§	8 (18.6)
Increased rheumatic disease activity$	14 (31.1)

* out of 51 patients, # out of 18 patients, ¶ out of 47 patients, ‡ out of 24 patients, § out of 43 patients, $ out of 45 patients.
MCTD- mixed connective tissue disease, AAV- ANCA associated vasculitis, PsA- psoriatic arthritis, pSS- primary Sjogren's syndrome, AS- ankylosing spondylitis, SSc- systemic sclerosis, cDMARDs- conventional disease-modifying antirheumatic drugs.

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Abstract Number: 0619

Racial and Ethnic Disparities in Pregnancy Outcomes Among Women with Rheumatic Diseases: A Systematic Literature Review and Quantitative Analysis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
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Background/Purpose: Women are disproportionately affected by rheumatic diseases (RD), with many of them carrying the diagnosis in their childbearing years. Pregnant women with RD have a high prevalence of adverse pregnancy outcomes (APO) owing to a multitude of factors. Racial/ethnic disparities in APO are well-recognized in the general population, however the understanding for this among women with RD is limited. While there are studies which have explored the impact of race/ethnicity on APO among patients with RD, limitations of RD type and race ascertainment

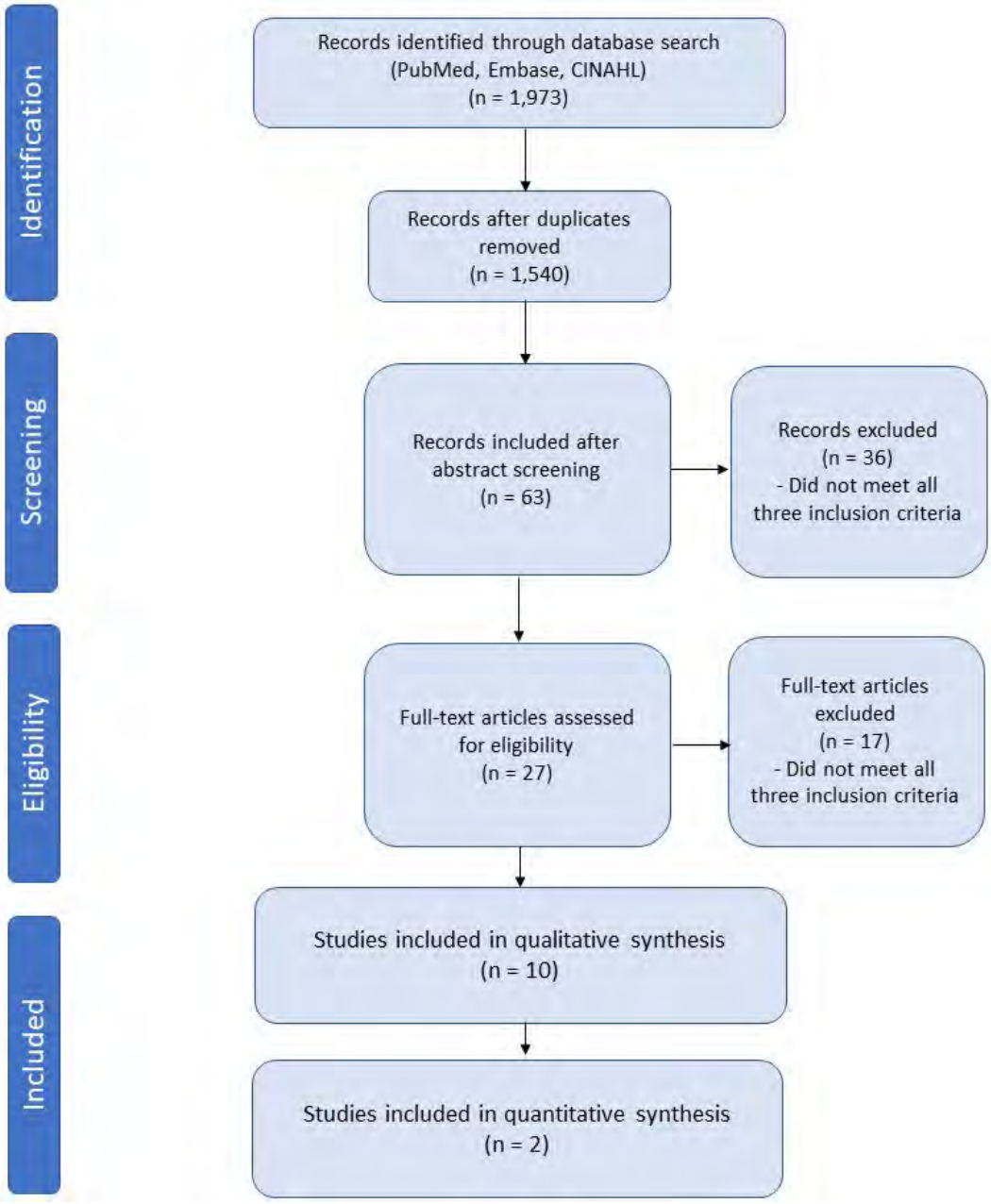

Figure 1. PRISMA Flow Diagram showing study selection process.

Table 1. Characteristics of studies included in the systematic literature review

Author last name /Publication year	Continent/Country	Rheumatic disease studied	Study period	Race/ethnicity	Adverse Pregnancy Outcomes
Kaplowitz 2017	North America	SLE, APS	Sept 2003–July 2014	White (non-hispanic), African American, Hispanic, Asian, American Indian	Fetal death after 12 weeks of gestation, neonatal death before hospital discharge due to complications of prematurity, preterm delivery before 36 weeks gestation due to pregnancy-induced hypertension, preeclampsia, placental insufficiency, and small for gestational age (SGA) neonate
Buyon 2015	North America	SLE	Sept 2003–Dec 2012	Non-Hispanic White, Hispanic White, African American, Asian, other	Fetal death after 12 weeks' gestation unexplained by chromosomal abnormalities, anatomical malformation, or congenital infection; neonatal death before hospital discharge due to complications of prematurity, placental insufficiency, pre-term delivery or termination of pregnancy at less than 36 weeks due to gestational hypertension, preeclampsia, or placental insufficiency; and 4) SGA neonate, defined as one with a birthweight below the fifth percentile without anatomical or chromosomal abnormalities.
Clowse 2016	US	SLE	2008-2010	White, Black, Hispanic	Preterm labor, preeclampsia, fetal growth restriction, stillbirth, premature rupture of membranes, chorioamnionitis, cervical incompetence, placental abruption, postpartum hemorrhage, gestational diabetes mellitus
Andrade 2008	US (Alabama, Texas, Puerto Rico)	SLE	Unknown – June 2005	Hispanic-Texan, Hispanic-Puerto Rican, African American, Caucasian	Miscarriage or abortion (<20 weeks), a stillbirth (≥ 20 weeks) and/or a moderate to severe preterm baby (<34 weeks)
Vinet 2011	Multiple (US, Canada, UK, Sweden)	SLE	Unknown	White, Black, Asian, Other	Standardized incidence ratio (SIR) of observed to expected live births
Shaharir 2020	Malaysia	SLE	Jan 2016 – Dec 2019	Malay, Chinese, Indian	APO includes early pregnancy loss (first 13 weeks), late pregnancy loss (after 13 weeks), intra-uterine death (fetal loss >= 20 weeks), intrauterine growth restriction (below 10th percentile), premature birth (before 37 weeks), pre-eclampsia, maternal death
Mohammed 2016	US	Juvenile rheumatoid arthritis (JRA)	2011 - 2012	Caucasian, African American, Hispanic	Preterm birth (delivery > 22 wks AND <37 weeks), SGA
Manzano-Gamero 2018	Spain	SLE and SLE plus APS	Sept 2013–Oct 2014	Caucasian, Roma	Fetal death, abortion
Anastasiou 2020	US (California)	SLE and RA	2016-2017	Caucasian, African American	Intrauterine fetal demise, pre-eclampsia/eclampsia
Sabih 2020	US (California)	SLE and RA	2007-2012	White, Black, Hispanic, Asian	Preterm Birth (less than 37 weeks)

prevent single studies from synthesizing a complete analysis. We conducted a systematic literature review to evaluate the impact of race/ethnicity on APO in women with RD.

Methods: Systematic literature searches in PubMed, Embase, and Cumulative Index for Nursing and Allied Health Literature (CINAHL) Complete were conducted to identify potentially eligible studies. Inclusion criteria consisted of all

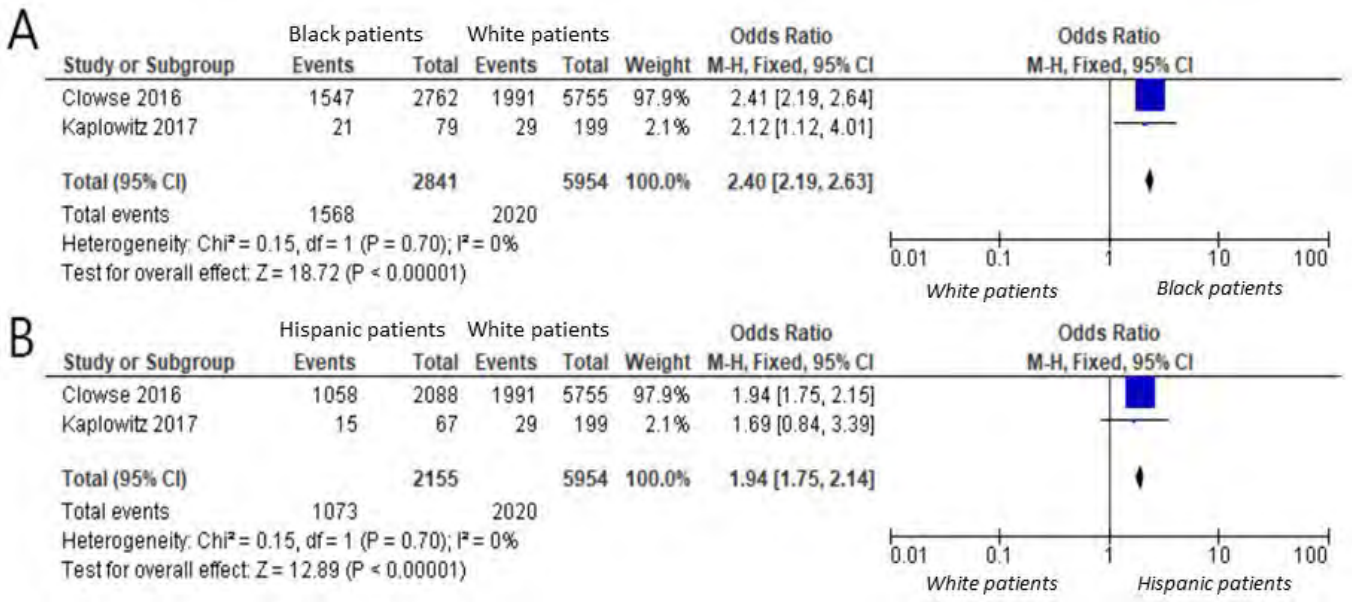

Figure 2. Forest plot comparing adverse pregnancy outcomes in SLE between A) Black and White patients, and B) Hispanic and White patients.

study designs except for case reports and narrative reviews, presence of RD and APO, and data pertaining to race/ethnicity. Conference abstracts published before 2015 and non-English articles were excluded.

Results: A total of 1540 references remained after duplicates were removed of which full text review was done for 27 articles (Figure 1). These were independently reviewed by three co-authors (GS, IJH, and MS) and discrepancies were resolved by a fourth co-author (NS). Study quality was assessed using Newcastle-Ottawa Scale. Ten studies met our eligibility criteria to be included in the literature review (Table 1).

Of the 10 studies, 7 were from North America, 1 from Europe, 1 from Asia, and 1 multicontinental. Most of them were cohort studies, except one that was a cross-sectional study. One study examined racial/ethnic disparities among patients with juvenile idiopathic arthritis (JIA). The remaining 9 studies looked at patients with systemic lupus erythematosus (SLE) of which 2 included patients with antiphospholipid antibody syndrome (APS), and 2 included patients with rheumatoid arthritis (RA).

Because of the significant differences between the studies, pooled analysis could only be carried out using two studies (Figure 2). Among patients with SLE, Black patients had higher odds of APO compared to White patients, with a pooled odds ratio (OR) of 2.40 [95% CI 2.19 - 2.63]. Similarly, Hispanic patients had higher odds of APO compared to White patients with a pooled OR of 1.94 [95% CI 1.75 - 2.14].

Conclusion: This systematic literature review highlights that racial/ethnic minority populations with RD are more prone to APO compared to their White counterparts. Eight out of the nine studies involving White patients are consistent with these findings. Pooled analysis was limited due to multiple factors including heterogeneity in the study population, variation in the outcomes of interest, and different definitions for APO. Standardized criteria for APO are necessary to allow direct comparisons between studies. SLE has been the focus in most of these studies and there is a paucity of data looking at other RDs. Further research is needed to explore the causes for the racial/ethnic disparities and how these can be addressed.

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Abstract Number: 0620

Is There a Difference in Disease Activity Between Genders in Axial Spondyloarthritis? 6-year Longitudinal Data from a Large National Cohort

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SESSION INFORMATION

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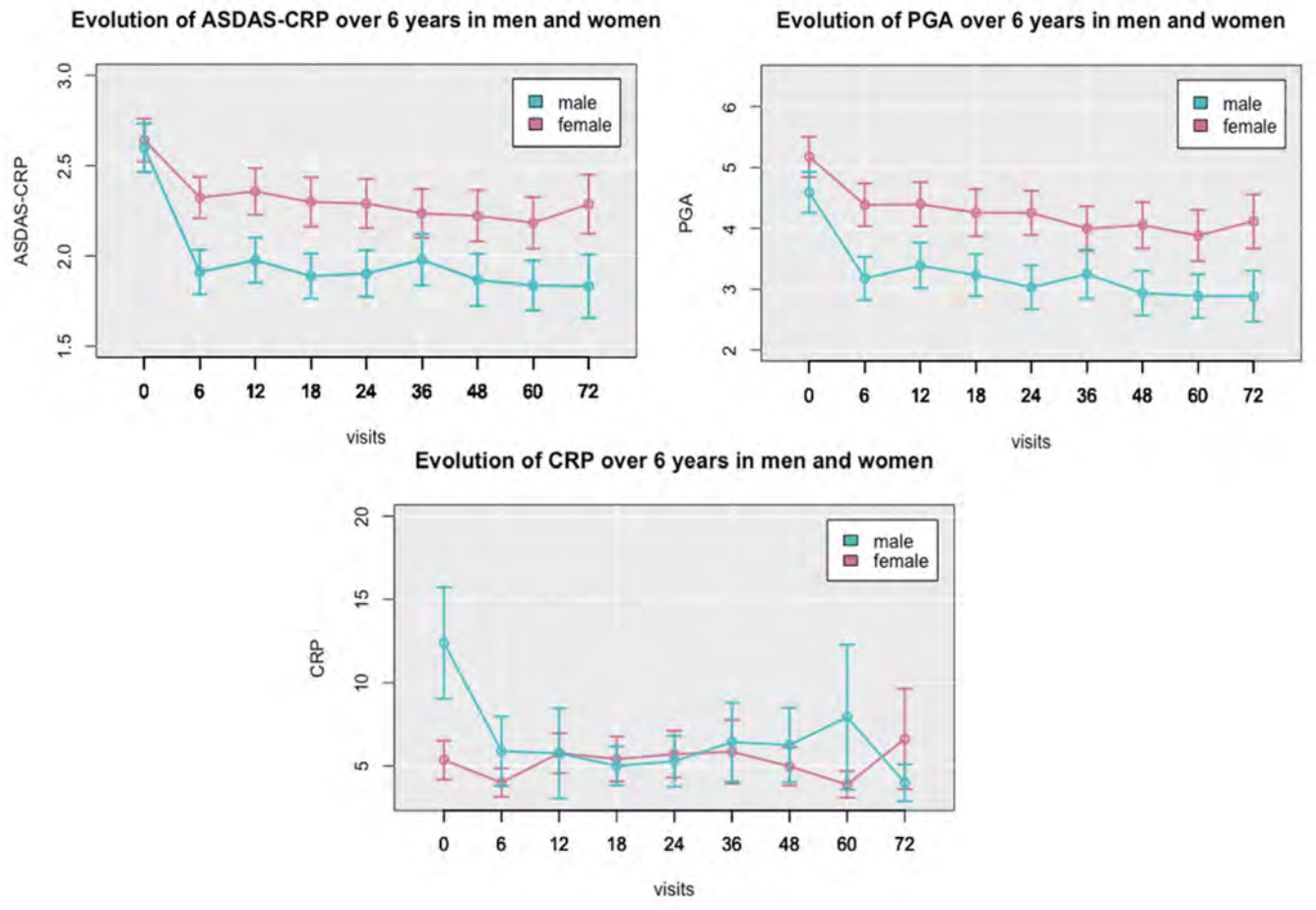
Background/Purpose: Recent data suggest differences between men and women with axial spondyloarthritis (axSpA), in terms of disease activity, disease progression and treatment response [1-3]. Overall, women tend to show



Comparison of evolution of disease activity (ASDAS, PGA, CRP) over 6 years of follow-up between genders.

higher perceived disease activity (mostly on the Bath Ankylosing Spondylitis Disease Activity Index: BASDAI) and extra-articular manifestations (mostly enthesitis), whereas men with axSpA tend to show more structural progression [2-3]. The objective of this study was to determine gender differences in disease activity in recent axSpA over 6 years of follow-up.

Methods: We analysed data collected during the first 6 years of follow-up of the prospective national multicentric DESIR cohort for patients with early inflammatory back pain suggestive of axial SpA and fulfilling the ASAS classification criteria for axSpA at any time (1) (n= 494). Self-reported gender was collected at baseline. Three main outcomes were compared between men and women: ASDAS-CRP (to assess disease activity), patient global assessment (PGA: ranging from 0-10), and CRP. To compare genders longitudinally and account for repeated measures over time (mo 6, 12, 18, 24, 36, 48, 60 and 72), a linear mixed-effect model analysis (LMM) was performed (using lme4 R package) with gender and time as fixed effects and subjects as random effect. There was no imputation of missing data.

Results: Of 708 at baseline, 494 patients (70%) were analysed: mean age was 31.9±7.5 years, mean disease duration 20.7±11.7 months; 50.4% were men. At baseline, mean ASDAS-CRP score was 2.6±1.0 in men versus 2.6± 0.9 in women (p=0.75), mean PGA score was 4.6±2.6 and 5.2±2.6 (p< 0.0001) and mean CRP was 10.7 ± 16.5 and 6.2 ± 8.3 (p< 0.0001) respectively. Over time, ASDAS-CRP, PGA and CRP all decreased in both men and women. However, there was more decrease in all aspects in men than women (Figure 1). The difference was significant in LMM for ASDAS-CRP and PGA (both p< 0.0001) but not for CRP (p=0.089). As an illustration, the mean ASDAS-CRP score was 1.8±1.0 in men versus 2.3±0.9 in women at 6 years, with mean PGA score of 2.9±2.6 versus 4.2±2.7 respectively.

Conclusion: Although disease activity was similar between genders at baseline, there were more improvements in all aspects of disease in men than in women over 6 years of follow-up, leading to higher disease activity and symptoms in women at 6 years, with similar CRP levels. Further research is needed to explore differences in disease activity between genders using imaging data. Gender is an important contextual factor in axSpA and should be taken into account.

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Abstract Number: 0621

Case Series of IgG4-related Disease in African American Patients at Two Large Academic Centers

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SESSION INFORMATION

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Background/Purpose: IgG4-related Disease (IgG4-rD) is a fibroinflammatory disease with highly variable manifestations that can be difficult to diagnose. Response to treatment with prednisone and/or rituximab is generally favorable. Unfortunately, it has not been well studied in African American patients, a population already affected by wider healthcare disparities. Better understanding how IgG4-rD may present and respond to treatment in African American patients is therefore of particular importance, especially in light of the meaningful phenotypic differences already described among other sub-populations including self-identifying Asians and women. Our aim is to describe manifestations and course of disease in a retrospective cohort of African American patients with biopsy-proven or highly suspected IgG4-rD.

Methods: The EMR systems for two academic centers in Washington, DC were queried for self-identifying African American patients with IgG4-rD by ICD-9 and ICD-10 codes applied from 2010 to present. IgG4-rD diagnosis (as documented by a treating rheumatologist) was then confirmed by manual chart review. Clinical data relevant to presentation, course, and management of disease were reviewed and recorded.

Results: 122 patients met initial screening criteria, 11 of whom (4 male) were confirmed to carry a diagnosis of IgG4-rD by manual chart review. 8 of these 11 patients met 2019 ACR classification criteria for IgG4-rD. The most commonly involved organs were lymph nodes (8) and orbits (5), and the mean number of organs involved was 2.8 +/- 1.3 (Figure 1). All 11 patients underwent tissue biopsy; common findings included lymphoplasmacytic infiltrate (5), >50/hpf IgG4-positive plasma cells (5), storiform fibrosis (2), no typical features (2), and obliterative phlebitis (1). Mean age at diagnosis was 51.5 +/- 11.3 years. Median time from symptom onset to diagnosis was 821 days (mean 1130 +/- 1149 days). 8 patients have achieved disease remission to date; mean time from diagnosis to remission was 222 +/- 97 days. Treatments included systemic steroids (10), rituximab (7), surgery (6), mycophenolate mofetil (1), and

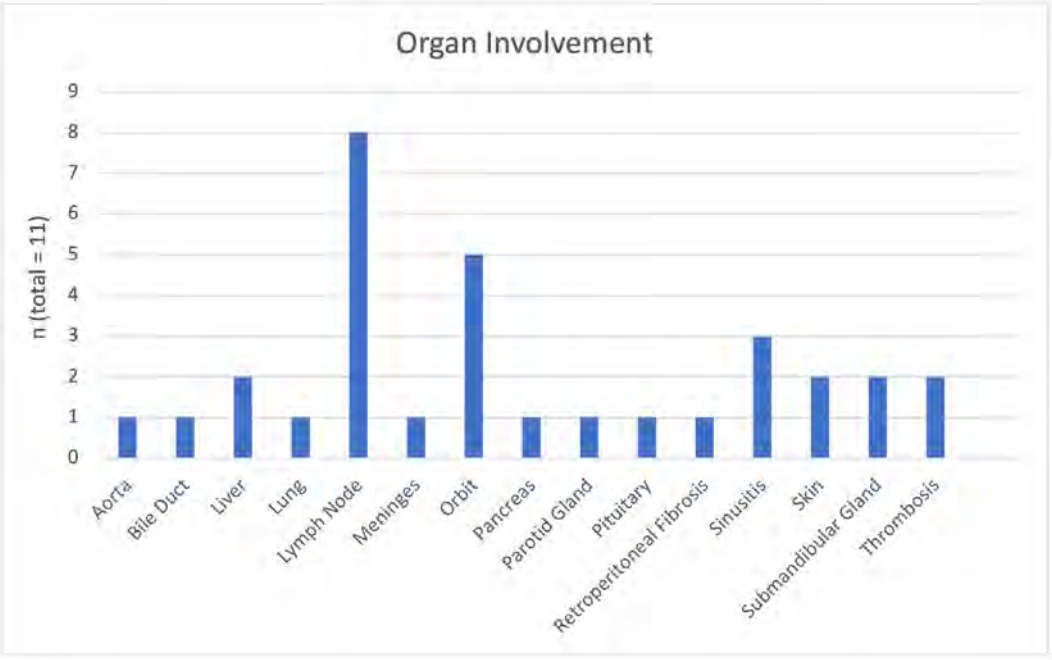

Figure 1. frequency of organ involvement in a case series of African American patients with IgG4-rD.

azathioprine (1). Serum IgG4 level was measured at or before the time of diagnosis in 8 patients (mean 304 +/- 220 mg/dL). A subsequent serum IgG4 was measured in 5 patients, all of whom had levels in the normal range by 1 year after diagnosis.

Conclusion: Presentation of IgG4-rD in this case series of African American patients was notable for prominent involvement of lymph nodes (73%), more than in previous analyses of largely Caucasian and Asian cohorts (estimated at 25-45%) [1,2]. Response to prednisone and/or rituximab was robust. The long median time from symptom onset to diagnosis of over 2 years may reflect underlying healthcare disparities but comparison data in other populations is lacking. This study was limited by small sample size. Inclusion of larger numbers of African American patients in future IgG4-rD research is needed.

1. Fong W et al. IgG4-related disease: features and treatment response in a multi-ethnic cohort in Singapore. 2018.

2. Wallace ZS et al. IgG4-Related Disease: Clinical and Laboratory Features in One Hundred Twenty-Five Patients. 2015.

Disclosure: J. Thaler, None; **S. Dia**, None; **F. Constantinescu**, None.

Abstract Number: 0622

Ethnic Disparities in Giant-Cell Arteritis: A Clinical Comparison Among Caucasian and Hispanic Patients in the Inland Empire of Southern California

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Healthcare Disparities in Rheumatology Poster (0594–0622)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Giant-Cell Arteritis (GCA) is the most common systemic vasculitis among North Americans, historically described in Caucasian populations, with limited clinical data in other ethnic backgrounds. Despite ongoing research in the field of Rheumatology many disparities remain. Our objective was to compare the demographic, clinical characteristics, comorbid conditions, and side effects to treatment in GCA patients with different ethnic backgrounds specifically Hispanics and Caucasians.

Methods: A single center retrospective chart analysis was performed on 400 patients with associated ICD10 code diagnosis of GCA seen at Loma Linda University Health from 2013 to 2020. 53 patients with a diagnosis of GCA, based on a positive temporal artery biopsy or meeting the ACR 1990 GCA classification criteria confirmed by an expert Rheumatologist were identified. We used Pearson's chi-square to test for independence between demographic and clinical categorical variables and ethnicity. We used independent samples t-test to test for mean differences in the continuous clinical variables between Caucasians and Hispanics and set alpha equal to 0.05 for statistical significance.

Results: We did not detect any proportional differences in average age, BMI, or gender between Caucasians and Hispanics in our cohort. A higher proportion of Caucasians had private insurance compared to Hispanics (70% vs

Table 1. GCA Demographic and Clinical Presentation in Caucasians and Hispanics, *n*=53.

	All	Caucasian	Hispanic	*p*-value[a]
Gender, % (*n*)				
Male	12	67% (8)	33% (4)	0.999
Female	41	63% (26)	36% (15)	
Insurance, % (*n*)				
Public	33	59% (19)	41% (13)	0.439
Private	19	70% (14)	30% (6)	
BMI, kg/m^2, mean ± SD	28.3 ± 6.9	28.7 ± 6.9	29.2 ± 7.6	0.792
Age, years, mean ± SD	71.2 ± 10.6	70.5 ± 10.6	70.8 ± 10.1	0.925
Initial Presenting Symptom, % (*n*)				
Headache	20	60% (12)	40% (8)	---
Visual Changes	8	63% (5)	37% (3)	
Headache & Visual Changes	23	65% (15)	35% (8)	
Other	2	100% (2)	---	
Visual Symptoms, % (*n*)				
No	13	54% (7)	46% (6)	0.372
Yes	40	68% (27)	32% (13)	
Jaw Claudication/Pain, % (*n*)				
No	33	70% (23)	30% (10)	0.279
Yes	20	55% (11)	45% (9)	
Abnormal Temporal Artery, % (*n*)				
No	36	64% (23)	36% (13)	0.954
Yes	17	65% (11)	35% (6)	
PMR Symptoms, % (*n*)				
No	20	60% (12)	40% (8)	0.682
Yes	32	66% (21)	34% (11)	

BMI=Body Mass Index. Percentages are estimated across rows and may not add to one-hundred due to rounding.

[a]*p*-value based on the chi-square statistic for categorical variables and independent samples t-test for continuous variables.

30%). Clinically, we found that a higher proportion of Caucasian patients reported headaches, visual symptoms, Polymyalgia Rheumatica, and had clinically documented abnormal temporal artery on physical exam at time of diagnosis when compared to Hispanics (Table 1).

We also examined associated risk factors/comorbidities and observed that Hispanics were proportionally more likely to have a diagnosis of Hyperlipidemia (HLD) compared to Caucasians and that this difference was statistically significant (p=0.021). Caucasian patients experienced a higher proportion of steroid side effects, overall, most notably weight gain (p=0.051) while on treatment compared to the Hispanic group (Table 2).

Interestingly our Caucasian cohort was more frequently diagnosed via abnormal biopsy (71% vs 29%) than the Hispanic group. We also investigated relapse data and noted Caucasians were more likely to relapse compared to Hispanics (p=0.066) and the relapse was occurring mostly after twelve months of diagnosis and treatment initiation (Table 3).

Conclusion: We observed some differences in Caucasians and Hispanics, specifically among their comorbidities, long term steroid side effects, and potential to relapse. We found that some conditions such as HLD are statistically

Table 2. Comorbid Conditions and Steroid Induced Side Effects in Caucasians and Hispanics, *n*=53.

	All	Caucasian	Hispanic	*p*-value[a]
Weight Gain, % (*n*)				
No	24	50% (12)	50% (12)	0.051
Yes	29	76% (22)	24% (7)	
Diabetes Mellitus, % (*n*)				
No	44	64% (28)	36% (16)	0.863
Yes	9	67% (6)	33% (3)	
Osteoporosis, % (*n*)				
No	30	63% (19)	37% (11)	0.982
Yes	22	64% (14)	36% (8)	
Infections Requiring Hospitalization, % (*n*)				
None	33	61% (20)	39% (13)	0.777
Bacterial/Viral	17	65% (11)	35% (6)	
Cerebral Vascular Events %(n)				
No	45	62% (28)	39% (17)	
Yes	7	86% (6)	14% (1)	0.224
Coronary Artery Disease %(n)				
No	35	66% (23)	34% (12)	
Yes	17	65% (11)	35% (6)	0.943
Hyperlipidemia %(n)				
No	28	77% (22)	21% (6)	
Yes	25	48% (12)	52% 13)	0.021
Hypertension % (n)				
No	14	77% (11)	21% (3)	
Yes	39	59% (23)	41% (16)	0.19
Diabetes Mellitus %(n)				
No	28	68% (19)	32% (9)	
Yes	25	60% (15)	40% (10)	0.552

Percentages are estimated across rows and may not add to one-hundred due to rounding.

[a]*p*-value based on the chi-square statistic for categorical variables.

more prevalent in our Hispanic population, while relapse and steroid side effects were more common in the Caucasian group. We also found some variations in the initial clinical manifestations in these two groups.

Further large-scale research across multiple centers with diverse populations could produce valuable insight into whether there is meaningful clinical variations or disease phenotypes based on ethnicity that can potentially affect therapeutic decisions and disease prognosis.

Table 3. GCA Modality of Diagnosis & Relapse in Caucasians and Hispanics, *n*=53.

	All	Caucasian	Hispanic	*p*-value[a]
Modality of Diagnosis, % (*n*)				
Clinical	36	61% (22)	39% (14)	0.502
Biopsy	17	71% (12)	29% (5)	
Relapsed, % (*n*)				
No	19	47% (9)	53% (10)	0.066
Yes	30	73% (22)	27% (8)	
Time from Treatment Start to Relapse, % (*n*)				
No Relapse	19	47% (9)	53% (10)	
0-3 Months	6	33% (2)	67% (4)	
4-6 Months	5	60% (3)	40% (2)	---
7-12 Months	---	---	---	
>12 Months	19	90% (17)	10% (2)	

Percentages are estimated across rows and may not add to one-hundred due to rounding.

[a]*p*-value based on the chi-square statistic for categorical variables.

Disclosure: K. D'Anna, None; **M. Hojjati**, None.

Abstract Number: 0623

Intervention to Improve SLE Medication Adherence

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Medication nonadherence is as high as 80% among SLE patients and leads to higher morbidity, mortality, and healthcare costs. Both the under-recognition of nonadherence by providers and patient-perceived poor communication with providers contribute to the problem. We developed and pilot tested an adherence intervention to reliably identify nonadherence and improve patient-provider communication regarding SLE medications. To conduct the intervention, the provider used commercial pharmacy refill data available in the electronic health records to monitor nonadherence and prompt a tailored discussion with the patient surrounding SLE medication use during

Table 1. Intervention effects on adherence when considering all SLE medications, HCQ alone, DMARDs combined, and MMF alone

	Improved Adherence	No Benefit	Persistent Good Adherence
Any SLE medication (n=130)	35 (27%)	41 (32%)	54 (42%)
HCQ (n=120)	23 (19%)	35 (29%)	62 (52%)
DMARDs (n=85)	16 (19%)	34 (40%)	35 (41%)
MMF (n=37)	4 (11%)	15 (41%)	18 (49%)

Table 2. Comparing socio-demographics and clinical characteristics among adherence groups

	Improved Adherence (N=35)	No Benefit (N=41)	Persistent Good Adherence (N=54)	p-value
Socio-demographics				
Age, years, median [IQR]	**38[31-51]**	**34[29-51]**	**46[38-53]**	**0.03**
Female gender, n (%)	34(97%)	40(98%)	49 (91%)	0.1
Non-White race, n (%)	**20(57%)**	**32(78%)**	**25(46%)**	**0.007**
<College education, n (%)	14(40%)	20(49%)	19(35%)	0.4
Married/cohabiting, n (%)	**13(37%)**	**11(27%)**	**28(52%)**	**0.04**
On disability, n (%)	13(37%)	11(27%)	14(26%)	0.5
Income ≤$50,000, n (%)	**19(54%)**	**29(71%)**	**23(43%)**	**0.02**
Private insurance, n (%)	21(60%)	23(56%)	34(63%)	0.8
Medicare/Medicaid, n (%)	16(46%)	16(39%)	25(46%)	0.8
Clinical characteristics				
SLAQ, median [IQR]	8.5[4-13]	9.5[5.5-12]	7[4-13]	0.8
SLEDAI, median [IQR]	2[0-4]	2[0-6]	0[0-4]	0.3
Active nephritis, n (%)	2 (6%)	5 (12%)	4 (7%)	0.9
PGA, median [IQR]	0.5[0-1]	0.6[0.3-1]	0.25[0-0.75]	0.07

PGA = Physician Global Assessment, 0-3; SLAQ = Systemic Lupus Activity Questionnaire

the clinic encounter. In this analysis, we explored the effect of the intervention on adherence and differences between patients who did and did not benefit from the intervention.

Methods: The intervention was pilot tested over 12 weeks at an academic lupus clinic during regular follow-up visits. Consecutive patients on SLE medications, including HCQ, MTX, AZA, MMF, LEF, and belimumab, were included. Adherence was assessed by medication possession ratio (MPR) based on pharmacy refill data, using MPR ≥80% as a cutoff for adherence.

MPRs 3-months before (pre-) and after (post-) the intervention visit for each SLE medication were collected. Patients were grouped into 1) Improved Adherence (MPR < 80% pre-intervention but ≥80% post-intervention), 2) No Benefit from the intervention (MPR < 80% both pre- and post-intervention, or MPR ≥80% pre-intervention but < 80% post-intervention), and 3) Persistent Good Adherence (MPR ≥80% both pre- and post-intervention).

Results: Among 130 patients included in the analysis, median age was 43, 95% were female, 59% were non-White, and 40% were married or cohabiting. A significant proportion of patients had < college education (41%), were medically disabled (29%), and the majority had income < $50,000/year (55%). During the 3-month periods before and after the intervention visit, 92% patients were prescribed HCQ, 28% MMF, 22% AZA, 12% MTX, 7% belimumab, and 2% LEF. Most (59%) were on ≥2 SLE medications.

Improved Adherence was found in 27% of patients, while 32% had No Benefit and 42% had Persistent Good Adherence when considering all SLE medications. A notable proportion of patients experienced Improved Adherence when

considering HCQ alone, MMF alone, or all DMARDs combined (Table 1). Compared to those who had No Benefit, those who had Improved Adherence after the intervention visit were more likely to be older, married or cohabitating, White, and have income >$50,000 (Table 2).

Conclusion: This simple intervention made routine use of a measurable, objective indication of adherence through pharmacy refill data and showed promising preliminary results in improving adherence in a significant proportion of SLE patients. However, additional research is needed to refine the intervention to best serve younger, non-White, and lower income patients, who often have more severe disease and are at highest risk for nonadherence.

Disclosure: K. Sun, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **J. Rogers**, Exagen, Inc, 5; **R. Sadun**, None; **L. Criscione-Schreiber**, None; **J. Doss**, Pfizer, 5; **M. Maheswaranathan**, None; **A. Barr**, None; **L. Eder**, None; **A. Corneli**, None; **H. Bosworth**, None; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5.

Abstract Number: 0624

Validation of a Self-reported Measure of Extent and Reasons for Nonadherence in SLE

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Construct validity correlating the refined DOSE-nonadherence measure of the extent of nonadherence with subjective and objective measures of adherence and the BMQ

	Pearson's correlation	p-value
Adherence measures		
MASRI (n=90)	0.60	<0.001
HCQ blood level (n=15)	-0.73	0.003
HCQ MPR (n=86)	-0.48	<0.001
Beliefs in Medicines Questionnaire		
Specific Necessity	-0.26	0.01
Specific Concern	0.32	0.002
General Overuse	0.29	0.005
General Harm	0.36	<0.001

MASRI = medication adherence self-report inventory;
MPR = medication possession ratio

Background/Purpose: Medication nonadherence is common in SLE and leads to increased hospitalizations, morbidity, and mortality. To better recognize nonadherence and address adherence barriers, there is a need for a validated and easily implemented tool. Based on our prior mixed-methods results and literature review, we adapted the Domains of Subjective Extent of Nonadherence (DOSE- nonadherence) questionnaire, a previously validated (in patients with hypertension and hepatitis C) self-reported measure of *extent of nonadherence* and *reasons for nonadherence,* to better illuminate nonadherence in SLE. This study aimed to refine and assess the validity of the DOSE-nonadherence in the context of SLE.

Methods: We refined the DOSE-nonadherence questionnaire through cognitive interviewing with SLE patients recruited from an academic lupus clinic and feedback from six lupus clinic rheumatologists. The instrument was then administered to patients taking any oral SLE medications. To assess its validity, we compared the results of the refined DOSE-nonadherence questionnaire to the Beliefs about Medicines Questionnaire (BMQ), the Medication Adherence Self-Report Inventory (MASRI), an existing self-reported adherence, medication possession ratio (MPR) based on pharmacy refill data, and available HCQ blood levels.

Results: Sixteen patients (median age 43, 100% female, 50% Black) participated in cognitive debriefing interviews to refine the DOSE-nonadherence. The refined DOSE-nonadherence was administered to 99 patients (median age 50, 96% female, 42% Black, 33% < college education, 55% married or cohabiting, 51% < $50K annual household income, 44% on Medicaid/Medicare). Of these, 85% were prescribed HCQ, 31% MMF, 14% AZA, 12% MTX, 1% LEF, and 5% belimumab.

Forty-four percent of patients reported nonadherence based on the refined DOSE-nonadherence. The *extent of nonadherence* score was highly correlated with MASRI (r=0.60) and HCQ blood levels (r=-0.73) and moderately correlated with HCQ MPR (r=-0.48), demonstrating convergent validity. The correlation between *extent of nonadherence* and BMQ was small (r=-0.26-0.36), demonstrating discriminant validity (Table 1).

Nonadherent patients reported on average 3.5 [IQR 1-6] reasons for nonadherence. The most common reasons were busyness and forgetting (n=25), physical fatigue (n=19), pill fatigue (n=15), feeling well (n=12), irregular schedule (n=11), and noticing no difference when skipping a dose (n=10).

Conclusion: Our results support the validity of the DOSE-nonadherence in assessing extent and reasons for nonadherence among SLE patients. In comparison to the MASRI, the DOSE-nonadherence helps identify *reasons for nonadherence*. This instrument can be used to identify, rigorously study, and guide the development of interventions to target the most common reasons for nonadherence in SLE.

Disclosure: K. Sun, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **D. Anderson**, None; **R. Sadun**, None; **L. Criscione-Schreiber**, None; **J. Doss**, Pfizer, 5; **J. Rogers**, Exagen, Inc, 5; **T. Coles**, Merck, 5; **C. Volis**, None; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5.

Abstract Number: 0625

Brief Tailored Clinic Intervention (A-MATIC) Targets Nonadherence During SLE Visits: Two-year Sustainability and Outcomes

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
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Background/Purpose: Up to 83% of SLE patients are nonadherent to hydroxychloroquine (HCQ) which can result in up to 8-fold higher risk of early death. Yet, adherence is *never* assessed during routine SLE visits. Current adherence tools are time-consuming and offer no guidance to clinicians for adherence discussions. Our prior study reported feasibility of using an adapted seven-item Assessing Medication Adherence & Tailoring Intervention in Clinic (A-MATIC) process that identifies nonadherence and facilitates tailored adherence discussions in 2.6 mins. This study examined the impact and sustainability of using A-MATIC during SLE visits.

Table 1. A-MATIC* Intervention Process. *A-MATIC is adapted from 2 validated gold-standard adherence tools (MASRI & BMQ). MASRI Medication Adherence Self-Report Inventory; BMQ Brief Medication Questionnaire

Step 1. Patient reports last month's adherence (0-140%) on MASRI Visual Analogue Scale (VAS)	
If <80% adherence – Proceed to **Step 2;** If ≥80% – **Stop**	
Step 2. Patient chooses barrier(s) category below (6 BMQ categories):	**Step 3.** Crosswalks clinician from Step 2. to categorized strategy options
1. System Inability to get refills	1. Give 90-day supplies; Use mail order pharmacy
2. Motivation Short-term med side effects	2. Conduct motivational interview; Use strategies to manage adverse effects
3. Understanding Lack of clarity on med role & response	3. Use teach back; Leverage visual aids on risk vs. benefits
4. Motivation & Understanding Long-term side effects & damage concerns	4. Discuss expected outcomes and timing; Use simple language
5. Recall Forgetfulness	5. Consolidate doses; Use pillboxes
6. Financial Inability to afford med	6. Offer low cost alternatives; Offer coupons
Step 4. Patient & clinician prepare personalized adherence plan using categorized strategy options. To complete intervention, clinician circles strategy options used and enters time spent	

Table 2. Patient Demographics

Table 2. Patient Demographics	
Total Patient-Visits	250
No. of Patients	87
Age (Mean ± SD)	46±17
Female	89%
Caucasian	87%
Hispanic/Other Ethnicities	18%
Active Smoker	4%
Baseline SLEDAI (Mean ± SD)	2.1±2.6

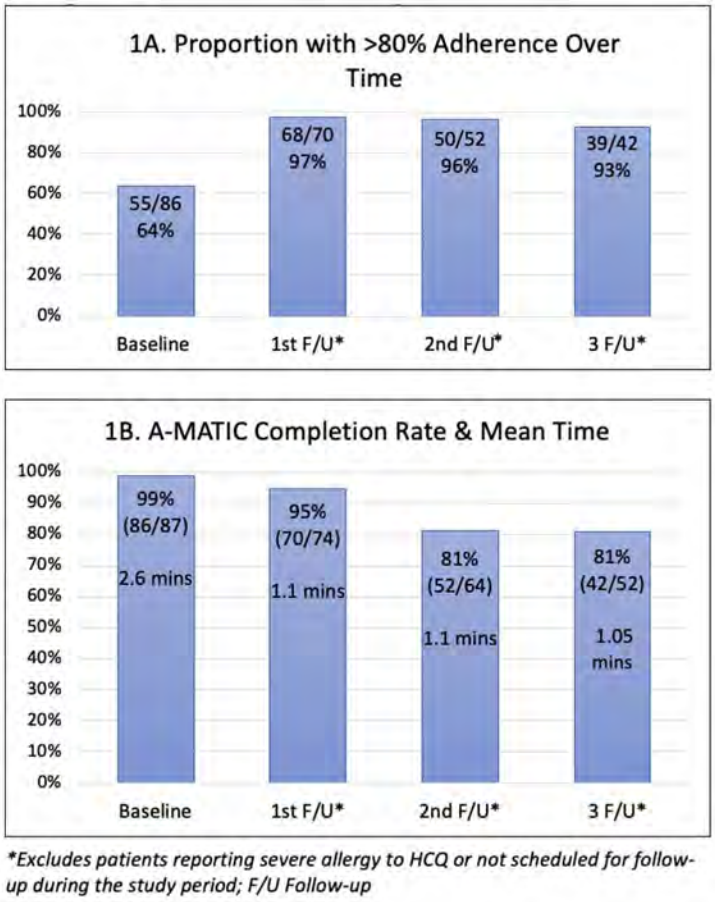

Figure 1. 1A. Graph showing impact of A-MATIC defined as proportion of adherence over two years; 1B. Graph showing sustainability of using A-MATIC during routine SLE visits over two years.

Methods: Our study included all patients seen at the UW SLE Clinic between 3/2019-5/2021. A-MATIC intervention is adapted from two standard adherence tools, Medication Adherence Self-Report Inventory (MASRI) and Brief Medication Questionnaire (BMQ), and includes 4 steps (Table 1): Step 1, assesses adherence using 0-140% MASRI visual analogue scale (VAS). The tool prompts patients reporting adherence < 80% to proceed to Step 2. Step 2, has 6-items BMQ-derived to identify key barriers. Step 3, contains adherence planning strategies that crosswalks from Step 2 barriers. Using these strategies, clinician can tailor an adherence plan based on patient choices in Step 4. Last, the clinician circles strategies used and time spent.

To assess impact, we examined the change in adherence across 3 follow-up (f/u) visits after patients participated in tailored patient-clinician discussions using A-MATIC compared to baseline adherence. We calculated the mean difference in adherence and examined the trend of adherence over time. To assess sustainability, we calculated the mean time spent and percentage of intervention completed at baseline, 1st, 2nd, 3rd f/u visits. Intervention completion was defined as patients and clinicians completing all steps.

Results: In study period there were 250 visits of 87 SLE patients with demographics shown in Table 2.

Impact – We found 36% (31/87) of the patients reported nonadherence at baseline. All patients reporting nonadherence participated in tailored adherence planning with their clinician. During the 1st f/u, 96% of these patients reported >80% HCQ adherence and resolution of underlying barriers; these patients reported HCQ adherence on their

subsequent f/u. We found 93% lower odds of reported nonadherence after completing the A-MATIC intervention and participating in adherence discussions (OR 0.07, CI 0.01-0.24, p < 0.001). Significant improvement in adherence was noted over time (Mean diff. 27%, CI 16%-38%, p < 0.001) (Fig. 1A). Finally, over 2 years, 95% of patients reported >80% adherence compared to 64% at baseline.

Sustainability – Over 2 years, the mean time to complete the intervention was 2.6±1 mins, 1.1±0.2 mins, 1.1±0.2 mins, 1.05±0.2 mins. during baseline, 1st, 2nd, 3rd f/u; the intervention was completed during 99%, 95%, 81%, 81% of the baseline, 1st, 2nd, 3rd f/u visits. (Fig. 1B).

Conclusion: A-MATIC intervention is a sustainable and impactful way to assess and facilitate adherence discussions between a patient and clinician, and helps sustain adherence over time. Next study will examine A-MATIC's role in targeting nonadherence in diverse SLE clinics.

Disclosure: S. Garg, None; **B. Chewning**, None; **S. Gomez**, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 0626

Does Higher Quality of Care in SLE Translate to Better Patient Outcomes?

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Quality of care (QOC) as measured by quality indicators (QIs) decreases damage accrual in SLE long term. We aimed to assess if high QOC in SLE results prospectively in improved outcomes, specifically patient reported quality of life (QOL) and non-routine health care utilization (HCU).

Methods: 140 consecutive patients meeting 1997 ACR classification criteria for SLE were recruited from the Rheumatology clinic at an academic center. Self-report questionnaires collected information on QOC and QOL (using the disease-specific tool LupusPRO, which assesses both health-related (HR) QOL and non (N)HRQOL) at baseline. Receipt of QIs was confirmed using chart review. Data on demographics, socio-economic and disease characteristics were collected. Disease activity and damage were measured using Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)- SLEDAI and SLICC-ACR damage index (SDI). Follow up QOL and HCU (routine: rheumatology, primary care physician (PCP) visits and non-routine: ER visits and hospitalizations) were collected prospectively at 6 months. High QOC was defined as those meeting ≥80% of the eligible QIs. Co-variates of high QOC were assessed. Univariate regression analyses were performed with QOC (continuous variable) and high QOC (binary variable) as independent variables and HRQOL and NHRQOL as the dependent variables at baseline and follow up. Multivariable regression models were adjusted for age, gender, public insurance, disease activity, damage, disease duration, fibromyalgia and Charlson comorbidity index. HCU was also included in the multivariate models for QOL at follow up. Similarly, univariate and multivariate regression analyses were performed to evaluate QOC (and high QOC) as the predictors of non-routine HCU and disease activity at follow up. P-value of ≤0.05 was significant.

Table 1. Regression analyses between QOC and LupusPRO at baseline

	LupusPRO-HRQOL			LupusPRO-NHRQOL		
	B	95% CI	P value	B	95% CI	P value
Univariate analysis						
QOC	14.24	-13.08, 41.56	0.304	**27.98**	**4.42, 51.64**	**0.021**
High QOC	4.63	-2.85, 12.12	0.222	**6.84**	**0.34, 13.34**	**0.039**
Multivariate analysis showing QOC and significant variables						
Model 1 with QOC						
QOC	20.33	-11.75, 52.41	0.211	**33.31**	**4.21, 62.42**	**0.025**
Gender	-	-	-	**17.21**	**4.32, 30.10**	**0.010**
Public insurance	**-9.87**	**-18.04, -1.69**	**0.019**	-	-	-
SELENA-SLEDAI	**-1.71**	**-3.08, -0.34**	**0.015**	-	-	-
Fibromyalgia	**-12.37**	**-22.81, -1.93**	**0.021**	-	-	-
Model 2 with high QOC						
High QOC	4.41	-3.58, 12.41	0.276	6.95	-0.37, 14.27	0.062
Gender	-	-	-	**17.69**	**4.70, 30.68**	**0.008**
Public insurance	**-9.55**	**-17.73, -1.37**	**0.023**	-	-	-
SELENA-SLEDAI	**-1.65**	**-3.02, -0.28**	**0.019**	-	-	-
Fibromyalgia	**-12.23**	**-22.69, -1.78**	**0.022**	-	-	-

*HRQOL includes 8 domains: lupus symptoms, lupus medications, physical health, emotional health, pain, sleep, vitality, procreation, cognition and body image and NHRQOL includes 4 domains: coping, social Support, satisfaction with care, and desires-goals.
*QOC (continuous variable); high QOC (binary variable those meeting ≥80% eligible QIs).
*Multivariate models adjusted for age, gender, public insurance, disease duration, SELENA-SLEDAI, SDI scores, Charlson comorbidity index and fibromyalgia.

Table 2. Regression analyses between QOC at baseline and LupusPRO at follow up

	LupusPRO-HRQOL			LupusPRO-NHRQOL		
	B	95% CI	P value	B	95% CI	P value
Univariate analysis						
QOC	4.08	-22.33, 30.51	0.759	15.06	-12.36, 42.49	0.278
High QOC	-0.43	-7.41, 6.55	0.903	6.80	-0.34, 13.93	0.069
Multivariate analysis						
Model 1 with QOC						
QOC	14.65	-20.26, 49.57	0.405	30.85	-6.38, 68.07	0.103
Model 2 with high QOC						
High QOC	0.75	-7.47, 8.97	0.857	**10.75**	**2.28, 19.23**	**0.014**

*HRQOL includes 8 domains: lupus symptoms, lupus medications, physical health, emotional health, pain, sleep, vitality, procreation, cognition and body image and NHRQOL includes 4 domains: coping, social Support, satisfaction with care, and desires-goals.
*QOC (continuous variable); high QOC (binary variable those meeting ≥80% eligible QIs).
*Multivariate models adjusted for age, gender, public insurance, disease duration, SELENA-SLEDAI, SDI scores, baseline QOL scores, Charlson comorbidity index, fibromyalgia, number of PCP, rheumatology, ER visits and hospitalizations.

	ER visit			Hospitalization			Follow up disease activity		
	OR	95% CI	P value	OR	95% CI	P value	B	95% CI	P value
Univariate analysis									
QOC	0.18	0.01, 6.56	0.349	0.60	0.01, 29.77	0.796	1.29	-5.30, 7.87	0.697
High QOC	0.89	0.34, 2.32	0.817	1.25	0.44, 3.56	0.676	0.52	-0.98, 2.03	0.490
Multivariate analysis showing QOC and significant variables									
Model 1 with QOC									
QOC	0.14	0.05, 27.21	0.466	46.97	0.01, 844374.35	0.441	1.48	3.98, 6.93	0.588
Age	-	-	-	**0.86**	**0.75, 0.99**	**0.037**	-	-	-
SELENA-SLEDAI	-	-	-	-	-	-	**0.51**	**0.32, 0.69**	**<0.0001**
Number of PCP visits	**1.71**	**1.05, 2.79**	**0.03**	**2.37**	**1.06, 5.26**	**0.034**	**0.44**	**0.01, 0.87**	**0.046**
Model 2 with high QOC									
High QOC	1.21	0.33, 4.37	0.772	5.49	0.43, 70.52	0.191	**1.20**	**0.06, 2.34**	**0.039**
Age	-	-	-	**0.83**	**0.70, 0.98**	**0.031**	-	-	-
SELENA-SLEDAI	-	-	-	-	-	-	**0.53**	**0.36, 0.71**	**<0.0001**
Number of PCP visits	**1.69**	**1.05, 2.72**	**0.031**	**2.62**	**1.12, 6.12**	**0.026**	**0.46**	**0.05, 0.87**	**0.027**
*QOC (continuous variable); high QOC (binary variable those meeting ≥80% eligible QIs). *Multivariate models adjusted for age, gender, public insurance, disease duration, baseline SELENA- SLEDAI, SDI scores, Charlson comorbidity index, fibromyalgia, PCP and Rheumatology visits.									

Table 3. Regression analyses between OQC at baseline and secondary outcomes at follow up

Results: Baseline and follow up data on 140 and 94 patients respectively were analyzed. Mean (SD) age was 45.3 (13.5) years, with 88.6% females. Mean (SD) cumulative performance rate (QOC) was 78.6 (13.4) with 52% patients in the high QOC group. Older age and longer disease duration were the only significant predictors of high QOC. On univariate analysis QOC (and high QOC) were associated with better NHRQOL at baseline but not with HRQOL (Table 1). QOC remained a significant correlate of baseline NHRQOL, even after adjusting for co-variates. Of all the NHRQOL domains, high QOC was associated with better treatment satisfaction.

QOC (or high QOC) was not predictive of HRQOL or NHRQOL at follow up on univariate analysis; however, high QOC at baseline predicted better NHRQOL at follow up on multivariate analysis (Table 2). QOC was not associated with non-routine HCU at follow up (Table 3). High QOC, baseline disease activity and number of PCP visits were significantly associated with higher disease activity at follow up on multivariate analysis.

Conclusion: Higher QOC predicted better NHRQOL by directly impacting treatment satisfaction, which has been noted to influence health behaviors and improve adherence and outcomes in SLE patients. Higher QOC was not associated with HRQOL, ER visits, hospitalizations, or improvement in disease activity at follow up.

Disclosure: S. Arora, None; **J. Block**, None; **A. Nika**, None; **W. Sequeira**, None; **P. Katz**, None; **M. Jolly**, Rush University, 10, AURINIA, 1.

Abstract Number: 0627

Increasing Rates of Standardized Depression Screening in Adolescents and Young Adults with Childhood-Onset Systemic Lupus Erythematosus in a Pediatric Rheumatology Clinic

Emily Datyner[1], Manda Mitchell[1], Brooke Fine[1], Barron Patterson[1], T. Brent Graham[1] and Alaina Davis[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt Universty Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Depression is common and adversely affects health outcomes in adolescents and young adults with childhood-onset systemic lupus erythematous (cSLE).[1,2] The aim of our quality improvement project was to increase rates of standardized depression screening for adolescents and young adults with cSLE in our pediatric rheumatology clinic.

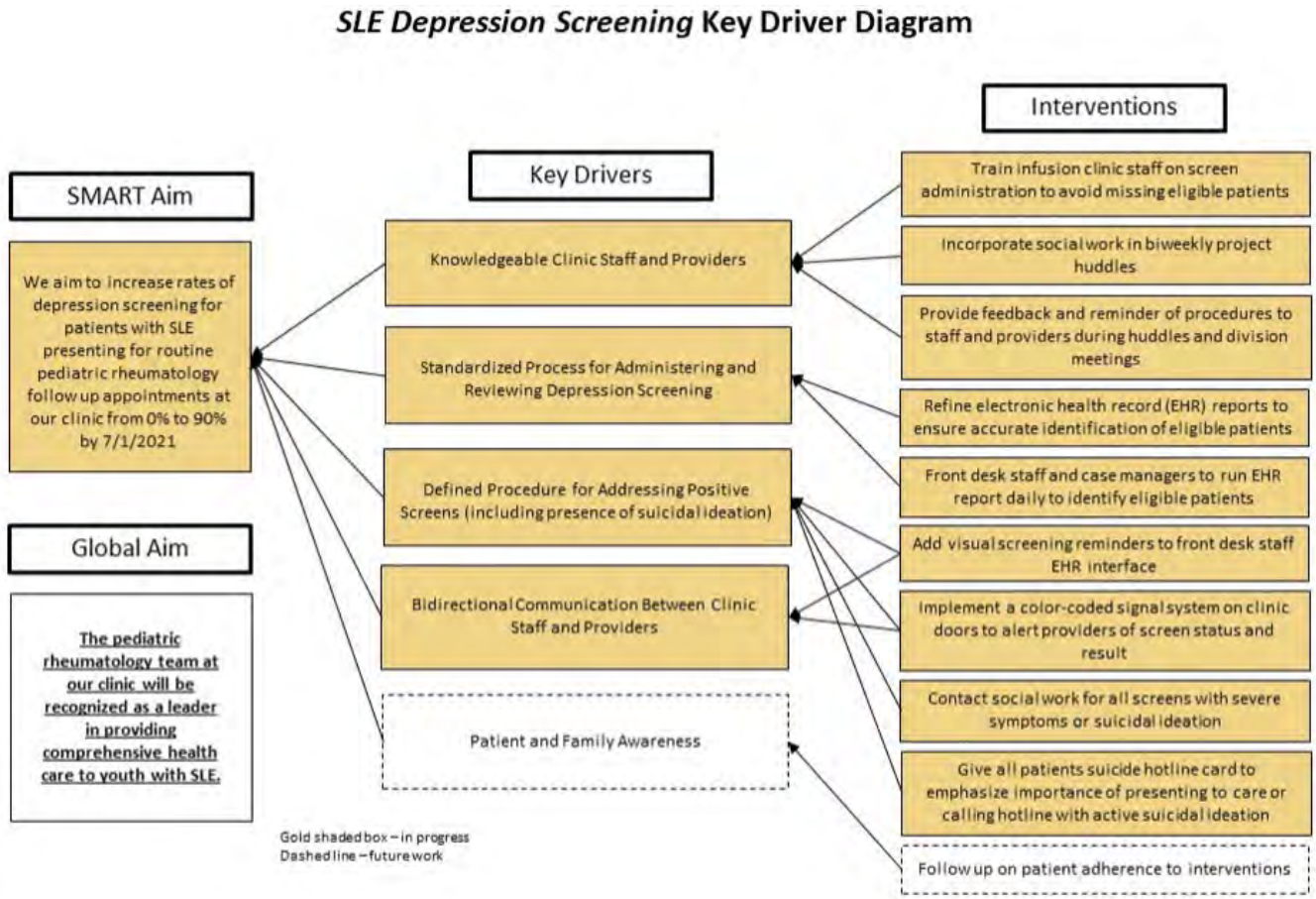

Figure 1. Key Driver Diagram - Depression Screening for Youth with SLE.

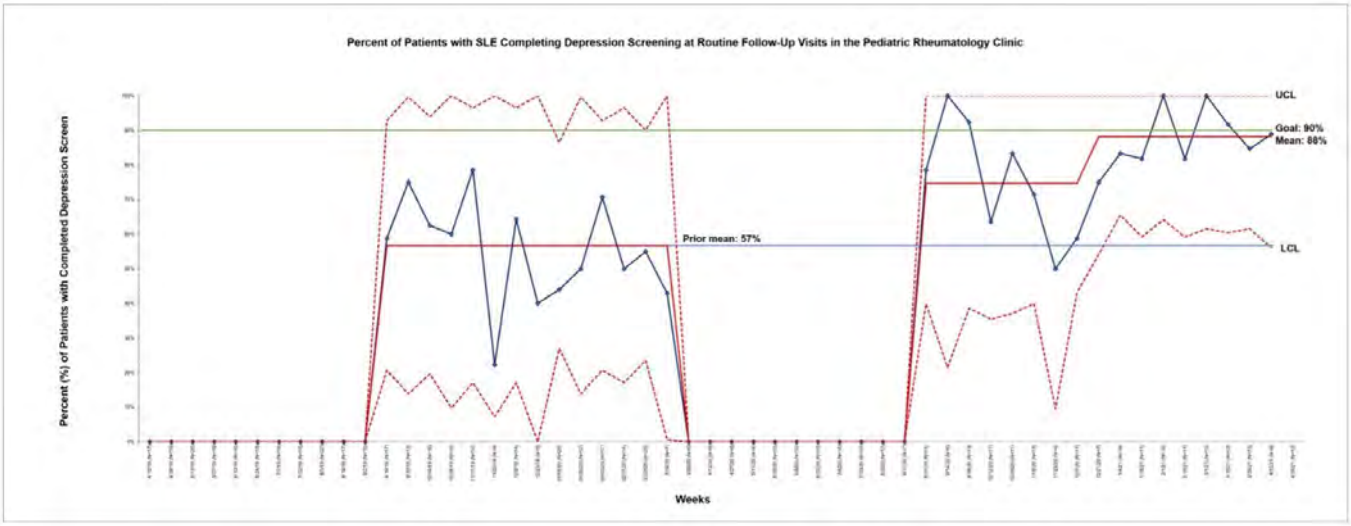

Figure 2. Control Chart - Percent of Patients Completing Depression Screening.

Methods: This was a second phase of an existing project that was halted March 2020 due to the SARS-COV2 pandemic. All patients with cSLE aged 12 years and older who were seen for routine follow-up in our pediatric rheumatology clinic August 31, 2020 through May 7, 2021 were included. Eligible patients were identified prior to their visit by an Electronic Health Record (EHR) generated report using ICD-10 codes for SLE. The Patient Health Questionnaire-9 modified for adolescents (PHQ-A) was used to screen for depressive symptoms. Patients completed the PHQ-A via an electronic tablet to maintain confidentiality. A designated clinic nurse immediately scored it and uploaded to the EHR for provider review. A multidisciplinary team developed a key driver diagram to organize potential interventions to improve rates of screening (Figure 1). Plan-Do-Study-Act (PDSA) cycles were used to prepare, implement, and evaluate these interventions. Statistical process control methods were used for data analysis.

Results: The percentage of eligible patient encounters where depression screening was completed increased from 57% to 88% following process improvements generated through PDSA cycles. This increase in completed screening represents special cause variation as evidenced by two separate data shifts on the control chart (Figure 2). Notable interventions included implementing a color-coded signal system to alert providers of screen status, adding screen reminders to front desk staff EHR interface, incorporating social work in biweekly huddles, and refining EHR reports to ensure accurate identification of eligible patients. Of the 176 depression screens completed, 33 (19%) were positive for moderate to severe symptoms and 16 (9%) were positive for suicidal ideation (SI). Clinic staff intervened on all screens that were positive for SI. Interventions for SI included social work consult, home safety planning, and referral to a behavioral health provider (or ensuring close follow up with an established behavioral health provider).

Conclusion: Rates of depression screening for adolescents and young adults with cSLE increased with process improvements made to our PHQ-A screening system. Future work will focus on improving rates further via full integration into the EHR.

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2. Chang JC, Davis AM, Klein-Gitelman MS, Cidav Z, Mandell DS, Knight AM. Impact of Psychiatric Diagnosis and Treatment on Medication Adherence in Youth With Systemic Lupus Erythematosus. Arthritis Care Res. 2021;73(1):30-38. https://doi.org/10.1002/acr.24450

Disclosure: E. Datyner, None; **M. Mitchell**, None; **B. Fine**, None; **B. Patterson**, None; **T. Graham**, None; **A. Davis**, None.

Abstract Number: 0628

Higher Quality of Care for Patients with Systemic Lupus Erythematosus in a Subspecialty Lupus Clinic: A Multi-Setting Cross-Sectional Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Healthcare quality for systemic lupus erythematosus (SLE) is a modifiable target for improving patient outcomes. Disease-specific subspecialty lupus clinics may offer experienced healthcare professionals, collaborative multidisciplinary teams and streamlined care processes. Superior performance of a subspecialty lupus clinic in the provision of quality care has been shown in the United States, where access to care based on insurance status is a major factor. We aimed to compare quality of care provided in a subspecialty lupus clinic with hospital and private general rheumatology clinics in a universal healthcare setting.

Methods: Patients with SLE (n = 258) were recruited in 2016 from various clinic settings in Australia, including a subspecialty lupus clinic (n = 147), two hospital general rheumatology clinics (n = 56) and two private rheumatology clinics (n = 55). Quality of care was assessed using 31 validated SLE quality indicators (QI) encompassing diagnostic work-up, disease and comorbidities assessment, drug monitoring, preventative care and reproductive health. Data were collected from both medical records and patient questionnaires. Overall QI performance was calculated as a percentage of the number of QIs met relative to the number of eligible QIs for each patient. Individual QI performance was measured as a percentage of the number of patients that met the QI relative to the number of patients eligible. Overall and individual QI performance were compared between the three clinic settings, and multivariable regression performed to adjust for sociodemographic, disease and healthcare factors.

Results: QI performance was generally high across clinic types for diagnostic work-up, comorbidity assessment, lupus nephritis, drug monitoring, prednisolone taper, osteoporosis management and pregnancy QIs. However, median [IQR] overall performance on eligible QIs was higher in the lupus clinic (66.7% [57.1-74.1]) than the hospital general rheumatology (52.7% [47.5-58.1]) and private rheumatology (50.0% [42.9-60.9]) clinics ($p < 0.01$) and remained significant after multivariable adjustment. The subspecialty lupus clinic significantly outperformed the other clinic settings on eligible individual QIs for disease activity, disease damage, cardiovascular risk factor and drug toxicity as-

sessments, pre-immunosuppression hepatitis and tuberculosis screening, new medication counselling, vaccinations, sun avoidance education and contraception counselling.

Conclusion: SLE patients managed in a subspecialty lupus clinic received higher quality of care compared to hospital and private general rheumatology clinics.

Disclosure: S. Sreedharan, None; **N. Li**, None; **G. Littlejohn**, AstraZeneca, 1, MSD, 1, AbbVie, 1, Janssen, 1, Pfizer, 1, Seqirus, 1; **R. Buchanan**, None; **M. Nikpour**, None; **E. Morand**, Amgen, 2, AbbVie, 2, Biogen, 2, Bristol Myers Squibb, 2, 5, AstraZeneca, 2, 5, 6, Genentech, 2, Servier, 2, Capella Biosciences, 2, Eli Lilly, 5, 6, EMD Serono, 5, 6, Janssen, 2, 5, UCB, 2, GlaxoSmithKline, 2, 5; **A. Hoi**, AstraZeneca, 2, 5, Janssen, 6, Abbvie, 6; **V. Golder**, None.

Abstract Number: 0629

Patient and Physician Satisfaction with Telemedicine Utilization for Delivery of Care in Patients with SLE – A Single Centre Experience

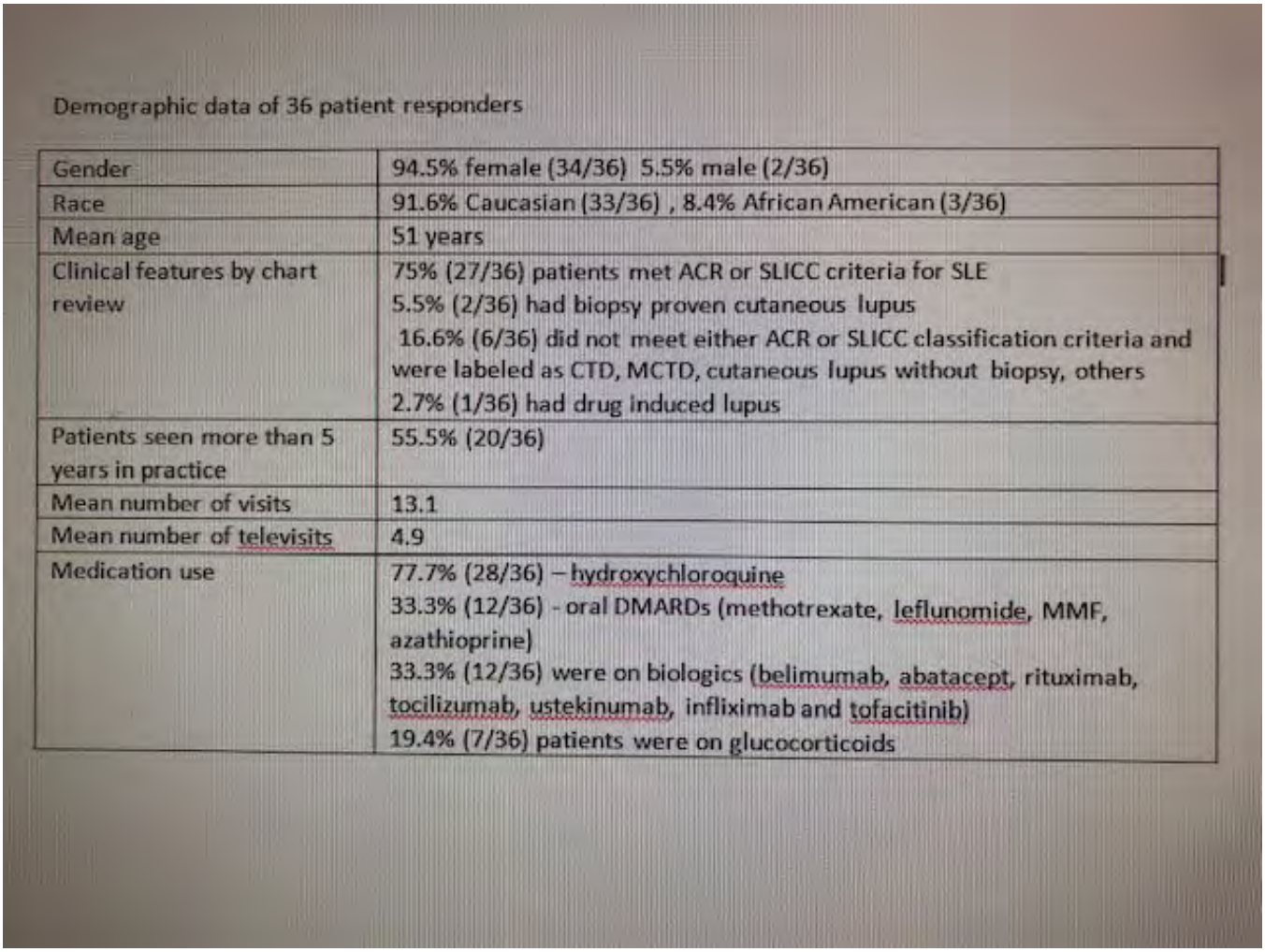
Tanmayee Bichile[1], Amanda Bembic[2], Susan Manzi[1] and Sonia Manocha[1], [1]Allegheny Health Network, Pittsburgh, PA, [2]Allgheny Health Network, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: COVID 19 has forced the healthcare system to utilize telemedicine to provide dependable and timely care for patients with SLE. Telemedicine has been used in patient care for RA, gout and CTD including SLE. Data on the use of telemedicine in patients with SLE is limited. The purpose of this study is to evaluate patient and physician satisfaction with use of telemedicine for SLE. This understanding can be utilized to provide timely access to care, improve gaps in delivery of care and address healthcare disparities.

Methods: After IRB approval,we queried EMR to identify patients with SLE (ICD10 codes M32.0-M32.9, L93.0-L93.2) seen as video visits (CPT codes 99201-99205,99211-99215) with providers in our division (Physicians and PAs= 18). Patients 18 years or older were included from 3/17/2020. Satisfaction Surveys were distributed to both patients and physicians. Chart review was performed on patient responders. A Likert scale was used to collect responses.

Results: 171 patients got the Patient satisfaction survey. 39 patients completed the survey, response rate was 22.8%. Chart review was done on 36 patients. 76.9% used telemedicine for the first time to seek care for SLE. 65.7% strongly agreed with ease to set up phone/computer. 94.8% visits started on time. 76.9% strongly agreed with visit convenience. 79.4% strongly agreed with adequate time to discuss questions/concerns . 69.2% strongly agreed with being comfortable with provider taking medical decisions. 66.6% strongly agreed with the satisfaction of the quality of care they received. 76.9% strongly agreed with the comfort of discussing problems. 47.2% patients received their telemedicine visit within a week from calling for appointment. 66.6% patients strongly agreed to another telemedicine visit but only 23.3% preferred telemedicine over in person visit. With Provider Satisfaction survey, 18 of 20 responded. 44.4% had used telemedicine to provide any medical care prior to pandemic while 22.2% had used telemedicine to provide care for SLE prior to the pandemic. 50% agreed and 22.2% strongly agreed with ease to set up hardware and software. 100% agreed that visits start on time. 61% agreed and 33.3% strongly agreed that visit was convenient. 55.5% agreed while 16.6% strongly agreed with the quality of care they provided. 100% were willing



Demographic data of 36 patient responders

Gender	94.5% female (34/36) 5.5% male (2/36)
Race	91.6% Caucasian (33/36) , 8.4% African American (3/36)
Mean age	51 years
Clinical features by chart review	75% (27/36) patients met ACR or SLICC criteria for SLE 5.5% (2/36) had biopsy proven cutaneous lupus 16.6% (6/36) did not meet either ACR or SLICC classification criteria and were labeled as CTD, MCTD, cutaneous lupus without biopsy, others 2.7% (1/36) had drug induced lupus
Patients seen more than 5 years in practice	55.5% (20/36)
Mean number of visits	13.1
Mean number of televisits	4.9
Medication use	77.7% (28/36) – hydroxychloroquine 33.3% (12/36) - oral DMARDs (methotrexate, leflunomide, MMF, azathioprine) 33.3% (12/36) were on biologics (belimumab, abatacept, rituximab, tocilizumab, ustekinumab, infliximab and tofacitinib) 19.4% (7/36) patients were on glucocorticoids

to order diagnostic and laboratory tests, prescribe medications. 61.1% were able to do some physical exam. 38.8% disagreed with preference of telemedicine over in person visit, 38.8% were neutral and 11.1% agreed and the rest 11.1% strongly disagreed.

Conclusion: Our study shows that telemedicine has an overall favorable satisfaction for SLE care among patients and providers. Our results indicate that patients with complex disease and medications and the providers could utilize telemedicine with favorable overall satisfaction. Over 50% patients had seen their rheumatologist for more than 5 years which indicates that an established patient-provider relationship is favorable for telemedicine use. Despite the overall satisfaction, both patients and providers seem to prefer an in person care over telemedicine only care for SLE.

Disclosure: T. Bichile, None; **A. Bembic**, None; **S. Manzi**, None; **S. Manocha**, None.

Abstract Number: 0630

Telemedicine in Rheumatology Care: A Systematic Review

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Summary of patient reported outcomes of included studies investigating use of telerheumatology. CCT, controlled clinical trial; CI, confidence interval; CSQ-8, Client Satisfaction Questionnaire-8; EQ-5D, EuroQol 5-domain questionnaire; GRC; Global Rating of Change Score; HAQ, Health Assessment Questionnaire; HAQ-DI, Health Assessment Questionnaire disability index; mHAQ, modified health assessment questionnaire; OR, odds ratio; RCT, randomized clinical trial; VSQ-9 score, 9-item visit-specific satisfaction questionnaire; WPAI; Work Productivity and Activity Impairment Questionnaire

Author (citation)	*Design (n)*	*Outcome and inference*
Patient Satisfaction		
Chew 2019	Observational (186)	Mean patient satisfaction score increased from 7.70 to 8.16 ($p < 0.05$) on 11-point Likert scale.
deThurah 2018	RCT (275)	>80% of patients in all groups (rheumatology or nursing telemedicine vs usual care) were "very satisfied".
Kavadichanda 2020	Observational (373)	90% reported satisfied or very satisfied with telemedicine on a 5-item Likert scale.
Kulcsar 2016	Observational (176)	Patient satisfaction for telerheumatology was 66%.
López-Medina 2020	Observational (644)	Mean patient satisfaction 64.7±35.8 (VAS scale 0-100).
Nguyen-Oghalai 2018	Observational (38)	37/38 patients rated highest level of satisfaction (10 out of 10) with telemedicine visit.
Palcu 2020	Observational (69)	87% agreed or strongly agreed that quality of care with telemedicine was same as in-person.
Phang 2020	Observational (127)	High patient satisfaction 4.0 and physician satisfaction 4.5 (on 5-point Likert scale).
Ramelet 2017	RCT (52)	Satisfaction by CSQ-8 significantly higher when receiving telemedicine (OR = 7.7, 95% CI: 1.8–33.6).
Shenoy 2020	Observational (100)	Median patient satisfaction 9 (IQR 8–10) on 0–10 scale.
Taylor-Gjevre 2018	RCT (54)	No significant between-group differences in VSQ-9 scores.
Wood 2019	CCT (85)	Patient satisfaction not statistically different between telemedicine and usual care groups.
Quality of Life		
Cuperus 2015	RCT (147)	No significant differences in HAQ-DI (mean group difference HAQ-DI (95% CI): -0.03 (-0.14, 0.07)).
deThurah 2018	RCT (275)	No differences between telehealth interventions and conventional follow-up by HAQ, EQ-5D, or self-efficacy.
Ferucci 2020	Observational (74)	No significant difference in functional status score with telemedicine versus in-person follow up.
Howren 2020	Observational (20)	No significant trends observed in WPAI, HAQ, or EQ-5D.
Kennedy 2017	CCT (76)	Immediate improved arthritis self-efficacy (mean change (95% CI): telemedicine 1.07 (0.67, 1.48) and usual care 1.48 (0.74, 2.23) with standardized effect size -0.24.
López-Medina 2020	Observational (644)	Patients who considered the phone consultation to be useful showed lower levels of axial pain (52.4±32.8 vs 63.7±29.8), peripheral stiffness (47.2±29.4 vs 56.1±29.0) and axial stiffness (47.6±32.7 vs 62.1±29.5).
Palmer 2021	Observational (25)	44% reported improvement in symptoms (GRC of ≥2); 52% reported symptoms had not changed (GRC Score of − 1, 0 or + 1); and 4% reported worsening of symptoms (GRC Score ≤ −2) after being provided with foot orthoses.
Ramelet 2017	RCT (52)	Morning stiffness (OR = 3.2, 95% CI: 0.97–7.15) and pain (OR = 2.64, 95% CI: 0.97–7.15) lower in the telemedicine group.
Taylor-Gjevre 2018	RCT (54)	No significant between-group differences in mHAQ, EQ-5D scores.
Preference (Telemedicine vs. usual care)		
Chew 2019	Observational (186)	61.5% preferred virtual monitoring clinic vs usual follow up.
Kavadichanda 2020	Observational (373)	76.1% considered that telemedicine better than in-person consultation in setting of COVID-19 pandemic.
Nguyen-Oghalai 2018	Observational (38)	67% of patients with inflammatory, rheumatic condition preferred face-to-face visit.

Table 2. Summary of objective outcomes of included studies investigating use of telerheumatology. €, Euro; £, Pound; CCT, controlled clinical trial; CI, confidence interval; CQR-5, 5-item Compliance Questionnaire Rheumatology; CRP, C-reactive protein; DAS28, disease activity score 28; ESR, erythrocyte sedimentation rate; MARS-5, Medication Adherence Report Survey; RADAI, rheumatoid arthritis disease activity index; RAPID3; Routine Assessment of Patient Index Data 3; RCT, randomized clinical trial; SGD; Singapore dollar

Author (citation)	*Design (n)*	*Outcome and inference*
Disease Activity		
Chew 2019	Observational (186)	Mean DAS28 increased from 2.56 to 2.78 (P < 0.05) and mean RAPID3 increased from 5.28 to 6.03 (P < 0.05) at 1-year.
deThurah 2018	RCT (275)	Noninferiority established; DAS28 score improved in telemedicine versus control -0.10 ([90% CI] -0.30, 0.13) (P = 0.45).
Ferucci 2020	Observational (74)	No significant difference in RAPID3.
Song 2020	RCT (77)	No significant difference in DAS28, ESR, CRP.
Taylor-Gjevre 2018	RCT (54)	No significant differences in DAS28-CRP, RADAI scores.
Wood 2019	CCT (85)	RAPID-3 not statistically different between telemedicine and usual care groups.
Cost, Travel, and Time Savings		
Cuperus 2016	RCT (147)	Difference in total societal costs non-significantly in favor of face-to-face program (difference €708; 95% confidence interval [95% CI] -€5,058, €3,642).
Kessler 2016	Observational (280)	Telemedicine group with smaller percentage spent on food compared to in-person visit (p < 0.001) and missed less time from work and school (p = 0.028, p = 0.003). Telemedicine group with significantly less median distance travelled (60 vs 175 miles, p < 0.001).
Kulcsar 2016	Observational (176)	Telemedicine services allowed savings of 200 driving miles per session (round trip), and average monetary savings of approximately $66.90 per session.
Nguyen-Oghalai 2018	Observational (38)	Patients travelled less distance for telemedicine compared to face-to-face visits (35 vs 63 miles).
Palmer 2021	Observational (25)	Cost savings with telephone consultation of £11.80 compared to face-to-face follow-up visit.
Phang 2020	Observational (127)	Cost savings estimate for patients requiring three telemedicine calls to reach target SUA would range from SGD$88.50 to SGD$273.00 for subsidized and private patients.
Wood 2019	CCT (85)	Significantly savings in mean distance travelled (Δ = −384.8 miles/visit, p < 0.01) and visit costs (Δ = −$113.8/visit, p < 0.01).
Medication Adherence		
deThurah 2018	RCT (275)	Medication nonadherence addressed in 31% of telemedicine and physician consultations .
Howren 2020	Observational (20)	No significant trends in CQR-5 level over 12 months (p = 0.31).
Phang 2020	Observational (127)	Median MARS-5 score was 24 (Q1:Q3 23-25).
Song 2020	RCT (77)	Significantly higher medication adherence (CQR score) in telemedicine compared to control group at 12th week (t = −2.528, p = 0.014) and 24th week (t = −2.073, p = 0.042).
Goal Serum Uric Acid		
Howren 2020	Observational (20)	72% achieved target serum uric acid < 360 µmol/L at 12 months.
Phang 2020	Observational (127)	57.5% achieved target serum uric acid < 360 µmol/L.

Background/Purpose: Coronavirus disease 2019 (COVID-19) pandemic led to a dramatic uptake of telemedicine in rheumatology. Given the impact of the pandemic on care delivery, we analyzed the recent published literature on the use of telemedicine for the diagnosis and management of inflammatory, noninflammatory and/or autoimmune rheumatic diseases.

Methods: We performed a registered systematic search (CRD42020202063) for interventional or observational studies in MEDLINE, Scopus, Cochrane Trials, Embase databases, and MedRXiv published between August 2015 and January 2021. We included studies that reported relevant outcomes (e.g., satisfaction, disease activity, quality of life) in ten or more people and that utilized telemedicine by rheumatologists for people with rheumatic disease. Pairs of reviewers screened manuscripts, extracted data and assessed studies for risk of bias using the Cochrane Collaboration's tool for randomized controlled trials and the Newcastle-Ottawa scale for nonrandomized studies.

Table 3. Results of Bias Assessment using the Risk of Bias 2.0 tool for randomized controlled trials

Authors and year of Publication	Randomization process	Deviations from intended interventions	Missing outcome data	Measurement of outcome	Selection of reported result	Overall Risk of Bias Judgement
Cuperus 2015	Low risk	Low risk	Low risk	Some concerns	Low risk	Some concerns
Cuperus 2016	Low risk	Low risk	Low risk	High risk	Low risk	High risk
DeThurah 2018	Some concerns	Low risk	Low risk	Low risk	Low risk	Some concerns
Ramelet 2017	Low risk	Some concerns	Low risk	High risk	Low risk	High risk
Song 2019	Some concerns	Some concerns	Low risk	High risk	Some concerns	High risk
Taylor-Gjevre 2018	Low risk	Some concerns	High risk	High risk	Low risk	High risk

Results: Of the 1,674 potentially eligible studies, 20 reports were included: eight observational trials (74%), six randomized clinical trials (21%), and two controlled clinical trials (6%) (Table 1). Studies included general rheumatology patients (n=9), rheumatoid arthritis (n=5), gout (n=2), osteoarthritis (n=2), unspecified inflammatory arthritis (n=1), and osteoporosis (n=1). Patient satisfaction with telemedicine was the most commonly reported outcome (n=12) with majority of studies demonstrating high levels of satisfaction. Disease activity was assessed in 6 studies with most demonstrating no significant difference between telemedicine and usual care groups. Seven studies included some component of cost analysis and found telemedicine to be generally cost-effective. Among interventional studies, the effect of telemedicine on the primary outcomes varied, with most finding that telemedicine was as good as usual or in-person care (in regards to disease activity, patient satisfaction, total societal costs, and other patient reported outcomes). One study demonstrated noninferiority of telemedicine relative to usual care (based on disease activity), and two studies demonstrated superiority of telemedicine over usual care (in regards to patient satisfaction and medication adherence). Effectiveness and feasibility were high across studies, though most demonstrated high risk of bias (Table 2 and Table 3). Meta-analysis was not feasible given heterogeneity of interventions and outcome instruments utilized.

Conclusion: Although the number of high quality studies to date is small, telemedicine may be an effective mode of care delivery for diagnosis and management of inflammatory, non-inflammatory, and autoimmune rheumatic disease. More randomized clinical studies are needed to determine the best uses of telemedicine for the diagnosis and management of rheumatic conditions.

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Abstract Number: 0631

Provider Assessment of Telehealth Utility During COVID-19

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SESSION INFORMATION
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Background/Purpose: The COVID-19 pandemic forced the provision of telehealth care to rheumatology patients with a broader range of diagnoses and disease activity than previously studied. In this study we seek to understand factors that associate with providers' perceptions of telehealth utility.

Methods: From 10/1/2020 – 1/31/2021, six providers at an academic medical center rated their telehealth visits according to perceived utility in making treatment decisions using the following Telehealth Utility Score (TUS) (1 = very low to 5 = very high). Ratings were entered immediately following each visit. 'Low telehealth utility' visits had a TUS between 1- 3 and 'high telehealth utility' visits had a TUS between 4-5. Providers also documented a provider global assessment of disease activity (0 = no activity to 10 = high activity). Data were obtained through the electronic data warehouse and manual chart review. Modified poisson regression models with robust error variance were used to assess the association between low versus high TUS and encounter diagnoses, current and prior patient-reported disease activity (RAPID3), provider global, and medication changes during the visit. Each analysis was performed unadjusted and adjusted according to age, race, insurance, and encounter mode (video/phone).

Results: A total of 481 telehealth encounters were included, of which 191 (39.7%) had a low telehealth utility score (Table 1). Patients with a diagnosis of inflammatory arthritis (IA) were more likely to have low telehealth utility compared to those with other diagnoses in unadjusted and adjusted models (aRR 0.806, 95% CI: 0.695-0.934, p=0.004). Furthermore, in patients with IA, the addition of a non-inflammatory musculoskeletal diagnosis made a telehealth encounter more likely to be of low utility in unadjusted and adjusted models (aRR 0.537, 95% CI: 0.344-0.838, p=0.006).

Higher patient and provider-reported measures of disease activity were significantly associated with low telehealth utility in unadjusted and adjusted models (Table 2), as follows: current RAPID3 (aRR 0.87, CI: p< 0.001), prior RAPID3 (aRR 0.89, p< 0.001), and provider global (aRR 0.83, 95% CI 0.79-0.87, p< 0.001).

An escalation in rheumatologic treatment was associated with low telehealth utility (aRR 0.7, p=0.015) and a de-escalation in rheumatologic treatment was associated with high telehealth utility (aRR 1.24, p=0.009), see Table 3.

Conclusion: Overall, telehealth was rated as a useful mode of care delivery for the majority of visits. A diagnosis of IA was associated with low telehealth utility, especially if a non-IA musculoskeletal diagnosis was also present, highlighting the need for in-person care for patients with active musculoskeletal symptoms. Intriguingly, higher disease activity by current and prior RAPID3 was associated with lower telehealth utility, suggesting that disease activity measures could help determine appropriateness for telehealth care. Finally, medication changes were associated with TUS, suggesting that providers feel comfortable decreasing medications during telehealth visits but prefer to escalate therapy in-person.

Table 1. Encounter Characteristics by Telehealth Utility Score (TUS)

Description	Low (N=191)	High (N=290)	Overall (N=481)
Age in years, Mean (SD)	56.5 (15.71)	56.0 (16.09)	56.2 (15.93)
Race, N (%)			
Black/African American	48 (25.1%)	64 (22.1%)	112 (23.3%)
Caucasian/White	128 (67.0%)	206 (71.0%)	334 (69.4%)
Other/Multiple	15 (7.9%)	15 (5.2%)	30 (6.2%)
Insurance, N (%)			
Commercial	84 (44.0%)	151 (52.1%)	235 (48.9%)
Medicare / Medicare Advantage	87 (45.5%)	112 (38.6%)	199 (41.4%)
Medicaid / Self-Pay / Other	20 (10.4%)	27 (9.3%)	47 (9.8%)
Encounter Modality, N (%)			
Phone	88 (46.1%)	98 (33.8%)	186 (38.7%)
Video	103 (53.9%)	192 (66.2%)	295 (61.3%)
Diagnosis Group, N (%) *			
Inflammatory Arthritis (IA)	103 (53.9%)	120 (41.4%)	223 (46.4%)
Non-inflammatory MSK	74 (38.7%)	67 (23.1%)	141 (29.3%)
Connective Tissue Disease	39 (20.4%)	69 (23.8%)	108 (22.5%)
Vasculitis	14 (7.3%)	21 (7.2%)	35 (7.3%)
Crystalline arthritis	12 (6.3%)	24 (8.3%)	36 (7.5%)
Other/Misc	5 (2.6%)	30 (10.3%)	35 (7.3%)
RAPID3 Value Present, N (%) **			
Current	105 (55.0%)	196 (67.6%)	301 (62.6%)
Prior	163 (85.3%)	264 (91.0%)	427 (88.8%)
Change from prior to current	94 (49.2%)	181 (62.4%)	275 (57.2%)
RAPID3 Scores, Mean (SD) **			
Current	4.3 (1.85)	2.6 (1.98)	3.2 (2.10)
Prior	4.5 (2.41)	3.1 (2.25)	3.6 (2.41)
Change from prior to current	0.1 (1.50)	-0.3 (1.71)	-0.1 (1.64)
Provider Global Score, Mean (SD)	4.0 (2.30)	1.6 (2.07)	2.6 (2.45)
Medication Actions During Visit			
De-escalation	14 (7.3%)	49 (16.9%)	63 (13.1%)
Escalation	41 (21.5%)	30 (10.3%)	71 (14.8%)
No Change	136 (71.2%)	211 (72.8%)	347 (72.1%)

Table Notes:

*Patients could have more than one diagnosis. IA=inflammatory arthritis, includes RA, juvenile arthritis, psoriatic arthritis, IBD-associated arthritis, ankylosing spondylitis, and reactive arthritis; Non-IA MSK=non-inflammatory arthritis musculoskeletal, includes OA, fibromyalgia, and regional MSK issues; CTD=connective tissue disease, includes SLE, MCTD, UCTD, Sjogren's syndrome, systemic sclerosis, inflammatory myopathy

**RAPID3: Current was within 7days of encounter, Prior was within 13 months, Delta was difference between current and prior RAPID3. The RAPID3 scale used was 0-10, where 0-1 = remission, 1.01-2 = low disease activity, 2.01-4 = moderate disease activity, and 4.01-10 = high disease activity

Table 2. Higher patient-reported disease activity, as measured with the RAPID3, is associated with lower utility of a telehealth visit. Model adjusted for age, race, insurance type, and encounter mode (video/phone).

Description	Unadjusted		Adjusted	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Per unit increase				
Current	0.87 (0.83,0.90)	<.001	0.87 (0.83,0.91)	<.001
Prior	0.88 (0.85,0.92)	<.001	0.89 (0.86,0.93)	<.001
Delta	0.96 (0.91,1.01)	0.104	0.94 (0.89,1.00)	0.067
Any	0.87 (0.84,0.90)	<.001	0.87 (0.84,0.91)	<.001

Table Notes
*We accounted for missing RAPID3 scores by centering all available RAPID3 scores about the mean and setting the derived value to 0 for all patients with missing scores. An indicator and interaction term were added, and the beta coefficient associated with the indicator was the relative risk given the presence vs absence of a RAPID3 score, while the interaction term was the change in risk per unit increase in RAPID3 among patients for whom the RAPID3 score is available.

Table 3. Treatment changes were associated with telehealth utility: providers rated telehealth visits in which they escalated treatment as having lower utility and visits in which they de-escalated therapy as having higher utility. Model adjusted for age, race, insurance type, and encounter mode (video/phone).

Description*	Unadjusted		Adjusted	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Escalation** vs no change	0.69 (0.52, 0.92)	0.012	0.70 (0.53, 0.93)	0.015
De-escalation*** vs no change	1.28 (1.09, 1.50)	0.002	1.24 (1.05, 1.45)	0.009

Table Notes
*Medications included prednisone, conventional DMARDs, biologic DMARDs, and targeted synthetic DMARDs
**Increase=medication started or dose increased
***Decrease=medication stopped, or dose decreased

Disclosure: C. Howe, None; **I. Smith**, None; **R. Overton**, Pfizer, 5; **R. Henao**, Pfizer, 5; **N. Economou-Zavlanos**, Pfizer, 5; **J. Doss**, Pfizer, 5; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **D. Leverenz**, Pfizer, 5.

Abstract Number: 0632

Impact of COVID-19 and Telehealth on RAPID3 Screening in an Academic Rheumatology Practice: Identifying Disparities in Care

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SESSION INFORMATION
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Background/Purpose: Measuring disease activity in patients with inflammatory arthritis is important for providing optimal treat-to-target care. The COVID-19 pandemic has widened disparities in care among racial minorities. The purpose of this study is to understand the impact of the COVID-19 pandemic and the resultant transition to telehealth on disease activity measurement to assess disparities in care.

Table 1. Patient Demographics, RAPID3 Documentation, and Mean RAPID3 Scores for Outpatient Rheumatology Encounters From July 1 to October 31 in 2019 and 2020

Description	2019 All Visits (N=4554)	2020 In Person (N=3548)	2020 Phone (N=688)	2020 Video (N=749)
Age Group, N (%)				
18 to 30	288 (6.3%)	199 (5.6%)	23 (3.3%)	65 (8.7%)
30 to 50	1293 (28.4%)	926 (26.1%)	148 (21.5%)	294 (39.2%)
≥50	2973 (65.3%)	2423 (68.3%)	517 (75.2%)	390 (52.1%)
Insurance, N (%)				
Commercial	2150 (47.2 %)	1696(47.8%)	238(34.6%)	438(58.5%)
Medicare / Medicare Advantage	2033 (44.6%)	1590(44.8%)	384(55.8%)	247(33%)
Medicaid / Self-Pay / Other	371(8.2%)	262(7.4%)	66 (9.6%)	64(8.5%)
Race, N (%)				
Black/African American	1267 (27.8 %)	929 (26.2%)	237 (34.5%)	179 (23.9%)
Caucasian/White	2935 (64.5%)	2337 (65.9%)	409 (59.5%)	499 (66.6%)
Other/Multi	309 (6.7%)	239 (6.7%)	34 (4.9%)	58 (7.7%)
Race Not Reported	43 (0.9%)	43 (1.2%)	8 (1.1%)	13 (1.7%)
RAPID3 Documentation by Race, N (%)*				
Overall	76.4%	74.8 %	23.8 %	83.3%
Black/African American	67.7%	70.5%	18.1%	75.4%
Caucasian/White	79.9%	76.4%	27.3%	88%
Other/Multi	77.7%	77.4%	26.5%	73.4%
Race Not Reported	79%	69.8%	0%	61.5%
RAPID3 Score by Race, Mean (SD)**				
Overall	3.7 (2.33)	3.7 (2.14)	3.6 (2.11)	3.4 (2.27)
Black/African American	4.2 (2.45)	4.3 (2.26)	4.3 (2.33)	3.9 (2.47)
Caucasian/White	3.5 (2.24)	3.5 (2.06)	3.3 (1.98)	3.2 (2.17)
Other/Multi	3.4 (2.41)	3.5 (2.10)	3.3 (2.14)	3.4 (2.15)
Race Not Reported	3.8 (2.75)	3.9 (2.13)	-	2.8 (3.50)

Table Notes:
*Percentages for RAPID3 availability by race reflect the percentage of each group with a RAPID3 documented within 7 days of the encounter.
**RAPID3 scores in this study range from 0 – 10, where 0-1 = remission, 1.01-2 = low disease activity, 2.01-4 = moderate disease activity, and 4-10 = high disease activity

Table 2. Relative Risk (RR) for Unadjusted and Adjusted Association with RAPID3 Documentation

Description	Unadjusted		Adjusted	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Year - 2020 vs 2019	0.91 (0.88, 0.93)	<0.001	0.69 (0.66, 0.73)	<0.001
2020 - Phone vs. In-Person	0.32 (0.28, 0.36)	<0.001	0.32 (0.28, 0.37)	<0.001
2020 – Video vs. In-Person	1.10 (1.06, 1.14)	<0.001	1.09 (1.05, 1.13)	<0.001
Black vs. White	0.85 (0.83, 0.88)	<0.001	0.87 (0.84, 0.89)	<0.001
Medicare vs. Comm	0.87 (0.85, 0.90)	<0.001	0.87 (0.84, 0.89)	<0.001
Age - 50+ vs. 18-<30	1.03 (0.98, 1.09)	0.238	1.07 (1.01, 1.13)	0.027
Male vs. Female	1.05 (1.02, 1.08)	<0.001	1.03 (1.00, 1.06)	0.032

Methods: This study assessed outpatient encounters at a single academic rheumatology practice between July 1st and October 31st in 2019 and 2020. Patients were included if they had a visit diagnosis of inflammatory arthritis (RA, JIA, PsA, AS, ReA, IBD-associated arthropathy) or SLE. All visits in 2019 were done in-person. Visits in 2020 were stratified by encounter type (in-person, phone telehealth, and video telehealth). Patient reported disease activity was

measured by RAPID3 (scale 0-10) either at clinic intake (in-person) or through the patient online EMR portal (phone, video, in-person). Descriptive statistics were used to evaluate the proportion of visits with a RAPID3 documented and average RAPID3 scores, stratified by race and visit modality. Modified Poisson regression was used to assess the association between RAPID3 documentation and year seen, age, race, insurance, and encounter type in unadjusted and adjusted models. We also calculated unadjusted year-over-year changes in RAPID3 documentation from 2019 to 2020 for each of these groups.

Results: There were 4554 visits during the study period in 2019 (all in-person) and 4985 in 2020 (3548 in-person, 699 phone, and 749 video; Table 1). In 2020, the proportion of visits completed by telehealth (phone or video) was similar among Black (31%) and white (28%) patients. However, telehealth encounters among Black patients were mostly by phone (60% of telehealth visits) whereas phone visits were the minority among white patients (45% of telehealth visits). In both 2019 and 2020 the RAPID3 was less likely to be completed by Black patients, though their RAPID3 score was higher, suggesting more rheumatic symptoms.

Encounters in 2020 were less likely to have a RAPID3 documented versus 2019 (adjusted risk ratio, aRR 0.69, $p< 0.001$, Table 2), driven by the absence of RAPID3 documentation among phone visits (phone vs. in-person: aRR 0.32, $p< 0.001$). The RAPID3 score is collected by electronic survey or during in-person check-in and our clinic did not have a systemic method to collect RAPID3 scores for phone visit patients. Over the entire study period, Black patients were significantly less likely to have a RAPID3 documented than White patients (aRR 0.87, $p< 0.001$, Table 2).

Conclusion: As telehealth use accelerated in 2020 in this academic clinic, the collection of patient-reported measure of disease activity remained stable for in-person and video visits, but decreased for patient visits completed by phone. The high use of phone visits among Black patient exacerbated the pre-existing disparity in RAPID3 collection between Black and White patients. These data necessitate a change in RAPID3 collection procedures to reduce systematic disparities in care for patients with inflammatory arthritis.

Disclosure: P. Apte, None; **R. Overton**, Pfizer, 5; **R. Henao**, Pfizer, 5; **N. Economou-Zavlanos**, Pfizer, 5; **J. Doss**, Pfizer, 5; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **D. Leverenz**, Pfizer, 5.

Abstract Number: 0633

Value of the Routine Assessment of Patient Index Data 3 (RAPID3) as a Disease Activity Measure in Patients with Psoriatic Arthritis

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Background/Purpose: The RAPID3 is a patient-reported pooled index of three measures: function, pain, and patient global estimate of status, that is used to classify disease severity[1]. It was developed in rheumatoid arthritis, but multiple studies have shown that it is useful in many rheumatic diseases, including Psoriatic Arthritis (PsA)[2,3]. We assessed the correlation of RAPID3 with other standard scores used in PsA in a private clinical practice setting.

Patients' demographic characteristics and disease activity measures

Patient Characteristics	N	mean	SD	Min	Max
Age	100	58.3	12.08	19.37	90.37
Disease duration (years)	91	9.85	7.97	0.21	39.9
Education (years)	100	13.64	1.89	10	17
CDAI	92	11.74	7.31	1	38
Rapid 3 (0-30)	97	10.91	6.9	0	25.99
cDAPSA	91	12.73	8.44	0	40
DAPSA	43	12.53	8.16	1.28	35.16

Methods: Adult patients with a diagnosis of PsA seen between February 2012 and November 2020 were retrospectively identified. We collected data including demographics, clinical measures and 4 disease activity measures: RAPID3,DAPSA, cDAPSA and CDAI from random routine care visits.

Spearman's correlations were calculated between RAPID3 and the other scores. Cross-test consistency of disease activity (remission, low, moderate, high) between different scores using kappa agreement analysis was calculated. Using ROC, we assessed the values of RAPID3 which best correlated with these levels of consistency. All calculations were performed using Stata Software v14 (Plano TX). IRB approval was obtained.

Results: The study included 100 patients with PsA. Patients' characteristics and scores are presented in table 1.

Spearman correlation analysis demonstrated a very strong correlation between RAPID3 and both DAPSA and cDAPSA (r=0.86) as well as a strong correlation between RAPID3 and CDAI (r=0.77).

There was strong agreement between RAPID3 remission score and DAPSA and cDAPSA remission scores, Kappa: 0.78 ($p < 0.0001$) and 0.71 ($p < 0.0001$) respectively.

The level of agreement dropped when we combined remission and low activity scores together, Kappa 0.56 ($p < 0.0001$) and 0.55 ($p < 0.0001$) respectively, although this remained in the moderate range.

Based on the ROC analysis, we redefined the RAPID3 score categories. A score of ≤3 was considered remission. >3 and ≤11 was considered low disease activity. >11 and ≤15 was considered moderate disease activity and >15 was considered high disease activity. Based on these categories, the level of agreement between RAPID3 and DAPSA and cDAPSA, when combining remission and low activity scores, significantly increased, Kappa 0.72 ($p< 0.0001$) and 0.71 ($p < 0.0001$) respectively.

Conclusion: This study supports the hypothesis that RAPID3 is as an effective disease activity measure in PsA. Our results show a strong to very strong correlation between RAPID3 and other standard scores such as DAPSA and cDAPSA used as a quantitative assessment of PsA disease activity at baseline and to measure treatment response. The advantage of RAPID3 compared to other disease activity measures is that it is a simple score that can be filled out entirely by the patients with minimal time or effort from the rheumatologist1,2,3.

We suggest that redefining the RAPID3 score categories to a score < 11 for low disease activity and >15 for high disease activity, will categorize disease activity more accurately.

Reference

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Abstract Number: 0634

Correlation Between the Functional Component of the Multidimensional Health Assessment Questionnaire (FN), Modified Health Assessment Questionnaire (MHAQ), Health Assessment Questionnaire II (HAQ-II) and a Single Functional Question (PF) in Patients with Rheumatic Disease

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Background/Purpose: There has been significant work developing questionnaires to find effective and reliable ways of characterizing the functional status of patients, to track disease progression and to measure response to treatment. However, these are often lengthy and difficult to perform, especially via telemedicine. We studied whether a VAS response (0-10) to a single question (Physical Function: "PF"): "We are interested in learning how your disease is affecting your ability to function in daily life" could replace the MDHAQ-FN (FN), MHAQ, HAQ-II to reliably predict the functional status of patients with rheumatic disease.

Methods: Pertinent data for adult patients with rheumatic disease collected as part of the routine practices from both a single private practice and an academic site was reviewed. Patients were asked to complete the MHAQ, FN, HAQ-II, and the single question. MHAQ is composed of 8 ADL items. FN is the functional component of the MDHAQ composed of the MHAQ plus 2 additional items. HAQ-II is composed of 10 ADL items. MHAQ, FN, and HAQ-II are scored by taking the mean item score, range 0-3. Spearman's correlations were used to compare scores from the MHAQ, FN, HAQ-II and the PF. All calculations were performed using Stata Software v14 (Plano TX). IRB approval was obtained.

Results: 1,298 patients (29% male, mean age = 60.87 years, mean disease duration 8.7 = years) were analyzed. Patient characteristics are presented in table 1. The FN, MHAQ and HAQ-II all had a very strong correlation to each other. The PF correlated strongly to scores of the FN, MHAQ and HAQ-II (Table 1.1). These correlations were generally maintained, regardless of the underlying diagnosis. Similar results were found at the UNMC.

Table 1. Pooled Data: Patient Characteristics

	Patient Characteristics		
Variable	N	Mean	Standard Deviation
Age	1298	60.87	15.20
Sex (% male)	1275	29.02	
Disease Duration (yrs)	1140	8.70	9.90
RA	214		
PsA	100		
AS	151		
OA	164		
FM	26		
SLE	27		
FN	1288	2.03	1.88
MHAQ	1269	0.41	0.50
HAQ-II	1127	0.81	0.71
PF	1298	7.50	6.05

Table 1.1. Spearman's correlation scores

Table 1.1	FN	MHAQ	HAQ-II
MHAQ	0.9189	1.0	
HAQ-II	0.9026	0.8036	1.0
PF	0.7346	0.6897	0.7217

Conclusion: This study demonstrates the utility of the PF: "We are interested in learning how your disease is affecting your ability to function in daily life" as a substitute for the FN, MHAQ and HAQ-II, questionnaires that have previously been validated as effective measures of functional status. The results were comparable, regardless of the underlying diagnosis. This single question is quick to administer and easy to score. In a time when telemedicine is becoming more prevalent, finding efficient and reliable ways of monitoring patients' wellbeing has become more important than ever. Incorporating this single question into general rheumatologic practice, in conjunction with other clinical tools, such as physical exam and lab values, can help streamline the collection of important data without sacrificing quality of care.

Disclosure: A. Healy, None; **J. Fares**, None; **M. Bergman**, AbbVie, 2, 6, Amgen Inc., 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, Bristol Myers Squibb, 2, Celgene, 2, Genentech, 2, Janssen, 2, Merck, 2, Johnson & Johnson, 11, Sandoz, 1, GSK, 6, Scipher, 2; **K. Michaud**, None; **A. Petro**, None; **H. Sayles**, None.

Abstract Number: 0635

Correlation Between Provider Documentation and Patient Experience with Contraceptive Counseling in an Academic Rheumatology Practice

Guiset Carvajal Bedoya[1], Tara Skorupa[2], Kristin Sturm[2], Ju Young Kwag[2], Kristen Demoruelle[3] and JoAnn Zell[3], [1]University of Colorado, aurora, CO, [2]University of Colorado, Denver, CO, [3]University of Colorado Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In a prior survey of providers and patients (Chakravarty 2014), it became apparent that clear gaps exist in provider-patient communication, affecting the delivery and success of contraceptive counseling for rheumatology patients. It is unclear how best to examine the prevalence of contraceptive counseling in clinical practice, but previous work has mainly relied on either medical chart review or patient survey to determine if counseling occurred. In this study we directly compare provider documentation of counseling with patient reported experience to assess if patient perspectives align with provider documentation. To our knowledge, this is the first study to investigate the prevalence of counseling in this manner.

Methods: Females of childbearing potential (ie, 18-50 years; no self-reported history of surgical sterilization, hysterectomy, menopause) with an established autoimmune condition were invited to complete on-line questionnaires. All patients were asked if they had ever received contraception counseling or been counseled about the potential pregnancy risks of their medications. In addition, a review of electronic medical records was performed for all patients

TABLE 1: PATIENT CHARACTERISTICS		N (%)
Rheumatologic diagnosis	RA	34 (31)
	SLE	36 (33)
	Other systemic autoimmune disease	39 (36)
Race/ethnicity	Non-Hispanic white	70 (64)
	African American	2 (2)
	Asian	4 (4)
	Hispanic	20 (18)
	Other	4 (4)
	More than one race	9 (8)
Medications currently taking (* = Teratogenic)	Steroids	22 (20)
	Methotrexate*	17 (1)
	Leflunomide*	1 (1)
	Cyclophosphamide*	0 (0)
	Mycophenolate*	14 (13)
	Any teratogenic medication	32 (29)
	Biologics	43 (39)
Medications currently or previously taking (* = Teratogenic)	Steroids	44 (40)
	Methotrexate*	21 (19)
	Leflunomide*	2 (2)
	Cyclophosphamide*	1 (1)
	Mycophenolate*	18 (17)
	Any teratogenic medication	40 (37)
	Biologics	44 (40)
Education	High school or less	9 (8)
	Some college	24 (22)
	College graduate	39 (36)
	Post-doctoral	37 (34)

TABLE 2: COMPARISONS OF PATIENT REPORTED COUNSELING WITH CHART DOCUMENTATION			
	Patient report of contraceptive counseling ever	Chart documentation of contraceptive counseling ever	Agreement*
All women	76/109 (70%)	59/109 (54%)	0.22
Women ever on a teratogenic medication	34/40 (85%)	28/40 (70%)	0.31
Women currently on a teratogenic medication	27/32 (84%)	22/32(69%)	0.41
Women with SLE	30/36 (83%)	21/36 (58%)	0.31
Women with RA	25/36 (69%)	21/36 (58%)	0.17
Women with other autoimmune disease	23/39 (59%)	19/3 (49%)	0.18
Women reporting no desire for pregnancy in the next year	56/84 (67%)	44/84 (52%)	0.27
*Agreement calculated based on Cohen's kappa statistic with 0.01-0.20=slight agreement, 0.21-0.40=fair agreement, 0.41-0.60=moderate agreement, 0.61-0.8=substantial agreement, 0.81-1=almost perfect agreement			

to identify provider documentation of contraceptive counseling. An anonymous on-line questionnaire was also given to clinical providers (8 rheumatology attending physicians, 6 rheumatology fellows and 2 rheumatology nurse practitioners) to assess their perception of how often they provide contraception counseling. Agreement between patient reported counseling and provider documentation of counseling was analyzed by Cohen's kappa (where k=1 is perfect agreement and k=0 is no agreement).

Results: We surveyed 109 women. The mean age was 34 years, 29% were currently or previously taking a teratogenic medication, 64% were non-Hispanic white and 92% had higher than a high school education. Overall, agreement was poor between women reporting having received contraception counseling and women with chart documentation of contraception counseling (Table 2, 70% vs. 54%, k=0.22). Agreement was slightly higher for women taking teratogenic medications (85% vs. 70%, k=0.41) and for women with lupus (83% vs. 58% k=0.31). Providers identified patient complexity as the major barrier to speaking to patients about family planning.

Conclusion: Women in an academic rheumatology practice were more likely to report having received counseling on contraception than was documented in their medical chart, suggesting that chart documentation of counseling may underestimate the true prevalence of this type of counseling that occurs in clinical care. More robust correlation was seen in patients with SLE or those currently on a teratogenic medication indicating that documentation may be more likely to occur for patients at risk for poor outcomes in the event of an unplanned pregnancy. These data showcase the need to improve the ease of documentation of contraception counseling in the medical record and continued commitment to the provision of discussions surrounding contraception with our patients.

Disclosure: G. Carvajal Bedoya, None; **T. Skorupa**, None; **K. Sturm**, None; **J. Kwag**, None; **K. Demoruelle**, Pfizer, 5; **J. Zell**, None.

Abstract Number: 0636

Contraceptive and Pre-conception Counseling in an Academic Rheumatology Practice: A Needs Assessment to Identify Gaps in Care

Tara Skorupa[1], Guiset Carvajal[2], Kristin Sturm[1], Ju Young Kwag[3], JoAnn Zell[1] and Kristen Demoruelle[1], [1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]University of Colorado, Colorado, CO, [3]University of Colorado, Denver, CO

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
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Background/Purpose: Systemic autoimmune conditions affect women of childbearing age, and teratogenic medications are commonly prescribed as treatment. In this study, we surveyed rheumatology patients to identify areas of focus that would be most effective to improve quality of care for female patients of childbearing potential.

Methods: We included 109 female patients who were seen in follow-up at an academic rheumatology practice, were 18-50 years old, had a diagnosis of any systemic autoimmune condition, were English-speaking and had no history of surgical sterilization or hysterectomy. An online survey was used to obtain patient perspectives on pregnancy, contraception, and their experiences with counseling about these topics. Definitions of teratogenic medications and highly effective, effective and less effective contraceptive methods are listed in Table 1.

Table 1. Patient characteristics		**N (%)**
Rheumatologic diagnosis	RA	34 (31)
	SLE	36 (33)
	Other systemic autoimmune disease	39 (36)
Age	<40 years	83 (76)
	≥40 years	26 (24)
Race/ethnicity	Non-Hispanic white	70 (64)
	African American	2 (2)
	Asian	4 (4)
	Hispanic	20 (18)
	Other	4 (4)
	More than one race	9 (8)
Medications currently or previously taking (* = Teratogenic)	Steroids	44 (40)
	Methotrexate*	21 (19)
	Leflunomide*	2 (2)
	Cyclophosphamide*	1 (1)
	Mycophenolate*	18 (17)
	Any teratogenic medication	40 (37)
	Biologics	44 (0)
Education	High school or less	9 (8)
	Some college	24 (22)
	College graduate	39 (36)
	Post-doctoral	37 (34)
Pregnancy history	Ever pregnant	56
	Never pregnant	53
Marital status	Married	47 (43)
	Living with someone/registered partnership	16 (15)
	Widowed/Divorced/separated	8 (7)
	Single	38 (35)
Current contraceptive method*	None	32 (29)
	Less effective	18 (9)
	Effective	18 (17)
	Highly effective	48 (44)

*Effectiveness of contraception defined as the following based on patient reporting of contraception used: 1) Highly effective=Intrauterine device, hormonal implant, male sterilization of partner, 2) Effective=oral contraceptive pills, vaginal ring or hormonal injection, 3) Less effective=Condoms or withdrawal method. Of note, 1 subject did not answer the type of contraception she was using.

Table 2. Factors influencing whether patients reported having ever received contraceptive counseling*			
Type of autoimmune disease	SLE (n=36)	Other (n=73)	p-value
	83%	63%	**0.03**
Teratogenic medication use	Ever	Never	
	85%	61%	**<0.01**
Self-reported race/ethnicity	Non-Hispanic white (n=86)	Other (n=22)	
	74%	50%	**0.04**
Marital status	Married (n=47)	Other (n=62)	
	72%	68%	0.61
Age	≥40 years (n=26)	<40 years (n=83)	
	50%	76%	**0.01**
Pregnancy history	Ever pregnant (n=56)	Never pregnant (n=53)	
	64%	75%	0.20
Education level	Completed college (n=76)	Did not complete college (n=33)	
	71%	67%	0.65
*All results represent the % of women in each category reporting that they had ever previously received counseling on contraception or the risks of their medications if they were to become pregnant			

Results: Patient characteristics are in Table 1. In all patients, 70% reported having ever been counseled about contraception or pregnancy risks of their medications by a rheumatologist. Reported rates of counseling were higher in women who took teratogenic medications ($p< 0.01$), had lupus ($p=0.03$), self-reported as non-Hispanic white ($p=0.04$) or were < 40 years old ($p=0.01$) (Table 2). Using multivariate logistic regression, ever use of teratogenic medications (OR=3.2, 95% CI 1.1-9.4, $p=0.03$) and non-Hispanic white race/ethnicity (OR=3.0, 95% CI 1.0-8.8, $p< 0.05$) remained significant predictors of ever counseling, after adjusting for age and lupus. In 31 women currently taking teratogenic medications, 84% reported ever counseling about contraception by a rheumatologist, but only 65% reported using effective or highly effective contraception. Those who reported ever counseling were more likely to be on effective/highly effective contraception compared to those who reported no counseling [24/26 (92%) vs. 2/5 (40%), $p=0.02$, respectively]. Regarding pre-conception counseling, among 56 women who had ever been pregnant, only 43% reported ever receiving pre-conception counseling by a rheumatologist or other health care provider.

Conclusion: In an academic rheumatology practice, women of childbearing potential reported moderately high rates of ever receiving counseling by a rheumatologist about contraception and/or pregnancy-related safety of their medications. However, we identified areas of focus that could improve counseling rates in our clinics, including a need to focus on improving counseling rates for non-white patients. The importance of contraception counseling is highlighted by our patients currently taking teratogenic medications, in whom we found an increased use of effective or highly effective contraception in women who had received counseling compared to women who had not. Our findings also highlight a need to improve pre-conception counseling rates in rheumatology patients, which were quite low at 43%. Further study is needed to determine what interventions will be most effective to ensure that all rheumatology patients with the potential for pregnancy receive appropriate counseling for either the prevention of unplanned pregnancy or planning for pregnancy, depending on each patient's preference.

Disclosure: T. Skorupa, None; **G. Carvajal**, None; **K. Sturm**, None; **J. Kwag**, None; **J. Zell**, None; **K. Demoruelle**, Pfizer, 5.

Abstract Number: 0637

Assessing the Rates of Cervical Cancer Screening in Women with Systemic Lupus Erythematosus and Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Prior studies have described increased incidence of cervical dysplasia and cervical cancer in women with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA), suggesting that these populations are at higher risk due to their disease state, their immunosuppressive medications, or both. The current US Preventive Services Task Force (USPSTF) guidelines recommend cervical cancer screening in women ages 21-65 years at intervals of 3-5 years based on age and HPV co-testing. Our aim was to assess the proportion of women with SLE and RA with documented cervical cancer screening per these guidelines.

Methods: This was a single-system retrospective chart review of women ages 21-65 years with SLE and RA. Included patients had a rheumatologist and primary care provider (PCP) within our university health system. For each patient, we documented the date and result of last Pap smear. We calculated each patient's age at last Pap smear, and for patients ages 21-29, we assessed for Pap smear within the last 3 years. For thoses ages 30-65, we assessed for Pap smear within 3 years or within 5 years with HPV cotesting. We excluded those with hysterectomy for non-cervical cancer reasons, and analyzed the proportion of remaining patients with abnormal cervical cancer screening results.

Results: Of the 371 patients included in the final analysis (Figure 1), 285 (76.8%) had age-appropriate cervical cancer screening documented in the medical record per USPSTF guidelines, compared to 81% of all women nationally. 50

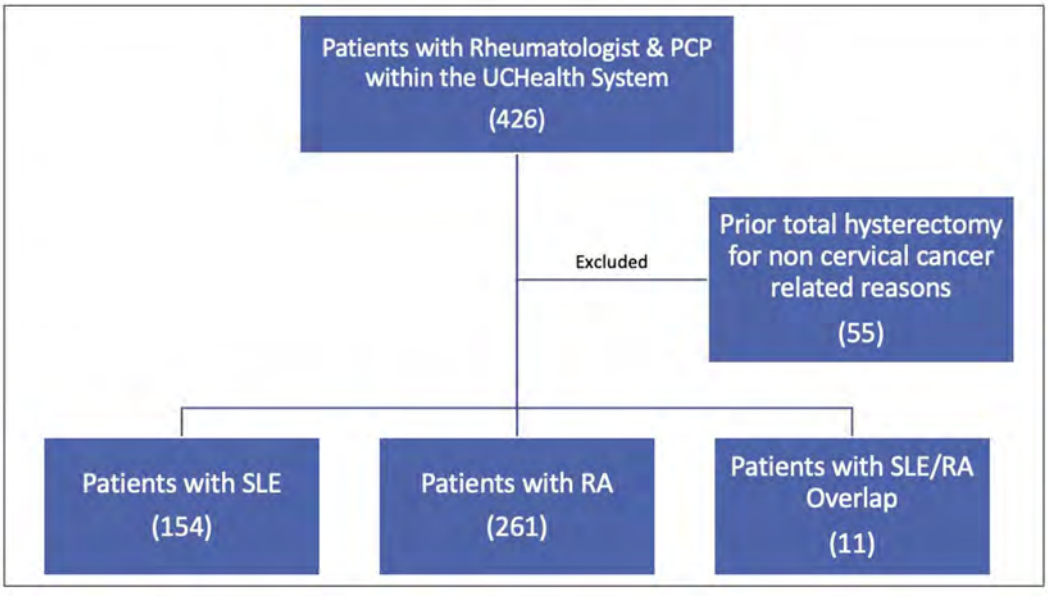

Figure 1. Patients included in the final analysis.

of the 371 patients (13%) had no prior cervical cancer screening data available in the chart. Of all 371 patients, last documented Pap smear was abnormal in 28 (7.5%). Of those patients, 18 had a positive HPV test. 3 rheumatology providers had ever documented the status of last Pap smear, and none documented counseling on cervical cancer screening.

Conclusion: Our results indicate that PCPs within our health system screen for cervical cancer in patients with SLE and RA at rates similar to the national average for all women. We acknowledge that our data may be underestimating the true number for our patients, as 13% had no prior documented Pap smear in the system. The current national average for cervical cancer screening is suboptimal, but it is even more unacceptable in patients with SLE and RA given their increased risk for cervical dysplasia. One barrier may be insufficient education about the association between these disease states and cervical cancer risk. We propose that there is an underutilized role for rheumatologists in educating patients and their PCPs about risk mitigation.

Disclosure: T. Skorupa, None; **S. Khatter**, None; **A. Freifeld**, None; **E. Weinstein**, None.

Abstract Number: 0638

Improving Safety in Rheumatology Patients by Closing Pre-screening Laboratory Care Gaps

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SESSION INFORMATION
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Background/Purpose: The Centers for Disease Control and Prevention and expert rheumatologists recommend screening for HBV and HCV prior to DMARD initiation and the ACR recommends screening for TB prior to biologic initiation. In our study, we aimed to improve patient safety by closing care gaps in the screening laboratories of our patients starting new DMARDs via collaboration with our pharmacists.

Methods: Hepatitis care gap closure for all patients starting a new DMARD was defined as meeting laboratory screening criteria for both HBV (HBsAg and HBcAb, at least IgM) and HCV (HCV Antibody or quantitative RNA). Additionally, TB screening (Purified Protein Derivative or QuantiFERON) was required to close the care gap in patients starting a new biologic. The study intervention consisted of Rheumatology pharmacist co-management protocols for all DMARDs and a pre-authorization smart-set with screening laboratory checks for new biologics. Data was extracted from our electronic health record (EHR) for patients with completed Rheumatology visits starting a new DMARD 1/1/2019 - 5/31/2020 at baseline and 6/1/2020 - 2/28/2021 post-intervention with pharmacist/physician collaborative screening. Screening was counted as present if there was documentation of completed tests in the chart any time prior to the DMARD initiation and up to one month after. For all new DMARD starts, the percent of HBV and HCV screened patients was calculated respectively. The hepatitis care gap closure for all new DMARDs was defined as meeting both HBV and HCV screening in this population. For all new biologic starts, the percent of HBV, HCV, and TB screened patients was calculated respectively. The care gap closure for new biologics was defined as meeting all three components. Two-sample t-tests were used to measure statistical significance of our screening laboratories.

Table 1. Hepatitis Screening and Care Gap Closures for All New DMARDs

	Month	% Hep B Completed	% Hep C Completed	% Hepatitis Care Gap Closure All New DMARDs
Pre-Intervention				
	6/1/2019	52/69 (75%)	51/69 (74%)	50/69 (72%)
	7/1/2019	61/75 (81%)	64/75 (85%)	61/75 (81%)
	8/1/2019	58/77 (75%)	62/77 (81%)	58/77 (75%)
	9/1/2019	51/65 78%)	52/65 (80%)	50/65 (77%)
	10/1/2019	54/71 (76%)	56/71 (79%)	53/71 (75%)
	11/1/2019	45/56 (80%)	48/56 (86%)	43/56 (77%)
	12/1/2019	44/55 (80%)	47/55 (85%)	43/55 (78%)
	1/1/2020	32/42 (76%)	32/42 (76%)	31/42 (74%)
	2/1/2020	77/93 (83%)	87/93 (94%)	77/93 (83%)
	3/1/2020	63/78 (81%)	66/78 (85%)	61/78 (78%)
	4/1/2020	74/106 (70%)	84/106 (79%)	72/106 (68%)
	5/1/2020	50/65 (77%)	50/65 (77%)	46/65 (71%)
Total %		661/852 (78%)	699/852 (82%)	645/852 (76%)
Post-Intervention				
	6/1/2020	58/74 (78%)	64/74 (86%)	55/74 (74%)
	7/1/2020	60/77 (78%)	66/77 (86%)	60/77 (78%)
	8/1/2020	50/66 (76%)	54/66 (82%)	48/66 (73%)
	9/1/2020	48/65 (74%)	53/65 (82%)	48/65 (74%)
	10/1/2020	64/75 (85%)	68/75 (91%)	64/75 (85%)
	11/1/2020	47/53 (89%)	46/53 (87%)	45/53 (85%)
	12/1/2020	45/54 (83%)	48/54 (89%)	44/54 (81%)
	1/1/2021	53/60 (88%)	54/60 (90%)	51/60 (85%)
	2/1/2021	37/42 (88%)	39/42 (93%)	37/42 (88%)
Total %		462/566 (82%)	515/566 (90%)	452/566 (80%)
p-Value		0.045	0.018	0.047

Results: New DMARD hepatitis screening and new biologic hepatitis/TB screening were examined in 852 and 562 patients at baseline and 566 and 390 patients respectively post-intervention. HBV and HCV screening for all DMARDs increased from 78% and 82% at baseline to 82% (p=0.045) and 90% (p=0.018) respectively post-intervention (Table 1). The care gap closure for total hepatitis screening in all patients starting new DMARDs increased from 76% to 80% (p=0.047) post-intervention (Table 1). For patients starting new biologics, TB screening increased from 88% to 93% (p=0.021) post-intervention while the average care gap closure for hepatitis and TB screening increased from 73% to 81% (p=0.049) post-intervention (Table 2). Figure 1 shows the improvement in care gap closure over time for all new DMARD and all new biologic starts respectively, from baseline through intervention.

Table 2. Hepatitis and Tuberculosis Screening and Care Gap Closures for All New Biologics

	Month	% Hep B Completed	% Hep C Completed	%TB Completed	% New Biologic Care Gap Closure
Pre-Intervention					
	6/1/2019	31/40 (78%)	31/40 (78%)	33/40 (83%)	27/40 (68%)
	7/1/2019	43/50 (86%)	46/50 (92%)	45/50 (90%)	40/50 (80%)
	8/1/2019	43/51 (84%)	45/51 (88%)	49/51 (96%)	42/51 (82%)
	9/1/2019	35/42 (83%)	36/42 (86%)	38/42 (90%)	30/42 (71%)
	10/1/2019	39/50 (78%)	40/50 (80%)	43/50 (86%)	34/50 (68%)
	11/1/2019	30/35 (86%)	29/35 (83%)	29/35 (83%)	26/35 (74%)
	12/1/2019	25/30 (83%)	25/30 (83%)	27/30 (90%)	24/30 (80%)
	1/1/2020	19/23 (83%)	19/23 (83%)	21/23 (91%)	18/23 (78%)
	2/1/2020	51/60 (85%)	55/60 (92%)	52/60 (87%)	48/60 (80%)
	3/1/2020	45/52 (87%)	45/52 (87%)	47/52 (90%)	41/52 (79%)
	4/1/2020	60/81 (74%)	68/81 (84%)	68/81 (84%)	53/81 (65%)
	5/1/2020	37/48 (77%)	37/48 (77%)	42/48 (88%)	30/48 (63%)
Total %		458/562 (81%)	476/562 (85%)	494/562 (88%)	413/562 (73%)
Post-Intervention					
	6/1/2020	37/45 (82%)	38/45 (84%)	39/45 (87%)	32/45 (71%)
	7/1/2020	44/54 (81%)	49/54 (91%)	48/54 (89%)	40/54 (74%)
	8/1/2020	34/44 (77%)	36/44 (82%)	40/44 (91%)	31/44 (70%)
	9/1/2020	32/40 (80%)	35/40 (88%)	35/40 (88%)	31/40 (78%)
	10/1/2020	49/52 (94%)	52/52 (100%)	50/52 (96%)	48/52 (92%)
	11/1/2020	37/40 (93%)	35/40 (88%)	38/40 (95%)	33/40 (83%)
	12/1/2020	30/35 (86%)	32/35 (91%)	33/35 (94%)	29/35 (83%)
	1/1/2021	46/52 (88%)	46/52 (88%)	51/52 (98%)	44/52 (85%)
	2/1/2021	29/30 (97%)	29/30 (97%)	29/30 (97%)	29/30 (97%)
Total %		338/390 (87%)	352/390 (90%)	363/390 (93%)	317/390 (81%)
p-Value		0.074	0.026	0.021	0.049

Conclusion: Avoiding harm to patients from the care that is intended to help them is essential. Using Rheumatology pharmacists to follow protocols driven by EHR tools, we have significantly improved our patient screening for hepatitis B, hepatitis C, and TB in DMARD-treated rheumatology patients. Today we are one step closer to fulfilling one of the aims of the framework set forth by the Institute of Medicine: Providing safer care for our rheumatic population.

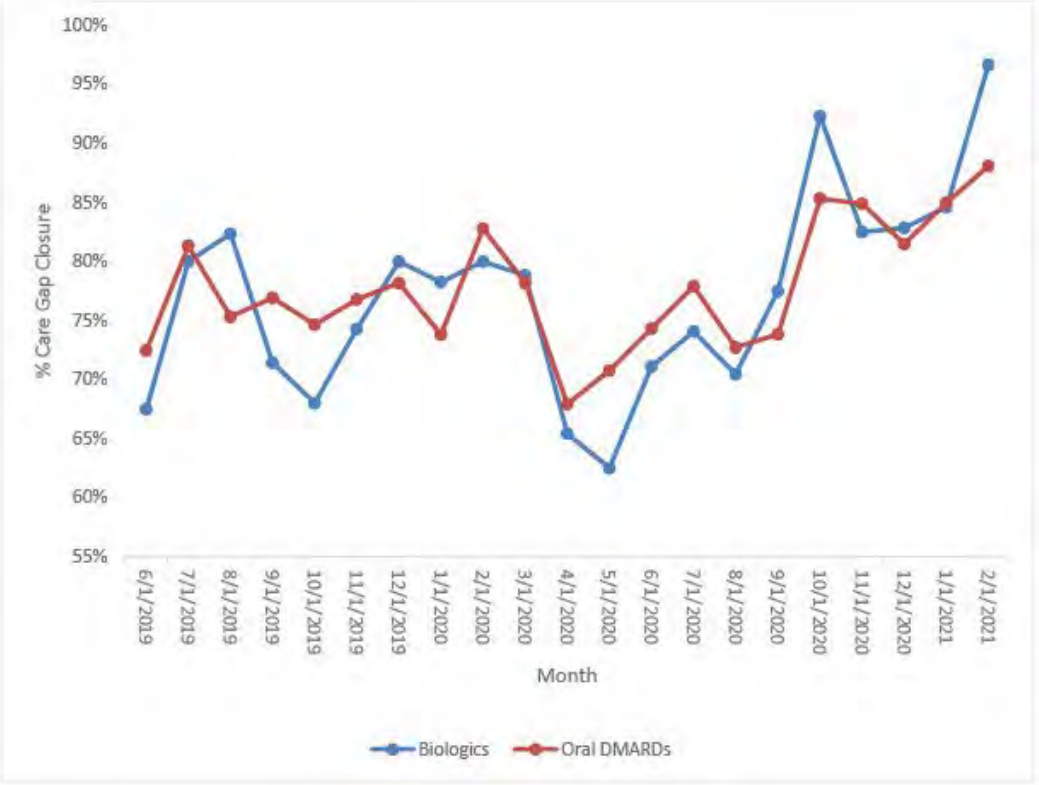

Figure 1. Care Gap Laboratory Improvement in All New DMARDs and Biologic Starts.

Disclosure: P. Nicholas, None; **J. Cote**, None; **D. Grassi**, None; **S. Thomas**, None; **J. Chronowski**, None; **D. Pugliese**, None; **E. Newman**, None.

Abstract Number: 0639

Improving Pre-biologic Infection Screening Using a Best Practice Alert in Electronic Health Records

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SESSION INFORMATION

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Background/Purpose: Biologics and small molecules (bDMARDs) are important immunomodulatory medications for management of patients with rheumatic diseases. Use of a bDMARD in patients with infection with pre-existing tuberculosis (TB), hepatitis B (HBV), or hepatitis C (HCV) can have serious consequences. Many national and international societies recommend timely screening for one or all of these exposures prior to initiation of certain bDMARDs, however, adherence to these recommendations varies widely. This quality improvement initiative focused on improving compliance with current standards using a best practice advisory (BPA) in the electronic health records (EHR).

Table 1. Comparison of screening rates of TB, HBV, and HCV captured pre-BPA and post-BPA. Displays captured screening rates of TB, HBV, and HCV before and after the initiation of the BPA

	Pre-BPA (N=758)		Post-BPA (N=63)		
	N	%	N	%	P-value
TB	516	68%	52	83%	0.00753
HBsAb	220	29%	18	29%	1.00000
HBcAB	248	33%	36	57%	0.00001
HBsAg	292	39%	27	43%	0.43639
HCV Ab	462	61%	52	83%	0.00026

Methods: Patients aged 18 years or older with at least two visits with a provider in the section of Rheumatology in the designated time frame were included. Upon a new prescription of a bDMARD, providers were alerted via a BPA pop-up in the EHR about the last available results if any, for TB, HBV, and HCV, and allowed for quick ordering as required. This BPA was implemented starting in December 2020. To assess the impact of the BPA, baseline rates of screening for TB (Quantiferon), HBV, and HCV for patients prescribed a new bDMARD from October 1, 2017 to November 30, 2020 (pre-BPA) were compared with those of patients with prescriptions from December 1, 2020 to April 9, 2021 (post-BPA). Data were collected for various bDMARDs targeting tumor necrosis factor (TNF), interleukin-17 (IL-17), interleukin-6 (IL-6), cytotoxic T-lymphocyte-associated protein 4 (CTLA-4), CD20, and Janus kinase (Jak).

Results: A total of 821 patients met the above inclusion criteria with 768 patients pre-BPA and 63 patients post-BPA implementation. The two patient populations were similar in gender, age, race/ethnicity, rheumatic disease diagnosis,

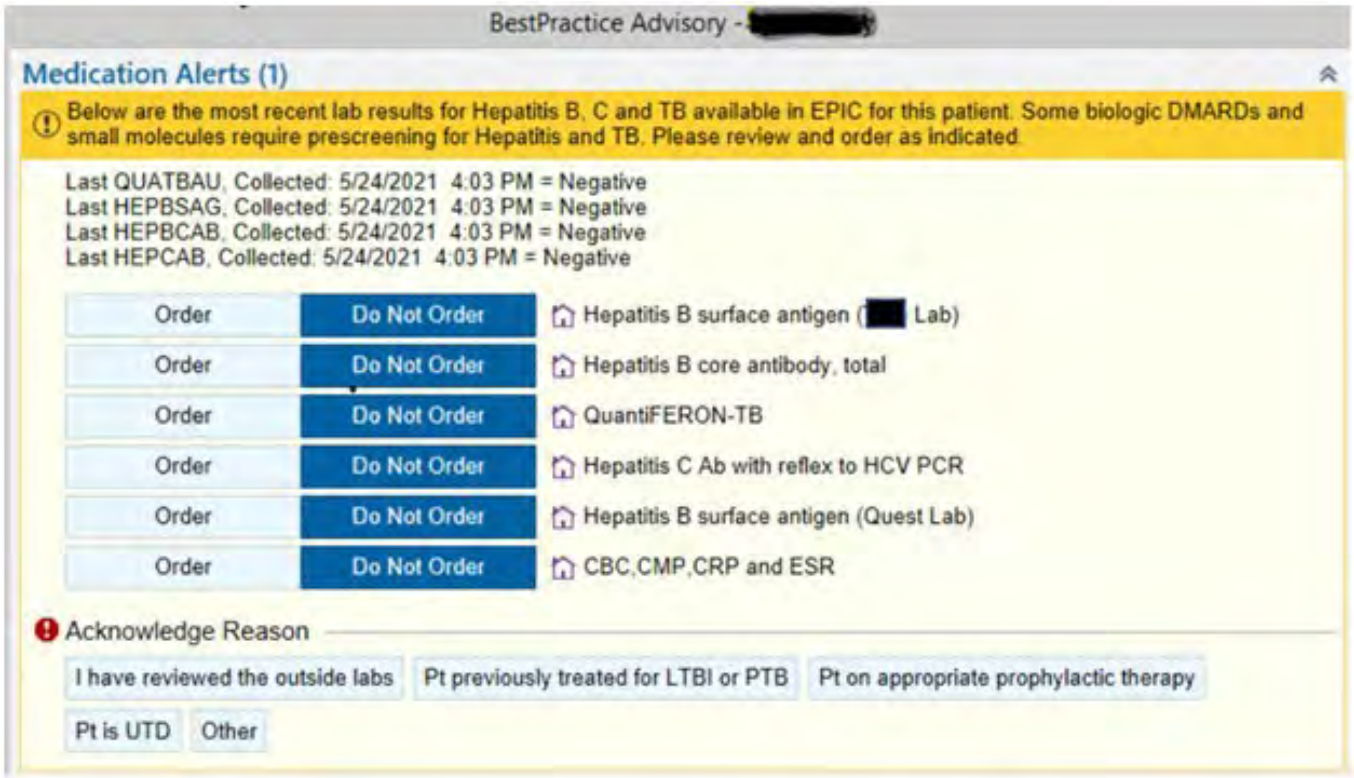

Figure 1. BPA notification. This is a visualization of the best practice advisory that appears on provider screens when ordering a biologic or bDMARD for a patient that does not have up-to-date infection screening within the defined time interval.

and a new bDMARD prescription. Median age of study population was 65 years, 70% were female, majority (77%) were white; most common rheumatic diseases were inflammatory arthritis (88%) and connective tissue disease (7%). TNFi (52%), IL-17 inhibitors (16%) and JAK inhibitors (15%) were most common bDMARDs prescribed. BPA implementation was associated with statistically significant improvement in screening for TB (pre-BPA 68% vs post-BPA 83% p=0.001), HCV (61% vs 83% p=0.0003) and hepatitis B core antibody (HBcAb) (33% vs 57% p=0.00001), numerical improvement in hepatitis B surface antigen (HBsAG) screening (39% vs 43% p=0.44) and no improvement in hepatitis B surface antibody (HBsAb) testing (29% each p=1.0) (Table 1).

Conclusion: Implementation of an electronic BPA in the EHR has the capacity to improve screening rates in patients who are started on a bDMARD. The BPA facilitates rapid review of screening tests and enhances provider experience and efficiency. Limitations include difficulty in capturing laboratory results performed outside the EHR.

Disclosure: H. Baker, None; **R. Fine**, None; **B. Hsiao**, None; **V. Chowdhary**, None; **L. Suter**, None; **A. Danve**, Abbvie, 1, Novartis, 5, 6.

Abstract Number: 0640

Implementation of Digital Prompt in Electronic Medical Records Improves Pneumonia Vaccination Rates in Patients Prescribed TNF-Inhibitors

Manjeet Bhamra[1] and Andras Perl[2], [1]SUNY Upstate Medical University, Syracuse, NY, [2]State University of New York, Syracuse, NY

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Tumor necrosis factor α inhibitors (TNFi) predispose to bacterial infections including pneumonia. In turn, vaccination with pneumococcal 13 valent (PCV13) and pneumococcal 23 valent (PPSV23) afford prevent pneumonia. We evaluated the prevalence of pneumonia and vaccination rates in patients prescribed TNFi. To improve vaccination rates of patients started on TNFi and prevent pneumonia in these patients, we implemented a digital prompt within the Electronic Medical Record (EMR).

Table 1. Pneumonia and vaccination rates in patients exposed TNF inhibitors Before and After Intervention via EMR prompt

	Pneumonia	No Pneumonia	Chi square	p-value
Before Intervention	256	3855	1.578	0.2006
After Intervention	37	433		

	Vaccination	No Vaccination	Chi square	p-value
Before Intervention	181	3930	110.3	<0.0001
After Intervention	76	394		

Methods: To improve vaccination rates of patients started on TNFi and prevent pneumonia in these patients, we implemented a digital prompt within the Electronic Medical Record (EMR). The digital prompt notifies providers of the vaccination status of PCV13 and PPSV23 for any patients for which a TNFi is prescribed at the time of the TNFi order entry. All adult patients from January 1, 2013-August 27, 2020 newly prescribed TNFi were put into a group labeled "Before Intervention." Adult patients prescribed TNFi from August 28, 2020-April 7, 2021 were put into a group labeled "After Intervention". Before and After Intervention corresponds to the start date of the digital prompt within our EMR. Diagnoses of pneumonia on ICD-10 codes, date of pneumonia diagnosis, pneumonia vaccinations, and date of initiation of the TNFi were collected for each group. A two-sided Chi Squared test was performed to find a relationship between vaccination and pneumonia occurrences in patients on TNFi in the before and after intervention groups.

Results: Data Collection shows 470 adults on TNFi from the After Intervention group and 4111 adults on TNFi in the Before Intervention Group. From the Before Intervention group, we assessed there is a 4.4% (181/4111) pneumonia vaccination rate and 6.2% (256/4111) prevalence of pneumonia in patients on TNFα-inhibitor (TNFi). In the After Intervention group, 16% (76/470) of patients on TNFi were vaccinated and there was a 7.9% (37/470) prevalence of pneumonia. There was a statistically significant increase in vaccination After Intervention group [p >0.0001] but there was no difference in pneumonia incidents [p=0.2006].

Conclusion: Our data shows that vaccinations of patients on TNFi improved after the implementation of the digital prompt. The rates of pneumonia did not improve. Our methods include pulling pneumonia based on the ICD-10 code. Notably, our data collection includes the COVID-19 pandemic. As such, there could be confounding factors, such as mask wearing, that might have reduced pneumonia incidence irrespective of receiving PCV13 and PPSV23 vaccines

Disclosure: M. Bhamra, None; **A. Perl**, None.

Abstract Number: 0641

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

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Smoking is a risk factor for rheumatologic conditions like lupus and rheumatoid arthritis and predicts worse outcomes. Smoking and rheumatic disease increase risk for cardiovascular disease, yet rheumatology clinics address smoking cessation in ≤10% of visits. An ACR quality measure reports cessation intervention rates. Tobacco Quit Lines (TQL) can increase cessation 4-fold via free coaching and nicotine replacement. Amid COVID, cigarette sales increased for the first time in years, yet 27% fewer sought TQL help.

Methods: *Quit Connect* (QC) supports rheumatology staff medical assistants or nurses via electronic health record (EHR) tools to *Ask* smokers about 30-day readiness to quit/cut back, *Advise* cessation support, and *Connect* ready

Table 1. Visit-level sociodemographics of population

	All visits
Current smoking	17.4%
Age (mean, SD)	51.27, 14.45
Sex (female)	80.3%
Black race	78.0%
White Non-Hispanic	4.6%
Unknown race	1.5%
Hispanic ethnicity	12.8%
Medicaid/Medicaid	52.7% [b]
Self-Pay	36.7%

[a]Demographic information is from 11/2019 to 1/2021; [b] Payor information is from 2016.

patients via EHR orders to receive cessation support via a TQL call or a cessation class. *QC* increased TQL referrals 26-fold in our prior study, and takes < 90 seconds. We implemented *QC* at a large public hospital rheumatology clinic in Atlanta, GA to test generalizability and increase TQL referrals.

Adults in the rheumatology clinic with current tobacco use were eligible. EHR tags captured process steps when a patient was *Asked* about smoking/quit readiness, *Advised* regarding cessation, and *Connected* via referral to TQL or cessation class. We compared performance pre-pandemic, during the COVID peak, and upon restart of the project. We assessed QC cost-effectiveness for clinics based on staff time and wages per our previous study.

Results: Across clinic visits, 80% were female, 78% Black race, 53% had public insurance, and 37% were uninsured. In 7 of 50 (14%) baseline audited visits, providers acknowledged current smoking, and only 3 visits (6%) included a quit line discussion. During *QC* implementation, across 2887 visits, 85% assessed tobacco use, and 17% identified current smoking (Table 1).

Compared to pre-intervention rates of 0%, after QC implementation, 21% of smokers were asked readiness to quit (Table 2). Questioning increased from 21% pre-pandemic to 35% during the restart phase. Of those asked, 70% were

Table 2. Completion of Quit Connect (QC) implementation process steps at distinct time points

	Baseline [a] Pre-QC	Pre-pandemic[b] n (%)	Pandemic[c] n (%)	Restart[d] n (%)	Total n (%)
In-person visits	2674	1370	702	815	2887
Smoking assessed at triage	(54)*	1192(87)	519 (74)	750 (92)	2461 (85)
Current smoking	535 (20)	206 (17)	93 (18)	130 (17)	429 (17)
Ready to quit asked	(0)*	43 (21)	3 (3)	46 (35)	92 (21)
Ready to quit *(% of current smokers)*	na	30 (70)	2 (67)	32 (70)	64 (70)
e-Referred to Quit Line *(% of ready to quit)*	(6)*	15 (50)	2 (100)	32 (100)	49 (77)
e-Referred to cessation class *(% of ready to quit)*	(0)*	16 (53)	0 (0)	2 (6)	18 (28)
e-Referred to Quit Line or class *(% of ready to quit)*	na	20 (67)	2 (100)	33 (100)	55 (86)

[a]Baseline: no EHR alerts or e-referral available; [b]Pre-pandemic: Nov 2019 through March 2020; [c]Pandemic: April 2020 through Nov 2020; [d]Restart: Dec 2020 through April 2021; [e]During the disruptions of Pandemic phase, intervention was suspended as was the cessation class. *Manually abstracted % from n=50 smokers prior to start of project.

Table 3. Results of offers to e-refer individuals ready to quit

Ready to quit n=64	n (%) Among ready to quit
Accepted e-referral to GA quit line or Grady cessation class	55 (86)
Accepted e-referral to class	18 (28)
Accepted e-referral to GA quit line[b]	49 (77)
Set quit date & accepted nicotine replacement therapy	5 (10)
Already registered/pending/other	16 (33)
Reached but declined services	11 (22)
Unreachable	17 (35)

[a]From Nov 2019 through April 2021. [b]Outcomes captured in EHR only for those e-referred to the GA Quit Line (Grady cessation class outcomes not available).

ready to quit. Among those ready to quit, 77% accepted referral to TQL and 86% accepted referral to TQL or class. Of those referred to TQL, 10% (n = 5) accepted nicotine replacement and set a quit date; 22% declined services, 35% were unreachable (Table 3).

Staff spent 920 seconds (15.3 minutes) to ask 92 patients readiness to quit and 4400 s (73.3 min) to offer referrals to 55 ready patients. With a total 88.6 min (1.47 hrs) multiplied by a staff rate of $15/hour, it cost $22.15 to refer 55 patients to tobacco cessation support ($0.40 each; $4.43 per quit attempt).

Conclusion: In a low resource rheumatology clinic serving predominantly Black patients with public insurance or uninsured, 70% of smokers were ready to cut back/quit when asked, and 86% of those individuals accepted referral to cessation support. Despite pandemic barriers, patients were connected directly to TQL and set a quit date and accepted nicotine replacement. Increasing the number of patients asked about readiness to quit may increase referrals. QC was feasible, cost-effective, and sustainable even during the COVID pandemic and could be considered for future dissemination to help rheumatology patients stop smoking.

Disclosure: J. Brandt, None; **E. Ramly**, None; **M. Messina**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 0642

Prevalence and Risk Factors for Cardio-metabolic Abnormalities in Patients with Inflammatory Arthritis Attending Cardio-rheumatology Primary Prevention Clinics

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

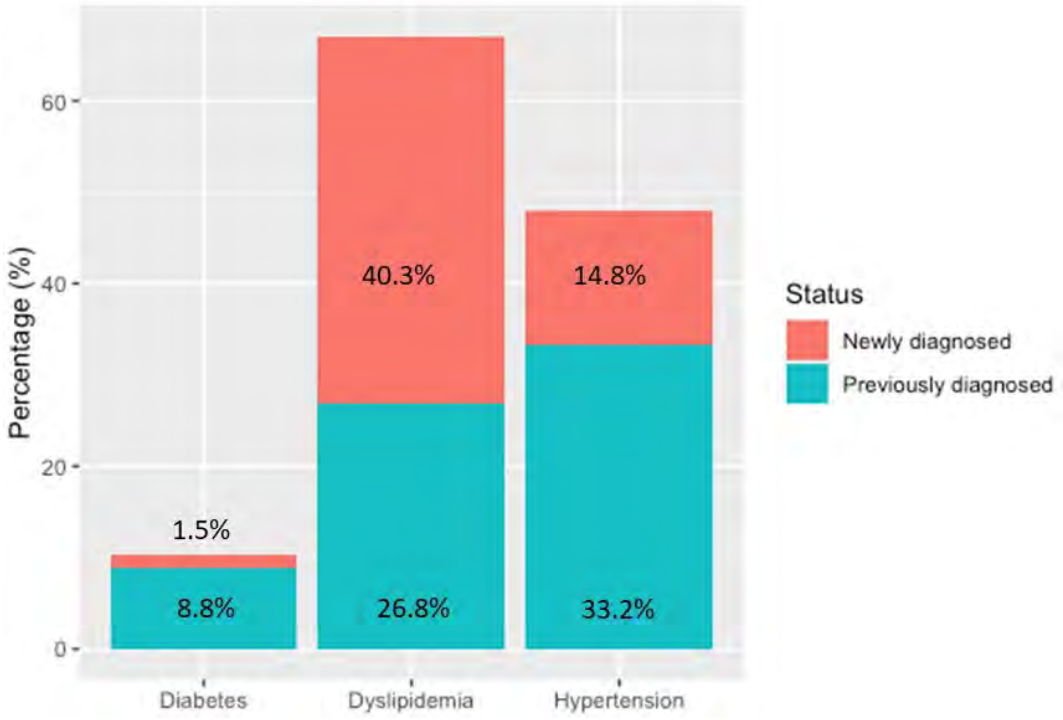

Figure 1. The prevalence of previously and newly diagnosed cardiovascular risk factors.

Background/Purpose: Cardio-metabolic abnormalities are common in patients with inflammatory arthritis (IA) but tend to be under-recognized and under-treated. We aimed to compare the prevalence and risk factors for cardio-metabolic abnormalities between patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS).

Methods: Consecutive patients enrolled in the University of Toronto Cardio-Rheumatology Network from 2017 to 2020 were analyzed. This is a primary prevention program that uses structured clinical, laboratory and multimodal imaging to diagnose and treat cardiovascular disease (CVD). Patients with a rheumatologist-confirmed diagnosis of RA, PsA or AS and no known CVD were evaluated. Information about IA diagnosis, medications and comorbidities was recorded. Each patient was evaluated by a cardiologist focusing on CVD risk assessment. We evaluated the prevalence of previously recorded and newly recognized cardio-metabolic risk factors including hypertension, dyslipidemia, obesity and diabetes. The prevalence of these abnormalities was compared between IA diagnoses. Regression models were used to assess the association between diagnosis and cardio-metabolic abnormalities after adjusting for demographics, smoking, BMI, measures of disease activity and medications.

Results: A total of 376 patients (219 RA, 124 PsA, 33 AS) were assessed (mean age 59±10.4 years, 69.7% female). Hypertension was reported in 33.2%, dyslipidemia in 26.8%, diabetes mellitus in 8.8% and overweight/obesity in 68.7%. Newly diagnosed dyslipidemia (elevated total cholesterol), elevated blood pressure and diabetes occurred in 40.3%, 14.8% and 1.5% of all patients (Figure 1). A total of 32% patients required a change or initiation of medications for their cardio-metabolic abnormalities (21.7% lipid-lowering therapy, 13.4% aspirin, 10.9% anti-hypertension therapy). Patients with PsA had the highest prevalence of cardio-metabolic abnormalities including dyslipidemia, obesity and hypertension (Figure 2). Having hypertension (prior or new diagnosis), elevated levels of triglycerides, non-HDL cholesterol, total cholesterol and BMI were associated with PsA vs. RA after adjusting for potential con-

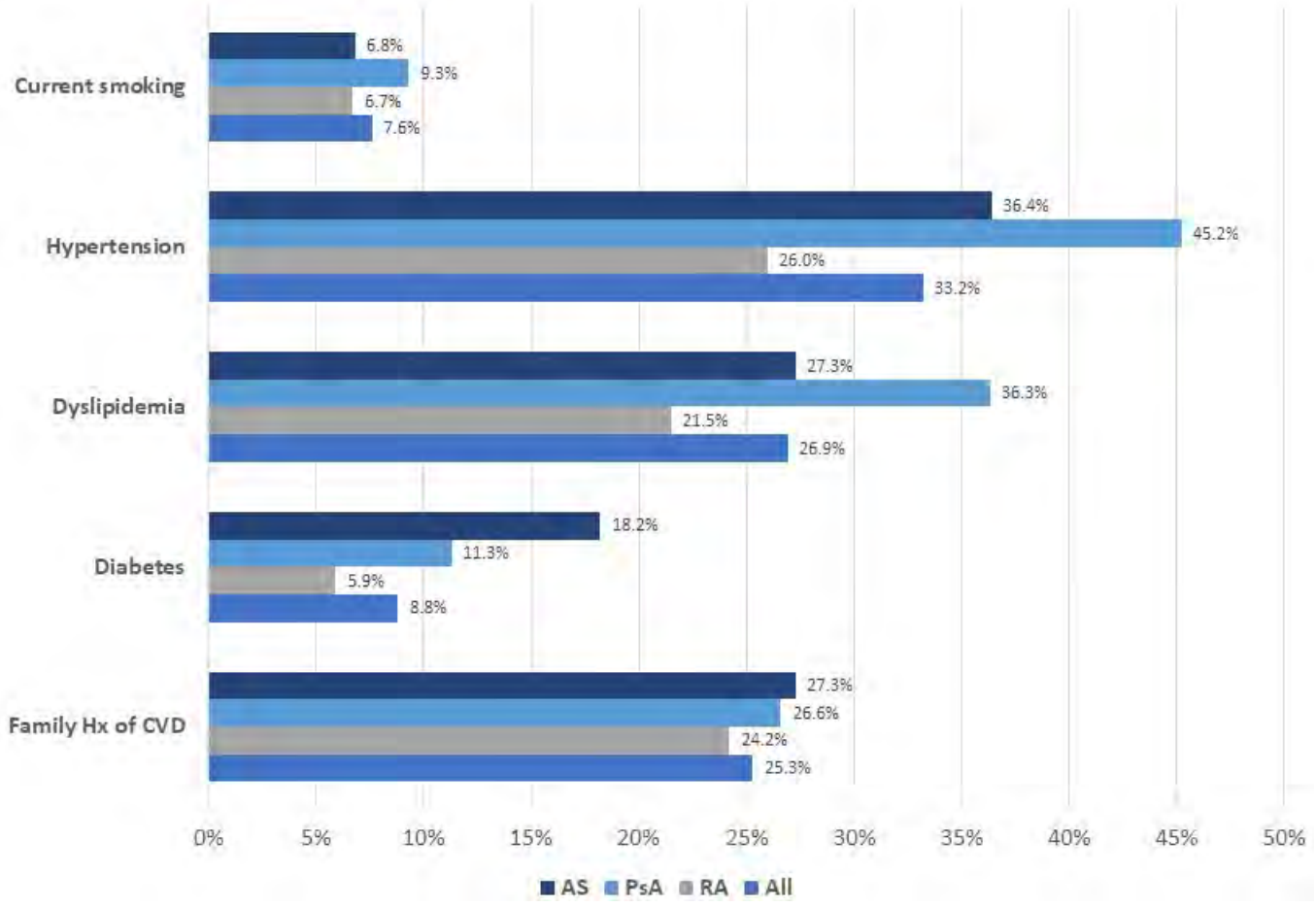

Figure 2. Prevalence of cardio-metabolic risk factors in patients with inflammatory arthritis by disease category.

founders (Figure 3). No significant association was found between cardio-metabolic abnormalities and AS vs. PsA or RA.

Conclusion: Dedicated cardio-rheumatology clinics have improved CVD screening and management in an IA population. The burden of cardio-metabolic abnormalities is elevated in PsA and suggests that tailored strategies to reduce adverse CVD events are particularly needed in this subgroup.

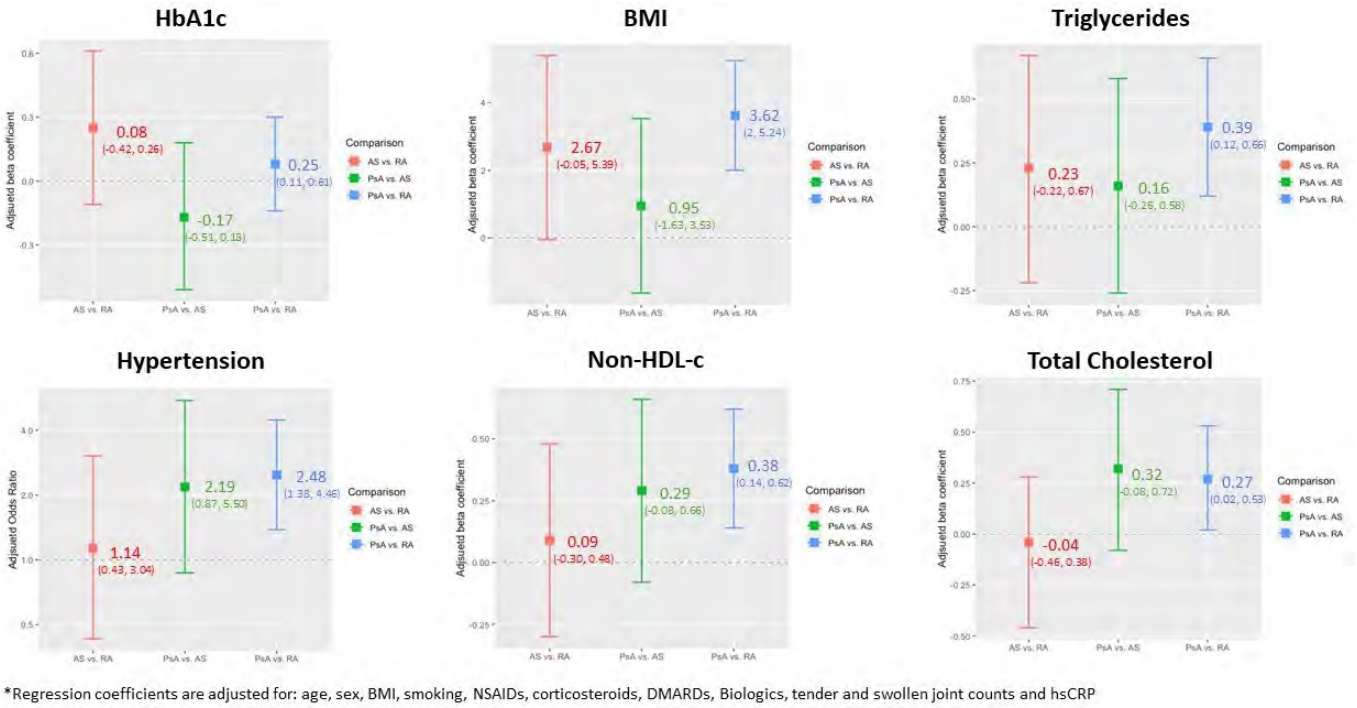

Figure 3. The Association between Disease Category and Cardiovascular Risk Factors by adjusted regression coefficients or Odds Ratio (95% Confidence interval)*.

Disclosure: L. Eder, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5; **S. Akhtari**, None; **D. Jerome**, Abbvie, 1, Novartis, 1, celltrion, 1, Gilead, 1, Lilly, 1; **J. Udell**, Boehringer-Ingelheim, 1, 5, Bayer, 5, Novartis, 1, 5, Sanofi, 1, 5, 6, Janssen, 5; **P. Lawler**, Novartis, 2; **P. Harvey**, None; **B. Kuriya**, None.

Abstract Number: 0643

Tailored BP Connect Protocol with Implementation Support for Rheumatology Clinic Staff Exceeds Non-tailored Protocol at Improving Primary Care Referrals for Blood Pressure Follow-up

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Many rheumatic diseases increase risk of cardiovascular disease, yet an important modifiable cardiovascular risk factor, high blood pressure (BP), often remains unaddressed during rheumatology visits. BP

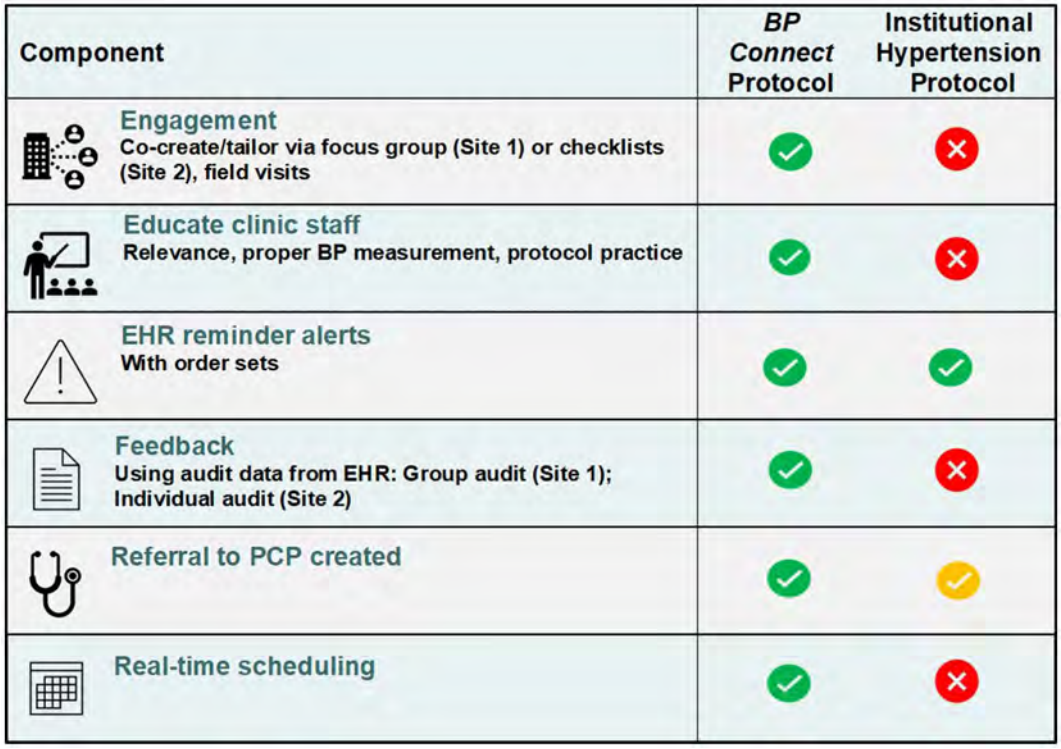

Figure 1. Comparison of protocol components for BP workflow implementation.

follow-up and control are also ACR quality measures. Some clinics have hypertension (HTN) protocols for clinic staff, however, various factors related to time constraints, technology limits, and specialty clinic staff buy-in, threaten uptake and sustainability. Our objective was to implement a tailored EHR-supported specialty clinic staff HTN protocol to empower clinic staff to confirm high BP and connect patients through follow-up orders or direct scheduling with primary care to address high BP.

Methods: We engaged 2 groups of medical assistants at urban (Site 1) and suburban (Site 2) academic rheumatology clinics to participate in the '*BP Connect*' protocol to compare effectiveness vs a prior institutional HTN protocol (Fig 1). Site 1 staff participated in a pre-intervention tailoring focus group and then monthly *group* audit-feedback on performance; Site 2 staff completed a pre-intervention tailoring checklist and monthly *individual* audit-feedback. EHR alerts instructed staff to re-measure BP if ≥ 140/90 and triggered education and offered scheduling of primary care follow-up if 2nd BP ≥ 140/90. Both groups received 1-hour education on HTN, cardiovascular risk in rheumatology, and hands-on BP measurement training and talking point practice. Using EHR data, we assessed how often staff re-measured high BPs, and if primary care follow-up was offered or accepted. The first 2 and last 2 months of the institutional process (protocol duration > 3 yrs) were compared to the 2 month *BP Connect* intervention period to report rate ratios (RR) and 95% CI's.

Results: We compared 269 *BP Connect* eligible intervention period visits with BPs ≥ 140/90 to 310-322 baseline visits at Site 1, and 27 intervention period visits to 15-37 baseline visits at Site 2 (Table 1). Baseline versus *BP Connect* period BP re-measurement rates at Site 1 ranged from 56-79% vs 74%. At Site 2, re-measurement rose from 20-81% baseline to 96% with *BP Connect*. After confirmed high BP, primary care referral offer rates rose at both sites. Site 1 increased from 22-37% to 68%, and at Site 2 offers increased from 50-67% to 100%. Across both sites, offered (RR 1.74 [1.41, 2.17]) and accepted primary care follow-up visits increased (RR 2.00 [1.21, 3.31]) in the *BP Connect* period even post-COVID.

Conclusion: A tailored rheumatology clinic staff intervention at sub/urban academic rheumatology clinics improved frequency of BP re-measurement, offers, and accepted primary care follow-up beyond an untailored HTN protocol.

Table 1. Process and outcomes of BP Connect vs institutional (inst.) HTN protocol

	BP Connect initial 2 mos. n (%)	Inst. HTN Protocol initial 2 mos. n (%)	Unadj. RR *BP Connect* vs Inst. HTN initial 2 mos. RR [95% CI]	Inst. HTN Protocol immed. 2 mos. before *BP Connect* n (%)	Unadj. RR for *BP Connect* vs 2 mos. before *BP Connect* RR [95% CI]
Site 1*					
1st High BP	269	310		322	
BP re-measured	198 (74)	246 (79)	0.93 [0.85, 1.02]	179 (56)	1.32 [1.17, 1.49]
High BP confirmed	146	157		135	
Referral Offered	99 (68)	35 (22)	3.04 [2.22, 4.16]	50 (37)	1.83 [1.43, 2.34]
Declined	58 (59)	33 (94)	0.62 [0.52, 0.75]	43 (86)	0.48 [0.37, 0.62]
Accepted	41 (41)	2 (6)	7.25 [1.85, 28.41]	7 (14)	2.96 [1.43, 6.11]
Site 2**					
1st High BP	27	15		37	
BP re-measured	26 (96)	3 (20)	4.81 [1.75, 13.28]	30 (81)	1.18 [0.10, 1.41]
High BP confirmed	15 (58)	2 (67)		18 (27)	
Referral Offered	15 (100)	1 (50)	1.99 [0.50, 7.95]	12 (67)	1.49 [1.07, 2.07]
Declined	4 (27)	0 (0)		5 (42)	0.64 [0.22, 1.87]
Accepted	11 (73)	1 (100)	0.81 [0.41, 1.57]	7 (68)	1.26 [0.71, 2.22]
Combined Sites 1 & 2					
Re-measured	**224 (76)**	**249 (76)**	**0.99 [0.90, 1.08]**	**209 (58)**	**1.30 [1.17, 1.45]**
Offered	**114 (71)**	**36 (22)**	**3.13 [2.31, 4.24]**	**62 (41)**	**1.74 [1.41, 2.17]**
Accepted	**52 (46)**	**3 (8)**	**5.47 [1.82, 16.47]**	**14 (23)**	**2.00 [1.21, 3.31]**

*Site 1 participated in a focus group for engagement and monthly group audit-feedback sessions. **Site 2 used an engagement checklist and monthly individual audit-feedback sessions.

It appears staff engagement with checklist tailoring was similar to a focus group (Site 2 vs. 1). Overall, *BP Connect*'s engagement, participatory education, and audit-feedback, components absent from the institutional protocol, appeared to improve performance. A trend suggests individual vs group audit-feedback may be more effective at improving performance which could inform future dissemination studies. *BP Connect's* tailored implementation improved rheumatology staff performance to connect primary care follow-up of high blood pressures.

Disclosure: D. Gazeley, None; **M. Messina**, None; **E. Ramly**, None; **A. Rosenthal**, None; **L. Lapp**, None; **L. Stewart**, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 0644

Follow-up Scheduling Appears Essential for Success of Rheumatology High Blood Pressure Protocol Across Health Systems

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Characteristics of eligible pre-post visits with high BP & outside HMO primary care (PC)

		Pre n=376	Post n=951 (n=400 confirmed high)	p
Age (mean (SD))		56.3 (12.5)	58.7 (12.4)	<0.01
Age category (%)	18-39	35 (9.3)	88 (9.3)	0.02
	40-59	175 (46.5)	361 (38.0)	
	60-79	153 (40.7)	473 (49.7)	
	≥80	13 (3.5)	29 (3.0)	
Sex (%)	Female	216 (57.4)	590 (62.0)	0.14
	Male	160 (42.6)	361 (38.0)	
Race (%)	Black	16 (4.3)	70 (7.4)	<0.01
	Other	35 (9.3)	49 (5.2)	
	White	325 (86.4)	832 (87.5)	
Language (%)	English	376 (100.0)	948 (99.7)	0.65
	Non-English	0 (0.0)	3 (0.3)	
Marital status (%)	Married/Partner	233 (62.1)	596 (62.7)	0.64
	Separated/Divorced,Widowed	58 (15.5)	129 (13.6)	
	Single	84 (22.4)	225 (23.7)	
Medicaid (%)	No	334 (88.8)	857 (90.1)	0.55
	Yes	42 (11.2)	94 (9.9)	
Tobaccouse (%)	Never	203 (54.3)	544 (57.3)	0.21
	Former	135 (36.1)	340 (35.8)	
	Current	36 (9.6)	65 (6.8)	
BMI (mean (SD))		32.61 (8.2)	31.95 (7.6)	0.16
BMI Category (%)	Underweight (<18.5)	4 (1.1)	6 (0.6)	0.80
	Normal weight (18.5-24.9)	57 (15.2)	157 (16.6)	
	Overweight (25-29.9)	114 (30.4)	287 (30.3)	
	Obesity (≥30)	200 (53.3)	498 (52.5)	

Background/Purpose: To address high blood pressure (BP), target of two ACR quality measures and *the* leading modifiable risk factor for cardiovascular disease, we previously developed *BP Connect*, a brief staff-driven protocol for rheumatology clinics. Across 28,000 visits, *BP Connect* cut rates of high BP visits in half and doubled timely in-system primary care (PC) follow-up [Adj. OR 2.0, (1.4-2.9)]. Yet many patients receive PC and rheumatology care in separate health systems. This study aimed to compare rates of timely outside system PC follow-up after high BP at rheumatology clinics before and after *BP Connect* implementation.

Methods: This post-hoc study examined pre-post rates of timely follow-up of high BP after *BP Connect* implementation among patients whose PC was in an outside Health Maintenance Organization (HMO). All adult patients with

Table 2. Odds of timely follow up (<1 mo.) compared across systems pre-post BP Connect

		Observed %	Unadjusted OR	(95% CI)
Outside PC	Pre Protocol-Any Timely Follow-up	38.0	Referent	
	Post Protocol-Any Timely Follow-up	43.8	1.27	(0.95, 1.69)
	Pre Protocol-PC Timely Follow-up	20.5	Referent	
	Post Protocol-PC Timely Follow-up	23.5	1.19	(0.85, 1.68)
In-System PC	Pre Protocol-PC Timely Follow-up	29*	Referent	
	Post Protocol-PC Timely Follow-up	42*	1.88*	(1.33, 2.66)

**Previously published rate of in-system primary care follow-up*

high rheumatology clinic BP and PC in that HMO were eligible. *BP Connect*'s EHR prompts ask rheumatology medical assistants, nurses, and schedulers to: Check, re-measuring high BP (>/=140/90), Advise CVD risk, and Connect patients to timely PC follow-up (< 1 mo per guidelines) using automated EHR orders in < 4 min. EHR follow-up orders prompt direct scheduling for patients with in-system PC, while outside HMO patients receive standardized recommendations printed on their after visit materials without direct scheduling. Staff steps were reinforced via monthly individual staff audit-feedback for the 6 mo. study period (late 2015-6), and then via email. For this study, we obtained outside EHR data on the next HMO PC visit with BP recorded after an eligible index rheumatology visit to evaluate rates and odds of timely follow-up pre-post using logistic regression. We compared results to our previously published rates and unadjusted OR for timely in-system follow-up.

Results: Across 1,327 rheumatology visits with high BP and outside HMO PC (2013-19), 951 occurred after 2015 *BP Connect* implementation and 400 had confirmed high BP. Differences in the post-implementation cohort included older age (58.7 vs 56.3) and more Black patient visits (7.4 vs 4.3%; Table 1).

After *BP Connect* implementation, among 400 visits with a confirmed high BP and outside HMO PC, any timely follow-up within 1 mo. increased modestly from 38 to 43.8%, and PC follow-up rose from 20.5 to 23.5% (Table 2). This contrasts with our prior published increase from 29 to 42% using a stricter 28-d. definition for in-system PC follow-up. Odds of timely BP follow-up among HMO PC patients changed insignificantly, [Any: OR 1.27, (CI 0.95, 1.69); PC: OR 1.19, (CI 0.85, 1.68)], vs. our prior published unadjusted OR of 1.88 (CI 1.33, 2.66) for timely in-system PC follow-up with direct scheduling.

Conclusion: Findings showed that in contrast to our prior published improvements for timely in-system PC follow-up with direct scheduling, *BP Connect* improvements were not significant for timely follow-up when PC was in an outside system. Printed patient instructions in after visit materials did not appear as effective as direct scheduling which patients with in-system PC received. Next steps include piloting a direct scheduling hotline with the outside HMO to improve timely BP follow-up and outcomes for rheumatology patients who receive PC in other systems.

Disclosure: C. Bartels, Pfizer, Independent Grants for Learning and Change, 5; **B. Hanlon**, None; **M. Messina**, None; **S. Ferguson**, None; **E. Ramly**, None.

Abstract Number: 0645

Time Burden of QTc Screening for HCQ Users at a Single VA Rheumatology Clinic

Iziegbe Ehiorobo[1], Anna Montgomery[2] and Gabriela Schmajuk[1], [1]University of California San Francisco, San Francisco, CA, [2]Department of Veterans Affairs, Tiburon, CA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is a commonly used medication in the treatment of rheumatic diseases. New guidance from the ACR supports routine monitoring of the QT interval among HCQ users, especially in patients at higher risk for QT prolongation, in order to avoid potentially fatal events related to Torsade de Pointes.

Table 1. Baseline characteristics of patients on San Francisco Veteran cohort on HCQ (N = 117)

	N (%) or Mean (SD)
Age, Mean [SD]	67 [13]
Male	96 (82.1)
Race	
White	79 (67.5)
Black	14 (11.9)
American Indian	4 (3.4)
Other /Unknown	3 (2.6)
Primary Rheumatic Diagnosis	
Rheumatoid Arthritis	73 (62.4)
Lupus	17 (14.5)
Other*	12 (10.3)
Calcium Pyrophosphate Deposition Disease	6 (5.3)
Inflammatory Arthritis	3 (2.6)
Sarcoidosis	3 (2.6)
Sjogren's	3 (2.6)
Comorbidities	
Cardiovascular disease	15 (12.8)
Alcohol liver disease	3 (2.6)
Hyperthyroidism	3 (2.6)
Receiving other QT-prolonging medications	24 (20.5)
ECG documented in the chart	
Yes - documented within 1 year	30 (25.6)
Yes – documented, but > 1 year	70 (59.8)
No	17 (14.5)
QTc (out of 100 pts with an ECG)	
Abnormal QTc on automated read	24 (24)
*Other included 1-2 pts with each of following diagnoses: Psoriatic arthritis, Osteoarthritis, Undifferentiated connective tissue disease, Lichen Planus, Skin Rash NOS, Joint pain NOS, Lichen sclerosis, Mixed Connective Tissue Disease, Antiphospholipid syndrome	

We assessed the time burden of implementing routine QTc monitoring for patients receiving HCQ in a single VA rheumatology clinic.

Methods: We identified patients receiving HCQ within the past year at our institution. Using chart review, we determined the date of the most recent ECG, the associated QTc interval, and whether it was abnormal (QTc > 450 ms for men and > 470 ms for women). We extracted information about other risk factors for QT prolongation, cardiac, renal, and endocrine comorbidities, and the use of other potential QT-prolonging medications. We implemented an algorithm (Figure 1) for when to order or repeat the ECG or place an e-Consult to cardiology. The total time taken to

Table 2. Average time spent executing the algorithm in Figure 1 to implement routine QTc monitoring for patients receiving HCQ in a single clinic

	N	Time in minutes executing algorithm in Figure 1 (Mean (SD))
No previously documented ECG	17	4.0 (1.0)
Recent ECG (≤1 year)		
With normal QTc	14	6.2 (2.4)
With abnormal QTc	16	11.0 (4.1)
Remote ECG (>1 year)		
With normal QTc	63	Pending
With abnormal QTc	7	4.7 (0.7)

perform each step for each patient was documented, including time for chart review; follow up of newly ordered ECG and consults ordered was not included.

Results: There were a total of 117 HCQ users at our institution, 96% were men, with mean (SD) age 67(13); most patients were using HCQ for the treatment of RA (see Table 1). 100 out of 117 (85.4%) had an ECG previously documented in the chart, with 30 out of 117 (25.6%) with an ECG performed within the last year. Out of 100 patients with an ECG, 24% had a prolonged QTc on the automated ECG read. Most patients with recent ECGs were using other

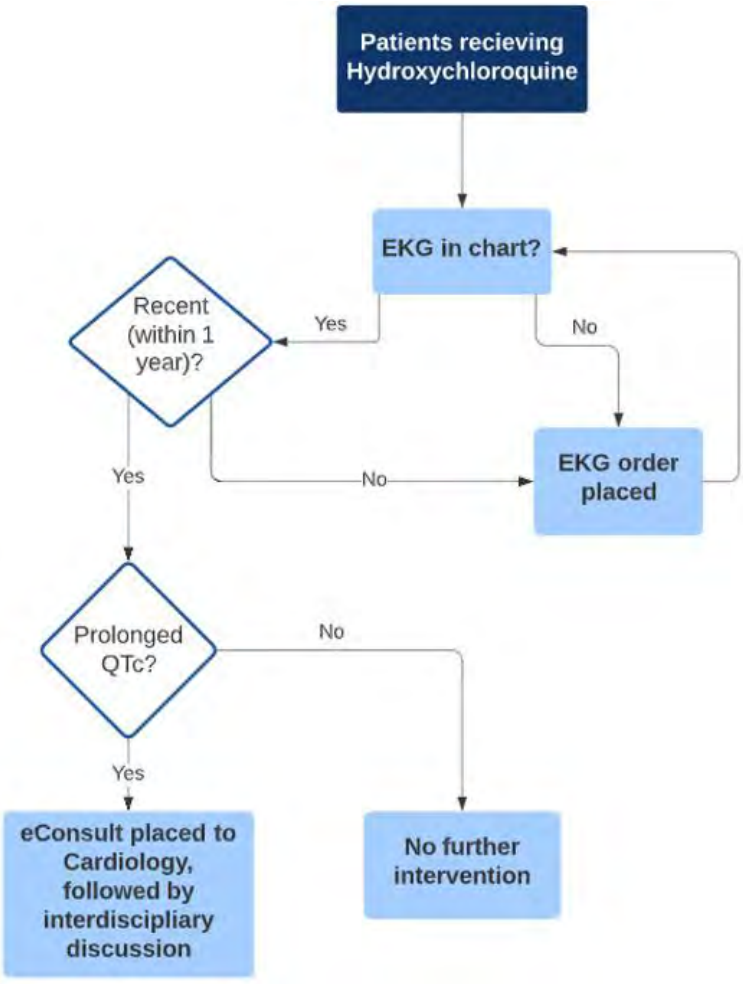

Figure 1. Flow chart depicting a process for implementing routine ECG monitoring patients receiving hydroxychloroquine.

QT-prolonging medications (63.3%); this proportion was higher in those with a prolonged QTc (70.5%). We executed the algorithm in Figure 1 for a subset of HCQ users, including those without any documented ECG (N=17); those with an ECG within the past year (N=30); and those with remote ECGs with a prolonged QTc (N=7), as these were the highest risk patients. We spent 4.1 (1.0) min for patients without any documented ECG; 9.3 (4.8) minutes for patients with a recent (< 1 year) ECG, and 4.7 (0.7) minutes for patients with remote ECGs that were abnormal (Table 2).

Conclusion: The time burden of implementing routine QTc monitoring for patients receiving HCQ in a single VA rheumatology clinic was about 6 minutes per HCQ user in this high-risk clinic population. Consultation with cardiology will result in confirmation of the automated ECG findings followed by a discussion of possible strategies to reduce the risk related to a prolonged QTc, including possible discontinuation of HCQ or other QT-prolonging medications. We plan to incorporate the additional time required to follow up updated ECG reports and recommendations from cardiology into these estimates as these data enter the chart. Future guideline development groups should compare the potential benefits of new recommendations to the time burden and other costs of implementation.

Disclosure: I. Ehiorobo, None; **A. Montgomery**, None; **G. Schmajuk**, None.

Abstract Number: 0646

Dark Adaptometry Screening for Hydroxychloroquine Retinopathy: A Pilot Study

Robert Yood[1], Elinor Mody[1], Bradley Daines[1], Kathryn Deliso[2], Eugenio Candal[1], Ahmed Ramram[1], Stephen Brimer[3], Alondra Msallem[2] and Larry Baitch[2], [1]Reliant Medical Group, Worcester, MA, [2]MCPHS University, Worcester, MA, [3]Saint Vincent Hospital, Worcester, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Background/Purpose: Hydroxychloroquine (HCQ) is widely used in the treatment of rheumatic diseases. The use of HCQ is complicated by HCQ-induced retinopathy, which may lead to irreversible visual loss. Current guidelines recommend annual screening for ocular damage with optical coherence tomography (OCT) and visual field (VF) testing beginning after 5 years of treatment with HCQ.

Dark Adaptometry (DA) tests the ability of the retina to recover its sensitivity after exposure to a bright, calibrated flash of light. This test shows high sensitivity and specificity as a biomarker for macular degeneration, a disease of the central retina. We hypothesized that DA might be more sensitive to retinal changes consequent to HCQ treatment than currently recommended tests and thus be useful as a novel screening test for HCQ retinopathy. We performed a pilot study to establish this test's diagnostic potential.

Methods: Patients aged 20-70 were eligible for participation if they had documentation of current treatment with HCQ and at least one prescription annually for the preceding 3 or more years. Exclusion criteria included diabetes mellitus, treatment with tamoxifen, active ocular disease and patients with high myopia. Patients were also excluded if they had not had an eye examination, including VF or OCT within the prior 18 months.

DA was performed using the Rapid Test protocol on all patients. In this protocol, patient subjects who did not reach a criterion level of sensitivity prior to 6.5 minutes were deemed to have failed the test.

Results: Thirty patients aged were recruited from a large multispecialty group practice and an academic optometry clinic. HCQ daily dosages at the time of the DA study ranged from 1.8 to 6.8 mg/kg with a median of 4.0 mg/kg. Cumulative dosages ranged from 420g to 4700g. with a median of 930g. The median number of years since HCQ was first prescribed was 9. No subjects had symptoms of HCQ retinopathy or positive indications of retinopathy in OCT imaging or VF testing.

Fifty-four eyes were successfully tested in 26 of the 30 study subjects. Of the eyes tested, 36 (67%) passed and 18 (33%) failed the DA test. Of the subjects tested, 40% showed at least one abnormal DA time. Of those eyes passing the test, 5 eyes (9% of the cohort) showed a "late normal" DA time between 6.0 and 6.4 minutes. There was no significant correlation with DA time for daily dosage, cumulative dosage, patient age or duration of HCQ treatment.

Conclusion: The high number of subjects with abnormal DA times was quite unexpected, given the absence of visual symptomology or objective abnormalities on OCT and VF testing. These results suggest that DA may provide a more sensitive biomarker for ocular changes due to HCQ than conventional OCT and VF testing. However, we do not know how specific this test is for retinopathy, i.e., whether those abnormal delays will precede changes on ocular coherence tomography, visual fields, or the onset of visual disturbances in patients with continued exposure to HCQ. This pilot study therefore warrants a larger cohort, longitudinal study to establish the specificity of dark adaptometry prior to its acceptance as a screening test to improve the safety of treatment with HCQ.

Disclosure: R. Yood, None; **E. Mody**, None; **B. Daines**, None; **K. Deliso**, None; **E. Candal**, None; **A. Ramram**, None; **S. Brimer**, None; **A. Msallem**, None; **L. Baitch**, Maculogix Inc, 6.

Abstract Number: 0647

Adherence to Hydroxychloroquine Dosing and Teleretinal Screening: Assessment and Quality Improvement

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SESSION INFORMATION
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Background/Purpose: Hydroxychloroquine (HCQ) is used in many rheumatologic diseases. The American Academy of Ophthalmology (AAO) put forth guidelines in 2012 regarding retinal screening and dosing of HCQ. These include a retinal exam in the first year after initiation of HCQ and a maximum dose of 5mg/kg/day of actual body weight. The Los Angeles County + University of Southern California Medical Center (LAC+USC MC) serves a largely underinsured urban population. LAC+USC MC utilizes an online third-party system for ophthalmology referrals. Our aim is to evaluate the LAC+USC MC rheumatology clinic's effectiveness at pursuing ophthalmologic care for HCQ patients and adhering to the appropriate dosing recommendations put forward by the AAO. Using this data, we plan to evaluate the effectiveness of a HCQ dosing calculator in increasing adherence to appropriate dosing recommendations.

Methods: First, a retrospective chart review was performed of rheumatology clinic patients prescribed HCQ in the LAC+USC MC rheumatology clinic. Charts of patients with clinic visits between March 2018 and May 2018 were reviewed. Patients were included if they had a clear first-time HCQ initiation date. Following the retrospective chart

Table 1. Sample patient characteristics	
Characteristic	**N (%)**
Age, *yrs* [a]	45.7 ± 14.2 (18 – 88)
Sex	
Female	121 (87.7%)
Male	17 (12.3%)
Ethnicity	
African American	9 (6.5%)
Asian	6 (4.4%)
Non-Hispanic Caucasian	3 (2.2%)
Hispanic	120 (87.0%)
Weight, *kg* [a]	68.2 ± 13.7 (36 – 109)
Diagnosis	
Systemic lupus erythematosus	42 (30.4%)
Rheumatoid arthritis	55 (39.9%)
Other	41 (29.7%)
AAO guideline adherence	
Prescribed HCQ dose over 10% of weight-based recommendations	39 (28.3%)
Appropriately screened/referred in first year	30 (21.7%)
System at fault [b]	
Physician	96 (89.8%)
System	3 (2.8%)
Patient	8 (7.4%)

[a] Mean ± SD; range
[b] Reported for n=108 patients who were not appropriately screened/referred.

review, a HCQ dosing calculator was implemented into the EMR in March 2020 that is prompted to appear whenever a patient is prescribed HCQ for the first time. Charts of patients prescribed HCQ between March 2020 and September 2020 were reviewed. Patients were included if they had a clear first-time HCQ initiation date after March 2020, a documented weight, and a clear HCQ daily dose. Prescribed dose and recommended weight-based dose of HCQ were noted.

Table 2. Patient characteristics by ophthalmologic screening status			
Variable	**Not screened (n=108)**	**Screened (n= 30)**	**p-value [b]**
Age, *yrs* [a]	46.6 ± 14.4	42.7 ± 13.4	0.19
Sex			
Female	93 (86.1%)	28 (93.3%)	0.36
Male	15 (13.9%)	2 (6.7%)	
Ethnicity			
African American	6 (5.6%)	3 (10.0%)	0.42
Asian	4 (3.7%)	2 (6.7%)	
Non-Hispanic Caucasian	2 (1.9%)	1 (3.3%)	
Hispanic	96 (88.9%)	24 (80.0%)	
Weight, *kg* [a]	68.6 ± 13.4	67.0 ± 14.7	0.57
Diagnosis			
Systemic lupus erythematosus	32 (29.6%)	10 (33.3%)	0.07
Rheumatoid arthritis	48 (44.4%)	7 (23.3%)	
Other	28 (25.9%)	13 (43.3%)	

[a] Mean ± SD reported; p-value by independent t-test.
[b] By Fisher's exact test

Results: One hundred and thirty-eight patients qualified for analysis in the initial retrospective chart review. Of the 138 patients, 30 (21.7%) received ophthalmologic assessment within the first year of HCQ use. Of the remaining patients who were not screened, 97 patients (89.8%) lacked a timely referral to ophthalmology. Thirty-nine (28.3%) patients were prescribed a HCQ dose higher than the AAO guidelines; the average amount in excess of the recommended dose was 24.3% (range 1-122%). Following implementation of the HCQ dosing calculator, forty-four patients qualified for analysis. Of these included patients, zero patients were prescribed a HCQ dose higher than the AAO guidelines.

Conclusion: Our findings demonstrate that providers are not meeting the guidelines for ophthalmologic screening when prescribing HCQ. Additionally, a large proportion of our patients are prescribed more than the recommended HCQ dose. We implemented a HCQ dosing calculator in order to address difficulty with individualized dosing as well as a lack of knowledge about the guidelines. The calculator was very successful in lowering the proportion of patients prescribed more than the recommended HCQ dose, with zero patients being inappropriately dosed after calculator implementation. We believe this promising method warrants further study and should be considered in other institutions. In the future we plan to address HCQ retinal screening deficiencies by educating providers on AAO guidelines and working with third party referral systems to ensure ease of referrals.

Disclosure: B. Cerk, None; **B. Toy**, None; **B. Situ**, None; **S. Savvas**, None; **L. Wise**, None.

Abstract Number: 0648

Improving Post-Rituximab Hypogammaglobulinemia Risk Assessments: A Fellows' Quality Improvement Initiative

Beth Rutstein[1], Melissa Argraves[2], Atiye Bilgic Dagci[2], Sarah Bayefsky[2], Julia Rood[2], Julie Chase[3], Jay Mehta[2], Melissa Lerman[2], Cory Stingl[4] and Jon Burnham[2], [1]Children's Hospital of Philadelphia, Wynnewood, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]The Children's Hospital of Philadelphia, Philadelphia, PA, [4]Children's Hospital of Philadelphia, Durham, NC

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Hypogammaglobulinemia following rituximab therapy is a potentially severe complication that can lead to infection-related morbidity and mortality. If recognized, clinicians may prevent infections by prescribing intravenous or subcutaneous immune globulin. Our goal was to improve hypogammaglobulinemia monitoring and documentation in pediatric rheumatology patients treated with rituximab therapy.

Methods: In September 2020, we identified patients prescribed rituximab within the previous 24 months and had a Rheumatology visit within the previous 6 months. We identified inconsistent IgG monitoring amongst providers and non-standardized documentation of hypogammaglobulinemia when identified. We then developed an IgG monitoring process based on adult guidelines and pediatric literature (Figure 1).

Our process measure, hypogammaglobulinemia risk assessment, was defined as 1) IgG testing based on algorithm recommendations, and 2) hypogammaglobulinemia documentation in the electronic health record problem list if IgG was low per scale. We aimed to increase the number of clinic visits fulfilling hypogammaglobulinemia risk monitoring between missed opportunities (goal > 6) by June 30, 2021. The outcome measure was the proportion of eligible patients with up-to-date hypogammaglobulinemia risk assessment (goal > 80%).

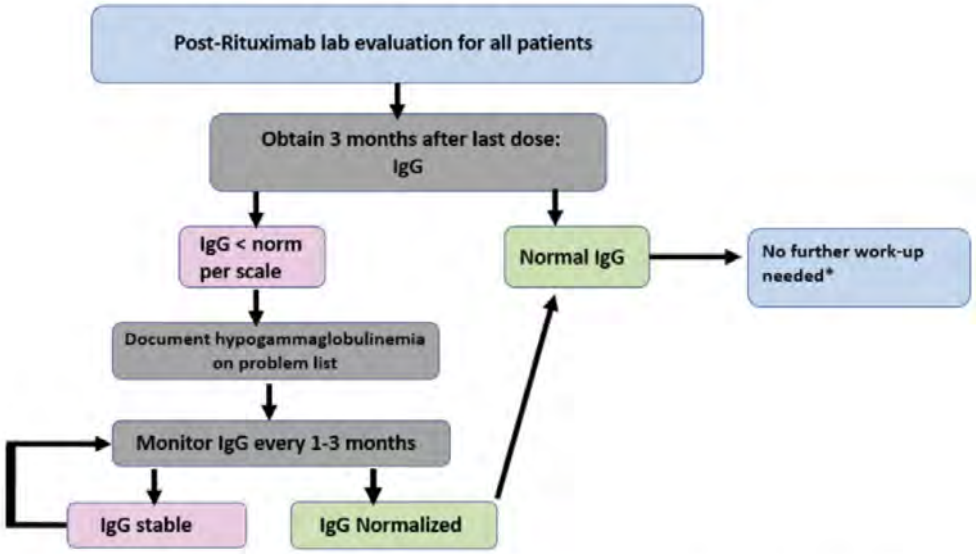

Figure 1. Standardized Post-Rituximab Hypogammaglobulinemia Monitoring Algorithm.
*Algorithm should be repeated with each Rituximab cycle

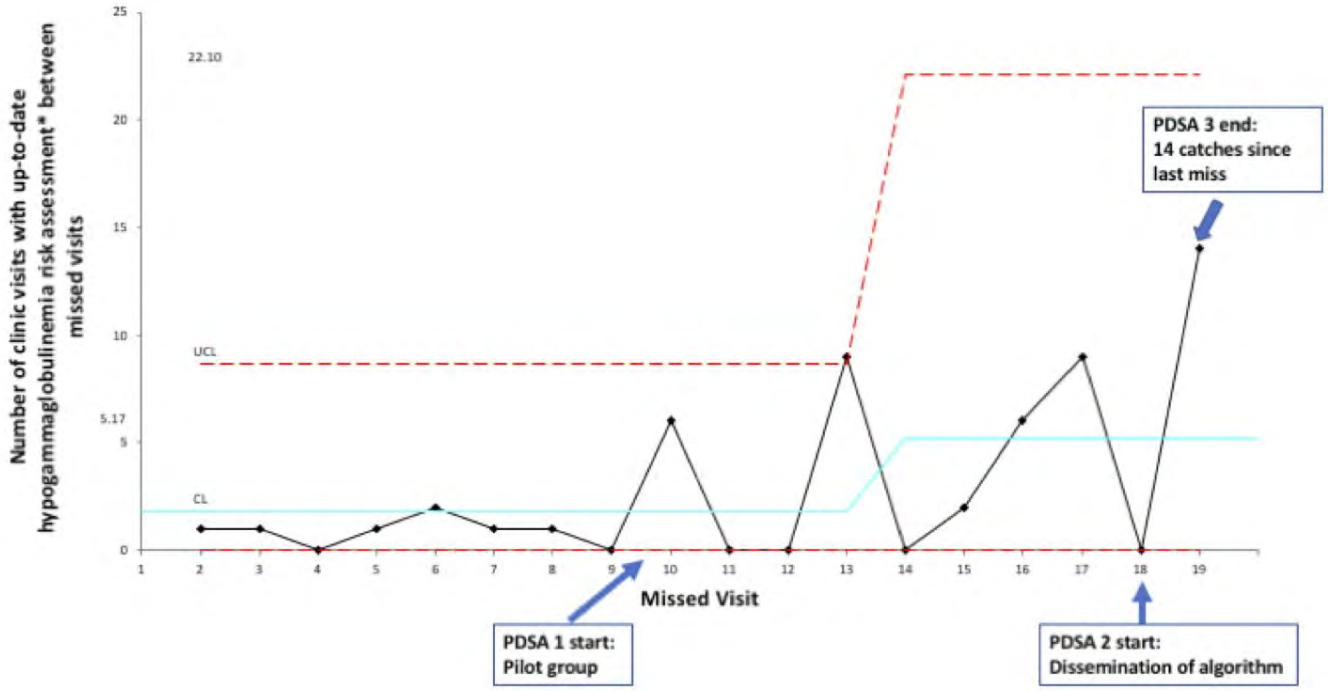

Figure 2. Number of clinic visits with documented up-to-date hypogammaglobulinemia risk assessment in between each missed visit. On the X-axis, visits in which an up-to-date hypogammaglobulinemia risk assessment was not documented for eligible patients is displayed chronologically from May 2020 through May 2021. Six months of baseline data (May – September 2020) demonstrated a median of 1.18 clinic visits with up-to-date documentation of clinical risk assessment for eligible patients between each missed clinic visit prior to intervention start. This increased to 5.17 visits between each missed visit by the end of PDSA 3.
* Hypogammaglobulinemia risk assessment = up-to-date IgG monitoring and documentation of hypogammaglobulinemia for IgG < normal per scale

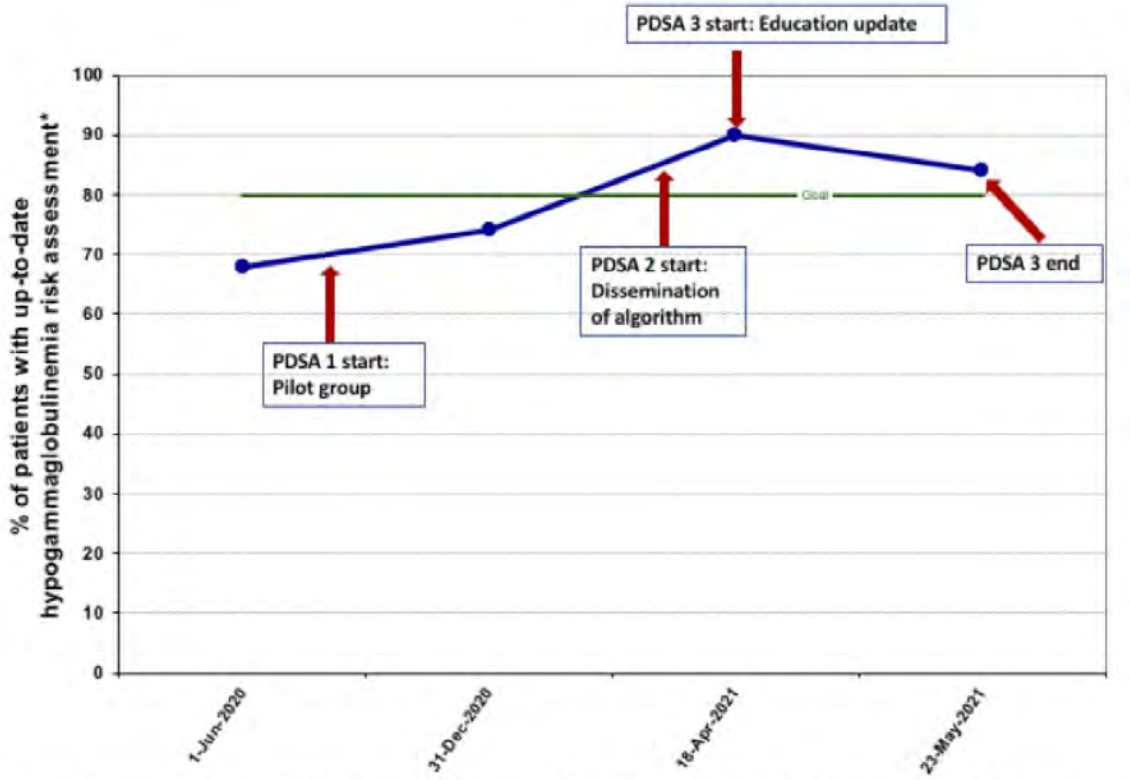

Figure 3. Improvement in Patient-Level Up-to-date Documented Hypogammaglobulinemia Risk Assessment Using Dissemination of a Standardized Algorithm and Division Education
* Hypogammaglobulinemia risk assessment = up-to-date IgG monitoring and documentation of hypogammaglobulinemia for IgG < normal per scale

We conducted the following "Plan-Do-Study-Act" (PDSA) cycles, beginning in September 2020: 1) pilot testing of algorithm, 2) division-wide dissemination of algorithm and provider-specific patient lists specifying those overdue for monitoring and/or documentation, and 3) education update reviewing divisional progress towards goals, algorithms, and provider-specific patient lists.

Data were analyzed for special cause variation using standard statistical process control and run chart methodology. Patients who received IgG replacement within the last 6 months, had transferred to an alternative practice, or were lost to follow-up (no visit within 12 months) were ineligible.

Results: Beginning in May 2020, the baseline median number of visits between missed hypogammaglobulinemia risk assessment opportunities was 1.18. Special cause variation criteria were met after the first PDSA cycle, with an increase in successful monitoring opportunities to 5.17 (Figure 2). Currently, we have successfully monitored 14 patients consecutively. Patients with an up-to-date clinical risk assessment increased from 68% (26/38) to 84% (21/25) (Figure 3). Documentation of identified hypogammaglobulinemia increased from 38% to 100%.

Conclusion: Provision of a standardized algorithm paired with intermittent provider-specific reminders improves identification and documentation of hypogammaglobulinemia in rheumatology patients who have received rituximab. We are nearing our risk assessment goal and will evaluate whether our improvements are sustained. Future directions include standardizing referrals to immunology for replacement immunoglobulin therapy and developing clinical decision support tools.

Disclosure: B. Rutstein, None; **M. Argraves**, None; **A. Bilgic Dagci**, None; **S. Bayefsky**, None; **J. Rood**, None; **J. Chase**, None; **J. Mehta**, None; **M. Lerman**, None; **C. Stingl**, None; **J. Burnham**, None.

Abstract Number: 0649

Optimizing SARS-CoV-2 Vaccine Timing in Rituximab-Treated Patients with Autoimmune Rheumatic Diseases: A Quality Improvement Intervention

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SESSION INFORMATION

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Table 1. Patient demographics, clinical, and immunologic data of autoimmune rheumatic disease patients receiving rituximab

Patient characteristics	Total (n=70)
Age (years), median (IQR)	61.5 (16)
Underlying disease:	
Rheumatoid arthritis, n (%)	31 (44.2)
ANCA-associated vasculitis, n (%)	16 (22.8)
Connective tissue disease*, n (%)	21 (30)
IgG4-related disease, n (%)	2 (2.8)
Rituximab Schedule	
Every 6 months, n (%)	60 (85.7)
Every 12 months, n (%)	10 (14.2)
Cumulative RTX (mg), median (IQR)	7000 (4000, 11500)
Concomitant DMARD, n (%)	38 (54.3)
Steroids ≥ 20mg/day, n (%)	2 (2.8)
B cell counts:	
Absolute CD19 count (#/uL), median (IQR): (n= 20)	15.33 (8.77, 19.73)
Absolute CD20 count (#/uL), median (IQR): (n= 20)	10.06 (5.99, 13.51)
History of hypogammaglobulinemia n, (%) (n=38)	19 (50)
Immunoglobulin M (mg/dL), median (IQR) (n=34)	47 (22.25, 67.5)
Immunoglobulin A, median (IQR) (n=35)	181 (113, 257.5)
Immunoglobulin G, median (IQR) (n=35)	901 (743, 1065)
Documented history of COVID-19 infection, n (%)	5 (8.3)
Influenza vaccine in 2020-2021 (yes/no) n (%) (n=53)	48 (90.5)
Patient group according to provider preference for SARS-CoV-2 vaccine:	
Universal recommendation for timing n (%)	40 (57.1)
Individualized approach to timing, n (%)	30 (42.8)
Patient reported data on SARS-CoV-2 vaccine (n=57)	
Refused, n (%)	0 (0)
Undecided, n (%)	2 (3.5)
Planned, n (%)	6 (10.5)
Received, n (%)	49 (85.9)
Timing of SARS-CoV-2 vaccination post RTX, median (IQR) (n= 49)	20.14 (12.4, 25.7)
SARS-CoV-2 nucleocapsid IgG (positive) n(%) (n=7)	1 (14.2)

*The connective tissue disease group is composed of systemic lupus erythematosus, inflammatory myopathies, anti-synthetase syndrome, overlap syndromes, and mixed connective tissue disease patients.

Table 2. Factors associated with SARS-CoV-2 vaccine timing after B-cell depleting therapy with rituximab

Clinical Factor	Vaccinated less than 20 weeks post RTX (n=24)	Vaccinated 20 or more weeks post RTX (n=25)	p-value
Provider preference for universal timing of vaccination, n (%)	11 (46)	19 (76)	0.04
Indication for RTX:			
Rheumatoid arthritis, n (%)	11 (46)	12 (48)	0.41
ANCA-associated vasculitis, n (%)	3 (12)	7 (28)	
Connective tissue disease*, n (%)	9 (38)	5 (20)	
IgG4-related disease, n (%)	1 (4)	1 (4)	
History of hypogammaglobulinemia, n (%)	8 (33)	8 (35)	1.00
Concomitant steroid dosing (daily prednisone equivalent), n (%)			
Less than 10mg daily	22 (92)	23 (92)	0.24
10-20mg daily	0 (0)	2 (8)	
Greater than 20mg daily	2 (8)	0 (0)	
Concomitant DMARD*, n (%)	14 (58)	14 (56)	1.00
Cumulative RTX dose (mg) median, (IQR)	8500 (5700, 13000)	5000 (3000, 8000)	
Planned to time vaccination (y/n), n (%)	21 (95)	24 (100)	0.48

* Concomitant DMARD list includes hydroxychloroquine, methotrexate, mycophenolate, leflunomide, azathioprine, sulfasalazine, intravenous immunoglobulin, one patient on omalizumab, and another on nintedanib and tacrolimus.

Background/Purpose: Experience with rituximab (RTX) in autoimmune rheumatic disease (AIRD) has shown a clear association with hypogammaglobulinemia, serious infections, and impaired humoral response to certain vaccines. The 2019 EULAR recommendations provide guidance to time future vaccines at least 24 weeks post-RTX and 4 weeks before the next course. We sought to educate faculty on the rationale for timing SARS-CoV-2 vaccines in AIRD patients on RTX and to assess timing of vaccination in clinical practice.

Methods: We performed a medical records review of AIRD patients treated with RTX from January 2020 through to February 2021 at our institution and conducted a quality improvement study to optimize vaccine timing for patients with AIRD on RTX. We first educated providers on the rationale for timing SARS-CoV-2 vaccines 24 weeks post RTX

Table 3. Patient reported side effects after SARS-CoV-2 vaccination

Reported symptom , n (%)	n=82*
Pain at injection site	43 (52.4)
Fatigue	33 (40.2)
Chills	13 (15.8)
Headache	13 (15.8)
Myalgias	10 (12.2)
Subjective fever	6 (7.3)
Arthralgias	6 (7.3)
Nausea	3 (3.6)
Swelling at injection site	2 (2.4)
Rash at injection site	2 (2.4)
Fever (documented >100.4° F)	2 (2.4)
Other (Suicidal ideations)	1 (1.2)
Lymph node swelling	0 (0)
Hives	0 (0)
Flare of Rheumatic disease	0 (0)

*If vaccine given in two shot series, symptoms were counted separately for each dose administered.

and recorded provider vaccine preference to either universally time all vaccines or to individualize the plan for each patient. We measured actual timing of vaccines through telephone survey of patients. In patients with available data, we then analyzed vaccine response in relation to vaccine timing and other clinical and immunologic parameters. This project was determined to be exempt by the institutional IRB.

Results: A total of 91 patients received RTX for AIRD during the COVID-19 pandemic. Seventy patients had plans to continue RTX at our institution in 2021. Of the 49 vaccinated patients, the median time of vaccination post RTX was 20.14 (12.4, 25.7) weeks with 14 (28.6%) patients vaccinated at least 24 weeks and 25 (51%) at least 20 weeks post RTX. Patients whose providers expressed universal intent to time vaccines were more likely to be vaccinated at least 20 weeks post-RTX than patients whose providers took an individualized approach to vaccine timing (p= 0.04). All patients who received Moderna or Pfizer vaccines received a second dose 2-7 weeks later. A higher cumulative RTX dose was associated with vaccination less than 20 weeks post-RTX (p= 0.03). Preliminary results for the 9 patients with SARS CoV2 Spike protein IgG Ab's revealed negative titers in the majority (78%) of patients despite a median time to vaccination post of 22.1 (19.7, 22.8) weeks.

Conclusion: While a majority of patients received dose 1 of the SARS-CoV2 vaccine more than 20 weeks after their last RTX infusion; most patients did not meet the primary endpoint of vaccination 24 weeks post-RTX despite a physician-directed educational program advocating for this. Patients of providers who indicated a preference to universally delay vaccination were more likely to receive their first vaccine dose at least 20 weeks post-RTX. Preliminary results are concerning for a low rate of SARS-CoV2 spike IgG Ab development in patients despite optimal vaccine timing and low steroid doses. These findings are of particular concern given emerging signals that RTX may be associated with particularly severe COVID-19 infections and warrant further study.

Disclosure: D. **Magliulo**, None; **S. Wade**, None; **V. Kyttaris**, Exagen Diagnostics, 5, GlaxoSmithKline, 1, Corbus Pharmaceuticals, 1.

Abstract Number: 0650

Use, Procurement Cost, and Adverse Events from IVIg Use in Rheumatic Disease

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
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Background/Purpose: Intravenous immunoglobulin (IVIg) is used in several systemic rheumatic diseases due to postulated immunomodulatory properties. However, IVIg is a scarce and costly resource and poses a risk of adverse events (AEs). We evaluated the safety, effectiveness, and procurement cost of IVIg in an ambulatory rheumatic disease sample.

Methods: Using our centre's blood bank records, we identified consecutive tertiary clinic patients receiving IVIg for rheumatic disease between January 2015 and September 2020. We performed retrospective chart reviews of all clinical encounters, from IVIg initiation until 3 months following the last infusion. We evaluated demographic and disease

Table 1. Characteristics of patients with and without a potential IVIg-related adverse event

	No IVIg-related AE (n=15)	At least one IVIg-related AE (n=7)
Age, mean (SD)	51.9 (15.9)	56.5 (10.8)
Sex female n (%)	12 (80)	4 (57)
IVIg duration (months) mean (SD)	9.3 (9.6)	4.9 (2.8)
Diagnosis n (%)		
Inflammatory myositis	12 (80)	6 (86)
SLE	2 (13)	1 (14)
Sjogren's	1 (7)	-
Cutaneous vasculitis	-	-
Indication n (%)		
Myositis	12 (80)	6 (86)
Chillblains	1 (7)	-
Lupus nephritis	1 (7)	-
Interstitial nephritis and pancytopenia	1 (7)	-
Cutaneous vasculitis	-	1 (7)
Concurrent prednisone n (%)	12 (80)	5 (71)
Concurrent immuno-suppressants n (%)	10 (67)	5 (71)
Recommended dose* n (%) * <= 10 g above target dose	9/12 (75)	2/3 (67)

characteristics and clinical effectiveness of IVIg, based on the treating clinicians' assessments 3 months after IVIg initiation and 3 months after cessation. Potential AEs and their severity documented in clinical encounter notes were adjudicated by two independent physicians using pre-established rating scales. An AE was classified as related to IVIg if there was >50% confidence of an IVIg-related adverse event. Finally, we determined if appropriate (ideal body weight-based) dosing was used and estimated the yearly procurement costs (CAN$).

Results: Of 25 patients receiving IVIg for rheumatic disease over the study period, 22 had sufficient clinical records to be included. Mean age was 53 years (range 19-74) and 16 (72%) were women. The treatment indication in 18 patients (82%) was inflammatory myositis (i.e., dermatomyositis, antisynthetase syndrome, overlap and necrotizing myositis); the remaining indications were SLE (n=2), Sjogren's syndrome (n=1), and cutaneous vasculitis (n=1). Patients had a mean of 15 infusions (SD 14) spanning 1271 total hours.

Of 21 patients with at least 3 months of follow-up after IVIg initiation, 18 (86%) showed clinical improvement. Of these 18 'responders', 14 had clinical follow-up at 3 months following cessation of therapy and of these, 10 (71%) had stable or quiescent disease while 4 (29%) had relapsed.

We identified 11 potential AEs in 7 patients, representing 3.2 events per 100 IVIg infusions (95% CI 1.8-5.8). AEs included headache (6), urticaria (3, one with angioedema), chills with back pain (1), and hypertension (1); none of these required an emergency room visit or hospitalization. One patient was switched from IV to subcutaneous Ig. The appropriate IVIg dose could be calculated for 15 patients (height not recorded in the remainder). We found that 7 (47%) received > 100 g excess IVIg over their treatment period and the total cumulative excess was 1242g. The cost of IVIg ranged from 61-90$/g, giving a total estimated procurement cost of $1.48 million during the study period.

Conclusion: The majority of our rheumatic disease patients received IVIg for inflammatory myositis. Most patients (86%) improved 3 months into therapy and a significant proportion of those (29%) relapsed after stopping therapy. Nearly 1 in 3 patients had a potential IVIg-related AE. A treatment course cost up to 254,964$, and one potential area of improvement is using recommended ideal body weight-based dosing.

Disclosure: F. Lambert-Fliszar, None; **E. Vinet**, None; **S. Bernatsky**, None; **A. Mendel**, None.

Abstract Number: 0651

Diagnostic Approach to Identifying Small Fiber Neuropathy in Patients with Sarcoidosis

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SESSION INFORMATION
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Background/Purpose: Sarcoidosis is a multisystem granulomatous disease that can affect the nervous system in about 5% of patients. Sarcoidosis associated small fiber neuropathy (SSFN) presents with neuropathic pain, numbness, and dysautonomia resulting from damage to thinly myelinated Aδ and unmyelinated C fibers. Recent studies, using variable screening instruments, have found that the prevalence of SSFN may in fact be as high as 32.8% -81%. This variability is due to the lack of gold standard diagnostic criteria. This study explores the diagnostic approach to peripheral neuropathy in sarcoidosis patients at VCU Health Systems (VCUHS).

Methods: We searched for patients that were coded for both sarcoidosis (at least 2 visits coded with ICD-10: D86) and polyneuropathy (ICD-10 codes: G62.9, G63, G62.89) at VCUHS . In total, 211 unique medical record numbers were generated. We retrospectively reviewed clinical notes, electromyography (EMG), skin biopsies, and labs of all 211 patients in Cerner electronic health records.

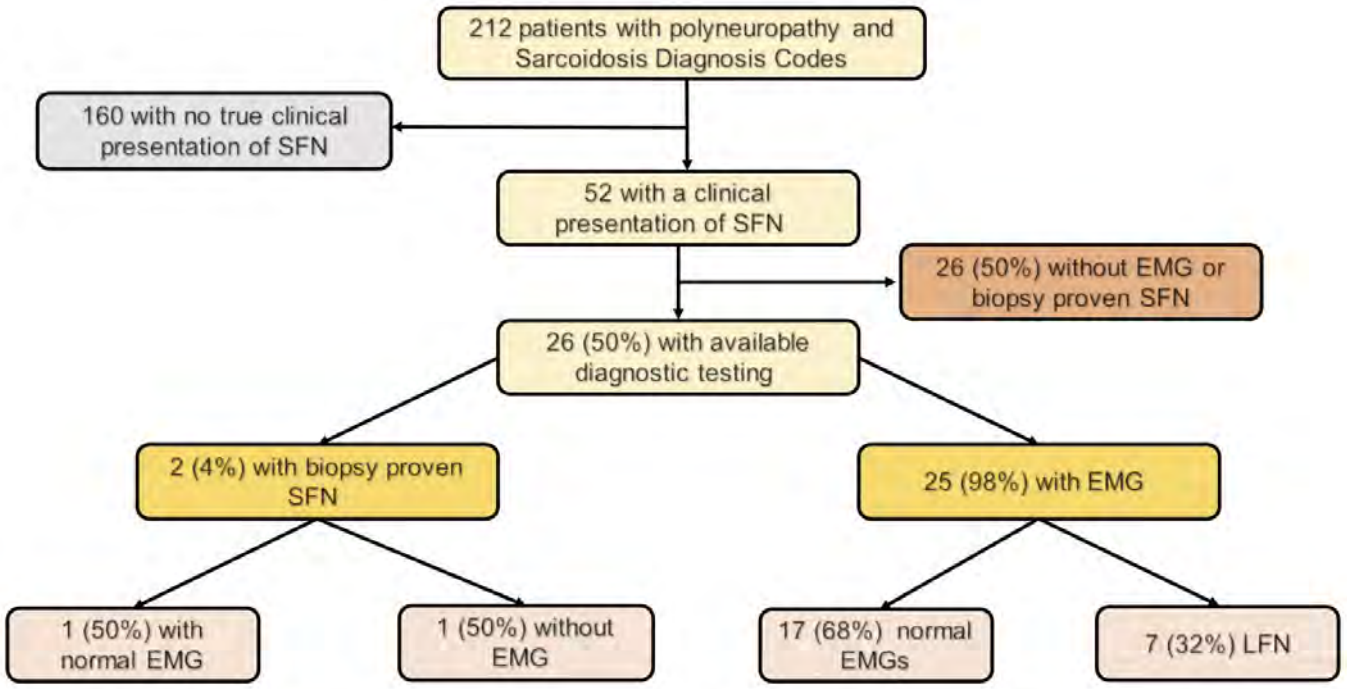

Figure 1. Flow chart of patient selection and methods used in diagnosing SSFN in patients with sarcoidosis. (SFN: small fiber neuropathy; EMG: electromyography; LFN: large fiber neuropathy).

Results: 52 patients had a clinical presentation of peripheral neuropathy upon further review. 69% were female, and 62% were African American. 35% had concomitant diabetes mellitus and 6% had vitamin B12 deficiency. There was no systematic diagnostic approach for any of the patients. 50% of patients had no studies (skin biopsy proven SFN or EMG). 96% of patients with available diagnostic testing had an EMG of which 68% were normal. The rest were consistent with large fiber neuropathy. 4% had skin biopsy proven SFN, half of which had an EMG which was normal. (Figure 1)

Conclusion: The majority of patients with small fiber neuropathy were diagnosed by their clinical presentation, without specific diagnostic criteria. Patients with SFN normally present with a normal EMG, however one patient with an abnormal EMG had a skin biopsy proven SFN, further emphasizing the need for more standardized diagnostic criteria. A SFN screening list has been previously validated in diagnosis of SSFN3, however it hasn't been correlated with other studies like skin biopsies. Given the debilitating effects of SSFN on physical functioning and ultimately the quality of life of patients with sarcoidosis, it is important to utilize a more standardized diagnostic approach to identify and manage these patients.

Disclosure: B. Bou Dargham, None; **N. Madanchi**, None; **K. Satkowiak**, None; **H. Syed**, None; **K. Gwathmey**, Alexion, 2, 6, Argenx, 2.

Abstract Number: 0652

Application of a GCA Probability Score to Patients Referred to a GCA Fast Track Clinic

Mmoloki Mathake[1], Julia Murdoch[2], Andrew Taylor[3], Jean-Louis deSousa[2], Kathy Jao[2], Rachel Li[2] and Helen Keen[4], [1]Fiona Stanley Hospital, Beckenham, Australia, [2]Royal Perth Hospital, Perth, Australia, [3]Fiona Stanley Hospital, Murdoch, Australia, [4]Fiona Stanley Hospital, Perth, Australia

SESSION INFORMATION
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Background/Purpose: Giant cell arteritis (GCA) is the most common large vessel vasculitis, and may be associated with irreversible blindness(1). It is therefore essential to make an early and secure diagnosis. However, GCA often presents a diagnostic challenge; whilst biopsy has been considered the gold standard, in recent years, imaging (ultrasound, MR angiography, CT angiography and PET) has also been validated in GCA. Pre-test probability of disease remains a critical component of GCA assessment and clinical decision making. Recently, the Southend pre-test probability score (PTPS) has been developed to aid GCA assessment (2,3).

We aimed to retrospectively apply the PTPS to patients seen through our GCA Fast Track Clinic (FTC) to assess the utility of this score.

Methods: Patients presenting to the Royal Perth Hospital GCA FTC were consented for prospective data collection. A clinical diagnosis of GCA was based on history, examination, temporal artery ultrasound, and temporal artery biopsy or additional imaging in select cases. We retrospectively calculated the PTPS from data collected between November 2019 and May 2021. We risk stratified patients into low-risk (PTPS < 9), intermediate risk (PTPS 9-12), and high risk (PTPS > 12) groups, and correlated these with the final clinical diagnosis. We then dichotomised the PTPS

into (1) low risk or (2) intermediate/high risk groups, to determine the sensitivity, specificity, positive predictive value and negative predictive value.

Results: Of 104 patients, 25 (24%) received the clinical diagnosis of GCA. Using the PTPS, 45 (43%) of the 104 patients were classified low risk, 34 (32%) intermediate and 25 (24%) high risk for GCA. In the low risk category, GCA prevalence was 0%, in the intermediate group GCA prevalence was 15%, and in the high risk category the prevalence was 80% ($p< 0.001$).

The Southend PTPS (dichotomised) had a sensitivity of 100%, Specificity 56.9%, positive predictive value of 42.3% and negative predictive value of 100%.

Conclusion: The PTPS (applied retrospectively) successfully stratifies patients referred to our fast track clinic into high and low risk for GCA, when using the clinical diagnosis as the gold standard. This tool may have a role in screening referrals to the GCA FTC; the negative predictive value suggests this tool is valuable to exclude GCA.

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Disclosure: M. Mathake, None; **J. Murdoch**, None; **A. Taylor**, AbbVie, 6, Novartis, 6, Gilead, 1, Janssen, 6, Pfizer, 6; **J. deSousa**, None; **K. Jao**, None; **R. Li**, None; **H. Keen**, Roche, 6, 12, educational support, Abbvie, 6.

Abstract Number: 0653

Adherence to the 2015 ACR Guidelines for the Management of Polymyalgia Rheumatica and Screening for Osteoporosis at a Tertiary Care Medical Center

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SESSION INFORMATION
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Background/Purpose: Since the first description of polymyalgia rheumatica (PMR) in the early 1950s, the ideal dose and duration of glucocorticoid therapy has varied. In 2015, the American College of Rheumatology (ACR) released guidelines for the management of PMR, and included recommendations on the starting dose of prednisone between 12.5-25mg/day, and suggested tapering strategies to achieve 10mg prednisone/day within 4-8 weeks. In order to evaluate the real world application of these guidelines, we conducted a retrospective analysis of patients diagnosed with PMR and managed by rheumatologists at a single clinic at a tertiary academic center. We further evaluated the

Table 1. Demographics and Lab Data

Table 1: Demographics and Lab Data	
Race, n (%)	39 (95%) Caucasian 2 (4%) African American 1 (2%) Asian
Gender, n (%)	25 (60%) Female 16 (40%) Male
Age (median), [Range], years	67, 52-85
ESR (median) mm/hour	43
CRP (median) mg/dL	2.8

screening characteristics for osteoporosis in this population with long term steroid use with a focus on quality improvement.

Methods: Diagnosis codes for PMR were queried for a single rheumatology clinic comprising four physicians and three advanced practice providers. Patients were included if they had an initial diagnosis between January 2015 and June 2020, and had at least four encounters for this diagnosis with a rheumatologist. A retrospective chart review was performed by a single reviewing physician; cases were excluded if they lacked initial laboratory testing for ESR or CRP or had presence of an additional inflammatory rheumatic disease including giant cell arteritis at the time of PMR diagnosis. By consecutive chart review, data was collected on age, race, and sex, ESR and/or CRP. DXA scan performance or physician documentation of known osteoporosis was recorded. Initial prednisone dose, time to taper to 10mg, and total duration of prednisone dose until observation period closed in June 2020 were recorded. Those patients still on prednisone at the end of the study were excluded from analysis for total duration of prednisone used.

Results: Of the 74 screened patients, 41 patients were enrolled in the cohort for analysis. The cohort consisted of 95% Caucasians, 4% African Americans and 2% Asians; 60% of the enrollees were women (*Table 1)*. The age ranged from 52 to 85 years at the time of diagnosis, with a median of 67 years old. The average starting dose for prednisone was 18mg, within the recommended dose range by the ACR. Only 60% of patients had prednisone tapered to 10mg by week 8. By the end of the observation period, 82% of patients had discontinued glucocorticoids. Of these 34 patients, 41% completed treatment within 7-12 months, 32% within 13-24 months, 17% within 25-36 months and

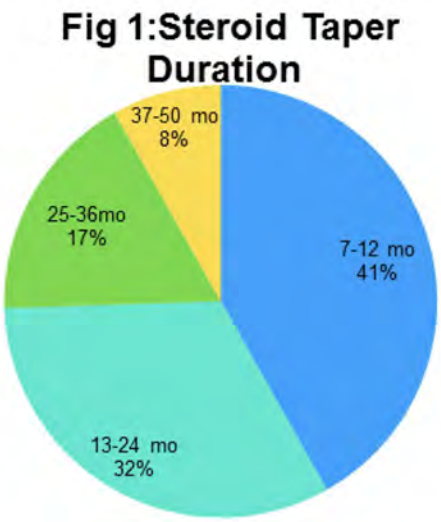

Figure 1. Duration of prednisone taper.

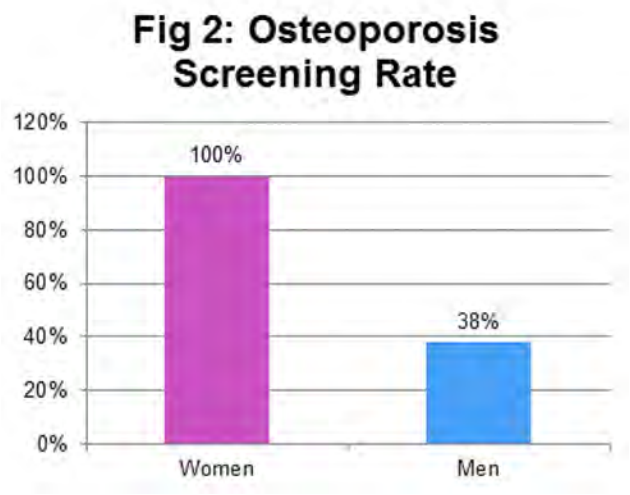

Figure 2. Osteoporosis Screening Rate.

8% between 37-50 months (*Fig 1)*. Osteoporosis screening was completed in 100% of women but only 38% of men despite the use of prednisone in most cases for longer than two years (*Fig 2*).

Conclusion: All rheumatology clinicians initiated prednisone treatment within ACR recommended dosing however goal taper prednisone dose of 10mg by 8 weeks was met by only 60% of patients. Male patients had markedly less DXA screening completed, suggesting that this population may be amenable to further quality improvement initiatives to limit steroid toxicity.

Disclosure: P. Parameswaran, None; **M. Lucke**, None.

Abstract Number: 0654

Assessing Provider Knowledge and Opinions of the 2017 Guidelines for Perioperative Management of Antirheumatic Medications in a Single Academic Center

Andrew Shaffer[1], Erica Mulcaire-Jones[2], Michael Battistone[3], Jeremy Gililland[4], Victor Carlson[4], Joshua Zimmerman[4], Kevin Lammert[4] and Dorota Lebiedz-Odrobina[4], [1]University of Utah, Sandy, UT, [2]Intermountain Healthcare, Salt Lake City, UT, [3]Salt Lake City VA, Salt Lake City, UT, [4]University of Utah, Salt Lake City, UT

SESSION INFORMATION

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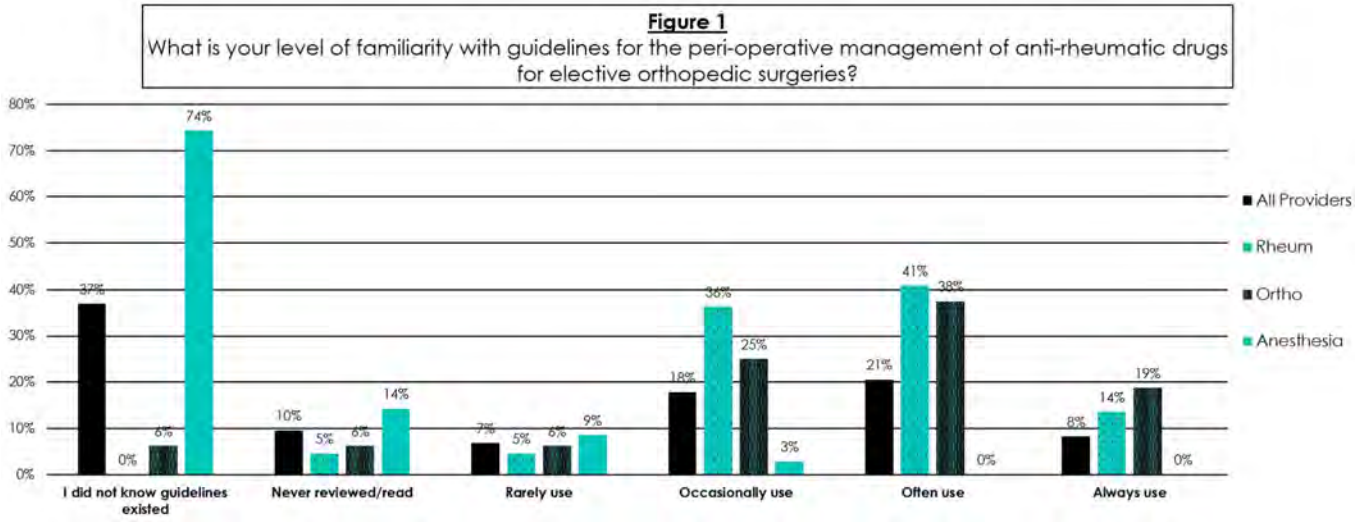
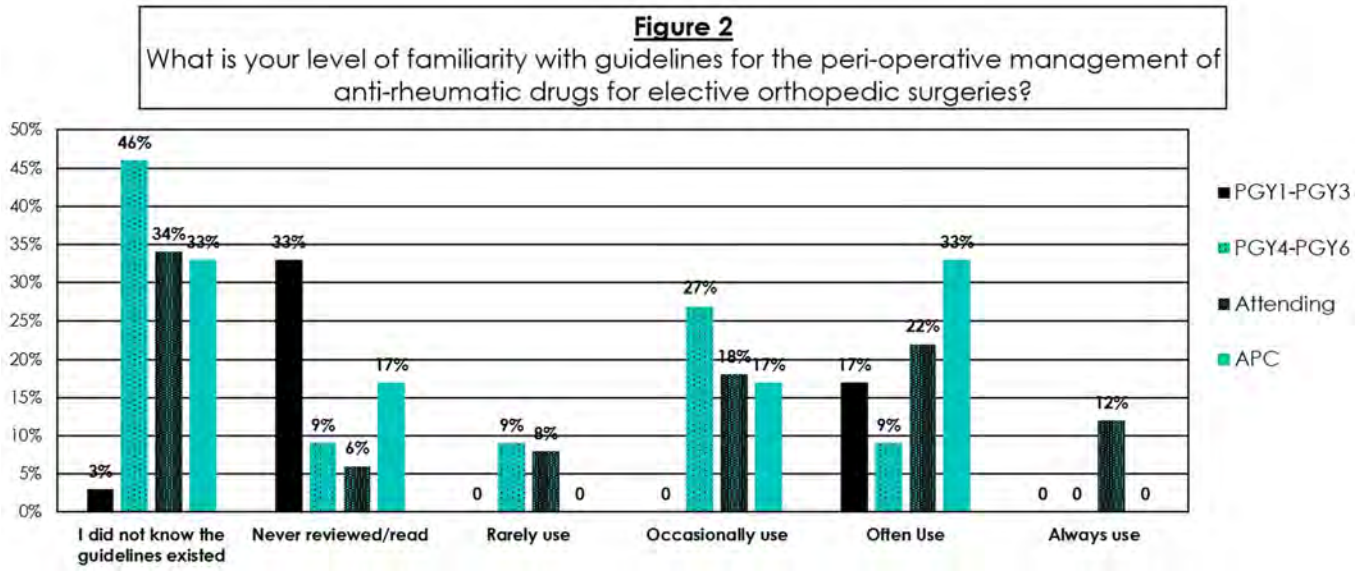
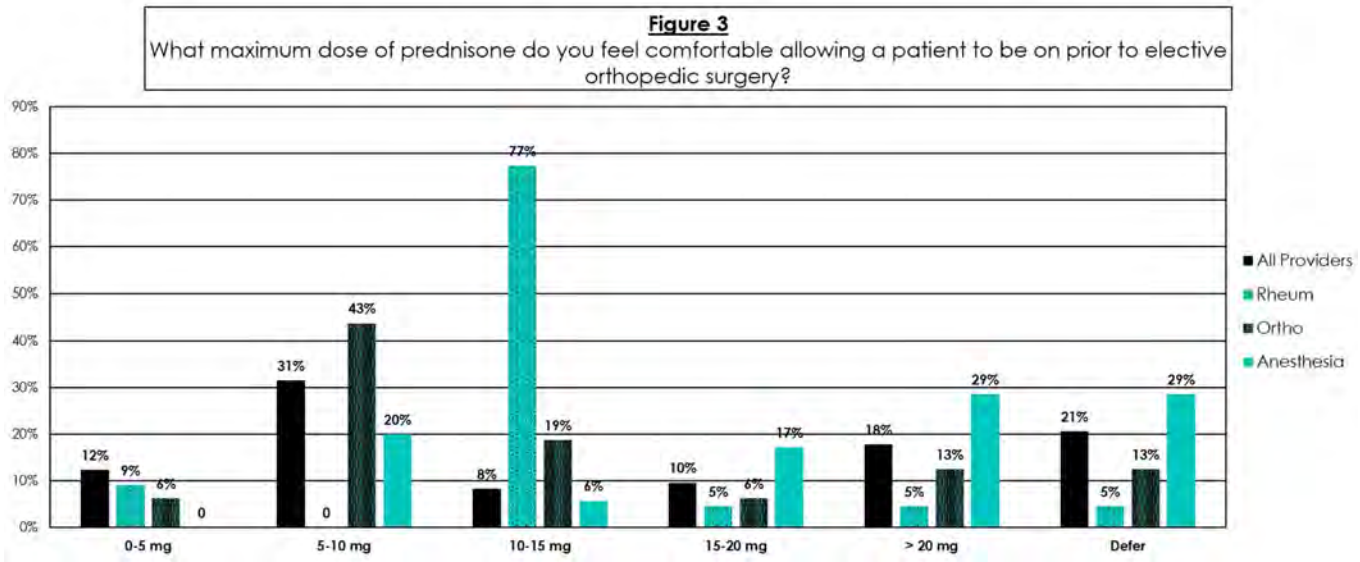
Background/Purpose: Guidelines for perioperative management of antirheumatic medications were released by the American College of Rheumatology (ACR) and American Association of Hip and Knee Surgeons (AAHKS) in 2017 (Goodman SM et al, 2017). Prior to this, no formal guidelines had been published. Their primary goal was to reduce infectious complications in the perioperative setting for elective total hip and knee replacements by guiding provider decision making. However, in order for the guidelines to standardize and improve patient care, providers must be familiar with them and take them into consideration during clinical decision making. In 2021, we surveyed a multispecialty provider cohort to determine provider knowledge and opinions of the ACR/AAHKS guidelines.



Methods: A 10-question survey was sent to all anesthesia, orthopedic surgery and rheumatology providers at a single academic center. Responses were stratified by specialty and level of training. Comparisons between groups were performed by chi-squared, Fisher's exact and Kruskal-Wallis testing.

Results: Seventy-three providers responded to the survey (22 rheumatologists, 16 orthopedic surgeons, 35 anesthesiologists). 6% of orthopedic surgeons and 74% of anesthesiologists were not aware that the guidelines existed. In contrast, all of the rheumatologists were aware that the guidelines existed. Awareness of the guidelines differed significantly between anesthesiologists and both orthopedic surgeons and rheumatologists ($p < 0.001$, figure 1). Awareness did not differ significantly by level of training (figure 2). The most common barrier to use of guidelines was lack of awareness that they existed (26% of respondents). When evaluating the understanding of the guidelines, 51% of respondents either did not correctly identify the recommended perioperative management of conventional synthetic disease modifying antirheumatic drugs (25%), or deferred the decision to another provider (26%). 18% of respondents indicated that they felt comfortable with patients on perioperative doses of prednisone ≥20mg prednisone/day, which is higher than the dose recommended by the guidelines (figure 3). 66% of respondents felt direct communica-





tion with a rheumatologist was a helpful intervention in making decisions regarding antirheumatic drug management. 63% of respondents felt rheumatologists should make the final decision on perioperative antirheumatic medications.

Conclusion: Increased awareness and understanding of the ACR/AAHKS guidelines is needed. This is particularly important for rheumatologists, who are the providers most often relied upon to make decisions related to the management of these medications. Direct communication with a rheumatologist is felt to be a preferred intervention in the decision-making process. As a next step, we plan to evaluate the adoption and impact of the guidelines on the rate of postoperative infectious complications after hip and knee arthroplasty.

Disclosure: A. Shaffer, None; **E. Mulcaire-Jones**, None; **M. Battistone**, None; **J. Gililland**, Stryker, 2, 5, OrthoGrid Systems, 1, 2, 5, 8, 9, 10, DJO Surgical, 2, Zimmer Biomet, 5, MiCare Path, 1, 8, 9; **V. Carlson**, None; **J. Zimmerman**, None; **K. Lammert**, None; **D. Lebiedz-Odrobina**, None.

Abstract Number: 0655

Depression and Fatigue: Two Forgotten Associated Comorbidities in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Background/Purpose: Rheumatoid arthritis (RA) is frequently associated with different comorbidities. Depression and fatigue are common in RA patients with a prevalence of 17-39-%[(1)] and 40%[(2)] respectively. However, the factors that determine these comorbidities, especially their association with disease activity have been little studied.

Tabla 1. Median differences between the 2 groups

Variables, median (IQR)	Total (n=75)	DAS28-ESR>3,2 (n=19)	DAS28-ESR≤3,2 (n=56)	p
Clinical				
TJC (0-28)	0 (0-2)	4 (1-6)	0 (0-0)	<0.001
SCJ (0-28)	0 (0-2)	3 (1-4)	0 (0-1)	<0.001
PATGL (0-10)	3 (1-4)	5 (3-7)	3 (1-3)	<0.001
PhyGL (0-10)	2 (1-3)	5 (3-5)	1 (1-3)	<0.001
Laboratory				
CRP	0.4 (0.4-0.4)	0.5 (0.4-2.2)	0.4 (0.4-0.4)	<0.001
ESR	8 (5-17)	23 (9-32)	6 (5-10)	<0.001
Composite Indices				
SDAI	6.8 (2.4-1.5)	16 (12.4-20.4)	4.4 (2.4-7.5)	<0.001
CDAI	6 (2-11)	15 (11-20)	4 (2-7)	<0.001
Questionnaires				
MDHAQ				
PN (0-10)	3.2 (0.5-5.5)	6,7 (3.2-8)	2,5 (0.5-5)	<0,001
FN (0-10)	1.7 (0.3-3.3)	4 (1.7-5.7)	1,3 (0.3-2.3)	<0.001
RAPID3 (0-30)	5.8 (1-10)	17 (7.4-19)	4 (1-7)	<0.001
FATIGUE (0-10)	3.75 (0.5-7)	6.5 (4.7-9.1)	2 (0-5.5)	<0.001
ROS60 (0-60)	7 (4-16)	16 (6-24)	5 (2-5.5)	0.04
Unidimensional				
FACIT-F (0-52)	40.1 (33-46)	31.5 (13.7-39.7)	42 (35.7-48)	<0.001
PHQ-9 (0-27)	4 (1-8)	8 (4-16)	3 (1-6)	0.001

We studied these two comorbidities: depression and fatigue in patients with RA, according to clinical activity, and the association between them.

Methods: Patients with RA (ACR/EULAR criteria, 2010) who agreed to participate in this study were included consecutively in the Rheumatology Department during a period of 3 months.

Table 2. Data from the Rho Spearman correlation analysis

	FACIT-F (0-52)	PHQ-9 (0-27)	ROS60 (0-60)	VASFatigue (1-10)	TJC (0-28)	SJC (0-28)	PATGL (0-10)	PhyGL (0-10)	CRP	ESR
FACIT-F (0-52)	1,000	r=-0,850 p<0,0001	r=0,766 p<0,001	r=-0,802 p<0,0001	r=-0,536 p<0,0001	r=-0,272 p=0,022	r=-0,517 p<0,0001	r=-0,428 p<0,0001	r=- 0,326 p=0,005	r=-0,334 p=0,004
PHQ-9 (0-27)	r=-0,850 p<0,0001	1,000	r=0,717 p<0,0001	r=0,721 p<0,0001	r=0,618 p<0,0001	r=0,392 p=0,001	r=0,616 p<0,0001	r=0,477 p<0,0001	r=0,287 p=0,018	r=0,304 p=0,012

Demographic variables (age, sex, BMI), years of disease duration, treatment, physical examination (TJC28, SJC28), patient (PATGL) and physician (PhyGL) global assessment, and laboratory tests (ESR, CRP) were collected. Patients completed 2 one-dimensional questionnaires: PHQ-9 for depression (0-27; cut-off point≥10) and FACIT-F for fatigue (0-52; lower scores indicate more fatigue) and the multidimensional health assessment questionnaire (MDHAQ) which includes a query for depression in the checklist review of 60 symptoms (ROS60) and one for fatigue measured in VAS of 0-10 (VAS_Fatigue). EULAR composite indices for clinical activity (DAS28-ESR and CRP, CDAI, SDAI) and self-reported clinical activity index with RAPID3 = function (FN) + pain (PN) + VGP were calculated.

Patients were compared in two groups according to disease activity (DAS28-ESR). Group 1: > 3.2 = moderate or high activity, and group 2: ≤3.2 = low activity or remission.

A bivariate statistical analysis was performed to compare groups (U Mann Whitney-test for quantitative variables and Chi^2-test for categorical). Finally, Spearman's Rho correlation was done.

Results: A total of 75 patients with RA were studied with a median of 14 years (IQR: 8-24) of disease duration, 84% women, with a median age of 63 (36-88) years and a BMI median of 24.22 (IQR: 22-27.4) and 64% with DMARDb treatment. 19 patients had moderate or high activity and 56 patients with low activity or remission. The clinical variables: TSC, SJC, laboratory tests (ESR, CRP) and all self-reported variables in MDHAQ (PN, FN, PTGL, self-RADAI, VAS_Fatigue, ROS60), PhyGL, FACIT-F and PHQ-9 showed significant differences between the two groups, with higher scores in patients of group 1. Also in the composite indices, as we expected (Table 1).

FACIT-F scores showed a very good negative correlation with VAS_Fatigue ($r = -0.802$; $p < 0.0001$), PHQ-9 ($r = -0.850$; $p < 0.0001$) and ROS60 ($r = -0.766$; $p < 0.0001$) and almost good with the rest of the variables (table 2). PHQ-9 scores showed high positive correlation with all the variables studied, remarkable in VAS_Fatigue ($r= 0.721$; $p < 0.001$) and in ROS60 ($r = 0.717$; $p < 0.001$) (Table 2).

Conclusion: In RA patients with a higher burden of disease (clinical, biological and self-reported) were observed high scores for fatigue and depression with a strong association to each other. These two comorbidities should be routinely studied in the follow-up of active RA patients.

References

1. Matcham F, *et al*. Rheumatology (Oxford) 2013.
2. Tournadre A, *et al*. Joint Bone Spine. 2019.

Disclosure: R. Morlà, None; **B. Frade-Sosa**, None; **N. Sapena**, None; **R. Gumucio**, None; **R. Sanmarti**, Abbvie, 6, BMS, 5, BMS, 6, Sandoz, 6, Pfizer, 6, Roche, 6, MSD, 6; **J. Gomez-Puerta**, Abbvie, 6, BMS, 6, GSK, 6, Galapagos, 6, Lilly, 6, MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 1.

Abstract Number: 0656

A Survey Based Descriptive Study to Assess the Quality of Sleep in Rheumatic Patients

Kezia Sam[1], David Lans[2] and Fulvia Milite[1], [1]White Plains Hospital, White Plains, NY, [2]New York Medical College, Valhalla, NY, New Rochelle, NY

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Sleeping difficulties although common in rheumatic patients, have often been overlooked presuming it to be part of a chronic illness. We conducted a survey-based study comparing the quality of sleep in patients with rheumatic diseases vs. healthy individuals employing the Pittsburg Sleep Quality Index (PSQI) and analyzing other factors, especially pain that effects sleep quality. PSQI is a self-rated questionnaire which assesses the sleep quality over a 1-month time interval. A total score > 5 is indicative of poor sleep quality.

Methods: Adult patients in an outpatient setting with rheumatic conditions were handed out the survey that included PSQI questionnaire and additional questions related to other factors affecting sleep quality. The rheumatic conditions included were Rheumatoid arthritis, Osteoarthritis, Psoriatic arthritis, Fibromyalgia, Polymyalgia rheumatica (PMR), Spondyloarthritis and Systemic lupus erythematosus (SLE). Healthy subjects were also handed out the surveys. Participation was anonymous and voluntary. Data were analyzed using descriptive statistics, t-tests, ANOVA, and regression analysis.

Results: The results have been obtained from questionnaires completed by 120 patients. Among them, 60 had rheumatic diseases (83% female with mean age 64, 17% male with mean age 49) and 60 were healthy subjects (78% female with mean age 62, 22% male with mean age 54). There was a statistically significant difference in the PSQI scores of patients with rheumatic conditions vs. those without rheumatic conditions ($p=2.2 \times 10^{-16}$, 95% CI: 6.4, 8.5) (Figure 1). The mean PSQI score was highest for patients with fibromyalgia (13) and lowest for those with PMR (7) (Table 1). There was no statistically significant difference in the PSQI scores between men and women with rheumatic conditions (p=0.6058, 95% CI: -2.92, 1.76). There is no statistically significant difference in PSQI scores between

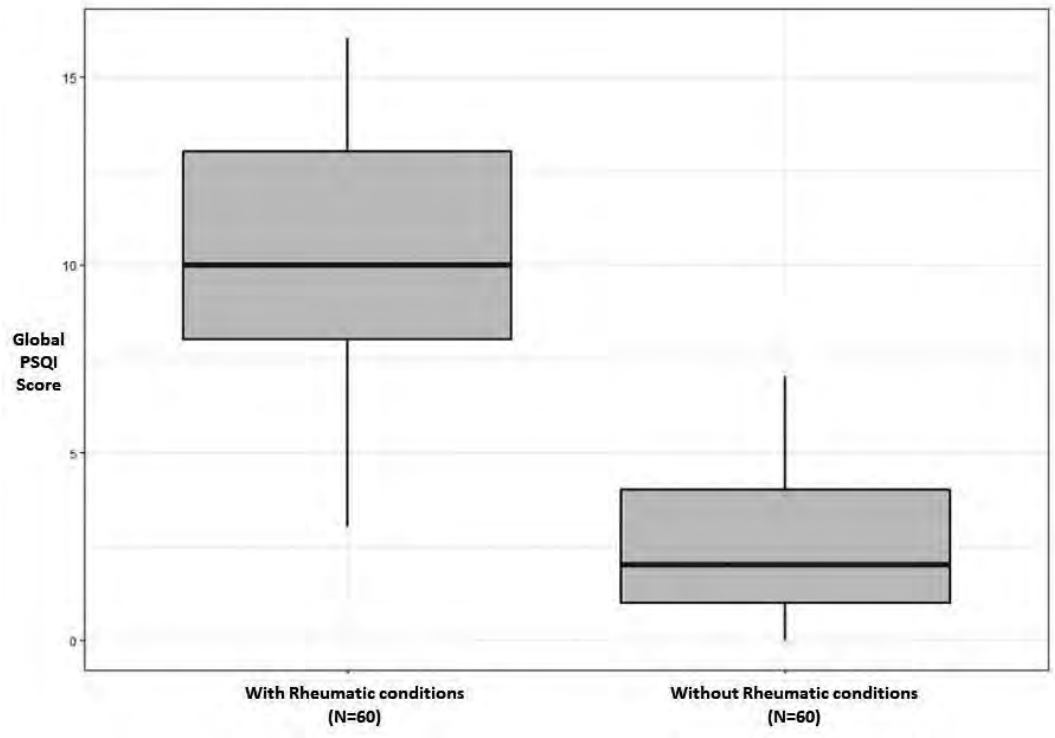

Figure 1. Box plot on PSQI scores of subjects with and without rheumatic conditions.

Table 1. Descriptive Statistics of Patients with Rheumatic Conditions and ANOVA Test Results

Rheumatic conditions	Number of Patients (N)	Mean PSQI Score	Std. Deviation of PSQI Scores
Fibromyalgia	7	12.86	2.73
SLE	3	11.67	2.52
Osteoarthritis	13	10.31	3.17
Polymyalgia Rheumatica	4	7.00	3.16
Psoriatic Arthritis	3	11.33	2.89
Rheumatoid Arthritis	27	9.11	3.46
Spondyloarthritis	3	11.33	6.35
Total	**60**	**10.02**	**3.57**

ANOVA Test Results

	Sum of Squares	df	Mean Square	F	Sig.
Between Groups	134.69	6	22.45	1.93	0.09
Within Groups	616.29	53	11.63		
Total	750.98	59			

patient groups with different rheumatic conditions, at 95% confidence interval (p value= 0.09) (Table 1 ANOVA Test Results). Based on regression analysis, the study confirmed that there is a linear relationship between PSQI Score and Pain Scale (Figure 2).

In addition to the PSQI questionnaire, questions on other factors contributing to poor sleep quality were included in the survey. 80% of the patients with rheumatic conditions were compliant with their medications. 25% of the subjects with rheumatic conditions received sleep education and 20% received sleep study referrals. Only 7% had the diagnosis of insomnia and 13% had the diagnosis of sleep apnea.

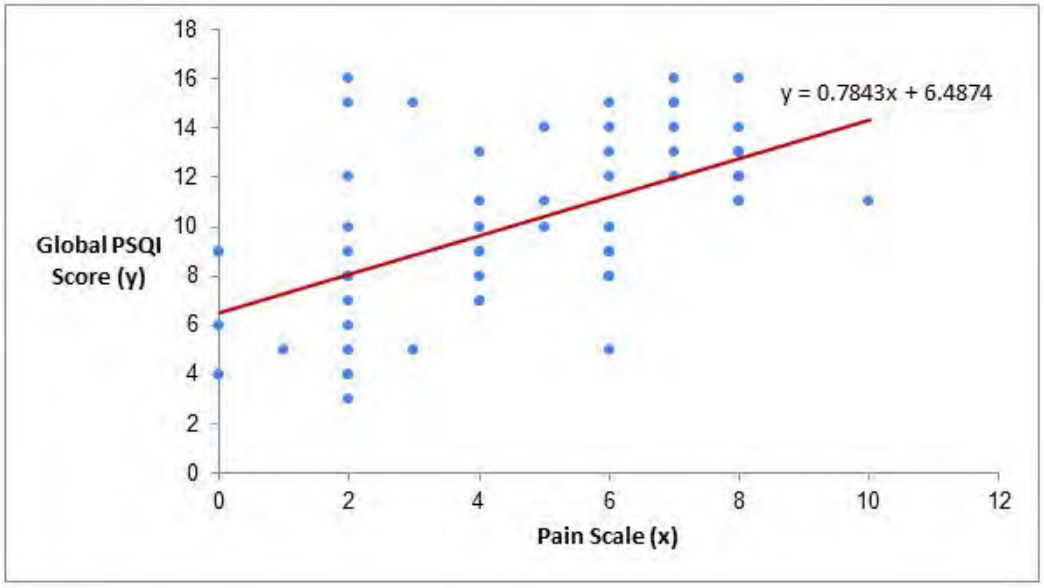

Figure 2. Regression Analysis of Global PSQI Score to Pain Scale for Patients with Rheumatic Conditions.

Conclusion: Poor sleep quality is often dismissed in patients with rheumatic diseases and often not taken into consideration as part of the management of patient care. Patients with rheumatic conditions have statistically significant poor sleep quality compared to those without rheumatic conditions. It is important to recognize those patients complaining of poor sleep and direct them to appropriate management keeping in mind that the better the quality of sleep, the higher the threshold for pain.

Disclosure: K. Sam, None; **D. Lans**, None; **F. Milite**, None.

Abstract Number: 0657

Assessing Patient Transition Outcomes from a Large Pediatric Rheumatology Center to Adult Healthcare

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Transitioning children with chronic diseases from pediatric to adult healthcare can be a challenging task, with high morbidity and mortality. In response, we have developed a transition pathway called the Baylor Rheumatology Initiative: Developing and Guiding Engagement (BRIDGE). Through the BRIDGE, patients are introduced to a clinic-specific transition policy, and providers are incentivized to discuss transition planning beginning in early adolescence, with the goal of effective transition to an adult provider. The Transition Planning Tool (TPT) is an electronic medical record-based flowsheet; TPT use is encouraged at clinic visits for patients aged 14-19. Our objective was to assess baseline transition outcomes for a legacy group of transitioned patients and to assess the correlation between TPT utilization and the rate of successful transition.

Methods: Twenty-seven patients who transitioned during the establishment of the BRIDGE pathway were followed for 1 year post-transition to assess the characteristics of their transition. TPT data was reviewed retrospectively for each patient, examining extent of TPT use and completion of TPT elements. We rigorously defined the primary outcome of successful transition as meeting all 3 of the following criteria: 1) first adult rheumatology appointment within 3 months from last pediatric visit; 2) prescriptions refilled from the adult provider within 3 months from transition; and 3) no rheumatology-related emergency (ER) visits or hospital admissions within 1 year of transition. Comparisons were made using Wilcoxon rank sum, Chi-square, and Fisher's exact tests.

Results: The majority of transitioned patients were female (78%) and privately insured (67%). The most common diagnosis was SLE (33%). Forty-four percent of patients met all goals for successful transition; 67% attended an adult appointment within 3 months (81% did within 4 months), 59% refilled medications within 3 months, and 85% avoided a rheumatology-related admission or ER visit within 1 year. There was no statistical significance between successfully transitioned patients and those who were not in number of times the TPT was accessed, number of unique TPT questions successfully answered, age, sex, diagnosis, insurance type, or disease severity. However, unadjusted logistic regression indicated that completion of some TPT questions, specifically #8 regarding alcohol/non-prescription drug use and #13 knowing who the adult provider will be, was associated with a higher probability of successful transition.

Conclusion: Although there is no significant link between TPT use and successful transition in this legacy cohort, there are some positive signals. For our next step, we will compare these outcomes to those of patients who have been in our formalized BRIDGE program for 1 year or longer before transition. Additionally, over the next quality improvement cycle, we hope to achieve successful transition metrics for 75% of our patients.

Disclosure: M. Robichaux, None; **B. Danna**, None; **M. Maher**, None; **D. McDonald**, None; **K. Nasto**, None; **A. Alexander**, None; **A. Coleman**, None; **D. Guffey**, None; **T. Vogel**, None.

Abstract Number: 0658

ACCORD: A Novel Rheumatology Transition Clinic Structure for Adolescent and Young Adult Patients with Childhood Onset Rheumatic Disease

Rebecca Overbury[1], Kelly Huynh[2], Tracy Frech[1], John Bohnsack[1] and Aimee Hersh[1], [1]University of Utah, Salt Lake City, UT, [2]Intermountain Health Care, Salt Lake City, UT

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The transition of health care from Pediatric to Adult providers for adolescents and young adults with childhood onset rheumatic disease continues to be associated with poor outcomes. In 2018, we initiated a novel transition clinic structure (ACCORD), integrating an Internal Medicine - Pediatrics trained Adult Rheumatologist in a Pediatric Rheumatology clinic to guide this transition. Our goal is to improve transition outcomes in childhood onset rheumatic disease. We report the preliminary outcomes of this intervention.

Methods: In the ACCORD clinic, the Adult Rheumatologist assumed medical management and guided the patient and their family through a transition curriculum. If they consented to do so, patients and their families were enrolled in a prospective observational outcomes research registry. Initial data from this transition clinic is reported. Descriptive statistics are employed.

Results: From November 2018 – December 2020, the ACCORD transition clinic Adult Rheumatologist saw 177 patients and enrolled 57 patients in the registry. From this registry, all patients reviewed the Transition Policy with the Adult Rheumatologist; 45 (78.9%) completed at least one Transition Readiness Assessment; 12 (21.1%) twice completed the Transition Readiness Assessment. 22 (38.6%) transitioned to an Adult Rheumatologist; 17 (29.8%) continued care post-transition with the ACCORD Adult Rheumatologist outside of the transition clinic. The median time between a last ACCORD clinic visit and a first Adult Rheumatology visit was 5.1 months (SD = 5.0, range 1.6 – 8.7). No transitioned patients enrolled in the Registry have failed to schedule with and be seen by an Adult Rheumatologist. There was no statistical significant difference in no-show rates between the ACCORD clinic and the general Pediatric Rheumatology clinic; both for patients of all ages, or for those limited to ≥ 16 years of age.

Conclusion: Our experience demonstrates the feasibility of our clinic model. Our registry shows transition rates of 100.0% and a median transition interval of 5.1 months. This is an improvement over transition rates reported elsewhere that did not implement our model. No-show rates in the ACCORD clinic are not different from our general Pediatric Rheumatology clinic. We believe this structure could be applied to other primary care and subspecialty clinics.

Table 1. ACCORD patients enrolled in the prospective observational registry (n = 57)

	Patients	
	Count	%
TOTAL	57	
Sex		
Female	43	75.4
Male	14	24.6
Self-Reported Race		
American Indian or Alaska Native	1	1.8
Asian	3	5.3
Black or African American	3	5.3
Native Hawaiian or Pacific Islander	1	1.8
Not Reported	1	1.8
Unknown	2	3.5
White	45	78.9
Other	1	1.8
Self-Reported Ethnicity		
Hispanic, Latino, or Spanish Origin	6	10.5
Not Hispanic, Latino, or Spanish Origin	48	84.2
Unknown	2	3.5
Not Reported	1	1.8
Age at Diagnosis		
1	2	3.5
2	2	3.5
3	2	3.5
4	1	1.8
6	1	1.8
7	1	1.8
8	4	7.0
9	2	3.5
10	2	3.5
11	1	1.8
12	2	3.5
13	2	3.5
14	3	5.3
15	11	19.3
16	11	19.3
17	8	14.0
18	1	1.8
19	1	1.8

Table 2. Diagnoses of ACCORD patients enrolled in the prospective observational registry (n = 57)

Diagnosis	Number of patients n (%)
JIA	36 (63.2)
Polyarticular RF negative	10 (17.5)
Polyarticular RF positive	4 (7.0)
Oligoarticular	8 (14.0)
Extended	4 (7.0)
Persistent	4 (7.0)
Psoriatic	1 (1.8)
Enthesitis related	3 (5.3)
Systemic	2 (3.5)
Undifferentiated	0
Other	0
SLE	8 (14.0)
MCTD	2 (3.5)
RA	12 (21.1)
Spondylarthritis	1 (1.8)
Psoriatic arthritis	2 (3.5)
Crystal arthropathy*	1 (1.8)
Dermatomyositis/polymyositis/inflammatory myositis	1 (1.8)
Auto inflammatory**	2 (3.5)
APS	0
Systemic Sclerosis	0
Linear scleroderma	0
Sarcoidosis	0

APS = antiphospholipid syndrome, JIA = juvenile idiopathic arthritis, MCTD = mixed connective tissue disease, RA = rheumatoid arthritis, RF = rheumatoid factor, SLE = systemic lupus erythematosus
* includes: gout
* includes: adult-onset still's disease and cryopyrin-associated periodic fever syndrome (CAPS)

Table 3. Clinic no-show rates

	ACCORD clinic % (*n*)	**ACCORD clinic ≥ 16 years old % (*n*)**	**General Pediatric Rheumatology clinic % (*n*)**	**General Pediatric Rheumatology clinic ≥ 16 years old % (*n*)**
Total no-show encounters	16.0 (69)	15.2 (56)	15.6 (1,458)	15.4 (303)

No-show encounters = no-show encounters + same day cancelations
Denominator is # of patients expected to be seen/scheduled in clinic 24 hours prior to clinic start

No-show encounters $X^2[1, N = 2,045] = 0.043, p = .83$
≥ 16 years of age, no-show encounters $X^2[1, N = 1,983] = 0.008, p = .93$

Disclosure: R. Overbury, None; **K. Huynh**, None; **T. Frech**, None; **J. Bohnsack**, Pfizer, 12, Site Investigator, Funded Research, Janssen, 12, Site Investigator, Funded Research, Bristol Myers Squibb, 12, Site Investigator, Funded Research, Abbvie, 12, Site Investigator, Funded Research, Roche, 12, Site Investigator, Funded Research, Baxter, 12, Site Investigator, Funded Research, General Electric, 11; **A. Hersh**, None.

Abstract Number: 0659

Understanding the Rheumatologic Population We Serve Through Objective Analysis of Referrals and Diagnoses: Does Perception Match Actual Data?

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Measures & Measurement of Healthcare Quality Poster (0623–0659)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Healthcare access in our Rheumatology Department is challenging. Fibromyalgia is perceived to occupy a large portion of clinic visits, leading to increased wait times for our rheumatic patients. We seek to understand our patient population and compare rheumatologist perception of wait times, types of disease referrals, and diagnoses to actual data.

Methods: Data on new clinic referrals between 1/1/19 - 6/30/19 were obtained via manual chart review in EHR. Table 1 lists definitions of rheumatic vs non-rheumatic diagnoses used to categorize disease. Rheumatologist perception of access to care and visit types seen was assessed via an 11-question survey (Table 2). Question 1 analyzed median wait time from date referred to seen while question 11 analyzed median visits per year of fibromyalgia patients. Their statistical analysis was calculated via Sign-test. Questions 2-10 analyzed types of conditions referred and diagnosed, referral accuracy, and fibromyalgia patients seen for a single visit. Statistical analysis was calculated using the mean via 1-proportion Z-test. A sub-analysis comparing actual diagnosis of self- vs physician-referrals was measured via Chi-Square test.

Results: There were 2,327 patient charts reviewed in EPIC. 94% of rheumatologists participated in the survey. Table 2 summarizes the results for questions 1-11. Median wait time from referral to clinic visit was 42 days. Discordance existed between physician perception and actual data for the percentage of patients referred and diagnosed with rheumatic disease, fibromyalgia and other disease. Physicians hypothesized that 47.5% of referrals are for rheumatic disease, 32.8% for fibromyalgia, and 24.4% for other disease compared to actual data of 62%, 7.8%, and 30.4%, respectively. They also hypothesized that 40% of patients are diagnosed with rheumatic disease, 38.4% with fibro-

Table 1. Our Definitions of Rheumatic versus Non-Rheumatic Diseases

Non-Rheumatic Diseases		Rheumatic Diseases (per ACR criteria)
Fibromyalgia/ Chronic Pain	Other	
1. Fibromyalgia 2. Myalgia 3. Chronic pain syndrome 4. Chronic non-inflammatory back pain	1. Osteoarthritis 2. Arthralgia/Arthritis/Joint pain (not clearly inflammatory) 3. Soft tissue disease (Tendinitis, Bursitis, Trigger finger, etc.) 4. Heritable diseases (Marfan's, EDS, Hypermobility, etc.) 5. Primary Raynaud's without underlying systemic CTD	1. Connective tissue diseases 2. Inflammatory arthritis (RA, undifferentiated, etc.) 3. Other inflammatory arthritis (infectious, paraneoplastic, drug-induced, etc.) 4. Inflammatory spondyloarthropathy 5. Inflammatory myopathies 6. Vasculitis (small, medium, large vessel) 7. Osteoporosis and other metabolic bone diseases (ex. Paget's, thyroid induced etc.)

myalgia, and 25.6% with other disease compared to 45.2%, 12.2%, and 45.9% of the actual diagnoses, respectively. Concordance existed for patients referred for non-rheumatic disease (13.5%), ultimately diagnosed with rheumatic disease (14.4%). Discordance existed between patients referred for rheumatic disease (51%), ultimately diagnosed with non-rheumatic disease (36%). 70% of fibromyalgia patients were seen for a single visit, concordant with physician perception. Fibromyalgia patients were seen less frequently per year than hypothesized (1 time vs 2). No association existed between type of referral (self vs physician) and ultimate diagnosis.

Conclusion: Timely rheumatologic care is essential to achieve the best outcomes and prevent disability. In order to achieve optimal patient access, we must first understand objective data on rheumatology referrals and diagnoses. Rheumatologist perception of high-volume fibromyalgia/chronic pain referrals was not reflective of the reality of visits in our clinic. Significantly less fibromyalgia/chronic pain was referred and ultimately diagnosed than hypothesized. Significantly more non-inflammatory disease, particularly osteoarthritis, was diagnosed than expected. This study helped us better understand the population we serve so we can more effectively redesign care to improve access and quality.

Table 2. Perception vs Observed Visit Types, Referrals, Diagnoses, and Wait times in Rheumatology Clinic

Question Number	Question	Physician Perception (Hypothesized)*	Observed Patient Data	P-value
Q1	Median wait time (days) from date referral placed to date seen in office	42	42 (IQR 13, 86)	0.7393
Q2	% Referred for Rheumatic disease	47.5%	62.0%	< 0.0001
Q3	% Referred for Fibromyalgia	32.8%	7.8%	< 0.0001
Q4	% Referred for Other Disease	24.4%	30.4%	< 0.0001
Q5	% Diagnosed with Rheumatic disease	40.0%	45.2%	< 0.0001
Q6	% Diagnosed with Fibromyalgia	38.4%	12.2%	< 0.0001
Q7	% Diagnosed with Other Disease	25.6%	45.9%	< 0.0001
Q8	% Referred for Non-Rheumatic disease but diagnosed with Rheumatic disease	13.5%	14.4%	0.3689
Q9	% Referred for Rheumatic disease but diagnosed with Non-Rheumatic disease	51.0%	36.0%	< 0.0001
Q10	% Fibromyalgia diagnoses alone seen for a single consult visit	67.7%	70.1%	0.4289
Q11	How many times per year are return patients with Fibromyalgia diagnosis alone seen	2	1 (IQR 1, 2)	< 0.0001

*Q2-Q10, physician perception hypothesized percentage is the mean of rheumatology physician perception estimates from the survey. Comparison analysis to observed data completed via 1-Proportion Z-Test. *Q1, Q11, physician perception hypothesized is the median of rheumatology physician perception estimates from the survey. Comparison analysis to observed data completed via Sign-Test.

Disclosure: K. Koons, None; **J. Cote**, None; **S. Shrestha**, None; **M. Band**, None; **D. Pugliese**, None; **E. Newman**, None.

Abstract Number: 0660

Improving the Gout Flare Chart Review Using Linked Claims-EHR Data

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Recurrent gout flares are the most crucial outcome in studies of gout treatment. However, gout flares is challenging to identify in a large population because it is episodic with limited data to distinguish encounters for a gout flare vs routine follow-up for gout. The objective of this study was to determine whether integrating information extracted from the narrative notes from the electronic health record (EHR) data using natural language processing (NLP) can improve the efficiency for identifying gout glares over claims data alone.

Methods: The study population was defined by first linking Medicare claims data (2007-16) with EHR data from two tertiary care centers. Subjects with age≥65, ≥1 gout ICD9/10 code, and initiated the urate-lowering therapy (ULT; allopurinol or febuxostat) were included in the study. Chart reviews were performed on a random sample of the study population to create a gold standard set of notes describing gout flare. A list of terms related to gout flare was created informed by the chart review (**Table 1**). Terms were further mapped to concepts as defined by the Unified Medical Language System (UMLS). Narrative notes for all subjects were processed using NLP to identify all notes

Table 1. Key terms used to create the list of natural language processing (NLP) terms for identifying gout flare.

Domains	Terms
Disease	gout;
State	flare; gout flare; gout attack; recurrent attacks;
Anatomy	joint; bursa; joint pain; arthralgia; arthritis; bursitis; synovial fluid; synovitis; podagra; gonagra; first metatarsophalangeal joint; first MTP; MTP1; big toe; great toe;
Pathophysiology	Monosodium urate crystals; MSU; urate; crystal;
Inflammation	red; redness; heat; warm; warmth; pain at rest; tender; tenderness; activity limitation; functional limitation;
Medications	Colchicine; Colcrys; glucocorticoid; glucocorticoid injection; steroid injection; depo-medrol; intraarticular injection; IA injection; Non-steroidal anti-inflammatory drugs; NSAIDs; indomethacin;
Final Terms*	gout; flare; gout flare; joint pain; bursitis; synovitis; podagra; gonagra; big toe; Monosodium urate crystals; MSU; uric acid; redness; warm; activity limitation; functional limitation; Colchicine; Colcrys; glucocorticoid; depo-medrol; intraarticular injection; allopurinol; NSAIDs; indomethacin

*These final terms were mapped to concepts as defined in the Unified Medical Language System (UMLS).

Table 2. Natural language processing (NLP) concepts ranked by largest difference in prevalence among months containing notes with describing gout flare compared to those without.

Rank	Concept ID	Name	Prevalence in month *without* gout flare mentioned	Prevalence in month *with* gout flare mentioned	Odds Ratio
1	C0332575	Redness	4.26%	42.86%	16.87 [3.40, 83.73]
2	C0149896	Primary Gout	4.26%	39.29%	14.56 [2.92, 72.58]
3	C0234233	Sore To Touch	4.26%	39.29%	14.56 [2.92, 72.58]
4	C0278140	Severe Pain	2.13%	17.86%	10.00 [1.10, 90.66]
5	C0041834	Erythema	6.38%	35.71%	8.15 [2.00, 33.09]
6	C0013604	Edema	19.15%	64.29%	7.60 [2.63, 21.96]
7	C0000737	Abdominal Pain	2.13%	10.71%	5.52 [0.55, 55.89]
8	C1517205	Flare	8.51%	28.57%	4.30 [1.16, 15.97]
9	C0268108	Chronic Gouty Arthritis	2.13%	7.14%	3.54 [0.31, 40.91]
10	C1565489	Renal Insufficiency	2.13%	7.14%	3.54 [0.31, 40.91]

Concept ID: concept unique identifier from the Unified Medical Language System (UMLS).

containing terms/concepts related to gout flare. Claims data were also used to segment notes by time period in two ways (claims time filter): (1) identify notes within the 12-month baseline before date of ULT initiation through ULT discontinuation; (2) notes occurring in months with ≥1 ICD9/10 gout code from claims within (1). We tested whether NLP and the application of temporally based claims-based rules could improve the prevalence of notes describing gout flares compared to ICD alone.

Results: A random sample of 69 patients with 10,845 notes was examined. NLP concepts representing signs and symptoms of a gout flare, e.g. redness, severe pain, differed the most among notes describing gout flares compared to those that were not (**Table 2**). After processing notes using NLP, 708 (6.5%) of 10,845 notes had concepts relevant to gout flare (**Table 3**); of the 708 notes, 24.4% described a gout flare. Applying claims time filter 1 alone to the 10,845 notes selected 2,198 (20%), of which 271 also had relevant NLP concepts. Claims time filter 2 selected 691 notes (6.4%), of which 169 also had relevant NLP concepts. Using a combination of NLP and claims time filter 2, which gave notes in months where an ICD9/10 gout code was used (nested within the 12-month baseline and during ULT use), resulted in 54% prevalence of gout flares among the selected notes.

Table 3. Reduction in the number of notes after applying NLP and claims-based time filters, and prevalence of notes with physician mentions of gout flares within the chose notes.

	Unfiltered	NLP Filter	NLP Filter + Time Filter 1	NLP Filter + Time Filter 2
N of patients	69	52	41	33
N of notes chosen	10,845	708	271*	169**
N of notes with physician mentions of gout flares	-	173 (24.4%)	121 (44.2%)	92 (54.4%)

Abbreviations: NLP filter: natural language processing filter (see **Table 1**); Time filter 1: 12-month baseline prior to drug initiation plus on-drug follow-up; Time filter 2: 12-month baseline prior to drug initiation plus on-drug follow-up AND ICD9/10 gout code (ICD9 274.00–03, 81, 82, 39, 9; ICD10 M10).

-: These were not directly checked as we avoided manually reviewing notes not passing the natural language processing (NLP) content-relevancy filter, which was designed to be very inclusive.
* 2,198 notes (66 patients) when the time filter 1 was applied in isolation.
** 691 notes (42 patients) when the time filter 2 was applied in isolation.

Conclusion: Certain NLP concepts may be useful in discriminating notes describing gout flare among a population of subjects with gout on ULT therapy. The combination of NLP as well as the use of claims data with a time component, e.g., segmented by months, can assist in selecting relevant notes describing a gout flare. Together, these provide data for the development of a gout flare phenotyping algorithm with month-level precision.

Disclosure: K. Yoshida, None; **T. Cai**, None; **L. Bessette**, None; **E. Kim**, None; **S. Lee**, None; **L. Zabotka**, None; **A. Sun**, None; **J. Liu**, None; **D. Solomon**, Abbvie, 5, Amgen, 5, Genentech, 5; **K. Liao**, None; **S. Kim**, AbbVie, 5, Roche, 5, Pfizer, 5, Bristol-Myers Squibb, 5.

Abstract Number: 0661

Effect of Omega-three Supplementation on Serum Urate and Gout Flares in People with Gout; A Pilot Randomized Trial

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), also known as omega-3 fats act as alternate COX substrates to arachidonic acid (AA). Their metabolism results in production of prostaglandins which are less inflammatory than those derived from AA. Thus omega-3 fatty acids can act as a "natural" anti-inflammatory drug. Regular use of anti-inflammatory doses of omega 3 fish oil may be particularly useful as a prophylaxis against gout flares during the introduction of urate lowering therapy, and acceptable to patients due to tolerability and lack of major adverse effects compared to other prophylactic medications. The aim of this study was determine the effect of omega-three supplementation with fish oil on serum urate (SU), weight and body mass index (BMI) in people with gout.

Methods: A pilot 6-month, randomized, open-label clinical trial was undertaken in people with gout with serum urate ≥6mg/dL/l. Forty participants were randomized to receive 6.2g omega-3 fish oil daily (manufactured by Melrose (Mt Waverley, Victoria, Australia)or no fish oil for 24 weeks. Blood was obtained monthly for SU and red cell EPA (20:5n-3) DHA (22:6n-3) were measured using a blood spot collection system. The primary efficacy outcome was the change in SU between baseline and week 24 (or the final visit for those who discontinued fish oil or were lost to follow-up). Secondary outcomes included (i) change in weight and BMI between baseline and week 24, (ii) mean number of flares per month between baseline and week 24, (iii) percentage of participants with flares at each month, (iv) cessation of fish oil therapy prior to week 24 due to adverse effects or intolerance and (v) change in oxypurinol, HBA1c, cholesterol, HDL, and LDL concentrations between baseline and week 24 for people on allopurinol.

Results: Five participants in the fish oil group discontinued the oil; three were unable to tolerate the taste, one commenced dabigatran and one found it inconvenient to take it. The baseline demographic and clinical features were well matched between randomized groups. There was no statistically significant difference in the mean (SEM) decrease in SU between baseline and week 24 between randomized groups: fish oil -0.021 (0.02) mmol/l vs. control -0.006 (0.02) mmol/l. There was no significant difference in change in weight or BMI between baseline and week 24 between randomized groups (Figure). There was a statistically significant correlation between red cell omega-three concentrations and the total number of flares per participant between week 12 and week 24; total omega-three r= -0.75 ($p \leq 0.001$),

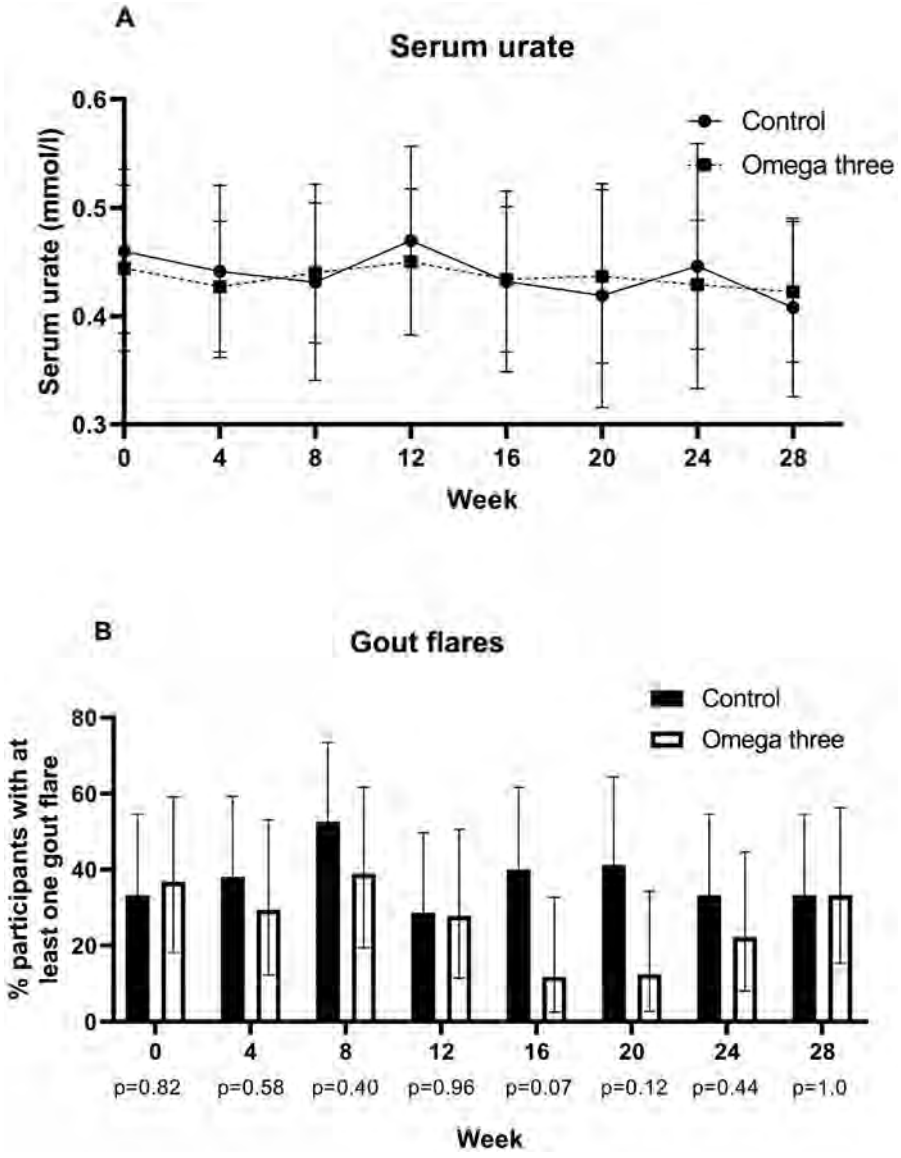

Figure 1. A) Serum urate and B) percentage of participants with at least one flare in the preceding four weeks over the study period in controls and those receiving omega three fish oil.

EPA r= -0.75 (p≤ 0.001) and DHA r= -0.76 (p≤ 0.001). In the omega-three fish oil group four participants reported gastrointestinal adverse effects definitely or probably related to the omega-three supplementation.

Conclusion: The lack of untoward effect of omega three fish oil supplementation on SU and BMI together with the relationship between higher omega-three concentrations and lower gout flares supports the development of further adequately powered clinical trials to determine the role of omega-three supplements as prophylaxis against gout flares in people starting urate lowering therapy.

Disclosure: L. Stamp, None; **R. Grainger**, Pfizer New Zealand, 6, 12, support to travel to conference, Jansenn Australia, 6, 12, travel to symposia, AbbVie New Zealand, 6, Cornerstones, 6, novartis, 1; **C. Frampton**, None; **J. Drake**, None; **C. Hill**, None.

Abstract Number: 0662

Serum Urate Reduction Is Causally Associated with Flare Outcomes in People with Gout: Evidence for Surrogate Status from a Pooled Analysis of 2 Randomized Trials

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Use of serum urate (SU) as a treatment target and outcome measure has become controversial in light of the American College of Physician Gout Guidelines which advocated a "treat-to-symptom", rather than a "treat-to-target SU" approach to management. The choice of SU as a treatment target measure implies that achievement of target SU is causally associated with improvement in patient-centered outcomes such as reduction

Table 1: Baseline demographics and clinical features for the NZ (15) and Nottingham studies (14). Data are present as n (%) or mean (SD).

	SU Responder		SU Non-Responder	
Variable	Nottingham	NZ	Nottingham	NZ
	(n=290)	(n = 53)	(n=227)	(n = 18)
Age (years)	62.7 (11.0)	61.5 (11.5)	63.1 (11.9)	55.9 (13.9)
Male, n (%)	259 (89.3%)	47 (89%)	202 (89%)	17 (94%)
Ethnicity, n (%)				
NZ European/European	280 (96.6%)	25 (47%)	221 (97.4%)	6 (34%)
Maori		17 (32%)		4 (22%)
Pacific Island		8 (15%)		7 (39%)
Asian		3 (6%)		1 (5%)
Duration of gout (years)	11.8 (10.3)	16.4 (11.8)	12.6 (10.1)	17.0 (11.4)
Serum urate baseline (mg/dL)	7.0 (1.8)	7.06 (1.46)	8.0 (1.2)	7.21 (1.49)
Serum urate month 12	4.3 (0.9)	5.18 (0.72)	7.7 (1.4)	5.75 (1.31)
Serum urate month 24	4.4 (1.2)	5.30 (1.01)	7.4 (1.7)	5.77 (1.50)
Creatinine (mmol/l)	92.7 (26.5)	146.5 (132.3)	96.4 (23.7)	125.8 (52.5)
CrCL (mL/min)	72.1 (15.9)	57.7 (25.8)	69.2 (15.9)	67.7 (31.6)
Body mass index (kg/m^2)	29.5 (5.2)	34.8 (7.1)	30.2 (4.8)	37.2 (9.3)
Flare frequency in the preceding year	4.0 (4.8)	5.9 (11.8)	4.1 (4.9)	10.1 (17.1)
Tophus	36 (12.4%)	19 (36%)	22 (9.7%)	6 (34%)

in the number of gout flares. The aim of this study was to assess the causal relationship between achieving target SU and occurrence of gout flares.

Methods: Individual patient data from two randomized trials were analyzed to determine the relationship between SU and flares. Study one (Nottingham, UK) was a 2-year randomized trial comparing nurse-led and GP-led gout care (n=517) (1). Study two (New Zealand) was a 2-year open label randomized trial assessing the safety and efficacy of allopurinol dose escalation (2, 3). Individuals who on average achieved SU < 6mg/dL at 6, 9 and 12 months post-baseline were defined as "SU responders". The primary endpoint was the proportion of participants having at least one gout flare from 12 to 24 months. The secondary endpoint was the actual number of flares from 12 to 24 months (collected as a number between 0 and 4 per month) and tophus regression. The individual patient data sets from New Zealand and Nottingham were combined and analyses undertaken for the primary and secondary outcome measures. These analyses were undertaken using the models as above with the addition of a fixed factor to account for New Zealand and randomization within the Nottingham dataset.

Results: Significantly fewer SU responders experienced a gout flare in months 12-24 compared to SU non-responders; unadjusted OR 0.20; 95%CI 0.15 to 0.29. In the Nottingham study, there was no effect of randomization on the relationship between serum urate response group and the presence or absence of gout flares (p=0.13) indicating that the reduction in SU is responsible for the absence of flares. The mean number of flares in months 12-24 was significantly lower in SU responders compared to SU non-responders, unadjusted mean difference -1.64; 95%CI -1.85 to -1.44. This association was also independent of the randomized treatment allocation. Combining the individual data for both NZ and Nottingham revealed those participants with a tophus at baseline, 38/55 (69.1%) of SU responders lost the sentinel tophus compared to 8/22 (36.4%) of the SU non-responders (OR 3.9; 95%CI 1.4 to >11.1).

Conclusion: We have shown using individual patient data from 2 RCTs that achieving an average SU < 6mg/dL over a 6-month period is likely causally associated with the subsequent absence of gout flares, a reduction in the number of gout flares, and resolution of tophi in people with gout during the second year of treatment.

Disclosure: L. Stamp, None; **C. Frampton**, None; **M. Morillon**, None; **W. Taylor**, Pfizer (NZ) Ltd, 1; **N. Dalbeth**, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **J. Singh**, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2, Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4; **M. Doherty**, None; **W. Zhang**, Eli Lilly, 1, Regeneron, 1; **H. Richardson**, None; **A. Sarmanova**, None; **R. Christensen**, None.

Abstract Number: 0663

Disappearing Digits: A National Retrospective Matched Cohort Study Examining the Risk of Lower Extremity Amputation in Gout

Quint Soto[1], Alison Petro[1], Bryant England[1], Harlan Sayles[1], Lindsay Helget[1], Punyasha Roul[1], Tuhina Neogi[2], James O'Dell[1], Brian LaMoreaux[3] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]Boston University School of Medicine, Boston, MA, [3]Horizon Therapeutics plc, Deerfield, IL

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Gout is associated with a number of comorbidities such as diabetes that are known risk factors for peripheral vascular disease. These comorbidities along with manifestations that mimic infection could place patients with gout at an increased risk of undergoing lower extremity amputation (LEA). The goal of this study was to determine if patients with gout are at a higher risk of undergoing LEA and to determine if this risk is independent of diabetes and other comorbidities.

Methods: We performed a retrospective matched cohort study using national Veterans Health Administrative (VHA) data from January 1999 to July 2015. Patients with gout were identified by the presence of ≥2 ICD9 codes (274.X). Gout patients were matched up to 1:10 by birth year, sex, and calendar year to patients without gout. Patients receiving LEA prior to the index date were excluded. LEA was defined using ICD9 procedure and common procedural terminology (CPT) codes and categorized as toe, transmetatarsal, below-the-knee, or above-the-knee. Diabetes and other comorbidities (e.g., peripheral vascular disease) were identified using ICD9 codes. Patients were followed until LEA or censoring due to death or end-of-study. Non-gout comparators developing gout later could "switch over", contributing at-risk time for gout after matching to 10 new controls. Associations of gout with LEA were examined using multivariable Cox proportional hazards regression accounting for demographics, body mass index, and comorbidities. In secondary analyses, patients were examined in 4 groups based on the presence/absence of gout and diabetes.

Results: We identified 556,521 gout patients and 5,368,397 matched non-gout controls. Patients had a mean age of 67 years and were predominantly male (99%). There were 4,970 LEAs over 4.2 million pt-yrs of follow-up in patients with gout and 24,583 LEAs over 40 million patient-years of follow-up in controls. The risk of LEA (overall and

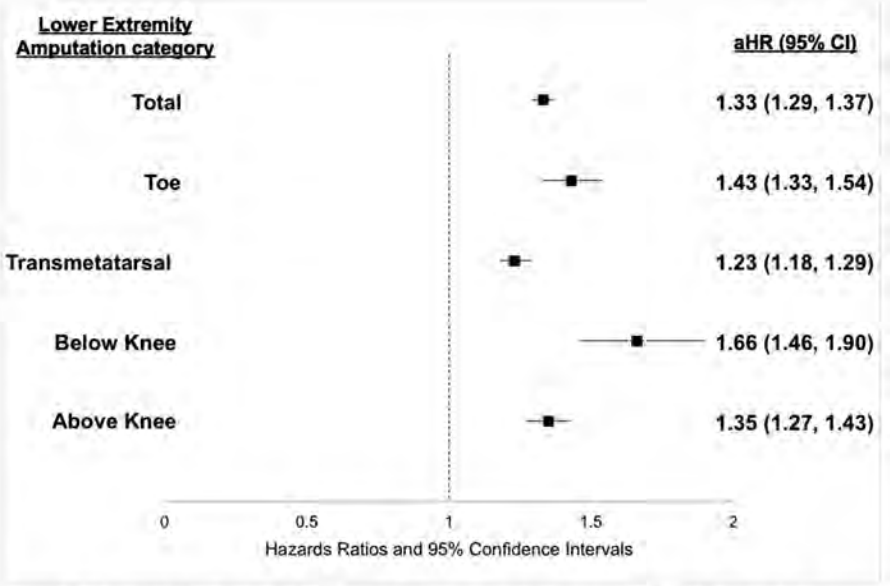


Figure 1: Associations of gout with undergoing lower extremity amputation, total and by type of surgery; adjusted hazard ratios and 95% confidence intervals generated with multivariable Cox proportional hazards regression adjusted for age, sex, race/ethnicity, body mass index, hypertension, cardiovascular disease, peripheral artery disease, cancer, cerebrovascular disease, chronic lung disease, dementia, diabetes and renal disease.

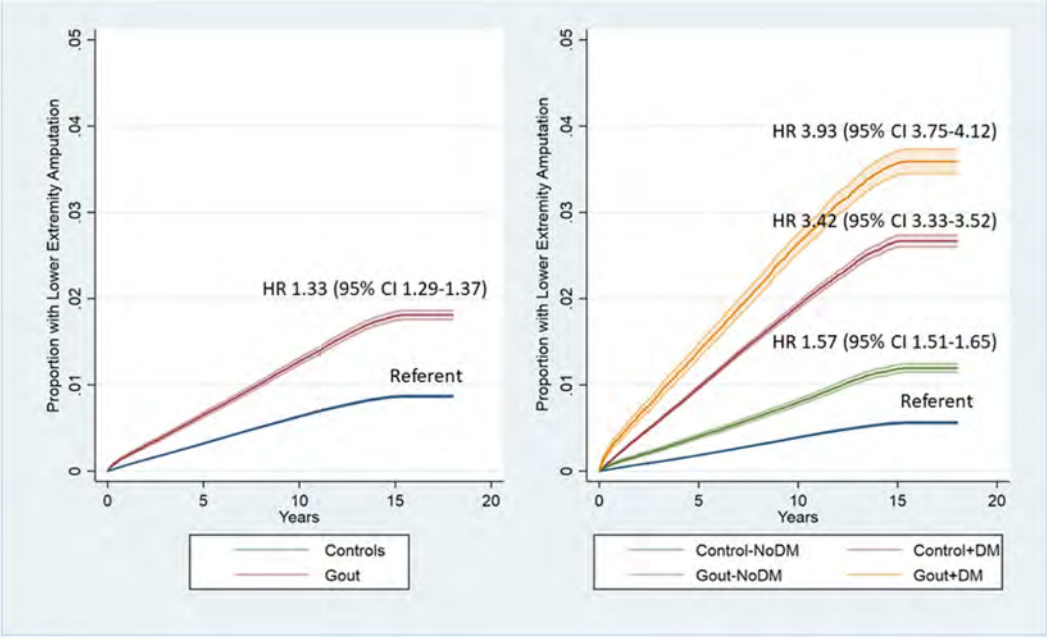


Figure 2: Cumulative incidence of lower extremity amputation based on gout vs. non-gout (left panel) and a combination of gout and diabetes (right panel). Hazard ratios and 95% confidence intervals shown calculated with multivariable Cox proportional hazards regression adjusted for age, sex, race/ethnicity, body mass index, hypertension, cardiovascular disease, peripheral artery disease, cancer, cerebrovascular disease, chronic lung disease, dementia, diabetes (left panel only) and renal disease.

Abbreviations: DM, diabetes mellitus

by category) in patients with gout is shown in **Figure 1**. After accounting for covariates, gout was associated with a significant increase in LEA risk (HR 1.33; 95% CI 1.29-1.37). This risk was highest for below-the-knee amputations (HR 1.66; 95% CI 1.46-1.90). Of other risk factors, diabetes (HR 3.23; 95% CI 3.15-3.32) was most strongly associated with LEA. Results based on dual gout and diabetes statuses are shown in **Figure 2**. In the absence of diabetes, patients with gout demonstrated a 1.57-fold increased risk (95% CI 1.51-1.65) of LEA. The highest risk of LEA was among patients with gout and diabetes, exceeding the risk posed by diabetes alone.

Conclusion: Patients with gout are at a 33% increased risk for undergoing LEA, with an even higher risk for below-the-knee amputations. This risk is independent of other comorbidities that have been associated with LEA including diabetes. Further research is needed to better understand the surgical indications for these procedures, whether tophi (which can mimic osteomyelitis) are associated with heightened risk, and to what degree LEA might be prevented in this patient population through enhanced diagnostics or improved gout management.

Disclosure: Q. Soto, None; **A. Petro**, None; **B. England**, Boehringer-Ingelheim, 2; **H. Sayles**, None; **L. Helget**, None; **P. Roul**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **J. O'Dell**, None; **B. LaMoreaux**, Horizon Therapeutics plc, 3, 11; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 0664

Which Attributes Are the Most and Least Important to Patients When Considering Gout Flare Burden over Time? A Best-worst Scaling Choice Study

Jeremy Holyer[1], William Taylor[2], Angelo Gaffo[3], Graham Hosie[1], Anne Horne[1], Borislav Mihov[1], Isabel Su[1], Gregory Gamble[1], Nicola Dalbeth[1] and **Sarah Stewart**[1], [1]University of Auckland, Auckland, New Zealand, [2]University of Otago Wellington, Auckland, New Zealand, [3]University of Alabama at Birmingham Medical Centre, Birmingham, AL

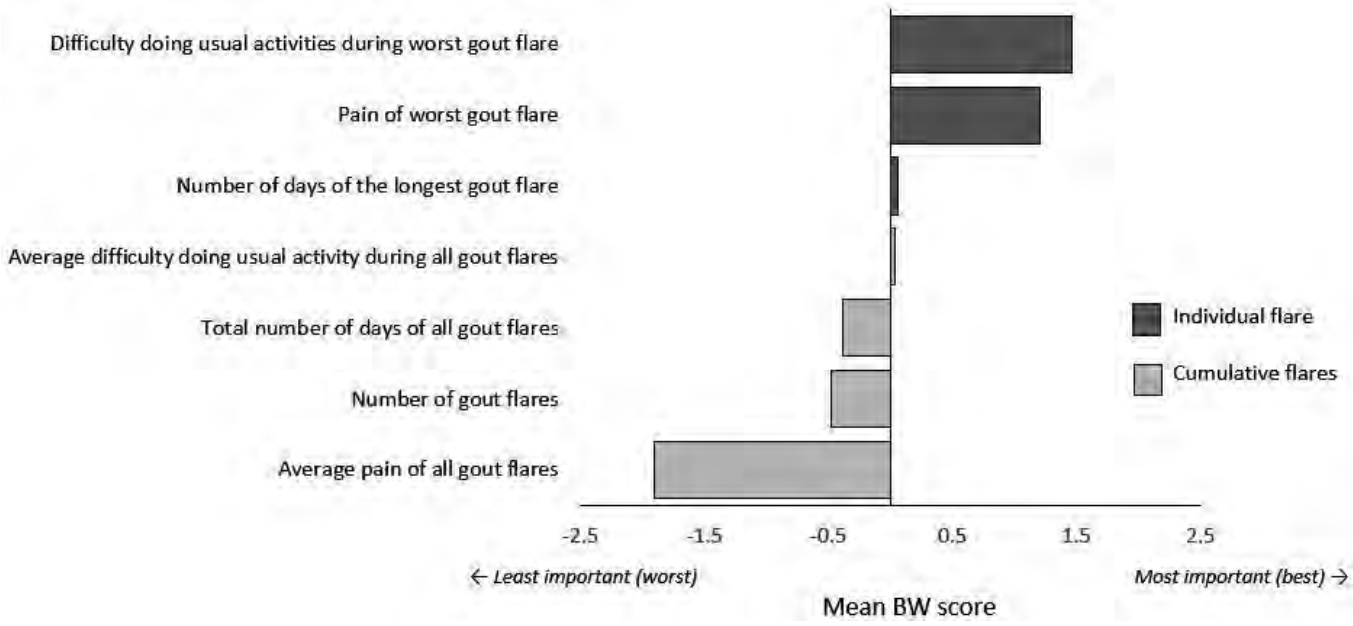
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Several factors contribute to the patient experience of gout flares, including pain intensity, duration, frequency, and disability. It is unknown which of these factors are most important to patients when considering flare burden over time, including those related to the cumulative experience of all flares, or the experience of a single worst flare. This study aimed to determine which flare attributes are the most and least important to the patient experience of flare burden over time.

Methods: Participants were recruited from existing databases of patients who had previously participated in research at the Clinical Research Centre, University of Auckland, Aotearoa/New Zealand. Participants with gout completed an anonymous online survey. Questions were aimed at identifying which attributes of gout flares were the most and least important over a hypothetical six-month period. Four attributes represented the cumulative burden of all flares (average pain of all gout flares, number of gout flares, total number of days of all gout flares, and average difficulty doing usual activities during all gout flares) and three attributes represented the burden of individual flares (pain of the worst gout flare, number of days of the longest gout flare, and difficulty doing usual activities during the worst gout flare). A best-worst scaling method was used to determine the importance hierarchy of the included attributes. Best (B) and worst (W) scores were calculated for each attribute representing the number of times that attribute was chosen as most and least important, respectively. The mean best-minus-worst (BW) score was also calculated to rank the attributes from most to least important, with positive values indicating the attribute being chosen more often as most important, and negative values indicating the attribute being chosen more often as least important.

Results: Fifty participants were included. The majority of participants were New Zealand European middle-aged males and 90% had experienced at least one gout flare in the previous 12 months, with 58% experiencing one to four gout flares in the previous 12 months. Difficulty doing usual activities during the worst flare and pain of the worst flare were ranked as the most important, while average pain of all flares was considered the least important. Overall, attributes related to the single worst gout flare were considered more important than attributes related to the cumulative impact of all flares (**Figure**).

Conclusion: When thinking about the burden of gout flares over time, patients rank activity limitation and pain experienced during their worst gout flare as the most important contributing factors, while factors related to the cumulative impact of all flares over time are relatively less important. Future studies investigating gout flare prevention should consider capturing outcomes related to the worst gout flare experienced during the follow-up period, specifically those related to activity limitation and pain.



Bar chart showing mean Best-Worst (BW) scores for each attribute. Positive scores indicate that attribute was chosen more frequently as the most important, while negative scores indicate that attribute was chosen more frequently as the least important.

Disclosure: J. Holyer, None; **W. Taylor**, None; **A. Gaffo**, None; **G. Hosie**, None; **A. Horne**, None; **B. Mihov**, None; **I. Su**, None; **G. Gamble**, None; **N. Dalbeth**, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **S. Stewart**, None.

Abstract Number: 0665

Pegloticase Treatment for Uncontrolled Gout in Kidney Transplanted Patients: Results of an On-going Multicenter, Open-Label, Efficacy and Safety Study

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Gout in kidney transplant (KT) recipients can be severe and particularly challenging to manage. Pegloticase (pegylated recombinant uricase) rapidly metabolizes urate and is a highly effective therapy for uncontrolled gout, but its efficacy can be limited in some pateints by the development of anti-drug antibodies. The addition of immunomodulators as co-therapy with pegloticase has been shown to improve response rates.[1-2] Few cases of pegloticase use in solid organ transplant patients have been reported and the phase 3 pegloticase trials excluded organ transplant recipients.[3-5] This ongoing Phase 4, open-label trial (PROTECT NCT04087720) examines the safety and efficacy of pegloticase in KT patients with uncontrolled gout.

Methods: Pegloticase treatment (8 mg IV infusion q2w for 24 wks) in KT recipients (KT >1 year ago, eGFR ≥15 mL/min/1.73m^2) with uncontrolled gout (serum urate [SU] ≥7 mg/dL, urate lowering therapy contraindication/inefficacy, and either tophi, chronic gouty arthritis, or ≥2 flares in past yr). Primary endpoint is proportion of pegloticase responders during Month 6 (SU < 6 mg/dL for ≥80% of time). Other endpoints included: eGFR and health assessment questionnaire (HAQ) pain (most severe: 100) and disability (max: 3) scores.

Results: At the time of analysis, 20 patients were enrolled (mean±SD; age: 53.9±10.9 yrs, KT 14.7±6.9 yrs ago, SU: 9.4±1.5 mg/dL, gout duration: 8.4±11.6 yrs; all on stable doses of ≥2 immunosuppresive medications) and 10 completed treatment, 3 discontinuted treatment (1 withdrew consent, 2 withdrew due to COVID-19 concerns), 2 patients met SU monitoring rules (pre-dose SU >6 mg/dL at 2 consecutive visits, nonresponders) and discontinued pegloticase, 5 were ongoing treatment. All patients experienced initial substantial reductions in SU, which was sustained in the majority; 2 met monitoring rules. No notable eGFR changes were observed. In patients who completed treatment, HAQ pain and disability improved by 26.7 ± 30.3 and 0.2 ± 0.5, respectively, at Week 24 (n=10). 7 SAEs (2 cellulitis, duodenal ulcer, sepsis, a-fib, diverticulitis, and localized infection), all deemed unrelated to pegloticase, were reported in 5 patients. No anaphylaxis or infusion reaction events have occurred.

Conclusion: On-going results from the PROTECT trial demonstrate promising outcomes treating uncontrolled gout in KT recipients with pegloticase with a substantial decrease in SU levels after initiating pegloticase therapy, which is maintained for the majority of patients. Patients also demonstrate a clinically meaningful reduction in pain (HAQ pain) and disability (HAQ-DI) with a stable eGFR. This phase 4, multicenter, open-label, efficacy and safety study will reach completion in Fall 2021.

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Disclosure: A. Abdellatif, Horizon Therapeutics plc, 2, 6, Amgen, 2, 6, Janssen, 2, 6, Relypsa, 2, 6, Keyrex, 2, 6, Mallinkrodt, 2, 6, Natera, 2, 6; **L. Zhao**, Horizon Therapeutics plc, 3, 11; **P. Peloso**, Horizon Therapeutics plc, 3, 11; **K. Cherny**, Horizon Therapeutics plc, 3, 11; **B. Marder**, Horizon Therapeutics plc, 3, 11; **J. Scandling**, Horizon Therapeutics plc, 2; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5.

Abstract Number: 0666

Process Mapping Gout Hospitalizations: A Deep Dive into an Avoidable Epidemic

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Hospital admissions for gout flares have increased dramatically in recent years. Strategies to reduce hospitalizations and improve uptake of urate-lowering therapy (ULT) are needed. We performed an in-depth review of gout hospitalizations at our centre, incorporating stakeholder input and process mapping, to identify strategies to prevent admissions.

Methods: We retrospectively reviewed all emergency department (ED) attendances and hospital admissions for gout flares at two large hospitals in London, UK, from 1st October 2020 to 31st December 2020. Primary and secondary admission diagnoses of gout were included. Data on multiple aspects of hospital and post-discharge care were analysed, including ULT initiation/uptitration, discharge delays and re-admission rates. A process map of the inpatient journey was constructed with input from multiple stakeholders, including patients and clinicians, and strategies to address care barriers were identified.

Results: Detailed case reviews were performed on 68 ED attendances or hospital admissions for gout flares. There was initial diagnostic uncertainty in 32 patients (47%); however, specialist input was rarely sought in ED, and joint aspiration was performed in only 9 patients, with a median delay of 3 days. For the 22 admitted patients, the median length of stay was 11 days (8 days for primary admissions; 17 days for secondary admissions). 18 patients (82%) had discharge delays, including delays in seeking rheumatology input and treatment of comorbid conditions. Forty patients (59%) had pre-existing gout, of whom 25% were on ULT at presentation (mean serum urate level, 6.6 mg/dL). ULT initiation and/or uptitration occurred in 7 patients (10%) during admission or in ED. Of 60 patients with post-discharge follow-up data available, 20 (33%) initiated and/or uptitrated ULT within 6 months (median delay, 32 days), 35 patients (58%) remained on no ULT, and only 2 patients (3%) achieved target serum urate levels. Seven patients (10%) re-presented to hospital within 6 months of discharge.

Through iterative process mapping and stakeholder input, strategies to address care barriers observed during gout hospitalizations were identified. Strategies included initiation of ULT during flares, treat-to-target ULT uptitration coordinated between secondary and primary care, provision of disease-specific patient education and flare management packs, and timely specialist input with joint aspiration and steroid injection as indicated.

Conclusion: We identified multiple barriers to optimal hospitalized gout care and strategies to address them. Effective implementation of evidence-based interventions during hospitalizations for gout could transform care for patients, reduce length of stay, and prevent re-admissions.

Disclosure: M. Russell, Lilly, 6, Pfizer, 6, UCB, 6, Menarini, 6; **B. Ellis**, Cellen Health, 1, Pfizer, 1; **B. Clarke**, Abbvie, 6; **D. Nagra**, None; **J. Galloway**, Abbvie, 6, Biovitrum, 6, BMS, 6, Celgene, 6, Chugai, 6, Gilead, 6, Janssen, 6, Lilly, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sanofi, 6, Sobi, 6, UCB, 6.

Abstract Number: 0667

Active Screening for Gout Permits Identifying a Larger Cardiovascular Population at High Mortality Risk

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: We have recently noted by active screening that about a third of gout cases in the cardiovascular population is not registered in records (Calabuig, *Front Med* 2020), highlighting the value of field studies. This study aims to assess whether gout screening in patients hospitalized for cardiovascular events may also help identify patients at higher risk of mortality after discharge.

Methods: A retrospective cohort field study carried out on 266 patients admitted for cardiovascular events in the Cardiology, Neurology and Vascular Surgery units of a tertiary centre in Spain. The presence of gout was established by records review and face-to-face interview, according to the 2015 ACR/EULAR criteria. The occurrence of mortality during follow-up and its causes were obtained from electronic medical records. The association between gout and subsequent mortality was tested using Cox regression models. Whether covariates affected the gout-associated mortality was also studied.

Results: Of 266 patients recruited at baseline, 17 were excluded due to loss to follow-up (>6mo), leaving a final sample of 249 patients (93.6%). Thirty-six cases (14.5% of the sample) were classified as having gout: twenty-three (63.9%) had a previously registered diagnosis, while 13 (36.1%) had not and was established by the interview.

After discharge, the mean follow-up was 19.9 months (SD ±8.6), with a mortality incidence of 21.6 deaths per 100 patient-years, 34.2% by cardiovascular causes.

Gout significantly increased the risk of subsequent all-cause mortality, with a hazard ratio (HR) of 2.01 (95%CI 1.13 to 3.58). The association remained significant when the analysis was restricted to gout patients with a registered diagnosis (HR 2.89; 95%CI 1.54 to 5.41).

The adjusted HR for all-cause mortality associated with gout was 1.86 (95% CI 1.01-3.40). Regarding the causes of death, both cardiovascular and non-cardiovascular were numerically increased.

Secondary variables raising the mortality risk in those with gout were age (HR 1.07; 1.01 to 1.13) and coexistent renal disease (HR 4.70; 1.31 to 16.84), while gender, gout characteristics or traditional risk factors showed no impact.

Conclusion: Gout was confirmed as an independent predictor of subsequent all-cause mortality in patients admitted for cardiovascular events. Active screening for gout allowed identifying a larger population at high mortality risk and may help tailor optimal management to minimize the cardiovascular impact.

Disclosure: S. **Ruiz-Simón**, None; **I. Calabuig**, None; **M. Gómez-Garberí**, None; **M. ANDRES**, Menarini, 6, Grunenthal, 5, 6.

Abstract Number: 0668

Patient Perspectives and Preferences Regarding Gout and Gout Management: Impact on Adherence

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Patient-centered management is becoming increasingly important in gout, but there are limited studies exploring patients' perspectives and preferences. We aimed to investigate patients' perspectives and preferences regarding gout and gout management, and their impacts on adherence to urate lowering therapy (ULT).

Methods: A paper-based survey was performed in patients with gout seen at the rheumatology outpatient clinics of 16 tertiary hospitals. The survey included questions regarding demographics, comorbidities, gout attacks, current treatment and adherence, and patients' perspectives and preferences regarding gout and gout management. Multivariate regression analysis was performed to determine the factors associated with ULT adherence.

Results: Of 809 surveyed patients with gout, 755 (94.5%) were using ULT. Among those using ULT, 89.1% had ≥ 80% adherence to ULT. Majority of the patients knew management strategies to some extent (94.8%), perceived gout as a life-long disease (91.2%), and were making efforts toward practicing at least one lifestyle modification (89.2%). Most patients (71.9%) obtained information about gout management during their clinic visits. Approximately half of the patients (53.6%) preferred managing their disease with both ULT and lifestyle modification, 28.4% preferred ULT only, and 17.4% preferred lifestyle modification only. Adherence was better in patients with older age (odds ratio [OR] 1.03), those with better knowledge of gout management strategies (OR 3.56), and those who had preference for ULT (OR 2.07).

Conclusion: Patients' perspectives and management preferences had high impacts on adherence to ULT in gout. Consideration of patients' perspectives and preferences is important for achieving the desired clinical outcome in gout.

Patients' perspectives and preferences regarding gout and gout management

	Total (N=809)	Patients receiving ULT (n=755)		
		ULT adherence≥80% (n=673)	ULT adherence<80% (n=82)	*P*
Know management strategies				
Know well	299 (37.0)	258 (38.3)	23 (28.0)	0.063
Know a little	467 (57.8)	387 (57.5)	52 (63.4)	
Do not know	42 (5.2)	28 (4.2)	7 (8.5)	
Perceive gout as a lifelong disease				
Strongly agree	344 (42.5)	297 (44.1)	28 (34.1)	0.322
Agree	394 (48.7)	315 (46.8)	45 (54.9)	
Disagree	16 (2.0)	15 (2.2)	1 (1.2)	
Strongly disagree	27 (3.3)	24 (3.6)	3 (3.7)	
Do not know	28 (3.5)	22 (3.3)	5 (6.1)	
Efforts toward making lifestyle modifications				
Any[a]	722 (89.2)	606 (90.0)	69 (84.1)	0.101
Regular exercise	449 (55.6)	380 (56.5)	40 (48.8)	0.181
Dietary modification	417 (51.6)	362 (53.8)	34 (41.5)	0.035
Alcohol restriction	614 (75.9)	522 (22.4)	25 (30.5)	0.104
Education preferences about gout management				
During clinic visit	582 (71.9)	492 (73.1)	57 (69.5)	0.490
Health education program	15 (1.9)	13 (1.9)	0 (0)	0.381
TV and radio programs	83 (10.3)	70 (10.4)	6 (7.3)	0.381
Written information (books, magazines, pamphlets)	33 (4.5)	30 (43)	1 (1.2)	0.239
Internet searching	283 (35.0)	229 (34.0)	36 (43.9)	0.077
Friends/family members with gout	58 (7.2)	50 (7.4)	5 (6.1)	0.661
Never sought	28 (3.5)	21 (3.1)	1 (1.2)	0.498
Treatment preferences				
ULT only	230 (28.4)	204 (30.3)	13 (15.9)	0.006
Lifestyle modification only	141 (17.4)	104 (15.5)	23 (28.0)	0.004
ULT and lifestyle modification	434 (53.6)	362 (53.8)	45 (54.9)	0.852
Others[b]	8 (1.0)	6 (0.9)	2 (2.4)	0.212

Data are presented as number (%). ULT = urate lowering therapy.

[a] Practicing at least one of regular exercise, dietary modification, and alcohol restriction.

[b] Others include natural supplements, herbal remedies, stress management, and joint injection.

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Abstract Number: 0669

Early-Onset Gout (EOG) Patients Are an Important and Recalcitrant Phenotype Warranting Further Investigation: A Systematic Review

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

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Background/Purpose: Data suggests that the number of patients with early-onset gout (EOG), defined as patients under the age of 40 years, is increasing[1]. There is a paucity of data related to the clinical features, comorbidity profile, and response to treatment for patients presenting with EOG although international guidelines recommend urate lowering therapy be initiated at time of diagnosis[2,3].

Methods: A systematic review of the literature was conducted to examine publications and abstracts providing insight into the overall profile of EOG patients. A comprehensive search was conducted in the PubMed Database and ACR Archived Abstracts to identify relevant publications. Identical Search Terms were used in both databases, and a full review of EOG literature identification and inclusion/exclusion criteria can be found in **Figure 1**.

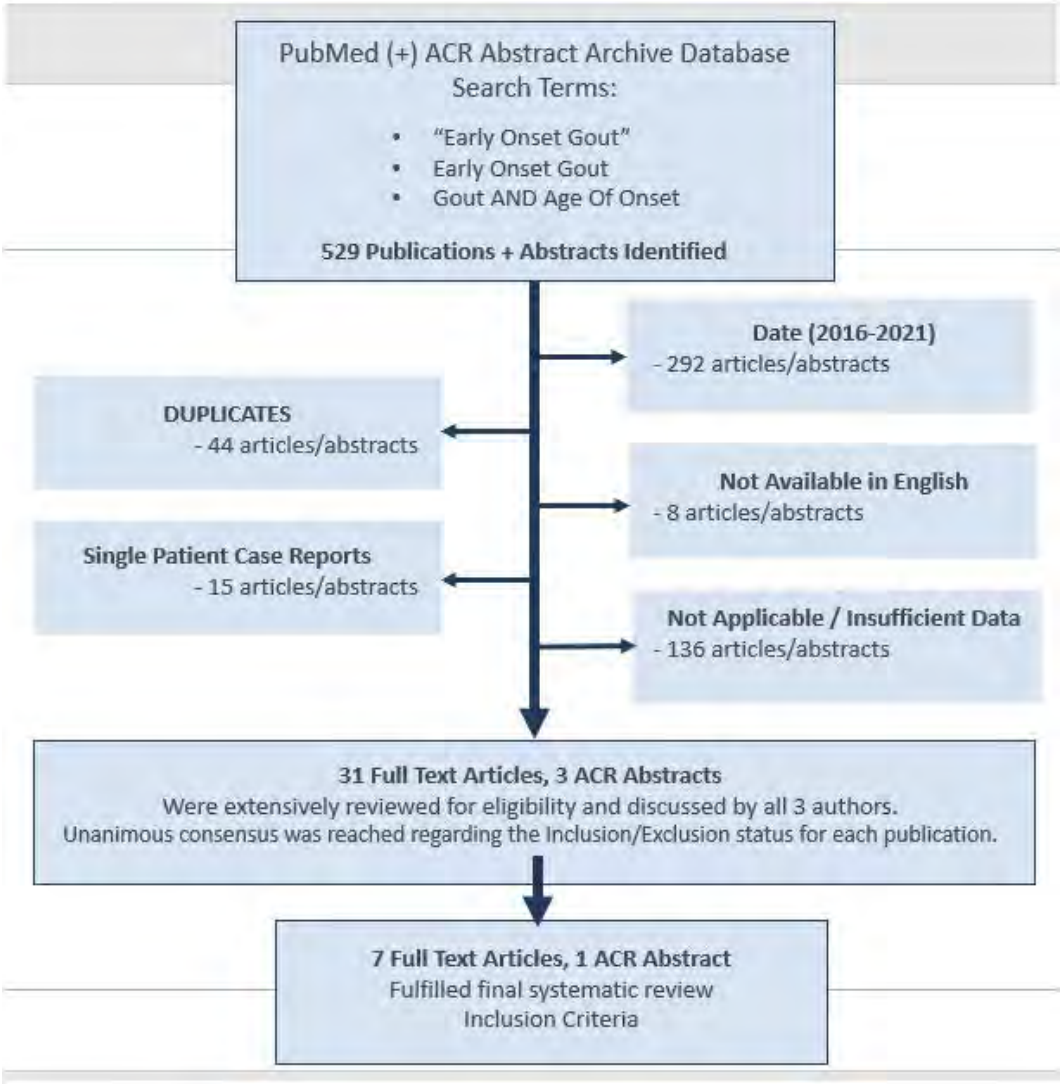

Figure 1. Flowchart of Early-Onset Gout Literature Identification and Selection.

Table 1. Clinical Features Analysis: Early-Onset Gout vs. Common Gout/Late-Onset Gout

Study	Patients, (n)	Gout PRECEDES onset of Cadio-Metabolic Comorbidities / Lower number of Comorbidities at Disease Onset	More Likely to have Preserved Renal Function	More Severe Joint Disease (recent flares frequency, polyarticular disease)	Less likely to achieve SU < 6mg/dL Or Higher baseline SU*
Pascart et al. (2019) GOSPEL 4 – Patients with early onset gout develop earlier severe joint involvement and metabolic comorbid conditions	985	✓	✓	✓	✓
Yan et al. (2019) Clinical Characteristics of Early-Onset Gout in Outpatient Setting	327	✓	✓	✓	✓
Zhang et al. (2016) Clinical Characteristics of early- and late-onset gout: a cross sectional observational study from a Chinese gout clinic	778	✓	✓	✓	✓*

Results: The search retrieved 529 references (**Fig 1**). 31 articles and 3 abstracts were reviewed for eligibility. 8 publications were included in the final review. 5 focused on the clinical characteristics of EOG patients; 3 of the 5 were retrospective or cross-sectional analyses comparing EOG patients to a group of Common Gout (CG) patients. All three cohorts with comparisons produced consistent insights into the clinical manifestations of EOG patients: either gout preceded the onset of cardio-metabolic comorbidities or fewer comorbidities were present at the time of gout diagnosis in EOGs; a large majority of EOGs had preserved renal function; EOGs had more severe joint disease (assessed by flare rates/polyarticular disease); finally all reported EOGs were less likely to achieve a target serum urate (SU) < 6 mg/dL or had higher SU levels at baseline compared to CG patients (**Table 1**). The remaining 3 publications focused on EOG patients' genetic predisposition for acquiring gout, concluding both ABCG2 and non-ABCG2 dysfunctional polymorphisms are more prevalent and likely contribute to the development of EOG.

Conclusion: The data reviewed examining EOG vs. CG comparators all produced consistent results. EOG patients are recalcitrant to ULTs, and present with more severe disease compared to CG patients.

SNPs (ABCG2, and other common and rare SNPs) that encode genetically dysfunctional urate transporters likely play an extensive role in development of EOG. The reviewed clinical and genetic data support the theory that gout operates within a "Common Disease, Multiple Common and Rare Variant" model.

EOG patients presented with less cardio-metabolic comorbidities upon diagnosis, suggesting a temporal separation between EOG diagnosis and development of other comorbidities. This suggests a window of opportunity to impact the development of comorbidities associated with gout.

Disclosure: A. Amatucci, Horizon Therapeutics, 3, 8; **B. LaMoreaux**, Horizon Therapeutics plc, 3, 11; **D. Bulbin**, Novartis, 2, Alexion, 2, 6, Sanofi, 6.

Abstract Number: 0670

Hemochromatosis Is Associated with CPPD Through Iron's Effect on Bone

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SESSION INFORMATION
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Background/Purpose: Hemochromatosis (HH) is one of the strongest known risk factors for calcium pyrophosphate (CPP) crystal deposition. The pathogenic mechanisms causing CPP crystal formation in HH patients remain unknown. CPP crystal formation is associated with increased levels of inorganic pyrophosphate (PPi). This process is controlled by transporters of extracellular ATP such as ANK, and a series of ectoenzymes that hydrolyze ATP or degrade PPi. Recently, alterations in bone such as increased osteoclastogenesis, have also been implicated in CPPD. Most end organ damage in HH is attributed to iron deposition; and *in vitro* studies mimic HH by exposing cells or tissues to high levels of iron. Prior work showed no clear effects of iron on factors affecting CPP crystal formation in articular cartilage. We sought to investigate the hypothesis that iron contributes to CPP crystal formation by stimulating osteoclastogenesis. We also explored other effects of iron on PPi regulatory factors in osteoclasts and osteoblasts.

Methods: RAW264.7 cells (pre-osteoclasts) were incubated with 10-20 ng/ml RANKL and 10-100 μM ferric ammonium citrate (FAC) or no additives for 4-6 days. Osteoclast formation was assessed using a quantitative TRAP assay. Many of the effects of iron are attributed to increased reactive oxygen species (ROS). We measured ROS in RAW

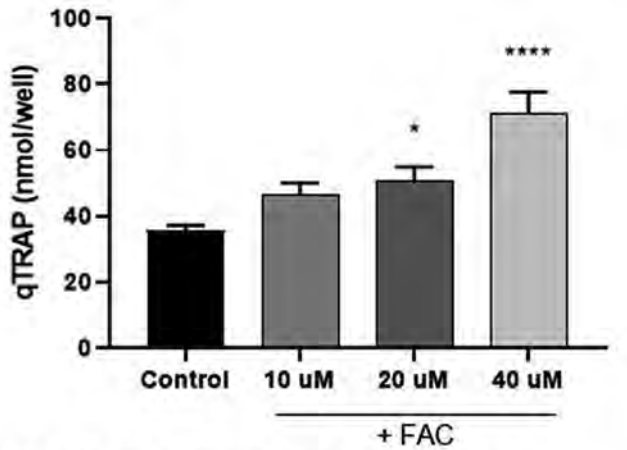

Figure 1. Iron increases osteoclastogenesis in pre-osteoclasts. RAW cells were incubated with 10 ng/ml RANKL and 10-40 μM FAC or no additives for 6 days. Osteoclast formation was assessed using a quantitative TRAP assay. Statistically significant differences were observed at 20 μM ($p=0.03$) and 40 μM ($p<0.0001$) FAC compared to control.

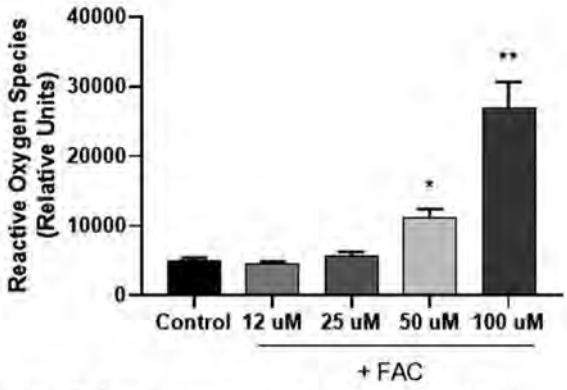

Figure 2. Iron increases reactive oxygen species in osteoclasts. RAW cells were incubated with 20 ng/ml RANKL and 12-100 μM FAC or no additives for 4 days. ROS formation was assessed using DCFDA dye. Statistically significant differences were observed at 50 μM (p=0.04) and 100 μM (p=0.002) FAC compared to control.

cells using DCFDA dye (Sigma). Because high levels of RANKL on osteoblasts stimulate osteoclast formation, we measured RANKL on osteoblasts in the presence of iron. Human osteoblasts (fOBs, Cell Applications) were exposed to 10-100 μM FAC or no additives for 9 days. RANKL levels were measured using RT-PCR. Other factors known to contribute to bone PPi homeostasis were measured in fOBs, including alkaline phosphatase (AP) activity, ANK levels, and levels of PPi. ANK was measured with RT-PCR and AP activity was measured with an assay from Abcam. PPi was measured in the conditioned media of fOBs and RAW cells using a highly sensitive radiometric assay.

Results: Ten-40 μM FAC significantly increased TRAP activity on RAW cells incubated with submaximal concentrations of RANKL at 6 days ($p< 0.0001$, N=15). Forty μM FAC increased TRAP activity by 2-fold (Figure 1). FAC also increased ROS ($p< 0.0001$, N=5) (Figure 2). Similar concentrations of FAC had no effects on fOB RANKL levels at 9 days in the absence or presence of differentiation factors (Data not shown). There was a small but significant decrease in alkaline phosphatase in fOBs at 100 μM FAC. Levels were 4.03± 1.3 nmol/well in fOBs with no iron exposure and 2.35± 0.6 U with FAC (p=0.02, n=5). FAC had no effects on ANK mRNA, and PPi levels were unmeasurable in both RAWs and fOBs. FAC toxicity was monitored using an LDH assay and was not significant at the concentrations tested.

Conclusion: We confirm here that iron increases TRAP positive osteoclasts *in vitro*. Increased osteoclast number is associated with premature severe CPPD caused by a loss of function mutation in osteoprotegerin. Further work will be necessary to determine the mechanisms through which osteoclast excess causes CPPD, but these findings add additional support to the hypothesis that some forms of CPDD are related to primary abnormalities in bone.

Disclosure: J. Velasco, None; **C. Gohr**, None; **E. MItton-Fitzgerald**, None; **A. Rosenthal**, None.

Abstract Number: 0671

Concomitant Immunomodulation and Pegloticase Therapy: Experiences with a Variety of Immunomodulatory Agents in Two Community Rheumatology Practices

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
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Background/Purpose: Patients with uncontrolled or refractory gout have heavy disease burden,[1] but few treatment options. Pegloticase is effective for lowering serum urate (SU) in these patients, though efficacy is limited by anti-drug antibody development in some patients.[2] Administering pegloticase in conjunction with an immunomodulating therapy meaningfully increased the number of patients with sustained urate lowering while on treatment.[3] However, case data in the literature remain limited. The current study reports experience from two busy rheumatology practices where immunomodulating therapy is routinely prescribed in patients undergoing pegloticase treatment.

Methods: Patients who underwent concomitant pegloticase/immunomodulation therapy (initiated 2017 or later) were included. Patient and treatment characteristics were examined, along with the proportion of patients who were considered pegloticase responders (≥12 pegloticase infusions and SU < 6 mg/dL at infusion 12). Patients who remained on therapy, but had not yet reached infusion 12 were not included in responder rate analyses. All patients received pre-infusion prophylaxis (125 mg IV methylprednisolone or 100 mg hydrocortisone, 180 mg oral fexofenadine or 25 mg IVP diphenhydramine). Estimated glomerular filtration rate (eGFR) was also examined before therapy and at last infusion. Data are presented as mean±SD or %.

Results: 34 patients (79% male, 62.4±16.3 years) with uncontrolled gout (SU = 9.1±2.0 mg/dL, 91% had tophi, 14.7±13.4 year gout history) were included. The most common comorbidities were hypertension (76%), obesity (71%), osteoarthritis (68%), and chronic kidney disease (CKD, 47%). Baseline eGFR was 65.4±25.2 ml/min/1.73 m^2 and 41% had eGFR< 60 ml/min/1.73 m^2. A mean of 14.6±7.1 pegloticase infusions were administered over 28.5±14.9 weeks. Immunomodulator co-therapy was initiated prior to (5.3±3.0 weeks, n=32) or at (n=2) first pegloticase infusion and included subcutaneous (subQ) methotrexate (MTX; 15.4±4.9mg/week [range: 10-25 mg/week], n=20), oral MTX (15.3±3.6 mg/week [range: 7.5-20 mg/week], n=9), oral mycophenolate mofetil (MMF; all 1000 mg/day, n=3), and oral azathioprine (AZA; all 100 mg/day, n=2). Overall treatment responder rate was 89.3% (n=28). Response rates were 93% for subQ MTX (n=14), 89% for oral MTX (n=9), 100% for MMF (n=3), and 50% for AZA (n=2). eGFR remained essentially unchanged during therapy (+10.3±16.9 ml/min/1.73 m^2) and CKD stage remained stable or improved in 85% of patients (Stage 1 to 2 [n=1], Stage 2 to 3a [n=1], Stage 3a to 3b [n=2],). 34 gout flares occurred in 19 patients (56%), no infusion reactions or infections were noted, and no new safety concerns were identified.

Conclusion: These data provide further support for concomitant immunomodulator/pegloticase therapy, showing similar efficacy rates to both an open-label trial with oral MTX (79%)[4] and a systematic literature review of all immunomodulators (83%).[3]

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Disclosure: A. Broadwell, Horizon, 6; **J. Albert**, Horizon, 6; **B. LaMoreaux**, Horizon Therapeutics plc, 3, 11; **L. Padnick-Silver**, Horizon Therapeutics plc, 3, 6.

Abstract Number: 0672

Does Obesity Affect Gout Risk Differently Among Genetically Predisposed Individuals?: Sex-Specific Prospective Cohort Study Findings over >32 Years

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Background/Purpose: Two recent analyses of the Global Burden of Disease Study reported on the rising global burden of gout (Safiri A&R 2020, Xia Rheumatology 2020). Addressing obesity, a major modifiable risk factor for gout, may help alleviate this burden. However, it is also recognized that there is a significant genetic contribution to the risk of hyperuricemia and gout according to genome-wide association studies (GWAS) (Tin Nat Genet 2019). It is unknown whether obesity affects gout risk differently among genetically predisposed individuals. Our objective was to prospectively investigate the association between obesity and the risk of incident gout according to genetic predisposition in two large US cohorts over >32 years, stratified by sex.

Methods: We investigated the joint effects of obesity and genetic predisposition on the future risk of incident gout in 18,247 women in the Nurses' Health Study (NHS) over 34 years and 10,899 men in the Health Professionals Follow-Up Study (HPFS) over 32 years. We derived a genetic risk score (GRS) using 114 serum urate single nucleotide polymorphisms from the latest GWAS (Tin), with higher GRS indicating higher genetic predisposition for hyperuricemia. We determined gene-body mass index (BMI) interactions among men and women separately. We also calculated the population attributable risk (PAR) for excess weight according to GRS stratum.

Results: We ascertained 1361 incident cases of self-reported gout in NHS and 1704 in HPFS. The baseline clinical gout risk factors were similar regardless of genetic predisposition within each cohort (**Table 1**). Among women, the multivariable relative risks (RR) of gout were 1.0, 1.24 (0.98 to 1.57), and 2.60 (2.09 to 3.24) among those with GRS below the mean and 1.55 (1.25 to 1.91), 2.74 (2.24 to 3.35), and 4.65 (3.80 to 5.68) among those with GRS above the mean for BMI categories < 25, 25-30, and >30, respectively (**Figure 1 and Table 2**). There was significant additive interaction with rate difference (RD) between BMI >30 relative to BMI ≤25 being 3.94 and 1.70/1000 person-years (PY) for GRS above and below the mean, respectively, resulting in relative excess risk due to interaction (RERI) of

Table 1. Baseline Gout Risk Factors by Genetic Scores in HPFS and NHS Participants

	HPFS		NHS	
	Genetic Score of 114 SNPs		Genetic Score of 114 SNPs	
	Below Mean (n = 5468)	Above Mean (n = 5431)	Below Mean (n = 9165)	Above Mean (n = 9082)
Age, years, mean (SD)	54.3 (8.6)	54.2 (8.7)	47.1 (6.9)	47.0 (6.9)
Systolic blood pressure, mm Hg, mean (SD)	128.7 (12.5)	128.7 (12.5)	123.9 (14.4)	124.2 (14.6)
Diastolic blood pressure, mm Hg, mean (SD)	81.3 (7.2)	81.2 (7.1)	78.8 (7.6)	79.1 (7.7)
Reported hypertension, %	21	21	15	17
BMI, kg/m^2, mean (SD)	25.6 (3.2)	25.6 (3.1)	24.5 (4.5)	24.5 (4.4)
Physical activity, MET-hours/week, mean (SD)	20.2 (23.5)	19.9 (23.7)	14.6 (20.8)	14.0 (19.3)
Alcohol, g/d, mean (SD)	12.1 (15.6)	12.4 (16.3)	6.5 (10.2)	6.6 (10.5)
Sweetened soft drink intake, servings/d, mean (SD)	0.3 (0.5)	0.3 (0.5)	0.3 (0.6)	0.3 (0.6)
Meat intake, servings/d, mean (SD)	1.6 (0.8)	1.6 (0.9)	1.1 (0.8)	1.1 (0.8)
Seafood intake, servings/d, mean (SD)	0.3 (0.3)	0.3 (0.3)	0.2 (0.2)	0.2 (0.2)
Low-fat dairy foods intake, servings/d, mean (SD)	1.0 (1.1)	1.0 (1.0)	0.9 (1.0)	0.9 (1.0)
High-fat dairy foods intake, servings/d, mean (SD)	1.3 (1.3)	1.3 (1.3)	1.4 (1.3)	1.4 (1.3)
Diuretic use, %	10.0	10.1	9.6	10.1

Values are age-adjusted (except for age).

1.48 (95% CI, 0.82 to 2.13) (p< 0.01). The results for men were similar in that the RR of excess weight appeared larger among men with GRS above the mean than below the mean (**Figure 1 and Table 2**); there was a similar trend, with a RD of 7.57 and 5.01/1000 PY for GRS above and below the mean, respectively, resulting in RERI of 0.58 (95% CI, -0.08 to 1.23) (p=0.08). Among women, excess weight accounted for a larger proportion of gout cases among those with GRS above the mean (PAR 48.5%, 95% CI, 38.8 to 55.9) compared to those with GRS below the mean (PAR 29.0%, 95% CI, 10.5 to 42.1). The PARs for men were similar within GRS strata (31.6% and 29.7%, respectively).

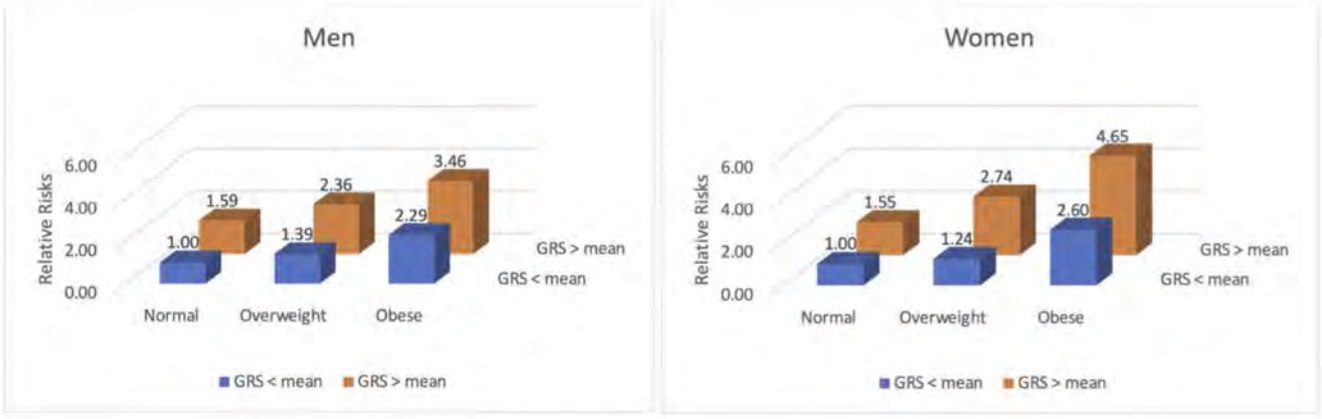
Conclusion: In these large prospective studies of men and women, we found a significant interaction between obesity and genetic predisposition among women, and a trend towards this in men. Maintaining healthy weight is an important gout prevention strategy, particularly among those with underlying genetic risk.

Table 2. Joint Association of Body Mass Index and Genetic Risk Score on the Relative Risk of Incident Gout

	HPFS [Men]			Additive Interaction (RERI)*			Multiplicative Interaction*		
	BMI					P			P
GRS	<25	25-30	>30	Estimate	95% CI	Value	Estimate	95% CI	Value
Below Mean	1.0 (ref)	1.39 (1.16, 1.66)	2.29 (1.84, 2.85)	0.58	-0.08, 1.23	0.08	0.94	0.71, 1.24	0.65
Above Mean	1.59 (1.33, 1.92)	2.36 (1.99, 2.78)	3.46 (2.93, 4.23)						
	NHS [Women]			Additive Interaction (RERI)*			Multiplicative Interaction*		
	BMI					P			P
GRS	<25	25-30	>30	Estimate	95% CI	Value	Estimate	95% CI	Value
Below Mean	1.0 (ref)	1.24 (0.98, 1.57)	2.60 (2.09, 3.24)	1.48	0.82, 2.13	<0.01	1.14	0.57, 1.51	0.33
Above Mean	1.55 (1.25, 1.91)	2.74 (2.24, 3.35)	4.65 (3.80, 5.68)						

*Comparing BMI >30 vs. <25

Figure 1: Joint Association of Genetic Risk Score (GRS) and Body Mass Index (BMI) on the Relative Risk of Incident Gout



Disclosure: C. Yokose, None; **N. McCormick**, None; **N. Lu**, None; **A. Joshi**, None; **H. Choi**, None.

Abstract Number: 0673

The Impact of Allopurinol on Blood Pressure and Renal Outcome in Gout Patients: A Retrospective Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The relationship between change in serum uric acid level and progression of chronic kidney disease and hypertension is still conflicting. In this study, we aim to determine if lowering uric acid had any beneficial effect on blood pressure (BP) and kidney function in gout patients.

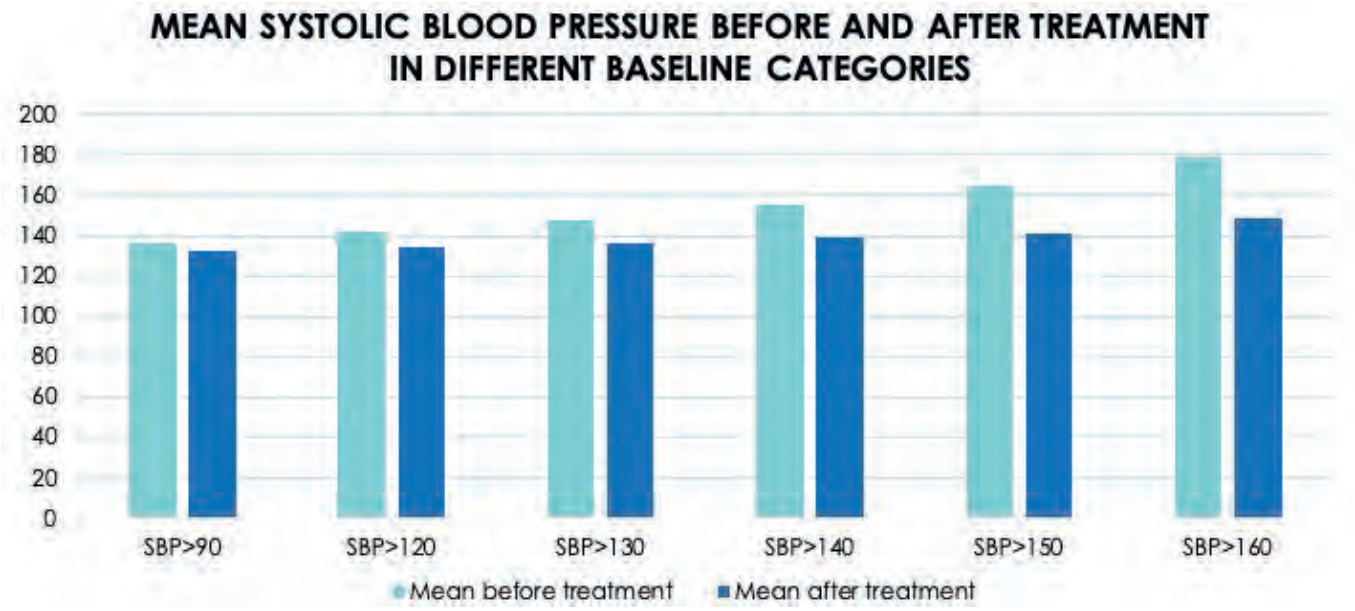
Methods: This was a retrospective study conducted in an outpatient clinic-based setting from December 2019 to December 2020. We obtained ethical approval from the Institutional Review Board of our hospital.

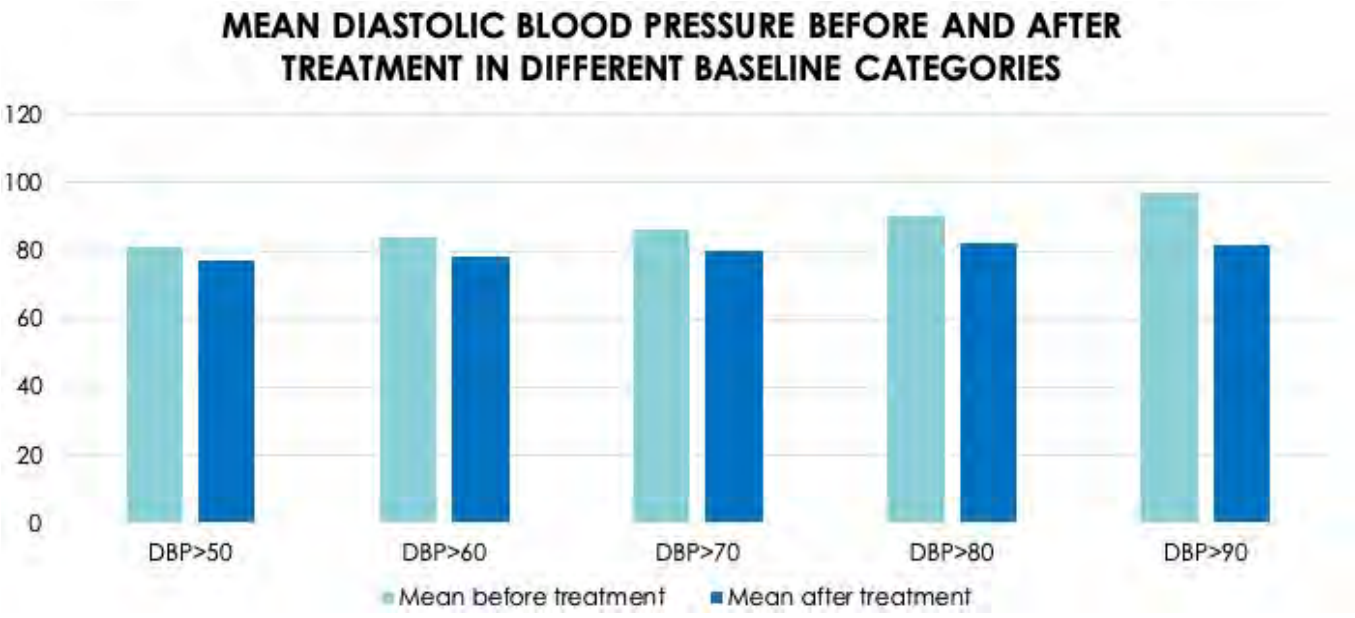
We recruited 77 patients on allopurinol therapy for gout based on the inclusion/exclusion criteria. All patients satisfied the 2015 Gout Classification Criteria by the American College of Rheumatology. Clinical determinants included mean BP (MBP), systolic BP (SBP), diastolic BP (DBP), estimated glomerular filtration rate (eGFR), creatinine, and uric acid. The change in clinical determinants was charted before initiation of allopurinol therapy and after being on treatment for 3-6 months. Patients clinical data was further divided into different subgroups based on gender male or female, age < 60 or >60, diabetic or non-diabetic, hypertensive or non-hypertensive, eGFR < 30, 30-59 and >60, SBP into six, and DBP into five subsets based on baseline SBP and DBP respectively. Potential confounders, like baseline co-morbidities and the antihypertensive treatment, were also charted. Patient data were recorded and analyzed through Excel sheets to obtain a p-value to explain the statistical significance.

Results: Patients on allopurinol treatment for gout for 3-6 months, showed a significant reduction in MBP 3.2 mm Hg (p-value 0.034) particularly in the group >60 years of age. SBP mean reduction was 3.7 mm Hg but didn't reach statistical significance. However, in the subgroup of patients with eGFR< 30, the reduction of SBP was statistically significant with a p-value of 0.05. DBP reduction was statistically significant in all patients with a mean reduction of 3.8 mm Hg (p-value 0.008). When we analyzed subgroups separately based on baseline SBP and DBP the greatest change was seen for the highest baseline systolic and diastolic BP and was statistically significant. The eGFR improved in subgroups of female, age >60, eGFR < 30, and eGFR 30-59, and creatinine improved in a subgroup of

The mean of different clinical determinants before and after treatment with Allopurinol

Clinical Determinants	Mean Before Treatment	Mean After Treatment	P-value
Mean Blood Pressure	98.5	95.3	0.034
Systolic Blood Pressure	136.3	132.6	0.087
Diastolic Blood Pressure	80.5	76.7	0.008
Estimated GFR	66.4	66.5	0.963
Creatinine	1.2	1.2	0.704
Uric Acid	8.1	5.6	<0.001





eGFR < 30, but didn't reach statistical significance. The uric acid reduction was highly statistically significant in all groups (p-value < 0.001).

Conclusion: Through this study, we were able to find a statistically significant change in MBP, DBP, and SBP (in a subgroup of patients with eGFR< 30) with allopurinol treatment. Though we were not able to demonstrate any statistically significant effect on eGFR and creatinine, there was an improvement noted in kidney function in a few subgroups. Such a result could be due to the small sample size for our study. The effect of allopurinol can be utilized in the future for BP control in hyperuricemic patients.

Disclosure: A. Faraz, None; **S. Islam**, None; **J. Grisanti**, None; **S. Iqbal**, None.

Abstract Number: 0674

A Behavioral Intervention to Improve Gout Outcomes in African Americans with Gout: A 12-month Multicenter, Randomized Controlled Trial

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Gout outcomes and severity are worst in African Americans compared to Caucasians with gout. Racial Disparities in gout are well-described. Few or no data exist for African Americans with gout from observational studies or randomized controlled trials (RCTs). Our objective was to assess if a culturally appropriate gout storytelling intervention is superior to an attention control for improving gout outcomes.

Methods: In a 12-month, multicenter, randomized controlled trial (RCT), African American (AA) Veterans with gout were randomized to gout storytelling intervention vs. a stress reduction video (1:1 ratio). The primary outcome was urate-lowering therapy (ULT) adherence measured with the MEMSCap™, an electronic monitoring system to measure medication adherence. Secondary outcomes included gout flares, serum urate, gout-specific health-related quality of life (HRQOL), and medication satisfaction

Results: The 306 male AA Veterans with gout, who met the eligibility criteria were randomized to the gout storytelling intervention (n=152) or stress reduction video (n=152; control); 261/306 (85%) completed the 1-year study. The mean age was 64 years, body mass index (BMI) was 33 kg/m^2, and gout disease duration was 3 years. The ULT MPR by MEMSCap™ (primary outcome) was similar in the intervention vs. control groups at each time point: 3-months, 73% versus 70%; 6-months, 69% versus 69%; 9-months, 66% versus 67%; and 12 months, 61% versus 64% (p >0.05 each). The number of gout flares in the last month were similar in the treatment versus control groups except at 9-months: 3-months, 1.4 versus 1.4 (p=0.55); 6-months, 1.3 versus 1.6 (p=0.53); 9-months, 0.7 versus 1.3 (p=0.03); and 12-months, 0.7 versus 1.0 (p=0.20; Figure 1). Serum urate levels and patient satisfaction with treatment were similar in the two groups at 6- and 12-months with no significant differences. Gout-specific health-related quality of life scores on GAQ-GIS were also similar in the treatment versus control group except lower/better scores in two subscale scores in the treatment group: gout medication side effects at 3-months, 32.8 vs. 39.6 (p=0.02); and unmet gout treatment need at 3-months, 30.9 vs. 38.2 (p=0.003), and at 6-months, 29.5 vs. 34.5 (p=0.03; Figure 1), respectively.

Conclusion: A culturally appropriate gout storytelling intervention was not superior to attention control for improving gout outcomes in AA Veterans with gout. More studies are needed to determine the subset of minorities with gout that can benefit from behavioral interventions such as this. We also need to design more effective behavioral interventions for people with gout, especially those with worse outcomes, such as racial/ethnic minorities.

Disclosure: J. Singh, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2,

Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **A. Joseph**, None; **S. Eisen**, None; **T. Shaneyfelt**, None.

Abstract Number: 0675

Urate-lowering Therapy for Prevention of Gout: Prespecified Analyses from the CKD-FIX Trial

Anushree Tiku[1], Neil Boudville[2], Fiona Brown[3], Alan Cass[4], Phiilip Clarke[5], Richard Day[6], Janak de Zoysa[7], Bettina Douglas[8], Randall Faull[9], David Harris[10], Carmel Hawley[11], Graham Jones[6], John Kanellis[3], Elaine Pascoe[11], Suetonia Palmer[12], Vlado Perkovic[13], Gopala Rangan[10], Donna Reidlinger[11], Laura Robison[11], Robert Walker[14], Giles Walters[15], David Johnson[11], Sunil Badve[13] and Nicola Dalbeth[7], [1]The George Institute of Australia, Sydney, Australia, [2]University of Western Australia, Perth, Australia, [3]Monash University, Melbourne, Australia, [4]Menzies School of Health Research, Darwin, Australia, [5]University of Oxford, Oxford, United Kingdom, [6]University of New South Wales, Sydney, Australia, [7]University of Auckland, Auckland, New Zealand, [8]Princess Alexandra Hospital, Brisbane, Australia, [9]University of Adelaide, Adelaide, Australia, [10]University of Sydney, Sydney, Australia, [11]University of Queensland, Brisbane, Australia, [12]University of Otago, Christchurch, New Zealand, [13]The George Institute for Global Health, Sydney, Australia, [14]University of Otago, Dunedin, New Zealand, [15]The Canberra Hospital, Canberra, Australia

SESSION INFORMATION

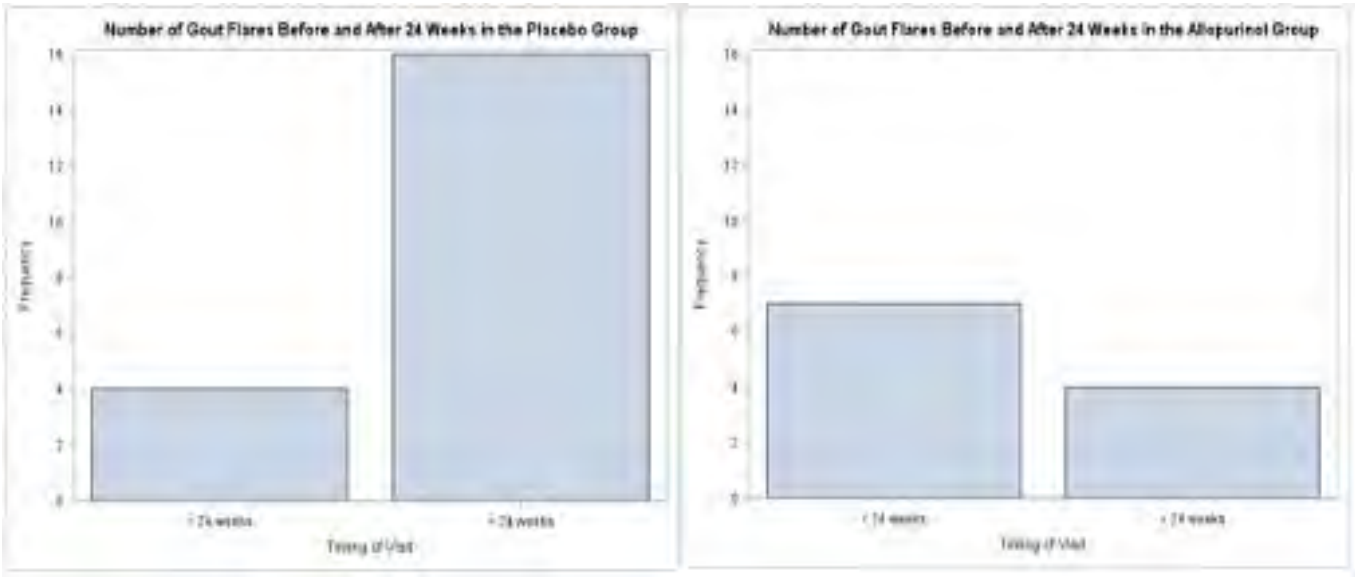
Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The CKD-FIX randomized controlled trial showed that allopurinol did not slow decline of estimated glomerular filtration rate (eGFR) over 104 weeks in patients with chronic kidney disease (CKD) at risk of progression. The aim of this pre-specified analysis was to assess if allopurinol prevents incident gout in the CKD-FIX trial population.



Number of gout flares before and after 24 weeks; placebo group shown in left panel, allopurinol group shown in right panel.

Methods: In the CKD-FIX trial, 369 adults with CKD stage 3 or 4, no history of gout, and risk of kidney disease progression (urinary albumin-to-creatinine ratio ≥265 mg/g or eGFR decrease ≥3.0 mL/min/1.73 m^2 in the preceding year) were randomized to receive placebo (n=184) or allopurinol up to 300mg daily (n=185). Gout flares were self-reported using a questionnaire at each study visit over 104 weeks. Additionally, the association of incident gout and baseline serum urate (normouricemia and hyperuricemia [based on a serum urate cut point of >6.8mg/dL], or as tertiles]) was analyzed.

Results: Three patients withdrew immediately after randomization. The remaining 363 patients (mean eGFR 31.7 mL/min/1.73 m^2, mean serum urate 8.2 mg/dL) were included in the analysis. At the end of the 12-week dose-escalation phase, 126 (69.2%) of 182 patients in the allopurinol arm were receiving 300mg daily. A total of 22 (6.1%) participants experienced 31 discrete flare episodes over 104 weeks (placebo group 20 flares in 13 patients; allopurinol group 11 flares in 9 patients). There was no significant difference between placebo and allopurinol groups in gout incidence. However, there were differences in timing of gout flares, with more flares in the allopurinol group in the first 24 weeks, and conversely more flares in the placebo group after 24 weeks (Figure, P=0.02). Across both groups, the most common affected joint region was the ankle. Of those participants who developed incident gout during follow-up, 19 (86%) had hyperuricemia at baseline. There was no association between incident gout and baseline serum urate stratified by hyperuricemia and normouricemia (P=0.14), however, there was an association between incident gout and baseline serum urate tertile, with the highest incidence of gout in those with serum urate in the highest tertile, that is, above 8.7mg/dL (P=0.004).

Conclusion: In people with CKD at risk of progression, incident gout is uncommon, and is associated with serum urate above 8.7mg/dL. Compared with placebo, allopurinol does not change the incidence of gout over a two year period, with more flares in the first 24 weeks of treatment, and fewer flares after 24 weeks.

Disclosure: A. Tiku, None; **N. Boudville**, None; **F. Brown**, None; **A. Cass**, None; **P. Clarke**, None; **R. Day**, None; **J. de Zoysa**, None; **B. Douglas**, None; **R. Faull**, None; **D. Harris**, None; **C. Hawley**, None; **G. Jones**, None; **J. Kanellis**, None; **E. Pascoe**, None; **S. Palmer**, None; **V. Perkovic**, None; **G. Rangan**, None; **D. Reidlinger**, None; **L. Robison**, None; **R. Walker**, None; **G. Walters**, None; **D. Johnson**, Baxter Healthcare, 2, 5, 6, 12, Travel Sponsorship, Fresenius Medical Care, 2, 5, 6, 12, Travel Sponsorship, AstraZeneca, 2, AWAK, 2, Bayer, 2, ONO, 6, 12, Travel Sponsorship, BI & Lilly, 6, Amgen, 12, Travel Sponsorship; **S. Badve**, None; **N. Dalbeth**, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5.

Abstract Number: 0676

Development, Refinement, and Validation of an Emergency Department Gout Flare Electronic Medical Record Alert

Lesley Jackson[1], Narender Annapureddy[2], Kenneth Saag[1], James Booth[3], Giovanna Rosas[1], Jeffrey Foster[1], Amy Mudano[1], Dongmei Sun[4], John Osborne[1], Tim Bongartz[5], Erik Hess[5], Colleen Lawrence[6], Leah Dunkel[6] and Maria I. Danila[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Department of Emergency Medicine, University of Alabama School of Medicine, Birmingham, AL, [4]Division of Clinical Immunology and Rheumatology, The University of Alabama at Birmingham, Birmingham, AL, [5]Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, TN, [6]Vanderbilt Institute for Clinical and Translational Research, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Key phrases and parameters used to identify acute gout flare in the gout flare alert. *Past medical history included the following terms (not case-sensitive): pmh, pmhx, hx, past medical history. †Pain locations included the following musculoskeletal sites: ankle, arm, elbow, leg, feet, finger, foot, hand, hip, knee, shoulder, thumb, toe, wrist

	Current gout in Chief Complaint	Both pain location + gout in Chief Complaint	Pain location in Chief Complaint + gout in problem list
Description	The term 'gout' listed before the past medical history* in the chief complaint	Both the term 'gout' and a 'pain location'† listed in chief complaint	'Pain location'† listed in the chief complaint or in the structured nursing form and 'gout' listed in the problem list
Examples	- captures "out of gout meds" - does not capture "pain in left knee past medical history gout" - does not capture "chest pain past medical history gout"	- does not capture "out of gout meds" - captures "pain in left knee past medical history gout" - does not capture "chest pain past medical history gout"	- captures "pain in left knee" with 'gout' listed in problem list - does not capture "chest pain" with 'gout' listed in problem list

Background/Purpose: Patients with acute gout are frequently treated in emergency departments (ED) and represent a typically underserved and understudied population. A key limitation of conducting gout research in the ED is the timely ability to identify potential gout patients during an ED encounter. The objective of our study was to develop a multi-criteria electronic medical record (EMR)-based gout flare alert for acute gout flares and determine its diagnostic properties for gout flare identification among ED patients.

Methods: The alert used EMR data entered by ED nursing staff and the medical problem list. The alert was triggered by: the term 'gout' preceding the past medical history in the chief complaint field, the term 'gout' and a musculoskeletal problem in the chief complaint, or the term 'gout' in the problem list and a musculoskeletal chief complaint (Table 1). We validated the presence/absence of gout through manual EMR review using adjudicated expert consensus (assessed with kappa coefficient) as the gold standard. We abstracted ED cases of possible gout patients in whom gout flare symptoms were not documented but who might have had gout based on other clinical parameters (e.g., those with an ICD-10 code for gout at the ED visit (M10.X), those who had an arthrocentesis performed in the ED and had an order placed for uric acid crystal analysis in the synovial fluid, and any patient who had an order for colchicine during their ED visit) to identify possible false negative cases.

Results: From January 1 to February 1, 2020, there were 38 patients with acute gout flare identified by the components of the gout flare alert and an additional 93 were identified as potentially having an acute gout flare and were

Table 2. Test characteristics of the electronic medical record gout flare alert system and the individual components of the algorithm. *listed are each of three components of the overall alert algorithm

	Alert cases identified n (%)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Gout Flare Alert, n = 38	38 (29)	70 (51 – 88)	80 (72 – 87)	42 (26 – 58)	93 (87 – 98)
Gout Flare Alert Subset #1*: Both pain location + gout in chief complaint	26 (20)	39 (19 – 59)	84 (77 – 91)	35 (16 – 53)	87 (80 – 93)
Gout Flare Alert Subset #2*: Current gout in chief complaint	8 (6)	22 (5 – 39)	97 (94 – 100)	63 (29 – 96)	85 (79 – 92)
Gout Flare Alert Subset #3*: Pain location in chief complaint + gout in problem list	8 (6)	17 (2 – 33)	96 (93 – 100)	50 (15 – 85)	85 (78 – 91)

included in the analysis of the alert characteristics. The positive predictive value (PPV) of the alert was 42% (95% CI [26 – 58%]) and the negative predictive value (NPV) was 93% (95% CI [87 – 98%]). The gout flare alert had a sensitivity of 70% (95% CI [51 – 88%]) and specificity of 80% (95% CI [72 – 87%]) (Table 2). Prevalence of a true gout flare was 16/38 (42%) among patients in whom the gout flare alert fired and 7/93 (8%) among patients in whom the gout flare alert did not fire. The kappa coefficient for agreement between the consensus expert determination of acute flare and the documented ED diagnosis of flare was 0.9. A second alert validation procedure occurred between October 24, 2020 to November 24, 2020. During this period, the gout flare alert had a lower overall PPV of 24% likely due to fewer gout flare cases seen in the ED due to the COVID-19 surge in our region.

Conclusion: We developed, refined, and validated a multi-component EMR gout flare alert with reasonable predictive properties to detect patients with an acute gout flare during the ED visit. This screening tool achieves good sensitivity and NPV, which preferentially increases the number of detected cases and allows the ED team to rule out false positives with secondary data. An automated EMR alert may help identify patients with acute gout flare in real time upon presentation to the ED. These patients may be approached for study recruitment or quality improvement strategies beyond the standard of care.

Disclosure: L. Jackson, None; **N. Annapureddy**, GSK, 2; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5; **J. Booth**, None; **G. Rosas**, None; **J. Foster**, None; **A. Mudano**, None; **D. Sun**, None; **J. Osborne**, None; **T. Bongartz**, None; **E. Hess**, None; **C. Lawrence**, None; **L. Dunkel**, None; **M. Danila**, Boehringer Ingelheim, 5, Amgen, 1, Amgen, 5, AbbVie, 1, Pfizer, 5, Pfizer, 11, Horizon, 5, Novartis, 1, WebMD, 12, writer.

Abstract Number: 0677

Pro-Inflammatory Diet and Increased Risk of Incident Female Gout: 30-Year Prospective Cohort Study of >170,000 Pre- and Post-Menopausal US Women

Natalie McCormick[1], Chio Yokose[2], Na Lu[3], Amit Joshi[1] and Hyon K. Choi[4], [1]Massachusetts General Hospital, Boston, MA, [2]Massachusetts General Hospital, Waltham, MA, [3]Arthritis Research Canada, Vancouver, BC, Canada, [4]Massachusetts General Hospital, Lexington, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Globally, the prevalence of gout is rising in females more than males,[1] but data on modifiable risk factors for female gout are scarce. Emerging evidence suggests inflammation may drive the progression from hyperuricemia to clinical gout,[2] but the role of extrinsic, modifiable sources of chronic inflammation on gout risk, such as diet, is unknown. Greater dietary inflammatory potential has been independently associated with increased risk of incident cardiovascular disease (CVD)[3] and type 2 diabetes (T2D),[4] conditions with higher prevalences among females with gout. We prospectively examined the relation between dietary inflammatory potential and gout risk in two large cohorts of US women over 30 years.

Table 1. Hazard Ratio (HR) of Incident Gout According to Quintiles of Inflammatory Diet Score

	Q1: (Lowest)	Q2	Q3	Q4	Q5: (Highest)	P for trend
N cases	662	812	998	1223	1588	
Person-years	863,160	864,059	863,926	863,411	862,713	
Incidence rate (per 1000 person-years)	77	94	116	142	184	
Incidence rate ratio	1.00 (Ref)	1.23	1.51	1.85	2.40	
Age-adjusted HR (95% CI)	1.00 (Ref)	1.22 (1.10 to 1.35)	1.50 (1.36 to 1.66)	1.86 (1.69 to 2.04)	2.48 (2.26 to 2.71)	<0.001
Multivariable HR (95% CI)*	1.00 (Ref)	1.18 (1.06 to 1.30)	1.37 (1.24 to 1.51)	1.59 (1.45 to 1.75)	1.89 (1.72 to 2.07)	<0.001
Multivariable HR (95% CI) (+ BMI)**	1.00 (Ref)	1.11 (1.00 to 1.23)	1.25 (1.13 to 1.38)	1.39 (1.26 to 1.53)	1.53 (1.39 to 1.68)	<0.001

*Multivariable (MV) models adjusted for age (month), White race, smoking, menopause, hormone use, physical activity (MET h/week), history of hypertension, and diuretic use. **MV + BMI models additionally adjusted for body mass index (BMI), a likely causal intermediate.

Methods: We studied 77,425 women from Nurses Health Study (NHS) (1986-2016) and 93,454 from NHS II (1989-2017) who were free of gout at baseline. Dietary intake and covariates were ascertained by validated questionnaires every 2-4 years, along with new cases of physician-diagnosed gout (every 2 years). Inflammatory potential of diet was evaluated using a food-based, empirical dietary index of inflammatory potential score (EDIP), pre-defined based on circulating levels of IL-6, C-reactive protein, adiponectin, and TNFαR2.[5]

We assigned an EDIP score for each woman, adjusted for total energy intake, and used Cox proportional hazards models to prospectively examine the relation between quintiles of cumulative average EDIP scores (reflection of *habitual* diet) and incident gout, adjusting for potential confounders. We further adjusted for body mass index (BMI), a potential causal intermediate, and conducted subgroup analyses.

Results: We documented 5,283 cases of incident gout over 4,317,270 person-years, including 3,670 in the NHS (mean age of 50 years at baseline; 49% post-menopausal) and 1,613 in NHS II (mean age 36 years; 3.6% post-menopausal). In pooled multivariable-adjusted (MV) analyses, women in the highest EDIP quintile had nearly two-times greater risk of gout (MV HR 1.9, 95% CI: 1.7 to 2.1) compared to women in the lowest quintile (**Table 1**). This remained positive with further adjustment for BMI, a likely causal intermediate (MV HR 1.5, 95% CI 1.4 to 1.7).

Effects were similar for the older and younger cohorts, with MV HRs of 1.9 (95% CI 1.7 to 2.1, p for trend < 0.001) and 1.9 (1.6 to 2.2, p < 0.001) before BMI adjustment, in the NHS I and II, respectively, and 1.6 (1.4 to 1.7, p < 0.001) and 1.5 (1.3 to 1.8, p < 0.001), respectively, after BMI adjustment. Estimates did not differ significantly across other subgroups.

Conclusion: In these large prospective cohorts of both older and younger women, habitual pro-inflammatory dietary pattern was independently associated with increased risk of incident gout, beyond the pathway through adiposity. Our findings support a role for chronic inflammation in development of female gout, similar to CVD[1] and T2D.[2]

Table 2. Hazard Ratio (HR) of Incident Gout According to Quintiles of Inflammatory Diet Score, by subgroups

	Q1: (Lowest)	Q2	Q3	Q4	Q5: (Highest)	P for interaction
Age, years						
< 60	1.00 (Ref)	1.20 (1.01 to 1.43)	1.37 (1.15 to 1.62)	1.61 (1.37 to 1.90)	1.97 (1.69 to 2.30)	0.16
≥ 60	1.00 (Ref)	1.16 (1.02 to 1.32)	1.36 (1.21 to 1.54)	1.58 (1.40 to 1.78)	1.83 (1.63 to 2.05)	
Body mass index, kg/m^2						
< 25	1.00 (Ref)	1.20 (1.01 to 1.42)	1.27 (1.07 to 1.51)	1.59 (1.34 to 1.88)	1.67 (1.40 to 1.99)	
25-29.9	1.00 (Ref)	1.08 (0.90 to 1.30)	1.13 (0.95 to 1.35)	1.27 (1.07 to 1.51)	1.55 (1.31 to 1.82)	0.68
≥ 30	1.00 (Ref)	1.09 (0.91 to 1.32)	1.36 (1.15 to 1.62)	1.44 (1.22 to 1.69)	1.58 (1.35 to 1.85)	
Physical activity, MET h/week						
< 25	1.00 (Ref)	1.18 (1.05 to 1.32)	1.39 (1.24 to 1.55)	1.60 (1.44 to 1.78)	1.91 (1.72 to 2.11)	0.68
≥ 25	1.00 (Ref)	1.18 (0.94 to 1.48)	1.29 (1.03 to 1.62)	1.56 (1.25 to 1.95)	1.86 (1.49 to 2.31)	
Alcohol use						
No	1.00 (Ref)	1.07 (0.82 to 1.38)	1.14 (0.89 to 1.46)	1.23 (0.97 to 1.56)	1.64 (1.31 to 2.05)	0.48
Yes	1.00 (Ref)	1.18 (1.06 to 1.32)	1.40 (1.26 to 1.56)	1.68 (1.51 to 1.86)	1.87 (1.68 to 2.08)	

Adhering to a diet with lower inflammatory potential may modulate systemic and metabolic inflammation, potentially reducing gout risk and these life-threatening comorbidities among women.

[1]Shen *Arthrit Rheum* (2021); PMID 33760368
[2]Xia *Rheumatology* (2020); PMID 31624843
[3]Li *JACC* (2020); PMID 32406924<
[4]Lee *Diabetes Care* (2020); PMID 32873589
[5]Tabung; PMID 27358416

Disclosure: N. McCormick, None; **C. Yokose**, None; **N. Lu**, None; **A. Joshi**, None; **H. Choi**, None.

Abstract Number: 0678

Is There a Difference in Self-reported Flare Frequency Between Men and Women?

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: There is increasing recognition of gout among women. The postmenopausal rise in serum urate levels in women increases the risk for the development of gout. Compared with men with gout, women with gout are older and had a more significant burden of comorbid conditions, including hypertension, diabetes, chronic kidney disease, obesity, and diuretic use (1). The risk of flares is associated with older age and cardiometabolic comorbidities. Female gout patients with cardiometabolic comorbidities were 60% more likely to have flared as compared with 10% in men (2,3). The profiles of women and men with gout are markedly different. Do women, especially women older than 65, have more frequent gout flares than men?

Methods: Using three cohorts of European gout patients from New Zealand (NZ European; 715 male, 147 female), USA (Ardea; 1,121 male, 57 female), and several European countries (GlobalGout; 726 male, 83 female) respectively, we analyzed sex differences between the number of self-reported flares in the last 12 months. We also filtered for individuals older than three age thresholds: > 65, > 75, and > 85 years old. Since there was significant skew in the flare data, we performed a non-parametric Wilcoxon rank-sum test in each cohort to statistically test for a difference in the mean number of flares between males and females. Bonferroni corrected P-value of 0.017 (0.05 / 3) was used for significance testing.

Results: There was a non-significant difference in flare rate between males and females within each cohort (Ardea p = 0.11, GlobalGout p = 0.51, NZ European p = 0.055). Figure 1 shows the distribution of flares in the past 12 months among males and females in each cohort, demonstrating the non-significant difference in flare rate between male-sand females within each cohort. In addition, no significant difference in flare rate between sexes when filtering for individuals older than either of three age thresholds: > 70 years old: 401 male, 125 female – p-value = 0.76; > 75 years old: 188 male, 76 female – p-value = 0.61.

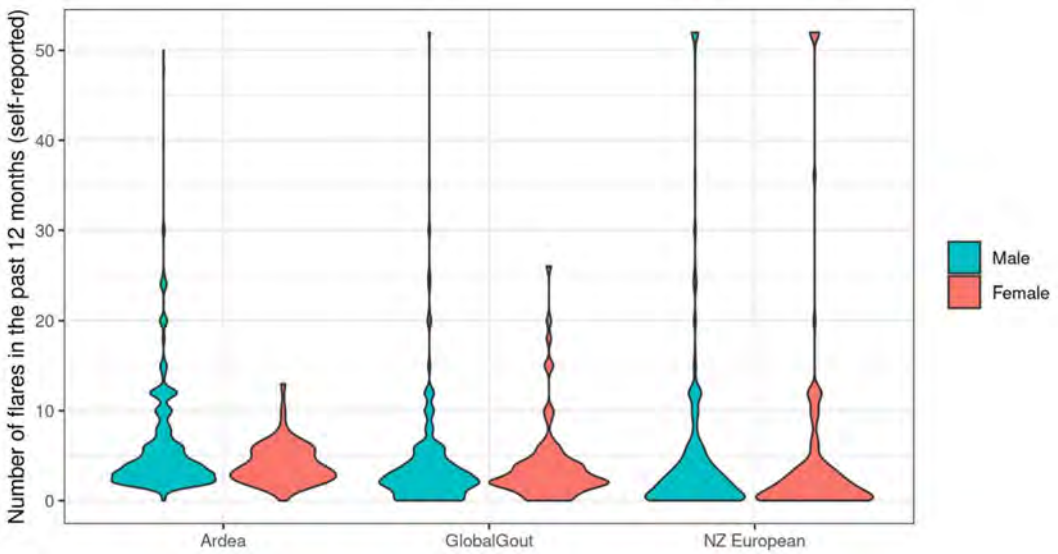

Figure 1. Violin plots showing distribution of self-reported flares in the past 12 months among males and females in three European gout cohorts.

Conclusion: In this large cohort of gout patients, we found the rate of self- -reported gout flares in women similar to those of men.

References

1. Lally et al. Arch Intern Med. 1986;146:2221–2225.
2. Harrold et al. BMC Musculoskelet Disord. 2017 14;18:108.
3. Primatesta et al. BMC Musculoskelet Disord 2011;12:103.

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Abstract Number: 0679

Cardiovascular Risk Associated with Treatment of Allopurinol and Benzbromarone in Patients with Gout

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies have shown that cardiovascular risk is increased in patients with gout. There are many studies on the effect of uric acid lowering therapy on CV risk in gout patients, but few studies have compared allopurinol and benzbromarone. A nationwide population-based cohort study is designed to compare cardiovascular risk according to the treatment of allopurinol and benzbromarone in Korean gout patients.

Methods: We used South Korea's database of the Health Insurance Review and Assessment service (HIRA) to identify gout patients 18 years of age or older who newly started allopurinol or benzbromarone between 2009 and 2015. The start date of allopurinol or benzbromarone is defined as the index date. We excluded patients who have been prescribed uric acid lowering agents or have been on dialysis for one year prior to the index date. During the study period, patients who used uric acid lowering agents other than allopurinol and benzbromarone or who used both drugs in combination were also excluded from the study. The primary outcome of the study was the occurrence of a composite cardiovascular endpoint, which included coronary revascularization, hospitalization due to MI, ischemic stroke, and transient ischemic attack (TIA). Cox proportional hazard regression analysis and Kaplan-Meier curves were used for the analysis.

Results: 257,097 allopurinol initiators and 7,868 benzbromarone initiators were included in the study. The mean age was 54.4 years, 86% were male. The mean adherence of drug administration was 68.2% for allopurinol initiators and 75.5% for benzbromarone initiators. In baseline, the benzbromarone initiator had more cardiovascular comorbidities and related drug administration than the allopurinol initiator. In allopurinol and benzbromarone initiators, the adjusted hazard ratio (aHR) of the composite CV endpoint was 1.01 (95% CI 0.83-1.21), which was not significantly different. No significant difference was found between the two groups in each of the items of the composite CV endpoint and

hospitalization for heart failure. The results did not change even when 1:3 propensity score matching was performed for baseline characteristics. In subgroup analysis of high risk patients with cardiovascular disease, there was no significant difference between allopurinol and benzbromarone initiators. However, when the analysis was limited to the group taking allopurinol ≥200mg and benzbromarone ≥50mg, there was no difference in primary outcome and other outcomes, but the risk of coronary revascularization was higher in benzbromarone initiator (aHR 1.58, 95% CI 1.16-2.14).

Conclusion: In our study, there was no significant difference in cardiovascular risk between allopurinol initiator and benzbromarone initiator. In the high risk group of cardiovascular disease, there was no difference in risk between the two drugs.

Disclosure: Y. Eun, None; **S. Kang**, None; **S. Lee**, None; **H. Kim**, None; **J. Lee**, None; **E. Koh**, None; **H. Cha**, None.

Abstract Number: 0680

Gout Stigma: Investigating the Existence of Gout Stigma and Its Impact on Patient Perceptions and Treatment Decisions

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Pegloticase is FDA-approved for uncontrolled gout and effectively lowers uric acid levels by conversion of circulating uric acid to allantoin, which is readily removed renally.1 One potential factor contributing to the hesitancy among rheumatologists in recommending pegloticase is the longstanding stigma associated with gout patients and perceptions of their ability or willingness to adhere to pharmacological treatments.3 Although rheumatologists may not explicitly endorse negative gout related stereotypes, it is possible that such stigma may unconsciously influence their perceptions of patients' illness and treatment efficacy, attributions for contributing factors, and treatment decisions. Therefore, we investigated, among practicing rheumatologists, the existence of stigmas associated with gout (compared to rheumatoid arthritis), perceptions of patient behavior, and treatment decisions in these conditions.

Methods: A sample of 27 practicing rheumatologists participated in an online survey that evaluated their causal beliefs, illness perceptions, and treatment recommendations for patients with gout, uncontrolled gout (UG), and rheumatoid arthritis (RA). Questions also focused on rheumatologists' perceptions of patient adherence in gout, UG, and RA, as well as the responsibility of patients' for their condition. All participants completed questions with reference to gout, UG, and RA, which were blocked and presented in random order. This design allows for an assessment of how rheumatologists' beliefs, perceptions, and recommendations vary across disease condition and its potential impact on treatment recommendations.

Results: Mean-level (95% CI) responses across disease condition are represented in the Figure. Responses to questions about gout and UG did not differ significantly ($p > 0.10$). However, patients with gout/UG vs RA were perceived as significantly more responsible for their own disease condition and less likely to adhere to prescribed treatments

($p < 0.05$). Additionally, patient personal behavior, diet, BMI, and lack of treatment adherence were perceived as greater contributing factors to gout/UCG vs RA; $p < 0.01$. Similarly, change in diet, increased exercise, and weight loss was perceived as more beneficial to the management of gout/UG vs. RA; $p < 0.01$, whereas biological pharmacological treatment was perceived as more effective at managing RA vs. gout or UG; $p < 0.01$.

Conclusion: Despite advanced training and high knowledge of gout, rheumatologists' causal beliefs and illness perceptions for patients with gout/UG compared to RA reflect negative gout related stereotypes, with implications for treatment recommendations. Patients with gout/UG vs. RA were perceived as more responsible for their own condition and less likely to adhere to or benefit from biological pharmacological treatment.

Disclosure: N. Edwards, None; **B. LaMoreaux**, Horizon Therapeutics, 3, 11; **J. Vitriol**, Horizon Therapeutics, 2; **A. Magerman**, Horizon Therpeutics, 2.

Abstract Number: 0681

Assessing Patterns of Inpatient Gout Management: Pathway for Optimal Patient Treatment Outcomes

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Gout is the most common inflammatory arthropathy worldwide. Despite having evidence-based guidelines, inconsistent management approaches remain a significant barrier to adequate treatment and prevention. As a result, recurrent gout flares lead to increased utilization of the healthcare system. The aim of this project was to assess inpatient gout management patterns at our health center with a focus on presence of urate lowering therapy (ULT), patient education, and follow-up. We hypothesized that patients admitted to the hospital with a gout flare had indications for ULT and should receive adequate discharge instructions or follow-up regarding gout.

Methods: We conducted a retrospective chart review of inpatients admitted to our tertiary care academic medical center between January 2017 and December 2019 using ICD-10 codes for gout flare (M10.9), as well as a serum uric acid (SUA) level greater than 7.0 mg/dL. Patients who either did not have a documented gout flare or died during their admission were excluded. Patient demographics, comorbidities, laboratory values including mean SUA, treatment modalities, discharge instructions, and follow-up plans were recorded. Continuous variables were summarized by means and standard deviations while categorical variables were summarized with frequencies and percentages. Simple logistic regression models were fit for each potential predictor to determine if an individual relationship existed with whether urate lowering therapy was given. A multivariable model was fit with appropriate predictors and control variables.

Results: Of 205 charts reviewed, 149 (73%) were analyzed. More than 50% of the patients had chronic kidney disease, congestive heart failure, dyslipidemia, or hypertension. 59 (40%) patients had ULT prescribed at time of discharge. Of those prescribed ULT, 47 (80%) were prescribed allopurinol at a dose less than 300 mg/day. The mean (SD) SUA of patients was 10.4 mg/dL (2.6) with a median of 10.2 mg/dL. Amongst all patients included in the

study, 46 (31%) had discharge instructions regarding gout and 85 (57%) were recommended to follow-up with their primary care physician or a rheumatologist. A univariate regression model suggested that both the number of flares (p=0.0039) and age (p=0.0012) were associated with whether ULT was prescribed. While controlling for age, the multiple logistic regression model demonstrated the odds of being prescribed ULT are 1.69, 95% CI (1.085, 2.629) for each additional gout flare after the first.

Conclusion: Only 40% of our studied patients received ULT despite all being at least conditionally recommended for ULT per the ACR 2020 gout guidelines. Of those prescribed ULT, 80% were on allopurinol dose less than 300 mg/day. We suspect ULT is both under prescribed and under dosed. ULT was more likely to be prescribed to patients who suffered from more than one gout flare during the study period, though these patients may have benefitted from earlier pharmacologic intervention. Furthermore, very few patients received discharge plans including education and follow up to reduce further gout flares. Our study reflects a significant opportunity to improve management of gout in the inpatient setting and upon hospital discharge.

Disclosure: E. Dombrosky, None; **Y. KC**, None; **J. Gavin**, None; **Y. Roman**, None; **N. Shah**, None.

Abstract Number: 0682

Gout Management and Outcomes During the COVID-19 Pandemic in Late 2020-2021: A Cross-sectional Internet Survey

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster I (0660–0682)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To assess gout management during the COVID-19 pandemic since September 2020.

Methods: We assessed urate-lowering therapy (ULT) use, healthcare utilization, gout-specific health-related quality of life (HRQOL; 0-100 range; higher scores = lower/pooper HRQOL), health literacy, illness perception, psychological distress using patient health questionnaire-4 (2 questions each for depression and anxiety; 0-6 each), and resilience using on Connor-Davidson Resilience Scale (CD-RISC2; range 0-8; higher=more resilient) scale in people with self-reported physician-diagnosed gout in a cross-sectional Internet survey.

Results: Among the 121 survey respondents with self-reported physician-diagnosed gout, 60% were prescribed urate-lowering therapy (ULT) and 33% were taking ULT daily since September 2020. The mean age of respondents was 62.8 years (standard deviation [SD], 12.6), 65% were male, and 82% were White. Regular daily use of gout medications was reported during the COVID-19 pandemic since September 2020 as follows: allopurinol, 31%; febuxostat, 4%; probenecid, 2%; colchicine, 7%; NSAIDs, 9%; glucocorticoids, 4%. Gout flares were common, i.e., 76% reported ≥1 gout flare. Overall, 29% of respondents reported more difficulty with managing their gout since September 2020.

Gout-specific HRQOL deficits were evident for all scales: (1) gout concern overall, 72.9 (SD, 25); (2) unmet gout treatment need, 54.2 (SD, 24.7); (3) gout concern during flare, 55.5 (SD, 24.5); (4) gout well-being during flare, 55.4 (SD, 23.6); and (5) gout medication side effects, 56.5 (SD, 25.5).

Table 1. Multivariable association of depression and anxiety with gout outcomes during COVID-19 pandemic in 2020-2021

	Depression (PHQ-2 score of 3 or more; **ref category**, score 0-2)	Anxiety (PHQ-2 score of 3 or more; **ref category**, score 0-2)
	Odds ratio (95% Confidence Interval)	
Regular ULT use	**0.29 (0.09 to 0.99)**	0.46 (0.13, 1.62)
Difficulty with getting healthcare for gout in		
Clinic	**6.50 (1.61 to 26.2)**	**9.94 (1.93 to 51.2)**
Emergency room or urgent care	**21.54 (1.90 to 244)**	**36.79 (1.75 to 734)**
Hospital	**37.29 (2.97 to 468)**	**20.39 (1.60 to 260)**
Difficulty getting gout flares treated	**14.85 (2.67 to 82.8)**	**23.91 (3.20 to 178)**
Difficulty avoiding gout flares,	**5.41 (1.21 to 24.11)**	3.56 (0.62, 20.46)
Difficulty avoiding complications from gout	**8.42 (2.10 to 33.77)**	**7.89 (1.67 to 36.35)**
Difficulty with daily activities	**3.88 (1.22 to 12.29)**	**5.72 (1.41 to 23.32)**
Difficulty with performing work	**5.30 (1.61 to 17.43)**	**5.02 (1.24 to 20.37)**
Bold represents statistically significant Odds ratios each with a p-value <0.05		

Psychological distress was moderate in 10% and severe in 14% (mild, 27%; none/normal, 50%). Resilience score was 6.5 (SD, 1.9). Health literacy was high with mean score of 18.5 (SD, 2.5; range 4-20).

Adjusted for age, and sex, compared to no depression or anxiety, depression with PHQ-2 score ≥3, and anxiety with PHQ-2 score of ≥3, were significantly associated with: (1) difficulty with getting healthcare for gout in clinic, emergency room or urgent care, and in-hospital; (2) difficulty getting gout flares treated, avoiding gout flares, and avoiding complications from gout; and (4) difficulty with daily activities, and performing work; and depression, but not anxiety with regular ULT use (**Table 1**).

Conclusion: Respondents with gout reported healthcare gaps, psychological distress, illness perception and HRQOL deficits since September 2020 during the COVID-19 pandemic. Anxiety and depression were associated with poorer ULT adherence and more difficulty managing gout. Interventions to address psychological comorbidity in gout are needed during the COVID-19 pandemic.

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Abstract Number: 0683

Predictors of Rapidly Progressive Interstitial Lung Disease and Mortality in Patients with Autoantibodies Against Melanoma Differentiation-Associated Protein 5 Dermatomyositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

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Background/Purpose: Anti-melanoma differentiation-associated protein 5 (MDA5) positive dermatomyositis (DM) is associated with rapidly progressive interstitial lung disease (RP-ILD) and high mortality. This multi-centre retrospective study aimed to evaluate whether RP-ILD was associated with increased mortality in anti-MDA5 positive DM in Hong Kong and to identify predictors for mortality and RP-ILD.

Methods: Anti-MDA5 positive DM patients were identified from the Hong Kong Myositis Registry and the Clinical Data Analysis and Reporting System. Diagnosis of DM was based on Bohan and Peter's criteria or EULAR/ ACR 2017 classification criteria. Diagnosis of CADM was defined as typical cutaneous features of DM confirmed by rheumatologist or dermatologist but minimal or no clinical features of myositis (hypomyopathic and amyopathic) with reference to the Sontheimer's criteria. Detailed clinical characteristics were reviewed. RP-ILD was defined as rapid progression of dyspnea or imaging finding of ILD within 1 month of onset of respiratory symptoms. Risk factors for mortality and RP-ILD were identified.

Results: Among the 101 recruited patients, 87 (86.1%) had ILD and 42 (41.6%) had RP-ILD. Over a period of 19.1±21.9 months, 38 (37.6%) patients died, in which 31 patients (81.6%) died within three months of diagnosis. Multivariate Cox regression analysis revealed that RP-ILD (HR 17.6, 95%CI 5.96-51.9), smoking (HR 6.40, 95%CI 1.43-28.7), ferritin level >2800pmol/L (HR 6.37, 95%CI 2.40-16.9) and fever at diagnosis (HR 3.11, 95%CI 1.14-8.53) were independent predictors of mortality. Early rituximab use was associated with better survival (HR 0.10, 95% CI 0.01-0.82). With regards to RP-ILD, multivariate Cox regression analyses showed that independent predictors included age >50 years (HR 3.02, 95%CI 1.43-6.38), baseline neutrophil to lymphocyte ratio (NLR) >7.5 (HR 2.45, 95%CI 1.05-5.71) and lactate dehydrogenase (LDH) level >300IU/L (HR 3.34, 95%CI 1.36-8.21). We proposed a prediction model, based on NLR >7.5, age >50 years old and LDH >300IU/L ("NAL"), to stratify risk of development of RP-ILD.

Conclusion: Anti-MDA5-associated RP-ILD is significantly associated with poor survival rates. The "NAL" model maybe useful to predict the development of RP-ILD in anti-MDA5 positive DM patients.

	N= 101
Anti-MDA5 positive DM patients, no.	101
Female, no. (%)	54 (53.5%)
Age of onset, years, mean (± SD)	52 (13)
Smoker, no. (%)	9 (8.9%)
Ethnicity, no. (%)	
Chinese	98 (97%)
Diagnosis	
DM, no. (%)	33 (32.7%)
CADM, no. (%)	68 (67.3)
PM, no (%)	0 (0%)
ILD, no. (%)	87 (86.1%)
RPILD, no. (%)	42 (41.6%)
Fever at presentation, no. (%)	51 (50.5%)
Cutaneous features	
Violaceous rash over elbow	23 (22.8%)
Violaceous rash over knee	7 (6.9%)
Cutaneous ulcer	21 (20.8%)
Cutaneous vasculitis	36 (35.6%)
Laboratory findings	
Lactate dehydrogenase, IU/L, mean	477
C-reactive protein, mg/dL, mean (normal <5)	16
Lymphocytes count ≤0.5	28 (27.7%)
Ferritin (ng/mL), mean	7834
Treatments and outcomes	
Steroid	98 (97%)
Cyclophosphamide, initial treatment	36 (35.6%)
Rituximab, initial treatment	34 (33.7%)
Overall Mortality, no. (%)	38 /101 (37.6%)
3- month survival rate	(73/101) 72.3%
1- year survival rate	(64/101) 63.4%

Patients' demographic, clinical features, treatments and outcomes

Variable	Hazard ratio	95% Confidence interval	P-value
Age at diagnosis >50 years old	3.020	1.431-6.376	**0.004**
Fever	1.570	0.781-3.158	0.205
Infection at diagnosis	1.792	0.874-3.674	0.111
NLR >7.5	2.445	1.046-5.714	**0.039**
LDH >300 IU/L at diagnosis	3.343	1.362-8.205	**0.008**
CRP >18 mg/dL at diagnosis	1.421	0.593-3.409	0.431

Results of multivariate Cox regression analyses for RP-ILD

Risk score	No. of RP-ILD	RP-ILD rate, %	% within RP-ILD
0	2	2.0%	4.8%
1	9	8.9%	21.5%
2	28	27.7%	66.7%
3	42	41.6%	100%

Prediction model for RP-ILD based on age >50, NLR >7.5 and LDH >300 IU/L at diagnosis

Disclosure: J. So, None; **L. Tam**, Janssen, 2, 5, Pfizer, 2, 5, GlaxoSmithKline, 5, AbbVie, 2, Novartis, 5, Amgen, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, Sanofi, 2; **P. Wong**, None; **L. Tam**, None; **T. Lam**, None; **C. Mok**, None; **C. To**, None; **Y. Chung**, None; **V. Wong**, None; **T. Wu**, None; **R. Ho**, None; **W. Li**, None; **C. Ho**, None; **H. So**, None.

Abstract Number: 0684

Extended Report: Successful Treatment anti-MDA5 Antibody-positive Interstitial Lung Disease with Plasma Exchange Therapy

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

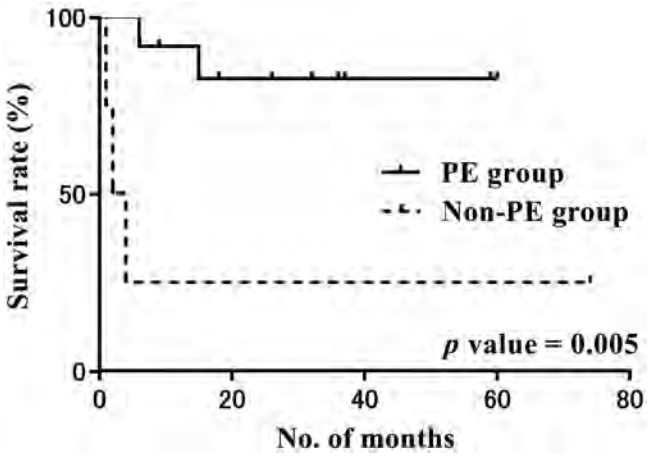
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: This study was extended report from our previous study that "Successful treatment of anti-MDA5 antibody-positive refractory interstitial lung disease with plasma exchange therapy" (Rheumatology (Oxford) 59(4):767-71, 2020). Anti-melanoma differentiation-associated gene 5 (MDA5) antibodies are a type of myositis-specific autoantibody. Anti-MDA5 antibodies are closely related to interstitial lung disease (ILD). Intensive immunosuppressive therapy with combination calcineurin inhibitor, and intravenous pulse cyclophosphamide was developed, because rapid progressive-ILD (RP-ILD) with anti-MDA5 antibodies is refractory and fatal. Intensive immunosuppressive therapy was shown to improve patient survival and prognosis. However, 20–30% of cases were still fatal, and we reported that the effectiveness of plasma exchange (PE) therapy for refractory RP-ILD. We aimed to reveal the effect of PE on survival in patients with refractory RP-ILD with anti-MDA5 antibodies.

Methods: We added 6 RP-ILD patients who were positive of anti-MDA5 antibodies with PE. Refractory RP-ILD was defined as radiological progression and/or oxygenation exacerbation within 4 weeks after intensive immunosuppressive



Kaplan-Meier curves for survivability comparing the overall PE group and non-PE group. The result of the log-rank test was P = 0.005. PE: plasma exchange therapy.

therapy. Study approval was obtained from the ethical committee of Juntendo University Hospital (approval number 17-274).

Results: The PE group included 6 former patients and 6 new patients such as 1 with newly refractory cases, 3 with relapsed refractory cases, and 2 with newly severe hypoxia cases that P/F ratio was less than 200. A total of 12 patients were included in the PE group. The 1-year survival rate of the PE group was significantly higher than that of the non-PE group (92% and 25%, respectively, P = 0.03). One patient who showed severe hypoxia at the start of treatment was improved from respiratory failure, but he died of candidemia due to vascular catheter infection.

Conclusion: We revealed the higher 1-year survival rate of PE for refractory or severe hypoxia RP-ILD in patients positive for anti-MDA5 antibodies. Physicians may consider that adding PE in refractory or severe hypoxia RP-ILD patients positive for anti-MDA5 antibodies.

Disclosure: Y. Abe, GlaxoSmithKline, 5; **M. Kogami**, None; **M. Kusaoi**, None; **K. Tada**, None; **K. yamaji**, None; **N. Tamura**, AbbVie Japan GK, 6, Bristol-Myers Squibb Co. Ltd, 6, Chugai Pharmaceutical Co. Ltd, 6, Eisai Co. Ltd, 6, Eli Lilly Japan K.K, 6, Glaxo Smith Kline K.K., 6, Janssen Pharmaceutical K.K., 6, Mitsubishi-Tanabe Pharma Co., 6, Novartis Pharma K.K, 6.

Abstract Number: 0685

Adipokines and Loss of Lean Mass Among Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with loss of muscle mass and quality that can have significant impacts on physical functioning and quality of life. Adipokines are fat and muscle-secreted hormones that

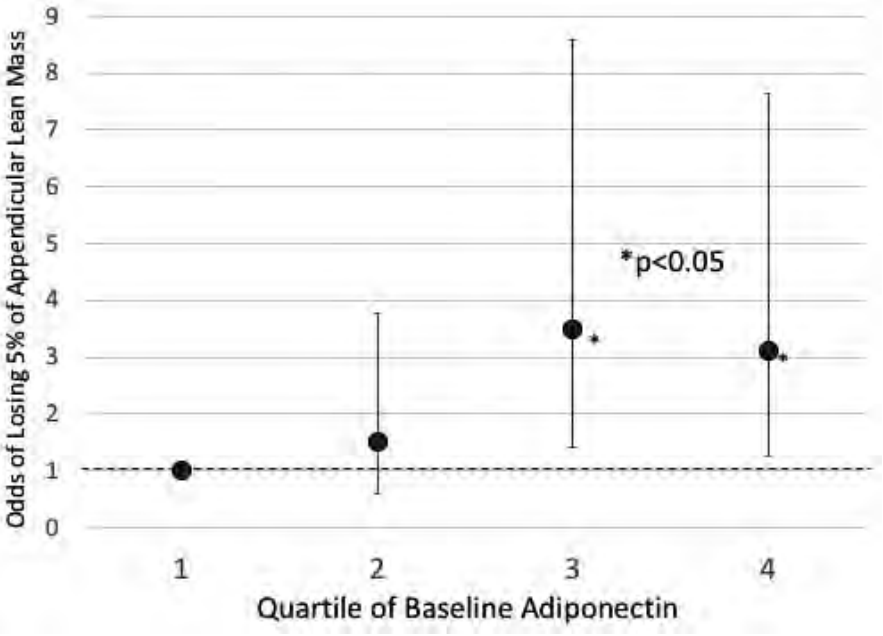

Figure. Adjusted odds of losing 5% of ALMI during follow-up by adiponectin quartile.

play a role in regulating metabolism and energy homeostasis and may play a role in the worsening of skeletal muscle deficits in RA. We determined whether adiponectin, leptin, and Fibroblast Growth Factor(FGF)-21 could predict significant declines in skeletal muscle mass over 2-3 years.

Methods: This study combined data from three longitudinal RA cohorts with assessments of whole-body dual-energy absorptiometry (DXA) measures including appendicular lean mass index (ALMI) and fat mass index (FMI). We

Table. Association between individual adipokines and their changes over follow-up and the adjusted odds of losing 5% of lean mass over follow-up

	Loss of 5% Lean Mass (individual adipokines)	
	OR (95% CI)	P
Baseline Adipokines*		
Adiponectin (per 1 SD)	1.55 (1.14, 2.49)	0.005
Leptin (per 1 SD)	0.82 (0.51, 1.30)	0.40
FGF-21 (per 1 SD)	1.82 (1.15, 2.88)	0.01
Change in Adipokines**		
Adiponectin (per 1 SD change)	2.36 (1.32, 4.23)	0.004
Leptin (per 1 SD change)	0.65 (0.37, 1.14)	0.13
FGF-21 (per 1 SD change)	0.67 (0.34, 1.35)	0.27

*Each adipokine is analyzed in a separate model and adjusted for age, sex, race, baseline ALMI, baseline FMI, study cohort, and follow-up time.
**as above and further adjusted for baseline adiponectin/leptin/FGF-21 levels.

defined a loss of lean mass as a decrease in ALMI of 5% or more and a loss of FMI as a decrease in FMI of 5% or more. Adiponectin, leptin, and FGF-21 were measured on stored samples. Values were log-adjusted and standardized so that one unit represents a 1 SD change in the exposure. Associations between adipokines at baseline and the change in adipokines during follow-up with long-term changes in ALMI and FMI were assessed using multivariable linear regression, adjusting for demographics, study cohort, and baseline body composition.

Results: A total of 75 (22%) out of 338 participants lost more than 5% of ALMI and 93 (28%) lost >5% of FMI by the time of their follow-up visit over a median (IQR) follow-up of 3 years (2, 3). Those who lost 5% of ALMI had higher adiponectin (per SD) levels at baseline [Mean (SD): 0.40 (1.10) v. -0.048 (1.06), p=0.001], but had similar levels of leptin [Mean (SD): 0.001 (1.04) v. 0.02 (0.96), p=0.87]. In a smaller cohort with FGF-21 levels, levels were higher (per SD) among the 31/159 (16%) who lost ALMI [Mean (SD): 0.28 (0.14) v. -0.17 (0.081), p=0.02]. A higher level of adiponectin (per 1 SD) was associated with a higher probability of losing 5% of ALMI (Figure 1). In multivariable models, participants with higher adiponectin levels had a significantly higher odds of losing 5% of ALMI [OR (per 1 SD): 1.55 (1.14, 2.10) p=0.005] (Table 1). Higher FGF-21 levels were also associated with a higher odds [OR: 1.82 (1.15, 2.88) p=0.01]. Leptin levels were not associated in similar models [OR (per 1 SD): 0.82 (0.51, 1.30), p=0.40]. In addition, after adjusting for baseline adiponectin levels, an increase in adiponectin during follow-up was associated with higher odds of losing 5% of ALMI [OR (per 1 SD change): 2.48 (1.37, 4.50), p=0.004]. Associations between adipokines and changes in ALMI were not attenuated by adjustment for C-Reactive Protein, pain scores, or results of the Health Assessment Questionnaire at baseline (not shown). Adipokines were not associated with loss of FMI.

Conclusion: Elevated adiponectin and FGF-21 levels as well as increasing levels of adiponectin are associated with declines in lean mass over long-term follow-up. These observations support the hypothesis that alterations in adipokines including elevations in adiponectin are associated with an adverse metabolic phenotype in patients with RA and may identify patients at risk of sarcopenia or cachexia. Further study is needed to determine whether elevations in adiponectin are associated with other long-term clinical outcomes in RA.

Disclosure: J. Baker, Bristol-Myers Squib, 2, Pfizer, 2; **J. Giles**, AbbVie, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 2, 5, UCB, 2; **P. Gould**, None; **P. Katz**, None.

Abstract Number: 0686

Is It Useful to Assess Muscle Involvement with Positron Emission Tomography in Patients with Idiopathic Inflammatory Myositis? A Case-Control Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Multiple diagnostic methods have been used to investigate muscle involvement in patients with idiopathic inflammatory myositis (IIM) such as electromyography (EMG) and muscle MRI. 18F-FDG PET-CT has been used to screen malignancy, and may also be beneficial in the investigation of myositis [1].

In this study, we aimed to evaluate the muscle involvement with PET – CT, which was performed for malignancy screening, and its association with clinical and laboratory parameters in patients with IIM.

Table 1: Comparison of PET-CT findings between patients with IIM and control group

Variables	IIM (n=34)	Control (n=14)	p value
Liver (SUV-max) (mean±SD; range)	3.1±1.2 (0.38-7.30	3.6±0.55 (2.6-4.6)	0.14
Mediastinum (SUV-max) (mean±SD; range)	2±0.85 (0.3-5.2)	2.1±0.36 (1.4-2.8)	0.7
Lumbar longus muscle (LLM) (SUV-max) (mean±SD; range)	1.28±0.6 (0.15-2.7)	1.13±0.3 (0.7-1.6)	0.4
Proximal upper extremity (SUV-max) (median)	1.7	1.15	***0.001****
Distal upper extremity (SUV-max) (median)	1.7	1.2	***0.036****
Proximal lower extremity (SUV-max) (median)	1.8	1.3	***0.003****
Distal lower extremity (SUV-max) (median)	1.9	1.2	***<0.001****
Muscle PET-CT positivity (n, %)			
According to liver uptake	13 (37.1)	0	***0.01***ǂ ***(OR:7.1)***
According to Mediastinum uptake	23 (65.7)	1 (7.1)	***<0.001***ǂ ***(OR:13.7)***
According to LLM uptake	32 (91.4)	13 (92.9)	0.9

*Mann Whitney U test, ǂ Fisher's exact test IIM: Idiopathic inflammatory myositis, SD: Standard deviation, SUV-max: Standardized uptake value-maximum, PET-CT: Positron emission tomography, LLM: Lumbar longus muscle

Table 2: Univariate analysis of clinical and laboratory characteristics of patients with IIM according to PET-CT findings

Variables	Positive muscle PET-CT result		
Diagnosis (n, %)	**Yes**	**No**	**p value**
Dermatomyositis	15 (60)	10 (40)	0.2
Polymyositis	7 (87.5)	1 (12.5)	
Muscle weakness (n, %)			
Yes	17 (77)	5 (23)	0.4
No	5 (63)	3 (38)	
Electromyography (n, %)			
Compatible with myositis	15 (78.9)	4 (21.1)	-0.047** (p=0.8)
Not compatible with myositis	5 (83.3)	1 (16.7)	
Positive muscle MRI (n, %)			
Yes	16 (88.9)	2 (11.1)	***0.412**(OR:4.1) (p=0.04)*
No	3 (50)	3 (50)	
Muscle biopsy (n, %)			
Compatible with myositis	8 (88.9)	1 (11.1)	0.418** (p=0.1)
Not compatible with myositis	2 (50)	2 (50)	
Malignancy (n, %)			
Yes	7 (70)	3 (30)	1
No	16 (70)	7	
Baseline CK levels (U/L) (median)	1264	115	***0.026****
Baseline LDH levels (U/L) (median)	589	301	***0.028****
Baseline ESR levels (mm/hour) (median)	22	22	0.6
Baseline CRP levels (mg/L) (median)	11	2	***0.032****

Ɨ Fisher's exact test, *Man Whitney U test, **kappa test SD: Standard deviation, CK: Creatinine kinase, LDH: Lactate dehydrogenase, ESR: Erythrocyte sedimentation rate, CRP: C-reactive protein, MRI: Magnetic resonance imaging

Methods: IIM patients who fulfilled EULAR/ACR classification criteria and had PET-CT scans during the active phase of myositis included into the study. PET-CT scans of IIM patients and non-IIM patients with malignancy as controls were assessed retrospectively by two experienced nuclear medicine specialists and decisions were made by consensus. Positive PET-CT for myositis was defined as higher FDG muscle uptake compared to liver, mediastinal vascular structures (mediastinum) and lumbar longus muscle (LLM). Univariate and multivariate analysis were performed according to FDG uptake compared to mediastinum which was found to have higher diagnostic accuracy.

Results: One hundred and sixty IIM patients were screened and 34 patients (of 64.7 % female) whose PET-CT results were available and 14 non-IIM patients included into the study. Mean age of the IIM patients was 55±13 (25-85). Median disease duration of IIM patients was 12 months. Liver, mediastinum and LLM uptakes were similar in patients with IIM and non-IIM groups; higher muscle uptake was observed in proximal and distal upper ($p=0.001$, $p< 0.001$, respectively) and lower extremity ($p=0.003$, $p< 0.001$, respectively) in patients with IIM compared to non-IIM. Sensi-

tivity and specificity of positive FDG muscle uptake were 37.1 % and 100 %, 65.7 % and 92.9 %, 91.4 % and 7.1 % compared to liver, mediastinum and LLM uptakes, respectively (Table 1).

In univariate analysis; increased CK, LDH and CRP levels (p=0.026, p=0.028 and p=0.032 respectively) and positive muscle MRI (p=0.04; OR:4.1) were associated with PET-CT positivity. There was significant agreement between PET-CT positivity and muscle MRI findings (κ=0.412; p=0.04) (Table 2). In multivariate analysis, high baseline CRP (p=0.017, CI 95%: 1.03-1.36, OR:1.18) and LDH (p=0.029, CI 95%: 1.001-1.017, OR:1.01) levels were associated with PET-CT positivity. Baseline muscle strength (r=-0.411, p=0.04) was negatively correlated with muscle FDG uptake.

Conclusion: In patients with active IIM, median muscle FDG uptake with PET-CT was higher compared to non-IIM and significantly increased compared to liver and mediastinum. Muscle FDG values compared to mediastinum had the highest sensitivity. PET-CT findings are correlated with biomarkers of inflammation and clinical activity. PET-CT may be used for the evaluation of extent and activity in patients with IIM although further prospective research is needed.

1. Tateyama, M., et al., BMJ Open, 2015. **5**(1): p. e006763

Disclosure: M. Bektaş, None; **E. Işık**, None; **F. Kemik**, None; **E. Oğuz**, None; **A. ABBASGHOLI ZADEH**, None; **B. Ince**, None; **Z. Gözde Özkan**, None; **Y. Yalcinkaya**, None; **B. Esen**, None; **A. Gül**, None; **M. İnanç**, None.

Abstract Number: 0687

Clinical Features and Prognosis of a Large North American Cohort of Adult MDA5+ Dermatomyositis

Christopher Mecoli[1], Eleni Tiniakou[2], William Kelly[2], Jemima Albayda[2], Julie Paik[2], Brittany Adler[2], Andrew Mammen[3], Cheng Ting Lin[1], Sonye Danoff[4], Livia Casciola-Rosen[5] and Lisa Christopher-Stine[2], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]National Institutes of Health, Bethesda, MD, [4]Johns Hopkins Medicine, Baltimore, MD, [5]Johns Hopkins, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: We describe a single-center North American adult cohort of MDA5-positive DM, with emphasis on the subgroup of patients that experience drug-free long-term remission.

Methods: From our entire IIM cohort, 52 patients were included that (1) Met either Bohan and Peter or 2017 American College of Rheumatology/European League Against Rheumatism classification criteria for dermatomyositis and (2) Were positive for anti-MDA5 autoantibodies by two methods: Euroimmun line blot (16 Ag IgG, Germany) and ELISA (MBL, Japan). All patients underwent structured telephone research interviews in 2019-2020 to update clinical status including symptoms and DM-specific therapies. Remission was defined as being off all immunosuppressive and immunomodulatory therapies > 1 year while remaining asymptomatic.

Results: Demographic and disease characteristics for the 52 MDA5-positive DM patients can be found in Table 1. Thirty-eight (73%) of the patients were women with a median age at DM symptom-onset of 47 (IQR 40-54). Twenty-five (48%) percent of patients were white, 16 (30%) were African American, 3 (6%) were Asian and 8 (16%) were other/declined to provide race. All patients had either Heliotrope or Gottron's sign, 29 (56%) had synovitis, and 18 (35%) had calcinosis. The majority of patients had interstitial lung disease, defined by fibrotic changes on HRCT (83%). With

Table 1. Demographic and Disease Characteristics of MDA5-positive DM Cohort, as well as those who experienced clinical remission. Physical examination findings are reported as ever/never recorded throughout longitudinal follow-up

	Total N=51	Chronic Course (n=42) Median (IQR)	Remission (n=9) Median (IQR)	p-value
Patient age at IIM symptom onset	47.3 (39.7-54.3)	47.6 (39.7-53.8)	47.1 (42.1-59.9)	0.770
Patient age at JH Cohort Entry	48.8 (41.1-55.3)	49.2 (41.1-55.0)	48.0 (43.3-61.3)	0.880
Male Sex	27%	26%	33%	0.690
Race				0.700
Caucasian	47%	45%	56%	
African American	31%	33%	22%	
Asian	6%	7%	0%	
Other	10%	7%	22%	
Declined	2%	3%	0%	
Unknown	4%	5%	0%	
Ethnicity				0.610
Hispanic	2%	2%	0%	
Not Hispanic	86%	83%	100%	
Unknown	12%	14%	0%	
Duration of follow-up	3.7 (1.4-5.9)	3.8 (1.7-6.3)	1.8 (1.1-3.8)	0.130
Ro52 Positive	42%	38%	56%	0.460
Gottron's sign or papules	98%	98%	100%	1.000
Heliotrope Sign	75%	76%	67%	0.680
Synovitis on physical examination	57%	57%	56%	1.000
Calcinosis on physical examination	35%	36%	33%	1.000
Elevated CPK	15%	19%	0%	0.320
Maximum CPK	101.0 (52.0-160.0)	106.5 (52.0-177.0)	56.0 (48.0-92.0)	0.130
Maximum aldolase	8.7 (6.9-10.8)	8.4 (6.9-10.8)	9.1 (6.4-12.6)	0.550
History of malignancy (ever)	12%	12%	13%	1.000
ILD on high-resolution CT	80%	81%	78%	1.000
Nadir FVC over longitudinal follow-up	70.5 (57.5-85.5)	75.0 (59.0-86.0)	59.0 (51.0-69.0)	0.096
Nadir TLC over longitudinal follow-up	68.5 (59.0-79.0)	70.0 (59.0-80.0)	61.0 (58.0-72.5)	0.320
Nadir DLCO over longitudinal follow-up	62.5 (45.5-78.5)	62.0 (45.5-79.5)	68.0 (51.0-78.0)	0.600
Ulcerations (composite) (digital ulcers, cutaneous ulcers, and mucosal ulcers)	67%	71%	44%	0.140
Ischemic digital ulcers on examination or pits	31%	31%	33%	1.000
Mucosal ulcerations (tongue, larynx, Vocal cords, mouth, NOT attributable to MTX or H!	35%	34%	43%	0.690
Cutaneous ulcerations on skin (hands or rest of body)	63%	67%	44%	0.270
Required intubation for rapidly progressive ILD (excludes elective/BAL/bx)	12%	14%	0%	0.570
Spontaneous pneumothorax or pneumomediastinum	8%	10%	0%	1.000
Proximal muscle weakness on examination	73%	79%	44%	0.093
Received pulse dose solumedrol	35%	40%	11%	0.130
Death	10%	12%	0%	0.570

regards to disease severity, 35% of patients required pulse-dose solumedrol at some point in their treatment course, 8% experienced a spontaneous pneumothorax or pneumomediastinum, 12% required intubation, and 10% died.

Over longitudinal follow-up, the median of which was 3.5 years (IQR 1.3-5.9), a total of 9 patients (18%) achieved clinical remission. One patient lost to follow-up could not be reached to ascertain clinical status. For the 9 patients that achieved clinical remission, the median time from DM-symptom onset to clinical remission was 4 years (IQR 2.4-5.0, range 1.8-5.6). The median duration of remission at the time of this study was 3.5 years (range 1.4-7.8). There were no demographic or disease characteristics that were significantly associated with clinical remission. There was no association between baseline MDA5 titer as obtained by MBL ELISA and clinical remission (median MBL MDA5 139 vs 140 units, Wilcoxon rank sum p=0.82). In patients who went into remission, there was no clear association with receiving more immunosuppression: A history of combination therapy use was equally likely in remission and non-remission groups, with a median number of concurrent medications of 3 throughout follow-up. Similarly, patients who went into remission had the same interval between DM-symptom onset to 1st immune-suppressing medication prescribed (median 0.25 years vs 0.25 years, rank sum p=0.185).

Conclusion: In a single center, tertiary referral population of MDA5+ DM, the largest North American cohort reported to date, approximately 20% of patients experienced long-term drug-free remission. No demographic, clinical sign/

symptom or laboratory factors were associated with remission. Future studies investigating other candidate biomarkers are warranted to identify this patient subgroup.

Disclosure: C. Mecoli, None; **E. Tiniakou**, None; **W. Kelly**, None; **J. Albayda**, None; **J. Paik**, Pfizer Inc, 5; **B. Adler**, None; **A. Mammen**, None; **C. Lin**, None; **S. Danoff**, None; **L. Casciola-Rosen**, None; **L. Christopher-Stine**, None.

Abstract Number: 0688

Standardized Prevalence Ratios of Cancer in Idiopathic Inflammatory Myositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Number of IIM patients, person-years of follow-up, and cancer standardized prevalence ratio in each autoantibody stratum. Time period is from cohort enrollment, median 1.6 (IQR 0.75-3.8) years after IIM-symptom onset. TIF1y was considered positive by two different MBL thresholds: >32 units per manufacturer, and >6 units (4 standard deviations above healthy control cohort mean)

Cancer site	Antibody	Person-years	No. observed	No. expected	Standardized Prevalence Ratio (95% CI)	p-value	N
All	All	6874	88	65.8	1.34 (1.07-1.65)	0.010	1062
All	TIF1y > 6	1555	25	14.4	1.73 (1.12-2.56)	0.014	240
All	TIF1y > 32	958	17	8.8	1.94 (1.13-3.10)	0.018	150
All	TIF1y ≤ 6	2963	27	26	1.04 (0.68-1.51)	0.900	456
All	TIF1y ≤ 32	3560	35	31.7	1.11 (0.77-1.54)	0.600	546
All	Ro52	1825	21	15.6	1.35 (0.83-2.06)	0.220	283
All	Ro52&TIF1y	185	3	1.4	2.18 (0.45-6.37)	0.320	34
All	EJ	80	1	0.8	1.18 (0.03-6.60)	0.990	11
All	Jo1	1062	12	9.5	1.26 (0.65-2.21)	0.500	156
All	Ku	232	4	2.3	1.71 (0.47-4.38)	0.420	38
All	PL7	191	1	1.5	0.67 (0.02-3.73)	0.990	30
All	PL12	164	1	1.3	0.75 (0.02-4.20)	0.990	30
All	OJ	39	0	0.5	0.00 (0.00-7.04)	0.990	7
All	EJ|Jo1|PL7|PL12|OJ	1518	15	13.5	1.11 (0.62-1.84)	0.750	229
All	Mi2	366	5	4.1	1.21 (0.39-2.81)	0.800	52
All	NXP2	438	7	3.9	1.78 (0.71-3.66)	0.210	71
All	SAE	111	4	1.2	3.25 (0.89-8.33)	**0.073**	17
All	Mi2|NXP2|SAE	900	15	9.2	1.64 (0.92-2.70)	**0.094**	138
All	MDA5	424	3	3.1	0.95 (0.20-2.78)	0.990	64
All	PM-Scl	280	0	2.3	0.00 (0.00-1.61)	0.200	41
All	HMGCR	939	16	12.6	1.27 (0.73-2.06)	0.400	142
All	SRP	383	2	3	0.66 (0.08-2.40)	0.840	68

Table 2. Number of IIM patients, person-years of follow-up, and cancer standardized prevalence ratio in each autoantibody stratum. Time period is from IIM symptom onset onwards. TIF1y was considered positive by two different MBL thresholds: >32 units per manufacturer, and >6 units (4 standard deviations above healthy control cohort mean)

Cancer site	Antibody	Person-years	No. observed	No. expected	Standardized Prevalence Ratio (95% CI)	p-value	N
All	All	10498	140	89.6	1.56 (1.31-1.84)	<0.001	1127
All	TIF1y > 6	2292	48	19.4	2.47 (1.82-3.27)	<0.001	266
All	TIF1y > 32	1468	31	12.3	2.53 (1.72-3.59)	<0.001	167
All	TIF1y ≤ 6	4485	43	35.3	1.22 (0.88-1.64)	0.230	479
All	TIF1y ≤ 32	5309	60	42.5	1.41 (1.08-1.82)	0.013	578
All	Ro52	2763	31	21.4	1.45 (0.98-2.05)	**0.060**	296
All	Ro52&TIF1y	314	6	2.2	2.76 (1.01-6.01)	0.047	37
All	EJ	118	1	1.1	0.87 (0.02-4.86)	0.990	11
All	Jo1	1601	15	12.9	1.17 (0.65-1.92)	0.620	159
All	Ku	356	7	3.4	2.05 (0.83-4.23)	0.117	42
All	PL7	292	2	2	1.00 (0.12-3.61)	0.990	33
All	PL12	229	3	1.7	1.76 (0.36-5.13)	0.490	32
All	OJ	84	0	0.9	0.00 (0.00-4.31)	0.850	7
All	EJ|Jo1|PL7|PL12|OJ	2262	20	18.1	1.11 (0.68-1.71)	0.710	236
All	Mi2	477	7	4.9	1.42 (0.57-2.93)	0.450	56
All	NXP2	657	10	5.2	1.93 (0.93-3.55)	**0.078**	74
All	SAE	143	6	1.5	4.04 (1.48-8.79)	0.009	19
All	Mi2|NXP2|SAE	1259	21	11.4	1.85 (1.14-2.82)	0.013	146
All	MDA5	578	5	4	1.26 (0.41-2.95)	0.720	66
All	PM-Scl	441	0	3	0.00 (0.00-1.22)	**0.096**	41
All	HMGCR	1457	22	17.1	1.29 (0.81-1.95)	0.280	150
All	SRP	613	6	4.2	1.42 (0.52-3.09)	0.500	73

Background/Purpose: Whether the likelihood of a cancer diagnosis in idiopathic inflammatory myopathy (IIM) patients differs by autoantibody type is not fully characterized. To inform cancer surveillance in IIM patients, in a large, tertiary referral IIM cohort, we determined whether cancer occurrence differs by autoantibody type from that expected based on the general US population.

Methods: Patients enrolled in our myositis cohort was retrospectively reviewed from 2007-2020 for adult patients who met one of these criteria: (i) Probable or definite DM/PM by Peter and Bohan, (ii) IMNM by the 2003 ENMC Criteria, (iii) Classic DM rash (Gottron's/heliotrope) and consistent histopathology on skin biopsy. Myositis specific and associated autoantibodies were determined systematically in our research lab using Euroimmun line blot (16 Ag IgG), ELISA (Mi2 and TIF1y by MBL, HMGCR by INOVA Diagnostics), and in-house immunoprecipitation (NXP2). Three time windows were analyzed: cohort enrollment onward, IIM symptom-onset onward, and within 3 years of IIM symptom onset (-3 to +3 years). The Surveillance, Epidemiology, and End Results (SEER) registry was used to compare the observed number of cancers to the expected number of cancers in the general population, adjusted for calendar year, age, sex, and race. Standardized prevalence ratios of cancer (SPR) – the observed/expected prevalence of cancer over an interval of time - were determined.

Results: 1174 patients, including 201 (17%) with a history of cancer, were studied. Median (IQR) time from IIM symptom onset to enrollment was 1.68 (0.75-3.8) yrs. From enrollment onward (5.21 [2.64-8.64] yrs; 89 diagnosed with cancer), patients with TIF1y autoantibodies (>6 units) had higher than expected cancer period prevalence (SPR=1.73, 95%CI 1.12-2.56), whereas patients negative for anti-TIF1y did not (SPR=1.04, 95%CI 0.68-1.51) [Table 1]. From IIM symptom onset onward (7.95 [4.92-11.86] yrs; 131 diagnosed with cancer, 25.2% within 0-1 yr, 28.2%

Table 3. Number of IIM patients, person-years of follow-up, and cancer standardized prevalence ratio in each autoantibody stratum. Time period is -3 to +3 years surrounding IIM symptom onset. TIF1γ was considered positive by two different MBL thresholds: >32 units per manufacturer, and >6 units (4 standard deviations above healthy control cohort mean)

Cancer site	Antibody	Person-years	No. observed	No. expected	Standardized Prevalence Ratio (95% CI)	p-value	N
All	All	6630	82	45.2	1.82 (1.44-2.25)	<0.001	1127
All	TIF1γ > 6	1540	34	10.6	3.22 (2.23-4.50)	<0.001	266
All	TIF1γ > 32	961	23	6.5	3.53 (2.24-5.29)	<0.001	167
All	TIF1γ ≤ 6	2826	28	17.6	1.59 (1.06-2.30)	0.026	479
All	TIF1γ ≤ 32	3405	39	21.6	1.81 (1.28-2.47)	<0.001	578
All	Ro52	1745	16	10.8	1.48 (0.85-2.41)	0.165	296
All	Ro52&TIF1γ	215	4	1.2	3.43 (0.93-8.78)	**0.062**	37
All	EJ	66	0	0.7	0.00 (0.00-5.63)	0.990	11
All	Jo1	950	5	5.8	0.86 (0.28-2.00)	0.940	159
All	Ku	243	6	1.8	3.40 (1.25-7.40)	0.019	42
All	PL7	190	2	1.1	1.76 (0.21-6.37)	0.630	33
All	PL12	188	2	1.1	1.83 (0.22-6.60)	0.600	32
All	OJ	42	0	0.4	0.00 (0.00-9.21)	0.990	7
All	EJ|Jo1|PL7|PL12|OJ	1402	8	8.9	0.90 (0.39-1.78)	0.950	236
All	Mi2	322	6	2.5	2.39 (0.88-5.19)	**0.086**	56
All	NXP2	437	6	3.2	1.85 (0.68-4.03)	0.220	74
All	SAE	109	3	1	3.03 (0.63-8.86)	0.157	19
All	Mi2|NXP2|SAE	852	14	6.5	2.16 (1.18-3.62)	0.014	146
All	MDA5	391	3	2.2	1.36 (0.28-3.98)	0.760	66
All	PM-Scl	246	0	1.2	0.00 (0.00-3.11)	0.610	41
All	HMGCR	885	9	8.5	1.06 (0.48-2.01)	0.950	150
All	SRP	427	6	2.3	2.62 (0.96-5.70)	**0.059**	73

>1-3 yrs, 14.5% >3-5 yrs, 32.1% >5 yrs), patients with anti-TIF1γ had higher than expected period prevalence of cancer, mainly breast (SPR=2.95, 95%CI 1.69-4.70) and ovarian (SPR=16.63, 95%CI 6.10-36.19). Patients with anti-SAE also had higher than expected cancer period prevalence (SPR=4.04, 95%CI 1.48-8.79). Patients with anti-Mi2 had higher than expected period prevalence of gastrointestinal cancers (SPR=6.03, 95%CI 1.24-17.61) [Table 2]. Within 3 yrs of IIM symptom onset (93 diagnosed with cancer), patients with anti-TIF1γ had higher than expected period prevalence of breast and ovarian cancer [Table 3]. Patients with DM autoantibodies (Mi2, SAE, or NXP2) had higher than expected cancer period prevalence.

Conclusion: In this tertiary referral center cohort, anti-TIF1γ was associated with higher occurrence of breast and ovarian cancers. Other DM-specific autoantibodies (Mi2, SAE, or NXP2) were associated with higher cancer occurrence. No cancer association (positive or negative) was observed for antisynthetase antibodies. These data suggest that intensive cancer surveillance is not needed in all IIM patients, and that autoantibody type may inform cancer occurrence, site and timing. Funded in part by NIAMS K23AR075898.

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Abstract Number: 0689

Incidence, Prevalence, and Mortality of Dermatomyositis: A Population-based Cohort

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Previous epidemiologic studies defined dermatomyositis (DM) using international codes of diseases (ICD) codes or Bohan & Peter 1975 criteria, and most were not population-based. Therefore, we aimed to determine the population-based incidence, prevalence, and mortality of DM, all using the new European League Against Rheumatism (EULAR)/American College of Rheumatology (ACR) 2017 DM classification criteria to define patients with DM.

Methods: This population-based cohort study included incident DM from 1/1/1995 and 12/31/2019 among all residents in a single geographical location. We used ICD codes for DM (710.3, M33.0-1, M33.9) and polymyositis (710.4, M33.2) to identify individuals with possible DM, and manually reviewed all to determine if they met criteria for DM by EULAR/ACR criteria (primary), rheumatologist/dermatologist physician diagnosis, and/or Bohan & Peter 1975 criteria. We defined index date of DM as date of EULAR/ACR 2017 criteria fulfilment. For incidence and prevalence, we age- and sex-adjusted our estimates to the United States White year 2000 population and provided 95% confidence intervals (CI). We estimated prevalence on 1/1/2015. For mortality calculations, we compared the survival of our cohort to expected survival rates from local life tables by age, sex, and year using standardized mortality ratios.

Table 1. Age- and sex-specific dermatomyositis incidence rates from 1995 to 2019

	Female		Male		Total	
Age	N	Rate (per 100,000)	N	Rate (per 100,000)	N	Rate (per 100,000)
18-29	1	0.29	0	0.0	1	0.2
30-39	4	1.5	1	0.4	5	0.9
40-49	4	1.6	0	0.0	4	0.8
50-59	6	2.7	1	0.5	7	1.6
60-69	4	2.6	1	0.7	5	1.7
70-79	3	3.0	0	0.0	3	1.6
80+	4	5.1	0	0.0	4	3.2
Total	26	1.8 (1.2,2.6)*	3	0.2 (0.0,0.5)*	29	1.1 (0.7,1.5)**

*Age-adjusted to the US White 2000 population
**Age- and sex-adjusted to the US White 2000 population

Table 2. Age- and sex-specific dermatomyositis prevalence rates on 1 January 2015

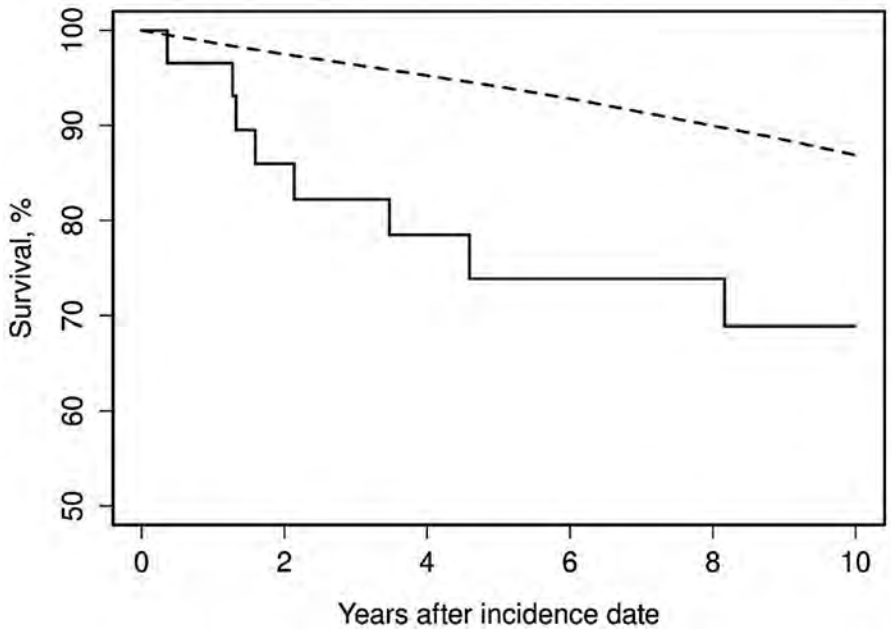
	Female		Male		Total	
Age	N	Rate (per 100,000)	N	Rate (per 100,000)	N	Rate (per 100,000)
18-29	0	0	0	0	0	0
30-39	1	9	0	0	1	4
40-49	2	22	0	0	2	11
50-59	2	18	1	10	3	14
60-69	2	25	1	14	3	20
70-79	4	81	0	0	4	44
80+	2	56	0	0	2	34
Total	13	21 (10,33)*	2	3.0 (0,7.2)*	15	13 (6,20)**

*Age-adjusted to the US White 2000 population

**Age- and sex-adjusted to the US White 2000 population

Results: We identified 40 cases of verified DM meeting at least one of the three DM criteria. Of those, 29 cases were incident DM in the study geographical location from 1995 to 2019 (mean age 57 years, 90% female). Median follow-up time was 8.2 years with interquartile range (IQR) 3.5 to 16.3 years. Of the 29, 17 (59%) had clinically myopathic DM, and 12 (41%) had clinically amyopathic DM (CADM). After age- and sex-adjusting to the US White 2000 population, the overall incidence of DM was 1.1 (95% CI 0.7 to 1.5) per 100,000 person-years (Table 1), and prevalence was 13 (95% CI 6 to 20) per 100,000 (Table 2). During the study period, 6 individuals with myopathic DM and 3 with CADM died (overall 10-year survival 69%; 95% CI 48-96%). Mortality of this DM cohort was higher than expected for their age-, sex-, and year-matched peers (Figure 1). The standardized mortality ratio was significantly elevated among the myopathic DM cases (3.1, 95% CI 1.1 to 6.8) but not CADM cases (1.1, 95% CI 0.2 to 3.3).

Conclusion: This population-based study using validated DM classification criteria found incidence and prevalence on the higher end of previous reports. Though confidence intervals were wide, mortality was significantly elevated for myopathic DM but not for CADM.



Overall survival of residents with incident dermatomyositis in 1995-2019 compared to expected rates from local lifetables

Disclosure: V. Kronzer, None; **B. Kimbrough**, None; **C. Crowson**, None; **J. Davis**, Pfizer, 5; **M. Holmqvist**, None; **F. Ernste**, Octapharma, 5, The Myositis Association, 4.

Abstract Number: 0690

Impact of Achieving 2016 ACR/EULAR Response Criteria on Patient Centered Outcome Measures in Myositis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
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Session Time: 8:30AM–10:30AM

Background/Purpose: The 2016 ACR/EULAR Myositis Response Criteria represent a composite measure that is increasingly being used as a primary end point in myositis clinical trials. The total improvement score (TIS) is calculated using differentially-weighted changes in six myositis core set measures, with thresholds for minimal, moderate and major improvement. It is unclear if achievement of these improvement levels truly reflects changes in symptoms, physical function, and physical activity in myositis patients. In this study, we examined the impact of achieving ACR-EULAR response criteria on patient-centered outcome measures.

Methods: Myositis patients were consecutively enrolled in an observational study with baseline, 3- and 6-month visits where six core set measures [extra-muscular, patient global, and physician global disease activity, manual muscle testing, HAQ-DI, and creatine kinase levels] were evaluated and TIS was calculated for each visit (https://www.niehs.nih.gov/research/resources/imacs/response_criteria/adult.html). The patient centered outcome measures included fatigue (VAS, SF-36), pain (VAS, SF-36), muscle strength (dynamometry), patient reported physical function (PROMIS PF-20, SF-36), task oriented physical function tests [sit-to-stand, timed up-and-go, and six-min walk test] and physical activity (Actigraph). Wilcoxon signed-rank test was used to assess significance of change in outcome measures over 3- and 6-months. Relative changes in outcome measures were compared between patients with improvement vs. those without improvement by using Mann-Whitney U test. Spearman correlation was used for correlations between TIS and changes in specified outcome measures.

Results: Fifty myositis patients were enrolled [mean age: 52, 60% female, 94% white], including 6 PM, 24 DM, 9 necrotizing myopathy and 11 with anti-synthetase syndrome. As per ACR/EULAR criteria, 22 patients had TIS scores satisfying criteria for improvement (13 minimal, 7 moderate, 2 major) at 3-months. Patient centered outcome measures including fatigue, pain, muscle strength, patient reported, and task oriented physical function measures demonstrated significantly greater changes in patients who met ACR/EULAR response criteria of at least minimal improvement compared to those who did not (Table 1). TIS correlated moderately-strongly with relative changes in most patient-centered outcome measures (Table 2). Similar results were noted at 6-months (n=39). Percentage agreement of improvement per TIS was 62% with patient-reported improvement and 90% with physician-reported improvement at 6-months. Patients who had at least minimal improvement also demonstrated significant improvement in pain, fatigue, muscle strength, PROMIS-PF, and task-oriented physical function tests over 6-months.

Table 1. Relative percent changes in patient-reported and clinical outcome measures [median (IQR)] using 2016 ACR EULAR myositis response criteria at 3 and 6 months

3 months	No improvement (n=21)	Improvement (n=22)	P value
Disease activity			
Muscle disease activity	0 [0-0]	-41.6 [(-66.6) – (-23.7)]	<0.0001
Muscle strength			
Dynamometry	-0.7 [(-14.7)-17]	18.7 [2.8 – 56]	0.02
Physical function (PRO)			
PROMIS t-score	-0.2 [(-7.6)-3.4]	4.6 [0.5 – 14.5]	0.01
SF36 PF10	-5.5 [(-20)-7.6]	25 [0-100]	0.01
Physical function (Task-oriented)			
Sit to stand	0 [(-11.1)-23]	9.5 [0 – 40]	0.1
Timed up and go	2.7 [(-3.3) – 15.3]	-9 [(-16.7) – 1.6]	0.009
6MWT (meters)	0.8 [(-12.3)-10.3]	12.8 [(-0.1) – 25]	0.01
Pain			
Pain VAS	0[0-100]	-47.8 [(-91.6) – 3.1]	0.004
SF36 Pain	0 [(-20) – 16.8]	48.8 [11.1 – 100]	0.004
Fatigue			
Fatigue VAS	0 [(-42.4) – 100]	-26.3 [(-67.5) – 35]	0.06
SF36 Fatigue	0 [(14.2) – 0]	75 [12.5 – 200]	0.0001
Physical activity (Actigraph)			
Peak 1-min cadence	-4.2 [(-13.1) – 3.7]	-0.8 [(-19.7) – 17.3]	0.5
Steps per minute	-4.7 [(-14.6) – 6.1]	0.1 [(-18.9) – 31.7]	0.6
Vector magnitude per minute	-5 [(16.6) – 9.9]	5.6 [(16.1) – 28.2]	0.4
6 months	**No improvement (n=18)**	**Improvement (n=21)**	**P value**
Disease activity			
Muscle disease activity	0 [(-5) – 0]	-62.5 [(-87.5) – 0]	<0.0001
Muscle strength			
Dynamometry	-9.8 [(-19.2) – 1.1]	33.3 [7.6 – 78.7]	<0.0001
Physical function (PRO)			
PROMIS t-score	-4 [(-8.7) – 0.7]	5.2 [(-1.6) – 23.2]	0.02
SF36 PF10	-5.2 [(18.3) – 2.6]	75 [0-200]	0.001
Physical function (Task oriented)			
Sit to stand	8.8 [(-9.3) – 21.2]	21.4 [9.7 – 52.7]	0.007
Timed up and go	-0.9 [(-7.4) – 14.6]	-11.5 [(-21.90) – 1.5]	0.06
6MWT (meters)	2.4 [(-6.1) – 10.2]	8.7 [(-1.6) – 54.6]	0.1
Pain			
Pain VAS	0 [0 – 100]	-20.8 [(-95.3) – 55.3]	0.04
SF36 pain	0 [(-23.5) – 0]	71.1 [0 – 122.2]	0.001
Fatigue			
Fatigue VAS	10.4 [0 – 100]	-23 [(-65) – 0]	0.001
SF36 fatigue	-8.3 [(-34.2) – 0]	26.5 [0-240]	0.001
Physical activity (Actigraph)			
Peak 1-min cadence	0.9 [(-14.3) – 11.4]	3.2 [(-17.6) – 36.2]	0.6
Steps per minute	-11.3 [(-28.1) – 9.7]	-7.7 [(-20.6) – 76.4]	0.3
Vector magnitude per minute	-13.4 [(-27.5) – 0.7]	1.3 [(-10.9) – 34.7]	0.02

Conclusion: Achieving improvement using the ACR/EULAR myositis response criteria was accompanied by significant improvement in several patient centered outcome measures including fatigue, pain, muscle strength, physical function, and physical activity. Our results reinforce the validity of the ACR/EULAR myositis response criteria and support their use as a clinically meaningful metric of improvement.

Table 2. Correlations of outcome measures with total improvement score using 2016 ACR/EULAR myositis response criteria at 3 and 6 months

Percent relative change	Correlation at 3 months (n=43)		Correlation at 6-months (n=39)	
	Rho	*p*	*Rho*	*p*
Disease activity				
Muscle disease activity	-0.81	<0.0001	-0.74	<0.0001
Muscle strength				
Dynamometry	0.45	0.01	0.67	<0.0001
Physical function (PRO)				
PROMIS t score	0.44	0.003	0.38	0.02
SF-36 physical function	0.36	0.02	0.59	0.0004
Physical function (Task-oriented)				
Sit-to-stand	0.25	0.11	0.46	0.003
Timed up-and-go	-0.32	0.04	-0.31	0.06
6MWT	0.31	0.05	0.29	0.08
Physical activity (Actigraph)				
Peak 1-min cadence	0.15	0.3	0.43	0.01
Steps per minute	0.10	0.5	0.41	0.02
Vector magnitude per minute	0.17	0.2	0.53	0.003
Pain				
Pain VAS	-0.39	0.009	-0.38	0.02
SF36 pain	0.50	0.001	0.60	0.0003
Fatigue				
Fatigue VAS	-0.23	0.13	-0.50	0.001
SF36 Energy/fatigue	0.59	<0.0001	0.53	0.002

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Abstract Number: 0691

Serum Cytokine Profiles of Patients with Adult Idiopathic Inflammatory Myopathy

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Idiopathic inflammatory myopathies are a heterogenous group of systemic autoimmune diseases characterized by muscle weakness. Serum cytokines and chemokines could shed light on disease pathogen-

Table 1. Baseline demographics and myositis core set measures of the three patient groups enrolled in the study

	Myositis patients with active disease (n=11)	Myositis patients in trial (n=10)	Myositis patients in remission (n=11)
Age	51.4 ± 20.9	51.4 ± 13.2	58.5 ± 15.9
Gender (Male/Female)	4/7	1/9	1/10
Diagnosis (PM/DM)	2/9	4/6	1/10
Manual muscle test (0-80)	67 [62-80]	59.2 [51.7-70]	80 [78-80]
HAQ-DI (0-3)	1.2 [0.5-1.8]	1.5 [0.2-1.6]	0.7 [0-1/3]
Physician-reported disease activity (0-10)	5 [3.7-5.7]	4.7 [2.6-6.5]	1.5 [0-3.5]
Patient reported disease activity (0-10)	5 [3-7]	5 [2-5.6]	5 [1-7.5]
Extra-muscular global disease activity (0-10)	1.5 [0.7-4.7]	2.1 [0.7-3.6]	0.6 [0-1.5]
Creatine kinase level (IU/L)	75 [51-213]	386 [66-2765]	162 [57.5-306]

esis and be used as biomarkers for prognostication, monitoring disease activity, and treatment response. We aimed to identify serum cytokine profiles of patients with active disease as compared to patients in remission and healthy controls, and explored correlations of these cytokines with clinical myositis outcome measures.

Methods: This was a prospective study of 3 clinical groups: (1) myositis patients with active disease, (2) patients in remission, and (3) healthy controls. All myositis patients fulfilled the Bohan-Peter criteria for DM/PM. Active disease was defined as requiring escalation of therapy within 6-months of screening. There were 3 study visits at baseline, 3- and 6-months. Plasma concentrations (pg/l) of 51 cytokines/chemokines/MMPs were obtained by utilizing a bead-based multiplex cytokine assay (Luminex). Physician- and patient-reported clinical outcome measures, functional measures, and creatine kinase levels were obtained for all the patients at each visit. T-test and false discovery rate for baseline differences as well as LASSO and random forest models were utilized to identify markers that best discriminate patients from controls, and patients with active disease from those in remission. GeneOntology was used for pathway analysis. Spearman correlation was used to assess correlations between cytokine levels and clinical outcome measures.

Results: 11 myositis patients in remission, 21 with active disease (including 10 enrolled in the open label trial of repository corticotropin injection) and 10 healthy controls were included in the study (Table 1). Results of the T-test,

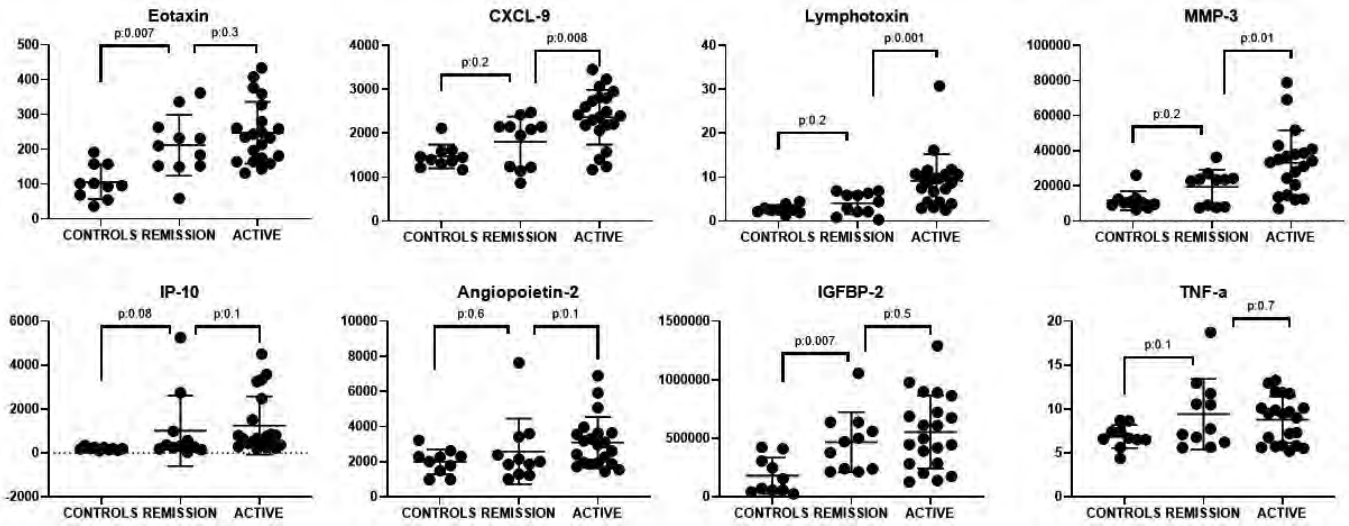

Figure 1. Distribution of cytokines/chemokine concentrations (pg/ml) among healthy controls, myositis patients with active disease and in remission.

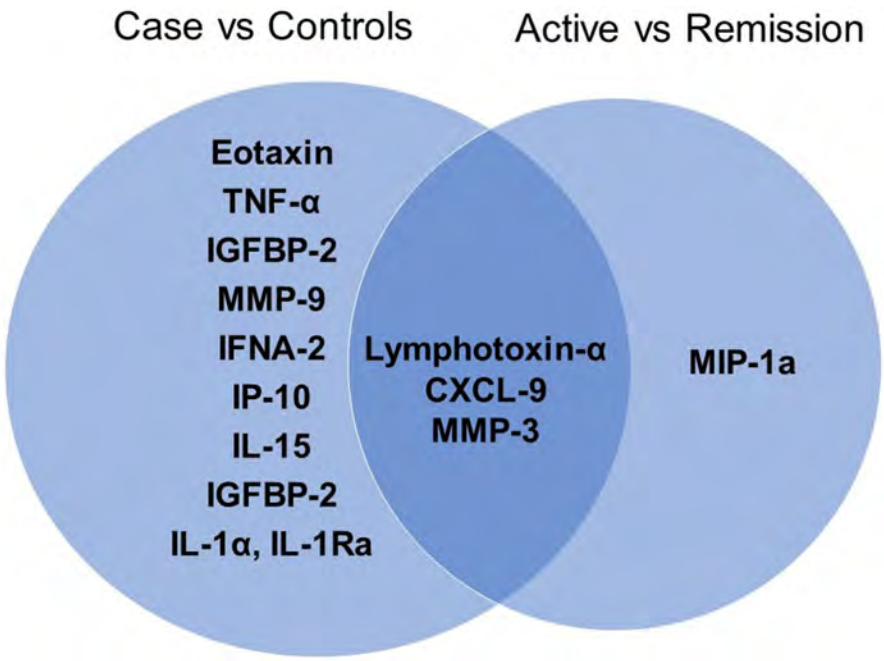

Figure 2. Upregulated cytokines that best differentiate cases from controls and patients with active disease from those in remission at baseline.

LASSO and random forest models revealed similar results. Myositis patients had elevated levels of chemokines that attract eosinophils (eotaxin) and dendritic cells, NK cells, cytotoxic T cells and monocytes/macrophages (CXCL-9, IP-10), cytokines that drive T-helper 1 responses (TNF-a, IL-1a, IL-1Ra, lymphotoxin-a, IFNA-2, IL-15), matrix degrading enzymes (MMP-3 and -9), and IGFBP-2 compared to healthy controls (Figure 1,2). Myositis patients with active disease had higher levels of lymphotoxin-a, CXCL-9, MIP-1b and MMP-3 than patients in remission. The pathways related to increased levels of these cytokines include chronic inflammatory responses, regulation of IL-1 mediated signaling, myoblast fusion, and tyrosine phosphorylation of STAT proteins. Eotaxin and CXCL-9 correlated with cutaneous and extramuscular global disease activity, IP-10 corelated with manual muscle strength test, and IL-1 correlated with HAQ as well as functional tests.

Conclusion: We identified key cytokines and chemokines that distinguish myositis patients from healthy controls as well as different disease activity states. Some cytokines correlated with clinical outcome measures, suggesting their potential use as biomarkers. Longitudinal analysis for the comparative changes in key cytokines and chemokines among different groups is currently ongoing. Larger longitudinal studies are needed to validate our findings.

Disclosure: D. **Saygin**, None; **P. Biswas**, None; **S. Nouraie**, None; **S. Moghadam-Kia**, None; **M. McGeachy**, None; **C. Oddis**, Genentech, 5, Pfizer, 2, Corbus, 5, CSL Behring, 5, EMD Serono, 2, 5; **S. Dzanko**, None; **D. Koontz**, None; **D. Ascherman**, None; **R. Aggarwal**, Mallinckrodt, 1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2.

Abstract Number: 0692

Immunophenotyping of Inclusion Body Myositis Blood T Cells: Pathogenic and Biomarker Implications

Namita Goyal[1], Jonathan Cauchi[1], Tyler Irani[1], Nadia Araujo[1], Leo Wang[2], Marie Wencel[1], Vivian Li[3], **Steven Greenberg**[4] and Tahseen Mozaffar[1], [1]University of California Irvine, Irvine, CA, [2]University of Washington, Seattle, WA, [3]University of California, Irvine, CA, [4]Brigham and Women's Hospital Department of Neurology, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The recent discovery of highly differentiated, killer cell lectin-like receptor subfamily G member 1 (KLRG1)+ T cells in the muscle of inclusion body myositis (IBM) patients raises the potential of targeting KLRG1 for therapeutic intervention. High-resolution mapping of blood KLRG1+ T cells and the broader T cell compartment of IBM patients is lacking. Here, we report the deep immunophenotyping of IBM blood T cell compartments and the relationship of derived biomarkers to IBM diagnosis, disease duration, and disease severity.

Methods: Patients providing informed consent who met the European Neuromuscular Centre (ENMC) criteria for clinically defined or probable IBM were included. Functional data and quality of life questionnaires were collected. Serological testing for NT5C1A antibodies and analysis of markers of T cell and NK subsets including KLRG1 isolated from peripheral blood through multiplex flow cytometry were done and compared with data from age-matched healthy donors.

Results: Data were obtained from 51 IBM patients and 19 healthy donors. A population of KLRG1+ T effector memory (TEM) and T effector memory re-expressing CD45RA (TEMRA) cells was expanded in both the CD4+ and CD8+ T cell subpopulations of IBM patients (Figure 1). KLRG1 expression in CD8+ T cells increased with T cell differentiation with the lowest levels in naïve T cells and highest in highly differentiated TEMRA and CD56+CD8+ T cells in IBM. The CD8+ TEMRA and KLRG1+ CD8+ TEMRA proportions were not associated with IBM disease severity, but modestly positively associated with disease duration. The KLRG1+CD4+ cells in IBM patients vs healthy controls had high

Table 1. Diagnostic performance of blood biomarkers of IBM

Biomarker	AUC	p-value
CD4% of CD3	0.70	0.0078
CD8 % of CD3	0.69	0.0127
CD8/CD4 Ratio	0.70	0.0100
KLRG1+ % of CD3	0.78	0.0002
KLRG1+ % of CD4	0.96	<0.0001
KLRG1+ % of CD8	0.72	0.0037
KLRG1+ % of CD8 TEMRA	0.66	0.0475
KLRG1+ % of CD4 TEM	0.65	0.0628
NK (CD56dim) %lymphs	0.57	0.3610
KLRG1+ % of NK	0.68	0.0191

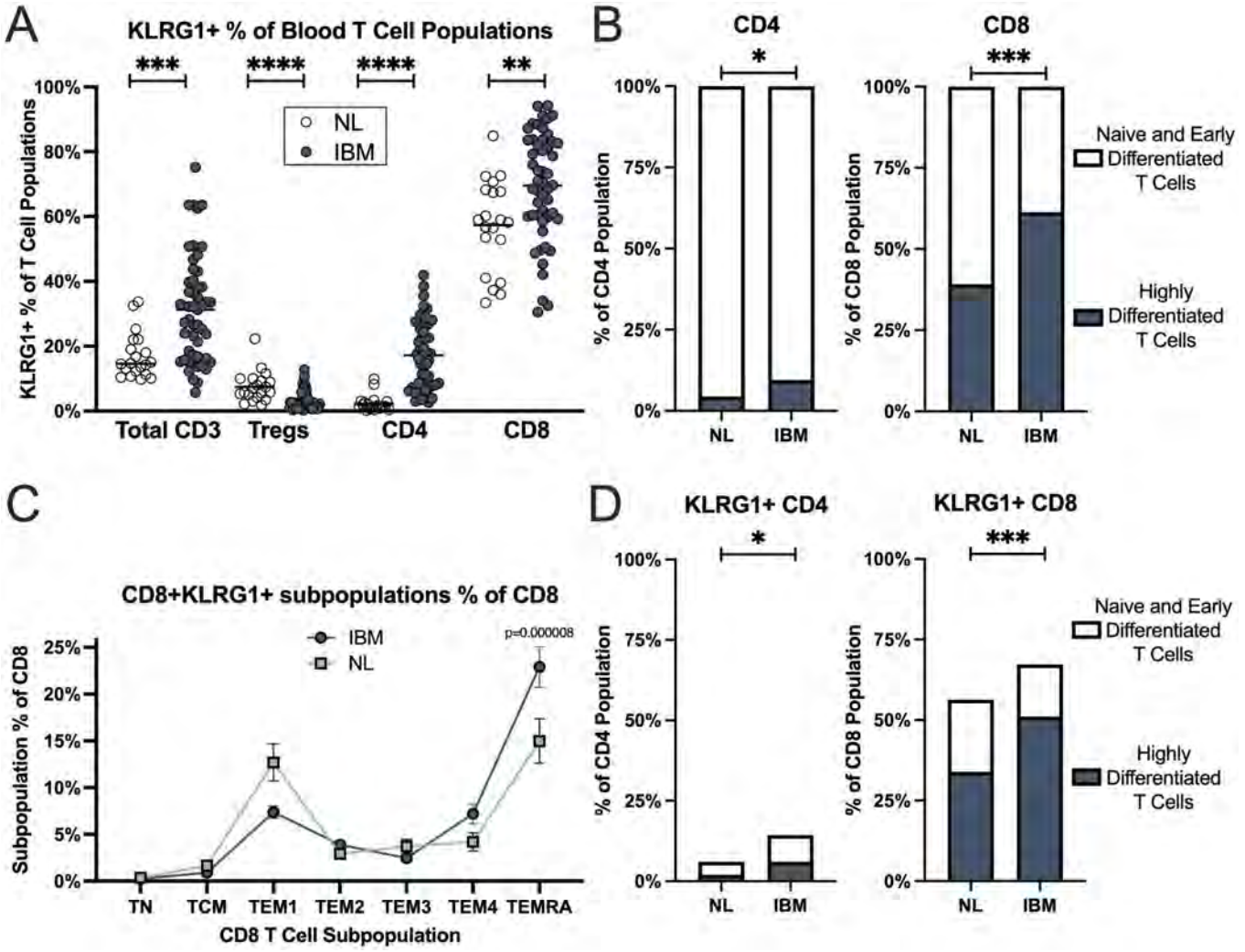

Figure 1. Skewed distribution of the blood T cell population in IBM towards highly differentiated CD8+ cytotoxic T cells. (A) Expansion of the KLRG1+ populations among total CD3+ T cells, Tregs, CD4+ T cells, and CD8+ T cells. (B) The proportion of blood naïve and early differentiated T cells (CD57-CD28+) and heterogenous highly differentiated T cells (CD57-CD28-; CD57+CD28-; CD57+CD28+) among CD4+ Tconv and CD8+ T cells. (C) KLRG1 expansion within and CD8+ TEM4 and TEMRA populations. (D) Expansion of the KLRG1+ T cell population lies largely within the highly differentiated compartments.

diagnostic performance (area under the curve=0.96; p< 0.0001) (Table 1). Minimal KLRG1 expression was present on regulatory T cells (3%) and no apparent alterations in NK cell phenotypes were identified in IBM.

Conclusion: Our findings reveal an expansion of blood KLRG1+ CD4+ and CD8+ TEMRA and TEM cells in IBM. Lack of association with disease activity suggests these cells may have a pathogenic role throughout the entire disease course. Measurement of these cells potentially allows for new blood diagnostic biomarkers.

Disclosure: N. Goyal, None; **J. Cauchi**, None; **T. Irani**, None; **N. Araujo**, None; **L. Wang**, None; **M. Wencel**, None; **V. Li**, None; **S. Greenberg**, Abcuro, Inc., 1, 2, 8, 10; **T. Mozaffar**, None.

Abstract Number: 0693

Discovery of Antigen Specific CD4+ T Cells in Anti-HMGCR-positive Immune Mediated Necrotizing Myopathy

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Background/Purpose: Anti-3-hydroxy-3-methylglutaryl coenzyme A reductase (HMGCR)-positive immune mediated necrotizing myopathy (anti-HMGCR+ IMNM) is a unique myopathy characterized by IgG autoantibodies against HMGCR and a strong association with a specific HLA class II allele (*HLA-DRB*1*11:01). Although this implicates HMGCR-specific CD4+ T cells in disease pathogenesis, no such cells have been identified thus far. In this study, we aimed to define HMGCR T cell epitopes using a natural antigen processing assay (NAPA).

Methods: Monocyte-derived dendritic cells (MoDCs) from 6 patients with anti-HMGCR+ IMNM were incubated with the C-terminal portion of HMGCR protein (amino acids 340-888) and presented peptides were identified using NAPA. Briefly, HLA-DR/peptide complexes were isolated by immunoprecipitation, and bound HMGCR peptides were sequenced by mass spectrometry. HMGCR peptides corresponding to the putative CD4+ T cell epitopes were synthesized and used to stimulate peripheral blood mononuclear cells (PBMCs) from 6 patients with anti-HMGCR+ IMNM and 6 patients with dermatomyositis, as negative controls. HMGCR-reactive CD4+ T cells were identified by flow cytometry based on activation status (CD154 upregulation).

Results: A total of 7 different naturally processed HMGCR peptides were identified using NAPA (Table 1). The number of distinct peptides presented per patient ranged from 1 to 5, with 5 epitopes being presented by at least two patients. All naturally presented HMGCR peptides elicited robust CD4+ T cell responses in the 6 anti-HMGCR+ IMNM

Table 1. Naturally processed HMGCR peptides identified by mass spectrometry. The naturally processed HMGCR peptides presented by each patient are indicated (+ = detected, - = not detected my mass spectrometry)

HMGCR+ Patient ID	1	2	3	4	5	6	7	#Peptides
9184	-	-	-	+	-	+	-	2
11054	-	+	-	+	-	-	+	3
12133	-	-	+	+	+	+	-	4
12168	+	+	-	+	+	-	+	5
13125	-	-	-	-	+	-	-	1
16024	-	-	-	+	-	+	-	2
#Patients	**1**	**2**	**1**	**5**	**3**	**3**	**2**	

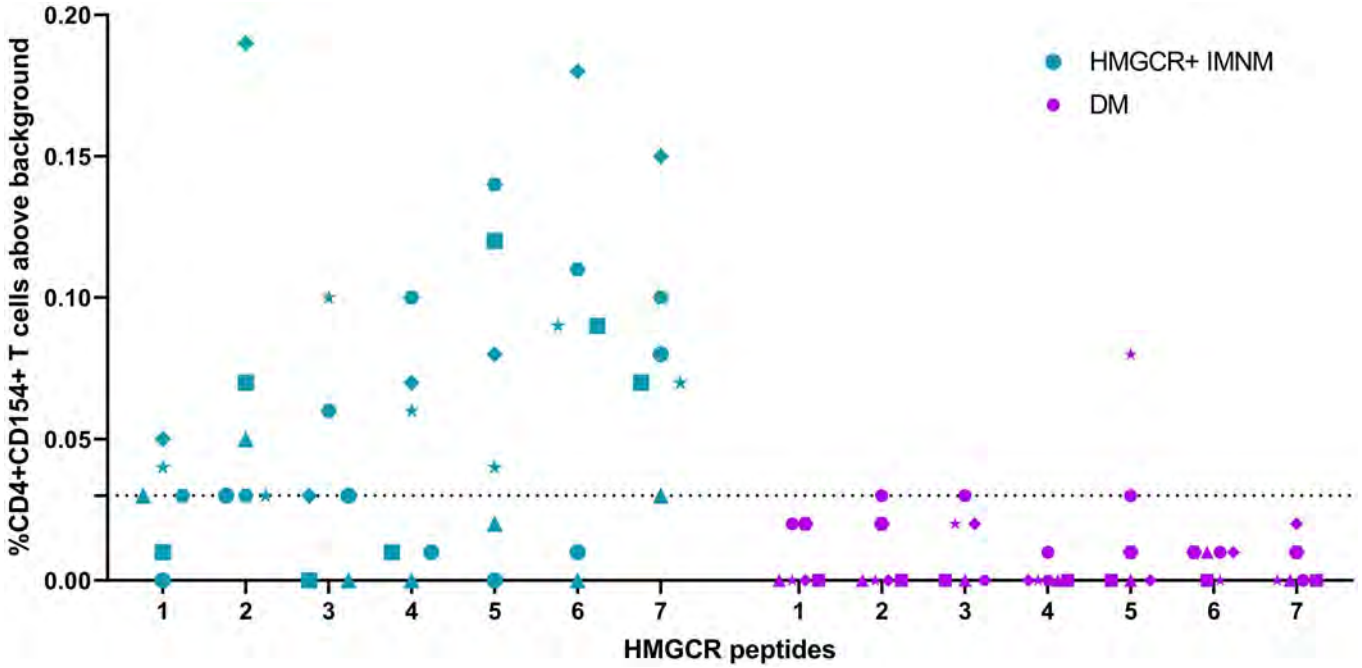

Figure 1. Anti-HMGCR+ IMNM patient T-cell responses to naturally processed HMGCR peptides. PBMCs from 6 anti-HMGCR+ IMNM patients were stimulated with the HMGCR peptides identified by NAPA and the % of CD4+CD54+ T cells above background observed with media alone was measured. Positive responses were considered those above the 95th percentile of the response of dermatomyositis (DM) controls (dotted line).

patients, compared to only 2/6 patients with dermatomyositis (p=0.014). All anti-HMGCR+ IMNM patients responded to 3-7 peptides (median 5.5) (Figure 1), and the T cell responses were significantly higher than those observed in patients with dermatomyositis (p< 0.0001).

Conclusion: Our findings represent the first report of antigen-specific CD4+ T cells in anti-HMGCR+ IMNM. Leveraging NAPA, we were able to define a core set of HMGCR peptides naturally presented by MoDCs from patients with anti-HMGCR+ IMNM, defining precise immunologically relevant autoantigenic CD4+ T cell epitopes. Definition of these epitopes is key in understanding disease pathogenesis and will aid in the future development of antigen-specific research and therapeutic tools.

Disclosure: E. Tiniakou, None; **A. Mammen**, None; **E. Darrah**, None.

Abstract Number: 0694

Glucagon-like Peptide-1 Receptor Agonist Suppresses Muscle Fiber Necroptosis and Muscle Inflammation and Ameliorates Muscle Weakness in Experimental Polymyositis

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: While glucocorticoids (GC) are the cornerstone of the treatment for polymyositis (PM), GC-induced myopathy is inevitable, which deteriorates muscle weakness. Therefore, novel therapeutic strategy that not only suppresses muscle inflammation but also improves muscle strength is awaited. Glucagon-like peptide-1 receptor (GLP-1R) agonists, which have been developed as an anti-diabetic therapy, have pleiotropic actions including anti-inflammatory effects, suppression of muscle wasting, and inhibition of cell death. We showed that the cell death of injured muscle fibers in PM is FASLG-mediated necroptosis, a form of regulated cell death accompanied with release of inflammatory mediators such as HMGB1. We also found that inhibition of necroptosis or HMGB1 ameliorated the muscle weakness and muscle inflammation in C protein-induced myositis (CIM), a murine model of PM. Accordingly, we hypothesized that GLP-1R agonists have beneficial effects on PM to recover muscle strength and to suppress muscle inflammation. The aims of this study are to examine the role of GLP-1R in PM and the effect of a GLP-1R agonist on PM models in vivo and in vitro.

Methods: Muscle specimens of PM patients and CIM were examined with immunohistological staining for the expression of GLP-1R. The effect of PF1801 (ImmunoForge, Seoul, South Korea), a GLP-1R agonist, on CIM was examined in monotherapy or in combination with prednisolone (PSL). C2C12-derived myotubes were treated with FAS ligand (FASLG) to induce necroptosis and used as an in vitro model of PM. The levels of HMGB1, TNF-α and IL-6 in the serum of CIM and the culture supernatant were measured by ELISA. The effect of PF1801 on the myotube necroptosis was examined using time lapse imaging and its effect on the activation of AMP-activated protein kinase (AMPK) and the expression of PGAM5 was assessed with western blotting. The levels of reactive oxygen species (ROS) were analyzed with CellROX® assay in vitro. The effect of PF1801 on the expression of antioxidant molecules was analyzed with quantitative real-time PCR in vitro.

Results: GLP-1R was expressed on the inflamed muscle fibers of PM and CIM. The treatment with PF1801 in monotherapy or in combination with PSL suppressed CIM-induced muscle weakness and the muscle weight loss as well as the severity of histological myositis while the monotherapy with PSL did not suppress muscle weakness and muscle weight loss. PF1801 decreased the levels of HMGB1, TNF-α and IL-6 in the serum of CIM. In vitro, PF1801 inhibited FASLG-induced myotube necroptosis and decreased the levels of HMGB1, TNF-α and IL-6 in the supernatant. The inhibitory effect of PF1801 on myotube necroptosis was dependent on the activation of AMPK. PF1801 activated AMPK and decreased the levels of PGAM5, which was crucial for FASLG-induced necroptosis of the myotubes. Furthermore, PF1801 upregulated the expression of antioxidant molecules including *Nfe2l2, Hmox1, Gclm,* and *Nqo1* and suppressed FASLG-induced ROS accumulation in the myotubes.

Conclusion: GLP-1R agonist could be a novel therapy for PM that recover muscle weakness and suppress muscle inflammation through suppressing muscle fiber necroptosis.

Disclosure: M. Kamiya, None; **F. Mizoguchi**, AbbVie, 5, 6, Asahi Kasei Pharma, 2, 6, Astellas Pharma, 5, Bristol-Myers Squibb, 5, 6, Chugai Pharmaceutical, 5, 6, Daiichi Sankyo Company, 5, Eizai, 5, 6, Eli Lilly and Company, 5, 6, ImmunoForge, 2, 5, Glaxo Smith Kline,, 6, Japan Blood Products Organization, 5, Mitsubishi Tanabe Pharma, 5, Novartis Pharma Japan, 5, Ono Pharmaceutical, 5, 6, Otsuka Pharmaceutical Factory, 5, Pfizer, 5, 6, Sanofi, 5, Takeda Pharmaceutical Company, 5, Teijin, 5; **H. Sasaki**, None; **N. Umezawa**, None; **S. Yasuda**, Abbvie, 5, 6, Asahi Kasei Corporation, 5, 6, Chugai Pharmaceutical, 5, 6, Bristol Myers Squibb, 5, 6, Ono pharmaceuticals, 5, 6, Eisai, 5, 6, Tanabe-Mitsubishi Pharmaceutical, 5, 6, Eli Lilly, 5, 6, GlaxoSmithKline, 6, Pfizer, 6.

Abstract Number: 0695

Safety and Tolerability of IVIg (Octagam 10%) in Patients with Active Dermatomyositis. Results of a Randomized, Double-Blind, Placebo-Controlled Phase III Trial

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SESSION INFORMATION
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Background/Purpose: Dermatomyositis (DM) is a chronic systemic autoimmune disease with characteristic skin rash and muscle weakness. Intravenous immunoglobulin (IVIg) has long been used as adjuvant treatment for DM and its efficacy was recently shown in a double-blind, randomized, placebo-controlled, phase III clinical trial (ProDERM study). The aim of this sub-analysis of the ProDERM study was to present detailed safety and tolerability data of IVIg in DM subjects.

Methods: The trial enrolled adults with definite or probable DM (Bohan & Peter criteria) with active disease and muscle weakness (MMT < 142/150). In the double-blind, placebo-controlled First Period, subjects were randomized 1:1 to either high dose IVIg (2g/kg every 4 weeks) or placebo.

After week 16, all patients on placebo and patients without clinical worsening while on IVIg entered the open label Extension Period, receiving 2 g/kg IVIg infusions every 4 weeks for an additional 24 weeks period. IVIg was given in equally divided doses over 2-5 consecutive days (=1 infusion cycle) every 4 weeks.

Results: A total of 95 adult DM patients (mean age: 53 years; 75% females) were enrolled and received at least one dose of IVIg. Baseline clinical characteristics were balanced between the 2 arms. Overall 96% and 73% patients completed the first and extension period, with 3 (3%) and 9 (10%) subjects discontinuing due to adverse events (1 of 3 and 6 of 9 due to IVIg related events), respectively.

A total of 664 infusions cycles were administered and 545 adverse events (AEs) were reported. Of these AEs, 282 in 62 (65%) subjects were assessed as being related to study drug. The majority of related AEs were mild (73.4%, 207), some were moderate (23.4%, 66) or severe (3.2%, 9). Most were infusion reactions (92%, 260). Headache (42% of subjects), pyrexia (19%) and nausea (16%) were the most common AEs (Table 1). Premedication for infusions was required by only 21.3% of patients before IVIg administration.

The incidence of serious AEs was similar in the two treatment groups during the First Period: 3 subjects (5.8%) experienced 5 serious AEs after IVIg and 2 subjects (4.2%) experienced 4 serious AEs after placebo.

Table 1. Related AEs reported > 2% of subjects (First and Extension Period)

Adverse event	% of subjects (N=95)
Headache	42.1
Fever	19
Nausea	15.8
Vomiting	8.4
Chills	7.4
Musculoskeletal pain	7.4
Blood pressure increased	6.3
Coombs test positive	5.3
Dizziness	4.2
Tachycardia	4.2
Infusion site condition	3.2
Haemoglobin decreased	3.2
Dyspnoea	3.2
Asthenia	2.1
Fatigue	2.1
Pain	2.1
Peripheral swelling	2.1
Arthralgia	2.1
Muscle spasms	2.1
Pain in extremity	2.1
Pulmonary embolism	2.1
Anaemia	2.1
Lymphopenia	2.1
Vision blurred	2.1

Overall, serious AEs were reported in 16 patients (Table 2). In 7 patients these were assessed as related to IVIg including thromboembolic events (TEE) in 5 subjects. All subjects with TEE had 1 or more other risk factors for TEE in addition to DM. During the study the exposure-adjusted incidence rate for TEE was efficiently lowered from 1.54 events per 100 patient months to 0.54 by reducing the maximum allowed infusion rate from 0.12 mL/kg/min to 0.04 mL/kg/min.

Conclusion: The safety and tolerability profile for high dose IVIg administration in patients with active DM was as expected with headache, pyrexia and nausea being most commonly reported during or after the infusions. Patients should be monitored for TEE (especially those with additional risk factors) with risk mitigation by using a low maxi-

Table 2. All serious adverse events (First and Extension Period) with intensity and relationship to IVIg

Treatment at time of event	Patient[a]	MedDRA Preferred Term	Intensity	Causality
First Period				
IVIg	*1*	Sepsis	Severe	Not related
		Pulmonary embolism	Moderate	
IVIg	**2**	**Muscle spasms**	**Severe**	**Probable**
		Dyspnoea	**Severe**	
IVIg	*3*	Ventricular extrasystoles	Moderate	Unlikely
Placebo	4	Tropical spastic paresis	Moderate	Not related
Placebo	5	Sinus tachycardia	Mild	Not related
		Sinus tachycardia	Mild	
		Hypertension	Moderate	
Extension Period (all IVIg)	6	Squamous cell carcinoma	Mild	Not related
	7	Condition aggravated	Moderate	Unlikely
		Atypical pneumonia	Moderate	
	8	**Deep vein thrombosis**	**Severe**	**Probable**
		Pulmonary embolism	**Severe**	
	9	**Loss of consciousness**	**Moderate**	**Probable**
	10	**Cerebrovascular accident**	**Moderate**	**Possible**
	11	**Cerebral infarction**	**Moderate**	**Possible**
	12	Condition aggravated	Severe	Not related
	13	**Hypoaesthesia**	**Mild**	**Possible**
	14	**Pulmonary embolism**	**Moderate**	**Possible**
	15	Pneumonia	Severe	Not related
		Cardiac failure congestive	Severe	
		Sepsis	Severe	
		Acute respiratory failure	Severe	
		Acute kidney injury	Severe	
	16	Escherichia bacteraemia	Severe	Unlikely

[a]# randomly assigned

mum infusion rate. This is the first large international, randomized, placebo-controlled phase III trial demonstrating the safety and tolerability of IVIg as a treatment for patients with DM.

Disclosure: R. Aggarwal, Mallinckrodt, 1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2; **C. Charles-Schoeman**, AbbVie, 2, 5, Bristol-Myers Squibb, 5, Pfizer Inc, 2, 5, Gilead Sciences, 2, Sanofi-Regeneron, 2; **J. Schessl**, Octapharma, 1; **Z. Bata-Csorgo**, Novartis, 1, 6, Sanofi-Genzyme, 1, 6, Ewopharma, 1, 6, Abbvie, 1; **M. Dimachkie**, Octapharma, 2, 5, CSL-Behring, 2, 5, Orphazyme, 2, 5, Kezar, 1, 2, 5, UCB, 1, 2, 5, Shire Takeda, 2, 5, Bristol-Myers Squibb, 5, Corbus, 5, FDA/OOPD, 5, IMACS,

4; **Z. Griger**, Octapharma, 1, Abbvie, 6, Roche, 6, Lilly, 6, CSL-Behring, 6, Boehringer Ingelheim, 6, Janssen-Cilag, 6; **S. Moiseev**, Octapharma, 12, Travel grant; **C. Oddis**, Genentech, 5, Pfizer, 2, Corbus, 5, CSL Behring, 5, EMD Serono, 2, 5; **E. Schiopu**, Octapharma, 2, 5; **J. Vencovsky**, AbbVie, 1, 6, Boehringer Ingelheim, 2, Eli Lilly, 1, 6, Gilead, 1, Octapharma, 1, Biogen, 6, MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6, Novartis, 6, Werfen, 6; **I. Beckmann**, Octapharma, 3; **E. Clodi**, Octapharma, 3; **T. Levine**, Octapharma, 1, NuFactor, 1; **a. Investigators**, None.

Abstract Number: 0696

Anti-Transcriptional Intermediary Factor 1-gamma Antibodies in Dermatomyositis with and Without Cancer - A Longitudinal Study

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: To longitudinally follow the levels of anti- transcriptional intermediary factor (TIF)1-gamma autoantibodies in patients with dermatomyositis with and without cancer.

Methods: We identified sera from 128 patients diagnosed with dermatomyositis (DM) between 1996 and May 2018 from a national myositis cohort. DM diagnosis was based on the new 2017 Eular/ACR classification criteria for inflammatory myopathies. Serum samples taken at DM diagnosis and after one and three years were tested for anti-TIF1-gamma autoantibodies by Enzyme-Linked ImmunoSorbent Assay (ELISA). Clinical data on DM and cancer was extracted from medical records, National Rheumatology Quality Register, National Myositis Network, International Myositis Register and National Cancer Register. Patients were grouped based on cancer within +/-3 years and anti-TIF1-gamma status into four mutually exclusive groups: DM negative or positive for anti-TIF1-gamma autoantibody

Table 1: The mean value and standard deviation (SD) in optical density (OD) of anti-TIF1-gamma autoantibodies at baseline 0, and after 1 year and 3 years from dermatomyositis (DM) diagnosis in patients with DM and cancer associated DM (CADM).

Time yr	Mean DM	SD DM	Mean CADM	SD CADM	P-value
0	2,07	0,91	2,49	0,88	0,171
1	1,37	0,86	1,75	0,96	0,444
3	1,02	0,84	1,22	0,71	0,651

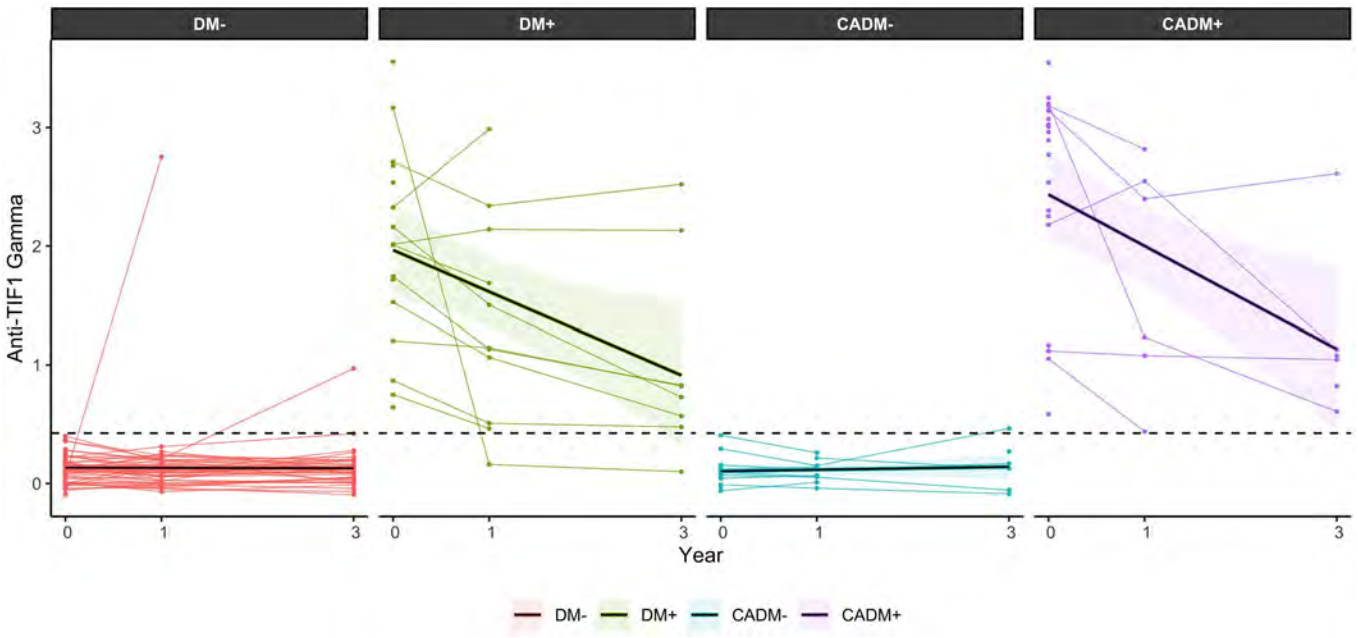

Figure 1. The mean value (one thin coloured line for each patient at baseline 0, 1 year and 3 years) and the overall slope (thick line) of anti-TIF1-gamma antibody. The filled area represents standard error. Dashed line = tif1gamma cutoff.

without cancer +/-3 years (DM- and DM+) and DM with cancer +/-3 years (CADM) negative or positive for anti-TIF1-gamma autoantibody (CADM- and CADM+). Levels of antibody over time were compared with healthy controls and between subgroups.

Results: For 41 patients only one serum sample was available, while 87 had longitudinal samples: 33 patients had 2 serum samples and 54 patients had 3 serum samples. Of all 128 patients, 34 (27%) had cancer within 3 years from myositis diagnosis and 36 (28%) of 128 were positive for anti-TIF1-gamma autoantibodies. We found 78 DM- (61%), 17 DM+ (13%), 19 CADM+ (15%) and 15 CADM- (12%). The mean serum level of anti-TIF1-gamma autoantibodies at baseline and after one and three years was higher in CADM+ patients compared to DM+ (table 1 and figure 1). Patients who tested positive at diagnosis for anti-TIF1-gamma autoantibodies, regardless of cancer status, lightly decreased in serum levels over time but remained in general persistently positive. During the observation time, only two patients changed their anti-TIF1-gamma autoantibody status from negative to positive and one from positive to negative.

Conclusion: The variation of anti-TIF1-gamma autoantibody levels over time did not differ in patients with DM with or without cancer and change in antibody status is rare, indicating that repeated serological tests might not be helpful in the clinical practice.

Disclosure: L. Dani, None; **S. Selickaja**, None; **A. Galindo-Feria**, None; **J. Svensson**, None; **P. Venalis**, None; **D. Leonard**, AstraZeneca, 1; **M. Hemberg**, None; **B. Hanna**, None; **I. Lundberg**, Corbus Pharmaceutical,, 2, EMD Serono Research & Development Institute, 2, Argenx, 2, Bristol Myers Squibb, 2, Janssen, 2, Kezaar, 2, Octapharma, 1, Orphazyme, 1, Roche, 11, Novartis, 11; **M. Holmqvist**, None.

Abstract Number: 0697

Detection of Autoantibodies Against Muscle-Specific Four-and-a-Half-LIM Domain 1 (FHL1) in Inflammatory Myopathies: Results from a Single-Center Cohort

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Autoantibodies targeting a muscle-specific autoantigen, four-and-a-half-LIM-domain 1 (FHL1), have been previously identified in patients with idiopathic inflammatory myopathies (IIM) (1).

The aim of this study was to determine the prevalence and associations of anti-FHL1 antibody in South Australian patients with histologically-confirmed IIM and autoimmune disease control group (systemic sclerosis (SSc)).

Methods: Sera from patients with IIM (n=267) from the South Australian Myositis Database (SAMD), and SSc (n=174) from the Australian Scleroderma Cohort Study (ASCS) followed at the Royal Adelaide Hospital, and healthy con-

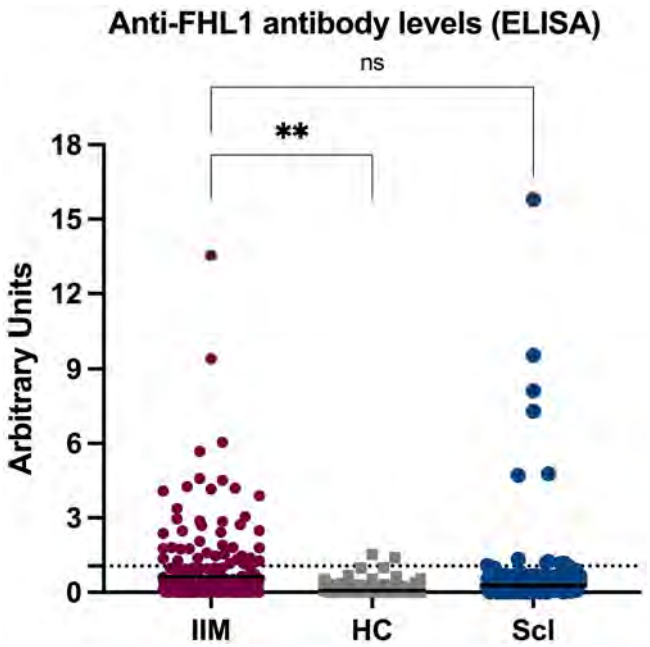

Figure 1. Sera from patients with IIM (DM, PM, IBM, IMNM and MNOS; n=267), SSc (n=174) and HC (n=100) were analyzed by ELISA using recombinant His-tagged FHL1. A cut-off value of 1.06 AU was calculated using a receiver operating characteristic (ROC) curve based on the HC, with an area under the curve (AUC) of 0.62 (CI 95% 0.56-0.68), sensitivity 15.52%, specificity 98%, and a likelihood ratio (LR) of 7.52. IIM, idiopathic inflammatory myopathy; HC, healthy controls; SSc, systemic sclerosis.

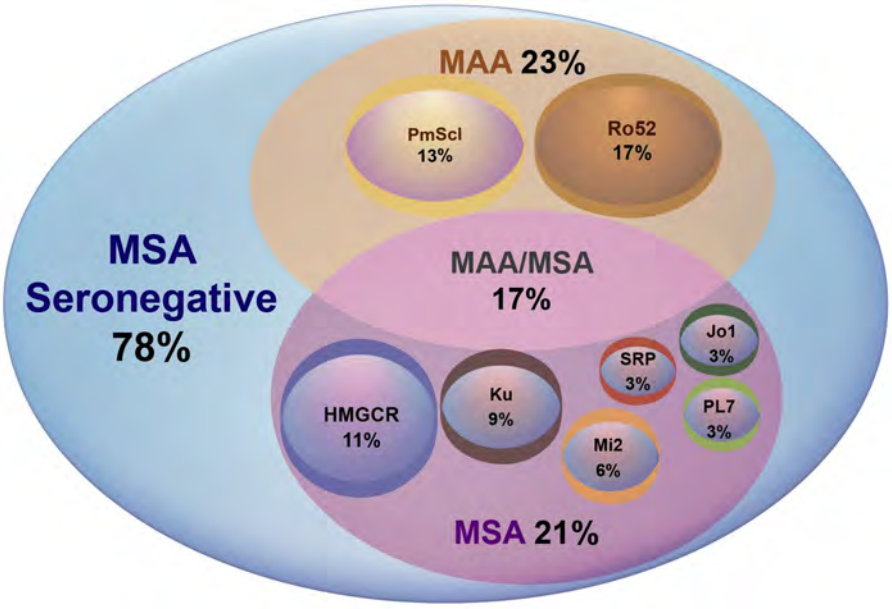

Figure 2. Frequency of IIM patients presenting MSA and MAA in anti-FHL1+ group. MSA, myositis-specific autoantibodies; MAA, myositis-associated autoantibodies

trols (HC, n=100) were analyzed for anti-FHL1 autoantibodies by Enzyme-Linked ImmunoSorbent Assay (ELISA) and transformed to Arbitrary Units (AU). Clinical, serological, and histological details were retrieved from the SAMD and the ASCS.

Results: Autoantibodies to FHL1 were more frequent in patients with IIM (37/267, 13.8%) compared with SSc (12/174, 7%) ($p< 0.02$) and HC (2/100, 2%) ($p< 0.001$) (Figure 1). There were no other myositis-specific autoantibodies (MSA) present in 28/37 (75%) anti-FHL1$^+$ patients (Figure 2). When analyzing the IIM subgroups, the presence of anti-FHL1 autoantibodies was more frequently found in the subgroups polymyositis (PM, 11/37) and Inclusion Body Myositis (IBM, 9/37) (Figure 3). In anti- FHL1$^+$ patients that were seronegative for other MSA (n=28), we found a higher frequency of vessel inflammation and marked fiber atrophy in muscle biopsies, less myalgia, lower CK median levels, and lower cellularity in the biopsy compared to anti-FHL1$^-$ patients. Objective weakness and marked fiber atrophy y in muscle biopsies was more frequent in anti-FHL1$^+$ compared to anti-FHL1- IBM patients. In the SSc patients, the

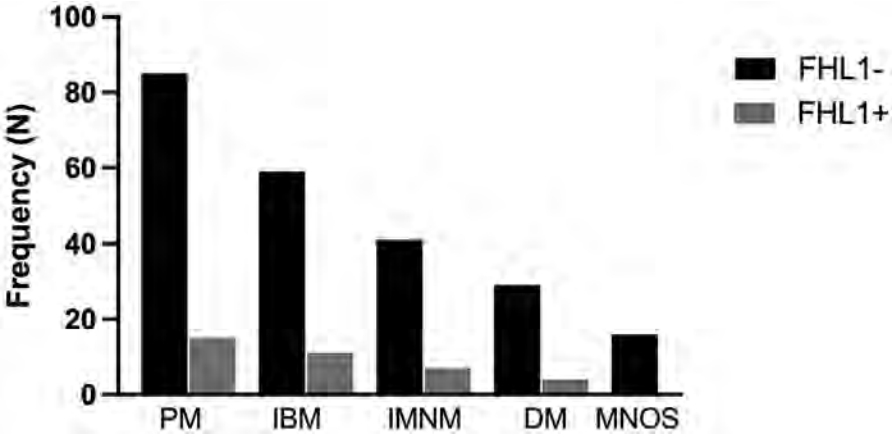

Figure 3. Frequency of IIM patients by disease subsets according to the presence of anti-FHL1+ or anti-FHL1- autoantibodies. IIM, idiopathic inflammatory myopathy; DM, dermatomyositis; PM, polymyositis; IBM, inclusion body myositis; IMNM, immune-mediated necrotizing myopathy; MNOS, myositis not-otherwise-specified

presence of anti-FHL1 autoantibodies was more frequent in limited compared to diffuse SSc, but did not have more frequent clinical diagnosis of myositis or atrophy in the muscle biopsy compared to anti-FHL1$^-$ patients.

Conclusion: The presence of anti-FHL1 autoantibodies was confirmed in a cohort of histologically-defined adult IIM of mixed ethnicity, and most anti-FHL1 positive cases were negative for known MSAs. We confirmed a clinical phenotype dominated by skeletal muscle involvement in patients with anti-FHL1 autoantibodies. We also found the presence of anti-FHL1 in SSc, and this finding warrants investigation in further SSc cohorts.

Disclosure: A. Galindo-Feria, None; **B. Horuluoglu**, None; **J. Day**, None; **C. Cerqueira**, None; **E. Wigren**, None; **S. Gräslund**, None; **S. Proudman**, Boehringer-Ingelheim, 1, Janssen, 1, Gossamer, 1, Janssen, 5; **I. Lundberg**, Corbus Pharmaceutical,, 2, EMD Serono Research & Development Institute, 2, Argenx, 2, Bristol Myers Squibb, 2, Janssen, 2, Kezaar, 2, Octapharma, 1, Orphazyme, 1, Roche, 11, Novartis, 11; **V. Limaye**, None.

Abstract Number: 0698

Flow Cytometry and Sorting of Single Antibody Secreting Cells from Frozen Muscle Tissue

Andrew Zlobin, Peter Pytel and **Vladimir Liarski**, University of Chicago, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) – dermatomyositis (DM), polymyositis, and inclusion body myositis - are poorly understood autoimmune muscle disorders. Isolation of relevant immune cell populations is made difficult by most protocols requiring fresh tissue. Our objective was to develop an approach to obtain intact antibody secreting cells from clinical samples of cryopreserved muscle biopsies.

Methods: Recent publications described the ability to isolate intact cells from frozen biopsies of human lupus nephritis and rheumatoid arthritis. These relied on collecting material in HypoThermosol FRS (HT), followed by freezing using CryoStor CS10 (CS) medium (both STEMCELL Technologies, Cambridge, MA) – a method not currently used in clinical practice. The authors achieved non-inferior results compared to fresh tissue. We integrated the above approach with published methods of preparing non-human primate muscle and tested tissue processing, freezing, and storage methods. Paired deidentified 1 cm^3 tonsil samples were subjected to variable collection media [HT or normal saline (NS)], freezing method [CS or liquid nitrogen-cooled isopentane (IP)], and digestion protocols. Flow cytometry was used to identify major antibody secreting cell subsets. Stored clinical DM and IBM samples were subjected to the final validated protocol and CD138$^+$ cells were sorted into 96-well plates. PCR was performed to confirm expression of heavy and light chain and PRDM1 and Bcl6.

Results: We recovered similar proportions of CD19$^+$ cells and downstream CD27$^+$IgD$^-$ and CD138$^+$ cell subsets by flow cytometry from tonsil collected with NS (**Fig. 1A**). Quantitation of our data showed that IP freezing was non-inferior to CS with statistically greater recovery of CD19$^+$ ($p=0.002$) and CD138$^+$ ($p< 0.001$) cells compared to fresh tissue (**Fig. 1B**). IP freezing outperformed CS conditions for CD19$^+$ ($p=0.001$) and CD27$^+$IgD$^-$ cells ($p=0.002$). Substitution of HT for NS did not alter results (data not shown).

Figure 1

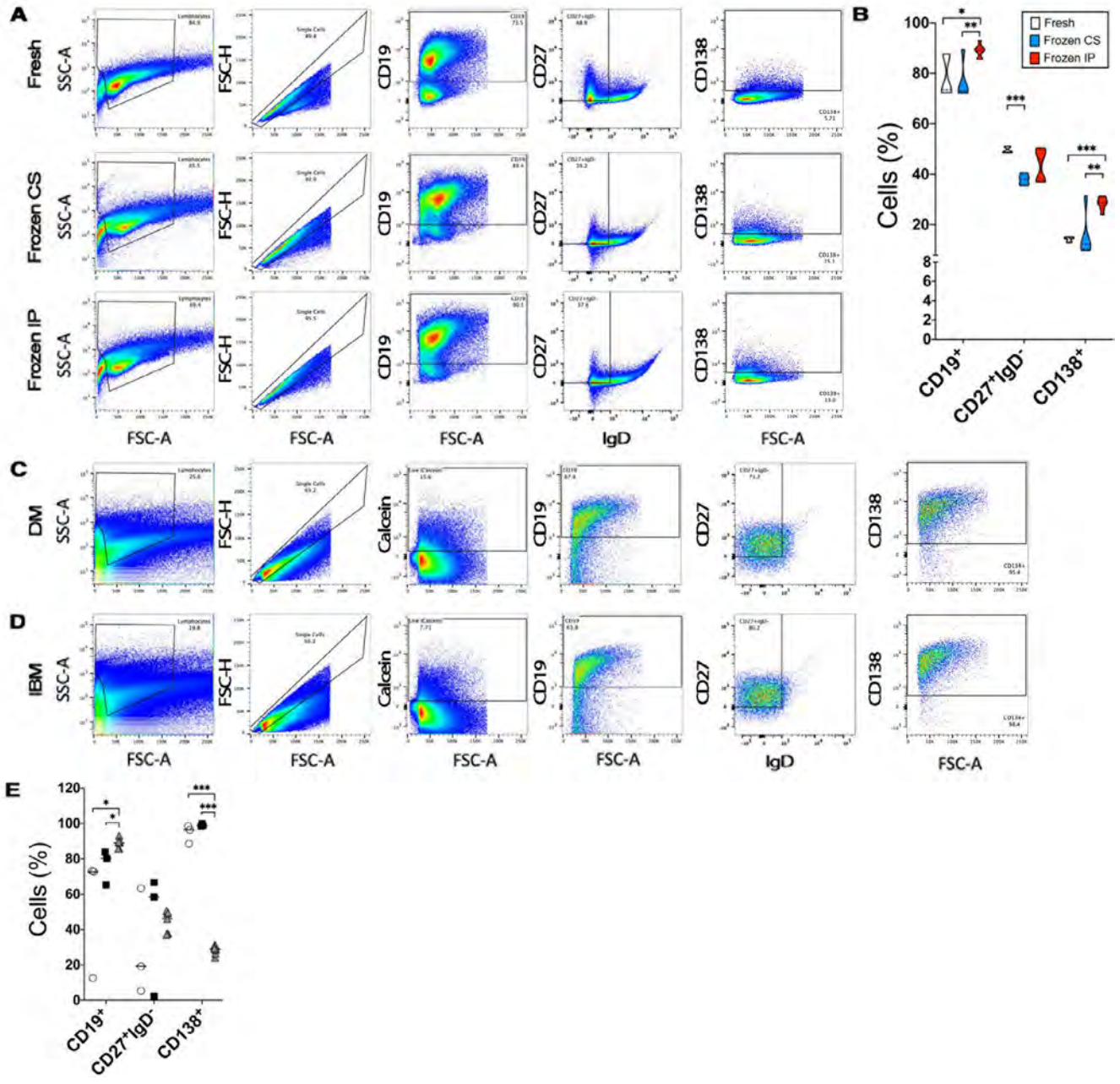

Figure 1. Development and validation of a frozen human tissue digestion protocol. (A) Representative flow cytometry plots performed on cell suspensions derived from digestion of fresh, CryoStor CS-10 (CS) frozen, or Isopentane (IP) frozen human tonsil tissue, collected in normal saline (NS). (B) Standard violin plot quantifying results in (A); fresh tonsil – white; CS – blue; IP – red. Total of 4 independent experiments. (C-D) Representative flow cytometry plots performed on cell suspensions derived from digestion of frozen biopsies of dermatomyositis (DM) (C) or inclusion body myositis (IBM) (D) patients. Calcein was added to confirm cell viability. (E) Quantitation of results in C and D for CD19+ B cells and indicated cell subsets in dermatomyositis (open circle), inclusion body myositis (closed square), and IP-frozen tonsil (closed grey triangle) samples, all collected in NS. Total of 3 independent experiments. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$, unpaired two-tailed t test. Central horizontal lines denote mean in E; median in B.

Applying the digestion protocol to 6 muscle biopsies (3 DM, 3 IBM) showed similar proportions of live $CD19^+$ B cells and downstream populations (**Fig. 1C and D**). All samples had recoverable cells despite an average sample age of 6.5 years. A quantitative comparison revealed no statistically significant differences in isolated cell populations between DM (open circle) and IBM (black square), while both disorders exhibited significantly greater proportions

Figure 2

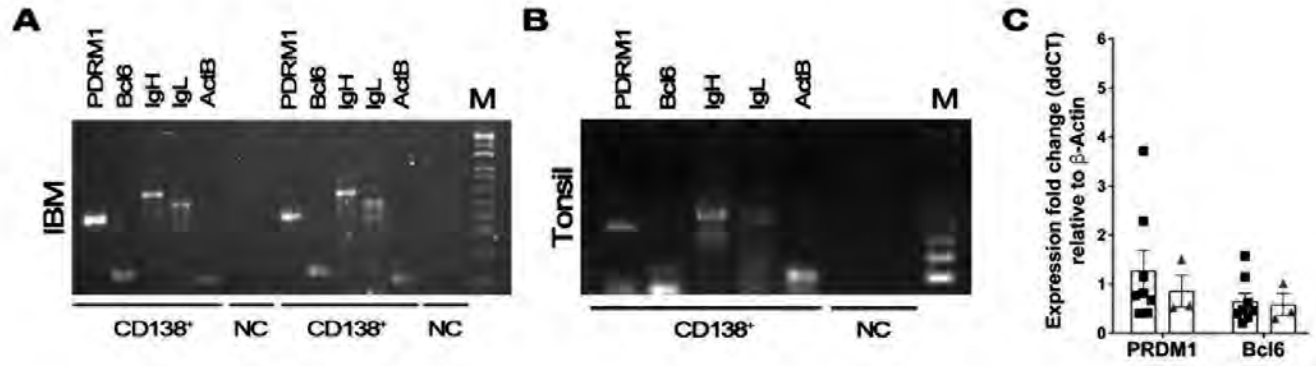

Figure 2. Confirmation of antibody secreting cell phenotype by PCR. Single sorted cells from inclusion body myositis (IBM) (A) or tonsil (B) were subjected to PCR for gene targets as labeled. Negative controls (NC) were performed on empty wells from the last two rows of collection plates. IgH: immunoglobulin heavy chain, ~550 bp; IgL: immunoglobulin light chain, ~400 bp; ActB: **β**-Actin; M: molecular weight marker. (C) Gel densitometry quantitative comparison of representative images A and B. CD138+ cells from IBM (black square) and tonsil (grey triangle) were analyzed. Values are expressed as fold change relative to **β**-Actin (ddCT). Total of 3 independent experiments. Error bars denote standard error.

of CD138$^+$ cells compared to tonsil ($p < 0.001$) (**Fig. 1E**). When subjected to PCR, examined single cells from IBM expressed immunoglobulin heavy and light chains (**Fig. 2A**). Levels of PDRM1 and Bcl6 from IBM (black square) were similar to tonsil controls (grey triangle) (**Fig. 2B)**.

Conclusion: By making it feasible to use stored samples of frozen muscle tissue, the diagnosis and histology of which are known, our approach serves to make a large impact on human translational research of myositis. A major benefit is that the derived muscle digestion protocol does not require specialized collection or freezing media and is compatible with standard clinical samples. We plan to use this approach in the study of antibody repertoire and *in situ* immune response in IIM.

Disclosure: A. Zlobin, None; **P. Pytel**, None; **V. Liarski**, None.

Abstract Number: 0699

Clinical Characteristics of Idiopathic Inflammatory Myositis Manifesting with Myoglobinuria: A 15 Year Retrospective Review

Lilian Vilar, William Moore and Ian Ward, Dwight D Eisenhower Army Medical Center, Fort Gordon

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The Idiopathic Inflammatory myopathies (IIM) are characterized by muscle damage and progressive weakness. Myoglobin is not typically released in high levels in IIM and myoglobinuria is more typically found in rhabdomyolysis. Myoglobinuria has been rarely described in inflammatory myositis. This study aims to describe the frequency, significance, and associated clinical characteristics of myoglobinuria in IIM patients receiving care through the military healthcare system.

Table 1. Demographics and Initial Labs at Time of Diagnosis

	Urine Myoglobin Positive N = 20	Urine Myoglobin OR Urine Hemoglobin positive N=44	IIM Cohort N=99	P-value
Age of onset, years, mean (range)	50.3 (19-72)	54.9 (19-87)	49.3 (18-82)	NS
Male Gender, n (%)	10 (50%)	29 (65.9%)	37 (37.4%)	0.002
BMI at onset, mean (range)	27 (18.4-38.4)	28.3 (18.4-47.4)	27.9 (18.8-48)	NS
Race				
Caucasian, n (%)	3 (15%)	9 (20.4%)	40 (40.4%)	0.014
African American, n (%)	14 (70%)	21 (47.7%)	30 (30.3%)	0.057
Hispanic, n (%)	1 (5%)	2 (4.5%)	3 (3%)	NS
Asian, n (%)	0 (0%)	7 (15.9%)	8 (8.1%)	NS
Other, n (%)	2 (10%)	5 (11.3%)	18 (18.1%)	NS
Labs				
Creatine Kinase, mean (range)	15734 (215-44240)	14741 (215-44240)	4372 (24-32550)	<0.0001
Aldolase, mean (range)	92.9 (7.7-250)	90.2 (7.7-250) *n=29	34.7 (4.9-231) *n=77	<0.0001
LDH, mean (range)	1960 (760-4995)	1448 (424-4995) *n=26	805 (218-3339) *n=35	0.016
ESR, mean (range)	34.9 (14-68)	35.6 (4-81)	33.7 (2-114) *n=94	NS
C-reactive Protein (CRP), mean (range) [mg/L]	21.9 (6.3-83.6)	20.3 (1-85)	24.5 (0.39-334.5) *n=83	NS
Antinuclear Antibody (ANA) >/= 1:320, n (%)	8 (40%)	13 (29.5%)	32 (34.4%) *n=93	NS
Myositis Specific Antibody present	13 (76.5%) *n=17	30 (81.0%) *n=37	61 (70.1%) *n=87	NS
Myositis Associated Antibody present	8 (40%)	15 (39.4%) *n=38	32 (38.6%) *n=83	NS
Necrotizing features on biopsy	13 (92.8%) *n=14	21 (72.4%) *n=29	20 (43.5%) *n=46	0.014

Methods: We performed a retrospective chart review of patients diagnosed with an inflammatory myositis within the Department of Defense (DoD) between January 2006 and December 2020. Patients were identified by ICD-10 diagnosis codes for inflammatory myositis and included if diagnosed at one of fifteen medical facilities within the DoD. All patients met either the Bohan and Peter 1975 or EULAR/ACR classification criteria for definite or probable myositis. Demographic and laboratory data were identified at initial presentation. Myositis complications and treatment regimens were collected during the follow up period. Clinical outcomes were based on the most recent documentation by the evaluating physician. We identified clinical evidence of myoglobinuria (urine myoglobin positivity or urinalysis with moderate to large blood and < 2 red blood cells on microscopy) at onset of disease and compared demographic, clinical and serologic parameters, treatments and outcomes with those patients without myoglobinuria. We performed Chi square tests to analyze categorical variables and Student's t-tests for continuous variables between groups.

Results: One hundred and forty three patients were included with follow-up time between 1 and 180 months. Forty four patients (30.8%) presented with evidence of myoglobinuria (Table 1) and were more likely to be males (p=0.002) and less likely to be of Caucasian race (p=0.014). Immune mediated necrotizing myopathy (IMNM) was the most common IIM subtype (p< 0.001) and muscle necrosis on biopsy was associated with myoglobinuria (p=0.014). Higher levels of creatine kinase (p< 0.0001), aldolase (p< 0.0001), and lactate dehydrogenase (p=0.016) at onset correlated with myoglobinuria, and these patients were more likely to have HMGCoA antibodies. Dysphagia and myocarditis were not associated with myoglobinuria, but there was significantly less incidence of interstitial lung disease (p=0.02).

Myoglobinuria was associated with less ongoing active disease at last follow up (p=0.03), but number of immunosuppressive agents needed was similar between groups.

Conclusion: We demonstrated that myoglobinuria occurs in over thirty percent of IIM. Non-Caucasian ethnicity, male sex, and IMNM were all more likely to present with myoglobinuria. These patients presented with more profound muscle involvement, but surprisingly had higher remission rates at follow up. The clinical profile identified herein will allow for recognition of severe but potentially highly treatment responsive myositis. We hypothesize this population, when recognized early, may respond well to treatment.

Table 2. Inflammatory Myositis Subtypes and Complications

	+ Urine Myoglobin N = 20	+ Urine Myoglobin OR + Urine Hemoglobin N = 44	Control N=99	P-value
Subtype				
Anti Synthetase Syndrome, n (%)	3 (15%)	7 (15.9%)	28 (28.2%)	NS
Cancer Associated, n (%)	1 (5%)	2 (4.5%)	10 (10.1%)	NS
Dermatomyositis, n (%)	6 (30%)	10 (22.7%)	36 (36.3%)	NS
Immune Mediated Necrotizing Myopathy, n (%)	8 (40%)	19 (43.1%)	14 (14.1%)	<0.001
Polymyositis, n (%)	2 (10%)	6 (13.6%)	11 (11.1%)	NS
Interstitial Lung Disease, n (%)	5 (25%)	10 (22.7%)	43 (43.9%) *n=98	0.02
Myocarditis, n (%)	2 (10%)	2 (4.5%)	3 (3.1%) *n=97	NS
Dysphagia, n (%)	5 (25%)	13 (29.5%)	25 (25.5%) *n=98	NS

IIM = idiopathic inflammatory myositis, BMI = body mass index, LDH = lactate dehydrogenase,

Table 3. Treatments at Time of Outcome

	+ Urine Myoglobin N = 19	+ Urine Myoglobin OR + Urine Hemoglobin N = 41	Control N=95	P-value
Steroid Free Remission	14 (73.6%)	28 (68.3%)	53 (55.8%)	NS
Remission on Steroids	4 (21.1%)	10 (24.4%)	18 (18.9%)	NS
Active Disease	1 (5.2%)	3 (7.3%)	22 (23.1%)	0.03
Death	0	0	2 (2.1%)	NS
Duration of Follow-up, months	51.9 (1-154)	56.3 (1-175)	58.6 (1-180)	NS
Disease Modifying Agents, total number	N = 19	N = 43	N=97	
Zero	0	4 (9.3%)	5 (5.2%)	NS
One	5 (26.3%)	11 (25.6%)	27 (27.8%)	NS
Two	5 (26.3%)	13 (30.2%)	35 (36.1%)	NS
Three or More	9 (47.4%)	15 (34.9%)	30 (30.9%)	NS

NS = not significant

Disclosure: L. Vilar, None; **W. Moore**, None; **I. Ward**, None.

Abstract Number: 0700

Clinical Outcomes in Idiopathic Inflammatory Myositis Within the Military Health System: A 15 Year Retrospective Review

David Mecham[1], William Moore[1] and Ian Ward[2], [1]Dwight D Eisenhower Army Medical Center, Fort Gordon, [2]United States Army, Evans, GA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The Idiopathic Inflammatory Myopathies (IIM) are often difficult to treat, require chronic steroid therapy, and can remain active despite multiple treatment regimens. The objective of this study is to identify clinical characteristics at time of diagnosis and follow on treatment strategies which have prognostic value related to disease outcomes.

Methods: We performed a retrospective chart review of patients diagnosed with an inflammatory myopathy within the Department of Defense (DoD) between January 2006 and December 2020. Identified by the ICD-10 diagnosis codes for inflammatory myositis, patients were included if diagnosed at one of fifteen hospitals within the DoD. All patients met either the Bohan and Peter 1975 or EULAR/ACR classification criteria for definite or probable myositis. Demographic and laboratory data were identified at initial presentation. Myositis complications and treatment regimens were collected during the follow up period. Clinical outcomes were based on the most recent evaluation. Patients were categorized into one of five clinical outcome groups. We used ANOVA modeling to identify significant parameters and performed Chi square tests for categorical variables and Student's t-tests for continuous variables within groups.

Results: Two hundred and eleven patients were followed between 2 and 180 months. Steroid free remission was achieved in 126 (59.7%) of which 39 (18.5%) achieved drug free remission. Thirty-eight patients (18.0%) remained with clinically active disease at end of study. African American ethnicity was associated with persistent disease activity ($p< 0.001$) (Table 1). There was no significant outcome associations for the subtypes of IIM, age, gender, and BMI. ESR was significantly lower in patients reaching steroid free remission compared to remission with steroids ($p=0.016$), but not with the active disease cohort. No other laboratory values correlated with outcomes. Dysphagia, but not interstitial lung disease or myocarditis, was associated with worse disease outcomes (Table 2). Patients who achieved any form of disease remission were more likely to see a 90% reduction in creatine kinase (CK) levels at 12 months of therapy than those with active disease (OR 2.7, CI 1.1 – 6.5). There was a trend with CK reduction of 87% at 3 months and end of study remission (OR 2.29, CI 0.99 – 5.24). Treatment regimens at final assessment did not correlate with specific outcomes, but historical exposure to second line agents mycophenolate ($p=0.03$), azathioprine ($p=0.008$), intravenous immunoglobulin (IVIg) ($p=0.007$) or rituximab ($p=0.002$) was associated with active disease (Table 3).

Conclusion: Steroid free remission was achieved in nearly 60% of the IIM population, but chronic steroid exposure and poor clinical outcomes were still common. African American ethnicity, dysphagia, and second line therapies were all associated with worse outcomes, identifying a need for more effective treatments strategies. Creatine kinase at time of onset did not correlate with outcomes, but a dramatic drop (>90% at 12 months) may have prognostic implications for remission, suggesting a need for a treat to target strategy.

Table 1. Clinical Characteristics at Time of Diagnosis

	Drug Free Remission N = 39	Steroid Free Remission N = 87	Remission with Steroids N = 40	Active Disease N = 38	Death N = 7
Age, years, mean (range)	50.2 (19-89)	50.1 (21-82)	48.4 (18-80)	49.1 (20-76)	67.7 (53-78)
Female, n (%)	24 (61.5%)	46 (52.9%)	23 (57.5%)	22 (57.9%)	7 (100.0%)
BMI, mean (range)	27 (19.4-36.5)	28.4 (18.4-40.7)	28.1 (18.8-48)	28.8 (19.6-44.6)	27.9 (18.8-48)
Ethnicity	*n=37	*n=85	*n=38	*n=38	*n=7
Caucasian, n (%)	16 (43.2%)	40 (47.1%)	15 (39.5%)	13 (34.2%)	5 (71.4%)
African American, n (%)	8 (21.6%)	25 (29.4%)	10 (26.3%)	20 (52.6%)	1/7 (14.3%)
Hispanic, n (%)	3 (8.1%)	3 (3.5%)	1 (2.6%)	1 (2.6%)	0
Asian, n (%)	5 (13.5%)	4 (4.7%)	6 (15.8%)	1 (2.6%)	1 (14.3%)
Other, n (%)	6 (16.2%)	13 (15.3%)	6 (15.8%)	2 (5.3%)	0
Labs					
Creatine Kinase, mean (range)	4212 (39-25937)	5870 (24-41760)	5269 (55-16398) *n=39	6849 (52-32550)	3253 (84-16167)
Aldolase, mean (range)	47.8 (4.6-231) *n=21	38.2 (3.7-250) *n=63	51.0 (5.1-253) *n=28	39.1 (2.9-158) *n=29	27.8 (7.6-114) *n=6
LDH, mean (range)	748 (159-2150) *n=17	1014 (136-4995) *n=29	891 (218-2205) *n=28	1137 (228-3339) *n=16	333 (193-410) *n=3
ESR, mean (range)	25.3 (2-75) *n=35	29.6 (2-114) *n=82	42.6 (4-114) *n=33	29.8 (2-114) *n=36	41 (16-74) *n=5
C-reactive Protein (CRP), mean (range) [mg/L]	13.6 (0.39-127.5) *n=25	24.3 (0.3-85) *n=66	31.3 (0.7-334.5) *n=30	19.1 (0.7-143.3) *n=29	8.4 (1.5-17.6) *n=5
Antinuclear Antibody (ANA) >/= 1:80, n (%)	12/38, (31.6%)	27/82 (32.9%)	12/36 (33.3%)	13/35 (37.1%)	4/5 (80%)
Myositis Specific Antibody present	17/31 (54.8%)	54/76 (71.1%)	27/37 (73.0%)	22/37 (59.5%)	3/5 (60%)
Myositis Associated Antibody present	10/34 (29.4%)	30/77 (39.0%)	9/34 (26.5%)	12/33 (36.4%)	2/6 (33.3%)

BMI = body mass index, LDH = lactate dehydrogenase, ESR = erythrocyte sedimentation rate

Table 2. Myositis Subtypes and Complications

	Drug Free Remission (DFR) N = 39	Steroid Free Remission (SFR) *N = 87	Remission on Corticosteroids (SR) N = 40	Active disease (AD) N = 38	Death (D) N = 7
Subtype					
ASS, n (%)	4 (10.3%)	20 (23.0%)	12 (30.0%)	9 (23.7%)	1 (14.3%)
CADM, n (%)	8 (20.5%)	10 (11.5%)	5 (12.5%)	2 (5.3%)	0
Cancer Associated, n (%)	3 (7.7%)	7 (8.0%)	1 (2.5)	2 (5.3%)	4 (57.1%)
DM, n (%)	12 (30.8%)	21 (24.1%)	15 (37.5%)	9 (23.7%)	1 (14.3%)
IMNM, n (%)	6 (15.4%)	19 (21.8%)	5 (12.5%)	10 (26.3%)	1 (14.3%)
PM, n (%)	6 (15.4%)	10 (11.5%)	2 (5.0%)	6 (15.8%)	0
Interstitial Lung Disease, n (%)	9 (23.1%)	29 (33.3%)	16 (40%)	15 (39.5%)	2 (28.6%)
Myocarditis, n (%)	0	3 (3.4%)	1 (2.5%)	1 (2.6%)	1 (14.3)
Dysphagia, n (%)	4 (10.3%)	13 (14.9%)	12 (30%)	14 (36.8%)	4 (57.1%)
Dysphagia p value	p = 0.001 - DFR + SFR + SR versus AD + D				
	p < 0.0001 - DFR + SFR versus SR + AD + D				
	p = 0.01 - DFR versus SFR		p = 0.01 - SR versus AD		
		p = 0.03 - SFR versus SR			

ASS = Antisynthetase Syndrome, CADM = clinically amyopathic dermatomyositis, DM = dermatomyositis, IMNM = immune mediated necrotizing myopathy, PM = polymyositis

Table 3. Treatment Exposure and Treatment at Outcome Assessment

	Drug Free Remission (DFR) N = 38	Steroid Free Remission (SFR) N = 87	Remission with Steroids (SR) N = 40	Active Disease (AD) N = 38	DFR+SFR+SR versus AD, p value
Treatment Exposure					
2 or more medications, n (%)	17 (44.7)	56 (64.4)	28 (70)	31 (81.6)	0.02
Methotrexate, n (%)	13 (34.2)	39 (44.8)	21 (52.5)	20 (52.6)	NS
Hydroxychloroquine, n (%)	10 (26.3)	33 (37.9)	11 (27.5)	14 (36.8)	NS
Azathioprine, n (%)	11 (28.9)	29 (33.3)	18 (45)	16 (42.1)	0.02
Tacrolimus, n (%)	0 (0)	5 (5.7)	2 (5)	3 (7.9)	NS
Mycophenolate, n (%)	5 (13.2)	19 (21.8)	13 (32.5)	15 (39.5)	0.03
IVIg, n (%)	4 (10.5)	24 (27.6)	14 (35)	18 (47.4)	0.007
Rituximab, n (%)	7 (18.4)	18 (20.7)	13 (32.5)	18 (47.4)	0.002
Adalimumab, n (%)	0 (0)	4 (4.6)	0 (0)	2 (5.3)	NS
Cyclophosphamide, n (%)	2 (5.3)	4 (4.6)	4 (10)	3 (7.9)	NS
Treatment at outcome assessment		N = 84	N = 38	N = 38	
2 or more medications, n (%)	n/a	26 (31.0)	13 (34.2)	18 (47.4)	NS
Average Prednisone dose, mg	n/a	n/a	9.1	20	
Methotrexate, n (%)	n/a	27 (32.1)	10 (26.3)	10 (26.3)	NS
Hydroxychloroquine, n (%)	n/a	24 (28.6)	6 (15.8)	7 (18.4)	NS
Azathioprine, n (%)	n/a	18 (21.4)	9 (23.7)	5 (13.2)	NS
Tacrolimus, n (%)	n/a	3 (3.6)	2 (5.3)	0 (0)	NS
Mycophenolate, n (%)	n/a	16 (19.0)	9 (23.7)	11 (28.9)	NS
IVIg, n (%)	n/a	10 (11.9)	5 (13.2)	9 (23.7)	NS
Rituximab, n (%)	n/a	9 (10.7)	7 (18.4)	5 (13.2)	NS
Adalimumab, n (%)	n/a	2 (2.4)	1 (2.6)	1 (2.6)	NS

IVIg = intravenous immunoglobulin, NS = not significant

Disclosure: D. Mecham, None; **W. Moore**, None; **I. Ward**, None.

Abstract Number: 0701

Use and Yield of Computed Tomography as a Cancer Surveillance Method in Idiopathic Inflammatory Myositis

Christopher Mecoli[1], Brant Chee[2], XingYao Wang[3], Mengkun Chen[4], William Kelly[3], Elizabeth Platz[4], Livia Casciola-Rosen[5], Lisa Christopher-Stine[3] and Ami Shah[6], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Applied Physics Laboratory, Baltimore, MD, [3]Johns Hopkins University, Baltimore, MD, [4]Johns Hopkins School of Public Health, Baltimore, MD, [5]Johns Hopkins, Baltimore, MD, [6]Johns Hopkins Rheumatology, Baltimore, MD

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: To inform guidance for cancer surveillance in patients with idiopathic inflammatory myositis (IIM), we conducted a retrospective cohort study in a single tertiary referral center to evaluate the use and yield of computed tomography (CT) for cancer surveillance within distinct myositis-specific autoantibody strata from 2007 through 2020.

Table 1. Time window of cohort enrollment onwards. Autoantibody, number of patients, # of cancers, and CT scans performed

Autoantibody	Patients (n)	# Cancers Diagnosed 0-3 Yr	CT Chest Positive for Cancer 0-3 Yr	Total CT Chest Ordered 0-3 Yr	% Positive CT Chest 0-3 Yr	CT A/P Positive for Cancer 0-3 Yr	Total CT A/P Ordered 0-3 Yr	% Positive CT A/P 0-3 Yr	# Cancers Diagnosed 3-5 Yr	CT Chest Positive for Cancer 3-5 Yr	Total CT Chest Ordered 3-5 Yr	% Positive CT Chest 3-5 Yr	CT A/P Positive for Cancer 3-5 Yr	Total CT A/P Ordered 3-5 Yr	% Positive CT A/P 3-5 Yr	# Cancers Diagnosed 5+ Yr	CT Chest Positive for Cancer 5+ Yr	Total CT Chest Ordered 5+ Yr	% Positive CT Chest 5+ Yr	CT A/P Positive for Cancer 5+ Yr	Total CT A/P Ordered 5+ Yr	% Positive CT A/P 5+ Yr
TIF1γ > 32	170	10	2	57	3.51%	1	43	2.33%	0	0	25	0.00%	0	21	0.00%	8	2	28	7.14%	0	26	0.00%
TIF1γ > 6	273	13	3	102	2.94%	2	79	2.53%	3	0	35	0.00%	0	29	0.00%	12	2	43	4.65%	0	37	0.00%
SRP	76	1	0	36	0.00%	0	28	0.00%	0	0	13	0.00%	0	5	0.00%	1	0	11	0.00%	1	5	20.00%
PL12	33	0	0	16	0.00%	0	8	0.00%	0	0	7	0.00%	0	3	0.00%	1	0	14	0.00%	0	8	0.00%
Jo1	165	3	0	73	0.00%	0	34	0.00%	2	1	37	2.70%	0	17	0.00%	7	0	56	0.00%	1	32	3.13%
OJ	7	0	0	3	0.00%	0	3	0.00%	0	0	1	0.00%	0	1	0.00%	0	0	1	0.00%	0	2	0.00%
MDA5	69	2	0	43	0.00%	1	28	3.57%	1	0	11	0.00%	0	4	0.00%	1	0	19	0.00%	0	9	0.00%
EJ	8	1	1	8	12.50%	0	2	0.00%	0	0	2	0.00%	0	1	0.00%	0	0	4	0.00%	0	1	0.00%
PL7	35	0	0	19	0.00%	0	12	0.00%	1	0	7	0.00%	0	4	0.00%	0	0	9	0.00%	0	5	0.00%
Ku	26	1	0	9	0.00%	0	9	0.00%	0	0	5	0.00%	0	1	0.00%	0	0	6	0.00%	0	3	0.00%
SAE	19	2	1	9	11.11%	1	5	20.00%	0	0	2	0.00%	0	2	0.00%	2	0	8	0.00%	1	4	25.00%
NXP2	82	3	1	31	3.23%	2	24	8.33%	3	0	13	0.00%	0	10	0.00%	2	0	8	0.00%	0	11	0.00%
Mi2	58	2	0	29	0.00%	2	23	8.70%	2	0	6	0.00%	0	3	0.00%	2	0	2	0.00%	0	6	0.00%
HMGCR	162	7	0	50	0.00%	1	44	2.27%	3	1	23	4.35%	0	19	0.00%	6	1	26	3.85%	0	29	0.00%
PM-Scl	41	0	0	19	0.00%	0	11	0.00%	0	0	7	0.00%	0	3	0.00%	0	0	10	0.00%	0	5	0.00%
All Ab+ IIM	1054	35	6	447	1.34%	9	310	2.90%	15	2	169	1.18%	0	102	0.00%	34	3	217	1.38%	3	157	1.91%

Table 2. Time window of IIM symptom onset onwards. Autoantibody, number of patients, # of cancers, and CT scans performed

Autoantibody	Patients (n)	# Cancers Diagnosed 0-3 Yr	CT Chest Positive for Cancer 0-3 Yr	Total CT Chest Ordered 0-3 Yr	% Positive CT Chest 0-3 Yr	CT A/P Positive for Cancer 0-3 Yr	Total CT A/P Ordered 0-3 Yr	% Positive CT A/P 0-3 Yr	# Cancers Diagnosed 3-5 Yr	CT Chest Positive for Cancer 3-5 Yr	Total CT Chest Ordered 3-5 Yr	% Positive CT Chest 3-5 Yr	CT A/P Positive for Cancer 3-5 Yr	Total CT A/P Ordered 3-5 Yr	% Positive CT A/P 3-5 Yr	# Cancers Diagnosed 5+ Yr	CT Chest Positive for Cancer 5+ Yr	Total CT Chest Ordered 5+ Yr	% Positive CT Chest 5+ Yr	CT A/P Positive for Cancer 5+ Yr	Total CT A/P Ordered 5+ Yr	% Positive CT A/P 5+ Yr
TIF1γ > 32	170	19	5	144	3.47%	4	127	3.15%	0	0	32	0.00%	0	27	0.00%	9	2	36	5.56%	0	32	0.00%
TIF1γ > 6	273	28	6	236	2.54%	5	201	2.49%	3	1	48	2.08%	0	37	0.00%	12	2	53	3.77%	0	44	0.00%
SRP	76	5	1	68	1.47%	1	49	2.04%	0	1	19	5.26%	0	7	0.00%	1	0	14	0.00%	1	7	14.29%
PL12	33	2	1	57	1.75%	0	20	0.00%	0	0	14	0.00%	0	5	0.00%	1	0	17	0.00%	0	8	0.00%
Jo1	165	5	1	172	0.58%	0	74	0.00%	2	1	54	1.85%	0	24	0.00%	8	0	67	0.00%	1	35	2.86%
OJ	7	0	0	6	0.00%	0	6	0.00%	0	0	2	0.00%	0	1	0.00%	0	0	2	0.00%	0	2	0.00%
MDA5	69	3	0	89	0.00%	1	58	1.72%	1	0	12	0.00%	0	6	0.00%	1	0	23	0.00%	0	12	0.00%
EJ	8	1	1	11	9.09%	0	3	0.00%	0	1	3	33.33%	0	1	0.00%	0	0	5	0.00%	0	1	0.00%
PL7	35	1	1	39	2.56%	0	19	0.00%	1	0	11	0.00%	0	5	0.00%	0	0	12	0.00%	0	6	0.00%
Ku	26	2	0	19	0.00%	0	18	0.00%	0	0	9	0.00%	0	2	0.00%	0	0	8	0.00%	0	4	0.00%
SAE	19	4	1	20	5.00%	2	14	14.29%	0	0	2	0.00%	0	2	0.00%	2	0	9	0.00%	1	4	25.00%
NXP2	82	5	1	71	1.41%	3	58	5.17%	3	0	17	0.00%	0	13	0.00%	2	0	13	0.00%	0	15	0.00%
Mi2	58	4	0	52	0.00%	2	47	4.26%	2	0	6	0.00%	0	3	0.00%	2	0	2	0.00%	0	6	0.00%
HMGCR	162	10	1	85	1.18%	2	72	2.78%	4	1	28	3.57%	0	23	0.00%	7	1	29	3.45%	0	31	0.00%
PM-Scl	41	0	0	42	0.00%	0	20	0.00%	0	0	13	0.00%	0	4	0.00%	0	0	13	0.00%	0	6	0.00%
All Ab+ IIM	1054	70	14	967	1.45%	16	659	2.43%	16	5	238	2.10%	0	133	0.00%	36	3	267	1.12%	3	181	1.66%

Methods: In 2020, we reviewed the electronic medical records of all patients who previously enrolled in our Myositis Research Registry to identify those who met the following criteria**:** (i) Probable or definite DM/PM by Peter and Bohan, (ii) IMNM by the 2003 ENMC Criteria, (iii) Classic DM rash (Gottron's/heliotrope) and consistent histopathology on skin biopsy. Myositis specific and associated autoantibodies were assayed using Euroimmun line blot (16 Ag IgG), ELISA (anti-Mi2 and anti-TIF1y [MBL], anti-HMGCR [INOVA Diagnostics]), and in-house immunoprecipitation (anti-NXP2). We also reviewed their charts and outside medical records for any CT chest and abdomen/pelvis studies ordered for cancer surveillance/screening purposes. Our myositis center's strategy for malignancy screening/surveillance includes at least one CT chest, abdomen, and pelvis upon IIM diagnosis. Data on CT imaging was collected with researchers blinded to both myositis-specific autoantibody and cancer status. Two time periods were analyzed: Cancer screening tests performed (i) after cohort enrollment, and (ii) after IIM-symptom onset, both through 12/31/2020.

Results: Among 1174 patients, 1054 patients had at least one myositis specific or associated autoantibody. From cohort enrollment onwards, the number of cancers that occurred within 0-3 yrs, 3-5 yrs, and >5 yrs after IIM symptom onset was 35, 15, and 34, respectively. The number/% of CT chest scans that were positive for cancer were 6/1.34% (0-3 yrs), 2/1.18% (3-5 yrs), and 3/1.38% (>5 yrs). The number/% of CT a/p positive for cancer was 9/2.90% (0-3 yrs), 0/0% (3-5 yrs), and 3/1.91% (>5 yrs). Of the 35 cancers diagnosed within 0-3 yrs from IIM symptom onset, more than half were diagnosed by methods other than CT chest, abdomen and pelvis imaging. Amongst 273 anti-TIF1g-positive patients, 181 CT chest or a/p scans were performed, 5 (2.7%) of which were positive within 0-3 yrs. In contrast, amongst 248 patients with Jo1, PL12, PL7, OJ, or EJ autoantibodies, 178 CT chest or a/p scans were performed, 1 (< 1%) of which was positive.

From IIM symptom onset onwards, the number of IIM patients diagnosed with cancer that occurred within 0-3 yrs, 3-5 yrs, and >5 yrs after IIM symptom onset was 70, 16, and 36. The percent of screening/surveillance CT chest and CT a/p scans that were positive for cancer was comparable to the time window from cohort enrollment onwards (Table 2).

Conclusion: In a tertiary referral center population, the number of patients needed to be screened by CT imaging to detect one cancer within the first 3 yrs of IIM was approximately 70 for CT chest and 40 for CT a/p. CT imaging is of higher yield in patients with anti-TIF1y antibodies compared to patients with antisynthetase autoantibodies. Whether CT imaging leads to improvement in cancer or IIM outcomes remains to be determined. Funded in part by NIAMS K2 3AR075898.

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Abstract Number: 0702

Performance of Commercial Autoantibody Testing in Comparison to Recognized Gold Standards in Myositis Autoantibody Testing

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The idiopathic inflammatory myopathies (IIM) are a heterogenous group of autoimmune conditions. The presence of myositis-specific autoantibodies (MSAs) and myositis-associated autoantibodies (MAAs) in patients are important for diagnosis and prognosis. The currently accepted gold standards for autoantibody testing are time consuming and difficult to perform. Commercial testing may offer a more cost-effective and time-efficient method for autoantibody testing. However, the relative performance characteristics of commercial testing methods are not well known. We sought to determine the relative performance characteristics of autoantibody (Abs) testing from a widely-used commercial lab compared to gold standard methodologies.

Methods: Laboratory testing by protein and RNA immunoprecipitation (IP) and IP-immunoblotting methods performed by the Oklahoma Medial Research Foundation (OMRF) was used as the gold standard for anti-Jo1, OJ, EJ, PL-7, PL-12, Mi-2, SRP, Ku, MDA5, P155, PM/Scl, and MJ autoantibodies. Testing by ELISA and confirmation by IP in the Mammen laboratory was used as the gold standard for anti-HMGCR autoantibodies. Immunoblotting results from Mammen and Greenberg labs were used as gold standards for the CN1A autoantibody. Commercial antibody testing was performed on archived samples by a commercial lab using laboratory developed ELISAs for HMGCR and CN1A assays and a laboratory developed line blot method for the remaining autoantibodies. Up to 10 adults and juveniles positive by gold standard testing for each autoantibody were selected to be evaluated in the commercial lab.

Results: Samples from 198 patients with diagnosed IIM were used, of which 137 were adult and 61 were juvenile.

Across those autoantibodies with more than 5 gold standard positive (GSP) test results, sensitivities were greater than 0.95 for Jo1 (0.96, 22 GSP), EJ (1.0, 6 GSP), PL-12 (1.0, 10 GSP), and Ku (1.0, 8 GSP), and > 0.85 for Mi-2 (0.89, 9 GSP), MDA-5 (0.95, 19 GSP), and SRP (0.88, 20 GSP). PM/Scl (0.75, 8 GSP), MJ (0.74, 19 GSP), HMGCR (0.7, 10 GSP), P155 (0.48, 23 GSP), CN1A (0.37, 21 GSP), OJ (0, GSP) exhibited sensitivities under 0.85.

Two autoantibodies had specificities under 0.95: SRP (0.88) and Mi-2 (0.89). All other autoantibodies tested had a specificity above 0.95.

Subgroup analysis by age showed differences in sensitivity greater than 0.2 between CN1A Abs in adult (0.83) and juvenile IIM (0.15) ($p = 0.004$) and in anti-HMGCR Abs in adult (0.4) and juvenile IIM (0.15) ($p = 0.038$).

Conclusion: Of the autoantibodies with at least 5 positive gold standard positive results, there was a large variation in the sensitivities among the Abs. Sample storage may have impacted commercial test sensitivity. However, the specificities were strong overall. Our results show that commercial testing can be used as a tool for initial autoantibody testing in myositis patients, but the gold standards still provide value for autoantibody groups with low sensitivities, including P155, CN1A, and OJ. Further research is needed to explain sensitivity differences between age groups.

Disclosure: S. Nazir, None; **L. Rider**, Eli Lilly and Company, 12, Drug, CureJM, 1, Bristol Meyer Squibb, 5, Hope Pharmaceuticals, 5; **I. Targoff**, Oklahoma Medical Research Foundation Clinical Immunology Laboratory, 2, 5, UpToDate, 9; **S. Naides**, EUROIMMUN US, 2, 6, Applied BioCode, 2, Seegene Technologies, 12, Guidepoint, 1, Laboratory Corporation of America, 2, AlphaSights, 1; **A. Mammen**, None; **S. Greenberg**, None; **A. Schiffenbauer**, Hope Pharmaceuticals, 5, Quest Diagnostics, 5, Astrazeneca, 5.

Abstract Number: 0703

CD8 Positron Emission Tomography (PET/CT) Imaging with 89Zr-Df-IAB22M2C in Patients with Inclusion Body Myositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Inclusion body myositis (IBM) is a slowly progressive autoimmune skeletal muscle disease for which no effective pharmacological therapy is available. A prominent feature of autoimmunity seen on microscopy is effector cytotoxic CD8+ T cells invading myofibers. Pathophysiologically, a quantitative approach to detection of CD8+ T cell burden in muscle would potentially distinguish IBM from other muscle diseases and provide a biomarker predicting disease progression, stratification for clinical trials, or a surrogate outcome for T cell directed therapies.

[89]Zr-Df-IAB22M2C is positron emission tomography (PET) tracer with high affinity for the CD8 glycoprotein.

In this pilot study we evaluated the safety, muscle distribution and sensitivity of [89]Zr-Df-IAB22M2C, to detect CD8+ T cell inflammation in the skeletal muscle of IBM patients.

Methods: Five patients with IBM from the University of Pennsylvania who met European Neuromuscular Center Criteria (ENMC) for probable IBM and were able to walk at least 10 feet without an assistive device were recruited. Patients on any immunomodulatory therapy or investigational agent were excluded. Screening and formal clinical evaluation by a neuromuscular neurologist (CQ) was performed within 28 days of imaging.

Table 1. Clinical Characteristics 1. Subject 1 was not included as this subject decided against imaging after clinical evaluation 2. IBM-FRS = IBM Functional Rating Scale. The IBM-FRS is a 10 question survey of functional status, including swallowing, arm and leg tasks. Each question is scored 0-4. The maximum score is 40. 3. IBM MRC Sum= A sum of medical research council grading scores, converted to a 10-point scale. This is a non-validated score measuring shoulder abduction, elbow flexion, elbow extension, long finger flexion (digit 2), long finger flexion (digit 4), hip flexion, knee extension, ankle dorsiflexion and ankle plantarflexion bilaterally

Subject[1]	Age (Years)	Gender	Disease Duration (Months)	IBM-FRS[2]	IBM MRC Sum[3]
2	77	M	132	22	124
3	61	F	132	26	148
4	60	M	7	34	154
5	64	F	121	25	117
6	73	M	23	20	118

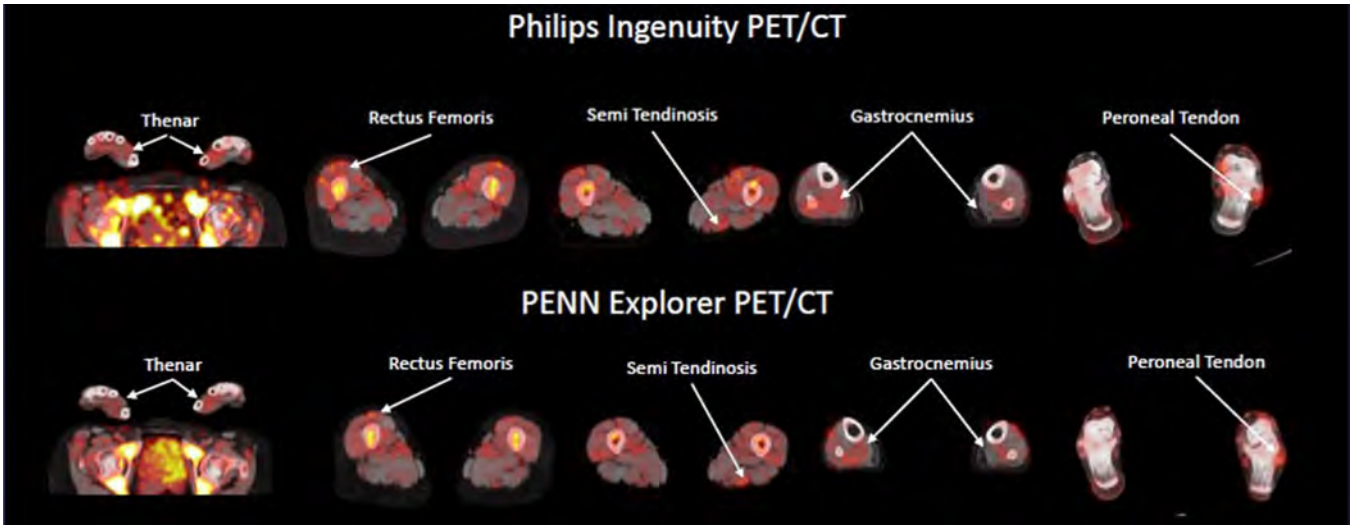
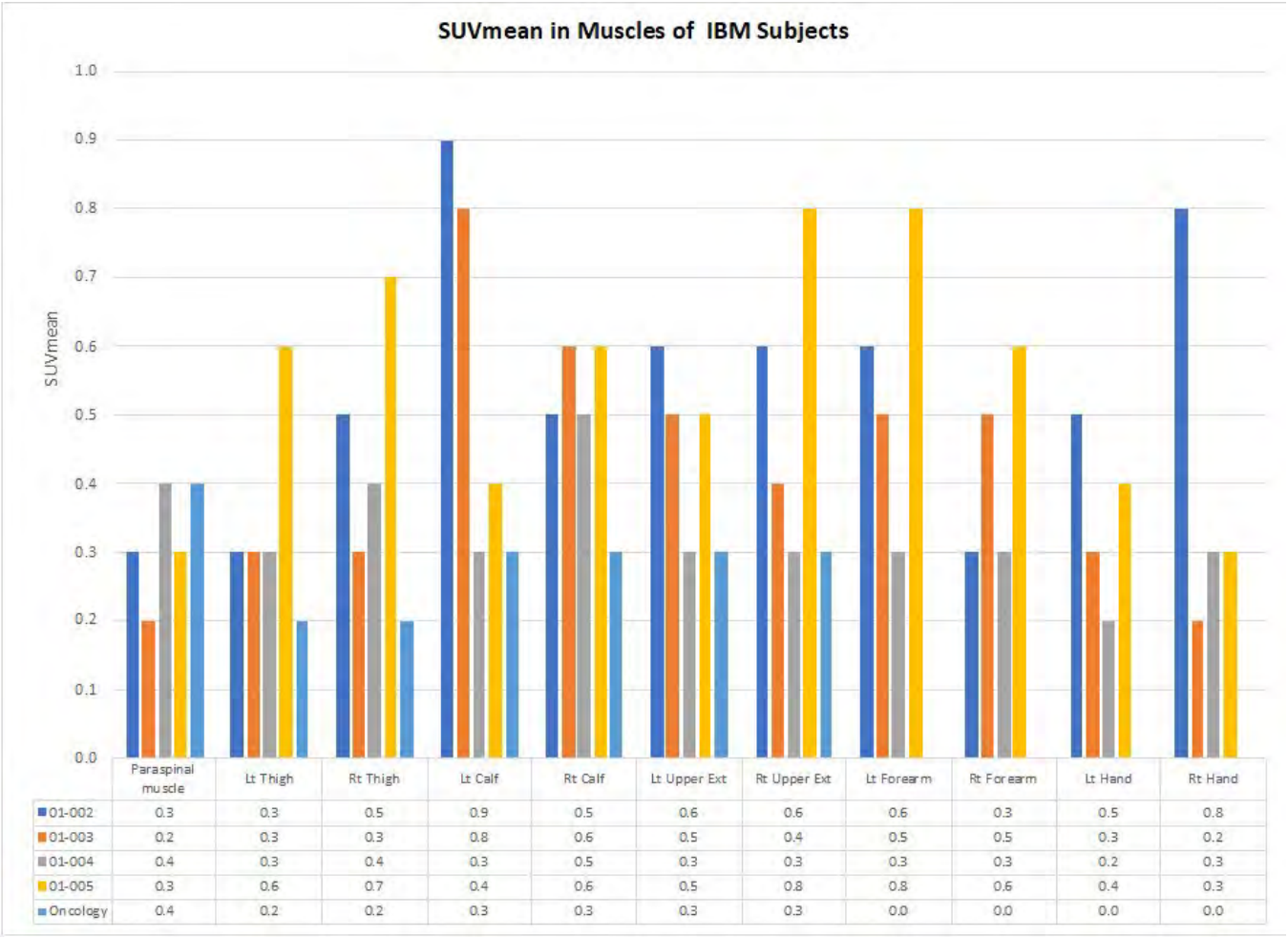


Figure 1. Representative PET/CT images from subject 4 demonstrating 89Zr-Df-IAB22M2C signal in the hands, anterior thigh and gastrocnemius muscles.



	Paraspinal muscle	Lt Thigh	Rt Thigh	Lt Calf	Rt Calf	Lt Upper Ext	Rt Upper Ext	Lt Forearm	Rt Forearm	Lt Hand	Rt Hand
01-002	0.3	0.3	0.5	0.9	0.5	0.6	0.6	0.6	0.3	0.5	0.8
01-003	0.2	0.3	0.3	0.8	0.6	0.5	0.4	0.5	0.5	0.3	0.2
01-004	0.4	0.3	0.4	0.3	0.5	0.3	0.3	0.3	0.3	0.2	0.3
01-005	0.3	0.6	0.7	0.4	0.6	0.5	0.8	0.8	0.6	0.4	0.3
Oncology	0.4	0.2	0.2	0.3	0.3	0.3	0.3	0.0	0.0	0.0	0.0

Figure 2. Muscle SUVmean. Subjects 2, 3, 4, 5 have been analyzed. A comparison control oncology patient is included. The highest uptake was seen in the calf (average SUVmean 0.58, SD 0.20), upper extremities (average SUVmean 0.50, SD 0.17), and forearms (average SUVmean 0.49, SD 0.18). The uptake in the paraspinal muscles (average SUVmean 0.30, SD 0.08) was similar to the control population.

Patients were imaged 24 h after administration of 0.7-1.1 mCI of ^{89}Zr-Df-IAB22M2C on both a standard clinical PET/CT scanner (Ingenuity TF; Philips Healthcare) and the PennPET Explorer, a whole-body scanner with approximately 40 times the sensitivity of a standard PET/CT instrument.

Outcome measures included safety and tolerability and a standard uptake value (SUV)-based quantitative analysis of tracer uptake in various muscle regions. SUV means were compared to a preexisting dataset from an oncology population where available.

Results: To date all 5 patients have undergone clinical assessment and PET imaging. Four patients have been analyzed. Clinical details of each patient are detailed in Table 1.

^{89}Zr-Df-IAB22M2C was well tolerated. One patient dropped out prior to receiving the tracer due to claustrophobia. A second patient experienced a fall the day after receiving the tracer deemed unrelated to the tracer, but the resulting delayed PET/CT evaluation left time for only PennPET Explorer imaging.

^{89}Zr-Df-IAB22M2C signal was detectable in the muscles of all patients (Figures 1 and 2). In all of the extremities assessed, the average muscle uptake was higher than in our control population, though some individual muscles were similar to control uptake. The highest uptake was seen in the calf (average SUVmean 0.58, SD 0.20), upper extremities (average SUVmean 0.50, SD 0.17), and forearms (average SUVmean 0.49, SD 0.18). The uptake in the paraspinal muscles (average SUVmean 0.30, SD 0.08) was similar to the control population.

Conclusion: ^{89}Zr-Df-IAB22M2C appears safe and well tolerated. This pilot study demonstrated clear uptake of ^{89}Zr-Df-IAB22M2C in the muscles of IBM patients at an intensity greater than the control population. Further studies should examine ^{89}Zr-Df-IAB22M2C uptake in other diseases and correlation with longitudinal changes related to measures of disease progression.

Disclosure: C. **Quinn**, Amicus Therapeutics, 1, Acceleron Pharma, 1, Amylyx Pharmaceuticals, 1, Biogen, 1, Sarepta Therapeutics, 1; **K. Moulton**, None; **R. Korn**, ImaginAb, 2, Imaging Endpoints, 3, 4, 8, 10, HonrHealth, 2, Globavir, 11, Verve, 8, Renobus, 8; **W. Le**, ImaginAb - Inglewood, CA, 3; **N. Goel**, Abcuro Inc, 3, 4, 8; **M. Farwell**, ImaginAb, 2, 5, BMS, 5, Merck, 5, Carisma, 5; **S. Greenberg**, Abcuro, Inc., 1, 2, 8, 10.

Abstract Number: 0704

Anti-SSa/SSb and Ro52 and Interstitial Lung Disease in Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In idiopathic inflammatory myopathies (IIM), SSa/SSb and Ro52 antibodies are frequently reported, especially in association with interstitial lung disease (ILD). However, limited literature exists on their prog-

Table 1. Demographics and clinical data.

		Anti-SSa/SSb (N=94)		Anti-Ro52 (N= 60)	
		positive (N =33)	negative (N =61)	positive (N =25)	negative (N=35)
Age (years)	Median (min- max)	54 (23-93)	57 (22-80)	54 (23-69)	55 (23-93)
Sex	female	78.8% (26)	75.4% (46)	72% (18)	71.4% (25)
	male	21.2% (7)	24.6% (15)	28% (7)	28.6 % (10)
Race	Caucasian	11 (33.3%)	30 (49.2%)	7 (28%)	16 (45.7%)
	African American	10 (30.3%)	18 (29.5%)	9 (36%)	11 (31.4%)
	Asian or Pacific Islander	6 (18.2%)	4 (6.6%)	5 (20%)	4 (11.4%)
	American Indian or Alaskan Naïve	1 (3.03%)	0	1 (4%)	0
	Unknown	5 (15.15%)	9 (14.7%)	3 (12%)	4(11.4%)
Myositis subset	DM	14 (42%)	33 (54.1%)	10 (40%)	17 (48.5%)
	PM	6 (18.1%)	9 (14.7%)	5 (20%)	6 (17.1%)
	DM and IMNM	1 (3.0%)	2 (3.27%)	3 (12%)	1 (2.8%)
	PM and IMNM	2 (6.0 %)	4 (6.5%)	1 (4%)	4 (11.4%)
	Overlap myositis	10 (30.3%)	9 (14.7%)	6 (24%)	7 (20%)
Antibodies subtypes	Jo-1 ab	26%	8%	16%	6%
	Pl-7 ab	0%	2%	0%	0%
	Pl-12 ab	3%	0%	4%	0%
	EJ ab	0%	3%	0%	6%
	OJ ab	0%	0%	0%	0%
	MDA-5 ab	9%	3%	16%	3%
	PM-Scl-100 ab	3%	2%	8%	3%
	RNP ab	15%	9%	8%	8%

DM-dermatomyositis, PM-polymyositis, IMNM-immune mediated necrotizing myopathy
UCTD-Undifferentiated Connective Tissue Disease

Table 2. Frequency of ILD and PFT results in anti-SSa/SSb positive and negative patients

	anti-SSa/SSb +	anti-SSa/SSb -	p-value
ILD n (%)	N = 33	N = 61	
ILD present	19 (55.9%)	15 (44.1%)	**0.003 ****
No ILD	14 (23.3%)	46 (76.7%)	
PFT %	N 16	N 31	
FEV1 median (min-max)	80 (33-131)	83 (42-125)	0.9555
FVC median (min-max)	77 (27-117)	78 (40-121)	0.7972
DLCO median (min-max)	61 (21-102)	67 (18-102)	0.2020

** statistically significant difference

nostic role and use in risk assessment. The aim of this analysis was to describe ILD spectrum and pulmonary function tests (PFTs) in IIM patients in relation to anti-SSa/SSb and anti-Ro52 positivity.

Methods: We queried the Northwell Myositis Center database for patients with IIM between 1/1/2007 to 4/6/2018. Patients were selected if they met 2017 European League Against Rheumatism /American College of Rheumatology classification criteria for IIM and had anti-SSa/SSb data available. Results of commercially available anti-SSa/SSb and anti Ro52 immunoassays were used. Anti-SSb was only found in association with anti-SSa in this cohort and anti-SSa/SSb were combined and analyzed as a single group. ILD was defined by the presence of NSIP, COP/BOOP, UIP and unspecified ILD patterns on CT chest. PFTs variables were collected. Statistical analyses included Chi-

Table 3. Frequency of ILD and PFT results in anti-Ro52 positive and negative patients

	anti-Ro52 +	anti-Ro52 -	p-value
ILD n (%)	N=25	N=35	
ILD present	16 (64 %)	9 (25.7%)	**0.004** **
No ILD	9 (36 %)	26 (74.3%)	
PFT %	N 14	N 19	
FEV1 median (min-max)	66 (33-105)	81 (42-131)	0.1165
FVC median (min-max)	64 (27-97)	80 (40-117)	0.1770
DLCO median (min-max)	47 (21-77)	68 (18-102)	**0.0226** **
** statistically significant difference			

square, Fisher's Exact test, and Wilcoxon Rank Sum test to determine statistical differences in group distributions and McNemar's test was performed to compare groups.

Results: 118 IIM adult (age ≥ 18) patient records were reviewed. 15 with no anti-SSa/SSb and anti-Ro52 data and 9 anti-SSa/SSb negative patients with low positive Ro52 antibodies were excluded. Of 94 patients included in the analysis 35.1% (33 /94) were anti-SSa/SSb positive. Of 60 patients with available anti-Ro 52 41.6% % (25/60) were positive. The anti-SSa/SSb positive (n=33) and negative (n=61) groups and anti-Ro52 positive (n=25) and negative (n=35) groups had similar distribution for age, gender, and race, as well as subtypes of IIM. Demographics, clinical characteristics are listed in Table1.

56% of patients with anti-SSa/SSb positive IIM had ILD compared to 44% of patient with negative anti-SSa/SSb (p = 0.003) regardless of anti-Ro52 status. 64% of patients with positive anti-Ro52 had ILD as compared with 36% of patient with negative anti-Ro52 (p= 0.004). NSIP and non-specified ILD were most reported irrespective of serological status, UIP was only seen in anti-SSa/SSb negative group. There was no statistically significant difference observed in FEV1, FVC, or DLCO between anti-SSA positive and anti-SSa negative patients. Interestingly, patients with positive Ro52 antibodies had a lower DLCO (47% vs. 68%; p = 0.003) than in anti-Ro52 negative patients, while there was no difference in FEV1 and FVC between groups.

Conclusion: While anti-SSa/SSb positivity is associated with higher rate of ILD, independent of anti-Ro 52 status, it does not confer an increased risk of ILD severity as measured with PFTs. DLCO in anti-Ro52+ group was significantly lower than that in anti-Ro52- group, indicating that anti-Ro 52 positivity is likely more applicable in predicting ILD severity than anti-SSa/SSb. This suggests that while both assays are useful in defining risk for ILD, anti-Ro52 is superior to the anti-SSa/SSb in determining severity of ILD in myositis patients.

Disclosure: S. Narain, None; **A. Valle**, None; **M. Barilla-Labarca**, None; **G. Marder**, GlaxoSmithKline, 5.

Abstract Number: 0705

Mitochondrial Calcification-Induced Inflammation in Human Skeletal Muscle and Immune Cells

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Children with juvenile dermatomyositis (JDM) have decreased autophagy, as also confirmed by our RNA seq data in JDM muscle, which may contribute to accumulation of harmful agents. Consistent with that interpretation, our prior work demonstrated accumulation of calcified mitochondria in degenerated muscle fibers of JDM patients. In further mechanistic studies, we demonstrated mitochondrial reactive oxygen species (mtROS) as the main driver of mitochondrial calcification in human skeletal muscle cells. However, what remains to be explored is the effect of mitochondrial calcification on inflammation in calcifying skeletal muscle cells and in phagocytosing immune cells that may participate in clearance of calcified extruded mitochondria.

Methods: Mitochondrial calcification was induced in human skeletal muscle cells (RH30 cells) by addition of moderately high calcium-phosphate medium (Ca-P), and detected by fluorescent stain osteoimage. MtROS was measured using MitoSOX. Targeted metabolomics was performed on RH30 cells to identify potential pathways enriched upon mitochondrial calcification. Inflammation in RH30 cells was measured by RT-qPCR and ELISA. Mitochondrial DNA was measured using qPCR. Cardiolipin exposure was measured by flow cytometry. THP-1 monocytes were used to investigate the inflammatory potential of calcified mitochondria.

Results: Consistent with the role of calcium in mitochondrial metabolism, we found a significant increase in mtROS of calcified RH30 cells compared to untreated cells ($p< 0.01$). Pathway enrichment analysis on metabolites significantly downregulated in Ca-P treated cells revealed several mitochondrial-related pathways including mitochondrial respiration. In RH30 cells, upon mitochondrial calcification, there is a significant induction of interferon-stimulated gene expression and release of inflammatory cytokines including IL-1β (135 pg/mL vs. 75 pg/mL, $p=0.0002$). Further, cellular supernatants from calcified RH30 cells enriched in mtDNA could induce interferon responses in an interferon reporter cell line suggesting the extrusion of inflammatory mitochondria-derived components upon calcification of skeletal muscle cells. Consistent with these findings, investigation on isolated calcified mitochondria demonstrated a propensity of calcified mitochondria to release significant amounts mtDNA compared to non-calcified mitochondria (2,233,494 copies/mL vs. 581,655 copies /mL, $p< 0.0001$) and a trend for increased cardiolipin exposure (aCL MFI 18,500 vs. 10,271, $p=0.07$), suggesting destabilization of calcified mitochondria. Consistent with the proinflammatory nature of calcified mitochondria, THP-1 monocytes stimulated with calcified mitochondria but not non-calcified mitochondria secreted significant levels of IL-1β.

Conclusion: Mitochondrial calcification, as occurs in JDM, contributes to inflammation in skeletal muscle cells as well as in phagocytosing immune cells.

Disclosure: B. Duvvuri, None; **L. Pachman**, None; **T. WANG**, None; **P. Hermanson**, None; **C. Lood**, Exagen Diagnostic, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 5, Horizon Diagnostic, 5.

Abstract Number: 0706

Mycophenolate Mofetil and Methotrexate Efficacy in Dermatomyositis

Madison Grinnell[1], Emily Keyes[2], DeAnna Diaz[2], Thomas Vazquez[3], Rui Feng[4] and Victoria Werth[2], [1]Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania and Philadelphia VAMC, OMAHA, NE, [2]Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania and Philadelphia VAMC, Philadelphia, PA, [3]FIU Wertheim College of Medicine, Virginia Beach, VA, [4]University of Pennsylvania Department of Biostatistics, Philadelphia, PA

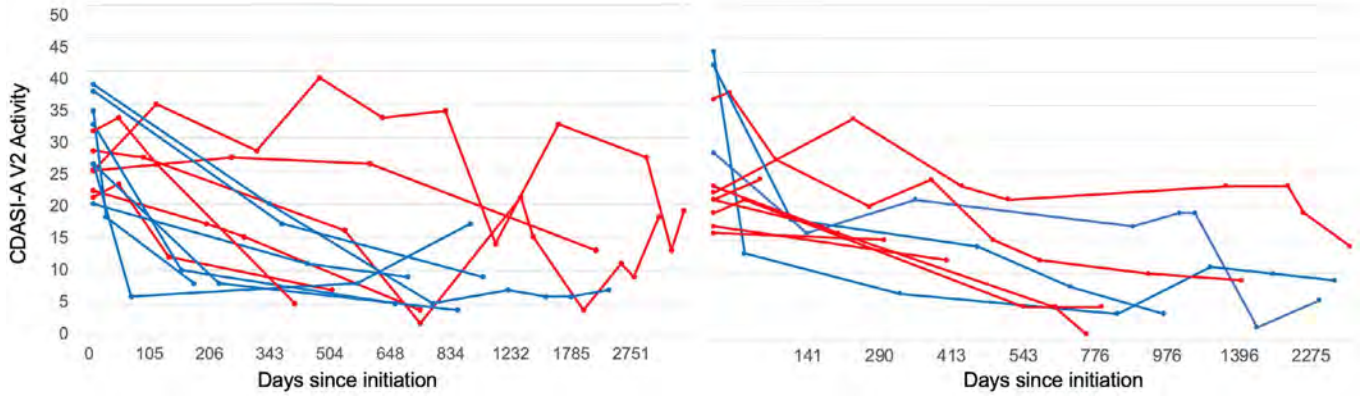
SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Treatment of dermatomyositis (DM) typically follows a stepwise sequence starting with either methotrexate (MTX) or mycophenolate mofetil (MMF) after an inadequate response to antimalarial therapy. However, data is scarce regarding the effectiveness of MTX and MMF.

Methods: A cohort of 24 patients with currently skin-predominant DM was identified using data from a prospective database at The University of Pennsylvania. Included patients took MTX or MMF and had ≥ two study visits within a retrospective observation period from October 2008 until February 2021. The Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) was used to assess severity and outcomes. Patients with mild disease activity, defined as a CDASI activity (CDASI-A) score < 14 (maximum sub-score of 100), were excluded from the analysis as were any patients on any other medications used to treat DM aside from MTX or MMF, with the exception of chronic antimalarials or topical medications.

Results: For both MMF (n=13) and MTX (n=11), there was no baseline difference in CDASI-A scores at initiation. There was no significant difference in the degree of improvement on either medication, with a mean difference in daily CDASI-A change between MTX and MMF of -0.0028 ± 0.0024 (p=0.2400) using a mixed linear effects model.



MMF Takers (Left) and MTX Takers (Right) CDASI Activity Scores (*Responders at first follow up displayed in blue, nonresponders displayed in red)

MMF		MTX	
Avg Age	62	Avg Age	62
Sex	10 Female, 3 Male	Sex	10 Female, 1 Male
Race	11 Caucasian, 2 Asian	Race	10 Caucasian, 1 Asian
Amyopathic	11	Amyopathic	8
Classic	2	Classic	3
# Switched	6	# Switched	1

Demographics

For MTX, the median percentage change in CDASI-A between the first and last study visit was -74%. For MMF, the median percentage change was -76%. A decrease of 40% or greater in the CDASI-A score has previously been associated with a meaningful change in quality of life (1). Defining responders as having a 40% or greater improvement in their CDASI-A score between their first and second observations (see Figure 1), 27% of the patients taking MTX were responders while 54% of patients taking MMF were responders. The range of time varied between the first and second visits with 50% of patients having a second study visit within 150 days. By last follow-up, 55% of patients taking MTX were considered responders and 77% of patients taking MMF met criteria to be considered responders. For MTX, the median follow-up for the second visit was 178 days and for the last visit was 776 days. For MMF, the median follow up was similar—147 days for the second visit, and for the last visit was 787 days. Of note, 7 patients in total had taken both MMF and MTX at some point in their disease course. More patients switched from taking MTX to MMF (see Table 1).

Conclusion: Although we do not have a large enough sample size to make a properly powered conclusion, MTX trended to a slightly delayed effect compared to MMF. Either MMF or MTX may be added to treatment plans for patients with DM who have not responded to antimalarial therapy. Moreover, our data suggest that responders continued to improve over many months (even years for some) while most non-responders showed little improvement at first follow-up (ranging from 2-6 months) during the observation period. Large cross over studies with safety data are needed to evaluate patient response to MMF and MTX in DM.

References

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Disclosure: M. Grinnell, None; **E. Keyes**, None; **D. Diaz**, None; **T. Vazquez**, None; **R. Feng**, None; **V. Werth**, None.

Abstract Number: 0707

Association of Pneumomediastinum with Poor Prognosis in Patients with Myositis-Associated Interstitial Lung Disease

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Background/Purpose: Pneumomediastinum is an important complication in patients with myositis-associated interstitial lung disease (ILD). Patients with myositis and ILD who had pneumomediastinum during the disease course have a poor outcome, often fatal, especially in the case of rapidly-progressive ILD (RP-ILD). The purpose of this study was to establish the clinical features and risk factors for mortality in patients with myositis-associated ILD accompanied by pneumomediastinum.

Methods: Retrospective study of patients attending Tokai University Hospital between 2011 and 2020, with idiopathic inflammatory myopathies (IIMs) satisfying the ACR/EULAR classification criteria and with ILD diagnosed based on the clinical course of respiratory symptoms, function and computed tomography. Patients´ sera were screened for autoantibodies using protein immunoprecipitation assays. Clinical features and prognostic risk factors were compared between patients with or without pneumomediastinum using univariate and multivariate analyses and multiple logistic regression models.

Results: Of 164 patients with IIMs accompanied by ILD, 23 (12 female, 11 male; mean age 58.6, range 36-80 years) developed pneumomediastinum during their clinical course. Seven of these patients had classic dermatomyositis (DM) and 11 had clinically amyopathic DM (CADM), 3 had polymyositis (PM) and 2 had anti-aminoacyl-tRNA synthetase (ARS) antibody syndrome. Twelve possessed antibodies specific for melanoma differentiation-associated gene 5 (MDA5) and 8 had anti-ARS antibodies (3 with anti-PL-7, 3 with anti-EJ, and 2 with anti-PL-12 antibodies). Frequencies of smoking and anti-MDA5 antibody-positivity were significantly higher in patients with pneumomediastinum than in those without (61% vs. 36%, P=0.027; 52% vs. 20%, P=0.001, respectively). By univariate analysis, pneumomediastinum during the clinical course was identified as an initial factor associated with subsequent mortality due to ILD. However, multiple regression analysis revealed that anti-MDA5-positivity, but not pneumomediastinum during the clinical course, was an independent factor associated with mortality due to ILD (HR= 4.84, 95% CI: 2.3, 10.7, P=0.01; HR= 2.42, CI: 1.0, 5.4, P=0.11, respectively).

Conclusion: These results indicate that pneumomediastinum frequently coexists with anti-MDA5-positivity and that the presence of anti-MDA5 antibody might be a potential confounding factor for pneumomediastinum with regard to mortality due to ILD in patients with myositis-associated ILD.

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Abstract Number: 0708

Cardiovascular Risk in Myositis Patients Compared to General Population – Preliminary Data from a Single-centre Cross-sectional Study

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Table 1: Baseline characteristics

	IIM (n = 39)	HC (n = 39)
Gender, n (%): female / male	32 (82) / 7 (18)	32 (82) / 7 (18)
Age (years); median (IQR)	56.0 (47.7 – 64.1)	56.0 (48.3 – 64.2)
BMI (kg/m²); median (IQR)	25.9 (23.2 – 31.1)	27.5 (23.9 – 31.7)
Disease subtype, n (%): DM / PM / IMNM	14 (36) / 18 (46) / 7 (18)	
Disease duration (years); median (IQR)	4.84 (1.96 – 8.83)	
Disease activity (MITAX); median (IQR)	0.13 (0.06 – 0.29)	
Disease damage (MDI); median (IQR)	0.05 (0.03 – 0.08)	
MMT-8; median (IQR)	64 (54 – 70)	
CRP (mg/L); median (IQR)	3.0 (1.4 – 5.0)	
ESR (mm/h); median (IQR)	13 (8 – 25)	
CK (µkat/L); median (IQR)	3.0 (1.3 – 9.4)	
LD (µkat/L); median (IQR)	3.7 (3.4 – 5.2)	
Myoglobin (µg/L); median (IQR)	93.6 (60.4 – 250.2)	
Glycaemia (mmol/L); median (IQR)	5.2 (4.8 –5.8)	
Current dose of GC - prednisolone equivalent dose (mg/day); median (IQR)	6.5 (3.75 – 15)	
IIM-associated clinical manifestations, n (%): MW / OD / SR / MH / RP / A / ILD / CI	35 (88) / 7 (18) / 5 (13) / 8 (21) / 10 (26) / 5 (13) / 16 (41) / 3 (8)	
Autoantibodies (positive), n (%): ANA / Mi-2 / TIF-1γ / CADM-140 / SAE / p140 / SRP / Jo-1 / PM-Scl / RNP / Ku / Ro / HMGCR	24 (62) / 3 (8) / 3 (8) / 0 (0) / 0 (0) / 0 (0) / 3 (8) / 10 (26) / 5 (13) / 5 (13) / 0 (0) / 16 (41) / 3 (8) / 2 (5)	
Treatment, n (%): GC / MTX / AZA / CSA / CPA / LEF / MMF	36 (92) / 11 (28) / 8 (21) / 5 (13) / 2 (5) / 2 (5) / 1 (3)	
Arterial hypertension (treated), n (%)	15 (38)	
Diabetes mellitus, n (%): Untreated / PAD / Insulin treatment	3 (8) / 1 (3) / 1 (3)	
Statin use, n (%): Current / Previous / Other current hypolipidemic drugs	0 (0) / 4 (10) / 1 (3)	
Smoking (current), n (%)	0 (0)	

Acronyms: IIM, idiopathic inflammatory myopathies; DM, dermatomyositis; PM, polymyositis; IMNM, immune mediated necrotising myopathy; HC, healthy controls; MITAX, Myositis Intention to Treat Activity Index; MMT-8, manual Muscle Testing-8; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CK, creatine kinase; LD, lactate dehydrogenase; MW, muscle weakness; OD, oesophageal motility disorder; SR, skin rash; MH, mechanic's hands; RP, Raynaud's phenomenon; A, arthritis; ILD, interstitial lung disease; CI, cardiac involvement ANA, antinuclear antibodies; Mi-2, anti-nuclear helicase 218/240 kDa; p155-140, anti-TIF1 (transcription factor-1); CADM-140, anti-MDA5 (antigen associated with melanoma differentiation); SAE, anti-SUMO1 (small ubiquitin-like activating enzyme); p140, anti-NXP2 (nuclear matrix protein); SRP, anti-signal recognition particles; Jo-1, anti-histidyl-tRNA synthetase; PM-Scl, anti-Pm-Scl (anti-core complex 11-16 proteins); RNP, anti-ribonucleoprotein; Ku, anti-Ku (against the nuclear DNA-protein kinase subunit); Ro, anti-Ro (52 / 60kDa, against cytoplasmic RNA and associated peptides); GC, glucocorticoids; MTX, methotrexate; AZA, azathioprine; CSA, cyclosporin A; CPA, cyclophosphamide; LEF, lefunomide; MFF, mycophenolate mofetil; PAD, per oral antidiabetic drugs

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are associated with systemic inflammation, limited mobility, and glucocorticoid treatment, which can have a negative impact on metabolic disease, atherogenesis, and cardiovascular risk. The aim of this study was to assess the cardiovascular risk in IIM patients and healthy controls (HC) and the association with disease-specific features.

Methods: 39 patients with IIM (32 females; mean age 56; disease duration 4.8 years; DM 14 / PM 18 / IMNM 7) and 39 age-/sex-matched HC (32 females, mean age 56) without rheumatic diseases were included. DM and PM patients fulfilled the Bohan/Peter criteria, IMNM patients fulfilled the ENMC criteria. In both groups manifest cardiovascular disease (angina pectoris, myocardial infarction, cerebrovascular, and peripheral arterial vascular events) were excluded by case history. Disease activity and damage were evaluated by MITAX and MDI, muscle involvement by manual muscle testing (MMT-8), and comorbidities and current treatment were recorded. All participants underwent an examination of carotid intima-media thickness (CIMT), pulse wave velocity (PWV), ankle-brachial index (ABI), body composition (densitometry: iDXA Lunar, bioelectric impedance: BIA2000-M). Physical activity was evaluated by Human Activity Profile (HAP) questionnaire. The risk of fatal CV risk events was evaluated by SCORE (charts for the European population). Data are presented as median (IQR).

Table 2: Cardiovascular (CV) parameters in patients with idiopathic inflammatory myopathies (IIM) and healthy controls (HC)			
Parameters of CV risk	**IIM** (n = 39)	**HC** (n = 39)	**p-value**
MAP (mmHg); median (IQR)	**95** (86 - 103)	**97.7** (89.3 - 107)	0.497
ABI; median (IQR)	**0.995** (0.92 – 1.06)	**1.05** (0,89 – 1.10)	0.265
PWV (m/s); median (IQR)	**8.0** (6.05 – 9.40)	**8.0** (7.05 – 9.38)	0.484
CIMT (mm) ; median (IQR)	**0.7** (0.6 – 0.8)	**0.7** (0.6 – 0.8)	0.356
Plaque; n (%)	**14** (35.9)	**10** (25.6)	0.462
Plaque thickness (mm); median (IQR)	**1.4** (1.3 – 1.8)	**1.6** (1.2 – 2)	0.978
BMI (kg/m²); median (IQR)	**25.9** (23.2 – 31.1)	**27.5** (23.9 – 31.7)	0.893
HAP; median (IQR)	**58.3** (47.8 – 69.8)	**83** (79 – 90.8)	**<0.001**
SCORE (%); median (IQR)	**2** (1 – 5)	**3** (1 – 5)	0.990

Acronyms: MAP, mean arterial pressure; ABI – ankle-brachial index; PWV – pulse wave velocity; CIMT – carotid intima-media thickness; BMI – body mass index; HAP, Human activity profile questionnaire; SCORE, systematic Coronary risk evaluation – risk of fatal cardiovascular event in 10 years (%)

Results: In IIM, baseline characteristics, disease activity, the dose of glucocorticoids, prevalence of comorbidities were evaluated (Table 1). Compared to HC, there was no significant difference in IIM regarding blood pressure, ABI, PWV, CIMT and risk of fatal CV events by SCORE. In IIM, there was a higher frequency of plaques, but no difference in the plaque thickness. IIM group recorded significantly lower physical activity (Table 2). In IIM, blood pressure (represented as MAP) correlated positively with age, BMI, parameters of inflammation (CRP, C3), triglycerides, atherogenic index and body fat %, but negatively with albumin and HDL-C. Decreased (unfavourable) values of ABI were associated with low HDL-C. Increased PWV was associated with higher age, longer disease duration, decreased disease activity (MITAX), and unfavourable parameters of body composition and nutritional status (decreased phase angle and cell quota, and higher extracellular/body-cell-mass ratio). Increased (unfavourable) values of CIMT and plaque thickness were associated with longer disease duration (Table 3).

Conclusion: No significant differences in cardiovascular risk parameters between our IIM patients and healthy age-/sex-matched individuals were detected. However, in IIM, cardiovascular risk factors were associated with age, disease duration, dose of glucocorticoids, and parameters of lipidogram and body composition. No association with decreased physical activity was observed.

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Table 3: Correlation of cardiovascular parameters and disease-specific features in all IIM patients (n=39)		
Correlated parameters	**Spearman's r**	**p-value**
MAP: Age; BMI CRP; albumin; C3; TG; HDL-C; AI BF (%, DXA); VF (kg, DXA); BF (%, BIA)	 0.567; 0.346; 0.324; -0.452; 0.451; 0.518; -0.418; 0.466 0.521; 0.512; 0.402	 <0.001; 0.042; 0.044; 0.014; 0.014; 0.004; 0,024; 0.011; 0.002; 0.002; 0.012
ABI: HDL-C	0.106	0.024
PWV: Age; disease duration; MITAX; albumin; Phase angle (BIA); ECM/BCM (BIA); Cell quota % (BIA)	 0.793; 0.368; -0.430; -0.430; -0.420; 0.793; -0.125	 <0.001; 0.049; 0.046; 0.010; 0.023; 0.023; 0.037
CIMT: disease duration	0.377	0.020
Plaque thickness: disease duration	0.438	0.029

Acronyms: MAP, mean arterial pressure; ABI – ankle-brachial index; PWV – pulse wave velocity; CIMT – carotid intima-media thickness; BMI – body mass index; CRP, C-reactive protein; C3, complement 3; TG, triglycerides; HDL-C, high-density lipoprotein; AI, atherogenic index of plasma = *log(TG/ HDL-C)*;BF, body fat; VF, visceral fat, DXA, dual X-ray absorptiometry; BIA, bioelectrical impedance; MITAX, Myositis Intention to Treat Activity Index; ECM/BCM, extracellular mass/body cell mass index

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Abstract Number: 0709

Lower HDL-associated Apolipoprotein A-I Levels Associate with Presence of Calcinosis in Adult Dermatomyositis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Calcinosis is a sequelae of juvenile and adult dermatomyositis (DM) associated with significant morbidity and poor quality of life. It is hypothesized that inflammatory vasculopathy may lead to dystrophic mineral deposition. Apolipoprotein A-I (apoA-I) is the major apolipoprotein component of HDL which normally prevents inflammation in the vessel wall. The current study aims to identify clinical and laboratory features associated with calcinosis in a cohort of adult patients with idiopathic inflammatory myopathies (IIM).

Methods: A cross sectional study was performed in 288 adult patients with IIM recruited at the University of California, Los Angeles between 2008-2020. Clinical and laboratory features including myositis autoantibodies were compared between patients with and without calcinosis. HDL-associated ApoA-I levels (HDL-apoA-I) were measured using sandwich ELISA. Patients were divided into HDL-apoA-I tertiles to compare the association of calcinosis with low (tertile 1) vs high (tertial 3) HDL-apoA-I. Stepwise multivariate logistic models were constructed to obtain odds ratios (ORs) that related calcinosis to various variables. Statistically significant bivariate variables were considered as predictors for the stepwise model. The final stepwise model was selected to minimize the Bayes Information Criterion (BIC).

Results: We identified 27 (9.3%) patients with calcinosis in our IIM cohort. All patients with calcinosis had dermatomyositis (DM), (12.6 % of DM cohort with calcinosis), with the exception of 1 patient who had polymyositis overlap with CREST syndrome. Five (19%) of the patients with calcinosis had juvenile onset DM. Patients with calcinosis were older and had significantly longer disease duration, higher MD global damage scores and lower total cholesterol (TC), LDL-cholesterol (LDL-C), and CPK levels. Among myositis autoantibodies, NXP2, SAE and PM-scl ab were more frequently seen in patients with calcinosis. In contrast, antisynthetase, HMGCR and SRP ab were less frequently seen in patients with calcinosis. None of the patients with calcinosis had a history of cancer compared to 28% in patients without calcinosis. Low (vs high) HDL-apoA-I levels were associated with calcinosis, and the association remained strong in multivariate analysis in addition to older age and longer disease duration. In fact, IIM patients with low HDL-apoA-I were 11.5 times more likely to have calcinosis compared to patients with high HDL-apoA-I.

Table 1. Clinical and laboratory features in IIM patients with and without calcinosis Values reported as mean±SD or N(%) unless specified *p <0.05 comparing calcinosis vs no calcinosis group using student's t test or Wilcoxon rank sum test. † Patient with polymyositis and overlap with CREST ‡ Myositis autoantibody testing results were available in 209/288 patients § Patients were divided into HDL-apoA-I tertiles: tertile 1 including patients with lowest apoA1, and tertile 3 including patients with highest apoA1 levels

	Calcinosis (n=27)	No Calcinosis (n=261)
Age	43±14*	50± 15
Sex, Female	23(85)	182(69)
Ethnicity, Hispanic	4(15)	56(21)
Race, White	17(62)	161(61)
IIM type		
Dermatomyositis	26(96)*	180(68)
Polymyositis	1(4)†	65(24)
Inclusion body myositis	0	16(6)
Disease duration, years	11 ±12*	3 ± 5
Myositis autoantibodies ‡		
Antisynthetase ab	1(4)*	45(17)
MDA5 ab	3(11)	18(7)
SRP/HMGCR ab	0(0)*	24(9)
Mi-2 ab	1(4)	10(4)
P155/140 ab	3(11)	29(11)
NXP2 ab	5(19)*	10(4)
U1/U2/U3 RNP ab	1(4)	2(1)
Ro/SSA ab	2(7)	12(4)
SAE ab	3(11)*	2(1)
Ku ab	0(0)	3(7)
PM-scl ab	2(7)*	2(1)
Unidentified ab	2(7)	17(7)
No myositis ab	0(0)	13(5)
IIM disease characteristics		
Hoarseness	4(15)	32(12)
Dysphagia	7(26)	85(32)
Amyopathic DM	8(30)	51(19)
Periungal erythema	1(4)	13(5)
Skin ulceration	2(8)	7(3)
Arthritis	12(44)	92(35)
Raynauds phenomenon	7(26)	42(16)
Mechanic's hands	1(4)	16(6)
Interstitial lung disease	8(32)	80(36)
Cancer	0*	18(28)
MD global activity VAS, 0-100mm	39±21	41±21
MD global activity likert, median (IQR)	2(1-2)	2(1-2)
MD global damage VAS, 0-100mm	44±20*	31±22
MD global damage likert, median (IQR)	2(1-3)*	1(1-2)
Laboratory values		
CPK, U/L, median (IQR)	87 (61-164)*	147 (65-401)
Aldolase, U/L	6.0 (4.5-8.2)	6.6 (5.0-11.4)
ESR, mm/hr	31±27	29±26
hsCRP, mg/L	5.2±8.1	5.7±9.6
Lipid panel, mg/dl		
Total cholesterol	173±39*	213±55
LDL cholesterol	97±37*	126±49
HDL cholesterol	55±18	62±31
Triglycerides	152±106	180±179
HDL-ApoA-I Low (Tertile 1 vs Tertile 3) §	15(75)*	79(47)

Conclusion: 12.6 % of dermatomyositis patients had calcinosis in our IIM cohort, which associated with older age, longer disease duration, and lower HDL-apoA-I levels. Further studies are warranted to evaluate the role of apoA-I in the development of calcinosis in patients with dermatomyositis.

Table 2. Multivariate stepwise logistic regression for presence of calcinosis Statistically significant bivariate variables were considered as predictors for the stepwise model. The final stepwise model was selected to minimize the Bayes Information Criterion (BIC)

MV predictors	OR	P value
Age	0.91 (0.84-0.97)	0.01
Disease duration	1.19 (1.06-1.32)	0.002
MD global damage VAS	1.05 (1.01-1.09)	0.01
HDL-apoA-I, Low (Tertile 1 vs Tertile 3)	11.49 (1.33-99.46)	0.04

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Abstract Number: 0710

Patients with Recent Onset, Active Polymyositis (PM), Dermatomyositis (DM) and Antisynthetase Syndrome (ASS) Have Reduced Muscle Endurance but Not Reduced Muscle Strength Compared to Patients with Established, Low-active Disease

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
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Session Time: 8:30AM–10:30AM

Background/Purpose: To analyze for differences in quadriceps maximal isometric voluntary contraction (MVIC), muscle endurance (ME), muscle mass and fat mass (m. vastus lateralis, mid-thigh) in patients with recent onset PM/DM and established PM/DM.

Table 1. Patient characteristics

	Recent onset PM/DM/ASS (n=8)	Established PM/DM/ASS (n=8)
Diagnosis, PM/DM/ASS, n	2/4/2	3/4/1
Age	54.5 (20-64)	53 (19-67)
Sex, n, M/F	1/7	1/7
Disease duration	5.5 (3-6) months	7.5 (6-36) years
Physical activity, min/week	225 (<30 - >300)	120 (60 - >300
Exercise, min/week	90 (0 - >120	120 (20 - >120)
Prednisone, mg/d	13.75 (2.5-30)	3.75 (0-8.75)
Physician VAS	20 (12-40)[1]	0 (0-20)[1]
Extra-muscular VAS	18 (0-50)[3]	0 (0-20)[1]
HAQ	0.63 (0-2.25)[1]	0.3 (0-1.38)[1]

All values in median (min-max) if not stated otherwise. Superscripted numbers showing numbers of cases with missing data.

Methods: All patients diagnosed with PM, DM or ASS during September 2017 to January 2020 at Karolinska University Hospital or Akademiska Hospital who met the inclusion criteria were asked to participate (n=16). So far 8 patients with established PM/DM/ASS have been identified to match 8 of the patients with recent onset disease, by age and gender. A dynamometer from Biodex was used to assess MVIC and ME starting with three warm-up 4-sec. contractions followed by three maximal contractions, all with a 3-minute rest in-between. Thereafter six sets of twelve submaximal contractions, starting on 20 % of MVIC and increasing by 10 % for each set, finishing on 70 % of MVIC. Each set ended with a new maximal contraction registered as percentage of initial MVIC. Muscle and fat mass was assessed by MRI. A blinded, experienced radiologist analyzed the muscle mass in m. vastus medialis and lateralis (distance femur - outer edge of the muscle) and fat mass (outer edge of muscle - inner edge of skin) in millimeters (mm). Examinations of muscle function and MRI were conducted at most two weeks apart.

Results: Patients with recent onset PM/DM had a median MVIC of 73 (53-93) Nm and established PM/DM had 75 (41-118) Nm (p=0.65). Median ME was 85 (63-89) % and 90.5 (83-98) % for the 8 patients with recent onset disease and established disease, respectively (p=0.007). Median muscle mass for patients with recent onset PM/DM was 38.5 (26-47) mm and 33 (20-55) mm for patients with established disease (p=0.41). Patients with recent onset disease had a median fat mass of 13 (7-21) mm and patients with established PM/DM had 10 (7-23) mm (p=0.49).

Conclusion: Patients with recent onset, active PM/DM/ASS had a significantly reduced muscle endurance (ME) compared to matched patients with established disease. No significant differences were found between the groups regarding maximal voluntary isometric contraction (MVIC), muscle mass or fat mass. Further data collection is needed to reach statistical power.

Disclosure: K. Andreasson, None; **H. Alexanderson**, None.

Abstract Number: 0711

Suppression of HDL-associated Apolipoprotein A-I (apoA-I) Levels in Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION
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Background/Purpose: Patients with idiopathic inflammatory myopathies have accelerated vascular disease, which contributes to higher disease morbidity and mortality. Apolipoprotein A-I (apoA-I) is the major protein component of HDL, which suppresses vascular inflammatory responses through promotion of cholesterol efflux and prevention of low density lipoprotein (LDL) oxidation. The current work assessed HDL-associated ApoA-I levels (HDL-apoA-I) in IIM patients compared to healthy controls, and evaluated associations of HDL-apoA-I with specific IIM disease characteristics.

Methods: HDL-apoA-I levels were measured by sandwich ELISA using a primary HDL antibody. HDL-apoA-I levels, demographic variables and traditional cardiovascular risk factors were compared in 122 IIM patients and 110 healthy controls (HC). HDL-apoA-I levels were also assessed separately in a large IIM extended patient cohort (n=274) in

Table 1. Clinical and laboratory characteristics of IIM patients and controls Values are mean±SD or N(%) unless specified *P<0.05, **P<0.0001 by student's t test and Wilcoxon rank sum test ‡Defined as first degree relative with MI at age <55 for male and <65 for female Abbreviations: MI, myocardial infarction; TIA, transient ischemic attack; BMI, body mass index; FHx, family history; hsCRP, high sensitivity C-reactive protein

	IIM (n=122)	Control (n=110)
HDL-apoA-I	45,888±44797**	159,507±65,674
Age, years	49±14	46±16
Sex, Female	85(70)	84(76)
Race, Caucasian	89(74)	79(74)
Ethnicity, Hispanic	25(20)	20(19)
Cardiovascular risk factors		
History of MI	2(2)	2(2)
Stroke/TIA	3(2)	1(1)
Hypertension	36(30)	17(20)
Dyslipidemia	28(23)	21(24)
Diabetes	18(15)*	2(2)
BMI	28±6	27 ±7
Ever smoker	16(16)*	23(37)
FHx of premature MI‡	12(12)	10(11)
Cholesterol medication use	17(14)	5(5)
Lipid panel, mg/dl		
Total cholesterol	216±62*	194±43
LDL-C	128±54*	111±35
HDL-C	61±27	60±19
Triglycerides	198±224*	116±67
ESR, median (IQR)	24 (8.25-44) *	12 (7.25-22)
hsCRP, median (IQR)	1.6(0.5-5.6)*	1.15(0.4-2.6)

relation to clinical and laboratory IIM disease characteristics. Multivariate linear regression analyses were performed to further assess predictors associated with HDL-apoA-I while adjusting for statistically significant univariate variables.

Results: HDL-apoA-I levels were significantly lower in IIM patients compared to HC (Table 1). The association between low HDL-apoA-I and IIM diagnosis remained strong after multivariate adjustment (Table 2). In linear regression analysis of the extended IIM patient group (Table 3), higher MD global disease activity scores by visual analog and likert scales as well as the presence of dermatomyositis (vs polymyositis or inclusion body myositis) and the presence of certain myositis specific autoantibodies (ab) (MDA5 and TIF1< ![if !msEquation] >< ![if !vml] >< ![endif] >< ![endif] > ab) were associated with lower HLD-apoA-I levels. In multivariate analysis, the presence of MDA5 or TIF1γ ab remained significantly associated with lower HDL-apoA-I levels (regression coefficient β= -1.35, p< 0.001 and β= -0.81, p=0.01 respectively).

Table 2. Multivariate Regression Analysis of Variables associated with HDL-apoA-I† activity in IIM patients and Healthy Controls (n=232) †Log transformation was used for skewed variables (apoA-I, hsCRP)

	Regression coefficient (95% CI)	P value
IIM (vs HC)	**-1.62 (-1.89, -1.34)**	**<0.0001**
Diabetes	-0.23 (-0.61,0.15)	0.24
Ever smoker	0.41 (0.11, 0.70)	**0.01**
Total cholesterol, 10mg/dl	0.01 (-0.04, 0.05)	0.73
LDL-C, 10mg/dl	0.01 (-0.04, 0.05)	0.74
Triglycerides, 10mg/dl	0.01 (-0.002, 0.001)	0.13
ESR, 10mm/hr	0.02 (-0.03, 0.08)	0.46
hsCRP†	0.01 (-0.08, 0.11)	0.75

Table 3. Univariate Linear regression Analysis of variables associated with HDL-apoA-I† levels in Patients with IIM including IIM disease specific variables (n=274) Values are mean±SD or N(%) unless specified *p<0.05 † Log transformation was used for skewed variables to fit linearity assumption, apoA-I, CK, ESR, hsCRP Abbreviations: MI, myocardial infarction; TIA, transient ischemic attack; BMI, body mass index; FHx, family history; VAS, visual analog scale; HAQ, health assessment questionnaire

	IIM (n=274)	Regression coefficient (95%CI)
Age, years	50±15	-0.004 (-0.02,0.01)
Sex, Female	195(71)	0.31 (-0.13, 0.75)
Race, White	205(75)	0.10 (-0.36,0.56)
Ethnicity, Hispanic	53(20)	**0.36 (0.06,0.65)***
CVD Risk factor		
History of MI	6(2)	0.49 (-0.86, 1.85)
History of Stroke/TIA	6(2)	-0.51 (-1.87,0.85)
Hypertension	83(30)	**0.67 (0.24, 1.09)***
Dyslipidemia	61(22)	**0.71 (0.24, 1.18)***
Diabetes	38(14)	0.49 (-0.08, 1.06)
BMI	27±6	0.02 (-0.02, 0.05)
Ever smoker	53(19)	0.23 (-0.27, 0.73)
FHx of premature MI	29(11)	0.18 (-0.46, 0.82)
Cholesterol medication use	33(12)	0.03 (-0.59, 0.64)
Lipid panel, 10mg/dl		
Total cholesterol	211±55	-0.01(-0.05, 0.03)
LDL-Cholesterol	125±49	-0.02(-0.06, 0.02)
HDL-Cholesterol	62±31	0.01(-0.05, 0.08)
Triglycerides	176±175	-0.004 (-0.01, 0.01)
IIM type		
Dermatomyositis	195	**-0.06 (-0.99, -0.12)***
Polymyositis	63	0.40 (-0.07, 0.87)
Inclusion body myositis	15	0.64 (-0.20, 1.49)
Disease duration, months, median (IQR)	14(3-62)	0.001 (-0.001,0.004)
Myositis Autoantibodies		
Antisynthetase	43 (16)	-0.05 (-0.60,0.50)
MDA5	21 (8)	**-1.47 (-2.20, -0.75)***
SRP	18 (7)	-0.63 (-1.43,0.17)
HMGCR	5 (2)	-1.25 (-2.73, 0.23)
Mi2	10 (4)	0.21 (-0.85, 1.27)
TIF1γ	32 (12)	**-0.83 (-1.44, -0.22)***
NXP2/MJ	15 (5)	-0.03 (-0.90, 0.85)
RNP	3 (1)	1.09 (-0.82, 3.00)
Ro/SSA	14 (5)	-0.60 (-1.50, 0.30)
SAE	5 (2)	-0.50 (-1.99, 0.99)
Ku	2 (1)	-1.80 (-4.12, 0.53)
PM-scl	3 (1)	-1.41 (-3.31, 0.49)
Unidentified ab	17 (6)	-0.78 (-1.60, 0.04)
None	13 (5)	-0.09 (-1.02, 0.85)
ILD	79(34)	-0.12 (-0.58, 0.34)
Cancer	19(25)	0.59 (-0.25, 1.42)
MD global activity VAS, 1-10cm	41±21	**-0.12 (-0.22,-0.02)***
MD global activity Likert, median (IQR)	2 (1-2)	**-0.31 (-0.57,-0.05)***
MD global damage VAS, 1-10	31±22	0.03 (-0.07,0.12)
MD global damage Likert, median (IQR)	1 (1-2)	-0.06 (-0.30,0.17)
HAQ, median (IQR)	0.88 (0.25-1.5)	-0.11 (-0.42, 0.21)
CK, median (IQR)†	121(62-352)	0.02 (-0.12, 0.17)
Aldolase	6.4(4.9-9.5)	0.25 (-0.04, 0.53)
ESR, median (IQR)†	23 (9-33)	-0.10(-0.28, 0.07)
hsCRP, median (IQR)†	1.6 (0.6-5.7)	0.09 (-0.04, 0.23)
Medications		
IVIG	54 (20)	**-0.90 (-1.37, -0.44)***
MMF	61 (22)	**-0.89 (-1.33,-0.44)***
AZA	22 (8)	0.57 (-0.12, 1.27)
MTX	51 (19)	0.01 (-0.48, 0.50)
HCQ	42 (15)	0.15 (0.37, 0.68)
TNFi	6 (2)	0.52 (-0.74, 1.77)
RTX	17 (6)	-0.04 (-0.81, 0.73)
CYC	10 (4)	**3.17 (1.90,4.45)***
Prednisone, yes	151 (55)	-0.22 (-0.68, 0.23)
Prednisone daily dose, median (IQR)	15 (5-35)	0.003 (-0.01, 0.01)

Conclusion: HDL-apoA-I levels were significantly lower in IIM patients compared to HC, and inversely associated with the presence of MDA5 and TIF1γ ab. Our results indicate a potential mechanism for the microvascular inflammation and damage in IIM, particularly in patients with MDA5 and TIF1γ ab.

Disclosure: S. Bae, None; **A. Shahbazian**, None; **J. Wang**, None; **C. Charles-Schoeman**, AbbVie, 2, 5, Bristol-Myers Squibb, 5, Pfizer Inc, 2, 5, Gilead Sciences, 2, Sanofi-Regeneron, 2.

Abstract Number: 0712

Immune Checkpoint Inhibitor-related Myotoxicity : Musculoskeletal and/or Neuromuscular Junction Disorder ?

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Immune checkpoint inhibitor (ICI)-related adverse events (irAE) recently emerged as new diseases in the field of auto-immunity. Among them, ICI-related myotoxicity has the highest fatality rate and is the second most frequent musculosketal irAE. Ir-myositis differs from its idiopathic counterpart by frequent oculomotor and bulbar symptoms as well as respiratory dysfunction. In addition, the presence of acetylcholine receptor antibodies (AchR Abs) in a subset of patients may suggest concurrent neuromuscular junction disorder. A comprehensive understanding of disease pathology underlying overlapping features of ir-myositis and ir-myasthenia gravis (MG) remains elusive, complicating disease stratification and management. Our study aimed to clarify the ir-myositis pathophysiology.

Methods: An observational, monocentric cohort study was conducted. Inclusion criteria were history of malignancy, ICI exposure, pathologically confirmed myositis, available AchR antibody testing and repetitive nerve stimulation, and absence of dermatomyositis skin rash. Post-mortem histopathology of the orbital muscles and diaphragm was examined in one and three patients, respectively.

Results: Twenty-two patients were enrolled. Median age was 71 [IQR 62-79] years; 14 patients (64%) were male. Two patients reported history of autoimmune disease. Lung (n=9/22), skin (n=3/22) and kidney (n=3/22) cancers were the most frequent indications for ICI therapy. Patients received anti-PD1 or anti-PDL1 monotherapy (77%; n=17/22) or combination therapy (23%; anti-LAG-3, n=1/22 and anti-CTLA4, n=4/22). Time to symptom onset was 25 [19-43] days. Clinical manifestations included proximal and axial muscle weakness (86%; n=19/22) and myalgia (63%; n=14/22). CK level was 3467 [1836-7659] U/L.

Additionally, patients frequently displayed diplopia and/or ptosis (45%; n=10/22) and dysphagia (53%; n=12/22). Respiratory failure requiring ventilatory assistance (invasive or non invasive) occured in a third of cases.

AchR Abs were detected at diagnosis in three patients (14%). We examined serum obtained prior to ICI exposure for presence of antibodies and retrieved positive results in all three cases. Electromyography showed a myopathic pattern in 13 patients (57%), whereas decrement on repetitive nerve stimulation was never observed.

Intensive care unit admission was required in 20 cases (91%). At follow-up (87 [36-255] days), mortality was 50%; death was related directly to myotoxicity in three patients (14%).

Post-mortem examination revealed muscle inflammation of both the oculomotor muscles and diaphragm.

Conclusion: Neuromuscular (oculomotor, bulbar and respiratory) signs typically observed in MG are frequent in ir-myositis and AchR Abs pre-exist in 14% of patients. In our cohort, based on electromyographic analysis, no evidence supports that the neuromuscular signs were related to a neuromuscular junction disorder. Necropsy findings may suggest that muscle inflammation underlies both oculomotor and respiratory dysfunction in ir-myositis patients. AchR Abs could be a biomarker of disease, however their pathogenic role is unclear.

Disclosure: H. Chassepot, None; **L. Plomp**, None; **D. Psimaras**, None; **T. Maisonobe**, None; **S. Leonard Louis**, None; **I. Plu**, None; **M. Touat**, None; **C. Anquetil**, None; **N. Wesner**, None; **N. Champtiaux**, None; **A. Rigolet**, None; **S. Demeret**, None; **N. Weiss**, None; **B. Abbar**, None; **M. Bretagne**, None; **B. Pinna**, None; **C. Morelot**, None; **M. Dres**, None; **T. Similowski**, None; **S. Ederhy**, None; **J. Salem**, None; **O. Benveniste**, None; **Y. Allenbach**, None.

Abstract Number: 0713

MDA5 Helicase Domains Identified as the Main Targets of Anti-MDA5 Autoantibodies in European Dermatomyositis Patients

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
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Session Time: 8:30AM–10:30AM

Background/Purpose: The presence of anti-melanoma differentiation associated protein 5 (MDA5) autoantibodies in myositis patients is associated with mucocutaneous ulcerations, (rapidly progressing) interstitial lung disease (RPILD), arthritis and mild muscle involvement. There are no biomarkers to identify patients that will develop RPILD, although early initiation of treatment is essential to rescue patients from respiratory failure. The aetiology is unresolved and it is unknown which domain of the MDA5 protein is the main elicitor of an immunogenic response.

The aim of this study is to identify the domains in the MDA5 protein that are the target of autoantibodies, which could lead to more insight into the disease mechanism.

Methods: The reactivity in sera from MDA5+ dermatomyositis patients at baseline (n=20, Karolinska Institutet) and purified IgG were measured in ELISA (OD). IgG were isolated from MDA5+ plasmapheresis samples (n=9, from

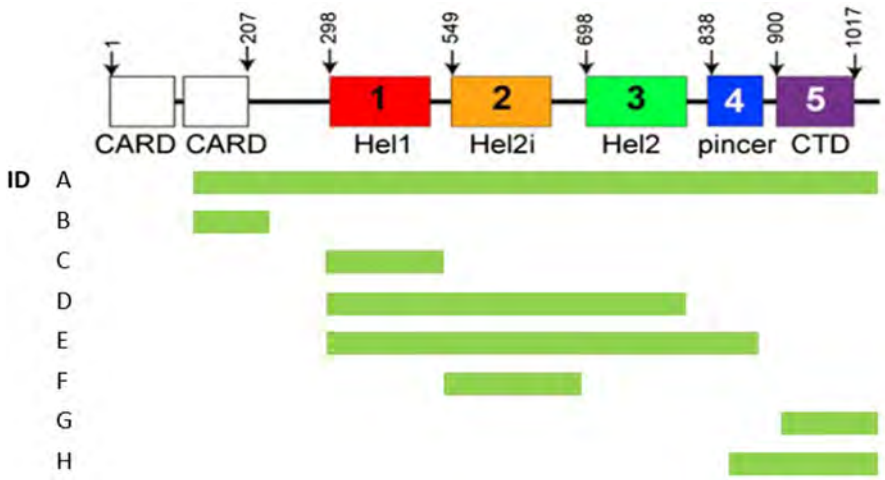

Figure 1. Graphical presentation of the MDA5 construct, each construct representing different (combinations of) domains of the MDA5 protein.

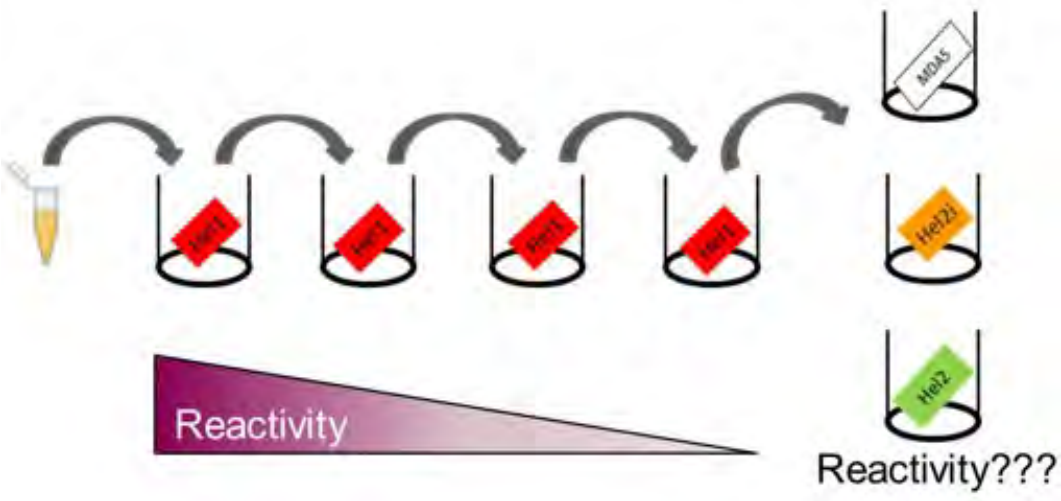

Figure 2. Graphical representation of the depletion ELISA. Samples were incubated with a primary construct to deplete all specific autoantibodies and then transferred to a secondary construct to assess if there were still specific antibodies towards the second construct.

France, Sweden and Belgium) by affinity chromatography as previously described (1). All target proteins, MDA5 constructs (UniProt ID Q9BYX4, *Figure 1*) and RIG-I (UniProt ID O95786), were produced in *E.coli*. A depletion ELISA was developed to assess the specificity of the reactivity towards the different domains. Briefly, the reactivity towards one construct was depleted in several incubation steps before the purified IgG were transferred to another construct to measure the remaining reactivity (*Figure 2*). The RIG-I protein was used as a negative control.

Results: All MDA5+ patients (n=20) showed reactivity towards the helicase (Hel) domains at the center of the MDA5 protein, but reactivity towards construct B was significantly lower compared to construct A (median OD 0.940 vs 3.13, $p< 0.0001$) and reactivity towards construct G varied between patients (median OD=2.285 [1.057-3.109]). There was no reactivity towards the RIG-I protein (0/29). After depleting antibodies that target Hel1 (or Hel2i), the reactivity towards Hel2i and Hel2 (or resp. Hel1 and Hel2) persisted.

Conclusion: Anti-MDA5 autoantibodies in plasma of dermatomyositis patients mainly target the helicase domains of the MDA5 protein. Our depletion experiments suggest that patients can have specific autoantibodies towards each

helicase domain, which implies that multiple epitopes are present on the MDA5 protein. The absence of reactivity towards construct B possibly suggests the structure of the autoantigen might differ from the endogenous MDA5 protein, but further experiments are necessary. The potential usage of anti-MDA5 reactivity as a biomarker for RPILD will be explored in an extended cohort.

Reference

(1) Ossipova E, Cerqueira CF, Reed E, Kharlamova N, Israelsson L, Holmdahl R, et al. Affinity purified anti-citrullinated protein/peptide antibodies target antigens expressed in the rheumatoid joint. Arthritis Res Ther. 2014;16(4).

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Abstract Number: 0714

Diagnostic Accuracy of Electromyogram for Myositis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The skeletal muscle biopsy is the gold standard for idiopathic **i**nflammatory myopathies (IIM) diagnosis. Myositis specific antibodies are diagnostic biomarkers for IIM but are present in only 60-70% of cases. Another non-invasive procedure: the electromyogram (EMG) maybe useful for IIM diagnosis but its diagnostic accuracy has been poorly investigated.

We aim to define the sensitivity, the specificity, and the positive and negative predictive values of EMG for IIM diagnosis.

Methods: We conducted a single-center retrospective study between January 2018 and October 2020. We selected all consecutive patients referred to the neuropathology department for a suspicion of IIM. Patients were enrolled if an EMG was performed in our department before the muscle biopsy.

Patients were diagnosed as IIM based on myopathological finding. Patients were subclassified into dermatomyositis (DM), anti-synthetase syndrome (ASyS), overlap myositis (OM), immune mediated necrotizing myopathy (IMNM), Inclusion body myositis (IBM) and immune checkpoint inhibitor induced myositis (ICI) based on ENMC criteria.

Results: Two hundred and thirty-one patients were screened and 182 patients were included. Patients were 57.8 ± 15.8 years and 62.6% were female.

	DM	ASyS	Overlap	IMNM	IBM	ICI myositis
N	30	16	47	20	27	17
Age	53.2 ± 19.2	53.1 ± 13.5	51.2 ± 14.4	61.3 ± 16.1	68.3 ± 83	70.1 ± 11.6
Female	21 (70)	15 (93.8)	29 (61.7)	9 (45)	16 (59.3)	5 (29.4)
Clinical finding						
Motor deficit	24	12 (75)	33 (70.2)	19 (95)	26 (96.3)	12 (70.6)
Cutaneous involvement	29	13 (81.3)	32 (68.1)	0	0	0
Interstitial disease	1	13 (81.3)	14 (29.8)	0	0	0
Arthritis/arthralgias	3	12 (75)	21 (44.7)	0	0	0
Biological Finding						
CK level	1886 ± 3042	4465 ± 4264	1495 ± 2511	6027 ± 5428	547 ± 663	2325 ± 2446
SMA	18 (60)	15 (93.8)	0	8 (40)	0	0
MAA	1 (3.3)	10 (62.5)	40 (85.1)	2 (10)	0	3
Muscle biopsy finding						
Atrophy	28 (93.3)	16 (100)	45 (95.7)	20 (100)	27 (100)	14 (82.4)
Necrosis/regeneration	22 (73.3)	14 (87.5)	39 (83.0)	19 (95)	26 (96.3)	14 (82.4)
Vacuolar change	14 (46.7)	1 (6.3)	9 (19.1)	5 (25)	19 (70.4)	0
HLA 1	28 (93.3)	16 (100)	46 (97.9)	16 (80)	27 (100)	17 (100)
Inflammation	24 (80)	12 (75)	42 (89.4)	7 (35)	27 (100)	16 (94.1)
Needle myography finding						
Fibrillation	9 (30)	8 (50)	18 (38.3)	15 (75)	12 (44.4)	3 (17.6)
PM discharge	3 (10)	3 (18.8)	4 (8.5)	4 (20)	4 (14.8)	0
Short MUP	27 (90)	15 (93.8)	40 (85.1)	19 (95)	23 (85.2)	5 (29.4)

EMG was described as myogenic in 74.1% of cases. Patients were diagnosed as IIM in 86.2% of cases.

The sensitivity was 82.2%, and the specificity was 76%. The positive likelihood ratio was 3.4. The positive predictive value was 95.6% and the negative predictive value 40.4%.

The presence of EMG abnormality was highly dependent on the IIM subgroup. The sensitivity was high in DM (90%), ASyS (93.8%) and IMNM (95%). The sensitivity also high in sIBM (85.2%) and in OM (85.1%) but low in ICI myositis (29.4%) (Table1).

Statistical analysis showed that factors associated with a false negative EMG (patients; n=28) were the use of corticosteroids prior to EMG (21.7% vs 46.4% p=0.01) and the absence of myositis specific antibody (68% vs. 88.9% p=0.03).

Conclusion: EMG was sensitive and specific for IIM diagnosis but its accuracy decrease with the use corticosteroids.

Disclosure: L. bolko, None; **S. Leonard Louis**, None; **J. Salmon**, None; **O. Benveniste**, None; **Y. Allenbach**, None; **T. Maisonobe**, None.

Abstract Number: 0715

High-Dimensional Analysis Reveals Abnormal B Cell Subsets Associated with Specific Changes to Circulating T and Myeloid Cell Populations in Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

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Session Time: 8:30AM–10:30AM

Background/Purpose: The idiopathic inflammatory myopathies (IIM) are a clinically heterogeneous group of conditions affecting the skin, muscle, joint, and lung in various combinations. This study aims to investigate the immunologic heterogeneity through detailed immunophenotyping of peripheral blood mononuclear cells (PBMCs) in IIM patients and healthy controls.

Methods: We collected PBMCs from 17 patients with a clinical diagnosis of inflammatory myositis in the inpatient or outpatient setting and 18 healthy controls. Immunophenotyping was performed using mass cytometry by time of flight (CyTOF) to simultaneously characterize B, T, and myeloid cell subsets. Data were analyzed using a combination of supervised biaxial gating and unsupervised clustering algorithms including t-distributed stochastic neighbor em-

Table 1. Patient Demographics

	IIM Patients (n=17)	Healthy Controls (n=18)
Average Age	56.8 ± 11.7	46.4 ± 11.7
Female Gender	8 (44.4%)	14 (82%)
Race		
Caucasian	13 (76.4%)	16 (88.8%)
African American	4 (23.5%)	1 (5.6%)
Other	0 (0%)	1 (5.6%)
Average Disease Duration in yrs (median, IQR)	0.9 (0.7,1.3)	
Clinical Categorization		
Dermatomyositis	6 (35.3%)	
Polymyositis	4 (23.5%)	
Anti-synthetase syndrome	7 (41.2%)	
Interstitial Lung Disease	14 (82.3%)	
Average %FVC (n=11)	56.9 ± 11.9%	
Average %DLCO (n=9)	49.1 ± 15.1%	
Supplemental oxygen use at enrollment	6 (42.9%)	
History of elevated creatinine kinase	9 (52.9%)	
Serologic Status		
+ANA	8 (47.0%)	
+Rheumatoid factor (n=14)	5 (35.6%)	
+Ro52	6 (35.3%)	
+Myositis specific or associated autoantibody	16 (94.1%)	
Probable or definite idiopathic inflammatory myositis according to 2017 classification criteria [53]	11 (64.7%)	

Data reported as mean ± standard deviation unless otherwise noted.
Abbreviations: FVC = forced vital capacity, DLCO = diffusing capacity of the lung for carbon monoxide, ANA = anti-nuclear antibodies,

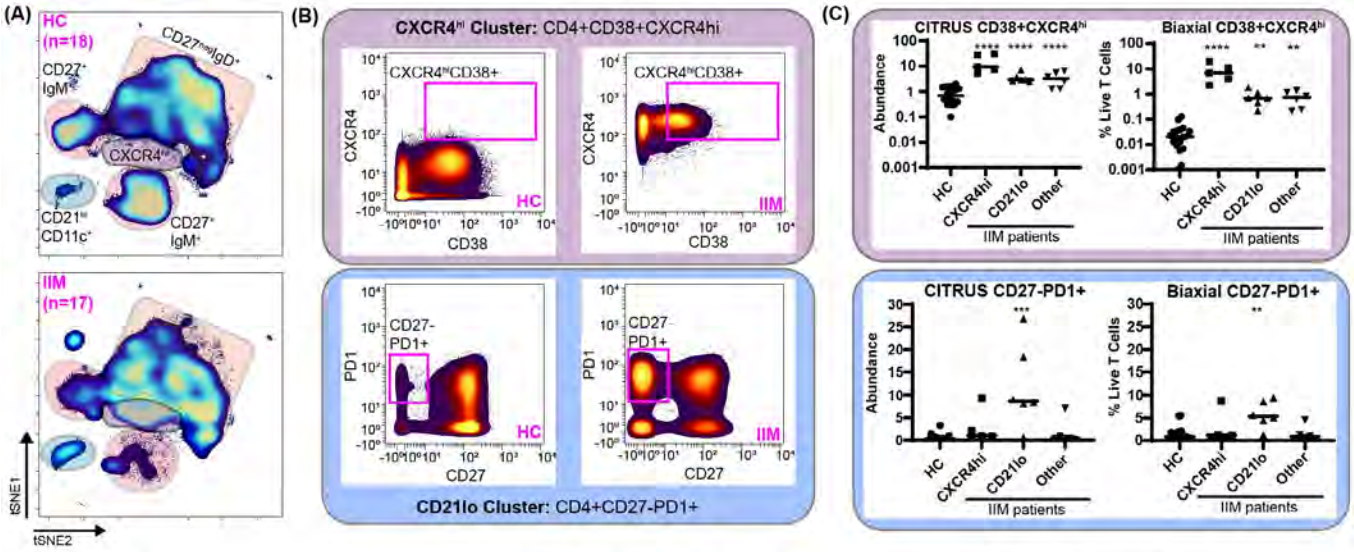

Figure 1. Preliminary immunophenotypes in the idiopathic inflammatory myopathies (IIM). (A) Density contour tSNE maps of concatenated CD19+ cells from healthy controls (HC) and IIM patients showing the increased CXCR4hi and CD21lo islands in IIM compared to healthy controls. (B) Biaxial flow cytometry plots of the CITRUS identified CD38+CXCR4hi and CD27-PD1+ CD4+T cell clusters. (C) CITRUS determined abundance and corresponding biaxial gating frequency for both the T cell clusters stratified by their B cell immunophenotype.

bedding (tSNE), cluster identification, characterization, and regression (CITRUS), and marker enrichment modeling (MEM).

Results: Patient demographics are shown in Table 1. We identified two distinct immune signatures amongst IIM patients (Figure 1). In one signature, increased CD19+CXCR4hiCCR7hi cells correlated with increased CD3+CXCR4hiCD38hi (Spearman r=0.62, p=0.009) and CD14+CD16-CXCR4+CD38+HLADR- (Spearman r=0.61, p=0.01) populations. Three out of five patients with a significant CD19+CXCR4hiCCR7hi island were critically ill with respiratory failure, a fourth was admitted with inability to swallow. In the second signature, increased CD19+CD21loCD11c+ cells correlated with an increased CD3+CD4+PD1+ (Spearman r=0.60, p=0.01) population. Of the six patients with a dominant CD19+CD21loCD11c+ island, four were Pm/Scl positive.

Conclusion: Based on circulating B cell phenotype, we identified two distinct immunologic signatures in IIM patients. Future work is needed to determine the significance of these immune signatures for clinical manifestations and treatment responses.

Disclosure: E. Wilfong, Boehringer-Ingelheim, 1, 5; **T. Bartkowiak**, None; **K. Vowell**, GSK, 3; **C. Westlake**, None; **J. Irish**, Incyte Corporation, 5, Janssen, 5, Pharmacyclics, 5, Kadmon, 5, Fluidigm, 12, Center of Excellence Agreement via Vanerbilt's Mass Cytometry Center of Excellence Core, Cytobank, 4, 11; **P. Kendall**, None; **L. Crofford**, Boehringer-Ingelheim, 5, UpToDate, 9; **R. Bonami**, Boehringer-Ingelheim, 5.

Abstract Number: 0716

Marked Capillary Basement Membrane Reduplication Is the Hallmark Histopathological Feature of Scleromyositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Scleromyositis (SM) is an emerging subset of autoimmune myositis (AIM) in patients with features of systemic sclerosis (SSc). SM patients may present without characteristic SSc skin thickening and without known SSc autoantibodies. We previously reported that SM was characterized by marked capillary basement membrane (BM) reduplication, even in patients with mild SSc features. The objective of this study was to confirm this histopathological finding in an independent cohort.

Methods: A standardized review of an independent cohort of SM cases and AIM controls was performed by 2 reviewers. In the absence of a gold standard, SM cases were selected based on clinicoserological features by a consensus of ≥2 experts. All stains recommended by the European NeuroMuscular Center (ENMC) for histopathological assessment of inflammatory muscle biopsy were performed. Muscle biopsies from SM cases and AIM controls were categorized using the ENMC criteria. Collagen IV immunofluorescence was performed to assess endomysial capillary abnormalities (dropout and/or mural thickening and/or luminal dilation) and electron microscopy to examine capillaries for BM reduplication (mild, 2-3 layers; marked, ≥4 layers).

Results: Twenty-four SM cases and 17 AIM controls (4 dermatomyositis (DM), 5 anti-HMGCR+ immune-mediated necrotizing myopathy (IMNM), 5 inclusion body myositis (IBM) and 3 antisynthetase syndrome) were reviewed. SM cases were predominantly females (63%) and mean age at diagnosis was 58 years (range, 27-81). Proximal muscle weakness was present in 74% of SM cases and mean CK level was 2561 IU/L (range, 180-9239). Eighty-three percent (19/23) of SM cases fulfilled the ACR/EULAR SSc criteria at the time of myositis diagnosis. SSc features supporting the diagnosis of SM in the 4 remaining cases included: Raynaud's phenomenon (n=4), positive ANAs and/or SSc-associated autoantibodies (n=3), SSc-type nailfold capillaroscopy (n=3), interstitial lung disease (n=2) and puffy fingers (n=1). Using the ENMC criteria, SM cases were mainly categorized as IMNM (54%), non-specific myopathic changes (17%), non-specific myositis (13%), unclassifiable (8%), IBM (4%) or polymyositis (4%). When using complementary techniques for capillary assessment, immunofluorescence identified abnormal capillaries in 95% (20/21) of SM cases vs 56% (5/9) of controls (p=0.0195), and electron microscopy demonstrated capillary BM reduplication in 83% of SM cases vs 35% of controls (p=0.0028). This difference in BM reduplication between SM and controls was even higher when only marked BM reduplication (≥4 layers) was considered (71% of SM vs 12% of controls,

p=0.0003). In SM patients who did not fulfill the ACR/EULAR criteria for SSc, 100% (4/4) showed BM reduplication; and in SM patients without known SSc autoantibodies, 83% (5/6) showed BM reduplication.

Conclusion: In this validation study, we confirmed that marked BM reduplication is the hallmark histopathological feature of SM. Ultrastructural evaluation of muscle capillaries is useful to support an accurate diagnosis of SM.

Disclosure: B. Ellezam, None; **Y. Troyanov**, None; **V. Leclair**, None; **I. Bersali**, None; **M. Giannini**, None; **S. Hoa**, None; **J. Bourré-Tessier**, None; **M. Satoh**, None; **M. Fritzler**, Inova Diagnostics Inc., 2, 6, Werfen International, 2, Alexion Canada, 6, Mitogen Diagnostics Corp., 3, 8, 9, 10; **B. Lannes**, None; **J. Senécal**, None; **M. Hudson**, None; **A. Meyer**, None; **O. Landon-Cardinal**, None.

Abstract Number: 0717

Association of Fatigue with Disease Activity in Myositis

Tissa Bijoy George[1], Anjana Chandrasekhara Pillai[2], Siamak Moghadam-Kia[3], Nicole Neiman[4], Dana Ascherman[3], Chester Oddis[3], Dianxu Ren[4] and Rohit Aggarwal[3], [1]UPMC McKeesport, Monroeville, PA, [2]UPMC, Pittsburgh, PA, [3]University of Pittsburgh, Pittsburgh, PA, [4]University of Pittsburgh Medical Center, Pittsburgh, PA

SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: The Idiopathic inflammatory myopathies are a heterogeneous group of rare systemic autoimmune diseases with muscle as the primary target. Fatigue is one of the most common and prominent symptoms reported by myositis patients. Activities of daily living are frequently affected by fatigue. In this study, we investigated the cross-sectional and longitudinal association of fatigue in myositis with established clinical outcome measures.

Methods: Myositis patients [Dermatomyositis (DM), necrotizing myopathy (NM), Polymyositis(PM), and anti-synthetase syndrome (AS)] evaluated at the University of Pittsburgh Myositis Center were prospectively enrolled. Patients with active disease (defined as the escalation of immunosuppressive therapy in the previous 6 months) and inactive disease were assessed at 0, 3, and 6 months. At each of these visits, myositis core set measures (CSMs) [muscle enzymes, manual muscle testing (MMT), patient and physician global disease activity, extra-muscular disease activity, and HAQ], task-oriented functional measures [Timed up and go (TUG), Sit to Stand (STS), 6 Minute Walk Distance (6-MWD)], and patient-reported outcomes [Patient-Reported Outcomes Measurement Information System-physical function (PROMIS-PF), Short Form- 36 (SF-36) physical and mental component summary (PCS, MCS)] were evaluated. Fatigue was evaluated using the vitality domain (energy/fatigue) of the SF-36 and a 10 cm Visual Analog Scale (VAS) for fatigue (mild 0-3; moderate 3-7; severe 7-10). The phenotypic and disease activity measures of the cohort were correlated with fatigue measures using Spearman at the baseline visit. Longitudinal changes were associated with clinical improvement (per 2016 ACR/EULAR myositis response criteria) as well as physician and patient global assessment of change using the Chi-square test.

Results: Fifty patients [mean age, 51.6 (±14.9); 60% females] were studied: 6 PM, 24 DM, 9 NM, and 11 AS (without clinical myositis). The mean (SD) severity of fatigue (0-10) was 4.2 (3), with most patients having moderate (51%) or severe (16%) fatigue at baseline. No difference was observed with respect to gender, disease subtypes (DM, non-DM), or age at enrollment. However, at baseline, fatigue (both VAS and SF-36 domain) was significantly associated with active myositis and having muscle weakness. Fatigue measures showed moderate to strong correlation with several

Table 1. Baseline association of fatigue (VAS and SF-36) with various disease activity, muscle strength, functional and laboratory measures

	Fatigue VAS		SF-36 Fatigue	
	Rho	p-value	Rho	p-value
Disease activity measures				
Cutaneous disease activity	-0.08	0.54	-0.04	0.78
Pulmonary disease activity	0.13	0.33	-0.14	0.33
Extra-muscular global disease activity*	0.22	0.11	-0.34	0.01
Muscle disease activity	0.40	0.004	-0.49	0.0005
MD Global disease activity*	0.44	0.001	-0.53	0.0001
Patient Global disease activity*	0.61	<0.0001	-0.67	<0.0001
Muscle enzymes*	0.36	0.009	-0.20	0.17
Pain measure				
VAS	0.70	<0.0001	-0.68	<0.0001
Muscle strength measure				
MMT-9*	-0.37	0.007	0.45	0.0013
Physical function measures				
PROMIS-PF theta score	-0.63	<0.0001	0.77	<0.0001
HAQ-DI*	0.59	<0.0001	-0.72	<0.0001
SF 36 PCS	-0.52	<0.0002	0.67	<0.0001
Mental health measure				
SF 36 MCS	-0.34	0.017	0.40	0.004
Task-oriented functional tests				
Sit-to-stand	-0.27	0.053	0.35	0.01
Timed-up and go	0.20	0.15	-0.14	0.35
Six-minute walk distance	-0.28	0.051	0.33	0.02
Serum muscle enzymes				
Creatine phosphokinase	0.40	0.007	-0.21	0.19
Aldolase	0.55	0.001	-0.41	0.02
Alanine aminotransferase	0.25	0.10	-0.12	0.46
Aspartate aminotransferase	0.29	0.06	-0.16	0.32

***Core Set Measures**

Table 2. Association of 6-month longitudinal change in fatigue (VAS and SF-36) with 2016 ACR/EULAR response criteria, physician-reported change and patient-reported change

	ACR/EULAR Improvement			Physician reported Improvement			Patient reported Improvement		
	No (n=26)	Yes (n=13)	p value	No (n=21)	Yes (n=15)	p value	No (n=27)	Yes (n=7)	p value
Change in Fatigue VAS (mean, SD)	0.28 (2.3)	-3.20 (4.3)	0.007	-1.95 (3.9)	0.40 (2.7)	0.03	-0.68 (2.8)	0.64 (4.0)	0.26
Change in SF 36 Fatigue domain (mean, SD)	-2.70 (16.6)	27.5 (26.1)	0.004	17.33 (23.6)	-6.66 (17.6)	0.005	9.60 (22.1)	15.83 (18.5)	0.03

myositis disease activity measures including CSMs, pain, and patient-reported outcomes of physical function (table 1). Physical function measures such as PROMIS-PF, HAQ-DI, SF-36 PCS, and MCS also had a statistically strong correlation with fatigue. The longitudinal analysis over the 6-month study period suggested that fatigue improved

significantly with improvement in myositis disease activity as assessed by 2016 ACR/EULAR response criteria as well as physician and patient-reported assessment of change in disease activity.

Conclusion: Fatigue is common in myositis and has a moderate to strong correlation with disease activity measures, muscle strength, and functional outcome measures. Further, an improvement in fatigue is associated with the clinical response using the ACR/EULAR myositis response criteria.

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Abstract Number: 0718

Pain Severity and Interference in Adult Autoimmune Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Although pain is one of the most common and highest priority symptoms reported by people with autoimmune inflammatory myopathies (AIM), large descriptive studies on pain in AIM are lacking. The objective of this study was to assess the prevalence, severity, functional impact, and clinical correlates of pain in AIM.

Methods: We undertook a cross-sectional study of adult AIM subjects in a large multicenter cohort. Standardized clinical histories, medical examinations, and self-administered questionnaires were collected at baseline study visit. Severity of pain was assessed using a Numeric Rating Scale (NRS; scores ranging from 0 (no pain) to 10 (very severe pain)). Pain interference with work (including both work outside the home and housework) was measured using the Short Form 36 (SF-36) (5-point Likert scale: not at all, a little bit, moderately, quite a bit, extremely). Global and skin disease activity were rated by the study physician using a NRS ranging from 0 (no activity) to 10 (maximum severity). Physical functioning was assessed using the Health Assessment Questionnaire (HAQ; scores ranging from 0 (no disability) to 3 (severe disability)). Ordinal logistic regression models were generated to determine the association between pain severity at baseline and selected clinical predictors.

Results: The study included 143 AIM subjects (69% female, median disease duration 1.6 years and mean age at diagnosis 56 years) with dermatomyositis (DM; 33%), overlap myositis (OM; 35%), anti-synthetase syndrome (ASS; 13%), inclusion body myositis (IBM; 13%), immune-mediated necrotizing myopathy (IMNM; 5%), and polymyositis/unspecified (PM/UNS; 2%) (Table 1). At baseline, 27% of subjects had myalgia, 59% active myositis, 39% interstitial

Table 1. Baseline characteristics of the cohort

Clinical features	DM n=47	OM n=50	ASS n=18	IBM n=18	IMNM n=7	PM/UNS n=3	All n=143	Missing
Female, n (%)	38 (81)	34 (68)	11 (61)	9 (50)	5 (71)	1 (33)	98 (69)	0
Age at diagnosis, mean (SD)	52 (17)	58 (13)	52 (14)	62 (10)	60 (8)	40 (3)	56 (14)	0
Disease duration in years, median [IQR]	1.2 [0.4-2.2]	2.0 [0.7-5.0]	0.9 [0.7-1.9]	9.6 [5.5-14]	4.4 [0.9-8.1]	4.4 [3.4-4.8]	1.6 [0.7-5.1]	7
Presence myositis-specific ab, n (%)	23 (50)	0	18 (100)	0	6 (86)	0	47 (33)	10
Manual muscle testing (MMT8; 0-150), median [IQR]	148 [141-150]	147 [142-150]	150 [148-150]	141 [119-143]	147 [131-148]	150 [150-150]	148 [140-150]	17
Baseline CK levels (UI/L), mean (SD)	2670 (10600)	526 (983)	929 (1620)	630 (655)	2250 (5230)	1280 (842)	1380 (6120)	6
Myalgia†, n (%)	14 (30)	12 (24)	4 (22)	6 (33)	2 (28)	1 (33)	39 (27)	1
Myositis†, n (%)	24 (51)	32 (64)	7 (39)	14 (78)	6 (86)	2 (67)	85 (59)	1
Dysphagia†, n (%)	17 (37)	14 (29)	4 (22)	8 (44)	2 (29)	0	45 (31)	1
Interstitial lung disease, n (%)	15 (32)	23 (46)	16 (89)	1 (6)	1 (14)	0	56 (39)	0
Arthritis†, n (%)	5 (11)	7 (14)	4 (22)	0	1 (14)	0	17 (12)	1
Raynaud's phenomenon, n (%)	11 (23)	30 (60)	5 (28)	0	1 (14)	1 (33)	48 (34)	1
Skin disease activity (NRS 0-10), mean (SD)	2.4 (1.8)	0.6 (1)	0.9 (1.2)	0	0	0	1.1 (1.6)	0
Global disease activity (NRS 0-10), mean (SD)	3.0 (2.3)	2.7 (1.8)	2.6 (2.1)	1.8 (0.9)	3.4 (2.1)	2 (2.7)	2.7 (2.0)	0
Health assessment questionnaire (HAQ; 0-3), median [IQR]	0.8 [0.1-1.6]	1.5 [0.4-1.9]	0.6 [0.1-0.9]	1.6 [1.1-2.5]	1.5 [0.2-2.2]	0 [0-0.4]	1 [0.3-1.9]	11

DM, dermatomyositis; OM, overlap myositis; ASS, anti-synthetase syndrome; IBM, inclusion body myositis; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis; UNS, unspecified; CK, creatine kinase; ab, autoantibodies; NRS, numerical rating scale; SD, standard deviation; IQR, interquantile range.
†Present at time of baseline visit as per Myosiits Disease Activity Assessment Tool (MDAAT).

lung disease, 12% arthritis and 34% Raynaud's phenomenon (Table 1). At baseline, mean (SD) skin activity was 1.1 (1.6), and mean (SD) global disease activity 2.7 (2.0). Mean (SD) creatine kinase (CK) was 1380 UI/L (6120). Median (IQR) HAQ score was 1 (0.3-1.9) indicating moderate functional disability.

Median (IQR) pain severity was 3 (1-7), with 64% of subjects reporting some level of pain (13% severe, 21% moderate, 30% mild pain) (Table 2). Pain interference with work affected 73% of patients (10% extremely, 27% moderately, 16% quite a bit, 20% a little bit). Among the AIM subsets, a higher percentage of patients with DM, OM, and ASS reported severe pain compared to other subsets. The IBM subjects reported more severe pain interference than in any other subset.

Univariate and multivariate logistic ordinal regressions showed statistically significant associations of baseline pain severity with age at diagnosis and arthritis (Table 3). After adjustment, patients with arthritis were almost 3 times more likely to report higher pain level than those without (OR [95%CI] 2.77 [1.04-7.48], p-value 0.04). By contrast, for every one-year increase in age at diagnosis, the odds of having pain decreased by 4% (OR [95%CI] 0.96 [0.94-0.99], p-value 0.008).

Table 2. Pain severity and interference with work at baseline

	DM n=47	OM n=50	ASS n=18	IBM n=18	IMNM n=7	PM/UNS n=3	All n=143
Pain severity, n (%)							
No pain (NRS 0)	16 (34)	20 (40)	6 (33)	7 (39)	2 (30)	1 (33)	52 (36)
Mild (NRS 1-4)	14 (30)	14 (28)	6 (33)	5 (28)	3 (43)	1 (33)	43 (30)
Moderate (NRS 5-7)	10 (21)	8 (16)	4 (22)	5 (28)	2 (29)	1 (33)	30 (21)
Severe (NRS 8-10)	7 (15)	8 (16)	2 (11)	1 (6)	0	0	18 (13)
Pain interference, n (%)							
Not at all	11 (23)	13 (26)	5 (28)	2 (11)	2 (29)	2 (67)	35 (25)
A little bit	6 (13)	12 (24)	4 (22)	4 (22)	2 (29)	0	28 (20)
Quite a bit	9 (19)	9 (18)	3 (17)	2 (11)	0	0	23 (16)
Moderately	13 (28)	8 (16)	5 (28)	10 (56)	1 (14)	1 (33)	38 (27)
Extremely	5 (11)	6 (12)	1 (6)	0	2 (29)	0	14 (10)
Missing	3 (6)	2 (4)	0	0	0	0	5 (4)

DM, dermatomyositis; OM, overlap myositis; ASS, anti-synthetase syndrome; IBM, inclusion body myositis; IMNM, immune-mediated necrotizing myopathy; PM, polymyositis; UNS, unspecified

Table 3. Predictors of pain severity at baseline

Variables	Univariate OR [95% CI]	Multivariate OR [95% CI]
Age at diagnosis	0.96 [0.95-0.99]**	0.96 [0.94-0.99]**
Female	1.37 [0.74-2.57]	1.10 [0.54-2.24]
Disease duration	0.94 [0.88-1.00]	0.92 [0.85-1.00]
Subset†		
Overlap myositis	0.83 [0.40-1.70]	0.92 [0.38-2.17]
Anti-synthetase syndrome	0.86 [0.33-2.20]	0.93 [0.34-2.47]
Immune-mediated necrotizing myopathy	0.76 [0.19-2.90]	2.06 [0.34-12.1]
Inclusion body myositis	0.76 [0.29-2.00]	2.67 [0.74-9.84]
Polymyositis/Unspecified	0.64 [0.08-4.46]	0.54 [0.05-4.17]
Baseline CK level††	1.14 [0.92-1.35]	1.14 [0.92-1.41]
Arthritis	3.39 [1.41-8.28]**	2.77 [1.04-7.48]*
Raynaud	1.25 [0.68-2.33]	1.64 [0.77-3.5]

Lipsitz test: LR statistic = 18.68, df = 10, p-value = 0.04453
*p <0.05,**p <0.01
†compared to DM
††creatine kinase (CK) values were log transformed

Conclusion: Pain is highly prevalent in adult AIM and interferes with work in 73% of subjects. Further research on correlates and trajectories of pain are urgently needed to inform effective management of pain in AIM.

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Abstract Number: 0719

Increased Risk of Venous Thromboembolism in Adult Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

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Background/Purpose: Idiopathic inflammatory myopathies (IIMs) patients have a higher risk of venous thromboembolism (VTE) [1]. We aimed to assess the incidence of thrombosis and associated factors in IIMs patients.

Methods: 93 IIMs patients (44 dermatomyositis and 49 polymyositis) were retrospectively reviewed to identify patients who had experienced a thrombosis during the follow-up period. The patients' clinical characteristics, association with cancer, presence of thrombophilia, APSL autoantibodies, and intravenous immunoglobulin (IVIG) therapy were systematically analysed.

Results: 93 cases with IIMs (64.5% female) were followed median 27.6 (IQR:11.6-75.4) months. The incidence of a thrombotic event in the total cohort was 8.6%. Median time to development of venous thromboembolism was 4 (IQR:1-28,75) months and 75% of the thrombotic events developed during the first year after IIM diagnosis (Table). Venous thromboembolism was not associated with age, sex, cancer or IVIG therapy.

Conclusion: The prevalence of thrombotic events was 8.6% in our cohort and the risk of VTE is highest in the first year of disease. Further studies are needed to identify high-risk patients and to test the role of thromboprophylaxis.

Table. Patients with polymyositis/dermatomyositis and venous thromboembolism

Patient	Diagnosis/ Onset age, years	Time from diagnosis to first thrombotic event, months	VTE	Malignancy	Thrombophilia	APSL autoantibodies
1	PM/35	6	Sinus thrombosis	No	Negative	Negative
2	PM/57	2	DVT	No	Not available	Negative
3	PM/67	0	Massive PE	No	Not available	Negative
4	PM/55	1	DVT/PE	No	Negative	Negative
5	DM/47	1	Iliac vein	No	Negative	Negative
6	PM/56	36	Portal vein	Breast	Not available	Negative
7	DM/63	7	Right cephalic vein, external iliac vein, vena saphena magna	Breast	Not available	Not available
8	PM/61	50	Popliteal vein	No	Negative	Negative

Abbreviatoins: PM: Polymyosisits; DM:Dermatomyositis; VTE: venous thrombosis; DVT: Deep vein thrombosis; PE: Pulmonary embolism,; Thrombophilia: include Factor V Leiden and prothrombin gene mutation; MTHFR gene mutation, homocysteine, antithrombin, Protein C, Protein S and Factor VIII, APSL: antiphospholipid

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Abstract Number: 0720

The Clinical Significance of anti-PC4 and SFRS1 Interacting Protein 1 Antibody in Polymyositis and Dermatomyositis Patients

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SESSION INFORMATION
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Background/Purpose: Many kinds of myositis specific autoantibodies are detected in sera from polymyositis (PM) and dermatomyositis (DM). Screening for autoantibodies is essential in the diagnostic workup of systemic autoimmune rheumatic diseases (SARD). It is noteworthy that recent reports suggest anti- PC4 And SFRS1 Interacting Protein 1 (PSIP1) are more prevalent in healthy individuals compared to SARD, especially systemic lupus erythematosus. However, it is still unclear its significance in PM/DM. Thus, we investigated the frequency of anti-PSIP1 Ab and the clinical features in PM/DM.

Methods: Adult Japanese PM/DM (N=87), SLE (N=17) patients who were treated at Tokai University hospital from 2012 to 2020 and healthy controls/non-SARD (N=41) were enrolled. Anti-ARS, SRP Ab were screened by RNA-immunoprecipitation and anti-MDA5, anti-TIF-1 Ab were detected by immunoprecipitation with [^{35}S]methionine-labeled HeLa cells. anti-PSIP1 Ab and anti-MDA5 Ab titers were measured using enzyme-linked immunoabsorbent assay (ELISA). Clinical data was retrospectively collected.

Results: The frequency of anti-PSIP1 Ab was 27.6% (24/87) in PM/DM, 7.3% (3/41) in healthy controls/non-SARD and 11.8% (2/17) in SLE.

Of note, the prevalence of anti-PSIP1 Ab was significantly higher in PM/DM compared to healthy control/non-SARD and SLE ($p < 0.05$). The prevalence of anti-PSIP1 Ab in PM/DM patients with anti-ARS, SRP, TIF1-γ and MDA5 Ab were 35.7% (10/28), 11.1% (1/9), 40% (4/10) and 22.5% (9/40), respectively. Among anti-ARS Ab positive PM/DM, none of anti-OJ (0/5) or anti-PL-7 (0/5) were positive for anti-PSIP1, while 66.7% (4/6) of anti-Jo-1 and 50% (6/12) of anti-PL-12 were. In addition, the change of anti-PSIP1 Ab titers were seemed to be correlated with those of anti-MDA5 Ab in the disease course.

Conclusion: In our study, anti-PSIP1 Ab was frequently detected in PM/DM, compared to healthy control/non-SARD and SLE. In addition, measurement of anti-PSIP1 Ab titers may be an indicator of disease activity in DM with anti-MDA5 Ab.

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Abstract Number: 0721

Timed Function Tests as Measures of Disease Activity and Functional Outcome in Inflammatory Myositis

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SESSION INFORMATION
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Background/Purpose: Manual muscle testing (MMT) and Functional index 2(FI-2) are the usual methods in assessing disease activity and functional status in IIM[1]. Limitations of MMT8 include low sensitivity to change and floor/ceiling effect[2] .FI-2 takes a longer time to administer. Several Timed function tests (TFTs) namely 2-minute walk test (2MWT), 30s raise from a chair test and 30s 1kg arm rise test have potential to measure both these aspects[2] and needs to be evaluated in IIM.

Our objective was to evaluate the performance of TFT in assessing muscle diseases at baseline and to evaluate the performance of TFTs to detect the longitudinal change in muscle power and endurance at 3 and 6 months.

Methods: This was an observational cohort study which included 42 patients with polymyositis and dermatomyositis satisfying EULAR/ACR classification criteria. MMT8, FI-2, FI-3 and TFTs were done at baseline, 3 months and 6 months. Individuals with a stable MMT-8 over last 1 month with no evidence of extra muscular disease activity were classified as inactive and the others as active disease.

Table 1. Mean MMT8, F-2, FI-3, and Timed function tests in active and inactive disease groups at baseline, 3 months, and 6 months

	Baseline (n=42)		3 months (n=42)		6 months (n=39)	
	Active disease (n=18)	Inactive disease (n=24)	Active disease (n=16)	Inactive disease (n=23)	Active disease (n=18)	Inactive disease (n=24)
Mean MMT8	62.6 ± 14.19	73 ± 2.2	69.7 ±8.6	75.1 ± 1.6	73.8 ±7.5	75.8 ± 2.1
Mean Fi-2	3.48±2.53	5.85±2.4	6.85±1.8	7.5±2.6	8.6 ± 2.3	7.8 ± 1.9
Mean Fi-3	1.24±0.53	3.65±1.4	2.8±0.84	3.8±0.62	3.6 ± 0.4	3.8 ± 1.2
Mean 30s rise from chair test	12±7.2	15±4.5	14.8±6.9	16±4.7	18 ± 5.4	17.3 ± 4
Mean 30s 1kg arm rise test	14.3±8.2	17±5.7	17.5±7.3	18.6±5.9	22.1 ± 4	20.1 ± 3
Mean 2MWD	82±5.1	128±30.3	105±45.3	134±26.8	126 ± 38	137 ± 24.2

MMT8- Manual muscle testing 8, Fi- Functional index, 2MWD- 2 Minute walk distance

Table 2. Correlation between TFT and MMT8, FI-2 & FI-3 at baseline in the study population

		Total study population (n=42)	Active disease (n=18)	Inactive disease (n=24)
Correlation of MMT8 with TFTs	**30s rise form chair**	**0.709***	0.581	**0.841***
	30s1kg arm lift	**0.699***	0.574	**0.762***
	2MWD	**0.806***	**0.781***	**0.649***
Correlation of FI-2 with TFTs	**30s rise form chair**	**0.755***	**0.811***	**0.658***
	30s1kg arm lift	**0.829***	**0.801***	**0.796***
	2MWD	**0.811***	**0.790***	**0.766***
Correlation of FI-3 with TFTs	**30s rise form chair**	**0.711***	**0.657***	**0.649***
	30s1kg arm lift	**0.804***	**0.621***	**0.769***
	2MWD	**0.789***	**0.709***	**0.779***

MMT8- manual muscle testing 8, Fi- Functional index, 2MWD- 2 Minute walk distance
*indicates p value<0.05

Results: All 42 [11 (27%) polymyositis, and 31 (73%) dermatomyositis] completed three month follow-up assessment and 39 underwent evaluation at 6 months. The mean MMT8 of the total study population at 59±12, 67 ±8 and 71 ± 9 at baseline, 3 and 6 months respectively. In the active disease subgroup the MMT-8 was 62.6 ± 18, 69.7 ± 9 (n=42), 73.8 ± 9.6 (n=39)at baseline, 3 and 6 months respectively. The 3 TFTs had moderate to high correlation with MMT8 and FI-2 adn FI-3 at baseline (Table 2). The change in TFTs showed a moderate to strong correlation with the change in FI-2 as well as FI-3 among the study population at three months and six months (Table 3). Among the TFTs 2MWD had the best performance with moderate correlation with both MMT8, FI-2 and FI-3 in active disease suggesting a role in assessing both disease activity and endurance.

Conclusion: Using timed function tests can be an excellent alternative to FI-2/3 in assessing muscle endurance. 2-minute walk distance could be a better alternative to conventional muscle testing as it measures both power and endurance, is simple to perform and could be a valid patient reported outcome measure.

Table 3. Correlation of change in TFT with change in composite MMT8, FI-2 at 3 months and 6 months

		At 3 months (n=42)		At 6 months (n=39)	
		Active disease (n=18)	Inactive disease (n=24)	Active disease (n=16)	Inactive disease (n=23)
Correlation of Δ MMT8 with	**Δ30s rise form chair**	0.143	0.346	0.200	0.347
	Δ30s1kg arm lift	0.018	0.284	0.362	0.168
	Δ2MWD	**0.755***	0.313	**0.482***	**0.334**
Correlation of ΔFI-2 with	**Δ30s rise form chair**	**0.784***	**0.495***	**0.486***	**0.424***
	Δ30s1kg arm lift	**0.671***	0.107	**0.704***	0.301
	Δ2MWD	**0.834***	**0.623***	**0.808***	**0.506***
Correlation of ΔFI-3 with	**Δ30s rise form chair**	**0.774***	**0.515***	**0.516***	**0.435***
	Δ30s1kg arm lift	**0.711***	0.214	**0.654***	0.201
	Δ2MWD	**0.704***	**0.616***	**0.754***	**0.468***

MMT8- manual muscle testing 8, Fi- Functional index, 2MWD- 2 Minute walk distance
*indicates p value<0.05

Disclosure: s. dunga, None; **C. Kavadichanda**, None; **V. Negi**, None.

Abstract Number: 0722

Myostatin in Idiopathic Inflammatory Myopathies: Seric Assessment and Disease Activity

Alexandrine Mahoudeau[1], Céline Anquetil[2], Nozomu Tawara[1], Hossein Khademian[1], Damien Amelin[1], Yves Allenbach[3] and Olivier Benveniste[3], [1]Center of Research in Myology, Sorbonne University, Paris, France, [2]Center of Research in Myology, Sorbonne University - AP-HP, Pitié-Salpêtrière Hospital, Department of Clinical Immunology and Internal Medicine, Paris, France, [3]Sorbonne University - AP-HP, Pitié-Salpêtrière Hospital, Department of Clinical Immunology and Internal Medicine, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Muscle Biology, Myositis & Myopathies Poster (0683–0722)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: In Idiopathic Inflammatory Myopathies (IIM) disease activity is very difficult to assess and IIM may induce severe muscle damage, especially in immune-mediated necrotizing myopathies (IMNM). We hypothesize that myostatin, a negative regulator of muscle mass, could be a new biomarker of disease activity and/or muscle damage.

Methods: Prospective assessment of myostatin protein level in 447 IIM sera samples (dermatomyositis (DM), n=157; inclusion body myositis (IBM), n=72; immune-mediated necrotizing myopathies, n=125; anti-synthetase syndrome (ASyS), n=93) and 59 healthy donors (HD) was performed by ELISA. A gene transcript analysis was also carried out on 18 IIM muscle biopsies and 6 HD to analyze the expression of myostatin and myostatin pathway genes.

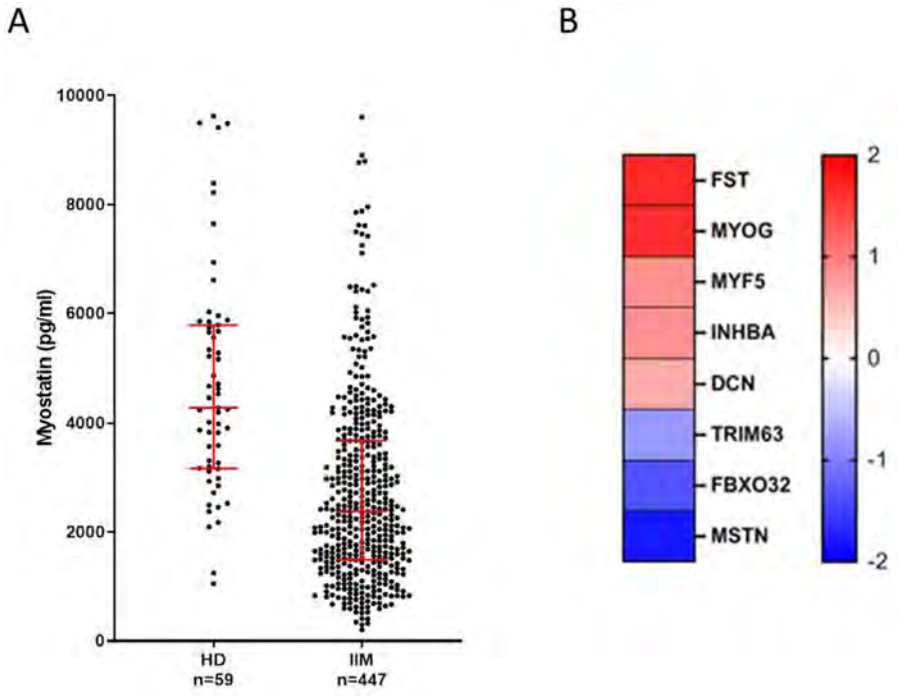


Figure 1. Quantification of circulating myostatin (A) and expression (Log2FC) of genes implicated in the myostatin pathway in IIM (B) compared to HD FST: follisatin, MYOG: myogenin, MYF5: myogenic factor 5, INHBA: inhibin A, DCN: decorin, TRIM63: Tripartite Motif Containing 63, FBXO32: F-box Protein 32, MSTN: myostatin.

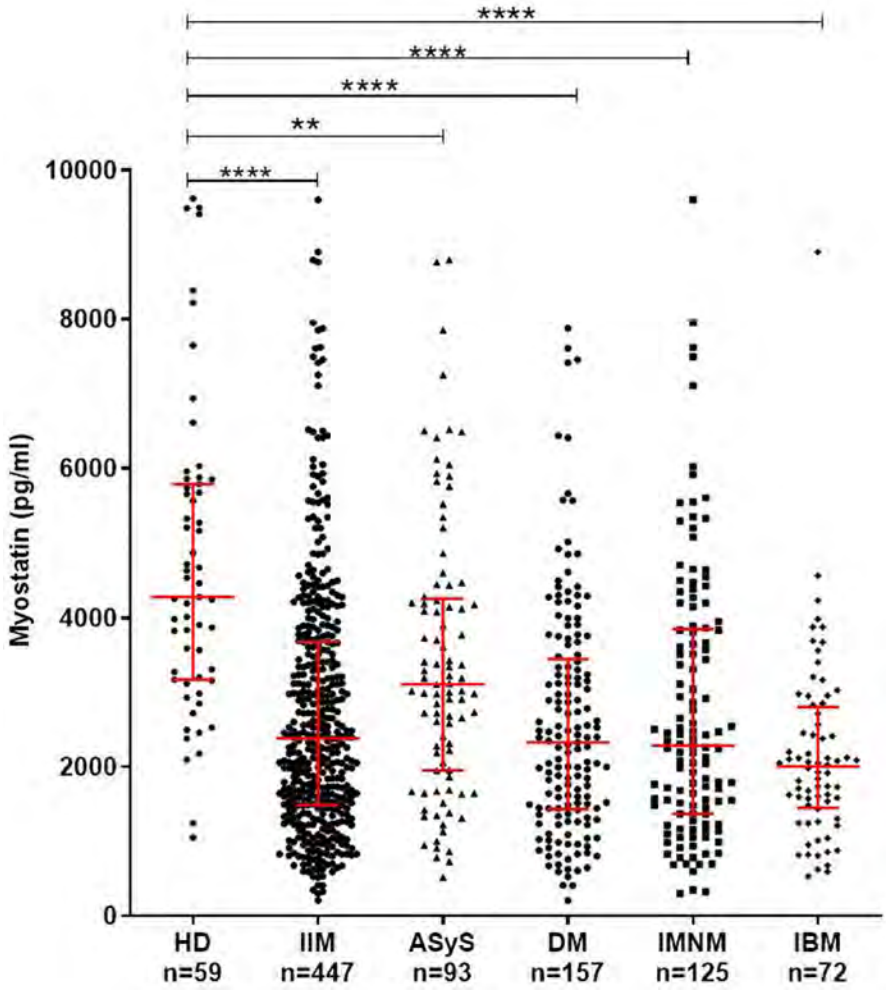


Figure 2 . Circulating myostatin levels in IIM subgroups.

Results: IIM patients had lower myostatin circulating protein levels and gene expression compared to HD (2379 [1490; 3678] pg/ml vs 4281 [3169; 5787] pg/ml; p< 0.0001 and log2FC=-1.83; p=0.0005 respectively) (Fig1). Myostatin-related genes expression varied accordingly. Myostatin circulating levels were then assessed for each subgroups. Myostatin levels were lower in ASyS (3109 [1952; 4258] pg/ml; p=0,001), DM (2327 [1431; 3446] pg/ml; p< 0.0001),

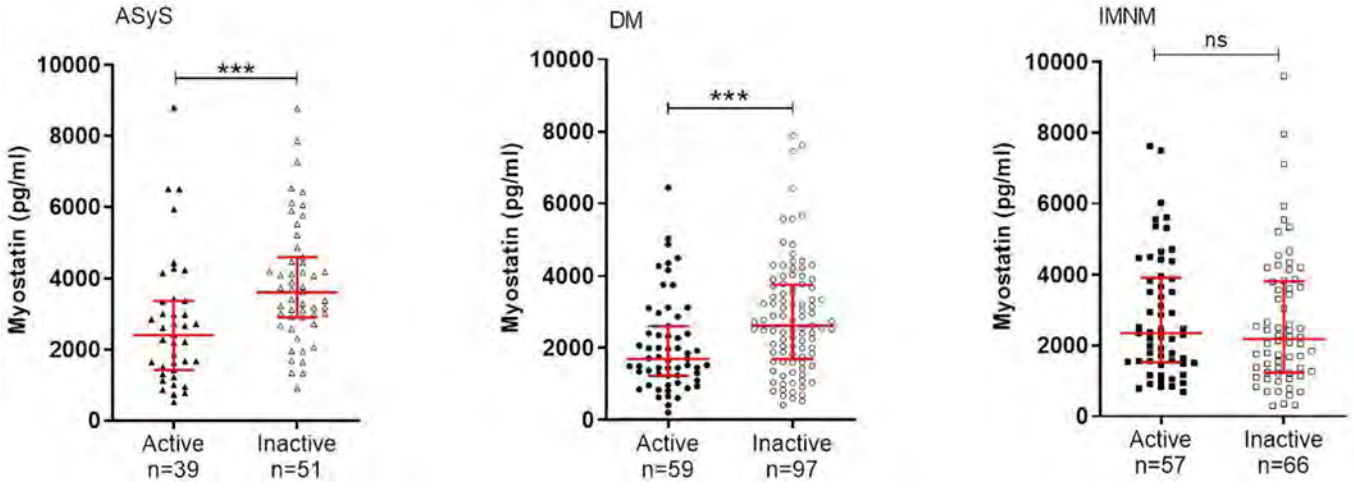


Figure 3 . Circulating myostatin levels in active vs inactive IIM patients.

IMNM (2285 [1371; 3851] pg/ml; p< 0.0001) and IBM (2005 [1449; 2803] pg/ml; p< 0.0001) compared to HD (4281 [3169; 5787] pg/ml) (Fig2). Based on the Physician Global Activity score, inactive IIM patients had higher myostatin levels than active ones. This was the case for all IIM subgroups, except IMNM patients where low myostatin levels were maintained (2186 [1235; 3815] vs 2349 [1518; 3922] pg/ml; p=0.4) even during remission (Fig3).

Conclusion: Myostatin protein and RNA levels are decreased in all IIM patients and circulating protein levels are correlated with disease activity. Inactive ASyS and DM patients have higher level of myostatin than active patients. Myostatin could be a marker of disease activity in these two subgroups. However, IMNM patients do not have a significant increase in myostatin levels after disease remission. This observation may highlight a new pathological disease mechanism in IMNM patients.

Disclosure: A. Mahoudeau, None; **C. Anquetil**, None; **N. Tawara**, None; **H. Khademian**, None; **D. Amelin**, None; **Y. Allenbach**, None; **O. Benveniste**, None.

Abstract Number: 0723

Size of Regression to the Mean in First-Line Interventions for Osteoarthritis: An Illusion of Effectiveness

Martin Englund and Aleksandra Turkiewicz, Lund University, Lund, Sweden

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Persons who seek treatment for osteoarthritis (OA) are likely doing so when experiencing a flare-up in pain. Due to natural fluctuation of pain, this will lead to regression to the mean (RTM), i.e. on average less pain at follow-up. In contrast to placebo response, RTM is deceiving as it constitutes *no* treatment response. Using reported results from two nation-wide exercise and education interventions, we estimated the size of the reported average improvement that could be attributable to RTM.

Methods: From the annual reports 2019, we retrieved average pain levels and reported improvement for knee OA patients enrolled in the Good Life with osteoArthritis in Denmark (GLA:D®) and Better Care for OA (BOA), Sweden. Both programs are similar first-line exercise and education programs for patients with OA.

To estimate mean levels of pain in subjects with symptomatic knee OA, i.e. the underlying population of GLA:D® and BOA, we used cohort data from the Osteoarthritis Initiative (OAI), USA, and the Malmoe OA study (MOA), Sweden. From OAI we included subjects with radiographic knee OA at baseline, 12 or 24 months, who reported knee pain, aching or stiffness on most days of at least one month the past 12 months at the baseline visit. MOA consisted of two parts: First, subjects responded to a postal questionnaire. Later, they had a clinic visit when knee X-rays were obtained. We included subjects who had signs of OA on X-rays and reported knee pain in the postal questionnaire. For OAI, we report pain values at both 12 and 24 months, and for MOA we report pain assessed at the clinic visit.

We used OAI data to estimate variability in pain over time, i.e. we determined the intra-class correlation coefficient (ICC) of two measurements (Table 1). To estimate the size of RTM expected in GLA:D®/BOA, we used a known formula: (1 - ICC)*($mean^{Pop}$ – $mean^{Int}$), where $mean^{Pop}$ is mean pain in the underlying population and $mean^{Int}$ is mean pain

Table 1. Standard deviation (SD) and intra-class correlation coefficient (ICC) of NRS pain over 12 months in OAI participants with radiographic knee OA (Kellgren Lawrence grade =2) and reporting knee pain, aching or stiffness on most days of at least one month the past 12 months knee pain on at least one follow-up between baseline and 48 months.

	NRS pain		
Visits	Between subjects, SD	Within subjects, SD	ICC (95%CI)*
12 months & 24 months	1.9	2.0	0.49 (0.46, 0.53)
36 months & 48 months	2.1	1.9	0.56 (0.52, 0.59)

*Based on these results, in RTM estimation using bootstrapping we sampled ICC from normal distribution with mean of 0.53 and standard deviation of 0.02.

in the intervention cohort at baseline. We assumed the difference in NRS pain between the underlying population and GLA:D®/BOA participants at baseline to vary from 0.4 to 1.3 (Table 2). To also address the uncertainty around the value of ICC we used bootstrapping. As a sensitivity analysis we evaluated the change in pain from baseline to 12 months in OAI.

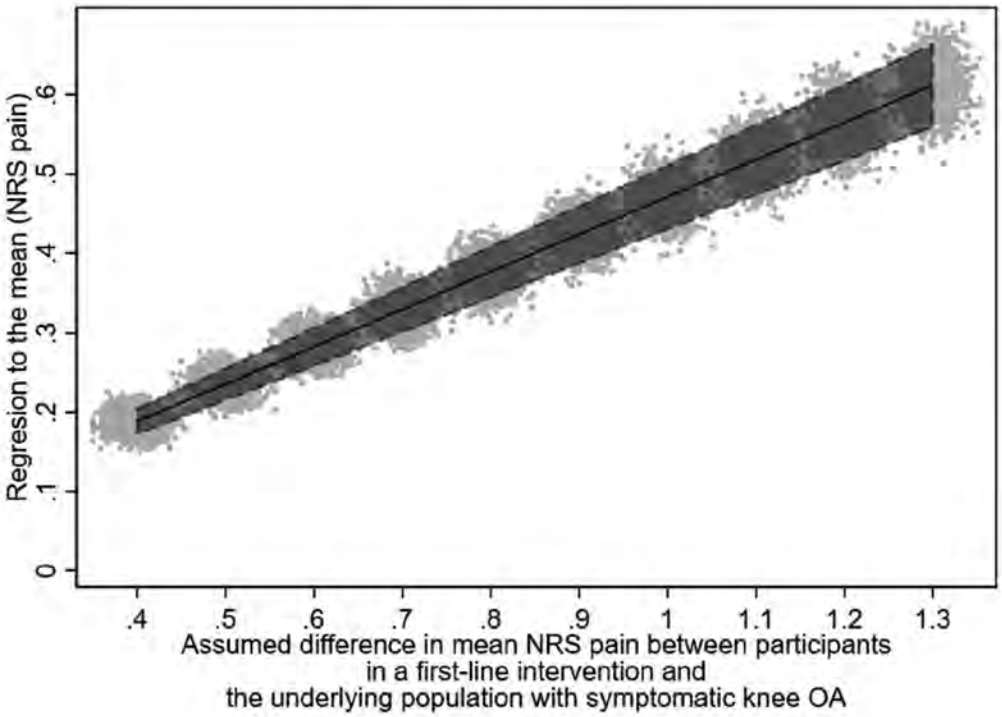
Results: The mean NRS pain levels at baseline in GLA:D® and BOA participants were *worse* than in persons with symptomatic knee OA from both the OAI and MOA (Table 2). An average ICC for NRS was ~0.53 (Table 2). We estimated the absolute improvement attributable to RTM in GLA:D®/BOA to range from 0.2 to 0.6 NRS points, depending on the assumptions (Figure 1) in line with the 0.5 NRS point improvement observed in OAI. The reported improvement in NRS from baseline to 12 months in GLA:D® was 1.3 and in BOA 1.0. Thus, in relative terms RTM ranges from 15% to 60% of the reported improvement in NRS pain.

Table 2. Key descriptive statistics for the OAI, MOA, GLA:D® and BOA participants.

	Persons with symptomatic knee OA, on a scheduled study visit			Knee OA patients self-enrolling in a first-line OA intervention	
	OAI, 12 months visit, n=1085	OAI, 24 months visit, n=1044	MOA, n=486	GLA:D®, baseline visit n=10 000*	BOA, baseline visit n=28 882*
Age, mean years	61	61	73	65	66
% women	56	56	65	68	69
BMI, mean kg/m^2	29	29	29	29	28
KOOS pain, mean	73	74	69	N/a	N/a
NRS pain, mean	3.9	4.0	4.3†	4.7§	5.2

N/a = Not available; data not collected or not presented in the annual report.
* Numbers as reported in each annual report 2019 for GLA:D® and BOA, respectively.
† The association between KOOS pain subscale and NRS pain in OAI data in persons with knee OA was linear with the formula: NRS=9.68-0.078*KOOS pain value. Thus, we used this formula to convert the mean KOOS pain in MOA of 69 to NRS value of 4.3.
§ We converted VAS values reported in GLA:D® to NRS values, by dividing by 10.

Figure 1. Size of the regression to the mean (in absolute NRS value), median (solid line), 2.5 and 97.5 percentile (dashed outer lines) of the estimated values (sampling 95% confidence intervals), depending on the difference in mean NRS pain in persons included in the first-line education and exercise programs and the underlying population with knee OA.



Conclusion: RTM in knee OA patients enrolled in a first-line intervention likely explains between 15% to 60% of the reported average improvement at 12 months. Results from OA interventions without control group(s) should not be inferred to as treatment effectiveness in reporting or marketing because the improvement is inflated by RTM which is neither an effect of the intervention, nor part of placebo response.

Disclosure: M. Englund, None; **A. Turkiewicz**, None.

Abstract Number: 0724

Dose (Exposure) Efficacy Response of Tanezumab Following Intravenous and Subcutaneous Administration Across Phase 2 and Phase 3 Studies in Patients with Osteoarthritis of Hip and Knee

Martin Boucher[1], Kenneth Verburg[2], Puneet Gaitonde[2] and Scott marshall[1], [1]Pfizer R&D Ltd., Sandwich, United Kingdom, [2]Pfizer Inc., Groton, CT

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Tanezumab is a humanized monoclonal antibody against nerve growth factor that has been evaluated for relief of chronic osteoarthritis pain by subcutaneous (SC) or intravenous (IV) administration every 8

Table. Predicted multiple imputation treatment differences (95% CI)

Endpoint	Tanezumab 2.5 mg vs placebo	Tanezumab 5 mg vs placebo	Naproxen vs placebo	Naproxen vs placebo (sensitivity analysis)
WPS	−0.75 (−0.84, −0.69)	−0.90 (−0.98, −0.84)	−0.25 (−0.36, −0.13)	−0.49 (−0.79, −0.19)
WOMAC Pain	−0.85 (−0.92, −0.79)	−1.00 (−1.10, −0.95)	−0.40 (−0.51, −0.30)	−0.52 (−0.84, −0.20)
WOMAC Physical Function	−0.91 (−1.00, −0.85)	−1.00 (−1.10, −0.97)	−0.28 (−0.43, −0.17)	−0.47 (−0.77, −0.17)

CI, confidence interval; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; WPS, weekly average pain score.

weeks. The current objectives were to (1) characterize the dose-response relationship between assigned dose and selected measures of efficacy at Week 16, (2) determine if average plasma tanezumab concentrations between 12 and 16 weeks ($C_{av12–16}$) could explain variability in the exposure-response, and (3) compare dose-response characterization for phase 2 vs phase 3 studies.

Methods: Data were pooled from 7 placebo-controlled clinical studies of tanezumab (2.5, 5, or 10 mg) administered via SC or IV routes in patients with osteoarthritis. Two of the 7 studies also included an active-controlled naproxen arm. Weekly average pain score (WPS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC*) Pain subscale score, and WOMAC Physical Function subscale score were evaluated. Population modeling analyses were conducted, using stepwise covariate modeling and multiple imputation methods consistent with the primary efficacy analysis to account for dropout. Sensitivity analyses used estimates of naproxen vs placebo, with study as an additional covariate on placebo response.

Results: Maximum effect models adequately described the dose-response relationship at Week 16 for all 3 endpoints; E_{max} point estimates (95% confidence interval [CI]) were: WPS −1.12 (−1.49, −0.76), WOMAC Pain −1.21 (−1.55, −0.87), and WOMAC Physical Function −1.22 (−1.55, −0.90). Model-based estimates of the treatment differences at Week 16 are shown in the **Table**; a 5 mg dose would provide only a 10–20% increase in effect over a 2.5 mg dose. Sensitivity analysis estimates (95% CI) of treatment differences for naproxen vs placebo for comparison with final model estimates are shown in the Table. Age was a significant covariate on E_{max} for all 3 endpoints; older patients had larger treatment effects compared with placebo than younger patients: between −0.15 and −0.24 for 75th age percentile and 25th age percentile, respectively. Exposure ($C_{av12–16}$) was not a significant covariate on E_{max} and route of administration (SC vs IV) was not a significant treatment effect modifier at Week 16 for any endpoint. The phase 2 study had a significantly lower placebo response and higher E_{max} compared with phase 3 studies for WPS and WOMAC Pain endpoints; after correcting for these differences, the estimated dose-response adequately covered the observed data across the phase 2 and phase 3 dose ranges.

Conclusion: Model-based simulations of E_{max} showed useful efficacy of pain relief with tanezumab 2.5 mg, with an increase in effect over naproxen. There was little effect gain at a higher tanezumab dose of 5 mg, and comparable efficacy between SC and IV routes of administration.

Disclosure: M. Boucher, Pfizer R&D UK LTD, 3, 8; **K. Verburg**, Pfizer Inc., 3, 8, 11; **P. Gaitonde**, Pfizer Inc., 3, 8; **S. marshall**, Pfizer R&D UK LTD, 3, 8.

Abstract Number: 0725

Efficacy of Subcutaneous Tanezumab for the Treatment of Osteoarthritis of the Knee or Hip: A Post Hoc Subgroup Analysis of Patients from a Randomized, NSAID-Controlled Study with a History of Depression, Anxiety, or Insomnia

Philip Mease[1], Theresa Mallick-Searle[2], Elizabeth Johnston[3], Lars Viktrup[3], Dominique Menuet[4], Ruoyong Yang[5] and Robert Fountaine[6], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [2]Stanford Health Care, Redwood City, [3]Eli Lilly and Company, Indianapolis, IN, [4]Pfizer SAS, Paris, France, [5]Pfizer Inc., New York, NY, [6]Pfizer Inc., Groton, CT

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

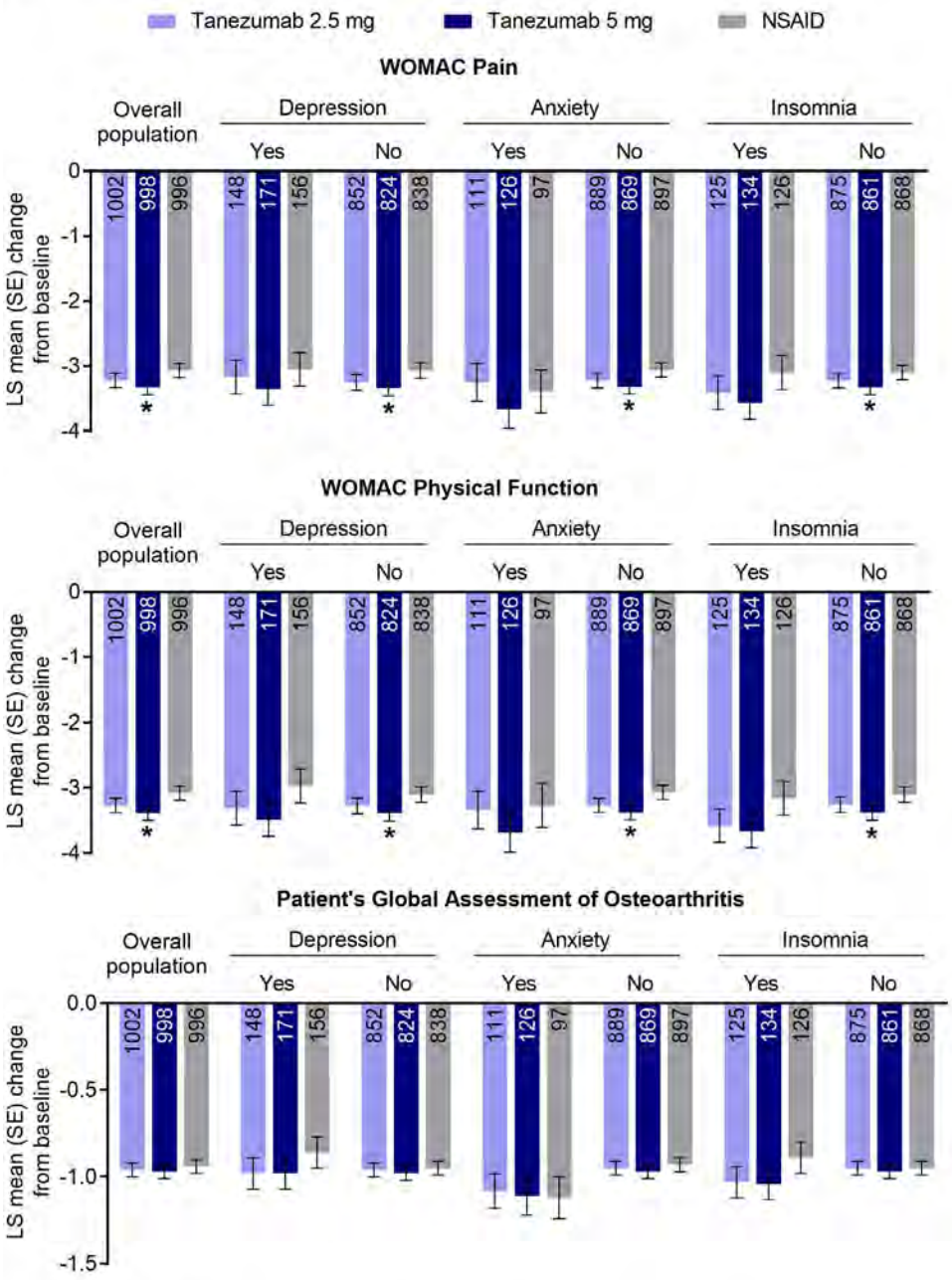
Background/Purpose: Tanezumab is a monoclonal antibody directed against nerve growth factor that is under study to treat moderate to severe chronic pain associated with osteoarthritis (OA) in adults for whom other treatments are ineffective or not appropriate. Phase 3 clinical trials have demonstrated the efficacy of subcutaneous (SC) tanezumab vs placebo for pain and function outcomes over various timepoints. Largely similar change from baseline was demonstrated in an oral NSAID-controlled study.[1-3] The efficacy of some other OA therapies can be dampened in patients with depression, anxiety, or insomnia.[4-6] A post hoc analysis explored efficacy of SC tanezumab after 16 weeks of treatment, as compared to oral NSAID, in patients with OA and a history of depression, anxiety, or insomnia at baseline.

Methods: A randomized, double-blind, double-dummy, active-controlled phase 3 study (NCT02528188) of tanezumab SC 2.5 or 5 mg every 8 weeks vs twice daily oral NSAID in patients (aged ≥18 y) with radiographically confirmed moderate to severe hip or knee OA (KL grade ≥2).[3] Co-primary efficacy endpoints were change from randomization to Week 16 in WOMAC Pain and Physical Function subscale scores (both ≥5/10 at baseline; higher scores indicate increasing pain/disability) and PGA-OA (≥3/5 at baseline; higher scores indicate poorer condition). Patients had a history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance/contraindication to tramadol or opioids, or unwillingness to take opioids. Patients were on a stable dose of NSAID for ≥30 days before screening. Data are presented as least squares (LS) mean change from baseline to Week 16 for the whole population and subgroups of patients with/without a history of depression, anxiety, or insomnia at baseline. Statistical analysis by ANOVA (P not adjusted for multiplicity). This exploratory analysis was not prespecified or included in any sample size calculations; comparisons between treatment arms or patient subgroups should be interpreted with caution.

Results: Overall, 2996 patients were randomized and received at least one dose of study treatment (SC tanezumab 2.5 mg: n=1002; 5 mg: n=998; oral NSAID: n=996). In patients with or without a history of anxiety, depression, or insomnia, all treatments were associated with notable and largely similar magnitude improvements in WOMAC Pain and Physical Function and PGA-OA at Week 16 (Figure). Across treatment groups, differences in LS mean change from baseline in patients with and without a history of depression, anxiety, or insomnia ranged between 0–0.34 for WOMAC Pain and Physical Function and 0–0.19 for PGA-OA.

Conclusion: Patients with a history of depression, anxiety, or insomnia did not appear to experience dampened improvements in pain or function with tanezumab or NSAID vs those without.

Figure 1: Co-primary efficacy endpoints after 16 weeks of treatment



*p<0.05 vs NSAID
LS, least squares; NSAID, nonsteroidal anti-inflammatory drug; SE, standard error; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.
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Funded by Pfizer and Eli Lilly.

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Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **T. Mallick-Searle**, AbbVie, 6, Allergan, 6, Eli Lilly and Company, 6; **E. Johnston**, Eli Lilly and Company, 3, 8, 11; **L. Viktrup**, Eli Lilly and Company, 3, 8; **D. Menuet**, Pfizer, 3, 8, 11; **R. Yang**, Pfizer Inc., 3, 8, 11; **R. Fountaine**, Pfizer Inc., 3, 8, 11.

Abstract Number: 0726

Joint Safety of Tanezumab versus NSAIDs; A Combined Assessment of Benefit and Harm

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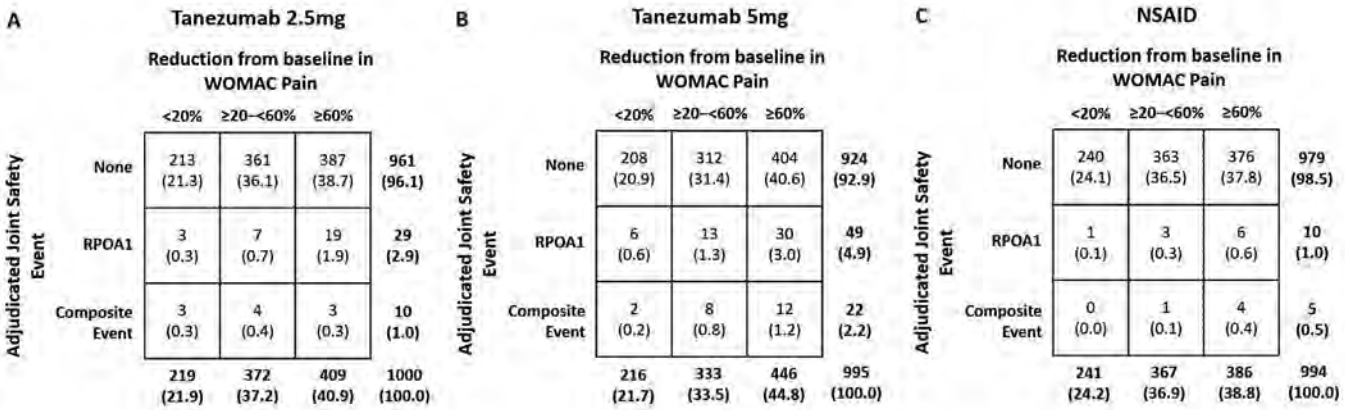
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Tanezumab, a monoclonal antibody against nerve growth factor, is in development for the relief of signs and symptoms of moderate to severe osteoarthritis (OA) in adult patients (pts) for whom use of other analgesics is ineffective or not appropriate. Previously, tanezumab has been associated with an increased incidence of joint safety events versus nonsteroidal anti-inflammatory drugs (NSAIDs)[1]. Our aim was to investigate the benefit/harm relationship for tanezumab and NSAIDs using the OMERACT 3x3 scale[2].

Methods: The study (NCT02528188) included pts with moderate to severe hip or knee OA with a history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance to tramadol or opioids; or unwillingness to take opioids. Pts were randomized to subcutaneous tanezumab 2.5mg or 5mg every 8 weeks or twice daily oral NSAIDs for a total of 56 weeks, with a 24-week post-treatment follow-up period. Benefit was assessed using 3 categories of reduction from baseline in Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)* Pain in the index joint at the primary efficacy endpoint of Week 16; < 20% (minimal improvement), ≥20–< 60% (moderate–substantial improvement) or ≥60% (very substantial improvement). Harm was assessed by considering 3 categories of joint safety outcomes; none (no adjudicated joint safety endpoints), rapidly progressive OA type 1 (RPOA1) or having an adjudicated composite joint safety endpoint (primary osteonecrosis, RPOA type 2, subchondral insufficiency fracture or pathological fracture) in any joint up to the end of the follow-up period or 26 weeks after the end of the treatment period, whichever was later.

Results: In the tanezumab 2.5mg group (n=1,000), 387 pts (38.7%) had the most favorable outcome of ≥60% improvement in WOMAC Pain with no joint safety events. 3 pts (0.3%) had the least favorable outcome of < 20% improvement in WOMAC Pain and a composite event (Figure 1A). In the tanezumab 5mg group (n=995), 404 pts

Figure 1. Assessment of benefit and harm using the OMERACT 3x3 scale



Patients, n (%), with each combination of outcomes is reported for the tanezumab 2.5mg (n=1,000), 5mg (n=995) and NSAID (n=994) groups. The total number and percentage of patients within each outcome category is presented at the end of the respective column or row.

Reduction from baseline in WOMAC Pain was assessed for the index joint at the primary study timepoint of Week 16. Adjudicated joint safety events were recorded for any joint up to the end of the follow up period or 26 weeks after the end of the treatment period, whichever was later.

NSAIDs, nonsteroidal anti-inflammatory drugs; RPOA1, rapidly progressive OA type 1; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

(40.6%) had the most favorable outcome and 2 pts (0.2%) had the least favorable outcome (Figure 1B). In the NSAID group (n=994), 376 pts (37.8%) had the most favorable outcome and 0 pts had the least favorable outcome (Figure 1C). Across all treatment groups, the incidence of RPOA1 increased with the category of benefit. The number of pts meeting the composite event increased with the category of benefit in the tanezumab 5mg and NSAID groups.

Conclusion: These analyses showed that ≥37.8% of pts had the most favorable outcome and ≤0.3% had the least favorable outcome; the proportion of pts with these outcomes was not notably different across treatments. An increased incidence of adjudicated joint safety events was associated with more favorable efficacy responses across treatments, with the exception of the composite event in the tanezumab 2.5mg group.

This study was sponsored by Pfizer and Eli Lilly. Medical writing support was provided by Steven Moore, PhD, of Engage Scientific Solutions and was funded by Pfizer and Eli Lilly.

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Abstract Number: 0727

Total Joint Replacements in Three Phase 3 Studies of Tanezumab in Patients with Osteoarthritis

John Carrino[1], Timothy McAlindon[2], Eric Vignon[3], Mark Brown[4], Aimee Burr[4], Robert Fountaine[4], Glenn Pixton[5], Lars Viktrup[6], Christine West[4] and Kenneth Verburg[4], [1]Hospital for Special Surgery, New York, NY, [2]Tufts Medical Center, Arlington, MA, [3]Université Claude Bernard Lyon 1, Lyon, France, [4]Pfizer Inc., Groton, CT, [5]Pfizer Inc., Morrisville, NC, [6]Eli Lilly and Company, Indianapolis, IN

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Osteoarthritis – Clinical Poster II (0723–0738)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Tanezumab (TNZ) is an antibody against nerve growth factor that has demonstrated efficacy in the management of osteoarthritis (OA). Due to the potential risk of rapidly progressive OA (RPOA), recent phase 3 studies of subcutaneous (SC) TNZ have included a comprehensive prospective assessment of joint safety. This analysis summarizes data on patients (pts) who underwent total joint replacement (TJR) in the recent phase 3 OA TNZ studies.

Table 1: Summary of Total Joint Replacements — Patient Level

		Tanezumab			
	Placebo n=514	2.5 mg n=1530	2.5/5 mg n=219	5 mg n=1282	NSAID n=996
Patients with ≥1 TJR, n (% pts in each treatment group)	23 (4.5)	84 (5.5)	15 (6.8)	100 (7.8)	26 (2.6)
TJRs during study, no. (% pts with TJR)					
1	20 (87.0)	77 (91.7)	13 (86.7)	87 (87.0)	25 (96.2)
≥2	3 (13.0)	7 (8.3)	2 (13.3)	13 (13.0)	1 (3.8)
TJR of index joint, no. (% pts with TJR)	20 (87.0)	74 (88.1)	14 (93.3)	77 (77.0)	22 (84.6)
Adjudicated joint safety outcomes, no. (% pts with TJR)					
RPOA1	0	4 (4.8)	1 (6.7)	8 (8.0)	2 (7.7)
RPOA2	0	3 (3.6)	0	10 (10.0)	1 (3.8)
Primary osteonecrosis	0	0	0	1 (1.0)	0
Pathological fracture	0	0	0	0	0
Subchondral insufficiency fracture	0	0	0	3 (3.0)	1 (3.8)
Normal progression of OA	21 (91.3)	73 (86.9)	14 (93.3)	73 (73.0)	22 (84.6)
Insufficient information to determine rapid vs normal progression of OA	0	2 (2.4)	0	0	0
Other joint outcome[a]	2 (8.7)	2 (2.4)	0	5 (5.0)	0

Includes TJR or adjudicated event up to the end of the follow-up period or 26 weeks after the end of the treatment period, whichever is later.

RPOA1 (rapidly progressive osteoarthritis type 1) is defined as a significant loss of joint space width ≥2 mm (predicated on optimal joint positioning) within ~1 year, without gross structural failure.

RPOA2 (rapidly progressive osteoarthritis type 2) is defined as abnormal bone loss or destruction, including limited or total collapse of ≥1 subchondral surface, that is not normally present in conventional end-stage osteoarthritis.

[a] Includes post-traumatic/post-procedure events and pre-existing conditions.

no., number of events; NSAID, nonsteroidal anti-inflammatory drug; OA, osteoarthritis; pt, patient; TJR, total joint replacement

Table 2: Characteristics of Replaced Joints — Joint Level

	Placebo n=514	Tanezumab 2.5 mg n=1530	Tanezumab 2.5/5 mg n=219	Tanezumab 5 mg n=1282	NSAID n=996
TJRs, n joints	26	91	17	114	27
Joint(s) affected, no. (% joints with TJR)					
Knee	13 (50.0)	55 (60.4)	10 (58.8)	64 (56.1)	15 (55.6)
Hip	13 (50.0)	35 (38.5)	7 (41.2)	46 (40.4)	11 (40.7)
Shoulder[a]	0	1 (1.1)	0	4 (3.5)	1 (3.7)
Index joint, no. (% joints with TJR)	20 (76.9)	74 (81.3)	14 (82.4)	77 (67.5)	22 (81.5)
Non-index joint, no. (% joints with TJR)	6 (23.1)	17 (18.7)	3 (17.6)	37 (32.5)	5 (18.5)
Baseline KL grade of replaced joint, no. (% joints with TJR)					
Not available	0	1 (1.1)	0	5 (4.4)	2 (7.4)
0	0	0	0	2 (1.8)	0
1	1 (3.8)	0	0	3 (2.6)	0
2	1 (3.8)	7 (7.7)	1 (5.9)	14 (12.3)	3 (11.1)
3	16 (61.5)	36 (39.6)	8 (47.1)	62 (54.4)	16 (59.3)
4	8 (30.8)	47 (51.6)	8 (47.1)	28 (24.6)	6 (22.2)

[a]KL grading was not conducted for shoulder joints.

KL, Kellgren-Lawrence; no., number of events; NSAID, nonsteroidal anti-inflammatory drug; TJR, total joint replacement.

Methods: In NCT02697773, pts with OA received placebo (PBO), TNZ 2.5 mg or 2.5 mg then 5 mg (TNZ 2.5/5 mg) for 16 weeks. In NCT02709486, pts received PBO or TNZ 2.5 or 5 mg for 24 weeks. In NCT02528188, pts received TNZ 2.5 or 5 mg or NSAIDs for 56 weeks. TNZ and matching PBO were given SC every 8 weeks; NSAID and matching PBO were taken orally twice daily. All studies had a 24-week safety follow-up period. Subgroup analyses were performed to explore potential associations between the incidence of TJR and baseline (BL) demographic/clinical characteristics or post-BL outcomes. In all studies, TJRs were adjudicated by a blinded external Adjudication Committee to determine any association with joint safety events including RPOA type 1, RPOA type 2, subchondral insufficiency fracture (SIF), primary osteonecrosis, or pathological fracture. For each pt, the most painful hip or knee joint with radiographic OA was selected as the index joint. Pain was assessed in all joints but efficacy assessments were only for the index joint. Pts could also have had OA in non-index joints.

Results: Across the 3 studies (N=4541 pts), 248 pts had ≥1 TJR (26 ≥2 TJRs) with an incidence of 2.6–7.8% across groups (**Table 1**). In all, 83% of pts with a TJR had surgery on their index joint, the proportion of which was similar in the PBO, TNZ 2.5 mg, and NSAID groups (84.6–88.1%), lower in the TNZ 5 mg (77.0%) group, and higher in the TNZ 2.5/5 mg (93.3%) group (**Table 1**). Most TJRs occurred in joints with Kellgren-Lawrence (KL) grade 3 or 4 at BL (**Table 2**). In the TNZ 5 mg group, 2 pts had TJR of a joint that was KL grade 0 at BL: 1 was adjudicated to be associated with RPOA2 and 1 as a post traumatic subchondral fracture following an accidental fall. The majority (73.3–81.0%) of pts across treatment groups had no prior history of TJR. Of the 275 TJRs reported across groups, 50.0–60.4% occurred in a knee, 38.5–50.0% in a hip and 0–3.7% in a shoulder (**Table 2**). Among PBO, TNZ 2.5 mg, TNZ 2.5/5 mg and NSAID groups, incidences of an adjudicated outcome of normal progression of OA were similar (84.6–93.3%; lower with TNZ 5 mg [73.0%]). The TNZ 5 mg group had the highest percentage of pts with a TJR with an adjudicated outcome of RPOA1, RPOA2 or SIF (**Table 1**). Subgroup analyses did not reveal any associations between BL demographic or clinical characteristics and the incidence of TJR (**Table 3**).

Conclusion: Pts treated with TNZ 5 mg had a greater incidence of TJR than those receiving TNZ 2.5 mg, PBO or NSAID. The occurrence of TJR in the index joint in pts receiving TNZ 2.5 mg was similar to those receiving PBO or

Table 3: Subgroups Analyzed for Potential Association With Total Joint Replacement

Subgroups	Details	Association with TJR
Demographic factors	• Age: <65 vs ≥65, <75 vs ≥75 • Gender: Male vs female • BMI: <25, 25 to <30, 30 to <35, ≥35	No association
Baseline disease severity	• Maximum KL grade (2, 3, or 4) at baseline • No. of joints with baseline KL grade ≥2 • Prior history of TJR • WOMAC[a] Pain subscale score at baseline (<7, ≥7) • WOMAC Physical Function subscale score at baseline (<7, ≥7) • Patient's global assessment at baseline (Fair, Poor/Very Poor)	No association
Adverse events	• Selected adverse events up to end of study: ○ Arthralgia or joint swelling ○ Arthralgia or joint swelling prior to TJR ○ Any adverse event of abnormal peripheral sensation[b] ○ Peripheral edema ○ Any fracture ○ Fracture of the lower limb ○ Any post-baseline fall	No association
Efficacy response: WOMAC Pain and Physical function	• Change from baseline in WOMAC Pain and Physical function scores at Week 16 and Week 56 (NCT02528188 only) for the index joint	No association
Other factors	• Use of intra-articular hyaluronic acid in year prior to study • Use of intra-articular corticosteroid in year prior to study • Any concomitant use with NSAID, cardiovascular prophylactic aspirin, intra-articular corticosteroid, bisphosphonate, or acetaminophen	No association
Concomitant NSAID use	• Use of NSAID prior to occurrence of TJR	No association
Baseline bone health	• Including history of osteopenia or osteoporosis	No association

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[b]Adverse events of peripheral sensation were allodynia, axonal neuropathy, burning sensation, carpal tunnel syndrome, decreased vibratory sense, demyelinating polyneuropathy, dysesthesia, formication, hyperesthesia, hyperpathia, hypoesthesia, hypoesthesia oral, intercostal neuralgia, neuralgia, neuritis, neuropathy peripheral, paresthesia, paresthesia oral, peripheral sensorimotor neuropathy, peripheral sensory neuropathy, polyneuropathy, polyneuropathy chronic, sciatica, sensory disturbance, sensory loss, tarsal tunnel syndrome, thermohypoesthesia.

BMI, body mass index; KL, Kellgren-Lawrence; NSAID, nonsteroidal anti-inflammatory drug; TJR, total joint replacement; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

NSAID. Across all treatment groups, the majority of TJRs were not associated with an adjudicated joint safety event but rather normal progression of OA and occurred in a joint with structural evidence of OA.

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Abstract Number: 0728

Intra-articular Canakinumab (anti-interleukin-1β) for Treatment of Symptomatic Knee Osteoarthritis: A Randomized, Double-blind, Placebo and Naproxen-controlled Phase II Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Knee osteoarthritis (OA) is a common musculoskeletal disease associated with pain and functional impairment. There are few effective therapies, often limited by side-effects.[1] This phase II study investigated the efficacy, safety, and pharmacokinetics of canakinumab, an anti-interleukin-1β antibody, in patients (pts) with knee OA (NCT01160822).

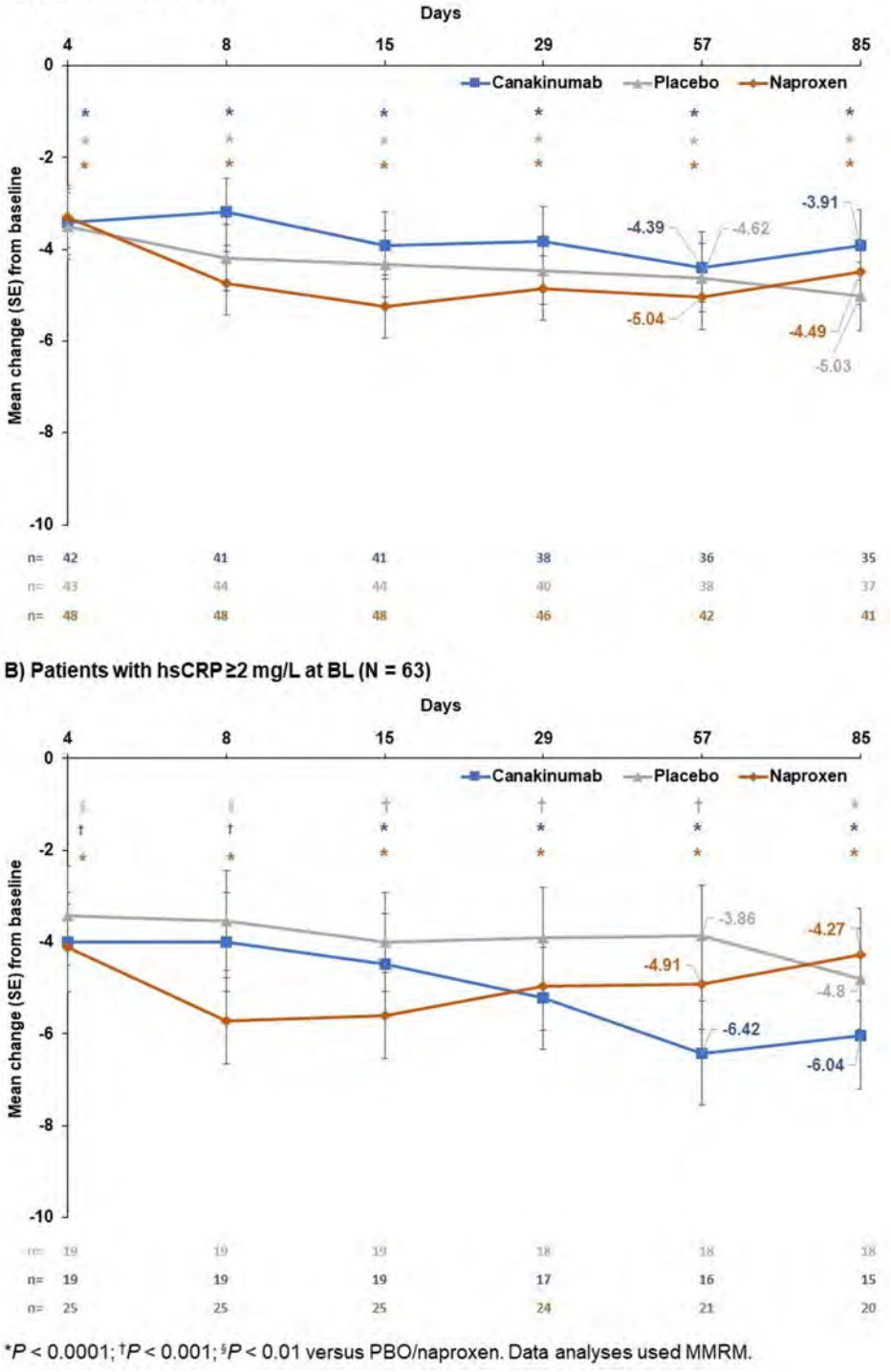
Methods: The study had a single placebo (PBO)-controlled ascending dose period assessing the safety of intra-articular (i.a.) canakinumab, and an 18-week randomized, double-blind, double-dummy PBO and naproxen-controlled period. Pts (N = 136) with symptomatic knee OA (VAS pain ≥40, Kellgren/Lawrence [K/L] grade 2 or 3) were enrolled to receive a single i.a. injection of canakinumab 600 mg or matched PBO at baseline (BL), and naproxen 500 mg twice daily or matched PBO. Co-primary endpoints were change from BL in knee OA pain (VAS 0-100] at Day 4 and in Western Ontario and McMaster OA Index (WOMAC) pain (scale 0-20) at Day 29.

Results: Canakinumab i.a was generally safe and well tolerated and had a short resident time in the joint with an early detection (1 hour) in the circulation after i.a. injection. The co-primary efficacy endpoints were not met. The rapid and clinically significant decreases from BL in VAS pain and WOMAC pain scores were largely comparable between canakinumab, PBO and naproxen (Figure 1A). In a post hoc analysis of pts with BL elevated high sensitive C-reactive protein (hsCRP) levels (≥2 mg/L), canakinumab had a more pronounced inhibitory effect on pain than PBO or naproxen (-2.56 [-5.16; 0.04], P = 0.11; adjusted mean (90% CI) from a mixed-effect model repeated measures [MMRM]) at Day 57. Furthermore, this subpopulation showed a (-1.24 [-3.87; 1.39], P = 0.44) reduction of WOMAC pain at Day 85 compared to PBO or naproxen (Figure 1B).

Conclusion: The effect of canakinumab on pain in a population with knee OA was not different from PBO or naproxen. An effect of canakinumab on pain was observed in a subpopulation with elevated BL hsCRP levels. In addition to the data published previously on the CANTOS study[2], these findings underscore the need to identify specific populations of pts with knee OA, who may benefit from anti-inflammatory treatment.

References: 1. Eymard F, Chevalier X. *Rev Prat*. 2019;69:515-9. 2. Schieker et al, *Ann Intern Med*. 2020;173:509-15.

Figure 1. Adjusted mean change from BL in WOMAC pain score



*$P < 0.0001$; †$P < 0.001$; ‡$P < 0.01$ versus PBO/naproxen. Data analyses used MMRM.

Disclosure: P. Conaghan, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **X. Chevalier**, Ibsa, 2, 5, 6, Sanofi, 2, Flexion therapics, 1, 2, magpharma, 1; **L. Mindeholm**, Novartis, 3, 12, Shareholder; **U. Schramm**, Novartis, 3, 12, Shareholder; **J. Praestgaard**, Novartis, 3; **A. Seroutou**, Novartis, 3; **R. Roubenoff**, Novartis, 3, 11; **M. Schieker**, Novartis, 3, 11.

Abstract Number: 0729

A Multicenter, Observational, Extension Study Evaluating the Safety, Tolerability, and Efficacy of a Single Lorecivivint Injection in Knee OA Subjects

Ismail Simsek[1], Christopher Swearingen[1], Heli Ghandehari[1], Sarah Kennedy[2], Jeyanesh Tambiah[1], Yusuf Yazici[3] and **Nebojsa Skrepnik**[4], [1]Biosplice Therapeutics, Inc., San Diego, CA, [2]Biosplice Therapeutics, Inc, San Diego, CA, [3]New York University School of Medicine, La Jolla, CA, [4]Tucson Orthopaedic Institute, Tucson

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Background/Purpose: Lorecivivint (LOR), a novel intra-articular (IA) CLK/DYRK inhibitor that modulates Wnt and inflammatory pathways, is in development as a knee osteoarthritis (OA) treatment. To further evaluate the safety and exploratory efficacy of a single LOR injection that was administered into the target knee joint of subjects with moderate to severe knee OA from two consecutive Phase 2 trials, an extension study was performed with the primary objective of evaluating serious adverse events (SAEs), as well as analyzing safety data for all doses and efficacy data for the (pivotal) 0.07 mg LOR dose.

Methods: This was a 5-year, Phase 3, multicenter, observational, extension study of completer subjects (NCT02951026) from a 12-month Phase 2a (Yazici, Y. et al. *Arthritis Rheumatol*. 72, 1694–1706 (2020)) and a 6-month Phase 2b (Yazici, Y. et al. *Osteoarthr. Cartil*. In Press, (2021)) trial of LOR. The study was terminated in Year 3 as relevant long-term safety information became limited in the absence of repeated LOR administration. Subjects received a single LOR or vehicle placebo (PBO) injection at their Phase 2 parent-trial baseline visit (Month 0). Pooled data from clinic visits at 6, 12, 24, and 36 months were used to analyze safety outcomes (serious AEs, knee-related AEs, and AEs of newly diagnosed conditions needing treatment). A post hoc baseline-adjusted ANCOVA on 0, 3, 6, 12, and 18-month data points (across current and parent trials) was used to compare changes from baseline in a subject subgroup (unilat-

Table 1. Subject characteristics by group

Mean(SD) or N(%)	Lorecivivint				Placebo	Sham
	0.03 mg	0.07 mg	0.15 mg	0.23 mg		
N	116	115	115	116	116	117
Age at Consent (years)	57.9 (7.9)	59.9 (8.6)	58.4 (8.3)	58.5 (9.0)	60.1 (9.0)	59.0 (8.0)
BMI (kg/m^2)	29.2 (3.8)	29.1 (3.6)	29.4 (4.1)	28.5 (4.4)	28.6 (4.3)	29.0 (3.8)
Female	76 (65.5)	66 (57.4)	69 (60.0)	61 (52.6)	64 (55.2)	70 (59.8)
KL Grade 3	63 (54.3)	74 (64.3)	68 (59.1)	63 (54.3)	72 (62.1)	58 (49.6)
Unilateral Symptomatic	59 (50.9)	62 (53.9)	63 (54.8)	63 (54.3)	61 (52.6)	62 (53.0)
Widespread Pain (WPI <4)	92 (79.3)	93 (80.9)	90 (78.3)	93 (80.2)	93 (80.2)	94 (80.3)
Race						
White	85 (73.3)	83 (72.2)	84 (73.0)	89 (76.7)	90 (77.6)	86 (73.5)
Black	24 (20.7)	22 (19.1)	25 (21.7)	21 (18.1)	17 (14.7)	24 (20.5)
Asian	5 (4.3)	5 (4.3)	6 (5.2)	5 (4.3)	6 (5.2)	3 (2.6)

Table 2. Key safety results (adverse events [AEs]) for all injected doses of lorecivivint and all controls (extension study reports only)

AEs Reported ≥1%	0.03 mg n=131	0.07 mg n=135	0.15 mg n=65	0.23 mg n=135	Other n=29	Control n=208^	All N=703
Total AEs/Unique subjects (%)	50 / 24 (18.3)	28 / 21 (15.6)	25 / 11 (16.9)	64 / 33 (24.4)	10/4 (13.8)	60/44 (21.2)	237 / 137 (19.5)
Osteoarthritis	13 / 9 (6.9)	6 / 6 (4.4)	1 / 1 (1.5)	6 / 5 (3.7)	1 / 1 (3.4)	6/6 (2.9)	33 / 28 (4.0)
Arthralgia	6 / 5 (3.8)	5 / 5 (3.7)	1 / 1 (1.5)	6 / 6 (4.4)	1 / 1 (3.4)	8/7 (3.4)	27 / 25 (3.6)
Meniscus Injury	3 / 3 (2.3)	2 / 2 (1.5)	1 / 1 (1.5)	1 / 1 (0.7)	0 / 0 (0.0)	2/2 (1.0)	9 / 9 (1.3)
Hypertension	2 / 2 (1.5)	0 / 0 (0.0)	2 / 2 (3.1)	2 / 2 (1.5)	0 / 0 (0.0)	6/6 (2.9)	12 / 12 (1.7)
Target Knee AEs (Total)	22 / 15 (11.5)	8 / 7 (5.2)	6 / 3 (4.6)	11 / 9 (6.7)	4 / 1 (3.4)	12/11 (5.3)	63 / 46 (6.5)
Osteoarthritis	8 / 8 (6.1)	2 / 2 (1.5)	1 / 1 (1.5)	2 / 2 (1.5)	1 / 1 (3.4)	4/4 (1.9)	18 / 18 (2.6)
Arthralgia	4 / 4 (3.1)	2 / 2 (1.5)	1 / 1 (1.5)	4 / 4 (3.0)	1 / 1 (3.4)	4/4 (1.9)	16 / 16 (2.3)
Meniscus Injury	2 / 2 (1.5)	2 / 2 (1.5)	1 / 1 (1.5)	1 / 1 (0.7)	0 / 0 (0.0)	1/1 (0.5)	7 / 7 (1.0)
Serious AEs							
Subjects Reporting SAEs	14 / 8 (6.1)	8 / 6 (4.4)	8 / 4 (6.2)	32 / 14 (10.4)	1 / 1 (3.4)	5/5 (2.4)	68 / 38 (5.4)

#AE / #subjects (%) reported.
Other: All subjects treated with anything other than the protocol-specified dose of LOR
^Control= Placebo, Sham, and 2 PBO subjects with dose of PBO not specified by protocol

eral symptoms, no widespread pain, 18-month post-injection radiograph at study termination) in WOMAC Pain and Function subscores and medial joint space width (mJSW) between 0.07 mg LOR and PBO groups.

Results: Of 703 subjects, 119 (17%) subjects discontinued prior to study termination. Subject characteristics are shown in Table 1. The safety analysis set included 495 LOR-treated subjects and 208 control subjects (Table 2). Four AEs in 3 (0.6%) subjects across LOR groups were considered related to the study drug; no subjects withdrew from the study due to a treatment-related AE. Incidence was similar between LOR and PBO groups. Sixty-eight SAEs in

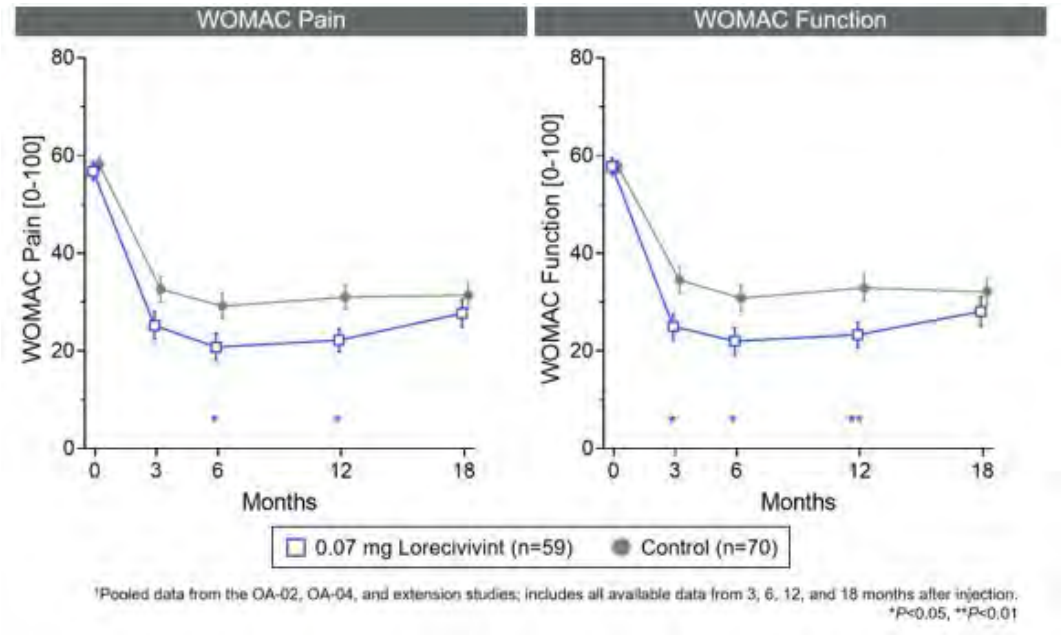

Figure 1. WOMAC Pain and Function scores over time in unilateral completers treated with intra-articular LOR (lorecivivint) or vehicle placebo (Control). Month 0 (baseline) is the subject's day of knee injection. Lower scores denote improvements. Statistical significance (asterisks) is shown for the groupwise comparison of mean changes from baseline for LOR and Control groups.

38 (5.4%) subjects were reported with none considered related to treatment by investigators. One death occurred in the control group. Post hoc efficacy analyses demonstrated that subjects in the 0.07 mg LOR group (n=59) showed greater mean improvements from baseline in both WOMAC Pain and Function at 6 (Pain: -8.16, 95% CI [-15.60, -0.71], *P*=0.032; Function: -9.47 [-17.09, -1.84], *P*=0.015) and 12 (Pain: -8.51 [-15.17, -1.85], *P*=0.013; Function: -9.62 [-16.83, -2.42], *P*=0.009) months vs. subjects in the control group (n=70) (Figure 1). No mJSW progression was observed in any group over 18 months. Limitations included using subjects (completers) more likely to be responders and not controlling for other treatments in the extension study period.

Conclusion: LOR appeared safe and well tolerated. Efficacy analyses on the described subset of completer subjects demonstrated durable symptom improvements in WOMAC Pain and Function for up to at least 12 months vs. contr ols.

Disclosure: I. Simsek, Biosplice, 3; **C. Swearingen**, Biosplice Therapeutics, Inc,, 3; **H. Ghandehari**, Biosplice Therapeutics, Inc., 3; **S. Kennedy**, Biosplice Therapeutics, Inc., 3; **J. Tambiah**, Biosplice Therapeutics, Inc., 3; **Y. Yazici**, Amgen, 2, BMS, 5, Biosplice, 3, 8; **N. Skrepnik**, Orthofix, 7, Regeneron, 2, Pfizer, 2.

Abstract Number: 0730

Safety, Tolerability, and Pharmacokinetics of an Intra-articular Corticosteroid Injection Administered 7 Days Before or After Intra-articular Lorecivivint Injection into the Same Knee of Healthy Volunteers: An Open-Label, Parallel-Arm Study

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Knee osteoarthritis (OA) is a painful condition leading to joint damage and impaired function. Intra-articular (IA) corticosteroid injections are frequently prescribed to treat pain. Lorecivivint (LOR), a novel IA CLK/DYRK inhibitor that modulates Wnt and inflammatory pathways, appeared safe and demonstrated patient-reported outcome pain and function improvements compared with placebo in a Phase 2b knee OA trial (Yazici, Y. et al. *Osteoarthr. Cartil*., 2021). While lorecivivint is proposed for stand-alone use, in clinical practice, providers might administer lorecivivint in close time proximity to IA corticosteroid. This open-label, parallel-arm, healthy volunteer study was conducted to assess potential safety and tolerability (primary objectives), and pharmacokinetic (PK) interactions (secondary objective), between lorecivivint and triamcinolone acetonide (TCA) when the two medications were administered 7 days apart.

Methods: Healthy volunteers were randomized to Treatment Arm 1 (IA 40 mg TCA on Day 1 followed by IA 0.07 mg lorecivivint on Day 8) or Treatment Arm 2 (IA 0.07 mg lorecivivint on Day 1 followed by IA 40 mg TCA on Day 8). All injections were performed on the right knee. For each treatment arm, treatment-emergent adverse events (TEAEs) were categorized by “epoch”, with Epoch 1 spanning from first until second injection, and Epoch 2 spanning from second injection until end of study. In Treatment Arm 1, plasma TCA levels were assessed on Days 1 (before TCA

Table 1. Treatment-emergent adverse events (TEAEs) by preferred term in the safety analysis set

	Treatment Arm 1				Treatment Arm 2			
	TCA (Epoch 1) (n=20)		TCA + LOR (Epoch 2) (n=20)		LOR (Epoch 1) (n=20)		LOR + TCA (Epoch 2) (n=20)	
Preferred Term	n (%)	Total Number of Events	n (%)	Total Number of Events	n (%)	Total Number of Events	n (%)	Total Number of Events
Total TEAEs	4 (20.0)	5	3 (15.0)	8	2 (10.0)	2	3 (15.0)	3
Injection site bruising	4 (20.0)	4	0	0	1 (5.0)	1	2 (10.0)	2
Injection site pain	0	0	1 (5.0)	2	0	0	0	0
Back pain	1 (5.0)	1	0	0	0	0	0	0
Flank pain	0	0	1 (5.0)	1	0	0	0	0
Musculoskeletal discomfort	0	0	1 (5.0)	1	0	0	0	0
Pain in extremity	0	0	1 (5.0)	1	0	0	0	0
Headache	0	0	1 (5.0)	1	1 (5.0)	1	0	0
Hypersensitivity	0	0	0	0	0	0	1 (5.0)	1
Skin abrasion	0	0	1 (5.0)	1	0	0	0	0
Adnexa uteri pain	0	0	1 (5.0)	1	0	0	0	0

All subjects in the safety analysis set received both study injections in a randomized manner in either Treatment Arm 1 (TCA then lorecivivint) or Treatment Arm 2 (lorecivivint then TCA). Epoch 1 spans the duration from the first injection until just prior to the second injection. Epoch 2 spans the duration from the second injection until the end of study phone visit/early termination. TEAEs were coded using MedDRA v23.1.
Abbreviations: LOR, lorecivivint; TCA, triamcinolone acetonide

dosing and up to 12 h after), 2 (24 h after), 3, 5, 8 (before lorecivivint dosing and up to 8 h after), 11, and 15. Plasma lorecivivint concentrations were assessed on Day 8 (before lorecivivint dosing and up to 8 h after). In Treatment Arm

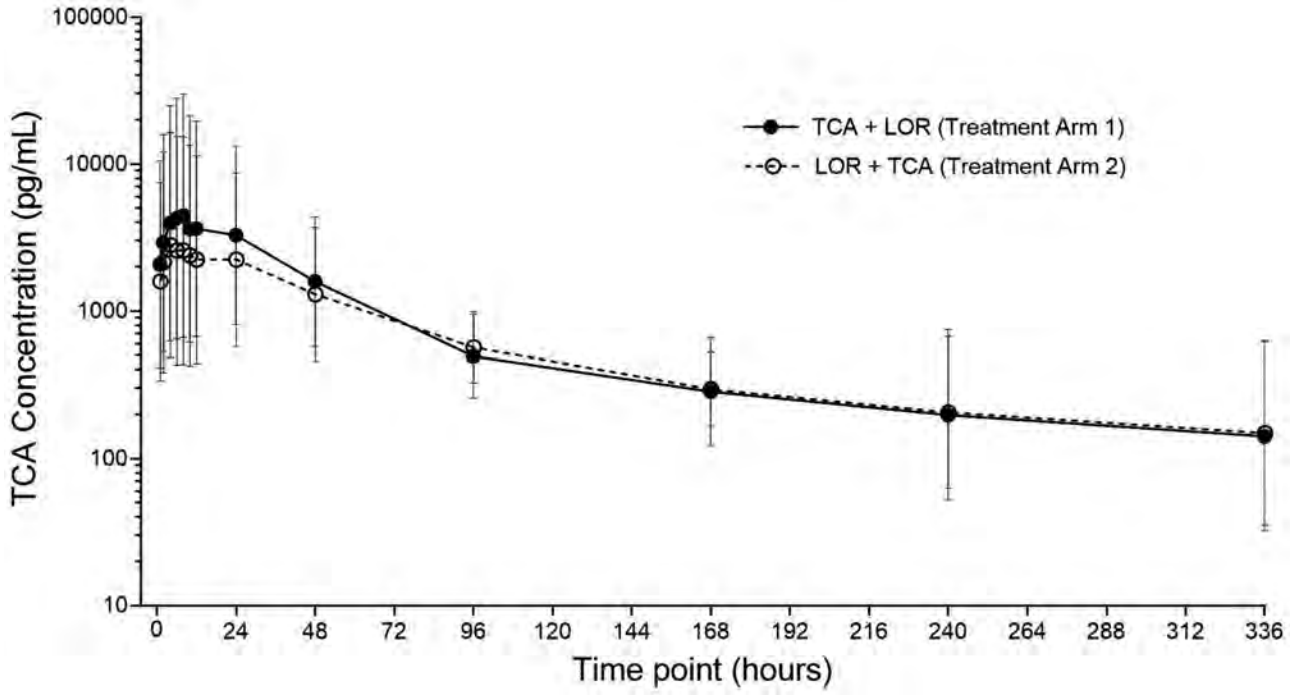

Figure 1. Plasma concentration of triamcinolone acetonide (TCA) following intra-articular (IA) knee injection (40 mg) 7 days before (Treatment Arm 1) and after (Treatment Arm 2) IA lorecivivint (LOR) (0.07 mg). Values shown are geometric means (geometric SD) for all post-injection time points. Values reported below the lower limit of quantification (LLOQ=20.0 pg/mL) were set to ½ × LLOQ.

2, plasma lorecivivint levels were assessed on Days 1 (before lorecivivint dosing and up to 8 h after), 8 (up to 8 h after TCA dosing), 9 (24 h after), 10, and 12. Plasma TCA levels were assessed on Days 8 (before TCA dosing and up to 12 h after), 9 (24 h after), 10, 12, 15, 18, and 22.

Results: Forty subjects (n=20/arm; age 41.3±7.2 years; BMI 27.8±2.98 kg/m^2; female 40.0%) were evaluated. A total of 18 TEAEs were reported by 11 (27.5%) subjects (Table 1). TEAEs were similar between arms and there were no serious adverse events. In all subjects and at all time points, plasma lorecivivint concentrations were below the limit of quantification (0.1 ng/mL). Geometric mean concentrations (Figure 1) and PK parameters for TCA were similar between treatment arms.

Conclusion: There were no quantifiable plasma concentrations of lorecivivint in either treatment arm, and the PK of TCA was unaffected by previous lorecivivint injection. No safety signals were observed. These results suggest that IA administration of lorecivivint and triamcinolone in close proximity (7 days apart) should not pose a safety concern.

Disclosure: A. Halseth, Biosplice, 3, 11, Neurana Pharmaceuticals, 3; **N. Lane**, Amgen, 2, Pfizer, 2, BriOri Biotech, 4, Makikroft, 2, 6, GSK, 2, UCB, 1; **S. Kennedy**, Biosplice Therapeutics, Inc., 3; **C. Swearingen**, Biosplice Therapeutics, Inc., 3; **V. Lopez**, Biosplice Therapeutics, Inc., 3; **I. Simsek**, Biosplice, 3; **M. Fineman**, Biosplice Therapeutics, Inc., 3, 8; **Y. Yazici**, Amgen, 2, BMS, 5, Biosplice, 3, 8.

Abstract Number: 0731

An Open-Label Study to Evaluate the Effect of Intra-articular Triamcinolone Acetonide Extended Release on Patients with Baseline Synovitis and Osteoarthritis of the Knee

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

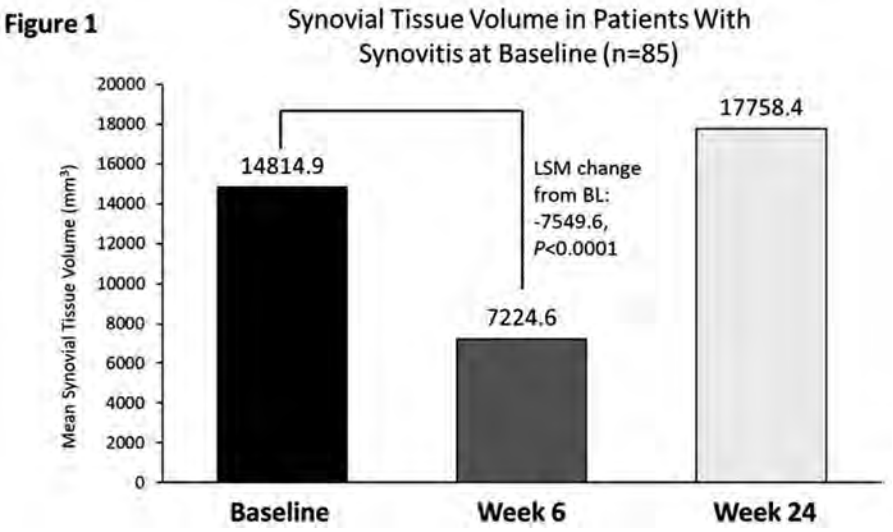
Background/Purpose: Synovial inflammation is common in knee osteoarthritis (OA) and is associated with pain and disease severity. Previous studies have suggested short-term (approximately 2 weeks) effects on synovial tissue from intra-articular (IA) steroid injection. This open-label Phase 3b study evaluated a single 32 mg intra-articular (IA) injection of triamcinolone acetonide extended release (TA-ER) on synovial tissue volume (STV), pain, stiffness, function, and quality of life (QOL) (NCT03529942).

Methods: Patients with KL grade 2-3 painful (Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC)-A total sum score ≥ 6) knee OA received TA-ER at baseline (BL). Assessments occurred at BL, Weeks 6, 12, 18, and 24, and included gadolinium MRI at BL, Weeks 6 and 24 using automated segmentation. MRIs were used to determine STV, with synovitis at BL defined as STV ≥3000 mm^3. Patients who had quality MRI data available at BL

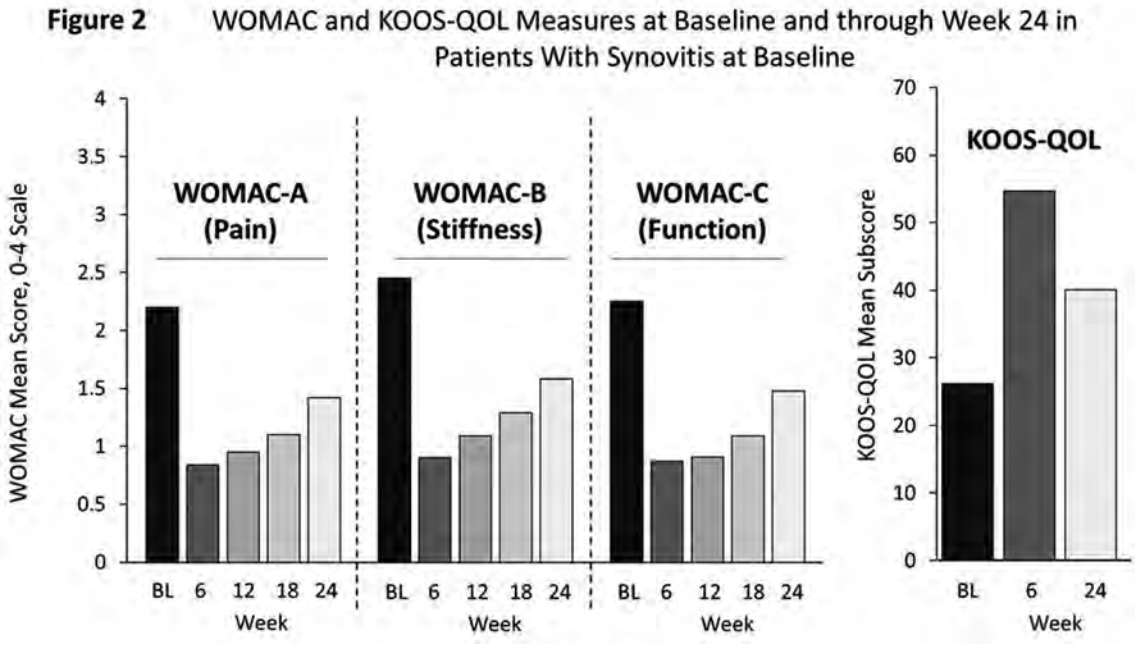
Parameter	Statistics	All Patients (N=129)	Patients With Synovitis* at BL (n=102)
Age, years	Mean (SD)	61.2 (8.0)	61.7 (7.9)
Female	%	62.8	61.8
BMI, kg/m^2	Mean (SD)	30.3 (4.7)	30.6 (4.5)
Years since diagnosis	Mean (SD)	9.0 (8.9)	8.9 (8.6)
Days with pain/month	Mean (SD)	29.2 (2.7)	29.2 (2.7)
Bilateral OA	%	69.8	65.7
Prior index knee surgery	%	26.4	30.4
Prior IACS	%	41.1	43.1
Prior IAHA	%	11.6	13.7
KL grade 2	%	48.8	40.2
KL grade 3	%	51.2	59.8
Joint space width, mm	Mean (SD)	4.7 (1.4)	4.5 (1.5)
WOMAC-A (pain)	Mean (SD)	2.2 (0.6)	2.2 (0.6)
WOMAC-B (stiffness)	Mean (SD)	2.4 (0.7)	2.5 (0.6)
WOMAC-C (function)	Mean (SD)	2.2 (0.6)	2.3 (0.6)
KOOS-QOL	Mean (SD)	27.2 (16.3)	26.2 (16.5)
Baseline STV, mm^3	Mean (SD)	11,876.6 (10,681.6)	14,814.9 (10,337.9)

*Synovitis was defined as STV ≥3000 mm^3 (3 mL) at baseline determined using gadolinium MRI.
BL, baseline; BMI, body-mass index; IACS, intra-articular corticosteroid; IAHA, intra-articular hyaluronic acid; KL, Kellgren-Lawrence; KOOS-QOL, Knee Injury and Osteoarthritis Outcome Score – Quality of Life; OA, osteoarthritis; SD, standard deviation; STV, synovial tissue volume; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index.

Figure 1



and at least one post-baseline timepoint were included in the Imaging Population. The primary study endpoint was mean standardized change in STV from BL to Week 6. Additionally, WOMAC-A (pain), WOMAC-B (stiffness), and WOMAC-C (function) were assessed at BL and Weeks 6, 12, 18, and 24; the Knee injury and Osteoarthritis Outcome Score – QOL (KOOS-QOL) was assessed at BL, Weeks 6 and 24. Treatment-emergent adverse events (TEAEs) were recorded.



Results: We enrolled 129 patients with typical knee OA characteristics (Table); 102 (79%) demonstrated BL synovitis (STV ≥3000 mm^3; range 3,005-45,113 mm^3). In patients with BL synovitis who were part of the Imaging Population (n=85), STV was significantly reduced at Week 6 ($P< 0.0001$; (Figure 1). The primary endpoint was met: standardized least squares mean (LSM) STV change at Week 6 was −0.90 (95% CI, −1.06 to −0.73; $P< 0.001$); at Week 24, STV change was 0.20 (95% CI, 0.04 to 0.36). In patients with BL synovitis following TA-ER, WOMAC-A, B, and C improved from BL at Weeks 6, 12, 18, and 24; also, KOOS-QOL improved from BL at Weeks 6 and 24 (Figure 2). Although STV returned to BL by Week 24, the clinical improvements observed in WOMAC and KOOS measures persisted through Week 24. Thirty-one patients (24%) experienced TEAEs; 9 (7.0%) patients had ≥1 index-knee TEAE. Most TEAEs were considered mild or moderately severe, however, one severe adverse event of nephrolithiasis occurred. None of the TEAEs were considered related to the study drug.

Conclusion: In patients with knee OA and BL synovitis, a single IA injection of TA-ER improved six-week synovitis, measured as reduced STV. TA-ER reduced OA symptoms of pain and stiffness and improved function and OA-related quality of life through Week 24. Overall, a single IA injection of TA-ER was well tolerated.

Disclosure: K. Huffman, Flexion, 5, Gilead Sciences Inc, 5; **A. Kivitz**, Pfizer, 2, 6, 11, 12, Sanofi, 2, 6, 11, 12, GlaxoSmithKline, 11, Gilead Sciences, Inc.,, 2, 11, Novartis, 2, 6, 12, AbbVie, 2, 6, 11, Boehringer Ingelheim, 2, Janssen, 2, Regeneron, 2, 6, 12, SUN Pharma Advanced Research, 2, Amgen, 11, Lilly, 6, Celgene, 6, 12, Flexion, 2, 6, Genzyme, 2, 6, 12, Merck, 6, 12, UCB, 6, Horizon, 6, 12; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **M. Bowes**, Imorphics, 3, 11, Novartis, 5, Pfizer, 5, Stryker, 3; **A. Brett**, Stryker, 3, 8, 11; **V. Kraus**, Novartis, 2, Paradigm Biopharma, 2, Gilead, 2, Flexion Therapeutics, Inc., 2, Zimmer Biomet, 5; **W. Maloney**, AAOS, 4, Flexion Therapeutics, Inc., 2, 11, Knee Society, 4, Stryker, 2, 9, 10, TJO, 11, Western Orthopedic Association, 4, Zimmer, 9, 10; **J. Parvizi**, Accumed, LLC, 11, Alphaeon, 11, Becton Dickenson, 12, Publishing royalties, financial or material support, Cerebell, 11, Corentec, 2, 9, 10, 11, Datatrace, 12, Publishing royalties, financial or material support, Elsevier, 12, Publishing royalties, financial or material support, Ethicon, 2, Fidia Pharm, 2, Heraeus, 2, Hip Innovation Technology, 11, Intellijoint, 11, Jaypee Publishers, 12, Publishing royalties, financial or material support, Joint Purification Systems, 11, Jointstem, 2, KCI / 3M (Acelity), 2, MD-Valuate, 11, MicroGenDx, 2, 11, Molecular Surface Technologies, 11, Nanooxygenic, 11, Parvizi Surgical Innovations and Subsidiaries, 11, Peptilogics, 2, PRN-Veterinary, 11, SLACK Incorporated, 12, Publishing royalties, financial or material support, Sonata, 11, Tenor, 2, Wolters Kluwer Health - Lippincott Williams & Wilkins, 12, Publishing royalties,

financial or material support, Zimmer Biomet, 2; **A. Cinar**, Flexion Therapeutics ,Inc., 3, 11; **N. Bodick**, Flexion Therapeutics, Inc., 2, 11; **S. Kelley**, Flexion Therapeutics, Inc., 3, 11.

Abstract Number: 0732

Topical Rofecoxib for OA of the Knee

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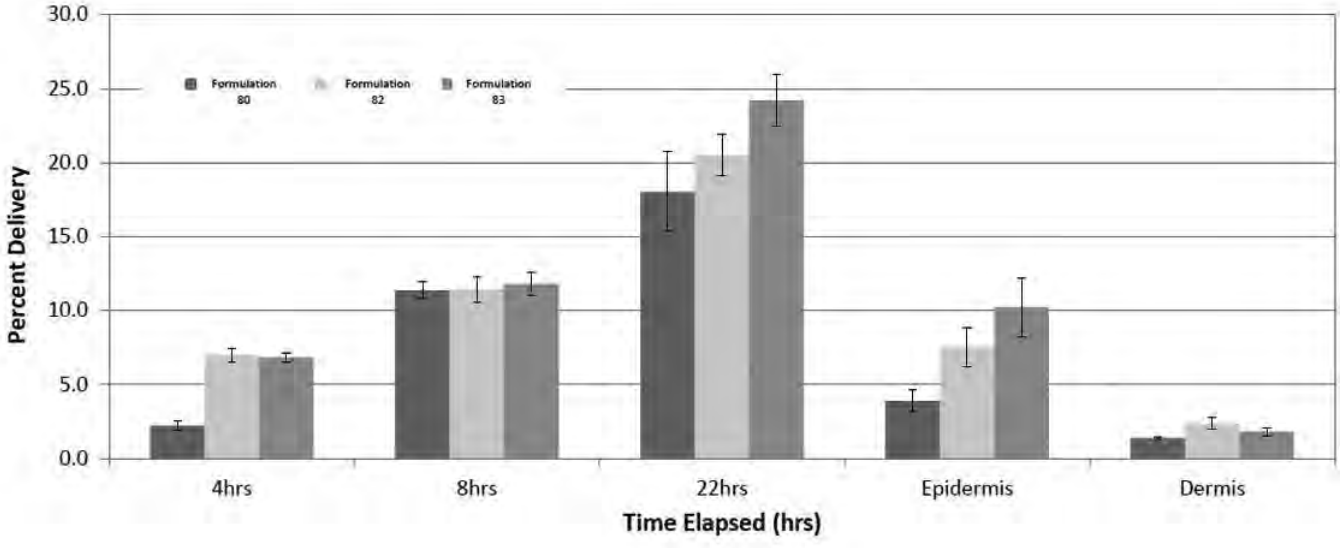
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis remains a highly prevalent disease in the elderly, and there are currently no approved treatments that can modify the disease course. Currently, both oral and topical nonsteroidal anti-inflammatory drugs (both COX-1 and COX-2 inhibitors) are frequently utilized to reduce pain and joint inflammation. These studies were done to demonstrate that rofecoxib topical may be an effective topical pain therapy.

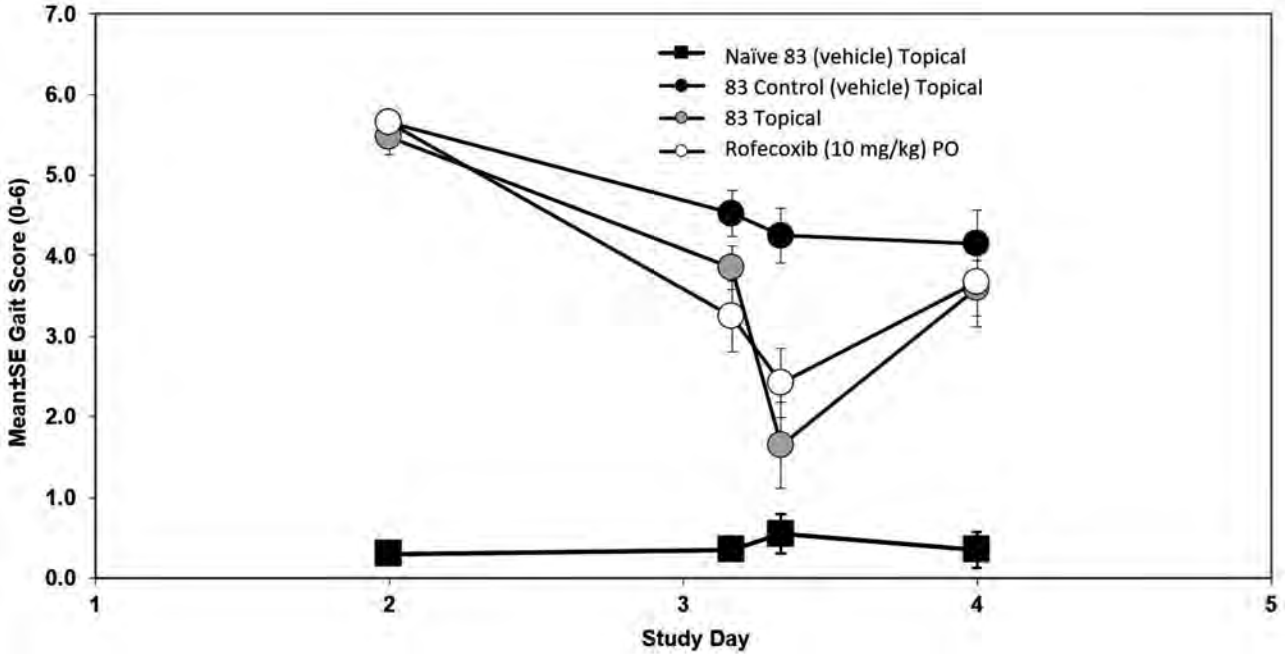
Methods: Three non-clinical experiments were performed to assess the utility of this newly formulated rofecoxib topical. The first experiment studied permeation across human cadaver skin, the second assessed the pain relief obtained in a rat inflammatory joint model, while a third experiment studied the dermal irritation and bioavailability of the topical drug.

Results: Human skin Franz diffusion cell studies (Figure 1) were performed using human cadaver skin. Rofecoxib transferences of 6% at 4 hours and up to 24% at 22 hours were measured. Topical Rofecoxib was tested in an

Figure 1



Human skin permeation of rofecoxib topical formulations.



Rat inflammatory joint model of rofecoxib topical.

adjuvant-induced model (Figure 2) of pain in Rats. Day 0. Rats were weighed and randomized by body wight. The animals were then anesthetized and injected with Freund's complete adjuvant into right rear joint to create severe joint inflammation and pain. Day 2. Rats were randomized by gait into groups of 10 with a score of "0" (normal) to "6" (hopping or carrying the leg). Day 3. Rats were dosed on the skin over the joint with: A. Ointment control (no API) on naive rats 100ul B. Ointment control (no API) C. Ointment with 2% API on test rats 100ul (1mg) D. Oral rofecoxib 10mg/kg. Following dosing the rats were gated for pain at 4, 8 and 24 hours. As shown in figure 2 at 8 hours topical rofecoxib showed efficacy equal to or greater than a super dose of oral rofecoxib. Study 3 was a Seven-Day Skin Irritation and Bioavailability Mini-Pig PK study (Table 1). Hanford miniature swine were dosed with topical rofecoxib for bioavailability. On day one 1.25ml of a 2% ointment was applied (25mg) to the 10% of the mini-pigs skin and a 24-hour pk study was done. On days 2 – 7 two applications of 1.25ml of the 2% ointment were applied and a 24-hour pk study was done on day 7. Draize scores for all animals through the end of the study on day 7 were all 0. One set of minipigs was dosed with 0.1mg/kg oral rofecoxib equivalent to a 12.5mg human dose of rofecoxib. The Day 1 t_{max} was the same as the oral rofecoxib demonstrating rapid absorption through the skin. The C_{max} on Day 1 was 15%

Table 1

C_{max} ng/ml	Day 1	% of Oral	Day 7	% of Oral
Oral (0.2mg/kg)	91.0		141.0	
Releven 2%[a]	14.5	15.9%	29.9	20.9%
AUC (ng*hours/ml)	**Day 1**	**% of Oral**	**Day 7**	**% of Oral**
Oral	610		579	
Releven 2%	39.5	6.4%	237	41.0%
t_{max} (hours)	**Day 1**		**Day 7**	
Oral	4.0		2.0	
Releven 2%	4.0		14.0	

Bioavailability of the topical rofecoxib.

of the oral and the AUC 6.4% of oral which will provide sufficient rofecoxib to the local area of inflammation for pain relief. The Day 7 C_{max} and AUC are significantly below the oral dose of rofecoxib reducing systemic exposure and potential side effects. No skin irritation was observed.

Conclusion: These data demonstrate that that topical rofecoxib diffuses through human skin rapidly resulting in a dose that provides pain relief in a rat model of inflammatory arthritis. In addition, the topical dosing in mini pigs has been shown to have a lower systemic exposure then oral rofecoxib given at the lowest approved human dose. These results suggest topical rofecoxib may be an effective topical analgesic.

Disclosure: B. **Register**, BriOri BioTech, 3, 8, 10; **N. Lane**, Amgen, 2, Pfizer, 2, BriOri Biotech, 4, Makikroft, 2, 6, GSK, 2, UCB, 1; **L. Simon**, eupraxia, 2, samumed, 2, horizon, 2, xalud, 2; **J. Newsam**, Encube Ethicals, Inc., 12, Employee of wholly-owned subsidiary; **E. Kisak**, Encube Ethicals, 12, Employee of wholly-owned subsidiar; **J. Pheneger**, None; **J. Galvin**, None; **J. Klein**, None; **M. Hochberg**, BriOri Biotech, 1, 2.

Abstract Number: 0733

A New Wearable Transcutaneous Electrical Nerve Stimulation Device (actiTENS®) Is More Efficient and Better Tolerated Than Weak Opioids in the Treatment of Knee Osteoarthritis Pain

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

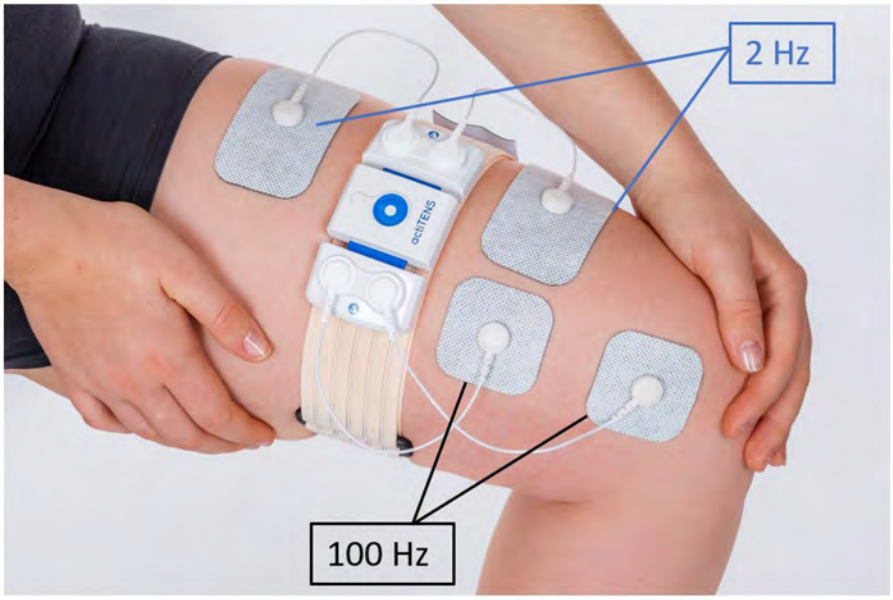
Background/Purpose: Knee osteoarthritis (KOA) is a frequent disease for which therapeutic possibilities are limited. In current recommendations, the first-line analgesic is acetaminophen. However, its low efficacy frequently leads to the use of weak opioids (WO) despite their poor tolerance, especially in elderly patients.

The primary objective was to compare the analgesic efficacy and safety of a new wearable transcutaneous electrical nerve stimulation (W-TENS) to weak opioids (WO) in the treatment of moderate to severe, nociceptive, chronic pain in KOA patients.

Methods: ArthroTENS study is a non-inferiority, multicentric, prospective, randomized, single-blinded for primary efficacy outcome, controlled, 2-parallel groups, clinical study. It compared W-TENS to WO over a 3-month controlled period with an additional optional non-controlled 3-month follow-up in W-TENS group.

Patients had KOA (ACR criteria) with baseline pain intensity (PI) ≥4 on a numerical rating scale (NRS), after failure to level 1 analgesics/NSAIDs, a Kellgren-Lawrence grade ≥2 and were assessed at baseline, M1 and M3.

The co-primary outcomes were PI at 3-month and the number of treatment-related adverse events (TRAEs) over 3 months. Secondary outcomes included WOMAC function, EuroQol, responder rates defined by PI reduction ≥30 and ≥50% and OMERACT-OARSI response criteria. The non-inferiority margin was defined as 0.825 on PI reduction.



Standardized positioning of W-TENS electrodes.

Measure population	W-TENS	WO	W-TENS - WO	
PP population				
n	52	47		Non inferiority demonstrated 95% CI < 0.825
Mean (SD)	3.87 (2.12)	4.65 (2.37)	-0.79 (0.44)	
95% CI	[3.28, 4.46]	[3.96, 5.35]	[-1.65, 0.08]	
ITT population				
n	55	55		Non inferiority demonstrated 95% CI < 0.825
Mean (SD)	3.84 (2.08)	4.73 (2.28)	-0.92 (0.40)	
95% CI	[3.27, 4.40]	[4.11, 5.35]	[-1.71, -0.12]	

Non-inferiority analyses on PI at M3. PP and ITT populations.

In W-TENS group, an advanced, mobile app enabled, wearable TENS was used. 100Hz and 2 Hz frequency stimulations were delivered via electrodes with standardized positioning (Figure 1).

Results: The non-inferiority of W-TENS was demonstrated in both the PP and ITT populations (Table 1). At M3, PI in PP population was 3.87 (2.12) compared to 4.66 (2.37) (delta: -0.79 (0.44); 95% CI (-1.65; 0.08)) in W-TENS and WO groups, respectively. Since the absolute value of the 95% CI of the between-treatments mean PI difference [-1.71, - 0.12] was above 0 in ITT set, the planned superiority analysis was performed, demonstrating that W-TENS was significantly superior to WO at M3 (P=0.0124).

In the ITT population, the number of potentially TRAEs was significantly lower (p< 0.001) in the W-TENS group (n=7) than in the WO group (n=36) during the 3-month controlled follow-up. The AEs observed in the W-TENS group were mainly local cutaneous reactions (erythema: 5.5%) due to the TENS technique, while those observed in the WO group were systemic and well known (dry mouth: 1.8%; vomiting: 1.8%; pruritus: 3.6%; dizziness: 5.5%; drowsiness: 7.3%; nausea: 10.9% and constipation: 12.7%) and limit their use and effectiveness in clinical practice. Thirty-nine (70.9%) patients wished to extend W-TENS treatment for 3 additional months. The efficacy was maintained throughout this additional therapeutic period. All secondary outcomes favored the W-TENS group at M1 and M3.

Conclusion: W-TENS was more effective and better tolerated than WO in the treatment of nociceptive KOA chronic pain and could represent an interesting non-pharmacological analgesic alternative for patients.

Disclosure: E. Maheu, SUBLIMED, 2, 6, TRB Chemedica, 6, MEDA-MYLAN, 2, CELGENE, 2, EXPANSCIENCE, 2, FIDIA, 2, PIERRE FABRE, 6; **S. Soriot-Thomas**, SUBLIMED, 2, 4, 5, 10, Grunenthäl, 2, 4, 5, 6; **E. Noël**, SUBLIMED, 2, Regenlab, 2; **H. Ganry**, SUBLIMED, 2, Ludocare, 2, UCB, 2, Grunenthäl, 2; **E. Lespessailles**, SUBLIMED, 2, MSD, 2, 5, THERAMEX, 2, ABBVIE, 2, 6, LILLY, 2, 6, NOVARTIS, 2, 6, GALAPAGOS, 2, 6, JANSSEN, 2, PFIZER, 6, AMGEN, 2, 6, UCB, 2, CELGENE, 5; **B. Cortet**, SUBLIMED, 2, Alexion, 6, Amgen, 6, Aptissen, 6, Expanscience, 6, Lilly, 6, Kyowa-Kirin, 6, Viatris, 6, MSD, 6, Novartis, 6, Theramex, 6, UCB, 6.

Abstract Number: 0734

Primary Total Knee Arthroplasty for Knee Osteoarthritis Among Younger versus Older Individuals: Cross-sectional Study of Surgical Appropriateness and Surgeon Decision-Making

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Rising rates of total knee arthroplasty (TKA) in younger adults with knee osteoarthritis (OA) has prompted concern about surgical appropriateness. We compared patient appropriateness for TKA, using previously validated criteria, and surgeons' recommendations for TKA, by patient age.

Methods: This cross-sectional study recruited patients with knee OA referred for TKA consultation to two centralized provincial arthroplasty intake centers in Alberta, Canada. Patients aged 30 years or older and determined by the surgeon to have primary knee OA on physical examination and imaging were eligible. Individuals with inflammatory arthritis were excluded. To examine age effects, recruitment continued until there was at least 200 individuals aged 30-59, 60-69 and ≥ 70 years. A pre-consult questionnaire assessed measures of patients' TKA appropriateness (need: knee symptoms, prior OA treatment; readiness/willingness to undergo TKA; health status; expectations) and contextual factors. Post-consultation, surgeons reported if TKA had been recommended and if not, why. Using multivariable logistic regression, we assessed the relationships between patient age (< 60 versus ≥ 60) and TKA appropriateness and receipt of surgeon recommendation for TKA.

Results: Of 2,064 participants, 26.0% were < 60 years of age, 68.0% female, 35.6% employed. Compared to older participants, younger participants reported significantly worse knee symptoms, higher use of OA therapies and similar TKA readiness/willingness. They were also more likely to have BMI >40 kg/m^2, smoke and endorse return to exercise/sports as a very important TKA outcome. TKA was offered to 1,525 individuals (73.9%). In multivariable analyses, controlling for TKA appropriateness, we found no relationship between patient age and surgeons' recommendations for TKA (OR, odds ratio, 0.81; 95% CI, confidence interval, 0.59 to 1.10). Surgeons were significantly

more likely to recommend TKA to those with TKA need, willingness and for whom improved ability to perform daily activities was very important. They were less likely to recommend surgery to smokers and for whom return to exercise/sport was important.

Conclusion: Among individuals referred for surgical consultation regarding TKA for knee OA, we found that younger patients (< 60 years old) had comparable TKA need, readiness and willingness as those aged 60 years or older. However, younger individuals were more likely to be obese, smoke, and desire to return to sport after TKA, which may increase risk for complications, including early revision. Incorporation of TKA appropriateness criteria into patient referral and patient-surgeon decision-making regarding TKA has potential to facilitate a balanced consideration of TKA benefits alongside the risks in a growing population of young, obese individuals with knee OA.

Disclosure: G. Hawker, None; **E. Bohm**, None; **M. Dunbar**, None; **A. Jones**, None; **T. Noseworthy**, None; **D. Marshall**, None.

Abstract Number: 0735

Walking Ability 12 Months After Total Knee Arthroplasty for Osteoarthritis – Gap Between Expectations and Reality: The BEST Knee Cohort Study

Lauren King, Esther Waugh and Gillian Hawker, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Improved ability to walk is a key driver for people with knee osteoarthritis (OA) to seek total knee arthroplasty (TKA). However, the extent to which patients' expectations of walking improvement are met following TKA is unknown. In individuals with knee OA undergoing primary TKA, we assessed: 1) pre-TKA expectations about walking ability and gait aid use after TKA; 2) TKA patient-reported improvement in walking ability and gait aid use pre-TKA and 12 months post-TKA; and 3) whether gender differences were present.

Methods: Participants with knee OA completed standardized questionnaires 1 month prior to and 12 months after primary, elective TKA. Pre-TKA, we assessed sociodemographic and clinical characteristics and patients' expectations for TKA (Hospital for Special Surgery Expectations Survey). Participants were asked to indicate how important "improved ability to walk" and "removed need for a gait aid" were to them as TKA outcomes (very important, yes/no). Both pre- and post-TKA, we assessed for perceived walking limitation (yes/no), gait aid use (yes/no) and walking ability (unlimited, 6-10 blocks, 1-5 blocks, < 1 block). At 12 months post-TKA, we assessed perceived change in walking ability (8-point Likert scale from "extremely worse" to "extremely better"). Values pre- and post-TKA were compared using McNemar tests. Chi-square tests compared gender differences in walking expectations pre-TKA and perceived walking ability at 12 months.

Results: 278 participants were included: mean age 67 years (SD 8.5), and 65.5% female. Pre-TKA, 97.5% indicated it was "very important" that TKA improve ability to walk and, of these, 98.1% desired to be able to walk medium-to-long distances. Of 68 (24.5%) who were using a gait aid pre-TKA, 84.0% indicated it was "very important" that TKA remove their need for one. At 12 months post-TKA, 73.6% reported walking "a lot" or "extremely better". Overall,

Table 1. Walking ability 1 month prior to and 12 months after total knee arthroplasty (n=278)

Variable	Pre-TKA	12mo post-TKA	p-value
Patient-reported walking ability			
Perceived distance can walk continuously, n (%)			<0.001
Unlimited	17 (6.16)	102 (37.09)	
6-10 blocks	55 (19.93)	85 (30.91)	
1-5 blocks	160 (57.97)	76 (27.64)	
<1 block	44 (15.94)	12 (4.36)	
Reported usual need for gait aid with waking, n (%)	81 (29.14)	50 (18.00)	0.002
Perceived limitation in walking ability, yes, n (%)	232 (83.45) *Of these 216 (93.51%) indicate due to knee*	90 (32.37) *Of these, 19 (21.11%) indicate due to knee*	<0.001
Patient reported change in walking ability after TKA			
Perceived change in walking ability, n (%)			
Extremely worse		-	
A lot worse		2 (0.72)	
Somewhat worse		6 (2.17)	
No change		20 (7.25)	
A little better		14 (5.07)	
Somewhat better		31 (11.23)	
A lot better		93 (33.70)	
Extremely better		110 (39.86)	

68.0% reported they could walk 6 or more city blocks, 60.5% of gait aid users pre-TKA no longer required one, and 67.6% reported no walking limitation; of those who did, only 21.1% ascribed the walking limitation to their operated knee (**Table 1)**. Pre-TKA, women and men had similar expectations of TKA to improve their ability to walk, but post-TKA, women were less likely to report being "unlimited" in walking ability compared to men (32.4% vs 46.2%, $p< 0.03$) and more likely to require a gait aid (21.4% vs 11.46%, $p< 0.04$).

Conclusion: This study confirmed the importance of improved ability to walk as a surgical outcome to patients undergoing TKA for knee OA, and elucidated that most expected TKA to enable walking medium to long distances. However, only two-thirds reported the ability to walk long distances post-TKA. A better understanding of causes of persistent walking limitation after TKA, as well as ways in which this can be addressed, are needed to support individuals with knee OA in meeting their walking expectations.

Disclosure: L. King, None; **E. Waugh**, None; **G. Hawker**, None.

Abstract Number: 0736

Decrease in Prevalence of Self-Reported Anxiety or Depression in Persons with Osteoarthritis After Total Knee Arthroplasty: The BEST KNEE Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: While anxiety and depression are highly prevalent in persons with symptomatic knee osteoarthritis (OA), few studies have assessed the effect of treatment of knee OA on these mood disorders. Further, it remains unclear which individuals will continue to have persistent anxiety and/or depression after OA treatment, limiting targeted intervention. Thus, the objectives of this study were to, in individuals with knee OA undergoing primary total knee arthroplasty (TKA): (1) describe the proportion of patients who report being anxious or depressed (A/D) pre TKA, 6 months post TKA, and 12 months post TKA; and (2) determine, in those with self-reported A/D pre TKA, the factors associated with persistence of mood disorder at 12 months post TKA.

Methods: In this prospective cohort study, patients with knee OA were assessed one month pre- and 6 and 12 months post-TKA. Questionnaires assessed sociodemographic factors, knee OA symptoms, comorbidities, and psychosocial factors. We assessed prevalence of self-reported A/D using the Anxiety/Depression dimension of the EQ-5D-3L. Self-reported A/D was defined as reporting being moderately or extremely anxious or depressed. Among individuals with self-reported A/D pre TKA, multivariable Poisson regression with a robust error variance was used to assess the association of sociodemographic factors, comorbidities, psychosocial factors, and knee OA symptoms with persistence of self-reported A/D at 12 months post TKA.

Results: 1259 patients were included: mean age 67.2 years, 60.8% female, mean pre TKA WOMAC pain 57.6 (SD 17.4) /100, and mean pre TKA KOOS-PS physical function 53.3 (SD 17.3)/100 (higher scores worse). The mean change from pre TKA to 12 months post TKA in WOMAC pain was -42.7 (SD 21.9), and in KOOS-PS was -29.6 (SD 21.5). Prevalence of self-reported A/D pre TKA was 624 (49.6%), at 6 months was 278 (22.1%), and at 12 months was 254 (20.2%). Of the 624 participants with self-reported A/D pre TKA, 197 (31.6%) self-reported A/D 12 months post TKA. In multivariable regression, persistence of A/D at 12 months post TKA was associated with reporting higher levels of knee OA pain post TKA (RR per WOMAC unit 1.02, 95% CI 1.01 to 1.03), greater knee OA functional impairment post TKA (RR per KOOS-PS unit 1.01, 95% CI 1.00 to 1.03), less pre TKA self-efficacy (RR per unit General Self-Efficacy Scale 0.97, 95% CI 0.94 to 0.99), and the presence of a pre TKA depression diagnosis (RR 1.89, 95% CI 1.44 to 2.48). Analyses stratified by sex, age (< 60/≥60 years), obesity, and reporting a prior diagnosis of depression were not appreciably different from the primary model.

Conclusion: A large proportion of individuals with knee OA report being anxious or depressed pre TKA. Of these individuals, greater than two-thirds report resolution of their mood disorder by 12 months post TKA. We found a higher risk of persistence in individuals with worse knee OA symptoms post TKA and among those with less self-efficacy. However, the strongest factor associated with persistence of A/D was a previous diagnosis of depression suggesting a group of individuals whose depression may not be related to their OA and would benefit from targeted mental health interventions to improve mood outcomes.

Disclosure: O. **Krystia**, None; **L. King**, None; **E. Waugh**, None; **G. Hawker**, None.

Abstract Number: 0737

Enhanced Arthrocentesis of the Flexed Knee with Pneumatic Compression

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

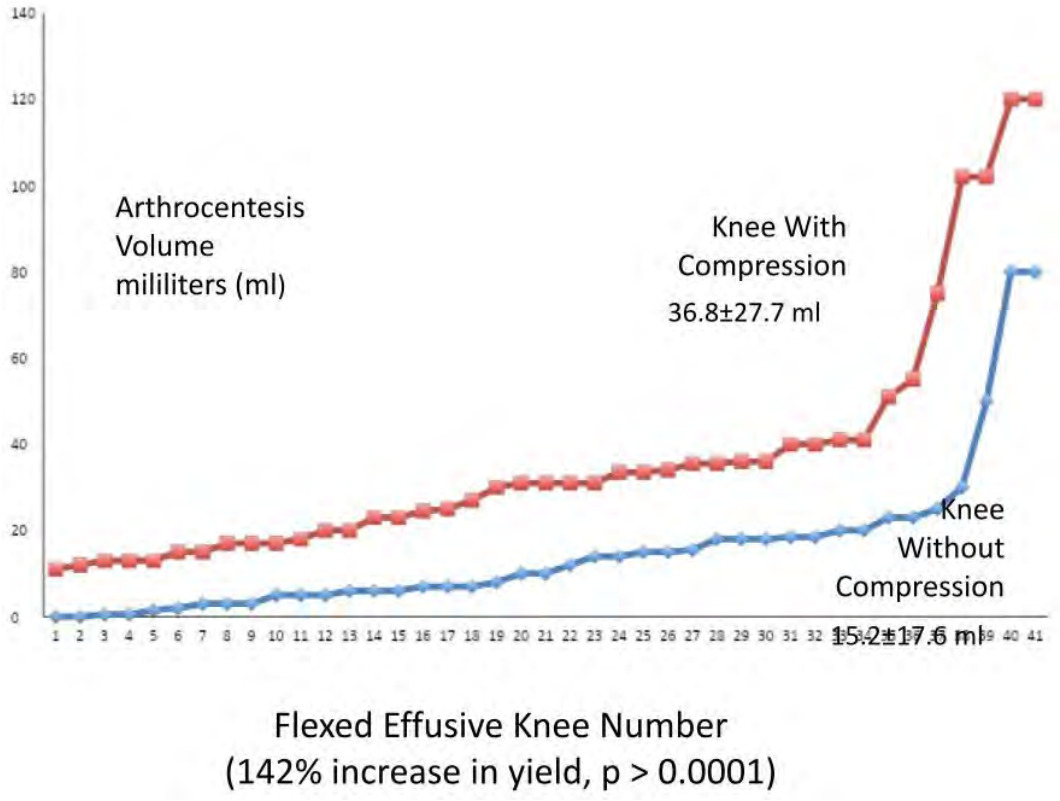
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)

Session Type: Poster Session B

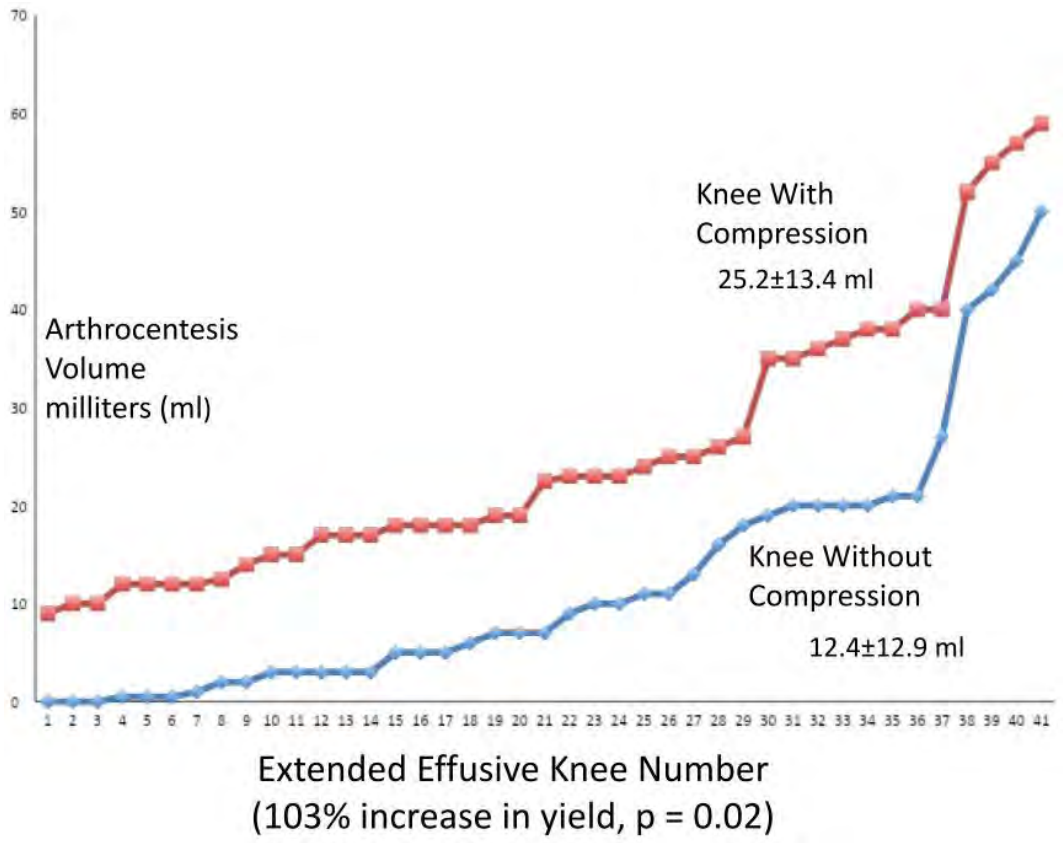
Session Time: 8:30AM–10:30AM

Background/Purpose: To explore an alternative to standard extended knee arthrocentesis using pneumatic compression of the flexed knee.

Methods: Using a paired sample design, 41 consecutive effusive knees underwent arthrocentesis in the flexed knee position first without and then with pneumatic compression of suprapatellar bursa. Arthrocentesis success and fluid yield in milliliters (ml) were measured. For comparison 41 consecutive patients who had undergone extended knee arthrocentesis without and with compression were also studied.



These graphs demonstrate the fluid yield with and without pneumatic compression of the flexed knee using the inferiolateral portal. Pneumatic compression causes a marked increase in fluid yield.



These graphs demonstrate the fluid yield with and without mechanical compression of the extended knee using the superiolateral portal (suprapatellar approach). Mechanical compression causes a marked increase in fluid yield similar to the increase in fluid yield with pneumatic compression shown in Figure 1.

Results: Successful diagnostic arthrocentesis (≥ 3 ml) of the effusive flexed knee was 85% (35/41) without compression and increased significantly to 100% (41/41) with pneumatic compression (p=0.027). Synovial fluid yields were significantly greater with pneumatic compression (36.8±27.7 ml) than without compression (15.2±17.6 ml) (increase of 142% or 21.6±17.6 ml more; 95% CI: 13.0 < 23.4< 33.8, p< 0.0001). Arthrocentesis yield for the extended knee position without compression (12.4±12.9 ml) was similar to the flexed knee without compression (15.2±17.6 ml; 95% -9.9412 < -3.1< 3.7412 (Wald) p=0.36). Arthrocentesis yield for the extended knee with compression (25.2±13.4 ml) was enhanced by 108% (12.8±13.2 ml) similar to the flexed knee with compression (142%, 21.6±17.6 ml).

Conclusions: Compression of the effusive flexed knee with a suprapatellar pneumatic cuff markedly improves the success and fluid yield of arthrocentesis and is non-inferior to standard extended knee arthrocentesis with or without compression. Arthrocentesis of the flexed knee with pneumatic compression is especially useful in patients who wish to remain seated or who cannot extend their knee due to flexion contracture, wheelchair confinement, pain or severe arthritis.

Conclusion: For individuals with knee contractures, the obese, wheelchair-bound individuals, the elderly, or those apprehensive individuals who involuntarily and forcefully contract the quadriceps muscles during a procedure, the standard extended knee superiolateral approaches for arthrocentesis can be difficult and/or inconvenient. Compression of the effusive flexed knee with a suprapatellar pneumatic cuff markedly improves the success and fluid yield of arthrocentesis and is non-inferior to standard extended knee arthrocentesis with or without compression. This pneumatic compression method that permits the patient to remain in the sitting position or equivalent with a flexed knee, but provides high levels of arthrocentesis success and fluid yield will be of obvious clinical utility.

Table 1. Clinical and Research Characteristics of the Study Populations

	Extended knee	Extended knee with compression	Flexed Knee	Flexed Knee with Compression
Number of Subjects	41	41	41	41
Age	62.0±11.3	62.0±11.3	66.8±12.1	66.8±12.1
Osteoarthritis of the knee	100% (41/41)	100% (41/41)	100% (41/41)	100% (41/41)
Male:Female Ratio	9:32 (65% female)	9:32 (65% female)	5:36 (89% female)	5:36 (89% female)
Preprocedural Pain (cm)	7.7± 1.1	7.7± 1.1	7.9 ± 1.5	7.9 ± 1.5 cm
Procedural Pain (cm)	2.4±1.5	2.4±1.5	4.4±2.2	4.4±2.2
Post-Procedural Pain (cm)	1.3±2.0	1.3±2.0	1.4±1.7	1.4±1.7
Diagnostic Arthrocentesis ≥ 3 ml	80 % (33/41)	100% (41/41)	85% (35/41)	100% (41/41)
Synovial Fluid Yields (ml)	12.4±12.9	25.2±13.4	21.6±17.6	36.8±27.7

Disclosure: S. Brahmbhatt, None; **A. Iqbal**, None; **F. Farshami**, None; **M. Muruganandam**, None; **J. Trost**, None; **D. Cisneros**, None; **A. Kiani**, None; **N. Emil**, None; **S. Nunez**, None; **W. Hayward**, None; **P. Band**, None; **W. Sibbitt**, None.

Abstract Number: 0738

Therapeutic Effects of Oral Chinese Patent Medicine on Knee Osteoarthritis

Weiheng Chen[1], Mengge Song[1], **Yan Jia**[1], Jigao Sun[1], Yan Zhao[2], Zhipeng Xue[3], Qianglong Chen[2], xiangrong Zeng[2] and Chenchen Wang[4], [1]The Third Affiliated Hospital of Beijing University of Chinese Medicine, Beijing, China (People's Republic), [2]2Wangjing Hospital, China Academy of Chinese Medical Sciences, Beijing, China (People's Republic), [3]1The Third Affiliated Hospital of Beijing University of Chinese Medicine, Beijing, China;, Beijing, China (People's Republic), [4]Tufts Medical Center, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Osteoarthritis – Clinical Poster II (0723–0738)
Session Type: Poster Session B
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Background/Purpose: Oral Chinese patent medicine (CPM) has been deemed to have analgesic and anti-inflammatory effects and is widely used as the first-line treatment for osteoarthritis (OA) in Asia countries. Despite this enthusiastic use of CPM for knee OA, its clinical efficacy remains unclear. We conducted an updated review to determine the effects of these therapies to inform clinical practice.

Methods: We performed a comprehensive search on PubMed, Cochrane Library, EMBASE, Biomedical Databases, National Knowledge Infrastructure, Wanfang, and VIP through May 2021. We included randomized controlled trials (RCTs) of oral CPM therapies as the first-line treatment in adults with knee OA. Knee OA was defined by the American College of Rheumatology criteria or the Chinese orthopedic association criteria. We also accepted the composite outcome criteria developed by the Chinese National Institute of Rheumatology as an endpoint (total effective rate,

Table 1: Eighteen RCTs of oral Chinese Patent Medicine for Knee Osteoarthritis

Author, Year	N[a]	Age[b] (yr)	Oral CPM group (Formula, Dose)[c]	Controls	Duration (wks)	Outcome Measures	Effect on Symptom (std. Mean Difference or Percentage Improvement)[d]	P value
Teekachunhateam S, 2004	200	63	Duhuo Jisheng Pill, 3g, 3 times/ day	Diclofenac, 25mg, 3 times/day	4	VAS pain Lequesne	0.18 ↓ 0.88 ↓	>0.05 >0.05
Xiao E, 2006	50	56	Jinwu Gutong Capsule, 1.5g, 3 times/ day	Ibuprofen, 200mg, 3 times/ day	4	Chinese composite Outcome	Treatment effect: ↑ 93.3% vs. 84.2%	< 0.05
Tao, 2008	80	53	Jinwu Gutong Capsule, 1.5g, 3 times/ day	Celebrex, 200mg, once/day	4	VAS pain Chinese composite outcome	-0.65 ↑ Treatment effect: ↓ 88% vs. 90%	< 0.05 > 0.05
Liang H, 2009	210	49	Biqi Capsule, 1.2g, 2-3times/ day	Meloxicam tablets, 7.5mg, twice/day	4	Chinese composite Outcome	Treatment effect: ↑ 93.3% vs. 75.0%	< 0.05
Shi, 2010	120	40-80	Jinwu Gutong Capsule, 1.5g, 3 times/ day	Diclofenac, 75mg, once/day	4	VAS pain Chinese composite outcome	-0.42 ↑ Treatment effect: ↑ 88.3% vs. 86.7%	< 0.05 >0.05
Liu, 2011	80	41-75	Biqi Capsule, 1.2g,3 times/ day	Diclofenac, 75mg, twice/day	4	Chinese composite outcome	Treatment effect: ↑ 92.5% vs. 62.5%	<0.05
Wang GY, 2013	72	66	Jintiange Capsule, 1.2g, 3 times/ day	Ibuprofen, 0.3g, twice/ day	12	Chinese composite outcome	Treatment effect: ↑ 75.0% vs. 44.4%	<0.05
Cao, 2015	60	62	Jintiange Capsule, 1.2g, 3 times/ day	Acetachlofenac, 0.1g, twice/day	4	Lequesne Chinese composite outcome	0.34 ↓ Treatment effect: ↓ 86.7% vs. 89.7%	>0.05 >0.05
Hu, 2015	60	57	Zhuanggu Guanjie Capsule, 0.9g, twice/day	Celebrex, 200mg, once/day	4	VAS pain Lequesne Chinese composite outcome	0.05 ↓ -2.70 ↑ Treatment effect: ↑ 93.3% vs. 73.3%	<0.05 <0.05 <0.05
Zhang XL , 2016	276	56	Zhuanggu Guanjie Capsule, 0.9g, twice/day	Celebrex, 200mg, once/day	4	Chinese composite outcome	Treatment effect: ↑ 89.7%vs. 89.2%	> 0.05
Niu, 2016	210	59	Jinwu Gutong capsule, 1.5g, 3 times/ day	Diclofenac, 100mg, once/day	4	VAS pain	-1.41 ↑	< 0.05
Zhou, 2017	78	53	Jintiange Capsule, 1.2g, 3 times/ day	Glucosamine, 60mg, twice/day	12	VAS pain Lequesne	0.01 ↓ -0.12 ↑	>0.05 >0.05
Zhang, 2017	76	63	Jinwu Gutong Capsule, 1.5g, 3 times/ day	Diclofenac, 75mg, once/day	4	Chinese composite outcome	Treatment effect: ↑ 94.7% vs. 68.4%	< 0.01
Peng, 2018	60	54	Jintiange Capsule, 1.2g, 3 times/ day	Etexoxib, 60mg, once/day	12	WOMAC pain Chinese composite outcome	-0.84 ↑ Treatment effect: ↑ 90.0% vs. 86.7%	<0.05 >0.05
Xiao DW, 2018	90	61	Jintiange Capsule, 1.2g, 3 times/ day	Piroxicam, 10mg, twice/day	12	Lequesne Chinese composite outcome	-2.50 ↑ Treatment effect: ↑ 84.4% vs. 55.6%	<0.05 <0.05
Liang ZL, 2018	120	73	Jintiange Capsule, 1.2g, 3 times/ day	Diclofenac sodium enteric-coated tablet, 25mg, 3 times/ day	4	WOMAC Pain	0.16 ↓	>0.05
Wang F, 2018	534	63	Xianling Gubao Capsule, 1.5g, twice/ day	Blank control	24	WOMAC pain	-0.78 ↑	<0.001
Wang LF, 2019	98	60	Zhuanggu Guanjie Capsule, 0.9g, twice/day	Celebrex, 200mg, once/day	4	VAS pain Lequesne Chinese composite outcome	-1.25 ↑ -2.64 ↑ Treatment effect: ↑ 93.9% vs. 77.6%	<0.05 <0.05 <0.05

[a] N= number of patients included; [b] Age reported in years as a mean; [c] Six oral CPM with the Chinese herbs have potential benefits in knee pain relief and physical function; [d] Between group comparisons. Visual Analogue Scale (VAS, range 0-10), Western Ontario and McMaster Universities Arthritis Index pain scores (WOMAC pain, range 0-20) and the Lequesne index (range 0-24), where a lower score indicates a better outcome (less pain or better physical function).

between 0-100%, higher score = better outcome), which assesses the overall pain, physical function and wellness. We extracted information on study characteristics, population characteristics, type, duration, frequency of interventions, and outcomes. Study quality was assessed in RevMan5.3 software using the Cochrane Risk of Bias Tool. The differences between treatment groups were reported as mean change or percentage improvement (P-value).

Results: We identified 1096 potentially relevant studies. Eighteen with a total of 2474 subjects (59% female, mean age = 59 years, mean pain duration = 3 years) met eligibility criteria. Seventeen studies were conducted in China and one in Thailand. **Table 1** summarized the eighteen RCTs concerned with the effectiveness of oral CPMs for knee OA. Six types of oral CPMs including Jintiange Capsule, Jinwu Gutong Capsule, Zhuanggu Guanjie Capsule, Biqi Capsule, Xianling Gubao Capsule and Duhuo Jisheng Pill were prescribed as the first-line treatment based on the syndrome differentiation. The treatment varied duration from one to three times per day and lengths of the treatment ranged from 4 to 24 weeks. The control group treatments included oral non-steroidal anti-inflammatory drugs (17 studies) and placebo (1 study). Ten studies showed significant pain relief compared to the controls (std, Mean Difference [SMD] = -0.50; 95% CI, -0.86 to -0.13; $p< 0.05$). Thirteen studies reported a significant improvement in overall clinical symptoms on both pain and function (RR = 1.15; 95% CI, 1.09 to1.22; $p< 0.00001$). There were no significant differences in Lequesne index between the groups in six studies (MD = -1.11; 95% CI, -2.57 to 0.34; p=0.13). No serious adverse events occurred. Constipation was the most common adverse reaction in the oral CPM group, followed by dizziness, nausea, stomach discomfort and rash, and the incidence of adverse events was significantly lower than the controls.

Conclusion: This review showed promising results for oral CPM that is a safe and potential beneficial effects for knee OA. Further high-quality randomized controlled trials with longer follow-up periods are warranted.

Disclosure: W. Chen, None; **M. Song**, None; **Y. Jia**, None; **J. Sun**, None; **Y. Zhao**, None; **Z. Xue**, None; **Q. Chen**, None; **x. Zeng**, None; **C. Wang**, None.

Abstract Number: 0739

Contextual Factors Should Complete the Assessment of Functioning in Patients with Axial Spondyloarthritis (axSpA)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Functioning of axSpA patients (pat.) is influenced by many factors, but how contextual factors influence functioning isn't well studied. According to the International Classification of Functioning, Disability and Health (ICF), functioning is a complex interaction between health status and contextual factors such as social support, relationships and attitudes. Resulting from impaired functioning, pat. reporting barriers might face definite limitations in participation. Thus, limitations in participation as well as barriers and facilitators of contextual factors need to be investigated in axSpA pat.

Methods: axSpA pat. were standardized assessed, thereby collecting pat. and disease characteristics, patient-reported outcomes (ASDAS, BASFI, BASMI, PHQ-9, ICF Measure of Participation and ACTivities questionnaire

Table 1. Presence of contextual factors, stratified for global functioning categories Table legend (below table): values given as number (%), Reference: 1 Kiltz et al. Ann Rheum Dis 2013;72(s3):572

ICF category	EFIS Item	Correlation between EFIS item and ASAS HI sum score	Global Functioning (ASAS HI 0-17)		
			Good ≤ 5 (n= 69)	Moderate <5 to <12 (n= 106)	Poor ≥ 12 (n= 25)
e3, Support and relationship	EFIS 1: As a result of my rheumatic disease, the children take more responsibility for household tasks.	0.5	11 (15.9)	55 (51.9)	21 (84)
e3, Support and relationship	EFIS 2: I don't like the way my friends act around me.	0.4	0 (0)	15 (14,2)	12 (48,0)
e3, Support and relationship	EFIS 3: I can't count on my relatives to help me with my problems	0.2	11 (15,9)	24 (22,6)	9 (36)
e1 Products and technologies	EFIS 4: I modify my home and work environments.	0.2	16 (23,2)	47 (44,3)	9 (36)
e5, Health services, disease control	EFIS 5: I have difficulties getting worsening of my disease acknowledged by a health care professional	0.4	3 (4,3)	21 (19,8)	16 (64)
e5, Health services, time constraints	EFIS 6: Treatment of my rheumatic disease is taking up time	0.4	22 (31,9)	73 (68,9)	22 (88)
e4, Attitudes friends, negative	EFIS 7: My friends expect too much of	0.2	1 (1,4)	18 (17,0)	7 (28)
e4, Attitudes family	EFIS 8: No one pays much attention to me at home	0.1	10 (14,5)	20 (18,9)	7 (28)
e4, Attitudes friends, positive	EFIS 9: My friends understand me	-0.1	56 (17,4)	83 (78,3)	12 (48)

values given as number (%), Reference: 1 Kiltz et al. Ann Rheum Dis 2013;72(s3):572

(IMPACT-S (0-100%)), ASAS Health Index (ASAS HI and environment factor item set (EFIS) (1). The EFIS contains 9 dichotomous questions addressing ICF categories of products and technologies (e1), support and relationship (e3), attitudes (e4) and health services (e5). Prior to the analysis, EFIS 1, 4 and 8 were assumed to act as facilitators. Validated cut-offs of ASAS HI were used to categorize global functioning: good ≤ 5, moderate < 5 to < 12, poor ≥ 12.

Results: A total of 200 axSpA pat. were included: 69% males, 44.3±12.5 years, symptom duration 17.9±12.6 years, ASDAS 2.5±1.1, BASFI 4.0±2.7, BASMI 3.5±1.8, ASAS HI 7.0±4.1. Pat. reported limitations in the IMPACT-S activity and participation domain (82.3% (15.2) and 83.5% (16.8)), respectively. The majority of pat. reported that treatment of axSpA requires time (e4, 58.5%) as a barrier. Some pat. reported needs such as (a) the support by family members (e3, 43.5%), (b) to modify home and work environment (e1, 39.5%) and (c) the inreliability of family members for help (e3, 22%) as barriers. Some pat. (< 20%) reported (a) comprehension problems with health care professionals when experiencing a flare (e5, 18.5%), (b) inadequate care of pat. at home (e4, 18.5%), (c) disliking friends' behavior toward them (e4, 13.5%), and (d) too demanding friends (e4, 13%) as barriers. The majority of pat. (e4, 75.9%) identified attitudes of friends as the only and major facilitator. All pat. reporting at least one barrier, had significantly worse global functioning (ASAS HI, IMPACT-S), and depression (PHQ-9) compared to pat. reporting no barriers in the respective ICF categories ($p < 0.01$). Similarly, pat. with poor functioning are more likely to report barriers in contextual factors compared to pat. with good functioning (Table 1). Pat., who have to ask for more support from their families, expressed the feeling that they cannot rely on that.

Conclusion: Barriers of contextual factors are more present in axSpA pat. than facilitators. This study shows that barriers of contextual factors are more common in pat. with impairments in self-reported and performed functioning as in those without impairments, underlining the importance of contextual factors in the management of axSpA pat. The controversial response to EF-Items 1, 4 and 8 suggests relevant differences in the individual interpretation of these questions.

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Abstract Number: 0740

Rheumatologists' and Patients' Mental Models for Treatment of RA Explain Low Rates of TTT

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

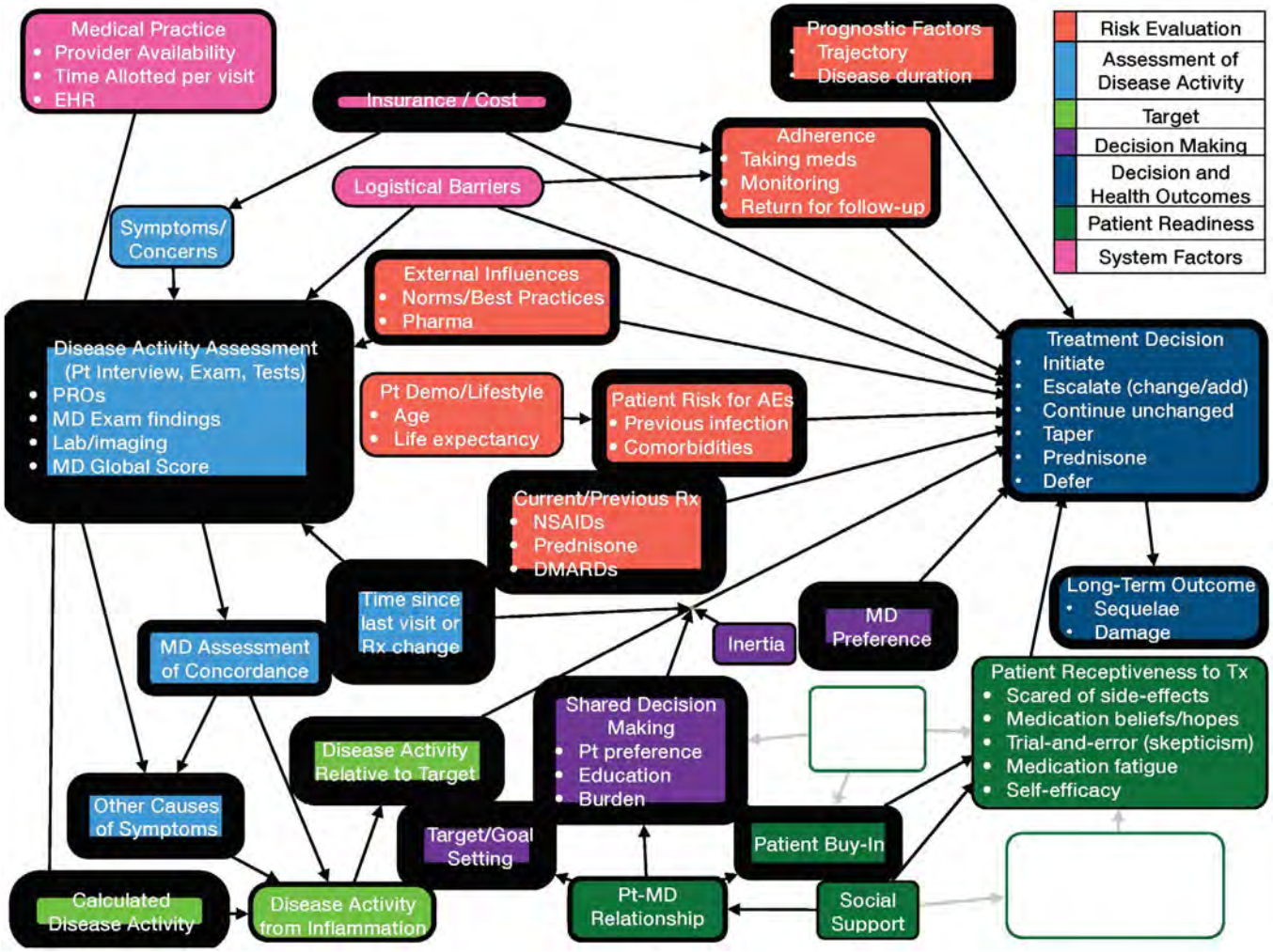
Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Concepts Raised by Physicians and Patients

Risk Evaluation	Physicians	Patients
Physician's Perceptions of Patient Adherence	29%	0%
• Returning for follow-up	43%	87%
• Taking medications	71%	47%
• Monitoring	43%	53%
Current or Previous Treatment	36%	7%
• DMARDs	86%	100%
• Non-steroidal anti-inflammatory drugs	7%	30%
• Prednisone	50%	37%
Patient Characteristics		
• Age	14%	3%
• Life expectancy	7%	0%
External Influences	50%	3%
• Norms/Best Practices	50%	3%
• Pharma	29%	30%
Prognostic Factors	71%	13%
• Disease duration	50%	0%
• DMARD response	36%	7%
• Trajectory	14%	7%
Patient Risk for Adverse Events	43%	3%
• Comorbidities	71%	7%
• Previous infection	50%	7%
Disease Activity Assessment		
Disease Activity Assessment	71%	3%
• PROs	86%	97%
• Physical exam findings	86%	80%
• Lab/imaging results	86%	87%
• Physician global assessment	36%	0%
Physician Assessment of Concordance between PROs and Exam	64%	10%
Causes other than RA of Symptoms or Exam/Lab Findings	71%	40%
Time Since Last Visit or Medication Change	93%	20%
Symptoms/Concerns	29%	90%
• Emotion-laden	0%	13%
Target		
Disease Activity Relative to Target	86%	83%
Calculated Disease Activity	93%	3%
• High	36%	0%
• Moderate	29%	0%
• Low	43%	3%
• Remission	29%	3%
Disease Activity Attributed to Inflammation	36%	7%
• High	21%	0%
• Moderate	7%	0%
• Low	21%	0%
• Remission	7%	0%

Decision and Health Outcomes		
Treatment Decision	86%	27%
• Initiate	86%	50%
• Escalate (change/add DMARDs)	100%	80%
• Continue unchanged	50%	20%
• Taper	21%	33%
• Prednisone	57%	27%
• Defer	21%	0%
Long-Term Outcome		
• Sequelae	29%	33%
• Damage	43%	0%
Decision Making		
Inertia/Preference for the Status Quo	50%	0%
Target / Goal Setting	93%	83%
Physician Preference	71%	87%
Shared Decision Making	64%	47%
• Patient preference	93%	93%
• Education	100%	100%
• Burden of decision making	0%	17%
Patient Readiness		
Patient Buy-In/Persuasion	64%	3%
Social Support	7%	93%
Patient Subjective Knowledge	0%	93%
Patient Receptiveness to Treatment	57%	93%
• Fear of side-effects	79%	87%
• Medication beliefs/hopes	36%	100%
• Trial-and-error (skepticism)	29%	80%
• Medication fatigue	0%	27%
• Self-efficacy/adaptation	93%	60%
Disease Impact	0%	33%
• Fear of pain/flares	0%	33%
• Concerns regarding long-term damage	0%	13%
• Patient global assessment/disease fatigue	14%	67%
Patient – Physician Relationship	50%	100%
System Factors		
Logistical Barriers	14%	17%
• Patient access	36%	57%
Medical Practice	14%	3%
• Provider availability	21%	73%
• Time allotted per visit	14%	27%
• Burden of electronic health record	29%	10%
Insurance/Costs	71%	90%
• Affordability	21%	50%
• Denial of treatment	21%	37%
• Barrier of paperwork	43%	13%

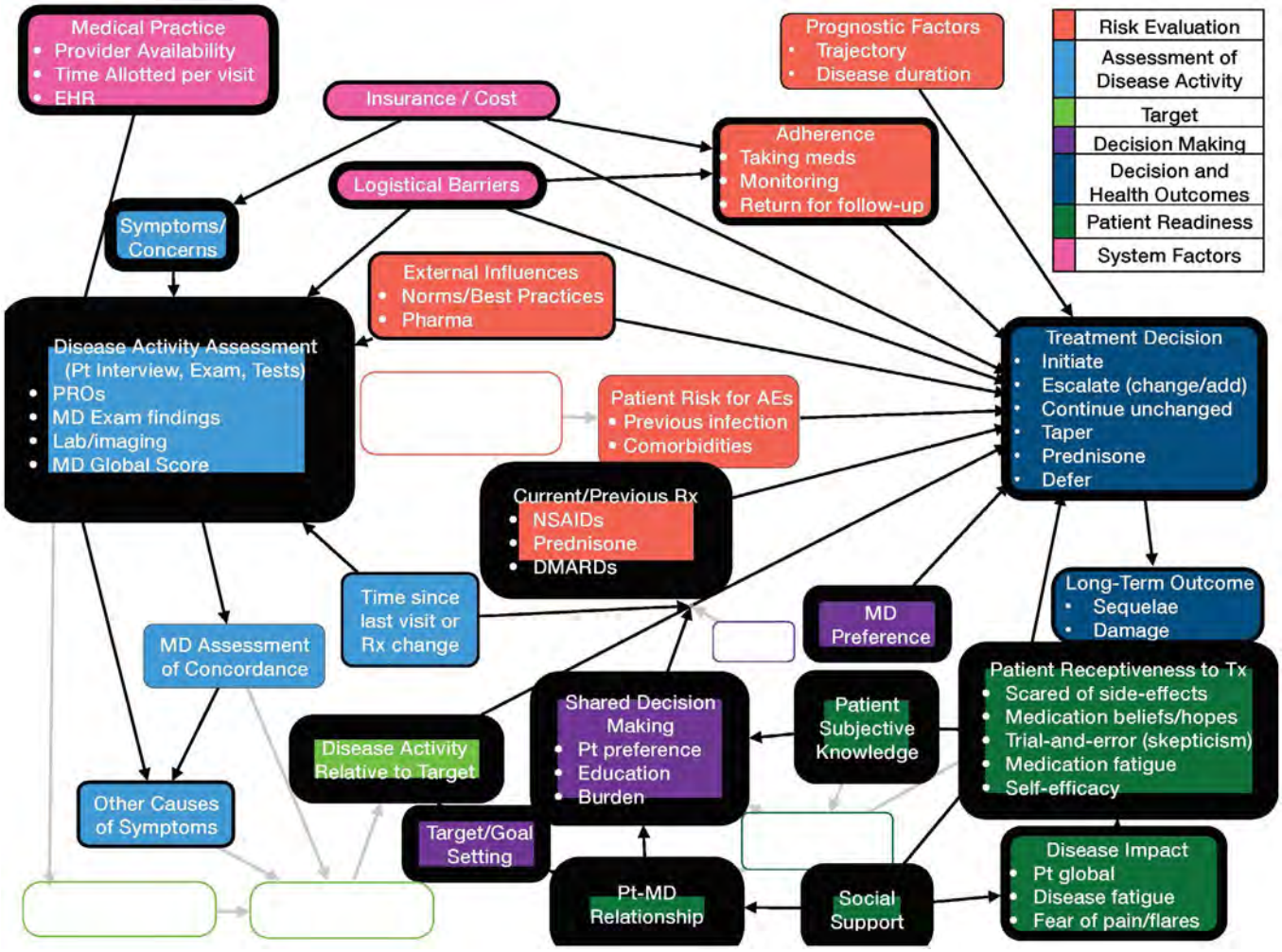


Physician Mental Model

Background/Purpose: Fewer than 50% of patients with rheumatoid arthritis (RA) are treated using a TTT strategy. The purpose of this study was to better understand rheumatologists' and patients' decision making regarding TTT using the Mental Models Approach to Risk Communication (MMARC). The MMARC provides a rigorous framework to develop interventions that address critical discrepancies between the mental models held by different populations, in this context, rheumatologists and patients.

Methods: We conducted semi-structured interviews with 14 rheumatologists and 30 patients to elicit respondents' views regarding treatment decisions in RA, with a focus on TTT. Interviews were transcribed and coded independently by two researchers. Final agreement between coders was high (kappa > 95%). We report the prevalence of each concept mentioned using the corresponding code. Because some ideas may not be expressed, these proportions represent a lower bound of their prevalence in people's mental models.

Results: Table 1 presents all factors raised in the interviews. Based on the codes assigned to each set of interviews, we created one model representing how rheumatologists conceptualize TTT (Figure 1) and another representing how patients conceptualize their treatment (Figure 2). Border thickness represent the frequency with which concepts were raised. Empty shapes highlight discrepancies between the rheumatologist and patient models. Several physicians stated that treatment decisions should be made based on overall trajectory of disease rather than at the point-of-care. They also described the importance of adherence and response to previous DMARDs on their decision making. Physicians recognized system barriers at the patient level (e.g., inadequate transportation), practice level, and insur-



Patient Mental Model

ance. Physicians also described how their own preferences and pharmaceutical company influences might affect their treatment decisions.

Notably absent from the patients' mental model is the cornerstone of TTT, i.e., disease activity measurement using validated instruments. Patients' anticipation of future experience on new medications. They described the necessity of feeling adequately informed, including from sources outside of their rheumatologist, in order to make treatment changes. Several discussed the burden of making treatment decisions. The uncertainty regarding whether one will benefit from a new DMARD and the risk of new side effects was frequently mentioned as an adverse aspect of changing medications. Concerns of the influence of pharmaceutical companies on rheumatologists' recommendations were also raised.

Conclusion: The TTT model of care is specific and prescriptive: measure disease activity and adjust treatment to achieve or maintain a predefined target using shared decision making. However, rheumatologists' and patients' mental models of treatment decision making in RA are much more complex and explain the low rates of TTT implementation. We found several discrepancies primarily related to differences in how patients and physicians value trade-offs that can serve as specific targets to improve patient-physician communication and ultimately inform interventions to improve uptake of TTT.

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Abstract Number: 0741

Assessing the Relationship of Patient Global Assessment of Disease Activity and Health Related Quality of Life by SF-36 with Other Patient-Reported Outcomes in Rheumatoid Arthritis: Post Hoc Analyses of Data from Phase 3 Trials of Baricitinib

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Improvements in patient-reported outcomes (PROs) were demonstrated in randomized controlled trials (RCTs) of baricitinib (BARI), an oral Janus kinase (JAK)1/JAK2 inhibitor, for the treatment of rheumatoid arthritis (RA). In these post-hoc analyses of BARI RCT data at baseline and 24 weeks, we examined the relative importance of PROs on the Patient Global Assessment of Disease Activity (PtGA) and health-related quality of life (HRQoL) and whether these differ in patients with good disease control compared with those not in low disease activity (LDA) or remission in different patient populations.

Methods: We analyzed data from three BARI phase 3 studies: 1) RA-BEGIN (NCT01711359) included 588 conventional synthetic DMARD-naive patients randomized 4:3:4 to receive methotrexate (MTX) monotherapy, BARI 4 mg, BARI + MTX; 2) RA-BEAM (NCT01710358) included 1307 MTX-inadequate response (IR) patients randomized 3:3:2 to placebo (PBO), BARI 4 mg, or adalimumab 40 mg; and 3) RA-BEACON (NCT01721044) included 527 biologic DMARD-IR patients randomized 1:1:1 PBO, BARI 2 mg, or BARI 4 mg. PtGA was measured by a visual analog scale (VAS, 0 to 100 mm) and HRQoL was measured by SF-36 physical component summary (PCS) and mental component summary (MCS) scores. PROs included pain (VAS, 0 to 100 mm), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), duration of morning joint stiffness (AMJtS), and Health Assessment Questionnaire-Disability Index (HAQ-DI). Good disease control was defined as either LDA or remission by Clinical Disease Activity Index (CDAI, ≤10 and ≤2.8, respectively). Within each RCT, treatment-agnostic correlation analyses at all time points from baseline to Week 24 were performed. Multiple regression analyses for the overall population and for patients in LDA, remission, or nonresponse were conducted; we present standardized parameter estimates from the regression analyses for each PRO to assess their relative importance on the PtGA, PCS score and MCS score.

Results: Across RCTs, pain strongly correlated with PtGA (r: 0.9); FACIT-F moderately correlated with PtGA, PCS, and MCS scores (r: 0.6 to 0.7; FACIT-F and PtGA are negatively correlated); and HAQ-DI moderately-to-strongly correlated with PtGA and PCS score (r: 0.6 to 0.8; HAQ-DI and PCS are negatively correlated). Duration of AMJtS was weakly correlated with the other PROs (r: -0.2 to -0.3 for PCS and MCS and 0.3 to 0.4 for PtGA). In regression

analyses across RCTs at baseline and Week 24 for the overall populations, the most significant factors were pain with PtGA (Table 1), HAQ-DI with SF-36 PCS score (Table 2]), and FACIT-F with SF-36 MCS score (Table 3). Similar results were observed in patients in LDA, remission, or nonresponse.

Conclusion: These results confirm prior findings, such as high correlations of pain with PtGA. We, however, observed that the relationships between other PROs with PtGA, PCS, or MCS scores were stable across time points over the first 6 months of treatment in differing patient populations, ranging from early to later disease. PtGA, PCS, and MCS scores were each associated with different PROs, indicating the importance of collecting multiple PROs in RCTs and real-world clinical practice.

	RA-BEGIN				RA-BEAM				RA-BEACON			
	Baseline		Week 24		Baseline		Week 24		Baseline		Week 24	
Overall	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**
Pain	**0.646**	**<0.0001**	**0.775**	**<0.0001**	**0.615**	**<0.0001**	**0.854**	**<0.0001**	**0.714**	**<0.0001**	**0.834**	**<0.0001**
FACIT-F	-0.040	0.2436	-0.088	0.0021	-0.115	0.0002	-0.025	0.1330	-0.094	0.0041	-0.083	0.0003
Duration of AMJtS	0.010	0.7139	0.013	0.5580	-0.012	0.6356	0.003	0.8130	0.021	0.4265	0.036	0.0381
HAQ-DI	0.174	<0.0001	0.062	0.0486	0.161	<0.0001	0.073	<0.0001	0.099	0.0034	0.047	0.0472

AMJtS: morning joint stiffness; B: standardized regression coefficient; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index

1) Regression model of Patient Global Assessment with PROs

	RA-BEGIN				RA-BEAM				RA-BEACON			
	Baseline		Week 24		Baseline		Week 24		Baseline		Week 24	
Overall	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**
Pain	-0.100	0.0056	-0.118	0.0007	-0.098	0.0008	-0.252	<0.0001	-0.135	0.0004	-0.217	<0.0001
FACIT-F	0.256	<0.0001	0.210	<0.0001	0.160	<0.0001	0.111	<0.0001	0.172	<0.0001	0.204	<0.0001
Duration of AMJtS	-0.046	0.1466	-0.031	0.2258	-0.031	0.2276	0.018	0.3717	-0.074	0.0311	-0.041	0.1632
HAQ-DI	**-0.426**	**<0.0001**	**-0.568**	**<0.0001**	**-0.576**	**<0.0001**	**-0.562**	**<0.0001**	**-0.447**	**<0.0001**	**-0.460**	**<0.0001**

AMJtS: morning joint stiffness; B: standardized regression coefficient; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index

2) Regression model of SF-36 Physical Component Summary with PROs

	RA-BEGIN				RA-BEAM				RA-BEACON			
	Baseline		Week 24		Baseline		Week 24		Baseline		Week 24	
Overall	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**	**B**	**p-value**
Pain	0.041	0.3249	-0.004	0.9343	0.003	0.9379	0.019	0.5405	0.031	0.4580	0.063	0.1530
FACIT-F	**0.516**	**<0.0001**	**0.803**	**<0.0001**	**0.715**	**<0.0001**	**0.800**	**<0.0001**	**0.578**	**<0.0001**	**0.875**	**<0.0001**
Duration of AMJtS	0.032	0.3684	0.060	0.0755	0.069	0.0238	0.023	0.3534	0.075	0.0485	0.031	0.3535
HAQ-DI	-0.121	0.0122	0.162	0.0007	0.117	0.0039	0.146	<0.0001	-0.016	0.7454	0.137	0.0033

AMJtS: morning joint stiffness; B: standardized regression coefficient; FACIT-F: Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI: Health Assessment Questionnaire-Disability Index

3) Regression model of SF-36 Mental Component Summary with PROs

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Abstract Number: 0742

Googling Rheumatic Diseases: Evaluating the Reliability of Information Found on the Internet

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. DISCERN criteria and JAMA core standards

DISCERN Questions*		*Mean*	*SD*
1.	Explicit Aims	4.25	0.98
2.	Aims achieved	3.96	0.82
3.	Relevance to patients	4.20	0.83
4.	Sources of information	2.43	1.63
5.	Currency (date) of information	3.20	1.53
6.	Bias and balance	3.78	1.00
7.	Additional sources of information	3.67	1.29
8.	Reference to areas of uncertainty	2.97	1.11
9.	How treatment works	3.19	1.47
10.	Benefits of treatment	4.05	1.27
11.	Risks of treatment	3.02	1.70
12.	Risks/benefits of no treatment	2.29	1.29
13.	Quality of life	3.03	1.13
14.	Other treatment options	4.00	0.93
15.	Shared decision making	4.13	1.10
16.	Overall quality	3.49	1.00
JAMA Core Standards**		*Mean*	*SD*
Authorship		0.44	0.50
Attribution		0.47	0.50
Disclosure		1	0
Currency		0.74	0.44

Mean and standard deviations are presented for all 100 websites

*16 questions/criteria used to assess the reliability of written consumer health information

**4 core standards presented in JAMA to assess quality of medical information online. Authorship= authors and contributors, their affiliations, and relevant credentials are provided. Attribution= References and sources for all content are listed clearly. Disclosure= Website ownership is prominent and fully disclosed with any sponsorship, advertising, commercial funding arrangements or support, and conflicts of interest. Currency= Dates that content was posted and updated are indicated

Table 2. DISCERN and JAMA scores for searched diagnoses

Disease		DISCERN*		JAMA**	
	N	*Mean*	*SD*	*Mean*	*SD*
Ankylosing Spondylitis	10	3.75	0.74	0.60	0.32
Fibromyalgia	10	3.40	0.53	0.68	0.29
Gout	10	3.34	0.58	0.73	0.30
Lupus	10	3.75	0.68	0.65	0.34
Osteoarthritis	10	3.19	0.53	0.60	0.27
Psoriatic Arthritis	10	3.57	0.53	0.65	0.32
Rheumatoid Arthritis	10	3.79	0.77	0.80	0.23
Scleroderma	10	3.22	0.71	0.65	0.30
Sjogren's	10	3.39	0.67	0.60	0.27
Vasculitis	10	3.39	0.80	0.68	0.33

*Score range 1-5 for each question; average of all questions was calculated for each website
**Score range 0= "not met", 1= "met" for each of 4 core standards; average of all core standards was calculated for each website
ANOVA, P=0.36 for DISCERN and P=0.91 for JAMA

Table 3. DISCERN and JAMA scores for major websites

Major Website		DISCERN*		JAMA**	
	N	*Mean*	*SD*	*Mean*	*SD*
WebMD	10	3.54	0.62	0.78	0.22
eMedicineHealth	4	4.33	0.31	1	0
MedicineNet	4	4.00	0.33	0.94	0.13
Wikipedia	5	3.85	0.25	0.75	0
Mayo Clinic	10	3.93	0.49	0.95	0.11
MedicalNewsToday	6	3.66	0.52	1	0
Healthline	8	4.13	0.57	1	0
CDC	4	3.30	0.82	0.63	0.25

*Score range 1-5 for each question; average of all questions was calculated for each website
**Score range 0= "not met", 1= "met" for each of 4 core standards; average of all core standards was calculated for each website

Background/Purpose: The internet is a significant source of information for health-related topics. Given the complexity of rheumatic diseases, rheumatologists may find their patients searching online for information related to their diagnosis, including treatment options and complications. Often, what patients find on the internet can steer their decisions on treatments and issues they discuss with their provider, regardless of how varied the quality and reliability of this information may be. This study was thus designed to critically evaluate the information found on common rheumatic diseases through Google search using two instruments (Table 1): Four core standards presented by the *Journal of American Medical Association* (JAMA) to promote accountability for information written on the internet and the DISCERN instrument which is the first standardized quality index developed to judge the quality of written consumer health information.

Methods: Google search was performed for 10 diseases commonly evaluated by rheumatologists: ankylosing spondylitis, fibromyalgia, gout, lupus, osteoarthritis, psoriatic arthritis, rheumatoid arthritis, scleroderma, Sjogren's, and vasculitis. The first 10 website search results for each diagnosis were included in the study to yield a total of 100 websites. All websites were classified into major medical information websites (websites that disseminate information on a wide variety of health topics) and non-major websites. Websites were then assessed using JAMA and DISCERN. Primarily descriptive statistics were utilized. One-way analysis of variance and two tailed t-tests were performed to assess differences in scores.

Results: Average DISCERN quality score and JAMA score for all 100 websites were 3.48 (SD 0.66) and 0.66 (SD 0.29), respectively. Only 24 websites scored ≥ 4 on the DISCERN instrument. Risks of no treatment was the most missed question on the DISCERN instrument and authorship was the most missed core standard on the JAMA in-

strument (Table 1). While there was no statistically significant difference in DISCERN scores and JAMA scores for the 10 different diagnoses (P =0.36 for DISCERN, P=0.91 for JAMA), websites on ankylosing spondylitis numerically scored highest on the DISCERN instrument and rheumatoid arthritis scored highest on the JAMA instrument (Table 2). We observed that the major medical information websites (n=49) scored higher than non-major websites (n=51, $P < 0.0001$) on both instruments with eMedicineHealth scoring highest on the DISCERN instrument (4.33, SD 0.31) (Table 3).

Conclusion: Information on common rheumatic conditions procured through Google searches is of moderate quality and lacks essential aspects such as authorship, sources, and thorough explanation of treatment options. Not surprisingly, major medical information websites present more reliable information than non-major websites. If patients are looking for information on the internet, rheumatologists should guide them towards more reliable resources for further reading.

References

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Disclosure: N. Chiruvolu, None; **M. Karim**, None; **V. Sandhu**, None.

Abstract Number: 0743

Pain Interference, Fatigue, Physical Function as Outcome Measures in Adult Myositis: Updates on the Validation Process by the OMERACT Myositis Working Group

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: People living with idiopathic inflammatory myositis (IIM) suffer impairments in health-related quality of life (HRQL), especially in the domains of pain interference, fatigue, and physical function. In 2021, the OMERACT Myositis Working Group 2021 Survey of PROM Construct Validity and Reliability was developed to evaluate specific patient-reported outcome measures (PROMs). The goal was to assess the measurement properties of construct validity and test-retest reliability for the Patient Reported Outcome Information System (PROMIS) Pain Interference 6a v1.0, Fatigue 7a v1.0, and Physical Function 8b v2.0 instruments.

OMERACT DOMAIN	Working Definition	Selected Instrument
Pain Interference	Aching, soreness, or tenderness attributable to IIM relating to the joints, muscles, and/or skin causing interference with routine daily function.	PROMIS Pain Interference 6a v1.0
Fatigue	A feeling of [extreme] tiredness or exhaustion attributable to IIM, interfering with usual and meaningful daily activities.	PROMIS Fatigue 7a v1.0
Physical Function	The ability to perform basic and desired activities of daily living that is affected by decreased use of muscles or other organ systems affected by IIM.	PROMIS Physical Function 8b v2.0

Table 1. OMERACT Core Domains of Interest.

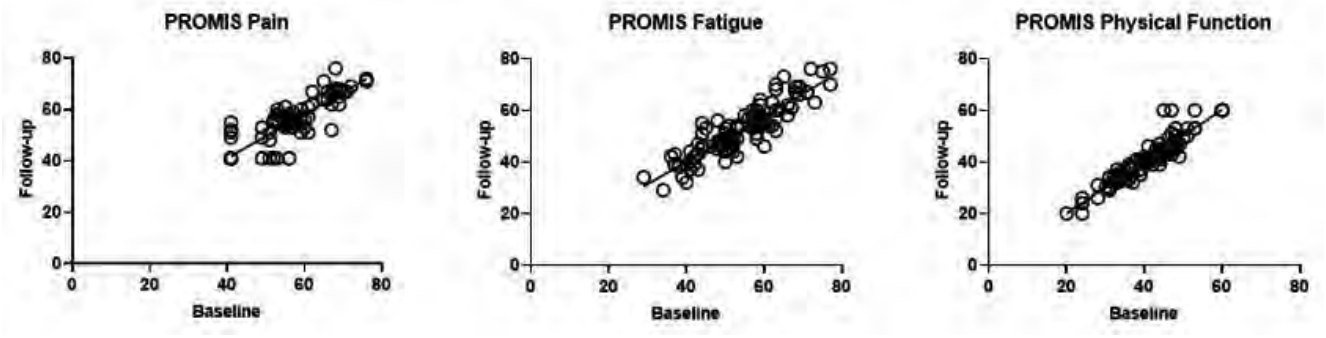

Figure 1. Test-Retest Correlation Matrices.

Methods: Formalized definitions of each domain were developed per methodological guidance from the OMERACT Instrument Selection Filter 2.2 (Table 1). PROMs for each domain of interest were deployed via Redcap to adult patients with confirmed IIM at a large tertiary care referral site (Baltimore, MD). Patient demographics and PROMIS v1.0 4a anxiety, depression, sleep disturbance, and social participation questionnaires were also administered, and identical questionnaires were given 7 days later. In addition, data from Sweden, Australia, South Korea, The Netherlands and the USA that was collected as part of the OMERACT Myositis Working Group 2019 Survey of PROM Content Validity and Feasibility was used which additionally included the Pain Disability Index (PDI), International Physical Activity Questionnaire (IPAQ), and Myositis Activities Profile (MAP). Raw PROMIS scores were converted to T-score measures and normalized to a score of 50 with a standard deviation of 10; higher scores indicate more of the concept being measured. Test/Retest reliability was calculated using intraclass correlation coefficients (ICC) and correlation matrices were constructed. Construct validity was determined via formulation of *a priori* hypotheses generated by working group members (Table 2); >75% member agreement was required for each hypothesis. Pearson's correlation was calculated for each construct pair.

Results: Domain definitions were formalized based on patient/expert consensus (Table 1). There were 287 adult participants with IIM who completed the baseline 2021 survey and 97 participants who completed the retest; the number of participants who completed the 2019 survey as relevant to this exercise varied (Table 2). Participants from the 2021 baseline survey were 76% female with a mean (SD) age of 60 (12). Test-retest reliability was high for pain interference, fatigue, and physical function with an ICC (95% CI) of 0.878 (0.823-0.917), 0.886 (0.822-0.925), and

Table 2. Construct Validity Assessment

OMERACT Myositis Working Group 2021 Survey of PROM Construct Validity and Reliability					
Construct	***A priori* hypothesis-expected correlation**	**Consensus Exercise, % Agreement of Group Members**	**Expected Results**	**Observed Pearson's rho**	**Hypothesis confirmed?**
PROMIS Pain Interference 6a v1, PROMIS Sleep Disturbance 4a v1: Pain interference should correlate moderately with one's sleep	Moderate	93%	r >0.25 but < 0.75	0.35	yes
PROMIS Pain Interference 6a v1, Pain Intensity (NRS): Pain interference should relate to pain intensity but not perfectly correlate.	Moderate-High	100%	r >0.50 and <0.90	0.87	yes
PROMIS Fatigue 7a v1, PROMIS Anxiety 4a v1.0: Fatigue is a complex symptom that should be partially driven by emotional distress.	Moderate	93%	r >0.25 but < 0.75	0.58	yes
PROMIS Fatigue 7a v1, PROMIS Sleep Disturbance 4a v1.0: Fatigue is a complex symptom that should moderately correlate to sleep disturbance but not to a high degree	Moderate	100%	r >0.25 but < 0.75	0.54	yes
PROMIS Physical function 8b v2.0, PROMIS Depression 4a v1: Physical function, or the perception of one's physical function, should be impacted by negative emotion.	Moderate (negative)	93%	r >0.25 but < 0.75	-0.49	yes
OMERACT Myositis Working Group 2019 Survey of PROM Content Validity and Feasibility					
PROMIS Pain interference 8a v1, sex: Pain interference should not differ between sexes	Low	57%	Item dropped	Item dropped	N/A
PROMIS Pain Interference 8a v1, age: Age should not be driving pain interference. N=65 observations.	Low	93%	r < 0.25	-0.18	Yes
PROMIS Pain interference 8a v1, Pain Disability Index (PDI): Pain interference and disability attributed to pain should be very similar in IIM. N=100 observations.	High	100%	r > 0.75	0.63	No
PROMIS Fatigue 7a v1, sex: Fatigue from IIM should not be related to sex. N=68 observations.	Low	100%	r < 0.25	0.17	Yes
PROMIS Fatigue 7a v1, age: Age should not be driving the degree of fatigue in IIM. N=68 observations.	Low	100%	r < 0.25	-0.18	Yes
PROMIS Physical function 8b v2.0, sex: Physical Function from IIM should not be impacted by sex. N=79 observations.	Low	100%	r < 0.25	-0.01	Yes
PROMIS Physical function 8b v2.0, age: Age should not be driving physical function in IIM. N=79 observations.	Low	100%	r < 0.25	-0.11	Yes
PROMIS Physical function 8b v2.0, International Physical Activity Questionnaire (IPAQ): One's physical activity should be related to/depend on one's physical function. N=100 observations.	Moderate	86%	r > 0.5	-0.134	No
PROMIS Physical Function 8b v2.0, Physical Activity: Myositis Activities Panel (MAP): One's physical activity should be related to/depend on one's physical function. N=100 observations.	Moderate	86%	r > 0.5	0.77	Yes

0.943 (0.917-0.962), respectively (Figure 1). For the construct validity exercise, member consensus was met for 12 of 13 *a priori* hypotheses. Hypotheses were correct for 3 out of the 4 available constructs for pain interference, 4 out of 4 constructs for fatigue, and 4 of 5 constructs for physical function (Table 2).

Conclusion: Both test-retest reliability and construct validity are high for pain interference, fatigue, and physical function when used in this IIM population. Further longitudinal validation is ongoing in Sweden, Australia, South Korea, The Netherlands and the USA.

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Abstract Number: 0744

MDHAQ (Multidimensional Health Assessment Questionnaire) and PROMIS-29 (patient-reported Outcomes Measurement Information System) Domains for Physical Function, Pain, Fatigue, Anxiety, Depression, Sleep, and Ability to Participate Provide Virtually Identical Information

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Table: Spearman correlation coefficients for MDHAQ scores and PROMIS T-scores for all patients.

MDHAQ scores:	Physical function T-score	Pain interference T-score	Fatigue T-score	Anxiety T-score	Depression T-score	Sleep T-score	Ability to participate T-score	Global pain (0-10)
Physical Function (0-10)	-0.82	0.70	0.54	0.46	0.52	0.43	-0.68	0.64
Pain (0-10)	-0.59	0.74	0.46	0.37	0.42	0.45	-0.52	0.86
Fatigue (0-10)	-0.57	0.59	0.73	0.48	0.44	0.51	-0.54	0.64
Anxiety (0-5.5)	-0.44	0.44	0.48	0.74	0.70	0.45	-0.44	0.37
Depression (0-5.5)	-0.45	0.46	0.48	0.71	0.77	0.47	-0.47	0.41
Sleep (0, 1.1, 2.2, 3.3)	-0.49	0.55	0.51	0.46	0.45	0.74	-0.48	0.56
Participate (0-5)	-0.72	0.61	0.49	0.40	0.43	0.39	-0.65	0.52
PATGL (0-10)	-0.65	0.76	0.53	0.41	0.46	0.44	-0.59	0.83
RAPID3 (0-30)	-0.75	0.82	0.57	0.46	0.52	0.50	-0.64	0.88
60-symptom checklist (0-60)	-0.53	0.56	0.64	0.53	0.54	0.53	-0.53	0.53
RADAI (0-54)	-0.56	0.62	0.45	0.46	0.48	0.45	-0.48	0.63

Background/Purpose: PROMIS-29 (patient-reported outcome measurement information system) has been extensively validated in many diseases according to standard deviations from normalized T-scores for 7 domains. It was developed through literature review, investigator consensus, item response theory analysis and expert review of scaling results from multiple PROMIS data sets. The domains are physical function, pain interference, fatigue, anxiety, depression, sleep quality and ability to participate, and it has construct validity and reliability in many diseases, including RA and other rheumatic diseases (Katz P et al Arth Care & Res. 2017;69:1312-21). An MDHAQ (multidimensional health assessment questionnaire) queries similar domains having been developed in clinical care by continuous quality improvement cycles. MDHAQ scores may be more intuitively understood by health professionals, and MDHAQ includes 3 indices which agree 80-90% with reference indices that require additional measures and are less feasible in busy clinical settings: RAPID3 (routine assessment of patient index data) to assess patient status; FAST4 (fibromyalgia assessment screening tool) to screen for fibromyalgia (Gibson, J Rheumatol. 2020;47:761-9); and DEP2 (Morla, Arth Care & Res 2021;73:120-9) to screen for depression (Dep). High correlations have been reported between PROMIS T-scores vs RAPID3 (Yun et al Arth Care & Res. 2020;72:553-60), suggesting a hypothesis that 7 PROMIS-29 vs MDHAQ domains may provide similar information, as studied here.

Methods: Both PROMIS-29 and MDHAQ were completed at the same routine rheumatology encounter. PROMIS-29 T-scores were obtained by submitting the data to the HealthMeasures Scoring Service, powered by Assessment Center^{SM} (https://www.assessmentcenter.net/ac_scoringservice). MDHAQ scores and indices were computed in the clinic. MDHAQ and PROMIS T-scores were compared in all patients, rheumatoid arthritis (RA) and non-RA patients by Spearman correlations and a series of linear regressions in which each PROMIS-29 T-score served as a dependent variable and MDHAQ scores as independent variables, and vice versa. Scores were also compared according to FAST4 status; (1 point each for pain >6/10, fatigue >6/10, symptom checklist >16/60, and self-report painful joint count >16/54 where 3/4 =FM).

Results: PROMIS-29 and MDHAQ were completed at the same visit by 571 patients, 225 with RA and 346 with other diagnoses. All 7 MDHAQ and PROMIS-29 domains were correlated significantly (rho=-0.65 to 0.82, $p< 0.001$) in all patients (Table), similar in RA and non-RA patients. Significantly poorer status was seen in both RA and non-RA patients with FM vs no FM according to FAST4 (data not shown). Regressions explained 53-81% of the variation in PROMIS T-scores by MDHAQ domains and 44%-82% of the variation in MDHAQ domains by PROMIS T-scores.

Conclusion: MDHAQ and PROMIS-29 give similar information in rheumatology patients. PROMIS has advantages for clinical research, while MDHAQ provides additional clinical information and is intuitive for busy clinical settings.

PATGL = Patient Global Assessment, RADAI = Rheumatoid Arthritis Disease Activity Index, RAPID3 = Routine Assessment of Patient Index Data 3. Participate (0-5) = Participate in Recreational Activities or Sports (0-3) + Social activity in 60-symptom (0 for No, 2 for Yes). Anxiety (0-5.5) = Anxiety (0-3.3) + Anxiety in 60-symptom (0 for No, 2.2 for Yes). Depression (0-5.5) = Depression (0-3.3) + Depression in 60-symptom (0 for No, 2.2 for Yes).

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Patient-reported Outcomes and Safety Measures in Patients with Rheumatic Diseases Who Switched from Reference or Other Biosimilar Etanercept to Biosimilar Etanercept GP2015 and in Biologic-naïve Patients Starting a Treatment with GP2015: 12-month Interim Analysis from a Real-world Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
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Session Time: 8:30AM–10:30AM

Background/Purpose: GP2015 is a biosimilar of etanercept (ETN). COMPACT is an ongoing, non-interventional study, evaluating the effectiveness, safety, and quality of life with GP2015 treatment in patients (pts) with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA) in real-world conditions.[1] Herein we present the pt-reported outcomes (PROs) and safety data focusing on pts who were either in treatment with reference ETN or biosimilar ETN (initial ETN; iETN) other than GP2015 and switched to GP2015 or biologic-naïve pts who started GP2015 as a first biologic therapy.

Methods: Pts aged ≥18 years who initiated treatment with GP2015 were enrolled. They were categorized based on prior treatment status.[1] PROs assessments through 12 months included 12-Item Short Form Survey (SF-12) score for mental/physical health and physical function as Health Assessment Questionnaire Disability Index (HAQ-DI) score. PROs and safety data are presented for switched pts (on clinical remission or low disease activity under treatment with iETN and switched to GP2015) and biologic-naïve pts (considered uncontrolled with conventional therapy and started with GP2015).

Results: A total of 1437 pts were recruited (analysis cut-off date: 16 Oct 2020), comprising 828 (57.6%) with RA as primary indication, 325 (22.6%) with axSpA, and 284 (19.8%) with PsA. There were 292, 159, and 116 switched pts; and 439, 124, and 134 biologic-naïve pts with RA, axSpA, and PsA, respectively. Comorbidities (switched and biologic-naïve pts) were more frequent in RA (70.2% and 65.8%), followed by PsA (58.6% and 59.7%) and axSpA (49.7% and 54.8%), respectively. After 12 months treatment with GP2015, we observed comparable HAQ-DI, SF-12 mental, and SF-12 physical scores between the switched and biologic-naïve pts (**Figure 1 A-C**). Incidences of adverse events (AEs) and serious AEs in pts with RA were 37.3% and 6.5% in switched, 43.7% and 7.3% in biologic-naïve; in pts with axSpA they were 25.8% and 3.1% in switched, 46.8% and 7.3% in biologic-naïve; and in pts with PsA they were 33.6% and 1.7% in switched, 43.3% and 6.0% in biologic-naïve. Injection-site pain was low across the groups (RA: 2.1% and 0.7% in switched and biologic-naïve pts; axSpA: 1.3% and 1.6% in switched and biologic-naïve pts; PsA: 0 and 0.7% in switched and biologic-naïve pts, respectively).

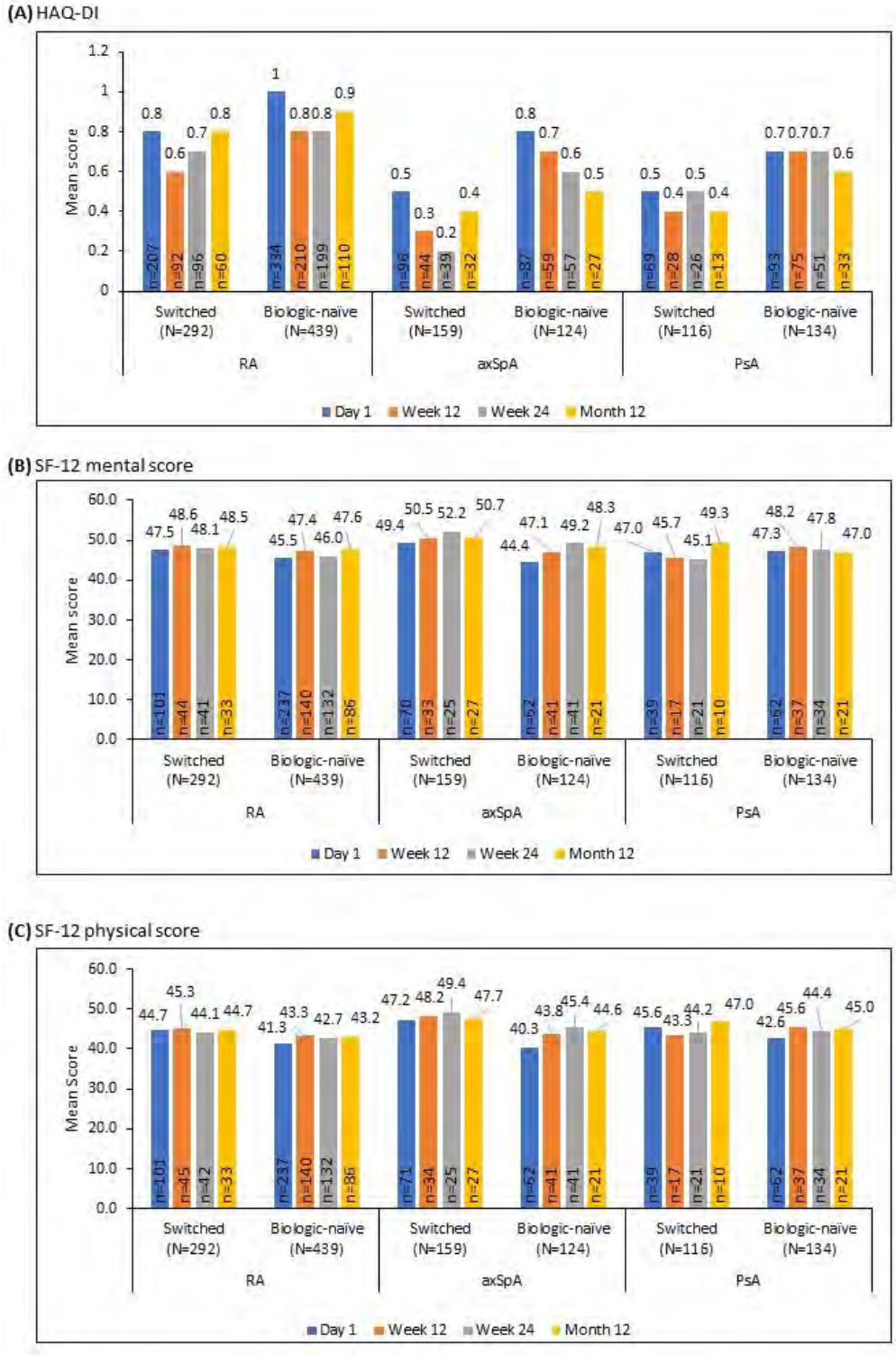

Figure 1. PROs in pts who switched from iETN to GP2015 and biologic-naïve started on GP2015.

Conclusion: This analysis shows comparable PRO scores obtained after 12 months of observation in pts under treatment with iETN who switched to GP2015 and in pts who were biologic-naïve and started GP2015 as a first-line biologic therapy, without any new safety signals in real-world conditions.

Reference

1. Schmalzing M, et al. ACR 2019, Atlanta, GA, United States. Poster No. 553.

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Abstract Number: 0746

Application of Existing Patient-Reported Outcome Measures for Telehealth Encounters: What's Feasible?

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Validated patient-reported outcome (PRO) measures play important roles in assessing and managing of patients with rheumatic diseases. However, use of these validated scales may not be feasible in the

Table 1. Correlations of single-item numeric rating scales with validated PROs

	RA				SLE				OA			
Time	1	2	3	4	1	2	3	4	1	2	3	4
n	2425	2270	1915	919	286	262	210	108	3601	990	839	379
Function												
HAQ	0.71	0.73	0.71	0.69	---	---	---	---	0.70	0.69	0.68	0.67
HAQ-II	0.74	0.74	0.76	0.75	0.78	0.79	0.77	0.77	0.72	0.73	0.73	---
PROMIS Physical Function	-0.72	-0.72	-0.72	-0.67	-0.76	-0.80	-0.77	-0.71	-0.73	-0.70	-0.71	-0.65
Pain												
PROMIS Pain Interference	0.66	0.70	0.70	0.69	0.75	0.74	0.76	0.74	0.64	0.63	0.75	0.66
Fatigue												
PROMIS Fatigue	0.82	0.80	0.79	0.75	0.83	0.80	0.83	0.82	0.82	0.80	0.82	0.78

Single item measures:
Pain: How much pain have you had in the past week because of your [illness]? 0 (no pain) – 10 (severe pain)
Function: In thinking about you're your [illness] affects your ability to function in daily life, how would you rate your functional limitations in the past week? 0 (no limitations) – 10 (severe limitations)
Fatigue: How much of a problem has fatigue or tiredness been for you in the past week? 0 (no problem) – 10 (major problem)

HAQ=Health Assessment Questionnaire; HAQ-II=Health Assessment Questionnaire II
PROMIS = Patient Reported Outcome Measurement Information System

Table 2. Correlations of changes in single-item numeric rating scales with changes in validated PROs									
	RA			SLE			OA		
Time	1-2	2-3	3-4	1-2	2-3	3-4	1-2	2-3	3-4
Function									
HAQ	0.21	0.26	0.17	-0.12	0.39	---	0.22	0.23	0.14
HAQ-II	0.22	0.25	0.16	0.18	0.19	0.15	0.23	0.31	0.52
PROMIS Physical Function	-0.23	-0.23	-0.19	-0.15	-0.30	-0.18	-0.25	-0.22	-0.22
Pain									
PROMIS Pain Interference	0.28	0.28	0.33	0.11	0.21	0.03	0.33	0.21	0.26
Fatigue									
PROMIS Fatigue	0.41	0.41	0.34	0.30	0.31	0.25	0.39	0.39	0.31

setting of telehealth encounters. Likewise, completion of physician-reported measures of disease activity may not be possible via telehealth because, for example, joint examinations and global assessments cannot be conducted reliably. In both cases, acceptable proxies are needed for use in telehealth as this method of care delivery remains widely used. We examined the relationship between (1) simple, single-item ratings of pain, function, and fatigue with validated scales measuring the same constructs, and (2) patient and physician ratings of disease activity in patients with rheumatoid arthritis.

Methods: Analysis 1 uses data from FORWARD, The National Databank for Rheumatic Diseases, a longitudinal registry of individuals with rheumatic diseases. Data are regularly collected via semi-annual questionnaires. Within each questionnaire, pain, function, and fatigue are assessed by both single-items and validated scales (Table 1). Spearman correlations examine the associations between single-item and scales for each construct at 4 different questionnaire administrations and between 6-month changes in item and scale responses. Analyses were conducted separately for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), and osteoarthritis (OA). Analysis 2 uses data from a study of people with rheumatoid arthritis in which both the Clinical Disease Activity Index (CDAI) and patient-reported Rheumatoid Arthritis Disease Activity Index (RADAI) were completed. Spearman correlations examine associations between CDAI and RADAI scores and components (global assessments, joint counts).

Results: Analysis 1: Participants with RA (n=7478) had mean age 68±11 years, were 92% white and 83% female; those with SLE (n=893) had mean age 63± 13 years, were 83% white, and 94% female; and those with OA (n=3371) had mean age 70± 10 years, were 95% white, and 86% female. Cross-sectional correlations between single items and scales were uniformly medium to large (Table 1). Correlations between change scores, however, were small (Table 2)..

Table 3. Correlation between CDAI and RADAI total scores and components (n = 48)	
	correlation
Total score	0.70
Components	
RADAI painful joints, CDAI swollen joints	0.36
RADAI painful joints, CDAI tender joints	0.71
Patient global, physician global	0.57

Analysis 2: Participants (n=48) had mean age 58 ± 12 years, were 76% female, 36% white, 7% Asian, 14% Black, and 43% other/multi-racial, and 36% LatinX ethnicity. Correlations between CDAI and RADAI total scores was 0.70, RADAI painful joint count and CDAI tender joints 0.71, and RADAI and CDAI global assessments 0.57.

Conclusion: Cross-sectional group associations between single-item and scale responses were high suggesting the potential for usefulness in telehealth settings where rheumatologists may not have sufficient time to complete longer validated measures nor data from a physical exam. Correlations in changes, however, were low, perhaps reflecting reduced precision of the single-item measures, which might limit the usefulness of these measures for following patients over time. The moderate-high associations between CDAI and RADAI scores and components suggests that remote patient-completed assessments of disease activity may be useful in telehealth settings.

Disclosure: P. Katz, None; **M. Subash**, None; **M. Bergman**, AbbVie, 2, 6, Amgen Inc., 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, Bristol Myers Squibb, 2, Celgene, 2, Genentech, 2, Janssen, 2, Merck, 2, Johnson & Johnson, 11, Sandoz, 1, GSK, 6, Scipher, 2; **K. Michaud**, None.

Abstract Number: 0747

Understanding Heterogeneity in Patients' Conceptualization of Treatment for Rheumatoid Arthritis: A Cluster Analysis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Uptake of treat to target strategies for the management of rheumatoid arthritis (RA) is low. While there are known system-related barriers to accessing treatment, poor primary (starting) and secondary (continuing) adherence are prevalent causes of suboptimal care. The objective of this study was to better understand the heterogeneity in patients' conceptualization of treatment of RA in order to inform interventions aimed at improving appropriate utilization of DMARDs.

Methods: Participants were recruited from an online research registry. Those meeting eligibility criteria [physician diagnosed RA currently being treated with DMARD(s)] rated 56 items (coded on 5-point scales with appropriate anchors) reflecting concepts raised during preparatory in-depth individualized patient interviews. To combine similar items for ease of analysis and interpretation we conducted a principal components analysis using Varimax rotation. We then entered mean scores, weighted by how heavily each item loaded onto each factor, into a k-means cluster analysis. We examined whether demographic characteristics differed across clusters using ANOVA and chi-square for continuous and categorical variables, respectively.

Results: Participants (N= 621) ranged in age from 22 to 93, with a mean of 57 years old (SD= 11.5). Most (89%) were female and reported themselves to be non-Hispanic white (89%); 27% reported having a post-graduate degree. A

Table 1. List of Items

Survey Item Text *(items with scores of 6 or higher are listed)*	Factor Loading	Mean (SD)
1. Access to high quality care and support (Variance Explained: 12.10%, Items: 21)		
Difficulty getting clear, complete answers in a timely manner from my rheumatologist (by email or telephone) in-between appointments if I have questions or concerns. (Reverse)	-0.72	1.83 (1.11)
Difficulty scheduling an appointment with my rheumatologist right away if my disease flares up. (Reverse)	-0.70	2.30 (1.24)
I feel like I don't have much of a say in making decisions about treating my RA. (Reverse)	-0.65	2.03 (1.11)
My rheumatologist gives me enough time to ask questions during my visits.	0.65	4.25 (0.89)
My rheumatologist wants me to stay on a medication even though I want to switch. (Reverse)	-0.63	1.72 (1.00)
My rheumatologist gives me enough information to decide which medication to take.	0.62	3.99 (1.10)
I feel like I have enough information from all sources to make good decisions about my medication.	0.60	3.91 (0.98)
2. Comfortable adding/switching DMARDs (Variance Explained: 9.73%, Items: 14)		
I worry about changing medication because I don't know if I will get new (or more) side effects. (Reverse)	-0.78	3.49 (1.31)
I worry about changing medication because I don't know if a new medication will work as well or any better than the one(s) I'm already taking. (Reverse)	-0.75	3.32 (1.30)
It is hard to decide whether to switch medication. (Reverse)	-0.65	2.93 (1.19)
It is hard to decide whether to add medication to the ones I am already taking. (Reverse)	-0.63	2.89 (1.21)
3. Perceived favorable DMARD risk/benefit ratio (Variance Explained: 8.74%, Items: 15)		
Medication is needed to keep my RA under control.	0.66	4.60 (0.69)
My life would be a real challenge without my RA medication.	0.63	4.50 (0.83)
4. Confidence that testing reflects disease activity (Variance Explained: 6.20%, Items: 6)		
Blood work shows whether I need more or different medication.	0.75	2.77 (1.23)
Blood work shows whether my medication is working.	0.69	2.90 (1.21)
Blood work shows if my RA is progressing. (Agree)	0.66	2.93 (1.31)
X-rays show whether I need more or different medication. (Agree)	0.66	2.37 (1.15)
X-rays show whether my medication is working. (Agree)	0.64	2.44 (1.12)
X-rays show if my RA is progressing. (Agree)	0.62	3.22 (1.15)

scree plot revealed that a 4-factor solution explaining 36.8% of the variance would provide desirable interpretability, with a discontinuous drop in eigenvalues for additional factors slowly tapering and adding little discriminability between later solutions. The four factors (% variance explained, number of items) were: 1) Access to high quality care and support (12.10%, n= 21); 2) Comfortable adding/switching DMARDs (9.73%, n= 14); 3) Perceived favorable

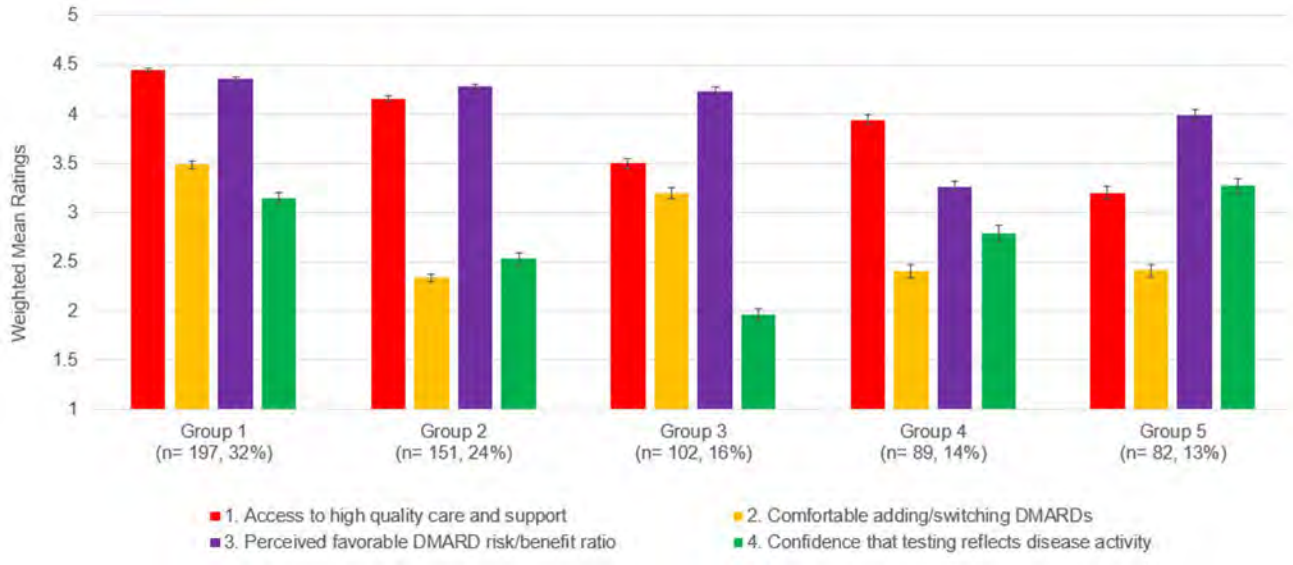

Figure 1. Weighted Ratings per Cluster.

Table 2. Participant Characteristics Across Groups

	Group 1 (n = 197)	Group 2 (n = 151)	Group 3 (n = 102)	Group 4 (n = 89)	Group 5 (n = 82)	p value
Age, mean (SD)	60.7 (9.6)	54.7 (11.6)	54.2 (11.8)	57.0 (12.7)	53.3 (11.3)	p= 0.1
Female, n (%)	173 (87.8%)	132 (87.4%)	93 (91.2%)	77 (86.5%)	75 (91.5%)	p= 0.6
White, Non-Hispanic n (%)	184 (93.4%)	137 (90.7%)	95 (93.1%)	72 (80.9%)	67 (81.7%)	p= 0.002
College degree or more, n (%)	111 (56.3%)	87 (57.6%)	61 (59.8%)	51 (57.3%)	33 (40.2%)	p= 0.01

DMARD risk/benefit ratio (8.74%, n= 15); and 4) Confidence that testing reflects disease activity (6.20%, n= 6). Table 1 lists the mean ratings for items with factor loading scores of 6 or greater. A 5-cluster solution showed the most stable convergence of cluster centers after 10 iterations. Figure 1 shows the weighted mean scores for each factor across clusters. While four out of the five groups perceived a favorable DMARD risk/benefit ratio, all groups voiced some discomfort with adding or changing DMARDs, with Groups 2, 4 and 5 having particularly low scores. Level of comfort adding/switching DMARDs was not mitigated by access to high quality care and support. There were a greater number of non-white participants in Groups 4 and 5, and less well-educated participants in Group 5 (Table 2). No differences in age or sex across groups were observed.

Conclusion: Patients' conceptualization of RA treatment varies. However, adding/switching DMARDs appears to be ubiquitous regardless of the perceived benefits associated with DMARDs and access to high quality care and support. Interventions outside of the traditional physician-patient relationship are needed to facilitate treatment escalation in patients with RA. Further research is required to understand residual variance not explained by our model.

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Abstract Number: 0748

Performance of Standardized Scores for Disease Assessment and Pain in Patients Withspondyloarthritis and Fibromyalgia

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Background/Purpose: The pathogenesis of spondyloarthritis (SpA) including axial SpA (axSpA) and psoriatic arthritis (PsA) differs from fibromyalgia (FM). However, symptoms partially overlap and both patient groups suffer from pain and stiffness. In addition, SpA patients may also develop a secondary form of FM. Classification criteria for SpA and

Table 1. Baseline characteristics of all diagnosis subtypes and comparison (p-values) to primary FM diagnosis. '+' : diagnosis with concomitant FM, '-': diagnosis without concomitant FM

Table 1	FM	axSpA-	*p-value*	axSpA+	*p-value*	PsA-	*p-value*	PsA+	*p-value*
Age	56.4±10.2	53.5±14.2	*0.086*	48.7±13.5	*0.026*	56.0±13.2	*<0.001*	58.5±10.4	*0.962*
Male	2%	67%	*<0.001*	0%	—	38%	*<0.001*	6%	*0.322*
HLAB27 pos.	0%	84%	—	71%	—	16%	—	50%	—
CRP (mg/dl)	0.353±0.47	1.09±2.09	*0.001*	0.5±0.3	*0.035*	1.408±3.0	*0.001*	0.5±0.5	*0.031*
NRS pain	7.5±1.6	6.1±2.4	*<0.001*	7.7±1.8	*0.768*	6.4±2.2	*<0.001*	7.3±1.1	*0.223*

diagnostic criteria for FM are used to differentiate between these subsets. Patient reported outcomes (PRO) often generated by questionnaires are used to assess severity and other disease features. We aim to study whether PROs developed for axSpA, PsA, and related physician-based information behave in a similar way in patients diagnosed with FM without an additional chronic inflammatory rheumatic disease (CIRD) as in patients with a primary diagnosis of SpA without or with secondary FM.

Methods: Patients were consecutively recruited. The main inclusion criterion was a clinical diagnosis of FM (without CIRD), axSpA or PsA (without or with secondary FM) and the indication for a treatment adaptation (escalation or change within the same class) for any reason, based on the judgement of experienced rheumatologists. Standardized assessment tools and lab parameters (BASDAI, ASDAS-CRP, DAPSA, patient´s and global assessment (NRS), CRP, BASFI, Fibromyalgia Impact questionnaire (FIQ), Leeds Enthesitis Index (LEI), Maastricht Ankylosing Spondylitis (MASES) and SpA Research Consortium of Canada (SPARCC) Enthesitis Score were assessed and compared between subgroups.

Table 2. Mean values (±standard deviation) of the assessed disease-specific indices and comparison (p-values) to primary FM diagnosis

Table 2	FM	axSpA-	*p-value*	axSpA+	*p-value*	PsA-	*p-value*	PsA+	*p-value*
BASDAI	6.9±1.4	5.2±2.0	*<0.001*	6.9±1.4	*0.858*	—	—	—	—
BASDAI Q1: Fatigue	7.4±1.9	5.7±2.6	*<0.001*	7.8±1.2	*0.667*	—	—	—	—
ASDAS-CRP	3.3±0.6	3.1±1.0	*0.086*	3.7±1.2	*0.208*	—	—	—	—
BASFI	6.4±2.1	5.4±2.5	*0.005*	7.1±1.8	*0.41*	—	—	—	—
DAPSA	43.0±17.8	—	—	—	—	32.0±18.6	*<0.001*	46.5±19.7	*0.37*
FIQ	68.5±13.5	53.9±21.2	*<0.001*	72.3±13.7	*0.352*	57.2±18.3	*<0.001*	68.5±11.6	*0.978*
LEI	4.0±1.6	1.5±1.7	*<0.001*	3.3±1.4	*0.179*	2.4±2.0	*<0.001*	3.6±2.0	*0.625*
MASES	8.6±3.0	3.4±3.3	*<0.001*	8.2±2.9	*0.642*	4.2±3.6	*<0.001*	7.1±3.6	*0.101*
SPARCC	9.4±3.4	3.5±3.4	*<0.001*	7.7±3.8	*0.139*	5.1±3.7	*<0.001*	8.1±3.9	*0.412*

Results: The baseline demographics of 300 recruited patients (100 FM. 100 axSpA and 100 PsA) are shown in Table 1. All patients with FM (primary or secondary to SpA) showed the highest scores in almost all assessments, and this was independent of the main diagnosis (Table 2). In comparison, patients with axSpA or PsA without secondary FM showed significantly lower scores in all PROs as compared to those with primary and secondary FM, with exception of (i) scores of ASDAS-CRP and (ii) duration of morning stiffness (Question 6 of BASDAI), which were not affected by the presence of secondary FM (Table 2).

Conclusion: Secondary FM is leading to significantly higher levels of SpA-specific scores. ASDAS-CRP was the only score that was not influenced by the presence of secondary FM in patients with axSpA even though it was also increased in patients with primary FM, while similar results were found for the duration but not the level of morning stiffness. On the other hand, FM-specific questionnaires also showed high scores in patients with axSpA and PsA with concomitant FM but not in those without.

Disclosure: X. Baraliakos, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **S. Tsiami**, None; **M. Gkelaki**, None; **P. Dukatz**, None; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Braun**, Abbvie, 2, 5, 6, Amgen, 2, 5, 6, Celltrion, 2, 5, 6, Chugai, 2, 5, 6, Medac, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, BMS, 2, 5, 6, Boehringer, 2, 5, 6, Celgene, 2, 5, 6, Centocor, 2, 5, 6, Mundipharma, 2, 5, 6, Sanofi-Aventis, 2, 5, 6, Eli Lilly, 2, 5, 6, EBEWE Pharma, 2, 6.

Abstract Number: 0749

Association Between Clinically Meaningful Back Pain Improvement and Patient-reported Outcomes and Disease Activity in Patients with Ankylosing Spondylitis: Results from a Phase 2/3 Trial

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
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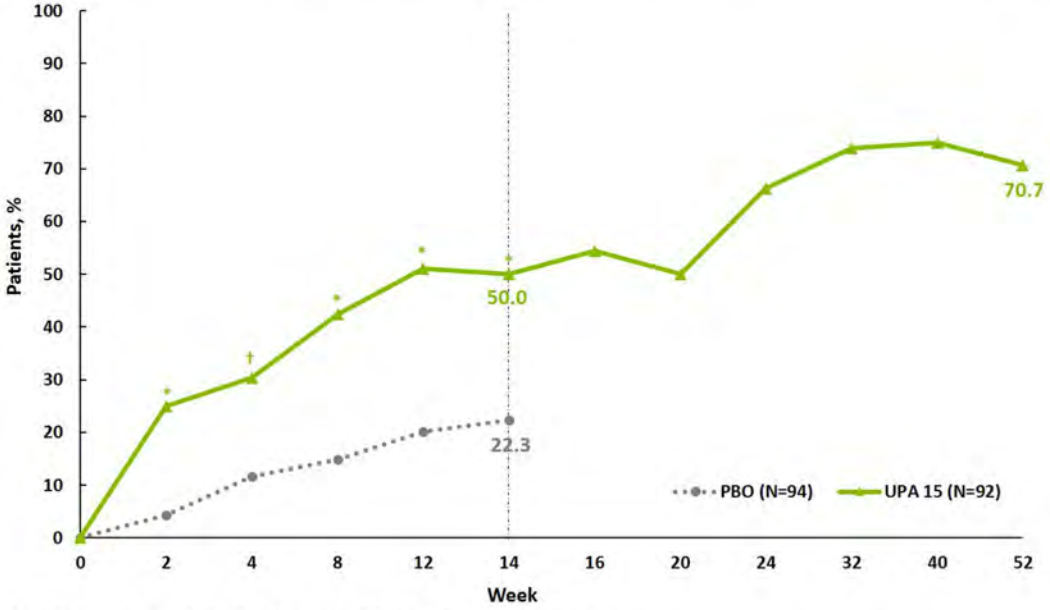
Session Time: 8:30AM–10:30AM

Background/Purpose: Back pain is the hallmark disease feature for patients (pts) with AS. However, the relationship between back pain and other patient-centric outcomes and disease activity measures has not been well characterized. The purpose of this study was to examine the association between meaningful back pain improvement and quality of life, disease activity, physical functioning, fatigue, sleep, and work productivity in pts with AS treated with upadacitinib (UPA) or placebo (PBO) in the phase 2/3 SELECT-AXIS 1 trial[1].

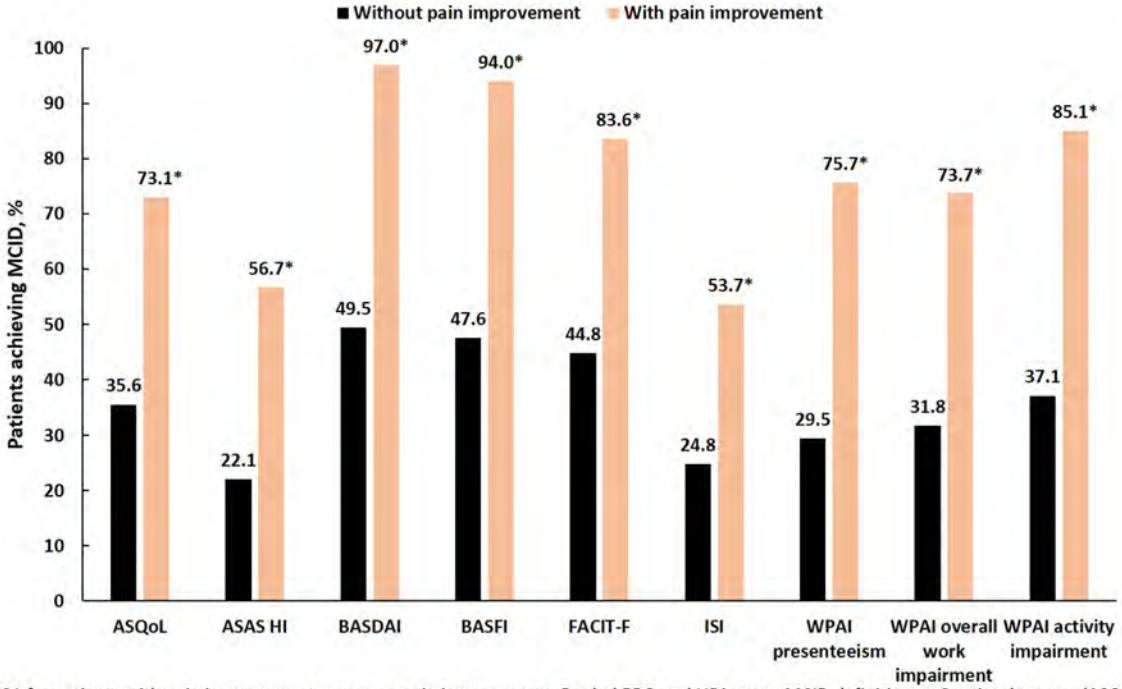
Methods: Active AS pts with an inadequate response to NSAID therapy received UPA 15 mg once daily or PBO for 14 weeks, followed by a 90-week open label extension period. Clinically meaningful back pain improvement was defined as achieving a score of < 4 and ≥2-point decrease from baseline in Patient's Assessment of Total Back Pain score

Figure 1. Proportion of patients achieving meaningful back pain improvement through Week 52 with treatment



*P<0.0001 vs placebo. †P<0.001 vs placebo. PBO, placebo; UPA, upadacitinib.

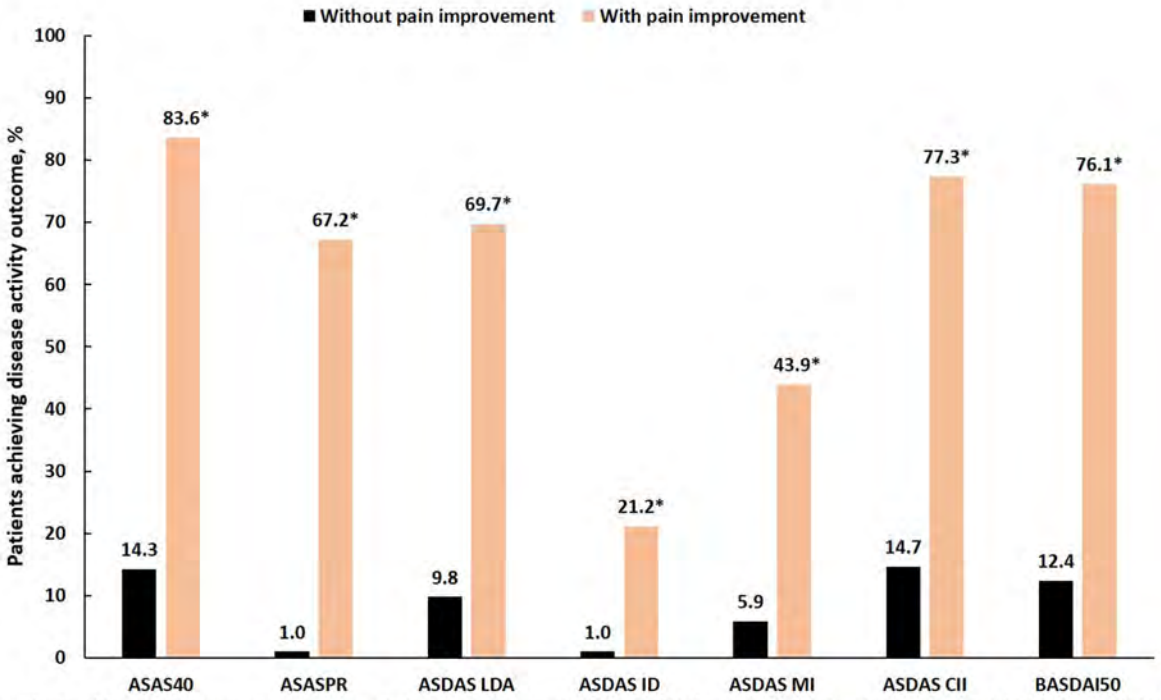
Figure 2. Proportion of patients with and without meaningful back pain improvement achieving MCID in PRO at Week 14



*P≤0.0001 for patients with pain improvement versus no pain improvement. Pooled PBO and UPA arms. MCID definitions: ≥3-point decrease (ASQoL and ASAS HI), ≥1.1-point decrease (BASDAI), ≥0.6-point decrease (BASFI), ≥4-point increase (FACIT-F), ≥6-point decrease (ISI), ≥20% decrease (presenteesism and activity impairment), and ≥15% decrease (overall work impairment).

ASAS HI, Assessment of SpondyloArthritis international Society-Health Index; ASQoL, Ankylosing Spondylitis Quality of Life; BASDAI, Bath Ankylosing Spondylitis Disease Index; BASFI, Bath Ankylosing Spondylitis Functional Index; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; ISI, Insomnia Severity Index; MCID, minimum clinically important difference; PRO, patient-reported outcomes; WPAI, Work Productivity and Activity Impairment.

Figure 3. Proportion of patients with and without meaningful back pain improvement achieving disease activity outcomes at Week 14



*$P \leq 0.0001$ for patients with pain improvement versus no pain improvement. Pooled PBO and UPA arms. ASDAS thresholds: <2.1 (ASDAS LDA), <1.3 (ASDAS ID), ≥2-point decrease (ASDAS MI), and ≥1.1-point decrease (ASDAS CII). ASAS, Assessment of SpondyloArthritis international Society; ASASPR, ASAS partial remission; ASDAS, Ankylosing Spondylitis Disease Activity Score; ASDAS CII, ASDAS clinically important improvement; ASDAS ID, ASDAS inactive disease; ASDAS LDA, ASDAS low disease activity; ASDAS MI, ASDAS major improvement; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

on a numeric rating scale and was assessed at all time points up to Week 52. The proportions of pts maintaining Week 4 meaningful back pain improvement at Week 14 and the proportion of pts at Week 14 in the pooled UPA and PBO arms reporting values ≥ minimum clinically important differences (MCID) in patient-reported outcomes (PROs: BASFI, BASDAI, BASFI, Assessment of SpondyloArthritis international Society-Health Index [ASAS HI], AS Quality of Life [ASQoL], Functional Assessment of Chronic Illness Therapy – Fatigue [FACIT-Fatigue], Insomnia Severity Index [ISI] scores, and Work Productivity and Activity Impairment [WPAI; presenteeism, overall work impairment, and activity impairment]), and achieving disease activity outcomes (ASAS40, ASAS partial remission, AS Disease Activity Score [ASDAS; low disease activity, inactive disease, major improvement, and clinically important improvement], and BASDAI50) as a function of meaningful back pain improvement were also assessed. Analyses were performed using either the Cochran-Mantel-Haenszel test, adjusting for high-sensitivity C-reactive protein with non-responder imputation for comparison between treatments, or Chi-Square test with as observed analysis for comparison between responders/non-responders. *P*-values < 0.05 were nominal.

Results: Meaningful improvement in back pain was achieved by a significantly greater proportion of pts with AS receiving UPA versus PBO starting at Week 2 ($P < 0.001$), with further improvements in the UPA group between Week 14 and Week 52 (Figure 1). Of pts achieving back pain improvement at Week 4, 92.9% of pts on UPA 15 compared to 54.5% of pts on PBO maintained this response at Week 14 ($P < 0.05$). A significantly greater proportion of pts who attained meaningful back pain improvement at Week 14 vs those who did not reported values ≥MCID in all PROs and had greater response across all disease activity outcomes ($P \leq 0.0001$, Figures 2 and 3).

Conclusion: A significantly greater proportion of pts with AS achieved meaningful improvement in back pain with UPA compared to PBO starting at Week 2, with continued improvement through 52 weeks of treatment. Meaningful

back pain improvement was associated with meaningful improvement in other PROs and achievement of important measures of AS disease activity.

Reference: 1. Van der Heijde *et al*. *Lancet*. 2019;394:2108–2117

Disclosure: X. Baraliakos, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **L. Bessette**, Amgen, 2, 5, 6, BMS, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Sanofi, 2, 5, 6, Sandoz, 2, 6, Fresenius Kabi, 2, 6, Teva, 2, 6, Gilead, 2, 5, Celgene, 5; **C. Salvarani**, AbbVie, 2, Pfizer, 2, Lilly, 2, Roche, 2, Novartis, 2, BMS, 2, Merck, 2; **N. Chen**, AbbVie, 3, 11; **R. Lippe**, AbbVie, 3, 11; **J. Patel**, AbbVie, 3; **I. Song**, AbbVie, 3, 11; **P. Zueger**, AbbVie, 3, 11; **P. Goupille**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Merck Sharpe & Dohme, 2, 5, 6, Nordic Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Medac, 2, 5, 6.

Abstract Number: 0750

Effect of Deucravacitinib on the Psoriatic Arthritis Impact of Disease Questionnaires 12 and 9: Analysis of a Phase 2 Study of Active Psoriatic Arthritis

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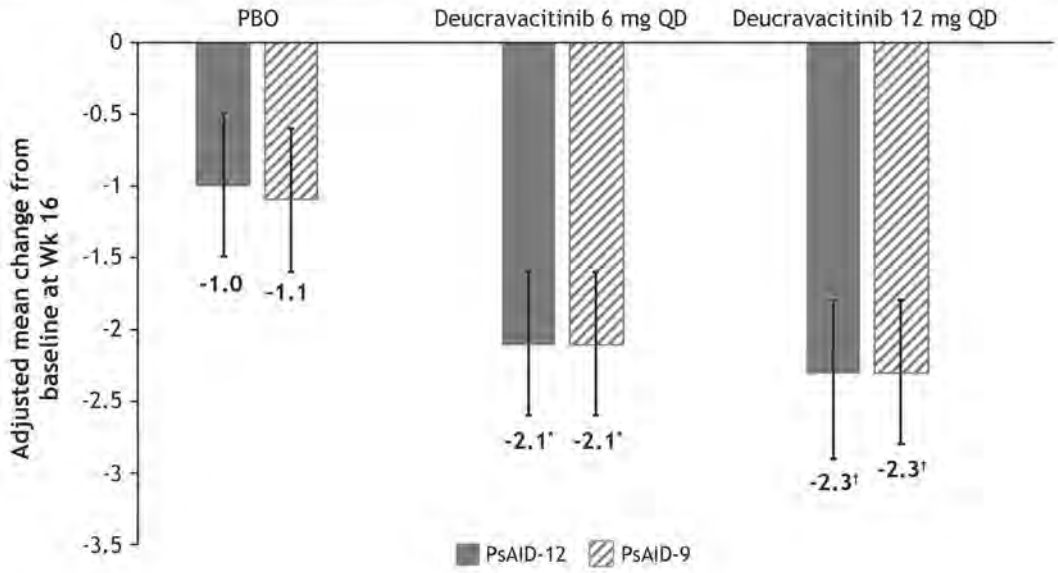
Background/Purpose: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling by cytokines, such as IL-23, IL-12, and IFNα/β, involved in the pathogenesis of PsA and other immune-mediated diseases. Deucravacitinib is a novel, oral selective inhibitor of TYK2 via the TYK2 nonconserved regulatory domain. Phase 2 results showed deucravacitinib was efficacious and well tolerated versus placebo (PBO) in patients (pts) with active PsA. The Psoriatic Arthritis Impact of Disease (PsAID) questionnaire is a validated instrument designed to specifically assess the impact of PsA on health-related quality of life from the pt's perspective and is available as separate versions for clinical practice (PsAID-12) and clinical trials (PsAID-9)[1] This analysis compared the effect of deucravacitinib vs PBO on PsAID-12 and PsAID-9 responses and assessed the relationships between PsAID scores and clinical and pt-reported outcome (PRO) measures.

Methods: In this 1-year, double-blind, Phase 2 trial (NCT03881059), pts with active PsA were randomized 1:1:1 to deucravacitinib 6 mg or 12 mg once daily (QD), or PBO for 16 weeks (Wk). PsAID-12 and PsAID-9, other PROs, and clinical response outcomes were assessed at baseline (BL) and Wk 16. Mean changes from BL in PsAID-12 and PsAID-9 total scores at Wk 16 were determined for each treatment group as well as by response outcomes (ie, achievement of response at Wk 16 for PROs and select clinical response outcomes). Spearman correlations between PsAID-12 and PsAID-9 scores and clinical and PRO measures were also assessed .

Figure. Adjusted mean change from baseline in PsAID-12 and PsAID-9 total scores at Wk 16



*$P \leq 0.002$ vs PBO; †$P \leq 0.0005$ vs PBO.
PBO, placebo; PsAID-9, 9-item Psoriatic Arthritis Impact of Disease questionnaire; PsAID-12, 12-item Psoriatic Arthritis Impact of Disease questionnaire; QD, once daily.

Results: Of 203 pts randomized, 180 (89%) completed 16 Wks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and BL disease characteristics were similar across groups. Mean age was 49.8 years and median PsA duration since diagnosis was 4.5 years. Adjusted mean changes from BL in PsAID-12 and PsAID-9 scores at Wk 16 were significantly greater in the deucravacitinib groups vs PBO (**Figure**). Significant improvements with deucravacitinib vs PBO were also observed in pts who achieved response for PROs and for Psoriatic Arthritis Disease Activity Score low disease activity and ≥75% improvement from BL in Psoriasis Area and Severity Index response (**Table**). In contrast, adjusted mean changes from BL were generally similar with deucravacitinib vs PBO in nonresponders. Spearman correlation analysis revealed significant correlations at BL and Wk 16 between PsAID-12 and PsAID-9 scores and clinical and PRO measures ($P < 0.0001$).

Conclusion: With deucravacitinib vs PBO, PsAID-12 and PsAID-9 scores were significantly improved vs BL at Wk 16. Both PsAID scores detected additional improvements among pts achieving response for multiple other PROs and select clinical outcome measures.

Reference: 1. Gossec L et al. *Ann Rheum Dis*. 2014;73:1012-9.

Table. Adjusted mean change from BL in PsAID-12 total scores at Wk 16 in patients who achieved PRO or clinical response

Response Definition	PBO n=66	Deucravacitinib 6 mg QD n=70	*P* value vs PBO	Deucravacitinib 12 mg QD n=67	*P* value vs PBO
PROs					
Patient global VAS (≤ -10.0)	-1.6 (n=40)	-2.8 (n=54)	0.0008	-2.9 (n=48)	0.0003
Patient pain VAS (≤ -10.0)	-2.3 (n=32)	-3.4 (n=44)	0.004	-3.3 (n=45)	0.004
HAQ-DI (≤ -0.35)	-2.8 (n=10)	-3.8 (n=27)	0.09	-3.8 (n=27)	0.11
FACIT-Fatigue (≥4.0)	-2.4 (n=27)	-3.3 (n=36)	0.02	-3.6 (n=41)	0.002
SF-36 PCS (≥2.5)	-1.7 (n=35)	-2.7 (n=44)	0.02	-3.1 (n=43)	0.001
SF-36 MCS (≥2.5)	-2.1 (n=21)	-3.5 (n=33)	0.005	-3.8 (n=31)	0.0009
Clinician assessments					
PASDAS (≤3.2)	-3.1 (n=6)	-4.2 (n=14)	0.004	-4.5 (n=15)	0.0006
PASI 75 (≥75% improvement from BL)	-2.4 (n=11)	-3.7 (n=25)	0.05	-3.9 (n=31)	0.02

PsAID-9 results were generally consistent with PsAID-12 (data not shown).
Response definitions based on published literature.
Higher FACIT-Fatigue scores indicate *less* fatigue.
Higher SF-36 PCS and SF-36 MCS scores indicate *less* disability.
BL, baseline: FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, Mental Component Summary; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PCS, Physical Component Summary; PRO, patient-reported outcome; QD, once daily; SF-36, 36-item Short Form Health Survey; VAS, visual analog scale.

Disclosure: L. Gossec, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **A. Ogdie-Beatty**, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **T. Lehman**, Bristol Myers Squibb, 3, 11; **M. Nowak**, Bristol Myers Squibb, 3, 11; **L. Wei**, Bristol Myers Squibb, 3, 11; **J. Ye**, Bristol Myers Squibb, 3, 11; **J. Choi**, Bristol Myers Squibb, 3, 11; **J. Zhuo**, Bristol Myers Squibb, 3, 11; **B. Becker**, Bristol Myers Squibb, 3, 11.

Abstract Number: 0751

Are Current Patient Reported Outcomes Instruments Optimized to Capture the Entire Patient Experience?

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic Arthritis (PsA) affects multiple attributes of patient health; to assess treatment effectiveness a compilation of Patient Reported Outcomes (PRO) have been utilized. While useful, most of these were originally created for other diseases and only later validated or adapted for use in PsA. More recent efforts have focused on development of PsA specific PRO tools, with inclusion of patient input and relevance for use in both clinical research and clinical care (1). Our research subjected a broad set of currently used PROs to patient assessment, giving clinicians insight into their usefulness in the clinic and informing ongoing efforts for optimization of PROs in PsA.

Methods: Four focus groups were conducted across three regionally-diverse areas in the United States from March 2016 to October 2016. Patients represented a range of disease history, symptoms, and severity. After trained facilitators encouraged open conversation about PsA, including symptoms, challenges and feelings about disease and treatment, patients were given time to review 13 currently utilized PROs and rate relevance of these instruments to reporting their disease experiences on a 3 point scale of Relevant, Somewhat Relevant, and Irrelevant. Verbal discussion followed on the merits and challenges of each rated PRO.

Results: PRO instruments ranged from overall global assessments to disease specific assessments (Table 1). The PROs received a variety of ratings, with Functional Assessment of Chronic Illness Therapy - Fatigue (FACIT-F) and Psoriatic Arthritis Impact of Disease (PsAID) judged as Very Relevant by the largest number of patients, followed by Health Assessment Questionnaire-Spondyloarthropathies (HAQ-S) and Pain VAS (Figure 1). Instruments receiving the most assessments of Not Really Relevant were Pt Global and PsA Quality of Life (PsAQOL). In the qualitative portion of the research, major patient critiques across PROs were the time frames listed on the questionnaires; some were too restrictive and disallowed reporting important recent disease activity. Preferences were for questions asked as '...since your last visit...'. Multiple participants also agreed that a visual tool allowing patients to circle specific joints to indicate pain would be useful.

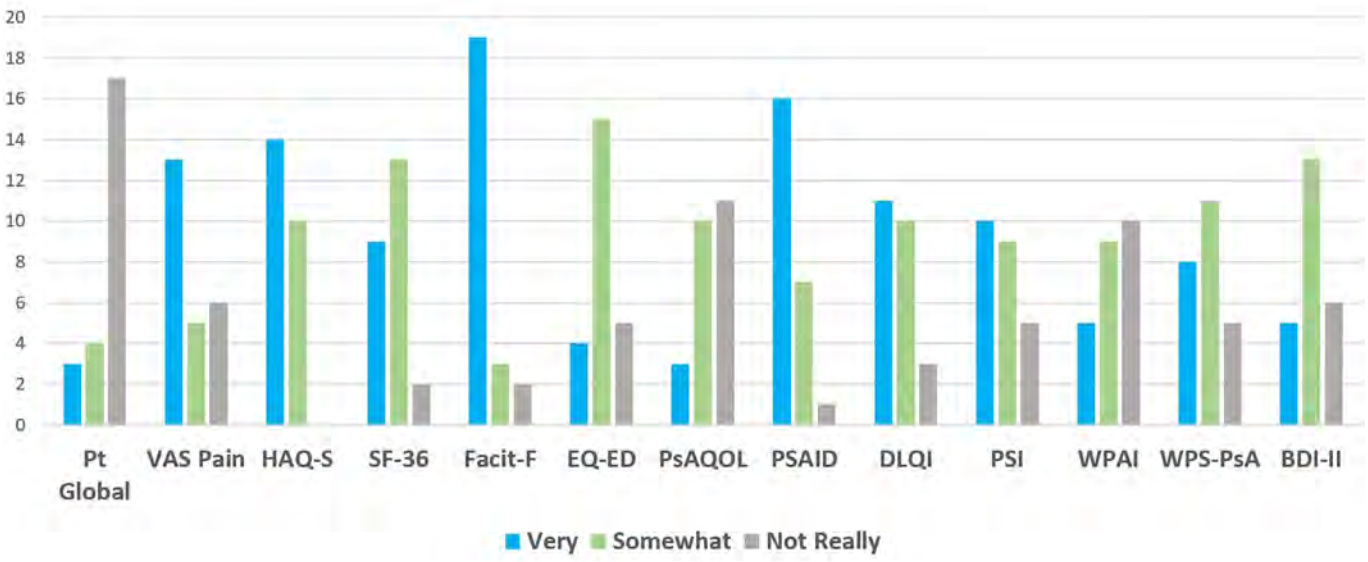
Conclusion: Currently utilized PROs in PsA evaluating domains of fatigue, function, pain, and disease specific manifestations were all important regarding new therapeutic agents. However, some are more relevant than others to patients, most notably FACIT-F and PsAID, the latter being an important example of a patient-led and disease-specific development effort. Allowing reporting of items of concern without restrictive time periods is important to patients. These preferences and comments can be utilized to better understand the value of PROs in clinical settings to optimize patient-clinician communications.

1. Gossec L, de Wit M, Kiltz U, et al. A patient-derived and patient-reported outcome measure for assessing psoriatic arthritis: elaboration and preliminary validation of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a 13-country EULAR initiative. Ann Rheum Dis 2014;73: 1012–9.

Table 1. Outcomes Instruments Assessed in the Study

Tool	Abbreviation	Time Period Queried
Patient Global	Pt GA	None Specified
Pain Visual Analog Scale	Pain VAS	In the past week
Health Assessment Questionnaire-Spondyloarthropathies	HAQ-S	Over the past week
Short Form - 36	SF-36	Different periods queried for different questions: Compared to a year ago; None Specified; Over the past 4 weeks
Functional Assessment of Chronic Illness Therapy - Fatigue	FACIT-F	Past 7 Days
EQ-5D and EQ Visual Analog Scale	EQ-5D-5L	Today
Psoriatic Arthritis Quality of Life	PsAQOL	None specified
Psoriatic Arthritis Impact of Disease	PsAID	During the last week
Dermatology Life Quality Index	DLQI	Over the last Week
Psoriasis Symptom Inventory	PSI	Last 7 days
Work Productivity and Activity Impairment: General Health	WPAI:GH	During the past 7 days
Work Productivity Survey - PsA	WPS-PsA	Last month
Beck Depression Inventory	BDI-II	During the past 2 weeks

Figure 1. Patient Ratings of the Relevance of Outcomes Instruments to Individual PsA Experience



Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **V. Strand**, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2; **D. Furst**, Actelion, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corbus, 2, 6, Galapagos, 2, 5, GSK, 6, Sanofi, 2, 5, 6, Roche/Genentech, 5, National Institutes of Health, 5, Novartis, 2, 5, Pfizer, 2, 5; **E. Siegel**, BMS, 2, Abbvie, 2, 6, Jannsen, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6; **M. Mcilraith**, None; **E. Husni**, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2; **M. Hay**, Novartis, 5, Novartis, 5.

Abstract Number: 0752

Intervening on Adverse Childhood Experiences in SLE—Self-Efficacy as a Potential Target

Kimberly DeQuattro[1], Andrea Seet[1], Laura Trupin[2], Stephanie Rush[1], Kamil Barbour[3], Maria Dall'Era[4], Jinoos Yazdany[1] and Patricia Katz[1], [1]University of California San Francisco, San Francisco, CA, [2]UC San Francisco, San Francisco, CA, [3]Centers for Disease Control, Atlanta, GA, [4]University of California San Francisco, Corte Madera, CA

SESSION INFORMATION
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Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Modifiable adaptations to adversity such as resilience (the ability to recover from difficulty) and self-efficacy (the belief in one's ability to succeed in a situation) may be protective for those with SLE who experience stress. We previously reported that patients with a history of adverse childhood experiences (ACEs) demonstrate worse patient-reported outcomes. There are gaps in how to ameliorate poor outcomes among patients who experienced ACEs. We seek to identify patterns of adaptations to adversity as potential targets for future interventions in this population.

Methods: Data are from the California Lupus Epidemiology Study (CLUES), a diverse sample of adult SLE patients with confirmed diagnosis of SLE (met (a) ≥4/11 ACR 1982/1997 criteria for the classification of SLE, (b) 3/11 ACR 1982/1997 criteria and treating rheumatologist's diagnosis of SLE, or (c) diagnosis of SLE nephritis). Participants completed a 10-item ACE questionnaire (range 0-10), a 4-item Brief Resilience Coping Score (BRCS, range 0-12), and the PROMIS self-efficacy survey. We examined associations for patient-reported measures of disease activity (SLAQ) and depression (PHQ-8) as well as ACEs with BRCS and self-efficacy using ANOVA and linear regression, controlling for age, gender, race/ethnicity, education, and disease duration. We also tested for interactions between ACE scores and resilience/self-efficacy.

Results: Of the 205 participants, 91.7% were female and 69.3% were non-white, with a mean ACE score of 1.76 (SD 2.1). Resilience was at the middle of the scale range (mean 8.4, SD 2.0) and the self-efficacy PROMIS measure was near the mean for the population distribution (mean 49.0, SD 9.1). There were similar levels of resilience and self-efficacy across ACE score categories (Table 1). As depicted (Table 2), there were significantly worse SLAQ and PHQ scores for people with higher ACE scores compared to people in the low ACE score category (0-1). Resilience showed no significant independent effect on SLAQ or PHQ, but self-efficacy was associated with better PHQ scores and SLAQ scores, although the latter did not reach statistical significance. Interactions between ACE score and resilience/self-efficacy were not statistically significant.

Table 1. Resilience, self-efficacy, disease activity, and depression among individuals with SLE (N=205) by Adverse Childhood Experience Score Category

	Adverse Childhood Experience Score Category			
	Low (0-1) (mean, sd) N = 121	Medium (2-3) (mean, sd) N = 44	High (4+) (mean, sd) N = 40	ANOVA p-value
Resilience	8.3 (2.0)	8.4 (2.0)	8.9 (1.8)	0.14
Self-Efficacy	48.6 (9.3)	49.2 (8.8)	49.2 (9.3)	0.67
SLAQ	7.6 (6.7)	10.9 (7.5)	14.0 (8.1)	<0.01**
PHQ-8	5.3 (4.6)	7.8 (5.8)	8.7 (5.1)	<0.01**

SLAQ - Systemic Lupus Activity Questionnaire; PHQ-8 - Patient Health Questionnaire depression scale
Self-Efficacy is a 4-item PROMIS subscale normed as T-scores with a population mean of 50 and standard deviation of 10

Table 2. Patient reported disease activity (SLAQ) and depression (PHQ-8) by Adverse Childhood Experience (ACEs) Score Category, Brief Resilience Coping Score, and PROMIS Self-Efficacy, from linear regression models adjusting for covariates[1]

	Disease Activity (SLAQ)		Depression (PHQ-8)	
	Beta ± SE	p-value	Beta ± SE	p-value
ACEs Score Category				
0-1	Ref	--	Ref	--
2-3	2.21 ± 1.21	0.07	2.02 ± 0.88	0.02*
≥4	4.96 ± 1.28	<0.01**	3.01 ± 0.93	<0.01**
Resilience	0.32 ± 0.25	0.20	-0.16 ± 0.18	0.38
Self-Efficacy	-0.11 ± 0.06	0.06	-0.13 ± 0.04	<0.01**

SLAQ - Systemic Lupus Activity Questionnaire; PHQ-8 - Patient Health Questionnaire depression scale
[1]Adjusted for age, gender, race, disease duration, education level.
Self-Efficacy is a 4-item PROMIS subscale normed as T-scores with a population mean of 50 and standard deviation of 10

Conclusion: Individuals with SLE with the highest ACEs exposures reported high disease activity and depression. Resilience did not show protective effects on the outcomes examined in this cohort. However, self-efficacy, for which interventions have been developed, was associated with less depression, suggesting the potential for interventions targeting self-efficacy to improve outcomes. Experiencing ACEs did not affect whether a participant was more or less resilient or self-efficacious. Additional targets for interventions, such as social support, merit exploration to better bolster SLE patients with a history of ACEs.

Disclosure: K. DeQuattro, None; **A. Seet**, None; **L. Trupin**, None; **S. Rush**, None; **K. Barbour**, None; **M. Dall'Era**, AstraZeneca, 2, Aurinia, 2, Biogen, 2, Bristol Myers Squibb, 2, GlaxoSmithKline, 2, Pfizer, 2; **J. Yazdany**, Astra Zeneca, 2, 5, Pfizer, 2, 6, Gilead, 5, BMS Foundation, 5; **P. Katz**, None.

Abstract Number: 0753

Patient-Reported Burden of Adverse Drug Reactions Attributed to the Use of Adalimumab and Etanercept in Patients with Inflammatory Rheumatic Diseases

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
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Background/Purpose: Health care professionals tend to focus on adverse drug reactions (ADRs) with the highest clinical impact. Subsequently, ADRs with less obvious clinical impact but with a high impact on patient's daily lives, might be overlooked. These ADRs may occur frequently and therefore constitute a considerable part of the total perceived burden of ADRs. To develop strategies to reduce the burden of ADRs, it is important to know which ADRs have the highest impact on patients' lives. The aim of the study was to gain insight into which patient-reported ADRs contribute most to the total experienced ADR burden attributed to the use of etanercept (ETN) and adalimumab (ADA).

Methods: Data of the Dutch Biologic Monitor (DBM) was used. In the DBM, immune-mediated inflammatory disease patients using biologicals were asked to fill out bimonthly questionnaires on experienced ADRs attributed to the biologic and the burden of the ADR using a five-point Likert-type scale ranging from 1 (no burden) to 5 (very high burden). Inclusion criteria for the present study were: patients with rheumatoid arthritis, psoriatic arthritis or spondyloarthritis using ADA or ETN, reporting an ADR with a burden score of 2 or higher. The ADRs reported for ADA and ETN were grouped into system organ classes (SOCs) according to the Medical Dictionary for Regulatory Activities. Every ADR in the SOC is multiplied with the corresponding burden score, summating the experienced burden per SOC. The total experienced burden of ADA and ETN is the sum of the experienced burdens of all SOCs. The proportion of the burden per SOC is calculated by dividing the burden per SOC by the total burden of all SOCs. ADRs per SOC were further stratified by ADA and ETN use, and analysed separately to identify possible differences.

Results: A total 196 patients met the inclusion criteria, of which 95 patients (48%) reported an ADR for adalimumab (575 ADRs) and 101 patients (52%) reported and ADR for ETN (793 ADRs), see Table 1. The proportion of experi-

Table 1 Demographics and characteristics of patients

	Total	Adalimumab	Etanercept
	N (%)	N (%)	N (%)
Characteristics	196 (100)	95 (48)	101 (52)
Gender (female)	136 (69)	63 (66)	73 (72)
Age (years) (mean ± SD)	55.6 ± 14.1	55.3 ± 14.0	55.9 ± 14.3
Biologic	196 (100)	95 (48)	101 (52)
Indication[a]			
Rheumatoid arthritis	124 (100)	52 (55)	72 (71)
Spondyloarthritis	40 (100)	22 (23)	18 (18)
Arthritis psoriatic	36 (100)	22 (23)	14 (14)
Drug-induced ADR burden (mean ± SD)	3.09 ± 0.56	3.04 ± 0.66	2.95 ± 0.49
Number of completed questionnaires (mean ± SD)	4.2 ± 7.0	3.6 ± 4.0	4.7 ± 9.0

[a]Patients could report more than one indication

Table 2 The proportion of burden of ADRs per system organ class (SOC) for adalimumab and etanercept

SOC	Proportion of the burden (%)	Mean burden	Number of reports
General disorders and administration site conditions	26,7	2,6	408
Infections and infestations	19,4	3,2	241
Skin and subcutaneous tissue disorders	13,1	2,9	177
Gastrointestinal disorders	9,5	2,8	133
Musculoskeletal and connective tissue disorders	8,1	3,2	98
Respiratory, thoracic and mediastinal disorders	6,6	2,7	95
Nervous system disorders	5,2	2,9	69
Eye disorders	4,3	3,2	54
Psychiatric disorders	1,7	3,1	21
Vascular disorders	1,3	2,6	20

enced burden attributed to ADA and ETN is summarized in Table 2. The ADRs that account for the highest proportion are general disorders (such as fatigue) and administration site conditions (such as injection site pain), infections and infestations (such as respiratory tract infections and nasopharyngitis), skin and subcutaneous tissue disorders (such

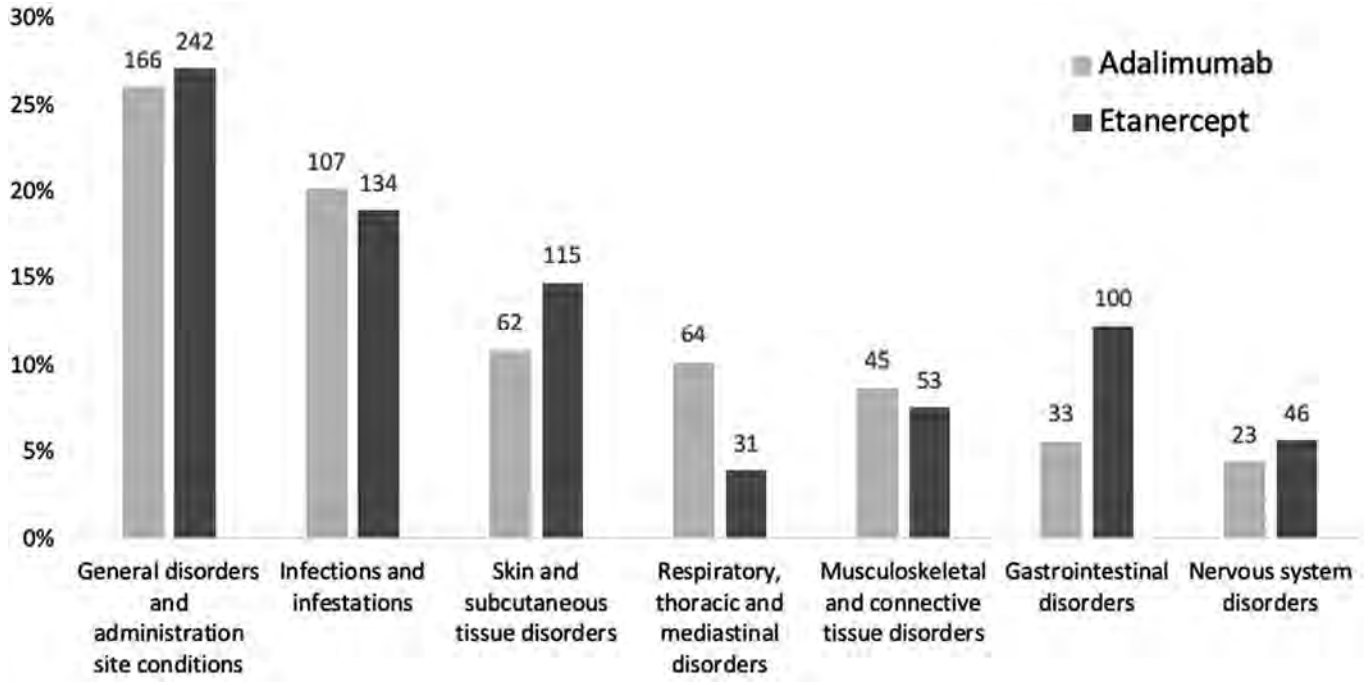

Figure 1. Proportion of experienced burden of adverse drug reaction per system organ class for adalimumab (575 ADRs) and etanercept (793 ADRs) with each their respective ADR count represented at the top of the bars.

as dry skin and pruritus). The proportion of burden of ADRs for ADA and ETN are comparable, except for skin and subcutaneous tissue disorders, respiratory, thoracic and mediastinal disorders, gastrointestinal disorders and vascular disorders (see Figure 1).

Conclusion: ADRs belonging to the SOCs General disorders and infections are the foremost contributors to the ADR burden. These ADRs are well-known and this outcome is as expected. Less known and new is information the high proportion of burden attributed to ADRs in the SOC skin and subcutaneous tissue disorders. Addressing these ADRs offers opportunities to reduce the burden associated with the use of ADA and ETN. Furthermore, although ADA and ETN are clinically considered comparable, our findings point to differences in proportions of experienced burden of ADRs grouped per SOC.

Disclosure: J. Davelaar, None; **N. Jessurun**, None; **S. Tas**, None; **M. Nurmohamed**, Abbvie, 4, Eli Lilly, 2, Celltrion, 2, GSK, 2, Novartis, 5, Janssen, 6, Pfizer, 5, Galapagos, 5; **B. van den Bemt**, None; **H. Vonkeman**, Novartis, 1, 6, Sanofi, 1, 6, Janssen-Cilag, 1, Roche, 6, Pfizer, 1, 6, Galapagos, 1.

Abstract Number: 0754

Bridging the Gap Between Patient-Reported Outcomes and Disease-Related Outcomes in Lupus – a Feasibility Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1. Patient Demographics.

Patient-Visits, No. of Patients	250 visits; 75 patients
Age (mean±SD)	37±19 years
Racial/Ethnicity	
White	52 (69%)
Other*	23 (31%)
Gender	
Female	70 (93%)
Male	5 (7%)
PROMIS-Physical Health (mean±SD)	12.7±1.9
PROMIS-Mental Health (mean±SD)	11.9±2.3
LupusQOL-Total Domain Score (mean±SD)	560±170
SLEDAI (mean±SD)	2.3±2.6
SLICC-DI (mean±SD)	0.82±1.03

Background/Purpose: Patients with SLE have significantly worse health-related quality of life (QOL) at an earlier age compared to patients with other chronic diseases. This highlights the importance of measuring and addressing patient-reported outcomes (PROs) to improve outcomes and QOL in SLE. Yet, QOL tools are lengthy and offer limited guidance to clinicians on use to impact disease-related outcomes in SLE. There is a need to improve feasibility such as using global short-form QOL measures. Therefore, we examined the feasibility of collecting global and lupus specific QOL measures in an academic SLE center and their correlation with disease-related outcomes.

Methods: Our study included all consecutive SLE follow-up visits at the UW SLE Clinic between 3/2019-5/2021. At each visit: 1) patients completed both the Patient Reported Outcome Measure Information System (PROMIS) Global Short Form and the LupusQOL; 2) physicians completed SLE disease activity index (SLEDAI) and SLICC-ACR damage index (SLICC DI). We calculated Pearson's correlation between PROMIS – Global physical and mental health scores, and LupusQOL domain scores and a total LupusQOL score. Next, we tested correlation between SLEDAI and PROMIS – global physical and mental health scores and LupusQOL domain and total scores, and SLICC-DI and both QOL scores.

Results: Between 1/1/19-4/1/21, there were 250 consecutive follow-up patient-visits of 75 patients with confirmed SLE at our clinic. Patients (Table 1) were 93% female, 69% White, and mean age at SLE diagnosis was 37 years. We noted that LupusQOL was completed in 106 patient visits (43%), PROMIS – Global was completed in 100 patient visits (40%), and SLEDAI, SLICC-DI completion rates were each 72%.

We found moderate correlation between both PROMIS-Global physical and mental health scores and total LupusQOL domain score ($r = 0.55$, $p < 0.001$; $r = 0.52$, $p < 0.001$) (Table 2). Further, PROMIS-Global physical health scores had moderate correlation with LupusQOL pain ($r = 0.56$, $p < 0.001$) and physical health (0.60, $p < 0.001$) domains (Table 2). While PROMIS-Global mental health scores only moderately correlated with all LupusQOL domains except the

Table 2. Correlations Between PROMIS Global Physical and Mental Health Scores & LupusQOL Domain Scores, n = 250 patient-visits

PROMIS Global Short-Form (Physical & Mental Health)	LupusQOL (8 domains)	Correlation Coefficient (95% CI)	p-value
PROMIS - Physical Health	**Pain**	**0.56 (0.41, 0.68)**	**<0.001**
PROMIS - Physical Health	Fatigue	0.38 (0.19, 0.54)	0.0014
PROMIS - Physical Health	**Physical Health**	**0.60 (0.45, 0.71)**	**<0.001**
PROMIS - Physical Health	Emotional	0.37 (0.18, 0.53)	<0.001
PROMIS - Physical Health	Burden	0.35 (0.16, 0.51)	0.004
PROMIS - Physical Health	Body Image	0.39 (0.21, 0.55)	<0.001
PROMIS - Physical Health	Intimate Relationship	0.33 (0.14, 0.50)	<0.001
PROMIS - Physical Health	Planning	0.46 (0.29, 0.55)	<0.001
PROMIS - Physical Health	**Total Domain Score**	**0.55 (0.38, 0.68)**	**<0.001**
PROMIS - Mental Health	Pain	0.48 (0.31, 0.62)	<0.001
PROMIS - Mental Health	Fatigue	0.46 (0.28, 0.61)	<0.001
PROMIS - Mental Health	Physical Health	0.48 (0.31, 0.62)	<0.001
PROMIS - Mental Health	Emotional Health	0.35 (0.16, 0.51)	0.005
PROMIS - Mental Health	Burden	0.23 (0.03, 0.41)	0.02
PROMIS - Mental Health	Body Image	0.41 (0.22, 0.56)	<0.001
PROMIS - Mental Health	Intimate Relationship	0.34 (0.15, 0.51)	<0.001
PROMIS - Mental Health	Planning	0.48 (0.31, 0.62)	<0.001
PROMIS - Mental Health	**Total Domain Score**	**0.52 (0.34, 0.65)**	**<0.001**

Moderate correlations shown in bold font.

burden domain. Next, we noted statistically significant correlation between high SLEDAI and low total LupusQOL scores (r = -0.31, p 0.0029), low LupusQOL emotional health scores (r = -0.30, p 0.004) and low LupusQOL fatigue scores (r=-0.31, p 0.002) (Table 3). We noted statistically significant but low correlation between high SLICC-DI and low LupusQOL pain score (r = -0.30, p 0.0023) (Table 3.). No correlations were noted between PROMIS and SLEDAI, and PROMIS and SLICC-DI.

Conclusion: Our findings highlight that specific LupusQOL domains correlate with disease-related outcomes which could be targeted in busy clinical settings to improve QOL. Further, the PROMIS global short-form moderately correlates with key LupusQOL domains thus, this could be utilized in busy practices to assess QOL. Given a moderate QOL completion rate, future studies are required to develop short, actionable tools to incorporate key specific LupusQOL domains that correlate with disease scores to improve disease and patient outcomes in SLE.

Table 3. Correlations Between SLEDAI & SLICC-DI, and PROMIS Global Physical and Mental Health Scores & LupusQOL Domain Scores, n = 250 patient-visits

Quality Of Life (QOL) Measures	Disease Related Outcomes	Correlation Coefficient (95% CI)	p-value
PROMIS - Physical Health	SLEDAI	-0.16 (-0.34, 0.04)	0.13
PROMIS - Mental Health	SLEDAI	-0.77 (-0.27, 0.12)	0.45
LupusQOL- Pain	SLEDAI	-0.13 (-0.3, 0.06)	0.16
LupusQOL- Fatigue	**SLEDAI**	**-0.31 (-0.48, -0.12)**	**0.0017**
LupusQOL- Physical Health	SLEDAI	-0.18 (-0.36, 0.02)	0.07
LupusQOL- Emotional Health	**SLEDAI**	**-0.30 (-0.46, -0.1)**	**0.004**
LupusQOL- Burden	SLEDAI	-0.19 (-0.37, 0.007)	0.059
LupusQOL- Body Image	SLEDAI	-0.21 (-0.39, -0.02)	0.054
LupusQOL- Intimate Relationship	SLEDAI	-0.20 (-0.38, 0.004)	0.054
LupusQOL- Planning	SLEDAI	-0.22 (-0.39, -0.02)	0.031
LupusQOL- Total Domain Score	**SLEDAI**	**-0.31 (-0.49, -0.11)**	**0.0029**
PROMIS - Physical Health	SLICC-DI	-0.10 (-0.28, 0.10)	0.34
PROMIS - Mental Health	SLICC-DI	-0.13 (-0.30, 0.017)	0.19
LupusQOL-Pain	**SLICC-DI**	**-0.30 (-0.46, 0.11)**	**0.0023**
LupusQOL-Fatigue	SLICC-DI	-0.06 (-0.13, 0.26)	0.53
LupusQOL-Physical Health	SLICC-DI	-0.23 (-0.4, -0.04)	0.018
LupusQOL-Emotional Health	SLICC-DI	-0.17 (-0.36, 0.024)	0.08
LupusQOL-Burden	SLICC-DI	-0.054 (-0.24, 0.14)	0.58
LupusQOL-Body Image	SLICC-DI	-0.15 (-0.33, -0.05)	0.15
LupusQOL-Intimate Relationship	SLICC-DI	-0.077 (-0.27, 0.12)	0.45
LupusQOL-Planning	SLICC-DI	-0.112 (-0.29, 0.08)	0.25
LupusQOL-Total Domain Score	SLICC-DI	-0.13 (-0.32, 0.08)	0.23

Significant correlations shown in bold font.

Disclosure: S. Garg, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 0755

Satisfaction with the Process versus Outcome of Care in Total Hip and Knee Arthroplasty

J. Alex Gibbons[1], Cynthia Kahlenberg[1], Bella Mehta[2], Vinicius Antao[1], Emily Ying Lai[1], Huong Do[1], Linda Russell[1], Peter Sculco[1], Mark Figgie[1] and Susan Goodman[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patient satisfaction, both with the process of care and the outcome of care, is critical for measuring the quality and value of elective procedures such as arthroplasty, leading the Centers for Medicare and Medicaid (CMS) to include patient satisfaction with the process of care in their payment models. The purpose of this study was to evaluate the association between patient-reported early postoperative satisfaction with the process of care and 2-year satisfaction with the outcome of care after primary total hip (THA) and total knee arthroplasty (TKA).

Methods: We identified patients that underwent primary THA or TKA from an institutional arthroplasty registry which administered a survey measuring satisfaction with the outcome of care to patients 2-years post-operatively. An overall satisfaction score was calculated using a previously validated score. Patient satisfaction with the process of care, as measured by the Press Ganey (PG) inpatient survey administered to patients shortly after discharge, was obtained and linked to the registry data. Both satisfaction measures have a range of 0-100, with higher scores indicating greater satisfaction. Spearman rank correlation coefficients were calculated to evaluate the association between satisfaction with the process of care (PG score) and the outcome of care (2-year score).

Results: The cohort included 721 TKA patients and 760 THA patients who underwent surgery at our institution and completed both the PG survey and 2-year satisfaction questionnaire (**Table 1)**. The mean age was 65.1 years, mean BMI was 28.8, and 56% were female. Satisfaction was high for both measures, with a mean PG score of 88.2 and a mean 2-year score of 95.6. Correlation between the two measures was fair to poor, with Spearman rank correlation coefficients of 0.23 for TKA patients ($p < 0.001$) and 0.13 for THA patients ($p < 0.001$). Bubble charts showing the distribution of patients by PG score and 2-year score for TKA and THA are presented in Figures 1a and 1b, respectively.

Conclusion: We found weak correlation between measurements of satisfaction with the process of care surrounding joint arthroplasty using the PG survey and satisfaction with the outcome of care after hip and knee arthroplasty using a validated 2-year satisfaction score. Policymakers should consider both facets of patient satisfaction when considering hospital performance and the value of elective surgical procedures.

Table 1. Demographic characteristics by TKA/THA

Variable, N (%)	Overall N = 1,481	TKA N = 721	THA N = 760
Age (mean)	65.1	67.1	63.3
BMI (mean)	28.8	30.1	27.6
Sex: Female	824 (55.6%)	425 (59.0%)	399 (52.5%)
Race			
Asian	9 (0.6%)	6 (0.8%)	3 (0.4%)
Black	38 (2.6%)	20 (2.8%)	18 (2.4%)
Hispanic	25 (1.7%)	17 (2.4%)	8 (1.1%)
Native/Pacific Islander	1 (0.1%)	—	1 (0.1%)
White	1391 (94.0%)	668 (92.8%)	723 (95.1%)
Other	16 (1.1%)	9 (1.3%)	7 (0.9%)
Primary Payer			
Medicare	792 (53.5%)	454 (63.0)	338 (44.5)
Medicaid	1 (0.07%)	—	1 (0.1)
Private Insurance	55 (3.7%)	29 (4.0)	26 (3.4)
Other	633 (42.7%)	238 (33.0)	395 (52.0)
Discharge Disposition			
Home	925 (62.5%)	351 (48.7%)	574 (75.5%)
Acute Care	6 (0.4%)	3 (0.4%)	3 (0.4%)
SNF/Rehab	550 (37.1%)	367 (50.9%)	183 (24.1%)
KOOS Baseline (mean)			
Pain	N/A	49.6	N/A
Stiffness	N/A	51.9	N/A
ADL	N/A	54.8	N/A
Sport	N/A	25.0	N/A
QOL	N/A	26.3	N/A
KOOS 2-year (mean)			
Pain	N/A	89.3	N/A
Stiffness	N/A	60.2	N/A
ADL	N/A	86.3	N/A
Sport	N/A	61.1	N/A
QOL	N/A	70.7	N/A
HOOS Baseline (mean)			
Pain	N/A	N/A	46.6
Stiffness	N/A	N/A	49.1
ADL	N/A	N/A	49.5
Sport	N/A	N/A	30.1
QOL	N/A	N/A	23.9
HOOS 2-year (mean)			
Pain	N/A	N/A	93.3
Stiffness	N/A	N/A	87.7
ADL	N/A	N/A	90.9
Sport	N/A	N/A	77.9
QOL	N/A	N/A	79.6
PCS Baseline (mean)	33.7	34.2	33.3
MCS Baseline (mean)	52.4	53.2	51.6
PCS 2-year (mean)	48.6	47.2	49.9
MCS 2-year (mean)	54.8	54.9	54.8
Charlson comorbidity index			
0	1110 (75.0%)	510 (70.7%)	600 (79.0%)
1	284 (19.2%)	160 (22.2%)	124 (16.3%)
2+	87 (5.8%)	51 (7.1%)	36 (4.7%)
ASA status			
1	79 (5.3%)	14 (1.9%)	65 (8.6%)
2	1164 (78.6%)	577 (80.0%)	587 (77.2%)
3	236 (15.9%)	129 (17.9%)	107 (14.1%)
4	2 (0.1%)	1 (0.1%)	1 (0.1%)
2-year Satisfaction score quartiles (total)			
Q1	87.5	87.5	93.75
Q2	100	100	100
Q3	100	100	100
Q4	100	100	100

Note: all values presented as N (%) unless stated otherwise.

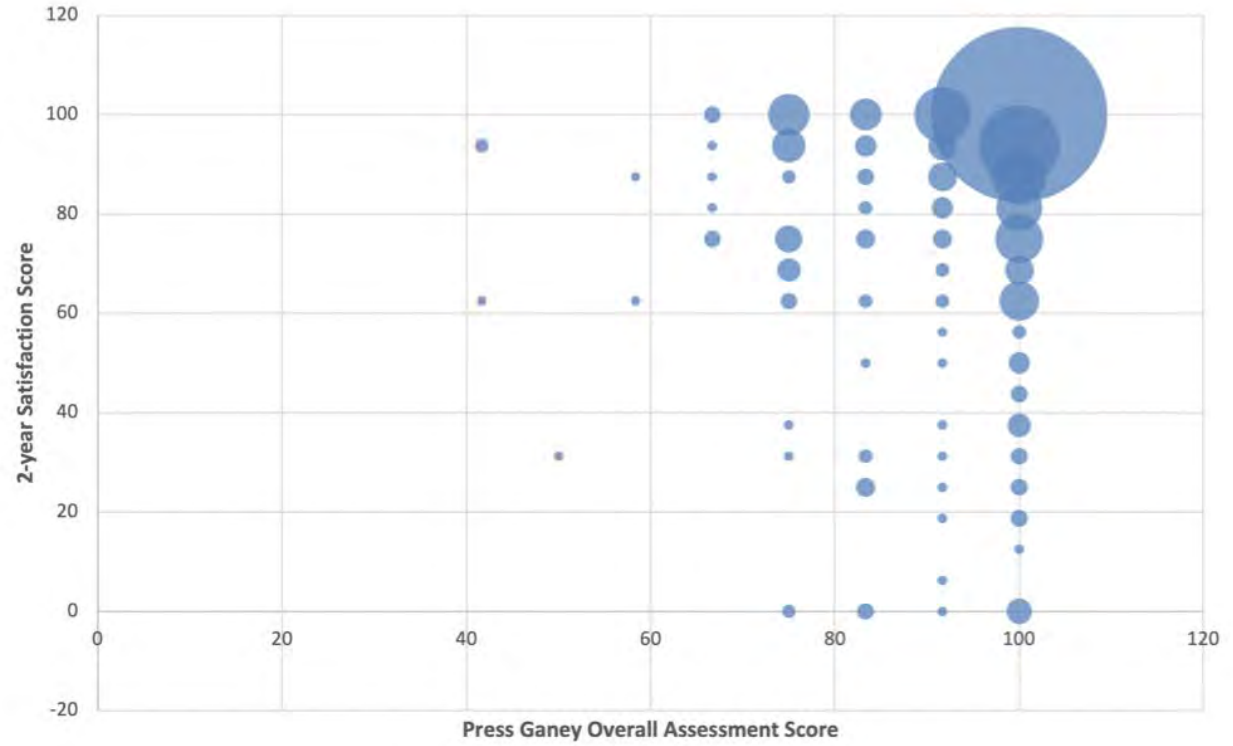

Figure 1a. Bubble Chart Displaying PG Score vs. 2-year Score for TKA patients. Bubble chart displaying Press Ganey Overall Assessment Score (PG Score) and 2-year Satisfaction Score (2-year Score) for TKA patients. Bubble size represents the proportion patients with the corresponding values of these scores.

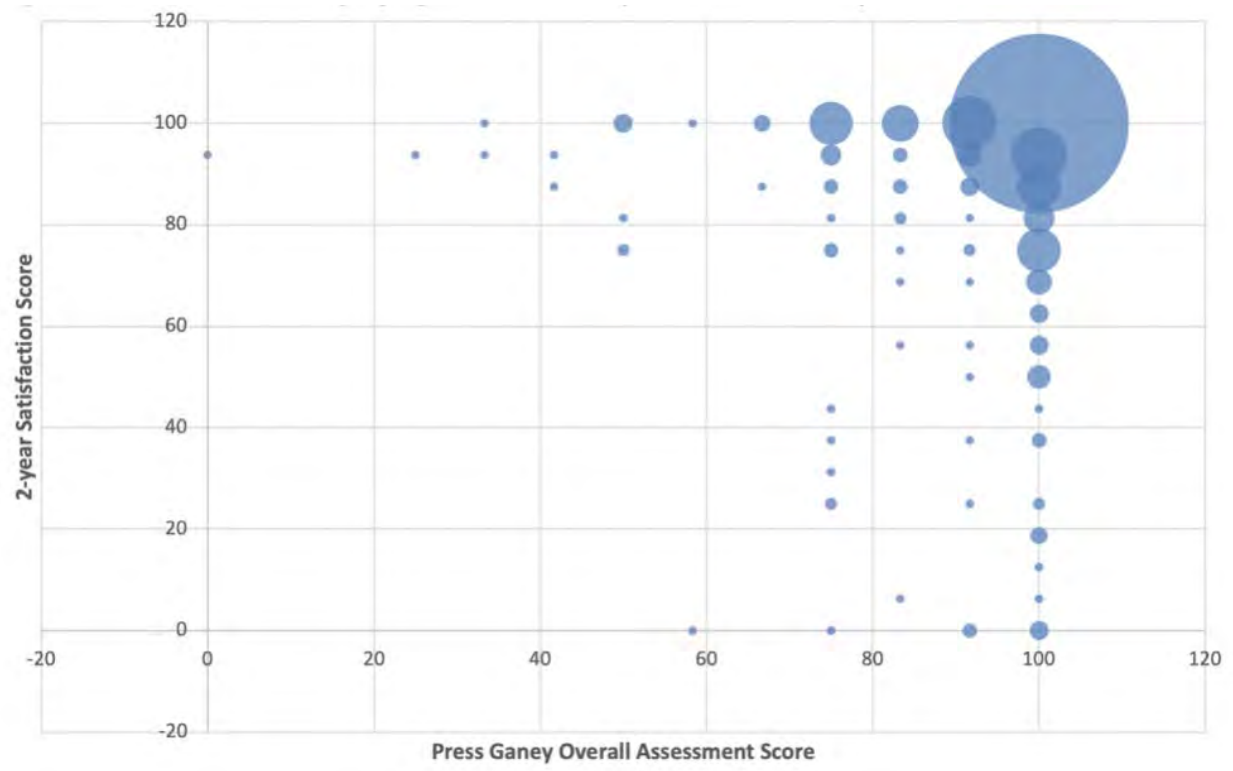

Figure 1b. Bubble Chart Displaying PG Score vs. 2-year Score for THA patients. Bubble chart displaying Press Ganey Overall Assessment Score (PG Score) and 2-year Satisfaction Score (2-year Score) for THA patients. Bubble size represents the proportion patients with the corresponding values of these scores.

Disclosure: J. Gibbons, None; **C. Kahlenberg**, None; **B. Mehta**, Novartis, 1, 6; **V. Antao**, None; **E. Lai**, None; **H. Do**, None; **L. Russell**, Arthritis Foundation, 4; **P. Sculco**, DePuy, 2, 6, EOS Imaging, 2, 6, Intellijoint Surgical, 2, 5, 6, 11, Lima Corporate, 2, Parvizi Surgical, 11, Zimmer, 2; **M. Figgie**, HS2, 11, Lima, 2, 10, mekanika, 11, Wishbone, 2, 10, 11; **S. Goodman**, UCB, 1, NOvartis, 5.

Abstract Number: 0756

Validation of Two Simple Patient-centered Outcome Measures for Virtual Monitoring of Patients with Idiopathic Inflammatory Myositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Changing landscape of patient care from in-person to virtual telemedicine-based consultation in times of a global pandemic has necessitated a wider use of patient-centered outcomes measures (PCOMs) and device-based measures for objective disease assessment. We prospectively validated 2 novel task based PCOMs for physical function, namely Arm Lift test (AL) & Two-Minute Walk Distance (2MWD) in idiopathic myositis (IIM) patients.

Methods: This was a prospective observational study with enrolment of adult patients with IIM in the MyoCite cohort (2017 ACR/EULAR criteria). Both active and inactive disease patients were enrolled. Active disease was defined as escalation of immunosuppression within 3 months, elevated muscle enzymes, physician VAS ≥2, skin disease worsening or fall in MMT8< 76 (any 2).

Two novel tests were performed at baseline; AL: Time taken for arm abduction ten times & 2MWD: distance walked in 2 minutes. We also evaluated all myositis core set measures [MMT 8, patient and physician global disease activity (PtGA and PhGA), HAQ-DI, extra-muscular disease activity as well as MDAAT & MDI]. Test-discriminant validity was tested between active and inactive myositis.

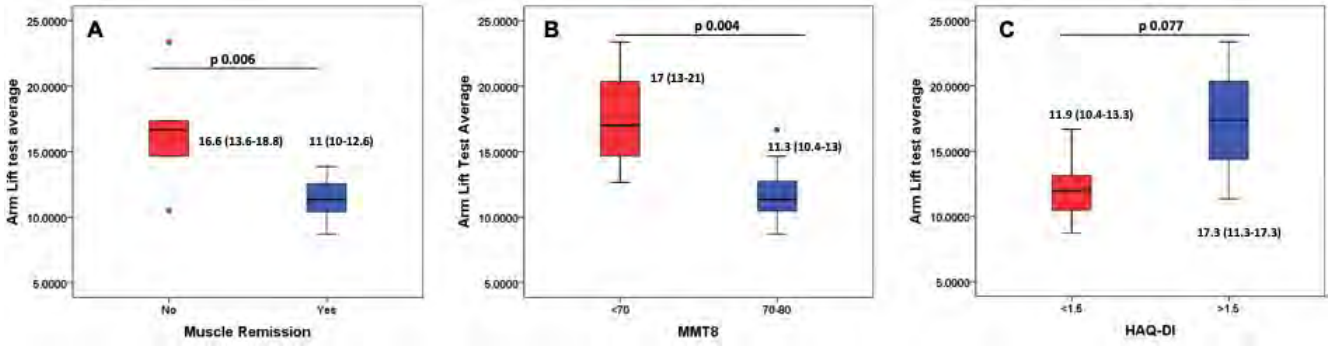

Figure 1. Arm lift test variation based on muscle disease remission (A), MMT8 (B) and HAQ-DI (C).

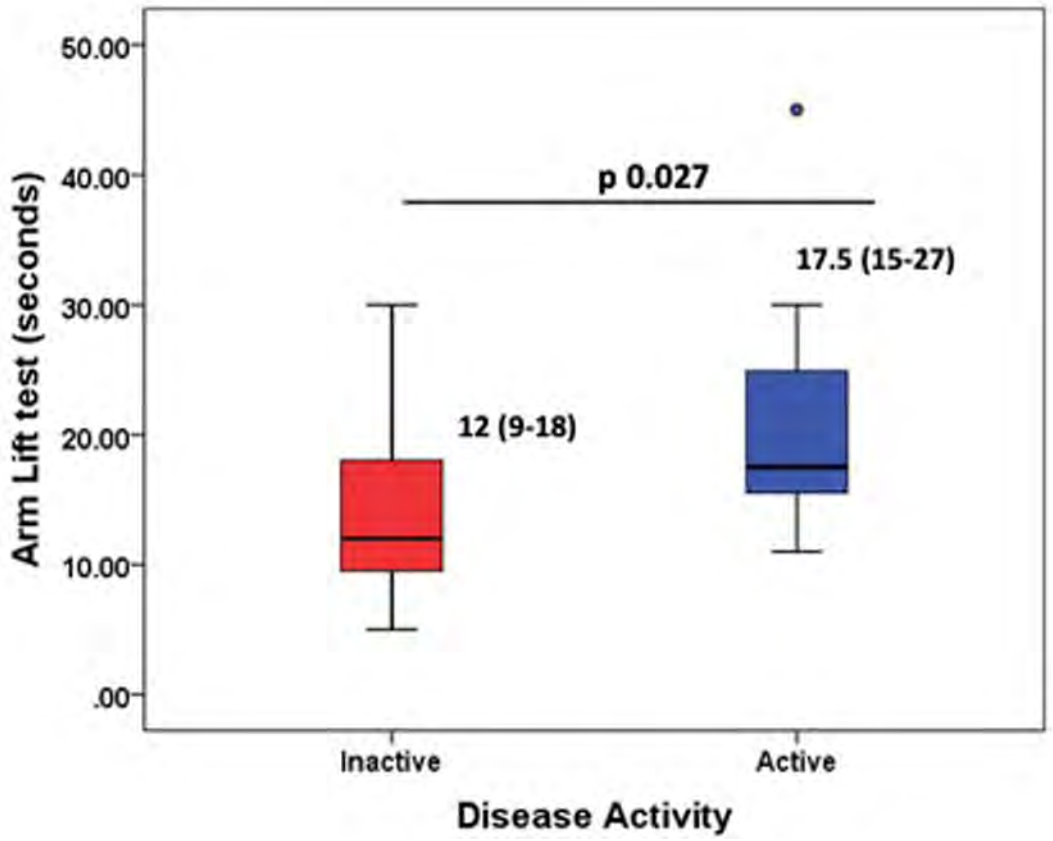

Figure 2. Arm Lift test in active versus inactive disease in Validation cohort (47 patient visits).

The results were validated in a larger Teleconsultation-based cohort to differentiate active vs. inactive disease. All values are in median(IQR).

Results: *Observation cohort*

22 adult IIM patients (68% female) of age 30.5 (19-62) years were enrolled. Median AL time, 2MWD and MMT-8 were 11.9 (10.5-14) seconds, 198 (167-225) metres and 79 (74-80) respectively.

AL and 2MWD showed excellent test-retest reliability (Cronbach's alpha 0.987 & 0.99 respectively, n=12). AL test had moderate to strong correlation all myositis core set measures including MMT8, PtGA, PhGA, HAQ-DI, Extra-muscular global (Ex-MuscGA), muscle enzyme (LDH, AST, ALT) and MYOACT (trend), but not with CK levels and MDI (table 1). In addition it showed moderately strong association with muscle disease VAS and muscle disease remission. In contrast, 2MWD had huge variability and no significant association with any of the core set or other measures except a moderate correlation with muscle VAS.

A higher AL time discriminated active and inactive myositis (16.6 vs 11 seconds, p=0.006) and discriminated between patients with and without muscle weakness (significant) and HAQ (non-significant trend) (Figure 1 A-C). However, 2MWD didn't discriminate based on muscle disease activity or other measures.

AUC for active versus inactive disease was 0.882 (p 0.006) with AL test. A cut-off of 12.8 seconds had 94% negative predictive values for active muscle disease (83% sensitivity, 83% specificity).

Table 1. Correlation of Arm lift test and 2MWD with disease parameters (Construct Validity) in observation cohort (n=22)

	Arm Lift test		2MWD	
	r	p	r	p
Core Set Measures				
PtGA	**0.725**	0.000	0.106	0.632
PhGA	**0.710**	0.000	0.100	0.651
MMT-8	**-0.784**	0.000	-0.074	0.736
HAQ-DI	**0.483**	0.023	0.204	0.363
Muscle enzymes				
AST (U/L)	**0.576**	0.004	0.103	0.639
ALT (U/L)	**0.586**	0.003	0.260	0.231
CK (U/L)	0.286	0.221	-0.048	0.841
LDH (U/L)	**0.753**	0.000	0.112	0.640
Ex-Musc GA	**0.479**	0.024	-0.413	0.056
Other measures				
MYOACT	0.365	0.087	**0.430**	0.041
Muscle disease VAS	**0.414**	0.050	**0.426**	0.043
MDI severity of damage score	-0.012	0.743	0.051	0.858
MDI extent of damage score	-0.059	0.789	-0.013	0.955
MDI extended damage score	-0.182	0.406	-0.133	0.545

AST- Aspartate transaminase, ALT- Alanine transaminase, CK – creatine kinase, ESR- Erythrocyte Sedimentation Rate, HAQ-DI Health Assessment Questionnaires disability index, LDH-Lactic Acid Dehydrogenase, MDI-Myositis Damage Index, MITAX-Myositis Intention to treat Activity Index, MITAX em- Myositis Intention to treat Activity Index extra-muscular, MYOACT-Myositis Disease Activity Assessment Visual Analogue Scales, MYOACT em- Myositis Disease Activity Assessment Visual Analogue Scales extra-muscular, PtGA- Patient global assessment VAS, PhGA-Physician Global Assessment VAS, PhEMS- Physician extra-muscular global assessment VAS, VAS-Visual Analogue Scale

Validation cohort

In 47 patient visits among 26 patients (81% female, 33 years median age), AL significantly differentiated between active vs. inactive patients (Figure 2).

Conclusion: AL correlated well with myositis disease activity measures including muscle weakness providing preliminary evidence for its role as PCOM in IIM especially in clinical trials and telemedicine consultation. 2MWD was not a good test for outcome evaluation of IIM patients. Larger longitudinal studies are needed to further validate these findings.

Disclosure: R. Naveen, None; **D. R Thakare**, None; **V. Agarwal**, None; **R. Aggarwal**, Mallinckrodt, 1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2; **L. Gupta**, None.

Abstract Number: 0757

Different Versions of the Patient Global Question in Rheumatoid Arthritis – Does It Really Matter? – Results of a Multi-center Observational Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The patient global assessment (PGA), typically assessed as *'Considering all of the ways your arthritis has affected you, how do you feel your arthritis is today?'* should reflect the patient's perception of disease activity. It is incorporated as core set measure of disease activity in rheumatoid arthritis (RA) but has been criticized to not adequately fulfill its construct validity.

We explore different versions of the PGA and assess agreement, factors of variance, change over time and effect on disease activity classification.

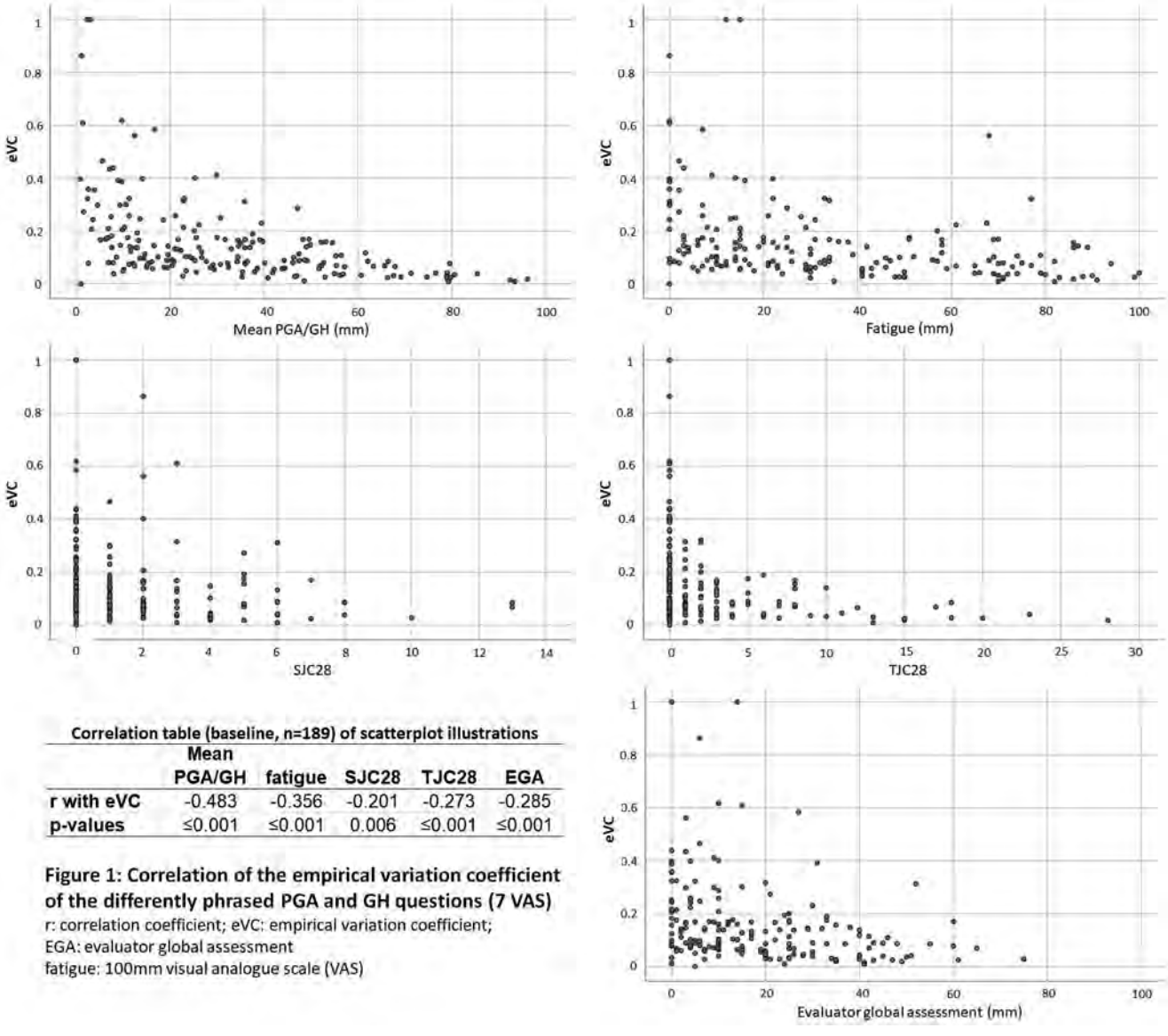
Methods: In a multicenter study (4 centers in US & Europe), RA patients were asked to score on global health (GH) and 6 differently phrased PGA questions using visual analogue scale covering 2 aspects: (1) providing more detailed explanation on disease activity *("Active arthritis can cause joint swelling OR stiffness, pain OR discomfort in your joints. WITH ACTIVE ARTHRITIS, You CAN BE tired during the day, even when you've slept well"* (ePGA) compared to traditional phrasing (tPGA); and (2) reference to 3 time periods: *today (TD), last week (LW)* or *last month (LM)*. This generated 3 tPGA versions (TD/LW/LM) and 3 ePGA versions (TD/LW/LM). Agreement was calculated with intra-class correlation (ICC) and comparisons between PGA were done with paired-analyses. The empirical variation coefficient (eVC: (SD/mean)/SQRT(n)) was calculated per patient. The influence of disease duration, HAQ >0.5 or ≤0.5, SJC28, TJC28, fatigue and evaluator global assessment (EGA) on scoring of PGA versions were assessed and the resulting variations in disease activity classification.

Results: At baseline (BL) 189 patients (82% female, 45%≥1 comorbidity, mean disease duration ±SD: 16.6±10.8, mean PGA: 31.8±22.7, mean eVC 0.15±0.15, mean SJC28: 1.6±2.3) and 138 with follow-up (FU) were subjected to analyses. In paired analyses ePGA were scored higher than tPGA ($p \leq 0.001$) and in both, scores were higher in longer reference periods. When comparing in between reference periods (Table 1), ICCs were all ranging >0.8. Changes in PGA between BL and FU reached high agreement, except for TD versus LM. Poor to moderate agreement both for BL, as well as change scores, were found between versions of PGA and GH (Table 1). BL to FU PGA changes correlated highly with changes in pain and moderately with changes in EGA. The difference between PGA and GH (LW, LM versions) increases with more swollen joints. Differences between phrasings were less pronounced in patients with HAQ >0.5 or with comorbidities. The variance in scores between questions was lower in people with higher disease

Intra-Class Correlation

	ePGA TD		ePGA LW		ePGA LM		GH		tPGA TD		tPGA LW	
	baseline	changes	baseline	changes	baseline	changes	baseline	changes	baseline	changes	baseline	changes
ePGA TD												
ePGA LW	0.877	0.83										
ePGA LM	0.827	0.693	0.919	0.798								
GH	0.619	0.555	0.677	0.606	0.629	0.616						
tPGA TD	0.875	0.861	0.864	0.821	0.794	0.624	0.662	0.558				
tPGA LW	0.862	0.724	0.913	0.861	0.848	0.701	0.713	0.588	0.896	0.805		
tPGA LM	0.781	0.607	0.892	0.743	0.889	0.632	0.724	0.648	0.851	0.666	0.889	0.7

Table 1: Intraclass correlation Cross table of different Patient Global Assessment (PGA) versions and Global Health (GH) & of its changes between baeline and follow-up. ePGA: explained version; tPGA: traditional version; TD: today; LW: last week; LM: last month



Correlation table (baseline, n=189) of scatterplot illustrations

	Mean PGA/GH	fatigue	SJC28	TJC28	EGA
r with eVC	-0.483	-0.356	-0.201	-0.273	-0.285
p-values	≤0.001	≤0.001	0.006	≤0.001	≤0.001

Figure 1: Correlation of the empirical variation coefficient of the differently phrased PGA and GH questions (7 VAS)
r: correlation coefficient; eVC: empirical variation coefficient;
EGA: evaluator global assessment
fatigue: 100mm visual analogue scale (VAS)

Shift in disease activity classification when using different PGA by CDAI			
	lose REM/LDA	achieve REM/LDA	Remain
tPGA LW > ePGA LW	2.1%	1.6%	64.0%
tPGA LW > GH	3.2%	3.2%	58.2%
ePGA LW > GH	2.6%	3.2%	57.7%
ePGA TD > ePGA LM	5.3%	2.1%	58.2%
tPGA TD > tPGA LM	4.8%	2.1%	61.4%
by ACR/EULAR Boolean remission			
	lose REM	achieve REM	Remain
tPGA LW > ePGA LW	2.6%	1.1%	14.8%
tPGA LW > GH	9.5%	2.1%	7.9%
ePGA LW > GH	8.5%	2.6%	7.4%
ePGA TD > ePGA LM	4.8%	1.6%	11.1%
tPGA TD > tPGA LM	3.2%	1.6%	14.8%
CDAI: clinicial disease activity index			
tPGA: traditional PGA; ePGA: explained PGA;			
TD: today; LW: last week; LM: last month			

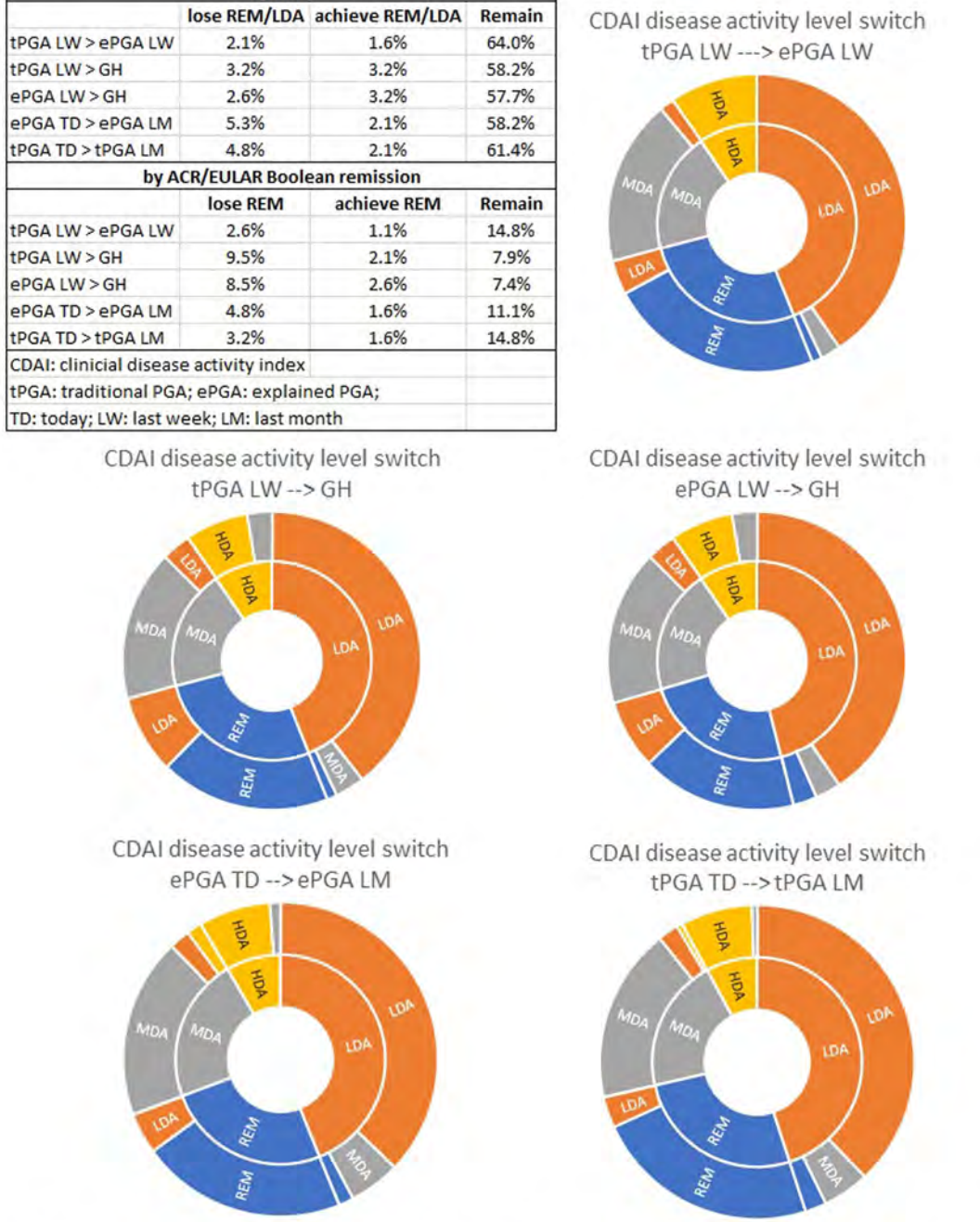


Figure 2: Sunburst Diagrams - Shift of classification of the patient in disease activity levels (measured by the clinical disease activity index – CDAI) when applying different versions of the Patient Global Assessment (PGA) or Global Health (GH).

activity. Higher mean PGA, fatigue, TJC, SJC and EGA correlated moderately with smaller eVC (Figure 1). The rate of patients switching CDAI disease activity level is around 8% when comparing tPGA with ePGA, but between 15% to 20% in PGA/GH and around 14% in TD/LM (Figure 2). Only up to 3% less achieve REM/LDA CDAI when switching to ePGA, however GH use instead of PGA coincides with 5 to 7% of patients less in Boolean remission.

Conclusion: Different versions of the PGA show high correlation, implicating that a more detailed phrasing would not increase construct validity. GH performs differently than PGA and may not be used interchangeably.

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Abstract Number: 0758

Outcome Reporting in Self-management Interventions for Inflammatory Arthritis Trials: A Systematic Review of Outcome Measures Covering Self-management Domains

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: A significant heterogeneity exists across outcome domains and outcome instruments measuring the effect of self-management interventions targeting people with inflammatory arthritis (IA). Thus, it is currently difficult to perform evidence synthesis assessing the effect of self-management interventions, and variability in the quality of the applied outcome measurement instruments exists. The objective of this study was to identify outcome measure instruments applied to measure the effect of self-management interventions targeting patients with IA.

Methods: Measures of self-management in IA were identified through an informative systematic literature review as described by OMERACT (1) and the Core Outcome Measures in Effectiveness Trials (COMET) (2) which focus on mapping outcome domains from earlier studies to inform the development of a COS. Trials were eligible for inclusion if the intervention was described as "self-management intervention", and the study population comprised of people with any IA: RA, PsA or SpA. Two authors independently assessed trials for eligibility and extracted information on study characteristics, outcome domains, and outcome measurement instruments reported. With discrepancies, discussion among all authors was conducted. Outcome domains and the outcome measurement instruments were sorted and categorized into domains and sub-domains using the OMERACT Framework based on 3 core areas: (*i*) Death, (*ii*) Life Impact, and (*iii*) Pathophysiological manifestations, plus resource use/economical evaluation which is highly recommended, but not defined as a mandatory core area.

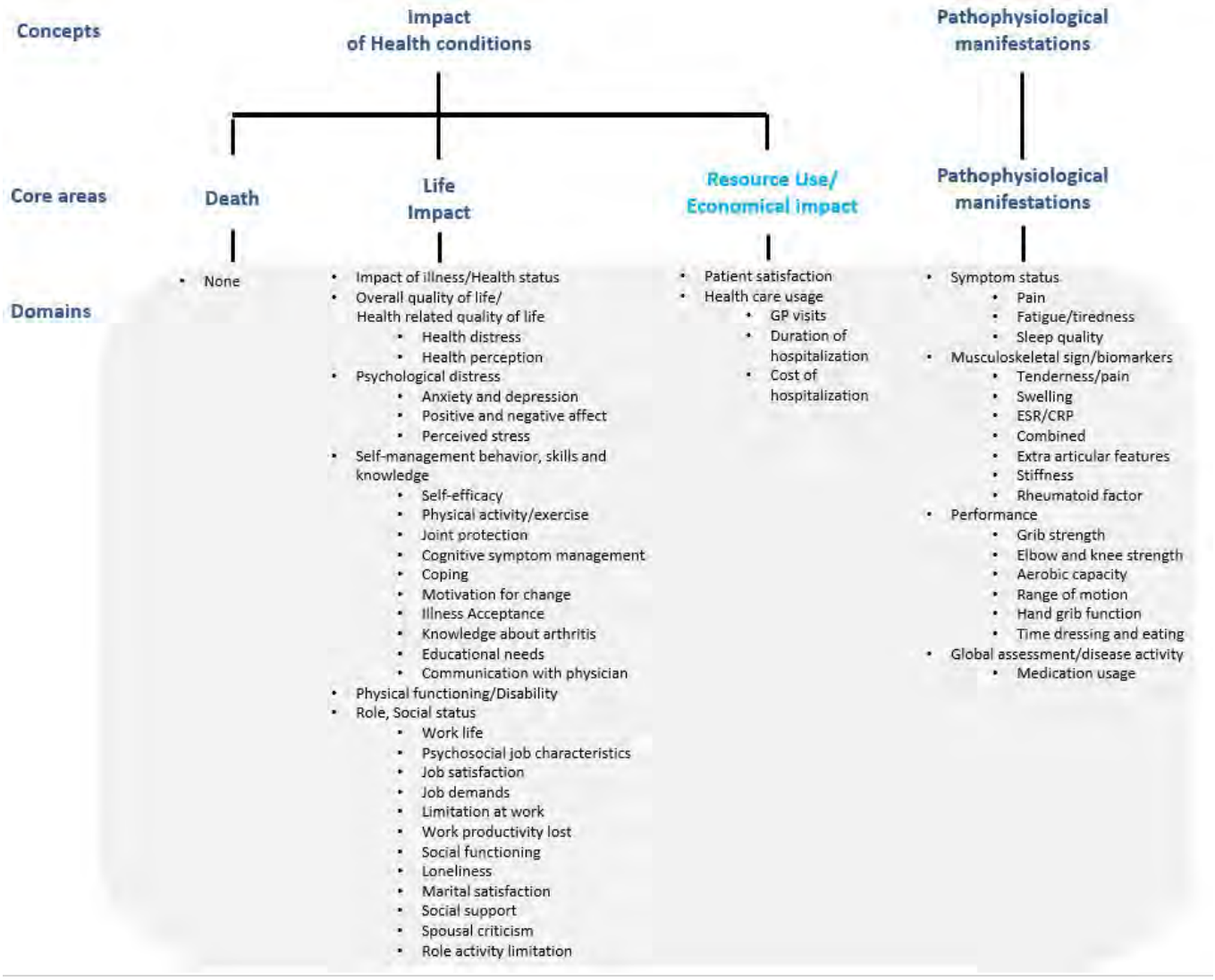

Figure 1. Overview of outcome domains and outcome sub-domains extracted from the 38 trials.

Results: From a total of 2502 records, we included 38 trials, published between 1988 and 2021. The studies most often based their self-management intervention on cognitive behavioral therapy and/or self-efficacy theory focusing on education of arthritis, medication, lifestyle, and self-management skill training involving problem-solving and goal setting. Across the trials, we identified 12 different outcome domains and 47 sub domains, comprising 128 different measurement instruments. The outcome domains and outcome sub-domains are illustrated in Figure 1. The identified outcome domains were primarily within the 'Life impact' core area. Self-efficacy and health-related quality of life was the most commonly applied domains in 30 and 16 studies, respectively. The domains and measurement instrument within the 'Life impact' core area are listed in Table 1.

Conclusion: The outcome domains and measurement instruments reported in self-management interventions including IA population, were widely diverse. This study provides a foundation for the development of a core outcome set for use in future trials.

Table 1. Measurement instruments applied within the Life Impact core area.

Domains	Sub-domains	Measurement instrument applied (Number of studies applying)
Impact of Illness/Health status		AIMS-2 (5), AIMS-2 SF (1), AIMS (1),
Overall quality of life/ Health related quality of life		SF-36 (5), RAQol (2), IIS (2), ASQol (1), EASi-Qol (1), ASAS-HI (1), PGI (1), EUROHIS-QUOL (1), SWLS (1), QLS (1).
	Health distress	HDQ (1), Stanford Health Distress (1)
	Health Perception	RAND-36 (1), SF-36 (1)
Psychological distress		
	Anxiety and depression	HADS (9), CES-D (6), AIMS depression and anxiety subscales (2), DS (1), Zung depression scale (1), STAI (1)
	Positive and negative affect	PANAS (2), MOS PA II scale (1), the Affective pain score (1)
	Perceived stress	PSS (1)
Physical functioning/Disability		HAQ (9), HAQ-DI (3), MHAQ (2), AIMS subscales (2), BASFI (2), DASH (1), HAQ-8 (1), HFAQ (1), Functional index (1)
Self-management behavior, skills and knowledge		PAM-13 (1), PAM (1), SMAS-S (1), EC-17 (1)
	Self-efficacy	ASES (15), ASES-8 (6), PSEQ (2), RASE (2), Coping Efficacy (2), SEMCD-6 (1), CDSES (1), JP self-efficacy (1)
	Physical activity/exercise	Stanford exercise behavior (2), IPAQ (1)
	Joint protection	JPBA (2), JPBA-S (1)
	Cognitive symptom management	Stanford cognitive symptom management (2)
	Coping	AHI (5), CORS (3), RAI (2), MPCI-F (1), CSQ (1), BECOMO (1), GSE (1), F-COPES (1)
	Motivation for change	NRS (1)
	Illness Acceptance	AIS (1)
	Knowledge about arthritis	ACREU (2), AS "what do you know" (1), JPKA (1)
	Educational needs	ENAT-2 (1)
	Communication with physician	Stanford Communication with physician (2)
Role, social status		
	Work life	WRF (1)
	Psychosocial job characteristics	demand-control model (1)
	Job demand	US social security (1)
	Job satisfaction	JCQ (1)
	Limitation at work	WLQ (1)
	Work productivity lost	EWPS (1), SPS-6 (1), WPAI-SHP (1)
	Social functioning/wellbeing	SPS (1), SSS (1)
	Loneliness	LS-3 (2)
	Marital satisfaction	MMQ (1)
	Social support	AIMS subscale (1)
	Spousal criticism	Spouse reaction questionnaire (1)
	Role activity limitation	MOS ACTIVELIM (1)

ACREU: arthritis community research and evaluation unit knowledge questionnaire, AHI: arthritis Helplessness Index, AIMS: Arthritis Impact Measurement Scale, AIMS-2: Arthritis Impact Measurement Scale version 2, AIMS-SF: Arthritis Impact Measurement Scale Short Form, AIS: Acceptance of Illness scale, ASAS-HI: Assessment of SpondylArthritis International Society Health Index, ASES: Arthritis Self-Efficacy Scale, BASFI: Bath Ankylosing Spondylitis Functional Index, BECOMO: The Bernese Coping Modes, CES-D: Center for Epidemiological Studies Depression Scale, CDSE: Chronic Disease Self-efficacy, CORS: Coping with Rheumatic Stressors, CSQ: Coping Strategies Questionnaire, DASH: the Disabilities of the Arm, Shoulder and Hand outcome measure, EASi-QoI: Evaluation of ankylosing spondylitis quality of life, EC-17: the Effective Consumer Scale, ENAT-2: Educational need Assessment Tool, EUROHIS-QUOL: European Health Interview Survey-Quality of life, EWPS: Endicott work productivity scale, F-Copes: Family crisis oriented personal evaluation scale, GSE: General, self-Efficacy, HADS: Hospital Anxiety and Depression Scale, HAQ: the Health Assessment Questionnaire, HAQ-DI: Health Assessment Questionnaire Disability Index, HDQ: Health Distress questionnaire, HFAQ: Hanover Functional Ability Questionnaire, IPAQ: International Physical Activity Questionnaire, ISS: Illness Intrusiveness Scale, JCQ: Job content questionnaire, JP: Joint Protection, IPBA: Joint Protection Behavior Assessment, JPKA: Joint Protection Knowledge Assessment, LS: Loneliness Scale, MMQ: Maudsley Marital Questionnaire, MPCI-F: Modified Pain Coping Inventory for Fatigue, MHAQ: Modified Health Assessment Questionnaire, MOS ACTIVELIM: Medical outcome study Activity Limitation Scale, MOS PA II scale: Medical Outcome Study Positive Affect Scale, NRS: Numerical rating scale, PANAS: Positive and Negative Affect Schedule, PAM: Patient Activation Measure, PGI: Patient Generated Index, PSEQ: Perceived self-efficacy Questionnaire, RAND-36: Research and development 36 Item Health Survey, PSS: Perceived Stress Scale, RAI: Rheumatology attitudes Index, RASE: Rheumatoid Arthritis Self-Efficacy, RAQol: The rheumatoid Arthritis quality of Life Questionnaire, SEMCD-6: Self-efficacy for Managing Chronic disease, SF-36: Short Form 36 Health Survey Questionnaire, SMAS-S: Self-management ability Scale, shorter scale, SPS: Social Perception Scale, SSS: Social Support Survey, SWLS: Satisfaction with Life Scale, WLO: Work limitation questionnaire, WPAI-SHP: Work productivity and activity impairment questionnaire specific Health problems, WRF: work role functioning, QLS: Quality of Life Scale.

Registration

The protocol was registered in **PROSPERO** (ID CRD42021238749).

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2. Williamson PR, Altman DG, et al. The COMET Handbook: Version 1.0, 2017. Available at: https://trialsjournal.biomedcentral.com/articles/10.1186/s13063-017-1978-4

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Abstract Number: 0759

The Patient as Assessor of Disease Status: A Graphical Evaluation of Relations Between Patient-Reported Outcomes in Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Current EULAR-guidelines recommend treating Rheumatoid Arthritis (RA) early, intensively and to-target. Patient-Reported Outcomes (PROs) can be important contributors for remote monitoring of disease status in patients with (early) RA to guide the interventions needed. However, which PROs are vital for such purposes is unknown. Therefore, we aimed to investigate the direct and indirect relations between different PROs in the Care in Early RA (CareRA) trial.

Methods: In CareRA, patients were asked to register the following PROs at baseline (BL), week 52 (W52), and week 104 (W104): Multi-Dimensional Fatigue Index (MF), Short Form 36 (SF36), Illness perception questionnaire (IPQ), Utre-

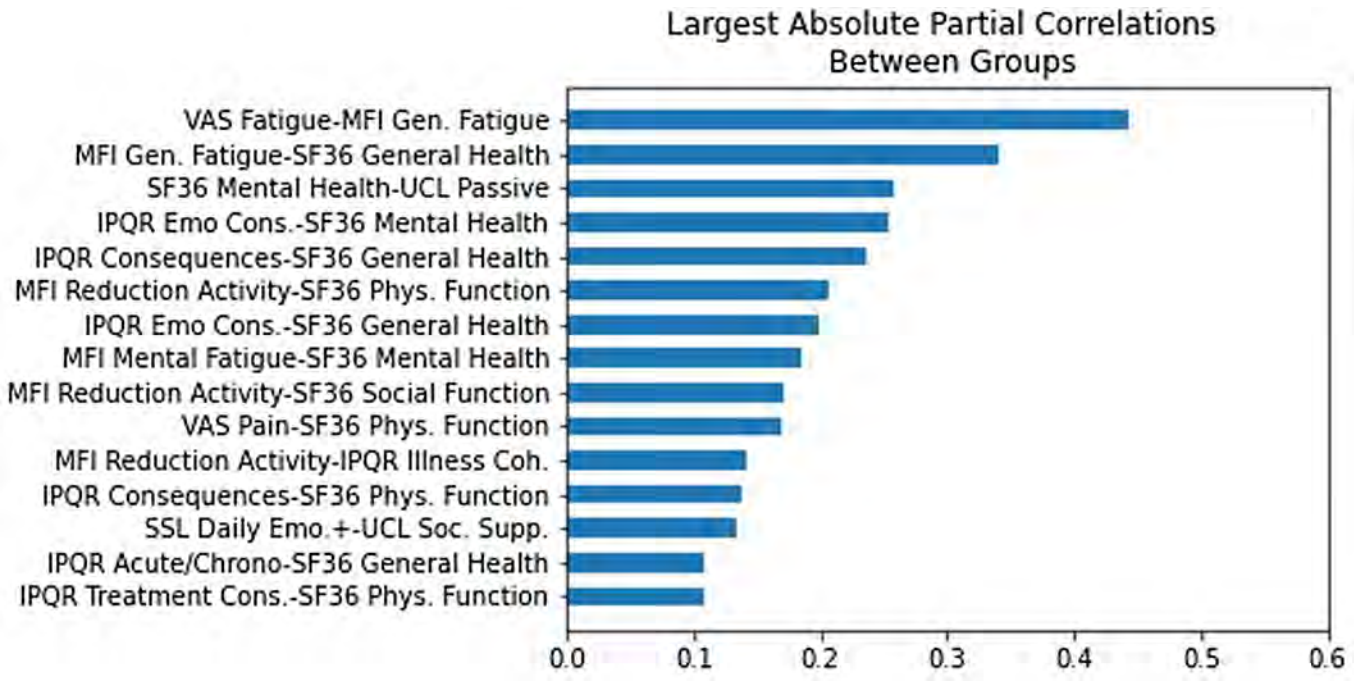

Figure 1 Estimated absolute (penalized) partial correlations between the (sub)scores at W104.

cht Coping List (UCL), Social Support List (SSL), Pittsburgh Sleep Questionnaire (PSQ), RA Quality of Life (RAQOL) and global health, pain and fatigue as measured by Visual Analogue Scale (VAS). Most questionnaires consist of different subdomains or subscores. Where applicable, these subscores were used, else the total score per questionnaire was used. The graphical lasso (GLASSO) method was used to estimate relations between PRO (sub)scores. GLASSO provides both an overview on indirect relations (via correlation) and on direct relations (via precision matrix). The GLASSO was run at BL, W52 and W104 to check for consistency over time.

Results: The GLASSO procedure suggested 168 direct relations out of 561 possible relations (±30%) at W104. Similar results were obtained at BL and W52. Fig 1 shows the 15 relations with the highest partial correlations between

Figure 2 Estimated direct relations (edges) between (sub)scores (nodes) at W104.

subscores from different PROs at W104. Absolute values of relationship strength showed slight variations, but the correlation scores appeared robust over time. Analyzed (sub)scores and relations estimated at W104 are presented in Fig 1. Three distinct groups of PROs were clearly identifiable from the GLASSO procedure. A first group consisting only of SSL subscores, a second group consisted only of UCL subscores and the last group consisted of all other PROs. There were many connections within each group and few between groups. This suggests that each group relates to a different underlying dimension.

Conclusion: Using the GLASSO-approach, we distinguished three distinct groups of PRO dimensions. Coping and social support constructs seem distinct from another heterogeneous group representing both mental and physical health topics. Correlation between these disease-activity-related PROs suggests not all PROs are required to get a representative view of patient health.

Disclosure: D. **De Cock**, None; **G. Verhavert**, None; **S. Pazmino**, None; **D. Bertrand**, None; **M. Doumen**, None; **R. Westhovens**, galapagos, 12, advisory board and principal investigator, gilead, 1, celltrion, 1; **P. Verschueren**, Pfizer, 12, Holder of the Pfizer Chair Early Rheumatoid Arthritis Management at the KU Leuven, Eli Lilly, 2, Nordic Pharma, 2, galapagos, 2, gilead, 2, ABBVIE, 2, Celltrion, 2, BMS, 2.

Abstract Number: 0760

The Performance of RA Disease Activity and Patient-Reported Outcomes in Rheumatoid Arthritis-Associated Interstitial Lung Disease in a Prospective Trial Using Pirfenidone in RA ILD (TRAIL1)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Both rheumatoid arthritis (RA) and idiopathic pulmonary fibrosis (IPF) have established measures of disease severity and patient reported outcomes (PROs) that measure health-related quality of life (HRQL). In IPF, established PROs correlate with severity of lung disease. In patients with interstitial lung disease (ILD) associated with RA, it is unknown if established RA disease severity indices and PROs correlate with ILD severity and available PROs used in IPF, which have been adapted for use in the TRAIL1 trial. Using baseline data collected in the TRAIL1 trial, we sought to examine correlations between PROs, measures of RA disease severity and severity of ILD and correlations between PROs used in RA and IPF.

Methods: Baseline data from 123 subjects randomized to the TRAIL1 trial were used for this analysis. All subjects underwent pulmonary function testing (PFT), baseline high-resolution computed tomography (HRCT) to determine extent of fibrosis and administration of PROs at enrollment. Disease severity for joint disease was measured with the disease activity score (DAS)28 in RA and disease severity for ILD was measured using forced vital capacity (FVC)%, diffusing capacity for carbon monoxide (DLCO)% and extent of fibrosis in ILD. PROs examined include the

	N=123
Age (years)	
Mean (SD)	67.7 (8.6)
Median [Min, Max]	69.1 [43.1, 84.6]
Sex, n (%)	
Female	46 (37%)
Male	77 (63%)
Pulmonary Function - FVC (% predicted)	
Mean (SD)	70.3% (14.8%)
Median [Min, Max]	70.6 [39.3, 111.7]
Pulmonary Function – DLCO (% predicted)	
Mean (SD)	48.7% (13.6)
Median [Min, Max]	47 [19.9, 91.0]
HRCT Fibrosis % (Reticulation + Honeycombing)	
Mean (SD)	22.4 (10.9)
Median [Min, Max]	20 [10, 60]
HRCT Pattern, n (%)	
UIP	81 (66%)
NSIP	13 (11%)
LIP	3 (2%)
Indeterminate	26 (21%)
Pulmonary Symptom Measures	
Dyspnea-12 [0-36, higher is worse]	
N	121
Mean (SD)	8.5 (7.8)
Median [Min, Max]	6 [0, 31]
SGRQ [0-100, higher is worse]	
N	122
Mean (SD)	43.6 (19.4)
Median [Min, Max]	42.6 [1.6, 87.4]
RA Disease Activity Measures	
Rapid3 [0-10, higher is worse]	
N	118
Mean (SD)	3.3 (2.4)
Median [Min, Max]	3 [0, 10]
DAS28 [0-10, higher is worse]	
N	104
Mean (SD)	4.3 (1.4)
Median [Min, Max]	4.25 [1.4, 9.3]

Footnote: SD=standard deviation, FVC=forced vital capacity, DLCO=diffusing capacity for carbon monoxide, HRCT=high resolution computed tomography, UIP=usual interstitial pneumonia, NSIP=nonspecific interstitial pneumonia, LIP=lymphocytic interstitial pneumonia, SGRQ=St. George's Respiratory Questionnaire, DAS=Disease Activity Score.

Baseline Characteristics of the TRAIL1 Population.

RAPID3 in RA and the St. George's Respiratory Questionnaire (SGRQ) and Dyspnea-12 for ILD. Spearman's rank correlation test was used to evaluate the relationship between candidate variables and correlation coefficients (r) were calculated.

	FVC %		DLCO%		% Fibrosis on HRCT	
	r	p	r	p	r	p
RAPID3	-0.13	0.17	-0.16	0.09	-0.07	0.47
SGRQ	-0.06	0.69	0.06	0.70	0.003	0.98
Dyspnea-12	-0.10	0.26	-0.10	0.30	0.08	0.38
DAS28	0.04	0.68	0.03	0.77	-0.11	0.27
Footnote: FVC=forced vital capacity, DLCO=diffusing capacity for carbon monoxide, HRCT=high resolution computed tomography, SGRQ=St. George's Respiratory Questionnaire, DAS=Disease Activity Score. r=Spearman correlation, p=p-value						

Correlations between PROs, DAS28 and ILD Disease Extent.

	SGRQ		Dyspnea-12	
	r	p	r	p
RAPID3	0.65	***<0.0001***	0.32	***0.0006***
DAS28	0.37	***0.02***	0.19	0.06
Footnote: SGRQ=St. George's Respiratory Questionnaire, DAS=Disease Activity Score. r=Spearman correlation, p=p-value				

Correlations between RAPID3, DAS28 and Lung-Specific PROs.

Results: Table 1 shows the baseline characteristics of the subjects randomized for the TRAIL1 trial. Most subjects were Caucasian males over 55 years old with a moderate amount of fibrosis. Baseline PROs revealed moderate RA activity; dyspnea and pulmonary-specific HRQL (as measured by the SGRQ) showed moderate impairment that was comparable to that seen in IPF. There was no association between DAS28 or PROs and disease severity for ILD (Table 2). There were strong correlations between the RAPID3 and the ILD-specific PROs (SQRQ and Dyspnea-12) (Table 3).

Conclusion: No correlations between joint-disease activity and RA-ILD disease severity as measured by PFTs and extent of fibrosis on HRCT were shown. Additionally, no correlations were apparent between ILD-specific PROs and severity of lung disease in RA-ILD, as is seen in IPF. While the small patient numbers may impact the results, these data suggest that RA-ILD has features that are unique compared to IPF, perhaps related to the systemic nature of the disease as well as the multicompartmental lung involvement that can be seen in RA. These differences may require the development of specific PROs that better correlate with lung function in the assessment of patients with RA-ILD. Furthermore, the correlation between RA and ILD-specific PROs may be important in the clinical management of patients with RA-ILD and requires further study.

Disclosure: P. Dellaripa, Boehringer Ingleheim, 5, Genentech, 5, bristol myers squibb, 5; **T. Doyle**, Bristol Myers Sqibb, 5, Boehringer Ingelheim, 2, Genentech, 5; **S. Danoff**, None; **H. Goldberg**, None; **M. Kolb**, None; **D. Chambers**, None; **F. Woodhead**, None; **C. Spino**, None; **I. Rosas**, None; **J. Solomon**, None.

Abstract Number: 0761

Development of a Symptom Diary for Use in Patients with Sjogren's Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren's Syndrome (SS) is a systemic autoimmune disease associated with a wide range of symptoms and long-term complications. While clinical indices are useful in diagnosis and assessment of disease activity, patient-reported outcome (PRO) measures are needed to measure the severity of symptoms from a patient perspective. The objective of this study was to develop a patient-reported diary for use in clinical trials to assess the severity of key symptoms of SS in alignment with Food and Drug Administration (FDA) PRO guidance documents.

Methods: Development began with targeted reviews of the literature and relevant PRO measures to identify symptoms of SS which are both highly prevalent in the patient population and have the potential to improve within the context and timeframe of a clinical trial. Following the development of an item pool addressing the initially identified symptoms, semi-structured interviews were conducted with clinical experts (n=2) to gather feedback on this preliminary item pool and to identify any additional concepts of importance. Following minor revisions to the draft items based on clinician feedback, three iterative sets of hybrid concept elicitation (CE) and cognitive debriefing (CD) interviews were conducted with a total of 17 patients with primary SS (64.7% female; median age 58.0 years [range 28-70 years]) to refine the diary and further assess its content validity.

Results: Based on the targeted literature review, the most prevalent symptoms of importance to patients with SS included dryness of the eyes, mouth, skin, and female genitalia along with fatigue and muscle or joint pain. While additional symptoms that tend to occur at later stages of the disease process were identified (e.g., brain fog, neuropathic pain), these symptoms would not be relevant across the full disease spectrum and thus were not included in the preliminary item pool. While the clinical experts generally endorsed the initial content of the diary, they recommended the exclusion of skin dryness, noting that this was not a common complaint among their patients.

The symptoms most commonly reported by patients participating in the qualitative interviews were consistent with those addressed in the preliminary item pool and final diary, including dry eyes (100%), dry mouth (100%), dry skin (47%), genital dryness (46% of female participants), fatigue (77%), and muscle or joint pain (53%). Of note, while the concept of skin dryness was not fully endorsed by the clinical experts, patients supported its inclusion in the final measure. With minor modifications, patients also indicated that the diary items were easy to understand and answer. Finally, no concept of importance was identified as missing from the diary by more than 3 of the 17 interview participants, and many of these were impacts rather than symptoms of SS (e.g., dental decay, depression).

Conclusion: The Sjögren's Syndrome Symptom Diary is a content valid measure designed for use in clinical trials to assess the severity of the symptoms most commonly experienced by patients with SS. Following psychometric evaluation, this measure will have the potential to support product labeling claims.

Disclosure: B. Ndife, Novartis, 3, 11; **S. Fenel**, Novartis, 2; **S. Lewis**, Novartis, 2; **N. Agashivala**, Novartis, 3, 11.

Abstract Number: 0762

Validity of the Musculoskeletal Health Questionnaire: Real World Analysis of Data Collection via an Electronic Patient Reported Outcome Platform

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: The Musculoskeletal Health Questionnaire (MSK-HQ) is a patient reported outcome measure (PROM) validated to assess disease outcomes in patients with MSK disorders. This study evaluates the validity of the MSK-HQ in an ePROM system as part of routine care in rheumatology. We assess reliability and validity of the MSK-HQ across different conditions and evaluate correlation of the total score and activity score with other PROMs.

Methods: Data were extracted via the King's College Hospital IMPARTS ePROM system which sends an SMS link 24hrs before a clinic appointment to complete PROMs tailored to the patient condition. The MSK-HQ includes 14 items summed to give a total score (0-56, higher scores indicate better quality of life) and a final item for physical activity in the past week. In addition, data were extracted for mental health (PHQ9 & GAD7), functional limitation (HAQ), and disease specific measures (BASDAI & DLQI). Data are reported as mean±SD with Pearson correlations estimated to test association and linear regression to test group differences.

Results: Data was available for 1323 encounters between 06/20 and 01/21. The MSK-HQ was completed on 1216 (92%) occasions (31.4±13.9). RA had the greatest impact compared to AS and PsA (RA: 30.3±14.4; AS:36.0±13.1; 33.3±12.8; other:31.1±13.6; $p < .001$). Chronbach's alpha coefficients indicated excellent reliability of the MSK-HQ total score (alphas:overall=.95;RA=.96;PsA=.96;AS=.95). Factor analysis confirmed a unidimensional solution supporting use of the total score.

Across all encounters patients reported 2.3±2.3 active days in the last week. Patients with RA, AS and PsA were active on 2.0± 2.2, 2.9± 2.3 and 2.6± 2.4 days respectively again suggesting RA has greater disease impact ($p < .001$). MSK-HQ scores were positively correlated with active days ($r=.36$, $p < .01$).

The MSK-HQ total score demonstrated good convergent validity with condition specific PROMs. BASDAI and BASFI in AS ($r=-.89$ $p < .001$ & $r=-.81$ $p < .001$ respectively) and DLQI in PsA ($r=-.44$, $p < .001$). BASDAI and BASFI strongly correlated with active days ($r=-.30$ $p < .05$ & $r=-.37$ $p < .05$ respectively) however DLQI didn't show significant correlation ($r=-.07$, $p=.42$).

Good convergent validity was demonstrated against HAQ. There was a $r=-.38$ correlation ($p < .05$) with active days per week. A HAQ score ≤1 was associated with a mean of 3.01 active days compared to a HAQ score >1 associated with a mean of 1.44 active days ($t=8.81$, $p < .05$).

Both MSK-HQ total score and number of active days could discriminate between those with and without mental health symptoms. The correlation between PHQ9 and GAD7 score and active days was $r=-.27$ and $r=-.19$ (both $p < .01$). Individuals with mild depressive symptoms were active 0.9 days less per week compared to those without

symptoms (t -4.06, p< .01). Individuals with probable major depression were active 1.4 days less per week compared to those with no symptoms (t -7.99, p< .01).

Conclusion: This study demonstrated acceptability and validity for both the MSK-HQ total score and activity score delivered via an ePROM system. The activity score in isolation discerned patients with and without symptoms of anxiety or depression highlighting the value of using this PROM in the healthcare setting.

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Abstract Number: 0763

What Does the Patient Well-Being Vas Tell Us When the Physician Global Assessmentscore Is Zero? Analysis of a Large Multinational Dataset

Francesca Ridella[1], Roberta Naddei[2], Maddalena Spelta[2], Cristina N. Herrera[3], Clara Malagon[4], Olga Arguedas[5], Amparo Ibanez Estrella[6], Nicola Ruperto[7], Angelo Ravelli[8] and Alessandro Consolaro[9], [1]Università degli Studi di Genova Genoa, Italy, Genova, Italy, [2]Istituto Giannina Gaslini, Genova, Italy, [3]Hospital de Ninos Roberto Gilbert Elizalde, Rheumatology, Guayaquil, Ecuador, Paediatric Rheumatology International Trials Organisation (PRINTO), Guayaquil, Ecuador, [4]Hospital Universitario Simon Bolivar, Clinica infantil Colsubsidio, Facultad de Medicina, Post Grado Reumatologia Pediatrica, Universidad El Bosque, Bogota, Colombia, Paediatric Rheumatology International Trials Organisation (PRINTO), Bogotà, Colombia, [5]Hospital Nacional de Ninos Dr Carlos Saenz Herrera, Servicio de Immunologia y Reumatologia pediatrica, San Josè, Costa Rica, Paediatric Rheumatology International Trials Organisation (PRINTO), San Josè, Costa Rica, [6]National Institute Salud del Nino, Rheumatology Service, Brena, Lima, Peru, Paediatric Rheumatology International Trials Organisation (PRINTO), Lima, Peru, [7]Istituto Giannina Gaslini, Paediatric Rheumatology International Trials Organisation (PRINTO), Genova, Italy, [8]Istituto Giannina Gaslini, Genoa, Italy, [9]Istituto Giannina Gaslini, Università degli Studi di Genova, Genova, Italy

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Measurements (0739–0763)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Parent- and child-reported outcomes (PCROs) reflect the parent and child perception of rheumatic disease course and effectiveness of therapeutic interventions. Among PCROs for the assessment of patients with juvenile idiopathic arthritis (JIA), the most widely adopted is the parent/patient global evaluation or well-being visual analogue scale (WB-VAS). Several studies in JIA have highlighted the discrepancies in the assessment of the disease status between the physician and the parent/patient. This difference might be due to the WB-VAS measuring a broader construct than the physician global assessment (PGA). Aim of this study is to evaluate in a large multinational sample of JIA patients the disease characteristics of subjects with a PGA score of 0 and with an increased WB-VAS score.

Methods: Data from the multinational dataset of patients in the Epidemiology Treatment and Outcome of Childhood Arthritis study were analyzed. We have included only subjects with a PGA score of 0. PCROs were collected through the juvenile arthritis multidimensional assessment report. We compared demographic features, socio-economic sta-

tus, level of education, subtype of JIA diagnosis and the main PCROs (pain level, presence of morning stiffness, count of joints with swelling or pain, functional ability, disease activity level, ongoing therapy, presence of medications side effects and health related quality of life between subjects with WB-VAS ≤ 1 and > 1.

Results: a total of 3537 patients were sorted into two groups according to the WB_VAS score: 2862 subjects were included in a first group (WB_VAS ≤1); 675 in a second one (WB-VAS >1). Respectively, 17,6% vs 18,1% of families belonged to the lower socio-economic status, 70,5% vs 71% to the intermediate, 11,9% vs 10,8% to the higher. The percentages of patients in the three levels of education was not different in the two groups:20,2% and 22% in the lower, 48,9% and 50,1% in the intermediate, 30,8% and 27,9% in the higher level of education. No significant difference was observed in the distribution of JIA categories in the two groups. Subjects in first group were younger at disease onset (5.6 vs 6.4 years). Comparison of main PCROs results is presented in the table.

PCROs	**WB_VAS ≤1**	**WB_VAS >1**	**p**
VAS_Pain (average)	0.3 (0.9)	2.4 (2.4)	< 0.001
Presence of morning stiffness (%)	227 (8.0)	285 (42.4)	< 0.001
Patients under treatment (%)	1919 (67.2)	540 (80.2)	< 0.001
Reporting side effects (%)	421 (22.1)	236 (43.9)	< 0.001
Juvenile Arthritis Functionality Scale (JAFS)Total Score (average)	0.5 (1.6)	3.0 (4.4)	< 0.001
JIA Quality of Life (JQL) Total Score (mean)	1.6 (2.3)	6.4 (4.4)	< 0.001
VAS-Disease Activity (average)	0.4 (1.3)	2.3 (2.4)	< 0.001
Count of active joints (average)	0.2 (0.7)	1.4 (2.2)	< 0.001

Conclusion: we have analyzed the variables that might determine a difference between the physician's assessment of inactive disease and the parent's/patient's perception of well-being. In particular, socio-economic status, level of education, and gender representation seem not to impact on the general perception of well-being, while pain seems to have the greatest influence on the parent/patient quality of life assessment. Finally, children with lower WB-VAS score had a younger disease onset.

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Abstract Number: 0764

Patients with Juvenile Systemic Sclerosis Have a Distinct Pattern of Organ Involvement: Results from the Juvenile Systemic Sclerosis Inception Cohort

Ivan Foeldvari[1], Jens Klotsche[2], Ozgur Kasapcopur[3], Amra Adrovic[4], Kathryn Torok[5], Maria Terreri[6], Ana Paula Sakamoto[7], Flavio Sztajnbok[8], Brian Feldman[9], Valda Stanevicha[10], Jordi Anton[11], Raju Khubchandani[12], Ekaterina Alexeeva[13], Sindhu Johnson[14], Maria Martha Katsicas[15], Sujata Sawhney[16], Vanessa Smith[17], Simone Appenzeller[18], Tadej Avcin[19], Mikhail Kostik[20], Thomas Lehman[21], Edoardo Marrani[22], Dieneke Schonenberg-Meinema[23], Walter Alberto Sifuentes-Giraldo[24], Natalia Vasquez-Canizares[25], Mahesh Janarthanan[26], Hana Malcova[27], Monika Moll[28], Dana Nemcova[29], Anjali Patwardhan[30], Maria José Santos[31], cristina battagliotti[32], Lillemor Berntson[33], Blanca Elena Rios Gomes Bica[34], Jürgen Brunner[35], Rolando Cimaz[36], Patricia Costa Reis[37], Despina Eleftheriou[38], Liora Harel[39], Gerd Horneff[40], Daniela Kaiser[41], Tilmann Kallinich[42], Dragana Lazarevic[43], Kirsten Minden[2], Susan Nielsen[44], Farzana Nuruzzaman[45], Siri Opsahl Hetlevik[46], Yosef Uziel[47] and Nicola Helmus[48], [1]Hamburger Zentrum fuer Kinder- und Jugendrheumatologie, Hamburg, Germany, [2]German Rheumatism Research Center, Berlin, Germany, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, İstanbul, Turkey, [4]Cerrahpasa Medical School, Istanbul, Turkey, [5]University of Pittsburgh, Pittsburgh, PA, [6]UNIFESP, São Paulo, Brazil, [7]Federal University of So Paulo (UNIFESP), São Paulo, Brazil, [8]UFRJ/UERJ, Rio de Janeiro, Brazil, [9]The Hospital for Sick Children, Toronto, ON, Canada, [10]Paediatric Rheumatology International Trials Organisation (PRINTO), Riga, Latvia, [11]Hospital Sant Joan de Deu, University of Barcelona, Barcelona, Spain, [12]Jaslok Hospital and Research Center, Mumbai, India, [13]Scientific Center of Children Health of RAMS, Moscow, Russia, [14]University of Toronto, Toronto, ON, Canada, [15]Hospital de Pediatria J.P Garrahan, Buenos Aires, Argentina, [16]Pediatric Rheumatology Department, Institute of Child Health, Sir Gangarm Hospital, New Delhi, India, [17]Department of Rheumatology and Internal Medicine, Ghent University Hospital, Ghent, Belgium, [18]Hospital das Clínicas da Universidade Estadual de Campinas, Campinas, Brazil, [19]University Medical Center Ljubljana, Ljubljana, Slovenia, [20]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia, [21]Hospital for Special Surgery, New York, NY, [22]University of Florence, Florence, Italy, [23]Emma Children's Hospital, Amsterdam, Netherlands, [24]Hospital Universitario Ramón y Cajal, Madrid, Spain, [25]Children's Hospital at Montefiore, Bronx, NY, [26]Sri Ramachandra University, Chennai, India, [27]Motol University Hospital, Prague, Czech Republic, [28]University Tuebingen, Tübingen, Germany, [29]Charles University, Prague, Czech Republic, [30]University of Missouri-Columbia, Columbia, MO, [31]Rheumatology Department, Hospital Garcia de Orta, Almada, Portugal, [32]Hospital de Niños Dr Orlando Alassia, Santa Fe, Argentina, [33]Uppsala University, Uppsala, Sweden, [34]Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [35]Medical University Innsbruck, Innsbruck, Austria, [36]ASST Gaetano Pini-CTO, Università degli Studi di Milano, Milan, Italy, [37]Hospital de Santa Maria, Lisbon, Portugal, [38]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [39]Scheiders Children Medical Center of Israel, Petah-Tiqva, Israel, [40]Paediatric Rheumatology International Trials Organisation (PRINTO), Sankt Augustin, Germany, [41]Luzerner Kantonsspital, Kinderspital, Luzern, Switzerland, [42]Charité University Medicine, Nuremberg, Germany, [43]Dept of Pediatric Rheumatology and Immunology Clinical Center Nis, Nis, Serbia, [44]Rigshospitalet, Copenhagen, Denmark, [45]Stony Brook Children's Hospital, Stony Brook, NY, [46]Oslo University Hospital, Oslo, Norway, [47]Meir Medical Center, Kfar Saba, Israel, [48]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile systemic sclerosis (jSSc) is a rare disease with a prevalence of around 3 in 1,000,000 children. To better capture the clinical manifestations of jSSc the juvenile systemic sclerosis inception cohort (jSScC) has been prospectively enrolling patients with predetermined clinical variables over the past 12 years. One of the goals is to study the demographic, clinical features, and physician and patient reported outcome differences between those with juvenile limited cutaneous (lc) compared to diffuse cutaneous (dc) disease subtypes, to determine if characteristics are similar or different between dc and lc jSSc.

Methods: Demographic, physical examination, organ system evaluation, autoantibody profile, treatment, and patient and physician reported outcome variables were evaluated from the jSSc Inception cohort and summary statistics applied using chi-square test and Mann Whitney U-test comparing lcjSSc and dcjSSc subtypes.

Results: At the time of data extraction, 187 jSSc patients were enrolled in the cohort, 80% were Caucasian and 80% female. Diffuse cutaneous jSSc subtype predominated (72%). Median Disease duration was 2.5 years (1 – 4.4). Median age at Raynaud´s was 10.4 years (7.2 – 13.1) and median age of first non-Raynaud´s was 10.9 (7.4 – 13.5). Significant differences were found between dcjSSc versus lcjSSc, regarding several clinical characteristics. Patients with diffuse cutaneous subtype had significantly higher modified Rodnan skin score ($p< 0.001$), presence of sclerodactyly ($p=0.003$), presence of Gottron's papules ($p=0.008$), presence of telangiectasia ($p=0.005$), history of digital tip ulceration ($p=0.001$). Cardiac involvement was significantly higher in limited cutaneous jSSc subtype ($p=0.001$). Diffuse cutaneous jSSc patients had significantly worse scores for Physician Global Assessment of disease activity (35 vs 20; $p< 0.001$) and disease damage (30 vs 15; $p< 0.001$).

Conclusion: Results from this large international cohort of jSSc patients demonstrate significant differences between dcjSSc and lcjSSc patients. According to the general organ involvement and physician global scores, the dcjSSc patients had significantly more severe disease. These observations strengthen our previous findings of the unique organ pattern of pediatric patients.

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Abstract Number: 0765

Male Juvenile Systemic Sclerosis Patients Have More Severe Disease: Results from the International Juvenile Scleroderma Inception Cohort

Ivan Foeldvari[1], Jens Klotsche[2], Ozgur Kasapcopur[3], Amra Adrovic[4], Kathryn Torok[5], Maria Terreri[6], Ana Paula Sakamoto[7], Flavio Sztajnbok[8], Brian Feldman[9], Valda Stanevicha[10], Jordi Anton[11], Raju Khubchandani[12], Ekaterina Alexeeva[13], Sindhu Johnson[14], Maria Martha Katsicas[15], Sujata Sawhney[16], Vanessa Smith[17], Simone Appenzeller[18], Tadej Avcin[19], Mikhail Kostik[20], Thomas Lehman[21], Edoardo Marrani[22], Dieneke Schonenberg-Meinema[23], Walter Alberto Sifuentes-Giraldo[24], Natalia Vasquez-Canizares[25], Mahesh Janarthanan[26], Hana Malcova[27], Monika Moll[28], Dana Nemcova[29], Anjali Patwardhan[30], Maria José Santos[31], cristina battagliotti[32], Lillemor Berntson[33], Blanca Elena Rios Gomes Bica[34], Jürgen Brunner[35], Rolando Cimaz[36], Patricia Costa Reis[37], Despina Eleftheriou[38], Liora Harel[39], Gerd Horneff[40], Daniela Kaiser[41], Tilmann Kallinich[42], Dragana Lazarevic[43], Kirsten Minden[2], Susan Nielsen[44], Farzana Nuruzzaman[45], Siri Opsahl Hetlevik[46], Yosef Uziel[47] and Nicola Helmus[48], [1]Hamburger Zentrum fuer Kinder- und Jugendrheumatologie, Hamburg, Germany, [2]German Rheumatism Research Center, Berlin, Germany, [3]Istanbul University-Cerrahpasa, Cerrahpasa Medical School, İstanbul, Turkey, [4]Cerrahpasa Medical School, Istanbul, Turkey, [5]University of Pittsburgh, Pittsburgh, PA, [6]UNIFESP, São Paulo, Brazil, [7]Federal University of So Paulo (UNIFESP), São Paulo, Brazil, [8]UFRJ/UERJ, Rio de Janeiro, Brazil, [9]The Hospital for Sick Children, Toronto, ON, Canada, [10]Paediatric Rheumatology International Trials Organisation (PRINTO), Riga, Latvia, [11]Hospital Sant Joan de Deu, University of Barcelona, Barcelona, Spain, [12]Jaslok Hospital and Research Center, Mumbai, India, [13]Scientific Center of Children Health of RAMS, Moscow, Russia, [14]University of Toronto, Toronto, ON, Canada, [15]Hospital de Pediatria J.P Garrahan, Buenos Aires, Argentina, [16]Pediatric Rheumatology Department, Institute of Child Health, Sir Gangarm Hospital, New Delhi, India, [17]Department of Rheumatology and Internal Medicine, Ghent University Hospital, Ghent, Belgium, [18]Hospital das Clínicas da Universidade Estadual de Campinas, Campinas, Brazil, [19]University Medical Center Ljubljana, Ljubljana, Slovenia, [20]Saint-Petersburg State Pediatric Medical University, Saint Petersburg, Russia, [21]Hospital for Special Surgery, New York, NY, [22]University of Florence, Florence, Italy, [23]Emma Children's Hospital, Amsterdam, Netherlands, [24]Hospital Universitario Ramón y Cajal, Madrid, Spain, [25]Children's Hospital at Montefiore, Bronx, NY, [26]Sri Ramachandra University, Chennai, India, [27]Motol University Hospital, Prague, Czech Republic, [28]University Tuebingen, Tübingen, Germany, [29]Charles University, Prague, Czech Republic, [30]University of Missouri-Columbia, Columbia, MO, [31]Rheumatology Department, Hospital Garcia de Orta, Almada, Portugal, [32]Hospital de Niños Dr Orlando Alassia, Santa Fe, Argentina, [33]Uppsala University, Uppsala, Sweden, [34]Faculdade de Medicina, Universidade Federal do Rio de Janeiro, Rio de Janeiro, Brazil, [35]Medical University Innsbruck, Innsbruck, Austria, [36]ASST Gaetano Pini-CTO, Università degli Studi di Milano, Milan, Italy, [37]Hospital de Santa Maria, Lisbon, Portugal, [38]Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom, [39]Scheiders Children Medical Center of Israel, Petah-Tiqva, Israel, [40]Paediatric Rheumatology International Trials Organisation (PRINTO), Sankt Augustin, Germany, [41]Luzerner Kantonsspital, Kinderspital, Luzern, Switzerland, [42]Charité University Medicine, Nuremberg, Germany, [43]Dept of Pediatric Rheumatology and Immunology Clinical Center Nis, Nis, Serbia, [44]Rigshospitalet, Copenhagen, Denmark, [45]Stony Brook Children's Hospital, Stony Brook, NY, [46]Oslo University Hospital, Oslo, Norway, [47]Meir Medical Center, Kfar Saba, Israel, [48]Hamburg Centre for Pediatric and Adolescence Rheumatology, Hamburg, Germany

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile systemic sclerosis (jSSc) is a rare disease with a prevalence of around 3 in 1,000,000 children. To better capture the clinical manifestations of jSSc the juvenile systemic sclerosis inception cohort (jSScC) has been prospectively enrolling patients with predetermined clinical variables over the past 12 years. One of the goals is to study the demographic, clinical features, and physician and patient reported outcome differences between male and female patients, to determine if characteristics are similar or different.

Methods: Demographics, organ involvement, laboratory evaluation, patient reported outcomes and physician assessment variables were compared between male and female jSSc patients enrolled in the prospective international juvenile systemic sclerosis cohort (jSScC) at their baseline visit.

Results: 175 jSSc patients were evaluated, 142 female and 33 male. Race, age of onset, disease duration, and disease subtypes (70% diffuse cutaneous) were similar between males and females. Active digital ulceration, very low body mass index, and tendon friction rubs were significantly more frequent in males. Physician global assessment of disease severity and digital ulcer activity was significantly higher in males. The composite pulmonary involvement was also more frequent in males, though not statistically significantly.

Conclusion: In this cohort, jSSc had a more severe course in males. This reflects the adult-onset SSc cohort data and parallels it in regards to increased digital ulcers, interstitial lung disease, and global severity. Differences from adult findings include no increased signal of pulmonary arterial hypertension or heart failure in male pediatric patients. While monitoring protocols of organ involvement in jSSc need to be identical for males and females, our findings suggest a higher index of suspicion of certain organ involvement in males.

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Abstract Number: 0766

Baseline Characteristics and Patient Reported Outcomes from a Juvenile Dermatomyositis Registry Inception Cohort

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile dermatomyositis (JDM), the most common inflammatory myopathy of children, is rare, with an estimated incidence of 2-4 in 1 million children. Given the challenges of studying JDM, large observa-

tional cohort studies are invaluable resources for disease characterization, long-term monitoring, and comparative effectiveness studies, to ultimately improve the care and outcomes of children with JDM.

The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry, designed a longitudinal inception cohort that includes the systematic data collection, including patient reported outcomes, planned over 10 years.

Table 1. Demographics, Diagnostic and Clinical Features

Age at diagnosis in years, median (IQR)	8 (4.0-11.5)
Age at disease onset in years, median (IQR)	7 (3.5-7.5)
Time to diagnosis in months, median (IQR)	3 (1-6.5)
Female, N (%)	76 (63.4)
Race, N (%)	
White	86 (72.3)
Hispanic, Latino, or Spanish origin	22 (18.5%)
Black, African American, African, or Afro-Caribbean	9(7.6)
Asian	7(5.9)
Native American, American Indian or Alaskan Native	3 (2.5)
Middle Eastern	3 (2.5)
Unknown	3 (2.5)
Other	4 (3.4)
Skin Predominant JDM, N (%)	38 (31.9)
History of, N (%)	
Proximal Muscle Weakness	86 (72.3)
Rash (Heliotrope or Gottron's)	110(92.4)
Elevated muscle enzymes	99(83.2)
EMG abnormality (n=4)	4
Muscle Biopsy abnormality (n=19)	18
MRI (81)	66
Autoantibodies, proportion	
ANA	75/96 (78.1%)
Myositis-specific antibodies	
Anti-MJ/NXP2	11/49 (22.4%)
Anti-p155/140/TIF1-γ	7/53 (13.2%)
Anti-Mi2	6/55 (10.9%)
Anti-MDA5	4/51 (7.8%)
Anti-Jo1	2/67 (3.0%)
Myositis-associated antibodies	
Anti-PM-Scl	3/43 (7.0%)
Anti-Smith	1/56 (1.7%)
Muscle Enzyme Elevation, N (%)	99 (83.2)
MMT8, median (IQR)	63.5 (51.0-75.0), N=32
CMAS, median (IQR)	43.5 (30.5-51.0), N=34
Skin Manifestations, N (%)	
Gottron's papules or sign	90(75.6)
Malar or facial erythema	78(65.5)
Periungal capillary loop changes	70(58.8)
Heliotrope Rash	64(53.8)
Linear Erythema	33 (27.7)
Cuticular overgrowth	24(20.2)
Non-sun exposed erythema	23(19.3)
Extensive cutaneous erythema	17(14.3)
Shawl Sign	13(10.9)

Table 2. Patient/Parent-Reported Outcome Measures

Global Assessments:	Median (IQR)	High symptom/low function scorers, n (%)*
Global Assessment of Disease Activity (patient), n=48	3 (1.75-5.25)	-
Global Assessment of Disease Activity (parent), n=33	3 (1-7)	-
PROMIS Pediatric Global Health 7 (patient), n=48	38.8 (33.6-42.1)	19 (39.6)
PROMIS Pediatric Global Health 7 (parent), n=34	34.6 (29.4-37.9)	18 (52.9)
Physical Function:		
CHAQ, n=102	0.75 (0.03-1.875)	-
PROMIS Mobility (patient), n=48	36.9 (32.9-48.4)	19 (39.6)
PROMIS Mobility (parent), n=33	32 (27-43)	22 (66.7)
PROMIS Upper Extremity (patient), n=31	35.4 (28.45-44.9)	16 (51.6)
PROMIS Upper Extremity (parent), n=28	23.5 (21-33.5)	20 (71.4)
Pain:		
Pain Intensity Now (patient), n=48	1 (0-4)	-
Pain Intensity Now (parent), n-35	1 (0-3)	-
Pain Intensity Past 7 Days (patient), n=48	3 (1-6)	-
Pain Intensity Past 7 Days (parent), n=35	2 (0-6)	-
Pain Frequency, # Days in Past 14 Days (patient), n=46	5 (1.25-13.25)	-
Pain Frequency, # Days in Past 14 Days (parent), n=30	4 (0.25-14)	-
PROMIS Pain Interference (patient), n=40	55.65 (50.33-61.4)	15 (37.5)
PROMIS Pain Interference (parent), n=30	62 (51.5-66.5)	21 (77.8)

*N=119 unless indicated in the table where missing data reduced the total number of patients analyzed

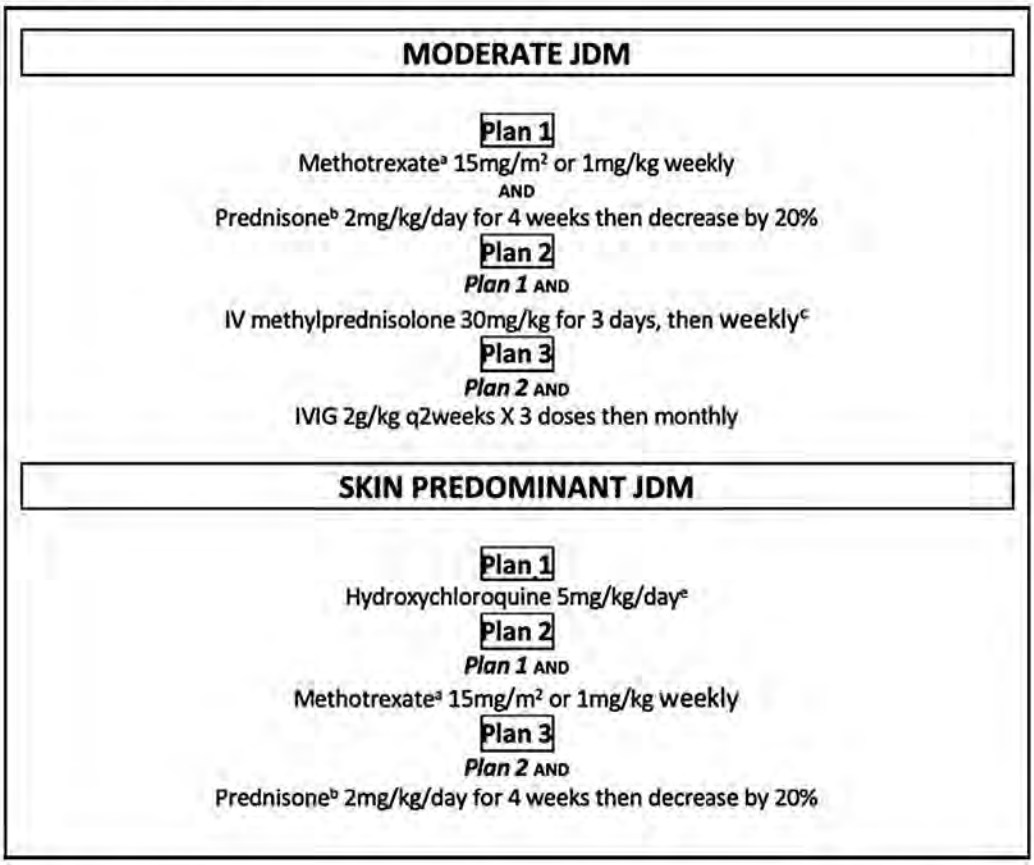
Here, we describe the baseline patient demographics, disease characteristics, initial assessments, patient/parent-reported outcomes and treatments for an inception cohort of children with JDM enrolled to the registry in the first year.

Methods: The CARRA Registry began enrollment of JDM subjects in January 2019. Eligible subjects were < 18 years of age at disease onset and diagnosed with JDM based on clinical judgement of the treating rheumatologist. Enrolled subjects had disease for < 6 months and treatment naïve or treated with systemic therapy for < 12weeks. This Registry is approved by Duke University Institutional Review Board (IRB) and each participating site. Consent/assent was obtained from eligible participants by the local investigators.

Results: 119 JDM subjects were enrolled from 41 sites. Most were female (63.4%), and white (72.3%) with a median diagnosis age 8.0 years (IQR 4.0-11.5), and median age of disease onset 7.0 years (IQR 3.5-7.5) (Table 1). They had characteristic rashes (92.4%), elevated muscle enzymes (83.2%), physician global score 4.0 (IQR 2.5-5.0) and manual muscle testing score 63.5 (IQR 51.0-75.0). Calcinosis (3%) and interstitial lung disease (< 1%) were uncommon.

CHAQ results (median 0.75, IQR 0.03-1.875), and patient/parent global assessments of disease activity (median 3, patient IQR: 1.75-5.25; parent IQR: 1-7) showed mild-moderate disability. PROMIS® Pediatric Global Health 7

Figure 1: Published Consensus Treatment Plans for JDM patients with Moderate, and Skin predominant disease



[a] Lesser of 15 mg/m² or 1 mg/kg (max 40 mg), [b] max 60mg, [c] optional, [d] max 70 grams, [e] max 400mg, [f] max 1500mg bid, [g] higher doses based on toxicity, efficacy

Published Consensus Treatment Plans for JDM patients with Moderate, Skin predominant disease.

scores, PROMIS measures for pain interference, physical function scores for mobility, and upper extremity function were commonly worse than 95% of the general pediatric population based on published normative data (Table 2).

Approximately half of subjects, 54.6% (n=64), were treated according to a Consensus Treatment Plans (CTP) (Figure 1).

Conclusion: In its first year 119 JDM patients were successfully enrolled into the CARRA Registry. They were similar to historic cohorts, with a trend toward earlier time to diagnosis and milder disease. PROs were also collected successfully, and our findings reveal moderate to severe patient and parent-reported disease impact. Published CTPs were also used to treat over half of the enrolled patients, suggesting that pragmatic trials may be feasible in the CARRA Registry.

This growing registry provides infrastructure to advance future clinical research and paired specimens in the CARRA biorepository will enable future translational research. Together, these efforts enhance trial readiness for future therapeutic studies, including comparative effectiveness trials which will help to advance care and outcomes for JDM.

Disclosure: J. Neely, None; **K. Ardalan**, None; **A. Huber**, None; **S. Kim**, None.

Abstract Number: 0767

Medication Use in Pediatric Lupus in the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Black and Hispanic children with pediatric lupus (pSLE) have higher morbidity and mortality, but the extent to which differences in outcomes may be related to disparities in treatment, including in medication regimens, is unknown. We aimed to characterize medication use in a large cohort of children with pSLE and determine whether use of steroids, antimalarials and rituximab in pSLE is associated with self-reported race and ethnicity.

Methods: We included patients with pSLE in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry enrolled from 2017-July 2020 with demographic, disease activity and medication data available at baseline visit. Central nervous system (CNS) lupus was defined as documented organic brain syndrome, psychosis, cerebrovascular accident, visual disturbance, cranial neuropathy, or seizure. Large versus small site of care was also included. Summary statistics were used to describe disease and demographic features and medication use in the cohort. We analyzed specific medication use: (1) use versus non-use of antimalarials (2) use of high (≥ 15mg or 0.3mg/kg prednisone equivalent daily) versus low/no prednisone dose at time of baseline visit and (3) use versus non-use of rituximab in the first year of Registry enrollment. Univariate logistic regression analysis was used to identify sociodemographic and disease-related factors associated with each medication outcome. Multivariable logistic regression was used to compare medication outcomes in Black and Hispanic patients to those of non-Black and non-Hispanic patients while adjusting for these covariates.

Results: We identified 572 patients with pSLE enrolled in the CARRA Registry with complete data at baseline visit and 273 patients with at least 1 year of follow up. Patient and disease characteristics are presented in Table 1. Median disease duration at baseline visit was 5.8 months. Overall, 90% of patients were prescribed an antimalarial at baseline visit and 49% were on high-dose steroids versus 51% on no or lower-dose steroids (Table 2). Of those with at least 1 year of follow up, 7.7% received rituximab. In multivariate regression, patients with lupus nephritis and those treated at large centers had increased odds of high-dose steroid regimens at their baseline visits; a trend toward higher dose was also seen in lower income patients (Table 3). Black race was associated with over three-fold higher odds of rituximab use within the first year of Registry enrollment even when controlling for disease activity. Antimalarial use at baseline was significantly associated with private insurance.

Conclusion: High dose steroid regimens were associated with higher SLEDAI score, lupus nephritis and large center size. Rituximab use was uncommon and associated with Black race and higher SLEDAI. Antimalarial use was high, though not universal, in this pSLE cohort, and use was associated with private insurance. Further research is needed to understand reasons for this variation and its impact on pediatric lupus outcomes.

Table 1. Patient Characteristics and Medication Use

	Count (%) or Median (IQR)
Sociodemographic Characteristics (n=572)	
Race/Ethnicity	
White	174 (30.4%)
Black/African American	170 (29.7%)
Hispanic/Latino	147 (25.7%)
Asian	89 (15.6%)
Native American, American Indian, Alaskan Native	13 (2.3%)
Middle Eastern/North African	6 (1.0%)
Native Hawaiian or Other Pacific Islander	5 (0.9%)
Female	483 (84.5%)
Age	15.5 (13.2, 17.0)
Family Income ($)	
<25,000	72 (12.6%)
25,000-49,999	86 (15%)
50,000-99,999	105 (18.4%)
Above 100,000	103 (18%)
Prefer not to answer	111 (19.4%)
Unknown	95 (16.6%)
Parental Education (n=540)	
Less than high school	47 (8.7%)
Graduated high school	114 (21.1%)
College	207 (38.3%)
Graduate school	77 (14.3%)
Prefer not to answer	95 (17.6%)
Insurance	
Private	273 (48.0%)
Non-military public	211 (37.1%)
Other	85 (14.9%)
Disease Features (n=572)	
Lupus Nephritis (n=570)	221 (38.8%)
CNS Lupus (n=570)	16 (2.8%)
SLEDAI Score (n=570)	4 (1, 10)
Age at Diagnosis (years) (n=566)	14.3 (12.0, 15.9)
Disease Duration at Enrollment (months) (n=566)	5.8 (1.4, 16.0)

Table 2. Medication Use Outcomes

Medication Use	
High dose steroid use at baseline visit (n=572)	281 (49.1%)
Antimalarial use at baseline visit (n=572)	513 (89.7%)
Rituximab use within 1st year (n=273)	21 (7.7%)

Table 3. Association of Medication Use with Disease and Sociodemographic Factors

	Antimalarial Use at Baseline Visit (n=572)		High Dose Steroid Use at Baseline Visit (n=572)		Rituximab Use in First Year of Follow Up (n=273)	
	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Race						
Black	1.4 (0.77-2.72)		1.02 (0.71-1.46)		3.54 (1.43-9.02)*	3.54 (1.44-9.89)*
Hispanic	1.02 (0.56-1.94)		1.49 (1.02-2.71)*		0.65 (0.18-1.83)	
Male	0.89 (0.45-1.93)		1.01 (0.64-1.6)		0.88 (0.2-2.76)	
Income						
Above 100,000	(reference)					
<25000	0.77 (0.28-2.14)		1.63 (0.89-3.02)	1.62 (0.80-3.3)	0.44 (0.02-3.62)	
25-49,999	0.82 (0.31-2.2)		1.33 (0.75-2.37)	1.35 (0.70-2.6)	2.59 (0.59-13.39)	
50-99,999	0.74 (0.29-1.84)		0.76 (0.44-1.32)	0.6 (0.32-1.12)	0.98 (0.17-5.53)	
Parent Education						
College	(reference)					
Less than high school	0.9 (0.34-2.82)		1.4 (0.74-2.7)		1.38 (0.19-6.47)	
High school	0.91 (0.43-1.99)		0.86 (0.54-1.35)		2.31 (0.73-7.55)	
Graduate school	1.07 (0.45-2.83)		0.79 (0.47-1.34)		1.78 (0.43-6.64)	
Insurance						
Private	(reference)					
Public	0.72 (0.39-1.33)	0.7 (0.36-1.35)*	1.45 (1.01-2.08)		1.11 (0.41-2.91)	
Other/none	0.44 (0.22-0.93)	0.4 (0.18-0.81)*	1.35 (0.83-2.2)		1.39 (0.3-4.9)	
Small site of care	0.97 (0.52-1.92)		0.77 (0.51-1.14)	0.55 (0.35-0.86)*	0.79 (0.22-2.23)	
Lupus Nephritis	1.55 (0.87-2.88)	1.9 (1.02-3.7)*	1.73 (1.23-2.44)*	2.01 (1.36-2.99)**	0.58 (0.2-1.48)	
SLEDAI Score	1.01 (0.97-1.05)		1.1 (1.07-1.14)*	1.1 (1.06-1.15) **	1.09 (1.03-1.15)*	1.07 (1.01-1.14)*
Age at Diagnosis	1.06 (0.96-1.16)		1.03 (0.97-1.09)		1 (0.86-1.18)	
Disease Duration at Enrollment	0.99 (0.97-0.99)*	0.98 (0.97-0.99)*	0.96 (0.94-0.97)**	0.96 (0.95-0.97)**	0.91 (0.83-0.97)*	0.93 (0.86-0.99)*

* p-value <0.05
**p-value <0.001

Disclosure: J. Roberts, None; **L. Berbert**, None; **M. Son**, None.

Abstract Number: 0768

Poverty and Length of Stay in Children Hospitalized with Pediatric Systemic Lupus Erythematosus: An Analysis of the 2016 Kids' Inpatient Database

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Prior studies have demonstrated alarming health disparities in adult patients with SLE, including higher disease severity and activity among Hispanic and Black patients. Pediatric studies have demonstrated similar racial disparities, including associations between Hispanic and Black race and end stage renal disease, increased health utilization, and death among hospitalized patients. Importantly, prior studies do not focus on modifiable risk factors of socioeconomic status (SES), such as income level, particularly important as exiting poverty demonstrated potential reversibility of disease damage in an analysis of the Lupus Outcomes Study. Our study aims to use the most recent iteration (2016) of the Kids' Inpatient Database (KID) – the largest all-payer pediatric inpatient care database in the U.S. – to investigate the relationship between income level and hospital length of stay (LOS) via cross-sectional analysis.

Methods: SLE hospitalizations were identified for children ages 2-20 by a primary ICD-10 diagnosis code of M32. Those with neonatal lupus (ICD-10 M32.8) were excluded. Baseline characteristics were compared by income level (Quartile 1, 2, 3, and 4) using descriptive statistics (ANOVA and Pearson's chi-squared exact tests, as appropriate). Negative binomial regression was used to analyze the effect of income level (by median income for zip code divided into quartiles) on length of stay unadjusted, then adjusted for sex and age, and finally adjusted for other covariates of interest (race/ethnicity, primary payer status) and confounders (APRDRG severity of hospitalization, presence of severe lupus features, and location/teaching status of hospital). Using this adjusted model, a marginal mean length of stay was calculated at each income quartile.

Results: A total of 1,586 primary lupus hospitalizations were identified (Table 1). The mean age at admission was 16 with a female predominance (84%). This cohort represented a diverse patient population (36% Black, 27% Hispanic, 8% Asian/Pacific Islander vs 14% White) with higher proportions of minority populations in the lower compared to upper income quartiles (i.e. Black 50% in Quartile 1 & 31% in Quartile 2 vs 27% in Quartiles 3 & 4). Private insurance coverage was more common in the highest income quartile (62% in Quartile 4 vs 26% in Quartile 1). In unadjusted analysis, income level was not associated with increased LOS though adjusted analysis did demonstrate an association with prolonged increased length of stay at the 2nd income level (IRR 1.17, p-value 0.032 – Table 2). Adjusted mean length of stay was higher than the mean for those with lower income levels (Quartile 1 and 2 - Figure 1).

Conclusion: Lower income level may be associated with prolonged LOS among children hospitalized with SLE though this association was only significant at the 2nd level of income quartile. This may reflect that those of lowest income are supported by resources not available to others in poverty who miss strict guidelines for assistance, such as housing support. Future work will include income as a predictor of readmissions and recurrent ED visits.

Table 1. Clinical Characteristics and Demographic Information of the SLE cohort in the 2016 Kids' Inpatient Database (KID)

	Total	$1-42,999	$43,000-53,999	$54,000-70,999	$71,000+	p-value
	N=1,586	N=572	N=383	N=332	N=299	
Age in years at admission	16 (3)	16 (3)	16 (3)	15 (4)	16 (3)	0.14
Sex						0.14
Male	251 (16%)	79 (14%)	74 (19%)	50 (15%)	48 (16%)	
Female	1,335 (84%)	493 (86%)	309 (81%)	282 (85%)	251 (84%)	
Race/Ethnicity						<0.001
White	227 (14%)	42 (7%)	66 (17%)	61 (18%)	58 (19%)	
Black	575 (36%)	285 (50%)	120 (31%)	89 (27%)	81 (27%)	
Hispanic	435 (27%)	160 (28%)	119 (31%)	94 (28%)	62 (21%)	
Asian or Pacific Islander	120 (8%)	21 (4%)	24 (6%)	29 (9%)	46 (15%)	
Native American	10 (1%)	4 (1%)	0 (0%)	2 (1%)	4 (1%)	
Other	96 (6%)	36 (6%)	21 (5%)	23 (7%)	16 (5%)	
Missing	123 (8%)	24 (4%)	33 (9%)	34 (10%)	32 (11%)	
Insurance						<0.001
Public	855 (54%)	380 (66%)	236 (62%)	148 (45%)	91 (30%)	
Private	586 (37%)	149 (26%)	110 (29%)	145 (44%)	182 (61%)	
Other (including self-pay and no charge)	145 (9%)	43 (8%)	37 (10%)	39 (12%)	26 (9%)	
Region of Hospital						<0.001
Northeast	279 (18%)	99 (17%)	61 (16%)	70 (21%)	49 (16%)	
Midwest	252 (16%)	104 (18%)	53 (14%)	48 (14%)	47 (16%)	
South	636 (40%)	266 (47%)	152 (40%)	116 (35%)	102 (34%)	
West	419 (26%)	103 (18%)	117 (31%)	98 (30%)	101 (34%)	
Location/teaching status of hospital						0.074
Rural	10 (1%)	6 (1%)	4 (1%)	0 (0%)	0 (0%)	
Urban non-teaching	124 (8%)	41 (7%)	24 (6%)	35 (11%)	24 (8%)	
Urban teaching	1,452 (92%)	525 (92%)	355 (93%)	297 (89%)	275 (92%)	
Length of stay	6 (8)	6 (8)	6 (9)	5 (7)	6 (9)	0.31
APRDRG: Severity of illness						0.004
Minor loss of function	246 (16%)	91 (16%)	68 (18%)	56 (17%)	31 (10%)	
Moderate loss of function	612 (39%)	212 (37%)	141 (37%)	126 (38%)	133 (44%)	
Major loss of function	513 (32%)	169 (30%)	127 (33%)	119 (36%)	98 (33%)	
Extreme loss of function	215 (14%)	100 (17%)	47 (12%)	31 (9%)	37 (12%)	
Any severe lupus feature						0.016
No	1,030 (65%)	372 (65%)	225 (59%)	230 (69%)	203 (68%)	
Yes	556 (35%)	200 (35%)	158 (41%)	102 (31%)	96 (32%)	
Any severe renal lupus feature						0.009
No	1,167 (74%)	414 (72%)	262 (68%)	260 (78%)	231 (77%)	
Yes	419 (26%)	158 (28%)	121 (32%)	72 (22%)	68 (23%)	
Any severe non-renal lupus feature						0.65
No	1,366 (86%)	494 (86%)	325 (85%)	292 (88%)	255 (85%)	

Table 2. Association of Income Level, Race/Ethnicity, and Insurance Status with Hospital Length of Stay (*IRR = Incidence rate ratio; **Achieving statistical significance at p-value <0.05; ***Multivariate negative binomial regression model adjusted for age, sex, hospital region, location/teaching status of hospital, presence of severe lupus features, APRDRG Severity Index + primary payer/income level and/or race/ethnicity)

	Unadjusted			Adjusted (Sex/Age)			Adjusted (Final Model***)		
	IRR*	95% CI	p-value	IRR*	95% CI	p-value	IRR*	95% CI	p-value
Income Level									
$1-42,999	1.08	0.85-1.38	0.532	1.07	0.84-1.37	0.567	1.13	0.99-1.28	0.067
$43,000-53,999	1.12	0.87-1.44	0.367	1.11	0.87-1.42	0.399	1.17**	1.01-1.35	0.032
$54,000-70,999	0.93	0.74-1.18	0.553	0.93	0.74-1.18	0.566	1.04	0.91-1.20	0.567
$71,000+	—	—	—	—	—	—	—	—	—
Race/ethnicity									
White	—	—	—	—	—	—	—	—	—
Black	0.89	0.69-1.14	0.357	0.88	0.69-1.14	0.333	0.96	0.81-1.13	0.595
Hispanic	1.06	0.84-1.34	0.623	1.03	0.82-1.30	0.807	1.04	0.88-1.24	0.636
Asian or Pacific Islander	1.38	0.96-1.98	0.085	1.32	0.91-1.93	0.143	1.34**	1.03-1.74	0.030
Native American	0.73	0.39-1.35	0.315	0.68	0.37-1.23	0.197	0.90	0.58-1.40	0.637
Other	1.09	0.71-1.68	0.698	1.07	0.69-1.67	0.753	1.01	0.77-1.33	0.920
Missing	0.93	0.72-1.20	0.582	0.88	0.67-1.15	0.347	0.92	0.75-1.13	0.434
Primary expected payer									
Public	0.96	0.80-1.16	0.678	0.94	0.78-1.12	0.477	0.93	0.83-1.03	0.173
Private	—	—	—	—	—	—	—	—	—
Other	0.84	0.63-1.11	0.222	0.85	0.66-1.09	0.201	0.91	0.75-1.09	0.308

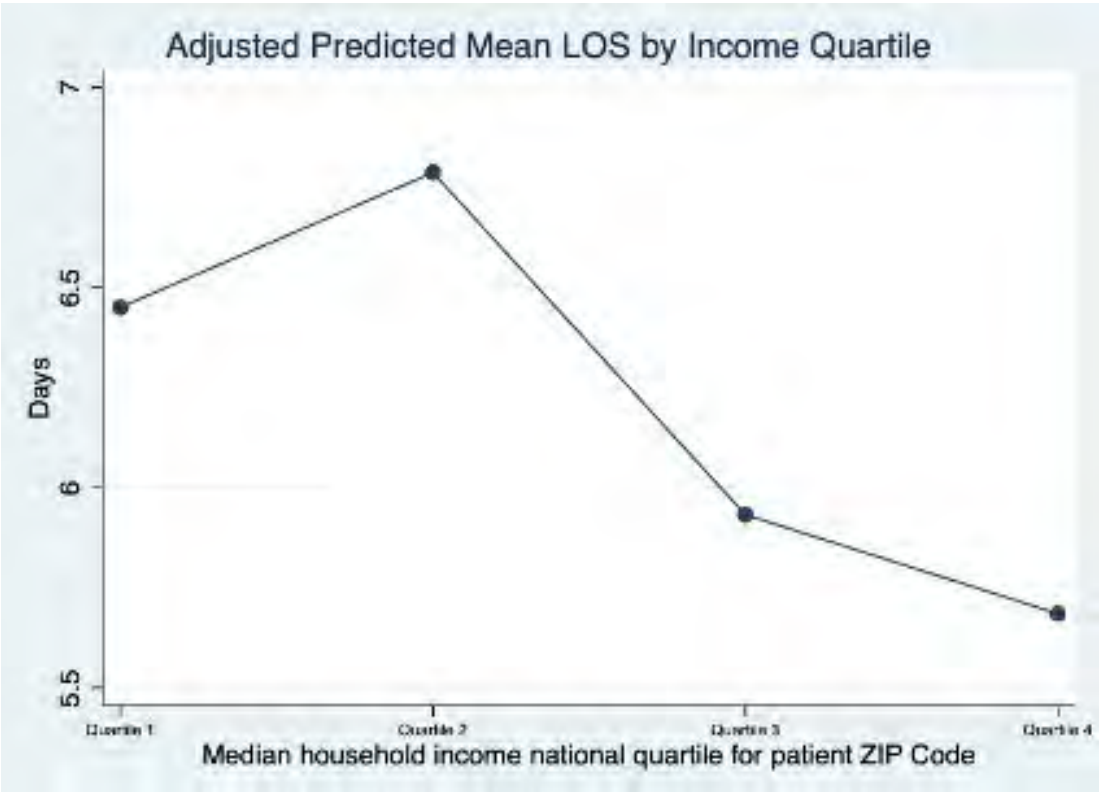

Figure 1. Adjusted* marginal mean length of stay by median household income for patient ZIP code categorized by quartile (*Multivariate negative binomial regression model adjusted for age, sex, race/ethnicity, insurance type, hospital region, location/teaching status of hospital, presence of severe lupus features, and APRDRG Severity Index).

Disclosure: W. Soulsby, None; **E. Lawson**, None; **M. Pantell**, None.

Abstract Number: 0769

Renal Outcomes in 1528 Childhood-onset Systemic Lupus Erythematosus Patients: A Brazilian Multicenter Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis is a frequent manifestation in childhood-onset systemic lupus erythematosus (cSLE) and has a great potential for chronic kidney disease (CKD), requiring dialysis and kidney transplantation, with great loss in health-related quality of life. The objective of this study was to analyze renal outcomes and CKD in cSLE and to assess its association with cumulative clinical and laboratory features, current disease activity and damage, cumulative treatments, and outcomes.

Methods: This is a multicenter, nationwide observational study of a cohort of 1,528 cSLE patients followed in 27 Brazilian pediatric rheumatology tertiary centers. All patients fulfilled the American College of Rheumatology (ACR) 1997 criteria for classification of SLE, with disease onset before 18 years of age. In this study, we investigated cumulative risk factors for KF in a large sample of cSLE patients.

Results: A total of 59/1528 (3.9%) of patients presented CKD. After Bonferroni´s correction for multiple comparisons ($p^{c}0.0013$), determinants significantly associated with CKD were urinary sediment alterations, neuropsychiatric involvement, higher scores of current SLEDAI-2K and SLICC/ACR-DI (especially renal involvement), as well as cumulative use of intravenous methylprednisolone, cyclophosphamide, and rituximab. In regression models, arterial hypertension (HR=15.42, 95%CI=6.12-38.83, $p \leq 0.0001$) and biopsy-proven proliferative nephritis (HR=2.83,

Table 1 – Demographic data, clinical and laboratorial features, disease activity and disease damage score, and treatment during follow-up in 1528 childhood-onset systemic lupus erythematosus (cSLE) patients with and without chronic kidney disease (CKD).

Variables	Total	End-stage renal disease (ESRD)		p
		With CKD (n=59)	Without CKD (n=1469)	
Demographic data				
Age at cSLE diagnosis, years, n=1528	12.1 (0.1-17.9)	11.2 (5.6-16.8)	12.1 (0.1-17.9)	0.085
Time of follow-up, years, n=1528	4.2 (0-22.3)	5.0 (0.05-15.5)	3.8 (0-22.3)	0.030
Male gender, n=1528	232 (15.1)	10 (16.9)	222 (15.1)	0.702
Clinical manifestations over time				
Constitutional manifestations, n=1528	1098 (71.7)	46 (61.4)	1048 (71.3)	0.094
Mucocutaneous involvement, n=1521	1326 (87.2)	52 (69.1)	1274 (87.1)	0.823
Musculoskeletal involvement, n=1519	1122 (73.9)	47 (79.7)	1075 (73.6)	0.901
Serositis, n=1518	518 (34.1)	25 (42.4)	493 (33.8)	0.173
Nephritis, n=1528	1136 (74.3)	59 (100)	1077 (73.3)	**<0.0001**
Hematuria, n=1514	832 (55.0)	51 (86.4)	781 (53.7)	**<0.0001**
Pyuria, n=1515	757 (50.0)	47 (79.7)	710 (48.8)	**<0.0001**
Urinary casts, n=1514	412 (27.2)	34 (57.6)	378 (26.0)	**<0.0001**
Proteinuria > 500mg/day, n=1517	868 (57.2)	56 (94.9)	812 (55.7)	**<0.0001**
Arterial hypertension, n=1516	516 (34.0)	54 (91.5)	462 (31.7)	**<0.0001**
Acute renal injury, n=1515	236 (15.6)	33 (55.9)	203 (13.9)	**<0.0001**
Classes III/IV LN, n=464	264 (17.2)	32 (54.2)	232 (15.8)	**<0.0001**
Neuropsychiatric involvement, n=1525	615 (40.3)	39 (66.1)	576 (39.3)	**<0.0001**
Central nervous system, n=1526	594 (38.9)	35 (59.3)	559 (38.1)	**0.001**
Peripheral nervous system, n=1528	59 (3.9)	5 (8.5)	54 (3.7)	0.073
Death, n=1528	63 (4.1)	14 (23.7)	49 (3.3)	**<0.0001**
Current disease activity score				
SLEDAI-2K, n=1415	4 (0-52)	8 (0-52)	2 (0-40)	**<0.0001**
Disease damage score				
SLICC/ACR-DI, n=1400	0 (0-7)	3 (0-7)	0 (0-6)	**<0.0001**
SLICC/ACR-DI without renal descriptor n=1400	NA	1 (0-4)	0 (0-6)	**<0.0001**
SLICC/ACR-DI ≥ 1, n=1395	398 (26.0)	49 (90.7)	349 (26.0)	**<0.0001**
Neuropsychiatric, n=391	152 (9.9)	17 (34.7)	135 (39.5)	0.521
Peripheral vascular, n=391	13 (0.8)	0 (0)	13 (3.8)	0.170
Ocular, n=391	88 (5.7)	6 (12.2)	82 (24.0)	0.066
Renal, n=391	88 (5.7)	39 (79.6)	49 (14.3)	**<0.0001**
Musculoskeletal, n=391	93 (6.0)	6 (12.2)	87 (25.4)	0.042
Cardiovascular, n=391	31 (2.0)	3 (6.1)	28 (8.2)	0.436
Hematological abnormalities, n=1528	1093 (71.5)	50 (84.7)	1043 (71.0)	0.022
Low complement levels (C3/C4/CH50), n=1499	1220 (81.4)	53 (91.4)	1167 (81.0)	0.046
Cumulative autoantibodies				
Anti-dsDNA, n=1512	1168 (77.1)	51 (88.4)	1115 (76.7)	0.062
Anti-P ribossomal, n=463	89 (13.6)	3 (9.5)	81 (13.8)	0.676
Treatment over time				
Prednisone, n=1528	1488 (97.5)	58 (98.3)	1430 (97.5)	0.869
Intravenous methylprednisolone n=1524	952 (62.5)	53 (89.9)	899 (61.4)	**<0.0001**
Total glucocorticoid dose (g), n=799	31.2 (0.4-430.5)	36.1 (6.7-120.7)	18.6 (0.4-430.5)	0.009
Antimalarial drugs, n=1527	1413 (92.5)	41 (69.5)	1372 (93.5)	**<0.0001**
Immunosuppressive agents				
Azathioprine, n=1526	822 (53.9)	33 (55.9)	789 (53.8)	0.745
Cyclosporine, n=1522	110 (7.2)	11 (18.6)	99 (6.8)	**<0.0001**
Methotrexate, n=1524	312 (20.5)	9 (15.3)	303 (20.7)	0.311
Mycophenolate mofetil, n=1527	380 (24.9)	24 (40.7)	356 (24.3)	0.004
Intravenous cyclophosphamide, n=1527	577 (37.8)	49 (83.1)	528 (36.0)	**<0.0001**
Cumulative dose (g), n=334	6.0 (0.1-36.0)	5.2 (1.0-18.0)	5.6 (0.1-36.0)	0.513
Rituximab, n=1526	42 (2.8)	9 (15.3)	33 (2.3)	**<0.0001**
Plasmapheresis, n=1511	10 (0.6)	1 (0.4)	9 (0.6)	0.594

Results are presented in n (%) and median (min-max).
The bold numbers express the p value that are statistically significant. *p value according to Bonferroni correction for multiple comparisons (p<0.0013).
CKD – chronic kidney renal disease, LN – Lupus Nephritis, SLEDAI-2K – Systemic Lupus Erythematosus Disease Activity Index 2000, SLICC-ACR/DI – Systemic Lupus International Collaborating Clinics/ACR-Damage Index, g – gram.

95%CI=1.70-4.72, p≤0.0001) increased the risk of CKD. The Kaplan-Meier overall curves showed significantly worse patient survival in cSLE patients with biopsy-proven proliferative nephritis (p=0.02) and CKD (p≤0.0001).

Conclusion: This study showed that cSLE patients with arterial hypertension and biopsy-proven proliferative nephritis exhibited higher hazard rates of progression to poor outcomes. Therefore, those patients could benefit from strict blood pressure control during follow-up, and better drug treatment for aggressive management of active lupus nephritis.

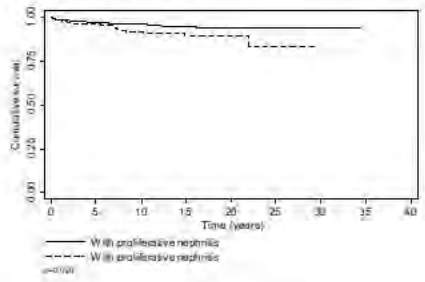
Table 2 – Regression analysis for prediction of risk of chronic kidney disease (CKD) in childhood-onset systemic lupus erythematosus (cSLE) patients

	Univariate Fine and Gray		Multivariate Fine and Gray			
			Initial Model		Final Model	
Characteristics	**Sub - Hazard Ratio (CI95%)**	**p**	**Sub - Hazard Ratio (CI95%)**	**p**	**Sub – Hazard Ratio (CI95%)**	**p**
Age (years)	0.96 (0.90 - 1.03)	0.236	1.01 (0.91 - 1.11)	0.875	-	-
SLEDAI-2K (score)	1.04 (1.02 - 1.06)	**<0.001**	1.01 (0.97 - 1.04)	0.751	-	-
Low complement	2.73 (1.17 - 6.38)	**0.020**	1.88 (0.81 - 4.35)	0.141	-	-
Anti-dsDNA	1.50 (0.84 - 2.66)	0.168	1.08 (0.54 - 2.16)	0.820	-	-
Proteinuria	9.43 (3.41 - 26.10)	**<0.001**	2.82 (0.77 - 10.35)	0.118	-	-
Arterial hypertension	19.97 (7.97 - 50.02)	**<0.001**	13.05 (4.21 - 40.43)	**<0.001**	**15.42 (6.12-38.83)**	**<0.001**
Biopsy-proven proliferative nephritis	5.17 (3.09 - 8.65)	**<0.001**	2.07 (1.15 - 3.73)	**0.016**	**2.83 (1.70-4.72)**	**<0.001**

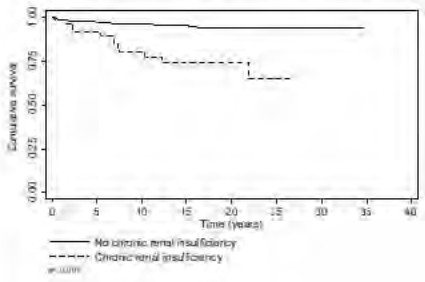
95% CI – 95% Confidence Interval
The bold numbers express statistically significant p values (p<0.05).

Figures 2 a-b and table c – Kaplan-Meier survival curves in 1528 cSLE patients

a – Renal survival due to proliferative nephritis



b – Renal survival due to chronic kidney disease (CKD)



c – Cumulative survival rate according to proliferative nephritis and CKD

	Cumulative survival rate (%)						*p*
	1 year	3 years	5 years	10 years	15 years	20 years	
Proliferative nephritis							**0.020**
No	98.56 ± 0.34	97.55 ± 0.44	97.33 ± 0.48	96.30 ± 0.61	95.08 ± 0.86	93.87 ± 1.20	
Yes	98.48 ± 0.76	96.45 ± 1.16	95.93 ± 1.27	91.97 ± 2.00	89.25 ± 2.79	89.25 ± 2.79	
CKD							**<0.001**
No	98.56 ± 0.31	97.71 ± 0.4	97.33 ± 0.44	96.28 ± 0.58	95.13 ± 0.82	94.11 ± 1.09	
Yes	98.31 ± 1.68	91.40 ± 3.68	91.40 ± 3.68	80.27 ± 5.69	73.98 ± 6.79	73.98 ± 6.79	

± Standard error
CKD – Chronic kidney disease
p – descriptive level of Log Rank test (Mantel-Cox)
The bold numbers express the p value that are statistically significant (p<0.05).
cSLE - childhood-onset systemic lupus erythematosus

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Abstract Number: 0770

Evaluation of the Lupus Low Disease Activity State (LLDAS) vs. the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2K Score in a Pediatric Systemic Lupus Erythematosus Cohort

Bridget Wilson, Tingting Qiu, Angela Merritt, Bin Huang and Hermine Brunner, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease which can affect any organ system, and ongoing disease activity leads to organ damage. The Lupus Low Disease Activity State (LLDAS) has been evaluated in adult patients, but not yet in pediatrics. In adults, achieving LLDAS was shown to decrease morbidity and mortality and was associated with improved quality of life. The Systemic Lupus Erythematosus Disease Activity Index (SLEDAI)-2K is a weighted scale measuring presence of SLE activity in nine organ systems. In children with SLE, disease activity measured by the SLEDAI-2K ≤ 4 (low SLEDAI-status) is considered to reflect good disease control currently. The purpose of the study was to compare LLDAS and low SLEDAI-status in children with SLE.

Table 1. Patient Demographics

DEMOGRAPHICS	Patients (N=117) N (%) or Mean±SD
Age at diagnosis (yrs)	15.02±2.96
Number of visits per patient	10.31±8.51
Gender	
Female	97 (82.91%)
Male	20 (17.09%)
Race	
White	56 (47.86%)
Black	48 (41.03%)
Other	11 (9.4%)
Unknown	2 (1.71%)
Ethnicity	
Non Hispanic	114 (97.44%)
Hispanic	3 (2.56%)

Table 2. Clinic Visits Achieving Low SLEDAI-2K Status and LLDAS

	Low SLEDAI-Status	Not Low SLEDAI-Status	
LLDAS	312	---	
Not LLDAS	473	---	
	785 (65%)	419 (35%)	1204 total visits

Methods: LLDAS metrics were recorded for 1204 clinic visits from 117 patients (83% female; 41% black) enrolled in the SLE Database at Cincinnati Children's Hospital Medical Center (see table 1). Visits with incomplete data to score the LLDAS were omitted. LLDAS criteria include: (1) low SLEDAI-status, without activity in major organ systems; (2) no new SLE disease activity compared with previous assessment; (3) physician global assessment (PGA) ≤1 (range 0-10); (4) current prednisolone (or equivalent) dose ≤ 7.5 mg/day; and (5) well tolerated standard maintenance doses of immunosuppressive drugs or approved biological agents, excluding investigational drugs.

Results: The majority (65%, 785/1204) of visits met low SLEDAI-status criteria, of which only 40% (312/785) met the LLDAS criteria (see table 2). Of those visits meeting low SLEDAI-status but not meeting LLDAS (N=473), 51% (N=241) presented new SLE activity from the previous visit; 50% (N=238) had current prednisolone (or equivalent) dose >7.5 mg daily, and 44% (N=209) had PGA >1 (see figure 1).

Conclusion: LLDAS is more stringent than low SLEDAI-status, which is the current treatment target. If confirmed that children with SLE accrue less disease damage with LLDAS versus low SLEDAI-status, this would change treatment targets, hence the standards of clinical care. The study also suggested the need to refine LLDAS for pediatric patients, particularly the criteria for prednisolone dosage.

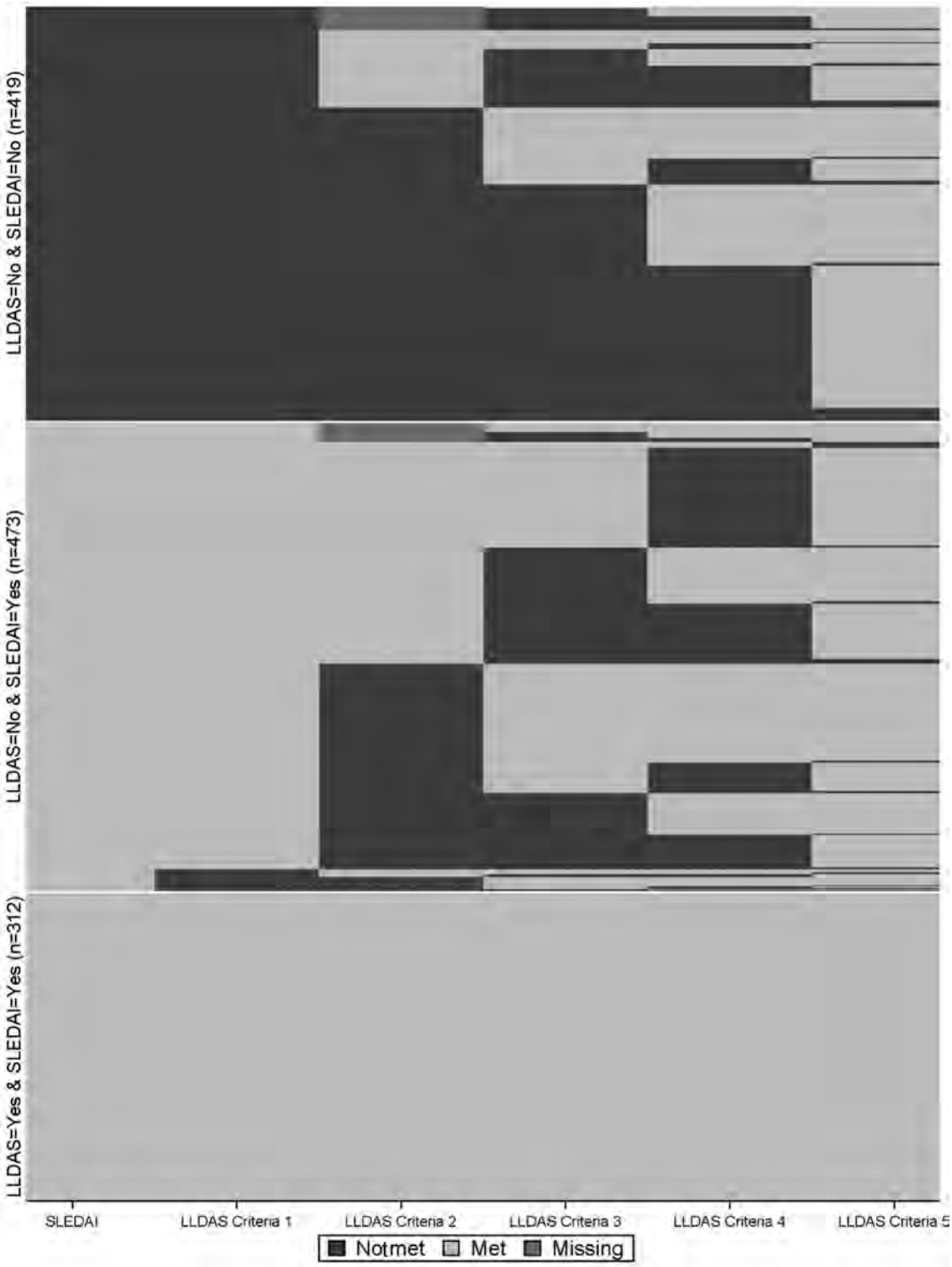

Figure 1. Heat Map of Clinic Visits Showing Low SLEDAI-2K Status and Particular LLDAS Criteria Met.

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Abstract Number: 0771

Race, Ethnicity and Patient-Reported Outcomes in Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The association of race/ethnicity with childhood-onset systemic lupus erythematosus (cSLE) outcomes has been well described, with non-White individuals experiencing a more severe disease phenotype including increased damage accrual and higher rates of renal involvement. However, there are limited data regarding patient-reported outcomes (PROs) across race and ethnic groups in cSLE. This study assesses the association of race/ethnicity with Pediatric Global Health [PGH-7], Pain Interference, and Physical Function Mobility as measured

Table 1. Characteristics by race/ethnicity in cSLE patients

	Features by race/ethnicity						P-value**
	Total N (%)	White	African American	Hispanic	Asian	Other or multiracial	
Demographics	588						
Female	492 (84.0)	142 (24.2)	137 (23.0)	109 (19.0)	62 (11.0)	29 (5.0)	0.66
Age diagnosis, mean (SD)		13.1 (3.0)	13.7 (2.8)	12.9 (3.5)	12.6 (3.2)	12.9 (3.4)	0.21
Household income < 25K	75 (19.0)	9 (2.3)	25 (6.4)	31 (8.0)	5 (1.3)	4 (1.0)	<0.001
No High School[1]	49 (10.5)	4 (1.0)	10 (2.1)	27 (6.0)	4 (1.0)	3 (1.0)	<0.001
Disease features[2]							
Rash	208 (35.4)	71 (12.0)	47 (8.0)	40 (7.0)	35 (6.0)	13 (2.2)	<0.05
Arthritis	319 (54.3)	89 (15.1)	98 (17.0)	68 (12.0)	38 (6.5)	19 (3.2)	0.65
Lupus nephritis	108 (18.4)	26 (24.1)	39 (36.1)	28 (26.0)	8 (7.4)	5 (5.0)	0.05
PLN[3]	81 (75.0)[3]	20 (19.0)	29 (27.0)	21 (19.0)	7 (6.5)	3 (3.0)	0.05
Leukopenia	254 (43.2)	59 (10.0)	98 (17.0)	51 (9.0)	31 (5.3)	9 (2.0)	<0.001
Anti ds-DNA	388 (71.2)	100 (18.4)	108 (20.0)	90 (17.0)	61 (11.2)	19 (3.5)	0.09
Anti-Sm	264 (52.2)	56 (11.1)	91 (18.0)	68 (13.4)	37 (7.3)	7 (1.2)	<0.001
SLEDAI, mean (SD)	5.8 (6.7)	5.2 (6.1)	6.2 (7.1)	6.1 (7.0)	5.5 (6.6)	6.6 (6.8)	0.65
PROs[2]							
PROMIS PGH-7, mean T-score (SD)	38.6 (6.2)	37.7 (6.1)	38.9 (6.9)	39.2 (5.7)	39.5 (5.9)	37.5 (7.3)	0.27
PROMIS Pain, mean T-score (SD)	53.7 (10)	53.3 (11)	54.9 (10.1)	54.5 (9.0)	51 (8.8)	53.6 (11.7)	0.46
PROMIS Function, mean T-score (SD)	47.8 (10.1)	47.6 (10.2)	47.6 (10.0)	47.9 (11.0)	50.1 (9.5)	45.5 (10.4)	0.27

** P-value global comparison across races/ethnicities
[1]Parental educational level (high school not completed)
[2]cSLE features and PROs at baseline visit
[3]PLN (proliferative lupus nephritis): 81/108 individuals had kidney biopsy consistent with PLN at baseline visit

by the Patient-Reported Outcomes Measurement Information System (PROMIS®) in cSLE patients at enrollment in the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry.

Methods: The CARRA Registry is a convenience cohort of pediatric patients with rheumatic diseases including cSLE. Sites are primarily North American. This study included cSLE patients enrolled in the CARRA registry within two years from cSLE diagnosis between May 2017 to January 2020 who met ≥ 4/11 ACR classification criteria and/or ≥ 4/11 SLICC classification criteria for lupus. Baseline demographics, laboratory, and disease features as well as PROs were

obtained. Analysis of variance (ANOVA) was used to assess the difference in the PROMIS summary T-score means across races/ethnicities. Relationships between SLEDAI and PRO scores were analyzed using Pearson's correlation coefficients. Multivariable linear regression analysis was used to examine the association of race and ethnicity with PROMIS scores at baseline. P-values < 0.05 were considered statistically significant.

Results: At the time of data extraction, 588 cSLE patients met inclusion criteria: 84% were female, 24.2% non-Hispanic White, 23% African American, and 19% Hispanic. The mean age at diagnosis was 13.2 years (SD 3.1). Household income and highest parental education varied by race/ethnic group, as did frequency of rash, leukopenia, and positive anti-Sm antibody (Table 1). The cohort had low-moderate baseline disease activity, with a mean SLEDAI of 6.14 (SD 6.8). There was no difference in disease activity across races/ethnicities in one-way ANOVA analysis. The overall PROMIS PHG-7 mean T-score was 38.6 (SD 6.4), which is more than 1 SD below the general population mean of 50. The mean Pain Interference T-score of 54 (SD 10) was slightly above, and the Physical Function Mobility mean T-score of 47.5 (SD 10.13) was slightly below the population mean of 50. There was a negative moderate correlation between PROMIS Pain Interference and Physical Function Mobility (Pearson correlation coefficient: - 0.52). There was no association between race/ethnicity and PROMIS scores in multivariable linear regression analysis.

Conclusion: In this large multiethnic CARRA pediatric lupus cohort, global health (PGH-7), pain interference, and physical function mobility as measured by PROMIS did not vary across races/ethnicities. The relatively low baseline disease activity may explain this lack of association. Long-term follow-up data is needed to assess for associations between PROs and race/ethnicity over time.

Disclosure: R. Borgia, None; **M. Gurka**, None; **S. Filipp**, None; **M. Elder**, None; **M. Cardel**, None; **N. Shiff**, Janssen Scientific Affairs, LLC., 3.

Abstract Number: 0772

Pediatric Craniofacial Scleroderma: Assessing Handheld 3D Stereophotogrammetric Imaging Feasibility and Reliability

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Craniofacial scleroderma (Cf-LS), also known as Parry-Romberg Syndrome or scleroderma *en coup de sabre*, is a subtype of localized scleroderma (morphea). Diagnosis and monitoring of Cf-LS is challenging due to the spectrum of clinical manifestations and lack of robust standardized assessment tools. Digital 3D facial maps help to provide objective assessment of longitudinal facial tissue changes between clinical visits. Traditional stationary camera systems are large, expensive, and require specialized training to use. In contrast, handheld 3D cameras are portable, low-cost, and easy to use. Handheld 3D cameras have been shown to produce reliably high-quality 3D facial maps in adults both with and without craniofacial differences. We set out to determine if the same holds true for children with Cf-LS.

Table 1. Baseline Enrollment Demographics and Characteristics (N = 22).

	n (%)
Female	13 (59)
Male	9 (41)
Diagnosis	
En coup de sabre (ECDS)	17 (77)
Parry-Romberg Syndrome (PRS)	3 (14)
Overlap (PRS+ECDS)	2 (9)
Facial Level Involvement*	
Top third	18 (82)
Middle third	13 (59)
Bottom third	8 (36)
	Median (IQR)
Age (years)	13.9 (9.8 – 16.7)
Disease Duration (years)	6.1 (4.6 – 14.0)
Height (centimeters)	155 (140 – 166)
Weight (kilograms)	51.7 (32.7 – 55.6)
Body Mass Index	19.4 (18.1 – 22.6)
Tri-ponderal Mass Index	13.7 (11.7 – 15.4)

*Facial involvement is defined by landmarks. Top third is the area superior to a horizontal line passing through nasion, middle third the area inferior to a horizontal line passing through nasion and superior to a horizontal line passing through subnasale, lower third inferior to a horizontal line passing through nasion and superior to a horizontal line passing through gnathion.

Methods: Digital facial images were obtained on 22 clinically stable Cf-LS patients < 23 years of age (IRB #19080205). Each subject was photographed with a handheld Vectra H2 (Canfield Scientific) and stationary 3dMD.head.t camera systems (3dMD), with a randomized order of acquisition. Number of trials and acquisition time to obtain a satisfactory image were recorded. Descriptive statistics were reported. Consensus facial landmarks (FaceBase Consortium) were digitally applied to each map by two trained individuals. Linear and curvilinear distances between landmarks were measured (VAM software). Reliability statistics and magnitude of error between instruments were calculated.

Results: Subjects ranged in age from 3.5 – 21.5 years with a median disease duration of 6.1 years (Table 1). Mean total image acquisition time was not significantly different between the 3dMD and Vectra camera systems (3dMD =

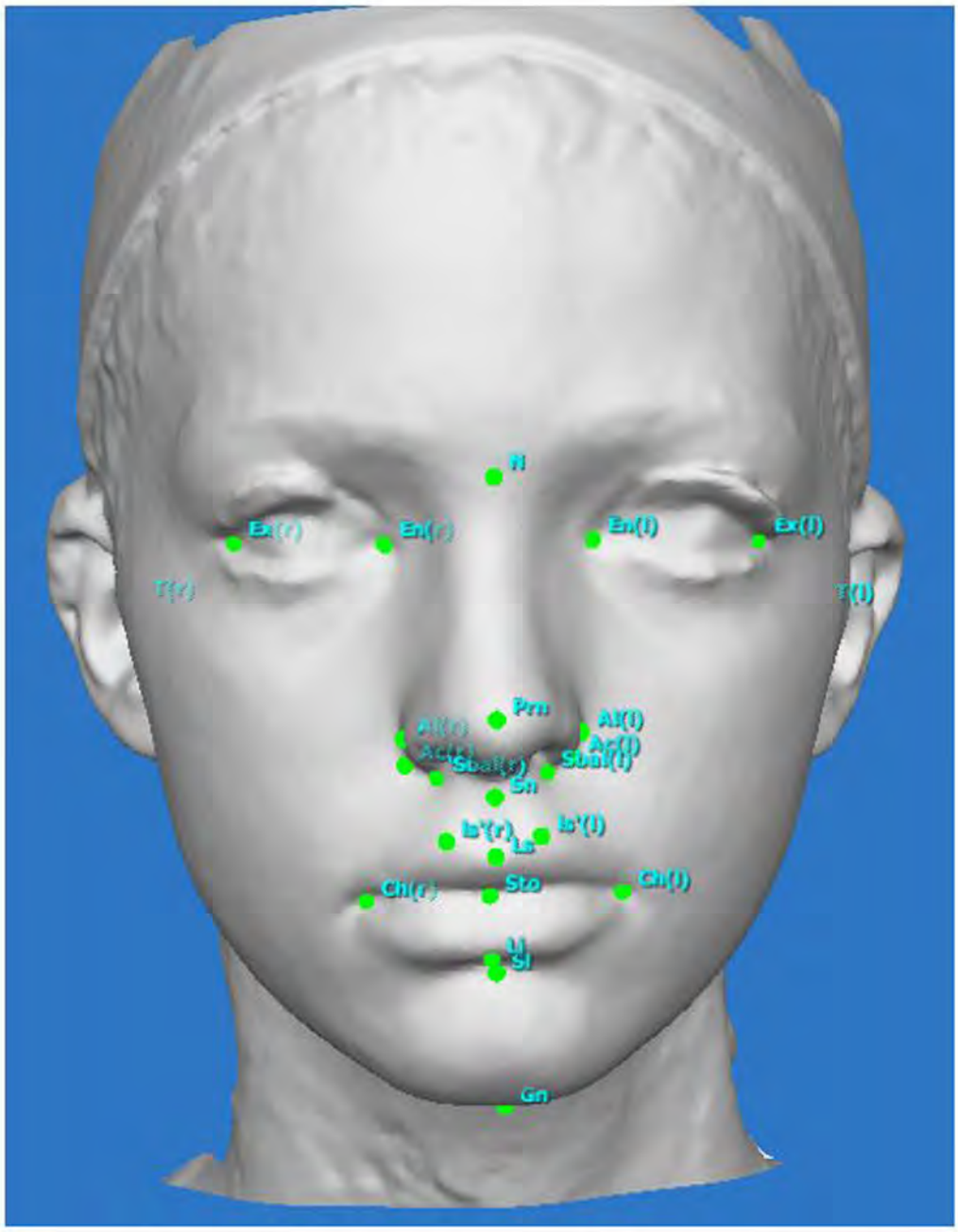

Figure 1. Twenty-four facial landmark locations for linear analysis on a representative 3D mesh. Inter-landmark distances were calculated using 3D coordinate positions of these landmarks.

59 seconds vs. Vectra = 61 seconds, p=0.71). Age was poorly related to acquisition time for both Vectra (Pearson r = -0.07) and 3dMD (Pearson r = -0.32) systems. Height was poorly related to acquisition time for the Vectra system (Pearson r = -0.21) but moderately related for the 3dMD system (Pearson r = -0.41).

Comparing the digital facial maps (Figure 1) from 3dMD and Vectra across 19 inter-landmark linear distances and 2 raters, the median technical error of measurement (TEM) was 1.91mm (range 0.6 – 9.08mm) and the median relative TEM (rTEM) was 3.85% (range 0.80% - 26.42%) (Table 2). Measurements with the highest TEM and rTEM values

Table 2. Single rater results for inter-landmark measurements comparing 3dMD to Vectra digital facial maps.

Landmarks	Mean Difference (mm)	Mean Signed Difference (mm)	TEM (mm)	rTEM (%)	Agreement Category*
Tragion(L) - Gnathion	1.42	0.12	1.03	0.80	Excellent
Gnathion - Tragion(L)	1.42	0.12	1.03	0.80	Excellent
Tragion(L) - Nasion	1.47	-0.17	1.11	0.99	Excellent
Tragion(L) - Subnasale	1.51	0.17	1.21	1.04	Very Good
Exocanthion(R) - Exocanthion(L)	1.73	-1.58	1.46	1.77	Very Good
Nasion - Stomion	1.34	-0.47	1.23	1.78	Very Good
Nasion - Gnathion	2.28	-1.28	2.04	1.83	Very Good
Alare(R) - Alare(L)	0.63	0.35	0.60	1.93	Very Good
Endocanthion(R) - Endocanthion(L)	0.87	-0.20	0.70	2.13	Very Good
Subnasale - Gnathion	2.26	0.78	2.00	3.27	Very Good
Nasion - Subnasale	2.52	-1.86	1.97	3.74	Very Good
Chelion(R) - Chelion(L)	2.05	-0.12	1.81	4.06	Good
Stomion - Gnathion	2.08	-0.81	1.84	4.10	Good
Sublabiale - Gnathion	2.35	-0.29	2.24	7.55	Moderate
Subnasale - Stomion	1.88	1.58	1.59	9.56	Moderate
Labiale superius - Stomion	1.06	0.68	0.92	12.16	Poor
Subnasale - Labiale superius	1.56	1.21	1.34	12.73	Poor
Stomion - Sublabiale	2.05	-0.52	2.01	13.09	Poor
Stomion - Labiale inferius	1.96	-0.60	2.28	26.42	Poor

* rTEM agreement categories include: < 1% (Excellent), 1 – 3.9% (Very Good), 4 – 6.9% (Good), 7 – 9.9% (Moderate), ≥ 10% (Poor).

usually involved oral and/or peri-oral landmarks. Only 36% of subjects had Cf-LS involvement of the lower third of the face. Measurements with the lowest TEM and rTEM values typically included landmarks along the midline of the face.

Conclusion: Handheld 3D cameras are easy to use and generate high quality digital facial maps in children as young as 3 years of age with craniofacial scleroderma, which are overall equivalent to images obtained by stationary cameras. Age and height did not impact the ease of obtaining handheld camera images. Measurements utilizing oral and peri-oral landmarks are most vulnerable to variation due to subtle changes in facial expression between acquisition on both camera systems. Future work will explore the accuracy of longitudinal digital facial maps for disease monitoring in the same population.

Disclosure: D. Glaser, None; **K. Schollaert-Fitch**, None; **C. Liu**, None; **J. Goldstein**, None; **K. Torok**, None.

Abstract Number: 0773

Janus Kinase (JAK) Inhibition with Baricitinib: Dosing and Patient-Reported Outcomes in Refractory Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

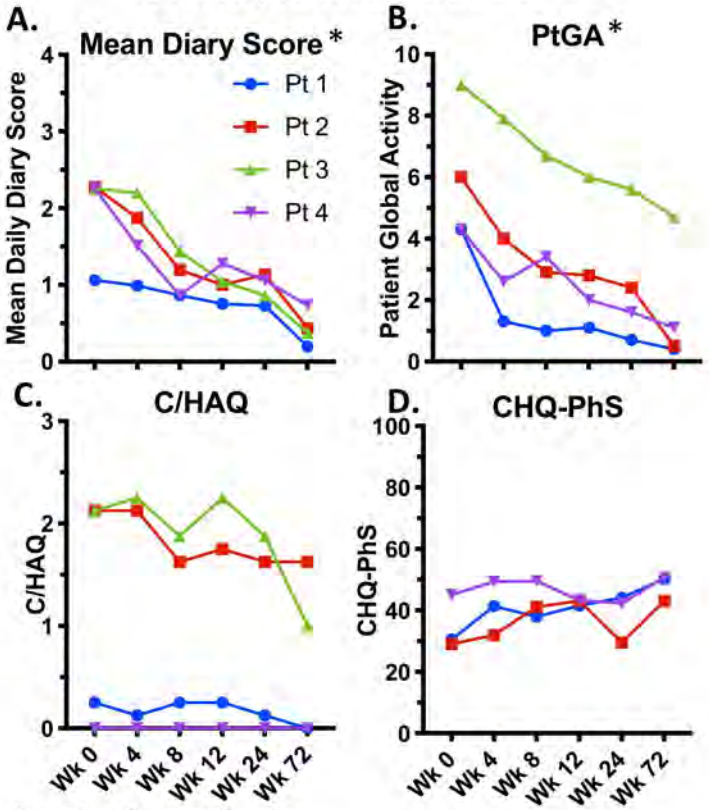
Background/Purpose: Juvenile dermatomyositis (JDM) is a systemic autoimmune disease with a prominent interferon (IFN) signature. Treatment often requires prolonged high-dose steroids and other immunosuppressive medications. In a compassionate use program, we assessed baricitinib (JAK 1/2 inhibitor) in active, refractory JDM and recently demonstrated efficacy by clinically relevant improvements in validated disease activity assessments and decreased IFN markers by 24 weeks.(1) Here we report patient-reported outcomes (PRO) and dosing with extended follow-up.

Methods: Baricitinib was dosed based on weight and renal function, with options to adjust dose based on established dosing and pharmacokinetics in pediatric interferonopathies.(2) One of the primary outcomes was reduction in symptom daily diary score (DDS) of weakness, fatigue, musculoskeletal pain, and rash. Each symptom was graded based on impact from 0 (no impact, not present) to 4 (maximal impact, highest grade), with symptom categories averaged for diary scores. DDS were collected for at least 2 weeks prior to starting investigational drug and then daily throughout the program. Other PROs included Patient/Parent Global Assessment (PtGA) by visual analog scale, (Childhood) Health Assessment Questionnaire (C/HAQ), and Childhood Health Questionnaire–Physical Summary Score (CHQ-PhS). Linear mixed models were used to compare measures to baseline. Safety and tolerability were assessed.

Results: Four patients with JDM (5.8-20.7 years old) were enrolled (NCT01724580), with at least 72 weeks of follow-up data collected. Patient diaries were collected for a total of 2167 days, with 2163 (99.8%) days of diary entries completed. At 72 weeks, DDS changed from a mean of 2.0/4.0 (range 1.1-2.3) to 0.4 (0.2-0.7; 68-83% decrease, $p< 0.01$) (Fig 1A). PtGA decreased from a mean of 5.9/10.0 (4.3-9.0) to 1.7 (0.4-4.7; 48-92% decrease, $p< 0.01$) (Fig 1B). C/HAQ decreased from mean 1.13/3.0 (range 0.0-2.13) to 0.66 (0.0-1.63, 0-100% decrease), indicating less disability (Fig 1C). CHQ-PhS (n=3) increased from mean 34.9/100 (29.1-45.0) to 48.0 (43.0-50.7; 13-65% increase), indicating improved physical function-related quality of life (Fig 1D). Patients were started on baricitinib 4-8mg PO per day divided BID or TID, and at last time point were on 5-12 mg/day divided BID. Dose adjustments were made based on renal function, safety laboratories, and/or efficacy in three patients. Baricitinib was generally well tolerated. There were no serious adverse events (AEs). Infections were the most common AE; Most common infection was upper respiratory infection. No AEs required holding/discontinuing baricitinib.

Conclusion: Patient-reported outcome data using baricitinib in four patients with refractory JDM supports shows continued improvement in symptoms with less disability and better physical function-related quality of life. Minor baricitinib dosing adjustments within the dosing range for pediatric interferonopathies were generally well tolerated.

Figure 1: Patient-reported outcomes in refractory JDM on baricitinib



*: p-value <0.1 versus baseline.

Patient-reported outcomes shown at baseline (week or wk 0), and then at week 4, 8, 12, and 24, and 72 for (A) mean Daily Diary score (DDS) out of 4, (B) Patient Global Activity (PtGA) out of 10, (C) Childhood Health Assessment Questionnaire (CHAQ) for 3 pediatric patients and Health Assessment Questionnaire (HAQ) for 1 adult patient out of 3, and (D) Childhood Health Questionnaire – Physical Function Summary Score (CHQ-PhS) out of 100 for 3 pediatric patients. A decrease indicates improvement for A-C, while an increase indicates improvement for D.

Disclosures: Baricitinib provided by Eli Lilly & Company, expanded access program sponsor. Other support: IRP of NIH, NIAMS, NIEHS, CC.

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1. Kim H et al, *Ann Rheum Dis*, 2020
2. Kim H et al, *Clin Pharmacol Ther*, 2018

Disclosure: H. Kim, Eli Lilly and Company, 12, Provide Drug; **L. Bergeron**, None; **S. Dill**, None; **M. O'Brien**, None; **X. Li**, None; **J. George**, None; **A. Brundidge**, None; **M. Millwood**, None; **L. Rider**, Eli Lilly and Company, 12, Drug, CureJM, 1, Bristol Meyer Squibb, 5, Hope Pharmaceuticals, 5; **R. Colbert**, Eli Lilly and Company, 12, Provide Drug.

Abstract Number: 0774

The Impact of Patient/Provider Discordance on Changes on Mood and Behavior in Adolescents with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Discordance between physicians' and patients' perceptions of disease severity can negatively impact treatment and disease outcomes; this has not yet been studied in children and adolescents with systemic lupus erythematosus (SLE). Neuropsychiatric symptoms, including depression and anxiety, can be present in up to 65% of adolescents with SLE. We propose to investigate the incidence of mood and behavioral changes, and its association with discordance between patient and physician perceptions of disease severity.

Methods: This is a multicenter pilot study conducted between September 2019 and April 2021. Patients over 12 years of age, diagnosed with SLE before their 19th birthdays, and who met ACR or SLICC Lupus classification criteria, were enrolled from two tertiary pediatric rheumatology centers in NY (one urban and one suburban). Data including demographics, disease manifestations, medications, and disease severity were collected. Patients completed standardized surveys assessing depression and various measures of quality of life. Global scores were obtained from individual patients and providers, analyzed via two-tailed t-tests, and compared with survey data using Pearson's correlations. A p-value of < 0.05 was considered significant.

Results: A total of 58 patients were enrolled, 40 from the urban center and 18 from the suburban center. Overall, the mean age at enrollment was 19 (13-23) years, with 81% female. The two cohorts identified ethnicity and race as 47% Hispanic, 38% Black, 6% White, and 3% as Alaskan Native/American Indian. There were no differences between the two cohorts on administered Kidscreen-52, Adverse Childhood Experience, and most Promis-25 survey subsections specifically focused on psychosocial factors, fatigue, mood, and cognition. However, the suburban cohort demonstrated higher depression scores on CES-D (mean 24.05, $p=0.008$), indicative of severe depression, and higher emotional scores on PedsQL (mean 9.58, $p=0.01$). The overall mean patient global score was 3.0 (range 0-9), and physician global was 1.44 (range 0-7). Patient/physician discordance was noted to be higher in the urban-based institution (p=NS), possibly indicating that patient perception of disease was often more severe than provider assessment. Discordance was also associated with items from PedsQL school ($r=0.41$, $p< 0.05$) and PROMIS depression subsections ($r=0.34$, $p< 0.05$).

Conclusion: We found that pediatric SLE patients in an urban based center demonstrated higher patient/physician discordance when compared to a suburban cohort. However, adolescents with SLE demonstrated higher rates of depression and emotional changes at a suburban-based center, despite physician perception of stable disease.

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Abstract Number: 0775

Decreased HDL Levels and Antioxidant Function in Juvenile Dermatomyositis

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

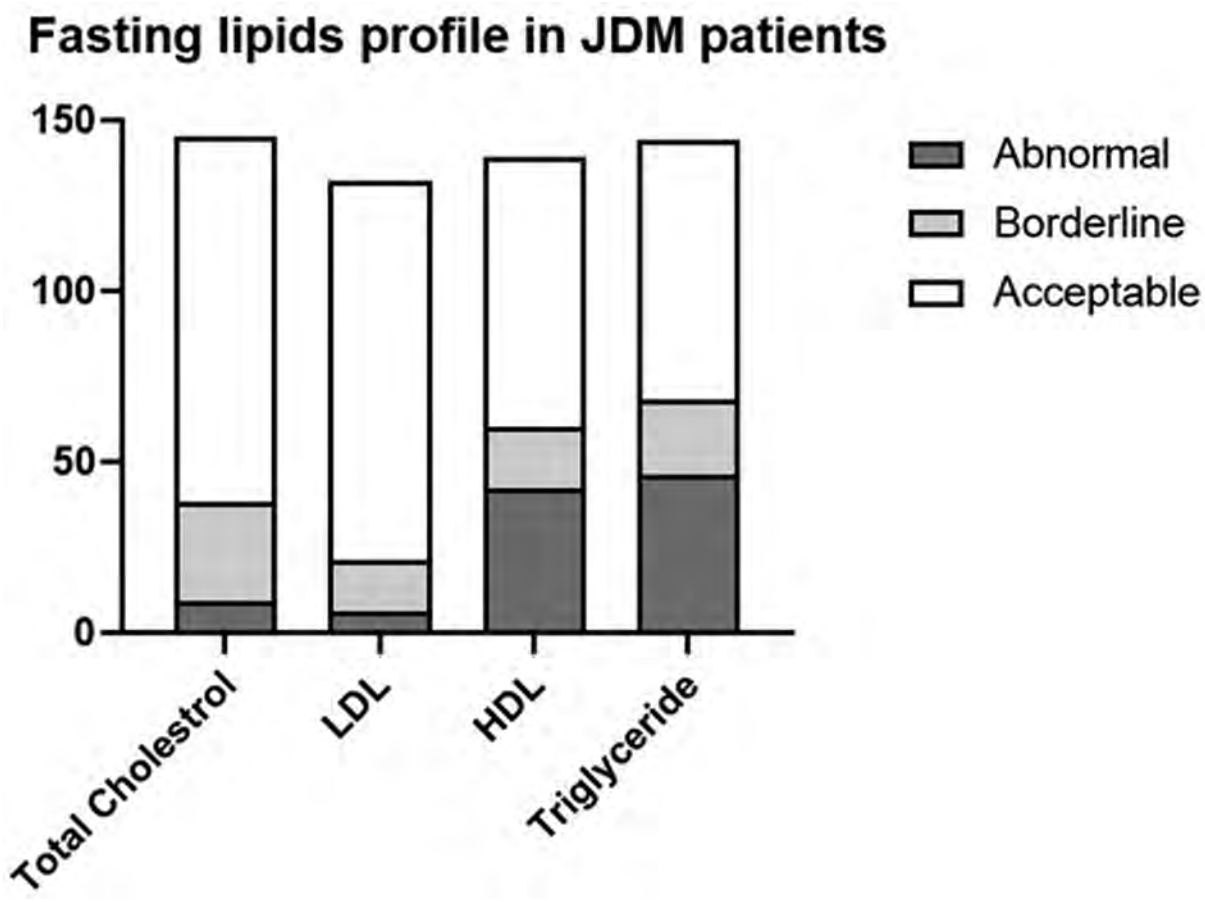
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile Dermatomyositis (JDM) is the most common inflammatory myopathy of childhood and is characterized by chronic inflammation targeting muscle and skin. Older patients who had JDM in childhood have a higher risk of atherosclerosis, documented by increased intima-media thickness. Paraoxonase 1 (PON1) is a hydrolytic enzyme associated with HDL and essential to protecting against LDL oxidation. Lower PON1 activity is linked with increased CAD risk. We hypothesize that, in JDM, dyslipidemia and HDL's antioxidant function is associated with the severity of systemic inflammation. We focused on the association of neopterin and dyslipidemia because TNF alpha, a proinflammatory cytokine produced by activated macrophage, can lead to dyslipidemia; elevated neopterin levels document macrophages activation.

Methods: This IRB-approved retrospective study was conducted at the Ann and Robert H. Lurie Children's Hospital of Chicago. All JDM patients (n= 143) who had fasting lipid profile, disease activity score (DAS), and neopterin level at the same visit were included. Normal, borderline and abnormal lipid profile values for children was defined based on the American Academy of Pediatrics guideline. HDL's antioxidant function evident by paraoxonase, lactonase, and arylesterase activity was measured by Dr. Charles-Schoeman's lab on 42 untreated JDM and 42 controls.

Results: Of 143 JDM patients included, 75% were female, and 70% were white. Only 12% of the subjects had lipid profiles before steroid treatment. While 88% of the untreated subject had low or borderline HDL and 75% had high or borderline triglycerides , only 13% had high or borderline LDL. Of the study population (n=143) 24% had elevated neopterin levels. Those with elevated neopterin levels had significantly lower mean HDL levels at 38.6 +/- 14.7 than JDM with normal neopterin at 51.6 +/- 14.9 and $p < 0.0001$. There was a significant negative correlation between HDL and various disease activity marker such as Neopterin ($R2=0.17$, $p < 0.0001$), DAS-total ($R2=0.16$ $p < 0.0001$), DAS-Muscle Weakness ($R2=0.19$, $p < 0.0001$) and DAS-Skin ($R2=0.07$, $p = 0.001$). We then examined the HDL antioxidative ability in 42 untreated JDM and age-matched control. JDM patients showed significantly lower lactonase activity (19.1 U/ml vs 23.9 U/ml p =0.005) and arylesterase activity (165.3 U/ml vs 189.4 U/ml p=0.04). Furthermore, there was a significant correlation between arylesterase enzyme activity and various disease activity markers such as Neopterin ($R2=0.22$, $p =0.004$), DAS-total ($R2=0.18$ p 0.005), DAS-Muscle Weakness ($R2=0.19$, $p =0.004$) and CMAS ($R2=0.16$, $p =0.01$). A similar correlation was found between lactonase as disease activity markers.

Conclusion: JDM patients have an increased prevalence of elevated TG and low HDL, especially before treatment. JDM patients with low HDL levels have more disease activity, as evidenced by DAS and elevated neopterin. Of note, the antioxidant capacity of HDL appeared to be reduced in JDM compared to control, and the degree of reduction



was associated with disease activity indicators. These findings suggest that early control of inflammation in JDM might improve HDL levels and their function.

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Abstract Number: 0776

Genetics of Neonatal Lupus Erythematosus Risk and Specific Manifestations

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Neonatal lupus erythematosus (NLE) is a passively acquired autoimmune disease in infants, secondary to the transplacental passage of maternal autoantibodies against Ro and/or La. The presence of anti-Ro

and/or La antibodies are necessary for NLE, but insufficient for disease suggesting additional risk factors. Genetics may impact NLE risk. We analyzed systemic lupus erythematosus (SLE) susceptibility loci in infants and their anti-Ro antibody positive mothers, with NLE risk and NLE specific manifestations.

Table 1. Cohort Demographics and NLE Manifestations. a Data includes 21 infants with self-reported ethnicity instead of genetically inferred ancestry, and 2 infants without genetically inferred or self-reported ethnicity. b Percentage of total cardiac NLE cases. c Percentage of total hematologic NLE cases. d Percentage of total rheumatic disease diagnoses.

Infants	n=287 (%) [a]
Female (%F)	148 (52)
Ethnicity	
European	118 (41)
East Asian	53 (18)
South Asian	45 (16)
Amerindian	22 (8)
African	21 (7)
Admixed	26 (9)
First born children	154 (54)
Previous sibling with NLE	24 (8)
NLE	156 (54)
Cardiac	20 (7)
Complete Heart Block	17 (85) [b]
Cutaneous	36 (13)
Hepatic	88 (31)
Neurologic	13 (5)
Hematologic	67 (23)
Neutropenic	61 (91) [c]
Thrombocytopenic	7 (10) [c]
Mothers	n=233 (%)
Rheumatic Disease Diagnosis	168 (72)
SLE	112 (67) [d]
Sjogren's Syndrome	32 (19) [d]
Hydroxychloroquine use during pregnancy	90 (39)

Table 2. Association between SLE-PRS and NLE Outcome. a a Models adjusted for PCs, prior NLE affected infants, maternal rheumatic disease and maternal hydroxychloroquine use during pregnancy.

	OR (95% CI) *P*-value		
	Infant PRS (n=264)	Mother PRS (n=423)	Mother-Infant PRS (n=212)
NLE	0.99 (0.79,1.26) 0.99	0.92 (0.71,1.19) 0.52	0.98 (0.74,1.30) 0.89
Cardiac NLE	1.04 (0.63,1.73) 0.87	1.19 (0.70,2.02) 0.52	1.20 (0.71,2.04) 0.49
Cutaneous NLE	0.83 (0.58,1.20) 0.33	0.87 (0.59,1.28) 0.48	1.22 (0.79,1.90) 0.37

Methods: We recruited infants born to anti-Ro positive mothers from the NLE clinic at The Hospital for Sick Children. Infants and mothers underwent genotyping on the Illumina Global Screening Array. Ancestry was genetically inferred from principal components (PCs) and Admixture, or self-reported based on Canada census categories. We created additive non-HLA SLE polygenic risk scores (PRSs) using 70 common SLE-risk SNPs from the largest SLE genome wide association study to date. Outcomes were defined as (1) any NLE, (2) cardiac NLE and (3) cutaneous NLE. We tested the association between SLE PRSs in the infant and in the mother with NLE outcomes, in logistic regression models using Generalized linear Mixed Model Association Tests (GMMAT). GMMAT enables inclusion of first-degree relatives in analyses by accounting for relatedness. In order to examine the degree of discordance between maternal and infant PRS, we regressed the difference between mother and infant PRS on NLE outcomes. Models were adjusted for PCs, prior NLE affected infants, maternal rheumatic disease status and hydroxychloroquine use during pregnancy.

Results: The study included 287 infants born to 233 anti-Ro positive mothers, with 212 genotyped maternal-infant pairs. The majority of infants were European (41%) or East Asian (18%), 52% were female, and 8% had a prior NLE affected sibling. Over half of the infants in the cohort had NLE (54%), including 7% with cardiac NLE and 13% with cutaneous NLE. Of the mothers, 41% were European and 21% were East Asian. A total of 168 mothers (72%) had a rheumatic disease diagnosis and 90 mothers (39%) were on hydroxychloroquine during pregnancy (Table 1).

We did not observe a significant association between infant, maternal or maternal-infant SLE-PRSs and any NLE, cardiac NLE or cutaneous NLE in adjusted GMMAT models (Table 2).

Conclusion: In our multiethnic cohort of infants born to Ro positive mothers, we did not identify a significant association between SLE genetics and risk of NLE or its manifestations. Additional studies are required to replicate our findings.

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Abstract Number: 0777

Potential Biomarkers of Cognitive Impairment in the Context of Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Cognitive complaints are common in children with childhood-onset systemic lupus erythematosus (cSLE), but neuropsychiatric lupus (NPSLE) remains challenging to diagnose and treat. To increase understanding of contributing mechanisms, we examined the association between cognitive function, disease measures and structural neuroimaging metrics.

Methods: We examined a cross-sectional sample of 24 patients with cSLE (ages 12-17) meeting ACR or SLICC classification criteria. Patients completed standardized traditional neurocognitive tests quantifying domains of attention and inhibition (CPT-3, Conners' Continuous Performance Test 3rd ed), working memory (WISC-V, Wechsler Intelligence Scale for Children 5th ed), and cognitive flexibility (D-KEFS, Delis-Kaplan Executive Function System). Cognitive impairment was defined as a score of 1.5 standard deviations below the mean in any domain. T1-weighted brain magnetic resonance images (MRI) were obtained using a 3T scanner. Advanced structural MRI analysis was used to extract volume, cortical thickness, and surface area metrics for brain segments. Demographic and disease measures were extracted from medical records. We used Partial Least-Squares Regression (PLS2), to examine the association between cognitive function (continuous outcome) and its potential predictors, comprised of structural brain metrics as well as disease and demographic measures. PLS2 analysis enables description of interactions between multivariate and potentially collinear data with a relatively small sample size. Each predictor's relevance criteria (i.e., stability and significance) were based on the bootstrapped sample distribution of its variable importance in projection (VIP) value, which measures the relative weight of a predictor across all outcome variables.

Results: Cognitive impairment was present in 42% (10/24) of patients; only one subject had a diagnosis of NPSLE (Table 1). In PSL2 analysis (Figure 1), 52 predictors were found to be relevant in the estimation of cognitive function (CI = 95%, VIP > 1.18). Of these, 50 were brain structure variables, with the most highly associated brain measures deriving from the frontal lobe (n=19), temporal lobe (n=11), occipital lobe (n=9) and cingulate cortex (n=7). The surface area and volume of the mid-posterior corpus callosum, total left and bilateral cortical volumes, the level of CRP and the age of patients at study visit were also found to be relevant predictors of cognitive function.

Conclusion: Objective cognitive impairment was prevalent in >40% of patients with cSLE. Impairment was strongly associated with several structural brain metrics, most of which derived from the frontal lobe. Only one disease-related factor (CRP) and one demographic factor (patient age) were found to be relevant predictors of cognitive function. Our results suggest that computational modeling has the potential to enhance diagnosis of NPSLE. Further study is needed to identify robust disease biomarkers that can be linked to functional and structural brain metrics with the use of machine learning models.

Table 1: Summary of demographic and lupus disease features in the cSLE cohort (n=24)	
Sex (Female, %)	20 (83%)
Age in years, Mean ± SD	15.4±1.7
Race (n, %)	
Asian	8 (33%)
White	8 (33%)
Black or African American	2 (8%)
Hispanic	2 (8%)
Mixed	2 (8%)
American Indian or Alaskan Native	1 (4%)
Middle Eastern	1 (4%)
Highest Household Education, n (%)	
College Diploma	6 (25%)
High School Diploma	6 (25%)
Bachelor's Degree	5 (21%)
Advanced Degree (Master's, Doctoral, Professional)	4 (16%)
Some College/University	3 (13%)
Household income (n, %)	
$90,000 or more	7 (29%)
$40,000 - <$90,000	13 (54%)
$15,000 - <$40,000	4 (17%)
Disease Measures	
Age at diagnosis of SLE in years, median (IQR)	13 (11-15)
Age at study visit in years, median (IQR)	16 (14-16)
Disease duration in years, median (IQR)	1.8 (1.0-3.1)
SLEDAI at study visit, median (IQR)	2 (1.5-4.2)
Mean SLEDAI in preceding year per patient, median (IQR)	3 (1.2-7)
Physician Global Assessment Scale (PGA) at study visit, median (IQR)	0.5 (0-2)
Level of C-Reactive Protein (CRP) at study visit, median (IQR)	0.6 (0.2-1.8)
Erythrocyte Sedimentation Ratio (ESR) at study visit, median (IQR)	17 (7-31)
Level of anti-double stranded DNA (anti-dsDNA) at study visit, median (IQR)	26.1 (9.8-130.7)

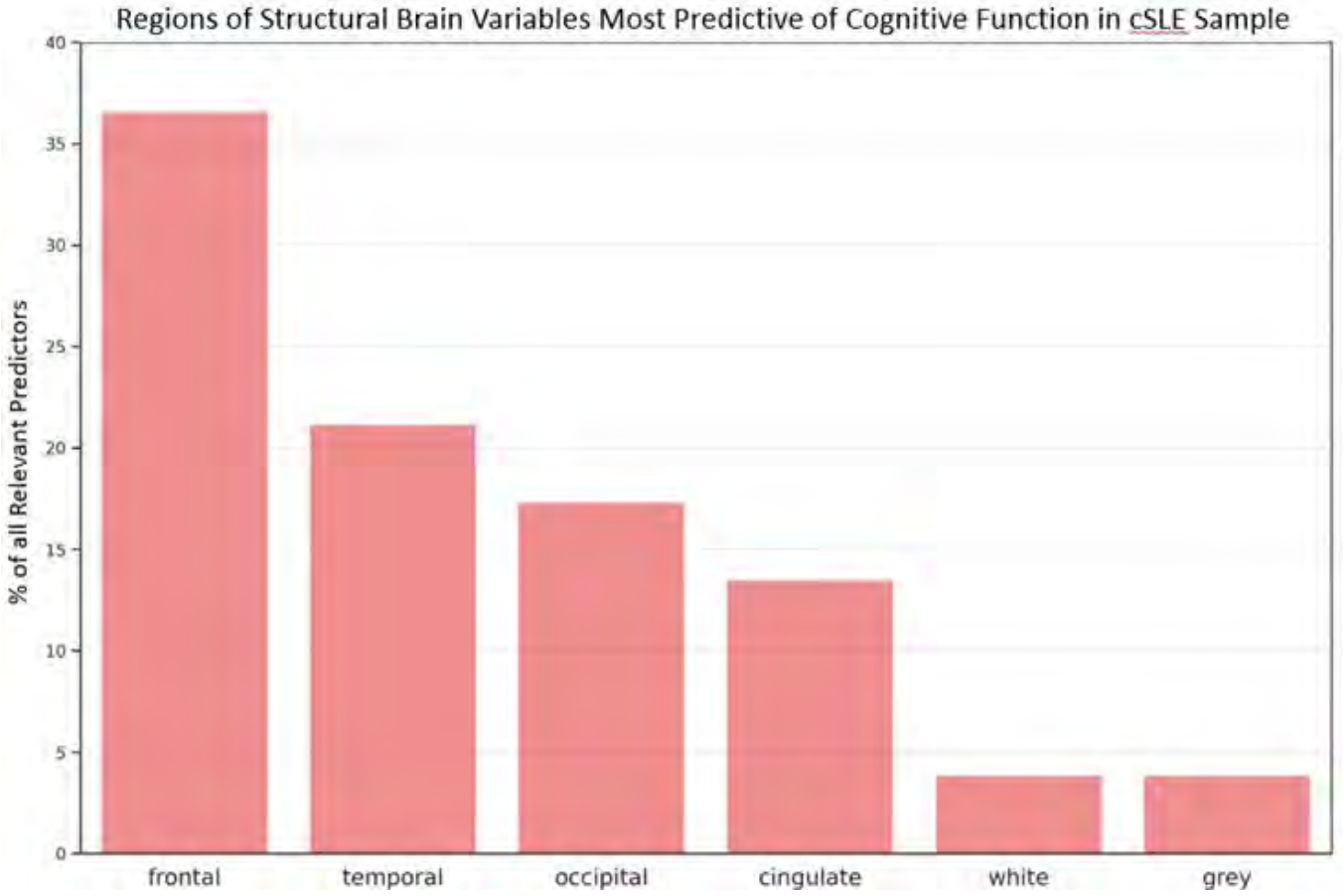

Figure 1. Shown is the distribution of the most relevant structural predictors of cognitive function in cSLE patients. Predictors are grouped per category and reported as a percentage of the all relevant predictors found in partial least squares analysis. Relevant white matter predictors are the area and volume of the mid-posterior corpus callosum. Relevant grey matter predictors are the total left and bilateral cortical volumes. No relevant predictors were found in the parietal lobe, subcortical structures, cerebellum or brainstem.

Disclosure: S. Arciniegas, None; **S. Mossad**, None; **T. El Tal**, None; **L. Ng**, None; **P. Moaf**, None; **H. Branson**, None; **A. Davis**, None; **L. Hiraki**, Novartis, 6; **D. Levy**, amgen, 6, sobi, 1, roche, 1, janssen, 1, medexus, 6; **A. Danguecan**, None; **A. Knight**, None.

Abstract Number: 0778

Autologous Stem Cell Transplantation with CD34-Selected Peripheral Blood Stem Cells in Patients with Treatment-Resistant Juvenile-Onset Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile-onset systemic sclerosis (jSSc) is a rare autoimmune disease associated with life-threatening multi-organ inflammation and fibrosis. As in adults, jSSc organ involvement includes vascular, cutaneous, gastrointestinal, pulmonary, and musculoskeletal systems. Treatment options are limited for aggressive and recalcitrant SSc, however advances in adult SSc therapies support Autologous Stem Cell Transplant (ASCT) as a safe option to reset the immune system and prevent eminent decline. Our center has developed reduced intensity conditioning protocols for both pediatric and adult onset SSc using CD34-selected peripheral blood ASCT, including our Immune Transplant and Therapy Center (ITTC) protocol (ClinicalTrials.gov Identifier: NCT03630211). We report initial safety and clinical response of three jSSc patients who received ASCT at our center (Table 1) with comorbidities too advanced even for our trial.

Methods: Patients with severe and progressive disease referred to our center were evaluated by pediatric rheumatologist (KT) and referred to BMT (PS, JB) if deemed to be refractory to standard clinical care. A dedicated multidisciplinary team evaluated the patients (Rheum, BMT, Cards, Pulm, GI) to determine baseline status and eligibility for an existing protocol (ITTC) or an Investigational New Drug (IND) application if more suitable. After IRB approval and consent, patients underwent ASCT with standardized safety, clinical outcome, and patient reported measures collected at baseline (pre-ASCT), 6, and 12 months-post ASCT.

Results: Three jSSc patients were eligible to receive ASCT by the multi-disciplinary team (Table 1); all failed to meet ITTC eligibility criteria due to poor respiratory function (FVC < 45% and/or DLCO < 40%; and 6MWT < 400m; see Table 1) and had individual INDs approved for ASCT. All consisted of Cyclophosphamide 120 mg/kg, total body irradiation (6 Gy in 3 fractions with liver and kidney shielding) and ATGAM. At time points of 15 months-post ASCT, 6 months-post ASCT, and engraftment for patients 1, 2, and 3, respectively, only patient 2 had a major safety concern, a significant ATGAM reaction requiring a brief ICU stay for increased supportive needs, with protocol resumption within 48 hours. Patient 3 had a milder ATGAM reaction. There have been no serious infections or organ dysfunction to date. All patients showed improvement in clinical outcomes of mRSS, range of motion, physical functioning (HAQ), and several PRO domains including dyspnea, Raynaud's phenomenon, and gastrointestinal symptoms (Table 2).

Conclusion: Our preliminary data supports the safety and efficacy of ASCT with CD34-Selected Peripheral Blood Stem Cells in jSSc. Two subjects had 7+ years of duration: one with more limited skin disease, and the other with overlap disease with myositis, both with positive outcomes. Expansion of ASCT eligibility to include children, adolescents and young adults and those with clinical features beyond classic early diffuse cutaneous SSc should be considered while maintaining an acceptable safety profile.

Table 1. Caption: a Clinical variables that would have failed adult SSc entry criteria ASCT trials: Autologous Stem Cell Transplantation International Trial (ASTIS) (van Laar et al JAMA 2014; 311(24)) and Scleroderma: Cyclophosphamide or Transplantation (SCOT) (Sullivan et al NEJM 2018; 378(11)). b Additional clinical variables that would have failed adult SSc entry criteria ITTC trial (6MWT >400). c Values represent percent predicted based on GLI2012 prediction equations for FVC and DLCO Quanjer et al. Eur Respir J 2012;40(6), and Rosenthal et al. Thorax 1993;48(8) for TLC. d Percent predicted based on Geiger et. al. J Pediatrics 2007; 150(4), pediatric prediction equations. e SpO2 was monitored continuously during 6MWT via forehead probe. Abbreviations: dcSSc (diffuse cutaneous systemic sclerosis); lcSSc (limited cutaneous systemic sclerosis); Scl-70 (scleroderma-70 anti-topoisomerase antibody); PM-Scl (polymyositis-scleroderma overlap antibody); ILD (interstitial lung disease); PHTN – (pulmonary hypertension)

Table 1. Baseline juvenile systemic sclerosis (jSSc) patient characteristics prior to autologous stem cell transplant (ASCT) and transplant outcomes.

	Patient 1	Patient 2	Patient 3
Demographics			
Age of onset jSSc (years)	15	7	13
Age at time ASCT (years)	18	15	21
Disease duration prior to ASCT (years)	3	8[a]	7[a]
Sex	Male	Female	Female
Ethnicity	Non-Hispanic	Non-Hispanic	Hispanic
Disease characteristics			
SSc subtype	dcSSc	lcSSc[a]	Overlap[a]
Auto-antibody positivity	Scl-70	None	Pm-Scl[a]
Modified Rodnan Skin Score (mRSS)	24	5[a]	23
Pulmonary features			
SSc ILD on HRCT	yes	yes	no
Pattern	UIP	NSIP	N/A
Total Lung Capacity (TLC)[c]	60	65	56
Forced Vital Capacity (FVC)[c]	52	48	40[a]
Diffusing capacity of the lungs for carbon monoxide (DLCO)[c]	35[a]	28[a]	59
6 Minute Walk Test (6MWT) (m)	480	320[b]	360[b]
6MWT (% predicted)[d]	73	47	50
Desaturation (>4%) during 6MWT	Yes	Yes	No
Exercise induced hypoxemia (SpO_2 <=88% during 6MWT)[e]	Yes	Yes	No
Maximal Respiratory Pressures (inspiratory/expiratory), % predict	96/41	67/71	48/57
PHTN on stress echocardiogram	No	No	No
PHTN on cardiac catheterization	No	--	--
Main clinical features	Progressive mod-severe ILD, Mod-severe mRSS, joint contracture small to large joints, Raynaud's phenomenon; GI esophageal dysmotility	Progressive severe ILD, Skin thickening minimal after Cytoxan; GI esophageal dysmotility	Progressive skin thickening, weakness, myositis; joint contracture small to large joints; restrictive lung disease from muscle weakness and ST; GI esophageal dysmotility
Previous treatments	Cytoxan, Rituximab, Mycophenolate Mofetil, Methotrexate	Cytoxan, Mycophenolate Mofetil, Prednisone (high dose)	Cytoxan, IVIG, Rituximab, Mycophenolate Mofetil, Methotrexate, Baricitinib
Transplant data			
Number of intended ATGAM doses given	6 of 6	3 of 6	2 of 6
CD34 dose (x 10^6/kg) infused	6.96	4.26	6.14
Day of neutrophil engraftment	10	15	11
Day of platelet engraftment (>50K)	20	16	19

Table 2. Baseline and post-ASCT Follow-up clinical variables and Patient reported outcomes (PROs).

	Patient 1		Patient 2		Patient 3	
	Time 1 – Baseline	Time 2 – 15 mos post ASCT	Time 1 – Baseline	Time 2 – 6 mos post-ASCT	Time 1 – Baseline	Time 2 – Engraftment post-ASCT
SKIN/MUSCULOSKELETAL						
mRSS (modified Rodnan skin thickness score)	24	1	5	0	23	14
Range of Motion	L1-L2 large and small joints UE and LE	Limitation L0-L1	L1 small and medium joints	L0	L1-L2 large and small joints UE and LE	L1-L2 large and small joints UE and LE
Finger To Palm (cm)	1.5	0.5	0.5	0	1.2	1.0
VAS scales SSc HAQ*						
• Pain (0 – 3)	0.78	0.0	0.73	0.15	1.90	1.33
• Hand (0 – 3)	0.80	0.0	0.00	0.00	2.02	1.29
• Disease (0 – 3)	2.69	0.1	1.52	0.46	0.56	1.04
Oral aperture (cm)	6.0	6.5	4.0	5.0	4.0	4.5
VASCULAR						
Nailfold capillary change (dermatoscope)	Moderate dilatation, drop out, hemorrhage	Mild dilatation only	Mild dilatation	Mild dilatation only	Mild dilation, few spot hemorrhages	Mild dilation, few spot hemorrhages
Raynaud's						
• Vascular VAS on SSc HAQ* (0-3)	1.64	0.06	0.00	0.00	2.23	1.56
GASTROINTESTINAL						
LES pressure (manometry)	8 mmHg	13 mmHg	14 mmHg	—	15 mmHg	—
24 hr pH probe						
• % time esophageal exposed acid	17%	3%	6%	—	20%	—
• Longest acidic reflux episode	48 min	2 min	14 min	—	106 min	—
GIT (GI scale) total* (0 – 3)	0.15	0.10	0.19	0.06	0.48	0.51
PULMONARY						
Pulmonary Function Test						
• FVC, % predicted	52	53	48	42	40	—
• DLCO, % predicted	35	35	28	24	59	—
6MWT (meters)	480	490[a]	320	400	360	—
OTHER PRO/GLOBAL						
CHAQ (0 – 3)*	0.25	0.00	0.75	0.38	1.63	1.50

Abbreviations: ASCT (autologous stem cell transplant); VAS (Visual Analog Scale); HAQ (Health Assessment Questionnaire); LES (lower esophageal sphincter); GIT (scleroderma gastrointestinal tract instrument); FVC (forced vital capacity); DLCO (diffusing capacity for carbon monoxide); 6MWT (6 minute walk test). GLI2012 prediction equations used for both FVC and DLCO. * Indicates a patient reported outcome. VAS scale on HAQ, GIT, CHAQ are 0 to 3; higher number reflects more interference of disease with function. a Comparability to prior tests is limited as patient's home portable oxygen concentrator, used on prior tests, was unavailable thus the patient carried a portable oxygen tank. 6MWT values here are likely not fully reflective of patient's ability.

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Abstract Number: 0779

Predictors of Mortality in a Series of 1528 Brazilian Childhood-onset Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Childhood-onset Systemic lupus erythematosus (cSLE) is an inflammatory autoimmune disease known for its complex and variable clinical presentation and disease course. Its severity may vary according to different organs involved and is usually life-threatening and have poorer outcome compared to adults (aSLE), leading to significant morbidity and mortality. The objectives of this study were to identify predictors of mortality of cSLE and to evaluate their association with clinical manifestations, laboratory features, disease activity and damage, current treatment, survival and causes of death.

Methods: This is a multicenter, nationwide observational study of a cohort of 1,528 cSLE patients followed in 27 Brazilian pediatric rheumatology tertiary centers. In this study, we investigated cumulative risk factors for mortality in a large sample of cSLE patients. We also compared its association with cumulative clinical and laboratory features, as well as disease activity and damage, cumulative treatment, outcome and causes of death.

Results: Mortality between patients was 4.1% (63/1528), occurring in a median period of 3.2 years after diagnosis, with predominance of girls (84.1%). The most frequent causes of death were sepsis/infectious disease in 29/63 (29%) and cSLE activity in 8/63 (12.7%). In 12/63 (19%) the cause was unknown. After Bonferroni´s correction for multiple comparisons ($p<0.0017$), determinants significantly associated with mortality were constitutional symptoms, skin vasculitis, pericarditis, arterial hypertension, acute renal injury, chronic kidney disease (CKD), neuropsychiatric (NP-SLE), thrombocytopenia, higher score of SLEDAI-2K at last visit or death, and SLICC/ACR-DI especially in renal domain. The use of intravenous methylprednisolone, cyclosporine, cyclophosphamide, and rituximab at last visit or death were also more frequent. In the multivariate regression model analysis, NP-SLE ($p=0.001$) and CKD ($p=<0.0001$) were significant factors associated to death. Patients with NP-SLE had 2.6 times higher risk of death (HR=2.56, 95%CI=1.48-4.42) compared to cSLE patients who did not present NP-SLE, and the risk of death in patients with CKD increases 4.3 times (HR=4.33, 95%CI=2.33-8.04). The Kaplan-Meier overall curve showed worse survival in patients with NP-SLE ($p=<0.0001$), proliferative nephritis ($p=0.02$) and CKD ($p=<0.0001$). Overall patient survival after diagnosis at 1, 5 and 10 years were 98.5%, 97% and 95.4% respectively.

Table 1 – Demographic data, clinical and laboratorial features, disease activity and disease damage score, and treatment at last visit/death in 1528 cSLE patients dead and alive.

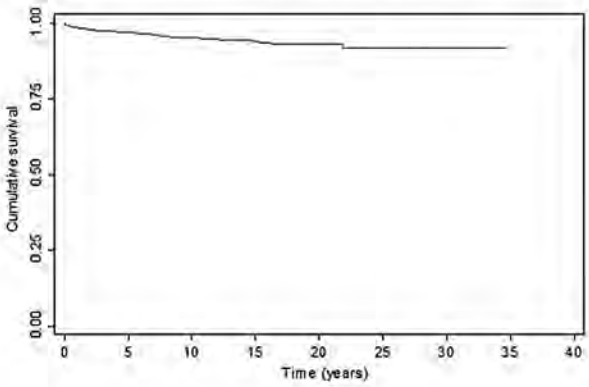
Variables	Death		p
	Dead (n=63)	Alive (n=1485)	
Demographic data			
Age at c-SLE diagnosis, years, n=1528	11.9 (3.2-16.5)	12.1 (0.1-17.9)	0.056
Time of follow-up, years, n=1528	3.2 (0-15.9)	4.6 (0-22.3)	0.004
Male gender, n=1528	10 (15.9)	222 (15.2)	0.976
Clinical manifestations			
Constitutional manifestations, n=1528	59 (93.7)	1037 (70.8)	**<0.0001**
Fever, n=1518	55 (87.3)	887 (59.6)	**<0.0001**
Weight loss > 2 kg, n=1518	34 (54.0)	500 (34.4)	**0.001**
Hepatomegaly, n=1517	30 (47.6)	266 (18.3)	**<0.0001**
Splenomegaly, n=1526	16 (25.4)	145 (10.0)	**<0.0001**
Mucocutaneous involvement, n=1521	54 (85.7)	1272 (87.2)	0.722
Rash, n=1519	45 (71.4)	947 (65.0)	0.297
Photosensitivity, n=1506	37 (58.7)	900 (62.3)	0.569
Vasculitis, n=1518	35 (55.6)	383 (26.4)	**<0.0001**
Musculoskeletal involvement, n=1519	46 (73.0)	1076 (73.9)	0.876
Serositis, n=1518	33 (52.4)	485 (33.3)	0.002
Pleuritis, n=1518	21 (33.3)	322 (22.1)	0.037
Pericarditis, n=1518	28 (44.4)	365 (25.1)	**<0.0001**
Nephritis, n=1526	54 (85.7)	1087(73.9)	0.035
Hematuria, n=1514	42 (66.7)	790 (54.4)	0.056
Pyuria, n=1515	40 (63.5)	717 (49.4)	0.028
Urinary casts, n=1514	27 (42.9)	385 (26.5)	0.004
Proteinuria > 500mg/day, n=1517	45 (72.6)	623 (56.6)	0.013
Arterial hypertension, n=1518	39 (61.9)	477 (32.8)	**<0.0001**
Acute renal injury, n=1515	27 (42.9)	209 (14.4)	**<0.0001**
CKD, n=1528	14 (22.2)	45 (3.1)	**<0.0001**
Classes III/IV LN, n=464	19 (30.2)	245 (16.7)	**<0.0001**
Neuropsychiatric involvement, n=1525	44 (69.8)	571 (39.1)	**<0.0001**
Central nervous system, n=1526	41 (65.1)	550 (37.8)	**<0.0001**
Peripheral nervous system, n=1528	4 (6.3)	55 (3.8)	0.295
Current disease activity score			
SLEDAI-2K, n=1415	13 (0-52)	2 (0-40)	**<0.0001**
Disease damage score			
SLICC/ACR-DI, n=1400	1 (0-7)	0 (0-6)	**<0.0001**
SLICC/ACR-DI ≥ 1, n=1395	31 (62.0)	367 (27.3)	**<0.0001**
Neuropsychiatric, n= 391	12 (19.0)	140 (9.6)	0.014
Ocular, n=391	6 (20.0)	82 (22.7)	0.732
Renal, n=391	16 (53.3)	72 (19.9)	**<0.0001**
Musculoskeletal, n=391	6 (20.0)	87 (24.1)	0.612
Cardiovascular, n=391	6 (20.0)	25 (6.9)	0.011
Hematological abnormalities, n=1526	55 (87.3)	1038 (70.9)	0.005
Autoimmune hemolytic anemia, n=1526	27 (42.9)	457 (31.2)	0.051
Leukopenia <4.000/mm³, n=1516	38 (60.3)	736 (50.6)	0.130
Lymphopenia <1.500/mm³, n=1527	50 (79.4)	1007 (68.8)	0.075
Thrombocytopenia, <100.000/mm³, n=1527	35 (55.6)	384 (26.2)	**<0.0001**
Low complement (C3/C4/CH50), n=1469	57 (95.0)	1163 (80.8)	0.006
Current treatment			
Nonsteroidal anti-inflammatory, n=1501	4 (6.3)	36 (2.4)	0.058
Prednisone, n=1493	51 (80.9)	1024 (69.9)	0.059
Intravenous methylprednisolone n=1471	8 (12.7)	83 (5.7)	0.020
Antimalarial drugs, n=1485	38 (60.3)	1185 (80.9)	**<0.0001**
Immunosuppressive agents			
Azathioprine, n=1485	24 (38.1)	461 (31.5)	0.268
Cyclosporine, n=1476	8 (12.7)	30 (2.0)	**<0.0001**
Methotrexate, n=1480	2 (3.2)	128 (8.7)	0.121
Mycophenolate mofetil, n=1485	8 (12.7)	275 (18.8)	0.224
Intravenous cyclophosphamide, n=1501	12 (19.0)	566 (38.7)	0.001
Rituximab, n=1504	2 (3.2)	9 (0.6)	0.018
Plasmapheresis, n=1498	3 (4.7)	1 (0.6)	**<0.0001**
Intravenous immunoglobulin, n=1500	9 (14.2)	8 (0.5)	**<0.0001**

Results are presented in n (%) and median (min-max).
The bold numbers express the p value that are statistically significant. *p value according to Bonferroni correction for multiple comparisons (p<0.0017).
NA: not analyzed.
CKD – Chronic kidney disease, LN – lupus nephritis, SLEDAI-2K – Systemic Lupus Erythematosus Disease Activity Index 2000, SLICC-ACR/DI – Systemic Lupus International Collaborating Clinics/ACR-Damage Index, VDRL – venereal disease research laboratory, g – gram.

Conclusion: This study showed that cSLE patients with CKD and NP-SLE exhibited higher hazard rates of progression to poor outcomes. Therefore, those patients could benefit from early aggressive management of active lupus nephritis and NP-SLE, especially within the first years after diagnosis.

Figure 1 a, table b – Kaplan-Meier survival curves in 1528 cSLE patients

a – Survival by the time of diagnosis to death or end of follow-up in 1528 cSLE patients



b – Kaplan Meier survival analysis by total

	Cummulative survival (%)					
	1 year	3 years	5 years	10 years	15 years	20 years
Total	98.55 ± 0.31	97.43 ± 0.42	97.07 ± 0.45	95.42 ± 0.64	93.88 ± 0.90	92.94 ± 1.11

±Standard error

Table 3 – Regression analysis for survival in 1528 in cSLE patients

	Univariate Cox regression		Multivariate Cox regression			
			Initial Model		Final Model	
Characteristics	**Hazard Ratio Rough (CI95%)**	**p**	**Adjusted Hazard Ratio (CI95%)**	**p**	**Adjusted Hazard Ratio (CI95%)**	**p**
Age (years)	0.95 (0.88 - 1.03)	0.212	0.95 (0.88 - 1.03)	0.243	-	-
Nephritis	1.68 (0.83 - 3.41)	0.151	1.08 (0.48 – 2.43)	0.847	-	-
Neuropsychiatric manifestations	2.88 (1.68 - 4.94)	**<0.001**	2.13 (1.21 - 3.74)	**0.009**	**2.56 (1.48 - 4.42)**	**0.001**
SLEDAI-2K (score)	1.03 (1.01 - 1.06)	**0.005**	1.02 (1.00 - 1.05)	0.095	-	-
SLEDAI-2K ≥ 8	2.28 (0.83 - 6.30)	0.111	-	-	-	-
Proliferative nephritis	1.88 (1.01 - 3.22)	**0.022**	1.24 (0.68 – 2.25)	0.487	-	-
Chronic kidney disease	5.25 (2.84 - 9.69)	**<0.001**	3.76 (1.91 – 7.41)	**<0.001**	**4.33 (2.33 - 4.72)**	**<0.001**

CI95% - Confidence Interval of 95%.
The bold numbers express the p value that are statistically significant (p<0.05).

Disclosure: A. Sakamoto, None; **C. Silva**, None; **A. Islabão**, None; **G. Novak**, None; **B. Molinari**, None; **R. Pereira**, None; **C. Saad-Magalhães**, None; **G. Clemente**, None; **M. Fraga**, None; **D. Pioto**, None; **C. Len**, None; **R. do Prado**, None; **M. Terreri**, Sanofi, 6, Alexion, 6, Pfizer, 6, Novartis, 6, Abbvie, 6, Roche, 6, Biomarin, 6, GSK, 6, Jansen, 12, Clinical studies, UCB, 12, Clinical studies, Bristol, 12, Clinical studies, Lilly, 12, Clinical studies.

Abstract Number: 0780

High Adolescent Health Needs and Relationship to Disease in Patients with Childhood-Onset Systemic Lupus Erythematosus

Chelsea DeCoste[1], Paris Moaf[1], Lawrence Ng[1], Dragana Ostojic-Aitkens[1], Fatima Faruq[2], Byran Maguire[3], Deborah Levy[1], Linda Hiraki[1], Alene Toulany[1] and Andrea Knight[4], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Research Institute, The Hospital for Sick Children, Toronto, ON, Canada, [4]Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE), with typical onset in adolescence, is a chronic life-threatening disease. In addition to dealing with cSLE, these adolescents endure the unique psychosocial and physical health challenges of this life stage. We aimed to characterize the burden of adolescent health issues faced by patients with cSLE, as well as demographic and disease characteristics associated with adverse adolescent health.

Methods: We conducted a retrospective cohort study of adolescents age 12-18 years with cSLE (meeting ACR and SLICC classification criteria) who were seen by Adolescent Medicine (AM) specialists in the Lupus Clinic at SickKids Hospital, between July 2018-July 2020. As part of our cSLE care model, patients presenting with adolescent health issues were routinely seen by AM in the clinic. Adolescent health issues were characterized using the HEADDSS framework (**H**ome, **E**ducation/**e**mployment, peer group **A**ctivities, **D**rugs, **S**exuality, and **S**uicide/depression), which was standardly recorded for all AM visits. Issues were classified as presenting and/or identified problems at each visit. Adolescent health burden was tabulated as the number of individual adolescent issues identified per patient. Multiple Poisson regression was used to examine associated patient factors, including age, gender, material deprivation score (measure of social marginalization that accounts for income, housing quality, educational attainment, and family structure), SLE disease activity and damage indices, and high-dose glucocorticoid exposure (>3 months and any-time dose of >30mg prednisone equivalent).

Results: 226 adolescents with cSLE were seen in the Lupus Clinic during the observation period, of which 106 (47%) were seen by AM. Of these, 88 (83%) were female. Median age at first visit was 14 years (IQR 13, 16). Additional patient characteristics are shown in Table 1. Patients had a median of 2 (1, 3) visits with AM over the study period. Figure 1 shows the range of adolescent health issues described across all visits, of which mood was identified as the top adolescent issue (presenting problem in 22%, and identified issue in 51% of patients). Patients had an average adolescent health burden of 2.8 ± 2.31, defined as the number of separate adolescent health issues identified over the study period. In multiple regression analyses, higher adolescent issue burden was associated with higher glucocorticoid exposure (RR=1.72, 95% CI 1.32-2.24), presence of damage (RR=1.30, 95% CI 1.30, 95% CI 0.99-1.70), higher material deprivation (RR=1.16, CI 1.03-1.29), and lower disease activity (RR=0.96, 95% CI 0.92-0.99). The most common service provided by AM was psychoeducation at 54% (Table 2).

Conclusion: Adolescents with cSLE experience a wide range of physical, emotional, and social issues in addition to their underlying disease. We found that increased cSLE disease severity and social marginalization put teens at higher risk of worse adolescent health issues. This highlights the need to discuss adolescent health during rheumatology clinic visits, and the importance of integrating AM specialists into routine cSLE care.

Table 1. Demographics & Disease Characteristics of Patients with cSLE in Adolescent Medicine Care (n=106)

Age in years, median (IQR)	14 (13.0, 16.0)
Female, N (%)	88 (83.0)
Race/Ethnicity, N (%)	
Asian	43 (40.6)
Black	22 (20.8)
White	20 (18.9)
Latin/Hispanic	10 (9.4)
Arab/Middle Eastern	7 (6.6)
Aboriginal	2 (1.9)
Unknown	2 (1.9)
Material deprivation score (range -3 to +3), median (IQR)	-0.2 (-0.7, 0.4)
Disease duration in years, median (IQR)	0 (0.0, 2.0)
Disease activity (SLEDAI-2K), median (IQR)	2 (1.0, 6.0)
Presence of damage on SLICC Damage Index (score >0), N (%)	21 (20.0)
Disease manifestations (ever), N (%)	
Cytopenias	85 (80.2)
Malar rash	76 (71.2)
Arthritis	65 (61.3)
Nephritis	42 (39.6)
Alopecia	38 (35.8)
Oral/nasal ulcers	25 (23.6)
Neuropsychiatric disease*	20 (18.9)
Serositis	12 (11.3)
Discoid rash	10 (9.4)
Anti-phospholipid syndrome	3 (2.8)
High-dose glucocorticoid exposure, N (%)	59 (56.0)
Comorbid psychiatric diagnosis, N (%)	31 (29.2)
Followed by Psychiatry, N (%)	30 (28.3)
Followed by Social Work, N (%)	35 (33.0)

*Neuropsychiatric disease consistent with the 1999 ACR nomenclature and case definitions for NPSLE.

Table 2. Adolescent Medicine Visit Outcomes and Services Provided for cSLE Patients (N=106)

Ongoing adolescent medicine follow-up, N (%)	75 (70.8)
Referral to mental health services at institution, N (%)	14 (13.2)
Acute	6 (5.7)
Outpatient	8 (7.5)
Referral to medical services at institution, N (%)	9 (8.5)
Referral to social work at institution, N (%)	7 (6.6)
Referral to community services mental health services, N (%)	22 (20.8)
Psychoeducation by Adolescent Medicine, N (%)	57 (53.8)
Educational materials, N (%)	27 (25.5)
Medication, N (%)	21 (19.8)
Prescribed by Adolescent Medicine	12 (11.3)
Recommended by Adolescent Medicine	14 (13.2)
Medical investigations ordered, N (%)	18 (17.0)

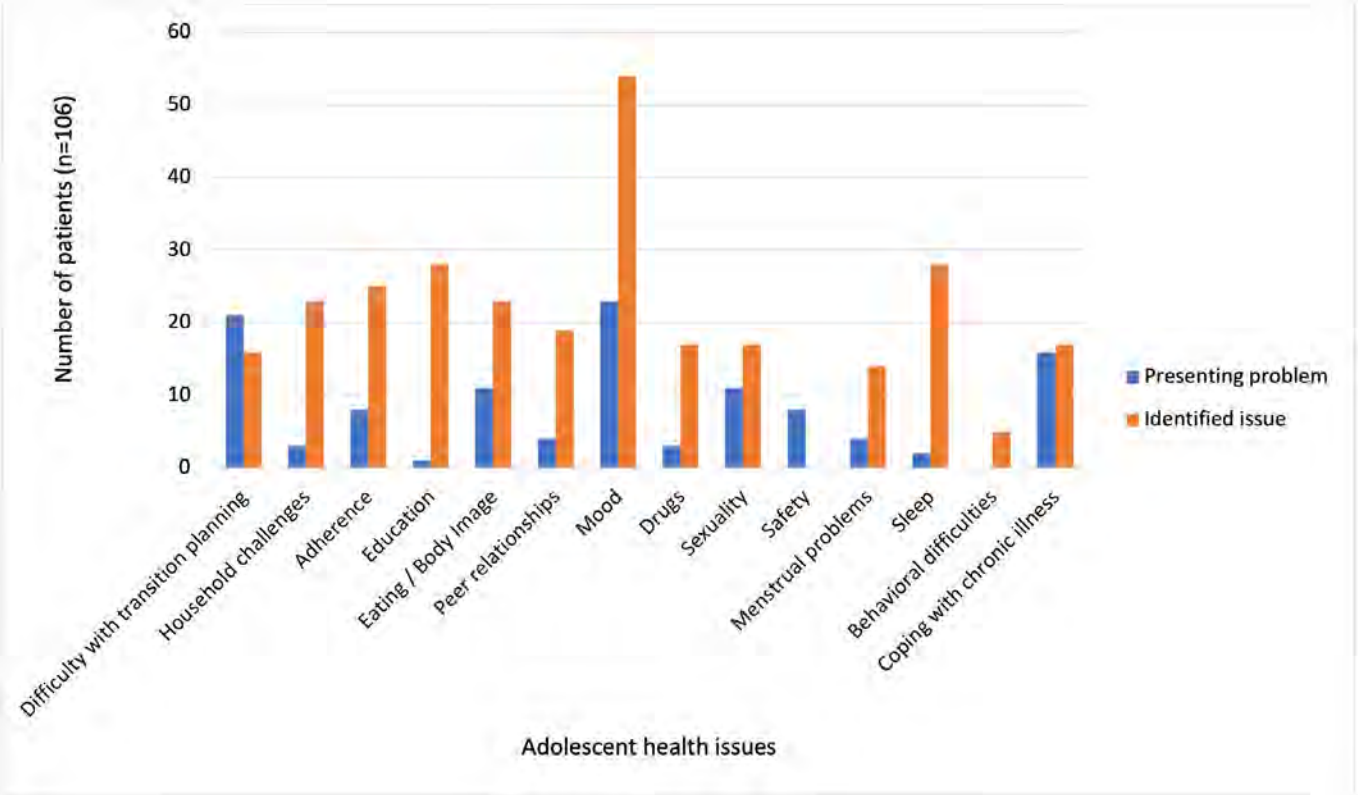


Figure 1. Adolescent Health Issues in cSLE Patients Across Adolescent Medicine Visits (N=106).

Disclosure: C. DeCoste, None; **P. Moaf**, None; **L. Ng**, None; **D. Ostojic-Aitkens**, None; **F. Faruq**, None; **B. Maguire**, None; **D. Levy**, amgen, 6, sobi, 1, roche, 1, janssen, 1, medexus, 6; **L. Hiraki**, Novartis, 6; **A. Toulany**, None; **A. Knight**, None.

Abstract Number: 0781

Long-Term Follow-up of Juvenile Localized Scleroderma Patients Treated with Methotrexate-Based Standardized Regimens (Consensus Treatment Plans)

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile localized scleroderma (jLS) is a rare chronic inflammatory and fibrosing disease associated with a high risk for morbidity in children. Methotrexate (MTX) has been identified as effective treatment, but data is limited as to the optimal duration, and need for corticosteroid (CS) treatment. The LS group of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed standardized regimens (consensus treatment plans, CTPs) for comparative effectiveness studies. The results of a 1-year follow-up of a pilot multi-center study of treating 50 patients with a MTX-based CTP were previously reported. Of the 44 (88%) patients that completed 1 year of follow-up, 33 (66%) were rated as responders and 11 (22%) as non-responders. We now report on the long-term follow-up of these patients.

Table. Characteristics of jLS study patients. JLS patients in the pilot CTP study were followed after they initiated treatment with one of 3 MTX-based CTPs. The characteristics of all the patients that completed the first year of treatment, patients that ever experienced a treatment failure (treatment failures), and patients that responded to the CTP (responders) are shown. Numbers are shown with % in parentheses unless otherwise stated. The % for number of patients is based upon the total initial cohort (50 patients). The other % are based upon the number of patients in the specific cohort. P-value was calculated for differences between the responders and treatment failures.

	All at 12 months	Responders	Treatment Failures	p-value
Number of patients	44 (88)	28 (56)	16 (32)	
Age of onset, years, median (IQR)	9.4 (6.1-11.7)	8.9 (5.1-10.4)	10.6 (8.5-13.4)	*0.052*
Disease duration, months, median (IQR)	12.5 (6-53.8)	24 (6.9-78)	11 (5.8-27)	*0.052*
Female	31 (70.5)	18 (64.3)	13 (81.3)	NS
Race:				NS
White		27	14	
African American		0	0	
Asian		0	2	
Mixed		1	0	
Hispanic		6	3	NS
Subtype:				NS
Circumscribed superficial	3 (7)	2 (7)	1 (6)	
Circumscribed deep	2 (4.5)	1 (4)	1 (6)	
Linear scleroderma	28 (64)	21 (75)	7 (44)	
Generalized morphea	1 (2)	0	1 (6)	
Pansclerotic morphea	1 (2)	0	1 (6)	
Mixed morphea	9 (20.5)	4 (14)	5 (31)	
Extracutaneous involvement	34 (77)	18 (64)	16 (100)	0.007
Arthritis	8 (18)	0	8 (50)	<0.001
Growth disturbance	21 (48)	12 (43)	9 (56)	NS
Craniofacial involvement	17 (39)	14 (50)	3 (19)	0.040
Prior systemic treatment	7 (16)	6 (21)	1 (6)	NS

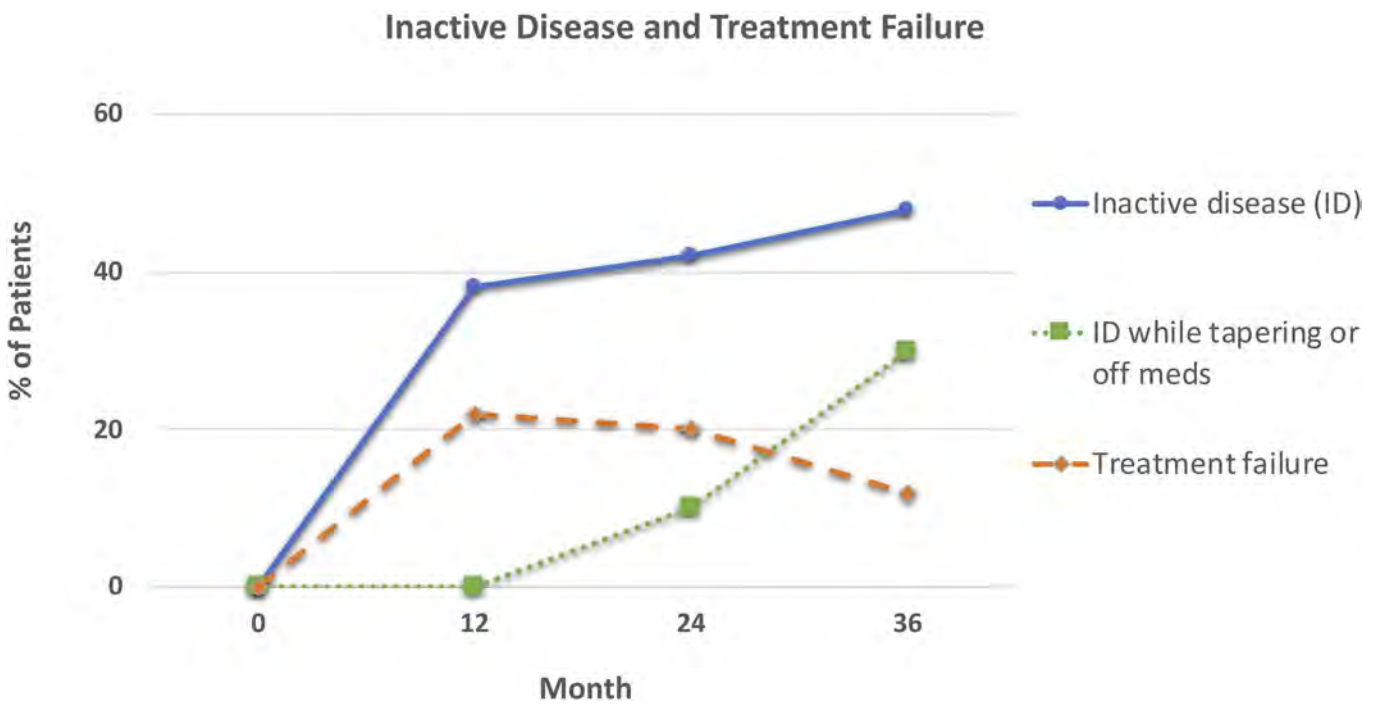

Figure 1. Percent of jLS patients achieving inactive disease or experiencing treatment failure over time. Patients initiating treatment with one of 3 MTX-based CTPs (no CS, concomitant oral CS, or concomitant intravenous CS) were followed for up to 36 months. There were 50 patients at 0 months, 44 at 12 months, 39 at 24 months, and 37 at 36 months. Inactive disease was defined as PGA-A = 0, treatment failure as active disease requiring additional treatment besides that specified by CTP.

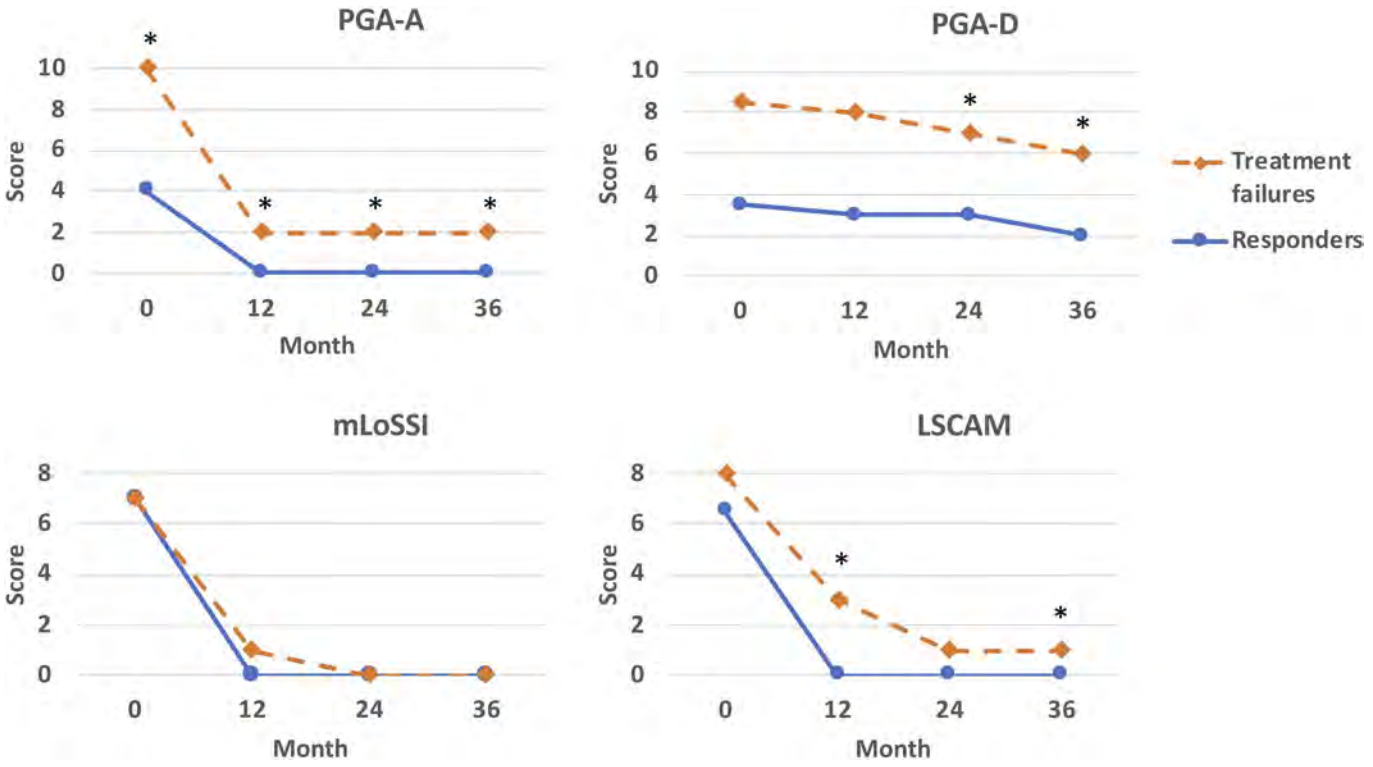

Figure 2. Comparison of scores in patients who experienced treatment failure to those who were responders to CTP. Significant differences are indicated by an * ($p < 0.05$). There were 28 patients who were responders and 16 who experienced treatment failure. mLoSSI: modified Localized Scleroderma Skin Severity Index; LSCAM: Localized Scleroderma Cutaneous Activity Measure; PGA-A: Physician global assessment of disease activity; PGA-D: physician global assessment of disease damage.

Methods: Patients enrolled in the pilot CTP study were eligible to enroll in the long-term extension, with study visits completed at 24 and 36 months. Each patient was evaluated by the same investigator for all 3 years of the study, using the same set of standardized clinical outcome measures for all visits. Treatments and adverse events that occurred since the last study visit were collected. Descriptive analysis was performed of all patients that had completed at least 12 months of follow-up, with p values calculated by Z-score or Mann Whitney U test. Inactive disease was defined as physician global assessment of activity (PGA-A) = 0, remission off medicine as PGA-A = 0 with the patient off treatment, and treatment failure as active disease requiring additional medication besides that specified in CTP. Patients who experienced treatment failures at any time during the study were compared to patients who were never treatment failures.

Results: Most patients were female (70%) and had linear scleroderma (Table). Thirty-seven (74%) of patients completed 36 months of follow-up (Figure 1). Over time, more patients achieved inactive disease, with 30% able to maintain inactive disease while tapering or discontinuing methotrexate (Figure 1). Treatment failures (TF) occurred most commonly in years 1 and 2 when ~20% of patients were non-responders. In addition to 11 patients who experienced TF in the first 12 months, 5 additional patients experienced TF by 24 months.

PGA-A and Skin scores declined significantly from 0 to 12 months for both responders and treatment failures. However, patients who experienced TF had higher PGA-A scores than responders at all visits (Figure 2). Skin activity scores, as measured by LSCAM, were also higher in patients who experienced TF at the 12- and 36-month visits than responders; no difference was identified by mLoSSI (Figure 2). PGA-Damage scores were higher at 24 and 36 months in patients who experienced TF than responders.

Conclusion: JLS patients treated with MTX-based standardized regimens were found to achieve further improvement in years 2 and 3 with continued treatment, with 20% able to achieve remission off medicine in year 3. Disease flares occurred in each year and overall, 16 (32%) patients were non-responders, with extracutaneous involvement, especially arthritis, associated with treatment failure. More work is needed to identify the at-risk patients and determine their optimal therapy.

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Abstract Number: 0782

Examining the Association of Socioenvironmental Factors with Depression and Anxiety Symptoms Among Youth with Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Depression and anxiety symptoms are prevalent in youth with childhood-onset system lupus erythematosus (cSLE). Healthcare disparities and trauma are associated with adverse mental health in adults with SLE. There is limited data on how these socioenvironmental factors impact mental health for children and adolescents with cSLE. We examined the association of socioenvironmental and disease-related factors with symptoms of depression and anxiety in a pediatric cSLE sample.

Table 1. Demographic, Socioenvironmental and Clinical Characteristics of Patients with cSLE

	Total Cohort (n=72)	Elevated symptoms of depression[a] (n=25)	Elevated symptoms of anxiety (n=28)
Demographic Characteristics			
Age, mean (SD) years	15.3(1.8)	15.8 (1.3)	15.5 (1.4)
Female, n (%)	59 (83%)	21 (84%)	24 (86%)
Race / ethnicity, n (%)	52 (75%)	17 (71%)	19 (70%)
Black/African-American	5 (7%)	1 (4%)	0 (0%)
East Asian	19 (27%)	4 (17%)	8 (30%)
South Asian	9 (13%)	6 (25%)	4 (15%)
Mixed race	4 (6%)	1 (4%)	2 (7%)
White	17 (25%)	7(29%)	8 (30%)
Other	15 (22%)	5(21%)	5 (18%)
Socioenvironmental Factors			
Exposure to traumatic experience, n (%)	25 (37%)	12 (52%)	10 (37%)
Marginalization total score, mean (SD)	2.9 (0.75)	3.1 (0.73)	2.8 (0.78)
Marginalization dimensions – % in most marginalized quartile			
Instability[b], n (%)	7(10%)	3(12%)	3(11%)
Material Deprivation[c], n (%)	14(19%)	8(32%)	6(21%)
Dependency[d], n (%)	3(4%)	2(8%)	2(7%)
Ethnic Concentration[e], n (%)	5(51%)	14(56%)	13(46%)
Clinical Characteristics			
Disease duration, mean months (SD)	45.3 (31.6)	31.8 (25.6)	44.6 (32.4)
Active disease (SLEDAI[f] > 4), n (%)	13 (18%)	5 (20%)	4 (14%)
Presence of damage (SDI[g]>0), n (%)	10 (14%)	6 (24%)	3 (11%)

[a] Elevated depression symptoms based on use of one of 3 self-rating scales

[b] The instability dimension reflects family and residential instability, which takes into account several indicators such as proportion of dwellings that are not owned and proportion of dwellings that are occupied by a single resident.

[c] The material deprivation dimension reflects the inability for residents to access basic material needs, and includes indicators such as proportion of single-parent households, proportion of population that received government transfer payments, and proportion of population that is considered low-income.

[d] The dependency dimension takes into the number of people (children, senior, adults) who do not have income from employment.

[e] The ethnic concentration dimension reflects the proportion of the population who are recent immigrants and/or belong to a 'visible minority' group.

[f] SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index

[g] SDI: Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage index

Table 2. Association of Patient Factors with Elevated Depression Symptoms in cSLE

	Univariate Analysis		Multivariate Analysis	
Variable	**Odds Ratio (95% CI)**	***p* value**	**Odds Ratio (95% CI)**	***p* value**
Age	1.29 (0.935-1.784)	0.120	-	-
Gender	1.11 (0.297-4.110)	0.881	-	-
Race (White/Non-White)	0.69 (0.225-2.140)	0.525	-	-
Socioenvironmental Factors				
Exposure to traumatic experience	2.60 (0.916-7.385)	0.073	1.82 (0.584-5.678)	0.302
Marginalization total score	1.93 (0.981-3.782)	0.057	1.67 (0.804-3.475)	0.169
Clinical Characteristics				
Disease duration	0.97 (0.955-0.994)	0.011	0.98 (0.956-0.999)	0.038
Active disease (SLEDAI > 4)	1.22 (0.352-4.214)	0.755	-	-
Presence of damage (SDI>0)	3.39 (0.858-13.434)	0.082	2.77 (0.491-15.669)	0.248

Shown are results of logistic regression models for predictors of elevated depression symptoms. Factors with univariate associations reaching significance of $p<0.10$ were included in the multivariate analysis.

Table 3. Association of Patient Factors with Elevated Anxiety Symptoms in cSLE

Variable	**Univariate Odds Ratio (95% CI)**	***p* value**
Age	1.08 (0.820-1.417)	0.590
Gender	1.37 (0.371-5.072)	0.636
Race (White/Non-White)	0.65 (0.214-1.960)	0.442
Socioenvironmental Factors		
Exposure to traumatic experience	0.98 (0.357-2.691)	0.969
Marginalization total score	0.68 (0.355-1.316)	0.255
Clinical Characteristics		
Disease duration	0.99 (0.984-1.014)	0.885
Active disease (SLEDAI > 4)	0.65 (0.179-2.348)	0.509
Presence of damage (SDI>0)	0.63 (0.150-2.689)	0.537

Shown are results of logistic regression models for predictors of elevated anxiety symptoms.

Methods: We examined a cross-sectional pediatric sample ages 9-17 years from a major tertiary hospital SLE outpatient clinic between August 2017 and April 2021. All patients met ACR or SLICC classification criteria for SLE. Self-report screening questionnaires for depression (one of: Center for Epidemiologic Studies Depression Scale for Children, Beck's Depression Inventory, Child Depression Inventory), and anxiety (the Screen for Childhood and Anxiety Related Disorders) were used to investigate current symptoms. Elevated depression/anxiety symptoms were determined based on established clinical cut-points. The Kiddie-Schedule for Affective Disorders and Schizophrenia (Version 5) interview recorded history of exposure to a traumatic event. Disease activity was measured by SLEDAI-2K and damage by the SLICC Damage Index (SDI). Area-level indicators of socioenvironmental disadvantage were obtained using the Ontario Marginalization Index. The association between elevated depression and anxiety symptoms

(binary outcomes), and disease-related (duration, activity, damage) and socioenvironmental (traumatic exposure, marginalization) factors were examined using univariate and multivariate logistic regression analyses.

Results: 72 youth (mean age 15.3 ± SD 1.8 years, 83% female, 75% self-identified as non-white) were included (Table 1). The mean ± SD disease duration was 46.3 ± 32.6 months. 18% had active disease (SLEDAI-2K > 4), and 14% had disease damage (SDI >0). History of traumatic exposure (e.g., witness of domestic violence) was present in 37%. The mean marginalization total score was 2.9 (range 1-5 with higher values reflecting greater marginalization). Elevated depression symptoms were present in 37% (n=25) and anxiety in 39% (n=28). In univariate analysis (Table 2), elevated depression symptoms were associated with shorter disease duration (OR=0.97, p=.011), presence of disease damage (OR=3.39, p=0.082), traumatic exposure (OR=2.60, p=.073), and higher marginalization level (OR=1.93, p=.057). Shorter disease duration was the only significant predictor in the multivariate analysis for depression. Analyses for anxiety (Table 3) did not identify any significant contributory factors.

Conclusion: In this pediatric sample of cSLE, depression and anxiety symptoms were prevalent, and levels of trauma exposure and social marginalization were high. Shorter cSLE disease duration was associated with elevated depression symptoms, which may reflect difficulty coping with the diagnosis. An approach for mental health care of youth with cSLE should consider early screening for mood problems, and underscores the need to assess the availability of psychological supports to enhance mental wellbeing.

Disclosure: D. Ostojic-Aitkens, None; **A. Danguecan**, None; **S. Mossad**, None; **M. Quilter**, None; **D. Korczak**, None; **R. Schachter**, None; **K. Cost**, None; **J. Couture**, None; **D. Dominguez**, None; **L. Ng**, None; **P. Moaf**, None; **T. El Tal**, None; **D. Levy**, amgen, 6, sobi, 1, roche, 1, janssen, 1, medexus, 6; **L. Hiraki**, Novartis, 6; **A. Knight**, None.

Abstract Number: 0783

Transmission Disequilibrium Testing Meets Next Generation Sequencing: Applying TDT to Whole Genome Data in Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disorder that is more severe in children than adults. Due to aggressive disease in childhood-onset SLE (cSLE), identification of genetic associations in this population could lead to insights into pathogenesis. Transmission disequilibrium test (TDT) is a family-based genetic association test performed on trios (affected patient and two unaffected parents) to compare the rate of transmission of an associated marker allele from the heterozygous parent to an affected offspring. Trio based TDT has increased power to detect association over a wide range of allele frequencies, but the empirical significance threshold has not been established for whole genome data. This is the first study to apply TDT to whole genome sequence data in a diverse, international cSLE cohort.

Table 1. Top gene based rvTDT results

Gene	p-value
DNAH11 (dynein axonemal heavy chain 11)	0.0009
PCDHB15 (protocadherin beta 15)	0.0009
TMEM63A (transmembrane protein 63A)	0.0009
FAM160A1 (family with sequence similarity 160 member A1)	0.0011
HNRNPUL2 (heterogeneous nuclear ribonucleoprotein U like 2)	0.0013
ADCY10 (adenylate cyclase 10)	0.0018
DAB2IP (DAB2 interacting protein)	0.0018
BCAM (basal cell adhesion molecule)	0.0019
CEBPZ (CCAAT enhancer binding protein zeta)	0.0024
SLFN14 (schlafen family member 14)	0.0026

Methods: SLE subjects met at least 4 of 11 revised American College of Rheumatology classification SLE criteria. cSLE subjects had disease onset prior to age 18. Whole blood samples collected from 81 subjects and 111 parents underwent whole genome sequencing via Illumina HiSeq X Ten. TDT was performed to assess for association of each variant allele with cSLE in the parents with heterozygous genotypes. TDT was performed as SNP-based and gene-based analyses. SNP-based TDT was performed using PLINK 1.9. Gene-based TDT analyses used EPACTS to annotate each SNP into genes. We then employed rvTDT, which uses multiple gene-based burden tests adapted for TDT including the burden of rare variants (BRV) test. Statistical significance was determined empirically by permutation for both the SNP-based and gene-based analyses.

Results: The SNP-based analysis did not return any genome-wide significant SNPs. A SNP of interest close to the empirical significance threshold was found to be associated with the Transmembrane Protein 132C gene (*TMEM132C*). In the gene-based TDT analysis, many significant genes were identified (Table 1). We cross-referenced our SNP and gene-based results with results from other SLE genetic analysis. *TMEM132C* was also present in our gene-based analysis, although again it did not reach statistical significance. The *TMEM132* family encodes for cell to cell junctions in the central nervous system. *TMEM132C* has not been associated with autoimmunity in prior studies, but previous genome wide association studies have found this gene to be associated with panic disorder, oncologic conditions, and hearing loss.

Conclusion: Our study identified novel genetic mutations that were statistically significant in a diverse childhood-onset lupus cohort. While no SNP reached significance across the genome, when we clustered SNPs by gene, we found many unrelated families were enriched in variants in the same gene. Future studies should be done to explore the role of *TMEM132C* in the pathogenesis of SLE. Our study is the first in rheumatology to apply TDT methodology to whole genome data. TDT methodology allowed for a robust analysis in a diverse patient cohort. Further studies in larger cohort of cSLE patient/parent trios will allow us to better evaluate significant SNP- and gene-based associations and identify candidate causal risk genes for SLE.

Disclosure: K. Vazzana, None; **A. Musolf**, None; **J. Bailey-Wilson**, None; **Z. Deng**, None; **M. Kaplan**, None; **L. Lewandowski**, None.

Abstract Number: 0784

Use of EuroLupus Cyclophosphamide Dosing for the Treatment of Lupus Nephritis in Childhood-Onset Systemic Lupus Erythematosus in North America

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Childhood-onset systemic lupus erythematosus (cSLE) has higher rates of lupus nephritis (LN) than adult-onset SLE, often requiring intensive immunosuppression. This study examined North American practices and preferences for the low-dose EuroLupus cyclophosphamide protocol, as compared to the high-dose National Institute of Health (NIH) cyclophosphamide protocol, to treat LN in cSLE.

Methods: A 35-item web-based survey was distributed to Childhood Arthritis and Rheumatology Research Alliance (CARRA) and Pediatric Nephrology Research Consortium (PNRC) providers. The survey assessed participant demographics, cyclophosphamide prescribing practices, perceptions of EuroLupus protocol, and LN vignette treatment decisions; one vignette was taken from a 2009 CARRA survey and responses were compared. Multivariable logistic regression analyzed provider factors associated with practices and preference for low- versus high-dose cyclophosphamide.

Results: Responses were provided by 185/421 (44%) CARRA physicians (Table 1). Among respondents who prescribed cyclophosphamide for pediatric LN over the past year (n=135), half reported using EuroLupus protocol. When presented the same vignette about an adolescent with class IV LN, 32% of pediatric rheumatologists chose EuroLupus dosing in 2020, versus only 6% in 2009 (Figure 1). Provider factors associated with choosing the low-dose regimen were familiarity with the protocol (OR 4.2, p=0.006) and greater perceived benefit (OR 1.6, p< 0.0001) (Table 2). Forty pediatric nephrologists had similar responses to the pediatric rheumatology providers. Overall, 78% of respondents perceived EuroLupus protocol efficacy to be equivalent to the high-dose protocol in cSLE LN.

Conclusion: Of pediatric specialists who prescribe cyclophosphamide for cSLE LN, more use low-dose cyclophosphamide compared to a decade prior. Nevertheless, familiarity with EuroLupus dosing remains low.

Table 1. Demographics of survey respondents. CARRA=Childhood Arthritis and Rheumatology Research Alliance PNRC=Pediatric Nephrology Research Consortium IV=intravenous LN=lupus nephritis

	Pediatric Rheumatologists CARRA (n=185)		Pediatric Nephrologists PNRC (n=40)	
Years in Practice				
Fellow	35	(19%)	8	(20%)
Faculty				
1-5	53	(29%)	9	(23%)
6-15	51	(27%)	16	(40%)
>16	46	(25%)	7	(17%)
Training Pathway				
Pediatric Rheumatology	166	(90%)	39	(98%)
Medicine/Pediatrics Rheumatology	19	(10%)	1	(2%)
Practicing both	14	(74%)	1	(2%)
Practicing pediatrics	4	(21%)	0	(0%)
Practicing adult	1	(5%)	0	(0%)
Practice Location				
North America				
United States	171	(92%)	36	(90%)
Canada	14	(8%)	1	(3%)
Other	0	(0%)	1	(3%)
Did not respond	0	(0%)	2	(5%)
Perceived as a Lupus Expert				
Yes	64	(35%)	15	(38%)
No	121	(65%)	25	(63%)
Ever initiated IV Cyclophosphamide				
Yes	172	(93%)	34	(85%)
No	7	(4%)	3	(8%)
Did not respond	6	(3%)	3	(8%)
Structure for Seeing LN Patients				
Co-management in a combined clinic	68	(37%)	17	(43%)
Co-management, no combined clinic	75	(40%)	14	(35%)
Rheumatology is primary	32	(17%)	1	(2%)
Nephrology is primary	9	(5%)	8	(20%)
Did not respond	1	(1%)	0	(0%)
Funneling LN to "Lupus Expert"				
Yes	15	(8%)	10	(25%)
No	170	(92%)	30	(75%)

CARRA=Childhood Arthritis and Rheumatology Research Alliance
PNRC=Pediatric Nephrology Research Consortium
IV=intravenous
LN=lupus nephritis

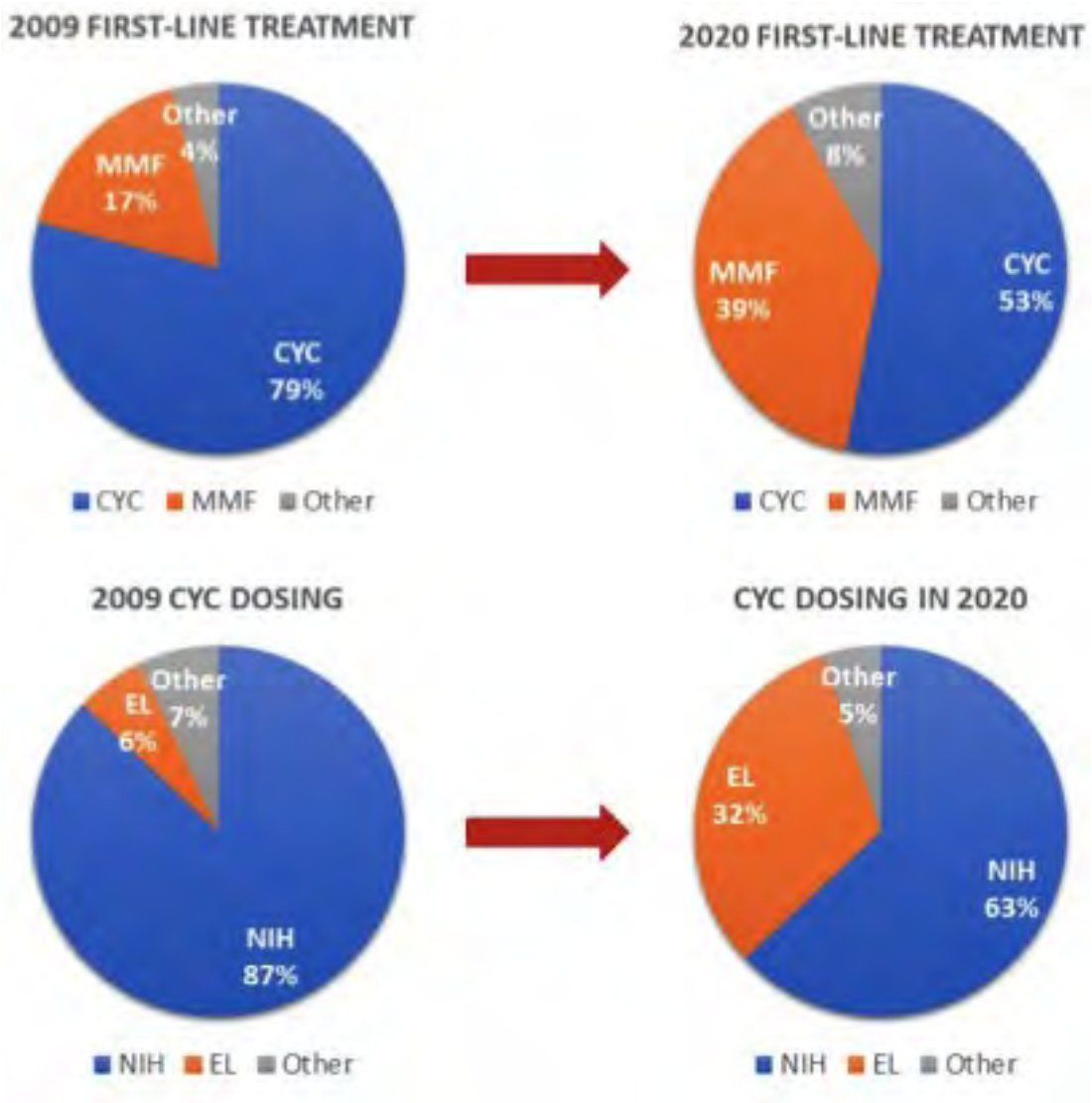

Figure 1. Change over a decade in pediatric rheumatologist preferences for first-line treatment of lupus nephritis in childhood-onset systemic lupus erythematosus. Survey respondents from the Childhood Arthritis and Rheumatology Research Alliance membership (n=134) were presented with the same clinical vignette that had been posed in 2009 (n=71) regarding first-line therapy for newly diagnosed SLE with class IV lupus nephritis in a 14-year-old girl. CYC=cyclophosphamide MMF=mycophenolate mofetil EL= EuroLupus NIH= National Institute of Health

Table 2. Provider factors associated with use of EuroLupus cyclophosphamide dosing based on results of logistic regression models. Shown are the results from a logistic regression model comparing provider factors for those selecting EuroLupus dosing vs NIH dosing who had prescribed cyclophosphamide for pediatric LN over the past 12 months (n=135). NIH= National Institute of Health LN= lupus nephritis

Variable	OR	95% CI	p-value
Training, Pediatrics Versus Medicine and Pediatrics	1.19	0.31-4.62	0.81
Familiarity with EuroLupus Dosing	5.24	2.24-12.26	0.0001
Years in Practice	1.00	0.96-1.04	0.92
Proportion of Benefits versus Disadvantages	1.52	1.23-1.87	0.0001

Shown are the results from a logistic regression model comparing provider factors for those selecting EuroLupus dosing vs NIH dosing who had prescribed cyclophosphamide for pediatric LN over the past 12 months (n=135).
NIH= National Institute of Health
LN= lupus nephritis

Disclosure: L. Cannon, None; **S. Wenderfer**, Bristol-Myers Squibb, 2; **L. Lewandowski**, None; **J. Cooper**, None; **B. Goilav**, None; **A. Knight**, None; **A. Hersh**, None; **S. Ardoin**, Aurinia, 2, American Board of Pediatrics, 4, Childhood Arthritis and Rheumatology Research Alliance, 4; **R. Sadun**, None.

Abstract Number: 0785

Decreased Peripheral Blood Natural Killer Cell Count in Untreated Juvenile Dermatomyositis Is Associated with Muscle Weakness

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Pediatric Rheumatology – Clinical Poster II: SLE, JDM, & Juvenile Scleroderma (0764–0785)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare pediatric autoimmune disease characterized by muscle and skin inflammation. The Pathophysiology of JDM is complex; it involves both adaptive and innate immune system dysregulation. The increase in type I and type II interferon signature is well documented in JDM patients.

IFN-α has been shown to enhance Natural Killer (NK) cell degranulation and inflammatory cytokine production. However, information about how NK cells contribute to the pathophysiology in JDM patients is lacking. This study aims to evaluate the changes in the NK cell count and its correlation with various disease activity markers.

Methods: This IRB-approved retrospective study was conducted at the Ann and Robert H. Lurie Children's Hospital of Chicago. 135 subjects (76% female, 74% white, 18.5 % Hispanic, 3% black) were included in this study. Clinical and laboratory variables, including age, race, gender, MSA, Disease Activity Scores (DAS skin, muscle, total), nailfold capillary count, neopterin, and muscle enzymes, were obtained from the Lurie Children's Juvenile Myositis Registry REDCap database. All subjects had flow cytometry (CD3, CD4, CD8, CD16/56, CD19, and HLA-Dr) before receiving treatment for JDM. To identify which NK cell subtype (CD56dim, CD56 bright) is affected in JDM, another flow cytometry was done with CD16 and CD56 on different fluorochromes in a smaller subset of the untreated JDM and control subjects.

Results: 57% of the untreated JDM children had low NK cells. Those with low NK cell count had more active disease with mean DAS-total 11.6 vs 9.6 (p= 0.001), DAS-muscle 5.8 vs 3.9 (p< 0.001), neopterin levels 22.1 vs 15.5 (p=0.003). Muscle enzymes were higher in the NK low groups as following: CPK 2733 vs 474 (p= 0.025), AST 147 vs 54(p= 0.003), LDH 491 vs 348(p= 0.006), Aldolase 23 vs 11(p= 0.013). There was no significant difference in the DAS-skin or nailfold capillary count between NK low group or normal. Among the different MSAs groups, the anti-MJ group has the Lowest mean NK cell count at 105+/- 52, and the anti P155/140 group has the highest level at 196 +/- 161; however, the difference was not statistically significant. Then we examined the NK cell subset in six JDM with low NK cells, three JDM with normal NK, and three healthy controls. CD56 dim NK cell percentage was significantly lower in NK low group than in control (0.55 % vs 4.6 % P< 0.001), whereas CD56 bright percentage did not differ significantly (0.45% vs 0.83% P=0.199).

Conclusion: Significant percentage of JDM children have low NK cells before treatment, suggesting that NK cells are likely to be contributing to the disease pathophysiology. Furthermore, JDM subjects with low NK cells show higher disease activity, especially in the muscle weakness and elevated muscle enzymes. Most of the NK cell count reduction is caused by the decreased number of the CD56 dim population, which is more cytotoxic with high perforin expression. Further studies of JDM muscle biopsies are in progress to determine if the CD56 dim NK cell counts are decreased in peripheral blood due to muscle infiltration.

Disclosure: A. Khojah, None; **A. Bukhari**, None; **C. Trinh**, None; **G. Morgan**, None; **L. Pachman**, None.

Abstract Number: 0786

Diagnostic Utility of FibroScan in Screening for Liver Injury in Patients with Inflammatory Arthritis on Treatment with Methotrexate (MTX)

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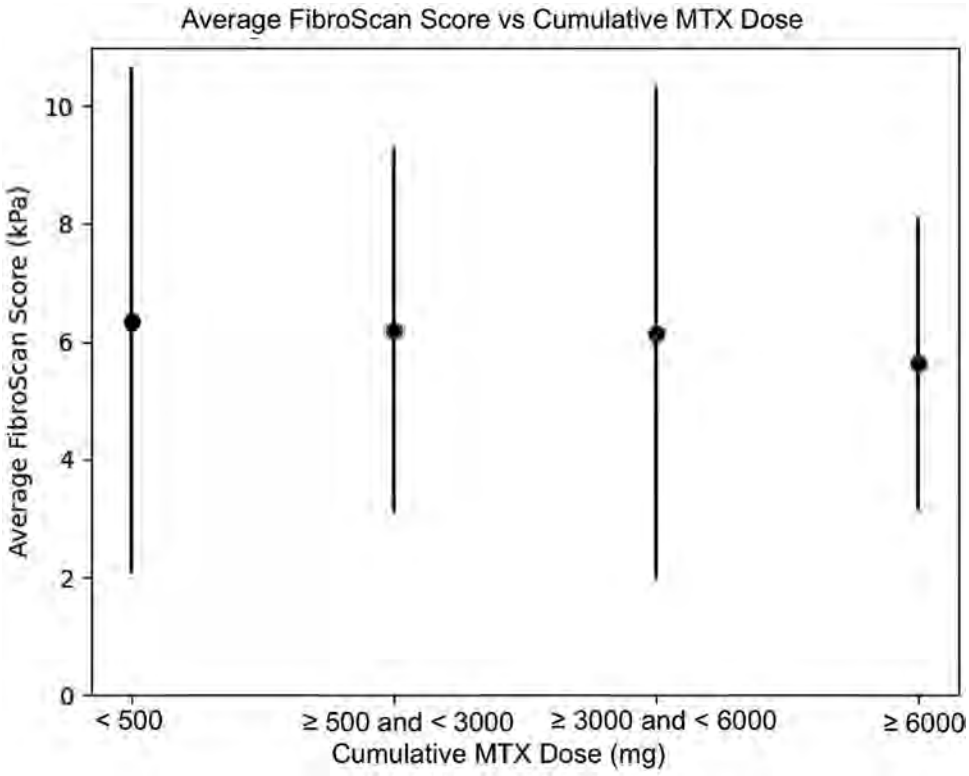
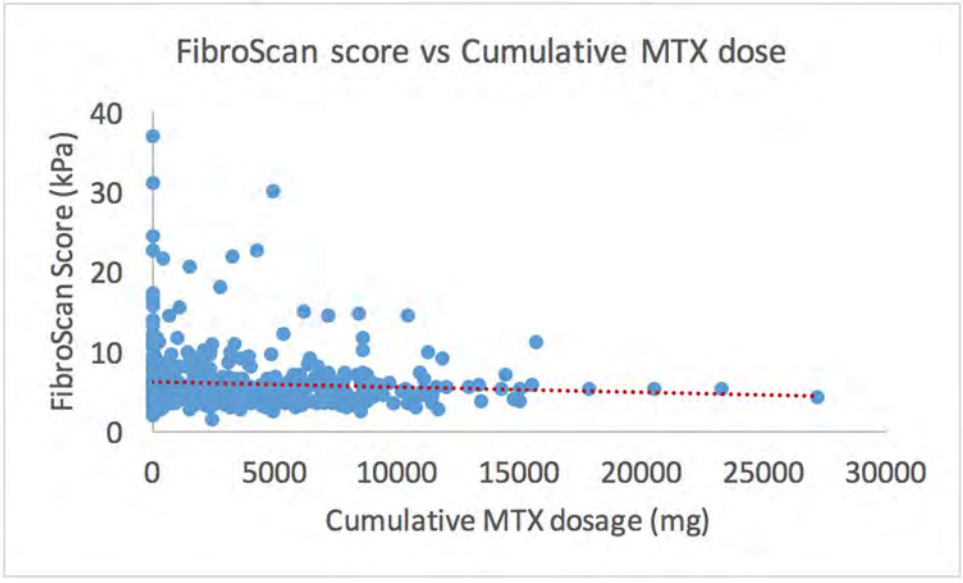
SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Methotrexate (MTX) is often the primary medication to treat various rheumatic diseases, including rheumatoid arthritis, psoriasic arthritis and many other inflammatory diseases. MTX is significantly less ex-



This table shows number (N) and percentage of participants with corresponding FibroScan scores in four cumulative MTX dosage subgroups and in the total study population. Also demonstrated are prevalence's of participants with stages F2+ and F3+ liver stiffness according to FibroScan measurements.



Scatterplot of the FibroScan score vs the cumulative MTX dosage among all participants. The plot shows that there is no significant correlation between the cumulative MTX dosage and the FibroScan score. The dotted line is the best linear fit to the data and the fact that it is almost horizontal indicates that the two variables (the cumulative MTX dosage and the FibroScan score) are almost independent from each other. Minimum cumulative MTX dosage = 0mg, maximum cumulative MTX dosage 27200mg, minimum FibroScan score = 1.5 kPa, maximum FibroScan score = 37.1 kPa.

Cumulative Dose of MTX Subgroup	Total N	F0-F1 N (%) (0.0 ≤ FS score < 7.1 kPa)	F2 N (%) (7.1 kPa ≤ FS score < 8.7 kPa)	F3 N (%) (8.7 kPa ≤ FS score < 10.4 kPa)	F4 N (%) (10.4 kPa ≤ FS score)	F2+ N (%) (FS score ≥ 7.1 kPa)	F3+ N (%) (FS score ≥ 8.7 kPa)
Group 1 (0-499 mg)	211	159 (75.4)	24 (11.4)	8 (3.8)	20 (9.5)	52 (24.6)	28 (13.3)
Group 2 (500-2999 mg)	95	73 (76.8)	6 (6.3)	10 (10.5)	6 (6.3)	22 (23.2)	16 (16.8)
Group 3 (3000-5999 mg)	104	89 (85.6)	3 (2.9)	5 (4.8)	7 (6.7)	15 (14.4)	12 (11.5)
Group 4 (6000+ mg)	110	93 (84.5)	7 (6.4)	4 (3.6)	6 (5.5)	17 (15.5)	10 (9.1)
Total	520	414 (79.6)	40 (7.7)	27 (5.2)	39 (7.5)	106 (20.4)	66 (12.7)

Average liver stiffness score per cumulative MTX dosage group. No significance difference between groups of different cumulative MTX dosage has been observed.

pensive than other alternatives and has been shown in randomized controlled trials to be effective in controlling disease activity, enhancing patient quality of life, and potentially decreasing mortality among patients with inflammatory disorders. Despite its advantages, however, a major concern has been the potential for hepatic fibrosis associated with long term MTX usage.

The present study investigates the association between cumulative MTX intake and development of liver fibrosis among patients with rheumatic diseases. We utilized non-invasive transient elastography (FibroScan) to assess for liver fibrosis among patients in a large academic outpatient rheumatology clinic.

Methods: All patients with inflammatory arthritis treated with MTX were offered screening with FibroScan. All patients who volunteered to participate were included. A certified FibroScan technician measured the liver stiffness after patients adhered to a minimal 90-minute fast. Health and medication information were collected from the patient. FibroScan measurements were recorded as both numerical values represented by the machine in kilopascal (kPa), as well as an ordinal classification from F0 (normal liver stiffness) to F4 (cirrhosis).

Results: Five hundred and twenty rheumatologic patients were included in the primary analysis. FibroScan scores ranged between 1.5 kPa and 37.1 kPa, with an average of 6.13 kPa ± 3.76 kPa. Univariate and multivariate linear and logistic regression models were used for analysis in this study. In multivariable linear regression analysis, statistically significant factors were BMI (regression coefficients: 0.060, p=0.001), waist circumference (0.041, p=0.015), male sex (0.109, p=0.004), and age (0.026, p=0.054). The population was then divided into quartiles based on the participant's cumulative dosage of MTX. The prevalence of F3/F4 liver fibrosis (i.e. FS ≥ 8.7 kPa) was 13.3% in the control group (MTX cumulative dosage < 500mg), 9.1% in subgroup 4 (MTX >6000mg) and 12.7% in the entire sample. Compared with subgroup 1 (control), MTX subgroups 2-4 were not significantly correlated with higher FS scores (p-values 0.82, 0.59, and 0.18 respectively).

Conclusion: FibroScan scores compatible with liver fibrosis were seen in all MTX subgroups; however, no significant correlation between the cumulative MTX dosage and liver stiffness was observed, even at high MTX doses. The analysis showed significant correlations between the FibroScan score and BMI, waist circumference, male sex, and age. Further studies are needed to assess agreement between liver function tests and FibroScan scores and to better

identify threshold FibroScan scores warranting methotrexate discontinuation, particularly in patients with additional risk factors such as high BMI and waist circumference.

Disclosure: S. Darabian, None; **j. Wade**, None; **S. Wade**, None; **J. Kur**, None; **M. Badii**, None.

Abstract Number: 0787

Association of Hemoglobin Levels and Radiographic Progression in the BRASS Registry

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To evaluate baseline hemoglobin (Hb) and radiographic progression over time for patients in the Brigham and Women's Hospital Rheumatoid Arthritis Sequential Study (BRASS) registry.

Methods: BRASS is a prospective observational study of over 1,500 patients diagnosed with RA at the Robert Breck Brigham Arthritis Clinic in Boston, MA (NCT01793103). The study began enrollment in March 2003 and has a 4-year average follow up retention rate of 80%. An extended follow-up of up to 18 years is available for some patients. BRASS Hb data and total Sharp score (TSS) data fields were matched with the main BRASS subjects by subject ID and visit date (±15 days). Hb at baseline was categorized as low (Hb < 120 g/L for women or < 130 g/L for men) and normal (Hb ≥120 g/L for women or ≥130 g/L for men) as per WHO guidelines. The distributions of Hb at baseline overall and within current medication subgroups at baseline (anti-TNF, biologic DMARD, non-biologic DMARD) and demographics and disease characteristics overall and by low/normal Hb were summarized. Hb and TSS values and changes over time were described (overall, by low/normal Hb and current medication at baseline). All analyses were descriptive.

Results: Patients with low Hb (N=224) at baseline had longer disease duration, higher disease activity, reported more pain, had lower income levels, less education, and were less frequently Caucasian. Compared with patients with normal Hb, those with low Hb were less frequently MTX-experienced, on a combination of anti-TNF and MTX, or on a biologic DMARD at baseline; low Hb was more frequently associated with baseline use of non-biologic DMARD and NSAIDs (Table 1). Over the 10-year observation period patients with low Hb at baseline continued to have lower Hb than patients with normal Hb; although, on average, patients in the low Hb subgroup exhibited a steady increase in Hb levels. This increase in Hb was observed in all baseline treatment subgroups. A larger increase in TSS over time was observed for patients with low Hb than for patients with normal Hb. No meaningful differences potentially attributable to medication use at baseline were detected.

Conclusion: Patients with low Hb who were treated with anti-TNFs, biologic DMARDs, or non-biologic DMARDs experienced sustained improvements in Hb levels over time. Patients with lower Hb levels at baseline tended to have increased radiographic progression as measured by TSS compared to RA patients with normal Hb levels. Future analyses may evaluate constant therapy and non-constant therapy cohorts and disease severity cohorts.

Table 1. Baseline demographic and clinical characteristics by Hb subgroup

Characteristic		Low Hb (N=224)	Normal Hb (N=890)	*P*-value
Age[a], years	Number Mean (SD)	224 60.38 (14.60)	890 55.53 (13.74)	<0.0001
Race[b], n (%)	Number Caucasian	219 187 (85.39%)	889 838 (94.26%)	<0.0001
Disease Duration[a]	Number Mean (SD)	223 14.05 (12.83)	890 11.71 (11.41)	0.0134
Early RA (<2 years)[b], n (%)	Number Yes	223 34 (15.25%)	890 127 (14.27%)	0.7107
Seropositive[b], n (%)	Number Yes	214 150 (70.09%)	832 569 (68.39%)	0.6315
RF Positive[b], n (%)	Number Yes	212 126 (59.43%)	808 498 (61.63%)	0.5586
Anti-CCP Positive[b], n (%)	Number Yes	212 140 (66.04%)	823 500 (60.75%)	0.1578
Income Level[b], n (%)	Number < $50,000	172 59 (34.30%)	707 196 (27.72%)	0.0881
Highest Education Level[b], n (%)	Number Graduate	224 166 (74.11%)	884 704 (79.64%)	0.0718
MDHAQ Score[a]	Number Mean (SD)	196 0.76 (0.56)	799 0.57 (0.50)	<0.0001
Modified RADAI[a]	Number Mean (SD)	196 3.99 (2.30)	795 3.31 (2.25)	0.0002
Pain VAS[a]	Number Mean (SD)	192 41.74 (27.84)	773 33.80 (27.22)	0.0003
Patient Global[a]	Number Mean (SD)	196 38.34 (24.75)	796 31.11 (25.27)	0.0003
Physician Global[a]	Number Mean (SD)	221 37.10 (21.63)	878 28.86 (20.81)	<0.0001
FSMHI5 Scale[a]	Number Mean (SD)	195 72.84 (18.20)	791 72.98 (17.84)	0.9213
Self-Efficacy Score[a]	Number Mean (SD)	196 69.86 (18.37)	791 71.49 (19.37)	0.2859
DAS 28-CRP4S[a]	Number Mean (SD)	195 4.46 (1.64)	791 3.53 (1.57)	<0.0001
Total Swollen Joints[a]	Number Mean (SD)	224 8.83 (7.85)	889 5.70 (6.89)	<0.0001
Total Painful Joints[a]	Number Mean (SD)	224 9.71 (8.74)	889 6.52 (7.36)	<0.0001
Medicines Ever Taken, n (%)				
Methotrexate[b]		163 (72.77%)	697 (78.31%)	0.077
Anti-TNF[b]		93 (41.52%)	406 (45.62%)	0.27
Plaquenil[b]		135 (60.27%)	531 (59.66%)	0.8689
Biologic DMARD		97 (43.30%)	412 (46.29%)	0.4222
Non-Biologic DMARD		210 (93.75%)	848 (95.28%)	0.3486
Non-Biologic DMARD, not including MTX or Plaquenil[b]		121 (54.02%)	414 (46.52%)	0.0446
Steroid[b]		182 (81.25%)	713 (80.11%)	0.7018
Current Medicines[b], n (%)				
Methotrexate		107 (47.77%)	491 (55.17%)	0.0471
Anti-TNF		67 (29.91%)	315 (35.39%)	0.1223
Anti-TNF and MTX		32 (14.29%)	170 (19.10%)	0.0945
Plaquenil		41 (18.30%)	163 (18.31%)	0.997
NSAIDs		133 (59.38%)	439 (49.33%)	0.0072
Any DMARD		192 (85.71%)	804 (90.34%)	0.0445
Biologic DMARD		74 (33.04%)	347 (38.99%)	0.1005
Non-Biologic DMARD		159 (70.98%)	673 (75.62%)	0.1538
Non-Biologic DMARD, not including MTX or Plaquenil		47 (20.98%)	139 (15.62%)	0.0543
Steroid		74 (33.04%)	252 (28.31%)	0.1651

N: Number of patients by baseline hemoglobin status; Number: Number of patients for each characteristic by baseline hemoglobin status. Percentages are based on 'Number'
[a]*P-value* is obtained using t test for equality of variance. In case equality of variance assumption is not met, Satterthwaite's p-value is provided.
[b]*P-value* is obtained using chi-square test. In case expected cell frequency is <5, Fisher's exact test is used.
MDHAQ, Multidimensional health assessment questionnaire; RADAI, Rheumatoid Arthritis Disease Activity Index; VAS, Visual analogue scale

Disclosure: N. Shadick, BMS, 5, Mallinckrodt, 5, Sanofi/Regeneron, 5, Crescendo Biosciences, 5; **O. Hagino**, Sanofi, 3, 11; **A. Praestgaard**, Sanofi, 3, 11; **S. Fiore**, Sanofi, 3, 10, 11; **M. Weinblatt**, BMS, 2, 5, Sanofi, 2, 5, Canfite, 11, Inmedix, 11, Vorso, 11, Eli Lilly, 2, 5, Scipher, 2, 11, Amgen, 2, 5, Abbvie, 2, Aclaris, 2, Chemocentryx, 2, Corrona,

2, Crescendo, 2, Eqrx, 2, Genosco, 2, GSK, 2, Gilead, 2, Horizon, 2, Johnson & Johnson, 2, Kaledio, 2, Kiniksa, 2, Novartis, 2, Pfizer, 2, Rami Therapeutics, 2, R Pharma, 2, Roche, 2, Sci Rhom, 2, Set Point, 2, Tremeau, 2; **G. Burmester**, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6.

Abstract Number: 0788

Red Cell Distribution Width Is Associated with Baseline 25-hydroxyvitamin D Level Before Methotrexate Therapy in Rheumatoid Arthritis

Shahdi Malakooti[1], Brigid Wilson[2], Taissa Bej[2], Lenche Kostadinova[3], Alyssa Lange[2], Megan O'Mara[2], David Zidar[2], Maya Mattar[4] and Donald Anthony[5], [1]Case Western Reserve University, UH Cleveland Medical Center, VA Medical Center, Cleveland, OH, [2]VA Medical Center, Cleveland, OH, [3]UH Cleveland Medical Center, VA Medical Center, Cleveland, OH, [4]Louis Stokes VA Medical Center, Mayfield Heights, OH, [5]Case, VA, Metro, Chardon, OH

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Peripheral blood red cell distribution width (RDW) correlates with disease activity in rheumatoid arthritis (RA) and is associated with subsequent mortality in non-RA patient populations. Although RDW and 25-hydroxyvitamin D (25(OH)D) levels are inversely correlated in community dwelling adults, the association between 25(OH)D status and RDW in RA has not been characterized. We investigated the relationships between baseline 25(OH)D status, RDW, and methotrexate (MTX) therapy in RA.

Methods: This was a retrospective cohort study of RA patients who fulfilled 1987 ACR classification criteria for RA and had a 25(OH)D level obtained within one year prior to MTX initiation at a single center VA Rheumatology Clinic (n=167). We evaluated vitamin D levels before and after MTX therapy start and evaluated the relationships between RDW, 25(OH)D levels, and 25(OH)D supplementation (multivitamin or higher dose supplementation) using Wilcoxon Signed Rank Test for paired analyses and Spearman Rank Sum Test for analyses of correlations.

Results: Prior to MTX therapy, 41% (n=69) were receiving 25(OH)D supplementation. After MTX therapy, 85% (n=142) were receiving 25(OH)D supplementation and 55% (n=92) were still receiving MTX at the last lab value. RDW inversely correlated with 25(OH)D levels prior to MTX (n=167; r=-0.19; p=0.01). This relationship also was observed in the subgroup where patients were receiving 25(OH)D supplementation (n=69; r=-0.25; p=0.04) but not in the subgroup not receiving supplementation (n=94; r=-0.07; p=0.52) prior to MTX.

25(OH)D level after any MTX therapy was significantly higher compared to baseline level (n=167; p< 0.001), and of those patients who remained on MTX therapy at last lab value significantly higher 25(OH)D level also was observed (n=92; p< 0.001). RDW was significantly higher compared to baseline level after any MTX therapy (n=167; p< 0.001), and of those patients who remained on MTX therapy at last lab value higher RDW again was observed (n=92; p< 0.001). After start of MTX therapy, the relationship between 25(OH)D level and RDW was no longer observed (n=92; r=0.13; p=0.21).

Conclusion: RDW and 25(OH)D levels are inversely correlated in RA patients on 25(OH)D supplementation prior to initiating MTX therapy. The relationship between 25(OH)D and RDW after MTX therapy start was no longer observed,

potentially secondary to MTX-driven anemia or MTX-mediated inflammatory control. Whether this relationship reflects overlapping inflammatory pathways driving RDW and 25(OH)D levels, or whether this is a causal relationship is yet to be determined. Specifically, whether 25(OH)D is a mediator of immunologic homeostasis in RA will need to be further elucidated.

Disclosure: S. Malakooti, None; **B. Wilson**, None; **T. Bej**, None; **L. Kostadinova**, None; **A. Lange**, None; **M. O'Mara**, None; **D. Zidar**, None; **M. Mattar**, None; **D. Anthony**, None.

Abstract Number: 0789

Adipokine Levels and Associations with Achievement of Low Disease Activity in Rheumatoid Arthritis

Joshua Baker[1], Bryant England[2], Michael George[1], Katherine Wysham[3], Gail Kerr[4], Andreas Reimold[5], Paul Monach[6], Gary Kunkel[7], Brian Sauer[7], Bartlett Hamilton[8], Carlos Hunter[2], Michael Duryee[2], Geoffrey Thiele[2] and Ted Mikuls[2], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]VA Puget Sound/University of Washington, Seattle, WA, [4]Washington D.C., Veterans Affairs Medical Center (VAMC)/Georgetown and Howard Universities, Washington, DC, [5]University of Texas – Southwestern Medical Center/Dallas Veterans Affairs Medical Center (VAMC), Dallas, TX, [6]Brigham and Women's Hospital, Boston, MA, [7]University of Utah, Salt Lake City, UT, [8]University of Nebraska, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Adipokines are fat-secreted proteins that serve as metabolic regulators. Prior studies have identified associations between adipokines and disease characteristics such as disease activity and radiographic progression in rheumatoid arthritis (RA) suggesting a link with disease phenotype, however, they have not been evaluated as prognostic biomarkers. In this study, we determined if circulating levels of adipokines were associated with the achievement of low disease activity (LDA) and clinical remission in RA. We also evaluated whether adipokines predicted the escalation of therapy to the use of biologic or targeted synthetic DMARDs.

Methods: This study evaluated patients with rheumatologist-diagnosed RA from Veteran patients who had moderate-high disease activity at enrollment in a registry study. Serum adiponectin, leptin, and fibroblast growth factor (FGF)-21 were assessed at enrollment using a multi-analyte panel. The primary outcome was the time to achievement of LDA (DAS28< 3.2). Secondary outcomes included the achievement of remission (DAS28< 2.6), achievement of low values for DAS28 subcomponents, and the incident use of bDMARDs or tsDMARDs. We used Cox proportional hazards models to evaluate the time to LDA by quartile of each adipokine among participants not in LDA at enrollment. Cox models were also used to assess the time to the initiation of bDMARDs or tsDMARDs among patients that were naïve to these therapies at enrollment regardless of disease activity. Models were comprehensively adjusted for demographics, calendar year, body mass index (BMI), disease characteristics, and comorbidity.

Results: Among 1276 patients [Mean age (SD): 70.9 (10.3) ; 89% male] that were eligible for inclusion, 827 achieved LDA and 598 achieved remission over 2,287 and 4,096 person-years of follow-up, respectively. Higher adipokine levels were associated with significantly lower rates of LDA and remission in a dose-dependent manner independent of a number of other clinical factors including BMI (Figure 1). Adipokines were also associated with lower rates of achievement of a low patient and evaluator global score and a low tender joint count, but not swollen joint count.

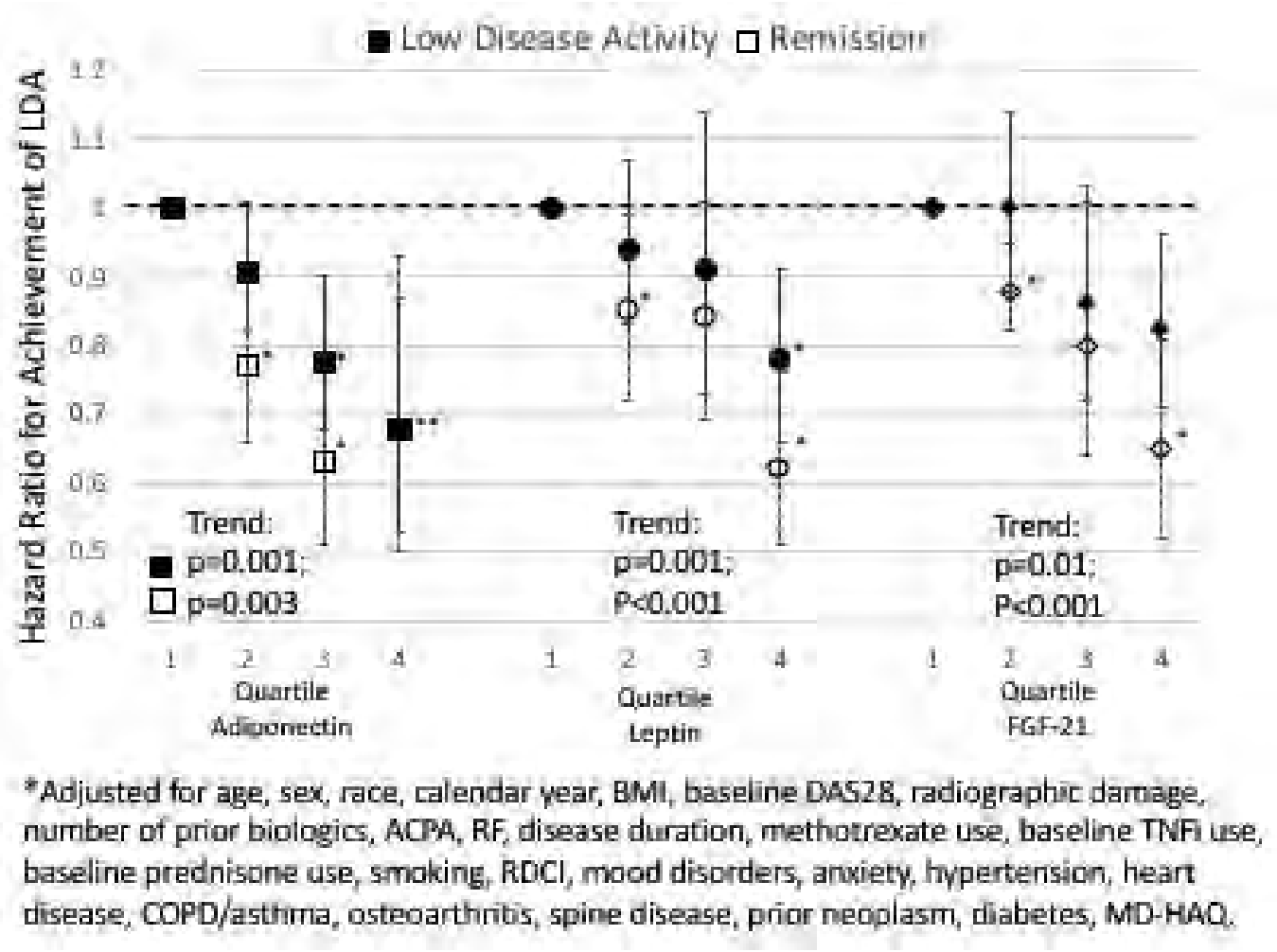

Figure 1. Adjusted risk of achieving low disease activity and remission by quartile of adipokines (adiponectin, leptin, and FGF-21).

Leptin was also associated with a lower likelihood of achievement of a low CRP. Among the 1352 biologic-naïve patients at enrollment total of 68 patients initiated a bDMARD or tsDMARD in 5,475 person-years of follow-up. Higher adipokine levels tended to be associated with a higher likelihood of initiation of new therapies (Figure 2).

Conclusion: Patients with high levels of adipokines demonstrate lower rates of achieving LDA and remission; an association that is independent of a number of clinical factors including baseline disease activity and BMI. In addition, patients with elevated adipokine levels, particularly adiponectin, might also be more likely to require escalation to a bDMARD or tsDMARD. While it remains unclear if adipokines play a causal role in promoting refractory disease, these data do support adipokines as prognostic biomarkers that may help to identify patients who are likely to experience more refractory disease over time. Further study is needed to further clarify the role of adipokines in the pathogenesis of the disease.

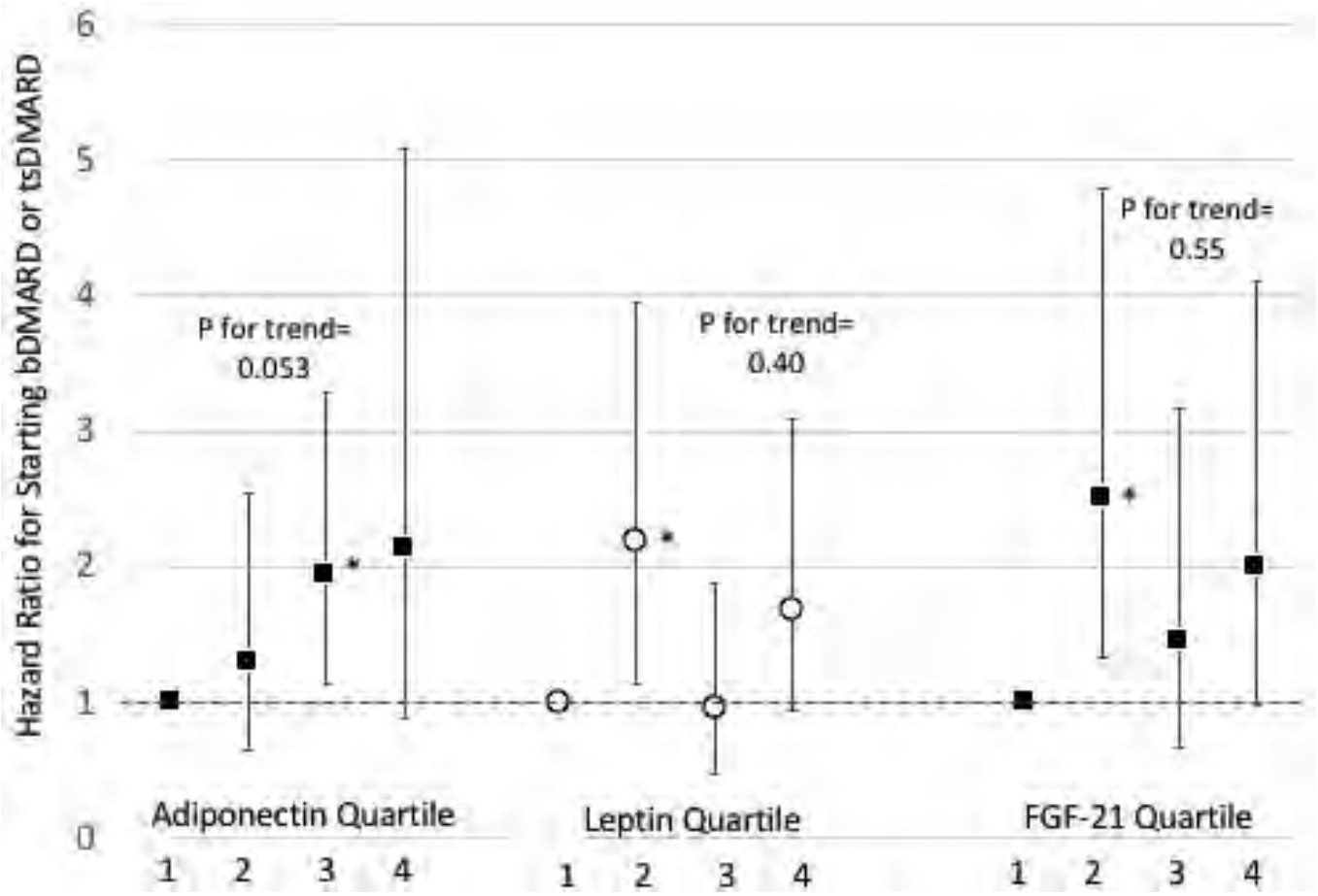

Figure 2. Hazard ratios for the risk of starting a new bDMARD or tsDMARD by adipokine quartile.

Disclosure: J. Baker, Bristol-Myers Squib, 2, Pfizer, 2; **B. England**, Boehringer-Ingelheim, 2; **M. George**, None; **K. Wysham**, None; **G. Kerr**, Aurinia, 6, Novartis, 5, Bristol Myers Squibb, 1, 5, Pfizer, 1, Horizon, 1; **A. Reimold**, None; **P. Monach**, Kiniksa, 1, Celgene, 2, Chemocentryx, 1; **G. Kunkel**, None; **B. Sauer**, None; **B. Hamilton**, None; **C. Hunter**, None; **M. Duryee**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 0790

Unraveling Heterogeneity Within ACPA-negative Rheumatoid Arthritis; The Subgroup of Patients with a Strong Clinical and Serological Response to Initiation of DMARD-treatment Favor Disease Resolution

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a heterogeneous disease, especially ACPA-negative-RA. This is reflected by differences in long-term outcomes, ranging from refractory RA to sustained-DMARD-free-remission(SDFR; sustained absence of synovitis after DMARD-cessation). Differentiation of RA-patients who are most likely to achieve SDFR can contribute to personalized treatment and tapering-strategies, however this subgroup remains scarcely discerned. Previous research demonstrated that RA-patients achieving SDFR are characterized by an early clinical response (DAS-remission after 4-months) after DMARD-start. We studied whether, in addition to this clinical response, a specific biomarker-response can further differentiate the subgroup of RA-patients most likely to achieve SDFR.

Methods: In 266 RA-patients, levels of 12-biomarkers(SAA/CRP/MMP-1/MMP-3/resistin/leptin/IL-6/TNF-R1/YKL-40/EGF/VEGF/VCAM-1) in the first 2-years after diagnosis, were studied in relation to SDFR, stratified for ACPA-status. Subsequently, biomarkers associated with SDFR-development were combined with early DAS-remission to study its additional value in defining subgroups. Since most biomarker-levels are not routinely measured in clinical practice, we explored how this subgroup could be recognized.

Results: ACPA-negative-RA-patients achieving SDFR(n=63) were characterized by a stronger decline in MMP-1/MMP-3/SAA/CRP 1-year after DMARD-start; respectively 1.30x/1.44x/2.12x/2.24x stronger. This effect was absent in ACPA-positive-RA. In ACPA-negative-RA, a strong biomarker-decline associated with early DAS-remission and the combination of both declines was present in a subgroup of ACPA-negative RA-patients achieving SDFR. This subgroup can be clinically recognized by the combination of high baseline CRP-levels(≥3-times ULN), and early DAS-remission ($DAS_{4\text{-months}} < 1.6$).

Conclusion: ACPA-negative RA-patients with early DAS-remission and a strong biomarker-response (or baseline CRP-levels≥3xULN) are most likely to achieve SDFR later-on. This could guide personalized treatment-decisions on DMARD-tapering/cessation in ACPA-negative-RA.

Disclosure: M. Verstappen, None; **H. van Steenbergen**, None; **P. de Jong**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 0791

Most Rheumatoid Arthritis (RA) Patients from Routine Care Reported in 2008-2021 Have Improved Outcomes vs Earlier Eras, but Most Remain in Moderate/high Disease Activity Rather Than Low Activity/remission: Are New Strategies for Earlier Treatment Needed in Addition to New Agents?

Juan Schmukler[1], Kyle Schroeder[2] and Theodore Pincus[2], [1]Mount Sinai Hospital - Rheumatology, Chicago, IL, [2]Rush University Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
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Background/Purpose: Treatment of rheumatoid arthritis (RA) has been advanced considerably by biological agents with capacity for stringent control of inflammation. A "treat-to-target" directive toward remission or low disease activity according to a quantitative index such as DAS28 (disease activity score), SDAI (simplified disease activity index), CDAI (clinical disease activity index), or RAPID3 (routine assessment of patient index data), is widely advocated, although it is recognized that the target must be adjusted in certain patients. The status of patients according to these indices in data from routine care has not been studied extensively and is analyzed here.

Methods: A PubMed search was conducted for "DAS28 categories - not trial," and for "CDAI" or "RAPID3" in lieu of DAS28 in separate searches. Many reports included several indices; if SDAI also was reported, it was included in analyses. Abstracts, reports of diseases other than RA, those that did not include index data or were restricted to subsets (e.g., elderly RA patients), were excluded. No further searches were done, with a goal to provide a general overview and not a comprehensive review. Means and medians of DAS28, CDAI, RAPID3 or SDAI were analyzed in cross-tabulations. The proportions of patients in 4 index categories – high, moderate, low, and remission - was analyzed in deciles.

Results: A total of 51 reports met inclusion criteria, including 1, 2, 3, or 4 indices; 43 reports presented only mean or median index values, 29 reports only different categories of index activity/severity, and 22 presented both types of data. In 79 available comparisons (including several indices in many studies), 18 for CDAI, 39 for DAS28, 13 for RAPID3, and 9 for SDAI, mean or median values indicated activity/severity that was high in 16 (20%), moderate in 55 (70%), low in 8 (10%), remission in none (Table 1). Similar results were seen for the 4 indices, with 56 -77% in moderate and 13-30% in high activity/severity (Table 1). In 60 available analyses of 4 categories of activity/severity (Table 2),

Table 1. Mean or median values for 4 RA indices for 4 categories of activity/severity, or remission in 79 reported comparisons

Activity	Remission	Low	Moderate	High	Total
CDAI	0	2 (11%)	11 (61%)	5 (28%)	18
DAS28	0	4 (10%)	30 (77%)	5 (13%)	39
RAPID3	0	0	9 (69%)	4 (31%)	13
SDAI	0	2 (22%)	5 (56%)	2 (22%)	9
Total		8 (10%)	55 (70%)	16 (20%)	79

Table 2. Proportion of patients in low activity or remission according to DAS28, SDAI, CDAI, and RAPID3 in 60 comparisons (2 studies "lumped" low activity and remission so no separate figure for remission)

	REMISSION					LOW ACTIVITY/REMISSION				
Percent	DAS28	SDAI	CDAI	RAPID3		DAS 28	SDA I	CDAI	RAPID3	
0-9.9	7	3	8	2	20 (34%)	2	0	0	0	2 (3%)
10-19.9	7	4	5	4	20 (34%)	5	1	3	0	9 (15%)
20-29.9	8	0	1	3	12 (21%)	3	3	3	4	13 (22%)
30-39.9	4	0	1	0	5 (9%)	10	0	3	2	15 (25%)
40-49.9	0	0	0	0	0	4	0	2	3	9 (15%)
50-59.9	1	0	0	0	1 (2%)	3	2	4	0	9 (15%)
60-69.9	0	0	0	0	0	1	1	1	0	3 (5%)
Total	27	7	15	9	58	28	7	16	9	60

remission was reported in 20% or more patients in 18/58 (31%) studies, 47%, 0%, 13%, and 33% for DAS28, SDAI, CDAI, and RAPID3, respectively. Low activity/remission was reported in 40% or more patients in 21/60 (35%) studies, 25%, 43%, 44%, and 33% for DAS28, SDAI, CDAI, and RAPID3, respectively (Table 2). Mean disease duration in all studies was 7.7 years. No differences were seen according to disease duration, or any trend toward better results between 2008 and 2021.

Conclusion: The findings indicate a considerable advance over historical results in RA treatment. Nonetheless, most patients were in moderate rather than low activity/severity or remission. This study is limited by a small number of reports, many from socioeconomically disadvantaged countries, some patients in remission may be seen rarely and not be included, and higher index scores may result from comorbid fibromyalgia and/or secondary osteoarthritis and other comorbidities. Nonetheless, the results may suggest a need for changes in treatment practices, such as strategies to see patients at shorter intervals after onset of symptoms, in addition to new agents, for optimal RA treatment.

Disclosure: J. Schmukler, None; **K. Schroeder**, None; **T. Pincus**, Medical History Services LLC, 8, 9, 10, 12.

Abstract Number: 0792

Remission Rates of Patients with Rheumatoid Arthritis in a Tertiary Care

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The main goal of treatment for patients (pts.) with rheumatoid arthritis (RA) is to achieve remission, in order to both, preserve physical function and to stop and prevent radiographic progression. Using the treat-to-target (T2T) approach this has recently been achieved in less than 50% of pts. in an early arthritis cohort in Germany[1]. Several influencing factors such as long symptom duration, impaired physical function, and a history of

Table 1. Patients' demographics and disease characteristics at clinical visits. Table legend on the bottom: *values are mean (SD)

Characteristics*	Patients with RA (N=137)
Age, in years	57.3 (14.5)
Gender female, n (%)	101 (73.3)
Education level university, n (%)	19 (13.9)
Employment, n (%)	64 (46.7)
Clinical pathway, second opinion, n (%)	60 (44.1)
Time since symptom onset, years	9.7 (8.6)
Anti-CCP positive, n (%)	78 (56.9)
Erosions, n (%)	44 (34.1)
At least one Comorbidity, n (%)	112 (81.1)
Charlson Comorbidity Index), 0-29	0.77 (1.1)
No. of patients on bDMARD, n (%)	64 (46.7)
No. of patients on tsDMARD, n (%)	17 (12.4)
No. of previous b- or tsDMARD, n (%)	1.5 (1.9)
Pain (NRS 0-10)	4.4 (2.4)
Patient Global (NRS 0-10)	4.4 (2.5)
DAS 28	3.5 (1.4)
SDAI	16.0 (12.4)
Patient Global (NRS 0-10)	4.4 (2.5)
DAS28-CRP, n (%)	
Remission	41 (29.9)
Low Disease Activity	21 (15.3)
Medium Disease Activity	57 (41.6)
High Disease Activity	18 (13.1)
HAQ-DI	1.3 (0.7)
HAQ-DI ≥1.28, n (%)	60 (44.1)
RAID, 0-10	4.1 (2.4)

*values are mean (SD)

Table 2. Comparing clinical characteristics at different visits. Table legend on the bottom: *values are mean (SD)

Characteristics*	Patients with RA (N=137)
Age, in years	57.3 (14.5)
Gender female, n (%)	101 (73.3)
Education level university, n (%)	19 (13.9)
Employment, n (%)	64 (46.7)
Clinical pathway, second opinion, n (%)	60 (44.1)
Time since symptom onset, years	9.7 (8.6)
Anti-CCP positive, n (%)	78 (56.9)
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High Disease Activity	18 (13.1)
HAQ-DI	1.3 (0.7)
HAQ-DI ≥1.28, n (%)	60 (44.1)
RAID, 0-10	4.1 (2.4)

*values are mean (SD)

multiple DMARD therapies were identified. Remission rates over longer periods of time in a real-life setting have not been well studied.

To evaluate the remission rate in a cohort of RA pts. treated in a tertiary care center in which a large proportion of pts. present for a second opinion.

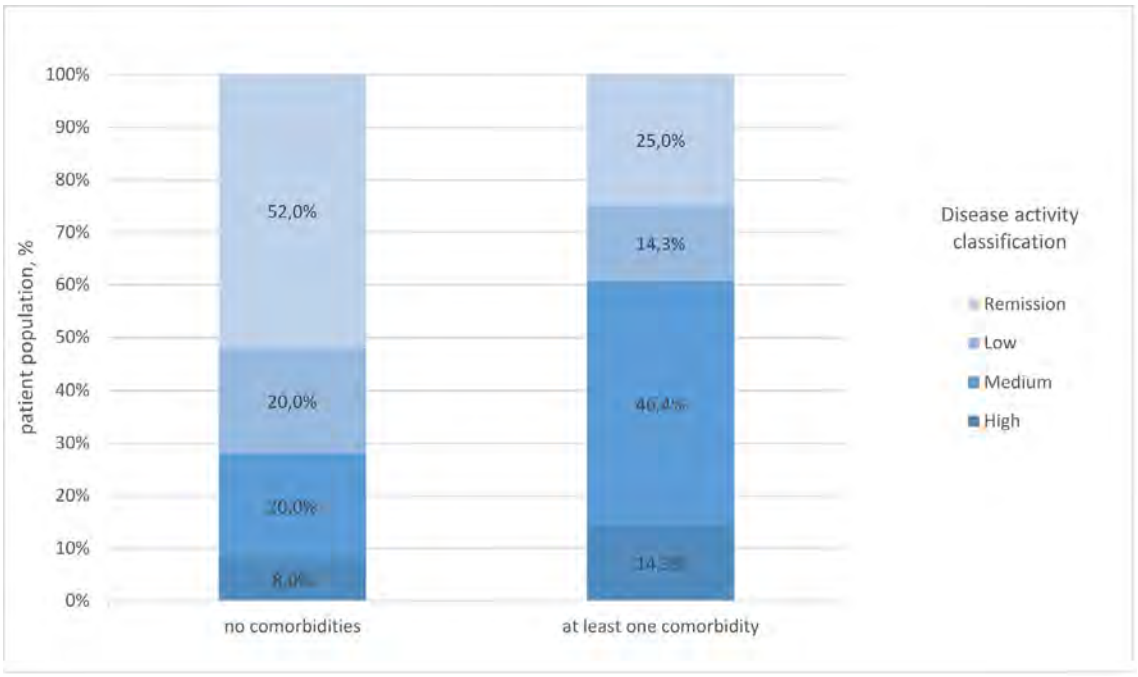

Figure 1. Disease activity DAS28-CRP at clinical visit.

Methods: Adult RA pts. were eligible for inclusion when their initial visit at our tertiary center was between January 2012 and December 2018. Patients and disease characteristics as well as standard assessments using validated outcome parameters for disease activity (DAS28-CRP, SDAI, and ACR/EULAR remission) and physical function (HAQ) were prospectively documented (clinical visit) and values were taken retrospectively from their initial visit (baseline visit) and from the visit at which remission criteria of DAS28-CRP < 2.6 occurred (remission visit).

Results: A total of 137 pts. were examined at their clinical visit between August 2020 and February 2021. Retrospective chart data were available for a follow-up of 33.7 (SD 18.0) months. One third of our cohort already had erosions and severe limitations in physical functioning (table 1). Cardiovascular comorbidities were as common as osteoporosis (both 13.1%). The vast majority of pts. (110 (80.3%)) achieved a state of clinical remission, (DAS28-CRP < 2.6) at least once in a time period of 47.9 (SD 18.9) months. At the clinical visit, 41 pts. (29.9%) were in DAS28 remission. However, using other outcome measures, 23 pts. achieved remission using SDAI (16.8%) and only 17 with Boolean criteria (12.4%), respectively. On average, remission by DAS28-CRP was reached 14.9 (SD 13.8) months after baseline visit. During the observation period pts. achieved remission for 15.8 (SD 10.4) months or 51.3% (SD 25.7) of the time, while 65 pts. (47.4%) achieved sustained remission for at least 6 months. Pts. with comorbidities reached remission less often than pts. without comorbidity (p=0.002). In accordance with the T2T strategy and EULAR recommendations, glucocorticoids were stopped in 47 pts. (34.3%) during the observation period. The remaining 53 pts. (38.7%) were still taking glucocorticoids at the clinical visit, but at a significantly lower dose than at baseline (table 2). The number of pts. on b/ts-DMARD therapy increased significantly from 14.7% at baseline to 59.1% at the clinical visit.

Conclusion: In this study pts. with RA reached remission more often when visited and observed more frequently and for longer periods of time. However, disease activity tends to come back for different reasons. This needs to be

further investigated. Moreover, the data also indicate that in a chronic disease more long term data are needed since short term results may show efficacy but this frequently changes over time in both directions.

Reference: 1 Albrecht Z Rheumatol 2021

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Abstract Number: 0793

Contributing Factors of Good Outcome in Difficult-to-treat Rheumatoid Arthritis: A Multicenter RA Ultrasound Prospective Observational Cohort Study in Japan

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The concept of difficult-to-treat rheumatoid arthritis (D2T RA) has emerged as the greatest unmet need in recent years. We have investigated the clinical characteristics and the contributing factors toward the outcome in patients with D2T RA in the real world setting using a multicenter RA ultrasound prospective observational cohort study.

Methods: We enrolled 366 RA patients from a multicenter prospective ultrasound observational cohort study [KUDOS study] who received biologic or targeted synthetic disease-modifying antirheumatic drugs (b/tsDMARDs) therapy. We evaluated the therapeutic efficacy by the patients' clinical disease activity scores and musculoskeletal ultrasound (MSUS) scores (sum of semi-quantitative evaluation from 22 joints from both wrist and finger joints) every 3 months during 12 months. We defined a D2T RA as a patient with (1) failure of ≥2 b/tsDMARDs and (2) at least moderate disease activity (DAS28-ESR >3.2 or CDAI >10) or inability to taper glucocorticoid treatment (≥7.5 mg/ day prednisone) at baseline. First, we compared characteristics between D2T RA and non-D2T RA. Second, we attempted to identify any variables that were independently contributing factors of the good outcome defined as CDAI remission and treatment continuation at 12 months from the patients' baseline characteristics and types of b/tsDMARD mode of action by performing a multivariate logistic regression analysis.

Results: Among 366 patients with RA, 74 (20.2%) were D2T RA. Disease duration, the positivity of rheumatoid factor, a complication of interstitial pneumonia, concomitant use of glucocorticoids, clinical disease activity scores and MSUS scores were significantly higher in D2T RA compared with non-D2T RA. There was no significant difference in

Table 1. Contributing factors of good outcome at 12 months in patients with D2T RA by multivariate logistic regression analysis

	Comparison	Odds ratio	95% CI	p-value
Age	1 increase	0.93	0.86-1.01	0.07
Rheumatoid factor	Positive	0.32	0.04-2.65	0.29
Concomitant use of MTX	presence	7.09	1.09-46.2	0.040
IL-6 inhibitor	presence	9.61	1.87-49.5	0.0068

the continuation rate at 12 months between D2T RA and non-D2T RA (60.8 vs 67.8%, p=0.44). Clinical and ultrasound remission (CDAI ≤2.8 and PD=0) rates at 12 months were significantly lower in D2T RA compared with non-D2T RA (9.5 vs 24.3%, p=0.0053). When good outcome at 12 months was defined as the achievement of CDAI remission with the continuation of b/tsDMARDs, 14 (18.9%) have achieved a good outcome. Multivariate logistic regression analysis showed that IL-6 inhibitor therapy (odds ratio 9.61, 95% confidence interval [CI] 1.87–49.5, p=0.0068) and concomitant use of methotrexate (MTX) (odds ratio 7.09, 95%CI 1.09–46.2, p=0.040) were independent contributors of good outcome (Table 1).

Conclusion: In our ultrasound cohort study, one-fifth of patients were classified as D2T RA at study entry. In patients with D2T RA, concomitant use of MTX and treatment with IL-6 inhibitors were associated with clinical remission and treatment continuation at 12 months.

Disclosure: S. Kawashiri, None; **T. Michitsuji**, None; **Y. Endo**, None; **A. Nishino**, None; **T. Shimizu**, None; **R. Sumiyoshi**, None; **T. Koga**, None; **N. Iwamoto**, None; **K. Ichinose**, None; **A. Kawakami**, None.

Abstract Number: 0794

Application of Treat to Target and Impact of Sustained Low Disease Activity or Remission on Function in Rheumatoid Arthritis Patients

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Session Time: 8:30AM–10:30AM

Background/Purpose: The aim of this analysis was to compare between enrolment periods RA treatment outcomes and frequency of treating to target, and to assess the impact of target type on long-term function.

Methods: This is a post-hoc analysis of data from the Biologic Treatment Registry Across Canada (BioTRAC). Patients with RA who initiated treatment with infliximab or subcutaneous golimumab were included. Patients were grouped into enrolment periods: 2002-2004, 2005-2008, 2009-2012, 2013-2015, 2016-2017. Achievement of LDA (CDAI LDA or SDAI LDA or SJC≤1), remission (CDAI remission or SDAI remission or SJC=0), and sustained LDA or remission (at 6 and 12 months) were compared between enrolment periods with the Chi-square test and multivariate logistic regression. The impact of achieving LDA or remission at 6 months, 12 months, or both (sustained) on HAQ-DI at 18 months was assessed with one-way ANOVA and generalized linear models.

Results: 1420 patients treated with anti-TNFs (IFX: n=890; GLM: n=530) were included. Over calendar time, a significant decrease in baseline disease duration and disease activity scores (CDAI, SDAI, SJC28, TJC28, HAQ) was observed ($p < 0.001$).

Across enrolment periods, significant differences were observed in target achievement with higher rates observed in more recent years. Upon adjusting for baseline CDAI and prior biologic exposure, no differences between enrolment periods were observed in achieving LDA, remission or sustained LDA/remission at 6 months; however, significantly (p=0.030) higher odds of achieving remission at 12 months were observed in more recent years.

Among patients not achieving LDA at 6 and 12 months, an intervention was applied in approximately 40% of patients, without significant differences between enrolment periods. Between 6 and 12 months, the most common intervention was anti-TNF discontinuation (64.9% of non-LDA achievers), followed by DMARD addition (9.8%), NSAID addition (8.8%), or steroid addition (7.2%). Similar results were obtained post 12 months.

Patients achieving sustained LDA, followed by those achieving LDA either at 6 or 12 months had significantly lower HAQ-DI at 18 months compared to patients not achieving LDA at either timepoint (0.8 vs. 1.1 vs. 1.4; $p< 0.001$). Similar results were observed when evaluating achievement of disease remission albeit with greater impact on HAQ-DI at 18 months (0.7 vs. 1.1 vs. 1.2; $p< 0.001$). Adjustment for baseline HAQ-DI did not impact the results.

Conclusion: Target achievement has increased over time although emphasis in treating to target may be placed in the first 6 months of treatment. Achieving stricter targets was associated with better long-term patient function.

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Abstract Number: 0795

Treatment Response and Several Patient-reported Outcomes Are Early Determinants of Future Self-efficacy in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Self-efficacy (SE), or patients' confidence in their ability to control disease and its consequences, was recently prioritised in EULAR-recommendations for self-management strategies for inflammatory arthritis (1). However, it remains unclear which factors influence SE in rheumatoid arthritis (RA), particularly during early disease.

Methods: We conducted a post-hoc analysis of the 2-year RCT Care in early RA (CareRA), which studied remission-induction treatment regimens for early RA. Participants completed the Arthritis Self-Efficacy Scale (ASES), Short

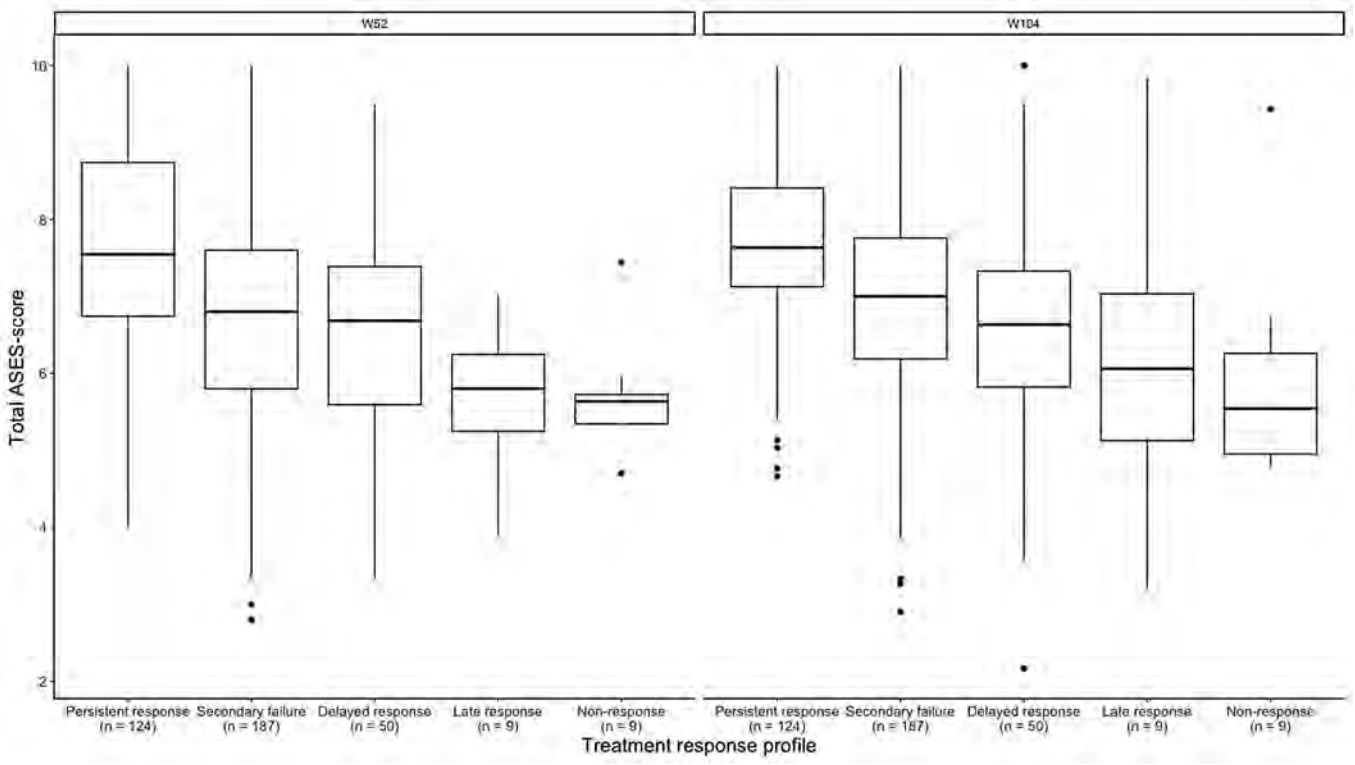

Figure 1. Total ASES-score at week 52 and week 104, stratified by treatment response profile. ASES = Arthritis Self-Efficacy Scale; Persistent response = sustained remission from week 16 to week 104; Secondary failure = loss of remission after week 16; Delayed response = first remission after week 16; Late response = first remission after week 52; Non-response = no remission within 104 weeks.

Form 36 (SF-36), Revised Illness Perception Questionnaire (IPQ-R), Utrecht Coping List (UCL), RAQoL and Health Assessment Questionnaire (HAQ). Depending on time to first remission (DAS28-CRP < 2.6) and persistence of remission, treatment response was defined as persistent response, secondary failure, delayed response, late response or non-response. The association between ASES scores and clinical/psychosocial factors was explored with Spearman correlation and multivariate linear mixed models. Baseline predictors of week 104 ASES were identified with exploratory simple linear regression followed by multiple linear regression of significant predictors adjusted for DAS28-CRP, HAQ, treatment arm, treatment response and demographic/serologic confounders. Models were adjusted for multiple comparisons, setting significance at a = 0.003.

Results: All 379 patients had a recent diagnosis of RA and were DMARD-naïve at study initiation. Most patients were women (69%) and RF/ACPA-positive (66%) and the mean (SD) age was 52 (13) years. For all tested outcome measures, better perceived health correlated with higher SE (Table 1). While patient-reported factors (HAQ, SF-36, RAQoL, IPQ-R, pain, fatigue and patient global assessment) showed moderate/strong correlations with ASES scores, correlations with physician-reported factors (physician global assessment, SJC28), TJC28 and DAS28-CRP were weak. In mixed models, only more favourable outcomes on patient-reported factors and DAS28-CRP were associated with higher ASES scores at each time point.

Table 1. Spearman-coefficients and linear mixed model output for the correlation between total ASES-score and clinical and psychosocial variables at all available time points. Bonferroni-correction for multiple comparisons was applied, setting the significance level at p < 0.003. ASES = Arthritis Self-Efficacy Scale, DAS28 = Disease Activity Score in 28 joints, HAQ = Health Assessment Questionnaire, VAS = Visual Analogue Scale, PGA = patient global assessment, SF-36 MCS = Short-Form 36 mental component score, IPQ-R = Revised Illness Perception Questionnaire, PhGA = physician global assessment, TJC28 = tender joint count in 28 joints, SJC28 = swollen joint count in 28 joints, CRP = C-reactive protein, ESR = erythrocyte sedimentation rate

	Spearman r	ß (95% CI)	P-value
DAS28-CRP	-0.37	-0.22 (-0.32, -0.11)	**<0.001**
HAQ	-0.55	-1.06 (-1.27, -0.84)	**<0.001**
Pain (VAS)	-0.50	-0.14 (-0.19, -0.09)	**<0.001**
Fatigue (VAS)	-0.51	-0.15 (-0.19, -0.10)	**<0.001**
PGA (VAS)	-0.51	-0.16 (-0.21, -0.11)	**<0.001**
SF-36 MCS	0.44	0.40 (0.29, 0.50)	**<0.001**
IPQ-R Illness Coherence	0.46	0.12 (0.09, 0.15)	**<0.001**
IPQ-R Treatment Control	0.46	0.16 (0.12, 0.20)	**<0.001**
IPQ-R Personal Control	0.30	0.09 (0.06, 0.11)	**<0.001**
IPQ-R Consequences	-0.65	-0.17 (-0.19, -0.15)	**<0.001**
IPQ-R Emotional Representations	-0.56	-0.11 (-0.12, -0.09)	**<0.001**
RAQoL	-0.67	-0.11 (-0.12, -0.09)	**<0.001**
PhGA (VAS)	-0.36	-0.12 (-0.19, -0.04)	**0.002**
TJC28	-0.34	-0.01 (-0.06, 0.03)	0.590
SJC28	-0.20	0.01 (-0.04, 0.07)	0.630
CRP	-0.07	0.00 (-0.01, 0.01)	0.550
ESR	-0.08	0.00 (0.00, 0.01)	0.320

Table 2. Baseline and treatment-related predictors of total ASES-score at week 104, based on multivariate linear regression. Predictors were first selected based on significance in univariate linear regression. Results were obtained from multivariate linear regression models predicting total ASES-score at week 104 by predictors that were significant in univariate analyses, and adjusting for age, gender, treatment arm and response, auto-antibody status and baseline HAQ and DAS28-CRP or its components. Bonferroni-correction for multiple comparisons was applied, setting the significance level at $p < 0.003$. ASES = Arthritis Self-Efficacy Scale, HAQ = Health Assessment Questionnaire, VAS = Visual Analogue Scale, PGA = patient global assessment, PhGA = physician global assessment, SF-36 = Short-Form 36, MCS = mental component score, IPQ-R = Revised Illness Perception Questionnaire, UCL = Utrecht Coping List

Variables	ß (95% CI)	P-value	Adjusted R^2
Clinical/demographic			
Gender (male)	0.33 (0.06, 0.60)	0.025	0.160
Treatment response	-0.47 (-0.63, -0.31)	**<0.001**	0.160
HAQ	-0.72 (-0.96, -0.48)	**<0.001**	0.160
Pain (VAS)	-0.01 (-0.08, 0.06)	0.82	0.160
Fatigue (VAS)	-0.04 (0.10, 0.02)	0.22	0.161
PGA	-0.01 (-0.08, 0.07)	0.82	0.160
PhGA	0.06 (-0.02, 0.15)	0.13	0.163
SF-36			
MCS	0.30 (0.18, 0.42)	**<0.001**	0.231
Vitality	0.15 (0.08, 0.23)	**<0.001**	0.212
Social Function	0.08 (0.02, 0.15)	0.009	0.194
Mental Health	0.20 (0.13, 0.28)	**<0.001**	0.236
Role Emotional	0.07 (0.04, 0.10)	**<0.001**	0.222
IPQ-R			
Illness coherence	0.07 (0.04, 0.10)	**<0.001**	0.217
Treatment control	0.09 (0.03, 0.14)	**0.002**	0.200
Personal control	0.05 (0.01, 0.09)	0.008	0.194
Emotional representations	-0.07 (-0.10, -0.05)	**<0.001**	0.262
Consequences	-0.06 (-0.10, -0.03)	**<0.001**	0.209
UCL			
Passive reacting	-0.08 (-0.12, -0.04)	**<0.001**	0.208
Active tackling	0.03 (-0.01, 0.07)	0.098	0.185
RAQoL	-0.04 (-0.07, -0.02)	**0.001**	0.203

An earlier, persistent treatment response predicted higher ASES scores at both week 52 and 104 (Fig. 1). Significant baseline predictors of week 104 ASES included HAQ; SF-36 dimensions Mental Component Score, Vitality, Mental Health and Role Emotional; IPQ-R dimensions Illness coherence, Treatment control, Emotional representations and Consequences; UCL dimension Passive reacting and the RAQoL (Table 2).

Conclusion: Patient-reported outcomes and treatment response were important early determinants of long-term SE in an early RA clinical trial. These results provide further relevance for the window of opportunity in an early treat-to-target strategy. In addition, our results could help to timely identify patients who might benefit the most from self-management treatment strategies or interventions to improve SE. Further prospective research is needed to confirm these findings.

(1) Nikiphorou E, et al. EULAR recommendations for the implementation of self-management strategies in patients with inflammatory arthritis. Ann Rheum Dis 2021

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Abstract Number: 0796

Validation of the Simplified Disease Activity Index (SDAI) with a Quick Quantitative C-reactive Protein Assay (SDAI-Q) in Patients with Rheumatoid Arthritis: A National, Multicenter Study

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SESSION INFORMATION

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Background/Purpose: Therapeutic decisions in RA patients should be based on regular disease activity assessment using scores like the Simplified Disease Activity Index (SDAI) or the Clinical Disease Activity Index (CDAI) [1]. The CDAI has the benefit of being immediately available, while the SDAI encompasses with the C-reactive protein (CRP) an acute phase reactant and therefore is the recommended score for the use in clinical trials. However, CRP

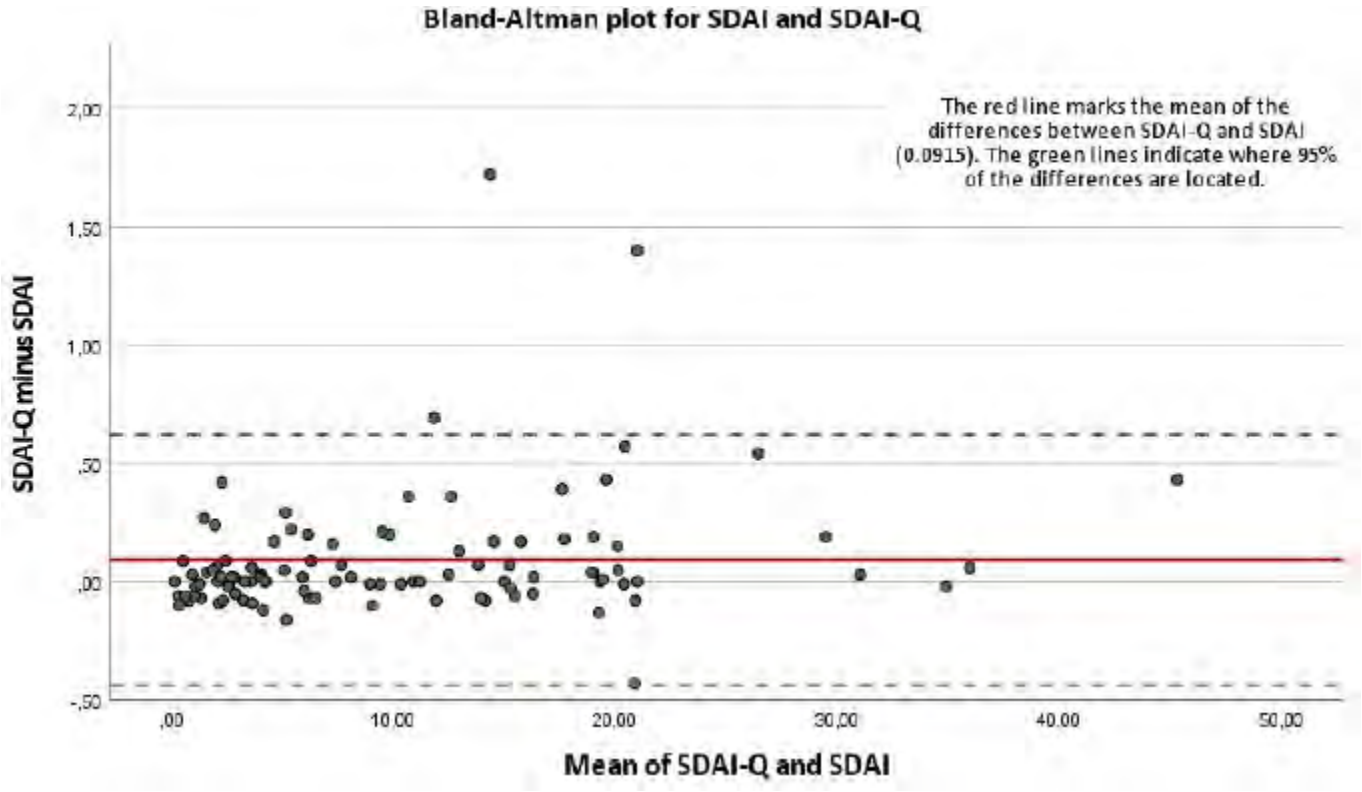
determination takes hours to days, thus hindering the treat-to-target concept using the SDAI. Quick quantitative CRP (qCRP) tests allow CRP measurement within a few minutes. Therefore, qCRP based SDAI (SDAI-Q) could combine the advantages of both scores. The objective of our study was to validate the SDAI-Q in a prospective, multicenter study of RA patients.

Table 1. A) Disease activity categories by SDAI-Q vs. SDAI; B) Disease activity categories by SDAI-Q vs.CDAI

A		SDAI-Q (n = 100)			
		Remission (≤ 3.3)	Low Disease Activity (> 3.3 and ≤ 11)	Moderate Disease Activity (> 11 and ≤ 26)	High Disease Activity (> 26)
SDAI	Remission (≤ 3.3)	28 (28.0%)			
	Low Disease Activity (> 3.3 and ≤ 11)		31 (31.0%)		
	Moderate Disease Activity (> 11 and ≤ 26)			35 (35.0%)	
	High Disease Activity (> 26)				6 (6.0%)

B		SDAI-Q (n = 100)			
		Remission (≤ 3.3)	Low Disease Activity (> 3.3 and ≤ 11)	Moderate Disease Activity (> 11 and ≤ 26)	High Disease Activity (> 26)
CDAI	Remission (≤ 2.8)	26 (26.0%)			
	Low Disease Activity (> 2.8 and ≤ 10)	2 (2.0%)	28 (28.0%)	2 (2.0%)	
	Moderate Disease Activity (> 10 and ≤ 22)		3 (3.0%)	33 (33.0%)	
	High Disease Activity (> 22)				6 (6.0%)

Fields highlighted in red indicate that disease activity categories do not match.
SDAI = Simplified Disease Activity Index;
SDAI-Q = SDAI calculated with a quick quantitative CRP assay;
CDAI = Clinical Disease Activity Index.



Bland-Altman plot for SDAI and SDAI-Q.

Methods: The study was conducted in five centers in Berlin, Germany. Consecutive adult (≥ 18 years) RA patients were included. In addition to a rheumatological assessment, including patient reported outcomes, routine CRP was measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument“ (Aidian Oy, Finland) was performed locally (measurement range 0.5 - 200 mg/l). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for CRP, qCRP, SDAI, SDAI-Q and CDAI.

Results: In this study 100 RA patients were included (mean age: 60.9 years, mean disease duration: 11.4 years, 73.0% were female, 63.0% RF positive, 57.0% ACPA positive, 49.0% positive and 29% negative for both parameters). 75.0% were treated with csDMARD, 15% with tsDMARDs, 39.0% with bDMARDs and 40% with glucocorticoids (mean prednisolone equivalent: 5.4 mg prednisolone/d). Mean CRP and qCRP-levels were 6.97 and 7.89 mg/l, respectively (ICC 0.992; 95%CI: 0.987; 0.995). Comparing SDAI-Q and SDAI, all patients (100%) achieved the same disease activity status (Table 1A); weighted Cohen´s kappa was 1.000 (95%CI: 1.000; 1.000). ICC for SDAI-Q- and SDAI-values was 1.000 (95%CI: 1.000; 1.000). The agreement of SDAI-Q and SDAI is shown in a Bland-Altman plot (Figure 1). When comparing the CDAI with the SDAI-Q 93 patients (93%) were assigned to the same disease activity category (Table 1B); weighted Cohen´s kappa was 0.929 (95%CI: 0.878; 0.981). ICC for numerical values of SDAI-Q and CDAI was 0.989 (95%CI: 0.978; 0.994).

Conclusion: SDAI-Q showed an absolute agreement with SDAI on the assignment to disease activity categories with the important advantage of time. With SDAI-Q, rheumatologists could base their clinical decision-making immediately on an index-based disease activity measurement by using a composite score considering acute phase reactants. Consequently, SDAI-Q can be integrated in clinical routine and clinical trials and could be implemented into the treat-to-target concept in RA patients.

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Abstract Number: 0797

Psychosocial Wellbeing and Illness Perceptions During the Early Disease Phase Predict Sustained Remission in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patient-reported outcomes (PROs) relating to global psychosocial wellbeing are rarely assessed in clinical trials for rheumatoid arthritis (RA), and specifically not to tailor additional interventions. Moreover, many patients with RA report ongoing pain, fatigue and suboptimal mental health despite satisfactory clinical disease control. We aimed to describe the association of early psychosocial wellbeing, coping and illness perceptions with sustained remission in early RA, and to identify patients with psychosocial unmet needs despite being in clinical remission.

Methods: Data were analysed from the 2-year randomised controlled treat-to-target trial Care in early RA (Care-RA). Patients completed the Short Form 36 (SF-36), Revised Illness Perception Questionnaire (IPQ-R) and Utrecht Coping List (UCL) among other PROs. Sustained remission was defined as continued DAS28-CRP < 2.6 from week 16 to week 104. SF-36 mental components, UCL and IPQ-R at baseline and week 16 were studied as predictors of sustained remission with multivariate logistic regression adjusting for age, gender, treatment arm, serology and 2-component DAS28 (1). Subgroups of patients in remission at week 16 were identified by Latent Profile Analysis (LPA) including significant psychosocial predictors from the regression models. Survival of remission was compared per subgroup by Kaplan-Meier analysis and Cox proportional hazards regression.

Results: All 379 included patients were recently diagnosed with RA and had not received DMARDs before study initiation. Most patients were women (69%) and RF/ACPA-positive (66%), with a mean age of 52 (SD 13) years. Sustained DAS28 CRP-remission was achieved by 124/379 (33%) patients. Sustained remission was associated with higher SF-36 scores and less passive coping at baseline, and with higher SF-36 scores and more positive IPQ-R reports at week 16 (Table 1). Among patients in DAS28-CRP remission at week 16 (n=287), two subgroups

Table 1. Psychosocial variables at baseline and week 16 predicting sustained remission. Results were obtained from multivariate logistic regression models with the specified variables as predictors and the odds of sustained DAS28-CRP-remission (from week 16 to week 104) as the dependent variable. All models contained age, gender, treatment arm, the presence of autoantibodies and 2C-DAS28 as covariates. OR = odds ratio, CI = confidence interval; SF-36 = Short Form 36, MCS = mental component score, VT = vitality, SF = social function, MH = mental health, RE = role emotional; IPQ-R = Revised Illness Perception Questionnaire; UCL = Utrecht Coping List; 2C-DAS28 = two-component Disease Activity Score in 28 joints

	Baseline		Week 16	
Variable	**OR (95% CI)**	**P-value**	**OR (95% CI)**	**P-value**
SF-36				
SF-36MCS	1.33 (1.08 – 1.64)	**0.011**	1.84 (1.38 – 2.45)	**<0.001**
SF-36VT	1.25 (1.11 – 1.41)	**<0.001**	1.44 (1.25 – 1.65)	**<0.001**
SF-36SF	1.17 (1.07 – 1.28)	**<0.001**	1.42 (1.25 – 1.62)	**<0.001**
SF-36MH	1.23 (1.08 – 1.40)	**0.003**	1.48 (1.26 – 1.74)	**<0.001**
SF-36RE	1.06 (1.00 – 1.12)	**0.047**	1.19 (1.10 – 1.29)	**<0.001**
IPQ-R				
Illness coherence	1.06 (1.00 – 1.13)	0.052	1.11 (1.04 – 1.19)	**0.006**
Treatment control	1.07 (0.97 – 1.17)	0.188	1.18 (1.07 – 1.31)	**0.008**
Personal control	1.02 (0.96 – 1.09)	0.521	1.08 (1.00 – 1.17)	**0.048**
Emotional representations	0.98 (0.94 – 1.02)	0.357	0.94 (0.90 – 0.98)	**0.005**
Consequences	0.97 (0.92 – 1.02)	0.277	0.88 (0.83 – 0.93)	**<0.001**
UCL				
Active tackling	0.99 (0.92 – 1.06)	0.841	1.07 (0.99 – 1.15)	0.156
Palliative reacting	0.98 (0.92 – 1.05)	0.685	0.97 (0.91 – 1.05)	0.303
Avoidance	0.98 (0.91 – 1.05)	0.508	0.96 (0.89 – 1.04)	0.175
Seeking social support	1.04 (0.97 – 1.12)	0.224	1.06 (0.98 – 1.15)	0.168
Passive reacting	0.92 (0.85 – 0.99)	**0.037**	0.93 (0.86 – 1.01)	0.086
Expression of emotion	1.01 (0.88 – 1.16)	0.727	1.10 (0.94 – 1.28)	0.340
Reassuring thoughts	0.98 (0.89 – 1.08)	0.666	1.03 (0.93 – 1.13)	0.625

were identified: a low-psychosocial-burden (n=231) and a high-psychosocial-burden group (n=56) (Fig. 1). The low-psychosocial-burden group retained remission longer (HR 0.51 [0.35-0.73]) (Fig. 2).

Conclusion: Suboptimal psychosocial wellbeing and illness perceptions were associated with lower odds of sustained remission in an early RA trial. Illness perceptions appeared to be more clinically relevant after 4 months of treatment. One-in-five patients still showed worse psychosocial outcomes despite being in early clinical remission, and these patients tended to lose remission earlier. Future research should focus on timely identification of unmet needs and person-centred interventions to target them.

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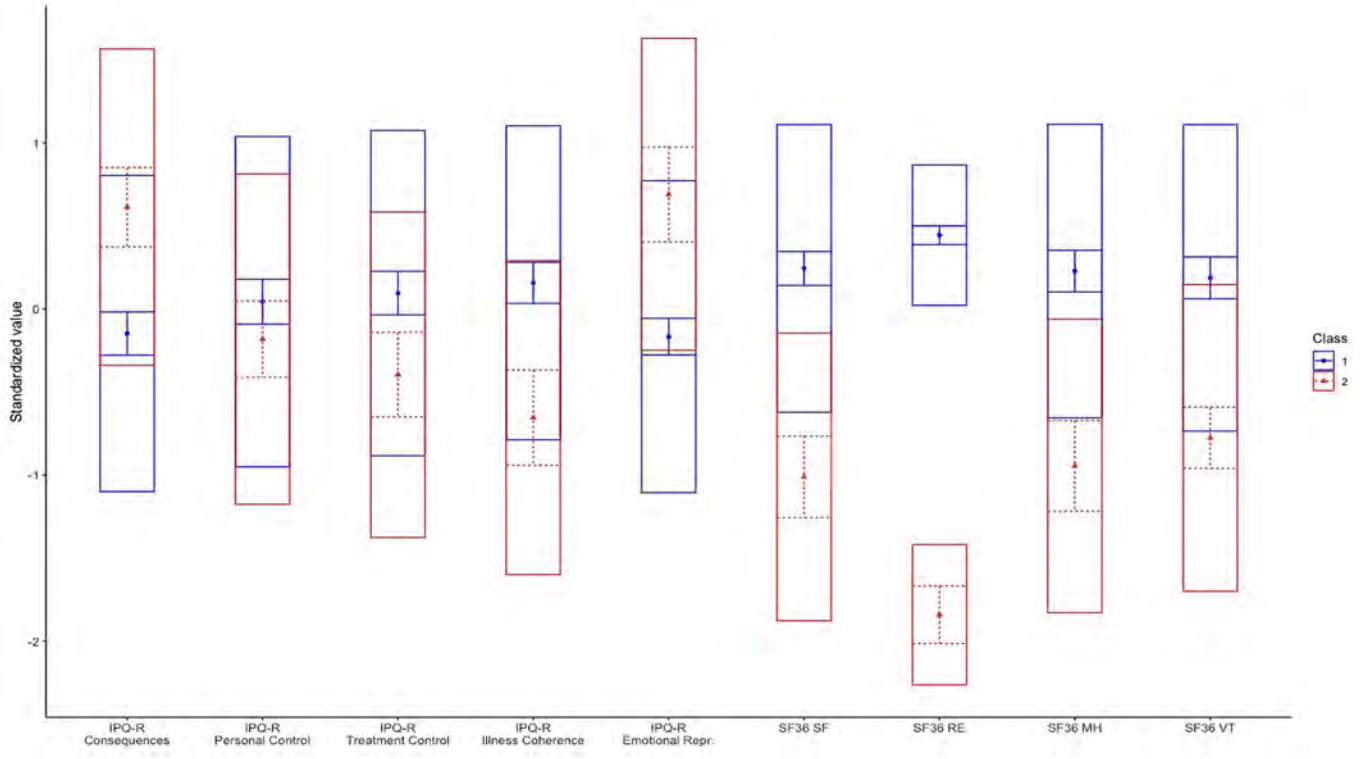

Figure 1. Clustering of patients in DAS28-CRP remission at week 16 by LPA of psychosocial variables. Results of latent profile analysis (LPA) of patients in DAS28-CRP remission at week 16, based on 9 psychosocial variables. Optimal model fit was obtained for 2 classes with equal variances and equal covariances. Class 1 consists of 231/287 patients (80%) and class 2 of 56/287 patients (20%). IPQ-R = Revised Illness Perception Questionnaire; SF36 = Short Form 36, VT = vitality, SF = social function, MH = mental health, RE = role emotional.

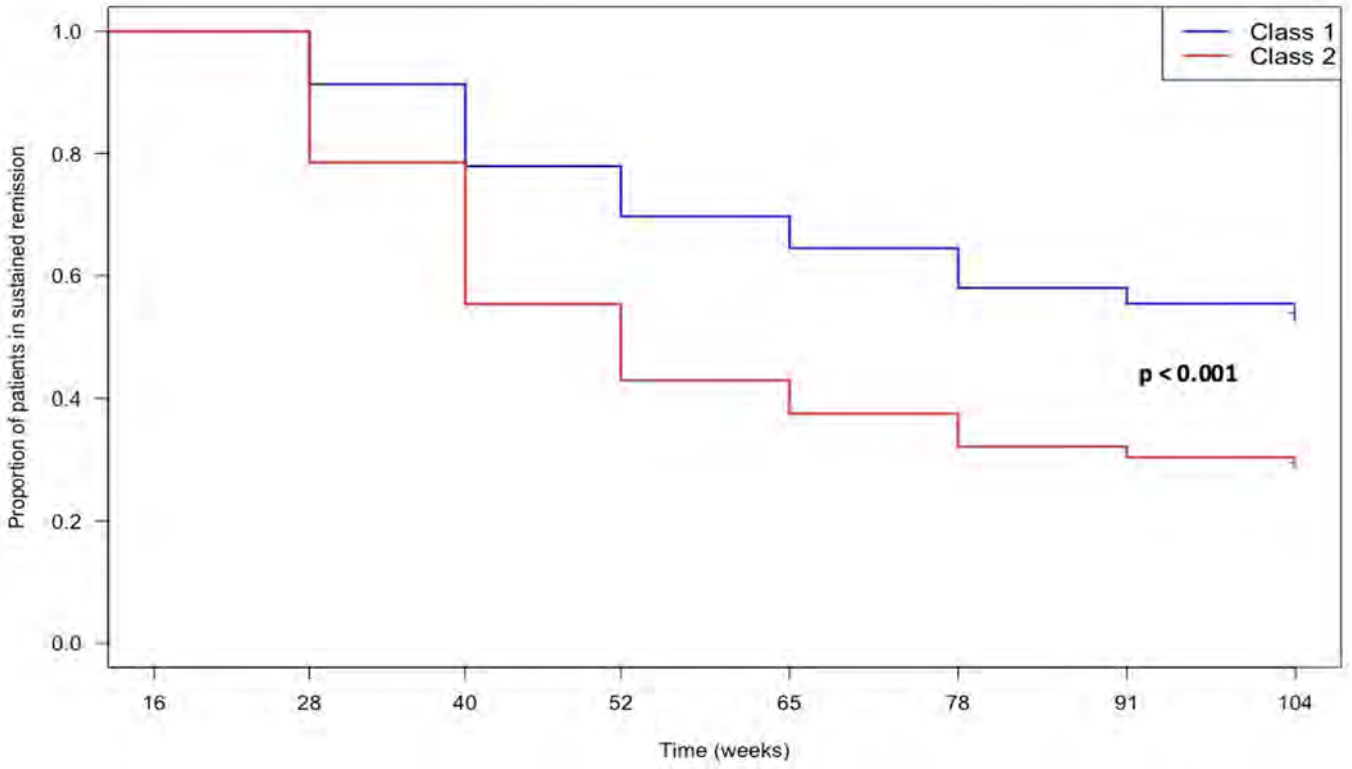

Figure 2. Kaplan-Meier (KM) curves for survival of DAS28-CRP remission, stratified by psychosocial class of patients in DAS28-CRP remission at week 16.

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Abstract Number: 0798

The Impact of Comorbidities on the Simple Disease Activity Index (SDAI) and Its Components over the First Year of Follow-up – an Analysis from the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

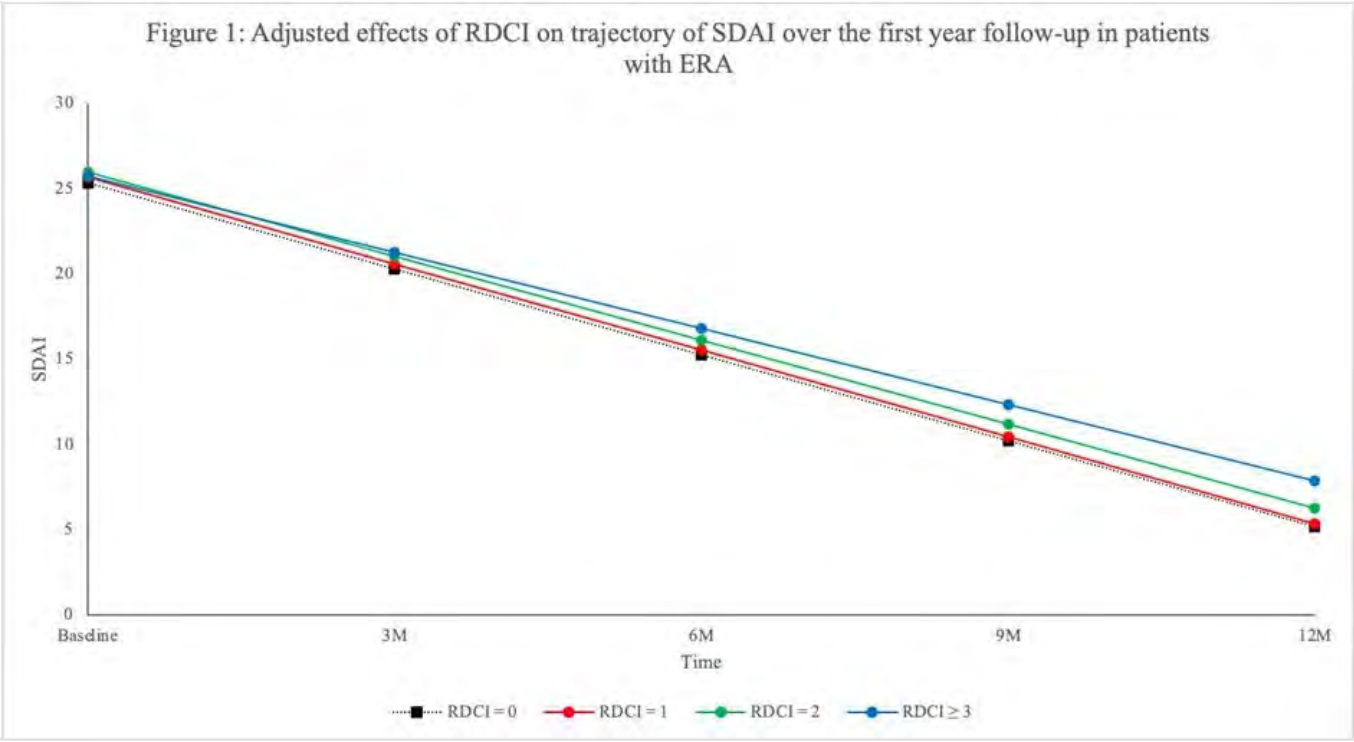
Session Date: Sunday, November 7, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Comorbid conditions have been shown to negatively influence the achievement of treatment targets in rheumatoid arthritis (RA) patients. The comorbid conditions may bias the subjective measures of the widely

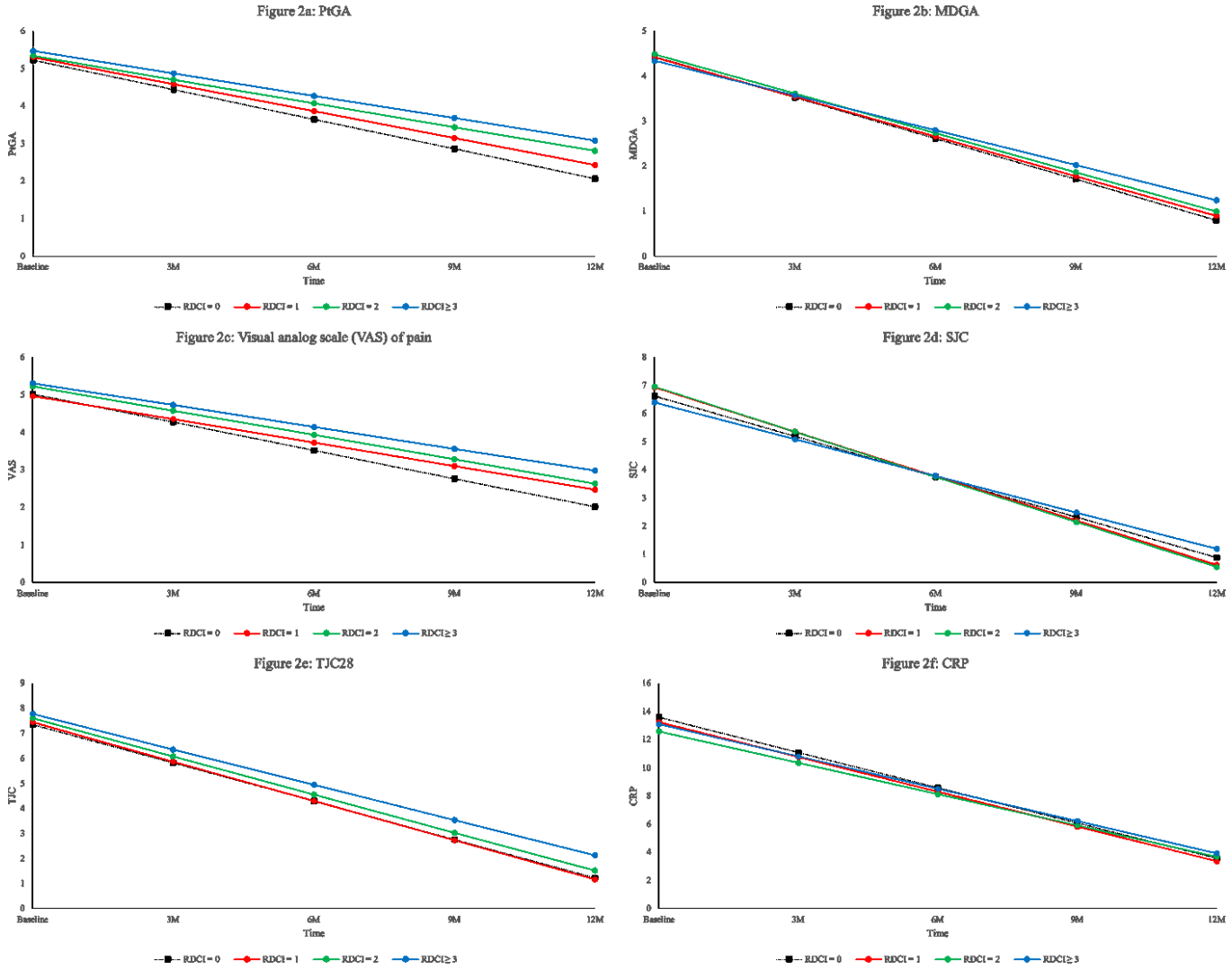


Adjusted effects of RDCI on trajectory (predictive margins) of SDAI over the first year follow-up in patients with ERA.

used indices for evaluation of disease activity. The objective is to look at the relationships between comorbidities and components of common clinical disease activity scores, such as tender (TJC) and swollen (SJC) joint count, patient global assessment (PtGA), physician global assessment (MDGA), C-reactive protein (CRP) and pain in early RA.

Methods: Using a validated tool for the assessment of comorbidity burden specifically developed for rheumatology, the Rheumatic Disease Comorbidity Index (RDCI), the influence of comorbidities on each component's trajectory in time has been assessed in early rheumatoid arthritis (ERA) patients over the first year of treatment with conventional synthetic DMARDS using data from the Canadian Early Arthritis Cohort (CATCH). The adjusted effects of RDCI scores (0, 1, 2, and ≥ 3) on the trajectory of the SDAI, on each component of the SDAI, and on pain (visual analog scale) was evaluated over the first year of follow-up with generalized estimating equations (GEE). Data were adjusted for possible confounders including baseline sociodemographic factors, disease activity and treatments.

Results: This sample size included 2248 ERA patients with a mean symptom duration (SD) of 5.71 (2.96) months; mean age (SD) was 55 (15) years old and 72% were female. At baseline, 1664 (74%) were treated with methotrexate with a mean weekly dose (SD) of 20.0 mg (4.2) and 1340 (60%) also received other conventional synthetic DMARDs. The mean (SD) SDAI at enrolment was 29 (15) and 90% were classified as having moderate-high SDAI. RDCI scores



Adjusted effects of RDCI on trajectory (predictive margins) of PtGA, MDGA, pain, and SJC over the first-year follow-up in patients with ERA.

of 0, 1, 2 or ³3 were obtained in 888 (40%), 547 (24%), 451 (20%), and 362 (16%) participants, respectively. Although disease activity did not differ by comorbidity status at baseline, patients with RDCI of 0 had better improvement (rate of change) in SDAI (Figure 1), PtGA, MDGA and pain (Figure 2a,b,c) over time relative to patients with multiple RDCI conditions ($p< 0.05$). A significant higher rate of change in SJC was observed in patients with RDCI of 1 and 2 compared with participants having higher RDCI score ($p= 0.01$) (Figure 2d). The RDCI scores were not significantly associated with the change of TJC and CRP (Figure 2e and f) over one year.

Conclusion: In this ERA cohort, having multiple comorbidities was associated with worse improvement and disease activity assessed by SDAI over the first year of treatment. SJC, PtGA, and MDGA were the components of SDAI that were most influenced by the presence of comorbidities. The results demonstrate a negative effect of having comorbidities at disease onset of RA on the evolution of both patients and physicians reported outcomes.

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Abstract Number: 0799

Relationships of Rheumatology Care and Patient Experiences to Rheumatoid Arthritis Remission

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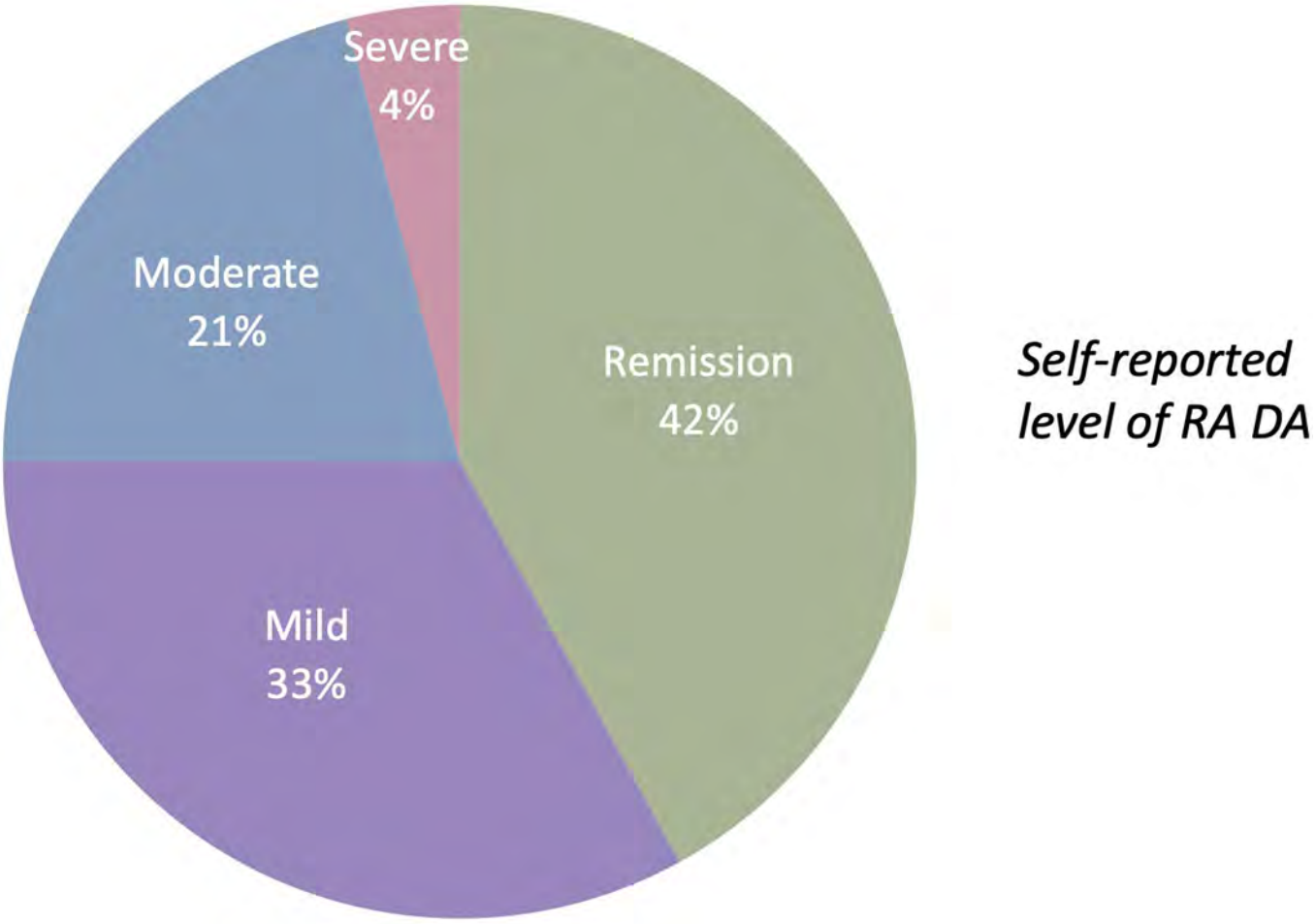
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

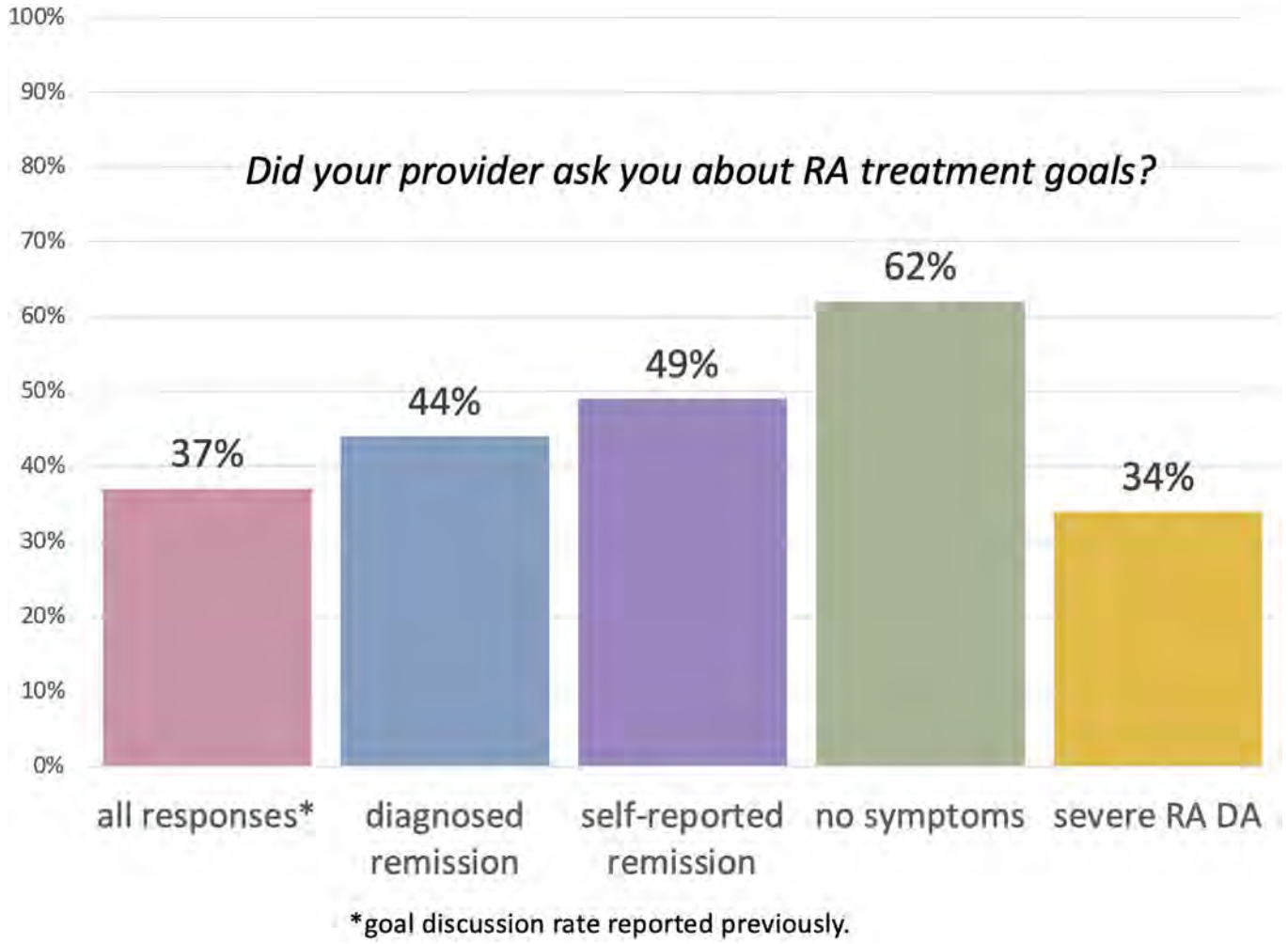
Background/Purpose: Remission is a well-established optimal outcome in rheumatoid arthritis (RA) treatment, yet a minority of patients reach this goal. There is not one recognized definition for RA remission, but several sets of criteria regarded as remission or low disease activity. Except aggressive treatment and less time between diagnosis and treatment, little is known of what factors may impact RA remission. Building on a long-term collaboration of a non-profit organization and an academic rheumatology center, we explored factors associated with RA remission.



Patient-assessed Disease Activity (DA) in Diagnosed RA Remission: Figure 1. Respondents replying "Yes" to "Does your doctor consider your RA to be in remission?" are divided by their replies to the question "What is your current level of RA disease activity?".

Methods: An anonymous survey was offered in 2019 on a secure online system. Participants were U.S. residents age ≥18 years with a self-reported RA diagnosis by a medical professional. They responded to questions on demographics, RA disease activity (DA), diagnosis and DMARD history, improvement from treatment, and RA treatment goals. Analyses included descriptive statistics with chi-square and rank sum tests for comparisons. Treatment goals were thematically coded and verified for reliability by a team using qualitative content analysis.

Results: The questionnaire was completed by 907 RA patients (90% women, 10% men), with 58 (11) mean (SD) years age and 11 (10) years since diagnosis. About twice as many reported being given an explicit diagnosis of RA remission (n=102; 11%) as patients who rated their DA as "in remission" (n=49; 5%). Patients rating their DA as in remission tried fewer different DMARDs than patients with more active disease (mean: remission 3.3; mild 4.2; moderate 5.7; severe DA 8.8). Those with diagnosed remission tried fewer mean DMARDs (4.7) than all respondents (5.8). Both self-reported remission and diagnosed remission were associated with less time between symptom onset and DMARD treatment. In both groups, about 35% were treated < 6 months of onset, but in all respondents, only 24% were treated this early. Both remission groups were associated with older current age and older age at diagnosis. Both remission groups were more likely to have had discussions with providers about RA treatment goals (diagnosed, 44% self-report, 51%) than all patients surveyed (37%).



RA Remission and Shared Treatment Goal Discussions: Figure 2. Patients in each category were asked whether their providers had discussed RA treatment goals with them.

Conclusion: This survey found previously unreported associations between remission and aspects of rheumatology care including time from symptom onset to treatment, age at diagnosis, and frequency of shared treatment goal discussions, independent of whether remission was clinically diagnosed or based on patient-reported DA levels. Our study is unique in that diagnosed remission is compared to self-reported DA "in remission," the former being twice as frequent. Further research should seek greater insight on patient experiences in remission and explore how factors associated with remission may be used to increase the rate of remission in people with RA.

Survey questions	Reported DA "in remission" n=49	Diagnosed remission n=102	All respondents n=907
Current age mean (SD)	60.3 (11.4)	60.1 (10.1)	57.9 (10.8)
Age at diagnosis mean (SD)	50.2 (13.3)	47.9 (15.2)	46.9 (12.9)
Years from diagnosis to treatment mean (SD)	1.7 (7.2)	1.4 (5.9)	0.9 (3.8)
Years since diagnosis mean (SD)	9.8 (8.6)	11.9 (10.8)	11.1 (10.1)
How many different DMARDs used mean (SD)	3.3 (3)	4.7 (3.7)	5.8 (4.4)
Highest level of improvement with DMARDs			
<20% improvement	1 (2%)	3 (3%)	129 (14%)
~20% improvement	2 (4%)	5 (5%)	157 (17%)
~50% improvement	2 (4%)	24 (24%)	277 (31%)
~70% improvement	13 (27%)	27 (26%)	197 (22%)
≥90% improvement	31 (63%)	43 (42%)	147 (16%)
How would you describe your current health?			
Very good	19 (19%)	17 (35%)	53 (6%)
Good	50 (49%)	23 (47%)	304 (34%)
Fair	24 (24%)	8 (16%)	355 (39%)
Poor	7 (7%)	0 (0%)	142 (16%)
Very poor	2 (2%)	1 (2%)	52 (6%)
Time from symptom onset to treatment			
<6 months (percent of group)	17 (35%)	36 (35%)	216 (24%)
6 months – 5 years	25 (51%)	42 (41%)	432 (48%)
>5 years	6 (12%)	23 (23%)	243 (27%)

Diagnosed remission in RA compared to patient-reported disease activity "in remission."

Disclosure: K. O'Neill, None; **K. Marks**, None; **P. Sinicrope**, None; **C. Crowson**, None; **E. Myasoedova**, None; **J. Davis**, Pfizer, 5.

Abstract Number: 0800

Digital Spatial Profiling Reveals Distinct Synovial Tissue Transcriptomic Signature of Sustained Disease Remission in Rheumatoid Arthritis Patients at Risk of Disease Flare After Treatment Tapering or Discontinuation

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Sustained disease remission is the treatment goal for Rheumatoid Arthritis (RA) leading patients to be eligible to treatment tapering or discontinuation. However, disease flare is an unpredictable event after treatment change representing a burden for RA. The study aims were to assess the impact of clinical classification on synovial tissue (ST) inflammation in sustained remission RA and to identify biomarkers of disease flare after treatment modification.

Methods: 152 RA in sustained clinical (84 RA with DAS< 1.6 and 68 RA fulfilling Boolean remission criteria for at least 9 months, respectively) and ultrasound (US) remission (PDneg) under Methotrexate with or without biological-Disease Modifying Anti-Rheumatic Drug (bDMARD) underwent US guided ST biopsy and were enrolled in the study. 240 naive RA were enrolled as comparison group. For each patient, synovitis degree was determined using a H&E-based semiquantitative score[1]. Some ST samples of naive RA and RA in remission were used for digital spatial profiling (GeoMx DSP, Nanostring) to quantitate transcript abundance in spatially distinct regions of interest (ROIs) within ST. RA in remission were randomly assigned to tapering/discontinuation (TAP/DISC) group (tapering c- or b-DMARD treatment for 6 months first and discontinuing c- or bDMARD afterwards) or maintaining the therapy unchanged (CONT). Each RA was followed every 3 months to assess disease flare rate after treatment modifications for at least 6 months.

Results: Considering the whole RA cohort, despite either DAS- and Boolean-defined remission RA had significantly lower KSS than naive RA (p< 0.0001 for both), RA in Boolean remission had lower KSS compared to RA in DAS-defined remission (p< 0.0001). In particular, ST of RA in Boolean remission showed lower stromal density (p< 0.0001) and inflammatory infiltrate scores (p=0.0003) together with lower lymphocytes (p=0.003) and plasmacells presence rates (p=0.015) than ST of RA with DAS-defined remission. Among the whole cohort, 54(35.5%) RA had a disease flare regardless the treatment change. Moreover, RA with DAS-defined remission who had a disease flare within at least 6 months follow-up had, at study entry, significantly higher KSS (p=0.0005) than RA who maintained a sustained remission, regardless to the treatment change (CONT:p=0.0275 and TAP/DISC:p=0.0112, respectively). Conversely, RA in Boolean-defined remission did not differ in terms of ST inflammation at study entry in the CONT (p >0.05) as well as in the TAP/DISC (p >0.05) subgroup. However, DSP analysis revealed that ROIs in ST of RA in Boolean remission had a unique transcriptomic signature characterized by 298 differentially expressed genes belonging to 26

pathways compared with RA in DAS-defined remission, whose over-expression, identifies ROIs from ST of RA who had disease flare.

Conclusion: DAS- and Boolean-based remission definitions in RA mirror differential degree of residual subclinical synovitis and are characterized by distinct ST transcriptomic signature which identifies RA in remission at higher risk of disease flare after treatment modification.

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Abstract Number: 0801

Early Remission at 6 Months as a Predictor of Longterm Remission in New Onset Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Early therapeutic intervention is crucial for patients with early rheumatoid arthritis (ERA). The goal of remission is achievable in a large proportion of ERA patients.

To evaluate the rate of patients in remission at 6 months and to correlate the 36 and 60 months remission rate in the Belgian CAP48 cohort and the UCLouvain Brussels cohort. To identify baseline characteristics differences between patients achieving remission or not.

Methods: We included patients with ERA from the CAP48 cohort and from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 RA classification criteria. All patients were naïve to csDMARDs therapy. We collected patient characteristics at baseline and clinical response was analysed at 6, 36 and 60 months.

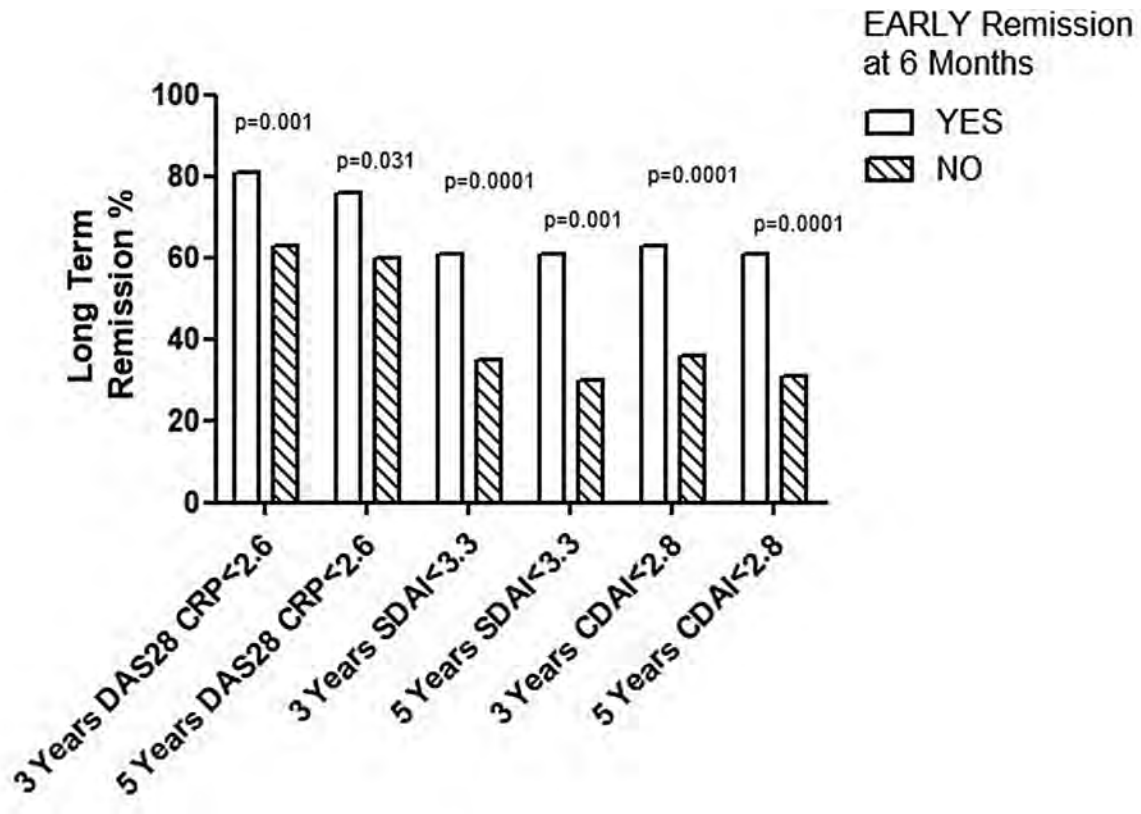
Results: 287 RA patients from our UCLouvain Brussels Cohort and the CAP48 cohort were analysed (211 Females, 76 Males, mean age 46.2 years, 43.4% with baseline erosion, 70.1% with ACPA, 70.3% with Rheumatoid Factor, mean HAQ 1.16, mean DAS28-CRP 4.67, mean SDAI 24.9 and mean CDAI 24.1).

The clinical results are summarized in the Table.

We divided the patients according to whether they achieved remission DAS28-CRP < 2.6 (group 1), or not (group 2) at 6 months.

Patient baseline characteristics were similar in the two groups respectively: age (46.7 vs 45.4 yrs); female (68.5 vs 77.3%); smoker (25.6 vs 27.0%); ACPA positive (70.1 vs 75.4%); baseline X-ray erosion (45.0 vs 54.7%).

DAS28-CRP, SDAI and CDAI at 6 months could predict long-term remission at 36 and 60 months (Figure).



In group 1 global remission (DAS28-CRP< 2.6, HAQ< 0.5 and no X-ray progression) was observed in 75.6% at 60 months. The majority of these patients (69.4%) are still treated with Methotrexate, the others were treated with combination therapy.

Conclusion: Early and long term remission is an achievable goal in our two cohorts. Early diagnosis is critical in standard of care. At 6 months, all remission index criteria are good predictor for long term remission and could be used in daily care.

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Abstract Number: 0802

Infection in Rheumatoid Arthritis Patients Treated with Golimumab

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SESSION INFORMATION
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Background/Purpose: Biologic use in RA is a well-characterized risk factors for infections. The aim of this analysis was to characterize the incidence of infection in RA patients treated with golimumab in Canadian routine care, as well as assess the impact of oral corticosteroid (CS) and DMARD use on infection.

Methods: This is a post-hoc analysis of the Biologic Treatment Registry Across Canada (BioTRAC). Patients with RA who initiated treatment with subcutaneous golimumab were included in this analysis. The incidence density rates (IDR) of total, serious (SI), and non-serious (NSI) infections were calculated for the overall follow-up period as well as by 6-month interval. Negative binomial and cox regressions were used to assess the impact of CS and DMARD use, as well as CS and methotrexate (MTX) dose levels. Time to first infection and time to treatment discontinuation were assessed with the Kaplan-Meier estimator of the survival function, and the impact of concomitant CS and DMARD use was assessed with the log rank test.

Results: 530 patients were included with a mean (SD) age of 57.7 (13.0) years and disease duration of 8.0 (8.3) years. Of these 74 (14.0%) were treated with ≤15mg/week MTX, 280 (52.8%) with >15mg/week MTX, while 173 (32.6%) were not on MTX. In terms of CS, 72 (13.6%) were treated with ≤5mg/day, 63 (11.9%) with >5mg/day, and 391 (73.8%) were not on CS.

Over a mean follow-up duration of 27.0 months, the IDR for total infections, NSI, and SI was 35.10 events/100 PYs, 32.90 events/100 PYs, and 2.23 events/100 PYs. Median estimated time to first infection was 52.9 months (SI: 84.9 months; NSI: 55.1 months). The incidence of total infections was 44.0, 37.3, 35.1, 29.4, 31.1, 35.7, 19.3, 7.4 and 0.0 events/100 PYs at 0-6 months, 6-12 months, 12-24 months, 24-36 months, 36-48 months, 48-60 months, 60-72

months, 72-84 months and 84-90 months, respectively. Longer follow-up duration was significantly associated with higher number of NSI (HR [95%CI]: 1.011 [1.006-1.017]) but not SI (1.011 [0.988-1.035]), while neither the use of DMARD, CS nor MTX was found to have an impact.

Conclusion: Higher IDR was observed during the first 6 months of treatment and decreasing thereafter. CS and DMARD treatment did not impact retention of golimumab treatment. These results support the notion that CS should be used concomitantly with anti-TNF for the shortest period possible to achieve remission, and then tapered.

Disclosure: L. Bessette, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Sandoz, 2, 5, 6, Sandoz, 2, 5, 6, Gilead, 2, 5, 6, Fresenius Kabi, 2, 5, 6, Teva, 2, 5, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **J. Kelsall**, None; **J. Purvis**, Pfizer, 1, Celltrion, 1, Sandoz, 1, Merck, 1, Roche, 1, Janssen, 1, Sanofi, 1, Amgen, 1; **E. Rampakakis**, None; **A. Lehman**, Janssen Inc., 3; **M. Rachich**, Janssen, 3, 11; **F. Nantel**, None; **O. Asin-Milan**, Janssen, 3.

Abstract Number: 0803

Rheumatoid Arthritis Practice Performance (RAPP) Project at 6 Years: Population Medicine (POPMED) Principles and Treat to Target (T2T) Care Yield Dramatic Improvements in Both Outcomes and Access for RA Patients and Productivity for Rheumatologists

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SESSION INFORMATION
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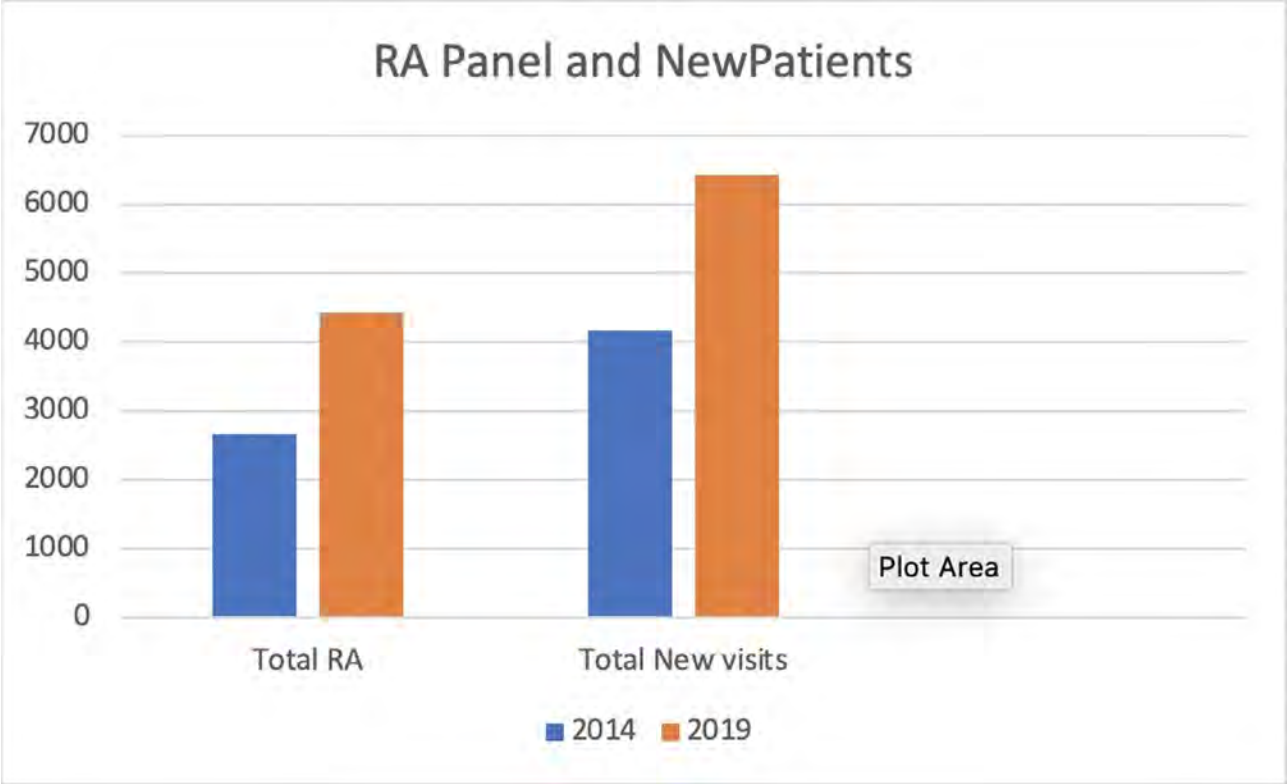
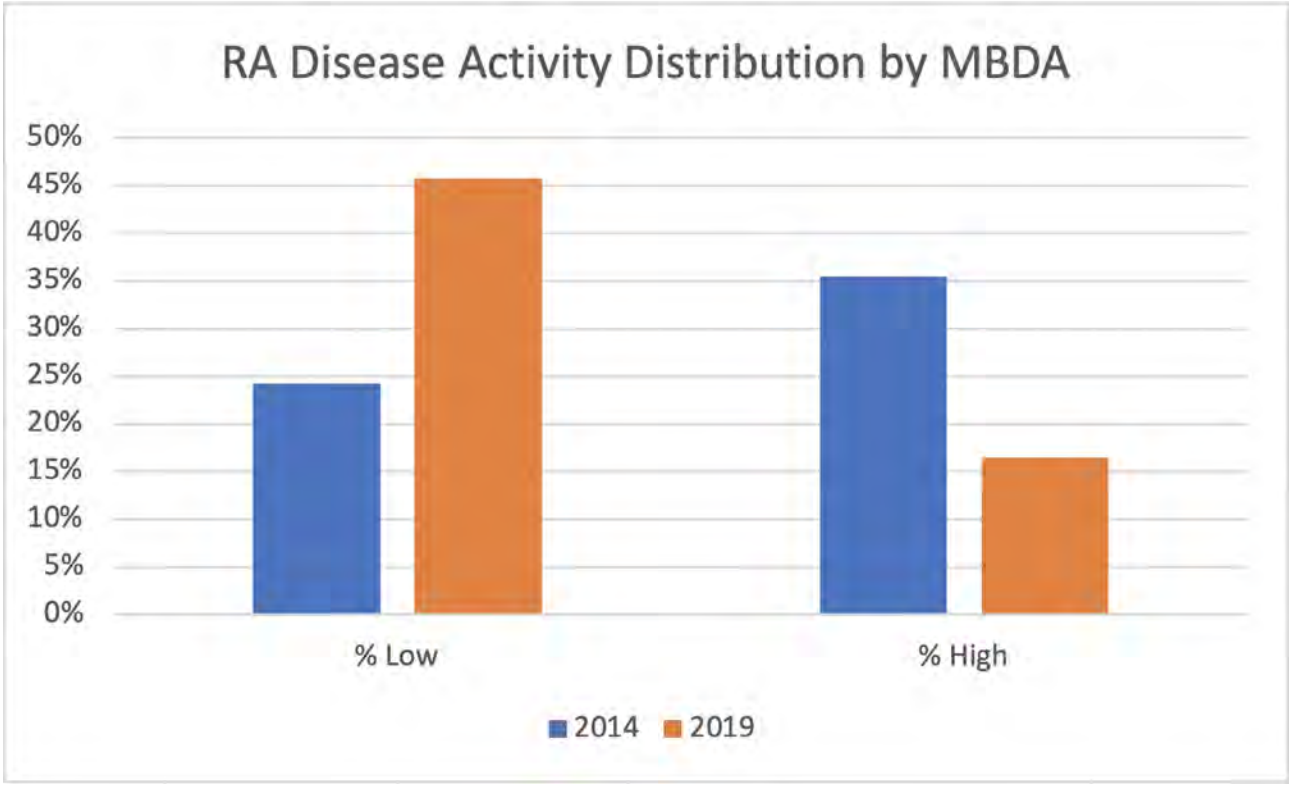
Session Time: 8:30AM–10:30AM

Background/Purpose: The RAPP quality improvement project is a voluntary consortium of practicing rheumatologists founded in 2013 by Timothy Harrington MD, MACR. The primary focus is to provide accurate, on-time disease activity assessments and necessary treatments for an entire RA population consistent with T2T recommendations. We identified a bottleneck at available physician appointments as a major impediment. To address this bottleneck, RAPP practices utilized principles of chronic disease management (POPMED) such as team care with advanced practice providers and medical assistants gathering pertinent clinical, lab and imaging data 1-2 weeks prior to the actual clinical visit with the Rheumatologist. We now report our experience with RA disease activity outcomes, timeliness of care and Rheumatologist productivity over 6 years in 4 RAPP practices that have implemented both T2T care and POPMED principles.

Methods: The 4 Rheumatology practices included in this analysis represent a spectrum of community-based, physician-owned Rheumatology providers including two large (>250 MDs) multispecialty groups, a 4 Rheumatologist practice and a solo practice. Timeliness of care was judged by fulfilling ACR/EULAR guidelines of assessments every 3 months for high or moderate disease activity (HDA) patients and 3-6 months for low or controlled disease activity (LDA) patients. RAPP practices also chose to use one or more composite disease activity profile from a panel



RA Panel and New Patients



RA Disease Activity Distribution by

(Rapid-3, CDAI, SJC, TJC, MD Global) . All or part of these were obtained by team members at each visit prior to the Rheumatologist seeing the patient. Only MBDA (Vectra) testing was utilized in all 4 practices at prescribed intervals.

Results: Over 6 years the 4 practices in total decreased the number of Rheumatologists from 11 to 10 while increasing the number of team members from 54 to 76. The added positions included 8 NP/PAs, 4 MAs and an assortment of other support staff. Total annual new patient visits increased 54% from 4165 to 6424(Image1).There was a 66% increase in the RA patient panel from 2673 (range 428 to 824) to 4428 (690-1307). MBDA scores demonstrated that initially 35% of RA patients had HDA and 42% were evaluated on time (Image 2). 6 years later only 16% of RA patients had HDA with 56% evaluated on time. A concomitant increase in RA patients with LDA from 24 to 46% was noted with on time evaluations increasing from 55% to 68%.

Conclusion: Creation of patient care teams and re-designing the patient visit into two components allowed almost 1800 additional patients with RA to access Rheumatology care despite an actual decrease in the number of Rheumatologists in the 4 practices. Associated with improved access, the number of RA patients with HDA declined dramatically (35% to 16%) and LDA increased (24 to 46%) as the timeliness of their visits improved. We conclude that Dr Harrington's vision of using T2T care and POPMED principles to improve quality and access to care for patients with RA has proven true.

Finally, the dramatic improvements in Rheumatologist productivity associated with implementing team care suggests the RAPP project can be a model to mitigate the shortage of Rheumatologists both now and projected in the future.

Disclosure: W. Arnold, Setpoint medical, 2; **E. Arnold**, Myriad, 6, SetPoint, 2; **D. Sikes**, Myriad, 2, Abbvie, 6; **G. Crump**, Myriad, 1, 6, AbbVie, 2, 6, Novartis, 1, 2, 6, UCB, 2, 6, Horizon, 1, 6, Amgen, 6, Exagen, 1; **K. Thomas**, None; **a. johnson**, None.

Abstract Number: 0804

Validation of the 2010 ACR/EULAR Classification Criteria of Rheumatoid Arthritis (RA) in a Nursing-led Triage Clinic

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: To shorten the waiting time to see rheumatologists, a nurse-led triage clinic was established in our hospital in September 2018 to triage new referrals for peripheral joint symptoms. Patients who were assessed to fulfil the ACR/EULAR criteria for rheumatoid arthritis (RA) were channeled for an early appointment while others a routine appointment in the rheumatology clinics. The objective of this study is to validate the performance of the 2010 ACR/EULAR classification criteria of RA in a nurse-led triage clinic.

Methods: Adult patients who presented with peripheral joint pain and referred to the medical clinics of Tuen Mun Hospital, Hong Kong between October 2018 and October 2020 were studied. Patients were seen face-to-face by a designated rheumatology nurse specialist (CMT) for assessment of the medical history, fulfillment of the ACR/

Performance of ACR/EULAR criteria	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
All patients (n=282)	92.1 (83.6-97.1)	86.4 (81.0-90.8)	71.4 (63.8-78.0)	96.7 (93.2-98.5)
Age ≥50 years (n=210)	93.2 (83.5-98.1)	84.1(77.3-89.5)	69.5 (61.2-76.9)	97.0 (92.5-98.8)
Age <50 years (n=72)	88.2 (63.6-98.5)	92.7 (82.4-98.0)	79.0 (59.0-90.7)	96.2 (87.4-99.0)
Male patients (n= 59)	80.0 (51.9-95.7)	84.1 (69.9-93.4)	63.2 (45.4-78.0)	92.5 (81.6-97.2)
Female patients (n= 223)	95.1 (86.3-99.0)	87.0 (80.9-91.8)	73.4 (64.9-80.5)	97.9 (94.0-99.3)

EULAR RA criteria and the number of tender and swollen peripheral joints. A final clinical diagnosis of RA made by the attending rheumatologists was regarded as the standard and the performance of the ACR/EULAR criteria for RA was validated by a 2x2 contingency tables according to a diagnosis of RA ("condition positive") and criteria fulfilment ("test positive") using standard formulas (sensitivity = true positive/[true positive+false negative]; specificity = true negative/[true negative+false positive]); positive predictive value (PPV) = true positive/true positive+false positive; negative predictive value (NPV) = true negative/true negative+false negative).

Results: A total of 336 patients were seen in the nurse-led clinic during the specified period. 51 patients were excluded because they were diagnosed to have RA by other specialists or private rheumatologists. Finally, 282 patients were studied (223 women [79%]; age 55.2±11.9 years [18-88]). All except 4 patients were ethnic Chinese. 73 (25.8%) patients were anti-CCP positive, 123 (43.5%) patients were rheumatoid factor (RF) positive, and 28 (9.9%) patients had more than 10 joints involved. A total of 98 patients fulfilled the ACR-EULAR criteria, 78 (79.6%) of whom were diagnosed clinically as RA by rheumatologists. The clinical diagnosis of patients who fulfilled the ACR-EULAR criteria but not clinical RA were: osteoarthritis (n=14), psoriatic arthritis (n=3), fibromyalgia (n=3), undifferentiated connective tissue disease (n=2), lupus (n=1), scleroderma (n=1) and others (n=4). The sensitivity and specificity of ACR/EULAR criteria for RA was 92.1% and 86.4%, respectively. Subgroup analyses showed that the ACR/EULAR RA criteria was less sensitive but more specific in younger patients (< 50 years). Both the sensitivity and specificity of the ACR/EULAR criteria for RA was lower in male patients.

Conclusion: The performance of the 2010 ACR/EULAR criteria for triage purpose in our nurse-led triage clinic is satisfactory. The higher specificity and sensitivity of the criteria as compared to other European and Asian cohorts is possibly related to the longer duration of joint symptoms in our patients before nursing assessment.

Disclosure: C. Tsang, None; **C. Mok**, None; **K. Chan**, None; **S. TSE**, None; **L. Ho**, None.

Abstract Number: 0805

A Real-world Prospective Observational Study of the Effectiveness of Golimumab in Adult Greek Patients with RA, PsA and Axial SpA and Inadequate Response to Initial TNFα Inhibitor Therapy

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SESSION INFORMATION

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Background/Purpose: Patients (pts) with immune-mediated rheumatic diseases and an insufficient response to previous treatment with TNFα inhibitors (TNFαi) are frequently encountered in clinical practice. This study assessed the effectiveness of golimumab (GLM) and its impact on patient-reported outcomes in this population.

Methods: GO-BEYOND was a real-world, prospective, 18-month study conducted in 25 sites in Greece. Eligible pts had active RA, PsA, or axSpA and had failed previous treatment with one TNFαi due to secondary non-response (defined as disease relapse following ≥6 months of treatment), intolerability, or inconvenience. The primary objective assessed the proportion of pts with: RA attaining low disease activity (LDA; DAS for 28 joints based on CRP [DAS28-CRP] < 3.2); PsA attaining minimal disease activity (MDA; defined by MDA criteria); and, axSpA attaining moderate disease activity (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] between 4 and 7) at 6 months. Disease activity, including inactive disease in axSpA pts (Ankylosing Spondylitis Disease Activity Score [ASDAS] < 1.3), was assessed at months 3, 12 and 18 as part of the secondary objectives, which also assessed work productivity and activity impairment (Work Productivity and Activity Impairment Questionnaire [WPAI]), QoL (EQ-5D-3L questionnaire), and healthcare resource utilization (HCRU) via a patient diary, at baseline (BL), 3, 6, 12, and 18 months in all indications. Drug persistence was evaluated using the Kaplan-Meier method.

Results: A total of 242 pts (RA: 117 [48.3%]; PsA: 63 [26.0%]; axSpA: 62 [25.6%]) were included, with a mean (SD) age of 55.1 (13.5). Most pts were female (173, 71.5%). The median (Q1-Q3) time from diagnosis to study entry was 3.6 (2.1-7.1) years. At BL, pts with RA had a median (Q1-Q3) DAS28-CRP of 4.8 (4.5-5.3), pts with PsA had a median (Q1-Q3) DAS28-CRP of 4.7 (4.3-5.1), and pts with axSpA had a median (Q1-Q3) BASDAI of 6.2 (4.7-6.9). Following 6 months of GLM treatment, 46.4% (45/97) of pts with RA achieved LDA and 57.1% (32/56) of pts with PsA achieved MDA; of pts with axSpA, 98.1% (53/54) achieved BASDAI≤7, 74.1% (40/54) achieved BASDAI < 4 and 31.3% (15/48) achieved inactive disease by ASDAS. Improvements in disease activity were also observed across each time point (3,

12 and 18 months) (Table 1). In the entire cohort (RA, PsA, and axSpA), the changes in all WPAI domain scores from BL to 3, 6, 12, and 18 months were significant ($p < 0.001$ all comparisons; Table 2), as were the respective changes in the EQ-5D-3L UK index score (Table 3). Of all pts, ~90.0% had disease-related laboratory tests performed and ~20.0% visited specialist physicians during the observation period; no hospitalizations were recorded. Finally, the persistence rates at 3, 6, 12 and 18 months were 93.7%, 89.0%, 85.1% and 85.1%.

Table 1. Disease Activity Measures by Disease Type

		Patients achieving each endpoint/ Patients with available data	%
RA patients – LDA (DAS28-CRP<3.2)			
3 months		35/108	32.4
6 months		45/97	46.4
12 months		50/91	54.9
18 months		59/76	77.6
PsA patients – MDA			
3 months		17/58	29.3
6 months		32/56	57.1
12 months		34/50	68.0
18 months		43/50	86.0
axSpA patients - BASDAI			
3 months	?7	52/56	92.9
	<4	28/56	50.0
6 months	?7	53/54	98.1
	<4	40/54	74.1
12 months	?7	51/51	100.0
	<4	46/51	90.2
18 months	?7	45/47	95.7
	<4	43/47	91.5
axSpA patients – Inactive Disease (ASDAS <1.3)			
3 months		8/55	14.5
6 months		15/48	31.3
12 months		17/49	34.7
18 months		16/41	39.0

LDA, Low Disease Activity; DAS28-CRP, DAS for 28 joints based on CRP; MDA, Minimal Disease Activity; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ASDAS, Ankylosing Spondylitis Disease Activity Score

Table 2. Work Productivity and Activity Impairment Questionnaire Domain Score Analysis. All study indications included

	Patients, N*	Domain score	p-value§
Median (Q1, Q3) baseline domain scores, %			
Absenteeism	118	6.7 (0.0,12.5)	-
Presenteeism	117	60.0 (50.0,70.0)	-
Work productivity loss	117	63.5 (53.5,77.8)	-
Activity impairment	233	70.0 (50.0,80.0)	-
Median (Q1, Q3) change in domain scores from baseline to 3 months, %			
Absenteeism	109	-2.4 (-6.6,0.0)	
Presenteeism	109	-20.0 (-40.0, -10.0)	<0.001
Work productivity loss	109	-18.4 (-42.1, -9.5)	
Activity impairment	215	-20.0 (-40.0, -10.0)	
Median (Q1, Q3) change in domain scores from baseline to 6 months, %			
Absenteeism	102	-2.8 (-7.0, 0.0)	
Presenteeism	102	-30.0 (-50.0, -20.0)	<0.001
Work productivity loss	102	-29.6 (-50.0, -18.7)	
Activity impairment	208	-30.0 (-50.0, -20.0)	
Median (Q1, Q3) change in domain scores from baseline to 12 months, %			
Absenteeism	93	-3.5 (-7.7, -0.2)	
Presenteeism	93	-40.0 (-50.0, -30.0)	<0.001
Work productivity loss	93	-40.0 (-50.5, -29.9)	
Activity impairment	182	-40.0 (-60.0, -30.0)	
Median (Q1, Q3) change in domain scores from baseline to 18 months, %			
Absenteeism	83	-3.2 (-7.0, -1.4)	
Presenteeism	83	-50.0 (-60.0, -40.0)	<0.001
Work productivity loss	83	-50.0 (-58.1, -39.4)	
Activity impairment	173	-50.0 (-60.0, -30.0)	

*Number of patients with available data. §By Wilcoxon signed-rank test for paired samples. Q1, first quartile; Q3, third quartile.

Conclusion: In a real - world setting in Greece, pts with active RA, PsA or axSpA, treatment with GLM over 18 months resulted in clinically relevant improvements in disease activity, while a high persistence rate was observed. Significant improvements in work productivity, activity impairment, and QoL were observed from BL to 3, 6, 12 and 18 months. HCRU was mostly driven by laboratory tests.

Table 3. EQ-5D-3L UK index score at baseline, 3, 6, 12 and 18 months, all study indications included

	Patients, N*	EQ-5D-3L UK index score Median (Q1-Q3)	Change in EQ-5D-3L UK index score from baseline Median (Q1-Q3)	p-value§
Baseline	240	0.5 (0.2-0.6)	-	-
3 months	225	0.6 (0.5-0.7)	0.1 (0.0-0.4)	<0.001
6 months	212	0.7 (0.6-0.9)	0.3 (0.1-0.5)	
12 months	192	0.7 (0.6-1.0)	0.3 (0.1-0.5)	
18 months	177	0.8 (0.7-1.0)	0.4 (0.2-0.5)	

*Number of patients with available data. EQ-5D-3L, 3-level EuroQol-5D questionnaire.
§By Wilcoxon signed-rank test for paired samples. Q1, first quartile; Q3, third quartile.

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Abstract Number: 0806

Coping with Recent-onset Rheumatoid Arthritis (RA): Validation of the Coping with Health Injuries and Problems (CHIP) Questionnaire in a Longitudinal Cohort

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Receiving a Rheumatoid Arthritis (RA) diagnosis presents a significant health stressor. Given that little is known about how patients cope with it, we aimed to validate for the first time the Coping with Health Injuries and Problems (CHIP) questionnaire (Endler NS et al. Psychol Assessm 1998;10:195) in early RA.

Methods: Between August 2006 and October 2020, 483 consecutive patients who met the criteria for RA were enrolled at the Centre Hospitalier Universitaire de Sherbrooke (CHUS). At baseline and at each scheduled yearly study visit, patients self-administered the CHIP questionnaire. CHIP is comprised of 32 items, with 4 subscales: Distraction, Palliative, Instrumental, Emotional. Each subscale is the sum of 8 items with a score ranging from 8 to 40. CHIP's validity was assessed for internal consistency with Cronbach's alpha, for sensitivity to change with mixed linear model with repeated measures as well as for factor structure with factorial analysis and confirmatory analysis.

Table 1. Cronbach's alpha for original subscales of the CHIP questionnaire

	Cronbach's alpha
Distraction	0.754
Palliative	0.736
Instrumental	0.763
Emotional	0.857

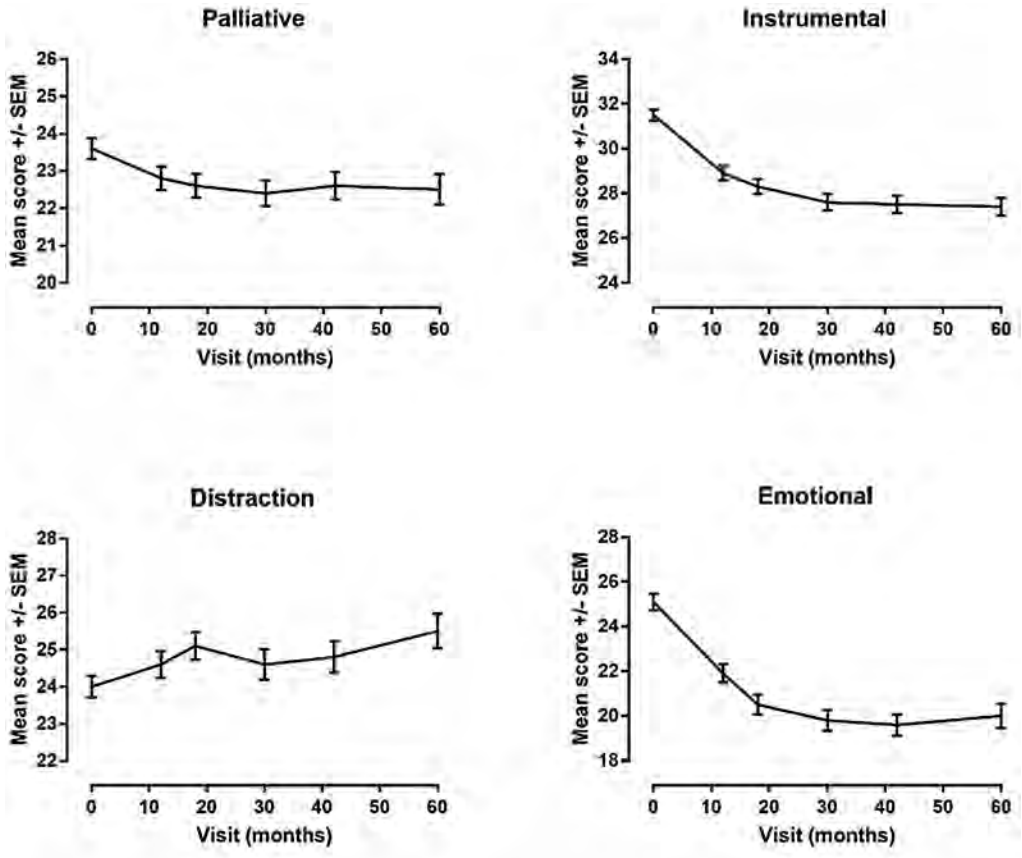

Figure 1. Evolution of CHIP subscales over the five years following RA onset

Results: A total of 420 patients were followed up to 5 years. The baseline mean (SD) of 4 subscales were 24.01 (6.46) for Distraction, 23.58 (6.07) for Palliative, 31.48 (5.35) for Instrumental and 25.10 (7.95) for Emotional. CHIP demonstrated good psychometric properties. Internal consistency (Cronbach's alpha) varied between 0.736 and 0.857 (Table 1); deleting each element separately did not improve the coefficient suggesting that each was an important contributor to the overall score. CHIP was sensitive to change with significant decreases (estimated ± SE) until 5 years for Instrumental (-4.25 ± 0.36, p< 0.001), Emotional (-5.87 ± 0.44, p< 0.001), Palliative (-1.27 ± 0.35, p< 0.001) and a significant increase for Distraction (1.15 ± 0.40, p=0.04) (Figure). Factor analysis suggested that all items were better represented on 7 subscales rather than 4; the 7-dimension solution explained 56.5% (versus 37.8%) of the total variability. The first subscale was defined by all 8 Emotional items; the second by 6 of 8 items of Distraction; five of the Instrumental items were found on dimension 3, the 3 others (linked to treatment adherence) were on dimension 5; Palliative items were split into 3 subscales (4, 6 and 7) that we called comfort, rest and well-being (Table 2). Confirmatory analyses showed that 7 subscales may be slightly better than the original 4, although Cronbach's alphas of the new 7 subscales were not improved when compared to the original 4.

Table 2. Results of factorial analysis using the 32 coping items of the CHIP questionnaire

	Fact 1	Fact 2	Fact 3	Fact 4	Fact 5	Fact 6	Fact 7
Original subscales	Emotional	Distraction	Instrumental	Comfort	Adherence	Rest	Well-being
Emotional							
4. Wonder "why me"	**0.676**	0.129	0.124	0.066	0.107	0.187	0.050
8. Feel angry	**0.737**	0.154	0.105	0.016	-0.078	0.128	-0.088
12. Become frustrated	**0.739**	0.029	0.073	0.047	-0.046	0.153	-0.075
16. Think about things I can't do	**0.599**	0.008	0.229	-0.134	0.090	-0.050	0.363
20. Fantasize about being healthy	**0.615**	0.188	0.034	0.106	0.020	-0.170	0.346
24. Wish it hadn' happened	**0.628**	0.093	-0.057	0.163	0.141	-0.003	0.205
28. Think about being vulnerable	**0.684**	-0.181	0.047	0.149	0.098	0.277	0.044
32. Worry about my health	**0.781**	-0.122	0.070	-0.011	0.112	0.079	0.097
Distraction							
1. Think about better times	0.159	**0.682**	-0.018	0.132	0.076	-0.009	0.054
5. Be with others	0.008	**0.704**	0.144	-0.038	0.082	0.264	-0.067
9. Daydream	-0.102	**0.678**	0.105	0.104	0.130	-0.001	0.083
13. Enjoy attention from people	0.037	**0.377**	0.182	0.173	0.135	0.011	0.492
17. Plan for the future	0.121	**0.477**	0.292	0.058	-0.046	0.095	0.112
25. Invite company	0.039	**0.540**	0.031	0.365	-0.033	0.004	0.119
21. Listen to music	-0.021	0.296	0.305	**0.342**	-0.032	0.122	0.011
29. Have nice things around	-0.011	0.376	0.207	**0.667**	0.052	-0.013	-0.103
Instrumental							
3. Find out more information	0.117	0.063	**0.743**	0.040	0.131	0.145	-0.060
7. Seek treatment quickly	0.163	0.019	**0.417**	-0.087	0.328	0.194	0.256
11. Focus on getting better	-0.033	0.258	**0.618**	-0.075	0.165	0,000	0.222
15. Learn more	0.130	0.115	**0.758**	0.192	0.039	0.139	0.020
31. Find out about treatments	0.198	0.062	**0.671**	0.347	0.130	-0.158	0.074
19. Comply with advice	0.069	0.076	0.209	0.043	**0.801**	-0.017	0.179
23. Follow doctor's advice	0.072	0.078	0.196	0.194	**0.797**	-0.056	0.098
27. Take medications on time	0.082	0.075	0.011	0.156	**0.737**	0.058	-0.065
Palliative							
22. Make surrounding quiet	0.163	0.140	0.113	**0.600**	0.136	0.216	0.175
26. Stay quiet	0.201	-0.159	-0.126	**0.607**	0.181	0.157	0.315
30. Get comfortable	0.035	0.262	0.144	**0.628**	0.275	0.027	0.144
2. Stay in bed	0.283	-0.017	0.083	0.235	-0.134	**0.645**	-0.020
6. Rest when tired	0.188	0.093	0.136	0.048	0.063	**0.647**	0.404
10. Sleep	0.101	0.253	0.066	0.047	0.078	**0.709**	0.047
14. Conserve Energy	0.251	-0.118	0.128	0.218	-0.026	0.310	**0.619**
18. Stay Warm	0.145	0.344	0.002	0.170	0.178	0.076	**0.539**
Eigenvalues	4.20	2.87	2.69	2.34	2.30	1.90	1.78
% of Variance explained	13.12	8.96	8.42	7.31	7.20	5.95	5.55
Cronbach's alpha	0.857	0.724	0.741	0.677	0.751	0.646	0.421

Conclusion: CHIP questionnaire describes patient's individual coping styles when facing recent-onset RA. Due to the prospective nature of our cohort, we could validate the questionnaire. Factor analysis suggested that coping in early RA was better characterized using 7 rather than 4 subscales, but Cronbach's alpha suggested that using the original tool might be as good, an observation that remains to be confirmed. Discussing a patient's results for CHIP may enable a rheumatologist to understand patients' perspectives and address their needs better, thereby strengthening their relationship. Results from CHIP may also be used as predictor of patients' outcomes pointing towards interventions that may help those in need to deal with their illness better.

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Baseline Coping Strategies as Predictors of Outcomes in Patients with Early-onset Rheumatoid Arthritis (RA)

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SESSION INFORMATION
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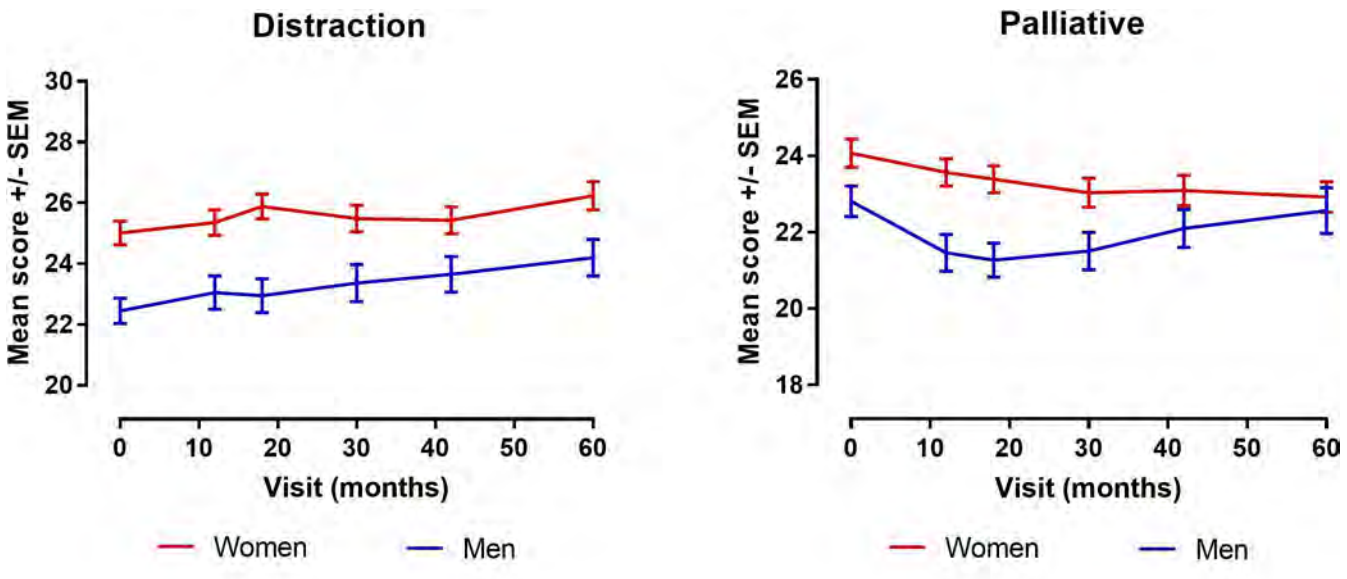
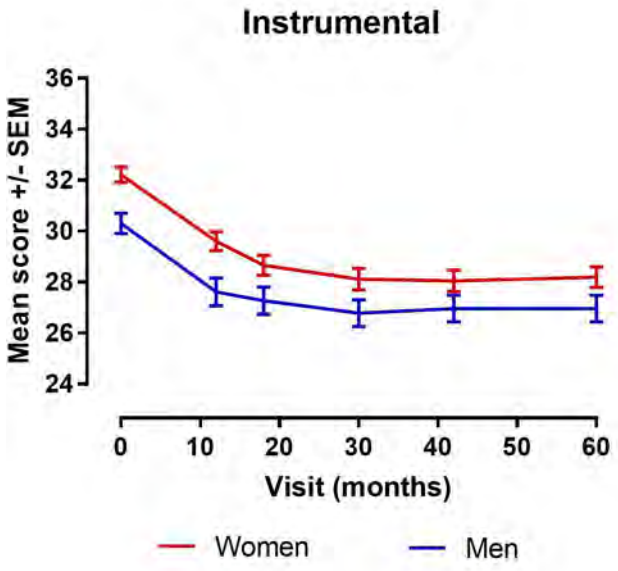
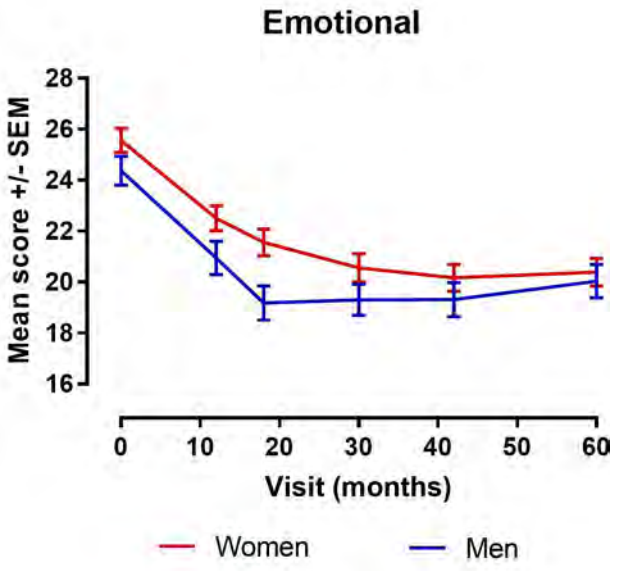
Background/Purpose: Patients recently diagnosed with RA employ various coping strategies. We aimed to describe these strategies over time and determine if specific strategies impacted patient outcomes.

Methods: Consecutive patients meeting the criteria for early RA identified at the Centre Hospitalier Universitaire de Sherbrooke(CHUS) self-administered the Coping with Health Injuries and Problems (CHIP) questionnaire at baseline and yearly follow-ups, up to 5 years. CHIP consists of 32 items with 4 subscales: Distraction, Palliative, Instrumental, Emotional, each containing 8 questions scored from 1 to 5. The scores (range 8-40) over time were examined by gender. Correlation between score and clinical variables at baseline were computed. Baseline scores were used to predict disease outcomes over time. The primary outcomes were: remission according to Simple Disease Activity Index (SDAI) and disability according to the Modified-Health Assessment Questionnaire (M-HAQ). CHIP scores were analyzed with the continuous scale and dichotomized according to the upper or lower third of the scale (≥30 or ≥18). P-values were calculated with linear mixed regression models for continuous outcomes or with generalized estimating equation for dichotomic outcomes.







	Distraction	Palliative	Instrumental	Emotional
p-value (Time)	<0.001	0.012	<0.001	<0.001
p-value (Gender)	<0.001	<0.001	<0.001	0.0214
p-value (Interaction)	0.038	0.033	0.199	0.374

Figure 1. Evolution of CHIP subscales over the five years according to gender.

Results: 482 patients were enrolled between August 2006 and October 2020 (61% female). Baseline mean scores (SD) were: 24.01 (6.46) for Distraction, 23.58 (6.07) for Palliative, 31.48 (5.35) for Instrumental and 25.10 (7.95) for Emotional.

Table 1. Correlation between CHIP subscales at baseline and clinicals variables at baseline

	Distraction		Palliative		Instrumental		Emotional	
	r	p-value	r	p-value	r	p-value	r	p-value
CHIP Distraction	1		0.416	**<0.001**	0.412	**<0.001**	0.129	**0.005**
CHIP Palliative	0.416	**<0.001**	1		0.382	**<0.001**	0.46	**<0.001**
CHIP Instrumental	0.412	**<0.001**	0.382	**<0.001**	1		0.283	**<0.001**
CHIP Emotional	0.129	**0.005**	0.460	**<0.001**	0.283	**<0.001**	1	
Age (years)	0.016	0.728	0.064	0.158	-0.005	0.921	-0.056	0.222
Female	0.212	**<0.001**	0.115	**0.012**	0.18	**<0.001**	0.072	0.114
Body mass index (kg/m2)	-0.064	0.162	-0.053	0.243	-0.027	0.554	-0.025	0.580
Disease duration (years)	0.116	**0.011**	-0.042	0.356	-0.019	0.678	-0.034	0.455
Smoking status (ever smoking vs no smoking)	-0.013	0.785	0.008	0.860	0.046	0.315	0.011	0.817
Depression, pain, fatigue								
Epidemiological Studies-Depression (CES-D)	-0.078	0.110	0.283	**<0.001**	0.048	0.323	0.577	**<0.001**
Fatigue (0-10 cm)	-0.013	0.779	0.208	**<0.001**	0.052	0.252	0.320	**<0.001**
Pain (0-10 cm)	0.037	0.415	0.172	**<0.001**	0.090	**0.05**	0.205	**<0.001**
Patient global assessment (0-10 cm)	0.073	0.111	0.208	**<0.001**	0.071	0.118	0.232	**<0.001**
Evaluator global assessment (0-10 cm)	-0.043	0.346	0.103	**0.024**	0.002	0.968	0.207	**<0.001**
Principal Outcomes								
Modified-Health Assessment Questionnaire (M-HAQ)	-0.008	0.874	0.214	**<0.001**	0.024	0.649	0.335	**<0.001**
Disease Activity Score-28 with CRP (DAS28-CRP)	0.008	0.862	0.156	**0.001**	0.053	0.247	0.173	**<0.001**
Simple Disease Activity Index (SDAI)	0.001	0.981	0.12	**0.009**	0.052	0.262	0.176	**<0.001**
Clinical Disease Activity Index (CDAI)	0.013	0.775	0.102	0.026	0.051	0.271	0.17	**<0.001**
Swollen joint count, 68 joints	0.010	0.834	0.057	0.215	0.035	0.442	0.104	**0.023**
Tender joint count, 66 joints	0.014	0.766	0.120	**0.009**	0.067	0.141	0.172	**<0.001**
Serology								
Anti-CCP2 positive	-0.023	0.610	-0.013	0.783	-0.021	0.641	0.090	**0.049**
Rheumatoid Factor positive	-0.031	0.498	0.003	0.948	-0.053	0.250	0.034	0.457
Anti-Sa positive	-0.02	0.672	-0.064	0.182	-0.079	0.100	-0.036	0.453
Erythrocyte sedimentation rate (ESR)	-0.096	**0.036**	0.119	**0.009**	-0.014	0.754	0.062	0.174
C-Reactive Protein (CRP)	-0.082	0.072	0.151	**0.001**	-0.019	0.682	0.073	0.110
Sharp van der Heijde Score	-0.01	0.850	-0.013	0.799	-0.015	0.770	0.002	0.967

For all subscales, females scored significantly higher than males and scores varied significantly over time (Figure 1). For Distraction and Palliative, scores declined faster in males than females, with significantly different slopes (interaction: gender*time).

At baseline, Emotional subscale was significantly correlated with depressive symptoms measured with Center for Epidemiological Studies-Depression (CES-D) (r=0.58) and with M-HAQ, fatigue, pain, disease activity according to the patient and the physician (r values between 0.20 to 0.33). Palliative subscale at baseline had significant correlations with the same variables, albeit weaker (r values 0.10 to 0.28) (Table 1).

Table 2. Impact of baseline CHIP on outcomes over time

Level (Third)	DAS28 remission		SDAI remission		CDAI remission		M-HAQ ≥1	
	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value	RR (95% CI)	p-value
Distraction								
Continuous	1.00 (1.00-1.01)	0.2833	1.01 (1.00-1.02)	0.2582	1.01 (1.00-1.02)	0.1419	0.99 (0.98-1.00)	0.1213
≥30 (Upper)	0.90 (0.79-1.03)	0.1306	0.85 (0.68-1.06)	0.134	0.92 (0.75-1.12)	0.4019	0.93 (0.65-1.32)	0.6646
≥18 (Lower)	0.94 (0.82-1.07)	0.3331	0.83 (0.67-1.04)	0.1359	0.92 (0.75-1.14)	0.4766	1.17 (0.84-1.64)	0.3224
Palliative								
Continuous	0.98 (0.97-0.99)	**<0.0001**	0.96 (0.95-0.97)	**<0.0001**	0.97 (0.96-0.98)	**<0.0001**	1.05 (1.04-1.07)	**<0.0001**
≥ 30 (Upper)	0.83 (0.72-0.96)	**0.0092**	0.58 (0.44-0.77)	**<0.0001**	0.63 (0.49-0.80)	**<0.0001**	1.75 (1.29-2.37)	**0.0036**
≥ 18 (Lower)	0.84 (0.74-0.96)	**0.0192**	0.72 (0.58-0.89)	**0.010**	0.78 (0.64-0.94)	**0.0223**	2.26 (1.32-3.86)	**0.0001**
Instrumental								
Continuous	0.97 (0.97-0.98)	**<0.0001**	0.96 (0.95-0.97)	**<0.0001**	0.96 (0.95-0.97)	**<0.0001**	1.05 (1.04-1.07)	**<0.0001**
≥ 35	0.89 (0.80-1.00)	**0.0372**	0.82 (0.67-0.99)	**0.0361**	0.82 (0.69-0.99)	**0.0279**	1.40 (1.07-1.82)	**0.0202**
≥ 30 (Upper)	0.97 (0.87-1.08)	0.5958	0.84 (0.70-1.00)	0.0663	0.90 (0.77-1.07)	0.2363	1.30 (0.98-1.73)	0.0628
≥ 18 (Lower)	0.92 (0.61-1.41)	0.7341	0.97 (0.44-2.10)	0.9306	1.08 (0.50-2.36)	0.8298	1.11 (0.30-4.16)	0.8704
Emotional								
Continuous	0.96 (0.96-0.97)	**<0.0001**	0.94 (0.93-0.95)	**<0.0001**	0.94 (0.93-0.95)	**<0.0001**	1.08 (1.07-1.10)	**<0.0001**
≥ 30 (Upper)	0.94 (0.84-1.05)	0.2574	0.69 (0.57-0.84)	**0.0001**	0.76 (0.64-0.91)	**0.0022**	2.04 (1.58-2.63)	**<0.0001**
≥ 18 (Lower)	0.81 (0.72-0.90)	**0.0011**	0.62 (0.52-0.74)	**<0.0001**	0.66 (0.56-0.78)	**<0.0001**	3.61 (2.24-5.82)	**<0.0001**

For baseline Emotional subscale, subjects with a score of ≥18 had less SDAI remission over time (RR 95% CI: 0.62 (0.52-0.74), p< 0.001) and higher M-HAQ over time (RR: 3.61 (2.24-5.82), p< 0.001) (Table 2). For Palliative, the best cut-off for SDAI remission was lower third (RR: 0.58 (0.44-0.77), p< 0.001) and upper third for M-HAQ (RR: 2.26 (1.32-3.86), p< 0.001). For Instrumental, the mean baseline score was above the upper third cut-off (≥30); the best cut-off for both remission and M-HAQ was thus set higher at ≥35.

Conclusion: CHIP questionnaire describes coping styles when facing health challenges such as recent-onset RA. Coping strategies vary across gender, female having the highest scores at baseline and over time. When maladaptive coping strategies dominate (e.g., emotional) poor outcomes are encountered. Our results indicate that CHIP may be a novel predictor for RA outcomes. Analyzing whether coping strategies add to existing models to predict outcomes in early RA patients is warranted.

Disclosure: Z. Akman, None; **G. Boire**, Abbvie, 1, 6, 7, BMS, 6, 7, Janssen, 1, 5, 6, Eli Lilly, 1, 7, Amgen, 7, Novartis, 6, 7, Pfizer, 7, Sandoz, 6, 7, Viatris, 1, 6, Samsung Bioepis, 1; **N. Carrier**, None; **S. Roux**, Amgen, 6; **A. Masetto**, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Amgen, 5, Merck, 5, Teva, 5; **A. deBrum Fernandes**, None; **P. Liang**, Janssen, 1, 5, 6, Hoffman-La Roche, 5, Novartis, 1, 6, Abbvie, 1, 6, BMS, 1, 6, Amgen, 1, 6, Merk, 1, 6; **P. Dobkin**, None; **A. Hugues**, Pfizer, 1, 6, Neomed, 7, Daiichi Sankyo, 7, Abbvie, 1, 6, Xencor, 7, Sanofi, 1, 6, Novartis, 1, 6, Amgen, 1, 6, Hoffmann-La Roche, 1, 6, Eli Lilly, 1, 6, Janssen, 1, 5, 6.

Abstract Number: 0808

Lower Serum MIP-1β Level Is Associated with CsDMARDs Response in Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The use of treat-to-target (T2T) strategy in managing early rheumatoid arthritis (ERA) had been highly advocated in the past decades. Various international guideline utilized a stepwise approach starting

Table 1. Baseline clinical features and disease activity in csDMARDs responder and non-responder

	csDMARDs responder		p
	No (n=18)	Yes (n=9)	
Age	50 ± 17	64 ± 5	**0.027**
Sex, female	15 83.3%	6 66.7%	0.326
Rheumatoid factor, +ve	14 77.8%	5 55.6%	0.233
Rheumatoid factor titre	99 ± 150	88 ± 82	0.844
ACCP, +ve	16 94.1%	7 77.8%	0.529
ACCP titre	195 ± 93	230 ± 33	0.197
VAS Pain, 0-100mm	62 ± 21	43 ± 25	**0.046**
Patients' global assessment, 0-100mm	65 ± 22	50 ± 18	0.100
Physicians' global assessment, 0-100mm	54 ± 20	53 ± 22	0.949
Tender joint count (0-28)	7 ± 3	8 ± 4	0.607
Swollen joint count (0-28)	4 ± 3	4 ± 2	0.100
Damaged joint count (0-28)	3 ± 2	2 ± 2	0.705
ESR, mm/1st hr	53 ± 27	75 ± 22	**0.043**
CRP, mg/L	16.4 ± 14.2	27.9 ± 21.7	0.109
DAS ESR	5.54 ± 0.87	5.72 ± 0.74	0.606
DAS CRP	4.70 ± 0.93	4.82 ± 0.78	0.589
CDAI	22.6 ± 7.4	21.9 ± 8.5	0.747
SDAI	24.3 ± 8.2	24.7 ± 8.9	0.814
NSAIDs, current use	11 61.1%	6 66.7%	0.767
Steroid, current use	4 22.2%	0 0.0%	0.216
csDMARDs, current use	0 0.0%	0 0.0%	-

ACCP – anticyclic citrullinated peptide; VAS – visual analogue scale; ESR – erythrocyte sedimentation rate; CRP – C-reactive protein; DAS- disease activity index; CDAI – clinical disease activity index; SDAI – simplified disease activity index; NSAIDs – Non-Steroidal Anti-Inflammatory Drugs; csDMARDs – conventional synthetic disease modifying anti-rheumatic drugs

Table 2. Logistic regression on predicting csDMARDs response at month 6

	Univariate analysis			Multi-variate analysis[1]		
	OR	95% CI	*p*	OR	95% CI	*p*
Age	1.16	1.01 to 1.33	0.035			
Sex, female	2.50	0.39 to 16.0	0.334			
ESR	1.03	0.99 to 1.07	0.057			
MIP1β	**0.93**	**0.88 to 0.99**	**0.017**	**0.87**	**0.76 to 0.99**	**0.034**
VAS pain	0.96	0.92 to 1.00	0.063			

[1]Age, sex and other variables with p<0.1 are listed. [2] adjusted for age, ESR and VAS pain at baseline. ESR – erythrocyte sedimentation rate; MIP-1β - Macrophage inflammatory protein-1β; VAS – visual analogue scale

with conventional synthetic disease modification anti-rheumatic drug (csDMARDs), and eventually escalate to biologic/targeted synthetic DMARDs (b/tsDMARDs) when the target is not met. The response rate to csDMARDs varies among individuals. Currently, there are limited biomarker data in predicting csDMARDs response. If certain biomarker could predict non-response towards csDMARDs, would early initiation of b/tsDMARDs improve disease prognosis remained uncertain.

Methods: This is a 6-month pilot prospective discovery cohort in patients with ERA. Patients received T2T treatment according to a standardized protocol with every 3-monthly follow up. Patients who achieved simplified disease activity index (SDAI) remission at month 6 is defined as csDMARDs responder. Serum blood sample was collected at baseline and 48 cytokines and chemokines Bio-Rad Bioplex assay was performed.

Results: Twenty-seven patients (age: 55±15 years; female: 21(78%)) who had completed month 6 follow up were included in the current analysis. All patient received csDMARDs treatment. After 6 months, significant improvement in disease activity was observed (SDAI: 24.4±8.3 at baseline vs 8.0±6.5 at month 6, $p< 0.001$). One third of them (9/27, 33%) achieved SDAI remission at month 6 and were regarded as csDMARDs responder (DR). Patients in DR+ group were older, had lower pain score and higher Erythrocyte sedimentation rate (ESR) (Table 1). There were no statistically difference between the use of drugs across the two groups during study period. Macrophage inflammatory protein-1β (MIP-1β) is a proinflammatory chemokine produced by macrophages. Baseline serum level of MIP-1β were dateable in all patients, and the level was significantly lower in DR (DR: 393±21 ng/ml vs non-DR: 437 ±46 ng/ml, $p=0.012$). Using multivariate logistic regression, lower MCP-1 was significantly associated with csDMARDs response (OR=0.87, 95%CI: 0.77 to 0.99, $p=0.034$) after adjustment of age, ESR and pain score at baseline. MIP-1β were also positively correlated with rheumatoid factor ($r=0.559$, $p=0.02$) at baseline and SDAI at month 6 ($r=0.412$, $p=0.012$).

Conclusion: Lower serum level of MIP-1β was associated with csDMARDs response in patients with ERA. Further validation will testify current findings.

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Abstract Number: 0809

The Impact of Flares on Clinical and Patient Reported Outcomes in Rheumatoid and Undifferentiated Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: There are many definitions of flare in rheumatoid arthritis (RA). Loss of low disease activity is associated with clinically relevant deterioration. Patients in DAS remission may flare to DAS≥1.6 but still have low disease activity. How does this affect outcomes? Therefore the objective of this study was to evaluate the prevalence of disease flares in patients treated to target DAS < 1.6, and to study the impact on clinical and patient-reported outcomes (PROs).

Methods: In the IMPROVED study 610 patients with early RA or UA were treated to target DAS< 1.6 for 5 years. Flares were defined as; **A)** DAS≥1.6 regardless of the previous DAS and ≥0.6 increase; **B)** DAS≥1.6 and previous DAS< 1.6 with ≥0.6increase. Kruskal Wallis tests were used to compare mean HAQ over time, HAQ at 5y, and median SHS progression at 5y between patients with different no. of flares. The OR for a significant deterioration of ≥20mm (from the preceding visit) on a visual analogue score (VAS) for disease activity, pain and morning stiffness during flares were calculated using a generalized linear mixed model.

Results: Over time 75% of patients had ≥1 flare **A**, and 68% ≥1 flare **B**. In 55% and 69% of cases, respectively, DAS remained ≤2.4. In 55% of flares A and B, a clinically relevant increase in HAQ of ≥0.22 occurred. This significantly (p< 0.01) increased to 68% in flares A and 76% in flares B if the DAS had increased to ≥2.4. More flares A per person were associated with a higher mean HAQ over-time and at 60 months and SHS progression at 5y (table 1). Also for the patient reported outcomes, there was a significant risk for a >20 mm deterioration (ORs ≥1 with 90% confidence intervals exceeding 1) for flares A and B (table 2).

Conclusion: In most patients, significant deterioration in PROs occurred when DAS increased to >1.6, even if DAS remained ≤2.4. Regardless of previous DAS, an increase in ≥0.6 DAS points was clinically relevant. Cumulative flares were associated with loss of and radiological progression at 5 years.

Table 1. Dose-response effect of the number of flares on functional ability and radiographic damage progression

	Frequency, N (%) patients		HAQ Month 8 - 60	HAQ[a] At month 60	SHS[a] Progression BL to month 60
	Total n = 585		Median (IQR)	Median (IQR)	Median (IQR)
No. of flare A					
0	147	(25)	0.1 (0.0-0.6)	0.0 (0.0-0.3)	0.0 (0.0-2.5)
1	154	(26)	0.5 (0.1-0.9)	0.3 (0.0-0.8)	0.0 (0.0-1.0)
2	143	(25)	0.5 (0.3-0.9)	0.5 (0.1-1.0)	0.5 (0.0-2.0)
≥	141	(24)	0.5 (0.2-1.0)	0.6 (0.1-1.0)	0.8 (0.0-3.5)
p-value[b]			*<0.01*	*<0.01*	*0.02*
No. of flare B					
0	189	(32)	0.3 (0.0-0.9)	0.3 (0.0-0.9)	0.5 (0.0-3.0)
1	171	(29)	0.5 (0.1-0.9)	0.4 (0.0-0.9)	0.0 (0.0-3.0)
2	146	(25)	0.5(0.3-0.8)	0.5 (0.1-0.9)	0.0 (0.0-3.0)
≥	79	(14)	0.3 (0.2-0.8)	0.5 (0.1-0.9)	0.5 (0.0-1.0)
p-value[b]			*0.25*	*0.13*	*0.09*

[a] completers analysis [b] p-values from Kruskal Wallis test on difference between the groups. HAQ: health assessment questionnaire; IQR: interquartile range; SHS: Sharp/van der Heijde score.

Table 2. Changes from the previous visit in visual analogue scores on patients assessment of disease activity, pain, and morning stiffness. Odds ratios for an increase in VAS of ≥20mm compared to the previous visit.

	Change in VASda		Change in VASpain		Change in VASms	
	≥20 mm increase[a]		≥20 mm increase[a]		≥20 mm increase[a]	
	OR[b]	95% CI	OR[b]	95% CI	OR[b]	95% CI
No flare A	*Ref.*		*Ref.*		*Ref.*	
Flare A	11.34	8.92;14.40	11.28	8.88;14.32	7.09	5.61; 8.96
No flare B	*Ref.*		*Ref.*		*Ref.*	
Flare B	10.93	8.46;14.12	10.89	8.43;14.07	7.70	5.99; 9.90

[a] Increase in VAS of ≥20mm compared to the VAS at previous visit. [b] Adjusted for time.

CI: confidence interval; IQR: interquartile range; OR: odds ratio; ref reference category; VASda: visual analogue scale of disease activity; VASpain: visual analogue scale of pain; VASms: visual analogue scale of morning stiffness

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Abstract Number: 0810

Persistent Disease Activity Impairs Work Productivity and Non-work Activity in Recent Onset Rheumatoid Arthritis

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SESSION INFORMATION

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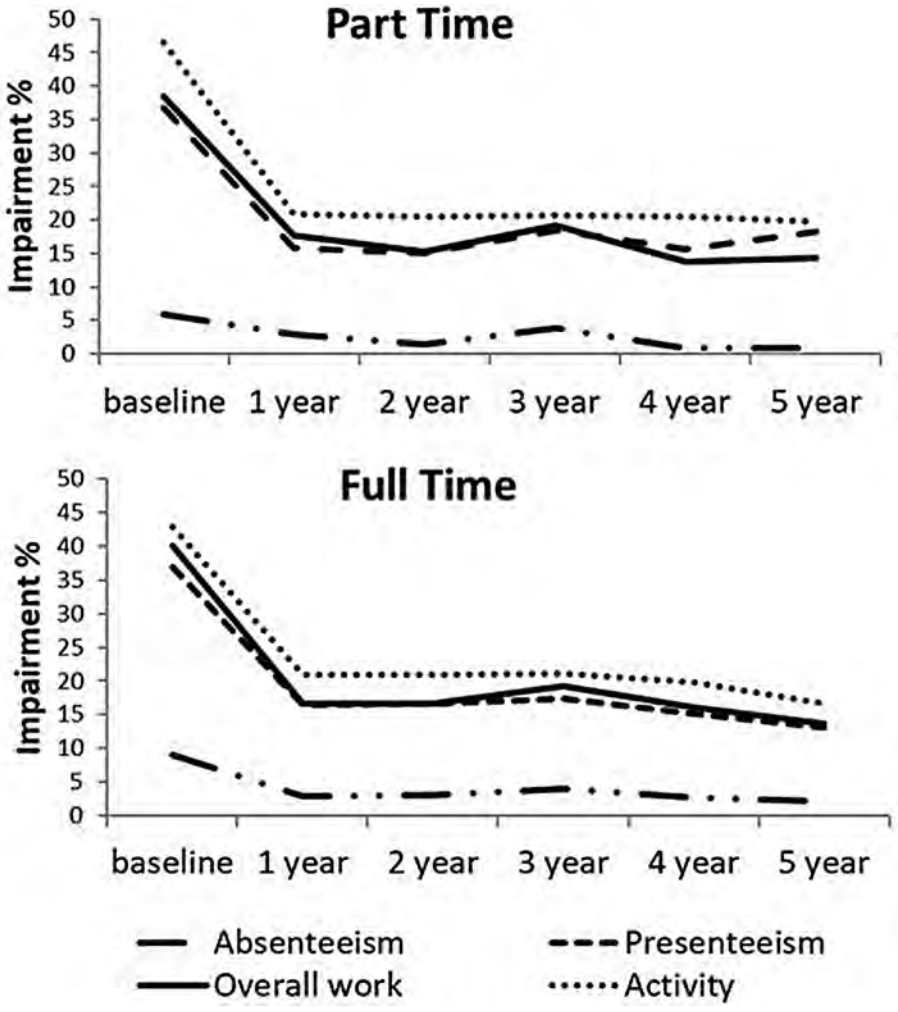
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Reduced work and activity productivity are significant contributors to the personal and societal costs associated with rheumatoid arthritis (RA). We sought to describe work productivity in newly diagnosed RA patients and to identify predictors of impaired productivity over time in patients managed according to contemporary treatment strategies.

Methods: Data were from working age, early RA patients (18-64 years; < 1 year of symptoms at baseline), followed by rheumatologists across Canada and treated with disease modifying anti-rheumatic drug therapies (DMARDs) according to Treat-2-Target guidelines. Between Nov 2011 and March 2020, participants reported baseline work status (employed, unemployed, retired) and annual work productivity was assessed using the Work Productivity and Activity Index (WPAI). WPAI scores for overall work productivity loss with subscores for absenteeism (time away from work) and presenteeism (reduced productivity at work) and scores for reduced general activity are expressed as impairment percentages (%) with higher numbers indicating greater impairment and less productivity. We used generalized estimating equations (GEE) to estimate associations between change in WPAI scores over the first five years of follow-up with time varying lagged disease activity (DAS28 at previous visit predicting WPAI at the next visit), while adjusting for baseline variables of age, sex, work commitment (full time; part-time) and comorbidity [Rheumatic Disease Comorbidity Index (RDCI; range 0-9); depression], and time-varying lagged therapy use (Methotrexate (MTX), biologic DMARDs/ JAKi, prednisone) at the previous visit.



Work productivity and activity impairment over the first five years of follow-up.

Results: At baseline, of 673 working age RA patients, 434 (65%) were employed [352 (82%) full time], 159 (24%) were unemployed and 74 (11%) were retired. Employed RA patients were mainly female (75%), Caucasian (81%), had some education beyond high school (68%) and had active RA with mean (SD) baseline DAS28 4.7(1.4) and mHAQ 0.5(0.5). At baseline, employed RA patients reported on average (SD) 39.8% (29.8) overall work impairment [absenteeism 8.4% (18.6); presenteesim 37.0 % (28.0)] and non-work activity impairment due to health of 43.5% (28.5). Work productivity scores improved after 1 year follow-up but remained relatively stable thereafter (Figure). In lagged multivariable GEE models, higher DAS28 was associated with more work impairment over time; mean change (95% confidence interval) in overall work impairment 7.1% (6.2, 7.9), absenteeism 1.9% (1.4, 2.5), presenteeism 6.6% (5.8, 7.4) and activity impairment 7.8% (7.1, 8.6). Baseline comorbidity was also associated with overall work impairment over time [RDCI mean change 1.9 % (0.1, 3.6); depression mean change 8.0 % (0.4, 15.7].

Conclusion: Patients with early RA report nearly 40% reduced work productivity, mainly from reduced effectiveness while at work, and have similar impairment in non-work activities. While work and activity productivity improve with treatment, persistent disease activity contributes to productivity impairment over time. Interventions to optimize continued engagement in work and addressing difficult to treat RA may improve productivity outcomes for RA patients and their employers.

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Abstract Number: 0811

Using a Smartphone App to Detect and Characterise Real-Time Patient-Reported Flares in Rheumatoid Arthritis

Julie Gandrup, Sabine N van der Veer, John McBeth and Will Dixon, University of Manchester, Manchester, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Miscellaneous Aspects of RA (0786–0812)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Flares are an intrinsic part of the rheumatoid arthritis (RA) disease course and may impact clinical and patient outcomes. Severity, frequency and duration of flares matter, but the clinical assessment is limited

by patient recall. Consumer technologies make it possible to capture and explore patient-reported flares in near real time. We used smartphone app data to explore the frequency of patient-reported flare weeks and their associations with various summary features of daily symptoms reported during the preceding week.

Methods: The Remote Monitoring of Rheumatoid Arthritis (REMORA) study aimed to improve monitoring of disease severity in RA. Patients tracked daily symptoms on a 0-10 scale (pain, fatigue, function, sleep, coping, physical and emotional wellbeing) and weekly flares on the REMORA smartphone app.

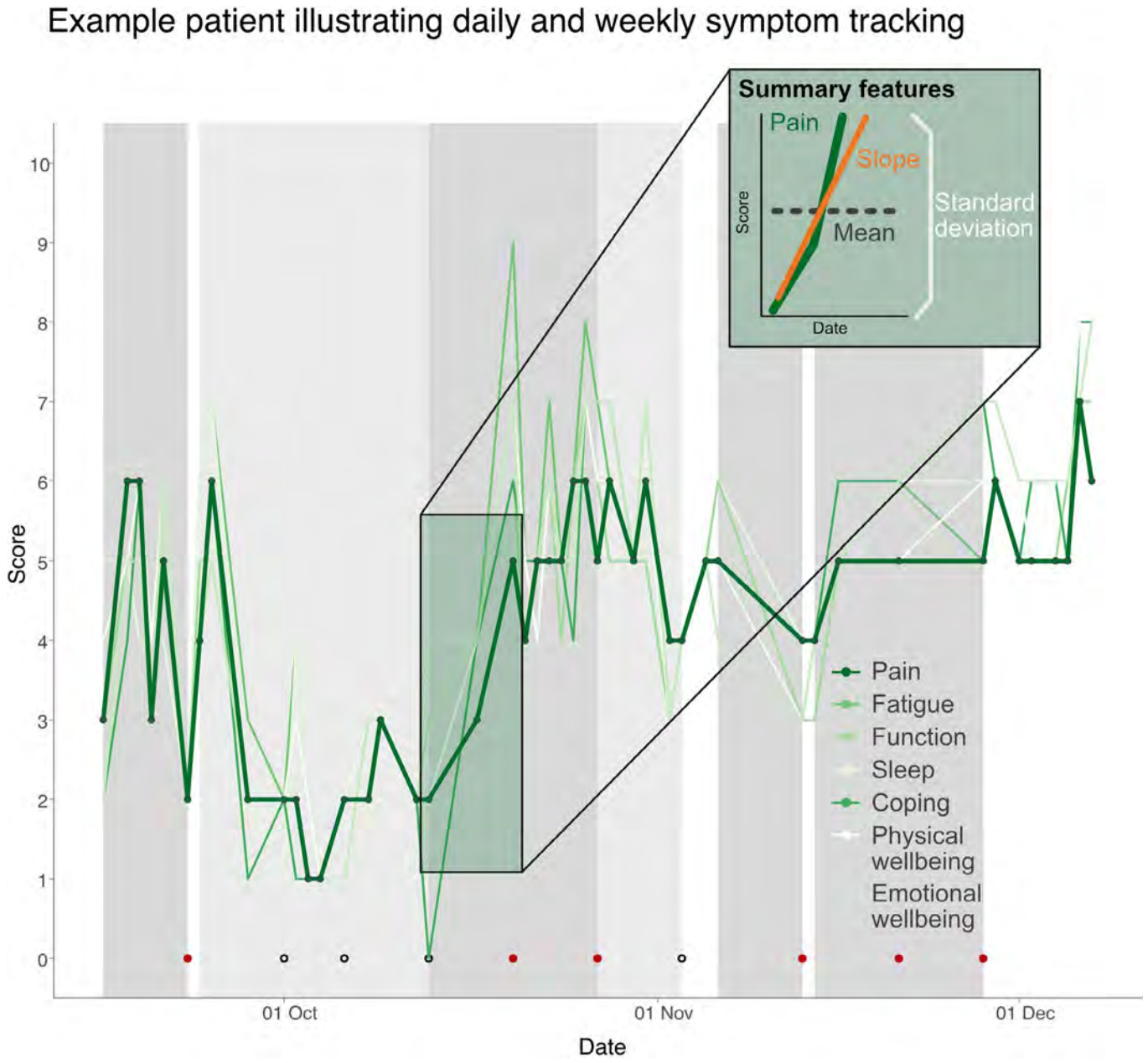

Figure 1. Example patient illustrating daily and weekly symptom tracking. The red circles indicate that the patient answered "yes" to the weekly flare question, the white circles when the patient answered "no". The seven days leading up to the flare question are marked with grey boxes to illustrate flare (darker) and non-flare (lighter) weeks. In the inset, the three summary features are highlighted for pain: 1) Mean, 2) Standard deviation, and 3) Slope.

A flare week was defined as the seven days leading up to the weekly flare-question "*Have you experienced a flare in the last week?*" where the patient answered "yes" (Fig. 1). We summarised the number of patient-reported flare weeks. Symptom scores in flare and non-flare weeks were compared.

For each week prior to a flare question, we calculated the following summary features for all daily symptoms: 1) mean score, 2) standard deviation (SD), and 3) slope (Fig. 1, inset). Mixed effects logistic regression models quantified the associations between flare weeks and each summary feature.

Results: Twenty patients tracked symptoms over three months. 60% were female, all but one were white British, and mean age was 56.9±11.1 years. The median number of days in the study was 81 (interquartile range (IQR) 80, 82). We included 168 participant weeks. In total, 15/20 participants reported at least one flare week, with 54 patient-reported flare weeks in total. Participants reported a median of two flare weeks (IQR 0.75, 3.5).

In paired analyses, all mean symptom scores were significantly higher (difference on average 0.67 (SD 0.22)) in flare weeks compared to non-flare weeks except for sleep ($p< 0.05$). The SDs, a measure of variability, were slightly higher in flare weeks, but only significantly different from non-flare weeks for emotional wellbeing. For slope, there was an increase for all symptoms in flare weeks, although only the slopes of pain, physical wellbeing, and coping were statistically significant.

Due to strong correlations between symptoms, multivariate modelling of all symptoms and their summary features was not possible. Rather, we modelled pain as an example using each of its three derived features. In the full pain model, mean pain scores appeared to be more clearly associated with a flare (odds ratio 1.83 (1.15; 2.97)) than the change in scores in the preceding week.

Conclusion: In our RA cohort, self-reported flares were frequent. Flare weeks were broadly associated with higher scores (for mean, variability, and slope) across a range of daily symptoms in the preceding week, but the absolute value seemed more important than the change. The correlation between daily symptoms made it impossible to disentangle the contribution of individual symptoms to the flare experience.

Future analysis of daily symptoms may allow us to predict imminent flares, opening the opportunity for just-in-time interventions.

Disclosure: J. Gandrup, None; **S. van der Veer**, None; **J. McBeth**, None; **W. Dixon**, Google, 2, Bayer, 2, Abbvie, 2.

Abstract Number: 0812

Are Biologic and Targeted Synthetic Disease Modifying Anti-Rheumatic Drugs Associated with Work Participation Improvement in Early Rheumatoid Arthritis? A Systematic Review and Meta-analysis

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Treatment of early RA with DMARDs is associated with particularly effective responses, resulting in sustained beneficial outcomes, including clinical and radiographic remission and optimal health related quality of life. The benefit of treatment with biological (b) and targeted synthetic (ts) DMARDs on work participation (WP), a top social role for RA patients, has been less frequently studied. Our aim was to review the evidence of treatment with b-/tsDMARDs in patients with early RA on WP outcomes.

Methods: Following PRISMA, a systematic literature review (SLR) was conducted in key electronic databases up to December 2020. The PICOT framework was: (P) RA with disease duration ≤3y; (I) b-/tsDMARDs; (C) any treatment/placebo (PBO); (O) employment status (ES), at-work productivity loss (presenteeism) and/or absence from paid work (sick leave - SL); (T) longitudinal studies (except cost-effectiveness) with any follow-up duration. Two reviewers independently identified eligible studies and extracted data using a self-composed extraction sheet. The Cochrane risk-of-bias tool for RCTs was used for the assessment of risk of bias. Odds ratios (OR) were computed for individual studies, and a pooled OR was obtained by random-effects meta-analysis. Statistical heterogeneity was assessed by I^2.

Results: From 5979 records (65 full-text articles screened), 9 studies were included in the SLR (6 RCTs in conventional synthetic (cs)DMARDs-naïve patients; 2 RCTs in bDMARD-naïve patients with inadequate response to csDMARDs; 1 RCT of bDMARD tapering after initial combination with methotrexate (MTX)). Studies assessed WP outcomes with validated and non-validated instruments (*Table 1*). Interventions comprised 4 bDMARDs (abatacept, adalimumab, etanercept and infliximab) and 1 tsDMARD (baricitinib). Most studies had MTX monotherapy(±PBO) (n=7;78%) as active comparator; in 2 studies bDMARD(±PBO) was added to background MTX. For presenteeism and SL, most between-group comparisons showed improvement in favour of b-/tsDMARDs, but not all comparisons were statistically significant – *Table 1*. A meta-analysis for ES (weeks 56 to 104) included 3 studies (total of 1124 patients) with

Table 1. Study characteristics of the included studies and overview of the between-group results.

Author (year)	Selected population	Intervention (I) Comparator (C)	N total (t) N employed (e)	Assessed Outcome	Instrument	Follow-up	Change (I vs C)$
Smolen, 2006# ASPIRE	RA ≤3 y csDMARDs naïve	I: IFX+MTX C: PBO+MTX	Nt= 621; Ne= 385 Nt=235; Ne=157	ES SL	Self-reported‡	54 w	+ (nt) + (nt)
Bejarano, 2008#	RA <2 y csDMARD naïve	I: ADA+MTX C: PBO+MTX	Nt=Ne=75 Nt=Ne=73	ES Pres	Self-reported‡	56 w	+* +*
Anis, 2009 COMET	RA for 3m-2y csDMARDs naïve	I: ETN+MTX C: MTX	Nt=Ne=105 Nt=Ne=100	ES Pres SL	Self-reported‡	52 w	+ (nt) +* +*
van Vollenhoven, 2010# PREMIER	RA <3 y csDMARDs naïve	I_1: ADA+MTX I_2: ADA+PBO C: PBO+MTX	Nt=219; Ne=130 Nt=231; Ne=125 Nt=214; Ne=110	ES Pres SL	Self-reported‡	104 w	+ (I_1 vs C)* / + (I_2 vs C) + (I_1 vs C)* / + (I_2 vs C) + (I_1 vs C)** / + (I_2 vs C)**
Eriksson, 2013 Swefot	RA <1 y csDMARDs-IR	I: INF + MTX C: csDMARD + MTX	Nt=109; Ne=97 Nt=101; Ne=83	SL	Social insurance registry	104 w	+
Emery, 2016 OPTIMA PROWD	RA <1 y csDMARDs naïve	I: ADA+MTX C: PBO+MTX	OPTIMA/PROWD: Nt=146/64; Ne=146/64 Nt=174/60; Ne=174/60	ES Pres SL	WPAI-RA	OPTIMA: 24 w PROWD: 26 w	+/- (nt) +/- +/-
Fleischmann, 2016, AMPLE	RA ≤3 y csDMARDs-IR	I: ABA+MTX C: ADA+MTX	Nt=328 Ne=NR Nt=318 Ne= NR	Pres SL	WPAI-RA	104 w	+§ (nt)
Wiland, 2016 PRIZE	RA ≤1 y csDMARDs naïve	I. ETN25/MTX C_1. PBO+MTX C_2. PBO+PBO	Nt=63 Ne=NR Nt= 65 Ne=NR Nt= 65 Ne=NR	Pres SL	WPAI-RA	117 w	+ (I vs C_1/C_2)* + (I vs C_1/C_2)*
Schiff, 2017 RA-BEGIN	RA < 2y csDMARDs naïve	I_1: BARI+MTX I_2: BARI+PBO C: PBO+MTX	Nt=159; Ne=67 Nt=215; Ne=117 Nt=210; Ne=94	ES Pres SL	WPAI-RA	52 w	+ (I_1/I_2 vs C) (nt) + (24w: I_1/I_2 vs C)** (52w: I_2 vs C**) + (24w: I_1/I_2 vs C)* (52w: I_2 vs C)*

ABA – abatacept; **ADA** – adalimumab; **BARI** – baricitinib; **csDMARDs** – conventional synthetic disease-modifying antirheumatic drugs; **ETN** – etanercept; **IFX** – infliximab; **IR** – irresponsive; **nt** – significance not tested; **PBO** – placebo; **RA** – rheumatoid arthritis; **SD** – standard deviation; **WPAI** – Work Productivity and Activity Impairment questionnaire.
Studies included in the meta-analysis; *$p \leq 0.05$ vs. Comparator; **$p \leq 0.001$ vs. Comparator; ‡ non-validated instrument; § includes both presenteeism and sick leave in a combined score; **"+"**: higher benefit for the intervention group; **"+/-"**: no meaningful differences between intervention and comparator groups; $ when more than one comparator and/or intervention were tested, the respective between-group comparison is presented.

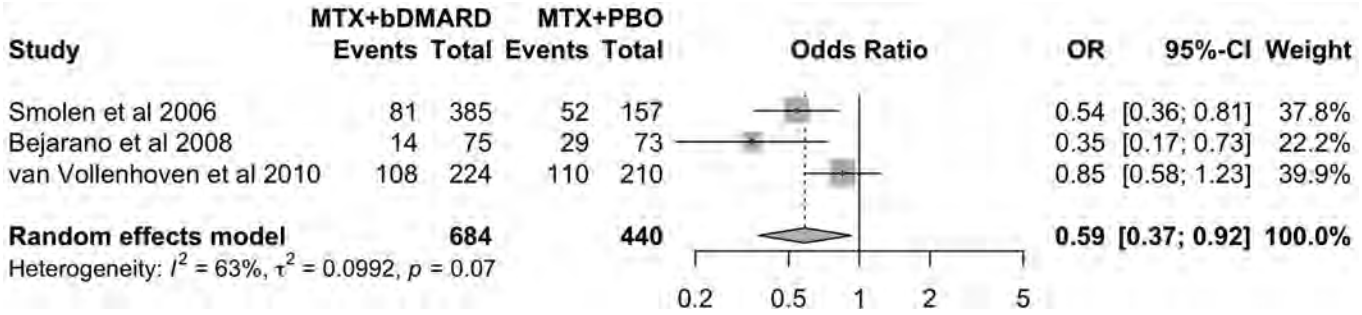

Figure 1. Random-effects meta-analysis of the employment loss in patients with early rheumatoid arthritis treated with MTX+bDMARD versus MTX in monotherapy. bDMARD – biologic disease-modifying antirheumatic drugs; MTX – methotrexate; PBO – placebo.

either adalimumab or infliximab as intervention (*Figure 1*). The pooled OR of the 3 studies showed a lower likelihood of employment loss in patients treated with MTX+bDMARDs (OR: 0.59; 95% CI:0.37 to 0.92) compared to MTX+PBO. High statistical heterogeneity was observed 63% [0.0%; 89.3%].

Conclusion: A protective effect against employment loss was observed in patients with early RA treated with MTX-+bDMARDs compared to MTX monotherapy. Although trends towards beneficial effects of b-/tsDMARDs were seen on presenteeism and SL, the methodological heterogeneity hampers clear conclusions. The additional role of b-/tsDMARD in a real world T2T approach should be further studied in long term (preferably population controlled) studies. Efforts to homogenize the design, analysis and reporting of future studies with WP as an outcome by following recently developed points to consider are crucial[1].

[1]Boonen A, et al. Ann Rheum Dis. 2021 https://doi.org/10.1136/annrheumdis-2020-219523

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Abstract Number: 0813

Improvement in Clinical Disease Activity and Patient-Reported Outcomes After 6 Months of Treatment with Abatacept, Stratified by Line of Therapy, in Patients with RA: Results from a Large, US, National Observational Study

Leslie Harrold[1], Keith Wittstock[2], Sheila Kelly[2], Sang Hee Park[2], Xue Han[2], Ying Shan[1], Carla Roberts-Toler[1], Nicole Middaugh[1] and Vadim Khaychuk[2], [1]CorEvitas, LLC, Waltham, MA, [2]Bristol Myers Squibb, Princeton, NJ

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

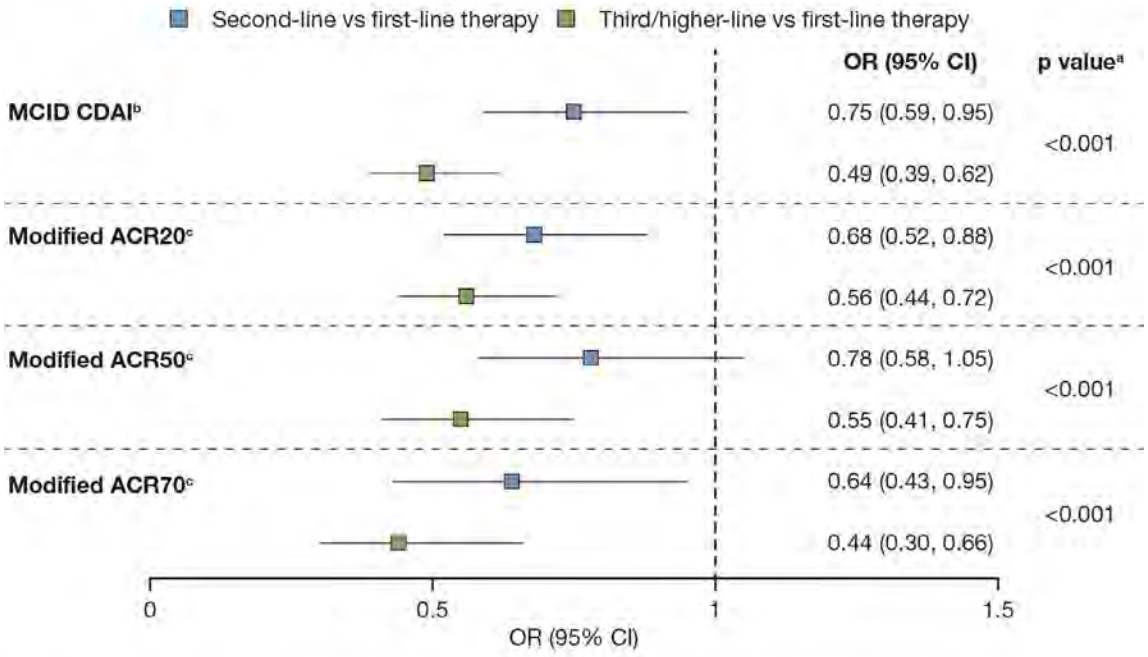
Background/Purpose: RA is more responsive to treatment in the early stages of disease, and early treatment may lead to better long-term outcomes.[1,2] Data on the effectiveness of specific drugs as first or later lines of therapy will help inform treatment sequencing. Data from patients enrolled in the Corrona RA Registry network were used to compare the effectiveness of abatacept across lines of therapy overall (primary cohort) and in a subset of patients who were ACPA+.

Table 1. Adjusted mean change in CDAI and patient-reported outcomes from BL to 6 months after initiation of abatacept by line of therapy (primary cohort)

Adjusted outcome, mean change (SE)	First-line (n = 440)	Second-line (n = 898)	Third/higher-line (n = 1515)	*P* value[a]
CDAI	−7.96 (0.33)	−7.49 (0.27)	−5.74 (0.19)	< 0.001
Patient-reported pain (VAS 0–100)	−9.43 (0.69)	−7.98 (0.47)	−7.70 (0.35)	0.074
Patient-reported fatigue (VAS 0–100)	−7.49 (0.71)	−5.87 (0.51)	−4.81 (0.36)	0.002
Patient-reported HAQ	−0.16 (0.01)	−0.12 (0.01)	−0.08 (0.01)	< 0.001

[a]Estimated by multiple linear regression model adjusted for age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain, and BL fatigue (factors that were identified *a priori* based on clinical experience or that differed significantly by line of therapy); *P* values reflect ANOVA overall test of differences across lines of therapy.
VAS, visual analog scale.

Figure 1. Adjusted odds ratio of achieving MCID CDAI or modified ACR20/50/70 at 6 months after initiation of abatacept by line of therapy (primary cohort)



[a]Estimated by multiple logistic regression analysis adjusted for age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain and BL fatigue (factors that were selected a priori based on clinical experience or differed significantly by line of therapy); p values reflect overall difference across lines of therapy.
[b]Reduction in CDAI score of 2 if BL disease activity was low (CDAI score ≤10); of 6 if BL disease activity was moderate (CDAI score >10 and ≤22); and of 11 if BL disease activity was high (CDAI score >22).
[c]Modified ACR criteria is based on 2 out of 4 measures (not using ESR or CRP).
Modified ACR20/50/70=20/50/70% improvement in modified ACR criteria; MCID=minimal clinically important difference; OR=odds ratio.

Methods: Patients with RA who initiated abatacept (January 2006 to October 2020), had 6 months' follow-up (within 4–9 months of starting abatacept), had baseline (BL) and follow-up CDAI scores available, and had BL CDAI > 2.8 were included. Outcomes were compared for first-, second- and third or higher-line therapy: 0, 1 or ≥ 2 prior biologic DMARDs or Janus kinase inhibitors, respectively. Continuous outcomes included change from BL to 6 months in mean CDAI and patient-reported pain, fatigue, and HAQ. Binary outcomes included rate of achieving minimal clinically important difference (MCID) in CDAI or modified ACR20/50/70 at 6 months. Continuous and binary outcomes were analyzed using multiple linear and logistic regression, respectively. The models included line of therapy, age, sex, disease duration, work status, SC nodules, history of hypertension and depression, BL CDAI, BL patient-reported pain, and BL fatigue. Additional subgroup analyses were carried out in patients with moderate/high disease activity (CDAI > 10) at BL.

Results: In total, 2876 patients (2327 with BL CDAI > 10; 890 ACPA+) were included; 442, 911, and 1523 patients initiated first-, second- or third/higher-line abatacept, respectively. Compared with patients on second/third/higher-line abatacept therapy, those on first-line abatacept were significantly older, had shorter disease duration, and had lower BL CDAI, pain and fatigue (all $P < 0.001$). In adjusted analyses, patients receiving abatacept as earlier lines of therapy had significantly greater improvement from BL in mean CDAI and in patient-reported fatigue and HAQ (**Table 1**). There was no significant difference between lines of therapy in change in patient-reported pain. Patients receiving first-line abatacept had significantly higher odds of achieving a MCID in CDAI or modified ACR20/50/70 response (**Figure 1**). Similar patterns were seen when the sample was limited to patients with moderate/high disease activity or in patients who were ACPA+.

Conclusion: There were significant differences in improvement in clinical disease activity and patient-reported outcomes across lines of therapy. Better treatment responses were observed with earlier lines of abatacept therapy in the overall population, in patients who were ACPA+ and in those with moderate/high BL disease activity.

References

1. Harrold LR, et al. *Clin Rheumatol* 2017;36:1215–1220.
2. Monti S, et al. *RMD Open* 2015;1(Suppl 1):e000057.
Medical writing: Claire Line, PhD (Caudex), funded by Bristol Myers Squibb

Disclosure: L. Harrold, Bristol Myers Squibb, 2; **K. Wittstock**, Bristol Myers Squibb, 3, 11; **S. Kelly**, Bristol Myers Squibb, 3; **S. Park**, Bristol Myers Squibb, 3; **X. Han**, Bristol Myers Squibb, 3; **Y. Shan**, CorEvitas, 3; **C. Roberts-Toler**, CorEvitas, 3; **N. Middaugh**, None; **V. Khaychuk**, Bristol Myers Squibb, 3.

Abstract Number: 0814

Patient Characteristics, Efficacy, and Treatment Patterns of Tofacitinib Monotherapy in Patients with RA: Contextualization of Randomized Controlled Trial Results with Real-world Data

Janet Pope[1], Axel Finckh[2], Lucia Silva-Fernández[3], Peter Mandl[4], Haiyun Fan[5], Jose L Rivas[6], Monica Valderrama[6] and María Montoro[6], [1]University of Western Ontario, London, ON, Canada, [2]University Hospital of Geneva, Geneve - Vesenaz, Switzerland, [3]Hospital Universitari Son Espases, Palma de Mallorca, Spain, [4]Division of Rheumatology, Medical University of Vienna, Vienna, Austria, [5]Pfizer Inc, Collegeville, PA, [6]Pfizer SLU, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Randomized controlled trials (RCTs) have long been considered the gold standard for clinical research, but can be complemented with real-world data (RWD) to further inform clinical decision-making. We evaluated patient (pt) characteristics, efficacy, and treatment patterns for tofacitinib monotherapy in pts with RA using RCT data and available RWD.

Methods: Three cohorts of pts receiving tofacitinib 5 mg BID monotherapy were defined for post hoc analyses of RCT data: Cohort (C)1, pts with an inadequate response to DMARDs from Phase (P)3 and P3b/4 RCTs (NCT00814307/

Table. Demographics and baseline disease characteristics for pts receiving tofacitinib monotherapy in RCTs and available RWD sources

	RCT data			RWD
	Cohort 1[a] (N=627)	Cohort 2[b] (N=373)	Cohort 3[c] (N=498)	Reed et al 2019[1] (N=238)
Age, yrs				
Median (range)	52.0 (21.0–81.0)	52.0 (18.0–76.0)	56.0 (19.0–82.0)	-
Median (IQR)	-	-	-	59 (52–68)
Female, n (%)	526 (83.9)	286 (76.7)	424 (85.1)	193 (81.1)
Race, n (%)				
Asian	82 (13.1)	68 (18.2)	216 (43.4)	-
Black	23 (3.7)	13 (3.5)	5 (1.0)	-
White	449 (71.6)	239 (64.1)	232 (46.6)	197 (82.8)
Other	73 (11.6)	53 (14.2)	45 (9.0)	-
Disease duration, yrs				
Median (range)	5.8 (0.2–42.3)	0.8 (0.0–44.0)	5.5 (0.0–38.0)	-
Median (IQR)	-	-	-	10 (5–16)
CDAI				
Median (range)	38.5 (10.7–75.3)	37.5 (11.5–74.3)	33.6 (11.8–71.9)	-
Median (IQR)	-	-	-	17.9 (9.8–27.0)
Concomitant glucocorticoids, n (%)	358 (57.1)	175 (46.9)	277 (55.6)	65 (27.3)[d]
Glucocorticoid dose, mean (SD) mg/day	4.3 (9.1)	3.6 (5.7)	6.2 (3.4)	4.4 (1.0)[d]
bDMARD-naïve, n (%)	626 (99.8)	373 (100.0)	498 (100.0)	23 (9.7)

[a]NCT00814307 and NCT02187055; [b]NCT01039688; [c]NCT00413699 and NCT00661661;
[d]Concomitant glucocorticoids were prednisone

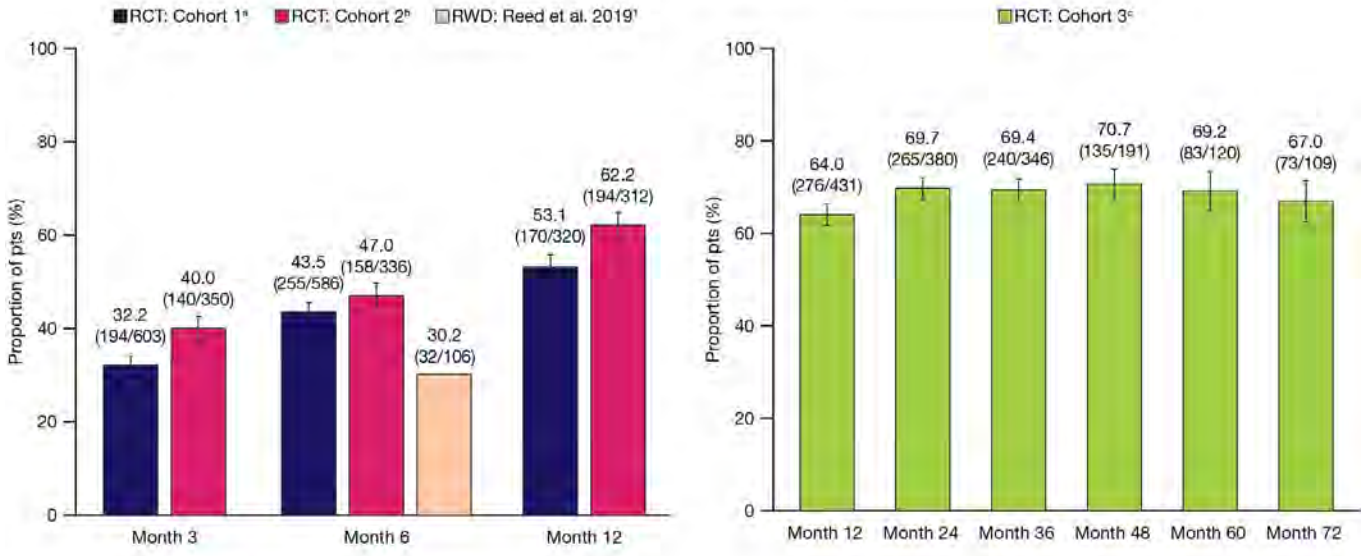
All pts included in the RCT cohorts received tofacitinib 5 mg BID monotherapy; only pts who received tofacitinib 5 mg BID monotherapy throughout the long-term extension studies were included in Cohort 3

- represents where the variable of interest was not reported

bDMARD, biologic DMARD; BID, twice daily; CDAI, Clinical Disease Activity Index; IQR, interquartile range; pts, patients; RCT, randomized controlled trial; RWD, real-world data; SD, standard deviation

1. Reed GW et al. Rheumatol Ther 2019; 6: 573-86

Figure 1. CDAI-defined LDA (CDAI ≤ 10) rates in pts receiving tofacitinib monotherapy in RCTs and available RWD sources



[a]NCT00814307 and NCT02187055; [b]NCT01039688; [c]NCT00413699 and NCT00661661
All pts included in the RCT cohorts received tofacitinib 5 mg BID monotherapy; only pts who received tofacitinib 5 mg BID monotherapy throughout the long-term extension studies were included in Cohort 3
RCT error bars represent standard error; these data were not available for RWD
BID, twice daily; CDAI, Clinical Disease Activity Index; LDA, low disease activity; pts, patients; RCT, randomized controlled trial; RWD, real-world data
1. Reed GW et al. Rheumatol Ther 2019; 6: 573-86

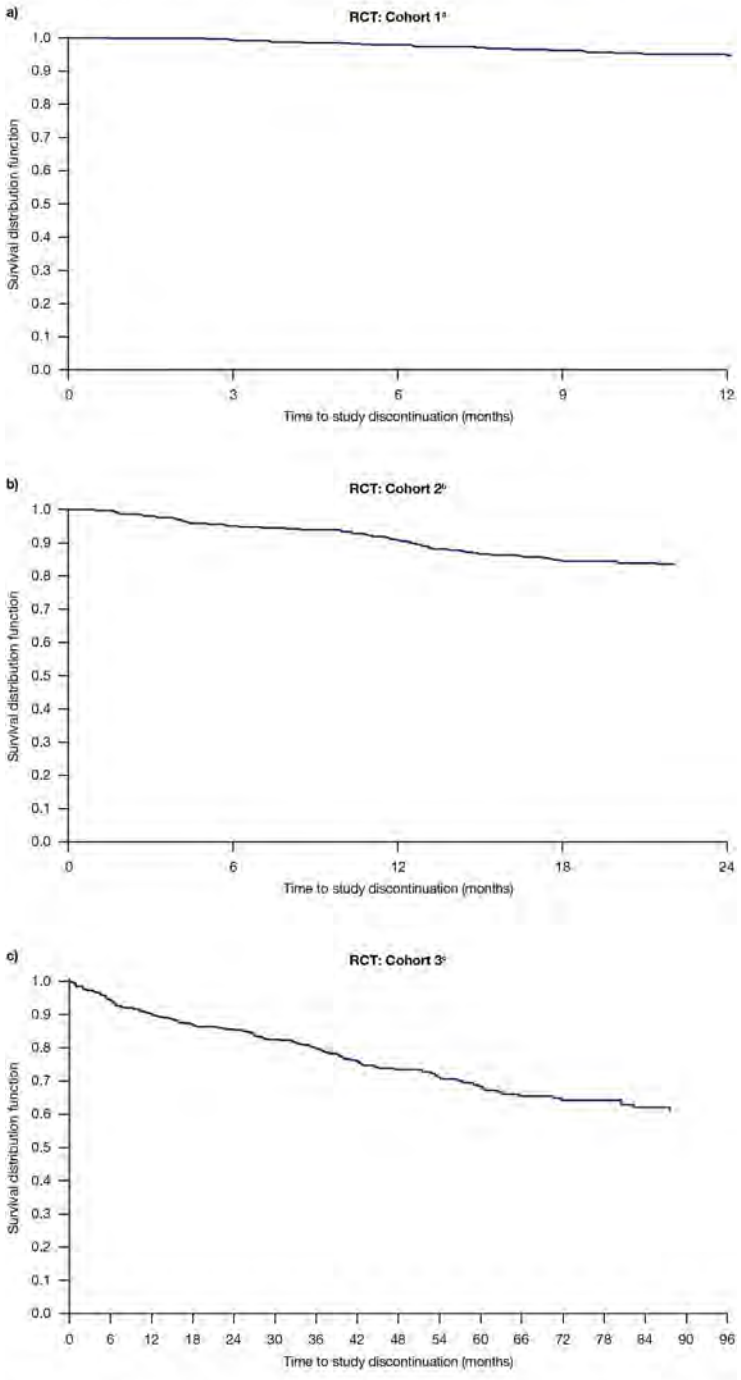
NCT02187055); C2, MTX-naïve pts from a P3 RCT (NCT01039688); and C3, pts who completed an index study and continued in any long-term extension study (NCT00413699/NCT00661661). Outcomes included Clinical Disease Activity Index (CDAI) low disease activity (LDA; scores ≤ 10) rates, and rates of/time to study discontinuation due to lack of efficacy or adverse events (AEs; per Kaplan–Meier plots). Across outcomes, available RWD are presented for contextualization, identified by non-systematic literature searches of PubMed, Embase, and ACR/EULAR abstracts, from 2013–2021.

Results: 1,498 pts treated with tofacitinib 5 mg BID monotherapy were included in the RCT analysis (C1, n=627; C2, n=373; C3, n=498); generally, baseline (BL) disease activity was high, most pts received concomitant glucocorticoids (GC) and were biologic (b)DMARD-naïve (Table). C1 and C2 CDAI LDA rates were ≥ 32.2% by Month (M)3 and sustained through M12 (Figure 1); C3 LDA rates ranged from 64.0–70.7% through M72 (Figure 1). In C1, C2, and C3, respectively, 4.0%, 15.6%, and 27.7% of pts discontinued due to lack of efficacy or AEs; Kaplan–Meier plots of time to discontinuation are presented in Figure 2. We identified 6 RWD publications that included tofacitinib monotherapy data; across publications, 16.6–59.2% of tofacitinib-treated pts received tofacitinib monotherapy.[1-6] Only 1 paper reported BL characteristics with tofacitinib monotherapy: median disease activity was moderate, pts had low GC use, and most were bDMARD-experienced[1] (Table 1). In the same paper, M6 CDAI LDA rates were 30.2% (Figure 1). Another paper estimated the 1-year retention rate for tofacitinib monotherapy as 59.7%.[6] While no RWD on treatment discontinuation specific to tofacitinib monotherapy were identified, 1 paper reported no significant differences in retention with tofacitinib monotherapy vs tofacitinib + conventional synthetic DMARDs (HR 1.11 [95% CI 0.91, 1.35]).[4]

Conclusion: Tofacitinib 5 mg BID monotherapy demonstrated good efficacy and persistence in post hoc analyses of RCT data. Variable monotherapy rates were seen in RWD; based on available data, tofacitinib monotherapy demonstrated good efficacy, and retention comparable with combination therapy.

1. Reed GW et al. Rheumatol Ther 2019; 6: 573-86
2. Babaeva A et al. Ann Rheum Dis 2020; 79: 635.

Figure 2. Kaplan–Meier plots of time to discontinuation of tofacitinib 5 mg BID monotherapy due to lack of efficacy or AEs in the RCT cohorts



[a]NCT00814307 and NCT02187055; [b]NCT01039688; [c]NCT00413699 and NCT00661661
All pts included in the RCT cohorts received tofacitinib 5 mg BID monotherapy; only pts who received tofacitinib 5 mg BID monotherapy throughout the long-term extension studies were included in Cohort 3
AE, adverse event; BID, twice daily; pts, patients; RCT, randomized controlled trial

3. Bird P et al. Clin Rheumatol 2020; 39: 2545-51.
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Abstract Number: 0815

Implementing Treat to Target (TTT) for Rheumatoid Arthritis (RA) Through a Virtual Learning Collaborative (LC) Program During COVID

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: TTT has been shown in multiple RCTs to be an effective paradigm for managing RA, however TTT has not been uniformly implemented in US rheumatology. In a prior RCT, we found improvement implementation of TTT at selected rheumatology practices during a face-to-face 9-month Learning Collaborative (LC) (1). An LC is a method for group-based quality improvement, which has been successfully used in healthcare. In the current study, we tested a 6-month virtual LC that took place during the COVID pandemic as a method for improving implementation and adherence with TTT in 18 rheumatology practices in the US.

Methods: During 2020-2021, we conducted a virtual LC for TTT in RA. All meetings used video-conferencing and a website allowed participants to share documents and data. The LC consisted of one 5-6 hour kickoff session and 6 monthly webinars. Faculty and participants discussed procedures for TTT, its rationale, and methods for quality improvement; we focused on Plan-Do-Study-Act (PDSA) cycles as a method for implementing TTT. Practices were asked to meet and carry-out PDSA cycles. Each monthly webinar discussed the PDSAs, reinforced topics from the kick-off, and demonstrated data on TTT adherence from the practices. Practices were asked to review 20-25 visit notes from RA patients and to input de-identified data into the website. The data were analyzed and shared in the monthly webinars. The webinars allowed sites to discuss the data and share best (and worst) practices. Adherence with TTT was measured as a percentage of the TTT component processes: 1) measure and document RA disease activity (any standard disease activity measure considered acceptable, e.g., CDAI, RAPID3, DAS28), 2) determine a target disease activity, 3) make treatment changes if not at target, and 4) document shared decision-making.

Results: 18 sites from 10 states (plus Washington DC) participated; they represented 45 rheumatology clinicians (MDs, nurse practitioners, and physician's assistants) who attended the kick-off and/or monthly webinars. During the 6 months, sites entered data on 1826 patient visits. Adherence with TTT improved over the six months from a mean of 50.7% at baseline to 83.7% at study completion (see **Figure 1**, p for trend < 0.001). Each aspect of TTT measured also improved (see **Figure 2**). The main reason for TTT non-adherence was that clinicians changed treatment in only 59% of visits where patients were not at target. Some reasons documented (not mutually exclusive) for not intensifying treatment when patients were not at target are shown in **Table 1**. They include patient preference (33%), clinician

Figure 1: Adherence with Treat to Target Across All Sites During the Learning Collaborative

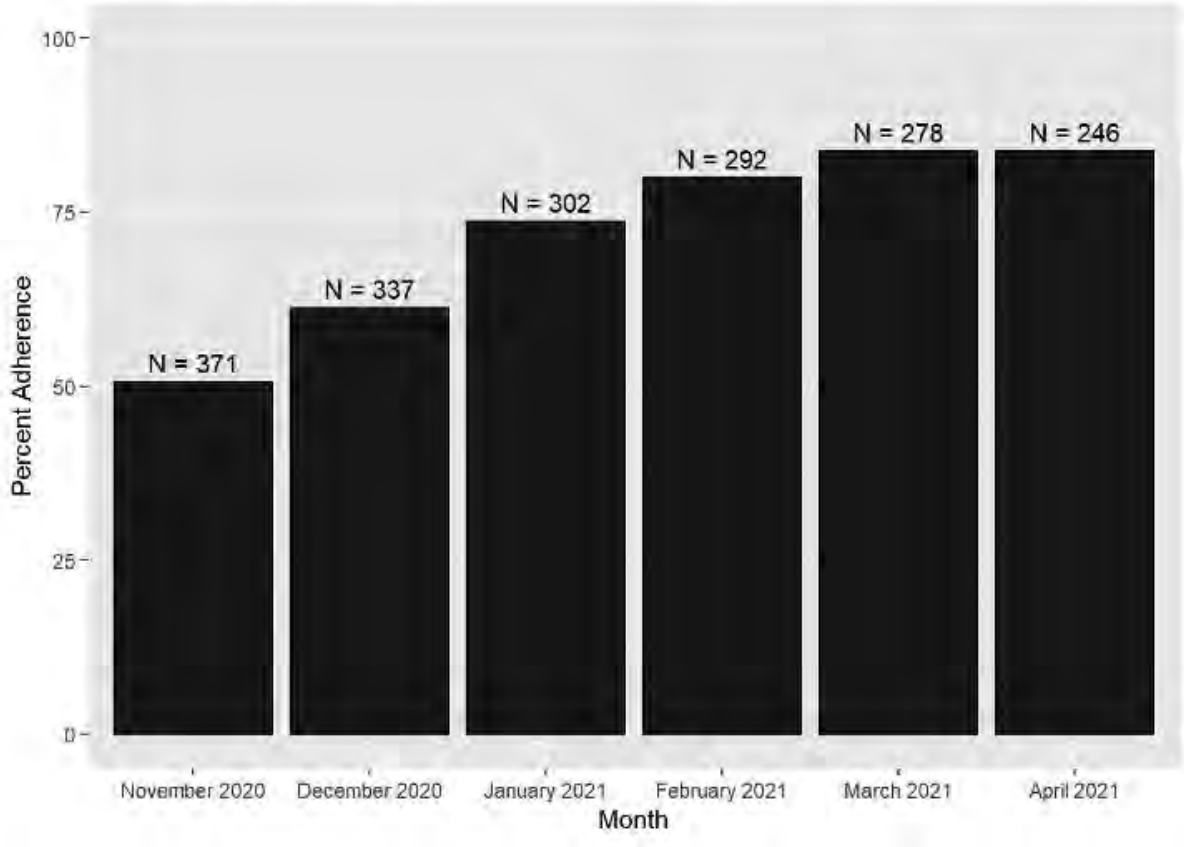

Figure 2: Adherence for the Four Components of TTT Adherence

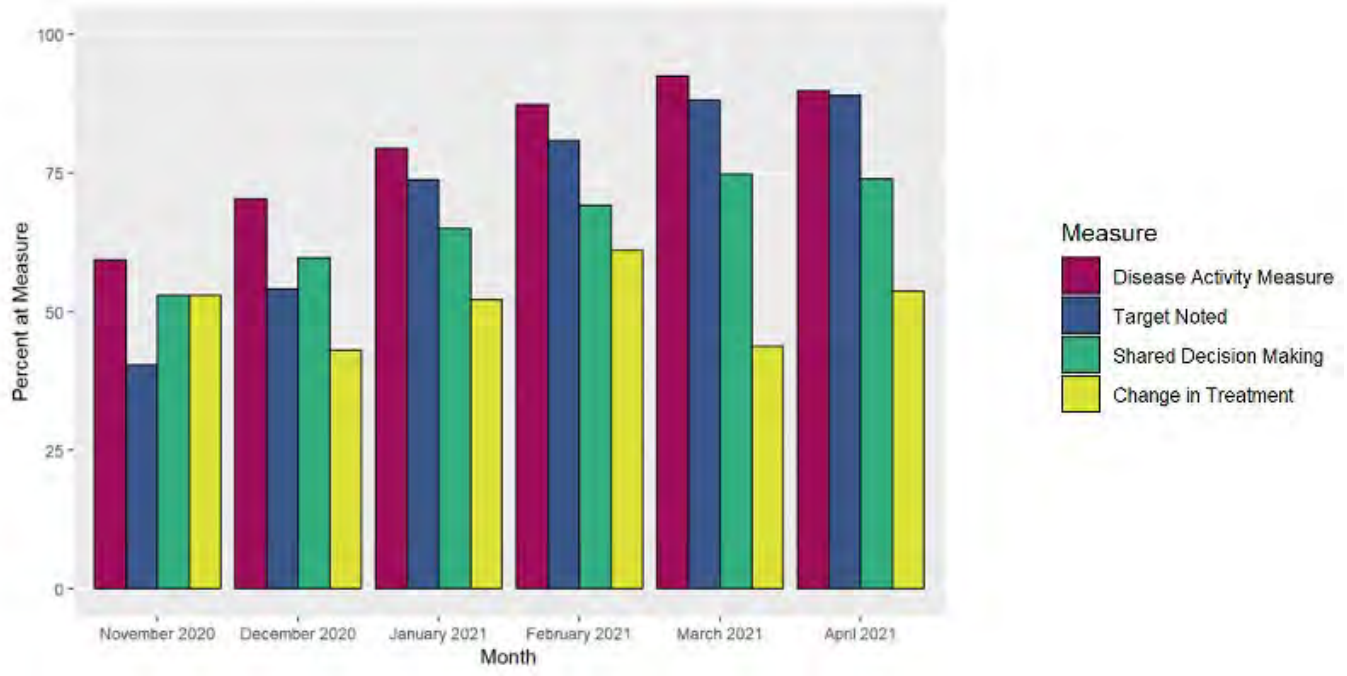

Table 1: Reasons for Not Changing RA Treatment when Patient Not at Target (n = 346)

Reasons	N (%)
Patient preference	115 (33.2)
Clinician preference	65 (18.8)
Pain not from rheumatoid arthritis	87 (25.1)
Wanted to give current treatment more time to work	65 (18.8)
Clinician/Patient did not want to make a change during COVID-19	5 (1.4)
Other reasons	9 (2.6)

preference (19%), clinician deemed symptoms were not from RA (25%), and the desire to observe the treatment effect for more time (19%).

Conclusion: Implementing TTT for RA can be improved through a relatively low-cost virtual LC. This improvement in TTT was observed despite the COVID pandemic. We would urge professional societies to experiment with implementing LC quality improvement programs virtually to facilitate wider dissemination of best practices.

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Abstract Number: 0816

Analysis of Abatacept Treatment Retention and Efficacy According to Disease Duration and Treatment Line in a Real-World Setting

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Longer disease duration and greater number of prior DMARDs have been associated with lower treatment efficacy in patients with RA.[1] Abatacept is a biologic (b)DMARD for treatment of moderate-to-severe

RA and is available in SC formulation, which may offer convenience benefits with efficacy similar to IV administration.[2] ASCORE (NCT02090556) was a 2-year, observational, prospective, multicenter study of SC abatacept for treatment of RA in routine clinical practice.[3] This *post hoc* analysis was conducted to determine if retention and efficacy of abatacept were impacted by disease duration and/or treatment line.

Methods: Eligible patients, aged ≥18 years, with active moderate-to-severe RA (ACR/EULAR 2010 criteria[4]) who were IV abatacept-naive and initiated SC abatacept 125 mg once weekly, were enrolled into 2 cohorts: bDMARD-naive patients and those with ≥1 prior bDMARD treatment failure. This *post hoc* analysis evaluated abatacept retention using Kaplan-Meier estimates, as well as disease activity scores (DAS28 [ESR]), CDAI and SDAI in patients with disease duration of ≤2, 3–5, 6–10 or >10 years, and in patients taking abatacept as first-line or ≥ second-line treatment.

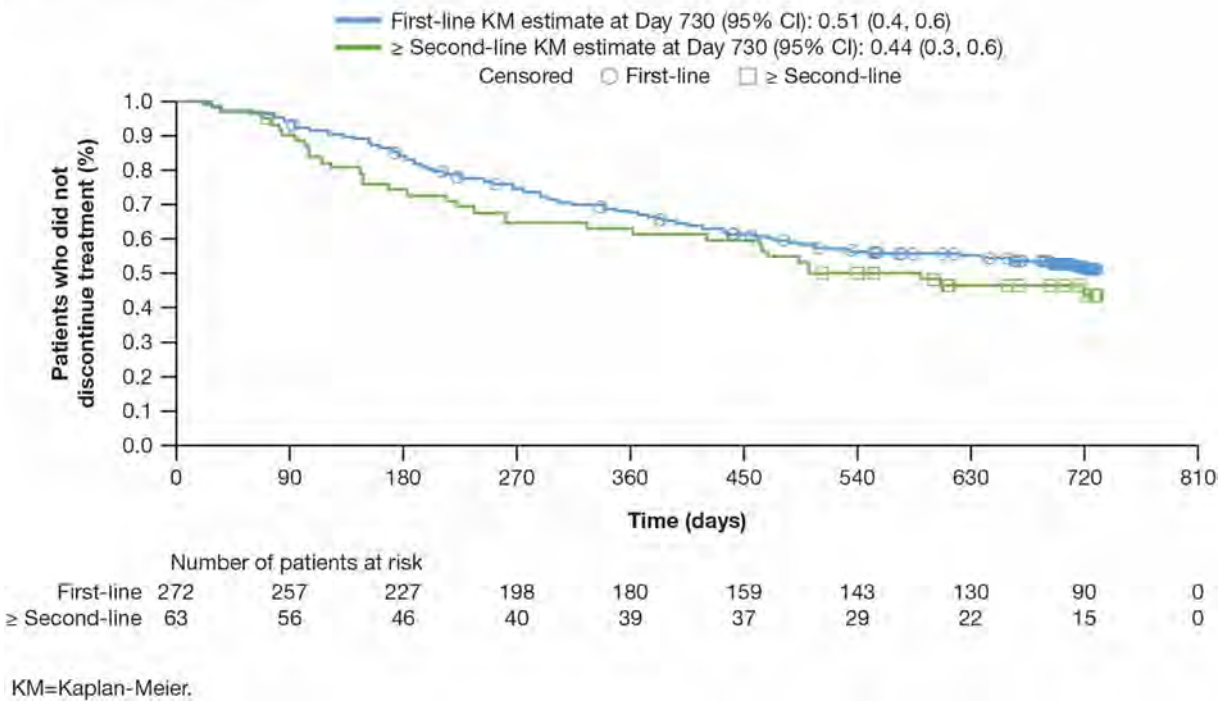
Results: Table 1 shows baseline characteristics. Mean age increased with disease duration; other characteristics were comparable across groups. Retention proportions (95% CIs) at Month 24 were 0.50 (0.4, 0.5), 0.47 (0.4, 0.5), 0.51 (0.5, 0.5) and 0.46 (0.4, 0.5) in the ≤2, 3–5, 6–10 and >10 years' duration groups, respectively. Proportion of patients (95% CI) with ≤2 years' duration retaining treatment at Month 24 were 0.51 (0.4, 0.6) among those using abatacept as first-line treatment and 0.44 (0.3, 0.6) among those using abatacept as a ≥ second-line treatment (Figure 1). Proportions (95% CI) at Month 24 were 0.51 (0.5, 0.6), 0.57 (0.5, 0.6) and 0.52 (0.5, 0.6) in first-line patients and 0.43 (0.4, 0.5), 0.48 (0.4, 0.5) and 0.44 (0.4, 0.5) in ≥ second-line patients in the 3–5, 6–10 and >10 years' duration

Table 1. Baseline characteristics (n=2872)

	RA disease duration, years			
	≤2 (n=338)	3–5 (n=655)	6–10 (n=686)	>10 (n=1193)
Age, years				
n	338	655	686	1193
Mean (SD)	55.2 (12.8)	55.6 (12.7)	56.9 (13.0)	59.9 (12.2)
Weight, kg				
n	327	629	665	1150
Mean (SD)	75.3 (18.1)	76.4 (19.0)	74.7 (17.4)	72.9 (16.0)
DAS28 (ESR)				
n	247	439	441	743
Mean (SD)	5.2 (1.3)	4.9 (1.3)	5 (1.2)	5.1 (1.3)
DAS28 (CRP)				
n	267	460	467	799
Mean (SD)	4.7 (1.2)	4.6 (1.2)	4.7 (1.1)	4.7 (1.2)
CDAI				
n	269	477	474	805
Mean (SD)	26.9 (12.7)	25.3 (12.2)	26.8 (12.4)	26.6 (12.2)
SDAI				
n	255	448	445	749
Mean (SD)	28.3 (13.3)	26.8 (12.9)	27.9 (12.6)	28.0 (12.7)
RF status, n (%)				
RF+	159 (47.0)	342 (52.2)	345 (50.3)	597 (50.0)
RF–	103 (30.5)	152 (23.2)	158 (23.0)	215 (18.0)
Anti-CCP status, n (%)				
Anti-CCP+	165 (48.8)	332 (50.7)	333 (48.5)	516 (43.3)
Anti-CCP–	89 (26.3)	126 (19.2)	137 (20.0)	175 (14.7)

Patients with missing duration of disease are excluded.

Figure 1. Treatment retention over 2 years among patients with RA with ≤2 years' disease duration



KM=Kaplan-Meier.

groups, respectively. Mean (SE) changes from baseline in DAS28 (ESR) at Month 24 were –2.12 (0.205), –1.86 (0.151), –2.07 (0.140) and –2.05 (0.115) in the ≤2, 3–5, 6–10 and >10 years' duration groups, respectively; respective mean (SE) changes in CDAI were –18.74 (1.604), –15.60 (1.099), –18.50 (1.038) and –17.68 (0.850); and respective mean (SE) changes in SDAI were –19.10 (1.873), –15.72 (1.345), –19.54 (1.103) and –17.07 (0.939).

Conclusion: In this *post hoc* analysis of the real-world ASCORE trial, patients with RA receiving abatacept in clinical practice as first-line therapy had better retention versus those receiving it as a ≥ second-line treatment, regardless of disease duration at baseline. Retention rates were similar across disease duration subgroups. Improvements in disease activity were seen in all duration subgroups, without consistently greater or lesser improvement seen with longer disease duration.

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3. Alten R, et al. *Ann Rheum Dis* 2019;78(suppl 2):A1639.
4. Aletaha D, et al. *Arthritis Rheum* 2010;62:2569–2581.

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Abstract Number: 0817

Biosimilar Infliximab Therapy in Rheumatoid Arthritis, Axial Spondyloarthritis and Psoriatic Arthritis: A Long-term Follow-up Study on Infliximab-naive Patients and Switched Patients from the Originator to the Biosimilar CT-P13

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: ReFLECT study has been carried out to investigate real life use of CT-P13, the first monoclonal antibody biosimilar to infliximab (IFX) originator.

Methods: ReFLECT is a multicentre, prospective, observational study conducted in France to determine the characteristics of patients (pts) receiving CT-P13, its effectiveness and safety in a real-life setting. Eligible pts were both IFX naive pts (IFX-N) starting CT-P13 and those who have been switched from infliximab originator (IFX-S) to CT-P13. Interim results in adult pts with rheumatic diseases using descriptive statistical analyses from inclusion to a 24-month-follow-up period are presented here.

Results: Among the 1370 adult pts included between October 2016 and April 2019, data were analysed for 142 pts with rheumatoid arthritis (RA; 23.9% males; mean age: 61.5±10.9 years; 80 IFX-N / 61 IFX-S), 411 with axial spondyloarthritis (axSpA; 58.9% males; 48.1±13.1 years; 228 IFX-N / 179 IFX-S), and 96 with psoriatic arthritis (PsA; 41.7% males; 53.4±14.1 years; 55 IFX-N / 40 IFX-S) after a median duration between 8.7 and 12.9 years since diagnosis. At

Figure 1. Change from 1st administration of CT-P13 in CRP and disease activity scores at month 24

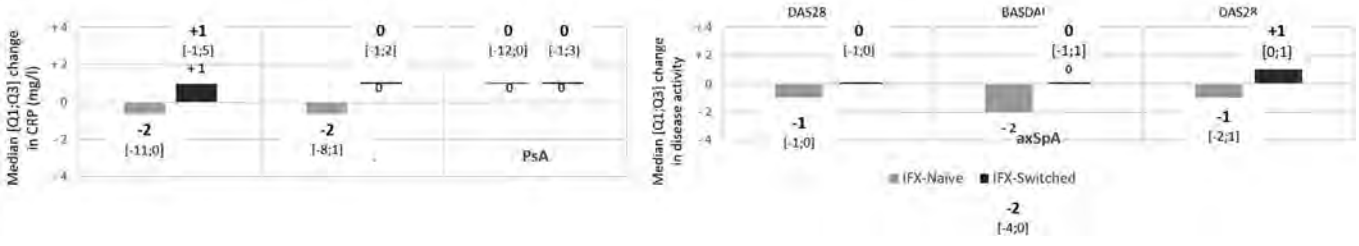

Table 1. CRP and disease activity scores after 24 months of treatment of CT-P13 since its 1st administration

Parameters in median [Q1;Q3]	Rheumatoid Arthritis		Axial Spondyloarthritis		Psoriatic Arthritis	
	Naive	Switched	Naive	Switched	Naive	Switched
CRP, mg/dl	**5** [2;9]	**5** [2;8]	**3** [2;9]	**3** [2;5]	**2** [1;4]	**2** [1;3]
Disease activity score *	**3** [3;4]	**2** [2;3]	**3** [1;4]	**2** [1;3]	**3** [2;3]	**3** [2;3]

* *DAS28 for RA and PsA, BASDAI for axSpA*

Table 2. Safety results

	RA (n = 142)	axSpA (n = 411)	PsA (n = 96)
Pts with ≥ 1 adverse event (AE)	67 (47.2%)	222 (54.0%)	48 (50.0%)
Pts with ≥ 1 AE related to CT-P13	33 (23.2%)	84 (20.4%)	19 (19.8%)
Pts with ≥ 1 serious AE	19 (13.4%)	42 (10.2%)	9 (9.4%)
Pts with ≥ 1 allergic infusion reaction †	4 (2.8%)	11 (2.7%)	1 (1.0%)
Pts with ≥ 1 infection ‡	10 (7.0%)	18 (4.4%)	3 (3.1%)

† *Including acute and delayed hypersensitivity reactions*
‡ *Including severe infections, tuberculosis, opportunistic infections, hepatitis*

inclusion, 67.9%, 24.1% and 50% had a concomitant treatment with methotrexate. At the time of the first administration of CT-P13, disease had been active in 94.2%, 76.6% and 83.3% of the IFX-N pts compared with 45.3%, 24.0% and 32.0% of the IFX-S pts respectively. From the first administration of CT-P13 to month 24, both CRP levels and disease activity remained stable in the IFX-S pts and as expected, improvement was observed in the IFX-N pts (Figure 1). In naive pts, after 24 months of treatment since its first administration, CT-P13 brought both CRP and disease activity down to levels comparable to those seen in pts having switched from the IFX originator to CT-P13 (Table 1). After 24 months of follow-up, 70 to 80% of pts in each group, whether IFX-N or IFX-S, remained on treatment with CT-P13, RA naive pts aside (53.8%). Main reason for CT-P13 withdrawing was treatment failure (including primary non-response and secondary loss of response) in both naive and switched pts: 31.6% and 13.1% of RA, 18.1% and 12.8% of axSpA, 9.1% and 15.8% of PsA pts respectively. Withdrawing for intolerance involved 6.3% and 1.6% of RA, 2.2% and 1.1% of axSpA, 1.8% and 2.6% of PsA in naive and switched pts respectively. Safety results are reported in Table 2.

Conclusion: Year 2 follow-up data indicate that CT-P13 effectively induced improvement in disease activity in pts with RA, axSpA and PsA receiving infliximab for the first time and maintained stable disease activity in pts having switched from IFX originator to CT-P13. This real-life study did not highlight any new safety concerns.

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Abstract Number: 0818

Biologics Initiation in Moderate vs Severe Rheumatoid Arthritis Patients: Prospective Observational Study from a Canadian Registry

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Prior studies have shown that in the real-world setting, rheumatoid arthritis (RA) patients have lower disease activity than those studied in clinical trials. However, randomized controlled trials for biologics continue to mainly recruit patients with severe disease. To assess the implications of this practice, our study investigates the proportion of patients achieving remission (DAS28-ESR ≤ 2.6), in RA patients with moderate disease activity and severe disease activity, at 12 months' post starting their first biologic, and identifies baseline predictors of biologic response.

Methods: This study included RA patients who have never been treated with a biologic and initiated their first biologic while enrolled in the Ontario Best Practices Research Initiative (OBRI) registry, between 2008 and 2019. Patients selected had either moderate RA (DAS28 ≥ 3.2 to ≤ 5.1) or severe RA (DAS28 > 5.1). Comparisons were made between the moderate and severe disease groups using the student's t-test for continuous variables, and the chi-square test for categorical variables. Multivariable logistic regression was used to test potential predictors of remission. Backward stepwise model selection was applied to select variables with *p*-value ≤0.10. Multiple imputation (MCMC method; n=20) was used to impute missing data.

	Moderate-RA (n=264)	Severe-RA (n=219)	*P*-Value
Remission, *n* (%)	111 (50)	45 (23)	<0.0001
Low disease activity, *n* (%)	151 (59)	74 (35)	<0.0001
Change in DAS from baseline ≥ 1.2, *n* (%)	168 (66)	164 (78)	0.0049
HAQ-DI change >0.22, *n* (%)	98 (53)	83 (52)	0.7974
Change in DAS28 from baseline, mean (SD)	-1.4 (1.3)	-2.2 (1.5)	<0.0001
Change in HAQ-DI from baseline, mean (SD)	-0.29 (0.57)	-0.30 (0.66)	<0.0001
Change in fatigue from baseline, mean (SD)	-0.98 (3.2)	-1.11 (3.2)	<0.0001
Change in sleep from baseline, mean (SD)	-0.85 (3.6)	-1.05 (3.9)	0.0004

Table 1. Outcomes at 12 months among patients with RA who initiated the first biologic.

Results: Overall, 641 patients initiated their first biologic, 483 had follow up data at 12 months (moderate disease activity=264; severe disease activity=219). In the moderate group, the mean age (SD) was 55.7 (13.1) and 80% were female. In the severe group, mean age (SD) was 58.4 (12.3) and 81% were female. At time of biologic initiation, the mean DAS28 for the moderate group was 4.1 (0.5), and 6.0 (0.6) for the severe group. After 12 months of starting a biologic, the proportion of patients achieving remission was 50% in the moderate group, and 23% in the severe group ($p< 0.0001$). In contrast, the proportion of patients achieving significant clinical change from baseline (improvement in DAS28 ≥ 1.2) was 78% in the severe group, compared to 66% in the moderate group ($p=0.0049$). More specifically, the absolute improvement in DAS28 after 12 months was higher in the severe group at 2.2 (1.5), compared to a change of 1.4 (1.3) in the moderate group ($p< 0.0001$). Negative predictors of remission include female gender (odds ratio (OR), 0.57, 95% confidence interval (CI), 0.33-0.97; $p=0.039$), and higher HAQ-DI score (OR 0.49, 95% CI 0.36-0.68; $p< 0.001$). In turn, moderate disease at time of biologic initiation (OR 2.38, 95% CI 1.50-3.79; $p=0.0390$) was identified as a positive predictor of remission.

Conclusion: This prospective cohort study found RA patients with moderate disease activity are more likely to reach targeted states (remission and low disease activity), whereas severe patients have greater absolute improvements in DAS28 and HAQ-DI but are less likely to achieve remission. Moderate disease is a positive predictor for remission, whereas female gender and a higher HAQ-DI score are negative predictors.

Disclosure: N. Guo, None; **X. Li**, None; **M. Movahedi**, None; **A. Cesta**, None; **C. Bombardier**, AbbVie, 2, 5, 6, Amgen, 5, BGP Pharma ULC, 1, 6, Gilead, 5, GSK, 1, 6, Janssen, 2, 5, 6, Lilly Pharmaceuticals, 5, Medreleaf/Aurora, 5, Merck, 1, 2, 5, 6, Pfizer Pharmaceuticals, 1, 5, Sandoz, 5, Samsung Bioepis, 2, 6.

Abstract Number: 0819

A Real-World 2-Year Prospective Study of Medication Tapering in Patients with RA in Sustained Remission in the RHEUmatoid Arthritis Medication TAPering (RHEUMTAP) Cohort

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Long term use of conventional synthetic DMARDs (csDMARDs) and biologics in RA has clinical risks including infection and malignancy. Patients with chronic RA remain interested in the question of medication tapering per our previous survey-based study within the RHEUmatoid Arthritis Medication TAPering (RHEUMTAP) cohort. Few RCTs and retrospective studies have systematically studied clinical outcomes of medication tapering in RA. In this study, we prospectively compared the clinical outcomes of different medication tapering groups within the RHEUMTAP cohort.

Methods: RHEUMTAP is a 2 year prospective cohort of patients with RA in sustained remission on biologics seen at Allegheny Health Network Rheumatology between 11/30/2018 and 11/30/2020 with at least 6 months follow up. Biologic tapering regimens were pre-determined based on provider consensus. Manual electronic health record (EHR) review was performed to confirm sustained remission on biologic therapy defined as CDAI≤2.8, stable RA medication

Table 1. Characteristics of Tapered and Not-Tapered groups

Variable	No taper (n=77)	Only biologic tapered (n=26)	Only csDMARD tapered (n=23)	Both biologic + csDMARD tapered (n=5)
Demographics				
Age	59.7 (±11)	60.3 (±11)	58.8 (±14)	57.8 (±12)
Female	60 (78%)	19 (73%)	22 (96%)	4 (80%)
Caucasian	70 (96%)	21 (88%)	22 (96%)	5 (100%)
BMI	29.3 (±5.8)	28.2 (±5.2)	30.5 (±7)	31.1 (±9)
Smoking history, yes	40 (52%)	11 (42%)	8 (35%)	2 (40%)
RA and Medication related variables				
Seropositive disease (RF ± CCP)	54 (70%)	17 (65%)	18 (78%)	4 (80%)
Erosive disease	21 (27%)	7 (27%)	5 (22%)	0
Baseline CDAI score	0 (0-1)	1 (0-1)	1 (0-1)	0.5 (0-1)
End visit CDAI score	4 (3-6)	8.5 (2-15)	4.5 (4-5)	18 (18-18)
Glucocorticoid use	14 (18%)	1 (3.9%)	2 (8.7%)	1 (20%)
Taper related variables				
Provider initiated taper	N/A	19 (73%)	12 (73%)	3 (60%)
Visit Taper Started				
Baseline visit	N/A	2 (7.7%)	2 (8.7%)	0
Visit#1		17 (65%)	15 (65%)	4 (80%)
Visit#2		5 (19%)	5 (22%)	1 (20%)
Visit#3		1 (3.9%)	1 (4.3%)	0
End visit		1 (3.9%)	0	0
End Visit Type, Virtual	21 (27%)	7 (30%)	9 (36%)	2 (40%)
Infection ± antibiotic use	7 (9.1%)	4 (15%)	2 (8.7%)	2 (40%)
Malignancy	1 (1.3%)	0	0	1 (20%)
Remission at end visit*	73 (95%)	20 (77%)	20 (87%)	1 (20%)
Flare*	4 (5.2%)	10 (38%)	3 (13%)	3 (60%)
Time to flare, days	305 (240-430)	29 (7-364)	98 (72-212)	297 (236-545)

Data are presented as mean (standard deviation) or median (interquartile range) for continuous variables, and frequency (percentage) for categorical variables. Variables with p value <0.05 are marked with *

use, and absence of flares for a period of at least 6 months. Taper meant a reduction in biologic and/or csDMARD dose, frequency, or discontinuation. Primary outcome was proportion of flares at the end of study period, and secondary outcome was time to flare. Flare was defined as provider diagnosed worsening RA requiring initiation, change

Table 2. Primary and secondary outcome (multivariable analyses)

	Only biologic tapered vs No-taper	p-value	Only csDMARD tapered vs No-taper	p-value	Both biologic and csDMARD tapered vs No-taper	p-value
Proportion of flares, Odds ratio (95%CI)	9.88 (2.5-39)	0.176	2.46 (0.46-13)	0.22	26.93 (2.5- 276)	0.048
Time to flare, Hazard ratio, (SE)	33.9 (1.2)	0.004	2.85 (1.1)	0.34	10.89 (0.91)	0.008

Variables with p<0.25 in univariate analysis were included in multivariable analysis. These variables included age, race, seropositive disease, and baseline DMARD use. Multivariable regression analysis was used for proportion of flares (primary outcome), and Cox regression analysis was used for time to flare (secondary outcome).

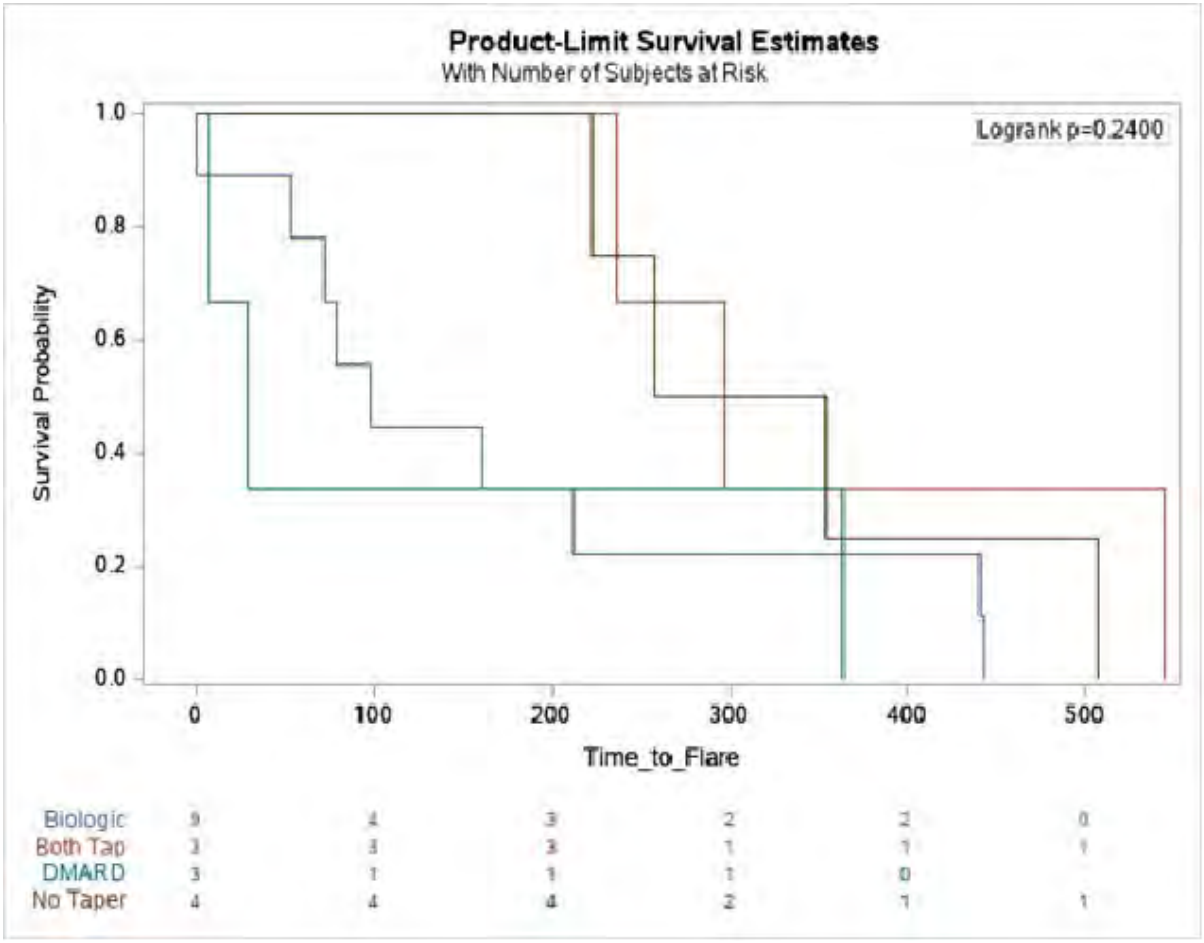

Figure 1. KM survival curve, without flare.

or increase in therapy. The 4 groups of comparison were: no taper, only biologic tapered, only csDMARD tapered, and both biologic and csDMARD tapered. Statistical analyses were completed using SAS Enterprise Guide 7.15 HF3 (SAS Institute, Inc, Cary, NC). Multivariable logistic regression analyses were used to estimate adjusted odds of flare. Kaplan Meier survival plots were created to determine the time to flare utilizing the log-rank test to determine significance.

Results: The RHEUMTAP cohort included 346 patients of which 131 patients were confirmed to have sustained remission on biologics +/- csDMARDs based on manual EHR review. Of these 131 patients, 54 patients underwent a medication taper. Flare was experienced by 20 (15%) patients during follow up period, of which 16 were in the taper groups and 4 in the no-taper group. There were no significant differences in characteristics between the groups (table 1). The most frequently tapered biologics were etanercept and adalimumab, and most frequent csDMARD tapered was methotrexate. Patients undergoing any taper (all groups combined) overall were 7.6 times more likely to experience a flare in the follow-up period compared to those not tapered (OR 7.68, 95% CI 2.4-24, p=0.0006). The both biologic and csDMARD tapered group was more likely to experience a flare (OR 26.93, 95% CI 2.5- 276, p< 0.048) and have a shorter time to flare (HR 10.89, SE 0.91, p=0.008) compared to the no-taper group (table 2).

Conclusion: RHEUMTAP is the first real-world prospective cohort study to report the outcomes of different medication tapering groups in RA in sustained remission. In our cohort, patients who tapered both biologics and csDMARDs were more likely to experience a flare and have a shorter time to flare. Larger studies are required to confirm our findings given our wide confidence intervals.

Disclosure: M. Tageldin, None; **M. Attur**, None; **N. Wilson**, None; **R. Schorr**, None; **T. Sharma**, None.

Abstract Number: 0820

The PROPER Study: Results of the First 48-week Interim Analysis of a Pan-EU Real-world Study of SB5 Biosimilar Following Transition from Reference Adalimumab in Patients with Rheumatoid Arthritis, Axial Spondyloarthritis or Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: SB5, an adalimumab (ADL) biosimilar, received EU marketing authorisation in August 2017, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated bioequivalence and comparable efficacy, safety and immunogenicity to reference ADL. There are few published data on longer-term follow-up of the transition from reference ADL to SB5 outside the controlled, randomised, clinical trial setting and in different disease cohorts. When complete, this umbrella study aims to evaluate candidate predictors of persistence on SB5 in EU patients across multiple indications.

Table 1: Patient baseline characteristics*

	RA (N=205)		axSpA (N=136)		PsA (N=169)	
	Mean (SD)	Q1, Q3	Mean (SD)	Q1, Q3	Mean (SD)	Q1, Q3
Age at initiation of SB5 (years)	60.4 (11.5)	54.0, 68.0	50.3 (13.6)	38.0, 61.0	53.0 (12.1)	44.0, 62.0
Age at diagnosis	44.6 (12.6)	37.0, 53.0	34.8 (13.1)	25.0, 43.0	39.7 (13.3)	31.0, 48.0
Duration of disease (years)	13.5 (11.5)	5.0, 19.5	18.7 (13.2)	9.0, 25.0	12.7 (9.9)	4.0, 20.0
			n (%)			
Women	148 (72.2)		40 (29.4)		79 (46.7)	
Tobacco use:						
Current	40 (19.5)		17 (13.0)		18 (11.2)	
Ex-	39 (19.0)		44 (33.6)		31 (19.3)	
Non-	126 (61.5)		70 (53.4)		112 (69.6)	
Work status:						
Full-time	73 (35.6)		68 (55.3)		84 (54.9)	
Part-time	19 (9.3)		16 (13.0)		16 (10.5)	
Unemployed	113 (55.1)		39 (31.7)		53 (34.6)	
Clinical Status (physician opinion)						
Remission	49 (24.0)		29 (23.8)		54 (32.7)	
Stable	139 (68.1)		83 (68.0)		100 (60.6)	
Active	16 (7.8)		10 (8.2)		11 (6.7)	
Pt awareness status:						
1. Received information on self-administration	185 (90.2)		103 (88.0)		145 (92.4)	
2. Knows to take SB5 out of the fridge 30 minutes prior to injection	188 (91.7)		108 (93.9)		150 (96.2)	
3. Knows can store SB5 < 25°C for up to 28 days	161 (78.5)		67 (58.3)		112 (71.8)	

SD, standard deviation; Q1, 1st quartile, Q3, 3rd quartile

* values based on n contributing to each data point.

Methods: This ongoing non-interventional study enrolled 1000 subjects with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA), ulcerative colitis or Crohn's disease who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference ADL, at clinics in Belgium, Germany, Ireland, Italy, Spain and the UK. Data are captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. This interim analysis provides insight into baseline characteristics, disease activity scores and dose regimen up to 48 weeks post-initiation of SB5 in subjects with RA, axSpA or PsA enrolled at 35 specialist sites and followed up to the data extract date of 3rd May 2021.

Results: This interim analysis includes 510 patients: 205 with RA, 169 with PsA and 136 with axSpA. Baseline clinical characteristics are outlined in Table 1 and changes in dosing regimens and disease activity scores in Table 2.

The majority of patients were in remission or had stable disease at transition, with no meaningful difference seen in disease score by Week 48 post-transition. Almost three quarters of patients in each cohort were transitioned to the same dose regimen of SB5 as received for reference ADL prior to transition, and the great majority of patients continued the same SB5 regimen to Week 48.

Table 2: SB5 Dose Regimen and Disease Score

		RA (N=205)		axSpA (N=136)		PsA (N=169)	
Dose Regimen		**n**	**%**	**n**	**%**	**n**	**%**
Baseline	40 mg Q2W	152	74.1	122	89.7	156	92.3
	*Other	53	25.9	14	10.3	13	7.7
Week 24	40 mg Q2W	134	74.0	102	87.9	137	91.9
	*Other	47	26.0	14	12.1	12	8.1
Week 48	40 mg Q2W	109	78.4	84	85.7	117	91.4
	*Other	30	21.6	14	14.3	11	8.6

Disease Score (paired)	**DAS28**		**BASDAI**		**PsARC (tender joint)**	
	n	**Mean (95% CI)**	**n**	**Mean (95% CI)**	**n**	**Mean (95% CI)**
Baseline		2.5 (2.3-2.6)		2.9 (2.4-3.3)		1.8 (0.9-2.7)
Week 24	126	2.5 (2.3-2.6)	52	3.3 (2.7-3.9)	55	3.8 (1.6-6.0)
Change from BL		*0.0 (-0.1; 0.2)*		*0.4 (-0.0; 0.9)*		*2.0 (0.3; 3.6)*
Baseline		2.4 (2.3-2.6)		2.6 (2.1-3.0)		1.8 (0.6-2.9)
Week 48	113	2.5 (2.3-2.7)	55	2.7 (2.1-3.2)	52	1.8 (0.5-3.1)
Change from BL		*0.0 (-0.1; 0.2)*		*0.1(-0.2; 0.5)*		*0.0 (-1.2; 1.3)*

	FFbH		**PsARC (swollen joint)**	
	n	**Mean (95% CI)**	**n**	**Mean (95% CI)**
Baseline		78.5 (70.3-86.7)		0.5 (0.2-0.8)
Week 24	26	77.6 (68.9-86.2)	55	1.0 (0.1-1.9)
Change from BL		*-0.9 (-2.9; 1.1)*		*0.5 (-0.4; 1.4)*
Baseline		78.8 (72.2-85.5)	52	0.6 (0.3-0.9)
Week 48	32	76.1 (68.7-83.4)		0.7 (0.2-1.2)
Change from BL		*2.8 (-6.3; 0.8)*		*0.1 (-0.4; 0.6)*

*Other includes all other reported doses and/or dosing intervals: 40 mg QW, 80 mg Q2W, and unspecified frequency.
BASDAI Bath Ankylosing Spondylitis Disease Activity Index; BL Baseline; CI, Confidence Interval; DAS-28 Disease Activity Score 28; FFbH Hanover Functional Ability Questionnaire; PsARC Psoriatic Arthritis Response Criteria; Q2W every 2 weeks.

Most patients were well educated about handling and self-administration of SB5.

Nine serious adverse events were reported: 5 in the PsA cohort (myocardial infarct [2], breast carcinoma [1], COVID-19 [1], gastrostomy [1]); 4 in the RA cohort (herpes zoster [1], pneumonia [2], facial numbness [1]). Herpes zoster and one case of pneumonia were considered to be causally related to study treatment.

Conclusion: This interim analysis has shown that effectiveness is maintained at 48 weeks after switching from reference to biosimilar ADL SB5 in a large, contemporary cohort of EU patients with established RA, axSpA or PsA. No new safety signals were observed.

Disclosure: U. Müller-Ladner, Biogen, 6; **K. Gaffney**, AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Lilly, 2, 5, 6, Pfizer, 2, 5, 6, Gilead, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, USD, 2, 5, 6; **D. Jadon**, Biogen, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Celgene, 2, 5, 6, Novartis, 5, 6, Janssen, 5, 6, AbbVie, 5, 6, Sandoz, 5, 6, Gilead, 2, 6, Roche, 6, Oxford University Press, 7; **U. Freudensprung**, Biogen International GmbH, 3, 11; **J. Addison**, Biogen Idec, 3, 11.

Abstract Number: 0821

Baseline Characteristics Predictive of Remission in Patients with RA Following Treatment with IV Abatacept: Post Hoc Analysis of a Real-world Observational Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

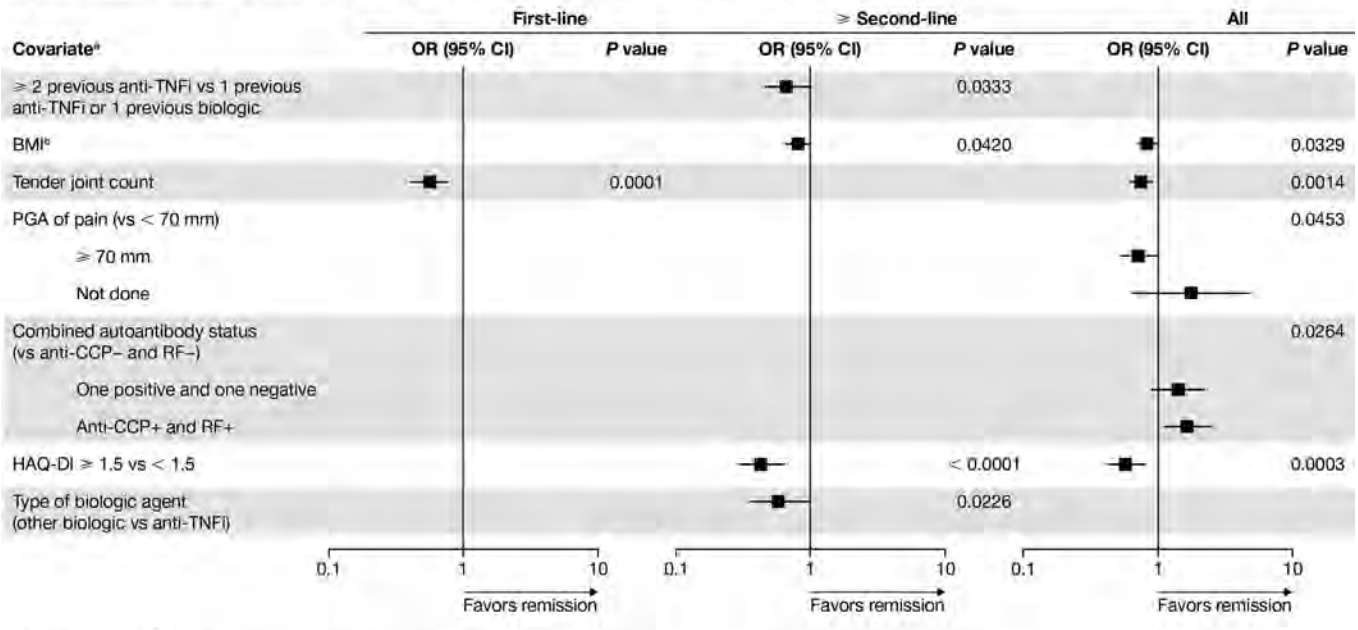
Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Identifying factors associated with treatment response and remission in patients with RA may assist with therapeutic decision-making. An international observational study evaluated efficacy and safety in patients with RA who initiated intravenous (IV) abatacept (AbataCepT In rOutiNe clinical practice [ACTION]; NCT02109666) and noted retention of 47.9% at 2 years.[1] This post hoc analysis identified baseline characteristics predictive of remission following abatacept treatment in patients with RA who participated in the real-world setting ACTION study.

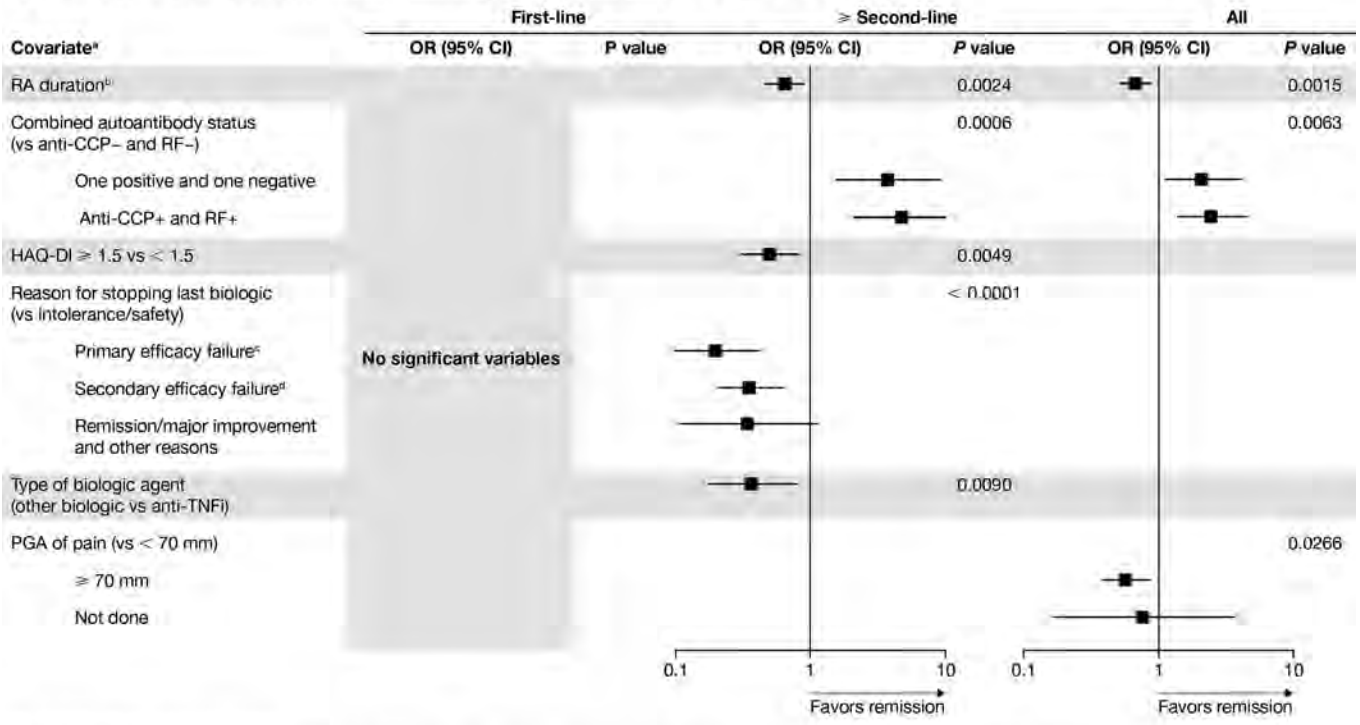
Methods: Patients (aged ≥ 18 years) with moderate-to-severe RA from ACTION who initiated IV abatacept as first- or ≥ second-line therapy and achieved DAS28 (CRP; < 2.6), Clinical Disease Activity Index (CDAI; ≤ 2.8) or Simplified Disease Activity Index (SDAI; ≤ 3.3) remission at 12 months were included. Univariate logistic regression analysis was performed to determine potential predictors of remission by treatment arm including baseline demographics, disease characteristics, serum markers, and previous treatments. Significant variables ($P < 0.2$) from the univariate analyses

Figure 1. Baseline factors predictive of DAS28 (CRP) remission by treatment line and overall, in multivariate analyses



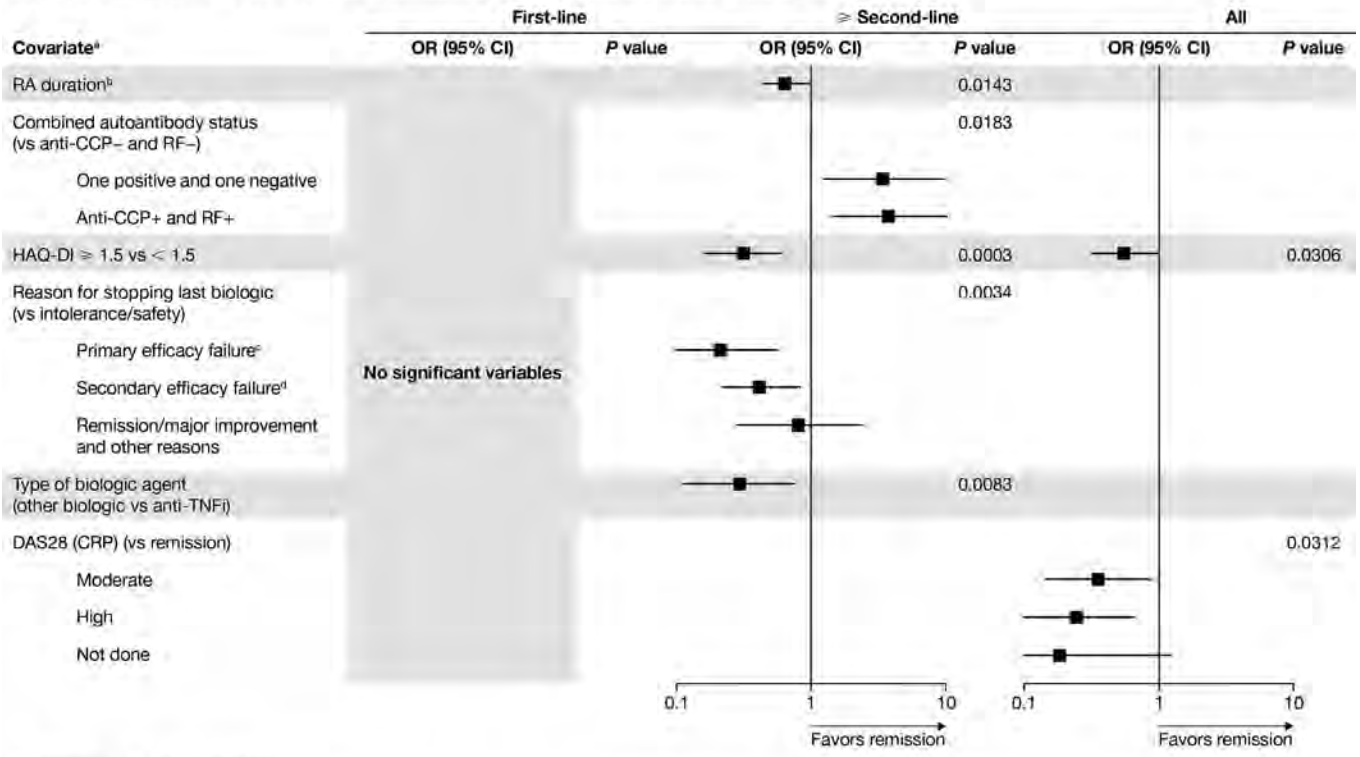
All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission; however, the OR varied by individual countries; [b]Continuous variables were standardized prior to multivariate analysis.
CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; PGA, patient global assessment; TNFi, TNFi inhibitor.

Figure 2. Baseline factors predictive of CDAI remission by treatment line and overall, in multivariate analysis



All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission; however, the OR varied by individual countries; [b]Continuous variables were standardized prior to multivariate analysis; [c]± secondary efficacy failure, remission, or other reasons; [d]± remission or other reasons.
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; PGA, patient global assessment, TNFi, TNF inhibitor.

Figure 3. Baseline factors predictive of SDAI remission by treatment line and overall, in multivariate analysis



All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission; however, the OR varied by individual countries; [b]Continuous variables were standardized prior to multivariate analysis; [c]± secondary efficacy failure, remission, or other reasons; [d]± remission or other reasons.
CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; SDAI, Simplified Disease Activity Index; TNFi, TNF inhibitor.

were evaluated by a multivariate backward elimination logistic regression model; odds ratios (95% confidence intervals) and *P* values were determined. Standardized values were used for the continuous baseline predictors.

Results: Overall, 2260/2364 enrolled patients were evaluable (643 first-line and 1617 ≥ second-line abatacept). For the overall population, DAS28 (CRP) (Figure 1) and CDAI remission (Figure 2) were more likely to be achieved in patients with seropositivity, while DAS28 (CRP) and SDAI remission (Figure 3) were more likely to be achieved in patients with less severe disability (HAQ-disability index [DI]). DAS28 (CRP) remission was more likely to be achieved with ≥ second-line therapy in patients who had low BMI, less severe HAQ-DI, and prior TNF inhibitor (TNFi) use (vs other biologic use). Lastly, in patients who received abatacept as ≥ second-line therapy, CDAI and SDAI remission were more likely to be achieved by patients with: seropositivity, less severe HAQ-DI, shorter RA duration, prior TNFi use (vs other biologic use), and lack of efficacy on last biologic.

Conclusion: This post hoc, multivariate analysis of the ACTION study showed several baseline factors, including seropositive RA and less severe disability (HAQ-DI), to be associated with remission at 12 months for patients treated with IV abatacept. These data support the earlier use of abatacept in patients with seropositive RA.

Reference: 1. Alten R, et al. *Clin Rheumatol* 2019;38:1413–1424.

Medical writing: Fiona Boswell, PhD (Caudex), funded by Bristol Myers Squibb

Disclosure: R. Alten, Abbvie, 1, Amgen, 1, Biogen, 1, Galapagos, 1, Gilead, 1, Janssen, 1, Lilly, 1, Novartis, 1, Pfizer, 1, Roche, 1, BMS, 1, Celltrion, 1; **X. Mariette**, BMS, 2, Galapagos, 2, Gilead, 2, GSK, 2, Janssen, 2, Pfizer, 2, UCB, 2; **M. Galeazzi**, None; **M. Chartier**, Bristol Myers Squibb, 3, 11; **C. Rauch**, Bristol Myers Squibb, 3, 11; **Y. Elbez**, Bristol Myers Squibb, 2; **K. Lozenski**, Bristol Myers Squibb, 3.

Abstract Number: 0822

Local Tolerance of GP2017, an Adalimumab Biosimilar with Low Citrate Concentration Formulation, in Healthy Volunteers and Patients with Rheumatoid Arthritis, Psoriatic Arthritis, and Psoriasis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Adalimumab (ADL) can be self-administered every 2 weeks as a subcutaneous (s.c.) injection in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), and psoriasis (PsO). Conflicting evaluations of local tolerance to formulations containing citrate buffer have created insecurity among health care professionals and patients.[1,2] Here, we evaluated local tolerance of SDZ-ADL (GP2017) a biosimilar ADL with low citrate concentration (1.2 mM), in 466 healthy volunteers (HV) and 408 patients (RA: 177; PsO: 231 including PsA: 52) from 4 phase I pharmacokinetic and 2 phase III confirmatory studies.

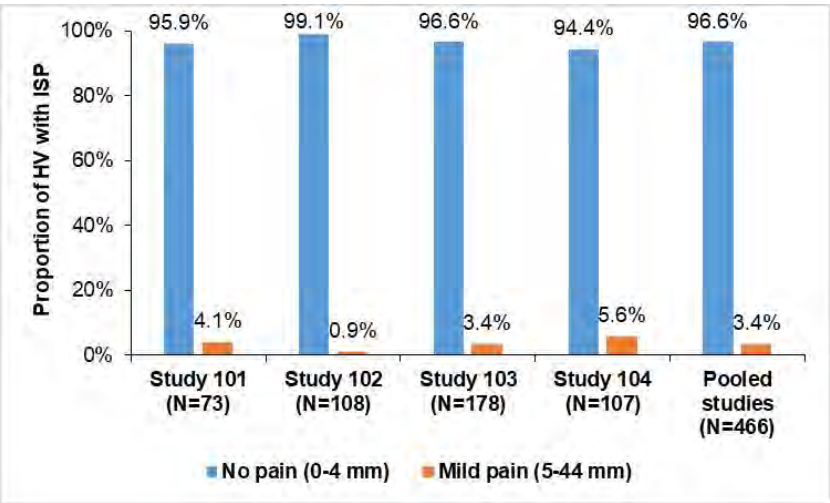

Figure. Proportion of HV with ISP in phase I PK studies.

Table. ISP and ISR results from phase I PK and phase III confirmatory studies

Phase I PK studies					
Study	**101 (N=73)**	**102 (N=108)**	**103 (N=178)**	**104 (N=107)**	**Pooled studies (N=466)**
VAS scores (mm) at 1-hour post-dose					
Mean (SD)	0.89 (2.07)	0.07 (0.52)	1.03 (1.71)	1.03 (2.49)	0.79 (1.84)
Median	0	0	1	0	0
ISR scores at 1-hour post-dose, n (%)					
None	73 (100)	106 (98.2)	178 (100)	99 (92.5)	456 (97.9)
Mild	0 (0)	1 (0.9)	0 (0)	8 (7.5)	9 (1.9)
Moderate	0 (0)	1 (0.9)	0 (0)	0 (0)	1 (0.2)

Phase III confirmatory studies				
	ADACCESS[4]* (PsO and PsA pts)		**ADMYRA[5]* (RA pts)**	
	W0–17 (N=231)	W0–51 (N=168; including pts re-randomized to continue SDZ-ADL after W17)	W0–24 (N=177)	W0–48 (N=177; all pts continued SDZ-ADL after W24)
Dosage	Induction 80 mg W0, then 40 mg EoW s.c.	40 mg EoW s.c.	40 mg EoW s.c.	40 mg EoW s.c.
Study duration, W	17	51	24	48
AEs - ISR, n (%), events	15 (6.5), 34	9 (5.4), 26	7 (4.0), 11	7 (4.0), 12
Mild	14 (6.1), 30	9 (5.4), 26	7 (4.0), 11	7 (4.0), 12
Moderate	1 (0.4), 4	0	0	0
AEs - ISP (reported as ISR), n (%)	3 (1.3)	1 (0.6)	2 (1.1)	2 (1.1)

*ADACCESS and ADMYRA were switch studies, therefore, only pts exposed to SDZ-ADL throughout the study period are included here. AEs, adverse events; EoW, every other week; ISP/ISR, injection site pain/reaction; N, number of HV or pts; HV, healthy volunteers; PK, pharmacokinetic; Pts, Patients; W, week

Methods: HV evaluated their injection site pain (ISP) using a Visual Analog Scale (VAS) of 0–100 mm. HV received a single 40 mg/0.8 mL s.c. injection and patients received SDZ-ADL every 2 week during 48–51week duration of study. Injection site reactions (ISR) as well as adverse events were assessed by investigators during the clinical studies. Detailed study designs have been reported previously.[3–6]

Results: Overall, 456 (97.9%) HV did not experience ISR while 10 (2.1%) HV experienced ISR. These were mostly of mild intensity; only 1 (0.2%) had an ISR of moderate intensity. At 1-hour post-dose, 96.6% of HV experienced no pain (VAS score, 0–4 mm) (**Figure**). In the phase III studies, a low number of mild/moderate ISR/ISP events were observed, which further decreased during the study. Detailed results are presented in the **Table**. No ISR/ISP led to treatment or study discontinuation in any study.

Conclusion: The proportion of HV and patients experiencing ISR and ISP after administration of SDZ-ADL was low, with no events leading to treatment or study discontinuation. These outcomes challenge the clinical impact of citrate in ADL formulations on the incidence and intensity of ISP/ISR.

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Abstract Number: 0823

Pharmacokinetic and Pharmacodynamic Evaluation of a Proposed Biosimilar MSB11456 versus Both the US-licensed and EU-approved Tocilizumab: Results of a Randomized, Double-blind, Parallel-group, Single-dose Trial in Healthy Adults

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Tocilizumab, a biologic disease-modifying antirheumatic drug, is a recombinant humanized monoclonal immunoglobulin G1 antibody against the interleukin-6 receptor (IL-6R). MSB11456 is a proposed biosimilar to US-licensed tocilizumab and EU-approved tocilizumab. Prior to initiation of its clinical development program, MSB11456 was considered highly similar to the reference products based on extensive *in vitro* pharmacological testing and functional activity assays. This double-blind, parallel-group phase I study (NCT03282851) assessed the pharmacokinetic (PK) and pharmacodynamic (PD) equivalence of MSB11456 to US-licensed and EU-approved tocilizumab and provided data on the similarity of safety profiles and immunogenicity of MSB11456 and the reference products in healthy adult subjects.

Methods: Healthy adult volunteers were randomized to receive a single 162 mg subcutaneous injection of MSB11456, US-licensed tocilizumab, or EU-approved tocilizumab. Samples for PK/PD and immunogenicity analysis were taken predose, up to 29 days postdose, and at the end of study visit (day 48). Primary endpoint PK parameters were natural log transformed and analyzed using analysis of covariance (ANCOVA) methods; results were then transformed back to the original scale. Secondary PD analysis measured serum soluble IL-6R and serum C reactive protein (sCRP) parameters, and data were analyzed using a method similar to that for PK data. Safety data were collected throughout the study and analyzed descriptively.

Results: 685 subjects were randomized and treated. Results of the primary PK analysis demonstrated bioequivalence between MSB11456 and both US-licensed and EU-approved tocilizumab, as well as between the reference

Results of primary PK analysis

Parameter	Treatment	n	Ratio of geometric LSMs (%)	90% CI of ratio
MSB11456 vs US-licensed tocilizumab				
$AUC_{0-\infty}$	MSB11456	194	106.16	96.80, 116.43
	US-licensed tocilizumab	190		
AUC_{0-t}	MSB11456	230	104.15	93.58, 115.90
	US-licensed tocilizumab	226		
C_{max}	MSB11456	230	104.45	95.05, 114.77
	US-licensed tocilizumab	226		
MSB11456 vs EU-tocilizumab				
$AUC_{0-\infty}$	MSB11456	194	104.03	94.96, 113.96
	EU-approved tocilizumab	200		
AUC_{0-t}	MSB11456	230	94.78	85.15, 105.50
	EU-approved tocilizumab	224		
C_{max}	MSB11456	230	94.83	86.28, 104.22
	EU-approved tocilizumab	224		
US-licensed vs EU-approved tocilizumab				
$AUC_{0-\infty}$	US-licensed tocilizumab	190	97.99	89.40, 107.41
	EU-approved tocilizumab	200		
AUC_{0-t}	US-licensed tocilizumab	226	91.01	81.71, 101.36
	EU-approved tocilizumab	224		
C_{max}	US-licensed tocilizumab	226	90.79	82.57, 99.84
	EU-approved tocilizumab	224		

AUC, area under the serum concentration-time curve (μg·h/mL); $AUC_{0-\infty}$, AUC from time zero to infinity; AUC_{0-t}, AUC from time zero to the time of the last quantifiable concentration; C_{max}, maximum concentration (μg/mL)

Results of primary PK analysis.

products, since all corresponding 90% confidence intervals (CIs) for the geometric least squares mean (LSM) ratios were within the predefined 80.00% to 125.00% equivalence margin (Table). PD analyses also demonstrated equivalence of MSB11456 and both US-licensed and EU-approved tocilizumab, as well as between the reference products. Safety, tolerability and immunogenicity were also comparable between treatments. The incidence of tocilizumab-specific neutralizing antibodies was low (< 3% for all three products).

Conclusion: PK and PD equivalence of MSB11456, US-licensed tocilizumab, and EU-approved tocilizumab were demonstrated with comparable immunogenicity, safety, and tolerability for the three products. This study adds to the totality of evidence in support of MSB11456 as a proposed biosimilar to tocilizumab.

Disclosure: C. Schwabe, None; **C. Wynne**, None; **A. Illes**, Fresenius Kabi SwissBioSim, 3; **M. Ullmann**, Fresenius Kabi SwissBioSim, 3; **E. Vincent**, Fresenius Kabi SwissBioSim, 3; **V. Ghori**, Fresenius Kabi SwissBioSim, 3; **C. Petit-Frere**, Fresenius Kabi SwissBioSim, 3; **A. Racault**, Fresenius Kabi SwissBioSim, 3; **J. Monnet**, Fresenius Kabi SwissBioSim, 3.

Abstract Number: 0824

Physicians' Reasons for Prescribing Janus Kinase Inhibitors (JAKi) in Patients with Rheumatoid Arthritis, and Associated Alignment Between Physicians and Patients in a Real-world Clinical Setting

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Shared decision making, a cornerstone of rheumatoid arthritis (RA) management[1], allows physicians and their patients to make informed decisions about their treatment goals and choice of care. As new treatments become available, it is important to understand rheumatologists' reasons for choosing Janus kinase inhibitors (JAKi), rheumatologist and patient satisfaction and alignment with this choice in patients with RA.

Methods: The Adelphi RA Disease Specific Programme™[2] is a large, multinational, point-in-time survey conducted amongst rheumatologists and their consulting patients with RA in Europe (Belgium, France, Germany, Italy, Spain, UK) between January and October 2020.

Physicians completed record forms for up to 10 consecutive RA patients, collecting demographic, clinical and treatment data, and reasons for current treatment choice. Patients were invited to complete a patient questionnaire to assess their satisfaction with ongoing treatment (5-point scale), and perceptions of shared decision making for the current treatment.

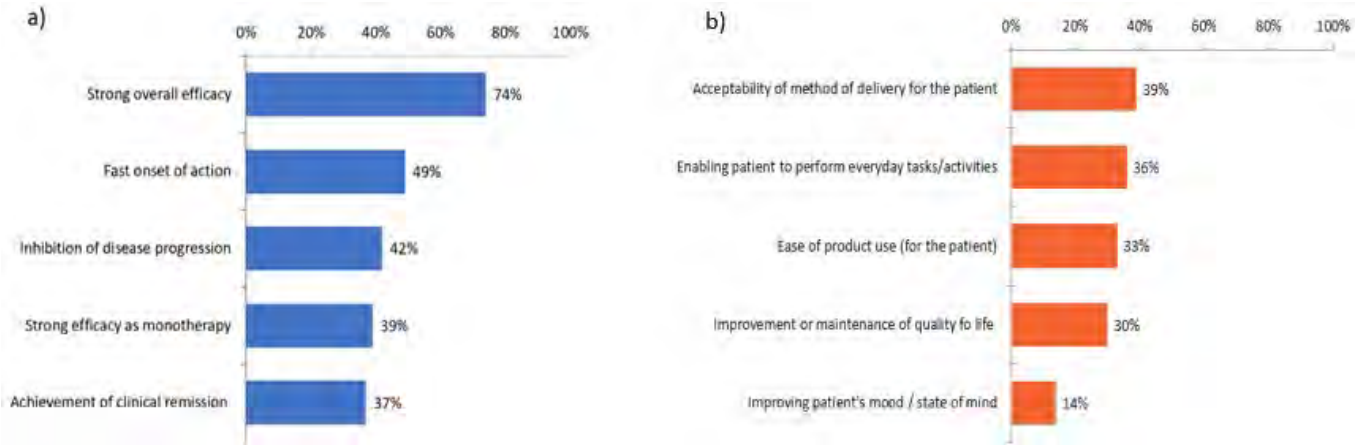

Figure 1. Physician stated reasons for prescribing a JAKi in their patients with RA, % of patients (n=397). a) Top 5 clinical reasons (Blue); b) Top 5 patient-centric reasons (Orange).

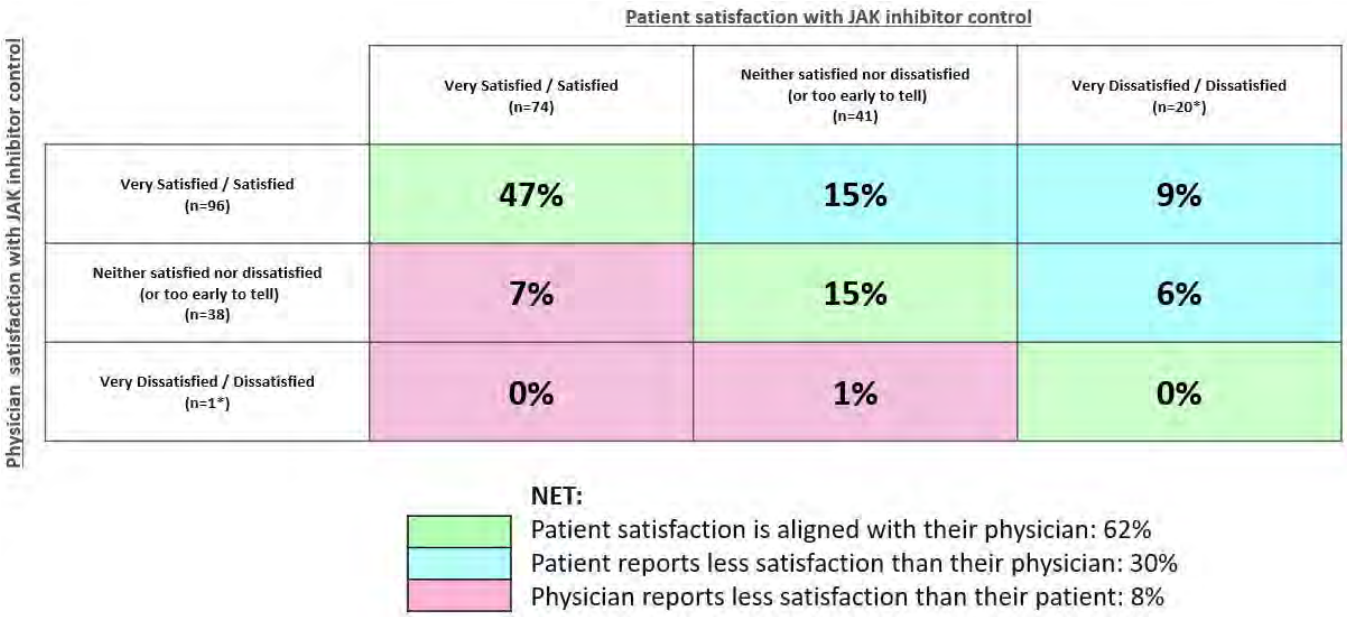

Figure 2. Level of alignment between physician and patient-reported satisfaction with JAKi.

Results: 316 rheumatologists provided data for 3121 patients, of whom 1130 (36.2%) completed patient reported questionnaires. Overall, 67% were female, mean age was 53 years (SD 14), 23% had moderate-high disease activity score (DAS28: >3.2). 68% of patients were currently receiving either a biologic or targeted synthetic DMARD (defined here as advanced therapy, AT), 72% were on first line AT.

Overall, physicians and their patients were aligned that a conversation took place about a treatment decision (n=855, 79% net alignment), and this was a shared treatment decision (n=814, 75% net alignment).

15% of patients not taking an AT were reported to have a clinical condition warranting one; reasons for not taking AT included patients' concerns about infection (24%), csDMARDs were tolerable and safe in the patient (18%), and patient dislike of infusions/injections (17%).

Of 2143 patients receiving AT, 19% were prescribed JAKi; 57% as monotherapy, 43% as combination therapy. For physician stated reasons for choice of JAKi, factors were driven by both perceptions of clinical efficacy and onset of action, as well as factors relating to patient acceptability such as method of delivery and ease of use (Figure 1).

With respect to JAKi treatment (n=135 patient-physician pairs), 62% of physicians and their patients were aligned on satisfaction, however 30% of patients reported less satisfaction than their consulting physician (Figure 2).

Conclusion: Communicating the choice of pharmacological therapy to patients with RA has become increasingly complex for physicians with expansion of approved treatments. In this subgroup of patients on JAKi, the drug attributes considered as reasons for prescribing were driven by clinical factors as well as by patient centric attributes. Although communications between patients and physicians were largely aligned, better understanding of patient expectations might serve to improve messaging about treatment options and resulting satisfaction.

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Disclosure: P. **Taylor**, Celgene, 5, Galapagos, 2, 5, Gilead Sciences, 2, 5, AbbVie, 1, GSK, 2, Janssen, 2, Eli Lilly, 2, Pfizer Inc, 2, Roche, 2, Nordic Pharma, 2, Fresenius, 2, Bristol-Myers Squibb, 2, Sanofi, 2, Celltrion, 2, UCB, 2, Biogen, 2; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **Y. Piette**, Abbvie, 2, Galapagos, 2, Sandoz, 2, Janssen, 2, Grünenthal, 2; **S. Romero-Yuste**, Abbvie, 2, 6, MSD, 5, Pfizer, 5, Novartis, 5, Biogen, 2, 6, Amgen, 6, Grünenthal, 6, Kern Pharma, 6, Lilly, 2, 6, Roche, 6, Sandoz, 6, Sanofi, 6, UCB, 6, Janssen, 2, 6, Fresenius Kabi, 2, Gebro, 2, BMS, 2, 5, Galapagos, 2; **J. Broen**, Galapagos, 2, Gilead, 2, UCB, 2, Novartis, 2, Pharming, 11; **M. Welcker**, Abbvie, 2, 5, 6, Actelion, 5, Aescu, 6, Amgen, 6, Biogen, 6, BMS, 2, 6, Berlin Chemie, 6, Celgene, 2, Galapagos, 2, 5, Gilead, 2, 5, GSK, 2, 5, 6, Hexal, 5, 6, Janssen, 6, Medac, 2, 6, MSD, 6, Mundipharma, 6, Mylan, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Riemser, 6, Sanofi, 2, 6, UCB, 2, 5, 6; **E. Holdsworth**, Adelphi Real World, 3; **M. Zignani**, Galapagos, 3; **K. Van Beneden**, Galapagos, 3, 11; **R. Caporali**, Abbvie, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Sanofi, 2, 6, Sandoz, 2, 6, Novartis, 6, MSD, 2, 6, Gilead Sciences, Inc., 2, 6, Galapagos NV, 2, 6, Roche, 2, 6, SamSung-Bioepis, 2, 6; **R. Alten**, Abbvie, 1, Amgen, 1, Biogen, 1, Galapagos, 1, Gilead, 1, Janssen, 1, Lilly, 1, Novartis, 1, Pfizer, 1, Roche, 1, BMS, 1, Celltrion, 1.

Abstract Number: 0825

An Investigator-initiated Multicenter Randomized Study in Early Rheumatoid Arthritis of Active Conventional Therapy versus Three Biological Treatments: 48 Week Clinical and Radiographic Results of the NORD-STAR Trial

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The optimal first-line treatment of patients (pts) with early rheumatoid arthritis (eRA) is yet to be established. The main objectives were to assess and compare clinical and radiographic outcomes after 48 weeks of active conventional therapy (ACT) with conventional synthetic (cs)DMARDs plus glucocorticoid versus each of three biological (b)DMARDs with different modes of action (certolizumab pegol, abatacept and tocilicumab), all combined with methotrexate (MTX).

Methods: The NORD-STAR trial (NCT01491815) was conducted in the Nordic countries and Netherlands (1). In this investigator-initiated, randomized, open-label, blinded-assessor study pts with treatment-naïve, eRA with DAS28 >3.2, and positive RF or ACPA, or CRP >10mg/L were randomized 1:1:1:1. Methotrexate (25 mg/week) was combined with: 1) ACT: oral prednisolone (tapered quickly; discontinued at wk 36); *or*: sulphasalazine, hydroxychloroquine and mandatory intra-articular (IA) glucocorticoid (GC) injections in swollen joints; 2) certolizumab 200 mg EOW SC (CZP); 3) abatacept 125 mg/wk SC (ABA); tocilizumab 162 mg/wk SC (TCZ). IA GC was allowed in all arms except wks 20-24 and 44-48. Co-primary outcomes were clinical disease activity index remission (CDAI≤2.8) at wk 48 and change in total van der Heijde-modified Sharp Score from baseline to wk 48 ($\Delta vdHSS_{w0\text{-}w48}$).

As predefined in the statistical analysis plan, 6 primary null hypotheses were tested: no difference between ACT and each of the 3 bDMARDs for each of the two co-primary outcomes. Multiplicity was handled by Bonferroni correction of the co-primary outcomes (resulting in a 0.025 significance level per outcome), and then applying Dunnet's multiple comparison procedure with ACT as reference within each outcome. Logistic regression with non-responder imputation (NRI) (dichotomous outcomes) and analysis of covariance (ANCOVA) (ΔvdHSS) were applied with inter- or extrapolation for missing values and adjusted for baseline value (only ANCOVA), gender, ACPA status and country.

Table 1. Demographics and patient characteristics at baseline (ITT population).

Parameter	ACT (n=200)	CZP+MTX (n=203)	ABA+MTX (n=204)	TCZ+MTX (n=188) §
Demographics				
Age (years)	55 (15)	55 (15)	55 (14)	52 (15)
Women, n (%)	139 (70%)	139 (69%)	140 (69%)	129 (69%)
Symptom duration, days	195 (167)	203 (166)	212 (168)	207.5 (155)
Time since diagnosis, days	13 (21)	12 (17)	16 (34)	16 (33)
Anti-citrullinated peptide antibody positive n (%)	163 (82%)	166 (82%)	169 (83%)	153 (82%)
Rheumatoid factor positive n (%)	151 (76%)	149 (73%)	159 (78%)	135 (72%)
Baseline characteristics, clinical				
CDAI	28.7 (12.1)	27.9 (12.4)	28.6 (11.3)	26.6 (11.7)
SDAI	30.9 (13.5)	30.0 (13.6)	30.5 (11.9)	28.5 (12.5)
DAS28	5.1 (1.1)	5 (1.1)	5.1 (1)	4.9 (1)
Tender Joint Count, 68 joints	17 (11)	15 (10)	16 (11)	15 (10)
Swollen Joint Count, 68 joints	11 (7)	11 (8)	11 (7)	10 (6)
Baseline characteristics, radiography				
Total vdHSS (0-448)	6.3 (8.2)	5.9 (7.6)	5.8 (9.8)	4.2 (6.7)
Total (0-448), median, IQR	4 [1 - 8.5]	3 [1 - 8]	3 [1 - 6]	2 [0.5 - 5]
vdHSS Erosion (0-280)	2.96 (4.45)	2.97 (4.58)	2.43 (4.64)	2.03 (4.33)
vdHSS Erosion (0-280), median [IQR]	1 [0 - 4]	1 [0 - 4]	1 [0 - 2.5]	0.5 [0 - 2]
vdHSS JSN (0-168)	3.36 (4.49)	2.96 (3.64)	3.39 (5.85)	2.2 (3.04)
vdHSS JSN (0-168), median [IQR]	2 [0 - 5]	2 [0 - 4.25]	2 [0 - 4]	1 [0 - 3]

Values are mean (standard deviation), if not otherwise indicated. §Finnish patients randomised to arm 4 (TCZ+MTX), but not receiving it owing to unavailability, are not included.

ABA: abatacept, ACT: Active conventional therapy CDAI: Clinical disease activity index; CZP: certolizumab pegol, DAS28: Disease activity score (28 joints, 4 variables, C-reactive protein), IQR: Interquartile range, JSN: Joint space narrowing, n: Number of patients, SDAI: Simple disease activity index, ITT: Intention to treat, TCZ: Tocilizumab, vdHSS: van der Heijde-modified Sharp Score.

Table 2. Primary and key secondary outcomes at week 48 (ITT population)

	ACT (n=200)	CZP+MTX (n=203)	ABA+MTX (n=204)	TCZ+MTX (n=188)[§]
Estimated adjusted outcome (ITT population)[1]				
Primary				
CDAI remission, w48	39.2% (32.5 to 45.9)	52.3% (45.5 to 59.1)	59.3% (52.6 to 66)	51.9% (44.9 to 59.0)
ΔvdHSS w0-w48	0.45 (0.31 to 0.59)	0.47 (0.33 to 0.61)	0.62 (0.48 to 0.76)	0.5 (0.36 to 0.64)
Key secondary				
ACR/EULAR Boolean remission, w48	31.6% (25.3 to 38)	46.3% (39.5 to 53.1)	51% (44.2 to 57.8)	44.6% (37.6 to 51.6)
DAS28 remission,w48	53.7% (46.9 to 60.6)	66.6% (60.1 to 73)	71.1% (65 to 77.3)	68.2% (61.6 to 74.7)
SDAI remission, w48	38.1% (31.5 to 44.8)	52.8% (45.9 to 59.6)	57.8% (51.1 to 64.6)	53.5% (46.5 to 60.6)
EULAR good response, w48	66.4% (59.9 to 72.9)	66.4% (59.9 to 72.9)	66.4% (59.9 to 72.9)	66.4% (59.9 to 72.9)
vdhSS progression ≤0.5, w0-w48	78.0% (72.3-83.8)	81.3% (75.9 to 86.7)	74.5% (68.5-80.5)	80.3% (74.6-86.0)
ΔErosion w0-w48	0.31 (0.21 to 0.4)	0.33 (0.23 to 0.42)	0.41 (0.31 to 0.5)	0.35 (0.25 to 0.45)
ΔJSN w0-w48	0.14 (0.05 to 0.23)	0.14 (0.05 to 0.23)	0.22 (0.13 to 0.31)	0.15 (0.06 to 0.24)
Estimated adjusted treatment difference (ITT population)[2]				
Primary				
CDAI remission, w48	Reference	**13.1% (3.5 to 22.6)***	**20.1% (10.6 to 29.5)****	12.7% (3 to 22.5)
ΔvdHSS w0-w48	Reference	0.02 (-0.17 to 0.22)	0.17 (-0.02 to 0.37)	0.05 (-0.15 to 0.25)
Key secondary				
ACR/EULAR Boolean remission, w48	Reference	14.7% (5.4 to 23.9)	19.4% (10.1 to 28.7)	13% (3.5 to 22.4)
DAS28 remission,w48	Reference	12.9% (3.5 to 22.2)	17.4% (8.2 to 26.6)	14.4% (5 to 23.9)
SDAI remission, w48	Reference	14.6% (5.1 to 24.1)	19.7% (10.2 to 29.1)	15.4% (5.7 to 25.1)
EULAR good response, w48	Reference	8.2% (-0.6 to 17.1)	11.3% (2.7 to 20)	2.9% (-6.3 to 12.2)
vdHSS progression ≤0.5, w0-w48	Reference	-3.3% (-11.1 to 4.6)	3.5% (-4.7 to 11.8)	-2.2% (-10.3 to 5.9)
ΔErosion w0-w48	Reference	0.02 (-0.12 to 0.16)	0.1 (-0.04 to 0.24)	0.04 (-0.1 to 0.19)
ΔJSN w0-w48	Reference	0 (-0.13 to 0.13)	0.08 (-0.05 to 0.21)	0.01 (-0.12 to 0.14)

[1]For dichotomous variables, values are estimated adjusted marginal proportions or estimated difference in proportions against ACT with 95% confidence limits. Confidence limits are calculated from the logistic regression model by the delta method. Missing data are imputed using worst outcome (non-responder imputation).

[2]For radiographic scores, values are estimated adjusted marginal mean change from baseline or estimated difference against ACT with 95% confidence limits from the ANCOVA model. Missing data are imputed using intra- or extrapolation.

Results are based on the intention to treat population; 17 Finnish patients allocated to tocilizumab and methotrexate group excluded([§]), since they could not receive tocilizumab because the drug was not available in the Finnish part of the study.

*Superiority of bDMARD compared with ACT was demonstrated; p=0.021. ** Superiority of bDMARD compared with ACT was demonstrated; p<0.001.

ABA: Abatacept, ACR: American College of Rheumatology, ACT: Active conventional therapy, bDMARD: Biological disease modifying anti-rheumatic drug, CDAI: Clinical disease activity index; CZP: Certolizumab pegol, DAS28: Disease activity score (28 joints, 4 variables, C-reactive protein), EULAR, European Alliance of Associations for Rheumatology, IQR: Interquartile range, JSN: Joint space narrowing, n: Number of patients, SDAI: Simple disease activity index, ITT: intention to treat, TCZ: Tocilizumab, vdHSS: van der Heijde-modified Sharp Score

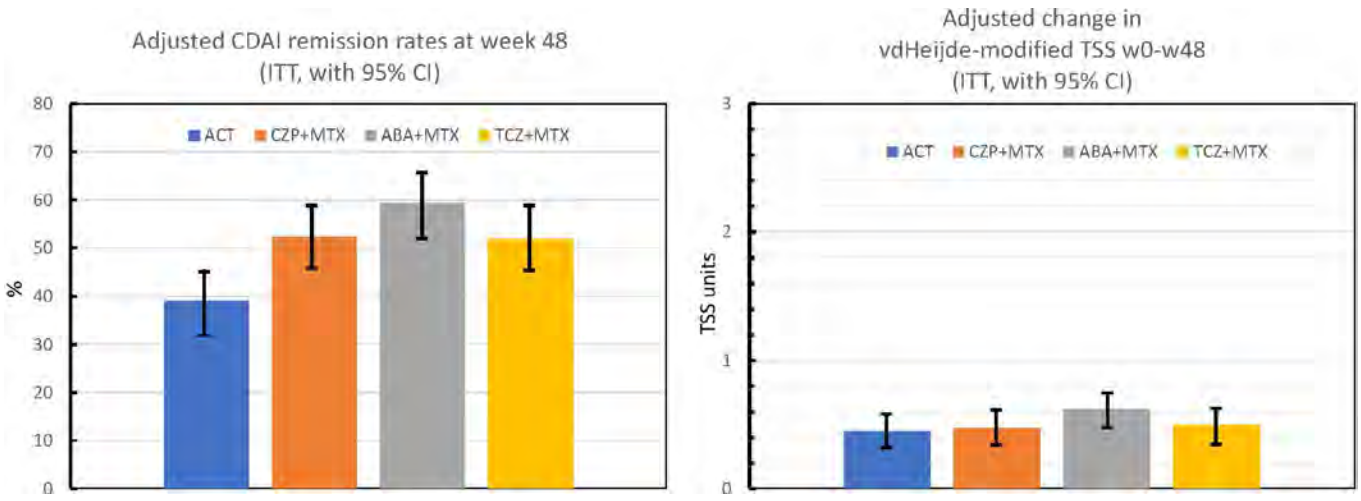

Figure 1. Adjusted CDAI remission rates at week 48 (left) and adjusted change in van der Heijde modified total Sharp score from baseline to week 48 (right).

Results: 812 pts were randomized. Table 1 shows baseline data.

Adjusted CDAI remission rates at w48 were: 59.3% (for ABA), 52.3% (CZP), 51.9% (TCZ) and 39.2% (ACT), with the null hypothesis formally rejected for ACT vs ABA (adjusted difference +20.1%; adjusted p< 0.001) and ACT vs CZP (+13.1; p=0.021), but not for ACT vs TCZ (+12.7; p=0.030). For key secondary clinical outcomes improved clinical outcomes in bDMARD groups compared to ACT were consistently found (Table 2).

Adjusted estimated mean $\Delta vdHSS_{w0\text{-}w48}$ was 0.62 (ABA), 0.47 (CZP), 0.50 (TCZ) and 0.45 (ACT), i.e consistently low. None of the radiographic null hypotheses were rejected (Table 2).

Safety profiles were as previously reported. The total number of serious adverse events (% patients with ≥1 event) were: ABA 21 (8.3%), CZP 28 (12.4%), TCZ 20 (9.2%) and ACT 23 (10.7%).

Conclusion: Compared with ACT (csDMARD+glucocorticoids), statistically significant superiority regarding CDAI remission rates was demonstrated for ABA+MTX and CZP+MTX, and not for TCZ+MTX. Radiographic progression was low, without significant differences between treatments.

References: 1. Hetland et al. BMJ 2020; 371:m4328

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Abstract Number: 0826

Diagnosis, Treatment and Utilization Changes in Rheumatoid Arthritis Patients Before and During COVID-19

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: During the COVID-19 pandemic, individuals were encouraged to shelter in place, specifically those considered high risk for COVID-19. Rheumatoid arthritis (RA) patients are known to be particularly susceptible to infections. During the pandemic, RA patients were found to cancel appointments and alter medications. This study aimed to understand the impact of COVID-19 on RA patients' diagnosis, treatment, and utilization during the pandemic.

Methods: This is a retrospective cohort study of RA patients insured by a large Commercial and Medicare health plan in the United States. To assess the impact of COVID-19 on newly diagnosed treatment and utilization rates, we compareda pre-COVID period (March 1 to December 31, 2019) to a COVID period (March 1 to December 31, 2020) to assess how COVID-19 impacted changes. We defined a new RA diagnosis as a patient with medical insurance but no paid claim for RA for at least six months before the initial claim with an RA diagnosis. We utilized both medical and pharmacy claims to identify utilization patterns.

Results: This study included 36,019 patients in 2019 and 35,880 patients in 2020. The newly diagnosed rate increased 6% ($p = 0.002$) for Medicare but not for Commercial patients. Infusion treatments decreased 7% ($p=0.03$) for Commercial but not for Medicare patients. During this time, there was a switch in infusion site of care from the hospital setting to the office setting of 3.1% ($p=0.05$) and 5.7% ($p< 0.001$) for Commercial and Medicare patients, respectively. There was also a switch from facility to office-based biologic drug administration for Commercial (1.8%, $p= 0.03$) and Medicare patients (2.6%, $p = 0.08$). From March to May 2020, there was an 18-19% decrease ($p < 0.001$) in new RA diagnoses for Commercial and Medicare patients with a rebound in the last six months of 2020. There was an 11-17% decrease ($p < 0.001$) in utilization among existing patients during this time. Having COVID-19 increased

the odds of being newly diagnosed with RA by 1.37 in Medicare patients and 1.91 in Commercial patients (both $p < 0.001$).

Conclusion: During the COVID-19 pandemic, we observed higher RA incidence rates. Additionally, infusion treatments decreased and changed from the hospital to the office setting. While new RA diagnosis and utilization rates of existing RA patients declined during the pandemic's height, both rates quickly rebounded in the last months of 2020. As a result, patients treated for COVID-19 were more likely to be newly diagnosed with RA, likely driving the higher incidence rates observed in this study. During the pandemic, some healthcare services were compromised to meet the demands of caring for COVID-19 patients. In some cases, patients canceled appointments or delayed care due to fear of exposure. The results of this study highlight the impact of a pandemic on healthcare.

Disclosure: M. Wang, CVS Health, 3, 11; **S. Lardeux**, CVS Health, 3, 11; **E. Avalos-Reyes**, CVS Health, 3, 11; **M. Hamburger**, None; **K. Johnson**, CVS Health, 3, 11.

Abstract Number: 0827

Discontinuation Rate of Tofacitinib as Monotherapy Is Similar Compared to Combination Therapy with Methotrexate in Rheumatoid Arthritis Patients: Pooled Data from Two Rheumatoid Arthritis Registries in Canada

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). We previously reported the similarity in retention between TOFA monotherapy and TOFA with MTX using data from two different registries separately; the Ontario Best Practices Research Initiative (OBRI) and the Quebec registry RHUMADATA.

Methods: RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Concurrent MTX use was defined as MTX use for more than 75% of the time while using TOFA. Multiple imputation (Imputation Chained Equation method, N=20) was used to deal with missing data for covariates at treatment initiation.

Time to discontinuation was assessed using Cox regression models. To deal with confounding by indication, we estimated propensity scores for selected covariates with an absolute standard difference greater than 0.1. We then adjusted Cox regression models for propensity quantile to compare the discontinuation of TOFA with MTX versus TOFA without MTX.

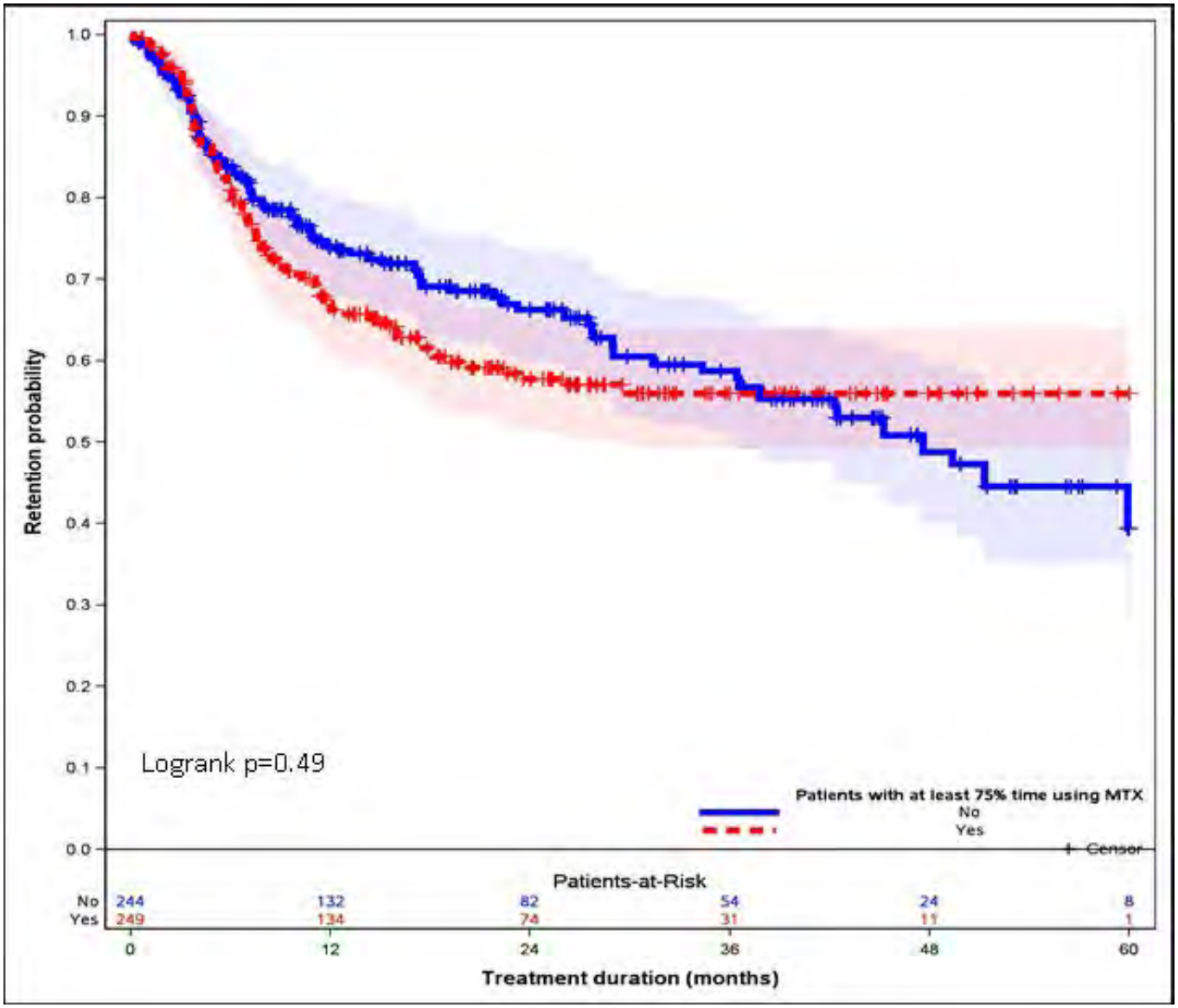

Figure 1. TOFA retention with and without MTX.

Results: A total of 493 patients were included. Of those, 244 (49.5%) and 249 (51.5%) were treated with MTX and without MTX, respectively. Compared to TOFA monotherapy, the TOFA with MTX group had a significantly lower mean HAQ-DI, fatigue score, and the number of prior biologic use at the time of TOFA initiation. A lower proportion of positive ACPA (59% vs. 66%), prevalence of hypertension (31% vs 37%), and concomitant use of Leflunomide (11% vs. 23%) were also observed for patients using TOFA with MTX.

Over a mean follow-up of 19.0 months, discontinuation was reported in 182 (36.9%) of all TOFA patients. After adjusting for propensity score quantile across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 1.12, 95% CI: 0.83-1.51; p=0.49) (Figure 1).

Conclusion: In this pooled real-world data study, we found that in patients with RA, the retention of TOFA is similar if it is used as monotherapy or in combination with MTX.

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Abstract Number: 0828

Long-Term Safety and Efficacy of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: Results at 3 Years from the SELECT-COMPARE Study

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

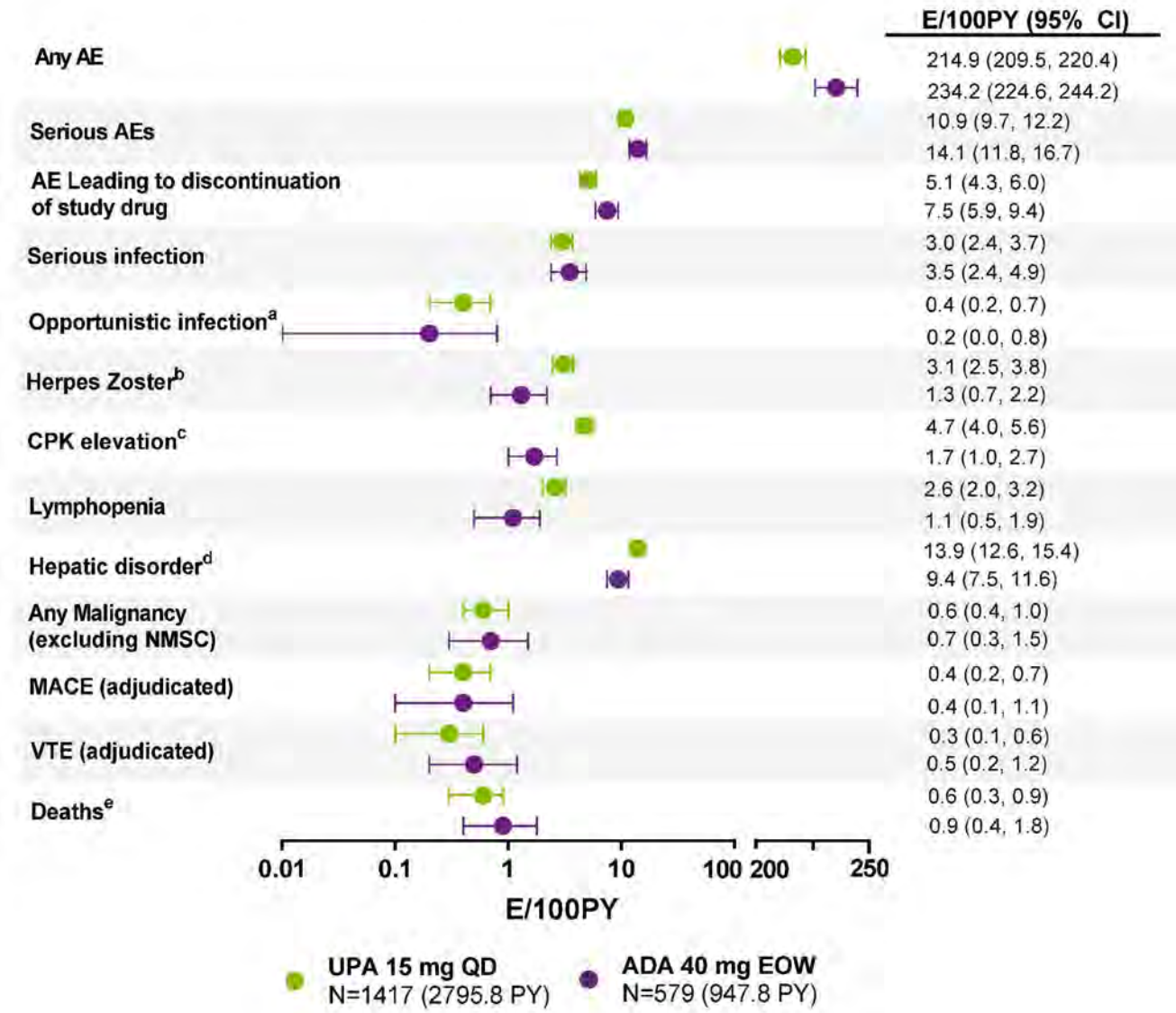
Background/Purpose: In the SELECT-COMPARE study, the Janus kinase inhibitor, upadacitinib (UPA), demonstrated significant improvement in the signs and symptoms of rheumatoid arthritis (RA) when administered at 15 mg once daily (QD) on background methotrexate (MTX) compared with adalimumab (ADA) plus MTX at Week 12 that were maintained through 72 weeks in patients with prior inadequate response to MTX.[1] The objective of this analysis was to assess the long-term safety and efficacy of UPA vs ADA over 3 years in the ongoing long-term extension (LTE).

Methods: Patients receiving background MTX were randomized 2:2:1 to UPA 15 mg QD, placebo (PBO), or ADA 40 mg every other week. Between Weeks 14-26, rescue was mandated for either lack of response (< 20% improvement in tender or swollen joint counts: Weeks 14, 18, 22) or failure to achieve a targeted disease outcome (CDAI low disease activity: Week 26). Patients who completed the 48-week double-blind period could enter an LTE for up to 10 years total. This analysis describes patients through 3 years of treatment. Treatment-emergent adverse events (TEAEs) per 100 patient years (PY), including events of special interest (AESI), were summarized up to 3 years based on exposure to UPA and to ADA. Efficacy was analyzed by original randomized groups. Patients who were rescued or prematurely discontinued study drug were categorized as non-responders for visits after rescue or discontinuation. Descriptive analyses were performed without formal statistical comparisons.

Results: In total, 651, 651, and 327 patients were randomized at baseline to receive UPA, PBO, and ADA, respectively. Between Weeks 14-26, 252 (39%) patients were rescued from UPA to ADA, 159 (49%) were rescued from ADA to UPA, and all PBO patients were switched to UPA by Week 26.[1] A higher proportion of patients randomized to UPA completed 3 years without rescue compared to those randomized to ADA (47% vs 36%, respectively). UPA was generally well-tolerated as assessed by the rates of TEAEs, including serious AEs, AEs leading to discontinuation of study drug, and AESIs, including serious and opportunistic infections, malignancies, adjudicated major adverse

cardiac events or venous thromboembolism; **Figure**). Consistent with previous analyses, the event rates of AESIs were generally comparable between the UPA and ADA groups, while herpes zoster, lymphopenia, hepatic disorder, and CPK elevation were reported at higher rates with UPA. Consistent with earlier time points, greater proportions of patients randomized to UPA achieved low disease activity and remission at 3 years based on CDAI, as well as DAS28(CRP) ≤3.2 or < 2.6, compared with patients randomized to ADA (**Table**).

Figure. Exposure-adjusted Event and Incidence Rates of Treatment-emergent AEs Over 3 Years



ADA, adalimumab; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rates; EOW, every other week; MACE, major adverse cardiovascular event; NMSC, non-melanoma skin cancer; PY, patient years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism.

Exposure adjusted incidence rates (EAIR) are reported for malignancy, MACE, VTE, and deaths; exposure adjusted event rates (EAER) are reported for the remaining events.

[a]Excluded tuberculosis and herpes zoster.

[b]Herpes zoster: majority of cases on UPA were non-serious and involved 1 or 2 dermatomes.

[c]CPK elevation: most were mild or moderate and asymptomatic, with no reports of rhabdomyolysis.

[d]Hepatic disorders: majority were transaminase elevations.

[e]Includes treatment-emergent and non-treatment emergent deaths.

Table. Efficacy Endpoints at 3 Years (NRI)

Endpoints, % (95% CI)	UPA 15 mg QD N=651*	ADA 40 mg EOW N=327*
CDAI ≤10	39 (36, 43)	29 (24, 34)
CDAI ≤2.8	24 (21, 28)	17 (12, 21)
DAS28(CRP) ≤3.2	37 (33, 41)	26 (21, 31)
DAS28(CRP) <2.6	32 (29, 36)	22 (17, 26)

ADA, adalimumab; CI, confidence interval; DAS28(CRP), Disease Activity Score for 28-joints C-Reactive Protein; CDAI, clinical disease activity index; EOW, every other week; NRI, non-responder imputation; QD, once daily; UPA, upadacitinib.
*Patients who were rescued prior to/at Week 26 were considered non-responders. 252/651 and 159/327 patients were rescued of those randomized to UPA and ADA, respectively.

Conclusion: The safety profile of UPA was consistent with the results reported previously and with the integrated Phase 3 safety analysis.[1,2] Higher levels of clinical response continued to be observed with UPA vs ADA through 3 years of treatment.

References

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2. Cohen SB, et al. *Ann Rheum Dis* 2020; https://doi.org/10.1136/annrheumdis-2020-218510.

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Abstract Number: 0829

Tapering and Withdrawal of Biologics or Targeted Synthetic Disease-Modifying Antirheumatic Drugs in Patients with Inflammatory Arthritis: A Systematic Review and Meta-Analyses of Randomised Trials

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Tapering and withdrawal of biological or targeted synthetic disease-modifying antirheumatic drugs (bDMARDs or tsDMARDs) in patients with inflammatory arthritis (IA) in remission or low disease activity (LDA) are a topic of great interest. This systematic review aimed to assess the risk of flare after tapering or withdrawing b- or tsDMARDs compared to continuation of standard dosage.

Methods: The protocol was registered at PROSPERO (CRD42019136905). Predefined search terms identified relevant articles in Cochrane Library, EMBASE, PubMed, and Web of Science (search date: 13-14/06/2019, rerun

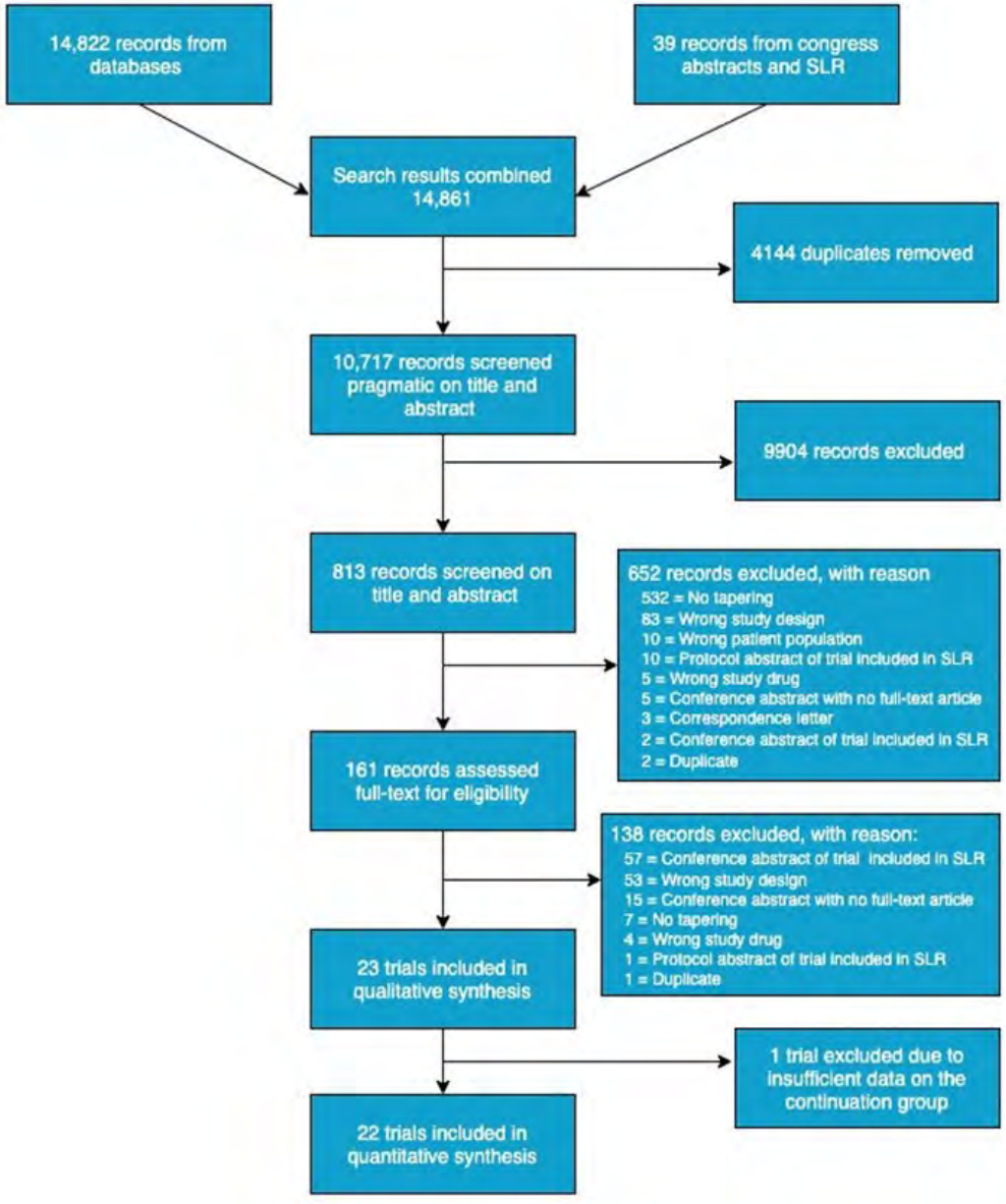

Figure 1. Flow diagram of study selection.

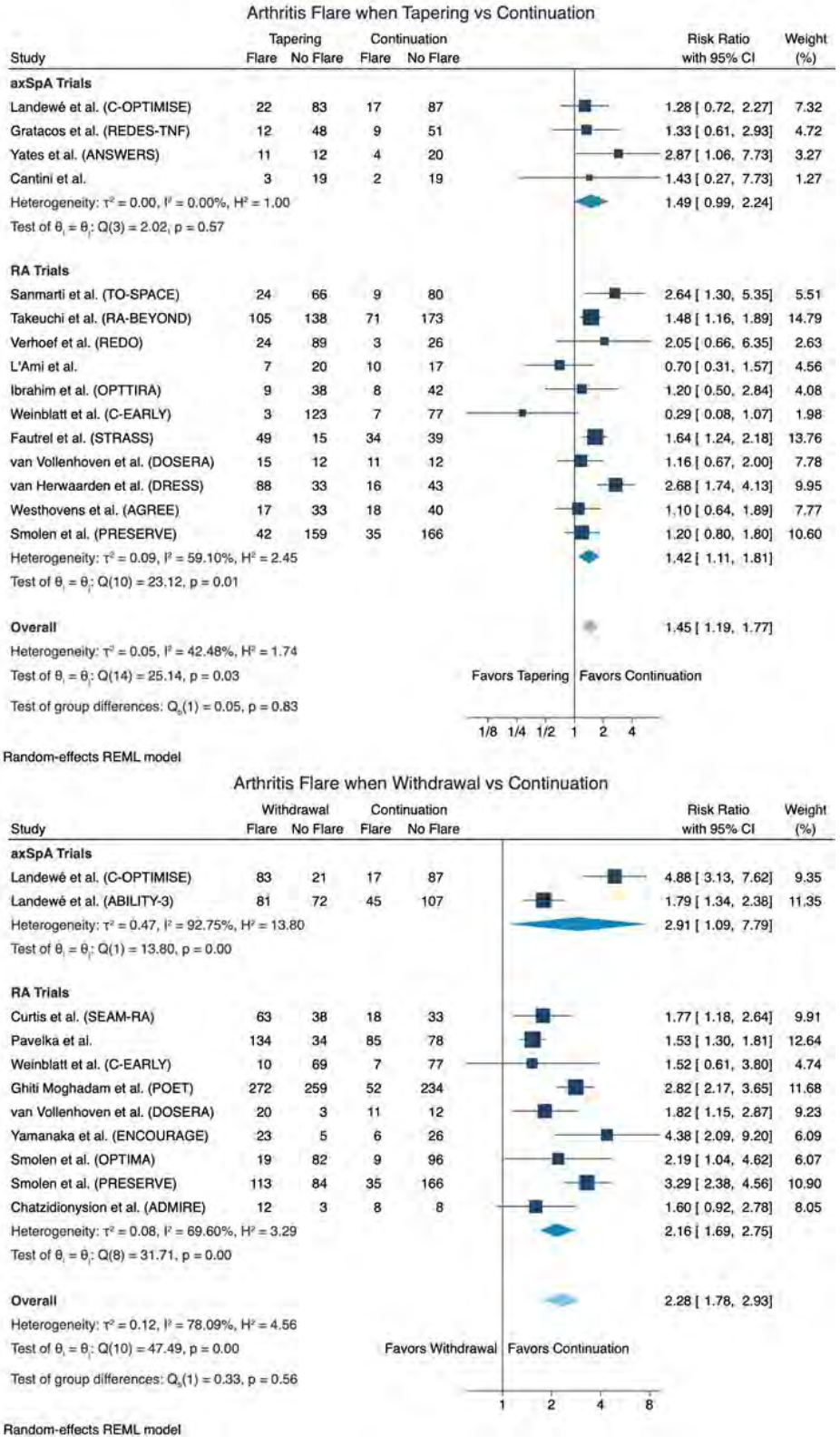

Figure 2. Meta-analysis of risk ratio with 95% confidence interval (95%CI) for flare by diagnosis (i.e. RA or axSpA) who A) Taper or B) Withdraw b- or tsDMARDs compared to continuation of standard dosage.

11/01/2021). Congress abstracts from ACR and EULAR after 01/01/2017 was evaluated for eligibility. Randomized trials comparing tapering or withdrawal of b- or tsDMARDs in patients with IA with continuation of standard dosage were included. Random-effects meta-analyses were performed to combine the risk ratio (RR) with 95% confidence interval (95%CI) for data on flare after either A) Tapering or B) Withdrawal of b- or tsDMARDs compared to continuation of standard dosage stratified by diagnosis. In trials with >1 tapering strategy, data for the different tapering strategies were combined initially before meta-analysis.

Results: 14,861 references were screened, and 22 trials were included in the meta-analyses of flare risk with data on 3,942 patients with RA and 828 patients with axSpA (*Figure 1*). An increased risk for developing flare(s) was demonstrated in the meta-analysis on 15 trials tapering of b- or tsDMARDs, RR = 1.45 (95%CI: 1.19 to 1.77; *Figure 2*). This corresponds to an absolute effect of number needed to treat (NNT [harm]) of 10 patients. Moreover, in 11 trials testing the effect of (abrupt) withdrawal of tumour necrosis factor inhibitors (TNFis), a highly evident increased risk was demonstrated, RR = 2.28 (95%CI: 1.78 to 2.93; *Figure 2*) with an absolute effect of NNT (harm) of 3 patients. As presented in *Figure 2*, no significant difference in the risk for flare was observed in subgroup meta-analyses when stratifying by diagnosis (i.e. axSpA or RA).

In summary, 431 patients (32.7%) in the tapering group had a flare and 888 patients (67.3%) did not whereas 830 patients (55.3%) in the withdrawal group experienced a flare and 670 patients (44.7%) did not. Thus, even though an increased risk for flare was demonstrated in the meta-analyses it is noteworthy that the proportion of patients with no flare was larger in the tapering group (67.3%) compared to the withdrawal group (44.7%).

Conclusion: Patients with IA who taper or withdraw their b- or tsDMARDs compared to continuation of standard dosage have an increased risk of flare with no significant risk difference between patients with axSpA or RA. However, a complete withdrawal was associated with a substantially increased flare risk; thus, the most favorable approach to reduce b- or tsDMARDs dose seems to be tapering.

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Abstract Number: 0830

Smartphone Assisted Patient Initiated Care Safely Reduces Outpatient Clinic Visits in Patients with Rheumatoid Arthritis: Results from a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The demand on outpatient rheumatology clinics is high due to protocolised visits of rheumatoid arthritis (RA) patients, including those in low disease activity or remission. We developed a mobile phone app for patients with RA, which allows them to self-monitor their disease activity in between clinic visits by answering a weekly routine assessment of patient index data (RAPID-3). The objective of this study is to assess efficacy and safety of self-initiated care assisted by a smartphone app in patients with RA.

Methods: A randomised controlled trial was performed with a study duration of one year. Inclusion criteria were: 1) diagnosed with RA by a rheumatologist, 2) disease duration of at least two years and 3) a Disease Activity Score 28 (DAS28) below 3.2 at the start of the study. Patients were excluded if they had initiated or discontinued conventional DMARDs or a biological in the previous 6 months. Patients were randomised to either app supported self-initiated care with only one scheduled follow-up consultation after a year (app-group) or to usual care. The app warned patients that they could be flaring when RAPID-3 scores increased more than 2 points and the overall score was over 4. The co-primary outcome was mean number of consultations with a rheumatologist and non-inferiority in terms of difference in DAS28 at 12 months. The non-inferiority limit was set at 0.5 difference in DAS28 between the groups. Secondary outcomes included consultations with nurses, satisfaction with healthcare and app usage.

Results: In total, 103 patients were randomised to usual care (n=53) or to the app group (n=50). Baseline characteristics were similar in both groups (table 1). At 12 months, the mean number (±SD) of outpatient or telephone consultations with the rheumatologist was significantly lower in the app group compared with usual care (1.7±1.8 vs 3.0±1.4, p< 0.001). The same applied to the nurse outpatient or telephone consultations (0.4±1.0 vs 0.9±1.1, p=0.03; table 2). Non-inferiority was established as the 95% confidence interval of the mean difference in DAS28 between the groups was within the non-inferiority limit: -0.04 in favour of the intervention group ([95% CI], -0,39, 0.30). Satisfaction with healthcare received was high (8.6 out of 10 ±1.3) in both groups and not statistically different. On average patients completed 56% (29/52, SD13.3) of the weekly questionnaires.

Table 1. Baseline characteristics. Data are mean (SD) or percentage.

	Telemonitoring (n=50)	Usual Care (n=53)
Age, years	58.4 ±12.6	57 ±10.8
Gender, % male	44	40
BMI	25.5 ±4.4	26.1 ±4.5
Disease duration, years	12.4 ±9.4	10.8 ±8.5
DAS28	1.7 ±0.7	1.5 ±0.7
RAPID 3	2.3 ±1.5	1.9 ±1.4
ACPA, % positive	66	75
RF, % positive	58	62

Table 2. Number of consultations per group. Means and standard deviation (SD) are presented. CI: 95% Confidence Interval.

	Telemonitoring (N=49)	Usual Care (N=53)	Mean Difference (CI)	P-value
Rheumatologist				
Telephone	1.4 ±1.6	2.0 ±1.3	0.6 (0.0-1.2)	0.04
Outpatient visits	0.3 ±0.6	1.1 ±0.8	0.8 (0.5-1.0)	<0.001
Total	1.7 ±1.8	3.0 ±1.4	1.2 (0.6-1.9)	<0.001
Nurse				
Telephone	0.3 ±0.8	0.5 ±0.9	0.2 (-0.2-0.5)	0.31
Outpatient visits	0.1 ±0.3	0.3 ±0.6	0.2 (0.0-0.4)	0.02
Total	0.4 ±1.0	0.9 ±1.1	0.5 (0.0-0.9)	0.03

Conclusion: The results of this study show that self-initiated care supported with weekly RAPID3 self-monitoring via a smartphone app reduces the number of outpatient visits and telephone consultations and is non-inferior to usual care in terms of the DAS28. We propose the implementation of this approach to optimise rheumatologic care for RA patients in low disease activity.

Disclosure: B. Seppen, None; **J. Wiegel**, None; **M. ter wee**, None; **D. van Schaardenburg**, None; **L. Roorda**, None; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5; **w. Bos**, Abbvie, 5, Pfizer, 5, Novartis, 5.

Abstract Number: 0831

Safety and Efficacy of Tofacitinib vs TNF Inhibitors in RA Patients Aged 50 Years or Older with One or More Cardiovascular Risks: Results from a Phase 3b/4 Randomized Safety Trial

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

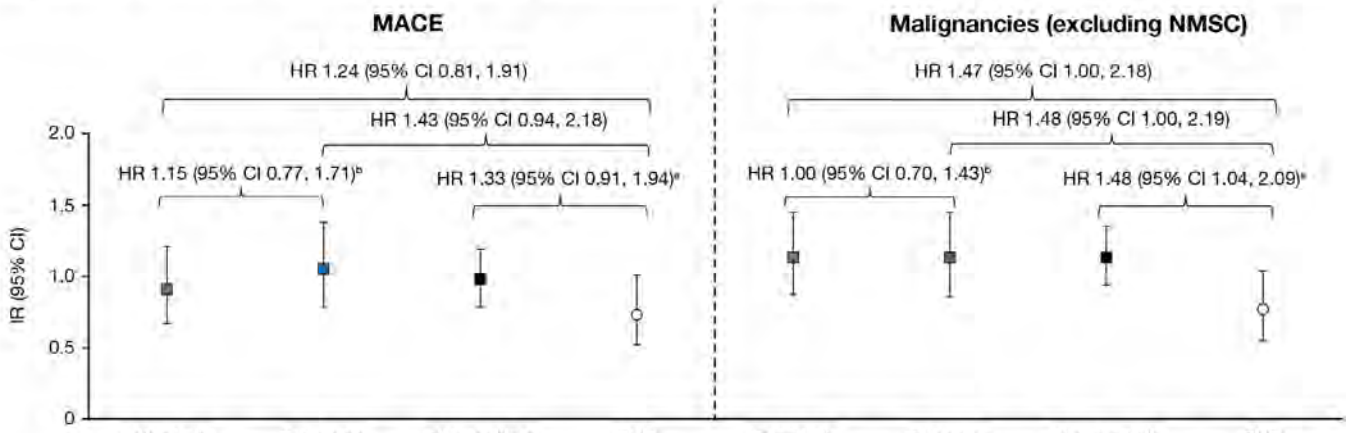
Session Time: 8:30AM–10:30AM

Background/Purpose: ORAL Surveillance (NCT02092467) was mandated by the US Food and Drug Administration to assess the relative risk of tofacitinib vs TNF inhibitors (TNFi), based on observed increases in lipids and malignancies in patients (pts) with RA following tofacitinib treatment. This analysis compared the risks of major adverse cardiovascular (CV) events (MACE) and malignancies (excluding non-melanoma skin cancer) in pts with moderate to severe RA aged ≥ 50 yrs with ≥ 1 additional CV risk factor receiving tofacitinib or a TNFi.

Methods: This Phase 3b/4 prospective, randomized, open-label, non-inferiority study (co-primary endpoints: adjudicated MACE and malignancies) was in high-risk pts with RA (aged ≥ 50 yrs, ≥ 1 additional CV risk factor), receiving MTX. Pts were randomized 1:1:1 to receive tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every other week or etanercept 50 mg every week). Adjudicators were blinded to treatment. Outcome differences were analyzed using univariate Cox proportional hazard models. The primary comparison was whether the upper limit of the 2-sided 95% confidence interval (CI) for the hazard ratio (HR) for tofacitinib doses combined vs TNFi was < 1.8; the secondary comparison was whether the upper limit for tofacitinib 10 vs 5 mg BID was < 2.0. Incidence rates (IRs; unique pts with events/100 pt-yrs) were calculated for co-primary endpoints and adverse events (AEs) of special interest. Efficacy outcomes for clinical disease activity and pt-reported outcomes were captured.

Results: Between Mar 2014–Jul 2020, 1,455, 1,456, and 1,451 pts received tofacitinib 5 mg BID, tofacitinib 10 mg BID, and TNFi, respectively. Median age was 60.0 yrs. For MACE and malignancies, primary assessments were not met for tofacitinib doses combined vs TNFi (HR [95% CI] 1.33 [0.91, 1.94] and 1.48 [1.04, 2.09], respectively; upper

Figure. HRs (95% CIs)[a,b] and IRs (95% CIs) for adjudicated MACE and adjudicated malignancies (excluding NMSC)



n/N	47/1,455	51/1,456	98/2,911	37/1,451	62/1,455	60/1,456	122/2,911	42/1,451
PY	5,166.32	4,871.96	10,038.28	5,045.27	5,491.48	5,311.71	10,803.19	5,482.30
IR (95% CI)	0.91 (0.67, 1.21)	1.05 (0.78, 1.38)	0.98 (0.79, 1.19)	0.73 (0.52, 1.01)	1.13 (0.87, 1.45)	1.13 (0.86, 1.45)	1.13 (0.94, 1.35)	0.77 (0.55, 1.04)
NNH[d] vs TNFi	567	319	412	--	276	275	275	--

The definition of MACE in this study was non-fatal myocardial infarction, non-fatal stroke, and all cardiovascular deaths, excluding death due to pulmonary embolism. For adjudicated MACE, the primary censoring time was the 60-Day On-Treatment period (defined as the time from the first until last study dose + 60 days or last contact date, whichever is earlier); for adjudicated malignancies (excluding NMSC), the primary censoring time was total time (defined as last contact date)

[a]The primary comparison (all tofacitinib doses combined vs TNFi) was whether the upper limit of the two-sided 95% CI for the HR was < 1.8

[b]The secondary comparison (tofacitinib 10 vs 5 mg BID) was whether the upper limit of the two-sided 95% CI for the HR was < 2.0

[c]The tofacitinib 10 mg BID treatment group included pts that were switched from 10 to 5 mg BID as a result of a study modification in 2019

[d]NNH was the number of PY of exposure needed for a treatment to have one more event relative to the reference; calculations were performed post hoc

BID, twice daily; CI, confidence interval; HR, hazard ratio; IR, incidence rate (pts with events per 100 PY); MACE, major adverse cardiovascular events; NNH, Number Needed to Harm; NMSC, non-melanoma skin cancer; pt, patient; PY, pt-yrs; TNFi, TNF inhibitor

Table. AEs of special interest

AE, n (%), IR [95% CI]	Tofacitinib 5 mg BID (N=1455)	Tofacitinib 10 mg BID (N=1456)	TNFi (N=1451)
Serious infection	141 (9.7)	169 (11.6)	119 (8.2)
	2.86 [2.41, 3.37]	3.64 [3.11, 4.23]	2.44 [2.02, 2.92]
All herpes zoster	180 (12.4)	178 (12.2)	58 (4.0)
(non-serious/serious)	3.75 [3.22, 4.34]	3.94 [3.38, 4.57]	1.18 [0.90, 1.52]
Pulmonary embolism[a]	9 (0.6)	24 (1.7)	3 (0.2)
	0.17 [0.08, 0.33]	0.50 [0.32, 0.74]	0.06 [0.01, 0.17]
Deep vein thrombosis[a]	11 (0.8)	15 (1.0)	7 (0.5)
	0.21 [0.11, 0.38]	0.31 [0.17, 0.51]	0.14 [0.06, 0.29]
Venous	17 (1.2)	34 (2.3)	10 (0.7)
thromboembolism[a]	0.33 [0.19, 0.53]	0.70 [0.49, 0.99]	0.20 [0.10, 0.37]
Arterial	47 (3.2)	45 (3.1)	41 (2.8)
thromboembolism	0.92 [0.68, 1.22]	0.94 [0.68, 1.25]	0.82 [0.59, 1.12]
All-cause mortality[a]	26 (1.8)	39 (2.7)	17 (1.2)
	0.50 [0.33, 0.74]	0.80 [0.57, 1.09]	0.34 [0.20, 0.54]

Censoring time was the 28-day on-treatment time (time from the first until last study dose + 28 days or last contact date, whichever was earlier)

[a]Adjudicated

AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (pts with events per 100 PY); pt, patient; PY, pt-yrs; TNFi, TNF inhibitor

limits of CIs were > 1.8); for tofacitinib 10 vs 5 mg BID, the upper limits of 95% CIs were < 2.0 (Figure). IRs for MACE and malignancies were numerically higher for tofacitinib vs TNFi (Figure). In post hoc analyses, most MACE and malignancies occurred in pts who were aged ≥ 65 yrs or had ever smoked (MACE: 83/98 [84.7%] and 29/37 [78.4%];

malignancies: 102/122 [83.6%] and 33/42 [78.6%]; with tofacitinib and TNFi, respectively). IRs of AEs of special interest were numerically higher with tofacitinib (10 > 5 mg BID) vs TNFi (Table). Efficacy was similar across treatment arms.

Conclusion: For MACE and malignancies, the primary assessments were not met for tofacitinib doses combined vs TNFi in this high-risk population. Pts most at risk were aged ≥ 65 yrs or had ever smoked. IRs for MACE and malignancies were < 1.5 across all treatment groups, with overlapping 95% CIs. The Numbers Needed to Harm for tofacitinib 5 and 10 mg BID, respectively, vs TNFi were 567 and 319 for MACE and 276 and 275 for malignancies. Efficacy was similar across treatment arms.

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Abstract Number: 0832

Consistency in Time to Response with Upadacitinib as Monotherapy or Combination Therapy and Across Patient Populations with Rheumatoid Arthritis

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SESSION INFORMATION

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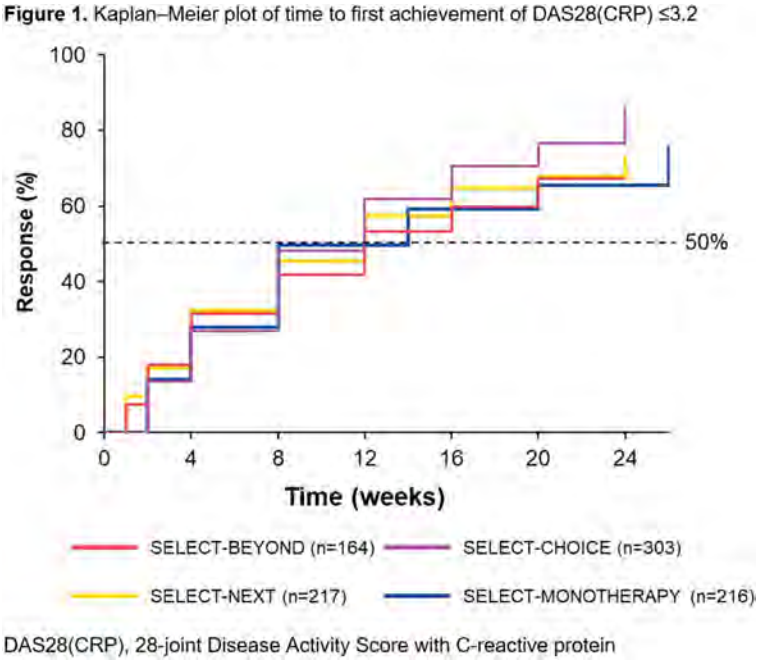

Figure 1. Kaplan–Meier plot of time to first achievement of DAS28(CRP) ≤3.2.

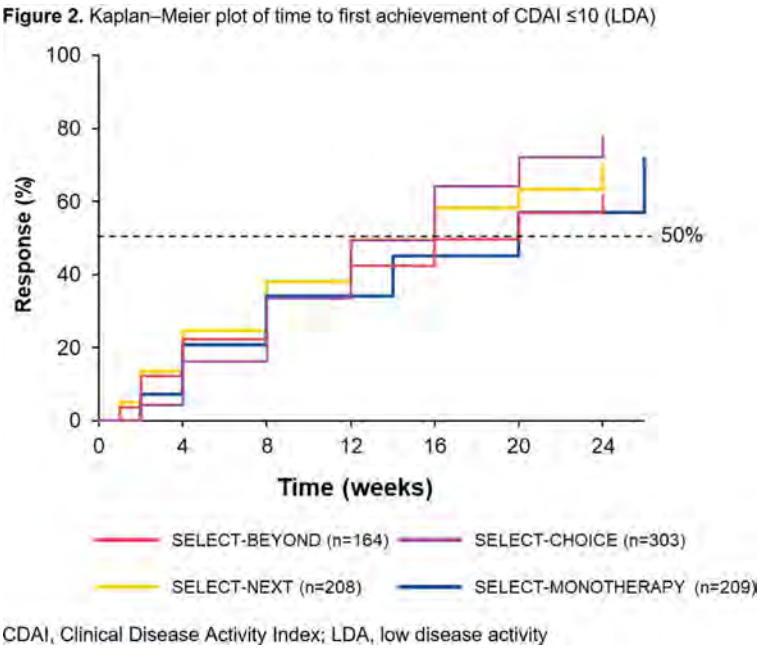

Figure 2. Kaplan–Meier plot of time to first achievement of CDAI ≤10 (LDA).

Background/Purpose: Upadacitinib (UPA) has demonstrated efficacy in patients with moderate-to-severe rheumatoid arthritis (RA) across various patient populations.[1–4] This post hoc analysis aimed to evaluate the consistency in time to achieving meaningful clinical response with UPA 15 mg + conventional synthetic (cs) DMARDs in biologic (b) DMARD-inadequate responder (IR) versus csDMARD-IR patients with RA as well as with UPA 15 mg monotherapy versus UPA 15 mg + csDMARDs in csDMARD-IR patients.

Methods: Patients originally randomized to UPA 15 mg once daily from four Phase 3 trials were included in this analysis: SELECT-BEYOND[1] and SELECT-CHOICE[2] (UPA 15 mg + csDMARDs in bDMARD-IR patients), SELECT-NEXT[3] (UPA 15 mg + csDMARDs in csDMARD-IR patients), and SELECT-MONOTHERAPY[4] (UPA 15 mg monotherapy in methotrexate-IR patients). Time to response was estimated using the Kaplan–Meier method for clinical outcomes over 24 weeks (26 weeks in SELECT-MONOTHERAPY). Clinical outcomes included achievement of 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP]) ≤3.2; low disease activity (LDA) defined as Clinical Disease Activity Index (CDAI) ≤10 and Simple Disease Activity Index (SDAI) ≤11; and 50% improvement in American College of Rheumatology (ACR) core components and morning stiffness (MS) duration/severity. Data presented were as observed.

Results: Overall, 905 patients were included (SELECT-BEYOND: n=164; SELECT-CHOICE: n=303; SELECT-NEXT: n=221; SELECT-MONOTHERAPY: n=217). csDMARD-IR patients had a mean disease duration of 7.3 (SELECT-NEXT) or 7.5 years (SELECT-MONOTHERAPY); bDMARD-IR patients had a mean disease duration of 12.4 years, with a more refractory population (≥3 prior bDMARDs) in SELECT-BEYOND (23%) than SELECT-CHOICE (10%). In general, the median time to DAS28(CRP) ≤3.2, CDAI LDA, 50% improvement in ACR core components, and 50% improvement in MS duration/severity were consistent across the studies in bDMARD-IR and csDMARD-IR patients. For SELECT-BEYOND, SELECT-CHOICE, SELECT-NEXT, and SELECT-MONOTHERAPY, the median (95% CI) time to achieve DAS28(CRP) ≤3.2 was 12 (12, 16), 12 (8, 12), 12 (8, 12), and 14 (8, 14) weeks, respectively **(Figure 1)**, and the median time to achieve CDAI LDA was 20 (12, 24), 16 (12, 16), 16 (12, 16), and 20 (14, 20) weeks, respectively **(Figure 2)**. A longer median (95% CI) time to achieve SDAI LDA was observed with UPA monotherapy (20 [14, 20] weeks) versus UPA + csDMARDs (12 [12, 16] weeks) in csDMARD-IR patients. Among bDMARD-IR patients, the median (95% CI) time to 50% improvement in pain was longer in SELECT-BEYOND versus SELECT-CHOICE (16 [12, 20] versus 8 [8, 12] weeks).

Conclusion: In diverse patient populations with RA, patients treated with UPA 15 mg, as monotherapy or with csDMARDs, generally demonstrated consistent time to achieving DAS28(CRP) ≤3.2, CDAI LDA, and 50% improvement in clinical outcomes.

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3. Burmester GR, et al. Lancet 2018;391:2503–12.
4. Smolen JS, et al. Lancet 2019;393:2303–11.

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Abstract Number: 0833

Effectiveness of Upadacitinib in Patients with Rheumatoid Arthritis in German Real-World Practice: Interim Results from a Post-Marketing Observational Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

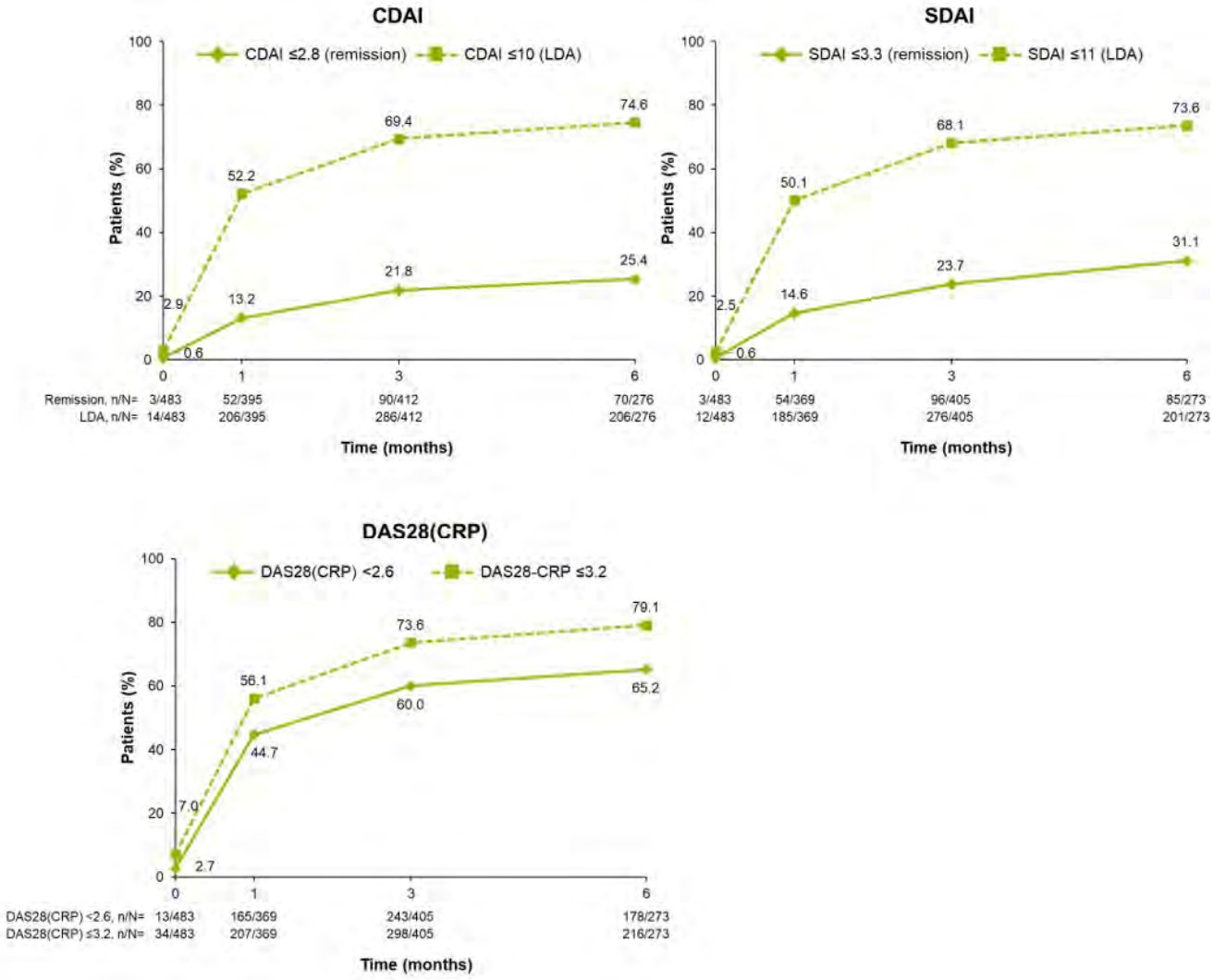
Session Time: 8:30AM–10:30AM

Table. Baseline characteristics

Parameter	UPA 15 mg QD	
	N	Baseline value[a]
Female, n (%)	483	369 (76.4)
Age, years	483	58.0 (12.3)
Disease duration, years	475	9.0 (8.0)
CRP, mg/dL	483	1.2 (1.8)
CRP >ULN, n (%)	483	274 (56.7)
RF+, n (%)	389	265 (68.1)
ACPA+, n (%)	271	178 (65.7)
TJC28	483	7.3 (5.9)
SJC28	483	5.5 (4.0)
Patient's Global Assessment	483	6.3 (1.8)
Physician's Global Assessment	483	5.9 (1.6)
CDAI	483	24.9 (10.3)
SDAI	483	26.1 (10.6)
DAS28(CRP)	483	4.6 (1.0)
Pain (RAID-1)	481	6.2 (2.2)
Fatigue (RAID-3)	481	5.5 (2.6)
HAQ-DI	471	1.3 (0.6)
Prior bDMARD or tsDMARD, n (%)	483	294 (60.9)
Prior tsDMARD, n (%)	483	85 (17.6)
Concomitant MTX[b], n (%)	399	195 (48.9)
Mean MTX dose, mg/week	195	12.7 (5.4)
Concomitant GCs, n (%)	399	175 (43.9)
Mean GC dose, mg/day	175	5.7 (3.3)
Prior HZ vaccination, Shingrix/Zostavax, n (%)	483	37 (7.7)/3 (0.6)

[a]Mean (SD) unless otherwise stated. [b]The study enrolled around 50% of patients receiving UPA monotherapy and 50% of patients receiving UPA + MTX at baseline per protocol.
ACPA, anti-citrullinated protein antibody; bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28(CRP), 28-joint Disease Activity Score using C-reactive protein; GC, glucocorticoid; HAQ-DI, Health Assessment Questionnaire-Disability Index; HZ, herpes zoster; MTX, methotrexate; QD, daily; RAID, Rheumatoid Arthritis Impact of Disease; RF, rheumatoid factor; SD, standard deviation; SDAI, Simple Disease Activity Index; SJC28/TJC28, swollen/tender joint count in 28 joints; tsDMARD, targeted synthetic disease-modifying antirheumatic drug; ULN, upper limit of normal; UPA, upadacitinib.

Background/Purpose: Upadacitinib (UPA) is a Janus kinase inhibitor that has been shown to be effective and well tolerated in patients with rheumatoid arthritis (RA) in the Phase 3 SELECT clinical trials.[1–6] However, data on the use of UPA in real-world clinical practice are limited. The UPwArds study aims to investigate the effectiveness and safety of UPA as monotherapy or in combination with methotrexate (MTX) in patients with RA in German clinical practice.



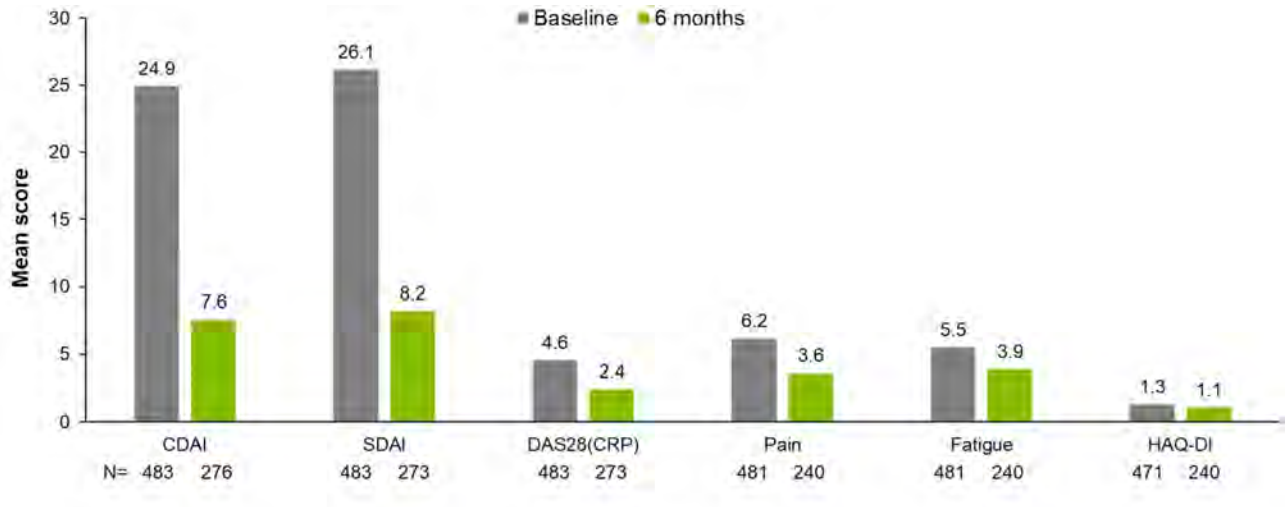
This descriptive interim analysis reports data based on observed case analyses for the patients who had completed Visit 3 (Month 6) by the cut-off date of March 22, 2021.

CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score using C-reactive protein; LDA, low disease activity; SDAI, Simple Disease Activity Index.

Figure 1. Proportions of patients achieving CDAI remission/LDA, SDAI remission/LDA, and DAS28(CRP) <2.6/≤3.2 over 6 months of upadacitinib treatment.

Methods: UPwArds is an ongoing, prospective, multicenter, non-interventional, post-marketing study in adult patients with moderate-to-severe RA who are treated with UPA 15 mg once daily according to the product label, with the decision to initiate UPA made prior to study participation. Per protocol, the study enrolled around 50% of patients receiving UPA monotherapy and 50% of patients receiving UPA + MTX. The primary endpoint was the proportion of patients achieving remission defined as Clinical Disease Activity Index (CDAI) ≤2.8 at 6 months. Key secondary endpoints included the proportion of patients achieving CDAI ≤2.8 and ≤10, Simple Disease Activity Index (SDAI) ≤3.3 and ≤11, and 28-joint Disease Activity Score using CRP (DAS28[CRP]) < 2.6 and ≤3.2 at each visit. Changes from baseline in disease activity and patient-reported outcomes were also assessed. This descriptive interim analysis reports data for the patients who had completed Visit 3 (Month 6) by the cut-off date of March 22, 2021. Data are presented as observed and summarized descriptively, with no statistical analyses conducted.

Results: Of the 483 patients at baseline (76.4% female; mean disease duration: 9 years), 60.9% had previously been treated with biologic (b) or targeted synthetic (ts) DMARDs **(Table 1)**. Of the patients with 6-month data, 25.4% (70/276) and 74.6% (206/276) achieved CDAI remission (primary endpoint) and LDA, respectively, after 6 months of UPA 15 mg treatment **(Figure 1)**. DAS28(CRP) < 2.6 and ≤3.2 at Month 6 were achieved by 65.2% (178/273) and 79.1% (216/273) of patients, respectively. The percentage of patients achieving any definition of LDA (DAS28[CRP] ≤3.2, CDAI ≤10, or SDAI ≤11) or remission (DAS28[CRP] < 2.6, CDAI ≤2.8, or Boolean remission) at 6 months was similar among those treated with UPA monotherapy (72.9%) or UPA + MTX (74.1%). Disease activity and patient-reported outcomes (including pain, fatigue, and physical function) improved within the first 6 months following initiation of UPA 15 mg **(Figure 2)**. The safety profile of UPA 15 mg was consistent with that seen in the Phase 3 trials with no new safety signals.[1–6]



This descriptive interim analysis reports data based on observed case analyses for the patients who had completed Visit 3 (Month 6) by the cut-off date of March 22, 2021.
CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score using C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; SDAI, Simple Disease Activity Index.

Figure 2. Disease activity and patient-reported outcomes after 6 months of upadacitinib treatment.

Conclusion: Consistent with previous clinical data, the 6-month interim results from this study suggest that UPA as monotherapy or in combination with MTX is associated with a favorable benefit–risk profile in real-world patients with RA.

1. Smolen JS, et al. Lancet 2019;393:2303–11.
2. Burmester GR, et al. Lancet 2018;391:2503–12.
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5. Fleischmann R, et al. Arthritis Rheumatol 2019;71:1788–800.
6. Rubbert-Roth A, et al. N Engl J Med 2020;383:1511–21.

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Abstract Number: 0834

Comparative Effectiveness of TNF Inhibitor vs IL-6 Receptor Inhibitor as Monotherapy or Combination Therapy with Methotrexate in Patients with Rheumatoid Arthritis: Analysis from CorEvitas' RA Registry

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SESSION INFORMATION
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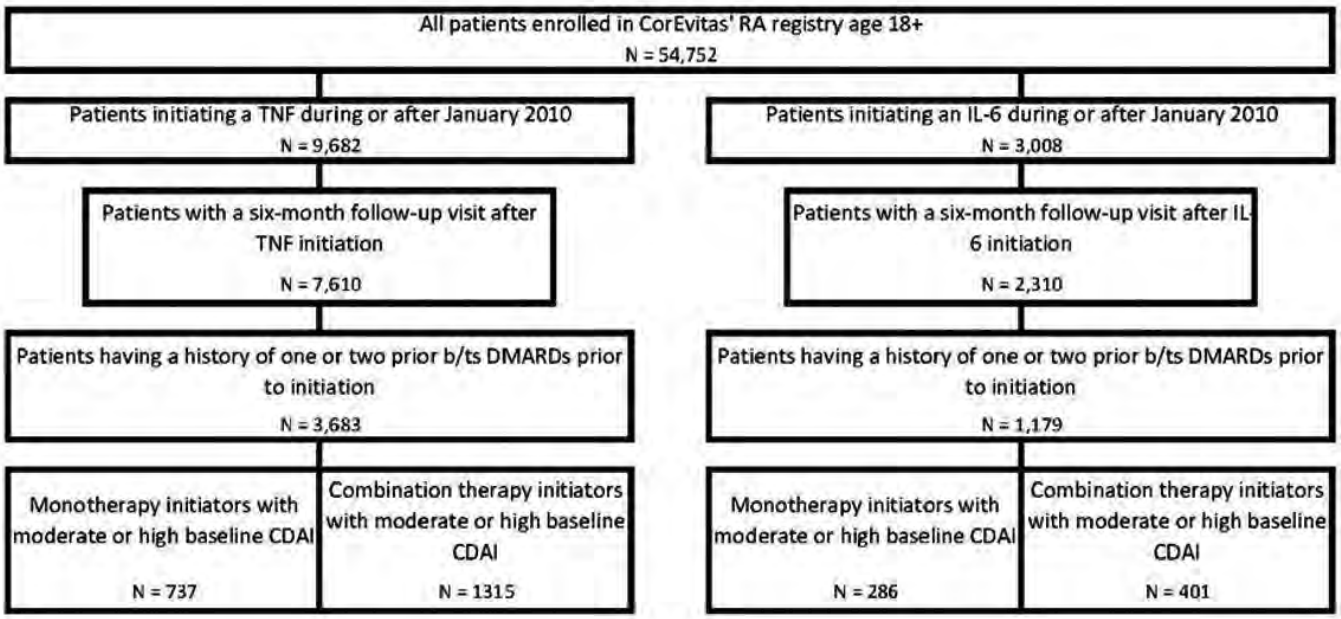
Session Time: 8:30AM–10:30AM

Background/Purpose: RA patients who fail to achieve treatment targets with conventional synthetic DMARDs (csDMARDs) can be treated with biologics. Randomized controlled trials (RCTs) have shown IL-6 receptor inhibitors (IL-6i) to be superior to TNF-α inhibitors (TNFi; adalimumab) as monotherapy in biologic-naïve patients with high disease activity. There is limited research comparing the effectiveness of TNFi vs IL-6i as monotherapy or in combination with csDMARDs in biologic-experienced RA patients with moderate/high disease activity. This real-world retrospective study based on CorEvitas' RA registry aimed to address the gap.

Methods: Adult RA patients who initiated a TNFi or IL-6i during or after January 2010 were included if they had: a history of 1 or 2 biologic/targeted synthetic DMARDs (b/tsDMARDs) prior to initiation, moderate/high disease activity at initiation, and a follow-up visit at 6 (± 3) months after initiation. Cohorts included TNFi and IL-6i initiators, both with subgroups initiating as mono- or combination (with MTX) therapy. Mixed effects regression models with random intercept for patients were used to evaluate the impact of therapy class on the following outcomes: disease burden (HAQ-DI, pain visual analog scale [VAS, 0-100], patient global assessment, and fatigue [1-item VAS, 0-100]), non-inflammatory pain (NIP; NIP1: tender joint count [TJC, 28] – swollen joint count [SJC, 28] ≥7; NIP2: SJC [28]/TJC [28] < 0.5), and clinical disease activity index (CDAI). Unadjusted and covariate-adjusted effects (β, 95% confidence interval [CI] for linear regressions and odds ratio [OR, 95% CI] for logistic regressions) were reported.

Results: Patients initiating IL-6i (n=286) vs TNFi monotherapy (n=737; **Figure 1**) were older (60.0 vs 55.4 years; *P*< 0.001), had longer history of RA (12.2 vs 10.0 years; *P*=0.001), higher CDAI at baseline (26.9 vs 24.9; *P*=0.02), and were more likely to initiate as 3rd line therapy (57.0% vs 30.9%; *P*< 0.001). IL-6i (n=401) vs TNFi (n=1315) combination therapy initiators had higher CDAI at baseline (26.7 vs 24.8; *P*=0.007) and were more likely to initiate as 3rd line therapy (56.4% vs 28.7%; *P*< 0.001; **Table 1**). There were no statistically significant differences in outcomes between IL-6i and TNFi initiators (as mono- or combination therapy). One-third of IL-6i and TNFi mono- (adjusted OR [aOR]: 0.99 [0.59, 1.67]) and combination therapy initiators (aOR: 0.96 [0.66, 1.38]) achieved low disease activity (**Table 2**).

Conclusion: In this real-world analysis, no significant differences were noted in the outcomes for IL-6i vs TNFi initiators (as mono- or combination therapy). Compared with prior RCTs, patients in this study were biologic-experienced, had lower disease activity, and were unblinded to treatment, which could have contributed to a reduced difference in effectiveness between these treatments. In addition, selection of therapy in this real-world study may be influenced by factors that cannot be measured or controlled.



b/ts DMARDs, biologic/targeted synthetic disease modifying anti-rheumatic drugs; CDAI, clinical disease activity index; IL-6, interleukin-6; N, number of patients; RA, rheumatoid arthritis; TNF, tumor necrosis factor.

Figure 1. Patient Disposition.

Table 1. Baseline demographic and clinical characteristics in monotherapy and combination therapy initiators by therapy class

Characteristic[a]	Monotherapy Initiators			Combination Therapy Initiators		
	TNFi	IL-6i	*P*-value	TNFi	IL-6i	*P*-value[b]
Total, N	737	286		1315	401	
Age, years	55.4 (13.6)	60.0 (12.9)	<0.001	57.5 (13.2)	58.1 (13.4)	0.42
Duration of RA, years	10.0 (9.7)	12.2 (10.1)	0.001	10.1 (9.2)	9.9 (9.3)	0.74
Female, n (%)	613 (83.2)	220 (76.9)	0.02	1055 (80.2)	305 (76.1)	0.07
Race (White), n (%)	616 (83.7)	231 (81.3)	0.37	1077 (82.3)	314 (78.7)	0.10
Smoking Status, n (%)			0.44			0.51
Never	354 (48.2)	129 (45.6)		665 (51.1)	192 (48.2)	
Previous/Current	380 (51.8)	154 (54.4)		637 (48.9)	206 (51.8)	
BMI, kg/m^2	30.1 (7.2)	29.3 (7.1)	0.13	31.2 (8.1)	30.8 (7.5)	0.33
BMI category, n (%)			0.32			0.98
Underweight/Normal weight (BMI<25)	184 (25.1)	87 (30.4)		297 (22.7)	90 (22.5)	
Overweight (25≤BMI<30)	227 (30.9)	78 (27.3)		382 (29.1)	115 (28.7)	
Obese (BMI≥30)	323 (44.0)	121 (42.3)		632 (48.2)	195 (48.8)	
CDAI	24.9 (12.3)	26.9 (12.4)	0.02	24.8 (12.2)	26.7 (12.2)	0.007
Tender joint count	9.0 (7.1)	9.6 (7.2)	0.23	9.0 (7.0)	10.0 (7.4)	0.01
Swollen joint count	6.0 (5.3)	6.9 (5.3)	0.02	6.6 (5.3)	6.7 (5.4)	0.60
Physician reported global assessment	42.8 (21.6)	45.5 (20.6)	0.06	40.8 (20.5)	44.3 (20.0)	0.003
Patient reported global assessment	56.5 (23.4)	58.4 (24.2)	0.26	52.2 (24.7)	55.5 (23.5)	0.02
HAQ-DI[c]	1.1 (0.7)	1.3 (0.7)	<0.001	1.1 (0.7)	1.2 (0.7)	0.08
Patient reported pain	59.8 (25.0)	62.2 (25.1)	0.18	54.3 (25.9)	57.3 (24.1)	0.04
Patient reported fatigue[c]	58.2 (27.3)	58.5 (27.7)	0.85	53.9 (27.7)	57.3 (26.9)	0.03
Morning stiffness, n (%)	678 (92.4)	274 (96.1)	0.03	1208 (92.4)	376 (94.5)	0.15
Morning stiffness duration, hrs[c,d]	2.3 (3.8)	2.4 (3.7)	0.64	2.2 (3.9)	2.3 (4.2)	0.66
NIP1, n (%)[e]	165 (22.4)	65 (22.7)	0.91	260 (19.8)	87 (21.7)	0.40
NIP2, n (%)[c,e]	228 (33.1)	82 (30.4)	0.41	356 (28.5)	119 (31.3)	0.28
Prior use of cDMARDs, n (%)			0.65			0.03
0	90 (12.2)	29 (10.1)				
1	275 (37.3)	109 (38.1)		642 (48.8)	221 (55.1)	
2+	372 (50.5)	148 (51.7)		673 (51.2)	180 (44.9)	
Prior use of TNFs, n (%)			<0.001			<0.001
0	69 (9.4)	32 (11.2)		104 (7.9)	34 (8.5)	
1	540 (73.3)	177 (61.9)		984 (74.8)	254 (63.3)	
2	128 (17.4)	77 (26.9)		227 (17.3)	113 (28.2)	
Prior use of any non-TNFs, n (%)	123 (16.7)	99 (34.6)	<0.001	202 (15.4)	130 (32.4)	<0.001
Prednisone use, n (%)			0.01			0.18
No use	517 (70.1)	190 (66.4)		928 (70.6)	261 (65.1)	
Current use, missing dose	6 (0.8)	< 5		21 (1.6)	6 (1.5)	
Current use, dose <10 mg	147 (19.9)	49 (17.1)		259 (19.7)	92 (22.9)	
Current use, dose ≥10 mg	67 (9.1)	46 (16.1)		107 (8.1)	42 (10.5)	
b/tsDMARD line of therapy, n (%)			<0.001			<0.001
Second	509 (69.1)	123 (43.0)		937 (71.3)	175 (43.6)	
Third	228 (30.9)	163 (57.0)		378 (28.7)	226 (56.4)	

[a] Values are mean (SD) unless indicated otherwise.
[b] *P*-values from unadjusted comparison tests of characteristic distributions between therapy groups.
[c] Variables (for monotherapy initiators) with more than 5% of missing.
[d] Only calculated for those reporting morning stiffness.
[e] NIP1: tender joint count [TJC, 28] – swollen joint count [SJC, 28] ≥7; NIP2: SJC [28]/TJC [28] <0.5.
BMI, body mass index; b/tsDMARD, biologic/targeted synthetic disease modifying anti-rheumatic drug; CDAI, clinical disease activity index; cDMARDs, conventional disease modifying anti-rheumatic drugs; HAQ-DI, Health Assessment Questionnaire-Disability Index; IL-6i, interleukin-6 receptor inhibitors; NIP, non-inflammatory pain; RA, rheumatoid arthritis; SD, standard deviation; TNF, tumor necrosis factor; TNFi, tumor necrosis factor inhibitors.

Table 2. Results from mixed models evaluating the impact of treatment class on disease burden, non-inflammatory pain, and disease activity among monotherapy and combination therapy initiators.

Outcomes	Six-Month Mean (SD)/Response Rate		Adjusted[a]			
	TNFi	IL-6i	β[b]	OR[b]	95% CI	*P*-value
Monotherapy Initiators						
Disease Burden						
HAQ-DI	1.0 (0.7)	1.2 (0.7)	0.01	–	−0.06, 0.08	0.853
Pain VAS	49.1 (28.5)	51.2 (28.5)	−0.03	–	−3.67, 3.61	0.988
Patient Global Assessment VAS	47.2 (26.7)	47.2 (27.2)	−1.47	–	−4.91, 1.98	0.404
Fatigue VAS	51.4 (28.9)	53.2 (29.1)	0.85	–	−2.73, 4.42	0.642
Non-inflammatory Pain						
NIP1: All initiators	120/731 (16.4%)	52/283 (18.4%)	–	1.38	0.58, 3.26	0.467
NIP2: All initiators	235/547 (43.0%)	86/213 (40.4%)	–	0.87	0.46, 1.67	0.682
Disease Activity						
CDAI	17.9 (13.4)	19.0 (13.9)	0.20	–	−1.54, 1.93	0.826
Achievement of LDA	270/729 (37.0%)	92/281 (32.7%)	–	0.99	0.59, 1.67	0.963
Achievement of remission	52/729 (7.1%)	20/281 (7.1%)	–	1.86	0.23, 15.05	0.560
Achievement of MCID in CDAI	326/729 (44.7%)	127/281 (45.2%)	–	1.06	0.67, 1.69	0.792
Combination Therapy Initiators						
Disease Burden						
HAQ-DI	1.0 (0.7)	1.1 (0.7)	0.01	–	−0.05, 0.07	0.714
Pain VAS	45.3 (28.4)	47.8 (27.5)	0.21	–	−2.66, 3.08	0.888
Patient Global Assessment VAS	42.0 (26.6)	45.5 (27.0)	1.30	–	−1.44, 4.04	0.352
Fatigue VAS	46.4 (29.1)	49.3 (29.1)	1.13	–	−1.77, 4.03	0.446
Non-inflammatory Pain						
NIP1: All initiators	165/1310 (12.6%)	71/398 (17.8%)	–	1.39	0.94, 2.06	0.101
NIP2: All initiators	332/978 (33.9%)	115/311 (37.0%)	–	1.06	0.70, 1.61	0.772
Disease Activity						
CDAI	16.7 (12.3)	18.7 (13.6)	0.48	–	−0.84, 1.81	0.475
Achievement of LDA	478/1301 (36.7%)	124/397 (31.2%)	–	0.96	0.66, 1.38	0.809
Achievement of remission	114/1301 (8.8%)	31/397 (7.8%)	–	1.23	0.34, 4.44	0.757
Achievement of MCID in CDAI	605/1301 (46.5%)	185/397 (46.6%)	–	0.97	0.71, 1.30	0.817

[a] Adjusted models include treatment indicators, baseline value of outcome, and covariates specified in the covariate list and those identified to be significantly different in baseline table (covariates of monotherapy initiators: biologic line of therapy, age, duration of RA, gender, work status, history of CVD, CDAI, and morning stiffness; covariates of combination therapy initiators: biologic line of therapy, history of CVD, CDAI, patient reported pain, prior use of cDMARDs, and narcotic use.)

[b] Based on covariate-adjusted regression analyses (β [95% CI] for linear regressions and OR [95% CI] for logistic regressions) using TNFi group as the reference; β represents the expected difference in the mean change of outcomes from baseline to six months for IL-6i group compared to TNFi group.

CDAI, clinical disease activity index; cDMARDs, conventional disease modifying anti-rheumatic drugs; CI, confidence interval; CVD, cardiovascular disease; HAQ-DI, Health Assessment Questionnaire-Disability Index; IL-6i, interleukin-6 inhibitors; LDA, low disease activity; MCID, minimal clinically important difference; NIP, non-inflammatory pain; OR, odds ratio; RA, rheumatoid arthritis; SD, standard deviation; TNFi, tumor necrosis factor inhibitors; VAS, visual analog scale.

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Abstract Number: 0835

Immunogenicity of Rituximab Biosimilar GP2013 in Chronic Inflammatory Rheumatic Disorders in Daily Clinical Practice

Jerome Avouac[1], Rodolphe Cougnaud-Murail[1], Claire Goulvestre[2], Sophie Dumas[3], Anna Molto[4], Corinne Miceli-Richard[5], ornella conort[3], Frederic Batteux[2] and Yannick Allanore[1], [1]Université de Paris, Service de Rhumatologie, Hôpital Cochin, AP-HP.CUP, Paris, France, [2]Université de Paris, Service d'Immunologie, Hôpital Cochin, AP-HP.CUP, Paris, France, [3]Université de Paris, Service de pharmacie, Hôpital Cochin, AP-HP.CUP, Paris, France, [4]Department of Rheumatology, University of Paris, Cochin Hospital, Paris, France, [5]Assistance Publique Hpitaux de PAris, Paris, France

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To study in daily practice the risk of immunogenicity of patients treated with rituximab (RTX) biosimilar GP2013 for their chronic inflammatory rheumatic disorder.

Methods: A prospective routine care study was carried out between September 2018 and May 2021 in the Rheumatology department of Cochin Hospital. We consecutively included patients treated with the biosimilar RTX GP2013, systematically used in the department since March 2018. Samples were taken before each infusion to quantify anti-RTX antibodies (ADAbs) and serum RTX trough levels by ELISA (Lisa Tracker Duo Rituximab, LTR005, Theradiag).

Results: We included 170 consecutive patients treated with GP2013 (134 women, 79%) with a mean age of 59±12 years and a mean disease duration of 18±11 years. Among these 170 patients, 114 (67%) had RA and 56 had another disease (17 systemic sclerosis (SSc), 13 mixed connective tissue disease (MCTD), 7 undifferentiated polyarthritis, 5 systemic lupus (SLE), 5 inflammatory myopathies (MI), 5 overlap syndrome, and 4 primary Sjögren syndrome). 146 patients (86%) were receiving associated disease-modifying therapy (DMARD), mainly methotrexate (MTX, 109/146 patients, 75%). 129 patients (76%) were in maintenance therapy with originator RTX (RTX exposure: 77±47 months and cumulative dose of RTX: 8±6g) before the switch to GP2013 in March 2018. Originator RTX was not re-established during the entire treatment period. The other 41 patients (24%) treated with GP2013 were naïve of originator RTX. During a mean follow-up of 25±10 months, 15 patients (8%), developed ADAbs, corresponding to a rate of 4 for 100 patient years (**Figure 1A**). Among the 15 patients with ADAbs, 9 had RA, 3 MCTD, 2 SSc and 1 SLE. The mean time to ADAbs detection was 11±6 months (range: 6-27 months). ADAb concentrations ranged from 6 to >100 ng/mL, with 3 patients with high ADAb concentrations >100 ng/mL. Patients with ADAbs had undetectable serum RTX trough levels. The frequency of immunization was higher among RTX-naïve patients (8/41, 19.5%) than in patients switching from originator RTX (7/129, 5%, p=0.004). Age, gender, disease duration, concomitant treatment with MTX, a body mass index >30 and the underlying disease were not predictive of immunization. Conversely, complete B cell depletion (CD19 < 18) was identified as protective of immunization (hazard ratio 0.04, 95% confidence interval, CI, 0.09-0.33, p=0.003) (**Figure 1B**). Moreover, ADAb concentrations correlated with CD19 counts (r=0.20, p=0.021). The presence of anti-RTX antibodies was not associated with increased disease flares or RTX discontinuation (**Figure 1C**). Regarding the 3 patients with ADAb concentrations >100 ng/mL, 1 patient experienced a severe allergic reaction leading to treatment discontinuation and the two others required RTX dose escalation from 500 mg to 1 g to maintain treatment efficacy.

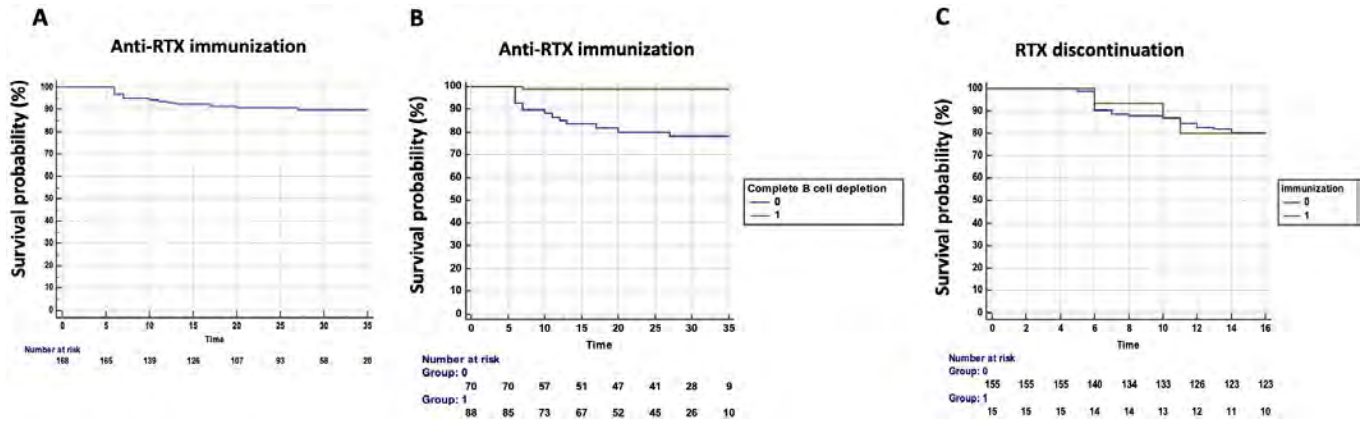

Figure 1. Kaplan Meyer Survival Analyses. A, risk of immunogenicity in patients treated with RTX biosimilar GP2013 during the follow-up period; B, risk of immunogenicity according to complete or incomplete B cell depletion and C, RTX discontinuation according to the presence of anti-RTX antibodies.

Conclusion: The immunogenicity of the biosimilar RTX GP2013 is a rare event associated with incomplete B cell depletion. Although development of anti-RTX antibodies had no impact on disease flares and treatment discontinuation, possible meaningful consequences may be observed in patients with high antibody levels.

Disclosure: J. Avouac, None; **R. Cougnaud-Murail**, None; **C. Goulvestre**, None; **S. Dumas**, None; **A. Molto**, None; **C. Miceli-Richard**, None; **o. conort**, None; **F. Batteux**, None; **Y. Allanore**, None.

Abstract Number: 0836

Flare After Switching from Intravenous Tocilizumab to Subcutaneous Formulation in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Interleukin-6 (IL-6) plays a key role in inflammatory and immune responses. Tocilizumab (TCZ) is a recombinant humanized monoclonal antibody of the IL-6 receptor which inhibits IL-6-mediated signaling. TCZ is available as an intravenous (IV) formulation (TCZ-IV) and a subcutaneous (SC) formulation (TCZ-SC). The present study aimed to evaluate the incidence and risk factors for RA flares after switching to TCZ-SC in stable RA patients as TCZ-IV.

Methods: We retrospectively evaluated the incidence of RA flares in patients who switched from TCZ-IV to TCZ-SC in single tertiary hospital between January 2013 and April 2020. Patients were divided into two groups based on RA disease activity as assessed by Disease Activity Score in 28 joints (DAS28) after switching from TCZ-IV to TCZ-SC ("SC inefficacy group" versus "SC efficacy group"). Factors associated with RA flares were evaluated by multivariate analysis.

Table 1. Clinical characteristics of the study patients at the time of switching from intravenous to subcutaneous tocilizumab

	SC inefficacy (n=11)	SC efficacy (n=26)	Total (n=37)	p-value
Age, years, mean (SD)	57.3 (11.4)	59.3 (13.3)	58.7 (12.6)	0.660
Female, n (%)	11 (100)	21 (80.8)	32 (86.5)	0.295
Disease duration, median (IQR)	138 (36-160)	92 (51-181)	104 (50-174)	0.868
IV TCZ duration, months, median (IQR)	9.0 (6.0-23.0)	13.5 (9.5-19.5)	13.0 (7.5-21.0)	0.433
TCZ dose, mg/kg, mean (SD)	8.2 (0.3)	7.7 (0.5)	7.9 (0.5)	0.002*
TCZ > 8 mg/kg, n (%)	7 (63.6)	5 (19.2)	12 (32.4)	0.018*
Concomitant medication				
MTX use, n (%)	5 (45.5)	21 (80.8)	26 (70.3)	0.0508
Dose of MTX, mg/week, median (IQR)	0 (0-10)	8.8 (7.5-15)	7.5 (0-10)	0.033*
Corticosteroid use, n (%)	6 (54.5)	6 (23.1)	12 (32.4)	0.122
Corticosteroids, mg/day, median (IQR)	2.5 (0-5)	0 (0-0.6)	0 (0-2.5)	0.062
Previous medication history, n (%)				
Biologics naïve	0	5 (19.2)	5 (13.5)	0.295
TNF-a inhibitor	7 (63.6)	21 (80.8)	28 (75.7)	0.404
Abatacept	5 (45.5)	3 (11.5)	8 (21.6)	0.035*
DAS28-ESR, mean (SD)	2.46 (0.58)	2.17 (0.57)	2.26 (0.58)	0.168
eGFR, mL/min/1.73 m^2, mean (SD)	111.6 (28.9)	89.2 (23.5)	95.9 (26.9)	0.018*

Table 2. Factors associated with disease exacerbation after switching from intravenous to subcutaneous tocilizumab

	Univariate			Multivariate		
	OR	CI	P value	OR	CI	P value
Dose of TCZ > 8mg/kg at switching	7.350	1.531-35.278	0.013*	33.441	1.573-710.83	0.024**
Duration of using TCZ-IV	1.005	0.948-1.066	0.857			
Concomitant MTX non-use at switching	5.040	1.085-23.419	0.039*	41.416	1.529-1121.73	0.027**
Dose of corticosteroids (mg/day)	1.366	0.970-1.923	0.074*			
h/o TNF inhibitors	0.417	0.087-2.000	0.274			
h/o JAK inhibitors	9.375	0.851-103.252	0.067*	119.796	0.951-15086	0.052
h/o Abatacept	6.389	1.179-34.624	0.031*	29.817	1.069-831.44	0.046**
eGFR at switching	1.038	1.003-1.073	0.032*	1.039	0.990-1.091	0.119
DAS28-ESR at switching	2.511	0.680-9.275	0.167			
Age at switching	0.987	0.931-1.045	0.651			

Results: Among 147 patients who were treated initially with TCZ-IV, 37 patients were switched to TCZ-SC after the acquisition of remission or low disease activity. The SC inefficacy and SC efficacy groups included 11 (29.7%) and 26 (70.3%) patients, respectively. At the time of switching, mean DAS28 was not different between the two groups. However, doses of TCZ-IV per weight and methotrexate were higher in the SC inefficacy group. In the multivariate analysis, the use of a high dose (more than 8 mg/kg) TCZ (odds ratio [OR] 33.441, 95% confidence interval [CI], 1.573–710.833, p=0.024), methotrexate non-user(OR 41.416, 95% CI, 1.529–1121.731, p=0.027), and history of prior abatacept use (OR 29.817, 95% CI, 1.069–831.442, p=0.046) were associated with the risk of RA flares after switching to TCZ-SC.

Conclusion: Methotrexate non-use and TCZ-IV overdose per weight were associated with a higher risk of RA flare after switching to TCZ-SC. Thus, we recommend checking these factors before switching from TCZ-IV to TCZ-SC to prevent RA flares.

Disclosure: S. Ahn, None; **J. Oh**, None; **H. Heo**, None; **S. Hong**, None; **C. Lee**, None; **B. Yoo**, None; **Y. Kim**, None.

Abstract Number: 0837

Sustainability of Response Between Upadacitinib and Adalimumab in Patients with Rheumatoid Arthritis: Results Through 3 Years from the SELECT-COMPARE Trial

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

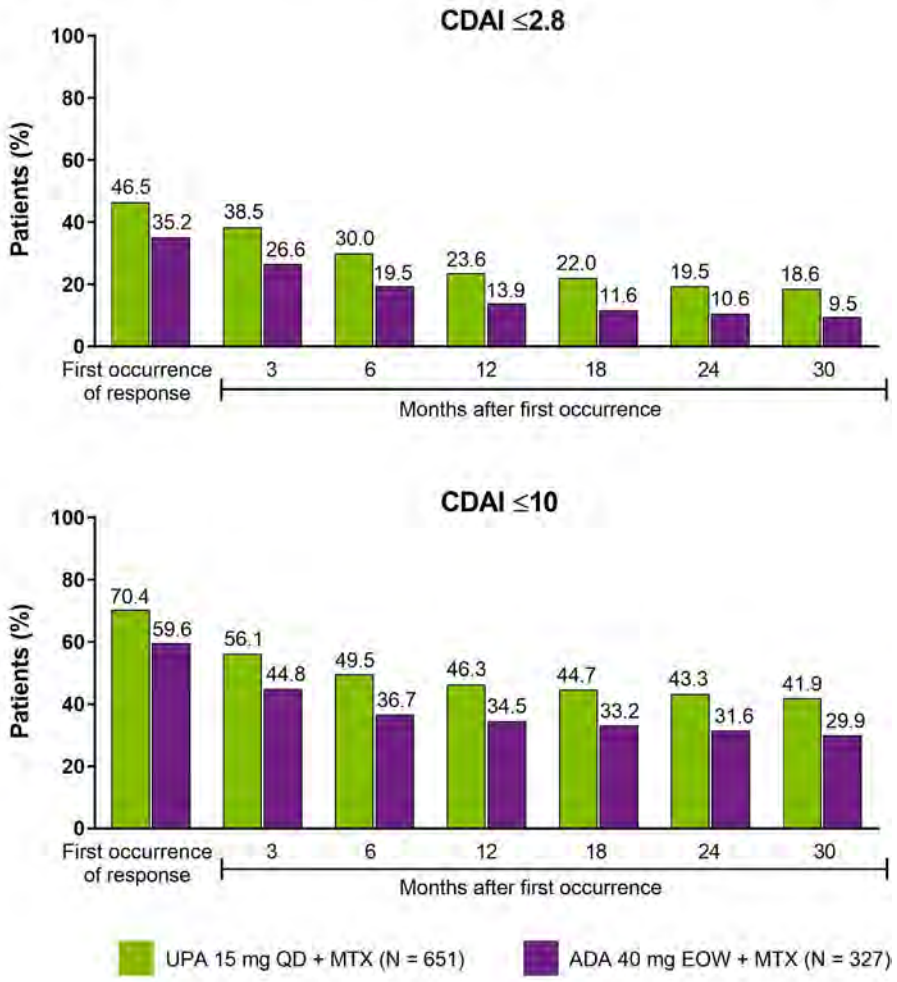
Background/Purpose: The primary treatment target for patients with active rheumatoid arthritis (RA) is sustained clinical remission (REM) or low disease activity (LDA).[1,2] A greater proportion of patients with RA and inadequate response to methotrexate (MTX) receiving the JAK inhibitor, upadacitinib (UPA), achieved REM/LDA compared with adalimumab (ADA), both with background MTX, through 26 weeks in the phase 3, SELECT-COMPARE trial.[3] Here we assessed sustainability of response over 3 years.

Methods: SELECT-COMPARE included a 26-week, double-blind, placebo (PBO)-controlled period, a 48-week, double-blind active comparator-controlled period, and an ongoing long-term extension for up to 10 years. Patients on background MTX received UPA 15 mg once daily, PBO, or ADA 40 mg every other week. Patients who did not achieve at least 20% improvements in tender and swollen joint counts (Weeks 14-22) or LDA (CDAI ≤10 at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA. This post hoc analysis evaluated clinical REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI ≤10; SDAI ≤11), and DAS28(CRP) < 2.6/≤3.2 at first occurrence (prior to treatment switch [rescue]), as well as over 3 years following initial response in patients randomized to UPA or ADA. For those patients who achieved REM/LDA, Kaplan-Meier was used to define the time from when the response was first achieved to the earliest date at which the response was lost at two consecutive visits, discontinuation of study drug, or losing

response at the time of rescue. The predictive ability of time to CDAI REM/LDA was assessed using Harrell's concordance (c)-index (range: 0 [all predictions wrong] to 1.0 [perfect predictive ability]. Non-responder imputation was used for missing data.

Results: Through 3 years, a significantly higher proportion of patients receiving UPA + MTX vs ADA + MTX achieved CDAI REM (47% vs 35%, *P* = 0.001) as well as CDAI LDA (70% vs 60%, *P* = 0.001). At 30 months after first occurrence of response, CDAI REM/LDA was sustained in 19%/42% of patients randomized to UPA and 10%/30% of patients randomized to ADA (**Figure 1)**. Time to initial clinical response did not appear to be predictive of sustained disease control. The c-index for CDAI REM/LDA was 0.50/0.60 on UPA vs 0.49/0.56 on ADA. Through the last

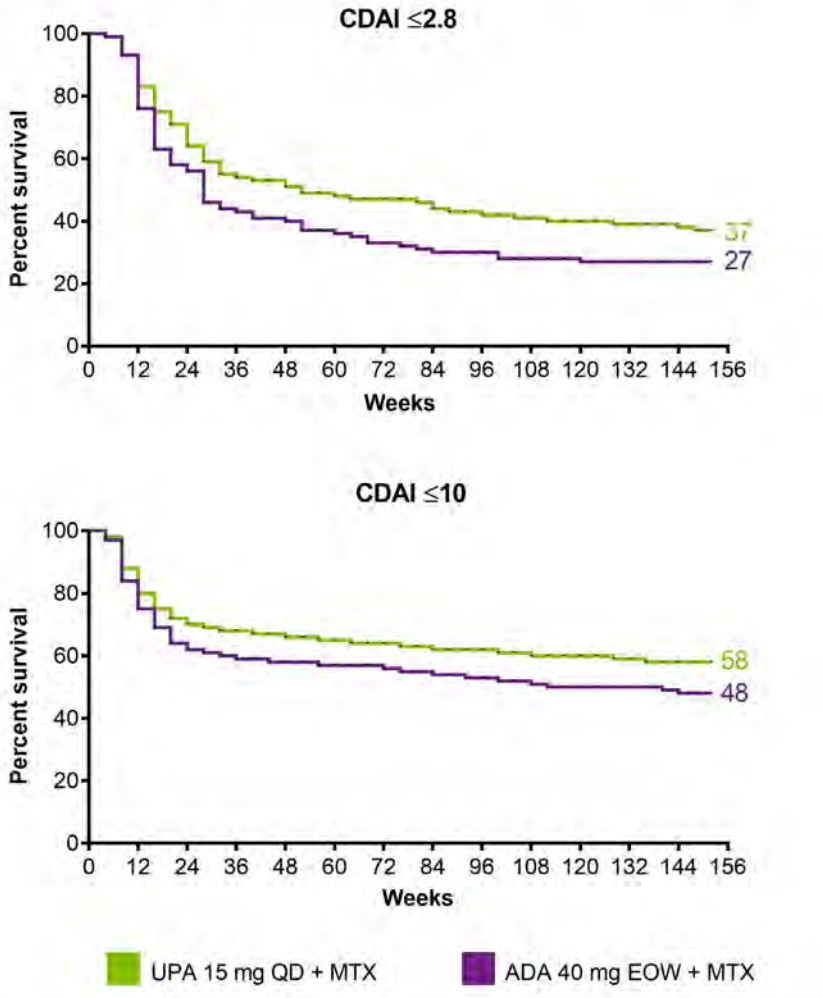
Figure 1. Proportion of Patients Sustaining CDAI Remission or Low Disease Activity Up to 30 Months After First Occurrence of Response Among the Total Randomized Population



Treatment groups are by initial randomization; non-responder imputation was used for missing data. Data are from patients who achieved initial CDAI response at any point during the 3-year study period, with 30 months post-initial response being the maximum time estimated for both treatment groups.

ADA, adalimumab; CDAI, Clinical Disease Activity Index; EOW, every other week; MTX, methotrexate; QD, once daily; UPA, upadacitinib.

Figure 2. Kaplan-Meier Analysis of Time to Loss of CDAI Remission or Low Disease Activity After the First Occurrence of Response Through 3 Years



Results are for patients who achieved CDAI clinical remission or low disease activity; treatment groups are by initial randomization. UPA 15 mg QD + MTX: CDAI ≤2.8: n = 303; CDAI ≤10: n = 458. ADA 40 mg EOW + MTX: CDAI ≤2.8: n = 115; CDAI ≤10: n = 195. Data were censored (i.e., data collection stopped) at 3 years, when all patients had reached Week 156 visit. Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.

ADA, adalimumab; CDAI, Clinical Disease Activity Index; EOW, every other week; MTX, methotrexate; QD, once daily; UPA, upadacitinib.

follow-up visit, 37%/58% of patients receiving UPA and 27%/48% on ADA remained in CDAI REM/LDA, respectively (**Figure 2**). Of patients who lost CDAI REM, 68% on UPA and 55% on ADA remained in LDA. Additionally, roughly similar proportions on UPA and ADA recaptured CDAI REM/LDA (UPA, 40%/17%; ADA, 48%/19%). Similar results were observed for REM/LDA based on SDAI and for DAS28(CRP) < 2.6/≤3.2.

Conclusion: Among patients with inadequate response to MTX, a higher proportion receiving UPA + MTX achieved remission or LDA across disease activity measures vs ADA + MTX. UPA-treated patients demonstrated a consistently higher sustained response rate over 3 years compared to those receiving ADA. Furthermore, significant proportions of patients who lost response on either UPA or ADA were able to recapture remission or LDA.

References

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2. Singh et al. Arthritis Rheumatol 2016;68:1–26.
3. Fleischmann et al. Arthritis Rheumatol 2019;71:1788–1800.

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Abstract Number: 0838

Predictors of Treatment for Inflammatory Arthritis with Immune Modulating Medications (IMM) in US Veterans

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Non-treatment and treatment delays contribute to suboptimal symptom control and irreversible joint damage in patients with inflammatory arthritis (IA). This investigations objective was to identify baseline patient factors associated with treatment initiation during the 12 months after the initial diagnosis of rheumatoid arthritis (RA), psoriatic arthritis (PsA), or ankylosing spondylitis (AS).

Methods: Active users of the Veteran Affairs Health System with an incident IA diagnosis between 1/1/2007 and 12/31/2019 were included (Figure 1). Data resources included the corporate data warehouse and the VA Informatics and Computing Infrastructure. Coded data were used to identify comorbidities, medications, laboratory data, provider visits and other encounters in the VA system. Natural language processing improved the accuracy of incident cohort identification and identifying erosions due to IA in the text of radiology reports. Treatment was captured during the 12 months following the initial IA diagnosis. Univariate analysis was used to explore patient factors associated with treatment. In normally distributed continuous variables means and standard deviations were compared, while medians and interquartile ranges were used for non-normally distributed variables.

Results: The study included 18,318 Veterans with incident IA (14,470 RA, 2380 PsA, 1468 AS). The mean age was 63.1 years and 90.7% were male. In the 12 month follow-up period, 40.7% did not use an IMM. VA system utilization was similar between groups (RR=1.000). Characteristics significantly associated with treatment included younger age (RR=0.9985), female gender (RR=0.9781), white race (RR=1.0179) non-Hispanic ethnicity (RR=1.0248), divorced marital status (RR=1.0118), and higher BMI (RR=1.0016). Estimates of socioeconomic status (measured by the area deprivation index [ADI]) were similar amongst patients with available data, but treatment was less frequent in patients with missing ADI (RR=1.0545). Higher comorbidity burden (RR=0.9883), alcohol dependence (RR=0.9718), heart failure (RR=0.9433), kidney disease (RR=0.9144), and osteoporosis (RR=0.9487) associated with non-treatment. Rheumatology (RR=1.2356), dermatology (RR=1.0462), gastroenterology (RR=1.0342), and orthopedic (RR=1.0232) visits were associated with treatment. Use of glucocorticoids (RR=1.1341), NSAIDS (RR=1.0785), and opiates (RR=1.0214) associated with treatment. Tests associated with therapy included: HLA-B27, RF, CCP, CRP, ESR. Positive results with RF, CCP, ESR, and articular erosions were associated with treatment (Table 2).

Conclusion: Several patient factors including certain demographics, subspecialty visits, additional medications, laboratory testing and erosions on imaging had a positive association with treatment. Other patient factors such as male gender, comorbidities and unknown addresses had a negative association with treatment. Future research with added analyses of these factors (multivariate analysis) and additional factors (health system and provider variables) may inform strategies to improve early treatment in appropriate patients with IA.

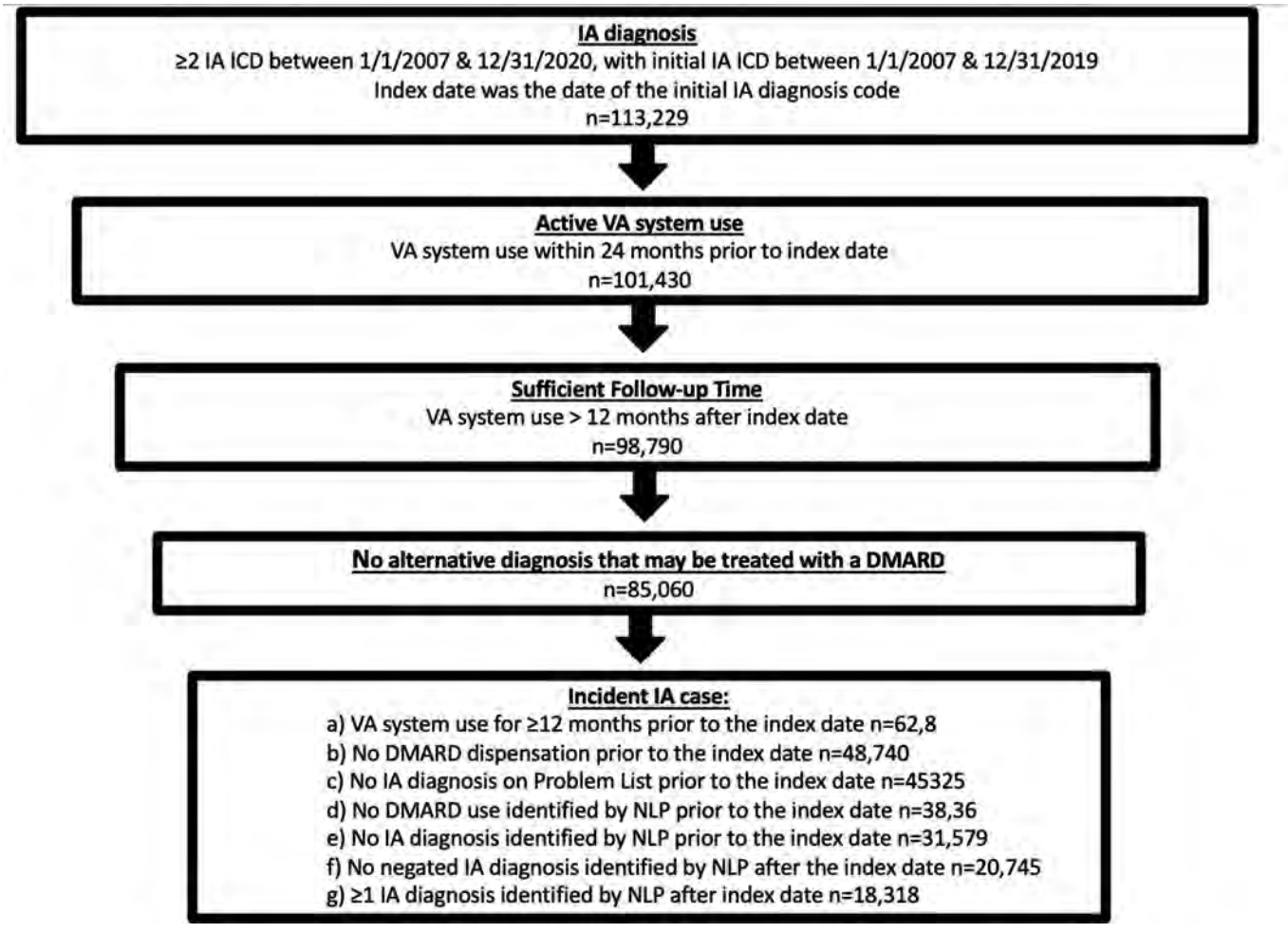

Figure 1. Attrition.

	Inflammatory Arthritis (Psoriatic Arthritis (n=2380) , Ankylosing Spondylitis (n=1468), Rheumatoid Arthritis (n=14470))				
	Non-Treatment (SD or %) or [IQR]	Treatment (SD or %) or [IQR]	p-value	Risk Ratio	Confidence intervals
n (%)	7450 (40.7)	10868 (59.3)			
Age, mean (SD)	64.19 (14.08)	62.40 (12.78)	<0.001	0.9985	0.9982-0.9988
Male Gender, (%)	6810 (91.4)	9799 (90.2)	0.005	0.9781	0.9637-0.9928
VA Utilization					
Encounters (median [IQR])	26.00 [12.00, 54.00]	30.00 [14.00, 56.00]	<0.001	1.0000	0.9999-1.0001
Encounters days/2 years (median [IQR])	17.00 [8.00, 35.00]	19.00 [9.00, 35.00]	<0.001	1.0000	0.9998-1.0001
Race					
White, (%)	5629 (75.6)	8437 (77.6)	0.001	1.0179	1.0070-1.0289
Black, (%)	1069 (14.3)	1454 (13.4)	0.064	0.9876	0.9748-1.0007
Other, (%)	424 (5.7)	624 (5.7)	0.911	1.0014	0.9824-1.0208
Unknown, (%)	328 (4.4)	353 (3.2)	<0.001	0.9512	0.9276-0.9754
Ethnicity					
Non-Hispanic (%)	6663 (89.4)	9873 (90.8)	0.002	1.0248	1.0091-1.0409
Hispanic, (%)	462 (6.2)	564 (5.2)	0.004	0.9711	0.9517-0.9909
Unknown, (%)	325 (4.4)	431 (4.0)	0.198	0.9848	0.9625-1.0077
Marital Status					
Divorced, (%)	1531 (20.6)	2375 (21.9)	0.036	1.0118	1.0009-1.0228
Married, (%)	4475 (60.1)	6674 (61.4)	0.07	1.0086	0.9994-1.0179
Never Married, (%)	723 (9.7)	974 (9.0)	0.094	0.9866	0.9713-1.0022
Separated, (%)	165 (2.2)	264 (2.4)	0.372	1.0142	0.9854-1.0439
Unknown, (%)	71 (1.0)	102 (0.9)	0.983	0.9977	0.9525-1.0450
Widowed, (%)	485 (6.5)	479 (4.4)	<0.001	0.9363	0.9164-0.9568
BMI, mean (SD)	29.63 (5.92)	30.01 (5.98)	<0.001	1.0016	1.0009-1.0024
Area Deprivation Index, mean (SD)	53.88 (25.42)	53.62 (24.51)	0.541	0.9999	0.9997-1.0001
# with ADI Data (%)	5527 (74.2)	8712 (80.2)	<0.001	1.0545	1.0428 -1.0663
Comorbidities					
Charleston Comorbidity Index, (median [IQR])	1.00 [0.00, 2.00]	1.00 [0.00, 2.00]	<0.001	0.9883	0.9853-0.9913
Alcohol related disorder, (%)	681 (9.1)	839 (7.7)	0.001	0.9718	0.9556-0.9882
Heart Failure, (%)	444 (6.0)	457 (4.2)	<0.001	0.9433	0.9227-0.9644
Kidney Disease, (%)	634 (8.5)	551 (5.1)	<0.001	0.9144	0.8963-0.9328
Osteoporosis, (%)	248 (3.3)	262 (2.4)	<0.001	0.9487	0.9216-0.9766
Sub-Specialty Evaluation					
Rheumatology, (%)	1351 (18.1)	5630 (51.8)	<0.001	1.2356	1.2256-1.2457
Dermatology, (%)	1006 (13.5)	1908 (17.6)	<0.001	1.0462	1.0342-1.0584
Gastroenterology, (%)	952 (12.8)	1690 (15.6)	<0.001	1.0342	1.0217-1.0468
Orthopedics, (%)	1113 (14.9)	1848 (17.0)	<0.001	1.0232	1.0111-1.0353
Non-DMARD Medication Use					
Glucocorticoids, (%)	545 (7.3)	1882 (17.3)	<0.001	1.1341	1.1222-1.1462
NSAID, (%)	1685 (22.6)	3587 (33.0)	<0.001	1.0785	1.0685-1.0885
Opioids, (%)	1767 (23.7)	2866 (26.4)	<0.001	1.0214	1.0111-1.0317
Laboratory Testing					
HLAB27 Tested, (%)	313 (4.2)	706 (6.5)	<0.001	1.0664	1.0480-1.0851
HLAB27 Positive, (%)	112 (1.5)	199 (1.8)	0.103	1.0298	0.9965-1.0641
RF Tested, (%)	2358 (31.7)	6205 (57.1)	<0.001	1.1669	1.1568-1.1770
RF Positive (%)	896 (12.0)	3019 (27.8)	<0.001	1.1464	1.1360-1.1569
CCP Tested, (%)	1024 (13.7)	4714 (43.4)	<0.001	1.2232	1.2134-1.2330
CCP Positive, (%)	242 (3.2)	2286 (21.0)	<0.001	1.2337	1.2241-1.2435
CRP Tested, (%)	1344 (18.0)	4563 (42.0)	<0.001	1.1754	1.1655-1.1853
CRP, (median [IQR])	6.90 [2.86, 24.75]	10.30 [4.20, 28.30]	0.001	0.9997	0.9996-0.9999
ESR Tested, (%)	1840 (24.7)	5337 (49.1)	<0.001	1.1652	1.1553-1.1751
ESR, (median [IQR])	20.00 [9.00, 42.00]	25.00 [12.00, 48.00]	<0.001	1.0004	1.0002-1.0006
Imaging					
Erosions (%)	389 (5.2)	1050 (9.7)	<0.001	1.0936	1.0783-1.1091

Table 1. Associations between patient factors and immune modulating medications for inflammatory arthritis (univariate analysis).

Disclosure: T. Braaten, Gilead, 1; **s. Pei**, None; **A. Rathod**, None; **G. Penmetsa**, None; **K. Douglas**, AbbVie, 3, 11; **J. Walker**, Abbvie, 3; **J. Clewell**, Abbvie Inc, 3, 11; **J. Walsh**, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5.

Abstract Number: 0839

Comparative Treatment Effectiveness in Rheumatoid Arthritis with and Without Concomitant Sjögren's Syndrome – Results from the Swiss Clinical Quality Management Cohort

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The variety of treatment options in RA contrasts with a lack of personalized medicine. The presence of concomitant SjS might be associated with differerences in RA pathobiology. We hypothesize that the clinical phenotype and treatment response differs in RA/SjS compared to RA alone with an inferior response to TNF-inhibitors (TNFi) over other target specific therapies.

Methods: In this retrospective observational cohort study data from the Swiss Clinical Quality Management in Rheumatic Diseases (SCQM) registry were obtained (01.01.2000-01.01.2021). All treatment courses (TC) from patients aged 18 and older with RA as diagnosed by the treating rheumatologist and definite SjS status undergoing TNFi, other modes of action (OMA) bDMARD (Abatacept, IL6-inhibitors, Rituximab) or JAK-inhibitors (JAKi) were assessed. Two group-comparison between RA/SjS and RA/non-SjS were performed. P-values are from Fisher test for nominal and Kruskal test for continuous variables. We estimated crude hazard ratios (HR) from univariate Cox models with the outcome of stop or start of a new bDMARD.

Results: A total of 9601 TCs were analyzed (5373 TNFi, 3201 OMA, 1027 JAKi). RA/SjS were more likely to be female, non-smoker, to have longer RA disease duration, a higher DAS28 and HAQ-score. Additionally, RA/SjS patients were more likely to receive OMA or concomitant steroid treatment and had a higher number of prior biologic treatments. Patients' characteristics at the start of each eligible TC are displayed in table 1. Figure 1 shows the Kaplan Meier plot for TNFi TCs (p-value corresponds to the log-rank test). Median retention time for RA/SjS versus RA/non-SjS was: TNFi 489 versus 714d; OMA 619 versus 768d; JAKi 693 versus 801d. There was evidence that RA/SjS have a higher hazard for stopping TNFi treatment than RA/non-SjS (crude HR 1.35, 95%; CI 1.05 to 1.74, p=0.02). No evidence was found for a difference in OMA (crude HR 1.13, 95% CI 0.92 to 1.39, p=0.23) or JAKi (crude HR 1.12, 95% CI 0.76 to 1.67, p=0.57).

Conclusion: The unadjusted Cox model suggests that patients with RA and associated SjS have an inferior response to TNFi than RA patients without SjS.

Table 1. Patient characteristics at the start of an eligible treatment course. Displayed are n (%) for nominal and median (Q1-Q3) for continuous variables

Variable	Levels	RA/non-SjS	RA/SjS	All patients	p value
Age [years]		57.6 (48.1-66.2)	62.8 (54.2-69.6)	57.8 (48.2-66.4)	<0.0001
Gender	Female	7058 (77.9)	243 (84.4)	7301 (78.1)	
	Male	1999 (22.1)	45 (15.6)	2044 (21.9)	0.009
Smoker	Current	1772 (26.1)	31 (12.1)	1803 (25.6)	
	Former	1994 (29.4)	90 (35.2)	2084 (29.6)	
	Never	3019 (44.5)	135 (52.7)	3154 (44.8)	0.0005
Time since RA diagnosis [years]		7.3 (2.9-14.7)	11.5 (5.3-20.4)	7.4 (3.0-14.8)	<0.0001
Anti-CCP	Positive	5115 (67.4)	190 (72.0)	5305 (67.6)	
	Negative	2469 (32.6)	74 (28.0)	2543 (32.4)	0.12
Rheumatoid Factor	Positive	6351 (72.2)	227 (81.7)	6578 (72.5)	
	Negative	2444 (27.8)	51 (18.4)	2495 (27.5)	0.00037
Drug class	TNFi	5122 (56.5)	86 (29.9)	5208 (55.7)	
	JAKi	980 (10.8)	43 (14.9)	1023 (10.9)	
	OMA	2955 (32.6)	159 (55.2)	3114 (33.3)	0.0005
Concomitant steroid therapy	No	5428 (60.0)	135 (46.9)	5563 (59.5)	
	Yes	3625 (40.0)	153 (53.1)	3778 (40.5)	<0.0001
Number of previous biologics	0	3710 (41.0)	50 (17.4)	3760 (40.3)	
	1	2459 (27.2)	74 (25.7)	2533 (27.1)	
	2	1423 (15.7)	58 (20.1)	1481 (15.9)	
	≥3	1460 (16.1)	106 (36.8)	1566 (16.8)	0.0005
HAQ		1.0 (0.5-1.6)	1.4 (0.9-1.8)	1.0 (0.5-1.6)	0.00035
DAS28-ESR		4.2 (3.3-5.2)	4.4 (3.6-5.4)	4.2 (3.3-5.2)	0.02

Disclosure: L. Christ, Novartis, 1, Gilead Sciences, 5, 11, F. Hoffmann-La Roche Ltd, 5, 11, Sanofi, 12, Pfizer, 5, Bristol-Myers Squibb, 6; **S. Kissling**, None; **R. Mueller**, None; **A. Finckh**, Eli Lilly, 5, 6, Pfizer Inc, 2, 5, 6, AbbVie, 2, 5, UCB, 2, Roche, 2, Galapagos, 5, MSD, 2, A2 Biotherapeutics, 2, Bristol-Myers Squibb, 2, 5; **B. Fisher**, Novartis, 2, BMS, 1, Janssen, 1, 5, Servier, 2, 5, Galapagos, 2, 5, Roche, 5; **B. Maurer**, Novartis, 2, 5, Boehringer Ingelheim, 1, 2, 6, Janssen Cilag, 2, Abbvie, 5, Protagen, 5, Pfizer, Roche, Actelion, mepha, MSD, 12, Congress Support; **B. Moeller**, Amgen, 5, Janssen, 6; **F. Kollert**, Roche, 3, Gilead, 5, Roche, 5, Pfizer, 5, Roche, 11, Pfizer, 1, Boehringer-Ingelheim, 1.

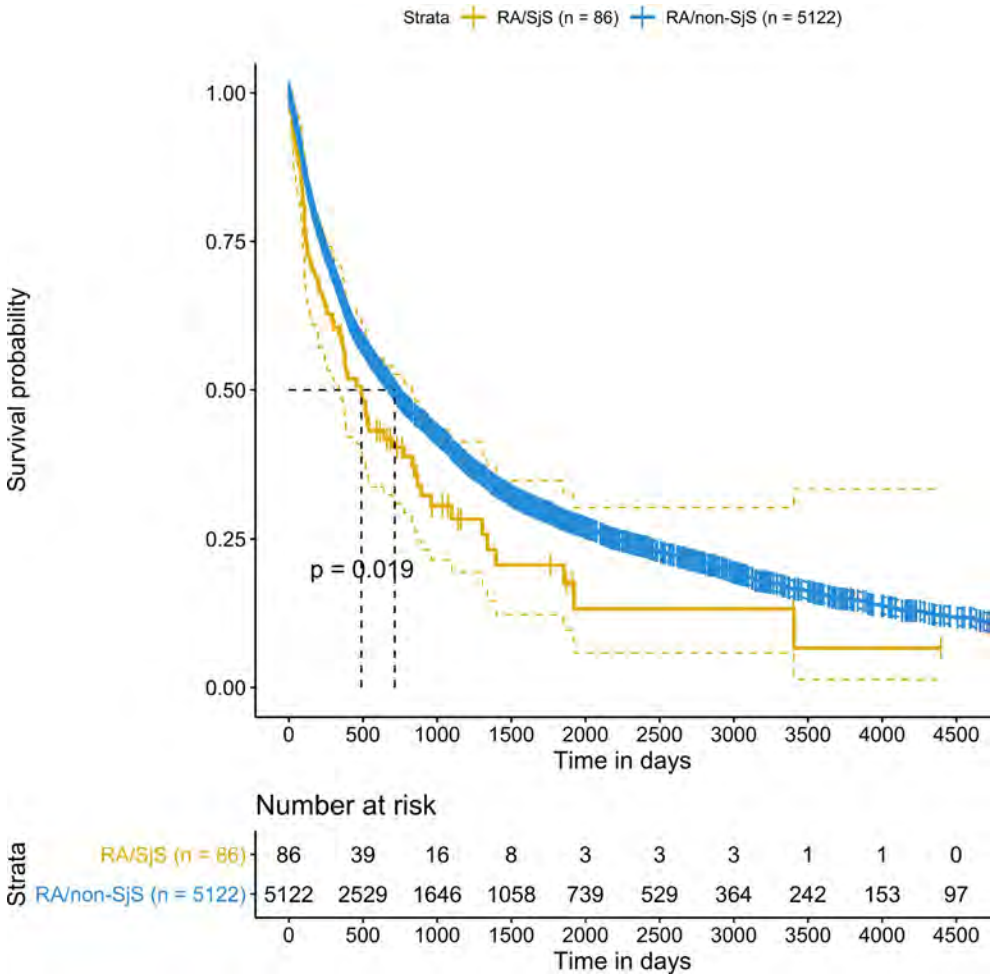

Figure 1. Kaplan Meier plot of retention time for eligible TNF-inhibitor treatment courses.

Abstract Number: 0840

Modelling of Disease Activity in Patients with Inflammatory Arthropathies Treated with Etanercept Originator or Biosimilar as First-Line Biologic: A Real-World Observational Study Using the OPAL Dataset

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The availability of biosimilars as non-proprietary versions of established biologic disease-modifying anti-rheumatic drugs (bDMARDs) has increased around the world. Since April 2017 both the originator and a biosimilar for etanercept have been available for use in Australia. This study aimed to model effectiveness of etanercept originator or biosimilar in reducing DAS28CRP in patients with RA, PsA or AS treated with either drug as first-line bDMARD as well as describe persistence on etanercept originator or biosimilar as first-line bDMARD in patients with RA, PsA or AS.

Methods: Clinical data were obtained from the Optimising Patient outcomes in Australian rheumatoLogy (OPAL) dataset, derived from electronic medical records. Eligible patients with RA, PsA or AS who initiated etanercept originator (n=977) or biosimilar (n=552) as first-line bDMARD between 1 April 2017 and 31 March 2021 were identified. Propensity score matching was performed to select patients on originator (n=280) or biosimilar (n=170) with similar characteristics in terms of diagnosis, disease duration, joint count, age, sex and concomitant medications. Data on clinical outcomes were recorded at 3 months after baseline, and then at 6-monthly intervals. Outcomes data that were missing at a recorded visit were imputed and propensity scores were re-calculated to include imputed outcomes data at baseline including DAS28CRP.

Effectiveness of the originator, relative to the biosimilar, for reducing DAS28CRP over time was modelled in the matched population using linear mixed models with both random intercepts and slopes to allow for individual heterogeneity. Time was modelled as a combination of linear, quadratic and cubic continuous variables. Individuals were weighted using inverse probability of treatment weights to ensure comparability between treatment groups. The average weighted baseline DAS28CRP were 4.95 and 4.94 for the originator and biosimilar, respectively.

Persistence on the originator or biosimilar was analysed using survival analysis (log-rank test).

Results: Reduction in DAS28CRP was associated with both time and etanercept originator treatment (Table 1). The conditional R-squared for the model was 0.28. The average model-predicted DAS28CRP at 3 months, 6 months, 9 months and 12 months were 3.0 and 3.3, 2.5 and 2.8, 2.3 and 2.5, and 2.1 and 2.3 for the originator and biosimilar, respectively, indicating a clinically meaningful effect of time for patients on either drug and an additional modest improvement for patients on the originator.

Median time to 50% of patients stopping treatment was 24.6 (16.8, 35.9) months for the originator and 24.1 (15.2, 32.2) months for the biosimilar (p=0.72). An adverse event was the reason for discontinuing treatment in 39 patients (11.4%) on the originator and 20 patients (13.4%) on the biosimilar.

Conclusion: Analysis using a large national real-world dataset showed treatment with either the etanercept originator or the biosimilar was associated with a reduction in DAS28CRP over time, with the originator being associated with a further modest reduction in DAS28CRP that was not clinically significant. Persistence on treatment was not different between the two drugs.

Table 1. Model summary for prediction of DAS28CRP using time and etanercept originator (relative to biosimilar)

Fixed Effect	Estimate	95% Confidence Interval	p-value
Time (linear)	0.91	0.91, 0.92	1.4e-64
Time (quadratic)	1.00	1.00, 1.00	1.2e-30
Time (cubic)	1.00	1.00, 1.00	1.2e-17
Originator	0.92	0.87, 0.96	6.7e-04

Disclosure: C. Deakin, None; **G. Littlejohn**, AstraZeneca, 1, MSD, 1, AbbVie, 1, Janssen, 1, Pfizer, 1, Seqirus, 1; **H. Griffiths**, AbbVie, 1, Lilly, 1, 6; **T. Smith**, None; **C. OSullivan**, None; **P. Bird**, Novartis, 1, Pfizer, 1, 6, Eli Lilly, 1, 6, Gilead, 1, 6, Janssen, 1, 6, AbbVie, 6.

Abstract Number: 0841

Persistence on JAK Inhibitors in Daily Practice: Evaluation of the Rhadar-registry

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The treatment strategy for rheumatoid arthritis (RA) includes achieving remission or at least low disease activity within six months of starting therapy. Active RA may be treated with either biological DMARDs (bDMARDs) or JAK inhibitors after inefficacy or intolerance of conventional DMARDs. To date, only few data are available on the persistence of the different treatment approaches in daily practice.

Methods: Regarding different mode of actions (MoA) for anti-rheumatic treatment, this analysis compares the persistence of JAK inhibitors with TNF inhibitors and other bDMARDs (nonTNFi) in RA patients from the German RheumaDatenRhePort (Rhadar) registry.

Data of 5154 RA patients from the pseudonymized Rhadar registry (Kleinert, S., P. Bartz-Bazzanella et. al. (2021). "A Real-World Rheumatology Registry and Research Consortium: The German RheumaDatenRhePort (RHADAR) Registry." J Med Internet Res 23(5): e28164.) entered by 22 rheumatologists were evaluated. Patients were included in the sample characterization if at least one registry entry was documented between July 1st, 2020, and March 31st, 2021. Only data of those patients that received a newly prescribed bDMARD or JAK inhibitor between June 1st, 2017 (shortly after the approval of tofacitinib and baricitinib in Germany) and March 31st, 2020, were compared regarding persistence. 3124 (60,6 %) of the evaluated patients suffered from a seropositive RA, 73,5% females, with a mean age of 64.5±13.9 years. 66.9% received monotherapy. The persistence of the respective MoA was calculated using Kaplan-Meier survival curves. Descriptive statistical analysis and drug survival were calculated using R (version 4.0.4) (R Core Team. R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vi-

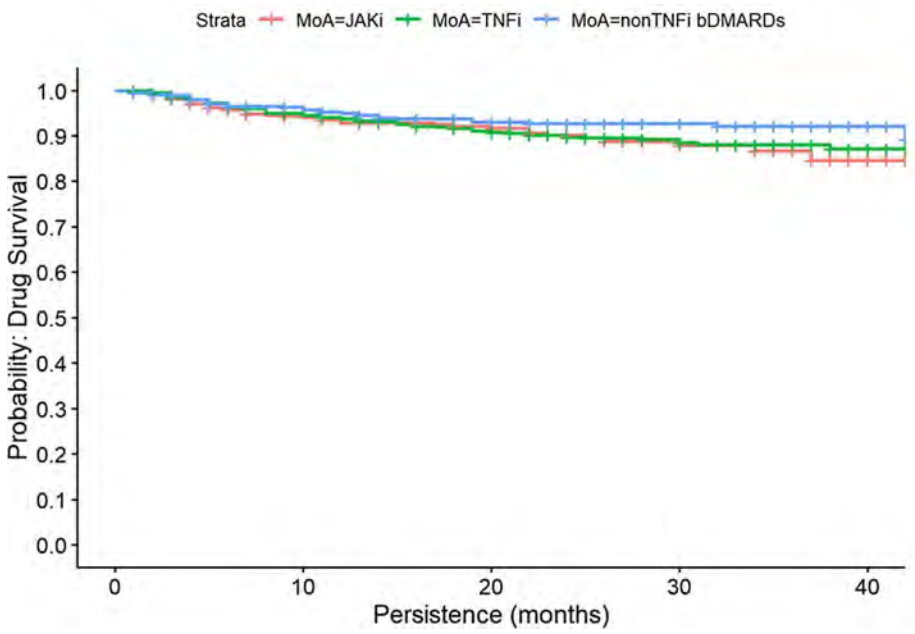

Figure 1. Persistence of the respective therapy principles (MoA = Mode of Action): (JAKi = JAK-inhibitor, TNFi = TNF-inhibitor, IL6i = IL6-receptor-inhibitor, CD20 = Rituximab, CD80/CD86 = Abatacept).

enna, Austria. 2018) and RStudio (version 1.4.1103) (RStudio Team. RStudio: Integrated Development for R. RStudio, Inc, Boston, MA. 2016).

Results: Prescription information of 4715 of the 5154 patients was available at database closure. Of these 4715 patients, 15.2% received a TNF inhibitor, 8.9% other bDMARDs and 10.0% a JAK inhibitor. JAK inhibitors were prescribed as monotherapy in 64.8%, TNF inhibitors only in 45.4% and other bDMARDs in 63.7% of the RA patients. The persistence on JAK inhibitors, TNF inhibitors and other bDMARDs was high (> 85% after 24 months) (fig. 1) and did not differ significantly between JAK inhibitors and TNF inhibitors ($p = 0.724$) or JAK inhibitors and other bDMARDs ($p = 0.084$) in a corresponding Cox proportional hazards model.

Conclusion: The persistence of therapy with JAK-inhibitors is high in daily practice, comparable to TNF inhibitors and other bDMARDs.

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Abstract Number: 0842

What Is the Success Rate in Clinical Trials of Discontinuation Glucocorticoids After Their Use as Bridging Therapy – a Systematic Literature Review

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)
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Background/Purpose: Short-term glucocorticoid (GC) bridging therapy results in rapid suppression of disease activity during the initial treatment of rheumatoid arthritis (RA) patients with DMARDs. But there are concerns that many patients may not be able to discontinue GC, risking adverse events. We reviewed the literature to investigate the success rate of GC discontinuation during 24 months of follow-up in trials using GC as bridging therapy.

Methods: A systematic literature search was conducted in PubMed, Embase, Web of Science, COCHRANE library, Emcare and Academic Search Premier to find clinical trials about RA patients treated with (also) initial GC bridging with at least 12 months follow-up. Studies were excluded according to a decision rule (see flowchart in *figure 1*). Heterogeneity was assessed based on pre-defined items, describing patient characteristics, initial GC bridging scheme, additional treatment and treatment adjustment protocols. Studies were assessed for continuation or restarting of GC after the induction scheme.

Results: The literature search identified 7160 abstracts (flowchart in *figure 1*). Based on reviewing the first 100 abstracts, we found a 97% interobserver agreement between the 3 reviewers (LO, ISN and SAB). The remaining abstracts were screened separately by the reviewers. 350 abstracts were included for full text analysis, resulting in 12 unique studies (*table 1*). The majority of included patients fulfilled the ACR/EULAR 2010 (53%) or the ACR 1987 (33%) criteria. At baseline, the mean symptom duration ranged from 4 to 7 months and the disease activity score (DAS) ranged from 3.0 to 5.2. All trials started with a DMARD at baseline next to the GC. In 83% of the studies oral GC bridging was used (initial dose ranging between 7.5 and 60 mg/day, the latter always followed by rapid tapering to 7.5 mg/day as maintenance dose, see *table 1*). Studies starting with a lower initial dose (5 studies) tapering to 5 mg/day (2/5, 40%) or directly to zero (3/5, 60%). Only 4/12 studies reported data on GC use after the GC induction phase, either at 12 (3/4) and/or at 24 (3/4) months follow-up (see *table 2*). The proportion of patients still using GC ranged from 23 to 44% at 12 months and 10 to 28% at 24 months. One study only started tapering at 12 months; at 24 months 45% of the patients were still using GCs (see *table 2*). Other outcome measures (e.g. cumulative or average GC dose, number of GC episodes) were reported in even fewer studies. Therefore, a meta-analysis was not performed.

Conclusion: The currently available data do not provide sufficient information on successful GC discontinuation after the induction phase, since initial type and dose of GC tapering schedules differed between studies and the total number of trials with pertinent data was small. However, preliminary data suggest that in the clinical trials assessed, up to 60% of patients have discontinued GCs initially at 12 months follow-up, and up to 70% at 24 months.

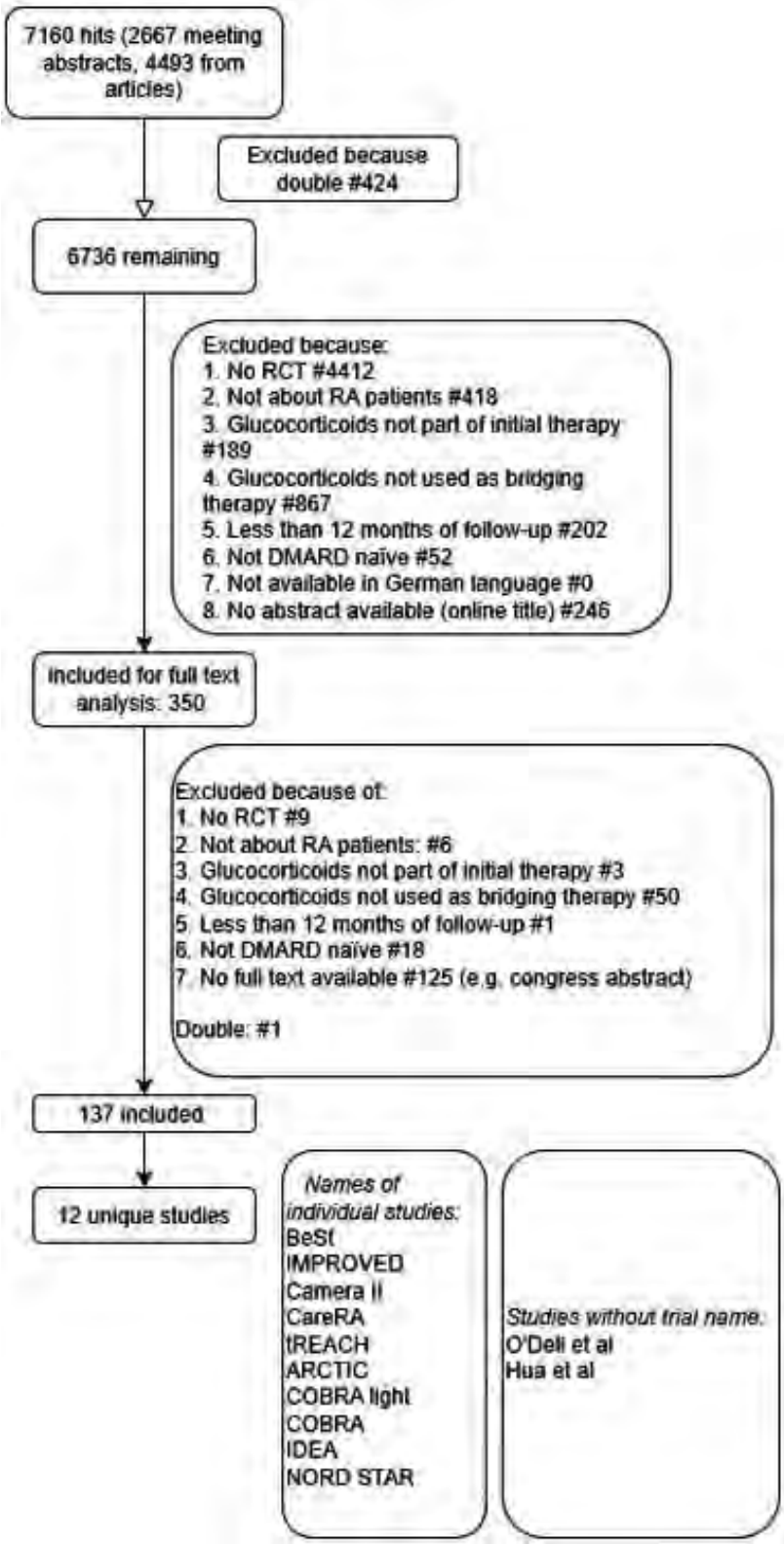
7160 hits (2667 meeting abstracts, 4493 from articles)
Excluded because double #424
6736 remaining
Excluded because:
1. No RCT #4412
2. Not about RA patients #418
3. Glucocorticoids not part of initial therapy #189
4. Glucocorticoids not used as bridging therapy #867
5. Less than 12 months of follow-up #202
6. Not DMARD naïve #52
7. Not available in German language #0
8. No abstract available (online title) #246
included for full text analysis: 350
Excluded because of:
1. No RCT #9
2. Not about RA patients: #6
3. Glucocorticoids not part of initial therapy #3
4. Glucocorticoids not used as bridging therapy #50
5. Less than 12 months of follow-up #1
6. Not DMARD naïve #18
7. No full text available #125 (e.g. congress abstract)
Double: #1
137 included
12 unique studies
Names of individual studies:
BeSt
IMPROVED
Camera II
CareRA
tREACH
ARCTIC
COBRA light
COBRA
IDEA
NORD STAR
Studies without trial name:
O'Dell et al
Hua et al

Table 1. Study overview

Study (year)	Journal	Type of GC	Initial GC dose	Tapering schedule
		Tapering early		
Cobra (1997)	Lancet	Prednisolone	60 mg/day	In 7 weeks to 7.5 mg/day. Stop possible after 28 weeks.
BeSt (2005)	Arthritis Rheum	Prednisone	60 mg/day	In 7 weeks to 7.5 mg/day. Stop possible after 28 weeks.
IDEA (2014)	Ann Rheum Dis	Methylprednisolone	250 mg iv once	N.A.
Cobra light (2015)	Ann Rheum Dis	Prednisolone	arm 1 60 mg/day arm 2 30 mg/day	arm 1: in 7 weeks to 7.5 mg/day arm 2: in 9 weeks to 7.5 mg/day Stop possible after 28 weeks.
IMPROVED (2014)	Ann Rheum Dis	Prednisone	60 mg/day	In 7 weeks to 7.5 mg/day. Stop possible after 28 weeks
ARCTIC (2016)	BMJ	Prednisolone	15 mg/day	In 7 weeks to 0
tREACH (2013)	Ann Rheum Dis	Arm 1: methylprednisolone or kenacort arm 2 & 3: prednisone	arm 1: 120 mg or 80 mg im once arm 2 & 3: 15 mg/day	In 10 weeks to 0
CareRA (2017) - *Classic* - *Slim* - *Avant garde*	Ann Rheum Dis	Prednisone	 - 60mg - 30mg - 30 mg	 - in 7 weeks to 7.5mg/day - in 6 weeks to 5mg/day - in 6 weeks to 5mg/day
Hua et al. (2020)	Medicine	Prednisone	10 mg/day	Tapering after 4 months, until 0 at 6 months.
Camera II (2012)	Ann intern med	Prednisone	10 mg/day	After 16 weeks to 5mg. Stop possible after 24 weeks.
Nord star (2020)	BMJ	Prednisolone	20 mg/day	In 9 weeks to 5 mg/day. Stop at 36 weeks.
		Tapering late		
O'Dell et al. (2001)	Arthritis Rheum	Prednisone	7.5 mg/day	Tapering possible at 12 months.

Table 2. Glucocorticoid use after the induction phase*

	N	% GC use 12 months	% GC use 24 months
BeSt study – arm 3	131	41	28
Cobra light – light group	81	42	-
Cobra light – cobra group	81	44	-
IMPROVED – early remission group	387	23	10
IMPROVED – arm 1	83	40	23
		Tapering late	
O'Dell et al.	60	ongoing induction phase	45

**studies shown which have data on GC use published*
Abbreviations: GC: glucocorticoids; N: number

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Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **J. Bijlsma**, None; **A. Kerschbaumer**, ABBVIE, 2, bristol-meyers squibb, 2, celgene, 2, Eli Lilly, 2, gilead, 2, Merck Sharp and Dohme, 2, Novartis, 2, Pfizer, 2; **T. Huizinga**, None; **R. Westhovens**, galapagos, 12, advisory board and principal investigator, gilead, 1, celltrion, 1; **C. Allaart**, Dutch College of Health Insurances, 5, Schering-Plough BV, 5, Centocor Inc., 5, Eli Lilly, 5; **S. Bergstra**, Pfizer, 5.

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Prevalence and Trends of Infections in Hospitalized Patients with Rheumatoid Arthritis in the United States

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SESSION INFORMATION
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Background/Purpose: Rheumatoid arthritis (RA) patients have a higher risk of developing infections as compared to the patients without the diagnosis, and this risk is further augmented by the use of biologics and immunosuppressant medications used for the treatment. This could be explained by the disease process itself, associated comorbidities, and immunomodulation as a result of the treatment modalities. We aim to identify national trends in terms of the common infectious etiologies in RA patients leading to hospitalizations in the patients admitted within a 15 year time period.

Methods: We used the Nationwide Inpatient Sample (NIS) database (years 1999-2014) and extracted all patients with Rheumatoid Arthritis using validated International Classification of Disease (ICD) codes. Further, six common hospitalized infections were identified: Urinary tract infection (UTI), Pneumonia, Skin and soft tissue infection (SSTI), Sepsis, Bacteremia, and Opportunistic infections. Data was analyzed using Statistical Analysis System (SAS) 9.4 software.

Results: A total of 1,351,284 cases of Rheumatoid arthritis were identified in the 15 year period (1999-2014). Mean age was 66.55 ± 15.34 years with females making up 74.95% (n= 1,012,532) of the patient population. As seen in Figure 1, an overall upward trend was noticed in all 6 selected infections ($p< 0.001$). It was found that UTI was the most prevalent infection in this population, which was on the rise from 10.38% in 1999 to 15.15% in 2011, with a steady decline to 14.74% in 2014, followed by Pneumonia (9.6% in 1999, 11.67% in 2014). Sepsis (3.34% in 2006 to 9.51% in 2014) and Bacteremia (3.91% in 2006 to 9.48% in 2014) had a dramatic increase since 2006.

Length of stay (LOS) in RA patients without any infection is 4.43 days and the average cost is $29,833.65 whereas in RA patients with any of the infections, LOS increases to 6.95 days and the average cost is $39,214.49.

Conclusion: The use of biological agents for the treatment of RA is associated with improved outcomes by decreasing inflammation and improving the overall mortality and morbidity in RA patients. However, at the same time, this has led to a higher rate of infections as a result of immune suppression in RA patients. It has been reported that

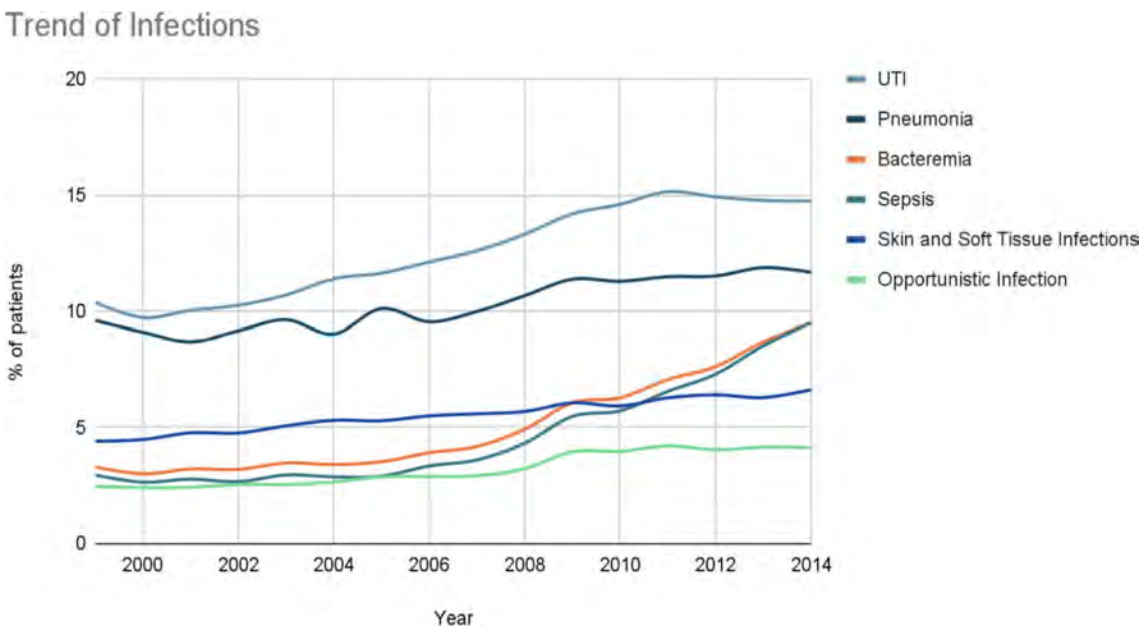

Figure 1. Trend of Infections over 15 years.

tumor necrosis (TNF) inhibitors are associated with a higher rate of infection when compared to conventional disease modifying agents, especially UTI, pneumonia and SSTI. In our study, we noticed that the common infections in hospitalized patients with RA included UTI and Pneumonia, both of which have risen since 1999. Higher UTI prevalence can also be explained by the female predominance. An increase in Sepsis was also seen which could be attributed to a higher infection rate, but maybe overestimated or correctly estimated as compared to past secondary to better coding and documentation of sepsis. Higher infection rates also contributed to longer hospital stays, thus leading to higher costs of care in these patients. Thus, there needs to be increased infection surveillance in this patient population, especially with the increasing use of biologic agents.

Disclosure: P. Khandwala, None; **A. Hussain**, None; **D. Desai**, None.

Abstract Number: 0844

Switching Biologics and Failure to Attain Remission in the First Year Predicts bDMARD Refractory Disease in Rheumatoid Arthritis: A 15-year Follow up of the Alberta Biologics Pharmacovigilance Cohort

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SESSION INFORMATION

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Table 1. RAPPORT Characteristics

Characteristics	All RAPPORT patients on bDMARDs N = 2338	Patients Not Receiving ≥3 Classes of Advanced Therapies. N = 2066	Patients Receiving ≥3 Classes of Advanced Therapies N = 272
Year of entry into RAPPORT: 2011 onwards, N (%)	1312 (56.1)	1184 (57.3)	128 (47.1)
Female sex, N (%)	1714 (73.3)	1511 (73.1)	203 (74.6)
Mother's race/ethnicity, N (%)			
Asian	111 (4.7)	100 (4.8)	11 (4.0)
Black	15 (0.6)	11 (0.5)	4 (1.5)
Caucasian	1852 (79.2)	1636 (79.2)	216 (79.4)
First nation	165 (7.1)	143 (6.9)	22 (8.1)
Other	195 (8.3)	176 (8.5)	19 (7.00)
Education, N (%)			
Less than secondary	188 (8.0)	177 (8.6)	11 (4.0)
Secondary	1099 (47.0)	949 (45.9)	150 (55.1)
Post-secondary	1016 (43.5)	912 (44.1)	104 (38.2)
Missing	35 (1.5)	28 (1.4)	7 (2.6)
Unemployed, N (%)	1134 (48.5)	990 (47.9)	144 (52.9)
Mean Age at entry in cohort, years (SD)	53.9 (14.0)	54.1 (14.1)	52.6 (12.8)
Mean RA duration at Baseline, years (SD)	10.0 (10.1)	10.0 (10.0)	10.2 (11.0)
Ever Methotrexate (Rheumatrex), N (%) [e]	1480 (63.3)	1310 (63.4)	170 (62.5)
Methotrexate dose (at baseline), N (%)			
Low dose: ≤ 15 mg	1559 (66.7)	1367 (66.2)	192 (70.6)
High dose: > 15 mg	779 (33.3)	699 (33.8)	80 (29.4)
Ever Hydroxychloroquine (Plaquenil), N (%) [f]	1082 (46.3)	973 (47.1)	109 (40.1)
Other csDMARDs at baseline, N (%)	91 (3.9)	82 (4.0)	9 (3.3)
Ever Prednisone, N (%) [g]	297 (12.7)	248 (12.0)	49 (18.0)
Mean dose prednisone, mg (SD)	11.0 (24.4)	10.4 (23.2)	13.2 (28.2)
JAK inhibitors, N (%) [a]	5 (0.2)	4 (0.2)	1 (0.4)
Anti TNF biologic, N (%) [b]	2004 (85.7)	1766 (85.5)	238 (87.5)
Other biologic, N (%) [c]	343 (14.7)	309 (15.0)	34 (12.5)
Smoking status, N (%)			
Current smoker	548 (23.4)	469 (22.7)	79 (29.0)
Ex-smoker	809 (34.6)	729 (35.3)	80 (29.4)
Never smoked	789 (33.7)	696 (33.7)	93 (34.2)
Missing	192 (8.2)	172 (8.3)	20 (7.4)
Rheumatoid Factor (RF), Positive (%) [d]	1143 / 1714 (66.7)	999 /1511 (66.1)	144 / 203 (70.9)
Anti CCP/ACPA, Positive (%)[d]	642 / 944 (68.0)	569 / 834 (68.2)	73 / 110 (66.4)
Mean CRP at baseline, (SD)[d]	18.8 (29.9)	18.6 (29.3)	20.8 (33.8)
Mean ESR at baseline, (SD)[d]	27.8 (24.6)	27.9 (24.8)	27.6 (23.0)
Obese (BMI 30 or greater), N (%)	543 (23.2)	476 (23.0)	67 (24.6)
Comorbidity, N (%)			
1 comorbidity	462 (19.8)	413 (20.0)	49 (18.0)
Greater than 1 comorbidity	1334 (57.1)	1168 (56.5)	166 (61.0)
Mean Number of tender joints, (SD)	13.3 (10.1)	13.1 (10.1)	14.8 (9.6)
Mean Number of swollen joints, (SD)	7.5 (5.6)	7.4 (5.6)	8.0 (5.6)
Mean Physician Global Assessment (PGA), (SD)	5.7 (2.5)	5.7 (2.5)	6.0 (2.5)
Mean Patient global assessment (PaGA), (SD)	5.8 (2.7)	5.8 (2.7)	6.3 (2.7)
Mean DAS28-CRP, (SD)	4.5 (1.3)	4.5 (1.3)	4.7 (1.3)
Mean CDAI, N (SD)	34.3 (16.4)	34.1 (16.3)	36.2 (16.6)
Mean SF-36 Global score, (SD)	43.0 (18.8)	43.4 (18.5)	39.9 (20.4)
Mean SF-36 physical component, (SD)	41.5 (27.4)	41.9 (27.2)	38.6 (28.8)
Mean SF-36 mental component, (SD)	56.5 (25.0)	57.0 (24.8)	53.1 (26.5)
Mean HAQ Index, (SD)	1.5 (0.7)	1.5 (0.7)	1.5 (0.8)

[a]**JAK inhibitors included**: tofacitinib and baricitinib. [b]**Anti-TNF biologic included**: etanercept, infliximab, golimumab, adalimumab and certolizumab. [c]**Other biologic** included other biologic drugs except the anti-TNFs. [d]The percentage for these variables was calculated based on the number of patients who had this test and whose lab results were known. [e]Included 10 patients exposed to methotrexate before baseline (10 non-MFAT). [f]Included 3 patients exposed to hydroxychloroquine before baseline (3 non-MFAT). [g]Included 9 patients exposed to prednisone before baseline (7 non-MFAT and 2 MFAT).

Background/Purpose: A subset of patients with rheumatoid arthritis (RA) experience refractory disease and do not attain remission imparting worse long-term outcomes. We evaluated RA patients with at least one year of follow-up on their first biologic, to identify characteristics associated with multiple failures of advanced therapies (MFAT) (biologics and/or JAK inhibitors).

Methods: The Rheumatoid Arthritis Pharmacovigilance Program and Outcomes Research in Therapeutics (RAPPORT) registry is a prospective inception cohort of northern Albertan RA patients starting their first biologic. We assessed RAPPORT patients with at least one year of follow-up on a biologic and identified RA patients with MFAT (defined as those exposed to 3 or more biologic classes or JAK inhibitors) developing over follow-up (i.e. forward from

Table 2. Cox regression Analysis: Univariate and Multivariable Analyses Evaluating Characteristics Associated with Developing Multiple Failures of Advanced Therapies (MFAT)

Characteristics	Unadjusted HR (95% CI)	Adjusted HR (95% CI)[a]
Female sex	1.01 (0.77, 1.33)	1.19 (0.82, 1.72)
Non-Caucasian mother race/ethnicity	1.33 (0.99, 1.79)	1.13 (0.76, 1.69)
Age at entry in the cohort, years	0.99 (0.99, 1.00)	0.99 (0.98, 1.01)
Disease duration at time zero	0.98 (0.97, 1.00)	0.99 (0.97, 1.01)
Secondary education	**1.32 (1.04, 1.69)**	0.99 (0.72, 1.35)
Unemployed	1.17 (0.91, 1.51)	1.07 (0.77, 1.49)
Obese (BMI 30 or greater)	1.13 (0.85, 1.50)	1.21 (0.85, 1.72)
Current smoker	**1.45 (1.11, 1.88)**	**1.49 (1.06, 2.09)**
Year of entry into cohort, 2011 onwards	**2.22 (1.70, 2.90)**	**2.07 (1.42, 3.03)**
Rheumatoid Factor (RF), positive	0.96 (0.71, 1.30)	0.86 (0.60, 1.23)
Ever hydroxychloroquine [e]	1.19 (0.94, 1.52)	0.86 (0.62, 1.19)
Ever methotrexate (MTX)[e]	1.23 (0.93, 1.65)	1.21 (0.83, 1.77)
Ever other csDMARDs [b,e]	1.06 (0.83, 1.36)	0.99 (0.72, 1.36)
Anti TNF biologic [c]	**0.56 (0.40, 0.80)**	**0.62 (0.40, 0.98)**
Ever prednisone [e]	**3.38 (2.66, 4.29)**	**3.06 (2.23, 4.19)**
DAS28-CRP (Reference: Remission)		
High disease activity	**2.37 (1.52, 3.68)**	2.94 (0.89, 9.76)
Moderate disease activity	1.46 (0.94, 2.27)	2.12 (0.64, 7.04)
Low disease activity	1.40 (0.77, 2.54)	2.39 (0.61, 9.37)
Achievement of remission[d]		
DAS28 remission at 3-4 months	**0.49 (0.35, 0.68)**	0.81 (0.53, 1.24)
DAS28 remission at one year	**0.36 (0.24, 0.56)**	**0.49 (0.27, 0.89)**
Switched bDMARD in first year [f]	**4.86 (3.79, 6.22)**	**3.53 (2.52, 4.92)**
Comorbid condition		
Heart disease	0.86 (0.49, 1.50)	1.14 (0.58, 2.26)
Lung disease	1.00 (0.62, 1.59)	1.00 (0.54, 1.86)
Diabetes	1.15 (0.70, 1.87)	1.07 (0.58, 1.97)
Kidney disease	0.58 (0.19, 1.82)	0.68 (0.21, 2.20)
Liver disease	**2.09 (1.07, 4.07)**	1.37 (0.62, 3.04)
Anemia or other blood disease	1.01 (0.68, 1.49)	1.25 (0.79, 2.00)
Cancer	1.04 (0.46, 2.35)	1.11 (0.39, 3.11)

[a]Adjusted for all variables shown. [b]**Other DMARDs Included**: chloroquine, leflunomide, gold,aAzathioprine, cuprimine, cyclophosphamide, minocycline, mycophenolate, cyclosporine and sulfasalazine. [c]**Anti-TNF biologic included**: etanercept, infliximab, golimumab, adalimumab and certolizumab. [d]**Achievement of remission** at 3-4 months or 1 year after baseline in this case (Yes/no). [e]These variables (drugs) are at time-dependant: Patients who had already taken these drugs. [f]Variable for whether or not the patient switched their biologic in the first year since the baseline in this case.

our time zero, which was from one year after biologic initiation). Cox regression analysis was performed to evaluate factors (demographics, clinical characteristics, and treatment) potentially associated with poor outcome.

Results: Of 2338 RAPPORT patients, baseline characteristics included low exposure to prednisone (12.7%), mean DAS-28-CRP 4.5 (SD 1.3), mean HAQ 1.5 (SD 0.7) and 86% with anti-TNF as their first biologic. 2107 had at least one year of follow-up on their first biologic (231 dropped out or were lost to follow-up prior to this point). Over an average of 6 years of follow-up beyond our time zero, 271/2107 (13%) of patients ultimately required ≥3 advanced therapies. Characteristics were similar between the two groups concerning age, sex, RA duration, Caucasian maternal race, body mass index, seropositivity for rheumatoid factor and anti-CCP (Table 1). Current smoker (29%) and unemployed (53%) were characteristics observed more frequently in the MFAT group. In univariate analyses, high disease activity and lower education were associated with requiring ≥3 advanced therapies, and lower risk of the outcome was seen in those with DAS28 remission at 3-4 months (HR 0.49, 95% CI 0.35- 0.68).

In unadjusted and adjusted models (Table 2), the risk of developing MFAT was associated with current smoking (time zero) (HR 1.49, 95% CI 1.06-2.09], entry into the cohort from 2011 onwards (HR 2.07, 95% CI 1.42-3.03], ever (up to time zero) used prednisone (HR 3.06, 95% CI 2.23-4.19]; and patients who switch bDMARD in the first year (HR 3.53, 95% CI 2.52-4.92). Lower risk of the outcome was associated with anti-TNF used as first biologic (HR 0.62 , 95% CI 0.40-0.98) and DAS28 remission at one year (HR 0.49, 95% CI 0.27-0.89). Results were similar when patients switching biologic in the first year were excluded. A potential limitation related to reasons for therapy changes beyond uncontrolled RA (e.g. adverse events).

Conclusion: Attaining disease remission within the first year of biologic initiation is a key factor associated with better longer-term RA outcomes. The greater risk of MFAT in early switchers may reflect the importance of personalized medicine and using the right treatment in the right patient in a timely manner. Subjects entering RAPPORT in the past decade were more likely to ultimately require ≥3 advanced therapies, possibly representing increasing therapy options and/or more aggressive approaches.

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Abstract Number: 0845

A Non-Interventional Prospective Observational Study of Treatment with Etanercept Biosimilar (SB4) in Rheumatoid Arthritis in Real Life Clinical Practice; Interim Analysis of the 'BENEFICIAL' Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: RA – Treatments Poster I: Comparative Effectiveness, Biosimilars, Withdrawal, & the Real World (0813–0845)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: SB4 is an etanercept biosimilar that obtained EU regulatory approval in 2016, and became available in Greece in 2018. Due to lack of published evidence about the use of etanercept biosimilars in the Greek setting, this study aims to generate real-world data on the impact of SB4 on patient-reported physical function and disease activity in RA patients.

Methods: BENEFICIAL is an ongoing 100-week non-interventional, multicenter, prospective study conducted in Greece, studying adult patients with moderate to severe active RA and inadequate response to conventional synthetic DMARDs. Patients were newly prescribed SB4 as monotherapy or combination therapy per the approved label in routine clinical practice. Patients who initiated SB4 >2 weeks before enrollment or who were previously treated with originator etanercept were excluded. Data are collected by routine clinical assessments, including tender/swollen joint count and physician's global assessment of disease activity, acute phase reactants, and patient-reported outcomes (PROs) at baseline (SB4 treatment initiation), and at 24, 52 and 100 weeks post-baseline. PROs include the validated Greek Patient-Reported Outcomes Measurement Information System Physical Function Short Form 20a (PROMIS PF SF-20), and the patient's global assessment of disease activity, joint pain intensity, and morning stiffness using visual analogue scales. We present the results of an interim analysis performed after all patients completed the 52-week observation period.

Results: Between 2/May/2019 and 9/Dec/2019, 132 eligible patients were enrolled in 9 rheumatology centers. Baseline characteristics are shown in Tables 1 and 2. Over a median (interquartile range; IQR) treatment duration of 50.1 (48.7-52.6) weeks, a median (IQR) of 50.0 (48.0-52.0) injections were received. The baseline median (IQR) PROMIS PF SF-20 total T-score was 28.7 (25.8-34.4).

A clinically important improvement from baseline physical function (≥2 point-change in PROMIS PF SF-20 total T-score) was observed in 82.1% (95% CI: 75.1-89.0) and 92.4% (95% CI: 87.3-97.5) of the patients at 24 and 52 weeks, respectively. Median PROMIS PF SF-20 total T-score and all item scores significantly increased from baseline

Table 1. Baseline patient characteristics.

Baseline patient characteristics	N=132
Age, median (IQR), years	66.3 (56.1-73.6)
Women (n=132), n (%)	118 (89.4)
Caucasian (n=132), n (%)	132 (100.0)
Urban residence (n=131), n (%)	82 (62.6)
Education ≤12 years (n=121), n (%)	96 (79.3)
Retired (n=130), n (%)	53 (40.8)
Married (n=127), n (%)	106 (83.5)
BMI (n=124), median (IQR), kg/m^2	26.7 (24.4-30.3)
Never-smoker (n=132), n (%)	99 (75.0)
At least 1 comorbidity (n=132), n (%)	76 (57.6)
Comorbidities in ≥10% (n=132), n (%)	
Hypertension	43 (32.6)
Dyslipidaemia[a]	32 (24.2)
Thyroid disorders[b]	21 (15.9)
Osteoporosis	14 (10.6)

[a]Includes hyperlipidaemia, dyslipidaemia, and hypercholesterolaemia. [b]Includes hypothyroidism and thyroid disorder. BMI: body mass index, IQR: interquartile range, N: total sample size, n: number of patients with available data.

at both timepoints (Figure 1). The proportions of evaluable patients achieving low disease activity or remission based on Simplified Disease Activity Index (score ≤11) at 24 and 52 weeks were 42.9% (33/77) and 80.0% (56/70). Among evaluable patients, ACR20, ACR50, and ACR70 responses were attained by 68.1% (64/94), 22.3% (25/112) and 8.0%

Table 2. Baseline disease and SB4 treatment characteristics

Baseline disease and SB4 treatment characteristics	N=132
Age at RA symptom onset (n=132), median (IQR), years	56.5 (46.5-66.8)
Age at RA diagnosis (n=132), median (IQR), years	59.1 (47.0-67.7)
Family history of RA (n=79), n (%)	9 (11.4)
Rheumatoid factor positive status (n=126), n (%)	58 (46.0)
Anti-CCP positive status (n=122), n (%)	40 (32.8)
Prior DMARD treatment for RA (n=132), n (%)	132 (100.0)
Conventional synthetic DMARDs	132 (100.0)
Biologic DMARDs	47 (35.6)
Targeted synthetic DMARDs	4 (3.0)
≥2 DMARDs	94 (71.2)
Prior systemic steroid treatment for RA (n=132), n (%)	40 (30.3)
Peripheral joint involvement (n=132), n (%)	132 (100.0)
Large and small joint involvement (n=132), n (%)	77 (58.3)
Radiographic evidence of joint erosion (n=85), n (%)	34 (40.0)
Number of swollen joints based on SJC28 (n=131), median (IQR)	5.0 (2.0-8.0)
Number of tender joints based on TJC28 (n=131), median (IQR)	7.0 (5.0-10.0)
PtGA of disease activity VAS score (0-100 mm) (n=132), median (IQR)	72.0 (58.5-80.0)
PhGA of disease activity VAS score (0-100 mm) (n=132), median (IQR)	70.0 (60.0-78.0)
Extra-articular manifestations related to RA (n=132), n (%)	46 (34.8)
Extra-articular manifestations in ≥5% (n=132), n (%)	
Osteoporosis	18 (13.6)
Subcutaneous rheumatoid nodules	12 (9.1)
Sjogren's syndrome	8 (6.1)
Patient-reported morning stiffness (n=132), n (%)	120 (90.9)
C-reactive protein levels (n=97), median (IQR), mg/dL	0.9 (0.5-1.8)
Erythrocyte sedimentation rate (n=96), median (IQR), mm/hour	36.0 (26.0-44.5)
DAS28-ESR score (n=95), mean (SD)	5.6 (0.7)
High disease activity based on DAS28-ESR score (>5.1) (n=95), n (%)	72 (75.8)
SDAI score (n=96), median (IQR)	28.4 (24.1-33.3)
High disease activity based on SDAI score (26.1-86.0) (n=96), n (%)	63 (65.6)
SB4 starting dosage: 50 mg once weekly (n=132), n (%)	132 (100.0)
In prefilled pen	118 (89.4%)
In prefilled syringe	14 (10.6%)
Concomitant csDMARD treatment for RA (n=132), n (%)	122 (92.4)
Methotrexate	78 (59.1%)
Hydroxychloroquine	45 (34.1%)
Leflunomide	19 (14.4%)
Ciclosporin	2 (1.5%)

CCP: cyclic citrullinated peptide, DAS28-ESR: disease activity score 28 with erythrocyte sedimentation rate, csDMARD: conventional synthetic disease modifying antirheumatic drug, IQR: interquartile range, N: total sample size, n: number of patients with available data, PhGA: physician's global assessment, PtGA: patients' global assessment, RA: rheumatoid arthritis, SD: standard deviation, SDAI: simplified disease activity index, SJC28: swollen joint count based on 28-joint assessment, TJC28: tender joint count based on 28-joint assessment, VAS: visual analog scale.

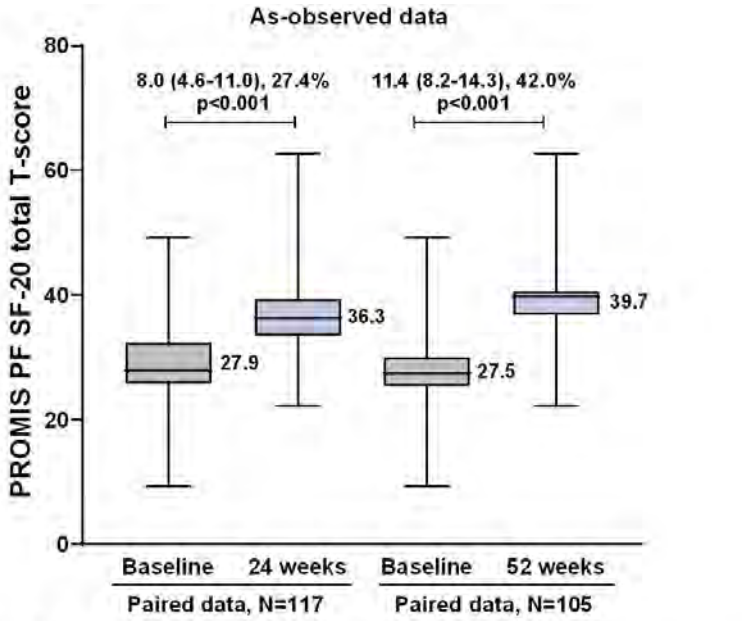

Figure 1. Change in PROMIS PF SF-20 total T-score from baseline at 24 and 52 weeks post-baseline, among patients with available paired data. Numbers next to bars indicate median values, while whiskers extend to minimum and maximum values at each timepoint. Median (interquartile range) differences and percent changes are displayed above the respective horizontal capped bars. Statistically significant increases (p<0.001, Wilcoxon signed-rank test) from baseline were observed both at 24- and 52- weeks post-baseline. N: number of patients with available data, PROMIS PF SF-20: Physical Function Short Form 20a.

Figure 1. Change in PROMIS PF SF-20 total T-score from baseline at 24 and 52 weeks post-baseline, among patients with available paired data. Numbers next to bars indicate median values, while whiskers extend to minimum and maximum values at each timepoint. Median (interquartile range) differences and percent changes are displayed above the respective horizontal capped bars. Statistically significant increases (p<0.001, Wilcoxon signed-rank test) from baseline were observed both at 24- and 52- weeks post-baseline. N: number of patients with available data, PROMIS PF SF-20: Physical Function Short Form 20a.

(9/113) of patients at 24 weeks, and by 86.8% (79/91), 58.1% (54/93) and 20.4% (19/93) at 52 weeks, respectively. The adverse event (AE) rate was 18.9% (25/132). AEs related to SB4 were reported for 3 (2.3%) patients (excluding events of 'drug ineffective') of whom one patient experienced 2 serious events.

Conclusion: These are the first real-world data on SB4 in a routine setting in Greece, indicating that the majority of patients in this study cohort demonstrated clinically meaningful improvement in their physical function and disease activity by 24 and 52 weeks post-initiation of SB4 for treatment of RA.

Disclosure: P. Athanassiou, None; **A. Bounas**, GENESIS PHARMA, 1, 2, 5, GSK, 1, 2, JANSSEN, 1, 2, MSD, 1, 2, 5, NOVARTIS, 1, 2, 5, PFIZER, 1, 2, 5, ROCHE, 1, 2, 5, UCB, 1, 2, 5, ABBVIE, 1, 2; **D. Boumpas**, unrestricted grant support through the research account of the University from various pharmaceutical companies., 5; **P. Sidiropoulos**, ABBVIE, 1, 5, 6, MSD, 1, 5, 6, PFIZER, 1, 5, 6, ROCHE, 5, 6, NOVARTIS, 1, 5, 6, ELI LILLY, 1, 5, 6, GILEAD, 1, 5, AMGEN, 5; **C. Tsalapaki**, None; **A. Garyfallos**, AbbVie, 6, BGP, 6, Roche, 6, Genesis Pharma, 2, UCB, 2, Pfizer, 2; **E. Grika**, None; **P. Voulgari**, Genesis Pharma SA, 3; **A. Kekki**, Genesis Pharma, 3; **Z. Anagnostopoulos**, Genesis Pharma, 3; **G. Karachalios**, Genesis Pharma, 3; **N. Antonakopoulos**, Genesis Pharma, 3.

Abstract Number: 0846

Psychometric Evaluation and Measurement Invariance of English and French Versions of the UCLA Loneliness Scale in Systemic Sclerosis: A Scleroderma Patient-Centered Intervention Network Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Research Methodology Poster (0846–0854)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Loneliness is a pervasive experience that has been associated with poorer health-related quality of life, and remains understudied in patients with systemic sclerosis (SSc). This study examined the psychometric properties of scores from the UCLA Loneliness Scale-6 (ULS-6; Neto, 1992), a self-report questionnaire not previously evaluated for SSc, and evaluated the equivalence of English and French versions.

Methods: This study used baseline data from 775 adults with SSc (89.9% female, 52.9% limited SSc, 66% English-speaking) enrolled in the Scleroderma Patient-Centered Intervention Network (SPIN) Cohort. Confirmatory factor analysis (CFA) was used to evaluate the single-factor structure of the ULS-6. Internal consistency reliability was assessed via McDonald's omega and Cronbach's coefficient alpha, and convergent validity was examined via Pearson product-moment correlations with measures of depression symptoms (PHQ-8) and social support (OSSS-3), number of people in the household, and social interaction frequency. Multiple group CFA (MGCFA) was used to determine whether the single-factor structure was supported in English and French-speaking subgroups. The MIMIC model was used to examine differential item functioning (DIF) for English versus French versions.

Results: The mean score on the ULS-6 was 7.00 (SD = 4.76, range 0-18), with a higher score representing greater loneliness. The CFA supported the expected single-factor structure (CFI = .96, SRMR = .03), although the RMSEA = .11 suggested less than adequate model fit. All standardized factor loadings for items were large and statistically significant (.62 to .86, all *p*s < .001). Omega and alpha were both 0.87, indicating high reliability. The ULS-6 total score correlated significantly (all *ps* < .001) and in expected directions with the total score for the PHQ-8 (*r* = .56), the total score on the OSSS (*r* = -.53), and frequency of social interactions with one person (*r* = -.162) and multiple people *(r* = -.24), but did not correlate significantly with number of people in the household (r = -.058, *p* = .11). The MGCFA indicated that the configural invariance model best fit the data ($\Delta\chi^2[8] = 56.14$, $p < .001$), suggesting non-equivalent factor loadings between language subgroups. However, unstandardized (.72 to 1.39, all *p*s < .001) and standardized (.48 to .90, all *p*s < .001) factor loadings were positive and statistically significant. The overall MIMIC model fit well and suggested cross-language metric equivalence (CFI = .939, SRMR = .044, RMSEA = .11). Statistically significant DIF were found for three items across language, although standardized differences were small (β(item 2) = .14, $p < .001$, β(item 4) = -.14, $p = .005$, β(item 6) = .13, $p < .001$).

Conclusion: Analyses demonstrated acceptable reliability and validity of the ULS-6 scores in English- and French-speaking adults with SSc, supporting its use to examine comparative experiences of loneliness. Although half of the items showed DIF across linguistic groups and the MGCFA did not support factor loading invariance, there were few practical implications for the total scores derived. Future studies of the ULS-6 across linguistic groups are needed to establish invariance for use with diverse SSc populations.

Disclosure: C. Rapoport, None; **A. Choi**, None; **L. Kwakkenbos**, None; **M. Carrier**, None; **K. Gottesman**, None; **S. Roesch**, None; **B. Thombs**, None; **V. Malcarne**, None.

Abstract Number: 0847

A Psychometric Analysis of the Self-Efficacy for Managing Chronic Disease Scale in Systemic Sclerosis: A Scleroderma Patient-Centered Intervention Network Cohort Study

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SESSION INFORMATION
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Session Title: Research Methodology Poster (0846–0854)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Self-efficacy is a key determinant of health behaviors and the target mechanism of self-management programs for patients with chronic diseases. The Self-Efficacy for Managing Chronic Disease (SEMCD) scale, a brief self-report instrument, has been widely used to measure self-efficacy in chronic disease populations and is validated in English for use in people with systemic sclerosis (SSc). However, it is essential that translations of measures be examined for psychometric equivalence across populations, and no research has yet ascertained that SEMCD scores are comparable across languages. The present study examined the cross-language measurement equivalence of the SEMCD in a sample of English- or French-speaking adults with SSc.

Methods: Adults with SSc (*N* = 2159; 87.4% female; 57.3% limited SSc; 68.3% English-speaking) from 46 centers were enrolled in the Scleroderma Patient-Centered Intervention Network (SPIN) Cohort. All participants were classified as having SSc according to the 2013 ACR/EULAR classification criteria. The SEMCD scale includes 6 items and higher scores indicate higher levels of self-efficacy. Confirmatory factor analysis (CFA) was used to confirm the single-factor structure of the SEMCD scale. Cronbach's coefficient alpha and McDonald's omega were used to evaluate internal consistency reliability. Multiple group confirmatory factor analysis (MGCFA) was used to determine whether the single-factor structure was supported in both languages. The Multiple-Indicator Multiple-Cause (MIMIC) model was used to examine differential item functioning (DIF).

Results: The mean total score on the SEMCD was 6.45 (SD = 2.26, range = 1-10). The SEMCD demonstrated good internal consistency reliability (α = .93, ω = .93). CFA indicated that a one-factor model fit well based on 2 of the 3

tested indices of model fit (Comparative Fit Index [CFI] = .96, Standardized Root Mean Residual [SRMR] = .03). The Root Mean Square Error of Approximation (RMSEA) indicated less than acceptable model fit (RMSEA = .14). Standardized factor loadings for all items were large and statistically significant (all *p*s < .001; range .755 to .879). Results from the MGCFA supported the metric invariance model as the best fit for the data ($\Delta\chi^2$ [10, *N* = 2159] = 13.32, *p* = .206), suggesting that the factor loadings are invariant across English and French language versions. The overall MIMIC model fit well and indicated that the SEMCD items demonstrate cross-language metric equivalence (CFI = .96, SRMR = .03, RMSEA = .12), although a statistically significant but small-magnitude DIF was found for one SEMCD item across language (β = .03, *p* < .05).

Conclusion: Findings support the use of the SEMCD as a reliable and valid single-factor measure of self-efficacy in SSc. SEMCD scores from English- and French-speaking individuals with SSc can be compared or combined for analysis. Future studies should examine the metric equivalence of the SEMCD across other linguistic and sociodemographic groups (e.g., race/ethnicity, sex).

Disclosure: A. Choi, None; **C. Rapoport**, None; **L. Kwakkenbos**, None; **M. Carrier**, None; **K. Gottesman**, None; **S. Roesch**, None; **B. Thombs**, None; **V. Malcarne**, None.

Abstract Number: 0848

Automatic Hand Segmentation from Hand X-rays Using Minimized Training Samples and Machine Learning Models

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Research Methodology Poster (0846–0854)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In many hand osteoarthritis (OA) studies (e.g., automatic Joint Space Width measuring), accurate hand segmentation is the first step towards making further analysis. However, it would be a difficult task to use only traditional image processing techniques due to inconsistencies like bands, rings, and low contrast X-rays (see Figure 1). To train a machine learning model to segment hand X-rays, one needs to set up a training set in which each hand X-ray should be manually delineated. To minimize the effort of manual delineation, we developed a novel iterative training strategy that requires only a small number of images to be manually segmented.

Methods: 3557 hand X-rays from the Osteoarthritis Initiative (OAI) were utilized in this study, where each X-ray contains one hand. We randomly separated the dataset into a training set with 3024 X-rays and a testing set with 533 X-rays, and the testing set was not exposed to the models during the training procedure. In round 1, we applied a traditional image segmentation algorithm on the training set and selected 132 good-quality results as a training set to train model 1. Round 2, we applied to model 1 to the training set with 3024 images and selected 25 of the worst predicted segmentations from the results. We manually segmented those 25 failed images and used them to train a new U-net model (model 2). In round 3, likewise, we applied to model 2 to the training set again and picked 11 failed segmentations from the results. We manually segmented those 11 failed cases and combined them with the 25 cases from round 2 to train a new model using a total of 36 training samples (model 3). In total, we only manually segmented 36 hand X-rays (25 in round 2 and 11 in round 3). To evaluate segmentation accuracy, two research as-

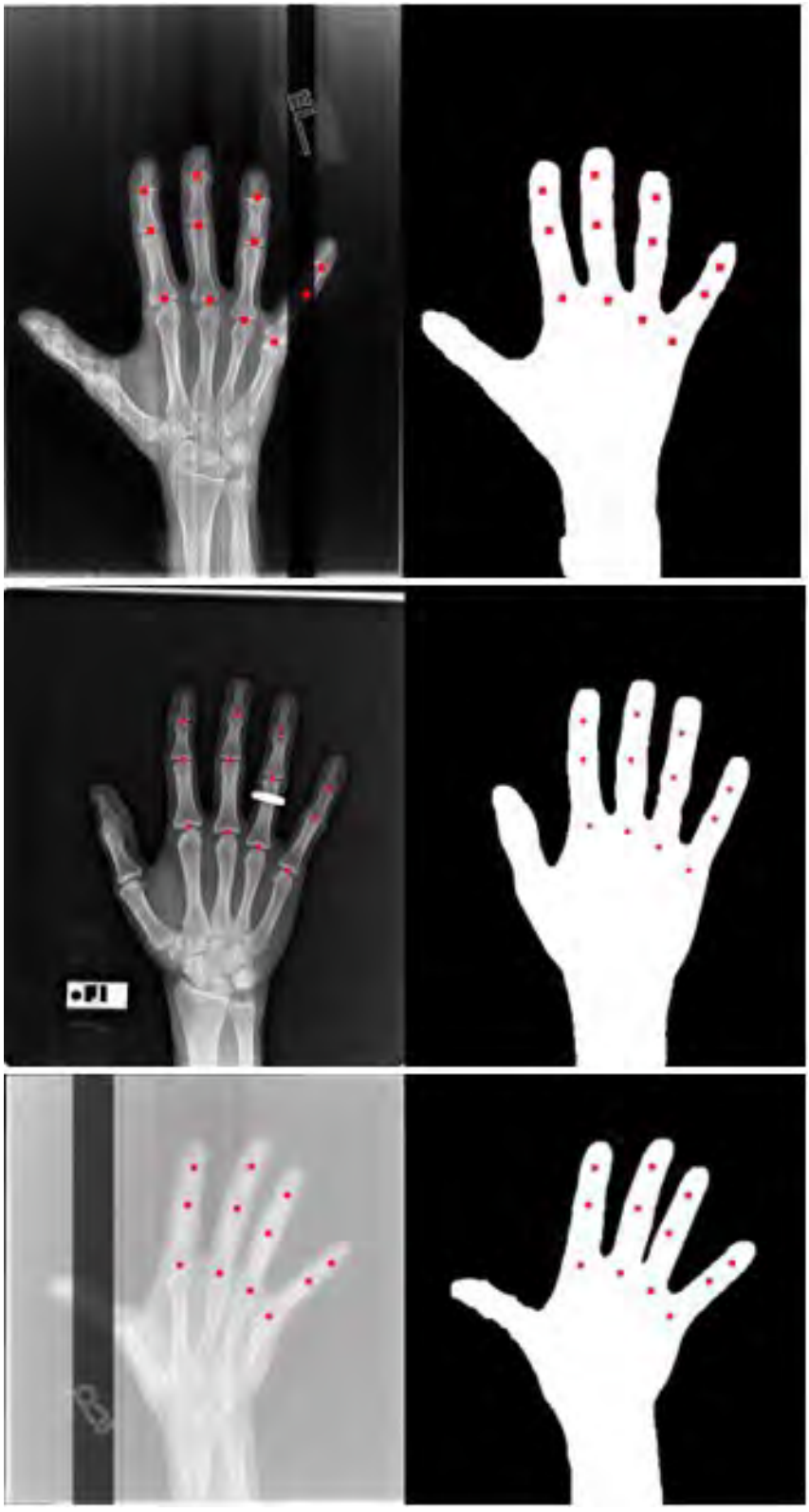

Figure 1. The first column contains challenge hand X-ray images with white bands, rings, and low contrast. The red dots are manual marks of 12 joint centers. The second column is the predicted hand masks by the machine learning model U-net (model 3).

Table 1. Hand segmentation accuracy

Model	# Training Samples	# Missing Joints / Total	Accuracy
Model 1	132	127/6396	98.01%
Model 2	25	24/6396	99.62%
Model 3	36	3/6396	99.95%

sistants manually marked the centers of 12 joints (excluding the thumb, Figure 1 red dots) on each of the 533 hands in the testing set. The reason that we used joint centers instead of segmenting the whole hand is to save labor. We evaluated the hand segmentation accuracy at the joint level: if a joint center is within the predicted hand mask, the joint is a match; otherwise, the joint is a miss. The overall accuracy of a model is equal to the number of matches divided by the number of total joints.

Results: Table 1 lists the accuracy for each model: model 1 performed the initial segmentation with the most training samples, but its accuracy was lowest; model 2 used only 25 training samples but improved the accuracy significantly; model 3 achieved the best accuracy (99.95%) with 36 training samples and only 3 joints out of 6396 joints were missed in the testing set.

Conclusion: Acquiring a large medical image dataset is a challenge in many studies and manually labeling is often a time-consuming procedure. In this paper, we proposed an iterative strategy to minimize the training samples that need to be manually labeled. In a dataset of 3557 hand X-rays, we only need to manually segment 36 images and achieved 99.95% accuracy for joint detection on the testing set. This strategy has potential usage in other medical image processing problems to save the manual labeling effort (e.g., knee cartilage segmentation, bone marrow lesion segmentation, etc.).

Disclosure: Z. Yang, None; **J. Shan**, None; **C. Guida**, None; **J. Blackadar**, None; **T. Cheung**, None; **J. Driban**, None; **T. McAlindon**, Kolon Tissue Gene, 1, Organogenesis, 1, Pfizer Inc., 1, Regeneron, 1, Remedium Bio, 1, Samumed, 1, Seikagaku, 1; **M. Zhang**, None.

Abstract Number: 0849

Myalgic Encephalomyelitis/Chronic Fatigue Syndrome: Creating a Foundation for Linking Patient Reported Outcomes Measures with the International Classification of Functioning, Disability and Health

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SESSION INFORMATION
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Session Title: Research Methodology Poster (0846–0854)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Myalgic Encephalomyelitis/Chronic Fatigue Syndrome (ME/CFS) is a devastating multisystem chronic disease, estimated to affect 1.5 million adults in the United States. The disease is associated with immune, neurological, metabolic, cognitive and sleep impairments compounded principally by Post-Exertional Malaise (PEM) and dysautonomia associated with a pathological level of fatigue. Among people with ME/CFS, 70%

cannot work; 25% are home- or bed-bound, and recovery is rare. There are no FDA-approved drugs or treatments. Diagnosis of ME/CFS is challenging due to many changing and persistent symptoms and often relies on a diagnosis of exclusion. Rheumatologists are among the handful of clinicians who treat patients with ME/CFS.

The National Institutes of Health (NIH) identified 119 Common Data Elements (CDEs) for use in people with ME/CFS. However, most CDEs are not targeted specifically for those with ME/CFS. The World Health Organization (WHO) International Classification of Functioning, Disability and Health (ICF) provides a framework to understand CDE items. The aim of this study is to use the ICF to categorize ME/CFS CDE items administered as Patient Reported Outcome Measures (PROMs). This work will provide a foundation to select the most appropriate CDE assessments and guide future development of an advanced, psychometrically-sound symptom based Computerized Adaptive Test (CAT) to assist rheumatology professionals in the treatment of patients with ME/CFS.

Methods: We reviewed all CDEs and excluded those that: 1) are not PROMs; 2) provide participant socio-demographic characteristics and medical history only; 3) use visual or pictographic scales; or 4) are for pediatric patients only.

We applied ICF linking rules[1] to identify and code meaningful concepts for all items. Items were divided among five researchers for independent coding and codes were compared. Coding discrepancies were noted and discussed until a consensus was achieved (Table 1. ICF Coding Example).

Results: We identified 36 PROMs comprised of 944 items (Figure 1). All coded items fit into two ICF components: *(1) Body Function (b codes) and (2) Activity and Participation (d codes)*. Body Function codes were as follows: *Energy and drive* (most frequently used), 14.9% (n=210) of the 1413 total codes; *Sensation of pain* 14.7% (n=208); *Sleep*

Table 1. Methods example of linking ICF categories to PROM items

PROM	ITEM	ICF CATEGORY	ADDITIONAL INFORMATION
CENTER FOR EPIDEMIOLOGIC STUDIES-DEPRESSION SCALE (CES-D)	I felt that I could not shake off the blues even with help from my family or friends.	b152 Emotional functions nc d7500 Informal relationships with friends d760 Family relationships	blues with help from
DEPAUL SYMPTOM QUESTIONNAIRE (DSQ)	Minimum exercise makes you physically tired	b4552 Fatiguability d5701 Managing diet and fitness	
FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY (FACIT)-FATIGUE	Because of my physical condition, I have trouble meeting the needs of my family	nd-ph d660 Assisting others d769 Family relationships	physical condition
WORLD HEALTH ORGANIZATION DISABILITY ASSESSMENT SCHEDULE (WHODAS)	In the past 30 days, how much difficulty did you have in: Standing for long periods such as 30 minutes?	d4154 Maintaining a standing position	

Key: nc = not covered by ICF, nd-ph = not definable physical health, b= Body function category, d = Activity and participation category.

Table 2a: ICF Body Function Codes for Core ME/CFS Symptoms

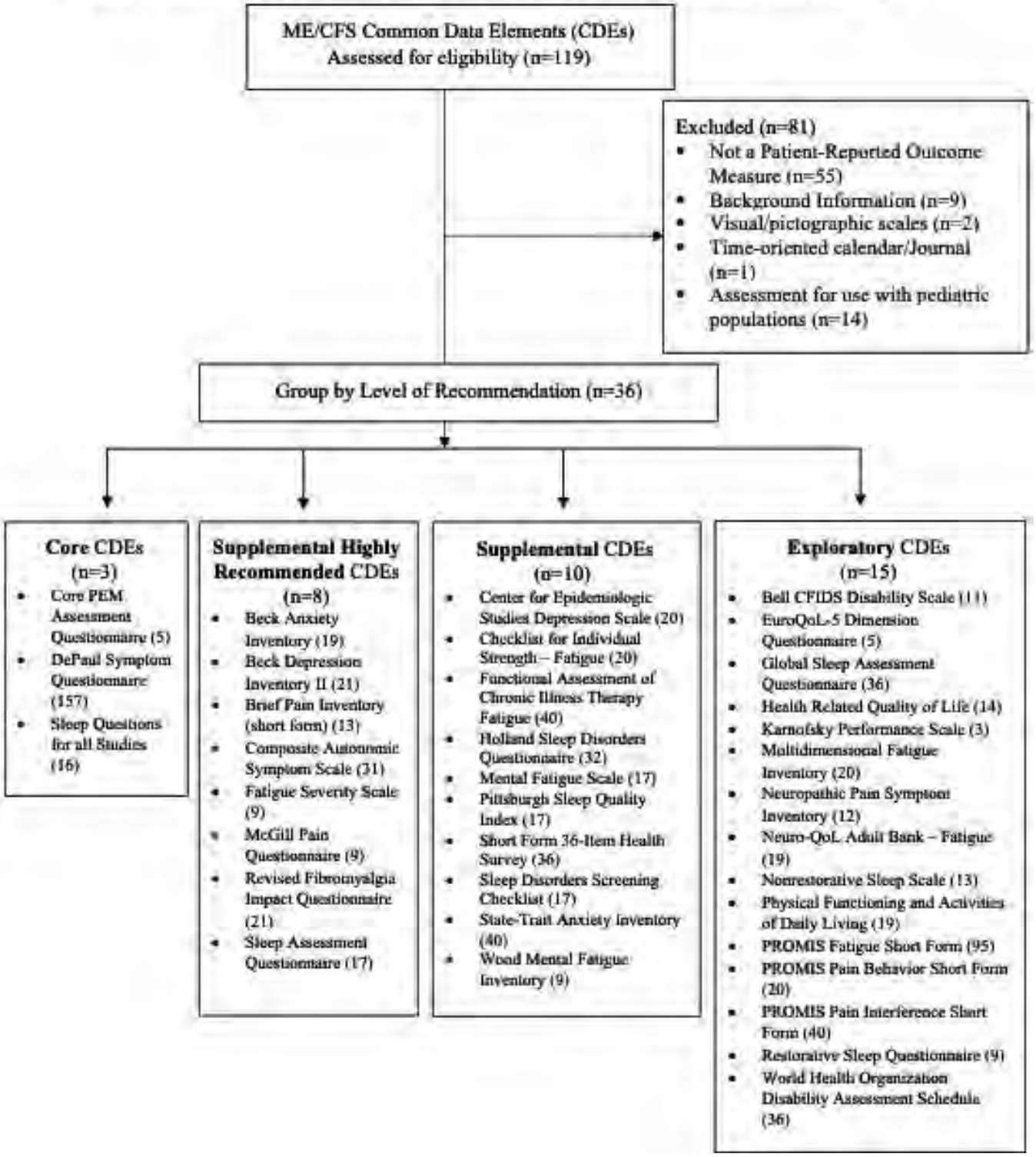
Pain	Sleep Unrefreshing	Post Exertional Malaise/Fatigue	Dysautonomia	Cognitive Impairment
b2 Sensory functions and pain b280 Sensation of pain b2800 Generalized pain b2801 Pain in body part b28010 Pain in head and neck b28011 Pain in chest b28012 Pain in stomach or abdomen	b134 Sleep functions b1340 Amount of sleep b1341 Onset of sleep b1342 Maintenance of sleep b1343 Quality of sleep b1344 Functions involving the sleep cycle	b130 Energy and drive functions b1300 Energy level b4552 Fatiguability	b2401 Dizziness b4100 Heart rate b4101 Heart rhythm b415 Blood vessel functions b515 Digestive functions b525 Defecation functions b550 Body temperature b5508 Thermoregulatory functions b620 Urination functions b6202 Urinary continence	b1 Mental functions b160 Thought functions b1600 Pace of thought b164 Higher-level cognitive functions b1641 Organization and planning b1644 Insight

Table 2b: ICF Activity and Participation Codes for Core ME/CFS Symptoms

Pain	Sleep Unrefreshing	Post Exertional Malaise/Fatigue	Dysautonomia	Cognitive Impairment
d Self-care d230 Carrying out daily routine d350 Conversations d4100 Lying down d4104 Standing d4153 Maintaining a sitting position d4154 Maintaining a standing position d4501 Walking long distances d460 Doing housework d4600 Moving around within the home d4602 Moving around outside the home or other buildings d570 Looking after one's health d5700 Ensuring one's physical comfort d5702 Maintaining one's health d710 Basic interpersonal interactions d850 Remunerative employment d 920 Recreation and leisure d9205 Socializing d5702 Maintaining one's health	d230 Carrying out daily routine d570 Looking after one's health	d177 Making decisions d2 General tasks and demands d210 Undertaking a single task d220 Undertaking multiple tasks d230 Carrying out daily routine d2302 Completing the daily routine d2303 Managing one's own activity level d350 Conversation d4100 Lying down d4103 Sitting d4153 Maintaining a sitting position d4154 Maintaining a standing position d450 Walking d4500 Walking short distance d4602 Moving around outside the home and other buildings d470 Using transportation d475 Driving d510 Washing oneself d550 Eating d570 Looking after one's health d5701 Managing diet and fitness d5702 Maintaining one's health d620 Acquisition of goods and services d640 Doing housework d7 Interpersonal interactions and relationship d7500 Informal relationships with friends d760 Family relationships d8 Major life areas d850 Remunerative employment d920 Recreation and leisure d9205 Socializing	d4104 Standing	d310 Communicating with receiving spoken messages d4104 Standing d6 Domestic life d640 Doing housework d850 Remunerative employment d9205 Socializing

functions 11.9% (n=168); *Fatiguability* 11.5% (n=163); and *Emotional functions* 9.7% (n=137). Only 11.1% (n=157) of items were coded in the *Activity and Participation* component. Table 2 presents ICF codes for core ME/CFS symptoms and functions.

Figure 1. NIH ME/CFS Common Data Elements ICF Coding Inclusion Flow Diagram



Conclusion: NIH ME/CFS CDEs are comprised of items that assess key areas of *Body function*; however, relatively few items assess the impact of ME/CFS symptoms on *Activity and Participation*. Extreme limitation in the ability to engage in physical and cognitive activities is a hallmark of ME/CFS. Results demonstrate the value of using the ICF conceptual framework to examine item content to assist rheumatology professionals in selecting appropriate assessments for their patients and to inform the future development of item banks for psychometrically-sound assessments.

1.Cieza A, et al. (2005). J Rehabil Med.

Disclosure: H. Bailey, None; **A. Vasudevan**, None; **E. Hickey**, None; **A. Ledingham**, None; **M. Slavin**, None; **L. Kazis**, MediWound, 2; **R. Tompkins**, None.

Abstract Number: 0850

Regression Methods for Modeling Western Ontario and McMaster Universities Arthritis Index (WOMAC) Pain Scores for Early Stage Knee Osteoarthritis

Benjamin Sweigart and Michael LaValley, Boston University School of Public Health, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Research Methodology Poster (0846–0854)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The Western Ontario and McMaster Universities Arthritis Index (WOMAC) pain score [range 0-20] is a common outcome measure for clinical trials and observational studies in knee osteoarthritis (OA). However, for early stage OA, the distribution of WOMAC pain is not symmetric, with many people reporting pain scores of 0, and very few high scores. Modeling non-symmetric outcomes with standard linear regression or t-tests can yield inaccurate estimates of association and prediction. We sought to determine whether alternative regression methods are better for modeling WOMAC pain scores for samples in early stage OA.

Methods: We analyzed WOMAC pain scores for the right knees of participants at the baseline exam of the Osteoarthritis Initiative (OAI) incidence cohort, which includes subjects at risk for symptomatic OA. We modeled the pain scores by fitting the following distributions to all participants: normal, log-normal, beta, and gamma. The log-normal and gamma distributions require values to be >0, and the beta distribution requires values to be >0 and < 1. To accommodate these restrictions, pain scores were transformed by adding 1 and dividing by 22 to range from 0.045 to 0.955. We assessed the best fits of distributions to the pain values visually, and with chi-square statistics comparing observed to expected counts after dividing the range into 10 intervals. We performed multivariable log-normal, beta and gamma regression including sex, age, and BMI as predictors of transformed pain values, and used the best fitting models to create 10,000 simulated datasets with pain score and predictor values distributed similarly to the OAI incidence cohort. We then fit log-normal, beta, gamma, and robust regression models to each simulated dataset with transformed pain as the outcome and age, sex and BMI as predictors. To measure regression accuracy and precision, we used the predicted mean on the original 0-20 WOMAC pain scale for each sex along with the 95% confidence interval coverage, average confidence interval width, bias, and mean square error of the predicted means.

Results: We included data from 3,282 individuals, 41% of whom were male, with an average age of 61.3 (SD 9.2) and BMI of 28.1 (SD 4.6). The median WOMAC pain score was 1.0 (interquartile range 0.0, 3.0). The normal and log-normal distributions were poor fits to the pain score data, while the beta and gamma distributions were better fits, both visually and from chi-square statistics (Figure 1). When simulated datasets were created using parameters from the beta regression, all of the regression models slightly under-predicted the true mean of WOMAC pain score for both males and females, but the beta regression resulted in highest coverage, shortest confidence intervals, and lowest mean square error (Table 1). Results were similar when simulated datasets were created using parameters from log-normal or gamma regressions.

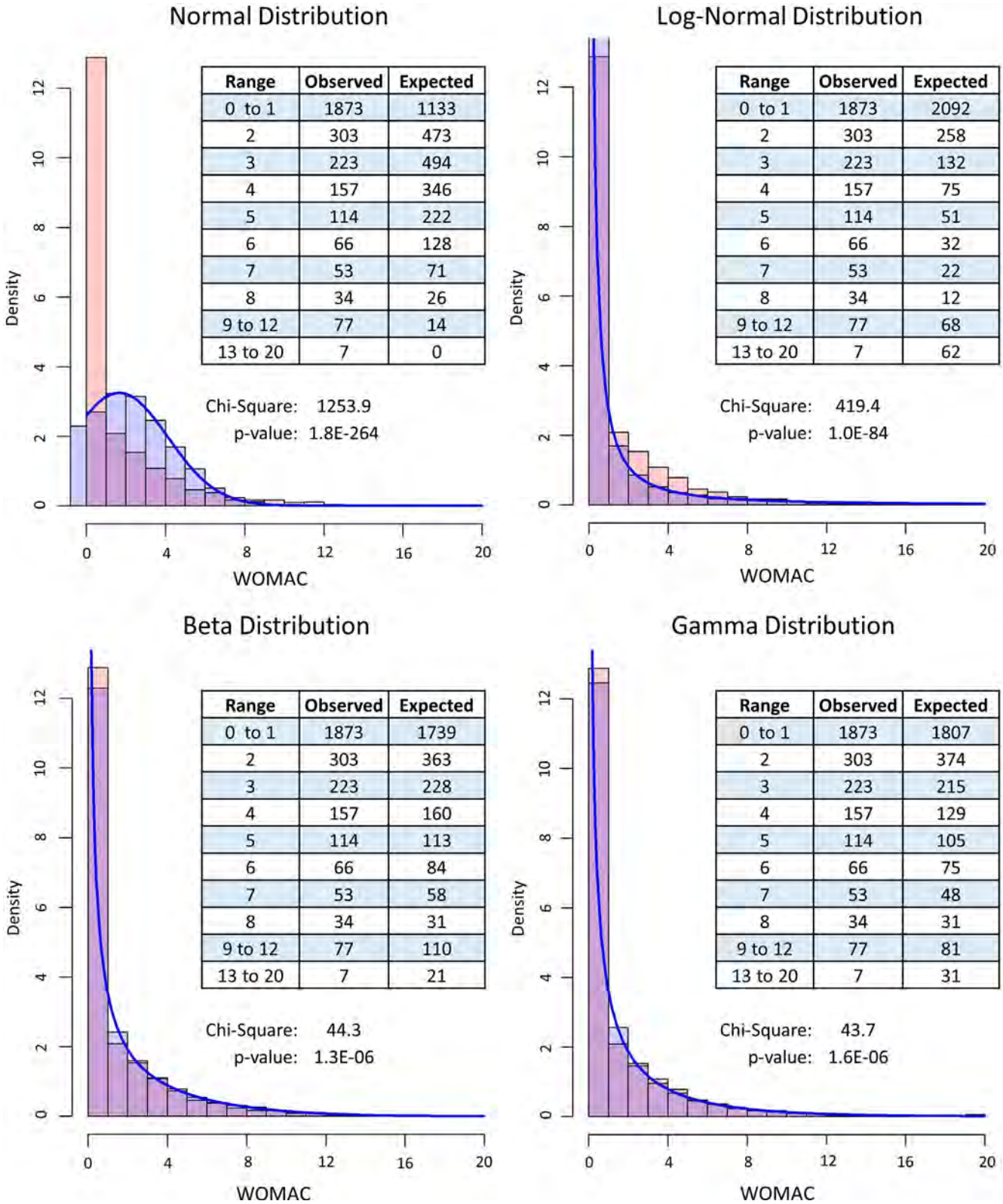


Figure 1. Goodness of fit of statistical distributions to the OAI Incidence Cohort WOMAC pain scores. Red = Actual OAI data; Blue = Fitted data; Purple = Overlap.

Table 1. Simulation results for predicted WOMAC pain score [0-20]: values for males and females, aged 60 years, with BMI 28 kg/m^2. Data were simulated from beta, gamma, and log-normal regression models and each simulated data set contained 3,282 observations. Results based on 10,000 simulations.

Data Generation Model	Regression Analysis Model	Males					Females				
		Mean WOMAC	Coverage	Mean CI Width	Bias	MSE	Mean WOMAC	Coverage	Mean CI Width	Bias	MSE
Beta Regression	*True WOMAC value*	*0.97*					*1.31*				
	Beta	0.86	**93%**	**0.6**	-0.11	**0.24**	**1.23**	**94%**	**0.8**	**-0.08**	**0.25**
	Normal	0.85	91%	1.7	-0.12	0.26	1.09	90%	1.6	-0.22	0.30
	Log-Normal	0.83	91%	1.4	-0.14	0.27	1.18	91%	1.5	-0.13	0.27
	Gamma	0.79	90%	1.5	-0.18	0.30	1.17	89%	1.6	-0.14	0.27
	Robust	**0.87**	90%	2.1	**-0.10**	0.33	1.01	92%	1.9	-0.30	0.33
Gamma Regression	*True WOMAC value*	*1.05*					*1.36*				
	Beta	**0.90**	**95%**	**0.7**	**-0.15**	**0.30**	1.26	**95%**	**0.8**	-0.10	**0.27**
	Normal	0.86	93%	1.1	-0.19	0.35	1.20	92%	1.3	-0.15	0.37
	Log-Normal	0.85	**95%**	0.8	-0.20	0.32	**1.29**	95%	0.9	**-0.07**	0.35
	Gamma	0.81	**95%**	0.8	-0.24	**0.30**	**1.29**	**96%**	0.9	**-0.07**	0.34
	Robust	0.89	94%	2.1	-0.16	0.44	1.12	94%	2.0	-0.24	0.36
Log-Normal Regression	*True WOMAC value*	*1.01*					*1.33*				
	Beta	0.90	94%	**0.7**	-0.11	0.31	**1.32**	**95%**	**0.8**	**-0.01**	0.30
	Normal	0.94	93%	1.1	-0.07	0.34	1.10	92%	1.2	-0.23	0.39
	Log-Normal	0.90	**95%**	0.8	-0.11	**0.27**	1.21	**95%**	**0.8**	-0.12	**0.29**
	Gamma	0.89	94%	0.8	-0.12	0.30	1.18	94%	0.9	-0.15	0.33
	Robust	**0.95**	94%	1.6	**-0.06**	0.39	1.08	93%	1.7	-0.25	0.35

Conclusion: Standard methods used to analyze WOMAC pain score data rely on assumed distributions that may poorly fit the data. For creating regression models to predict the WOMAC pain score, beta regression may have better statistical properties than either normal or log-normal regression.

Disclosure: B. Sweigart, None; **M. LaValley**, None.

Abstract Number: 0851

Application of a Modified Recursive Feature Elimination Machine Learning Algorithm to Select Predictors of Mortality in Those with and Without Osteoarthritis

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SESSION INFORMATION
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Session Title: Research Methodology Poster (0846–0854)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Radiographic osteoarthritis (rOA) and joint symptoms at the knee and hip are predictors of mortality. However, questions remain about the nature of the relationship and if there are other predictors, or combinations of predictors, that contribute to increased mortality. Since non-steroidal anti-inflammatory drugs (NSAIDs) have been shown to increase risk of death and are widely used by those with OA, we applied novel statistical methods to identify a set of predictors of mortality, and whether these predictors interact with NSAID use

Methods: Data were from 4,156 participants in the Johnston County Osteoarthritis Project (JoCoOA), a longitudinal community-based cohort of Black and White men and women aged ≥45 years. Vital status was assessed using the National Death Index records to capture date of death through December 2015. Clinical exams, radiographs and questionnaires were completed at baseline and at up to 3 follow-up time points. Socio-demographic and clinical characteristics, including comorbidities and joint symptoms, were considered as predictors and NSAID use was considered as an effect modifier. Multiple imputation was used for missing data.

We applied a time-varying covariate stratified cox model with recursive feature elimination (RFE). RFE searches for a subset of predictors starting with a full model including all predictors in the training dataset, and successively removing one at a time. Our model initially included 57 predictors, with NSAID use entered as an interaction term with all other predictors. A model with the smallest change in log-likelihood from the full model was selected and that predictor, along with its interaction with NSAID use, was dropped. This process was repeated until no predictors remained in the model. Using a plot of the log-likelihoods after each elimination, the final model was selected based on an inflection point prior to a notable decrease in log-likelihood (Figure 1). All observations were stratified by the time point, and hazard ratios (HR) and 95% confidence intervals (CI) were estimated.

Results: Mean age of the participants at baseline was 61 years, 63% were female and 66% were white (Table 1). More than 34% of participants reported taking NSAIDs at baseline, which increased to 51%, 67%, and 70% at the first, second, and third follow-up, respectively, over which time 1,812 deaths occurred.

In the RFE model, we found that after iterative predictor elimination, 13 predictors showed an important contribution to excess death (Figure 1, Table 2). The strongest contributors were current smoking status, cancer, diabetes and male sex. Left knee pain was associated with a 19% increased HR. We observed an NSAID-modified association with right knee injury where those with a knee injury and no NSAID use had a 30% lower hazard of mortality, whereas little association was observed for right knee injury among those who used NSAIDs.

Table 1. Demographic characteristics over study visits, JoCoOA Study.

Table 1. Demographic characteristics over study visits, JoCoOA Study

	Study Visit			
	Baseline (n=4156)	1st FU (n=2436)	2nd FU (n=1448)	3rd FU (n=556)
	n (%) or mean (SD)	n (%) or mean (SD)	n (%) or mean (SD)	n (%) or mean (SD)
Demographics				
Baseline to follow-up (years)	—	6.0 (1.2)	12.2 (2.7)	18.4 (1.8)
Age at visit (years), mean (SD)	61.1 (10.6)	65.9 (9.9)	69.9 (8.7)	73.3 (7.0)
Female, n (%)	2626 (63.2)	1613 (66.2)	978 (67.5)	367 (66.0)
African American, n (%)	1418 (34.1)	772 (31.7)	442 (30.5)	157 (28.2)
<High School Education, n (%)	1493 (35.9)	730 (30.0)	313 (21.6)	77 (13.8)
Non-professional occupation, n (%)	2322 (55.9)	1324 (54.4)	782 (54.0)	274 (49.3)
BMI (kg/m^2), mean (SD)	29.6 (6.5)	30.5 (6.7)	31.3 (6.8)	30.9 (6.4)
Past Smoker, n (%)	1154 (27.8)	940 (38.6)	642 (44.3)	263 (47.3)
Current Smoker, n (%)	918 (22.1)	354 (14.5)	137 (9.5)	35 (6.3)
Cigarettes per day (current), mean (SD)	4.0 (9.1)	2.5 (7.3)	1.4 (5.2)	0.8 (3.9)
NSAID use, n (%)	1422 (34.2)	1246 (51.1)	969 (66.9)	389 (70.0)
Number of timepoints using NSAIDs since baseline, mean (SD)	—	0.8 (0.5)	0.8 (0.8)	1.3 (1.0)
0, n (%)	—	1619 (66.5)	592 (40.9)	130 (23.4)
1, n (%)	—	817 (33.5)	534 (36.9)	203 (36.6)
2, n (%)	—	—	322 (22.2)	156 (28.1)
3, n (%)	—	—	—	67 (12.1)
Comorbidities				
Cancer, n (%)	50 (1.2)	61 (2.5)	68 (4.7)	54 (9.7)
Asthma, n (%)	254 (6.1)	205 (8.4)	179 (12.4)	80 (14.4)
Emphysema, n (%)	120 (2.9)	100 (4.1)	65 (4.5)	23 (4.1)
Cardiovascular disease, n (%)	906 (21.8)	790 (32.4%)	606 (41.9)	264 (46.6)
Diabetes, n (%)	537 (12.9)	459 (18.8)	367 (25.3)	164 (29.5)
Depression, n (%)	532 (12.8)	261 (10.7)	157 (10.8)	63 (11.3)
Knee & Hip KL Grade/Pain Variables				
Knee injury, left, n (%)	445 (10.7)	411 (16.9)	264 (18.2)	122 (21.9)
Knee injury, right, n (%)	509 (12.2)	448 (18.4)	288 (20.0)	109 (19.6)
Hip injury, left, n (%)	156 (3.8)	131 (5.4)	85 (5.9)	38 (6.8)
Hip injury, right, n (%)	166 (4.0)	135 (5,5)	89 (6.1)	35 (6.3)
Knee KL Grade, left, n (%)				
0, n (%)	2209 (53.2)	979 (40.2)	335 (23.1)	81 (14.6)
1, n (%)	1122 (27.0)	742 (30.5)	514 (35.5)	220 (40.0)
2, n (%)	464 (11.2)	332 (13.6)	249 (17.2)	110 (19.8)
3, n (%)	224 (5.4)	216 (8.9)	166 (11.5)	52 (9.4)
4, n (%)	102 (2.5)	112 (4.6)	155 (8.0)	62 (11.2)
Replacement, n (%)	35 (0.8)	55 (2.3)	69 (4.8)	31 (5.6)
Knee KL Grade, right				
0, n (%)	2065 (49.7)	919 (37.5)	306 (21.1)	75 (13.5)
1, n (%)	1151 (27.7)	781 (32.1)	539 (37.2)	208 (37.4)
2, n (%)	556 (13.4)	331 (13.6)	232 (16.0)	105 (18.9)
3, n (%)	213 (5.1)	222 (9.1)	164 (11.3)	65 (11.7)
4, n (%)	132 (3.2)	119 (4.9)	129 (8.9)	68 (12.2)
Replacement, n (%)	39 (1.0)	69 (2.8)	78 (5.4)	35 (6.3)
Hip KL Grade, left				
0, n (%)	1266 (30.5)	436 (17.9)	133 (9.2)	29 (5.2)
1, n (%)	2031 (48.9)	1370 (56.2)	860 (59.4)	307 (55.2)
2, n (%)	772 (18.6)	558 (22.9)	403 (27.8)	190 (34.2)
3, n (%)	40 (1.0)	27 (1.1)	16 (1.1)	10 (1.8)
4, n (%)	20 (0.5)	11 (0.5)	5 (0.3)	6 (1.1)
Replacement, n (%)	26 (0.6)	34 (1.4)	31 (2.1)	14 (2.5)
Hip KL Grade, right				
0, n (%)	1042 (25.1)	380 (15.6)	182 (12.6)	43 (7.7)
1, n (%)	2299 (55.3)	1495 (61.4)	901 (62.2)	349 (62.8)
2, n (%)	709 (17.1)	481 (19.7)	301 (20.8)	132 (23.8)
3, n (%)	60 (1.4)	35 (1.4)	16 (1.1)	9 (1.6)
4, n (%)	25 (0.6)	18 (0.7)	5 (0.3)	6 (1.1)
Replacement, n (%)	21 (0.5)	27 (1.1)	43 (3.0)	17 (3.1)

FU=Follow-up; SD=Standard deviation; BMI=body mass index NSAIDs=non-steroidal anti-inflammatory drugs; KL=Kellgren-Lawrence

Conclusion: We show that an application of a RFE algorithm is useful to both select the important predictors, and to quantify predictive validity, on excess mortality. The model demonstrated good performance in selecting a set of predictors and identifying characteristics most important in premature death that can be explored in future analyses.

Table 2. Final prediction model

Predictor	HR (95% CI)
Demographics	
Age	1.10 (1.09, 1.10)
Female	0.64 (0.58, 0.71)
<High School Education	1.17 (1.06, 1.29)
Past Smoker	1.18 (1.05, 1.32)
Current Smoker	2.05 (1.79, 2.35)
NSAID Use	1.01 (0.91, 1.13)
Comorbidities	
Cancer	1.69 (1.32, 2.17)
Asthma	1.24 (1.06, 1.47)
Cardiovascular disease	1.38 (1.25, 1.53)
Diabetes	1.64 (1.47, 1.84)
Depression	1.27 (1.10, 1.46)
Knee & Hip KL Grade/Pain Variables	
Knee Pain, left	1.19 (1.08, 1.32)

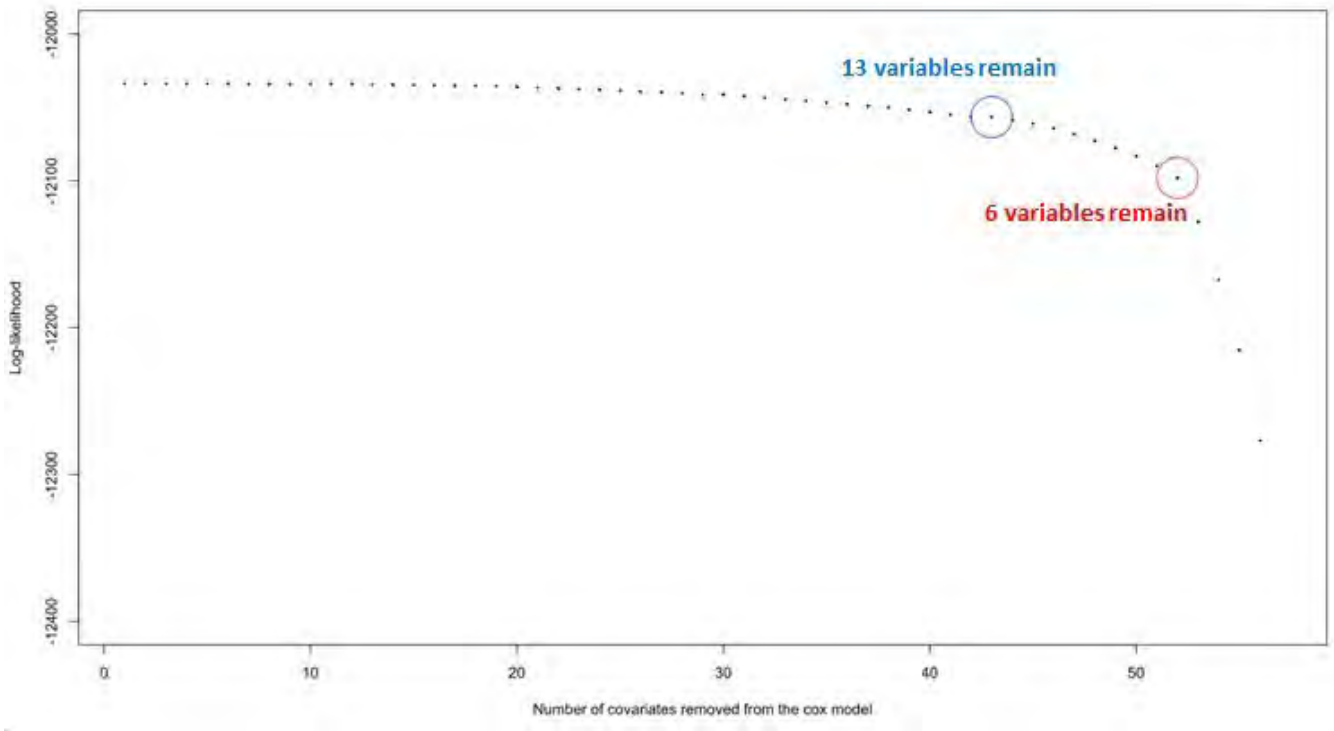

Figure 1. Plot of Log-likelihood values by number of variables dropped in each iteration indicating inflection points.

Disclosure: S. Kim, None; **S. Xiang**, None; **L. Arbeeva**, None; **C. Alvarez**, None; **A. Nelson**, Lilly, 1; **Y. Golightly**, None; **L. Callahan**, None; **M. Kosorok**, None; **B. Cleveland**, None.

Abstract Number: 0852

Bone Marrow Lesion Segmentation Using Synthetic Data and Deep Learning Models

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SESSION INFORMATION
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Background/Purpose: Bone marrow lesions (BML) are indicators for knee osteoarthritis (OA) and can be detected from magnetic resonance imaging (MRI). Due to the small size, low contrast, and various positions that BML may occur, it is challenging to automatically segment BMLs. Besides, not all patients with OA have BML, and for those patients with BML, not every slice has BML. The limited data becomes an obstacle to train machine learning models. In this work, we developed a novel strategy to synthesize MRI images with BML and trained deep learning models using the augmented dataset.

Methods: 300 cases from the Osteoarthritis Initiative (OAI) database were utilized in this study, where each case has sagittal intermediate weighted fat-suppressed (IWFS) sequence that is composed of a sequence of 36 MRI images. The BMLs in the dataset were manually delineated by domain experts as ground truth. We randomly separated the dataset into training, validation, and testing sets with 210/45/45 cases, respectively. To generate synthetic images with BML, we used images from the training set only. Three strategies were proposed. In strategy 1, for each image with BML in the training set, we selected a clean image without BML from the training set. We cropped out the BML from the original image and overlaid it on the clean image. To decide where to overlay it, we first calculated the center of the femur bone, the angle to the vertical direction, and the projected point on the bone edge in the original image, as shown in Figure 1. We also calculated the distance from the center to the lesion, and from the center to the bone

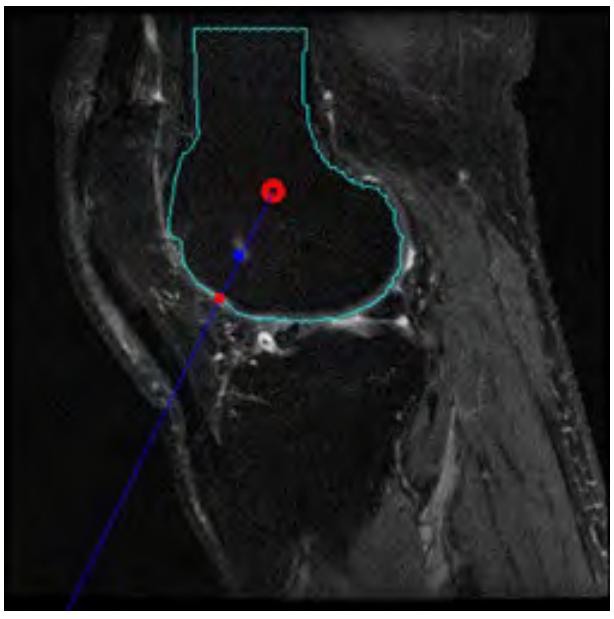

Figure 1. Bone center and projection on the edge (red point). BML is marked by the blue point.

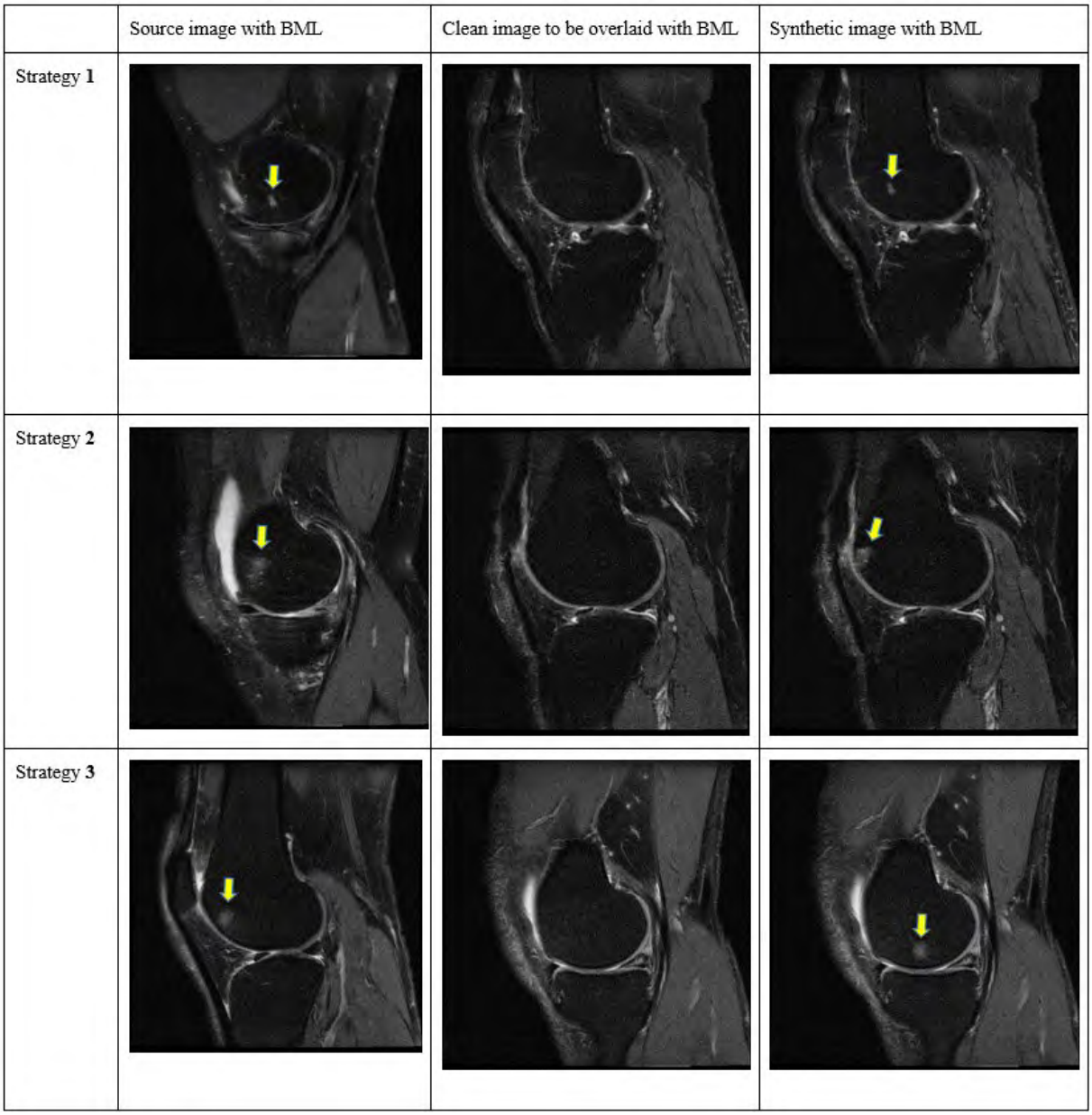

Figure 2. Example images for each strategy (the highlighted arrows mark the BML location).

Table 1. BML segmentation performance on the testing set using different augmentation strategies.

	Dice Coefficient (average)	Similarity (average)
Baseline Data (Original Images with BML)	0.4029	0.2998
Baseline Data + Synthetic Data from Strategy 1	0.5190	0.3963
Baseline Data + Synthetic Data from Strategy 2	**0.5192**	**0.3862**
Baseline Data + Synthetic Data from Strategy 3	0.4378	0.3274

edge. Then we applied the same distance percentage and same angle when overlaying the BML to the clean image. In strategy 2, everything is the same as strategy 1 except a fixed distance percentage was used to make sure the lesion is close to the bone boundary. In strategy 3, we introduced variations about the angle. A random angle from a range of -20 to +20 degrees from the vertical direction of the bone was applied when overlaying the BML. Figure 2 shows examples of the three strategies. After data generation, we first trained a deep learning model, called U-net, using the original BML images from the training set, as our baseline. Then for each strategy, a separate U-net model was trained, using the combination of original BML images plus the synthetic images.

Results: We reported the Dice coefficient and Similarity for each model in Table 1. An interesting finding is that for all the strategies, using 50% of the synthetic data produced higher accuracy than using 100% of the synthetic data. Therefore, we presented the results of using 50% of the synthetic data for each strategy. As Table 1 shows, the best accuracy was achieved by strategy 2, with more than 0.1 improvement in Dice and around 0.1 improvement in Similarity.

Conclusion: We developed an effective synthetic image generation method for BML segmentation. The accuracy was improved after adding the synthetic images to the training set. Future work could focus on refining the strategies for more realistic images and find the balanced combination between original images and synthetic images.

Disclosure: B. Michaely, None; **M. Zhang**, None; **J. Shan**, None.

Abstract Number: 0853

A Combined Patient Registry and Biobank Laboratory Information System for Prospective Multisite Chronic Rheumatic Disease Research Using REDCap

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Background/Purpose: As we enter the big data revolution, comprehensive informatics solutions are essential to realising precision medicine for rheumatic and other chronic disease patients, especially for curating high-quality,

large-scale and longitudinal biospecimen and linked data collections. In establishing the Australian Arthritis and Autoimmune Biobank Collaborative (A3BC), we sought to develop a low-cost, nation-scale data management system capable of managing our multi-site longitudinal biobank-registry and its complex biobank and data requirements. This included broad life-course data from adults and children across clinical/phenotypic, biological, patient-reported

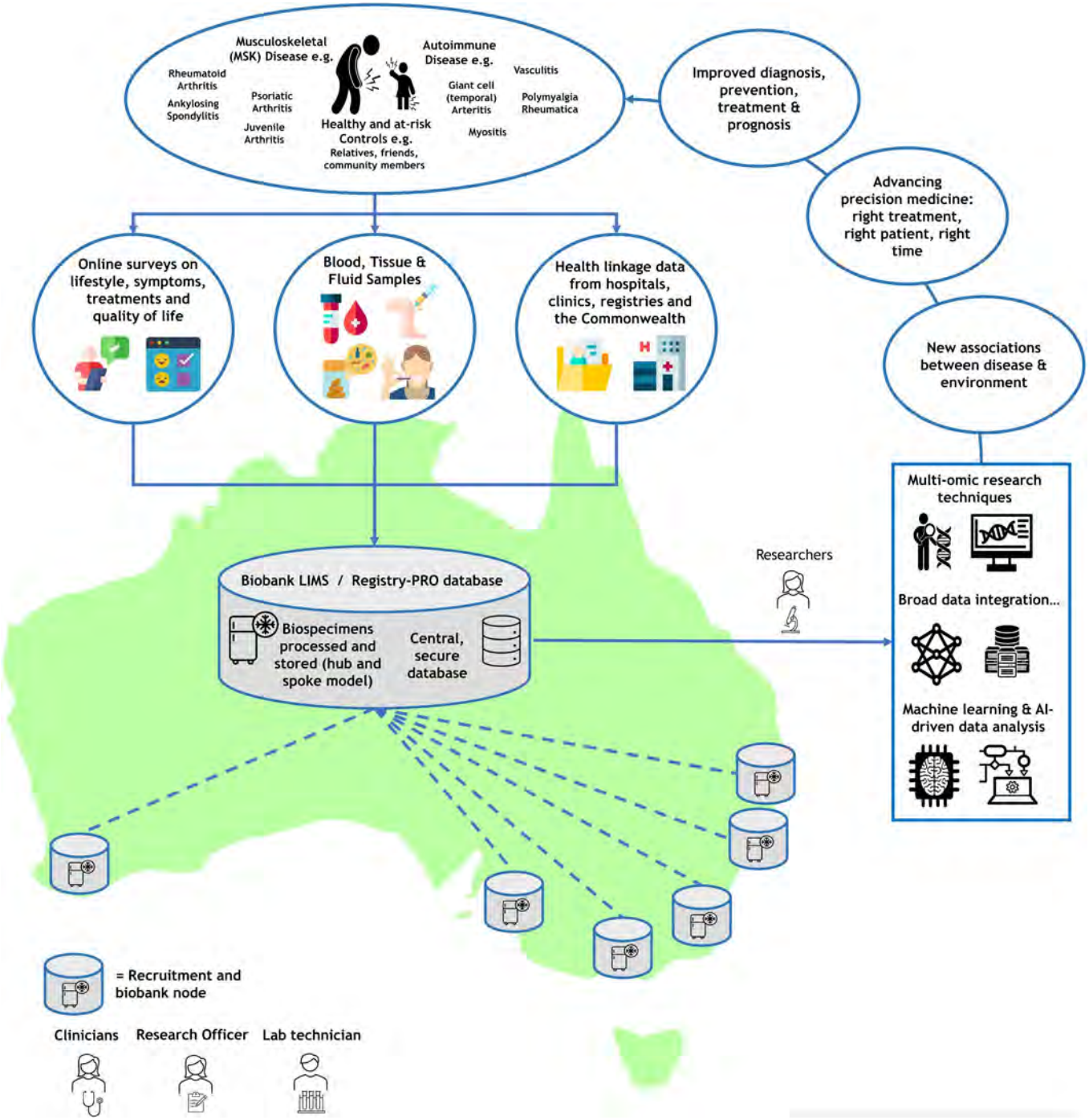

Figure 1. The A3BC is a national arthritis and autoimmune disease biobank-registry network developing state-of-the-art data collection, data linkage and big data analytics (incl. machine-learning) capabilities for better enabling and translating research discovery. It integrates a broad range of 'omic' (genomic, microbiomic etc), patient-reported (demographics, treatment, quality of life, diet etc), medical and administrative health data from people adults and children across Australia. Collected data and biological samples are deidentified and made available for ethics-approved research into understanding the causes, improving treatments or preventions, and finding cures for arthritis and autoimmune conditions.

and administrative health data domains, collected to enable holistic multidisciplinary research towards improved outcomes for people living with arthritis and autoimmune conditions (Figure 1).

Methods: We assessed several international commercial and non-profit software platforms using standardised system requirement criteria and follow-up interviews. Vendor compliance scoring was prioritised to meeting our project-critical requirements. Consumer / end-user co-design was integral to refining our system requirements for optimised adoption. Customisation of the selected software solution was performed to optimise field auto-population between participant timepoints and forms, using external modules that do not impact core code. Institutional and independent testing was used to ensure data security.

Results: We selected the widely used research web application, Research Electronic Data Capture (REDCap), which is "free" for non-profit REDCap Consortium members. REDCap is highly configurable and customisable to a variety of biobank and registry needs and can be developed/ maintained by end-users with modest IT skill, time and cost. We created a secure, comprehensive participant-centric biobank-registry database that includes best practice data security measures (incl login for multi-site access using academic and government user credentials), permission-to-contact and dynamic itemised e-consent (Figure 2A), a complete chain of custody from consent to biospecimen/data collection to publication, complex longitudinal patient-reported surveys, a fully integrated biobanking workflow (Figure 2B), disease-specific case report forms (Figure 2C), integration of record-level extracted/ linked participant data, significant form auto-population for streamlined data capture, and native dashboards for operational visualisations. The system (Figure 3) has the capacity to enrol participants with a range of diagnoses as well as healthy or at-risk controls (e.g. first degree relatives).

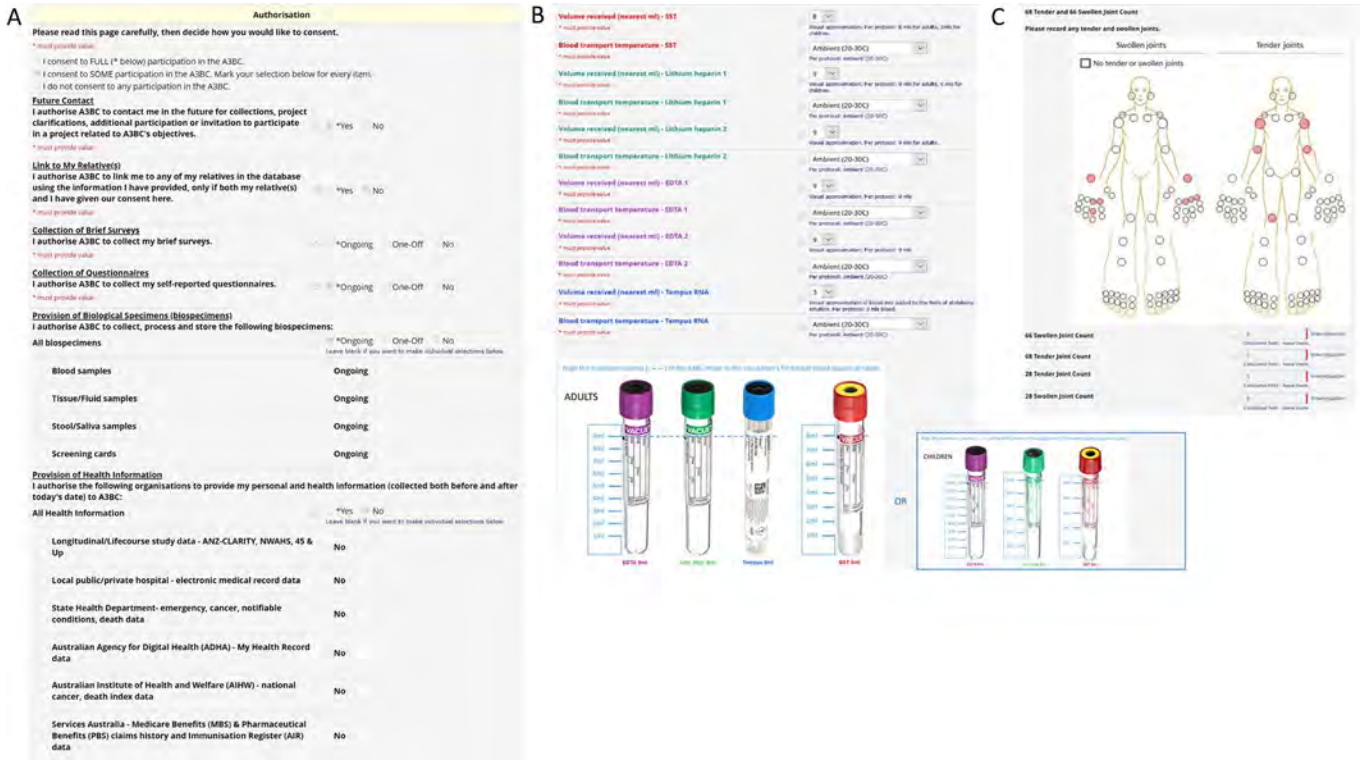

Figure 2. (A) In line with global trends in clinical research we created a Permission to Contact (PTC) and dynamic electronic consent (eConsent) strategy to maximise patient engagement in our biobank-registry. (B) We made extensive use of REDCap's action tag, smart variable and external module functionalities for defining auto-population and branching logic rules to dramatically reduce user effort in recording pre-analytical variables, an important aspect of biobank quality management and tracking for downstream applications. (C) An interactive 66 swollen / 68 tender joint count data collection tool was designed and implemented in our electronic case report form (eCRF) using the REDCap Image Map external module. Joint map image use permission granted by the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA)-Outcome Measures in Rheumatology (OMERACT).

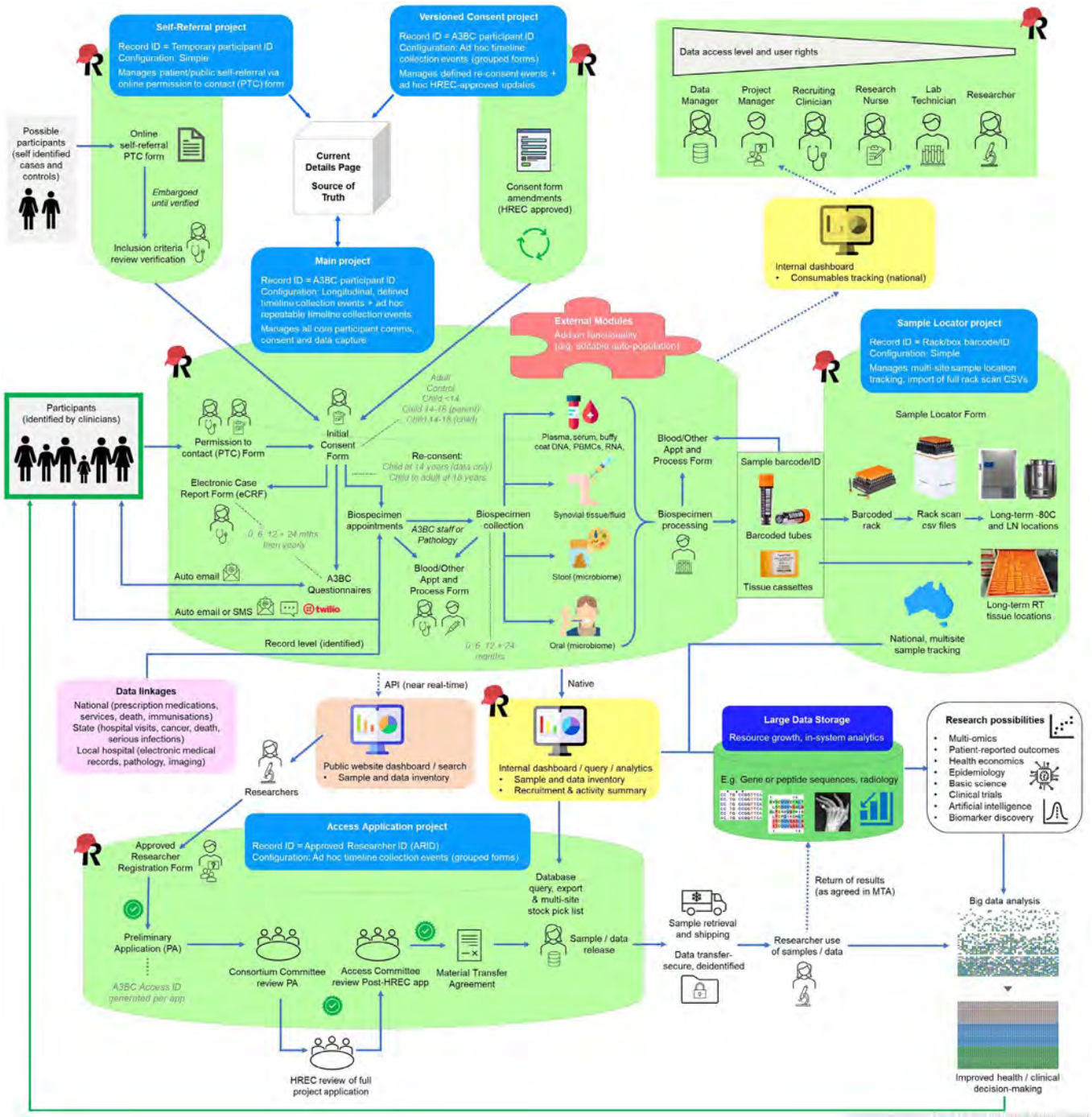

Figure 3. To enable both participant- and sample-centric functionalities, the system was designed as five linked REDCap projects, each representing a relational data table. Several unique linkage keys are used across the A3BC database tables to ensure a complete chain of custody is maintained from the point of collection through to storage, transfer, return of results and publication. Of note, we customised a 'Current Details' form as our central source of truth for participant contact details, consent status and collected samples. This form uses an underlying external module for hierarchical field auto-population to pull changes in specified fields from different locations across the Main project into a single location.

Conclusion: We utilised REDCap to develop an economical, easily-adaptable and sustainable model and recommend it for prospective chronic disease biobanks or biobank-registry projects supporting research into disease prediction, targeted treatments and prevention strategies.

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Abstract Number: 0854

Confirmatory Factor Analysis of the Fatigue Assessment Instrument and Fatigue Severity Scale in Systemic Sclerosis

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Background/Purpose: Fatigue is a prevalent, debilitating symptom across chronic diseases that is difficult to treat and negatively impacts patients' quality of life. Patients with rheumatologic diseases, such as systemic sclerosis (SSc), report high levels of fatigue. The 29-item Fatigue Assessment Instrument (FAI) is an expanded version of the 9-item Fatigue Severity Scale (FSS). The FAI is multidimensional and yields 4 subscales measuring different components of fatigue (global severity, situation specific, psychological consequences, responds to rest/sleep), while the FSS is unidimensional and has been more widely used to assess fatigue in chronic disease populations. However, there have been few psychometric studies of the FAI and FSS in SSc, and structural validity has yet to be assessed. The present study examined the previously established 1-factor structure of the FSS and the 4-factor structure of the FAI in an SSc sample.

Methods: SSc patients (*N* = 390; 84.1% female; 59.0% diffuse SSc; 52.1% White, 26.2% Hispanic, 17.7% Black) were sampled from the *G*enetics versus *EN*vironment *I*n *S*cleroderma *O*utcome *S*tudy (GENISOS). GENISOS is a

multicenter, prospective cohort study of early SSc patients based in Texas. All patients fulfilled the ACR/EULAR classification criteria for SSc and had disease duration < 5 years at enrollment. Confirmatory factor analysis was used to assess the 1-factor structure of the FSS and the 4-factor structure of the FAI. Cronbach's coefficient alpha and McDonald's omega were used to evaluate internal consistency reliability.

Results: The 1-factor model of fatigue demonstrated good model fit for the FSS based on 2 indices (Comparative Fit Index [CFI] = .96, Standardized Root Mean Residual [SRMR] = .04). The Root Mean Square Error of Approximation (RMSEA) indicated slightly less than acceptable model fit (RMSEA = .09). All standardized factor loadings for items were statistically significant (all *p*s < .001), with values ranging from .338 to .842. The 4-factor model of fatigue demonstrated acceptable model fit for the FAI based on 2 indices (SRMR = .07, RMSEA = .08). However, the Comparative Fit Index (CFI) indicated less than acceptable model fit (CFI = .86). All standardized factor loadings for items were statistically significant (all *p*s < .001), with values ranging from .23 to .82. The FSS (α = .89, ω = .90) and the global fatigue severity subscale of the FAI had adequate internal consistency reliability (α = .92, ω = .92). The other 3 FAI subscales had Cronbach's coefficient alpha and McDonald's omega values ranging from .62 to .69.

Conclusion: Findings provided support for the expected factor structure of both the FSS and the FAI. However, given the superior model fit of the FSS, the lower internal consistency reliability of 3 subscales of the FAI, and that only 22 of the 29 items on the FAI are scored, the FSS is recommended for use as a general, more efficient measure of fatigue in SSc patients.

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Abstract Number: 0855

Asymptomatic Coronary Artery Disease Assessed by Coronary Computed Tomography in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
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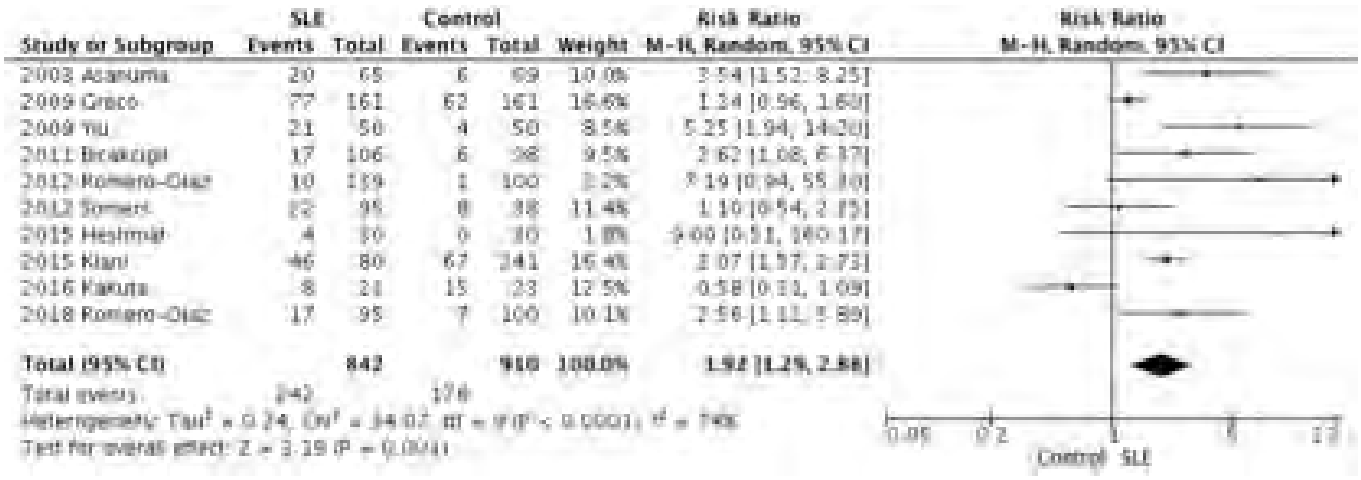
Session Time: 8:30AM–10:30AM

Background/Purpose: To date, the prevalence and prognosis of coronary artery disease (CAD) according to the coronary calcium score (CCS) and coronary artery calcification (CAC) using coronary computed tomography in patients with rheumatic diseases, including systemic lupus erythematosus (SLE), have been investigated in various studies, but with conflicting results. The latest American Heart Association and American College of Cardiology (AHA/ACC) guidelines for the primary prevention of atherosclerotic cardiovascular disease (CVD) permit the CAC score to be used in intermediate-risk patients, in whom additional individual risk-enhancing clinical factors such as chronic inflammatory disease, such as SLE are present, if the risk level is uncertain.

Table 1. Characteristics of the studies included

Author and publication year	N (SLE/Controls)	Type of controls	Ethnicity SLE%/Controls %	Type of CT scanner
Asanuma 2003	65/69	Age, sex and race-matched controls	Caucasian 72/75	EBCT
Kao 2008	105/105	Age and race-matched healthy controls	Caucasian 96.2/96.2	EBT
Greco 2009	161/161	Age and race- matched healthy women from population study	Caucasian 88/90	EBCT
Yiu 2009	50/50	Age and sex-matched controls	Chinese 100/100	MDCT
Bicakcigil 2011	106/98	Age, sex, BMI, waist/hip-matched controls	NA	MDCT
Romero-Diaz 2012	139/100	Age and sex-matched controls	Hispanics 100/100	MDCT
Somers 2012	95/38	Age and sex-matched controls from population study	White 84.2/89.5	MDCT
Heshmat 2015	30/30	Age and sex-matched control	Egyptian 100/100	MDCT
Kiani 2015	80/241	Controls from population study	Caucasians 65/41 African American 31/59	MDCT
Kakuta 2016	21/23	NA	Japanese 100/100	MDCT
Romero-Diaz 2018	95/100 (only men)	Age-matched controls	Hispanics 100/100	MDCT
Purmalek 2019	64/30	Age and gender-matched controls	Caucasians 39/53 African American 20/17	MDCT
Stojan 2020	72/100	Not matched controls	Caucasians 70.8/71.3 African American 23.6/5.3	MDCT

EBCT: electron beam computed tomography; MDCT: multi-detector computed tomography; NA: not available.



Meta-analysis of the weighted mean differences (WMD) of coronary calcium score in patients with SLE compared to controls.

The aim of this systematic review and meta-analysis was to synthesize the evidence on this topic.

Methods: Relevant literature was identified and evaluated from inception until January 2021 through multiple search strategies on PubMed, Embase, Web of Science and Cochrane library. Cross-sectional or cohort (baseline data) studies reporting CAC prevalence and the extent of CAC identified by the CCS were included. Data extracted from eligible studies were used to calculate estimated effect sizes (ESs) and 95% confidence intervals (95%CI) and weighted mean differences (WMD) with 95% CI (PROSPERO registration number: CRD42021228710).

Results: The search retrieved 80 articles, of which 23 were eligible for inclusion. For the CAC prevalence, 10 studies were included (842 SLE patients and 910 controls) and the pooled prevalence of the random effect size was 28.7% (95%CI 25.7-31.9%) for SLE patients and 19.3% (95%CI 16.2-21.4%) in controls (RR 1.92, 95%CI 1.3 to 2.9; p< 0.0001) with substantial heterogeneity (I^2= 74%, p < 0.0001) (Fig 1) and there was no significant increase in the WMD for CCS (MD= 0.32, 95%CI -5.55 to 6.20, p= 0.91 and I2= 50%, p= 0.06) compared with controls (Fig 2), using data from 7 studies. Limited evidence suggests that patients with SLE had more multivessel CAD. Greater organ damage was associated with a higher CCS. Glucocorticoid use was associated with both prevalence or progression in CAC. According to two studies, coronary computed tomographic angiography showed the calcified and non-calcified plaque burden were increased in SLE patients compared with controls.

Conclusion: In patients with SLE, asymptomatic CAD by CAC is more prevalent and shows more multivessel disease compared with controls without lupus. However, the extent of CAC was not increased in SLE patients.

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Abstract Number: 0856

Identifying COVID-19 Infection Rates and Outcomes in Patients with Systemic Lupus Erythematosus

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Background/Purpose: The risk of COVID-19 infection among patients with Systemic Lupus Erythematosus (SLE) is poorly understood. Patients with SLE often take medications which modulate the immune system, and some were of interest as possible therapies for COVID-19. It is not fully understood if taking these medications may be associated with an increased or decreased risk of contracting COVID-19. This survey sought to investigate the rate of COVID-19 infection among our patients with SLE, identify disease severity among infected patients, and identify any correlation between ongoing treatment and the diagnosis of COVID-19.

Methods: We identified all patients with SLE seen in the Rheumatology clinic between January 2018 and March 2020. Patients were contacted via telephone from June 2020 through August 2020 to complete a questionnaire. Data were collected by chart review and by a telephone questionnaire. We recorded data on patient demographics, medication regimen, COVID-19 diagnosis and complications, and social distancing practices. A logistic regression was performed to identify possible risk factors for being diagnosed with COVID-19.

Results: 245 patients with SLE were identified. 129 (52%) completed the telephone questionnaire. The COVID-19 status was known for 137 patients, either through chart review or by the telephone survey. The most commonly used medications were hydroxychloroquine (82.2%), prednisone (45.7%), and mycophenolate mofetil (32.6%).14 (10.2%) patients were diagnosed with COVID-19. Among these patients, 4 were hospitalized, 2 received intensive care-unit level of care, and 3 died. There were no deaths attributed to active lupus in the patients that were surveyed. The odds

of being diagnosed with COVID-19 were not significantly higher in patients treated with steroids (OR 1.08, 95% CI 0.36 to 3.28), hydroxychloroquine (OR 0.84, 95% CI 0.22 to 3.27), mycophenolate mofetil (OR 0.57, 95% CI 0.15 to 2.14), belimumab (OR 2.76, 95% CI 0.51 to 14.82), leflunomide (OR 3.08, 95% CI 0.30 to 31.77) or azathioprine (OR 1.01, 95% CI 0.20 to 4.94). Known contact with someone who had COVID-19 was associated with an increased risk of being diagnosed with COVID-19 (OR 7.79, 95% CI 1.43 to 42.38). The odds of contracting COVID-19 were not increased with comorbid lung disease (OR 0.61, 95% CI 0.16 to 2.31), gender (OR 1.09, 95% CI 0.12 to 8.76), smoking history (OR 1.49, 95% CI 0.43 to 5.15), age above median (47 years, OR 0.51, 95% OR 0.16 to 1.61), or weight above median (76.7 kg, OR 1.02, 95% CI 0.34 to 3.07). The median subjective disease activity score determined by the patient on a scale of 0-10 was 3.

Conclusion: Immunosuppressive treatment was not associated with increased odds of contracting COVID-19. Our infection rate of 10.2% is within the range of percentage of total Brooklyn residents testing positive for COVID-19 (3.08% - 13.97% per the New York Times New York City Coronavirus Map and Case Count database). Patients with SLE do not appear to have an elevated risk of COVID-19 compared to the general population. Surveyed patients felt that their SLE was fairly well controlled during the pandemic.

Disclosure: A. Hall, None; **M. Trevisonno**, None; **E. Murray**, None; **O. Tisor**, None; **E. Stanford**, None; **J. Gaines**, None; **N. Anvery**, None; **E. Ginzler**, None.

Abstract Number: 0857

Association of Telomere Length with Phenotypic Frailty in Systemic Lupus Erythematosus

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Session Date: Sunday, November 7, 2021
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Background/Purpose: Frailty is a novel risk factor for adverse health outcomes in systemic lupus erythematosus (SLE). Although frailly is conceptualized as "accelerated aging," whether the frailty phenotype is associated with physiologic biomarkers of aging is unclear. Shortened telomere length reflects cellular senescence in older adults.

Table 1. Prevalence of frailty and individual components by frailty definition

Fried phenotype (N=52)		**FRAIL scale (N=52)**	
Component	N (%)	*Component*	N (%)
Weight loss	13 (25.0)	Weight loss	13 (25.0)
Fatigue	21 (40.4)	Fatigue	27 (51.9)
Slow gait	9 (17.3)	Ambulation	20 (38.5)
Weakness	28 (53.8)	Resistance	21 (40.4)
Inactivity	9 (17.3)	Not applicable	
Not applicable		Comorbidity	2 (3.8)
Overall	N (%)	*Overall*	N (%)
Frail	12 (23.1)	Frail	13 (25.0)

Table 2. Characteristics of women by frailty classification

Characteristic (Median and interquartile range unless otherwise specified)	Fried phenotype (N=52)			FRAIL scale (N=52)		
	Non-frail (N=40)	Frail (N=12)	p-value	Non-frail (N=39)	Frail (N=13)	p-value
Age (years)	39.0 [28.0, 56.0]	52.0 [43.0, 64.0]	0.07	44.0 [30.0, 56.0]	50.0 [33.0, 59.5]	0.37
Race, N (%)†			0.11			0.37
Asian	1 (2.5)	0 (0)		1 (2.6)	0 (0)	
Black or African American	7 (17.5)	6 (50.0)		8 (20.5)	5 (38.5)	
White	9 (22.5)	1 (8.3)		8 (20.5)	2 (15.4)	
Other or declined to state	23 (57.5)	5 (41.7)		22 (57.4)	6 (46.1)	
Ethnicity, N (%)†			0.10			0.08
Hispanic	11 (27.5)	2 (16.7)		12 (42.9)	1 (11.1)	
Non-Hispanic	17 (42.5)	7 (58.3)		16 (57.1)	8 (88.9)	
SLE disease duration (years)	12.0 [8.5, 24.5]	11.5 [6.5,14.5]	0.38	12.0 [8.0, 22.0]	12.0 [10.0, 16.0]	0.37
SELENA-SLEDAI* score	4.0 [2.0, 5.0]	4.0 [2.0, 7.0]	0.51	4.0 [2.0, 5.0]	3.0 [1.0, 5.5]	0.45
SLICC/ACR Damage Index** score	0 [0 1.0]	1.5 [1.0, 3.5]	<0.01	0.0 [0.0, 2.0]	1.0 [1.0, 3.0]	<0.01
Charlson Comorbidity Index	2.5 [1.0, 3.0]	3.5 [2.5, 5.0]	0.01	2.0 [1.0, 3.0]	4.0 [3.0, 4.0]	<0.01
Current prednisone dose (milligrams)	1.5 [0, 7.8]	5.0 [2.0, 10.0]	0.19	0 [0, 8.0]	5.0 [2.0, 10.0]	0.03
Ever smoking, N (%)	3 (7.5)	5 (41.7)	0.01	2 (5.1)	6 (46.2)	<0.01
Self-reported fibromyalgia, N (%)	9 (22.5)	3 (25.0)	0.99	11 (28.2)	1 (7.7)	0.11
Telomere length (kilobases)	7.3 [6.7, 7.6]	6.5 [6.4, 6.9]	<0.01	7.2 [6.5, 7.6]	6.7 [6.4, 7.3]	0.18

*SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Scores range from 0-105, with higher scores indicating greater disease activity.

**SLICC/ACR Damage Index: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Scores range from 0-46, with higher scores indicating greater damage.

†>10% missing

Although preliminary evidence suggests that telomere length is not associated with a SLE-specific cumulative deficits definition of frailty in adult women with SLE [1], to our knowledge, the relationship between telomere length and phenotypic definitions of frailty has not been assessed in women with SLE. We aimed to evaluate differences in telomere length between frail and non-frail women with SLE and to assess whether telomere length is independently associated with frailty after controlling for multiple potential confounders.

Table 3. Cross-sectional association of telomere length with frailty

Model	Fried phenotype (N=52)		FRAIL scale (N=52)	
	Odds ratio	*95% confidence interval*	*Odds ratio*	*95% confidence interval*
Unadjusted	0.19	0.06-0.65	0.60	0.25-1.46
Adjusted for age	0.26	0.07-0.96		
Adjusted for age and disease damage	0.21	0.04-1.03		

Methods: Women ≥18 years old with SLE validated according to the 2019 European League Against Rheumatism/ American College of Rheumatology Classification Criteria were enrolled at a single center. Frailty status according to both the Fried phenotype (FP), which includes objective and self-report components, and the FRAIL scale (FS), an exclusively self-report instrument, were measured at a single study visit. Telomere length was determined from whole blood drawn at the same visit using Southern analysis of terminal restriction fragments. Sociodemographic features and physician-reported disease activity and damage also were collected. Differences between frail and non-frail participants were evaluated using Fisher's exact or Wilcoxon rank sum tests. The association of telomere length with frailty was assessed using logistic regression.

Results: Data from 52 participants were available for this interim analysis. 12 (23.1%) and 13 (25.0%) of women were classified as frail according to the FP and the FS, respectively, despite median age of 50-52 years old (Tables 1 and 2). Frail women according to both metrics had greater comorbidity burden (FP: p=0.01; FS: p< 0.01), more organ damage (FP: p< 0.01; FS: p< 0.01), and a higher prevalence of cigarette smoking (FP: p=0.01; FS: p< 0.01) than non-frail women; frail women according to the FS also were taking more glucocorticoids compared to non-frail women (p=0.03) (Table 2). Telomere length was significantly shorter among frail versus non-frail women according to the FP (p< 0.01), but not the FS (p=0.18) (Table 2). Similarly, telomere length was significantly associated with frailty according to the FP (Odds ratio [OR] 0.19, 95% confidence interval [CI] 0.06-0.65), but not the FS. This relationship was attenuated for the FP after adjustment for age (OR 0.26, 95% CI 0.07-0.96) and further attenuated after adjustment for organ damage (OR 0.21, 95% CI 0.04-1.03) (Table 3).

Conclusion: Approximately a quarter of women with SLE were frail according to two validated frailty measures. Shorter telomere length was associated with frailty according to the FP, but not the FS, suggesting that the FP is a better measure of accelerated aging in women with SLE. Further study is needed to identify the longitudinal impact of frailty on the health of women with SLE.

Reference

1. Lima K et al. *Arthritis Rheumatol* 2020;72(suppl 10).

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Abstract Number: 0858

Effect of COVID Infection and COVID Vaccination on SLE Activity, Including Antiphospholipid Antibodies

Michelle Petri[1], Jessica Li[2] and Daniel Goldman[1], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: SLE patients may have a particular propensity to some viral infections including zoster and CMV. International studies have suggested that prednisone and rituximab may be risk factors for COVID in rheumatic disease patients. One study found that 50% of hospitalized patients (not SLE) made antiphospholipid antibodies. In this study we compared disease activity, and antiphospholipid antibodies both before and after COVID-19 infection and vaccination.

Methods: Patients enrolled in a lupus cohort had data on COVID-19 testing and vaccination status prior to May, 2021 collected. A positive RNA test was required to confirm COVID-19 infection. Dates of vaccination and vaccine source were recorded. All patients met ACR and/or SLICC criteria for SLE. The lupus activity index (0-3 visual acuity scale: LAI), SELENA SLE disease activity index (SLEDAI) and laboratory values were collected at each visit. To compare the pre and post COVID infection/vaccination, paired t-test was used for continuous variables and McNemar's test was used for categorical variables.

Results: Out of 860 patients in the cohort, 65 patients had a positive COVID-19 RNA test. 38 of these patients had at least one visit within 6 months before and after the COVID date. Table 1 shows the effect of COVID-19 on disease activity and laboratory values. On average, the LAI-rash score was lower after COVID infection. Anticardiolipin (aCL) IgG and anticardiolipin IgM increase after COVID infection. 228 patients had COVID-19 vaccine: 10 had Johnson & Johnson; 94 had Moderna; 124 had Pfizer. 13 patients were positive for COVID-19 prior to vaccination. 98 patients had at least 1 visit within 6 months before vaccine and at least one visit after vaccine. Table 2 shows the effect of COVID-19 vaccination on disease activity and laboratory values.

Conclusion: : COVID infection did not lead to an increase in SLE activity. Instead there was a decrease in cutaneous activity (perhaps explained by quarantine). There was an increase in aCL IgG and IgM post infection, but COVID vaccination did not increase SLE activity and did not increase antiphospholipid antibody levels.

Table 1. Effect of COVID infection on disease activity and laboratory measurements

		Average of visits within 210 days before and after infection			Closest visit before and after infection		
	n	Before COVID infection	After COVID infection	p-value	Before COVID infection	After COVID infection	p-value
PGA	31	0.81 (0.6)	0.73 (0.77)	0.4861	0.81 (0.62)	0.73 (0.77)	0.5035
SLEDAI	31	3.02 (2.7)	2.06 (1.97)	0.0794	3.26 (3.33)	2.06 (1.97)	0.0635
LAI-fatigue	31	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-rash	31	0.19 (0.3)	0.1 (0.2)	**0.0325**	0.19 (0.31)	0.1 (0.2)	**0.0314**
LAI-joints	31	0.34 (0.43)	0.21 (0.4)	0.1752	0.34 (0.45)	0.21 (0.4)	0.2111
LAI-serositis	31	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-neuro	31	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-renal	31	0.34 (0.68)	0.42 (0.84)	0.4594	0.37 (0.73)	0.42 (0.84)	0.6125
LAI-pulmonary	31	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-hematologic	31	0.11 (0.28)	0.07 (0.21)	0.0908	0.1 (0.24)	0.07 (0.21)	0.3915
Log(Anti-DNA)	34	0.79 (1.55)	0.93 (1.62)	0.2638	0.78 (1.59)	0.93 (1.62)	0.2484
C3	34	125.81 (22.14)	126.59 (19.43)	0.7179	127.65 (23.52)	126.59 (19.43)	0.6443
C4	34	22.44 (9.12)	22.06 (9.01)	0.5224	22.79 (9.74)	22.06 (9.01)	0.2491
RVVT	30	37.31 (8.82)	37.73 (11.79)	0.7640	36.63 (11.52)	38.2 (11.66)	0.4017
aCL IgG	32	9.26 (1.92)	10.63 (2.34)	**0.0016**	9.75 (2.17)	10.63 (2.34)	**0.0102**
aCL IgM	32	15.6 (23.97)	17.69 (24.97)	**0.0068**	16.25 (25.33)	17.69 (24.97)	**0.0533**
aCL IgA	32	9.34 (3.72)	9.69 (2.52)	0.3869	9.66 (3.59)	9.69 (2.52)	0.9293
aB2 IgG	12	8.25 (0.45)	8.17 (0.39)	0.3388	8.25 (0.45)	8.17 (0.39)	0.3388
aB2 IgM	12	8.67 (1.44)	11.5 (5.76)	0.0803	8.67 (1.44)	11.5 (5.76)	0.0803
aB2 IgA	12	20.67 (38.89)	21.33 (41)	0.4739	20.17 (39.02)	21.33 (41)	0.3810
Triamcinolone	31	5 (16.1%)	3 (9.7%)	0.4142	4 (12.9%)	3 (9.7%)	0.6547

Table 2. Effect of COVID vaccination on disease activity and laboratory measurements

		Average of visits within 210 days before and after vaccine			Closest visit before and after vaccine		
	n	Before COVID vaccine	After COVID vaccine	p-value	Before COVID vaccine	After COVID vaccine	p-value
PGA	35	0.83 (0.58)	0.85 (0.69)	0.9050	0.87 (0.61)	0.82 (0.7)	0.7058
SLEDAI	35	3.17 (2.55)	2.46 (2.8)	0.1729	3.18 (2.73)	2.55 (2.85)	0.2783
LAI-fatigue	35	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-rash	35	0.25 (0.41)	0.14 (0.38)	0.0489	0.24 (0.47)	0.14 (0.38)	0.0897
LAI-joints	35	0.53 (0.48)	0.47 (0.59)	0.4648	0.61 (0.56)	0.45 (0.6)	0.0670
LAI-serositis	35	0 (0.02)	0.09 (0.37)	0.1994	0 (0)	0.09 (0.38)	0.1837
LAI-neuro	35	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-renal	35	0.28 (0.57)	0.37 (0.69)	0.3956	0.23 (0.54)	0.34 (0.68)	0.2914
LAI-pulmonary	35	0 (0)	0 (0)	/	0 (0)	0 (0)	/
LAI-hematologic	35	0.06 (0.2)	0.11 (0.25)	0.2004	0.07 (0.21)	0.12 (0.25)	0.2125
Log(Anti-DNA)	63	1.42 (2.08)	1.47 (2.11)	0.6158	112.33 (26.57)	110.63 (24.52)	0.2532
C3	63	111.94 (26.88)	111.11 (24.03)	0.5417	22.67 (8.86)	23.25 (9.19)	0.1807
C4	59	22.28 (8.52)	23.21 (9.27)	0.0178	1.37 (2.11)	1.44 (2.08)	0.5479
RVVT	58	42.75 (14.06)	42.56 (12.09)	0.8466	43.22 (15.46)	42.62 (12.02)	0.6189
aCL IgG	60	12.35 (7.95)	12.82 (4.18)	0.4290	12.82 (7.58)	12.82 (4.11)	1.0000
aCL IgM	58	11.89 (6.08)	11.81 (6.26)	0.7752	12.97 (11.32)	11.78 (6.16)	0.0932
aCL IgA* all titers were between 8 and 10 units	58	9.43 (0.72)	9.67 (0.73)	0.0045	9.62 (0.74)	9.68 (0.72)	0.3983
aB2 IgG	11	8.55 (1.51)	8.55 (1.81)	1.0000	8.46 (1.39)	8.46 (1.66)	1.0000
aB2 IgM	11	22.18 (42.87)	8 (0)	0.2983	20 (39.5)	8 (0)	0.2948
aB2 IgA	11	16.64 (20.72)	17.27 (23.49)	0.6282	16.92 (19.41)	18.15 (22.4)	0.3448
Triamcinolone	35	21 (60%)	12 (34.3%)	0.0027	17 (48.6%)	11 (33.3%)	0.0956

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Abstract Number: 0859

Evaluation of the Montreal Cognitive Assessment as a Screening Tool for Cognitive Dysfunction in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Cognitive dysfunction (CD) affects approximately 40% of SLE patients (1), impacting on employment, daily function, and quality of life (2)(3). Diagnostic neuropsychological testing is time-consuming and requires specialised staff, limiting access and resulting in under-detection in routine practice. Therefore, effective screening of SLE patients in the clinical setting is essential in selecting patients for formal cognitive testing. The Montreal Cognitive Assessment (MoCA) is a brief screening tool, initially designed to screen for mild cognitive impairment (MCI) or dementia, which preliminary studies suggest may have utility in SLE. This study aimed to comprehensively evaluate the MoCA as a screening tool for CD in SLE.

Methods: We tested SLE patients (n=95) and demographically matched healthy control (HC) participants (n=48) using the MoCA and the one-hour neuropsychiatric test battery recommended by the ACR for use in SLE (4). CD in SLE patients was defined using standard deviations from the HC group mean. We compared three CD

Table 1. Multivariate Analysis of the Montreal Cognitive Assessment (MoCA), Age and Cognitive Test Results in SLE. CI = Confidence Interval, *p value <0.05 **p value <0.005. Premorbid IQ was highly collinear with MoCA score and therefore was not included in the multivariate model. 1) Impairment defined by number of cognitive domains either 1.5 or 2 SD below healthy control group mean. 2) Specific cognitive tests used for each domain are as follows: Visual Memory - Rey Ostrrieth Complex Figure Test Recall Score, Verbal Memory -California Verbal Learning Test trials 1-5, Verbal Fluency - Controlled Oral Word Association Test FAS Sum, Working Memory - Letter Number Sequencing score, Processing Speed - Coding score, Complex Attention - Trail making test B time inverse, Psychomotor speed - finger tap test dominant hand score. Test scores were expressed as Z-scores in comparison to healthy control group data.

	Cognitive Impairment Definitions[1]			**Individual Cognitive Domains[2]**						
	2 domains 1.5 SD below	1 domain 2 SD below	2 domains 2 SD below	Visual Memory	Verbal Memory	Verbal Fluency	Working Memory	Processing Speed	Complex attention	Psychomot or Speed
	Odds ratio (CI) using logistic regression			Coefficient (CI) using linear regression						
Age	**1.08**** (1.02-1.13)	**1.07*** (1.02-1.12)	**1.10*** (1.02-1.17)	**-0.04**** (-0.06--0.02)	**-0.02*** (-0.03- -0.01)	0.004	-0.01	**-0.02**** (-0.03- -0.01)	**-0.03**** (-0.05- -0.02)	**-0.03**** (-0.05- - 0.02)
MoCA score	**0.44**** (0.31-0.63)	**0.49**** (0.36-0.67)	**0.49**** (0.35-0.69)	**0.26**** (0.17-0.36)	**0.16**** (0.09-0.22)	**0.24**** (0.17-0.30)	**0.14**** (0.08-0.20)	**0.12**** (0.06-0.18)	**0.28**** (0.20-0.36)	0.07

definitions, all based on thresholds from the 2007 ACR response criteria for neurocognitive impairment in SLE clinical trials (5). We used regression analyses to determine associations between MoCA and cognitive test scores, and assessed sensitivity, specificity, positive predictive value and negative predictive value of various MoCA cut-offs for predicting CD. We then determined the diagnostic accuracy of MoCA cut-off thresholds using receiver operator curves.

Results: The SLE and HC groups were well matched with no significant differences in age, gender, ethnicity, premorbid IQ or education level. The median age was 45 (range 22-64), 60% were Caucasian and the rest predominantly Asian, and all had good English proficiency. The prevalence of CD in the SLE group varied from 19% to 49% depending on the definition used; the median MoCA score was 26 (range 19-30). On multivariate analysis, MoCA score correlated significantly with nine of the ten cognitive endpoints studied (all $p < 0.001$; Table 1). Receiver operator curve analysis suggested that the MoCA cut-off of < 27 yielded the highest diagnostic accuracy across the three cognitive impairment definitions (AUC 0.76-0.78; Figure 1). The MoCA cut-off of < 28 had sensitivity of 83-94% with specificity of 46-58%, depending on the impairment definition used (Table 2).

Table 2. Sensitivity, Specificity, Positive Predictive Value and Negative Predictive Value of Montreal Cognitive Assessment (MoCA) for detection of Cognitive Impairment in SLE. 1) Defined by number of cognitive domains either 1.5 or 2 SD below healthy control group mean. Acronyms: HC – Healthy Control, PPV – Positive Predictive Value, NPV – Negative Predictive Value.

Table 2a: Sensitivity and Specificity of Montreal Cognitive Assessment (MoCA) for detection of Cognitive Impairment in SLE

	Cognitive Dysfunction Definitions[1]					
	2 domains ≥1.5 SD below HC		1 domains ≥2 SD below HC		2 domains ≥2 SD below HC	
MoCA cut off	Sensitivity	Specificity	Sensitivity	Specificity	Sensitivity	Specificity
<24	21.3%	100.0%	23.1%	98.2%	38.9%	96.1%
<25	36.2%	97.9%	38.5%	94.6%	61.1%	90.9%
<26	46.8%	93.8%	48.7%	89.3%	72.2%	84.4%
<27	72.3%	83.3%	74.4%	76.8%	88.9%	66.2%
<28	83.0%	58.3%	87.2%	55.4%	94.4%	45.5%
<29	91.5%	35.4%	92.3%	32.1%	100.0%	26.0%
<30	95.7%	20.8%	97.4%	19.6%	100.0%	15.6%

Table 2b: Positive and Negative Predictive Value of Montreal Cognitive Assessment (MoCA) for detection of Cognitive Impairment in SLE

	Cognitive Impairment Definitions[1]					
	2 domains 1.5 SD below		1 domains 2 SD below		2 domains 2 SD below	
MoCA cut off	PPV	NPV	PPV	NPV	PPV	NPV
<24	100.0%	56.5%	90.0%	64.7%	70.0%	87.1%
<25	94.4%	61.0%	83.3%	68.8%	61.1%	70.0%
<26	88.0%	64.3%	76.0%	71.4%	52.0%	92.9%
<27	81.0%	75.5%	69.1%	81.1%	38.1%	96.2%
<28	66.1%	77.8%	57.6%	86.1%	28.8%	97.2%
<29	58.1%	81.0%	48.7%	85.7%	19.0%	95.2%
<30	54.2%	83.3%	45.8%	91.7%	21.7%	100.0%

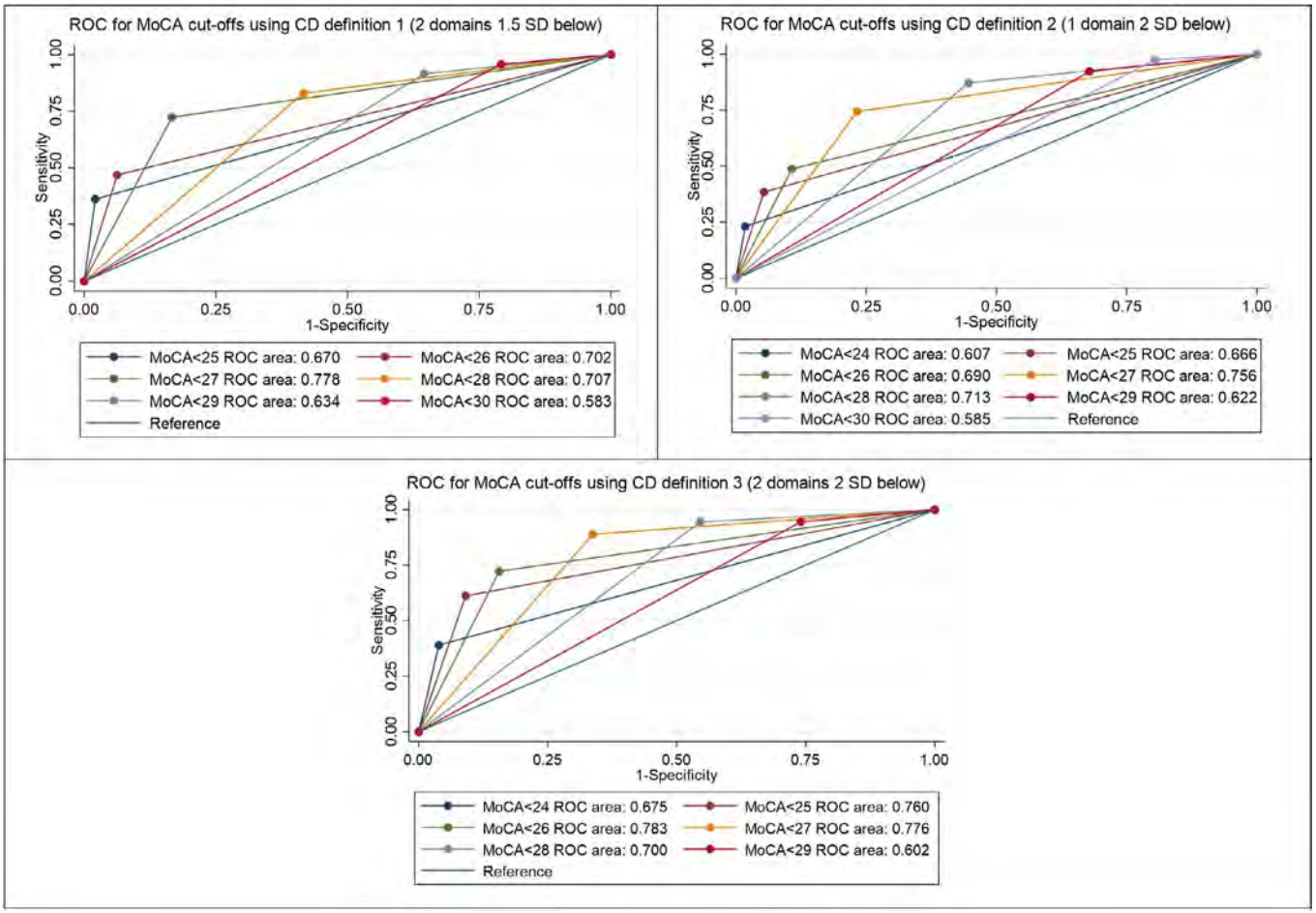

Figure 1. Receiver Operating Curves (ROC) for different Montreal Cognitive Assessment (MoCA) cut-offs by Cognitive Dysfunction (CD) Definition. Area under the curve interpretation: 0.7-0.9 = moderate accuracy, 0.5-0.7 = low accuracy, ≤0.5 = equal to chance.

Conclusion: The MoCA correlates strongly with gold-standard cognitive test results in SLE and is sufficiently sensitive for use in screening. We recommend the MoCA cut-off of < 28 as the threshold with the optimal sensitivity for screening for CD in SLE to ensure potential cases are detected. This threshold is higher than the MoCA cut-off used for MCI and dementia. This brief, freely available and practical tool for screening SLE patients for CD should be considered for inclusion in SLE management guidelines.

References: 1) Al Rayes et al. Semin Arthritis Rheum 2018. 2) Arntsen et al. Joint report by Lupus Research Alliance, Lupus Foundation of America & Lupus and Allied Diseases Association 2018. 3) Appenzeller et al. Arthritis Rheum 2009. 4) Liang et al. Arthritis Rheum 1999. 5) Mikdashi et al. Lupus 2007.

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Abstract Number: 0860

Associations Between Tricarboxylic Acid Cycle Plasma Metabolites and Fatigue Phenotypes in Black Females with Systemic Lupus Erythematosus: An Untargeted Metabolomics Analysis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) occurs predominantly in women and Black women have disproportionately poorer health outcomes across the trajectory of their disease compared to women of other race/ethnicities. Specifically, Black women with SLE report higher symptom burden with pervasive impacts on quality of life. Fatigue is highly prevalent in SLE patients, and is a major driver of negative disease perception and patient difficulty with steroid therapy discontinuation. However, the underlying biochemical mechanisms of fatigue in Black women with SLE are largely unknown. We conducted untargeted metabolomic plasma profiling in Black females with SLE and Black female non-SLE controls to identify metabolites and metabolic pathways associated with SLE. We then identified which of these SLE metabolites and pathway predictors were correlated with patient-reported symptoms of fatigue.

Methods: Blood samples were collected from 23 Black female patients with diagnosis of SLE during a routine outpatient rheumatology visit and from 21 Black female non-SLE controls. SLE clinical data were obtained via EMR review and all subjects completed identical, reliable and valid measures of fatigue (Multidimensional Fatigue Inventory [MFI]) and PROMIS symptom measures. A US-based commercial metabolomics analysis company conducted

MFI Subscales →	General Fatigue	Physical Fatigue	Mental Fatigue	Reduced Activity	Reduced Motivation
Citrate	-0.12	0.20	**-0.34***	-0.14	-0.23
Aconitate	0.02	0.10	-0.18	-0.09	-0.24
Alpha-ketoglutarate	0.04	**0.33***	-0.12	0.17	0.10
Succinate	0.27	**0.52***	-0.06	0.04	0.07
Fumarate	-0.14	0.19	**-0.32***	-0.21	0.02
Malate	-0.09	0.26	-0.17	-0.12	-0.03
Depression	0.03	0.37	**0.39***	**0.46***	0.27
Sleep Disturbance	0.24	0.10	**0.35***	**0.37***	**0.40***
Cognitive Function	**-0.43***	**-0.40***	**-0.60***	**-0.37***	-0.24
Pain	0.31	0.15	0.20	**0.48***	0.18
Age	-0.20	0.18	**-0.32***	-0.03	0.11
Disease Activity	**-0.40***	-0.03	-0.23	-0.29	0.1
Years with Lupus	**-0.32***	-0.27	-0.17	-0.21	0.13
BMI	**0.46***	**0.39***	0.16	0.18	-0.04
Comorbidities	-0.26	-0.12	-0.22	-0.06	0.05
Hypertension	**-0.43***	-0.28	-0.28	**-0.43***	0.15

Note: * $p < .05$, TCA Cycle metabolites noted in *italics*.

Correlations Between MFI Fatigue Subscales, TCA Cycle Metabolites, Co-Occurring Symptoms, and Clinical Variables in SLE Subjects (n=21).

untargeted metabolomics on the 44 plasma samples using ultrahigh performance liquid chromatography/tandem mass spectrometry along with metabolite identification and quantification to examine differences between SLE/non-SLE groups. Metabolites and symptom data were correlated using Kendall's Tau with a two tailed alpha of $p < .05$.

Results: All SLE subjects met 2019 EULAR/ACR diagnostic criteria. SLE subjects were significantly younger (42.5 years ± 12.2 vs. 63.2 years ± 6.4), had a lower BMI (30.3 ± 9.4 vs. 34.9 ± 4.1), and greater co-morbidities (2.3 ± 1.3 vs. 1.1 ± 1.3) than non-SLE controls. Welch's two sample t-tests revealed 290 biochemicals that were significantly different ($p \leq .05$) between SLE and non-SLE groups; with Random Forest analysis yielding a predictive accuracy of 91% in differing between the two groups. While significant metabolic differences between groups were noted in biochemicals within pathways associated with glycolysis, the TCA cycle, fatty acid metabolism, branched chain amino acids, sterols, and heme catabolism, the metabolites that associated with fatigue were within the TCA cycle, also called the Kreb's Cycle, and responsible for energy production (See table). Increased MFI physical fatigue was significantly correlated with alpha-ketoglutarate, succinate, lower cognitive function, and greater BMI. Increased MFI mental fatigue was significantly associated with fumarate, depression, sleep disturbance, lower cognitive function, and increased age.

Conclusion: Metabolites from the TCA cycle, identified through untargeted metabolomics, were significantly associated with physical and mental fatigue phenotypes in Black females with SLE. Validating these findings in a larger sample would inform potential biomarkers for fatigue as well as targets for intervention.

Disclosure: L. Kimble, None; **A. Khosroshahi**, None; **G. Brewster**, None; **N. Carlson**, None; **R. Eldridge**, None; **E. Corwin**, None.

Abstract Number: 0861

Systemic Lupus Erythematosus, a Pilot Study of a New Disease Activity Score

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous, waxing and waning, multisystem autoimmune disease. The complexity and clinical unpredictability of SLE challenge the assessment of disease activity over time, especially in every day clinical practice. Multiple clinical disease monitoring instruments have been developed, however they are limited in ability to detect change in disease activity over time or too cumbersome to be utilized in daily practice. The aim of the study is to construct a new disease activity score which will simplify and improve disease activity assessment in daily practice, and possibly serve as a better tool for clinical studies.

Methods: The new instrument for the assessment of SLE activity is comprised of 6 visual analogue scales (VAS), which separately address the physician's global assessment and 5 organ systems including: mucocutaneous, musculoskeletal, cardiorespiratory, renal and neuropsychiatric systems. Changes in blood counts, serology, and medica-

tions are recorded. The patient's own assessment, as well as treatment changes will be included in the final score. In order to assess the reliability and validity of the new score, as well as the score's sensitivity to change in disease activity, 4 paper cases, including 2 visits for each case, were constructed. Each of the visits was scored by 5 experienced rheumatologists who were not involved in the construction of the new score, using 3 validated scoring instruments: BILAG, SLEDAI, LFA-REAL, and our proposed score. The order of the instruments utilized for each scored visit and the order of patients scored by each physician were randomized.

Results: The inter-rater reliability (i.e. agreement between physicians) of the new score was good for all systems represented in the paper cases, both for single visit scores and for the change in disease activity between 2 consecutive visits (ICC (2,1) range 0.75-0.95), except for a borderline value for changes in disease activity in the renal system (0.59). The inter-rater reliability values of the new score were comparable with those of the BILAG and the LFA-REAL scoring systems. The construct (convergent) validity of the new score, as evaluated by correlation with the other 3 validated scoring instruments was good for single visit scores (Spearman correlation coefficients range 0.48-0.94). Correlation of our proposed score with the BILAG score, regarding changes in disease activity, was good when scoring the mucocutaneous, musculoskeletal and cardiorespiratory systems (0.66, 0.75, 0.83, respectively) but was poor when scoring the renal system (0.11).

Conclusion: This paper case evaluation of the new disease activity score suggests a promising and simple tool, with overall good reliability and construct validity. Further studies are ongoing to evaluate a greater diversity of real-life patients with SLE. Further psychometric evaluation is needed to refine the score and to incorporate laboratory and medication data and patient assessment.

Disclosure: D. **Paran**, None; **M. Ben-Am**, None; **L. Mendel**, None; **A. Polachek**, None; **V. Furer**, None; **O. Elalouf**, None; **J. Wollman**, None; **S. Kivity**, None; **N. Agmon-Levin**, None.

Abstract Number: 0862

Prevalence and Risk Factors for Herpes Zoster Reactivation in 1542 Patients with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To study the prevalence and risk factors of herpes zoster (HZ) infection in patients with rheumatic diseases.

Methods: Medical records of patients with rheumatic diseases who attended our out-patient rheumatology clinics between March and August, 2019 were retrospectively reviewed. Patients who were using biological or targeted DMARDs were excluded. Episodes of HZ infection were identified and the prevalence over time was calculated. Laboratory parameters (total white cell count, neutrophil-to-lymphocyte ratio, serum albumin, globulin & creatinine), history of diabetes mellitus and the highest doses of immunosuppressive medications within 6 months of the first ep-

isode of HZ infection were compared with those within 6 months of last follow-up in patients who did not have HZ infection. Cox regression analysis was performed to identify factors associated with the first HZ infection in all patients.

Results: 1542 patients were studied (88% women, age 46.4±15.0 years). The underlying diseases were SLE (38%), rheumatoid arthritis (26%) and other rheumatic diseases (36%). After a total follow-up of 11,515 patient-years since diagnosis (7.5±7.0 years), 122 (7.9%) patients developed 146 episodes of HZ infection, giving an overall prevalence of 1.27/100-patient years. The prevalence rates of HZ in SLE, RA and non-SLE/RA patients were 1.70, 0.64 and 0.76 per 100 patient-years, respectively. Patients who experienced HZ reactivation were younger (41.6±14.7 vs 46.8±15.0 years; p< 0.001), more likely to have SLE (74% vs 35%; p< 0.001) and diabetes mellitus (17% vs 7.3%; p=0.01), and had a significantly lower albumin (38.6±5.6 vs 41.3±3.5; p< 0.001) and higher neutrophil-to-lymphocyte ratio (4.9±6.2 vs 2.8±2.6; p< 0.001). More patients with HZ reactivation were treated with prednisolone (54% vs 22%; p< 0.001), azathioprine (20% vs 8%; p< 0.001), mycophenolate mofetil [MMF] (21% vs 12%; p=0.006), cyclophosphamide [CYC] (4.9% vs 0.1%; p< 0.001) and hydroxychloroquine (48% vs 34%; p=0.002) in the preceding 6 months compared with those who did not have HZ infection. Among those using immunosuppressive drugs, the doses of MMF (1.42±0.64 vs 1.02±0.31g; p=0.005) and prednisolone (15.6±15.9 vs 5.5±4.5mg; p< 0.001) were significantly higher in those with HZ infection. The cumulative risk of having HZ reactivation in SLE patients at 24 and 48 months since diagnosis was 5.9% and 8.6%, respectively, which was significantly higher than that in non-SLE patients (1.9% and 2.5%, respectively; p< 0.001 by log rank test). Cox regression analysis revealed that having a diagnosis of SLE (HR 1.97 [1.17-3.31]), albumin level (HR 0.93 [0.90-0.97] per g/L; p=0.001), serum creatinine (HR 0.995 [0.990-1.00] per umol/L), higher neutrophil/lymphocyte ratio (HR 1.08 [1.05-1.11]) and the use of CYC (HR 6.69 [2.56-17.5]) and prednisolone (HR 1.61 [1.02-2.45]) in the preceding 6 months were independently associated with the development of HZ infection.

Conclusion: Reactivation of HZ is fairly common in patients with rheumatic diseases. Underlying SLE, prednisolone/cyclophosphamide therapy and the neutrophil/lymphocyte ratio, but not age, sex or other laboratory parameters, are the major risk factors for HZ reactivation.

Disclosure: C. Mok, None; **L. Ho**, None; **S. TSE**, None; **K. Chan**, None; **C. To**, None.

Abstract Number: 0863

Serum Proprotein Convertase Subtilisin/kexin Type 9 (PCSK9) and Cardiovascular Risk in Systemic Lupus Erythematosus: A Longitudinal Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To study the predictive value of serum PCSK9 level on cardiovascular complications in Chinese patients with systemic lupus erythematosus (SLE).

Methods: Consecutive patients who fulfilled ≥4 1997 ACR criteria for SLE and consented for a biomarker study between 2009 and 2012 were included. Stored serum samples from these patients were assayed for PCSK9 using a commercial ELISA kit. New ischemic vascular events in these patients during follow-up were evaluated. ROC analysis was performed to adopt the best cut-off value of PCSK9 for the prediction of a new vascular event. Patients were divided into two groups according to this cut-off value. The cumulative incidence of new vascular event and mortality over time was studied by Kaplan-Meier's analysis and compared between the high and low PCSK9 subgroups. Cox regression was performed to study the effect of the PCSK9 subgroups on new vascular events and mortality, adjusted for other confounding factors.

Results: 539 SLE patients were studied (93% women, age 41.9±14.0 years; disease duration 106±90.4 months at entry). The mean PCSK level at baseline was 265±158ng/ml and a cut-off of 243.25ng/ml best predicted a new vascular event by the maximum Youden's index (ROC analysis: AUC 0.63[0.51-0.74]; sensitivity 69%; specificity 61%). 220 SLE patients had baseline PCSK9 level of ≥243.25ng/ml (high PCSK9) and 319 patients had level below 243.25ng/ml (low PCSK9). No significant difference in SLE manifestations and autoantibody profile was observed between the high and low PCSK9 groups except the former had a significantly higher prevalence of lupus nephritis. 31 new vascular events (13 ischemic stroke, 13 acute coronary syndrome and 5 peripheral vascular disease) developed in 29 patients over a mean follow-up of 91.3±18.6 months. Patients with a new vascular event had a significantly higher baseline PCSK9 level than those without (350±225 vs 260±153ng.ml; p=0.02). The cumulative incidence of a first vascular event at 5 years from study entry was 7.8% in the high PCSK9 group and 1.9% in the low PCSK9 group (log rank test; p=0.003, univariate hazard ratio [HR] 3.08[1.39-6.80]). At last follow-up, 40 patients succumbed (10 due to vascular event [vascular death]). Kaplan-Meier's analysis showed that the high PCSK9 group had a significant higher cumulative risk of all-cause mortality (log rank test p=0.003; HR2.68[1.39-5.14]) and vascular mortality (log rank test p=0.002; HR12.4[1.56-98.4]) over time than the low PCSK9 group. Cox regression analyses showed that high PCSK9 was significantly associated with new vascular events (HR2.56[1.10-5.99]; p=0.03) independent of age, sex, SLE duration, diabetes mellitus, hypertension, body mass index, atherogenic index, smoking, antiphospholipid antibody, past history of vascular events, and the use of statins, aspirin, hydroxychloroquine, prednisolone, mycophenolate mofetil, azathioprine and the calcineurin inhibitors at study entry.

Conclusion: A higher serum PCSK9 level is a strong risk factor for ischemic vascular events in patients with SLE, which is independent of age, sex, traditional atherosclerotic risk factors, antiphospholipid antibody and the use of statins and immunosuppressive medications.

Disclosure: C. Mok, None; **L. Ho**, None; **K. Chan**, None; **S. TSE**, None; **C. To**, None.

Abstract Number: 0864

Does Obesity Affect Disease Activity Outcomes in Systemic Lupus Erythematosus?

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Increased Body Mass Index (BMI) affects cardiovascular risk and is related to worse health-related quality of life measures in patients with systemic lupus erythematosus (SLE). However, its impact on disease activity over time is not known. The aim of the present study was to assess the impact of increased BMI on measures of disease activity in SLE.

Table 1. Demographic, clinical, serological and therapeutic characteristics of patients at baseline

VARIABLE	Normal weight BMI=18-24.9 N=257	Overweight BMI=25-29.9 N=101	Obese BMI=30 N=61	*p*
Age (y)	33.2 ± 13.6	35.8 ± 14.3	35.4 ± 12.9	0.202
Females (n, %)	232 (90.3%)	89 (88.1%)	55 (90.2%)	0.827
Blacks (n, %)	46 (17.9%)	23 (22.8%)	14 (23.0%)	0.004
Caucasians (n, %)	116 (45.1%)	57 (56.4%)	36 (59.0%)	
Chinese (n, %)	50 (19.5%)	7 (6.9%)	2 (3.3%)	
Others (n, %)	45 (17.5%)	14 (13.9%)	9 (14.8%)	
SLE duration (y)	4.8 ± 6.4	6.3 ± 7.4	7.1 ± 8.3	0.03
SLEDAI-2K	8.7 ± 7.4	7.6 ± 7.3	8.1 ± 6.6	0.431
SDI	0.3 ± 0.7	0.4 ± 0.9	0.4 ± 0.9	0.186
CNS involvement (n, %)	21 (8.2%)	13 (12.9%)	8 (13.1%)	0.282
Renal involvement (n, %)	48 (18.7%)	21 (20.8%)	5 (8.2%)	0.099
Hypertension (=130/80 mmHg or antihypertensives) (n, %)	111 (43.4%)	64 (63.4%)	44 (72.1%)	<.001
Systolic BP (mmHg)	115.2 ± 15.0	119.2 ± 17.5	125.9 ± 16.6	<.001
Diastolic BP (mmHg)	72.2 ± 10.0	75.8 ± 10.0	79.4 ± 10.3	<.001
Dyslipidemia (abnormal TC or LDL or treatment with statins) (n, %)	85 (33.3%)	40 (39.6%)	25 (41.0%)	0.365
Abnormal total cholesterol (n, %)	80 (31.4%)	37 (36.6%)	23 (37.7%)	0.486
Abnormal triglycerides (n, %)	30 (11.8%)	9 (8.9%)	5 (8.2%)	0.593
Diabetes (n, %)	6 (2.3%)	4 (4.0%)	0 (0.0%)	0.277
Current Smoker (n, %)	31 (12.2%)	7 (7.0%)	10 (16.9%)	0.15
Increased anti-dsDNA (n, %)	173 (67.3%)	55 (54.5%)	38 (62.3%)	0.074
Low C3 (n, %)	135 (52.5%)	39 (38.6%)	19 (31.1%)	0.002
Low C4 (n, %)	87 (33.9%)	19 (18.8%)	19 (31.1%)	0.019
hs-CRP	5.8 ± 12.3	4.2 ± 7.3	10.1 ± 15.6	0.015
eGFR	106.4 ± 35.2	104.3 ± 35.9	101.6 ± 37.5	0.609
Lupus Anticoagulant (n, %)	28 (12.1%)	12 (13.5%)	4 (7.1%)	0.487
Anticardiolipin antibodies (n, %)	29 (12.6%)	14 (16.1%)	7 (12.5%)	0.702
Glucocorticoids (n, %)	179 (69.6%)	65 (64.4%)	36 (59.0%)	0.237
Antimalarials (n, %)	157 (61.1%)	60 (59.4%)	30 (49.2%)	0.234
Immunosuppressives (n, %)	103 (40.1%)	46 (45.5%)	19 (31.1%)	0.194
Biologics (n, %)	2 (0.8%)	0 (0.0%)	0 (0.0%)	0.531
Anticoagulation / Antiplatelet (n, %)	22 (8.6%)	14 (13.9%)	9 (14.8%)	0.19

SLEDAI-2K: SLE Disease Activity Index 2000, SDI: Systemic Lupus International Collaborating Clinics Damage Index, CNS: central nervous system, BP: blood pressure, TC: total cholesterol, LDL: low-density lipoprotein, hs-CRP: high sensitivity C-reactive protein, eGFR: estimated glomerular filtration rate

Methods: Patients with documented weight and height in their first two clinic visits and at least three consecutive years of follow-up were retrieved from our long-term longitudinal database. They were divided into three groups according to their BMI (normal BMI=18-24.9, overweight with BMI=25-29.9 and obese with BMI ≥30). Patients were followed for three years for outcomes of disease activity (primary) including the time-adjusted mean SLE Disease Activity Index 2000 (AMS), number of flares (defined as any increase in SLEDAI-2K, any increase ≥4 in SLEDAI-2K and systemic treatment escalation), percentage of patients achieving clinical remission and low disease activity state (LDA, defined as clinical SLEDAI-2K 2 regardless of therapy), time spent in remission and/or LDA, cumulative glucocorticoid dose and adjusted high sensitivity C-reactive protein (hs-CRP). Secondary outcomes included new damage accrual (increase in Damage Index) as well as new atherosclerotic vascular events (AVEs), osteoporosis and osteonecrosis. Outcomes were compared among groups by ANOVA test for mean values and Chi-Square test for binary variables; post-hoc multi-testing adjustments were applied in case of statistical difference. The associated effect of obesity on AMS in three years was evaluated using Linear regression analysis.

Results: There were 419 eligible patients (257 with normal BMI, 101 overweight, 61 obese). The baseline characteristics are shown in Table 1. Obese patients had a longer disease duration and higher prevalence of hypertension and higher hs-CRP at baseline. Other variables did not differ significantly between groups. The outcomes after three years

Table 2. Primary and secondary outcomes at 3 years

VARIABLE	Normal weight BMI=18-24.9 N=257	Overweight BMI=25-29.9 N=101	Obese BMI=30 N=61	*p*
Adjusted Mean SLEDAI-2K	5.2 ± 3.6	4.4 ± 3.7	4.7 ± 4.0	0.185
Number of flares (SLEDAI-2K increase = 1)	1.5 ± 1.3	1.4 ± 1.3	1.4 ± 1.2	0.596
Number of flares (SLEDAI-2K increase =4)	0.9 ± 1.0	0.9 ± 1.1	0.8 ± 1.0	0.797
Number of flares (treatment escalation)	2.1 ± 1.8	1.8 ± 1.8	1.6 ± 1.7	0.065
Remission (clinical SLEDAI-2K=0) at 3rd year	157 (61.1%)	59 (58.4%)	38 (62.3%)	0.86
LDA (clinical SLEDAI-2K=2) at 3rd year	187 (72.8%)	75 (74.3%)	44 (72.1%)	0.946
Time in remission (y)	1.6 ± 1.0	1.6 ± 1.1	1.7 ± 0.9	0.569
Time in remission or LDA (y)	1.9 ± 1.0	2.1 ± 1.0	2.1 ± 0.9	0.283
Cumulative glucocorticoid dose (g)	13.9 ± 19.7	15.8 ± 24.4	14.7 ± 23.9	0.747
Adjusted mean hs-CRP	3.8 ± 7.1	4.1 ± 4.2	7.0 ± 7.2	0.004
SDI increase	0.5 ± 0.9	0.5 ± 0.8	0.5 ± 0.9	0.996
New AVEs in 3 years	3 (1.2%)	6 (5.9%)	3 (4.9%)	0.03
New osteonecrosis in 3 years	20 (7.8%)	6 (5.9%)	5 (8.2%)	0.808
New osteoporosis in 3 years	21 (8.2%)	6 (5.9%)	4 (6.6%)	0.741

SLEDAI-2K: SLE Disease Activity Index 2000, LDA: low disease activity, AVEs: atherosclerotic vascular events

of follow-up are shown in Table 2. There were no differences in terms of adjusted mean SLEDAI-2K, flare rate and time spent in remission and/or low disease activity after three years of follow-up between normal weight, overweight and obese patients. However, obese patients had higher time-adjusted hs-CRP. Overweight patients developed more frequently AVEs. Linear regression analysis with AMS as the dependent outcome did not confirm obesity to significantly affect this measure of disease activity.

Conclusion: Obese patients had a higher time-adjusted CRP over three years indicating persistent inflammation. However, this was not associated with increased lupus inflammatory burden. These patients more frequently developed atherosclerotic cardiovascular events that could be explained both by the persistence of inflammation (as expressed by the CRP) and traditional atherosclerotic risk factors.

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Abstract Number: 0865

Lupus Low Disease Activity State Attainment Provides Significant Protection Against Mortality: A Multi-National, Longitudinal Observational Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

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Background/Purpose: Mortality in patients with systemic lupus erythematosus (SLE) is high compared to the general population. Attainment of the Lupus Low Disease Activity State (LLDAS) is validated as protective against adverse outcomes including organ damage accrual and flare. We examined whether LLDAS attainment provided protection against mortality in patients with SLE. In addition, we examined remission (Definitions for Remission in SLE (DORIS) definitions).

Methods: Data from a 13-country longitudinal SLE cohort on patients meeting either ACR or SLICC criteria were collected between 2013 and 2020 using standard case report files. LLDAS was defined as in Golder *et al*., 2019 (SLEDAI≤4, no new activity, PGA ≤1, pred ≤7.5 mg/d, antimalarials (AM) and immunosuppressants (IS) allowed. Remission definitions were as in Vollenhoven *et al*, 2016 included clinical remission on treatment (CROT: clinical SLEDAI=0, AM and IS allowed, prednisolone ≤5 mg/d), and a variation disallowing glucocorticoid (CROT-off-steroid). Longitudinal associations of mortality were examined using survival (Cox regression) analysis.

Results: The study cohort included 4,020 SLE patients followed over a median of 2.6 years [IQR: 1.0 to 5.1] (Table 1). Ninety-one patients died during the study observation period; the crude mortality rate was ~ 7/1000 person-years. About 68% of deaths were related to infections; ~49% were related to SLE; ~24% related to cardiovascular causes and about 13% related to malignancy.

Disease activity and organ damage were strongly and independently associated with mortality. A 1 point increase in SLEDAI-2K was associated with an increased risk of mortality of 15% after accounting for confounders (adjusted HR: 1.15 (1.07, 1.23), p< 0.001). A 0.3-increase in PGA increased the risk of mortality by 33% (adjusted HR = 1.33 (1.13, 1.56), p=0.001). Every 1 unit increase in SDI score increased the mortality hazard by 53% (adjusted HR = 1.53 (1.38, 1.70), p< 0.001). While the associations of cumulative prednisolone exposure and flares with mortality were significant in univariable analysis, they attenuated in multivariable analysis.

48% of all patients achieved ≥50% observed time in LLDAS (LLDAS-50) but only 21% of those who died (Table 2). LLDAS-50 reduced mortality by 60% (adjusted HR = 0.40 (95% CI: 0.23, 0.69) p< 0.001) (Table 2). Clinical remission on treatment ≥50% of observed time (CROT-50) was achieved in 36% of patients and reduced mortality by 50% (HR = 0.50 (0.27, 0.92), p=0.026). A greater reduction in mortality was observed in patients who spent ≥50% time on CROT-off-steroid (HR=0.13 (0.02,0.96), p=0.045), but this was only achieved in 13% of patients (Table 2).

Table 1. Patient demographics of the study cohort

Patient demographics and clinical indicators	All patients N=4,020	Deceased patients N = 91
	Median [IQR] (range) or n (%)	
Age at enrolment (years)	39 (30, 50)	41 (28, 54)
Age at diagnosis (years)	29 (21, 39)	31 (21, 39)
Disease duration at enrolment (years)	8 (3, 15)	7 (3, 13)
Study duration (years)	2.6 (1.0, 5.1)	2.1 (0.7, 3.5)
Patients with ≥2 visits	3750 (93%)	80 (88%)
Females	3697 (92%)	81 (90%)
Asian ethnicity	3552 (89%)	52 (90%)
Tertiary level education	1963 (53.4%)	29 (35%)
Time adjusted mean SLEDAI-2K (AMS)	2.9 (1.3, 4.7)	5.0 (2.7, 7.1)
Time adjusted mean PGA	0.4 (0.2, 0.7)	0.8 (0.5, 1.3)
Prednisolone-ever	3417 (85%)	89 (98%)
Time adjusted mean prednisolone mg/day	5.0 (2.5, 8.8)	9.0 (5.7, 15.5)
Cumulative prednisolone dose (g)	3.6 (0.7, 9.6)	6.3 (2.1, 13.0)
Organ damage present at the end of study follow-up	1707 (47.8%)	60 (72%)
Damage accrual during study period	707 (19.8%)	27 (33%)

Table 2. Longitudinal associations of LLDAS and DORIS remission attainment with mortality

Treat-to-Target (T2T) endpoints	All patients Total=3,750	Deceased patients Total = 80	Multivariable Cox regression analysis
	N (%)	N (%)	HR[1] (95% CI), p-value
LLDAS-50[2]	1,800 (48%)	17 (21%)	0.40 (0.23,0.69), p=0.001
CROT-50[3]	1,353 (36%)	13 (16%)	0.50 (0.27,0.92), p=0.026
CROT-off-steroids-50[4]	498 (13%)	1 (1.3%)	0.13 (0.02,0.96), p=0.045

[1] *HR = Hazard ratios adjusted for GDP (PPP) and SDI score.*

[2] *Lupus Low Disease Activity State, defined as SLEDAI≤4, no new activity, PGA ≤1, prednisolone ≤7.5 mg/day, antimalarials and immunosuppressants allowed, for ≥50% of observed time*

[3] *Clinical Remission on Therapy, defined as cSLEDAI=0; antimalarials and immunosuppressants allowed; Prednisolone ≤5mg/day, for ≥50% of observed time*

[4] *Clinical Remission on Therapy but Off Steroids, defined as cSLEDAI=0; anti-malarial and immunosuppressants allowed; no corticosteroids, for ≥50% of observed time*

Conclusion: The attainment of LLDAS and DORIS remission conferred significant protection against mortality in SLE. LLDAS was more attainable than remission. Compared to LLDAS, clinical remission on treatment was not more protective, while clinical remission off steroids was maximally protective. Steroid free remission should be the goal of treatment in SLE.

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Characteristics Associated with Poor COVID-19 Outcomes in People with Systemic Lupus Erythematosus (SLE): Data from the COVID-19 Global Rheumatology Alliance (GRA)

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Preliminary data in people with SLE suggested that disease activity as well as SLE treatment at time of COVID-19 acquisition impact COVID-19 outcomes over and above other known risk factors. We assessed characteristics associated with poor outcomes in a global population of people with SLE and COVID-19.

Methods: People with SLE reported in the COVID-19 Global Rheumatology Alliance (GRA) physician-reported registry from March 24th 2020 to April 12th 2021 were included. Variables collected included age, gender, region [Europe, North America, South America and other (Africa, Asia and Australia)], comorbidities (chronic renal disease, cardiovascular disease, and the number of other comorbidities), physician global assessment of disease activity, calendar

Table 1: Characteristics associated with poorer COVID-19 outcomes in individuals with SLE (n=1734)*.

	OR (95% CI)
Age (per year, continuous)	1.03 (1.02, 1.04)
Gender	
Female	Ref.
Male	1.74 (1.22, 2.49)
Region	
Europe	Ref.
North America	1.26 (0.52, 3.07)
South America	1.37 (0.59, 3.19)
Other (Asia, Africa and Australia)	3.77 (1.85, 7.69)
Calendar Period	
March 24-June 15, 2020	Ref.
June 16-Sept 30, 2020	0.61 (0.42, 0.89)
Oct 1, 2020- April 12, 2021	0.42 (0.30, 0.59)
Baseline Glucocorticoid Dose	
0 mg/day	Ref.
1-5 mg/day	1.87 (1.39, 3.04)
6-9 mg/day	2.46 (1.35, 4.46)
=>10 mg/day	2.32 (1.63, 3.32)
Baseline Medication Category	
Antimalarial monotherapy for SLE	Ref.
No SLE treatment	2.05 (1.39, 3.04)
IS drugs as monotherapy (MMF, tacrolimus, cyclophosphamide, cyclosporine, azathioprine, methotrexate, leflunomide, sulfasalazine only)	1.04 (0.77, 1.42)
Biologic/targeted monotherapy	1.05 (0.45, 2.45)
Biologic/targeted monotherapy + IS	1.30 (0.82, 2.06)
Chronic renal insufficiency or end stage renal disease	3.21 (2.31, 4.46)
Cardiovascular/Hypertension	1.64 (1.24, 2.16)
Number of Comorbidities (Other than Renal/Cardiovascular/Hypertension)	1.51 (1.15, 1.98)
Physician-reported SLE Disease Activity	
Remission	Ref
Minimal or low	0.99 (0.73, 1.35)
Moderate	1.78 (1.19, 2.64)
Severe or high	4.18 (2.50, 6.97)

IS: immunosuppressive; b/ts: biologics/target synthetic; OR: Odd ratio; CI: confidence interval

*The ordinal outcomes was: 1 not hospitalized, 2 hospitalized without supplementary oxygen or with non-invasive ventilation, 3 hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 4 death. This assumed that the relationship between each pair of outcome groups is of the same direction and magnitude.

period, glucocorticoid dose, and SLE treatment at the time of COVID diagnosis. SLE treatment was categorized into five groups: antimalarials only (reference), no SLE drugs, non-biologic immunosuppressant (IS) monotherapy, biologics/target synthetic IS, and combination IS therapy. An ordinal outcome was defined as: 1) not hospitalized, 2) hospitalized without supplementary oxygen or with non-invasive ventilation, 3) hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 4) death. We constructed a multivariable ordinal logistic regression model to assess the relationship between COVID-19 severity and demographic characteristics, comorbidities, medications and disease activity.

Results: 1734 patients were included; 1567 (90.4%) were female, median age was 44.3 (SD: 14.3) years. A total of 1291 (74.5%) patients were not hospitalized; 148 (8.5%) patients were hospitalized without oxygen or with non-invasive ventilation, 195 (11.2%) patients were hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 100 (5.6%) died. In our multivariable model, more severe COVID-19 outcomes were seen in older patients (odds ratio, OR=1.03 per year), males (OR =1.74), patients outside Europe and North and South America (OR=3.77), patients on prednisone (0-5 mg/d OR=1.87, 5-10 mg/d OR=2.46, and >10 mg/d OR=2.32), no SLE therapy (OR =2.05), chronic renal disease (OR =3.21), cardiovascular disease (OR =1.64), the number of other comorbidities (OR=1.51) and moderate and high disease activity (OR =1.78 and OR=4.18, respectively). There was evidence of a calendar period effect, with worse outcomes in those with a COVID diagnosis earlier in the pandemic (before June 15, 2020); these data are summarized in Table 1.

Conclusion: These results demonstrate patterns similar to the general rheumatic disease population, and underscore the importance of controlling disease activity in people

with SLE patients during the COVID-19 pandemic.

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Abstract Number: 0867

A Proteomic/Transcriptomic Analysis Associates with Subclinical Vascular Disease in Systemic Lupus Erythematosus

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is associated with enhanced cardiovascular (CV) risk linked to both traditional Framingham risk factors and lupus-specific immune dysregulation. Characterizing an immunological signature at the transcriptional and protein level that associates with subclinical vascular disease and predicts atherosclerosis progression has been challenging.

Methods: SLE patients and matched healthy controls underwent assessments of vascular stiffness (cardio-ankle vascular index (CAVI)), vascular inflammation by FDG-PET CT, and coronary artery plaque by coronary computed tomography angiography (CCTA). Whole blood RNA sequencing was performed in samples from a subset of those patients including 10 controls and 20 SLE patients. In a larger subset of these patients including 24 controls and 64 SLE patients, measurement of several inflammatory biomarkers using the Olink platform was performed. The findings were correlated with clinical and vascular assessments.

Results: In initial pathway analyses, transcriptional regulation of genes related to cell cycle processes was observed in SLE patients with more severe vascular disease compared to SLE patients with milder vascular phenotypes. Additionally, upregulation of pathways related to cytokine-mediated signaling and response to interferon-gamma was also noted between these groups but was driven by changes in expression of only a small selection of genes. Within SLE patients, proteomic analyses revealed fourteen immunologic and inflammatory-linked proteins (CCL11, IL18R1, IL20RA, IL6, IL7, LIF, CDCP1, IL22RA, LAP TGF-β1, LIFR, MCP3, TNFSF14, TRANCE, X4EBP1) which correlate with more than one cardiovascular readout. Of specific interest, these analyses reveal four proteins that correlate significantly with non-calcified plaque burden (IL6, LIFR, IL22RA1, IL4) and thirteen different proteins which correlate with dense calcified plaque burden (CCL11, IL1α, IL20, IL20RA, IL2RB, IL2, IL5, IL7, LIF, MCP3, MCP4, MMP1, TNFSF14),). Of note, decreased leukemia inhibitory factor receptor (LIFR) and increased IL6 were associated with both increased vascular inflammation, total plaque burden and non-calcified plaque burden in SLE patients.

Conclusion: Several inflammatory serum markers associate with enhanced vascular damage in SLE. Of note, dysregulation of the LIF/IL6 axis, described to be involved in regulation of the fate of T-cells, may represent both a marker of increased atherosclerotic plaque burden risk and a mechanism by which plaque burden worsens in SLE patients, potentially driven by changes in lymphocyte composition. Thus, further investigation of the influence of the LIF/IL6 axis and T-cell subsets is warranted in understanding the pathogenesis of cardiovascular disease in SLE. Additionally, given the transcriptomic data, investigation of the role of cell cycle processes in cardiovascular risk in SLE may also prove valuable.

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Abstract Number: 0868

Cell-bound Complement Activation Products (CB-CAPs) Predicts Type 1 SLE Activity

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: SLE is a multisystem autoimmune disease that displays diverse manifestations that can be categorized into two broad types. Type 1 SLE activity includes inflammatory manifestations such as arthritis and nephritis. Type 2 SLE activity, which has a less clear relationship to inflammation, includes findings such as fatigue and widespread pain and can be assessed using patient-reported outcome measures (PROs). Cell bound-activation products (CB-CAPs), erythrocyte-bound C4d (EC4d), and B-lymphocyte-bound C4d (BC4d) in a multi-analyte assay with algorithm (MAP) provide valuable diagnostic information in SLE. In this study, we evaluated EC4d, BC4d, and MAP as markers of current Type 1 SLE activity.

Methods: This was a cross-sectional study of SLE patients (ACR 1997 or SLICC criteria) from June 2020 to March 2021. ANA and other autoantibodies were measured by ELISA. Anti-dsDNA was determined by immunofluorescence using Crithidia luciliae. CB-CAPs were measured by flow cytometry. The multi-analyte assay panel with algorithm (MAP) was determined using a 2-tier algorithm.

We used SLEDAI, the Polysymptomatic Distress Score (PSD, patient-reported pain and symptoms), and a PGA (physician's global assessment; a 3-point visual analog scale) for Type 1 and for Type 2 SLE activity to define 3 bookended patient groups based on current SLE activity:

- Type 1 SLE activity: SLE Disease Activity Index (SLEDAI-2k) ≥6, clinical SLEDAI ≥4, renal SLEDAI ≥4 or Type 1 PGA ≥1.5, with or without Type 2 SLE activity
- Type 2 SLE: PSD score ≥8, Type 2 PGA ≥1.5, SLEDAI=0, and Type 1 PGA ≤0.5
- Minimal SLE: PSD score of ≤3, SLEDAI=0, Type 1 PGA ≤0.5 and Type 2 PGA ≤0.5.

Differences across groups were analyzed by Fisher's exact test. Logistic regression analysis examined predictors of Type 1 activity.

Results: In this bookended cohort of 52 patients (90% female, 54% Black, mean age 46 years), 50% had current Type 1 activity, 31% had Type 2 SLE without Type 1 activity, and 19% had minimal SLE activity. Patients with Type 1 activity were younger, but there was no difference in race, ethnicity, length of disease, historical renal disease, hydroxychloroquine, or immunosuppression use across the groups (Table 1). The median MAP score and BC4d and EC4d levels were significantly higher in patients with current Type 1 activity (Table 2). Additionally, BC4d, EC4d, and

	Type 1 Activity n=26	Type 2 SLE n=16	Minimal SLE n=10	Overall n=52	p-value
Demographics:					
Mean age (SD)	42.1 (16.3)	52.6 (11.3)	44.4 (12.4)	45.8 (14.7)	**0.03**
% Female	24 (92%)	16 (100%)	7 (70%)	47 (90%)	**0.04**
Black	13 (50%)	7 (44%)	8 (80%)	28 (54%)	0.2
Ethnicity Hispanic	4 (15%)	0 (0%)	0 (0%)	4 (8%)	0.2
SLE Characteristics:					
Mean length of disease	12.45 (10.7)	17.76 (11.1)	11.30 (5.2)	13.92 (10.1)	0.3
% Historical renal disease	13/26 (50%)	4/16 (25%)	7/10 (70%)	24 (46%)	0.08
Current SLE Activity Scores:					
Type 1 PGA Mean (SD)	1.2 (0.6)	0.2 (0.2)	0.1 (0.1)	0.7 (0.7)	**<0.001**
Type 2 PGA Mean (SD)	1.1 (0.6)	1.1 (0.5)	0.1 (0.2)	0.9 (0.6)	**<0.001**
SLEDAI Mean (SD)	5.8 (2.9)	0 (0)	0 (0)	2.9 (3.6)	**<0.001**
Current Medications:					
Hydroxychloroquine	19 (73%)	11 (69%)	6 (60%)	36 (69%)	0.7
DMARD (MTX, Aza, MMF)	16 (62%)	11 (69%)	4 (40%)	31 (57%)	04
Prednisone >5mg	9 (35%)	5 (31%)	4 (40%)	18 (35%)	0.9
Belimumab, Rituximab, or Cyclophosphamide	5 (19%)	3 (19%)	1 (10%)	9 (17%)	0.9

Demographics and SLE Characteristics.

	Type 1 Activity	Type 2 SLE	Minimal SLE	Overall	
Cell-Bound Activation Markers: (Dichotomous)	n(%)	n(%)	n(%)	n(%)	p-value
BC4d positive (> 60 MFI)	11/24 (46%)	0/15 (0%)	1/10 (10%)	12/49 (25%)	**0.002**
BC4d (> 40 MFI)	15/24 (62%)	1/15 (7%)	1/10 (10%)	17/49 (35%)	**<0.001**
EC4d positive (>14 MFI)	12/26 (46%)	1/16 (6%)	3/10 (30%)	16/52 (31%)	**0.02**
BC4d (>60 MFI) and/or EC4d positive	15/25 (60%)	1/15 (7%)	3/10 (30%)	19/50 (38%)	**0.002**
MAP positive (>0)	16/24 (67%)	6/15 (40%)	5/10 (50%)	27/49 (55%)	0.3
Cell-Bound Activation Markers: (Continuous)	Median (IQR)	Median (IQR)	Median (IQR)		
MAP score	1.8 (3.3)	-0.6 (2.1)	0.7 (0.9)	0.6 (4.1)	**0.01**
BC4d (log MFI)	3.8 (1.6)	3.1 (1.1)	3.0 (0.5)	3.4 (1.2)	**0.01**
EC4d (log MFI)	2.5 (0.9)	1.5 (0.6)	2.2 (0.7)	2.1 (1.3)	**0.003**
Traditional SLE Activity Biomarkers:					
dsDNA positive	8/26 (31%)	1/16 (6%)	1/10 (10%)	10/52 (19%)	0.1
Low C3 and/or C4	7/26 (27%)	0/16 (0%)	0/10 (0%)	7/52 (14%)	**0.02**
dsDNA positive and/or Low C3 and/or C4	10/26 (39%)	1/16 (6%)	1/10 (10%)	12/52 (23%)	**0.03**
Extractable Nuclear Antibodies:					
Ro-60 positive	17/26 (65%)	5/16 (31%)	0/10 (0%)	22/52 (42%)	**0.001**
Sm positive	3/26 (12%)	0/16 (0%)	1/10 (10%)	4/52 (8%)	0.4
U1RNP positive	8/26 (31%)	3/16 (19%)	4/10 (40%)	15/52 (29%)	0.5

Biomarkers and Serologies.

Ro-60 were more frequently positive in patients with current Type 1 activity. Only 39% of patients with Type 1 SLE had positive dsDNA and/or low complement. MAP positivity, Sm, and U1-RNP did not distinguish between the groups. In a predictive model, the presence of BC4d >40 or Ro-60 >20 resulted in an 84.6% sensitivity, 73.1% specificity, and diagnostic odds ratio of 14.9 for Type 1 SLE activity.

Conclusion: CB-CAPs may serve as effective biomarkers to categorize current SLE activity using the Type 1 and Type 2 model. MAP scores as well as BC4d, EC4d, and Ro-60 positivity, but not traditional SLE-related antibodies, differentiated current Type 1 SLE activity from Type 2 SLE and low disease activity patients. The addition of CB-CAPs to PROs assessing Type 2 SLE enhances the rheumatologist's ability to categorize more completely the spectrum of SLE symptomatology.

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Abstract Number: 0869

Comparison of Two Frailty Definitions in Women with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Frailty is a novel risk factor for adverse health outcomes in systemic lupus erythematosus (SLE). Multiple definitions of frailty, including the Fried definition (FD), a disease-agnostic phenotypic definition, and the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI), a SLE-specific cumulative deficits definition, have been used to measure frailty in SLE [1,2]. However, the relationship between these two definitions of frailty has not been evaluated. We aimed to determine the prevalence of frailty according to the FD and the SLICC-FI in a single center cohort of adult women with SLE, as well as the cross-sectional association of each frailty definition with self-reported disability.

Methods: Women 18-70 years of age with SLE validated according to the 1997 Update of the 1982 American College of Rheumatology Revised Classification Criteria were enrolled. Frailty status according to the FD and the SLICC-FI was measured at a single study visit. Agreement between frailty metrics was determined using a kappa statistic. Sociodemographic features, physician-reported disease activity and damage, Patient Reported Outcome Measurement Information System (PROMIS) computerized adaptive tests, and Valued Life Activities (VLA) self-report disability were assessed. Differences between frail and non-frail participants were evaluated using Fisher's exact, Chi-squared, or Wilcoxon rank sum tests. The cross-sectional association of frailty according to each metric and VLA disability was assessed using logistic regression.

Results: Data from 67 participants were available for analysis. 12 (17.9%) and 18 (26.7%) of women were classified as frail according to the FD and the SLICC-FI, respectively. There was moderate agreement between frailty metrics (kappa = 0.41, $p< 0.01$). Compared to non-frail women, frail women had lesser educational attainment (FD: $p=0.05$; SLICC-FI: $p=0.03$) and greater disease damage (FD and SLICC-FI: $p< 0.01$) (Table 1). Frail women according to the FD were also older ($p=0.05$) with greater comorbidity burden ($p< 0.01$) and more likely to have smoked over their

Table 1. Characteristics of women with SLE by frailty classification

Characteristic (Median and interquartile range unless otherwise specified)	Fried definition (N=67)			SLICC-FI (N=67)		
	Non-frail (N=55)	Frail‡ (N=12)	p-value	Non-frail (N=49)	Frail‡‡ (N=18)	p-value
Age (years)	41.0 [31.0, 57.0]	57.0 [52.5, 62.0]	0.05	46.0 [29.0, 57.0]	53.5 [36.0, 64.0]	0.15
Race, N (%)			0.18			0.34
Asian	5 (9.1)	0 (0)		5 (10.4)	0 (0)	
Black or African American	15 (27.3)	7 (63.6)		14 (29.2)	8 (44.4)	
White	19 (34.6)	2 (18.2)		17 (35.4)	4 (22.2)	
Other or declined to state	16 (29.1)	2 (18.2)		12 (25.0)	6 (33.3)	
Ethnicity, N (%)			0.72			0.10
Hispanic	15 (27.8)	4 (36.4)		11 (23.4)	8 (44.4)	
Non-Hispanic	39 (72.2)	7 (63.4)		36 (76.6)	10 (55.6)	
Educational attainment			0.05			0.03
High school or less	6 (10.9)	4 (33.3)		4 (8.2)	6 (33.3)	
Some college	13 (23.6)	3 (25.0)		10 (20.4)	6 (33.3)	
College	22 (40.0)	3 (25.0)		21 (42.9)	4 (22.2)	
Graduate or professional school	14 (25.4)	2 (16.7)		14 (28.6)	2 (11.1)	
SLE disease duration (years)	13.0 [6.0, 23.0]	15.0 [12.5, 32.0]	0.17	13.0 [6.0, 2.0]	12.0 [10.0, 16.0]	0.06
SELENA-SLEDAI* score	4.0 [0, 4.0]	1.0 [0, 7.5]	0.58	2.0 [0, 4.0]	4.0 [4.0, 7.0]	<0.01
SLICC/ACR Damage Index** score	0 [0, 2.0]	3.5 [2.5, 6.0]	<0.01	0 [0, 1.0]	3.5 [2.0, 5.0]	<0.01
Charlson Comorbidity Index	2.0 [1.0, 3.0]	3.5 [2.5, 6.0]	<0.01	2.0 [2.0, 3.0]	3.0 [1.0, 5.0]	0.14
Current prednisone dose (milligrams)	5.0 [4.0, 9.0]	5.0 [5.0, 5.0]	0.79	5.0 [5.0, 10.0]	5.0 [3.0, 5.0]	0.12
Ever smoking, N (%)	6 (10.9)	5 (41.7)	0.02	6 (12.2)	5 (27.8)	0.15
Self-reported fibromyalgia, N (%)	8 (14.6)	4 (33.3)	0.21	7 (14.3)	5 (27.8)	0.28

*SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Scores range from 0-105, with higher scores indicating greater disease activity.

**SLICC/ACR Damage Index: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Scores range from 0-46, with higher scores indicating greater damage.

‡Defined by presence of ≥3 criteria.

‡‡Defined by SLICC-FI score >0.21.

lifetime (p=0.02) than non-frail women (Table 1). Frail women according to the SLICC-FI had greater disease damage (p< 0.01) than non-frail women (Table 1). Frail women according to either definition had worse PROMIS scores across multiple domains (p< 0.01) and greater VLA disability (p< 0.01) than non-frail women (Table 2). After adjusting for age, frailty according to either definition was still significantly associated with greater odds of VLA disability (Table 3).

Table 2. Patient-reported outcome measures among women with SLE by frailty classification

Characteristic (Median and interquartile range)	Fried definition (N=67)			SLICC-FI (N=67)		
	Non-frail (N=55)	Frail‡ (N=12)	p-value	Non-frail (N=49)	Frail‡‡ (N=18)	p-value
PROMIS* measure						
Mobility	46.4 [40.2, 49.7]	34.1 [31.9, 38.1]	<0.01	46.4 [41.4, 49.7]	37.2 [33.0, 39.4]	<0.01
Pain behavior	43.9 [39.8, 48.5]	32.7 [26.7, 35.5]	<0.01	44.8 [40.1, 50.1]	36.5 [32.6, 40.0]	<0.01
Pain interference	56.6 [49.7, 59.8]	60.5 [57.6, 63.1]	<0.01	54.2 [48.5, 58.7]	61.4 [59.7, 63.4]	<0.01
Fatigue	55.6 [49.1, 62.7]	72.8 [64.0, 73.9]	<0.01	55.4 [48.5, 62.7]	65.0 [58.7, 73.9]	<0.01
Depression	51.3 [44.7, 57.5]	56.5 [48.1, 69.5]	0.12	51.3 [44.6, 57.5]	54.7 [48.1, 65.8]	0.13
Anxiety	54.1 [50.6, 51.5]	61.2 [48.1, 69.0]	0.33	53.6 [50.4, 61.3]	61.5 [52.9, 65.1]	0.15
Valued Life Activities† disability	0.5 [0.2, 0.9]	1.2 [1.1, 1.8]	<0.01	0.4 [0.1, 0.9]	1.1 [0.9, 1.5]	<0.01

*PROMIS: Patient Reported Outcome Measurement Information System. Scored using a T score metric, with 50 representing the population mean and a difference of 5 considered clinically significant.
†Valued Life Activities: Scores range from 0-3, with higher scores indicating greater disability.
‡Defined by presence of ≥3 criteria.
‡‡Defined by SLICC-FI score >0.21.

Table 3. Cross-sectional association of frailty with disability in women with SLE

Model	Fried phenotype (N=66)		SLICC-FI (N=66)	
	Odds ratio	*95% confidence interval*	*Odds ratio*	*95% confidence interval*
Unadjusted*	6.2	1.6-23.5	5.0	1.5-16.5
Adjusted for age	4.7	1.2-18.8	4.6	1.3-15.8

*Odds of Valued Life Activities disability score in the top quartile in frail versus non-frail women.

Conclusion: Frailty prevalence was higher according to the SLICC-FI than the FD in this single center cohort of women with SLE. Agreement was moderate and clinical characteristics differed between participants classified as frail according to each metric, suggesting differences in frailty constructs. Further studies are needed to explore discrepancies in frailty metrics to determine which may best predict relevant health-related outcomes in patients with SLE.

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Abstract Number: 0870

Blood Brain Barrier Integrity and Brain Imaging Patterns in Patients with SLE

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SESSION INFORMATION

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Background/Purpose: The pathogenesis of neuropsychiatric SLE (NPSLE) has not been fully elucidated. Recent evidence suggests impaired blood brain barrier (BBB) integrity as a possible mechanism leading to neuropsychiatric damage. We aimed to assess brain imaging patterns in patients with SLE, NPSLE and healthy controls utilizing multi-parametric MRI methods to assess cerebral atrophy, tissue and BBB integrity. We also aimed to assess correlations between imaging findings, clinical characteristics and cognition.

Methods: Twenty-three consecutive patients attending the Lupus clinic (NPSLE n=11, non-NPSLE n=12), and 20 age and gender matched healthy subjects were recruited. The MRI protocol included high-resolution T1 sequence (MP2RAGE), diffusion tensor imaging and dynamic contrast enhanced imaging utilizing a 3-Tesla MRI scanner. Brain segmentation was performed to assess volumetric changes, tissue integrity and BBB permeability in various brain regions. Clinical parameters, quality of life and cognition were assessed. Patients were divided into subgroups based on presence of NPSLE, SLE disease activity, disease duration, accrued damage and presence of antiphospholipid antibodies (aPL). Comparisons were performed between the entire patient group and the control group and between subgroups.

Results: The NPSLE group was significantly younger than the non-NPSLE group and significantly less educated compared to the healthy controls and the non-NPSLE group. The NPSLE group had significantly shorter disease duration, more accrued damage, more hypertension compared to the non-NPSLE group and a higher percentage were treated with anticoagulants.

Abnormal findings on conventional MRI (cMRI) were seen in 67% of the non-NPSLE group and 82% of the NPSLE group. Brain atrophy was seen in 43% of the patients and was not limited to NPSLE. In the NPSLE group a negative correlation was observed between the volume of grey matter and disease duration. The grey matter volume was significantly reduced in the NPSLE group and in patients with aPL as compared to healthy controls. The volume of the nucleus accumbens was significantly reduced in patients with a damage index of ≤ 1 as compared to those without damage and compared to healthy controls. Impairment of BBB integrity, as expressed by increased permeability values compared to healthy controls was seen in 5 of the SLE patients (25%), 3 of whom were non-NPSLE. Increased

permeability was detected in several cerebral grey and white matter regions. All 5 patients had significantly longer disease duration (>10years) and as a group had a smaller volume of the anterior segment of the corpus callosum. One patient with SLE underwent MRI scanning during active disease and repeat scan when the disease was better controlled showing a reduction in BBB permeability by 25% in 8 brain regions.

Conclusion: In the present study we detected abnormal cMRI findings, brain atrophy and impaired BBB integrity among patients with SLE, which was not limited to patients with NPSLE. Our results suggest that impairment of the BBB occurs in patients with long disease duration and possibly during active disease, even in patients with SLE without overt NPSLE.

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Abstract Number: 0871

The Association of Hydroxychloroquine Dosing with Adverse Cardiovascular Events in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Current guidelines recommend use of hydroxychloroquine (HCQ) at doses not exceeding 5mg/kg based solely on the increased risk of retinopathy at higher doses. This recommendation does not consider the impact of HCQ dose in comorbidities, disease activity or outcomes. Both protective and toxic effects of HCQ on cardiovascular health have been reported but how HCQ dose influences this balance is uncertain. We aimed to determine if HCQ dose is associated with all-cause heart failure with reduced ejection fraction (HFrEF), life-threatening arrhythmia or cardiac death in SLE.

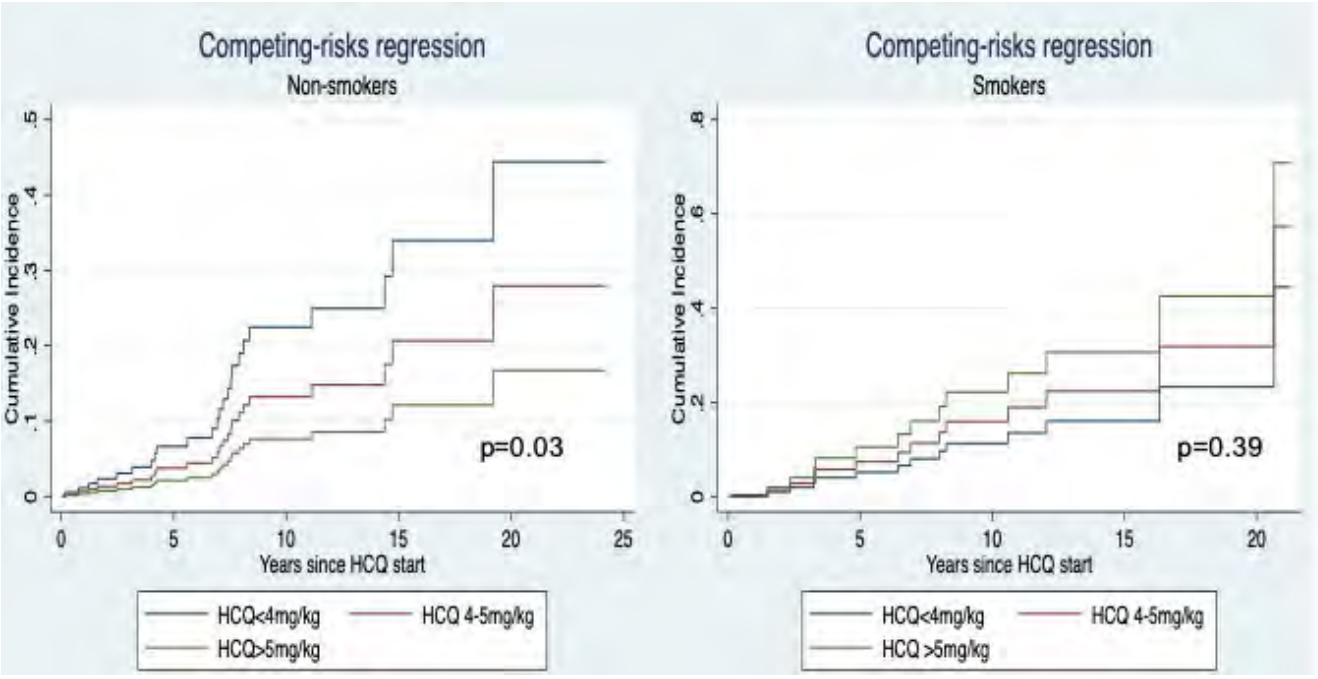
Methods: This was a retrospective cohort study of SLE patients followed at a tertiary care center in the Bronx, New York between January 2005 and January 2021. SLE patients on HCQ with at least one echocardiogram were included. HCQ weight-based doses at HCQ start date and through follow up were recorded. The primary outcome was incident all-cause HFrEF, life-threatening arrhythmia or cardiac death. HFrEF was defined as documentation of clinical heart failure and a systolic ejection fraction < 50% on echocardiogram. Arrhythmia was defined as ventricular arrhythmia, sudden cardiac death, or need for implantable cardiac device or pacemaker. We used competing risk regression to study the association of HCQ dose with the composite outcome. Due to a significant interaction between smoking and HCQ exposure, models were stratified by smoking status.

Results: Of 296 patients, 38 (13%) developed the outcome over a median (IQR) follow up time of 7.0 (3.3,11.8) years. Mean age at baseline (HCQ start date) was 33 ± 13.6 years. A total of 267 (90%) were female and 278 (94%) self-identified as Hispanic or Black. At baseline, 97 (33%) had lupus nephritis, 44 (15%) had chronic kidney disease stage

Competing Risk Regression Analysis								
	Non-smokers n=225				Smokers n=67			
	Unadjusted SHR (95% CI)	p	Adjusted* SHR (95% CI)	p	Unadjusted SHR (95% CI)	p	Adjusted** SHR (95% CI)	p
Baseline Doses								
HCQ weight-based dose, per mg/kg	0.76(0.57,1.0)	0.05	0.72(0.53,0.98)	0.03	1.12(0.82,1.53)	0.47	1.12(0.77,1.65)	0.56
HCQ mg/kg categories								
<4mg/kg	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
4-5mg/kg	0.23(0.06,0.83)		0.27(0.08, 0.94)		2.39(0.43,13.3)		2.63(0.33, 20.64)	
>5mg/kg	0.32(0.14,0.75)		0.3(0.11,0.83)		2.31(0.43, 12.3)		2.58(0.32,21.02)	
p for trend		0.02		0.03		0.33		0.39
Average Doses								
HCQ average weight-based dose, per mg/kg	0.69(0.51,0.93)	0.01	0.72(0.52,1.0)	0.05	1.1(0.80, 1.52)	0.55	1.09(0.77,1.56)	0.62
HCQ average mg/kg categories								
<4mg/kg	1 (ref)		1 (ref)		1 (ref)		1 (ref)	
4-5mg/kg	0.71(0.27,1.87)		0.59(0.2, 1.78)		1.05(0.21,5.18)		1.06(0.21,5.34)	
>5mg/kg	0.36(0.12,0.96)		0.43(0.15,1.21)		1.70(0.46, 6.34)		1.69(0.45,6.38)	
p for trend		0.03		0.1		0.4		0.4

*Models adjusted for age, chronic kidney disease, thromboembolism and diabetes
** Shown models adjusted for age

Competing Risk Regression Analysis Stratified by Smoking Status.



Cumulative Incidence Curves Stratified by Smoking Status.

3 or higher, 26 (9%) had a history of thromboembolism or antiphospholipid syndrome, 101 (34%) had hypertension, 68 (23%) were smokers, 11 (4%) had diabetes and 7 (2%) had coronary artery disease. Mean HCQ weight-based dose was 5.2 ± 1.5 mg/kg at baseline and 5.1 ± 1.5 in average through follow up. Median (IQR) HCQ duration and cumulative dose were 6.5 (3.1, 11.3) years and 828 (328, 1467) grams, respectively. In non-smokers (n=225), multivariable analysis adjusted for age, chronic kidney disease, diabetes and thromboembolism showed that the risk of HFrEF or arrhythmia decreased by 28% per mg/kg of baseline HCQ dose, HR 0.72 (95% CI 0.53, 0.98), p=0.03

(Table). The cumulative incidence of the outcome was the lowest at doses >5mg/kg (Figure). Conversely, there was no significant association between higher baseline HCQ doses and the risk for the outcome among smokers (n=67), HR 1.12 (95% CI 0.77, 1.65) per mg/kg, p=0.56.

Conclusion: Higher HCQ doses were associated with a lower risk HFrEF, life-threatening arrhythmia or cardiac death among non-smoker SLE patients and no increased risk among smokers. If confirmed with future studies, these results would support the inclusion of the potential cardiovascular benefits derived from higher HCQ dosing into HCQ dosing risk-benefit considerations, beyond the risk for retinopathy.

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Abstract Number: 0872

Lack of Association Between Cognitive Test Performance and Cognitive Symptoms in Systemic Lupus Erythematosus (SLE)

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Background/Purpose: Cognitive dysfunction (CD) is reported to affect approximately 40% of SLE patients (1). Mood disorders have been associated with both cognitive symptoms and cognitive function in SLE, but the associations of fibromyalgia with these are unclear. We investigated the relationships between patient-reported cognitive symptoms and objective cognitive test results in SLE, and associations of fibromyalgia and mood disorders with both.

Methods: We tested SLE patients (n=87) and demographically matched healthy control (HC) participants (n=48) with the one-hour neuropsychiatric test battery recommended by the ACR for use in SLE (2) and applied three binary definitions of CD and seven cognitive test z-scores. We assessed patient-reported cognitive symptoms, mood disorder symptoms, fibromyalgia symptoms, and fatigue using the Cognitive Symptoms Inventory (CSI), Hospital Anxiety and Depression Scale (HADS), Central Sensitivity Score (CSS) derived from the 2016 ACR fibromyalgia diagnostic criteria (3) and the Functional Assessment of Chronic Illness Therapy Fatigue Scale (FACIT), respectively. We performed multivariate regression analysis to determine associations with cognitive endpoints; likelihood ratio tests were used to select for inclusion from collinear pairs. We used unpaired t tests to compare CSI scores between groups.

Table 1. Characteristics of Study Groups. 1) Sociodemographic variables were compared between the SLE and control groups using Mann-Whitney, Chi squared and T tests. 2) Premorbid IQ measured by Test of Premorbid Functioning scaled score. 3) HADs – Hospital Anxiety and Depression Scale. 4) Central Sensitivity Score = Widespread Pain Index plus Symptom Severity Score as per 2016 ACR Fibromyalgia Diagnostic Criteria. 5) Meeting 2016 ACR Fibromyalgia Diagnostic Criteria. 6) Impairment defined by number of cognitive domains either 1.5 or 2 standard deviations (SD) below healthy control group mean.

Table 1: Characteristics of Study Groups			
	SLE group N=87	**HC group** N=48	**Comparison[1]** (p-value)
Age, median (range)	45 years (22-64)	46 years (23-62)	0.88
Gender, female	92%	92%	0.95
Premorbid IQ[2], mean ± SD	108.7 ± 7.2	110.8 ± 8.3	0.12
History of Psychiatric Illness (any)	49%	8%	<0.0001
History of Depression	38%	6%	<0.0001
History of Anxiety	26%	6%	0.004
HADS[3] Depression, median (range)	5 (0-15)	1 (0-9)	<0.00001
HADS[3] Anxiety, median (range)	6 (0-20)	4.5 (0-13)	0.0005
Central Sensitivity Score (CSS)[4], median (range)	8 (0-27)	3 (0-9)	<0.00001
Fibromyalgia – meeting criteria[5]	14%	0%	0.009
Cognitive Impairment[6]:			
2 domains ≥1.5 SD below	48%	15%	<0.001
1 domain ≥2 SD below	39%	10%	<0.001
2 domains ≥2 SD below	16%	0%	0.001

Table 2. Multivariate Analysis of Mood Disorders, Fibromyalgia and Cognitive Test Results and Symptoms in SLE. Significant results bolded: *p value <0.05 **p value <0.005. 1) Impairment defined by number of cognitive domains either 1.5 or 2 SD below healthy control group mean. 2) Specific cognitive tests used for each domain are as follows: Visual Memory - Rey Ostrrieth Complex Figure Test Recall Score, Verbal Memory -California Verbal Learning Test trials 1-5, Verbal Fluency - Controlled Oral Word Association Test FAS Sum, Working Memory - Letter Number Sequencing score, Processing Speed - Coding score, Complex Attention - Trail making test B time inverse, Psychomotor speed - finger tap test dominant hand score. 3) for FACIT scores higher scores represent less fatigue (better functioning). Acronyms: TIA - transient ischaemic attack, CSS – Central Sensitivity Score derived from 2016 Fibromyalgia diagnostic criteria, HADS – Hospital Anxiety and Depression Scale, FACIT - Functional Assessment of Chronic Illness Therapy Fatigue Scale. CSI - Cognitive Symptoms Inventory, SD – standard deviations.

Table 2: Multivariate Analysis of Mood Disorders, Fibromyalgia and Cognitive Test Results and Symptoms in SLE											
	Cognitive Dysfunction Definitions[1]			**Individual Cognitive Domains[2]**							**Cognitive symptoms**
	2 domains 1.5 SD below	1 domain 2 SD below	2 domains 2 SD below	Visual Memory	Verbal Memory	Verbal Fluency	Working Memory	Processing Speed	Complex attention	Psychomotor Speed	Cognitive Symptoms Inventory
	Odds ratio (logistic regression)			Coefficient (linear regression)							
Age	**1.07****	**1.07***	**1.07***	**-0.04****	**-0.02***			**-0.02****	**-0.03***	**-0.03****	
Premorbid IQ	**0.88****	**0.85****	**0.84***	**0.06****	**0.04****	**0.07****	**0.03***	0.02	**0.05****	0.02	
Past seizures					**-0.80***				-0.61	-0.16	
Past strokes or TIA	6.55	10.6					**-0.95****	**-0.53***			
Narcotics ever			2.75					-0.28		**-0.64***	
Alcohol Intake											
CSS	**1.09***							**-0.03***			**0.56****
HADS depression											
HADS anxiety		**1.16***			-0.04		-0.02			-0.03	
Depression History			**5.36***	-0.47		-0.28			**-0.60***		
Anxiety History											3.47
FACIT total											

Results: Among SLE patients, the median (range) age was 45 (22-64). Compared to HC, CSS scores were higher (< 0.00001), fibromyalgia was more common (p 0.009) and a history of depression or anxiety was more frequent (p< 0.0001) in SLE patients (Table 1). Cognitive symptoms (CSI score) were worse in SLE patients than HC (median (range) 33 (19-52) vs. 26.5 (21-35), p < 0.0001). At all thresholds, cognitive dysfunction was also more frequent in SLE patients than HC. Age and premorbid IQ were significantly associated with multiple cognitive test endpoints but not with CSI score. On multivariate analysis, CSS, a history of depression, and HADS Anxiety each had significant associations with at least one CD endpoint, but history of anxiety or FACIT score did not. On univariate analysis, cognitive symptoms (CSI) consistently correlated with CSS, FACIT and all mood disorder covariates (CSI) (p 0.02 - < 0.001); on multivariate analysis, after selecting from collinear pairs, only CSS remained significant (p< 0.0001) (Table 2). There were no associations between cognitive symptoms and cognitive test results. Correspondingly, there was no significant difference in cognitive symptoms (CSI score) between cognitively impaired and unimpaired SLE patients at any cognitive impairment threshold (p values 0.22-0.47).

Conclusion: Cognitive impairment, and cognitive symptoms, are each common in patients with SLE, but there were no associations between patient-reported cognitive symptoms and objective cognitive test results. Depression, anxiety and fibromyalgia were more strongly associated with cognitive symptoms than with test results. The distinction between cognitive symptoms and cognitive function needs to be considered when assessing SLE patients with CD.

References: 1) Al Rayes et al. Semin Arthritis Rheum 2018. 2) Liang et al. Arthritis Rheum 1999. 3) Wolfe et al. Semin Arthritis Rheum 2016.

Disclosure: S. Raghunath, None; **Y. Glikmann-Johnston**, None; **E. Guymer**, None; **E. Morand**, Amgen, 2, AbbVie, 2, Biogen, 2, Bristol Myers Squibb, 2, 5, AstraZeneca, 2, 5, 6, Genentech, 2, Servier, 2, Capella Biosciences, 2, Eli Lilly, 5, 6, EMD Serono, 5, 6, Janssen, 2, 5, UCB, 2, GlaxoSmithKline, 2, 5; **J. Stout**, Zindametrix, Pty Ltd, 4; **A. Hoi**, AstraZeneca, 2, 5, Janssen, 6, Abbvie, 6.

Abstract Number: 0873

Clinical and Serological Characteristics of Latin American Patients with Lupus Enteritis: A Case-Control Study

Marcela Muñoz-Urbano[1], Julian Sanchez-Bautista[2], Yeison Santamaria-Alza[1], Diana C. Quintero-González[3], Andres Ramirez[2], Adriana Lucía Vanegas-García[4], Gloria M. Vasquez[1] and Luis Alonso Gonzalez[3], [1]Rheumatology section, Universidad de Antioquia, Medellín, Colombia, [2]Department of internal medicine, Universidad de Antioquia, Medellín, Colombia, [3]Division of rheumatology, Universidad de Antioquia, Medellín, Colombia, [4]Division of rheumatology, Universidad de Antioquia – Hospital San Vicente Fundación, Medellín, Colombia

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus enteritis (LE) is a potentially life-threatening manifestation of systemic lupus erythematosus (SLE), with an incidence ranging from 8% to 27%. Timely diagnosis is essential for prompt treatment and the prevention of complications. As the clinical and immunological characteristics of LE have not been established in Latin American patients (1-2), we conducted a case-control study to investigate the clinical and serological characteristics compared with non-LE patients.

Methods: We performed a case-control study in SLE patients (per ACR criteria) at a tertiary care academic center from January 2012 to December 2019. Eleven patients with LE (cases) were matched with twenty-four non-LE patients (controls), who were similar in age and gender distribution to those of the group of cases. Descriptive statistics were used to compare them.

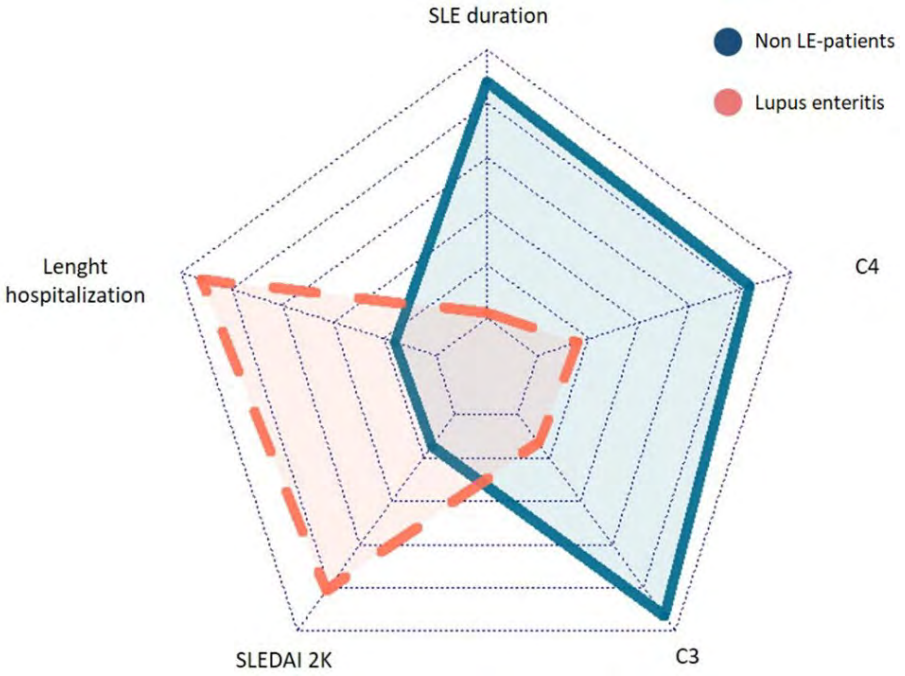

Figure 1. Spider diagram of quantitative variables with significant differences between the groups.

Table 1. Demographic, clinical, and immunological characteristics in patients with and without LE.

Variable	LE (n=11)	Non-LE (n=24)	p-value
Age, mean years ± SD	28.9±15.8	28.3±10.8	0.929
Female (%)	11 (91)	24 (96)	0.536
Disease duration, months ± SD	51±80.6	75±67.7	**0.046**
Long of stay, days ± SD	28.7±17.5	8.9±6.0	**0.0007**
SLEDAI-2K ± SD	22.3±8.2	6.6±6.2	**0.0001**
Hemoglobin, g/dl ± SD	11.2±2.1	10.4±1.9	0.286
Platelet, /mm3 ± SD	235.8±107.3	212.2±104.6	0.423
Erythrocyte sediment rate, mm/h ± SD	51.7±44.8	47.1±31.3	0.700
Serum creatinine, mg/dl ± SD	1.1±0.8	1.9±2.2	0.270
C3, mg/dl ± SD	55.2±25.5	85.9±22.0	**0.004**
C4, mg/dl ± SD	10.4±12.5	18.0±9.1	**0.014**
Anti-Ro antibody (%)	5 (55)	5 (33)	0.260
Anti-La antibody (%)	3 (33)	0	**0.042**
Anti-Sm antibody (%)	2 (22)	6 (40)	0.332
Anti-RNP antibody (%)	4 (44)	7 (47)	0.625
Concomitant kidney involvement (%)	10 (91)	22 (92)	0.691
Concomitant skin involvement (%)	7 (64)	20 (83)	0.194
Concomitant joint involvement (%)	7 (64)	18 (75)	0.380
Concomitant hematologic compromise (%)	7 (64)	18 (75)	0.380
Concomitant serositis (%)	6 (54)	9 (37)	0.281

LE, Lupus enteritis; non-LE, non-enteric lupus; SD, standard deviation.

Results: LE patients were predominantly women (91%) and had a median age of 29 years. In seven (63.6%) patients LE was an initial presentation of SLE, 2 (18%) patients had a recurrence of LE, and 10 (90.9%) patients had concomitant lupus nephritis (LN). The most common clinical manifestations were abdominal pain (90.9%), nausea or vomiting (72.7%), fever (63.6%), and diarrhea (63.6%). Imaging studies revealed the target sign (63.6%), increased attenuation of mesenteric fat (18%), and bladder wall thickening (9.1%). Only one death was recorded and was due to sepsis. All patients received steroids as initial treatment, 82% intravenous (IV) pulses of methylprednisolone, 72.7% IV cyclophosphamide, 9.1% azathioprine, 9.1% mycophenolate mofetil, 9.1% rituximab, and 9.1% IV immunoglobulin. Among the eight patients who received cyclophosphamide, seven had LN or another severe SLE manifestation, which was the main indication for the additional immunosuppressant. LE patients had a significantly shorter disease duration (51 vs 75 months, p=0.046), longer hospital stay (28.7 vs 8.9 days, p=0.0007), higher SLEDAI-2K scores (22.3 vs 6.6, p=0.0001), lower levels of C3 (55.2 vs 85.9 mg/dL, p= 0.004) and C4 (10.4 vs 18.0 mg/dL, p= 0.014), and higher positivity of anti La antibodies (33.3% vs 0%, p= 0.042) compared to non-LE patients.

Conclusion: In Latin American patients, LE is an early SLE manifestation and often with coexistent LN. LE patients had evidence of more active disease than those without LE and had a moderate recurrence rate despite aggressive immunosuppressive therapy.

Disclosure: M. Muñoz-Urbano, None; **J. Sanchez-Bautista**, None; **Y. Santamaria-Alza**, None; **D. Quintero-González**, None; **A. Ramirez**, None; **A. Vanegas-García**, None; **G. Vasquez**, None; **L. Gonzalez**, None.

Abstract Number: 0874

Serum Galectin-9 and CXCL-10 but Not Their Urinary Levels Reflect Lupus Activity

Pankti Mehta, Pratibha Singh and Amita Aggarwal, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: SLE is characterized by increased type I IFN signature in the blood and immune cells. Traditionally, type I IFN signature is measured by gene expression analysis however it is difficult to compute in routine clinical practice. IFN alpha levels are very low and need a highly sensitive assay for its measurement, thus we aimed to look at proteins affected by IFN-alpha like galectin-9 and CXCL-10 as markers of SLE activity as well as for lupus nephritis.

Methods: Patients with SLE (fulfilling SLICC criteria) were included and clinical parameters recorded. They were divided based on renal involvement and disease activity into—active (SLEDAI≥4) renal, active non-renal and inactive subgroups. 20 healthy controls (HC) were also included. Serum and urine galectin-9 and CXCL-10 levels were measured by ELISA. Urine galectin-9 and CXCL-10 were normalized with spot urine creatinine values. Follow-up serum and urine galectin-9 levels were measured for those in the active renal group at six-months. Non-parametric test like Kruskal Wallis test, Spearman's correlation coefficient, and ROC curve analysis were used.

Results: 97 patients with SLE (26 years; 89 females) were categorized into active renal disease (35), inactive disease (32) and active non-renal disease (30). 20 HC (25 years; 15 females) were enrolled.Themedian duration of disease was 24 months (6-48)and SLEDAI 2K was 9 (2-15).

Patients with SLE had higher serum galectin-9 (5.652 vs 1.702 ug/ml, p=0.0001) but not urine galectin-9 (0.538 vs 0.317 ug, p=0.7) levels as compared to HC. Serum galectin-9 but not urine galectin-9 was higher in patients with active as compared to inactive lupus (12.912 in active renal, 16.777 in active non-renal vs 3.565 ug/ml, p=0.04 and 0.005). There was no significant difference in serum or urine galectin-9 between active renal and active non-renal disease.

Patients with SLE had higher CXCL-10 (0.164 vs 0.046ug/ml, p=0.0003) and urine CXCL-10 levels (0 vs 0 ug, p=0.01) as compared to HC. Patients with active non-renal disease had higher serum CXCL-10 levels as compared to inactive lupus (0.365 vs 0.086 pg/ml, 0.02), however, urine CXCL-10 was not significantly different between active renal and

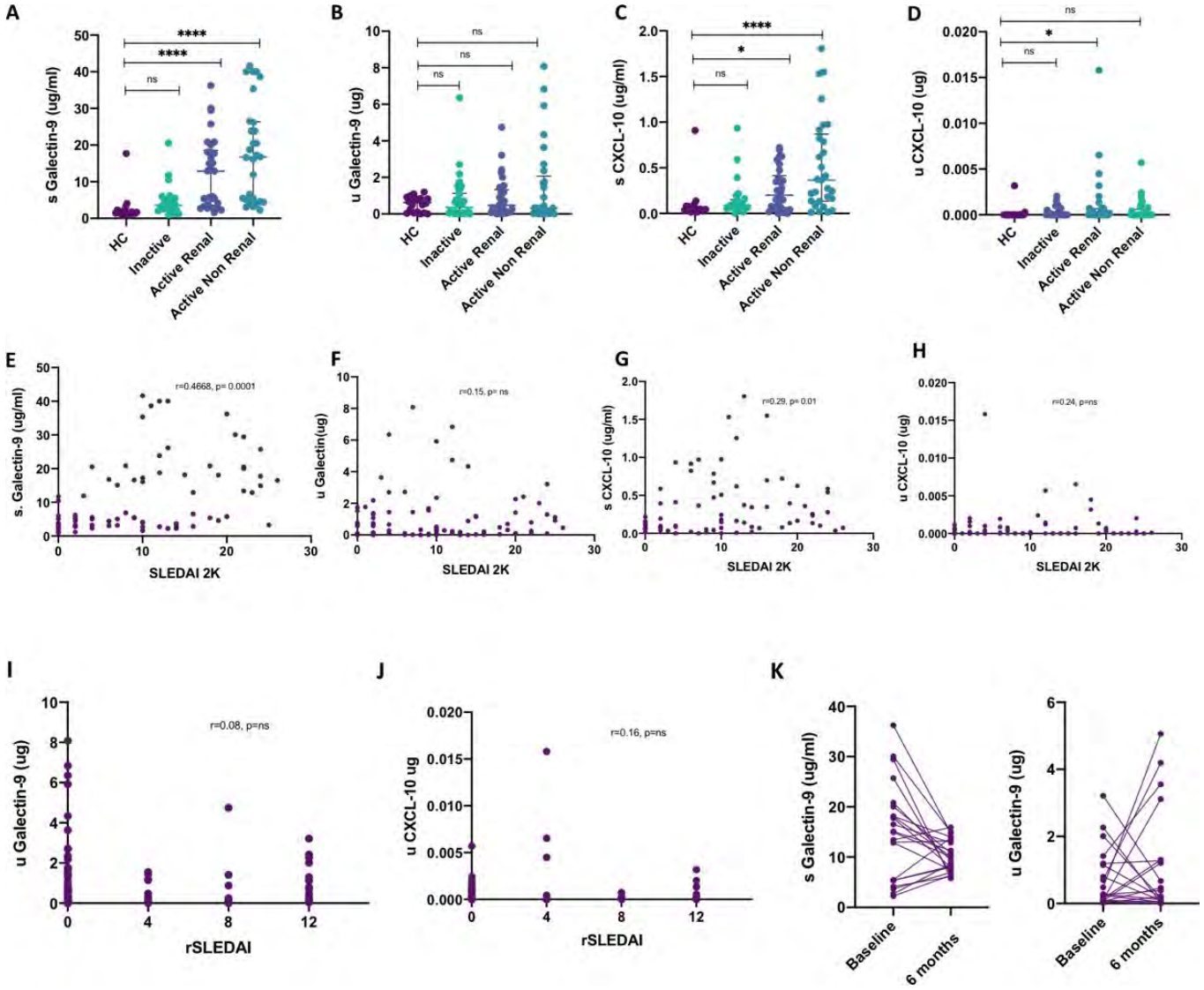

Figure 1. Comparison of serum galectin-9 (A), urine galectin-9 (B), serum CXCL-10 (C) and urine CXCL-10 (D) across active renal, active non-renal, inactive renal and healthy controls. Correlation of serum galectin-9 with SLEDAI 2K (E), urine galectin-9 with SLEDAI 2K (F), serum CXCL-10 with SLEDAI 2K (G) and urine CXCL-10 with SLEDAI 2K (H). Correlation of urine galectin-9 and CXCL-10 with renal SLEDAI (I, J). Follow up levels of serum and urine galectin 9 in the active renal subgroup at baseline and 6 months (K).

inactive subgroup. There was no difference in serum or urine CXCL-10 between active renal and active non-renal disease. [Fig 1A-D]br>

Serum galectin-9 and serum CXCL-10 showed a good association with SLEDAI2K however urinary galectin-9 and CXCL-10 had no association with SLEDAI2K [Fig 1E-H]. Serum galectin-9 and CXCL-10 levels had a modest correlation (r=0.4) with SLEDAI2K, both the urinary markers did not show any association with rSLEDAI. [Fig I-J]

In a subset of patients with active renal disease, serum galectin-9 levels significantly reduced after six-months whereas urine galectin did not show a significant fall [Fig 1K]. Serum galectin-9 showed a greater AUC than CXCL-10 (0.77 vs 0.67) in differentiating active SLE from inactive disease.

Conclusion: Serum Galectin-9 and CXCL10 are good markers of lupus activity however they do not differentiate between active renal and active non-renal disease. Urinary Galectin-9 & CXCL10 do not reflect renal activity.

Disclosure: P. **Mehta**, None; **P. Singh**, None; **A. Aggarwal**, None.

Abstract Number: 0875

Renal Function, Adherence and Low Hydroxychloroquine Dosing Predict HCQ Blood Levels and Lupus Disease Activity

Shivani Garg[1], Karen Hansen[2], Betty Chewning[1] and Christie Bartels[2], [1]UW Madison, Madison, WI, [2]University of Wisconsin School of Medicine and Public Health, Madison, WI

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Despite weight-based dosing, hydroxychloroquine (HCQ) efficacy varies between individuals. Our meta-analysis based on several studies found that low HCQ levels increased risk of lupus flare, while high levels increased the risk of macular toxicity. Aside from body weight, factors influencing HCQ levels are not well defined. Understanding such factors could guide clinicians to adjust HCQ doses, with the aim of controlling lupus disease activity while minimizing toxicity. Thus, we examined individual factors associated with variations in HCQ levels. We also evaluated the impact of HCQ levels on SLE disease outcomes.

Methods: Inclusion criteria were: a) age ≥18 years, b) 1997-ACR, 2012-SLICC or 2019-ACR/EULAR confirmed SLE, c) prescribed HCQ ≥1 month before enrollment. We measured consented patients' whole blood HCQ levels after clinic visits. We abstracted data on patients' demographics, disease characteristics, laboratory values, SLE disease activity index (SLEDAI), and patient-reported adherence (0-100% MASRI Visual analogue scale (VAS); ≥80% adherence) on the day of the visit. We measured HCQ blood levels by liquid chromatography mass spectrometry. We used linear and logistic regression models to test associations between interindividual factors and HCQ blood levels, and between HCQ levels and SLE outcomes.

Results: Patient and clinical characteristics are summarized in Table 1. Among 82 samples collected from 70 patients between 8/1/20 and 5/20/21, mean±SD HCQ levels were 813±502 ng/ml. HCQ dosing, renal function and adherence were the key variables predicting HCQ levels. We noted that regardless of adjustment for body weight, patients taking

200 mg/day had lower HCQ levels (Mean Difference -415 ng/ml, CI -134, -697; p 0.005, Table 2). We found an inverse relationship between renal function and HCQ blood levels. For every 10 mL/min increment in glomerular filtration rate (GFR), there was a 44 ng/mL decline in HCQ levels (CI -43, -84; p 0.03). Further, we found that patients with CKD stage ≥3 had significantly higher HCQ levels by 345 ng/ml (CI 42, 648; p 0.02, data not shown). Finally, we found that every 10% increase in patient-reported adherence predicted an 83 ng/ml increase in HCQ levels (CI 45, 120; p < 0.001). We found no associations between weight and HCQ levels.

HCQ levels ≥500 ng/ml predicted 40-fold higher odds of patient-reported adherence by VAS (p 0.0007, data not shown). There was a good correlation between HCQ levels and patient-reported adherence (0.55, p < 0.001, data

Table 1. Demographics Table (n = 70 patients)

Table 1. Demographics Table (n = 70 patients)

Age (Mean ± SD)	46±15 years
Gender	
Male	5 (7%)
Female	65 (93%)
Race	
White	43 (62%)
Other Race/Ethnicity*	27 (38%)
Active Smoker	1 (1%)
Body Weight (Mean ± SD)	81±19 Kgs
GFR (Mean ± SD)	95±29 mL/min
CKD Stage ≥3	9 (13%)
SLEDAI ≥6	14 (20%)
Reported Nonadherence	10 (14%)
Dose 200 mg/d	14 (20%)

**Includes Hispanic ethnicity*

Table 2. Interindividual factors affecting HCQ blood levels using multivariable linear regression, n = 82 blood samples

Table 2. Interindividual factors affecting HCQ blood levels using multivariable linear regression, n = 82 blood samples

Variables	Mean Change in HCQ Blood Levels (ng/ml), 95% CI	p-value
Age (in 10 years increments)	-34 (-110, 43)	0.39
Gender		
Male	ref	
Female	-3.4 (-394, 388)	0.99
Racial/Ethnic Groups		
White	ref	
Other Race/Ethnicity*	1.7 (-200, 204)	0.99
Weight (in 1 Kg increments)	-4.1 (-9.8, 1.8)	0.16
GFR (in 10 mL/min increments)	**-44 (-82, -43)**	**0.03**
Prescribed HCQ Dose**		
400 mg Daily	ref	
200 mg Daily	**-415 (-697, -134)**	**0.005**
200 & 400 mg Alternate Days	-237 (-517, 44)	0.097
300 mg Daily	-217 (-1071-637)	0.62
200 mg BID	23 (-260, 305)	0.87
Patient-reported Adherence (in 10% increments)	**83 (45, 120)**	**<0.0001**

**Includes Hispanic ethnicity; Significant findings bolded; **No patients were on <200 mg/day dose*

Table 3. Multivariable Analysis of HCQ Blood Levels Predicting Active SLE, SLEDAI ≥6 in Age, Gender, Race, and Patient-Reported Adherence Model; n = 82 blood samples

Table 3. Multivariable Analysis of HCQ Blood Levels Predicting Active SLE, SLEDAI ≥6 in Age, Gender, Race, and Patient-Reported Adherence Model; n = 82 blood samples

Variables	OR Active SLE (95% CI)	p-value
HCQ Level Categories		
<250 ng/ml	*ref*	*ref*
>250-500 ng/ml	0.77 (0.65, 8.6)	0.83
>500-750 ng/ml	1.1 (0.15, 8.8)	0.95
>750-1000 ng/ml	0.18 (0.01, 2.3)	0.21
>1000 ng/ml	**0.06 (0.002-0.77)**	**0.04**

**Includes Hispanic ethnicity; Significant findings bolded*

not shown). Finally, we noted that HCQ levels ≥1000 ng/ml predicted 94% lower odds of active SLE (SLEDAI ≥6) (OR 0.06, CI 0.002-0.77, p 0.039, Table 3) and clinically meaningful change in SLEDAI (-2.7, CI -1.1, -4.4, p 0.036).

Conclusion: We found that HCQ dose, adherence and renal function predicted significant variations in HCQ blood levels. Patients with CKD stage ≥3 had markedly higher HCQ levels, which could portend higher HCQ toxicity in this group. Conversely, prescribing lower HCQ doses could permit higher flare risk. Our findings support that individualizing HCQ dosing based on GFR could benefit SLE patients. Future work will focus on how to effectively individualize dosing to reduce toxicity and flares in diverse SLE patients.

Disclosure: S. Garg, None; **K. Hansen**, None; **B. Chewning**, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 0876

Antibody Response in Patients with Systemic Lupus Erythematosus After a Two-dose Regimen with SARS-CoV-2 Vaccines (Preliminary Results)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) often receive immunosuppressive treatment for many years, resulting in higher risk of infections, including COVID-19, and infections may trigger disease flares. Patients with SLE show reduced immunogenicity against influenza and pneumococcal vaccination, however the immune response depends on immunosuppressive therapy and disease activity. Our aim was to investigate the immune response during a 24-month follow-up period in patients with SLE following COVID-19 vaccination with a two-dose regimen.

Methods: Patients with SLE (≥18 years of age) in the Region of Southern Denmark were invited to participate in the study. Blood samples were drawn approximately 3 weeks after the first vaccination and 4 and 8 weeks after

Table 1. Preliminary results from 90 patients eight weeks after a two-dose regimen of COVID-19 vaccination

Table 1. Preliminary results from 90 patients eight weeks after a two-dose regimen of COVID-19 vaccination

	N (%)
Sex (females)	79 (87.8)
Age (years, median; IQR)	52; 42-64
Vaccine type	
BNT162b2 (Pfizer)	87 (97.7)
AZD1222 (AstraZeneca)	2 (2.2)
mRNA-1273 (Moderna)	1 (1.1)
Active smokers (n=88)	12 (13.6)
SLE disease duration at time of vaccination (years, median; IQR)	13; 6-25
Influenza vaccination during the previous year	71 (78.9)
Medical treatment of SLE	
*DMARD**	43 (38.7)
Hydroxychloroquine	67 (60.3)
*Biologics***	5 (4.5)
Prednisolone (daily dose<7.5 mg)	25 (22.5)
Prednisolone (daily dose>7.5 mg)	5 (4.5)
No treatment	12 (10.8)

** Methotrexate, Azathioprine, Mycophenolic acid, Mycophenolate mofetil. Not including Hydroxychloroquine*

*** TNFα inhibitors, Belimumab, Rituximab.*

the second vaccination. SLEDAI-score and SLICC damage were assessed between vaccinations and 8 weeks after the second vaccination. Patients' hospital records were reviewed for clinical information and treatment data. Anti-SARS-CoV-2 Spike IgG was determined using Abbotts SARS-CoV-2 IgG II Quant. Resulting concentrations (AU/ml were converted to IU/ml using a lot-specific factor calibrated against the "First WHO International Standard for anti-SARS-CoV-2 immunoglobulin (20/136)). A positive cut off for Anti-SARS-CoV-2 Spike IgG was set at >8.7 IU/ml. Nucleocapsid IgG was determined using Abbotts SARS-CoV-2 IgG.

Results: A total of 128 patients with SLE were included in the study. We report the preliminary results of antibody response to the SARS-CoV-2 spike antigen of 90 patients who have completed the two-dose vaccine regimen in this ONGOING STUDY (Table 1). Of these, 55 (49.5%) of the participants had blood samples drawn for IgG antibodies after the first vaccination and seropositive SARS-CoV-2 spike IgG antibody titers were detected in 31 (56.4%) with an overall mean of 92.7 IU/ml (±327.6).

The response rate was increased to 93.3% (84) four weeks after the second dose with an overall mean of 1601.3 IU/ml (±1752.6). Of participants with a positive response 81 (96.4%) recieved the BNT162b2 vaccine, 2(2.4%) recieved the AZD1222 vaccine and 1(1.2%) recieved the mRNA-1273 vaccine.

The median SLEDAI score was 2 (IQR: 0-6) and SCLICC damage score was 1 (IQR: 0-2) between vaccinations, and there was no significant difference between responders and non-responders (Mann-Whitney, P=0.2113 and P=0.0623, respectively). All participants were negative for SARS-CoV-2 nucleocapsid IgG, suggesting that none of the patients had COVID-19 prior to vaccination.

Conclusion: Patients with SLE had a good antibody response after COVID-19 vaccination, without secondary flare of disease activity.

Disclosure: E. Stavnsbjerg Larsen, None; **A. Nilsson**, None; **U. Stenz Justesen**, None; **A. Voss**, None; **I. Somuncu Johansen**, None.

Abstract Number: 0877

Association of HCQ Blood Levels with Type 1 and 2 SLE Activity

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Background/Purpose: HCQ levels reflect adherence and have been shown to correlate with SLE outcomes. However, HCQ levels have not been studied in the context of a novel conceptual model which categorizes SLE activity into Type 1 (including arthritis, rash, nephritis) and Type 2 manifestations (including myalgias, mood disturbance, and cognitive dysfunction). We hypothesized that HCQ levels would inversely correlate with Type 1 but not Type 2 SLE activity.

Methods: Those meeting ACR or SLICC classification criteria for SLE were recruited from an academic lupus clinic. We measured whole blood HCQ levels using liquid chromatography coupled to mass spectrometry. Patients were categorized by HCQ levels as under-exposed (HCQ < 200 ng/ml), subtherapeutic (HCQ between 200-1000 ng/ml), or

Table 1. Comparing socio-demographics, self-reported adherence, and HCQ dosing information among patients with different HCQ levels.

	Total cohort (n=81)	Under-exposed HCQ (n=12)	Subtherapeutic HCQ (n=32)	Therapeutic HCQ (n=37)	p-value
Socio-demographics					
Age in years	42[30-49]	33[27-37]	44[32-53]	38[30-49]	0.07
Female gender	90%	92%	94%	86%	0.6
Black	73%	92%	66%	73%	0.2
Less than a College Education	51%	75%	50%	43%	0.2
Married/cohabitating	39%	33%	47%	34%	0.5
Income over $50,000	29%	8%	23%	42%	0.06
Private Insurance	58%	42%	47%	73%	0.04
Self-Reported Adherence:					
Self-reported adherence ≥90%	75%	67%	78%	76%	0.7
HCQ Dosing Information:					
Creatinine					
<1.4	89%	100%	93%	83%	0.04
1.4-4.9	8%	0%	0%	17%	
≥5	3%	0%	7%	0%	
HCQ dose					
>5mg/kg	24%	33%	27%	19%	0.04
4-5mg/kg	31%	25%	13%	47%	
<4mg/kg	45%	42%	60%	33%	
Weight in kg	85[68-108]	77[68-92]	78[65-111]	87[74-100]	0.6

Footnotes: continuous variables are summarized by median [interquartile range]

Table 2. Comparing measures of Type 1 and Type 2 SLE activity among patients with different HCQ levels.

	Under-exposed HCQ (n=12)	Subtherapeutic HCQ (n=32)	Therapeutic HCQ (n=37)	p-value
Type 1 SLE Activity:				
Type 1 PGA	1[0.5-1.5]	0.5[0.1-1.3]	0.25[0-0.8]	0.04
Type 1 PGA ≥1	67%	34%	19%	0.008
SLEDAI	5[0-9]	2[0-4]	2[0-4]	0.3
Type 2 SLE Activity:				
Type 2 PGA	1.4[0.5-2]	0.5[0.3-1.1]	0.5[0.25-1.3]	0.03
Type 2 PGA ≥1	67%	34%	35%	0.1
Depression (PHQ-2)	15%	11%	17%	0.6
Polysymptomatic Distress Score[1]	16[12-23]	8[4-12.5]	8[3.5-11]	0.01
Widespread Pain Index	8[3.5-12.5]	3.5[1-7]	3[1-6]	0.07
Symptom Severity Score	7[5-10]	4[2-5]	4[1.5-6]	0.07
Fatigue[2]	67%	63%	35%	0.07
Cognitive dysfunction[2]	44%	8%	12%	0.03
Unrefreshed sleep[2]	78%	31%	25%	0.02

Footnotes: continuous variables are summarized by median [interquartile range];
[1]Polysymptomatic distress score is the sum of widespread pain index and symptom severity score; [2]Fatigue, cognitive dysfunction, and unrefreshing sleep are components of the symptom severity score; the percentage of patients reporting moderate-severe levels of these symptoms.

therapeutic (HCQ >1000 ng/ml). Type 1 SLE activity measures included Type 1 Physician Global Assessment (PGA) and SLEDAI. Type 2 SLE activity measures included Type 2 PGA, patient-reported Polysymptomatic Distress (PSD) score, and depression based on the Patient Health Questionnaire-2. SLE groups were defined as Minimal (low Type 1 and 2 activity), Type 1 (high Type 1 and low Type 2 activity), Mixed (high Type 1 and 2 activity), and Type 2 (low Type 1 and high Type 2 activity). Self-reported adherence was measured using the visual analog scale of the Medication Adherence Self-Report Inventory. We used the Chi-squared and Kruskal-Wallis tests to examine differences across patient groups.

Results: This analysis included 81 patients (median age 42, 90% female, 73% Black, 51% < college education, 39% married or cohabiting, 29% with annual household income >$50,000, and 58% with private insurance). HCQ levels were under-exposed in 15%, subtherapeutic in 39%, and therapeutic in 46% of patients (Table 1).

Patients with therapeutic HCQ levels were more likely to have private insurance and a trend for older age and higher income. Self-reported adherence was similarly high among the three HCQ groups. Patients with lower HCQ levels are more likely to have lower creatinine, but weight and HCQ dose prescribed did not appear to play a consistent role in therapeutic drug level.

Lower HCQ levels were significantly associated with both higher Type 1 and Type 2 SLE activity. Patients with lower HCQ levels self-reported a higher PSD score, more cognitive dysfunction and nonrestorative sleep. There was also a trend for patients with lower HCQ blood levels to have more fatigue, areas of pain, and higher symptom severity scores (Table 2).

Comparing HCQ levels across SLE groups, patients with Mixed SLE activity had significantly lower HCQ levels compared to all other patients (Table 3).

Conclusion: More than half of the patients had lower than therapeutic HCQ blood levels, and surprisingly, this was associated with both higher Type 1 and Type 2 SLE activity. Although Type 2 SLE manifestations are conventionally

Table 3. Comparing HCQ levels across SLE groups.

	Minimal (n=37)	Type 1 (n=11)	Mixed (n=20)	Type 2 (n=7)	p-value
HCQ level	1005 [708-1247]	1005 [660-1581]	502 [18-992]	1402 [1338-1418]	0.048
HCQ<200	3%	18%	35%	0%	0.007
HCQ 200-1000	46%	27%	40%	14%	
HCQ>1000	51%	55%	25%	86%	

Footnotes: continuous variables are summarized by median [interquartile range]

High Type 1 SLE activity is defined by: SLEDAI ≥6, clinical SLEDAI ≥4, active lupus nephritis, or Type 1 PGA ≥1.0; High Type 2 is defined by: FSS ≥8 or Type 2 PGA ≥1.0

SLE groups are defined as: Minimal (low Type 1 and 2 activity), Type 1 (high Type 1 and low Type 2 activity), Mixed (high Type 1 and 2 activity), and Type 2 (low Type 1 and high Type 2 activity).

thought to be noninflammatory, their inverse association with HCQ blood levels in patients with concurrent Type 1 SLE activity suggest that in some SLE patients, immunologic activity may contribute to these debilitating symptoms.

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Abstract Number: 0878

Investigating the Neutrophil to Lymphocyte Ratio as a Marker of SLE Disease Activity, Health-Related Quality of Life and Depression

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The need for readily available markers of SLE activity has led to the evaluation of laboratory parameters, such as the neutrophil to lymphocyte ratio (NLR). Our goal was to ascertain the association of NLR with SLE activity and damage, and further evaluate its association with disease specific health-related quality of life (HRQoL) and depression.

Methods: This cross-sectional study included data from 134 patients from the Cyprus SLE registry. All patients fulfilled the SLICC classification criteria 2012. The following data were captured: NLR, demographic parameters, patient self-rated health (poor/fair vs. good/excellent), SELENA-SLEDAI index (score ≥4 was defined as active disease), SLICC/ACR damage index (DI) (damage defined as score ≥1). HRQoL was assessed by the Lupus QoL, a disease specific measure that includes 8 domains (physical health, pain, planning, intimacy, burden to others, emotional health, body image, and fatigue). Each domain score ranges from 0 to 100, with higher scores indicating better QoL. Depression was evaluated by the patient health questionnaire (PHQ-9) and higher scores suggest the presence of im-

Table 1. Activity index - SELENA-SLEDAI, Damage index - SLICC/ACR DI, Lupus QoL and PHQ9 indices							
	Overall		NLR<2.73		NLR>=2.73		
	N	Median [Q1, Q3] or n (%)	N	Median [Q1, Q3] or n (%)	N	Median [Q1, Q3] or n (%)	p-value
Activity index -SELENA-SLEDAI	134	2 [0, 5]	87	2 [0, 4]	47	4 [2, 8]	**0.002**
Active disease (SELENA-SLEADI ≥ 4)		61 (45.5%)		33 (37.9%)		28 (59.6%)	**0.016**
Damage index - SLICC/ACR DI	134	0 [0,1]	87	0 [0,1]	47	0 [0,2]	0.054
Damage (SLICC/ACR DI ≥1)		43(32.1%)		23 (26.4%)		20 (42.6%)	0.057
Lupus QoL							
Physical health	131	68.8 [34.3, 87.5]	85	75.0 [53.1, 93.7]	46	59.4 [28.1, 81.3]	**0.012**
Pain	131	75.0 [41.6, 91.7]	85	75.0 [50.0, 100.0]	46	66.6 [41.6, 83.3]	0.155
Planning	131	75.0 [41.6, 100.0]	85	83.3 [50.0, 100.0]	46	58.3 [33.3, 91.6]	**0.010**
Intimacy	60	75.0 [50.0, 75.0]	40	75.0 [50.0, 81.2]	20	50.0 [31.3, 75.0]	0.108
Burden to others	130	75.0 [58.0, 100.0]	84	79.0 [58.3, 100.0]	46	75.0 [50.0, 100.0]	0.286
Emotional health	131	79.1 [58.3, 91.6]	85	79.1 [66.6, 91.6]	46	72.9 [50.0, 88.0]	0.154
Body image	130	87.5 [66.6, 100.0]	85	91.6 [75.0, 100.0]	45	80.0 [55.0, 100.0]	**0.028**
Fatigue	131	68.7 [50.0, 87.5]	85	62.5 [50.0, 87.5]	46	68.7 [37.5, 81.2]	0.502
PHQ 9							**0.033**
% Minimal depression 0-4		54 (40.9%)		35 (40.7%)		19 (41.3%)	
% Mild depression 5-9		37 (28.0%)		28 (32.6%)		9 (19.6%)	
% Moderate depression 10-14		25 (18.9%)		18 (20.9%)		7 (15.2%)	
% Moderately severe depression 15-19		9 (6.8%)		3 (3.5%)		6 (13.0%)	
% Severe depression 20-27		7 (5.3%)		2 (2.3%)		5 (10.9%)	
Depression (PHQ≥10)							0.143
% Yes		41(31.1%)		23 (26.7%)		18 (39.1%)	
% No		91(68.9%)		63 (73.3%)		28 (60.9%)	
Moderately Severe or Severe Depression (PHQ≥15)							**0.002**
% Yes		16 (12.1%)		5 (5.8%)		11 (23.9%)	
% No		116 (87.9%)		81 (94.2%)		35 (76.1%)	
PHQ 9 score	131	6 [3, 11]	86	6 [2, 10]	45	7 [3, 14]	0.082

Abbreviations: SELENA-SLEDAI, Safety of Estrogens in Lupus Erythematosus National Assessment - Systemic Lupus Erythematosus Disease Activity Index; SLICC/ACR DI, Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index; Lupus QoL, Lupus Quality Of Life; PHQ, Patient Health Questionnaire; NLR, Neutrophil to lymphocyte ratio.

paired depressive symptoms. Scores ≥15 are consistent with severe or moderately severe depression. Patients were separated in two groups using an NLR cutoff of 2.73, which corresponds to the 90th percentile of healthy individuals. Mean ± SD and median (q1, q3) were reported for normally and not normally distributed variables and compared using the student's t-test and Wilcoxon test, respectively. Categorical variables were compared using the $\chi 2$ test of independence. Unadjusted and adjusted logistic regression models were used, adjusting for age, sex, and BMI and odds ratios (OR) with the corresponding 95% CIs and p-values were reported. All tests performed were two-tailed, using an alpha level of significance of 0.05

Results: Out of the 134 SLE patients, 47 (35%) had NLR ≥2.73 and among them the mean age was 47 years old and 85% were females. Compared to the NLR< 2.73 group, SLE patients with NLR ≥2.73 were more likely to report poor/fair self-rated health (53.2% vs. 28.7%, p=0.005) and higher activity based on the SELENA-SLEDAI-index (median

4 vs. 2, p=0.002). There was no statistically significant difference between the groups in SLICC/ACR DI (p=0.054) or presence of damage (p=0.057). Several LupusQoL domains such as physical health (p=0.012), planning (p=0.010), and body image (p=0.028), were significantly lower in the high NLR group (Table 1). While no significant difference was found in the presence of depression (PHQ ≥10) (p=0.143) or overall PHQ-9 score (p=0.082), there were significantly more patients with moderately severe or severe depression (PHQ ≥15) in the high NLR group (23.9% vs. 5.8%, p=0.002). Adjusted logistic regression models revealed a significant association between high NLR and moderately severe or severe depression (OR=7.21), poor/fair self-reported health (OR=2.79), high disease activity (SLEDAI≥4) (OR=2.23) and the presence of damage (SLIC/ACR DI ≥1) (OR=2.51).

Conclusion: High NLR in SLE patients is associated with active disease, damage, severe depression, and worse HRQoL and self-rated health.

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Abstract Number: 0879

Anti-dsDNA Antibodies Increase Systemic Lupus Erythematosus Cardiovascular Risk Impairing the Immune and Cardiovascular Systems

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: This study aimed to delineate the role of anti-dsDNA antibodies on the alterations observed in the gene profile and the activity of immune and vascular cells in systemic lupus erythematosus (SLE) patients, as well as on their cardiovascular risk.

Methods: Eighty SLE patients were included. Extensive clinical/analytical evaluation was performed, including parameters related to cardiovascular diseases (CVD) such as endothelial function, proatherogenic dyslipidemia, and carotid intima-media thickness. Gene and protein expression profiles were evaluated in monocytes from patients positive and negative for anti-dsDNA antibodies by using Nanostring and cytokine arrays respectively. NETosis was assessed in both, neutrophils and plasma through analysis of nucleosomes, neutrophil elastase, and myeloperoxidase. The circulating inflammatory profile was also quantified by Luminex assays.

Results: Positivity and persistence of anti-dsDNA antibodies in SLE patients were found associated with endothelial dysfunction, pro-atherogenic dyslipidemia, and accelerated atherosclerotic process. In parallel, anti-dsDNA antibodies were linked to the aberrant activation of innate immune cells, so that anti-dsDNA(+) SLE monocytes showed distinctive gene and protein expression/activity profiles, and neutrophils were more prone to suffer NETosis in com-

parison with anti-dsDNA(-) patients. Anti-dsDNA(+) patients further displayed altered levels of numerous circulating mediators related to inflammation, NETosis, and enhanced CV risk. In vitro, Ig-dsDNA promoted NETosis on neutrophils, apoptosis on monocytes, modulated the expression of inflammation and thrombosis-related molecules, and induced endothelial activation, at least partially, by FcR-binding mechanisms.

Conclusion: Anti-dsDNA antibodies increase the cardiovascular risk of SLE patients by altering key molecular features that drive a distinctive and coordinated immune and vascular activation.

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Abstract Number: 0880

Health Information Use by SLE Patients Pre and During COVID-19

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: The spread of COVID-19 misinformation is especially serious for individuals with complex diseases like SLE; conflicting and/or unfounded information can complicate a patient's health decision making and exacerbate stress. We assessed how SLE patients access and trust health information pre and during COVID-19.

Methods: Canadian and international patients fulfilling the ACR or Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for SLE were recruited from 15 observational SLE research cohorts, and patients self-reporting SLE were recruited through five patient advocacy organizations. Participants completed an online survey from June 2020-April 2021 regarding the sources of health information they accessed in the 12 months preceding

(pre 03/11/2020) and during the COVID-19 (post 03/11/2020) pandemic. We calculated the percentage of patients accessing each source of information, their preferred sources, and the level of trust in each source. McNemar tests were used to compare frequencies pre and post 03/11/2020 in the Canadian and international samples.

Results: 845 Canadian and 1090 international (Asia n=201, Europe n=324, Latin America n=118, US n=447) patients completed the survey (40.4% and 21.0% response rates, respectively); 78.0% were recruited through SLE research cohorts, 92.7% were female, 35.2% reported non-white race/ethnicity, mean age at diagnosis was 32.0 years (SD 13.3) and mean disease duration was 16.6 years (SD 12.0). 76.6% of participants had completed post-secondary education, and 2.1% reported a positive COVID-19 test. Canadian and international patients accessed news media more frequently during vs pre pandemic (44.6% of Canadians accessed sometimes/often/always pre vs 52.1% during; 59.8% of international participants accessed pre vs 68.9% during), while access to family physicians, lupus specialists, pharmacists and alternative care providers decreased in both samples during the pandemic (Table 1). Lupus specialists and family physicians were ranked the most preferred information sources (Table 2) and considered the most trustworthy (Table 3) pre and during the pandemic. News media was more preferred post vs pre 03/11 (Table 2), yet was considered less trustworthy in Canada (44.5% rated online news media as somewhat/very trustworthy pre vs 41.8% post) and internationally (43.0% pre vs 40.2% post) during COVID-19 (Table 3). In both samples, patient

Table 1. Health Information Source Frequency of Access, Pre and Post March 11, 2020

	Health Information Source Accessed *					
	Canada			International		
	Pre 03/11/20 %	Post 03/11/20 %	95% CI for Post-Pre Difference	Pre 03/11/20 %	Post 03/11/20 %	95% CI for Post-Pre Difference
Family Physicians	59.6	48.5	**-11.1 (-14.6, -7.7)**	53.4	49.9	**-3.5 (-6.4, -0.6)**
Lupus Specialists	72.0	57.8	**-14.2 (-17.7, -10.7)**	82.8	77.7	**-5.1 (-7.6, -2.7)**
Pharmacists	53.3	45.8	**-7.5 (-10.8, -4.1)**	40.7	36.5	**-4.2 (-6.8, -1.6)**
Alternative Care Providers	23.6	14.6	**-9.0 (-11.7, -6.3)**	17.0	12.6	**-4.4 (-6.3, -2.6)**
Peers	35.9	34.7	-1.2 (-4.4, 2.1)	42.9	46.7	**3.8 (1.0, 6.5)**
Patient Advocacy Organizations	31.1	28.6	-2.5 (-5.3, 0.3)	40.9	44.1	**3.2 (0.8, 5.7)**
News Media	44.6	52.1	**7.6 (3.9, 11.0)**	59.8	68.9	**9.1 (6.1, 12.0)**
Social Media	31.2	32.8	1.5 (-1.3, 4.4)	44.8	47.6	**2.8 (0.3, 5.4)**
**Respondents who reported health information source access sometimes/often/always*						

Table 2. Preferred Health Information Sources, Pre and Post March 11, 2020

	Canada		International	
	Pre 03/11/20	Post 03/11/20	Pre 03/11/20	Post 03/11/20
Lupus Specialists	1	1	1	1
Family Physicians	2	2	2	2
Pharmacists	3	4	6	7
News Media	4	3	4	3
Patient Advocacy Organizations	5	5	3	4
Peers	6	7	7	6
Alternative Care Providers	7	8	8	8
Social Media	8	6	5	5
Respondents ranked their three most preferred sources. Sources were then scored and ranked from most preferred (1) to least preferred (8)				

Table 3. Trustworthiness of Health Information Source, Pre and Post March 11, 2020

	Trust in Source *					
	Canada			International		
	Pre 03/11/20 %	Post 03/11/20 %	95% CI for Post-Pre Difference	Pre 03/11/20 %	Post 03/11/20 %	95% CI for Post-Pre Difference
Family Physicians	80.8	78.8	-2.0 (-4.8, 0.8)	71.1	72.8	1.7 (-0.5, 3.8)
Lupus Specialists	89.8	89.5	-0.4 (-2.4, 1.7)	92.7	92.6	-0.1 (-1.6, 1.4)
Pharmacists	79.5	78.5	-1.1 (-3.4, 1.2)	60.0	58.3	-1.7 (-4.0, 0.5)
Alternative Care Providers	32.8	29.0	**-3.8 (-6.0, -1.6)**	23.8	21.4	**-2.4 (-4.3, -0.5)**
Peers	25.9	27.1	1.2 (-1.4, 3.8)	25.5	27.2	1.7 (-0.5, 4.0)
Patient Advocacy Organizations	54.2	50.1	**-4.1 (-6.7, -1.6)**	61.8	56.8	**-5.0 (-7.2, -2.9)**
Newspaper	28.9	28.0	-0.8 (-3.5, 1.8)	34.7	29.9	**-4.8 (-7.1, -2.5)**
Online News Media	44.5	41.8	**-2.7 (-5.4, -0.1)**	43.0	40.2	**-2.8 (-5.0, -0.6)**
Radio	28.8	26.3	**-2.5 (-4.9, -0.1)**	29.7	24.8	**-5.0 (-6.9, -3.0)**
Television	40.4	38.7	-1.7 (-4.3, 1.0)	37.9	35.7	-2.2 (-4.4, 0.0)
Facebook	12.0	12.7	0.7 (-1.1, 2.5)	17.0	14.8	**-2.2 (-4.1, -0.3)**
Instagram	5.8	6.4	0.6 (-0.9, 2.0)	9.8	8.9	-0.9 (-2.4, 0.5)
Internet Blog	8.5	8.4	-0.1 (-2.0, 1.7)	13.3	11.0	**-2.3 (-3.9, -0.7)**
Twitter	5.7	5.8	0.1 (-1.3, 1.6)	8.3	8.1	-0.3 (-1.5, 0.9)
YouTube	12.2	11.5	-0.7 (-2.4, 1.0)	18.1	16.8	-1.3 (-3.1, 0.6)
Other Social Media (e.g., LinkedIn, Pinterest, Reddit, TikTok)	7.8	6.9	-0.9 (-2.5, 0.6)	8.1	7.2	-0.8 (-2.3, 0.6)
**Respondents who reported source as somewhat/very trustworthy*						

advocacy organizations were accessed less frequently pre and during COVID-19 than other less preferred and trusted sources (e.g., peers, social media), and trust in advocacy organizations decreased during the pandemic in both Canadian and international samples by 4.1% and 5.0%, respectively.

Conclusion: Although lupus specialists and family physicians were ranked as the most preferred and trustworthy health information sources, patients accessed these sources less frequently during the pandemic and accessed news media, a less trusted source, more frequently. To increase accessibility to preferred and trusted sources, virtual visits should be promoted where not already in place. This research will improve existing information dissemination pathways valued by SLE patients.

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Abstract Number: 0881

Economic Evaluation of Neuropsychiatric (NP) Lupus in an International Inception Cohort Using a Multistate Model Approach

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Little is known about the economic burden of NP lupus. We estimated annual and cumulative direct and indirect costs (DC, IC) associated with NP events attributed to SLE and non-SLE causes using multistate modelling in a multicentre, multi-ethnic inception cohort.

Methods: Patients fulfilling revised ACR classification criteria for SLE from 31 centres in 11 countries were enrolled within 15 months of diagnosis. NP events were documented annually using ACR NP case definitions and attributed to either SLE or non-SLE causes. At each assessment and for both SLE and non-SLE events, patients were stratified into 1 of 3 NP states (no, resolved, or new/ongoing NP event). The change in NP status characterized by transition rates between states was analyzed over time, using multistate modelling for SLE attributed NP events and non-SLE attributed NP events (*Hanly. A&R 2021;* https://doi.org/10.1002/art.41876*)* (Fig 1).

At each assessment, annual DC and IC were based on health resource use and lost work-force/non-work-force productivity over the preceding year. Resource use was costed using 2021 Canadian prices and lost productivity using Statistics Canada age-and-sex specific wages. Costs associated with each SLE and non-SLE NP state were

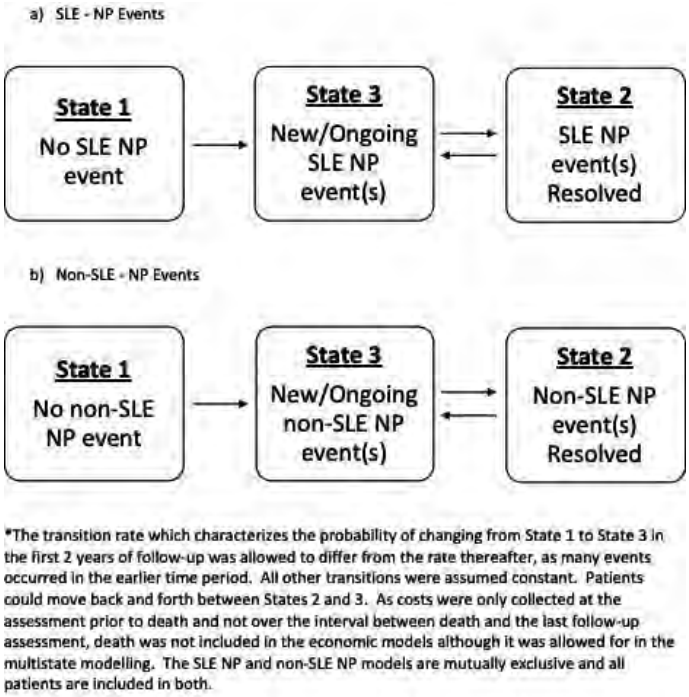

Figure 1. Reversible Multistate Patient Level Models for Observed Transitions* in a) SLE NP Events and b) Non-SLE NP Events.

Table 1. Observed Annual Unadjusted Costs (in 2021 Canadian dollars), Stratified by a) SLE NP State and b) Non-SLE NP State

a) SLE NP States

Current NP State	Patients no. *	Observations, no. (%)	Direct Costs Mean (95%CI)	Indirect Costs Mean (95%CI)
State 1**	1487	11155 (80)	6474 (5752, 7196)	24459 (23130, 25788)
State 2	235	1562 (11)	8254 (6449, 10058)	28224 (25059, 31390)
State 3	273	1270 (9)	10721 (8409, 13033)	35921 (32318, 39524)

b) Non-SLE NP States

Current Non-SLE NP State	Patients no.	Observations, no. (%)	Direct Costs Mean (95%CI)	Indirect Costs Mean (95%CI)
State 1	1280	8169 (58)	5874 (5238, 6511)	22322 (20828, 23815)
State 2	504	2922 (21)	8430 (6622, 10238)	30317 (28050, 32584)
State 3	620	2896 (21)	8789 (7381, 10198)	34454 (31638, 37271)

*The number of patients exceeds 1697 as a single patient may have multiple NP states during the study duration and will contribute observations to multiple states.

** State 1 = no NP event; State 2 = resolved NP event; State 3 = new/ongoing NP event

calculated by averaging all observations in each NP state. Multiple regressions including age at diagnosis, sex, race/ethnicity, disease duration, geographic region, and smoking adjusted for possible confounding of these variables on the association of annual DC and IC and NP state. 5 and 10-year cumulative costs for each NP state were predicted

Table 2. Predicted Annual and 5 and 10-Yr Direct and Indirect Costs (in 2021 Canadian dollars), Stratified by SLE and Non-SLE NP States*

a) SLE NP States

		State 1**	State 2	State 3	Difference State 1 & 2	Difference State 1 & 3	Difference State 2 & 3
Direct Costs	1 year	6715	9020	10809	2304 (-2439, 7048)	**4093 (114, 8072)**	1789 (-3769, 7346)
	5 years	35567	45782	52060	10215 (-12590, 33020)	16493 (-4056, 37041)	6278 (-20421, 32976)
	10 years	72307	91193	99496	18886 (-25576, 63348)	27188 (-14884, 69261)	8302 (-43120, 59725)
Indirect Costs	1 year	24805	25133	34939	328 (-5191, 5846)	**10134 (4310, 15958)**	**9806 (3024, 16589)**
	5 years	136970	138257	172674	1287 (-25270, 27844)	**35704 (7705, 63702)**	**34417 (2800, 66033)**
	10 years	289343	293639	339156	4296 (-48915, 57506)	49813 (-5662, 105287)	45517 (-15111, 106145)

b) Non-SLE NP States

		State 1	State 2	State 3	Difference State 1 & 2	Difference State 1 & 3	Difference State 2 & 3
Direct Costs	1 year	6401	8225	8868	1824 (-1412, 5059)	2467 (-676, 5610)	644 (-3117, 4404)
	5 years	34587	41847	44002	7259 (-9411, 23930)	9414 (-6907, 25736)	2155 (-16778, 21088)
	10 years	70890	83515	86262	12625 (-22051, 47301)	15372 (-18829, 49574)	2747 (-35895, 41390)
Indirect Costs	1 year	22866	28195	34225	**5330 (466, 10193)**	**11359 (6000, 16717)**	**6029 (428, 11630)**
	5 years	131194	151794	171979	20599 (-3717, 44915)	**40785 (14979, 66591)**	20186 (-6291, 46662)
	10 years	279874	316701	342434	36827 (-13437, 87091)	**62560 (10663, 114457)**	25733 (-26882, 78348)

*Values are the mean (95% CI).

** State 1 = no NP event; State 2 = resolved NP event; State 3 = new/ongoing NP event

Boldface indicates differences which are significant as the 95% CI does not include 0.

by multiplying adjusted annual costs associated with each state by the expected duration in each state, forecasted using the multistate model.

Results: 1697 patients (89% female, 51% non-Caucasian race/ethnicity, mean age at enrolment 35.1 years) were followed for a mean of 8.8 years. 1971 NP events occurred in 956 patients, 32% attributed to SLE. Across 13,987 assessments, the majority of observations were provided by patients with no NP event (Table 1.) For the SLE NP events, annual DC were higher in those with a new/ongoing vs no event ($10809 vs $6715) (Table 2). Although 5 and 10-yr cumulative DC trended higher in the new/ongoing vs no event, the differences were not significant. However, annual and 5-yr IC were higher in the new/ongoing vs no event and new/ongoing vs resolved event. (5-yr: new/ongoing vs no: $172674 vs $ $136970). For the non-SLE NP events, although all DC trended higher in the new/ongoing vs no event, the differences were not significant. However, annual IC were higher in the new/ongoing vs no

event, new/ongoing vs resolved event, and resolved vs no event and 5 and 10-yr IC were higher in the new/ongoing vs no event (10-yr: new/ongoing vs no: $342434 vs $279874). For all NP states, IC exceeded DC between 2.8 and 4-fold.

Conclusion: IC are approximately 1.3-fold higher in patients with new/ongoing vs no NP events, attributed to either SLE or non-SLE. While DC trended higher in those with new/ongoing events, they did not differ significantly. Impaired productivity associated with both ongoing and resolved NP lupus is substantial and underscores the previously documented reduced quality of life in NP lupus.

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Abstract Number: 0882

COVID-19 Impact Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Initial studies of SLE patients with COVID-19 revealed an increased risk for severe disease in people with distinct demographic features such as advanced age and/or underlying comorbidities comparable to

that of the general population. However, uncertainty remains around the real impact SARS-CoV-2 has in SLE. In this context, we conducted a cross-sectional survey in SLE patients who follow at our tertiary care lupus cohort.

Methods: We designed a questionnaire using the REDCap tool to capture information about demographics, clinical and serological variables related to SLE and COVID-19. The survey was sent between June 1st to August 31st, 2020 to 87 participants. Additional information was gathered from the lupus registry database. After the survey ended subjects underwent SARS-CoV-2 IgG antibody testing.

Results: A total of 79 subjects completed the survey. From these, 6 patients developed COVID-19 infection with many of them disclosing an epidemiologic link. All infected patients were female and the mean age was significantly higher in COVID-19 patients compared to those who did not get infected (p 0.04). We also found a significant relationship between COVID-19 status and race (p 0.02) with the majority of the infected individuals having black ancestry. COVID-19 serology was tested in 46 individuals, showing only one positive result in someone who reported COVID-19 infection. Interestingly, among 4 infected subjects whose serology was obtained only one had evidence of persistent immunity against SARS-CoV-2 10 months after the infection. Additionally, we observed a numeric trend in patients' global disease activity (60 v 41), SLE duration (17 v 12 years), SLICC-DI score (1.8 v 0.7), and mean daily dose of prednisone (3 v 2 mg) in COVID-19 patients compare to non-infected subjects, respectively. In regards to COVID-19 features in SLE, the most common symptoms were headache, shortness of breath, and cough. Despite a prolonged illness and a relative more severe SLE, the majority of infected patients presented with a favorable disease course including the patient who was hospitalized. Moreover, the use of immunosuppressive drugs was not found to be associated with severe infection. COVID-19 related hydroxychloroquine shortage affected up to 16.5% of SLE patients, but at least short-term consequences were not evident. Lastly, we identified that 69% of the respondents were

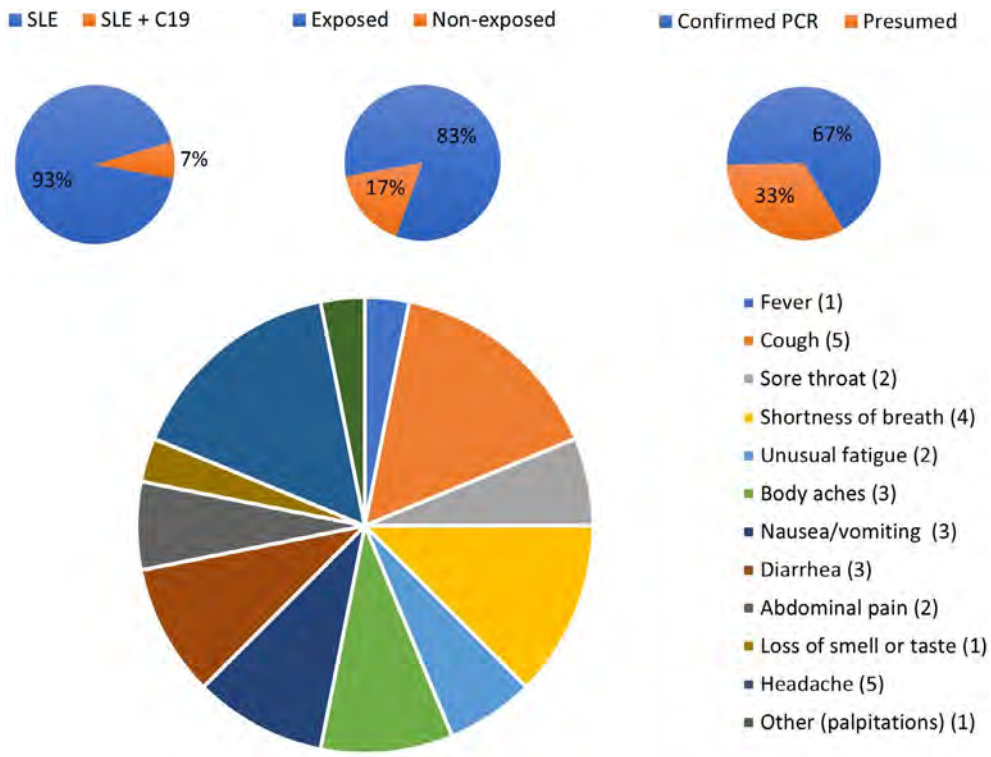

Figure 1. COVID-19 prevalence and symptoms in SLE patients. The prevalence of COVID-19 in patients with SLE (SLE, SLE+C19) is shown on the upper leftmost panel. Exposure history and PCR positivity in SLE patients with COVID-19 are plotted in the middle and rightmost panel, respectively. The prevalence of different symptoms in patients with SLE and COVID-19 are depicted in the lower panel.

Table 1. Characteristics of the surveyed SLE patients

	Total (n=79)	SLE-C19 (+) (n=6)	SLE-C19 (-) (n=73)	P value
Age, years (mean, SD)	42.6 ±12.7	52.3 ±9.7	41.8 ±12.6	**0.04**
Sex n° (%)				
Women	71 (89.9)	6	65	
Men	8 (10.1)		8	
Race n° (%)				**0.02**
White	38 (48.1)	1	37	
Black	30 (38)	4	26	
Asian	10 (12.6)	-	10	
Hispanic	1 (1.3)	1	-	
Comorbidities n° (%)				
Hypertension	15 (19)	2	13	
Diabetes	6 (7)	1	5	
Chronic lung disease	4 (5)	1	3	
SLE duration (mean years, SD)	12.4 ±8.9	16.5 ±8.5	12.1 ±8.9	0.27
SLICC DI (mean score)	0.82 ±1.2	1.8 ±2.1	0.7 ±1.08	0.26
Lupus nephritis n° (%)	26 (32.9)	1	25	
Lupus medications n° (%)				
Hydroxychloroquine Mean daily dose (mg), SD	71 (89.8) 297.97 ±127.5	6 323.6 ±98.3	64 295.8 ±129.9	0.53
Prednisone Mean daily dose (mg), SD	25 (31.6) 2.14 ±3.6	3 3.33 ±4.08	22 2.04 ±3.6	0.48
Mycophenolate	28 (35)	3	25	
Azathioprine	14 (17.7)	1	13	
Belimumab	9 (11)		9	
Methotrexate	6 (7)		6	
Others (LEF, CsA, Anakinra)	4 (5)	1	3	
SARS-CoV-2 IgG antibody n° (%)	46	1	45	

SLE: systemic lupus erythematosus; SLICC-DI: Systemic Lupus International Collaborative Clinics Damage Index; LEF: leflunomide; CsA: cyclosporine A; PGA: patient global assessment; C19: Coronavirus disease 2019.

able to continue medical care through telehealth during the surge, and 87% were eager to make use of telemedicine services in the foreseeable future.

Conclusion: Despite study limitations, our data confirm that age and race are important risk factors for COVID-19 infection in SLE. Importantly, we also noted that neither underlying SLE nor the use of immunosuppressive drugs was found to be risk factors for severe COVID-19 illness though further studies are needed. Finally, our results demonstrated that having COVID-19 infection does not necessarily mean prolonged immunity as this can wane over time. In any case, as the pandemic continues to unfold, rheumatologists should continue stressing preventive measures, recommending vaccination, and offering optimal virtual care when needed to avoid undesirable outco mes.

Table 2. Survey of COVID-19 in SLE

	Total (n=79)	SLE C19 (+) (n=6)	SLE C19 (-) (n=73)	P value
Employment status n° (%)				
Before the pandemic				
Employed (full/part-time)	55/9 (69/11)			
Unemployed	5 (6)			
Other (disabled, retired)	10 (14)			
During the pandemic				
Employed (full/part-time)	50/8 (63/10)			
Unemployed	10 (12.6)			
Other (disabled, retired)	11 (15)			
Continue using immunosuppressive drugs n° (%)	79 (100)			
HCQ shortages n° (%)	13 (16.5)			
PGA score (0 – 100)	40.3 ±29.4	59.75 ±26	40.64 ±29	0.21
Telehealth follow up n° (%)	55 (69)			
Future virtual visits n° (%)	69 (87)			

SLE: Systemic Lupus Erythematosus; HCQ: Hydroxychloroquine; PGA: Patient Global Assessment; C19: Coronavirus disease 2019.

Disclosure: J. Rubio, None; **S. krishfield**, None; **V. Kyttaris**, Exagen Diagnostics, 5, GlaxoSmithKline, 1, Corbus Pharmaceuticals, 1.

Abstract Number: 0883

Multimorbidity Burden in Systemic Lupus Erythematosus: A Nationwide Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have an increased risk of osteoporosis, end-stage renal disease, cardiovascular disease, and other comorbidities. The presence of multiple chronic conditions (multimorbidity) is associated with disability and premature death. We aimed to compare the burden of multimorbidity in SLE patients with the general population.

Methods: An SLE cohort was assembled using OptumLabs Data warehouse (OLDW) from 1/2006-9/2015. SLE cases were identified using ≥ 3 SLE ICD-9 codes separated ≥ 30 days, the date of the third SLE code was considered the index date. SLE patients were matched to non-SLE comparators on age, sex, race, and enrollment date. Diagnosis codes from the period between enrollment and index date were used to determine the presence of comorbidities. Comorbidities were identified using the ICD-9 chronic condition indicator of the clinical classification software

Table. Top 10 most prevalent chronic conditions in SLE vs Non-SLE			
Comorbidity	SLE, N (%) 34,869	Non-SLE, N (%) 34,869	Odds ratio (95%CI)
Essential hypertension	10053 (28.8)	5411 (15.5)	2.6 (2.5-2.7)
Hyperlipidemia	6199 (17.8)	4538 (13.0)	1.5 (1.5-1.6)
Thyroid disorders	4964 (14.2)	2123 (6.1)	2.7 (2.5-2.8)
Osteoarthritis	3798 (10.9)	1092 (3.1)	4.2 (3.9-4.5)
Mood disorders	3634 (10.4)	1701 (4.9)	2.3 (2.2-2.5)
Chronic pain disorders	2989 (8.6)	713 (2.0)	4.6 (4.2-5.0)
Spondylosis; intervertebral disc disorders; other back problems	2957 (8.5)	1164 (3.3)	2.7 (2.5-2.9)
Esophageal disorders	2935 (8.4)	996 (2.9)	3.2 (3.0-3.5)
Diabetes mellitus without complication	2884 (8.3)	2158 (6.2)	1.4 (1.3-1.5)
Anxiety disorders	2117 (6.1)	1053 (3.0)	2.1 (1.9-2.3)

(healthcare cost and utilization project). SLE, cutaneous lupus, and rheumatoid arthritis ICD-9 codes were excluded from the analysis. Two or more ICD-9 codes at least 30 days apart were used to define a comorbidity. We defined multimorbidity as the presence of 2 or more comorbidities (excluding SLE) and substantial multimorbidity as the presence of 5 or more comorbidities. Conditional logistic regression models were performed.

Results: A total of 34,869 SLE patients were matched to 34,869 non-SLE comparators. The mean age was 48 (SD 14.2) years and 90.6% were female. 66.4% were White, 18.4% Black, 3.4% Asian and 18.4% Hispanic. The mean observation time from enrollment to index date was 2.3 (SD 2.4) years. Multimorbidity was present in 58.0% SLE vs. 26.3% non-SLE subjects (OR 5.0; 95%CI 4.8-5.2) and substantial multimorbidity was present in 21.2% SLE patients vs. 6.5% non-SLE subjects (OR 4.6; 95%CI 4.4-4.9). Of the 172 chronic conditions examined, 134 (78%) were more common in SLE than in non-SLE (Table).

Conclusion: In this nationwide commercial insurance database study, patients with SLE were five times as likely to suffer from multimorbidity and substantial multimorbidity compared to the general population. Most comorbidities were overrepresented in SLE patients. It is unclear if multimorbidity in SLE is driven by the disease activity, medication such as steroids, socioeconomic factors, or a combination of these.

Disclosure: A. Duarte-Garcia, None; **H. Heien**, None; **N. Shah**, None; **C. Crowson**, None.

Abstract Number: 0884

Genetics of Longitudinal Disease Activity in Adults with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

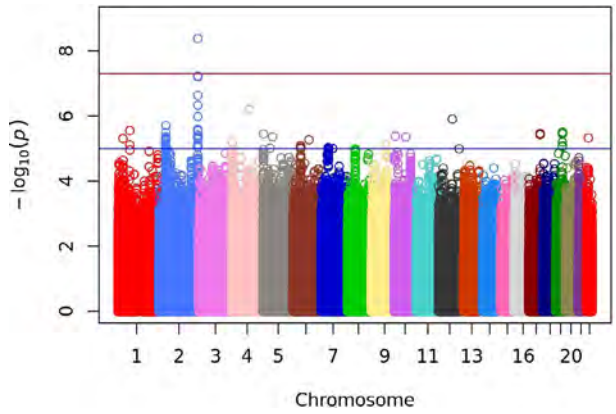

Figure. Manhattan plot for meta-genome-wide association of adjusted mean SLEDAI and corticosteroid exposure over time (AMSG).

Background/Purpose: Genetics and gene expression has been shown to correlate with systemic lupus erythematosus (SLE) disease severity. Our aim was to identify genetic risk loci for disease activity measures over time, representing disease activity burden.

Methods: The cohort study included participants from a tertiary care centre dedicated Lupus Clinic. Participants all met ≥4 of the ACR/SLICC classification criteria for SLE or 3 criteria and a positive biopsy. All participants had prospectively collected clinical data including repeated measures of disease activity evaluated with the Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K). We restricted to participants with a first Lupus clinic visit within 3 years of SLE diagnosis and at least 2 clinic visits within 5 years. Participants were genotyped on the Illumina Multi-Ethnic Global Array, Global Screening Array or Omni 1-Quad array. Ungenotyped SNPs were imputed and ancestry was inferred using principal components (PCs) (1000 Genomes Project reference). The outcome was adjusted mean SLEDAI-2K and corticosteroids (AMSG), the calculated area under the curve of SLEDAI-2K over time, accounting for corticosteroid dose. Continuous square-root of AMS-G was the outcome of interest, transformed to improved normality. We included variants with minor allele frequency (MAF) of ≥0.01 and imputation quality r2 >0.3. Genome-wide additive allelic linear regression models were adjusted for sex and 5 PCs, stratified by array (MEGA+GSA and OMNI) and results were meta-analyzed using inverse variance weighting. A genome-wide significance threshold ($p< 5x10^{-8}$) was used to indicate statistical significance.

Results: The cohort included 538 individuals with SLE. The majority (75%) had a first clinic visit within 1 year of SLE diagnosis. The majority were of European ancestry (54%) with 16% of East Asian ancestry and 12% African ancestry. The median ASMG was 5.5 (IQR 3.2, 8.8). Meta-GWAS identified a genome-wide significant SNP for ASMG (rs4561613) on chromosome 2 intronic to *AGAP1* (Beta 0.34, SE 0.06, *P*=4.2x10-9) (Figure). The overall MAF is 0.43, with a higher risk allele frequency for increased ASMG in non-European ancestral groups (0.67 in African ancestry; 0.41 East Asian ancestry) compared to those of European ancestry (0.36).

Conclusion: We identified a genome-wide significant locus for SLE disease activity burden as measured by AMSG. Variants in *AGAP1* has been linked with body mass index and red blood cell indices. The mechanism by which AGAP1 variants impact disease activity and severity in SLE is unclear. Future studies are required to replicate these findings in independent cohorts.

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Abstract Number: 0885

SLE Phenotypes Formed from Machine Learning and Their Associations with Cognitive Impairment

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Cognitive impairment (CI) in SLE is a significant problem with limited treatment options. This is in part due to the uncertainty regarding the multifaceted cause. Factors associated with CI include depression, pain, fatigue, medications, as well as more specific SLE factors such as disease damage, autoantibodies and inflammation. We aimed to phenotype CI in SLE using machine learning techniques to better enable future personalised targeted treatments.

Methods: SLE patients aged 18-65 years attending a single lupus centre (January 2016 - October 2019) completed the ACR Neuropsychological Battery (ACR-NB) cognitive assessment. Age and gender matched normative data

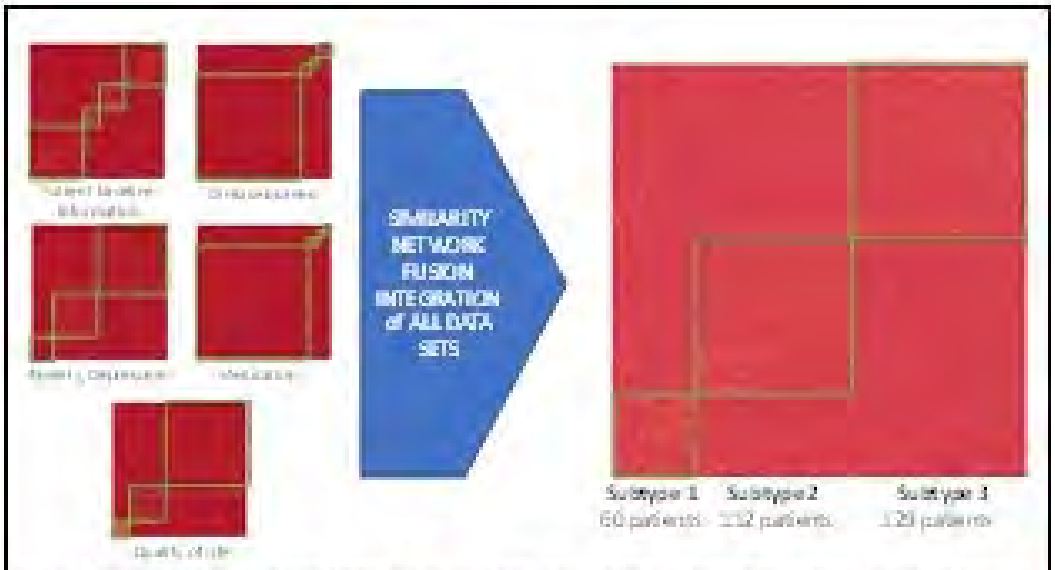

Figure 1. Similarity network fusion (SNF) for first visit data. Three subtypes defined by patterns in patient baseline information, health-related quality of life (HRQoL), depression, anxiety, fatigue, and medication usage. Demographic and clinical variables used within the patient baseline and disease burden information included; age, sex, marital and employment status, education and income level, age at diagnosis, disease damage, disease activity and fibromyalgia status.

were used to obtain z-scores on all 19 tests of ACR-NB. The ACR-NB tests were reduced using principal component analysis (PCA) to generate a factor score (CI Factor Score).

Demographic, and clinical data, and patient reported outcomes including, SF-36, LupusQoL, the PDQ-20 (perceived cognitive deficits), Beck Depression Inventory-II, Beck Anxiety Inventory, and the fatigue severity scale (FSS) were analysed using similarity network fusion (SNF) to identify patient subtypes. Differences between the SNF identified subtypes were evaluated using Kruskal-Wallis tests and chi-square tests.

Results: Of the 301 patients, 89% were women, mean age 40.9 ± 12.1 and mean disease duration 14 ± 10.1 years at study visit. The CI Factor Score accounted for 28.8% of the variance and was associated predominantly with tests of executive function and verbal memory. The SNF analysis defined **subtypes** with distinct patterns in health-related quality of life (HRQoL), depression, anxiety, fatigue, fibromyalgia, medication usage, and disease damage (**figure 1**). The CI Factor Score was significantly different between the subtypes (p=0.008). Examining specific cognitive domains revealed the most significant differences in the language processing (p=0.0008) and executive function tests (p=0.008; p=0.009; p=0.0009). Subtype 3 performed worst on the majority of the different cognitive domains (**figure 3**). Further exploration revealed statistical differences with depression, anxiety, fatigue, and fibromyalgia between the subtypes (**figure 2**). Differences were also found relating to organ involvement within the last ten years and damage within specific organs. No differences were found for SLE disease activity (**figure 2**). Subtype 3 had higher levels of all conditions and disease damage, Subtype 2 had lower levels and Subtype 1 mixed levels.

Conclusion: The subtype with the greatest psychiatric and disease burden and reduced HRQoL performed worse on cognitive testing, specifically in domains of language processing and executive function. This subtype also had more musculoskeletal (MSK) and cardiovascular involvement. MSK involvement affects pain levels, which can impact cognition. Cardiovascular damage may be linked to cerebral small vessel disease, which is known to affect cognitive function SLE patients. Overall, these results aid with phenotyping CI in SLE and provide a baseline for our future longitudinal results. This will then help to determine personalised CI trajectory and treatment options in SLE.

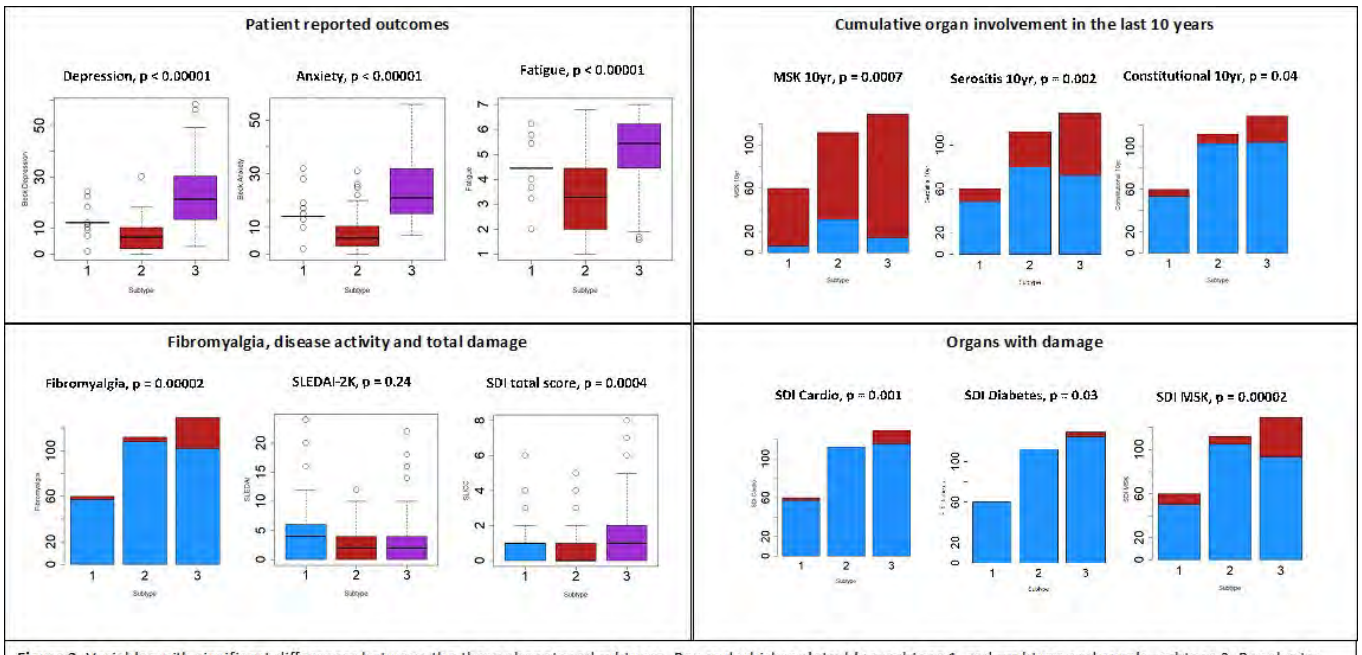

Figure 2. Variables with significant differences between the three phenotyped subtypes. Box and whisker plots: blue=subtype 1, red =subtype and purple=subtype 3. Bar charts: red=number of participants with variable and blue=number without.

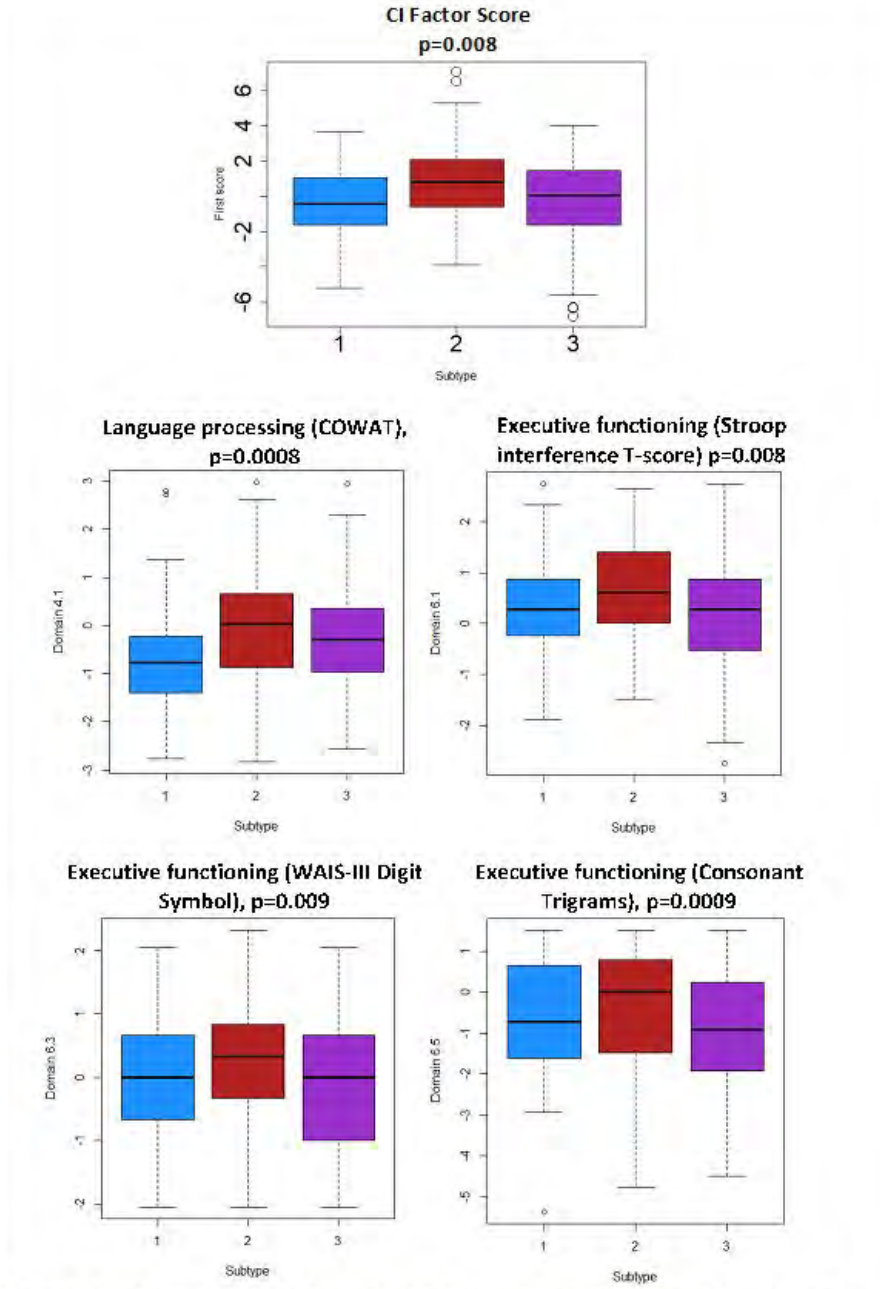

Figure 3. Significant differences between the three subtypes for the PCA determined CI Factor Score and the different cognitive domains tested. Lower score indicates greater cognitive impairment.

COWAT= Controlled Oral Word Association Test
Stroop interference T-score = Predicted interference (word and colour)
WAIS-III= Wechsler Adult Intelligence Scale
Consonant Trigrams = An average score between 0-3 was determined for repetitions of three letters after delays of 9, 18 and 36 seconds. These scores were converted to z-scores and the lowest of the three z-score is represented here.

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8, 9, 10; **D. Bonilla**, None; **D. Beaton**, None; **B. Parker**, Roche, 2, Eli Lily, 2, Fresenius Kabi, 2, Abbvie, 2; **R. Green**, None; **P. Katz**, None; **I. Bruce**, Astra Zeneca, 2, 6, GSK, 2, 5, 6, UCB, 2, 6, Eli Lilly, 2, Aurinia, 2; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6.

Abstract Number: 0886

Determinants of Accessing Social and News Media and Experiencing Negative Impacts During COVID-19 in an International SLE Sample

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SESSION INFORMATION

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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
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Background/Purpose: The spread of COVID-19 misinformation through social/news media is a health risk in SLE. We assessed the determinants of SLE patients accessing health information in social and news media, and self-reporting negative health impacts associated with accessing health information from these sources.

Methods: International patients meeting ACR or Systemic Lupus International Collaborating Clinics Classification Criteria for SLE were recruited from 15 patient cohorts, and patients self-reporting SLE were recruited from five advocacy organizations.They completed an online survey (06/2020-04/2021) about sources of health information accessed preceding (pre 03/11/2020) and during (post 03/11/2020) the COVID-19 pandemic. Logistic regression was used to explore factors (region, sociodemographics, SLE characteristics, access to/trust in sources) associated with: 1) accessing social media, 2) news media, and 3) self-reported negative impacts from health information accessed through these sources.

Results: 1935 patients (Asia n=201, Canada n=845, Europe n=324, Latin America (LA) n=118, US n=447) completed the survey (27.1% response rate): 92.7% female, 35.2% non-white race/ethnicity, mean age at diagnosis 32.0 years (SD 13.3), mean disease duration 16.6 years (SD 12.0), and 76.6% had post-secondary education. 21.6% and 37.0% accessed health information often/always from social and news media, respectively, and 17.0% reported being negatively impacted by health information accessed through these sources.

Table 1. Logistic regression results: access to social and news media often/always*+

Explanatory Variables	Social Media		News Media	
	Adjusted Odds Ratio	95% Confidence Interval	Adjusted Odds Ratio	95% Confidence Interval
Region				
Canada (ref)	1.00	-	1.00	-
Asia	1.26	(0.83, 1.91)	0.97	(0.65, 1.45)
Europe	1.46	(1.03, 2.07)	1.77	(1.26, 2.49)
Latin America	2.19	(1.36, 3.56)	1.71	(1.03, 2.83)
US	0.58	(0.40, 0.84)	0.79	(0.56, 1.10)
Sociodemographics				
Age	0.98	(0.97, 0.99)	1.00	(1.00, 1.01)
Female	2.02	(1.17, 3.49)	1.53	(0.98, 2.37)
Time[a]	-	-	3.18	(1.65, 6.14)
Access/Trust in Health Information Sources				
Access – Family Physicians[b]	0.70	(0.54, 0.92)	0.64	(0.50, 0.80)
Access – Peers[b]	2.33	(1.79, 3.03)	3.16	(2.51, 3.98)
Access – Patient Advocacy Organizations[b]	1.56	(1.19, 2.04)	-	-
Access – News Media[b]	5.78	(3.92, 8.53)	-	-
Access – Social Media[b]	-	-	4.83	(3.74, 6.22)
Trust – News Media[c]	-	-	4.33	(3.40, 5.52)
Trust – Social Media[c]	3.18	(2.45, 4.14)	0.63	(0.48, 0.83)

* Sociodemographics (region, age, gender, marital status, household size, employment status, ethnicity, post-secondary education), disease characteristics (antimalarial, steroid and immunosuppressive use, disease duration, positive COVID-19 test), number of days to survey completion since 03/11, and access to and trust in sources (family physicians, SLE specialists, pharmacists, alternative care providers, peers, advocacy organizations, social media, news media) were considered in the models. Only significant variables are presented here.

+ Variables with a – were not included in the final model. All geographic variables were forced in the model, and other variables were chosen through backwards selection.

[a]Time (years) of survey completion since March 11, 2020
[b]Respondents accessing source for health information sometimes/often/always since March 11, 2020
[c]Respondents reporting source as somewhat/very trustworthy since March 11, 2020

Respondents in Europe and LA vs Canada were more likely to access social (Europe: OR 1.46, 95% CI 1.03, 2.07; LA: OR 2.19, 95% CI 1.36, 3.56) and news media (Europe: OR 1.77, 95% CI 1.26, 2.49; LA: OR 1.71, 95% CI 1.03, 2.83), and those in the US were less likely to access social media (OR 0.58, 95% CI 0.40, 0.84) (Table 1). Females were more likely (OR 2.02, 95% CI 1.17, 3.49), while older subjects were less likely to access social media (OR 0.98, 95% CI 0.97, 0.99). Patients accessing family physicians during COVID-19 were less likely to access social (OR 0.70, 95% CI 0.54, 0.92) and news (OR 0.64, 95% CI 0.50, 0.80) media, and those reporting trust in social (OR 3.18, 95% CI 2.45, 4.14) and news media (OR 4.33, 95% CI 3.40, 5.52) were more likely to access each, respectively. Those in Asia vs Canada (OR 0.34, 95% CI 0.17, 0.66) and older participants (OR 0.97, 95% CI 0.96, 0.99) were less likely to report negative impacts, and females (OR 2.27, 95% CI 1.15, 4.47) were more likely to report negative impacts (Table 2). While subjects with post-secondary education were less likely to be negatively impacted (OR 0.60, 95% CI 0.40, 0.90), those with post-secondary education in Europe (OR 3.56, 95% CI 1.75, 7.30) and LA (OR 4.37, 95% CI 1.44, 13.30) were more likely to report negative impacts.

Conclusion: Region, age, gender, accessing family physicians, and education were associated with accessing social/news media and/or self-reporting negative impacts of accessing health information from these sources. Education was inversely associated with reporting a negative impact, yet in Europe and LA the relationship is reversed, likely due to local context. This study emphasizes the need for targeted health messaging.

Table 2. Logistic regression results: self-reported negatively impacted by accessing health information through social/news media

Explanatory Variables	Adjusted Odds Ratio	95% Confidence Interval
Region		
Canada (ref)	1.00	-
Asia	0.34	(0.17, 0.66)
Europe	0.88	(0.47, 1.64)
Latin America	0.64	(0.24, 1.70)
US	1.40	(1.00, 1.97)
Sociodemographics		
Age	0.97	(0.96, 0.99)
Female	2.27	(1.15, 4.47)
Post-secondary education	0.60	(0.40, 0.90)
Europe x Post-secondary education[a]	3.56	(1.75, 7.30)
Latin America x Post-secondary education[a]	4.37	(1.44, 13.30)
Access/Trust in Health Information Sources		
Access - Alternative Care Providers[b]	1.59	(1.11, 2.28)
Trust - News Media[c]	0.62	(0.47, 0.80)

[a]Interaction terms between region and post-secondary education as well as trust in news media were added to explore their effects on self-reporting being negatively impacted by accessing health information through social/news media

[b]Respondents accessing source for health information sometimes/often/always since March 11, 2020

[c]Respondents reporting source as somewhat/very trustworthy since March 11, 2020

Disclosure: F. Cardwell, None; **S. Elliott**, None; **R. Chin**, None; **L. Rowbottom**, None; **Y. St.Pierre**, None; **M. Choi**, MitogenDx, 1, 2; **M. Urowitz**, GlaxoSmithKline, 2, 5, 6, UCB, 2, Lilly, 6, AstraZeneca, 2; **G. Ruiz-Irastorza**, None; **S. Bernatsky**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **S. Manzi**, Astra Zenecs, 2, 5, Cugene, 2, Eli Lilly, 2, Exagen, 2, 5, 10, UCB, 2, GSK, 2; **C. Peschken**, AstraZeneca, 2, GlaxoSmithKline, 2, Eli Lilly, 2; **R. Ramsey-Goldman**, None; **P. Fortin**, Lilly, 1, AbbVie, 1, AstraZeneca, 1; **J. Shin**, None; **S. Bae**, None; **J. Cho**, None; **A. Mak**, None; **J. Hanly**, None; **A. Askanase**, GSK, 2, 5, AstraZeneca, 1, 5, Amgen, 1, Aurinia, 2, Abbvie, 1, Pfizer, 5, Eli Lilly, 5, Idorsia, 5; **J. Romero-Diaz**, None; **R. Nieto**, None; **B. Pons-Estel**, Janssen, 5, Glaxo Smith Kline, 6; **I. Bruce**, Astra Zeneca, 2, 6, GSK, 2, 5, 6, UCB, 2, 6, Eli Lilly, 2, Aurinia, 2; **D. Wallace**, GlaxoSmithKline, 2, 6, Eli Lilly and Company, 2, 6, AstraZeneca, 2, 6, Aurunia, 2, 6, EMD Serono, 2; **A. Clarke**, AstraZeneca, 2, GSK, 6, BMS, 2, Exagen Diagnostics, 2.

Abstract Number: 0887

Association of Mycophenolate and Azathioprine Use with Cognitive Function in SLE

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Background/Purpose: Cognitive dysfunction (CD) is a common manifestation of systemic lupus erythematosus (SLE) which can have detrimental consequences for those affected. To date, no treatments have been approved for SLE-associated CD (SLE-CD). This study aims to assess the association of azathioprine (AZA) and mycophenolate (MMF) use with SLE-CD, given that these medications have demonstrated neuroprotective qualities in prior studies.

Methods: Consecutive adult SLE patients presenting to a single center were screened. The American College of Rheumatology (ACR) neuropsychological battery (NB) for SLE, evaluating 6 cognitive domains, was administered to consenting participants at 0, 6 and 12 months. Age and gender matched normative data were used to obtain z-scores. CD was determined by a z-score of £-1.5 in ³2 cognitive domains. Non-CD was defined as no z-score £-1.5. MMF and AZA use were recorded as cumulative dose (grams per kilogram [g/kg]), duration of treatment (number of years) and current use for ³6 months from visit day. Clinical and demographic characteristics were verified at each visit. Baseline characteristics by cognitive status and medication use were documented. Mixed-effects logistic regression models were constructed to estimate the odds of CD and non-CD with respect to AZA and MMF use over the three follow-up periods.

Results: Three hundred participants representing 676 patient visits completed the study; 157 (52%) met criteria for CD at baseline. Mean age was 41.1 years (SD 12.1) and 267 participants (89.0%) were female. Table 1 outlines baseline characteristics by CD and non-CD status. There were no significant differences in mean age, glucocorticoid dose, disease duration, SLE Disease Activity Index-2000 (SLEDAI-2K) scores, or SLICC-ACR Damage Index (SDI) scores. In contrast, there were significantly more participants with CD who identified as Black or Chinese, and significantly fewer participants identifying as White. There were also fewer married participants with CD. Table 2 documents baseline characteristics by AZA and MMF use with respect to CD status. Participants taking AZA or MMF had significantly higher SLEDAI-2K scores and higher prevalence of nephritis; participants taking MMF had higher rates of hypertension, higher daily doses of glucocorticoid medications and lower rates of smoking.

Table 3 shows results of the mixed effects models for AZA and MMF use versus CD. For each g/kg of cumulative AZA, there was on average a 24% reduced odds of CD: OR 0.76, 95% CI 0.61, 0.96, p=0.02. For each year of AZA treatment there was on average a 32% reduced odds of CD: OR 0.68 (0.50, 0.94), p=0.02. AZA use as binary variable (yes versus no) demonstrated a consistent trend toward reduced odds of CD with AZA use without reaching statistical significance: OR 0.29 (0.08, 1.12), p=0.07. Cumulative AZA dose was not significantly associated with non-CD status: 1.08 (0.91, 1.27), p=0.38 (not shown). MMF use was not associated with CD or non-CD.

Conclusion: Despite higher disease activity scores in participants taking AZA compared to those not taking AZA, cumulative AZA dose and increasing AZA treatment duration were associated with significantly lower odds of SLE-CD. MMF use was not associated with SLE-CD.

1) CD: cognitive dysfunction. Defined as a z-score of ≤-1.5 on ≥2 cognitive domains, based on neuropsychological testing. 2) Completion of post-secondary schooling including a College (≥2 years) or University (≥4 years) degree. 3) Positive lupus anticoagulant testing, and/or anti-beta2glycoprotein1 IgG or IgM, and/or anti-cardiolipin IgG or IgM above laboratory specific upper limit of normal, at baseline and again after ≥12 weeks. 4) Psychosis, seizures, stroke, neuropathy and/or transverse myelitis. 5) Known risk factors for cognitive dysfunction not captured elsewhere. 6) SLICC ACR: Systemic Lupus International Collaborating Clinics / American College of Rheumatology Damage Index.

7) SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000. 8) SLEDAI-2KG: Systemic Lupus Erythematosus Disease Activity Index 2000 Glucocorticoid Index. 9) Beck Depression Inventory score of 0–13 is considered minimal, 14–19 mild, 20–28 moderate and 29–63 severe. 10) Beck Anxiety Inventory score of 0-7 is considered minimal, 8-15 mild, 16-25 moderate and 26-63 severe.

Table 1. Baseline characteristics of participants by cognitive function

	Total n=300	Non-CD[1] n=143 (47.7%)	CD[1] n=157 (52.3%)	Absolute Standardized Differences (%)	p-values
Sex, n (%)					
Female	267 (89.0%)	129 (90.2%)	138 (87.9%)	0.1%	0.52
Male	33 (11.0%)	14 (9.8%)	19 (12.1%)		
Age in years, mean ± SD	41.1 ± 12.1	41.4 ± 11.6	40.8 ± 12.5	6.4%	0.53
Ethnicity					
Black	59 (19.7%)	19 (13.3%)	40 (25.5%)	**31.1%**	**0.01**
White	162 (54.2%)	93 (65.0%)	69 (43.9%)	**43.2%**	**<0.01**
Chinese	33 (11.0%)	10 (7.0%)	23 (14.7%)	**24.8%**	**0.03**
Others	46 (15.3%)	21 (14.7%)	25 (15.9%)	3.4%	0.77
Education Level, highest achieved, n (%)					
12[th] Grade or lower	60 (20.0%)	22 (15.4%)	38 (24.2%)		
College or University Degree[2]	240 (80.0%)	121 (84.6%)	119 (75.8%)	**28.6%**	0.06
Employment Status, n (%)					
Employed or student	195 (65.0%)	100 (69.9%)	95 (60.5%)	**30.9%**	0.09
Other	105 (35.0%)	43 (30.1%)	62 (39.5%)		
Marital Status, n (%)					
Married or common Law	119 (39.9%)	66 (46.2%)	53 (33.8%)	**32.0%**	**0.04**
Other	179 (60.0%)	77 (53.8%)	102 (65.0%)		
SLE Manifestations, n (%)					
Antiphospholipid positivity[3]	46 (15.3%)	25 (17.5%)	21 (13.4%)	**15.8**	0.32
Nephritis	91 (30.3%)	42 (29.4%)	49 (31.2%)	1.2%	0.97
Mucocutaneous	172 (57.5%)	85 (59.9%)	87 (55.4%)	**13.2%**	0.44
Musculoskeletal	112 (37.5%)	49 (34.5%)	63 (40.1%)	7.2%	0.32
Other NPSLE manifestation[4]	75 (25.0%)	31 (21.7%)	44 (28.0%)	3.8%	0.21
Serositis	26 (8.7%)	16 (11.3%)	10 (6.4%)	3.4%	0.13
Additional CD risk factors[5], n (%)					
Hypertension	124 (41.3%)	63 (44.1%)	61 (38.9%)	10.1%	0.36
Obesity	97 (32.3%)	44 (30.8%)	53 (33.8%)	**14.7%**	0.58
Smoker	18 (6.0%)	8 (5.6%)	10 (6.4%)	2.0%	0.78
Disease Duration in years, median (IQR)	12.4 (6.0, 21.6)	13.4 (6.4, 22.7)	12.0 (5.5, 19.7)	**15.5%**	0.20
SLICC ACR Damage Index[6] score					
Median (IQR)	1.0 (0.0-2.0)	0.0 (0.0-2.0)	1.0 (0.0-2.0)		
Mean ± SD	1.05 ± 1.45	1.00 ± 1.41	1.09 ± 1.49	10.3%	0.52
SLEDAI-2K[7] score					
Median (IQR)	2.0 (0.0, 4.0)	2.0 (0.0, 4.0)	2.0 (0.0, 4.0)		
Mean ± SD	3.3 ± 3.8	3.1 ± 3.4	3.4 ± 4.1	4.2%	0.87
SLEDAI-2KG[8] score					
Median (IQR)	3.1 (0.9-6.2)	3.0 (0.93-6.1)	3.2 (0.8-6.2)		
Mean ± SD	4.4 ± 4.7	4.1 ± 4.4	4.6 ± 5.0	7.1%	0.77
Glucocorticoid dose, mg/day					
Mean ± SD	4.3 ± 8.1	4.2 ± 7.7	4.5 ± 8.4	9.2%	0.84
Immunosuppressant use, n (%)					
Antimalarials	224 (82.4%)	109 (82.6%)	115 (82.1%)	2.6%	0.93
Azathioprine	52 (17.3%)	32 (22.4%)	20 (12.7%)	**14.3%**	**0.03**
Belimumab	2 (0.7%)	1 (0.7%)	1 (6.4%)	10.2%	0.86
Cyclophosphamide	2 (0.7%)	2 (1.4%)	0 (0.0%)	10.8%	0.14
Cyclosporine	2 (0.7%)	1 (0.7%)	1 (6.4%)	7.5%	0.95
Glucocorticoids	132 (48.5%)	65 (49.2%)	67 (47.9%)	0.8%	0.82
Methotrexate	25 (8.8%)	10 (7.0%)	15 (9.6%)	5.5%	0.42
Mycophenolate	96 (32.0%)	41 (28.7%)	55 (35.0%)	3.5%	0.24
Rituxan	14 (4.7%)	7 (4.9%)	7 (4.5%)	2.6%	0.95
Prior Immunosuppressant Use, n (%)					
Azathioprine	2 (0.7%)	1 (0.7%)	1 (0.6%)	0.8%	0.95
Cyclophosphamide	0	0	0	-	-
Cyclosporine	0	0	0	-	-
Methotrexate	2 (0.7%)	0	2 (1.3%)	**16.1%**	0.18
Mycophenolate	23 (7.7%)	11 (7.7%)	12 (7.6%)	0.2%	0.99
Cumulative dose in g/kg, median (IQR)					
Azathioprine	2.29 (0.58, 4.89)	3.2 (1.0, 8.2)	1.9 (0.3, 3.1)	**28.0%**	**0.01**
Mycophenolate	37.6 (14.5, 78.6)	37.5 (14.2, 84.1)	43.5 (15.4, 88.9)	6.8%	0.22
Years of treatment, median (IQR)					
Azathioprine	4.9 (1.6, 12.0)	4.8 (1.5, 12.4)	3.0 (0.8, 5.5)	**57.8%**	0.21
Mycophenolate	4.5 (1.7, 8.6)	4.1 (1.1, 7.0)	4.4 (1.4, 8.4)	**18.2%**	0.41
Beck Depression Inventory[9] score					
Median (IQR)	14.9 (7.2, 18.3)	13.4 (6.2, 16.4)	14.9 (8.3, 21.0)	**21.7%**	0.67
Beck Anxiety Inventory[10] score					
Median (IQR)	15.6 (7.0, 20.0)	14.0 (6.0, 18.0)	15.6 (9.0, 21.0)	**21.6%**	0.39

Table 2. Characteristics of participants by AZA and MMF[1] use

	No AZA use n=248	AZA use n=52	Absolute Standardized Differences	p-value	No MMF use n=204	MMF use n=96	Absolute Standardized Differences	p-value
SLICC-ACR Damage Index[1]								
Median score (IQR)	1.0 (0.0, 1.0)	1.0 (0.0, 2.0)	**13.4%**	0.40	0.0 (0.0, 1.1)	1.0 (0.0, 2.0)	1.9%	0.32
Mean score ± SD	1.0 ± 1.4	1.2 ± 1.5			1.0 ± 1.5	1.1 ± 1.4		
Disease Duration in years, median (IQR)	12.7 (5.8, 21.9)	11.9 (6.7, 16.6)	**13.6%**	0.48	13.2 (6.0, 22.2)	11.6 (6.0, 19.4)	**19.4%**	0.22
SLEDAI-2K[2]								
Median score (IQR)	2.0 (0.0, 4.0)	4.0 (2.0, 6.0)	**21.9%**	**<0.01**	2.0 (0.0, 4.0)	3.5 (0.0, 6.0)	**23.3%**	**0.03**
Mean score ± SD	3.1 ± 3.8	4.3 ± 3.6			2.9 ± 3.5	4.0 ± 4.2		
SLEDAI-2KG[3]								
Median score (IQR)	2.3 (0.0, 6.0)	2.1 (1.5, 7.3)	**16.2%**	**<0.01**	2.0 (0.0, 6.0)	4.0 (2.0, 7.8)	**35.0%**	**<0.01**
Mean score ± SD	4.2 ± 4.9	5.5 ± 3.8			3.8 ± 4.1	5.7 ± 5.7		
Other Immunosuppressant use, n (%)			W					
Antimalarials	183 (82.1%)	41 (83.7%)	4.3%	0.79	152 (82.6%)	72 (81.8%)	3.2%	0.87
Belimumab	11 (4.4%)	3 (5.8%)	**12.8%**	0.68	10 (4.9%)	4 (4.2%)	4.7%	0.78
Cyclophosphamide	2 (0.8%)	0	**11.9%**	0.52	2 (1.0%)	0	**13.4%**	0.33
Cyclosporine	2 (0.8%)	0	8.4%	0.52	2 (1.0%)	0	9.5%	0.33
Methotrexate	23 (9.3%)	2 (3.9%)	**21.2%**	0.20	23 (11.3%)	2 (2.1%)	**40.5%**	**0.01**
Rituximab	2 (0.8%)	0	**15.8%**	0.52	1 (0.5%)	1 (1.0%)	2.3%	0.58
Prior Immunosuppressant Use, n (%)								
Azathioprine	-	-	-	-	2 (1.0%)	0	**14.1%**	0.33
Cyclophosphamide	0	0	-	-	0	0	-	-
Cyclosporine	0	0	-	-	0	0	-	-
Methotrexate	2 (0.8%)	0	**12.8%**	0.52	2 (1.0%)	0	**14.1%**	0.33
Mycophenolate	5 (2.0%)	18 (34.6%)	**92.9%**	**<0.01**	-	-	-	-
Glucocorticoid Dose, mg/day								
Mean ± SD	4.4 ± 8.5	4.2 ± 5.8	**12.3%**	0.23	3.1 ± 5.5	7.0 ± 11.4	**42.3%**	**<0.01**
SLE manifestations, n (%)								
Cognitive dysfunction	137 (55.2%)	20 (38.5%)	**19.8%**	**0.03**	102 (50.0%)	55 (57.3%)	3.7%	0.24
Antiphospholipid positivity[4]	34 (13.7%)	12 (23.0%)	**21.5%**	0.09	28 (13.7%)	18 (18.8%)	**14.4%**	0.26
Nephritis	68 (27.5%)	25 (48.1%)	**37.0%**	**<0.01**	43 (21.1%)	50 (52.6%)	**64.6%**	**<0.01**
Mucocutaneous	137 (55.5%)	35 (67.3%)	5.8%	0.12	117 (57.4%)	55 (57.9%)	0.2%	0.93
Musculoskeletal	90 (36.4%)	22 (42.3%)	**12.1%**	0.43	76 (37.3%)	36 (37.9%)	2.6%	0.92
Other NPSLE manifestation[5]	66 (26.6%)	9 (17.3%)	**31.8%**	0.16	50 (24.5%)	25 (26.0%)	3.9%	0.78
Serositis	20 (8.1%)	6 (11.5%)	5.1%	0.42	15 (7.4%)	11 (11.6%)	**25.0%**	0.23
Additional CD Risk Factors[6], n (%)								
Hypertension	100 (40.3%)	24 (46.2%)	**14.5%**	0.44	76 (37.3%)	48 (50.0%)	**21.1%**	**0.04**
Obesity	83 (33.5%)	14 (26.9%)	**23.3%**	0.36	63 (30.9%)	34 (35.4%)	10.4%	0.43
Smoker	14 (6.1%)	3 (5.8%)	**17.9%**	0.94	16 (7.8%)	2 (2.1%)	**20.1%**	**0.05**
Ethnicity								
Black	50 (20.2%)	9 (17.3%)	7.3%	0.64	36 (17.6%)	23 (24.0%)	**15.5%**	0.20
White	132 (53.2%)	30 (57.7%)	8.9%	0.56	111 (54.4%)	51 (53.1%)	2.6%	0.84
Chinese	27 (10.9%)	6 (11.5%)	2.1%	0.89	18 (8.8%)	15 (15.6%)	**20.8%**	0.08
Others	39 (15.7%)	7 (13.4%)	6.4%	0.68	39 (19.1%)	7 (7.3%)	**35.4%**	**0.01**
Education Level, highest achieved, n (%)								
12th Grade or lower	45 (18.1%)	15 (28.8%)			40 (19.6%)	20 (20.8%)		
College or University Degree[2]	203 (81.9%)	37 (71.2%)	**25.3%**	0.08	164 (80.4%)	76 (79.2%)	3.0%	0.80

AZA: azathioprine; MMF: mycophenolate; CD: cognitive dysfunction; NPSLE: neurologic and psychiatric manifestations of systemic lupus. 1) SLICC-ACR DI: Systemic Lupus International Collaborating Clinics American College of Rheumatology Damage Index. 2) SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000. 3) SLEDAI-2KG: Systemic Lupus Erythematosus Disease Activity Index 2K Glucocorticoid. 4) Positive lupus anticoagulant testing, and/or anti-beta2glycoprotein1 IgG or IgM, and/or anti-cardiolipin IgG or IgM above laboratory specific

Table 3. Mixed logistic regression results for azathioprine and mycophenolate use versus cognitive dysfunction[1]

	Cumulative dose, g/kg n=676		Use for ≥6 months n=676		Treatment duration, years n=676	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
Azathioprine	**0.76 (0.61, 0.96)**	**0.02**	0.29 (0.08, 1.13)	0.07	**0.68 (0.50, 0.94)**	**0.02**
Mycophenolate	1.00 (0.99, 1.01)	0.44	0.83 (0.34, 2.05)	0.69	1.12 (0.96, 1.30)	0.15

upper limit of normal, at baseline and again after ≥12 weeks 5) Psychosis, seizures, stroke, neuropathy and/or transverse myelitis. 6) Known risk factors for cognitive dysfunction not captured elsewhere.

1Cognitive dysfunction was defined as a z-score of ≤-1.5 on ≥2 cognitive domains based on comprehensive neuropsychological testing. OR: odds ratio; CI: confidence interval. Covariates included in the models: Systemic Lupus Erythematosus Disease Activity Index-2000 Glucocorticoid (SLEDAI-2KG) score (incorporates glucocorticoid dose with the SLE Disease Activity Index 2000 [SLEDAI-2K]), Systemic Lupus International Collaborating Clinics (SLICC) - American College of Rheumatology (ACR) Damage Index score (SDI), additional CD risk factors not captured elsewhere (hypertension, obesity, active smoker), persistent antiphospholipid antibody positivity (positive lupus anticoagulant testing, and/or anti-beta2glycoprotein1 IgG or IgM, and/or anti-cardiolipin IgG or IgM above laboratory specific upper limit of normal, at baseline and again after ≥12 weeks, recorded as binary variable), history of lupus nephritis, active use of an additional immunomodulator (antimalarials, belimumab, calcineurin inhibitor, cyclophosphamide, methotrexate, rituximab), prior use of an immunomodulator (AZA, calcineurin inhibitor, cyclophosphamide, methotrexate, MMF), Beck Depression Inventory (BDI) scores, Beck Anxiety Inventory (BAI) scores, age in years, sex (male versus female), ethnicity (Black, Caucasian, Chinese or other), education level (completion of a College or University degree recorded as binary variable), employment status (employed or full time student versus other) and marital status (married or common-law partner versus other).

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Abstract Number: 0888

Disease Flares in Lupus Are Concordant with *Ruminococcus Blautia Gnavus* Blooms Within Unstable Gut Microbiota Communities

Doua Azzouz[1], Ze Chen[1], Zhi Li[1], Jing Deng[1], Peter Izmirly[1], David Fenyo[1], Jill Buyon[1], Alexander Alekseyenko[2] and **Gregg Silverman**[1], [1]NYU Grossman School of Medicine, New York, NY, [2]Medical University of South Carolina, Charleston, SC

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus is the archetypic systemic autoimmune disease in which dysbiosis in the gut microbiome has been postulated to contribute to disease development in genetically-susceptible

individuals. To investigate for dynamic-relationships between gut-microbial community shifts and disease activity, we performed taxonomic surveys using 16S rRNA gene amplicon-libraries from female patients and healthy controls (CTL).

Methods: To study the gut microbial communities in disease-affected individuals, we examined two to six sequential fecal samples obtained from 16 individual lupus patients, representing 44 samples obtained over 24-291 weeks. For comparisons, we also evaluated 72 samples from 22 healthy adult female volunteers, with 2 to 12 samples from 9 of these CTL. To assess the diversity within these bacterial communities, fecal DNA was extracted, followed by targeted amplification of a standard interval to generate 144 individual 16S rRNA gene amplicon libraries. Community-wide multivariate analysis were used to estimate subject variances in libraries from individual donors based on Jensen-Shannon Divergence with the Tw2 statistic,

Results: Lupus gut communities commonly displayed significant imbalances in alpha and beta microbiota diversity as compared to control subjects. The communities in each individual lupus patients exhibited unique differences from other patients -- a pattern of disease-associated heterogeneity in dysbiotic responses termed *the Anna Karenina Principle*. From community-wide ecological multivariate analysis, we documented significantly greater intra-individual longitudinal microbiota community instability in Lupus patients than in healthy individuals and more so in Lupus Nephritis (LN) patients. Taxonomic analyses also documented transient spikes of several potentially pathogenic bacterial species, and by far the most prevalent were blooms of *Ruminococcus blautia gnavus* documented in 4/9 LN and 1/7 non-renal patients. From libraries obtained over many months to several years, RG blooms were concordant with disease flares.

Conclusion: As many Lupus patients suffer relapsing illness despite appropriate follow-up, evaluation, and treatment, we speculate that gut blooms of pathogenic bacteria, which impair gut barrier function and stoke systemic inflammation, directly contribute to lupus immunopathogenesis. We propose that future therapeutic interventions that

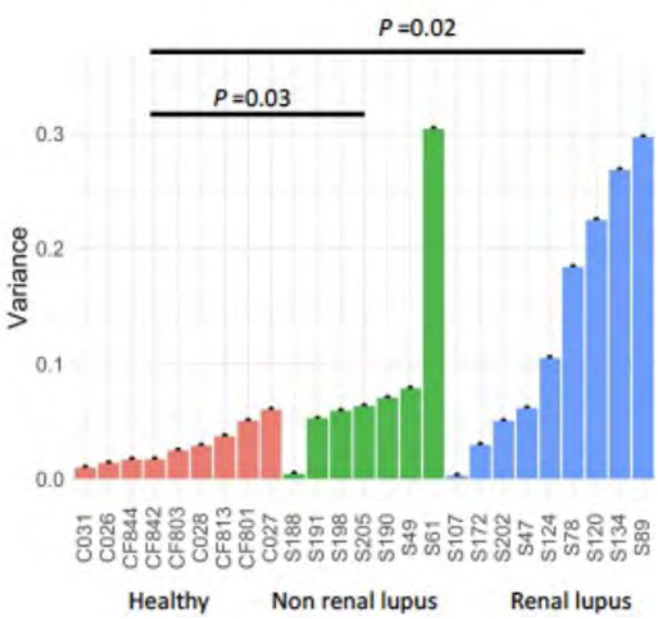

Figure 1. Lupus patients have more unstable gut microbiota than healthy individuals. To compare the overall dynamics of shifts in fecal communities sampled overtime in individual subjects, community-wide multivariate analysis were used to estimate subject variances based on Jensen-Shannon Divergence with the Tw2 statistic (Hamidi et al. (2019) Microbiome 7(1):51). Patients were assigned to the renal group was based on ACR criteria. The variance in these three groups were significantly different (Kruskal Wallis ANOVA, p = 0.03). Variance of gut microbiota in the healthy subjects were significantly different than communities in the renal lupus group, as well as the non-renal lupus group (two-sided Mann-Whitney test, p = 0.02 and p = 0.03, respectively).

are designed to promote a durable cure, consider the necessity to target both the immunologic/inflammatory abnormalities and re-establish stability in the gut microbiota community.

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Abstract Number: 0889

Association of Subjective Cognitive Report Using PDQ-20 to a Neuropsychological Battery in a Cohort of SLE Patients

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) can lead to a number of neuropsychiatric manifestations including cognitive impairment (CI). Previous meta-analyses have reported the prevalence of CI at 38% (95% confidence interval: 33-43%), with a range of 15-79%. Comprehensive neuropsychological battery (NB) of tests is considered the gold standard when diagnosing CI. We aim to compare a subjective questionnaire, the perceived deficits questionnaire (PDQ-20) to the NB and also to other patient reported outcomes, in an SLE cohort.

Methods: This is a cross-sectional study of consecutive consenting patients, aged 18-65 years, who attended a single center (Jul 2016 – Mar 2019). Each patient completed a comprehensive NB evaluating six cognitive domains including: manual motor speed and dexterity, simple attention and processing, visual spatial construction, verbal fluency, learning and memory (verbal and visuospatial) and executive function. They also completed the 20 item PDQ-20 questionnaire (subjective cognitive function) along with other patient reported outcome questionnaires such as the Beck anxiety score, Beck depression score, fatigue severity score (FSS), Short Form Health Survey (SF-36) domains [Role Physical, Mental Health, Bodily Pain, General Health, Physical Functioning, Emotional, Social Functioning, and Vitality domains].

The variable of main interest was the total score of 19 tests in NB, along with patients' demographics, lupus disease activity, organ damage, treatment and other PROs. Mean ± std., median (interquartile range) and count (%) were calculated for these variables. Univariate and multivariable linear regressions were performed to evaluate the associated factors with total PDQ-20 scores. Least Absolute Shrinkage and Selection Operator (LASSO) method was used in the variable selection in multivariable model building process. Linear model assumptions were tested by residual density plots and quantile-quantile plots.

Results: Data on 238 patients was analysed; 89.9% were females with an average age and SLE duration at baseline visit of 41.1 ± 12.1 and 14.3 ± 10.0 years, respectively. In the univariate analysis, PDQ-20 was associated with the

Table 1. Linear regression univariate/multivariate analyses using PDQ-20 as the dependent variable

	Univariate Analysis				Multivariate Analysis			
Predictor	Parameter Estimate	Lower 95% CI	Upper 95% CI	p value	Parameter Estimate	Lower 95% CI	Upper 95% CI	p value
Female vs. Male	8.02	0.92	15.12	0.02	-	-	-	-
Age @ 1st visit	0.11	-0.07	0.29	0.22	-	-	-	-
SLE Disease Duration	0.07	-0.15	0.29	0.53	-	-	-	-
Caucasian (yes vs. no)	-0.57	-4.9	3.77	0.79	-	-	-	-
High Education (>= college)	-4.57	-9.66	0.52	0.07	-	-	-	-
SLEDAI Score	0.03	-0.6	0.66	0.92	-	-	-	-
SDI	1.84	0.41	3.27	0.01	-	-	-	-
Fatigue Severity Score	6.01	4.98	7.05	<.0001	2.15	0.98	3.32	0.001
BECK depression score	0.87	0.74	1.01	<.0001	0.22	0.02	0.42	0.03
BECK anxiety score	0.85	0.72	0.98	<.0001	0.25	0.06	0.44	0.01
SF-36 Bodily Pain	-0.36	-0.42	-0.29	<.0001	-0.05	-0.13	0.03	0.23
SF-36 General Health	-0.33	-0.41	-0.25	<.0001	-	-	-	-
SF-36 Mental Health	-0.42	-0.5	-0.34	<.0001	-	-	-	-
SF-36 Physical Functioning	-0.31	-0.38	-0.24	<.0001	-	-	-	-
SF-36 Role Emotional	-0.21	-0.25	-0.17	<.0001	-0.07	-0.11	-0.02	0.002
SF-36 Role Physical	-0.22	-0.26	-0.18	<.0001	-0.04	-0.09	0.01	0.10
SF-36 Social Functioning	-0.35	-0.41	-0.29	<.0001	-0.02	-0.11	0.06	0.59
SF-36 Vitality	-0.38	-0.45	-0.31	<.0001	-	-	-	-
Glucocorticoids within 3 month (yes vs. no)	-2.06	-6.37	2.26	0.34	-	-	-	-
Glucocorticoids dose (mg/day)	-0.07	-0.32	0.19	0.60	-0.31	-0.48	-0.14	0.001
Antimalarials treatment (yes vs. no)	0.05	-5.56	5.66	0.98	-	-	-	-
Immunosuppressives treatment (yes vs. no)	-0.99	-5.33	3.35	0.65	-	-	-	-
Battery total score	-0.2	-0.37	-0.03	0.01	-	-	-	-

NB, SDI, fatigue severity score (FSS), BECK anxiety and depression score and all SF-36 domains (Table 1). In the multivariate analysis, PDQ-20 was significantly associated with female gender, SDI, fatigue, BECK depression and anxiety scores, SF-36 Role Emotional domain and glucocorticoid dosage. PDQ-20 was not associated with the NB. There was also no association with age at first visit, SLE disease duration, ethnicity, education level, SLEDAI score, anti-malarial or immunosuppressive treatment with the PDQ-20 score.

Conclusion: Subjective cognitive report by PDQ-20 was associated with the NB in univariate analysis but not multivariate analysis. While PDQ-20 was associated with all SF-36 domains in the univariate analysis, this association was

significant only with Role Emotional in the multivariate analysis. There was a clear association of PDQ-20 with other subjective patient reported outcomes (such as fatigue, anxiety and depression, and SF-36 Role Emotional domain).

Disclosure: A. Gupta, None; **S. Johnson**, None; **J. Su**, None; **A. Knight**, None; **J. Diaz-Martinez**, None; **K. Bingham**, None; **M. Kakvan**, None; **M. Tartaglia**, None; **L. Ruttan**, None; **J. Wither**, None; **M. Choi**, MitogenDx, 1, 2; **M. Fritzler**, Inova Diagnostics Inc., 2, 6, Werfen International, 2, Alexion Canada, 6, Mitogen Diagnostics Corp., 3, 8, 9, 10; **D. Bonilla**, None; **D. Beaton**, None; **P. Katz**, None; **R. Green**, None; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6.

Abstract Number: 0890

Depression Is Associated with Frailty in Systemic Lupus Erythematosus Patients: Multicenter Retrospective Analysis Using Systemic Lupus Erythematosus International Collaborating Clinics-Frailty Index

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus International Collaborating Clinics-Frailty Index (SLICC-FI) is a novel health measure in systemic lupus erythematosus (SLE) and was reported to have impact on outcomes including mortality. The objective of the study was to evaluate the association of depression and frailty in SLE patients.

Methods: SLE patients who fulfilled 1997 American College of Rheumatology (ACR) classification criteria were enrolled from five teaching hospitals in Korea and the participants filled out questionnaires at outpatient clinic. Electronic medical records were reviewed for laboratory results, disease activity at enrollment, medications and damage

Table 1. Risk factors of frailty in systemic lupus erythematosus patients (multivariable logistic regression analysis)

	Odd ratio (95% C.I)	P-value	
Age	1.09 (1.03-1.14)	0.002	
ESR	1.03 (1.00-1.06)	0.030	
SLEDAI-2K	1.18 (1.02-1.37)	0.026	
PHQ-9 score	1.27 (1.14-1.40)	<0.001	
SDI score	3.22 (2.00-5.32)	<0.001	

ESR, erythrocyte sedimentation rate; PHQ-9, patient health questionnaire-9; SLEDAI-2K, systemic lupus erythematosus disease activity index-2000; SDI, SLICC/ACR damage index

index score and SLICC-FI was calculated. To assess the severity of depression, patient health questionnaire-9 (PHQ-9) was used. Logistic regression analysis was used to evaluate the factors associated with frailty in SLE patients

Results: In total, 247 patients were recruited. Mean (standard deviation, SD) age of the cohort was 50.5 (1.6) and 91.9% of the cohort was female. The mean (SD) of SLE disease activity index-2000 (SLEDAI-2K) was 3.5 (4.0). According to SLICC-FI, 36 (14.6%) patients were classified as frail. Mild depression (PHQ-9 score ≥ 5) was observed in 97.2% of frail patients and 54.5% of not-frail patients. Severe depression (PHQ-9 ≥ 20) was observed in 22.2% of frail patients and 1.4% of not-frail patients. In multivariable logistic regression analysis, age (1.09), ESR (1.03), SLEDAI-2K (1.18), PHQ-9 score (1.27) and SLICC/ACR damage index (3.22) were associated with frailty (odds ratio in parenthesis).

Conclusion: Depression in SLE patients was associated with frailty. Rheumatologists should pay attention to early detection and intervention of depression in SLE patients to improve outcomes.

Disclosure: K. Shin, None; **I. Choi**, None; **E. Lee**, None; **S. CHOI**, None; **J. Yeo**, None; **Y. Lee**, None; **S. Yoo**, None; **B. Hahm**, None; **J. Park**, None; **J. Lee**, None; **Y. Song**, None; **J. Kim**, None.

Abstract Number: 0891

Quality of Life Assessment in an Indian Inception Cohort (INSPIRE) of SLE Using Lupus QoL Questionnaire

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus quality of life (Lupus QoL) questionnaire is a disease specific patient reported outcome that is available in multiple languages[1]. Indian SLE inception cohort for research (INSPIRE) is a multi-institutional cohort having patients from different parts of India who speak different languages[2]. The study aimed to assess the QOL in this cohort and study its association with measures of disease activity.

Methods: Patients satisfying the SLICC classification criteria for lupus enrolled in the INSPIRE cohort[1] were asked to fill the Lupus QoL questionnaire in their native language. Any help needed in understanding a question was provided by the study nurse or the physician. Internal consistency of the questions in the various domains of the Lupus QoL was assessed using Cronbach's Alpha. Associations between Lupus QoL domains with age, SLEDAI, and BILAG were analyzed using Spearman correlation.

Results: Seven hundred and eighty-one lupus patients answered the Lupus QoL in either Hindi, Telugu, Tamil, Kannada, Urdu, Punjabi, Bengali and English. The mean age of the patients was 28± 10 years. Disease duration was less than three years. The median (IQR) HAQ score was 0.5(0.25-1.0). The mean SLEDAI was 10.9± 8.1. The internal

Table 1. Internal consistency in different language version of LupusQoL

Domain name	Question no.	Cronbach's alpha N=781	Hindi n=197	Telugu n=197	Tamil n=193	Kannada N=72	Urdu n=22
Physical Health	1-8	0.90	0.89	0.91	0.94	0.78	0.90
Pain	9-11	0.80	0.71	0.83	0.87	0.80	0.75
Planning	12-14	0.84	0.80	0.85	0.92	0.72	0.92
Intimacy	15,16	0.91	0.82	0.94	0.89	0.94	0.92
Burden to others	17-19	0.83	0.75	0.86	0.85	0.82	0.91
Emotional health	20-25	0.90	0.83	0.90	0.95	0.93	0.94
Body image	26-30	0.81	0.80	0.84	0.91	0.62	0.91
Fatigue	31-34	0.79	0.78	0.72	0.86	0.79	0.62

Table 2. The mean scores in Lupus QOL domains across different languages

Language / LQOL domains	Hindi (n=197)	Telugu (n=197)	Tamil (n=193)	Kannada (n=72)	Urdu (n=22)
Physical Health	60.3	60.2	53.3	54.8	68.9
Pain	55.9	58.8	54.6	54.6	66.3
Planning	66.3	65.1	54.8	57.4	75.8
Intimacy	57.5	57.5	51.2	56.6	65.9
Burden to others	52.8	57.4	52	49.2	64
Emotional health	59.9	62.5	57.8	52.5	73.7
Body image	59.3	64.6	55.5	54.7	74.2
Fatigue	57.9	60.7	45.6	58.7	67

consistency of the questions in various domains of the translated LupusQOL was high with Cronbach's Alpha varying from 0.79-0.91 (Table1)

The mean scores in each domain of Lupus QoL among the patients were as follows: physical health 58.1, pain 55.9, planning 63, intimacy 54.8, burden to others 55, emotional health 59.7, body image 59.3 and fatigue 57.5 (Table 2). Higher SLEDAI scores correlated with poor LupusQoL across all domains, though the correlation was at mild.

Table 3. Correlation with clinical disease activity *p<0.05, ** p<0.01

	Physical Health	Pain	Planning	Intimacy	Burden	Motion	Body Image	Fatigue
SLEDAI	-.219**	-.184**	-.206**	-.170**	-.157**	-.164**	-.126**	-.170**
BILAG domains								
Constitutional	-.201**	-.186**	-.160**	-0.044	-.087*	-0.053	-.106**	-.101**
Mucocutaneous	-.084*	-.073*	-.136**	-0.037	-0.062	-.092**	-.165**	-.097**
Neuropsychiatry	-.091*	-.075*	-.081*	-0.074	-0.058	-0.056	-0.056	-0.069
Musculoskeletal	-.252**	-.245**	-.179**	0.008	-.139**	-.125**	-.089*	-.170**
Cardiopulmonary	-.098**	-.117**	-.100**	-0.057	-0.067	-0.062	-0.052	-0.050
Gastrointestinal	-0.038	-0.035	-0.036	-0.040	-0.015	0.027	-0.017	-0.003
Ophthalmic	0.019	0.007	0.004	0.052	0.049	0.003	0.040	0.029
Renal	-0.058	-0.036	-.074*	-.132**	-.097**	-0.066	-0.039	-0.004
Hematological	-.117**	-.124**	-.114**	-.098*	-0.070	-.086*	-0.063	-.082*

Looking at impact of different organ involvement on LUPUS QoL Physical health was affected by constitutional and musculoskeletal(MSK) domain and pain scores correlated with MSK domain, (Table 3).

Conclusion: Hindi, Telugu, Tamil, Kannada and Urdu translations of Lupus QoL have good internal consistency. Indian lupus patients have significantly impaired quality of life. only some part of which could be accounted for by disease activity. Thus other factors contributing to poor QoL need to be addressed while managing patients.

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Abstract Number: 0892

Screening for Cognitive Impairment with the Automated Neuropsychological Assessment Metrics in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: The American College of Rheumatology Neuropsychological Battery (ACR-NB) is the standard screening test for cognitive impairment (CI) in systemic lupus erythematosus (SLE). While the ACR-NB is vali-

dated for classifying definite, indeterminate, or non-CI, it requires expensive administration by specialists that limits widespread use. Towards an accessible alternative, we developed a CI index with the Automated Neuropsychological Assessment Metrics (ANAM) in a SLE population with definite or non-CI. Although our work provided evidence for the validity of the ANAM relative to the ACR-NB, one third of SLE patients are classified as indeterminate CI in practice. In this study, we further assessed the ANAM as a screener for CI in a population more reflective of clinical settings. Our objectives were to: (i) identify ANAM subtests predictive of CI, (ii) develop an initial approach for classifying definite, indeterminate, or non-CI, (iii) evaluate performance relative to the ACR-NB.

Methods: 211 adult SLE patients were given the ACR-NB and ANAM on the same day at a single center in 2016-2018 **(Table 1)**. The ACR-NB scores across the 6 domains are standardized by age and gender to define CI as: definite: z-score ≤ -1.5 in ≥ 2 domains, indeterminate: z-score ≤ -1.5 in 1 domain, or non: z-scores in all domains > -1.5. The ANAM has 7 domains with 15 subtests scored with the mean reaction time (MR), percentage correct responses (PCT), the coefficient of variation of the MR (CV), and/or throughput (TH).

To classify ACR-NB CI status (definite/indeterminate/non-CI) with the ANAM subtests, we fit 6 models with all subtests and different score types: 4 with one score each, one with MR, CV, and PCT, and one with MR, CV, PCT, and TH. In each setting, we fit a proportional odds cumulative logit model with the adaptive elastic net penalty using the log transformed ANAM subtest scores. The penalized fitting identifies relevant subtests by shrinking coefficients of irrelevant subtests to zero. The initial estimates for penalization were obtained with ridge regression and the tuning parameter selected with cross-validation using the Akaike information criteria. Performance estimates relative to the ACR-NB were obtained with weighted 3-fold cross-validation.

Results: The best performing model included the MR, CV, and PCT scores and selected 36 subtest scores across the 7 ANAM domains for classification of CI. The estimates of the nonzero coefficients are presented in **Table 2**. **Figure 1** summarizes the overall classification accuracy of the model relative to the ACR-NB CI classifications. While the model tends to overcall the indeterminate group as definite CI and the non-CI group as indeterminate and definite CI, it performs well for definite CI compared to ACR-NB. Used as a screening test for CI relative to indeterminate or non-CI, the model has a sensitivity of 0.62 (95% confidence interval: 0.48, 0.76), specificity of 0.72 (0.60, 0.88), and area under the curve of 0.76 (0.69, 0.80).

Conclusion: This is the first study to evaluate the ANAM in discriminating definite, indeterminate, and non-CI in a real world SLE population. The ANAM holds promise as a CI screener and warrants further assessment.

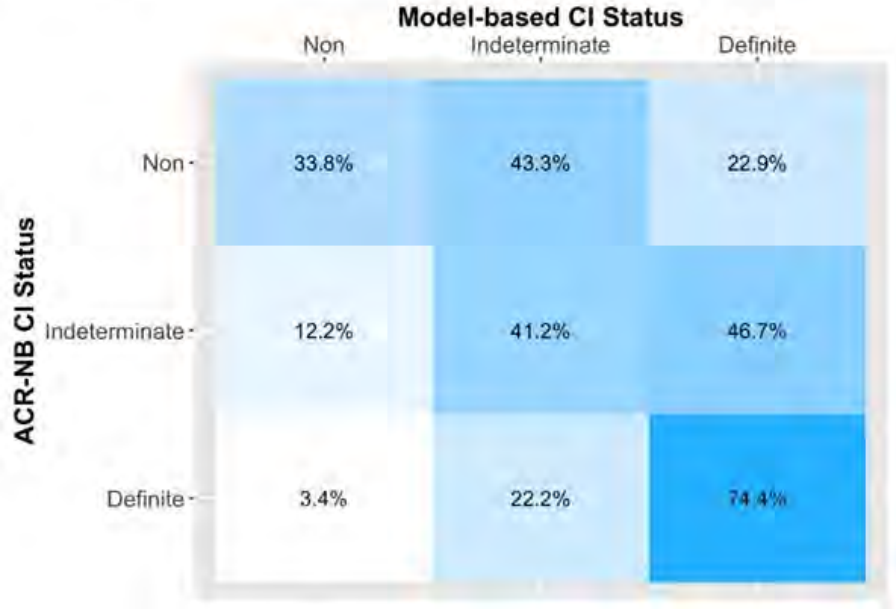
Table 1: Characteristics of the patient population.

	ACR-NB CI Status		
	Non (N=42)	Indeterminate (N=69)	Definite (N=100)
Female sex(%)	40(95.2%)	59(85.5%)	86(86.0%)
Age(yr)	41.3±12.3	40.9±11.7	39.6±12.8
Diagnosis duration(yr)	16.2±11.7	14.2±9.7	12.9±9.2
Ethnicity(%)			
Black	4(9.5%)	7(10.1%)	25(25.0%)
Caucasian	28(66.7%)	48(69.6%)	48(48.0%)
Chinese	4(9.5%)	3(4.3%)	14(14.0%)
Others	6(14.3%)	11(15.9%)	13(13.0%)

Table 2: ANAM subtests selected for classification of ACR-NB CI status from the proportional odds cumulative logit model.

ANAM Domain	Subtest	Score	Standardized Coefficient	SE
Fine Motor Processing	Tapping Right	CV	-0.07	0.08
	Tapping Left	MR	-0.23	0.32
		CV	-0.01	0.11
Attention and Processing Speed	Simple Reaction Time	MR	0.32	0.25
	Procedural Reaction Time	MR	-0.45	0.32
		PCT	-0.21	0.19
	Simple Reaction Time-repeated	MR	0.03	0.03
		CV	-0.10	0.18
	Two Choice Reaction Time	MR	-0.32	0.30
		PCT	-0.18	0.29
		CV	0.21	0.24
	Running Memory	MR	0.33	0.29
		PCT	0.16	0.19
		CV	-0.13	0.14
Visual-spatial Perception	Spatial Processing	MR	0.53	0.23
		PCT	-0.05	0.11
		CV	0.39	0.20
Language Processing	Logical Relations	MR	-0.08	0.08
		PCT	0.15	0.17
		CV	-0.17	0.15
Learning Memory	Code Substitution Learning	MR	-0.14	0.13
		PCT	0.05	0.15
		CV	0.15	0.20
	Match to Sample	MR	0.17	0.14
		PCT	0.06	0.09
		CV	-0.05	0.12
	Code Substitution Delayed	MR	0.44	0.30
		PCT	0.53	0.23
		CV	-0.09	0.11
Executive Functioning	Math Processing	MR	-0.03	0.13
		PCT	0.48	0.23
		CV	-0.08	0.11
	Go No Go Hits	MR	-0.06	0.12
		PCT	0.06	0.18
	Tower Test	MR	-0.01	0.07
		CV	0.02	0.13

Figure 1: Overall accuracy of the proportional odds cumulative logit model for classifying ACR-NB CI status based on the ANAM subtests. The rows correspond to the ACR-NB classification and the columns correspond to the model classification. The diagonal from left to right contains the percentage of patients correctly classified by the model, while the off-daigonal entries contain the percentage of misclassifications.



Disclosure: R. Pan, None; **J. Diaz-Martinez**, None; **J. Gronsbell**, None; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6.

Abstract Number: 0893

Trajectories of Depressive Symptoms in Systemic Lupus Erythematosus over 7 Years

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

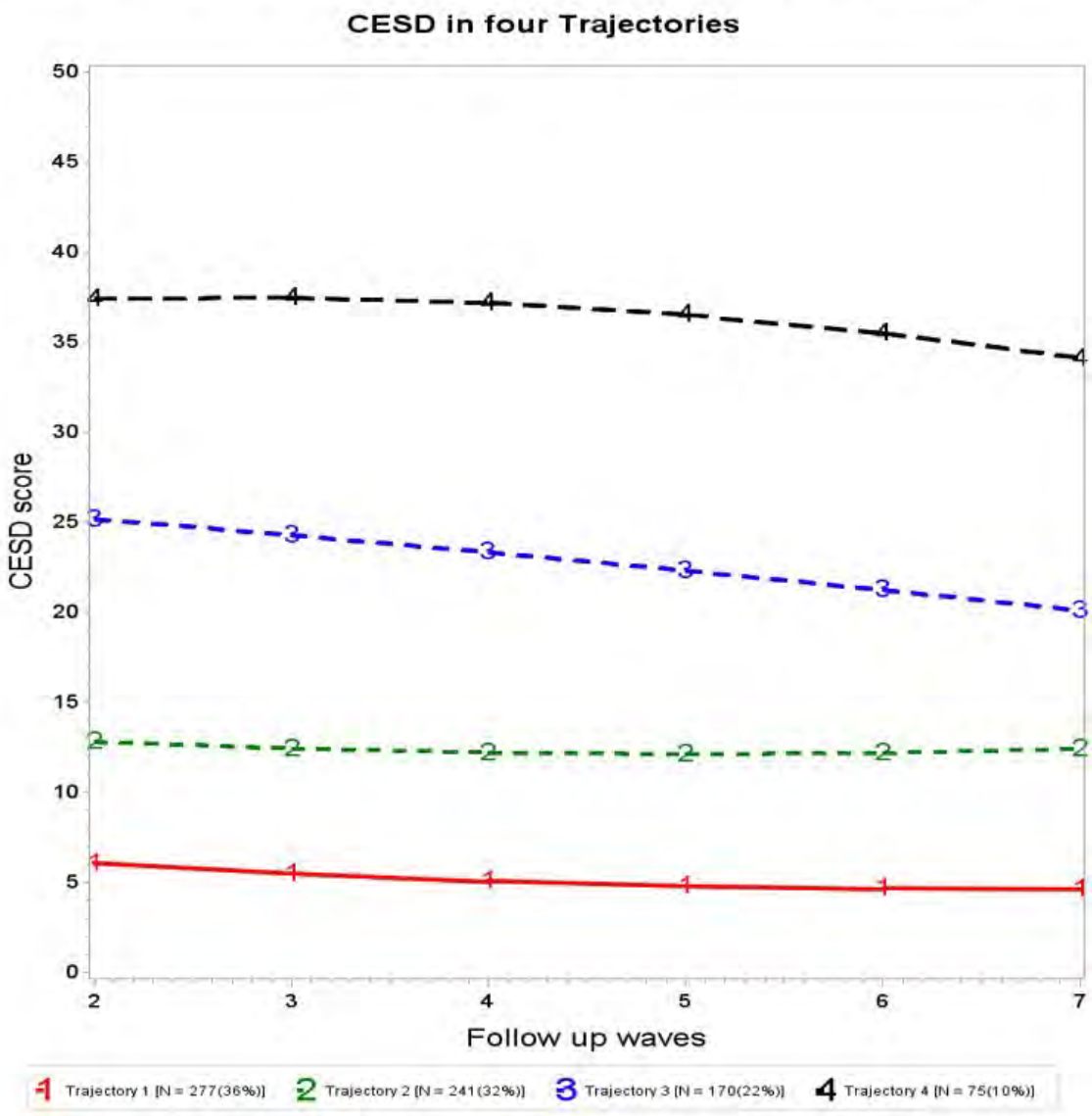
Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Depression remains one of the most frequently observed psychiatric disorders in patients with SLE with a pooled prevalence of 35.0% (95% CI: 29.9%-40.3%). Nevertheless, the trajectory of depression in this population remains uncharacterized. Our aims were to: 1) determine longitudinal trajectories of depressive symptoms in patients with SLE, 2) identify baseline factors that predict a patient's trajectory of depression.

Methods: Longitudinal data on 763 adults with SLE followed over 7 years from a single center were analyzed. Depressive symptoms were assessed with the Centre for Epidemiologic Studies Depression Scale (CESD) annually in years 2-7 providing 6 waves of observation (wave 2 is the baseline assessment for CESD). Patients with two or more

Figure 1. Membership and trajectories of four latent classes using CESD over 7 years



waves of data for CESD were included. Group-based joint trajectory modelling was used to model latent classes. Using only members with latent class posterior probability > 0.8, univariable and multivariable analyses were used to examine baseline factors association with latent classes memberships. The outcomes were the ordinal worse classes of depression represented by latent classes. The assumption of proportionality of the model was checked and satisfied between the four latent classes.

Results: Depressive symptoms were mapped into four trajectories: 1) lowest CESD scores (no depression, 36%), 2) low CESD scores (no depression, 32%), 3) high CESD scores (depression, 22%), and 4) highest CESD scores (depression, 10%). **Figure 1** shows the longitudinal trajectories of four latent classes based on their CESD values over 7 years.

Table 1 shows the baseline demographic information in four classes of patients after they were grouped into four trajectories.

Table 1. Baseline characteristics of patients by classes (n=763)					
	Descriptive	Class 1 Lowest CESD scores	Class 2 Low CESD scores	Class 3 High CESD scores	Class 4 Highest CESD scores
Variables	VALUE	N=277	N=241	N=170	N=75
Female	Yes	253 (91.3%)	220 (91.3%)	157 (92.4%)	75 (100.0%)
Ethnicity	Missing	18	8	7	4
	Caucasian	187 (72.2%)	170 (73.0%)	117 (71.8%)	48 (67.6%)
	Hispanic	17 (6.6%)	16 (6.9%)	16 (9.8%)	6 (8.5%)
	African-American	13 (5.0%)	12 (5.2%)	15 (9.2%)	7 (9.9%)
	Asian	29 (11.2%)	19 (8.2%)	9 (5.5%)	5 (7.0%)
	Other	13 (5.0%)	16 (6.9%)	6 (3.7%)	5 (7.0%)
Age	Mean ± SD	49.1 ± 13.5	50.7 ± 13.2	50.8 ± 11.1	50.6 ± 9.8
SLE Disease duration	Mean ± SD	15.9 ± 9.3	15.9 ± 8.0	14.8 ± 8.0	15.9 ± 8.8
Education	1 - Less than high school	1 (0.4%)	4 (1.7%)	3 (1.8%)	7 (9.3%)
	2 - High school graduate	20 (7.2%)	25 (10.4%)	24 (14.1%)	14 (18.7%)
	3 - Some college/no degree	68 (24.5%)	75 (31.1%)	54 (31.8%)	19 (25.3%)
	4 - Associate degree/trade or vocational school	42 (15.2%)	36 (14.9%)	34 (20.0%)	25 (33.3%)
	5 - College graduate (Bachelor's degree)	82 (29.6%)	53 (22.0%)	37 (21.8%)	5 (6.7%)
	6 - Masters/PhD/professional degree	64 (23.1%)	48 (19.9%)	18 (10.6%)	5 (6.7%)
Deceased	Yes	23 (8.3%)	33 (13.7%)	27 (15.9%)	8 (10.7%)

Data on 584 (76%) patients satisfied the posterior probability 0.8 and were analyzed in the ordinal logistic regression. In the multivariable analyses, older age at baseline, Caucasian, higher education level and less SF-36 Bodily Pain were associated with better CESD classes while higher fatigue score and SLE disease activity by SLAQ were associated with worse CESD classes (**Table 2**).

Conclusion: Four distinct trajectories for depressive symptoms were found. Baseline factors that were associated with latent classes were identified that may be helpful in identifying individuals with SLE who are at the greatest risk of developing persistent depressive symptoms over time. These results will serve as a more comprehensive guide for prognosis and clinical decisions to improve overall treatment outcomes.

Class 1) lowest CESD scores (no depression, 36%), Class 2) low CESD scores (no depression, 32%), Class 3) high CESD scores (depression, 22%), and Class 4) highest CESD scores (depression, 10%)

Table 2. Multivariable ordinal logistic regression of baseline factors of class membership, using only members with posterior probability > 0.8

Variables	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	P values
Age	0.98	0.96	0.99	0.007
Caucasian vs. non-Caucasian	0.67	0.45	0.99	0.046
Education levels 1 to 6, higher vs. lower level	0.84	0.74	0.96	0.010
Fatigue score at wave two (each one unit increase)	1.04	1.02	1.05	<.0001
Any of Immunosuppressives, yes vs. no	1.42	0.96	2.10	0.076
SF-36 Physical Functioning Score (higher is better, each one unit increase)	0.99	0.99	1.00	0.137
Lupus activity, scale of 0 to 10, where 0 is no activity and 10 is the most activity	1.13	1.04	1.22	0.003
Income was above or below 125% of the US federal poverty threshold, based on income and household size	1.59	0.92	2.77	0.099
Kidney problems because of lupus, Yes vs. no	1.39	0.91	2.13	0.127
SF-36 Bodily Pain score (higher is better, each one unit increase)	0.94	0.92	0.96	<.0001

Disclosure: S. Chawla, None; **J. Su**, None; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6; **P. Katz**, None.

Abstract Number: 0894

Help-seeking Behaviors and Treatment Preferences for Sleep Problems Among Persons with Lupus

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Sleep disturbances, including difficulty initiating sleep, maintaining sleep, and/or early morning awakenings are prevalent among persons with lupus and have been shown to contribute to worsening of symptoms including fatigue, pain, depression and health related quality of life. Cognitive behavioral therapy for insomnia (CBTi) is considered first-line treatment for insomnia, but accessibility is limited. Internet delivered CBTi has the potential to overcome accessibility barriers. To guide the tailoring of an internet delivered CBTi for persons with lupus experiencing insomnia, an on-line needs assessment was conducted to identify help-seeking behaviors, strategies for managing insomnia and treatment preferences among persons with lupus.

Methods: We conducted a cross-sectional on-line survey with 119 individuals with lupus (mean age = 47.4 years ± 13.7) recruited through social media ads posted by Lupus Canada and other Canadian and provincial lupus Face-

book pages. Participants completed self-report questions assessing their sleep quality, insomnia symptoms (Insomnia Severity Index – ISI), help-seeking behaviors, barriers to help-seeking, treatment preferences for sleep problems and sociodemographics. Means, medians, and percentages were calculated for continuous values, and percentages were calculated for categorical values.

Results: Of the total sample in the past year, 46% had used at least once prescription medications and 37.2% had used over the counter medication to specifically facilitate sleep. Among participants with probable insomnia (ISI score ≥ 8, n=103), 71.3% had ever discussed their sleep problem with a health care provider and 44.6% perceived a need to talk to a health care provider about their sleep problems in the past year but decided not to seek care. Most commonly endorsed reasons for not seeking treatment were perceptions of insomnia as a problem that one should be able to handle on one's own (54.8%), that insomnia gets better by itself (50%), or that insomnia is not amenable to change (48.9%). Among patients with probable insomnia, 45.4% rated medication treatment as very acceptable, while 56.7% rated nonmedication treatment as very acceptable, and 98% reported that they would be likely or very likely to try a nonmedication approach delivered over the internet and tailored to lupus to improve sleep.

Conclusion: Given the prevalence, chronicity and adverse consequences associated with insomnia in individuals with lupus, this study suggests that efforts designed to reduce the perception of insomnia as transient and to increase awareness of the effectiveness of behavioral treatments are needed. Behavioral interventions such as CBTi are acceptable to individuals with lupus and these findings will guide the evaluation of an internet delivered CBTi program tailored to persons with lupus experiencing insomnia.

Disclosure: D. Da Costa, None; **J. Savard**, None; **E. Rahme**, None; **P. Fortin**, Lilly, 1, AbbVie, 1, AstraZeneca, 1.

Abstract Number: 0895

Insight into Intraindividual Variability Across Neuropsychological Tests and Its Association with Cognitive Dysfunction in Patients with Systemic Lupus Erythematosus

Jennifer He[1], Juan Diaz-Martinez[2], Kathleen Bingham[3], Jiandong Su[4], Mahta Kakvan[4], Maria Tartaglia[4], Lesley Ruttan[3], Dorcas Beaton[5], Joan Wither[4], May Choi[6], Marvin Fritzler[7], Nicole Anderson[4], Dennisse Bonilla[4], Robin Green[4], Patricia Katz[8] and Zahi Touma[9], [1]Western University, London, ON, Canada, [2]UHN, Toronto, ON, Canada, [3]University of Toronto, University Health Network, Toronto, ON, Canada, [4]University Health Network, Toronto, ON, Canada, [5]Institute for Work & Health, Toronto, ON, Canada, [6]Brigham and Women's Hospital | University of Calgary, Calgary, AB, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]University of California San Francisco, San Francisco, CA, [9]University of Toronto, Mississauga, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Dispersion is defined as the variability in an individual's performance across multiple tasks at a single assessment visit. This measure has been studied in a number of neurodegenerative and neurodevelopmental disorders, in which increased dispersion was generally found to be associated with cognitive dysfunction (CD). We aim to compute a dispersion score using the tests of the American College of Rheumatology Neuropsychological battery (ACR-NB) and to determine the association between this dispersion score and the risk of CD in SLE patients.

Methods: This retrospective longitudinal study included patients who attended the Lupus Clinic from January 2016 to October 2019. A total of 301 adult SLE patients were administered the ACR-NB at their initial visit, 6 months and

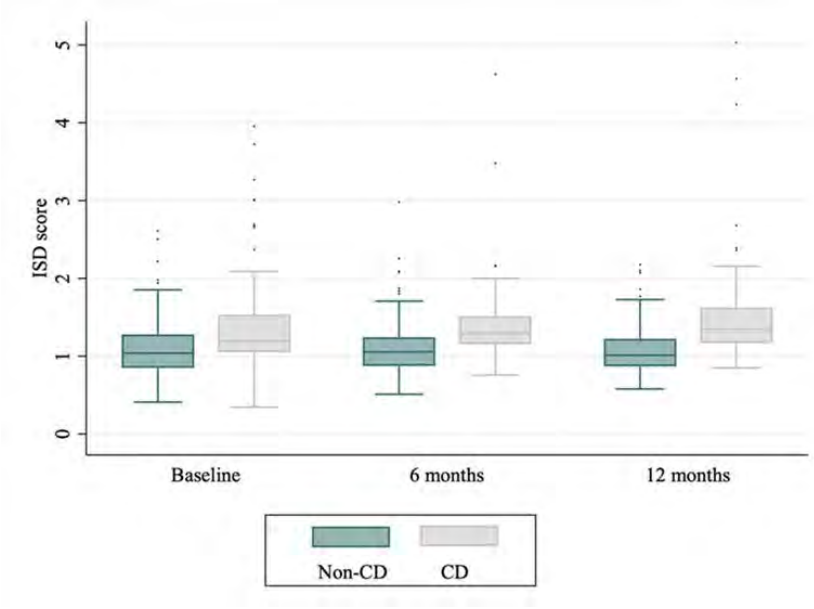

Figure 1. Intraindividual standard deviation (ISD) scores across three assessment visits for non-CD patients and CD patients.

Table 1. Multivariable random intercept logistic regression model

	Odds ratio	95% CI	P-value
ISD			
ISD	13.56	4.80-38.31	<0.0001
1/10th ISD	1.3	1.17-1.44	
Anxiety or depression (ref. = No)			
Yes	1.13	0.49-2.41	0.78
Socioeconomic status (ref. = Lowest)			
Medium-Low	1.28	0.33-4.91	0.72
Middle	0.57	0.15-2.21	0.42
Medium-high	1.02	0.25-4.20	0.98
Highest	0.62	0.14-2.81	0.54
Education level (ref. = 8th grade)			
High School	1.26	0.09-16.78	0.86
College	0.8	0.06-9.90	0.86
University	0.5	0.04-6.14	0.59
Ethnicity (ref. = Black)			
White	0.08	0.02-0.28	<0.0001
Chinese	0.16	0.03-0.89	0.04
Others	0.22	0.05-0.96	0.04
Employment (ref. = Employed)			
Retired	2.56	0.11-58.15	0.56
Homemaker	1.28	0.20-8.37	0.8
Student	0.35	0.06-1.87	0.22
Disabled	2.35	0.73-7.61	0.15
Sick Leave	2.47	0.32-19.00	0.38
Looking for Work	5.18	0.33-81.38	0.22
Others	1.83	0.09-37.17	0.70

12 months. CD was defined as a z-score of ≤-1.5 on ≥2 domains or z ≤-2 on ≥1 domain. The 19 tests of the ACR-NB were used to compute a type of dispersion score, the intraindividual standard deviation (ISD). To obtain the ISD, the standard deviation of the age- and sex- adjusted z-scores was calculated for each visit, resulting in a maximum of 3 scores per patient. To estimate the association between ISD and patient's cognitive status (CD and non-CD), we used multi-level logistic regression, adjusting for clinically important covariates.

Results: CD was observed in 106 patients (35.2%) at baseline, 52 patients (27.8%) at 6 months, and 53 patients (28.0%) at 12 months. Among all observations across 3 visits, the mean age- and sex-adjusted ISD was 1.40 ± 0.55. Prior to adjustment for covariates, the mean ISD for the non-CD group was 1.10 ± 0.31 compared with 1.50 ± 0.70 for the CD group. After adjusting for ethnicity, education, employment, socioeconomic status and anxiety/depression, there was a statistically significant association between ISD and cognitive status (odds ratio [OR] for one unit increase in ISD: 13.56, 95% CI: 4.80-38.31; OR for 1/10th unit increase in ISD: 1.30, 95% CI: 1.17-1.44). Findings were robust to multiple sensitivity analyses. Multivariable random intercept logistic regression modelling is provided in **Table 1**. ISD scores across 3 assessment visits for non-CD and CD patients is provided in **Figure 1**.

Conclusion: Dispersion scores such as ISD have been explored as a pragmatic and sensitive marker of cognitive function in different patient populations. We showed that among adult SLE patients, increased ISD across the cognitive tests of the ACR-NB was associated with an increased likelihood of having CD, adjusting for important covariates. Additional research is warranted to evaluate the promise of dispersion scores in clinical practice.

Disclosure: J. **He**, None; **J. Diaz-Martinez**, None; **K. Bingham**, None; **J. Su**, None; **M. Kakvan**, None; **M. Tartaglia**, None; **L. Ruttan**, None; **D. Beaton**, None; **J. Wither**, None; **M. Choi**, MitogenDx, 1, 2; **M. Fritzler**, Inova Diagnostics Inc., 2, 6, Werfen International, 2, Alexion Canada, 6, Mitogen Diagnostics Corp., 3, 8, 9, 10; **N. Anderson**, None; **D. Bonilla**, None; **R. Green**, None; **P. Katz**, None; **Z. Touma**, AbbVie Inc, 2, UCB Biopharma SRL, 2, Sarkana Pharma Inc., 1, 4, Janssen Inc., 2, GlaxoSmithKline Inc., 6.

Abstract Number: 0896

Systemic Lupus Erythematosus Disease Flares After SARS-CoV-2 Vaccination

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Manifestations (0855–0896)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Vaccination against SARS-CoV-2 is particularly important for patients with systemic lupus erythematosus (SLE), who may be at increased risk of hospitalization for COVID-19. However, the most common reason for vaccine refusal in patients with SLE is fear of SLE disease flare. Additionally, the SARS-CoV-2 mRNA vaccines could potentially induce interferon production, associated with increased SLE disease activity. Thus far, no population-based data exist regarding whether SARS-CoV-2 vaccines trigger SLE flares.

Methods: We emailed a secure web-based survey on March 5, 2021 to 7,094 patients aged ≥18 years evaluated at least once between 2018-2020 by a rheumatologist at a single Rheumatology Division in New York City. We included individuals who received at least one vaccine dose. ICD-10-CM codes identified patients with SLE. A self-reported disease flare was defined as "a sudden worsening of your rheumatology condition or arthritis" within two weeks of the vaccine dose. To prevent misleading conclusions, we did not perform statistical testing on these interim results.

Results: As of March 30, 2021, 136/466 (29.2%) respondents with SLE (mean[SD] age 54.7 [13.9] years; 93.4% female; 67.7% White; 13.2% Hispanic/Latinx ethnicity) reported receiving at least one COVID-19 vaccine dose.

Table 1. Vaccine Characteristics in Outpatients with SLE, Stratified by Flare Status Post-COVID-19 Vaccination				
	1st COVID-19 Vaccine Dose N=136		2nd COVID-19 Vaccine Dose N=72	
	Flare N=9 (6.6%)	No Flare N=127 (93.4%)	Flare N=5 (6.9%)	No Flare N=67 (93.1%)
Vaccine Manufacturer*, N%				
Pfizer	4 (44.4)	77 (60.6)	2 (40.0)	41 (61.2)
Moderna	5 (55.6)	43 (33.9)	3 (60.0)	23 (34.3)
Johnson &Johnson	0 (0)	4 (3.2)	N/A	N/A
Medications taken for Prevention of COVID-19 Vaccine Side Effects (Prior to Vaccine) (N,%)**				
Benadryl	1 (11.1)	6 (4.7)	1 (20)	2 (3)
Corticosteroids	1 (11.1)	2 (1.6)	1 (20)	0 (0)
Acetaminophen	0 (0)	9 (7.0)	1 (20)	4 (6)
NSAIDs/CoX-2 inhibitors	0 (0)	2 (1.6)	0 (0)	0 (0)
No Medications	7 (77.8)	110 (86.6)	3 (60)	60 (89.6)
Medications taken for Treatment of COVID-19 Vaccine Side Effects (After Vaccine) (N,%)**				
Epi pen	0 (0)	0 (0)	0 (0)	0 (0)
Benadryl	1 (11.1)	3 (2.4)	1 (20)	2 (3)
Corticosteroids	1 (11.1)	1 (0.8)	1 (20)	0 (0)
Acetaminophen	3 (33.3)	33 (26.0)	4 (80)	26 (38.8)
NSAIDs/CoX-2 inhibitors	2 (22.2)	9 (7.1)	1 (20)	6 (9)
No Medications	4 (44.4)	86 (67.7)	0 (0)	35 (52.2)
Flare defined as self-reported "sudden worsening of rheumatology condition or arthritis" within 2 weeks of COVID-19 vaccination. *Column numbers do not add up due to missing data.				

Eighty-one patients (59.6%) received Pfizer, 48 (39.3%) received Moderna, and 4 (2.9%) received Janssen. Of patients receiving Pfizer or Moderna, 72 (54.5%) received 2/2 doses. Twelve patients (8.8%) reported SLE flare within two weeks of COVID-19 vaccination. Only 1 patient (8.3%) with flare reported a history of suspected/confirmed COVID-19, similar to those without flare (8.4%). Patients reporting SLE flare were older (59.0 [14.0] vs. 54.3 [13.9] years) and White (83.3% vs. 61.1%). Flares occurred in 12.5% of patients receiving Moderna and 7.4% receiving Pfizer (6 patients each). Out of 7 patients receiving both vaccine doses, 2 flared only after the first dose, 3 flared only after the second dose, and 2 flared after both doses. Of the 14 flare episodes, 9 occurred after the first dose, and 5 occurred after the second dose. Medications were used for prevention or treatment of vaccine side effects by both the flare and non-flare groups (Table 1). Most flares after the first vaccine dose were mild (77.8%), and after the second vaccine were moderate (60%). 12/14 flares (85%) were described as "typical", predominantly characterized by joint pain, muscle aches, and fatigue (Table 2). While 8/14 flares started 1 day after vaccination, 4/14 started 4-7 days later. None started >7 days post-vaccination. Most SLE flares resolved within 7 days of onset; however, 4/14 lasted 8-21 days and 2/14 lasted >21 days.

Conclusion: Our data suggest >91% of SLE patients did not experience a disease flare post-SARS-CoV-2 vaccination; of those that did, most had mild flares. Given almost all patients reported that their post-vaccine flare was "typical" of their SLE flares, vaccine side effects alone may not explain these findings. This information can help inform vaccine decision-making among patients with SLE. Future analyses will evaluate whether modifying immunosuppressive medications to enhance vaccine efficacy increased SLE flare risk.

Table 2. Flare Characteristics in Outpatients with SLE, Stratified by Flare Status Post-COVID-19 Vaccination		
	1st COVID-19 Vaccine Dose	2nd COVID-19 Vaccine Dose
	Flare N=9 (6.6%)	Flare N=5 (6.9%)
Flare Severity (N,%)		
Mild	7 (77.8)	1 (20)
Moderate	1 (11.1)	3 (60)
Severe	1 (11.1)	1 (20)
Flare described as "Typical" (N,%)		
Yes	8 (88.9)	4 (80)
No	0 (0)	1 (20)
Not Sure	1 (11.1)	0 (0)
Flare Symptoms (N,%)*		
Fever	3 (33.3)	1 (20)
Joint pain	5 (55.6)	4 (80)
Joint swelling	1 (11.1)	3 (60)
Skin rash	2 (22.2)	1 (20)
Fatigue	7 (77.8)	5 (100)
Muscle aches	5 (55.6)	4 (80)
Other**	2 (22.2)	1 (20)
Number of days after vaccine when flare started (N,%)		
1 day	5 (55.6)	3 (60)
2-3 days	1 (11.1)	1 (20)
4-7 days	3 (33.3)	1 (20)
>7 days	0 (0)	0 (0)
Length of flare (N,%)		
1 day	1 (11.1)	0 (0)
2-3 days	0 (0)	2 (40)
4-7 days	4 (44.4)	1 (20)
8-21 days	2 (22.2)	2 (40)
>21 days	2 (22.2)	0 (0)

*Rows not mutually exclusive.
**Other flare symptoms indicated by patients at 1st COVID-19 vaccine dose: Brain fog, mouth sores; Other symptoms at 2nd vaccine dose: increased neuropathy pain, neck pain, knee pain.

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Abstract Number: 0897

Age-Stratified Trend of Spinal Radiographic Damage Progression in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies investigating the course of spinal structural progression in patients with ankylosing spondylitis (AS) using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) have shown highly variable rates of mSASSS progression among individuals. Furthermore, a substantial radiographic progression has been noted both in young patients at an early stage of disease as well as in elderly patients at an advanced stage, indicating a within-individual variation in the progression of long-term structural damage in the spine. Thus, exploring the extent to which spinal radiographic damage worsens according to age can be helpful in providing insights into the understanding of the natural course of structural disease progression. The aim of this study was to estimate the course of spinal radiographic progression for specific age range categories using a longitudinal dataset in a real-life setting.

Methods: In total, 4016 radiographic intervals were obtained from 1125 AS patients with consecutive spinal radiographs available at a single hospital. The included radiographic intervals were categorized into five groups based on the age at each radiograph: age < 20 (n=122); 20–29 (n=1124); 30–39 (n=690); 40–49 (n=794); and ≥50 years (n=286). Radiographic progression rate was defined as the mSASSS change per year. Age-stratified mSASSS change per year was estimated using the generalized estimating equations (GEE) for longitudinal data after adjusting for predictors of radiographic progression. A subgroup analysis was performed to estimate the course of radiographic progression, stratified for identified risk factors.

Results: The mean (SD) follow-up duration was 8.4 (2.9) years and the mean number of radiographs was 4.6 (1.2) per patient. The mean radiographic progression rate of the overall intervals was 0.8 (1.9). In the GEE multivariable analysis, smoking, peripheral joint involvement, eye involvement, log-transformed C-reactive protein (CRP) values at each radiograph, and preexisting syndesmohyte were significant and independent factors for predicting structural damage progression.

GEE-estimated radiographic progression was highest at age group 30–39 (estimated mean mSASSS change per year was 1.148), followed by 40–49 (1.003), 20–29 (0.868), ≥50 (0.779), and < 20 (0.643) . However, radiographic damage scores rapidly increased among younger age groups with risk factors. The estimated mean mSASSS change per year for the age group 20–29 was 1.244 with elevated CRP levels and 2.505 with preexisting syndesmophytes, respectively.

Table 1. Characteristics of radiographic intervals, overall and by age-stratified groups

Variable	Total intervals (n=4016)		Radiographic intervals by age-stratified groups, years				
	No. with data	Value	<20 (n=122)	20–29 (n=1124)	30–39 (n=1690)	40–49 (n=794)	≥50 (n=286)
Age, years	4016	34.7 (9.5)	17.6 (1.5)	25.4 (2.8)	34.3 (2.8)	43.6 (2.8)	55.9 (5.1)
Symptom duration, years	3457	12.7 (7.8)	3.9 (3.0)	7.9 (4.6)	13.3 (6.4)	16.6 (8.2)	19.9 (11.3)
Male gender	4016	3572 (88.9%)	112 (91.8%)	1008 (89.7%)	1528 (90.4%)	696 (87.7%)	228 (79.7%)
HLA-B27 positive	4006	3878 (96.8%)	119 (98.3%)	1100 (98.2%)	1637 (97.1%)	756 (95.3%)	266 (93.0%)
Smoking ever	3860	2384 (61.8%)	35 (29.9%)	519 (48.9%)	1100 (67.7%)	555 (71.3%)	175 (62.7%)
Eye involvement ever	3564	1410 (39.6%)	21 (22.1%)	327 (33.2%)	620 (41.0%)	328 (45.8%)	114 (44.5%)
Peripheral joint involvement ever	3529	1539 (43.6%)	51 (54.8%)	433 (44.5%)	637 (42.3%)	298 (42.3%)	120 (47.4%)
CRP, mg/dL	3957	1.6 (1.9)	1.9 (2.4)	1.9 (2.2)	1.5 (1.8)	1.5 (1.9)	1.4 (1.6)
Elevated CRP	3957	1585 (40.1%)	50 (41.7%)	501 (45.4%)	656 (39.4%)	275 (35.0%)	103 (36.3%)
ESR, mm/h	3961	22.9 (25.1)	25.1 (28.8)	23.8 (26.3)	21.4 (23.4)	23.1 (25.2)	26.4 (28.1)
BASDAI (0–10)	2684	3.4 (2.2)	4.1 (2.7)	3.6 (2.3)	3.4 (2.2)	3.3 (2.1)	3.7 (2.0)
Elevated BASDAI (≥4)	2684	946 (35.2%)	21 (48.8%)	243 (38.9%)	412 (34.0%)	186 (31.4%)	84 (39.3%)
TNF inhibitor use ever	4016	2306 (57.4%)	78 (63.9%)	625 (55.6%)	957 (56.6%)	458 (57.7%)	188 (65.7%)
Sacroiliitis grade at baseline	3796	2.9 (0.9)	2.3 (0.8)	2.6 (0.9)	3.0 (0.9)	3.1 (0.9)	2.9 (0.9)
Syndesmophytes presence at baseline	4016	1146 (28.5%)	0 (0.0%)	84 (7.5%)	494 (29.2%)	397 (50.0%)	171 (59.8%)
mSASSS change/year	4016	0.8 (1.9)	0.1 (0.5)	0.5 (1.5)	1.0 (2.0)	1.1 (2.0)	0.8 (1.8)
Cervical segment	4016	0.3 (1.2)	0.0 (0.4)	0.2 (1.0)	0.4 (1.3)	0.5 (1.2)	0.3 (1.3)
Lumbar segment	4016	0.5 (1.2)	0.1 (0.3)	0.3 (0.9)	0.6 (1.3)	0.6 (1.4)	0.5 (1.5)

Continuous variables are presented as mean (standard deviation).

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; ESR, erythrocyte sediment rate; HLA, human leukocyte antigen; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score; TNF, tumor necrosis factor.

Conclusion: In AS, spinal structural damage with age progresses in an increasing trend in which periods of relatively rapid increase and slow increase may alternate, and it seems to progress the most in the 30s. However, patients with risk factors show a rapid progression from under the 30s.

Table 2. Age-stratified radiographic progression rate estimated from GEE multivariable models

	Radiographic intervals by age-stratified groups, years				
	<20	20–29	30–39	40–49	≥50
Estimated mSASSS change/year	0.643 (0.484, 0.801)	0.868 (0.711, 1.026)	1.148 (1.027, 1.268)	1.003 (0.837, 1.170)	0.779 (0.519, 1.038)
Cervical segment	0.211 (0.086, 0.336)	0.316 (0.200, 0.432)	0.478 (0.375, 0.582)	0.492 (0.390, 0.594)	0.343 (0.186, 0.500)
Lumbar segment	0.324 (0.205, 0.444)	0.477 (0.374, 0.580)	0.684 (0.595, 0.773)	0.557 (0.439, 0.674)	0.511 (0.309, 0.714)

Values are balanced marginal means (95% CI) of mSASSS change/year which were averaged over the levels of independent predictors of radiographic progression (smoking, eye involvement, peripheral joint involvement, log-transformed CRP, and preexisting syndesmophyte).

CI, confidence interval; GEE, generalized estimating equations; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Table 3. GEE-estimated radiographic progression rate, by the presence or absence of risk factors

		Radiographic intervals by age-stratified groups, years				
		<20	20–29	30–39	40–49	≥50
Smoking	Yes (n=2068)	0.753 (0.464, 1.040)	1.036 (0.784, 1.290)	1.364 (1.201, 1.530)	1.235 (1.017, 1.450)	0.709 (0.384, 1.030)
	No (n=1252)	0.519 (0.337, 0.701)	0.757 (0.586, 0.928)	0.932 (0.750, 1.113)	0.835 (0.620, 1.049)	1.078 (0.666, 1.489)
Eye involvement	Yes (n=1308)	0.848 (0.502, 1.190)	1.112 (0.783, 1.440)	1.305 (1.104, 1.510)	1.047 (0.842, 1.250)	0.703 (0.359, 1.050)
	No (n=2012)	0.550 (0.375, 0.726)	0.774 (0.616, 0.931)	1.075 (0.926, 1.224)	1.063 (0.804, 1.323)	0.895 (0.518, 1.271)
Peripheral joint involvement	Yes (n=1467)	0.747 (0.530, 0.965)	0.802 (0.574, 1.031)	1.019 (0.844, 1.195)	1.011 (0.803, 1.220)	0.915 (0.557, 1.274)
	No (n=1853)	0.649 (0.397, 0.901)	1.024 (0.799, 1.250)	1.332 (1.153, 1.511)	1.141 (0.892, 1.391)	0.787 (0.407, 1.166)
Elevated CRP	Yes (n=1351)	0.885 (0.601, 1.170)	1.244 (0.991, 1.500)	1.627 (1.412, 1.840)	1.141 (0.882, 1.400)	0.829 (0.306, 1.350)
	No (n=1969)	0.440 (0.274, 0.607)	0.544 (0.364, 0.724)	0.787 (0.656, 0.918)	0.899 (0.694, 1.104)	0.612 (0.318, 0.906)
Preexisting syndesmophyte	Yes (n=947)	-	2.505 (1.640, 3.370)	1.751 (1.514, 1.990)	1.321 (1.039, 1.600)	0.755 (0.453, 1.060)
	No (n=2373)	0.243 (0.116, 0.370)	0.373 (0.284, 0.462)	0.711 (0.568, 0.854)	0.790 (0.610, 0.969)	1.098 (0.696, 1.499)
Preexisting syndesmophyte & elevated CRP (n=525)		-	2.770 (1.951, 3.600)	2.310 (1.928, 2.700)	1.440 (1.052, 1.820)	1.050 (0.531, 1.570)

Values are balanced marginal means (95% CI) of mSASSS change/year which were averaged over the levels of independent predictors of radiographic progression (smoking, eye involvement, peripheral joint involvement, log-transformed CRP, and preexisting syndesmophyte).

CI, confidence interval; CRP, C-reactive protein; GEE, generalized estimating equations; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score.

Disclosure: T. Lee, None; **B. Koo**, None; **B. Nam**, None; **S. Lee**, None; **K. Joo**, None; **T. Kim**, AbbVie, 6, Celltrion, 6, Kirin, 6, Lilly, 6, Novartis, 6.

Abstract Number: 0898

MRI Vertebral Corner Inflammation and Fat Deposition Are Associated with Whole Spine Low Dose CT Detected Syndesmophytes: A Multilevel Analysis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

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Session Time: 8:30AM–10:30AM

Background/Purpose: In previous studies vertebral corner inflammation (VCI) and vertebral corner fat deposition (VCFD) were associated with syndesmophyte formation on cervical and lumbar conventional radiography. We studied associations between patterns of VCI, VCFD and a combination of both on magnetic resonance imaging (MRI) and the development of new or grown syndesmophytes on whole spine low dose computed tomography (ldCT), thereby studying these associations also in the thoracic spine.

Methods: Patients in the Sensitive Imaging in Ankylosing Spondylitis cohort underwent MRI at baseline, 1 year and 2 years, and ldCT at baseline and 2 years. MRI lesions were scored by 3 central readers, using the SPARCC method for VCI and the CanDen method for VCFD, and coded as absent or present per timepoint and per reader. MRI patterns over time (Table) were deemed present if seen by ≥2 out of 3 readers. The patterns reflect hypothetical associations between presence and absence of VCI and VCFD, independently and combined, on ldCT detected new or grown syndesmophytes. Individual reader change scores were used for ldCT images, scored by 2 central readers with the Computed Tomography Syndesmophyte Score. New (CTSS 0 à 1, 2 or 3) and grown (CTSS 1 à 2 or 3; 2 à 3) syndesmophytes were grouped together to represent bone formation. Corners not at risk for the outcome due to presence of a bridged syndesmophyte at baseline were excluded. Multilevel generalized estimated equations were used, with separate models per MRI pattern, accounting for correlations within patients and between ldCT readers.

Results: Fifty patients were included, contributing a total of 4600 vertebral corners. Their mean age was 49.3 years (SD 9.8), 86% were male and 78% were HLA-B27+. Presence of VCI and VCFD patterns ranged from 43 (0.9%) to 3108 (67.6%) corners (Table), with the lowest frequency being for VCI preceding VCFD. Protection against syndesmophyte development was seen in case of absence of both VCI and VCFD (OR 0.35) and positive associations with ORs ranging from 1.87-2.58 were observed for various VCI/VCFD patterns. Nevertheless, out of all corners with a new or grown syndesmophyte, 47.3% of corners according to reader 1 and 43.9% according to reader 2 had neither VCI nor VCFD preceding the bone formation.

Conclusion: Presence of VCI or VCFD and combinations of the two increased odds of bone formation 2 years later, whereas absence of both VCI and VCFD decreased the odds, showing that VCI and VCFD have some role in the development of syndesmophytes. However, almost half of all bone formation occurred in corners without VCI or VCFD, suggesting the presence of these lesions in yearly MRIs does not fully explain the development of syndesmophytes.

Table. Effect of vertebral corner inflammation and vertebral corner fat deposition on syndesmophyte formation

Patterns of lesions over time on MRI	Corners with VCI/VCFD pattern N(%)	OR (95% CI)
1. VCI at any TP, irrespective of VCFD	691 (15.0%)	**2.37 (1.49-3.78)**
2. VCFD at any TP, irrespective of VCI	1080 (23.5%)	**2.58 (1.97-3.39)**
3. VCI on ≥1 TP and absence of VCFD on all TPs	372 (8.1%)	**1.90 (1.15-3.13)**
4. VCFD on ≥1 TP and absence of VCI on all TPs	754 (16.4%)	**1.87 (1.41-2.48)**
5. VCI precedes VCFD	43 (0.9%)	2.20 (0.83-5.86)
6. VCI precedes or coincides with VCFD. VCFD does not precede VCI	198 (4.3%)	**2.33 (1.47-3.69)**
7. Absence of VCI and VCFD on all TPs	3108 (67.6%)	**0.35 (0.25-0.49)**

VCI, vertebral corner inflammation; VCFD, vertebral corner fat deposition; TP, timepoint.

This study confirmed that there is an association between VCI and VCFD and bone formation also for the thoracic spine and on ldCT compared to conventional radiography.

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Abstract Number: 0899

Comparison of Sacroiliac CT Findings in Patients with and Without Ankylosing Spondylitis Aged 50 Years or Older: Preliminary Results of the CASIAGE Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)
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Background/Purpose: Diagnosis of axial spondyloarthritis (SpA) is nowadays commonly made with pelvic radiography or MRI. However, there is an important inter-observer variability for radiographs, and MRI is subject to possible false positives and is not the best modality for studying structural lesions. Conversely, pelvic CT has an excellent

Table 1. Sacro-iliac CT findings using a score modified from Diekhoff et al.

Finding	AS Patients	Controls	p-value
Mean (SD) total score (range 0-108)	73.13 ± 38.07	7.51± 12.42	< 0.0001
Global positivity, n (%)	60 (89.55 %)	13 (19.40 %)	< 0.0001
Bilateral ankylosis, n (%)	39 (58.21 %)	1 (1.49 %)	< 0.0001
Positive joint space score, n (%)	59 (88.06 %)	12 (17.91 %)	< 0.0001
Positive erosion score, n (%)	18 (26.87 %)	2 (2.99%)	0.0001
Significant sclerosis, n (%)	16 (23.88 %)	10 (14.93%)	0.19
Intra-articular gas, n (%)	18 (26.87 %)	45 (67.16 %)	< 0.0001
DISH, n (%)	3 (4.48 %)	23 (34.33 %)	< 0.0001

specificity and appears to be more effective than radiography for the diagnosis of SpA. However, CT findings in patients over 50 years of age have not been studied. Therefore, we conducted a study to describe sacroiliac (SI) joint CT characteristics in patients with ankylosing spondylitis (AS), aged 50 years or older.

Methods: An observational, retrospective study was performed using medical records from Besançon University Hospital's rheumatology department, which were screened to identify patients with AS, according to the 2009 ASAS criteria. A search was then carried out for patients over 50 years old in the hospital's imaging archiving system to identify those who had undergone a CT which included the SI joints in their entirety. Non-inclusion criteria were the existence of pelvic bone lesions and a history of pelvic radiotherapy. Each patient was then matched with a control of the same age and sex, recruited through the hospital's imaging archiving system.

For each individual, CT was interpreted by two independent readers using a score previously used by Diekhoff et al.[1], dividing each SI joint into 12 regions, for each of which joint space narrowing (JSN), erosions, and sclerosis are assessed. For this study, we also observed the existence of intra-articular gas and diffuse idiopathic skeletal hyperostosis (DISH) lesions for each region. Quantitative variables are expressed as mean ± standard deviation and were compared using Student's t-test. Qualitative variables are expressed as numbers and percentages and were compared using the Chi-2 test.

Results: 67 patients and 67 controls were included. Mean age was 65.45 ± 10.62 years in the AS group and 65.34 ± 10.70 years in the control group. 44 (65.67%) were male in both groups. In the AS group, 48 (87.27%) were HLA-B27 positive. Mean disease duration was 22.57 ± 14.88 years. 23 (35.38%) had a bamboo spine. CT findings are described in table 1. The majority of AS patients had a positive JSN score, but significant erosions were found in only a minority of cases. This is partly explained by the fact that 39 (58.21%) patients had at least one complete bilateral ankylosis (and therefore no erosions) on the slices studied.

Bilateral ankylosis was associated with longer disease duration (p=0.0007) and presence of bamboo spine (p=0.0003). The distribution of patients' lesions appeared to be homogenous over all 24 regions studied (Figure 1).

The rate of significant JSN and erosion was significantly higher in the AS group. On the contrary, the rate of DISH and intra-articular gas was significantly higher in the control group.

Conclusion: CT findings in AS patients over 50 years of age are mostly represented by changes in joint space, with bilateral ankylosis present in half of the patients, and show more erosions and JSN changes, but less intra-articular gas than controls. AS appears to be a protective factor for DISH.

1. Diekhoff T et al. *Ann Rheum Dis*. 2017;76(9):1502-1508.

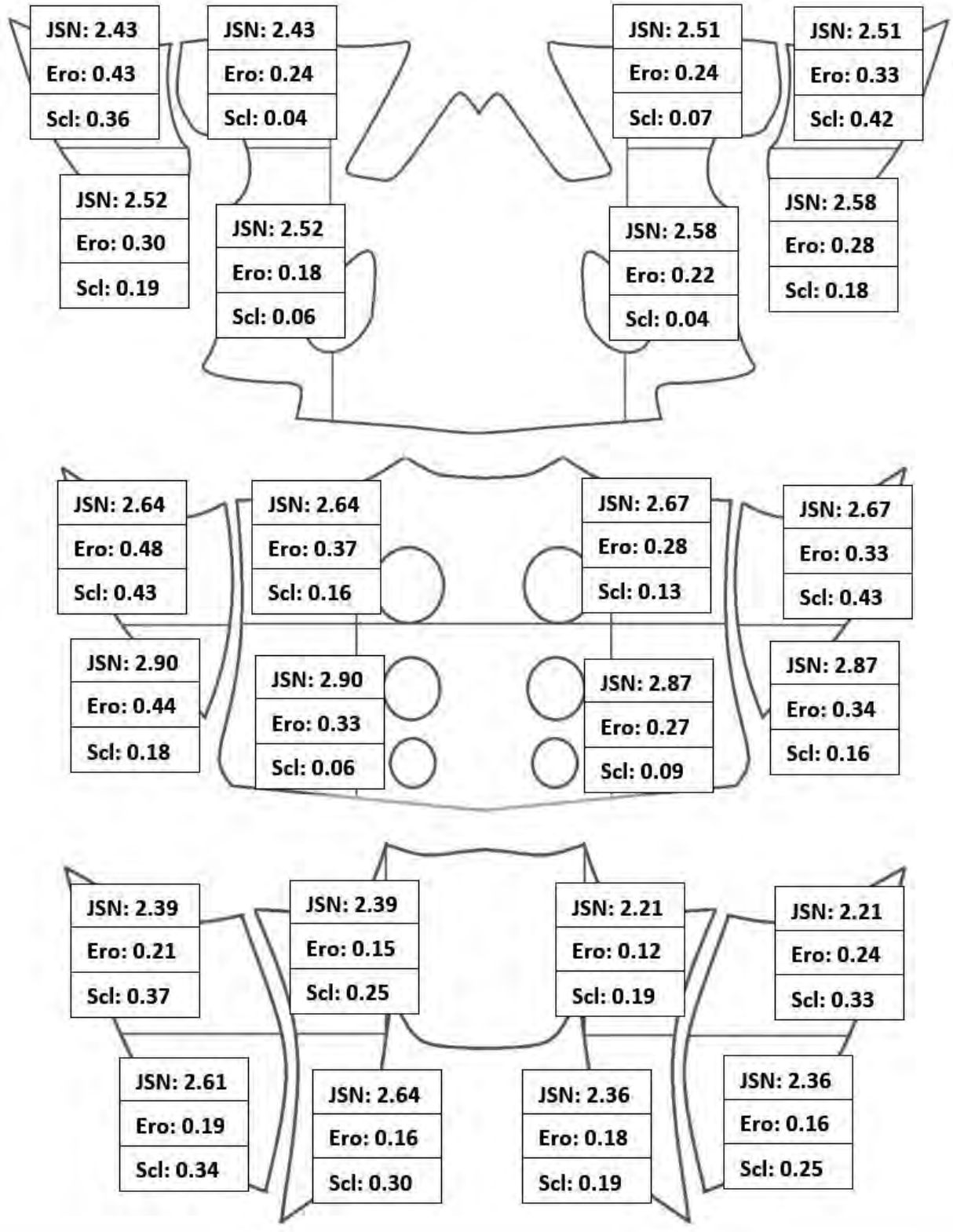

Figure 1. Mean scores per region in the anterior, central, and posterior SI slices (JSN: joint space narrowing (0-4), Ero: erosions (0-3), Scl: sclerosis (0-2)) for AS patients.

Disclosure: O. **Fakih**, None; **M. Chouk**, None; **C. Prati**, None; **D. Wendling**, None; **F. Verhoeven**, None.

Abstract Number: 0900

The Phenomenon of Fused Sacroiliac Joints but Absent Syndesmophytes in Long Standing Ankylosing Spondylitis Patients: Data from a Prospectively Followed Cohort

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SESSION INFORMATION

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Session Type: Poster Session B

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Background/Purpose: Ankylosing Spondylitis describes disorders of inflammation and damage to the spine and sacroiliac (SI) joints. Clinicians have observed, on occasion, AS subjects with fused SI joints but little or no spinal involvement; is there truly a subgroup with fused SI joints and long-standing disease but absent radiographically demonstrated spinal syndesmophytes? No study has assessed the subset with long standing disease with fused SI joints but no radiographic spinal disease. Using a large multi-center cohort, the purpose of this study was to identify factors associated with discordant SI joint and spinal radiographic severity in AS patients.

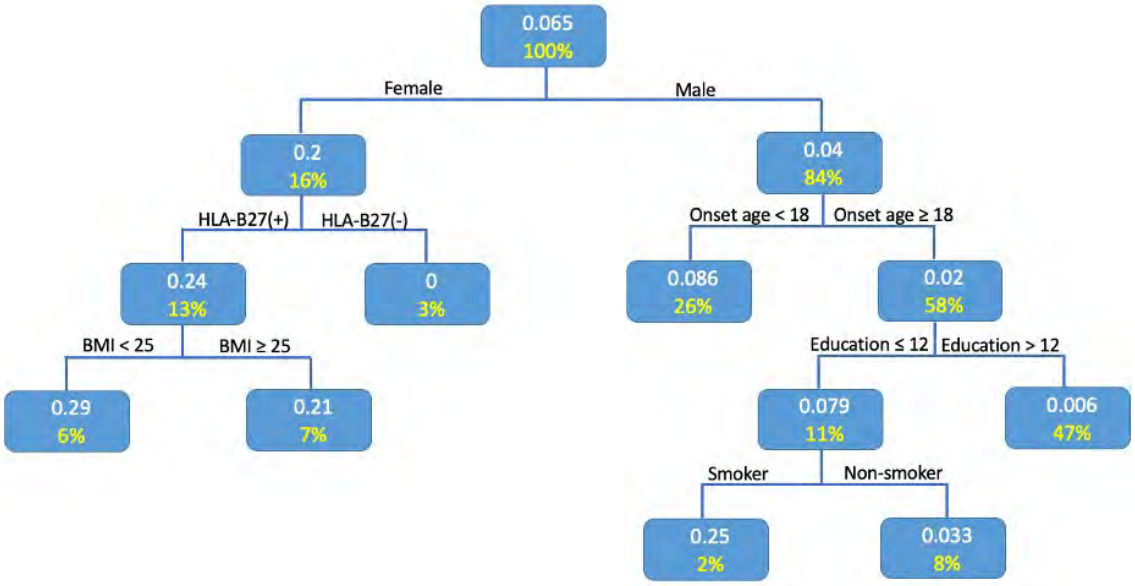

Figure 1. CART Analysis. Yellow values = percentages of the total subgroup population. White values = likelihood of not having syndesmophytes.

Table 1. Factor associated with syndesmophytes for patients with disease duration ≥20 years and grade IV sacroiliitis based on univariable logistic regression model (N=354 patients).

Variable	Syndesmophytes N=331	No-Syndesmophytes N=23	Odds Ratio (95% CI)	p-value
Gender				
Male, n (%)	286 (86.40)	12 (52.17)	5.83 (2.43, 14.00)	<0.001
Female, n (%)	45 (13.60)	11 (47.83)	0.17 (0.07, 0.41)	
Race				
White, n (%)	288 (87.01)	18 (78.26)	1.86 (0.66, 5.27)	0.243
Non-white, n (%)	43 (12.99)	5 (21.74)	0.54 (0.19, 1.52)	
HLA-B27				
Plus (+), n (%)	278 (83.99)	23 (100.00)	NA*	0.956
Minus (-), n (%)	53 (16.01)	0 (0.00)	NA*	
Education level (last available)				
High school or less, n (%)	60 (18.13)	6 (26.09)	1.59 (0.60, 4.21)	0.347
College or more, n (%)	271 (81.87)	17 (73.91)	0.63 (0.24, 1.66)	
Age of onset (year)				
<18, n (%)	106 (32.02)	11 (47.83)	0.51 (0.22, 1.20)	0.125
18-45, n (%)	219 (66.16)	12 (52.17)	1.79 (0.77, 4.19)	0.178
>45, n (%)	6 (1.81)	0 (0.00)	NA**	0.985
BMI (last available)				
Normal (<25), n (%)	34 (28.57)	5 (45.45)	0.41 (0.14, 1.18)	0.099
Overweight (25-30), n (%)	42 (35.29)	4 (36.36)	0.69 (0.22, 2.13)	0.519
Obese (>30), n (%)	43 (36.13)	2 (18.18)	1.57 (0.36, 6.92)	0.553
Smoker (last available)				
Yes, n (%)	32 (10.19)	4 (18.18)	0.51 (0.16, 1.60)	0.249
No, n (%)	282 (89.81)	18 (81.82)	1.96 (0.62, 6.14)	
IBD (last available)				
Yes, n (%)	21 (6.5)	2 (9.52)	0.66 (0.14, 3.03)	0.594
No, n (%)	302 (93.5)	19 (90.48)	1.51 (0.33, 6.94)	
Ever Uveitis				
Yes, n (%)	141 (43.79)	10 (45.45)	0.94 (0.39, 2.23)	0.879
No, n (%)	181 (56.21)	12 (54.55)	1.07 (0.45, 2.55)	
Presence of hip disease (last available)				
Yes, n (%)	181 (55.02)	11 (47.83)	1.33 (0.57, 3.11)	0.504
No, n (%)	148 (44.98)	12 (52.17)	0.75 (0.32, 1.75)	
Presence of enthesitis (last available)				
Yes, n (%)	66 (20.12)	5 (21.74)	0.91 (0.33, 2.53)	0.852
No, n (%)	262 (79.88)	18 (78.26)	1.10 (0.40, 3.08)	
Presence of peripheral arthritis (last available)				
Yes, n (%)	76 (23.03)	4 (17.39)	1.42 (0.47, 4.30)	0.535
No, n (%)	254 (76.97)	19 (82.61)	0.70 (0.23, 2.13)	

NA*: All patients with no-syndesmophytes have HLA-B27+
NA**: All patients with age of onset >45 have syndesmophytes

Methods: Patients met the modified New York criteria for AS. Study visits every 4-6 months included CRP levels, demographic and social information. Radiographs of the pelvis and lateral spine were performed every 2 years. We included 354 patients with fused SI joints and disease duration of at least 20 years. We employed classification and regression trees (CART) analysis to examine the subset of patients with fused SI joints but no syndesmophytes. We defined no-syndesmophytes as mSASSS< 2 at all cervical- and lumbar-spine levels, and the presence of syndesmophytes as mSASSS≥ 2. We also conducted logistic regression models.

Results: Of the 354 patients with long standing disease and fused SI joints, 6.5% did not have syndesmophytes. Gender was the strongest factor associated with lack of syndesmophytes on CART analysis. Females accounted for

Table 2. Factors associated with syndesmophytes for patients with disease duration ≥ 20 years and grade IV sacroiliitis based on multivariable logistic regression with first-order interactions (N=354 patients).

Variable	Adj. OR (95% CI)	p-value
Education level (High school or less vs. College or more)	0.33 (0.04, 2.99)	0.325
BMI (Overweight [BMI 25 to 30] vs. Normal [18.5 to <25])	1.00 (0.21, 4.68)	0.999
BMI (Obese [BMI ≥30] vs. Normal [18.5 to <25])	1.79 (0.29, 11.07)	0.532
Gender (Male vs. Female)		
Age of onset <18	1.44 (0.24, 8.68)	0.691
Age of onset ≥18	35.65 (2.81,451.60)	0.006

16% of the subgroup, and of these, 20% did not have syndesmophytes. Males were 84% of the subgroup and 4% did not have syndesmophytes (*Figure 1*). Univariable logistic regression modeling corroborated this finding with OR 5.83 (95% CI 2.43, 14.00), *p*-value was < 0.001 with females more likely to not have syndesmophytes (*Table 1*).

In men, age of onset was the next important predictor. 26% of males had age of symptom onset less than 18 years, and 8.6% of these did not have syndesmophytes (*Figure 1*). Investigating interactions between male gender and age of symptom onset, on multivariable analysis the *p*-value was 0.006 with OR 35.65 (95% CI 2.81, 451.60) (*Table 2*) with men who had age of symptom onset < 18 years being less likely to have syndesmophytes.

All 23 patients who did not have syndesmophytes were HLA-B27 positive.

Conclusion: Of our subgroup, 6.5% of patients lacked syndesmophytes. Gender was the most important variable, with women being more likely to lack syndesmophytes despite having complete SI fusion with long disease duration. Age of symptom onset may also be an important variable in male gender subjects. All of the non-syndesmophyte group were HLA-B27 positive raising the possibility that HLA-B27 positivity may be more associated with sacroiliitis than proliferative spinal bone disease. Our study is distinct in assessing this subpopulation of fused SI joints with long disease duration but no spinal disease. Further studies are needed to elucidate why AS disease behaves differently in this and other subgroups.

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Abstract Number: 0901

Low Dose Dual Energy CT Scan for the Detection of Bone Marrow Edema and Erosions in Axial Spondyloarthritis

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SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Table 1: Sensitivity, specificity, positive predictive value & negative predictive value

Variables	Readers	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)
DECT BME compared with MRI	Reader 1	28.9	90.0	78.57	50.0
	Reader 2	35.29	87.50	75.0	56.0
MRI Erosion compared with DECT	Reader 1	85.4	81.5	87.5	78.6
	Reader 2	82.5	80.8	86.8	75

Table 2: Measure of Agreement: Kappa Analysis- inter-rater agreement between reader 1 and reader 2.

Variables	Kappa Value	Standard Error	P value
MRI BME	0.880	0.058	<0.001
DECT BME	0.57	0.12	<0.001
MRI Erosion	0.939	0.042	<0.001
DECT Erosion	0.683	0.092	<0.001

Background/Purpose: Bone marrow edema (BME) and erosions of the sacroiliac (SI) joints are key imaging features in the diagnosis of axial spondyloarthritis (axSpA). MRI with a fluid sensitive sequence is the most common technique for confirming BME but disadvantages include cost and accessibility. Traditional CT is considered superior for detection of erosions but may be limited by radiation exposure. Low dose CT is a technique associated with a similar amount of radiation as conventional radiography and low dose dual energy CT (ldDECT) may be able to detect BME without the need for higher doses of radiation.

We aim to compare the ability of ldDECT and MRI STIR for the detection of BME and erosions of the SI joints in an inception cohort of patients presenting with undiagnosed back pain and psoriasis, iritis, colitis, or positive HLA-B27.

Methods: Consecutive patients ≤ 45 years of age with ≥ 3 months of undiagnosed low back or buttock pain with any one of psoriasis, uveitis, inflammatory bowel disease, or positive HLA-B27 underwent routine clinical evaluation by a rheumatologist for axSpA followed by both MRI and ldDECT of the SI joints done within 3 months of each other.

Two musculoskeletal fellowship trained radiologists were given 17 cases for calibration which were not included in the study. MRI images were scored for presence of BME, presence of large BME lesions, erosions, number of erosions, and radiologist global assessment for presence/absence of sacroiliitis with confidence scale (0-10) blinded to clinical information and ldDECT images. ldDECT images were scored in the same manner and discordant reads were adjudicated by a third radiologist.

Results: 68 patients were recruited with 27 (39.7%) diagnosed with axSpA (mean age 33.2, male 63%, mean symptom duration 8.7 years, HLA-B27 positive 85%). Uveritis, psoriasis, and IBD were present in 20, 23, and 6% of patients respectively.

ldDECT had a sensitivity of 28.9 and 35.3% and a specificity of 90 and 87.5% between two readers for detection of BME compared with MRI (Table 1).

MRI had a sensitivity of 85 and 82.5% and a specificity of 81.5 and 80.8% between two readers for detection of erosions compared with ldDECT.

Inter-reader reliability was higher for MRI detected BME and erosions compared with DECT (Table 2).

Amongst patients who were diagnosed by a rheumatologist as having axSpA (n=27), 21 had sacroiliitis seen on both CT and MRI, 2 only on CT, 1 only on MRI, and 3 on neither.

Conclusion: ldDECT displayed a reduced sensitivity but was highly specific for BME compared to MRI STIR sequence as a reference standard. MRI revealed reasonable sensitivity and specificity for erosions compared to ldDECT as a reference standard. ldDECT has good reproducibility for the interpretation of erosions but has moderate inter-reader reliability for BME.

Amongst patients where BME was detected, 86% had evidence of erosive changes suggesting a marginal benefit with addition of dual energy scanning. Only 1 patient eventually diagnosed with axSpA had sacroiliitis on MRI not seen on ldDECT. Given the potential lower cost and accessibility of ldDECT, further studies may reveal whether utilizing ldDECT as the initial imaging modality would reduce the need for an MRI and thus increase accessibility and reduce costs.

Disclosure: J. Chan, Pfizer, 5, Abbvie, 5, UCB, 2, 5, Novartis, 2, 5, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sandoz, 2, Roche, 2, Gilead, 2, Merck, 2, Fresenius Kabi, 2; **S. Nicolaou**, Siemens, 12, UBC has a master reserach agreement with Siemens; **Y. Yan**, None; **M. Osman**, None; **H. Ouellette**, None; **S. Jalal**, None.

Abstract Number: 0902

Does Imaging of the Sacroiliac Joint and Spine Differ in Patients Presenting with Undiagnosed Back Pain and Psoriasis, Acute Anterior Uveitis, and Colitis: An Inception Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Diagnosis and classification of axial spondyloarthritis (axSpA) relies considerably on imaging evidence of sacroiliitis which has led to the development of classification criteria which also rely on imaging. However, it has been suggested that such criteria may not be appropriate for axSpA patients presenting with other forms of

Imaging Feature	Colitis (n=30)	Psoriasis (n=19)	Iritis (n=52)	P value
Unilateral sacroiliitis (grade ≥2), N(%)	1 (3.3%)	0 (0%)	2 (3.8%)	0.69
mNY criteria +, N(%)	5 (16.7%)	6 (31.2%)	15 (28.8%)	0.39
Grade of sacroiliitis, mean(SD)	1.8 (2.2)	2.1 (2.7)	2.2 (2.4)	0.76
MRI of Sacroiliac Joints (n=101)				
MRI indicative of axSpA, N(%)	15 (50.0%)	11 (57.9%)	32 (61.5%)	0.60
MRI indicative of axSpA (confidence ≥5/10), N(%)	14 (46.7%)	10 (52.6%)	30 (57.7%)	0.63
MRI active lesion typical of axSpA, N(%)	6 (20.0%)	6 (31.6%)	18 (34.6%)	0.37
MRI structural lesion typical of axSpA, N(%)	11 (36.7%)	7 (36.8%)	18 (34.6%)	0.98
MRI with unilateral lesion (any)	2 (6.7%)	3 (15.8%)	11 (21.2%)	0.22
MRI with unilateral lesion (BME)	1 (3.3%)	2 (10.5%)	5 (9.6%)	0.54
MRI with unilateral lesion (Erosion)	0 (0%)	0 (0%)	3 (5.8%)	0.23
MRI with unilateral lesion (Sclerosis)	1 (3.3%)	1 (5.3%)	3 (5.8%)	0.89
MRI with unilateral lesion (Fat)	0 (0%)	0 (0%)	0 (0%)	NA
MRI with iliac lesion	17 (56.7%)	12 (63.2%)	32 (61.5%)	0.88
MRI with sacral lesion	12 (40.0%)	11 (57.9%)	31 (59.6%)	0.21
MRI of Spine (41 of 101 patients also had spine MRI)				
	Colitis (n=14)	Psoriasis (n=9)	Iritis (n=18)	P value
MRI indicative of axSpA, N(%)	3 (21.4%)	2 (22.2%)	9 (50.0%)	0.17
MRI indicative of axSpA (confidence ≥5/10), N(%)	3 (21.4%)	2 (22.2%)	4 (22.2%)	1.0
MRI indicative of axSpA only in spine and not SIJ, N(%)	0	0	0	NA
Any active lesion in spine but not SIJ, N(%)	2 (14.3%)	1 (11.1%)	2 (11.1%)	0.96
Any structural lesion in spine but not SIJ, N(%)	1 (7.1%)	1 (11.1%)	0	NA
No(%) with ≥1 vertebral corner BME lesion	6 (42.9%)	5 (55.6%)	8 (44.4%)	0.82
No(%) with ≥4 vertebral corner BME lesions	3 (21.4%)	1 (11.1%)	4 (22.2%)	0.77
No(%) with ≥5 vertebral corner fat lesions	0	1 (11.1%)	2 (11.1%)	NA

SpA, especially psoriatic, because imaging features may vary in frequency and/or may be atypical. This hypothesis has never been tested in a prospective inception cohort of patients presenting with undiagnosed back pain. We aimed to compare the spectrum of radiographic and MRI abnormalities in the sacroiliac joint (SIJ) and spine of an inception cohort of patients presenting with undiagnosed back pain and psoriasis, iritis, and colitis.

Methods: We used data from the prospective multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study, which is aimed at early detection of axial SpA in patients referred by the respective specialist after first presenting with these disorders. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or colitis undergo routine clinical evaluation by a rheumatologist for axial SpA followed by imaging. In SASPIC I, MRI evaluation of the SIJ and whole spine was ordered per rheumatologist decision. In SASPIC II, MRI evaluation of the SIJ was ordered for all patients. Radiographs and MRI scans were assessed by two central readers and comparisons of the three groups were based on concordant assessments of imaging features. Evaluation of MRI scans included both global assessment for presence/absence of axSpA with confidence scale (-10 to +10), active and structural lesions typical of axSpA per recent ASAS definitions, and granular assessment of individual lesions according to SIJ quadrants and halves in consecutive semicoronal slices through the SIJ as well as detailed evaluation of active and structural lesions in individual discovertebral units of the spine on consecutive sagittal slices. Groups were compared by ANOVA and the chi-square test.

Results: A total of 240 patients were recruited, 143 from SASPIC I and 97 from SASPIC II, 101 (42.1%) being diagnosed with axSpA (65.3% male, mean age 34.4 years, mean symptom duration 8.7 years, B27 positive 55.4%). Mean age of colitis (N=101), psoriasis (N=61), iritis (N=78) patients were 33.4, 36.6, 34.3 years, respectively, mean symptom duration was 6.8, 7.2, 9.4 years, respectively, and % males were 45.5%, 52.5%, 51.3%, respectively. MRI scans of the SIJ were available in 101 patients and of these 41 also had MRI of the spine. There were no significant group differences for unilateral versus bilateral radiographic sacroiliitis and no significant differences in the frequencies, type,

or distribution of MRI lesions in the SIJ and spine(Table). In particular, there was not a single case where there was an MRI indicative of axSpA in the spine that was not also evident in the SIJ.

Conclusion: Data from the SASPIC prospective inception cohort does not support the view that imaging of the SIJ and spine differs in psoriatic axSpA, which appears similar to axSpA associated with iritis or colitis. These data support the umbrella concept of axSpA.

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **U. Weber**, None; **J. Chan**, Pfizer, 5, Abbvie, 5, UCB, 2, 5, Novartis, 2, 5, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sandoz, 2, Roche, 2, Gilead, 2, Merck, 2, Fresenius Kabi, 2; **R. Carmona**, None; **J. Yeung**, None; **S. Aydin**, Abbvie, 6, Celgene, 6, UCB, 6, Novartis, 6, Jannsen, 6, Pfizer, 6, Sanofi, 6; **J. Reis**, None; **L. Martin**, None; **A. Masetto**, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Amgen, 5, Merck, 5, Teva, 5; **O. Ziouzina**, None; **D. Mosher**, None; **S. Keeling**, AbbVie, 1, 6, Amgen, 2, Pfizer, 2, 5, AstraZeneca, 2, UCB, 2, 6, Janssen, 2, 6, Sandoz, 2, 5, 6, Merck, 2, 5, GSK, 2, FresniusKabi, 2, Eli Lilly, 2, Novartis, 2; **S. Rohekar**, None; **R. Dadashova**, None; **J. Paschke**, None; **A. Carapellucci**, None; **R. Lambert**, Pfizer, 2.

Abstract Number: 0903

Scoring MRI Structural Lesions in Sacroiliac Joints of Patients with Axial Spondyloarthritis: How Many Slices Are Optimal?

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: There is no international consensus on the optimal number of slices for evaluation of MRI structural lesions in the SIJ. An "all slice" method evaluates lesions from the most anterior slice, defined as the first slice with vertical height of ≥1cm of the SIJ joint cavity, up to the most posterior slice, defined as the most posterior slice where ≥1cm vertical height of the cartilaginous portion is still visible. The SPARCC method scores the transitional slice between cartilaginous and ligamentous compartments as the first slice and then an additional 4 slices anterior to the transitional slice. We aimed to investigate inter-reader reliability, the extent of detection of lesions, and frequency of cases with a positive MRI for structural lesions when using an "all slice" approach versus the SPARCC scoring of 5 central slices.

Table 1.

MRI Lesion	"All slice"	Central 5 slices	Peripheral slices	P value central vs peripheral slices	P value "all slice" vs central slices
Mean (SD) Lesion Score Per Case					
Erosion	2.4 (4.5) (0-22.9)	1.8(3.4) (0-17.1)	0.6 (1.4) (0-10.1)	<0.001	< 0.001
Fat lesion	2.5 (5.9) (0-34.0)	1.8 (4.5) (0-25.1)	0.7 (1.8) (0-9.9)	< 0.001	<0.001
Sclerosis	2.0 (4.9) (0-39.0)	1.5 (3.6) (0-26.1)	0.5 (1.5) (0-12.9)	< 0.0001	0.0003
Backfill	0.5 (1.5) (0-12)	0.4 (1.2) (0.0-9.3)	0.1 (0.4) (0-2.7)	< 0.0001	0.84
Ankylosis	0.5 (3.4) (0-30.7)	0.3 (2.3) (0-20.0)	0.2 (1.2) (0-11.3)	0.10	0.18
Mean (SD) (Range) % of Total Lesion Score in Central vs Peripheral slices					
% of total erosion score (mean (SD) (range)) n=73 where erosion is present	100%	76.4% (28.9%) (0-100%)	23.6% (28.9%) (0-100%)	<0.001	
% of total fat lesion score (mean (SD) (range)) n=58 where fat lesion is present	100%	75.4% (26.5%) (0-100%)	24.6% (26.5%) (0-100%)	<0.001	
% of total sclerosis score (mean (SD) (range)) n=74 where sclerosis is present	100%	79.5% (22.9%) (0-100%)	20.5% (22.9%) (0-100%)	<0.001	
% of total backfill score (mean (SD) (range)) n=30 where backfill is present	100%	86.0% (20.2%) (0-100%)	14.0% (20.2%) (0-100%)	<0.001	
% of total ankylosis score (mean (SD) (range)) n=15 where ankylosis is present	100%	59.0% (36.4%) (0-100%)	41.0% (36.4%) (0-100%)	0.56	

Table 2 ICC of 7 readers Mean (SD) (Range)

	All slices	Central 5 slices	Peripheral slices
Erosion	0.54 (0.15) (0.28-0.84)	0.58 (0.13) (0.34-0.85)	0.40 (0.17) (0.10-0.66)
Fat lesion	0.61 (0.18) (0.30-0.89)	0.63 (0.16) (0.35-0.88)	0.52 (0.20) (0.19-0.82)
Sclerosis	0.73 (0.18) (0.36-0.94)	0.73 (0.16) (0.36-0.91)	0.67 (0.19) (0.27-0.94)
Backfill	0.37 (0.21) (0.10-0.85)	0.39 (0.19) (0.14-0.83)	0.18 (0.23) (0.0-0.80)
Ankylosis	0.97 (0.02) (0.91-0.99)	0.99 (0.01) (0.97-1.0)	0.85 (0.10) (0.62-0.98)

Methods: MRI T1W images with DICOM series were available from 148 cases who had MRI performed in the ASAS-Classification Cohort. Seven central readers recorded MRI lesions in an eCRF that recorded global assessments of presence/absence of changes suggestive of axSpA and structural lesions typical of axSpA. Structural lesions per the ASAS definitions were also recorded in consecutive semicoronal slices using the "all slice" approach, but also recording the transitional slice, according to their presence/absence in SIJ quadrants (erosion, fat lesion, sclerosis) or halves (backfill, ankylosis). Structural lesion frequencies were assessed descriptively according to majority agreement (≥4/7) of central readers and also any 2 central readers. Reliability for detection of MRI lesions was compared between central and local readers using the ICC.

Results: The mean (SD) (range) number of anterior and posterior slices peripheral to the 5 central slices was 1.0 (1.0) (0-4) and 2.2 (1.8) (0-6) per case, respectively. There were 2 cases (1.4%) where ≥2 readers scored structural lesions in peripheral slices but not in the 5 central slices. The mean percentage of the total structural lesion score that was captured by the 5 central slices was >75% for all types of lesions except ankylosis (59%) (Table 1). Inter-reader reliability was greater for all lesions when assessing the 5 central slices and especially for erosion and backfill (Table 2).

Conclusion: The major component of structural lesion data is captured by assessment of 5 slices, which includes the transitional slice and the subsequent 4 anterior slices. Moreover, reliability for detection of structural lesions is substantially worse in peripheral slices.

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **U. Weber**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **S. Pedersen**, None; **J. Sieper**, AbbVie, 2, 5, 6, Merck, 2, 5, 6, Pfizer, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6, Roche, 2, 6; **S. Wichuk**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **M. Rudwaleit**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, UCB Pharma, 2, AbbVie, 6, Eli Lilly, 6, Novartis, 6, Novartis, 2, UCB Pharma, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **J. Paschke**, None; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **R. Lambert**, Pfizer, 2.

Abstract Number: 0904

Data-driven Definitions Based on Inflammatory Lesions for a Positive MRI of the Spine Consistent with Axial Spondyloarthritis

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SESSION INFORMATION

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Background/Purpose: The ASAS definition of a positive MRI for inflammation in the spine (ASAS-MRI+) is intended for classification of patients as having axSpA but is often misused for diagnostic purposes. This is problematic because bone marrow edema (BME) in the spine may occur in 20-40% of both healthy individuals as well as those with mechanical back disorders. The ASAS MRI group has generated updated consensus lesion definitions that describe each of the MRI lesions in the spine. These definitions have been validated by 8 readers from the ASAS-MRI group on MRI spine images from the ASAS Classification Cohort. We aimed to identify quantitative cut-offs based on numbers of vertebral corners that define a positive MRI for axSpA, there being two gold standards: A. majority central reader decision as to the presence of spine MRI findings consistent with axSpA B. rheumatologist expert opinion diagnosis of axSpA

Methods: Eight ASAS-MRI readers recorded MRI lesions in the spine of 62 cases recruited to the ASAS classification cohort according to recently updated ASAS definitions in an eCRF that comprises global assessment (are the findings on this MRI scan consistent with axSpA? (yes/no)), and detailed scoring of lesions for all sites in the spine, including vertebral bodies, lateral and posterior elements. We calculated sensitivity and specificity for numbers of vertebral corners with BME (VC-BME) where a majority of readers (≥5/8) agreed as to the presence of MRI findings consistent with axSpA. We selected optimal cut-offs with ≥95% specificity. These cut-offs were analyzed for their predictive utility for rheumatologist diagnosis of axSpA by calculating positive and negative predictive values (PPV, NPV) and selecting those cut-offs with PPV of ≥95%. Both specificity of ≥95% for MRI consistent with axSpA as well

Table 1. Majority readers agree MRI findings consistent with axSpA are present is the gold-standard external reference

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)
BME in ≥1 vertebral corner	87.5(47.3 - 99.7)	83.3 (70.7 - 92.1)
BME in ≥2 vertebral corners	87.5 (47.3 - 99.7)	87.0 (75.1 - 94.6)
BME in ≥ 3 vertebral corners	87.5 (47.3 - 99.7)	94.4 (84.6 - 98.8)
BME in ≥4 vertebral corners	**75.0 (34.9 - 96.8)**	**98.2 (90.1 - 100.0)**
BME in ≥5 vertebral corners	62.5 (24.5 - 91.5)	98.2 (90.1 - 100.0)
Cases with ≥1 additional non-corner site inflammatory lesion		
BME in ≥1 vertebral corner	37.5 (8.5 - 75.5)	94.4 (84.6 - 98.8)
BME in ≥2 vertebral corners	37.5 (8.5 - 75.5)	94.4 (84.6 - 98.8)
BME in ≥3 vertebral corners	**37.5 (8.5 - 75.5)**	**98.2 (90.1-100.0)**
BME in ≥4 vertebral corners	37.5 (8.5 - 75.5)	100.0 (93.4-100.0)
BME in ≥5 vertebral corners	37.5 (8.5 - 75.5)	100.0 (93.4-100.0)
Cases with ≥2 vertebral corner fat lesions		
BME in ≥1 vertebral corner	**62.5 (24.5 - 91.5)**	**100.0 (93.4-100.0)**
BME in ≥2 vertebral corners	62.5 (24.5 - 91.5)	100.0 (93.4-100.0)
BME in ≥ 3 vertebral corners	50.0 (15.7 - 84.3)	100.0 (93.4-100.0)
BME in ≥4 vertebral corners	50.0 (15.7 - 84.3)	100.0 (93.4-100.0)
BME in ≥5 vertebral corners	37.5 (8.5 - 75.5)	100.0 (93.4 -100.0)

Table 2. Predictive values of cut-offs for number of vertebral corners with BME according to the diagnostic ascertainment of the rheumatologist

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV
MRI findings consistent with axSpA ≥any 2 readers	52.5 (36.1 - 68.5)	94.7 (74.0 - 99.9)	95.5 (75.3 - 99.3)	48.6 (40.2 - 57.2)
MRI findings consistent with axSpA ≥majority read	20.0 (9.1 - 35.6)	100.0 (82.4 - 100.0)	100.0	37.3 (33.7 - 40.9)
BME in ≥ 4 vertebral corners	**17.5 (7.3 - 32.8**	**100.0 (82.4 - 100.0)**	**100.0**	**36.5 (33.3 - 39.9)**
Cases with ≥1 additional inflammatory lesion				
BME in ≥ 3 vertebral corners	**10.00 (2.8 - 23.7)**	**100.00 (82.4 - 100.0)**	**100.0**	**34.5 (32.2 - 36.9)**
Cases with ≥2 vertebral corner fat lesions				
BME in ≥1 vertebral corner	**12.50 (4.2 - 26.8)**	**100.00 (82.4 - 100.0)**	**100.0**	**35.2 (32.6 - 37.9)**

as a PPV of ≥95% for rheumatologist diagnosis were considered requirements for preliminary designation of MRI cut-offs defining a positive spine MRI consistent with axSpA.

Results: MRI findings consistent with axSpA were observed in the spine by majority read in 8 (20%) of 40 cases diagnosed with axSpA, and 0 (0%) of 19 cases without axSpA. Cut-offs achieving specificity of ≥95% for MRI findings consistent with axSpA were 4 VC-BME (sensitivity 75%) for all cases, 3 VC-BME (sensitivity 37.5%) for cases with ≥1 additional location with inflammation, 1 VC-BME (sensitivity 62.5%) in cases with ≥2 vertebral corner fat lesions (Table 1). All of the above cut-offs also had very high positive predictive values (≥95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist (Table 2).

Conclusion: A cut-off of BME in ≥4 vertebral corners, or ≥3 corners in the setting of additional inflammatory lesions at other locations or corner fat, are primary candidates for defining a positive MRI of the spine consistent with axSpA. The PPV performance of these MRI cut-offs for rheumatologist diagnosis of axSpA apply to typical patients referred to a rheumatologist with a high index of suspicion of axSpA and may not be appropriate in other populations.

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **R. Lambert**, Pfizer, 2; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **S. Pedersen**, None; **I. Eshed**, Novartis, 6, Abbvie, 6; **U. Weber**, None; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **M. de Hooge**, None; **J. Sieper**, AbbVie, 2, 5, 6, Merck, 2, 5, 6, Pfizer, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6, Roche, 2, 6; **S. Wichuk**, None; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **M. Rudwaleit**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, UCB Pharma, 2, AbbVie, 6, Eli Lilly, 6, Novartis, 6, Novartis, 2, UCB Pharma, 6; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6.

Abstract Number: 0905

Artificial Neural Network for the Recognition of Active Inflammatory Changes Compatible with Axial Spondyloarthritis on Magnetic Resonance Imaging of Sacroiliac Joints

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SESSION INFORMATION

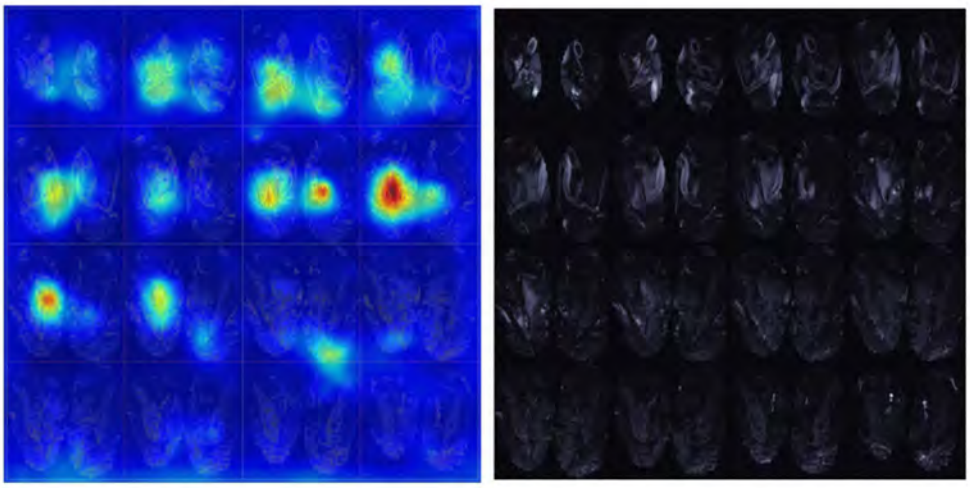
Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Figure 1. Inference of the convolutional neural network on a pre-processed 2D grid of an MRI of sacroiliac joints from the validation dataset.



This exemplary gradient-weighted class activation map (left panel) shows that the CNN correctly focusses on the periarticular bone marrow edema that is evident on a preprocessed 2D grid image of an exemplary STIR sequence (right panel).

Background/Purpose: Active inflammatory changes in sacroiliac joints (SIJ) compatible with axial spondyloarthritis - axSpA (first of all, subchondral bone marrow edema – BME / osteitis) as detected by magnetic resonance imaging (MRI) play a pivotal role in diagnostic and classification approaches. Artificial intelligence/machine learning methods such as a trained artificial convolutional network (CNN) offer a potential for the development of assistant tools to be used by radiologists and rheumatologists in clinical practice.

The present study is aimed to evaluate the possibility of detection of active inflammatory changes compatible with axSpA on MRI of SIJ.

Methods: A total of 6 trained and calibrated readers evaluated MRIs of SIJ (STIR, semicoronal views) of 476 patients with and without axSpA from 4 cohorts (GESPIC-AS, GESPIC-Crohn, GESPIC-Uveitis, and OptiRef). Readers indicated the presence or absence of active inflammatory changes compatible with axSpA and specified the type of changes. Active inflammatory changes were considered present if at least 4 out of 6 readers deemed them positive. Images with an undetermined classification were adjudicated in a consensus reading session. These results were used for the training and validation of the CNN. First, we used an object detection approach to train a 3D CNN to detect the SIJ on all available MRIs to generate dilated masks of the SIJs to focus subsequent model training to the SIJs and periarticular areas. Secondly, we used a classification task to train a 2D CNN (ResNet34) to predict the presence of active inflammatory changes compatible with SpA on these grid MRI images. MRIs from the ASAS classification Cohort annotated by 7 readers (Maksymowych WP, at al. Ann Rheum Dis 2020;79:935-942) formed the holdout dataset that was used to test for CNN generalizability.

Results: A total of 403 STIR-MRIs were included in the training, 73 in the validation sets and 122 in the holdout set. The trained classification CNN achieved an accuracy of 91.8%, a sensitivity of 88.9% and a specificity of 93.5% in detecting active inflammatory changes in SIJ compatible with axSpA in the validation set (n=73). The accuracy of MRI classification in the independent holdout set (ASAS) was 81.5% with a sensitivity of 67% and a specificity of 84.5%. Figure 1 shows an exemplary class activation map of the CNN.

Conclusion: Our study shows the principal possibility of detecting active inflammatory changes compatible with axSpA on MRI of SIJs. Detection of structural changes and overall contextual interpretation of the findings are warranted for the subsequent development steps.

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Abstract Number: 0906

Measurement of Vertebral Hounsfield Units in Low Dose Computed Tomography – a Reliable Methodology for Assessing Bone Mineral Density at the Vertebral Level in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Bone loss paradoxically coexists with bone formation in radiographic axial spondyloarthritis (r-axSpA). Assessing bone mineral density (BMD) in r-axSpA poses challenges, namely because of possible overestimation due to ectopic bone formation. The measurement of Computed Tomography (CT) Hounsfield Units (HU) at the individual vertebral level has been shown to correlate with BMD as measured by Dual-energy X-ray absorptiometry in trauma patients.[1] However, its value in r-axSpA has never been studied. Whole spine low dose CT (ldCT) has been suggested as the ideal method to assess both bone formation and bone loss in r-axSpA. By using ldCT scans, we aimed to cross-sectionally describe HU measurements and their inter-reader reliability at the vertebral level from C3 to L5 in patients with r-axSpA.

Methods: We used ldCT scans of r-axSpA patients included in the Sensitive Imaging in Ankylosing Spondylitis (SIAS) study, a multicenter (Leiden, the Netherlands and Herne, Germany) 2-year prospective cohort. A standardized protocol was applied in both centers and automatic exposure control calibration in ldCT imaging acquisition was used. For the present study, baseline ldCT scans were independently assessed by two trained readers. The HU measurement was performed as described in *Figure 1* – using OsiriX software (v6.5.1). Inter-reader reliability was assessed using intraclass correlation coefficients (ICC) absolute agreement, applying two-way mixed effect models. Agreement was assessed using the smallest detectable difference (SDD = 1.96 x $SD_{difference}$ /(√k), in which $SD_{difference}$ is the standard deviation of the differences in status scores between two readers, and k=2 (number of readers) and Bland-Altman plots.

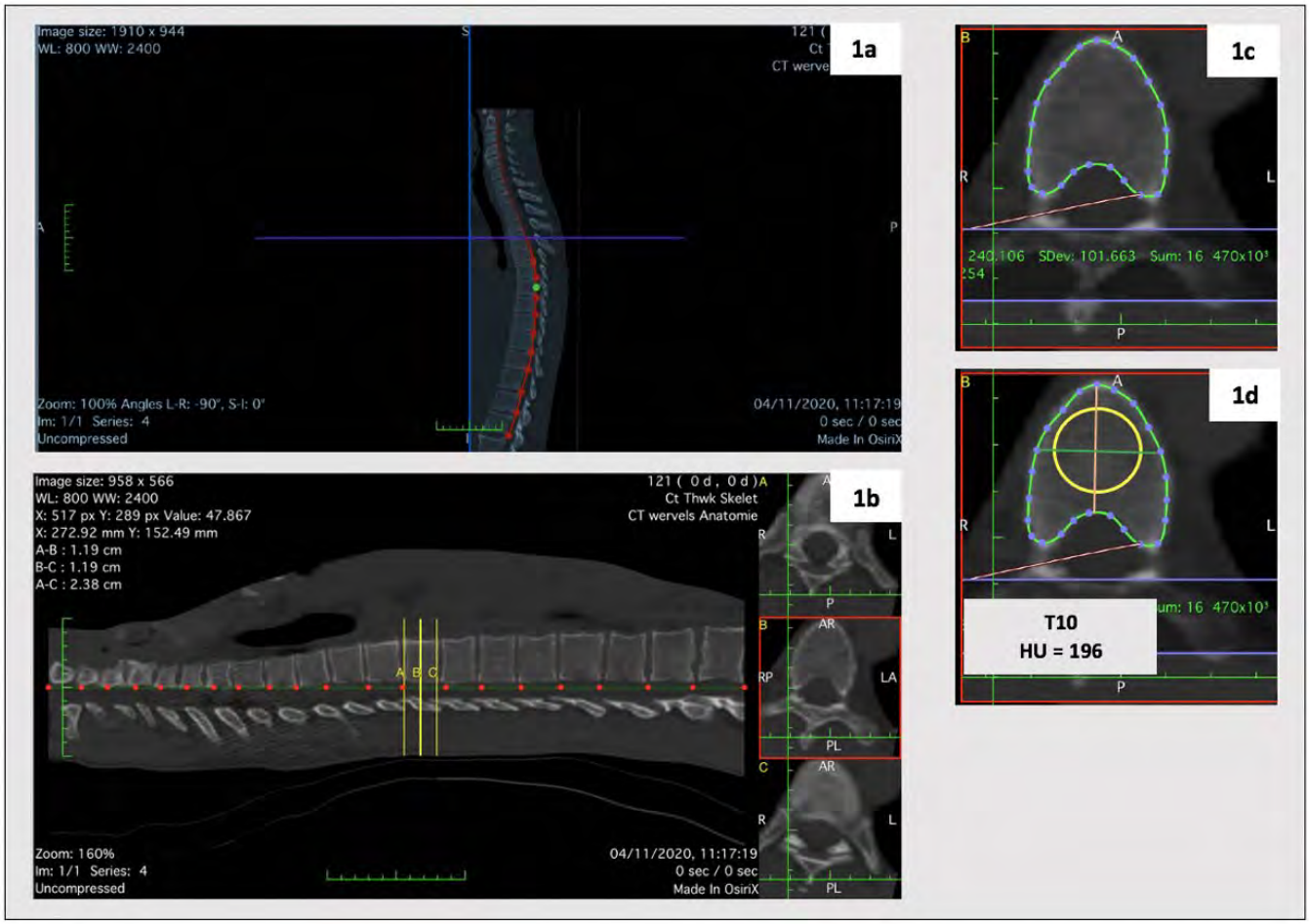

Figure 1. Methodology of Hounsfield Units (HU) measurement. Using a three-dimensional curved-multiplanar reconstruction (3D Curved-MPR) we identify the curve of the spine from the spinal canal (1a). On the obtained sagittal image, the individual vertebral levels are identified. At each vertebral level, two lines of reference are positioned at the superior (yellow line A) and inferior (yellow line C) limits of the vertebra. Equidistant to A and C, the yellow line B will be positioned at the center of the vertebral body (1b). Vertebral HU measurements are taken from a reconstructed cross-sectional slice positioned at the center of the vertebra as defined by the selection process described above (1c). A circular sample region of this slice is used, centered at the body origin and having a diameter equal to 75% of the average of distances posteroinferior-to-anteroinferior, and posterosuperior-to-anterosuperior. The density of the vertebra is calculated as the average image intensity within the sample region, reported in HU (1d).

Results: Whole spine ldCT scans from 50 r-axSpA patients (mean (SD) age of 49 (10) years; 43 (86%) male and 42 (84%) HLA-B27 positive) were included. In total, 220 cervical, 588 thoracic and 245 lumbar vertebrae were assessed by both readers. The HU values decreased from the cervical to the lumbar spine – *Table 1*. For both readers, the highest mean (SD) value for HU was obtained at C3 (354 (106) and 355(108), for reader 1 and 2 respectively), and the lowest at L3 (153 (65) and 150 (65), for reader 1 and 2 respectively). Inter-reader reliability was shown to be excellent (cervical spine ICC: 0.90 to 1.00; thoracic spine ICC: 0.97 to 1.00; lumbar spine ICC: 0.89 to 0.91). SDD varied from 4 to 8. A small degree of systematic error was observed between the two readers, i.e., for the majority of vertebrae, reader 1 scored somewhat higher than reader 2 (mean difference of scores ranging from -0.6 HU to 2.9 HU). Bland-Altman plots show homoscedasticity throughout the whole spine. Representative examples from vertebrae of each segment of the spine are presented in *Figure 2*.

Conclusion: Low dose CT measurement of HU is a reliable method to assess BMD at each vertebra from C3 to L5. This methodology can aid the future study of bone loss in r-axSpA, a disease affecting the whole spine. Further validation and longitudinal assessment of reliability are warranted in future studies.

Table 1. Descriptive statistics of Hounsfield Units (HU) per vertebral level, according to reader 1 and 2 measurements

Vertebra§	Mean (SD) HU Reader 1	Range HU Reader 1	Mean (SD) HU Reader 2	Range HU Reader 2
C3	354 (106)	162 to 643	355 (108)	158 to 647
C4	350 (113)	119 to 661	350 (113)	122 to 668
C5	333 (109)	83 to 601	333 (109)	88 to 605
C6	290 (88)	82 to 481	289 (88)	83 to 479
C7	271 (83)	79 to 447	270 (82)	81 to 440
T1	229 (86)	69 to 431	224 (87)	67 to 426
T2	246 (59)	55 to 382	240 (58)	57 to 384
T3	230 (71)	88 to 402	223 (69)	90 to 407
T4	222 (69)	41 to 333	210 (66)	43 to 335
T5	208 (56)	59 to 369	204 (57)	53 to 362
T6	205 (63)	31 to 319	194 (63)	32 to 312
T7	198 (78)	-9 to 353	187 (74)	-10 to 359
T8	185 (68)	7 to 299	177 (65)	3 to 306
T9	194 (72)	-15 to 307	181 (69)	-17 to 304
T10	194 (73)	18 to 375	181 (71)	23 to 372
T11	176 (60)	29 to 305	168 (60)	30 to 302
T12	177 (62)	28 to 367	166 (58)	23 to 372
L1	165 (55)	11 to 325	162 (54)	6 to 317
L2	158 (51)	-13 to 258	153 (51)	-9 to 253
L3	154 (65)	-37 to 345	150 (65)	-34 to 346
L4	163 (84)	-35 to 459	156 (82)	-37 to 461
L5	159 (65)	-12 to 292	158 (63)	-8 to 286

§ Cervical spine values are based on a total of 44 vertebrae scored at each level (C3 to C7) by both readers. The values for thoracic and lumbar spine are based on a total of 50 and 49 vertebrae scored at each level (T1 to L5) by reader 1 and 2 respectively.

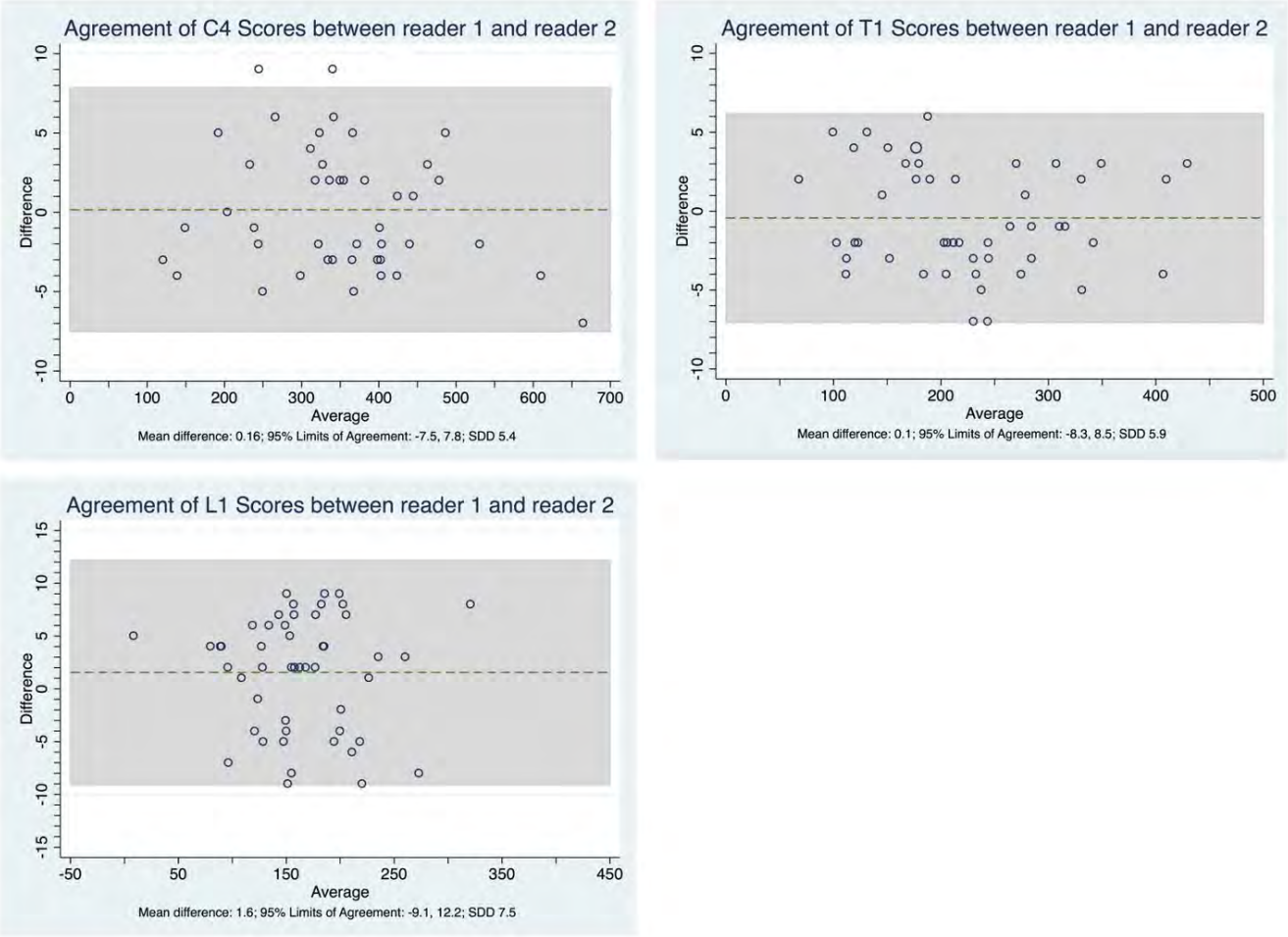

Figure 2. Bland-Altman plots for representative examples from vertebrae of each segment of the spine: C4, T1, and L1. The scatter of differences is homoscedastic.

[1]Shaun P. Patel, et al. J Clin Exp Orthop. 2016;2(1:14):1–7.

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Abstract Number: 0907

Radiographic Sacroiliitis Progression up to Six Years of Follow-Up in Patients with Non-Radiographic Axial Apondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster II: Imaging in Spondyloarthritis (0897–0907)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: In two years, approximately 10% of patients with non-radiographic axial spondyloarthritis (nr-axSpA) progresses to ankylosing spondylitis (AS). There are no data available of more long-term follow-up. The objective of this study was to assess the rate of progression of nr-axSpA to AS in patients with up to six years of follow-up.

Methods: Patients enrolled in the ongoing Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort, classified as nr-axSpA at baseline with a baseline pelvic radiograph and at least one two-year follow-up radiograph, were selected for our analyses. These baseline, two-, four- and six-year radiographs were randomized with radiographs of AS patients in a three-to-one ratio and scored with known time sequence according to the modified New York (mNY) criteria by two trained readers (SK and RW). In case of discrepancy in classification, the score of a third independent reader (AS) was used. Progression to AS was defined as progression in mNY sacroiliitis score to ≥2 bilaterally or ≥3 unilaterally.

Table 1. Patients classified with nr-axSpA progressing to AS according to mNY-criteria for radiographic sacroiliitis, evaluated with two-year intervals.

Population	Size	nr-axSpA	AS	Follow-up data not yet available
Baseline	79	79	N/A	N/A
+2 years	79	71	8	N/A
+4 years	48	44	4	23
+6 years	24	21	3	20

Results: 79 patients were clinically classified as nr-axSpA at baseline confirmed by radiographic score. At baseline, mean age was 39 ± 10 years, 48% was male, median symptom duration was 6 (IQR 3-17) years, mean ASDAS was 2.8 ± 1.1, and 71% was HLA-B27+. After two, four and six years, 8/79 (10.1%), 4/48 (8.3%) and 3/24 (12.5%) nr-axSpA patients progressed to AS. In total, 23 and 20 patients did not yet reach follow at four and six years, respectively (Table 1).

Conclusion: In our observational cohort of patients with axial spondyloarthritis with up to six years of follow-up, every two years approximately 10% of patients progressed from nr-axSpA to AS. The next step will be to evaluate associations with patient and disease characteristics.

Disclosure: S. Kieskamp, Novartis, 5; **R. Wilbrink**, None; **F. Wink**, Janssen-Cilag, 6, Novartis, 5; **R. Bos**, None; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2; **S. Arends**, None; **A. Spoorenberg**, Novartis, 5, Abbvie, 2, Novartis, 2, Pfizer, 2, MSD, 2, UCB, 2, 5.

Abstract Number: 0908

Evaluation of the Nonsteroidal Anti-Inflammatory Drug-Sparing Effect of Secukinumab in Patients with Ankylosing Spondylitis: Multicenter, Randomised, Double-blind, Phase IV Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Nonsteroidal anti-inflammatory drugs (NSAIDs) are used to treat inflammatory back pain in patients (pts) with ankylosing spondylitis (AS). However, an increased risk of side effects associated with NSAIDs and their dosage has been reported[1]. Therefore, lower doses and a dose reduction is desirable. The objective of this study is to evaluate the short-term NSAID sparing effect of secukinumab (SEC) in AS pts with NSAID intake.

Methods: In a prospective controlled trial, 211 adult pts with active AS Bath Ankylosing Spondylitis Disease Activity Index (BASDAI ≥4) and an inadequate response (IR) to at least 2 NSAIDs at the highest recommended/tolerated dose and pts with an IR, or those who were naïve/intolerant to a maximum of 2 tumor necrosis factor inhibitors (TNFi) were enrolled. NSAID intake was evaluated using the Assessment in Ankylosing Spondylitis (ASAS)-NSAID score. To be eligible, pts had to take at least 50% of the highest recommended/tolerated NSAID dose regularly. Pts were randomised (1:1:1) to receive SEC 150 mg s.c. from Week (Wk) 0 (group [gp] 1), Wk 4 (gp 2) and Wk 16 (gp 3). All groups received SEC 150 mg from Wk 16. NSAID tapering was allowed in all groups from Wk 4 onwards. The primary endpoint (PE) was an ASAS20 response of pooled gp 1 and gp 2 *vs*. gp 3 at Wk 12.

Results: There were 71 pts in gp 1, 70 in gp 2 and 70 in gp 3. Baseline (BL) characteristics were comparable across groups; mean age (SD) was 45.2 (12.3) years (yrs), time since diagnosis was 7.4 (9.8) yrs, 57.8% male, 79.0% human

Table. Effect of SEC 150 mg s.c. in AS pts (Intention-to-Treat-population) at Wk 16				
(%), unless otherwise specified		**Group 1 (N=71)** (SEC 150 mg from BL until Wk 20)	**Group 2 (N=70)** (PBO from BL until Wk 4; SEC 150 mg from Wk 4)	**Group 3 (N=70)** (PBO from BL until Wk 16; SEC 150 mg from Wk 16)
ASAS20*		56.3	50.0	41.4
ASAS40*		43.7§	32.9	21.4
ASAS5/6*		39.4‡	32.9	21.4
ASAS-PR*		8.5	20.0‡	5.7
ASAS20	TNF-IR‡*	60.0‡‡	26.3	45.0
	TNF-naïve‡‡*	54.9	58.8‡	40.0
ASAS40	TNF-IR‡*	45.0	15.8	25.0
	TNF-naïve‡‡*	43.1‡	39.2‡	20.0
ASDAS-CRP change (mean±SD)**		-1.2±0.9§	-1.0±0.9‡	-0.7±0.8
BASDAI change (mean±SD)***		-2.3±1.9‡	-2.0±2.0	-1.7±2.0
BASDAI50+		32.4	28.6	22.9
ASAS-NSAID score change (mean±SD)++		-51.5±46.2‡	-42.5±68.6	-33.7±38.8
ASAS-NSAID score	decrease ≥50%*	64.8‡	58.6	42.9
	<10*	52.1§	45.7‡	28.6
	=0*	32.4‡	38.6§	17.1

AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis International Society; ASDAS, AS Disease Activity score; BASDAI, Bath AS Disease Activity Index; BL, baseline; CRP, C-reactive protein; IR, inadequate responder; NSAID, non-steroidal anti-inflammatory drug; N, total number of subjects in each treatment group; PBO, placebo; PR, partial remission; pts, patients; SD, standard deviation; SEC, secukinumab; TNFi, tumor necrosis factor inhibitor; Wk, week.

†p<0.001; §p<0.01 and ‡p<0.05 *vs*. gp 3; ‡‡p<0.05 *vs*. gp 2

*p-values are from a logistic regression model with treatment, TNFi status (IR / naive) and CRP status (>/ ≤ central lab ULN) as factors. Missing values were imputed as non-response.

+p-values are from MMRM with treatment, TNFi status (IR / naive), CRP status (>/ ≤ central lab ULN) and visit as factors, BL value as continuous covariate. Missing values were imputed as non-response.

Observed data (pts) for gp 1, 2, 3, respectively:

**67, 66, 62

***67, 66, 63

++67, 67, 65

‡20, 19, 20

‡‡51, 51, 50

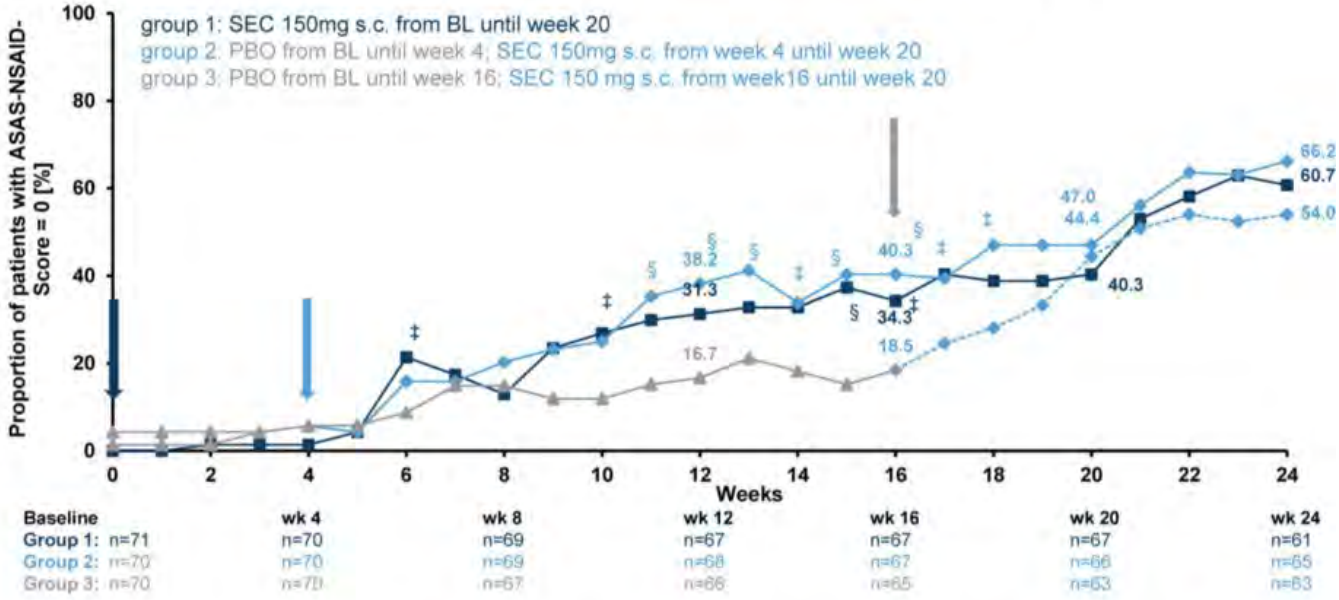
leukocyte antigen (HLA)-B27 positive 48.6% pts had an elevated C-reactive protein (CRP) 40.8% were current/ever smoker and 72.0% were TNFi-naïve. The ASAS-NSAID (SD) scores at BL were: gp 1 *vs*. gp 2 *vs*. gp 3: 82.9 (37.7) *vs*. 79.9 (45.3) *vs*.82.3 (39.1). BASDAI and Ankylosing Spondylitis Disease Activity Score (ASDAS)-CRP scores were similar between groups: 6.0 (1.4) *vs*. 6.2 (1.5) *vs*. 6.2 (1.3), and 3.4 (0.7) *vs*. 3.3 (0.8) *vs*. 3.4 (0.7), respectively. The ASAS20 response at Wk 12 of pooled gp 1 and 2 *vs*. gp 3 was 51.1% *vs*. 44.3% but the PE was not met (p=0.35). A higher proportion of pts in gp 1 and 2 achieved ASAS40 and BASDAI50 and other secondary outcomes at Wk 16 (**Table**). More pts in gp 1 and 2 reduced their NSAID intake from BL through Wk 16 *vs*. gp 3 **(Table and Figure)**.

Conclusion: In this population of pts with AS, SEC provided clinical improvements in conventional clinical outcomes and a short-term NSAID sparing effect.

References

1. Burmester G, et al. *Ann Rheum Dis*. 2011;70:818-822.

Figure: Proportion of patients reaching ASAS-NSAID score=0 through Week 24



ASAS, Assessment of SpondyloArthritis international Society; NSAID, non-steroidal-anti-inflammatory drug; N, total number of pts in each treatment group; n, number of observed pts; PBO, placebo; pts, patients; SEC, secukinumab; s.c., subcutaneous; Wk, week;

Data presented descriptively as observed through Wk 24;

As PE failed, statistical analysis is exploratory; p-values are from a logistic regression model with treatment, TNF inhibitor status (inadequate responder / naïve) and CRP status (> central lab ULN / ≤ lab ULN) as factors †p<0.001; §p<0.01 and ‡p<0.05 vs group 3; Arrows indicate first application of SEC in group 1, group 2 and group 3.

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **J. Brandt-Jrgens**, Abbvie, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, Novartis, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, UCB, 2, 6, BMS, 2, 6, Janssen, 2, 6, Medac, 2, 6; **U. Wagner**, Roche, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, BMS, 5; **S. Lieb**, Novartis, 3; **C. Sieder**, Novartis, 3; **C. Mann**, Novartis, 3; **J. Braun**, Abbvie, 2, 5, 6, Amgen, 2, 5, 6, Celltrion, 2, 5, 6, Chugai, 2, 5, 6, Medac, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, BMS, 2, 5, 6, Boehringer, 2, 5, 6, Celgene, 2, 5, 6, Centocor, 2, 5, 6, Mundipharma, 2, 5, 6, Sanofi-Aventis, 2, 5, 6, Eli Lilly, 2, 5, 6, EBEWE Pharma, 2, 6.

Abstract Number: 0909

How Does Gender Affect Secukinumab Treatment Outcomes and Retention Rates in Patients with Ankylosing Spondylitis? – Real World Data from a German Observational Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Current studies suggest that the phenotype of spondyloarthritis differs between genders and that this may influence the subsequent diagnostic approach and therapeutic decisions[1]. The German non-interventional study AQUILA provides real-world data on the influence of gender on therapeutic effectiveness and retention rate under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.

The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate secukinumab treatment outcomes on disease activity, depressive mood and retention rate depending on the gender of PsA patients.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including more than 3000 patients with active AS or psoriatic arthritis. Patients were observed from BL up to week (w) 52 according to clinical routine. Real-world data was assessed prospectively and analyzed as observed. Validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of SpondyloArthritis-Health Index, ASAS-HI) and severity of depressive mood (Beck´s Depression Inventory version II, BDI-II). Patient reported outcomes were reported using patient´s global assessment (PGA). In addition, retention rates (time from study inclusion until premature secukinumab treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on the subgroups of male and female AS patients.

Results: At BL, 683 AS patients were included: 59.7% (n=408) male and 40.3% (n=275) female. Demographic data (Table 1) of male and female AS patients differed numerically in the following parameters: proportion of obese patients, smokers, pretreatment with disease-modifying antirheumatic drugs (csDMARDs), and biologicals/biosimilars (b-bsDMARDs).Mean BASDAI and PGA were comparable between male and female AS patients over time (♂: 5.2 at BL to 3.8 at w52, ♀: 5.3 at BL to 4.1 at w52 and ♂: 5.9 at BL to 4.1 at w52, ♀: 5.6 at BL to 4.3 at w52, respectively). Mean ASAS-HI over time was higher in women; nevertheless, improvements in global functioning were comparable for both genders from BL to week 52 (Fig. 1A). Severity of depressive mood was numerically lower in male patients; nevertheless, BDI-II reductions were comparable across the genders (♂: 11.2 at BL to 10.0 at w52, ♀: 13.1 at BL to 11.0 at w52). Secukinumab treatment retention rate for men was (not significantly) higher than for women (Fig. 1B).

Conclusion: In a real-world setting, secukinumab improved disease activity, global functioning and severity of depressive mood in AS patients in both men and women. Women showed overall higher disease burden. Altogether, real-world data of this interim analysis are in line with those of Phase 3 studies and show that secukinumab is an effective treatment up to 52 weeks with high treatment retention rates, irrespective of gender.

Table 1. Overview of baseline characteristics in AS patients depending on gender

Demographics*	Male (N=408)	Female (N=275)
Age, years	45.6 (12.1)	47.8 (12.2)
BMI, kg/m²	27.4 (4.5)	27.6 (5.7)
BMI >25 to ≤30 kg/m², n (%)	178 (45.1)	88 (32.4)
BMI >30 kg/m², n (%)	94 (23.8)	83 (30.5)
Smoker, n (%)	150 (36.8)	67 (24.4)
BASDAI	5.2 (1.9)	5.3 (1.9)
PGA	5.8 (4.9)	5.6 (5.6)
ASAS-HI	7.4 (3.5)	8.2 (3.5)
BDI-II	11.2 (10.2)	13.1 (13.0)
Medication prior to secukinumab initiation, n (%):		
NSAID	330 (80.9)	222 (80.7)
csDMARD	145 (35.5)	137 (49.8)
b-bsDMARD	249 (61.0)	190 (69.1)

*variables given as mean (SD)

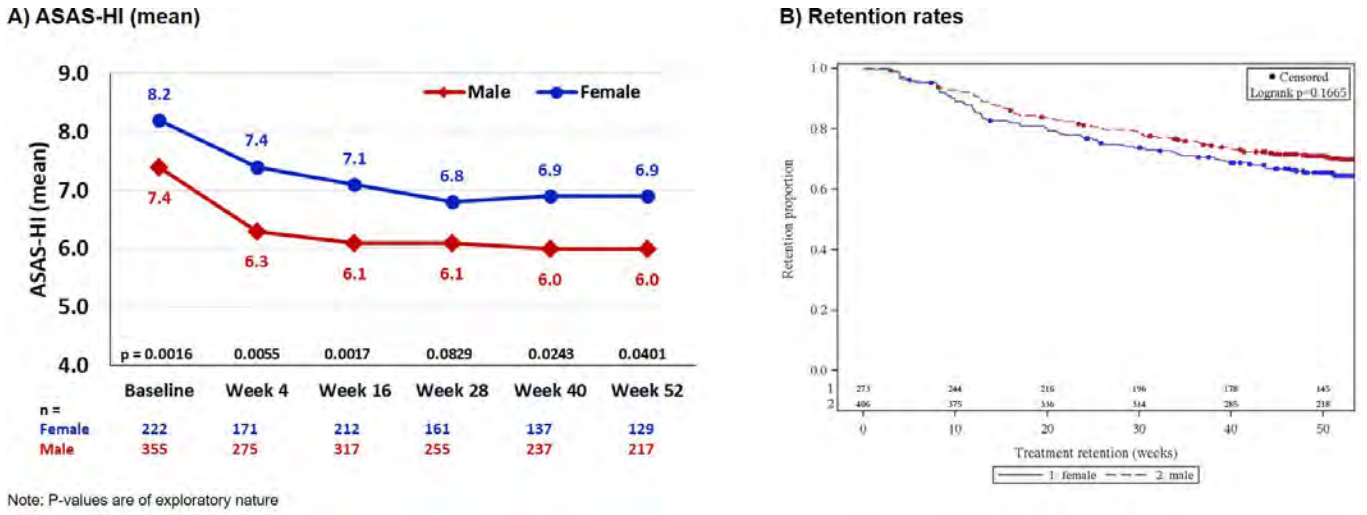

Figure 1. Global functioning and secukinumab treatment retention in AS patients stratified by gender.

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Brandt-Jrgens**, Abbvie, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, Novartis, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, UCB, 2, 6, BMS, 2, 6, Janssen, 2, 6, Medac, 2, 6; **P. Kästner**, Chugai, 2, Novartis, 2; **E. Riechers**, AbbVie, 2, 5, Chugai, 2, 5, Eli Lilly, 5, Janssen, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 5, UCB, 2, 5; **D. Peterlik**, Novartis, 3; **H. Tony**, AbbVie, 2, Astra-Zeneca, 2, BMS, 2, Chugai, 2, Janssen, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, Roche, 2, Sanofi, 2.

Abstract Number: 0910

The Association of TNF Inhibitor Use with Incident Hypertension in Ankylosing Spondylitis: Data from the PSOAS Cohort

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Ankylosing spondylitis (AS) is associated with greater cardiovascular (CV) risk than in the general population. The impact of tumor necrosis factor inhibitors (TNFi) on CV risk in AS, including on the development of hypertension, an important CV risk factor, remains unclear. We aimed to determine the association of TNFi use with incident hypertension in a longitudinal AS cohort.

Table 1. Baseline demographic and clinical characteristics of subjects without hypertension at baseline, stratified by baseline TNFi use

Variables	Whole cohort (n=630)	TNFi users (n=269)	TNFi non-users (n=361)
Age, years	39.4 ± 12.9	39.1 ± 12.2	39.6 ± 13.3
Male	72%	74%	70%
White	80%	80%	80%
Age at symptom onset, years	23.8 ± 9.2	23.8 ± 9.3	23.9 ± 9.2
BASDAI (0-10)	3.7 ± 2.4	3.3 ± 2.4	3.9 ± 2.4
Elevated CRP	37%	26%	46%
Continuous NSAID use	32%	25%	37%
Obese BMI	22%	25%	19%
Cardiovascular disease	2%	2%	3%
Diabetes	1%	2%	1%
Current smoking	10%	10%	10%

Methods: Adults with AS were enrolled in a prospective cohort during 2002-2018 and examined every 4-6 months. TNFi use during the preceding six months was ascertained at each study visit. We defined hypertension by patient-reported hypertension, anti-hypertensive medication use, or, on two consecutive visits, systolic blood pressure ≥140 mm Hg or diastolic ≥90 mm Hg. We evaluated the association between TNFi use and the development of hypertension with marginal structural models, estimated by inverse probability weighting, to account for time-dependent confounders (nonsteroidal anti-inflammatory drug use and disease activity) and informative censoring.

Results: We included 630 participants without baseline hypertension, and at least one year of follow-up. Of these, 72% were male, with a mean age at baseline of 39±13 years, and 43% used TNFi at baseline. On follow-up (median 5 years), 129 developed incident hypertension. TNFi use was not associated with incident hypertension (adjusted hazard ratio 1.11, 95% CI 0.86-1.44).

Conclusion: In this prospective AS cohort, there was no conclusive evidence to support an increased risk of incident hypertension with TNFi use, after accounting for important baseline and time-dependent confounding factors.

Disclosure: J. Liew, Pfizer, 5; **S. Jafarzadeh**, Pfizer, 5; **M. Dubreuil**, UCB, 2; **S. Heckbert**, None; **S. Mooney**, None; **M. Brown**, None; **M. Ishimori**, None; **J. Reveille**, UCB, 1, Eli Lilly, 1, Eli Lilly, 5, Novartis, 1; **M. Ward**, None; **M. Weisman**, Novartis, 2, Gilead, 2, GSK, 2, UCB, 2; **L. Gensler**, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2.

Abstract Number: 0911

Drug Retention of Tumor Necrosis Factors and IL-17 Inhibitors in Axial Spondyloarthritis: A Multi-Center Comparative Analysis

Thibaut Delépine[1], Peggy PHILIPPE[2], Emeline CAILLIAU[3], Eric HOUVENAGEL[4], Tristan Pascart[5], Xavier DEPREZ[6], Rene-Marc FLIPO[7] and Jean-Guillaume LETAROUILLY[2], [1]Lille University Hospital, Lille, France, [2]Rheumatology Department, University Hospital of Lille, Lille, France, [3]Assessment of Health Technologies and Medical Practices Department, University Hospital of Lille, Lille, France, [4]Rheumatology Department, Lille Catholic Hospitals, Lomme, France, [5]Groupement Hospitalier de l'Institut Catholique de Lille, Lomme, France, [6]Rheumatology Department, Hospital Center of Valenciennes, Valenciennes, France, [7]Rheumatology Department, Lille University Hospital, Lille, France

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Biological disease-modifying antirheumatic drugs (bDMARDs) should be considered in patients with active axial spondyloarthritis (AxSpA) despite treatment with nonsteroidal anti-inflammatory drugs. The objective of this study was to compare drug retention in patients with active AxSpA treated with tumor necrosis factor inhibitors (TNFi) and secukinumab (SEC), an interleukin 17 inhibitor.

Methods: AxSpA patients from three tertiary care centers starting SEC or TNFi in 2016-2019 were included. Hazard-ratios (HR) for treatment discontinuation were calculated using propensity score and after overlap weighting.

Results: A total of 279 patients were included (TNFi 178, SEC 101). Mean (SD) age was 45.1 (13.1) years and 45.5% were women. Most of them were diagnosed with radiographic sacroiliitis (63.4%), few were bDMARD-naïve (33.7% and 14.9% for TNFi and SEC, respectively). Before matching, patients of the SEC group were older, more likely to present with peripheral joint manifestations, radiographic sacroiliitis, had a higher prevalence of male gender,

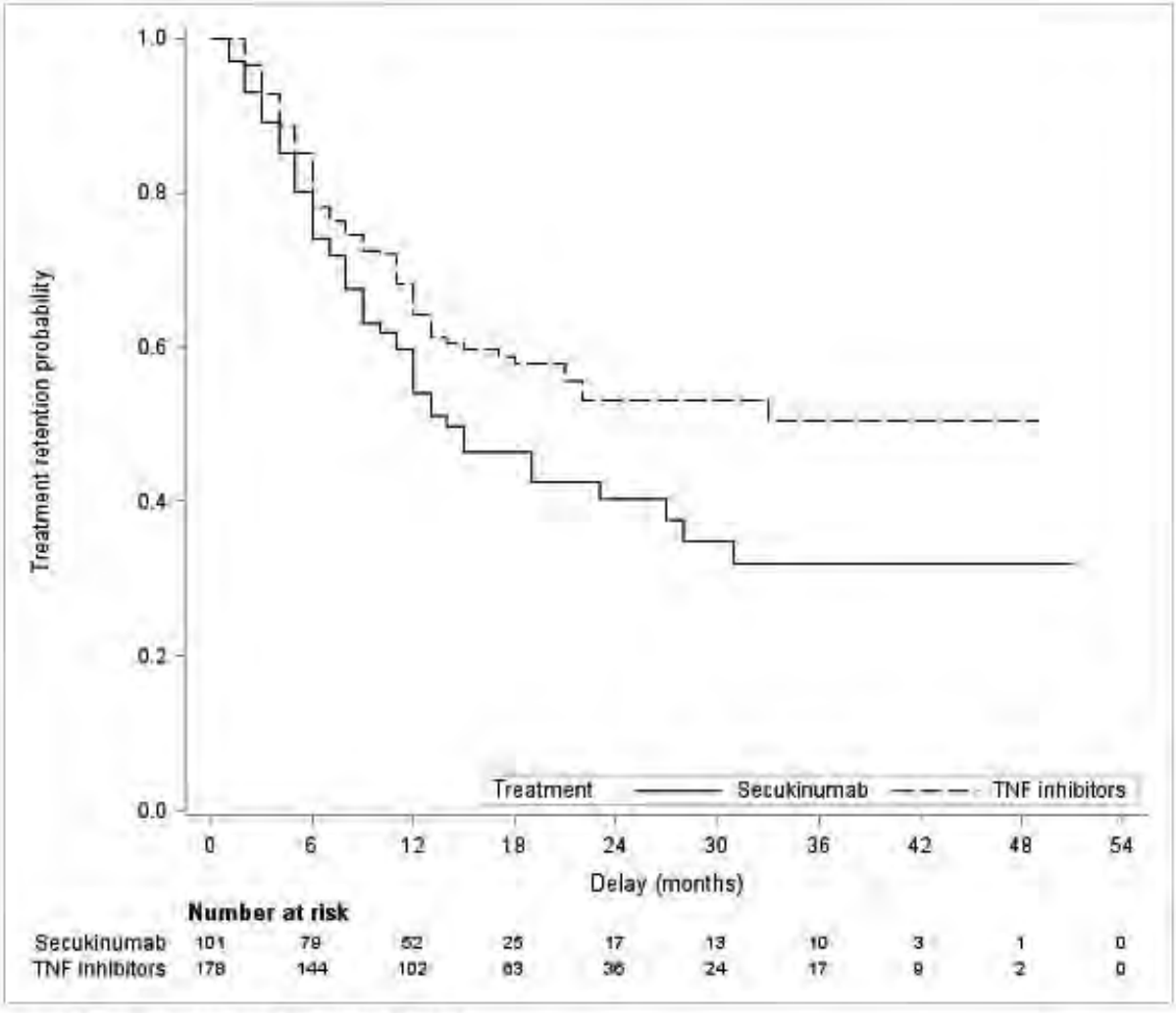

Figure 1. Persistence with SEC versus TNFi

HLA-B27 positive status, fibromyalgia and comorbidities. 77 matched pairs (mean values of the 10 imputed datasets) were found.

Out of 279 patients, 128 (45.9%) discontinued treatment (Figure 1). In unadjusted analyses, a better drug retention was observed with TNFi compared with SEC (Hazard Ratio HR for treatment discontinuation: 1.46 95% CI: 1.03 to 2.08; p=0.033). The HR for treatment discontinuation in overlap-weighting and matched cohort were 1.46 (95%CI:

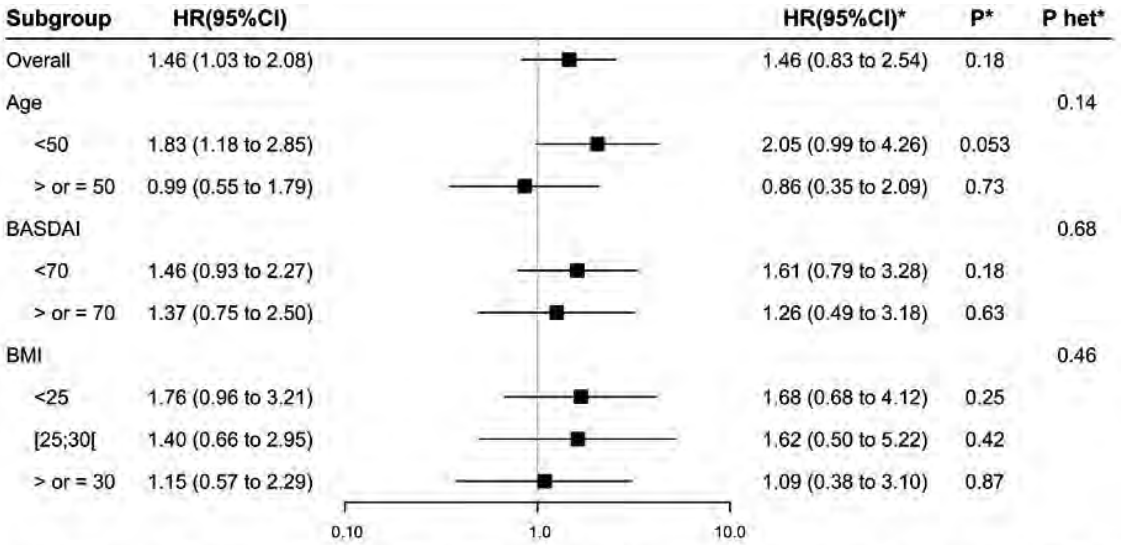

Figure 2. Treatment retention between SEC and TNFi, before and after Overlap Weighting. Abbreviations: BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BMI: body mass index; CI: confidence interval; CRP: C-reactive protein; HR: hazard ratio. Hazard ratios were calculated for patients treated with Secukinumab versus those treated with TNF inhibitors. * after overlap weighting

Table 1. Reason for treatment discontinuation according to treatment.

	TNF inhibitors n = 178	Secukinumab n = 101
Discontinued treatment, n (%)	73 (41.0)	55 (54.5)
Reason for discontinuation		
Primary non-response, n (%)	33 (45.2)	22 (40.0)
Secondary inefficacy, n (%)	23 (31.5)	19 (34.5)
Adverse events, n (%)	14 (19.2)	11 (20.0)
Hepatic cytolysis, n	1	0
Infection, n	6	3
Generalised drug eruption, n	1	1
Injection site reaction, n	3	0
Headache, n	0	3
Dizziness, n	0	2
Inflammatory bowel disease, n	0	1*
Abdominal pain, n	2	0
Paradoxical psoriasis, n	1	1
Remission, n (%)	3 (4.1)	0 (0.0)
Other, n (%)	0 (0.0)	3 (5.5)†

* One new-onset inflammatory bowel disease

† One death not treatment related, one progression of multiple sclerosis, one progression chronic lymphocytic leukemia

0.83 to 2.54; p=0.18) and 1.46 (95%CI: 0.86 to 2.50; p=0.16), respectively. 6-month and 12-month SEC retention rates were 74% and 54%, respectively. Subgroup analyses (age, BASDAI at diagnosis, BMI) showed no difference between TNFi and SEC (Figure 2).

Reasons for discontinuation of TNFi and SEC treatments are demonstrated in Table 1. The main reason for discontinuating both treatments was inefficacy. The overall rate of adverse events leading to treatment discontinuation was similar for both treatment groups (19.2% and 20.0% for TNFi and SEC, respectively).

Conclusion: In this real-world AxSpA cohort, drug retention of SEC and TNFi were similar. In subgroups analyses, age, BASDAI at diagnosis and BMI did not favour any group. These results should be supplemented by head-to-head trials.

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Abstract Number: 0912

Efficacy and Safety of Intravenous Golimumab in Ankylosing Spondylitis Patients with Early versus Late Disease Through Week 52 of GO-ALIVE Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The GO-ALIVE study assessed efficacy and safety of intravenous golimumab (IV GLM) in patients with ankylosing spondylitis (AS).[1,2] In this post hoc analysis, we assessed IV GLM efficacy and safety in AS patients with early disease (ED) vs late disease (LD) based on patient-reported duration of inflammatory back pain (IBP).

Methods: In this Phase 3, double-blind, placebo (PBO)-controlled trial, patients with active AS were randomized (1:1) to receive IV GLM 2 mg/kg at Week (W) 0, W4, then every 8 weeks (Q8W) or PBO at W0, W4, and W12 with crossover to IV GLM at W16, W20, then Q8W through W52. The primary endpoint was the Assessment of SpondyloArthritis International Society 20% improvement response (ASAS 20) at W16. In this post hoc analysis, 208 patients were grouped into quartiles based on self-reported duration of IBP symptoms. Efficacy and safety in 60 patients with ED (1st quartile) were compared with 52 patients with LD (4th quartile).

Results: For the overall study population, mean duration of IBP symptoms was 10.9 years and mean time since diagnosis was 5.5 years. For ED patients, the mean duration of IBP symptoms ranged from 2.3 years (IV GLM) to 2.6 years (PBO), and for LD patients ranged from 23.5 years (IV GLM) to 24.4 years (PBO). At W16, ASAS 20 was

Table. Efficacy Outcomes

	ED				LD			
	Week 16		Week 52		Week 16		Week 52	
	PBO (n=25)	IV GLM (n=35)	PBO→IV GLM (n=25)	IV GLM (n=35)	PBO (n=28)	IV GLM (n=24)	PBO→IV GLM (n=28)	IV GLM (n=24)
ASAS 20	32%	71%	68%	71%	21%	67%	68%	63%
ASAS 40	12%	46%	56%	60%	4%	42%	57%	42%
BASDAI 50	12%	40%	64%	60%	7%	33%	57%	42%
ASDAS inactive disease (score <1.3)	4%	17%	44%	37%	0%	8%	14%	4%
ASDAS major improvement (decrease ≥2.0)	n=24 4%	57%	n=24 54%	51%	0%	n=23 48%	46%	n=23 30%
ASDAS clinically important improvement (decrease ≥1.1)	n=24 29%	77%	n=24 75%	77%	18%	n=23 91%	61%	n=23 65%
Mean change from baseline (SD) in BASFI	n=23 -0.4 (2.0)	-2.3 (2.1)	n=23 -2.7 (2.7)	-2.8 (2.6)	n=27 -0.3 (1.8)	n=24 -2.2 (1.7)	n=27 -2.4 (2.2)	n=23 -2.3 (1.7)
Mean change from baseline (SD) in BASMI	n=23 -0.3 (0.7)	-0.4 (0.7)	n=23 -0.6 (0.7)	-0.3 (0.5)	n=27 0.01 (0.5)	n=21 -0.3 (0.6)	n=27 -0.4 (0.7)	n=20 -0.3 (0.7)
Mean change from baseline (SD) in enthesitis score	n=23 0.1 (3.6)	-2.9 (2.9)	n=23 -2.0 (4.4)	-3.2 (2.5)	n=27 -0.6 (3.4)	n=21 -2.5 (3.0)	n=27 -2.5 (3.1)	n=20 -3.5 (5.9)

ASAS=Assessment of SpondyloArthritis International Society, ASDAS=Ankylosing Spondylitis Disease Activity Score, BASDAI=Bath Ankylosing Spondylitis Disease Activity Index, BASFI=Bath Ankylosing Spondylitis Functional Index, BASMI=Bath Ankylosing Spondylitis Metrology Index, ED=early disease, GLM=golimumab, IV=intravenous, LD=late disease, PBO=placebo, SD=standard deviation

achieved by 72% IV GLM vs 32% PBO patients with ED and by 67% IV GLM vs 21% PBO patients with LD. Patients with ED had numerically better response than those with LD in Bath Ankylosing Spondylitis Functional Index (BASFI), Bath Ankylosing Spondylitis Metrology Index (BASMI), and across more stringent endpoints, including ASAS 40, Bath Ankylosing Spondylitis Disease Activity Index 50% improvement (BASDAI 50), and Ankylosing Spondylitis Disease Activity Score (ASDAS) inactive disease and major improvement (Table). Response rates at W16 among IV GLM-treated patients were generally consistent through 1 year in both ED and LD subgroups; also in ED and LD subgroups, patients crossing over to IV GLM at W16 demonstrated response at W52 consistent with patients who started IV GLM at W0. At W16, improvements in enthesitis score were similar for patients with ED (mean change -2.9 for IV GLM vs 0.1 for PBO) and LD (mean change -2.5 for IV GLM vs 0.6 for PBO); improvements were maintained at W52 for ED and LD patients. Treatment-emergent adverse events and serious adverse events through 1 year were 46% and 3% for patients with ED compared with 61% and 2% for patients with LD, respectively.

Conclusion: While IV GLM provided clinically meaningful improvements in signs and symptoms of AS in patients regardless of disease duration, response generally appeared numerically better in patients with ED than in patients with LD. This supports the principle of prompt diagnosis and early treatment.

References

1. Deodhar A, et al. *J Rheumatol*. 2018;45:341-348.
2. Reveille J, et al. *J Rheumatol*. 2019;46:1277-1283.

Disclosure: A. Deodhar, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **S. Kafka**, Janssen Research and Development, LLC, 3; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **K. Lo**, Janssen Research and Development, LLC, 3; **K. Lilianne**, Janssen Research and Development, LLC, 3; **S. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **J. Reveille**, UCB, 1, Eli Lilly, 1, Eli Lilly, 5, Novartis, 1.

Abstract Number: 0913

Long-Term Safety and Efficacy of Certolizumab Pegol in Patients with Active Non-Radiographic Axial Spondyloarthritis: 3-Year Results from a Phase 3 Multicenter Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Certolizumab pegol (CZP) has demonstrated clinical efficacy in patients with active non-radiographic axial spondyloarthritis (nr-axSpA) and objective signs of inflammation (sacroiliitis on MRI and/or elevated C-reactive protein levels) treated during the 52-week placebo-controlled period of C axSpAnd.[1] We evaluate long-term safety and changes in clinical outcomes in patients with active nr-axSpA treated with CZP for up to 3 years during the C-axSpAnd double-blind period and open-label (OL) safety follow-up extension (SFE).

Methods: C-axSpAnd (NCT02552212) was a 3-year, phase 3, multicenter study consisting of a 1-year double-blind, placebo-controlled period (Weeks 0–52) followed by a 2-year OL SFE (Weeks 52–156).[1] Patients were randomized 1:1 to placebo (PBO) or CZP (400 mg at Weeks 0, 2, 4, then 200 mg every 2 weeks [Q2W]), which they received in addition to non-biologic background medication for 52 weeks. Switching to OL CZP (or other biologics) was permitted at any point. At Week 52, patients completing the double-blind phase (on CZP, PBO or OL CZP) who enrolled into the SFE received OL CZP 200 mg Q2W for an additional 104 weeks. We report safety and clinical outcomes (Ankylosing Spondylitis Disease Activity Score [ASDAS], BASDAI and BASFI, ASDAS Major Improvement [ASDAS-MI], Assessment of SpondyloArthritis international Society 40% response [ASAS40]) up to Week 156 for patients who entered the SFE according to whether they were initially randomized to CZP or PBO. As efficacy outcomes for the SFE were assessed at Weeks 52 and 156 only, data are reported as observed case (OC).

Results: 243/317 patients who entered C-axSpAnd continued into the SFE, including 120 patients from the CZP-randomized arm and 123 from the PBO-randomized arm. During the double-blind period, prior to SFE entry, 75/123 PBO patients had switched to OL CZP, compared to 10/120 of CZP patients. In total, 102/120 (85.0%) and 104/123 (84.6%) SFE patients from the CZP- and PBO-randomized arms, respectively, completed the study up to Week 156.

Table. Safety outcomes up to Week 156 of the C-axSpAnd study

	Double-blind period Weeks 0–52		Safety follow-up extension Weeks 52–156	
n (%) [#]	CZP 200 mg Q2W (n=159)	PBO (n=158)	CZP 200 mg Q2W (n=120)	PBO → CZP 200 mg Q2W (n=123)
Any TEAE	120 (75.5) [476]	101 (63.9) [333]	73 (60.8) [193]	76 (61.8) [212]
Serious TEAEs	8 (5.0) [9]	3 (1.9) [3]	6 (5.0) [6]	9 (7.3) [14]
Subject discontinuations due to TEAEs	3 (1.9) [4]	3 (1.9) [3]	1 (0.8) [2]	4 (3.3) [4]
Permanent withdrawal of study medication due to TEAEs	3 (1.9) [4]	3 (1.9) [3]	1 (0.8) [2]	5 (4.1) [5]
Drug-related TEAEs	48 (30.2) [111]	23 (14.6) [61]	13 (10.8) [33]	23 (18.7) [46]
Severe TEAEs	5 (3.1) [5]	4 (2.5) [4]	4 (3.3) [4]	5 (4.1) [8]
Frequently reported TEAEs by preferred term [a]				
Diarrhea	8 (5.0) [11]	10 (6.3) [10]	1 (0.8) [1]	3 (2.4) [3]
Upper respiratory tract infection	30 (18.9) [38]	16 (10.1) [23]	14 (11.7) [20]	7 (5.7) [11]
Nasopharyngitis	21 (13.2) [24]	13 (8.2) [17]	18 (15.0) [23]	8 (6.5) [10]
Bronchitis	8 (5.0) [9]	5 (3.2) [5]	5 (4.2) [6]	5 (4.1) [5]
Tonsilitis	7 (4.4) [7]	2 (1.3) [2]	6 (5.0) [7]	6 (4.9) [7]
Increased blood creatine phosphokinase	8 (5.0) [9]	4 (2.5) [4]	1 (0.8) [1]	2 (1.6) [2]
Arthralgia	9 (5.7) [12]	10 (6.3) [12]	3 (2.5) [3]	3 (2.4) [3]
Axial spondyloarthritis	11 (6.9) [13]	12 (7.6) [13]	4 (3.3) [4]	1 (0.8) [1]
Headache	11 (6.9) [15]	7 (4.4) [9]	4 (3.3) [4]	5 (4.1) [7]
Cough	6 (3.8) [6]	8 (5.1) [10]	1 (0.8) [1]	2 (1.6) [2]
Deaths	0	0	0	0

For Weeks 0–52, data are reported for double-blind safety set (N=317), and for Weeks 52–156 for the SFE safety set (N=243). [a] Reported in ≥5% patients. #: number of individual TEAE occurrences; CZP: certolizumab pegol; PBO: placebo; Q2W: every 2 weeks; TEAE: treatment-emergent adverse event.

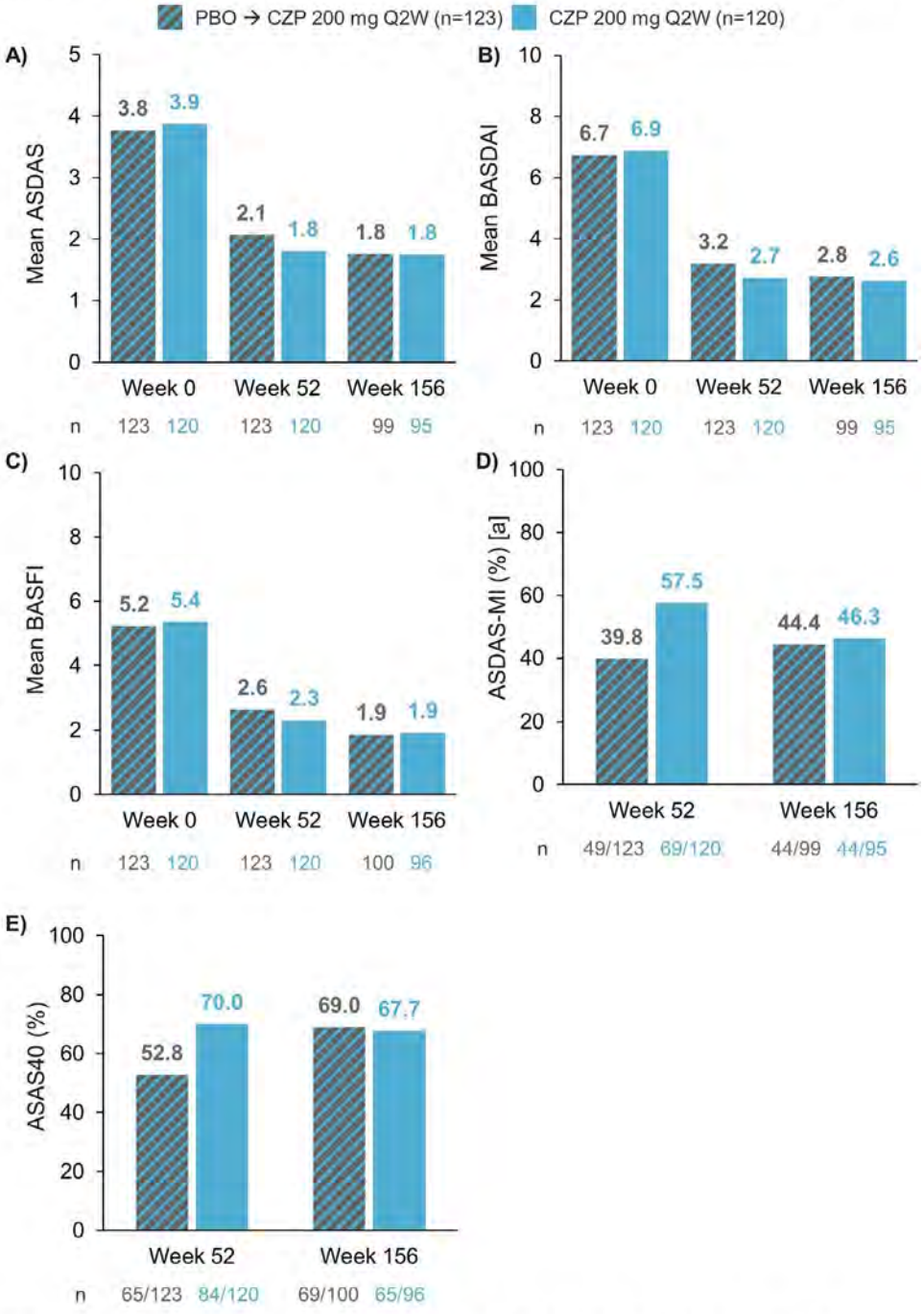
During the SFE, 405 TEAEs were reported for 149 (61.3%) patients, including 20 serious TEAEs in 15 (6.2%) patients (**Table**). Over a period of up to 3 years of CZP treatment, no new safety signal was identified.

At Week 52 (SFE baseline), using OC data, there were substantial improvements from Week 0 in ASDAS, BASDAI and BASFI, and in ASDAS-MI and ASAS40 response rates (**Figure**). As the majority of PBO-randomized patients had switched to OL CZP during the double-blind period, improvements were also observed in this arm at Week 52. Responses were maintained to Week 156 in both arms, and by Week 156, improvements across all reported efficacy outcomes in patients initially randomized to PBO were comparable to those initially randomized to CZP (**Figure**).

Conclusion: This analysis reports safety and clinical outcomes in the nr-axSpA patients who entered the C-axSpAnd SFE and received OL CZP treatment. During the SFE, CZP was shown to be well tolerated in patients with nr-axSpA, in line with 1-year data.[1] In patients receiving CZP treatment for up to 3 years, observed improvements in signs and symptoms after 1 year were maintained up to 3 years.

References: 1. Deodhar A. Arthritis Rheum 2019;71:1101–11.

Figure. (A) ASDAS, (B) BASDAI, (C) BASFI, (D) ASDAS-MI and (E) ASAS40 up to Week 156 in patients who entered the C-axSpAnd SFE (observed case data)



All patients entering the SFE received CZP for at least 2 years. Data are reported as observed case.
[a] Reduction of ≥2 units from baseline. ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; ASDAS-MI: ASDAS Major Improvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CZP: certolizumab pegol; PBO: placebo; SFE: safety follow-up extension.

Disclosure: D. van der Heijde, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and

Rheumatology BV, 4; **L. Gensler**, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2; **W. Maksymowych**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **M. Rudwaleit**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, UCB Pharma, 2, AbbVie, 6, Eli Lilly, 6, Novartis, 6, Novartis, 2, UCB Pharma, 6; **L. Bauer**, UCB Pharma, 3, 11; **B. Hoepken**, UCB Pharma, 3, 11; **T. Kumke**, UCB Pharma, 3; **M. Kim**, UCB Pharma, 3, 11; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2.

Abstract Number: 0914

Response to Certolizumab Pegol in Patients with Non-Radiographic Axial Spondyloarthritis by Baseline C-Reactive Protein Cut-Offs: Post-Hoc Analysis from a Phase 3 Multicenter Study

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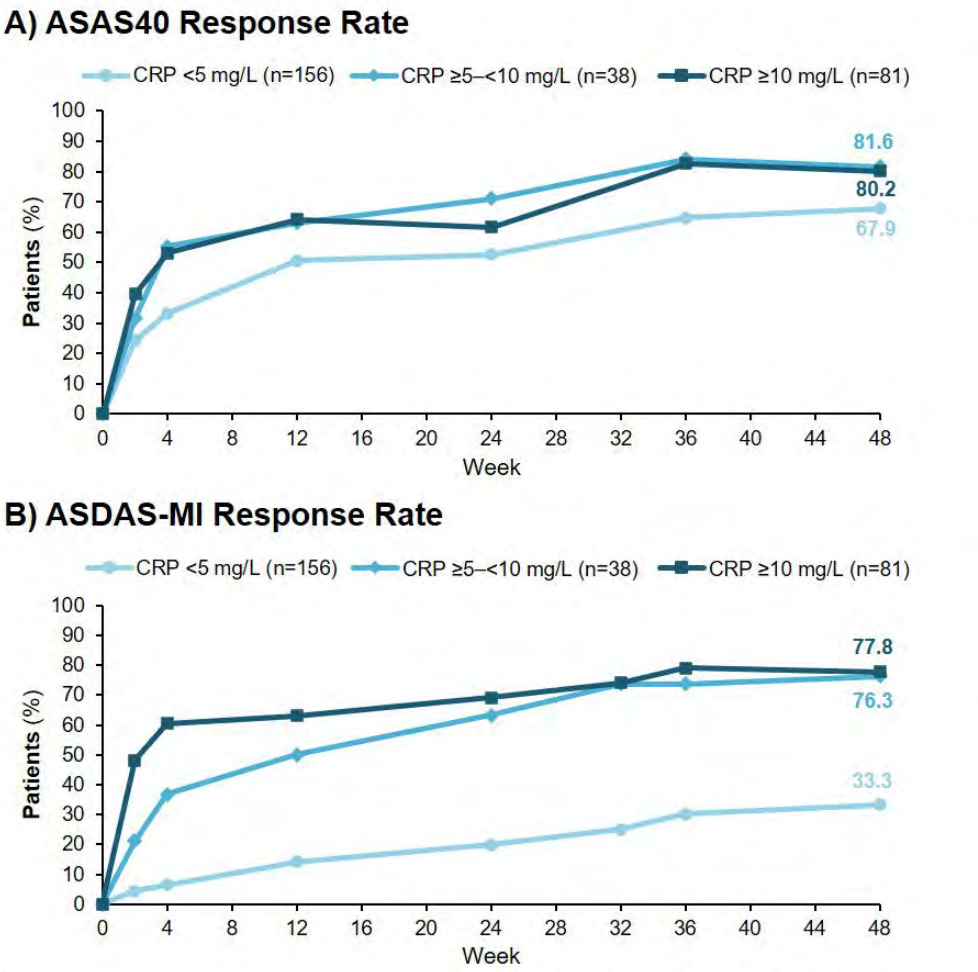
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Certolizumab pegol (CZP), an Fc-free, PEGylated tumor necrosis factor (TNF) inhibitor, has previously demonstrated efficacy and safety in patients with radiographic (r) and non-radiographic (nr) axial spondyloarthritis (axSpA).[1,2] In nr-axSpA patients, CZP has demonstrated efficacy across all C-reactive protein (CRP) subgroups, including patients with normal baseline CRP levels.[3] However, the association between CZP efficacy and baseline CRP levels has not been investigated in the subset of nr-axSpA patients with positive magnetic resonance imaging (MRI+; defined as the presence of active sacroiliitis on MRI based on the Assessment of SpondyloArthritis international Society [ASAS] criteria).[4] This post-hoc analysis explores the association between baseline CRP levels and CZP efficacy in MRI+ nr-axSpA patients from the C-OPTIMISE trial.

Methods: C-OPTIMISE (NCT02505542) was a two-part, multicenter, phase 3b study in adult patients with r-axSpA or nr-axSpA.[1,2] In the open-label run-in period (0–48 weeks), patients received CZP 400 mg at Weeks 0, 2, and 4, then CZP 200 mg every 2 weeks thereafter. This analysis included the subset of MRI+ nr-axSpA patients in the C-OPTIMISE cohort who received ≥1 dose of study medication in the open-label period. Efficacy outcomes were evaluated and stratified by baseline CRP levels (<5 mg/L, ≥5– < 10 mg/L and ≥10 mg/L). The upper limit of normal of the CRP assay was defined as 9.99 mg/L by the central laboratory. The lower limit of quantification (LLoQ) was 4 mg/L; where CRP levels < LLoQ, a CRP value of 2 mg/L was used to calculate Ankylosing Spondylitis Disease Activity Score (ASDAS).[5] Outcomes included ASAS ≥40% improvement (ASAS40), ASDAS – major improvement (ASDAS-MI), ASAS partial remission (ASAS PR), ASDAS, BASDAI, and BASFI.

Results: In total, 275 MRI+ nr-axSpA patients were included in this analysis (CRP <5 mg/L: n=156; CRP ≥5– <10 mg/L: n=38; CRP ≥10 mg/L: n=81). Response rates for ASAS40 increased over the treatment period and were com-

Figure 1. (A) ASAS40 and **(B)** ASDAS-MI response rates in CZP-treated patients by baseline CRP category (non-responder imputation)



ASAS40: Assessment of SpondyloArthritis international Society ≥40% improvement; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; CRP: C-reactive protein; CZP: certolizumab pegol.

parable across CRP subgroups (**Figure 1A**). Response rates for ASDAS-MI were higher in the CRP ≥10 mg/L and CRP ≥5– <10 mg/L subgroups than the CRP <5 mg/L subgroup (**Figure 1B**). Across other efficacy measures, improvements were observed at Week 48 compared with baseline in all CZP-treated CRP subgroups (**Table 1**).

Conclusion: Clinically relevant responses were observed in MRI+ nr-axSpA patients treated with CZP, across CRP subgroups and measured outcomes. The responses in each subgroup were consistent with those previously reported in total nr-axSpA patient group.[1] ASDAS-MI response rates were lower in the CRP <5 mg/L subgroup, however, CRP is a key factor in ASDAS derivation. It is unlikely that ASDAS-MI could be achieved in patients in the CRP <5 mg/L subgroup since most of them had CRP levels < LLoQ.

References: 1. Landewé R et al. Rheumatol Ther 2020;7:581–99. **2**. Landewé R et al. Ann Rheum Dis 2020;79:920–28. **3**. Robinson P et al. Int J Rheum Dis 2020;23:67–8. **4**. Rudwaleit M et al. Ann Rheum Dis 2009;68:1520–7. **5**. Machado P et al. Arthritis Rheumatol 2015;67:408–13.

Table 1. Clinical responses in CZP-treated patients by baseline CRP category

		CRP <5 mg/L (n=156)	CRP ≥5–<10 mg/L (n=38)	CRP ≥10 mg/L (n=81)
ASAS40 % (n)	*Baseline*	–	–	–
	Week 48	**67.9** (106)	**81.6** (31)	**80.2** (65)
ASDAS-MI % (n)	*Baseline*	–	–	–
	Week 48	**33.3** (52)	**76.3** (29)	**77.8** (63)
ASAS PR % (n)	*Baseline*	–	–	–
	Week 48	**50.0** (78)	**73.7** (28)	**67.9** (55)
ASDAS Mean (SD)	*Baseline*	**3.1** (0.5)	**3.6** (0.5)	**4.3** (0.6)
	Week 48	**1.6** (1.0)	**1.3** (1.0)	**1.5** (1.0)
BASDAI Mean (SD)	*Baseline*	**6.7** (1.4)	**6.5** (1.6)	**6.9** (1.3)
	Week 48	**2.6** (2.5)	**1.6** (2.4)	**1.7** (2.2)
BASFI Mean (SD)	*Baseline*	**5.0** (2.0)	**4.7** (2.3)	**5.5** (2.1)
	Week 48	**1.9** (2.3)	**1.4** (2.3)	**1.3** (1.9)

ASDAS-MI, ASAS40 and ASAS PR are reported using non-responder imputation.
ASDAS, BASDAI and BASFI are reported using the last observation carried forward.
ASAS: Assessment of SpondyloArthritis international Society; ASAS40: ASAS ≥40% improvement; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; CRP: C-reactive protein; CZP: certolizumab pegol; PR: partial remission; SD: standard deviation.

Disclosure: P. Robinson, Abbvie, 1, Novartis, 1, 5, 6, Atom Biosciences, 1, Janssen, 5, 6, Eli Lilly, 1, 2, 6, Gilead, 6, UCB Pharma, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 6; **S. Hall**, AbbVie, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Bristol-Myers Squibb, 2, 5, Merck, 2, 5, 6; **B. Hoepken**, UCB Pharma, 3, 11; **L. Bauer**, UCB Pharma, 3, 11; **E. Demas**, UCB Pharma, 3; **M. Kim**, UCB Pharma, 3, 11; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2.

Abstract Number: 0915

Biomarkers of Extracellular Matrix Turnover Reflect Treatment Response and Pharmacodynamic Effects of TNF-α Inhibitory Therapy in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease associated with extracellular matrix (ECM) remodeling of the cartilage, bone, and connective tissues. Quantification of ECM-mediated biomarkers may be useful to determine treatment response in axSpA. The aim of this study was to identify biomarkers reflecting the pharmacodynamic effect and the treatment response of adalimumab in two placebo-controlled axSpA studies.

Methods: Biomarkers reflecting the degradation of collagen type I (C1M), II (C2M and T2CM), III (C3M), IV (C4M), VI (C6M), formation of collagen type II (PRO-C2), III (PRO-C3), IV (PRO-C4) and VI (PRO-C6) and inflammation (CRPM, PROM, and VICM) were measured in serum from the ASIM study (n=45) and the DANISH study (n=49) at baseline, week 6 or 12 (ASIM and DANISH, respectively), and week 24. Patients received treatment with adalimumab 40 mg or placebo the first 6 or 12 weeks (ASIM and DANISH, respectively) followed by adalimumab 40 mg for an additional 18 or 12 weeks (ASIM and DANISH, respectively). Differences in fold change of biomarker levels between week 6 or week 12 (ASIM and DANISH, respectively) and baseline were evaluated by a linear regression model to investigate treatment pharmacodynamics. A linear regression model adjusted by treatment (active treatment or placebo for the first 6 or 12 weeks, ASIM and DANISH, respectively) were applied to investigate treatment response. Response to treatment was evaluated as a reduction of at least 50% in BASDAI index from baseline to week 24.

Table 1. Pharmacodynamic effect of adalimumab in the ASIM (Baseline to 6 weeks) and DANISH (Baseline to 12 weeks) studies, presented as fold change of the investigated serum biomarkers.

Biomarker (fold change mean, [95% CI])	ASIM			DANISH		
	Active treatment (n=22)	Placebo (n=23)	P-value	Active treatment (N=24)	Placebo (n=25)	P-value
C1M	0.5[0.41,0.70]	1.2[0.90,1.49]	**<0.001**	0.5[0.32,0.66]	1.1[0.75,1.50]	**0.002**
C2M	1.0[0.91,1.08]	1.0[0.91,1.08]	0.976	1.0[0.82,1.25]	1.2[0.94,1.41]	0.386
T2CM	1.0[0.94,1.07]	1.0[0.93,1.05]	0.698	1.0[0.89,1.08]	1.0[0.91,1.10]	0.727
C3M	0.9[0.81,0.95]	1.1[0.99,1.16]	**<0.001**	0.9[0.80,0.96]	1.0[0.93,1.10]	**0.020**
C4M	0.8[0.76,0.89]	1.1[0.98,1.15]	**<0.001**	0.8[0.73,0.90]	1.0[0.88,1.09]	**0.015**
C6M	0.8[0.69,0.85]	1.1[0.98,1.19]	**<0.001**	0.7[0.64,0.86]	1.0[0.84,1.11]	**0.011**
CRPM	0.9[0.81,0.99]	1.0[0.89,1.09]	0.180	0.9[0.85,1.01]	1.0[0.94,1.12]	0.100
PROM	1.1[0.93,1.19]	1.0[0.85,1.08]	0.274	1.0[0.95,1.10]	1.0[0.91,1.05]	0.336
VICM	0.8[0.57,1.01]	1.1[0.82,1.45]	0.078	0.7[0.52,0.95]	0.9[0.66,1.20]	0.259
PRO-C2	1.1[0.96,1.23]	1.0[0.90,1.14]	0.416	1.0[0.91,1.09]	1.0[0.89,1.07]	0.78
PRO-C3	1.0[0.95,1.11]	1.0[0.88,1.03]	0.198	1.0[0.94,1.10]	1.0[0.92,1.08]	0.773
PRO-C4	0.9[0.88,0.96]	1.0[0.95,1.04]	0.018	0.9[0.89,0.99]	1.0[0.93,1.03]	0.304
PRO-C6	1.0[0.94,1.07]	1.0[0.92,1.05]	0.673	0.9[0.88,1.02]	1.0[0.92,1.05]	0.434
PRO-C2/C2M	1.1[0.97,1.25]	1.0[0.90,1.16]	0.426	1.0[0.77,1.27]	0.8[0.67,1.08]	0.392
PRO-C3/C3M	1.2[1.05,1.31]	0.9[0.80,1.00]	**0.001**	1.2[1.03,1.30]	1.0[0.88,1.10]	0.051
PRO-C4/C4M	1.1[1.05,1.19]	0.9[0.88,1.00]	**<0.001**	1.2[1.08,1.26]	1.0[0.93,1.08]	**0.009**
PRO-C6/C6M	1.3[1.16,1.47]	0.9[0.81,1.02]	**<0.001**	1.3[1.09,1.50]	1.0[0.87,1.19]	**0.049**

C1M: metalloproteinase (MMP)-degraded type I collagen; C2M: metalloproteinase (MMP)-degraded type II collagen; T2CM: MMP-1 and -13 mediated degradation of type II collagen; C3M: MMP-degraded type III collagen; C4M: MMP-degraded type IV collagen; C6M: MMP-degraded type VI collagen; CRPM:C-reactive protein metabolite; PROM: MMP-1 and -13 mediated degradation of prolargin; VICM: citrullinated and MMP-degraded vimentin; PRO-C2: pro-peptide of type II collagen; PRO-C3: pro-peptide of type III collagen; PRO-C4: pro-peptide of type IV collagen; PRO-C6: pro-peptide of type VI collagen; Type 2: formation/degradation ratio of type II collagen; Type 3: formation/degradation ratio of type III collagen; Type 4: formation/degradation ratio of type IV collagen; Type 6: formation/degradation ratio of type VI collagen.

Table 2. Response to adalimumab treatment from baseline to week 24 in the ASIM and the DANISH studies, presented as fold change of the investigated serum biomarkers.

Biomarker (fold change mean, [95% CI])	ASIM			DANISH		
	Responders (n=32)	Non-responders (n=10)	P-value	Responders (n=43)	Non-responders (n=3)	P-value
C1M	0.6[0.47,0.71]	0.9[0.60,1.26]	0.06	0.5[0.36,0.57]	0.6[0.26,1.50]	0.48
C2M	1.0[0.91,1.10]	1.1[0.91,1.28]	0.45	1.0[0.94,1.05]	1.2[0.96,1.50]	0.10
T2CM	1.0[0.94,1.06]	1.0[0.86,1.08]	0.58	1.0[0.89,1.04]	0.9[0.69,1.29]	0.93
C3M	0.9[0.87,0.98]	1.0[0.87,1.07]	0.49	0.9[0.83,0.96]	1.2[0.92,1.56]	**0.04**
C4M	0.9[0.81,0.93]	1.0[0.85,1.10]	0.16	0.8[0.73,0.87]	1.1[0.82,1.54]	**0.04**
C6M	0.8[0.76,0.89]	1.0[0.84,1.09]	0.05	0.7[0.68,0.83]	1.1[0.72,1.54]	0.09
CRPM	0.8[0.75,0.95]	1.0[0.83,1.28]	0.11	1.0[0.90,1.03]	1.2[0.96,1.61]	0.06
PROM	1.0[0.91,1.01]	1.0[0.90,1.09]	0.54	1.0[0.95,1.05]	0.9[0.73,1.05]	0.16
VICM	0.8[0.67,0.96]	0.8[0.59,1.11]	0.97	0.5[0.42,0.69]	0.6[0.25,1.63]	0.70
PRO-C2	1.1[0.95,1.26]	1.2[0.89,1.49]	0.74	1.0[0.89,1.05]	1.1[0.78,1.42]	0.58
PRO-C3	1.0[0.92,1.09]	1.0[0.84,1.13]	0.71	1.0[0.92,1.03]	1.1[0.89,1.37]	0.25
PRO-C4	0.9[0.86,0.93]	1.0[0.91,1.06]	**0.04**	0.9[0.88,0.96]	1.1[0.92,1.25]	0.06
PRO-C6	1.0[0.94,1.05]	1.1[0.95,1.17]	0.30	1.0[0.90,1.01]	1.0[0.77,1.20]	0.93
PRO-C2/C2M	1.1[0.97,1.23]	1.1[0.86,1.32]	0.84	1.0[0.91,1.05]	0.9[0.67,1.15]	0.46
PRO-C3/C3M	1.1[0.99,1.19]	1.0[0.85,1.20]	0.45	1.1[0.99,1.20]	0.9[0.64,1.33]	0.37
PRO-C4/C4M	1.0[0.95,1.11]	1.0[0.88,1.16]	0.83	1.2[1.08,1.24]	1.0[0.74,1.23]	0.15
PRO-C6/C6M	1.2[1.10,1.32]	1.1[0.94,1.30]	0.33	1.3[1.13,1.44]	0.9[0.57,1.47]	0.18

C1M: metalloproteinase (MMP)-degraded type I collagen; C2M: metalloproteinase (MMP)-degraded type II collagen; T2CM: MMP-1 and -13 mediated degradation of type II collagen; C3M: MMP-degraded type III collagen; C4M: MMP-degraded type IV collagen; C6M: MMP-degraded type VI collagen; CRPM:C-reactive protein metabolite; PROM: MMP-1 and -13 mediated degradation of prolargin; VICM: citrullinated and MMP-degraded vimentin; PRO-C2: pro-peptide of type II collagen; PRO-C3: pro-peptide of type III collagen; PRO-C4: pro-peptide of type IV collagen; PRO-C6: pro-peptide of type VI collagen; Type 2: formation/degradation ratio of type II collagen; Type 3: formation/degradation ratio of type III collagen; Type 4: formation/degradation ratio of type IV collagen; Type 6: formation/degradation ratio of type VI collagen.

Results: In the ASIM vs. DANISH study 56% vs. 78% of the patients were male, the mean (SD) age of the patients was 37.6 (9.9) vs. 39.5 (11.2) and frequency of HLA-B27 78% vs. 88%. The 22 patients representing the primarily actively treated group in the ASIM study presented significantly lower fold change in C1M, C3M, C4M, C6M, and PRO-C4 over the first 6 weeks as compared to the placebo group ($p< 0.001$, $p< 0.001$, $p< 0.001$, $p< 0.001$, $p= 0.018$, respectively Table 1), and showed a significantly higher fold change in the ratios of formation/degradation of collagen type III, IV and VI (all $p< 0.001$). The 24 patients from the actively treated group in the DANISH study had a significantly lower fold change over the first 12 weeks in C1M, C3M, C4M, C6M as compared to the placebo group ($p=0.002$, $p=0.02$, $p=0.015$, $p=0.011$, respectively, Table 1), and had a significantly higher fold change in the ratios of formation/degradation of collagen type IV and VI ($p=0.009$, $p=0.049$, respectively). Thirty-two out of 45 patients were considered responders in the ASIM study, and 43 out of 46 patients in the DANISH study (Table 2). In the ASIM study, levels of PRO-C4 presented a significantly lower fold change in responders compared to non-responders ($p=0.042$), while in the DANISH study, levels of C3M and C4M had both a significantly lower fold change in responders compared to non-responders (both $p=0.04$, Table 2).

Conclusion: The biomarkers C1M, C3M, C4M, and C6M may have potential as pharmacodynamic biomarkers, while the biomarkers C3M and C4M were associated with response to adalimumab treatment after 24 weeks.

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Abstract Number: 0916

Disease Activity and Inflammation in Axial Spondyloarthritis Patients Who Did Not Experience Flares Following Certolizumab Pegol Withdrawal, Dose Reduction or Dose Continuation

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

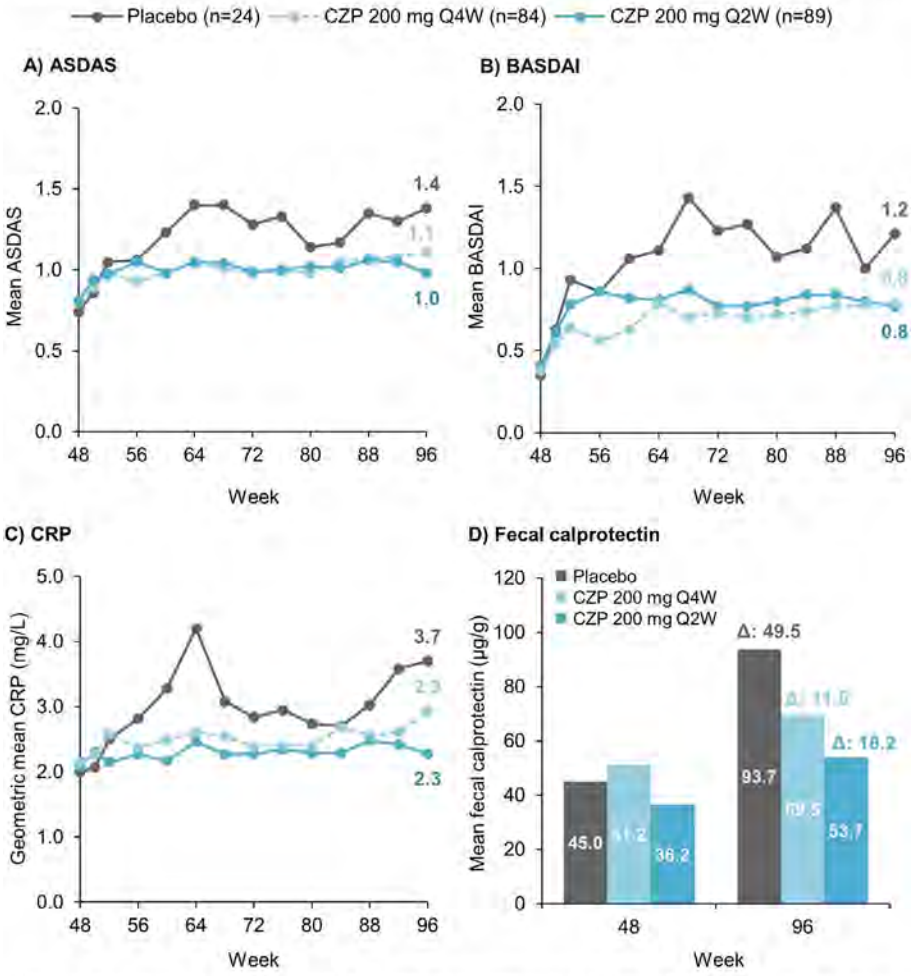
Session Time: 8:30AM–10:30AM

Background/Purpose: C-OPTIMISE was a phase 3b study investigating certolizumab pegol (CZP) maintenance dose continuation, reduction or withdrawal following achievement of sustained remission in patients with axial spondyloarthritis (axSpA). During the C-OPTIMISE maintenance period, the majority of patients randomized to CZP, either the full or reduced maintenance dose, did not experience disease flares. Conversely, in those who had CZP withdrawn, only a minority of patients remained flare-free.[1] This post-hoc analysis evaluates disease activity and clinical markers of inflammation in patients who did not experience a disease flare following randomization to CZP full maintenance dose, CZP reduced maintenance dose or placebo (PBO) during the C-OPTIMISE maintenance period (Weeks [Wks] 48–96).

Methods: C-OPTIMISE (NCT02505542) was a multicenter, double-blind, parallel-group, randomized phase 3b study with a 48-wk open-label run-in period.[1] Adult patients with early (< 5 years' symptom duration) active axSpA received open-label CZP 200 mg every 2 wks (Q2W) for the first 48 wks; from Wk 48, patients who achieved sustained remission (Ankylosing Spondylitis Disease Activity Score [ASDAS] < 1.3 at Wk 32/36 and Wk 48) were randomized 1:1:1 to double-blind CZP 200 mg Q2W (full maintenance dose), CZP 200 mg Q4W (reduced maintenance dose) or PBO for a further 48 wks (maintenance period). A flare was defined as ASDAS ≥2.1 at two consecutive visits or ASDAS >3.5 at any visit. We report ASDAS, BASDAI, and C-reactive protein (CRP) and fecal calprotectin levels during Wks 48–96 in CZP- and PBO-randomized patients who did not experience a flare (completed Wk 96 on randomized treatment). Missing data were imputed using last observation carried forward.

Results: Of 313 patients entering the maintenance period at Wk 48 (CZP 200 mg Q2W: 104; CZP 200 mg Q4W: 105; PBO: 104), 197 (62.9%) completed Wk 96 on randomized treatment without experiencing a flare; of these, 89 (85.6%) and 84 (80.0%) patients were in the CZP 200 mg Q2W and CZP 200 mg Q4W arm, respectively, with only 24 (23.1%) patients randomized to PBO not experiencing a flare. Baseline characteristics of patients are shown in the **Table**. During Wk 48–96, disease activity (ASDAS, BASDAI) and CRP levels were comparable between the CZP full and reduced maintenance dose group, and lower in both CZP arms than in PBO (**Figure A–C**). From Wk 60 up to Wk 96, PBO patients who did not flare had consistently higher mean ASDAS, BASDAI and CRP levels compared with CZP-randomized patients (**Figure A–C**). Similarly, there was a greater increase in fecal calprotectin levels between Wks 48 and 96 in the PBO arm compared with both CZP arms (**Figure D**).

Figure. (A) ASDAS, (B) BASDAI, (C) CRP and (D) fecal calprotectin in patients who did not experience a flare during the C-OPTIMISE maintenance period (Weeks 48–96)



Missing data were imputed using last observation carried forward. Δ values for fecal calprotectin show change from Week 48. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; CZP: certolizumab pegol; Q2W/Q4W: every 2/4 weeks.

Table. Baseline (Week 0) characteristics of patients who did not experience flares during the C-OPTIMISE maintenance period

	Placebo (n=24)	CZP 200 mg Q4W (n=84)	CZP 200 mg Q2W (n=89)
Age (years), mean (SD)	29.8 (7.4)	32.9 (6.7)	32.4 (7.2)
Male, n (%)	19 (79.2)	69 (82.1)	69 (77.5)
Time since diagnosis (years)			
Mean (SD)	2.0 (1.8)	2.0 (1.7)	2.5 (1.6)
Median	1.2	1.2	2.7
Symptom duration (years)			
Mean (SD)	2.7 (1.7)	3.4 (1.9)	3.9 (2.9)
Median	2.8	3.5	3.9
ASDAS, mean (SD)	3.4 (0.8)	3.7 (0.8)	3.7 (0.7)
BASDAI, mean (SD)	6.3 (1.1)	6.6 (1.5)	6.4 (1.4)
CRP (mg/L), geometric mean	6.28	7.88	7.35
Fecal calprotectin (µg/g), mean (SD)	71.8 (111.4)	87.1 (110.5)	81.0 (120.0)

ASDAS: Ankylosing Spondylitis Disease Activity Score; CZP: certolizumab pegol; Q2W: every 2 weeks; Q4W: every 4 weeks; SD: standard deviation.

Conclusion: Despite not meeting the threshold for a flare, numerically higher disease activity and increases in serologic and inflammatory biomarkers were observed in PBO-randomized patients who did not experience a flare compared to those who remained on CZP. These findings confirm that patients with axSpA who achieve sustained remission benefit from continued CZP treatment, either with the full or reduced maintenance dose, over treatment withdrawal.

References: 1. Ritchlin CT. Lancet 2020;395:427–40; **2**. McInnes IB. ARD 2020;79:1153–4.

Disclosure: L. Gensler, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **L. Bauer**, UCB Pharma, 3, 11; **B. Hoepken**, UCB Pharma, 3, 11; **T. Kumke**, UCB Pharma, 3; **M. Kim**, UCB Pharma, 3, 11; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6.

Abstract Number: 0917

Efficacy of Secukinumab and HLA-B27 Subtypes: Results from a Phase IIIb Randomised Controlled Trial in Axial SpA

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Human Leukocyte Antigen (HLA)-B is strongly associated with axial spondyloarthritis (axSpA); over 100 subtypes of HLA-B27 are currently recognized and designated as HLA-B*2701 to HLA-B*27106, defined by their DNA sequence.[1,2] The association of these subtypes with the clinical features of axSpA patients or their response to therapy has not been determined so far. In this post hoc analysis, we explored the potential association of the HLA-B27 subtypes with the effect of secukinumab (SEC) in axSpA patients from the SKIPPAIN trial (NCT03136861).

Methods: SKIPPAIN, a 24 week (wk), randomised, double-blind, placebo (PBO) controlled, multicenter trial, enrolled adult axSpA patients with active disease fulfilling ASAS classification criteria (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] score ≥4 and average spinal pain numerical rating scale [NRS] score >4 at baseline [BL]) and inadequate response to ≥2 NSAIDs for ≥4 wks. Patients were randomized (3:1) to receive subcutaneous SEC 150 mg or PBO wkly followed by every 4 wks (q4w) starting at Wk 4. At Wk 8, PBO patients were re-randomized to SEC 150 or 300 mg q4w up to Wk 24. HLA-B27 subtypes were tested by PCR-reverse sequence-specific oligonucleotide probe on a baseline blood sample. Average spinal pain scores were analysed using a repeated measures analysis of covariance (ANOVA) model.

Results: Overall 380 patients with axSpA (269 [70.8%] AS and 111 [29.2%] nr-axSpA) were randomised to SEC 150 mg (N=285) or PBO (N=95). Demographic and BL characteristics were previously reported.[3] Most patients enrolled in the study were HLA-B27 positive in both treatment groups (233 [81.8%] in the SEC vs. 76 [80.0%] in the PBO

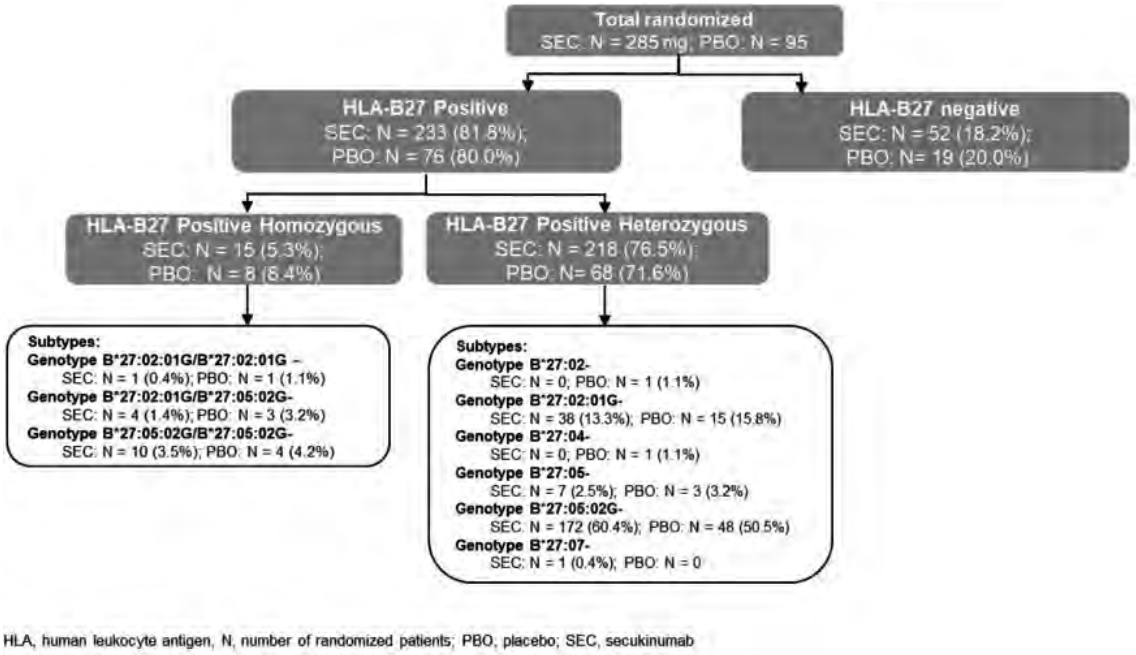

Figure 1. Distribution of HLA-B27 subtype patients.

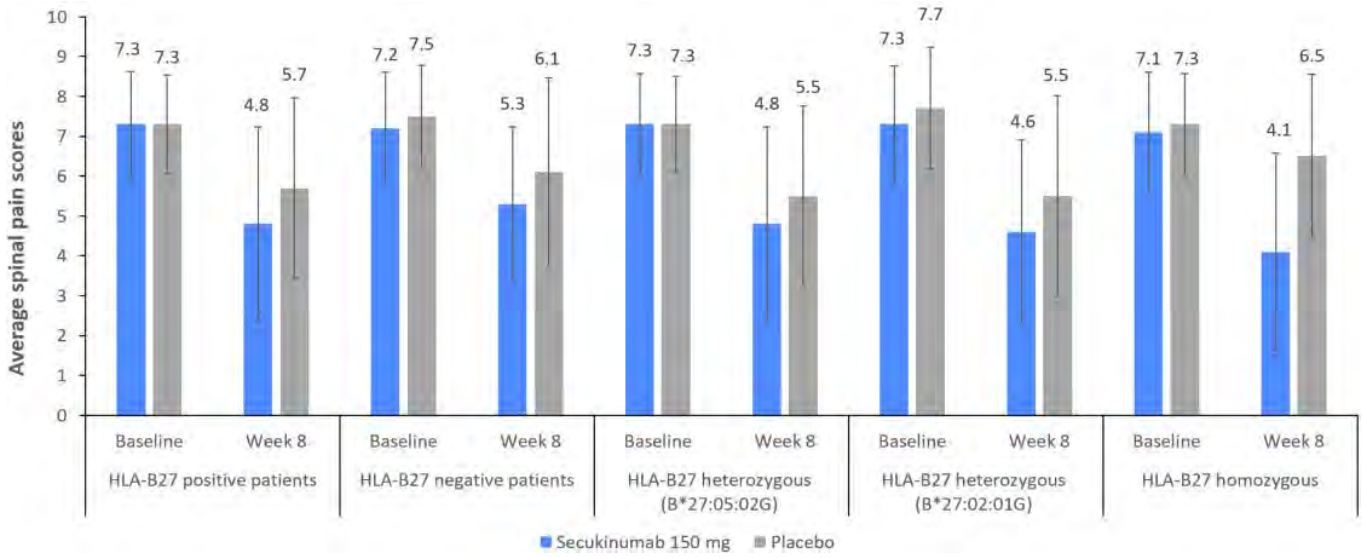

Figure 2. Average spinal pain scores in treatment groups by HLA-B27 status.

group). The distribution of HLA subtypes was consistent with what is expected in a typical European population[1], with HLA-B*27:05:02G as the most common allele **(Figure 1)**. In the HLA-B*27 homozygous group, a higher proportion of patients had uveitis, peripheral arthritis, enthesitis and a family history of spondyloarthritis, when compared to the heterozygous group; disease severity or burden of disease was similar between the two groups. Male predominance was more evident in the HLA-B*27 homozygous group who were younger by one year and reported longer duration of symptoms by an average of 8 months. Disease severity was comparable while disease burden was higher in B*27:05:02G compared with B27:02:01G heterozygous group. There were notable differences in the back pain response associated with B27 subtypes although the level of statistical significance could not always be reached due to the size of the subgroups (**Figure 2 and Table**).

Table 1. Average spinal pain scores (LS mean) at Week 8 and difference of LS Mean between the treatment groups, according to HLA-B27 status

Treatment Group	n	LS mean (SE)	LS mean difference (SE) between SEC vs PBO	95% CI	P-value
HLA-B27 positive patients					
Secukinumab 150 mg	279	5.1 (±0.19)	−0.9 (±0.27)	−1.47 to −0.42	**0.0004**
Placebo	92	6.0 (±0.27)			
HLA-B27 heterozygous (B*27:05:02G)					
Secukinumab 150 mg	167	5.1 (±0.24)	−0.9 (± 0.37)	−1.62 to −0.17	**0.0152**
Placebo	48	6.0 (±0.38)			
HLA-B27 heterozygous (B*27:02:01G)					
Secukinumab 150 mg	37	5.8 (±0.64)	−0.53 (±0.73)	−1.99 to 0.94	0.4748
Placebo	13	6.3 (±0.82)			
HLA-B27 homozygous					
Secukinumab 150 mg	15	4.7 (±1.23)	−2.45 (±1.26)	−5.23 to 0.32	0.0778
Placebo	8	7.2 (±1.45)			

Average spinal pain scores were analysed using a repeated measures analysis of covariance model with treatment, country, and the stratification factor of HLA-B27 as factors and the respective BL spinal pain score as covariate
CI, confidence interval; HLA, human leukocyte antigen; LS, least square; SE, standard error.

Conclusion: The spinal pain response after 8 weeks of treatment showed notable differences between HLA-B27 subgroups. Further studies or pooled analyses are warranted to investigate associations of the HLA-B27 subtypes with the clinical features of axSpA or of less prevalent HLA-B27 subtypes with response to treatment.

References

1. Bowness P. *Annu Rev Immunol* 2015;33:29-48
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3. Poddubnyy D, et al. *ARD* 2020;79:1624-1625

Disclosure: D. Poddubnyy, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **E. Pournara**, Novartis, 3, 11; **B. Schulz**, Novartis, 3; **S. Sadhu**, Novartis, 3; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **H. Marzo-Ortega**, Janssen, 2, 5, 6, Takeda, 6, Novartis, 2, 5, 6, UCB, 2, 5, 6, Celgene, 2, 6, AbbVie, 2, 6, Lilly, 2, 6, Pfizer, 2, 6.

Abstract Number: 0918

Individual Components Contributing to the Achievement of Assessment in SpondyloArthritis International Society 40 Response in Biologic Naïve Patients with Radiographic Axial Spondyloarthritis: Results from the COAST V Trial

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Ixekizumab (IXE), an IL-17A antagonist, is effective in patients with radiographic axial spondyloarthritis (rad-axSpA). Assessment in SpondyloArthritis International Society (ASAS) 40 response – the primary study endpoint – was achieved at week (wk) 16 by 48% of those treated with 80mg subcutaneous IXE every 4 wks (Q4W) in the phase 3 COAST V trial (NCT 02696785) [1]. Until now, no information has been available on the efficacy of IXE on the components of the ASAS40 composite endpoint. Our objective is to describe which individual components of ASAS40 drive the achievement of efficacy response.

Methods: This exploratory post-hoc analysis was based on COAST V data. Patients enrolled in COAST V met ASAS criteria for rad-axSpA and were biological disease-modifying antirheumatic drug (bDMARD)-naïve. Patients were assigned 1:1:1:1 to subcutaneous placebo (PBO), IXE Q4W, IXE Q2W or 40 mg adalimumab (ADA). Only data for approved doses are shown.

To reach ASAS40 response, patients must have an improvement of at least 40% and at least 2 units for at least 3 of 4 individual components which define response (patient global assessment of disease activity, spinal pain, inflammation (defined as the mean of Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) questions 5 and 6), and function (Bath Ankylosing Spondylitis Functional Index - BASFI)), without worsening in the remaining component. We describe the percentage of patients who achieved this change, had an insufficient response, or deteriorated in each component out to wk 16 for IXE Q4W, ADA and PBO. The time course of the change from baseline in individual components of the ASAS response is depicted descriptively per treatment arm by use of the mean and standard deviation. Observed data have been utilised.

Table 1. Observed changes from baseline (CFB), percentage improvements and response status of patients enrolled in COAST V trial at wk 16

Measure	*Observed CFB (SD)*	*Observed % improvement (SD)*	*Improvement >=40% and >=2 units, n (%)*	*Insufficient response, n (%)*	*Deteriorated, n (%)*
IXE Q4W (N=78)					
Patient global assessment	-2.6 (2.9)	32.3 (51.1)	39 (50.0)	30 (38.5)	9 (11.5)
Spinal pain	-3.3 (2.7)	43.4 (34.4)	47 (60.3)	27 (34.6)	4 (5.1)
Inflammation*	-3.2 (2.5)	46.8 (32.8)	47 (60.3)	25 (32.0)	6 (7.7)
Function	-2.5 (2.3)	39.6 (31.0)	34 (43.6)	37 (47.4)	7 (9.0)
ADA (N=88)					
Patient global assessment	-2.6 (2.4)	35.2 (33.4)	35 (39.8)	48 (54.5)	5 (5.7)
Spinal pain	-2.6 (2.4)	36.8 (34.7)	38 (43.2)	44 (50.0)	6 (6.8)
Inflammation*	-2.6 (2.4)	38.4 (36.9)	42 (47.7)	37 (42.0)	9 (10.2)
Function	-2.1 (2.2)	35.2 (34.3)	31 (35.2)	48 (54.6)	9 (10.2)
PBO (N=86)					
Patient global assessment	-1.5 (2.0)	18.0 (37.9)	21 (24.4)	54(62.8)	11(12.8)
Spinal pain	-1.9 (1.9)	25.8 (26.7)	23 (26.8)	55(64.0)	8(9.3)
Inflammation*	-1.4 (1.9)	20.9 (33.9)	19 (22.1)	53 (61.6)	14 (16.3)
Function	-1.3 (1.8)	19.1 (31.6)	16 (18.6)	51 (59.3)	19 (22.1)

Inflammation is mean of BASDAI 5 (Morning stiffness severity) and BASDAI 6 (Morning stiffness duration)

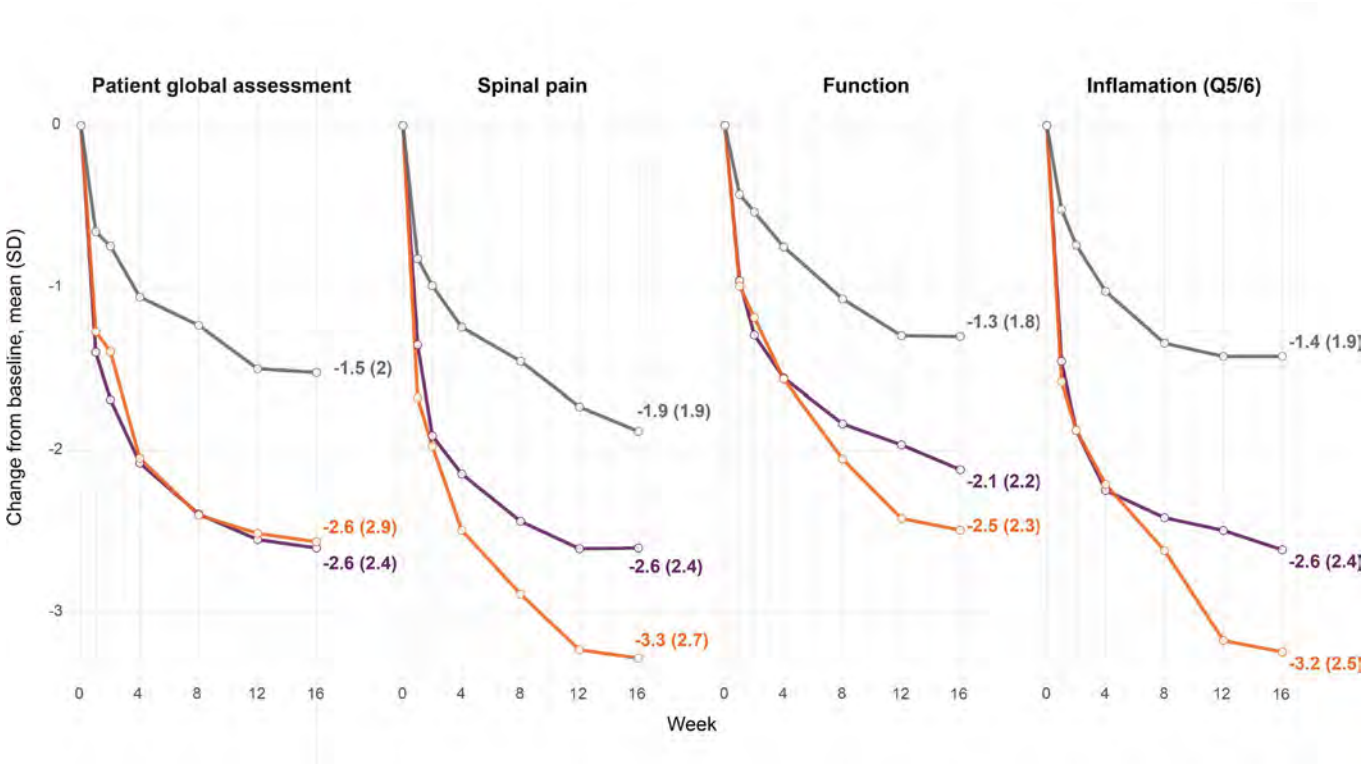

Figure 1. Mean (SD) change from baseline (observed) on individual components of ASAS 40 response by treatment arm and wk.

Results: IXE Q4W response at 16 wks was driven by all 4 individual components of the ASAS40 with the largest improvements for patients treated with IXE Q4W seen in inflammation and spinal pain (Fig. 1).

At wk 16, at least 50% of all patients treated with IXE Q4W achieved response on spinal pain (60.3%), inflammation (60.3%) and patient global assessment (50%), with 43.6% of patients meeting the response criteria for function (Table 1). The corresponding results for ADA were 43.2%, 47.7% 39.8%, and 35.2%.

Conclusion: Our findings show that meeting ASAS40 response criterion for an individual component at 16 wks by patients treated with IXE Q4W was broadly similar between individual components. However, a clinically relevant improvement was more frequently observed for the spinal pain and inflammation components.

1). Dougados, M., et al. (2020). Ann Rheum Dis **79**(2): 176-185.

Disclosure: D. **Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **S. Attar**, None; **M. Nissen**, AbbVie, 2, Eli Lilly and Company, 2, 6, Janssen, 2, 6, MSD, 2, Novartis, 2, 6; **E. Fillipi**, Eli Lilly and Company, 3, 11; **H. Russ**, Eli Lilly and Company, 3; **A. Erdogan**, Eli Lilly and Company, 3, 11; **Y. Schymura**, Eli Lilly and Company, 3, 11; **S. Liu-Leage**, Eli Lilly and Company, 3, 11; **E. Collantes-Estevez**, Novartis, 1, Eli Lilly and Company, 1, Janssen, 1, AbbVie, 1, UCB, 1; **F. Ciccia**, Eli Lilly and Company, 1, 2, 6, AbbVie, 1, 2, 6, Celgene, 1, 2, 6, Amgen, 1, 2, 6, Novartis, 1, 2, 6, Janssen, 1, 2, 6, UCB, 1, 2, 6, Roche, 1, 2, 6, Pfizer, 1, 2, 6, Galapagos, 1, 2, 6, Glaxo, 1, 2, 6.

Abstract Number: 0919

Ixekizumab Shows a Distinct Pattern of Pain Improvement Beyond Measurable Inflammation as Assessed by MRI or CRP or BASDAI Questions 5 & 6 in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Ixekizumab (IXE) demonstrated rapid efficacy in patients (pts) with AS at week (W) 16 in the absence of elevated inflammation as measured by baseline serum CRP values or spinal MRI Spondyloarthritis Research Consortium of Canada (SPARCC) score.[1] This analysis evaluated the improvement in pain with IXE based on longitudinal status of objective measures of inflammation by MRI, CRP value, and BASDAI 5/6 over 16W.

Methods: The Phase III COAST-V (NCT02696785) 52W, multi-center, randomized, double-blind, placebo (PBO)-controlled study examined the efficacy of IXE in pts with active AS. Adalimumab (ADA) was used as an active reference arm for the first 16W. Pts originally assigned to PBO or ADA were re-randomized to IXE at W16. Change in spinal pain at night (SP-N) and Short Form 36 Health Survey Questionnaire (SF-36) Bodily Pain were measured during study visits and analyzed while controlling for inflammation status using MRI, CRP levels and mean of BASDAI 5/6 (Q5: Duration, Q6: Intensity of morning stiffness). Observed data analyses are presented for each group stratified by treatment arm. Initial analysis: 'controlled inflammation' is defined as MRI SPARCC SI joint <4 and MRI SPARCC Spine $<3^2$ at W16, CRP < 5mg/L at every visit W4-16, or BASDAI 5/6 improvement of ≥2 points W12 and W16. 'Not Controlled' are noted in figure legends. Second analysis: control is defined as CRP < 5 mg/L at every week between W4-16 and MRI SPARCC SI joint <4 at W16 and MRI SPARCC Spine <3 at W16.

Results: When inflammation is controlled per MRI, pts treated (tx) with IXEQ4W (-3.9 $p < 0.001$) and ADA (-2.8 $p=0.02$) experienced significant reduction in SP-N vs PBO (-1.6) at W16, further improvements were experienced in pts rerandomized to IXE by W52 (Fig1A). When inflammation was not controlled per MRI, IXEQ4W (-3.5 $p < 0.01$) and ADA (-3.1 $p=0.02$) experienced significant reduction in SP-N at W16, all IXE tx pts had further reductions at W52 (Fig1B). When inflammation was controlled per MRI+CRP, IXEQ4W (-3.8 $p=0.2$) and ADA (-3.1 $p=0.4$) had reduction in SP-N at W16 vs PBO (-2.4), all IXE groups had further improvements at W52 (Fig2A). When inflammation was not controlled as measured by MRI+CRP, IXEQ4W (-3.7 $p < 0.001$) had significant reduction in SP-N vs PBO (-1.7), whereas improvement with ADA (-2.6 $p=0.06$) was not significant, all IXE tx pts had further reduction by W52 (Fig1B). For SF-36 bodily pain, improvements were observed at W16 and W52 whether inflammation was controlled or not controlled per MRI, CRP, MRI+CRP, or BASDAI 5/6 (Table 1).

Conclusion: This analysis adds support to the hypothesis that IXE improves pain in pts with and without measurable inflammation.

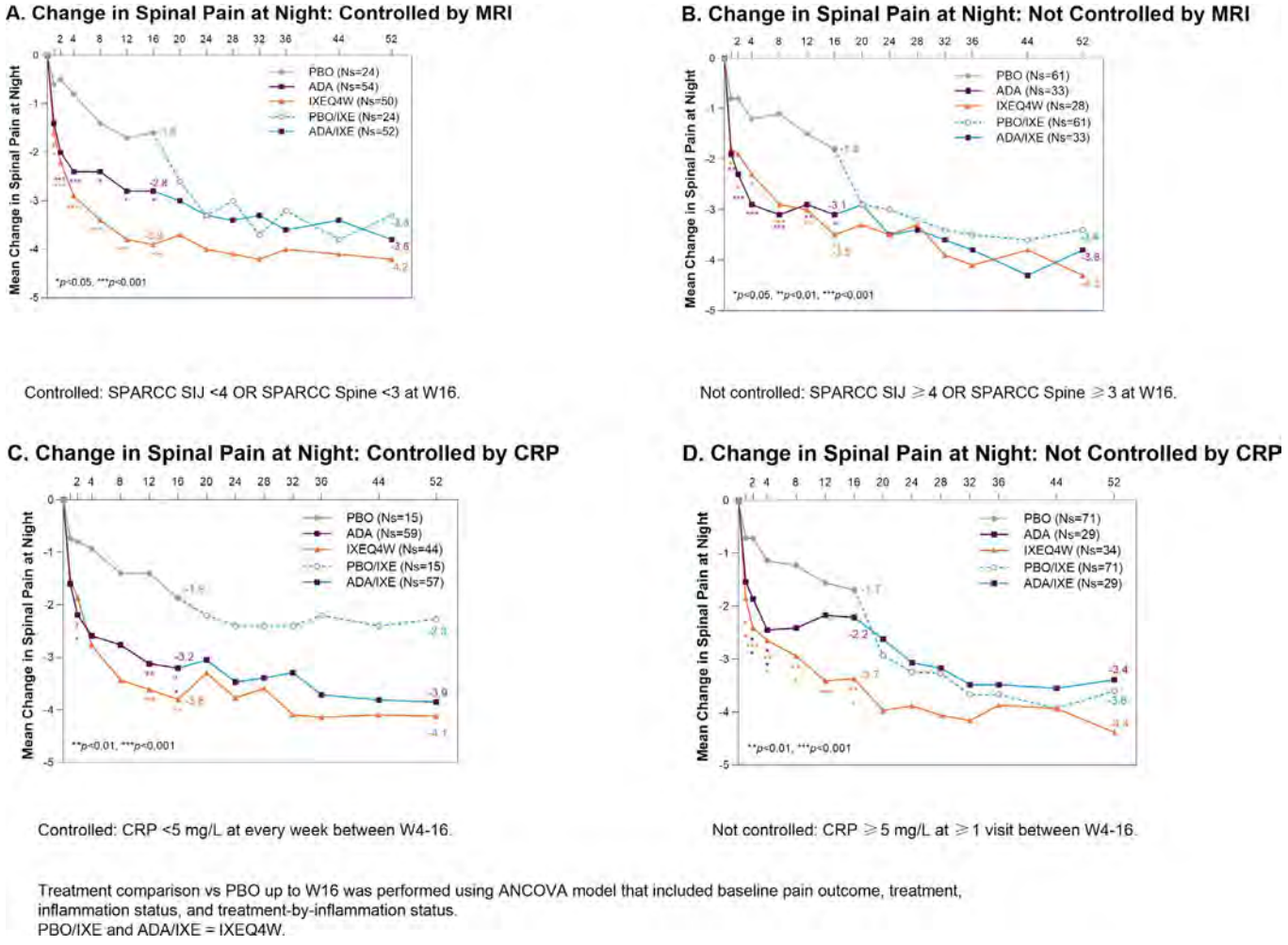


Figure 1. Change in Spinal Pain at Night over 52 weeks by MRI and CRP.

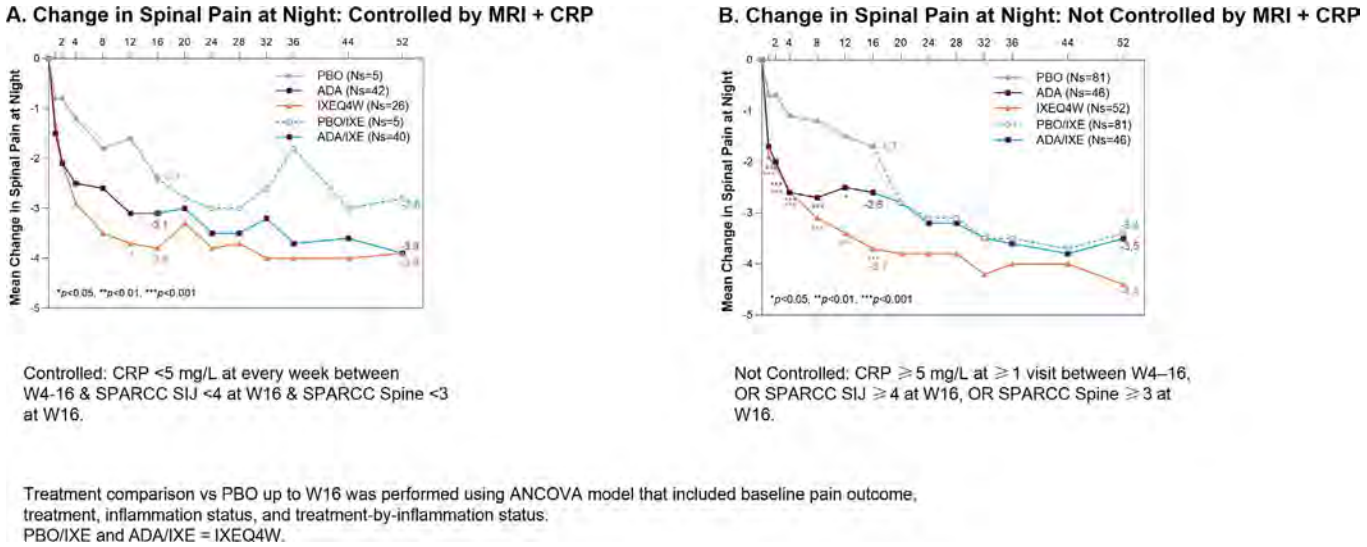


Figure 2. Change in Spinal Pain at Night over 52 weeks by MRI + CRP.

	Controlled			Not Controlled		
	Change in Spinal Pain at Night by BASDAI 5/6 (≥ 2-point improvement in BASDAI Inflammation at Week 12 and Week 16)					
	PBO (Ns=24)	IXEQ4W (Ns=48)	ADA (Ns=43)	PBO (Ns=62)	IXEQ4W (Ns=30)	ADA (Ns=45)
Baseline (mean (SD))	7.1 (1.9)	7.1 (1.6)	7.3 (1.8)	7.1 (1.6)	7.0 (1.1)	6.6 (1.7)
Week 16	-3.2 (2.0)	-4.7 (2.2) **	-4.6 (2.3) **	-1.2 (1.6)	-2.2 (2.7) *	-1.2 (1.8)
	PBO/IXE (Ns=24)	IXEQ4W (Ns=48)	ADA/IXE (Ns=42)	PBO/IXE (Ns=62)	IXEQ4W (Ns=30)	ADA/IXE (Ns=44)
Week 52	-4.6 (2.1)	-4.9 (2.2)	-4.9 (2.3)	-2.9 (2.7)	-2.9 (2.3)	-2.5 (2.4)
	Change in SF-36 Bodily Pain by MRI (SPARCC SIJ <4 and SPARCC Spine <3 at Week 16)					
	PBO (Ns=24)	IXEQ4W (Ns=50)	ADA (Ns=54)	PBO (Ns=61)	IXEQ4W (Ns=28)	ADA (Ns=33)
Baseline (mean (SD))	37.0 (19.8)	40.0 (15.9)	38.6 (16.2)	34.0 (16.0)	35.4 (16.9)	35.8 (14.8)
Week 16	11.9 (17.3)	22.5 (21.9) *	19.4 (19.0)	10.9 (16.4)	22.3 (19.7) **	23.0 (21.8) **
	PBO/IXE (Ns=24)	IXEQ4W (Ns=50)	ADA/IXE (Ns=52)	PBO/IXE (Ns=61)	IXEQ4W (Ns=28)	ADA/IXE (Ns=33)
Week 52	22.3 (24.6)	25.7 (21.6)	21.9 (19.6)	24.3 (19.2)	31.6 (26.4)	29.8 (18.3)
	Change in SF-36 Bodily Pain by CRP (CRP <5 mg/L at every week between Weeks 4-16)					
	PBO (Ns=15)	IXEQ4W (Ns=44)	ADA (Ns=59)	PBO (Ns=71)	IXEQ4W (Ns=34)	ADA (Ns=29)
Baseline (mean (SD))	33.2 (12.3)	38.4 (17.6)	38.4 (14.7)	35.2 (17.9)	38.3 (14.6)	35.6 (17.4)
Week 16	11.8 (12.5)	24.3 (21.5) **	23.7 (20.5) **	10.6 (17.6)	20.0 (20.4) **	13.0 (19.6)
	PBO/IXE (Ns=15)	IXEQ4W (Ns=44)	ADA/IXE (Ns=57)	PBO/IXE (Ns=71)	IXEQ4W (Ns=34)	ADA/IXE (Ns=29)
Week 52	14.7 (15.7)	28.8 (24.5)	26.2 (21.9)	25.8 (21.3)	26.0 (21.6)	21.8 (14.5)
	Change in SF-36 Bodily Pain by MRI + CRP (SPARCC SIJ <4 and SPARCC Spine <3 at Week 16 + CRP <5 mg/L at every week between Weeks 4-16)					
	PBO (Ns=5)	IXEQ4W (Ns=26)	ADA (Ns=42)	PBO (Ns=81)	IXEQ4W (Ns=52)	ADA (Ns=46)
Baseline (mean (SD))	41.8 (14.2)	40.6 (16.7)	39.5 (14.4)	34.5 (17.2)	37.2 (16.1)	35.7 (16.6)
Week 16	16.0 (8.8)	23.7 (21.1)	22.2 (18.8)	10.5 (17.1)	21.8 (21.1) ***	18.3 (22.4) *
	PBO/IXE (Ns=5)	IXEQ4W (Ns=26)	ADA/IXE (Ns=40)	PBO/IXE (Ns=62)	IXEQ4W (Ns=30)	ADA/IXE (Ns=44)
Week 52	12.2 (8.1)	25.6 (20.6)	23.5 (21.8)	24.5 (21.2)	28.8 (24.8)	25.6 (18.0)
	Change in SF-36 Bodily Pain by BASDAI 5/6 (≥ 2-point improvement in BASDAI Inflammation at Week 12 and Week 16)					
	PBO (Ns=24)	IXEQ4W (Ns=48)	ADA (Ns=43)	PBO (Ns=62)	IXEQ4W (Ns=30)	ADA (Ns=45)
Baseline (mean (SD))	38.2 (19.0)	37.4 (17.9)	36.0 (15.4)	33.6 (16.2)	39.9 (13.4)	38.9 (15.8)
Week 16	21.2 (17.9)	31.3 (21.0) *	31.5 (18.2) *	6.8 (14.6)	8.2 (10.9)	9.4 (17.1)
	PBO/IXE (Ns=24)	IXEQ4W (Ns=48)	ADA/IXE (Ns=42)	PBO/IXE (Ns=62)	IXEQ4W (Ns=30)	ADA/IXE (Ns=44)
Week 52	29.5 (19.7)	35.0 (24.1)	32.5 (18.1)	21.6 (20.9)	14.0 (14.0)	17.0 (18.2)

Data presented as observed change (standard deviation) unless otherwise stated. *$p<0.05$; **$p<0.01$; ***$p<0.001$
Not Controlled definitions: BASDAI=<2 point improvement in BASDAI Inflammation at W12 OR W16; MRI=SPARCC SIJ ≥4 OR SPARCC Spine ≥3 at W16; CRP= CRP ≥5 mg/L at ≥1 visit between W4-16; MRI + CRP= CRP ≥5 mg/L at ≥1 visit between W4–16, OR SPARCC SIJ ≥4 at W16, OR SPARCC Spine ≥3 at W16. Treatment comparison vs PBO up to W16 was performed using ANCOVA model that included baseline pain outcome, treatment, inflammation status, and treatment-by-inflammation status. PBO/IXE and ADA/IXE = IXEQ4W.

Table 1. Change in Spinal Pain at Night by BASDAI 5/6, and Change in SF-36 by MRI, CRP, MRI + CRP and BASDAI 5/6.

References

1. Maksymowych et al. ACR. 2021.
2. Maksymowych et al. Rheumatology (in press) https://doi.org/10.1093/rheumatology/keab099.

Disclosure: K. de Vlam, Amgen, 6, 7, AbbVie, 6, Celgene, 2, 5, 6, Eli Lilly, 2, Johnson & Johnson, 2, Novartis, 2, 6, Galapagos, 2, 7, UCB, 2, 6, 7; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **V. Krishnan**, Eli Lilly and Company, 3, 11; **R. Bolce**, Eli Lilly and Company, 3, 11; **D. Sandoval Calderon**, Eli Lilly and Company, 3; **S. Park**, Eli Lilly and Company, 3, 11; **G. Gallo**, Eli Lilly and Company, 3; **W. Maksymowych**, Abbvie, 2, 5, 6, BMS, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0920

Influence of Baseline Demographics on Improvements in Disease Activity Measures in Patients with Ankylosing Spondylitis Receiving Upadacitinib: A Post Hoc Subgroup Analysis

Filip Van den Bosch[1], Denis Poddubnyy[2], Jayne Stigler[3], Andrew Ostor[4], Salvatore D'Angelo[5], Victoria Navarro-Compán[6], In-Ho Song[3], Tianming Gao[3], Fabiana Ganz[3] and Lianne Gensler[7], [1]Dept. of Rheumatology - Ghent University Hospital, Ghent, Belgium, Ghent, Belgium, [2]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [3]AbbVie Inc., North Chicago, IL, [4]Monash University, Cabrini Hospital, and Emertius Research, Malvern, Australia, [5]Rheumatology Institute of Lucania (IReL) – Rheumatology Department of Lucania, "San Carlo" Hospital of Potenza and "Madonna delle Grazie" Hospital of Matera, Potenza, Italy, [6]Rheumatology service, Hospital Universitario La Paz-IdiPaz, Madrid, Spain, [7]Department of Rheumatology, University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Upadacitinib (UPA), an oral Janus kinase inhibitor, has demonstrated efficacy and safety through 14 weeks in the SELECT-AXIS 1 study in biologic disease-modifying antirheumatic drug-naïve patients with

Table PBO-corrected mean change from baseline (95% CI) in ASDAS(CRP) at Week 14 in patients receiving UPA 15 mg by baseline subgroups (MMRM)

		n		ASDAS(CRP)
Subgroup		**UPA 15 mg**	**PBO**	**PBO-corrected mean change from baseline (95% CI)**
Gender	Male	58	62	–1.11 (–1.37, –0.84)
	Female	26	22	–0.44 (–0.92, 0.03)
Age	<40 years	24	36	–1.00 (–1.42, –0.58)
	40–<65 years	51	46	–0.88 (–1.17, –0.59)
Body mass index	<25 kg/m²	32	37	–0.92 (–1.30, –0.55)
	≥25 kg/m²	52	47	–0.89 (–1.20, –0.59)
AS symptom duration	<5 years	16	17	–0.90 (–1.46, –0.34)
	≥5 years	68	67	–0.92 (–1.18, –0.66)
Baseline hsCRP	≤2.8 mg/L	23	19	–0.59 (–1.02, –0.15)
	>2.8–<10 mg/L	39	34	–0.59 (–0.95, –0.23)
	≥10 mg/L	22	31	–1.64 (–2.01, –1.27)
Inflammation based on SPARCC MRI scores	Positive[a]	56	57	–0.98 (–1.27, –0.69)
	Negative[b]	21	16	–0.60 (–1.08, –0.12)
HLA-B27 status	Positive	62	66	–0.97 (–1.24, –0.71)
	Negative	20	17	–0.73 (–1.28, –0.17)

[a]Spine SPARCC score ≥2 or sacroiliac joint SPARCC score ≥2. [b]Spine SPARCC score <2 and sacroiliac joint SPARCC score <2

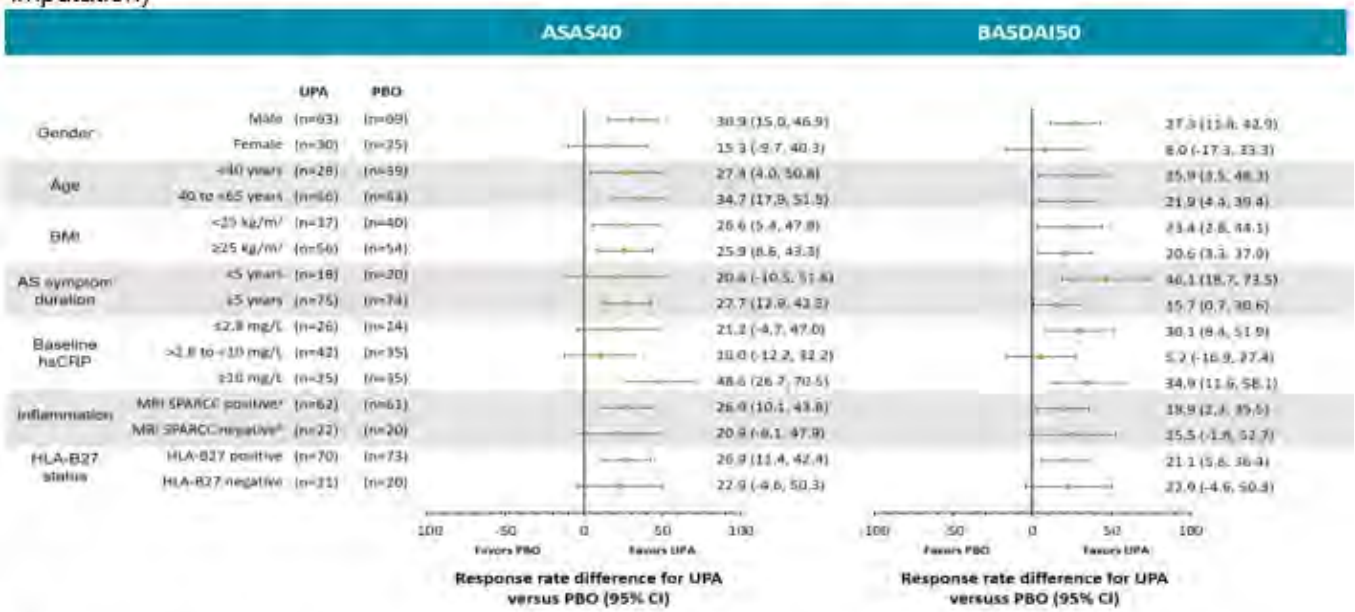
ASDAS(CRP), Ankylosing Spondylitis Disease Activity Score with C-reactive protein; CI, confidence interval; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; MMRM, mixed model repeated measures; MRI, magnetic resonance imaging; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib

active ankylosing spondylitis (AS).[1] The objective of this analysis was to evaluate the efficacy of UPA 15 mg once daily (QD) in selected subgroups of patients with AS based on different baseline characteristics.

Methods: In SELECT-AXIS 1, patients were randomized to 14 weeks of blinded treatment with UPA 15 mg QD or placebo (PBO). This post hoc analysis evaluated the proportions of patients achieving ≥40% improvement in Assessment of SpondyloArthritis International Society criteria (ASAS40), ≥50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), and change from baseline in Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS[CRP]) at Week 14 across subgroups based on the following baseline patient characteristics: gender, age, body mass index, AS symptom duration, C-reactive protein (CRP) levels, Spondyloarthritis Research Consortium of Canada Magnetic Resonance Imaging index, and human leukocyte antigen B27 status. For missing data, non-responder imputation analysis was used for ASAS40 and BASDAI50, and mixed model repeated measures analysis was used for ASDAS(CRP).

Results: Baseline disease characteristics were balanced between the treatment groups at randomization, as previously reported.[1] ASAS40 and BASDAI50 response rates at Week 14 were numerically higher with UPA 15 mg versus PBO across the demographic and disease characteristic subgroups evaluated (**Figure**), including some subgroups with small sample sizes, such as patients with disease duration < 5 years and female patients. Improvements from baseline in ASDAS(CRP) were also consistently greater with UPA 15 mg versus PBO across the subgroups evaluated (**Table**).

Figure Response rate difference for UPA versus PBO (95% CI) for ASAS40 and BASDAI50 responses at Week 14 in patients receiving UPA 15 mg by baseline subgroups (non-responder imputation)



[a]Spine SPARCC score ≥2 or sacroiliac joint SPARCC score ≥2. [b]Spine SPARCC score <2 and sacroiliac joint SPARCC score <2

AS, ankylosing spondylitis; ASAS40, ≥40% improvement in Assessment of SpondyloArthritis International Society criteria; BASDAI50, ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; CI, confidence interval; HLA-B27, human leukocyte antigen B27; hsCRP, high-sensitivity C-reactive protein; MRI, magnetic resonance imaging; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; UPA, upadacitinib

Conclusion: Within subgroups evaluated, most patients with active AS receiving UPA 15 mg demonstrated greater improvements versus PBO in disease activity measures assessed by ASAS40, BASDAI50, and change from baseline in ASDAS(CRP). There was some evidence that gender, AS symptom duration, and baseline CRP levels seemed to influence outcomes, though results should be interpreted with caution due to small sample sizes for some subgroups.

Reference: 1. van der Heijde D, et al. *Lancet* 2019;394:2108–17.

Disclosure: F. Van den Bosch, AbbVie, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Galapagos, 2, 6, Gilead, 2, 6; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **J. Stigler**, AbbVie, 3, 11; **A. Ostor**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Janssen, 1, 2, UCB, 1, 2, Paradigm, 1, 2; **S. D'Angelo**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, UCB, 2, 6; **V. Navarro-Compán**, Abbvie, 5, Lilly, 5, Novartis, 5, Pfizer, 5, UCB, 5, Janssen, 5; **I. Song**, AbbVie, 3, 11; **T. Gao**, AbbVie, 3, 11; **F. Ganz**, AbbVie, 3, 11; **L. Gensler**, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2.

Abstract Number: 0921

Effect of Secukinumab on Radiographic Progression and Inflammation in Sacroiliac Joints and Spine in Patients with Non-radiographic Axial Spondyloarthritis: 2-year Imaging Outcomes from a Phase III Randomized Trial

Juergen Braun[1], Ricardo Blanco[2], Helena Marzo-Ortega[3], Lianne Gensler[4], Filip Van den Bosch[5], Stephen Hall[6], Hideto Kameda[7], Denis Poddubnyy[8], Marleen van de Sande[9], Désirée van der Heijde[10], Tingting Zhuang[11], Anna Stefanska[12], Aimee Readie[11], Hanno Richards[13] and Atul Deodhar[14], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany, [2]Hospital University Marqués de Valdecilla, IDIVAL, Division of Rheumatology, Santander, Spain, [3]NIHR Leeds Biomedical Research Centre and University of Leeds, Leeds, United Kingdom, [4]Department of Rheumatology, University of California San Francisco, San Francisco, CA, [5]Dept. of Rheumatology - Ghent University Hospital, Ghent, Belgium, Ghent, Belgium, [6]Emeritus Research and Monash University, Melbourne, Australia, Melbourne, Australia, [7]Division of Rheumatology, Department of Internal Medicine, Faculty of Medicine, Toho University, Tokyo, Japan, [8]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany, [9]Amsterdam UMC, University of Amsterdam, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, [10]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands, [11]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [12]Novartis Ireland Limited, Dublin, Ireland, Dublin, Ireland, [13]Novartis Pharma AG, Basel, Switzerland, [14]Oregon Health & Science University, Portland, OR

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

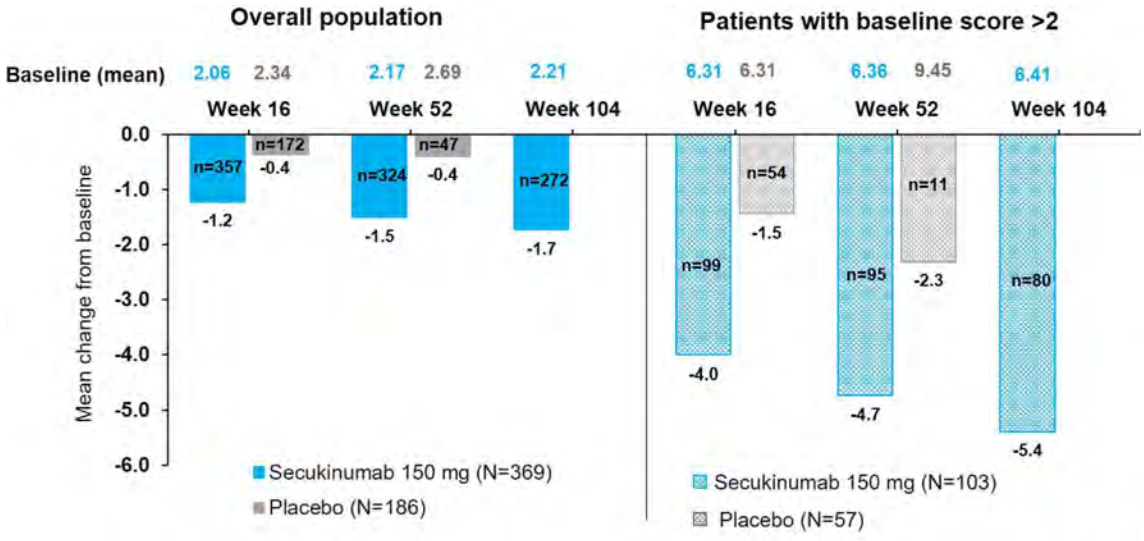
Background/Purpose: Axial spondyloarthritis (axSpA) is characterized by inflammation of the sacroiliac joints (SIJ) and the spine. Secukinumab (SEC) treatment was clinically efficacious and reduced SIJ bone marrow edema as detected by magnetic resonance imaging (MRI) in patients with non-radiographic (nr)-axSpA through 52 weeks in PREVENT (NCT02696031) study.[1] Here, we report radiographic progression and the course of inflammation as assessed by X-ray and MRI of SIJ and spine, over 2 years in the study.

Methods: Study design, key endpoints have been reported.[1] In total, 555 patients were randomized (1:1:1) to receive SEC 150mg with (LD) or without loading (NL) doses, or placebo (PBO). Switch to open-label (OL) SEC or standard of

care (SoC) was permitted after Week 20. All patients (except those who switched to SoC) received OL SEC from Week 52. Radiographs of the spine and SIJ were collected at baseline (BL) and Week 104; MR images of the spine and SIJ were collected at BL, Weeks 16, 52, and 104. Spinal radiographs were scored using the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) and SIJ radiographs according to modified New York criteria (mNYC). Spinal MR images were assessed for signs of inflammation with the Berlin score. SIJ bone marrow edema was assessed according to the Berlin Active Inflammatory Lesions Scoring. All images were evaluated in blinded fashion independently by two central readers. All data are reported from the Week 104 reading session and are presented as observed.

Results: The vast majority (98%) of patients treated with SEC 150mg (pooled LD and NL) showed no structural progression, defined as change in total mSASSS score ≤ smallest detectable change (SDC) of 0.760 (80% agreement level) over 2 years. At BL, 62 patients (43 in SEC 150mg, 19 in PBO) presented with at least one syndesmophyte (at least one vertebral unit scored by at least 1 reader). Among these patients, 9 in the SEC 150mg (20.9%) and 7 in the PBO (36.8%) groups had developed at least one new syndesmophyte by Week 104. Among 237 (SEC 150mg) and 117 (PBO) patients without syndesmophytes at BL, only 4 patients on SEC 150mg (1.7%) and 4 patients on PBO (3.4%) developed at least one new syndesmophyte by Week 104. SIJ radiographs showed that 88% (SEC 150mg) and 86% (PBO) patients had no progression in SIJ [defined as change ≤ SDC (0.458) in total mNYC score] by Week 104. No patient had an increase in that score of 2 or more. Spinal inflammation on MRI (Berlin score) was low at BL: mean 0.82 (SEC 150mg) and 1.07 (PBO) with no change at Week 104: 0.56 (SEC 150mg). SEC reduced SIJ bone marrow edema score versus PBO at Week 16 and Week 52 with sustained reduction through Week 104 in the overall patient population, with greater reduction in patients with BL score > 2 (**Figure)**.

Conclusion: Secukinumab reduced SIJ inflammation (SIJ bone marrow edema) in patients with active nr-axSpA. The majority of patients initially randomized to secukinumab or placebo showed no radiographic progression through 2 years.



Data presented are as observed. Secukinumab (pooled) included patients who continued on secukinumab to Week 104. Placebo included only patients randomized to placebo who remained on placebo to Week 52. At each time point, only patients with a value at both Baseline and that time point are included.
MRI, magnetic resonance imaging; n, number of evaluable patients; N, total number of randomized patients; SIJ, sacroiliac joint

Mean change in SIJ bone marrow edema score by MRI in the overall population and in patients with baseline score >2 through Week 104.

References

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Abstract Number: 0922

Bimekizumab Shows Sustained and Meaningful Long-Term Improvements in Health-Related Quality of Life in Ankylosing Spondylitis: Interim Results After 3 Years of Treatment in an Ongoing Phase 2b Study

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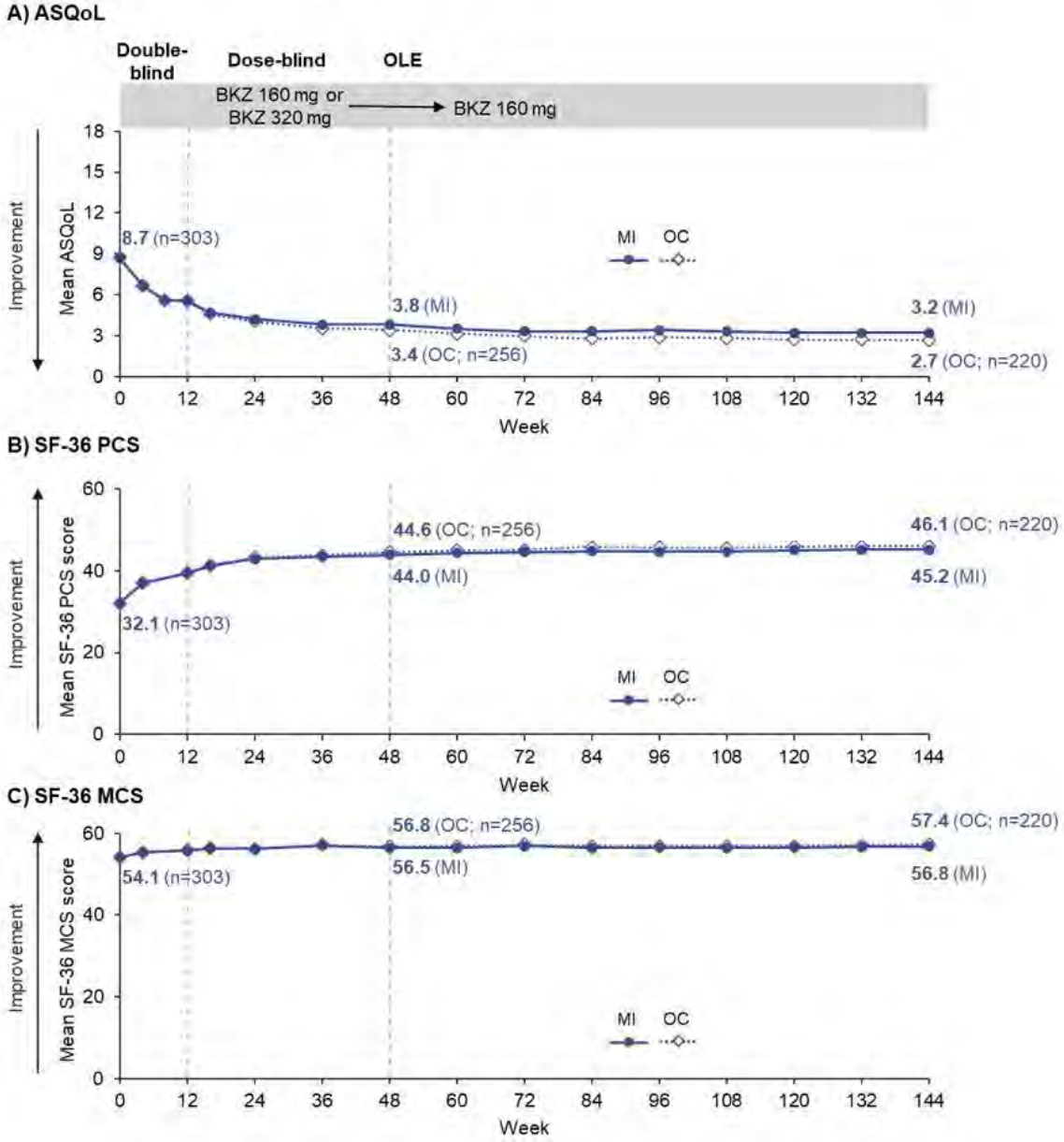
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that selectively inhibits both interleukin (IL)-17F and IL-17A, has been demonstrated to be efficacious and well tolerated in patients (pts) with ankylosing

spondylitis (AS) treated for up to 3 years (yrs).[1–3] We report 3-yr interim health-related quality of life (HRQoL) in pts with active AS from a 1-yr phase 2b study (BE AGILE; NCT02963506) and its ongoing 4-yr open-label extension (OLE; NCT03355573).

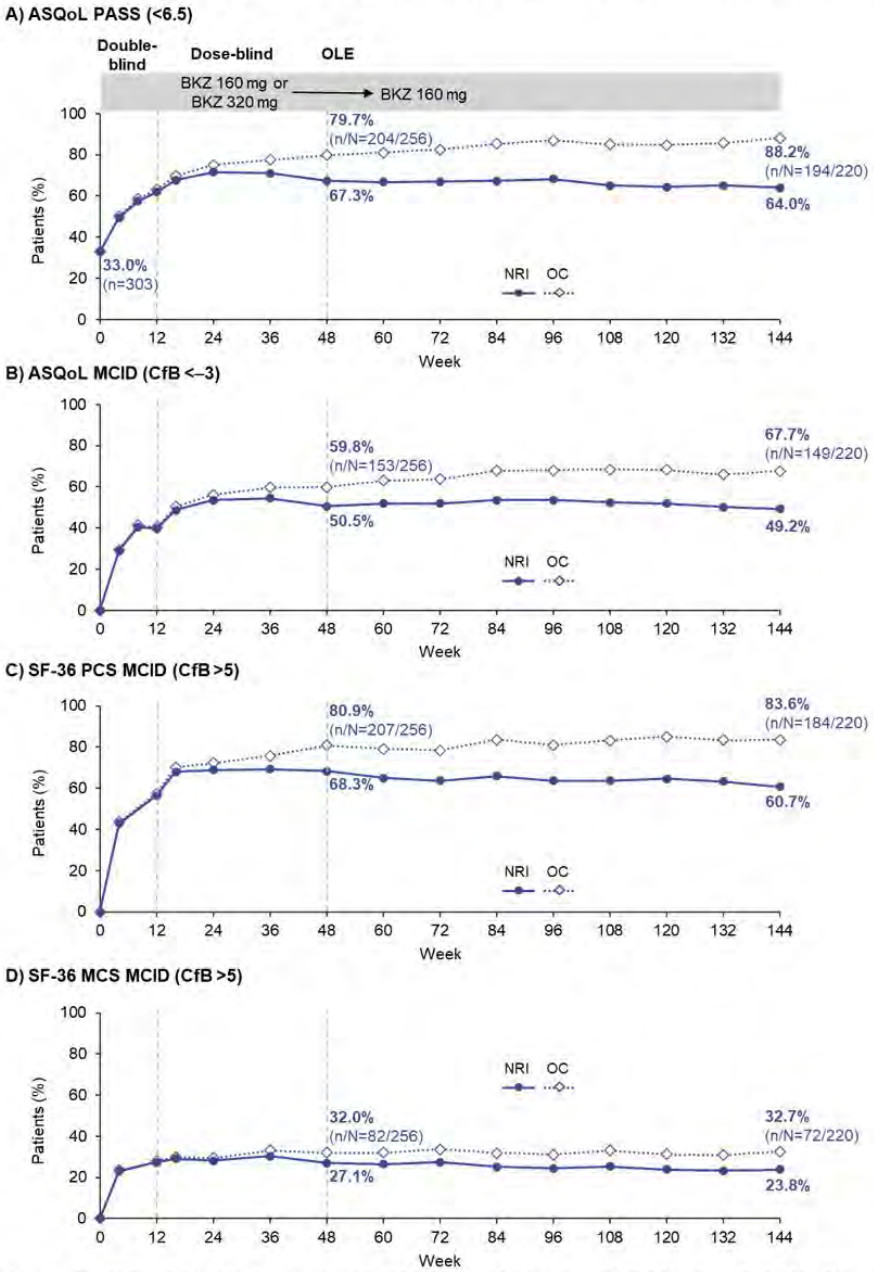
Figure 1. Change over time in HRQoL outcomes from baseline to Week 144 (multiple imputation and observed case)



Full analysis set (N=303). All patients received BKZ 160 mg during the OLE (Weeks 48–144) after completing BKZ 160 mg or 320 mg in BE AGILE. During the double-blind period (Weeks 0–12), 60/303 (19.8%) patients received placebo. MI and OC data are shown for all timepoints from BE AGILE baseline to Week 144. SF-36 MCS scores were high from baseline (≥US population normal mean score).
ASQoL: Ankylosing Spondylitis Quality of Life; BKZ: bimekizumab; HRQoL: health-related quality of life; MCS: mental component summary; MI: multiple imputation; OC: observed case; OLE: open-label extension; PCS: physical component summary; SF-36: Short Form-36.

Methods: The BE AGILE study design has been described previously.[1] Following the 12-week (wk) double-blind, placebo-controlled dose-ranging period, pts received BKZ 160 mg or 320 mg every 4 wks (Q4W) in the dose-blind period to Wk 48. Pts completing Wk 48 were eligible to enter the OLE where all pts received BKZ 160 mg Q4W.

Figure 2. Proportion of patients meeting clinically relevant thresholds for HRQoL outcomes from baseline to Week 144 (non-responder imputation and observed case)



Full analysis set (N=303). All patients received BKZ 160 mg during the OLE (Weeks 48–144) after completing BKZ 160 mg or 320 mg in BE AGILE. During the double-blind period (Weeks 0–12), 60/303 (19.8%) patients received placebo. NRI and OC data are shown for all timepoints from BE AGILE baseline to Week 144; in the NRI analyses, patients who completed BE AGILE to Week 48 but did not enter the OLE were considered non-responders from Week 48 onwards. ASQoL: Ankylosing Spondylitis Quality of Life; BKZ: bimekizumab; CfB: change from baseline; HRQoL: health-related quality of life; MCID: minimal clinically important difference; MCS: mental component summary; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PASS: patient acceptable symptom state; PCS: physical component summary; SF-36: Short Form-36.

We report HRQoL following a total of 3 yrs of treatment for the BE AGILE full analysis set (all randomized patients who received ≥1 dose of investigational medicinal product and had a valid measurement of the ASAS components at baseline). Change over time in ASQoL and SF-36 scores are reported using multiple imputation (MI) and observed case (OC) methodology. Additionally, for ASQoL, we report the proportion of pts achieving a pt acceptable symptom state (PASS) of < 6.5 and a reduction from baseline greater than a minimal clinically important difference (MCID) of 3;[4,5] for SF-36 PCS and MCS scores, we report the proportion of pts with an improvement in score greater than an MCID of 5.[6] These analyses utilized non-responder imputation (NRI) and OC methodology; for NRI, pts who did not enter the OLE were considered non-responders from Wk 48 onwards.

Results: 296/303 (97.7%) pts randomized at BE AGILE study baseline entered the dose-blind period at Wk 12; 262/303 (86.5%) pts completed Wk 48 on BKZ. At Wk 48, 256/303 (84.5%) pts entered the OLE, of whom 255 received BKZ 160 mg Q4W; 220/303 (72.6%) pts completed the HRQoL instruments at Wk 144. ASQoL and SF-36 PCS scores at baseline were indicative of impaired physical function in this patient population with long-standing disease; mean scores (both OC and MI) improved up to Wk 48 and these improvements were maintained up to Wk 144 (**Figure 1A, B**). Baseline SF-36 MCS mean was indicative of non-impaired psychological function; the slight improvement trend shown at Wk 48 was maintained over 144 wks of BKZ treatment (**Figure 1C**). At baseline, 33.0% pts were in a PASS for ASQoL (score < 6.5); this increased to 67.3% and 64.0% at Wk 48 and Wk 144 respectively in the NRI analysis, and 79.7% and 88.2% in the OC analysis (**Figure 2A**). The proportion of pts with clinically relevant improvements (≥MCID) was maintained from Wk 48 to Wk 144 for ASQoL (NRI: 50.5% to 49.2%; OC: 59.8% to 67.7%), as well as SF-36 PCS (NRI: 68.3% to 60.7%; OC: 80.9% to 83.6%) and MCS (NRI: 27.1% to 23.8%; OC: 32.0% to 32.7%; **Figure 2B–D**).

Conclusion: Clinically relevant improvements in HRQoL demonstrated at Wk 48 were sustained over 144 wks of BKZ treatment.

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1. van der Heijde D. Ann Rheum Dis 2020;79:595–604;
2. Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10):1364;
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Disclosure: A. Deodhar, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **M. Dougados**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **K. Gaffney**, AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Lilly, 2, 5, 6, Pfizer, 2, 5, 6, Gilead, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, USD, 2, 5, 6; **R. Sengupta**, Merck Sharp & Dohme, 1, 5, 6, AbbVie, 1, 5, 6, Biogen, 1, 5, 6, Celgene, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, UCB, 1, 5, 6; **M. Magrey**, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5; **N. de Peyrecave**, UCB Pharma, 3, 11; **M. Oortgiesen**, UCB Pharma, 3; **T. Vaux**, UCB Pharma, 3; **C. Fleurinck**, UCB Pharma, 3; **V. Taieb**, UCB Pharma, 2; **C. de la Loge**, UCB Pharma, 2; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2.

Abstract Number: 0923

Minimal Impact of the COVID-19 Pandemic on Patient-Reported Disease Activity and Health-Related Quality of Life in Patients with Ankylosing Spondylitis Receiving Bimekizumab: Post Hoc Analyses from a Phase 2b Study

Philip Robinson[1], Pedro Machado[2], Nigil Haroon[3], Lianne Gensler[4], John Reveille[5], Vanessa Taieb[6], Thomas Vaux[6], Carmen Fleurinck[7], Marga Oortgiesen[8], Natasha de Peyrecave[7] and Atul Deodhar[9], [1]University of Queensland School of Clinical Medicine, Brisbane, Queensland, Australia, Herston, Australia, [2]Centre for Rheumatology & Department of Neuromuscular Diseases, University College London, London, United Kingdom, [3]Division of Rheumatology, Toronto Western Hospital, University of Toronto, Toronto, ON, Canada, [4]Department of Rheumatology, University of California San Francisco, San Francisco, CA, [5]Division of Rheumatology, The University of Texas Health Science Center at Houston, Houston, TX, [6]UCB Pharma, Slough, United Kingdom, [7]UCB Pharma, Brussels, Belgium, [8]UCB Pharma, Raleigh, NC, [9]Oregon Health & Science University, Portland, OR

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

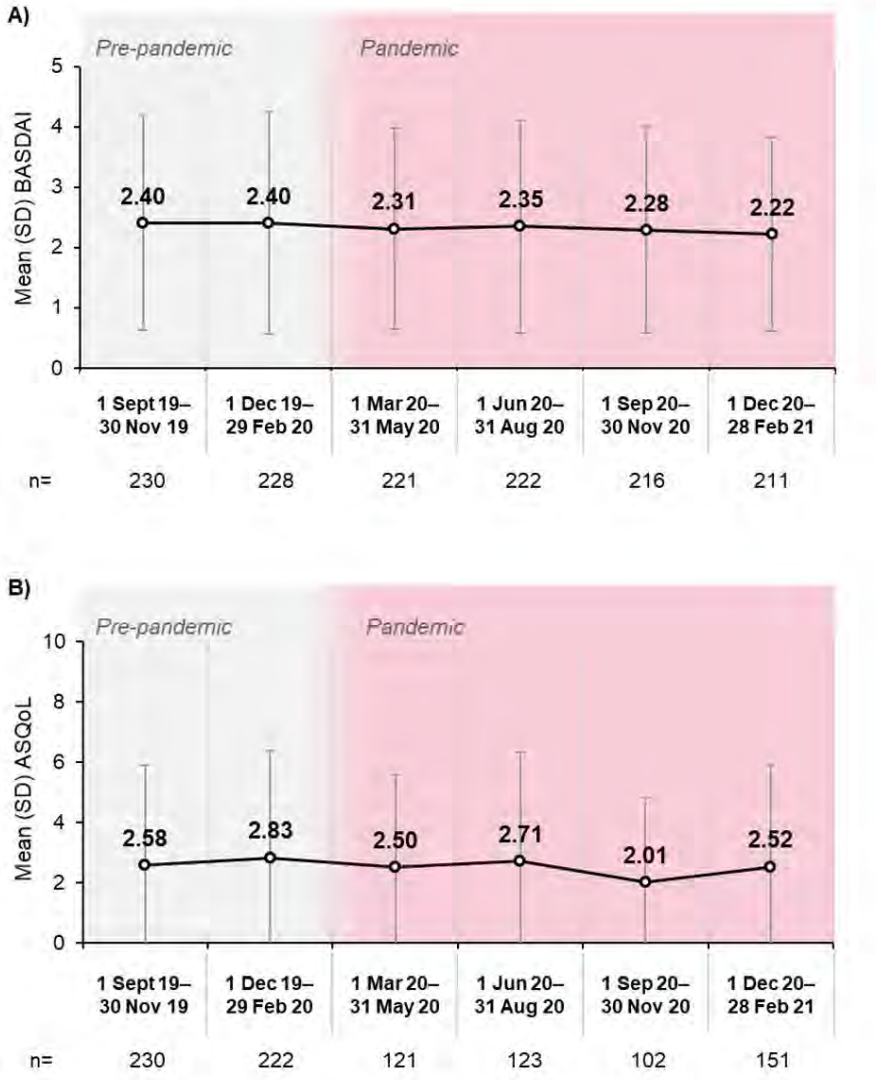
Session Time: 8:30AM–10:30AM

Background/Purpose: Bimekizumab (BKZ), a monoclonal IgG1 antibody that inhibits both interleukin (IL)-17A and IL-17F, has been demonstrated to be efficacious and well tolerated in patients (pts) with ankylosing spondylitis (AS) treated for up to 3 years in the BE AGILE study and its open-label extension (OLE).[1–3] At the start of the COVID-19 pandemic in March 2020, most pts in BE AGILE had received >3 years of BKZ treatment and outcomes were stable.[3] Findings from real-world studies evaluating the impact of the pandemic on disease activity and quality of life in pts with axial spondyloarthritis have been conflicting.[4–6] We assess whether the COVID-19 pandemic and associated societal changes have impacted pt-reported disease activity and health-related quality of life (HRQoL) among pts with active AS receiving BKZ in the ongoing OLE (NCT03355573) of a phase 2b dose-ranging study (BE AGILE; NCT02963506).

Methods: The BE AGILE study design has been described previously.[1] Pts treated with BKZ 160 mg or 320 mg every 4 weeks (Q4W) at Week 48 in BE AGILE were eligible for OLE entry. All OLE pts received BKZ 160 mg Q4W. For the OLE full analysis set, we report descriptive statistics for BASDAI (measured every 12 weeks) to show overall disease activity and Ankylosing Spondylitis Quality of Life (ASQoL; measured every 12 weeks up to Week 156, then every 24 weeks) to show HRQoL for selected time periods before and during the pandemic. For this post hoc analysis, the start of the pandemic was defined as 11 March 2020, as per the World Health Organization's declaration. Analyses included data collected between September 2019–April 2021.

Results: Of the 255 pts (safety set) who entered the OLE and received BKZ 160 mg, 229 (89.8%) were based in Eastern Europe (most were from Poland [n=89; 34.9%], the Czech Republic [n=72; 28.2%] or Russia [n=32; 12.5%]), 18 (7.1%) in Western Europe and 8 (3.1%) in North America. Study discontinuation rate was low, with 224/255 (87.8%) pts remaining in the study at Week 156; very few BKZ doses and study visits were missed for any reason. Across 3-monthly periods before and during the pandemic, BASDAI or ASQoL scores appeared to be stable (**Figure 1**). During the pandemic period between March 2020 and April 2021, there were no notable changes in these outcomes since the last pre-pandemic visit (last visit before 11 March 2020; **Figure 2**).

Figure 1. Mean (A) BASDAI and (B) ASQoL scores during the pre-pandemic and pandemic periods in patients receiving BKZ 160 mg Q4W during the BE AGILE OLE (observed data)

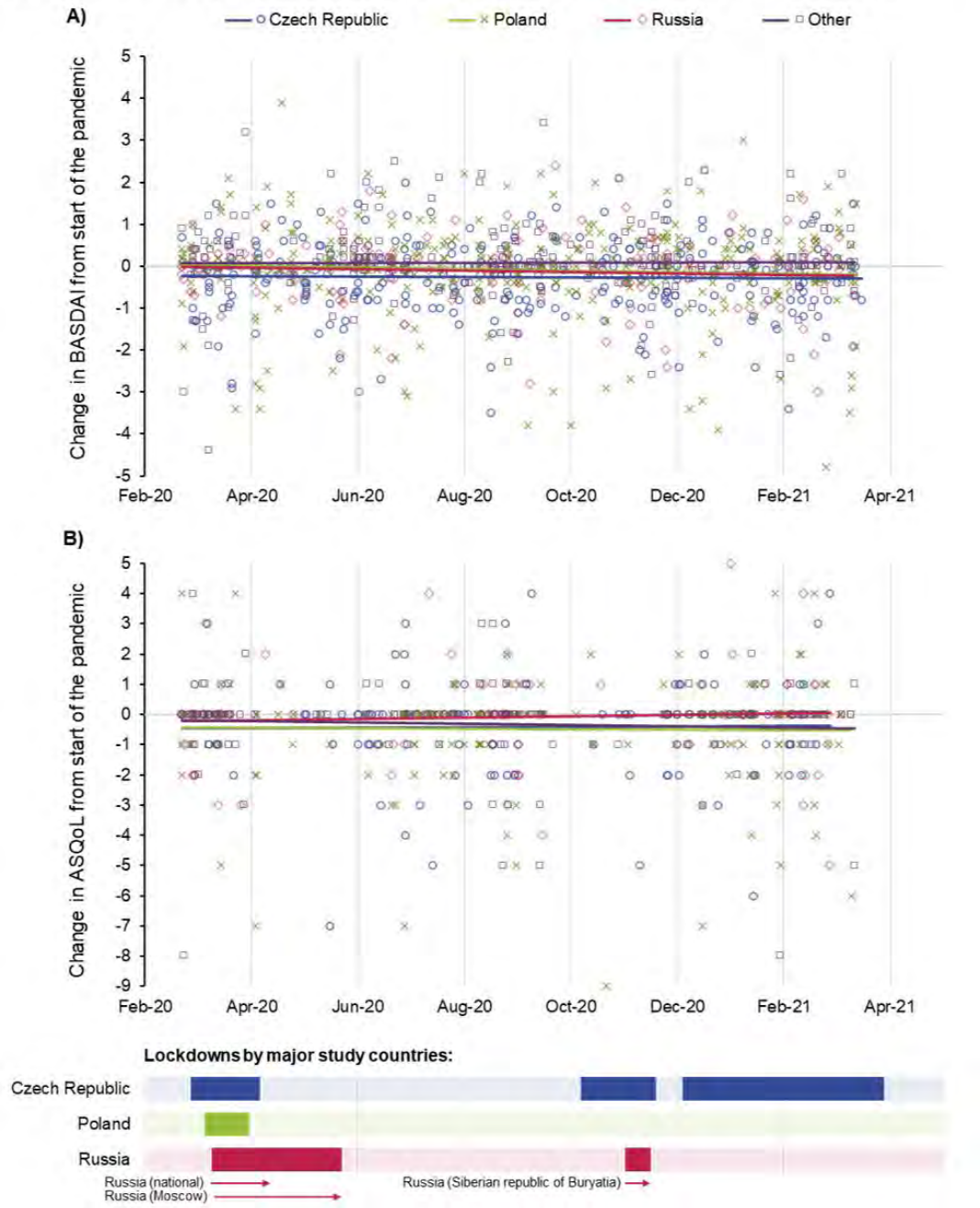


Data are reported for the OLE full analysis set (patients who entered the OLE and had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement in the OLE; N=254). Error bars show SD. Patient numbers appear lower for ASQoL than BASDAI during the pandemic period because ASQoL assessments were conducted every 24 weeks from Week 156, whereas BASDAI assessments were conducted every 12 weeks. Data for the period 1 Mar 2021–30 Apr 2021 are not shown as data were only available for a limited number of patients at the time of writing. ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; OLE: open-label extension; SD: standard deviation; Q4W: every 4 weeks.

Conclusion: In pts with AS receiving BKZ in this OLE study, disease activity (BASDAI) and HRQoL (ASQoL) remained stable during the pandemic; there was no indication that the pandemic had a detrimental impact on these outcomes. Our findings, which differ from some recent real-world studies evaluating the impact of the pandemic on pts with rheumatic disease,[4–6] may partly reflect the clinical trial setting of this study.

References: 1. van der Heijde D. Ann Rheum Dis 2020;79:595–604; **2**. Baraliakos X. Arthritis Rheumatol 2020;72 (suppl 10):1364; **3**. van der Heijde D. Ann Rheum Dis 2021;80 (suppl 1):332–3; **4**. Liew JW. ACR Open Rheumatol 2020;2:533–9; **5**. Ciurea A. Ann Rheum Dis 2021;80:238–41; **6**. Garrido-Cumbrera M. RMD Open 2021;7:e001546.

Figure 2. Change in (A) BASDAI and (B) ASQoL scores since the start of the pandemic in patients receiving BKZ 160 mg Q4W during the BE AGILE OLE (observed data)



The start of the pandemic is defined as the last visit before 11 March 2020. Each marker represents a single patient visit; linear trendlines for each of the countries/regions are shown. Data are reported for the OLE full analysis set (N=254). Patient numbers appear lower for ASQoL than BASDAI because ASQoL assessments were conducted every 24 weeks from Week 156, whereas BASDAI assessments were done every 12 weeks. Lockdowns (national, unless otherwise indicated) for the major study countries are shown by dark-colored bars. ASQoL: Ankylosing Spondylitis Quality of Life; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BKZ: bimekizumab; OLE: open-label extension; SD: standard deviation; Q4W: every 4 weeks.

Disclosure: P. Robinson, Abbvie, 1, Novartis, 1, 5, 6, Atom Biosciences, 1, Janssen, 5, 6, Eli Lilly, 1, 2, 6, Gilead, 6, UCB Pharma, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 6; **P. Machado**, Abbvie, 6, BMS, 6, Celgene, 6, Eli Lilly, 2, Janssen, 2, MSD, 6, Galapagos, 6, Novartis, 2, 6, Pfizer, 6, Roche, 6, UCB, 2, 6, Orphazyme, 5, 6; **N. Haroon**, AbbVie, 2, Amgen,

2, Eli Lilly, 2, Janssen, 2, MSD, 2, Novartis, 2, Pfizer, 2, UCB, 2; **L. Gensler**, Novartis, 5, UCB, 5, Eli Lilly, 2, Gilead, 2, Pfizer, 2, Pfizer, 5, Janssen, 2, UCB, 2; **J. Reveille**, UCB, 1, Eli Lilly, 1, Eli Lilly, 5, Novartis, 1; **V. Taieb**, UCB Pharma, 2; **T. Vaux**, UCB Pharma, 3; **C. Fleurinck**, UCB Pharma, 3; **M. Oortgiesen**, UCB Pharma, 3; **N. de Peyrecave**, UCB Pharma, 3, 11; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2.

Abstract Number: 0924

Efficacy and Safety of Upadacitinib in Patients with Active Ankylosing Spondylitis: 2-Year Results from a Randomized, Double-Blind, Placebo-Controlled Study with Open-Label Extension

Désirée van der Heijde[1], Atul Deodhar[2], Walter Maksymowych[3], Joachim Sieper[4], Filip Van den Bosch[5], Tae-Hwan Kim[6], Mitsumasa Kishimoto[7], Andrew Ostor[8], Bernard Combe[9], Yunxia Sui[10], Yuanyuan Duan[11], Alvina D. Chu[11] and In-Ho Song[12], [1]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands, [2]Oregon Health & Science University, Portland, OR, [3]Department of Medicine, University of Alberta, Alberta, Canada, Edmonton, AB, Canada, [4]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [5]Dept. of Rheumatology - Ghent University Hospital, Ghent, Belgium, Ghent, Belgium, [6]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [7]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan, [8]Monash University, Cabrini Hospital, and Emertius Research, Malvern, Australia, [9]Montpellier University, Montpellier, France, [10]AbbVie, North Chicago, IL, [11]AbbVie Inc, North Chicago, [12]AbbVie Inc., North Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The objective of this long-term analysis of the SELECT-AXIS 1 study was to report safety and efficacy of upadacitinib (UPA) in active AS through 2 years.

Methods: SELECT-AXIS 1 (NCT03178487) included a placebo-controlled, 14-week (wk) period followed by a 90-wk open-label extension.[1] The study enrolled patients (pts) with active AS (fulfilling modified New York criteria) who had an inadequate response to NSAID therapy and were biologic DMARD naive. At baseline (BL), pts were randomized to UPA 15 mg once daily (QD) or PBO; at wk 14, pts continued to receive UPA 15 mg QD (continuous UPA) while PBO pts were switched to UPA. Efficacy assessments related to signs and symptoms included Assessment of SpondyloArthritis international Society (ASAS) 40 response, ASAS partial remission (PR) and AS Disease Activity Score (ASDAS) inactive disease (ID) and low disease activity (LDA). Imaging assessments included changes from BL in MRI Spondyloarthritis Research Consortium of Canada (*SPARCC*) spine and SI joint scores and in modified Stoke Ankylosing Spondylitis Spine Score (mSASSS) at wk 104. As observed (AO) and non-responder imputation (NRI) data for binary endpoints and mixed-effect model repeated measures for continuous efficacy endpoints are reported. UPA treatment-emergent adverse events (AEs) were monitored throughout the study.

Results: Of 187 pts randomized at BL, 178 pts (each n=89 for UPA and PBO) completed wk 14 on study drug and entered the open-label extension; 144 pts (77%) completed wk 104 (UPA, n=71; PBO to UPA, n=73). ASAS40 response was maintained through 2 years among pts receiving continuous UPA; similar results at wk 104 were observed among pts who switched from PBO to UPA at wk 14 (**Figure)**. A similar pattern and maintenance of response was

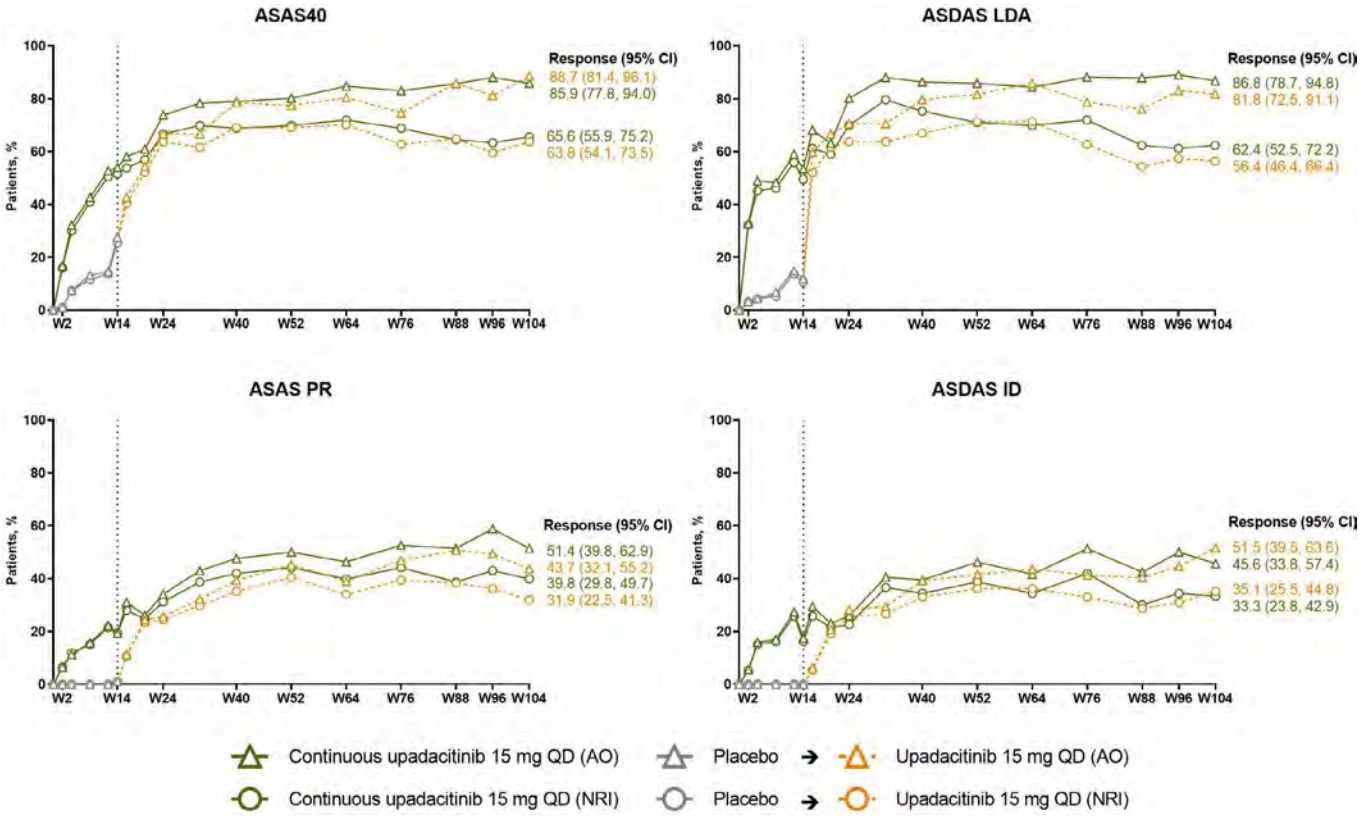


Figure 1. Clinical Efficacy Endpoints Over Time.

Table 1. Baseline Mean and Mean Change From Baseline in MRI SPARCC score and mSASSS.

Mean (95% CI)	UPA 15 mg QD	PBO to UPA 15 mg QD	Total
MRI SPARCC Spine*			
Baseline, mean (SD)	11.3 (15.4) n=85	12.7 (16.5) n=81	12.0 (15.9) n=166
Week 14, mean (95% CI) Δ	−7.2 (−10.2, −4.2) n=69	−2.0 (−3.7, −0.2) n=60	—
Week 104, mean (95% CI) Δ	−7.3 (−10.8, −3.7) n=71	−7.9 (−11.2, −4.6) n=67	—
MRI SPARCC SI joints*			
Baseline, mean (SD)	9.0 (12.7) n=84	6.1 (10.4) n=80	7.6 (11.7) n=164
Week 14, mean (95% CI) Δ	−6.1 (−8.5, −3.7) n=68	−0.8 (−2.3, 0.7) n=59	—
Week 104, mean (95% CI) Δ	−5. 3 (−7.6, −3.1) n=70	−4.9 (−7.0, −2.8) n=66	—
mSASSS			
Baseline, mean (SD)	7.5 (11.1) n=92	8.8 (12.1) n=94	8.1 (11.6) n=186
Week 104, mean (95% CI) Δ	0.59 (0.05, 1.12) n=69	0.78 (0.15, 1.40) n=67	0.68 (0.27, 1.09) n=136

Δ, change from baseline; mSASSS, modified Stoke Ankylosing Spondylitis Spine Score; SPARCC, Spondyloarthritis Research Consortium of Canada.
95% CIs are calculated based on the t-distribution.
*Data were obtained in a dedicated reading session that included baseline, week 14, and week 104 images.

Table 2. Treatment-emergent Adverse Events Throughout the Study.

Events (E/100 PY)	Any UPA 15 mg QD N=182 (308.6 PY)
AE	749 (242.7)
Serious AE	19 (6.2)
AEs leading to discontinuation	17 (5.5)
Infections	246 (79.7)
Opportunistic infections excluding TB and herpes zoster*	2 (0.6)
Herpes zoster†	5 (1.6)
Creatine phosphokinase elevation‡	35 (11.3)
Hepatic disorder§	32 (10.4)
Neutropenia‖	9 (2.9)
Anemia‖	5 (1.6)
Lymphopenia‖	3 (1.0)
Malignancy¶	1 (0.3)
Adjudicated venous thromboembolic events**	1 (0.3)
Inflammatory bowel disease††	1 (0.3)
Uveitis‡‡	16 (5.2)
Deaths	0

AE, adverse events; PY, patient years; QD, once daily; TB, tuberculosis; UPA, upadacitinib
*Two non-serious events of esophageal candidiasis in the same patient.
†Five events in 4 patients (3 from Japan); all non-serious, mild or moderate, and limited to 1 dermatome.
‡All but 1 event were non-serious and none led to study drug discontinuation; majority were asymptomatic, and the 3 symptomatic patients had muscle pain due to alternative explanations, such as increased physical activity
§Majority based on asymptomatic alanine aminotransferase/aspartate aminotransferase elevations; all were non-serious and none led to study drug discontinuation.
‖All events were non-serious and none led to study drug discontinuation.
¶Squamous cell carcinoma of tongue (stage IV) in 61-year-old male former smoker (approximately 40 pack-years).
**Pulmonary embolism in 1 female patient with history of thrombosis of the lower leg prior to study entry, impaired glucose tolerance, cigarette smoking, sedentary lifestyle, and obesity.
††Event of colitis with appendix swelling in patient with no prior history of inflammatory bowel disease.
‡‡16 uveitis AEs in 10 patients; 9 patients were HLA-B27 positive, 9 patients had a history of uveitis, and 15 of 16 events were mild or moderate. Most events were transient, resolved with local treatment (corticosteroid eye drop), and did not lead to interruption of study drug or study drug discontinuation (except 1 patient with mild uveitis who discontinued the study); all were non-serious.

also observed for other efficacy endpoints (**Figure**). MRI SPARCC spine and SI joint scores decreased from BL to wk 14 and were maintained thereafter to wk 104 with continuous UPA; a similar magnitude of decrease was seen at wk 104 in pts who switched from PBO to UPA at wk 14 (**Table 1**). The mean (95% CI) change from BL to wk 104 in the mSASSS was 0.68 (0.27, 1.09) in the total group (**Table 1**). Overall UPA treatment-emergent AE rate was 242.7/100 patient-years (PY). Infections were the most common AEs; no serious infections, active tuberculosis, adjudicated major adverse cardiovascular events, lymphoma, non-melanoma skin cancer, renal dysfunction, or gastrointestinal perforations were observed. Five (1.6/100 PY) non-serious herpes zoster infections (limited to 1 dermatome), 1 event of colitis (0.3/100 PY), 16 (5.2/100 PY) non-serious uveitis events (mostly in HLA-B27 positive pts with a history of uveitis), and 35 (11.3/100 PY) mostly asymptomatic and transient events of creatine phosphokinase elevation were observed throughout the 2 years among pts receiving UPA (**Table 2**).

Conclusion: UPA 15 mg QD showed sustained and consistent efficacy over 2 years for ASAS40 (primary endpoint) and other clinically relevant endpoints (ASDAS ID, ASDAS LDA, and ASAS PR). A low rate of radiographic progression was observed based on spinal radiographs. No new safety findings were observed.

1. van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.

Disclosure: D. van der Heijde, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2,

Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **W. Maksymowych**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **J. Sieper**, AbbVie, 2, 5, 6, Merck, 2, 5, 6, Pfizer, 2, 5, 6, Janssen, 2, 6, Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6, Roche, 2, 6; **F. Van den Bosch**, AbbVie, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Galapagos, 2, 6, Gilead, 2, 6; **T. Kim**, AbbVie, 6, Celltrion, 6, Kirin, 6, Lilly, 6, Novartis, 6; **M. Kishimoto**, AbbVie, 2, 6, Amgen-Astellas BioPharma, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, BMS, 2, 6, Celegene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **A. Ostor**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Janssen, 1, 2, UCB, 1, 2, Paradigm, 1, 2; **B. Combe**, AbbVie, 2, 4, 5, 6, Lilly, 2, 4, 5, 6, Gilead, 2, 4, Galapagos, 2, 4, Janssen, 2, 5, BMS, 2, Celltrion, 2, Novartis, 2, Roche-Chugai, 2, Sanofi, 2, Merck, 6; **Y. Sui**, AbbVie, 11; **Y. Duan**, AbbVie, 11; **A. Chu**, AbbVie, 11; **I. Song**, AbbVie, 3, 11.

Abstract Number: 0925

Impact of Achieving ASDAS LDA on Disease Activity and Patient-Reported Outcome Measures Among Patients with Ankylosing Spondylitis Treated with Biologic DMARDs

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Although Ankylosing Spondylitis Disease Activity Score (ASDAS) low disease activity (LDA) is a common treatment target for disease control when managing AS, real-world research describing ASDAS LDA achievement among patients treated with biologic DMARDs (bDMARD) is limited. The aim of this study was to describe disease activity and patient-reported outcome measures (PROMs) among patients with AS who achieved and did not achieve ASDAS LDA after 6 months of bDMARD treatment.

Methods: This analysis included patients diagnosed with AS in CorEvitas' PsA/SpA Registry, a prospective, observational, disease-based registry. Eligible patients initiated bDMARD treatment (baseline) between March 2013 and March 2021, were not in ASDAS LDA at initiation, and had a 6-month follow-up visit. Baseline demographic and clinical characteristics were compared between patients who did and did not achieve ASDAS LDA (ASDAS < 2.1) at follow-up using t-tests, Wilcoxon ranked-sum tests, chi-square tests, or Fisher exact tests. Clinical outcomes at 6 months (assessment in AS [ASAS] 20, 40, and partial remission [PR]) were described for both groups.

Results: Of 130 patients, 25% (n=33) achieved ASDAS LDA 6 months after bDMARD initiation and 75% (n=97) did not. At baseline, a greater percentage of ASDAS LDA achievers were naïve to conventional DMARDs (79% vs 58%; *P*=0.03), and ASDAS LDA achievers were more likely to be naïve to bDMARDs (76% vs 44%; *P*=0.002; **Table 1**). AS-

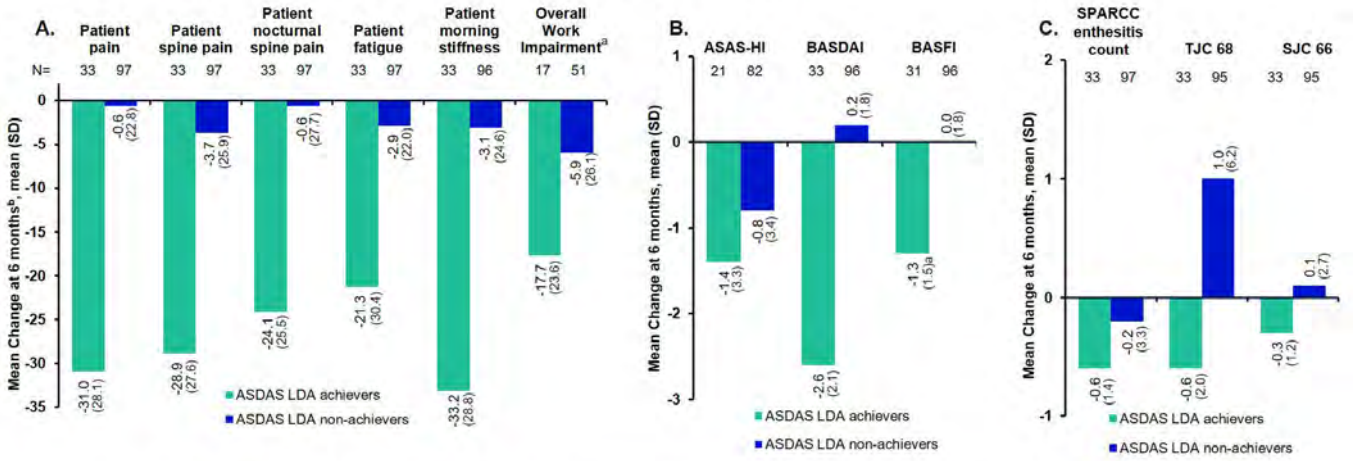
Table 1: Baseline demographics and clinical characteristics among AS patients who did and did not achieve ASDAS LDA 6-months following biologic DMARD initiation

	ASDAS LDA Status		
	Achievers N=33	Non-Achievers N=97	*P*-value[a]
Age, mean (SD)	46 (15)	51 (12)	0.06
Female, n (%)	11 (34)	60 (62)	0.01
White race, n (%)	32 (97)	84 (87)	0.10
BMI Category, n (%)			0.41
Under/normal weight	9 (28)	17 (18)	
Overweight	6 (19)	18 (19)	
Obese	17 (53)	62 (64)	
Time since AS symptom onset (y), mean (SD)	14 (11)	14 (11)	0.97
Time since AS diagnosis (y), mean (SD)	7 (11)	6 (8)	0.50
Comorbidities, n (%)			
Depression	<5	30 (31)	N/A
Uveitis	<5	14 (14)	N/A
IBD	<5	9 (9)	N/A
Conventional DMARD-naïve, n (%)	26 (79)	56 (58)	0.03
Biologic DMARD-naïve, n (%)	25 (76)	43 (44)	0.002
Monotherapy, n (%)	28 (85)	69 (71)	0.12
Prior NSAID use, n (%)	11 (33)	23 (24)	0.28
HLA-B27 positive, n (%)	22 (76)	48 (67)	0.37
Elevated CRP[b], n (%)	8 (24)	35 (36)	0.21
Enthesitis[c], n (%)	9 (27)	44 (45)	0.07
Tender Joint Count (68) ≥1, n (%)	14 (42)	45 (47)	0.63
Swollen Joint Count (66) ≥1, n (%)	9 (27)	28 (29)	0.81
Patient-reported measures at baseline[d]			
Patient pain, mean ± SD	55.5 ± 25.6	66.8 ± 21.6	0.004
Patient spine pain, mean ± SD	49.7 ± 24.8	62.5 ± 25.1	0.004
Patient nocturnal spine pain, mean ± SD	45.1 ± 30.2	59.7 ± 28.0	0.003
Patient fatigue, mean ± SD	55.6 ± 24.1	65.6 ± 24.7	0.02
Patient morning stiffness, mean ± SD	57.4 ± 25.3	68.9 ± 22.1	0.004
Overall work impairment[e] (%), mean ± SD	30.8 ± 25.9	52.1 ± 26.7	<0.001
Clinical evaluation measures at baseline			
ASAS-HI, mean ± SD	7.2 ± 3.4	9.9 ± 3.4	<0.001
BASDAI, mean ± SD	5.1 ± 1.9	6.2 ± 1.8	<0.001
BASFI, mean ± SD	3.3 ± 2.3	5.4 ± 2.3	<0.001
SPARCC enthesitis count, mean ± SD	1.1 ± 2.4	2.4 ± 3.3	0.01
TJC 68, mean ± SD	1.7 ± 2.7	4.9 ± 8.9	0.02
SJC 66, mean ± SD	0.9 ± 1.8	1.5 ± 3.4	0.25

[a]*P*-values from two sample t-tests or Wilcoxon ranked-sum tests for continuous variables, and from chi-square or Fisher exact tests for categorical variables. [b]Defined as CRP >0.8 mg/dL. [c]Enthesitis was defined as SPARCC index score ≥1. [d]Measured using a 100-point visual analog scale. [e]Only measured for those reporting that they are working at baseline (n = 106). ASAS-HI, Assessment of Spondyloarthritis International Society Health Index; ASDAS, Ankylosing Spondylitis Disease Activity Score; AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; CRP, C-reactive protein; HLA-B27, human leukocyte antigen B27; IBD, irritable bowel disease; LDA, low disease activity; N/A, not applicable; SD, standard deviation; SJC 66, swollen joint count 66; SPARCC, Spondyloarthritis Research Consortium of Canada; TJC 68, tender joint count 68; y, year.

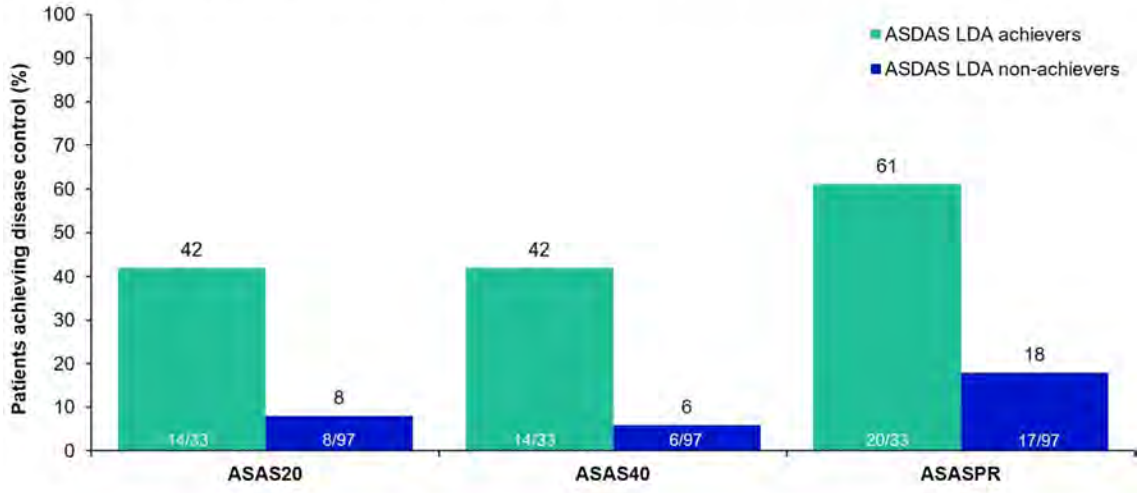
DAS LDA achievers were less likely to be women compared with the non-achiever group (34% vs 62%; *P*=0.01). A higher number of ASDAS LDA non-achievers had comorbidities such as depression, uveitis, and inflammatory bowel disease. After 6 months of bDMARD therapy, those who achieved ASDAS LDA reported substantial improvements (mean change [standard deviation]) in PROMs (measured on a 0-100-point visual analog scale), including patient-

Figure 1. Mean change in patient-reported outcome and clinical evaluation measures among ASDAS LDA achievers and non-achievers who initiated a biologic DMARD, from baseline to 6 months



[a]Overall work impairment was only assessed in patients who reported current employment. [b]All assessments are measured on a 0-100 visual analog scale (Panel A). ASAS-HI, assessment of spondyloarthritis international society health index; ASDAS, ankylosing spondylitis disease activity score; BASDAI, bath ankylosing spondylitis disease activity index; BASFI, bath ankylosing spondylitis functional index; LDA, low disease activity; SJC 66, swollen joint count 66; SPARCC, Spondyloarthritis Research Consortium of Canada; TJC 68, tender joint count 68.

Figure 2. Disease control among ASDAS LDA achievers and non-achievers who initiated a biologic DMARD, from baseline to 6 months



ASAS20, assessment in ankylosing spondylitis, 20% improvement; ASAS40, assessment in ankylosing spondylitis, 40% improvement; ASASPR, assessment in ankylosing spondylitis, partial remission; ASDAS, ankylosing spondylitis disease activity score; LDA, low disease activity.

reported pain (-31.0 [28.1]), spine pain (-28.9 [27.6]), nocturnal spine pain (-24.1 [25.5]), fatigue (-21.3 [30.4]), morning stiffness (-33.2 [28.8]), and overall work impairment (-17.7 [23.6]) (**Figure 1A**). ASDAS LDA achievers had improved clinical characteristics of peripheral arthritis, including Spondyloarthritis Research Consortium of Canada enthesitis count (mean change [standard deviation]; -0.6 [1.4]), tender joint count (-0.6 [2.0]), and swollen joint count (-0.3 [1.2]) (**Figure 1B-C**). Patients with ASDAS LDA achievement had numerically higher rates of ASAS20, ASAS40, and ASASPR attainment than non-achievers (42% vs 8%, 42% vs 6%, 61% vs 18%, respectively) (**Figure 2**).

Conclusion: Among our real-world patients with AS, those who achieved ASDAS LDA demonstrated substantial improvements in PROMs and achievement of key clinical milestones of ASAS20, ASAS40, and ASASPR, suggesting ASDAS LDA as an important target for disease control when managing patients with AS. Key patient characteristics

such as sex and comorbidities were different between patients who did and did not achieve ASDAS LDA and may need to be considered when managing patients with AS.

Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **R. McLean**, CorEvitas, 3; **T. Blachley**, CorEvitas, 3; **M. Marchese**, CorEvitas, 3; **L. Anatale-Tardiff**, CorEvitas, 3; **C. Saffore**, AbbVie, 3, 11; **D. Quach**, AbbVie, 3; **A. Biljan**, AbbVie, 3, 11; **A. Ogdie**, Amgen, 2, AbbVie, 2, 11, BMS, 2, Celgene, 2, CorEvitas, 2, Gilead, 2, Janssen, 2, Lilly, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer, 2, 5, Novartis, 2, 5.

Abstract Number: 0926

Predictors of 1-Year Treatment Response Among Upadacitinib-Treated Patients with Ankylosing Spondylitis: A Post Hoc Analysis

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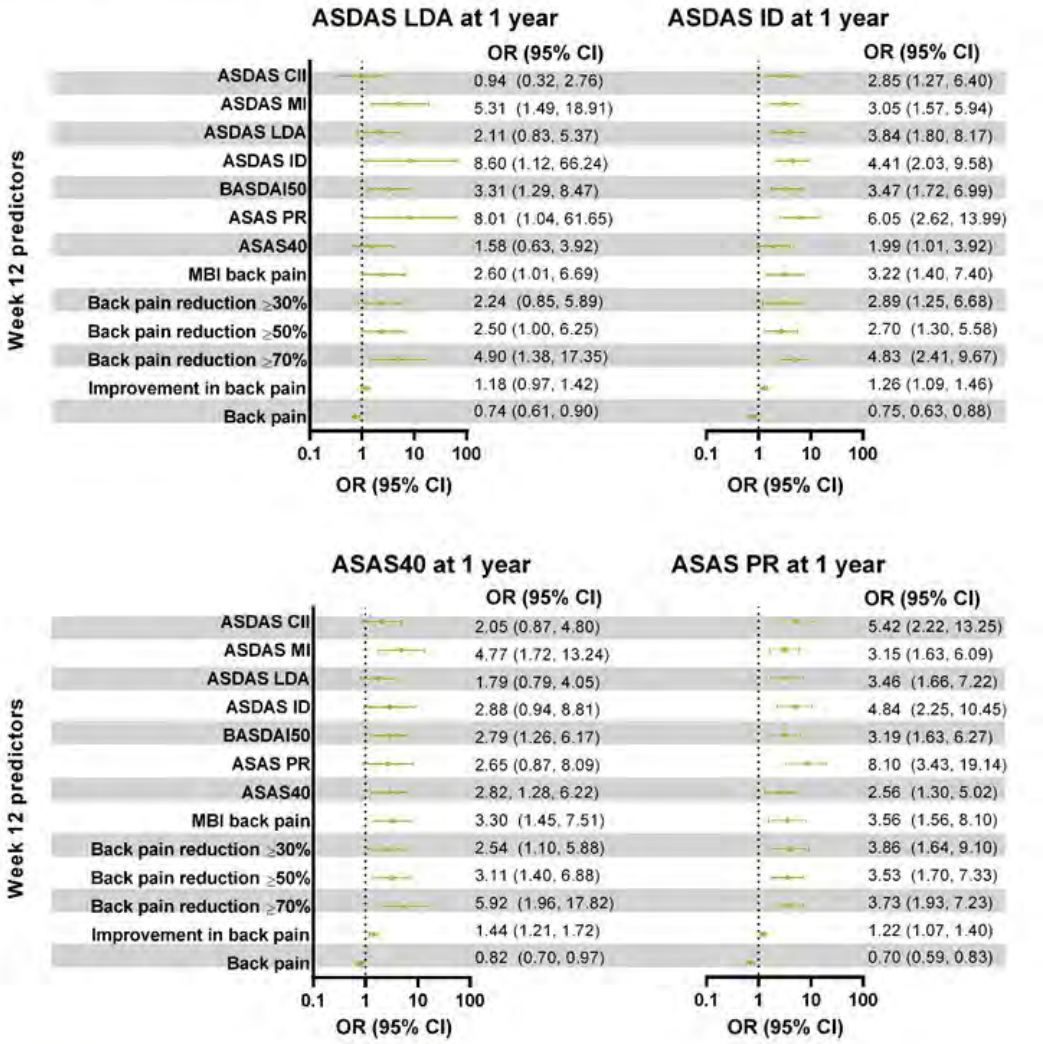
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Upadacitinib (UPA) is an oral Janus kinase inhibitor that has demonstrated efficacy and safety among patients with ankylosing spondylitis (AS) in the phase 2/3 SELECT-AXIS 1 study.1 If identified, early predictors of treatment response may inform treat-to-target strategies and optimize patient outcomes in AS. The objective of this analysis was to determine whether baseline (BL) characteristics or early responses predict clinical response at 1 year in UPA-treated patients with AS.

Methods: In the double-blind, randomized, placebo (PBO)-controlled SELECT-AXIS 1 study, patients received UPA 15 mg once daily or PBO until Week 14.[1] At Week 14, PBO-treated patients switched to UPA 15 mg; patients originally randomized to UPA continued UPA therapy. Data from patients in the PBO and UPA arms were combined based on overall exposure to UPA; in the switch arm, exposure was defined as current visit minus 14 weeks (time of switch). The following outcomes were assessed at 1 year: Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS[CRP]) inactive disease (ID; < 1.3) and low disease activity (LDA; < 2.1), Assessment of SpondyloArthritis International Society (ASAS) partial remission (PR), and ≥40% improvement in ASAS criteria (ASAS40) response. The ability of BL characteristics, efficacy at Week 12, and back pain at Week 12 to predict 1-year outcomes was assessed using a univariable logistic regression model generating odds ratios (ORs; 95% confidence intervals). LASSO regression was used to select the best-fitted multivariable model at Week 12 for each outcome measure.

Results: Among 187 patients who received or switched to UPA 15 mg, 70 (37.4%), 134 (71.7%), 73 (39.0%), and 131 (70.1%) achieved ASDAS(CRP) ID, ASDAS(CRP) LDA, ASAS PR, and ASAS40, respectively, following 1 year of UPA treatment. No meaningful predictors of 1-year efficacy outcomes were identified based on BL demographics

Figure Association between Week 12 response or back pain at Week 12 and achievement of efficacy outcomes at 1 year (univariable analysis)



All ASDAS scores are calculated using C-reactive protein

ASDAS CII: change from BL ≥1.1; ASDAS MI: change from BL ≥2.0; MBI back pain: ≥2-point reduction in absolute score and ≥33% reduction from BL on a 0–10 NRS

ASAS, Assessment of SpondyloArthritis International Society; ASAS40, ≥40% improvement in ASAS criteria; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI50, ≥50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; CI, confidence interval; CII, clinically important improvement; ID, inactive disease; LDA, low disease activity; MBI, much better improvement; MI, major improvement; NRS, numeric rating scale; OR, odds ratio; PR, partial remission

(including disease duration, gender, and human leukocyte antigen B27 status) or BL disease characteristics (including ASDAS, Bath Ankylosing Spondylitis Disease Activity Index, and CRP levels). In univariable analyses, Week 12 responses based on several disease activity measures and patient-reported outcomes (PROs), including reductions

(much better improvement [MBI], ≥30/≥50/≥70% reduction, or improvement) in back pain score, along with lower scores for back pain at Week 12, were associated with the achievement of ASDAS(CRP) ID, ASDAS(CRP) LDA, ASAS PR, and ASAS40 at 1 year (**Figure**). In a multivariable analysis, improvement from BL to Week 12 in back pain score consistently predicted several efficacy outcomes at 1 year.

Conclusion: In upadacitinib-treated patients with AS, improvement in PROs and reduction in back pain score at 12 weeks predicted clinical outcomes at 1 year.

Reference: 1. van der Heijde D, et al. *Lancet* 2019;394:2108–17.

Disclosure: M. Magrey, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5; **S. Ramiro**, AbbVie, 2, Eli Lilly, 2, MSD, 2, Novartis, 2, Sanofi, 2, UCB, 2, MSD, 5; **M. Pinheiro**, AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2; **T. Gao**, AbbVie, 3, 11; **F. Ganz**, AbbVie, 3, 11; **I. Song**, AbbVie, 3, 11; **A. Biljan**, AbbVie, 3, 11; **N. Haroon**, AbbVie, 2, Amgen, 2, Eli Lilly, 2, Janssen, 2, MSD, 2, Novartis, 2, Pfizer, 2, UCB, 2; **M. Rudwaleit**, AbbVie, 2, Celgene, 2, Eli Lilly, 2, Janssen, 2, UCB Pharma, 2, AbbVie, 6, Eli Lilly, 6, Novartis, 6, Novartis, 2, UCB Pharma, 6.

Abstract Number: 0927

Whole Blood Transcriptional Changes Following Treatment with Filgotinib in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Ankylosing spondylitis (AS) – also referred to as radiographic axial spondyloarthritis – is a chronic inflammatory disease that affects the sacroiliac joints and spine. Inhibition of Janus kinase 1 (JAK1) has the potential to simultaneously block multiple inflammatory pathways and lessen disease severity. In the recently completed TORTUGA study, filgotinib (FIL), a preferentially selective JAK1 inhibitor, significantly reduced AS disease activity compared with placebo (PBO).[1] The current study was conducted to evaluate the impact of FIL on transcriptional biomarkers in adult patients with active AS from the TORTUGA study.

Methods: TORTUGA (Clinicaltrials.gov identifier: NCT03117270) is a phase 2 double-blind, PBO-controlled study in which 116 AS patients with an inadequate response to >1 NSAID were randomized 1:1 to receive FIL 200 mg or PBO orally once daily for 12 weeks. Whole blood samples from patients were collected in PAXgene tubes at baseline and weeks 1, 4 and 12. Illumina TruSeq Stranded mRNA (50M 100bp PE) was generated for 414 samples from 96 patients, FIL 200 (n=49) and PBO (n=47). Gene-level quantification of RNA-seq counts and transcripts/million (TPMs) was conducted using Salmon (v0.8.2, and gencode GRCh38.p7 v25). Pathway analysis was performed using single sample gene set enrichment analysis (ssGSEA) based on Hallmark 50 pathways from the MSigDB. Treatment effect was evaluated using differential expression analysis by limma.

Results: The JAK-STAT, Inflammatory Response, Complement and Coagulation Hallmark 50 pathways were significantly correlated with the C-reactive protein (CRP) levels at baseline, whereas ASDAS correlated with Inflammatory

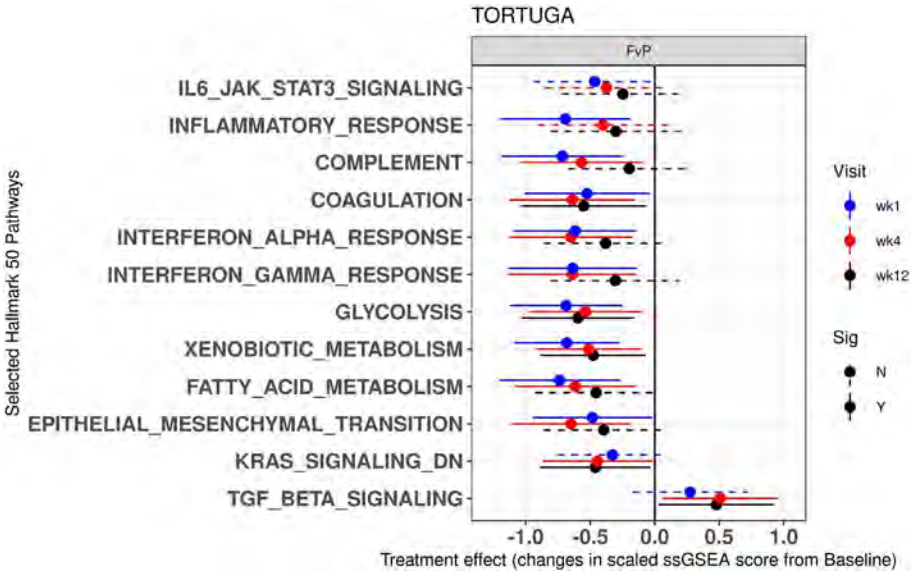

Figure 1. Filgotinib treatment effect on selected Hallmark 50 pathways. Whole blood transcriptomic analysis of PBO-subtracted FIL gene expression changes at weeks 1, 4 and 12 compared to baseline. Center dots represent the mean changes of the pathway ssGSEA scores from baseline and the horizontal bar indicate the 95% CI. Treatment effect significance at each time point is indicated by a solid line and is based on the nominal p-value generated by Limma.

Response and Coagulation pathways, among others. Treatment with filgotinib rapidly decreased several immune pathways at week 1 (Coagulation, Inflammatory Response Complement, Interferon), metabolic pathways (Glycolysis, Fatty Acid Metabolism) and increased the TGF-β Signaling pathway at weeks 4 and 12 (Figure 1). At the gene level, CRP-associated genes such as FAM20A, as well as the JAK-STAT pathway member CISH were downregulated following treatment with FIL.

Changes in circulating cellular composition were observed following filgotinib treatment comprising a decrease in percentage of neutrophils (weeks 1, 4), a transient decrease in monocytes (weeks 1, 4), an increase in B cells (weeks 4, 12) and a transient increase in lymphocytes (weeks 1, 4). These cellular fluctuations accounted for a portion of the changes in gene expression observed, including loss of some gene expression changes over time and upregulation of many genes at weeks 4 and 12.

Conclusion: In patients with active AS, FIL treatment meaningfully decreased inflammatory pathways and genes associated with disease activity in AS, and increased TGF-β signaling pathways as a result of changes in inflammatory gene expression and alterations in circulating cellular composition.

Reference

1. van der Heijde D, Baraliakos X, Gensler LS, et al. *Lancet*. 2018;392:2378–87.

Disclosure: D. **Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **Y. Liu**, Gilead Sciences, 3, 11; **W. Barchuk**, Gilead Sciences, 3, 11; **R. Besuyen**, Galapagos, 3, 11; **R. Galien**, Galapagos NV, 3, 11, 12, Warrant holder; **Y. Tian**, Gilead Sciences, 3, 11; **V. Malkov**, Gilead Sciences, 3, 11; **A. Hertz**, Gilead Sciences, 3, 11.

Abstract Number: 0928

Filgotinib Treatment Results in Reduction of Inflammatory and Matrix Remodeling Biomarkers Associated with Disease in Patients with Ankylosing Spondylitis

Walter Maksymowych[1], Yuan Tian[2], Jingting Xu[2], William Barchuk[3], René Galien[4], Robin Besuyen[5], Yihua Liu[2], Vlad Malkov[2] and Angie Hertz[2], [1]Department of Medicine, University of Alberta, Alberta, Canada, Edmonton, AB, Canada, [2]Gilead Sciences, Foster City, CA, [3]Gilead Sciences, Inc., Foster City, CA, [4]Galapagos NV, Romainvulle, France, [5]Galapagos BV, Leiden, Netherlands

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Ankylosing spondylitis (AS) – also referred to as radiographic axial spondyloarthritis – is a chronic inflammatory disease that affects the sacroiliac joints and spine. In the recent TORTUGA study, filgotinib (FIL), a preferentially selective Janus kinase 1 (JAK1) inhibitor, significantly reduced AS disease activity compared with placebo (PBO).[1] JAK1 inhibition by FIL has the potential to block multiple inflammatory pathways. Thus, we analyzed circulating biomarker concentrations in samples from adult patients with active AS in TORTUGA and age, gender and BMI-matched healthy volunteers (HV) using exploratory multiplex biomarker panels and high sensitivity immunoassays to assess the impact of disease on circulating biomarkers at baseline and evaluate the effect of FIL treatment over 12 weeks.

Methods: TORTUGA (Clinicaltrials.gov identifier NCT03117270) was a 12-week, randomized, double-blind, placebo-controlled, phase 2 study. Patients were randomized 1:1 to FIL 200 mg (n=58) or PBO (n=58) once-daily and serum and plasma samples (FIL n=56, PBO n=53) were collected at baseline (BL) and weeks 1, 4 and 12. The samples were analyzed using immunoassays from Meso Scale Diagnostics (Rockville, MD, USA), EMD Millipore (Burlington, MA, USA), Nordic Biosciences (Herlev, Denmark) and Nexelis (Seattle, WA, USA). Biomarker concentration changes from BL were analyzed on paired patient data and reported for weeks 1, 4 and 12, and clustering analysis was performed. Correlation between the biomarkers and selected clinical scores were assessed by Spearman rank correlation analysis. Mean of log-fold-changes in biomarker levels from BL to week 4 and week 12 were compared between arms using PBO-adjusted estimates from a linear mixed effects model.

Results: Five clusters of biomarker response were identified based on the kinetics and magnitude of percent changes from BL with FIL treatment. As compared to PBO, a reduction in the inflammatory biomarkers CRP, SAA and IL-6 was observed, as well as a reduction in matrix metalloproteinase-degraded collagen fragments C1M, C3M, C6M and MMP1 (Figure 1). The change in several of these biomarkers correlated with changes in numerous clinical characteristics from BL to week 12, notably a correlation of MMP1, C6M and ICAM1 with Ankylosing Spondylitis Disease Activity Score (ASDAS), CRP, Spondyloarthritis Research Consortium of Canada (SPARCC) MRI spine score and patient-reported pain. Comparisons to HV were made on a subset of biomarkers and BL ICAM1 and VCAM1 were elevated in AS patients as compared to HV. However, after 1 week of treatment with FIL, both were reduced to levels comparable to HV and remained low for the 12-week duration of the study.

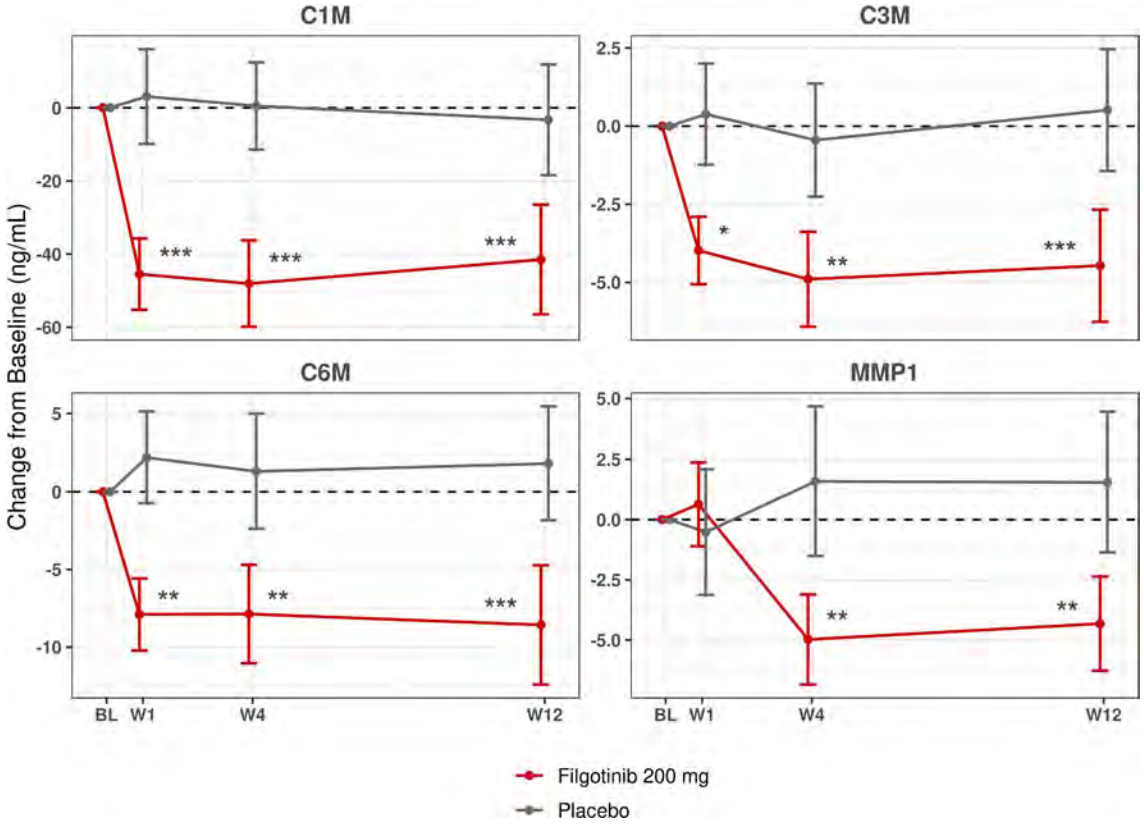

Figure 1. Circulating levels of matrix remodeling biomarkers are reduced with FIL treatment. The change from baseline resulting from PBO or FIL treatment on C1M, C3M, C6M and MMP1 levels at BL, weeks 1, 4 and 12 was calculated using a linear mixed effects model (adjusted for age, sex, BMI, BL ASDAS and BL spine SPARCC MRI scores) including a treatment by visit multiplicative interaction. The data are presented as the mean and 95% CI. FDR-corrected p-values: *Adj.p <0.05; **Adj.p <10–3; ***Adj.p <10–6.

Conclusion: In patients with active AS, FIL treatment reduced the levels of inflammatory cytokines associated with disease including systemic inflammatory cytokines, matrix remodeling biomarkers and cellular adhesion molecules. The observed decrease in biomarkers is consistent with the reduced AS disease activity in TORTUGA and suggest that FIL treatment can rapidly reduce a range of inflammatory cytokines involved in AS pathobiology.

Reference

1. van der Heijde D *et al. Lancet* 2018;392:2378–87

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **Y. Tian**, Gilead Sciences, 3, 11; **J. Xu**, Gilead Sciences, 3, 11; **W. Barchuk**, Gilead Sciences, 3, 11; **R. Galien**, Galapagos NV, 3, 11, 12, Warrant holder; **R. Besuyen**, Galapagos, 3, 11; **Y. Liu**, Gilead Sciences, 3, 11; **V. Malkov**, Gilead Sciences, 3, 11; **A. Hertz**, Gilead Sciences, 3, 11.

Abstract Number: 0929

Tapering of TNF Inhibitors in Patients with Axial Spondyloartritis – Can Flare Be Predicted?

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with axial spondyloarthritis (axSpA) in clinical remission tapered Tumor Necrosis Factor inhibitor (TNFi) treatment according to a clinical guideline and were followed for 2-years. We aimed to investigate 1) potential 'baseline' predictors of flare within 16 weeks after tapering to 2/3, 1/2, 1/3 and 0 of standard dose and 2) if change in clinical and/or imaging variables in the previous 16-weeks (i.e. during the previous dose reduction step) could predict flare within 16 weeks after tapering to 1/2, 1/3 and 0 dose.

Methods: In all, 109 patients (78(72%) on standard dose, 31(28%) on reduced dose) in clinical remission with Bath ankylosing spondylitis disease activity index (BASDAI)< 40, physician global score< 40 and no signs of disease activity the previous year tapered TNFi to 2/3 of standard dose at baseline, 1/2 at week 16, 1/3 at week 32 and withdrew at week 48. Patients who experienced clinical, BASDAI or magnetic resonance imaging (MRI) flare stopped tapering and escalated to the previous dose. Prediction analyses were done by multivariable regression.

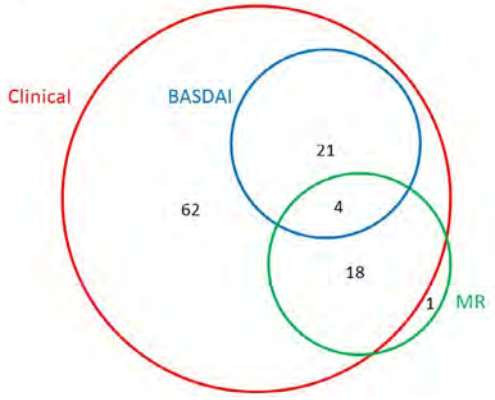
Results: Of 107 patients who followed the tapering algorithm for 2 years, 106 patients flared: 30 (28%) flared at 2/3 of standard dose, 20 (19%) at 1/2, 29 (27%) at 1/3 and 27 (25%) after discontinuation of TNFi (Table 1). Of the 106 patients who flared, 105 had clinical flare, 25 BASDAI flare and 23 MRI flare (Figure 1). Higher baseline physician global score was an independent predictor of flare after tapering to 2/3 (Odds ratio (OR)=1.21 (95% Confidence Interval=1.05 to1.44); p=0.007). When changes from baseline to week 16 in addition to demographics were investigated as predictors of flare, higher age predicted flare within 16 weeks after tapering to 1/2 dose (OR=1.07(1.01 to 1.15); p=0.015) (Table 2). Prediction analyses on lower dose steps were not possible due to small sample sizes.

Conclusion: In axSpA patients in clinical remission who tapered TNFi according to a clinical guideline, higher baseline physician global score was the only independent predictor of flare within 16 weeks after tapering to 2/3 of standard dose.

Table 1. Baseline characteristics of patients stratified by the dose on which they experienced flare (n=107)

	2/3 dose (n=30)	1/2 dose (n=20)	1/3 dose (n=29)	Discontinuation (n=27)	No flare (n=1)	p-value
Baseline demographics						
Male gender, n (%)	26 (87%)	17 (85%)	25 (86%)	23 (85%)	1 (100%)	1
Age, years	42 (35,50)	48 (43,55)	40 (32,50)	44 (41,54)	47 (47,47)	0.077
Time since diagnosis, years	9 (5,13)	9 (6,16)	7 (3,14)	14 (10,24)	12 (12,12)	**0.008**
Current smoker, n (%)	5 (17%)	2 (10%)	7 (25%)	9 (33%)	0 (0%)	0.344
HLA-B27 positivity, n (%)	23 (82%)	15 (83%)	27 (93%)	23 (85%)	1 (100%)	0.654
Disease characteristics at baseline						
TNF inhibitor, n (%)						
Adalimumab	11 (37%)	9 (45%)	7 (24%)	10 (37%)	1 (100%)	0.291
Etanercept	2 (7%)	1 (5%)	4 (14%)	5 (19%)	0 (0%)	
Certolizumab pegol	0 (0%)	1 (5%)	2 (7%)	0 (0%)	0 (0%)	
Golimumab	9 (30%)	5 (25%)	10 (34%)	2 (7%)	0 (0%)	
Infliximab	8 (27%)	4 (20%)	6 (21%)	10 (37%)	0 (0%)	
CRP >3 mg/l, n (%)	5 (17%)	2 (10%)	4 (14%)	7 (26%)	0 (0%)	0.601
SPARCC Enthesitis Index (0-16)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0.781
BASMI (0-100)	10 (0,30)	10 (0,22)	10 (0,20)	20 (0,40)	10 (10,10)	0.404
Back pain (yes), n (%)	8 (27%)	2 (11%)	2 (7%)	0 (0%)	0 (0%)	**0.023**
Inflammatory back pain (yes), n (%)	0 (0%)	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0.721
Physician global VAS (0-100)	5 (4,8)	4 (3,6)	5 (3,6)	4 (3,8)	5 (5,5)	0.532
ASDAS	1.1 (0.9,1.4)	1.0 (0.5,1.3)	1.0 (0.6,1.3)	0.9 (0.6,1.2)	0.4 (0.4,0.4)	0.253
VAS physician confidence to taper (0-100)	71 (62,79)	73 (65,76)	74 (69,86)	70 (56,76)	94 (94,94)	0.136
VAS patient confidence to taper (0-100)	50 (47,73)	50 (47,78)	85 (62,100)	71 (28,90)	95 (95,95)	**0.008**
PROs at baseline						
BASDAI (0-100)	16.0 (8.3,22.0)	10.4 (3.5,22.3)	10.8 (4.0,20.2)	8.2 (4.3,13.7)	5.0 (5.0,5.0)	0.148
BASFI (0-100)	11.1 (4.3,21.7)	14.7 (1.3,22.1)	9.5 (4.0,13.0)	7.6 (3.2,23.9)	5.8 (5.8,5.8)	0.871
Patient pain VAS (0-100)	10 (6,20)	10 (2,21)	6 (1,11)	5 (2,10)	8 (8,8)	0.168
Patient fatigue VAS (0-100)	20 (8,33)	17 (6,32)	15 (7,28)	11 (2,24)	7 (7,7)	0.242
Patient global VAS (0-100)	12 (7,20)	12 (4,23)	8 (3,12)	7 (1,14)	7 (7,7)	0.172
Physician global VAS (0-100)	5 (4,8)	4 (3,6)	5 (3,6)	4 (3,8)	5 (5,5)	0.532
HAQ-S (0-3)	0.2 (0.1,0.4)	0.2 (0.0,0.3)	0.1 (0.1,0.2)	0.2 (0.0,0.5)	0.0 (0.0,0.0)	0.362
EQ-5D (0-1)	0.9 (0.8,0.9)	0.9 (0.8,1.0)	0.9 (0.9,1.0)	0.9 (0.8,1.0)	1.0 (1.0,1.0)	0.186
ASAS Health index (0-17)	3.0 (1.0,5.8)	2.0 (0.0,3.4)	3.0 (2.0,5.0)	1.0 (0.0,3.0)	0.0 (0.0,0.0)	0.106
Imaging variables at baseline						
mNYc positive, n (%)	17 (61%)	16 (80%)	17 (61%)	20 (77%)	0 (0%)	0.220
mSASSS (0-72)	0 (0,18)	2 (0,12)	0 (0,5)	10 (0,37)	0 (0,0)	0.059
SPARCC SIJ Inflammation Index (0-72)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0.876
SPARCC spine total inflammation (0-108)	0 (0,2)	2 (0,5)	0 (0,2)	0 (0,5)	0 (0,0)	0.304
CANDEN posterolateral elements inflammation subscore (152)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0.634
SPARCC SSS Fat (0-40)	10 (0,18)	13 (3,25)	17 (7,30)	14 (3,21)	1 (1,1)	0.302
SPARCC SSS Erosion (0-40)	0 (0,1)	0 (0,0)	0 (0,1)	0 (0,0)	0 (0,0)	0.265
SPARCC SSS Backfill (0-20)	0 (0,5)	1 (0,10)	2 (0,11)	0 (0,1)	0 (0,0)	0.137
SPARCC SSS Ankylosis (0-20)	1 (0,15)	3 (0,10)	0 (0,11)	4 (0,15)	0 (0,0)	0.818
CANDEN MRI spine fat score (510)	2 (0,10)	3 (0,11)	4 (0,12)	2 (1,12)	2 (2,2)	0.987
CANDEN MRI spine bone erosion score (208)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0 (0,0)	0.979
CANDEN MRI spine NBF score (0-460)	6 (0,34)	24 (4,52)	6 (0,18)	13 (2,42)	2 (2,2)	0.400

Figure 1. Venn diagram showing overlaps between flare types



Values are median (IQR) unless otherwise stated. Kruskal-Wallis, chi-squared or Fisher's test was used for analysing between-group differences, as appropriate; bold indicates statistically significant p-values; p-value<0.05 was considered statistically significant.

Table 2. Univariate and multivariable logistic regression analyses for predictive value of baseline variables for flare after tapering to 2/3 dose and for predictive value of changes in variables prior to tapering to 1/2 dose for flare within following 16 weeks

Clinically relevant variables						
Patients tapered to 2/3 dose (n=78)						
	Univariate analyses			Final multivariable analyses		
Predictor	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Male gender	1.03	(0.26 - 4.41)	0.970			
Age	1.00	(0.95 - 1.04)	0.848			
Time since diagnosis	1.01	(0.96 - 1.06)	0.790			
Current smoker	0.71	(0.20 - 2.25)	0.568			
HLA-B27 positive	0.74	(0.21 - 2.71)	0.638			
previous bDMARDs	1.35	(0.70 - 2.65)	0.363			
Patient pain VAS	1.02	(0.98 - 1.06)	0.426			
Physician global VAS	1.21	(1.05 - 1.44)	**0.008**	1.21	(1.05 - 1.44)	0.008
ASDAS	1.62	(0.68 - 3.96)	0.275			
mNYc positive	0.63	(0.24 - 1.67)	0.352			
SPARCC SIJ Inflammation Index	1.01	(0.90 - 1.11)	0.911			
CANDEN Total inflammation	0.91	(0.60 - 1.21)	0.539			
SPARCC SSS Erosion	1.10	(0.90 - 1.36)	0.335			
CANDEN Fat	0.99	(0.96 - 1.02)	0.665			
AUC (95% CI)				0.67 (0.56 - 0.80)		
Change in clinically relevant variables						
Patients tapered to 1/2 dose (n=48)						
	Univariate analyses			Final multivariable analyses		
Predictor	OR	(95% CI)	p-value	OR	(95% CI)	p-value
Male gender	0.44	(0.07 - 2.79)	0.372			
Age	1.07	(1.01 - 1.15)	**0.017**	1.07	(1.01 - 1.15)	0.017
Time since diagnosis	1.03	(0.97 - 1.11)	0.335			
Current smoker	0.40	(0.05 - 1.93)	0.267			
HLA-B27 positive	0.36	(0.06 - 2.04)	0.241			
previous bDMARDs	0.93	(0.33 - 2.31)	0.879			
16 weeks prior change in patient pain VAS	0.98	(0.91 - 1.04)	0.481			
16 weeks prior change in global physician VAS	1.06	(0.92 - 1.22)	0.403			
16 weeks prior change in ASDAS	2.14	(0.56 - 9.94)	0.271			
16 weeks prior change in CANDEN Total inflammation	1.04	(0.68 - 1.49)	0.847			
16 weeks prior change in SPARCC SIJ Inflammation Index	0.50	(0.09 - 1.50)	0.247			
16 weeks prior change in SPARCC SSS Erosion	1.18	(0.24 - 5.47)	0.820			
16 weeks prior change in CANDEN Fat	1.27	(0.46 - 4.50)	0.648			
AUC (95% CI)				0.71 (0.57 - 0.88)		

Predictors were selected by applying backward selection in stacked imputed data. p-values by likelihood ratio tests. Bold indicates p-values<0.1 in univariate analyses. Results of final multivariable analyses were derived in non-imputed data (no missing values in selected predictors) and CIs were given as profile likelihood CIs. AUC was estimated based on internal validation by bootstrapping with 1000 samples.

Disclosure: M. Wetterslev, None; **S. Georgiadis**, None; **S. Christiansen**, Novartis, 5, BMS, 6, GE, 6; **S. Juhl Pedersen**, MSD, 5, 6, Pfizer, 6, AbbVie, 1, 5, 6, Novartis, 1, 5, 6, UCB, 6; **I. Sørensen**, None; **M. Lund Hetland**, Bristol-Myers Squibb, 5, AbbVie, 5, Roche, 5, 12, Novartis, 5, MSD, 5, 12, Biogen, 5, 12, Elly Lilly, 12, Orion Pharma, 12, CellTrion, 12, Samsung Bioepis, 12, Janssen Biologics BV, 12, Pfizer, 5, 12; **A. Duer**, None; **M. Boesen**, Image Analysis Group, 2, 5, 6, Esaote, 2, 5, 6, AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Eli-Lilly, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Novo, 2, 5, 6, GSK, 2, 5, 6, Takeda, 2, 5, 6, Geurbet, 2, 5, 6, Biogen, 2, 5, 6, Radiobotics, 2, 5, 6, Chondrometrics, 2, 5, 6; **K. Kjærulf Gosvig**, None; **J. Møllenbach Møller**, None; **M. Bakkegaard**, None; **C. Heegaard Brahe**, None; **N. Krogh**, None; **B. Jensen**, None; **O. Rintek Madsen**, None; **J. Christensen**, None; **A. Hansen**, None; **J. Nørregaard**, None; **H. Røgind**, None; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6.

Abstract Number: 0930

Effect of Tofacitinib on Spinal Vertebral Body and Posterolateral Element Inflammation and Structural Lesions Using the Canada-Denmark MRI Scoring System in Patients with Ankylosing Spondylitis: Results from a Phase 2 Study

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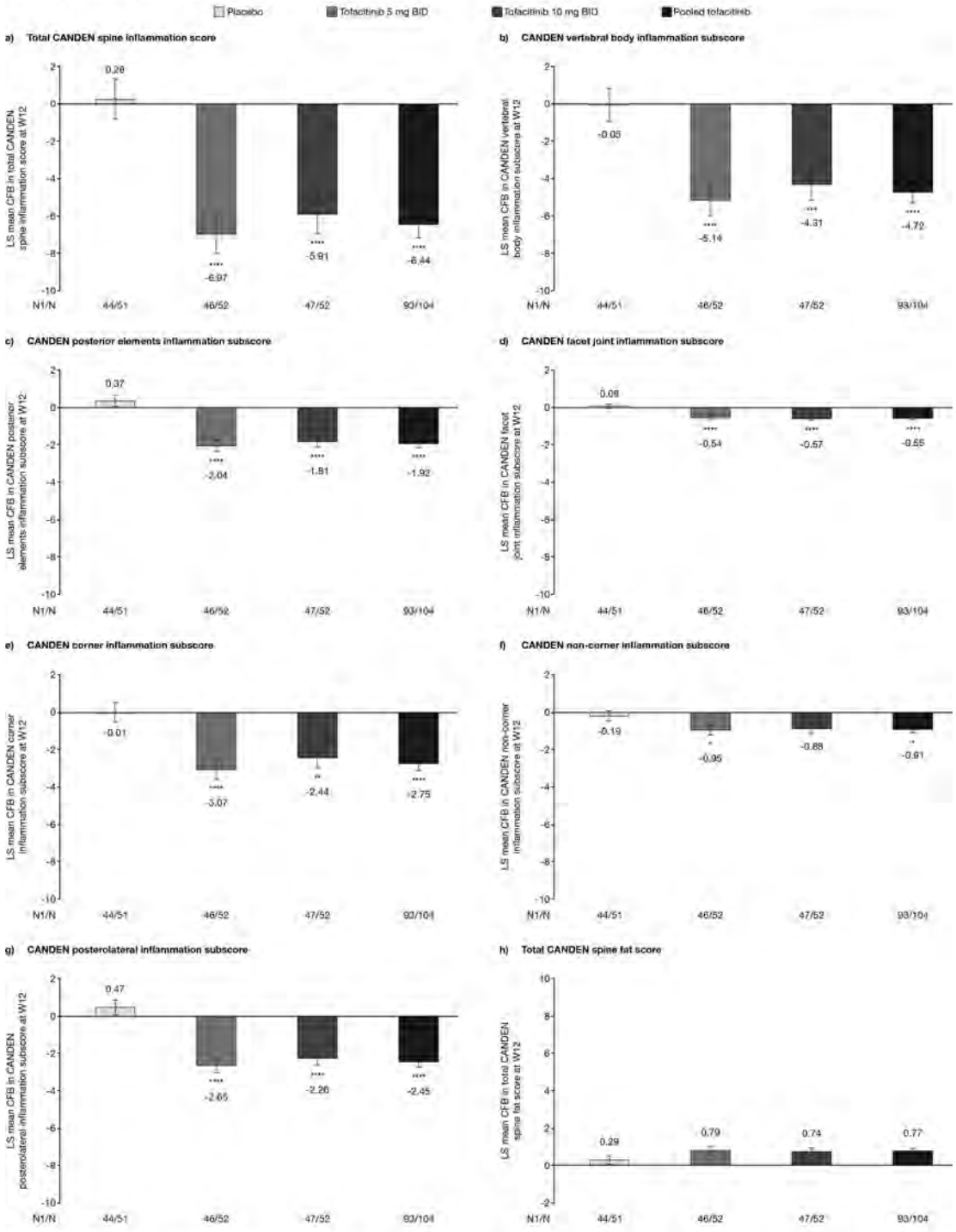
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: The Canada-Denmark (CANDEN) MRI scoring system enables detailed anatomy-based evaluation of inflammatory and structural lesions in spinal vertebral bodies and posterior elements in patients (pts) with AS.[1] Tofacitinib is an oral Janus kinase inhibitor under investigation for the treatment of adult pts with AS. In a Phase (P)2 dose-ranging study (NCT01786668), tofacitinib showed greater efficacy vs placebo (PBO) in reducing signs, symptoms, and inflammation based on Spondyloarthritis Research Consortium of Canada MRI SI joint and spine scores in biologic-naïve pts with AS.[2] This post hoc analysis evaluated the efficacy of tofacitinib on MRI outcomes for spinal vertebral body and posterolateral element inflammation and structural lesions in pts with AS, assessed with the CANDEN MRI scoring system.

Methods: Biologic-naïve adult pts with active AS (per modified New York criteria) were randomized 1:1:1:1 to tofacitinib 2, 5, or 10 mg twice daily (BID), or PBO in a 16-week (12-week treatment; 4-week follow-up), double-blind P2 study. Spine MRI assessments were performed at baseline (BL) and Week (W)12. This post hoc analysis comprised data from re-evaluation of MRI images in pts in the tofacitinib 5 or 10 mg BID, or PBO groups. Images were read

pairwise (both time points displayed simultaneously) by 2 independent readers blinded to time point/treatment, and scored using the CANDEN MRI scoring system. In cases of substantial disagreements between readers, a third reader adjudicated. Least squares mean changes from BL to W12 were reported for CANDEN-specific MRI outcomes, including total spine inflammation score and subscores, and total spine fat score. An analysis of covariance was

Figure. LS mean change from BL at W12 (FAS, LOCF) in CANDEN MRI scoring system: a) total spine inflammation score; b) vertebral body inflammation subscore; c) posterior elements inflammation subscore; d) facet joint inflammation subscore; e) corner inflammation subscore; f) non-corner inflammation subscore; g) posterolateral (costovertebral joints, transverse processes, spinous processes, and soft tissues) inflammation subscore; and h) total spine fat score



Data are LS mean (SE)
*p < 0.05; **p < 0.01; ***p < 0.001; ****p < 0.0001 for LS mean difference vs placebo
The pooled tofacitinib group included data from pts treated with tofacitinib 5 or 10 mg BID. An analysis of covariance with fixed effects of treatment and BL value was used. The FAS included pts who were randomized to tofacitinib 5 or 10 mg BID or placebo and received ≥ 1 dose of study drug. BL value was defined as the last observation prior to or on the date of the first dose of study drug. If a pt discontinued from the study ≥ W6, the pts' MRI was required at the early termination visit. MRI images obtained at the early termination visit were used for the W12 visit (LOCF)
BID, twice daily; BL, baseline; CANDEN, Canada-Denmark; CFB, change from BL; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; MRI, magnetic resonance imaging; N, number of pts in the FAS; N1, number of pts with both BL and W12/early termination MRI images in the FAS, evaluable by CANDEN MRI scoring system, included in analyses; pt, patient; SE standard error; W, Week

used for the primary comparison of pooled tofacitinib 5 and 10 mg BID groups vs PBO and for comparisons between tofacitinib 5 or 10 mg BID groups vs PBO. P values without adjustment to multiplicity are reported.

Results: MRI data for 137 pts were evaluated. At W12, significantly greater reductions were seen in the pooled tofacitinib group vs PBO for total CANDEN spine inflammation score ($p < 0.0001$; Fig a), and CANDEN vertebral body ($p < 0.0001$; Fig b), posterior elements ($p < 0.0001$; Fig c), facet joint ($p < 0.0001$; Fig d), corner ($p < 0.0001$; Fig e), non-corner ($p=0.0310$; Fig f), and posterolateral (costovertebral joints, transverse processes, spinous processes, and soft tissues; $p < 0.0001$; Fig g) inflammation subscores. Similar reductions were seen for these outcomes in the tofacitinib 5 or 10 mg BID groups vs PBO. Regarding fat infiltration, a numerically greater increase in total spine fat score was seen in the pooled tofacitinib group vs placebo (Fig h).

Conclusion: In biologic-naïve pts with AS, tofacitinib treatment was associated with significant reductions in MRI spinal inflammation, as assessed by the CANDEN MRI scoring system. Tofacitinib reduced inflammation in the posterolateral elements of the spine and the facet joints, which has not been described previously.

1. Krabbe S et al. RMD Open 2019; 5: e001057.

2. van der Heijde D et al. Ann Rhem Dis 2017; 76: 1340-7.

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Disclosure: M. Ostergaard, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **J. Wu**, Pfizer Inc, 3, 11; **L. Fallon**, Pfizer Canada, 3, 11; **S. Sherlock**, Pfizer Inc, 3, 11; **C. Wang**, Pfizer Inc, 3, 11; **D. Fleishaker**, Pfizer Inc, 3, 11; **K. Kanik**, Pfizer Inc, 3, 11; **W. Maksymowych**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0931

Early Improvement in Disease Activity Indices Predicts Achievement of Long-term Clinical Remissions, ASDAS Inactive Disease and Low BASDAI with Normal CRP, During TNF-α-inhibitor Therapy in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: As biologic agents including tumor necrosis factor (TNF)-α inhibitors (TNFi) have been proven to improve enormously clinical outcomes for patients with ankylosing spondylitis (AS), treat-to-target (T2T) is an emerging management strategy in AS. According to the concept of T2T strategy, clinical remission, which means

mainly achievement of ASDAS inactive disease (ASDAS-ID) or, alternatively, low BASDAI with normal CRP (BASDAI-CRP) or ASAS partial remission, should be accomplished and then be maintained throughout TNFi therapy. In this study, we evaluated to determine the possibility of achieving clinical remission and to investigate the predictors of attainment of clinical remission in AS patients treated with TNFi.

Methods: This was a retrospective observational study in 139 adult AS patients treated with TNFi up to 33 months. All outcome measures were performed at baseline and month 3, and then every six month up to month 33. Clinical remission selected were ASDAS-ID and BASDAI < 2 with normal CRP level (BASDAI-CRP). The longitudinal relationship between early improvement in clinical parameters and achievement of clinical remission was assessed using generalized estimating equations (GEEs).

Results: Responders of ASDAS-ID increased from 32.4 at month 3 to 68.9% at month 33 and that of BASDAI-CRP increased from 39.9% at month 3 to 75.2% at month 33. Patients satisfied with ASDAS-ID or BASDAI-CRP were almost redundant. The responders of ASDAS-ID or BASDAI-CRP showed a significantly better functional and metrological indices than the non-responders.

The analysis using univariable GEE model demonstrated that age [OR: 0.71 (95% confidence interval (CI), 0.54-0.92)] and all of 3-month improvement in ASDAS-CRP [OR: 1.57 (CI, 1.11-2.23)], BASDAI [OR: 1.78 (CI, 1.40-2.26)], physician's global assessment (PhGA) [OR: 1.47 (CI, 1.26-1.71)], patient's global assessment (PtGA) [OR: 1.40 (CI, 1.26-1.71)], and pain [OR: 1.32 (CI, 1.13-1.53)] were significant variables. On the multivariable GEE analysis, age [OR: 0.67 (CI, 0.49-0.93)] and 3-month BASDAI improvement [OR: 1.70 (CI, 1.19-2.41)] were associated with achievement of ASDAS-ID.

On the univariable GEE analysis, age [OR: 0.76 (CI, 0.60-0.96)], 3-month improvement in BASDAI [OR: 1.66 (CI, 1.32-2.10)], PhGA [OR: 1.23 (CI, 1.06-1.42), PtGA [OR: 1.19 (CI, 1.04-1.38)], and pain [OR: 1.25 (CI, 1.09-1.45)], and normalized ESR [OR: 2.87 (CI, 1.26-6.55)] and CRP [OR: 2.56 (CI, 1.22-5.34)] at month 3 were independent predictors of achievement of BASDAI-CRP. On the multivariable GEE analysis, age [OR: 0.75 (CI, 0.59-0.96)], 3-month BASDAI improvement [OR: 1.75 (CI, 1.29-2.36)], normalized ESR [OR: 2.93 (CI, 1.20-7.16)] and CRP at month 3 [OR: 2.98 (CI, 1.30-6.83)] were independent predictors of attainment of BASDAI-CRP.

Conclusion: The proportion of achievement of BASDAI-CRP was higher than that of ASDAS-ID during long-term TNFi therapy and patients satisfied with ASDAS-ID and BASDAI-CRP were almost redundant. On the analysis of mul-

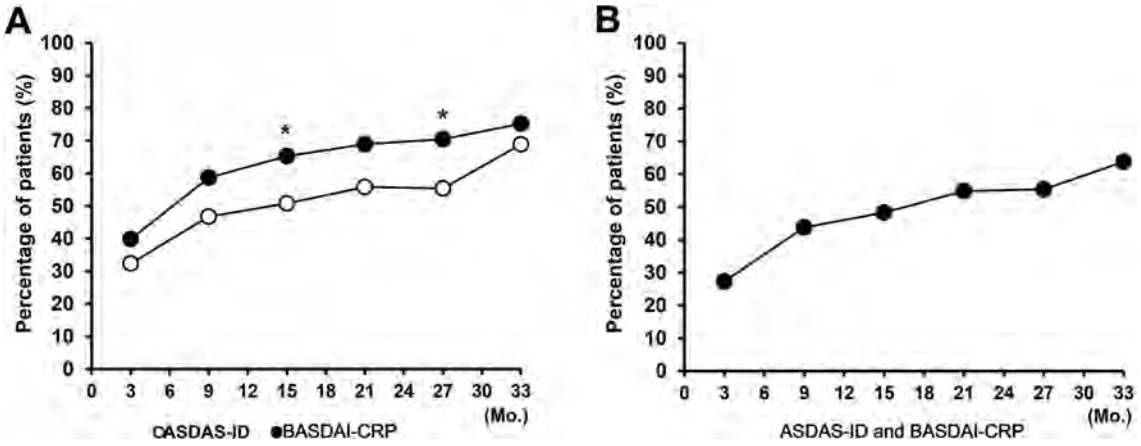

Figure. Response to TNF-α-inhibitor therapy as measured by ASDAS inactive disease (ASDAS-ID) and BASDAI + CRP criteria. These graphs show the proportion of achievement of (A) ASDAS-ID or BASDAI-CRP and (B) both ASDAS-ID and BASDAI- CRP criteria. *p <0.05.

tivariable GEE model, age and 3-month BASDAI improvement were independent predictors of achievement of both clinical remission criteria and normalized ESR and CRP at month 3 were predictors of achievement of BASDAI-CRP.

Disclosure: S. Lee, None; **N. Kim**, None; **E. Nam**, None.

Abstract Number: 0932

Sequential Treatment in Axial Spondyloarthritis - Real World Data from a Network of German Rheumatologists

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Increasing immunmodulatory treatment options are available for axial spondyloarthritis. Little is known about sequential treatment in clinical routine.

Methods: The pseudonymized RHADAR database (Kleinert, S. et al, J Med Internet Res. 2021;23(5):e28164) was analyzed with a special emphasis on patients with axSpA and with databank entries in the last 9 months before March 31st 2021. Their current and previous therapies were analyzed using the statistic software R (version 3.5.1) and RStudio (version 1.1.453). Documented therapies between 2011 and 2021 were included.

Results: Characteristics of the 1050 axSpA-patients are displayed in table 1. In 986 patients at least two timepoints of therapy could be analyzed. 77.2% stayed on the treatment of timepoint 1, 21.8% patients changed treatment at timepoint 2, and 4.2 % changed again at a 3rd timepoint.

At timepoint 1, 501 patients were on anti-TNF treatment; of which 379 (75.6%) therapy remained unchanged . At timepoint 2 57 (11,4%) changed to a different TNF blocker, 33 (6,6%) to NSAID only, 16 (3,2%) to anti-IL17 treatment, and 2 (0,4%) to treatment with a Janus kinase inhibitor.

NSAID therapy was applied in 335 patients at timepoint 1, of those, 281 (83.9%) remained on same therapy., 45 (13,4%) changed to anti-TNF treatment, 6 (1,8%) to anti-IL17 treatment at timepoint 2.

Among the 52 (5.3%) patients on anti-IL17 treatment at timepopint 1 38 (73,1%) continued their therapy unchanged, 7 changed to NSAIDs, 4 to a different anti-IL17 inhibitor, and 2 to anti-TNF treatment.

Table 1. Patients' characteristics.

	n (available)	% (available)	Mean	SD	Median	25% Quantile	75% Quantile
Age	1050	100.0	50.1	14.0	51.0	39.0	60.0
Age (female)	454	43.2	51.3	13.7	53.0	40.0	60.8
Age (male)	596	56.8	49.1	14.2	49.0	38.0	59.0
Disease duration	1041	99.1	14.4	12.2	11.0	6.0	21.0
Disease duration (female)	453	43.1	12.5	11.8	9.0	5.0	17.0
Disease duration (male)	588	56.0	15.9	12.3	13.0	6.0	22.0
BASDAI	1009	96.1	3.2	2.1	2.8	1.5	4.7
BASFI	961	91.5	2.8	2.5	2.2	0.8	4.5
BASMI	376	35.8	1.9	2.5	1.0	0.0	3.0
ASDAS	522	49.7	2.0	0.9	1.9	1.4	2.5
Treatment Timepoint 1	986						
- NSAID	335	34.0					
- Anti TNF	501	50.8					
- Anti IL17	52	5.3					
- different (Sulfasalazine, Methotrexat)	101	10.2					

Conclusion: The majority of the patients 50,8% (501/986) were treated with an TNF-inhibitor, 34% (335/986) received NSAIDs only, while 5,3% were on IL17-inhibitor at timepoint 1. Regardless of the treatment modality at timepoint 1 majority of axSpA-patients continued their therapy unchanged. The most likely explanation to this observation is the low disease activity as reflected by the disease activity indices in table 1.

The emerging immunomodulatory therapeutic options will offer further alternative pathways in the sequential treatment of axSpA patients.

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Abstract Number: 0933

Sustained Functional Remission in Axial Spondyloarthritis (axSpA): Which Are the Primary Outcomes That Should Be Targeted to Achieve This?

Walter Maksymowych[1], Robert Inman[2], Louis Bessette[3], Proton Rahman[4], Emmanouil Rampakakis[5], Odalis Asin-Milan[6], Meagan Rachich[6], Anne Marilise Marrache[6] and Allen Lehman[6], [1]Department of Medicine, University of Alberta, Alberta, Canada, Edmonton, AB, Canada, [2]University Health Network, Toronto, ON, Canada, [3]Centre de l'Ostoporose et de Rhumatologie de Qubec, Québec City, QC, Canada, [4]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [5]JSS Medical Research, Montréal, QC, Canada, [6]Janssen Inc., Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: A treat-to-target (T2T) strategy has been advocated for the management of axSpA although no consensus exists as to the most appropriate target or the outcome to be monitored to achieve this target. Structural damage assessed by radiography is not a feasible target in axSpA as it is insensitive to change. Functional impairment is associated with inflammation and structural damage and is assessed in axSpA using the Bath Ankylosing Spondylitis (AS) Functional Index (BASFI). Sustained (≥6 mos duration) low BASFI (< 3) may therefore be an appropriate target for a T2T strategy in axSpA. There is also no consensus as to which outcome(s) should be monitored in a T2T strategy although there is agreement that the key domain is disease activity. The AS Disease Activity Score (ASDAS) is recommended although the Bath AS Disease Activity Index (BASDAI) is more feasible. Our objectives were to determine 1) to what degree duration of low disease activity impacts function and 2) which patient and disease characteristics predict sustained low BASFI focusing on a comparison of sustained (≥6 mos) low ASDAS versus BASDAI.

Methods: Biologic Treatment Registry Across Canada (BioTRAC) was a multi-centre, prospective, registry that collected real-world patient reported outcomes, clinical, and laboratory data on axSpA patients treated with infliximab or golimumab between 2002-2018. Data were collected every 6 mos. The impact of achieving low BASDAI (< 3) and/or ASDAS-inactive disease (ID) (< 1.3) at 6 and 12 mos, at only 6 or 12 mos, or at neither time point, and the interaction of CRP at 6 and 12 mos with BASDAI, on the BASFI score at 18 mos was analyzed by generalized linear models (GLM) adjusted for age, gender, baseline disease duration, and baseline BASFI. Generalized estimating equations (GEE) were used in univariate and multivariate analyses to test baseline patient demographic and disease character-

Table 1. Predictors of low BASFI (<3) Between 12 and 18 Months

Parameter	OR	95% CI	P-Value
BASFI-Baseline	0.7	0.6, 0.8	**<0.001**
Low BASDAI (<3): M6 and M12 vs persistent BASDAI >3	10.5	4.0, 27.2	**<0.001**
Low BASDAI (<3): M6 or M12 vs. persistent BASDAI>3	5.2	2.4, 11.1	**<0.001**
ASDAS-ID: M6 and M12 vs. persistent ASDAS>1.3	3.7	1.1, 13.1	**0.040**
ASDAS-ID: M6 or M12 vs. persistent ASDAS>1.3	2.2	0.8, 6.0	0.144

Table 2. Predictors of BASFI at 18 Months

Parameter	B*	95% CI	P-Value
BASFI-Baseline	0.30	0.19, 0.41	**<0.001**
Low BASDAI (<3): M6 and M12 vs. persistent BASDAI >3	-2.45	-3.35, -1.55	**<0.001**
Low BASDAI (<3): M6 or M12 vs. persistent BASDAI >3	-2.14	-2.88, -1.41	**<0.001**
ASDAS-ID: M6 and M12 vs. persistent ASDAS>1.3	-1.10	-2.15, -0.05	**0.041**
ASDAS-ID: M6 or M12 vs. persistent ASDAS>1.3	-0.70	-1.62, 0.22	0.136
Age (Years)	0.04	0.02, 0.07	**0.001**
Male vs. Female	0.35	-0.22, 0.92	0.228
Baseline Disease Duration (Years)	-0.02	-0.05, 0.01	0.121

**Positive Beta coefficient indicates increased BASFI score at 18 months*

istics, treatment, sustained low BASDAI and/or ASDAS-ID at 6 and 12 mos, in predicting low BASFI (< 3) between 12 and 18 mos.

Results: A total of 1620 pts were enrolled, 33.7% and 15% with sustained low BASDAI and ASDAS-ID, respectively. In univariate GEE of baseline variables, only age and baseline BASDAI, BASFI, and ASDAS were significant predictors of sustained low BASFI. In univariate GEE of follow up variables, sustained low BASDAI and ASDAS-ID were also predictors. In multivariate GEE, sustained low BASDAI and baseline BASFI were the only predictors of low BASFI (Table 1). Sustained ASDAS-ID was a weak predictor when forced into the model.

Similarly, in GLM models, sustained low BASDAI and baseline BASFI plus age were strong predictors of BASFI score at 18 mos, while sustained ASDAS-ID was a weak predictor (Table 2). A significant interaction was observed between duration of low BASDAI and normal CRP (< 5mg/L at 6 and 12 mos) with CRP remission identified as an independent predictor of function among patients on sustained low BASDAI.

Conclusion: Aiming for sustained low BASDAI (< 3) may be a valid and more feasible T2T treatment strategy than ASDAS-ID for routine care in axSpA. Further validation of these real-world findings is required to aid in achieving consensus on which outcome should be monitored in a T2T strategy.

Disclosure: W. Maksymowych, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6; **R. Inman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Lilly, 2, Novartis, 2, Pfizer, 2, Sandoz, 2; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **E. Rampakakis**, None; **O. Asin-Milan**, Janssen, 3; **M. Rachich**, Janssen, 3, 11; **A. Marrache**, Janssen, Inc (a subsidiary of Johnson & Johnson), 3, 11; **A. Lehman**, Janssen Inc., 3.

Abstract Number: 0934

Baseline Characteristics and Treatment Response to Ixekizumab Categorised by Sex in Radiographic and Non-Radiographic Axial Spondylarthritis Patients Through 52 Weeks: Data from 3 Phase III, Randomized, Controlled Trials

Irene van der Horst-Bruinsma[1], Rebecca Bolce[2], Theresa Hunter[3], David Sandoval Calderon[2], Danting Zhu[2], Vladimir Geneus[2], Jeffrey Lisse[4], Soyi Liu-Leage[5] and Marina Magrey[6], [1]Amsterdam UMC, Amsterdam, Netherlands, [2]Eli Lilly and Company, Indianapolis, IN, [3]Eli Lilly and Company, Indianapolis, IN, USA, Indianapolis, IN, [4]Eli Lilly and Company, Tucson, AZ, [5]Eli Lilly and Company, Neuilly sur Seine, France, [6]Case Western Reserve University, MetroHealth Medical Center, Cleveland, OH, USA, Richfield, OH

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease of the axial skeleton comprising two subtypes within the same spectrum: radiographic (r-axSpA) and non-radiographic (nr-axSpA). Previous studies have shown that clinical presentation and treatment response of males and females may differ[1] despite simi-

lar disease burden.[2] Ixekizumab (IXE), a high-affinity monoclonal antibody that selectively targets interleukin-17A, has demonstrated superior efficacy to placebo in the treatment of patients with r-axSpA (COAST-V/W [bDMARD- naïve/ TNFi-experienced]) and nr-axSpA (COAST-X [bDMARD-naïve]).[3] Here we report baseline characteristics and treatment response to IXE categorised by sex in patients with r-axSpA and nr-axSpA for up to 52 weeks.

Methods: Patients fulfilled the ASAS classification criteria for r-axSpA or nr-axSpA. Patients were randomized to receive 80 mg subcutaneous IXE every 2 weeks (Q2W) or 4 weeks (Q4W), or to placebo (PBO) [16 weeks COAST-V/W; 52 weeks COAST-X]. Baseline characteristics and treatment outcomes were assessed. Patients were categorised by sex, missing data was controlled for using non-responder imputation (NRI) and modified baseline observation carried forward (mBOCF) analysis was conducted on continuous efficacy variables.

Table 1. Baseline Characteristics of Patients Categorised by Sex

	Patients with r-axSpA (COAST-V/W) (n=376)			Patients with nr-axSpA (COAST-X) (n=198)		
Characteristic	**Male (n=298)**	**Female (n=78)**	**p value**	**Male (n=99)**	**Female (n=99)**	**p value**
Age at onset (yrs), mean (SD)	26.5 (8.7)	30.1 (10.1)	**0.002***	27.9 (7.7)	32.0 (10.7)	**0.002***
Symptom duration (yrs), mean (SD)	16.7 (10.5)	17.8 (12.2)	0.420	9.5 (9.2)	12.3 (11.3)	0.057
ASDAS, mean (SD)	4.0 (0.8)	3.9 (0.7)	0.304	3.7 (0.8)	3.9 (0.8)	0.143
BASDAI, mean (SD)	7.10 (1.4)	7.4 (1.5)	0.179	6.9 (1.4)	7.4 1.4)	**0.013***
Fatigue/tiredness (BASDAI Q1), mean (SD)	7.4 (1.6)	7.8 (1.5)	**0.036***	7.0 (1.6)	7.9 (1.5)	**<0.001***
Spinal pain (BASDAI Q2), mean (SD)	7.9 (1.5)	8.0 (1.5)	0.682	7.5 (1.4)	7.9 (1.5)	**0.029***
Pain/swelling in other joints (BASDAI Q3), mean (SD)	6.5 (2.1)	6.9 (2.2)	0.129	6.6 (2.3)	7.2 (1.9)	**0.039***
Tenderness to touch/pressure (BASDAI Q4), mean (SD)	6.8 (1.8)	7.0 (1.9)	0.339	6.6 (1.9)	6.8 (1.8)	0.404
Morning stiffness (BASDAI Q5), mean (SD)	7.5 (1.6)	7.7 (1.8)	0.504	7.3 (1.7)	7.7 (1.9)	0.137
Morning stiffness duration (BASDAI Q6), mean (SD)	6.5 (2.3)	6.5 (2.8)	0.944	6.3 (2.3)	6.6 (2.5)	0.392
Spinal pain at night NRS, mean (SD)	7.4 (1.5)	7.8 (1.7)	**0.033***	7.0 (1.8)	7.6 (1.8)	**0.027***
BASFI, mean (SD)	6.8 (1.8)	7.0 (2.0)	0.466	6.2 (1.8)	6.7 (2.1)	0.108
SF-36 PCS, mean (SD)	30.9 (8.3)	28.9 (8.2)	0.075	33.1 (7.7)	32.1 (7.2)	0.348

p-value from Fisher's exact test analysis of variance (ANOVA) with sex as a factor for continuous data. Data includes pooled IXEQ2W and IXEQ4W.

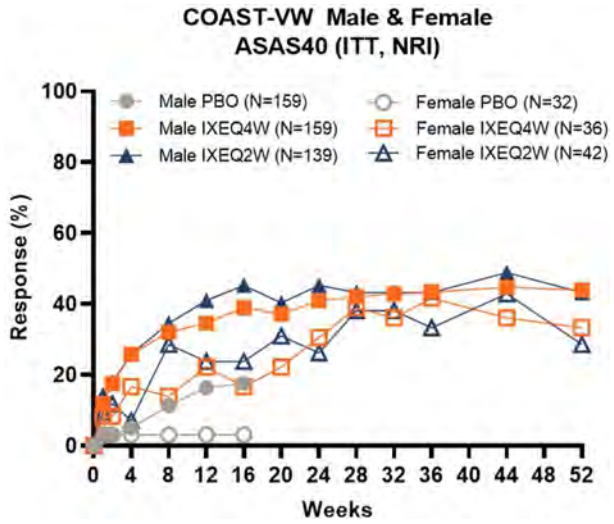

Figure 1. COAST-V/W ASAS40 (ITT, NRI) Patients initially randomized to PBO in COAST-V/W switched to IXEQ2W or Q4W at week 16 by study design; PBO data are summarised up to week 16.

Results: At baseline, females were older, with significantly higher pain and fatigue scores and peripheral joint symptoms (table 1). ASAS40 response rate with IXEQ4W was achieved in 39% of males with r-axSpA by week 16, and 44% by week 52. Females achieved 16.7% at week 16, and 33.3% at week 52. In nr-axSpA, 46% of IXEQ4W males achieved ASAS40 at week 16 and 30% at week 52. 23.9% of females achieved ASAS40 at week 16, increasing to 30.4% at week 52.

Conclusion: This analysis demonstrates that for the axSpA disease spectrum, females present with higher disease burden as reflected by higher scores in fatigue/tiredness, and spinal pain at night. Our findings indicate that males and females respond to IXE; however, females experience this benefit later in their treatment course, with a more prolonged attainment of peak response.

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2. Zhao SS, et al. Rheumatology. 2019;58:2025-2030.
3. Deodhar A, et al. Lancet. 2020;395:53-64.

Disclosure: I. van der Horst-Bruinsma, None; **R. Bolce**, Eli Lilly and Company, 3, 11; **T. Hunter**, Eli Lilly and Company, 3, 11; **D. Sandoval Calderon**, Eli Lilly and Company, 3; **D. Zhu**, Eli Lilly and Company, 3; **V. Geneus**, Eli Lilly and Company, 3; **J. Lisse**, Eli Lilly and Company, 3, 11; **S. Liu-Leage**, Eli Lilly and Company, 3, 11; **M. Magrey**, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5.

Abstract Number: 0935

Effects of Ixekizumab Treatment on Structural Changes in the Sacroiliac Joints Based on MRI Assessments at 16 Weeks in Patients with Non-Radiographic Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: To evaluate the effect of treatment with ixekizumab versus placebo (PBO) on structural lesions in the sacroiliac joints (SIJ) at 16 weeks in patients with non-radiographic axial spondyloarthritis (nr-axSpA).

Methods: Patients with active nr-axSpA who were biologic-naïve (COAST-X, NCT02757352) were randomized 1:1:1 to receive double-blinded ixekizumab 80 mg every 4 (Q4W) or 2 weeks (Q2W) with an 80-mg or 160-mg starting dose at week 0 or PBO. SIJ magnetic resonance imaging (MRI) was assessed by Spondyloarthritis Research Consortium of Canada (SPARCC) SIJ structural score (SSS). Treatment comparisons used analysis of covariance based on observed cases.

Results: Of 303 randomized patients, 266 patients (Q4W: n=85, Q2W: n=91, PBO: n=90) with an MRI scan available at baseline and week 16 were included in this analysis. Mean SPARCC SSS for PBO and ixekizumab dose groups were similar at baseline (Figure 1 and Table). Significant reduction in SPARCC SSS for erosion was observed in both ixekizumab dose groups versus PBO (Fig. 1A). Increased erosion scores occurred for fewer patients in both ixekizumab dose groups versus PBO (Fig. 1B). Decreased erosion scores occurred for more patients in both ixekizumab dose groups versus PBO (Fig. 1B). Mean change from baseline in SPARCC SSS was significantly greater for ixekizumab for fat metaplasia (Q4W) and backfill (Q4W and Q2W) versus PBO (Table). Changes in ankylosis were generally not observed (Table).

Conclusion: Treatment with ixekizumab versus PBO led to significant reductions in erosions and significant increases in fat metaplasia and backfill in the SIJ in patients with nr-axSpA assessed at 16 weeks of treatment.

MRI SPARCC SSS Change from Baseline (CFB) at Week 16 (observed)

Parameters	PBO N=105	IXE Q4W N=96	IXE Q2W N=102
Bone erosion			
Number of patients[a]	90	85	91
Baseline mean	3.36	3.19	3.03
LS mean CFB (SE)	0.16 (0.13)	-0.39 (0.13)	-0.40 (0.13)
p-value versus PBO	NA	0.003	0.002
Fat metaplasia			
Number of patients[a]	90	85	91
Baseline mean	1.41	1.71	1.05
LS mean CFB (SE)	-0.04 (0.058)	0.16 (0.059)	0.10 (0.057)
p-value versus PBO	NA	0.013	0.067
Backfill			
Number of patients[a]	90	84	91
Baseline mean	0.59	0.54	0.54
LS mean CFB (SE)	-0.10 (0.085)	0.21 (0.087)	0.22 (0.084)
p-value versus PBO	NA	0.011	0.006
Ankylosis			
Number of patients[a]	90	85	91
Baseline mean	0.06	0.38	0.08
LS mean CFB (SE)	0 (0.003)	0 (0.003)	0.01 (0.003)
p-value versus PBO[a]	NA	NA	NA

Note: The ANCOVA model for observed case analysis includes treatment, geographic region, screening MRI/CRP status, and baseline value.

[a]Only one patient in the IXE Q2W group had a change of 0.5; all other patients had no change.

ANCOVA: analysis of covariance; CFB: change from baseline; CRP: C-reactive protein; IXE: ixekizumab; LS: least squares; MRI: magnetic resonance imaging; N: number of patients in the analysis population; NA: not applicable; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; SE: standard error; SIJ: sacroiliac joints; SPARCC: Spondyloarthritis Research Consortium of Canada; SSS: SIJ structural score.

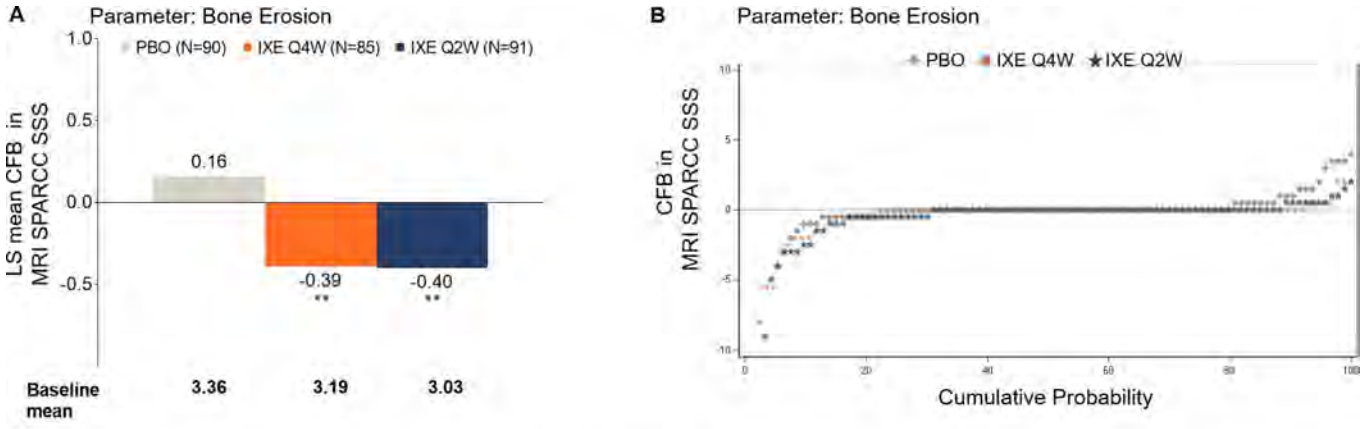

Figure 1. Mean CFB for IXE 80 mg versus placebo to week 16 in MRI SPARCC SSS bone erosion for A) summary data and B) individual patient-level data. The ANCOVA model for observed case analysis includes treatment, geographic region, screening MRI/CRP status, and baseline value. **p<.005 versus PBO. ANCOVA: analysis of covariance; CFB: change from baseline; CRP: C-reactive protein; IXE: ixekizumab; LS: least squares; MRI: magnetic resonance imaging; N: number of patients with an MRI scan available at baseline and week 16; PBO: placebo; Q2W: every 2 weeks; Q4W: every 4 weeks; SIJ: sacroiliac joints; SPARCC: Spondyloarthritis Research Consortium of Canada; SSS: SIJ structural score.

Disclosure: W. Maksymowych, Abbvie, 2, 5, 6, BMS, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Janssen, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **R. Lambert**, Pfizer, 2; **R. Landewé**, AbbVie, 5, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB, 5, 6, Astra-Zeneca, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli-Lilly, 6, Janssen, 6, Gilead, 6, Galapagos, 6, Glaxo-Smith-Kline, 6; **D. Sandoval Calderon**, Eli Lilly and Company, 3; **H. Carlier**, Eli Lilly and Company, 3; **J. Lisse**, Eli Lilly and Company, 3, 11; **X. Li**, Eli Lilly and Company, 3; **M. Hojnik**, Eli Lilly and Company, 3; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6.

Abstract Number: 0936

Factors Associated with the Development of Anti-drug Antibodies to Tumour Necrosis Factor Inhibitors in Patients with Axial Spondyloarthritis; A Two Year Follow-up Study

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)

Session Type: Poster Session B

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease affecting sacroiliac joints and spine as well as peripheral joints and entheses. Tumour necrosis factor inhibitors (TNFi) are widely used in patients with persistently high disease activity despite non-steroidal anti-inflammatory drugs. Some patients

Table 1. Baseline demographic and disease characteristics

	All patients (n=180)
Age, years median (IQR)	43 (16)
Sex, male, n(%)	119 (66.1)
The presence of extraspinal involvement history	
Periferal arthritis, n (%)	21/102 (20.6)
Enthesitis, n (%)	8/102 (7.8)
Dactylitis, n (%)	2/95 (2.1)
Anterior uveitis, n (%)	1/102 (1)
Psoriasis, n (%)	3/102 (2.9)
İnflamatory bowel disease, n (%)	5/92 (5.4)
Disease activity	
BASDAI (0 to 10), mean ± SD	5.8 ± 16.7
BASFI (0 to 10), mean ± SD	5.2 ± 2.5
ASDAS-CRP, mean ± SD	3.7 ± 0.9
CRP (mg/dl), median (IQR)	12 (22.5)

Table 2. Factors associated with the development of anti-drug antibodies

	Model 1			***Model 2***		
	B	95% CI	*P*	B	95% CI	*P*
Age years	-0.061	-0.109;-0.012	***0.015***	-0.058	-0.107;-0.010	***0.018***
TNFi Treatment						
ETN	-1.981	-4.369; -0.134	*0.104*	-2.475	-4.791; -0.076	***0.036***
ADA	1.438	-0.002; 0.407	*0.073*	1.275	-0.119; -0.160	*0.064*
INF	1.550	3.010; 3.102	*0.050*	1.255	2.666; 2.629	*0.073*
GOL	0[a]			0[a]		
Presence of	-0.824	-1.451; -.0198	***0.010***	-0.835	-1.461; -0.208	***0.009***

fail to respond or loose responsiveness during therapy with TNFi. The development of anti-drug antibodies (ADA) might play a role in non-response or some adverse events. However it has never been evaluated for 2-years period.

Objectives: Therefore, the aim of the present study was to evaluate the development of ADA against TNFi longitudinally during 2-years period in axSpA patients and factors associated with it.

Methods: In total 180 axSpA patients according to ASAS classification criteria with a new TNFi prescription in the last two weeks period were included in this observational study. Clinical data and serum samples were collected at baseline and at every 12 weeks. Serum drug levels and ADAs were measured on 12, 24, 52 and 104 weeks of treatment by ELISA in one center to avoid inter-assay variability. The development of ADA over time was investigated by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.

Results: 180 biologic naive axSpA patients (116 male, median [IQR] 44,5 [14,5] years) who started anti-TNF agents (infliximab [20%], adalimumab [27,2%], etanercept [32,2%] and golimumab [20,6%]) were included in the analysis (Table 1). In comparison to baseline values BASDAI, ASDAS-CRP and CRP values were significantly decreased in third months of follow-up (Figure 1). In total 172 patients had at 12 weeks, 154 at 24, 121 at 52, and 73 at 104 week serum samples available for ADA determination. In longitudinal analysis; baseline age and TNFi type, as well as longitudinal BASDAI, ASDAS, serum CRP levels and the development of adverse events and discontinuation of the drug were found to be associated with the development of ADA. In order to determine independent association/s with the development of ADA two longitudinal multivariable models were run; (a) with ASDAS as an activity measure, (b) with BASDAI and CRP levels and produced that all the variables were independently associated with longitudinally development of anti-drug antibodies (Table 2). Antibodies to adalimumab were related with lower serum drug levels.

Conclusion: The results of the present study with up to 2 years of follow-up, revealed that the development of ADA against TNFi therapy is associated with high disease activity, the development of adverse events and treatment discontinuation in patients with axSpA. And etanercept might be negatively associated with the development of ADA.

Disclosure: E. **Ediboglu**, None; **D. Solmaz**, Roche, 6, Farmanova, 6, Pfizer, 6, Lilly, 6; **G. Kabadayi**, None; **M. Ozmen**, None; **K. Kaya**, None; **M. Çınar**, None; **G. Sargın**, None; **G. Hatemi**, Celgene, 5, AbbVie, 6, Novartis, 6, UCB, 6; . **Karadağ**, None; **G. Kınıklı**, None; **O. Gercik**, None; **U. Kalyoncu**, None; **S. Yılmaz**, None; **T. Şentürk**, None; **G. Keser**, None; **F. Yargucu**, None; **A. Cefle**, None; **D. Kozacı**, None; **B. Kısacık**, None; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6.

Abstract Number: 0937

Evaluation of the Safety of Vedolizumab in Combination with Other Immunosuppression Biological Therapy in Patients with Inflammatory Bowel Disease

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory bowel disease (IBD) causes a wide range of symptomology frequently leading to co-management of disease activity between gastroenterologist and rheumatologists. Recently in efforts to optimize treatment, there has been interest in using combination biological therapy with vedolizumab.

Methods: A retrospective single center study was performed on individual patients, between the ages 18 to 80, treated with combination therapy with vedolizumab and any other biological (etanercept, adalimumab, golimumab, certolizumab, infliximab, ustekinumab, JAK inhibitors) between 2014 and May 2021. Patients were identified through a database search via diagnosis code and medication list review with subspecialty clinics. Individual patient charts were then reviewed to confirm IBD diagnosis and use of combination therapy during their time of follow-up at this institution. Additional data was abstracted regarding baseline characteristics, infections, cancer diagnoses, and mortality.

Results: Sixteen patients meeting the study criteria for a complete retrospective chart review were identified. The mean age at initiation of combination therapy was 39.8 years of age. 56% of the patients were male. 81.2% of the patients were diagnosed with Crohn's disease and 18.8% with ulcerative colitis. 56.25% had complaints of joint pain and 37.5% were evaluated by rheumatology. Dual biological therapy was initiated for IBD control in 75% of patients and for joint pain in 25% of patients. 69% received adalimumab, 44% received ustekinumab, and 6% received certolizumab. One of the patients received adalimumab then transitioned to ustekinumab. The mean duration of dual biological therapy was 11.9 months. 14 of 16 patients remained on dual therapy during the duration of the study. One patient developed antibodies against adalimumab which lead to discontinuation. One patient had to discontinue dual therapy due to insurance authorization. The minimum duration of combination therapy was 1 month and the maximum duration was 22 months. Seven total infections occurred in 4 patients (25%). Serious infections requiring hospitalization or IV antibiotics occurred in two patients (12.5%). None of the patients developed a new diagnosis of cancer or experienced a reoccurrence of cancer. No deaths occurred during the time of follow-up.

Conclusion: This retrospective study reviewing 16 cases of patients treated with vedolizumab and dual biological combination therapy demonstrates additional data regarding infection, cancer, and mortality rates. Further studies are needed to better characterize and evaluate the safety profile of vedolizumab combination therapy in IBD patients for intestinal and extra-intestinal manifestations.

Disclosure: G. Chesini, None; **E. Parrott**, None; **L. Fox**, None; **J. Beatty**, None; **C. Effken**, None; **N. Yu**, None; **F. Hosseini-Aslinia**, None; **M. Krause**, None.

Abstract Number: 0938

Comparative Effectiveness and Treatment Survival of Different TNF Inhibitors for Axial Spondyloarthritis in Real-World Clinical Practice

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Tumor necrosis factor (TNF) inhibitors are the mainstay treatment for NSAID refractory axial spondyloarthritis (axSpA). However, few data exist on their use during routine clinical practice. The primary aim of

this study was to evaluate the effectiveness and treatment survival of different TNF blocking agents within a cohort of patients with axSpA.

Methods: We obtained data from patients who fulfilled the ASAS 2011 classification criteria for axSpA, who were treated with a TNF inhibitor and had clinical follow-up from 2003 to 2019. Effectiveness was evaluated based on the BASDAI50 response at 6 months of therapy. Multivariable linear regression models were used to estimate the predictors of improvement in BASDAI. Treatment persistence was analyzed using Kaplan-Meier survival analysis and Cox proportional hazards model.

TNF inhibitor during first treatment	BASDAI50 (%)
Adalimumab	39/71 (54.9%)
Certolizumab	1/3 (33.3%)
Etanercept	16/33 (48.5%)
Golimumab	24/52 (46.2%)
Infliximab	7/12 (58.3%)
Total	87/171 (50,9%)

Table 1. Percentage of patients obtaining a BASDAI50 by molecule during first TNF inhibitor treatment (n=171); p=0,812[b]

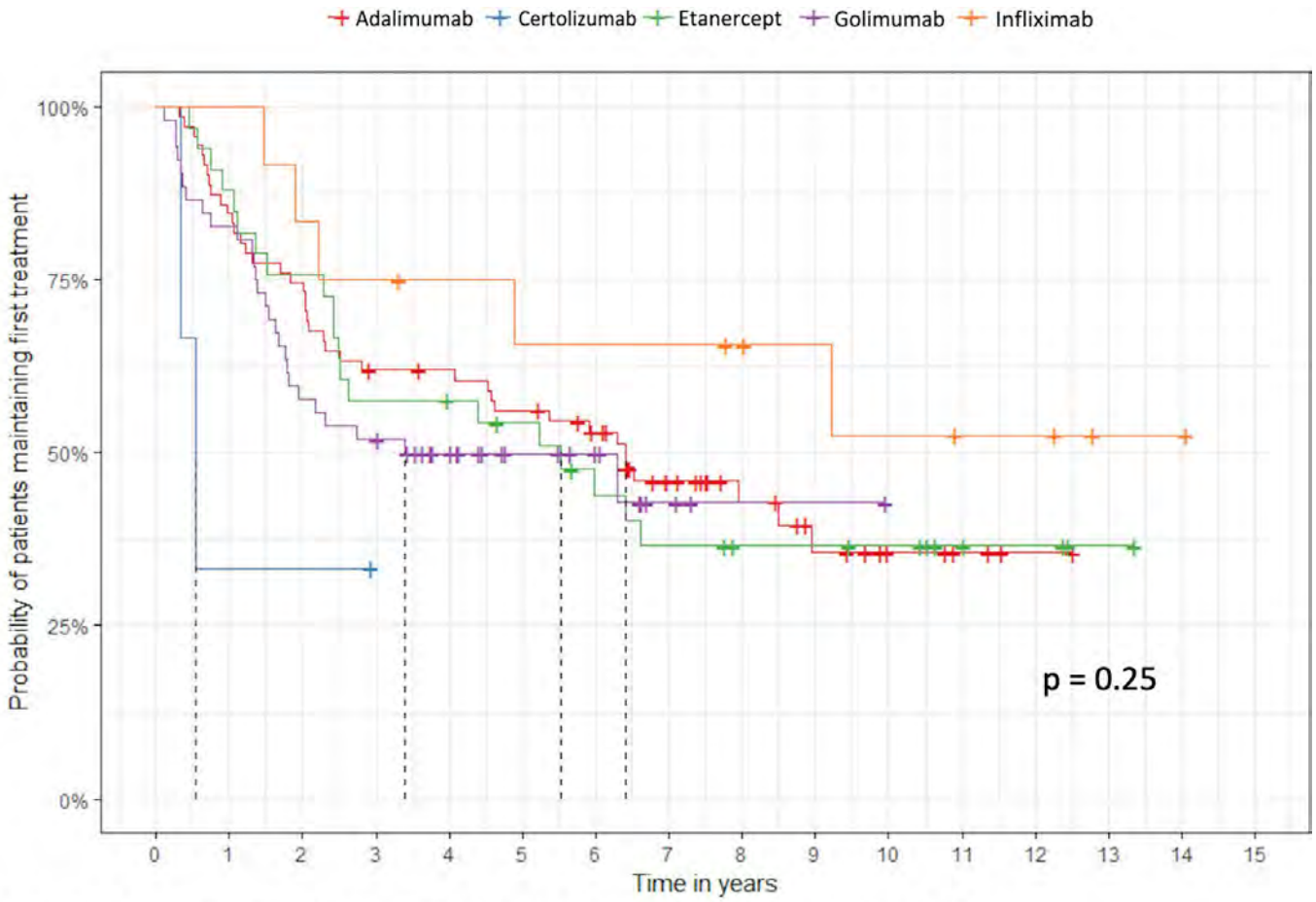

Figure 1. Drug survival for different TNF inhibitors as first treatment in axSpA

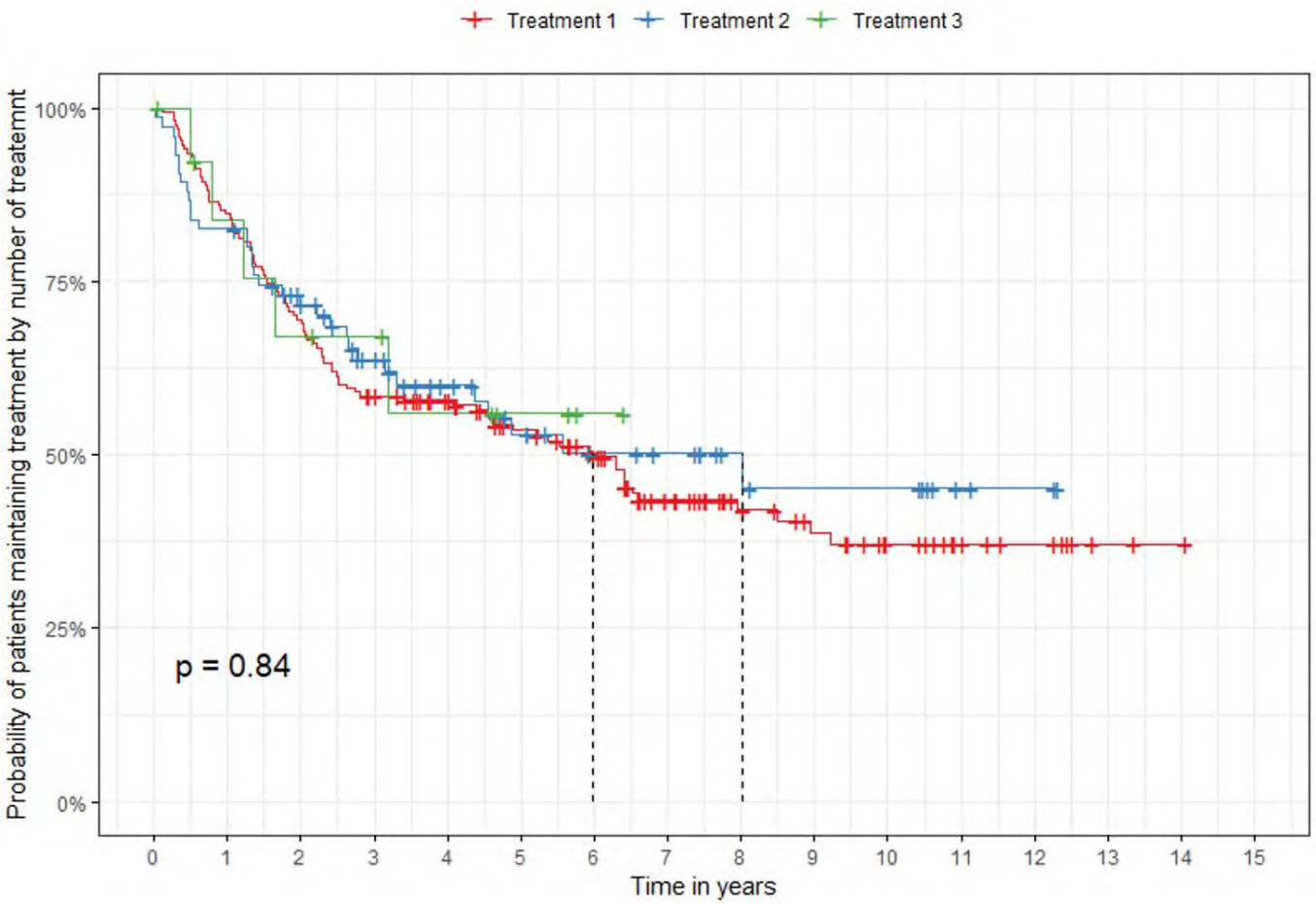

Figure 2. Drug survival of first and subsequent TNF inhibitor treatments

Results: The study comprised 171 patients. The median age was 45 years and 57% were males. Mean baseline BASDAI and BASFI were 6.1 and 5.5 respectively. At 6 months, 50.9% reached a BASDAI50 response and no differences were observed within the different TNF inhibitors **(Table 1)**. In the adjusted analysis, smokers were less likely to achieve a BASDAI50 response compared with nonsmokers HR 0.15 (95% CI 0.059 - 0.375) $p < 0.0001$. In contrast, patients with a higher baseline BASDAI score were more likely to reach a BASDAI50 at 6 months HR 1.29 (95% CI 1.072 - 1.564) $p = 0.007$. No other variables demonstrated an association with BASDAI50. The median survival for the first TNF inhibitor therapy was 5.9 years (95% CI 4.5-7.4) without significant difference in treatment survival between TNF inhibitors. There was a trend for a better survival with infliximab, but this was not statistically significant (Figure 1). In the non-radiographic (nr-axSpA) group (n=51), 57% reached a BASDAI50 response, compared to 48% in the ankylosing spondylitis (AS) group (n=119) (p=0.28) during the first TNF inhibitor treatment. The median survival, for the first TNF blocking therapy, was 5.3 years (95% CI 1.58-9.15) in the nr-axSpA group and 6,3 years in the AS group (95% CI 4.58-8.01).

After a first TNF inhibitor failure, the BASDAI50 response for subsequent second and third TNF inhibitor therapies, was 48.7% and 38.5% respectively, with no significant difference in treatment survival (Figure 2). The reasons for discontinuation of the first TNF inhibitor were primary failure 14.7%, secondary failure 61.1%, adverse events 14.7%, and others 9.5%.

Conclusion: Most patients who received TNF blocking agents for axSpA during routine clinical care showed improvement in disease activity. TNF inhibitor effectiveness and drug survival were comparable to published data.

There were no significant differences in effectiveness or treatment survival among the different TNF inhibitors. Effectiveness and drug survival was not different between nr-axSpA and AS. Failure to a first TNF inhibitor did not diminish effectiveness or drug survival of subsequent TNF inhibitor treatments. The main reason for treatment discontinuation was secondary failure.

Disclosure: J. Marrugo, None; **M. Bonin**, None; **G. Boire**, Abbvie, 1, 6, 7, BMS, 6, 7, Janssen, 1, 5, 6, Eli Lilly, 1, 7, Amgen, 7, Novartis, 6, 7, Pfizer, 7, Sandoz, 6, 7, Viatris, 1, 6, Samsung Bioepis, 1; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **A. Masetto**, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, Janssen, 2, 5, 6, Amgen, 5, Merck, 5, Teva, 5.

Abstract Number: 0939

Non-steroidal Anti-inflammatory Drug Use Is Associated with Disease Activity and Reduced Significantly in Patients with Axial Spondyloarthritis Treated with Tumor Necrosis Factor Inhibitors; Data from a Real Life Experience

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster I: Axial Spondyloarthritis (0908–0939)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Bacground: Non-steroidal anti-inflammatory drugs (NSAIDs) is the first line treatment option in axial spondyloarthritis (axSpA) patients suffering from pain and stiffness. However there is only limited data regarding the concomitant use of NSAIDs during tumour necrosis factor inhibitor (TNFi) treatment.

Objectives: To evaluate longitudinal concomitant NSAIDs use with the TNFi treatment and the determinant of the ASAS-NSAID index in patients with axSpA.

Methods: In total 429 axSpA patients (253 [59%] male; 272 [63%] with AS and 157 [37%] with nonradiographic (nr)-axSpA) who have followed up one year were included in this observational study (Table 1). The data regarding disease activity and serum CRP levels were collected on 12, 24 and 52nd week. At each visit NSAID usage, type, dosage and frequency were recorded in order to calculate ASAS-NSAID index. The longitudinal relationship between NSAID-index and other factors tested by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality

Results: At baseline 127/138 (92%) patients starting TNFi and 239/291 (82%) conventionally treated patients were using NSAID. Both the rate (p=0.007) and the median (IQR) ASAS-NSAID index were higher in biologic treatment group (100 [50] vs 70.8 [89.4]; $p< 0.001$). During follow-up ASAS-NSAID index was decreased significantly in patients treated with TNFi (median 100 to 8.0;$p< 0.001$), however ASAS-NSAID index was not changed in conventionally

Table 1: Baseline demographic and disease characteristics

	All group (n=429)	Biological treatment (n=139)	Conventional treatment (n=290)	*p*
Age, years median (IQR)	40 (18)	39 (19)	41 (17)	0.49
Sex, male, n(%)	253 (59)	94 (67.6)	160 (55)	**0.014**
Diagnosis, n (%) r-AxSpA	273 (63.6)	106 (76.3)	166 (57.4)	**<0.001**
HLA-B27 positivty n (%)	209/342 (61.1)	64/95 (67.4)	146/248 (58.9)	0.15
Duration of symptoms, median yrs (IQR)	12 (12)	14 (11)	11 (12)	**0.004**
Time since diagnosis, median yrs (IQR)	5 (7)	7 (8)	4 (5)	**<0.001**
The presence of extraspinal involvement history				
Periferal arthritis, n (%)	127/407 (31.2)	60/123 (48.8)	67/285 (23.5)	**<0.001**
Enthesitis, n (%)	108/377 (48)	52/99 (52.5)	129/279 (46.2)	0.30
Dactylitis, n (%)	14/414 (3.4)	7/126 (5.6)	7/288 (2.4)	0.11
Anterior uveitis, n (%)	45/413 (10.9)	17/126 (13.5)	28/287 (9.8)	0.26
Psoriasis, n (%)	17/411 (4.1)	5/126 (4)	12/285 (4.2)	0.91
İnflamatory bowel disease, n (%)	10/369 (2.7)	5/96 (5.2)	5/273 (1.8)	0.08
Disease activity, median (IQR)				
BASDAI (0 to 10)	4 (3)	4.9 (2.8)	3.6 (2.8)	**<0.001**
BASFI (0 to 10)	2.9 (4.2)	4.4 (3.7)	2.2 (3.9)	**<0.001**
BASMI (0 to 10)	2 (3)	3 (3)	2 (2)	**0.009**
ASDAS-CRP	2.8 (1.5)	3.5 (1.4)	2.4 (1.4)	**<0.001**
CRP (mg/dl)	1 (8)	7 (15.8)	1 (0.5)	**<0.001**

treated patients (p=0.154) (Figure 1). In univariate longitudinal analysis revealed that ASAS-NSAID index was significantly associated with BASDAI, ASDAS, BASFI scores and patient global assessment of disease activity, serum levels of CRP and education. We established two multivariable models (Table 2) to assess the associated factors/covariates with ASAS-NSAID index over time (one with ASDAS and the other BASDAI+CRP as disease activity index)

Table 2: The factors associated with ASAS-NSAII index in biologic treated patients

	Model 1			Model 2		
	B	95%CI	p	B	95% CI	p
BASFI	-0.55	-4.384; 4.275	*0.980*	0.943	-3.795; 5.682	*0.696*
BASMI	0.951	-1.511; 3.413	*0.449*	-0.098	-2.430; 2.234	*0.934*
PGA	0.535	0.210; 0.860	***0.001***	0.759	0.432; 1.086	***0.000***
CRP	-0.068	-0.220; 0.084	*0.380*			
BASDAI	5.718	2.487; 8.949	***0.001***			
ASDAS-CRP				1.771	-6.571; 10.113	*0.677*

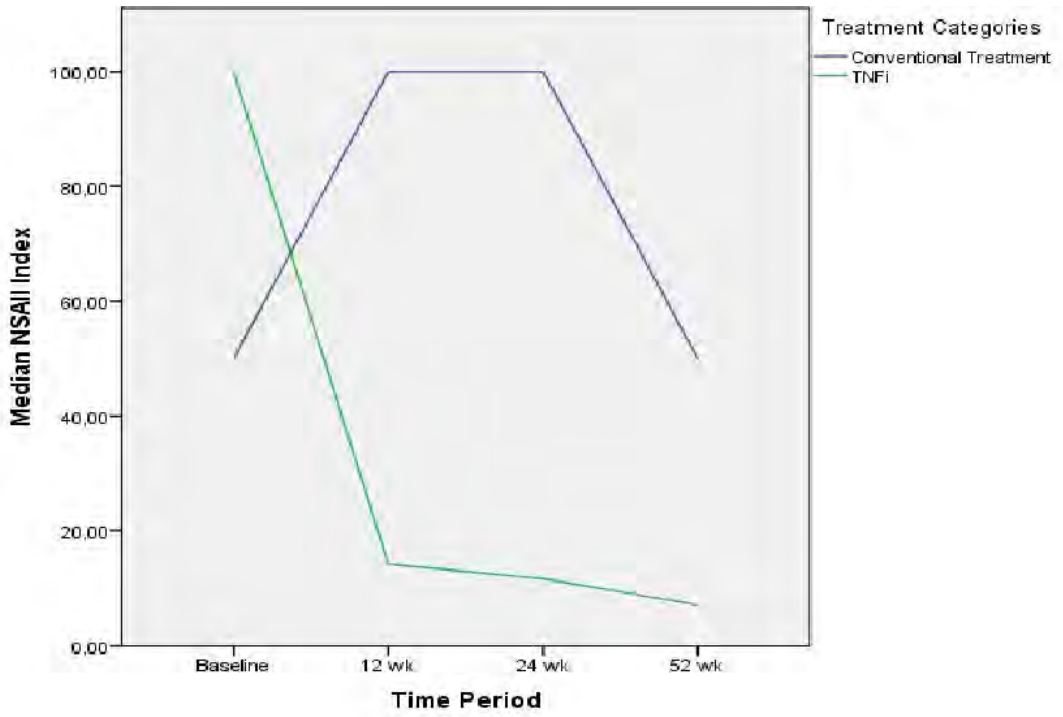

Figure 1. Mean change in disease activity and CRP levels during follow-up duration.

(P values for 3rd months BASDAI<0.0001, CRP<0.001, ASDAS-CRP<0.001 respevtively)

and showed that BASDAI and patient global assessment of disease activity were independent determinants of NSAID dosage in biologic treated patients. However, in multivariate analysis there was no significant predictor for NSAID index in conventional treatment group.

Conclusion: Our results showed that NSAID prescription was significantly higher in axSpA patients who have TNFi indication. NSAID use was decreased significantly over time with TNFi and still independently determined by disease activity. However, it is stable in conventionally treated axSpA patients.

Disclosure: E. Ediboglu, None; **D. Solmaz**, Roche, 6, Farmanova, 6, Pfizer, 6, Lilly, 6; **G. Kabadayi**, None; **e. otman**, None; **H. Cinaklı**, None; **G. Alp**, None; **E. Erpek**, None; **S. Gücenmez**, None; **M. Ozmen**, None; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6.

Abstract Number: 0940

Overactivation of the Kinase IKK2 Causes a Hand Osteoarthritis-Like Phenotype in Mice

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (0940–0943)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Hand osteoarthritis (OA) presents the highest prevalence among rheumatic diseases. Synovitis is a defining feature in hand OA that has been associated with radiographic progression and bone erosion. Synovitis is mediated by the activation of several signalling pathways, such as the NF-κB pathway, which remain active within the synovial joint. Activation of NF-κB takes place after phosphorylation of the kinase IKK2, an event that converges in overexpression of inflammatory molecules that play a critical role in hand OA. These mediators include cytokines, chemokines, and degradative enzymes released by fibroblast-like synoviocytes (FLS), contributing to cartilage degeneration and bone erosion. Pathogenic mechanisms driving hand OA remain unclear, and no animal models exist; however, activating specific cell types within the joint could represent a better approach to elucidate disease mechanisms. In order to characterize a hand OA model, our lab induced a constitutive IKK2 activation in Prg4-expressing cells, such as FLS and superficial chondrocytes, as a strategy to study *in situ* inflammation within the synovial joint of mice paws.

Methods: The *R26Stop*^{FL}*ikk2ca-Prg4*^{CreERT2} mouse model that expresses a constitutively active form of IKK2 was used in this study. IKK2 activation was induced in the homozygous mouse model in a tamoxifen-inducible Prg4 CreER-dependent way by intraperitoneal injections to 2-month old mice. Isolation of FLS was performed after four weeks of tamoxifen injections. Bulk RNA-seq was performed from total RNA extraction obtained from FLS at passages 2 to 4. Additionally, single-cell RNA-seq was accomplished in live-sorted cells from the paws joint to identify cell clusters

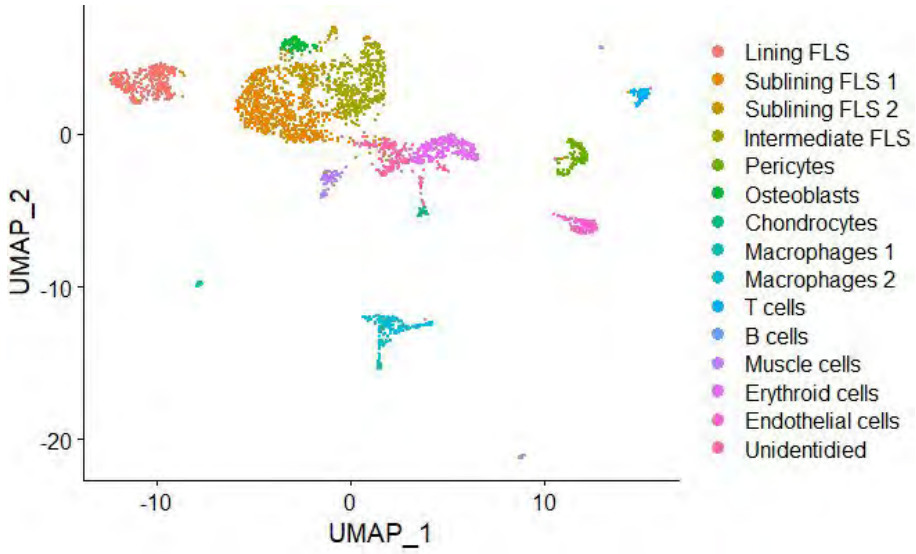

Figure 1. Single-cell RNA-seq clustering in the IKK2ca model. UMAP shows fifteen cell clusters identified in our model. Cluster names are located at the far right of the plot.

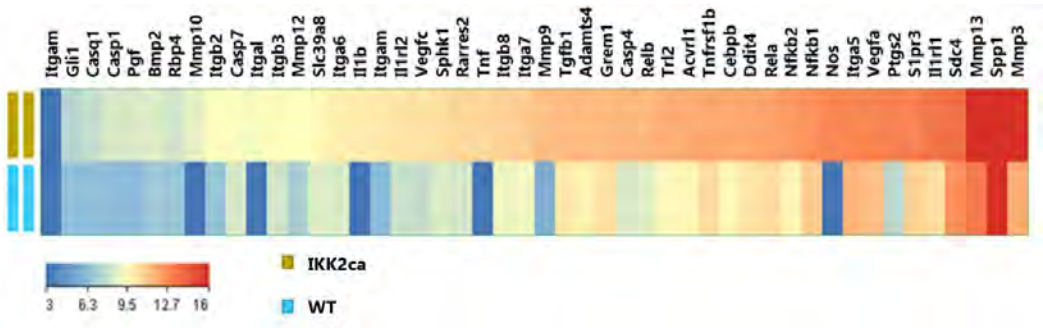

Figure 2. Top DE genes observed in the osteoarthritis signalling canonical pathway. Bulk RNA-seq from IKK2ca vs WT mice FLS was performed. IPA was carried out by using DE genes obtained from bulk RNA-seq. Top DE genes between IKK2ca and WT FLS observed in the OA signalling canonical pathway are shown in the heatmap.

in our model. Public available data was used for bioinformatics analysis to compare DE genes between paws from IKK2ca mice and hand OA [European Nucleotide Archive (ENA) codes PRJEB14422 and PRJEB14595].

Results: Bulk RNA-seq data analysis showed high expression of proinflammatory mediators in FLS obtained from IKK2ca mice compared with WT. Besides, scRNA-seq allowed us to identify fifteen cell clusters in our mice. We observed an increased number of cells in both the osteoblast and macrophage clusters when we compare IKK2ca vs WT. Differential expression (DE) gene analysis between IKK2ca and WT mice showed upregulation of MMPs and NF-κB signalling pathway activation molecules. Interestingly, ingenuity pathway analysis (IPA) from those DE genes revealed the osteoarthritis pathway as one of the top five canonical pathways in the IKK2ca model. Additionally, bioinformatics analysis revealed an overlap of key up and down-regulated genes involved in inflammation and cartilage degeneration in IKK2ca compared with hand OA.

Conclusion: Overactivation of IKK2 induced a hand OA-like phenotype characterized by overexpression of MMP's, cytokines, and NF-κB signalling molecules that contributed to cartilage degeneration.

Disclosure: S. Ramirez-Perez, None; **k. Jones**, None; **U. Gangishetti**, None; **P. Bhattaram**, None.

Abstract Number: 0941

Lorecivivint (SM04690), an Intra-articular, Small-Molecule CLK/DYRK Inhibitor That Modulates the Wnt Pathway, Provided Cartilage-Protective Effects in an Animal Model of Post-traumatic OA

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (0940–0943)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Osteoarthritis (OA) is characterized by increased cartilage thinning, bone remodeling, and inflammation. Post-traumatic OA, which develops after acute direct trauma to the joints, accounts for approximately 12% of all OA cases.[1] Current therapeutic options focus on alleviating symptoms and pain rather than disease

Table 1: OARSI scores

Week-2 injection	Sham-operated (14 weeks after surgery)	Baseline (BL) (2 weeks after surgery)	Vehicle (12 weeks after injection)	LOR (12 weeks after injection)
Total score	5.99	19.17	31.36	19.19
SEM	1.07	1.55	2.48	1.81
***P* value versus BL**				0.9999
***P* value versus vehicle**				0.0004

Week-3 injection	Sham-operated (15 weeks after surgery)	Baseline (BL) (3 weeks after surgery)	Vehicle (12 weeks after injection)	LOR (12 weeks after injection)
Total score	6.09	23.17	30.45	21.20
SEM	1.25	1.36	1.42	1.00
***P* value versus BL**				0.4522
***P* value versus vehicle**				0.0001

Week-4 injection	Sham-operated (16 weeks after surgery)	Baseline (BL) (4 weeks after surgery)	Vehicle (12 weeks after injection)	LOR (12 weeks after injection)
Total score	6.97	16.88	24.95	18.63
SEM	1.32	1.04	1.74	1.61
***P* value versus BL**				0.6257
***P* value versus vehicle**				0.0111

modification. Lorecivivint (LOR; SM04690), an intra-articular (IA), small-molecule CLK/DYRK inhibitor that modulates the Wnt pathway, has been shown in animal studies to induce chondrogenesis, protect cartilage, and reduce inflammation and, thereby, improve joint health.[2] A single IA LOR injection was evaluated in a rat model of knee instability to determine its protective and regenerative effects when injected at different timepoints after induction of post-traumatic OA.

Methods: Knee instability/post-traumatic OA was surgically induced in rats by combining anterior cruciate ligament transection with partial medial meniscus transection (ACLT+pMMx). LOR (0.3 µg) or vehicle was injected into the IA space of the damaged knee at 2, 3, or 4 weeks after induction of OA. OA-induced (n=10/group) or sham-operated (surgery without ACLT+pMMx; n=5/group) rats were sacrificed at the injection timepoint (baseline) or 12 weeks after LOR/vehicle injection (study conclusion). Histological grades were evaluated using the summed OARSI scores (stage and grade of cartilage damage)[3] of the anterior and posterior medial femoral condyle (MFC) and medial tibial plateau (MTP). Weight distribution analysis was performed using an incapacitance meter at several timepoints. Statistical analysis was performed using one-way ANOVA with Dunnett's multiple comparison test.

Results: ACLT+pMMx surgeries led to increased OARSI scores in rats by 2 weeks compared with sham surgeries. LOR treatment at Weeks 2, 3, and 4 led to significant decreases ($P< 0.05$) in total OARSI scores (Table 1) at the end of the study compared with vehicle treatment. Rats treated with LOR for 12 weeks and rats at injection baseline had similar OARSI scores, suggesting that LOR treatment arrested the progression of cartilage damage. Significant improvements ($P< 0.05$) were also observed in the weight distribution of LOR-treated rats in the 3- and 4-week groups at 6 and 12 weeks after their respective IA injections compared with vehicle-treated rats.

Conclusion: LOR exhibited cartilage-protective effects and slowed disease progression in the ACLT+pMMx model in vivo and, therefore, has potential as a structure-modifying treatment for OA.

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Disclosure: T. Seo, Biosplice Therapeutics, Inc, 3, 11, GNF, 3; **V. Deshmukh**, Biosplice Therapeutics, Inc., 3; **Y. Yazici**, Amgen, 2, BMS, 5, Biosplice, 3, 8.

Abstract Number: 0942

Transcriptional Regulation of Synovial Macrophages in the Aging Joint

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (0940–0943)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Macrophages are critical in maintaining tissue homeostasis, as well as in inflammation and immune response, but their function deteriorates with age increasing susceptibility to arthritis. In the joint synovium, we and others have shown that several distinct populations of macrophage co-exist at steady-state and differ in their ontogeny, localization, and function. Our prior work demonstrated that the epigenomic landscape of macrophages is specified by a combination of transcription factors (TFs) that become active during differentiation or in response to the local environment: however, these processes may be disrupted over time. Here, we investigate how the transcriptional regulation of synovial macrophages is altered in the aging joint.

Methods: We use young (3-6 months), old (20-24 months) mice with a C57BL/6 background. Ankles were dissected, muscle resected, and bone marrow removed. Synovium is exposed and digested into a single-cell suspension for Fluorescence-Activated Cell Sorting (FACS). Macrophages were identified as CD45+CD11B+Ly6G-Ly6C-CD64+ cells and further subdivided into four populations by expression of MHCII and CX3CR1. In addition, monocytes were sorted from the blood and bone marrow. Either RNA-seq or ATAC-seq was performed and sequenced on Illumina Nextseq. Sequencing files were demultiplexed and resulting fastq files were trimmed and aligned to mm10 followed by either mappin to genes with HTseq (RNA-seq) or peak calling and annotation with HOMER (ATAC-seq).

Results: We isolate four macrophage subpopulations which we characterize based on their steady-state identity as CX3CR1+MHCII- tissue-resident synovial lining, CX3CR1+MHCII+ newly infiltrating cells; CX3CR1-MHCII- tissue-resident interstitial, CX3CR1-MHCII+ monocyte-derived interstitial. These populations have distinct epigenomic landscapes in the young joint with the tissue-resident macrophage populations exhibiting more similar transcriptional profiles than the monocyte-derived populations. However, as the mouse ages, the gene expression of all the subpopulations converges on a transcriptional profile similar to young infiltrating macrophages. This is consistent with the observation that there are increased numbers of monocyte-derived macrophages in the joint. Moreover, our results suggest a decrease in the activity of the TF, Mef2C, associated with the expression of tissue-resident genes. By comparing the epigenomic landscape of monocytes in young and aged mice, we observe an decrease in chromatin accessibility at the binding sites of cell-type-specific TFs, such as KLF and PU.1. Thus, the dysfunction of aged synovial macrophages traces back to changes in monocytes, whose contribution increases over time.

Conclusion: These results further our understanding of how the function of different macrophage subpopulations change with age. Future studies will investigate specific targets to reprogram the synovial macrophage compartment in aging.

Disclosure: S. Chen, None; **A. Montgomery**, None; **A. Woo**, None; **G. Gadhvi**, None; **H. Perlman**, Kiniksa, 1, 2; **C. Cuda**, None; **D. Bowdish**, None; **D. Winter**, None.

Abstract Number: 0943

Metabolomic Profiling of Synovial Tissue of Patients with Osteoarthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Osteoarthritis & Joint Biology – Basic Science (0940–0943)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Increasing evidence indicates that osteoarthritis (OA) progression is mediated not simply by progressive degeneration of cartilage, but also by low-grade synovial inflammation (synovitis) that is associated with increased symptoms in knee OA (KOA). Ongoing inflammatory responses are associated with dramatic shifts in tissue metabolism. The objective of this work is to explore the metabolomic profiling in synovial tissue (ST) from OA patients and its association with synovial inflammation.

Methods: 37 ST samples (28 knees and 9 hips) were collected from patients with OA during hip or knee replacement. ST was either fixed in formalin for histology analysis, cultured (explants) for 24 hours to collect supernatant for cytokine analysis, or snap-frozen for metabolomic analysis. ST samples were categorized as inflammation 0-I vs II-III according

Table 1. Comparison of cytokines from explants (pg/ml) and metabolites from ST (μM) concentrations between stages of inflammation.

	Inflammation 0-I n=13	Inflammation II-III n=24	p
IL-6	22801 ± 27542	56793 ± 48175	0.06
CXCL2	756 ± 756	2229 ± 1966	0.05
Alanine	3.41 ± 1.24	5.53 ± 2.64	0.002
Fumarate	0.15 ± 0.10	0.24 ± 0.11	0.012
Glutamine	2.17 ± 1.32	3.90 ± 2.61	0.032
Glycine	1.70 ± 2.40	4.51 ± 4.18	0.014
Lactate	27.17 ± 13.53	40.63 ± 19.22	0.032
Leucine	1.80 ± 1.02	2.59 ± 1.01	0.030
Lysine	1.93 ± 1.10	3.00 ± 1.37	0.020
Methionine	0.34 ± 0.23	0.50 ± 0.39	0.019
TMNO	0.19 ± 0.10	0.36 ± 0.26	0.007
Tryptophan	0.26 ± 0.15	0.046 ± 0.21	0.017
Valine	1.36 ± 0.76	2.28 ± 1.02	0.01

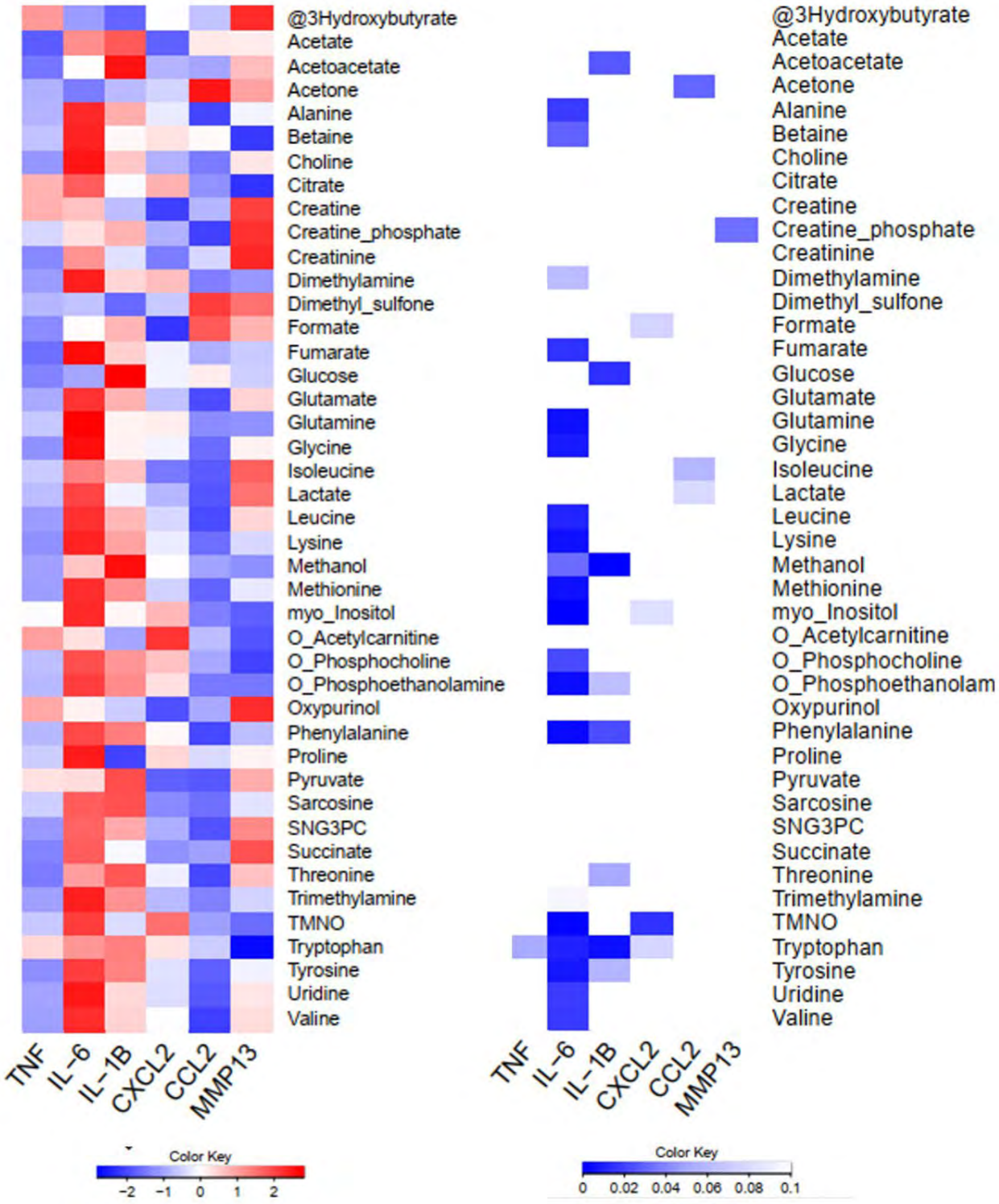

Figure 1. Pearson correlation between polar metabolites in ST obtained by 1H-NMR and proinflammatory mediators quantified from explants. A) The strength of association of each pair were used to form a cluster heatmap to lend insight into which mediator were correlated with which group of polar metabolites; B) Correlation p values are displayed in B. TNF: Tumor necrosis factor; IL-6: Interleukin 6; IL-1B: Interleukin 1β; CXCL2: Chemokine (C-X-C motif) ligand 2; CCL2: C-C motif chemokine 2; MMP13: Matrix metallopeptidase 13.

to the Krenn histopathological synovitis score. We also categorized our samples in fibrosis 0-I vs fibrosis II-III with Masson's trichrome staining. A 600 MHz Bruker Avance III spectrometer ^{1}H-NMR was used to acquire NMR spectra of ST samples. Software Chenomx NMR suite 8.5 professional was used for metabolite identification and quantifi-

cation. The samples were normalized by volume/weight and the concentrations are reported in μM. Proinflammatory mediators were measured by ELISA. Metaboanalyst 5.0, SPSS v26, and R studio were used for statistical analysis.

Results: 51 metabolites were detected in the ST by 1H-NMR. ST samples were divided in inflammation 0-I (n= 13) vs inflammation II-III (n=24), and fibrosis 0-I (n=18) vs fibrosis II-III (n=19). Only 4 metabolites were different between the 2 fibrosis categories (acetoacetate, creatine phosphate, tryptophan and proline). However, the levels of several metabolites (lactate alanine, fumarate, glutamine, glycine, leucine, lysine, methionine, trimethylamine N-oxide, tryptophan and valine) were elevated in ST with inflammation II-III compared to 0-I (Table 1). Proinflammatory mediators (TNF, IL-1b, IL6, CCL2, CXCL2 and MMP13) from ST explants (n-24, 9 with inflammation 0-I, and 15 with inflammation II-III) were measured in the supernatants. CXCL2 and IL-6 levels were higher in ST explants supernatants with inflammation II-III than with 0-I (Table 1). IL-6, but also IL-1β, correlated positively with several metabolites (Figure 1).

Conclusion: Metabolomic profiling of synovial tissue can identify metabolic changes associated with inflammation. Further studies are needed to determine whether metabolomic profiling of synovial tissue can identify new therapeutic targets in inflammatory osteoarthritis.

Student t test was used to evaluate the differences between groups. $P<0.05$ was considered significant. Continous variables are expressed in mean ± standard deviation. TMNO: Trimethyalamine N-oxide.

Disclosure: J. Murillo Saich, None; **R. Coras**, None; **R. Meyer**, None; **M. Guma**, novartis, 5, pfizer, 5, gilled, 5, genentech, 6.

Abstract Number: 0944

A Characterization of the Gut and Cutaneous Microbiome of Monozygotic Twins Discordant for Psoriatic Disease

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Basic Science (0944–0947)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Psoriasis (PsO) is an inflammatory, immune-mediated skin disorder affecting ~3% of the population worldwide. It is associated with multiple comorbidities, including psoriatic arthritis (PsA), which occurs in up to a third of patients. While genes contribute to the pathogenesis of psoriatic disease, twin studies demonstrate substantial discordance in PsO and PsA, suggesting that epigenetics and environmental factors play a significant role. In fact, there is increasing evidence that the microbiome has an impact on psoriatic disease pathogenesis. However, prior investigations were performed in populations of unrelated individuals and could not discern environmental from genetic influences. To characterize the host-microbiome relationship, we studied the gut and skin microbiome of monozygotic (MZ) twins discordant for psoriatic disease in order to determine disease-specific microbial perturbations that are independent of host-genes.

Methods: Stool and skin swabs were collected from subjects with psoriatic disease and their unaffected MZ twin siblings (pairs=9, n=18). Non-lesional (NL) or healthy skin was swabbed at three separate sites: bicep, scalp, and elbow/forearm. Fecal samples underwent shotgun metagenomic sequencing to deeply characterize the gut microbiome taxonomy and functional pathways at high resolution. Sequences were processed with the HUMAnN and MetaPhlAn2 pipelines. Skin swab samples underwent 16S rRNA sequencing to characterize the cutaneous bacterial microbiome. Forward sequences were processed with the QIIME2 pipeline and SILVA reference database. Downstream computational analysis was performed using several libraries in R, including DESeq2.

Results: In gut samples, the relative abundance of *Ruminococcus bromii* species was significantly reduced and two pathways related to tetrahydrofolate biosynthesis were upregulated in psoriatic twins compared to their corresponding unaffected siblings (Fig 1; p< 0.05, Mann-Whitney). In NL skin samples from psoriatic twins, there was a

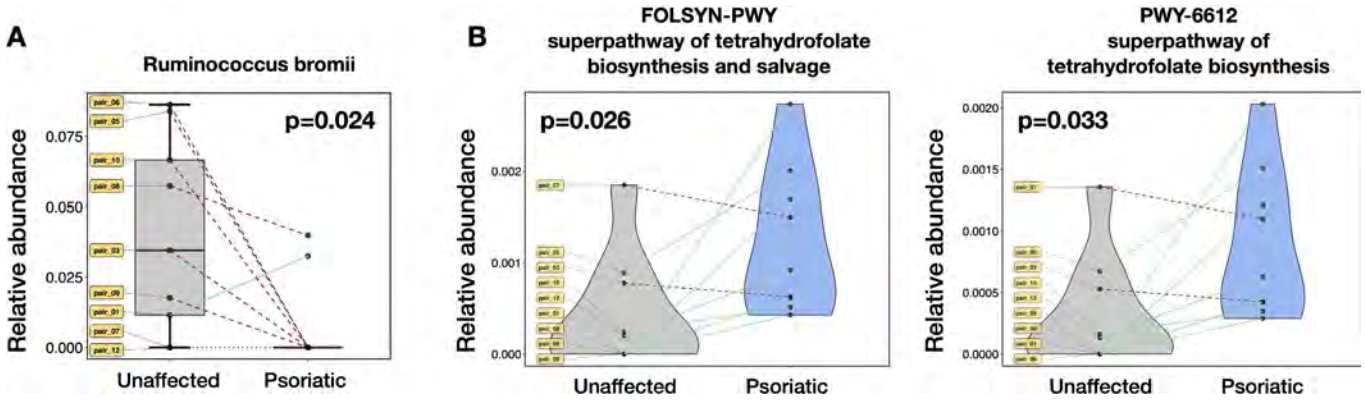
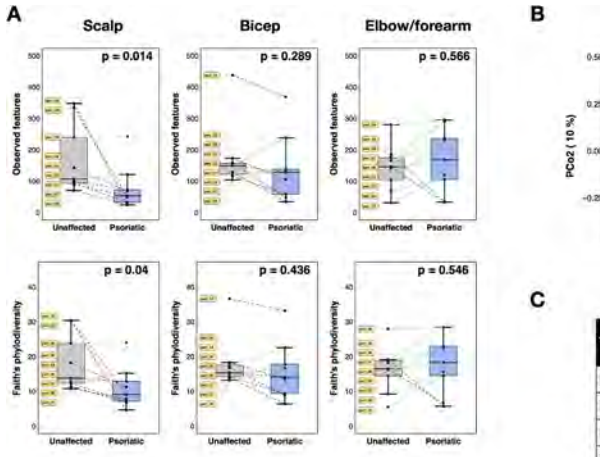
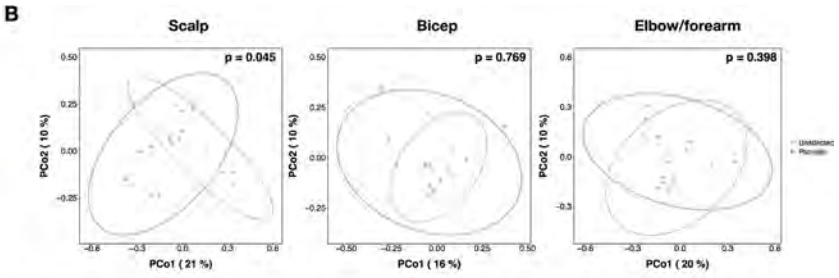


Figure 1. Monozygotic (MZ) twins discordant for psoriatic disease demonstrate differences in their gut microbial features. Psoriatic twins show a significant reduction in Ruminococcus bromii species (A), and a higher abundance of two tetrahydrofolate biosynthesis pathways (B) compared to their unaffected siblings (p<0.05, Mann-Whitney).





C

Taxon	Log2-fold change (Psoriatic/Healthy)	p-value	p-value with FDR adjustment	Mean relative abundance (%)
Bacilli (c)	2.831	0.001	0.018	63.661
Deinococcales (o)	-21.331	6.40E-13	2.88E-11	0.175
Fusobacteriales (o)	-3.429	0.002	0.037	0.641
Bacillales (o)	2.557	0.0007	0.016	57.615
Deinococcaceae (f)	-21.459	4.66E-13	4.05E-11	0.175
Deinococcus (g)	-21.912	1.55E-13	2.48E-11	0.175

Figure 2. The cutaneous microbiome of non-lesional (NL) skin from the scalp of monozygotic (MZ) psoriatic twins is different from corresponding healthy skin of their unaffected siblings. (A) Alpha diversity is significantly reduced in the scalp of psoriatic twins compared to their unaffected siblings (p<0.05, Mann-Whitney; observed features and Faith's phylodiversity), but not in the bicep or elbow/forearm. (B) There is a significant difference in the beta diversity of scalp microbial communities between psoriatic and unaffected twins (p<0.05, Permanova; unweighted UniFrac), but not in the bicep or elbow/forearm. (C) Differential abundance analysis with DESeq2 demonstrates a higher abundance of the Bacillales order and related taxa, and a lower abundance of the Deinococcus genus and related taxa in psoriatic twins compared to their unaffected siblings (p<0.05 with FDR correction). Prior to DESeq2 analysis, features were filtered to ensure that every feature was present in at least 2 samples in order to minimize outliers.

significant reduction in alpha diversity and beta diversity differences in microbial communities of the scalp, but not the bicep or elbow/forearm, compared to healthy samples from unaffected twins (Fig 2A-B; $p< 0.05$, Mann-Whitney and Permanova). Differential analysis of taxa in the scalp identified a higher abundance of the *Bacillales* order and related taxa, as well as a lower abundance of the *Deinococcus* genus and related taxa in psoriatic twins compared to their unaffected siblings (Fig 2C; $p< 0.05$ with FDR correction).

Conclusion: This is the first study exploring microbial differences in MZ twins discordant for psoriatic disease. In agreement with our previous results, we found that *Ruminococcus* is reduced or virtually absent in the gut of psoriatic patients, and may therefore be associated with psoriatic disease. Additionally, we discovered that even healthy-appearing NL skin of psoriatic subjects, particularly in the scalp, exhibited microbial perturbations and decreased diversity compared to unaffected twins. A further understanding of these changes and their downstream effects should shed light into the pathogenesis of psoriatic disease beyond genetic susceptibility.

Disclosure: J. Manasson, None; **M. Stapylton**, None; **R. Medina**, None; **R. Castillo**, None; **P. Vasudevanpillai Girija**, None; **A. Heguy**, None; **C. Ubeda**, None; **M. (MATR)**, None; **J. Clemente**, None; **J. Scher**, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, AbbVie, 2, Sanofi, 2, Kaleido, 2, UCB, 2.

Abstract Number: 0945

A Single-cell Atlas of Human Synovial Endothelial Cells in Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Basic Science (0944–0947)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Dysregulated endothelial cell (EC) function and altered (lympho)angiogenesis crucially contribute to synovial pathology in inflammatory arthritis. Additionally, endothelium plays a key role in the positional identity of sublining synovial fibroblasts and their pathogenic expansion in RA. Here, we utilized single-cell RNA sequencing (scRNA-seq) to characterize the diversity of synovial vascular and lymphatic ECs and functionally annotate synovial ECs across inflammatory arthritides.

Methods: We obtained synovial tissue from 12 knees, 8 wrists, 8 metacarpophalangeal and one sternoclavicular joint from 14 RA, 5 SpA, 3 PsA and 3 patients with undifferentiated arthritis (UA, 2 mono-, 1 polyarthritis) using ultrasound-guided synovial biopsy. We dissociated synovium into a single cell suspension through a combined mechanical-enzymatic dissociation. Additional tissue was formalin-fixed and paraffin-embedded for immunohistology (Krenn

synovitis score, pathotype). We created scRNA-seq libraries with 10x Genomics Chromium and sequenced them on NovaSeq6000 (min. 50'000 reads/cell). We mapped the reads to the reference genome GRCh38.p13 (transcripts from GENCODE Release 32) and analysed the scRNA-seq data with R/Bioconductor tools, including quality control, filtering, graph-based clustering, manual and computational cell-type annotation, differential abundance (DA), and differential state analysis. We visualized data using iSEE.

Results: Our dissociation protocol yielded highly viable (median 90%) single-cell suspensions from which we generated 107'438 high quality synovial single cell profiles. We could classify synovial pathotypes in 86% of the samples (24% diffuse myeloid, 29% lympho-myeloid, 33% pauci-immune). Krenn synovitis score ranged from 2 to 8 (median 4), suggesting a moderate inflammation in most synovia. ScRNA-seq analysis identified 6 principal and 4 minor synovial cell populations forming 38 distinct synovial cell clusters (Fig 1A). PECAM1^{+} ECs (n=10'231) represented 4-15% (25Q-75Q, median 9%) of all synovial cells, comprising 8 distinct cell subpopulations: ACKR1^{high} SELE^{high} ICAM1^{high} IL6^{+} venous ECs, ACKR1^{high} SELE^{high} IL6^{-} venous ECs, ACKR1^{high} SELE^{low} IL6^{-} venous ECs, COL3A1^{+} and

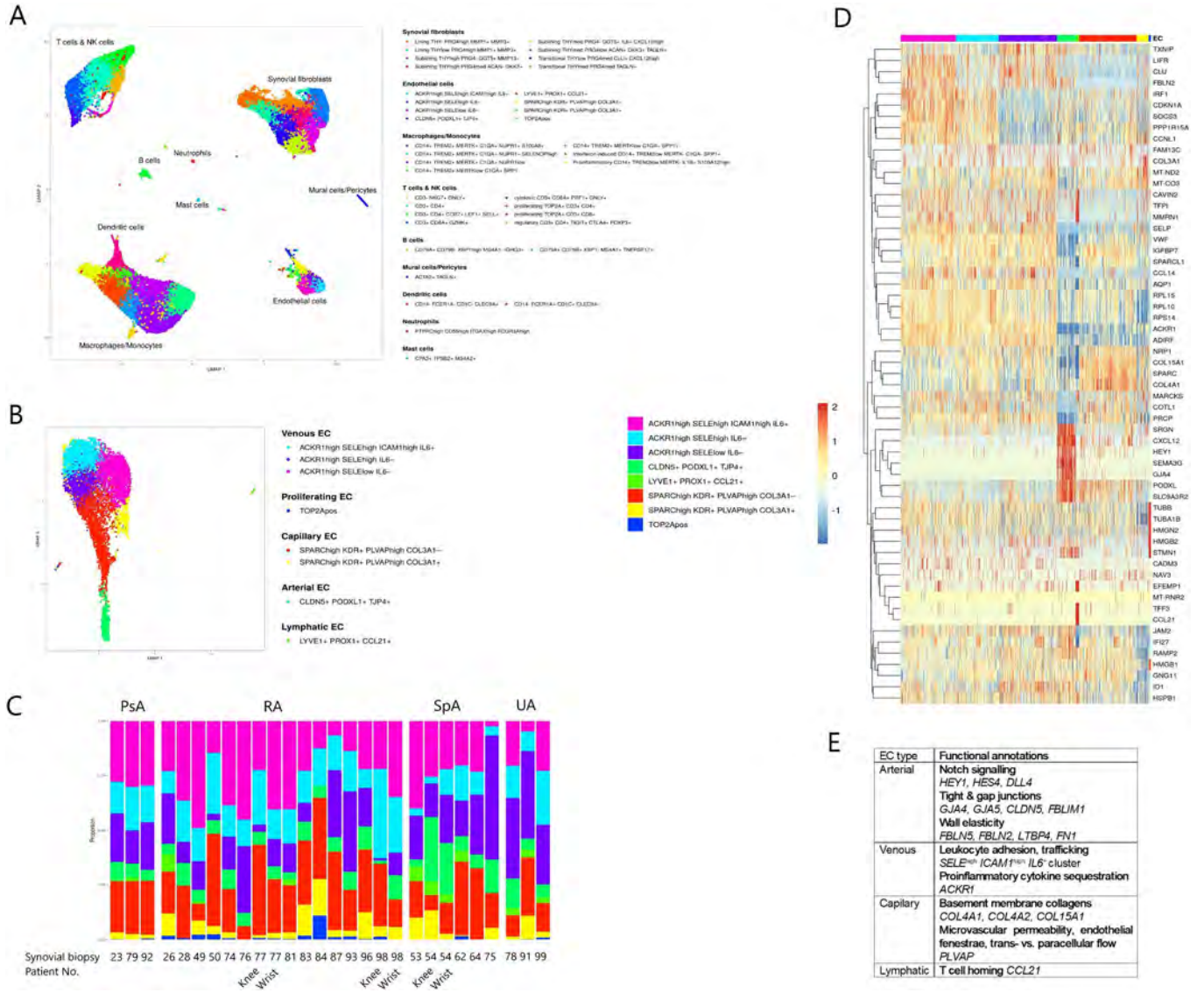

Figure 1. ScRNA-seq: UMAP plots with annotations of (A) all synovial cells and (B) ECs. (C) A heterogeneous distribution of the eight EC subpopulations across patients with PsA, RA, SpA and UA. The EC subpopulations are specified with the colour palette. (D) Top 10 cluster marker genes per each of the eight EC subpopulations. The EC subpopulations are specified with the colour palette at the top of the heatmap. (E) Core enriched genes in EC subpopulations inferring EC functions.

COL3A1^{-} SPARC^{high} KDR+ PLVAP^{high} capillary ECs, highly proliferative TOP2A^{+} ECs, CLDN5^{+} PODXL1^{+} TJP4^{+} arterial ECs and lymphatic LYVE1^{+} PROX1^{+} CCL21^{+} ECs (Fig 1B). EC subpopulations were heterogeneously distributed across patients (Fig 1C), but none of the EC subpopulations was significantly enriched in RA, PsA and SpA synovia in our patient cohort. We defined synovial pan-endothelial and subtype-specific EC markers (Fig 1D) and identified genes that infer the core EC subtype-specific functions (Fig 1E).

Conclusion: We created a comprehensive single-cell atlas of synovial ECs in patients with inflammatory arthritis. Our EC dataset comprises more than 10'000 EC profiles, representing a reference dataset for annotating synovial ECs and guiding EC subtype-specific functional studies.

Disclosure: S. Edalat, None; **R. Gerber**, None; **M. Houtman**, None; **R. Micheroli**, Gilead Sciences, 2, Eli Lilly, 2, Pfizer Inc, 2, AbbVie, 2; **K. Buerki**, None; **N. Izanc**, None; **B. Burja**, None; **T. Kuret**, None; **S. Sodin-Šemrl**, None; **A. Ciurea**, AbbVie, 6, Eli Lilly, 6, MSD, 6, Novartis, 6, Pfizer Inc, 6; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2; **C. Ospelt**, Novartis Foundation for Biomedical Research, 5; **C. Pauli**, None; **M. Robinson**, None; **M. Frank-Bertoncelj**, AbbVie, 5.

Abstract Number: 0946

Distinct Lipidomic Signatures in Synovium and Synovial Fluid of Patients with Rheumatoid Arthritis versus Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Basic Science (0944–0947)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: The differential diagnosis of Rheumatoid Arthritis (RA) and Psoriatic arthritis (PsA) is often difficult due to the similarity of symptoms and the unavailability of reliable clinical biomarkers. Lipid alterations have been suggested to contribute to the pathophysiological processes in the knee joint, and chronic inflammation induces significant changes in the synovium and synovial fluid (SF) lipidome. Therefore, we aimed to evaluate whether differences in the lipid profiles from synovial membrane (SM) and SF could support the differential diagnosis of these diseases.

Methods: SM samples of patients affected by RA (n=6), PsA (n=12) and control donors (n=10) were compared using Matrix-Assisted Laser Desorption Ionization Mass Spectrometry Imaging (MALDI-MSI) for spatially resolved lipid analysis. To this end, tissue sections were measured on a RapifleX MALDI-TOF/TOF instrument. Next, a targeted approach based on multiple reaction monitoring (MRM-MS) was performed to further validate the lipidomic alterations reported by MALDI-MSI between RA and PsA tissues. In this case, lipids extracted from SF (control donors (n=4), RA (n=21) and PsA (n=27)) were analyzed in a QTRAP 4000 mass spectrometer coupled with an ExpressHT™-Ultra HPLC system for the targeted analysis of 84 lipid species. Principal component analysis (PCA) and discriminant analysis (DA) were used for data interpretation.

Results: Lipid profiles of PsA and RA synovial membranes were unequivocally distinguished by MALDI-MSI followed by PCA-DA. Interestingly, several lipid species, including sphingomyelins, phosphatidylcholines (PC) and phosphatidylethanolamines (PE), presented the greatest separation power to classify RA and PsA tissue samples. On the other hand, the lipid profile of arthritic SM samples was also discriminated from control tissues. Specifically, several lysophosphatidylcholines showed the greatest discriminative capability for separating groups. The abundance of those lipid species with discriminatory potential were further compared using ANOVA. This analysis found 35 lipid species significantly different among the study groups, where most of them were significantly increased in RA and PsA compared to controls. Particularly, 11 lipids showed higher levels in PsA tissues compared with RA, including several PC and PE such as PE 34:1 and PE 36:1. The spatial distribution of these PE species was associated with areas of the sublining layer with increased vascularity and inflammatory cell infiltrates, according to MALDI-MSI images. On the other hand, RA and PsA patients were also correctly classified based on the SF levels of all quantified lipid species

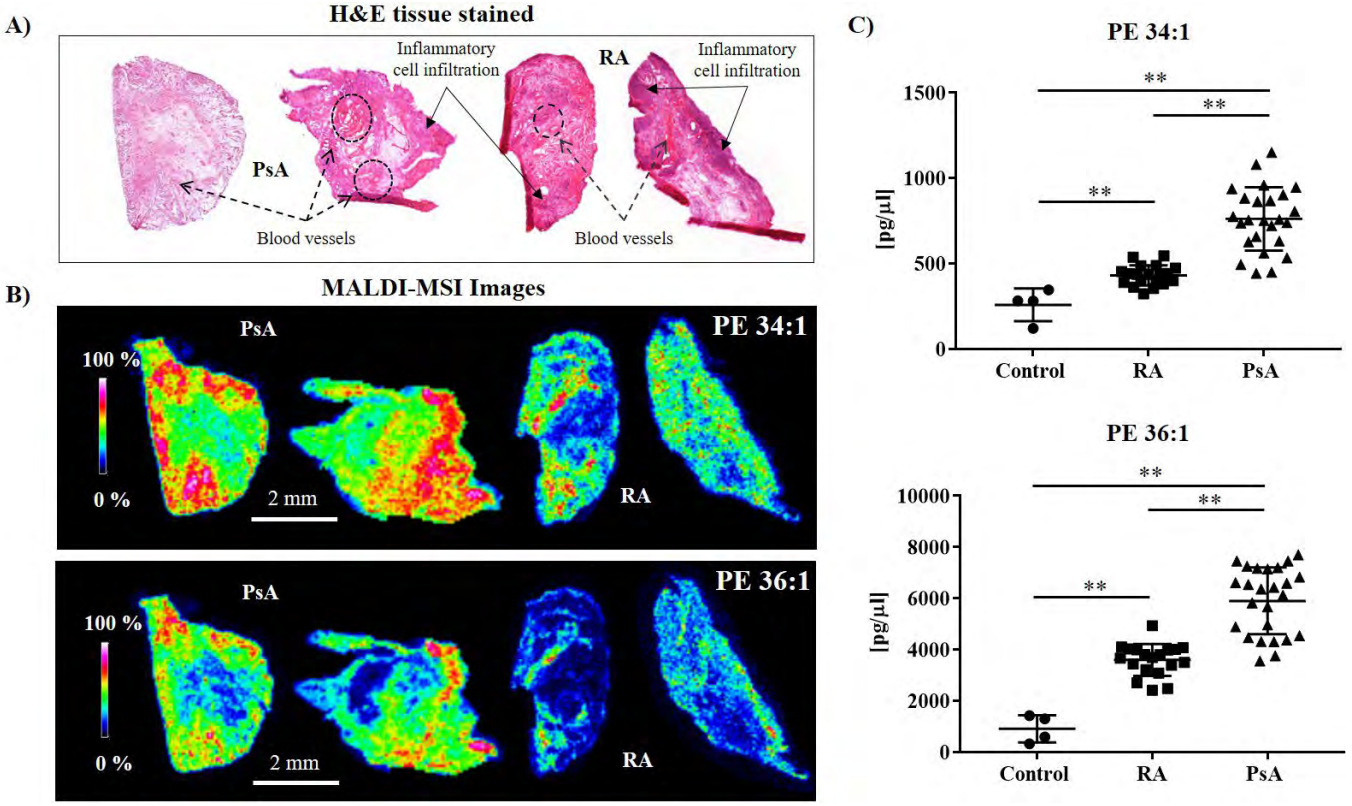

Figure 1. Increased levels of PE 34:1 and PE 36:1 in the PsA synovium and synovial fluid compared to RA. A) Images show samples from two representative RA and PsA biopsies stained with hematoxylin and eosin. B) MALDI-MSI images showing the differences in the abundance and spatial distribution of PE 34:1 and PE 36:1 in PsA synovium compared to RA samples. The colour scale at the bottom left indicates the relative abundance. Pink or white denote higher abundances, while blue or black denote lower abundances. C) SF levels of PE 34:1 and PE 36:1 are increased in PsA patients compared to RA. Y-axis represents concentrations in pg/µl. **p-value < 0.01. PE, phosphatidylethanolamine; RA, rheumatoid arthritis; PsA, psoriatic arthritis; SF, synovial fluid.

according to PCA and clustering analysis. Finally, we were able to validate the increased levels of PE 34:1 and PE 36:1 in the SF of PsA patients compared to RA (Figure 1).

Conclusion: Our study shows a distinct lipid profile between RA and PsA synovium and synovial fluid, and reports potential clinically useful lipid markers for the differential diagnosis of these diseases.

Disclosure: B. Rocha, None; **B. Cillero-Pastor**, None; **A. Illiano**, None; **V. Calamia**, None; **G. Pinto**, None; **A. Amoresano**, None; **C. Ruiz-Romero**, None; **J. Cañete**, Abbvie, 6, Pfizer, 6, Janssen, 6; **R. Heeren**, None; **F. Blanco-García**, None.

Abstract Number: 0947

Cytokine Competent Gut-joint Migratory T Cells Contribute to Inflammation in the Joint

Adam Lefferts[1], David Claypool[1], Eric Norman[1], Uma Kantheti[1] and Kristine Kuhn[2], [1]University of Colorado, Anschutz Medical Campus, Aurora, CO, [2]University of Colorado Anschutz Medical Campus, Aurora, CO

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Basic Science (0944–0947)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Although studies have identified the presence of gut-associated cells in the enthesis of joints affected by spondyloarthritis, a direct link through cellular transit between the gut and joint has yet to be formally demonstrated. Using the KikGR transgenic mice to label in situ and track cellular trafficking from the distal colon to the joint under inflammatory conditions of both the gut and joint, we aimed to determine the relative roles of gut-trafficked T cells in the joint.

Methods: KikGR x $TNF^{DARE/+}$ mice, which spontaneously develop Crohn's like intestinal inflammation and spondyloarthritis-like joint inflammation, and KikGR x $TNF^{+/+}$ controls underwent colonoscopy-guided photo-labeling of the distal colon epithelium. At 72 hours after photo-labelling, we harvested the popliteal lymph nodes (PLNs) from both KikGR x $TNF^{DARE/+}$ and KikGR x $TNF^{+/+}$ mice. Following magnetic sorting of T cells by negative selection, T cells were stimulated with anti-CD3 anti-CD28 for 4 hours in the presence of protein transport blockade. T cells then were evaluated by flow cytometry for activation, cytokine production, and transcription factors. To assess the contribution of gut-derived T cells to disease, we reconstituted $Rag1^{-/-}$ mice with colon epithelium associated T cells from and $TNF^{DARE/+}$ and $TNF^{+/+}$ donors harvested by negative selection magnetic sorting. After 8 weeks of homeostatic proliferation, we assessed joint inflammation by histology 5 days following injection of complete Freund's adjuvant (CFA) into the left hind hock.

Results: 72 hours following photo-labeling, gut-trafficked T cells are observed in the Achilles enthesis in equal proportions (~10% of total T cells) between $TNF^{DARE/+}$ and $TNF^{+/+}$ mice. In the PLNs, photo-labeled T cells expressed markers of terminal differentiation, with 51% of labeled cells Foxp3+ and 19% Roryt+, compared to 10% and 1.7% in the unlabeled fraction, respectively ($P< 0.01$), similar in both $TNF^{DARE/+}$ and $TNF^{+/+}$ mice. Ex vivo stimulation of T cells isolated from the PLNs demonstrated significant enrichment of TNF and IL-17A production in the photo-labeled gut-derived T cells compared to unlabeled cells. As expected, gut-derived T cells derived from $TNF^{DARE/+}$ animals produced higher levels of TNF compared to littermate controls (45% vs 5%, $P=0.1$); However, while we observed a

large and significant enrichment for Il-17A positivity in greater proportion within gut-derived cells in $TNF^{+/+}$ mice (41% vs 1%, P< 0.0001) this enrichment was smaller and not significant in the $TNF^{DARE/+}$ (29% vs 5% P =0.2). Transfer of gut-derived T cells into $Rag1^{-/-}$ mice resulted in moderately increased inflammation in recipients of $TNF^{+/+}$ T cells (P=0.056), and a significant increase in inflammation in recipients of $TNF^{DARE/+}$ cells (P=0.01), compared to unmanipulated $Rag1^{-/-}$ mice, when challenged with hock injection of CFA.

Conclusion: Our data demonstrate a direct link between the gut and joint through trafficking of gut-derived T cells with the potential to be directly pathogenic through production of pro-inflammatory cytokines like IL-17 and TNF and exacerbation of joint inflammation. Altogether our data suggest a means by which gut-derived T cells may drive joint pathology.

Disclosure: A. **Lefferts**, None; **D. Claypool**, None; **E. Norman**, None; **U. Kantheti**, None; **K. Kuhn**, None.

Abstract Number: 0948

Immunometabolism of Neutrophils in Antiphospholipid Syndrome (APS)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Antiphospholipid Syndrome (0948–0951)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Neutrophil hyperactivity and neutrophil extracellular trap (**NET**) release (**NETosis**) appear to play roles in APS pathophysiology. Until recently, it was thought that neutrophils relied primarily on glucose uptake and glycolysis to fulfill their energy needs. Accumulating evidence now suggests that metabolic plasticity guides both physiologic and pathologic neutrophil functions. Our previous work characterizing the transcriptome of APS neutrophils found that genes related to glycogenolysis and the pentose phosphate pathway were markedly upregulated. We now begin to characterize how neutrophil metabolism may impact APS-relevant NETosis.

Methods: Primary human neutrophils were stimulated with phorbol myristate acetate (**PMA**), calcium ionophore A23187 (**Ca iono**), or affinity-purified anti-β_2GPI IgG (**aβ_2GPI**). PMA and Ca iono were chosen as mechanistic anchors given their divergent mechanisms for triggering NETosis (NADPH oxidase-dependent and -independent, respectively). Inhibitors included 2-deoxy-D-glucose (**2-DG**, a competitive inhibitor of glycolysis) and 6-aminonicotinamide (**6-AN**, a glucose-6-phosphate dehydrogenase inhibitor that blocks the pentose phosphate pathway). Metabolic flux analysis was conducted using a Seahorse analyzer. NETosis was quantified with SYTOX Green. APS-associated thrombosis was modeled in C57BL/6 mice via electrolytic activation of the inferior vena cava (**IVC**) endothelium.

Results: In the metabolic flux analysis, Ca iono triggered an earlier peak in oxygen consumption than did PMA (30 min vs. 90 min). Peak Ca iono-induced oxygen consumption decreased by 30% with 2-DG and by 74% with 6-AN. For PMA, the decreases were 39% (2-DG) and 47% (6-AN). Interestingly, as compared with healthy control neutrophils, neutrophils isolated from primary APS patients (n=3) demonstrated a pattern of oxygen consumption indicative of more robust mitochondrial reserve. When NETosis was considered, PMA-induced NETosis was sensitive to both 2-DG (46% reduction) and 6-AN (57% reduction). In contrast, Ca iono-induced NETosis was insensitive to both in-

hibitors. Importantly, aβ_2GPI-induced NETosis mirrored PMA and was sensitive to both 2-DG (< 0.05) and 6-AN (p< 0.05). In a mouse model of APS, transfer of IgG from APS patients into mice (n=8-10/group) doubled IVC thrombus size (mean 9.7 mm vs. 5.1 mm) at 24 hours. When APS mice were administered daily 2-DG (250-1000 mg/kg) for two weeks prior to thrombus induction, thrombus size was decreased back to the baseline of 5 mm (p< 0.0001); this was accompanied by a reduction in plasma NET remnants.

Conclusion: We demonstrate for the first time that inhibitors of glycolysis and the pentose phosphate pathway attenuate aβ_2GPI-induced NETosis. Furthermore, neutrophils isolated from patients with primary APS appear to have baseline characteristics suggestive of a more robust mitochondrial network, which may hint at metabolic plasticity *in vivo*. The potential clinical applicability of these studies are emphasized by the ability of 2-DG to restrain APS-associated thrombosis in mice. Numerous studies are now underway to further dissect these metabolic (and potentially modifiable) underpinnings of APS pathophysiology.

Disclosure: A. Tambralli, None; **A. Harbaugh**, None; **S. Estes**, None; **S. Yalavarthi**, None; **C. Hoy**, None; **G. Sule**, None; **J. Knight**, None.

Abstract Number: 0949

Single-Cell RNA Sequencing of APS Skin Reveals Endothelial Pathology and Cellular Interactions

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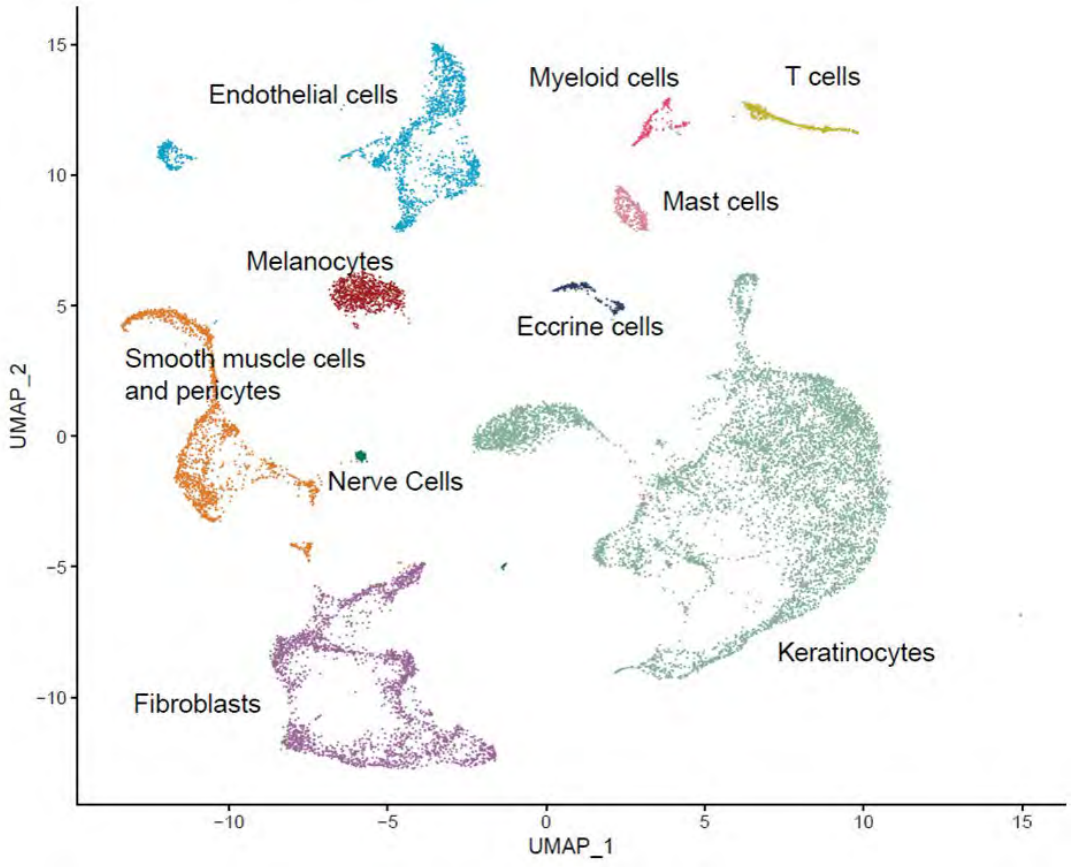
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Antiphospholipid Syndrome (0948–0951)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

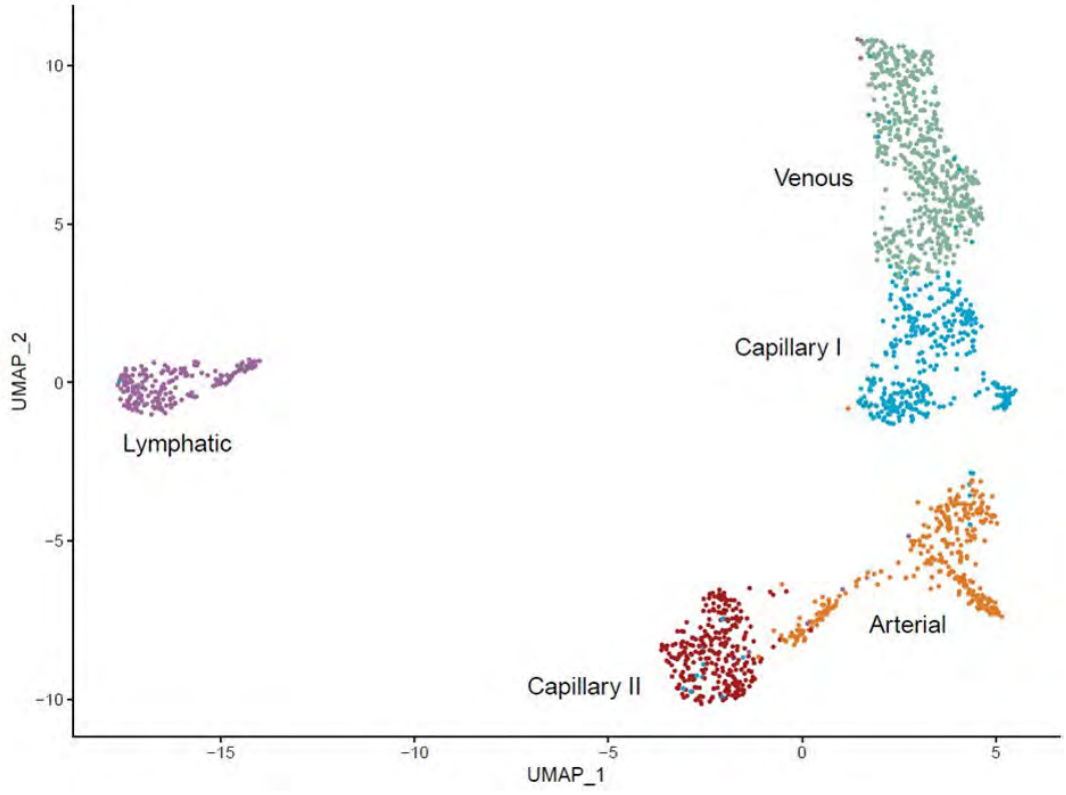
Background/Purpose: Although antiphospholipid syndrome (**APS**) regularly presents with discrete thrombotic events, many patients will also acquire organ damage over time secondary to occlusive neointimal formation in small vessels. The presence of livedo reticularis is predictive of various "internal" manifestations of APS including cerebrovascular disease. Although the interplay between antiphospholipid antibodies (**aPL**) and endothelial cells is likely a key driver of APS vasculopathy in skin and other organs, APS microvascular endothelial cells have been studied only sparsely. Here, we employed skin biopsy and sc-RNAseq to characterize APS endothelial cells with an eye toward identifying the dysregulated pathways and cellular crosstalk that may conspire to promote APS vasculopathy over time.

Methods: We applied sc-RNAseq to skin biopsies of three primary APS patients with livedo reticularis and four healthy controls with neither APS nor livedo. Uniform manifold approximation and projection (UMAP) was used to discriminate cell types, and differential gene expression analysis was identified. Pathway enrichment was determined by Ingenuity Pathway Analysis. Ligand-receptor pairs from the Database of Interacting Proteins were used to identify potential intra- and inter-cellular communication. Immunohistochemistry (IHC) was performed to verify protein expression in APS and control skin. Control human MVECs were cultured with APS sera in pursuit of discerning transcriptional expression of upregulated genes.

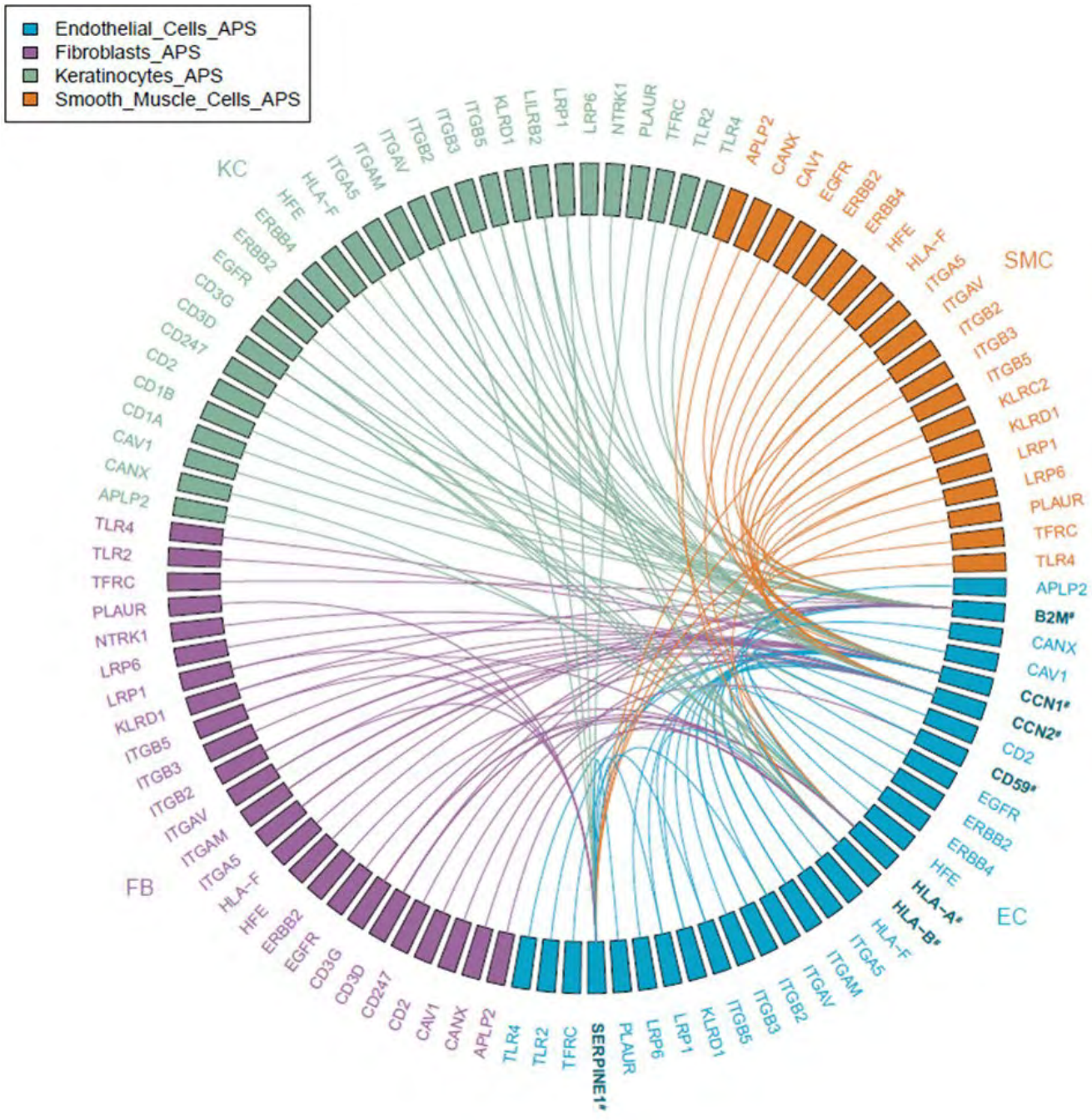
Results: We identified ten cell types in skin (**Figure 1**). Within the main endothelial cell population, there were four distinct subsets that we named Arterial, Capillary I, Capillary II, and Venous based on differential expression of key



Cell type-specific subsets in APS and control skin.



Endothelial cell subsets in APS and control skin.



Interactions between ligands upregulated in APS endothelial cells (bolded) and receptors expressed by endothelial cells and other cell types. EC=endothelial cells, SMC=pericytes/smooth muscle cells, KC=keratinocytes, and FB=fibroblasts.

genes (**Figure 2**). We compared gene expression profiles between APS and control endothelial cells and found significant upregulation of various genes associated with cell proliferation, most notably CCN1 (CYR61), CCN2 (CTGF), and SERPINE1 (PAI-1) in APS. These changes were most pronounced in the Capillary I and Venous subsets. By pathway analysis, we found the APS endothelial cell expression profile to be enriched for Hippo-YAP1/TAZ and TGF-β pathways. Anchored by differentially-expressed ligands of APS endothelial cells, interaction analysis suggested strong communication between endothelial cells (especially ligands CCN1 and CCN2) and both pericytes/smooth muscle cells and fibroblasts (**Figure 3**). IHC staining confirmed higher expression of CCN1 and CCN2 in APS skin as

compared with control skin. In these same biopsies, APS endothelial cells were more likely to display YAP1 nuclear translocation as compared with control endothelial cells. *In vitro*, culture of control MVECs with APS sera upregulated CCN1, CCN2, and SERPINE1.

Conclusion: To our knowledge, this is the first direct analysis of gene expression in APS endothelial cells and local interacting cells. These data suggest that APS endothelial cells demonstrate a pattern of ligand gene expression with potential to drive the proliferation of neighboring cells including pericytes/smooth muscle cells and fibroblasts, which may have significant relevance for the neointimal formation of APS vasculopathy.

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Abstract Number: 0950

Mammalian Target of Rapamycin (mTOR) Pathway Assessment in Antiphospholipid Antibody Positive Patients with Livedo Reticularis/ Racemosa

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Antiphospholipid Syndrome (0948–0951)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Endothelial proliferation is a key finding in antiphospholipid antibody (aPL)-positive patients with microvascular disease. The mTOR pathway plays a role in the endothelial proliferation leading to aPL-related nephropathy; however, the role of mTOR pathway is not well determined in patients with livedo, which is discolorization of the skin due to reactive dilation of peripheral dermal venules triggered by reduced blood flow in the center. Thus, our primary objective was to investigate mTOR pathway activation in the skin biopsies of aPL-positive patients with livedo reticularis/racemosa.

Methods: This cross-sectional study included patients with livedo reticularis/racemosa: a) those with aPL-positivity (LA, aCL IgG/M > 40U, and/or aβ2GPI IgG/M > 40U) with/without systemic lupus erythematosus (SLE); and b) aPL-negative SLE patients as a control group. We collected demographics and aPL-related history. We performed two 5-mm skin biopsies (epidermis) on each patient, one from the erythematous-violaceous peripheral area (lesional) and the second from the non-violaceous central area (non-lesional). Specimens were stained for phosphorylated S6 ribosomal protein (P-S6RP) and protein kinase B (AKT) as a marker of mTOR complex-1 activity. We manually counted cells in the upper superficial and lower basal layers of epidermis and compared the number of cells stained positive for mTOR between different groups (lesional and non-lesional samples in aPL-positive patients vs aPL-negative SLE controls) using chi square test.

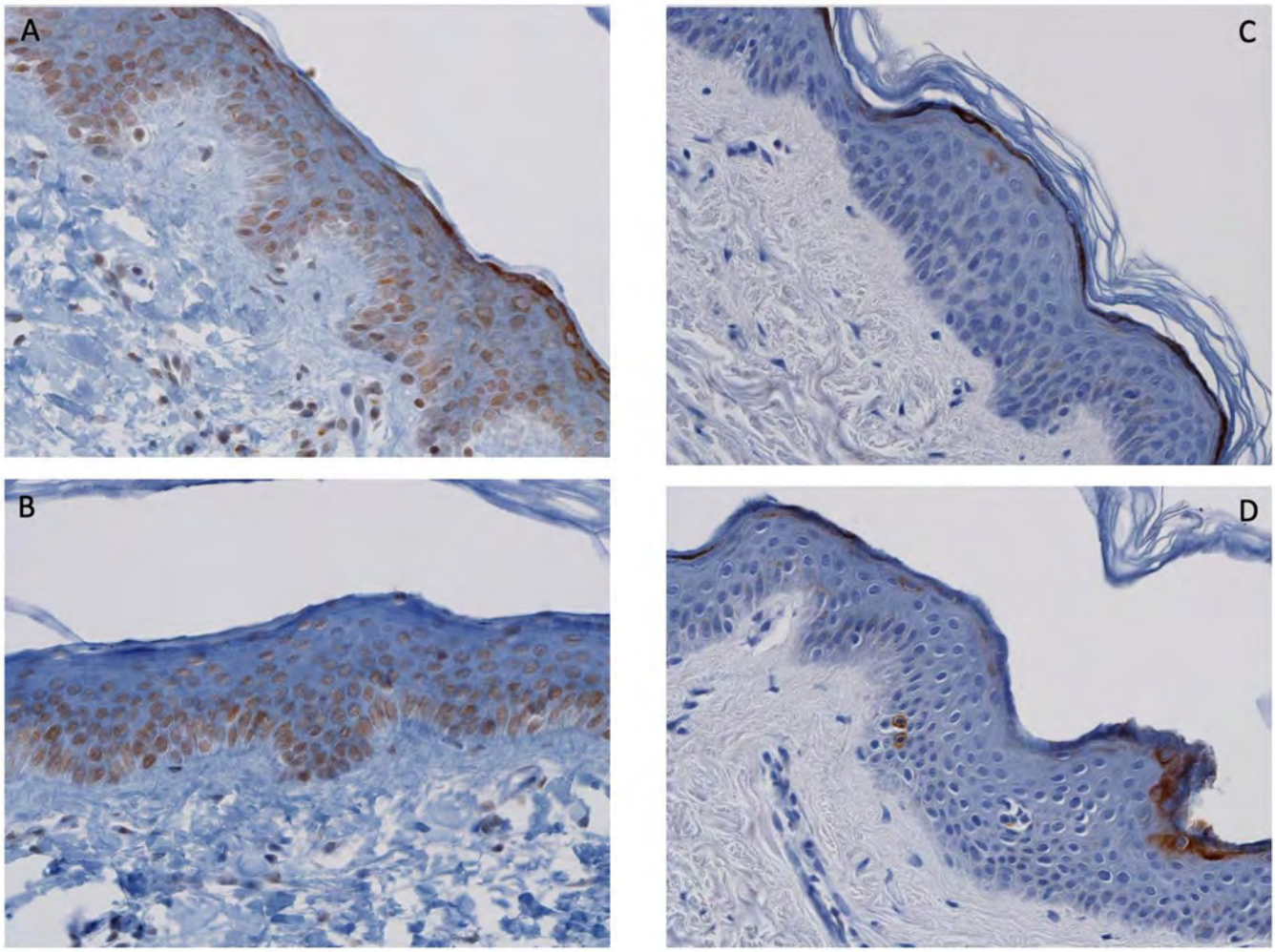

Figure. Increased mTOR Activity Suggested by the S6RP Staining (brown) in the Lesional (A) and Non-lesional (B) Skin Biopsies of an Antiphospholipid Antibody Positive SLE Patient with Livedo, (no similar mTOR activity was observed in the Lesional [C] or Non-lesional [D] skin biopsy of the aPL-negative SLE patient with livedo [C, D]).

Results: Ten patients were enrolled (aPL-positive without SLE: 4 [APS classification met: 3], aPL-positive SLE: 4 [APS classification met: 3], and aPL-negative SLE [control]: 2); nine females; all Caucasian; mean age: 45±13.6y. In all aPL-positive patients (n: 8), there was significantly increased mTOR activity in both lesional and non-lesional skin biopsies, compared to the aPL-negative SLE controls (n:2), more pronounced in the lower basal layers (Figure; Table 1). Furthermore, increased mTOR activity in aPL-positive patients was more prominent in the lesional samples, compared to non-lesional (Table 2).

Conclusion: We found increased mTOR activity in livedoid lesions of aPL-positive patients with or without SLE, compared to aPL-negative SLE patients, suggesting there is a role of mTOR pathway activation in aPL-positive patients with livedo. Our results also showed more profound mTOR activity in: a) lower basal layers of epidermis (compared to upper surface layer), more accountable to present the underlying pathology given the cellular proliferation initiates from the basal layers and the upper layer uptake might be non-specific; and b) in non-violaceous central areas (compared to erythematous-violaceous peripheral areas), consistent with the pathophysiology of livedoid lesions given the vascular stenosis occurring in arterioles located in the center leads to livedo at the periphery.

Table 1: Comparison of mTOR-positive Cell Counts Between aPL-positive (with/without SLE) and aPL-negative SLE Patients	aPL without SLE (n: 4)	aPL with SLE (n: 4)	aPL-negative SLE (n: 2)	p
P-S6RP (Positive cells/Total Cells (%))				
Lesional				
Upper Surface Layer	457/1241 (37)	1128/1567 (72)	452/1484 (30)	*<0.001*
Lower Basal Layer	1547/2346 (66)	3039/3530 (86)	693/3247 (21)	*0.000*
Total	2004/3587 (57)	4167/5097 (82)	1145/4731 (24)	*0.000*
Non-lesional				
Upper Surface Layer	833/1836 (23)	1712/2439 (70)	942/3570 (26)	*<0.001*
Lower Basal Layer	2195/2872 (76)	3917/4400 (89)	1889/5450 (35)	*0.000*
Total	3028/4708 (64)	5629/6839 (82)	2831/9020 (31)	*0.000*
AKT (Positive cells/Total Cells (%))				
Lesional				
Upper Surface Layer	247/1215 (20)	201/1411 (14)	21/261 (8)	*<0.001*
Lower Basal Layer	982/1710 (57)	1185/1967 (60)	151/571 (26)	*<0.001*
Total	1229/2925 (42)	1386/3378 (41)	172/832 (21)	*<0.01*
Non-lesional				
Upper Surface Layer	468/2852 (16)	456/4117 (11)	38/1773 (2)	*<0.001*
Lower Basal Layer	2544/4048 (63)	1784/5656 (32)	301/1916 (16)	*0.001*
Total	3012/6900 (44)	2240/9773 (23)	339/3689 (9)	*0.000*

P-S6RP: Phosphorylated S6 Ribosomal Protein; **AKT:** Protein Kinase B

Table 1. Comparison of mTOR-positive Cell Counts Between aPL-positive (with/without SLE) and aPL-negative SLE Patients.

Table 2: Comparison of mTOR-positive Cell Counts Between Lesional vs Non-Lesional Skin Samples in aPL-positive Patients (n:8)	Lesional Skin Samples	Non-Lesional Skin Samples	p
S6RP (Positive cells/Total Cells (%))			
Upper Surface Layer	1585/2805 (57)	2545/4275 (60)	*0.0115*
Lower Basal Layer	4586/5876 (78)	6112/7272 (84)	*<0.0001*
Total	6171/8684 (71)	8657/11547 (75)	*<0.0001*
AKT (Positive cells/Total Cells (%))			
Upper Surface Layer	448/2626 (17)	924/6969 (13)	*<0.0001*
Lower Basal Layer	2167/3677 (34)	4328/9704 (45)	*<0.0001*
Total	2615/6303 (41)	5252/11421 (32)	*<0.0001*

P-S6RP: Phosphorylated S6 Ribosomal Protein; **AKT:** Protein Kinase B

Table 2. Comparison of mTOR-positive Cell Counts Between Lesional vs Non-Lesional Skin Samples in aPL-positive Patients (n:8).

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Abstract Number: 0951

Associations Among Antiphospholipid Antibody Types, Isotypes, and Titers: Results from the AntiPhospholipid Syndrome Alliance for Clinical Trials and InternatiOnal Networking (APS ACTION) Clinical Database and Repository ("Registry")

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SESSION INFORMATION

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Session Type: Abstract Session

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Background/Purpose: Several antiphospholipid antibody (aPL) profiles are associated with a higher risk for the clinical manifestations of the antiphospholipid syndrome (APS). These include "triple positivity" (lupus anticoagulant [LA], anticardiolipin antibodies [aCL], and anti-b2 glycoprotein I antibodies [ab2GPI]), and LA positivity itself. Further risk is associated with higher levels of aCL and ab2GPI, and with aPL persistence. LA test can detect antibodies to b2GPI and/or prothrombin of any isotype; ab2GPI immunoassays detect isotype-specific antibodies to human b2G-PI. Although the putative antigen in aCL tests is cardiolipin, these tests primarily detect isotype-specific antibodies to bovine b2GPI (present in the blocking buffer/sample diluent). Given that the three aPL tests do not detect discrete antibody populations, but rather partially overlapping sets of antibodies, the primary goal of this study was to further characterize the associations among aPL tests using validated APS ACTION Core Laboratory data.

Methods: The APS ACTION Registry was created to study the natural course of persistently aPL-positive patients with or without autoimmune disorders over at least 10 years. The inclusion criteria are positive aPL according to Updated Sapporo Classification Criteria tested within one year prior to enrollment. Patients are followed every 12±3 months with clinical data and blood collection for APS ACTION Core Laboratory aPL confirmation. We analyzed

Table 1: Prediction of Positive Lupus Anticoagulant (LA) Test by Anticardiolipin Antibody (aCL) and Anti-β2 glycoprotein-I (aβ2GPI) IgG/M Levels ≥ 40 (n: 351)

	OR	95% CI	p value
aCL IgG ≥40U	5.2	2, 14	.001
aCL IgM ≥ 40U	3.6	1.3, 10.5	.02
aβ2GPI IgG ≥ 40U	3.2	1.1, 9.3	.03
aβ2GPI IgM ≥ 40U	14	1.9, 103.6	.01

OR: Odds Ratio, CI: Confidence Interval. In patients with negative LA test, the frequency of all aPL ELISA titers <40 Units was 82%, while in patients with positive LA test it was 41% (p<.0001).

Table 2: Contribution of Number of Anticardiolipin Antibody (aCL) and Anti-β2 glycoprotein-I IgG/M ≥40U ("aPL Load") to Positive Lupus Anticoagulant Test (n: 351)			
	OR	95% CI	p value
At Least 1-2 aCL/aβ2GPI IgG/M ≥ 40U*	6.1	2.6, 14.2	<.001
At Least 3-4 aCL/aβ2GPI IgG/M ≥ 40U*	10.7	1.4, 80.4	.02

*OR: Odds Ratio, CI: Confidence Interval. * 47% IgG only, 30% IgM only, and 23% IgG and IgM.*

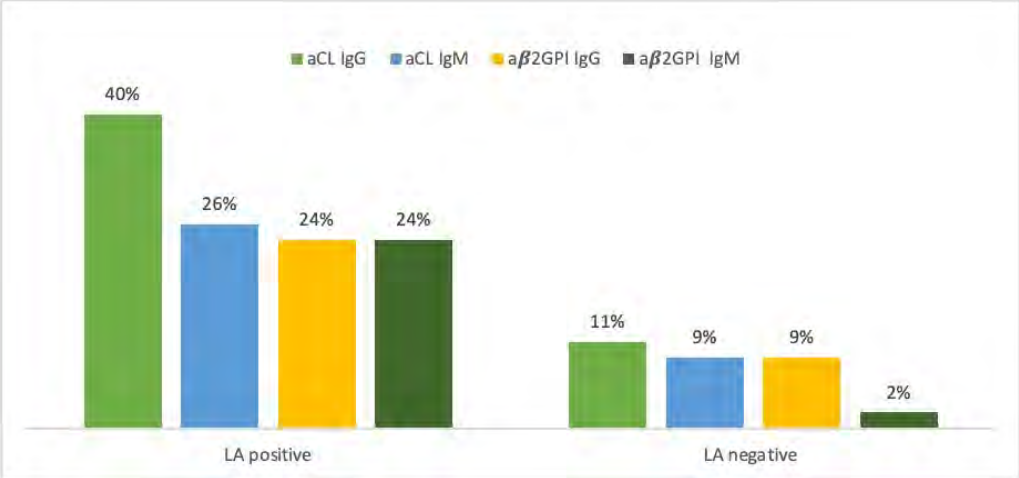

Figure 1. The Frequency of Anticardiolipin Antibody (aCL) and Anti-beta 2 glycoprotein-I IgG/M >=40U Based on the Lupus Anticoagulant (LA) Results (n=351; LA positive=306, LA negative=45).

baseline and prospective Core Laboratory aPL data for associations. Spearman's rank correlation with Bonferroni adjusted significance level for multiple comparisons was used to assess correlation between all available aPL ELISA test results (Inova Diagnostics). Univariate logistic regression was used to assess laboratory predictors of positive LA test.

Results: As of 1/2021, 854 patients were included; 567 patients had Core Laboratory aPL profiles at baseline and follow up. Based on four (aCL/ab$_2$GPI IgG/M) same sample tests (n: 1008) at baseline and follow up, a strong correlation was identified between aCL IgG and ab$_2$GPI IgG, and aCL IgM and ab$_2$GPI IgM (r=0.75, p< .001 for both). There was no correlation between IgG and IgM isotypes. Based on five (aCL/ab$_2$GPI IgG/M and LA) same sample tests at baseline, patients with: a) aCL/ab$_2$GPI IgG/IgM ≥40U had a higher chance of a positive LA test, compared to those with lower titers (Table 1); b) one or two positive tests ≥ 40U among aCL/ab$_2$GPI IgG/IgM had 6.1 times higher odds of a positive LA test; and c) three or four positive tests ≥ 40U among aCL/ab$_2$GPI IgG/IgM had 10.7 times higher odds of a positive LA test (Table 2). The frequencies of aCL IgG, ab$_2$GPI IgG, aCL IgM, and ab$_2$GPI IgM levels ≥40U in LA-positive and LA-negative patients are shown in Figure 1.

Conclusion: Using a large scale international aPL/APS database, we confirmed a strong association between aCL IgG and ab2GPI IgG and, similarly, aCL IgM and ab2GPI IgM, that is likely explained by the b2GPI dependence of aCL tests. Both aPL ELISA levels ≥ 40U and a higher number of aPL ELISA tests ≥ 40U were predictive of a positive LA test, introducing the concept of "aPL load", that may provide a mechanistic explanation of a positive LA test.

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Abstract Number: 0952

Outcomes of COVID-19 Infection in Patients with Primary Systemic Vasculitis and Polymyalgia Rheumatica: Results from the COVID-19 Global Rheumatology Alliance Physician Registry

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Vasculitis – ANCA-Associated (0952–0955)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Patients with primary systemic vasculitis (PSV) and polymyalgia rheumatica (PMR) may be at high risk for poor COVID-19 outcomes due to the treatments used, the potential organ damage caused by PSV, and demographic factors such as older age that are associated with these conditions. We investigated factors associated with COVID-19 outcomes in patients with PSV and PMR in a large multinational registry.

Methods: We analyzed PSV and PMR cases from the COVID-19 Global Rheumatology Alliance registries (12/Mar/2020-12/Apr/2021). PSV diagnoses included ANCA vasculitis (AAV), giant cell arteritis (GCA), Behçet's syndrome, and other vasculitides. The ordinal COVID-19 severity outcome was: 1) no hospitalization, 2) hospitalization without oxygen, 3) hospitalization with oxygen/ventilation, or 4) death. Relevant covariates included age, sex, race, season, number of comorbidities, BMI, smoking status, disease activity, immunosuppresive therapies (conventional synthetic and biologic/targeted synthetic DMARDs), glucocorticoid (GC) (daily dose prednisolone-equivalent), and region. Multivariable ordinal logistic regressions were used to estimate odds ratios (ORs) for being one level higher on the ordinal outcome. Analyses were also stratified by disease (GCA, AAV, or PMR).

Results: Of 1,202 included patients, 61.0% were female; mean age was 63.8 years. Diagnoses were PMR (31.1%), AAV (29.3%), GCA (15.2%), Behçet's syndrome (9.4%), and other vasculitis (15.0%). Overall, 508 (49.8%) patients

Figure 1. Global distribution of primary systemic vasculitis and polymyalgia rheumatica patients with COVID-19 infection in the COVID-19 Global Rheumatology Alliance Physician Registry

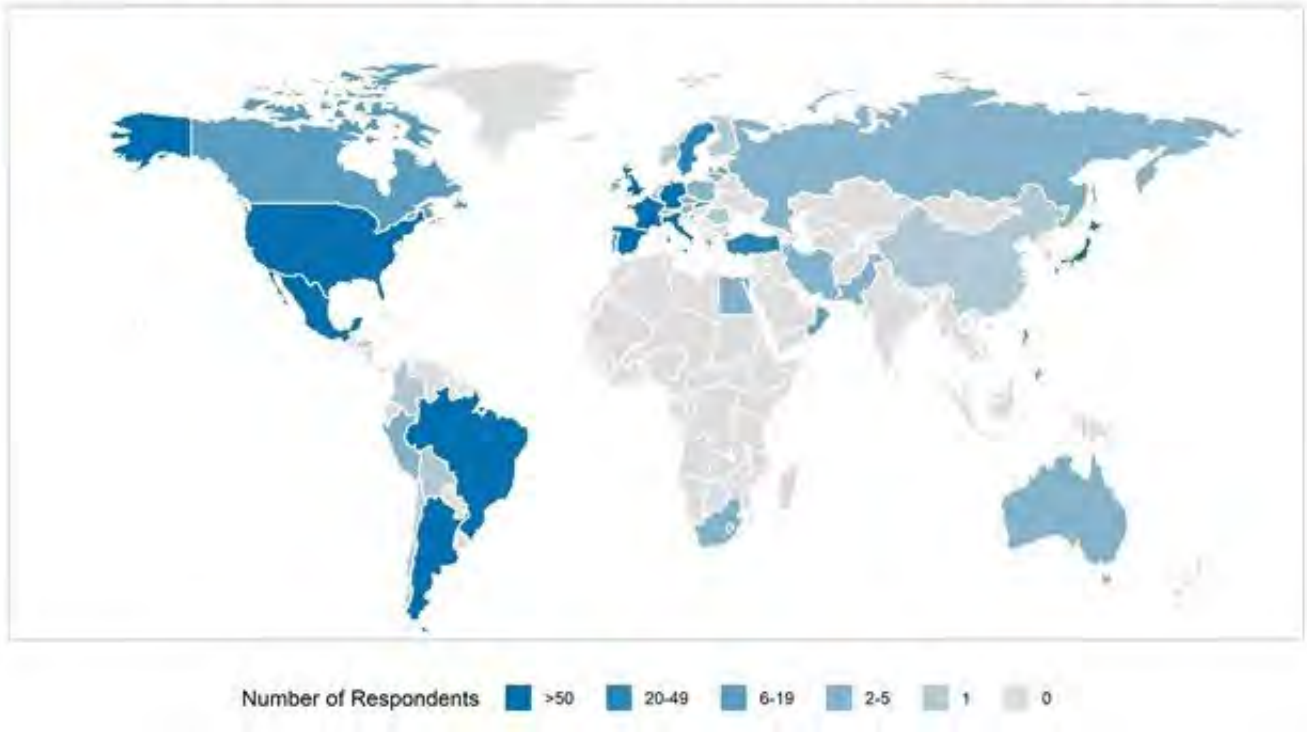

Figure 1.

Table 1.

Table 1. Frequencies and proportions of outcomes in the ordinal COVID-19 severity scale according to diagnosis*

COVID-19 Severity scale	Overall (N = 1020)	GCA (N = 158)	AAV (N = 293)	PMR (N = 323)	Behcets (N = 98)	Other vasculitis (N = 148)
Not Hospitalized	512 (50.2)	69 (43.7)	110 (37.5)	187 (57.9)	84 (85.7)	77 (52.0)
Hospitalization with No Oxygenation	114 (11.2)	19 (12.0)	30 (10.2)	30 (9.3)	11 (11.2)	20 (13.5)
Hospitalization with Any Ventilation or Oxygenation	239 (23.4)	38 (24.1)	88 (30.0)	71 (22.0)	1 (1.0)	30 (20.3)
Death	155 (15.2)	32 (20.3)	65 (22.2)	35 (10.8)	2 (2.0)	21 (14.2)

* Excluding 182 cases with missing outcome data
COVID-19, Coronavirus Disease 2019; AAV, ANCA-associated vasculitis; GCA, giant cell arteritis; PMR, polymyalgia rheumatica.

Table 2.

Table 2. Multivariable† logistic regression analysis of factors associated with the ordinal COVID-19 severity outcomes for patients with primary systemic vasculitis or polymyalgia rheumatica

Factors	OR (95% CI)	p-value
Age (per decade)	1.46 (1.33, 1.60)	<0.01**
Sex		
Female	REF	
Male	1.46 (1.12, 1.91)	<0.01**
Season		
Prior to June 15, 2020	REF	
June 16-Sept 30, 2020	1.07 (0.71, 1.61)	0.76
Oct 1,2020- April 12,2021	0.47 (0.35, 0.63)	<0.01**
Number of Comorbidities	1.38 (1.22, 1.57)	<0.01**
Smoking	0.95 (0.70, 1.28)	0.73
Obesity	1.26 (0.91, 1.75)	0.16
Glucocorticoid (prednisone equivalent)		
No glucocorticoid use	REF	
1-5 mg/day	1.14 (0.81, 1.59)	0.45
6-9 mg/day	1.30 (0.80, 2.11)	0.29
≥ 10 mg/day	2.14 (1.48, 3.09)	<0.01**
Disease Activity		
Remission/Minimal or low	REF	
Moderate/Severe or high	2.32 (1.60, 3.36)	<0.01**

†Adjusted for sex, age, region, medication category, season, number of comorbidities, disease activity, and random effects of region
* $p < 0.05$
** $p \leq 0.005$
The effect size is the odds of being one level higher on the ordinal scale than the reference group.
COVID-19, Coronavirus Disease 2019

were hospitalized, and 155 (15.2%) patients died (Table 1). Older age (OR 1.46, 95% CI 1.33-1.60), male sex (OR 1.46, 95% CI 1.12-1.91), GC dose ≥ 10 mg/day (OR 2.14, 95% CI 1.48-3.09), moderate/severe or high disease activity (OR 2.32, 95% CI 1.60-3.36) and number of comorbidities (OR 1.38, 95% CI 1.22-1.57) were associated with worse outcome (Table 2). In the disease-specific stratified analysis, 20.3% and 22.2% of patients with GCA and AAV, respectively, died. Risk factors for poorer outcomes were: for GCA patients, older age (OR 1.79, 95% CI 1.21-2.65) and obesity (OR 3.04, 95% CI 1.17-3.04); for AAV patients, older age (OR 1.45, 95% CI 1.18-1.79), rituximab (OR 2.50, 95% CI 1.33-4.68) or cyclophosphamide use (OR 6.43, 95% CI 1.48-28.01), and moderate/severe or high disease activity (OR 2.71, 95% CI 1.21-6.07); and for polymyalgia rheumatica, older age (OR 2.69, 95% CI 1.99-3.63) and higher comorbidity burden (OR 1.31, 95% CI 1.03-1.67). Overall, severe outcomes were less likely if COVID-19 infection developed between October 1, 2020, and April 12, 2021 (OR 0.47, 95% CI 0.35-0.63). This was also observed in the disease-specific analysis.

Conclusion: Patients with GCA or AAV who had COVID-19 infection had higher rates of severe outcomes compared to PMR and other vasculitis, even despite similar ages of the GCA and PMR groups. Risk factors identified for different PSV subtypes may inform mitigation strategies for these patients.

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Abstract Number: 0953

An International Delphi Exercise to Identify Items of Importance for Measuring Response to Treatment for ANCA-associated Vasculitis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Vasculitis – ANCA-Associated (0952–0955)
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Background/Purpose: ANCA-associated vasculitis (AAV) is characterized by fluctuating levels of disease activity. Randomized controlled trials (RCTs) in AAV have used multiple instruments to define active disease or remission as a dichotomous outcome. However, no formal criteria exist to measure treatment response in AAV. This Delphi exercise aimed to reach consensus about which measures are considered by patients and physicians to be most important when assessing treatment response in RCTs in AAV.

Methods: An international 3-round online Delphi exercise was conducted in English. Survey participants included experts in AAV and patients with AAV. Items in the Delphi were based on a systematic literature review of outcome measures in RCTs in AAV, and suggestions from a Steering Committee comprised of vasculitis experts and patients with AAV.

Survey participants were asked to rate (on a scale of 1-9) the importance of each item when assessing response to treatment (improvement) in a RCT in AAV. Items scored 7-9 by ≥70% participants were considered to be highly important, and items scored 1-3 by ≥70% participants were considered to be of limited importance.

Results: 265 participants completed three rounds of the Delphi, including 176 physicians with expertise in AAV and 89 patients with AAV. Physicians were from six continents; the majority from Europe [n=81 (46%)] or North America [n=50 (28%)]. Most physicians specialized in rheumatology [n=105 (60%)] or nephrology [n=50 (28%)]. All physicians were in practice for at least 2 years (two-thirds >10 years) and responsible for managing ≥30 patients with AAV; over half of the physicians managed >75 patients with AAV. Patients with AAV were from four continents, with most located in North America [n=63 (71%)] or Europe [n=23 (26%)] with a diagnosis of GPA [n=71 (80%)] or MPA [n=16 (18%)]. The majority of patients with AAV were female [n=61 (69%)], ages 50-79 years [n=67 (75%)], were diagnosed in the past 10 years [n= 62 (70%)], and were currently on treatment [n=61 (69%)].

The most highly rated items of response (Table 1) involved disease activity [reduction in BVAS, extent of organ involvement, and physician global assessment] and patient-reported outcomes [patient global assessment and health-related quality of life]. Achievement of BVAS ≤1 and BVAS of 0 were highly rated more often by physicians than by patients. Pain and fatigue were highly rated by patients, but not by physicians. Changes on urinalysis and acute phase reactants were highly rated only by patients. Additional items related to organ damage, glucocorticoid tapering, and

Table 1: Results of the Delphi exercise rating importance of items to measure when assessing response to treatment in a clinical trial in ANCA-associated vasculitis. Items rated as highly important by physicians and/or patients after 3 rounds of the Delphi.

	Delphi Item	Physicians (n=176) (% rated highly important)	Patients (n=89) (% rated highly important)
Patient-reported outcomes	Improved patient global assessment	72%	73%
	Improved HRQoL measures	75%	87%
	Improved pain	28%	75%
	Improved fatigue	14%	71%
Disease activity	**BVAS**		
	≥50% reduction in BVAS	72%	76%
	BVAS ≤1	94%	70%
	BVAS of 0	94%	67%
	Kidney function		
	Improved kidney function (eGFR)	96%	83%
	No development of ESRD	97%	97%
	Ability to discontinue dialysis	84%	88%
	Resolution of hematuria on urinalysis	42%	79%
	Resolution of proteinuria on urinalysis	50%	81%
	Other		
	No new/worse major organ involvement	96%	95%
	No new/worse minor organ involvement	80%	93%
	Improved physician global assessment	80%	80%
	No rise in acute phase reactants	27%	71%
	No worsening of chest CT	70%	88%
	Survival	100%	97%
Damage	No new major organ damage	94%	97%
	No new non-major organ damage	80%	88%
Glucocorticoid taper	Ability to taper prednisone to ≤5 mg/day	88%	84%
	Ability to stop prednisone	81%	84%
Adverse events	Severe medication-related adverse events	95%	91%
	Severe infections	97%	94%

HRQoL = Health-related quality of life, BVAS = Birmingham Vasculitis Activity Score (any version), eGFR = estimated glomerular filtrate rate, ESRD = end-stage renal disease, CT = computerized tomography.

treatment-related adverse events were highly rated by both patients and physicians. There were no items rated of limited importance by both patients and physicians.

Conclusion: In this Delphi exercise, there was consensus between international experts in AAV and patients with AAV on many items considered important to measure when assessing treatment response in RCTs in AAV. There were also some items rated as highly important by only experts or only patients. These data provide insights into how to evaluate this complex form of vasculitis and will inform the next steps in the development of treatment response criteria in AAV.

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Abstract Number: 0954

The Association of Rituximab- vs. Cyclophosphamide-Based Remission Induction Strategies with Risk of End-Stage Renal Disease and Death in ANCA-Associated Vasculitis

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SESSION INFORMATION

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Background/Purpose: The RAVE trial established the non-inferiority of rituximab (RTX) vs cyclophosphamide (CYC) for remission induction of ANCA-Associated Vasculitis (AAV). Patients in RAVE were followed for 18 months so little

Table 1: Demographic and Disease-Specific Features of Cohort

	Overall n=553	RTX-Based n=313	CYC-Based n=240	P-Value
Age (mean, SD)	59.6 (17.5)	59.6 (18.0)	59.6 (16.7)	0.98
Male (N, %)	236 (43)	131 (42)	105 (44)	0.7
BMI	28.6 (6.3)	28.6 (6.3)	28.6 (6.4)	0.96
Race (N, %)				0.99
White	475 (86)	270 (86)	205 (85)	
Black	14 (3)	8 (3)	6 (3)	
Asian	10 (2)	5 (2)	5 (2)	
Hispanic	10 (2)	6 (2)	4 (2)	
Other	15 (3)	9 (3)	6 (3)	
Smoking (N, %)				0.3
Current	42 (8)	20 (6)	22 (9)	
Past	244 (44)	135 (43)	109 (45)	
Never	265 (48)	156 (50)	109 (45)	
PR3-ANCA (N, %)	174 (32)	92 (29)	82 (34)	0.2
CCI (mean, SD)	1.7 (2.4)	1.5, 2.4	2.0, 2.3	0.05
Disease Activity				
BVAS/WG (mean, SD)	5.1 (2.2)	5.3 (2.4)	4.8 (1.9)	0.004
DAH (N, %)	80 (15)	49 (16)	31 (13)	0.3
Hematuria	64 (12)	43 (14)	21 (9)	0.07
RBC Casts	292 (53)	156 (50)	136 (57)	0.1
Rise in Creatinine	290 (52)	149 (48)	141 (59)	0.009
Any Renal	376 (68)	208 (66)	168 (70)	0.4
No of Major Items (mean, SD)	1.5 (1.1)	1.5 (1.1)	1.6 (1.0)	0.3
Labs (Median, IQR)				
Creatinine (mg/dL)	1.8 [1.0, 4.2]	1.15 [0.98, 3.5]	2.4 [1.2, 5.2]	<0.001
eGFR (mL/min/1.73 m^2)	32.3 [12, 67]	40 [14, 70]	23 [9, 59]	0.001
CRP (mg/L)	4.4 [1.4, 16.2]	4.1 [1.4, 13.9]	5.2 [1.7, 22.2]	0.1
ESR (mm/hr)	17 [8.0, 38.0]	15.0 [8.0, 32.0]	24.0 [10.0, 56.0]	<0.001

Abbreviations: RTX: Rituximab; CYC: Cyclophosphamide; BMI: Body Mass Index; CCI: Charlson Comorbidity Index; BVAS/WG: Birmingham Vasculitis Activity Score/Wegener's Granulomatosis; DAH: Diffuse Alveolar Hemorrhage; RBC: Red Blood Cell; GFR: Glomerular filtration rate; CRP: C-reactive protein; ESR: Erythrocyte Sedimentation Rate

is known regarding the long-term outcomes of these remission induction strategies in real world practice. Here, we evaluated the association of remission induction treatment strategy with the risks of end-stage renal disease (ESRD) and death, two key outcomes in AAV.

Methods: The data source was a consecutive inception cohort of PR3- or MPO-ANCA+ AAV patients assembled in a large healthcare system between 2002 and 2019. Baseline demographics and disease-specific features, including baseline manifestations and laboratory values, were extracted from the electronic health records (EHR) and data warehouse. The primary exposure was RTX- vs CYC-based remission induction regimens, ascertained by manual review. ESRD and vital status, the composite outcome of interest, were ascertained by EHR review as well as linkage to the United States Renal Data System and National Death Index, respectively. A propensity score (PS) model for treatment with RTX vs CYC was created using demographic and disease-specific variables present at baseline, including age, sex, comorbidities, ANCA type, AAV manifestations, and renal function. We first examined the association of RTX vs CYC with the risk of ESRD or death in unadjusted and multivariable adjusted Cox proportional hazard models. We then performed the same analysis after one to many matching RTX users to CYC users by PS.

Results: We identified 553 patients who received RTX- or CYC-based regimens (**Table 1**). The mean (SD) age was 59.6 (17.5) years, 236 (43%) were male, and 475 (86%) were White. The majority were MPO-ANCA+ (379, 68%) and had renal involvement (376, 68%). The mean (SD) BVAS/WG score was 5.1 (2.2). Baseline demographics were similar between RTX- and CYC-users (**Table 1**). RTX-users had a higher BVAS/WG (5.3 [2.4] vs 4.8 [1.9], p=0.004) and CYC-users had a higher creatinine (2.4 [1.2, 5.2] vs 1.2 [1.0, 3.5], p< 0.001). Over a total follow-up of 64,686 days, there were 182 events (ESRD or death). The incidence of the primary outcome was 3.0/1,000 days in RTX-users vs 2.7/1,000 days in CYC-users (**Table 2**). In the multivariable adjusted Cox model (n=553), the risk of ESRD or death was similar in RTX- vs CYC-users (1.26, 95% CI 0.89 to 1.79). Our results remained similar in analyses limited to those with renal involvement and those with any major disease. Baseline demographics and disease-specific features were

Table 2: The Association of Rituximab- vs Cyclophosphamide-Based Remission Induction Regimens with the Composite Outcome of ESRD or Death

	RTX-Based Treatment	CYC-Based Treatment
Standard Cox Regression		
Entire Cohort	313	240
Number of Events	74	108
Follow Up (person days)	24466	40220
Incidence Rate (/1000 days)	3.0 (2.3-3.7)	2.7 (2.2-3.2)
Unadjusted (HR, 95% CI)	1.03 (0.75, 1.42)	1.0 (Ref)
Partially Adjusted*	0.99 (0.73, 1.35)	1.0 (Ref)
Fully Adjusted^	1.26 (0.89, 1.79)	1.0 (Ref)
Renal Involvement Only	208	168
Number of Events	52	83
Follow Up Time	15764	25322
Incidence Rate	3.30 (2.40, 4.20)	3.30 (2.60, 4.00)
Unadjusted	0.86 (0.59, 1.24)	1.0 (Ref)
Partially Adjusted*	0.92 (0.63, 1.33)	1.0 (Ref)
Fully Adjusted†	0.94 (0.63, 1.39)	1.0 (Ref)
Major Involvement Only	242	191
Number of Events	62	92
Follow Up Time	17487.9	29749.9
Incidence Rate	3.50 (2.70, 4.40)	3.10 (2.50, 3.70)
Unadjusted	0.99 (0.70, 1.41)	1.0 (Ref)
Partially Adjusted*	0.97 (0.69, 1.38)	1.0 (Ref)
Fully Adjusted**	1.05 (0.73, 1.52)	1.0 (Ref)
Propensity-Score Matching	223	128
PS-Matched	1.19 (0.75-1.89)	1.0 (Ref)

Adjusted for age, sex, race, smoking; ^Adjusted for age, sex, race, smoking, ANCA type, CCI score, BVAS Score, GFR, CRP, ESR; † Adjusted for age, sex, race, smoking, ANCA type, CCI score, GFR; **Adjusted for age, sex, race, smoking, ANCA type, CCI score, GFR, BVAS

well-balanced after PS-matching. In the PS-matched analysis (n=351), the risk of ESRD or death was similar in RTX- vs CYC-users (1.19, 95% CI 0.75-1.89).

Conclusion: In this large multi-center AAV cohort, there were no significant differences in the risk of ESRD or death associated with RTX- vs CYC-based therapy for remission induction. Our observations remained consistent in analyses using propensity score matching to robustly address confounding by indication. These results will inform the care of patients with AAV for whom there remains some uncertainty regarding initial choice of immunosuppression.

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Abstract Number: 0955

The Effect of Treatment with the Complement C5a Receptor Inhibitor Avacopan on Health-Related Quality of Life in ANCA-Associated Vasculitis

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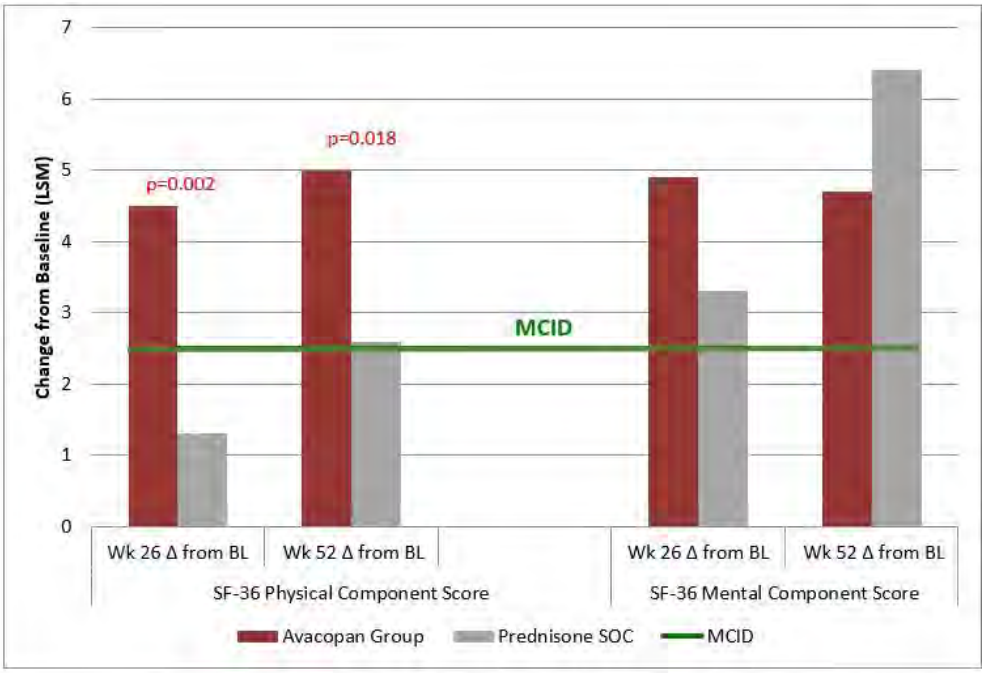
Background/Purpose: Avacopan, an oral C5a receptor inhibitor, was evaluated in ANCA-associated vasculitis (AAV). Efficacy and safety results were reported previously. Health-related quality of life (HRQoL) changes are reported here.

Methods: A 52-week blinded trial (ADVOCATE) randomized 331 AAV patients 1:1 to either full-dose daily oral prednisone with taper ('Prednisone SOC'), or avacopan with no daily oral prednisone ('Avacopan Group'). Both received standard of care (SOC): rituximab induction *or* cyclophosphamide. Glucocorticoid (GC) exposure including pre-randomization tapering into the blinded treatment period, co-administration with rituximab, and flares was expected and balanced between groups. The total dose of prednisone was ~2500 mg less with avacopan treatment over the entire trial. Primary efficacy endpoints were % patients achieving disease remission at Week 26 and sustained remission at Week 52 using Birmingham Vasculitis Activity Score (BVAS). HRQoL was assessed by Short Form-36 Health Survey version 2 (SF-36), a generic measure of HRQoL that performs well across vasculitis trials, including AAV[1] and giant cell arteritis[2], and EuroQoL Group 5-Dimensions 5-Levels Questionnaire (EQ-5D-5L).

Results: Week 26 improvements in physical component summary (PCS) score with Avacopan Group: 4.5 points vs Prednisone SOC: 1.3 points (least squared means, LSM, for all analyses); statistically significant (p=0.002) and >minimum clinically important difference (MCID) = 2.5 points[3] (**Fig. 1**). Mental component summary scores (MCS) were: Avacopan Group: 4.9 points; Prednisone SOC: 3.3 points, > MCID in both groups. At Week 26 improvements in physical function (PF), role physical (RP), general health (GH), vitality (VT) and role emotional (RE) domains with Avacopan Group were large (3.1 to 16.8 points); statistically significant vs Prednisone SOC (p< 0.002 to p=0.002), and >MCID of 5.0 points in 4 domains (**Fig. 2**). This reflects improvements in physical function and activities; also fatigue, energy, emotional role limitations, and general health perceptions.



	Physical Component Score (PCS)			Mental Component Score (MCS)		
	Avacopan Group n=165	Prednisone SOC n=160	P-value	Avacopan Group n=166	Prednisone SOC n=160	P-value
Baseline	39.2	40.1	–	42.1	44.2	–
Wk 26 Change	4.5	1.3	p=0.002	4.9	3.3	ns
Wk 26 Score	44.2	42.1	–	49.4	47.1	–
Wk 52 Change	5.0	2.6	p=0.018	4.7	6.4	ns
Wk 52 Score	44.8	43.1	–	50.9	48.8	–
MCID: minimum clinically important difference; ns: not significant; SOC: standard of care						

Least Squares Mean Improvements in SF-36 Physical and Mental Component Scores.

Week 52 improvements with Avacopan Group vs Prednisone SOC were maintained or improved. PCS score was 5.0 vs 2.6 points, clinically meaningful, and statistically significant (p=0.018). Improvements in PF and GH domains exceeded MCID and were statistically significant (p< 0.049 and p< 0.002). The health utility score, SF-6D, based on calculation across all 8 domains of SF-36, indicated broad improvements in patient-reported health status. Improvements at Weeks 26 and 52 were greater with Avacopan Group compared to Prednisone SOC **(Fig. 3)**; >MID (0.041)[3] and consistent with reported improvements in EQ-5D-5L utility score, which was statistically significant at week 52 (p=0.009).

Conclusion: Treatment of AAV with avacopan and a reduced-dose glucocorticoid regimen led to significant improvements in HRQoL compared to SOC. These findings have important clinical implications for treatment of patients with AAV.

1. Pugnet G, et al. *Clin Exp Rheumatol*. 2016; 34(3 Suppl 97):S54-S59
2. Strand V, et al. *Arthritis Res Ther*. 2019; 21:64
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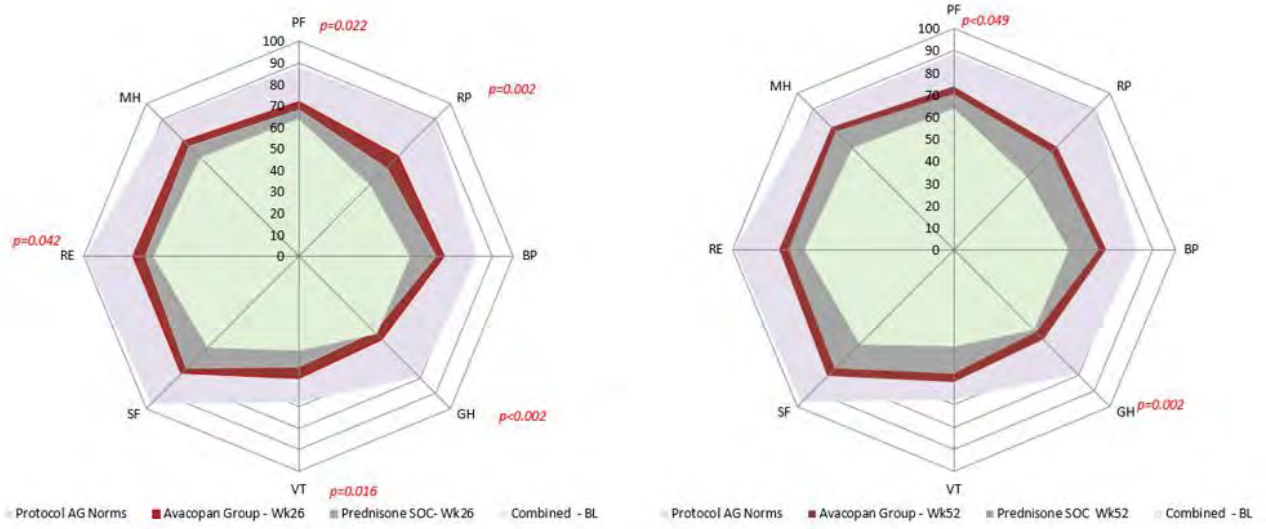

	PF	RP	BP	GH	VT	SF	RE	MH
Avacopan Group - BL	63.74	46.07	51.40	51.44	44.65	61.14	67.77	67.20
Prednisone SOC - BL	64.10	47.49	52.71	51.11	42.91	59.06	67.08	62.55
Avacopan Group - Wk26	71.93	65.67	67.64	54.71	57.01	77.19	77.22	75.91
Prednisone SOC - Wk26	67.90	57.83	63.85	49.59	51.44	73.72	71.28	71.96
Avacopan Group - Wk52	73.93	65.88	68.84	57.32	59.50	80.62	79.00	78.16
Prednisone SOC Wk52	70.58	62.46	65.40	52.53	55.69	75.95	74.54	75.40
Protocol AG Norms	**88.20**	**89.90**	**82.95**	**79.38**	**67.70**	**97.10**	**98.91**	**89.06**
Combined - BL	63.9	46.8	52.1	51.3	43.8	60.1	67.4	64.8

Spydergrams of SF-36 Domains vs Age and Gender Matched Norms – Baseline to Week 26 (left) and Week 52 (right).

	SF-6D Utility		EQ-5D-5L Utility	
	Avacopan Group	Prednisone SOC Group	Avacopan Group	Prednisone SOC Group
Baseline	0.675	0.668	0.752	0.774
Wk 26 Change	0.067	0.050	0.023	-0.001
Wk 26 Score	0.742	0.718	0.789	0.782
Wk 52 Change	0.079	0.066	0.047	-0.004*
Wk 52 Score	0.754	0.734	0.809	0.779
*p=0.009 Age/Gender normative value SF-6D: 0.834				

SF-6D and EQ-5D-5L Utility Scores Demonstrating Improvement in Patient-Reported Health Status from Baseline to Weeks 26 and 52.

Disclosure: V. Strand, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2; **P. Bekker**, ChemoCentryx, 2, 3; **H. Yue**, ChemoCentryx, 3; **D. Jayne**, ChemoCentryx, 2, 5, GSK, 2, 5, Roche/Genentech, 5, Sanofi-Genzyme, 5, AstraZeneca, 2, Boehringer-Ingelheim, 2, Celgene, 2, InflaRx, 2; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9.

Abstract Number: 0956

Racial Disparities in Renal Outcomes over Time Among Hospitalized Children with SLE and Effects of Hospital Minority Composition

Joyce Chang[1], Cora Sears[2], Veronica Torres[3] and Mary Beth Son[1], [1]Boston Children's Hospital, Brookline, MA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Temple University, Bucks County, PA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Plenary II (0956–0961)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: Racial and ethnic minorities are disproportionately affected by pediatric-onset SLE and have worse outcomes compared to their white counterparts. With ongoing advances in pediatric SLE care, it is not known how these gaps are changing. We determined whether changes in renal outcomes over time of hospitalized children with SLE varied by race/ethnicity, and whether these trends differed by hospital minority composition.

Table 1. Characteristics of Hospitalized Children with SLE by Race/Ethnicity

	Non-Hispanic White N=1,667	Black N=2,370	Asian[a] N=563	Hispanic White N=1,217	Hispanic Other N=891	Non-Hispanic Other[b] N=1,617
Year of index admission, n (%)						
2006-2010	506 (30)	941 (40)	152 (27)	533 (44)	240 (27)	262 (36)
2011-2015	647 (39)	712 (30)	210 (37)	323 (27)	347 (39)	241 (33)
2016-2019	514 (31)	717 (30)	201 (36)	361 (30)	304 (34)	223 (31)
Age at index admission, mean (SD)	14.5 (3.1)	14.6 (3.0)	13.8 (3.1)	14.2 (3.1)	13.9 (3.4)	14.2 (3.0)
Female Sex, n (%)	1335 (80)	1993 (84)	478 (85)	990 (81)	717 (80)	601 (83)
Insurance type, n (%)						
Public	641 (38)	1423 (60)	245 (44)	823 (68)	640 (72)	389 (54)
Private	907 (54)	761 (32)	285 (51)	284 (23)	183 (21)	257 (35)
Other/Unknown	119 (7)	186 (8)	33 (6)	110 (9)	68 (8)	80 (11)
Census Region, n (%)						
Midwest	459 (28)	487 (21)	90 (16)	84 (7)	120 (13)	130 (18)
West	374 (22)	226 (10)	283 (50)	594 (49)	473 (53)	244 (34)
Northeast	211 (13)	263 (11)	46 (8)	49 (4)	85 (10)	171 (24)
South	623 (37)	1394 (59)	144 (26)	490 (40)	213 (24)	181 (25)
Urban area hospital	1339 (80)	2108 (89)	525 (93)	1078 (89)	785 (88)	649 (89)
Income Quartile[c]						
<$31,061	237 (14)	680 (29)	45 (8)	277 (23)	188 (21)	136 (19)
$31,061 - $39,625	361 (22)	568 (24)	98 (17)	351 (29)	247 (28)	174 (24)
$39,626 - $52,223	462 (28)	545 (23)	129 (23)	311 (26)	270 (30)	192 (26)
>= $52,224	557 (33)	511 (22)	273 (49)	248 (20)	161 (18)	204 (28)
Unknown/Missing	50 (3)	66 (3)	18 (3)	30 (2)	25 (3)	20 (3)
Diagnosis for comorbid condition/organ involvement assigned at any hospital encounter during observation period						
Nephritis	839 (50)	1429 (60)	359 (64)	775 (64)	523 (59)	406 (56)
ESRD	96 (6)	262 (11)	46 (8)	114 (9)	66 (7)	68 (9)
Seizure	126 (8)	261 (11)	49 (9)	113 (9)	85 (10)	64 (9)
Stroke	56 (3)	130 (5)	24 (4)	53 (4)	41 (5)	41 (6)
Mental health disorder[d]	585 (35)	787 (33)	129 (23)	372 (31)	286 (32)	219 (30)

[a] Includes Pacific Islanders (n=132)
[b] Includes Other race (n=1117) and American Indian race (n=93)
[c] Median household income for zip code
[d] Child and Adolescent Mental Health Disorders Classification System (CAMHD-CS) diagnosis groups

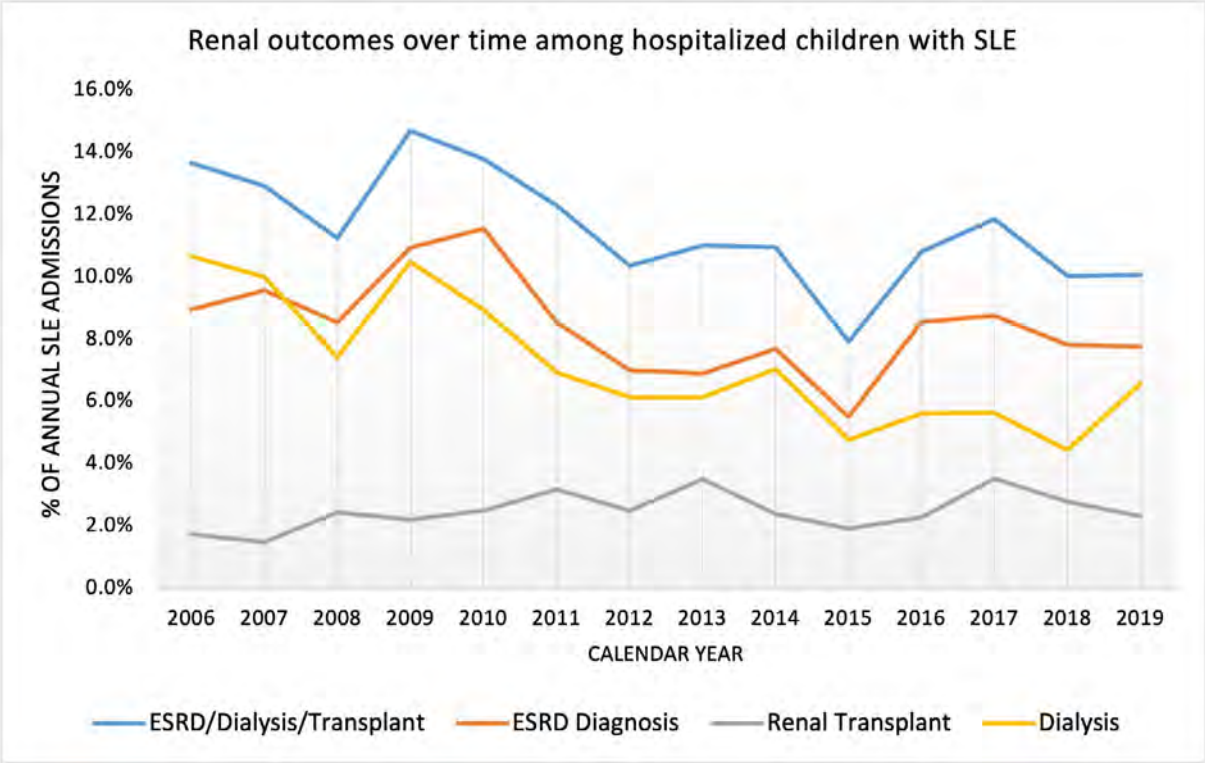

Figure 1. Proportion of SLE admissions in each calendar year that were assigned an ESRD diagnosis code, dialysis procedure code, or renal transplant procedure code, and composite outcome.

Methods: We identified patients ≤21 years old with an ICD-9/10 hospital discharge diagnosis of SLE in the Pediatric Health Information System® inpatient database from 2006-2019. Adverse renal outcomes were defined by assignment of an end-stage renal disease (ESRD) diagnosis code, dialysis procedure code, or renal transplant, analyzed separately and as a composite outcome. We used logistic regression models with fixed effects for time (calendar period), demographic and disease characteristics, and hospital-level random effects to estimate odds of a) an adverse renal outcome at any single hospital encounter or b) incident hospitalization for an adverse renal outcome, after which subsequent encounters were censored. We tested interactions between race and time to assess if change over time differed by race/ethnicity. Hospitals were further dichotomized by whether ≥50% of SLE patients were Black or ≥50% were Hispanic (Creanga et al. 2014) to test multiplicative interactions between hospital minority composition, race and time.

Results: There were 7,434 unique SLE patients with a total of 20,893 admissions at 50 hospitals. Racial/ethnic composition and patient characteristics are shown in **Table 1**. The proportion of SLE admissions with any adverse renal outcome, ESRD, or dialysis decreased over time from 2006 to 2019 (Fig. 1, $p< 0.01$ for trends). However, Black children remained significantly more likely to have an adverse renal outcome at any hospital encounter (adjusted OR 2.5, 95% CI [1.8-3.5]) over time compared to non-Hispanic whites. Black and Asian children were also more likely to have an incident hospitalization for an adverse renal outcome (OR 1.4 [1.1-1.8] and OR 1.5 [1.0-2.4], respectively). There were no significant changes in the magnitude of disparity over time. However, there were significant differences in both the magnitudes of disparities and changes in disparity levels over time between hospitals in which Black or Hispanic minorities comprised ≥50% of SLE patients vs. < 50% (p-values for interactions < 0.01). At hospitals with ≥50% Hispanic SLE patients, renal outcomes failed to improve at the same rate among Black and Hispanic white patients compared to non-Hispanic whites (**Fig. 2A/B**). At hospitals with ≥50% Black SLE patients, rates of renal outcomes improved less over time among black vs. non-Hispanic white children and worsened among Hispanic white children (**Fig. 2C/D**).

Conclusion: On average, adverse renal outcomes among hospitalized children with SLE decreased over a 13 year period, but racial disparities persisted without significant narrowing of the existing gap. There is a specific need to

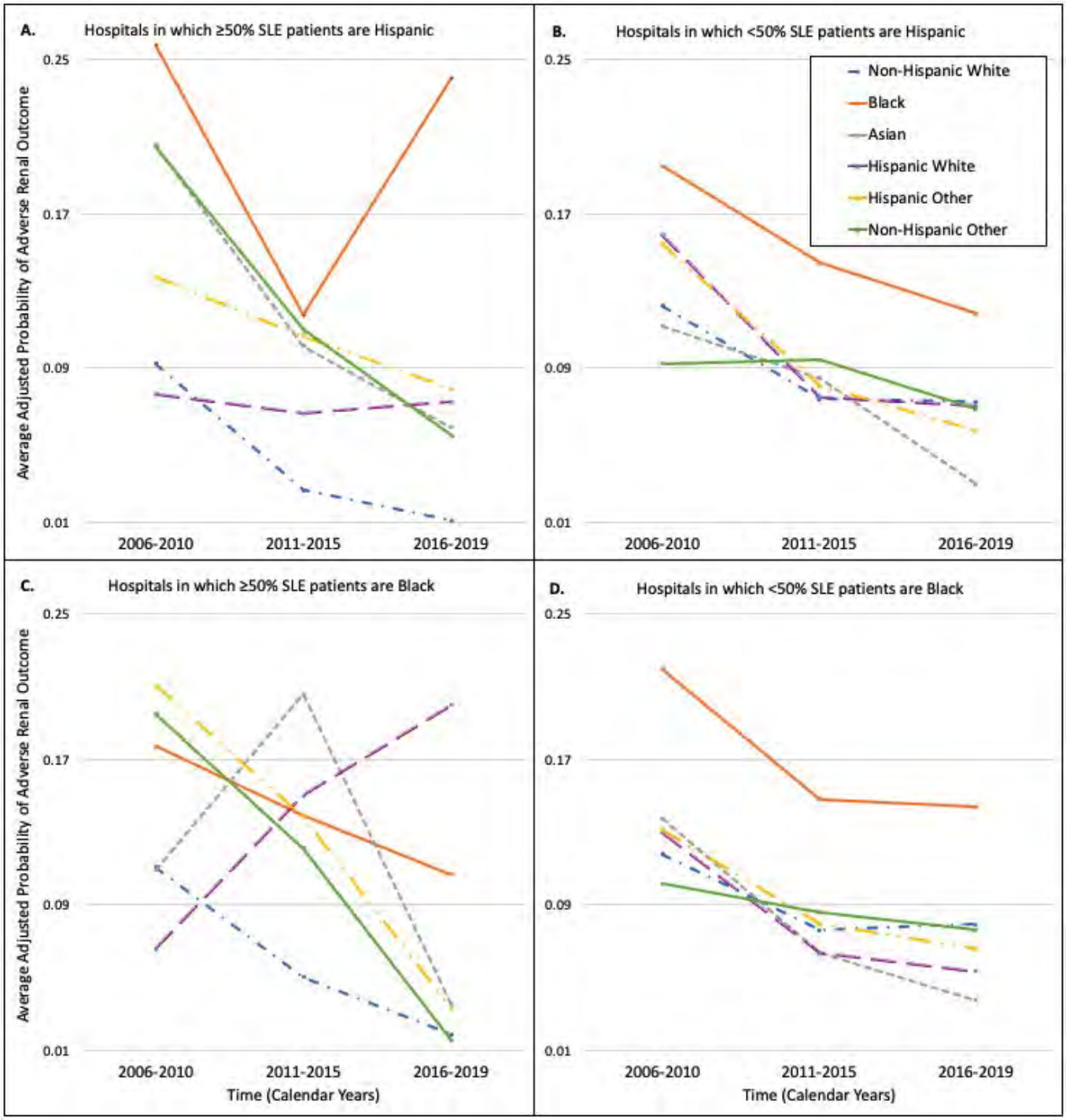

Figure 2. Marginal predictions of the average adjusted probability of adverse renal outcomes at any hospital encounter (composite of ESRD diagnosis, dialysis, renal transplant) over time by racial/ethnic category, stratified either by hospitals in which Hispanic patients comprise A) ≥50% of admitted SLE patients (N=7 hospitals) vs. B) <50% of SLE patients (N=43 hospitals), or by hospitals in which C) ≥50% of SLE patients are Black (N=18 hospitals) vs. D) <50% of SLE patients are Black (N=32 hospitals). All models are adjusted for age, census region, median household income, insurance type, APR-DRG severity of illness, and seizure.

address greater or widening disparities that are systematically concentrated in local contexts despite population level improvements.

Disclosure: J. Chang, GlaxoSmithKline, 5; **C. Sears**, None; **V. Torres**, None; **M. Son**, None.

Abstract Number: 0957

Vitamin D and Marine n-3 Fatty Acid Supplementation and Prevention of Autoimmune Disease in the VITAL Randomized Controlled Trial

Jill Hahn[1], Nancy Cook[2], Erik Alexander[3], Sonia Friedman[3], Vadim Bubes[3], Joseph Walter[3], Gregory Kotler[3], I-Min Lee[3], JoAnn Manson[3] and **Karen Costenbader**[4], [1]Harvard T.H. Chan School of Public Health, Boston, MA, [2]Brigham and Womens' Hospital, Boston, MA, [3]Brigham and Women's Hospital/ Harvard Medical School, Boston, MA, [4]Brigham and Women's Hospital, Belmont, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Plenary II (0956–0961)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: In observational studies, vitamin D has been inconsistently associated with reduced risk of several autoimmune diseases, and a large randomized, controlled trial has been lacking. Dietary marine-derived long-chain omega-3 (n–3) fatty acids decrease systemic inflammation and ameliorate symptoms in some autoimmune diseases, but no trials have tested whether supplementation lowers risk of developing autoimmune disease. We tested both vitamin D_3 and n-3 fatty acids for the prevention of autoimmune disease within a large nationwide randomized, controlled trial.

Methods: VITamin D and Omeg**A**-3 Tria**L** (**VITAL**), a U.S. nationwide randomized, double-blind, placebo-controlled trial, enrolled men at least 50 years and women at least 55 years of age in a two-by-two factorial design. Randomiza-

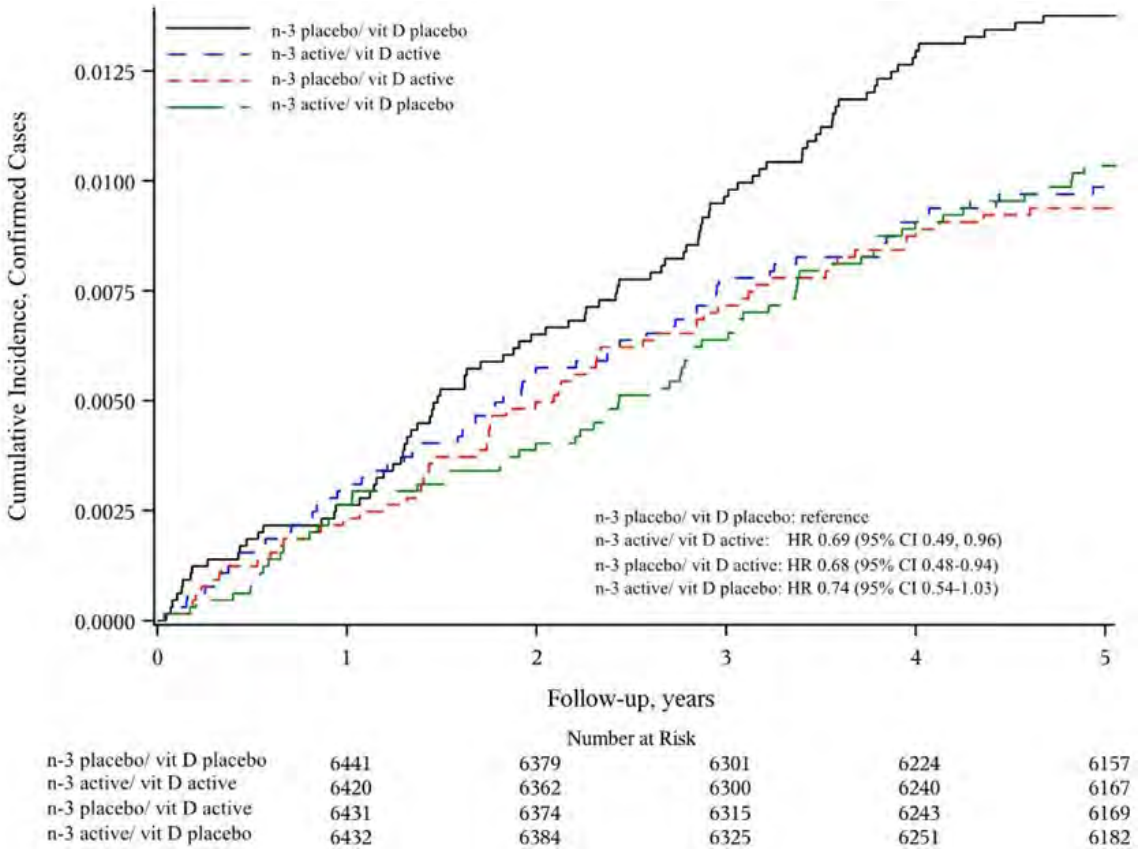

Figure 1. Incident Autoimmune Disease in the Four Arms of VITAL over 5.3 years Mean Follow-up, including Confirmed Cases.

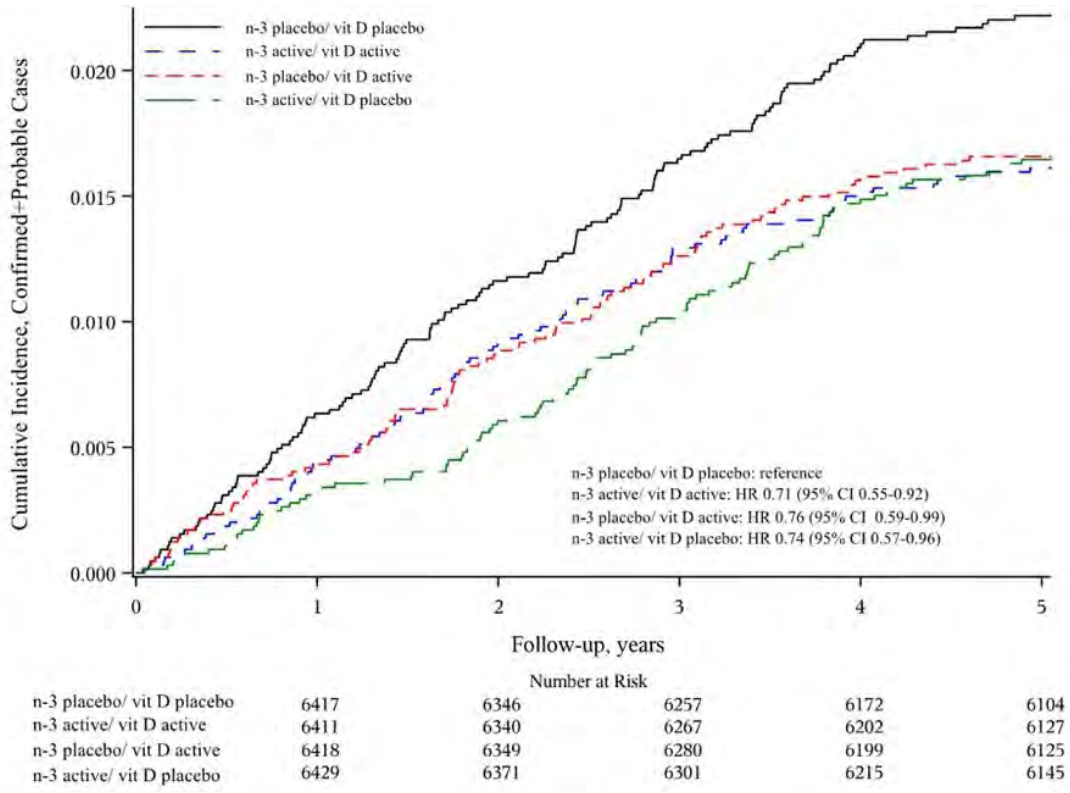

Figure 2. Incident Autoimmune Disease in the Four Arms of VITAL over 5.3 years Mean Follow-up, including Confirmed and Probable Cases.

tion to vitamin D_3 (2000 IU/d) and/or n-3 fatty acids (1000 mg/d) or placebo occurred from November 2011 to March 2014, and treatment continued through December 2017. (VITAL parent trial for cancer and cardiovascular disease prevention was reported in *NEJM*, January 3, 2019). We tested effects of vitamin D_3 and n-3 fatty acids upon autoimmune disease incidence. Incident doctor-diagnosed autoimmune diseases were reported by participants annually and confirmed by medical record review by expert physicians for classification criteria (if existing). The primary endpoint was total incident autoimmune diseases, including rheumatoid arthritis, polymyalgia rheumatica, autoimmune thyroid disease, psoriasis, and all others. Pre-specified secondary endpoints included individual most common autoimmune diseases; and probable autoimmune disease (evidence of incident autoimmune disease but lacking enough medical record data to confirm). Results were displayed in cumulative incidence curves and Cox regression models calculated hazard ratios (HR) of incident autoimmune diseases.

Results: 25,871 participants were randomized: 71% self-reported non-Hispanic Whites, 20% Black, and 9% other racial/ethnic groups, 51% women, mean age 67.1 years. During median follow-up of 5.3 years, confirmed autoimmune disease was diagnosed in 117 participants in the vitamin D_3 group and 150 in the placebo group (HR 0.78, 95% confidence interval 0.61-1.00, p=0.04). Excluding the first 2 years in pre-specified analyses of the primary endpoint, the HR for vitamin D_3 was 0.61 (0.43 - 0.86; 137 cases). Confirmed autoimmune disease was diagnosed in 123 participants in the n-3 fatty acids group and 144 in the placebo group (HR 0.85 (0.67-1.09). Excluding the first 2 years, the HR for the primary endpoint was 0.90 (0.64-1.26). (**Table 1**) When analyzed by factorial design subgroups, HRs for all three active arms vs. placebo/placebo were reduced by 25-30% (**Figures 1-2**). The number needed to treat with both agents for 5 years to prevent one autoimmune disease was 167 (94-769).

Conclusion: Supplementation for 5 years with vitamin D_3 and/or n-3 fatty acids reduced incident autoimmune disease by 25-30% in older adults vs. those who received neither supplement. The effect of vitamin D_3 appeared stronger after 2 years of supplementation.

Table 1. Hazard Ratios and 95% Confidence Intervals for the Primary and Secondary Endpoints, according to Randomized Assignment to (A) Vitamin D3 or Placebo or (B) N-3 Fatty Acids or Placebo

Table 1A. Hazard Ratios and 95% Confidence Intervals (95% CI) for the Primary and Secondary Endpoints, according to Randomized Assignment to Vitamin D_3 or Placebo[a]

Endpoint	Vitamin D_3	Placebo	Hazard Ratio	p value
	(N=12,927)	(N=12,944)	(95% CI)	
	Number of participants with event			
Primary Endpoint				
Confirmed autoimmune diseases	117	150	0.78 (0.61-1.00)	0.04
Secondary Endpoints				
Confirmed+probable autoimmune diseases	199	235	0.85 (0.70-1.02)	0.09
Analyses excluding all pre-randomization AD				
Confirmed autoimmune diseases	98	123	0.79 (0.61-1.03)	0.08
Confirmed+probable autoimmune diseases	161	197	0.81 (0.66-1.00)	0.05
Analyses excluding the first 2 years of follow-up				
Confirmed autoimmune diseases	52	85	0.61 (0.43-0.86)	0.005
Confirmed+probable autoimmune diseases	90	130	0.69 (0.53-0.91)	0.007
Individual autoimmune diseases				
Confirmed rheumatoid arthritis	14	24	0.58 (0.30-1.13)	0.11
Confirmed+probable rheumatoid arthritis	17	27	0.63 (0.34-1.16)	0.14
Confirmed polymyalgia rheumatica[b]	30	43	0.70 (0.44-1.12)	0.14
Confirmed+probable polymyalgia rheumatica	31	43	0.72 (0.46-1.15)	0.17
Confirmed autoimmune thyroid disease	18	11	1.63 (0.77-3.45)	0.20
Confirmed+ probable autoimmune thyroid disease	92	87	1.05 (0.78-1.41)	0.74
Confirmed psoriasis[c]	15	21	0.72 (0.37-1.39)	0.32
Confirmed+probable psoriasis	16	23	0.70 (0.37-1.32)	0.27
Confirmed other autoimmune disease	39	53	0.74 (0.49-1.12)	0.15
Confirmed+probable other autoimmune disease	44	60	0.73 (0.50-1.08)	0.12

Table 1B. Hazard Ratios and 95% Confidence Intervals for the Primary and Secondary Endpoints, according to Randomized Assignment to N-3 Fatty Acids or Placebo[a]

Endpoints	N-3 Fatty Acids	Placebo	Hazard Ratio	p-value
	(N=12,933)	(N=12,938)	(95% CI)	
	Number of participants with event			
Primary Endpoint				
Confirmed autoimmune disease	123	144	0.85 (0.67-1.09)	0.20
Secondary Endpoints				
Confirmed+probable autoimmune disease	196	238	0.82 (0.68-0.99)	0.04
Analyses excluding all pre-randomization autoimmune disease				
Confirmed autoimmune disease	111	119	0.91 (0.70-1.18)	0.48
Confirmed+probable autoimmune disease	180	199	0.90 (0.73-1.10)	0.30
Analyses excluding the first 2 years of follow-up				
Confirmed autoimmune disease	67	74	0.90 (0.64-1.26)	0.54
Confirmed+probable autoimmune disease	110	117	0.94 (0.72-1.23)	0.66
Individual autoimmune diseases				
Confirmed rheumatoid arthritis	14	24	0.58 (0.30-1.13)	0.11
Confirmed+probable rheumatoid arthritis	16	26	0.57 (0.31-1.06)	0.07
Confirmed polymyalgia rheumatica[b]	34	39	0.87 (0.55-1.38)	0.55
Confirmed+probable polymyalgia rheumatica	34	40	0.85 (0.54-1.34)	0.48
Confirmed autoimmune thyroid disease	10	19	0.53 (0.25-1.14)	0.10
Confirmed+ probable autoimmune thyroid disease	79	100	0.80 (0.59-1.07)	0.13
Confirmed psoriasis[c]	22	14	1.57 (0.81-3.07)	0.18
Confirmed+probable psoriasis	23	16	1.44 (0.76-2.72)	0.26
Confirmed other autoimmune disease	42	50	0.84 (0.56-1.26)	0.40
Confirmed+probable other autoimmune disease	45	59	0.76 (0.52-1.12)	0.17

[a]Analyses from Cox regression models controlled for age, sex, race, and other (n-3 fatty acid or vitamin D_3) randomization group
[b]14 confirmed cases of PMR without giant cell arteritis (GCA), 18 confirmed GCA without PMR, and 2 confirmed cases with both
[c]No cases of psoriatic arthritis

Disclosure: J. Hahn, None; **N. Cook**, None; **E. Alexander**, None; **S. Friedman**, None; **V. Bubes**, None; **J. Walter**, None; **G. Kotler**, None; **I. Lee**, None; **J. Manson**, None; **K. Costenbader**, Neutrolis, 11, Merck, Exagen, Gilead, 5, Astra Zeneca, Neutrolis, 2.

Abstract Number: 0958

Risk Factors for Major Adverse Cardiovascular Events in Patients Aged ≥ 50 Years with RA and ≥ 1 Additional Cardiovascular Risk Factor: Results from a Phase 3b/4 Randomized Safety Study of Tofacitinib vs TNF Inhibitors

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

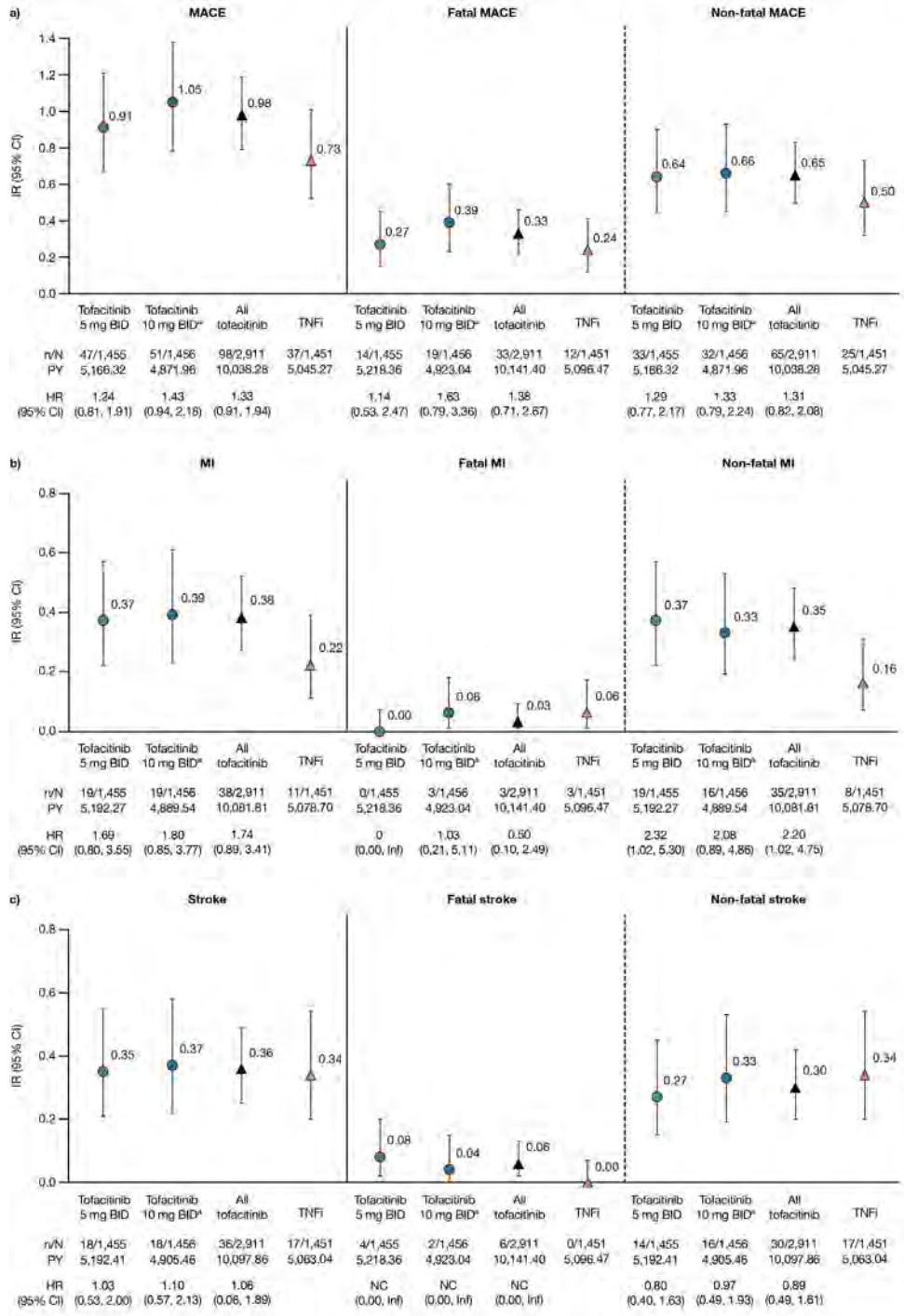
Session Title: Plenary II (0956–0961)

Session Type: Plenary Session

Session Time: 10:30AM–12:00PM

Background/Purpose: To identify independent risk factors for major adverse cardiovascular (CV) events (MACE) in ORAL Surveillance (NCT02092467), a long-term, randomized, open-label, non-inferiority, Phase 3b/4 safety study of tofacitinib vs TNFi in high-risk (aged ≥ 50 yrs with ≥ 1 additional CV risk factor) patients (pts) with RA and an inadequate MTX response.

Figure. IRs (95% CI, unique pts with events per 100 PY) and HRs (95% CI; tofacitinib vs TNFi) for a) MACE, b) MI, and c) stroke, including fatal and non-fatal events



[a]The tofacitinib 10 mg BID group included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019
MACE included CV death (excluding CV death due to pulmonary embolism), non-fatal MI, and non-fatal stroke
HRs (95% CI) were based on 2 univariate Cox models (one for comparing All tofacitinib vs TNFi, and the other for comparing tofacitinib 5 and 10 mg BID vs TNFi) with treatment as the only covariate; NC is shown where HR was not calculated due to 0 events in the denominator (TNFi) of the treatment comparison
Risk period was to 60 days beyond the last dose or to the last contact date, whichever was shorter. The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date. PY included time to first event for pts with events, otherwise pts with no events were censored at the end of this risk period
AE, adverse event; BID, twice daily; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; Inf, infinity; IR, incidence rate; MACE, major adverse cardiovascular events; MI, myocardial infarction; NC, not calculated; pt, patient; PY, pt-yrs; TNFi, tumor necrosis factor inhibitor

Methods: Pts on stable doses of MTX were randomized 1:1:1 to receive tofacitinib 5 or 10 mg BID or a TNFi (adalimumab 40 mg every 2 weeks or etanercept 50 mg every week). Incidence rates (IRs; unique pts with events/100 pt-yrs) and hazard ratios (HRs; tofacitinib vs TNFi) were evaluated for the co-primary endpoint of adjudicated MACE, as well as myocardial infarction (MI) and stroke; MACE was defined as CV death (excluding CV death due to pulmonary embolism), non-fatal MI, and non-fatal stroke. Across outcomes, IRs and HRs are also presented for fatal and non-fatal events. A post hoc analysis identified independent overall risk factors for MACE across treatment groups by Cox regression models. Baseline (BL) categorical covariates were initially screened in 2 univariate Cox analyses (main risk factor $p < 0.1$ and risk factor–treatment interaction $p \geq 0.2$) and were then selected in the final multivariate Cox model using backward selection, with $p < 0.1$ stay criteria. IRs and HRs for MACE were then stratified by the 4 most important risk factors identified (per largest HRs and smallest p values in the multivariate Cox model).

Results: 4,362 pts were included (tofacitinib 5 mg BID, n=1,455; tofacitinib 10 mg BID, n=1,456; TNFi, n=1,451). Median (range) age was 60.0 (50.0–88.0) yrs. MACE was reported by 47 pts, 51 pts, and 37 pts receiving tofacitinib 5 mg BID, tofacitinib 10 mg BID, and TNFi, respectively (Figure). IRs for MACE, MI, fatal and non-fatal MACE, and non-fatal MI were numerically higher with both tofacitinib doses vs TNFi (95% CIs overlapped; Figure a, b). Generally, IRs for fatal MI, and stroke (including fatal/non-fatal events), were similar across treatment groups (Figure a–c). HRs for MACE, MI, and stroke were generally > 1 for tofacitinib vs TNFi (Figure a–c); HR 95% CIs for non-fatal MI excluded 1 for tofacitinib 5 mg BID and all tofacitinib vs TNFi. BL covariates identified as the most important independent overall risk factors for MACE were current smoking, aspirin use, age ≥ 65 yrs, and male sex (Table 1). In pts with 1 of these

Table 1. Multivariate analysis of BL covariates as potential independent overall risk factors for MACE across all treatment groups

BL covariate	HR (95% CI)	p value
Current smoking	2.18 (1.50, 3.16)	< 0.0001
Aspirin use	2.11 (1.40, 3.19)	0.0004
Age ≥ 65 yrs	1.81 (1.27, 2.59)	0.0011
Male sex	1.81 (1.25, 2.61)	0.0015
History of diabetes	1.72 (1.16, 2.54)	0.0064
History of coronary artery procedures	1.71 (0.98, 2.99)	0.0598
History of hypertension	1.51 (1.00, 2.29)	0.0526
Total cholesterol/HDL-c ratio > 4	1.50 (1.06, 2.14)	0.0240

The tofacitinib 10 mg BID group included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019

MACE included CV death (excluding CV death due to pulmonary embolism), non-fatal MI, and non-fatal stroke

A backward selection algorithm was used on a multivariate Cox model, which included effects of treatment (tofacitinib 5 mg BID, tofacitinib 10 mg BID, and TNFi; not subject to backward selection) and a pre-selected set of potential independent overall risk factors (ie risk factors which affect the incidence rates of an event equally across all 3 treatment groups) based on 2 Cox univariate models, where the p value for the risk factor was < 0.1 in a main effect model, and for the risk factor–treatment interaction was ≥ 0.2 in an interaction effect model. This pre-selected set of risk factors were subject to backward selection, with $p < 0.1$ stay criteria (except for treatment, which was mandatorily included in the model)

The 8 independent overall risk factors shown were selected from the backward selection algorithm; of these, the top 4 with the smallest p values were identified as the most important independent risk factors for MACE. The HR (95% CI) and p value presented for each risk factor are for Yes vs No (or the reference level)

Risk period was to 60 days beyond the last dose or to the last contact date, whichever was shorter. The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date

AE, adverse event; BID, twice daily; BL, baseline; CI, confidence interval; CV, cardiovascular; HDL-c, high-density lipoprotein-cholesterol; HR, hazard ratio; MACE, major adverse cardiovascular events; MI, myocardial infarction; pt, patient; TNFi, TNF inhibitors

Table 2. IRs (95% CI, unique pts with events per 100 PY) and HRs (95% CI; tofacitinib vs TNFi) for MACE, stratified by BL covariates identified as independent overall risk factors for MACE by Cox regression modeling

	Tofacitinib 5 mg BID			Tofacitinib 10 mg BID[a]			All tofacitinib			TNFi	
BL covariate	n/N	IR (95% CI)	HR (95% CI)	n/N	IR (95% CI)	HR (95% CI)	n/N	IR (95% CI)	HR (95% CI)	n/N	IR (95% CI)
Smoking status											
Current smoking	22/411	1.55 (0.97, 2.34)	1.31 (0.67, 2.55)	17/402	1.29 (0.75, 2.06)	1.08 (0.53, 2.20)	39/813	1.42 (1.01, 1.94)	1.20 (0.65, 2.21)	14/353	1.19 (0.65, 1.99)
Past smoking	13/309	1.22 (0.65, 2.09)	1.92 (0.77, 4.82)	15/302	1.53 (0.86, 2.53)	2.43 (0.99, 5.96)	28/611	1.37 (0.91, 1.98)	2.17 (0.95, 4.96)	7/326	0.64 (0.26, 1.32)
Never smoked	12/735	0.45 (0.23, 0.78)	0.77 (0.37, 1.63)	19/752	0.74 (0.44, 1.15)	1.28 (0.66, 2.50)	31/1,487	0.59 (0.40, 0.84)	1.02 (0.56, 1.87)	16/772	0.58 (0.33, 0.94)
Aspirin use											
Yes	18/212	2.41 (1.43, 3.81)	1.66 (0.78, 3.51)	19/231	2.60 (1.57, 4.07)	1.79 (0.85, 3.76)	37/443	2.51 (1.76, 3.45)	1.72 (0.88, 3.38)	11/224	1.46 (0.73, 2.62)
No	29/1,243	0.66 (0.44, 0.94)	1.08 (0.64, 1.84)	32/1,225	0.77 (0.53, 1.09)	1.28 (0.76, 2.15)	61/2,468	0.71 (0.55, 0.92)	1.18 (0.74, 1.86)	26/1,227	0.61 (0.40, 0.89)
Age											
≥ 65 yrs	19/413	1.38 (0.83, 2.15)	1.51 (0.76, 3.02)	27/478	1.88 (1.24, 2.74)	2.06 (1.08, 3.93)	46/891	1.63 (1.20, 2.18)	1.79 (0.99, 3.26)	14/462	0.91 (0.50, 1.52)
< 65 yrs	28/1,042	0.74 (0.49, 1.07)	1.12 (0.65, 1.95)	24/978	0.70 (0.45, 1.04)	1.07 (0.60, 1.89)	52/2,020	0.72 (0.54, 0.94)	1.10 (0.67, 1.79)	23/989	0.66 (0.42, 0.99)
Sex											
Male	18/286	1.85 (1.10, 2.92)	1.37 (0.69, 2.73)	21/332	1.95 (1.21, 2.98)	1.45 (0.75, 2.81)	39/618	1.90 (1.35, 2.60)	1.41 (0.78, 2.57)	15/334	1.35 (0.75, 2.22)
Female	29/1,169	0.69 (0.46, 0.99)	1.24 (0.71, 2.16)	30/1,124	0.79 (0.53, 1.13)	1.42 (0.82, 2.46)	59/2,293	0.74 (0.56, 0.95)	1.33 (0.81, 2.16)	22/1,117	0.56 (0.35, 0.85)
Age and smoking status											
≥ 65 yrs or ever smoked	40/932	1.23 (0.88, 1.68)	1.33 (0.82, 2.14)	43/963	1.39 (1.00, 1.87)	1.50 (0.94, 2.40)	83/1,895	1.31 (1.04, 1.62)	1.41 (0.93, 2.15)	29/926	0.93 (0.62, 1.33)
50–< 65 yrs and never smoked	7/523	0.36 (0.15, 0.75)	0.87 (0.32, 2.41)	8/493	0.45 (0.19, 0.89)	1.10 (0.41, 2.93)	15/1,016	0.41 (0.23, 0.67)	0.98 (0.42, 2.31)	8/525	0.42 (0.18, 0.82)

[a]The tofacitinib 10 mg BID group included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019

MACE included CV death (excluding CV death due to pulmonary embolism), non-fatal MI, and non-fatal stroke

HRs (95% CI) were based on 2 univariate Cox models (one for comparing All tofacitinib vs TNFi, and the other for comparing tofacitinib 5 and 10 mg BID vs TNFi) with treatment as the only covariate at each level of the risk factors

Risk period was to 60 days beyond the last dose or to the last contact date, whichever was shorter. The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date

AE, adverse event; BID, twice daily; BL, baseline; CI, confidence interval; CV, cardiovascular; HR, hazard ratio; IR, incidence rate; MACE, major adverse cardiovascular event; MI, myocardial infarction; pt, patient; PY, pt-yrs; TNFi, TNF inhibitors

risk factors present, IRs for MACE were numerically higher with both tofacitinib doses vs TNFi (95% CIs overlapped; Table 2). Across treatment groups, in pts without these risk factors present, IRs for MACE were similar (Table 2). Generally, HRs for MACE were > 1 for tofacitinib vs TNFi, in pts with or without risk factors present (Table 2).

Conclusion: The incidence of MACE was numerically higher with tofacitinib vs TNFi treatment. Across treatment groups, the BL covariates, current smoking, aspirin use, age ≥ 65 yrs, and male sex were identified as independent overall risk factors in pts experiencing MACE; tofacitinib vs TNFi treatment in pts with any of these risk factors present was associated with numerically higher incidence of MACE.

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Abstract Number: 0959

Impact of Systemic Lupus Disease Activity State on Flare Risk After Hydroxychloroquine Maintenance, Reduction or Discontinuation in a Multinational Inception Cohort

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SESSION INFORMATION
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Background/Purpose: Physicians and patients often consider reducing or discontinuing hydroxychloroquine (HCQ) among SLE patients in remission or very low disease activity to limit HCQ-induced toxicity. We evaluated how disease activity status is associated with SLE flare after HCQ reduction or discontinuation, compared with HCQ maintenance.

Methods: We analyzed prospective data from the SLICC cohort (33 sites in Europe, Asia, and North America), which enrolls patients within 15 months of diagnosis and follows them annually since 1999. In patients initially receiving HCQ, we identified events of HCQ dose reduction and discontinuation. We created two cohorts of person-time, with time zero being date of first HCQ reduction in one cohort, and discontinuation in the other. For each cohort, we formed a comparison cohort of person-time on HCQ maintenance, matched on HCQ duration at time-zero (Figure

1). Patients were censored at death, lost to follow-up, end of study (April 2019), or when they started contributing person-time to the other cohorts. SLE flare was defined as either subsequent SLE therapy augmentation (steroids, immunosuppressives, HCQ, chloroquine, or biologics), increase of ≥4 points in the SLE Disease Activity Index-2000 (SLEDAI-2K) or hospitalization for SLE (information available only after 2014, for 60% of patients). We estimated crude flare rates, adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) of the first flare in the HCQ reduction and discontinuation cohorts (vs HCQ maintenance). Analyses were then stratified by low disease activity state or clinical remission (see the definitions in the footnote to Table 1). All models were adjusted for demographics and clinical characteristics at time-zero.

Results: A total of 1460 patients were included (89% female, 52% Caucasian). The HCQ reduction cohort contributed 1063 person-years (N=564) and were compared with 1242 HCQ maintenance person-years (N=778). The HCQ discontinuation cohort contributed 657 person-years (N=389) and were compared with 924 maintenance person-years (N=577). We estimated that 5% of patients may have reduced HCQ therapy as result of the AAO guidelines, 55% because of low disease activity state, and the remainder (40%) for other reasons (possibly intolerance or patient preference). Among those who discontinued HCQ, 4% had retinal changes of concern, 15% were in clinical remission and the remainder stopped for unknown reasons (possibly intolerance, or patient preference). Cohorts reducing or discontinuing HCQ tended to have more SLE flares versus those maintaining HCQ (Table 1). Maintaining HCQ was associated with lower SLE flares particularly among patients already in low disease activity state or in remission at time zero (Table 1). However, patients who were not in remission or low activity state, were likely to flare if HCQ was either maintained or reduced, but the flare risk was higher if they discontinued HCQ (Table 1).

Conclusion: Maintaining HCQ was associated with a lower flare risk in all subgroups evaluated. Even among SLE patients in remission, lowering or stopping HCQ was associated with a 2-fold increase in flare risk compared to HCQ maintenance.

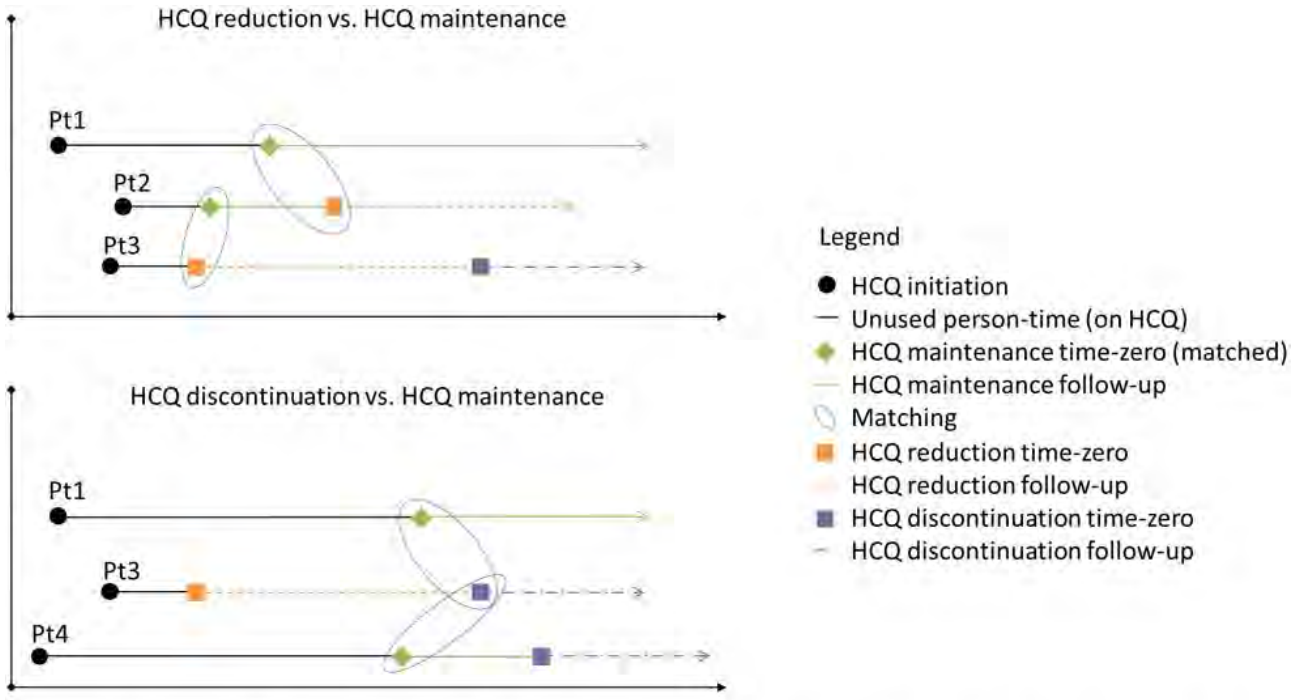

Figure 1. Example of 4 cohort patients (Pt1-4). A single patient could contribute person-time to one or more cohorts. HCQ maintenance person-time was matched (2:1) to the reduction or discontinuation groups on HCQ duration at time-zero.

Table 1. Adjusted hazard ratios with 95% confidence intervals (CIs) for SLE flares associated with HCQ reduction/discontinuation versus maintenance: main and stratified analyses

	HCQ reduction vs maintenance			HCQ discontinuation vs maintenance		
	No. of patients	Absolute flare rate/100 person-years (95% CI)	Adjusted HR (95% CI)*	No. of patients	Absolute flare rate/100 person-years (95% CI)	Adjusted HR (95% CI)*
Main analysis	1342	42.3 (38.6, 46.4) vs. 35.6 (32.4, 39.1)	1.13 (0.98, 1.30)	966	43.1 (38.3, 48.4) vs. 34.2 (30.6, 38.2)	1.41 (1.19, 1.67)
Stratified analyses:						
Low disease activity[a] state at time zero						
Yes	815	38.7 (34.2, 43.8) vs. 31.4 (27.8, 35.5)	1.26 (1.04, 1.51)	592	36.7 (31.5, 42.7) vs. 30.1 (26.0, 34.8)	1.52 (1.21, 1.91)
No	527	48.1 (41.8, 55.4) vs. 43.9 (38.0, 50.8)	1.00 (0.80, 1.23)	374	56.9 (47.5, 68.1) vs. 42.2 (35.6, 50.0)	1.37 (1.06, 1.77)
Clinical remission[b] at time zero						
Yes	196	26.2 (20.1, 34.1) vs. 13.2 (9.4, 18.4)	2.14 (1.34, 3.43)	133	24.7 (17.7, 34.6) vs. 12.2 (8.0, 18.8)	2.77 (1.46, 5.26)
No	1146	46.3 (41.9, 51.1) vs. 41.7 (37.8, 46.0)	1.07 (0.92, 1.24)	833	47.9 (42.3, 54.2) vs. 39.2 (35.0, 43.9)	1.35 (1.13, 1.62)

*Adjusted for sex, race, age at SLE diagnosis, education, geographic residence, and the following variables assessed at time zero: SLE duration, renal damage according to SLICC Damage Inex, body mass index, smoking, prednisone, immunosuppressives and biologics. The main analysis was additionally adjusted by disease activity at time zero. [a]Low disease activity state was defined as SLEDAI-2K<4 and current prednisone dose ≤7.5 mg/day. [b]Clinical remission was defined as SLEDAI-2K=0 and no prednisone or immunosuppressives use during the last year.

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Abstract Number: 0960

The Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA (STOP-JIA) Study: 24-Month Outcomes

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Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: The CARRA STOP-JIA study compared the effectiveness of the CARRA Consensus Treatment Plans (CTPs) in achieving clinical inactive disease (CID) in untreated polyarticular JIA (pJIA) at 12 months using a prospective, observational study design. The primary results were reported previously ["The CARRA STOP-JIA Study: A Comparative Effectiveness Study of CARRA Consensus Treatment Plans for Untreated Polyarticular JIA", Kimura et al, Arthritis Rheumatol, In press]. Patients were enrolled into the CARRA Registry, which allows for long-term follow-up of this cohort. Here we report on the impact of initial CTP choices on outcomes at 24 mo.

Methods: STOP-JIA compared 3 CARRA CTPs: 1) Step Up (SU) – starting conventional synthetic disease modifying anti-rheumatic drug (csDMARD), adding biologic (b)DMARD if needed after ≥ 3 months; 2) Early Combination (EC) - csDMARD and bDMARD started together; and 3) Biologic First (BF) – starting bDMARD monotherapy, adding csDMARD if needed after ≥ 3 months. There was no randomization. Data were collected every 3 months using the CARRA Registry for the first 12 months and every 6 months thereafter. Patients with 24 months of follow-up were included in this analysis. The primary outcome was the proportion of children achieving CID off glucocorticoids (GC) at 24 months. Propensity score (PS) weighting (linear probability model) was used to balance baseline differences in potential confounders between CTPs. Secondary outcomes included the clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS10), the Pediatric ACR 70 (pACR70) and patient-reported outcomes (PROs).

Results: 291 participants had a 24 month visit (188 Step Up, 76 Early Combination, 27 Biologic First). There were significant baseline differences between CTP groups for several variables, including JIA categories, number of active joints, Physician Global Assessment of Disease Activity, and cJADAS10 scores (Table 1). Patients in CID at 24 months was 42% for SU, 52% EC, and 44% BF (at 12 months: 32%, 37%, and 24% respectively), with a statistically significant difference (p=0.006) between the SU and EC groups after PS weighting at 24 months (Table 2). There were no significant differences between proportions of patients achieving cJADAS10 inactive disease (ID) (≤2.5) or the pACR70. All groups continued to improve at 24 months compared to 12 months. At 12 months/24 months, proportion of cJADAS10 ≤2.5 in SU: 45% vs 59%; EC: 60% vs 66%; BF: 48% vs. 57%. At 12 months/24 months, proportion of

Table 1. Baseline characteristics for all participants with complete data for CID at 24 months

	Overall	Step up	Early Combination	Biologic First	P-value	Missing (%)
n	275	177	73	25		
Age (median [range])	10.7 [1.1, 17.8]	10.5 [1.2, 17.8]	10.7 [1.2, 17.8]	11.6 [1.4, 16.6]	0.21	0.0
Sex = Female (%)	199 (72.4)	128 (72.3)	56 (76.3)	15 (60.0)	0.27	0.0
Race (%)					0.99	0.0
Black	17 (6.2)	10 (5.6)	5 (6.8)	2 (8.0)		
Other	58 (21.1)	38 (21.5)	15 (20.5)	5 (20.0)		
White	200 (72.7)	129 (72.9)	53 (72.6)	18 (72.0)		
Months since symptom onset (median [range])	5.4 [0.2, 171.5]	5.2 [0.2, 171.5]	6.8 [1.0, 122.5]	4.5 [0.9, 111.6]	0.33	0.0
Months since JIA diagnosis (median [range])	0.0 [0.0, 149.0]	0.0 [0.0, 149.0]	0.0 [0.0, 113.8]	0.5 [0.0, 107.6]	0.19	0.0
JIA Category (%)					0.20	0.0
Enthesitis-related	17 (6.2)	8 (4.5)	6 (8.2)	3 (12.0)		
Extended oligoarticular	11 (4.0)	10 (5.6)	0 (0.0)	1 (4.0)		
Polyarticular (RF-)	161 (58.5)	111 (62.7)	39 (53.4)	11 (44.0)		
Polyarticular (RF+)	57 (20.7)	32 (18.1)	20 (27.4)	5 (20.0)		
Psoriatic	19 (6.9)	11 (6.2)	5 (6.8)	3 (12.0)		
Undifferentiated	10 (3.6)	5 (2.8)	3 (4.1)	2 (8.0)		
Physician Global (median [range])	5.50 [1, 10]	5.0 [1, 10]	7.0 [1, 10]	7.0 [1, 10]	<0.001	1.1
Pt Global (median [range])	5.0 [0, 10]	4.0 [0, 10]	5.0 [0, 10]	5.50 [0, 9]	0.006	8.4
cJADAS10 (median [range])	18.0 [6.0, 29.0]	17.0 [7.0, 29.0]	21.0 [6.0, 29.0]	19.50 [10.0, 28.5]	<0.001	9.1
Active joint count (median [range])	10 [5, 50]	9 [5, 47]	15 [5, 50]	8 [5, 41]	0.001	0.0
ESR abnormal (%)	89 (42.4)	51 (38.9)	31 (51.7)	7 (36.8)	0.22	23.6
CRP abnormal (%)	67 (31.9)	38 (29.0)	22 (36.7)	7 (36.8)	0.51	23.6
CHAQ (median [range])	0.9 [0.0, 3.0]	0.8 [0.0, 3.0]	1.0 [0.0, 2.6]	0.9 [0.0, 3.0]	0.04	8.7

Abbreviations: RF=rheumatoid factor; Physician Global=Physician Global Assessment of Disease Activity; Pt Global=Patient/parent Global Assessment of Overall Well-being; cJADAS10=clinical Juvenile Arthritis Disease Activity Score based on 10 joint maximum; ESR: erythrocyte sedimentation rate; CRP: C reactive protein; CHAQ: Childhood Health Assessment Questionnaire.

Table 2. Between Group Differences in Clinically Inactive Disease (ACR) off Glucocorticoids, Pediatric ACR 70 Scores and cJADAS10 at 24 months

*A. Between-group difference estimates in CID off GC: estimates from PS-weighted model with adjustment**

	Difference in CID	Lower 95%	Upper 95%	P-value
Biologic First vs Step Up	7.2	-17.8	32.2	0.572
Early Combination vs Step Up	19.1	4.5	33.6	0.011
Biologic First vs Early Combination	-11.8	-38.0	14.3	0.375

*B. Between-group differences in cJADAS10 Inactive Disease (ID) (≤2.5): estimates from PS-weighted model with adjustment**

	Difference in ID	Lower 95%	Upper 95%	P-value
Biologic First vs Step Up	-2.1	-27.6	23.5	0.875
Early Combination vs Step Up	10.0	-5.9	25.8	0.219
Biologic First vs Early Combination	-12.0	-38.6	14.6	0.376

*C. Between-group differences in ACR70: estimates from PS-weighted model with adjustment**

	Difference in ACR70	Lower 95%	Upper 95%	P-value
Biologic First vs Step Up	-3.8	-28.6	21.0	0.765
Early Combination vs Step Up	9.1	-3.8	22.1	0.169
Biologic First vs Early Combination	-12.9	-38.7	12.9	0.328

* Adjusted for severity factors

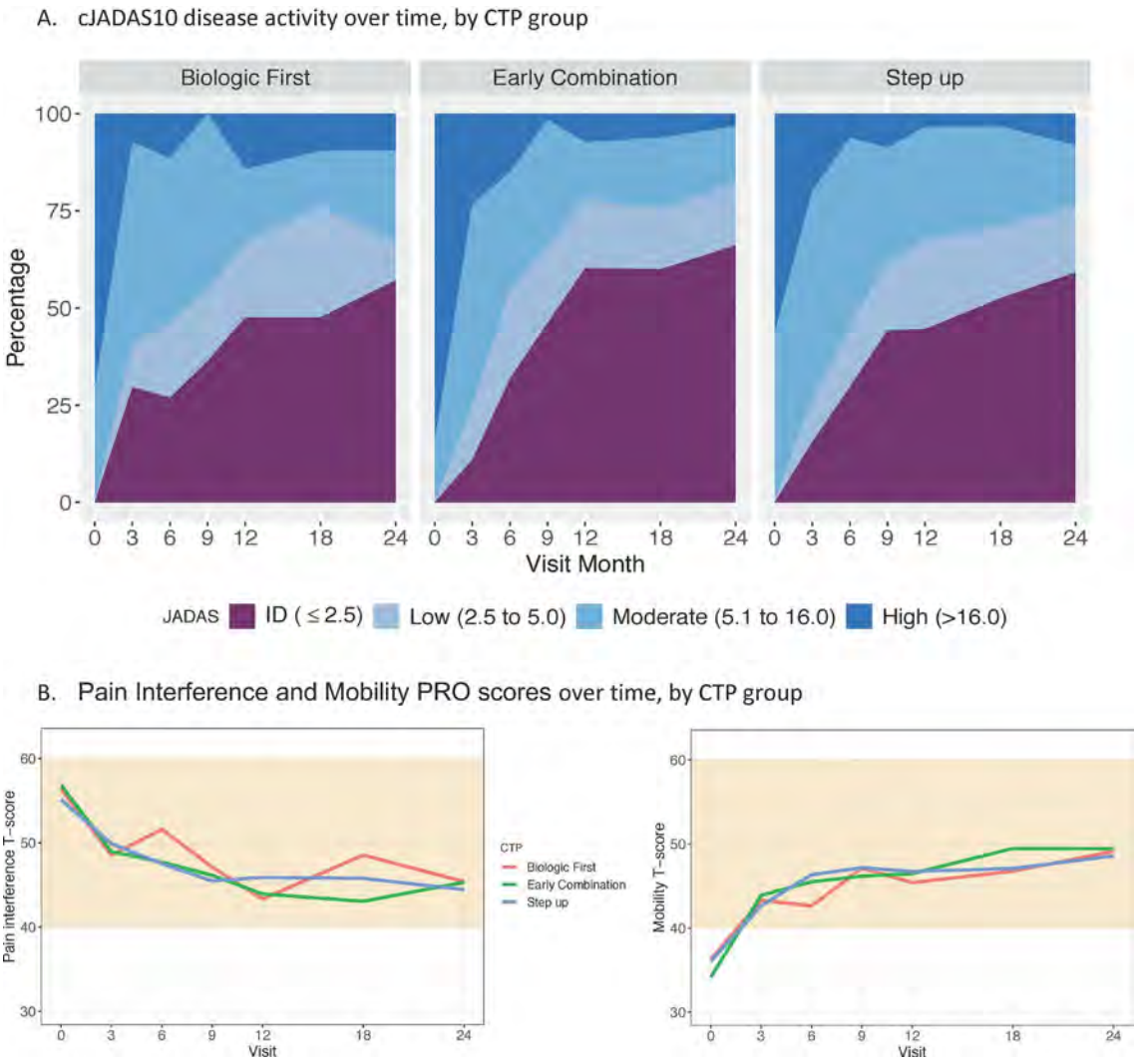

Figure 1. cJADAS10 and PRO measures over time.

pACR70 in SU: 47% vs 74%; EC: 59% vs 83%; BF: 44% vs 74%. Figure 1A shows the proportions of each group's JADAS activity over the 24 months. All groups also showed improvement in PROMIS® pain interference or mobility measures from baseline (Figure 1B). Seventeen SAEs were reported, most commonly infections.

Conclusion: While there was a significant difference in CID favoring Early Combination versus Step Up at 24 months, there were no significant differences between CTPs for other study outcomes. All groups did continue to improve in cJADAS10 and PRO measures. Additional analyses will include comparison of remission on medications (CID for 12 months) and patients ever achieving CID between CTPs.

Disclosure: Y. Kimura, Genentech, 5, UpToDate, 9, CARRA, 4, 12, Salary support; **S. Ringold**, UpToDate, 9, CARRA, 4, 5, BMS, 12, co-PI on PCORI funded study for which BMS is supplying abatacept; **G. Tomlinson**, None; **L. Schanberg**, UCB, 12, DSMB member, Sanofi, 12, DSMB member, SOBI, 2, BMS, 5; **A. Dennos**, None; **M. Riordan**, None; **V. Del Gaizo**, CARRA, 3; **K. Murphy**, None; **P. Weiss**, Lilly, 1, 2, Pfizer, 1, 2, Biogen, 2; **B. Feldman**, Pfizer, 12, DSMB member, AB2 Bio, 12, DSMB member; **M. Natter**, None; **T. CARRA Registry Investigators**, None.

Abstract Number: 0961

Proteomic Profiling of MIS-C Patients Reveals Heterogeneity Relating to Interferon Gamma Dysregulation and Vascular Endothelial Dysfunction

Caroline Diorio[1], Rawan Shraim[1], Laura Vella[1], Josephine Giles[2], Amy Baxter[2], Derek Oldridge[2], Scott Canna[1], Sarah Henrickson[1], Kevin Mcnerney[1], Frances Balamuth[1], Chakkapong Burudpakdee[1], Jessica Lee[1], Tomas Leng[1], Alvin Farrell[1], Michele Lambert[1], Kathleen Sullivan[1], John Wherry[3], David Teachey[1], Hamid Bassiri[1] and **Edward Behrens**[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]UPenn, Philadelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Plenary II (0956–0961)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: Multi-system Inflammatory Syndrome in Children (MIS-C) is a major complication of the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) pandemic in pediatric patients. Children with MIS-C present with varying degrees of cardiovascular and hyperinflammatory symptoms. We performed a comprehensive analysis of the plasma proteome of more than 1400 proteins in children with SARS-CoV-2. We hypothesized that the proteome would reflect heterogeneity in hyperinflammation and vascular injury, and further identify pathogenic mediators of disease.

Methods: Between April 2020 and October 2020, we enrolled 63 hospitalized patients with MIS-C (N=22), Severe COVID-19 ("Severe", N=15)) or asymptomatic or mild SARS-CoV-2 infection ("Minimal", N=26). In addition, we included remnant plasma samples from otherwise healthy patients ("Healthy", N=25). We utilized the Olink Explore 1536/384 protein biomarker platform to interrogate the plasma proteome of all 88 patients. All statistical analyses were performed in RStudio (RStudio, PBC, Boston, MA).57 Data were assumed to be non-parametric unless normality was demonstrated.

Results: To understand how the overall proteome of patients with MIS-C changes over time, we first created a PCA mapping all proteins and all patients. We then PCA transformed data for convalescent samples on that space. Convalescent samples shifted towards the healthy controls, implying that following treatment, the proteome in MIS-C patients returns towards a baseline state. We examined CXCL9 as the key protein associated with IFNg response and

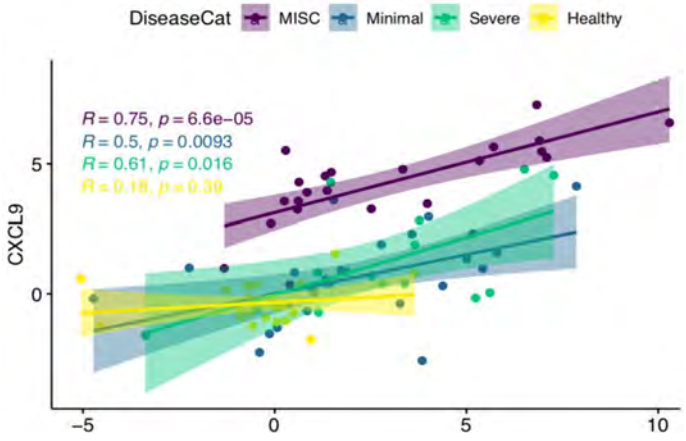

Figure 1. MISC patients are hyperresponsive to IFNg. Compared to all other groups, MISC patients make increased amounts of the IFNg responsive protein CXCL9 relative to their serum levels of IFNg.

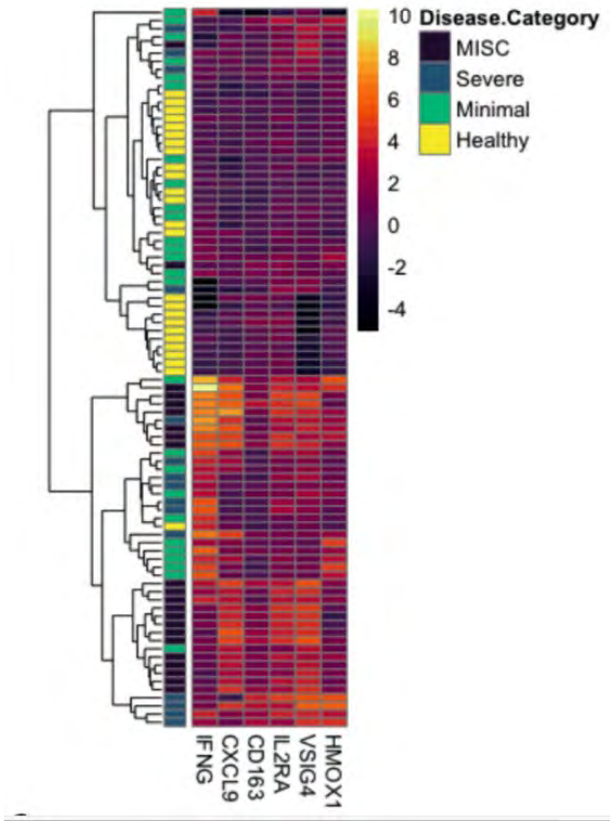

Figure 2. Clustering of patients based on MAS protein biomarkers. A panel of 6 protein biomarkers that are elevated in MAS cluster MISC patients away from healthy controls, asymptomatic SARS-CoV-2 infected patients, and severe COVID19 patients. There are two MAS/MISC clusters, one with an IFNg high signature, and one with an IFNg low signature.

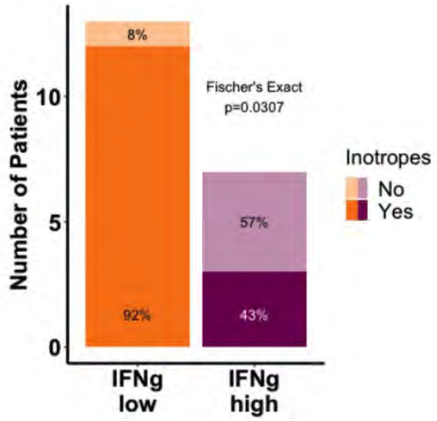

Figure 3. MISC patients with higher levels of IFNg are protected from inotrope requirement.

found that all patients with SARS-CoV-2 infection showed a positive CXCL9 response to increasing IFNg. Strikingly, MIS-C patients had a disproportionately high CXCL9 response to IFNg compared to the other groups. Consistent with a derepression of IFNg signaling, MIS-C patients expressed less TRIM21 compared to healthy controls. Unsupervised hierarchical clustering revealed two distinct groups of MIS-C patients that had elevations in multiple Macrophage Activation Syndrome (MAS) markers. These two clusters primarily differed by their IFNg expression with an IFNg-high versus IFNg-low group evident. Hierarchical clustering identified that SC5B9 correlated most highly with PLA2G2A, PDGFC, SELE, CALCA, NOS3, VWA1 and TYMP, demonstrating a signature consistent with thrombotic

microangiopathy (TMA). Patients with elevations in MAS or TMA markers were more likely to meet clinical criteria for MAS or TMA respectively. Interestingly, MISC patients with an Interferon gamma low signature were at higher risk of requiring inotropes.

Conclusion: We used proteomic analysis to begin to unravel the complex and heterogeneous pathophysiology associated with MIS-C. We identify PLA2G2A as a candidate biomarker for MIS-C and show that PLA2G2A is associated with clinical features of TMA. We demonstrate that MIS-C patients are characterized by a disproportionately high CXCL9 response to IFNg, implying a dysregulated response to IFNg. Patients with MIS-C showed heterogeneity based on IFNg expression, and surprisingly, patients with higher IFNg levels were less likely to require inotropes.

Disclosure: C. Diorio, None; **R. Shraim**, None; **L. Vella**, None; **J. Giles**, None; **A. Baxter**, None; **D. Oldridge**, None; **S. Canna**, Simcha Therapeutics, 2, Novartis, 5, AB2Bio, Ltd, 5, IMMvention Therapeutix, 5; **S. Henrickson**, None; **K. Mcnerney**, None; **F. Balamuth**, None; **C. Burudpakdee**, None; **J. Lee**, None; **T. Leng**, None; **A. Farrell**, None; **M. Lambert**, None; **K. Sullivan**, None; **J. Wherry**, Merck, 1, 2, Elstar, 1, 2, Janssen, 1, 2, Related Sciences, 1, 2, Synthekine, 1, 2, Surface Oncology, 1, 2, 8, Arsenal Biosciences, 8, Roche/Genentech, 10; **D. Teachey**, Janssen, 1, Amgen, 1, Sobi, 1, Humanigen, 1, La Roche, 1; **H. Bassiri**, CSL Behring, 11; **E. Behrens**, None.

Abstract Number: 0962

Association of Antiphospholipid Antibodies with Thromboembolic Events and Severe Outcomes in COVID-19

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Infection-related Rheumatic Disease (0962–0965)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Although several studies indicate that patients with COVID-19 produce antiphospholipid antibodies (aPL), it is unclear which aPL subtype predominates and whether aPL correlates with thrombosis or severe COVID-19 outcomes. We tested aPL in a large prospective cohort of patients with and without COVID-19, and determined if aPL are associated with thromboembolic events and other severe outcomes in hospitalized COVID-19 patients.

Methods: Symptomatic patients undergoing SARS-CoV-2 nasopharyngeal PCR testing at a Canadian tertiary centre were enrolled in a prospective biobank cohort from March-July 2020. All PCR results (including those performed at other centres), demographics, medical history, hospitalization details and clinical outcomes were collected with a standard report form. Subjects were classified as COVID+ (≥1 positive PCR prior/at baseline) or non-COVID (all PCR negative prior/after enrolment). Biobanked plasma (day 0-7 after enrolment) was tested for anticardiolipin (aCL) IgM and IgG, anti-domain I of ß2-glycoprotein I (aD1ß2GP1) IgM and IgG, anti-phosphatidylserine/prothrombin (aPS/PT) IgM and IgG (Inova Diagnostics, San Diego), as well as lupus anticoagulant (LAC; Precision BioLogic, Halifax) using manufacturers' cut-offs. All plasma was also tested for SARS-CoV-2 IgM and IgG. We compared aPL prevalence (including subtypes) between COVID+ and non-COVID subjects. In hospitalized COVID+ subjects, we performed multivariate logistic regressions evaluating aPL (and subtypes) and thrombotic events (deep vein thrombosis, DVT, pulmonary embolism, PE, stroke, transient ischemic attack, TIA, myocardial infarction, MI), as well as acute kidney injury (AKI), intensive care unit (ICU) stay, mechanical ventilation, and death, adjusting for age and sex.

Table 1. Characteristics and aPL status of COVID+ and non-COVID subjects (n=656)

Characteristic	COVID + subjects n=291	Non-COVID subjects n=365
Age in years, mean (SD)	67 (18)	64 (20)
Female sex, n (%)	151 (52)	183 (50)
Hospital admission, n (%)	241 (83)	224 (61)
Prospective follow-up, mean days (SD)	70 (48)	60 (51)
Positive SARS-CoV-2 serologies IgM and/or IgG[1], n (%)	201/288 (70)	11/362 (3)
Antiphospholipid status, n (%)		
Any aPL	123/289 (43)	116/361 (32)
aCL IgM	74/289 (26)	36/361 (10)
aCL IgG	37/289 (13)	36/361 (10)
aD1 β2GP1 IgM	18/289 (6)	20/359 (6)
aD1 β2GP1 IgG	2/289 (1)	3/359 (1)
aPS/PT IgM	24/284 (8)	22/352 (6)
aPS/PT IgG	17/284 (6)	18/352 (5)
LAC	9/214 (4)	12/274 (4)

Abbreviations : aPL, antiphospholipid antibody; aCL, anticardiolipin, aD1β2GP1, anti-domain-1 of β2-glycoprotein-1; aPS/PT, anti-phosphatidylserine/prothrombin; LAC, lupus anticoagulant
[1]SARS-CoV-2 serologies were performed by Luminex xMAP SARS-CoV2 multi-antigen (IgG) and DiaSource COVID ELISA (IgM and IgG), with cutoffs according to manufacturers' recommendations

Table 2. Outcomes in hospitalized COVID+ subjects according to aPL status (n=241)

aPL subtypes	Venous thrombosis[1] n (%)	Arterial thrombosis[2] n (%)	AKI n (%)	ICU n (%)	Mechanical ventilation n (%)	Hospital death n (%)	Any death n (%)
Any aPL							
(+) n=112	11 (10)	5 (4)	53 (47)	33 (29)	28 (25)	20 (18)	24 (21)
(-) n=129	10 (8)	7 (5)	38 (29)	33 (26)	17 (13)	14 (11)	17 (13)
aCL IgM							
(+) n=66	8 (12)	4 (5)	30 (46)	22 (33)	19 (29)	12 (18)	14 (21)
(-) n=175	13 (7)	9 (5)	11 (35)	44 (25)	26 (15)	22 (13)	27 (15)
aCL IgG							
(+) n=32	6 (19)	2 (6)	17 (53)	14 (44)	11 (34)	6 (19)	7 (22)
(-) n=209	15 (7)	10 (5)	74 (35)	52 (25)	34 (16)	28 (13)	34 (16)
aD1 β2GP1 IgM							
(+) n=17	0 (0)	0 (0)	9 (53)	5 (29)	4 (24)	2 (12)	2 (12)
(-) n=224	21 (9)	12 (5)	82 (37)	61 (27)	41 (18)	32 (14)	39 (17)
aD1 β2GP1 IgG							
(+) n=2	0 (0)	0 (0)	2 (100)	0 (0)	0 (0)	2 (100)	2 (100)
(-) n=239	21 (9)	12 (5)	89 (37)	66 (28)	45 (19)	32 (13)	39 (16)
aPS/PT IgM							
(+) n=21	1 (5)	1 (5)	9 (43)	4 (19)	3 (14)	5 (24)	6 (29)
(-) n=217	20 (9)	11 (5)	81 (37)	60 (28)	42 (19)	28 (13)	34 (16)
aPS/PT IgG							
(+) n=15	0 (0)	0 (0)	7 (47)	3 (20)	3 (20)	0 (0)	0 (0)
(-) n=223	21 (9)	12 (5)	83 (37)	61 (27)	42 (19)	33 (15)	40 (18)
LAC							
(+) n=8	0 (0)	0 (0)	3 (38)	1 (13)	0 (0)	1 (13)	1 (13)
(-) n=171	16 (9)	10 (6)	69 (40)	54 (32)	42 (25)	24 (14)	31 (18)

Abbreviations : AKI, acute kidney injury ; ICU, intensive care unit ; aPL, antiphospholipid antibody; aCL, anticardiolipin, aD1 β2GP1, anti-domain-1 of β2-glycoprotein-1; aPS/PT, anti-phosphatidylserine/prothrombin; LAC, lupus anticoagulant
[1] venous thrombosis : deep vein thrombosis or pulmonary embolism
[2] arterial thrombosis : any of stroke, transient ischemic attack, myocardial infarction

Table 3 Association of aPL with thromboembolic events and severe outcomes among hospitalized patients with COVID-19 (n= 241)

	Adjusted Odds ratio (95% CI) for outcomes of interest						
	Any thrombo-embolic event	AKI	ICU	Mechanical ventilation	Hospital death	Any death	ICU stay or hospital death
Any aPL+	1.2 (0.5-2.5)	**1.9 (1.1-3.3) ***	**1.8 (1.0-3.5)***	**3.7 (1.7-7.8) ***	1.3 (0.6-2.9)	1.3 (0.6-2.8)	**1.9 (1.1-3.4) ***
aCL IgM+	1.2 (0.5-2.8)	1.4 (0.8-2.6)	**2.0 (1.0-3.9) ***	**3.1 (1.5-6.4) ***	1.3 (0.6-3.0)	1.3 (0.6-2.7)	1.8 (1.0-3.3)
aCL IgG+	2.3 (0.9-6.0)	2.0 (0.9-4.2)	**3.0 (1.3-6.8) ***	**3.1 (1.3-7.4) ***	1.3 (0.5-3.6)	1.2 (0.5-3.3)	**2.8 (1.3-6.2) ***
aD1b2GP1 IgM+	-[3]	2.1 (0.7-5.7)	1.2 (0.4-3.7)	1.5 (0.5-5.0)	0.8 (0.2-4.0)	0.6 (0.1-3.1)	1.0 (0.4-2.9)
aPS/PT IgM+	0.8 (0.2-3.6)	1.0 (0.4-2.6)	0.7 (0.2-2.4)	0.8 (0.2-2.8)	1.3 (0.4-4.1)	1.4 (0.5-4.2)	0.9 (0.3-2.4)
aPS/PT IgG+	-	1.4 (0.5-4.2)	0.7 (0.2-2.9)	1.2 (0.3-4.8)	-	-	0.5 (0.1-1.7)
LAC+	-	0.7 (0.2-3.3)	0.3 (0.0-3.0)	-	0.4 (0.0-4.4)	0.3 (0.0-2.8)	0.5 (0.1-2.8)

Abbreviations : AKI, acute kidney injury; ICU, intensive care unit ; aPL, antiphospholipid antibody; aCL, anticardiolipin, aD1 β2GP1, anti-domain-1 of β2-glycoprotein-1; aPS/PT, anti-phosphatidylserine/prothrombin; LAC, lupus anticoagulant

[1] each OR adjusted for age and sex

[2] analysis not performed for aD1 β2GP1 IgG+ due to too few subjects

[3] multivariate analyses for some outcomes could not be performed since no event occurred in those positive for the aPL subtype

Results: We studied 291 COVID+ and 365 non-COVID patients. The two groups were similar in age and sex, but more COVID+ patients were hospitalized (83% vs 61%) and had positive SARS-CoV-2 serology (70% vs 3%) vs non-COVID patients (Table 1). At baseline, 43% of COVID+ patients were positive for at least one aPL versus 32% of non-COVID patients (difference in proportion 11%; 95% CI 3, 18). In hospitalized COVID+ patients, 13% had a thromboembolic event, 38% developed AKI, 27% had an ICU stay, 19% had mechanical ventilation, and 17% died. In multivariate analyses, presence of any aPL was associated with AKI (OR 1.9; 95% CI 1.1, 3.3), ICU stay (OR 1.8; 95% CI 1.0, 3.5) and mechanical ventilation (OR 3.7; 95% CI 1.7, 7.8). Both aCL IgM and aCL IgG were strongly and independently associated with ICU stay and mechanical ventilation (Table 3). We saw a strong trend for more thrombotic events associated with aCL IgG (OR 2.3; 95% CI 0.9, 6.0), though the CI included the null value.

Conclusion: In this large prospective sample, over 40% of COVID-19 patients had aPL early in their clinical course. In hospitalized COVID-19 patients, aPL were associated with substantial increased risk of severe outcomes, with a strong trend for association between aCL IgG and thrombotic events. Our findings suggest that aPL, in particular aCL, might be useful markers for risk stratification in COVID-19.

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Abstract Number: 0963

Immunogenicity of COVID-19 Vaccines in Patients with Autoimmune and Inflammatory Rheumatic Diseases (AIIRDs)

Gordon Lam[1], Andrew Laster[2], Sarah McCarter[2], Heather Gladue[3], Ahmad Kashif[2], Erin Siceloff[2], Victoria Lackey[3], Cheryl Robertson[3], Ashley Toci[2] and Leonard Calabrese[4], [1]Arthritis and Osteoporosis Consultants of the Carolinas, Cornelius, NC, [2]Arthritis and Osteoporosis Consultants of the Carolinas, Charlotte, NC, [3]Arthritis & Osteoporosis Consultants of the Carolinas, Charlotte, NC, [4]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Infection-related Rheumatic Disease (0962–0965)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: AIIRD patients may have a blunted immune response to the COVID-19 vaccines, but this is largely uncharacterized as these individuals were not included in clinical trials. Vaccine response may be affected by patients' underlying disease processes and the systemic immunomodulatory therapies used to treat them, although the evidence for this is uncertain. To better understand the immunogenicity of the COVID-19 vaccines in this patient population and their treatment regimens, we quantified humoral responses to the SARS-CoV-2 spike protein in AIIRD patients.

Methods: This exploratory, descriptive, prospective cohort study enrolled patients from a single-specialty practice in Charlotte, NC who received the BNT162b2 (Pfizer), mRNA-1273 (Moderna) or Ad26COV2.S (Johnson & Johnson) vaccine from 3/17/21-5/14/21. Those with prior COVID-19 by self-report were excluded. We collected demographics, AIIRD diagnoses and immunomodulatory regimens of these patients. Antibody (Ab) testing was performed at least 14 days after completion of their vaccine series. SARS-CoV-2 IgG Ab levels to the S1 spike antigen RBD were measured using a semi-quantitative assay (Siemens Atellica; Quest). Associations between clinical characteristics and Ab responses were evaluated.

Results: Characteristics of 291 AIIRD patients studied are listed in Table 1. Overall, 71% developed an Ab response with a mean Ab titer of 12.72 (< 1 index). There was no difference based on gender. The likelihood of an absent Ab response increased with age, and there was a decline in mean levels with aging in Ab+ patients.

Treatment associations are listed in Table 2. Patients receiving rituximab were less likely to develop an Ab response (13%) and had a lower mean Ab titer (7.55) compared to the overall cohort. Dosing appeared to affect response rates with a single dose (1000 mg) Ab+ rate of 38% compared to a paired dose (1000 mg x2) rate of 7% (Table 3). Patients receiving abatacept IV were also less likely to develop an Ab response (45%). Detectable antibodies were seen in nearly all patients on JAKi (91%), belimumab (86%), TNFi (82%), IL-17i (80%), IL-6i (78%), IL-23i (100%) and IL-12/23i (100%).

Without concomitant targeted therapy, Ab+ rates with mycophenolate (75%) and MTX (80%) were decreased compared to sulfasalazine (100%), leflunomide (100%) and azathioprine (89%). 82% of patients receiving prednisone without biologics were Ab+ (average daily dose ≤10 mg). Overall dose effect is shown in Table 3.

Table 1. Demographics and Clinical Characteristics of Patients with Autoimmune and Inflammatory Rheumatic Disease patients

Gender				
	N	Ab (-)	Ab (+)	Mean Ab+ titer
Female	217 (75%)	63 (29%)	154 (71%)	12.82
Male	74 (25%)	20 (27%)	54 (73%)	12.45
Total	291	83 (29%)	208 (71%)	12.72
Age (mean 64.3 years)				
Age Category	N	Ab (-)	Ab (+)	Mean Ab+ titer
20-29	5 (1.7 %)	0 (0%)	5 (100%)	14.37
30-39	10 (3.4%)	1 (10%)	9 (90%)	17.20
40-49	32 (11%)	6 (19%)	26 (81)	16.93
50-59	44 (15.1%)	8 (18%)	36 (82%)	12.73
60-69	77 (26.5 %)	24 (31%)	53 (69%)	13.13
70-79	95 (32.6 %)	35 (37%)	60 (63%)	10.86
80-89	26 (8.9%)	8 (31%)	18 (69%)	8.52
90-99	2 (0.7%)	1 (50%)	1 (50%)	10.00
Race				
	N	Ab (-)	Ab (+)	Mean Ab+ titer
CAUCASIAN	252 (86.6%)	75 (30%)	177 (70%)	12.80
Black or African American	29 (10.0%)	7 (24%)	22 (76%)	13.22
Asian or Pacific Islander	2 (0.7%)	0	2	6.78
AMERICAN INDIAN/ALASKAN NATIVE	1 (0.3%)	1	0	N/A
Hispanic	3 (1.0%)	0	3	10.22
Multiracial	2 (0.7%)	0	2	5.59
Not Reported	2 (0.7%)	0	2	16.91

Diagnosis				
Diagnosis	N	Ab (-)	Ab (+)	Mean Ab+ titer
Rheumatoid Arthritis	185 (64%)	58 (31%)	127 (69%)	12.33
SLE	34 (12%)	6 (18%)	28 (82%)	13.09
Psoriatic Arthritis	28 (10%)	6 (25%)	22 (75%)	14.47
Sjogren's	11 (4%)	5 (45%)	6 (55%)	14.87
Axial Spondyloarthritis	7 (2%)	0	7	15.55
IBD (Crohn's/UC)	8 (3%)	3 (38%)	5 (63%)	14.15
UCTD	6 (2%)	1 (17%)	5 (83%)	10.67
GPA	5 (2%)	3 (60%)	2 (40%)	20.00
Sarcoid	4 (1%)	1 (25%)	3 (75%)	0.00
Dermatomyositis/Polymyositis	5 (2%)	2 (40%)	3 (60%)	12.44
Inflammatory Arthritis	3 (1%)	0	3	20.00
PSS	1 (0.3%)	0	1	1.57
Stills	1 (0.3%)	0	1	11.87
Uveitis	1 (0.3%)	1	0	0.00
Bechet's	1 (0.3%)	0	1	20.00
Alopecia	1 (0.3%)	0	1	12.08
Atopic Dermatitis	1 (0.3%)	0	1	20.00
MG	1 (0.3%)	0	1	8.00
Susac Syndrome	1 (0.3%)	1	0	0

Vaccine Type				
	N	Ab (-)	Ab (+)	Mean Ab+ titer
Pfizer	206 (71%)	66 (32%)	140 (68%)	11.74
Moderna	74 (25%)	9 (12%)	65 (88%)	15.49
J&J	11 (4%)	8 (73%)	3 (27%)	1.9
Total	291	86 (29%)	208 (71%)	
No patients have had self-reported COVID infection post SARS CoV2 Vaccine				

Table 2. Patient immunomodulatory therapies and vaccine responses. IgG antibodies to SARS CoV-2 S1 RBD antigen were measured using a semi-quantitative chemiluminescent immunoassay (Siemens Atelllica IM/Siemens Atellica IM Analyzer; QUEST) in which negative/nonreactive was <1.0, and positive/reactive was reported from 1.00 to 20.00 or > 20.00. https://www.siemens-healthineers.com/en-us/laboratory-diagnostics/assays-by-diseases-conditions/infectious-disease-assays/sars-cov-2-igg-assay

Drug	N (%)	Ab – (%)	Ab + (%)	P value	Mean Ab+ titer	Mean mg dose AB (-)	Mean mg dose Ab (+)	Mean mg dose (ALL)
Rituximab	38 (13%)	33 (87%)	5 (13%)	<0.001	7.55			
Single dose:	8	5 (62.5%)	3 (37.5%)		3.22			
Double dose:	30	28 (93%)	2 (7%)		5.66			
Abatacept	27 (9%)	13 (48%)	14 (52%)	0.02	12.15			
IV	20	11 (55%)	9 (45%)		11.11	931.82	805.56	875.0
SC	7	2 (29%)	5 (71%)		14.01			
Mycophenolate	16 (5%)	6 (38%)	10 (63%)	0.40	12.80	1370	1238	1287.5
monotherapy	4	1 (25%)	3 (75%)		5.8			
+ biologics	4	2 (50%)	2 (50%)		5.4			
+ csDMARD	8	2 (25%)	6 (75%)		20.00			
Belimumab	14 (5%)	2 (14%)	12(86%)		10.32			
IV	9	1 (11%)	8 (89%)		7.96			
SC	5	1 (20%)	4 (80%)		12.69			
Methotrexate	110 (38%)	27 (25%)	83 (75%)	0.28	11.59	18.70	17.08	17.5
no biologic	51	10 (20%)	41 (80%)		11.21			
JAK Inhibitors	23 (8%)	2 (9%)	21 (91%)	0.03	10.68			
Tofacitinib	20	1 (5%)	19 (95%)		15.70			
Upadacitinib	3	1 (33%)	2 (67%)		5.66			
Baricitinib	0	0	0		0.00			
Prednisone	77 (26%)	29 (38%)	48 (62%)	0.05	12.36	6.37	5.39	5.7
no biologic	28	5 (18%)	23 (82%)		12.66			
TNF Inhibitors	57 (20%)	10 (18%)	47 (82%)	0.39	11.47			
Infliximab	17	4 (24%)	13 (76%)		12.07			
Etanercept	10	5 (50%)	5 (50%)		13.31			
Adalimumab	12	0	12		13.43			
Golimumab	13	2 (15%)	11(85%)		7.32			
Certolizumab	4	0	4		11.22			
IL-6 Inhibitors	9 (3%)	2 (22%)	7 (78%)		10.35			
Tocilizumab	9	2 (22%)	7 (78%)		10.35			
Sarilumab	0	N/A	N/A		N/A			
IL-17 Inhibitors	5 (2%)	1 (20%)	4 (80%)		18.11			
Secukinumab	4	1 (25%)	3 (75%)		16.22			
Ixekizumab	1	0			20.00			
IL-23 Inhibitors	2(1%)	0	2		20.00			
Guselkumab	2	0	2		20.00			
Risankizumab	0	N/A	N/A		N/A			
Ustekinumab	2 (1%)	0	2		0.00			
Apremilast	1 (0.3%)	0	1		20.00			
Anakinra	1 (0.3%)	0	1		20.00			
Vedolizumab	1 (0.3%)	1	0		0.00			
HCQ	61 (21%)	21 (34%)	40 (66%)		15.28			
no biologic	31	8 (26%)	23 (74%)		16.39			
Leflunomide	23 (8%)	8 (35%)	15 (65%)		11.54			
no biologic	8	0 (0%)	8 (100%)		11.84			
Sulfasalazine	5 (2%)	0 (0%)	5 (100%)		17.26			
no biologic	3	0 (0%)	3 (100%)		20.00			
Azathioprine	11 (4%)	1 (9%)	10 (91%)		13.22			
no biologic	9	1 (11%)	9 (89%)		11.53			

Table 3. Dose effects of rituximab and prednisone on vaccine responses in AIIRD patients

Rituximab				
	N	**Ab (-)**	**Ab (+)**	**Mean Ab titer**
Total	38	33 (87%)	5 (13%)	7.55
Mean days last RTX infusion to first vaccine dose	79.95 days	79.4 days	83.8 days	
Single dose (1000mg)	8 (21%)	5 (62.5%)	3 (37.5%)	3.22
monotherapy	5	3(60%)	2 (40%)	3.22
combination therapy	3	2 (67%)	1 (33%)	20.00
Paired dose (1000mg x 2 @2 wks)	30 (79%)	28 (93%)	2 (7%)	5.66
monotherapy	11	11(100%)	0 (0%)	0
combination therapy	19	17 (89%)	2 (11%)	5.66
Prednisone (all patients)				
Average Daily Dose (mg)	**N**	**AB (-)**	**AB (+)**	**Mean Ab titer**
≤ 5 mg	61	**21 (34%)**	40 (66%)	**12.52**
6-10 mg	12	**5 (42%)**	7 (58%)	**10.38**
11-15 mg	2	2	0	0.00
16-20 mg	1	1	0	0.00
>20 mg	1	0	1	20.00

Conclusion: A majority (71%) of AIIRD patients developed detectable anti-SARS-CoV-2 RBD Abs. Ab response rates and titers were age dependent. Patients receiving rituximab and abatacept IV were less likely to develop an Ab response with the former having a dose effect. Among csDMARDs, response rates were decreased in patients receiving MTX and mycophenolate. Low dose prednisone without biologics did not appear to influence Ab+ rates. Limitations of this study include its single center, non-randomized design and lack of residual confounder measures. Additional measures of humoral immune response and T cell function are also needed. However, this real-world study may provide further guidance for COVID-19 vaccination in patients with AIIRDs on immunomodulatory drugs.

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Abstract Number: 0964

Rituximab Treatment Dramatically Reduces Neutralizing Humoral Response to mRNA SARS-COV-2 Vaccines in Patients with Autoimmune Diseases

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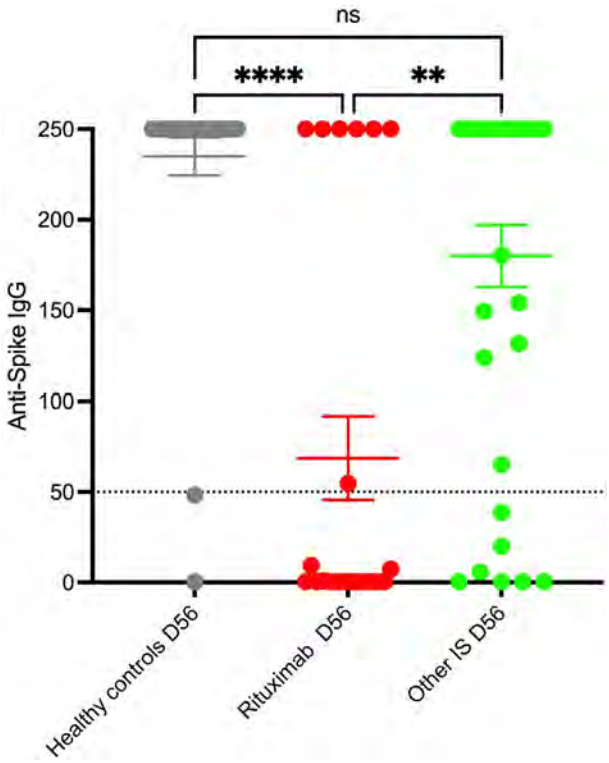
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Infection-related Rheumatic Disease (0962–0965)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: The global COVID-19 pandemic is starting to be controlled by massive vaccination. Some immunosuppressed patients have already paid a high price to the pandemic with increased risk of death in cancer patients and in autoimmune diseases patients treated with rituximab (hazard ratio of death: 4,04 (2,32-7,03). Despite the tremendous efficacy of novel mRNA vaccines, some immunocompromised patients seem not to respond at the same level compared to healthy controls to these vaccines when anti-spike antibodies are considered.

Objectives: To compare autoimmune diseases patients treated with either rituximab (RTX) or other immunosuppressants (other IS) and controls regarding response to mRNA vaccines.

Methods: Patients and healthy controls (HC) were vaccinated with BNT162b2 at days 0 and 28 and sampled at days 28 and 56. Patients with detectable levels of anti-nucleocapsid at any time points were excluded. Patients were divided into 2 groups: “RTX group” if they had received RTX ≤1 year, or “other IS group” if they were treated with other immunosuppressants. Serological assessment of vaccine response (ECLIA Cobas, Roche) and neutralization (iFlash-2019-nCoV Nab assay, Ylho) was performed. According to preliminary data, a threshold ≥ 50 of anti-Spike IgG was defined as a response to vaccine (since it is the value were patients had detectable neutralizing antibodies in the neutralization test). T-cell response against spike peptides using intra-cellular staining of TNF, IFNg, IL6, granzyme and perforine on activated CD4 and CD8 T cells will also be analyzed in all patients and will be presented at the time of the ACR meeting.

Results: 28 HC and 57 patients with autoimmune diseases were included: 24 patients in rituximab group and 33 in other IS group. On day 28, HC had significantly higher median levels of anti-Spike IgG (46.7 IQR 146) compared to



RTX and other Is : 0.4 IQR 3.8 and 4.5 IQR 20.5 respectively. At day 56, compared to both control (250 IQR 0) and other IS groups (250 IQR 141), the RTX (0.4 IQR 250) group had significantly lower median levels of anti-spike IgG (see figure). The RTX group also had a lower response rate : 29,2% in RTX group vs.79.4% in other IS group and 92,2% in HC There was no difference in anti-Spike IgG levels or percentage of response between the HC and other IS group. Within the RTX group, the median time to last RTX infusion was significantly lower in the non-responders (81 days IQR 147) compared to responders (231 days IQR 89). None of the patients having received RTX in the previous 6 months responded to the vaccine.

Conclusion: In patients with autoimmune disorders treated with immunosuppressors, responses after 1 dose of mRNA COVID vaccine were lower to that of HC. However, assessed one month after the second dose responses remained significantly impaired only in RTX treated patients (lower response rate and IgG anti-spike levels), but not in patients with patients treated with other IS. In RTX treated patients, the main factor associated with lack of response was time since last infusion. Given the low frequency of patients on RTX having a humoral response, it will be key to assess if these patients will have or not a cellular response. Data will be presented at the congress.

Disclosure: S. Bitoun, None; **J. Henry**, None; **C. Vauloup Fellous**, Roche Diagnostics, 2, Abbott Diagnostics, 2, DiaSorin, 2; **R. Seror**, None; **L. Mouna**, None; **C. Joly**, None; **D. Desjardins**, None; **M. Bitu**, None; **R. Le Grand**, None; **A. Roque Afonso**, None; **X. Mariette**, GlaxoSmithKline, 2, BMS, 2, Servier, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 0965

Anti-TNF Usage in Patients with HIV Infection 2003-2021: Long Term Safety and Followup

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Infection-related Rheumatic Disease (0962–0965)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: There are concerns about using immunosuppressive agents for treatment of rheumatic diseases in patients with HIV infection due to concerns of opportunistic infection. We previously reported a series of eight HIV positive patients primarily seen at a County Outpatient Rheumatology Clinic treated with anti-TNF agents between 2003 and 2008 (Cepeda et al, Ann Rheum Dis 67: 710-12, 2008). The purpose of this study is to report the safety and efficacy of anti-TNF agents in these patients over time to the present and to update our experience with biologic agents in this setting in additional patients.

Methods: All but three of the patients were seen at the Harris County HIV Outpatient Clinic. At baseline visit, sociodemographic characteristics, CD4 counts, HIV viral load and medications were collected. Patients with rheumatoid arthritis or spondyloarthritis were initially treated with NSAIDs and nonbiologic disease modifying antirheumatic drugs(DMARDs) (methotrexate, sulfasalazine) and intra-articular/intralesional corticosteroids. Those patients with persistent disease activity despite conservative therapy were begun on anti-TNF agents, provided CD4 counts were

Table 1. Clinical, Sociodemographic and Current Status of Initial Seven HIV Patients Treated with Anti-TNF Agents 2003-2006

Patient Number	1	2	3	4	5	6	7*
Age at First Visit	48	31	49	44	39	47	52
Gender	Male	Male	Female	Female	Male	Female	Male
Ethnicity	White	Black	Black	Black	Black	Black	White
Rheumatic Status	Rheumatoid Arthritis	Reactive Arthritis	Peripheral SpA	Rheumatoid Arthritis	Psoriatic Arthritis	Psoriatic Arthritis	Psoriatic Arthritis
Anti-TNF Agent Usage Status	Currently taking	Not taking	Not taking	Not taking	Not taking	Switched to Ustekinumab	Lost to Follow Up
Taking HAART	Yes	No	Yes	No	No	Yes	Yes
Baseline CD4 (cells/μL)	631	745	373	1300	970	365	268
Baseline Viral (copies/mL)	Undetectable	Undetectable	Undetectable	Undetectable	27829	15667	Undetectable
Duration of anti-TNF Treatment	2003-2011, 2016-Present	2003-2005	2003-2017	2004-2005	2004-2007	2006-Present	2003-2007
Still Followed	Current Patient	Last Visit 2015	Current Patient	Current Patient	Last Visit 2018	Current Patient	Last Seen 2015
Lowest CD4 on Anti-TNF Treatment (cells/μL)	357	923	580	1082	750	382	240
Highest Viral Load on Anti-TNF Treatment (copies/mL)	103	Undetectable	120,000	Undetectable	428,503	<400	Undetectable
Most Recent CD4 Count (cells/μL)	468	535	1026	993	37	1121	417
Most Recent HIV Viral Load	Undectable	193	Undectable	Undetectable	501,000	Undetectable	Undetectable
Anti-TNF or Other Agent Used	Etanercept, Adalimumab	Etanercept	Etanercept, Adalimumab, Infliximab	Etanercept	Etanercept, Infliximab, Adalimumab	Etanercept, Adalimumab, Infliximab, Cosentyx	Etanercept, Infliximab
Clinical Response To Therapy	Excellent response	Excellent response	Partial response	Excellent response	Etanercept- transient Infliximab- excellent, Adalimumab-partial	Adalimumab- no response	Etanercept-no response, infliximab- excellent
Complications of Anti-TNF Treatment	Facial abscess, dental problems, psoriasis on Etanercept	Acute anterior uveitis	None	None	Transient rise in viral RNA, infusion reaction (infliximab)	Etanercept allergy, Golimumab shingles, Cosentyx allergy	Facial abscess (infliximab)

Table 2. Clinical and Sociodemographic Features of HIV Patients with Rheumatic Disease Treated with Anti-TNF Agents after 2006

Patient Number	8	9	10	11	12	13	14	15	16
Age at First Visit	35	30	49	36	48	49	36	53	49
Gender	Male	Male	Female	Male	Male	Male	Male	Female	Female
Ethnicity	Black	Hispanic	Black	Black	Black	Black	Hispanic	Black	Black
Rheumatic Status	Enteropathic Arthritis	Psoriatic Arthritis	Ankylosing Spondylitis	Psoriatic Arthritis	Rheumatoid Arthritis	Axial SpA	Reactive Arthritis	Axial SpA	Periperal SpA
Anti-TNF Agent Usage Status	Not Taking	Currently taking	Not Taking	Currently Taking	Currently Taking	Not Taking	Currenty Taking	Currently Taking	Currently Taking
Taking HAART	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Baseline CD4 (cells/μL)	583	185	614	562	1608	440	1300	827	2618
Baseline Viral (copies/mL)	1788	535	Undetectable	4500	2,000,000	Undetectable	Undetectable	Undetectable	Undetectable
Duration of anti-TNF Treatment	2006-2010	2010-Present	2013-2013	2010-Present	2013-2016, 2020-Present	2014-2014	2019-Present	2020-Present	2020-Present
Still Followed	Last Seen 2015	Current Patient	Current Patient	Current Patient	Current Patient	Current Patient	Current Patient	Current Patient	Current Patient
Lowest CD4 on Anti-TNF Treatment (cells/μL)	403	303	677	217	599	389	1144	815	1416
Highest Viral Load on Anti-TNF Treatment (copies/mL)	35,200	43,700	Undetectable	45,500	384	Undetectable	Undetectable	8390	Undetectable
Most Recent CD4 Count (cells/μL)	583	771	925	323	643	592	2166	1803	2402
Most Recent HIV Viral Load	164,000	38	Undetectable	35,800	Undetectable	Undetectable	Undetectable	Undetectable	Undetectable
Anti-TNF or Other Agent Used	Adalimumab	Etanercept, Adalimumab	Etanercept	Adalimumab, Etanercept	Etanercept	Etanercept	Adalimumab	Adalimumab	Adalimumab
Clinical Response To Therapy	Partial response	Etanercept- transient , Adalimumab-good	Good response	Adalimumab-Transient, Etanercept-Good response	Good response	Dc'd because of only transient response	Excellent respnse	Good response	Good response
Complications of Anti-TNF Treatment	Stopped due to rising viral load and CD4 drop	Symptoms persisting with Etanercept	Patient discontinued treatment	None	None	Patient discontinued due to lost of insurance	None	None	None

above 200 cells/µl and HIV viral load < 60,000 copies/ml (as per guidelines for use of immunosuppressive agents in the face of HIV infection).

Results: In total, 18 patients were treated with anti-TNF agents, including 8 treated with anti-TNF agents between 2003 and 2006 (two RA, two peripheral spondyloarthritis (SpA), of whom we have follow-up data on seven, and an additional nine treated with anti-TNF agents since then. There were no major infectious episodes that necessitated discontinuation of the medications, although one patient seen after 2006 had his adalimumab discontinued by his primary care doctor because of rising HIV viral load. The data on seven of the original eight are shown in Table 1 (one patient was seen only transiently in 2004 and was lost to followup).Of these original seven patients, four are still currently followed (of whom one is on adalimumab and one ustekinumab, the other two in remission) and all seven have been seen in the past six years. Of the nine patients begun on anti-TNF agents since 2006, all but one are currently being followed. by us, of whom six are still taking anti-TNF agents. Three had discontinued them, one due to lack of efficacy, one because of a rising HIV viral load, and one due to fears of toxicity(though no actual event was recorded).

Conclusion: In this series of 17 HIV positive patients, followed up to 18 years, the largest and longest followed reported to date, our data underscore the safety of using anti-TNF agents in patients with HIV infection over long duration, provided standard precautions of using immunosuppressive agents in the setting of HIV infection are followed.

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Abstract Number: 0966

Integrated Single Cell RNA-Sequencing Analysis of Tissue-Localized T Cells in Cutaneous Lupus and Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0966–0969)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is commonly present in patients with systemic lupus erythematosus (SLE), but can also exist as an isolated manifestation without further systemic involvement. Single cell RNA-sequencing (scRNAseq) has previously been employed to define the T cell states present in SLE and lupus nephritis (LN), which has helped reveal insights into the pathogenesis of the disease. Similar scRNAseq studies targeted at skin lesions in SLE could likewise help define the cellular landscape of cutaneous lupus, and could facilitate comparisons of cell infiltrates in different target tissues in SLE. Here, we present the scRNAseq profile of T and NK cell populations within both lesional and non-lesional skin biopsies of patients with cutaneous lupus. We further integrate this dataset of skin-localized T cells with scRNAseq data from T cells from LN kidneys to compare and contrast T cell infiltrates at these two target sites.

Methods: Skin biopsies were obtained from both lesional and non-lesional sites of patients with cutaneous lupus, and from healthy donors. Single cells were encapsulated and sequenced using the 10x Genomics Chromium platform, and data were processed using the Cell Ranger pipeline (10x Genomics). Broad T/NK cell clusters were subset

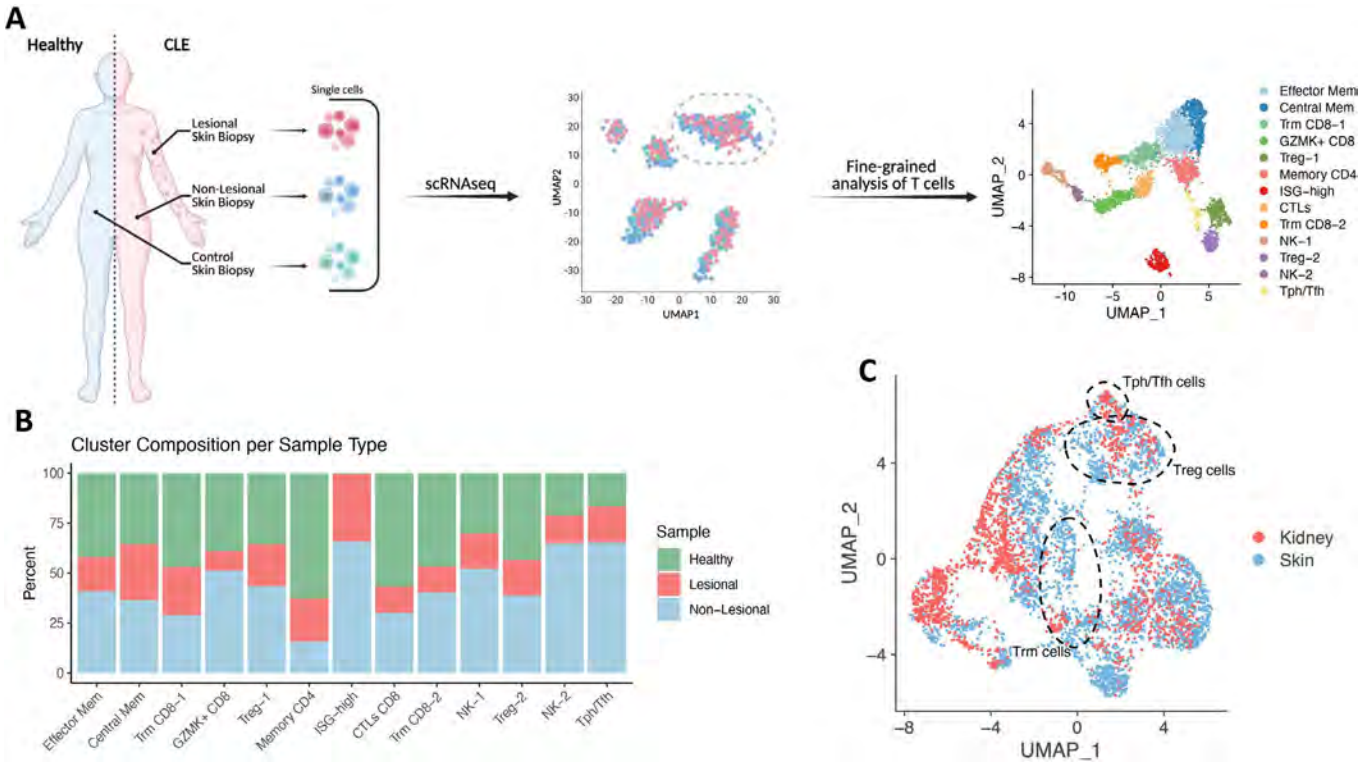


Figure 1. Analysis of T cells subsets across cutaneous lupus and lupus nephritis. (A) Graphical representation of pipeline for cutaneous lupus sample collection and analysis. (B) Breakdown of sample-type representation per cluster in the cutaneous lupus T cell dataset. (C) Integration of cutaneous lupus and lupus nephritis T cell datasets. Several conserved cell subsets, including Tregs, resident memory CD8 T cells, and Tph/Tfh-like cells, are highlighted.

from this dataset and were processed using Seurat for quality control filtering and subcluster analysis. scRNAseq data from LN T cells was obtained from the AMP RA/SLE Phase LN immune cell dataset. Integration of datasets was performed in Seurat using CCA analysis.

Results: Following filtering, paired lesional and non-lesional skin biopsies from 6 SLE patients and 1 isolated CLE patient, along with biopsies from 13 healthy donors, yielded 3,499 T and NK cells. Clustering of these cells revealed 13 subclusters. A population of strongly interferon-responding cells were present in patients with CLE but absent in healthy donors. Within CLE patients, both lesional and non-lesional cells across clusters expressed elevated levels of interferon simulated genes (ISGs), mirroring the ISG upregulation previously seen in scRNAseq studies of LN and blood T cells of lupus patients. Other populations enriched in lupus skin biopsies include a peripheral helper/follicular helper-like CD4 T cells (Tph/Tfh-like) population characterized by expression of CXCL13, MAF, and ICOS, and a population of NK cells expressing PRF1, GNLY, and GZMB. Integration of this dataset with T cells from LN samples using CCA revealed many shared T cell states, including populations of resident memory CD8 T cells, regulatory T cells, Tph/Tfh-like cells, cytotoxic CD8 T cells, ISG-high cells, and NK cells.

Conclusion: This data represents the first analysis of the transcriptomics of T and NK cells in cutaneous lupus at the single cell level. We defined the populations of T cells present in lesional skin as compared to non-lesional skin from the same patients, as well as skin from healthy controls. We identified a strong ISG upregulation in samples collected from CLE patients, and also noted an overrepresentation of helper T cells and NK cells among these samples. Integration of CLE and LN further revealed numerous conserved states, serving as a base for deeper analysis across tissues in lupus.

Disclosure: G. Dunlap, None; **A. Billi**, None; **F. Ma**, None; **J. Gudjonsson**, Almirall, 5, Eli Lilly, 5, BMS, 5; **J. Kahlenberg**, astrazeneca, 1, Janssen, 5, Bristol Myers Squibb, 1, 5, q32 Bio, 5, Ventus Therapeutics, 2, Eli Lilly, 1, GlaxoSmithKlein, 1; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6.

Abstract Number: 0967

Antigen-specific and Bystander Autoreactive T Cell Control in Peripheral Blood of ACPA+ Rheumatoid Arthritis Patients Administered Antigen-specific Tolerising Immunotherapy

Pascale Wehr[1], Ranjeny Thomas[2], Nishta Ramnoruth[3], Swati Patel[3], Jamie Rossjohn[4] and Hugh Reid[4], [1]University of Queensland Diamantina Institute, Brisbane, Australia, [2]University of Queensland, Diamantina Institute, Brisbane, Australia, [3]University Of Queensland, Brisbane, Australia, [4]Monash University, Melbourne, Australia

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0966–0969)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: The control of autoreactive T cells in an antigen-specific manner in autoimmune diseases is a major clinical research goal. Various regulatory immune signatures have emerged from the analysis of patients with type 1 diabetes (T1D), multiple sclerosis or allogeneic stem cell transplantation who achieve prolonged disease remission or a favorable response to immunotherapies designed to control T cells. These include CD4+CD25+CD127hi T helper (Th) cells producing Th2 cytokines, IL-10-producing CD4+ regulatory type 1 (Tr1) T cells, and EOMES+-TIGIT+KLRG1+ "partially exhausted" CD8+ T cells. Transcriptomic and T cell receptor (TCR) sequencing analysis of rheumatoid arthritis (RA) peripheral blood (PB) and synovial T cells has identified large populations of clonally expanded CD4+ and CD8+ cytotoxic T cells (CTL) in RA patients. DEN-181 is a liposome immunotherapy encapsulating 40mg/ml collagen $II_{259-273}$ (CII) peptide + 400ng/ml calcitriol, which is presented by lymph node dendritic cells after s.c. injection. Here we assessed the impact of a single ascending dose of DEN-181 on PB CII-specific and bystander citrullinated (Cit) Cit64vimentin$_{59-71}$ autoreactive T cell responses, CD4+ T cells, and CTL.

Methods: Stored PBMC from 11 ACPA+ HLA-DRB1*0401 or *0101+ RA patients who received vehicle or 3 dose levels of DEN-181, in clinical trial protocol A-RA—0081, were evaluated for number of CII- and Cit64vimentin$_{59-71}$-specific CD4+ T cells 0, 7 and 28 days post-dosing with flow cytometry using haplotype-specific tetramers in a recently-qualified assay. CD45+ leukocytes from cryopreserved PBMC of one patient per cohort at 0 and 28 days post-dose were sequenced using 5' RNA/TCR single-cell 10x Genomics kits. We identified clonally expanded TCR and mapped the clonotypes to their respective transcriptome using the Seurat package in R.

Results: The number of CII-specific T cells and Cit64vimentin$_{59-71}$-specific bystander T cells decreased at day 7 and 28 relative to baseline with similar trends in cohorts receiving 1ml or 3ml but not 0.3ml DEN-181 or placebo. Transcriptomics identified 16 unique CD3+TCR+ PB populations, including activated and exhausted CTL, naïve, Th2-like memory and regulatory CD4+ T cells. The most expanded clonotypes were CD8+ CTL. While the polyfunctional CD8+ CTL cluster decreased at day 28 after 0.3, 1 or 3ml DEN-181, exhausted CTL uniquely increased after 1ml DEN-181. In contrast to 0.3 or 3ml, all but one of the TCR clonotypes shared across time points after 1ml DEN-181 expanded its proportion of exhausted cells at day 28. Naïve-like T cells decreased and $CD4^{lo}$ central memory Th-like T cells increased uniquely after 1ml DEN-181.

Conclusion: In T1D, CTL exhaustion reflects a favorable response to T cell immunotherapy. One ml of antigen-specific tolerising immunotherapy, DEN-181, controlled antigen-specific and autoreactive bystander CD4+ T cell numbers, and enhanced bystander CTL clonal exhaustion in RA PB.

Disclosure: P. Wehr, None; **R. Thomas**, Merck, 5, CSL, 1, 5, BMS, 6, Janssen-Cilag, 2, 6; **N. Ramnoruth**, None; **S. Patel**, Thermo Fisher, 3; **J. Rossjohn**, None; **H. Reid**, None.

Abstract Number: 0968

Granzyme K$^+$ CD8 T Cells Form the Core Population of Inflamed Human Tissue-associated CD8 T Cells

Anna Helena Jonsson[1], Fan Zhang[2], Emma Gomez-Rivas[1], Gerald Watts[1], Garett Dunlap[3], Heather Faust[1], Karishma Rupani[1], Joseph Mears[1], Deepak Rao[1], Runci Wang[4], Gregory Keras[1], Nida Meednu[5], Jonathan Coblyn[1], Elena Massarotti[1], Derrick Todd[1], Andrew McDavid[6], Jennifer Anolik[5], Accelerating Medicines Partnership AMP: RA/SLE Network[7], Kevin Wei[1], Soumya Raychaudhuri[1] and Michael Brenner[8], [1]Brigham and Women's Hospital, Boston, MA, [2]Harvard Medical School, Boston, MA, [3]Harvard University, Somerville, MA, [4]Brigham and Women's Hospital, Boston, MA, [5]University of Rochester Medical center, Rochester, NY, [6]University of Rochester, Rochester, NY, [7]NIH/FNIH, Bethesda, MD, [8]Brigham and Women's Hospital, Harvard Medical School, Newton, MA

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0966–0969)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: T cell-derived pro-inflammatory cytokines are a major driver of rheumatoid arthritis (RA) pathogenesis. While CD4 T cells have traditionally been assumed to be the main cytokine-producing T cells, CD8 T cells rival CD4 T cells in terms of both cell numbers and production of IFNγ and TNF. We found that the majority of CD8 T cells in synovial tissue and fluid are defined by high granzyme K (GzmK) expression and intermediate granzyme B (GzmB) expression, a pattern rare in blood. Here, we characterize the functions and differentiation of these tissue CD8 T cell subsets and describe the effects of GzmK on synovial fibroblasts.

Methods: Blood, synovial fluid, and synovial tissue were obtained from patients meeting the 2010 ACR criteria for RA. Single-cell RNA-seq data sets were generated by integrating new and publicly available data from synovial tissue and fluid from patients with RA and from blood from healthy controls. Synovial fibroblasts were stimulated with recombinant GzmK and/or cytokines for 24 hours prior to harvest of supernatants and RNA. Cytokine production was assessed by intracellular cytokine staining and flow cytometry or by enzyme-linked immunosorbent assay (ELISA). Gene expression changes were analyzed by RT-PCR or bulk RNA-sequencing (RNA-seq). In cross-disease analysis, GzmK and GzmB gene signatures were derived from RA synovial tissue data and applied to other tissue CD8 T cell profiles from publicly available scRNA-seq data.

Results: The vast majority of synovial CD8 T cells have a phenotype that is distinct from classic cytotoxic T lymphocytes, which express high levels of cytotoxic proteins such as granzyme B (GzmB), perforin, and granulysin (Fig. 1A). Instead, synovial CD8 T cell populations are dominated by GzmK$^+$ GzmB$^+$ CD8 T cells with low expression of perforin. Unlike GzmB, which activated caspases to induce target cell death, we find that GzmK does not induce cell death of synovial fibroblasts. Instead, we find that GzmK induces synovial fibroblasts to produce inflammatory factors such as IL-6 and CCL2. Moreover, GzmK can potentiate the effects of IFNg and TNF on synovial fibroblasts, thereby amplifying the effects of these T cell-derived cytokines in RA synovium (Fig. 1B). Using single-cell TCR repertoire studies to track sister clones among matched blood and synovial CD8 T cells, we have identified migration and differentiation pathways that lead to the accumulation of GzmK$^+$ GzmB$^+$ CD8 T cells in inflamed joints. Further, we found transcriptomically similar CD8 T cells in both healthy and diseased tissues, including bowel from patients with inflammatory bowel disease and bronchoalveolar lavage fluid from patients with severe COVID-19 (Fig. 1C).

Conclusion: These findings suggest that GzmK$^+$ GzmB$^+$ CD8 T cells form a core population of tissue-associated T cells in humans that has the potential to drive inflammation both by production of inflammatory cytokines and by direct effects of granzyme K on other cells.

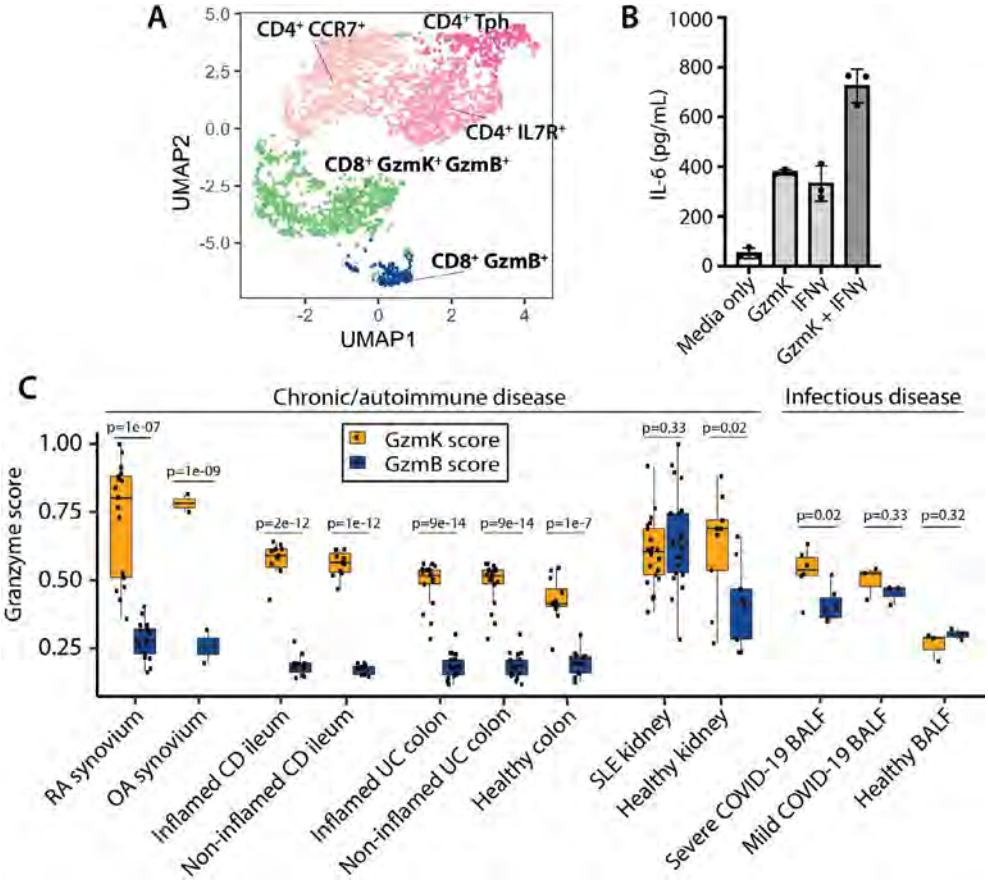


Figure 1. (A) UMAP plot of Louvain clustering of 4,111 single-cell RNA-seq profiles from synovial tissue T cells. (B) IL-6 production by synovial fibroblasts after stimulation with recombinant GzmK and/or IFNg for 24 hours. (C) GzmK and GzmB scores were derived from scRNA-seq data from CD8 T cells from RA synovial tissue and applied to publicly available scRNA-seq profiles of CD8 T cells from other healthy and diseased tissues.

Disclosure: A. Jonsson, Amgen, 5; **F. Zhang**, None; **E. Gomez-Rivas**, None; **G. Watts**, None; **G. Dunlap**, None; **H. Faust**, None; **K. Rupani**, None; **J. Mears**, None; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6; **R. Wang**, None; **G. Keras**, Takeda, 3; **N. Meednu**, None; **J. Coblyn**, CVS, 1; **E. Massarotti**, None; **D. Todd**, Up to Date, 9; **A. McDavid**, None; **J. Anolik**, None; **A. AMP: RA/SLE Network**, Several (FNIH-sponsored consortium), 5; **K. Wei**, Mestag, 2; **S. Raychaudhuri**, Mestag Therapeutics, 2, 12, Founder, Johnson & Johnson, 1, 2, Pfizer, 1, 2, Biogen, 5, Gilead Sciences, 2; **M. Brenner**, GSK, 2, 4FO Ventures, 2, Mestag Therapeutics, 2, 11.

Abstract Number: 0969

Loss of Balance Between Protective and Pro-inflammatory Synovial Tissue T Cell Polyfunctionality Predates Clinical Onset of Rheumatoid Arthritis

Achilleas Floudas[1], Nuno Neto[2], Carl Orr[3], Mary Canavan[4], Phil Gallagher[3], Conor Hurson[5], Michael Monaghan[2], Nagpar Sunil[6], Ronan Mullan[7], Douglas Veale[8] and Ursula Fearon[2], [1]Molecular Rheumatology Trinity Biomedical Sciences Institute, Dublin, Ireland, [2]Trinity College Dublin, Dublin, Ireland, [3]St Vincent's Hospital, Dublin, Ireland, [4]Trinity College, Santry, Ireland, [5]St Vincents University Hospital, Dublin, Ireland, [6]Janssen R&D, Spring House, PA, [7]Tallaght University Hospital, Dublin, Ireland, [8]University College Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: T Cell Biology & Targets in Autoimmune & Inflammatory Disease (0966–0969)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

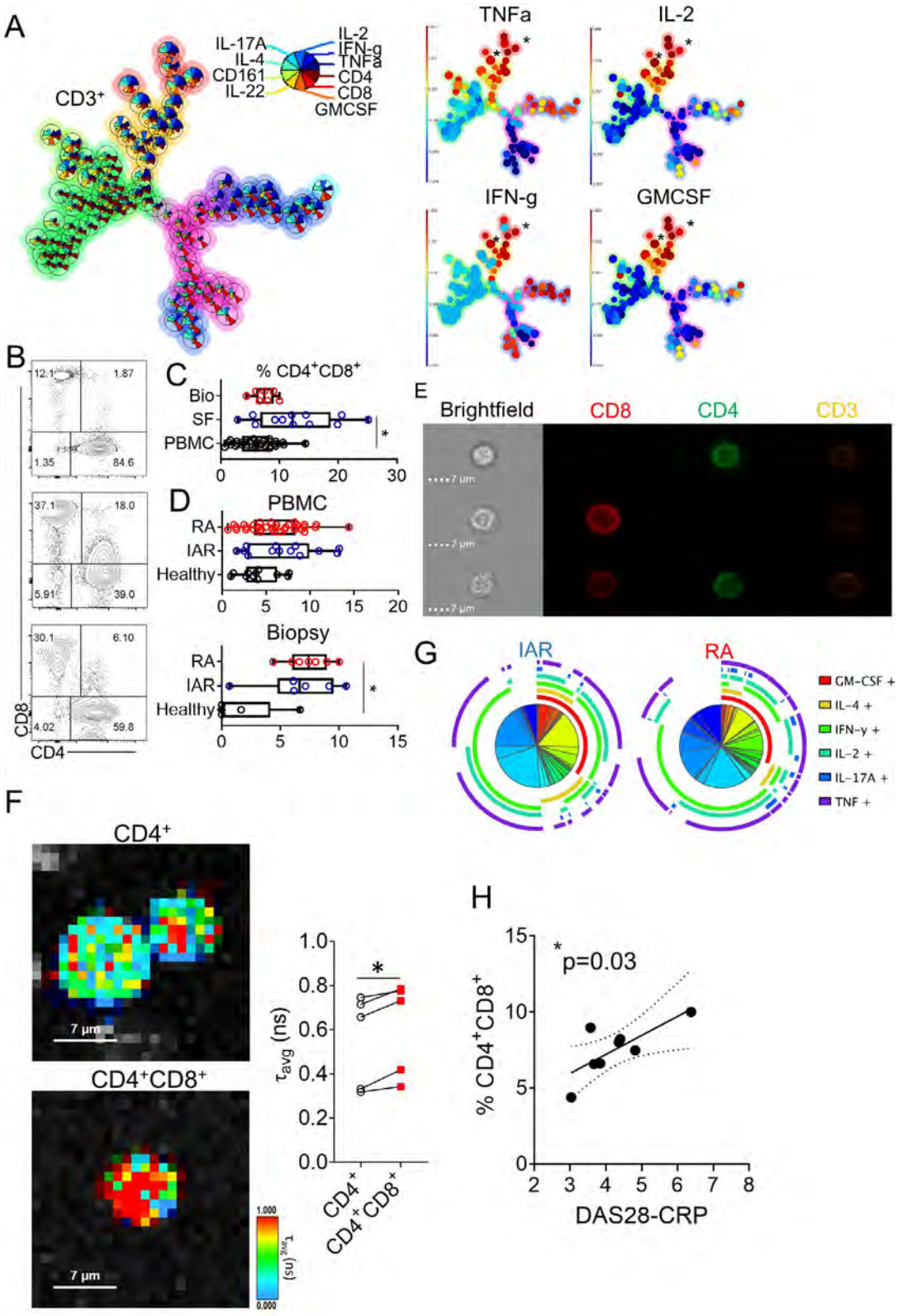
Background/Purpose: Effective treatment of Rheumatoid arthritis (RA) patients is achievable within a short window of opportunity. T-cells are early drivers of synovial inflammation of RA, therefore, identification of pathogenic T-cell subsets at the synovial tissue of pre-RA, individuals at risk (IAR), would greatly improve our understanding of disease pathogenesis. Comparative analysis of healthy control, IAR subject and RA-patient derived synovial tissue T-cell responses will lead to the identification of pathogenic as well as protective cytokine milieu, thus enabling the identification of early therapeutic targets to help steer the immune response towards resolution.

Methods: Synovial biopsies from RA, IAR and HC by arthroscopic surgery followed by RNAseq analysis (Guo et al., PLoS One, 2018). Single cell synovial tissue cell suspensions from RA, IAR and HC and paired PBMC were stimulated *in vitro* and polyfunctional synovial T-cell subsets examined by flow cytometric analysis, SPICE visualization and FlowSom clustering. Flow-Imaging, was utilised to confirm T-cell cluster identification. Fluorescent Lifetime Imaging Microscopy (FLIM) was used to visualise metabolic status of specific T-cell populations.

Results: T-cell associated pro-inflammatory gene pathways were increased in RNAseq analysis of RA-patient and IAR compared to HC synovial tissue biopsies. Flow cytometric analysis of pro-inflammatory cytokine (TNF-a, IFN-γ, IL-2, GM-CSF, IL-17A, IL-22) production and SPICE analysis of *ex vivo* stimulated T-cells revealed marked polyfunctionality of IAR synovial T-cells, thus providing evidence for a dysregulated synovial T-cell response that pre-dates clinical onset of disease. Importantly, HC synovial tissue harbours a small, albeit surprisingly polyfunctional, CD4 T-cell population characterised by significantly increased IL-4 and GM-CSF cytokine production compared to arthralgia subject ($P< 0.001$ and $P=0.01$) and RA-patient ($P< 0.001$ and $P=0.004$) synovial tissue. However, not all polyfunctional T-cells are equal in their pathogenic potential. Therefore, in order to identify highly pathogenic synovial T-cells, cluster analysis of flow cytometric data using the unsupervised algorithm FlowSom was performed and led to the identification of specific T-cell clusters with unique polyfunctionality characteristics. Specifically a cluster of $CD4^{+}CD8^{+}$ double positive (DP) T-cells with high polyfunctionality scores was identified. Hybrid flow cytometry and imaging technique confirmed the co-expression of CD4 and CD8 by a synovial T-cell population. DP T-cells are enriched in RA-patient synovial fluid and synovial tissue and IAR synovial tissue, but are absent from HC synovial tissue. Importantly, DP T-cell synovial accumulation strongly ($P=0.002$) correlates with DAS28(CRP) of RA-patients. Utilisation of the novel, non-invasive FLIM technique for visualisation of cellular NAD, revealed that DP T-cells have a metabolic profile indicative of activated memory T-cells.

Conclusion: These data highlight a key early loss of balance between protective and pathogenic synovial T-cell polyfunctionality and the emergence of specific, highly polyfunctional and pathogenic T-cell clusters in RA.

A. FlowSom unsupervised clustering algorithm analysis of RA patient synovial CD3+ T cells for the identification of phenotypically distinct highly polyfunctional T cell clusters. Symbols indicate polyfunctional CD4+CD8+ DP T cells. B. Representative flow cytometric analysis of paired RA patient peripheral blood, synovial fluid and synovial tissue CD3+ T cells. C. Frequency of CD4+CD8+ DP T cells in the periphery (n=34), synovial fluid (n=13), and synovial tissue (n=7), of RA patients. D. Frequency of CD4+CD8+ DP T cells in the periphery and synovial tissue of HC (n=11 and n=5 respectively), IAR (n=13 and n=6 respectively), subjects and RA (n=34 and n=7 respectively) patients. E. Representative imaging flow cytometry of RA patient synovial fluid CD4+, CD8+ and CD4+CD8+ DP T cells. F. FLIM images and cumulative data of RA patient flow sorted peripheral blood CD4+ and CD4+CD8+ DP T cells, (n=5). H. Linear regression graph for the synovial tissue frequency of RA (n=8) patient CD4+CD8+ DP T cells and disease severity score (DAS28-CRP).



Disclosure: A. Floudas, None; **N. Neto**, None; **C. Orr**, None; **M. Canavan**, None; **P. Gallagher**, None; **C. Hurson**, None; **M. Monaghan**, None; **N. Sunil**, None; **R. Mullan**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6; **U. Fearon**, Abbvie, 1, 5, 6, BMS, 1, Pfizer, 1, 5, Janssen, 5, Eli Lilly, 5, UCB, 5, GSK, 6.

Abstract Number: 0970

Hippo Signaling Is a Novel Regulator of Apoptosis and Photosensitivity in Lupus Keratinocytes

Grace Hile[1], Patrick Coit[2], Bin Xu[1], Shannon Estadt[1], Jacob Martens[3], Rachael Wasikowski[1], Lam Tsoi[1], Ramiro Iglesias-Bartolome[4], Celine Berthier[1], Allison Billi[5], Johann Gudjonsson[5], Amr Sawalha[2] and J. Michelle Kahlenberg[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Pittsburgh, Pittsburgh, PA, [3]Graduate Program in Immunology, University of Michigan, Ann Arbor, MI, USA, Ann Arbor, MI, [4]NIH, National Cancer Institute, Bethesda, MD, [5]Department of Dermatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: SLE – Etiology & Pathogenesis (0970–0973)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: Skin inflammation and photosensitivity are common manifestations of cutaneous (CLE) and systemic lupus erythematosus (SLE), yet the mechanisms underlying heightened cell death and epidermal inflammation remain unclear. Non-lesional lupus keratinocytes (KCs) sustain an interferon (IFN)-rich, inflammatory profile even through several weeks of culture, suggesting possible epigenetic changes that drive this phenotype. Here we identify differential methylation of the Hippo signaling pathway as a novel regulator of apoptosis and photosensitive responses in lupus skin.

Methods: Genome-wide DNA methylation analysis was performed on extracted KC DNA from SLE patients and HC skin biopsies. Single-cell and bulk RNA sequencing was used to analyze RNA expression in cultured primary KCs from SLE patients and HC.*In vivo* protein and phospho-protein expression was assessed by immunofluorescent staining of HC and non-lesional lupus skin. A spontaneously immortalized KC line (N/TERTs) expressing a tetracycline inducible TEAD inhibitor (TEADi) that prevents colocalization of YAP-TEAD was used to evaluate the role of YAP signaling in apoptosis and UVB-mediated cell death. Apoptosis was analyzed via TUNEL staining and caspase 3/7 assay.

Results: Genome-wide DNA methylation analysis on cultured KC DNA from non-lesional, non-sun exposed skin biopsies of SLE patients and HC identified Hippo signaling as the top differentially-methylated pathway. We found significant hypomethylation of WWC1 in lupus KCs compared to control ($\Delta\beta$=-0.17,*P*= 4.36 X 10-9) which promotes phosphorylation and thus cytosolic sequestration of YAP, attenuating TEAD-mediated transcription of pro-proliferative target genes. To determine functional relevance, we compared IFNγ or IFNα stimulated RNA-seq samples from the KCs used for our methylation studies. We found a negative correlation between IFN responses and methylation signatures. As confirmation, we analyzed Hippo regulated genes using single-cell RNA sequencing of nonlesional KC isolated from skin biopsies of lupus vs. HC and found downregulation of pro-proliferative YAP target genes such as SLP1, MYC, and AREG. Consistent with modulation of Hippo signaling as predicted by our methylation data, WWC1 expression was significantly increased in SLE vs. HC KC ($p = 0.0142$). Further, immunofluorescent microscopy of frozen non-lesional biopsies identified a significant increase in phosphorylated YAP in lupus skin compared to controls. TEADi induction in a spontaneously immortalized KC line resulted in a robust increase in UVB-mediated apoptosis as measured by TUNEL staining and caspase 3/7 activation, suggesting that the cytoplasmic retention of YAP observed in SLE KCs may contribute to enhanced UV-mediated KC apoptosis.

Conclusion: Collectively, our work describes a novel mechanistic paradigm in lupus KC in which hypomethylation of key regulators of the Hippo pathway restrict coactivation of TEAD transcriptional activity through cytoplasmic reten-

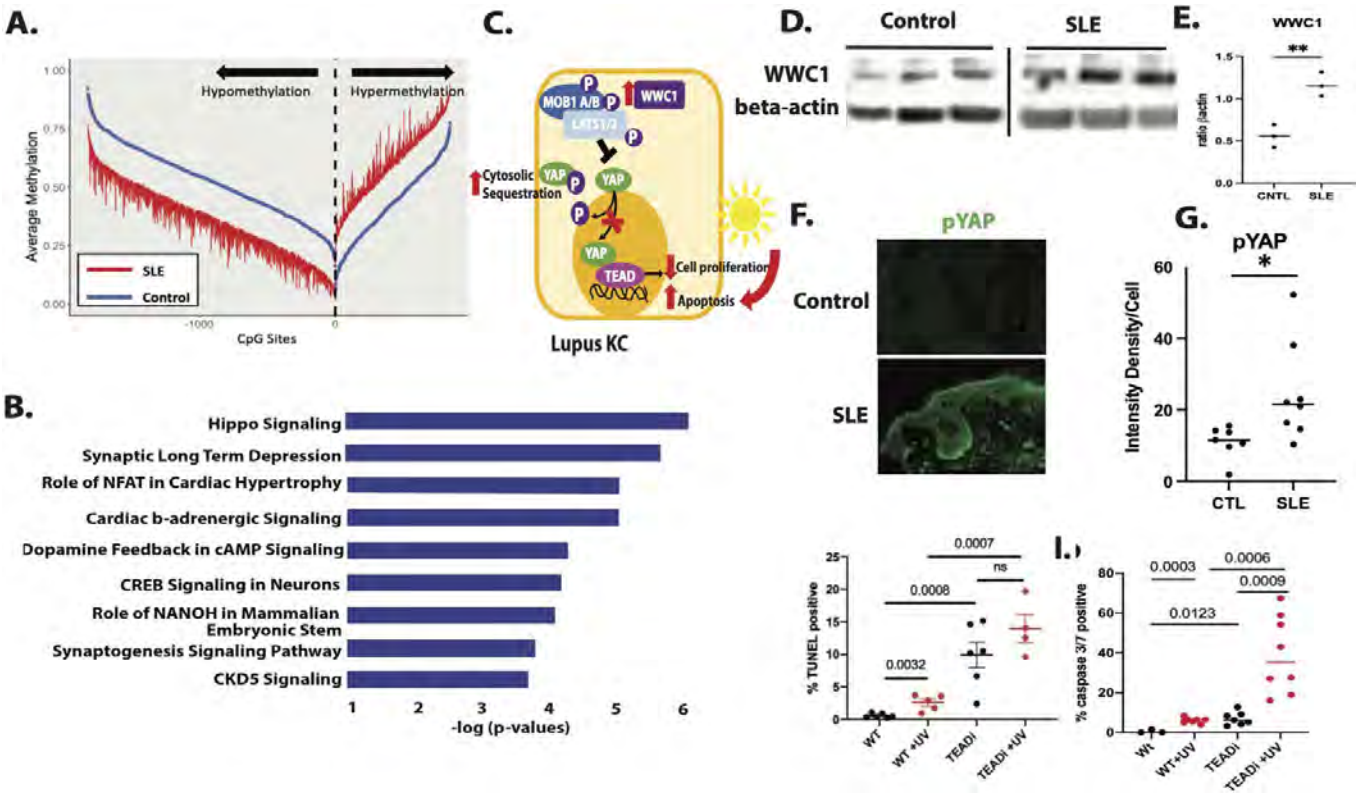


Figure 1. Deactivation of Hippo signaling in SLE KCs leads to increased UVB-mediated apoptosis. A. Illumina methylation arrays of non-lesional SLE vs. control KCs (age, sex, race matched, n=7 each) identified differential methylation in SLE KCs and B. KEGG analysis (via DAVID) revealed Hippo signaling as the top significantly differentially methylated pathway. C. Schematic of Hippo signaling in SLE KCs: increased WWC1 leads to phosphorylation of LATS1/2 which then phosphorylates YAP and leads to cytosolic retention and decreased transcription of proliferative genes and increased transcription of pro-apoptotic genes. D. Western blot of WWC1 and beta-actin in 3 healthy control and 3 SLE KC cultures. E. Quantification of WWC1 in 3 HC and 3 SLE KC lines. F. Immunofluorescent staining of healthy control and SLE non-lesional skin identifies increased phospho-YAP staining in SLE vs. HC. G. Quantification of pYAP in 3 SLE and 3 HC lines. H and I. Induction of a protein which interrupts YAP-TEAD binding results in increased UVB mediated apoptosis (treated with 50 mJ/cm2) as measured by TUNEL staining (H) and active caspase 3/7 (I).

tion of YAP. This results in a propensity for apoptosis after UVB. Thus, modulation of the Hippo pathway could serve as a novel target for abrogation of photosensitivity in SLE and CLE patients.

Disclosure: G. Hile, None; **P. Coit**, None; **B. Xu**, None; **S. Estadt**, None; **J. Martens**, None; **R. Wasikowski**, None; **L. Tsoi**, None; **R. Iglesias-Bartolome**, None; **C. Berthier**, None; **A. Billi**, None; **J. Gudjonsson**, Almirall, 5, Eli Lilly, 5, BMS, 5; **A. Sawalha**, None; **J. Kahlenberg**, astrazeneca, 1, Janssen, 5, Bristol Myers Squibb, 1, 5, q32 Bio, 5, Ventus Therapeutics, 2, Eli Lilly, 1, GlaxoSmithKlein, 1.

Abstract Number: 0971

Longitudinal CyTOF Immunophenotyping Reveals Distinct Patterns of T cell-B Cell Dysregulation in SLE

Takanori Sasaki[1], Sabrina Bracero[1], Lin Chen[1], Ye Cao[2], Emma Stevens[1], Yujie Qu[3], Guoxing Wang[4], Joshua Keegan[1], James Lederer[5], Stephen Alves[3], Karen Costenbader[6] and Deepak Rao[2], [1]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Merck & Co., Inc., Boston, MA, [4]Merck & Co., Inc, Boston, MA, [5]Brigham and Women's Hospital and Harvard Medical School, Millis, MA, [6]Brigham and Women's Hospital, Belmont, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: SLE – Etiology & Pathogenesis (0970–0973)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Mass cytometry (CyTOF), a powerful tool to broadly assess immuno-phenotypes, has previously revealed that T follicular helper (Tfh) cells, T peripheral helper (Tph) cells, and age-associated B cells (ABCs) are robustly expanded in patients with newly diagnosed SLE. However, how these and other immune cell populations change over time in SLE remains unclear.

Methods: We employed CyTOF with two 39 marker panels (T and B cell) in cryopreserved peripheral blood mononuclear cells (PBMCs) from 9 patients with newly diagnosed immunosuppressant-naïve SLE, 15 patients with established SLE, and 14 non-inflammatory controls. FlowSOM (Flow Self-Organizing Maps) and marker analysis by tSNE (t-distributed Stochastic Neighbor Embedding) used to identify and quantify clusters based on their 39-parameter characterization. For the newly diagnosed cohort, PBMCs were analyzed at 3 time points (A = at diagnosis, B = 6 months after the diagnosis, C = 12 months after the diagnosis). Serum samples were also analyzed to quantify 65

Figure 1

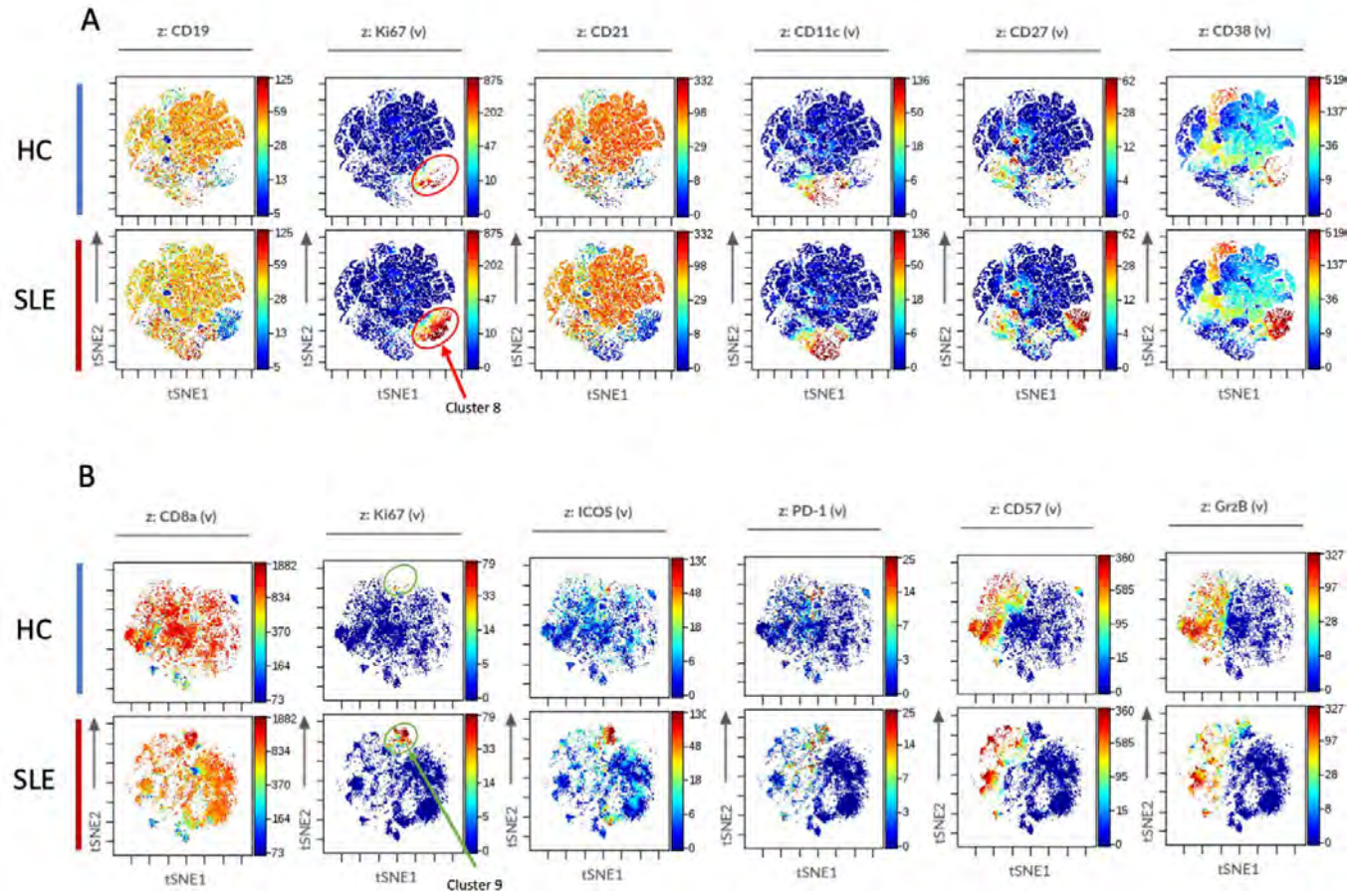


Figure 1. Expanded two Ki67+ populations in PBMCs of SLE patients. A. tSNE plot of CD19+ cells revealed that CD21low, CD11clow, CD27hi, CD38hi plasmablasts were expanded in SLE (Cluster 8). B. tSNE plot of CD8+ cells revealed that Ki67hi, ICOShi, PD-1int, CD57low, GrzBint CD8 T cells were expanded in SLE (Cluster 9).Figure 1. Expanded two Ki67+ populations in PBMCs of SLE patients. A. tSNE plot of CD19+ cells revealed that CD21low, CD11clow, CD27hi, CD38hi plasmablasts were expanded in SLE (Cluster 8). B. tSNE plot of CD8+ cells revealed that Ki67hi, ICOShi, PD-1int, CD57low, GrzBint CD8 T cells were expanded in SLE (Cluster 9).

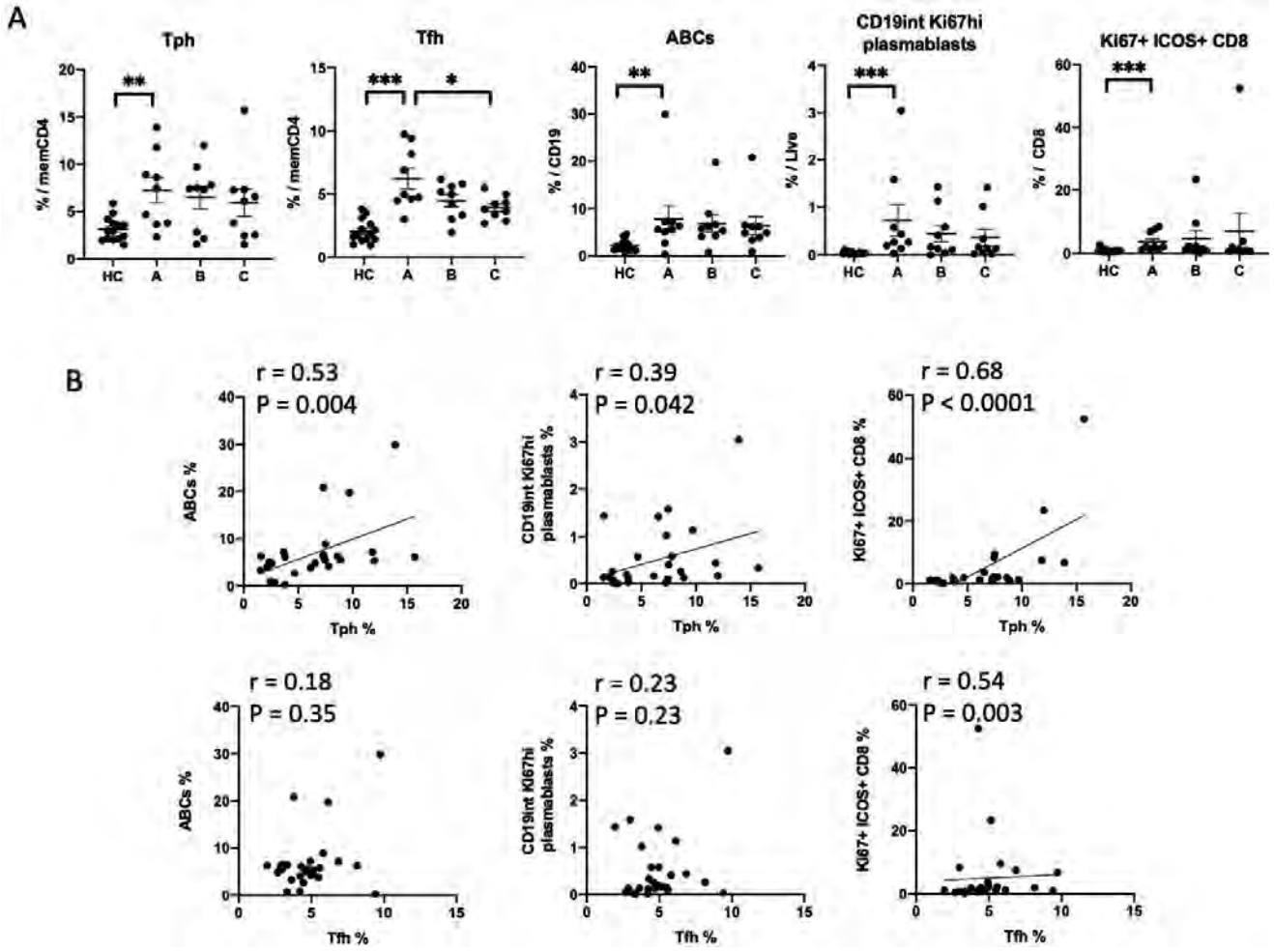


Figure 2. Longitudinal CyTOF analysis of PBMCs in SLE patients. A. Time course changes of Tph, Tfh, ABCs, CD19int Ki67hi plasmablasts, and Ki67+ ICOS+ CD8 T cells in SLE. Timepoint A = at diagnosis, timepoint B = 6 months after the diagnosis, timepoint C = 12 months after the diagnosis. B. Correlation analysis between dysregulated T cell, B cell subsets and cytokine in SLE. HC and A were compared by Mann-Whitney U test. A, B, and C were compared by Wilcoxon test. *p<0.05, **p<0.01, ***p<0.001. Correlation was assessed by Spearman's test.

cytokines by Luminex multiplex assay, and associations between cell types and cytokines assessed by Spearman correlation.

Results: We first confirmed that among CD4 T cells, Tfh cells (PD-1^{hi} CXCR5^{+} CD4^{+} T cells) and Tph cells (PD-1^{hi} CXCR5^{-} CD4^{+} T cells) were significantly increased in SLE patients. A broad analysis of B cells identified 3 clusters as significantly increased in the patients with SLE. Two of these clusters contained CD11c^{+} CD21^{-} ABCs, consistent with prior analyses. A third cluster, cluster 8, contained a CD19^{int} Ki67^{hi} B cell population. This CD19^{int} Ki67^{hi} cluster was also CD21^{low}, CD11c^{low}, CD27^{hi}, and CD38^{hi}, consistent with a Ki67^{hi} plasmablast population (**Figure1A**). Among CD8 T cells, we identified one highly expanded cluster in SLE patients compared to controls, which expressed Ki67^{hi}, ICOS^{hi}, PD-1^{int}, CD57^{low}, and granzyme B^{int} (**Figure1B**). In longitudinal analyses, the frequency of Tfh cells decreased over the first year of SLE, while Tph cells, ABCs, CD19^{int} Ki67^{hi} plasmablasts, and Ki67^{+} ICOS^{+} CD8 T cells remained elevated at 12 months (**Figure 2A**). Tph cells, but not Tfh cells, were correlated with ABCs ($r = 0.53$, $p = 0.004$) and CD19^{int} Ki67^{hi} PB ($r = 0.39$, $p = 0.042$). Ki67^{+} ICOS^{+} CD8 T cells were correlated with Tph cells and Tfh cells, but more strongly in Tph cells ($r = 0.68$, $p < 0.0001$) (**Figure 2B**). Correlation analyses including both immune cell frequencies and cytokines revealed an association of Tph cells, Ki67^{+} ICOS^{+} CD8 T cells, ABCs, and CD19^{int} Ki67^{hi} plasmablasts. These associated populations, but not Tfh cells, were also significantly correlated with CXCL13 and TSLP (**Figure 3**).

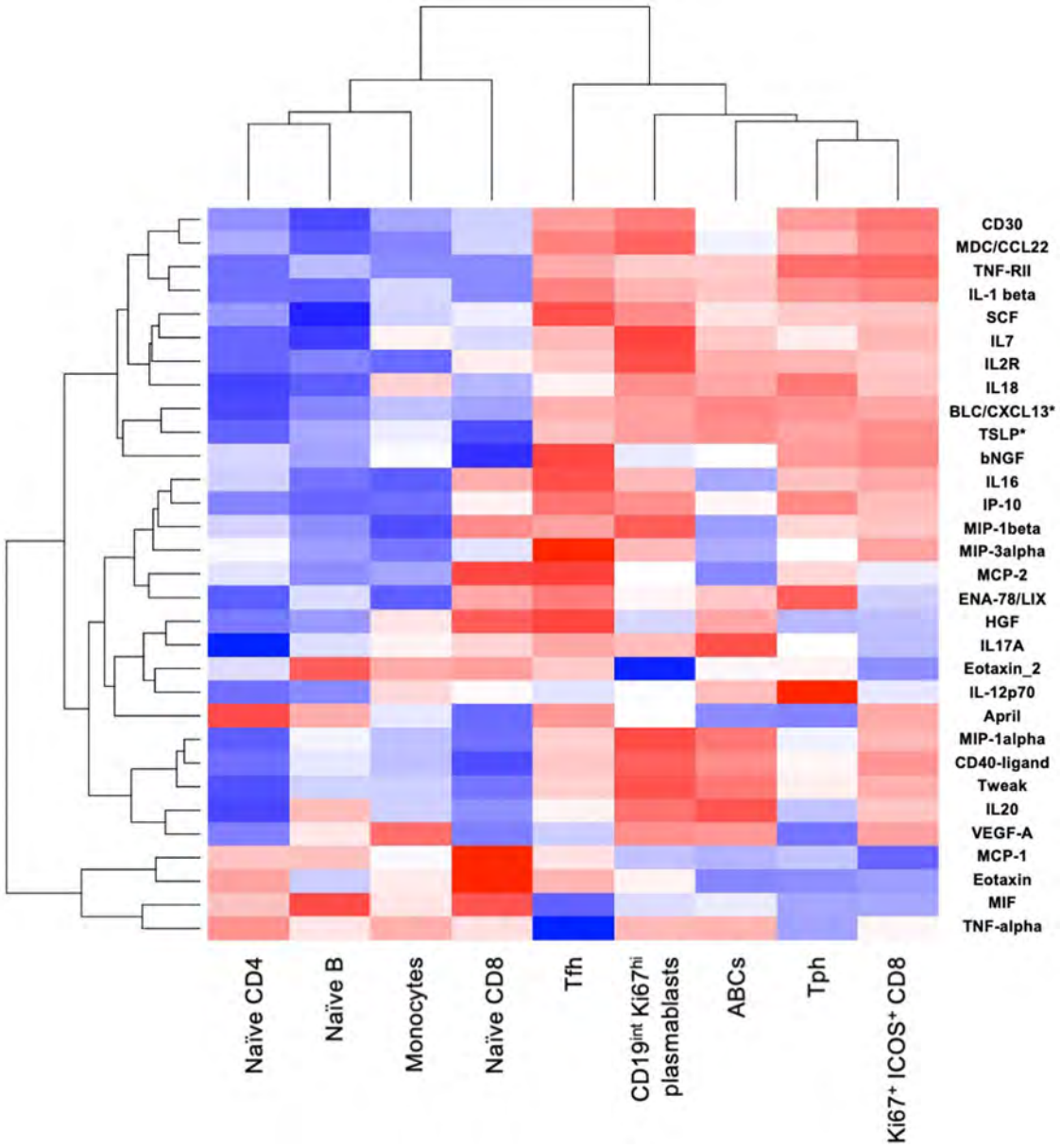


Figure 3. A hierarchical clustering heatmap with immune cell frequencies and cytokines in SLE. Among 65 cytokines, 31 cytokines were detected. Correlation coefficients calculated by Spearman's test were used for the heatmap. *p<0.05 in Tph cells, Ki67+ ICOS+ CD8 T cells, ABCs, and CD19int Ki67hi plasmablasts, but not in Tfh cells and other populations.

Conclusion: Tph cells, ABCs, and the two different Ki67^{+} proliferating populations were consistently elevated during the first year after diagnosis of SLE, while Tfh cells decreased in frequency over the same timeframe. This longitudinal immunophenotyping and cytokine profiling approach thus highlights persistent activation of a Tph-CXCL13-ABC-plasmablasts axis in both early and established phases of SLE.

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Abstract Number: 0972

Hypoxia Promotes the Expression of ADAM9 by Tubular Epithelial Cells Which Enhances TGF-β1 Activation and Promotes Tissue Fibrosis in Lupus Nephritis

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: SLE – Etiology & Pathogenesis (0970–0973)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Enhanced expression of transforming growth factor-beta (TGF-β) in the kidneys of patients with lupus nephritis (LN) can lead to progressive fibrosis, resulting in end-organ damage (J Immunol. 180, 1903-1912. 2008). We previously reported that a disintegrin and metalloproteinases 9 (ADAM9) enhances Th17 cell differentiation and autoimmunity by activating TGF-β1 (PNAS. 118, 2021). We hypothesized that ADAM9 in the kidney may accelerate fibrogenesis by activating TGF-β1.

Methods: We assessed the expression of ADAM9 in kidneys from MRL/*lpr* mice and control MPJ mice and determined the expression levels of ADAM9 in kidney cells. We conducted *in vitro* experiments using tubular epithelial cells (TEC) isolated from B6 mice and explored the mechanisms responsible for the upregulation of ADAM9 in tubular epithelial cells (TEC) and the subsequent activation of TGF-β1 by ADAM9 expressed in TEC. To assess the role of ADAM9 in the development of tubular-intestinal fibrosis in LN, we generated MRL/*lpr.Adam9-/-* mice and compared the intensity of renal fibrosis between *Adam9* sufficient and deficient MRL/*lpr* mice.

Results: We identified ADAM9 to be highly expressed in tubules from MRL/*lpr* mice. The transcription factor hypoxia-inducible factor-1 alpha (HIF-1α) was found to promote the transcription of ADAM9 in TEC. TEC from *Adam9*-deficient mice exposed to the hypoxia inducer dimethyloxalylglycine (DMOG) failed to cleave the latency-associated peptide to produce bioactive TGF-β1 from latent TGF-β1. Co-culture of TEC from *Adam9*-deficient mice and fibroblasts with DMOG and latent TGF-β1 showed decreased production of type I collagen and alpha-smooth muscle actin (αSMA) by fibroblasts. *Adam9*-deficient MRL/*lpr* mice showed mitigated tubular-intestinal fibrosis.

Conclusion: Our findings have revealed that hypoxia promotes the expression of ADAM9 by TEC which is responsible for the development of interstitial fibrosis in LN by promoting the generation of fibroblast bioactive TGF-β1 [hypoxia (HIF-1α) **->** ADAM9 **->** TGF-β1 **->** production of collagen I and αSMA by resident fibroblasts].

Disclosure: M. Umeda, None; **A. Satyam**, None; **N. Yoshida**, None; **R. Bhargava**, None; **R. Hisada**, None; **S. Jamaly**, None; **C. Owen**, AstraZeneca Biopharmaceuticals Inc, 3; **G. Tsokos**, None.

Abstract Number: 0973

Modeling of Clinical Phenotypes in SLE Based on Platelet Transcriptomic Analysis and FCGR2a Biallelic Variants

MacIntosh Cornwell[1], Hanane EL Bannoudi[2], Elliot Luttrell-Williams[1], Khrystyna Myndzar[1], Alexis Engel[3], Peter Izmirly[4], H. Michael Belmont[5], Robert Clancy[6], Jeffrey Berger[1], Kelly Ruggles[1] and Jill Buyon[6], [1]New York University, New York, NY, [2]NYU Langone Health, New York, NY, [3]NYU Langone Health, New Yok, NY, [4]New York University School of Medicine, New York, NY, [5]NYU School of Medicine, New York, NY, [6]NYU Grossman School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: SLE – Etiology & Pathogenesis (0970–0973)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: The clinical heterogeneity of SLE with its complex pathogenesis remains challenging as we strive to provide optimal management. The contribution of platelets to endovascular homeostasis, inflammation and immune regulation highlights their potential importance in SLE. Prior work from our group showed that the Fcγ receptor type IIa (FcγRIIa)–R/H131 biallelic polymorphism is associated with increased platelet activity and cardiovascular risk in SLE. The study was initiated to investigate the platelet transcriptome in patients with SLE and evaluate its association across FcγRIIa genotypes and distinct clinical features.

Methods: RNA-sequencing was done on platelets isolated from 51 patients fulfilling criteria for the classification of SLE based on recent EULAR/ACR definitions, and 18 healthy controls matched on age, sex, and race. Unsupervised clustering, differential gene expression, and gene set enrichment analysis (GSEA) were used to analyze differences between SLE patients and controls, and SLE subpopulations, based on SELENA SLEDAI Hybrid disease activity, specific organ manifestations, and FcγRIIa genotype. Weighted Gene Correlation Network Analysis (WGCNA) was performed to create a modular transcriptomic framework.

Results: Our cross-sectional SLE cohort (N=51, age = 41.1±12.3, 100% female, 45% Hispanic, 24% black, 22% Asian, 51% white, SLEDAI = 4.4±4.2) was comprised of patients consecutively enrolled excluding those on aspirin or anticoagulants. Compared to the 18 controls, there were 2290 ($p.adj < 0.05$) differentially expressed genes. (**Figure 1 A,B)** GSEA revealed positive enrichment for pathways related to interferon response, TNFa signaling, and coagulation in SLE. (**Figure 1C)** WGCNA was used to create a modular transcriptomic framework. (**Figure 2A**) Modules enriched for platelet activity, immune response, and WNT signaling were significantly increased in SLE versus controls. Moreover, modules enriched for interferon response and WNT signaling paralleled increases in disease activity. (**Figure 2B)** When analyzing patients with proteinuria, modules associated with oxidative phosphorylation and platelet activity were unexpectedly decreased. **(Figure 2C)** Analyzing the ratio of fold changes between SLE/Control vs SLE Proteinuria/SLE No Proteinuria, genes increased in SLE and those with proteinuria were enriched for immune effector processes, while genes increased in SLE but decreased in proteinuria were enriched for coagulation and cell adhesion. **(Figure 2D)** The module enriched for FCR activation was decreased in SLE and was affected by the FcγRIIa genotype. **(Figure 3A)** FcγRIIa R131 and H131 patients showed significantly different platelet transcriptomes. **(Figure 3B)** The combination of SLE with an FcγRIIa R131 variant leads to a significant increase in the platelet activity module not seen in controls. **(Figure 3C)**

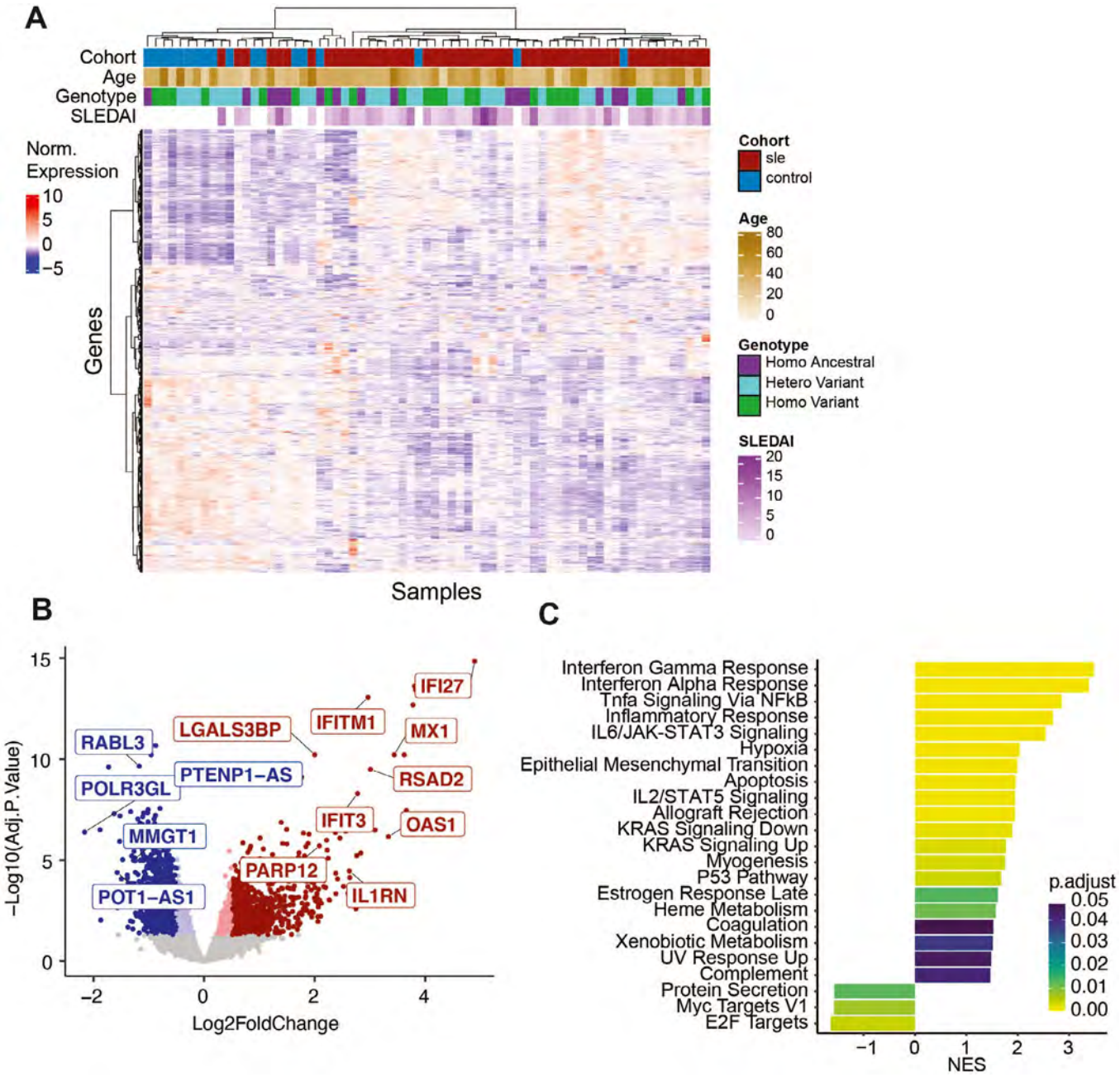

Figure 1. Transcriptomic analyses reveal differences between SLE and Control platelet transcriptomes. (A) Unsupervised clustering of out cohort based on the top 10% of varied genes. (B) Volcano plot depicting differential expression between the SLE and Control cohorts. (C) Gene Set Enrichment Analysis (GSEA) normalized enrichment scores and p values for pathways differentially enriched between our cohorts.

Conclusion: These analyses reveal that SLE patients have a significantly different platelet transcriptome from controls, different phenotypic presentations of SLE patients associate with distinct platelet transcriptomic signatures, and FCGR2a variants may differentially influence the role of platelets in the contribution to SLE disease activity.

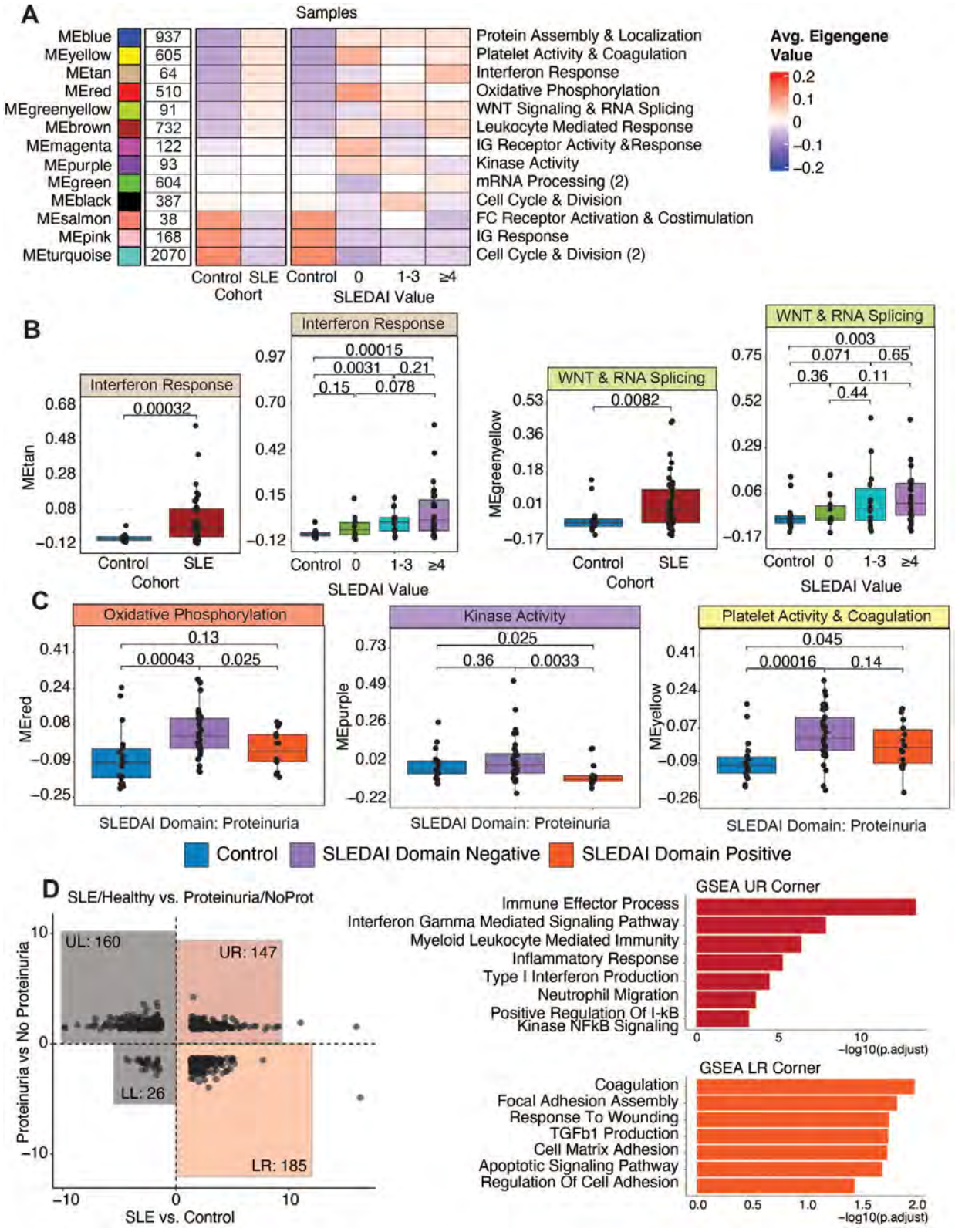

Figure 2. Modular analyses of the lupus cohort demonstrate differences between SLE patients. (A) Weighted Gene Correlation Network Analysis (WGCNA) derived modules and their average values between our control and SLE cohort, and between control and our SLE cohort when divided by SLEDAI value. (B) Boxplots for the individual patient values of the Interferon Response module and WNT & RNA Splicing modules seen in our SLE cohort. (C) Boxplots for the Oxidative Phosphorylation, Kinase Activity, and Platelet Activity & Coagulation modules seen in our cohort when separated into control, proteinuria, and no proteinuria. (D) Scatterplot of log2fc values for SLE vs control, and proteinuria vs no proteinuria, divided into quadrants associated with the directionality of the two log2fc ratios. GSEA analysis was performed on the UR (upper right) quadrant and the LR (lower right) quadrant.

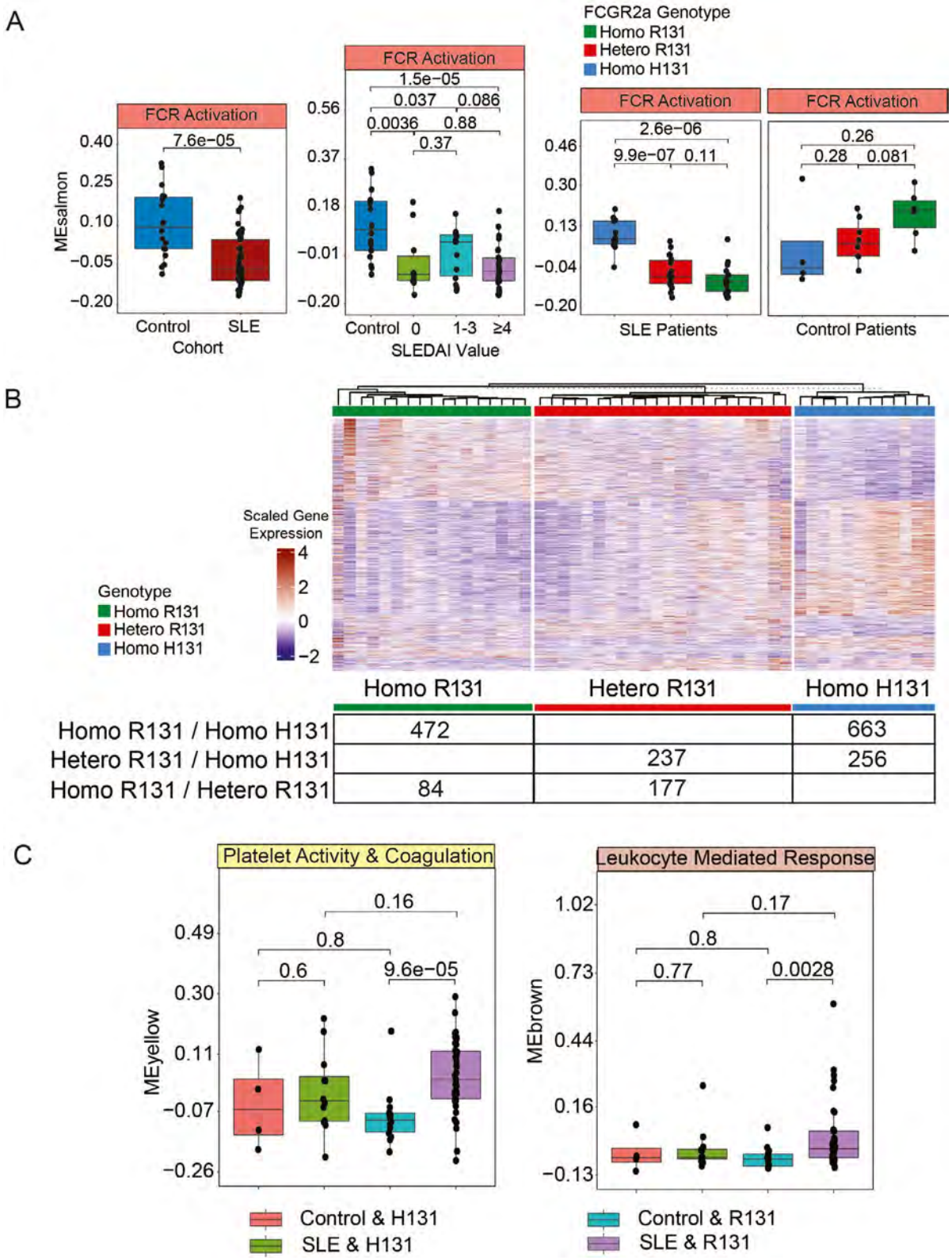

Figure 3. FCGR2a variants significantly affect the platelet transcriptome. (A) The WGCNA module enriched for FCR activation represented as boxplots when our cohort is split by (1) SLE vs control, (2) control vs SLEDAI groups, and (2) SLE and Control cohorts split by their FCGR2a genotype. (B) Heatmap of differentially expressed genes derived from the pairwise comparisons of our three genotype groups: Homozygous R131, Heterozygous R131, and Homozygous H131. The table shows number of genes up in the respective group for each pairwise comparison (e.g. Homozygous R131 / Homozygous H131 had 472 genes upregulated in Homo R131, and 663 genes upregulated in Homo H131) (C) WGCNA Modules for Platelet Activation and Leukocyte Mediated Response when split by diagnosis and FCGR2a genotype.

Disclosure: M. Cornwell, None; **H. EL Bannoudi**, None; **E. Luttrell-Williams**, None; **K. Myndzar**, None; **A. Engel**, None; **P. Izmirly**, Momenta/Janssen, 1; **H. Belmont**, Alexion, 6; **R. Clancy**, None; **J. Berger**, None; **K. Ruggles**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2, Dagamma, 12, In-kind donation of fetal heart rate monitors for clinical trial.

Abstract Number: 0974

Use of Disease-Modifying Anti-Rheumatic Drug Associated with Lower Incidence of Anti-Tumor Necrosis Factor Induced Psoriasis in Children with Inflammatory Bowel Disease and Juvenile Idiopathic Arthritis

Katelyn Baggett[1], Timothy Brandon[1], Rui Xiao[2], Zachary Valenzuela[1], Lisa Buckley[3] and **Pamela Weiss**[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Vanderbilt Children's Hospital, Nashville, TN

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Pediatric Rheumatology – Clinical (0974–0979)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Tumor necrosis factor inhibiting (TNFi) therapies are associated with new-onset psoriasis in children with inflammatory bowel disease (IBD) and juvenile idiopathic arthritis (JIA). We aimed to compare the differential effect of three TNFi therapies and to examine whether the addition of a nonbiologic disease-modifying anti-rheumatic drug (DMARD) impacts the incidence of psoriasis in children with IBD and JIA.

Methods: This was a single-center retrospective cohort study of electronic health record data from 2008 to 2020. Inclusion criteria were: 1) 2 ICD-9 or ICD-10 codes for JIA, IBD, or chronic nonbacterial osteomyelitis (CNO); 2) age at diagnosis of under 19 years; 3) at least 2 visits with a study center rheumatologist or gastroenterologist. Subjects with psoriasis prior to the diagnosis of JIA, IBD, or CNO were excluded. TNFi exposure was defined as at least 1 prescription for infliximab, etanercept, or adalimumab (ever/never). DMARD exposure was dichotomized as ever/never and included methotrexate. The primary outcome was incident psoriasis defined as the first ICD-9/10 code for psoriasis during a visit with a study center rheumatologist, gastroenterologist, or dermatologist. Incidence rates (IRs) were calculated and stratified by underlying diagnosis, TNFi agent, and DMARD use. IRs for CNO were not calculated due to small sample size.

Results: 5088 children met inclusion criteria – 3799 (75%) had IBD, 1185 (23%), had JIA, and 104 (2%) had CNO. 1335 (66%), 304 (15%), and 382 (19%) of children were prescribed infliximab, etanercept, or adalimumab, respectively. 1430 (71%) and 593 (29%) had TNFi exposure with or without a DMARD, respectively. The number of follow-up years, cases, and IRs for the entire cohort and for each diagnosis are presented in Table 1. The IR for psoriasis was higher in patients with JIA than IBD in both the TNFi alone and TNFi plus DMARD groups with a risk difference of 7.9 and 4, respectively. Amongst all patients, the IR for psoriasis was lowest for infliximab (12.4) and similar in etanercept and adalimumab (17.1 and 17.2). The IR for infliximab remained lower than the other 2 TNFi when stratified by DMARD use but differed by underlying diagnosis. There were no IBD patients treated with etanercept and of the limited number of JIA patients treated with infliximab (N=21), none developed psoriasis. The IR of psoriasis was lower amongst children on a TNFi who were DMARD-exposed (12.2) versus those unexposed (15.1).

Conclusion: The IR of TNFi-induced psoriasis was lowest for patients exposed to infliximab, even after stratifying by DMARD exposure. For patients with exposure to any of TNFi evaluated, the IR was lower in those also exposed to DMARD.

Table 1. Incidence rates of psoriasis for entire cohort and for each underlying disease according to TNFi type and presence of methotrexate

	All TNFi exposed			TNFi only			TNFi plus methotrexate		
	All*	IBD	JIA	All*	IBD	JIA	All*	IBD	JIA
Follow-up (person-years)									
All TNFi	6504	4924	1538	3965	3490	449	2539	1434	1089
infliximab	4283	4179	84	3052	3011	34	1231	1168	49
etanercept	1220	0	1214	309	0	306	911	0	917
adalimumab	997	740	240	603	477	109	394	263	160
Cases									
All TNFi	91	64	25	60	50	10	31	14	15
infliximab	53	51	0	41	41	0	12	10	0
etanercept	21	0	21	8	0	8	13	0	16
adalimumab	17	13	4	11	9	2	6	4	5
IR (per 1000 person years)									
All TNFi	14	13	16.3	15.1	14.3	22.2	12.2	9.8	13.8
infliximab	12.4	12.2	0	13.4	13.6	0	9.7	8.6	0
etanercept	17.2	–	17.3	25.9	–	26.2	14.3	–	17.4
adalimumab	17.1	17.6	16.6	18.3	18.9	18.3	15.2	15.2	31.2

*IBD, JIA, and CNO IR: incidence rate; IBD: inflammatory bowel disease; JIA: juvenile idiopathic arthritis; CNO: chronic nonbacterial osteomyelitis; TNFi: tumor necrosis factor inhibitor

Disclosure: K. Baggett, None; **T. Brandon**, None; **R. Xiao**, None; **Z. Valenzuela**, None; **L. Buckley**, None; **P. Weiss**, Lilly, 1, 2, Pfizer, 1, 2, Biogen, 2.

Abstract Number: 0975

Data-driven MRI Definitions for Active and Structural Sacroiliac Joint Lesions in Juvenile Spondyloarthritis Typical of Axial Disease

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: Pediatric Rheumatology – Clinical (0974–0979)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Determining optimal cut-offs for active and structural imaging lesions of juvenile spondyloarthritis (JSpA) with axial disease is important for diagnosis, therapeutic management, and classification. We aimed to determine quantitative sacroiliac joint (SIJ) imaging lesion thresholds to 1. define a positive MRI for inflammatory and structural lesions typical of axial JSpA and 2. evaluate the lesions associated with assessment of axial disease by a panel of SpA experts.

Methods: Subjects were a retrospective cohort of children who had an MRI as part of their evaluation for suspected axial disease. MRI scans were reviewed by 6 central raters blinded to clinical details. Raters provided a yes/

Table 1. Performance of cut-offs for presence of definite inflammatory and structural lesions of axial disease

Cut-offs for number of SIJ quadrants (any location)	Sensitivity (95% CI)	Specificity (95% CI)
Majority (≥4/6) rater agreement for definite active lesion		
BME score ≥1	100 (95-100)	85.9 (79.7-90.7)
BME score ≥2	100 (95.0-100)	93.5 (88.7-96.7)
BME score ≥3	98.6 (92.5-100)	96.5 (92.5-98.7)
BME score ≥4	95.8 (88.3-99.1)	97.1 (93.3-99.0)
Inflammation in erosion cavity (any)	56.2 (44.1-67.8)	98.3 (95.0-99.6)
BME score ≥3 *or* inflammation in erosion cavity (any)	98.6 (92.5-100)	95.3 (90.9-97.9)
Majority (≥4/6) rater agreement for definite structural lesion		
Erosion score ≥1	97.1 (90.1-99.7)	91 (85.4-95)
Erosion score ≥2	95.7 (88-99.1)	96.8 (92.7-99)
Erosion score ≥3	91.4 (82.3-96.8)	98.7 (95.4-99.8)
Sclerosis score ≥1	74.3 (62.4-84)	95.5 (91-98.2)
Sclerosis score ≥2	62.9 (50.5-74.1)	98.1 (94.5-99.6)
Fat score ≥1	31.4 (20.9-43.6%)	96.8 (92.7-99%)
Fat score ≥2	22.9 (13.7-34.4%)	98.7 (95.4-99.8%)
Backfill score ≥1	24.3 (14.8-36)	99.4 (96.5-100)
Backfill score ≥2	20 (11.4-31.3)	100 (97.7-100)
Ankylosis score ≥1	2 (0.4-5.7)	100 (94.9-100)
Ankylosis score ≥2	1.3 (0.2-4.7)	100 (94.9-100)
Any structural lesion*	98.6 (92.3-100)	89.7 (83.9-94)
Erosion score ≥2 *plus* ≥1 of the following lesions: sclerosis, fat score, back fill, ankylosis	80 (68.7-88.6)	99.4 (96.5-100)

Table 2. Diagnostic test statistic performance for active, structural or any lesion (defined in Table 1) consistent with SpA using majority expert final assessment of case as the reference standard.

	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)
Active lesions				
Inflammation in erosion cavity	41.2 (30.6-52.4)	95.8 (91.9-98.2)	81.4 (66.6-91.6)	78.5 (72.7 (83.6)
BME ≥3 quadrants	80.6 (69.5-88.9)	89.8 (84.1-93.9)	77.3 (66.2-86.2)	91.4 (86-95.2)
BME ≥3 quadrants *or* inflammation in erosion cavity	80.6 (69.5-88.9%)	88.6 (82.7-93%)	75.3 (64.2-84.4%)	91.3 (85.8-95.2%)
Structural lesions				
Erosion ≥2 quadrants	72.2 (60.4-82.1)	88 (81.7-92.7)	74.3 (62.4-84.0)	86.8 (80.4-91.8)
Erosion ≥2 quadrants *plus* at least one of the following: sclerosis, fat lesion, backfill, ankylosis	59.7 (47.5-71.1)	90.7 (84.8-94.8)	75.4 (62.2-85.9)	82.4 (75.7-87.9)
Erosion ≥2 quadrants *or* at least one of the following: sclerosis, fat lesion, backfill, ankylosis	80.6 (69.5-88.9)	83.3 (76.4-88.9)	69.9 (58.8-79.5)	89.9 (83.7-94.4)
Active or structural lesion combinations				
Any active *or* structural lesion^	89.3 (80.1-95.3%)	81.5 (74.8-87.1%)	68.4 (58.2-77.4%)	94.5 (89.4-97.6%)
BME ≥3 *or* erosion ≥2 quadrants	82.7 (72.2-90.4)	85.7 (79.5-90.6)	72.1 (61.4-81.2)	91.7 (86.3-95.5)

no response and confidence levels to the following parameters: 1) Are there typical active inflammatory lesions compatible with axial SpA present in the SIJs or at entheseal sites outside the SIJ? 2) Are typical chronic inflammatory lesions present in or around the SIJs? Raters assessed lesions in SIJ quadrants or halves on consecutive semi-coronal slices on a web-based interface for: a) bone marrow edema (BME), b) inflammation in erosion cavity, c) erosion, d) sclerosis, e) fat lesion, f) backfill, and g) ankylosis. Optimal sensitivity and specificity of MRI score cut-offs for each lesion were calculated using central imaging majority (≥4/6 raters) designation of high confidence (≥+3 on confidence scale from -5, "Definitely No", to +5, "Definitely Yes") in the presence of MRI active or structural lesions typical of axial SpA as the reference standard. All clinical and imaging data were assessed by 3 of 14 SpA expert panelists. JSpA experts assessed their confidence that the case was "JSpA with axial disease" with the anchors -3 (very unlikely) to +3 (very likely). Cases classified by majority (≥2/3) experts with high confidence (≥+2) were used as the reference standard. Test statistic properties of the quantitative lesion-based MRI thresholds were assessed against this reference standard.

Results: Imaging from 243 subjects, 61% male, median age 14.9 had sequences available for detailed MRI scoring. The lesion-based cut-offs achieving specificity ≥95% with the highest sensitivity for a definite active inflammatory lesion were: BME in ≥3 quadrants or ≥1 inflammation in an erosion cavity (Table 1); combining the two types of lesions did not add incremental value. For definite structural lesion, the lesion cut-offs achieving ≥95% specificity with the highest sensitivity were the following: erosion in ≥2 quadrants, sclerosis in ≥1 quadrant, fat lesion in ≥1 quadrant, and backfill in ≥1 quadrant (Table 1); combinations of the lesions did not add incremental value. PPV and NPV of the quantitative threshold definitions for active, structural, or any lesions typical of axial SpA using the majority expert final assessment as the reference standard are shown in Table 2. The PPV and specificities were highest for BME ≥3 quadrants, erosion in ≥2 quadrants or a combination of the 2.

Conclusion: We propose cut-offs for definite active and structural lesions on MRI typical of axial disease in JSpA that have high PPV and specificity for clinical assessment. These cut-offs have applicability for diagnosis, therapeutic management, and classification.

*Any structural lesion with the following score thresholds: Erosion in ≥2 quadrants, sclerosis in ≥1 quadrant, fat lesion in ≥1 quadrant, backfill in ≥1 quadrant, or ankylosis ≥1 quadrant. Erosion SIJ quadrants = upper ilium, lower ilium, upper sacrum, lower sacrum for left and right SIJ; # of quadrants = total # of quadrants with detectable BME across all slices of study. Bone Marrow edema: An ill-defined area of high bone marrow signal intensity on fluid-sensitive sequences within the subchondral bone of the ilium or sacrum compared to the signal intensity of the iliac crest, edges of the vertebrae, and triradiate cartilage and in comparison to physiological changes normally seen on MRI examinations of age- and sex-matched children, and visible in 2 planes [1]. Inflammation at the site of an erosion: Increased signal on STIR and/or T1-weighted fat suppressed (FS) post-gadolinium at the site of erosion [2]. Erosion: A defect in subchondral bone associated with full-thickness loss of the dark appearance of the subchondral cortex at its expected location, with loss of signal on a T1-weighted sequence compared with the normal bright appearance of adjacent bone marrow [2]. Sclerosis: A substantially wider than normal (of ≥ 5 mm in adolescents) area of low subarticular bone signal on T1-weighted and fluid sensitive images [1]. Fat lesion: Homogeneous increased signal intensity within the subchondral bone on T1-weighted non-FS image presenting with a distinct border of the lesion [2]. Backfill: Bright signal on a T1-weighted sequence in a typical location for an erosion or confluent erosions, with signal intensity greater than normal bone marrow, which meets the following requirements: a) associated with complete loss of the dark appearance of the subchondral cortex at its expected location. B) clearly demarcated from adjacent bone marrow by an irregular band of dark signal reflecting sclerosis at the border of the original erosion [2]. Ankylosis: Presence of signal equivalent to regional bone marrow continuously bridging a portion of the joint space between the iliac and sacral bones [1]. BME = bone marrow edema; SIJ = sacroiliac joint; CI = confidence interval.

Confidence level was reported for each case on a scale of highly confident the case is not axial disease (-3) to highly confident the case is axial disease (+3). Cases rated as high confidence by the experts in having axial disease ≥+2 were used as the reference standard. ^Bone marrow edema in ≥3 quadrants, inflammation in an erosion cavity, Erosion in ≥2 quadrants, sclerosis, fat lesion, backfill, or ankylosis. PPV = positive predictive value; NPV = negative predictive value; CI = confidence interval; BME = bone marrow edema.

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NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties; **J. Smith**, None; **M. Stoll**, None; **S. Tse**, None; **F. Van den Bosch**, AbbVie, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Galapagos, 2, 6, Gilead, 2, 6; **R. Lambert**, Pfizer, 2; **D. Biko**, None; **N. Chauvin**, None; **M. Francavilla**, None; **J. Jaremko**, MEDO.ai, 8; **N. Herregods**, None; **O. Kasapcopur**, Novartis, 6, Pfizer, 6, Roche, 6, Abbvie, 6; **M. YILDIZ**, None; **A. Hendry**, None; **W. Maksymowych**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Boehringer Ingelheim, 2, Celgene, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Janssen, 2, 6, Novartis, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6.

Abstract Number: 0976

Cumulative Social Disadvantage Predicts an Arthritis Diagnosis: A Cross-sectional Analysis of the National Survey of Children's Health (NSCH)

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Background/Purpose: The impact of social determinants of health in juvenile idiopathic arthritis (JIA) remains poorly understood. Racial disparities exist in JIA, including increased pain and joint damage among Black and Latinx children. Adverse childhood events (ACEs) have been associated with increased odds of childhood arthritis, suggesting an association with chronic stress exposure. However, studies on the impact of poverty and insurance status have yielded mixed results. Data suggests social risk may have a cumulative impact on health, with recent analyses using combined scoring systems to measure social determinants of health. Our aim was to calculate a cumulative social risk score (including income, race/ethnicity, education, and ACE data) and assess its association with arthritis in the National Survey of Children's Health (NSCH).

Methods: This is a cross-sectional analysis utilizing the 2017-2018 version of the NSCH, a federally administered survey focused on physical and emotional health of children 0-17 years of age in the US. Social risk score was generated, with a score of 1 given for each of the following domains: education (high school or less), income level (0-199% of Federal Poverty Level), insurance status (public or uninsured), and high ACE score (4). The cohort was dichotomized by the presence of currently reported arthritis and compared using descriptive statistics (Kruskal Wallis and Pearson's chi-squared or Fisher's exact tests, as appropriate). Univariate and multivariate logistic regression were used to measure the impact of social risk score on the odds of an arthritis diagnosis, controlling for age, sex, and race/ethnicity. An analogous method was used to investigate parent-reported severity of arthritis (moderate/severe versus mild) within the arthritis cohort.

Results: 146 children reported current arthritis, yielding a population estimate of 199,725 children using appropriate survey weights (Table 1). Families of children with arthritis reported lower income (40% vs 28%), lower education level (27% vs 15%), greater likelihood of having public insurance or being uninsured (40% vs 24%), and greater likelihood of having an ACE score ≥4 (16% vs 7%), as compared to children without arthritis (p-value < 0.001). In multivariate logistic regression, higher social risk score was predictive of an arthritis diagnosis (Table 2, p=0.009) with highest

odds among those with a score of 3 (adjusted OR 3.93, p=0.002). Among the arthritis cohort, social risk score predicted increased parent-reported arthritis severity (Table 3), though this was not statistically significant (p=0.2).

Conclusion: In this nationally representative sample, children with arthritis were more likely to come from households with lower income and education level and were more likely to have public insurance or be uninsured, yielding higher social risk scores than their peers without arthritis. In adjusted analysis, social risk factors predicted increased odds

Table 1. Demographic characteristics of the National Survey of Children's Health (NSCH) 2017-2018 by arthritis diagnosis

	Total	No Arthritis	Arthritis	p-value
	N=52,129	N=51,983	N=146	
Age (Mean)	9 (5)	9 (5)	13 (4)	<0.001
Sex				0.001
Male	27,044 (52%)	26,988 (52%)	56 (38%)	
Female	25,085 (48%)	24,995 (48%)	90 (62%)	
Race/ethnicity				0.011
Hispanic	6,099 (12%)	6,082 (12%)	17 (12%)	
White, non-Hispanic	35,977 (69%)	35,882 (69%)	95 (65%)	
Black, non-Hispanic	3,336 (6%)	3,317 (6%)	19 (13%)	
Other/Multi-racial, non-Hispanic	6,717 (13%)	6,702 (13%)	15 (10%)	
Insurance				<0.001
Public health insurance only	10,421 (20%)	10,368 (20%)	53 (36%)	
Private health insurance only	36,775 (71%)	36,701 (71%)	74 (51%)	
Public and private insurance	1,968 (4%)	1,956 (4%)	12 (8%)	
Uninsured	2,227 (4%)	2,221 (4%)	6 (4%)	
Unknown	738 (1%)	737 (1%)	1 (1%)	
Household poverty level				0.006
0-199% FPL	14,625 (28%)	14,566 (28%)	59 (40%)	
200-299% FPL	8,301 (16%)	8,279 (16%)	22 (15%)	
300-399% FPL	7,582 (15%)	7,561 (15%)	21 (14%)	
400% FPL or greater	21,621 (41%)	21,577 (42%)	44 (30%)	
Parental education level				<0.001
High school or less	8,041 (15%)	8,002 (15%)	39 (27%)	
Some college or technical school	12,305 (24%)	12,264 (24%)	41 (28%)	
College degree or higher	31,783 (61%)	31,717 (61%)	66 (45%)	
Cumulative social risk score				<0.001
0	30,474 (58%)	30,415 (59%)	59 (40%)	
1	9,848 (19%)	9,820 (19%)	28 (19%)	
2	7,057 (14%)	7,027 (14%)	30 (21%)	
3+	4,750 (9%)	4,721 (9%)	29 (20%)	
Lower income level	14,625 (28%)	14,566 (28%)	59 (40%)	<0.001
Lower education level	8,041 (15%)	8,002 (15%)	39 (27%)	<0.001
Lower insurance coverage	12,648 (24%)	12,589 (24%)	59 (40%)	<0.001
High ACE score (4+)	3,432 (7%)	3,408 (7%)	24 (16%)	<0.001

Table 2. Using cumulative social risk score to predict an arthritis diagnosis among children in the 2017-2018 National Survey of Children's Health (*Model adjusted for age, sex, and race/ethnicity)

Cumulative social risk	Unadjusted OR	95% CI	p-value	Wald Test	Adjusted OR*	95% CI	p-value	Wald Test
0	—	—	—	0.0048	—	—	—	0.009
1	2.64	1.17-5.94	0.019		2.38	1.06-5.31	0.035	
2	1.50	0.72-3.12	0.274		1.48	0.67-3.27	0.328	
3	4.02	1.76-9.18	0.001		3.93	1.66-9.32	0.002	

Table 3. Using cumulative social risk score to predict moderate to severe versus mild parent-rated severity of arthritis among children with a reported diagnosis of arthritis in the 2017-2018 National Survey of Children's Health (*Model adjusted for age, sex, race/ethnicity)

Cumulative social risk	Unadjusted OR	95% CI	p-value	Wald Test	Adjusted OR*	95% CI	p-value	Wald Test
0	—	—	—	0.167	—	—	—	0.202
1	2.27	0.50-10.17	0.286		0.64	0.15-2.72	0.543	
2	4.30	1.15-16.06	0.030		2.38	0.36-15.76	0.370	
3	3.09	0.64-14.86	0.158		2.73	0.57-13.05	0.209	

of an arthritis diagnosis. There was a trend towards increased parent-reported severity of arthritis among children with more social risk, though this finding did not achieve statistical significance.

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Abstract Number: 0977

Enhancement of Patient and Clinician Partnerships in Juvenile Idiopathic Arthritis Management Using a Point-of-Care Dashboard: Development and Pilot Testing

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SESSION INFORMATION

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Background/Purpose: Health outcomes improve when people living with chronic conditions partner with their clinicians to coproduce care based on their values, preferences, goals, and the best scientific evidence. Patient-facing dashboards can be used to support coproduction by aggregating longitudinal data for review during clinical encounters, such as patient-reported outcomes (PROs), clinical data, and medications. We developed and implemented a point-of-care dashboard to enhance collaboration between families of children with juvenile idiopathic arthritis (JIA) and their clinicians and care teams.

Methods: The dashboard was developed through a co-design process including patients, parents, clinicians, and care team members. Delphi voting achieved consensus on dashboard data elements. The dashboard leveraged an Epic electronic health record (EHR) tool that was customized and integrated at four medical centers. The dashboard resides within each site's EHR and aggregates PROs and clinical data in real-time for review by the family and clinician together (Figure 1). A convenience sample of JIA patients and parents completed an anonymous 19-item feedback survey following their clinic visit to assess the utility and usability of the dashboard. A subset of patients and parents completed 30-minute interviews with the research team. Feedback from clinicians was collected during biweekly meetings, and via surveys and interviews. Data were collected between July 2020 and April 2021.

Results: During the development phase, end-users agreed that a dashboard needed to be easy to use and trend data over time. Data elements included: (1) PROs of pain interference, upper extremity function, mobility, patient questions/concerns, medication adherence, medication side effects; (2) clinical data including active joint count, disease activity score, and liver toxicity; and, (3) current and past medications (Table 1). There was some variability in implementation among sites due to factors such as programmer availability, workflow changes, and clinic staff. During the testing phase, 101 JIA families completed a post-visit feedback survey: 93% agree or strongly agree the dashboard was useful during discussions, 89% indicated that it helped to talk about what mattered most, and 81% reported that it helped to make healthcare decisions. The Net Promoter Score, which rated the likelihood of families to recommend the dashboard to a friend or peer, was a +68 (>50 = excellent). Families valued the ability to share questions/concerns in advance of the visit, insight into clinical assessment data used by clinicians, and visualization of data over time to inform shared treatment decisions with their clinicians.

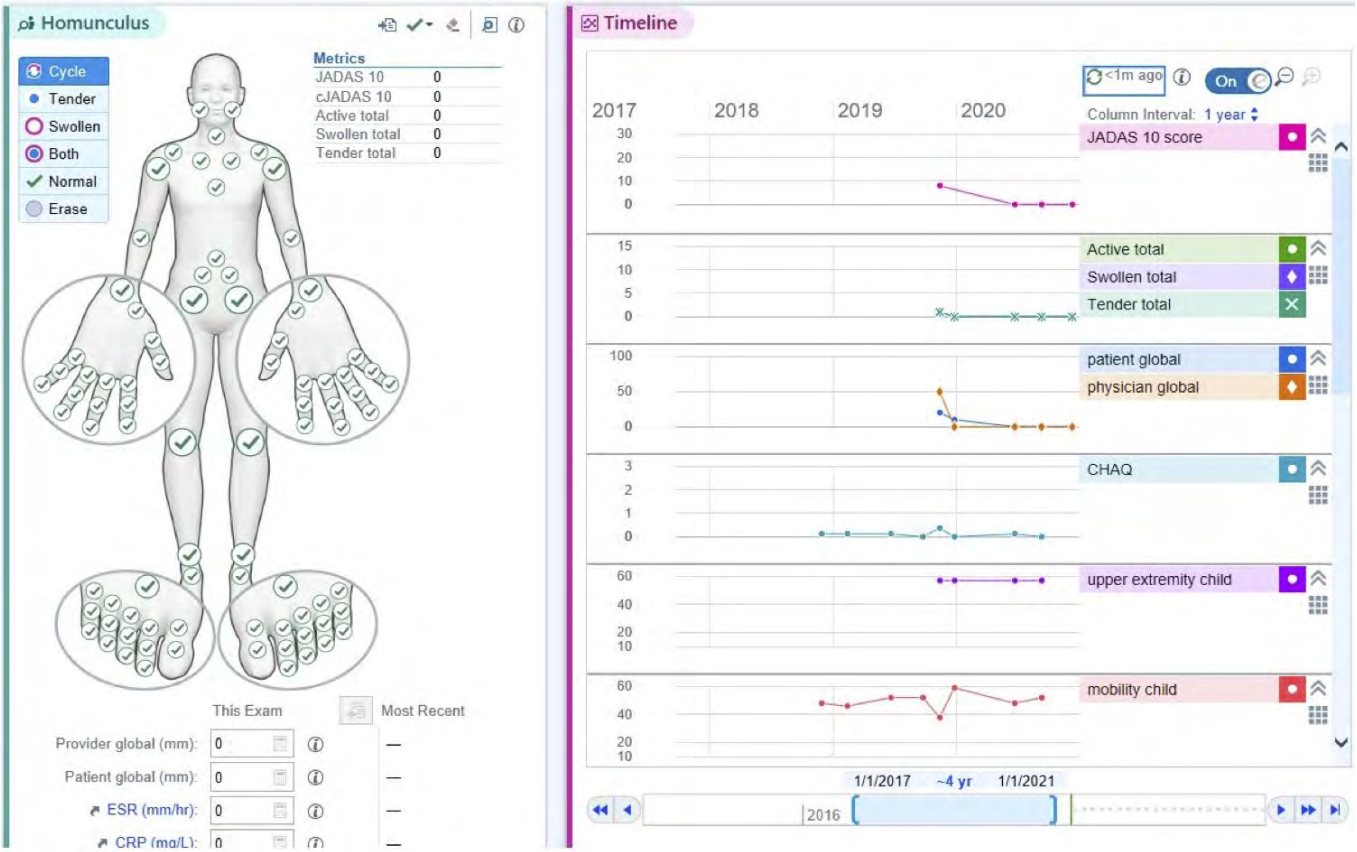

Figure 1. Pediatric Rheumatology Dashboard displaying longitudinal patient-reported and clinical data.

Table 1. Recommended Data Elements for inclusion in the JIA Dashboard

Domain	Data Element Description
Patient-Reported Outcomes	
Concerns, Questions	Free text patient and parent questions or concerns for discussion in the visit
Patient Global Assessment	Ordinal 0-10 scale, indicates patient's overall well-being
Medication Adherence	5-point Likert Scale, indicates how often medications are being taken as prescribed, includes option of "I am not currently taking any prescribed rheumatology medications"
Physical Function	PROMIS 1.0 Pediatric Upper Extremity short form raw summed score; PROMIS 1.0 Pediatric Mobility short form raw summed score
Medication Side Effects	List of symptoms from medications being taken
Pain, Pain Interference	Ordinal 0-10 current rating of pain; PROMIS 1.0 Pain Interference short form raw summed score
Clinical Data	
Joint Count	Total number of tender joints; total number of swollen joints
Provider Global Assessment	Ordinal 0-10 scale, provider's assessment of patient's overall disease activity
Disease Activity	0-30 composite score, incorporates patient global assessment, provider global assessment, joint count
Liver Toxicity	Alanine Aminotransferase (ALT)
Medications	
Medications	Medication name, dose, route, and frequency

Conclusion: Building upon basic Epic functionality, we implemented a JIA dashboard at four sites, informed by a human-centered design approach with a diverse group of stakeholders. Data demonstrated that the dashboard effectively facilitates shared decision making between JIA families and their clinicians. Additional efforts are ongoing to spread the dashboard use to other clinicians and to determine optimal use of the dashboard during telehealth visits.

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Abstract Number: 0978

Immunological and Clinical Features of Untreated Juvenile Dermatomyositis Patients with Elevated Neopterin

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Background/Purpose: Neopterin is a metabolic product of guanosine triphosphate, which is produced by macrophages upon stimulation with interferon-gamma from activated T helper cells. Despite the initial studies showing elevated neopterin in children with active Juvenile Dermatomyositis, the broad adoption of neopterin as biomarkers in clinical practice is still limited. We aim to study the immunological and clinical differences between newly diagnosed JDM patients with elevated and normal serum neopterin levels.

Methods: Children with JDM who had serum neopterin before initiating medical therapy were included. Elevated serum neopterin was defined by levels $\geq$ 10 nmol/l. We assessed T, B, and NK cell populations, Myositis-specific antibodies, Muscle enzymes and Disease Activity Score for skin (sDAS), muscle (mDAS), Total (tDAS). Student's t-test and chi-square to compare the baseline characteristics, disease activity markers, and among the two groups.

Results: 113 subjects (77% female, 77% white, 3.5 % black, 14.2 % Hispanic) were included in this study. 80% of untreated JDM patients had elevated serum neopterin. The mean age of onset was similar in the two groups however the duration of untreated disease was significantly shorter in the patients with elevated neopterin (7.7 months vs 14.1 months p = 0.007). Among the different MSAs group, anti-MJ group has the highest the mean neopterin at 26.7+/- 4.4 nmol/l and the Mi2 group has the lowest level at 14.2 +/- 6.0 nmol/l however the difference was not statistically significant . Also, the group with elevated neopterin had significantly more active disease with mean tDAS 11.7 vs 9.0 (p=0.0009), mDAS 5.7 vs 3.7 (p=0.005), sDAS 6.0 vs 5.4 (p =0.04), CK level 475.9 vs 274.1 IU/L (p= 0.006), Aldolase 21.0 vs 7.8 U/L (p=0.05) and ESR 19 vs 10.7 mm/hr (p=0.01). The flow cytometry showed reduced T cells (1517 vs 2348 /mm3 p < 0.001) and NK cells (144 vs 248 /mm3 p =0.002). TNFalpha-308AA/AG polymorphism was more common in subject with elevated neopterin than TNFalpha-308GG (chi-square p = 0.05). Of note, there was a positive correlation between the levels of serum neopterin and tDAS (R^2 = 0.14, p = < 0.001) and mDAS (R^2 = 0.17, p = < 0.001) but not sDAS.

Conclusion: Elevated serum neopterin is seen in 80 % of untreated JDM. JDM Patients with elevated have more muscle weakness and elevated muscle enzymes. Also, elevated neopterin is associated with an increased frequency of TNFalpha-308AA/AG polymorphism and decreased absolute NK, and T cells count.

Disclosure: A. Khojah, None; **G. Morgan**, None; **L. Pachman**, None.

Abstract Number: 0979

Autoantibody Testing in Juvenile Localized Scleroderma and Systemic Sclerosis: Comparing Antibody Profiles and Clinical Correlations

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SESSION INFORMATION

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Background/Purpose: Pediatric scleroderma encompasses juvenile onset localized scleroderma (jLS) and juvenile onset systemic sclerosis (jSSc), both of which present with varied cutaneous fibrosis and systemic involvement. Autoantibodies (Aab) help serve as a prognostic tool for adult onset SSc disease manifestations; however, their clinical relevance for jSSc and jLS remains unclear. Development of commercially available Aab panels facilitates testing

Table 1: Comparison of Aab frequencies

EUROLINE	Healthy (n=42)	LS (n=143)	SSc (n=75)	FIDIS	Healthy (n=42)	LS (n=143)	SSc (n=75)
Scleroderma-related							
Scl-70	2%	8%	35%	Scl-70	2%	1%	24%
CENP A	0%	9%	11%				
CENP-B	0%	17%	15%	CENP-B	0%	6%	13%
NOR90	0%	10%	5%				
Th/To	2%	1%	0%				
Myositis overlap-related							
PM-Scl75	2%	3%	5%				
PM-Scl100	0%	7%	9%	PMScl	2%	12%	20%
Ku	2%	4%	4%				
				Sm	2%	11%	17%
				Sm-RNP	2%	20%	35%
				Jo-1	2%	0%	1%
Sjogrens/Lupus-related							
Ro-52	2%	3%	7%	Ro-52	0%	6%	11%
				SSA Ro60	0%	1%	1%
				SSB	2%	3%	4%
				ds-DNA	2%	2%	1%
Other							
PDGFR	0%	6%	0%				
RP11	0%	1%	0%				
RP155	2%	3%	5%				
Fibrillarin	0%	0%	0%				
				Histones	2%	0%	0%
				Ribosomal P	2%	14%	21%
				PCNA	0%	6%	7%

Legend

- Euroimmun Assay
- FIDIS Assay
- Significantly more than Control
- Significantly more than both Control and LS

but requires clinical validation in pediatric cohorts. Using two of these panels, we sought to compare Aab profiles between jLS and jSSc, and investigate the association of Aabs in jLS with clinical characteristics.

Methods: Sera from 42 age-matched pediatric healthy controls (HC), 75 jSSc patients, and 143 jLS patients (IRB #STUDY19080297) underwent Aab phenotyping with the FIDIS™(F) Connective Profile addressable laser bead immunoassay (ALBIA) (TheraDiag, Paris, France) and the EUROLINE™(E) SSc Profile line immunoassay (LIA) (Euroimmun, Germany) comprising 26 distinct Aabs. Cutoffs were defined from HC and applied to jLS and jSSc samples to determine Aab positivity. Chi-square analysis was used to compare Aab profiles between cohorts and determine

Table 2: Clinical characteristics based on poly-positivity in localized scleroderma (LS)

Poly-positivity	NSITES	MLOSSI	LOSDI	PGAACT	PGADAMG	PGASEVER
0 Aabs (n=51)						
Median	2	2	5	11	31	38
Interquartile Range	1 - 3	0 - 4	3 - 10	0 - 32.5	26 - 43	30 - 50.75
1 Aabs (n=24)						
Median	3	4	7	23	28	32
Interquartile Range	1 - 5	0 - 8	3.75 - 14.25	0 - 40.75	16.75 - 39.25	25.5 - 49.5
2 Aabs (n=19)						
Median	1	3	5	22	33	49
Interquartile Range	1 - 3	0 - 6.5	2.5 - 8.5	2.5 - 40.5	23.5 - 48	32 - 50
3+ Aabs (n=5)						
Median	2	7	6	41	31	47
Interquartile Range	1 - 2	2 - 7	2 - 7	12 - 63	23 - 49	30 - 63.25

Legend

NSITES	Number of sites
MLOSSI	LS skin severity index
LOSDI	LS damage index
PGAACT	Physician global assessment of disease activity
PGADAMG	Physician global assessment of disease damage
PGASEVER	Physician global assessment of disease severity

significant ($p< 0.05$) relationships with clinical variables. For Aabs significantly higher in frequency than HC, poly-positivity profiles (3 or more Aab) were analyzed.

Results: Overall, Aab were positive in 80% of jSSc patients and 41% of jLS patients. Significant Aab elevation compared to HC, unique to jSSc, included Scl-70 (both), PM-Scl100 (E), PM-Scl (F), Sm (F), and Ro-52 (F) (Table 1). Whereas NOR90 (E) was unique to jLS compared to HC. Shared Aabs between jLS and jSSc, significantly elevated compared to HC, included CENP-A (E), CENP-B (E), Sm-RNP (F) and ribosomal P (Rib P) (F). Among jSSc, the most common Aabs were Scl70 (36%), Sm-RNP (35%), and Rib P (25%). Scl70 was the most common among single positive patients (41%), while combination of Sm-RNP, Sm, and Rib P were present among all polypositive jSSc patients. Most frequent Aabs in jLS were Sm-RNP (20%), CENP-B (17%), and Rib P (15%), with the combination of Sm-RNP/Rib P (53%) in polypositive patients. In jLS, those with 3+ Aabs had significantly elevated skin and global disease activity scores (Table 2). Rib P Aab positivity associated with jLS face/scalp involvement (OR 3.056, 95% CI: 1.16-10.55, p=0.026).

Conclusion: Using two scleroderma-targeted Aab panels, we observed that jLS patients have a lower frequency of Aab positivity compared to jSSc. This jSSc cohort had predominant Scl-70 positivity, as adult SSc, but differs in higher frequency of overlap Aab including PM-Scl and Sm-RNP. jLS patients share a number of Aabs with jSSc, namely Sm-RNP, Rib P, and anti-centromere (CENP-A, CENP-B) suggesting a degree of pathophysiologic overlap. Unique Aab patterns emerged based on the quantity of positive Aabs present and were associated with skin and global disease activity parameters. Rib P Aabs were associated with head involvement among jLS patients. Overall, our findings suggest that the jLS Aab profile is similar, but distinct from, jSSc and may be related to clinical disease characteristics.

Disclosure: J. Li, None; **E. Mirizio**, None; **K. Buhler**, None; **M. Choi**, MitogenDx, 1, 2; **H. Hou**, Mitogen Diagnostics Corp, 3; **G. Werner**, None; **A. Sanyal**, None; **K. Schollaert-Fitch**, None; **M. Fritzler**, Inova Diagnostics Inc., 2, 6, Werfen International, 2, Alexion Canada, 6, Mitogen Diagnostics Corp., 3, 8, 9, 10; **K. Torok**, None.

Abstract Number: 0980

Relationship Between Paraoxonase-1 Genotype, Activity, and Malignancies in Patients with RA Receiving Tofacitinib

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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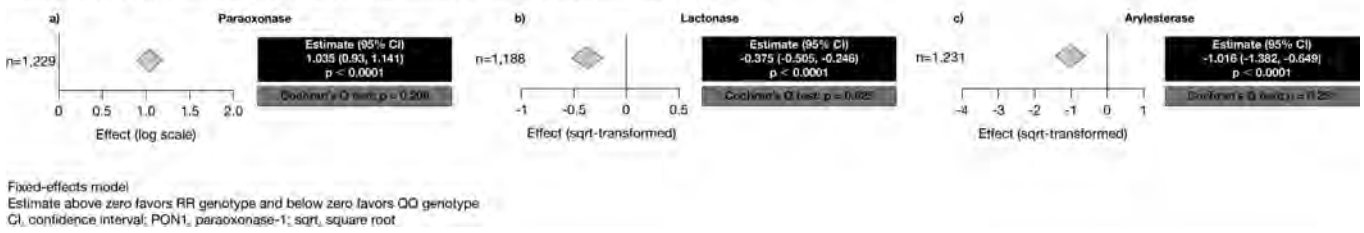
Background/Purpose: Paraoxonase-1 (PON1) is a high-density lipoprotein-associated enzyme with paraoxonase, lactonase, and arylesterase activities.[1] PON1 gene polymorphisms at the Q192R allele (rs662) have been associated with a reduced risk of cancers, although larger samples are needed to confirm any prognostic role.[1,2] This post hoc analysis investigates the relationship between PON1 genotype/activity and risk of malignancies in the tofacitinib RA clinical program.

Methods: Data were pooled from patients (pts) enrolled in 9 Phase 2/3 studies of tofacitinib in RA (completed by March 31, 2015). Enzyme activities in pt plasma samples were measured at individual study baseline (BL), and at follow-up visits, using 3 substrates: paraoxon (paraoxonase activity), dihydrocoumarin (lactonase activity), and phenylacetate (arylesterase activity). The effect of the PON1 Q192R genotype (QQ, QR, or RR) on BL paraoxonase/lactonase/arylesterase activity was assessed using linear regression for each study, with age and sex as covariates; a fixed-effects meta-analysis assessed effects across studies. The risk of malignancies excluding non-melanoma skin cancer (NMSC), and NMSC events by enzyme activity, was determined using Cox proportional hazards regression, stratified by clinical studies. Univariate regression against BL enzyme activity and other risk factors, as well as both minimally and fully adjusted multivariable regressions against time-varying enzyme activity, are presented.

Results: The analysis included 1,969 pts with RA who received ≥ 1 dose of tofacitinib and had ≥ 1 PON1 activity measure available at BL; 53 pts had ≥ 1 malignancy event excluding NMSC, and 56 pts had ≥ 1 NMSC event. Compared with the QQ genotype, the RR genotype had a highly significant positive association with BL paraoxonase activity, and a highly significant negative association with BL lactonase and arylesterase activity (Figure 1). In the univariate analysis, age, RA duration, and smoking status ('ex-smoker/never smoked') were identified as risk factors for both malignancies excluding NMSC (Figure 2) and NMSC (data not shown). Time-varying models found a highly significant association of increased paraoxonase activity over time with lower risk of future malignancies excluding NMSC (Figure 3), but not with NMSC events (data not shown), even after controlling for risk factors including RA duration, age, and smoking status. No such trend was observed for lactonase and arylesterase for malignancies excluding NMSC or for NMSC events (data not shown).

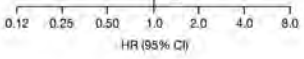
Figure 1. Effect of PON1 Q192R genotype (RR vs QQ) on a) paraoxonase, b) lactonase, and c) arylesterase enzyme activities



Fixed-effects model
Estimate above zero favors RR genotype and below zero favors QQ genotype
CI, confidence interval; PON1, paraoxonase-1; sqrt, square root

Figure 2. Associations between BL covariates and occurrence of malignancies excluding NMSC (univariate analysis)

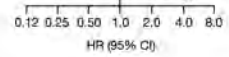
Covariate	Events / Pts	HR	95% CI	p value (nominal)	p value (FDR)
Log(paraoxonase)[a]	52 / 1,898	0.828	(0.624, 1.1)	0.193	0.351
sqrt(lactonase)[a]	51 / 1,826	0.858	(0.646, 1.14)	0.289	0.444
sqrt(arylesterase)[a]	53 / 1,902	0.855	(0.645, 1.13)	0.274	0.444
Age (10 yrs)	53 / 1,905	1.54	(1.19, 2)	0.0012**	0.00801**
Sex (male/female)	53 / 1,905	1.8	(0.97, 3.34)	0.0625	0.156
Average tofacitinib dose (10 mg/5 mg)	53 / 1,905	0.415	(0.213, 0.808)	0.00972**	0.0389*
BMI (kg/m^2)	53 / 1,905	1.04	(1.01, 1.08)	0.0218*	0.0621
RA duration (yrs)	53 / 1,905	1.05	(1.02, 1.08)	0.000365***	0.00365**
Glucocorticoid use (Y/N)	53 / 1,905	1.03	(0.597, 1.79)	0.904	0.951
Methotrexate use (Y/N)	53 / 1,905	1.46	(0.217, 9.85)	0.697	0.775
Statin use (Y/N)	53 / 1,905	1.96	(0.905, 4.26)	0.0879	0.176
Smoking status (ex-smoker/never smoked)	53 / 1,905	2.83	(1.46, 5.49)	0.00213**	0.0106*
Smoking status (smoker/never smoked)	53 / 1,905	3.48	(1.6, 6.73)	0.000208***	0.00365**
Hypertension (Y/N)	53 / 1,905	1.14	(0.656, 1.98)	0.639	0.752
Diabetes (Y/N)	53 / 1,905	1.37	(0.491, 3.61)	0.55	0.752
Total cholesterol[b]	42 / 1,570	0.922	(0.671, 1.27)	0.617	0.752
LDL cholesterol[b]	42 / 1,558	0.927	(0.679, 1.27)	0.632	0.752
HDL cholesterol[b]	42 / 1,569	0.762	(0.558, 1.04)	0.0865	0.176
Triglycerides[b]	42 / 1,570	1.42	(1.08, 1.88)	0.0136*	0.0455*



*p < 0.05, **p < 0.01, ***p < 0.001
[a]All paraoxonase activities were standardized after transformation (mean = 0; SD = 1)
[b]All lipids were log-transformed and standardized (mean = 0; SD = 1)
BL, baseline; CI, confidence interval; FDR, false discovery rate; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; N, no; NMSC, non-melanoma skin cancer; pts, patients; SD, standard deviation; sqrt, square root; Y, yes

Figure 3. Associations between BL and time-varying covariates and occurrence of malignancies excluding NMSC (univariate and adjusted multivariable analyses)

Variable	Model	Events / Observations	HR	95% CI	p value
Time-varying log(paraoxonase)[a]	Univariate	53 / 4,977	0.749	(0.597, 0.94)	0.0126*
Time-varying log(paraoxonase)[a]	Minimally adjusted	53 / 4,977	0.733	(0.574, 0.937)	0.0131*
Time-varying log(paraoxonase)[a]	Fully adjusted	53 / 4,977	0.706	(0.546, 0.912)	0.00773**
Time-varying log(paraoxonase)[a]	Fully adjusted + HDL cholesterol[b]	42 / 4,207	0.75	(0.554, 1.015)	0.0624
Time-varying log(paraoxonase)[a]	Fully adjusted + LDL cholesterol[b]	42 / 4,189	0.73	(0.541, 0.985)	0.0393*
Time-varying log(paraoxonase)[a]	Fully adjusted + total cholesterol[b]	42 / 4,208	0.731	(0.54, 0.988)	0.0416*
Time-varying log(paraoxonase)[a]	Fully adjusted + triglycerides[b]	42 / 4,208	0.746	(0.554, 1.006)	0.0545
Time-varying log(paraoxonase)[a]	Fully adjusted + rs662 in European pts	44 / 3,312	0.726	(0.47, 1.121)	0.149
BL log(paraoxonase)[a]	Fully adjusted BL model	52 / 1,898	0.846	(0.638, 1.122)	0.247
BL log(paraoxonase)[a]	Fully adjusted BL model + rs662	43 / 1,229	0.989	(0.66, 1.48)	0.956
rs662 QR vs QQ[c]	rs662 multivariate BL model	44 / 1,233	0.877	(0.464, 1.659)	0.687
rs662 RR vs QQ[c]	rs662 multivariate BL model	44 / 1,233	0.668	(0.199, 2.241)	0.514
rs662 QR vs QQ[c]	Fully adjusted + rs662 in European pts	44 / 3,312	1.172	(0.558, 2.46)	0.675
rs662 RR vs QQ[c]	Fully adjusted + rs662 in European pts	44 / 3,312	1.048	(0.272, 4.034)	0.945
HDL cholesterol[b]	Fully adjusted + HDL cholesterol[b]	42 / 4,207	0.815	(0.602, 1.103)	0.185
LDL cholesterol[b]	Fully adjusted + LDL cholesterol[b]	42 / 4,189	0.823	(0.609, 1.112)	0.205
Total cholesterol[b]	Fully adjusted + total cholesterol[b]	42 / 4,208	0.765	(0.555, 1.054)	0.102
Triglycerides[b]	Fully adjusted + triglycerides[b]	42 / 4,208	1.132	(0.846, 1.515)	0.403
Age (10 yrs)	Fully adjusted	53 / 4,977	1.417	(1.064, 1.887)	0.0172*
RA duration (yrs)	Fully adjusted	53 / 4,977	1.054	(1.025, 1.084)	0.000205***
Average tofacitinib dose (10 mg/5 mg)	Fully adjusted	53 / 4,977	0.474	(0.245, 0.919)	0.0271*
Smoking status (ex-smoker/never smoked)	Fully adjusted	53 / 4,977	2.558	(1.287, 5.084)	0.00736**
Smoking status (smoker/never smoked)	Fully adjusted	53 / 4,977	4.544	(2.296, 8.995)	1.39e-05***



*p < 0.05, **p < 0.01, ***p < 0.001
Minimally adjusted model covariates: tofacitinib dose (10 mg/5 mg) and age
Fully adjusted model covariates: tofacitinib dose (10 mg/5 mg), age, RA duration, and smoking status
[a]All paraoxonase activities were standardized (mean = 0; SD = 1)
[b]All lipids analyzed were time-varying, log-transformed, and standardized (mean = 0; SD = 1)
[c]Analysis only conducted in European population
BL, baseline; CI, confidence interval; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; NMSC, non-melanoma skin cancer; pts, patients; SD, standard deviation

Conclusion: In this post hoc analysis, higher paraoxonase activity over time was associated with a significantly reduced risk of future malignancies excluding NMSC in pts with RA receiving tofacitinib, after controlling for risk factors such as RA duration, age, and smoking. Based on these findings, further investigation of PON1 as a novel functional lipid biomarker to assess malignancy risk in pts with RA is warranted.

1. Mackness M & Mackness B. Gene 2015; 567: 12-21

2. Pan X et al. Biomed Res Int 2019: 2019: 5897505.

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Abstract Number: 0981

Clinical and Economic Burden of Herpes Zoster in Patients with Rheumatoid Arthritis: A Retrospective Cohort Study Using Administrative Claims

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
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Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Inflammatory arthritis (IA) is an autoimmune disease targeting multiple joints and characterized by joint destruction caused by osteoclasts (OC), leading to physical disability. However, the precise cellular origins of OC are poorly understood. Myeloid lineage cells including OC and macrophages can derive from either hematopoietic stem cells (HSC) or erythro-myeloid progenitors (EMP). Previous studies in vitro suggest that in IA, HSC-derived monocytes differentiate into OC and others showed that macrophages can fuse to form OC under the influence of inflammatory cytokines. We hypothesized that in IA, embryonically derived Erythro-Myeloid Progenitor macrophages and Hematopoietic Stem Cell-derived progenitors can independently contribute to the formation of OC in vivo. These cell lineage tracing systems will allow to discriminate among distinct OC populations by their cell surface phenotype and selectively target them for therapeutic purpose.

Methods: To test this hypothesis, we used bone frozen sections and immunofluorescence, as well as flow cytometry (FACS) from cell lineage tracing systems, to discriminate among these progenitors. We used $Flt3^{Cre}$;$Rosa26^{LSL\text{-}YFP}$mice to label HSC and their progeny and both $Csf1r^{Mer\text{-}iCre\text{-}Mer}$;$Rosa26^{LSL\text{-}tdTomato}$ and $Cx_3cr_1^{CreERT2}$;$Rosa26^{LSL\text{-}tdTomato}$ mice, pulsed with 4-hydroxytamoxifen at E8.5 and E9.75 respectively, to label EMP-derived progenitors.

Results: Histology of ankle joints from healthy $Flt3^{Cre}$;$Rosa26^{LSL\text{-}YFP}$ embryos at E16.5, newborn at P0 and 8 week-old mice showed that ~7 % of synovial F4/80+ or CD68+ cells were of HSC origin, suggesting that EMPs are the major source of synovial macrophages. We confirmed, using both $Csf1r^{Mer\text{-}iCre\text{-}Mer}$;$Rosa26^{LSL\text{-}tdTomato}$ and $Cx_3cr_1^{CreERT2}$;$Rosa26^{LSL\text{-}tdTomato}$ mice, that ~40% of all F4/80+ synovial macrophages were TdTomato+, showing for the first time an EMP-origin. To test the HSC origin of OC in IA, adult $Flt3^{Cre}$;$Rosa26^{LSL\text{-}YFP}$ mice were treated with K/BxN arthritogenic serum and

Figure 1a. Study schematic for patients with RA and HZ

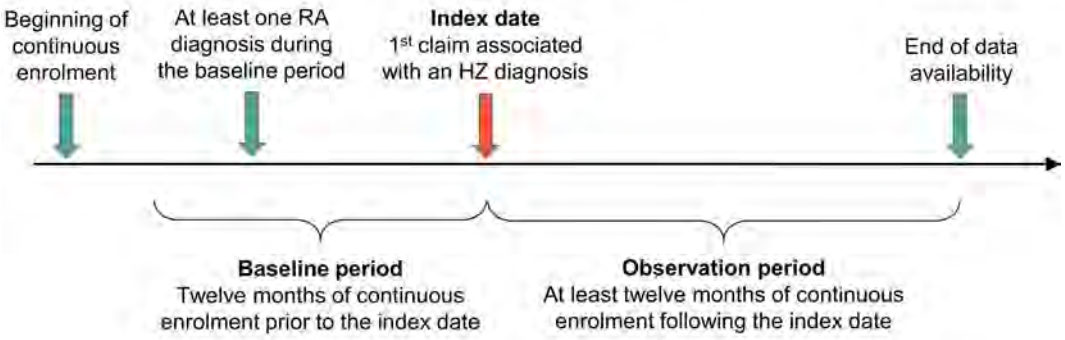
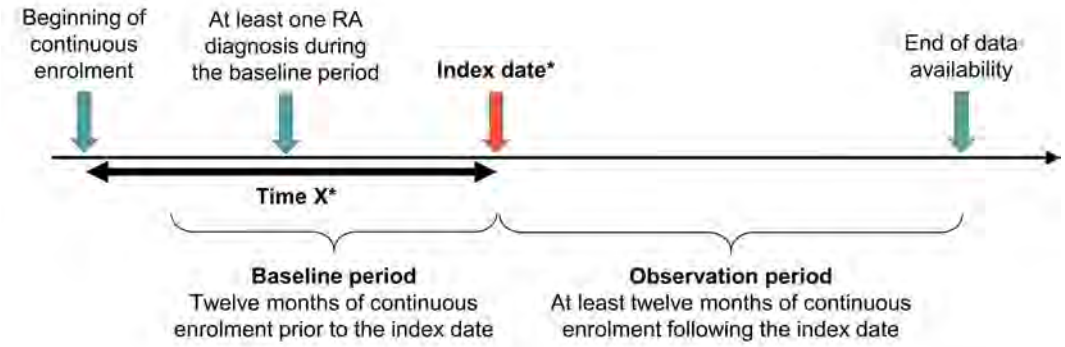


Figure 1b. Study schematic for patients with RA only



***The index date was randomly assigned based on the distribution of time from the start of continuous enrolment to index date in the RA and HZ cohort. Time X represents this distribution of time from the beginning of continuous enrolment to the assigned index date.**

HZ, herpes zoster.

ankle joints were harvested at day 10 (peak inflammation). Unexpectedly, we found that only 56% of OC were YFP-positive, indicating that a large proportion of synovial OC are not HSC-derived. Further, we identified CD68+TRAP+ cells localized to periosteal surfaces as candidate progenitors of synovial OC. Consistent with the dual origin of synovial OC, CD68+TRAP+ progenitors derive from both HSC (27%) and non-HSC (73%) lineages.

Conclusion: These data suggest that both HSC-derived and EMOP-derived osteoclast precursor cells independently contribute to OC formation in IA. These cell lineage tracing systems will help us to identify unique differences among OC of distinct origins. These differences will allow for differential targeting of OC via unique cell surface markers and for the development of new targets to inhibit OC formation and prevent bone and cartilage erosions in IA.

Table 1. Baseline demographic, clinical, and cost information for patients with RA and HZ and patients with RA only

	RA and HZ (n=1,866)	RA only (n=38,846)	Standardized difference[1]
Age, mean (SD)	68.3 (11.6)	66.2 (12.7)	17.1%
Female, n (%)[2]	1,489 (79.8)	29,521 (76.0)	9.2%
Geographic region, n (%)			
South	806 (43.2)	17,595 (45.3)	4.2%
West	461 (24.7)	8,943 (23.0)	3.9%
Midwest	421 (22.6)	8,633 (22.2)	0.8%
Northeast	178 (9.5)	3,655 (9.4)	0.4%
Unknown	0 (0.0)	20 (0.1)	3.2%
Index year, n (%)			
2016	167 (8.9)	2,430 (6.3)	10.2%
2017	745 (39.9)	15,285 (39.3)	1.2%
2018	825 (44.2)	18,533 (47.7)	7.0%
2019	129 (6.9)	2,598 (6.7)	0.9%
Insurance type n (%)			
Medicare advantage	1,338 (71.7)	26,166 (67.4)	9.4%
Commercial	528 (28.3)	12,680 (32.6)	9.4%
Modified Charlson-Quan comorbidity index, mean (SD)[3]	1.3 (1.7)	1.1 (1.6)	10.2%
Use of RA-related medications at index, n (%)			
NSAIDs	435 (23.3)	8,063 (20.8)	6.2%
Systemic steroids	731 (39.2)	11,013 (28.4)	22.9%
Conventional synthetic DMARDs	1,046 (75.3)	29,055 (74.8)	1.3%
Biologic DMARDs	555 (29.7)	11,382 (29.3)	1.0%
Targeted synthetic DMARDs (JAK inhibitors)	86 (4.6)	1,011 (2.6)	10.8%
Total costs, mean (SD)	$52,625 (67,774)	$46,332 (65,480)	9.4%

[1]For continuous variables, the standardized difference was calculated by dividing the absolute difference in means of cohorts RA+HZ vs RA only by the pooled SD of both groups. The pooled SD was the square root of the average of the squared SDs. For categorical variables with two levels, the standardized difference was calculated using the following equation where P_1 was the proportion of participants with an event in cohort RA+HZ, and P_2 was the proportion of participants with an event in cohort RA only: $(P_1-P_2)/\sqrt{p(1-p)}$, where $p = (P_1+P_2)/2$.
[2]One patient in cohort RA only had "unknown" gender and was imputed "female" gender.
[3]The Modified Charlson-Quan comorbidity index excluded rheumatologic disease.
Standardized differences of 20%, 50% and 80% can be interpreted to represent small, medium and large differences, respectively (Cohen J. Statistical Power Analysis for the Behavioral Sciences. 2nd edition: Lawrence Erlbaum Associates; 1988.).

HZ, herpes zoster; JAK, Janus kinase; n, number; NSAIDs, non-steroidal anti-inflammatory drugs; SD, standard deviation.

Table 2. Healthcare resource use and costs during 12 months after index date for patients with RA and HZ and patients with RA only

	RA and HZ (n=1,866)	RA only (n=38,846)	
HCRU, n (%) of patients			P-value (unadjusted, chi-square test)
Inpatient admissions	405 (21.7)	6,301 (16.2)	<0.001
ED visits	770 (41.3)	11,810 (30.4)	<0.001
Outpatient Visits	1,866 (100.0)	38,508 (99.1)	<0.001
HCRU, Incidence rate PPPY			Adjusted incidence rate ratio (95% CI)[2]
Inpatient admissions	0.33	0.24	1.16 (1.04, 1.30)
ED visits	1.03	0.77	1.34 (1.21, 1.47)
Outpatient visits	26.33	22.22	1.11 (1.08, 1.14)
Costs, mean (SD)[1]			Adjusted cost difference (95% CI)[3]
Total costs	$57,291 (75,481)	$50,562 (75,213)	$3,325 (-58, 7,345)
Medical costs	$40,033 (69,732)	$33,404 (68,319)	$3,428 (446, 6,781)
Inpatient	$19,511 (56,906)	$15,310 (56,037)	$1,953 (-17, 4,473)
ED	$2,870 (8,429)	$1,832 (5,501)	$705 (430, 1,003)
Outpatient	$16,790 (26,179)	$15,459 (28,775)	$168 (-798, 1,118)
Pharmacy costs	$17,258 (29,997)	$17,158 (31,295)	-$833 (-1,846, 386)

[1]All costs are presented in 2020 US Dollars.
[2]Adjusted incidence rate ratios are calculated using generalized linear model assuming a negative binomial distribution and log link, controlling for propensity score and key baseline measures. Propensity scores included variables selected based on expert review.
[3]Cost differences were estimated using the two-part modelling approach: (1) In the first part, the probability of observing a positive cost was modelled using logistic regression; (2) in the second part, a generalized linear model with a gamma distribution and log link was used to predict costs among patients with positive costs. Both models included the patients' propensity scores and relevant baseline characteristics. The 95% CI and approximate p-values were estimated from nonparametric bootstrap procedures with 499 replications.

CI, confidence interval; ED, emergency department; HCRU, healthcare resource use; HZ, herpes zoster; n, number; SD, standard deviation; PPPY, per patient per year; US, United States.

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Abstract Number: 0982

B Cells Repertoire Repartition Predicts Response to Methotrexate at 6 and 12 Months in Naïve RA: A Machine Learning Driven Approach

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: The adaptive immune system plays a central role in Rheumatoid Arthritis (RA) pathogenesis. Moreover, the composition of the B cell repertoire and its perturbation are known to exist across disease phenotypes (i.e., ACPA positive versus ACPA negative). However, the influence of underlying B-cell repertoire changes in RA according to their response to treatment, and the ability of these to constitute as predictive biomarkers of response to Methotrexate (MTX) are not yet known. The objective of this analysis was to create a nomogram capable of predicting response to MTX at 6 and 12 months based on properties of the baseline B cell repertoire.

Methods: Peripheral blood leukocytes (PBL) from patients from the Scottish Early Rheumatoid Arthritis SERA cohort (1) were included in the analysis and classified into 3 categories according to their response to MTX measured by CDAI or DAS 28 at 6 and 12 months: responders (n=36), non-responders (n=35) and relapsing responders (n=28). BCR sequence repertoires were explored through IGH sequencing via the IGH-LR assay and the Gene Studio S5, sequencing to a target of 1.5M reads per sample. Data were analyzed via Ion Reporter 5.12 and 5.16. A gradient-boosting supervised learning method was used to build a prediction model of MTX response at 6 months and 1 year.

Results: 99 patients, with a mean age of 60.5 (SD 13.72) were included for analysis. Of interest, differences in class-switching and repartition of naïve B cells were observed across all groups. Notably, untreated patients displayed higher levels of IgA, IgE and IgG clones compared to after 12 months of MTX (p=0.003). At baseline, isotypes were more frequently switched towards IgA, IgE and IgG in non-responders than responders (p=0.008). Baseline levels of circulating IgD+ B cells clones were more frequent in responders compared to non-responders (p=0.004) while IgA1+ and IgA2+ clones tended to be more frequently represented in non-responders (p=0.069 and p=0.001 respectively). Over the course of the treatment with MTX, responders and non-responders tended to show an increased frequency of IgM+IgD+ clones whilst a depletion in IgG1+ clones was observed only in responders (p=0.034). In the relapsing responders' group, no significant depletion at both 6 and 12 months was observed. When analyzing somatic hypermutation (SHM) levels in the BCR variable regions, the levels of SHM were consistently lower in non-responders compared with responders, although the number of SHM tended to increase over time for most isotypes. The top

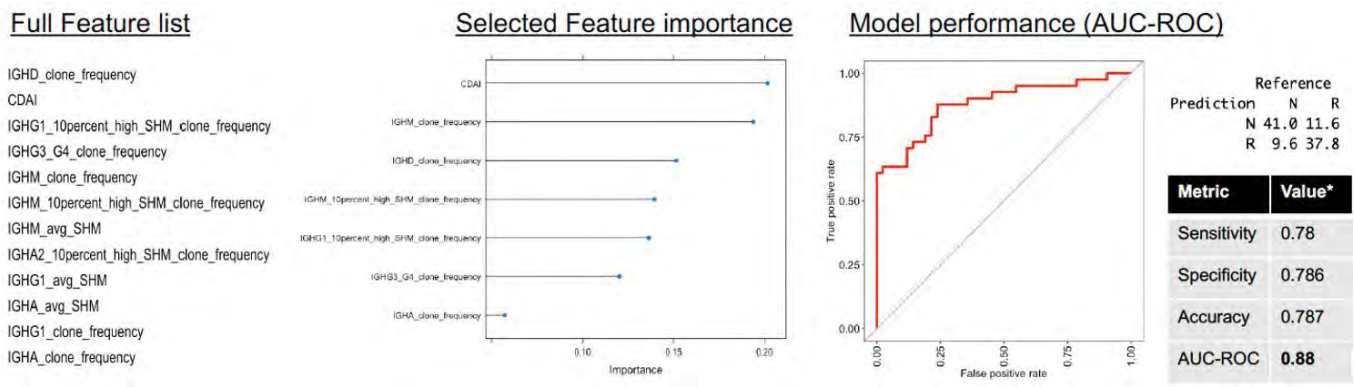

Figure 1. Final Prediction Model For Patient Response to Methotrexate. AUC: area under the curve; SHM: somatic hypermutations.

7 baseline features were selected from a preliminary random forest model: IgM, IgD, IgG3, IgG4 and IgA clone frequency, frequency of IgM and IgG clones with >10% SHM and CDAI. Additional training and optimization of a new gradient boosting model, revealed that the response to MTX in the cohort could be predicted with a sensitivity of 0.78, a specificity of 0.786 and an area under the curve of 0.88 (Figure 1).

Conclusion: This model, based on an innovative machine learning approach in conjunction with a cutting-edge B cell repertoire analysis in RA, constitute the first immunology-based prediction model for response to MTX to our knowledge. This could be further used for personalized therapy in RA.

Disclosure: A. Najm, UCB, 1, Bristol-Meyers Squibb, 1, 6, Novartis, 5; **S. Sarda**, None; **M. Toro**, None; **L. Pickle**, None; **S. Ostresh**, None; **F. Morton**, None; **G. Lowman**, None; **A. Felton**, None; **C. Goodyear**, Astra Zeneca, 5, Bristol-Meyers Squibb, 5, Galvani, 5, Istesso, 5, Janssen, 5, Lilly, 1, 5, MedAnnex, 1, 5, MedinCell, 1, MiroBio, 1, Oxford BioDynamics, 5, ThermoFisher, 5, UCB, 5.

Abstract Number: 0983

Anti-S1 Antibodies After Vaccination with Anti SARS-CoV-2 mRNA Vaccines in Patients with Rheumatoid Arthritis Differ in Magnitude and Kinetics from Healthy Controls: Results from a Prospective, Observational Controlled Study

Andrea Rubbert-Roth[1], Nicolas Vuilleumier[2], Burkhard Ludewig[3], Kristin Schmiedeberg[4], Yella Rottlaender[4], Ian Pirker[5] and Johannes VonKempis[6], [1]Kantonspital St Gallen, St.Gallen, Switzerland, [2]Departement Diagnostique, University of Geneva, Switzerland, Geneva, Switzerland, [3]Institute of Immunobiology, Cantonal Hospital St Gallen, St Gallen, Switzerland, [4]Division of Rheumatology, Cantonal Hospital St Gallen, St Gallen, Switzerland, [5]Kantonsspital St. Gallen, St.Gallen, Switzerland, [6]Division of Rheumatology and Immunology, St. Gallen, Switzerland

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes I: Bugs & Drugs (0980–0983)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Long-term vaccine-induced immunity to SARS-CoV-2 is critical to combat the pandemic. Vaccination against anti SARS-CoV-2 is recommended in patients with rheumatic diseases, but limited data are

Table 1. Baseline characteristics of RA patients and healthy control individuals

	RA patients (n=77)	Healthy controls (n=21)	p-value
Age (yrs), mean (± SD)	64 (12.5)	44.1 (13.8)	< 0.0001
Female sex, n (%)	46 (59.7)	15 (71.4)	0.45 (NS)
Vaccination type/schedule			
mRNA-1273, n (%)	12 (15.6)	0 (0)	0.06
BNT162b2, n (%)	65 (84.4)	21 (100)	
Mean interval between 1st vaccination and sampling (days ± SD)	21.4 ± 2.3	21.8 ± 2	0.33 (NS)
Mean interval between 2nd vaccination and sampling (days ± SD)	14.9 ± 2.5	15.1 ± 1.6	0.22 (NS)
Mean interval between 1st and 2nd vaccination (days ± SD)	34.5 ± 4	32.9 ± 5.9	0.15 (NS)
RA disease characteristics			
ACPA ± RF, n (%)	47/75 (62.7)	NA	
RA disease duration (yrs ± SD)	9.2 (8.7)	NA	
DMARD therapy			
Monotherapy of csDMARDs, n (%)	22/77 (28.6)	NA	
bDMARDs, n (%)	35/77 (45.5)	NA	
Monotherapy of bDMARDs, n (%)	14/35 (40)	NA	
JAK inhibitors, n (%)	20/77 (26)	NA	
Monotherapy of JAK inhibitors, n (%)	8/20 (40)	NA	
Prednisone, n (%)	25/77 (32.5)	NA	
Mean daily dose prednisone (mg ± SD)	5.6 ±3.6		

Table 2. Anti-S1 levels (U/l) in RA patients and healthy control individuals

	RA patients (n=77)	Healthy controls (n=21)	p-value
Baseline (pre-vaccination), n (%)	0.4 (100)	0.4 (100)	NS
Anti-NP at baseline, n (%)	4/77	0/21	NS
3 weeks after 1st vaccination			
median (IQR) (n = 73)	0.4 (0.4-4.65)	115 (24.8-172)	p < 0.00001
% of patients > 133 U/l, n (%)	1/73 (1.4)	9/21 (42.9)	p = 0.0001
% of patients > 15 U/l, n (%)	11/73 (15.1)	19/21 (90.5)	p < 0.0001
2 weeks after 2nd vaccination			
median (IQR) (n = 73)	657 (135-2500)	2500 (2500-2500)	p < 0.0001
% of patients > 133 U/l, n (%)	55/73 (75.3)	21/21 (100)	p= 0.01
% of patients > 15 U/l, n (%)	63/73 (86.3)	21/21 (100)	p= 0.11 (NS)
12 weeks after 1st vaccination			
median (IQR) (n = 43)	293 (121-1218)	2243 (1394-2500)	p < 0.00001
% of patients > 133 U/l, n (%)	31/43 (72.1)	20/20 (100)	p = 0.007
% of patients > 15 U/l, n (%)	39/43 (90.7)	20/20 (100)	p = 0.3 (NS)

available in patients on immunosuppressive therapy. The objective of this study is to analyse magnitude and kinetics of mRNA vaccine induced anti-S1 titers in patients with rheumatoid arthritis (RA) on DMARD therapy and healthy controls (HC).

Methods: 77 consecutive RA patients and 21 HC were eligible for vaccination according to federal guidelines and were enrolled in the prospective RECOVER trial (Rheumatoid>Covid-19 Vaccine Immune>Response) between 10th January and March 15th 2021. Vaccination itself was not part of the study. The anti-SARS-CoV-2 vaccines mRNA-1273 and BNT162b2 were applied according to the manufacturers` recommendations. All patients continued their DMARD therapy, patients on rituximab were excluded. Serum samples were obtained before the first vaccine, 3 weeks after

the first, 2 weeks after the second vaccine and after 12 weeks. Quantitative antibody testing was performed using the Roche Elecsys® Anti-SARS-CoV-2 S1 assay that measures antibodies to the S1 protein (range 0.4-2500 U/l) and nucleoprotein to exclude subclinical SARS-CoV-2 infection. A threshold level of anti-S1 that correlates to neutralization has been proposed at 133 U/l.[1] . More recently, even lower cut-off levels (>15 U/l) have been suggested.[2]

Results: Baseline characteristics are summarized in Tab. 1. Levels of anti-S1 antibodies after vaccination are presented in Table 2. 4/77 patients with antibodies to nucleoprotein at baseline were excluded from the analysis. At present, 43/73 patients reached the 12 week timepoint after the first vaccine dose. Median titers of anti-S1 antibodies were significantly lower in RA patients at all time points. 3 weeks after the first vaccine dose, 9/21 HC but only 1/73 RA patients developed anti-S1 titers exceeding 133 U/l (p = 0.0001) or 15 U/l (19/21 HC versus 11/73 RA patients). Two weeks after the second vaccine, the proportion of RA patients with anti-S1 titers exceeding 133 u/l was still significantly lower than in HC (75.3% versus 100%, p = 0.01). Of note, significantly fewer RA patients on abatacept (n=9) or JAK inhibitors (n = 19) achieved both threshold levels compared to patients on csDMARDs and/or anti-cytokine directed biologics.

Conclusion: The development of anti-S1 titers after vaccination with mRNA vaccines against SARS-CoV-2 in patients with RA is overall slower and results in lower antibody titers in comparison to healthy controls. Our data suggest that patients on abatacept or on JAK inhibitors have an increased risk of an impaired anti-S1 response compared to RA patients on csDMARDs or anti-cytokine directed biologics. Strategies need to be developed to optimize vaccine induced humoral immunity in patients with RA.

Ref.: [1]Resman Rus K et al *J Clin Virol 2021*, [2]Rubio-Acero R et al *medRxiv 2021*

Disclosure: A. Rubbert-Roth, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 2, 6, Roche, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sanofi, 2, 6, Amgen, 2, 6, Novartis, 2, 6; **N. Vuilleumier**, None; **B. Ludewig**, None; **K. Schmiedeberg**, None; **Y. Rottlaender**, None; **I. Pirker**, None; **J. VonKempis**, None.

Abstract Number: 0984

Human Papillomavirus Infection Increases Risk of Primary Sjogren's Syndrome: A Population-based Cohort Study over a 15-year Follow-up

Kevin Sheng-Kai Ma, Center for Global Health, Perelman School of Medicine, University of Pennsylvania, Philidelphia, PA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science (0984–0987)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Viral infection has been considered as an exogeneous risk factor for primary Sjogren's syndrome (pSS). We determined whether human papillomavirus (HPV) infection was associated with the risk of pSS in this population-based propensity score-matched cohort study.

Methods: In this cohort study, 47,300 patients with HPV infection and 189,200 propensity score-matched controls without HPV infection were enrolled. A Cox proportional hazard model was utilized to estimate the risk of pSS and survival analysis was adopted to assess the time-dependent effect of HPV infection on pSS. Subgroup analyses stratified by age, gender, and follow-up years were conducted to identify susceptible populations.

Results: Of all patients with HPV, 493 developed pSS (incidence rate=13.61 per 100,000 person-months, 95%CI=12.46-14.86). Patients with HPV infection were more likely to develop pSS than controls without HPV infection (incidence rate ratio=1.81, 95%CI=1.63-2.01; hazard ratio, HR =1.64, 95% CI =1.47–1.83, P < 0.0001), which persisted in the survival analysis (log-rank test P < 0.0001). The effect of HPV on pSS was significant in HPV-infected patients from both genders and all age subgroups, including male patients (HR=1.83, 95% CI = 1.47–2.28, P < 0.0001), female patients (HR=1.58, 95% CI = 1.40–1.79, P < 0.0001), patients aged between 16 and 45 (HR=1.60, 95% CI = 1.34–1.91, P < 0.0001), and patients older than 45 (HR=1.67, 95% CI = 1.46–1.91, P < 0.0001), all compared with respective matched controls without HPV infection.

Conclusion: This is the first longitudinal study that addresses the relationship between HPV infection and risk of pSS. Based on the observed relationship, regular follow-up in the rheumatology clinic is recommended for patients with HPV infection.

Disclosure: K. Ma, None.

Abstract Number: 0985

Sjögren's Symptom Burden Drives Immunomodulatory Therapies but Correlates Poorly with Disease Severity Markers

Sara McCoy[1], Miguel Woodham[1], Ian Saldanha[2], Esen Akpek[3], VATINEE BUNYA[4] and Alan Baer[5], [1]University of Wisconsin, Madison, WI, [2]Brown University School of Public Health, Providence, RI, [3]Wilmer Eye Institute, JHU, Baltimore, MD, [4]University of Pennsylvania, Penn Valley, PA, [5]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science (0984–0987)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Sjögren's syndrome (SS) patients have lower quality of life driven by symptoms of pain, depression and fatigue. These symptoms often do not respond to traditional immunosuppressive therapy and may not be effectively addressed by physicians, driving a discordance between patient and provider expectations. Classification of SS patients into symptom-based categories has the potential to increase patient-provider harmony and impact therapeutic strategies. Our objective was to define relevant differences between clusters with respect to symptoms, treatment, disease activity, and laboratory profile.

Methods: We used the Sjögren's International Collaborative Clinical Alliance (SICCA) registry to analyze 1,541 adults fulfilling the 2016 ACR/EULAR criteria for SS. Unsupervised hierarchical clustering was applied to identify the optimal phenotypically similar clusters by: 1) dryness (a composite score derived from Vitali C et al. 2002 consensus criteria ranging 0-100), 2) fatigue (5-point Likert scale from "not at all" to "nearly every day"), and 3) pain (5-point Likert scale from "not at all" to "extremely"). We reported demographic features, symptoms, medication use, organ involvement and laboratory values within each cluster. We used ANOVA or Chi-square to identify cluster differences, controlling for recruitment site, age, sex, race, ethnicity and education.

Results: The analysis yielded 4 clusters among 1,454 participants with complete data on the 3 key symptoms (Figure 1). Clusters were characterized by low symptom (LS; 10% prevalence) and high symptom frequency/severity (HS; 37%) in all categories; high pain (HP; 23%) and low pain (LP; 30%). Depression, measured by mean PHQ9, was

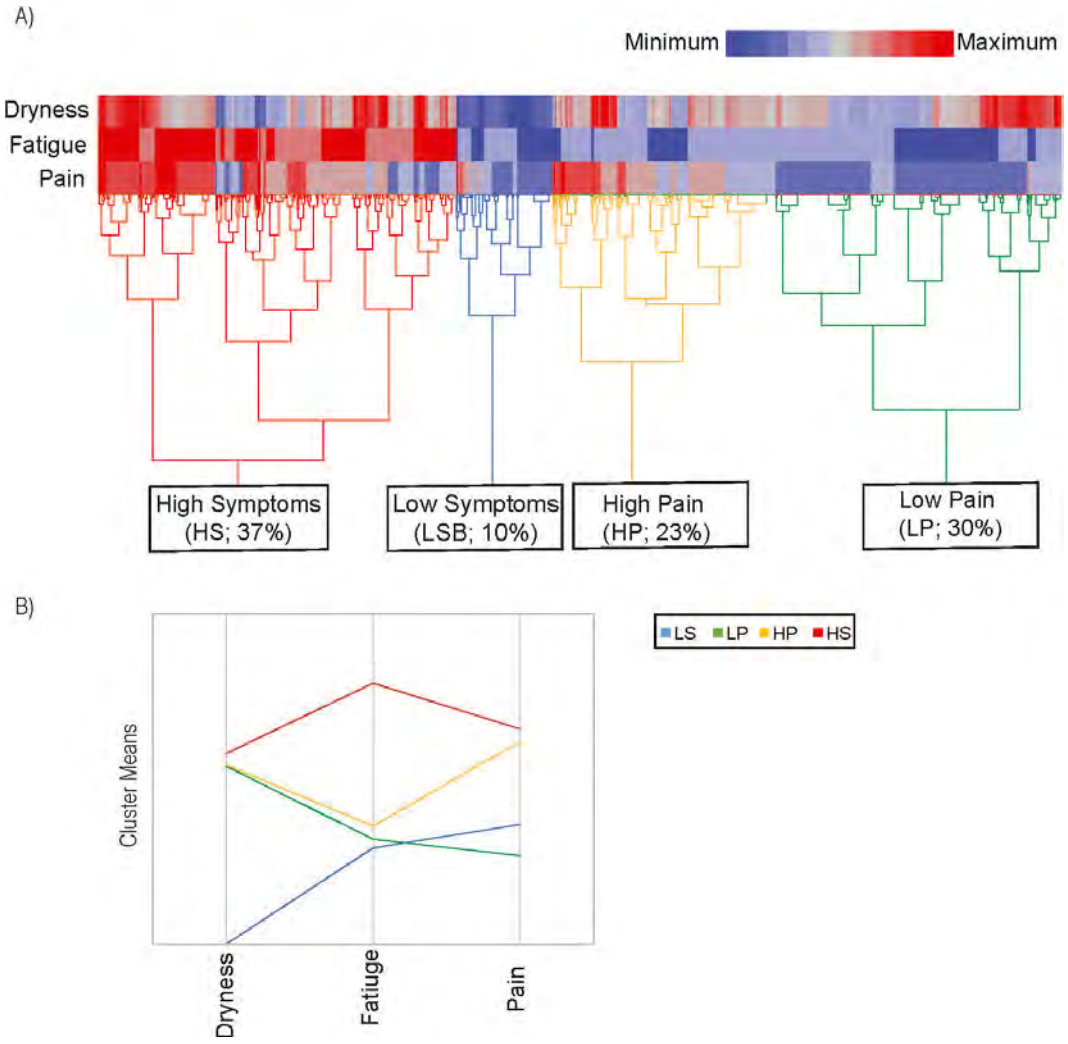

Figure 1. SS symptom-based hierarchical clusters. A) Clusters identified by Ward's method and generated on symptoms including dryness (a composite score of five questions: 1. presence of dry mouth, 2. need sips of liquid to swallow food, 3. presence of dry eye, 4. presence a gritty sensation in eyes, and 5. use of tear substitutes), fatigue (Likert from none of the time to all of the time) and pain (Likert from none of the time to all of the time); B) Cluster means for low symptoms (LS), low pain (LP), high pain (HP), and high symptoms (HS).

worse in the HS group (11.3) compared to the LS group (2.2) ($p< 0.0001$). Health related quality of life, measured by the short form (SF) 12 (6 questions related to physical health, 5 question to mental health, and 1 question to both), was best in the LS group (mental) and LP group (physical) (Figure 2). The HP group was treated with corticosteroids and DMARDs most (20% & 6%). Extraglandular manifestations occurred most often in the LP group, though not reaching significance due to low frequencies of these manifestations (Figure 3A). Interestingly, synovitis occurred most frequently in the HP group (11%). Both the LS and LP groups had higher IgG than the HS and HP groups (Figure 3 B&C). Rheumatoid factor and focus scores were highest in the LP group (Figure 3 D&E).

Conclusion: Here we identify four clusters of SS patients based on dryness, pain and fatigue severity and show that symptom burden does not correlate well with traditional disease markers of severity. Additionally, treatments differed by cluster. The HP group received DMARDs and steroids most often; however, the LP group had the most prominent organ involvement and laboratory abnormalities, yet received immune modulating medication less frequently than the

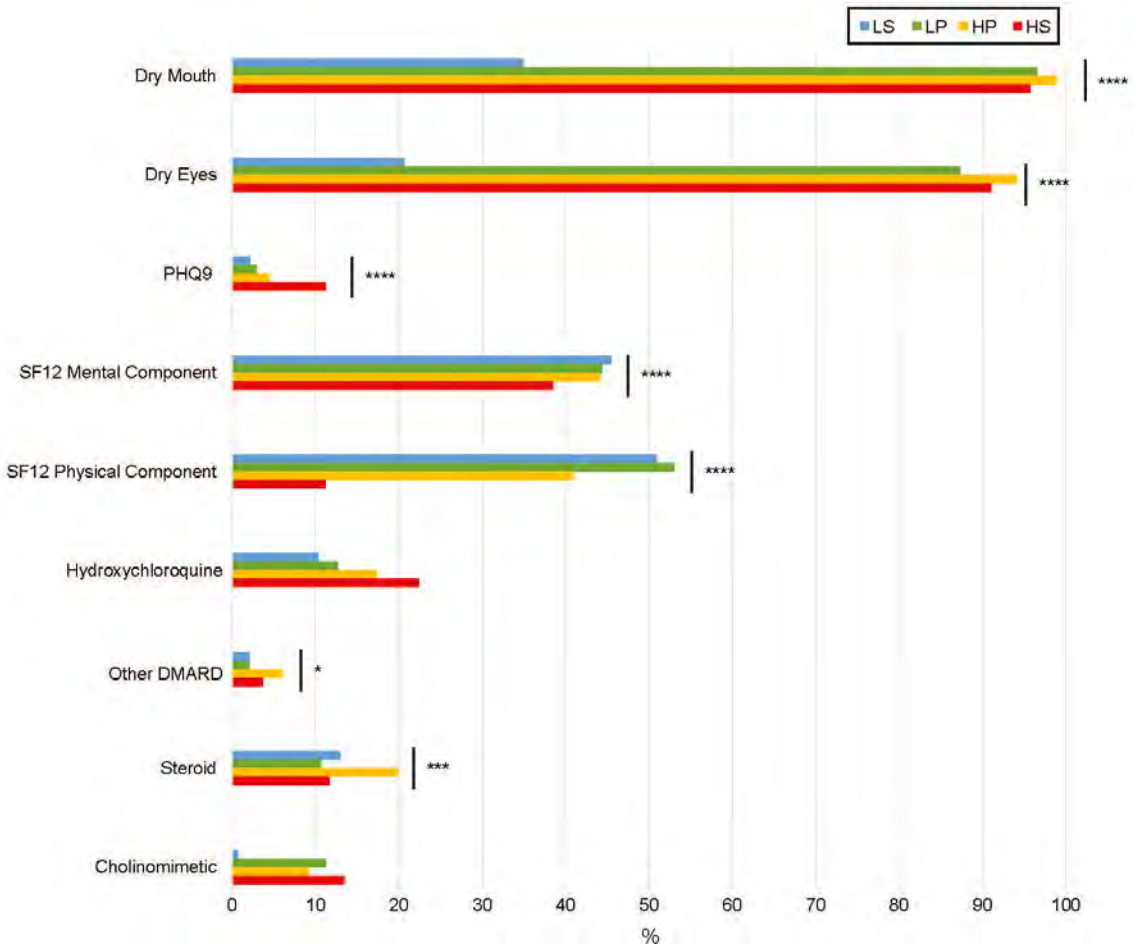

Figure 2. Frequency of patient experience and medication use within four symptom-based clusters. LS=low symptoms of dryness, fatigue, and pain; LP=low pain with some dryness and low fatigue; HP=high pain with some dryness and low fatigue; HS=high symptoms of dryness, fatigue and pain. *<0.05, **<0.01, ***<0.001, ***<0.0001.

HS and HP groups. These findings highlight discordance between disease activity and treatments; symptoms drive therapies as opposed to disease activity. We propose future research defining these subsets to optimize treatment approaches in order to harmonize patient-provider expectations.

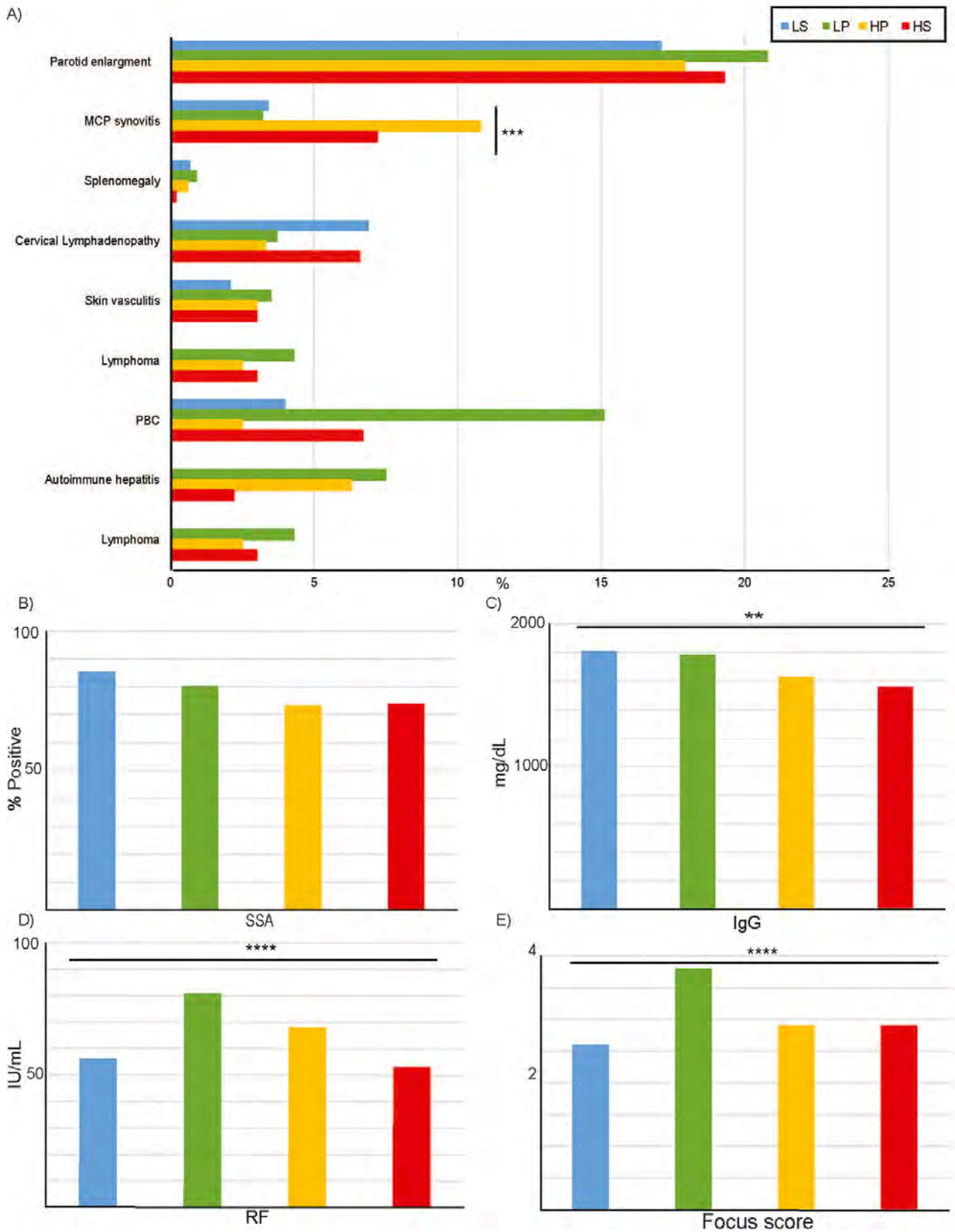

Figure 3. Organ involvement and laboratory findings within SS syptom-based clusters. A) Frequency of organ involvement among clusters; B) Frequency of anti-SSA antibody positivity; C) IgG levels; C) RF levels; D) Focus score. LS=low symptoms of dryness, fatigue, and pain; LP=low pain with some dryness and low fatigue; HP=high pain with some dryness and low fatigue; HS=high symptoms of dryness, fatigue and pain; IgG=immunoglobulin G; RF=Rheumatoid Factor; *=adjusted p <0.05, **=adjusted p <0.01, ***=adjusted p <0.001, ***=adjusted p <0.0001. Models adjusted for age, sex, race, ethnicity, education, and recruitment site.

Disclosure: S. McCoy, BMS, 2, Novartis, 1, Boehringer Ingelheim, 6; **M. Woodham**, None; **I. Saldanha**, None; **E. Akpek**, Novartis, 5, OcularTherapeutix, 5, W.L. Gore & Associates, 5, Dompe, 1, 2, Sinqi, 1, 2, ClearView Health Care Partners, 1, 2, Regeneron, 1, 2, Up-To-Date, 9; **V. BUNYA**, None; **A. Baer**, Bristol Myers Squibb, 2, UpToDate, 9.

Abstract Number: 0986

Ianalumab (VAY736) Safety and Efficacy in Patients with Sjögren's Syndrome: 52 Week Results from a Randomized, Placebo-controlled, Phase 2b Dose-ranging Trial

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science (0984–0987)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Sjögren's syndrome (SS) is an autoimmune disease affecting excretory glands and characterized by B-cell hyperactivity. Ianalumab (VAY736) is a human monoclonal antibody to B-cell activating factor receptor,

Table. Key Safety Data (All Study Periods up to Week 52) †

n (EAIR)[1]	5 mg 24 Wks (N=47)	50 mg 24 Wks (N=47)	150 mg 28 Wks* (N=47)	Any 300 mg (N=47)
Any AE	**43 (517.5)**	**43 (423.3)**	**44 (621.0)**	**45 (544.6)**
Any SAE	**3 (5.9)**	**5 (10.7)**	**8 (19.9)**	**8 (13.6)**
Infections and infestations (SOC)[2]	**33 (154.1)**	**31 (119.2)**	**34 (162.0)**	**38 (127.7)**
Nasopharyngitis[3]	7 [15.5]	4 [8.5]	9 [22.1]	9 [16.5]
Upper respiratory tract infections[3]	6 [12.8]	8 [17.8]	5 [11.6]	8 [13.6]
Bronchitis[3]	3 [6.2]	3 [6.2]	4 [9.5]	4 [6.6]
Tracheobronchitis[3]	1 [2.0]	0 [0.0]	0 [0.0]	3 [5.0]
Pneumonia[3]	1 [2.0]	0 [0.0]	1 [2.2]	2 [3.3]
Blood & Lymphatic Disorders (SOC)[2]	**8 (18.0)**	**9 (20.8)**	**6 (14.3)**	**9 (16.8)**
Lymphopenia[3]	4 [8.4]	4 [8.6]	3 [6.8]	2 [3.3]
Neutropenia[3]	5 [10.7]	1 [2.1]	2 [4.5]	4 [6.9]
Injection site reaction[3]	**4 (8.3)**	**9 (21.4)**	**17 (52.7)**	**27 (90.8)**

†Includes all safety data from TP1, TP2 and post-treatment follow-up; cut-off 06-Feb-2020
*150 mg also includes placebo-controlled patients who were switched to VAY736 150 mg at Week 24
[1]EAIR, incidence rate per 100 subject years. For patient with an event, exposure time is censored at time of first event
[2]Number of patients with at least one AE in SOC
[3]PT, preferred term
AE, adverse event; SAE, serious adverse event; SOC, system organ class; Wks, weeks.

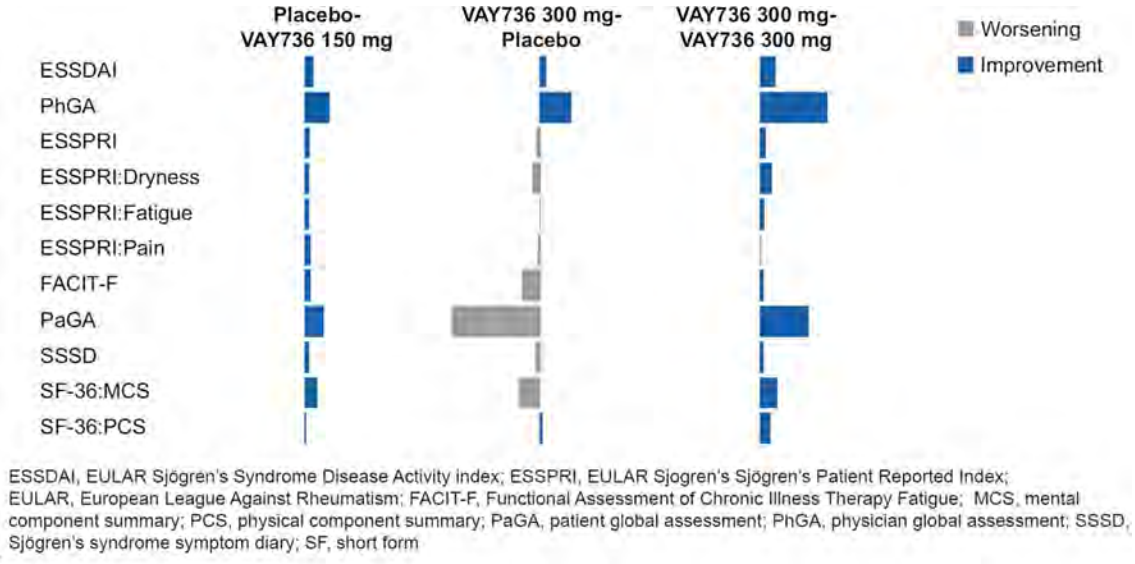

Figure. Summary of Efficacy data at Week 52 (Treatment Period from Wk 24 to Wk 52).

engineered for direct ADCC-mediated B-cell depletion. A Phase 2b study evaluated the dose-response of VAY736 vs placebo (PBO) in EULAR SS Disease Activity Index (ESSDAI) change from baseline (CHB) and other secondary endpoints. Primary results at Week (Wk) 24 were reported previously[1]. Here we report 52 Wks safety and efficacy from extended blinded treatment period 2 (TP2).

Methods: 190 patients were randomized equally to receive s.c. doses of VAY736 (5, 50, 300 mg) or PBO every 4 Wks (q4w). Eligible patients fulfilled American European Consensus Group (AECG) criteria, were anti-Ro/SSA+, had ESSDAI ≥6 and EULAR SS Patient Reported Index (ESSPRI) ≥5. At Wk 24, after completion of the first blinded TP (TP1), PBO-treated patients were switched to VAY736 150 mg, and patients on 300 mg were re-randomized to continue 300 mg or PBO for 28 Wks in TP2. Patients were followed post-treatment for ≥20 Wks. Safety was assessed for all periods. Due to lack of PBO-control in TP2, descriptive efficacy analysis was performed for ESSDAI, ESSPRI, Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F), Physician's (PhGA) and Patient's Global Assessments (PaGA), 36-Item Short Form Survey (SF-36), and SS symptom diary (SSSD).

Results: Overall, there was no dose dependency of treatment emergent adverse events (TEAEs) except for injection site reactions, which were mostly mild to moderate in severity. Lymphopenia and neutropenia were mostly grade (G)1 and G2, and none G4. Most common TEAEs were infections and infestations in exposure-adjusted analysis of incidence rates. Nasopharyngitis and upper respiratory tract infections were the most common TEAEs, with no dose response (**Table**). Tracheobronchitis and pneumonia, were mild to moderate severity, not associated with absolute neutrophil count G3, and none led to treatment withdrawal.

At Wk 52, efficacy was sustained for patients who continued 300 mg in TP2 (ESSDAI, ESSPRI, PaGA, PhGA CHB: –9.06, –1.91, –22.03, and –35.80, respectively). Efficacy was partially lost for patients who switched to PBO at Wk 24 (**Figure**). Improvement was noted for PBO patients who switched to 150 mg. Stimulated whole salivary flow at Wk 24 was improved for 300 mg (PBO-adjusted CHB 0.20 ml/min; P=0·037); last measurement at Wk 48 was 0.45 and 0.22 ml/min CHB in patients who continued 300 mg or PBO in TP2, respectively.

Conclusion: Ianalumab 300 mg was well tolerated up to 52 Wks. Exploratory efficacy measures showed that continuous dosing of 300 mg s.c. q4w provided sustained clinical benefit. PaGA was the outcome that showed the most prominent change following switch to PBO or VAY736.

Reference

1. Dörner T, et al. [OP0302]. *Ann Rheum Dis*. 2020;79(suppl 1):187.

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Abstract Number: 0987

Rituximab Prevents the Progression of B-cell Driven Inflammatory Infiltrate in the Minor Salivary Glands of Primary Sjogren's Syndrome by Downregulating Immunological Pathways Key in Ectopic Germinal Centre Organization: Results from the TRACTISS Trial

Elena Pontarini[1], Farzana Chowdhury[1], Elisabetta Sciacca[1], Sofia Grigoriadou[1], Felice Rivellese[1], Davide Lucchesi[1], Katriona Goldmann[1], Liliane Fossati-Jimack[1], Paul Emery[2], Wan-Fai NG[3], Nurhan Sutcliffe[4], Colin C Everett[5], Catherine Fernandez[5], Anwar Tappuni[6], Myles Lewis[1], Costantino Pitzalis[7], Simon J Bowman[8] and Michele Bombardieri[1], [1]Queen Mary University of London, William Harvey Research Institute, London, United Kingdom, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Leeds NIHR Biomedical Research Centre, Leeds, United Kingdom, [3]Translational and Clinical Research Institute, Newcastle University,, Newcastle, United Kingdom, [4]Royal London Hospital, Bart's Health NHS Trust, London, United Kingdom, [5]Leeds Institute for Clinical Trials Research, University of Leeds, Leeds, United Kingdom, [6]Oral Immunobiology and Regenerative Medicine, Institute of Dentistry, Queen Mary University of London, London, United Kingdom, [7]Queen Mary University of London, London, United Kingdom, [8]Department of Rheumatology, University Hospitals Birmingham NHS Foundation Trust, Birmingham, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Sjögren's Syndrome – Basic & Clinical Science (0984–0987)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: The pathogenic role of B-cells in primary Sjögren's Syndrome (pSS) is well established and B cell abnormalities are hallmarks of the disease. Because of the substantial role of B-cells, rituximab (RTX), has been considered a potential biologic disease modifying drug in pSS. To date, the TRial for Anti-B-Cell Therapy In patients with pSS (TRACTISS) is the largest multi-centre, placebo-controlled trial with RTX. Despite the unmet primary end-points (30% reduction in fatigue or oral dryness, measured by visual analogue scale), RTX treated patients showed an improvement in unstimulated whole salivary flow. The study provides the first longitudinal transcriptomic and histological analysis at 3 time points over 48 weeks of labial salivary glands (SGs) of pSS patients treated with RTX, in comparison to placebo, from the TRACTISS cohort.

Methods: 26 pSS patients randomised to RTX or placebo arm consented for labial SG biopsies at baseline, weeks 16 and 48. Patients received two 1000mg cycles of RTX or placebo at baseline and week 24. The histological analysis was performed by digital imaging (QuPath software), RNA was extracted from matched labial SG lobules and sequenced with Illumina platform.

Results: Placebo-treated labial SGs showed a worsening of inflammation with an increment of B-cell density, development of new follicular-dendritic cell (FDC) networks, and a higher ectopic germinal centre (GC) prevalence at week 48, compared to RTX-treated patients. RTX downregulated genes involved in immune cell recruitment and inflammatory aggregate organisation (e.g. CCR7, CCL19, CD52, and PDCD1) and gene signature-based analysis of 64 immune cell types highlighted how RTX preferentially blocked class-switched- and memory-B-cells infiltration in SGs at week 48. Pathway analyses confirmed the downregulation of leukocyte migration, MHC class II antigen presentation, and T-cell co-stimulation immunological pathways, such as the CD40 receptor complex pathway. The analysis of placebo SGs transcriptomic at week 48 showed a higher expression of genes linked to ectopic GC organisation in female compared to male subjects. Gender was confirmed as a key co-variate responsible for most of the variation in the PrincipalComponentAnalysis, together with the SG focus score and the *foci* area fraction.

Conclusion: Treatment with RTX showed beneficial effects on labial SG inflammatory infiltration in pSS, by downregulating genes involved in immune cell recruitment, activation and organisation in ectopic GCs. Although a clear association with the clinical improvement in unstimulated salivary flow observed at week 48 in RTX-treated patients could not be established given the low number of patients consenting to 3 longitudinal biopsies it is conceivable that RTX is responsible for preserving exocrine function through the above-described mechanisms.

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Abstract Number: 0988

Risk Prediction Models for Incident Systemic Lupus Erythematosus Using Lifestyle/Environmental Risk Factors and a Genetic Risk Score

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Epidemiology & Public Health I: Risk in Rheumatic Diseases (0988–0991)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: The identification of lifestyle/environmental and genetic factors, influencing SLE risk introduces the potential to develop risk prediction models. We examined SLE risk prediction incorporating a lifestyle/en-

vironmental factors and a genetic risk score for SLE in predicting SLE risk among women in the prospective Nurses' Health Studies (NHS).

Methods: Within the prospective cohorts of female nurses, Nurses' Health Study (NHS) (1976-2016) and NHSII (1989-2018), lifestyle, environmental, and medical data were collected at baseline and on subsequent biennial questionnaires. Incident physician diagnosed SLE was self-reported on biennial questionnaires and confirmed by medical record review to meet 1997 ACR classification criteria. Genotyping was performed on blood samples collected in 1989 (NHS) and 1997 (NHSII) from ~25% of participants. We conducted a nested case-control study in which women who had donated a blood sample and developed incident SLE were matched on age (± 4 years) and race to women who had donated a blood sample but did not develop SLE. Our previously derived and published SLE weighted genetic risk score, (wGRS, Cui J et al, *Arthritis Rheum*, 2019) includes 86 single nucleotide polymorphisms (SNPs) and 10 classical *HLA* alleles associated with SLE risk. Lifestyle/environmental variables, including smoking, alcohol use, socioeconomic status, U.S. region, menarchal age, oral contraceptive use, menopausal status/postmenopausal hormone use, body mass index, were assessed on the questionnaire prior to SLE diagnosis (or matched index date). We used multivariable logistic regression to develop sequential models of SLE risk prediction, calculating the area under the receiver operating characteristic curve (AUC). Three models were generated: 1) SLE wGRS, 2) age, race, cohort, lifestyle and environmental factors and 3) model 2 + SLE wGRS. Models were internally validated using a bootstrapped estimate of optimism of the AUC. This measure of overfitting is based on average difference between predictive ability of model using original sample, and that of models using each bootstrap sample.

Results: 138 incident cases of SLE were matched to 1136 women who did not develop SLE. Characteristics of the SLE cases and their matched controls are shown in Table. The results of our three successive prediction models are shown in Figure. The expanded model 3, including both lifestyle and genetic factors, had the best discrimination, with an AUC of 0.721 and optimism corrected AUC of 0.691.

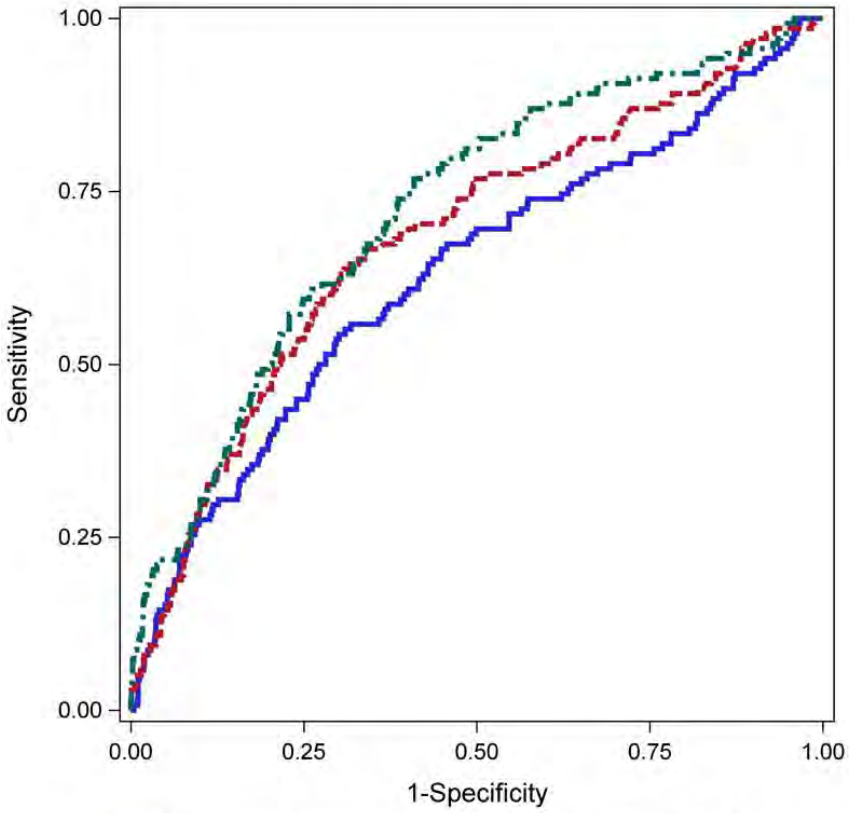
Conclusion: A combination of lifestyle and environmental factors and weighted genetic risk score accurately classified future SLE risk with good AUC of 0.721. To our knowledge, this is the first SLE prediction model using environmental and genetic factors and might be feasibly employed in at-risk populations. The NHS cohorts include few non-White women with blood samples, and mean age at incident SLE was in early 50s given enrollment age, limiting generalizability and calling for further research in more diverse cohorts.

Table. Demographic and Clinical Characteristics of the Female Nurses' Health Study SLE Cases and their Matched Controls at Index Date of SLE Diagnosis

	NHS SLE Cases (138)	NHS Controls (1136)
Mean age in years (SD)	51.8 (10.9)	53.5 (10.3)
Non-European ancestry %	1.5	1.4
Never/Distant Smoker %	82.6	85.1
Current/Recent* Smoker %	17.4	14.9
Mean number of 1997 American College of Rheumatology Criteria for SLE Classification (SD)	4.7 (1.2)	--
ANA+ %	94.9	--
Arthritis %	76.1	--
Hematologic involvement %	53.6	--
Renal involvement %	14.5	--
dsDNA+ %	39.1	--

* quit within 4 years

Figure. Receiver Operating Characteristic (ROC) Curves for SLE Risk Prediction in Nested Case-Control Study within Nurses' Health Study Cohorts (1976-2018)



------ **Model 1**: SLE weighted genetic risk score (wGRS, 86 SNPs and 10 HLA) **(0.6288)**
------ **Model 2**: Age, race, cohort and lifestyle/environmental factors (smoking (current/recent vs. past/never), alcohol use (≤ vs. >5 gms/day), socioeconomic status (zip-code level median household income), U.S. region, menarchal age (< vs ≥ age 10), oral contraceptive use (current/past/never), menopausal status/ postmenopausal hormone use, body mass index (non-obese vs. obese > 35 kg/m^2) **(0.6820)**
------ **Model 3**: Model 2 + SLE wGRS **(0.7209)**

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Abstract Number: 0989

Risk Factors for Hydroxychloroquine Retinopathy and Its Subtypes – Prospective Adjudication Analysis of 4,899 Incident Users

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SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: Epidemiology & Public Health I: Risk in Rheumatic Diseases (0988–0991)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: Hydroxychloroquine (HCQ) is a key treatment for patients with lupus and other rheumatic diseases; however, the known risk factors for HCQ retinopathy (its major toxicity), are mostly derived from prevalent case analyses. We determined the risk factors for incident HCQ retinopathy within a large-scale, longitudinal incident user cohort.

Methods: We conducted a nested case-control study within a large cohort of incident HCQ users identified from a US integrated health network who continued HCQ for ≥5 years during the study period, 1997-2020. We assessed the outcome of retinopathy by prospective assessment of spectral domain-optical coherence tomography (SD-OCT) scans. All scans were reviewed by an expert ophthalmologist (RM), and a second expert ophthalmologist (MM) reviewed all abnormal scans and a random subset of normal scans. Discrepant cases were adjudicated by consensus between the two readers. We identified the dates of earliest abnormal scans. Each SD-OCT scan was graded as

Table 1. Characteristics of Retinopathy Cases and Age-, Sex-, and HCQ Initiation Year-Matched Controls Among Long-Term HCQ Users

Characteristics	Cases (n= 159)	Controls (n=755)
Age at cohort entry, mean (SD)	56 (12)	56 (12)
Female sex, n (%)	146 (91)	699 (92)
Race/ethnicity, n (%)		
White, non-Hispanic	83 (52)	384 (51)
Asian	32 (20)	100 (13)
Hispanic	23 (15)	132 (18)
Black	10 (6)	89 (12)
Other	11 (7)	50 (7)
Year of cohort entry, median (interquartile range)	2004 (2000, 2007)	2004 (2001, 2007)
Actual body weight (kg), mean (SD)	71.0 (17.2)	75.0 (18.5)
Ideal body weight (kg), mean (SD)	55.2 (8.1)	55.8 (8.2)
Primary Indication, n (%)		
Rheumatoid Arthritis	76 (48)	379 (50)
Systemic lupus erythematosus	25 (16)	107 (14)
Other Connective Tissue Disease	5 (3)	38 (5)
Discoid lupus	6 (4)	20 (3)
Other Inflammatory Arthritis	9 (6)	93 (12)
Other	24 (15)	54 (7)
Comorbidities, n (%)		
Chronic Kidney Disease	23 (15)	61 (8)
Liver Disease	3 (2)	35 (5)
Diabetes Mellitus	18 (11)	114 (15)
Tamoxifen use, n (%)	6 (4)	10 (1)
Duration of HCQ use (months), mean (SD)	128.8 (46.4)	113.6 (47.3)
Cumulative dispensed dose (g), mean (SD)	1303.5 (532.2)	979.6 (503.4)
HCQ dose, mean (SD)		
Average daily dose (mg)	331.3 (62.4)	279.8 (73.5)
Average daily dose per actual body weight (mg/kg)	4.9 (1.3)	3.9 (1.3)
Average daily dose per ideal body weight (mg/kg)	6.1 (1.3)	5.1 (1.4)

HCQ, hydroxychloroquine

Table 2. Risk Factors for HCQ Retinopathy Among Long-term Users

Risk Factors	Crude OR (95% CI)	Multivariable* OR (95% CI)
Race/Ethnicity		
White, Non-Hispanic	1.0 (reference)	1.0 (reference)
Asian	1.48 (0.92-2.37)	1.66 (1.01-2.73)
Hispanic	0.83 (0.50-1.38)	1.06 (0.62-1.80)
Black	0.53 (0.26-1.06)	0.60 (0.29-1.23)
Chronic Kidney Disease		
No Kidney Disease	1.0 (reference)	1.0 (reference)
Chronic Kidney Disease Stage ≥3	1.95 (1.15-3.31)	2.19 (1.24-3.85)
Duration of HCQ use		
Duration of use, per 12 months	1.24 (1.12-1.38)	1.15 (1.04-1.27)
Duration of use, per 5 years	2.98 (1.79-4.96)	2.00 (1.23-3.24)
Cumulative HCQ dose, per 500g	3.05 (2.28-4.07)	4.28 (2.69-6.81)
Average daily dose, per 100mg	2.53 (1.99-3.21)	2.96 (2.09-4.20)
Average daily dose, per ABW		
≤5mg/kg	1.0 (reference)	1.0 (reference)
>5mg/kg	4.20 (2.81-6.28)	2.87 (1.85-4.47)
Average daily dose, per IBW		
≤6.5mg/kg	1.0 (reference)	1.0 (reference)
>6.5mg/kg	4.93 (3.11-7.80)	3.59 (2.18-5.90)
Duration of use with daily dose >5mg/kg ABW, per 5 years	1.36 (1.03-1.81)	1.35 (1.00-1.81)
Duration of use with daily dose >6.5mg/kg IBW, per 5 years	1.50 (1.10-2.06)	1.72 (1.24-2.40)
Average HCQ daily dose, per ABW		
Less than 4mg/kg	1.0 (reference)	1.0 (reference)
Between 4- <5 mg/kg	3.36 (2.12-5.35)	2.76 (1.67-4.58)
Between 5-<6mg/kg	5.12 (3.10-8.67)	3.97 (2.24-7.04)
Greater than or equal to 6mg/kg	10.36 (5.34-20.10)	7.36 (3.49-15.50)
Average HCQ daily dose, per IBW		
Less than 5.2 mg/kg	1.0 (reference)	1.0 (reference)
Between 5.2- <6.5 mg/kg	2.84 (1.77-4.55)	2.40 (1.45-3.93)
Between 6.5-<7.8 mg/kg	7.49 (4.42-12.71)	6.10 (3.47-10.74)
Greater than or equal to 7.8 mg/kg	9.74 (4.15-22.83)	8.45 (3.42-20.89)

ABW, actual body weight; IBW, ideal body weight; CKD, chronic kidney disease
*For all models, patients were matched by age, sex, and HCQ initiation year. For race/ethnicity, models adjusted for CKD and number of prescription days covered. For CKD, model adjusted for race/ethnicity and number of prescription days covered. For duration of use, models adjusted for race/ethnicity, CKD, and average daily dose per 100mg. All other models adjusted for race/ethnicity, CKD, and number of prescription days covered.

mild, moderate, or severe retinopathy, no retinopathy, or non-HCQ retinopathy (such as macular degeneration), and retinopathy cases were subclassed as parafoveal or pericentral pattern. Cases with incident HCQ retinopathy were matched with up to 5 controls by age, sex, and HCQ initiation year using risk set sampling. Using pharmacy dispensing records, we assessed HCQ duration of use, cumulative dose, average daily dose, and dose per actual body weight (ABW) and ideal body weight (IBW). Candidate risk factors also included race/ethnicity and chronic kidney disease (CKD). We used conditional logistic regression to assess the association between potential risk factors and the risk of HCQ retinopathy overall, by severity, and by pattern.

Results: Of 4,899 long-term HCQ users, we identified 164 patients with incident HCQ retinopathy (100 mild, 38 moderate, and 26 severe cases), with a parafoveal pattern in 131 and pericentral pattern in 33 patients. We matched 159 cases with 755 controls. The mean age at HCQ initiation was 56 years; over 90% were female (**Table 1**). The risk of HCQ retinopathy doubled for every additional 5 years of use (**Table 2**). Cumulative dose was associated with an

Table 3. Risk Factors for Moderate/Severe HCQ Retinopathy Among Long-term Users

Characteristics	Crude OR (95% CI)	Multivariable* OR (95% CI)
Race/Ethnicity		
White, Non-Hispanic	1.0 (reference)	1.0 (reference)
Asian	3.72 (1.83-7.55)	3.51 (1.69-7.30)
Hispanic	1.23 (0.55-2.76)	1.48 (0.63-3.47)
Black	1.04 (0.37-2.91)	1.02 (0.35-2.98)
Chronic Kidney Disease		
No Kidney Disease	1.0 (reference)	1.0 (reference)
Chronic Kidney Disease Stage ≥3	3.03 (1.45-6.36)	3.07 (1.37-6.87)
Duration of HCQ use		
Duration of use, per 12 months	1.15 (1.02-1.30)	1.08 (0.96-1.23)
Duration of use, per 5 years	1.99 (1.09-3.64)	1.49 (0.80-2.76)
Cumulative HCQ dose, per 500g	2.28 (1.53-3.40)	4.44 (2.06-9.61)
Average Daily Dose, per 100mg	2.72 (1.71-4.35)	3.03 (1.79-5.15)
Average daily dose, per ABW		
≤5mg/kg	1.0 (reference)	1.0 (reference)
>5mg/kg	1.99 (1.56-2.52)	1.89 (1.45-2.47)
Average daily dose, per IBW		
≤6.5mg/kg	1.0 (reference)	1.0 (reference)
>6.5mg/kg	5.15 (2.59-10.25)	4.86 (2.28-10.36)
Duration of use with daily dose >5mg/kg ABW, per 5 years	1.39 (0.93-2.09)	1.46 (0.93-2.28)
Duration of use with daily dose >6.5mg/kg IBW, per 5 years	1.65 (1.02-2.67)	2.07 (1.22-3.50)
Average HCQ Daily Dose, per ABW		
Less than 4mg/kg	1.0 (reference)	1.0 (reference)
Between 4-<5 mg/kg	3.02 (1.34-6.83)	2.89 (1.23-6.78)
Between 5-<6mg/kg	4.33 (1.79-10.47)	3.33 (1.26-8.77)
Greater than or equal to 6mg/kg	14.50 (5.53-38.01)	10.79 (3.70-31.52)
Average HCQ daily dose, per IBW		
Less than 5.2 mg/kg	1.0 (reference)	1.0 (reference)
Between 5.2-<6.5 mg/kg	2.49 (1.13-5.50)	2.23 (0.97-5.14)
Between 6.5-<7.8 mg/kg	7.63 (3.20-18.24)	6.61 (2.59-16.86)
Greater than or equal to 7.8 mg/kg	9.26 (2.83-30.36)	10.06 (2.69-37.57)

ABW, actual body weight; IBW, ideal body weight; CKD, chronic kidney disease
*For all models, patients were matched by age, sex, and HCQ initiation year. For race/ethnicity, models adjusted for CKD and number of prescription days covered. For CKD, model adjusted for race/ethnicity and number of prescription days covered. For duration of use, models adjusted for race/ethnicity, CKD, and average daily dose per 100mg. All other models adjusted for race/ethnicity, CKD, and number of prescription days covered.

adjusted risk ratio of 4.28 (95% CI 2.69-6.81) per additional 500g, and dosing category per mg/kg of ABW or IBW strongly correlated with the risk of retinopathy. Asian patients had an increased risk of HCQ retinopathy overall, moderate/severe grade, and the pericentral pattern. CKD was associated with 2x higher risk of overall retinopathy and a 3x higher risk of moderate/severe retinopathy (**Table 3**).

Conclusion: The risk of incident HCQ retinopathy increases with higher dosing per ABW and per IBW in a dose-response manner. We found cumulative HCQ dose, duration of use, CKD, and Asian race to be independent risk factors for incident HCQ retinopathy including moderate/severe cases. Patients with these risk factors may warrant closer monitoring.

Disclosure: A. Jorge, None; **R. Melles**, None; **C. Conell**, None; **N. Lu**, None; **M. Marmor**, None; **L. Young**, None; **N. McCormick**, None; **Y. Zhang**, None; **H. Choi**, None.

Abstract Number: 0990

Lower Incidence of COVID-19 but Higher Mortality in Patients with Inflammatory Arthritis Compared to Controls in Wales, United Kingdom: A Population Epidemiological Study

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SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Abstracts: Epidemiology & Public Health I: Risk in Rheumatic Diseases (0988–0991)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: The COVID-19 pandemic has caused over 3 million deaths. Having inflammatory arthritis (IA) and anti-rheumatic medications increase the risk of infections. Comorbidities, common in IA, have been associated with increased mortality with COVID-19. In the U.K, including Wales, governments advised vulnerable individuals including many patients with IA to self-isolate at home (shielding) by letters.

A small primary care cohort and the global rheumatology registry found an increased risk of severe disease and mortality in patients with rheumatic diseases (4-5). Comorbidities and a moderate to a high dose of glucocorticoids were associated with a higher risk of being hospitalised.

Using the complete COVID-19 test data for the entire nation of Wales, U.K, we compared the incidence and mortality of COVID-19 in patients with IA with controls for an entire nation with a 3 million population

Methods: All individuals who tested positive for COVID-19 from 1/3/20 to 12/05/21 formed the population. Primary care and hospital healthcare records were linked anonymously using a multiple encryption system by NHS Wales Informatics Service (6). Individuals with diagnosis codes for Rheumatoid Arthritis, Psoriatic Arthritis and Ankylosing Spondylitis comprised the IA patients, while those without these codes were the control population. Individuals who were under 18 years of age when tested for COVID-19 were excluded from the analysis.

The incidence rate of COVID-19 was assessed by Chi-square statistics. COX proportional hazard models were used to generate hazard ratios (HR) of death following COVID-19 for IA patients compared to controls. Univariable analysis informed the significant candidate variables (at $p< 0.05$ level of significance) to be added to the final model in a stepwise model. Analyses were conducted for 1st (Mar-Jun 20) and 2nd (Sep 20-May 21) waves as well as in between these periods.

Results: Over 3 million COVID-19 tests were conducted. The incidence rate of COVID-19 for patients with IA was 2,031/100,000, compared to 22,755/100,000 for those without IA (Chi-Square p=0.0001). Patients with IA were statistically significantly older and had more comorbidities.

The proportion of patients with IA admitted to hospital post-COVID test was statistically significantly higher compared to those without IA (1st wave: difference 24.5%, 95% CI: 18.4-30.7). The proportion of patients deceased following COVID-19 was statistically significantly higher in IA patients during the first wave (difference 21.4, 95% CI: 15.7 to 27.4) and second wave (difference 10.9, 95% CI: 8.6 to 13.6) (Table 1).

Table 1: Hazard ratio of risk of death of IA patients compared to controls across the pandemic

	Wave 1:		Period between waves		Wave 2	
	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)	Univariable analysis HR (95% CI)	Multivariable analysis HR (95% CI)
Rheumatoid arthritis	3.32 (2.61 to 4.22)*	-	2.87 (1.18 to 6.99)*	-	4.55 (3.76 to 5.51)*	-
Psoriatic arthritis	1.23 (0.66 to 2.30)	-	1.17 (0.16 to 8.36)	-	0.94 (0.49 to 1.81)	-
Ankylosing spondylitis	2.39 (1.20 to 4.79)*	-	*	-	2.58 (1.46 to 4.54)*	-
Shielding	3.47 (3.13 to 3.84)*	1.43 (1.35 to 1.64)*	5.90 (4.35 to 8.01)*	2.28 (1.58 to 3.27)*	6.41 (5.92 to 6.94)*	1.84 (1.67 to 2.02)*
Mean age at test	1.08 (1.07 to 1.08)*	1.07 (1.07 to 1.08)*	1.08 (1.07 to 1.09)*	1.08 (1.07 to 1.09)*	1.10 (1.10 to 1.10)*	1.07 (1.06 to 1.07)*
Female	0.51 (0.46 to 0.55)*	0.68 (0.60 to 0.76)*	0.64 (0.49 to 0.83)*	0.55 (0.40 to 0.76)*	0.64 (0.60 to 0.69)*	0.62 (0.57 to 0.97)*
Ever smoked	2.02 (1.85 to 2.21)*	1.16 (1.02 to 1.32)*	2.45 (1.83 to 3.28)*	-	2.05 (1.9 to 2.20)*	-
Diabetes	3.37 (3.06 to 3.71)*	1.36 (1.19 to 1.55)*	3.82 (2.77 to 5.25)*	-	5.73 (5.31 to 6.19)*	1.28 (1.18 to 1.40)
Previous Serious infections (hospitalised)	4.70 (4.31 to 5.14)*	1.56 (1.38 to 1.76)*	3.56 (2.71 to 4.67)*	-	4.21 (3.94 to 4.51)*	1.03 (1.01 to 1.02)*
cDMARDs	2.22 (1.82 to 2.73)*	-	1.59 (0.70 to 3.57)	-	2.82 (2.49 to 3.43)*	-
Antimalarial only	0.68 (0.42 to 1.11)	-	1.44 (0.26 to 7.93)	-	1.74 (1.18 to 2.58)*	-
Glucocorticoids	2.36 (2.16 to 2.57)*	-	2.81 (2.13 to 3.69)*	-	2.71 (2.52 to 2.9)*	1.10 (1.01 to 1.19)*

** Significant at p<0.05*

Adjusted COX hazard models showed that being a shielded individual, advanced age, ever smoker, diabetes, previous history of serious infection requiring hospitalisation and glucocorticoids were associated with increased risk of death in IA patients compared to controls (Table 1). Being female was associated with a reduced risk of death.

Conclusion: Patients with IA have a lower risk of contracting COVID perhaps due to shielding. Mortality was significantly higher in IA patients compared to controls which was due to older age and had more comorbidities. The only IA related risk factor associated with higher mortality was corticosteroids.

Disclosure: R. Cooksey, None; **M. Atkinson**, None; **E. Choy**, Bio-Cancer, 2, 5, Biogen, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi, 1, 2, 5, 6, UCB, 1, 2, 5, 6, Amgen, 2, 5, 6, Biocon, 2, Chugai Pharma, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, 12, Support for attending meetings and/or travel, Gilead, 1, 2, 5, 6, 12, Support for attending meetings and/or travel, Janssen, 2, 5, Regeneron Pharmaceuticals, Inc., 2, 5, 6, Abbvie, 2, 12, Support for attending meetings and/or travel, Bristol Myers Squibb, 2, 5, 6, Galapagos, 1, 2, 6, Merck Serono, 2, Boehringer Ingelheim, 2, 5, 6, AstraZeneca, 2, 5, Celgene, 2, 5, Chelsea Therapeutics, 2, 5, Daiichi Sankyo, 2, 5, Ferring Pharmaceuticals, 2, 5, GlaxoSmithKline, 2, 5, Hospira Pharmaceuticals, 2, 5, Ionis Pharmaceuticals, 2, 5, Jazz Pharmaceuticals, 2, 5, MedImmune, 2, 5, Merck Sharp & Dohme, 2, 5, 6, Merrimack Pharmaceuticals, 2, 5, Napp, 2, 5, Novimmune, 2, 5, ObsEva, 2, 5, R-Pharm, 2, 5, SynAct Pharma, 2, 5, Tonix, 2, 5.

Abstract Number: 0991

Does Diet Affect Gout Risk Differently Among Genetically Predisposed Women?: Prospective Female Cohort Study Findings over 34 Years

Chio Yokose[1], Natalie McCormick[2], Na Lu[3], Amit Joshi[2] and Hyon K. Choi[4], [1]Massachusetts General Hospital, Waltham, MA, [2]Massachusetts General Hospital, Boston, MA, [3]Arthritis Research Canada, Vancouver, BC, Canada, [4]Massachusetts General Hospital, Lexington, MA

SESSION INFORMATION

Session Date: Sunday, November 7, 2021

Session Title: Abstracts: Epidemiology & Public Health I: Risk in Rheumatic Diseases (0988–0991)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: Gout has long been considered a male disease. However, several recent analyses of the Global Burden of Disease (GBD) Study report a disproportionate worsening of gout burden among women (Xia Rheumatology 2020), suggesting intensive dietary measures for gout prevention are indicated, especially in women. The Dietary Approaches to Stop Hypertension (DASH) diet lowers serum urate and is associated with a lower risk of incident gout while the Western diet is associated with an increased risk (Rai BMJ 2017). However, whether the dietary impact is affected by genetic risk remains unknown. We investigated the potential interaction between genetic predisposition and diet on the risk of incident gout among women.

Methods: We examined the role of genes on the association between two dietary patterns (DASH and Western) on the risk of incident gout in 18,247 women from the Nurses' Health Study (NHS) over 34 years. Using validated food frequency questionnaires, for each participant we derived: 1) DASH score emphasizing fruits, vegetables, nuts and legumes, whole grains, low-fat dairy, and reduced intake of saturated fat and sugar-sweetened beverages (SSBs) and 2) Western diet score characterized by high intake of red and processed meats, SSBs, desserts, French fries, and refined grains. The DASH and Western diet scores were categorized into quintiles, with higher quintiles indicating higher adherence to these dietary patterns. We derived a genetic risk score (GRS) using 114 serum urate single nucleotide polymorphisms from the latest GWAS (Tin Nat Genet 2019), with a higher GRS indicating a higher genetic predisposition for hyperuricemia.

Table 1. Baseline Gout Risk Factors by Genetic Risk Score

	NHS	
	Genetic Score of 114 SNPs	
	Below Mean (n = 9165)	Above Mean (n = 9082)
Age, years, mean (SD)	47.1 (6.9)	47.0 (6.9)
Systolic blood pressure, mm Hg, mean (SD)	123.9 (14.4)	124.2 (14.6)
Diastolic blood pressure, mm Hg, mean (SD)	78.8 (7.6)	79.1 (7.7)
Reported hypertension, %	15	17
BMI, kg/m^2, mean (SD)	24.5 (4.5)	24.5 (4.4)
Estrogen use, %		
Physical activity, MET-hours/week, mean (SD)	14.6 (20.8)	14.0 (19.3)
Alcohol, g/d, mean (SD)	6.5 (10.2)	6.6 (10.5)
Sweetened soft drink intake, servings/d, mean (SD)	0.3 (0.6)	0.3 (0.6)
Meat intake, servings/d, mean (SD)	1.1 (0.8)	1.1 (0.8)
Seafood intake, servings/d, mean (SD)	0.2 (0.2)	0.2 (0.2)
Low-fat dairy foods intake, servings/d, mean (SD)	0.9 (1.0)	0.9 (1.0)
High-fat dairy foods intake, servings/d, mean (SD)	1.4 (1.3)	1.4 (1.3)
Diuretic use, %	9.6	10.1

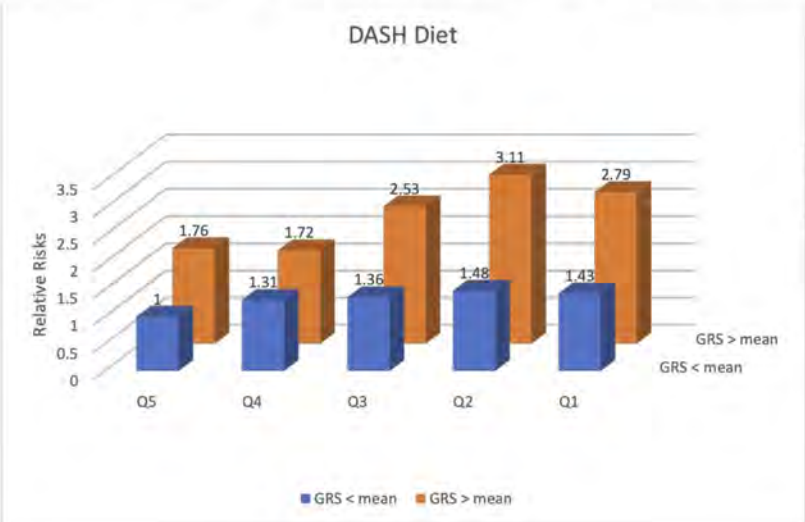
Values are age-adjusted (except for age).

Table 2. Joint Associations of Diet and Genetic Risk Score on the Relative Risk of Incident Gout

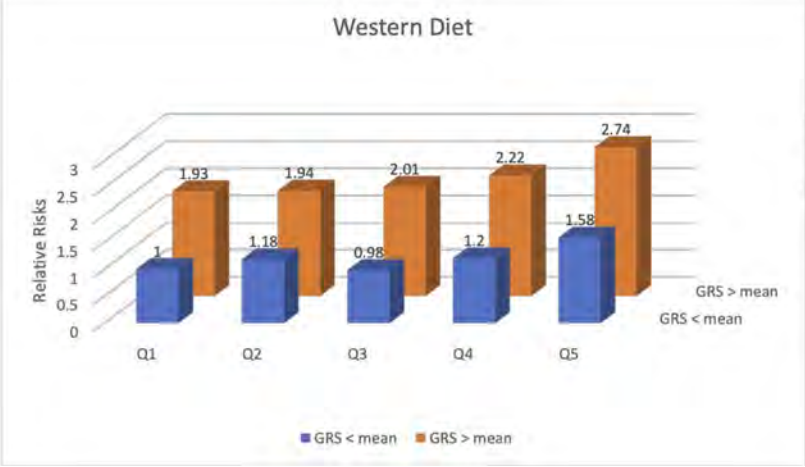
	DASH									
	Below Mean					Above Mean				
	Q5	Q4	Q3	Q2	Q1	Q5	Q4	Q3	Q2	Q1
No. Cases	92	73	123	109	84	154	94	224	224	163
Person-Years	75010	44684	72624	59702	49169	72389	43843	70639	57902	49079
Age-Adjusted RR	1.0 (ref)	1.36 (1.00, 1.85)	1.43 (1.09, 1.87)	1.57 (1.19, 2.08)	1.54 (1.14, 2.07)	1.75 (1.35, 2.27)	1.81 (1.35, 2.41)	2.67 (2.09, 3.40)	3.39 (2.66, 4.33)	3.05 (2.36, 3.95)
MV-Adjusted* RR	1.0 (ref)	1.31 (0.96, 1.78)	1.36 (1.04, 1.79)	1.48 (1.12, 1.96)	1.43 (1.06, 1.92)	1.76 (1.36, 2.28)	1.72 (1.29, 2.30)	2.53 (1.98, 3.23)	3.11 (2.43, 3.97)	2.79 (2.15, 3.61)
	Western									
	Below Mean					Above Mean				
	Q1	Q2	Q3	Q4	Q5	Q1	Q2	Q3	Q4	Q5
No. Cases	76	99	84	102	120	136	159	171	185	208
Person-Years	60640	61330	61813	59615	57840	57727	60372	60424	58614	56723
Age-Adjusted RR	1.0 (ref)	1.21 (0.90, 1.63)	1.00 (0.74, 1.37)	1.26 (0.93, 1.69)	1.59 (1.19, 2.13)	1.91 (1.44, 2.53)	2.00 (1.52, 2.63)	2.10 (1.60, 2.76)	2.34 (1.79, 3.07)	2.85 (2.18, 3.71)
MV-Adjusted* RR	1.0 (ref)	1.18 (0.87, 1.59)	0.98 (0.71, 1.34)	1.20 (0.88, 1.62)	1.58 (1.17, 2.14)	1.93 (1.46, 2.56)	1.94 (1.47, 2.55)	2.01 (1.53, 2.65)	2.22 (1.69, 2.92)	2.74 (2.07, 3.62)

*Adjusted for age (continuous), menopause, use of hormone therapy (never, past or current), history of hypertension, systolic and diastolic blood pressure (continuous), alcohol (continuous), total energy intake (continuous), and intake of meat, seafood, and dairy foods (continuous).

Figure 1. Joint Association of GRS and Diet on Relative Risk of Incident Gout



RERI (additive interaction): 0.57 (p=0.06)
Multiplicative interaction: 1.12 (p=0.56)



RERI (additive interaction): 0.20 (p=0.52)
Multiplicative interaction: 0.90 (p=0.57)

Results: We ascertained 481 incident cases of self-reported gout among women without a genetic predisposition and 859 incident cases among women with a genetic predisposition in NHS. The baseline clinical gout risk factors were similarly distributed among women with and without a genetic predisposition (Table 1). For the DASH diet, the multivariable relative risks (RR) of gout for quintiles 5 through 1 were 1.0, 1.31, 1.36, 1.48, 1.43 (95% CI, 1.06 to 1.92) among those without a genetic predisposition and 1.76, 1.72, 2.53, 3.11, 2.79 (95% CI, 2.15 to 3.61) among those with a genetic predisposition, respectively (Figure 1 and Table 2). Comparing quintiles 5 vs. 1, this yielded a relative excess risk due to interaction (RERI) of 0.57 (95% CI, -0.02 to 1.17) which approached statistical significance (p=0.06). For the Western diet, the RR of gout for quintiles 1 through 5 were 1.0, 1.18, 0.98, 1.20, 1.58 (95% CI, 1.17 to 2.14) among those without a genetic predisposition and 1.93, 1.94, 2.01, 2.22, 2.74 (95% CI, 2.07 to 3.62) among those with a genetic predisposition, respectively (Figure 1 and Table 2). This yielded RERI of 0.20 (95% CI, -0.40 to 0.81, p=0.52).

Conclusion: In this large prospective female cohort with 34 years of follow-up, regardless of genetic predisposition, DASH diet was associated with lower risk of incident gout while Western diet was associated with higher risk. The impact of DASH diet appeared stronger among those with a genetic predisposition to gout. These data support the recent GBD study's recommendation for intensive dietary measures for gout prevention, especially in females.

Disclosure: C. Yokose, None; **N. McCormick**, None; **N. Lu**, None; **A. Joshi**, None; **H. Choi**, None.

Abstract Number: 0992

Inflammatory Arthritis in HIV-Infected Humanized Mice

Can Sungur[1], Ayse Ozanturk[1], Hongbo Gao[1], Li-ping Yang[1], Liang Shan[1] and Wayne Yokoyama[2], [1]Washington University, St Louis, MO, [2]Washington University School of Medicine, St. Louis, MO

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Human immunodeficiency virus (HIV) remains a significant life-threatening agent and burden on public health. Lesser studied and understood aspects of HIV include HIV-associated inflammatory arthritis. By utilizing humanized mice with human cytokine knock-ins that better support a human immune system than other models, we studied HIV-associated arthritis and enthesitis to understand their development and progression.

Methods: MISTRG-IL15 mice (human M-CSF/GM-CSF, IL-3, SIRPα, TPO, RAG2 -/-, IL2rg-/-, and IL-15 knocked into the respective endogenous mouse loci) were reconstituted with CD34+ hematopoietic stem cells obtained from human fetal cord blood. After checking for engraftment after 6-8 weeks, we infected reconstituted mice with HIV. Synovial tissues were obtained from the knee joints of the hind limbs at different time points and processed into single cell suspensions. Intercellular staining was performed on cells incubated with PMA/Ionomycin for 4 hours and then permeabilized and fixed for flow cytometry. NK cells were defined as CD3-CD56+. Histochemistry was also performed on hind paws that were fixed in 4% paraformaldehyde. Samples were then sectioned and stained with H&E for histologic analysis. Different chemokine receptor-tropic HIV viruses were also utilized to determine importance of specific infected cells on development of inflammation.

Results: Humanized MISTRG-IL15 mice developed inflammatory arthritis as well as enthesitis after HIV infection. Significant increases in total inflammatory cells and NK cells were seen in the synovial tissue throughout the course

of infection. GM-CSF producing NK cells also increased throughout the course of HIV infection. Late in the course of infection, IFNγ- and granzyme B-producing NK cells increased, along with a pro-inflammatory environment in the synovial tissue. Histologic analysis showed increased cellular infiltrate in the synovium and tendons of mice infected by HIV infection with erosive changes that worsened during course of infection. Antiretroviral therapy (ART) eliminated cellular infiltration while cessation of therapy resulted in return of cellular infiltration in synovial tissue. Use of a chemokine receptor-tropic HIV virus that does not infect macrophages (X4-tropic) showed reduced pro-inflammatory cytokine production by NK cells, strongly suggesting HIV-infected macrophages induced the NK cell changes.

Conclusion: We have developed a unique humanized mouse model of HIV infection which allows opportunities to study HIV-associated arthritis and enthesitis in depth. In addition to providing a model to study arthritis induced by other human pathogens, findings from such studies will provide mechanistic understanding of inflammatory arthritis and enthesitis.

Disclosure: C. **Sungur**, None; **A. Ozanturk**, None; **H. Gao**, None; **L. Yang**, None; **L. Shan**, None; **W. Yokoyama**, None.

Abstract Number: 0993

The Mechanistic Basis of anti-CD6 as a Novel Form for the Treatment of Autoimmune Diseases and Cancer

Mikel Gurrea-Rubio[1], Jeffrey Ruth[1], Qi Wu[1], Eliza Pei-Suen Tsou[1], Phillip Campbell[1], Peggy Randon[1], M.Asif Amin[1], Nora Singer[2], Feng Lin[3] and David Fox[1], [1]University of Michigan, Ann Arbor, MI, [2]The MetroHealth System, Cleveland, OH, [3]Cleveland Clinic, Cleveland, OH

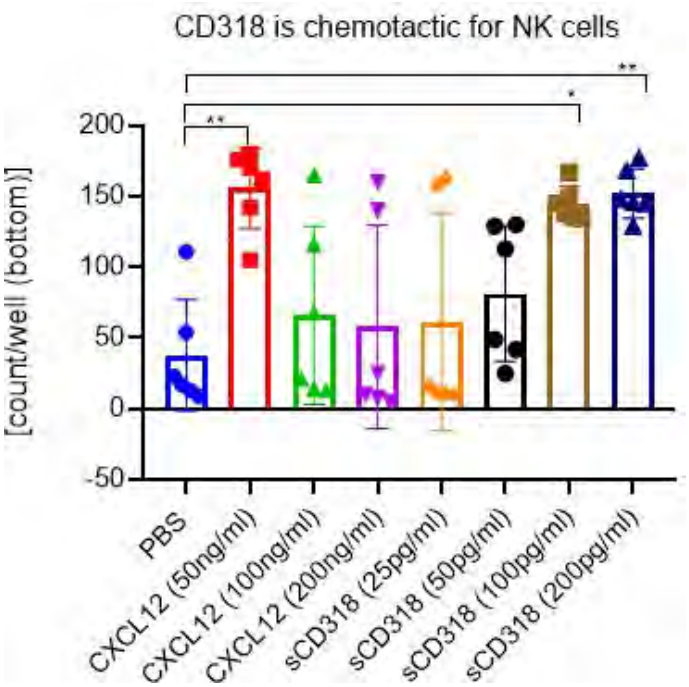
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The use of Immune Checkpoint Inhibitors (ICIs) is limited by the induction of immune-related adverse events. CD6 is expressed by most T lymphocytes and a subset of natural killer (NK) cells, and engages the ligands *CD166/ALCAM* and *CD318*. Interrupting CD6 interaction with its ligands using UMCD6 (anti-CD6) reverses autoimmunity in mouse models of rheumatoid arthritis, multiple sclerosis and uveitis, due to suppression of differentiation of effector Th1 and Th17 cells. Recently, we have demonstrated that UMCD6 directly activates CD8+T and NK cells, enhancing these cells to kill breast, lung, and prostate cancer lines, even more robustly than ICIs directed to the PD-1/PD-1L pathway. We now explore the mechanisms by which UMCD6 activates NK cells while controlling the differentiation of CD4 cells.

Methods: RNAseq was used to study the molecular changes occurring during NK activation by CD6 blockade. Data analysis was conducted using DESeq2 software, and genes showing a Padjusted ≤0.05 were considered significantly differentially expressed.

Chemotaxis of NK cells was assessed by the number of isolated human NK cells using an IncuCyte® Chemotaxis System assay. One-way ANOVA was used to compare groups. Significance was defined as $p < 0.05$.

To identify NK structures that are involved with the functional pathway that is triggered by UMCD6, we generated monoclonal antibodies from Balb/C mice immunized with NK-92 cells.



Results: Our RNAseq data from UMCD6-treated NK cells demonstrate extensive changes in gene expression induced by UMCD6. Expression of 180 genes was altered significantly. These genes included: i) activating NK receptors (e.g., Hcst [DAP10], and CD244 [2B4]), and ii) genes whose protein products are important in the immunoregulatory signaling pathways PI3K, AKT, and mTOR.

NK cells migrate in response to sCD318 with a peak response at 200 pg/ml ($p < 0.01$). This concentration of sCD318 is detectable in supernatants of cancer cell lines that we have used as targets for UMCD6-stimulated lymphocytes. NK cells also migrate toward stromal cell-derived factor (SDF)-1α (CXCL12) at a concentration of 25 ng/ml ($p < 0.01$), consistent with studies of NK chemotaxis to CXCL12 into sites of inflammatory responses or malignancies.

Hybridoma supernatants from Balb/C mice immunized with NK-92 cells have been screened to select antibodies whose corresponding surface structures are up-or down-regulated by UMCD6, co-internalize with UMCD6, and/or inhibit or augment target cell killing by NK cells. Thus far, 10 hybridomas have been selected based on informative positive results from this screening process.

Conclusion: The profound changes in gene expression induced by UMCD6 (anti-CD6) are consistent with our previous studies showing UMCD6 to concurrently control autoimmunity through effects on CD4+ lymphocyte differentiation while enhancing killing of cancer cells through activation of CD8+ and NK cells. The chemotactic properties of sCD318, a ligand of CD6, toward NK cells also demonstrates the importance of CD6 in migration of cytolytic lymphocytes into the tumor microenvironment. Altogether, these data point to a potential new approach to cancer immunotherapy that would suppress rather than instigate autoimmunity.

CD318 is chemotactic for NK cells. Chemotaxis of NK cells was assessed by the number of isolated human NK cells using an IncuCyte® Chemotaxis System assay. NK cells migrate in response to sCD318 with a peak response at 200 pg/ml ($p<0.01$). NK cells also migrate toward stromal cell-derived factor (SDF)-1α (CXCL12) at a concentration of 25 ng/ml ($p<0.01$). PBS was used as negative control.

Disclosure: M. Gurrea-Rubio, None; **J. Ruth**, None; **Q. Wu**, None; **E. Tsou**, None; **P. Campbell**, None; **P. Randon**, None; **M. Amin**, None; **N. Singer**, None; **F. Lin**, None; **D. Fox**, None.

Abstract Number: 0994

Role of SLE Associated Cytokines in Generation of Mature Neutrophils

Neelakshi R. Jog, Julia Nguyen and Judith James, Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a systemic autoimmune disease characterized by autoantibody production and periods of elevated disease activity. Recent studies indicate that along with dysfunctional adaptive immune responses, neutrophils are also important in disease pathogenesis. SLE patients have higher numbers of low-density granulocytes (LDGs) in peripheral blood that express neutrophil markers and are hyperresponsive to external stimuli. LDGs are suggested to be pathogenic in lupus. However, the mechanisms leading to increased LDGs in SLE patients are unclear.

Methods: Peripheral blood mononuclear cells from 19 SLE patients with varying disease activity and 11 controls were enriched by density gradient centrifugation. LDG numbers were determined by flow cytometry. Plasma cytokines were measured by xMAP assays. Induced pluripotent stem cells (iPSC) derived from adult peripheral blood CD34+ cells were differentiated into neutrophils using feeder-culture conditions. Cultures were supplemented with IL-13 at different stages of differentiation: day 7 (hemangioblasts-like cells to CD34+ hematopoietic stem cells (HSC)), day 12 (HSC into CD45+ hematopoietic cells), day 18 (CD45+ cells into neutrophil precursors), day 23 (maturation to segmented neutrophils).

Results: SLE patients with elevated disease activity had significantly higher frequency of immature LDGs as determined by surface marker expression (p=0.005). IL-13 levels were higher in SLE patients with elevated disease activity compared to low disease activity patients (p=0.01) and controls (p=0.006), and the levels correlated negatively with absolute neutrophil numbers (r = -0.4404, p= 0.0354). Our goal was to test whether abnormal timing and excessive IL-13 exposure of hematopoietic stem cells (HSC) leads to generation of immature neutrophils in SLE patients due to defective differentiation. The iPSC cultures were induced into neutrophilic differentiation. By day 23 of differenti-

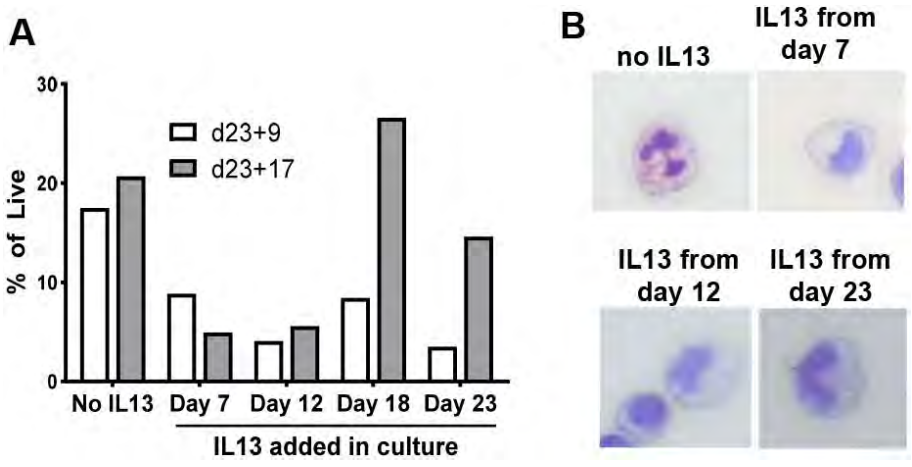


Figure 1. Early IL-13 exposure inhibits neutrophil differentiation. CD45+cells from day 23 of iPSC differentiation were allowed to mature into neutrophils additional 17 days. A. Flow cytometry was performed on day 9 (Day 23+9) and 17 (Day 23+17). Percent of mature neutrophils are shown. B. Giemsa staining on cytospins of differentiating cells. Days are the day of differentiation IL-13 supplementation was started.

ation, presence of IL-13 reduced frequencies of neutrophilic cells. The presence of IL-13 did not inhibit early stages of neutrophil differentiation. However, the frequencies of more mature band and segmented cells was significantly reduced when exposed to IL-13 at day 7. In the cultures where IL-13 supplementation was started at day 18 and day 23, neutrophils were generated when allowed to differentiate for a longer duration (Fig 1). Thus, although delayed, maturation was restored with late IL-13 exposure. Although IL-13 inhibited neutrophilic differentiation, it did not affect the generation of CD34+ HSC or CD45+ cells.

Conclusion: Our data suggest that SLE patients may have dysregulated development of myeloid cells in the bone marrow due to the cytokine milieu during elevated disease activity. Abnormal timing and exposure to IL-13 may increase immature neutrophils in SLE patients, possibly by altering the differentiation potential of CD34+ HSC. The functional responses of these newly generated neutrophils may differ due to differences in the bone marrow transit time. The dysregulation of granulopoiesis therefore may generate neutrophils that further exacerbate autoimmune response.

Disclosure: N. Jog, None; **J. Nguyen**, None; **J. James**, Progentec Diagnostics, Inc., 2.

Abstract Number: 0995

Innate Immune Tolerance Attenuates Zymosan-Induced Arthritis, Inflammatory Gene Expression and Synovial Neutrophil Infiltration

Richard Bell, Chao Yang, Caroline Brauner, Upneet Sohki, Rouxi Yuan, Bikash Mishra, Mahesh Bachu and Lionel Ivashkiv, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Zymosan (Zym) induces arthritis through TLR2- and Dectin-1-activated NK-κB signaling and inflammatory myeloid cell infiltration into the synovium of the injected joint. Innate immune tolerance after an initial TLR challenge dampens inflammatory responses induced by a second challenge. It is currently unknown if this innate immune tolerance affects Zym responses and can attenuate the effector phase of inflammatory arthritis. We hypothesize that LPS preconditioning dampens zymosan-induced innate inflammatory response and arthritis.

Methods: C57BL6 mice were administrated 10ul/g PBS or 0.5mg/kg lipopolysaccharide (LPS) intraperitoneally for 24 h and then given intraarticular (IA) injections of 180μg Zym in the right knees (n=5-12/group). H&E histology on D7 after IA Zym was performed to measure synovitis. Serum cytokine analysis at 3 h after IA Zym (n=3-4/group) and flow cytometry (FC) for myeloid cell subsets in the periarticular tissue at D2 and D7 after IA Zym (n=6-8/group) were conducted. $CD14^+$ cells from healthy human whole blood donors were isolated, cultured with M-CSF overnight, and either allowed to “rest” (R), treated with 10 ng/ml LPS for 24 h (L), stimulated with 16 μg/ml Zym for 3 h (Z), or LPS-24 h + Zym-3 h (L+Z). Cells were then harvested for mRNA expression (n=7) or stained for intracellular cytokine (n=3) analysis via FC. Western blot of TBK1, NF-κB and MAPK p38 signaling activation at 5, 15, 30, and 60 min after Zym treatment was performed (n=3).

Results: IA injection of Zym significantly induced synovitis, periarticular inflammation and immune cell infiltration while LPS pretreatment significantly attenuated synovitis (Fig 1). Serum neutrophil chemoattractant proteins CXCL1

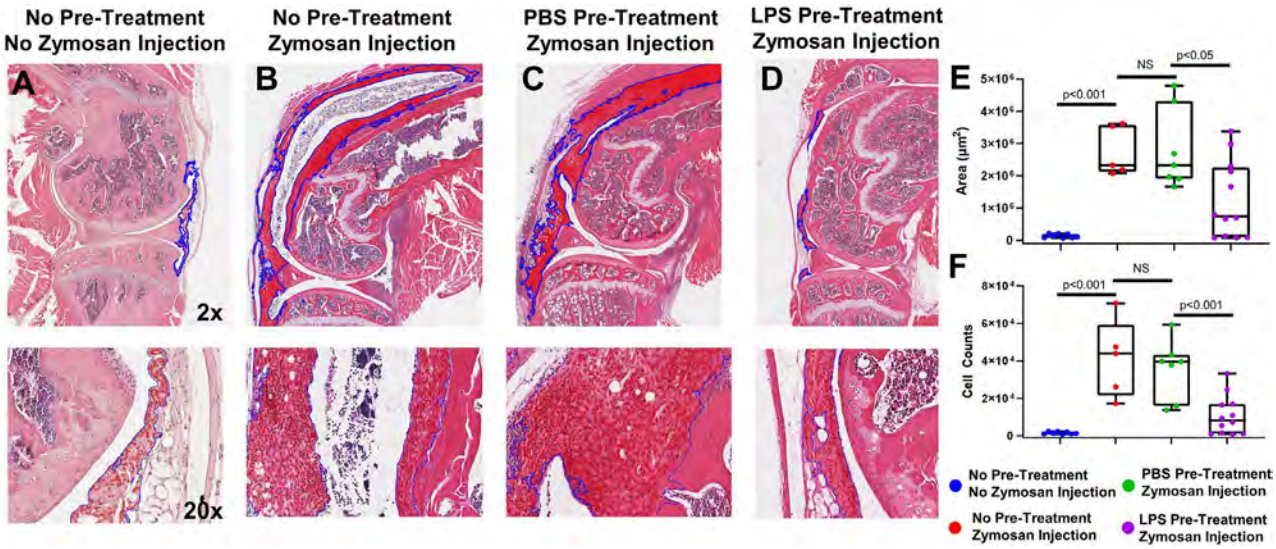


Figure 1. LPS pre-treatment attenuates zymosan induced arthritis. Compared to the un-injected knee (A), zymosan intraarticular injection induces synovitis (B) with no change in the PBS pre-treatment. However, LPS pretreatment reduces the amount of synovitis that occurs 7 days after Zym injections. Quantification of the synovial area by semi-automated segmentation (Blue outline in A-D) showed a significant expansion of area with zymosan injections with a decrease with LPS pretreatment (E). Nuclei counting via a watershed nuclei identification algorithm (Red Outline in A-D) within the segmented area showed a similar result (F). Statistical analysis performed with an ANOVA and Tukey's post-hoc test (NS = Not Significant, Data are the average of 1-3 histologic levels per knee).

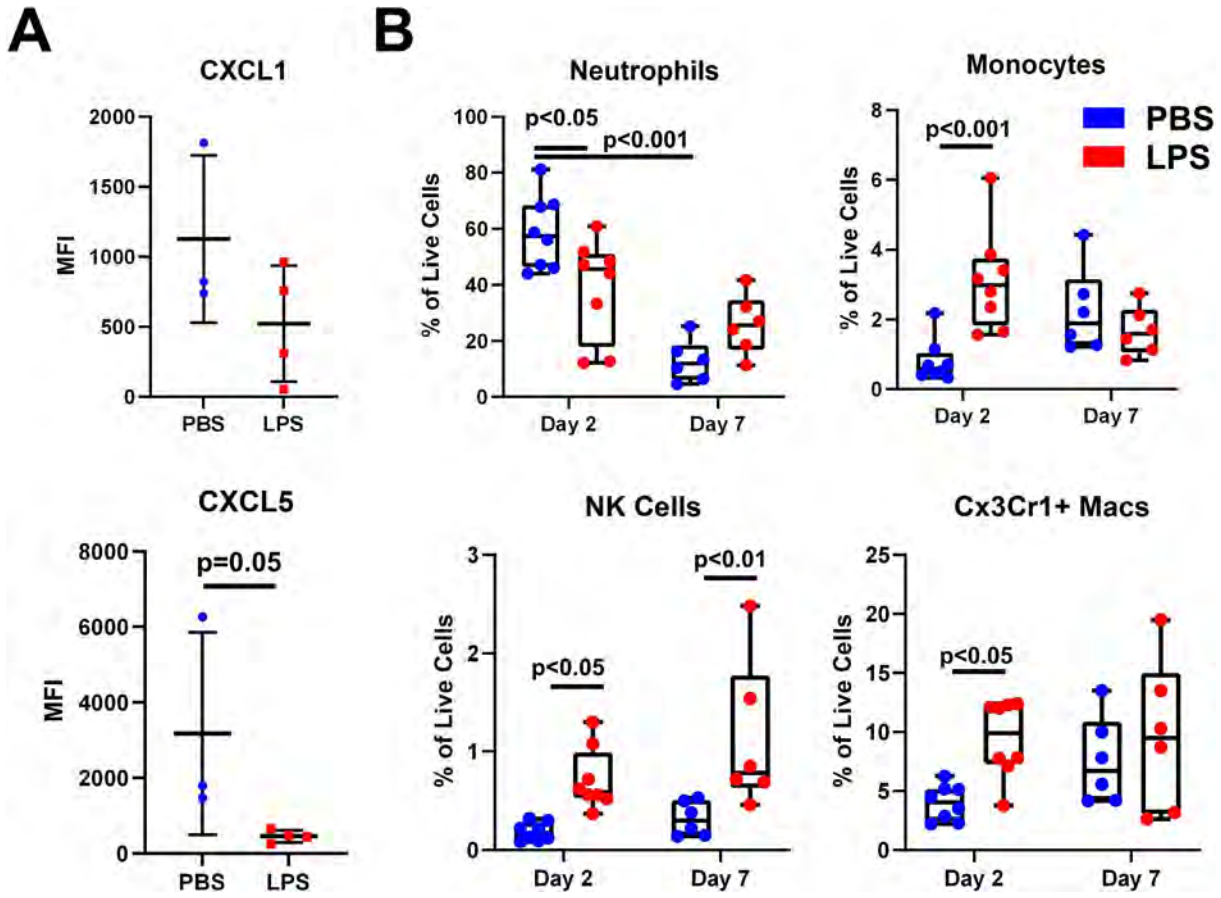


Figure 2. Neutrophil infiltration into the synovium is suppressed at day 2 after zymosan injection. Serum collected at 3 hours after zymosan IA injection in PBS and LPS treated mice suggest that the neutrophil chemokines Cxcl1 and Cxcl5 are lower in LPS treated mice (A). Flow cytometry analysis demonstrates that neutrophile infiltration in to the synovial tissue is decreased at day 2 while monocytes, NK cells and Cx3Cr1 macrophages are all increased at day 2. Statistical analysis was performed with either a Mann-Whitney test or 2-way ANOVA with Tukey's post-hoc test.

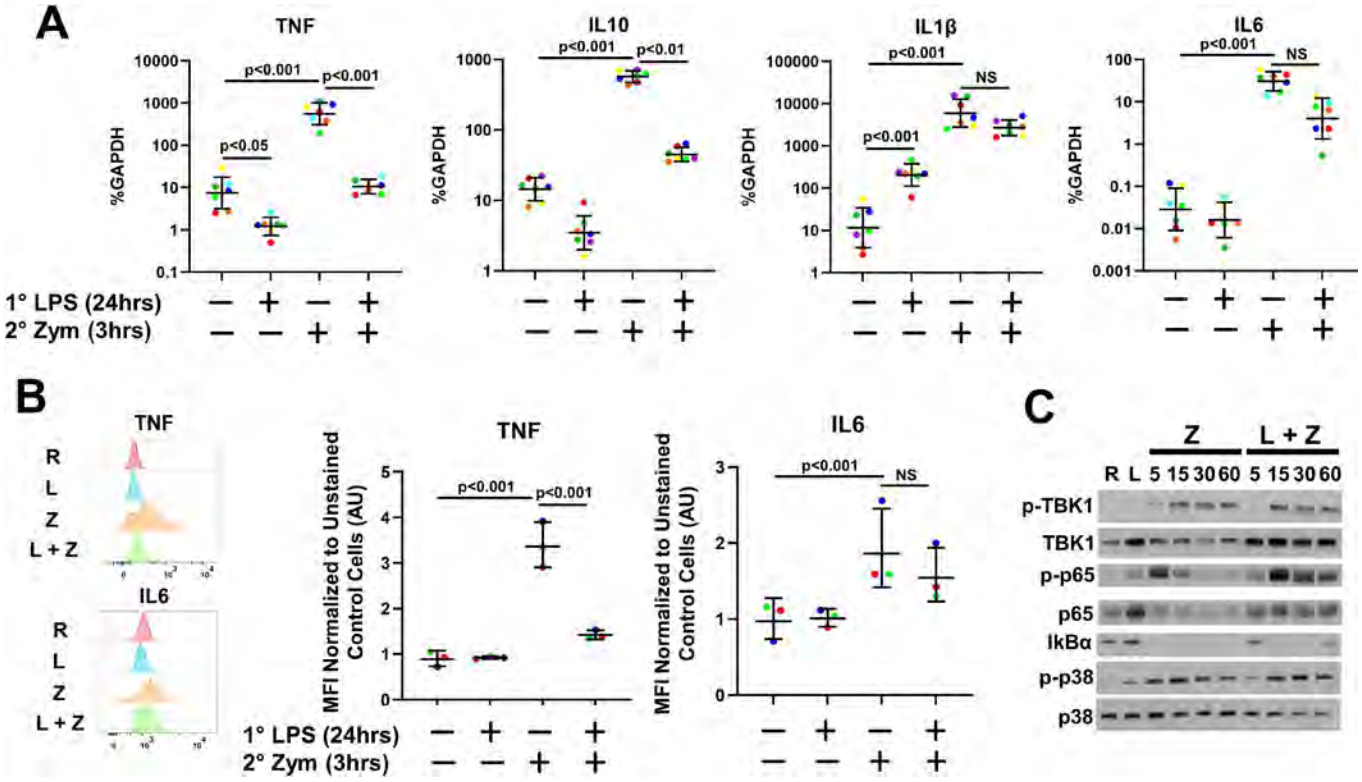


Figure 3. Gene specific tolerization by LPS of the Zymosan inflammatory response in human CD14+ cells. CD14+ cells stimulated with Zym for 3h have increased gene expression and intracellular cytokine staining of TNF, IL10, IL1β and IL6 compared to the resting condition (A, B). However, when these cells are pretreated with LPS for 24h only TNF and IL10 displayed reduced expression. Western blot analysis demonstrates zymosan induced phosphorylation of TBK1, p65, p38 and degradation of IκBα is largely unaffected by LPS pre-treatment (C). Statistical analysis was performed by log transformation of gene expression values with 2-way Repeated Measures ANOVAs and a Tukey's post-hoc test (Each colored dot indicates an individual donor).

and CXCL5 were reduced at 3 h after IA Zym in the LPS pretreated group compared to PBS group (Fig 2A). FC analysis revealed a significant reduction of synovial neutrophils at D2, while Ly6C+/Cd11c- monocytes, NK cells and CX3CR1+/CD11b+/F4-80+ macrophages were increased at D2 after arthritis induction (Fig 2B). RNA and intracellular cytokine expression of CD14+ cells challenged with Zym showed gene-specific tolerization of *Tnf* and *Il10* expression by LPS pretreatment, while *Il1b* and *Il6* induction remained intact (Fig 3 A, B). Western blots of NF-kB, TBk1 and MAPK p38 signaling suggested that LPS pretreatment minimally affects Zym-induced signaling (Fig 3C). Zym-induced expression of *CXCL2* and *CXCL8* in the human monocytes was also suppressed by LPS.

Conclusion: LPS attenuated production of neutrophil chemokines in vivo and in vitro and reduced neutrophil abundance in the synovium, thereby decreasing Zym induced synovitis. LPS pretreatment displayed gene-specific tolerization of Zym-induced gene expression in human monocytes in vitro. Monocyte, macrophage and NK cell infiltration were increased in vivo, however, our in vitro data suggests these populations could be partially tolerized. Interestingly, gene-specific tolerance occurred in the context of intact signaling, suggesting epigenetic mechanisms of gene silencing. Overall, these results suggest that LPS significantly disrupts the inflammatory response to Zym and that innate immune memory could play a role in the effector phase of inflammatory arthritis.

Disclosure: R. Bell, None; **C. Yang**, None; **C. Brauner**, None; **U. Sohki**, None; **R. Yuan**, None; **B. Mishra**, None; **M. Bachu**, None; **L. Ivashkiv**, Eli Lilly, 12, nonpaid consultant.

Abstract Number: 0996

The Stimulator of Interferon Genes (STING) Protects from Bone Loss Through Regulation of Tonic and Induced Type I Interferon Pathways

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The intracellular DNA sensing Stimulator of Interferon Genes (STING) pathway is critical for detection of viral and bacterial pathogen DNA. Hyperactivating mutations in this innate immune pathway are associated with autoinflammatory and autoimmune diseases, including gain of function mutations in STING that lead to STING-Associated Vasculopathy with onset in Infancy (SAVI). Type I interferons (IFN-I) are downstream of STING and regulate many cellular processes. An often under-appreciated aspect of IFN-I signaling, tonic (constitutive) IFN-I signaling, has been proposed as a critical element of cellular homeostasis. Vital for maintaining a balanced threshold of immune genes, tonic interferon-stimulated genes (ISGs) serve to regulate immune responses. We have focused on the role of the STING pathway in both tonic and inducible type I interferon (IFN-I) signaling and its impact on bone homeostasis.

Methods: STING deficient, myeloid specific STING-deficient ($STING^{flox/flox}$LysM $cre^{+/}$), and SAVI mice (activating murine point mutants STING V154M) were studied. Osteoclastogenesis assays were performed *in vitro*, osteoclasts were enumerated *in vivo*, and serum C terminal pyridinoline cross-linked peptide (CTX), a marker of bone resorption, was determined by ELISA. RNA sequencing was performed on osteoclast precursors before and during differentiation with M-CSF and RANKL. In SAVI osteoclastogenesis assays, differentiation was tested in the absence and presence of an IFN-I blocking antibody.

Results: We previously reported that STING-deficient and $STING^{LysM}$-deficient osteoclast precursors form greater numbers of osteoclasts *in vitro* and that STING-deficient mice lose trabecular bone faster than littermate controls, an effect consistent with increased osteoclast activity. Myeloid STING is sufficient for this effect, as ovariectomized $STING^{LysM}$-deficient mice exhibit a significantly greater loss of bone compared to controls. We extend these findings by showing that both STING-deficient and $STING^{LysM}$-deficient mice have increased osteoclast numbers *in vivo,* with evidence of increased bone resorption by serum CTX assays. To address mechanism, bulk RNAseq was performed and showed that STING-deficient osteoclast precursors exhibit a marked reduction in both tonic ISG expression prior to and following RANKL stimulation (Figure 1). To further test whether STING-mediated IFN-I limits osteoclast differentiation, osteoclastogenesis assays were performed using precursor cells from STING gain of function (SAVI) mice. SAVI osteoclast precursor cells showed significantly inhibited osteoclastogenic potential, associated with a decreased expression of differentiation factors. Importantly, blockade of IFNAR1 restored the ability of SAVI precursor cells to form osteoclasts, indicating that STING-regulated IFN-I limits osteoclastogenesis (Figure 2).

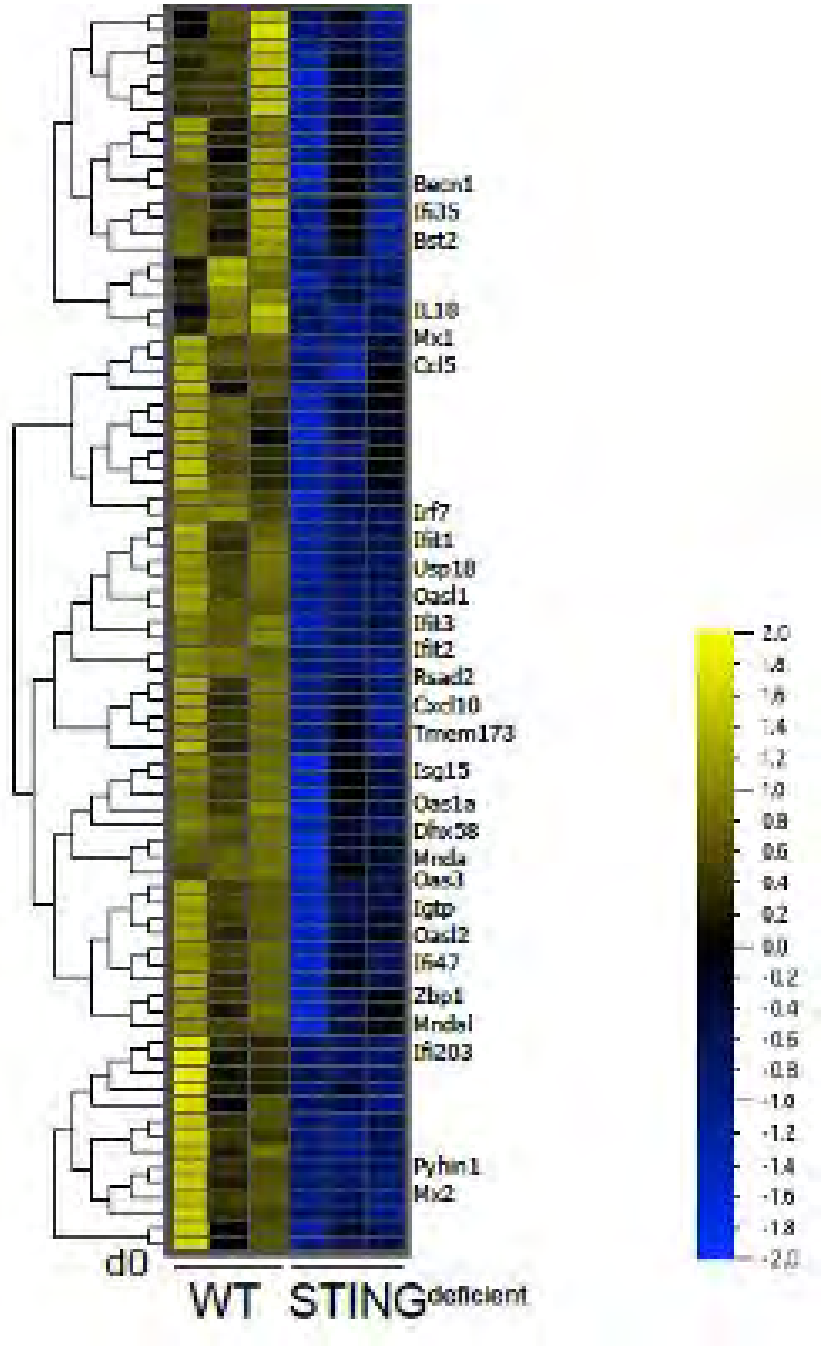

Figure 1. Analysis of the osteoclast precursor transcriptome reveals a STING-dependent tonic IFN-I signature. Heatmap representation shows multiple downregulated ISGs at d0 in STING-deficient osteoclast precursors compared to WT.

Conclusion: STING is an upstream mediator of both tonic and RANKL-induced IFN-I signaling, providing a break on osteoclast formation and protection from bone loss. These data also demonstrate that in settings in which the STING pathway is abnormal or is therapeutically altered, there may be important effects on bone.

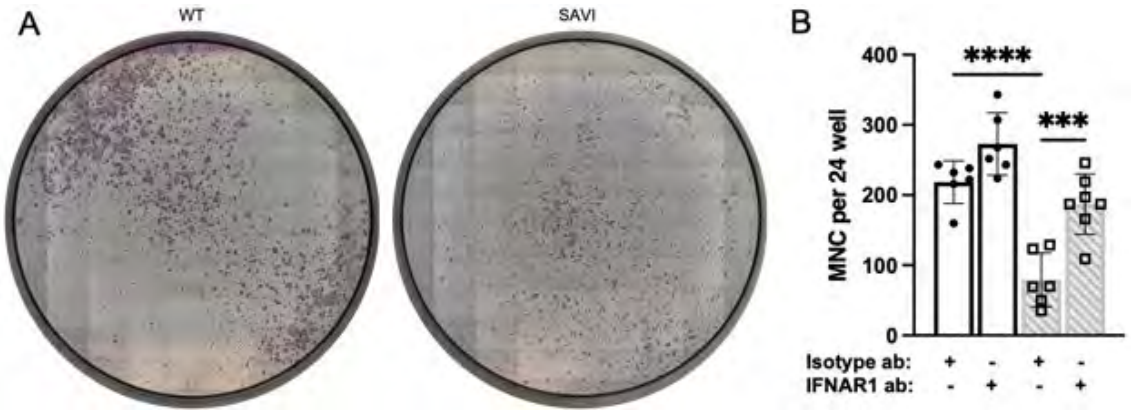

Figure 2. STING activation by SAVI point mutation limits osteoclast formation in an IFNAR1-dependent fashion. A) Representative low magnification images of TRAP stained (purple) WT and SAVI osteoclastogenesis assays at d5. B) More multinuclear cells (MNCs) form in WT (white bars) than SAVI (grey bars), which is reversed in the presence of IFN-blocking antibody (IFNAR1 ab) compared to isotype treated controls.

Disclosure: S. MacLauchlan, None; **P. Kushwaha**, None; **A. Tai**, None; **J. Chen**, None; **C. Manning**, None; **K. Fitzgerald**, None; **S. Sharma**, None; **E. Gravallese**, None.

Abstract Number: 0997

Citrullinated Vimentin Induces Epigenetic Memory of the Innate Immune System

Katerina Laskari[1], Shweta Sabu[2], Oliver Distler[3], Emmanuel Karouzakis[2] and Michel Neidhart[2], [1]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zürich, Switzerland, [2]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich, University of Zurich, Zurich, Switzerland, [3]Center of Experimental Rheumatology, Department of Rheumatology, University Hospital Zurich/University of Zurich, Zurich, Switzerland

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: During trained immunity, monocytes and macrophages undergo a functional and transcriptional reprogramming toward activation, which is induced by a priming stimulus and results in enhanced responsiveness to subsequent triggers. We aimed to investigate if citrullinated vimentin (c-vimentin), a damage-associated pattern in rheumatoid arthritis (RA), induces trained immunity in vitro in healthy individuals.

Methods: Monocytes isolated from the peripheral blood (EDTA blood, n=22; buffy coats, n=6) of healthy donors by Ficoll-paque centrifugation and negative selection, were stimulated with c-vimentin (0.1 μg/ml) for 24h and re-stimulated 5 days later with the lipopolysaccharide of E.coli (LPS) (10 ng/ml). Protein release (ELISA, Western blot) and gene expression levels (RNA sequencing) were measured. Chromatin accessibility changes were assessed by ATAC sequencing. The methylation of histone H3 at lysine 4 (H3K4) was examined by chromatin immunoprecipitation. The ligand-receptor glycocapture technology was used to identify candidate cell surface targets of c-vimentin.

Results: Priming with c-vimentin induced training in human monocytes, as suggested by the significantly increased levels of secreted interleukin-6 (IL-6), the chemokine CXCL1 and CCL20/Macrophage Inflammatory Protein 3a, upon

restimulation with LPS (1.29-2.32-fold increase, n=22, all p< 0.001). A significant increase in proinflammatory cytokine and chemokine expression was also shown in RNA sequencing (n=4), beside up-regulation of genes related to glucose and lipid metabolism as well as epigenetic effectors. Exposition to c-vimentin induced chromatin rearrangement (n=4), with increased proportion of accessible promoters (14.4% on day 6 vs. 2.4% on day 1), and a positive correlation to gene expression (r=0.35). Besides, c-vimentin induced H3K4 methylation with increased levels of this mark in the promoter of the IL-6 gene (n=6, p=0.020). Interestingly, we observed an upregulation in the expression of histone methyltransferase PRDM8 (37-fold, SD +/-10.8). At the same time, by inhibiting histone methyltransferases with methylthioadenosine (1 mM), trained immunity was reversed (8.43-fold decrease in IL-6 release, n=6, p=0.031). A shift in metabolism was supported by high lactate production measured by ELISA in the trained cells (n=9, p=0.004), while by inhibiting the metabolic pathway of glycolysis with 2-deoxyglucose (11 mM), the induction of trained immunity could be counteracted (5.32-fold decrease in IL-6 release, n=6, p=0.030). Finally, STING was identified as cell surface receptor for the ligand c-vimentin. Indeed, c-vimentin induced activation of TBK1, which is implicated in the STING signaling pathway, by phosphorylation, while STING inhibition with the covalent small molecule H151 (2 μM) abolished this effect, and decreased IL-6 release (1.61-fold decrease, n=5, p=0.051).

Conclusion: C-vimentin induces epigenetic and metabolic changes in monocytes, probably through a STING and TBK1-dependent activation, resulting in enhanced cytokine and chemokine production upon restimulation. Inhibition of the STING signaling pathway may be a novel therapeutic target against myeloid activation in RA.

Disclosure: K. **Laskari**, None; **S. Sabu**, None; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2; **E. Karouzakis**, None; **M. Neidhart**, None.

Abstract Number: 0998

Increasing Age Impairs the Metabolic Adaptation of Human Neutrophils to Glucose Deprivation

Moritz Pfeiffenberger[1], Pierre-Louis Krau[2], Yuling Chen[3], Thomas Buttgereit[4], Alexandra Damerau[1], Timo Gaber[1] and Frank Buttgereit[4], [1]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [2]Charit Universittsmedizin Berlin, corporate member of Freie Universitt Berlin, Humboldt-Universitt zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany, [3]Charité University Medicine Berlin, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Age-related impairment of characteristic neutrophil functions is well described (Fortin, McDonald et al. 2008). However, experimental evidence for age-related alterations of neutrophil metabolic adaptation towards nutrient deprivation -a feature of neutrophil battlefields- remains elusive. Moreover, differences in neutrophil metabolic adaptation may contribute to age-related pathologies such as autoimmune diseases including rheumatoid arthritis or other pathologies as atherosclerosis or cancer.

Therefore, we hypothesized that metabolic adaptation of human neutrophils to glucose deprivation is impaired with increasing age.

Methods: In order to test the hypothesis, we compared isolated human peripheral CD15+ neutrophils from four healthy young donors (mean age: 23.4 ± 2.7) with four healthy elderly donors (mean age of 58.7 ± 2.4). First, we analyzed the survival of neutrophils either stimulated with PMA or left untreated and subsequently incubated for 0 h and 6 h under various glucose concentrations (0, 1, 5, and 10 mM). To address this, we performed 7-AAD staining by flow cytometry, while basal respiration, ATP-bound respiration, maximal respiration, and spare capacity were determined using Seahorse™ technology.

Results: We observed that neutrophils (purity > 97%) survived for 6 hours *in vitro*, independent of treatment with PMA or glucose concentrations in the culture medium. With minor differences between the various concentrations of glucose used, the percentage of living cells after 6 h was 95% ± 2.5 without PMA and 75% ± 4.7 with PMA stimulation. No differences were uncovered between the two age groups. However, Seahorse™ technology revealed significant differences in basal, maximal, and spare respiratory capacity. Briefly, oxygen consumption rate (OCR; pmol/min/cell count) with respect to basal, maximal and reserve respiratory capacity was lower in the elderly donors compared to the young donors. For instance, with a concentration of 5 mM glucose, the OCR was 17 ± 0.7 in elderly donors compared to 22.5 ± 1 in young donors, while the maximal respiration was 25 ± 0.8 in elderly and 41 ± 0.6 in the young donor group. Interestingly, these differences were independent of glucose concentrations in the medium.

Conclusion: Our initial experiments show that basal metabolic parameters differ between neutrophils from young and older donors. Further experiments are needed to understand in detail the mechanisms and effects of age-related differences in metabolism on neutrophil functions.

Disclosure: M. Pfeiffenberger, None; **P. Krau**, None; **Y. Chen**, None; **T. Buttgereit**, None; **A. Damerau**, None; **T. Gaber**, None; **F. Buttgereit**, Horizon Therapeutics, 2, 5, Mundipharma, 5, Roche, 1, 5, Pfizer, 1, 5, 6.

Abstract Number: 0999

UVB-irradiated Keratinocyte-derived Extracellular Vesicles Induced Proinflammatory Responses in Macrophages

Yubin Li[1], Thomas Vazquez[2], DeAnna Diaz[3], Mariko Momohara[4] and Victoria Werth[4], [1]Corporal Michael J. Crescenz VAMC, Department of Dermatology, U Penn, Philadelphia, PA, [2]FIU Wertheim College of Medicine, Virginia Beach, VA, [3]Philadelphia College of Medicine, Philadelphia, PA, [4]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultraviolet B irradiation (UVB) contributes to skin inflammation. As UVB mostly affects the epidermis, with just 10% getting into the dermis, the crosstalk between epidermis and dermis in the response to UVB warrants investigation. Extracellular vesicles (EVs), lipid bilayer membrane vesicles secreted by many cells, can carry lipids, proteins and nucleic acids to mediate signal transduction. As a critical sensor and adaptor for the host immune response to cytosolic DNA and cyclic dinucleotides, stimulator of interferon genes (STING) plays critical roles in immunity and inflammation. Initiated by cytosolic pattern recognition receptors, inflammasome activation-mediated pyroptosis is a highly inflammatory form of programmed cell death. Thus, we hypothesized that EVs derived from UVB-irradiated keratinocytes might trigger STING and inflammasome-mediated proinflammatory responses in dermal cells; The goal here was to evaluate the crosstalk between STING and the inflammasome during EVs-mediated proinflammatory responses in dermal cells.

Methods: Human keratinocytes (HaCaT) cells were irradiated with UVB light. After irradiation, cells were cultured for 24 hours and the supernatant was harvested for EV collection. EVs were isolated by ultracentrifugation and used to stimulate fibroblasts or macrophages with/without STING or inflammasome signaling inhibitors. The supernatant was harvested for ELISA and the lysed cells were collected for Western blot. C57BL/6J (Stock No.: 000664) and C57BL/6J-Sting1gt/J (Stock No.: 017537) mice purchased from Jackson Laboratory were treated with or 100 mJ/cm^2 UVB for five consecutive days. Dorsal skin samples were collected for histological analysis.

Results: UVB irradiated HaCaT cells released more extracellular vesicles than unirradiated cells (1.78x10^9/mL vs. 3.31x10^8/mL), with a similar mean size (74.7nm *vs* 73.5nm). UVB-irradiated-keratinocyte-derived EVs (KEV-UVB) expressed more small extracellular vesicle surface markers (CD81, CD9, CD63) than non-irradiated-KEVs. KEV-UVB triggered more interferonb (IFNb) release from macrophages than fibroblasts (111.1±21.45 vs. 4.85±0.72 pg/mL $P<$ 0.05 n=3). STING antagonist H-151 attenuated KEV-UVB triggered IFNb production in macrophages (13.18±6.38 vs. 111.1±21.45 pg/mL $P<$ 0.05). TBK1 inhibitor MRT67307 also showed a similar effect (12.6±0.71 vs. 304.6±94.4 pg/mL $P<$ 0.05). Inhibition of the STING signaling pathway also suppressed KEV-UVB triggered interleukin 1b (IL1b) production in macrophages (60.52±11.41 vs. 325.2±62.68 pg/mL $P<$ 0.05), while suppression of the inflammasome pathway by VX765 and Ac-YVAD-cmk only attenuated KEV-UVB triggered IL1b (22.00±5.01 vs. 34.67±5.85 pg/mL $P<$ 0.05) but not IFNb production in macrophages (636.9±165.1 vs. 680.8±147.1 pg/mL $P>$0.05). Furthermore, UVB irradiation triggered more skin inflammation in STING knockout mice than WT mice *in vivo*.

Conclusion: KEV-UVB were mediators of inflammation, and triggered both STING and inflammasome-mediated cytokine release. Targeting the STING signaling pathway may provide insight into a potential therapeutic approach for UVB-induced skin inflammation.

Disclosure: Y. Li, None; **T. Vazquez**, None; **D. Diaz**, None; **M. Momohara**, None; **V. Werth**, None.

Abstract Number: 1000

Molecular Mechanism of Inhibition of CD38 in Attenuation of Monosodium Urate Crystal-induced Inflammatory Responses in Macrophages

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: CD38 can function as a degrading enzyme of nicotinamide adenine dinucleotide (NAD), a critical metabolic intermediate serving as enzyme cofactor in redox reactions and as a co-substrate by many enzymes such as sirtuins (SIRTs). We have recently observed that expression of CD38 is increased in PBMCs of gout patients compared to health controls, and inhibition of CD38 attenuated monosodium urate (MSU) crystal-induced acute inflammatory responses in mice *in vivo*. In this study, we investigated the molecular mechanism mediating beneficial effect of inhibition of CD38 in macrophages in response to MSU crystals *in vitro*.

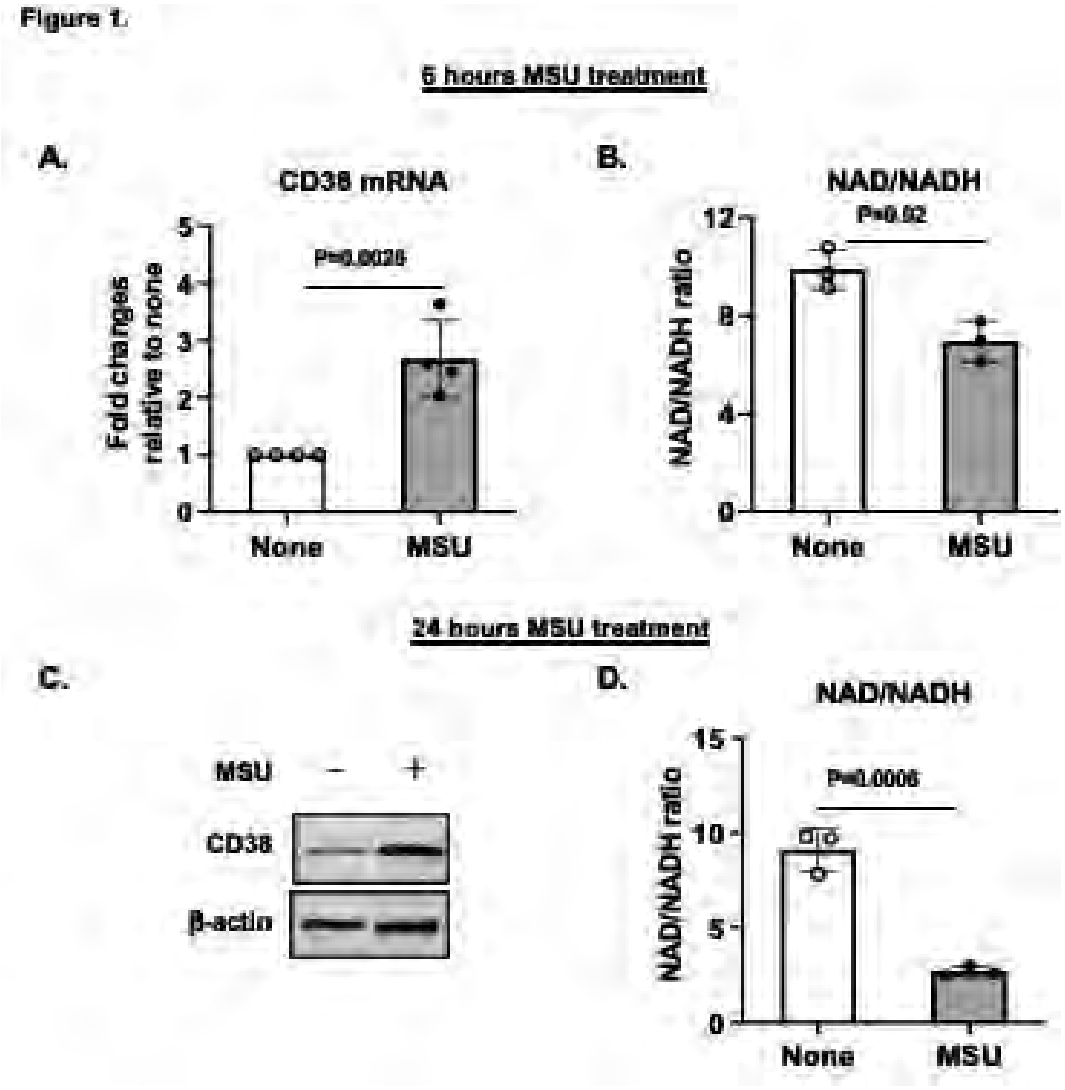

Figure 1. Induction of CD38 expression by MSU crystals correlated with decreased NAD/NADH ratio in mouse BMDMs.

Methods: Bone marrow derived macrophages (BMDMs) prepared from CD38 knockout (KO) and wild type (WT) were treated with MSU crystals (0.2 mg/ml) in the presence or absence of apigenin (25 μM), a flavonoid that selectively inhibits CD38 for 6 and 24 hours. Expression of CD38 was examined at both mRNA and protein levels by qRT-PCR and Western blot analysis. The NADH/NAD Quantification Kit (BioVision) was used to measure the intracellular NAD, NADH and their ratio. Western blot analysis was carried out to examine expression of NAD-dependent SIRT3 and acetylated SOD2, expression of NLRP3 and cleaved caspase-1. ELISA was performed to determine the release of IL-1β from the conditioned media. RNA sequencing analysis was also carried out to profile differentially expressed genes.

Results: The NAD/NADH ratio was significantly reduced in BMDMs treated with MSU crystals at both 6 and 24 hours, correlated with increased CD38 expression at both mRNA and protein levels, respectively. Apigenin inhibited CD38 expression, prevented a decrease in NAD/NADH ratio, prohibited a decrease in expression of SIRT3 and an increase in expression of acetylated SOD2, an antioxidant enzyme in the mitochondria, in BMDMs treated with MSU crystals. Apigenin also suppressed NLRP3 expression at both mRNA and protein levels, inhibited expression of cleaved casepase-1, and attenuated IL-1ß release in response to MSU crystals. RNA-seq analysis showed that 163 genes upregulated in WT+MSU BMDMs ($log_2FC \geq 1$)were downregulated in both WT+MSU+apigenin and CD38KO BMDMs

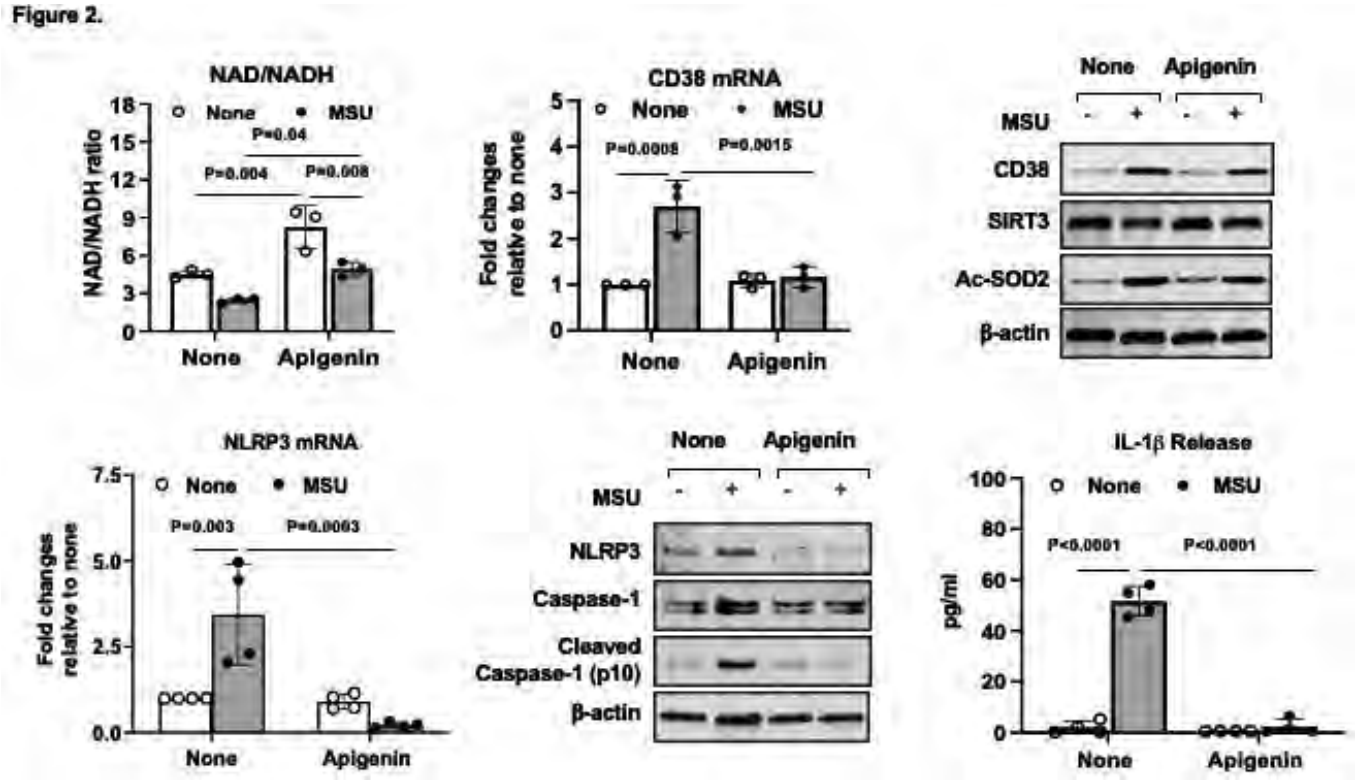

Figure 2. Apigenin inhibited CD38 expression, prevented a decrease in NAD/NADH ratio, prohibited a decrease in expression of SIRT3 and an increase in expression of acetylated SOD2, suppressed NLRP3 expression at both mRNA and protein levels, inhibited expression of cleaved casepase-1, and attenuated IL-1b release in response to MSU crystals in macrophages.

($log_2FC \leq 1$). KEGG Pathway enrichment analysis revealed several inflammatory pathways including cytokine-cytokine receptor interaction, chemokine, TNF, NF-κB, JAK-STAT, HIF-1α, TLR and MAPK signaling. Interestingly, a top differentially expressed gene six-transmembrane epithelial antigen of prostate 4 (Steap4) was upregulated in WT+MSU BMDMs ($log_2FC=8.14$) but was downregulated in WT+MSU+apigenin BMDMs ($log_2FC= -7.18$) and CD38KO+MSU BMDMs ($log_2FC= -4.43$). Steap4 is a metalloreductase that has the ability to reduce both Fe(3+) to Fe(2+) and Cu(2+) to Cu(1+), using NAD(+) as acceptor. Increased Steap4 expression has been shown to lead to mitochondrial iron accumulation and enhanced reactive oxygen species production. Thus, downregulation of Steap4 expression induced by MSU crystals through inhibition of CD38 may help maintain mitochondria homeostasis.

Conclusion: Inhibition of CD38 can attenuate inflammatory response to MSU crystals in macrophages by prohibiting NAD decline and preventing mitochondrial dysfunction.

Disclosure: H. Qin, None; **P. Oliveira**, None; **T. Yan**, None; **R. Terkeltaub**, SOBI, 2, Selecta, 2, Allena, 2, Horizon, 2, Astra-Zeneca, 2, Astra-Zeneca, 5; **R. Liu Bryan**, None.

Abstract Number: 1001

Exosomes Mediate a Cooperative Mechanism of Macrophage/Fibroblast Activation in Systemic Sclerosis

Rajan Bhandari[1], Heetaek Yang[2], Noelle Kosarek[3], Michael Whitfield[4] and **Patricia Pioli**[1], [1]Geisel School of Medicine at Dartmouth, Lebanon, NH, [2]Geisel School of Medicine, Hanover, NH, [3]Dartmouth Geisel School of Medicine, Hartford, VT, [4]Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Prior work demonstrates that macrophages (MØs) from patients with Systemic Sclerosis (SSc) produce fibrotic and pro-inflammatory mediators and that cocultured MØs and SSc fibroblasts engage in reciprocal activation. However, the factors responsible for pro-fibrotic MØ activation in SSc are unknown. Given the proximity of MØs and fibroblasts in SSc patient skin, we hypothesize that fibroblast-derived mediators contribute to SSc MØ activation. In this study, we identify SSc dermal fibroblast-derived exosomes as inducers of MØ activation and demonstrate that exosome-activated MØs stimulate fibroblast production of inflammatory cytokines and extracellular matrix (ECM) components (Figure 1).

Methods: Fibroblasts were isolated from skin biopsies obtained from 9 SSc patients or 7 healthy age and gender-matched control subjects following written informed consent. $CD14^+$ monocytes were purified from PBMCs obtained from whole blood of 7 healthy consented donors. Dermal fibroblasts were cultured with 5 ng/ml TGF-beta in media supplemented with exosome-depleted FBS for 72 hours prior to exosome isolation from cell supernatants. Exosomes were quantified using NanoSight and exosome purity was assessed by immunoblot for canonical markers. Monocytes were differentiated into MØs by incubation with M-CSF for 5 days and then were cultured with exosomes

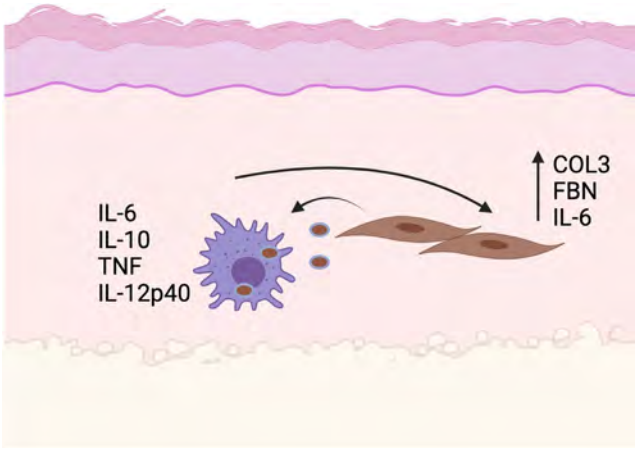

Figure 1. Model of SSc Fibroblast-derived Exosome-mediated Induction of MØ Activation in SSc. In our model, dermal fibroblasts from SSc patients release exosomes containing miR cargo that are internalized by MØs. Uptake of SSc fibroblast-derived exosomes induces pro-inflammatory and pro-fibrotic MØ activation, resulting in release of cytokines and fibrotic mediators by MØs that further stimulate SSc fibroblast activation. Cooperative activation results in dermal inflammation and increased ECM deposition.

from control or SSc fibroblasts for an additional 48 hours. MØs were immunophenotyped using flow cytometry, qRT-PCR and multiplex. For mutual activation studies, exosome-activated MØs were co-cultured with SSc fibroblasts using Transwells.

Results: MØs activated with dermal fibroblast-derived exosomes from SSc patients upregulate surface expression of CD163, CD206, and MHC Class II compared with MØs incubated with healthy control fibroblasts (Figure 2). This pattern of expression is consistent with the previously identified surface marker profile established for human SSc MØs. In addition, SSc fibroblast-derived exosomes elicit elevated levels of secreted IL-6, IL-10, IL-12p40, and TNF from MØs (Figure 3). Exosome cargo from SSc and healthy control fibroblasts was sequenced and differential expression of microRNAs (miRs) was noted between the cell types, which may account for the enhanced inflammatory activation of SSc MØs. Co-culture studies demonstrate that exosome-stimulated MØs and SSc fibroblasts engage in reciprocal activation, as production of collagen and fibronectin is significantly increased in fibroblasts receiving signals from SSc exosome-stimulated MØs.

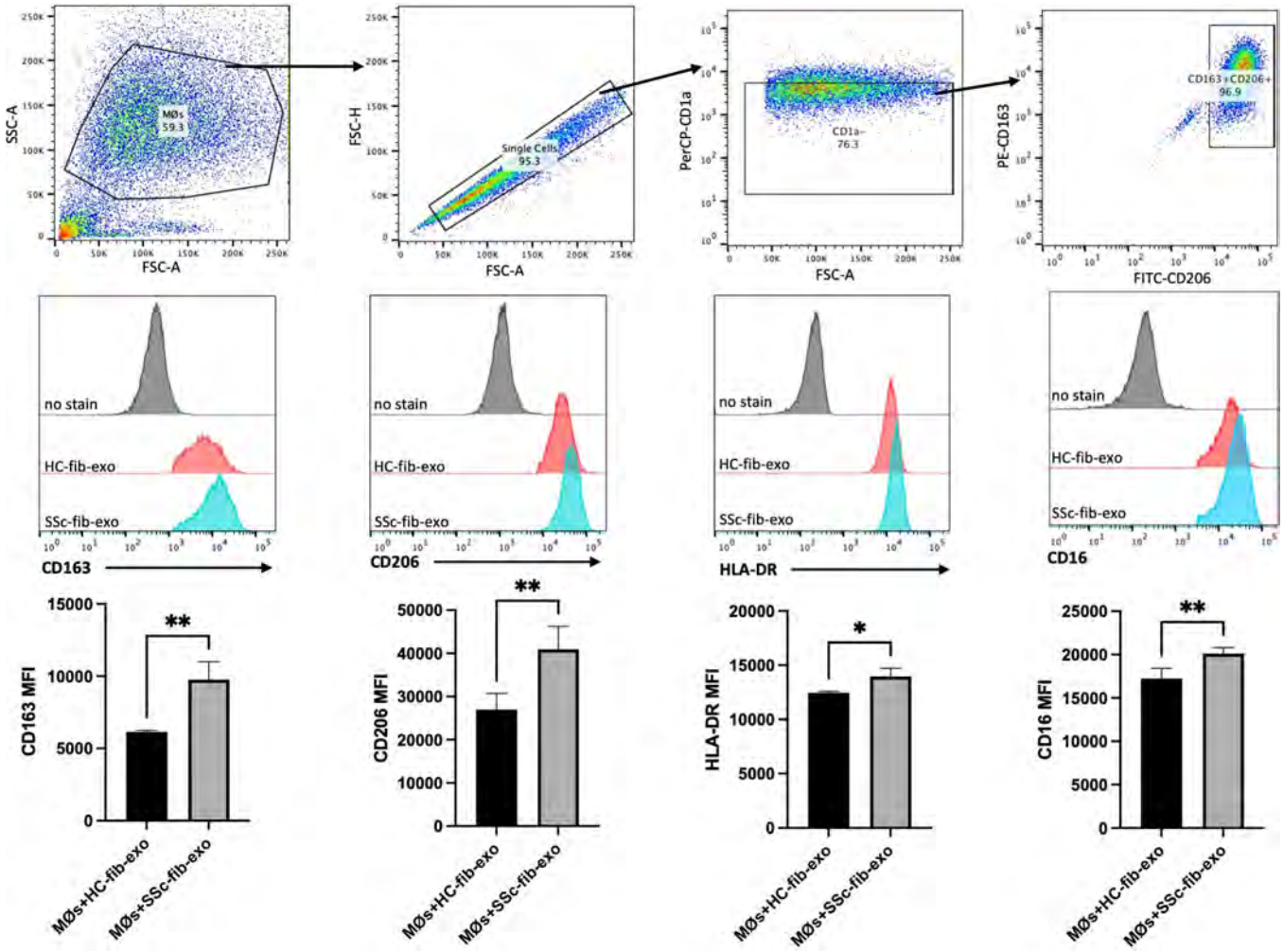

Figure 2. Induction of Surface Marker Expression on MØs by SSc Fibroblast-derived Exosomes. MØs were incubated with exosomes released from TGF-beta-stimulated SSc dermal or healthy control fibroblasts for 48 hours. Exosome uptake was verified in MØs using immunofluorescence, and activated MØs were immunophenotyped using flow cytometry. As demonstrated, internalization of SSc fibroblast-derived exosomes upregulated surface marker expression of CD163, CD206, and MHC Class II, which were previously identified as characteristic of pro-fibrotic SSc MØs.

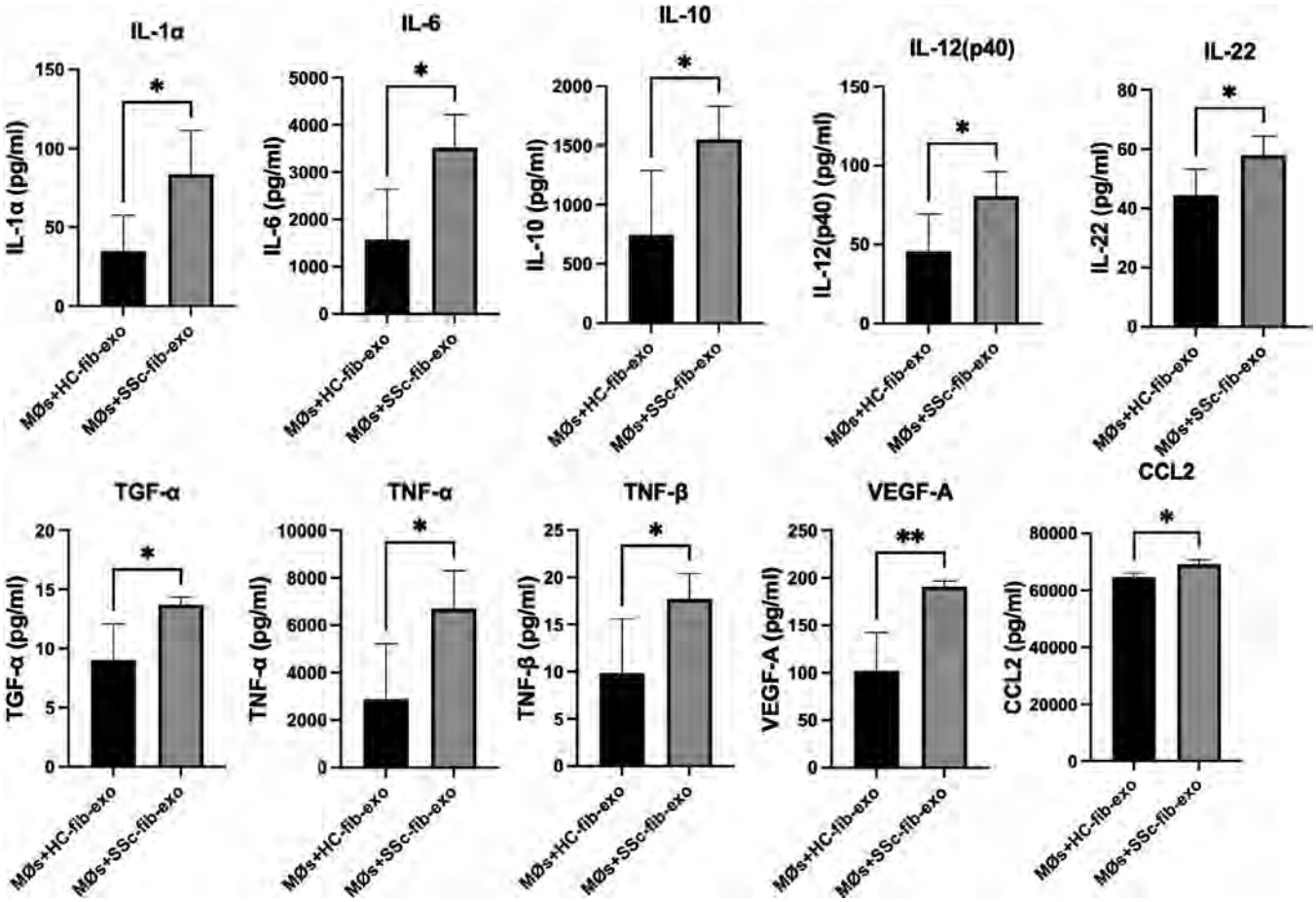

Figure 3. Pro-inflammatory and Pro-fibrotic Cytokines Are Induced in MØs Activated with SSc-Fibroblast-derived Exosomes. Exosomes were isolated from the supernatant of TGF-beta stimulated SSc or healthy control fibroblasts and cultured with MØs for 48 hours. Exosome uptake was confirmed using immunofluorescence and MØ surface phenotype was monitored by flow cytometry. Supernatants were collected from activated MØs and analyzed using multiplex analysis.

Conclusion: In this work, we demonstrate for the first time that human SSc dermal fibroblasts can mediate MØ activation through exosomes. Consistent with prior studies, we show that MØs express surface markers and release mediators associated with both alternative and inflammatory MØ activation. Our findings suggest that MØs and fibroblasts engage in cross-talk in SSc skin that results in mutual activation, inflammation, and ECM deposition. Collectively, these studies implicate MØs and fibroblasts as cooperative mediators of fibrosis in SSc and suggest dual therapeutic targeting of these cell types may provide maximal benefit in ameliorating disease in SSc patients.

Disclosure: R. Bhandari, None; **H. Yang**, None; **N. Kosarek**, None; **M. Whitfield**, Celdara Medical, LLC, 2, 5, 8, 12, Scientific Founder, Bristol Myers Squibb, 2, 5, 6, Acceleron, 2, Corbus Pharmaceuticals, 2, 6, Abbvie, 6, Kadmon, 6; **P. Pioli**, Celdara Medical, 5, Pfizer, 5.

Abstract Number: 1002

Nerve and Airway-associated Tissue Resident Pulmonary Macrophages Limit Infiltration and Alter Phenotype of Infiltrating Monocytes and Fibrocytes to Reduce Pulmonary Fibrosis

Robert Freilich[1] and Kamal Khanna[2], [1]New York University Department of Rheumatology, New York, NY, [2]New York University Department of Rheumatology & Microbiology, New York, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Macrophages and monocytes are increasingly implicated in the pathogenesis of autoimmune induced pulmonary fibrosis. In addition to the well-recognized classes of tissue resident macrophages alveolar macrophages (AMs) and interstitial macrophages (IMs), recent studies have identified a novel class lung tissue resident macrophage termed CD169+ Nerve and Airway-associated Macrophages (NAMs) whose role in autoimmune pulmonary pathology is unclear. Further, recent studies have demonstrated monocytes playing a critical role in the progression of pulmonary fibrosis. Interestingly, monocytes can be further subdivided into classical, non-classical, intermediate and fibrocytes, that are thought to play a key role in fibrosis/wound healing, but whose exact roles in autoimmune induced pulmonary fibrosis are unknown.

Methods: We utilized the bleomycin-induced murine model of pulmonary fibrosis in C57BL/6 wild-type (WT) mice in combination with transgenic murine models that selectively deplete AMs, NAMs, or both AMs/NAMs upon Intraperitoneal injection of diphtheria toxin (DT). DT injection (1000ng) were given 16 hours prior to bleomycin treatment (2.5u/kg). Mice were sacrificed on days 4, 11, 18 and 42. Lungs were fixed, sectioned and stained for IF or disassociated into a single cell suspension, stained, and analyzed by flow cytometry for both surface and intracellular targets, including a-Smooth Actin (aSMA)/Collagen-1a (Col1a).

Results: Bleomycin-treated mice whose NAMs were depleted were sicker than WT littermates, with greater weight loss (34% vs. 24%), reduced survival (35% vs 65%) and increased lung dry weight (67.7mg vs 55.9mg) Interestingly, NAM depletion resulted in increased monocytic infiltration compared to WT bleomycin-treated littermates. We further characterized the infiltrating monocytic compartment, via flow cytometry, as either 'true' monocytes (CD45+,CD11b+,CD140a-,SMA-,Col1a-), putative fibrocytes (CD45+,CD11b+,CD140a+,aSMA+, Col1a+) or a transitioning population (CD45+,CD11b+,CD140a+,aSMA+, Col1a-). Our analyses demonstrates that depletion of NAMs alters the infiltrating monocytic compartment in two key ways. First, we observed a 39% increase in the numbers of infiltrating monocytes that are (CD45+,CD11b+,CD140a-) (p=0.0195). However, these monocytes were noted to have more fibrocytic phenotype with higher levels of aSMA or Col1a expression, 23% (aSMA+/Col1a-) (p=0.0426), and 16% (aSMA+/Col1a+) (p=0.0292).

Conclusion: Depleting tissue-resident macrophages led to an increase in infiltrating monocytes skewed towards a more pro-fibrotic phenotype and resulting in a poorer clinical outcome. Taken together, these findings potentially provide insight into the mechanisms of inflammatory pulmonary fibrosis in autoimmune diseases.

Disclosure: R. Freilich, None; **K. Khanna**, None.

Abstract Number: 1003

Significant Enrichment of Pathogenic CD206+CD163+ Macrophages in Rheumatoid Arthritis Synovial Tissue with Distinct Transcriptional Signatures

Megan Hanlon[1], Mary Canavan[2], Nuno Neto[3], Qingxuan Song[4], Phil Gallagher[5], Ronan Mullan[6], Conor Hurson[7], Barry Moran[3], Michael Monaghan[3], Sunil Nagpal[8], Douglas Veale[9] and Ursula Fearon[3], [1]Molecular Rheumatology, Dublin, Ireland, [2]Trinity College, Santry, Ireland, [3]Trinity College Dublin, Dublin, Ireland, [4]Janssen Research & Development LLC, Spring House, PA, [5]St Vincent's Hospital, Dublin, Ireland, [6]Tallaght University Hospital, Dublin, Ireland, [7]St Vincents University Hospital, Dublin, Ireland, [8]Janssen Research, Collegeville, PA, [9]University College Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Synovial tissue macrophages are an exquisitely plastic pool of innate cells that play a key role in RA disease progression. However, the precise nature, diversity, and function of macrophage subsets within the inflamed joint remains unexplored. Therefore, the aims of this study are to phenotypically, transcriptionally and functionally characterise synovial tissue macrophages residing within the inflamed joint.

Methods: Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA), Osteoarthritis (OA), Arthralgia and healthy control synovial tissue biopsies and synovial fluid mononuclear cells were analysed using the following panel (CD40,-CD45,-CD64,-CD68,-CD163,-CD206,-CD253,-CCR4,-CCR7,-CXCR1,-CXCR3). CD206+CD163+ and CD206-CD163- macrophages were sorted from RA synovial-tissue by FACSAria sorter; RNAseq and FLIM analysis, autologous T-cell co-culture and heathy synovial fibroblast experiments were performed. Cytokine expression was measured by MSD.

Results: A spectrum of macrophage activation states exists within the inflamed synovium. Within this spectrum, significant enrichment of dominant CD206+CD163+ macrophage subtype is present in synovial-tissue versus fluid ($p< 0.05$). CD206+CD163+ synovial tissue macrophages express significantly more CD40 than synovial fluid ($p< 0.0003$), positively correlating with disease activity ($r=0.6$, $p< 0.01$), with baseline levels predicting response to therapy ($p< 0.05$). Moreover, CD206+CD163+CD40+ macrophages are enriched in RA synovial tissue compared to PsA and OA pathotypes ($p< 0.05$). While the CD206+CD163+ subset is present in healthy synovial tissue, expression of CD40 is completely absent in healthy synovium ($p< 0.05$). Protective barrier-like CX_3CR1-expressing macrophages are depleted in RA synovial tissue and this occurs prior to clinical manifestations. RNA-seq analysis indicates that CD206+CD163+ population is transcriptionally distinct from synovial tissue CD206-CD163-, synovial fluid CD206+CD163+, and RA monocyte-derived M1/M2 macrophages, with unique tissue-resident gene signatures. Moreover, differing metabolic demands between CD206+CD163+ and CD206-CD163- subsets was demonstrated by RNAseq and FLIM analysis. Finally, CD206+CD163+ macrophages spontaneously secrete high levels of key pro-inflammatory mediators (reversed through inhibition of CD40 signalling) which in turn can activate healthy synovial fibroblasts, thus further contributing to the local inflammatory response.

Conclusion: This data identifies for the first-time enrichment of a previously undescribed dysfunctional dominant and transcriptionally distinct macrophage subtype in RA synovial tissue. Taken together, this data provides a greater understanding of the critical role tissue-resident macrophages play in perpetuating inflammation in RA. Further investigation of the molecular patterns and cues that shape specific synovial macrophage subsets may provide opportunities to reinstate RA joint homeostasis.

Disclosure: M. Hanlon, None; **M. Canavan**, None; **N. Neto**, None; **Q. Song**, Janssen Research and Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **P. Gallagher**, None; **R. Mullan**, None; **C. Hurson**, None; **B. Moran**, None; **M. Monaghan**, None; **S. Nagpal**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6; **U. Fearon**, Abbvie, 1, 5, 6, BMS, 1, Pfizer, 1, 5, Janssen, 5, Eli Lilly, 5, UCB, 5, GSK, 6.

Abstract Number: 1004

Manipulation of B7 Family Member Expression Demonstrates Synovial Macrophage Plasticity and Possible Future Targets for Treatment of Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Infiltration of monocyte-derived macrophages into the synovial tissue (ST) is a hallmark of rheumatoid arthritis (RA). These infiltrating cells lead to inflammation, local joint effusion, and joint damage via the production of inflammatory cytokines. Macrophages express an array of co-stimulatory receptors, particularly those of the B7 protein family, including the programmed death protein 1 (PD-1) ligands, PD-L1 and PD-L2, and the B7-related protein VSIG4.

In the healthy state, interaction between PD-1 and its ligands results in an inhibitory signalling cascade in the PD-1 expressing T cell, which can in turn inhibit cell proliferation and cytokine release. However, in RA, PD-L1 is conspicuously absent from the ST (Guo, et al., 2018), leaving disease-driving cells expressing PD-1 (such as T peripheral and T follicular helper cells) unchecked. This imbalance in PD-1 signalling may contribute to disease progression and may provide a target for treatment.

Herein, we investigate the potential of 'reprogramming' inflammatory synovial fluid macrophages to upregulate inhibitory co-signalling molecules such as PD-L1 and PD-L2, to provide a proof-of-concept study into using these cells as a future cellular-based therapy. Such a therapy may provide a locally administered, anti-T cell based therapeutic approach.

Methods: Synovial fluid mononuclear cells (SFMC) were obtained from patients with active early RA (< 1 year; fulfilling 2010 classification criteria). Cryopreserved SFMCs were cultured for 48 hours in the presence of 10 ng/mL interferon (IFN)-γ or 50 ng/mL dexamethasone, or neither. Following culture, cells were stained for flow cytometry using antibodies against CD14, CD16, CD68, CD163, CD45, PD-L1, PD-L2 and VSIG4 (BD Biosciences), and the viability dye Zombie NIR (BioLegend). Cells were analysed using a Beckman Coulter CytoFLEX flow cytometer and data interpreted using FlowJo software.

Results: SF macrophages were characterised by their expression of CD14, CD16, CD68 and CD163. Flow cytometric analysis revealed that SF macrophages were amenable to phenotypic modulation by exogenous mediators. As ex-

pected, Dexamethasone resulted in an increase in a CD163$^+$, M2 like phenotype. Comparison of unstimulated control SF macrophages and those cultured with IFNγ showed significantly elevated levels of PD-L1 and PD-L2, and significantly reduced expression of VSIG4. Conversely, SF cells stimulated with dexamethasone exhibited significantly reduced levels of PD-L1, and significantly elevated levels of VSIG4.

Conclusion: Our findings demonstrate, for the first time in RA, the phenotypic plasticity of SF macrophages *in vitro*. Specifically, we found that culture of RA SF macrophages in the presence of IFNγ increased the expression of PD-L1 and PD-L2, demonstrating the potential of these cells to 'rebalance' the PD-1 pathway. Interestingly, these cells exhibited decreased surface protein levels of VSIG4, a B7 family related protein with overlapping function with PD-L1 and PD-L2. Culture with dexamethasone induced the opposite. These findings suggests that while PD-L1, PD-L2 and VSIG4 have similar regulatory characteristics, these proteins may exert differential functions in specific environments.

Disclosure: A. Small, None; **K. Williams**, None; **A. Ferrante**, None; **M. Smith**, None; **S. Proudman**, janssen, 1, 5, Glaxo Smith Kline, 5, Boehringer Ingelheim, 1, Corbus, 12, PI on clinical trial, CSL, 12, PI on clinical trial, Emerald, 12, PI on clinical trial, Pfizer, 5, Roche, 5, Bayer, 5; **H. Weedon**, None; **M. Wechalekar**, Janssen Research and Development, Philadelphia, USA, 5.

Abstract Number: 1005

CD209/CD14$^+$ Dendritic Cells Characterization in Rheumatoid and Psoriatic Arthritis Patients: Activation, Synovial Infiltration and Therapeutic Targeting

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Dendritic cells (DCs) are a heterogeneous population of professional antigen-presenting cells which are at the interface between innate and adaptive immunity. A specific subset of DCs is known to derive from monocyte and has a key role in inflammation and infection.

This study aimed to identify and characterize the CD209$^+$/CD14$^+$ DC subset and evaluate their characteristics in the periphery of patients with inflammatory arthritic (IA) together with their enrichment and activation at the site of inflammation, the joint of rheumatoid (RA) and psoriatic arthritic (PsA) patients.

Methods: Peripheral blood and synovial fluid mononuclear cells (PBMC and SFMC) were isolated by Ficoll density gradient from healthy subjects (HC), RA and PsA patients. Single-cell synovial tissue suspension (ST) from RA and PsA patients was obtained by enzymatic digestion. PBMC, SFMC and ST were analysed by flow cytometry to identify the CD209$^+$/CD14$^+$ DC subset, its frequency and the expression of chemokines receptors (CCR6, CCR7/CXCR3/CXCR4/CXCR5) and activation markers (CD40 and CD80) on the surface of the DC subset. In addition, PBMC were

stimulated with different TLR (LPS, CPG, Poly I:C) and intracellular staining for IL12/TNFα/IL1β/IL6 was performed. $CD209^+$ DC were isolated with a two-step isolation protocol. Lineage negative cells ($CD3/CD19/CD56^-$) were stimulated with GMCSF/IL4 in the presence or absence of the JAK/STAT inhibitor Tofacitinib or the TNF inhibitor Humira and the $CD209^+/CD14^+$ DC was evaluated by flow cytometry.

Results: We identified, for the first time, the $CD209^+/CD14^+$ DC population in PBMC of RA and PsA patients, with similar frequency observed when compared to HC. However, we observed activation of circulating $CD209/CD14^+$ DC from both RA and PsA patients, with higher production of cytokines (IL12/TNFα), in addition to expression/co-expression of chemokine receptors (CCR6/CCR7/CXCR3/CXCR4/CXCR5). Interestingly, we observed that this DC population was enriched at the site of inflammation, in SFMC and ST and displayed a mature phenotype, with a significant increase in CD40 and CD80 and co-expression of specific chemokine receptors, displaying unique patterns between PsA and RA. We developed a protocol of magnetic isolation for $CD209^+$ DC from blood and observed that culturing HC CD209+DC with IA synovial fluid SF was sufficient to induce the development of $CD209/CD14^+$ DC, leading to a poly-mature phenotype. Finally, we observed that JAK/STAT inhibition, but not TNF inhibitor, reduced the generation and development of $CD209^+/CD14^+$ DC.

Conclusion: We identified, for the first time, a monocyte-derived DC population characterized as $CD209^+/CD14^+$ DC in the periphery of RA and PsA patients. This population was enriched at the site of inflammation displaying a unique chemokine receptor profile and activation markers, suggesting cells, already activated in the periphery of IA patients, are then recruited activated further into the joint of IA patients. We observed that IA SF induce the development of $CD209/CD14^+$ DC and their maturation. In addition, we demonstrated that the $CD209^+/CD14^+$ DC development is sensitive to JAK/STAT, but not TNF inhibition.

Disclosure: V. Marzaioli, None; **M. Canavan**, None; **A. Floudas**, None; **K. Flynn**, None; **R. Mullan**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6; **U. Fearon**, Abbvie, 1, 5, 6, BMS, 1, Pfizer, 1, 5, Janssen, 5, Eli Lilly, 5, UCB, 5, GSK, 6.

Abstract Number: 1006

MAA Modified and/or Citrullinated Proteins Stimulate Macrophages and Human Fibroblast-Like Synoviocytes to Increase the Secretion/Expression of Fractalkine Ligand (CX3CL1) and Fractalkine Receptor (CX3CR1)

Nozima Aripova, Michael Duryee, Peter Maloley, Bryant England, James O'Dell, Ted Mikuls and Geoffrey Thiele, University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Innate Immunity Poster (0992–1006)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

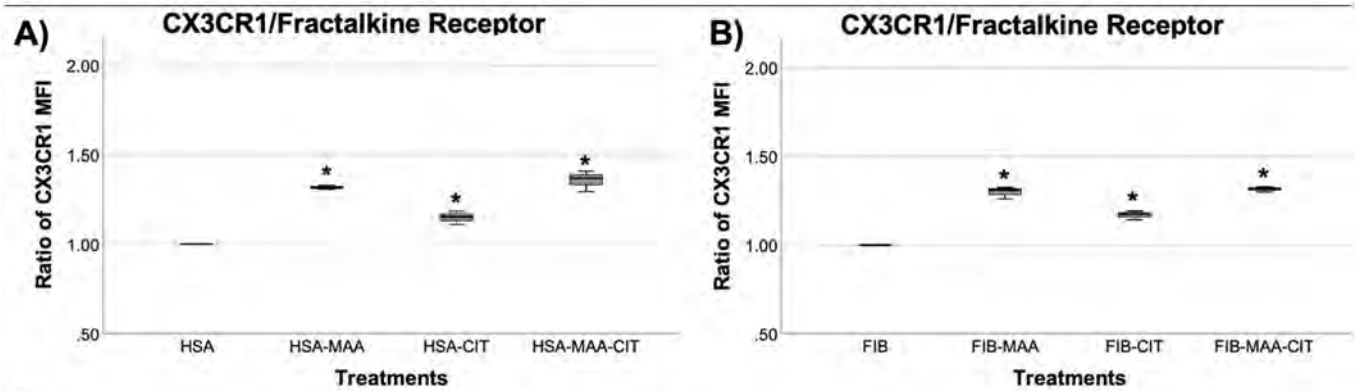
Background/Purpose: In rheumatoid arthritis (RA) synovium, activated synovial fibroblasts and macrophages release inflammatory mediators that affect surrounding cells and accelerate disease progression. One such chemokine axis, we and others have shown to be present in RA, is CX3CL1/Fractalkine ligand and its receptor CX3CR1(Fractalkine receptor). Malondialdehyde and acetaldehyde adducts (MAA) and/or citrullinated (CIT) proteins in isolation or in combination induce inflammatory and fibrotic responses by macrophages and fibroblasts. Recent preliminary

data from our laboratory using the VARA cohort (N=2342) suggests that anti-MAA antibodies negatively correlated with serum CX3CL1 levels (R=-0.04123, p< 0.05). Therefore, it was the purpose of this study to evaluate the effects of MAA and/or CIT modified proteins on the expression of CX3CL1 and CX3CR1 by macrophages (U937 cells), and human fibroblast-like synoviocytes from RA synovium (HFLS-RA).

Methods: Both HFLS-RA and U937 cells, separately, were stimulated with MAA, CIT, and MAA-CIT modified or unmodified human serum albumin (HSA) or fibrinogen (FIB) for 24 hours. Afterward, supernatants were assayed using a cytokine capture assay for CX3CL1. CX3CR1 expression was measured using both PCR and flow cytometry. In a separate experiment, U937 cells were incubated with previously collected HFLS-RA supernatants (following antigen stimulation as above) and mRNA was isolated to evaluate inflammatory markers with PCR: TNF-α, IL-1β. One-way ANOVA with Tukey's-b post-hoc was used to compare normalized values across exposure groups to appropriate native proteins.

Results: U937 cells do not secrete the CX3CL1, and HFLS-RA cells do not express the CX3CR1 in response to any modification of HSA or FIB. However, stimulation of U937 with modified antigens significantly increased CX3CR1 expression by flow cytometry [**Fig.1A,B**]. Stimulation with dually modified (MAA-CIT) HSA and FIB demonstrated the highest CX3CR1 expression by PCR [**Fig.1C**]. Treatment of HFLS-RA with HSA-MAA had the highest significant CX3CL1 release, followed by HSA-MAA-CIT [**Fig.2A**]. Treatment with FIB-MAA-CIT significantly increased levels of CX3CL1 release, followed by FIB-CIT [**Fig.2B**]. When U937 cells were stimulated with HSA-MAA-CIT [**Fig.3A**] or FIB-CIT [**Fig.3B**] supernatants from HFLS-RA cells, mRNA levels of TNF-α and IL-1β increased, but to a significantly lesser extent than respective stimulations without HFLS-RA supernatants. HSA-MAA treated HFLS-RA supernatants significantly increased U937 mRNA levels for TNF-α and considerably, to a lesser extent, IL-1β as compared to direct stimulation of U937 with HSA-MAA antigen without HFLS-RA supernatants [**Fig.3A**].

Conclusion: Our data demonstrate for the first time that fibroblasts and macrophages can express CX3CL1 and CX3CR1, respectively, in response to HSA and FIB modified proteins. Macrophages showed significantly diminished inflammatory responses when exposed to supernatants from stimulated HFLS-RA cells. These studies suggest that the CX3CL1-CX3CR1 axis could link immune cells and fibroblasts, thereby regulating inflammatory mediators in response to MAA and/or CIT modified proteins.



C)

	HSA	HSA-MAA	HSA-CIT	HSA-MAA-CIT	FIB	FIB-MAA	FIB-CIT	FIB-MAA-CIT
Rq for *CX3CR1*	1.0(0.3)	1.4(0.1)	1.4(0.5)	3.1(0.7*)	1.1(0.1)	1.0(0.2)	0.3(0.1)	3.8(0.6*)

Figure 1. Altered CX3CR1/Fractalkine receptor expression from monocytes stimulated with post-translationally modified albumin and fibrinogen. U937 cells were incubated with human serum albumin (HSA) and fibrinogen (FIB) modified antigens. Panels (A) and (B) show CX3CR1/Fractalkine receptor expression from flow cytometry with HSA (A) and FIB (B) modified antigens; the data are represented using mean fluorescent intensity (MFI) and are normalized tβ o native protein. Panel (C) summarizes mean relative quantity (Rq) mRNA levels of CX3CR1/Fractalkine receptor by PCR. *p<0.001, n=3.

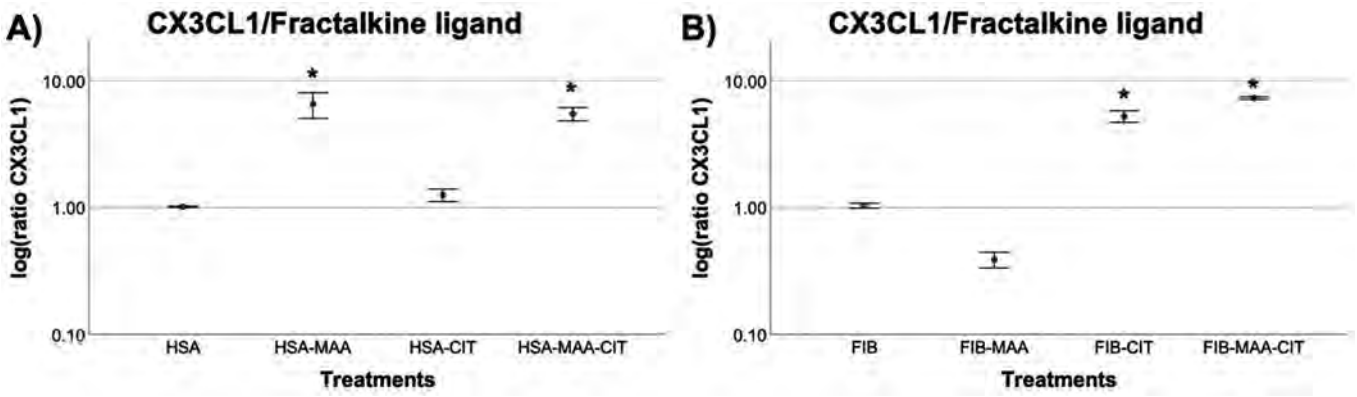


Figure 2. CX3CL1/Fractalkine ligand release from stimulated HFLS-RA cells. HFLS-RA cells were incubated with HSA (A) and FIB (B) modified antigens for 24 hours. Afterwards, the supernatants were collected for analysis for CX3CL1/Fractalkine ligand release using Mesoscale Discovery assay kit. The concentration of CX3CL1/Fractalkine ligand was measured in pg/mL and normalized to native protein. Log based 10 ratio of modified protein to native protein is represented on y-axis (HSA and FIB respectively). *p<0.001, n=3.

A)

	With supernatants from HFLS-RA cells				*Without supernatants from HFLS-RA cells*			
	HSA	**HSA-MAA**	**HSA-CIT**	**HSA-MAA-CIT**	**HSA**	**HSA-MAA**	**HSA-CIT**	**HSA-MAA-CIT**
TNF-α	1.0(0.0)	**11.9(1.9*)**	0.4(0.2)	0.6(0.1)	1.0(0.0)	**8.0(0.9*)**	1.2(0.2)	**8.4(0.8*)**
IL-1β	1.0(0.0)	**34.3(2.9*)**	1.5(0.7)	1.4(0.3)	1.0(0.0)	**52.4(2.4*)**	1.3(0.3)	**36.3(0.7*)**

B)

	With supernatants from HFLS-RA cells				*Without supernatants from HFLS-RA cells*			
	FIB	**FIB-MAA**	**FIB-CIT**	**FIB-MAA-CIT**	**FIB**	**FIB-MAA**	**FIB-CIT**	**FIB-MAA-CIT**
TNF-α	1.0(0.1)	1.1(0.1)	0.7(0.1)	1.3(0.1)	1.1(0.1)	0.9(0.1)	**6.6(0.5*)**	1.1(0.2)
IL-1β	1.0(0.1)	1.1(0.2)	**2.4(0.2*)**	1.7(0.5)	1.0(0.1)	1.0(0.2)	**20.5(1.4*)**	**2.2(0.2#)**

Figure 3. PCR for mRNA levels of inflammatory markers from stimulated U937 cells. U937 cells were stimulated with either supernatants from modified antigens treated HFLS-RA cells or with directly modified antigens. RNA was collected from U937 cells and categorized as incubation with HSA (A) or FIB (B) modified antigens. The data is represented as relative quantity (Rq) of inflammatory markers. #p<0.05, *p<0.001, n=3.

Disclosure: N. Aripova, None; **M. Duryee**, None; **P. Maloley**, None; **B. England**, Boehringer-Ingelheim, 2; **J. O'Dell**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6.

Abstract Number: 1007

Vascular Deposition of Oxidized LDL Is Increased in Children with Untreated Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Pediatric Rheumatology – Basic Science Poster (1007–1013)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a systemic vasculopathy associated with metabolic derangements and possible increased risk for premature atherosclerosis. Oxidation of low-density lipoprotein (LDL) in the endothelial wall of blood vessels is an early step in atherosclerotic plaque formation. The primary aim of this study was to compare deposition of oxidized LDL in the vasculature of muscle biopsies (MBx) from patients with untreated JDM compared to pediatric controls.

Methods: After informed consent, MRI-directed MBx were obtained from 20 female patients with JDM (mean age = 6.3+/-2.2) before the start of therapy and 5 female controls (mean age = 14.4+/-1.8). Frozen muscle sections were stained with DAPI and fluorescently labeled antibodies against von Willebrand factor (vWF) and LDL oxidized by copper (oxLDL) and were imaged by a Leica DMR-HC upright microscope. ImageJ (NIH, Bethesda, MD) was used to identify blood vessel areas, defined by the presence of vWF, and measure the fluorescence of the area and intensity of oxLDL within the vessel walls. For each vessel visualized, the intensity of oxLDL was calculated for the area of the vessel and corrected for background intensity. The total fluorescence for each muscle biopsy was calculated by dividing the sum of the intensities of the individual vessels by the sum of the area of the vessels. Data was analyzed using t-tests and Pearson correlation.

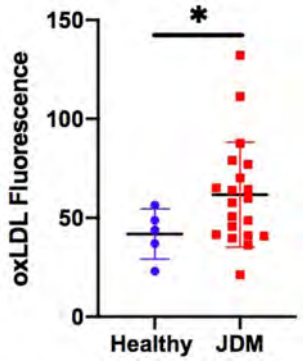

Figure 1. Fluorescence of oxLDL (intensity/area) in the walls of muscle vasculature is increased in JDM muscle biopsies compared to healthy controls (p=0.03). The mean value is indicated by the line, and the standard deviation is indicated by the whiskers. JDM patients, n=20, and healthy controls, n=5.

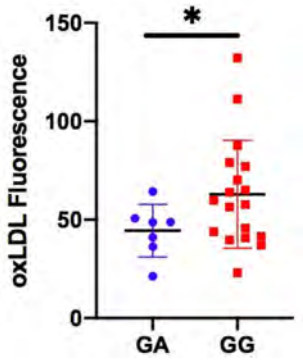

Figure 2. Fluorescence of oxLDL (intensity/area) in the walls of muscle vasculature is increased in subjects with the GG polymorphism at the TNFa-308 gene locus compared to subjects with the GA polymorphism (p=0.04).

Results: Children with untreated JDM demonstrated higher fluorescence of oxLDL in the walls of muscle vasculature compared to healthy children (p=0.03, Figure 1). Secondary analysis revealed significantly higher oxLDL fluorescence in muscle biopsies of patients with the TNF-a-308 G allele compared to biopsies of patients with the A allele (p=0.04, Figure 2). Within the JDM cohort, there was a trend towards increased oxLDL fluorescence with longer duration of untreated disease at time of MBx. There was no significant correlation found between oxLDL fluorescence and markers of disease activity including disease activity (DAS) scores, nailfold capillary end row loops, muscle enzymes, serum vWF antigen, or neopterin.

Conclusion: Increased deposition of oxLDL within blood vessels of children with JDM supports the concern that these children are at increased risk for premature atherosclerosis. Additional longitudinal studies are needed to better understand the long term impact on morbidity and mortality.

Disclosure: J. Spitznagle, None; **A. Kacha-Ochana**, None; **J. Cook-Mills**, None; **A. Khojah**, None; **G. Morgan**, None; **L. Pachman**, None.

Abstract Number: 1008

Synovial Fluid IL-36γ in Patients with Enthesitis Related Arthritis (ERA) Correlates with Disease Activity and Leads to Production of IL-6 by Fibroblast Like Synoviocytes

Amita Aggarwal, **Sanjukta Majumder** and Shivika Guleria, Sanjay Gandhi Post Graduate Institute of Medical Sciences, Lucknow, India

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Pediatric Rheumatology – Basic Science Poster (1007–1013)
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Session Time: 8:30AM–10:30AM

Background/Purpose: IL-36 has been implicated in the pathogenesis of spondyloarthropathies (SpA) like psoriasis and IBD. Enthesitis related arthritis (ERA) category of juvenile idiopathic arthritis (JIA) is a form of juvenile SpA; however, no data is available regarding the role of IL-36 in this disease. Thus, we studied the involvement of IL-36 in ERA.

Methods: 84 patients with ERA (ILAR criteria), 20 patients with rheumatoid arthritis (RA) and 24 healthy subjects were enrolled in the study after ethics approval and informed consent.

IL-36α, β, γ and IL-36R was determined in PBMCs and SFMCs at the mRNA levels using RTqPCR; and IL-36α, γ, IL-36Ra, IL-6 and IL-17 levels were measured in serum and synovial fluids (SF) by ELISA. Fibroblast like synoviocytes (FLS) were stimulated with recombinant IL-36γ, IL-6, IL-17, IL-6+IL-17 and TNF-α as well as with SF from patients with ERA in presence or absence of IL-36Ra. For ELISA, cells were stimulated for 8 h and supernatants were removed, cells were washed and further cultured for 16 h. Post stimulation expression of IL-6 and IL-36γ levels were measured at mRNA and protein levels. All results are expressed as median ±IQR.

Results: Among 84 JIA-ERA patients, 77 were boys. Their mean age was 16.8 ± 3.5 years and mean disease duration was 60.3 ± 48.8 months. All had active disease with mean ESR of 62.3 ± 34.9 mm and mean Juvenile Spa disease activity score of 3.4 ± 1.4.

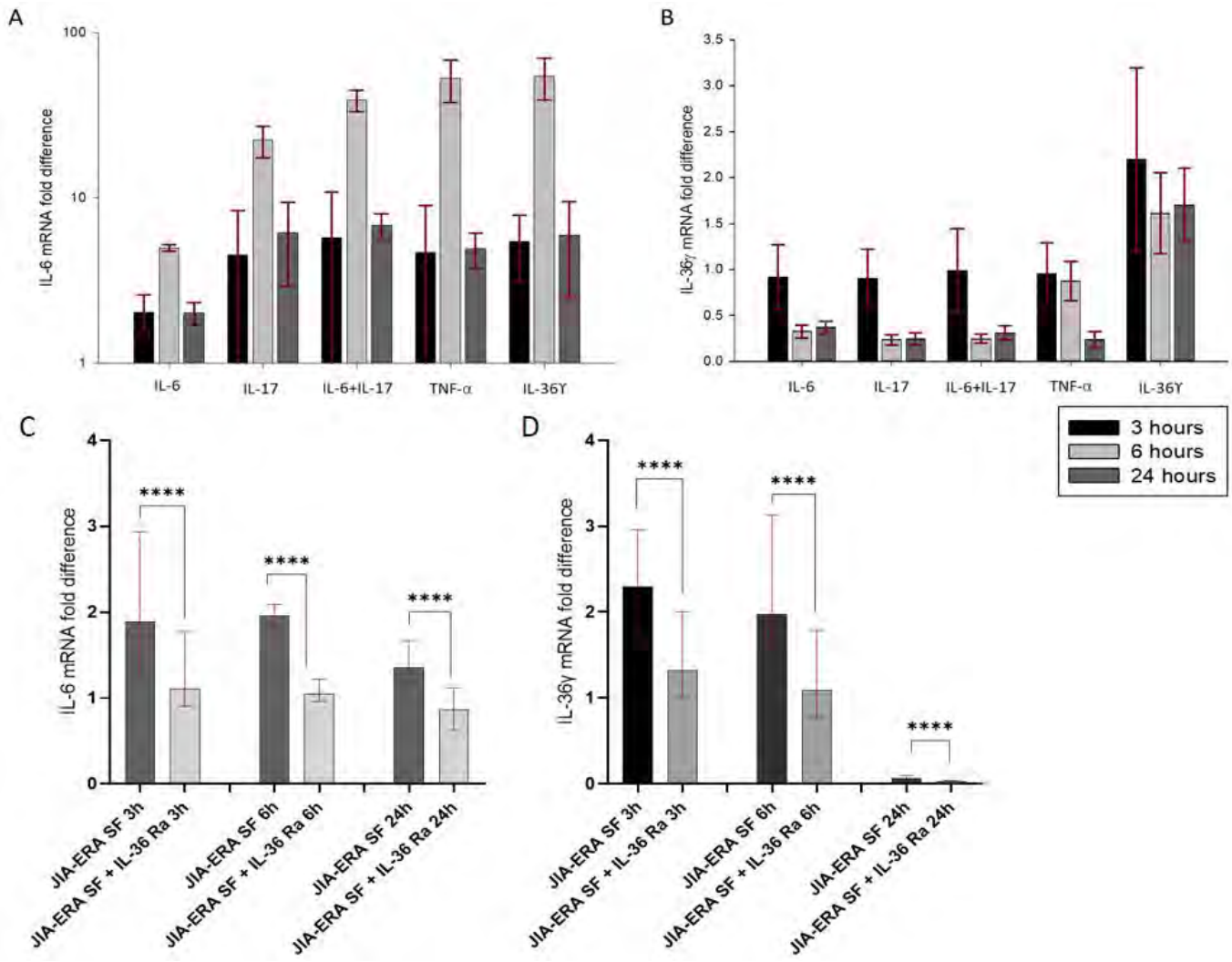

Figure. Fold difference in mRNA expression of IL-6 and IL-36**γ** in FLS post stimulation. (A) mRNA expression of IL-6 upon stimulation of FLS with pro-inflammatory cytokines. (B) mRNA expression of IL-36**γ** upon stimulation of FLS with pro-inflammatory cytokines. (C) mRNA expression of IL-6 in FLS upon stimulation with SF from JIA-ERA patients in presence or absence of IL-36Ra. (D) mRNA expression of IL-36**γ** in FLS upon stimulation with SF from JIA-ERA patients in presence or absence of IL-36Ra.

mRNA levels of IL-36α, IL-36γ and IL-36R were increased in PBMCs of ERA patients as compared to healthy controls. However, at protein level only IL-36γ was detectable in a significant proportion of subjects and was higher (0 ± 42.1 pg/mL) than controls (0 ± 0) ($p< 0.01$) but lower than RA patients (198.2 ± 672.9 pg/mL).

In SFMCs, all 4 mRNA were detectable with levels lower than RA patients. SF levels of IL-36γ were also enhanced (0 ± 26.78 pg/mL) but were lower than RA patients (460 ± 1345 pg/mL). SF IL-36γ levels correlated significantly with disease activity (JSpaDA) ($r=0.51$, $p< 0.0001$), and with SF levels of IL-6 ($r=0.4$, $p= 0.0063$) and IL-17 ($r=0.57$, $p=0.0018$). Patients on treatment with DMARDs had significantly lower SF IL-36γ levels than those not receiving DMARDs.

When FLS were stimulated with IL-36γ and other pro-inflammatory cytokines, mRNA expression of IL-36γ; and mRNA and protein expressions of IL-6 were found increased. Protein expression of IL-36γ was not detectable by ELISA in cell supernatants and no expression of IL-17 at RNA or protein level was noted.

When FLS were stimulated with SFs from JIA-ERA patients (n=5), increased expressions of IL-36γ mRNA and IL-6 mRNA and protein were seen, compared to controls. However, in presence of IL-36Ra, expressions of both cytokines were significantly reduced ($p< 0.0001$ in all cases).

Conclusion: The data suggests that pro-inflammatory cytokines aid in upregulation of IL-36γ which in turn upregulates expression of IL-6 and this might lead to a positive feedback loop leading to amplification of inflammation in ERA. Association of SF levels of IL-36g with disease activity further supports this possibility.

Disclosure: A. Aggarwal, None; **S. Majumder**, None; **S. Guleria**, None.

Abstract Number: 1009

Expanded B Cell-Helper T Cells in ANA+ Oligoarticular Juvenile Idiopathic Arthritis

Amelie Jule[1], Maria Taylor[2], Kacie Hoyt[3], Kevin Wei[4], Maria Gutierrez-Arcelus[1], Siobhan Case[1], Mia Chandler[1], Margaret Chang[2], Ezra Cohen[1], Fatma Dedeoglu[1], Olha Halyabar[1], Jonathan Hausmann[5], Melissa Hazen[1], Erin Janssen[1], Jeffrey Lo[2], Mindy Lo[1], Esra Meidan[2], Jordan Roberts[1], Mary Beth Son[1], Robert Sundel[2], Pui Lee[6], Talal Chatila[1], Peter Nigrovic[1], Deepak Rao[4] and Lauren Henderson[7], [1]Boston Children's Hospital, Boston, MA, [2]Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, [3]Virginia Tech Carilion School of Medicine, Roanoke, VA, [4]Brigham and Women's Hospital, Boston, MA, [5]Beth Israel Deaconess Medical Center, Boston, MA, [6]Boston Children's Hospital, Newton, MA, [7]Division of Genetics and Genomics, Boston Children's Hospital, Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

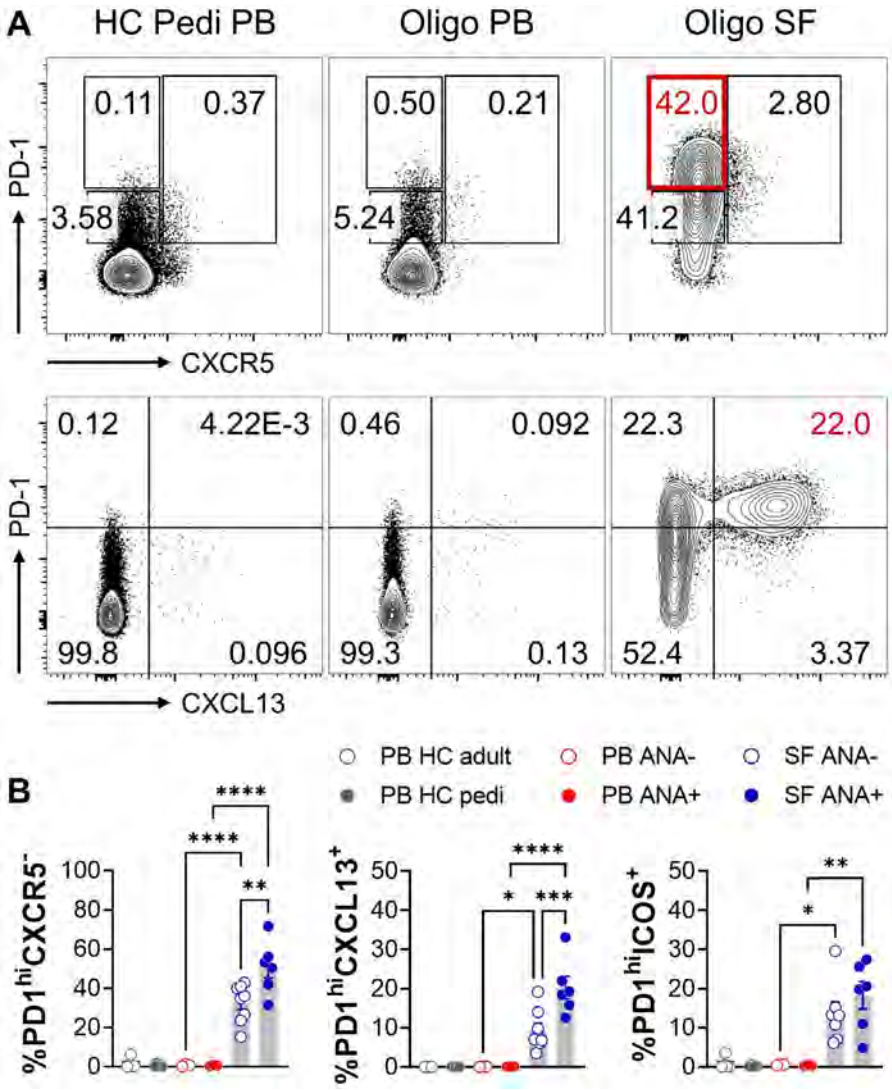
Background/Purpose: Oligoarticular juvenile idiopathic arthritis (oligo JIA) is defined by limited joint involvement (< 5 joints) in the first 6 months of disease. A subgroup of patients presents with distinct clinical features, including early age at disease onset (< 6 years), female sex, increased risk for uveitis and antinuclear antibody (ANA) positivity. The biological processes that drive clustering of these clinical features in ANA^+ oligoarthritis are not understood. The presence of autoantibodies in this oligo JIA subgroup suggests a role for abnormal B cell responses. To better understand interactions between T and B cells in oligo JIA, we characterized $CD4^+$ T cells with a B cell-helper T cell profile in ANA^+ and ANA^- oligo JIA.

Methods: Synovial fluid (SF) and, where possible, paired peripheral blood (PB) samples were collected from oligo JIA patients, defined by ILAR criteria. PB was obtained from healthy controls (HC). PB and SF mononuclear cells were evaluated with flow cytometry. T effector ($CD4^+CD25^-$, Teff) and T regulatory ($CD4^+CD25^+CD127^{lo}$) cells were sorted from the SF of 2 patients (one ANA^+ and one ANA^-), stained with hashing antibodies, pooled together in equal ratio, and processed for single-cell RNA sequencing (scRNA-seq) coupled with T cell receptor (TCR) repertoire using 10X. Transcriptomic data were analyzed in R using Seurat v3.1.5.

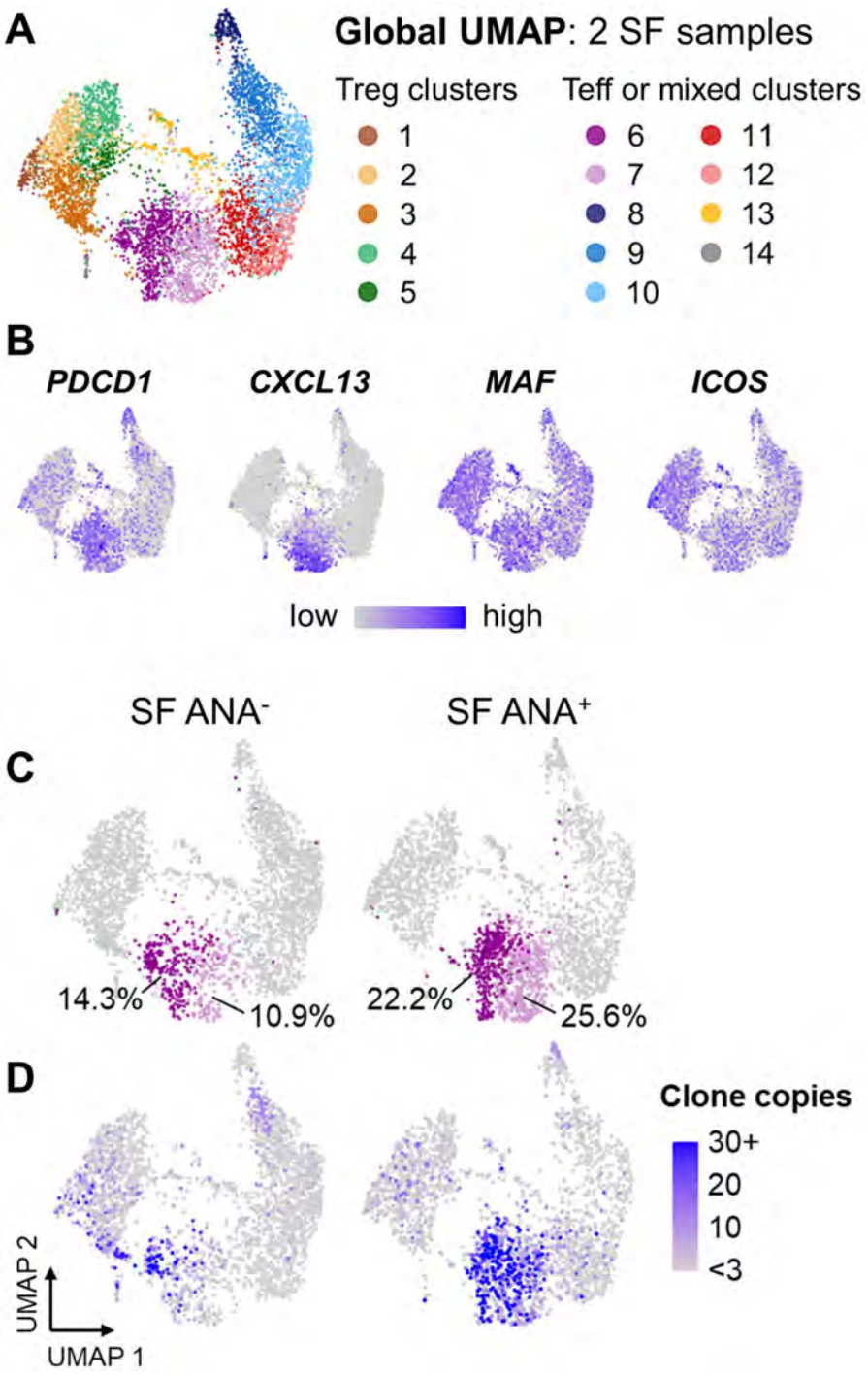
Results: 14 oligo JIA patients and 10 controls were studied. T follicular helper cells ($CD4^+PD\text{-}1^{hi}CXCR5^+$, Tfh) are found in secondary lymphoid organs and express factors (PD1, ICOS, IL-21, CXCL13) promoting B cell maturation and antibody production. Compared to the PB of controls and patients, Tfh cells were not significantly enriched in the SF of ANA^+ or ANA^- oligo JIA. In peripheral tissues, B cells are driven to mature and generate autoantibodies by T peripheral helper cells ($CD4^+PD\text{-}1^{hi}CXCR5^-$, Tph). Flow cytometry studies showed a significant enrichment of Tph cells in the SF of oligo JIA patients. ANA^+ patients had the highest proportion of Tph cells, with 50.8% ± 5.5 (mean ± SEM) of Tph

among total CD4⁺ T cells, compared to 32.5% ± 3.4 in ANA⁻ patients. In contrast, Tph cells were rare in the PB of patients and controls (< 6.5% of CD4⁺ T cells). Tph cells in SF expressed markers of B cell-helper T cells, including ICOS and the B cell chemoattractant CXCL13. scRNA-seq studies of SF CD4⁺ T cells revealed 2 clusters with Tph features, including cells co-expressing high levels of *PDCD1* (gene encoding PD1) and *CXCL13* alongside transcription factors previously identified in Tph cells (*MAF* and *BATF*). A greater proportion of Teff cells from the ANA⁺ patient (48%) compared to the ANA⁻ patient (25%) was found in Tph clusters. TCR repertoire analysis showed that clonally expanded T cells (with at least 3 clonal TCR copies) concentrated in Tph clusters and were mostly observed in the ANA⁺ patient.

Conclusion: Our results show that T cells with features of B cell-helper T cells preferentially accumulate in the joints of children with ANA⁺ oligo JIA. These results suggest that beyond the clinical features that characterize early-onset, ANA⁺ oligo JIA, disordered T cell-mediated help to B cells may further define this patient subset. Further studies are needed to delineate the functionality of Tph cells in oligo JIA.



T peripheral helper (Tph) cells are enriched in the synovial fluid (SF) of ANA+ oligo JIA. A) Representative flow cytometry dot plots gated on live CD3+CD4+ T cells. Frequencies of Tph cells (PD1hi, CXCR5-) and of the B-cell chemoattractant CXCL13 in oligo JIA SF are highlighted in red. B) Mean frequency ± SEM of CD3+CD4+ T cells expressing the corresponding markers. Statistical testing: ANOVA with correction for multiple comparisons; p-value <0.05 *; <0.01 **, <0.001 ***, <0.0001 **** (for readability, not all significant comparisons are shown).



Single-cell RNA sequencing of SF CD4+ T cells reveal clonally expanded cells with features of Tph cells in ANA+ oligo JIA. Sorted Tregs (CD4+CD25+CD127lo) and Teffs (CD4+CD25-) from the SF of 2 oligo JIA patients were studied with 10X. A) Uniform manifold approximation and projection (UMAP) of global dataset (both subjects, 6190 cells), color-coded by cluster. Clusters 6 & 7 contain Tph cells. B) UMAP of global dataset, showing gene expression levels of key Tph cell markers. C) UMAP of dataset, split by patient. The percent of T effector cells found in each Tph cluster for each patient is shown. D) UMAP projection, split by patient, highlighting T cell clones with strictly more than 3 copies across the dataset (expanded clones). A clone is defined by its paired TCRα and TCRβ chain.

Disclosure: A. Jule, None; **M. Taylor**, None; **K. Hoyt**, None; **K. Wei**, Mestag, 2; **M. Gutierrez-Arcelus**, None; **S. Case**, None; **M. Chandler**, None; **M. Chang**, None; **E. Cohen**, None; **F. Dedeoglu**, Novartis, 2, UptoDate, 9; **O. Halyabar**, None; **J. Hausmann**, Novartis, 2, Biogen, 2, Pfizer, 2; **M. Hazen**, None; **E. Janssen**, None; **J. Lo**, None; **M. Lo**, None; **E. Meidan**, None; **J. Roberts**, None; **M. Son**, CARRA, 5, UpToDate, 5; **R. Sundel**, None; **P. Lee**, None; **T. Chatila**, None; **P. Nigrovic**, AbbVie, 5, Bristol-Myers Squibb, 5, Novarits, 5, Pfizer, 5, Sobi, 5, CARRA, 5, UpToDate, 9; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6; **L. Henderson**, None.

Abstract Number: 1010

Proton Pump Inhibitors Suppress IL-1 Mediated Carditis in a Murine Model of Kawasaki Disease

Paul Tsoukas[1], Melissa Kleinau[2], Lysa Langevin[2], Lily Morikawa[3], Trang Duong[1], Suzanne Tam[4] and Rae Yeung[5], [1]Hospital for Sick Children, Toronto, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]The Hospital for Sick Children, Toronto, ON, [4]Hospital for Sick Children, Toronto, ON, [5]The Hospital for Sick Children, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Pediatric Rheumatology – Basic Science Poster (1007–1013)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Kawasaki disease (KD), is the leading cause of acquired heart disease in childhood. Up to 20% of patients may develop coronary artery lesions (CAL) despite standard of care treatment with intravenous immunoglobulin (IVIg).

Murine and patient data indicate Interleukin-1 (IL-1) contributes to CALs. Proton pump inhibitors (PPI), a class of medications used to limit gastric acid secretion, have also been shown to have anti-inflammatory properties: 1) decreasing macrophage IL-1β secretion in vitro and 2) improving clinical outcomes in IL-1 mediated murine models.

This study aims to determine if PPIs inhibit IL-1β production and resulting CAL in the Lactobacillus casei cell wall extract (LCWE) induced coronary arteritis murine model of KD.

Methods: Bone marrow derived macrophages (BMDMs) were obtained from adult mice and stimulated with Pam-3Cys and Lactobacillus casei cell wall extract (LCWE), in the presence or absence of PPIs. To exclude toxic effects, viability was tested via flow cytometry and trypan blue exclusion. Electrolyte flux was measured via fluorescent imaging plate reader. In vivo, KD was induced by intraperitoneal LCWE injection. Mice were injected with LCWE alone, LCWE+PPI, saline or PPI alone. Coronary artery inflammation was scored by a blinded pathologist. Using ELISA, serum IL-1β and NT-proBNP were measured.

Results: Following stimulation with either Pam3Cys or LCWE, PPIs inhibited BMDM IL-1β production in a dose-dependent and drug class independent manner. Inflammasome activation was prevented by PPI inhibition of signal two. In vivo, compared to untreated KD diseased mice, those treated with PPI were shown to have significantly reduced coronary artery inflammation.

Conclusion: IL-1 is essential for the development of LCWE induced murine KD and anti-IL-1 therapy have been shown to prevent myocardial inflammatory changes. Our data indicate that PPIs have extra-gastrointestinal anti-inflammatory properties in a murine KD model preventing IL-1 induced coronary artery inflammation. PPIs may be a novel inexpensive, oral, and safe adjuvant anti-IL-1 medication to treat KD.

Disclosure: P. Tsoukas, None; **M. Kleinau**, None; **L. Langevin**, None; **L. Morikawa**, None; **T. Duong**, None; **S. Tam**, None; **R. Yeung**, None.

Abstract Number: 1011

Validation of Bioinformatics Pipeline to Detect NEMO-Deleted Exon 5 Autoinflammatory Syndrome (NEMO-NDAS) and Preliminary Clinical and Immunologic Characterization

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: Splice site variants in *IKBKG* that lead to exon 5 deletion cause NEMO-deleted exon 5 autoinflammatory syndrome (NEMO-NDAS). NEMO-NDAS clinically mimics the interferonopathy chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) but treatment with JAK inhibitors provides only partial benefit. Because an *IKBKG* pseudogene complicates the genetic diagnosis of NEMO-NDAS by standard methods, we developed and validated a bioinformatics approach to diagnose these patients (pts). We further characterized the complex immunodysregulation present in NEMO-NDAS.

Methods: A bioinformatics pipeline to mask the *IKBKG* pseudogene was refined using splice prediction tools (SpliceAi, TraP and MaxEntScan). Screening of *IKBKG* exon 5 ± 30bp was validated in 701 samples from subjects enrolled in an IRB-approved protocol, and in internal (n=2655, whole exome sequencing (WES)) and public (n=2498, whole genome sequencing (WGS)) databases. The variants detected were validated by Sanger or amplicon deep sequencing (seq) and spliced product was confirmed by Western blot, cDNA seq and RNA-seq. Nanostring gene expression, PBMC stimulation and cytokine assays were performed. CRISPR generated U937 cell line clones were functionally assessed.

Results: 13 pts (9 females and 4 males) had 9 different de novo splice site variants in *IKBKG*. cDNA seq (12/12) or Western blot (5/5) confirmed the splice product in all pts tested. RNA-seq (n=12) showed a high frequency of exon 5 skipping (median 55% (35-80%)). *IKBKG* exon 5 splice site variants were screened in internal and public WES/WGS databases (n=5149) and 11 variants in 22 subjects passed filters. Sanger seq confirmed 1 of the 11 variants (9%);

amplicon deep seq is pending. The most common clinical features in NEMO-NDAS pts were panniculitis with systemic inflammation (100%), ectodermal dysplasia (83%), hepatosplenomegaly (77%) and B-cell lymphopenia (80%). Compared to CANDLE pts (n=5), NEMO-NDAS pts' skin biopsies (n=7) showed histiocytic panniculitis, vacuolar interface changes and dyskeratosis. Liver biopsies (n=3) showed granulomatous hepatitis; 2 other pts had portal hypertension. All pts were steroid-dependent with partial responses to anti-TNF (n=9) or JAK inhibition (n=9). Nanostring IFN and NF-κB scores were elevated in all 13 pts. Pts with NEMO-NDAS had higher serum levels of IFN-γ, IL-12p40, IL-17 and IL-23 than seen in CANDLE pts ($p< 0.0001$ for all). Stimulated M1 and M2 macrophages from NEMO-NDAS pts (n=3) produced higher levels of CCL3/4 (MIP1-α/β) than healthy control (HC) cells (n=7)($p< 0.05$). NEMO-NDAS pts (n=2) had normal T and B cell proliferation, and Fas-induced T cell death was comparable to HC. U937 cell line clones lacking exon 5 normally degraded IκBα upon LPS stimulation and mutant U937 clones showed enhanced TNF induced cell death compared to wildtype and PSMB8-/- clones.

Conclusion: Our bioinformatics pipeline masking *IKBKG* pseudogene provides a sensitive diagnostic tool for the early recognition of NEMO-NDAS pts. The role of cytokine dysregulation and TNF induced cell death in the specific pathogenesis of NEMO-NDAS is being evaluated to improve therapeutic options.

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Disclosure: A. Almeida de Jesus, None; **B. Lin**, None; **E. Karlins**, None; **D. Kahle**, None; **A. Rastegar**, None; **J. Mitchell**, None; **S. Torreggiani**, None; **F. Bhuyan**, None; **S. Alehashemi**, None; **K. Cetin Gedik**, None; **K. Uss**, None; **C. Lee**, None; **H. Kuehn**, None; **S. Rosenzweig**, None; **K. Calvo**, None; **M. Walkiewicz**, None; **J. Lack**, None; **E. Hanson**, None; **A. Khojah**, None; **E. Wu**, None; **C. Scott**, None; **T. Ronan Leahy**, None; **E. MacDermott**, None; **O. Kileen**, None; **T. Arkachaisri**, None; **Z. Gucev**, None; **K. Cook**, None; **V. Mammadova**, None; **G. Nasrullayeva**, None; **S. Canna**, Simcha Therapeutics, 2, Novartis, 5, AB2Bio, Ltd, 5, IMMvention Therapeutix, 5; **D. Kuhns**, None; **C. Dalgard**, None; **T. Moran**, None; **A. Oler**, None; **R. Goldbach-Mansky**, Lilly, 5, IFM, 5.

Abstract Number: 1012

Altered T Cell Responses, and Synergistic Regulation of Synovial Fibroblasts Function in Children with Down's Syndrome-Associated Arthritis

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SESSION INFORMATION
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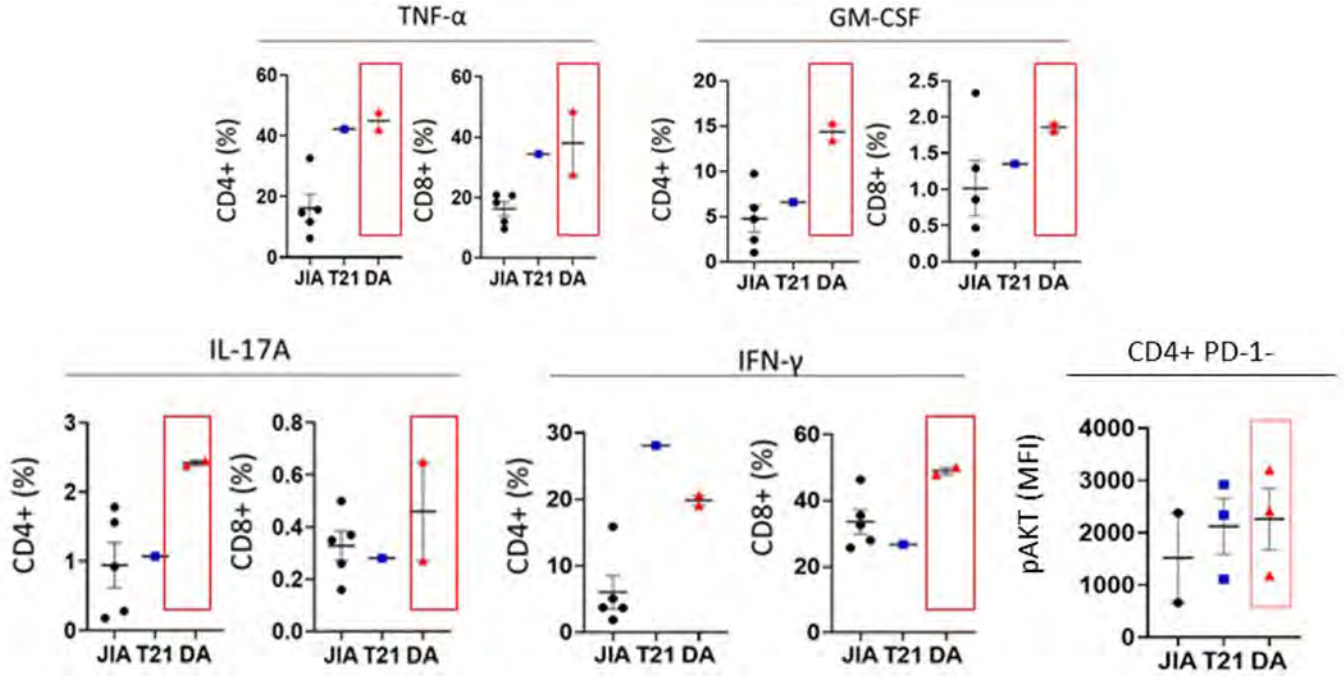
Session Time: 8:30AM–10:30AM

Background/Purpose: Juvenile idiopathic arthritis (JIA) was thought to be the most common inflammatory arthritis in children. However an aggressive, erosive arthritis of little-known immunologic mechanism occurs 20 times more frequently in children with Down's syndrome. This study was undertaken to characterize the distinct immune cell responses and synovial fibroblast invasiveness in children with Down's syndrome-associated arthritis (DA) in comparison to JIA.

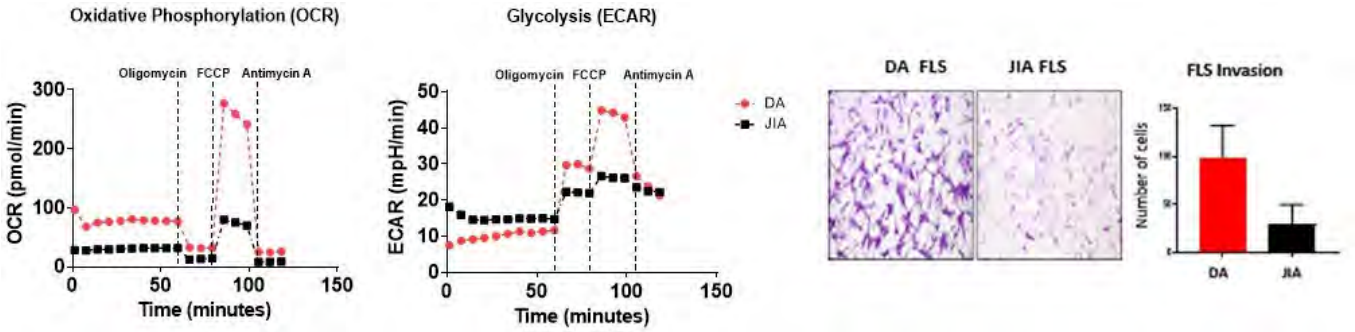
Methods: Multiparametric flow cytometric analysis was used to examine peripheral blood T cell, B cell and monocyte populations. In addition, T cell cytokine responses and their metabolic profile in children with DA, JIA, Down's Syndrome (trisomy 21 [T21]), and in healthy controls were assessed. The function of DA primary synovial fibroblasts (FLS) was assessed in response to stimulation with pro-inflammatory mediators alone and in combination (TNF-α, IL-17a, IFN-γ, GM-CSF). The two major energy pathways glycolysis (ECAR) and oxidative phosphorylation (OCR) were quantified by the Seahorse XFe96 Analyser. Migration, adhesion, invasion and cytokine/chemokine secretion were quantified wound repair scratch assays, Transwell collagen invasion chambers, adhesion binding assays, flow cytometry and ELISAs.

Results: T cell frequencies were higher in DA compared to JIA and T21 in contrast to B cell frequencies which were decreased. T cell responses in DA were characterized by increased frequencies of CD4+ and CD8+ TNF-a, IFN-g and GM-CSF producing T cells. The frequency of T peripheral helper cells were elevated in children with DA compared to all other groups, paralleled by an increase in their metabolic profile evident by higher phosphorylation of mTOR pathway component, AKT. Comparison of DA and JIA FLS demonstrated that DA FLS display a more invasive/migratory capacity and are more metabolically active. Based on the increased cytokine profile from DA T cells, we next examined the effect T cell derived cytokines TNF-α, IL-17a, IFN-γ and GM-CSF alone and in combination on DA FLS function. TNF-α, IL-17a and IFN-γ elevated IL-6, RANTES and MCP-1, with no effect observed for GM-CSF. Furthermore, TNF-α, and IL-17a induced DA FLS migration and increased PBMC adhesion to DA FLS. Finally, IL-17a and IFN-γ potentiated the effects TNF-α had on IL-6 and MCP-1 secretion compared to stimulation alone.

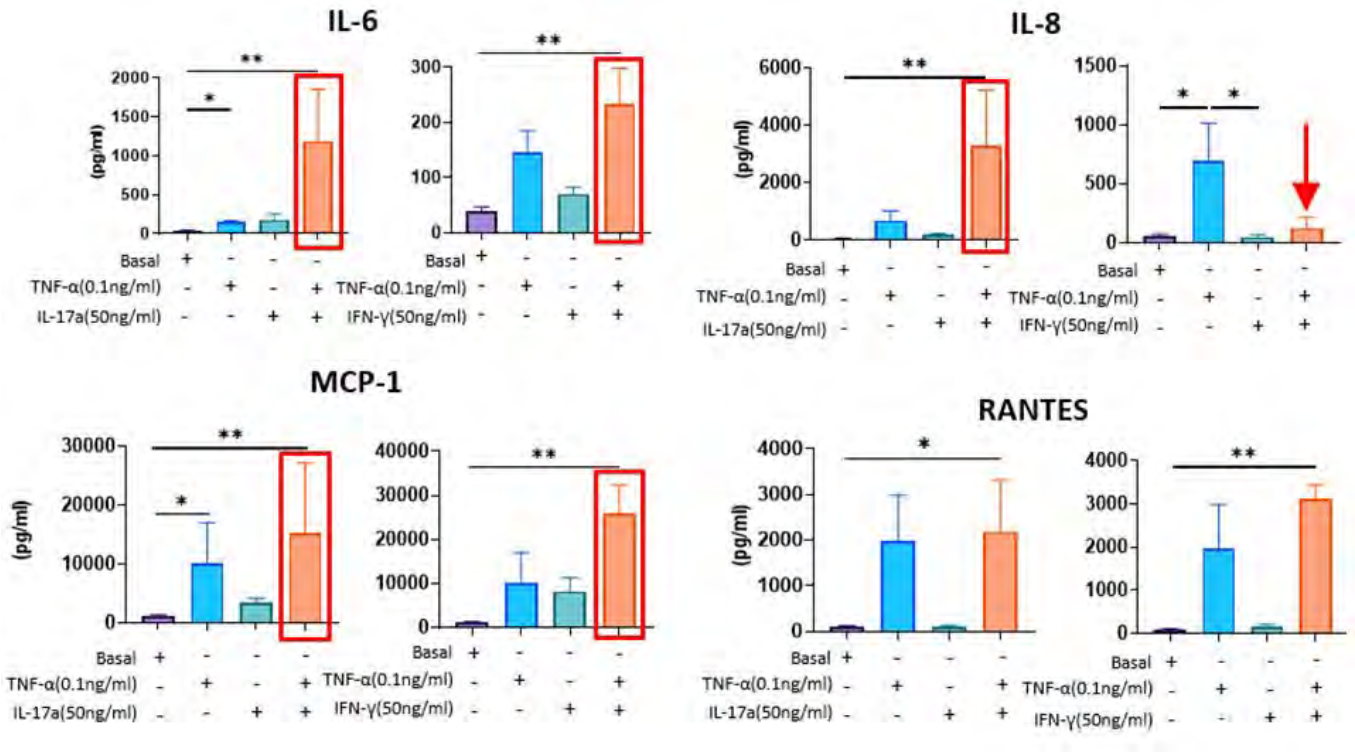
Conclusion: DA is a more common and aggressive form of arthritis compared to JIA. It is characterized by increased T cell responses and a more invasive FLS phenotype compared to that of JIA, with T cell derived cytokines alone and in combination further inducing the DA FLS pathogenic mechanisms. This suggests a synergistic relationship between cytokines. These effects mirror the increased erosive disease observed clinically.



CD4+ and CD8+ T cells in DA expresses higher TNF-α, GM-CSF and IL-17a. CD8+ T cells from DA show increased IFN-γ expression while DA CD4+ PD-1- T cells have elevated pAKT compared to JIA and T21.



Higher metabolic profiles and higher invasive capacity in DA FLS compared to JIA FLS.



Cytokine synergy between TNF-α, IL-17a and IFN-γ induces proinflammatory mediators in DA FLS.

Disclosure: S. Foo, None; **A. Floudas**, None; **A. O' Brien**, None; **S. Ansboro**, None; **R. Mullan**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/ Gilead, 1, 6; **E. MacDermott**, None; **D. Deely**, None; **C. Foley**, None; **O. Killeen**, None; **U. Fearon**, Abbvie, 1, 5, 6, BMS, 1, Pfizer, 1, 5, Janssen, 5, Eli Lilly, 5, UCB, 5, GSK, 6.

Abstract Number: 1013

SARS-CoV-2 Antibody Phenotype and Immune Gene Expression in Multi-system Inflammatory Syndrome in Children

Kate Webb[1], Thandeka Moyo-Gwete[2], Simon Mendelsohn[3], Claire Butters[4], Simone Richardson[5], Heidi Facey-Thomas[4], Debbie Abrahams[4], Mashudu Madzivhandila[5], Zanele Makhado[5], Frances Ayres[5], William Horsnell[6], Neilia Manamela[5], Richard Baguma[3], Stanley Kimbung Mbandi[3], Mzwandile Erasmus[3], Thomas Scriba[3], Liesl Zühlke[7], Penny Moore[5], George Kassiotis[8] and Christiaan Scott[4], [1]Paediatric Rheumatology University of Cape Town/ Francis Crick Institute, Cape Town, South Africa, [2]National Institute of Communicable Diseases/University of Witwatersrand, Johannesburg, South Africa, [3]South African TB vaccine initiative, IIDM, University of Cape Town, Cape Town, South Africa, [4]Paediatric Rheumatology, University of Cape Town, Cape Town, South Africa, [5]National Institute of Communicable Diseases/ University of Witwatersrand, Cape Town, South Africa, [6]University of Cape Town, Cape Town, South Africa, [7]Paediatric Cardiology, University of Cape Town, Cape Town, South Africa, [8]Retroviral Immunology, Francis Crick Institute, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Pediatric Rheumatology – Basic Science Poster (1007–1013)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Multi-system Inflammatory Syndrome in Children (MIS-C) is a severe disease that affects a small proportion of children exposed to Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). Differences in SARS-CoV-2 antibody responses and immune gene expression between SARS-CoV-2-infected children who develop MIS-C and those who do not may provide insight into the mechanism of MIS-C.

Methods: Healthy children presenting for elective surgery and those with MIS-C were recruited between 22 June 2020 and 5 November 2020 from a single paediatric hospital during the first wave of SARS-CoV-2 in the region. Clinical data, whole blood RNA and serum were collected. Titres of SARS-CoV-2 spike-specific antibody (SAb) and their capacity to perform neutralization, antibody-dependent cellular phagocytosis (ADCP) and antibody dependant cellular cytotoxicity (ADCC) were measured. Whole blood RNA gene expression was measured using multiplex Fluidigm quantitative Polymerase Chain Reaction (qPCR) with a panel of 84 immune genes. Principal component analysis was performed to assess for differences in gene expression. A linear regression model was developed with a forward stepwise model selection method to assess which genes associated with C-reactive protein (CRP) in MIS-C after controlling for the neutrophil to lymphocyte ratio (NLR).

Results: Twenty-three children with MIS-C and 25 healthy children were recruited. Nine healthy children had detectable SARS-CoV-2 serum antibodies (healthy exposed). No children had preceding clinical disease related to SARS-CoV-2 infection. Comparing children with MIS-C and healthy exposed children showed no difference in SAb binding responses (p=0.372) or ADCC (p=0.992). Increased neutralisation titre (p=0.084) and ADCP (p=0.086) in children with MIS-C was observed although was non-significant. Antibody function or titre did not change over time or with treatment in MIS-C. There was a clear distinction in immune gene expression between healthy children and those with MIS-C. Immune gene expression in MIS-C resolved to become indistinct from healthy children with time. Whole blood immune gene expression associated with an abundance of neutrophils in MIS-C. In a model that accounted for 66% of the variance in CRP (adjusted R^2 = 0.66) the expression of the gene for interleukin 27 (*IL27)* accounted for 64% of the model effect (B=35; p< 0.001) followed by NLR (15%, B=6.6, p=0.002) and the expression of the gene for monocyte chemoattractant protein 2 (*MCP2)* (11%, B=-14.59, p=0.008).

Conclusion: Comparing children infected with SARS-COV-2 from the same time period and region with or without MIS-C provides unique mechanistic insight into the disease. A trend towards higher SAb titres and ADCP implies a distinct humoral immune response to SARS-COV-2 in children with MIS-C, although further studies are required to validate this observation. The resolution of the abnormal immune gene expression in MIS-C implies a monophasic immune perturbation. The association of *IL27* and *MCP2* with CRP suggests that these may be important targets in future studies for possible pathogenicity and as potential biomarkers in MIS-C.

Disclosure: K. Webb, None; **T. Moyo-Gwete**, None; **S. Mendelsohn**, None; **C. Butters**, None; **S. Richardson**, None; **H. Facey-Thomas**, None; **D. Abrahams**, None; **M. Madzivhandila**, None; **Z. Makhado**, None; **F. Ayres**, None; **W. Horsnell**, None; **N. Manamela**, None; **R. Baguma**, None; **S. Kimbung Mbandi**, None; **M. Erasmus**, None; **T. Scriba**, None; **L. Zühlke**, None; **P. Moore**, None; **G. Kassiotis**, None; **C. Scott**, None.

Abstract Number: 1014

Enhanced Expression of Rheumatoid Arthritis Related Autoantibodies Following Airborne Endotoxin Exposure in the Setting of Collagen-Induced Arthritis

Ted Mikuls[1], Rohit Gaurav[1], Geoffrey Thiele[1], Bryant England[1], Madison Wolfe[1], Brianna Shaw[1], Kristina Bailey[1], Amy Nelson[1], Michael Duryee[1], Carlos Hunter[1], Debra Romberger[1], Dana Ascherman[2] and Jill Poole[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: In addition to inflammatory arthritis, collagen-induced arthritis (CIA) recapitulates cardinal features of rheumatoid arthritis (RA) including autoreactive T cells, peptidyl-arginine deiminase expression, and citrullination of synovial antigens. However, CIA is not characterized by robust ACPA expression, a key limitation of this model since ACPA are highly disease specific and play a pathogenic role in RA. Airborne biohazards such as cigarette smoke have been linked with airway generation of citrullinated antigens, ultimately leading to tolerance loss and ACPA production. In prior work, we have shown that combining the inhalant exposure of lipopolysaccharide (LPS; a component of relevant environmental/occupational exposures in RA) with CIA amplifies arthritis and shifts airway inflammation seen with LPS alone towards lung fibrosis. In this study, we examined the effect of repetitive exposure to airborne LPS on airway formation of autoantigens and circulating autoantibodies in CIA.

Methods: DBA/1J male mice were assigned to 4 groups: 1) Sham (saline injection/saline inhalation); 2) CIA alone (CIA injection/saline inhalation); 3) LPS alone (saline injection/LPS 100 ng inhalation); and 4) CIA+LPS (CIA injection/LPS inhalation). Serum and lung tissues were harvested at 5 weeks. ACPA (IgG) and antibody to malondialdehyde-acetaldehyde (IgG anti-MAA [also increased in RA] and anti-MAA-CIT antibody) were measured using ELISA. Lung tissues were examined for citrulline (CIT), MAA adducts, and extracellular matrix proteins (fibronectin, vimentin) using immunohistochemistry. Pearson R^2 values were calculated as measures of tissue co-localization.

Results: Serum ACPA, anti-MAA, and anti-MAA-CIT antibodies were strikingly potentiated in CIA+LPS vs. all other groups ($p< 0.01$; **Figure 1**). Both CIT- and MAA-modified lung proteins were significantly increased in CIA, LPS, and CIA+LPS vs. Sham, with the highest expression in CIA+LPS ($p< 0.01$ vs. all other groups) (**Figure 2**). CIT and MAA

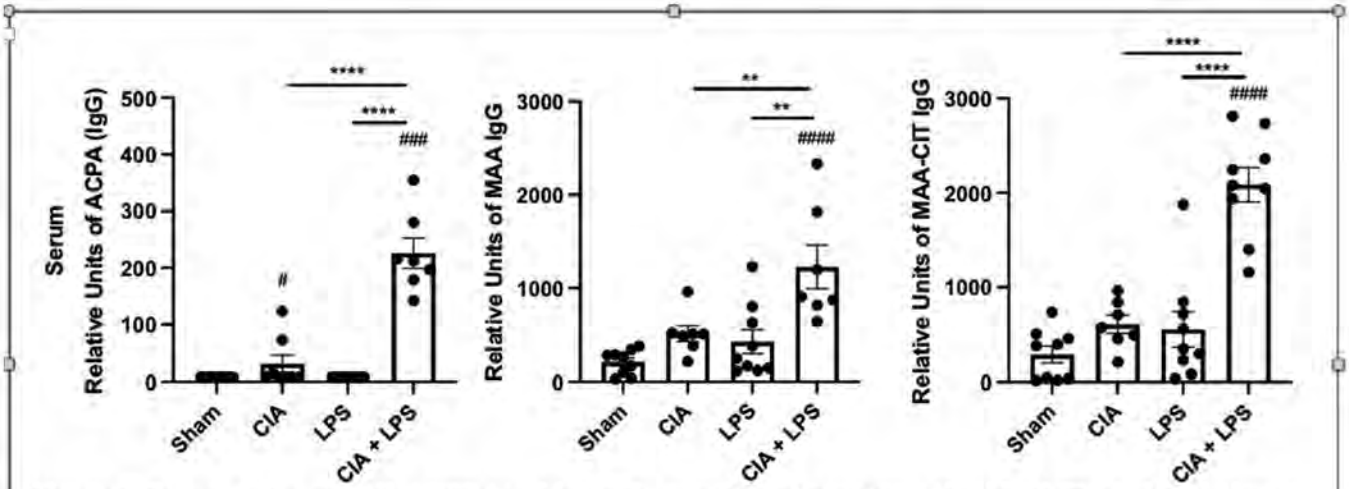


Figure 1. Serum autoantibodies with combining the repetitive lipopolysaccharide (LPS)-induced airway inflammation and collagen-induced arthritis (CIA) animal modeling systems. Serum levels of IgG anti-citrullinated protein antibody (ACPA) levels to citrullinated (CIT) peptides, IgG antibody to malondialdehyde-acetaldehyde (MAA)-modified proteins, and combined anti-MAA-CIT autoantibodies. Statistical difference versus sham (#p<0.05, ###p<0.001, ####p<0.0001) and between groups as noted by lines (**p<0.01, ****p<0.0001).

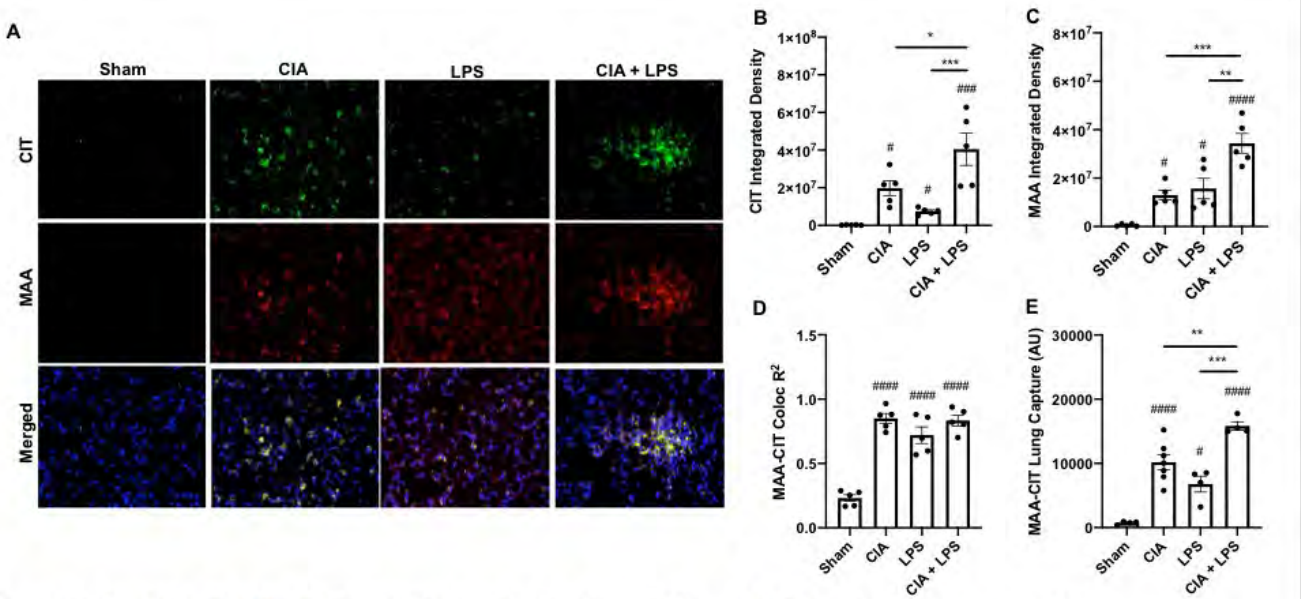


Figure 2. Combined CIA+LPS modeling modulates lung CIT and MAA autoantigen expression.
(A) Confocal images of lung tissue from treatment groups stained for citrulline (CIT; green) and malondialdehyde-acetaldehyde (MAA; red) modified proteins and merged with nuclei staining (DAPI, blue) shown at 40x magnification. Images were analyzed using Zen 2012 software (Zeiss). Scatter plots depict integrated density with SE bars of (**B**) CIT and (**C**) MAA-modified proteins quantified per each mouse. (**D**) R^2-values demonstrating co-localization of MAA-CIT within each treatment group. (**E**) Co-capture of MAA-CIT from lung tissue homogenates by sandwich ELISA (AU; arbitrary units). Statistical difference versus sham (#p<0.05, ###p<0.001, ####p<0.0001) and between groups as noted by lines (*p<0.05, **p<0.01, ***p<0.001).

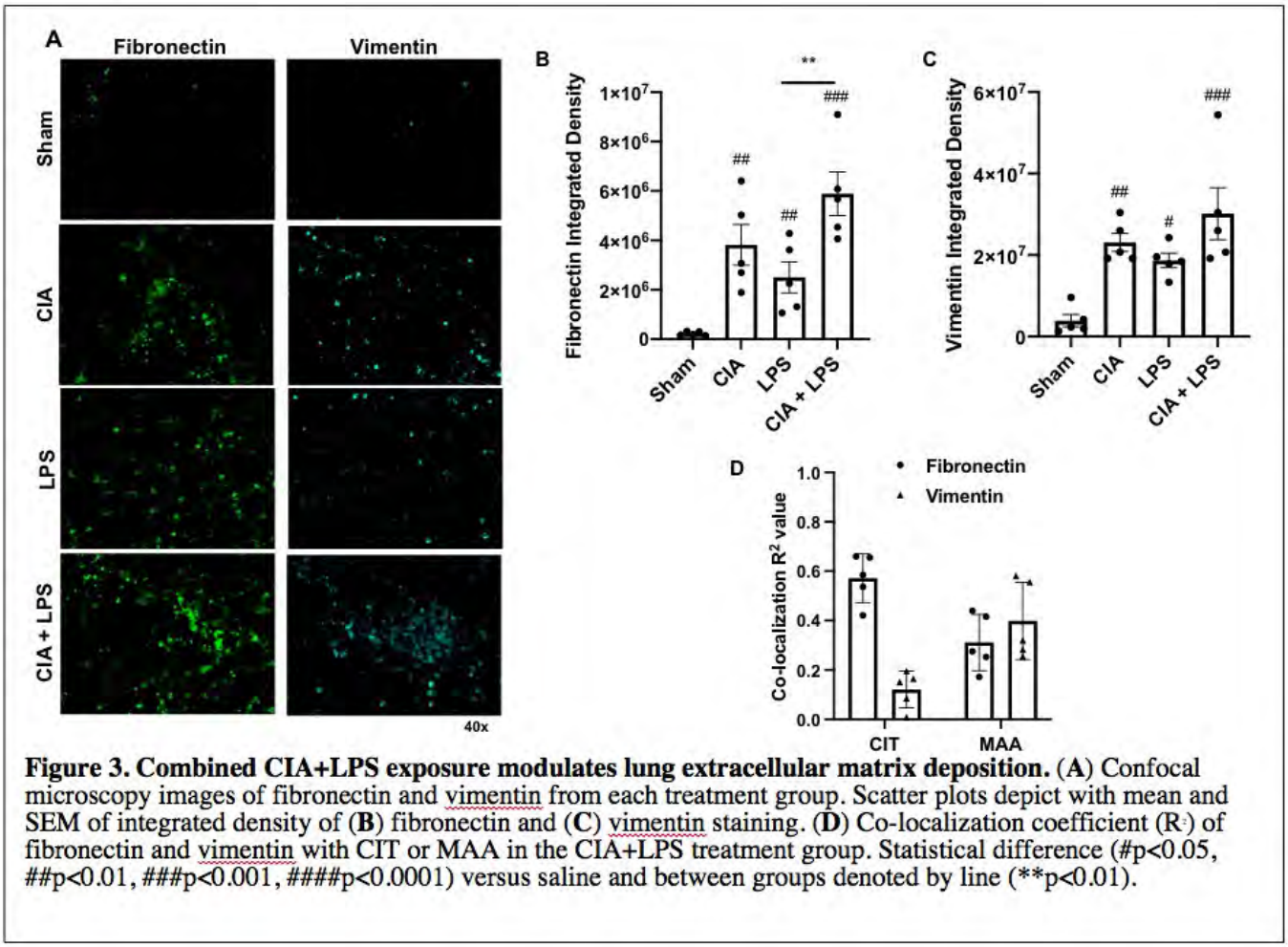


Figure 3. Combined CIA+LPS exposure modulates lung extracellular matrix deposition. (**A**) Confocal microscopy images of fibronectin and vimentin from each treatment group. Scatter plots depict with mean and SEM of integrated density of (**B**) fibronectin and (**C**) vimentin staining. (**D**) Co-localization coefficient (R^2) of fibronectin and vimentin with CIT or MAA in the CIA+LPS treatment group. Statistical difference (#p<0.05, ##p<0.01, ###p<0.001, ####p<0.0001) versus saline and between groups denoted by line (**p<0.01).

co-localization were similarly increased across groups vs. Sham. Lung fibronectin was increased with CIA and LPS and its expression was enhanced in CIA+LPS (**Figure 3**). Vimentin expression was increased in CIA, LPS, and CIA+LPS vs. Sham, but there were no differences between treated groups. In CIA+LPS lung tissues, CIT co-localized with fibronectin (R^2=0.6) but not vimentin (R^2=0.12), whereas MAA co-localized with both fibronectin (R^2=0.3) and vimentin (R^2=0.4).

Conclusion: In the context of arthritis induction, exposure to endotoxin (a ubiquitous airborne biohazard) led to substantial increases in the lung expression of post-translationally modified proteins implicated in RA. Moreover, these combined exposures led to striking increases in serum autoantibodies including a >30-fold increase in ACPA and a 6-fold increase in anti-MAA antibody, yielding an autoantibody profile more closely mimicking human disease. These results emphasize that an underlying predisposition to autoimmunity plus a "second hit" such as an airborne biohazard exposure could be driving tolerance loss and autoimmunity that characterize RA.

Disclosure: T. Mikuls, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **R. Gaurav**, None; **G. Thiele**, Regeneron, 6; **B. England**, Boehringer-Ingelheim, 2; **M. Wolfe**, None; **B. Shaw**, None; **K. Bailey**, None; **A. Nelson**, None; **M. Duryee**, None; **C. Hunter**, None; **D. Romberger**, None; **D. Ascherman**, None; **J. Poole**, None.

Abstract Number: 1015

Preclinical Investigation of the First-in-Class SIK2/SIK3 Inhibitor GLPG3970 in Models of Arthritis

Catherine Jagerschmidt[1], Stephanie Lavazais[1], Maikel Colli[2], Michael Drennan[2], Erik Verschueren[2], David Amantini[1], Nicolas Desroy[1] and **Steve De Vos**[2], [1]Galapagos SASU, Romainville, France, [2]Galapagos NV, Mechelen, Belgium

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Improved management of rheumatoid arthritis (RA) and psoriatic arthritis (PsA) remains an unmet need. Salt-inducible kinases (SIKs) modulate immune cells by a dual mechanism of action (MoA) in inflammatory conditions.[1–3] SIK2/SIK3 inhibition governs a molecular transcriptional switch resulting in reduced expression of pro-inflammatory mediators coupled with enhanced immunoregulatory activity. GLPG3970 is a first-in-class SIK2/SIK3 inhibitor in development for inflammatory indications. We evaluated the therapeutic activity of GLPG3970 in murine arthritis models.

Methods: GLPG3970's selectivity and potency were profiled in biochemical and target-based cell assays. The dual MoA of SIK2/SIK3 inhibition with GLPG3970 was evaluated in LPS-stimulated human whole blood measuring TNFα and IL-10 release and by performing RNA sequencing. Functional enrichment analysis of KEGG pathways among the differentially expressed genes (DEGs) was performed using a standard hypergeometric test.

Three doses of GLPG3970 treatment were evaluated in two murine models of arthritis: the IL23-induced PsA model and the collagen-induced-arthritis (CIA) model. First, B10.RIII mice received hydrodynamic i.v. injection of 0.1 µg mIL-23 enhanced Episomal Expression Vector to induce PsA disease. Efficacy of 5 weeks of treatment with GLPG3970 was evaluated by clinical score analysis and X-ray imaging (analysis of osteophyte formation). Inflammatory media-

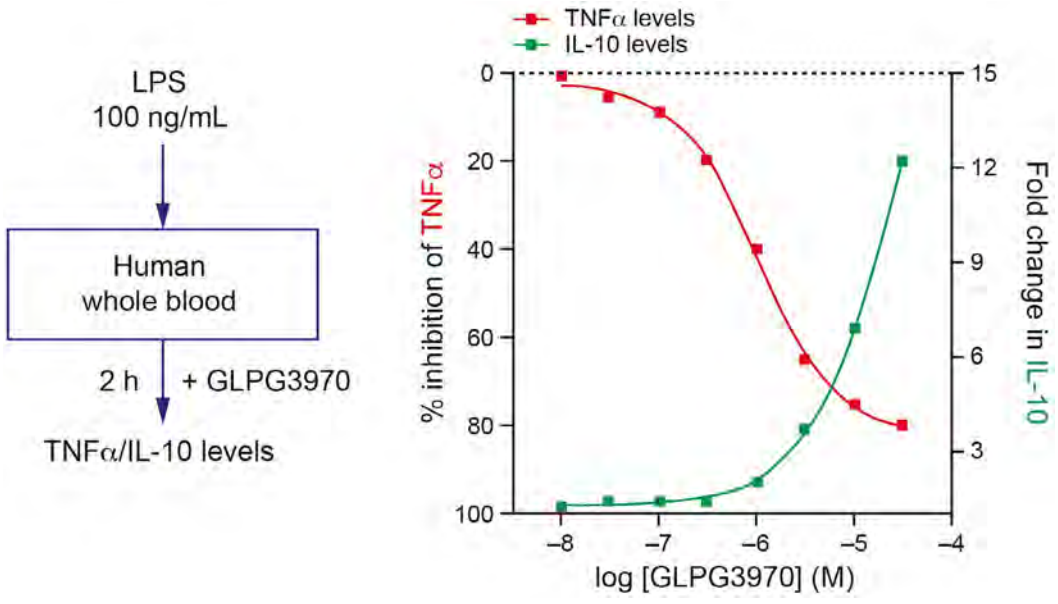


Figure 1. GLPG3970 activity in LPS-stimulated human whole blood assay (mean values, n=52, healthy donors).

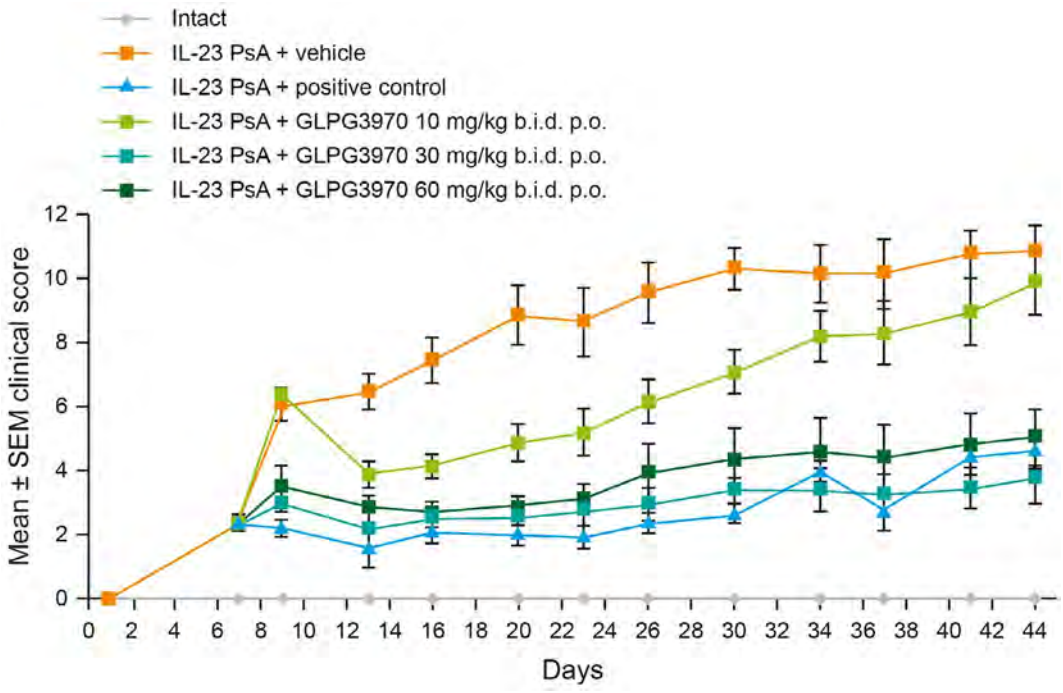


Figure 2. Clinical score over time in PsA model (IL-23 induced).

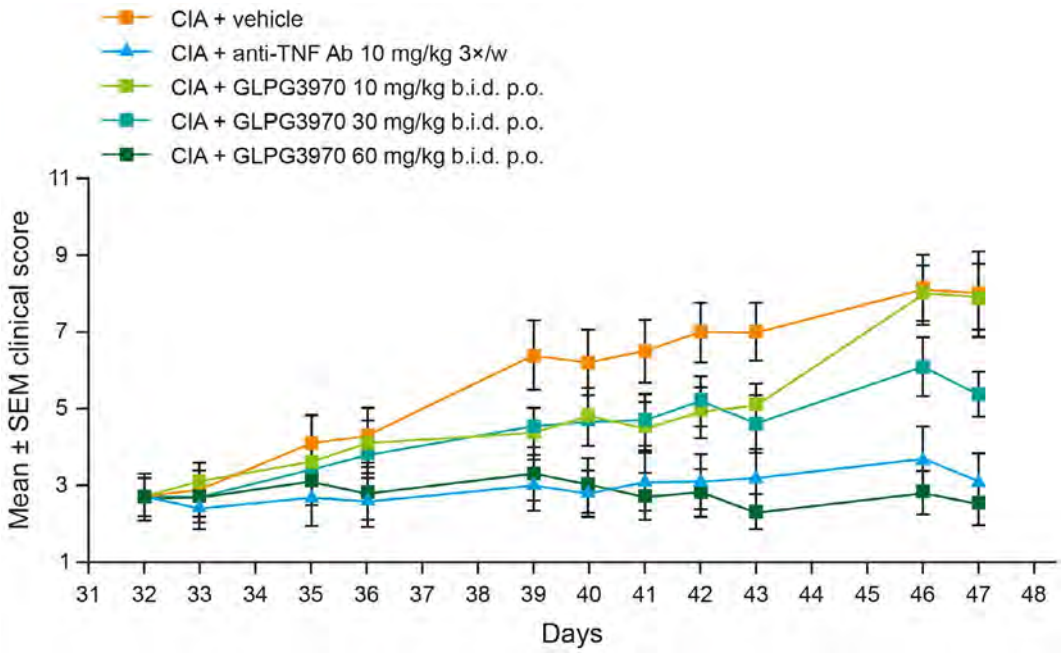


Figure 3. Clinical score over time in RA model (therapeutic CIA model).

tors were quantified in paws. Second, in the CIA model, DBA1J mice were classically immunized with a type II bovine collagen emulsion on day 1 and day 21. Efficacy of GLPG3970 treatment from day 32–47 was compared with an anti-TNF agent (Enbrel®) and evaluated by clinical score analysis and bone erosion (Larsen score after X-ray imaging). Anti-collagen type-II antibodies were quantified in serum.

Results: GLPG3970 was shown to inhibit SIK2/SIK3 with high selectivity against a panel of 372 kinases. Activity in LPS-stimulated whole blood led to dose-dependent reduction of TNFα levels coupled with increased IL-10 release (Fig 1). GLPG3970 DEGs in LPS-stimulated whole blood were functionally enriched with RA as part of the top 3 most

statistically significant pathways from the KEGG database. GLPG3970 treatment in the PsA model decreased clinical score (Fig 2), osteophyte formation and pro-inflammatory mediators. GLPG3970 reduced clinical score in the CIA model (Fig 3). The highest dose effect was comparable with anti-TNF treatment and correlated with reduced Larsen score and anti-collagen type-II antibody levels.

Conclusion: This study associates the underlying mechanism of SIK2/SIK3 inhibition with RA and highlights the therapeutic activity of GLPG3970 in murine arthritis models, supporting GLPG3970 as a promising novel approach for the treatment of arthritis. GLPG3970 is being tested in a phase 2a study in patients with RA (NCT04577781).

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2. Lombardi M *et al. J Leukoc Biol* 2016;99:711–21.
3. Darling N *et al. Biochem J* 2017;474:521–37.

Disclosure: C. Jagerschmidt, Galapagos NV, 3; **S. Lavazais**, Galapagos NV, 3; **M. Colli**, Galapagos NV, 3; **M. Drennan**, Galapagos NV, 3; **E. Verschueren**, Galapagos NV, 3; **D. Amantini**, Galapagos NV, 3; **N. Desroy**, Galapagos NV, 3; **S. De Vos**, Galapagos NV, 3.

Abstract Number: 1016

Assessment of Pre-Inflammatory Mesenchymal (PRIME) Cells as a Biomarker of Tumor Necrosis Factor-Induced Arthritis in Mice

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Recently, CD45–CD31–Podoplanin (PDPN)+ synovial fibroblast-like cells, termed pre-inflammatory mesenchymal (PRIME) cells were found to be differentially expressed and circulate in the blood of rheumatoid arthritis (RA) patients before an arthritic flare (1). PRIME cells are hypothesized to be stimulated from an inflammatory trigger and recruited to the synovium from blood to facilitate flares, suggesting that their presence in circulating blood can be a biomarker for inflammatory arthritis. However, the presence of a PRIME cell population in rodent animal models of RA has yet to be determined. TNF-transgenic (TNF-Tg) mice are a model of RA in which the constitutive expression of pro-inflammatory cytokines characterizes a persistent inflammation during disease development. Identification of PRIME cells in rodent models, and specifically in the TNF-Tg mice, may be utilized to further elucidate the role of PRIME cells in inflammatory arthritis. Thus, we hypothesized that arthritic TNF-Tg mice express a population of circulating PRIME cells that are increased compared to wild-type (WT) controls.

Methods: Flow cytometry analysis of peripheral blood and bone marrow was performed on 6-9-month-old TNF-Tg and WT male littermates (n=3 mice/group). PRIME cells were determined as CD45-CD31-PDPN+ gated cells, and for each experimental sample, populations were compared with the percentage of gated cells and the total count

of PRIME cells (Fig 1). Groups were analyzed using unpaired t-tests, and values are reported as mean ± standard deviation.

Results: At 6-9 months, both TNF-Tg and WT mice showed PRIME cell populations in circulating blood (2.28 ± 1.98% TNF-Tg vs 2.21 ± 3.52% WT; 31.33 ± 45.88 TNF-Tg vs 31.33 ± 53.41 WT) and bone marrow (7.70 ± 13.34% TNF-Tg vs 12.11 ± 20.98% WT; 25 ± 43.3 TNF-Tg vs 35.33 ± 61.20 WT). There was no significant difference in PRIME cell populations between TNF-Tg and WT mice.

Conclusion: These preliminary results suggest that PRIME cells can be detected in blood and bone marrow of both TNF-Tg mice with advanced arthritis and their WT littermates. However, by late stage arthritis, the PRIME cell population in TNF-Tg mice is not greater than that found in WT controls, and therefore ineffective as a biomarker of chronic disease in this model. Future studies looking at early disease and flare are warranted to further clarify the use of PRIME cells as biomarkers in TNF-induced arthritis.

1. Orange D.E. et al. *N Engl J Med* 383(3):218-228. 2020.

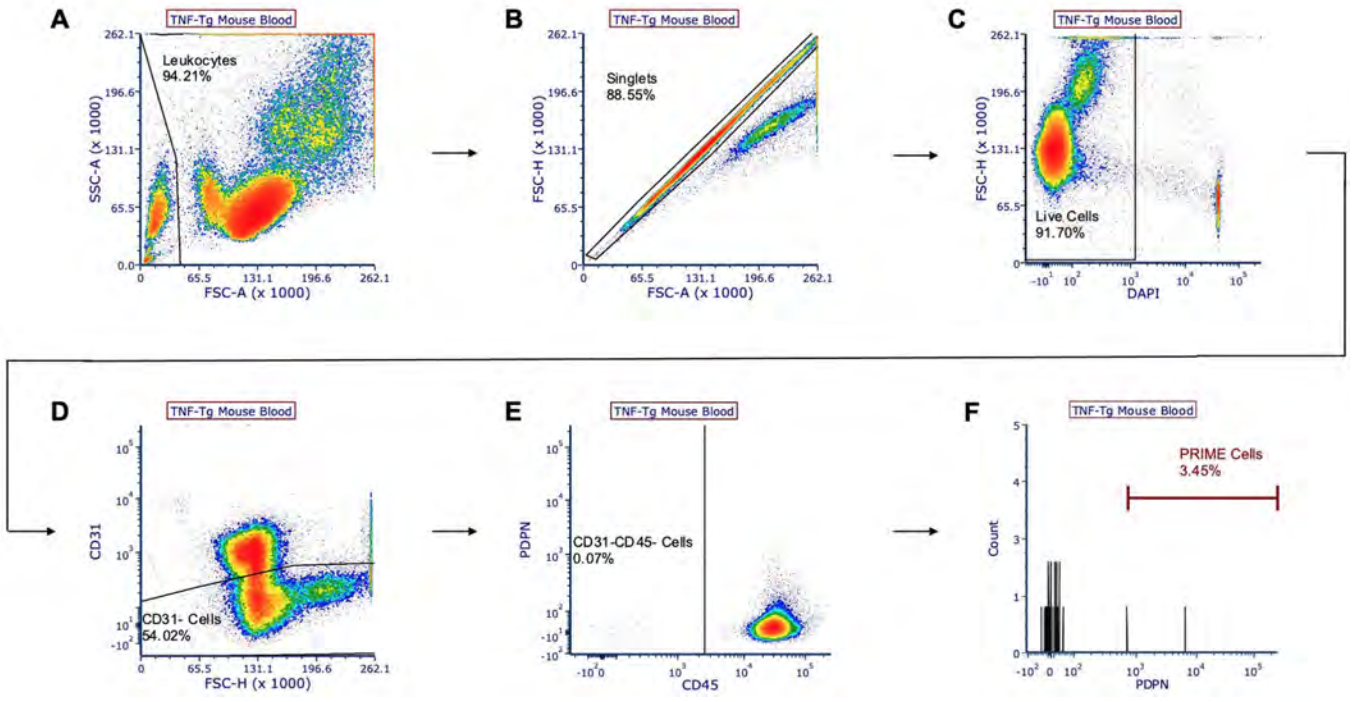

Figure 1. Gating strategy of representative TNF-Tg mouse blood for CD45-CD31-PDPN+ PRIME cells. TNF-Tg mouse peripheral blood (male; 6.5-months old) was harvested and stained with CD45, CD31, and podoplanin (PDPN) antibodies and DAPI viability stain. Live, single-cell leukocytes were gated (A-C), and PRIME cells were identified as CD31- (D), CD45- (E), and PDPN+ (F) cells. Each value represents the percentage of gated cells.

Disclosure: K. Chen, None; **X. Lin**, None; **L. Xing**, None; **H. Kenney**, None; **R. Bell**, None; **E. Schwarz**, Janssen, Johnson & Johnson, 12, Anti-TNF and placebo antibodies were a gift from Janssen, J&J; **H. Rahimi**, None.

Abstract Number: 1017

Osteoclast-Specific Transmembrane Protein (OC-STAMP) Regulates Osteoclastogenesis and Inhibits Inflammation in an Acute Arthritis Model

Maria de la Luz Garcia-Hernandez[1], Javier Rangel-Moreno[1], Ananta Paine[1], Jacob R. Jones[1], Marc Nuzzo[1], Lidsay N. Schnur[2] and Christopher Ritchlin[1], [1]Division of Allergy, Immunology, and Rheumatology, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY, [2]University of Rochester, Rochester, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Dendritic Cell (DC)-Specific Transmembrane Protein (STAMP) expressed by osteoclast precursors is required for cell-cell fusion in the formation of the osteoclast (OC) polykaryon. Genetic ablation of DC-STAMP results in mononuclear OCs and an osteopetrosis phenotype. Absence of DC-STAMP in the TNF-Tg arthritis model markedly reduces synovitis and inflammatory bone loss. OC-STAMP is another molecule required for cell-cell fusion and absence of either DC or OC-STAMP blocks multinucleation. To date, it is unknown if both molecules have redundant or cooperative functions and if their combined absence results in decreased bone damage and synovitis in inflammatory arthritis. We hypothesize that dual absence of OC-STAMP and DC-STAMP will ameliorate inflammation and bone erosion in a mouse model of acute arthritis (K/BxN).

Methods: OC-STAMP floxed mice were crossed with DC-STAMP$^{-/-}$ and global B6-Cre mice to generate OC-STAMP$^{-/-}$ and OC-STAMP$^{-/-}$ x DC-STAMP$^{-/-}$ animals. We injected WT, OC-STAMP$^{-/-}$ and OC-STAMP$^{-/-}$ x DC-STAMP$^{-/-}$ mice with serum collected from 8-week old K/BxN mice to induce acute inflammatory arthritis. We evaluated bone loss and local inflammation by micro-CT scan and histology, respectively. We isolated CD115^{+} cells, macrophages, neutrophils, dendritic cells (DCs), T cells and differentiated M1/M2 macrophages from WT mice to assess OC-STAMP expression by quantitative qPCR. We also quantified mRNA changes in IL13, IL10 and arginase I in WT and OC-STAMP deficient M2 macrophages.

Results: k/bxn-treated OC-STAMP deficient mice demonstrated extensive bone loss in the tibia (10 ± 0.9 Vs 22 ± 2, p = 0.0001), femur (12 ± 1 Vs 26 ± 2.5, p = 0.0001), talus (53 ± 2 Vs 58 ± 2, p = 0.0001), and increased pannus infiltration compared to WT mice. Surprisingly, the absence of DC-STAMP in OC-STAMP deficient mice treated with k/bxn sera was associated with decreased bone resorption in femur (16.3 ± 5, p = 0.05), tibia (15 ± 5, p =0.01) and ankle (51 ± 3.6, p = 0.02), compared to WT but bone loss was significantly lower than observed previously in DC-STAMP$^{-/-}$ TNF-Tg mice. We assessed OC-STAMP expression by quantitative PCR in immune cells and found that OC-STAMP is expressed by spleen macrophages (51.9 ± 0.6, p ≤ 0.001), DCs (304 ± 24, p = 0.002), neutrophils (126 ± 13, p = 0.003), M2 macrophages (350 ± 17, p = 0.001), CD4 (1.8 ± 0.014) and CD8 T cells (7.9 ± 0.5, p = 0.0002). Its expression was low or absent in M1 macrophages (4.5 ± 0.01, p ≤ 0.0001) and CD115^{+} cells (1 ± 0.01, p ≤ 0.001), respectively. OC-STAMP deficient M2 macrophages showed impaired expression of IL13 (14.5 ± 1.6 Vs. 0.1 ± 0.005, p = 0.004), arginase I (55 ± 6.7, Vs. 1.3 ± 0.07, p = 0.006) and IL10 (0.056 ± 0.03, Vs 79 ± 1.9, p ≤ 0.001) compared with WT macrophages.

Conclusion: Ablation of OC-STAMP in the K/RxN arthritis model dramatically enhanced synovitis and bone loss in direct contrast to the findings observed with DC-STAMP knockout mice. OC-STAMP modulates synovial inflammation

by inducing the expression of immunosuppressive cytokines and factors expressed by M2 macrophages. In the DC-STAMP/OC-STAMP knockout the arthritis phenotype is dominated by the absence of OC-STAMP.

Disclosure: M. Garcia-Hernandez, None; **J. Rangel-Moreno**, None; **A. Paine**, None; **J. Jones**, None; **M. Nuzzo**, None; **L. Schnur**, None; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2.

Abstract Number: 1018

Joint-Draining Popliteal Lymphatic Vessels Exhibit Lymphatic Muscle Cell Dysfunction in TNF-Tg Mice with Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Lymphatic dysfunction is a factor in the onset and progression of rheumatoid arthritis (RA) (1). Our prior studies demonstrated reduced lymphatic clearance in the hands of symptomatic RA patients vs. healthy controls (2). We reported similar findings in the tumor necrosis factor transgenic (TNF-Tg) mouse model of RA, which exhibits reduced contractility of joint-draining popliteal lymphatic vessels (PLVs) (3,4). Remarkably, anti-TNF therapy in flaring TNF-Tg mice recovers PLV contractions concomitant with amelioration of arthritis (4). Based on this result, we hypothesize that PLV dysfunction correlates with arthritis and is caused by: 1) chronic TNF-mediated lymphatic muscle cell (LMC) damage (4), and/or 2) paracrine factors known to inhibit lymphatic contractions from accumulated peri-lymphatic inflammatory cells during chronic inflammation (5). To specifically assess LMC tissue damage, herein we tested the hypotheses that: 1) alpha-smooth muscle actin ($\alpha SMA)^+$ PLV-LMC coverage is reduced in TNF-Tg mice with severe arthritis, and 2) anti-TNF therapy recovers LMC integrity by promoting turnover of bromodeoxyuridine $(BrdU)^+$ PLV-LMCs associated with return of lymphatic and joint homeostasis.

Methods: BrdU (0.1mg/g/day/i.p.) was administered to 8-month-old wild-type (WT, n=8 mice) and TNF-Tg (placebo or anti-TNF therapy, n=5 mice each; i.p. 10mg/kg/week) mice for 6-consecutive weeks, followed by whole mount immunofluorescent microscopy for αSMA^+ and $BrdU^+$ PLV-LMCs, as previously described (6). Talus bone volumes were measured by μCT longitudinally every 3-weeks as a biomarker of ankle arthritis. Preliminary scanning electron microscopy (SEM) was performed on WT PLVs (n=2 mice) to assess the feasibility of evaluating LMC coverage with ultrastructural analysis.

Results: αSMA^+ PLV-LMC coverage was reduced in TNF-Tg placebo mice vs. WT littermates (61.32±23.47% placebo vs 84.99±10.79% WT; $p< 0.0001$). However, anti-TNF therapy failed to recover αSMA^+ PLV-LMC coverage (68.86±20.41%) **(Figure 1)**, consistent with no change in LMC turnover (< 2% $BrdU^+/\alpha SMA^+$ cells for all groups) **(Figure 2)**. In contrast, anti-TNF therapy restored talus bone volume, and there was no relationship with αSMA^+ PLV-LMC coverage and bone volume (R^2=0.1106) **(Figure 1)**. SEM of PLVs confirmed the ability to further interrogate LMC coverage with ultrastructural imaging, and also unexpectedly identified a predominant peri-lymphatic mast cell population that may explain previous findings of increased peri-lymphatic cells in TNF-Tg mice **(Figure 3)**.

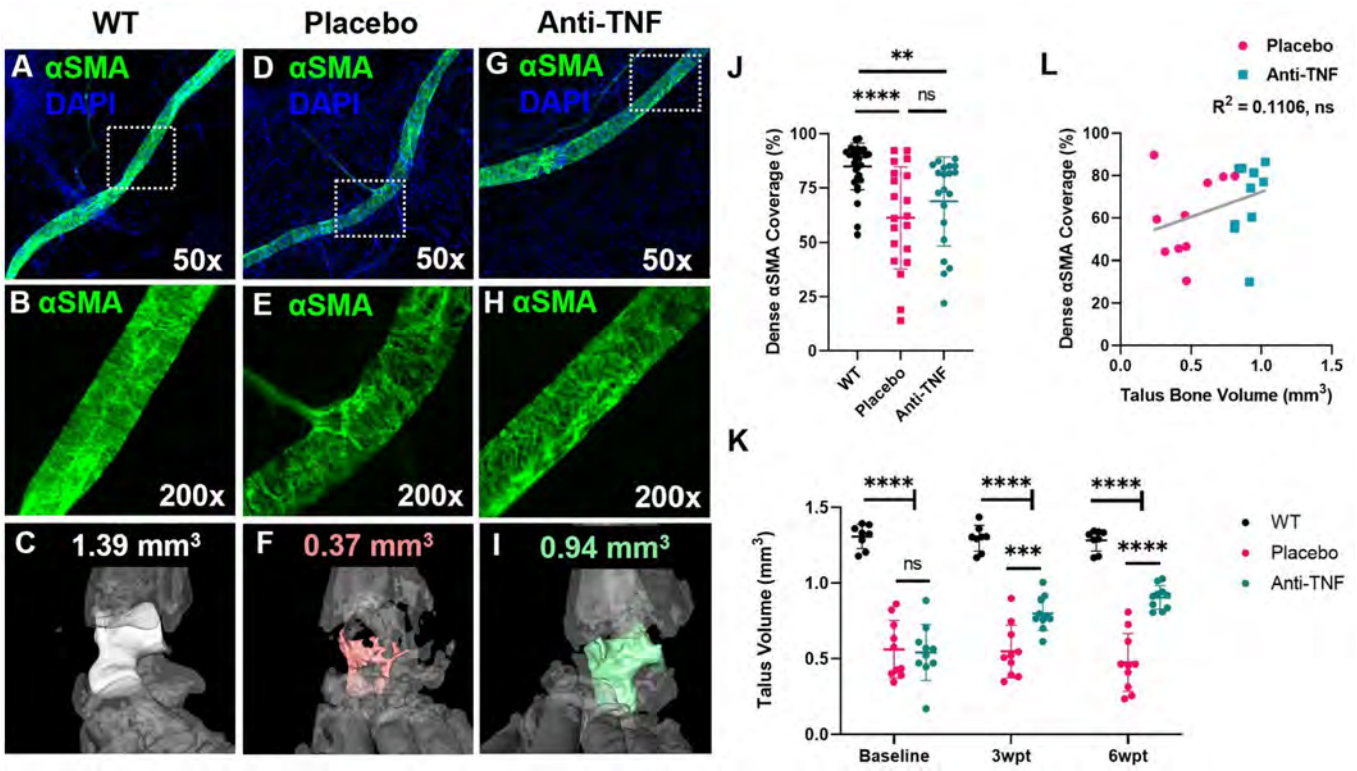

Figure 1. 6-weeks of anti-TNF therapy ameliorates bone erosions despite persistence of reduced PLV-LMC **α**SMA coverage in TNF-Tg mice. TNF-Tg mice (8-month-old) were treated with anti-TNF or placebo (10mg/kg/week, i.p.) for 6-consecutive weeks, while WT littermates received volume-matched vehicle PBS. Following treatment, PLVs were harvested and processed for whole mount immunofluorescent microscopy. Talus bone volumes were evaluated longitudinally at 3-week intervals by **μ**CT. Representative images of **α**SMA+ PLV-LMC coverage (green) and segmented taluses (colored bone within the remaining transparent grey ankle joint) (WT A-C; TNF-Tg D-F; anti-TNF G-I) with quantification of **α**SMA coverage (J, **α**SMA coverage as a percent of total PLV area), talus bone volumes (K), and the correlation between these outcomes (L) are shown for all groups. Note the similar reduction in intensity of **α**SMA signal for both placebo and anti-TNF treated TNF-Tg cohorts despite talus bone recovery with anti-TNF therapy. Each data point for **α**SMA coverage represents individual PLVs, while correlation with talus bone volumes was performed with the average between the two PLVs present in each limb. Statistics: All data is reported as mean ± standard deviation (SD). One-Way ANOVA (J; **** $p < 0.0001$, ** $p < 0.01$); Two-Way ANOVA (K; **** $p < 0.0001$, *** $p < 0.001$); and linear regression (L; no significance (ns) $p > 0.05$).

Conclusion: Chronic inflammation reduces αSMA⁺ PLV-LMC coverage. While 6-weeks of anti-TNF therapy reverses bone loss in TNF-Tg mice, this short-course does not enhance αSMA investiture or LMC turnover in damaged PLVs. Thus, future work will focus on the recent discovery of mast cell accumulation in the peri-lymphatic tissue of joint-draining PLVs during chronic inflammation, known to inhibit LMC contractility.

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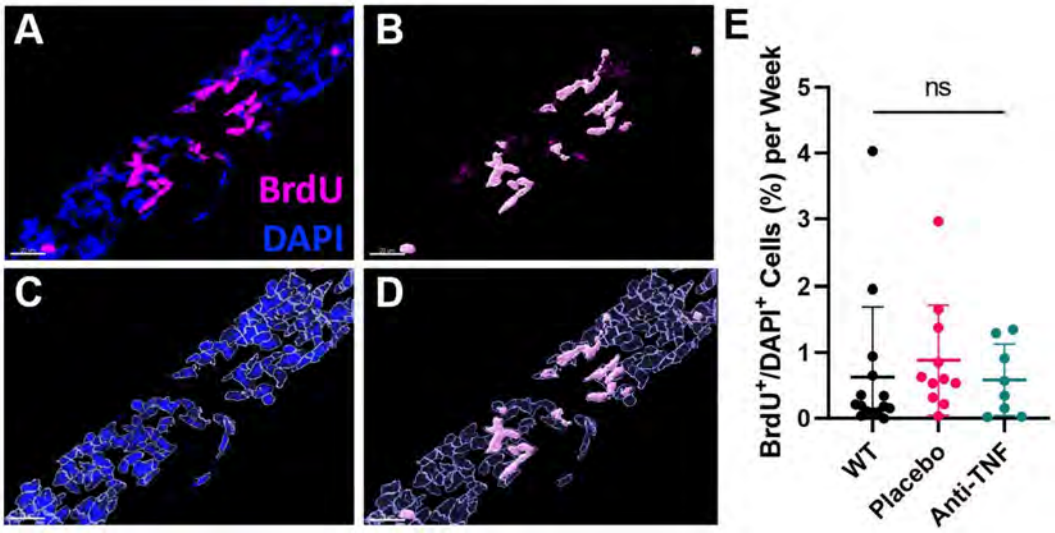

Figure 2. LMC turnover of joint-draining PLVs is unchanged during inflammation or therapy. Imaris software was used to analyze DAPI+/BrdU+ cell colocalization within an **α**SMA+ mask in 200x confocal stacks across the entire length of PLVs (~5mm) (A). Segmentation of individual BrdU+ (B) and DAPI+ nuclei (C) was performed to evaluate the ratio of BrdU+/DAPI+ cells (D). WT and TNF-Tg (placebo or anti-TNF as in Figure 1) were treated with BrdU for 6-consecutive weeks (0.1mg/g/day, i.p., as previously described (6)), and quantification of BrdU labeled cells in the PLVs indicates no difference in PLV cellular turnover between groups (E). Each data point represents a single PLV. Statistics: All data is reported as mean ± SD. One-Way ANOVA (E; ns $p > 0.05$ all comparisons).

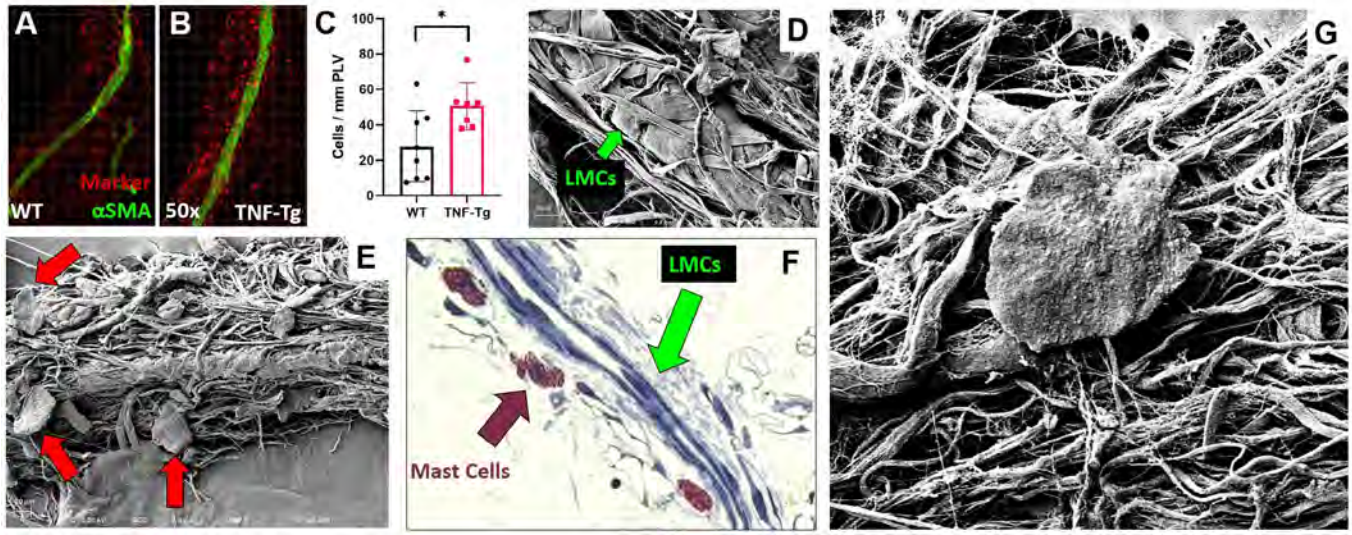

Figure 3. Increased mast cell numbers around PLVs in TNF-Tg mice with inflammatory arthritis. PLVs harvested from TNF-Tg mice exhibited increased cell accumulation in the peri-lymphatic region compared to those of WT controls by whole mount immunofluorescent microscopy (A,B), and the number of positive cells is quantified for each PLV (C). To elucidate the identity of these cells, scanning electron microscopy (SEM) was performed on WT PLVs, which identified LMCs (1,000x) (D) with mast cells embedded within the peri-lymphatic tissue (500x) (E), which was validated by histologic staining using toluidine blue (F). These findings suggest that during chronic inflammation, mast cells accumulate in the peri-lymphatic region surrounding joint-draining PLVs and inhibit lymphatic contractility associated with progression of arthritis in the afferent ankle. Future studies will target these identified mast cells (5,000x) (G) to further elucidate the mechanisms of lymphatic dysfunction in inflammatory arthritis. Statistics: All data is reported as mean ± SD. Unpaired t-test (C; * $p < 0.05$).

Disclosure: H. Kenney, None; **Y. Peng**, None; **K. de Mesy Bentley**, None; **C. Galloway**, None; **H. Rahimi**, None; **L. Xing**, None; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **E. Schwarz**, Janssen, Johnson & Johnson, 12, Anti-TNF and placebo antibodies were a gift from Janssen, J&J.

Abstract Number: 1019

Cigarette Smoking Induces Post-translational Protein Modifications in Both *in Vitro* and *in Vivo* Models of Rheumatoid Arthritis-associated Interstitial Lung Disease

Alyssa Gregory[1], Corrine Kliment[1], Geoffrey Thiele[2], Michael Duryee[2], Ted Mikuls[2], Bryant England[2], Jill Poole[2] and **Dana Ascherman**[3], [1]University of Pittsburgh School of Medicine, Pittsburgh, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Animal Models Poster (1014–1021)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Cigarette smoking has been epidemiologically linked to the development of ACPA+ rheumatoid arthritis (RA) and, by extension, RA-associated interstitial lung disease (RA-ILD). Providing strong evidence for the contribution of gene-environment interactions to disease pathogenesis, the risk for ACPA+ RA is increased

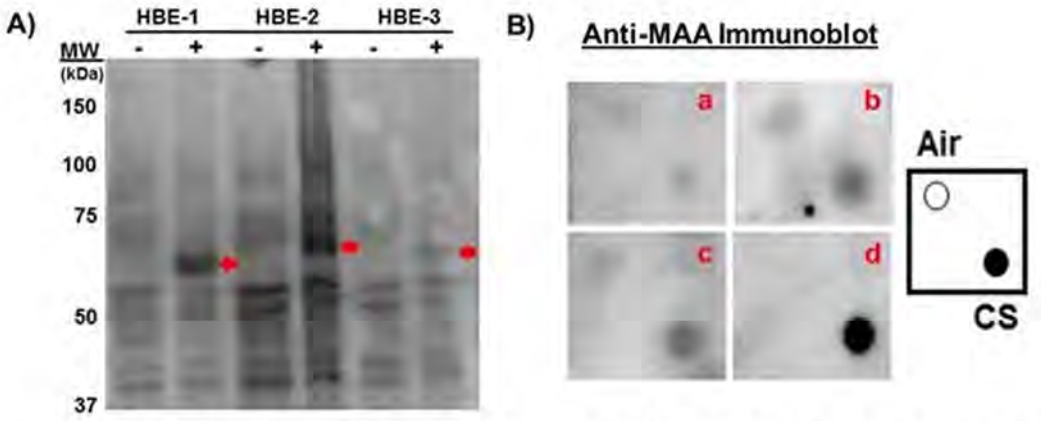

Figure 1. Cigarette smoke-induced PTMs in Human Bronchial Epithelial cells (HBEs) exposed to cigarette smoke. (**A**) Paired lanes depict equal amounts of HBE cell extract probed with anti-modified citrulline antibody (EMDMillipore) 18 hours after exposure to air (-) vs. cigarette smoke (+). Arrowheads designate specific proteins citrullinated in response to an 8 cigarette dose. (**B**) Panels a-c depict dot blots of paired extracts derived from HBE cells exposed to air (upper left) vs. cigarette smoke (4-8 cigarette dose, lower right). Specificity of the polyclonal anti-MAA antibody used to probe these blots is shown in panel d comparing recognition of unmodified (upper left) vs. MAA-modified human serum albumin (1 μg). Results are representative of at least two independent experiments for each extract.

more than 20 fold in cigarette smokers who also possess HLA-DRB1*0401 or other shared epitope alleles. This link between smoking, the shared epitope, and risk of RA/RA-ILD is thought to arise from immune responses targeting *in situ*, smoking-induced post-translational modifications (PTMs) such as citrullination. However, because most of the data linking smoking and PTMs has been "associative," we examined the ability of cigarette smoke to directly induce PTMs in both *in vitro* and *in vivo* model systems.

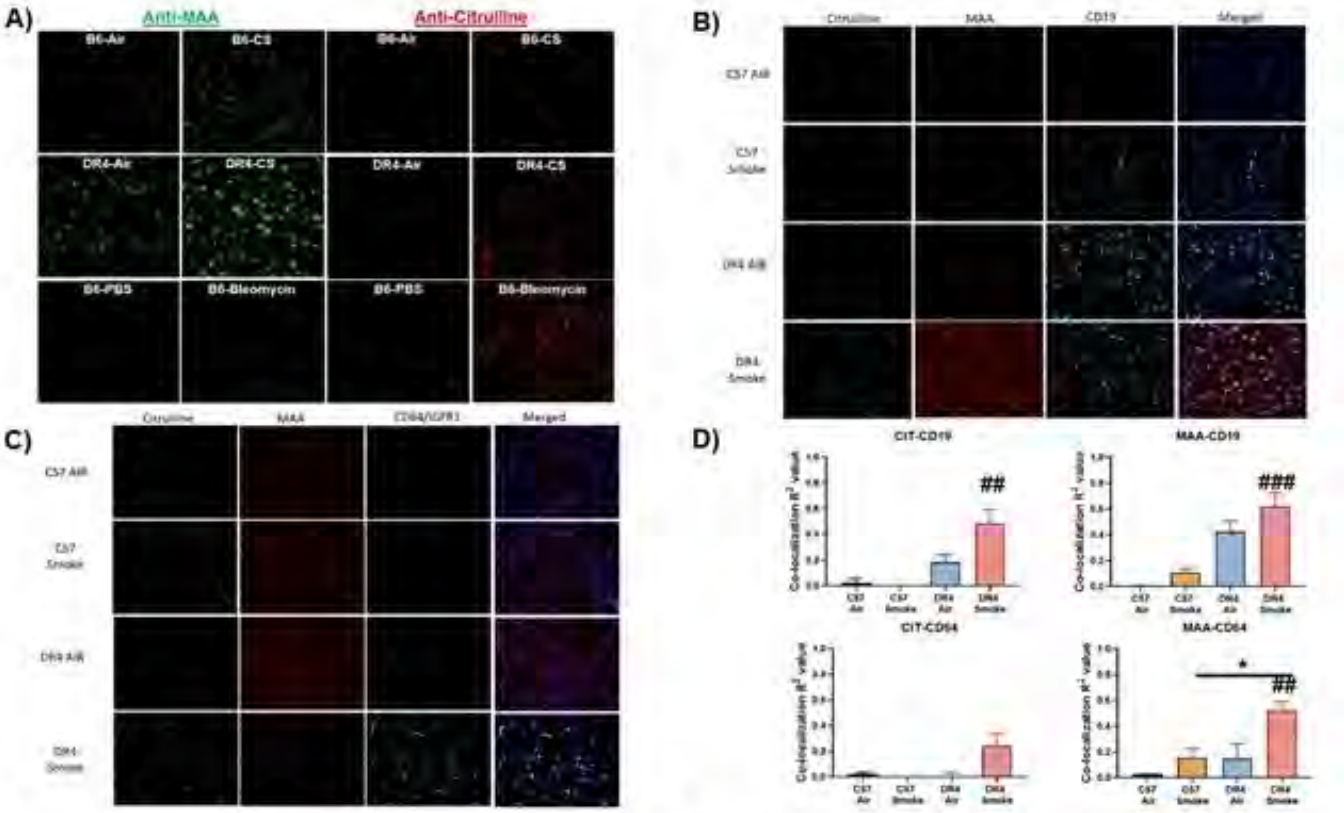

Figure 2. Cigarette smoke-induced PTMs in mouse lung tissue. A) Immunohistochemical staining of mouse lung tissue derived from C57BL/6 WT and HLA-DR4 transgenic mice following exposure to cigarette smoke demonstrates increased MAA-modified (columns 1-2) and citrullinated (columns 3-4) proteins relative to air-exposed lungs. Lung tissue from B6 WT mice following administration of intraperitoneal PBS versus bleomycin is shown for comparison. Panels B-C demonstrate co-localization of anti-MAA, anti-Cit, anti-CD19 (B), and anti-CD64 (C) staining. D) Corresponding grafts depict the degree of co-localization (represented by R^2 values) for these PTMs and CD19+ B cells or CD64+ macrophages. While significant differences between smoking groups and C57 WT-air are indicated by # symbols (#p<0.05, ##p<0.01, ###p<0.001), differences between DR4-smoking and C57 WT-smoking are denoted by asterisks and lines (*p<0.05).

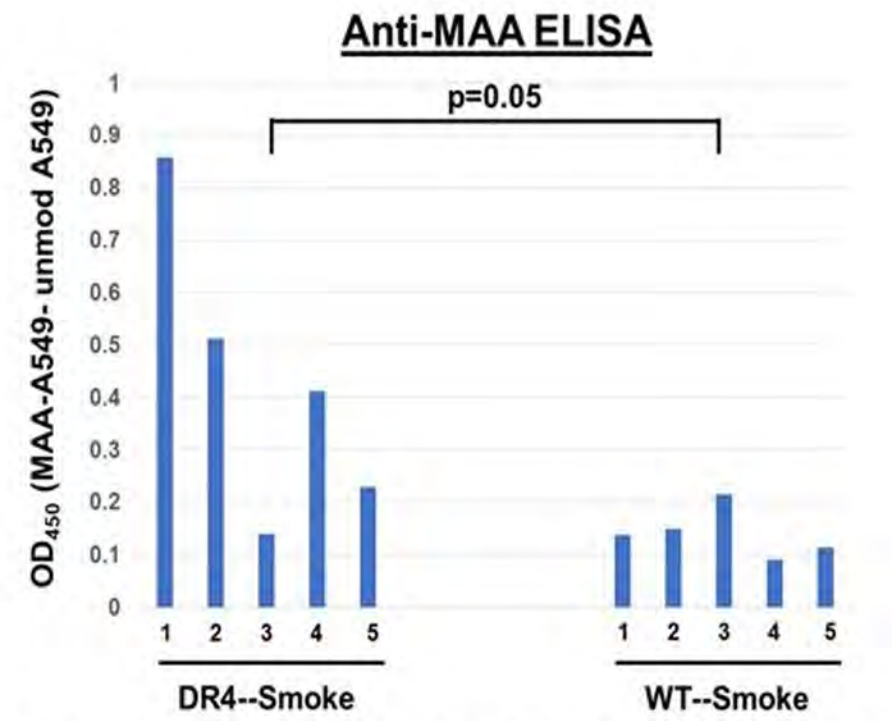

Figure 3. Cigarette smoke-induced anti-MAA antibody formation. Bars represent relative titers of antibodies targeting MAA-modified A549 lung epithelial cell extract in individual DR4 TG vs. B6 WT mice exposed to daily cigarette smoke for 2 months; negligible error bars are not shown.

Methods: Primary human bronchial epithelial cells (HBEs) were isolated, cultured at the air-liquid interface, and robotically exposed to defined doses of cigarette smoke vs. air prior to harvesting and preparation of cell extracts. Following SDS-PAGE, separated proteins were transferred to nitrocellulose membranes and probed with anti-modified citrulline antibody (EMD Millipore). Alternatively, extracts were transferred directly to membranes and probed with polyclonal antibody recognizing malondialdehyde-acetaldehyde (MAA)-modified proteins. Complementing these *in vitro* studies, HLA-DR4 transgenic (DR4) and C57BL/6 (WT) mice were exposed to daily cigarette smoke for 2 months and then harvested for immunofluorescence (IF) staining of lung tissue and ELISA-based analysis of PTM-targeted autoantibody production. Lung tissue from WT mice with bleomycin-induced pulmonary fibrosis was used as a control for PTM formation.

Results: Immunoblots of HBE cell extracts demonstrated smoke-induced citrullination as well as MAA-modification (**Figure 1**). Similarly, *in vivo* administration of cigarette smoke induced both citrullination and MAA modification of lung tissue, particularly in DR4 TG mice (**Figure 2A**). Additional IF staining revealed that these PTMs co-localized with CD19+ B cells and CD64+ macrophages (**Figure 2B-D**), both of which were increased in the lung tissue of cigarette smoke-exposed DR4 TG mice ($p < 0.01$ for CD19+ cells and < 0.0001 for CD64+ cells, DR4 TG-smoke vs. WT-smoke). ELISAs also demonstrated preferential formation of anti-MAA antibodies in the serum of DR4 TG mice exposed to cigarette smoke (**Figure 3**), but a limited profile of ACPA were not detected. Mice showed no evidence of overt arthritis in any of the treatment groups.

Conclusion: *For the first time*, these studies *directly* demonstrate that cigarette smoke can induce PTMs such as citrullination and MAA modification in lung tissue/cells. Corresponding development of PTM-targeted immune responses in DR4 TG mice support a paradigm in which cigarette smoke triggers a breach of immune tolerance in immunogenetically predisposed hosts as a foundation for the development of RA/RA-ILD.

Disclosure: A. Gregory, None; **C. Kliment**, None; **G. Thiele**, Regeneron, 6; **M. Duryee**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **B. England**, Boehringer-Ingelheim, 2; **J. Poole**, None; **D. Ascherman**, None.

Abstract Number: 1020

Enhancing Endothelial Cell Barrier Function via Sphingosine -1 Phosphate Receptor 1 (S1PR1) – a Novel Treatment for Experimental Arthritis

Nathalie Burg, Ryan Malpass, Carl Blobel and Jane Salmon, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: S1PR1 signaling plays critical roles in EC barrier function and vascular health, but until now, research on S1PR1 modulation in autoimmune rheumatic disease has been focused on lymphocyte trafficking. Importantly, endothelial cells have never been targeted for the treatment of autoimmune rheumatic disease. In prior work, we showed that S1PR1 modulators attenuated immune complex (IC) mediated vascular injury in skin and lung. In vitro, S1PR1 agonists rescued EC barrier function and decreased loss of VE-cadherin expression in human umbilical vein ECs (HUVEC) challenged with IC activated neutrophils. In this study we asked whether EC S1PR1 signaling limits experimental arthritis and whether it does so, at least in part, by limiting VE-cadherin shedding.

Methods: Mice with an EC specific S1PR1 KO or gain of function (GOF) were subjected to K/BxN serum induced arthritis (SIA) by injecting 100 µl of serum days 0 and 2. To determine how pharmacologic modulation of S1PR1 signaling affected SIA, WT animals were treated with S1PR1 agonist, CYM-5442 or antagonist NIBR-0213 30 mg/kg or vehicle controls. Clinical scores were obtained daily after day 2 in a blinded manner and mice were sacrificed on days 2-3 or on day 8. Synovial fluids from arthritic ankles obtained on days 2-3 were assessed by ELISA and western blot for soluble VE-cadherin. H&E-stained paraffin sections were scored by a pathologist in a blinded manner. HUVECs treated with S1PR1 inhibitor NIBR-0213 or vehicle control were assessed by western blot.

Results: S1PR1 ECKO mice had augmented arthritis at earlier time points and mice with EC S1PR1 GOF had delayed disease compared to controls (n=7-8 animals/group, $p< 0.05$; Fig 1). Similarly, the S1PR1 agonist CYM-5442 delayed the onset of arthritis (n= 7 mice/group $p< 0.05$; Fig 2), while an S1PR1 antagonist NIBR induced earlier and more severe disease (n=4 animals/group p= 0.05). Synovial fluid from S1PR1 ECKO mice showed increased VE-cadherin shedding (n= 6; $p \leq 0.01$) and Evans blue extravasation (n=6; p= 0.1) at early time points after SIA compared to controls, suggesting that increased vascular permeability via VE-cadherin shedding contributed to arthritic damage. S1PR1 ECKO mice also showed increased VE-cadherin shedding in their bronchoalveolar lavage fluid at baseline, suggesting that S1PR1 signaling inhibits VE-cadherin at homeostasis. To determine whether blockade of S1PR1 signaling induce VE-cadherin shedding in vitro, we treated HUVEC with NIBR-0213 (Fig 3). There was a marked increase

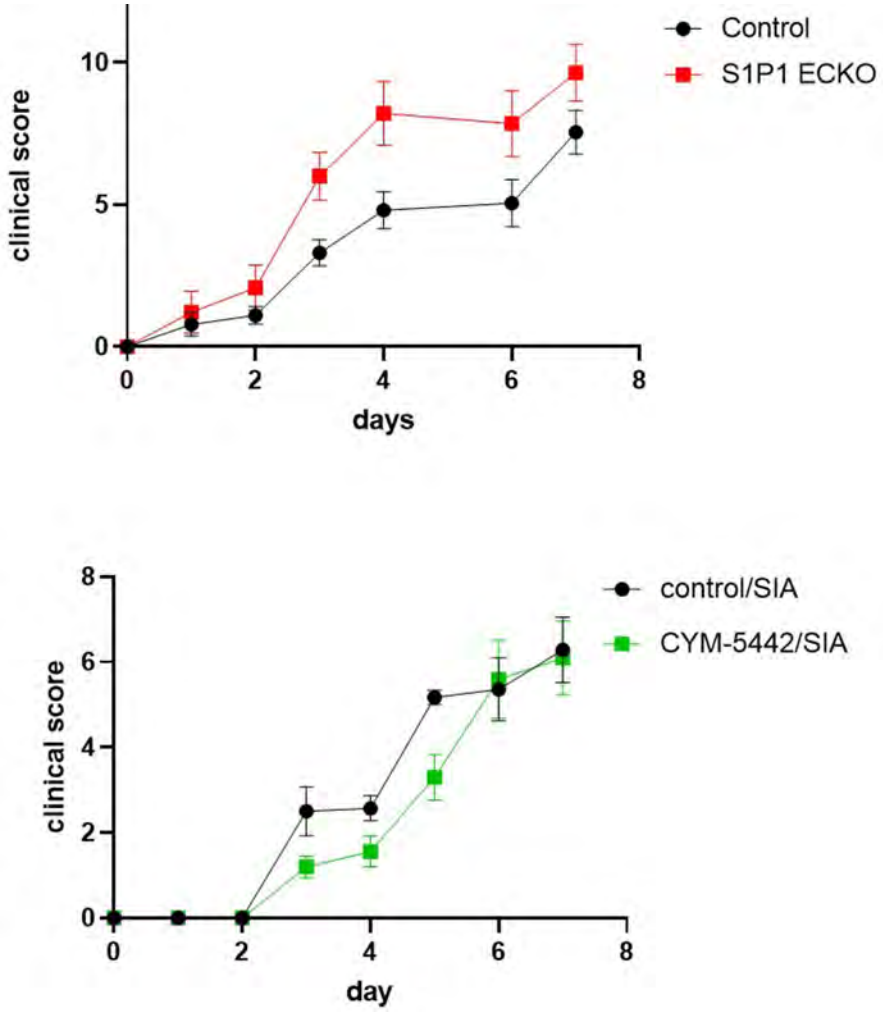

Figure 1. S1PR1 ECKO mice show increased inflammatory injury in response to SIA.
Figure 2. The S1PR1 agonist CYM-5442 delays SIA in WT mice.

in VE-cadherin shedding which was blocked by non-specific metalloprotease inhibitor marimastat (MM). Human RA single cell RNA seq data in ECs from the Accelerated Medicine Partnership (AMP) show that expression of EC S1PR1 and EC Sphingosine kinase 1, a key enzyme for the production of the endogenous ligand, S1P, are both statistically significantly lower than in OA controls.

Conclusion: Our data reveal that S1PR1 signaling restrains VE-cadherin shedding and maintains EC vascular barrier function and thereby attenuates arthritis. Augmenting EC S1PR1 signaling is a potential novel, non-immunosuppressive approach to treat inflammatory arthritis.

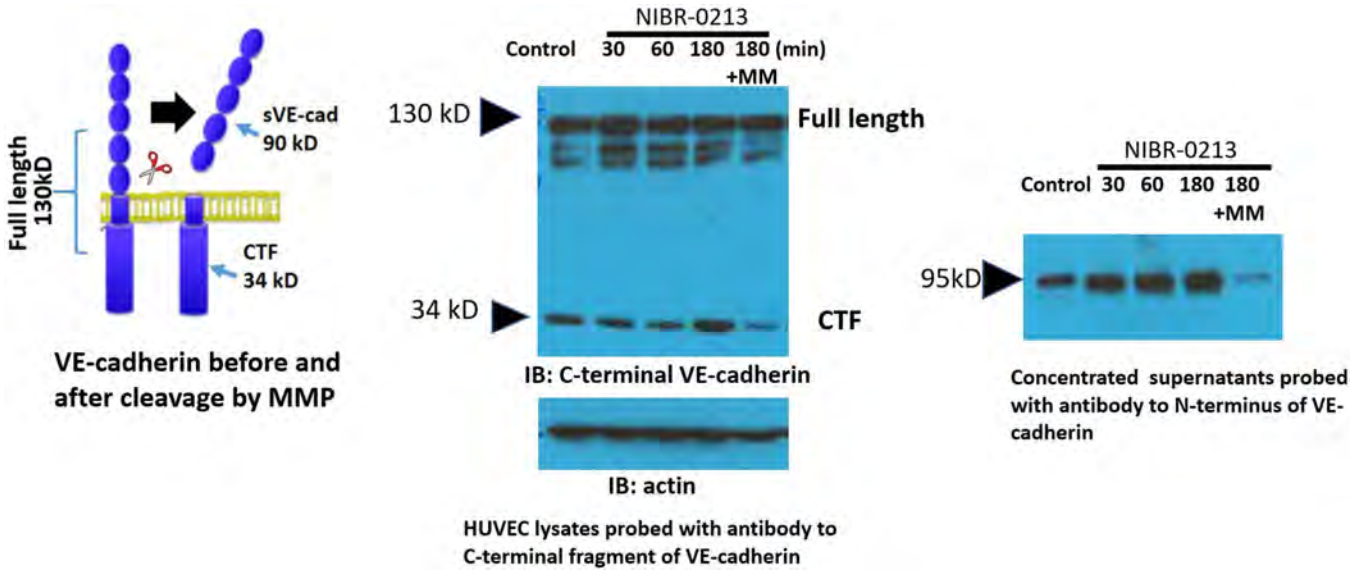

Figure 3. S1PR1 antagonist NIBR-0213 induces shedding of VE-cadherin in HUVEC that is blocked by the MMP inhibitor Marimastat (MM).

Disclosure: N. Burg, None; **R. Malpass**, None; **C. Blobel**, SciRhom, 1, 2, 5, 8, 10; **J. Salmon**, UCB, 1, 5, BMS, 1, Aurinia, 1.

Abstract Number: 1021

Organic Dust Exposure Induces Post-translational Protein Modifications and a HLA-DR4-dependent Pro-inflammatory Lung Phenotype in a Murine Model of Interstitial Lung Disease

Jill Poole[1], Ted Mikuls[1], Amy Nelson[1], Rohit Gaurav[1], Michael Duryee[1], Geoffrey Thiele[1], Bryant England[1] and **Dana Ascherman**[2], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: RA – Animal Models Poster (1014–1021)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Environmental and occupational exposures have been epidemiologically linked to the development of rheumatoid arthritis-associated interstitial lung disease (RA-ILD). Previous investigation and modeling have also suggested that airborne inflammatory biohazards can trigger post-translational modifications (PTMs) capable of stimulating immune response against neo-epitopes. For PTMs such as citrullination, this immune response is strongly associated with HLA-DRB1*0401 and other shared epitope alleles. To further elucidate mechanisms linking environmental insults, immunogenetic background, and PTM-targeted immune responses to the development of RA-ILD, we utilized the established organic dust extract (ODE) airway inflammatory exposure model in HLA-DR4 transgenic (DR4 TG) versus C57BL/6 wild type (WT) mice.

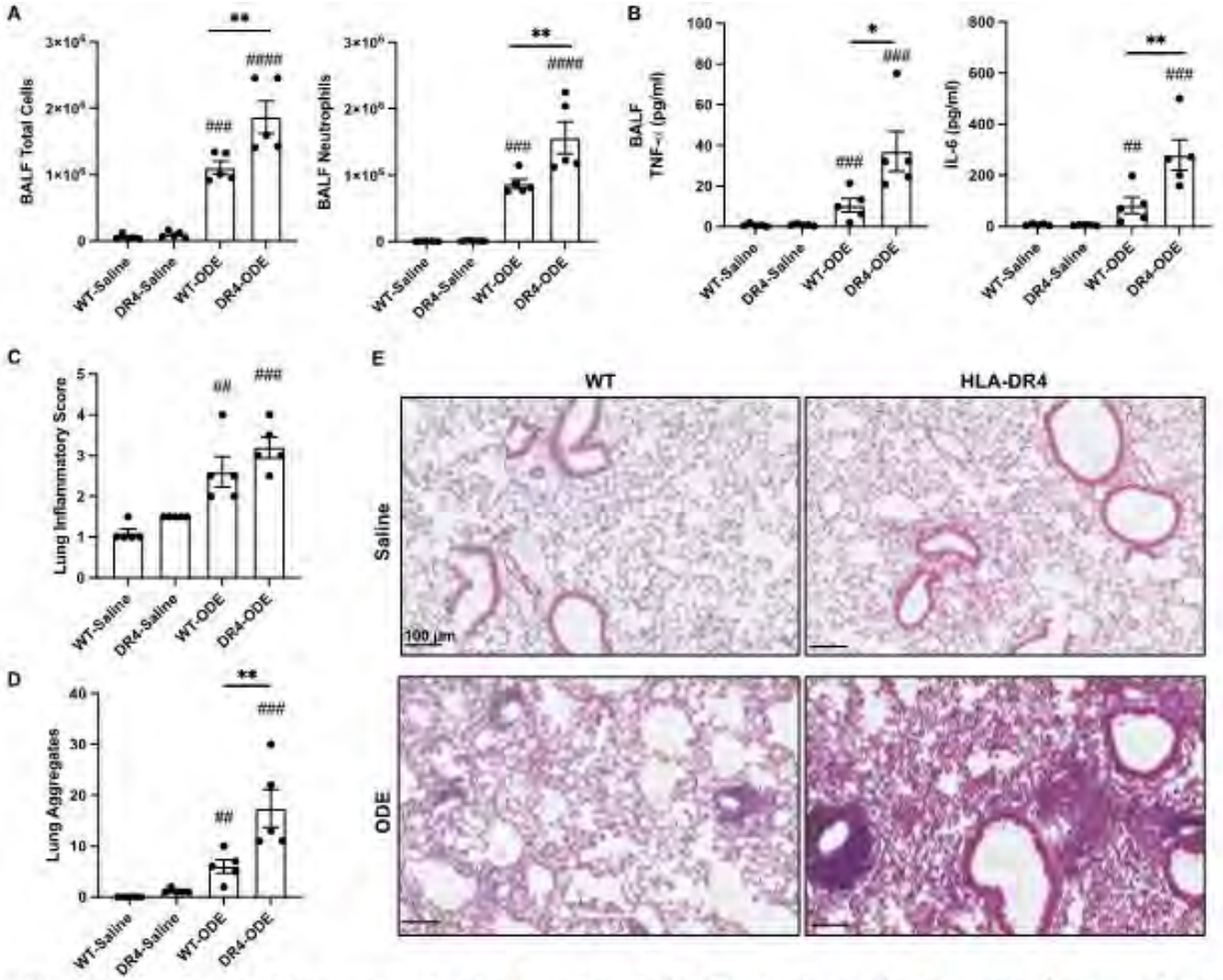

Figure 1. Repetitive organic dust extract (ODE)-induced airway inflammatory response is increased in HLA-DR4 transgenic mice. Scatter plots depict mean with standard error of (**A**) total cell and neutrophil influx and (**B**) levels of TNF-α and IL-6 in bronchoalveolar lavage fluid (BALF). (**C**) Semi-quantitative lung inflammatory score and (**D**) number of ectopic lung lymphoid aggregates are depicted; n=5 mice/group. (E) A representative H&E-stained lung section of one mouse per treatment group. While significant differences between ODE treatment groups and WT-saline are indicated by # symbols (##p<0.01, ###p<0.001, ####p<0.0001), differences between WT-ODE and DR4 TG-ODE are denoted by asterisks and lines (*p<0.05, **p<0.01).

Methods: WT and DR4 TG mice were exposed to intranasal inhalation of ODE (12.5%) versus sterile saline (n=5 mice/treatment group/strain) on a daily basis for 4 weeks. Following this 4 week treatment period, bronchoalveolar lavage fluid (BALF) was collected for cellular and cytokine analysis. Serum was also collected for ELISA-based assessment of autoantibodies targeting citrullinated and MAA (malondialdehyde-acetaldehyde)-modified substrate antigens. Lung tissue was subjected to immunofluorescence (IF) staining using antibodies recognizing peptidyl-

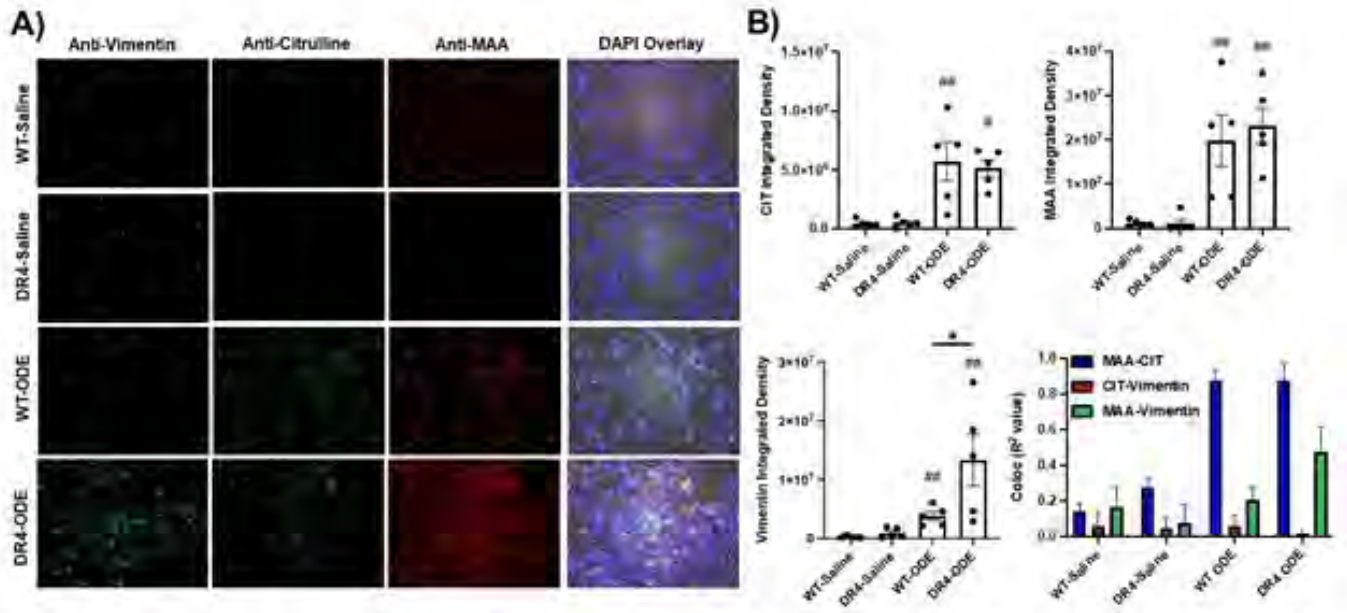

Figure 2. Post-translational protein modifications induced by repetitive ODE exposure. A) Representative images demonstrate immunofluorescent staining of lung tissue derived from WT and DR4 TG mice exposed to saline versus ODE using antibodies against vimentin, citrulline, and MAA. B) Corresponding grafts depict fluorescent signal intensity (image density) as well as the degree of co-localization (represented by R^2 values) for these proteins/PTMs. While significant differences between ODE treatment groups and WT saline are indicated by # symbols (#p<0.05, ##p<0.01), differences between WT-ODE and DR4 TG-ODE are denoted by asterisks and lines (*p<0.05).

citrulline (clone F95, EMDMillipore), MAA-modified proteins (rabbit polyclonal), and vimentin (Bioss). Quantitative scoring of fluorescence in combined regions of interest was compared using one-way ANOVA and Student's t-tests.

Results: ODE-induced airway cellular influx driven by neutrophils was significantly increased in DR4 TG versus WT mice, with corresponding increases in BALF levels of TNF-a and IL-6 ($p< 0.01$ for both cytokines, DR4 TG-ODE vs. WT-ODE) (**Figure 1A-B**). Lung histopathology demonstrated an increased number of ectopic lymphoid aggregates as well as overall lung inflammation in DR4 TG relative to WT mice after repetitive ODE exposure (**Figure 1C-E**). Corresponding IF staining of lung tissue showed that PTMs such as citrullination and MAA modification were strikingly enhanced in both DR4 TG-ODE and WT-ODE mice (**Figure 2**). Additional analysis revealed increased co-localization of vimentin and MAA staining that was most pronounced in DR4 TG mice (**Figure 2A-B**). Custom ELISAs demonstrated an increase in anti-MAA modified protein antibodies (including anti-MAA-vimentin antibodies) following ODE treatment that was amplified in DR4 TG mice ($p< 0.05$, **Figure 3**). Mice demonstrated no evidence of arthritis and had no detectable ACPA.

Conclusion: ODE-induced lung inflammation is more pronounced in DR4 TG relative to WT mice. This disease phenotype is accompanied by enhanced PTM formation and humoral immune responses targeting post-translationally-modified proteins. Overall, these results support a model in which environmental insults trigger PTM formation that,

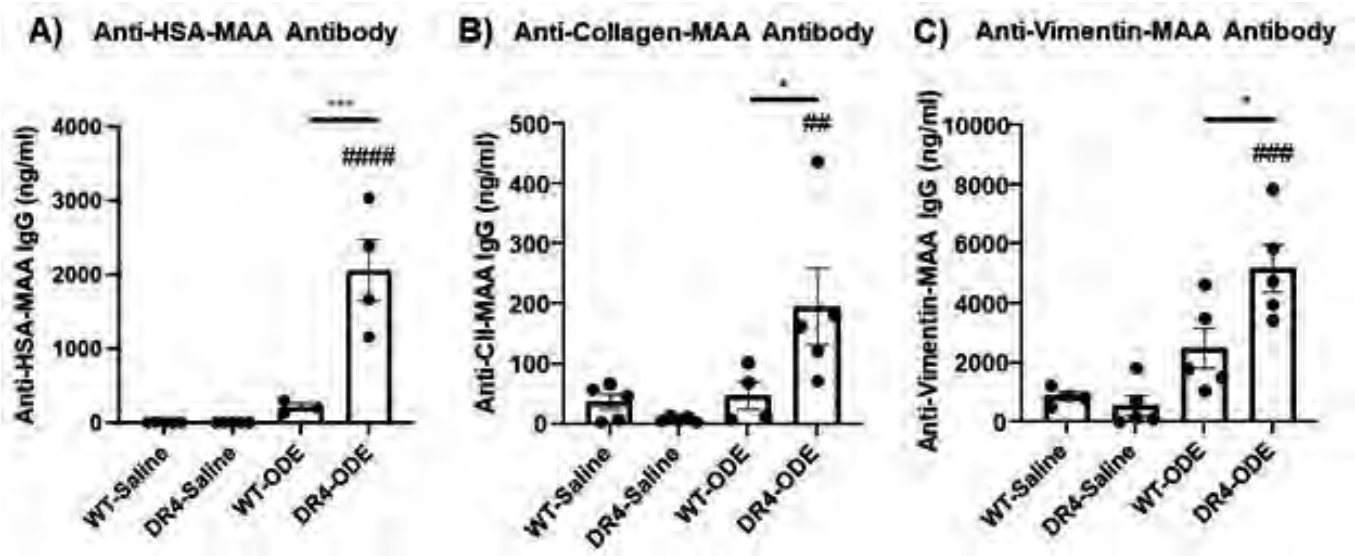

Figure 3. Anti-MAA modified protein antibody responses following repetitive ODE exposure. Panels A-C depict titers (ng/ml) of IgG anti-MAA modified protein antibodies detected in the serum of WT and DR4 mice repetitively exposed to inhaled ODE vs. Saline. While significant differences between ODE treatment groups and WT-saline are indicated by # symbols (##p<0.01, ###p<0.001, ####p<0.0001), differences between WT-ODE and DR4 TG-ODE are denoted by asterisks and lines (*p<0.05, ***p<0.001). HSA=human serum albumin.

in the selected immunogenetic background of HLA-DR4 TG mice, generates lung-centered, PTM-targeted immune responses and a tissue phenotype sharing immunopathological features with RA-ILD.

Disclosure: J. Poole, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **A. Nelson**, None; **R. Gaurav**, None; **M. Duryee**, None; **G. Thiele**, Regeneron, 6; **B. England**, Boehringer-Ingelheim, 2; **D. Ascherman**, None.

Abstract Number: 1022

Incidence of Antisynthetase Syndrome and Risk of Malignancy in a Population-based Cohort (1998-2019)

Caitrin Coffey[1], Li Wang[1], Stephanie Duong[1], Cassondra Hulshizer[1], Cynthia Crowson[2], Jay Ryu[1] and Floranne Ernste[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The antisynthetase syndrome (ASSD) is a distinct subgroup of the idiopathic inflammatory myopathies characterized by myositis, interstitial lung disease, inflammatory arthritis, Raynaud's phenomenon and an aminoacyl tRNA synthetase autoantibody. Population-based epidemiology studies are lacking. Our aims were to determine the incidence and prevalence of ASSD in a well-defined geographic area over a 22-year period, and to assess malignancy risk among incident ASSD patients within 3 years of diagnosis.

Methods: A retrospective, population-based cohort of adult patients with incident ASSD in a geographically well-defined area from Jan 1, 1998 to Dec 31, 2019 was assembled. Fulfillment of Solomon et al. criteria (1) and clinical data were collected by manual chart review via a validated medical records linkage system. Malignancy was defined by physician diagnosis in the medical record. Patients were followed until death, migration from the area, or December 31, 2019. Incidence rate was age- and sex-adjusted to the 2010 U.S. white population. Point prevalence rate was obtained on Jan 1, 2015.

Results: 13 patients with ASSD who fulfilled Solomon et al. criteria were identified in the 22-year study period. 7 (54%) were female, 13 (100%) Caucasian, median age 44.9 years (IQR: 41.9, 58.3) at time of meeting criteria.

At time of meeting criteria, 11 (85%) of patients had interstitial lung disease diagnosed by a physician. Of these 8 patients (73%) had an NSIP pattern. 11 patients (85%) had myositis: 6/12 (50%) had a positive EMG, 1 (8%) with a positive muscle MRI. 5 patients had muscle biopsy performed, and 100% demonstrated inflammatory myopathy. 13 (100%) had positive anti-nuclear antibody; 12 (92%) had positive Jo-1 antibody. A myositis-specific panel was positive in 1 out of 4 patients showing PL-7 antibody.

The age- and sex-adjusted incidence of ASSD was 0.56 (95% CI: 0.25-0.87) per 100,000 population. The age-adjusted incidence was 0.59 (95% CI: 0.15-1.03) per 100,000 for females, and 0.52 (95% CI: 0.10-0.94) per 100,000 for males. Incidence rate was highest in the 50-59 age group, at 1.01 per 100,000 population. Age- and sex- adjusted prevalence of ASSD on Jan 1, 2015 was 9.2 per 100,000 (95% CI: 3.4-15.0).

2/13 (15%) were diagnosed with a malignancy (Hodgkin's lymphoma, leiomyosarcoma) within the follow-up interval; none within 3 years of ASSD diagnosis. Mean time to malignancy diagnosis from ASSD criteria was 52 (range: 40-64) months.

At a median 11.9 (IQR: 7.0, 13.4) years of follow-up, 12/13 (92%) of patients were alive.

Conclusion: Antisynthetase syndrome is rare, with incidence of 0.56 per 100,000 population and prevalence of 9 per 100,000. Incidence appears similar in our cohort between males and females, differing from previous estimates of higher incidence in females, and highest in persons age 50-59. None of the patients in this cohort developed malignancy within 3 years of ASSD diagnosis.

(1) Solomon J, Swigris JJ, Brown KK. Myositis-related interstitial lung disease and antisynthetase syndrome. J Bras Pneumol. 2011;37(1):100-109.

Disclosure: C. Coffey, None; **L. Wang**, None; **S. Duong**, None; **C. Hulshizer**, None; **C. Crowson**, None; **J. Ryu**, None; **F. Ernste**, Octapharma, 5, The Myositis Association, 4.

Abstract Number: 1023

Racial and Ethnic Distribution of Rheumatic Diseases in Health Systems of the National Patient-Centered Clinical Research Network

William Nowell[1], Edward L. Barnes[2], Nupur Parikh[1], Shilpa Venkatachalam[1], Michael Kappelman[2], Jeffrey Curtis[3], Peter Merkel[4], Dianne Shaw[5], Kalen Young[5] and Michael George[4], [1]Global Healthy Living Foundation, Upper Nyack, NY, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, [4]University of Pennsylvania, Philadelphia, PA, [5]Vasculitis Foundation, Kansas City, MO

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Ensuring adequate representation of racial/ethnic minorities in research necessitates understanding the prevalence of rheumatic and musculoskeletal diseases in these populations. We sought to evaluate the relative prevalence of 8 rheumatic diseases across racial and ethnic groups within the National Patient-Centered Clinical Research Network (PCORnet), an integrated partnership of diverse health systems across the US that incorporate electronic health record data to answer clinical questions affecting patients' lives.

Methods: We queried electronic health records from 50 health systems of PCORnet from January 1, 2013 to December 31, 2018 and identified adult patients having ≥ 2 encounters separated by 90 days with diagnosis codes for rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), osteoporosis (OP), or several types of vasculitis (eosinophilic granulomatosis with polyangiitis (EGPA), granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), giant cell arteritis (GCA), and Takayasu's arteritis (TAK)). We restricted to patients with race/ethnicity data and excluded those reporting more than one race or other. To assess representativeness of PCORnet data we com-

Table 1. Racial/ethnic characteristics of patients with selected rheumatic diseases in PCORnet, 2013-2018

	2015 US Census Data		PCORnet		Rheumatoid Arthritis		Systemic Lupus Erythematosus		Osteoporosis		Granuloma-tosis with Polyangiitis		Eosinophilic Granuloma-tosis with Polyangiitis		Giant Cell Arteritis		Microscopic Polyangiitis		Takyasu's Arteritis	
Adult Patients	n=251,736,641		n=28,059,546		n=271,752		n=98,915		n=557,269		n=4,379		n=3,224		n=8,505		n=1,699		n=1,029	
	n	%	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]	n	%[a]
Race																				
American Indian or Alaska Native	4,617,759	2	96,440	0	1,174	0	381	0	1,156	0	0	0	0	0	0	0	0	0	0	0
Asian	15,644,372	6	641,178	3	4,202	2	2,302	3	13,275	3	46	1	45	2	43	1	46	2	32	4
Black or African American	33,081,436	13	4,175,087	18	36,070	15	28,881	34	36,042	8	227	6	338	12	691	9	227	9	96	12
Native Hawaiian or Pacific Islander	1,007,939	0	59,617	0	308	0	177	0	523	0	0	0	0	0	0	0	0	0	0	0
White	197,544,694	78	18,485,134	79	195,204	82	52,706	63	415,492	89	3,464	93	2,338	86	6,675	91	3,464	90	647	84
Hispanic Ethnicity																				
Hispanic	38,967,150	15	3,238,126	13	26,031	11	12,711	14	39,634	8	289	7	191	7	305	4	104	7	83	9
Non-Hispanic	212,769,491	85	21,725,620	87	216,066	89	75,030	86	448,491	92	3,687	93	2,738	93	7,280	96	1,437	93	822	91

[a] Column presenting percentages of patients with known race or ethnicity designation, with other/missing data removed for calculation of percentages.

Note: US Census data presented as annual estimates of the resident population by race alone or in combination with other races, as individuals may report more than one race. Data is presented in US Census estimates, with single race categories, instead of "other/more than one race". Hispanic origin is considered an ethnicity.

Table 2. Odds of diagnosis of rheumatic diseases among adult and pediatric patients in PCORnet, 2013-2018, stratified by race/ethnicity

	Rheumatoid Arthritis OR vs. all patients in PCORnet (95% CI)	Systemic Lupus Erythematosus OR vs. all patients in PCORnet (95% CI)	Osteoporosis OR vs. all patients in PCORnet (95% CI)	Granulomatosis with Polyangiitis OR vs. all patients in PCORnet (95% CI)	Eosinophilic Granulomatosis with Polyangiitis OR vs. all patients in PCORnet (95% CI)	Giant Cell Arteritis OR vs. all patients in PCORnet (95% CI)	Microscopic Polyangiitis OR vs. all patients in PCORnet (95% CI)	Takyasu's Arteritis OR vs. all patients in PCORnet (95% CI)
Adult Patients with rheumatic disease, n	**n=271,752**	**n=98,915**	**n=557,269**	**n=4,379**	**n=3,224**	**n=8,505**	**n=1,699**	**n=1,029**
American Indian or Alaska Native vs. White	1.15 (1.09 – 1.22)	1.39 (1.25 – 1.53)	0.53 (0.50 – 0.57)	n/a	n/a	n/a	n/a	n/a
Asian vs. White	0.62 (0.60 – 0.64)	1.26 (1.21 – 1.31)	0.92 (0.91 – 0.94)	0.59 (0.44 – 0.79)	0.56 (0.41 – 0.75)	0.19 (0.14 – 0.25)	0.38 (0.29 – 0.51)	1.43 (1.00 – 2.03)
Black or African American vs. White	0.82 (0.81 – 0.83)	2.43 (2.39 – 2.46)	0.38 (0.38 – 0.39)	0.64 (0.57 – 0.72)	0.55 (0.49 – 0.61)	0.46 (0.42 – 0.50)	0.29 (0.25 – 0.33)	0.66 (0.53 – 0.81)
Native Hawaiian or Pacific Islander vs. White	0.82 (0.81 – 0.83)	1.04 (0.90 – 1.21)	0.39 (0.36 – 0.43)	n/a	n/a	n/a	0.82 (0.81 – 0.83)	0.56 (0.52 – 0.61)
Hispanic vs. Non-Hispanic	0.81 (0.80 – 0.82)	1.14 (1.12 – 1.16)	0.59 (0.59 – 0.60)	0.53 (0.47 – 0.59)	0.47 (0.40 – 0.54)	0.28 (0.25 – 0.32)	0.49 (0.40 – 0.59)	0.68 (0.54 – 0.85)

Note: White used as reference group for all comparisons of race

pared racial/ethnic distributions in PCORnet to 2015 US census data. We then compared prevalence of rheumatic conditions across racial/ethnic groups to the PCORnet population and used univariable logistic regression to assess associations between race/ethnicity with different rheumatic diagnoses within PCORnet.

Results: A total of 28,059,546 adult PCORnet patients were included. Among the PCORnet patients with race/ethnicity data, 21% were non-white race and 13% Hispanic, similar to US Census data (Table 1). Compared to the wider PCORnet population, a higher percentage of adults with OP (89%) were white, while a higher percentage of patients with SLE (34%) were black/African-American (Table 1). African-American patients were more likely than white patients to have a diagnosis of SLE (OR 2.43, 95% CI 2.39-2.46, Table 2). American Indian/Alaska Native patients were more likely than white patients to have a diagnosis of RA (OR 1.15, 95% CI 1.09-1.22) and of SLE (OR 1.39, 95% CI 1.25-1.53), and Asian patients were more likely to have a diagnosis of Takayasu's Arteritis than were white patients (OR 1.43, 95% CI 1.00-2.03).

Conclusion: Certain rheumatic diseases disproportionately affect people of color in the US population, and PCORnet, a data resource potentially useful for studying the epidemiology and outcomes of rheumatic and musculoskeletal diseases, mirrored these expected differences. An improved understanding of the demographics and epidemiology of rheumatic disease among patients of different races and ethnicities presents an opportunity to enroll patients into research studies in a more inclusive and representative manner, and will provide an improved framework for studies of genetic and/or environmental differences, and of clinical outcomes.

Disclosure: W. Nowell, Global Healthy Living Foundation, 3, AbbVie, 5, Amgen, 5, Eli Lilly, 5; **E. Barnes**, AbbVie, Inc., 2, Takeda Pharmaceuticals, 1, Gilead, 1, Pfizer, 1, Target RWE, 2; **N. Parikh**, None; **S. Venkatachalam**, None; **M. Kappelman**, Abbvie, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Takeda, 2, 5, Pfizer, 2, 5; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **D. Shaw**, None; **K. Young**, None; **M. George**, None.

Abstract Number: 1024

Medical Care Seeking Is Frequent and Associated with Overuse of Low-Value Care for Low Back Pain in Portugal: Results from a Nationwide Population-Based Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Low back pain (LBP) constitutes an important cause of disability and morbidity in general population. Appropriate care for LBP includes non-pharmacological interventions based on a biopsychosocial framework of patient education and advice. World Health Organization recommends that excessively medical solutions should be avoided. This study aimed to estimate prevalence of medical care seeking and characterize diagnostic workup and management procedures for LBP in the adult Portuguese population. We also aim to compare the medical framework for LBP diagnostic and management between primary and secondary care.

Methods: The present study was conducted under the scope of EpiReumaPt (2011-2013), a population-based study including a representative sample of non-institutionalized Portuguese adults (n=10,661 habitants). A sample of individuals who self-reported history of medical care seeking for LBP within the previous 12 months (n=2,618) were considered. Patients' self-reported data collected through a structured questionnaire was explored to characterize medical care seeking, and diagnostic and management procedures for LBP. Prevalence was computed as weighted proportions, and inference statistics used to compare medical procedures between different levels of care.

Results: A prevalence of medical care seeking for LBP of 38.0% (95%IC, 35.9 to 40.1%) was found. Primary care in isolation (45.3%), multiple care (primary plus secondary care) (28.8%) and secondary care in isolation (25.9%) were the sought levels of care for LBP. Emergency departments (25.9%) and orthopedics (19.4%) were the secondary medical specialties most used. Several distinct structural-based diagnosis and specific/ serious underlying diseases were diagnosed by physicians, mainly supported by laboratory and imaging tests performed to 91.1% of individuals. Disc herniation (20.4%) and osteoarthritis (19.7%) were the most frequent diagnosis, while x-rays (63.7%), clinical history/ observation (44.4%), blood tests (38.2%), urinalysis (34.4%), and CT scans (32.4%) were the most frequent diagnostic procedures. Only 8.5% of individuals were evaluated based on a clinical history/ observation procedure in isolation. Lastly, 75.1% of individuals self-reported being treated for LBP by their physician, 80.4% with oral medication/ pills and 15.3% with injectables. The mean duration of pharmacological treatment was 104.24 (266.80) days. The use of structural-based diagnosis, laboratory and imaging tests, and pharmacological treatment were generally aggravated when secondary care, in isolation or complementarily with primary care, was considered compared with primary care in isolation ($p< 0.05$).

Conclusion: Our results show that medical seeking for LBP is frequent and is associated to overdiagnosis through a diagnostic label despite there being no reliable way of determining the pathoanatomical source of pain for the great majority of patients. Medical seeking is also associated with overuse of pharmacological treatment. Funding and delivery actions should be prioritized to assure appropriate care of LBP and reduce this low-value care overuse within local health systems.

Disclosure: L. Gomes, None; **E. Cruz**, None; **A. Henriques**, None; **J. Branco**, None; **H. Canhão**, None; **A. Rodrigues**, None.

Abstract Number: 1025

Survival of Patients with Idiopathic Inflammatory Myopathy in Slovenia

Alojzija Hocevar[1], Andrej Virscek[2], Monika Krosel[1], Matija Tomšič[3] and Ziga Rotar[3], [1]UKC Ljubjana, Ljubjana, Slovenia, [2]Statistical Office of the Republic of Slovenia, Ljubljana, Slovenia, [3]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of rare systemic diseases associated with significant morbidity and mortality. The aim of our study was to study for the first time the survival of IIM patients in Slovenia.

Methods: We included IIM patients diagnosed between January 2005 and December 2020, and followed at our secondary/tertiary rheumatology center. To evaluate mortality the censor date of April, 14 2021 was set. Kaplan–Meier analysis was used to analyze mortality. A standardized mortality ratio (SMR) was calculated using data of age and sex matched Slovenian population as the reference. Logistic regression was used to study prognostic risk factors in IIM.

Results: During the 16-year observation period, we identified 174 new IIM patients (121 (69.5%) females, median (IQR) age 63.5 (52.1-73.1) years, range 22 to 94 years). We diagnosed polymyositis, dermatomyositis, antisynthetase syndrome, other overlap IIM, necrotizing myopathy and inclusion body myositis in 15 (8.6%), 66 (37.9%), 47 (27.0%), 23 (13.2%), 21 (12.1%), and 2 (1.1%) patients, respectively.

Patients were followed for a median (IQR) 56.6 (20.8 – 107.0) months. During follow up 57/174 (32.8%) IIM patients deceased. The causes of death were cancer (18/57 (31.6%)), infections (13/57 (22.8%)), cardiovascular disease (14/57 (24.6%)), and active IIM (4/57 (5.3%)). In 9 patients the cause of death was unknown. One- and five-year survival rate was 86.7% and 71.6%, respectively. We found no significant sex related differences in the net survival estimates during the first five years of follow up (p=0.13). Figure 1 shows the survival curve of IIM patients and general population as a comparator according to Kaplan–Meier analysis. The mortality of patients with IIM patients was significantly higher compared to matched general population. In the table 1 the standardized mortality ratios in IIM patients are presented. In the first year following IIM diagnosis the SMT was almost 8-times higher compared to the

Table 1. The standardized mortality ratio of IIM patients

Time of FU	Observed deaths	Expected deaths	SMR (95% CI)	P value
1 year	23	2.9	7.95 (5.04-11.93)	<0.01
2 years	7	2.6	2.74 (1.1-5.64)	0.033
3 years	2	2.4	0.84 (0.09-3.02)	0.852
4 years	6	2.4	2.51 (0.92-5.46)	0.071
5 years	6	1.9	3.19 (1.17-6.95)	0.026

Legend: FU follow up; SMR Standardized mortality ratio; CI confidence interval

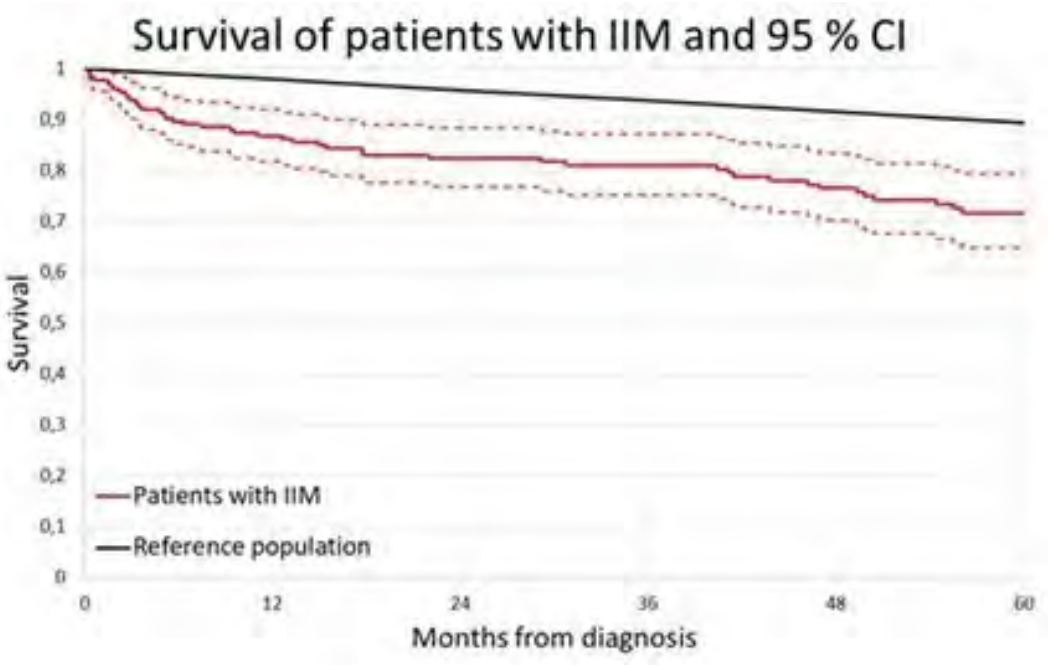

Figure 1. Survival curve according to Kaplan–Meier analysis in IIM.

general population (SMR 7.95 (95%CI 5.04-11.93). The risk remained higher also during the following four years. As prognostic risk factors emerged increasing age (OR 1.08 (95%CI 1.05-1.12); p< 0.001), antisynthetase syndrome (OR 2.61 (95%CI 1.09-6.28); p< 0.032), Raynaud phenomenon (OR 0.21 (95%CI 0.07-0.66); p< 0.007), and cancer (OR 6.21 (95%CI 2.29-16.85); p< 0.001).

Conclusion: The survival of patients with IIM patients was substantially worse compared to matched general population. Cancer was the leading cause of death in our IIM cohort.

Disclosure: A. Hocevar, None; **A. Virscek**, None; **M. Krosel**, None; **M. Tomšič**, None; **Z. Rotar**, None.

Abstract Number: 1026

Factors Impacting Likelihood of Discontinuing Immunosuppression in Adult Dermatomyositis: A Single-Center Study

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

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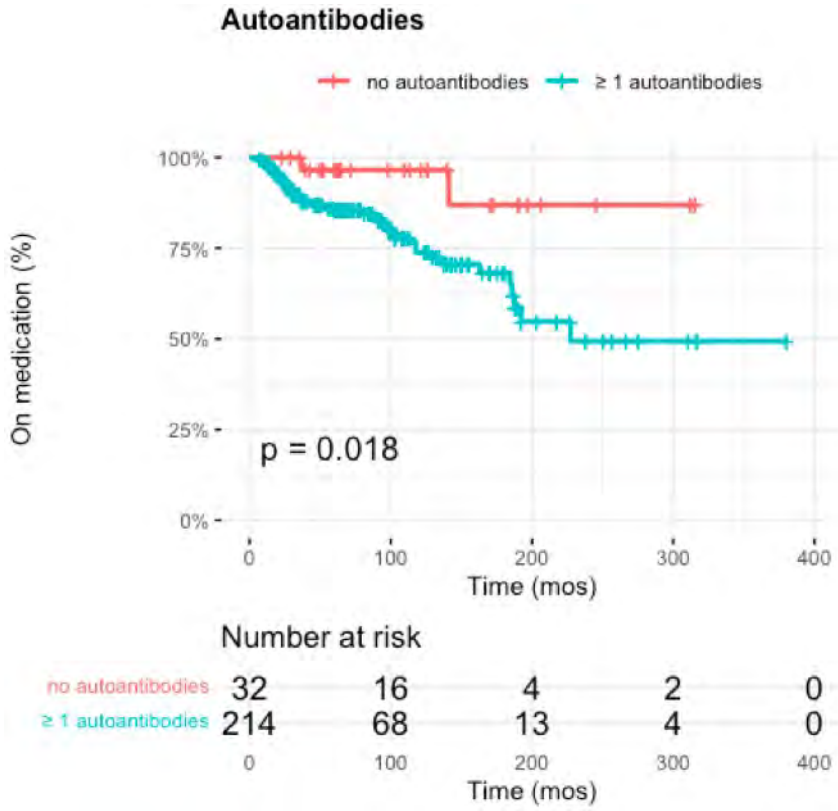
Session Time: 8:30AM–10:30AM

Background/Purpose: Dermatomyositis (DM) is a chronic idiopathic inflammatory myopathy with variable clinical course, but little is known regarding factors associated with remission of disease. We conducted a retrospective cohort study of 246 adult patients at Stanford to determine the rate of discontinuation of systemic immunosuppressive therapy as a proxy for clinical remission.



Factor associated with medication cessation in patients with dermatomyositis. Patients with at least one myositis specific autoantibody had a significantly shorter time to medication cessation.

Methods: Inclusion criteria included patients diagnosed with DM after 18 years of age and seen for at least one clinic visit at the Stanford multidisciplinary rheumatology/dermatology clinic between January 1, 2013 to December 31, 2020. Included patients were exposed to at least one immunosuppressive medication for at least 3 months. Patients not returning to clinic were contacted via phone or email to determine status of medication use. Survival analysis was performed using Kaplan-Meier curves and log rank analyses. Variables significantly associated with medication cessation or with p-value < 0.15 on univariable analysis were used to perform multivariate analysis using Cox proportional-hazards models.

Results: 47 patients (19%) discontinued medications over a median follow-up time from disease onset of approximately 7 years. The median time to medication cessation from disease onset was approximately 3 years. Log rank analysis indicated that patients with at least one DM-specific autoantibody ceased all medication use significantly earlier than those without (p= 0.018) (Figure 1). In particular, those with anti-MDA5 autoantibodies had significantly shorter time to medication cessation compared with the negative autoantibody group (p=0.03). Multivariable modeling was performed including demographic features, specific organ involvement, and autoantibody status as covariates. Clinically amyopathic patients were 2.6-fold (CI 1.29-5.27) more likely to discontinue medications than those with muscle disease. In addition, those with anti-MDA5, anti-NXP2, and anti-SAE1 antibodies had increased likelihood of medication cessation with hazard ratios of 11.4 (CI 2.42-53.7), 12.0 (CI 2.31-62.7), and 10.2 (CI 2.07-50.3) respectively when compared to patients with no DM-specific autoantibodies.

Conclusion: We found that almost 20% of our DM cohort were able to discontinue immunosuppressive medications over the course of several years. Those with clinically amyopathic disease, anti-MDA5, anti-NXP2, and anti-SAE1 antibodies were associated with a higher likelihood of medication cessation.

Disclosure: S. Cho, None; **L. Chung**, Boerhinger Ingelheim, 1, 5, 6, Genentech, 2, Eicos, 1, Reata, 1; **D. Fiorentino**, None.

Abstract Number: 1027

Epidemiology of Latent Tuberculosis Infection in Patients with Rheumatic Immune-mediated Diseases: Single University Study of 1117 Patients

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Background: Patients with rheumatologic immune-mediated diseases (R-IMID) with Latent tuberculosis infection (LTBI) requiring biologic therapy (BT) are at an increased risk of active tuberculosis (TB). Screening of LTBI with tuberculin skin test (TST) and/or Interferon (IFN)-γ release assays (IGRA) is recommended before starting of BT.

Purpose: In patients with R-IMID previously to BT our aim was to assess a) prevalence of LTBI, b) importance of using a booster test in negative TST and c) to compare TST with the IGRA test.

Methods: Cross-sectional single University Hospital study including all patients diagnosed with R-IMID who underwent a TST and/or IGRA in the last five years (2016-2020).

Table. Results of TST (+booster) and IGRA test

		IGRA				
		Positive	Negative	Indeterminate	Unavailable	Total
TST (+Booster)	Positive	89	142	45	48	324
	Negative	30	500	130	133	793
	Total	119	642	175	181	1117

* Cohen's kappa coefficient: 0.381

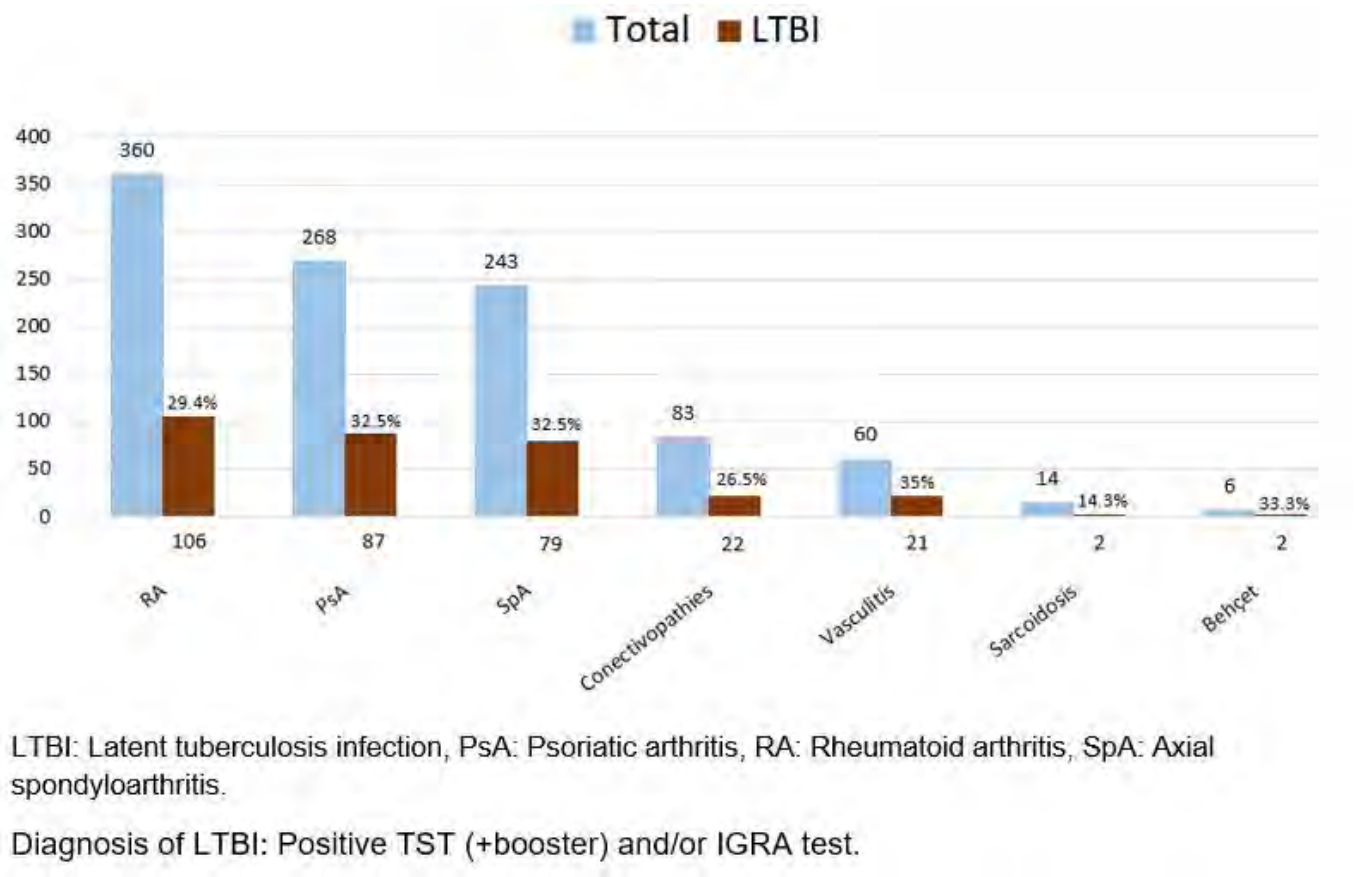

FIGURE. Prevalence of LTBI in different underlying R-IMID.

TST was performed by a subcutaneous injection of 0.1 ml of purified protein derivative (PPD) with a reading after 72 hours. TST was considered positive with an induration of more than 5 mm of diameter. If the first TST was negative, a new TST (Booster) was performed between 1 and 2 weeks after the first TST.

LTBI was diagnosed by a positive IGRA and/or TST and absence of active TB (Chest radiograph). Diagnosis with IGRA vs TST was compared (Cohen's kappa coefficient).

Results: We included 1117 patients (741 women/376 men), mean age 53±15 years with LTBI. Chest radiograph was normal in most of the patients, only 39 patients (3.5%) presented signs of previous TB infection, mostly granuloma. Total LTBI prevalence was 31.7% (354/1117). LTBI prevalence in different underlying R-IMID ranges from 35% in vasculitis up to 26.5% in conectivopathies (FIGURE).

Booster was positive in 66 patients (7.7%) out of 859 patients with a negative simple TST. Results of TST (+booster) and IGRA tests are shown in TABLE. TST (+booster) was positive in 187 patients (22.9%) out of 817 with a negative or indeterminate IGRA test. IGRA test was positive in 30 (3.8%) out of 793 patients with a negative TST (+booster). Cohen's Kappa coefficient between TST (+booster) and IGRA, was 0.381.

Conclusion: LTBI is frequent between patients with R-IMID. Booster after negative simple TST may be useful, since it can detect false negatives for LTBI. IGRA and TST(+booster) show a low grade of agreement. Therefore, performing both tests before BT may be recommendable.

Disclosure: D. Martinez-Lopez, None; **J. Osorio-Chávez**, None; **C. Álvarez-Reguera**, None; **V. Portilla**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1028

Knee Osteoarthritis and Mortality: The Osteoarthritic Initiative

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: A recent international individual participant data (IPD) meta-analysis (n=10,723) reported a 35-37% increased mortality risk among individuals with painful knees (no radiographic OA) and symptomatic radiographic knee OA (Leyland K et al 2021). We examined whether these results could be replicated in the Osteoarthritis (OAI) cohort (not included in the international IPD) using complete, long-term data on participant deaths from the OAI.

Methods: The OAI is a prospective cohort study investigating risk factors and biomarkers associated with the development and progression of knee OA. A total 4,796 adults age 45-79 years with or at high risk of developing knee OA were recruited at five US clinical sites. A National Death Index search was initiated to identify all deaths from 2004-2018. We used OAI baseline data on radiographic knee OA (K-L grade >=2), knee symptoms (pain on most days of a month in past year) and symptomatic OA (radiographic OA and symptoms in the same knee) to classify participants into four groups: symptomatic OA in one or both knees; no symptomatic OA but has radiographic OA in one or both knees; no radiographic OA but has symptoms in one or both knees; no radiographic OA or symptoms in either knee (referent group). Cox proportional hazards models were used to calculate hazard ratios (HR) for mortality, and their 95% confidence Intervals (CI), adjusted for covariates, in each group compared to the referent group. We excluded those who had a knee replacement at baseline (n=63) and missing data on covariates.

Table: Risk of Mortality by Baseline Radiographic Knee Osteoarthritis (OA) and Symptom Status

	Number of Deaths/N (%)	Model 1[a] Hazard ratio (95% CI)	Model 2[b] Hazard ratio (95% CI)
No Radiographic OA; no symptoms	117/1201 (9.7)	1.0 referent	1.0 referent
No Radiographic OA; with symptoms	64/784 (8.2)	1.13 (0.83, 1.53)	1.08 (0.79, 1.47)
Radiographic OA[c]; no symptoms	166/1243 (13.3)	0.92 (0.72, 1.16)	0.91 (0.72, 1.17)
Symptomatic radiographic OA	168/1348 (12.5)	1.28 (1.00, 1.62)	1.26 (0.99, 1.61)

[a] Model 1= age, sex, race, site

[b] Model 2=Model 1 + alcohol consumption, body mass index, cardiovascular disease, diabetes and smoking.

[c] K-L score $\geq$ 2 in either knee

Results: The mean age of the cohort at baseline was 61 years; 80% were white; 58% were women. Over an average follow-up of 9.2 years, 515 (11.3%) died. Of those with no radiographic OA and no symptoms, 9.7% died; no radiographic OA with symptoms, 8.2% died; radiographic OA and no symptoms, 13.4% died and radiographic OA and symptoms, 12.5% died, p< 0.0005, See Table. In multivariable adjusted models there was a marginally significant 28% increase in mortality (p=0.065) in participants with symptomatic knee OA at baseline. The association with mortality was stronger in those with symptomatic knee OA with a K-L grade 3 or 4 HR= 1.32 (1.00, 1.73) compared with those symptomatic OA with K-L score of 2, HR=1.17(0.85, 1.63). We also examined the association between frequent knee symptoms in either knee, adjusting for K-L grade; those with frequent knee pain had an increased risk of death, HR= 1.19 (0.99, 1.43).

Conclusion: These results with complete long-term follow-up data from the OAI cohort are consistent with those from the individual level meta-analysis showing increased mortality among those with symptomatic knee OA.

Disclosure: J. Cauley, None; **M. Nevitt**, None; **K. Sun**, None; **J. Maeda**, None; **C. Kwoh**, Lilly, 5, Abbvie, 5, Kolon Tissue Gene, 12, DSMB, Regeneron, 1, LG Chem, 1; **L. Sharma**, None; **R. Jackson**, None; **S. Rubin**, None; **M. Hochberg**, BriOri Biotech, 1, 2.

Abstract Number: 1029

Evaluation of the EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus in a Population-Based Registry

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The Manhattan Lupus Surveillance Program (MLSP) is a multi-racial/ethnic population-based registry with the primary goal to determine the prevalence and incidence of Systemic Lupus Erythematosus (SLE). In this study, we compare the three most commonly used classification criteria for SLE (1997 revised ACR, Systemic Lupus International Collaborating Clinics (SLICC) and the recent EULAR/ACR classification criteria) to identify cases that fulfilled only one of the classification criteria and explore each criteria set's unique cases. In addition, we used the EULAR/ACR criteria to determine the incidence and prevalence of SLE in Manhattan.

Methods: MLSP cases were identified from Manhattan-based hospitals and rheumatologists, and state population databases. For this analysis, SLE cases were defined as fulfilling 1) the 1997 ACR classification criteria, 2) the SLICC criteria or 3) EULAR/ACR classification criteria. We quantified the number of cases that uniquely associated with each classification criteria and the number that fulfilled all three classifications. Prevalence (2007) and incidence

Table 1. Explanations for patients meeting ACR criteria only

PATIENTS MEETING ACR CRITERIA ONLY (N=50)	Number	Example
REASONS FOR NOT MEETING EULAR/ACR CRITERIA:		
No ANA for entry:	N=35	
ANA unknown/not documented:	N=15	
Sufficient points to meet EULAR/ACR if ANA known/positive:	N=15 [points range 10-23, mean 15.1]	*e.g. malar, arthritis, leukopenia, proteinuria*
ANA documented negative:	N=20	
Sufficient points to meet EULAR/ACR if ANA was positive:	N=18 [points range 10-21, mean 14.38]	*e.g. malar, oral ulcer, arthritis, pericarditis*
Insufficient points to meet EULAR/ACR criteria if ANA was positive:	N=2 [points range 6-8, mean 7]	
Unique criteria:	N=2	*e.g. serositis, [lymphopenia], anti-cardiolipin, [non-RBC casts]*
Overlapping criteria within same domain:	N=1	*e.g. malar, photosensitivity, discoid, oral ulcer*
ANA <1:80, not sufficient for entry:	N=6	
Sufficient points to meet EULAR/ACR if ANA titer was sufficient:	N=4 [points range 10-12, mean 10.75]	*e.g. ANA, malar, photosensitivity, dsDNA*
Insufficient points to meet EULAR/ACR if ANA titer was sufficient:	N=2 [points range 5-6, mean 5.5]	*e.g. ANA, arthritis, [anti-cardiolipin], [lymphopenia]*
ANA positive/sufficient titer for entry, not meeting points threshold ≥ 10:	N=9 [points range 0-9, mean 6.1]	
Unique criteria	N=7	*e.g. ANA, [lymphopenia], malar, [photosensitivity]*
REASONS NOT MEETING SLICC CRITERIA:		
No immunologic criteria:	N=35	
ANA unknown/not documented:	N=15	
< 4 criteria met – unique criteria:	N=2	*e.g. photosensitivity, arthritis, pleuritis, [lymphopenia]*
< 4 criteria met – combined criteria:	N=1	*e.g.* ***malar, photosensitivity****, arthritis, lymphopenia*
ANA negative:	N=20	
< 4 criteria met:	N=2	*e.g. malar, oral ulcer, arthritis, [lymphopenia]*
Immunologic criteria met:	N=15	
ANA <1:80, < 4 criteria met:	N=6	
Lymphopenia not met by SLICC:	N=5	
APL not met by SLICC:	N=2	
Malar/photosensitivity combined in SLICC:	N=1	
ANA ≥ 1:80, <4 criteria met:	N=9	
Lymphopenia not met by SLICC:	N=3	
APL not met by SLICC:	N=3	
Renal not met by SLICC:	N=2	
Malar/photosensitivity combined in SLICC:	N=1	

Bolded font: overlapping criteria falling within the same domain
[Brackets]: criteria not part of, or does not meet, the specified classification system

rates (2007-2009) using the EULAR/ACR classification criteria and associated 95% confidence intervals (CI) were calculated using denominators obtained from the US Census data (revised 2000-2009 intercensal population files) for Manhattan.

Results: Overall 1,568 cases fulfilled at least one of the three classification criteria. Of those, 1008 (64.3%) cases fulfilled all three classification criteria, 166 (10.5%) fulfilled only the SLICC criteria, 50 (3.2%) fulfilled only the 1997 ACR criteria and 36 (2.3%) fulfilled the EULAR/ACR criteria with the remaining cases fulfilling a combination of two classification criteria. Cases that only met one of the classification criteria, and the reasons why they did not meet the other two classification criteria with example cases, are detailed in Tables 1-3. Based on the EULAR/ACR classification criteria, the age-adjusted overall prevalence and incidence rates of SLE in Manhattan were 59.8 (n=1,029, 95%CI:56.1- 63.6) and 4.9 (n=245, 95%CI 4.3-5.5) per 100,000 population. Prevalence was 9 times higher and incidence was 6.9 times higher among females compared to males. The age-adjusted prevalence per 100,000 was highest among non-Hispanic Black females (198.9), followed by Hispanic females (133.1), non-Hispanic Asian/Pacific Islander females (97.7) and non-Hispanic White females (59.8). Age-adjusted incidence rates per 100,000 were highest in non-Hispanic Black females (15.8), followed by Hispanic females (7.5), non-Hispanic Asian/Pacific Islander females (7.3) and non-Hispanic White females (6.3). Prevalence and incidence rates for males followed a similar pattern.

Conclusion: Applying the three commonly used classification systems to a multi-racial/ethnic population-based registry allowed for identifying unique cases of SLE who only fulfilled one classification system. The EULAR/ACR classification criteria revealed similar prevalence and incidence estimates and gender and racial/ethnic disparities to the previously published results from the MLSP using the 1997 revised ACR and SLICC classification criteria.

Table 2. Explanations for patients meeting SLICC criteria only

PATIENTS MEETING SLICC CRITERIA ONLY (N=166)	Number	Example
REASONS FOR NOT MEETING EULAR/ACR CRITERIA:		
No ANA for entry:	N=53	
ANA unknown/not documented:	N=28	
Sufficient points to meet EULAR/ACR if ANA known/positive:	N=24 [points range 12-29, mean 18.75]	*e.g. dsDNA, low complement, malar, Class IV LN, leukopenia*
Insufficient points to meet EULAR/ACR criteria if ANA known/positive:	N=3 [points range 7-8, mean 7.3]	*e.g. APL, arthritis, [neuropathy], [lymphopenia]*
Sufficient points to meet EULAR/ACR, but immunologic criteria only:	N=1	*e.g. dsDNA, Smith, APL, low C4, [urinary casts]*
ANA documented negative:	N=25	
Sufficient points to meet EULAR/ACR if ANA was positive:	N=21 [points range 10-21, mean 13.95]	*e.g. dsDNA, alopecia,* ***leukopenia, thrombocytopenia***
Insufficient points to meet EULAR/ACR if ANA was positive:	N=4 [points range 7-9, mean 8]	
Overlapping criteria:	N=3	*e.g. low complement, oral ulcer, [neuropathy],* ***leukopenia, thrombocytopenia***
Unique Criteria:	N=2	*e.g. low complement, [photosensitivity], leukopenia [lymphopenia], thrombocytopenia, [DAT]*
ANA <1:80, not sufficient for entry:	N=17	
Sufficient points to meet EULAR/ACR if ANA titer was sufficient:	N=4 [points range 10-12, mean 10.75]	
Overlapping criteria within same domain:	N=2	*e.g. ANA (1:40), Sm, alopecia,* ***leukopenia****, [lymphopenia],* ***thrombocytopenia***
Unique criteria:	N=1	*e.g. ANA (1:40), arthritis, [peripheral neuropathy], leukopenia, [lymphopenia]*
Insufficient points to meet EULAR/ACR criteria if ANA titer was sufficient:	N=13 [points range 0-9, mean 6.7]	
Overlapping criteria within same domain:	N=7	*e.g. ANA (1:40),* ***malar, discoid, alopecia***
Unique criteria:	N=6	*e.g. ANA (1:40), [photosensitivity], [neuropathy], [lymphopenia]*
ANA positive, sufficient titer, but not meeting point threshold of ≥ 10:	N=95 [points range 2-9, mean 6.9]	
Overlapping criteria:	N=30	*e.g. ANA, discoid,* ***leukopenia, thrombocytopenia***
Unique criteria:	N=35	*e.g. ANA, low C3, [panniculitis], alopecia, leukopenia, [lymphopenia]*
ANA positive, sufficient points, but immunologic criteria only:	N=1	*e.g. ANA, DNA, low complement, [RBC casts]*
REASONS NOT MEETING ACR CRITERIA:		
3 criteria only:	N=102	
Low complement - not part of ACR:	N=40	*e.g. [low complement], arthritis, pericarditis, [lymphopenia]*
Alopecia - not part of ACR:	N=37	*e.g. ANA, malar, [alopecia], leukopenia, [lymphopenia]*
Unique NPSLE criteria not part of ACR:	N=24	*e.g. ANA, arthritis, [peripheral neuropathy], leukopenia*
Unique cutaneous criteria not part of ACR:	N=0	
Lymphopenia not met by ACR:	N=10	*e.g. ANA, APL, arthritis, [lymphopenia – NON-ACR]*
≤ 2 criteria only:	N=64	
Low complement - not part of ACR:	N=34	*e.g. ANA, [low C3],* ***lymphopenia, thrombocytopenia***
Alopecia - not part of ACR:	N=30	*e.g. dsDNA, [alopecia],* ***leukopenia, thrombocytopenia***
Unique NPSLE criteria not part of ACR:	N=22	*e.g. [low complement], photosensitivity, arthritis, [peripheral neuropathy]*
Unique cutaneous criteria not part of ACR:	N=3	*e.g. ANA, [bullous lesions], oral ulcer, [alopecia], [lymphopenia]*
Lymphopenia not met by ACR:	N=7	*e.g. ANA, malar, [neuropathy], [lymphopenia]*

Bolded font: overlapping criteria falling within the same domain; [Brackets]: criteria not part of, or does not meet, the specified classification system

Table 3. Explanations for patients meeting EULAR/ACR criteria only

PATIENTS MEETING EULAR/ACR CRITERIA ONLY (N=34)	Number	Example
REASONS FOR NOT MEETING SLICC CRITERIA:		
3 criteria only (ANA + 2 additional criteria):	N=34	*e.g. ANA, dsDNA, arthritis*
Lymphopenia not met by SLICC:	N=3	*e.g. ANA, arthritis, low complement, [lymphopenia]*
REASONS FOR NOT MEETING ACR CRITERIA:		
3 criteria only (ANA + 2 additional criteria):	N=31	*e.g. ANA, dsDNA, arthritis*
Low complement not part of ACR:	N=2	*e.g. ANA, arthritis, [low complement], lymphopenia*
Overlapping criteria within same domain:	N=1	*e.g. ANA, arthritis,* ***lymphopenia, thrombocytopenia***
2 criteria only (ANA + 1 additional criteria):	N=3	
Lymphopenia not met by ACR (only documented once):	N=2	*e.g. ANA, arthritis, [low complement], [lymphopenia]*

Bolded font: overlapping criteria falling within the same domain
[Brackets]: criteria not part of, or does not meet, the specified classification system

Disclosure: A. Guttmann, None; **B. Denvir**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **M. Aringer**, Boehringer Ingelheim, 1, 6, Roche, 1, 6; **H. Belmont**, Alexion, 6; **S. Sahl**, None; **J. Salmon**, UCB, 1, 5, BMS, 1, Aurinia, 1; **A. Askanase**, GSK, 2, 5, AstraZeneca, 1, 5, Amgen, 1, Aurinia, 2, Abbvie, 1, Pfizer, 5, Eli Lilly, 5, Idorsia, 5; **J. Bathon**, None; **L. Geraldino**, None; **Y. Ali**, None; **E. Ginzler**, None; **C. Putterman**, equllium, 2, 5, Progentec, 2, Kidneycure, 2; **C. Gordon**, Centre for Disease Control, 2, 6, Astra-Zeneca, 2, 6, MGP, 2, 6, Sanofi, 2, 6, UCB, 2, UCB, 5, 6; **C. Helmick**, None; **H. Parton**, None; **P. Izmirly**, Momenta/Janssen, 1.

Abstract Number: 1030

Critical Illness in Modern Rheumatology: Analysis of Admissions to Australian and New Zealand ICUs

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

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Background/Purpose: Patients with systemic rheumatic diseases (SRD) have an increased risk of admission to the Intensive Care Unit (ICU) relative to the general population, secondary to SRD chronicity, expanding options for concomitant immunosuppression, co-morbidities, deconditioning, and multi-organ disease. Despite this, there is paucity of data within this population regarding outcomes of ICU admission over time, and whether subgroups of patients with SRD exhibit differential outcomes. This study aims to further the understanding of SRD in the context of critical

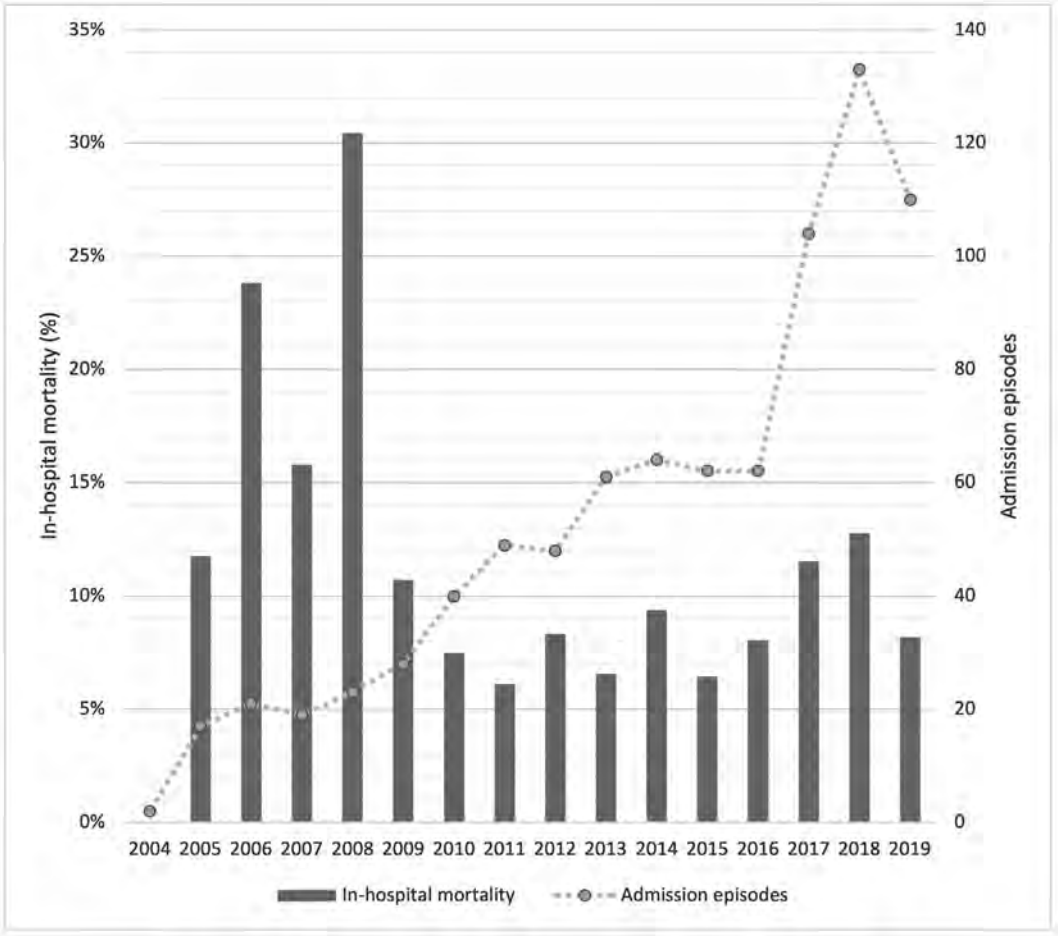

Figure 1. Admission episodes and in-hospital mortality over time.

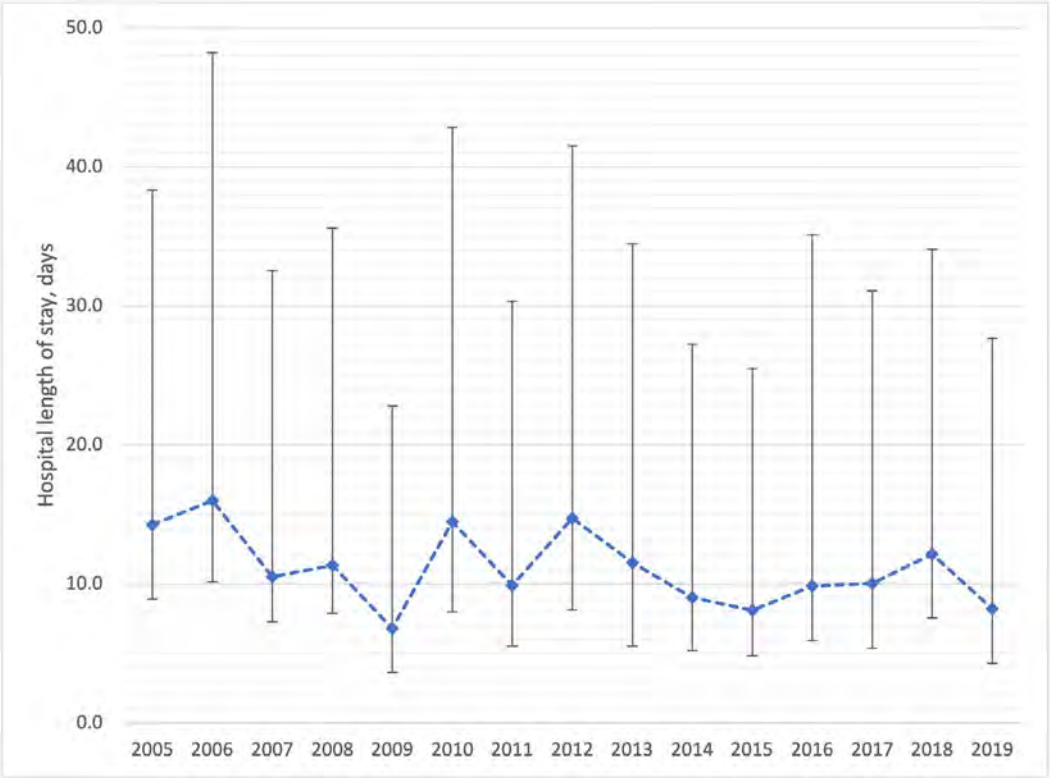

Figure 2. Median (IQR) length of hospital stay by year.

illness by examining a population-based registry, the Australia New Zealand Intensive Care Society Adult Patient Database (ANZICS-APD).

Methods: The ANZICS-APD mandates disease-category based reporting across all ICUs in ANZ, including mortality and length of stay both within ICU and hospital. Retrospective data (2004-2019) from ICU admissions across hospitals in Australia and New Zealand was analysed. Eligible records were those where the primary reason for admission was SRD. These were identified through the use of database specific codes and excluded sepsis, rhabdomyolysis and viral myositis. We sought to analyse the trends over time, mortality and length of stay across SRDs. Severity of critical illness on ICU admission was measured by the Australian and New Zealand Risk of Death (ANZROD) score.

Results: 1,478 admission episodes (52% females) were included, from 155 Australian sites (95%) and 16 New Zealand sites (5%). Reasons for admission were musculoskeletal/skin (42%), musculoskeletal medical (38%), vasculitis (7%), connective tissue disease (5%), SLE (3%), scleroderma (2%) and rheumatoid arthritis (RA; < 2%). Predicted mortalities for each diagnosis (derived from the ANZROD scoring system) were: connective tissue disease 17%, vasculitis 17%, SLE 15%, musculoskeletal-medical 10%, scleroderma 10%, musculoskeletal-skin disease 9.3% and RA 5.2%. Considering temporal changes, annual ICU admissions with SRD increased in a linear fashion from 2004 to 2019, consistent with growth in the size of the database over time. Change in hospital mortality over time was not statistically significant and remained stable or decreased over this period (Figure 1). Median length of hospital stay did not demonstrate a temporal trend (Figure 2). In-hospital mortality by SRD category was connective tissue disease (17%), vasculitis (10%), SLE (9%), musculoskeletal-medical (9%), scleroderma (20%), musculoskeletal/skin (7%) and RA (4%).

Conclusion: Analysis of a large dataset from Australian and New Zealand ICUs reveals that: 1) There has been a large increase in the number of patients with SRD admitted to ICUs each year since 2004, a change reflected in the ANZICS-APD more broadly 2) In-hospital mortality in this cohort remained stable or decreased over time; 3) No tem-

poral trend with respect to length of ICU stay is apparent; 4) Patients with connective tissue disease, vasculitis and SLE are sicker on presentation relative to other SRD diagnoses; and 5) In-hospital mortality is greatest in patients with scleroderma or connective tissue disease.

Disclosure: R. Lambert, None; **S. Bihari**, None; **M. Wechalekar**, Janssen Research and Development, Philadelphia, USA, 5; **D. Pilcher**, None; **E. Pontifex**, None.

Abstract Number: 1031

Clinical and Humanistic Burden of Dermatomyositis and Polymyositis in the United States: A Systematic Literature Review

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SESSION INFORMATION
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Background/Purpose: Dermatomyositis (DM) and polymyositis (PM) are rare heterogenous systemic autoimmune disorders of the skin, muscles, and other organs that may have a devastating impact on patients and care partners life. The objective of this study was to systematically review and synthesize evidence on clinical and humanistic burden and unmet needs in the management of DM/PM.

Methods: A systematic literature review (SLR) was conducted in MEDLINE and Embase databases to identify studies in children and adults with DM/PM, published in the English language between 2011–2021. Only primary studies of any design enrolling 10 or more patients were included, irrespective of country or region. The current abstract summarizes preliminary SLR results on the clinical and humanistic burden of DM/PM in the United States (US).

Results: A total of 3624 records were retrieved from medical databases, 393 records underwent full-text review, and 210 were included in data abstraction. An additional 8 papers were included from searching reference lists of identified studies. There were 32 US studies that reported on the natural history of the disease and/or comorbidities (n=27) and quality of life (QoL) of patients or caregivers (n=8). There were 24 retrospective and 8 prospective studies, with a sample size ranging from 17 to more than 160,000 patients. Patients with DM/PM had an increased risk of comorbidities, including various types of infections (19–42%), malignancies (6–17%) and cardiovascular-related disorders (1–20%), compared to unmatched or matched non-DM/PM controls. Concerns about malignancy risk contributed to increased depression and anxiety. Remission occurred in only 33–38% of adult DM patients. About 26–50% of patients with juvenile DM/PM (JDM/JPM) often had a chronic course of disease characterized by persistently active disease, and a 36% rate of active disease 10-years post-diagnosis. Diseases flares were reported by 73% of patients within the past year and their increased frequency trended with a longer mean duration of illness ($p< 0.001$). Disease flares significantly contributed to poorer QoL due to increased disability and pain ($p< 0.001$). Adult patients with DM, compared to other dermatologic disorders such as cutaneous T-cell lymphoma and non-melanoma skin cancer/actinic keratoses, had a significantly worse Skindex-29 emotional subscore, worse SF-36 role-emotional, physical, and social functioning subscore, and greater fatigue compared to healthy controls ($p< 0.05$). DM had a detrimental

impact on QoL which correlated with skin disease activity. JDM affected the entire family with difficulties in family functioning, communication problems, sibling distress, and increased number of conflicts. Parents of patients with JDM reported higher levels of worry, anger, depression, and reduced physical functioning, than parents of children with chronic diseases.

Conclusion: DM/PM are associated with multiple comorbidities affecting multiple QoL domains, especially in the physical and social/emotional realm. Despite various therapies available, a notable proportion of patients seem not to achieve sustainable remission indicating a high residual unmet need.

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Abstract Number: 1032

Causes of Death Among Populations with Systemic Lupus Erythematosus by Race and Ethnicity

Tiffany Taylor[1], Christine Anastasiou[1], Stephanie Rush[1], Laura Trupin[2], Maria Dall'Era[3], Patricia Katz[1], Kamil Barbour[4], Jinoos Yazdany[1] and Milena Gianfrancesco[1], [1]University of California San Francisco, San Francisco, CA, [2]UC San Francisco, San Francisco, CA, [3]University of California San Francisco, Corte Madera, CA, [4]Centers for Disease Control, Atlanta, GA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease with manifestations that vary widely in severity. Data indicate that minority populations are at higher risk of developing SLE and have more severe outcomes, including mortality. However, whether specific causes of death vary by race and ethnicity has largely been unexplored, particularly for Asians and Hispanics.

Methods: The California Lupus Surveillance Project identified potential SLE cases using community rheumatology and nephrology clinics, community hospitals, and integrated healthcare systems among individuals who were residents of San Francisco County, CA during January 1, 2007 – December 31, 2009. SLE cases were defined using American College of Rheumatology Classification Criteria (≥4 of the 11 revised criteria as defined in 1982 and updated in 1997) or two alternative definitions: SLE diagnosed by the patient's treating rheumatologist plus 3 ACR criteria; or lupus-related kidney disease (World Health Organization class II-VI lupus nephritis upon biopsy or documented record of SLE diagnosis and dialysis or renal transplantation). Cases were matched to the 2007-2017 National Death Index (NDI) data, which included the underlying cause of death for each individual. Chi-squared tests were used to examine differences in underlying cause of death by race (white, Black, Asian), ethnicity (Hispanic, non-Hispanic), and sex (female, male). Age-standardized mortality ratios (SMRs) between SLE patients and the general San Francisco county population were calculated for the leading cause of death, and estimated observed versus expected deaths by sex, race, and Hispanic/Latino ethnicity.

Results: During the study time period, 812 deaths related to SLE were identified. Cardiovascular disease (CVD) was the leading cause of death among SLE patients overall (33%), and across all racial and ethnic groups. Other top

Table 1. Standardized mortality ratios of cardiovascular disease (CVD) in SLE patients compared to the general San Francisco county population, age-standardized, 2007-2017

		CVD as Underlying Cause of Death		
	Total SLE Population #	Observed CVD Deaths in CLSP	Expected CVD Deaths*	SMR (95% CI)
Overall	809	45	12.4	3.63 (2.65, 4.86)
Race				
White	311	13	5.3	2.43 (1.29, 4.16)
Black	164	16	5.5	2.89 (1.65, 4.70)
Asian	294	14	3.7	3.83 (2.09, 6.42)
Ethnicity				
Hispanic	123	7	1.1	6.45 (2.59, 13.29)
Non-Hispanic	604	36	10.6	3.39 (2.37, 4.69)
Sex				
Female	728	40	8.6	4.65 (3.32, 6.34)
Male	81	5	1.4	3.48 (1.13, 8.12)

SMR= Age-standardized mortality ratio
#Three patients excluded from SMR analyses, as rates from CDC Wonder were not available for ages < 15 years.
*Expected rate calculated from age-specific crude mortality rates from cardiovascular disease in San Francisco county

causes included rheumatic disease (18%) and hematological/oncological conditions (18%) overall, and across all racial groups. Overall, CVD as the underlying cause of death was over three times higher among SLE cases than in the general population of San Francisco County (SMR=3.63) (Table 1). CVD deaths for those with SLE were nearly four times higher for Asians and over six times higher for Hispanic/Latinos. CVD deaths were also elevated for females (SMR=4.7) and males (SMR=3.5) with SLE compared with their non-SLE counterparts.

Conclusion: These findings indicate that CVD is the leading underlying cause of death among SLE patients across various racial and ethnic groups, and that SLE patients experience a disproportionate burden of CVD mortality compared with the general population.

Disclosure: T. Taylor, None; **C. Anastasiou**, None; **S. Rush**, None; **L. Trupin**, None; **M. Dall'Era**, AstraZeneca, 2, Aurinia, 2, Biogen, 2, Bristol Myers Squibb, 2, GlaxoSmithKline, 2, Pfizer, 2; **P. Katz**, None; **K. Barbour**, None; **J. Yazdany**, Pfizer, 2, Astra Zeneca, 5, Eli Lilly, 2, University of California, San Francisco, 3; **M. Gianfrancesco**, None.

Abstract Number: 1033

Physical Inactivity Among Adults with Specific Chronic Conditions, by Arthritis Status, 49 States and District of Columbia, Behavioral Risk Factor Surveillance System, 2019

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Arthritis is associated with reduced physical activity (PA). PA can improve functional status, brain health, and weight management, reduce pain, prevent chronic disease, falls, and premature mortality, and prevent or delay disability. Arthritis is frequently comorbid with numerous chronic conditions for which PA is recommended for disease management, but information on physical activity among adults with arthritis across a range of comorbid chronic conditions is limited. We examined physical inactivity prevalence, stratified by arthritis status, among adults with 9 chronic conditions for which clinical guidelines recommend physical activity for disease management.

Methods: We analyzed 2019 Behavioral Risk Factor Surveillance System data from 49 states and District of Columbia for adults ≥18 years (n=380,418). Physical inactivity was no leisure-time PA in the past month. Arthritis was "yes" to "Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis,

Table 1. Distribution (weighted(1) percentages(2)) of sociodemographic characteristics for adults aged ≥18 years(3), by arthritis(4) status, 49 states and District of Columbia(5), Behavioral Risk Factor Surveillance System, 2019

	Arthritis (n= 130,259)		No Arthritis (n= 250,159)	
	n[6]	% (95% CI)	n[6]	% (95% CI)
Sociodemographic Characteristics				
Age (years)				
18-44	11,058	15.9 (15.4–16.4)	96,191	56.3 (56.0–56.7)
45-64	45,861	40.9 (40.4–41.5)	84,433	29.2 (28.8–29.5)
≥65	73,340	43.2 (42.6–43.7)	69,535	14.5 (14.3–14.7)
Sex				
Men	49,771	41.0 (40.4–41.5)	123,311	51.4 (51.0–51.8)
Women	80,488	59.0 (58.5–59.6)	126,848	48.6 (48.2–49.0)
Race/Hispanic Ethnicity				
White, non-Hispanic	106,182	73.9 (73.3–74.5)	185,533	60.2 (59.8–60.6)
Black, non-Hispanic	9,647	11.3 (10.9–11.7)	18,578	11.6 (11.3–11.8)
Hispanic	4,961	9.1 (8.7–9.6)	23,448	19.0 (18.6–19.4)
Asian, non-Hispanic	1,096	2.2 (2.0–2.5)	6,575	6.2 (5.9–6.5)
American Indian/Alaska Native, non-Hispanic	2,150	1.3 (1.2–1.5)	3,871	0.9 (0.9–1.0)
Other/Multiple race, non-Hispanic	3,784	2.1 (2.0–2.3)	7,964	2.1 (2.0–2.2)
Education				
Less than high school graduate	10,210	13.6 (13.2–14.1)	16,011	12.1 (11.8–12.4)
High school or equivalent	37,325	29.0 (28.5–29.5)	63,542	27.2 (26.8–27.5)
Technical school/Some college	39,097	33.3 (32.8–33.8)	67,962	30.6 (30.2–30.9)
College degree or higher	43,352	24.0 (23.6–24.4)	101,995	30.1 (29.8–30.5)
Employment status				
Employed/Self-employed	40,917	37.3 (36.7–37.8)	147,359	64.7 (64.3–65.0)
Unemployed	4,270	4.4 (4.1–4.6)	9,947	5.2 (5.1–5.4)
Retired	60,860	37.2 (36.7–37.7)	59,081	13.0 (12.8–13.2)
Unable to work/Disabled	17,342	15.4 (15.0–15.8)	10,134	3.9 (3.8–4.1)
Other	6,299	5.7 (5.5–6.0)	21,826	13.1 (12.9–13.4)

CI: confidence interval

[1] Due to BRFSS's complex sampling design, sampling weights, derived using iterative proportional fitting (raking), were applied to make estimates representative of each state.

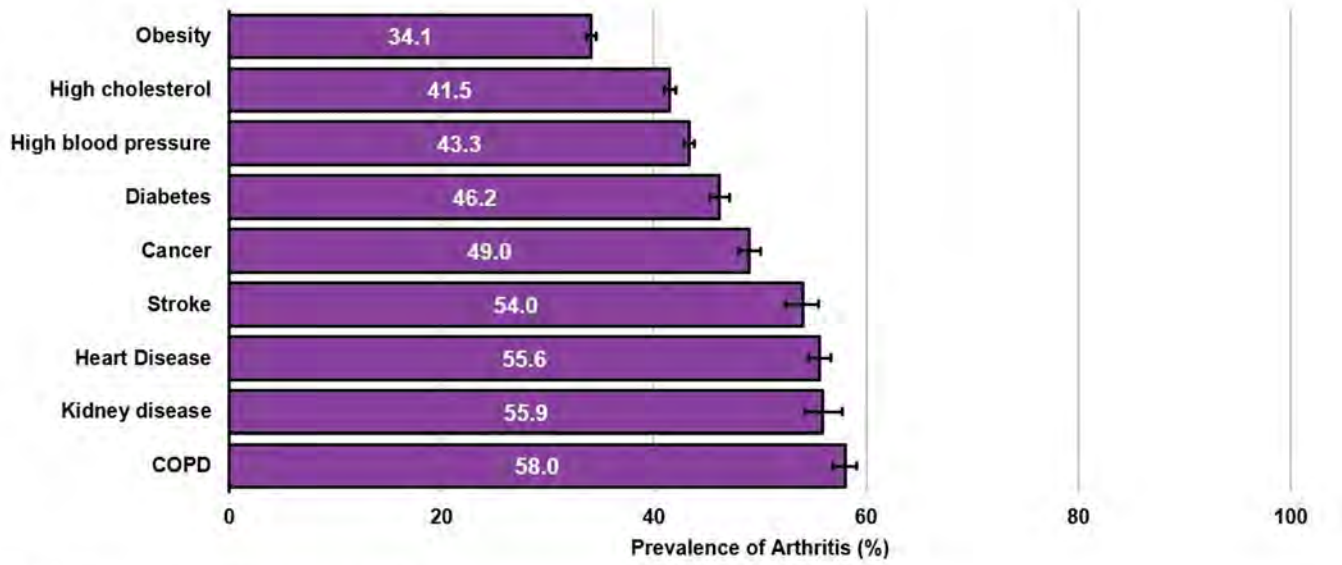
[2] Values may not sum to 100.0 because of rounding.

[3] Study inclusion criteria were: adults ≥18 years who reported age, arthritis status, and physical activity status.

[4] Arthritis was defined as "yes" in response to "Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"

[5] 49 states and DC were studied. In 2019, New Jersey did not collect sufficient data to meet the minimum requirement for inclusion in the BRFSS public-use dataset.

[6] Due to missing data, number of respondents (n) for each variable does not sum to the total n.



COPD: chronic obstructive pulmonary disease
[1] Due to BRFSS's complex sampling design, sampling weights, derived using iterative proportional fitting (raking), were applied to make estimates representative of each state.
[2] Arthritis was defined as "yes" in response to "Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"
[3] Study inclusion criteria were: adults ≥18 years who reported age, arthritis status, and physical activity status.
[4] Physical activity is recommended as part of the management of each of these 9 chronic conditions.
[5] 49 states and DC were studied. In 2019, New Jersey did not collect sufficient data to meet the minimum requirement for inclusion in the BRFSS public-use dataset.

Figure. Weighted(1) prevalence and 95% confidence intervals of arthritis(2) among adults aged ≥18 years(3), across each of 9 chronic conditions(4), 49 states and District of Columbia(5), Behavioral Risk Factor Surveillance System, 2019.

gout, lupus, or fibromyalgia?" The 9 comorbid conditions were cancer (excluding skin), chronic obstructive pulmonary disease (COPD), diabetes, heart disease, high blood pressure, high cholesterol, kidney disease, obesity, and stroke. We estimated chronic condition-specific prevalence of 1) arthritis; and 2) physical inactivity (unadjusted and age-standardized), by arthritis status. We compared age-standardized estimates by arthritis status using t-tests (α=0.05).

Results: Distributions of sociodemographic characteristics by arthritis status differed most for age and employment status (Table 1). In 2019, the chronic condition-specific arthritis prevalence was highest for adults with COPD (58.0%), kidney disease (55.9%), and heart disease (55.6%) (range: 34.1%–58.0%) (Figure). Unadjusted physical inactivity prevalence among adults with a specific chronic condition and arthritis was highest for COPD (46.8%), stroke (44.0%), and diabetes (44.0%) (range: 33.0%–46.8%) (Table 2). Age-standardized physical inactivity prevalence was higher for adults with each chronic condition and arthritis versus those without arthritis ($p < 0.05$ for 6 conditions). Percentage point differences ranged from 3.7–9.0; largest differences were high cholesterol (9.0), diabetes (8.9), and high blood pressure and cancer (both 7.7).

Conclusion: Adults with arthritis had a notably higher physical inactivity prevalence for all comorbid chronic conditions; the pattern was significant for 6 of the 9. Observed differences may be attributed to arthritis-related barriers that need to be addressed. Health care providers can help their patients address arthritis-specific and generic PA barriers by recommending PA and chronic disease self-management education programs. Community organizations delivering these programs may be ideal partners for referrals, and expanded program delivery could reduce PA barriers and improve quality-of-life and health outcomes.

Table 2. Weighted(1) unadjusted and age-standardized(2) prevalence of physical inactivity(3) among adults(4) aged ≥18 years, overall and for each of 9 chronic conditions(5), by arthritis(6) status, 49 states and District of Columbia(7), Behavioral Risk Factor Surveillance System, 2019

	Arthritis (n= 130,259)			No Arthritis (n= 250,159)			Percentage point difference[8]
	n	Physical Inactivity % (95% CI)		n	Physical Inactivity % (95% CI)		
		Unadjusted	Age-standardized[2]		Unadjusted	Age-standardized[2]	
Overall	42,960	32.8 (32.2–33.3)	30.2 (29.4–31.0)	59,093	23.7 (23.4–24.1)	23.9 (23.6–24.2)	6.3[9]
Heart disease[10]	8,307	41.4 (40.0–42.8)	37.5 (34.0–41.2)	4,713	34.7 (33.0–36.4)	33.8 (30.5–37.2)	3.7
Kidney disease	4,123	43.4 (41.2–45.6)	36.9 (31.7–42.5)	2,066	35.8 (33.3–38.4)	32.4 (29.4–35.6)	4.5
Stroke	4,429	44.0 (42.0–46.0)	39.9 (36.0–44.0)	2,807	39.2 (36.8–41.7)	35.4 (32.0–39.1)	4.5
COPD	9,623	46.8 (45.5–48.2)	41.6 (39.1–44.1)	5,102	39.8 (38.1–41.5)	36.5 (34.4–38.6)	5.1[9]
Obesity (BMI ≥30)	19,648	38.9 (38.1–39.7)	35.3 (34.0–36.6)	19,743	28.8 (28.2–29.5)	29.1 (28.4–29.7)	6.2[9]
Cancer (non-skin)	7,315	36.5 (35.1–37.8)	34.9 (31.7–38.2)	5,311	28.0 (26.6–29.4)	27.2 (24.6–30.0)	7.7[9]
High blood pressure	28,069	37.0 (36.3–37.7)	34.9 (33.4–36.4)	22,593	28.6 (28.0–29.3)	27.2 (26.4–27.9)	7.7[9]
Diabetes	11,789	44.0 (42.8–45.2)	41.7 (38.9–44.7)	8,996	34.7 (33.4–35.9)	32.8 (31.1–34.7)	8.9[9]
High cholesterol	21,438	34.9 (34.2–35.7)	34.0 (32.2–35.8)	17,563	26.2 (25.5–26.9)	25.0 (24.1–25.8)	9.0[9]

CI: confidence interval; COPD: chronic obstructive pulmonary disease; BMI: body mass index
[1] Due to BRFSS's complex sampling design, sampling weights, derived using iterative proportional fitting (raking), were applied to make estimates representative of each state.
[2] Estimates were age-standardized to the 2000 projected US adult population using 3 age groups: 18–44 years, 45–64 years, and ≥65 years.
[3] Physical inactivity was defined as no leisure time physical activity in the past month.
[4] Study inclusion criteria were: adults ≥18 years who reported age, arthritis status, and physical activity status.
[5] Physical activity is recommended as part of the management of each of these 9 chronic conditions.
[6] Arthritis was defined as "yes" in response to "Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"
[7] 49 states and DC were studied. In 2019, New Jersey did not collect sufficient data to meet the minimum requirement for inclusion in the BRFSS public-use dataset.
[8] Percentage point difference between age-standardized physical inactivity prevalences for adults with versus without arthritis.
[9] Indicates statistically significant t-test ($p<0.05$) for difference between age-standardized physical inactivity prevalences for adults with versus without arthritis.
[10] Heart disease included coronary heart disease and myocardial infarction.

Disclosure: D. Guglielmo, None; **C. Helmick**, None; **M. Boring**, None; **K. Theis**, None; **L. Murphy**, None; **K. Watson**, None; **L. McGuire**, None; **L. Duca**, None.

Abstract Number: 1034

Racial/ethnic Differences in Lupus Pregnancy Outcomes over 1 Decade: A US National Study

Bella Mehta[1], Yiming Luo[2], Deanna Jannat-Khah[3], Jiehui Xu[4], Lisa Sammaritano[3], Jane Salmon[3], Michael Lockshin[1], Susan Goodman[3] and Said Ibrahim[5], [1]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [2]National Institutes of Health, Bethesda, MD, [3]Hospital for Special Surgery, New York, NY, [4]Weill Cornell Medicine, New York, NY, [5]Weill Cornell Medicine, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) disproportionately affects women and minorities of childbearing age. Although maternal and fetal outcomes of pregnancy among women with SLE have improved over time, it is not known whether the improved outcomes are shared equally among different racial/ethnic groups.

Methods: We used the National Inpatient Sample to conduct a retrospective cross-sectional analysis of SLE pregnancy related admissions from 2008 to 2017. Patients were identified using ICD-9/10 codes. Race/ethnicity was the primary exposure variable (Caucasian, African American, Hispanic, Asian/Native American/Others). We studied pregnancy outcomes including in-hospital maternal mortality, fetal mortality, non-delivery related admissions and Cesarean section (C-section). We performed multiple imputation to account for missing data on race. Weights were applied to represent the nationwide estimates.

Results: From 2008 to 2017, there were a total of 61,012 SLE pregnancy related hospitalizations (Table 1). African American and Hispanic pregnant women (29 yrs) with SLE were younger compared to Caucasian (30 yrs) and Asians (31 yrs). Similarly, they were more likely to be on Medicaid (51% for African American, 49% for Hispanic, 30% for Caucasian and 33% for Asian/Native American/Other). During the 10-year study period, fetal mortality, and non-delivery related admissions and C-section rates improved in all racial/ethnic groups (Figure 1). Maternal mortality rates were very low throughout the study period, with none observed among Caucasians. Overall fetal mortality declined in all racial/ethinic groups, with a numerically greater reduction in Hispanic (from 291 in 2008-2009 to 101 in 2016-2017 per

Table 1 Demographic of hospitalized pregnant women with SLE among different racial/ethnic groups

	Caucasian	African American	Hispanic	Asian/Native American/Other
	n=24611	n=29849	n=32238	n=23131
Age (mean years)	30	29	29	31
Primary Payer				
Medicare	4%	10%	5%	3%
Medicaid	30%	51%	49%	33%
Private insurance	60%	35%	40%	59%
Other	6%	4%	6%	5%
median income quartiles for ZIP Code area				
0-25th percentile	20%	45%	33%	19%
26-50th percentile	23%	22%	26%	19%
51-75th percentile	28%	19%	24%	23%
76-100th percentile	29%	14%	17%	39%
Hospital Bedsize				
Small	11%	7%	9%	8%
Medium	25%	25%	21%	22%
Large	64%	68%	70%	70%
Hospital Location and Teaching Status				
Rural	7%	4%	3%	3%
Urban non-teaching	29%	18%	27%	25%
Urban teaching	64%	78%	71%	72%
Hospital Regions				
Northeast	19%	17%	17%	23%
Midwest	23%	21%	10%	15%
South	38%	52%	33%	24%
West	20%	10%	40%	38%
Elixhauser Comorbidity Index				
0	9%	9%	8%	9%
1 to 4	89%	87%	89%	89%
5+	2%	4%	3%	2%

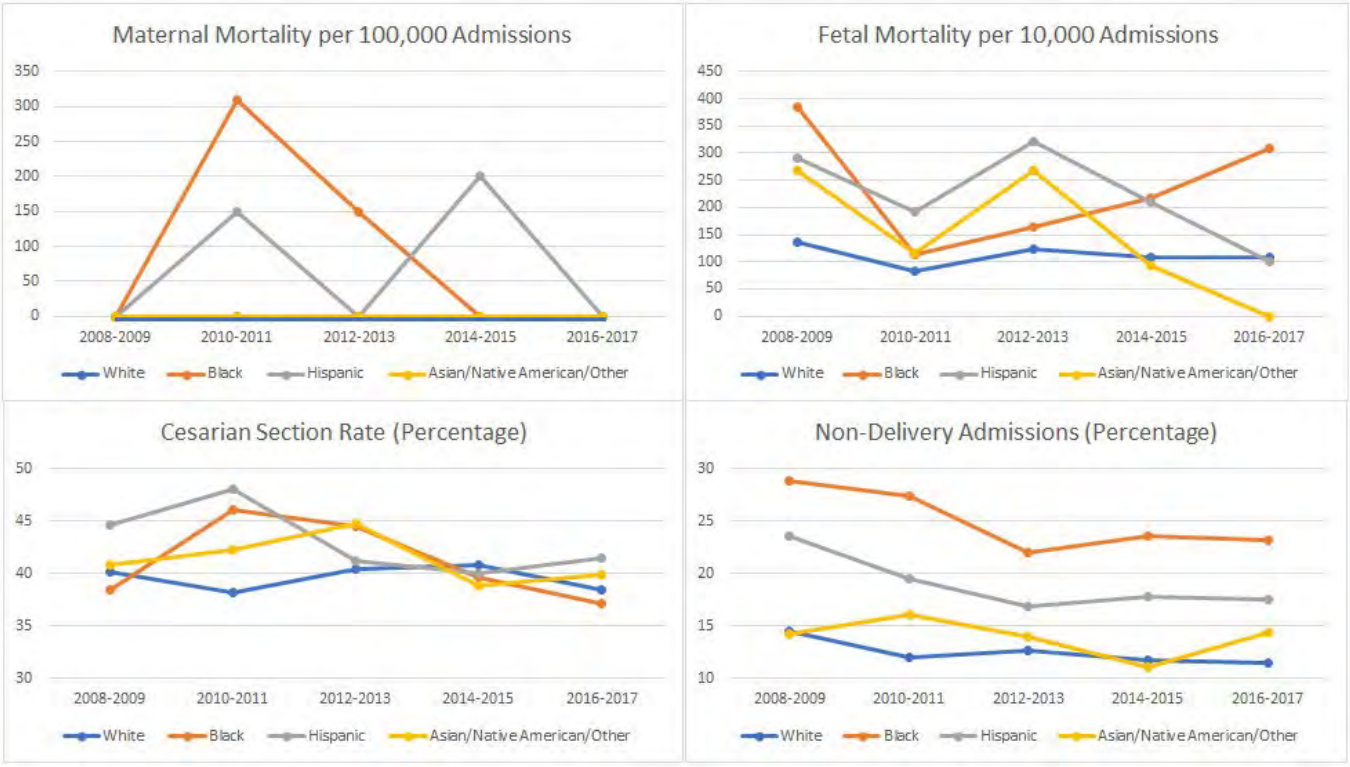


Figure 1. Trends in pregnancy related outcomes over a 10 year period.

10,000 admissions) and Asian/Native American/Other(from 267 in 2008-2009 to no observations in 2016-2017 per 10,000 admissions) than Caucasian (from 136 in 2008-2009 to 108 in 2016-2017 per 10,000 admissions) and African American (from 385 in 2008-2009 to 308 in 2016-2017 per 10,000 admissions).

Conclusion: Pregnancy outcomes in women with SLE improved in all racial/ethnic groups over the past decade however, persistent disparities in African Americans and Hispanics remain.

Disclosure: B. Mehta, Novartis, 1, 6; **Y. Luo**, None; **D. Jannat-Khah**, Cytodyn, 12, own shares of stock, Walgreens, 12, Own stock shares, AstraZeneca, 12, own stock shares, GW Pharmaceuticals, 12, stock ownership; **J. Xu**, None; **L. Sammaritano**, None; **J. Salmon**, UCB, 1, 5, BMS, 1, Aurinia, 1; **M. Lockshin**, None; **S. Goodman**, UCB, 1, NOvartis, 5; **S. Ibrahim**, None.

Abstract Number: 1035

The ELSA-Brasil Musculoskeletal Cohort (ELSA-Brasil MSK): Design, Implementation and Prevalence of Chronic Musculoskeletal Pain and Radiographic Knee Osteoarthritis at Baseline

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Musculoskeletal (MSK) disorders, including low back pain and osteoarthritis (OA), are ranked among the top causes of years lived with disability and increased risk-attributable disability-adjusted life-years. ELSA-Brasil MSK is an ancillary study of the ELSA-Brasil that investigates the incidence and risk factors for MSK disorders. Here we briefly describe the design and implementation of the cohort and presented prevalence of chronic musculoskeletal pain (CMP) and knee OA at baseline.

Table 1. Prevalence of chronic musculoskeletal pain according to sociodemographic and general health characteristics at baseline of ELSA-Brasil MSK (n=2,901, 2012-2014).

Characteristics	CMP ≥1 site N=1,597 (55.1%) %	Multisite CMP N=553 (19.1%) %	Generalized CMP N=299 (10.3%) %
Sex			
Male	44.6	11.6	5.57
Female	64.3	25.9	14.6
Age, years			
38 – 44	45.0	12.1	6.2
45 – 54	54.1	18.5	9.2
55 +	57.5	20.9	11.8
Self-declared race/skin color			
White	53.7	17.1	8.4
Non-White	56.2	21.1	12.1
Education level			
Secondary school or higher	54.1	18.7	10.0
Primary school or lower	58.5	24.1	13.8
Work status			
Active	53.5	18.0	9.3
Retired	62.2	24.3	15.2
Body mass index (kg/m²)			
Non-obese (BMI<30)	52.4	17.2	8.9
Obese (BMI ≥ 30)	64.1	25.9	15.3
Comorbidity[a]			
0	49.1	14.6	7.2
1-2	59.0	22.7	12.4
3+	71.0	26.0	18.3
Depression			
No	53.8	17.9	9.5
Yes	77.1	40.9	25.8

BMI, body mass index. MSK, musculoskeletal. CMP, chronic musculoskeletal pain. CLBP, chronic low back pain. aComorbidity: hypertension, diabetes, myocardial infarction, heart failure, stroke, kidney disease, COPD, cirrhosis, cancer.

Table 2. Tibiofemoral compartment according to Kellgren-Lawrence score, ELSA-Brasil MSK (n=5,638 knees, 2012-2014)

Tibiofemoral Kellgren-Lawrence score	N (%)
0	3,526 (62.5)
1	1,452 (25.8)
2	430 (7.6)
3	170 (3.0)
4	60 (1.1)

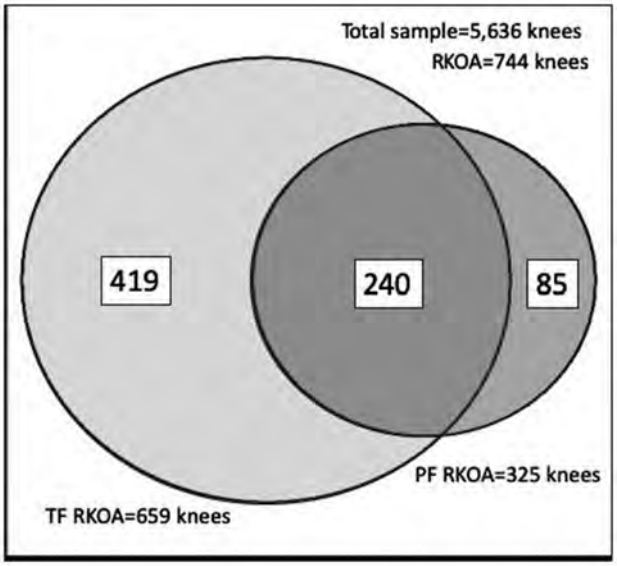

Figure 1. Venn Diagram of radiographic OA in ELSA-Brasil MSK (n=5,636 knees*, 2012-2014) *n=5,636 knees tibiofemoral and patellofemoral radiographic images.

Methods: ELSA-Brasil MSK includes active and retired civil servants from one of the investigation centers (IC) of ELSA-Brasil (IC-Minas Gerais) who completed assessments on five different domains concerning MSK health (rheumatic diseases and symptoms; disability and physical functioning; mechanical risk factors; personal beliefs; care seeking) at study baseline (2012-2014). Cohort surveillance has been performed through annual telephone interviews and return visits (scheduled every 4 years after enrollment), collecting extensive information on exposures, subclinical and clinical outcomes. A total of 2,901 participants were assessed for CMP (≥ 6 months in the past year) at nine body sites: neck, shoulders, upper back, elbows, lower back, wrists/hands, hips/thighs, knees, ankles/feet. CMP was described as multisite (>3 sites) and generalized (3 regions: upper + lower limbs + axial skeleton). 2,830 participants underwent hand and/or knee radiography for the diagnosis of OA along with the assessment of frequent hand/knee pain (pain on most days of at least 1 month). Radiographic knee OA (RKOA) was defined as the presence of tibiofemoral (TF) (KL ≥2) and/or patellofemoral (PF) (definitive osteophyte ≥2 or joint space narrowing ≥2 +bone abnormality) OA and symptomatic knee OA (SKOA) as the presence of RKOA + frequent knee pain in the corresponding knee.

Results: Participants were aged between 38 and 79 years old (mean 56.0 SD 8.9), 52.9% were women. CMP in at least one site was observed in 55.1% of participants and there was a high prevalence of multisite (19.1%) and generalized (10.3%) CMP. CMP was more commonly observed among females and participants who were older, non-white, less educated, retired, with depression, and those with higher body mass index and number of comorbidities (Table 1). The prevalence RKOA and SKOA was 18.1% and 7.8%, respectively. TF compartment was scored as KL in 2 in 7.6%, 3 in 3.0% and 4 in 1.1% of 5,638 knee images (Table 2). Most knees with RKOA (n=740) showed isolated TF OA (56.6%), with isolated PF OA in 11.4% of knees (Figure 1).

Conclusion: The high prevalence of CMP and knee OA indicates a large burden of MSK disorders in Brazil. Future longitudinal analyses in ELSA-Brasil MSK will provide an unique opportunity to fill current knowledge gaps about psychosocial and biological determinants of these disorders in a middle-income country.

Funding: ELSA-Brasil is supported by the Brazilian Ministry of Health and of Science and Technology (FINEP and CNPq-BR), (Grants 01 06 0010.00 RS, 01 06 0212.00 BA, 01 06 0300.00 ES, 01 06 0278.00 MG, 01 06 0115.00 SP, 01 06 0071.00 RJ). ELSA-Brasil MSK has been supported by CAPES-BR (054/2010), FAPEMIG-BR (APQ-00921-16) and CNPq-BR (42358520169).

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Abstract Number: 1036

The Association of Patient Uncertainty with Mental Health in Systemic Autoimmune Rheumatic Diseases

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with systemic autoimmune rheumatic diseases (SARDs) face uncertainty regarding disease flare or progression, management, how to interpret physiologic changes in their bodies, and new roles, including when and how to engage in medical visits and tests. ANCA-associated vasculitis (AAV), systemic sclerosis (SSc), and IgG4-related disease (IgG4-RD) are prototypic SARDs with differing treatments, natural histories, and manifestations that may lead to differences in the impact of illness-related uncertainty. Little is known about the psychological profiles and psychosocial and health needs of illness-related uncertainty among adults with these unique SARDs.

Methods: We invited English-speaking patients with AAV, SSc, and IgG4-RD from a single center to participate. Participants provided details of sociodemographics and SARD history and completed surveys: Mishel Uncertainty in Illness Scale (MUIS, (range 22-110), Patient Health Questionnaire depression scale (PHQ-8, range 0-12), General Anxiety Disorder (GAD-7, range 0-21), Sickness Impact Profile (SIP, range 0-22), and a survey of psychosocial needs.

Table 1: Demographics of Survey Respondents

	Total	AAV	IgG4-RD	SSc
N	132	41	61	30
Age (Mean, SD)	64.7, 11.3	64.7, 10.3	64.5, 12.0	64.9, 11.8
Race/Ethnicity n (%)				
American Indian or Alaskan Native	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Asian	13 (9.8)	2 (4.9)	9 (14.8)	2 (6.7)
Black or African American	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Hispanic or Latino	6 (4.5)	1 (2.4)	3 (4.9)	2 (6.7)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
White	110 (83.3)	38 (92.7)	46 (75.4)	26 (86.7)
Other	4 (3.0)	1 (2.4)	3 (4.9)	0 (0.0)
Sex n (%)				
Female	69 (52.3)	23 (56.1)	17 (27.9)	29 (96.7)
Relationship status n (%)				
Single, never married	12 (9.1)	7 (17.1)	2 (3.3)	3 (10.0)
Married/Living with partner	101 (76.5)	28 (68.3)	54 (88.5)	19 (63.3)
Widowed/Divorced	16 (12.1)	5 (12.2)	4 (6.6)	7 (23.3)
Other	2 (1.5)	1 (2.4)	0 (0.0)	1 (3.3)
Children n (%)				
Yes	102 (77.3)	33 (80.5)	49 (80.3)	20 (66.7)
Caretaker n (%)				
Yes	22 (16.7)	6 (14.6)	12 (19.7)	4 (13.3)
Level of Education n (%)				
High school or some college	27 (20.5)	7 (17.1)	9 (14.8)	11 (36.7)
College degree	47 (35.6)	18 (43.9)	21 (34.4)	8 (26.7)
Advanced degree	57 (43.2)	16 (39)	30 (49.2)	11 (36.7)
Employment status n (%)				
Full-time	37 (28)	12 (29.3)	19 (31.1)	6 (20.0)
Part-time	10 (7.6)	6 (14.6)	2 (3.3)	2 (6.7)
Unemployed and looking for work	5 (3.8)	1 (2.4)	3 (4.9)	1 (3.3)
Unable to work due to caring for family or home	2 (1.5)	2 (4.9)	0 (0.0)	0 (0.0)
Unable to work due to disability or illness	6 (4.5)	2 (4.9)	1 (1.6)	3 (10.0)
Retired	69 (52.3)	16 (39.0)	36 (59.0)	17 (56.7)
Student	1 (0.8)	1 (2.4)	0 (0.0)	0 (0.0)
Other	2 (1.5)	1 (2.4)	0 (0.0)	1 (3.3)
Annual household income n (%)				
Less than 20,000	4 (3.0)	1 (2.4)	3 (4.9)	0 (0.0)
20,000-39,999	16 (12.1)	4 (9.8)	6 (9.8)	6 (20.0)
40,000-59,999	11 (8.3)	6 (14.6)	2 (3.3)	3 (10.0)
60,000-79,999	14 (10.6)	4 (9.8)	5 (8.2)	5 (16.7)
80,000-99,999	8 (6.1)	3 (7.3)	3 (4.9)	2 (6.7)
100,000 and over	64 (48.5)	20 (48.8)	35 (57.4)	9 (30.0)
Don't know	1 (0.8)	0 (0.0)	1 (1.6)	0 (0.0)
Prefer not to answer	14 (10.6)	0 (0.0)	6 (9.8)	0 (0.0)
Health Insurance n (%)				
Employer-sponsored	54 (40.9)	20 (48.8)	21 (34.4)	13 (43.3)
Individual insurance	8 (6.1)	4 (9.8)	4 (6.6)	0 (0.0)
Medicare	64 (48.5)	15 (36.6)	32 (52.5)	17 (56.7)
Medicaid	2 (1.5)	1 (2.4)	1 (1.6)	0 (0.0)
Military health care	2 (1.5)	0 (0.0)	2 (3.3)	0 (0.0)
Don't know	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Other	2 (1.5)	1 (2.4)	1 (1.6)	0 (0.0)
No health insurance	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Comorbidities n (%)				
Cardiovascular disease (i.e. heart disease, stroke, high blood pressure, high cholesterol)	59 (44.7)	16 (39.0)	27 (44.3)	16 (53.3)
Diabetes	15 (11.4)	3 (7.3)	11 (18.0)	1 (3.3)
Kidney disease	17 (12.9)	4 (9.8)	11 (18.0)	2 (6.7)
Liver disease	3 (2.3)	0 (0.0)	3 (4.9)	0 (0.0)
Lung disease (e.g., asthma, COPD, sleep apnea)	43 (32.6)	20 (48.8)	16 (26.2)	7 (23.3)
Overweight/obesity	26 (19.7)	9 (22.0)	12 (19.7)	5 (16.7)
Underweight	2 (1.5)	0 (0.0)	0 (0.0)	2 (6.7)
Other	31 (23.5)	11 (26.8)	13 (21.3)	7 (23.3)
Rheumatic disease n (%)				
ANCA- associated Vasculitis	41 (31.1)			
IgG4-related disease	61 (46.2)			
Scleroderma	30 (22.7)			
Self-Reported Disease activity n (%)				
In remission	56 (42.4)	21 (51.2)	32 (52.5)	3 (10.0)
Not in remission	42 (31.8)	13 (31.7)	13 (21.3)	16 (53.3)
I do not know	34 (25.8)	7 (17.1)	16 (26.2)	11 (36.7)

Participants could complete surveys by paper, electronically, or by phone. We assessed the correlation of MUIS with PHQ-8, GAD-7, and SIP using Pearson's correlation coefficient. The association of psychological measures with self-reported needs were assessed using P-for-trend analyses. A two-sided p-value < 0.05 was considered significant.

Results: Of 368 patients invited, 132 (36%) with AAV (41, 31%), IgG4-RD (61, 46%), or SSc (30, 23%) participated (**Table 1**). The mean (SD) age was 65 years (11) and the majority (n=69, 52%) were female and white (n=110, 83%).

Table 2: The Association of Uncertainty with Mental Health

	Correlation coefficient	p-value
Overall		
MUIS and PHQ-8	0.426	<.0001
MUIS and GAD-7	0.332	<.0001
MUIS and SIP	0.280	0.0012
AAV		
MUIS and PHQ-8	0.559	0.0001
MUIS and GAD-7	0.451	0.0031
MUIS and SIP	0.565	0.0001
IgG4-RD		
MUIS and PHQ-8	0.168	0.1992
MUIS and GAD-7	0.217	0.0932
MUIS and SIP	0.012	0.9260
SSc		
MUIS and PHQ-8	0.595	0.0007
MUIS and GAD-7	0.250	0.1834
MUIS and SIP	0.593	0.0005

AAV: ANCA-Associated Vasculitis; IgG4-RD: IgG4-Related Disease; SSc: Systemic Sclerosis; MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder (GAD-7), SIP: Sickness Impact Profile

Fifty-six (42%) reported remission and 42 (32%) active disease. The median [IQR] MUIS, PHQ-8, GAD-7, and SIP scores were 55.0 [48.0, 62.0], 3.0 [1.0, 6.0], 2.0 [0.0, 5.5], and 1.0 [0.0, 6.0]; 46 (35%) had at least mild depression and 42 (32%) had at least mild anxiety. We observed variations in these measures across SARDs. Across the full sample, illness-related uncertainty was positively correlated with depression (PHQ-8, r=0.43, p=< 0.0001), anxiety (GAD-7, r=0.33, p= < 0.0001), and sickness impact (SIP, r=0.28, p=0.001). We further observed variations in these measures across SARDs, such that uncertainty was more strongly associated with depression and sickness impact for individuals with AAV or SSc as compared to individuals with IgG4-RD (**Table 2**). Most commonly, patients endorsed needing help with physical symptoms (n=70, 53.0%), emotional concerns (n=32, 24.2%), and strategies to increase self-care (n=49, 37.1%), with greater needs significantly positively correlated with illness-related uncertainty (**Table 3**).

Conclusion: For rheumatology patients with prototypic SARDs, illness-related uncertainty is a significant correlate of levels of depression, anxiety, and sickness impact, as well as their chief psychosocial needs. Considering the relatively stronger associations among patients with AAV and SSc rather than IgG4-RD, there may be key differences in natural history and needs for targeted interventions to address uncertainty and patient-reported needs.

Table 3: Needs Identified by Patients According to Uncertainty and Mental Health (N=132)

		Managing physical symptoms		Coping with emotional concerns		Managing social concerns or lack of support		Learning strategies to increase self-care		Managing sexual and reproductive concerns		Finding resources to help with daily concerns	
	Total	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend	N (%)	P for trend
PHQ8													
Total	132 (100.0)	68 (51.5)	**0.0332**	31 (23.5)	0.0704	10 (7.6)	**0.0079**	48 (36.4)	**0.0317**	4 (3.0)	0.0656	9 (6.8)	0.3488
Minimal (0-4)	84 (63.6)	42 (50.0)		15 (17.9)		2 (2.4)		25 (29.8)		1 (1.2)		4 (4.8)	
Mild (5-9)	31 (23.5)	14 (45.2)		11 (35.5)		5 (16.1)		16 (51.6)		2 (6.5)		4 (12.9)	
Moderate (10-14)	5 (3.8)	3 (60.0)		1 (2.0)		1 (20.0)		1 (20.0)		0 (0.0)		0 (0.0)	
Moderately Severe (15-19)	5 (3.8)	4 (80.0)		2 (40.0)		1 (20.0)		2 (40.0)		0 (0.0)		0 (0.0)	
Severe (20-24)	5 (3.8)	5 (100.0)		2 (40.0)		1 (20.0)		4 (80.0)		1 (20.0)		1 (20.0)	
< 10	115 (87.1)	56 (48.7)	**0.0229**	26 (22.6)	0.3611	7 (6.1)	0.0581	41 (35.7)	0.4076	3 (2.6)	0.3938	8 (7.0)	0.9669
>= 10	15 (11.4)	12 (80.0)		5 (33.3)		3 (20.0)		7 (46.7)		1 (6.7)		1 (6.7)	
GAD7													
Total	132 (100.0)	70 (53.0)	0.516	32 (24.2)	**<.0001**	10 (7.6)	**0.0106**	49 (37.1)	**0.0332**	4 (3.0)	**0.0076**	11 (8.3)	0.0761
Minimal (0-4)	90 (68.2)	48 (53.3)		12 (13.3)		4 (4.4)		30 (33.3)		1 (1.1)		6 (6.7)	
Mild (5-9)	34 (25.8)	16 (47.1)		15 (44.1)		4 (11.8)		13 (38.2)		2 (5.9)		3 (8.8)	
Moderate (10-14)	6 (4.5)	4 (66.7)		3 (50.0)		1 (16.7)		4 (66.7)		0 (0.0)		1 (16.7)	
Severe (15-21)	2 (1.5)	2 (100.0)		2 (100.0)		1 (50.0)		2 (100.0)		1 (50.0)		1 (50.0)	
MUIS													
Total	132 (100.0)	70 (53.0)	**0.0028**	32 (24.2)	**0.039**	10 (7.6)	**0.0342**	49 (37.1)	**0.0366**	4 (3.0)	0.8634	11 (8.3)	0.7692
Q1 (22-44)	21 (15.9)	7 (33.3)		1 (4.8)		1 (4.8)		6 (28.8)		0 (0.0)		1 (4.8)	
Q2 (44-66)	97 (73.5)	51 (52.6)		26 (26.8)		5 (5.2)		33 (34.0)		4 (4.1)		10 (10.3)	
Q3 (66-88)	13 (9.8)	11 (84.6)		5 (38.5)		4 (30.8)		10 (76.9)		0 (0.0)		0 (0.0)	
Q4 (88-110)	1 (0.8)	1 (100.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	
SIP													
Total	132 (100.0)	70 (53.0)	0.2665	32 (24.2)	0.1673	10 (7.6)	0.7647	49 (37.1)	0.2117	4 (3.0)	**0.0012**	11 (8.3)	0.0781
Q1 (0-5)	92 (69.7)	47 (51.1)		19 (20.7)		6 (6.5)		32 (34.8)		0 (0.0)		4 (4.3)	
Q2 (6-11)	34 (25.8)	18 (52.9)		11 (32.4)		4 (11.8)		13 (38.2)		3 (8.8)		7 (20.6)	
Q3 (12-16)	6 (4.5)	5 (83.3)		2 (33.3)		0 (0.0)		4 (66.7)		1 (16.7)		0 (0.0)	
Q4 (17-22)	0 (0.0)	0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)		0 (0.0)	

MUIS: Mishel Uncertainty in Illness Scale; PHQ-8: Patient Health Questionnaire depression scale; GAD-7: General Anxiety Disorder (GAD-7); SIP: Sickness Impact Profile

Disclosure: Z. Wallace, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2; **C. Cook**, None; **L. Finkelstein-Fox**, None; **X. Fu**, None; **F. Castelino**, Boehringer Ingelheim, 2, Kadmon, 5; **H. Choi**, None; **C. Perugino**, Viela Bio, 2; **J. Stone**, Principia Biopharma Inc, a Sanofi Company, 5, 12, personal fees; **E. Park**, None; **D. Hall**, None.

Abstract Number: 1037

Variations in Total Knee Replacement Utilization and Outcomes in USA and Canada: The Role of Geography and Socioeconomic Factors

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1: Characteristics of patients who underwent Total Knee Arthroplasty in Ontario, Canada and Pennsylvania, US

TKA	Lowest quintile community Income			2nd – 4th quintile community Income			Highest quintile community Income		
Variable, n (%)	Ontario N=26,393	Pennsylvania N = 35,096	p	Ontario N=102,788	Pennsylvania N = 113,577	p	Ontario N=32,063	Pennsylvania N = 59,343	p
Age, mean ± SD	67.93 ± 9.68	65.1 ± 10.1	<0.001	67.76 ± 9.14	66.3 ± 9.80	<0.001	67.69 ± 8.90	67.3 ± 9.53	<0.001
Age <50	702 (2.7%)	2001 (5.70%)	<0.001	2,046 (2.0%)	4785 (4.21%)	<0.001	575 (1.8%)	1749 (2.95%)	<0.001
Age 50-64	8,988 (34.1%)	14785 (42.1%)	<0.001	35,722 (34.8%)	43710 (38.5%)	<0.001	11,004 (34.3%)	20917 (35.2%)	0.005
Age >=65	16,703 (63.3%)	18310 (52.2%)	<0.001	65,020 (63.3%)	65082 (57.3%)	<0.001	20,484 (63.9%)	36677 (61.8%)	<0.001
Sex:			<0.001			0.001			0.005
Female	17,805 (67.5%)	23109 (65.8%)		63,028 (61.3%)	70425 (62.0%)		19,051 (59.4%)	35830 (60.4%)	
Male	8,588 (32.5%)	11987 (34.2%)		39,760 (38.7%)	43152 (38.0%)		13,012 (40.6%)	23513 (39.6%)	
Elixhauser index:									
0	14,120 (53.5%)	3326 (9.48%)	<0.001	60,159 (58.5%)	12766 (11.2%)	<0.001	19,116 (59.6%)	7132 (12.0%)	<0.001
1-4	12,206 (46.2%)	28715 (81.8%)	<0.001	42,451 (41.3%)	92807 (81.7%)	<0.001	12,907 (40.3%)	48136 (81.1%)	<0.001
>= 5	67 (0.3%)	3055 (8.70%)	<0.001	178 (0.2%)	8004 (7.05%)	<0.001	40 (0.1%)	4075 (6.87%)	<0.001
Volume of cases (by facility and year):									
< 25 procedures	<=5 (0.0%)	593 (1.69%)	<0.001	28 (0.0%)	1121 (0.99%)	<0.001	<=5 (0.0%)	479 (0.81%)	<0.001
25-99 procedures	720 (2.7%)	3847 (11.0%)	<0.001	3,051 (3.0%)	7924 (6.98%)	<0.001	351 (1.1%)	2348 (3.96%)	<0.001
100-199 procedures	2,142 (8.1%)	8356 (23.8%)	<0.001	8,049 (7.8%)	20237 (17.8%)	<0.001	1,645 (5.1%)	5422 (9.14%)	<0.001
200-299 procedures	1,983 (7.5%)	4198 (12.0%)	<0.001	6,667 (6.5%)	14110 (12.4%)	<0.001	1,151 (3.6%)	9246 (15.6%)	<0.001
>= 300 procedures	21,546 (81.6%)	18102 (51.6%)	<0.001	84,993 (82.7%)	70185 (61.8%)	<0.001	28,911 (90.2%)	41848 (70.5%)	<0.001
Urban/rural (based on patient zipcodes):			<0.001			<0.001			<0.001
rural	3,775 (14.3%)	9179 (26.2%)		20,865 (20.3%)	20915 (18.4%)		1,170 (3.6%)	189 (0.32%)	
urban	22,618 (85.7%)	25917 (73.8%)		81,923 (79.7%)	92662 (81.6%)		30,893 (96.4%)	59154 (99.7%)	

Comparisons of continuous variables were performed with the use of one-way analysis of variance, comparisons of categorical variables were performed with the use of logistic regression.

Background/Purpose: Total Knee Arthroplasty (TKA) is an effective treatment option for end-stage knee osteoarthritis. The US is well known for having striking wealth-based disparities in healthcare access and outcomes. While it is assumed that disparities in the US are larger than in other countries, there are few population-based studies that directly compare wealth-based disparities in the US with other high income countries. Our objective was to examine the relationship between neighborhood income and TKA utilization and outcomes in the US and Canada.

Methods: We used population-based administrative data fromPennsylvania(PA), USA and Ontario(ON) Canada to identify all patients age >18 who were hospitalized for primary TKA between 2012 to 2018 using ICD-9/10 codes. We linked patient-level data from each jurisdiction to community median household income using zip code of residence. In each country we independently stratified patients into neighborhood income quintiles. The primary outcome of interest was age and sex standardized per capita utilization of TKA (per 10,000 population per year) for patients in each country stratified by income quintile. Secondary outcomes included 90-day mortality, 90-day readmission, and 1-year revision rates.

Results: We identified 161,244 primary TKAs in ON and 208,016 TKAs in PA (Table 1). TKA utilization per 10,000 population per-year was significantly higher in PA than ON (29.5 vs. 22.8, $p < 0.001$). Across all income groups, utilization

Table 2: Outcomes in patients who underwent primary TKA in Ontario and Pennsylvania*

TKA Outcomes	Lowest quintile community income			2nd – 4th quartile community income			Highest quintile community income		
	Ontario N=26,393	Pennsylvania N = 35,096	p	Ontario N=102,788	Pennsylvania N = 113,577	p	Ontario N=32,063	Pennsylvania N = 59,343	p
Utilization rate, per 10,000 per year	17.5	31.4	<.001	24.4	26.1	<.001	22.8	37.5	<.001
90-day readmission, n (%)	1,744 (6.6%)	3118 (8.88%)	<0.001	5,681 (5.5%)	8480 (7.47%)	<0.001	1,634 (5.1%)	4378 (7.38%)	<0.001
90-day mortality, n (%)	61 (0.2%)	108 (0.31%)	0.07	212 (0.2%)	263 (0.23%)	0.21	46 (0.1%)	113 (0.19%)	0.11
1-year revision, n (%)	124 (0.5%)	354 (1.01%)	<0.001	405 (0.4%)	932 (0.82%)	<0.001	120 (0.4%)	387 (0.65%)	<0.001
Length of stay, mean ± SD	3.27 ± 2.03	2.72 ±1.42	<0.001	3.06 ± 1.92	2.62 ± 1.33	<0.001	2.98 ± 1.87	2.42 ± 1.30	<0.001
Discharge disposition, n (%)									
Died in hospital	18 (0.1%)	21 (0.06%)	0.68	50 (0.05%)	47 (0.04%)	0.43	9 (0.03%)	17 (0.03%)	0.96
Discharged home	24,255 (91.9%)	11145 (31.8%)	<0.001	97,204 (94.6%)	38462 (33.9%)	<0.001	30,476 (95.1%)	20778 (35.0%)	<0.001
Transfer to another acute-care hospital	159 (0.6%)	28 (0.08%)	<0.001	461 (0.4%)	70 (0.06%)	<0.001	42 (0.1%)	37 (0.06%)	0.001
Post-acute care	1,773 (6.7%)	6445 (18.4%)	<0.001	4,569 (4.4%)	16736 (14.7%)	<0.001	1,410 (4.4%)	9202 (15.5%)	<0.001
Other	188 (0.7%)	17456 (49.7%)	<0.001	504 (0.5%)	58256 (51.3%)	<0.001	126 (0.4%)	29309 (49.4%)	<0.001
In-hospital surgery complications:									
Myocardial infarction, n (%)	66 (0.3%)	49 (0.14%)	0.002	202 (0.2%)	133 (0.12%)	<0.001	42 (0.1%)	60 (0.1%)	0.20
Prosthetic device complication, n (%)	29 (0.1%)	26 (0.07%)	0.14	121 (0.1%)	102 (0.09%)	0.04	31 (0.1%)	49 (0.08%)	0.49
Surgical wound infection, n (%)	67 (0.3%)	33 (0.09%)	<0.001	174 (0.2%)	97 (0.09%)	<0.001	44 (0.1%)	39 (0.07%)	0.001
Venous thromboembolism, n (%)	10 (0.04%)	87 (0.25%)	<0.001	39 (0.04%)	341 (0.30%)	<0.001	11 (0.03%)	187 (0.32%)	<0.001

*TKA = total knee arthroplasty

Comparisons of continuous variables were performed with the use of one-way analysis of variance, comparisons of categorical variables were performed with the use of logistic regression.

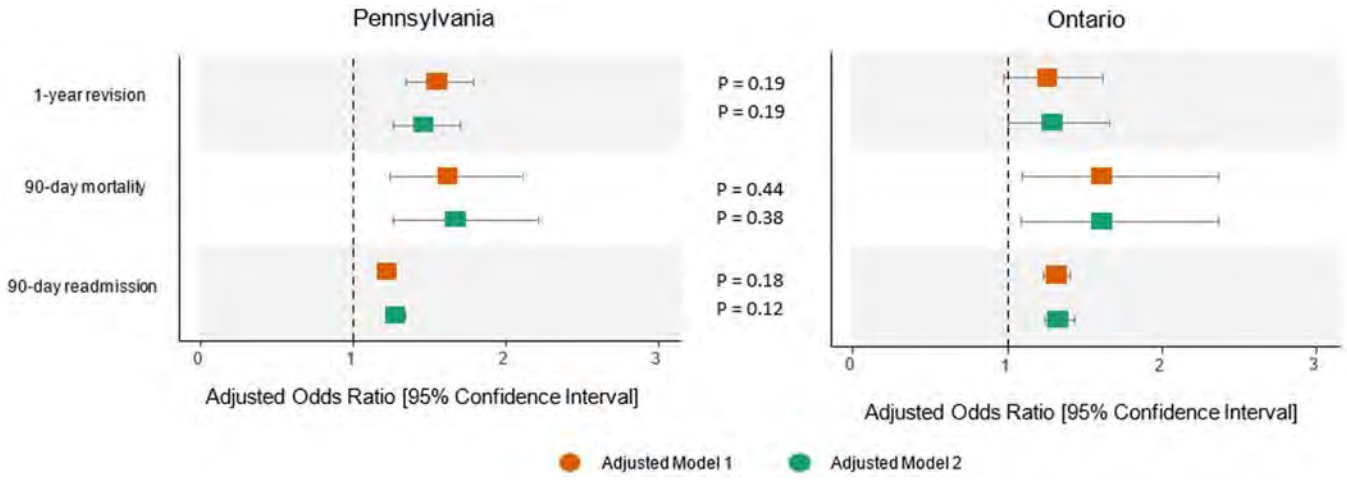

Figure 1. Adjusted odds ratio of three TKA outcomes (1-year revision, 90-day mortality, 90-day readmission) for patients who lived in the lowest income quintile compared to patients living in the highest income quintile in Pennsylvania and Ontario. Adjusted model 1 adjusted for age, sex, hospital volume of cases, rural/urban Adjusted model 2 adjusted for age, sex, hospital volume of cases, rural/urban, Elixhauser Index Comparison tests for country differences based on model estimates.

rates were significantly higher in PA compared to ON (31.4 vs. 17.5, p < 0.001 in lowest income quintile; 37.5 vs. 22.8, p < 0.001 in highest income quintile). (Table 2). In both PA and ON, those in the highest income quintile, had significantly increased odds of 90-day mortality (aOR = 1.58 in PA, 1.47 in ON) and 90-day readmission (aOR = 1.24in PA, 1.30 in ON) compared to lowest income quintile. For 1-year revision were only significant in PA (aOR = 1.44) (Figure 1)

Conclusion: The population-based utilization of TKA is higher in PA, USA compared to ON, Canada. We observed significantly lower rates of TKA for residents of lower income neighborhoods in both the US and Canada and the relative difference between low and high income communities is similar in both countries. In the context of the ongoing debate over healthcare reform in the US, our findings suggest that a single-payer system is unlikely to eliminate income-based disparities.

Disclosure: B. Mehta, Novartis, 1, 6; **K. Ho**, None; **V. Ling**, None; **S. Goodman**, UCB, 1, NOvartis, 5; **M. Parks**, Zimmer Biomet, 2; **B. Ravi**, None; **S. Banerjee**, None; **S. Ibrahim**, None; **P. Cram**, None.

Abstract Number: 1038

Outcomes of Hydroxychloroquine Screening for Retinopathy in a Cohort of Patients with Rheumatological Conditions

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is used to treat rheumatoid arthritis (RA), connective tissue disease (CTD) and other inflammatory conditions. In 2018, the United Kingdom Royal College of Ophthalmologists (RCOphth) published new screening guidelines to monitor the risk of HCQ associated retinopathy, recommending patients be referred for screening if patients had been on HCQ for ≥5 years and included a list of risk factors to guide the screening process: dosage >5mg/kg/day absolute body weight (ABW), concurrent tamoxifen use and impaired renal function (eGFR < 60ml/min/1.73m²). This report aims to audit the 1) HCQ dosing based on RCOphth 2018 guidelines 2) the number of patients appropriately referred for screening and 3) the outcome of screening.

Methods: In July 2018 (when the RCOphth guidelines were published), a list of all patients started on HCQ from April 2013-2014 and received the first prescription from hospital was obtained from hospital pharmacy records. These patients' electronic patient records were reviewed between Jul-Oct 2018 to extract data on demographic and clinical parameters, drug persistence including reason for cessation of drug and suitability for referral for HCQ retinopathy monitoring if they continued the drug. Referral for eye screening took place between Oct 2018-May 2019. These patients were followed until the most recent follow-up visit by May 2021 to determine the outcome of screening (Figure 1).

Results: 100 patients were identified. The median age of the cohort was 57 years (46-70), with 67% of the cohort being female. Many patients (67%) were started on HCQ for RA, 16% for SLE and 17% for other rheumatological diagnoses. The median HCQ dose was 4.6mg/kg/day (3.4-5.7). 37% of patients were prescribed a starting dose of > 5mg/kg/day. 9 patients had an eGFR of < 60 ml/min/1.73m^2. No patients were on concurrent tamoxifen (Table 1).

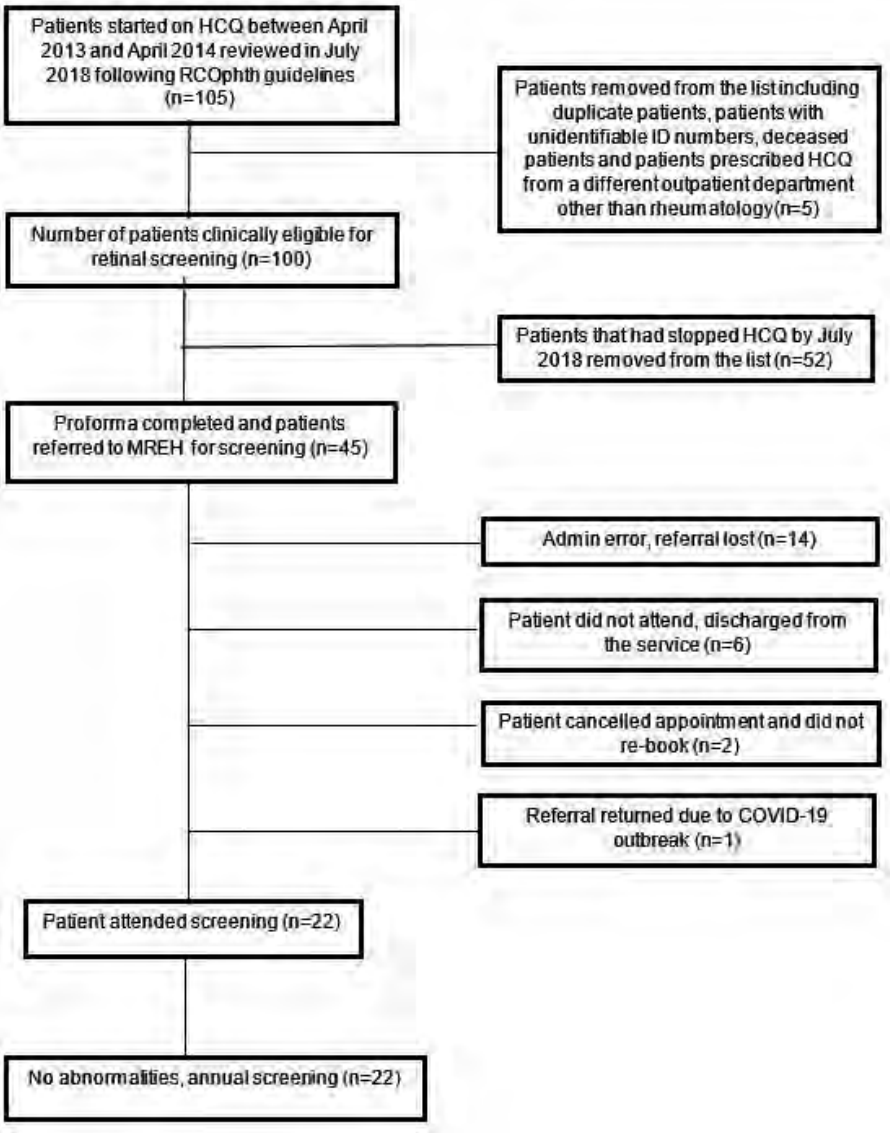

Figure 1. Flowchart showing the process of filtering patients who were clinically suitable to be referred for HCQ retinopathy screening and the outcome of screening (HCQ=hydroxychloroquine).

By July 2018 (median 5 years of follow-up from 2013), 48% of patients remained on HCQ. 52% of patients were no longer on HCQ for a variety of reasons including side effects (33%) and ineffectiveness (10%). Of the 48 patients that remained on HCQ, 3 died before they could be referred and the remaining 45 were referred for eye screening. Of the 45 who were referred, 22 were screened and all showed no evidence of retinopathy, 14 referrals were lost, 6 did not attend and were discharged, 2 cancelled and did not rebook and 1 referral was returned due to the COVID-19 outbreak (Figure 1). Of the 22 patients with normal screening, 2 had renal impairment and 7 were prescribed ≥5mg/kg/day and 2 had both renal impairment and were dosed over 5mg/kg.

Conclusion: After 5 years of follow-up, the drug survival for HCQ is 50%. By knowing the number of patients prescribed and started on HCQ annually and stop therapy after 5 years, this will influence screening service capacity issues. Of those patients who attended for screening after 5 years of therapy, none had evidence of HCQ retinopathy which is reassuring including 11 patients who were either dosed ≥5mg/kg/day (n=7) or had renal impairment (n=2) or both (n=2). In 2013, over a third of patients were started on a HCQ dose >5mg/kg/day, we need to ensure that dosage is appropriate and monitor for other factors to reduce their risk of developing HCQ retinopathy.

Table 1. Baseline characteristics of cohort that started HCQ between April 2013-2014 (ABW = absolute body weight, HCQ=Hydroxychloroquine, IQR= interquartile range, RA=Rheumatoid Arthritis, SLE= Systemic Lupus Erythematous, BMI= Body Mass Index, eGFR= estimated Glomerular Filtration Rate).

Characteristic	N=100
Median age (IQR), years	57 (46-70)
Age >60 years, n	45
Females, n	71
Rheumatological diagnosis, n RA SLE Other	 67 16 17
Median height (IQR), m Height data not available, n	1.62 (1.57-1.71) 29
Median weight (IQR), (kg Weight data not available, n	73.5 (61.0-86.6) 0
Median BMI (IQR), kg/m^2 BMI data not available, n **unavailable data on heights*	27.3 (22.6-32.2) 29
How many were dosed >5mg/kg/day ABW, n	37
Median HCQ dose (IQR), mg/kg/day	4.6 (3.4-5.7)
Median eGFR at time of prescription (IQR), ml/min/1.73m^2	77.5 (70.8-87.0)
No. of people with impaired renal function defined as eGFR <60 ml/min/1.73m^2 at the time HCQ prescription, n	9

Disclosure: G. Tehseen, None; **A. Chadwick**, None; **S. Wills**, None; **A. Low**, None.

Abstract Number: 1039

Healthcare Resource Utilization and Costs of Dermatomyositis and Polymyositis in the United States: A Systematic Literature Review

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Dermatomyositis (DM) and polymyositis (PM) are rare heterogenous systemic autoimmune disorders with primary target of muscle, skin, but can also impact multiple other organs. The objective of this study was to systematically review and synthetize evidence on healthcare resource utilization (HCU) and cost of treating DM/PM in the United States (US).

Methods: A systematic literature review was conducted using MEDLINE and Embase databases. Primary studies of any design enrolling 10 or more patients with DM/PM, published in the English language between 2011–2021 were included irrespective of country or region. Each eligible article was independently reviewed by two reviewers. The title and study abstracts were reviewed to assess eligibility for full-text review. Data on the clinical, humanistic, and economic burden in DM/PM patients in the US were extracted. The economic burden data is presented below.

Results: A total of 3624 records were retrieved from medical databases, 393 records underwent full-text review, and 210 were included in data abstraction. Additional 8 papers were included from searching reference lists of identified studies. HCU and/or costs related to DM/PM in the US were reported in 13 studies. Patients with DM/PM had a significantly higher number of medical visits (>50% directly related to DM/PM care), inpatient admissions, emergency room visits, as well as visits to rheumatologists, neurologists and physical therapy care, compared to matched controls (Table 1). When hospitalized, patients with DM/PM required more specialized tests and procedures, typically with 1.11 to 1.88-day longer length of stay, compared to controls. The total annual cost of hospitalization due to DM

Table 1. Healthcare resource utilization in DM/PM (References: 1 Bradford Rice 2016; 2 Robinson 2016; 3 Ungprasert 2020; 4 Tripathi 2020; 5 Kwa 2017; 6 Kwa 2018; 7 Shah 2013; 8 Christopher-Stine 2020; 9 Zhang 2019)

OUTCOME	N of PATIENTS	STUDY POPULATION	CONTROL / REFERENCE	RESULTS	DIFFERENCE vs CONTROL; p-value (when applicable)
HEALTHCARE RESOURCE UTILIZATION (comparative studies)					
Medical visits/year, mean[1]	2587	DM/PM	Matched non-DM/PM	31 vs 23.6	**+7.4 (57% directly related to DM/PM care); p<0.001**
Inpatient admissions/ year, mean[1]	2587	DM/PM	Matched non-DM/PM	3.6 vs 2.5	**+1.1; p<0.001**
ED visits/year, mean[1]	2587	DM/PM	Matched non-DM/PM	0.8 vs 0.6	**+0.2; p<0.001**
Any outpatient visit/year, mean[1]	2587	DM/PM	Matched non-DM/PM	21.8 vs 17.2	**+4.6; p<0.001**
• Rheumatologist visits[1]	2587	DM/PM	Matched non-DM/PM	1.8 vs 0.6	**+1.2; p<0.001**
• Neurologist visits[1]	2587	DM/PM	Matched non-DM/PM	0.8 vs 0.4	**+0.4; p<0.001**
• Physical therapy[1]	2587	DM/PM	Matched non-DM/PM	3.7 vs 2.6	**+1.1; p<0.001**
• Other visits[1]	2587	DM/PM	Matched non-DM/PM	4.8 vs 3.4	**+1.4; p<0.001**
Prescriptions filled/year, mean[1]	2587	DM/PM	Matched non-DM/PM	32.2 vs 27.5	**+4.7; p<0.001**
Unique drugs / year, mean[1]	2587	DM/PM	Matched non-DM/PM	12.5 vs 10.1	**+2.4; p<0.001**
Dermatology visits, median[2]	103	DM	Healthy controls	7 vs 3	**+4; p<0.0001**
LOS, mean [days][1]	2587	DM/PM	Matched non-DM/PM	2.2 vs 2.0	+0.2; p=0.174
LOS, mean [days][3]	160,528 (admissions)	DM/PM	Non-PM/DM	7.0 vs 5.3	**+1.7 (95% CI: 1.6-1.8); p<0.01**
LOS, mean [days][4]	39,253 (admissions)	DM, malignancy	DM, no malignancy	6.09 vs 5.76	+0.33; p=0.2334
LOS, geometric mean [days][5]	2,042 (admissions)	DM (prim. diagn.)	Non-DM	5.38 vs 3.5	**+1.88 (+54%); p<0.0001**
	9,050 (admissions)	DM (second. diagn.)		4.61 vs 3.5	**+1.11 (+31%); p<0.0001**
LOS, geometric mean [days][6]	909 (admissions)	Juvenile DM (prim. diagn.)	Non-DM	2.5 vs 2.7	-0.2; p>0.05
	495 (admissions)	Juvenile DM (second. diagn.)		3.75 vs 2.7	**+1,05 (+39%); p<0.0001**
ICU admission (during hospitalization)[2]	160,528 (admissions)	DM/PM	Non-DM/PM	NR	**OR=1.94 (95% CI: 1.84-2.05); p<0.01**
Angiography (during hospitalization)[2]	160,528 (admissions)	DM/PM	Non-DM/PM	NR	**OR=1.15 (95% CI: 1.06-1.25); p<0.01**
Use of MRI (during hospitalization)[2]	160,528 (admissions)	DM/PM	Non-DM/PM	NR	**OR=1.68 (95% CI: 1.35-2.09); p<0.01**
Use of tomography scans (during hospitalization)[2]	160,528 (admissions)	DM/PM	Non-DM/PM	NR	**OR=1.90 (95% CI: 1.50-2.41); p<0.01**
HEALTHCARE RESOURCE UTILIZATION (non-comparative studies)					
Ever hospitalized (%)[7]	33 354	Juvenile PM Juvenile DM	NA	71.9% (23/33) 52.1% (176/354)	
Ever wheelchair used (%)[7]	33 354	Juvenile PM Juvenile DM	NA	31.3% (10/33) 16.9% (58/354)	
Hospitalization/year (%)[8]	524	DM	NA	22.1% (116/524)	
• Myositis-related/year (%)[8]	524	DM	NA	10.7% (56/524); **increasing trend with an increasing disease flare freq. (6.1% – none to 15.7% - ≥4 flares/year; p=0.029)**	
ED/urgent care visits/year (%)[8]	524	DM	NA	41% (210/524)	
• Myositis-related/year (%)[8]	524	DM	NA	17/9% (94/524); **increasing trend with an increasing disease flare freq. (9.1% - none to 23.1% - ≥4 flares/year; p=0.009)**	
30-day readmission rate/year (%)[9]	NR	DM	NA	26.6%	
• All-cause/year (%)[8] • Same-cause/year (%)[9]	NR	DM	NA	18.3% 30.8%	

Table 2. Direct and indirect cost of DM/PM (References: 1 Bradford Rice 2016, 2 Ungprasert 2020; 3 Kwa 2017; 4 Kwa 2018; 5 Zhang 2019; 6 Christopher-Stine 2020)

OUTCOME	N of PATIENTS	STUDY POPULATION	CONTROL / REFERENCE	RESULTS	DIFFERENCE vs CONTROL; p-value (when applicable)
DIRECT COST					
Medical and prescription cost, mean [USD][1]	2587	DM/PM	Matched non-DM/PM	14,622 vs 14,276	+346; p=0.115
Total hospitalization charge, mean [USD][2]	39,253 (admissions)	DM/PM	Non-DM/PM	55,774 vs NR	**+13,531 (95% CI: 12,184-14,789), p<0.001**
Hospitalization cost (inpatient care), mean [USD][2]	39,253 (admissions)	DM/PM	Non-DM/PM	16,817 vs NR	**+4,216 (95% CI: 3,869-4,563); p<0.01**
Total hospitalization cost [USD][3]	11,092 (admissions)	DM (prim. diagn.)	DM (second. diagn.)	168,076,970 vs 643,816,887	NR
Hospitalization cost, geometric mean [USD][3]	2,042 (admissions)	DM (prim. diagn.)	Non-DM	11,682 vs 7,620	**+53%; p<0.0001**
	9,050 (admissions)	DM (second. diagn.)	Non-DM	9,712 vs 7,620	**+27%; p<0.0001**
Total hospitalization cost [USD][4]	1,404 (admissions)	Juvenile DM (prim. diagn.)	Juvenile DM (second. diagn.)	49,339,995 vs 49,784,853	NR
Hospitalization cost, geometric mean [USD][4]	909 (admissions)	Juvenile DM (prim. diagn.)	Non-DM	7,350 vs 4,479	**+64%; p<0.0001**
	495 (admissions)	Juvenile DM (second. diagn.)	Non-DM	7,352 vs 4,479	**+64%; p<0.0001**
Total cost of readmission [USD][5]	NR	DM	NA	29.3 million between years 2010-2014	
INDIRECT COST					
Workdays lost/year, mean[1]	616	DM/PM	Matched non-DM/PM	17.5 vs 15.5	**+2; p<0.001**
• Medically-related workday loss[1]	616	DM/PM	Matched non-DM/PM	10.7 vs 9.5	**+1.2; P<0.001**
• Disability-related workday loss[1]	616	DM/PM	Matched non-DM/PM	6.8 vs 6.0	+0.8; p=0.977
Total myositis-related productivity loss/past week, mean (SD) [% of workdays][6]	215	DM/PM	NA	**27.65% (28.7%); Increasing trend with increasing disease flare freq. (4.56% - none to 42.15% - ≥4 flares/year, p<0.001)**	
• Myositis-related work time loss/past week (absenteeism), mean (SD) [% of workdays][6]	215	DM/PM	NA	**8.97% (20.72%); increasing trend with increasing disease flare freq. (0.63% - none to 15.23% - ≥4 flares/year, p=0.046)**	
• Myositis-related time impaired while working/past week (presenteeism), mean (SD) [% of workdays][6]	215	DM/PM	NA	**22.15% (23.07%); Increasing trend with increasing disease flare freq. (4% - none to 32.5% - ≥4 flares/past year, p<0.001)**	

in the US was estimated at $49 million and $168 million for juvenile and adult patients, respectively, with a substantial cost increase to $644 million for hospitalizations due to various morbidities or comorbidities in adult patients (DM as secondary inpatient diagnosis). These costs were increased by 27–64% when compared with inpatients without DM. On average, mean hospital costs to payers were $55,000, which was $13,000 higher relative to inpatients without DM/PM (Table 2). Two studies evaluated indirect costs related to DM/PM and showed an increased, disease-related productivity loss (on average, 2 workdays loss vs matched controls, or 27.65% missed workdays/week) that was also associated with disease flare frequency.

Conclusion: Most of the published evidence focuses on direct hospital care suggesting DM/PM generate significant costs to the healthcare system. Moreover, there is significant direct and indirect economic burden related to the treatment of DM/PM, suggesting unmet need for exploring novel therapeutics in clinical trials to safe and efficacious therapies. Given the limited evidence on the HCU and associated costs of DM/PM in the US, additional research on this topic is warranted.

Disclosure: R. Aggarwal, Mallinckrodt, 1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2; **K. Gwathmey**, Alexion, 2, 6, Argenx, 2; **R. Leff**, Multiple Pharmaceutical Companies, 2, 11; **K. Pisarczyk**, Kezar Life Sciences, Inc, 2; **I. Aleksanderek**, None; **K. Palaniswamy**, None; **N. Henig**, Kezar Life Sciences, 4, 10, 11.

Abstract Number: 1040

Monoclonal Gammopathy in Autoimmune Diseases: Analysis and Follow-up of 160 Cases in a Tertiary Center in China

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Monoclonal gammopathy (MG) in patients with autoimmune diseases (AID) is pretty common, but the outcomes and predictors for hematological neoplasm (HN) progression have not been well characterized.

Methods: Patients diagnosed of AID complicated with MG in Peking Union Medical College Hospital from January 2010 to June 2017 were systematically reviewed, and followed up. Recognition of HN was set as the primary observational endpoint. Cox proportional hazard regression analysis was applied to identify possible risk predictors.

Results: Of 160 patients with AID and MG, the median time between AID diagnosis and MG diagnosis was 0.6 months (IQR: 0-42.3 months) with 87 (54.4%) patients diagnosed with AID and MG simultaneously. The most common AID was primary Sjögren's syndrome (37, 23.1%), followed by rheumatoid arthritis (28, 17.5%) and systemic lupus erythematosus (25, 15.6%). About 62.5% (n=100) of AID patients in our cohort were having active disease at the detection of M protein. Thirty-nine (24.4%) patients developed HN during the follow-up (median: 3.7 years, IQR: 0.3-5.5 years) including multiple myeloma (22, 56.4%), lymphoma (9, 23.1%), macroglobulinemia (4, 10.3%), amyloidosis (3, 7.7%), and plasmacytoma (1, 2.6%) (Table 1.). The cumulative probability of HN progression was 21.8% at 1 year, 22.6% at 3 years, and 29.3% at 6 years after the finding of MG, respectively (Fig. 1A). High levels of monoclonal protein (M protein > 14.35% of total serum protein) (HR 11.71, 95%CI: 5.37-25.54, p< 0.001), significant weight loss (HR 6.24, 95%CI: 2.87-13.59, p< 0.001), and reduction of other types of immunoglobulins (HR 3.02, 95%CI: 1.40-6.48, p=0.005) were independent risk indicators. Types of M protein (Fig. 1B), disease activity, and treatment of AID (Fig. 1C) seemed unrelated to HN in our cohort.

Conclusion: Around one-fourth of MG in patients with AID develop HN, indicating that though MG mostly is a benign process in patients with AID, it can be the prelude for HN in certain group of this population. High levels of M protein, weight loss, and the reduction of other immunoglobulins are predisposing factors that warrant vigorous follow-up and monitoring.

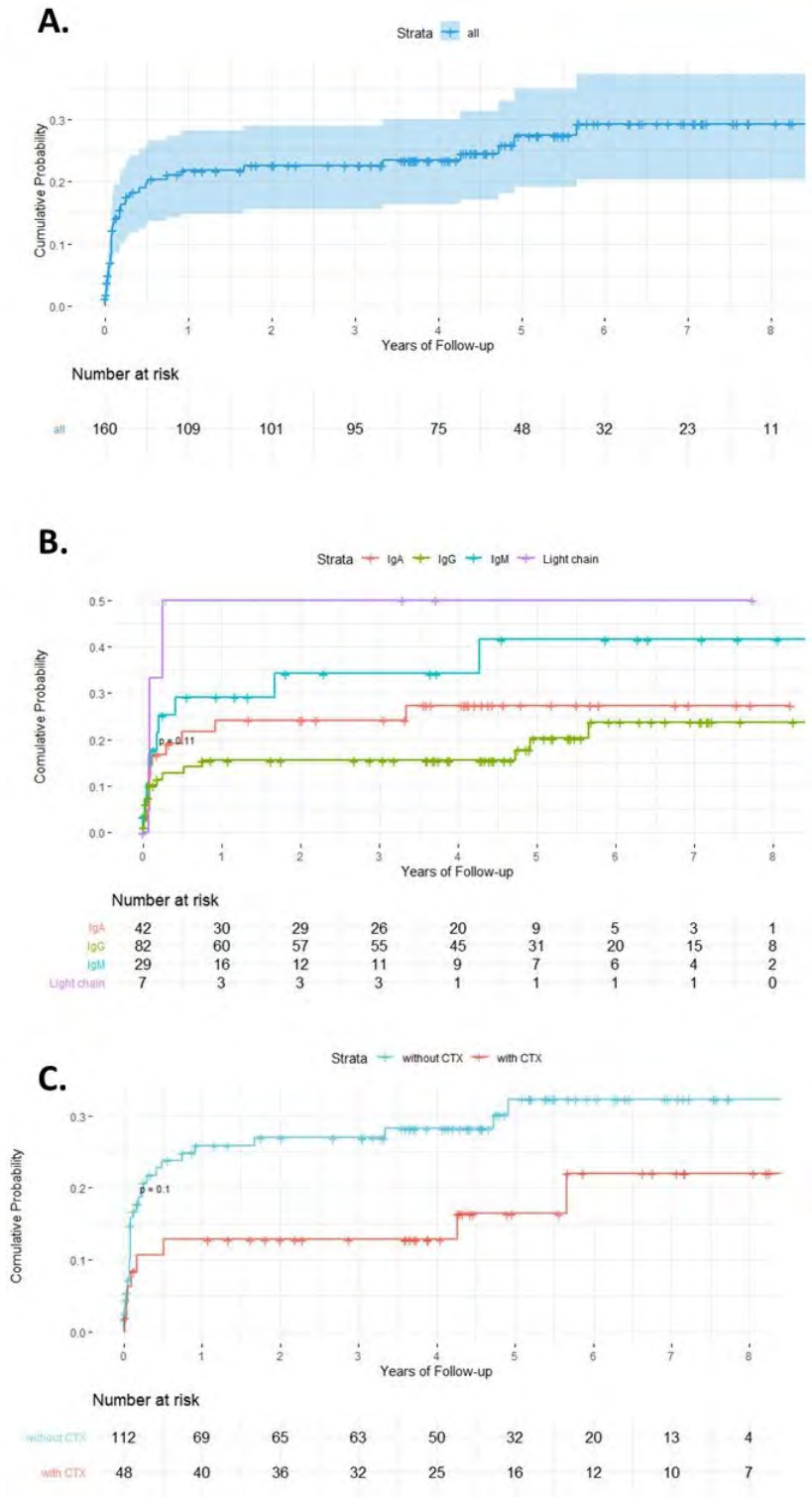

Figure 1. Survival analysis of patients with autoimmune diseases (AID) and monoclonal gammopathy. (A) Kaplan-Meier HN cumulative probability of monoclonal gammopathy patients with AID. (B) Kaplan-Meier hematological neoplasm (HN) cumulative probability of patients stratified with the type of M protein. (C) Kaplan-Meier HN cumulative probability of patients stratified with the use of cyclophosphamide. CTX: cyclophosphamide.

Table 1. Demographics of the autoimmune disease patients who developed hematological neoplasms during follow-up.

	Total	Plasma cell neoplasms		Lymphoma	Other plasma cell neoplasms	
		Multiple myeloma	Plasmacytoma		Macroglobulinemia	Amyloidosis
Number	39	22 (56.4%)	1 (2.6%)	9 (23.1%)	4 (10.3%)	3 (7.7%)
Sex, female (n, %)	27 (69.2%)	12 (54.5%)	1 (100%)	8 (88.9%)	3 (75.0%)	3 (100%)
Age at HN diagnosis (mean (SD), years)	60 (12)	60 (12)	33	59 (11)	65 (16)	59 (10)
Time between AID diagnosis and HN diagnosis (median (IQR), months)	7.3 (1.0-59.8)	5.6 (0.9-41.9)	42.43	62.7 (27.3-328.7)	15.2 (0.7-47.0)	1.0 (0.1, 3.0)
Type of M protein						
IgG (n, %)	15 (38.5%)	12 (54.5%)	1 (100%)	1 (11.1%)	0	1 (33.3%)
IgA (n, %)	11 (28.2%)	7 (31.8%)	0	4 (44.4%)	0	0
IgM (n, %)	10 (25.6%)	2 (9.1%)	0	4 (44.4%)	4 (100%)	0
Light chain (n, %)	3 (7.7%)	1 (4.5%)	0	0	0	2 (66.7%)
Type of AID						
SLE (n, %)	5 (12.8%)	5 (22.7%)	0	0	0	0
RA (n, %)	9 (23.1%)	7 (31.8%)	0	1 (11.1%)	1 (25.0%)	0
pSS (n, %)	9 (23.1%)	4 (18.2%)	0	4 (44.4%)	1 (25.0%)	0
SSc (n, %)	3 (7.7%)	2 (9.1%)	0	0	1 (25.0%)	0
IIM (n, %)	1 (2.6%)	0	0	1 (11.1%)	0	0
Vasculitis (n, %)	2 (5.1%)	1 (4.5%)	0	1 (11.1%)	0	0
PMR (n, %)	1 (2.6%)	1 (4.5%)	0	0	0	0
PBC (n, %)	1 (2.6%)	0	0	1 (11.1%)	0	0
IgG4-RD (n, %)	3 (7.7%)	1 (4.5%)	0	1 (11.1%)	1 (25.0%)	0
AS (n, %)	1 (2.6%)	1 (4.5%)	0	0	0	0
UCTD (n, %)	4 (10.3%)	0	1 (100%)	0	0	3 (100%)

SLE: systemic lupus erythematosus; RA: rheumatoid arthritis; pSS: primary Sjögren's syndrome; SSc: systemic sclerosis; IIM: idiopathic inflammatory myopathies; PMR: polymyalgia rheumatica; PBC: primary biliary cirrhosis; IgG4-RD: IgG4-related disease; AS: ankylosing spondylitis; UCTD: undifferentiated connective tissue disease

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Abstract Number: 1041

Do Cancer Risks Increased in the Five Major Autoimmune Diseases? A Large Cohort Study in China

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Cancer is a comorbidity of concern for the long-term prognosis in autoimmune disease (AID) patients. This study investigated cancer incidence and risks in five major AIDs in a large cohort of Chinese patients, compared with the general population.

Methods: The cohort retrospectively enrolled 8120 AID inpatients with SLE, RA, SS, SSc, or IIM admitted to Peking Union Medical College Hospital from January 2006 to April 2015. Cancer occurrences were consecutively followed

Table 1. Demographics, follow-up, and cancer occurrence of the cohort and AID-CA patients

Variables	All CTDs n=8120	SLE n=3794	RA n=1658	SS n=1329	IIM n=964	SSc n=375
Median age at cohort entry (years) (median, IQR)	43.8 (29.8-57.9)	31.2 (21.1-41.4)	57.8 (48.9-66.8)	53.7 (43.6-63.7)	48.3 (38.2-58.4)	48.8 (38.8-58.4)
Gender ratio (Female/Male)	4.82 (6726/1394)	6.66 (3299/495)	3.02 (1246/412)	9.55 (1203/126)	2.31 (673/291)	4.36 (305/70)
Follow-up time (person-years)	58726.53	19601.91	6787.29	6390.49	6144.29	1802.58
Observed cancer (n)	430	90	162	84	67	27
Expected cancer*	127.42	34.92	40.64	29.18	15.53	7.16
SIR (95%CI)	3.37 (3.06-3.71)	2.58 (2.07-3.17)	3.99 (3.40-4.65)	2.88 (2.30-3.56)	4.31 (3.34-5.48)	3.77 (2.49-5.49)
Incidence rate (per 100,000 person-years)	1110.35	459.14	2386.82	1314.45	1616.68	1497.85
Age at cancer diagnosis, median (IQR) (years)	57.5 (48.8-66.2)	49.1 (39.8-58.5)	61.5 (53.3-69.6)	61.6 (51.8-71.3)	59.7 (52.5-67)	49.2 (43.1-55.3)
Gender ratio of AID-CA patients (Female/Male)	4.58 (353/77)	21.50 (86/4)	2.77 (119/43)	15.80 (79/5)	2.05 (45/22)	8.00 (24/3)
Time interval between AID and CA diagnosis, Median (IQR) (months)	79.8 (14.2-145.4)	115.2 (62.4-166.8)	121.2 (48.0-194.4)	54.0 (4.8-103.2)	7.2 (0-20.4)	42.0 (3.6-80.4)

*Expected cancer was calculated by multiplying person-years and the cancer incidence of general Chinese population. The estimated cancer incidence rates were age, gender, and site-specific rates in 2006-2015, reported by the National Central Cancer Registry (NCCR) of China.
Abbreviations: AID, autoimmune diseases; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; SS, Sjögren's syndrome; IIM, idiopathic inflammatory myopathies; SSc, systemic sclerosis. IQR: interquartile range; SIR, standardized incidence ratio, CI: confidence interval.

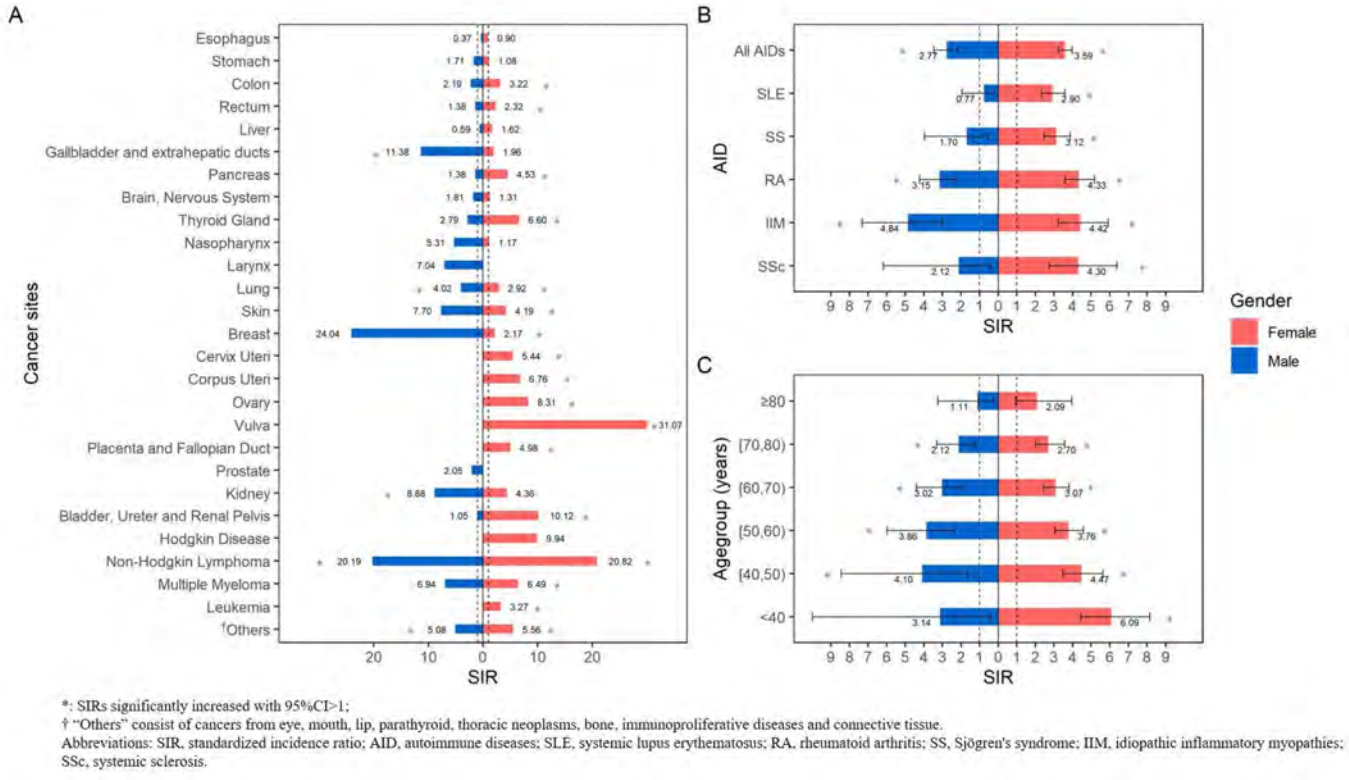
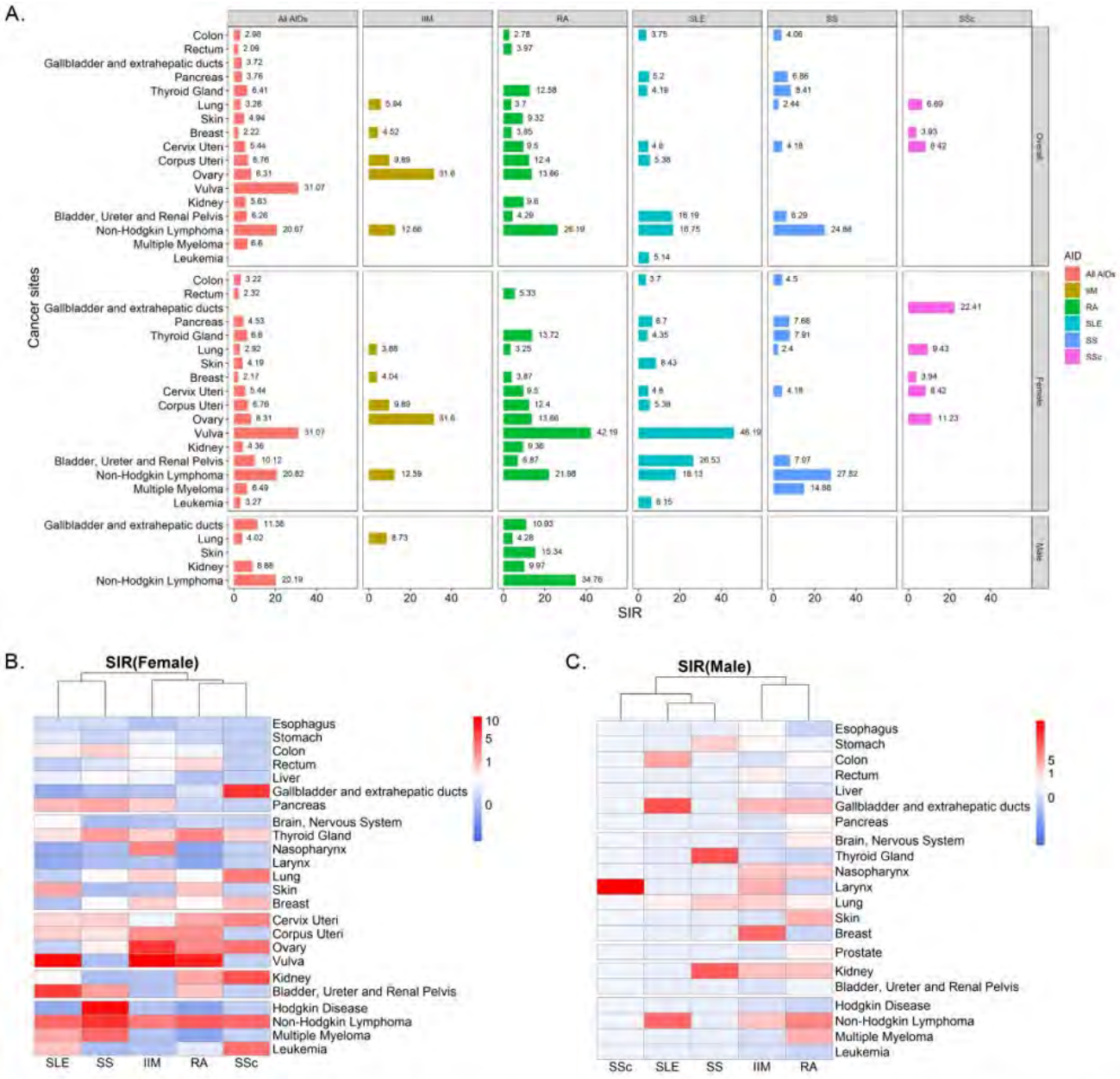


Figure 1. Gender- and age-specific standardized incidence ratios (SIRs) in AID patients and subgroups. (A) SIRs of site-specific cancers for female and male. (B) SIRs in all and each type of AID patients for female and male. (C) SIRs in different age groups (every 10 years) for female and male.



Abbreviations: SIR, standardized incidence ratio; AID, autoimmune diseases; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; SS, Sjögren's syndrome; IIM, idiopathic inflammatory myopathies; SSc, systemic sclerosis.

Figure 2. Site-specific standardized incidence ratios (SIRs) in AID patients and subgroups. (A) Significantly increased SIRs for high-risk cancer in all AID and five types of AID patients. (B) Heatmaps of SIRs in female patients clustered by type of AID. (C) Heatmaps of SIRs in male patients clustered by type of AID.

up by direct contact with the attending clinician or telephone. The demographics, distributions, and standardized incidence ratios (SIRs) were analyzed and compared among the five AIDs.

Results: During 38726.55 person-years of follow-up, 430 (5.3%) patients developed cancer, with a median age of 57.5 (IQR: 48.8-66.2) years and disease duration of 79.8 (IQR: 14.2-145.4) months after the diagnosis of AID (Table 1.). The estimated SIR in all AIDs was 3.37 (95%CI: 3.06-3.71), with the highest in IIM (4.31, 95%CI 3.34-5.48), followed by RA (3.99, 95%CI 3.40-4.65), SSc (3.77, 95%CI 2.49-5.49), SS (2.88, 95%CI 2.30-3.56) and SLE (2.58, 95%CI 2.07-3.17). Gender discrepancy of cancer risks existed, with SIR for female patients (3.59, 95% CI 3.23-3.99)

higher than male (2.77, 95% CI: 2.19-3.46) (Fig. 1A, Fig. 1B). And SIR for younger patients (age< 50) was generally higher than older patients (age≥50) (Fig. 1C). Compared among the five major AIDs, each AID had distinctive features related to cancer (Fig. 2A-C). SLE had significantly increased SIRs of hematologic malignancies and solid tumors located in the urinary tract, female genital organs, pancreas, thyroid, and colon. SS also had a high SIR of non-Hodgkin's lymphoma (NHL). IIM was closely associated with cancer, with 74.6% of cancers diagnosed within 3 years and had increased SIRs of ovarian, corpus uteri, lung, breast, and NHL. In RA populations, a wide distribution of cancers was detected after 15 years since the diagnosis of RA. For SSc, increased SIRs were observed in cervix uteri, lung, and breast cancers.

Conclusion: AID patients in China had an overall increased cancer risk than the general population, with varied site-specific cancer risks in gender, age groups, and AID types.

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Abstract Number: 1042

Multimorbidity Prevalence in Systemic Lupus Erythematosus: A Population-Based Study

Ali Duarte-Garcia[1], Maria Valenzuela-Almada[2], Mehmet Hocaoglu[3], Jesse Dabit[1], Shirley-Ann Osei-Onomah[1], Sebastian Vallejo-Ramos[1], Kurt Greenlund[4], Tina Gunderson[1], Kamil Barbour[4] and Cynthia Crowson[5], [1]Mayo Clinic, Rochester, MN, [2]Division of Rheumatology, Mayo Clinic, Rochester, MN, [3]University of Maryland Medical Center, Midtown Campus, Baltimore, MD, [4]Centers for Disease Control, Atlanta, GA, [5]Mayo Clinic, Eyota, MN

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have a 3-fold increase in all-cause mortality, compared to the general population. Young patients with SLE are 40 and 60 times more likely to have cardiovascular disease and end-stage renal disease, respectively, and have at least twice the risk for psychiatric comorbidities (e.g., depression) than people of comparable age without SLE (Manzi et al. AJE 1997; Choi et al. Medicine 2019)). These and other chronic conditions have emerged as factors contributing to the excess morbidity and shorter lifespan of patients with SLE. To date, characterization of age-, disease- and treatment-related comorbidities associated with SLE has relied almost exclusively on individual comorbidity assessment. We aimed to compare the prevalence of multimorbidity in SLE patients with the general population.

Methods: Prevalent cases of SLE who met the ACR/EULAR classification criteria and were residents in a 27-county area of the United States on January 1, 2015 were included in the study. SLE patients were age-, sex-, race-, and county-matched to subjects from the same underlying population. Diagnosis codes within a five-year lookback period were used to determine the presence of comorbidities; 2 or more codes at least 30 days apart were used to define a comorbidity. A previously published list of 44 comorbidities was considered (England et al. ARD 2020). SLE and cutaneous lupus codes were excluded from the analysis. We defined multimorbidity as the presence of 2 or more comorbidities (excluding SLE) and substantial multimorbidity as the presence of 5 or more comorbidities. Logistic regression models adjusted for age and sex were performed.

Table. Prevalence on 1-1-2015 and odd ratios of comorbidities and multimorbidity (2 or more, 5 or more) in 479 patients with systemic lupus erythematosus (SLE) compared to 479 patients without SLE.

Outcome/Comorbidity	Non-SLE N (%)	SLE N (%)	OR [95%CI] SLE vs non-SLE
Multimorbidity (2 or more)	277 (57.8)	376 (78.5)	**2.96 [2.20-4.02]**
Substantial multimorbidity (5 or more)	122 (25.5)	228 (47.6)	**3.06 [2.28-4.12]**
Pulmonary Circulation Disorders	1 (0.2)	36 (7.5)	**39.0 [8.38-694]**
Anemia	22 (4.6)	141 (29.4)	**8.82 [5.61-14.50]**
Renal Disease	12 (2.5)	75 (15.7)	**7.38 [4.10-14.50]**
Interstitial Lung Disease	4 (0.8)	26 (5.4)	**6.93 [2.67-23.7]**
Valvular Heart Disease	13 (2.7)	48 (10)	**4.20 [2.29-8.24]**
Peptic Ulcer Disease	1 (0.2)	4 (0.8)	4.05 [0.59-79.5]
Osteoporosis	17 (3.5)	57 (11.9)	**3.94 [2.27-7.17]**
Peripheral Vascular Disease/Aneurysm	14 (2.9)	46 (9.6)	**3.74 [2.05-7.24]**
Osteoarthritis	53 (11.1)	126 (26.3)	**3.51 [2.40-5.20]**
Gout	3 (0.6)	10 (2.1)	**3.46 [1.04-15.60]**
Coronary Artery Disease	23 (4.8)	62 (12.9)	**3.22 [1.95-5.50]**
Cancer	18 (3.8)	49 (10.2)	**3.10 [1.78-5.61]**
Fibromyalgia	25 (5.2)	67 (14)	**2.98 [1.87-4.89]**
Inflammatory Skin Diseases	16 (3.3)	44 (9.2)	**2.93 [1.66-5.43]**
Cardiac Arrhythmias	37 (7.7)	90 (18.8)	**2.85 [1.90-4.35]**
Neuropathy	18 (3.8)	45 (9.4)	**2.70 [1.56-4.87]**
Chronic Obstructive Pulmonary Disease	13 (2.7)	33 (6.9)	**2.70 [1.43-5.41]**
Liver Disease	12 (2.5)	31 (6.5)	**2.69 [1.40-5.52]**
Severe Vision Reduction	57 (11.9)	113 (23.6)	**2.63 [1.81-3.85]**
Cerebrovascular Disease	14 (2.9)	34 (7.1)	**2.57 [1.38-5.03]**
Sleep Disorder	27 (5.6)	55 (11.5)	**2.19 [1.37-3.60]**
Chronic Headache	45 (9.4)	82 (17.1)	**2.02 [1.37-3.00]**
Hypertension	148 (30.9)	212 (44.3)	**2.00 [1.49-2.68]**
Congestive Heart Failure	3 (0.6)	36 (7.5)	**13.30 [4.74-55.5]**
Hypothyroid	56 (11.7)	95 (19.8)	**1.97 [1.36-2.88]**
Gastroesophageal Reflux Disease	61 (12.7)	97 (20.3)	**1.79 [1.25-2.56]**
Prostatic Hyperplasia*	6 (7.1)	9 (10.6)	1.66 [0.53-5.61]
Chronic Back Pain	97 (20.3)	139 (29)	**1.63 [1.21-2.20]**
Drug Abuse	6 (1.3)	9 (1.9)	1.51 [0.54-4.56]
Diverticulitis/Diverticulosis	16 (3.3)	23 (4.8)	1.49 [0.77-2.96]
Depression	88 (18.4)	118 (24.6)	**1.46 [1.07-1.99]**
Asthma	26 (5.4)	35 (7.3)	1.37 [0.82-2.34]
Anxiety	71 (14.8)	90 (18.8)	1.33 [0.95-1.88]
Non-Inflammatory Gynecologic Disorders*	69 (17.5)	84 (21.3)	1.28 [0.90-1.83]
Obesity	56 (11.7)	67 (14)	1.23 [0.84-1.80]
Urinary Incontinence	13 (2.7)	15 (3.1)	1.16 [0.54-2.53]
Hyperlipidemia	146 (30.5)	155 (32.4)	1.11 [0.82-1.51]
Hearing Loss	19 (4)	19 (4)	1.00 [0.51-1.95]
Diabetes	41 (8.6)	38 (7.9)	0.92 [0.57-1.47]
Post-Traumatic Stress Disorder	5 (1)	4 (0.8)	0.80 [0.20-3.04]
Alcohol Abuse	12 (2.5)	9 (1.9)	0.74 [0.30-1.78]
Bipolar Disorder	5 (1)	2 (0.4)	0.40 [0.06-1.85]
Dementia	1 (0.2)	0 (0)	0.34 [0.00-6.29]
Parkinson's Disease	3 (0.6)	1 (0.2)	0.32 [0.02-2.6]

*Percentages reflect sex-specific totals for Non-Inflammatory Gynecologic Disorders (N=394 each group) and Prostatic Hyperplasia (N=85 each group).

Results: A total of 479 SLE patients were matched to 479 non-SLE comparators. The mean age was 53.2 (SD 16.2) years and 82.3% were female. 86% were non-Hispanic White. Patients with SLE had 5.3 comorbidities compared to 2.9 among non-SLE subjects. Multimorbidity was present in 78.5% SLE vs. 57.8% non-SLE subjects (OR 2.96; 95%CI 2.2-4.0) and substantial multimorbidity was present in 47.6% SLE patients vs. 25.5% non-SLE subjects (OR 3.06; 95%CI 2.28-4.1). Of the 44 conditions examined, 27 were more common in SLE than in non-SLE (Table).

Conclusion: In this population-based cohort, patients with SLE were 3 times as likely to suffer from multimorbidity and substantial multimorbidity compared to the general population. Most comorbidities were overrepresented in SLE patients. These findings highlight the complex care needs of SLE patients.

Disclosure: A. Duarte-Garcia, None; **M. Valenzuela-Almada**, None; **M. Hocaoglu**, None; **J. Dabit**, None; **S. Osei-Onomah**, None; **S. Vallejo-Ramos**, None; **K. Greenlund**, None; **T. Gunderson**, None; **K. Barbour**, None; **C. Crowson**, None.

Abstract Number: 1043

Prevalence of Multimorbidity in Cutaneous Lupus Erythematosus: A Population-Based Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) patients report impaired quality of life due to cutaneous and psychological morbidity. Previous literature on the prevalence of comorbidities in CLE patients is scarce and the extent of multimorbidity is uncertain. In this population-based study, we aimed to characterize the prevalence of multimorbidity in CLE patients.

Methods: Prevalent CLE cases from a well-defined 27-county region in the United States were included in our study. Cases with concomitant systemic lupus erythematosus (SLE) meeting ACR/EULAR 2019 criteria were excluded. Subjects identified as CLE were age-, sex-, race-, and county-matched to non-CLE subjects from the same population. A five-year lookback period was used for diagnostic codes to determine the presence of comorbidities. Two or more codes ≥30 days apart were used to define a comorbidity. A previously published list of 44 comorbidities was considered (England et al. ARD 2020). CLE and SLE codes were excluded from the analysis. Two or more comorbidities were defined as multimorbidity, 5 or more as substantial multimorbidity. Logistic regression models adjusted for age and sex were used.

Results: 303 CLE patients were matched to 303 non-CLE controls from the same population. The mean age was 59.4 (SD 15.7) years. 72.9% were female. 90.8% were White. CLE patients had 4.7 comorbidities on average compared to 4.0 of non-CLE subjects. Multimorbidity was present in 79.5% CLE vs. 65.7% non-CLE (OR:2.27; 95CI:1.53-3.38) and substantial multimorbidity was present in 43.9% CLE patients vs. 34.3% non-CLE subjects (OR:1.65; 95CI:1.14-2.38). Fibromyalgia, liver disease, chronic obstructive pulmonary disease (COPD), hypertension, anemia, and hypothyroidism were significantly more common in CLE patients compared to controls (Table).

Conclusion: In this population-based study, CLE patients were 2 times more likely to have multimorbidity compared to the general population. It is unclear if the driver of multimorbidity in CLE is the disease itself, treatments, or a combination thereof.

Table. Prevalence on 1-1-2015 and odd ratios of comorbidities and multimorbidity (2 or more, 5 or more) in 303 patients with cutaneous lupus erythematosus (CLE) compared to 303 patients without CLE.

Outcome/Comorbidity	Non-CLE N (%)	CLE N (%)	OR [95%CI] CLE vs non-CLE
Multimorbidity (2 or more)	199 (65.7)	241 (79.5)	**2.27 [1.53-3.38]**
Substantial comorbidities (5 or more)	104 (34.3)	133 (43.9)	**1.65 [1.14-2.38]**
Fibromyalgia	13 (4.3)	37 (12.2)	**3.16 [1.68-6.33]**
Liver Disease	7 (2.3)	17 (5.6)	**2.52 [1.07-6.62]**
Renal Disease	5 (1.7)	12 (4.0)	2.47 [0.89-7.96]
Chronic Obstructive Pulmonary Disease	15 (5.0)	28 (9.2)	**1.97 [1.04-3.88]**
Hypertension	104 (34.3)	139 (45.9)	**1.81 [1.26-2.62]**
Peripheral Vascular Disease/Aneurysm	15 (5.0)	24 (7.9)	1.68 [0.85-3.43]
Anemia	37 (12.2)	55 (18.2)	**1.66 [1.04-2.68]**
Hypothyroid	43 (14.2)	63 (20.8)	**1.64 [1.06-2.56]**
Prostatic Hyperplasia	6 (7.3)	9 (11.0)	1.62 [0.53-5.30]
Inflammatory Skin Diseases	23 (7.6)	35 (11.6)	1.60 [0.92-2.82]
Severe Vision Reduction	61 (20.1)	78 (25.7)	1.56 [0.99-2.48]
Peptic Ulcer Disease	2 (0.7)	3 (1.0)	1.50 [0.25-11.47]
Coronary Artery Disease	29 (9.6)	39 (12.9)	1.44 [0.84-2.51]
Anxiety	52 (17.2)	69 (22.8)	1.43 [0.96-2.15]
Non-Inflammatory Gynecologic Disorders	33 (14.9)	43 (19.5)	1.42 [0.84-2.40]
Depression	65 (21.5)	82 (27.1)	1.37 [0.94-2.01]
Chronic Headache	31 (10.2)	40 (13.2)	1.36 [0.81-2.27]
Interstitial Lung Disease	6 (2.0)	8 (2.6)	1.33 [0.46-4.11]
Valvular Heart Disease	14 (4.6)	18 (5.9)	1.29 [0.61-2.78]
Osteoporosis	23 (7.6)	28 (9.2)	1.27 [0.67-2.42]
Chronic Back Pain	78 (25.7)	91 (30.0)	1.25 [0.87-1.79]
Sleep Disorder	20 (6.6)	24 (7.9)	1.22 [0.66-2.28]
Alcohol Abuse	10 (3.3)	12 (4.0)	1.21 [0.51-2.94]
Drugs	5 (1.7)	6 (2.0)	1.21 [0.35-4.35]
Pulmonary Circulation Disorders	6 (2.0)	7 (2.3)	1.16 [0.38-3.67]
Gastroesophageal Reflux Disease	45 (14.9)	50 (16.5)	1.14 [0.73-1.78]
Neuropathy	23 (7.6)	26 (8.6)	1.14 [0.63-2.07]
Congestive Heart Failure	15 (5.0)	17 (5.6)	1.11 [0.52-2.40]
Hearing Loss	19 (6.3)	21 (6.9)	1.10 [0.55-2.18]
Asthma	22 (7.3)	23 (7.6)	1.05 [0.57-1.93]
Post-Traumatic Stress Disorder	2 (0.7)	2 (0.7)	0.99 [0.12-8.47]
Osteoarthritis	62 (20.5)	61 (20.1)	0.97 [0.63-1.48]
Cardiac Arrhythmias	36 (11.9)	34 (11.2)	0.92 [0.55-1.55]
Cancer	17 (5.6)	16 (5.3)	0.92 [0.45-1.89]
Urinary Incontinence	9 (3.0)	8 (2.6)	0.88 [0.32-2.34]
Bipolar	6 (2.0)	5 (1.7)	0.83 [0.24-2.79]
Gout	5 (1.7)	4 (1.3)	0.79 [0.19-3.05]
Hyperlipidemia	122 (40.3)	108 (35.6)	0.79 [0.55-1.13]
Obesity	43 (14.2)	34 (11.2)	0.76 [0.47-1.23]
Cerebrovascular Disease	15 (5.0)	12 (4.0)	0.76 [0.33-1.69]
Diverticulitis/Diverticulosis	13 (4.3)	10 (3.3)	0.74 [0.31-1.74]
Diabetes	49 (16.2)	26 (8.6)	0.48 [0.28-0.79]
Dementia	2 (0.7)	0 (0.0)	0.18 [0.00-2.32]

Disclosure: M. Hocaoglu, None; **M. Davis**, None; **M. Valenzuela-Almada**, None; **J. Dabit**, None; **S. Osei-Onomah**, None; **S. Vallejo-Ramos**, None; **T. Gunderson**, None; **K. Greenlund**, None; **K. Barbour**, None; **C. Crowson**, None; **A. Duarte-Garcia**, None.

Abstract Number: 1044

Older Patients with Rheumatic Disease Are Commonly Prescribed Potentially Inappropriate Medications

Christine Anastasiou, Michael Evans, Gabriela Schmajuk and Jinoos Yazdany, University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

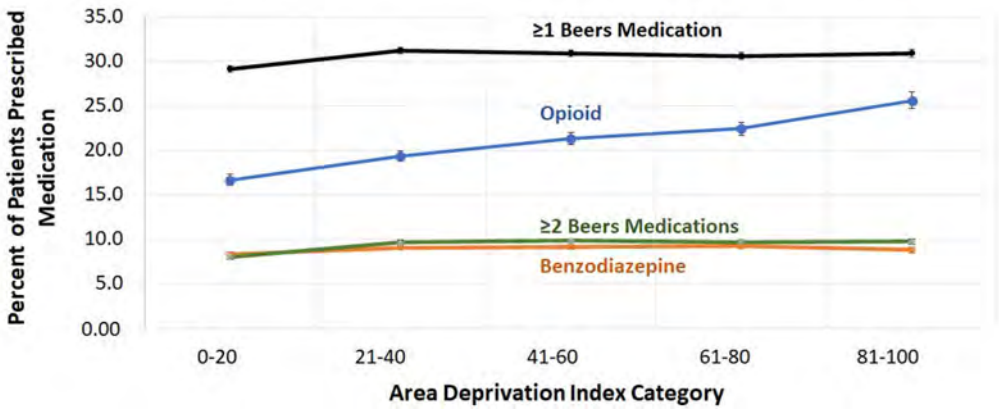
Session Time: 8:30AM–10:30AM

Background/Purpose: Reducing exposure to potentially inappropriate medications (PIMs) in older adults may minimize adverse drug events. The American Geriatrics Society (AGS) Beers Criteria® of Potentially Inappropriate Medication Use provides guidance regarding medications that should be avoided in older adults. Since opioids are associated with an increased risk of cognitive impairment, falls with fracture, and adverse drug-drug interactions in older adults, we also included opioids in the analysis. We used a population-based sample of older adults seen by rheumatologists to assess PIM use and identify risk factors.

Methods: Adult patients ≥ 65 years old with ≥ 2 visits in 2018 at a clinical rheumatology practice participating in the RISE registry were included. We focused on patients with 6 rheumatic diseases commonly associated with pain: OA, gout, RA, PsA, SLE, and SSc. Diagnosis was defined by ≥ 2 ICD-10 CM codes ≥ 30 days apart. Each patient was given one diagnosis for this analysis based on a simple predetermined hierarchy (OA, gout, RA, PsA, SLE, SSc). Medications of interest were those listed by the AGS Beers Criteria® with a 'strong recommendation to avoid', or opioids. The frequency and percent of patients with these medications listed on their medication list was determined. We developed several logistic regression models in which the outcome estimated the odds of patients taking these medications (≥1 Beers Medication, ≥2 Beers Medication, opioid, or benzodiazepine) and covariates included patient area deprivation index, age, gender, rheumatic diagnosis, Deyo-Charlson comorbidity index, insurance, and race/ethnicity. Marginal predictions and 95% confidence intervals were obtained.

Results: We included 178,833 older adults (mean age 75+/-7) from 217 practices. Forty percent of older adults seen in these rheumatology practices had a PIM on their medication list. Rates differed slightly between diseases (45% OA, 37% gout, 37% RA, 39% PsA, 42% SLE, 40% SS). Patients were most likely to have a prescription for opioids (17%), NSAIDs (12%), benzodiazepines (7%), or anticholinergics (4%). Older adults living in more socioeconomically disadvantaged neighborhoods were more likely to have an opioid prescription. Other factors associated with a higher odds of opioid prescription included female gender; OA, gout or PsA diagnosis; Medicaid insurance; and American Indian or Alaskan Natives race/ethnicity. Lower odds of opioid prescription was associated with older age and Asian race/ethnicity. Area deprivation index was not associated with other assessed PIM use (Figure).

Figure. Percent of Older Adults with Potentially Inappropriate Medication Use Based on Area Deprivation Index



Conclusion: Older adults with rheumatic disease were more likely to have an opioid prescription if they lived in a socioeconomically disadvantaged area. In contrast, other PIM prescriptions assessed did not vary based on the level of disadvantage in the area of residence. Future research should evaluate ways to reduce potentially harmful medications such as opioid and benzodiazepine use in older patients with rheumatic disease, and determine what factors are driving the increased opioid prescriptions associated with living in more deprived areas.

Beers Medication refers to medications listed in the American Geriatrics Society (AGS) Beers Criteria® with a strong recommendation to avoid. Marginal predictions and 95% confidence intervals from several logistic regression models with outcomes shown (≥1 Beers Medication, ≥2 Beers Medication, Opioid, or Benzodiazepine) based on patient area deprivation index and including age, gender, rheumatic diagnosis, Deyo-Charlson comorbidity index, insurance, and race/ethnicity as covariates.

Disclosure: C. Anastasiou, None; **M. Evans**, None; **G. Schmajuk**, None; **J. Yazdany**, Astra Zeneca, 2, 5, Pfizer, 2, 6, Gilead, 5, BMS Foundation, 5.

Abstract Number: 1045

Composition of Phospholipid Fatty Acids in Erythrocyte Membranes from Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: To investigate the composition of phospholipid fatty acids in erythrocyte membranes from patients with ankylosing spondylitis (AS), and determine the correlations between the percentage of fatty acids and inflammation level, disease activity and functional capacity in a cross-sectional study.

Methods: Fatty acids in erythrocyte membranes of 20 healthy subjects and 59 patients with AS, who fulfilled the modified New York criteria, were measured using gas chromatography-mass spectrometric (GC-MS). Inflammation level was measured by the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Disease activity was quantified using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS), and functional capacity was Bath Ankylosing Spondylitis Functional Index (BASFI).

Results: Lower docosahexaenoic acid (DHA) and higher palmitic acid and dihomo-γ-linolenic acid (DGLA) were found in erythrocyte membranes from patients with AS compared with healthy subjects (Table 1). There were negative correlations of palmitic acid with BASDAI and BASFI ($r=-0.38$ and $r=-0.36$, respectively, $p<0.05$; Table 2), and there were positive correlations of DGLA with ESR, CRP and ASDAS ($r=0.36$, $r=0.35$ and 0.47, respectively, $p<0.05$). DHA was negatively correlated to ESR and CRP ($r=-0.38$ and $r=-0.35$, respectively, $p<0.05$).

Table 1. Composition of phospholipid fatty acids in erythrocyte membranes from 20 healthy controls and 59 patients with ankylosing spondylitis

No.	Fatty acids (in Total FA,%)		Healthy Controls(n=20)	AS Patients(n=59)
1	Octanoic acid	C8:0	0.00(0.00)	0.00(0.00)
2	Decanic acid	C10:0	0.00(0.00)	0.00(0.00)
3	Lauric acid	C12:0	0.08(0.13)	0.12(0.11)
4	Myristic acid	C14:0	0.23(0.14)	0.27(0.16)
5	Pentadecanoic acid	C15:0	0.00(0.07)	0.00 (0.00)
6	Palmitic acid	C16:0	24.77±1.31	25.23±1.31*
7	Palmitoleic Acid	C16:1	0.00(0.00)	0.00(0.00)
8	Heptadecanoic acid	C17:0	0.21(0.05)	0.20(0.06)
9	Stearic acid	C18:0	19.22±1.36	19.27±1.05
10	Oleic acid	C18:1 n-9	11.75(10.00)	12.19(2.00)
11	Linoleic acid (LA)	C18:2 n-6	10.53(3.00)	10.30(3.00)
12	α-Linolenic acid (ALA)	C18:3 n-3	0.00(0.00)	0.00(0.00)
13	γ-Linolenic acid	C18:3 n-6	0.00(6.14)	0.00(0.00)
14	Arachidic acid	C20:0	0.41±0.12	0.43±0.10
15	Eicosenic acid	C20:1	0.00(0.00)	0.00(0.15)
16	Eicosadienoic acid	C20:2	0.25(0.33)	0.27(0.10)
17	Dihomo-γ-linolenic acid (DGLA)	C20:3 n-6	1.12±0.26	1.29±0.33*
18	Arachidonic acid (AA)	C20:4 n-6	15.81±2.33	15.35±1.40
19	Eicosapentaenoic acid (EPA)	C20:5 n-3	0.07(0.39)	0.00(0.26)
20	Behenic acid	C22:0	1.70(0.25)	1.74(0.41)
21	Docosahexaenoic acid (DHA)	C22:6 n-3	4.96±1.47	4.05±1.43*
22	Lignoceric acid	C24:0	4.56±0.62	4.62±0.48
23	Nervonic acid	C24:1	4.15(0.56)	3.94(0.83)
24	Total SFA		51.96(5.00)	51.87(2.00)
25	Total PUFA		48.04(4.54)	48.13(1.576)
26	n-3 PUFA		5.18±1.70	4.17±1.00
27	n-6 PUFA		26.97(12.00)	26.80(2.00)
28	n-6 PUFA / n-3 PUFA		5.53(4.76)	6.76(3.31)

*$p<0.05$. SFA: saturated fatty acids; PUFA: polyunsaturated fatty acids.

Conclusion: Different composition of fatty acids in erythrocyte membranes was found between healthy subjects and patients with AS, and palmitic acid, DGLA and DHA were correlated to inflammation level, diseases activity and functional capacity.

Table 2. Correlations of Palmitic acid, DGLA, DHA, ω-3 index, n-6 D6D with ESR, CRP, BASDAI, BASFI, ASDAS

	C16:0		C20:3 n-6		C22:6 n-3		ω-3 index		n-6 D6D	
	r	p	r	P	r	p	r	p	r	p
ESR	-0.04	0.769	0.36*	0.006	-0.38*	0.004	-0.36*	0.007	-0.42*	0.001
CRP	-0.17	0.204	0.35*	0.007	-0.39*	0.002	-0.31*	0.018	-0.44*	0.001
BASDAI	-0.38*	0.016	0.21	0.203	0.05	0.774	0.02	0.906	-0.18	0.285
BASFI	-0.36*	0.025	0.26	0.106	-0.09	0.573	-0.10	0.557	-0.24	0.136
ASDAS	-0.19	0.259	0.47*	0.003	-0.27	0.102	-0.23	0.151	-0.40*	0.011

*p<0.05. n-6 D6D: delta-6-desaturase in n-6 PUFA synthesis.

Disclosure: J. Chen, None; **X. Huang**, None; **Q. Huang**, None; **Z. Huang**, None; **Y. Huang**, None; **Y. Liu**, None; **L. Huang**, None; **S. Sun**, None; **Z. ji**, None; **T. Li**, None.

Abstract Number: 1046

Risk of Ocular Comorbidities and Blindness Among Patients with Behçet's Disease: A Nationwide Population-based Cohort Study in Korea

SE RIM CHOI[1], Anna Shin[2], Joo Young Shin[3], Hokyung Choung[3], You-Jung Ha[2], Yun Jong Lee[4], Eun bong Lee[1], Jin Kyun Park[1] and Eun Ha Kang[2], [1]Seoul National University Hospital, Seoul, Republic of Korea, [2]Division of Rheumatology, Department of Internal Medicine, Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [3]Department of Ophthalmology, Seoul National University College of Medicine, SMG-SNU Boramae Medical Center, Seoul, Republic of Korea, [4]Seoul National University Bundang Hospital, Seongnam-si, Republic of Korea

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: To examine the risk of ocular comorbidities in a nation-wide cohort of patients with Behçet's disease (BD) compared to general population in Korea.

Methods: We conducted a population-based cohort study using 2002-2017 Korean National Health Insurance Service database to examine the risk of diverse ocular comorbidities associated with BD compared to general population. Patients with BD and controls were matched on age and sex at a ratio of 1:5. The primary outcome was blindness. Secondary outcomes were uveitis, and surgical procedure requiring cataract, glaucoma, or retinal diseases. Cox proportional hazard ratio models were used to estimate the hazard ratios (HRs) and 95% confidence interval (CIs) for the outcomes comparing BD patients and controls.

Results: A total of 32,288 BD patients and 161,440 controls were included in the study. During a mean 9.38 years of follow-up, the incidence rate per 100 person-years was 0.12 in the BD group and 0.025 in the control group, respectively. The corresponding HR (95% CI) for the primary outcome was 4.92 (4.27 to 5.69). The risk of all secondary

Table 1. Prevalence rates of blindness and ocular complications in the study population

N (%) of affected patients	BD n= 32,288	Control n= 161,440
Blindness	838 (2.60)	963 (0.60)
Uveitis	7,004 (21.69)	4,244 (2.63)
Cataract	3,250 (10.07)	9,414 (5.83)
Glaucoma	295 (0.91)	281 (0.17)
Retinal disorder	403 (1.25)	797 (0.49)
Retinal detachments and breaks	139 (0.43)	316 (0.20)
Retinal vascular occlusions	25 (0.08)	57 (0.04)
Macular/posterior pole degeneration	118 (0.37)	265 (0.16)
Peripheral retinal degeneration	14 (0.04)	36 (0.02)

Table 2. Incidence rates of blindness disability ocular complications

	BD			Controls			HR (95% CI)
	Events	PY	IR (95% CI)	Events	PY	IR (95% CI)	
Blindness	360	298,378	0.12 (0.11–0.13)	386	1,545,268	0.03 (0.02–0.03)	4.92 (4.27–5.69)
Uveitis	4,450	277,375	1.60 (1.56–1.65)	4,042	1,546,354	0.26 (0.25–0.27)	6.23 (5.97–6.51)
Cataract	3,135	301,098	1.04 (1.01–1.08)	9,116	1,545,340	0.59 (0.58–0.60)	1.80 (1.72–1.87)
Glaucoma	276	302,603	0.09 (0.08–0.10)	277	1,550,379	0.02 (0.016–0.020)	5.20 (4.40–6.14)
Retinal disorder	387	302,703	0.13 (0.12–0.14)	791	1,550,132	0.05 (0.05–0.06)	2.55 (2.26–2.88)
Retinal detachments and breaks	135	302,884	0.05 (0.04–0.05)	312	1,550,292	0.02 (0.018–0.022)	2.26 (1.84–2.76)
Retinal vascular occlusions	25	302,966	0.01 (0.005–0.011)	57	1,550,529	0.004 (0.003–0.005)	2.28 (1.43–3.65)
Macular/posterior pole degeneration	113	302,949	0.04 (0.030–0.044)	265	1,550,480	0.02 (0.015–0.019)	2.22 (1.78–2.77)
Peripheral retinal degeneration	14	303,013	0.01 (0.002–0.007)	36	1,550,497	0.002 (0.002–0.003)	2.03 (1.10–3.77)

* The hazard ratios represent the risk for Behçet's disease patients relative to controls.

outcomes was significantly elevated among the patients with BD, with the HR (95% CI) of 6.23 (5.97 to 6.51) for uveitis, 1.80 (1.72 to 1.87) for cataract, 5.20 (4.40 to 6.14) for glaucoma, and 2.55 (2.26 to 2.88) for retinal disorders.

Conclusion: This large population-based study showed that BD patients were at higher risk of diverse ocular comorbidities compared to the general population. In particular, the risk of low vision including blindness was the 4.92 tim es.

Disclosure: S. CHOI, None; **A. Shin**, None; **J. Shin**, None; **H. Choung**, None; **Y. Ha**, None; **Y. Lee**, None; **E. Lee**, None; **J. Park**, None; **E. Kang**, None.

Abstract Number: 1047

Exposure to Industrial Pollutants and Mortality Due to Inmune-mediated Inflammatory Systemic Diseases (IMD) in Spain

ana Perez[1], Arturo Rodriguez Pérez[2], Pablo Fernandez-Navarro[3], Fernando Albarran[4], Cristina Bohorquez[4], Atusa Movasat[4], Lucia Ruiz[4], Paula Pretel[4], elena Rabadan[4], Valentina Emperiale[4], Adrian abbasi[5], julio suarez[5], Lorena Montano[4], emilio rico[5], alfredo prieto[2], melchor Alvarez de Mon[5] and beatriz perez[3], [1]Hospital Universitario Príncipe de Asturias. Rheumatology. Medicine Faculty. Alcala University Department., Madrid, Spain, [2]Faculty of Medicine. Alcala University, Alcala de Henares, Spain, [3]Department of Epidemiology of Chronic Diseases.National Center of Epidemiology/CIBERESP. Instituto de Salud Carlos III, Madrid, Spain, [4]Hospital Universitario Príncipe de Asturias, Rheumatology Department, Alcala de Henares, [5]Hospital Universitario Príncipe de Asturias, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The etiology of many IMD is largely unknown; however, available data suggest that environmental contaminants could play a role in their origin. Industrial facilities are sources of exposure to pollutants in general population. Their possible association with IMD has not been studied.

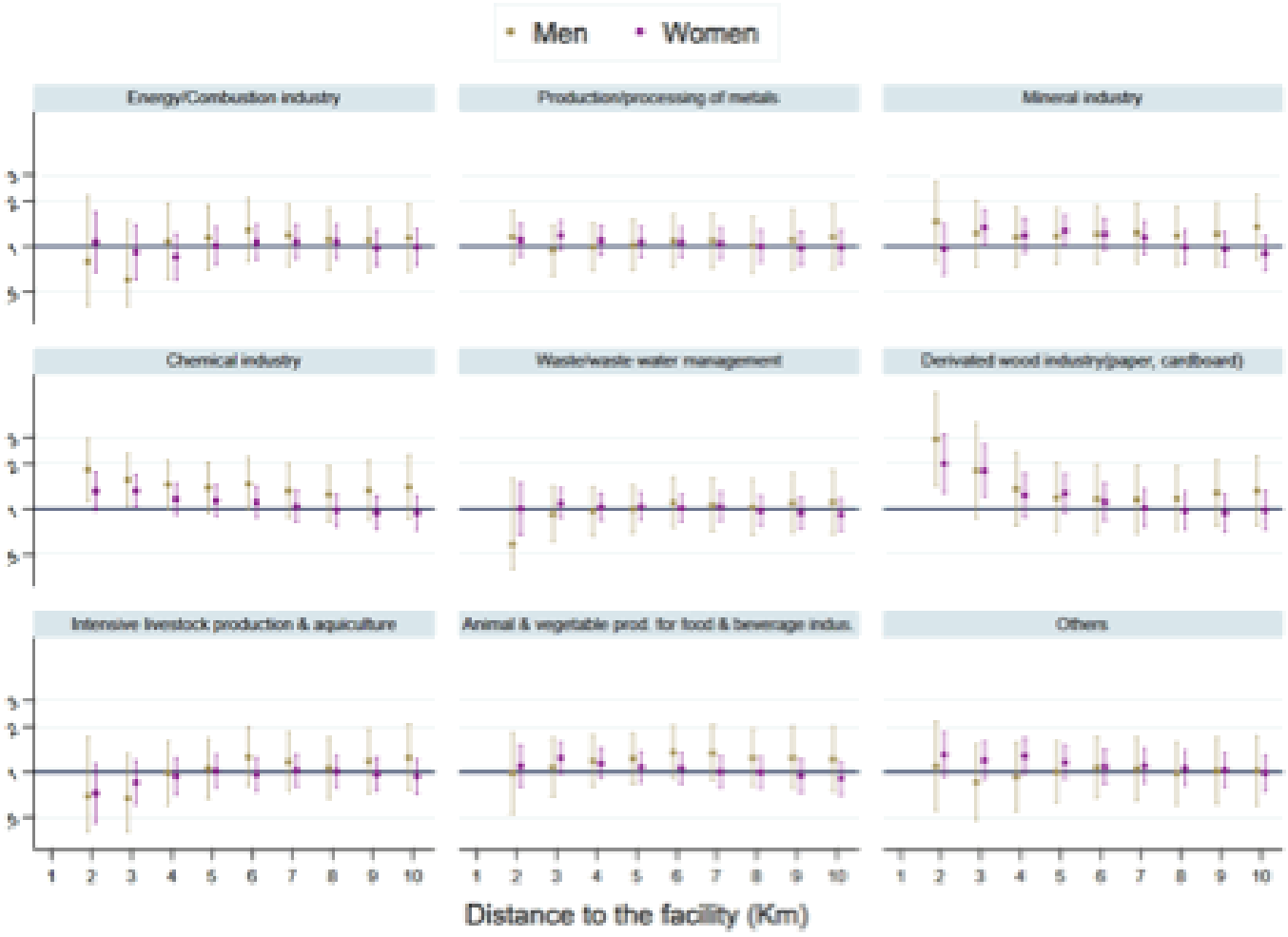


Figure 1. Mortality due to SSc related to distance of industries.

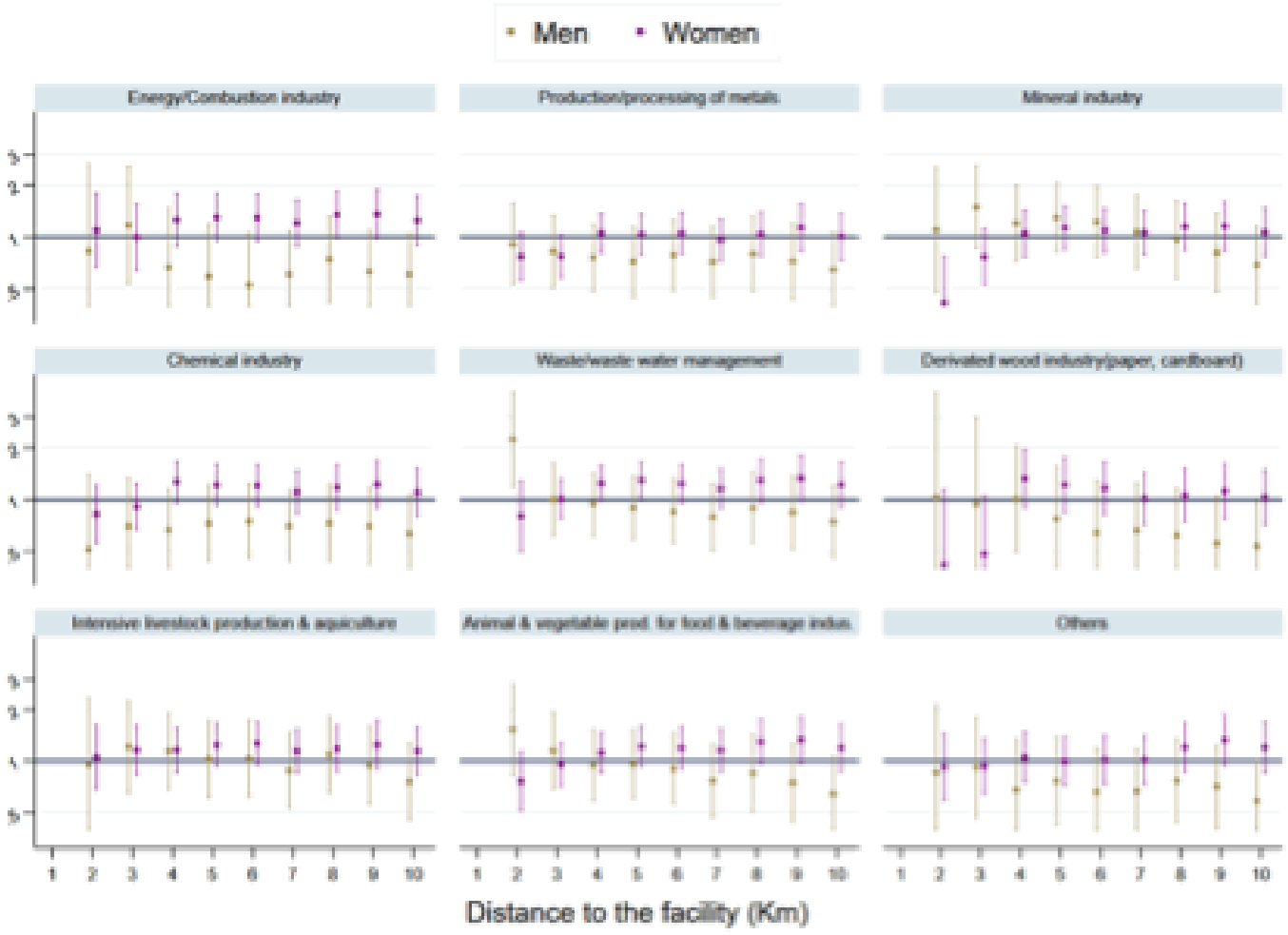


Figure 2. Mortality due to SLE related to distance of industries.

Our purpose was to study whether mortality due to SSc/SLE/Systemic Vasculitis is related to the exposure to environmental pollutants of industrial origin in Spain.

Methods: We obtained mortality due to SSc/SLE/Vasculitis & population data (2005-2014) for each municipality in Spain (8097 towns) from the National Institute of Statistics, & estimated the sex-specific age-adjusted expected deaths with Spain as reference. We collected the coordinates of a) the center of each town; and b) the industrial facilities included in the *Spanish Register of Emissions and Pollutant Sources* (https://prtr-es.es/). Then, we created concentric sectors of different radius (2-10 km) around the pollutant sources to define municipalities' exposure to industrial pollution based on the distance of their population centers to the facilities. Relative risks (RR) between exposed & unexposed municipalities were estimated with Bayesian conditional autoregressive models, using the "Integrated nested approximations" method as inference method (R-INLA library, R statistical program)

Results: SYSTEMIC SCLEROSIS (Figure 1): In both sexes, the highest risks of death due to SSc were found in the vicinity of chemical industries (RR_{men} at 2 km:1.82; 95%CI:1.13-2.94, RR_{women}:1.31;95%CI: 0.98-1.77) and near of paper and wood processing facilities (RR_{men} at 2 km:2.92; 95%CI:1.42-6.00, RR_{women}:2.00; 95%CI:1.28-3.14). In addition, they decreased with increasing distance of the pollutant sources. A less marked association was also found for males with mining industry (RR at 2km:1.21; 95%CI:0.73-2.02).

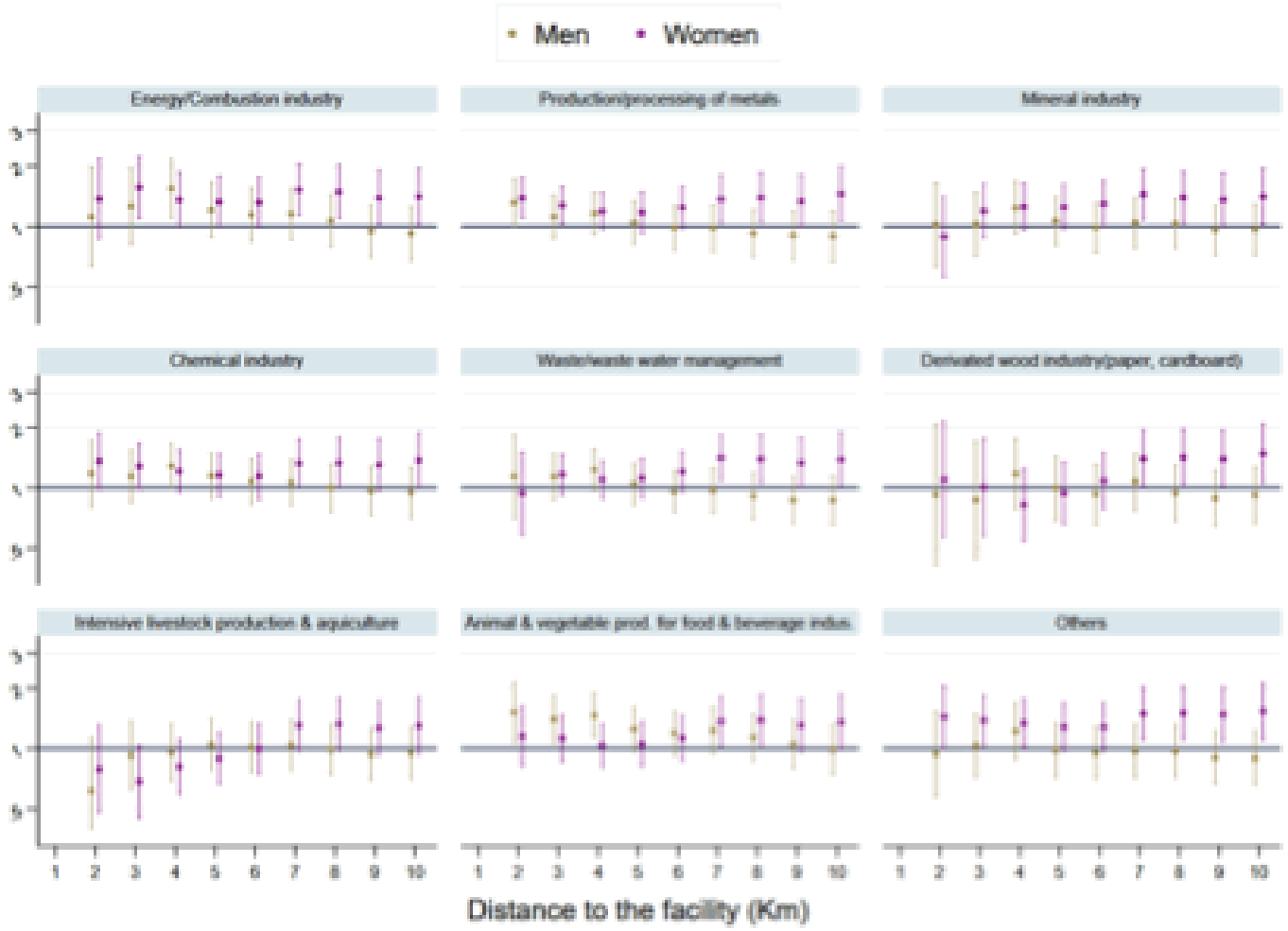


Figure 3. Mortality due to Vasculitis related to distance of industries.

SYSTEMIC LUPUS (Figure 2): In women we did not observe any association; however, in men, there were three sectors with high risks in the closeness of the industries that decreased progressively when moving away: mining facilities (RR at 3 km: 1.50; 95%CI:0.87-2.59), those related to resource and wastewater management (RR at 2 km: 2.23; 95%CI:1.18-4.19) and food industry (RR at 2 km 1.51;95%CI: 0.82-2.78).

SYSTEMIC VASCULITIS (Figure 3): In women, high risk of death was found in the industries of energy & combustion (RR at 2 km:1.38; 95%CI:0.87-2.23), metal processing (RR:1.39; 95%CI:1.10-1.76), chemical (RR:1.36; 95%CI:0.99-1.89) & "other activities" (related to use of organic solvents) (RR: 1.44; 95%CI: 1.01-2.06), but they did not decrease clearly with the distance. For men, there were high RR in the metal (RR:1.32;95%CI:1.00-1.73) and food industries (RR:1.51; 95%CI:1.08-2.14), which decreased with distance from the emitting source.

Conclusion: Residing in the vicinity of certain industries might be a risk factor for dying due to SSc/SLE/Systemic Vasculitis. These results support the possible role of environmental pollution in the origin of these diseases. However, these ecological studies are only exploratory; their results should be confirmed with other studies.

Disclosure: a. Perez, None; **A. Rodriguez Pérez**, None; **P. Fernandez-Navarro**, None; **F. Albarran**, None; **C. Bohorquez**, None; **A. Movasat**, None; **L. Ruiz**, None; **P. Pretel**, None; **e. Rabadan**, None; **V. Emperiale**, None; **A. abbasi**, None; **j. suarez**, None; **L. Montano**, None; **e. rico**, None; **a. prieto**, None; **m. Alvarez de Mon**, None; **b. perez**, None.

Abstract Number: 1048

Estimating the Weight of Rheumatologic Diseases in Mortality in Spain: Basic Cause of Death vs Multiple Cause Analysis

ana Perez[1], Fernando Albarran[2], Cristina Bohorquez[2], Atusa Movasat[2], Lucia Ruiz[2], Paula Pretel[2], elena Rabadan[2], Valentina Emperiale[2], Adrian abbasi[3], julio suarez[3], lorena montano[3], emilio rico[3], alfredo prieto[4], Inmaculada Leon[5], melchor Alvarez de Mon[3] and beatriz perez[6], [1]Hospital Universitario Príncipe de Asturias. Rheumatology. Medicine Faculty. Alcala University Department., Madrid, Spain, [2]Hospital Universitario Príncipe de Asturias, Rheumatology Department, Alcala de Henares, [3]Hospital Universitario Príncipe de Asturias, Madrid, Spain, [4]Faculty of Medicine. Alcala University, Alcala de Henares, Spain, [5]Communicable Diseases. Instituto de Salud Carlos III, Madrid, Spain, [6]Department of Epidemiology of Chronic Diseases.National Center of Epidemiology/CIBERESP. Instituto de Salud Carlos III, Madrid, Spain

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Classical statistics provide information on mortality rates for basic causes of death. Although many inflammatory rheumatic diseases decrease life expectancy, they are generally not a direct cause of death. Since 2016, the Spanish Institute of Statistics provides information on all causes appearing on certificates, in addition to the basic one; this may help to estimate the real burden of this group of diseases on mortality in Spain.

Methods: Population estimates and individual death records for inflammatory rheumatic diseases [ICD10 M05-14; M30-36; M45-46] for 2016-2018 were available from the National Institute of Statistics. We calculated age-adjusted mortality rates by sex and by age group (0-44, 45-64 and ≥ 65) a) using only the basic cause (BC) (Table 1); and b) using the certificates in which these diseases appear anywhere, either as a basic, immediate, intermediate or

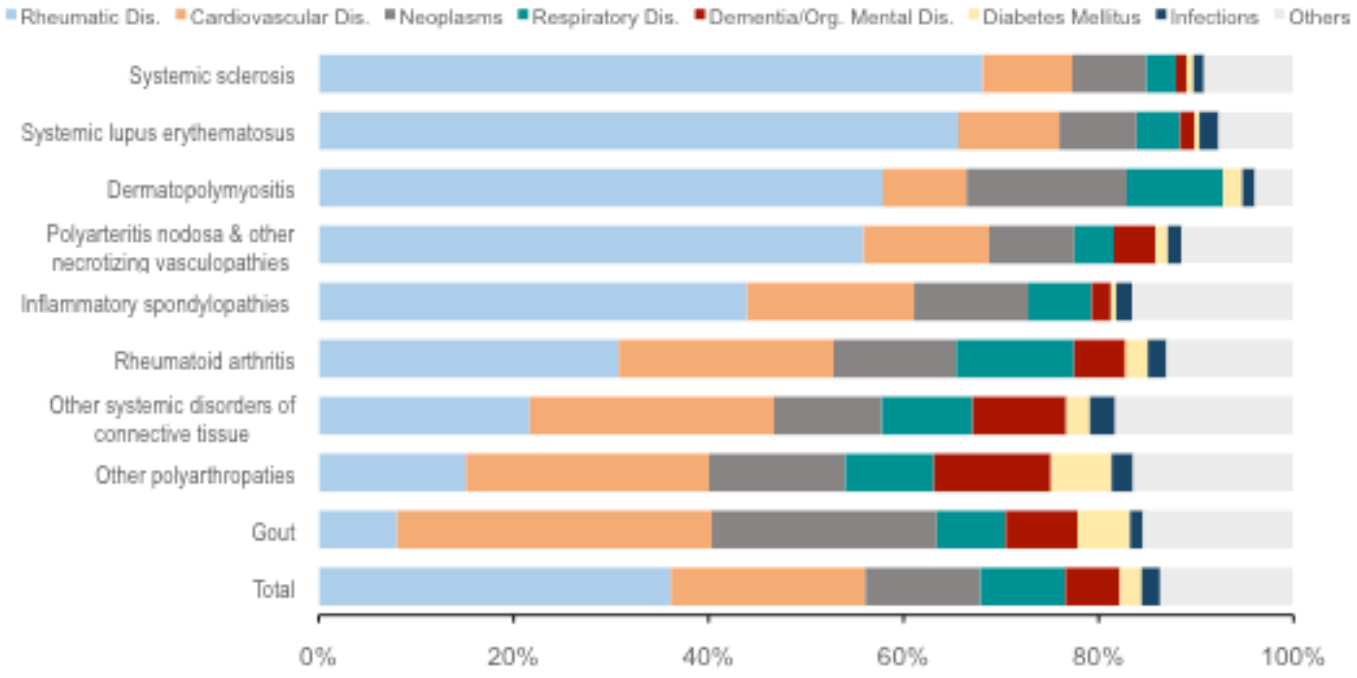


Figure 1. Basic cause of death among deceases registering inflammatory rheumatic diseases in the death certificate. Spain, 2016-2018.

Table 1. Age-adjusted mortality rates in Spain in 2016-18 for all inflammatory rheumatic syndromes using MCD and BC approaches

Inflammatory rheumatic diseases	Age-adjusted* mortality rates (deaths/100.000)												Basic cause deaths/multiple causes deaths (%)					
	Based on basic cause of death						Considering multiple causes of death											
	Global	Men	Women	<45	45-64	>64	Global	Men	Women	<45	45-64	>64	Global	Men	Women	< 45	45-64	> 64
Rheumatoid arthritis	0.21	0.16	0.25	0.01	0.14	2.20	0.71	0.59	0.80	0.01	0.53	7.31	29.4	26.7	30.7	66.7	27.5	29.4
Gout	0.00	0.01	0.00	0.00	0.00	0.05	0.07	0.14	0.02	0.00	0.05	0.72	6.2	3.8	16.7	_	0.0	6.2
Other arthropaties	0.02	0.00	0.03	0.01	0.01	0.13	0.33	0.11	0.10	0.01	0.06	1.09	13.3	3.3	20.0	100	12.5	13.3
Polyarteritis nodosa & other necrotizing vasculopathies	0.12	0.12	0.12	0.03	0.09	1.01	0.29	0.21	0.29	0.04	0.18	1.70	54.6	57.3	52.5	66.7	52.2	54.6
Systemic lupus erythematosus	0.09	0.04	0.14	0.04	0.15	0.62	0.15	0.06	0.23	0.07	0.23	0.72	60.0	61.9	59.6	50.0	65.5	60.0
Dermatopolymyositis	0.03	0.02	0.03	0.01	0.02	0.21	0.05	0.04	0.06	0.01	0.06	0.40	49.1	43.8	51.4	66.7	37.5	49.1
Systemic sclerosis	0.13	0.06	0.19	0.02	0.26	0.81	0.19	0.09	0.27	0.02	0.33	1.32	65.3	65.8	65.2	87.5	79.1	65.3
Other systemic disorders of connective tissue	0.09	0.06	0.11	0.02	0.08	0.74	0.31	0.24	0.37	0.02	0.17	3.16	23.6	25.0	23.0	66.7	30.0	23.6
Inflammatory spondyloarthropathies	0.07	0.11	0.03	0.00	0.08	0.58	0.15	0.26	0.07	0.00	0.19	1.36	46.3	45.3	48.9	50.0	44.0	46.3
Total	0.76	0.59	0.92	0.12	0.85	6.14	1.91	1.72	2.08	0.17	1.76	17.54	34.6	31.6	36.4	64.2	47.2	34.6

* WHO World Standard Population 2001

fundamental cause (MCD) (Table 1). In the latter case, we also describe which are the non-rheumatic basic causes of death in the certificates mentioning rheumatic pathology (Figure1).

Results: Inflammatory rheumatic syndromes appeared in 6998 death certificates (2333 annual average, 63% women), although BC were considered in only 36% of them (833 deaths per year; 66% women), with age-adjusted mortality rates for MDC and BC of 1.56 and 0.64 deaths/100,000 inhabitants, respectively. In the certificates mentioning rheumatic pathology (MCD) in which this was not the basic cause, death was mainly attributed to cardiovascular disease (20%), cancer (12%) and respiratory diseases (10%).

Within age groups, the adjusted rate of MDC for deaths in those under 45 years of age was 0.17 per 100,000 (0.12 as a basic cause); 1.76 for the 45 to 64 range (0.85 as a basic cause); and 17.54 for those over 64 years of age (6.14 as a basic cause). Overall, the rates in women were somewhat higher, although the main differences between sexes were observed in systemic sclerosis and lupus (almost three times more frequent in women) and in spondyloarthritis (in which the male rates were double those of women). Rheumatoid arthritis, as expected, had the highest mortality in both sexes, with adjusted rates based on MDC more than three times higher than those calculated with BC alone (MDC: 0.56/100,000; BC: 0.17/100,000). The change in rates using MDC is rather less marked in the more aggressive entities, such as systemic sclerosis or systemic lupus erythematosus, and especially in deaths in persons younger than 45 years. In these subgroups, rheumatologic diseases are the basic cause of death in almost two thirds of the certificates in which they appear, and in almost 90% if we are talking about deaths in young people with systemic sclerosis.

Conclusion: At the population level, these syndromes have a non-negligible importance in terms of mortality, which is underestimated in the classic mortality statistics, based only on basic causes. The underestimation is less in the more severe rheumatologic processes. The rates provided here probably portray a picture closer to reality of the burden that these diseases represent in Spanish mortality.

Disclosure: a. Perez, None; **F. Albarran**, None; **C. Bohorquez**, None; **A. Movasat**, None; **L. Ruiz**, None; **P. Pretel**, None; **e. Rabadan**, None; **V. Emperiale**, None; **A. abbasi**, None; **j. suarez**, None; **I. montano**, None; **e. rico**, None; **a. prieto**, None; **I. Leon**, None; **m. Alvarez de Mon**, None; **b. perez**, None.

Abstract Number: 1049

Multimorbidity Differences Between Systemic Lupus Erythematosus Patients and Comparators in Different Age Groups: A Large Nationwide US Study

Ali Duarte-Garcia[1], Herbert Heien[1], Nilay Shah[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

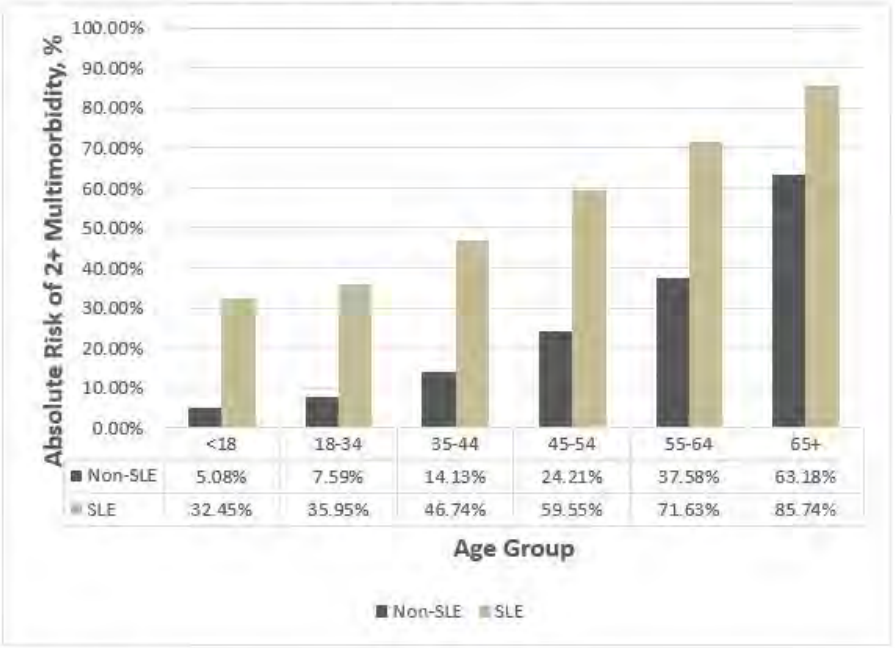
Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) have an increased burden of multimorbidity. Age is strongly associated with accumulation of comorbidities. Patients with SLE may experience multimorbidity at younger ages than their non-SLE controls due to exposure to toxic treatments, disease activity or accelerated aging. We aimed to compare multimorbidity among different age groups of patients with SLE and comparators without SLE.

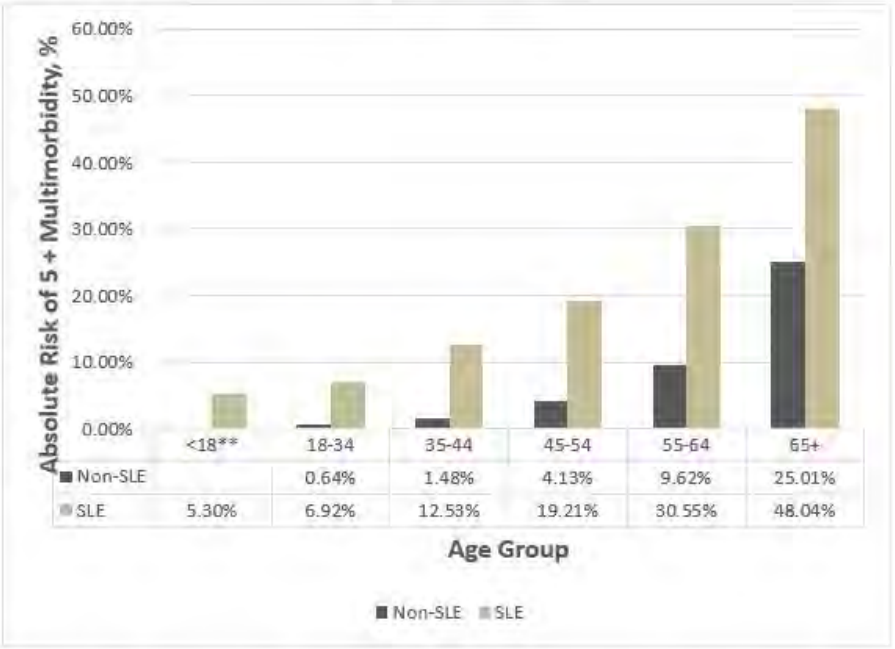
Methods: We used the OptumLabs Data Warehouse (OLDW), a real-world data asset with de-identified administrative claims to identify cases of SLE and matched comparators. Cases were defined as patients with ≥3 diagnoses of SLE between 1/2006 and 9/2015. Comparators were persons without SLE matched 1:1 on age, sex, race/ethnicity, and enrollment date. Race was classified as White, Black, Asian and Hispanic. Multimorbidity (2 or more comorbidities) was defined using 172 chronic comorbidities from the chronic condition indicator of the clinical classification software (healthcare cost and utilization project). Two or more ICD-9 codes at least 30 days apart were used to define a comorbidity. SLE, cutaneous lupus, and rheumatoid arthritis codes were excluded from the analysis. A secondary analysis was performed including those with 5 or more comorbidities. Conditional logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI) adjusted for region.

Results: 34,752 cases with SLE and 34,752 matched non-SLE comparators were included. Mean age was 48 (SD 14.2) years, and 90.6% were female for both cohorts. 66.4% of the patients in both cohorts were White, 18.4% Black, 3.4% Asian and 18.4% Hispanic. 1.3% of patients were < 18 years old; 17% 8-34; 21.3% 35-44; 27.1% 45-54; 22.1% 55-64 and 11.2% >65 years. Patients with SLE had more multimorbidity than non-SLE subjects (58.1% vs 26.3%). Multimorbidity increased with age in both cohorts (**figure**). Multimorbidity differences between SLE and non-SLE were present throughout all the age groups, in general patients with SLE compared to non-SLE had a difference of 27-34% in the prevalence of multimorbidity on all age groups except those age >65 where the difference was 23%. Young patients with SLE had a multimorbidity burden similar to non-SLE comparators who were three decades older (SLE 18-34, 35.95%, non-SLE 55-64, 37.58%). Young patients with SLE were 6-9 times as likely to suffer from multimorbidity compared to matched non-SLE patients in the same age group (**table**), these differences decreased in older age groups but persisted even in those SLE patients that were >65 (OR 3.5, 95%CI 3.12-3.90). Secondary analysis on patients with 5 or more comorbid conditions showed similar findings (**figure and table**).

Conclusion: This large nationwide study showed increased occurrence of multimorbidity in SLE versus non-SLE patients, with substantial burden of multimorbidity through all age groups and even persistent during elderhood. Young

Figure. Prevalence of multimorbidity by age groups in SLE and non-SLE patients. Top panel, 2 or more comorbidities. Bottom panel, 5 or more comorbidities.





** < 11 Non-SLE patients <18 years (number suppressed to protect confidentiality

patients with lupus have a multimorbidity burden of similar to individuals 3 decades older. This study highlights the striking comorbidity burden patients with lupus endure. The effects of multimorbidity on compliance, healthcare burden and outcomes deserve further research.

Table. Comparison of multimorbidity prevalence by age group between patients with SLE and non SLE		
	Multimorbidity (2+ conditions) Odds ratio*	Multimorbidity (5+ conditions) odds ratio*
Age group (compared to non-SLE)		
<18 years	9.06 (5.97-14.41)	12.69 (2.90-54.07)
18-34	6.83 (6.12-7.62)	11.43 (8.18-15.97)
35-44	5.32 (4.91-5.76)	9.48 (7.76-11.59)
45-65	4.59 (4.3-4.87)	5.48 (4.89-6.14)
55-64	4.18 (3.91-4.48)	4.10 (3.75-4.49)
65+	3.49 (3.12-3.9)	2.76 (5.51-3.04)
*Adjusted region		

Disclosure: A. Duarte-Garcia, None; **H. Heien**, None; **N. Shah**, None; **C. Crowson**, None.

Abstract Number: 1050

Epidemiology and Clinical Features of Ophthalmological Manifestations in Behçet's Disease: Study of 50 Patients of a Series of 120 Patients in a Region in Northern Spain

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Ophthalmological involvement is one of the most feared manifestations of Behçet's disease. The aim of this study was to define the main demographic and clinical features of ophthalmological involvement in a well-defined cohort of patients with Behçet's disease.

Methods: Descriptive study of a cohort of 120 patients diagnosed with Behçet's disease from January 1, 1980 to December 31, 2019. Finally, following the 2014 International Criteria for Behçet's Disease (ICBD) (J Eur Acad Dermatol Venereol 2014; 28:338-47) 94 patients were chosen for this study.

Results: 50 patients (28 men/22 women; male to female ratio of 1:0.8) had ocular involvement. Mean age at diagnosis was 37.6±11.8 years. Mean ICBD score was 5.8±1.3 points. Neurological involvement was the most frequent

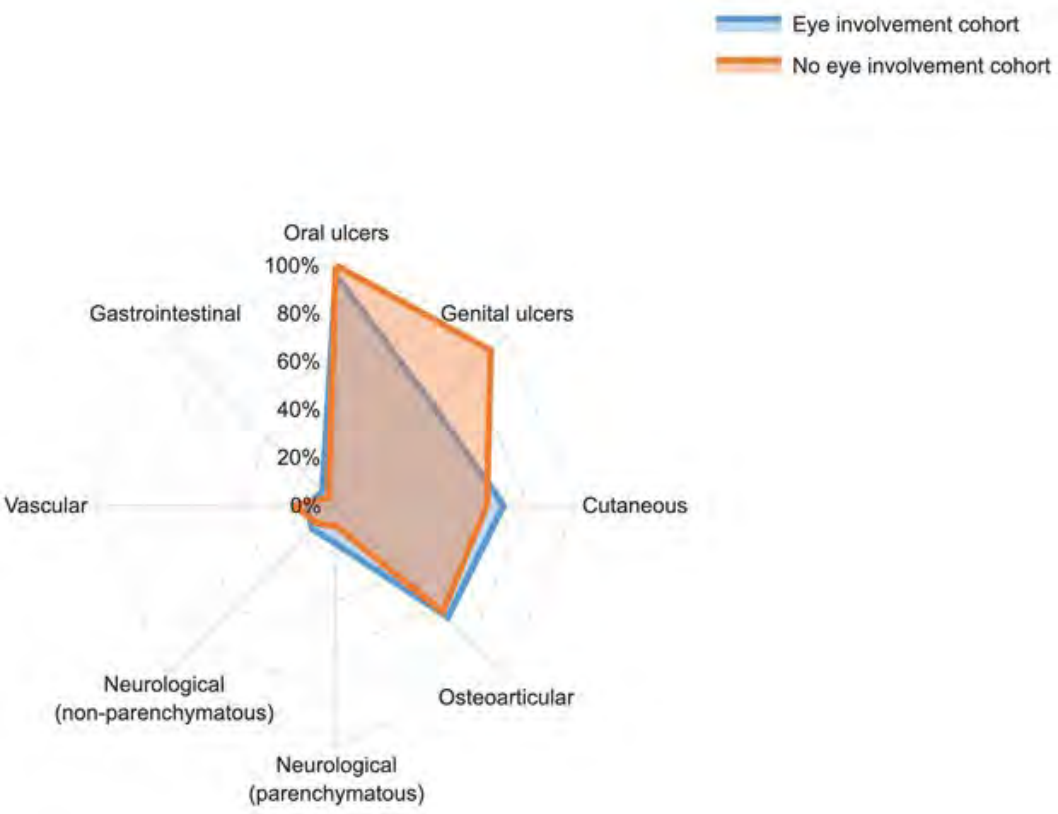

Figure. Comparison between clinical domains in patients with and without ophthalmological involvement.

Table. Clinical characteristics of ocular Behçet's disease

	n (%)	Unilateral, n (%)	Bilateral, n (%)
Uveitis	44 (88.0)	26 (59.1)	18 (40.9)
Anterior	17 (38.6)	13 (76.5)	4 (23.5)
Intermediate	2 (4.5)	-	2 (100)
Posterior	14 (31.8)	9 (64.3)	5 (35.7)
Panuveitis	11 (25.0)	4 (36.4)	7 (73.6)
Retinal vasculitis	5 (10.0)	-	-
Dry eye	5 (10.0)	-	-
Cystoid macular edema	4 (8.0)	-	-
Episcleritis	3 (6.0)	3 (100)	-
Optic neuritis	2 (4.0)	-	-

manifestation in this group. Genital ulcers were more frequent in the non-ophthalmological involvement group. Systemic clinical domains are shown in **Figure**.

The most frequent ocular manifestations were uveitis (n=44, 88.0%), retinal vasculitis (n=5, 10%) and dry eye (n=5, 10%). Likewise, the most frequent type of uveitis was anterior (n=17, 38.6%), followed by posterior uveitis (n=14, 31.8%). 26 (59.1%) of all uveitis were unilateral. Panuveitis was more frequent among patients under 60 years. Similarly, anterior uveitis was predominant in patients older than 70 years. There were no remarkable differences between genders. Main clinical features are shown in **Table**.

Conclusion: Ophthalmological involvement in Behçet's disease was more frequent in men. Uveitis and retinal vasculitis were the most frequent ocular manifestation. No remarkable differences in clinical features were observed between genders.

Disclosure: A. Herrero-Morant, None; **G. Suárez-Amorín**, None; **R. Demetrio-Pablo**, None; **L. Sánchez-Bilbao**, None; **C. Álvarez-Reguera**, None; **D. Martinez-Lopez**, None; **R. Fernandez**, None; **J. Martin-Varillas**, None; **C. Mata-Arnaiz**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1051

Variance of Joint Space Width Across the Tibiofemoral Joint on Knee Radiographs: A Novel Measure of Structure and Progression

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: The FDA accepts medial minimum joint space width (mJSW) in the tibiofemoral (TF) compartment as the standard for structural change in clinical trials of potential disease modifying OA drugs (DMOADs) for knee osteoarthritis (OA). Historical and novel imaging biomarkers of knee OA should be investigated in terms of their ability to predict clinically important outcomes. Quantitative radiographic OA scores (QROS), software developed to read fixed-flexion knee radiographs based on an anatomical coordinate system, generates medial mJSW and other quantitative measures. Our objective was to compare the clinical relevance of QROS-generated radiographic measurements based on their contributions to predicting time to knee replacement, and to assess a novel measure of structure, variance of JSW across the TF joint.

Methods: We selected knees with a baseline radiograph graded Kellgren-Lawrence (KL) 2 or 3 and QROS assessment at baseline and year 2, from the Osteoarthritis Initiative, a longitudinal observational study. QROS was used to measure medial mJSW and corresponding location, JSW measured at fixed locations across the joint (Figure 1), femoral tibial angle, width of the femoral condyles, distance from the tibial plateau to the tibial rim closest to the femoral condyle as a measure of knee positioning, and x-ray beam angle. We calculated the variance of fixed JSW measurements across the joint. Participants reported knee replacements up to 10 years following the year 2 clinic visit, confirmed by medical records and/or radiographs.

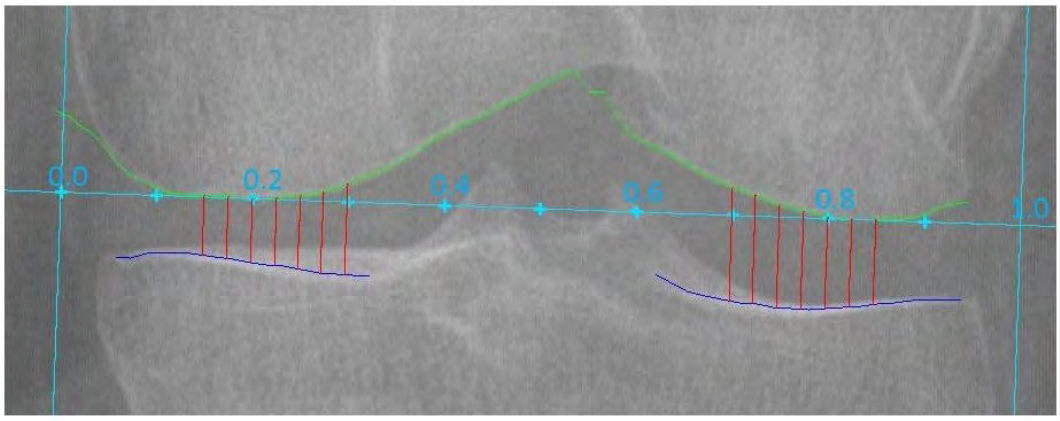

Figure 1. Fixed-location joint space width (JSW) measurements provided by quantitative radiographic OA scores (QROS) software. The variance of fixed-location JSW across the tibiofemoral joint (TF) may reflect degree of bone curvature, asymmetry of cartilage thickness in the TF joint, and/or uneven joint loading.

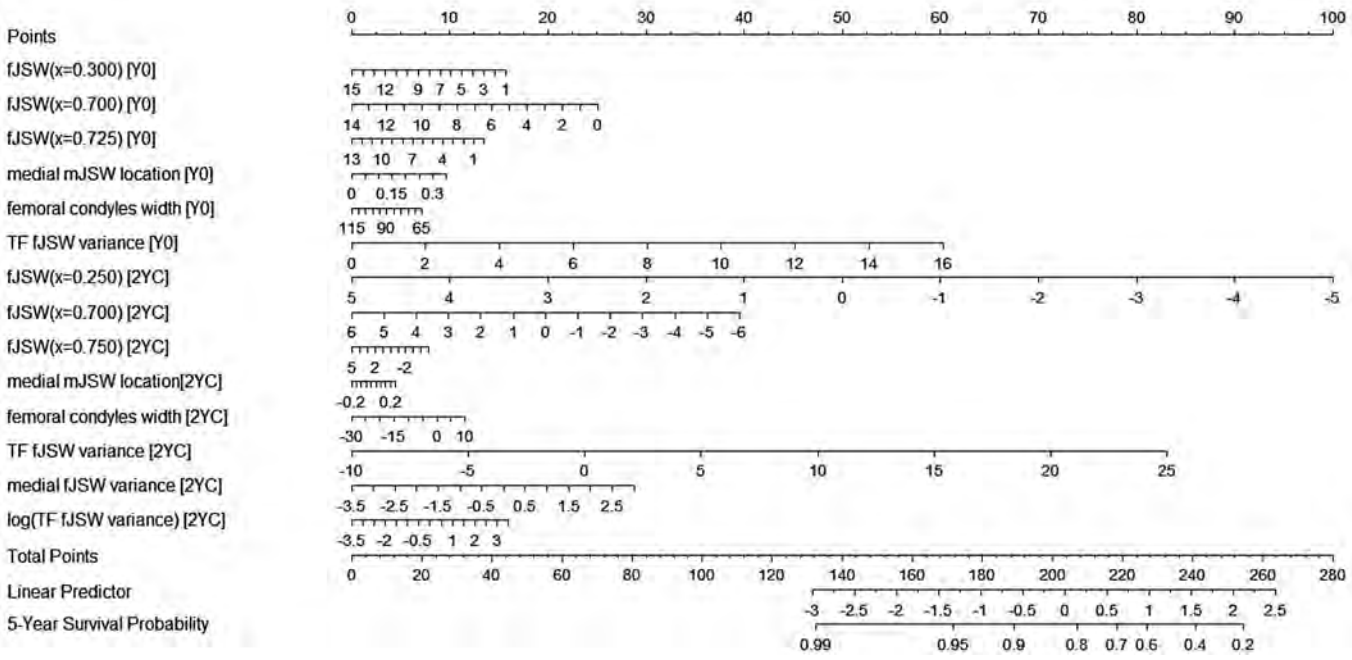

Figure 2. QROS predictors of 5-year survival. Nomogram visualization of exploratory analysis shows model-based points for lasso-selected predictors and mapping between total points and 5-year probability of survival from knee replacement. Y0 indicates OAI year 0 (baseline), and 2YC indicates 2-year change (from baseline to year 2).

We fit lasso penalized Cox models, including baseline measurements and change over 2 years, selecting the penalty parameter that achieved a partial log-likelihood deviance within one standard error of the minimum in 10-fold cross validation. Technical problems prevented some measurements in up to 9% of knees; we used multivariate imputation by chained equations to account for uncertainty in missing values. Model discrimination was evaluated with a bootstrap estimate of the time-dependent area under the receiver operating characteristic curve (AUC), and model calibration was visually inspected by plotting predicted versus observed survival probabilities.

Results: The sample included 3,082 KL 2,3 knees with 327 knee replacement outcomes over a median of 6.9 years, contributed by 2,101 participants. Lasso-selected predictors of time to knee replacement are shown in Figure 2. Important predictors included baseline and 2-year change of fJSW at specific locations in the TF joint, baseline and 2-

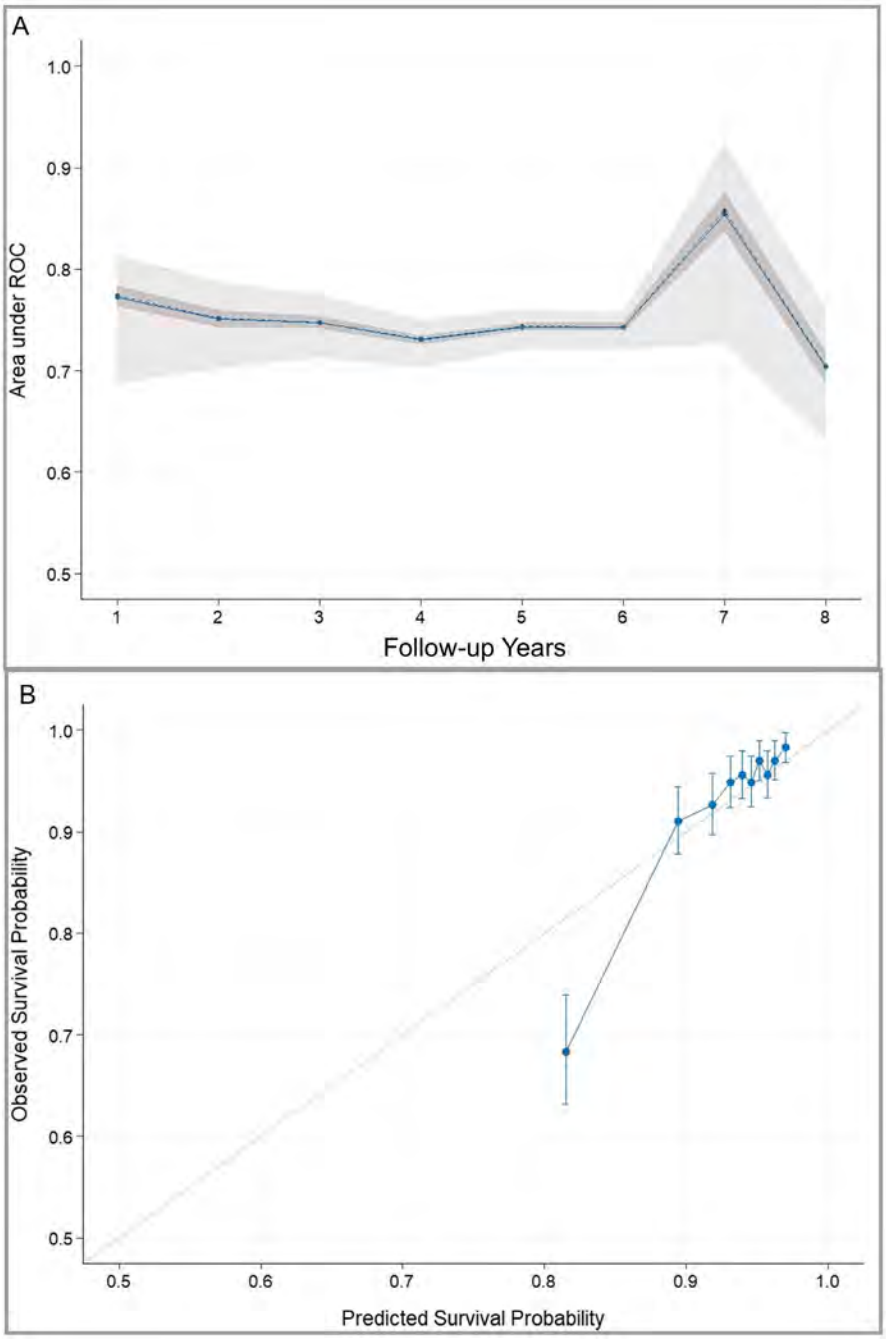

Figure 3. Model Performance. A) Discrimination: Time-dependent area under the receiver operating characteristic curve (AUC), estimated with a bootstrap. The darker interval in the plot shows the 25% and 75% quantiles and the lighter interval shows the minimum and maximum AUC from the bootstrap samples. B) Calibration: Predicted vs observed knee replacement survival at 5 years of follow-up, in 10 model-based risk groups. Bars represent 95%CI for survival probability estimated by Kaplan-Meier method.

year change of TF fJSW variance, baseline and 2-year change of medial mJSW location as well as 8 other variables. Model performance, as summarized by model discrimination and model calibration, is shown in Figure 3.

Conclusion: We developed an innovative measure of knee OA structure and progression, TF fJSW variance, which may reflect degree of bone curvature, asymmetry of cartilage thickness, and/or uneven joint loading. Baseline and 2-year change of TF fJSW variance, as well as other quantitative measures from QROS, were identified as important predictors of time to knee replacement. Further work needs to be done to validate TF fJSW variance as a potential imaging biomarker of knee OA progression.

Disclosure: K. Kwoh, Regeneron, 2, LG Chem, 2, Express Scripts, 2, Abbvie, 12, Principal investigator for pharma sponsored clinical trials, UCB, 12, Principal investigator for pharma sponsored clinical trials, Eicos, 12, Principal investigator for pharma sponsored clinical trials, Cumberland, 12, Principal investigator for pharma sponsored clinical trials, Mitsubishi, 12, Principal investigator for pharma sponsored clinical trials, GSK, 12, Principal investigator for pharma sponsored clinical trials, Kolon TissueGene, 4, Avalor Therapeutics, 4; **E. Ashbeck**, EMD Serono, 2; **E. Bedrick**, None; **X. Sun**, None; **J. Duryea**, Biosplice LLC, 5.

Abstract Number: 1052

Female Reproductive Factors and Risk of Joint Replacement Arthroplasty of the Knee and Hip Due to Osteoarthritis in Postmenopausal Women: A Nationwide Cohort Study of 1.36 Million Women

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Background/Purpose: Previous studies of the relationships between female reproductive factors and osteoarthritis (OA) have shown conflicting results. In this study, we aimed to explore the relationships between reproductive factors and joint replacement arthroplasty of the knee (TKRA) and hip (THRA) in a large nationwide population-based cohort of postmenopausal Korean women.

Methods: We included 1,218,257 subjects who participated in national health examinations in 2009 in the study. The study outcomes were incident THRA or TKRA due to severe hip or knee OA. The relationships between reproductive factors and THRA or TKRA were evaluated using a multivariate-adjusted proportional hazards model.

Results: During a mean follow-up duration of 8.2 years, 1,733 incident THRA cases and 65,108 incident TKRA cases were observed. Later age at menarche, longer breastfeeding, HRT and OC use were associated with increased risk of TKRA for severe knee OA, while later age at menopause and longer reproductive span were associated with decreased risk. With regard to THRA for severe hip OA, later menarche, longer breastfeeding, and HRT more than 5 years were associated with higher risk. The associations between reproductive factors and severe OA were more pronounced in underweight and younger subjects.

Conclusion: We found that shorter estrogen exposure was associated with higher risk of joint replacement therapy due to severe OA, and such associations were more pronounced in underweight and younger subjects.

Disclosure: Y. Eun, None; **J. Yoo**, None; **K. Han**, None; **D. Kim**, None; **J. Lee**, None; **D. Lee**, None; **D. Lee**, None; **D. Shin**, None; **H. Kim**, None.

Abstract Number: 1053

Temporal Trends and Geographic Variations of Premature Mortality Related to Musculoskeletal(MSK) and Connective Tissue Disorders in the United States: A 20-Year Analysis from WONDER Database

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SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Musculoskeletal system and connective tissue disorders (arthropathies, systemic connective tissue disorders, soft tissue disorders) may contribute to premature mortality likely due to associated comorbidities related to disease and treatment. Worldwide MSK-related mortality rate showed a downward trajectory between 1986 and 1997, an uptrend till 2001, again followed by a decrease thereafter in both sexes (1). However, data regarding premature MSK-related mortality is lacking. We sought to analyze the temporal trends and geographical variations of MSK-related premature mortality (age ≤ 65 years) over the last 20 years in the United States (U.S.). We hypothesized that increased surveillance, early diagnosis or improvement of treatment, and increased survival would have led to a downward trend in premature mortality during the last two decades.

Methods: Death certificate data were retrieved from the Centers for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (WONDER) database for 1999-2018. WONDER database is publicly available de-identified data collected by CDC that reports the underlying cause of death across the United States. Premature mortality, for MSK and connective tissue disease (ICD-10 code M00-M99) as an underlying cause of death, for age<

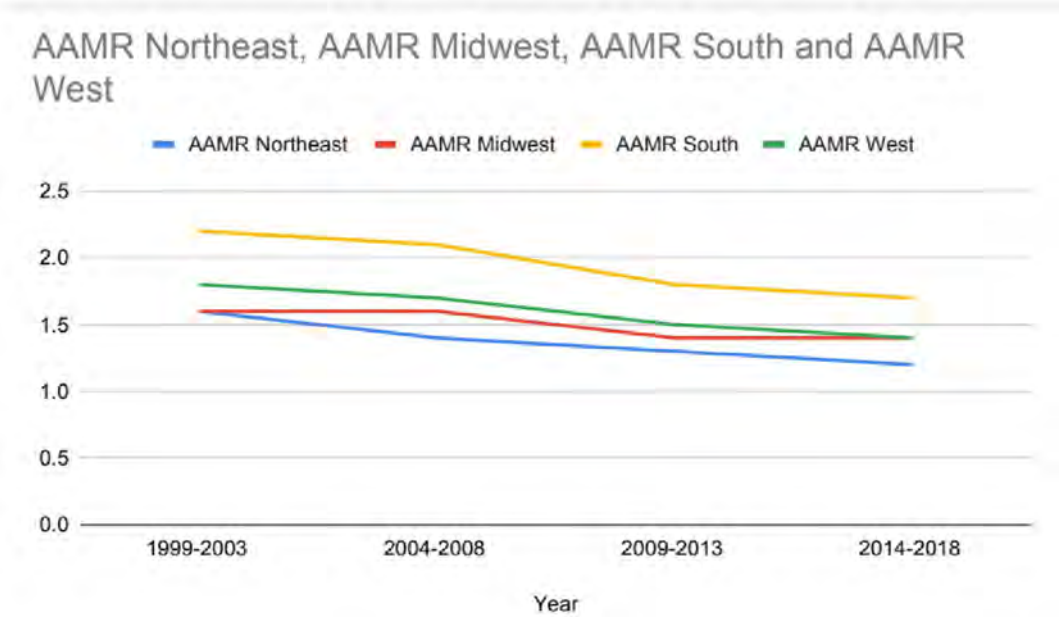

Figure 1. Illustrates temporal trends and regional MSK and connective tissue related AAMRs from 1999-2018.

Table 1. Regional age-adjusted MSK and connective tissue related mortality rate in the U.S Census regions

Census region	Year	Deaths	Population	Crude mortality rate	Age adjusted mortality rate (95% CI)	% of total deaths
Northeast CR1	1999-2003	2862	178,310,928	1.6 (1.5-1.7)	1.6 (1.5-1.6)	16.20%
	2004-2008	2863	183,913,328	1.6 (1.5-1.6)	1.4 (1.4-1.5)	15.10%
	2009-2013	2,795	187,574,515	1.5 (1.4-1.5)	1.3 (1.2-1.3)	15.30%
	2014-2018	2,615	187,169,280	1.4 (1.3-1.5)	1.2 (1.1-1.2)	14.20%
Midwest CR2	1999-2003	3,577	213,449,994	1.7 (1.6-1.7)	1.6 (1.6-1.7)	20.30%
	2004-2008	3872	220,236,056	1.8 (1.7-1.8)	1.6 (1.6-1.7)	20.50%
	2009-2013	3,659	223,299,604	1.6 (1.6-1.7)	1.4 (1.4-1.5)	20.00%
	2014-2018	3,754	222,536,045	1.7 (1.6-1.7)	1.4 (1.4-1.5)	20.40%
South CR3	1999-2003	7,399	338,492,277	2.2 (2.1-2.2)	2.2 (2.1-2.2)	42.00%
	2004-2008	8,022	365,766,080	2.2 (2.1-2.2)	2.1 (2.0-2.1)	42.40%
	2009-2013	7,804	386,389,995	2.0 (2.0-2.1)	1.8 (1.8-1.9)	42.70%
	2014-2018	7,985	400,900,424	2.0 (1.9-2.0)	1.7 (1.7-1.8)	43.40%
West CR4	1999-2003	3793	214,594,655	1.8 (1.7-1.8)	1.8 (1.8-1.9)	21.50%
	2004-2008	4154	232,214,406	1.8 (1.7-1.8)	1.7 (1.7-1.8)	22.00%
	2009-2013	3,999	245,003,898	1.6 (1.6-1.7)	1.5 (1.4-1.5)	21.90%
	2014-2018	4,064	254,179,315	1.6 (1.5-1.6)	1.4 (1.4-1.5)	22.10%
Overall	1999-2003	17631	944,847,854	1.9 (1.8-1.9)	1.9 (1.8-1.9)	100%
	2004-2008	18,911	1,002,129,870	1.9 (1.9-1.9)	1.8 (1.7-1.8)	100%
	2009-2013	18,257	1,042,268,012	1.8 (1.7-1.8)	1.6 (1.5-1.6)	100%
	2014-2018	18,418	1,064,785,064	1.7 (1.7-1.8)	1.5 (1.5-1.6)	100%

Table 2. All-cause mortality in the United States

Year	All-cause AAMR	Deaths	Population	Crude mortality rate	Age adjusted mortality rate (95% CI)	Standard error for AAMR
1999-2003	300.7	3,602,568	1,158,686,801	310.9	300.7 (300.4 - 301.0)	**0.2**
2004-2008	289.2	3,110,657	1,002,129,870	310.4	289.2 (288.9 - 289.5)	0.2
2009-2013	275.3	3,235,557	1,042,268,012	310.4	275.3 (275.0 - 275.6)	0.2
2014-2018	285.5	3,490,246	1,064,785,064	327.8	285.5 (285.2 - 285.8)	0.2

65 years was queried. This duration was further stratified into five-year periods. Age-adjusted mortality rate (AAMR) per 100,000 population was calculated with 95% CI for the four U.S. census regions (CR1 Northeast, CR2 Midwest, CR3 South, and CR4 West). Figure 1 illustrates the regional trends.

Results: A total of 73,217 premature MSK and connective tissue deaths occurred among individuals aged 15-65 years in the last 20 years. Overall, AAMR per 100,000 deaths declined by 22% during the study period. From 1999-2018 AAMR for Northeast declined from 1.6 to 1.2; for Midwest 1.6 to1.4; for West 1.8 to 1.4; for South 2.2 to 1.7 (Figure-1) Regional AAMR declined by 25% in the Northeast, 22.7% in the South, 22.2% in the West, and 12.5% in Midwest. Table 1 gives Total deaths and crude mortality rates in each region. All-cause AAMR declined (~5%) from 300.7 to 285.5 per 100,000 during 1999 to 2018 (Table 2).

Conclusion: This analysis of nationally representative data shows a decline in the AAMR for premature MSK and connective tissue diseases. Overall and regional AAMR showed a downward trajectory from 1999-2018. Our study underscores the importance of high-quality and evidence-based practices in rheumatology that may have played a significant role in decreasing MSK and connective tissue disorders compared with overall all-cause mortality. The regional disparities in premature mortality among different census regions warrant further investigations. Study limitations include inherent weaknesses of database studies that misclassify the cause of mortality.

Disclosure: I. Kaur, None; **M. Mughal**, None; **H. Mirza**, None; **H. Jagdey**, None; **P. Bansal**, None; **E. Capitle**, None; **F. Aslam**, None.

Abstract Number: 1054

Metabolomics as an Innovative Tool for Cardiac Risk Stratification in Patients with Rheumatic Diseases: Results from a Pilot Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatic diseases (RMD) face an increased cardiovascular (CV) mortality compared to the general population. Still, risk stratification based on traditional cardiovascular risk factors fail prediction in these patients. Particular metabolites and lipid homeostasis are of high interest as both are described to play a crucial role in cardiovascular disease (CVD) development.

In this pilot study, we aimed to identify a metabolite profile in patients with systemic lupus erythematodes (SLE), ANCA-associated vasculitis (AAV) or psoriatic arthritis (PsA) that identifies patients at cardiovascular risk, which in future can be adapted and used independently from traditional risk factors.

Methods: Plasma samples of patients with PsA (n=21), AAV (n=16) and SLE (n=16) were analyzed with a combined approach using targeted LC-MS/MS-analysis for low-concentrated lipid mediators, non-targeted LC-HRMS analysis for abundant lipids and the Biocrates MxP Quant 500 Kit a total of 685 metabolites and lipids could be detected. Compounds of interest for discrimination of patients with CV risk were selected using machine-learning with random forest algorithm, whereas 70% of the data was used for training and 30% for testing using stratified randomization. Prior training a Spearman correlation matrix and recursive feature elimination were applied to reduce the number of metabolites.

Included patients had a comparable low disease activity at inclusion with a DAS28-CRP of 2.31±0.9 (PsA), a BVAS of 2.37 ±1.45 (AAV) and a SLEDAI-2K of 2.37±1.96 (SLE). 31 of the 53 included patients had a traditional CV risk factor or a CVD, with a proportion of 22.58% male in patients with CVD and 36.36% in patients without CVD.

Patients with CVD had a mean age of 60.83 years (yrs) ±11.58 and a mean RMD duration of 16.83±12.82 yrs, compared to non-CVD patients with 43.81yrs±9.98 of mean age and 15.61±25.36 yrs of disease duration.

Results: Our machine-learning model can classify patients with and without CVD or CV risk with an accuracy of 86.67% and an ROC-AUC of 0.963 (77.78% sensitivity, 100% specificity). This model based on 14 metabolites including different amino acids, kynurenine, hexoses, acylcarnitine, palmitoyl ethanolamine, phospholipids and trigylcerides.

Conclusion: In this pilot study, we identified a panel of metabolites that can stratify patients with PsA, AAV and SLE based on CVD and traditional CV risk factors with a high sensitivity and specificity. The identified panel and a machine-learning model will be validated in larger cohorts to assess a risk stratification that is independent from traditional CV risk factors. Furthermore, the role of the selected metabolites in the pathophysiology of CVD might help to better understand the complex interaction of pathways leading to CVD development in patients with RMD.

Disclosure: S. Mojtahed Poor, German Society for Rheumatology (DGRh Forschungsinitiative 2020), 5; **L. Hahnefeld**, None; **F. Behrens**, Chugai, 5, 6, AbbVie, 6, Amgen, 6, GlaxoSmithKline, 5, Janssen, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Boehringer Ingelheim, 6, Celgene, 6, Eli Lilly, 6, Merck, 6, Novartis, 6, Sanofi, 6, UCB, 6; **H. Burkhardt**, None; **M. Köhm**, None; **G. Gerd**, None; **G. Robert**, None.

Abstract Number: 1055

How to Optimize E-Recruitment Strategies: Lessons Learned from over 3000 Participants in an International Arab Online Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The use of online surveys as a recruitment tool for clinical research has increased during the COVID-19 pandemic and will likely continue to expand. However, good practice guidance for investigators and steering committees to optimize their digital recruitment strategies is still needed. The aim of this study was to identify the most effective strategies for digital recruitment (e-recruitment) in an international Arab online study about the perceptions of patients with rheumatic diseases regarding the COVID-19 vaccination.

Methods: This is a post hoc analysis of the ARCOVAX (Arab League of Associations for Rheumatology (ArLAR) COVID Vaccination) study, which included patients with rheumatic diseases and health care professionals (HCPs, serving as a control group). The ARCOVAX questionnaire was an anonymous web survey adapted from the VAXICOV study (Felten et al. Lancet Rheumatol. 2021 Apr;3(4):e243-e245) and disseminated in Arabic, English, and French from April 13th until May 11th, 2021 by an ArLAR special interest group (Arab Adult Arthritis Awareness (AAAA) group), through multiple social media channels. The steering committee conducted 6 different actions to boost recruitment: promoting on social media and WhatsApp groups, sharing recruitment status on AAAA WhatsApp group, sending personalized WhatsApp messages to recruiters, disseminating e-posters and QR codes, addressing recruiters' technical issues (technical support), and announcing count-down for survey closing through a promotional video. The impact of each action was correlated with the number of enrolled participants, first in the whole population then by countries stratified according to the Gross Domestic Product (GDP) level as per the World Bank Classification.

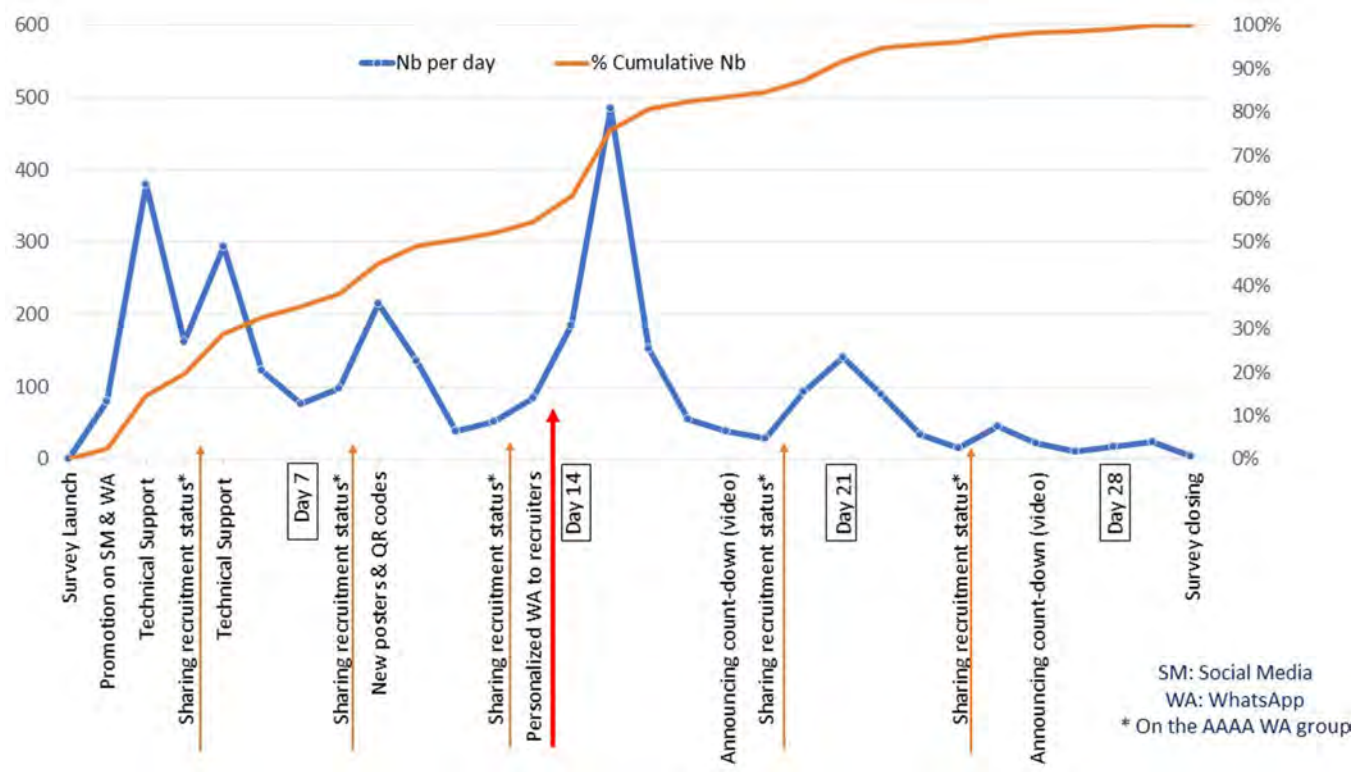

Figure 1. Enrollment of Patients For the e-Survey and Correlation with the Recruitment Strategies.

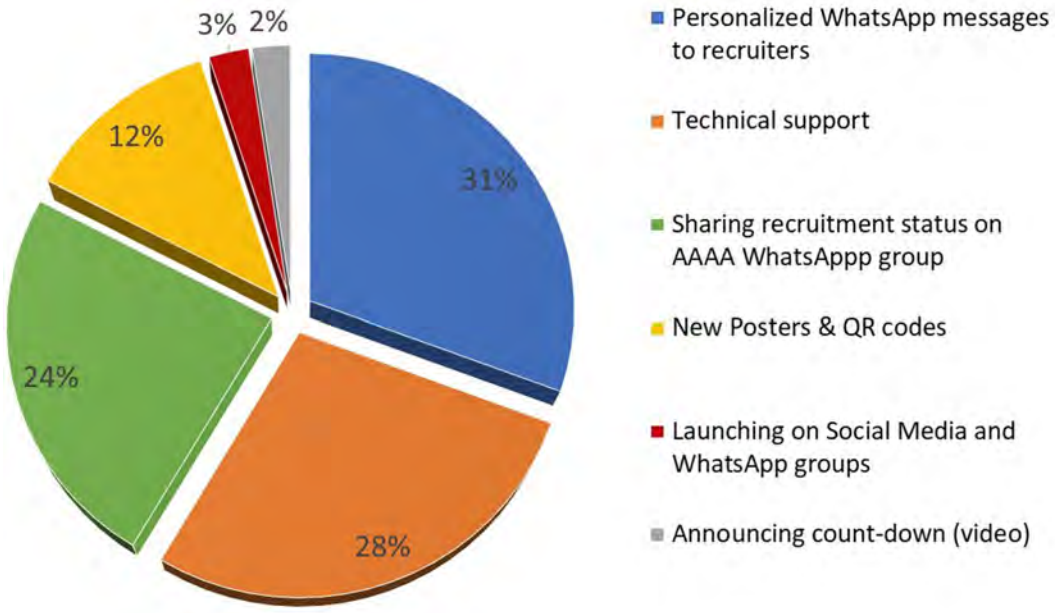

Figure 2. Percentage of recruited participants with regards to the strategy.

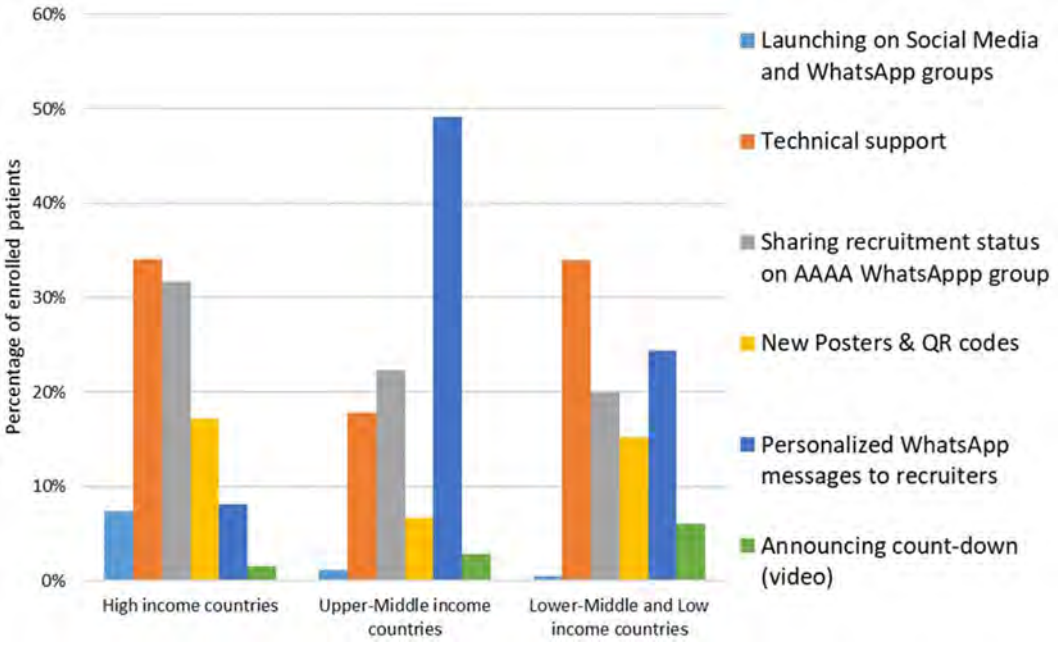

Figure 3. Impact of recruitment strategies on the number of enrolled participants by Gross Domestic Product.

Results: A total of 3,176 participants from 19 Arab countries completed the survey (1,594 patients and 1,517 HCPs). The enrollment of participants was highly fluctuating (Figure 1) and the e-recruitment strategies had different impacts: 31% of participants were recruited after sending personalized WhatsApp messages to recruiters in different countries, 28% after prompt technical support by the steering committee to resolve issues faced by the recruiters, 24% after sharing recruitment status on AAAA WhatsApp group, 12% after disseminating e-posters and QR codes via

social media and WhatsApp groups, 3% after initially launching on social media and WhatsApp groups and 2% after sharing a motivational video announcing the count-down of the last week of recruitment (Figure 2). The impact of these strategies was different according to the countries' GDP level, where technical support and sharing recruitment status had the most impact in high-income countries, and personalized messages resulted in higher recruitment in the upper-middle-income countries (Figure 3).

Conclusion: The most effective strategy was the use of personalized WhatsApp messages to the recruiters. The research team must be active (mobilizing teams to participate), reactive (prompt technical support), and proactive (sharing updates regularly). Further studies are needed to identify the appropriate action for each phase of e-recruitment and for each specific region.

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Abstract Number: 1056

Characterization of the Patterns of Care, Access and Direct Costs of Systemic Lupus Erythematosus in Brazil: Findings from the Macunaíma Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: This study evaluated the patterns of care, access and direct costs related to the management and treatment of patients with systemic lupus erythematosus (SLE) in Brazil.

Methods: This cross-sectional study (GSK Study 207353) assessed patients ≥18 years of age with SLE (ACR, 1997 classification criteria) who had been receiving SLE care for ≥1 year at 5 SLE reference facilities. The study period was 12 months. Patients retired or on leave owing to another illness were excluded. Clinical information and resources used in clinical practice were obtained by interviewing patients and medical records. Direct resources were categorized as: (1) health-related hospital resources: consultations, tests, medications, hospitalization; (2) non–health-related hospital resources: transportation, home adaptation, spending on caregivers. The drugs were categorized as: (1) specific for SLE, according to coverage by the Brazilian public system; (2) adjuvants, used in the management of

Table 1. Distribution of sociodemographic characteristics, clinical classification and treatment for patients with SLE

	Overall (N=300)	Midwest	Northeast	North	Southeast	South	p-value
Age, mean (SD) years	41.9 (12.8)	41.1 (12.5)	40.5 (10.8)	37.2 (11.5)	43.5 (14.5)	47.1 (12.4)	<0.001
Female, n (%)	277 (92.3)	54 (90.0)	58 (98.3)	56 (93.3)	54 (90.0)	54 (90.0)	
Race, n (%)							<0.001
White	76 (25.3)	10 (16.7)	10 (16.7)	5 (8.3)	16 (26.7)	35 (58.3)	
Black	56 (18.7)	19 (31.7)	4 (6.7)	1 (1.7)	19 (31.7)	13 (21.7)	
Others	7 (2.3)	2 (3.3)	1 (1.7)	1 (1.7)	2 (3.3)	1 (1.7)	
Mixed race	161 (53.7)	29 (48.3)	45 (75.0)	53 (88.3)	23 (38.3)	11 (18.3)	
SLE Classification Criteria (ACR, 1997), most frequent, n (%)							
Nonerosive arthritis	221 (73.7)	24 (40.0)	52 (86.7)	53 (88.3)	48 (80.0)	44 (73.3)	<0.001
Immunologic disorder	190 (63.3)	35 (58.3)	40 (66.7)	32 (53.3)	35 (58.3)	48 (80.0)	0.023
Photosensitivity	180 (60.0)	19 (31.7)	42 (70.0)	53 (88.3)	27 (45.0)	39 (65.0)	<0.001
Malar rash	166 (55.3)	21 (35.0)	36 (60.0)	49 (81.7)	25 (41.7)	35 (58.3)	<0.001
Renal disorder	141 (47.0)	16 (26.7)	23 (38.3)	42 (70.0)	30 (50.0)	30 (50.0)	<0.001
Hematologic disorder	140 (46.7)	11 (18.3)	36 (60.0)	23 (38.3)	32 (53.3)	38 (63.3)	<0.001
Stopped school education because of SLE, n (%)	46 (15.3)	9 (15.0)	6 (10.0)	15 (25.0)	7 (11.7)	9 (15.0)	0.047
Employment, n (%)							0.020
Active	79 (26.3)	15 (25.0)	17 (28,3)	11 (18.3)	20 (33.3)	16 (26.7)	
Retired or on sick leave because of SLE	100 (33.3)	17 (28.3)	12 (20.0)	25 (41.7)	22 (36.7)	24 (40.0)	
Unemployed	65 (21.7)	17 (28.3)	10 (16.7)	16 (26.7)	12 (20.0)	10 (16.7)	
Others	56 (18.7)	11 (18.3)	21 (35.0)	8 (13.3)	6 (10.0)	10 (167)	
Access to care							
Time between onset of symptoms and start of treatment, mean (SD) months	21.6 (39.6)	16.4 (28.2)	26.0 (35.2)	16.9 (30.2)	17.6 (24,7)	31.4 (65.6)	0.158
Travel time from home to facility, mean (SD) hours	4.4 (12.6)	3.52 (4.3)	1.7 (1.3)	11.5 (25.4)	3.7 (8.3)	1.80 (1.7)	<0.001
Missing medical appointments for any reason, study period, mean (SD)	0.72 (1.3)	0.46 (10.9)	0.35 (0.9)	0.7 (1.1)	1.7 (1.8)	0.3 (0.8)	<0.001
Number of medications per day, mean (SD)	6.59 (3.9)	3.92 (2.5)	6.0 (2.7)	6.2 (2.4)	8.5 (3.7)	8.3 (5.3)	<0.001
Immunosuppressants or biological medicines most used, n (%)							
Hydroxychloroquine or chloroquine	222 (74.0)	33 (55.0)	42 (70.0)	39 (65.0)	53 (88.3)	55 (91.7)	<0.001
Mycophenolate mofetil	90 (30.0)	2 (3.3)	15 (25.0)	27 (45.0)	29 (48.3)	17 (28.3)	<0.001
Azathioprine	77 (25.7)	12 (20.0)	12 (2.0)	15 (25.0)	15 (25.0)	23 (38.3)	0.131
Methotrexate	48 (16.0)	12 (20.0)	17 (28.3)	5 (8.3)	7 (11.7)	7 (11.7)	0.019
Cyclophosphamide	27 (9.0)	7 (11.7)	2 (3.3)	11 (18.3)	4 (6.7)	3 (5.0)	0.029
Cyclosporine	6 (2.0)	0 (0.0)	0 (0.0)	2 (3.3)	4 (6.7)	0 (0.0)	0.025
Rituximab	11 (3.7)	1 (1.7)	4 (6.7)	3 (5.0)	2 (3.3)	1 (1.7)	0.648
Belimumab	13 (4.3)	11 (18.3)	2 (3.3)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Tacrolimus	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.7)	0 (0.0)	1.000

Note 1: The sources for valuing the resource items were: A) For specific drugs: shopping list from the Ministry of Health, broken down by the Medicines Market Regulation Chamber (CMED). Available at: https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/precos (last accessed April 4, 2021); B) Other health-related resource items were obtained from the price list of the Brazilian Medical Association (2019) and from the price list of the Management System of the SUS Procedures, Medicines and OPM Table (Sistema de Gerenciamento da Tabela de Procedimentos, SIGTAP). Available at: http://sigtap.datasus.gov.br/tabela-unificada/app/sec/inicio.jsp?first=10 (last accessed April 4, 2021).

Note 2: The conversion of the values to United States Dollar (USD) was made from the average of the values of the dollar for the 4 quarters in the period of the study (2019-2020) provided by the Central Bank of Brazil. Available at https://www.bcb.gov.br/conversao (last accessed April 4, 2021). Based on this, US$1.00 is equivalent to 4.24 Brazilian Real (BRL).

comorbidities. Costs were calculated at the unit value of each resource in relation to the quantity consumed. A multivariate regression model sought to explore cost predictors in this group of patients.[1]

Results: Three hundred patients with SLE (92.3% female, mean [standard deviation, SD] duration of disease of 11.8 [7.9] years) were included. Overall, the time (mean [SD]) between the onset of the first symptoms and the start of treatment was 21.6 (39.6) months (**Table 1**). Forty-six (15.3%) patients stopped schooling because of the disease and 33.3% were retired or on sick leave because of SLE. Mean (SD) travel time from home to a care facility was 4.4 (12.6) hours. Antimalarials were the drugs most used by patients (n=222 [74.0%]) followed by mycophenolate mofetil (n=90 [30.0%]). The mean total cost for SLE in Brazil was US$3123.53 per patient per year (median [interquartile range, IQR] US$1618.51 [678.66; 4601.29]). The main item that contributed to the expenditure was medication, with

Table 2. Distribution of the cost of SLE, per patient per year, according to geographic region and type of resource consumed, in US$ [2,3]

Resources used (median [IQR])	Overall (N=300)	Midwest	Northeast	North	Southeast	South	p-value
Medicine	910.62 (460, 4033.51)	312.8 (119.4, 937.6)	694.6 (462.4, 3712.8)	1334.5 (615.5, 4391.8)	1751.2 (654.2, 5141.5)	950.7 (489.0, 3336.3)	<0.001
Hospitalization	900.60 (382.10, 2106.41)	1891.1 (382.4, 4194.9)	430.9 (377.4, 1858.0)	1007.7 (673.0, 1182.9)	1836.0 (598.0, 3145.1)	711.2 (475.5, 1395.1)	0.29
Caregiver	849.06 (283.02, 235.85)	NA (NA, NA)	283.0 (212.3, 1981.1)	424.5 (254.7, 583.7)	1202.8 (336.1, 1981.1)	1132.1 (1061.3, 1273.6)	0.336
Examinations	130.85 (73.70, 191.58)	38.3 (18.5, 74.8)	153.7 (117.2, 207.2)	102.6 (59.9, 174.5)	153.1 (97.6, 189.9)	187.4 (123.4, 229.4)	<0.001
Home adaptation because of SLE	70.75 (23.58, 235.85)	1179.2 (1179.2, 1179.2)	NA (NA, NA)	235.8 (188.7, 528.3)	188.7 (117.9, 202.8)	21.2 (15.9, 35.4)	0.02
Aids and support for disability	35.38 (14.15, 51.89)	82.5 (44.2, 121.5)	28.7 (16.1, 40.0)	18.9 (15.3, 40.1)	47.2 (14.2, 94.3)	14.2 (14.2, 14.2)	0.086
Consultation	34.67 (23.11, 63.56)	23.1 (17.3, 34.3)	40.4 (28.9, 59.2)	34.7 (23.1, 44.0)	63.6 (37.6, 87.3)	28.9 (17.3, 52.0)	<0.001
Transportation	9.43 (5.42, 18.87)	9.4 (7.9, 18.3)	7.9 (3.3, 10.1)	6.8 (3.5, 19.1)	9.4 (9.4, 42.5)	9.4 (9.0, 18.9)	<0.001
Total cost	**1618.51 (678.66, 4601.29)**	**545.3 (193.0, 3246.3)**	**1334.1 (645.1, 4234.0)**	**2569.0 (927.7, 4559.3)**	**4036.6 (1225.5, 5971.3)**	**1556.5 (706.6, 3551.7)**	**<0.001**

Note 1: The sources for valuing the resource items were: A) For specific drugs: shopping list from the Ministry of Health, broken down by the Medicines Market Regulation Chamber (CMED). Available at: https://www.gov.br/anvisa/pt-br/assuntos/medicamentos/cmed/precos (last accessed April 4, 2021); B) Other health-related resource items were obtained from the price list of the Brazilian Medical Association (2019) and from the price list of the Management System of the SUS Procedures, Medicines and OPM Table (Sistema de Gerenciamento da Tabela de Procedimentos, SIGTAP). Available at: http://sigtap.datasus.gov.br/tabela-unificada/app/sec/inicio.jsp?first=10 (last accessed April 4, 2021).

Note 2: The conversion of the values to USD was made from the average of the values of the dollar for the 4 quarters in the period of the study (2019-2020) provided by the Central Bank of Brazil. Available at https://www.bcb.gov.br/conversao (last accessed April 4, 2021). Based on this, US$1.00 is equivalent to 4.24 BRL.

a median (IQR) cost of US$910.62 (460; 4033.51), followed by hospitalization (US$900.60 [382.10; 2,106.41]; **Table 2**). According to the regression model, mycophenolate use increased the cost by 3.664 times ($p< 0.001$). Also, inflammatory monitoring (erythrocyte sedimentation rate [ESR] or C-reactive protein) reduced expenditure by 0.381 times ($p< 0.001$; **Table 3**).

Conclusion: The cost of SLE in Brazil is driven by the use of immunosuppressants or by its frequent monitoring, and hospitalization.

Funding: GSK

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Table 3. Multivariate regression model to assess the factors that influence the total cost per patient per year

	Coefficient	std err	z	P>|z|	[0.025	0.975]	Exponential of the coefficient
Medications: methotrexate	-0.312	0.138	-2.261	0.024	-0.582	-0.041	0.732
Medications: mycophenolate	1.299	0.112	11.579	0.000	1.079	1.518	3.664
Examinations: liver function tests	0.275	0.110	2.491	0.013	0.059	0.491	1.317
Lupus classification: arthritis	-0.524	0.111	-4.733	0.000	-0.741	-0.307	0.592
Damage accrual: SLICC-DI	0.163	0.052	3.119	0.002	0.061	0.266	1.177
Examination: ESR or C-reactive protein	-0.964	0.219	-4.400	0.000	-1.394	-0.535	0.381
Medications: antihypertensive or antidigitalis or antianginal medicines	0.623	0.131	4.769	0.000	0.367	0.879	1.864
HRQoL: SF-12 physical component	-0.232	0.048	-4.884	0.000	-0.326	-0.139	0.793
Medical history: hypertension	-0.246	0.125	-1.977	0.048	-0.491	-0.002	0.782
Schooling (years)	0.154	0.048	3.189	0.001	0.059	0.248	1.166
Brazilian economic classification criterion (C2)	0.350	0.096	3.628	0.000	0.161	0.538	1.418
Medical appointment: nursing	0.381	0.172	2.207	0.027	0.043	0.719	1.463
Examinations: transthoracic echocardiogram or transesophageal echocardiogram	0.286	0.124	2.304	0.021	0.043	0.529	1.331
Examinations: urea or creatinine test	0.849	0.260	3.270	0.001	0.340	1.358	2.337
Examinations: echo Doppler carotid arteries or subclavian or lower members	0.69	0.195	3.425	0.001	0.286	1.052	1.952
Lupus classification: hematological manifestations	0.264	0.096	2.753	0.006	0.076	0.451	1.302
Time between initial symptoms and initial treatment (months)	0.181	0.049	3.728	0.000	0.086	0.277	1.199
Time from symptom onset to first consultation with rheumatologist (years)	-0.140	0.047	-2.986	0.003	-0.232	-0.048	0.869
SLICC: cataract	-0.290	0.137	-2.115	0.034	-0.558	-0.021	0.748
Caregiver cost	0.530	0.174	3.042	0.002	0.188	0.871	1.699
SLEDAI score: 2–6	-0.280	0.111	-2.518	0.012	-0.497	-0.062	0.756
Examinations: myocardial injury biomarker	0.350	0.152	2.307	0.021	0.053	0.646	1.418
Intercept	7.032	0.220	32.034	0.000	6.602	7.462	1132.519

HRQoL, health-related quality of life; SF-12, 12-Item Short Form Survey; SLEDAI, SLE Disease Activity Index; SLICC-DI, Systemic Lupus International Collaborating Clinics – Damage Index

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Abstract Number: 1057

Impact of Osteoarthritis in Younger Adults

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: OA is a disease frequently perceived as a disease of the elderly and an inevitable result of aging. Consequently, epidemiological and clinical studies of OA are often restricted to older adults and there is limited information on OA in the younger population. The current study takes advantage of available population-based OA data to describe OA across a wide age range comparing younger and older adult age groups.

Methods: Data source: 2009 Survey on Living with Chronic Diseases in Canada - Arthritis (SLCDC-A), a nationally representative survey of Canadians aged 20+ years who reported diagnosed arthritis in the 2008 Canadian Community Health Survey (CCHS). Analyses were restricted to individuals reporting OA and no other kind of arthritis (n=1614). Comparisons to the general population used CCHS data.

Age categories: 20-44/45-54/55-64/65-74/75+ years. SLCDC-A respondents reported OA characteristics including painful joints in the past month, severity (1-10 scale) and frequency of pain and fatigue, arthritis-attributed limitations in daily activities, and extent to which arthritis affected their lives. Both SLCDC-A and CCHS respondents also reported their life satisfaction and physical and mental well-being.

Results: The average age at diagnosis of OA was 50 years: 30.4% were diagnosed before the age of 45. At the time of the survey 27.1% of respondents reporting OA were younger than 55, with 7.2% aged 20-44 years.

Table 1. Characteristics and severity of OA by age

	Age groups				
	20-44	45-54	55-64	65-74	75+
Mean number of painful joints	3.5	3.1	3.5	3.9	3.5
Joint pain - Severe and frequent*	31.4%	22.4%	25.9%	28.6%	29.3%
Fatigue - Severe and frequent*	27.2%	26.2%	16.4%	18.4%	18.0%
Limited in bathing/dressing (yes)	36.1%	32.0%	36.8%	40.2%	40.0%
Limited in getting around the house (yes)	52.9%	39.6%	33.9%	41.1%	46.0%
Limited in doing household chores (yes)	58.9%	49.2%	58.0%	53.7%	57.8%
Limited in running errands/shopping (yes)	55.0%	48.6%	46.3%	52.1%	56.3%
Limited in recreation, leisure, hobbies or social activities (yes)	78.5%	60.8%	66.0%	57.9%	59.8%
Overall effect of OA on life					
Not at all	8.4%	12.6%	8.2%	10.4%	11.4%
A little bit/Moderately	58.9%	60.2%	71.7%	71.0%	58.7%
Quite a bit/Extremely	32.6%	27.2%	20.1%	18.6%	29.9%

*Severe joint pain was defined as pain intensity seven or more out of ten and was considered frequent if experienced "always" or "often". Severe and frequent fatigue was defined analogously.

Table 2. Health status of people with OA compared to the general population (Pop)

	Life satisfaction*		Self-rated health†		Self-rated mental health‡		Life stress§	
Age	OA	Pop	OA	Pop	OA	Pop	OA	Pop
20-44	15.2%	2.0%	30.0%	6.6%	18.3%	6.6%	35.6%	24.6%
45-54	7.6%	3.3%	25.7%	10.5%	18.5%	7.0%	28.2%	29.1%
55-64	7.9%	3.9%	23.9%	15.3%	13.4%	6.9%	20.6%	21.5%
65-74	6.7%	3.0%	29.5%	17.7%	5.3%	5.2%	12.1%	11.8%
75+	4.1%	3.9%	32.8%	25.9%	2.9%	5.9%	11.4%	4.2%

*Dissatisfied or very dissatisfied; †Fair or poor self-rated general health; ‡Fair or poor self-rated mental health; §Quite a bit or extremely stressful

The characteristics of OA for the younger and older respondents were remarkably alike, with a similar number of reported painful joint sites and similar proportions with severe and frequent joint pain, and most activity limitations (Table 1). Younger individuals were more likely to report having severe and frequent fatigue and being limited in recreation, leisure, hobbies or social activities.

The proportion of individuals in the 20-44 and 45-54 age groups reporting that their arthritis affected their life quite a bit/extremely was similar to those in the 75+ year age group. Overall, only 10% of respondents with OA reported that their OA had no effect on their lives.

Compared with the general population, in the 20-44 age group those with OA had a nearly 8-fold higher proportion reporting low life satisfaction; a nearly 5-fold higher proportion reporting low self-rated general health; and a nearly 3-fold higher proportion reporting low self-rated mental health (Table 2). Differences between individuals with OA and the general population were considerably smaller among older respondents.

Conclusion: OA is not an uncommon experience among young and middle aged adults in Canada, despite the frequently held perception that it is a condition predominantly of older people. Findings for young and middle aged adults in this study are likely to represent the initial experience of the disease for a substantial proportion of all people with OA. It appears that irrespective of age, OA is accompanied by a similar degree of symptoms and severity, suggesting that younger individuals with OA live for many years with the 'full' consequences of OA. Given the relatively little attention that has been paid to OA in young age groups, more epidemiological and clinical attention is warranted.

Disclosure: E. Badley, None; **J. Wilfong**, None; **A. Perruccio**, None.

Abstract Number: 1058

Sex-Specific Associations Between Knee Synovial Fluid Biomarkers and Knee Osteoarthritis Pain

Anthony Perruccio, Elizabeth Badley, J Denise Power, Mayilee Canizares, Nizar Mahomed, Kahlid Syed, Rajiv Gandhi, J. Roderick Davey, Mohit Kapoor, Christian Veillette and Y Raja Rampersaud, Schroeder Arthritis Institute, University Health Network, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Sex has received limited attention in osteoarthritis (OA) clinical studies assessing relationships between biomarkers and pain. In prior work we reported sex-specific associations between knee pain and systemic inflammatory biomarkers. The current study investigated associations with knee synovial fluid (SF) biomarkers, focusing on whether associations differed by sex.

Methods: Patients (n=180) with knee OA scheduled for total joint arthroplasty at a tertiary care hospital in Toronto, Canada. Eligibility: 35+ years of age. Exclusions: acute trauma/injury or inflammatory arthritis. Health questionnaires and blood draws were completed in-clinic and knee SF drawn prior to surgical incision. Questionnaire data included knee pain (WOMAC subscale), sex, age, height and weight (BMI was calculated), comorbidity, and symptomatic joints. SF (and blood) biomarker analyses included leptin (adipokine), IL-8 (pro-inflammatory cytokine) and MMP-1 and -2 (matrix metalloproteinases) using Luminex bead-based ELISA assays. Concentration values were log-transformed for analyses. Two linear regression models were estimated (dependent variable: knee pain score). The first included each of the SF biomarkers, adjusted for sex, age, BMI, comorbidity and symptomatic joint count. The second added interaction terms between sex and factors found to have sex-specific influences.

Results: Mean age of the sample was 64 years (range 43-89), 56.2% were female. Females had higher comorbidity and joint counts, and worse knee pain scores than males. Median marker concentrations for leptin and MMP-1 were higher in females. No difference was found for IL-8 and MMP-2. In adjusted analyses, initially without sex-specific consideration, none of the biomarkers were associated with pain scores. When sex-specific effects were assessed, all biomarkers were significantly associated with pain, but differently for males and females. The association between leptin and pain was positive in males, negative in females (p=0.004). For IL-8, a negative association was found in males (p=0.022) but none in females. For MMP-2, a negative association was found only in females (p=0.008). Finally, MMP-1 was similarly positively associated with pain in males and females. Sensitivity analyses: additional adjustment for corresponding systemic biomarkers showed a positive association between systemic IL-8 and pain in males and negative association in females (p=0.002); SF biomarker associations were unchanged.

Conclusion: Findings provide evidence of sex-specific associations between SF biomarkers and knee OA pain, suggesting drug targets for OA symptom management may need to be sex-specific. They further highlight that sex considerations in OA clinical/epidemiological studies are essential.

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Abstract Number: 1059

The Association of Pain and Sleep in Relation to Depressive Symptoms Among Older Adults with Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The primary symptom of arthritis is chronic pain which has widespread consequences on an individual's sleep and mental health. Research suggests that sleep and chronic pain may synergistically impact depression. However, to date no study has examine the joint effect that sleep and chronic pain may have on the development of depressive symptoms.

Methods: Data for this study was utilized from the 2010-2016 waves of Health and Retirement Survey (HRS). The study included data from 6,933 individuals with arthritis and were free of depressive symptoms at the baseline (2010). We performed a multivariable-adjusted Cox proportional hazards regression to estimate the hazard ratio for the joint effect of pain and sleep problem relative to having neither conditions on the development of depressive symptoms (CES-D≥3). Sex, gender, race, smoking status, comorbidity count, physical activity limitation, and BMI were all con-

Table 1. Associatons between demographics and Pain problems and sleep problems exposure for Health and Retirement Survey Baseline

	Exposure Status				
Factors	Pain and Sleep (n = 2,604)	Sleep Only (n = 3,181)	Pain Only (n = 347)	Neither (n = 801)	Total N=6933
Sex *					
Male	944(14.9)	1172(17.7)	155(2.4)	344(5.1)	2615(39.9)
Female	1660(23.4)	2009(27.9)	192(2.6)	457(6.2)	4318(60.1)
Age (years)**	64.30(0.4)	66.03(0.4)	63.82(0.6)	65.81(0.6)	64.54(0.4)
Race*					
Non-Hispanic White	2028(32.9)	2515(39.9)	267(4.3)	628(9.9)	5438(87.0)
Non-Hispanic Black	85(1.0)	76(0.7)	13(0.1)	16(0.1)	190(1.9)
Hispanic	443(3.5)	513(3.9)	57(0.4)	145(1.1)	1158(8.9)
Other	48(0.2)	77(1.1)	10(0.2)	12(0.2)	147(2.2)
No. of Comorbidities**	0.95(0.02)	0.65(0.01)	0.77(0.03)	0.61 (0.03)	0.76(0.01)
Smoking Status*					
Ever Smoke	1553(23.0)	1694(24.2)	193(2.8)	460(6.6)	3900(56.6)
Never Smoke	1051(15.2)	1487(21.4)	154(2.1)	341(4.7)	3033(43.4)
Arthrititis Limits Activity*					
Yes	1613(24.1)	783(11.2)	196(2.9)	159(2.2)	2751(40.3)
No	991(14.1)	2398(34.4)	151(2.1)	642(9.1)	4182(59.7)

* Values expressed as N and weighted total percent **Values shown are median and (standard error)

Table 2. The Joint effect of pain and sleep problems on the development of depressive symptoms of our unadjusted and adjusted models using cox regressional hazards

	Unadjusted				Adjusted*			
	Hazard Ratio	95% CI	RERI	AP	Hazard Ratio	95% CI	RERI	AP
Pain and Sleep	3.85	[2.88,5.15]	0.88	0.23	2.94	[2.14,4.04]	0.38	0.13
Sleep Only	2.21	[1.60,3.00]			2.08	[1.51,2.87]		
Pain Only	1.76	[1.19,2.61]			1.48	[1.00,2.19]		
Neither	1.00	Referent			1.00	Referent		

*adjusted for age, sex, smoking status, comorbidity count, race, arthritis limiting activity; RERI- Relative excess risk due to interaction; AP- Attributable proportion due to interaction

Table 3. The Joint effect of pain and sleep problems on the development of depressive symptoms stratified by sex

Unadjusted	Male				Female			
	Hazard Ratio	95% CI	RERI	AP	Hazard Ratio	95% CI	RERI	AP
Pain and Sleep	4.3	[2.94,6.50]	2.1	0.49	3.56	[2.40,5.29]	0.16	0.04
Sleep Only	2.05	[1.35,3.13]			2.21	[1.43,3.40]		
Pain Only	1.15	[0.57,2.31]			1.88	[1.32,3.66]		
Neither	1.00	Referent			1.00	Referent		
Adjusted*								
Pain and Sleep	3.3	[2.16,5.05]	1.43	0.43	2.81	[1.84,4.30]	-0.23	0.08
Sleep Only	1.92	[1.26,2.93]			2.16	[1.40,3.33]		
Pain Only	0.95	[0.47,1.93]			1.88	[1.14,3.12]		
Neither	1.00	Referent			1.00	Referent		

*adjusted for age, smoking status, comorbidity count, race, arthritis limiting activity; RERI- Relative excess risk due to interaction; AP- Attributable proportion due to interaction

sidered for our modeling procedures. We calculated the relative excess risk due to interaction, comparing the joint effect with that of pain alone and sleep problem alone. Analysis was further stratified by sex.

Results: There was evidence of a synergistic effect of pain and sleep on risk of depressive symptoms adjusted-HR (95% CI):2.87(2.80,4.99) and RERI of 0.38. When stratified by sex, a similar synergistic effect was observed in men with adjusted-HR(95% CI):3.30(2.16,5.05) and RERI of 1.43.

Conclusion: Findings from this study suggest that sleep and pain are synergistically linked to the development of depressive symptoms. Understanding the joint effect of pain and sleep on individuals' increased risk of depressive symptoms can help target treatment options for arthritis patients.

Disclosure: U. Nguyen, None; **C. Zielke**, None; **N. Peeri**, None.

Abstract Number: 1060

Temporal Trends of Arthropathies Related Mortality in the United States and Its Regional Variations from 1999-2018

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Epidemiology & Public Health Poster III: Other Rheumatic & Musculoskeletal Diseases (1022–1060)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Temporal trends of arthropathies-related mortality in the United States are not well studied. Arthropathies include Infectious arthropathies, Inflammatory poly-arthropathies, osteoarthritis, and other joint disor-

Table 1. shows crude and age-adjusted mortality rate with 95% CI, from 1999-2018 for arthropathies as the underlying cause of death in four U.S census regions

Census region	Year	Deaths	Population	Crude rate, 95% CI	Age adjusted rate	% of total deaths
Northeast CR1	1999-2003	3,384	269,332,043	1.3 (1.2 - 1.3)	1.1	15.50%
	2004-2008	3,184	272,926,710	1.2 (1.1 - 1.2)	1	15.50%
	2009-2013	3,036	277,676,103	1.1 (1.1 - 1.1)	0.9	15.80%
	2014-2018	2,916	281,227,394	1.0 (1.0 - 1.1)	0.8	16.70%
Midwest CR2	1999-2003	6,287	323,564,615	1.9 (1.9 - 2.0)	1.9	28.80%
	2004-2008	5,692	330,130,356	1.7 (1.7 - 1.8)	1.6	27.80%
	2009-2013	5,153	335,698,460	1.5 (1.5 - 1.6)	1.3	26.70%
	2014-2018	4,683	340,082,035	1.4 (1.3 - 1.4)	1.1	26.80%
South CR3	1999-2003	7,593	508,781,830	1.5 (1.5 - 1.5)	1.5	34.80%
	2004-2008	7,152	545,314,353	1.3 (1.3 - 1.3)	1.3	34.90%
	2009-2013	6,672	579,791,769	1.2 (1.1 - 1.2)	1.1	34.60%
	2014-2018	5,810	611,686,927	0.9 (0.9 - 1.0)	0.8	33.20%
West CR4	1999-2003	4,557	321,485,667	1.4 (1.4 - 1.5)	1.6	20.90%
	2004-2008	4,448	343,655,563	1.3 (1.3 - 1.3)	1.4	21.70%
	2009-2013	4,413	363,985,531	1.2 (1.2 - 1.2)	1.2	22.90%
	2014-2018	4,094	383,293,645	1.1 (1.0 - 1.1)	1	23.40%

Table 2. shows overall AAMR for arthropathies as the underlying cause of death in the U.S from 1999-2008

Overall	Year	Deaths	Population	Crude rate, 95% CI	AAMR	Percentage deaths
	1999-2003	21,821	1,423,164,155	1.5 (1.5 - 1.6)	1.6	100.00%
	2004-2008	20,476	1,492,026,982	1.4 (1.4 - 1.4)	1.3	100.00%
	2009-2013	19,274	1,557,151,863	1.2 (1.2 - 1.3)	1.1	100%
	2014-2018	17,503	1,616,290,001	1.1 (1.1 - 1.1)	0.9	100%

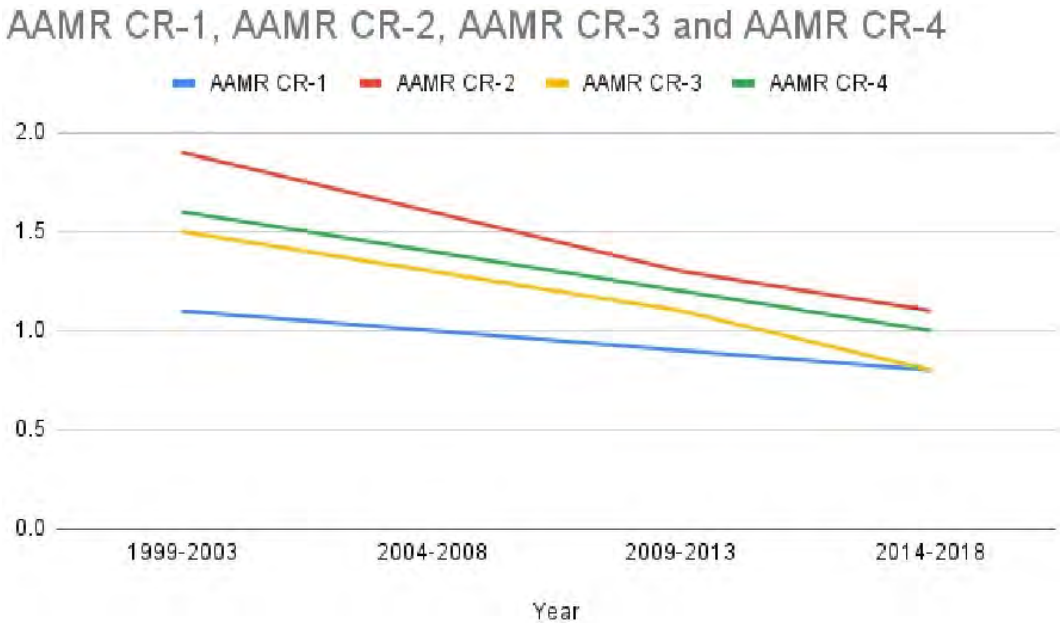

Figure 1. illustrates the age-adjusted mortality rate per 100,000 population due to arthropathies (M00-M25) in four U.S census regions from 1999-2018

ders. It is reasonable to speculate that with the advancement in the field of rheumatology, availability of new immune therapies, and persistent guideline-based high-quality treatment, arthropathies-related mortality rates would have trended down over the last two decades. We wanted to investigate the mortality rates and temporal trends of arthropathies related mortality in the United States using nationwide data.

Methods: In this retrospective study death certificate data were retrieved from the Center for Disease Control and Prevention's Wide-Ranging Online Data for Epidemiologic Research (WONDER) database for 1999-2018. WONDER database is publicly available de-identified data collected by CDC that reports the underlying cause of death across the United States. Mortality, for arthropathies (M00-M25) as an underlying cause of death, was queried. This duration was further stratified into five-year periods from 1999-2018. Age-adjusted mortality rate (AAMR) per 100,000 population was calculated with 95% CI for the four U.S. census regions (CR1 Northeast, CR2 Midwest, CR3 South, and CR4 West).

Results: From 1999-2018 overall arthropathies-related age-adjusted mortality rate (AAMR) declined by 43.75%. Arthropathies-related AAMR for Northeast (CR-1) declined by 18.18 %, for Midwest (CR-2) declined by 42.10%, for South (CR-3) declined by 46.66%; for West (CR-4) declined by 37.5%. Regional and overall crude rates with 95% CI, are reported in Table-1; and Table 2. Temporal trends are illustrated in Figure-1.

Conclusion: Our study shows a downward trajectory of arthropathies-related mortality in all U.S census regions. Regional variations warrant further discovery. This data reinforces the continuation of high-quality care and evidence-based practices that may have played a role in declining AAMR for arthropathies-related mortality in the U.S. Major limitation of our study is the inherent weakness of the WONDER database and the inability to report AAMR for different MKS related disorders (SLE, rheumatoid arthritis).

Disclosure: H. Akbar, None; **W. Mughal**, None; **H. Mirza**, None; **I. Kaur**, None; **H. Jagdey**, None; **M. Mughal**, None.

Abstract Number: 1061

Comparing Consultation Patterns Across Telehealth Platforms and Face-to-Face Clinic in the Military Health System

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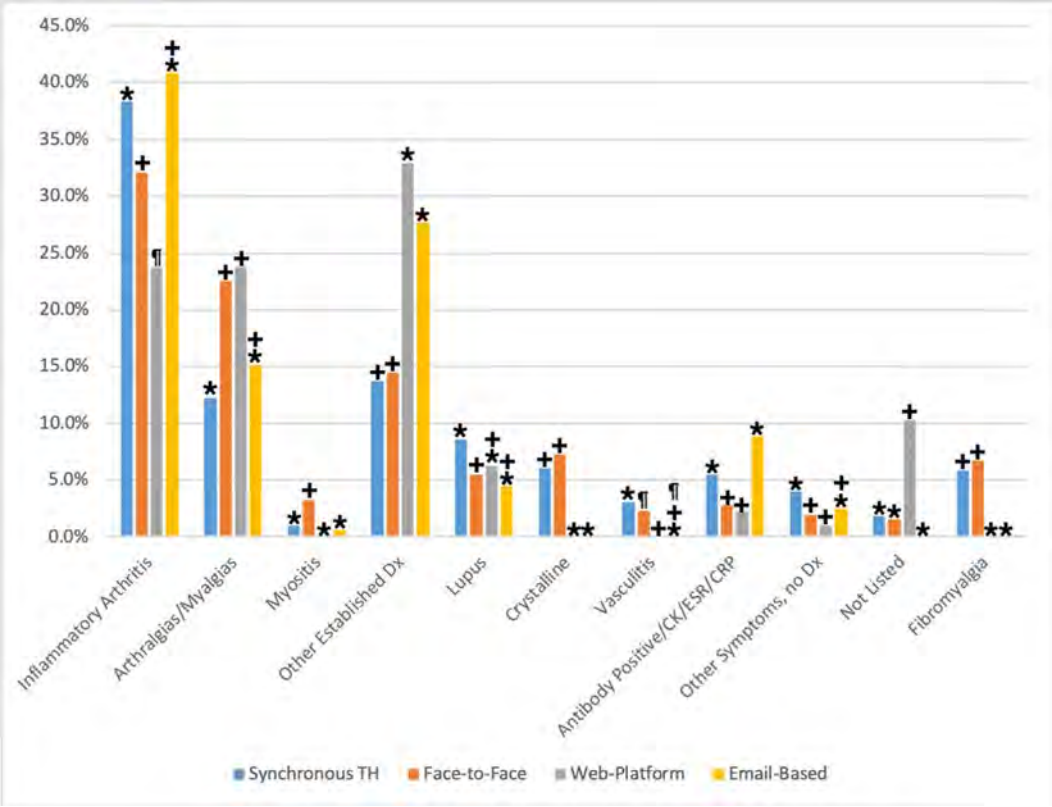
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatic diseases are often diagnostically challenging not only due to rarity, but also because symptoms can develop piecemeal before the diagnosis is clear. Access to care is another hurdle. By 2025 the majority of the US population will have only 0.5-1 rheumatologist per 100,000 people despite an aging population, resulting in an estimated shortage of 3,269 rheumatologists and increasing to a shortage of 4,133 by 2030. Practice in the military health system (MHS) adds additional challenges—transitions of care and practice in austere environments. Multiple telehealth modalities have been implemented to mitigate these challenges.

Methods: We conducted a retrospective review comparing face-to-face consults during 2019 with telehealth consults from three virtual systems in the MHS: an asynchronous email-based system from May 2006 to Feb 2018, a web-based platform from 2014 to 2018, and synchronous telehealth consults from March 2020 to March 2021. We review the diagnosis resulting from consultation and if face-to-face follow up or medical evacuation was required.



Results: Leading diagnoses across platforms were inflammatory arthritis, noninflammatory arthritis, and a composite of other diagnoses. Inflammatory arthritis was the leading diagnosis for the email-based model (65 cases, 40.9%), synchronous telehealth model (429 cases, 38.4%), and face-to-face consultations (1416 cases, 32.0%). Chi-square testing revealed that inflammatory arthritis comprised significantly more consults in the synchronous telehealth and email-based models than in the web-based and face-to-face models. The composite of other diagnoses was the leading diagnosis for the asynchronous web-based model (164 cases, 32.9%), which did not differ proportionately from the asynchronous email model and was significantly more than the synchronous telehealth and face-to-face systems.

Considering outcomes, in the email-based model consultation resulted in medical evacuation in 15.7% of cases and prevented 5 unnecessary evacuations. In the web-based model, consultation prompted medical evacuation in 20.1% of cases. In the synchronous model, face-to-face follow up was recommended in 15.0% of cases.

Conclusion: Modality of rheumatology consultation influences the type of cases are seen. In the asynchronous models, there were fewer referrals for crystalline arthropathies, fibromyalgia, vasculitis, and composite of other diagnoses, suggesting a qualitative difference in referral patterns in different telehealth mediums. Despite these differences, both synchronous and asynchronous telerheumatology models were able to answer consult questions without referral for face-to-face evaluation in 79.9-85.0% of cases, suggesting teleconsultation is a viable method to increase access to high-quality rheumatology care.

Proportion of diagnosis across consultation platforms. Matching symbols indicate that proportions are not statistically different across platforms; different symbols indicate a statistically significant difference.

Disclosure: M. Loncharich, None; **D. DeSena**, None; **A. Collamer**, None; **J. Edison**, None.

Abstract Number: 1062

Telemedicine Enriched Care Model to Optimize Care for Patients with Autoinflammatory Diseases

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SESSION INFORMATION
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Background/Purpose: Autoinflammatory diseases (AID) are severe potentially life-threatening conditions requiring personalized therapy and monitoring which only few expert centers can provide. Long travel distances impede health equity and optimal AID care, especially in emergencies. Individualized care models based on integrative telemedicine consultations (video-c) with AID experts for primary care providers and patients could optimize AID care "close to patients' homes". Data on the acceptance of such care models for AID are scarce. The aim of this study was to evaluate the acceptance and influencing factors of a telemedicine enriched AID care model (video-c).

Methods: This prospective study investigated the influence of usefulness and ease of use on attitude and intention to use video-c in "close to home" AID care. Primary care providers caring for AID patients with ≥1 AID-center visit since

01/2019 were included. Personal expertise, desire for support in AID care and acceptance of video-c were recorded. Acceptance was assessed based on the Technology Acceptance Model (TAM; 7-point Likert scale) with 1 meaning no agreement and 7 meaning strong agreement. Influencing factors were tested by structural equation modeling (SEM). Analysis was performed using IBM SPSS Statistics 26 and MPLUS 7.

Results: The response rate was 54% (62/115). 87% of participants were pediatricians, 10% family physicians, and 3% internal medicine physicians; 40% were female. In AID treatment, 27.4% felt (very) unexperienced, 27.4% (very) experienced; 45.2% neutral. More support from AID experts was desired by 71%. Technical equipment for video-c was available to 56% of primary care providers. 64% indicated a positive attitude (≥5/7 points) towards video-c for AID care "close to home"; 60% would use video-c in practice (≥5/7 points). SEM confirmed acceptable model fitting (WRMR=0.81, CFI/TLI=0.98/0.98). Ease of use showed a significant association with perceived usefulness (β=0.66, p< 0.001). Perceived usefulness was positively associated with attitude towards video-c (β=0.98, p< 0.001). Ease of use and usefulness explained 94% of the variance in attitude towards video-c (R2=0.94). Perceived usefulness combined with attitude explained 93% of the variance in intention to use a video-c (R2=0.93).

Conclusion: Three out of four primary care providers wished for more expert support in AID patient care "close to patients' home". Integrative telemedicine enriched care models (video-c) for primary care providers and patients with AID experts can optimize local AID care. Perceived usefulness and ease of use are significant influencing factors that should be considered when conceptualizing video-c and implementing such care models.

Disclosure: L. Oefelein, None; **J. Klotsche**, None; **S. Benseler**, Novartis, 1, Sobi, 1; **J. Kuemmerle-Deschner**, Novartis, 1, 2, 5, 6, SOBI, 1, 2, 5, 6; **T. Welzel**, None.

Abstract Number: 1063

Use of Telemedicine for Rheumatology Practice in Queensland, Australia: Experiences Before and During the COVID-19 Pandemic

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SESSION INFORMATION
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Background/Purpose: In Australia there is a nationwide rheumatologist shortage potentially translating to poorer clinical outcomes for those living with rheumatic diseases. [1] A possible solution to improve patient care in this setting is telemedicine (TM). During the COVID-19 pandemic TM consultations increased significantly resulting in an opportunity to review rheumatologists' use of TM. The aim of this study was to examine the utilisation and provider perceptions of TM in rheumatology. This study investigated the usage of TM by rheumatologists before and during the COVID-19 pandemic and explored the models of care utilised and the challenges experienced.

Methods: A sequential mixed-methods study design was adopted and rheumatologists completed a questionnaire including demographics, clinical practice, TM uptake, models of care applied and clinician perceptions of TM. The

qualitative phase utilised purposeful sampling of active users of TM through in-depth semi-structured interviews. The impact of COVID 19 pandemic on TM use for rheumatology practise was explored.

Results: Thirty Queensland rheumatologists participated in surveys with 76.7% actively utilising TM. Usage of TM was limited prior to the COVID-19 with 9.5% seeing more than 5 patients per week. Patient populations served by TM included capital city (n=16, 53.3%), regional (n=19, 63.3%) and rural/remote (n=7, 23.3 %). A significant association between rheumatologists (n=29) having ever practised in a rural/remote setting (n=19, 65.5%) and use of TM within the last 24 months (n=17, 58.62%), p=0.030 was seen with no association found for formal training in TM or years of experience as a rheumatologist and TM usage. Of the active TM users prior to the COVID-19 pandemic 90% commenced conventional DMARDs and 55% biological DMARDS through TM. One of the major barriers to wider usage included low to medium confidence with joints assessments through TM (n= 15/19). Qualitative analysis further identified barriers to TM uptake including limited distribution of technology, administrative and peripheral clinical staff involvement and lack of financial incentives particularly in the private sector. During the COVID-19 pandemic, a significant expansion of TM as telephone calls occurred with rheumatologists reporting low confidence and satisfaction with this, whilst identifying that telephone calls and TM may be an acceptable model for monitoring stable patients with low disease activity.

Conclusion: Familiarity with TM exists in this rheumatology cohort, however its usage in routine practise is limited due to multiple barriers. The COVID 19 pandemic highlighted lower confidence in telephone calls as a form of TM and concerns regarding new or unstable patients.

Disclosure: D. Jhaveri, None; **F. Alele**, None; **A. Strom**, None; **T. Emeto**, None; **H. Benham**, None.

Abstract Number: 1064

Pharmacist-Led Multidisciplinary Approach to Opioid Tapering in a Private Rheumatology Practice: Patient Outcomes

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SESSION INFORMATION
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Background/Purpose: With the evolution of disease modifying anti-rheumatic drugs medications, the need for opioids in the treatment of rheumatic diseases has decreased. However, rheumatology professionals are often presented with patients in whom chronic opioid therapy was started prior to the availability of newer DMARDs and may require reductions in opioid doses. Current guidelines suggest opioid tapering should be considered in patients with chronic noncancer pain on ≥90 mg morphine equivalent daily dose (MEDD) daily or in combination with other high-risk medications.

Methods: The pharmacy team developed a three phased program starting in June 2019 including provider/staff education, updates to workflows, and implementation of individualized patient taper plans. Patients identified by providers are enrolled in the pharmacy service. The pharmacy team serves as a continuous resource to providers and works directly with patients enrolled in the service. Baseline characteristics, historical data on opioid related efficacy/side effects, and daily morphine equivalents are collected/tracked for each patient.

Results: Provider and staff education sessions led by the pharmacy team occurred in June 2019, October 2019 and December 2019. Controlled substance contract workflow changes were implemented in December 2019. The number of signed contracts reportable at baseline was 0. To date, a total of 253 signed controlled substance contracts (including tramadol and pregabalin) are documented in TCFR electronic health record. As of April 2021, a total of 124 patients have active prescriptions (defined as a refill in the last 3 months) for opioids including codeine, hydrocodone, oxycodone, methadone, and morphine. Since implementation of our program, 6, 33, and 10 patients have discontinued opioids prescribed by TCFR providers in the years 2019, 2020, and 2021. A total of 19 patients have been enrolled in the pharmacist-led opioid taper service. All patients are co-managed by the pharmacist and the provider. Daily initial starting doses ranged from 20 to 200 MEDD. A total of 5 patients (26%) have successfully tapered off opioids. Nine patients (47%) have had reductions in MEDD. Five patients (26%) have remained on the same initial dose. A total of 9 patients enrolled in the service had an MEDD ≥ 90. Of those patients, 56% reduced MEDD ≤90, of which 2 patients are no longer on opioids. The average MEDD percent reduction for all patients enrolled in the service was 48%. The average duration of all patients enrolled with the service is 11 months with a range from 5-20 months. The duration of taper for patients who have successfully tapered off opioids ranged from 1 to 3 months.

Conclusion: Successful opioid tapering is a time intensive process and requires a multidisciplinary approach. This provides an opportunity for pharmacists to play an essential role as part of a team-based approach to ensure a successful opioid taper or discontinuation while minimizing adverse events.

Disclosure: J. Farrell, Abbvie, 6, Pfizer, 6, Cumberland Pharmaceuticals, 2, 6, Janssen, 5; **M. Miller**, None; **K. Hennig**, None; **K. McCarthy**, None; **C. Katche**, None; **J. Cleary**, Genomind, 2, 6, AcelRX, 1, Remitigate, 2.

Abstract Number: 1065

Optimizing Joint Pain EConsult Referrals in an Underserved Region of Southern California

Neha Chiruvolu[1] and Vaneet Sandhu[2], [1]UC Riverside School of Medicine, Riverside, CA, [2]Loma Linda University Health, Loma Linda, CA

SESSION INFORMATION
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Background/Purpose: Electronic consultations (eConsults) are increasingly utilized to supplement or replace face to face (FTF) visits in different medical specialties. They are especially valuable in underserved communities where timely access for a FTF visit with a rheumatologist is limited by various factors including transportation and limited rheumatology workforce in the area. Further, eConsult assistance with obtaining rheumatology diagnostic evaluations prior to FTF visits expedites patient care. Unfortunately, care is delayed if vital information is not included in eConsults to rheumatology. This study was thus designed to identify gaps in the eConsult referral process for chief complaints of joint pain through the Inland Empire Health Pan (IEHP), the largest insurance plan in an underserved region of Southern California.

Methods: Seven rheumatologists at Loma Linda University Health were surveyed on what information in the eConsult interface would provide the rheumatologist with necessary information to triage the patient into 3 categories: 1. Close for FTF visit, 2. Change in specialty, 3. Hold on FTF pending trial of medication or further diagnostics. 100 eConsult referrals to rheumatology for joint pain were then randomly selected and retrospectively reviewed for this information,

Table 1. Information provided in history of personal illness

Which joints?	
Joints specified	54
Joint pain indicated as "generalized"	12
Not specified	34
Description of joint pain	34
Whether or not pain/stiffness worse in morning	12
Whether or not patient has stiffness	17
Whether pain/stiffness improved or worsened with physical activity	3
Whether or not patient has joint swelling	21

Table 2. Pertinent workup ordered for joint pain

Lab	Ordered (*N*)	Result available at time of referral (*N*)
CRP	56	45
ESR	65	54
RF*	78	66
CCP**	56	48
Uric Acid	21	17
ANA	68	59
Xray	39	29

*RF: Rheumatoid Factor
**CCP: Cyclic citrullinated peptide Ab
Note: CCP was ordered along with RF in 54 patients. Solitary CCP was ordered in 2 patients.

which included: description of joint pain in patient's history of personal illness (HPI; to include description of involved joints, inflammatory vs mechanical pain, presence of swelling, stiffness, association with physical activity), laboratory workup, and x-rays of affected joints.

Results: Among 100 referrals for joint pain, affected joints were specified in 54 and generalized joint pain noted in 12 (Table 1). Information to differentiate between inflammatory vs mechanical joint pain was only provided in 34 consults with presence or absence of swelling noted in 21(62%) of these patients. Rheumatoid factor was ordered in 78 patients, of whom 54 (69%) also had a serum CCP evaluated (Table 2). ANA was ordered in 68 patients, however only seven of these patients had symptoms or indications of connective tissue disease noted in their HPI: 5 with rash, 1 with alopecia and rash, 2 with shortness of breath, 1 with anemia. X-rays were ordered in 39 patients and results were available in 29 at the time of rheumatology appointment. In total, 84 referrals were triaged to a FTF visit, 6 resulted in a change in referral specialty, and 10 were recommended trial of medication or further diagnostics prior to FTF visit.

Conclusion: We find that joint pain referrals made through the IEHP eConsult interface lack important information to guide rheumatologists in their diagnosis and appropriate triage of patients. This can potentially lead to delays in treatment. To optimize the process, a checklist can be displayed in the interface at time of referral to assure that joint pain is thoroughly described in the HPI, associated symptoms are included, and related labs and imaging are ordered in a timely manner. We plan to expand this study to include referrals for positive immunological markers such as ANA.

Disclosure: N. Chiruvolu, None; **V. Sandhu**, None.

Abstract Number: 1066

Evaluation of a Non-Face to Face Multidisciplinary Health Care Model in a Population with Rheumatoid ArthritisVulnerable to Covid-19 in a Health Emergency Situation

Pedro Santos-Moreno[1], Rosangela Casanova[2], Gabriel-Santiago Rodríguez-Vargas[2], Laura Villareal[1], Jaime-Andrés Rubio[2], Josefina Chávez-Chávez[2], Diana Patricia Rivera-Triana[2], Ruth Alexandra Castiblanco-Montañez[2], Sandra Milena Hernández-Zambrano[2] and Adriana Rojas-Villarraga[2], [1]BIOMAB IPS, Bogotá, Colombia, [2]Fundación Universitaria de Ciencias de la Salud-FUCS, Bogotá, Colombia

SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic impacted everyday practice pattern of health care in rheumatoid arthritis (RA) patients. The objective was to evaluate the implementation of a tele-consultation program in adult population with RA

Methods: This was an analytical observational study-prospective cohort (Clinical trials NCT04768413) that evaluated the effectiveness of a teleconsultation model compared with a face-to-face consultation model in RA adult patients. Patients were followed 12 weeks (Jul-Oct 2020) at a RA center of excellence in Colombia. Simple random sampling was done. Two groups were included: Group A, patients who assisted to tele-consultation care and Group B, those who wish to continue with the usual face-to-face consultation. Data regarding activity of disease (Week 0,6,12) [Patient Activity Scale (PAS) in both groups and DAS28 in group B], and Quality of life [EQ-5D-3L], disability [Health Assessment Questionnaire (HAQ)], therapeutic adherence [Morisky-Green Adherence Scale (MGLS)] and self-care capacity [Appraisal of Self-care Agency Scale -Revised (ASA-R)] was evaluated (weeks 0-12). Outcomes regarding COVID-19 were evaluated. Bivariate analysis was done (StataV-13; P-value< 0.05)

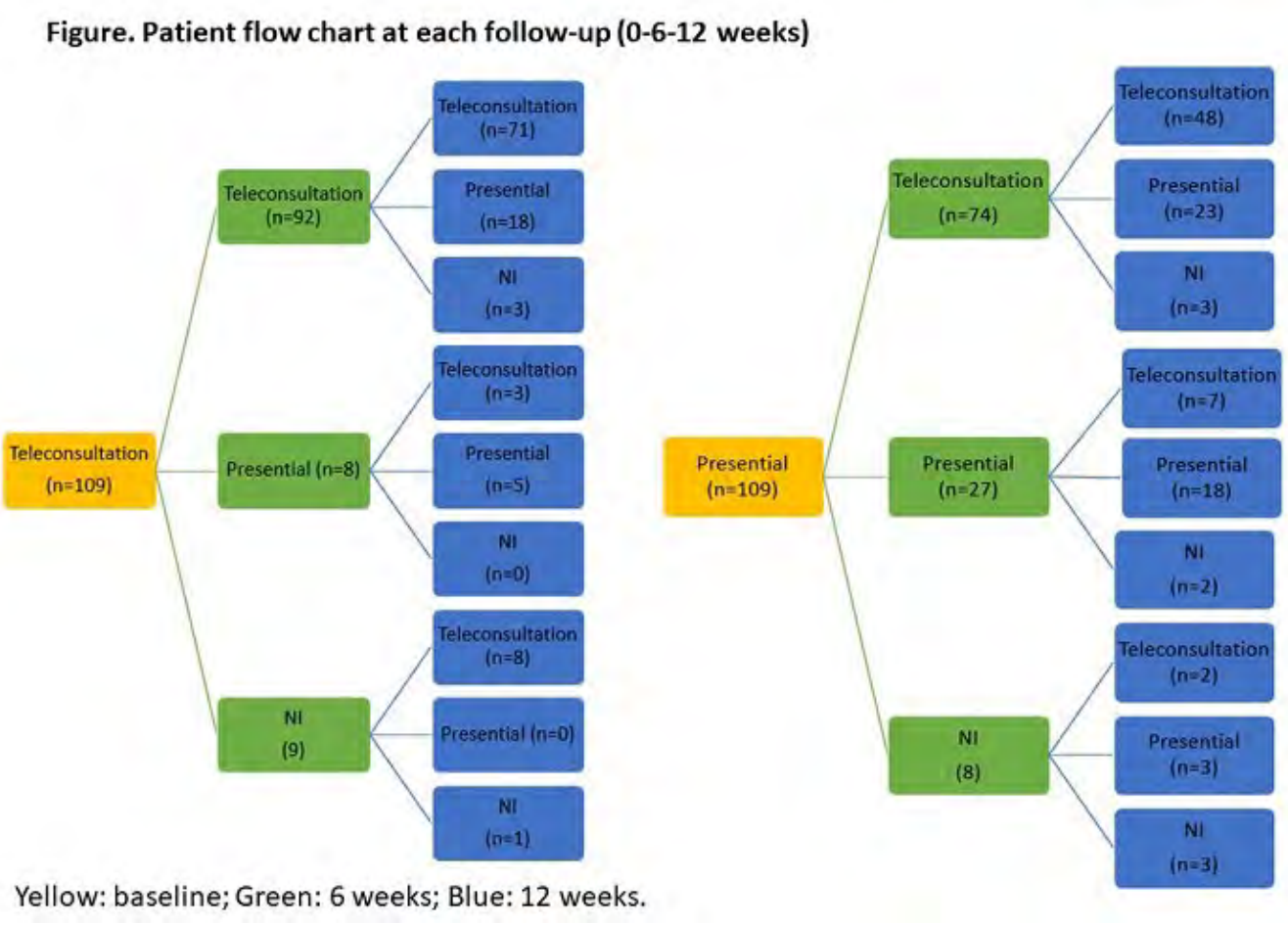
Results: 218 adults were included: (109 in Group A and 109 in Group B). The groups did not differ in general characteristics (See Figure-Table). In Group A: (n=71), no statistically significant differences were observed in the median scores of VAS global, VAS pain, PAS, HAQ, EQ-5D and ASA-R, while increase in adherence was demonstrated (MGLS, without statistical significance), during follow-up. In Group B: (n=18), a significant decrease in adherence (MGLS, p= 0,019) and increase in self-care (ASA-R, p= 0,0077) were found, no other differences were found (including DAS-28). A third group was conformed by patients (n=129) that transited between the two models during follow-up (See figure). An increase in in self-care (ASA-R) was demonstrated in the group presential >remote >presential (p=0,0001), the same result was documented in the group presential >remote >presential, with a decrease in adherence (p=0,033). 7 patients developed COVID-19 (one patient hospitalized/group A and one patient died/mixed model)

Conclusion: The teleconsultation model favors that patients remain without deteriorating their commitment to RA, without major differences compared to the face-to-face model. It is important to know these results due to the impact they have given the changes that will follow in the care of RA patients due the current pandemic. Studies with a longer follow-up period are required to corroborate the results

Table. Main characteristics of patients

Variable		Teleconsultation n=109*		Face to Face n=109*		p-valor
Age		61.1	12.6	61.9	12.5	0.6079
Age at onset		47.7	13.6	46.7	13.5	0.593
Age at diagnosis		50.2	13.7	49.9	13.3	0.872
Variable		n	(%)	n	(%)	
Sex	Female	90	82.6	87	79.8	0.603
Marital status	Married	44	40.4	51	46.8	
	Single	34	31.2	21	19.3	0.055
	Other	31	28.4	37	33.9	
Socioeconomic status (presential n=106)	Low	61	56	58	54.7	0.794
	Middle or high	48	44	48	45.6	
Residence	Bogotá	77	70.6	89	81.7	0.57
	Outside Bogotá	32	29.4	20	18.4	
Occupational status	Household duties	46	42.2	48	4.0	
	Intellectual/ office work	18	16.5	4	3.7	0.000
	Manual work	24	22.0	18	16.5	
	Household duties	46	42.2	48	44	
	Other	21	19.3	39	35.8	
Educational level	None	1	0.9	0	0	
	Primary school	47	43.1	34	31.2	
	Secondary school	35	32.1	50	45.9	0.124
	Technician	21	19.3	15	13.8	
	University	4	3.7	9	8.3	
	Postgraduate	1	0.9	1	0.9	
Comorbidities (Teleconsultation n=108)	Arterial hypertension	36	33.0	38	34.9	0.775
	Osteoarthritis	82	75.9	86	78.9	0.600
	Fibromyalgia	2	1.8	11	10.1	0.010
	Hypothyroidism	27	24.8	25	22.9	0.751
	Osteoporosis	38	34.9	47	43.5	0.192
Previous surgical procedures		89	84.0	74	67.9	0.000
Erosivity		50/102	49.0	44	40.4	0.206
Polyautoimmunity	Systemic Lupus Erythematosus	2	1.8	2	1.8	
	Sjögren's syndrome	5	4.6	5	4.6	
	Systemic Sclerosis	2	1.8	2	1.8	0.087
	Other	9	8.3	2	1.8	

*median (Standard deviation)



NI: No Information

Disclosure: P. Santos-Moreno, None; **R. Casanova**, None; **G. Rodríguez-Vargas**, None; **L. Villareal**, None; **J. Rubio**, None; **J. Chávez-Chávez**, None; **D. Rivera-Triana**, None; **R. Castiblanco-Montañez**, None; **S. Hernández-Zambrano**, None; **A. Rojas-Villarraga**, None.

Abstract Number: 1067

Experiences of Self-Care During the COVID-19 Pandemic Among Individuals with Rheumatoid Arthritis: A Qualitative Study

Jenny Leese[1], Catherine L. Backman[1], Jasmin Ma[1], Cheryl Koehn[2], Alison Hoens[3], Kelly English[3], Eileen Davidson[4], Shanon McQuitty[3], James Gavin[5], Jo Adams[5], Stephanie Thierren[6] and Linda Li[1], [1]University of British Columbia, Vancouver, BC, Canada, [2]Arthritis Consumer Experts, Vancouver, BC, Canada, [3]Arthritis Research Canada Arthritis Patient Advisory Board, Vancouver, BC, Canada, [4]Arthritis Research Canada Arthritis Patient Advisory Board, Burnaby, BC, Canada, [5]University of Southampton, Southampton, United Kingdom, [6]Arthritis Research Canada, Richmond, BC, Canada

SESSION INFORMATION

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Background/Purpose: The COVID-19 pandemic poses new challenges for individuals with rheumatoid arthritis (RA) to manage their self-care, such as being physically active, maintaining emotional wellbeing, and accessing necessary medications. The aim of this qualitative study was to explore how the pandemic influenced self-care from the perspectives of individuals living with RA.

Methods: The study was jointed designed and conducted with patient partners living with RA. Between March and October 2020, we conducted one-to-one semi-structured interviews (30-60 mins) with participants with RA. These participants were purposively sampled from two ongoing randomized controlled trials (RCT) testing a web-based self-care intervention. To be eligible for either RCT, participants must have had: 1) a physician confirmed diagnosis of RA; 2) no joint surgery in the past 6 months; 3) no history of acute injury to any joints in the past six months; 4) an email address and daily access to a computer or mobile device. In the present qualitative study, we aimed for maximum variation in age, sex, and education among participants. An inductive thematic analysis approach was used. Preliminary findings were shared during consultations with 5 local patient partners and 13 patient partners living with RA in a different country to explore transferability of findings.

Results: Twenty-six of 33 eligible participants (aged 27-73; 23 females) agreed to be interviewed. Eighteen (69%) held a university degree or trade certificate. We identified 3 main themes: 1) *Adapting to maintain self-care* described how participants took measures to continue self-care activities while preventing virus transmissions. While spending more time at home, some participants reported improved self-care; 2) *Managing emotions* describes resilience-building strategies such as keeping perspective, positive reframing, and avoiding negative thoughts. Participants described both letting go and maintaining a sense of control to accommodate difficulties and emotional responses; 3) *Changing communication with health professionals* outlined positive experiences of remote consultations with health professionals, particularly if good relationships had been established pre-pandemic. Consultations with patient partners in a different country indicated experiences typically resonated across these different geographical, political and health service contexts that experienced a total or partial lockdown during the pandemic.

Conclusion: Findings describe the adaptations that adults with RA used to maintain their self-care and overall well-being. Insights gained may serve to inform researchers and clinicians in supporting adaptation and resilience among persons with arthritis more broadly during the pandemic and beyond. Findings also reveal opportunities to further examine remote consultations to optimize patient engagement and care.

Disclosure: J. Leese, None; **C. Backman**, None; **J. Ma**, None; **C. Koehn**, None; **A. Hoens**, None; **K. English**, None; **E. Davidson**, None; **S. McQuitty**, None; **J. Gavin**, None; **J. Adams**, None; **S. Thierren**, None; **L. Li**, None.

Abstract Number: 1068

Analysis of Tweets Containing Information Related to Rheumatological Diseases on Twitter

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Twitter is an indicator of the interests of its users in the real world, and therefore, is an appropriate setting to assess the content on rheumatological diseases related tweets. The objective of this research was to analyze the content of the tweets referring to rheumatological diseases.

Methods: We analyzed the content of the tweets published between the 25 of January and 20 February, 2020, in English or Spanish, out of six rheumatological diseases: vasculitis, systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), Sjögren's syndrome (SS), osteoarthritis (OA) and spondyloartopathies, including spondylitis, ankylosing spondylitis, psoriatic arthritis and reactive arthritis. At least 10% of tweets were randomly selected from each disease. It was classified as medical content (diagnosis, treatment or other aspects of the disease) or non-medical (conversation between users, request for help, etc.). It also has been evaluated the type of user and the suitability of the medical content -appropriate or fake.

Results: 15,250 original tweets were published, selecting 1,628: 1,093 classified as medical, 421 as non-medical and 168 as unclassifiable (Figure 1). We analyzed a total of 1,039 tweets: 1,093 classified as medical and 421 as non-medical.

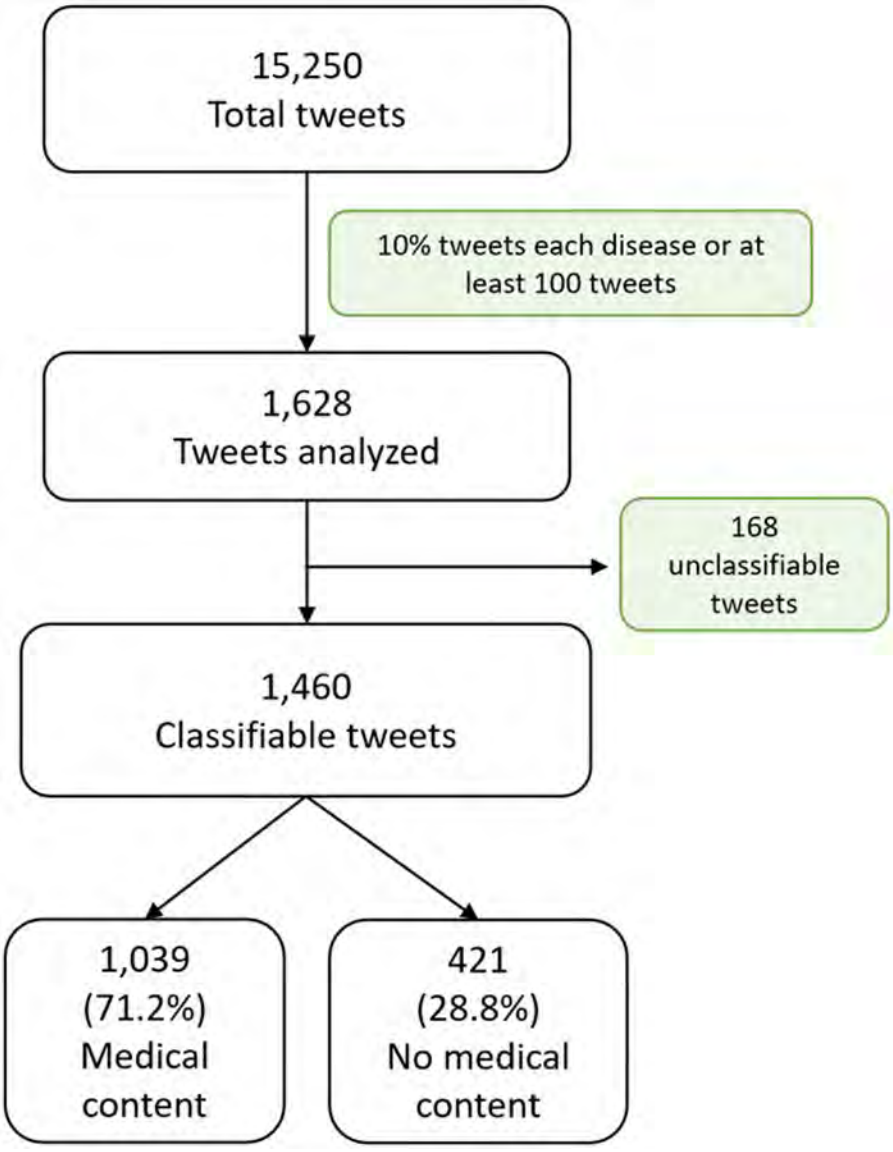

Figure 1. Flowchart illustrating the process followed for the analysis of the tweets, along with the number of tweets included and excluded.

Table 1. Number of tweets with medical contents and of those with fake information related to the rheumatic diseases

	Total tweets with medical content		Fake tweets	
Related to specific rheumatic diseases	**n**	**% of total tweets**	**n**	**% of total tweets with medical content**
Vasculitis	73	67.0%	0	0.0%
Systemic lupus erythematosus (SLE)	108	90.0%	0	0.0%
Spondyloarthropathy	171	60.0%	4	2.3%
Osteoarthritis	337	75.6%	18	5.3%
Rheumatoid arthritis	313	70.7%	24	7.7%
Sjogren's syndrome	37	64.9%	0	0.0%
Total	1039	71.2%	46	4.4%
Area of medical content	**n**	**% of total tweets**	**n**	**% of total tweets with medical content**
Diagnosis	71	6.8%	0	0.0%
Therapeutic	275	26.5%	16	5.8%
Comorbidities	69	6.6%	1	1.4%
Radiology	20	1.9%	0	0.0%
Information for patients	158	15.2%	2	1.3%
Pathophysiology	68	6.5%	0	0.0%
Other	378	36.4%	27	7.1%
Total	1039	100.0%	46	4.4%
Type of user that posted the tweet	**n**	**% of total tweets**	**n**	**% of total tweets with medical content**
Patient/Family member	32	3.1%	3	9.4%
Health professional	186	17.9%	0	0.0%
Health institutes	59	5.7%	0	0.0%
Other	762	73.3%	43	5.6%
Total	1039	100.0%	46	4.4%

The p-value of the Chi square test for the differences between the number of fake tweets by medical content, rheumatic diseases, and type of user were $p = 0.002$, $p = 0.001$ and $p = 0.001$, respectively

As shown in Table 1, medical tweets related to RA and OA accounted for 62%, followed by tweets regarding SpA.

Next, we investigated the content of the tweets (Table 1 and Figure 2). Concerning the specific medical contents, it was found that most of the tweets were related to the treatment of the disease (26.5%) followed by information for patients (15.2%). The percentage of tweets with contents referred to the diagnosis, comorbidities and pathophysiology were minor. Within the medical tweets, the content of these varied according to the disease. The specific analysis of the type of medical content among the investigated diseases showed a significative heterogenous distribution ($p< 0.001$). Contents related to diagnosis were mainly observed in those of vasculitis and SS, and were marginal in those of OA and RA. In contrast, the percentage of treatment related tweets were markedly elevated in those of OA and RA and minimum in those of SS.

Finally, we analyzed the fake content of the tweets (Table 1). Interestingly, a low percentage of tweets with fake content regarding RA, OA and SpA was observed. Furthermore, it was observed that the content of theses fake tweets was mainly focused in the treatment of the diseases. In fact, 5.8 % of the tweets related to treatment showed wrong information. The fake content came from unidentified users. Notably, no fake tweets were encountered among those posted by health professionals or health institutions.

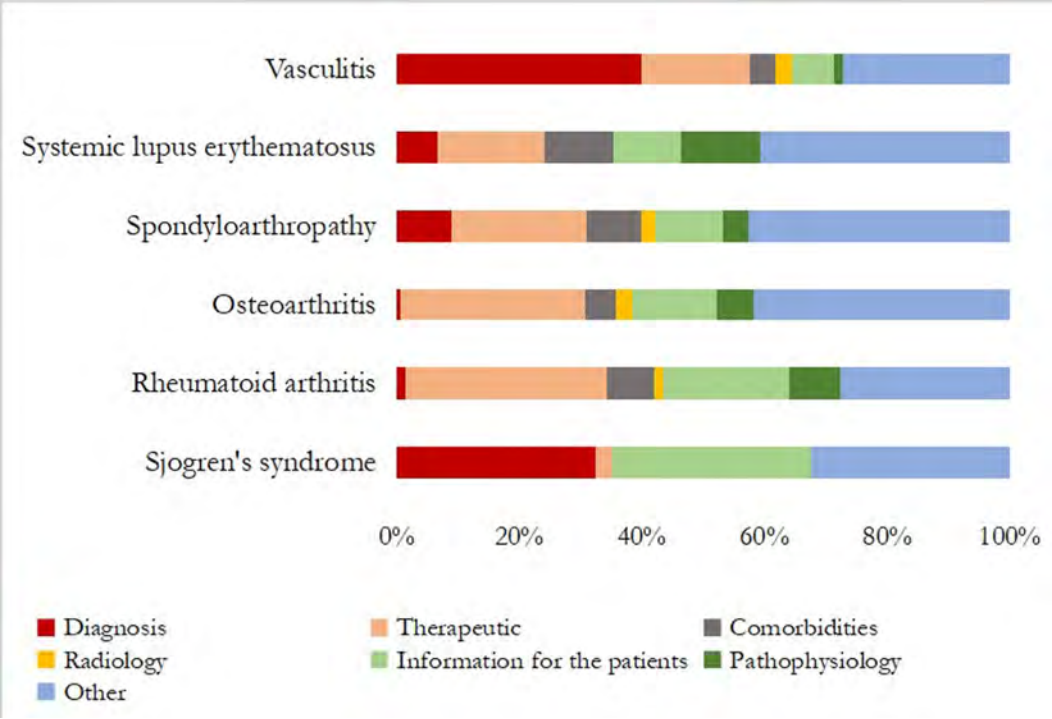

Figure 2. Proportion of the different medical contents among the tweets related to each rheumatic disease.

Conclusion: The data show that the interest of Twitter community in rheumatic diseases is high according to the number of tweets. The diseases with more tweets were the most prevalent. Given the interest raised by medical content posted on Twitter, the involvement of health institutions and health care providers in medical related conversations over social media appears to be desirable. However, the content posted by healthcare professionals is always appropriate, although there is some spreading of fake content by unidentified users.

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Abstract Number: 1069

Supporting Patient-Centered Care in the Pediatric Rheumatology Setting: Patient, Family and Provider Experiences with OurNotes

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)
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Background/Purpose: Health information transparency enabled by the widespread adoption of patient portals and open notes has truly transformed the way healthcare is delivered. However, broader applications of this technology are needed to promote meaningful team-based collaboration in a way that is interactive, personalized to the patient

Empowering Patients and Families as Partners
• "It made us feel like a little team all together. Our voices can be heard, and we feel like we're part of her journey, her treatment journey, whether it's good or bad we can be involved." (Parent 8)
• "I definitely see that it facilitates that structure and helps develops that collaboration which is great." (Parent 2)
• "I think it's important to think about long term goals and speaking up for how I want my medical journey to look like in the future. So, I think that goal setting is a very important thing that I hadn't thought about before, but I'm glad that the survey helps me think about it." (Patient 6)
• "I think it just goes back to the, I have a say in this, and I've got a little bit more control. It's not just the doctor, it's all of us. We have an opportunity to contribute, and I think can only be a positive thing." (Parent 6)
• "I think it's really helpful for me to get my questions out there…just to kind of gather any kind of information to help me better understand her diagnosis. I just want to make sure I cover all bases, so I can better provide care and be more attentive to what she may need, to get these questions answered I can at least kind of accommodate her through the good days and bad days." (Parent 9)
• "I think it just feels like we mean something, we're not just a number. We're not just another patient, like they've taken time to really understand our current situation, what's top of mind for us. So, I just think that improves that relationship." (Parent 6)
• "I feel like it makes the patient feel like they're actually being valued during their doctor's visits, that their doctors actually like taking into consideration their portion of the visit, like knowing that they're being heard and there's concerns are valid…it gives me as a patient more confidence. I felt like we're more connected together than just, you know, a doctor and patient. I felt like my doctor actually knew me so well." (Patient 5)
• "I think it's important because a lot of times your health is more complex than just test results and maybe clinical observations. I guess in some sense, it just adds like more data points to better inform like treatment options and things like that. So, I guess you're getting a more like holistic picture than maybe if you just had the perspective of the doctor." (Patient 1)
• "…it helps my provider kind of see my personality and just see how living with the condition affects me on a daly to day life, and so I think it had kind of a personal aspect to it." (Patient 6)
• "I think it's a positive thing because there's things that come up on the day to day that are part of just how she's doing and how she's feeling that are important to consider in her case as well…not just the clinical stuff but also just the little things that come up, and so I like that what we're seeing is also being included in her medical record. I think it just completes the picture." (Parent 14)
Impact on Care Delivery
• "I feel like our needs and specific questions got answered without me having to like rapid fire at her at the end. [The provider] kind of came in prepared knowing what I wanted to ask and where our visit was going to go, which was really great". (Parent 1)
• "If you if you're a person who has questions and…you just feel like intimidated bringing them up or whatnot, then I think this is a good avenue." (Parent 4)
• "I think it was helpful, because I'm kind of the type of patient who doesn't really say much. I think it was helpful to let my provider know what my problems were for that specific visit because if she doesn't ask, I usually don't say it. I've been with this doctor for a long time, but it's little more sensitive for me to talk about like mental health. So, it was beneficial that I could share that without having to say it to her in the moment." (Patient 2)
• "Instead of going through like more general like topics, it's like easier to pinpoint what exactly would be the best use of time, to go over what areas are you having like more trouble with. I thought it made it a little more targeted, not that it was like unproductive before." (Patient 1)
• "…just knowing that then [provider name] could process that information before we showed up, made the in-person conversation that we had during our visit much more efficient. That's what I found to be the most beautiful." (Parent 2)
• "It's a good way to organize your thoughts and be prepared for the doctor's visits, so you're not wasting the doctors time, you're not wasting your own time. I would hope that it's something that would make the appointment more efficient, and you would get more information than if you just kind of walked in blindly without any notes or thinking of anything in advance.
Especially as a parent with young kids, you're trying to make sure they're behaving themselves and sitting still you know? You're trying to focus on what the doctor is saying. I think for me having all my questions listed out beforehand…I know she's making sure we cover everything. It's like one less thing to worry about." (Parent 12)
• "Without sitting down to think about it or have some time to think about it, I can envision or probably have forgotten some of those components when you're in a in-person meeting or asked a question, right? Maybe something's more top of mind than others. So, having some time to think about things in a less time constrained format is helpful." (Parent 11)
• "You're sort of like forced to like go a little bit deeper and think about your answers like in a more meaningful way." (Patient 1)
• "There is a like a limited amount of time the doctor can spend with us right, so in that sense, having this questionnaire filled in and then the doctor reviewing it before the appointment, I think it helps to make sure that we are kind of on the same page, and that we have the same objectives for that appointment. I think we can go to the appointment with more like clarity, what we want to know, what we want to ask, what our goals are going forward." (Parent 16)
• "It does help me to kind of sit down and put my thoughts down before we all meet…we often have a lot of questions, so it's good to kind of have, okay, what are the top three things that we want to know, that we were concerned about. So, I think it was helpful to sit down and prioritize and have this thought process before we met the doctor." (Parent 14)
• "The questions on the questionnaire I feel were pointed in a constructive way, they kind of got my gears thinking in the right direction." (Parent 2)

Themes and Illustrative Quotes

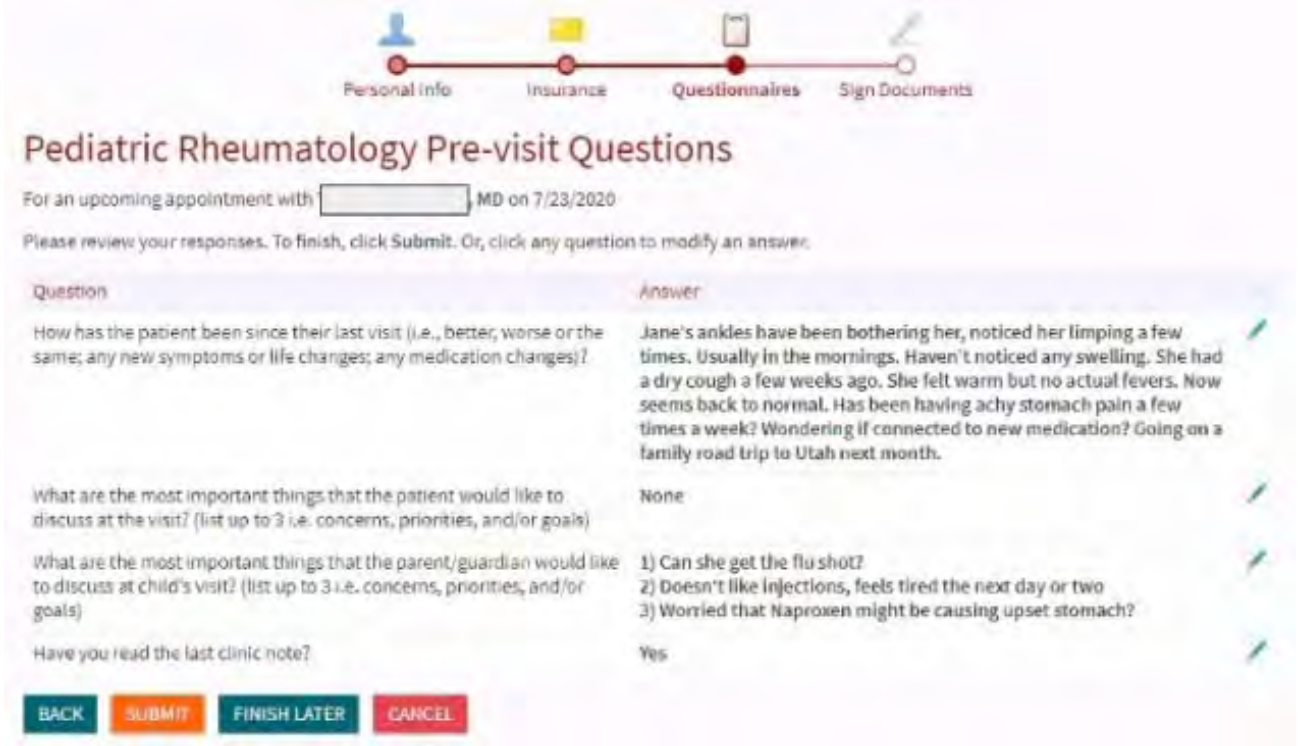
encounter, and facilitates joint decision-making regarding complex decisions. These aspects of care are particularly relevant in improving health outcomes among those with pediatric rheumatic conditions and aid in reducing the growing burden of disease in this population. Through this study, we introduced OurNotes, a portal-based pre-visit tool that leverages patient-generated health data, enabling patients and caregivers to actively contribute to their medical record and the co-generate clinical notes with their provider. We conducted a qualitative study exploring patient and caregiver experiences and attitudes related to the adoption of OurNotes in the pediatric rheumatology setting.

Methods: Patients and/or their caregivers were recruited as a convenience sample across four pediatric rheumatology ambulatory sites at Stanford Children's Health, a tertiary care academic medical center. We conducted individual semi-structured interviews following participants' clinic or telemedicine visits. Interviews were recorded and transcribed, and we employed an inductive reflexive thematic analysis approach outlined by Braun and Clark to analyze the data.

Results: Twenty-four participants (7 adult patients, 17 patient-caregiver dyads) were invited to participate in semi-structured interviews following their clinic or telemedicine visits. Patient diagnoses included juvenile idiopathic arthritis (JIA), systemic lupus erythematosus (SLE), juvenile dermatomyositis (JDM), and localized scleroderma, Inflammatory Bowel Disease-associated spondyloarthropathy. We identified four major themes and ten sub-themes that characterized patient and caregiver experiences, attitudes and perceptions on how OurNotes may foster strategies for enhancing their rheumatology care experience. Major themes included *Empowering Patients and Families as Partners, Impact on Care Delivery, Information Impact, and User Experience*. The results are summarized concisely in Table 1 with supportive illustrative excerpts.

Information Impact
• "When I read providers chart notes versus the notes that I take, it's kind of like a check and balance to make sure that this is what we are going to do, this is our plan. This is what I understood and that's what you guys understood. That way, there's no mishap or incorrect diagnosis or incorrect miscalculation of medication. So, it's definitely helpful for me to just make sure that, yes, we are on the same page. And if we're not, or if I don't see something in in your guys' notes like, you know, I'll email you guys and just be like, hey, you know, I noticed I was going through your notes, and you didn't say anything about so and so or whatever it is. Is this still the plan?" (Parent 9)
• "I just think it's good to have a central place to kind of look back at all of the notes from different appointments. Sometimes it's hard because we have some outside providers, so if the information is being transferred back and forth, it's just nice to refer back to the notes. Especially if I'm speaking to someone else and telling what happened in that appointment." (Parent 5)
• "I actually thought that that was helpful information to have access to. It was just very factual, and kind of a summary of where she was at. I thought it was interesting to read [the provider's] perspective on where things were in her words. I think it was it's just helpful sometimes to hear things you know just in a different way…I think it just added more clarity." (Parent 14)
• "Yes, I always try to read the doctor's notes either after the visit or before the next visit. I think it's always important that I know my health history and that I'm aware of everything in the doctor's notes, and I think it always helps me prepare questions for the next visit. It's also great to see the evolution of my health history over time, I think it's very important." (Patient 6)
• "I think what it helps is that during the appointment we talk, but we don't remember everything, right? So, basically what the doctor says, especially certain medications that are discontinued or no longer used or for example if there is any lab result, we need to be paying more attention to. What I find in the notes is that everything is written and captured, so I can go and review it and relate back to what we discussed during the appointment. So, in that sense it's kind of, rather than kind of just having that ambiguity in that what was discussed during the visit, the written note makes it more concrete" (Parent 16)
• "I find it helpful if I need to go back and reference something that they said that I couldn't remember. The amount of information, you get in an appointment is overwhelming and if you're juggling a small kid, it's hard to take notes, and so I think it is nice sometimes to go back. I mean, probably not everything is in there, but majority of stuff you could probably find, or I have found answers to in the past by having access to that." (Parent 12)
• "I think it's a good idea that this questionnaire gets integrated into the doctor notes. I think it's nice for both, us, and the provider, to review on both sides. So, in the future when you want to look back and see what our concerns were at a certain point in time, and what the doctor decided the plan was going to be, it may be helpful." (Parent 16)
• "It's so many different medicines and this disease is extremely complicated. A lot goes into it on a day-to-day basis and changes happen rapidly. I just to like to stay on board and you don't want to do the wrong thing. So, it's good to have a reference and then you know sometimes if you have to call your doctor's office, sometimes they're busy and you get a machine and then you gotta wait for them to call you back. So, this like provides clear messages, what the doctor said, and how to do things. It's very thorough and it's an amazing system, I think." (Parent 4)
• "…I really want to focus on him and we're there. I try to give him all my attention to help him manage his emotions and manage what he's going through. So, having my attention divided, I can sometimes miss something. I try to take notes in the moment, but it doesn't always happen. I've been able to look over his notes and make sure that I know where we're going with his treatment plan, and I know what to expect in the future." (Parent 1)
User experience
• "I'm so comfortable with everything now, and so familiar with everything we went through, but in the beginning, there was so much that I think that having this would have even made me feel more comfortable and confident in going into every appointment." (Parent 8)
• "I think that the only drawback is my time, like the effort that I'm willing to put in, and I think that it really did put the pressure, not pressure, but like just enough for me to feel like I really need to prepare and make sure that I'm walking in knowing what's going on. So, I enjoyed that. I think maybe for some people the time might be an issue." (Parent 1)
• "It depends on the week. The week that we had it, we had time to sit and go over it. Sometimes things just get crazy and busy, and it might just be another thing to do, but I think it's beneficial if you take the time to do it." (Parent 7)
• "I think I did get a little nervous. I was like oh, I better make sure that this sounds intelligent. But I realized like, it's just it's a document like any other and it's there for communication and record keeping. So, anything that I share is I think adds value, you know, and so I chilled out about it. Yeah, I find it really exciting that I get to contribute to his file." (Parent 1)
• "I think it's a great idea for parents to be able to put in their concerns. Sometimes I think I can be over worried, so that would be my only concern, listing things that may not be of immediate concern. If it's going to be solidified in the notes, I would want it to just be accurate and not my worries. I would just be afraid that would clutter up the actual detail of the note." (Parent 17)
• "I think that the questionnaire seemed very secure, and I feel like I would have been comfortable expressing any concerns in the survey, because I know that it's through a safe website and it's going directly to my provider and to people within the system that care about my health and well-being." (Patient 6)
• "I'm a very open person. So, I kind of feel like all cards are on the table, and I would put it in the chart if it's important to me and if I feel like I really need to discuss it, even though it may be embarrassing. I'm mindful, for the fact that I'm an adult, and nobody has access to my MyHealth or MyChart except for me, but if I was like a teenager who wanted to talk about something that my parents might have access to, I don't know if I would feel comfortable putting it in there." (Patient 7)
• "The only thing that I can think of would be just access. If people don't have access, right? The mobile version is more robust in some ways, but it's less user friendly. If you only have access through your cell phone, I don't think that you could do the question nearly as easily. I did it on my laptop, and so just, you know, having access to the Internet and access to a device is needed. What if you're not tech savvy?" (Parent 2)

Themes and Illustrative Quotes



Conclusion: OurNotes represents a novel application of the electronic health record that has the potential to bridge inefficiencies in care among patients and families with chronic rheumatic conditions by enhancing information flow, fostering active collaboration and supporting more personalized and productive care interactions. Clinical transparency and inclusivity afforded by this approach empowered patients and families to effectively participate in care with greater autonomy in decision-making. Participants also endorsed a better understanding of their care, improved dialogue during visits and greater trust and satisfaction with their providers. More research is needed to demonstrate the best practices of OurNotes, paying special attention to clinical workflow integration, equitable access, and patient privacy and confidentiality.

Disclosure: U. Khalsa, None; **R. Pooni**, None; **C. Sandborg**, None; **I. Balboni**, None; **K. Wayman**, None; **T. Lee**, None.

Abstract Number: 1070

Experiences of Wearable Technology by Persons with Knee Osteoarthritis Participating in a Physical Activity Counselling Intervention Study: A Relational Ethics Lens

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Background/Purpose: Current evidence indicates wearable physical activity trackers could support persons with knee osteoarthritis (OA) to be more physically active. Recent empirical evidence also identifies, however, some persons with arthritis experience guilt or worry while using a wearable if they are not as active as they should be. Questions remain around how persons with knee OA experience benefits or downsides in using a physical activity wearable in their everyday lives. Better understanding of these experiences are needed if wearable technology is to be incorporated in arthritis self-management in ways that are ethically aware. Our aim was to use an ethics lens to describe a range of experiences (positive or negative) from persons with knee OA who used a wearable as part of a physical activity counselling intervention study.

Methods: This is a secondary analysis of qualitative interviews (60-90 mins) nested within a randomized controlled trial (RCT). Guided by phenomenography, we explored the experiences of persons with knee OA, following their participation in a physical activity counselling intervention. The intervention consisted of participants attending a 1.5-hour education session about physical activity, using a Fitbit Flex, and receiving 4 biweekly phone calls for activity counselling with a study physiotherapist (PT) in an 8-week period. All PTs were trained in the Brief Action Planning approach, whereby they guided participants to identify activity goals, develop an action plan, and identify barriers and solutions. Benefits or downsides in participants' experiences of using the wearable were identified using a relational ethics lens, with attention paid to any impacts on their relationships with themselves (i.e., their self-perception) or the study PT.

Results: Interviews with 21 participants (12 females; 9 males) aged 40-82 years were analyzed. Education ranged from high school graduate (n=4) to bachelor's degree or above (n=11). Three categories of description were identified: 1) Participants experienced their wearable as a motivating or nagging influence to be more active, depending on how freely they were able to make autonomous choices about physical activity in their everyday lives; 2) Some participants felt a sense of accomplishment from seeing progress in their wearable data, which fuelled motivation. One participant experienced negative emotions (e.g., self-blame) if his wearable data indicated physical activity goals were not met; 3) For some participants, sharing wearable data helped to build mutual trust in their relationship with the study PT. They also expressed, however, there was potential for sharing wearable data to undermine this trust if, for example, they perceived the data as inaccurate.

Conclusion: To our knowledge, this is the first qualitative study that uses a relational ethics lens to explore how persons with arthritis experienced changes in their relationship with a health professional when using a wearable during research participation. Findings also provide an early glimpse into positive and negative emotional impacts of using a wearable that can be experienced by participants with knee OA when participating in an RCT to support physical activity participation.

Disclosure: J. Leese, None; **G. Macdonald**, None; **A. Townsend**, None; **C. Backman**, None; **L. Nimmon**, None; **L. Li**, None.

Abstract Number: 1071

Experiences Using Wearable Technology by Persons with Rheumatoid Arthritis Participating in a Physical Activity Counselling Intervention Study: A Relational Ethics Analysis

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Background/Purpose: Using wearables to self-monitor physical activity is a promising approach to support self-management among persons with arthritis. Evidence indicates, from perspectives of persons with arthritis, using a wearable influences interaction with health professionals in positive and negative ways. Questions remain about benefits and downsides that may be experienced by persons with arthritis in relationships with themselves (i.e., self-perception) and others, if using a wearable in self-management. Relational ethics is a suitable conceptual lens to explore positives or negatives encountered in these relationships. Our aim was to use this ethics lens to better understand how persons with rheumatoid arthritis (RA) experience their use of a wearable as part of a physical activity counselling intervention study involving a physiotherapist (PT).

Methods: A constructivist grounded theory design and a relational ethics lens guided data collection and analysis. A sample of persons with RA took part in an initial and follow-up interview following participation in an 8-week randomized controlled trial. Participants used a Fitbit-Flex-2 paired with a new web-based application to self-monitor physical activity, received education and counselling from a study PT and received 4 biweekly calls from the PT. We

took a systematic approach of coding transcripts, and forming concepts and key categories to construct a conceptual framework underpinned by concepts of relational ethics.

Results: Initial interviews took place with 14 participants (12 female; 2 male) aged 29-71 years. Of these, 11 took part in a follow-up interview. A conceptual framework was developed to illustrate key categories identified in analysis. These categories describe positive and negative influences of using a wearable with the PT on how participants constructed a valued moral identity: 1) Participants expressed how being active intertwined with moral values placed on self-control within cultural norms in which they lived. For some, using a wearable helped to "do something right" by reaching step goals or sitting less. Some, however, felt ambivalent (feeling both justified and at fault) when they could not reach a physical activity goal; 2) Participants described how their distrust of wearable data raised moral tensions in their relationship with the PT, which had implications for how mutual trustworthiness was negotiated; 3) Participants conveyed being active as a means of preserving or regaining respect for themselves as an independent and productive person. Some described how interpreting wearable data with the PT helped them to affirm this valued sense of self.

Conclusion: This study contributes a situated relational ethics conceptual framework grounded in empirical evidence to sparse literature on how persons with arthritis experience their use of a physical activity wearable positively or negatively. It brings to light salient ethical issues pertaining to autonomy, mutual trust, and respect for further study in the context of everyday self-management. It is a key step to informing how to incorporate wearable-enabled programs that support physical activity participation in ways that are ethically aware.

Disclosure: J. Leese, None; **S. Zhu**, None; **A. Townsend**, None; **C. Backman**, None; **L. Nimmon**, None; **L. Li**, None.

Abstract Number: 1072

The Multidisciplinary Approach with Patient Collaboration Improve the Clinical Effectiveness of the Intervention

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Background/Purpose: We have developed a multidisciplinary unit for patients in treatment with biological therapies (BT) with the collaboration of Dermatology (Der), Gastroenterology (GE), Rheumatology (Rheu), Ophthalmology (Oft), Endocrinology , M Preventive, Nursing and Pharmacy. Diseases: rheumatoid arthritis (RA), spondyloarthritis (SpA), psoriatic arthritis (PsA), inflammatory bowel disease (IBD) and psoriasis (Ps). Patients collaborate in the management of the unit.

Objective: To check the changes that the new model can offer in accessibility, efficiency effectiveness, and quality of life, as well as delving into the concept of multidisciplinarity.

Table 1: effectiveness results

	Rheu		GE		Der	
	2019	2020	2019	2020	2019	2020
Patients clinical remission (%)	52.3	62.4	67.3	72.6	78.4	82.8
Hospital admissions, any cause (%)	10.7	6.4	15.9	9.8	3.8	4.3
ER admissions, any cause (%)	25.6	20.3	37.4	24.5	17.1	12.4

Methods: Unit began in January 2019 and results of 2020 have been compared with 2019. Indicators: number of patients attended, patients starting BT, patients from another health area, proportion of patients who need to be attended by more than a specialty, proportion of patients in clinical remission, percentage of patients admitted to hospital or emergency room for any cause, annual cost of BT per patient, proportion of patients on biosimilar, EuroQol, hospital scale of depression and anxiety (HAD), labor productivity questionnaire (WPAI).

Results: In 2020, 8,156 medical consultations, 11,014 nursing consultations, 2,311 pharmaceutical care and 4,093 treatments were carried out in the day hospital. 2020 and (2019) indicators: Accessibility: 2,940 (2,280) patients, patients starting BT: 145 (140); BT patients: Rheu 1011 (868), digestive 640 (652), dermatology 210 (211); patients from another healthcare area: Rheu 43.8% (40.1%), GE 46.6% (41.9%), Der 30.8% (25.0%). The effectiveness results are shown in the attached table. Efficiency: average annual cost BT, RA € 5,747 (€ 6,371), SpA € 5,757 (€ 6,371), PsA € 6,331 (€ 6,895), IBD € 7,977 (€ 8,693), Ps 6,945 € (€ 7,210); Patients on biosimilar treatment, RA 55.2% (55.7%), SpA 38.0% (28.4%), PsA 34.7% (31.9%), EII 57.3% (48, 9%), Ps 25.9% (13.6%). Quality of life: Median EuroQol (IQR): Rheu: 75 (60-85) vs 70 (50-80) in 2019; GE 80 (60-86) vs 75 (69-80) in 2019; Der 80 (70-90) vs 77.5 (67.5-90.0) in 2019. Median HAD (IQR): Rheu 13 (-22) vs 11 (6-18) in 2019; GE 8 (5-16) vs 9 (7-10) in 2019; Der 6 (3-7) vs 5.5 (4-11) in 2019. WPAI hours / week, mean (SD): Rheu 3.9 (11.1) vs 4.3 (11.6); GE 3.9 (10.5) vs 2.7 (6.9), Der 0 vs 0.8 (2.1). Multidisciplinariety in 2020: Reu 23.3%, GE 20.5%, Der 46.8%, Oft 24.6%.

Conclusion: We observed an improvement in the quality of care in our multidisciplinary unit for patients treated with biological therapies with their collaboration in the management. Noteworthy was the improvement in the effectiveness of BT, measured by the percentage of patients in clinical remission and the decrease in patients admitted to hospital or to the emergency room. However, the improvement in the quality of life with the instruments used is not so evident. We need to deepen the analysis of the indicators used and the procedures of our model to confirm this improvement.

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In Favor of the Subspecialty Clinic Model for Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)
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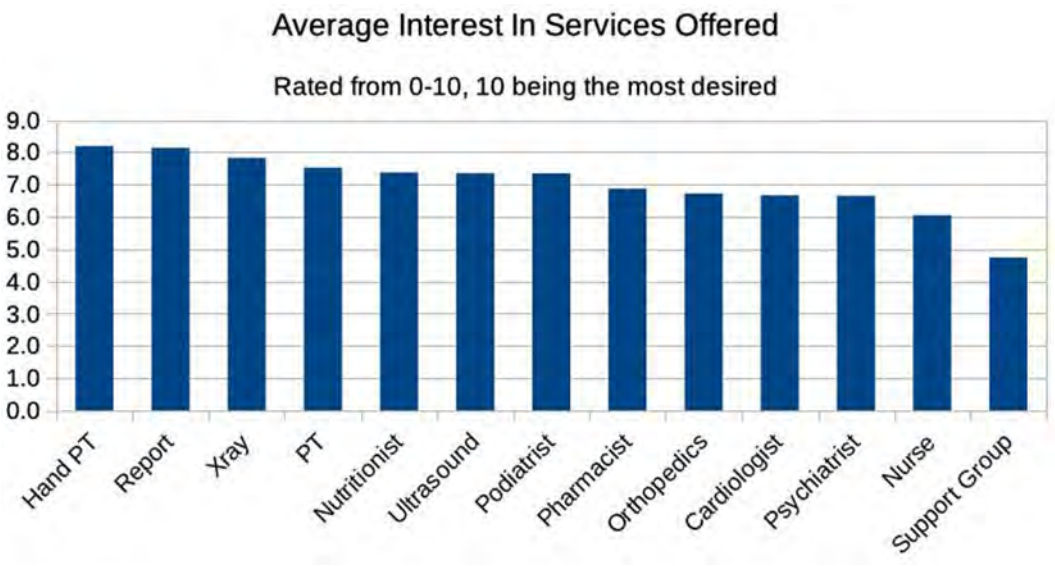
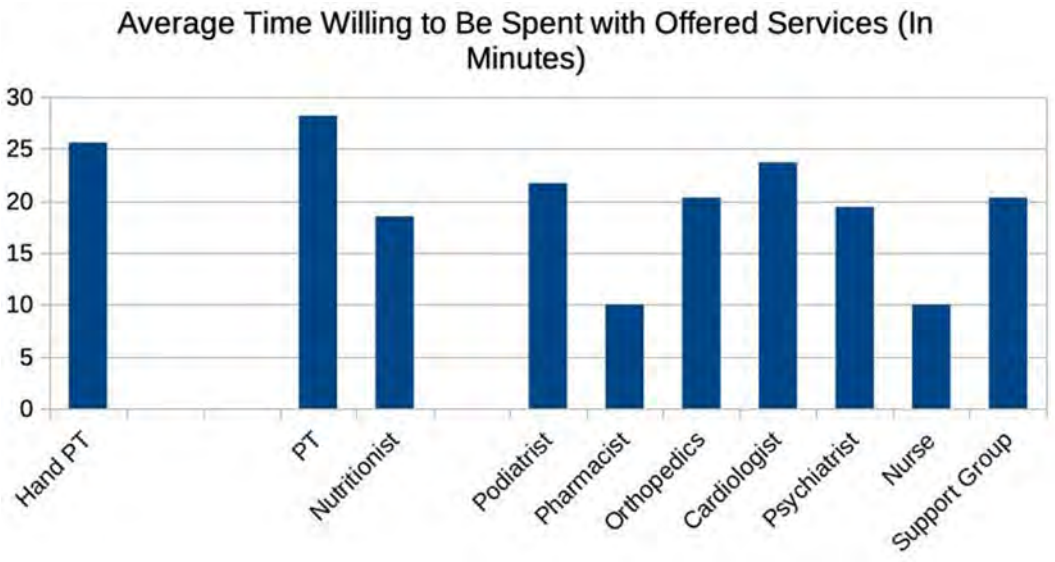
Background/Purpose: The Subspecialty Clinic Model (SCM) which seeks to allow for collaborative care and services by stratifying patients with a particular disease or need to a specialized clinic has been growing in popularity in rheumatology. This model has been shown to not only improve patient satisfaction but also patient outcomes. While the SCM is popular in other rheumatologic diseases such as lupus, it is less popular for rheumatoid arthritis. In this study, we sought to collect patients' perspectives on a SCM for RA. **To our knowledge, this is the first study to take into account patient perspectives in designing a RA subspecialty clinic**.

Methods: 54 adult patients with a diagnosis of RA based on ICD-10 diagnostic codes were surveyed at an outpatient rheumatology clinic. Participants were asked to complete a survey rating their interest (0-10, with 10 being the most desired) in having a service (pharmacist, nurse, physical therapist, hand therapist, orthopedics, podiatrist, psychiatrist, cardiologist, support group, xray, ultrasound), the time (0, 5, 15, 20, 30, 45, 60 minutes) they were willing to have with said services, whether they would agree to be billed for the services, how often they would attend a clinic under the SCM, and if they would transfer care to a SCM. Statistical measures of location were used to analyze the data.

Results: Among those surveyed, 88% of respondents were interested in having at least one of the services that were described. Almost all participants (94%) expressed interest in getting an annual report. Having a psychiatrist help improve pain perception was the least popular service, but over half the respondents still expressed interest (62%). Among respondents who were interested in a service, the service that evoked the strongest interest was hand physical therapy (average of 8.19). The service that evoked the weakest response was a support group (average of 4.74). Participants were willing to spend the most time with a physical therapist (average 28 minutes) and the least time





with a pharmacist and nurse (average 10 minutes). More than 75% of respondents were willing to be billed for xrays, ultrasound, physical therapy, hand therapy, and orthopedics. Less than 60% of respondents were willing to be billed for the remaining services. 74% of participants reported that they would attend a clinic under the SCM at least yearly and 50% were willing to transfer their care in order to access these services.

Conclusion: Patient perspective and satisfaction has recently become a focus in medicine as it often positively correlates to patient outcomes. The response from our participants were strongly in favor of the SCM for rheumatoid arthritis. This indicates that movement to the SCM may be advisable.

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Satisfaction with a Virtual Learning Collaborative Aimed at Implementing Treat to Target (TTT) in Rheumatoid Arthritis (RA)

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SESSION INFORMATION
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Background/Purpose: Learning collaboratives (LC) have been used widely for quality improvement in healthcare, and a recent 9-month in person LC was found effective for improving treat to target (TTT) in RA (1). However, there is relatively little information about the experiences of participants in a virtual LC and little qualitative data or participant feedback on how this format can be improved.

Methods: During the COVID pandemic, we conducted a virtual LC with 18 rheumatology practices. The LC focused on implementing TTT in RA and included a virtual kick-off meeting (run over 5-6 hours) and monthly webinars. The

Table 1. Site Characteristics Based on Site Surveys (N = 18)

	Category	N (%)
Practice Type	Solo	1 (5.9%)
	Group Rheumatology	9 (50%)
	Group Multi-Specialty	6 (33%)
	Other	2 (11%)
Practice Setting	Academic Medical Center	12 (67%)
	Private Practice with Academic Affiliation	2 (11%)
	Private Practice Non-Academic Affiliation	3 (17%)
	Community Safety-Net Hospital	1 (5.6%)
Practice Size (RA patients)	1-300 patients	5 (28%)
	301-600 patients	1 (5.6%)
	601-900 patients	3 (17%)
	901-1200 patients	4 (22%)
	1201-1500 patients	1 (5.6%)
	>1500 patients	2 (11%)
	Unknown	2 (11%)
Percentage of Visits That Were Virtual at Each Site Across Collaborative	0-5%	3 (17%)
	6-10%	5 (28%)
	11-30%	4 (22%)
	31-60%	3 (17%)
	61-80%	2 (11%)
	>80%	1 (5.6%)
Number of Individuals Involved in Learning Collaborative at Practice	1-2	9 (50%)
	3-5	8 (45%)
	6+	1 (5.6%)
Frequency of Learning Collaborative Planning Meetings and PDSA Discussions	Never	2 (11%)
	Weekly	1 (5.6%)
	Every other Week	4 (22%)
	Monthly	9 (50%)
	Other	2 (11%)
Number of PDSAs Submitted Across 6 Months of Learning Collaborative	1-2	8 (45%)
	3-4	7 (39%)
	5-6	3 (17%)

Table 2: Role in and Satisfaction with Learning Collaborative Based on Individual Surveys (N=35)

		Category	N (%)
Respondent's Characteristics and Role in Learning Collaborative	Respondents Role at Site	Rheumatologist	24 (69%)
		Nurse Practitioner (NP)	4 (11%)
		Physician Assistant (PA)	1 (2.9%)
		Other	6 (17%)
	Number of Monthly Webinars Attended	0	2 (5.7%)
		1-2	7 (20 %)
		3-4	4 (11%)
		5-6	22 (63%)
	Number of Months With Chart Review Submissions (clinicians only)	0-1	1 (2.9%)
		2-3	1 (2.9%)
		4-5	6 (17%)
		6	23 (66%)
		N/A (Not clinician)	4 (11%)
	Level of Participation in Monthly PDSA Planning	Very Active	21 (60%)
		Somewhat Active	13 (37%)
		Not Active	1 (2.9%)
Respondent's General Satisfaction with Learning Collaborative	Overall Satisfaction With Collaborative	Very Satisfied	26 (74%)
		Somewhat Satisfied	7 (20%)
		Neutral	2 (5.7%)
		Somewhat Dissatisfied/ Dissatisfied	0 (0%)
	How Likely Are You to recommend a Similar Collaborative to a Colleague?	Very Likely	23 (66%)
		Likely	10 (29%)
		Neutral	2 (5.7%)
		Not Likely/Very Unlikely	0 (0%)
Respondent's Satisfaction with Components of Learning Collaborative	Kickoff Meetings	Useful or very useful	30 (86%)
	Monthly Data and PDSA Submission	Useful or very useful	28 (80%)
	Monthly Speakers	Useful or very useful	29 (83%)
	Data Visualization and Feedback	Useful or very useful	28 (80%)
	Website	Useful or very useful	22 (63%)
	Meeting Recordings	Useful or very useful	20 (57%)
	Brigham Collaborative Support Team	Useful or very useful	33 (94%)
	Discussion with Other Participants (Inter-site)	Useful or very useful	29 (83%)
	Discussion with Members at Site (Intra-site)	Useful or very useful	26 (74%)

kick-off meeting introduced topics and discussed plan-do-study-act (PDSA) cycles as a main tool for quality improvement. Practices prepared for the monthly webinars with 20-25 chart reviews and submission of PDSA cycles. At the end of the collaborative, leaders of each practice received an anonymous 12 question survey on site characteristics. All 45 participants, including site leads, received a separate anonymous survey focused on their experience in the LC. These questions asked participants to reflect on their participation and evaluate the LC. The following analyses describe the survey responses.

Results: All 18 active rheumatology practices and 35 of 45 participants (78%) responded to the site and individual surveys, respectively. Characteristics of the practices are shown in **Table 1** and included multiple practice types, with 12 academic rheumatology practices, 2 academically affiliated practices, and 4 non-academic practices. The number of RA patients seen regularly at participating practices ranged widely from < 450 RA patients to > 1000. The number of participants in the LC at practices ranged from 1 to 8. As noted in **Table 2**, 63% of respondents indicated they attended 5 or 6 of the monthly webinars. 97% of respondents indicated they were somewhat or very active in monthly PDSA planning and approximately 77% of clinicians submitted chart reviews for 5 or 6 months of the collaborative.

Table 3: Future Learning Collaborative Suggested Medium and Topics Based on Individual Surveys (N = 35)

	Type of Collaborative	N (%)
Preferred Collaborative Medium	Virtual	13 (37%)
	Hybrid	18 (51%)
	In-Person	4 (11%)
	Topic	N (%) "Very Interested/Interested"
Future LC Topics with High Reported Levels of Interest ("Interested/Very Interested")	Improving Management of Steroid Induced Osteoporosis	29 (83%)
	Improving Adherence to Vaccination Schedules	24 (69%)
	Cardiovascular Risk Factor Management	26 (74%)
	Reproductive Health Counseling	27 (77%)
	Laboratory Monitoring for Drugs and Diseases	30 (86%)
	Obesity and Weight Management	25 (71%)

Table 2 shows that 94% of respondents indicated they were either somewhat or very satisfied with the LC, and 94% of respondents said they would recommend a similar LC to a colleague. Regarding LC format, 37% of respondents indicated they would prefer a virtual LC, and 51% indicated they would prefer a hybrid (virtual and in-person) model (**Table 3**). Respondents noted that they would be very interested in future LCs on a range of rheumatology-specific topics (**Table 3**), including improving management of glucocorticoid induced osteoporosis, cardiovascular risk factor management, reproductive health counseling, and laboratory monitoring for drugs and diseases.

Conclusion: Virtual multi-center LCs are feasible, and participants were very satisfied with the virtual format. Virtual LCs are highly valued by rheumatologists, trainees, and their practice staffs. Potential topics were identified for future LCs that could improve the quality of care delivered to rheumatology patients.

1. Solomon, D. H., et al. Implementation of Treat-to-Target in Rheumatoid Arthritis Through a Learning Collaborative: Results of a Randomized Controlled Trial. Arthritis Rheumatol 2017;69:1374-1380.

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Abstract Number: 1075

The Impact of an Integrated Care Management Program on Acute Care Use for Potentially Avoidable Conditions Among High-Risk Patients with SLE

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Background/Purpose: Patients with SLE are disproportionately from populations with lower socioeconomic status and poorer access to health care, placing them at risk for potentially avoidable acute care use (emergency department [ED] visits and hospitalizations that could be avoided if high-quality outpatient care were provided). We defined potentially avoidable acute care conditions using the Agency for Healthcare Research and Quality's 10 prevention quality indicators for adults and a recently published set of 25 SLE-specific, ambulatory care-sensitive outcomes[1] (**Table 1**). A nurse-led, primary care-based integrated care management program (iCMP) at our multihospital system coordinates care for patients at high-risk for frequent acute care use due to comorbidities, demographics, and prior use patterns. We studied whether iCMP was effective at decreasing rates of potentially avoidable ED visits and hospitalizations among patients with SLE.

Methods: We identified adults with SLE enrolled in iCMP from January 2012-February 2019. We then used electronic health record (EHR) data linked to insurance claims to compare incidence rates of potentially avoidable ED visits (composite variable and individual conditions) and potentially avoidable hospitalizations (composite variable and individual conditions) during iCMP enrollment vs. during the 12-months prior to iCMP enrollment. We used Poisson regression to compare incidence rate ratios (IRR) during iCMP versus pre-iCMP for each utilization measure, adjusted for age, sex, race/ethnicity, number of comorbidities, and calendar year, accounting for within-patient clustering. All upper gastrointestinal (GI) bleeds and osteoporotic fractures were considered potentially avoidable as we did not have information about whether patients were taking GI protectants or osteoporosis therapy.

Results: We identified 67 iCMP enrollees with SLE and linked EHR-claims data. Sixty-one of 67 met 1997 ACR criteria for SLE; 4 met 2012 SLICC criteria and 2 did not meet criteria but were diagnosed by a rheumatologist. The mean age was 60 years; 93% were female, 55% were white, 25% Black, 16% other race, and 3% Asian; 21% were Latinx. Median iCMP enrollment time was 33 months. During iCMP enrollment, there was a decrease in the overall rate of potentially avoidable ED visits (IRR 0.50; 95% CI 0.28-0.88; see **Table 2**) and potentially avoidable hospitalizations

Table 1. Potentially Avoidable Conditions for Emergency Department Visits or Hospitalizations Among Patients with SLE[1]

Infections
Community-acquired pneumonia
Influenza
Herpes zoster
Urinary tract infection
Hepatitis B
Meningococcal disease
Pneumococcal disease
Pneumocystis pneumonia while receiving moderate-to-high dose glucocorticoids
Cardiovascular Disease
Hypertension
Congestive heart failure
Angina without procedure
Recurrent myocardial infarction
Pulmonary Disease
Chronic obstructive pulmonary disease
Asthma
Renal Disease
Chronic kidney disease or end-stage renal disease among patients with known lupus nephritis
Thromboembolic Disease
Vascular thrombosis among SLE patients with antiphospholipid antibody syndrome
Embolic stroke among SLE patients with antiphospholipid antibody syndrome
Vascular thrombosis among SLE patients with positive antiphospholipid antibodies receiving estrogen-based contraception
Diabetes Mellitus-Related
Diabetes long-term complication
Diabetes short-term complication
Uncontrolled diabetes
Complications from uncontrolled glucocorticoid-induced diabetes mellitus
Lower-extremity amputation among patients with diabetes
Medication-Related
Vision loss from hydroxychloroquine toxicity
Chronic opioid use
Opioid overdose
Osteoporotic fracture among patients with SLE receiving glucocorticoids
Avascular necrosis among patients with SLE receiving prolonged glucocorticoids
Gastrointestinal bleed on glucocorticoids, non-steroidal anti-inflammatory drugs, or anticoagulation
Obstetrics/Gynecology-Related
Fetal anomalies on teratogenic medications
Neonatal lupus/congenital heart block in the offspring of a patient with positive anti-Ro or anti-La antibodies
Spontaneous abortion in an SLE patient receiving teratogenic medications
Obstetrical complications among SLE patients with antiphospholipid syndrome
Premature ovarian insufficiency/infertility in a patient following standard dose cyclophosphamide
High-grade cervical dysplasia/cervical cancer
General Preventive Care
Lupus flare in the absence of ultraviolet light protection

SLE=systemic lupus erythematosus 1. Feldman CH et al. Development of a Set of Lupus-Specific, Ambulatory Care-Sensitive, Potentially Preventable Adverse Conditions: A Delphi Consensus Study. Arthritis Care Res (Hoboken). 2021; 73: 146-57.

(IRR 0.37; 95% CI 0.21-0.65; see **Table 3**). We also found that during iCMP enrollment, there was an increase in the rate of ED visits for upper GI bleed (IRR 1.28; 95% CI 1.15-1.42).

Conclusion: We found that a nurse-led, primary care-based integrated care management program is effective at decreasing the rate of potentially avoidable ED visits and hospitalizations among high-risk SLE patients. We hypothesize that this is due to optimization of outpatient care. ED visits for upper GI bleeds also increased during iCMP, possibly due to medication use (for example, steroids). Further multicenter studies of integrated care management programs are needed to confirm these findings.

Table 2. Incidence Rate Ratios (IRR) for Potentially Avoidable Emergency Department (ED) Visits During the Integrated Care Management Program (iCMP) as Compared to Pre-iCMP (Reference)

Primary Discharge Diagnosis	Pre-iCMP IR* (95% CI)	During iCMP IR* (95% CI)	IRR (95% CI) (Ref=pre-iCMP)
All potentially avoidable conditions	12.0 (4.0-32.0)	6.0 (2.0-15.0)	**0.50 (0.28-0.88)**
Hypertension	1.2 (0.2-8.7)	0.6 (0.2-2.5)	0.52 (0.05-5.67)
Congestive heart failure	6.1 (2.2-17.1)	3.9 (2.0-7.4)	0.63 (0.18-2.23)
Urinary tract infection	3.1 (1.0-9.6)	2.7 (1.4-5.2)	0.87 (0.33-2.28)
Community-acquired pneumonia	2.5 (0.6-9.7)	2.6 (1.2-5.8)	1.04 (0.21-5.29)
Osteoporotic fracture	2.6 (0.7-9.7)	3.2 (1.4-7.2)	1.24 (0.29-5.29)
Upper gastrointestinal bleed	3.4 (1.7-7.2)	4.4 (2.1-9.2)	**1.28 (1.15-1.42)**
COPD	2.0 (0.1-29.1)	5.2 (0.9-29.5)	2.61 (0.82-8.24)

*IR per 1000 person-years; IR=incidence rate; CI=confidence interval; Ref=reference; COPD=chronic obstructive pulmonary disease; all primary discharge diagnoses which were present in our data are presented above.

Table 3. Incidence Rate Ratios (IRR) for Potentially Avoidable Hospitalizations During the Integrated Care Management Program (iCMP) as Compared to Pre-iCMP (Reference)

Primary Discharge Diagnosis	Pre-iCMP IR* (95% CI)	During iCMP IR* (95% CI)	IRR (95% CI) Ref=pre-iCMP
All potentially avoidable conditions	14.0 (5.0-37.0)	5.0 (2.0-14.0)	**0.37 (0.21-0.65)**
Congestive heart failure	11.4 (4.4-29.8)	7.6 (4.5-12.9)	0.67 (0.26-1.71)
Influenza	1.3 (0.2-8.6)	1.0 (0.2-4.2)	0.77 (0.07-8.66)
Osteoporotic fracture	4.5 (1.4-15.1)	4.2 (2.0-9.0)	0.93 (0.31-2.78)
Urinary tract infection	2.5 (0.6-10.3)	2.6 (1.2-5.7)	1.04 (0.29-3.71)
Hypertension	1.2 (0.2-8.7)	1.3 (0.3-5.9)	1.04 (0.09-12.76)
Upper gastrointestinal bleed	3.2 (1.1-9.8)	5.6 (2.4-13.2)	1.75 (0.98-3.12)
Community-acquired pneumonia	2.4 (0.6-9.9)	4.5 (2.6-7.9)	1.86 (0.43-8.12)

*IR per 1000 person-years; IR=incidence rate; CI=confidence interval; Ref=reference; all primary discharge diagnoses which were present in our data are presented above.

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Abstract Number: 1076

Combining Fuzzy Logic with Time-Driven Activity Based Costing Within the Rheumatoid Arthritis Care Cycle: Insights from a Dutch Hospital

Fiona Koster[1], Deirisa Lopes Barreto[2], Marc Kok[3] and Angelique Weel-Koenders[1], [1]Maasstad Hospital Rotterdam, Rotterdam, Netherlands, [2]Maasstad Hospital Rotterdam, Rotterdam, [3]Maasstad Hospital, Rotterdam, Netherlands

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)

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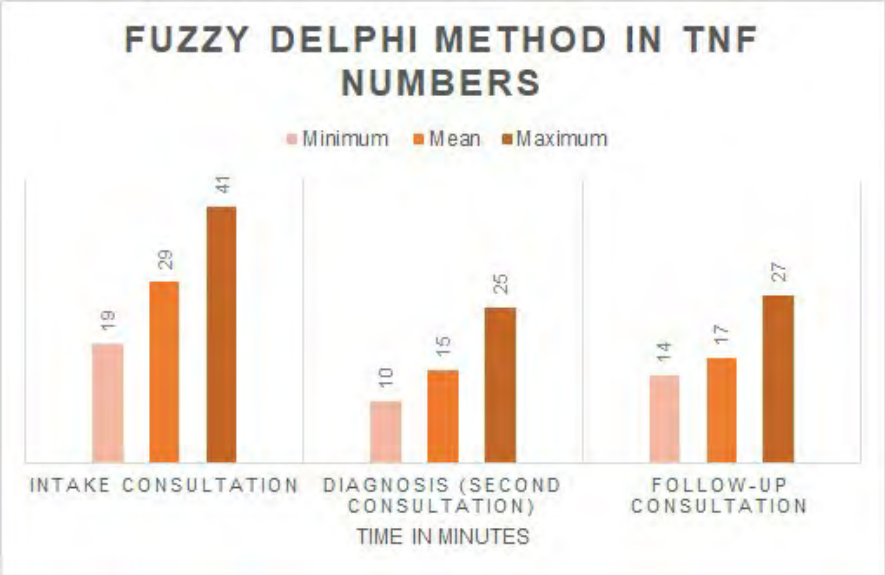
Session Time: 8:30AM–10:30AM

Background/Purpose: Transparency and management of healthcare costs is warranted for rheumatoid arthritis (RA) as the disease places a great economic burden on a patient and societal level. Time-Driven Activity Based Costing (TDABC) is a cost accounting method that may support value-based healthcare (VBHC) management programs. A flaw of TDABC is the inaccuracy of the time estimates due to heterogeneity in patients' care needs, presence of



Graph 1. Results of fuzzy Delphi method displayed in TNF numbers.

(multi)morbidity and the variety of providers. Thus, we aimed to gain knowledge in the costs of the RA care cycle and improve the accuracy of the cost estimates with the fuzzy logic method.

Methods: The data was retrieved from the outpatient department of rheumatology at Maasstad hospital. The care delivery value chain (CDVC) and the corresponding process map serves as a base for the assessment of the costs of the RA care cycle. To correct for the imprecision and ambiguity of the parameters in the TDABC model, the fuzzy logic Delphi method was applied and expressed in triangular fuzzy numbers (TNF). The average TNF numbers were obtained by focus groups and surveys for consultations with the medical team; rheumatologists, nurse practitioners, physician assistants, rheumatology nurses and doctor's assistants. Minimum, average and maximum time estimates were compared to the standard time frames of the procedures and finally, utilized to calculate the total costs of the RA care cycle.

Results: Conducting the Delphi method gave insight in the time estimations of staff members. With respect to the rheumatologists, a distinction was made between the intake, diagnosis and the follow-up consultations. Graph 1 shows the results of the fuzzy Delphi method concerning the average estimates of the rheumatologists. With respect to the first consultation, the estimates of the physicians were considerably lower compared to the standard determined value of 50 minutes. The highest estimate, namely 45 minutes for the maximum TNF, is not even close to the standard time for the intake consult. Remarkable is the fact that the diagnosis consult is valued at 25 minutes regarding the maximum time needed. No distinction is made between the diagnosis and follow-up consult with respect to the standard time values, despite the fact that the time of the diagnosis consultation is significantly lower compared to the follow-up consultations (i.e. 40 minutes). The spread concerning time estimates are on average lowest for the follow-up consultations.

Conclusion: Fuzzy logic was combined with TDABC to encounter the deficiencies related to the TDABC methodology. To provide an accurate and precise estimate of the costs concerning the RA care cycle, time estimates of the complex and expensive procedures are calculated as TNF numbers. The results will depict the resource costs of the RA care cycle in three ways, namely the minimum costs of the care cycle, the mean costs and the maximum costs. Hence, the fuzzy logic estimates reflect reality more properly. As TDABC is still in its infancy, this research contributes to the investigation of a convenient cost accounting method concerning care cycles.

Disclosure: F. Koster, None; **D. Lopes Barreto**, None; **M. Kok**, None; **A. Weel-Koenders**, None.

Abstract Number: 1077

Effectiveness of Non-Pharmacological Interventions to Promote Work Participation of People with Rheumatic and Musculoskeletal Diseases: A Systematic Review and Meta-Regression Analysis

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Table. Stratified analyses of effectiveness of non-pharmacological interventions (disease, baseline risk status, setting and intervention components)

	Sick leave		Work status		Presenteeism	
	SMD	**95% CI**	**SMD**	**95% CI**	**SMD**	**95% CI**
Overall	-0.23	-0.33, -0.13	-0.38	-0.63, -0.12	-0.25	-0.39, -0.12
Disease						
Non-specific pain	-0.07	-0.33, 0.19	-0.50	-0.93, -0.08	-0.19	-0.50, 0.12
Other RMDs*	-0.35	-0.57, -0.14	-0.28	-0.49, -0.07	-0.20	-0.39, 0.00
Baseline risk status						
Not on SL or not at risk	-0.35	-0.67, -0.03	NA	NA	-0.44	-0.73, -0.15
On SL or at risk	-0.11	-0.19, -0.02	-0.38	-0.62, -0.14	-0.17	-0.31, -0.02
Setting						
Clinical	-0.12	-0.21, -0.02	-0.31	-0.65, 0.03	-0.14	-0.44, 0.16
Workplace	-0.38	-0.98, 0.22	NA	NA	-0.19	-0.63, 0.25
Combined	-0.09	-0.53, 0.36	NA	NA	-0.13	-0.56, 0.30
Other	-0.24	-0.40, -0.08	-0.35	-0.61, -0.09	-0.34	-0.70, 0.01
Components						
Single	-0.25	-0.42, -0.08	-0.51	-0.93, -0.08	-0.09	-0.44, 0.27
Multiple	-0.12	-0.22, -0.03	-0.28	-0.49, -0.07	-0.22	-0.41, -0.04

*SMD = standardized mean difference, CI = confidence interval, RMDs = rheumatic and musculoskeletal diseases, *inflammatory RMDs, degenerative RMDs, mixed populations or unspecified , SL = sick leave, NA = not available*

Background/Purpose: Despite improvements in the treatment of rheumatic and musculoskeletal diseases (RMDs), reduced work participation persists when compared to the general population. A Task Force within the European Alliance of Associations for Rheumatology (EULAR) aimed to establish Points to Consider to support people with RMDs in healthy and sustainable work participation. Non-pharmacological interventions could have an important role in this regard. The objective of the evidence synthesis was to summarize the effectiveness of non-pharmacological interventions to promote work participation in people with RMDs.

Methods: Randomized controlled trials (RCTs) and observational studies assessing non-pharmacological interventions until August 2020 were eligible. Records addressing people with any non-work-related RMD and assessing at least one work participation outcome domain (sick leave, work status, presenteeism) were eligible. Two reviewers screened titles, abstracts and full-texts. Data on study, population and intervention characteristics, and effectiveness were extracted for qualitative and quantitative synthesis. For quantitative synthesis per outcome domain, standardized mean differences (SMDs) were used as effect size measure, with a negative SMD favoring intervention. RCTs were included in Mixed Effects Meta-Regression Analyses and a fixed effect for the specific study, stratifying for population and intervention characteristics.

Results: Out of 8,864 records, 73 were included for extraction and analysis. These 73 records described 64 studies of 71 interventions. Studies included a mixed population of RMDs (42%), followed by musculoskeletal pain (36%). Sick leave was the most frequently assessed outcome domain (88% of studies). The majority of interventions were conducted in a clinical setting (62%) and had multiple components (80%), such as vocational support (46%) and physical training (61%). In the qualitative synthesis, including 64 studies, 30%/50%/29% of interventions were considered to be possibly effective (interpretations of reviewers) on sick leave/work status/presenteeism, respectively. In the quantitative synthesis, 37 RCTs (42 interventions) were included. Their population and intervention characteristics were largely similar to those of the total sample. Interventions showed significant, but small to moderate effect sizes, favoring intervention over comparator: SMD=-0.23 (95%CI -0.33 to -0.13) for sick leave, SMD=-0.38 (-0.63 to -0.12) for work status and SMD=-0.25 (-0.39 to -0.12) for presenteeism (Table). Stratified analyses showed that interventions were effective in both populations not at risk and populations at risk or already on sick leave. Both single- and multiple-component interventions had a small positive effect on sick leave and presenteeism respectively. Of note, there was substantial heterogeneity between studies.

Conclusion: Overall, non-pharmacological interventions may have a small effect on sick leave, work status and presenteeism in RMDs. This effect varies substantially between subgroups. This synthesis suggests tailoring non-pharmacological work-related support to individuals' needs and contextual factors.

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Abstract Number: 1078

Rural Veterans with Gout – "Rheum" for Improvement

Jennifer Barton[1], Elizabeth Hooker[2], Christopher Larsen[2], Rachel Matsumoto[2] and Allison O'Neill[2], [1]VA Portland Health Care System/OHSU, Portland, OR, [2]Center to Improve Veteran Involvement in Care/VA Portland Health Care System, Portland, OR

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Gout is a form of inflammatory arthritis that can be "cured" with appropriate urate-lowering therapy to achieve a goal uric acid of 6mg/dL or lower. Rheumatology specialty care is associated with improved control, however access to specialty care for rural Veterans can be a challenge. Our objectives were to explore factors associated with poorly controlled gout among rural Veterans and the impact of dose among those receiving allopurinol.

Methods: Veterans residing in VISN 20 in rural areas were identified using the Corporate Data Warehouse (CDW). Inclusion criteria: in 2019, Veterans: 1) received care from VA, 2) had ≥ 2 ICD codes for gout, 3) were age 18 years or older, and 4) had at least 1 serum uric acid (sUA) measurement. Data on gender, age, race/ethnicity, body mass index (BMI), and visit type (primary care or rheumatology) were extracted from CDW. Controlled status over the course of a panel-year was determined as follows: no sUA elevation (≤6 mg/dl) and no diagnosis code for tophus. Gout med-

Table. Observed and predicted percentages of rural VA patients in VISN 20 with controlled gout^ in 2019

		Observed difference		Unadjusted difference [a] Percentage points (95% CIs)		Adjusted difference [a] Percentage points (95% CIs)	
	N	Rate, %	Difference, %	Unadjusted models	p-value	Model 1[b]	p-value
Overall	**896**	**34.6**					
Gender							
Male	879	34.6	Ref	Ref		Ref	
Female	17	35.3	0.7	2.8 (-21.1, 26.6)	0.82	1.9 (-21.6, 25.5)	0.87
Age							
<= 50	80	23.3	Ref	Ref		Ref	
51 to 64	182	34.3	11.1	11.8 (0.8, 22.8)	0.04	12.7 (1.6, 23.9)	0.03
65 to 80	489	36.0	12.8	13.2 (3.3, 23.0)	<0.01	13.2 (3.3, 23.1)	<0.01
>80	98	37.8	14.5	16.2 (2.9, 29.4)	0.02	14.8 (1.4, 28.2)	0.03
Race							
White	738	35.5	Ref	Ref		Ref	
Other	121	28.9	-6.6	-5.9 (-14.8, 2.9)	0.19	-5.6 (-14.6, 3.3)	0.22
Hispanic	24	29.2	-6.3	-9.4 (-27.6, 8.8)	0.31	-7.6 (-26.5, 11.3)	0.43
Missing	13	46.2	10.7	10.6 (-16.7, 37.9)	0.45	12.2 (-15.6, 40.0)	0.39
BMI							
Normal	39	46.2	Ref	Ref		Ref	
Overweight	154	35.1	-11.1	-12.2 (-29.8, 5.3)	0.17	-10.0 (-27.5, 7.5)	0.26
Obese	451	32.6	-13.6	-15.1 (-31.6, 1.3)	0.07	-12.4 (-29.1, 4.2)	0.14
Missing	252	36.1	-10.0	-10.9 (-27.8, 6.1)	0.21	-8.4 (-25.4, 8.6)	0.33
Visit Type							
PC – none	2						
PC	894						
Rheumatology – none	510	32.2	Ref	Ref			
Rheumatology	386	37.8	5.7	5.9 (-0.5, 12.4)	0.07		
Medications rx'd in 2019							
Allopurinol – none	215	21.4	Ref	Ref			
Allopurinol	681	38.8	17.4	17.0 (10.3, 23.7)	<0.01		
Febuxostat – none	839	34.1	Ref	Ref			
Febuxostat	57	42.1	8.0	9.2 (-4.2, 22.7)	0.18		
Colchicine – none	521	38.0	Ref	Ref			
Colchicine	375	29.9	-8.1	-7.6 (-13.9, -1.3)	0.02		
Prednisone – none	640	35.8	Ref	Ref			
Prednisone	256	31.6	-4.1	-3.8 (-10.6, 3.0)	0.28		
Indomethacin/Naproxen – none	695	39.1	Ref	Ref			
Indomethacin/Naproxen	201	18.9	-20.2	-20.5 (-27.0, -13.9)	<0.01		

[a] Mixed logistic regression with clustering for site
[b] Model 1: Adjusted for patient characteristics, clustered for site
^ controlled gout defined as: no serum uric acid (≤6 mg/dl), no diagnosis code for tophus

ications included any receipt of urate lowering therapy (allopurinol or febuxostat), colchicine, prednisone and non-steroidal anti-inflammatories (NSAIDs) within 2019. Descriptive statistics are presented for patient characteristics. Mixed logistic regression models with clustering for site were run to examine the association between age, race/ethnicity, BMI, and controlled gout.

Results: A total of 2,421 Veterans were identified as having gout and received care at VA in 2019 with VISN 20, 896 (37%) of whom resided in a rural area. Among rural-residing Veterans, 311 (35%) met the definition of controlled gout compared with 31% of urban Veterans. The majority of the rural population were male (98%), between 65 and 80 years old (55%), white (82%) and overweight or obese (68%). In a model with age, race, and BMI, rural Veterans in all age groups over 50 years old were significantly more likely to have controlled gout compared with those under 50 years old (predicted percentage (PP) controlled gout (95% CI): Age < =50 years: 23.3% (14.3-32.2); Age >80 years: 37.8% (28.2-47.4); p= 0.03). There was no significant variation by race or BMI category. Urate lowering therapy with allopurinol was common (76.0%) among rural Veterans with many fewer receiving febuxostat (6.4%). In an unadjusted model, Veterans with receipt of any allopurinol in 2019 had a significantly higher likelihood of controlled gout compared to those without any allopurinol receipt (PP 17% (95% CI 10.3, 23.7).

Conclusion: In this study of rural Veterans who receive care in VA, only one third had controlled gout using serum urate levels. Interventions that share rheumatology best practices and expertise for managing gout with VA primary care teams, such as the VA Rheumatology ECHO program and expansion of telehealth within VA rheumatology, should be developed and tested to enhance quality of care for rural Veterans.

Disclosure: J. Barton, None; **E. Hooker**, None; **C. Larsen**, None; **R. Matsumoto**, None; **A. O'Neill**, None.

Abstract Number: 1079

A Multifaceted Approach to Increasing Enrollment and Activation of Pediatric Rheumatology Patient Portal Profiles

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SESSION INFORMATION
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Background/Purpose: Patient portals provide patients and caregivers the opportunity to be more engaged in their healthcare, as it promotes autonomy and encourages patients and caregivers to take an active role in their care. The adoption of patient portals in the pediatric population compared to the adult population is complex as healthcare providers need to balance the privacy of the patient whilst providing information access to the caregiver. Since the implementation of an electronic medical record system at our pediatric institution in 2018, the enrollment and activation of patients/caregivers profiles to the patient portal has been low. The objectives of this quality improvement project were a) to double the patient/caregiver enrollment and activation of the patient portal profiles from the baseline rate

over one-year period; b) to understand barriers to enrollment and activation; and c) to identify and create systems to facilitate enrollment and activation of the patient portal.

Methods: Iterative Plan-Do-Study-Act (PDSA) cycles were used to create culture change amongst the healthcare team to promote increased patient portal enrollment and activation. Strategies were initially launched with the quality improvement team champions and were later spread to other members of the healthcare team. Results from the PDSA cycles were reviewed and shared with the healthcare team on regular intervals. Feedback from the team were used to inform each successive iterative cycle.

Results: Strategies employed during PDSA cycles that were directed at the healthcare team included educational sessions, pre-clinic identification of patients with inactive profiles, reminders within the electronic medical record, email reminders, and weekly updates. Strategies targeted to patients/caregivers in PDSA cycles included the creation of patient/caregiver activation instructions, and placement of the registration link in email signatures of healthcare team members, after visit summaries, and appointment reminder emails.

The combined strategies increased enrollment and activation from the baseline rate of 15% to 41% over a one-year period. Using a multi-pronged strategy, which informed patients about the opportunity to enroll at various points of contact with the clinic, created a redundancy mechanism that also facilitated enrollment. Barriers to enrollment and activation included patients/caregivers not activating their profile within the eligible period, patient/caregivers not wanting to enroll due to privacy concerns, healthcare team forgetting to offer enrollment, activation emails being misdirected to patients'/caregivers' spam, and the need for patients to re-enroll at ages 12 and 16.

Conclusion: Strategic planning and education of stakeholders are important in the implementation of new programs. Designing small changes that stakeholders are willing to adopt into their daily routine also facilitates this process. Helping stakeholders understand the benefit of patient portal access augmented their willingness to assist enrolling patients/caregivers. Similarly, patients/caregivers were eager to enroll after understanding the functionalities of the application.

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Abstract Number: 1080

Effect of Triage by a Rheumatologist in a Primary Care Setting

Elke van Delft[1], Deirisa Lopes Barreto[2], Huub Han[1], Ilja Tchetverikov[3], Adrie Evertse[4], Martijn Kuijper[1], Mieke Hazes[5] and Angelique Weel-Koenders[1], [1]Maasstad Hospital Rotterdam, Rotterdam, Netherlands, [2]Maasstad Hospital Rotterdam, Rotterdam, [3]Albert Schweitzer Hospital, Dordrecht, Netherlands, [4]Medical Centre Molenaar, Oud-Beijerland, Netherlands, [5]Erasmus Medical Center Rotterdam, Rotterdam, Netherlands

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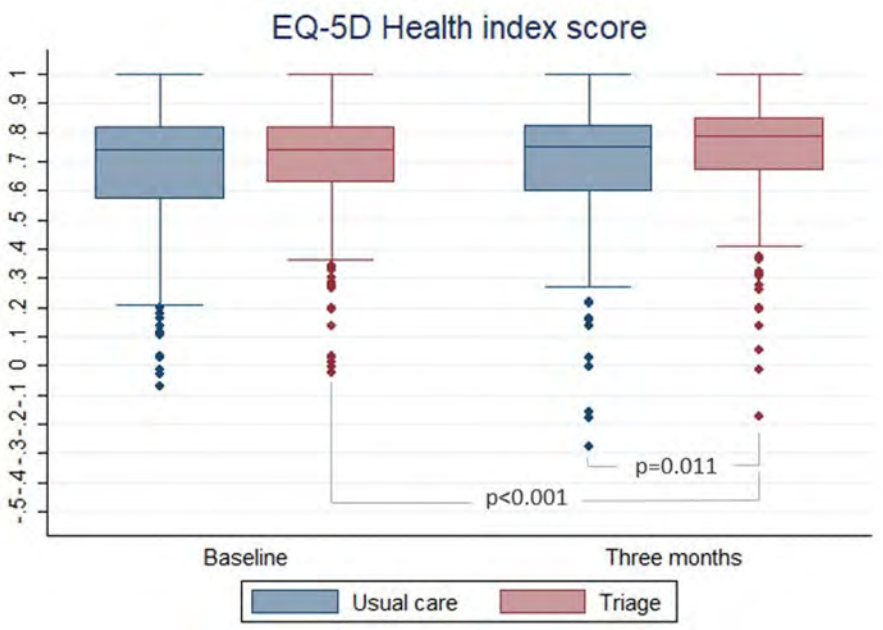

Figure 1. Change of quality of life measured by the health index score over three months after initial visit to rheumatologist.

Background/Purpose: General practitioners have difficulties recognising inflammatory rheumatic diseases (IRD), reflected by a low incidence rate of IRD in newly referred arthralgia patients. On the other hand, IRD needs to be diagnosed and treated as early as possible to overcome progression.

The objective of this study is to assess whether triage by a rheumatologist in a primary care setting effectively increases the number of appropriately referred patients to secondary care and to investigate its impact on health care utilization and patient experience.

Methods: This study follows a cluster randomized controlled trial design and is performed in the Netherlands. Triage by an experienced rheumatologist in a primary care setting will be compared to usual care where patients are referred to a rheumatologist in secondary care by advice of their own general practitioner. The primary outcome was the percentage of IRD diagnoses in referred patients as assessed by a rheumatologist. Health care utilization (iMCQ), quality of life (EQ-5D) and quality of care (CQI) were determined after three months of follow-up.

Results: A total of 544 participants were included with a mean age of 51.4 years and 24% were men. Of all referred patients, 51% had an IRD in the triage group versus 21% in the usual care group (OR 3.85, p< 0.001). After three months, triage patients showed to have a lower health care utilization (p=0.009) mainly regarding secondary care, and higher quality of life (p=0.011), without a decline in quality of care (p=0.712).

Conclusion: Triage by a rheumatologist in primary care provides appropriate care at the right place with good quality for patients with MSC. While these results are encouraging, more long term evidence is needed of value on cost-effectiveness before implementing this strategy in daily practice.

Disclosure: E. van Delft, None; **D. Lopes Barreto**, None; **H. Han**, None; **I. Tchetverikov**, None; **A. Evertse**, None; **M. Kuijper**, None; **M. Hazes**, None; **A. Weel-Koenders**, None.

Abstract Number: 1081

Improving Rheumatology Resource Utilization and Access to Specialty Care for Patients with Early Inflammatory Arthritis Through Enhanced Triage

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Background/Purpose: In many health care jurisdictions the demand for rheumatology consultation exceeds the capacity to provide timely access for all referrals. This has highlighted the importance of enhanced triage to ensure timely access to care for those with the most urgent need. The purpose of this project was to design and evaluate a systematic centralized triage system to improve identification of patients with new onset inflammatory arthritis.

Methods: In this prospective randomized study, half of new referrals received for arthritis at a single academic health care centre with 10 attending staff rheumatologists were assigned to the "enhanced" centralized triage process (intervention); the other 50% of referrals were assessed using the "standard" current triage system (control). Referrals were randomly assigned to a triage arm using a randomization schedule generated through REDCap. In the intervention arm, referrals were triaged based on the probability of inflammatory arthritis using a combination of laboratory data including rheumatoid factor, anti-cyclic citrullinated peptide antibodies, C-reactive protein twice the upper limit of normal and a scoring algorithm using a validated early inflammatory arthritis questionnaire. Referrals in the control arm were triaged by individual rheumatologists as per their usual practice. Data regarding referral content, patient

Table 1: Demographic and Referral Data for the 198 Patients Included in the Study

		Enhanced (n=99)	Standard (n=99)
Average Age		52.667	53.040
Sex	Female	69 (69.7%)	72 (72.7%)
	Male	30 (30.3%)	27 (27.3%)
Referral Source	Family Physician	85	81
	Nurse Practitioner	3	3
	Specialist	5	14
	Other	6	1
Referral Declined		24	9
Telephone Consult Between Referring Physician and Rheumatologist		2 (1 went on to be booked as urgent)	3
Total Number of Patients Managed Without an Initial In-Person Appointment		25	12
Triage Category Assigned	Urgent	68	64
	Semi-Urgent	6	23

Table 2: Diagnosis and Time to Assessment for Urgent Referrals

	Enhanced (n=68)	Standard (n=64)
Inflammatory Arthritis	37	30
Crystalline Arthritis	6	7
Diagnosis Unclear	1	1
Connective Tissue Disease	0	4
Non-inflammatory Condition (tendonitis/fibromyalgia/OA etc.)	24	22
Average time from referral to first assessment for patients with Inflammatory Arthritis (days)	70.24	87

demographics, diagnosis, triage category, disease activity and time from receipt of referral to first assessment were collected and entered into a REDCap database.

Results: 198 patients were included in the study, 99 patients in each arm (Table 1). A higher percentage of patients requiring urgent assessment were confirmed to have inflammatory arthritis in the intervention arm compared to the control arm (54.4% vs .46.9%) although this did not reach statistical significance (P = 0.384). More patients in the intervention arm compared to the control arm (25 vs 12; P = 0.018) were managed without requiring an in-person clinic appointment, in which case initial treatment recommendations were sent directly to the referring physician. This reduced in person clinic visits and avoided prolonged delays in treatment implementation. In addition, wait times for rheumatology assessment for those with inflammatory arthritis was 17 days shorter in the intervention arm (70.2 vs. 87 days) although this did not reach statistical significance (P = 0.191).

Conclusion: For patients referred for suspected inflammatory arthritis, a systematic centralized triage system may lead to improved outcomes; these include better agreement between triage suspected diagnosis and rheumatologist confirmed diagnosis of inflammatory arthritis, improved wait times and more referrals managed without an unnecessary rheumatology assessment.

Disclosure: K. Roche, None; **J. Hanly**, None; **J. MacKinnon**, None; **S. Parlee**, None; **T. Taylor**, Abbvie, 1, Amgen, 1, Janssen, 1, Pfizer, 1, UCB, 1, Lilly, 1, Novartis, 1; **V. Bakowsky**, Pfizer, 1, Abbvie, 1, Gilead, 1, Jannsen, 1, Lilly, 1, Sandoz, 1, Teva, 1; **C. Gunn**, None; **N. Harris**, None; **J. Roberts**, Lilly, 1, Pfizer, 1, Abbvie, 1, Pfizer, 6, BMS, 6.

Abstract Number: 1082

The Rheumatology Workforce in Canada: Results of the Workforce and Wellness Survey

Stephanie Kulhawy-Wibe[1], Jessica Widdifield[2], Jason Kur[3], Jennifer Lee[4], Carter Thorne[5], Elaine Yacyshyn[6], Michelle Batthish[7], Dana Jerome[4], Rachel Shupak[8], Konstantin Jilkine[9], Jane Purvis[10], Justin Shamis[4], Janet Roberts[11], Jennifer Burt[12], Nicole Johnson[1], Cheryl Barnabe[1], Nicole Spencer[1] and Claire Barber[1], [1]University of Calgary, Calgary, AB, Canada, [2]Sunnybrook Research Institute; ICES; Institute of Health Policy, Management & Evaluation, University of Toronto, Toronto, ON, Canada, [3]University of British Columbia, Vancouver, BC, Canada, [4]University of Toronto, Toronto, ON, Canada, [5]Southlake Regional Health Centre, Newmarket, ON, Canada, [6]University of Alberta, Edmonton, AB, Canada, [7]McMaster University, Hamilton, ON, Canada, [8]St. Michael's Hospital, University of Toronto, Toronto, ON, Canada, [9]University of Manitoba, Winnipeg, MB, Canada, [10]Peterborough Education, Peterborough, ON, Canada, [11]Dalhousie University, Halifac, NS, Canada, [12]Eastern Health, St. John's, NL, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Health Services Research Poster II: Care Models and Innovation (1061–1082)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: A rheumatology workforce survey conducted in Canada in 2015 predicted a looming critical shortage of rheumatologists, with one third of surveyed rheumatologists indicating plans to retire between 2020-2025[1]. Moreover, the demographics of the available workforce are changing as females and millennials now comprise a larger proportion of practicing rheumatologists. The Canadian Rheumatology Association (CRA) distributed the 2020 Workforce and Wellness Survey to update the Canadian rheumatology workforce characteristics. As the survey was launched during the COVID-19 pandemic, it provided the opportunity to understand the impact of the pandemic on rheumatologists' practices and burnout.

Methods: The survey was developed from the 2015 iteration and expanded to include the additional aims. It consisted of 26 questions including demographic and practice information, how the pandemic impacted practice, and the Mini-Z questionnaire[2] was used to assess burnout. After pilot testing by 8 rheumatologists, French and English versions of the electronic survey were distributed to CRA members with 12 email reminders. The survey was open for responses from 10/14/2020-03/05/2021. We estimated the number of full-time equivalent (FTE) rheumatologists per 75,000 population from the median proportion of time in clinical practice multiplied by provincial rheumatologist numbers from the Canadian Medical Association.

Results: The response rate was 43% (183/430) of expected practicing rheumatologists (149 adult and 34 pediatric). The median age was 47 years, 62% were female, and 28% planned to retire within the next 5-10 years. Rheumatologists spent a median of 70% of their time in clinical practice, holding a median of 6 (IQR 3-7) half-day clinics, with 6 (IQR 4-12) new consultations and 40 (IQR 25-60) follow-ups seen per week. We estimated between 0 and 0.70 FTE rheumatologists per 75,000 population in each province/territory and 0.62 per 75,000 population in Canada. This represents a deficit of 1 to 78 FTE rheumatologists per province/territory and a total of 194 FTE rheumatologists needed in Canada to meet the CRA recommendation of 1 rheumatologist per 75,000 population.

As a result of the pandemic, rheumatologists were more engaged in virtual care (97% increase). There was a reported reduction in the number of half-day clinics per week, with fewer new and follow-up patients seen per week, and more time spent on clinical paperwork.

Over half of rheumatologists (51%) reported burnout. Women were at 2.86 (95%CI 1.42, 5.93) increased odds of burnout. Age was protective against burnout, with a decrease in odds of 0.95% (95%CI 0.92, 0.99) per year of age.

Conclusion: We highlight the ongoing shortage of rheumatologists in Canada and that this is likely to worsen in the near future without increasing new graduates to cover retirements. This problem may be compounded by the threat of burnout to the retention and productivity of the current workforce. The pandemic has significantly impacted patient volume, likely affecting rheumatologist remuneration and contributing to delayed care.

1. Barber et al; J Rheumatol 2017;44(2):248-57.

2. Olson et al; Stress Health 2019;35(2):157-75.

Disclosure: S. Kulhawy-Wibe, None; **J. Widdifield**, None; **J. Kur**, Pfizer, 1, Novartis, 1, Merck, 1, Fresenius Kabi, 1, Sandoz, 1, Abbvie, 1; **J. Lee**, None; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **E. Yacyshyn**, Hoffman-La Roche Limited, 6, Otsuka Canada, 12, Market research; **M. Batthish**, Abbvie, 5, Novartis, 6, Mylan, 1, Sobi, 1; **D. Jerome**, Abbvie, 1, Novartis, 1, celltrion, 1, Gilead, 1, Lilly, 1; **R. Shupak**, None; **K. Jilkine**, None; **J. Purvis**, Pfizer, 1, Celltrion, 1, Sandoz, 1, Merck, 1, Roche, 1, Janssen, 1, Sanofi, 1, Amgen, 1; **J. Shamis**, Abbvie, 6, Janssen, 6; **J. Roberts**, Lilly, 1, Pfizer, 1, Abbvie, 1, Pfizer, 6, BMS, 6; **J. Burt**, None; **N. Johnson**, None; **C. Barnabe**, Pfizer, 1, Gilead, 1, Novartis, 6, Sanofi, 6, Celltrion, 1; **N. Spencer**, None; **C. Barber**, None.

Abstract Number: 1083

Outcomes of COVID-19 Illness in Systemic Autoinflammatory Diseases and Changes in Flares During the COVID-19 Pandemic: An International Survey

Samira Nazzar Romero[1], Lakshmi Moorthy[2], Jennifer Tousseau[3], Sivia Lapidus[4], Mariana Correia Marques[5], Leanne Mansfield[6], Marinka Twilt[7], Grant Schulert[8], Maria Gutierrez[9], Saskya Angevare[10], Fatma Dedeoglu[11] and Karen Durrant[12], [1]University of California Los Angeles, Los Angeles, CA, [2]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [3]Autoinflamamtory Alliance, Lincoln, CA, [4]The Joseph M. Sanzari Children's Hospital, Hackensack Meridian Health, Montclair, NJ, [5]UPMC Children`s Hospital of Pittsburgh, Pittsburgh, PA, [6]Hospital for Special Surgery, New York, NY, [7]Alberta Children's Hospital, Calgary, AB, Canada, [8]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [9]John's Hopkins, Baltimore, MD, [10]Autoinflammatory Alliance / Kaisz / ENCA as patient organizations, Amersfoort, Netherlands, [11]Boston Children's Hospital, Boston, MA, [12]Autoinflammatory Alliance, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The exaggerated inflammatory responses to the SARS-CoV-2 virus and the paucity of data on COVID-19 infection risk in systemic autoinflammatory disease (SAID) patients posed many unanswered questions, in addition to the profound overall impact of the pandemic.

The aim of this study is to determine if SAID patients had any changes in flare frequency or fevers during the COVID-19 pandemic, and to assess the outcome of SAID patients infected with the SARS-CoV-2 virus.

Methods: The CARRA Autoinflammatory Working Group collaborated with the Autoinflammatory Alliance to conduct an anonymous online survey which was distributed via social media and online autoinflammatory patient groups globally. Data collection was carried out from January 2021 through May 2021.

Results: A total of 647 surveys were completed. In those, 452 of the surveyed listed a specific SAID affecting them and/or their children. (Table 1)

Data for 593 patients showed that the frequency of flares (compared to pre-pandemic) were unchanged in 56% (n=334) of patients overall. The distribution of our data included 57% of patients from the United States, US territories and Canada and 70% of the international patients. Globally 54% of individuals reported that fevers during flares were either lower (n=31) or absent (n=58) since March 2020, and (n=31) found that their fevers were higher with flares.

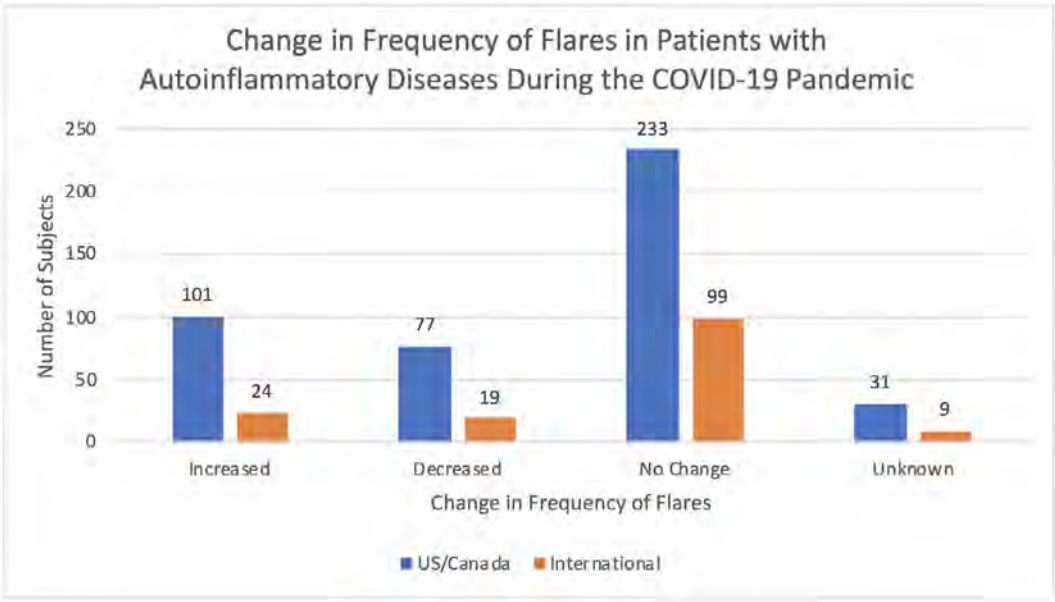
Specific Diagnosis of Autoinflammatory Diseases of Subjects in the Survey			
	US territories, Canada	Other countries	Total
CAPS (all forms)	77	32	109
unclassified SAID	58	12	70
PFAPA	49	15	64
SJIA & Still's	31	6	37
TRAPS	25	7	32
FMF	23	8	31
Behçet's	21	8	29
MKD/HIDS	13	6	19
NLRP12 (FCAS2)	8	3	11
CRMO/CNO/SAPHO	5	3	8
NOD2 (not Blau)	7	0	7
Others*	22	13	35
Totals	**339**	**113**	**452**

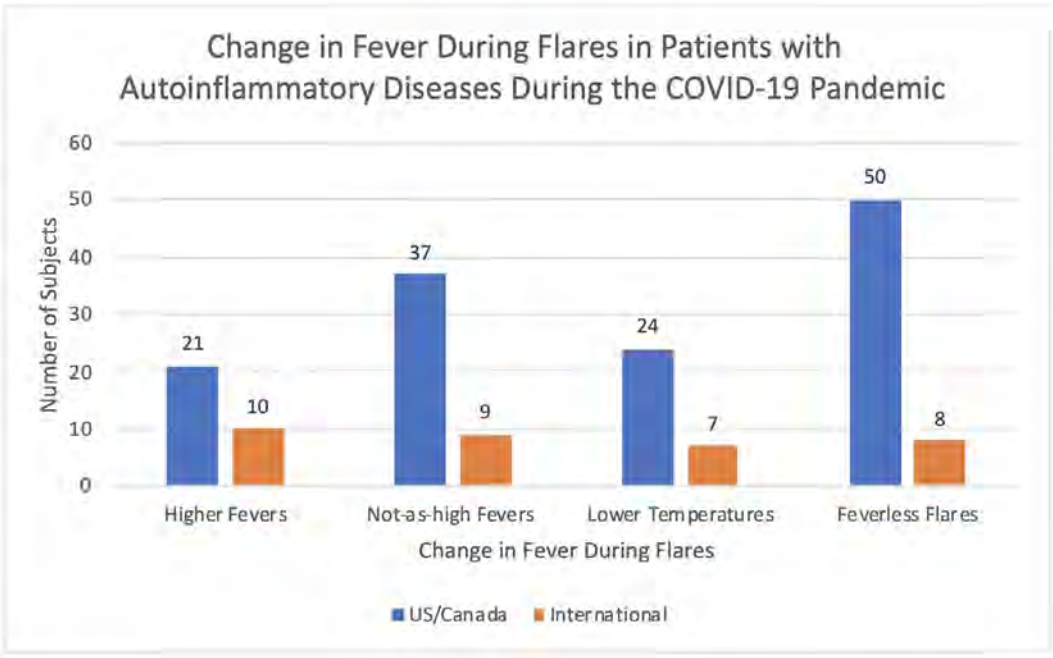
CAPS: Cryopyrin-associated periodic syndrome; PFAPA: Periodic Fever, Aphthous Stomatitis, Pharyngitis, and cervical Adenitis; SJIA: Systemic Juvenile Idiopathic Arthritis; TRAPS: Tumor necrosis factor receptor-associated periodic syndrome; FMF: familial Mediterranean fever; MKD: mevalonate kinase deficiency; HIDS: Hyper-IgD syndrome; *NLRP12*: NOD-like receptor family pyrin domain containing-3; FCAS2: Familial cold autoinflammatory syndrome-2; CRMO: Chronic Recurrent Multifocal Osteomyelitis; CNO: Chronic Non-bacterial Osteomyelitis; SAPHO: Synovitis Acne Pustulosis Hyperostosis Osteitis; *NOD2*: Nucleotide-binding oligomerization domain-containing protein- 2.

* Each diagnosis had between 1 and 4 subjects and include: autoinflammatory syndrome familial Behçet's-like (AIBSL/HA20); Aicardi Goutières; Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE); Deficiency of adenosine deaminase- 2 (DADA2); Deficiency of IL-1 receptor antagonist (DIRA); Hidradenitis suppurativa; *LPIN* mutation with periodic fevers; pyogenic sterile arthritis, pyoderma gangrenosum and acne syndrome; PAPA- PASH; PAPASH; *PLCG2* associated antibody deficiency and immune dysregulation (PLAID or FCAS3); STING-associated vasculopathy with onset in infancy (SAVI); Schnitzler syndrome; Sweet syndrome; Trisomy 8 related autoinflammatory disease (TRIAD).

(Graphic 1) Most individuals were sheltering from work or school and 50% had no changes in their medication for SAID.

SARS-CoV-2 positivity occurred in 35 subjects. 20% (n=7) were asymptomatic, 40% (n=14) had mild infection, 31% (n=11) suffered with moderate illness at home and three (8%) were hospitalized in the regular ward. From the patients who contracted SARS-CoV-2, 31% (n=11) had a flare of their underlying SAID, either concurrently (20%, n=7) or after recovering from COVID-19 infection (11%; n=4). (Table 2) Ten (29%) SARS-CoV-2 positive patients reported lingering symptoms after resolution of acute COVID-19, such as headaches, fatigue, respiratory issues, myalgia and joint pain. Twenty patients reported physician-diagnosed presumed COVID-19, including a Neuro-Behçet's patient requiring intensive care (ICU). Of these, 60% (n=12) had persistent symptoms post-COVID. One case of Multisystem Inflammatory Syndrome in children (MIS-C) and one case of Multisystem Inflammatory Syndrome in adults (MIS-A) with macrophage activation syndrome (MAS) occurred in patients with physician-diagnosed presumed COVID-19.





Conclusion: These data reflect the largest known global cohort of SAID patients' experiences during the COVID-19 pandemic. Most patients had no change in flare frequency from their baseline SAID but many had a reduced intensity of their fevers during flares. The majority of SAID patients with COVID-19 infection reported mild to moderate illness with approximately a third who presented with an exacerbation of their baseline SAID with COVID-19 and lingering symptoms.

Outcomes of Patients with SAID who had Confirmed or Presumed COVID-19 infection by Specific SAID Diagnosis													
COVID-19 Status	Specific Disease	Cases Per Disease	COVID-19 Illness Presentation in Patients with SAID					Flares related to COVID-19				Persistent post-COVID symptoms	
			Asymptomatic	Mild symptoms	Moderate symptoms	Hospitalized	Intensive Care Unit	During COVID	Post-COVID	Unsure	No flare	Number of Subjects	Specific symptoms reported
Positive COVID-19 Test	CAPS (all types)	10	1	5	4	0	0	0	3	2	1	4 (40%)	1*; 2 + ! ^; 3 x; 1 /
	FMF	1	-	1	-	-	-	-	-	-	1	0	0
	Not stated	8	3	2	3	-	-	2	-	-	2	1 (13%)	1 +, x, /,^
	PFAPA	4	1	3	-	-	-	-	-	1	3	0	0
	CRMO	2	-	-	-	2	-	2	-	-	-	0	0
	TRAPS	1	-	-	1	-	-	1	-	-	-	0	0
	SAVI	1	-	1	-	-	-	-	2	-	-	1 (100%)	1 lasting joint pain
	NLRP12	2	-	-	2	-	-	-	2	-	-	2 (100%)	1 x, ^, >; 1 n
	Behçets	1	-	1	-	-	-	1	-	-	-	1 (100%)	1 x, increased asthma
	SJIA-ILD	1	1	-	-	-	-	-	-	-	1	0	0
	uSAID	2	-	-	1	1	-	1	-	-	-	1 (50%)	1 Hemi Migraine, >, w
	Blau	1	-	1	-	-	-	-	-	-	-	0	0
	Sweet's	1	1	-	-	-	-	-	-	-	1	0	0
	TOTAL COVID+	**35**	**7**	**14**	**11**	**3**	**0**	**7**	**4**	**3**	**9**	**10 (29%)**	
Physician Diagnosed-Presumed COVID-19	CAPS (all types)	7	-	4	3	-	-	-	3	4	-	4 (57%)	4 x, 1^;1 !; 1*, swelling
	FMF	1	-	-	1	-	-	1	-	-	-	1 (100%)	1 x,+,kidney disease,♡
	Not stated	3	-	1	1	1	-	-	-	-	-	3 (100%)	1 MIS-C;1x;^;1 cognitive
	PFAPA	1	-	-	1	-	-	-	-	1	-	1 (100%)	PFAPA onset post COVID
	PLAID	1	-	1	-	-	-	-	-	1	-	1 (100%)	1 prolonged recovery
	Neuro-Behçets	1	-	-	-	-	1	1	-	-	-	1 (100%)	1 ♡, x, n, seizures
	TRAPS	3	-	1	2	-	-	1	-	-	-	0	0
	Adult Still's	1	1	-	-	-	-	-	-	-	1	0	0
	uSAID	2	-	-	2	-	-	1	1	-	-	1 (50%)	1 *, MIS-A & MAS
	TOTAL Presumed	**20**	**1**	**7**	**10**	**1**	**1**	**4**	**4**	**6**	**1**	**12 (60%)**	
	GRAND TOTAL	55	8	21	21	4	1	11	8	9	10	22 (40%)	

Symptoms key: * = Dr Dx PASC; ! = pain; x = Respiratory; n = neuro; + = fatigue; ^ = Headache; w = limb weakness; ♡= new cardiovascular issues ; /= loss taste/smell; > = long systemic flaring

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Abstract Number: 1084

COVID-19 Among Patients with Inflammatory Arthropathies Participating in the RHUMADATA Clinical Database and Registry

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has hit the world since 2019. The province of Québec in Canada has not escaped this plague. Our goal is to compare inflammatory arthropathies patients with and without COVID-19 and compare the cumulative rate of COVID-19 infections in our cohort to that of reference populations.

Methods: RHUMADATA® clinical database and registry collect patient data that includes socio-demographics, patient-reported outcomes, disease activity indices, laboratory variables, clinical exam data, concomitant medications, inflammatory disease treatments, comorbidities, and infections. Patients followed either in person or by phone were systematically asked about their COVID-19 status since March 2019. More specifically, patients were asked about signs and symptoms of COVID-19, actual positive/negative test results and history of contact and travels. We

matched four patients without COVID-19 (controls) to each patient with COVID-19. The matching was made based on primary diagnosis, gender, age at diagnosis, and year of last treatment. The analyses were performed on data extracted on May 11, 2021. We used the number of reported COVID-19 infections to develop estimates of the burden of infection in our cohort. We further compared these estimates to that of reference populations.

Results: Fifty-four patients are known to have had COVID-19 in the RHUMADATA cohort. The crude rate of confirmed COVID- 19 cases among active RHUMADATA patients is estimated at 1324 per 100,000 (95% CI = [1021,1715]) or alternatively 13.9 cases per 1000 person-years of follow-up (95% CI = [10.5,18.0]). The treatment, clinical, and comorbidity profiles of patients with COVID-19 were like their matched controls. Overall, most subjects were women (68%). Three deaths were observed in our cohort; two occurred in the COVID-19 group and were attributed to COVID-19. As of May 27, 2021, the estimated cumulative rate of confirmed COVID-19 cases in the province of Québec is 4302 per 100,000, the second-highest rate among Canadian provinces. The reported rates from "local service networks" located around Montréal (Montréal, Laval, Montérégie) ranged from 2573 to 9214 cases per 100,000.

A matched cohort study using national Veterans Affairs data compared COVID-19 rates of RA and non-RA patients (1). Estimated rates were of 27.3 [25.5, 29.2] and 20.5 [19.0, 22.1] per 1000 person-years.

A recent seroprevalence study produced by *Héma Québec* estimated that 15% of the Québec population developed COVID-19 antibodies (10% because of an infection and 5% due to vaccination).

Conclusion: The rate of COVID-19 infections in the RHUMADATA cohort is lower than rates observed in the general population in the region of Montreal and among VA RA and non-RA patients. These differences may result from under-reporting, gender-ethnic-cultural differences, adherence to protective measures due to efficacy beliefs, and methodological differences.

1. England et al. (2021), Risk of COVID-19 in Rheumatoid Arthritis: A National Veterans Affairs Matched Cohort Study in At-Risk Individuals. Arthritis & Rheumatology. Accepted Author Manuscript.

2. Press release accessed at https://www.hema-quebec.qc.ca on May 27, 2021.

Disclosure: D. Choquette, AbbVie, 2, 5, Amgen, 2, 5, Celltrion, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 2, 5, Sanofi, 2, 5, Teva Pharmaceuticals, 2, Gilead Sciences, 2; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **L. Choquette Sauvageau**, None; **B. Haraoui**, Amgen Inc., 2, 6, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Merck, 2, 6, UCB, 2, 6, Celgene, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sandoz, 2, 6, Sanofi-Genzyme, 2, 6; **I. Ferdinand**, AbbVie, 2, Amgen, 2, 6, Novartis, 2, Pfizer, 2, 6; **F. Massicotte**, AbbVie, 2, Pfizer, 2, Janssen, 2, 6, Eli Lilly, 2; **V. Nadon**, None; **J. Pelletier**, ArthroLab Inc., 8, TRB Chemedica SA, 2, 5; **J. Raynauld**, ArthroLab Inc., 2; **M. Rémillard**, AbbVie, 2, 6, Amgen, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sandoz, 2, 6; **D. Sauvageau**, None; **E. Villeneuve**, UCB, 2, Celgene, 2, Roche, 2, 6, Pfizer, 2, 6, Amgen, 2, AbbVie, 2, 6, Sanofi-Genzyme, 2; **L. Coupal**, None.

Abstract Number: 1085

COVID 19 Infection in Patients with Rheumatic Immune-mediated Diseases in a Single University Hospital: Matched Case-control Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: COVID19 may present different degrees of severity. It is generally thought that viral infections in patients with rheumatic inflammatory diseases (R-IMID) or receiving immunosuppressive treatment tend to present more severe disease. However, data comparing the severity of the disease between R-IMID and the general population are scarce.

Our aim was to assess the predisposing factors, clinical-analytical features and severity of COVID-19 infection in R-IMID compare to patients without R-IMID.

TABLE. Main clinical and analytical features of patients with R-IMID and matched controls

	R-IMID patients (n=274)	Controls (n=274)	P
Age	59.1±18	58.8±17.3	0.842
Sex F/M, n, (%)	185/89 (67.5/32.5)	185/89 (67.5/32.5)	1
Comorbidities (n,%)			
Hypertension	119 (43.4)	84 (30.7)	**0.0026***
Dyslipidemia	119 (43.4)	79 (28.8)	**0.0005***
Obesity	49 (17.9)	49 (17.9)	1
Diabetes mellitus	36 (13.1)	37 (13.5)	1
Pulmonary disease	29 (10.6)	32 (11.7)	0.79
Cardiovascular disease	45 (16.4)	33 (12)	0.18
Severity of the disease (n, %)			
Mild	209 (76.3)	204 (74.5)	0.69
Moderate	35 (12.8)	47 (17.2)	0.19
Severe	9 (3.3)	14 (5.1)	0.39
Critical	21 (7.7)	9 (3.3)	**0.04***
Deaths	17 (6.2)	7 (2.6)	**0.0076***
Analytical values, median [IQR]			
CRP	4.7 [2-9.3]	3.9 [1-7.3]	0.176
Creatinine (mg/dl)	0.91 [0.7-1.1]	0.79 [0.7-1.1]	0.214
Lymphocytes (x10^3 /µL)	1 [0.6-1.5]	1.1 [0.8-2.5]	0.711
Platelets (x10^3 /µL)	179 [141-237]	174 [155-211]	0.722
D-Dimer (ng/mL)	999 [342-1417]	548 [336-997]	**0.032***

CRP: C-reactive protein.

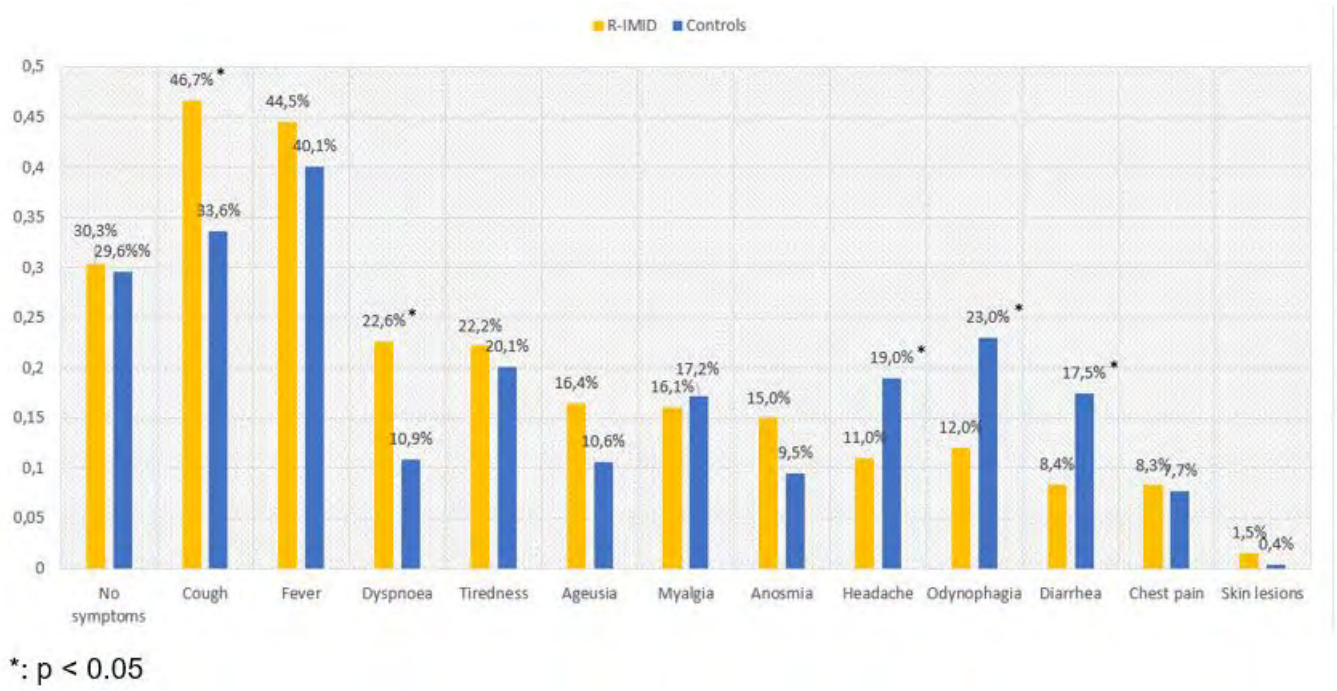


FIGURE. Symptoms in R-IMID patients and matched controls.

Methods: Case-control study in a single University Hospital. We included all consecutive patients with a diagnosis of a R-IMID and a positive test for COVID-19 up to March 31st, 2021.

A total of 274 controls were selected for each case, and matched by sex, age (± 5 years), and without previous diagnosis of R-IMID or use of immunosuppresive therapy.

Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2.

COVID-19 case severity was divided into mild, moderate, severe and critical according to the United States National Institute of Health (NIH) COVID-19 guidelines. Mild/moderate COVID19 was compared with critical.

Results: We included 274 patients (185 women/89 men), mean age 59.1 18 years.

More frequent R-IMID were: Rheumatoid arthritis (RA) (n=87, 31.8%), Axial spondyloarthritis/ Psoriatic arthritis (SpA/PsA) (n=90, 32.8%), Polymyalgia Rheumatica (PMR) (n=22, 8%) and Systemic Lupus Erythematosus (SLE) (n=22, 8%)

We also included 274 age and matched controls. Main characteristics of patients with R-IMID and controls are shown in **TABLE**.

Concerning comorbidities, hypertension and dyslipidemia were more frequent in patients with R-IMID ($p< 0.05$).

COVID-19 symptoms' distribution is shown in **FIGURE**.

Cough and dyspnoea were more frequent and headache, odynophagia and diarrhea were less frequent in the R-IMID group.

The only analytical difference was D-Dimer that was significantly higher in patients with R-IMID.

Although most of the cases were mild, critical cases and deaths were more frequent in R-IMID ($p < 0.05$).

Conclusion: Most of the patients present a mild COVID-19. However, a more severe syndrome was observed in R-IMID

Disclosure: D. Martinez-Lopez, None; **D. Prieto-Peña**, None; **L. Sánchez-Bilbao**, None; **C. Álvarez-Reguera**, None; **A. Herrero-Morant**, None; **F. Benavides-Villanueva**, None; **C. Corrales-Selaya**, None; **M. Trigueros-Vazquez**, None; **R. Wallmann**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1086

Lack of Effect of SARS-CoV-2 Vaccination on Cell Bound Complement Activation Products (CB-CAPs), Multianalyte Assay Panel (MAP) with Algorithm, and Inflammatory Biomarkers

Mark Rudolph, Anja Kammensheidt and Roberta Alexander, Exagen Inc., Vista, CA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

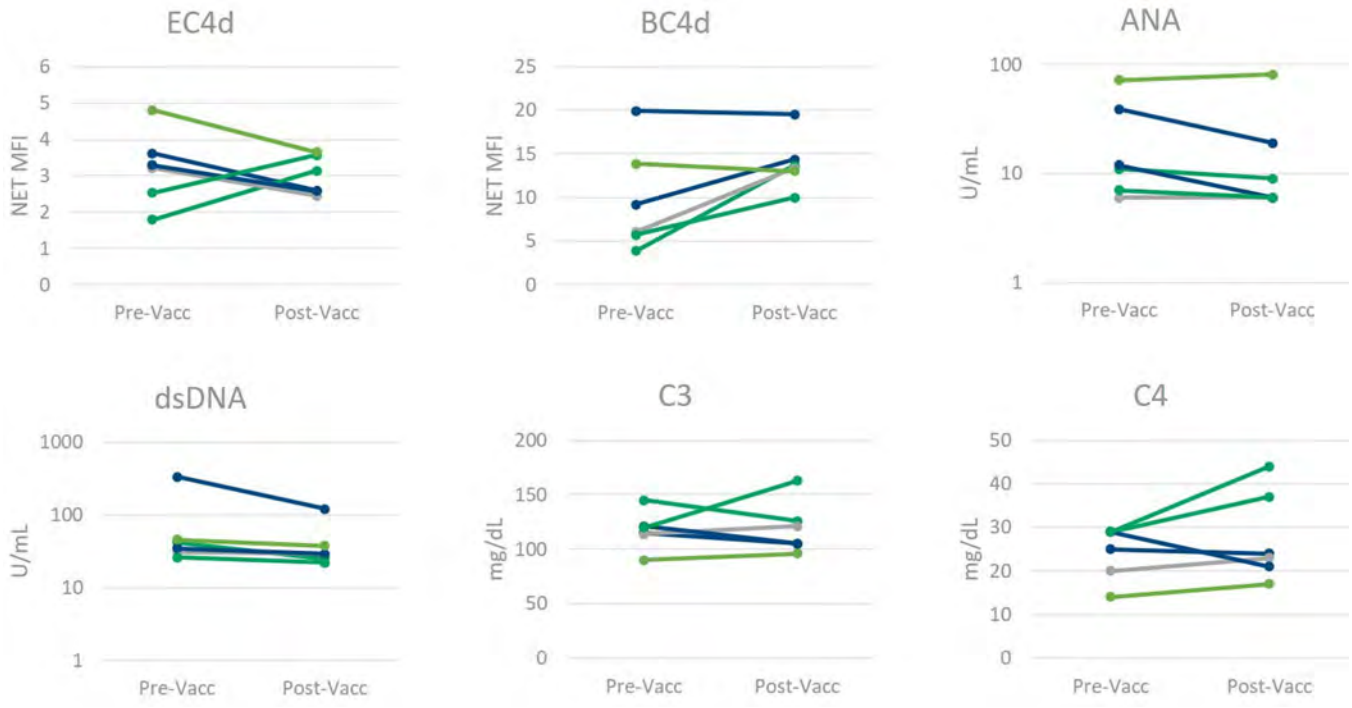


Figure 1. Multianalyte Assay Panel (MAP) components remain constant following SARS-CoV-2 Vaccination. The levels of erythrocyte- and B-cell bound C4d (measured by flow cytometry, reported as Net MFI), anti-nuclear antibodies (ANA) and anti-dsDNA (measured by ELISA, reported in Units/mL), and complement proteins C3 and C4 (measured by immunoturbidimetry, reported as mg/dL) do not significantly change in normal healthy individuals following SARS-CoV-2 vaccination. (Confirmed by paired, two-tailed homoscedastic t-test for all but anti-dsDNA (heteroscedastic).

Table 1. Normal healthy median and interquartile range values pre- and post-SARS-CoV-2 vaccination. Results of EC4d and BC4d (Net MFI), ANA and anti-dsDNA (U/mL), C3 and C4 concentration (mg/dL), and cytokine concentrations (interferon-gamma (IFN**γ**), interleukins (IL)-6, -8, -10, -17A, and 18, tumor necrosis factor-alpha (TNF**α**), IFN**γ**-induced protein-10 (IP-10), interferon-alpha-2a (IFN-**α**2a), and monocyte chemoattractant protein-1 (MCP-1) (pg/mL) in normal healthy volunteers prior to and following SARS-CoV-2 vaccination. Multianalyte Assay Panel (MAP) score is calculated by a combination of CB-CAP and auto-antibody test results, and where a score below 0 is determined to be a negative result

Unit	Biomarker	Pre-Vacc Median (IQ)	Post-Vacc Median (IQ)	p-value
NET MFI	EC4d	3.25 (2.35 – 3.92)	2.86 (2.54 – 3.59)	0.655
	BC4d	7.62 (5.26 – 15.40)	13.53 (12.25 – 15.63)	0.162
U/mL	ANA	11.5 (6.75 – 47.25)	7.5 (6.0 – 34.5)	0.841
	Anti-dsDNA	38.5 (29.75 – 118.25)	29.0 (24.25 – 59.0)	0.456 (unequal var.)
mg/dL	C3	117.5 (108.0 – 127.0)	113.0 (102.8 – 135.3)	0.883
	C4	27.0 (18.5 – 29.0)	23.5 (20.0 – 38.75)	0.517
	MAP Score	-2.5 (-3.325 - -1.25)	-2.3 (-2.425 - -1.575)	0.627
pg/mL	IFNγ	27.2 (17.45 – 42.43)	27.1 (18.6 – 51.55)	0.710
	IL-6	2.86 (2.34 – 3.78)	3.76 (3.0 – 3.83)	0.310
	IL-8	5.88 (4.13 – 17.61)	5.21 (3.94 – 10.73)	0.597
	IL-10	0.65 (0.43 – 0.89)	0.60 (0.40 – 1.11)	0.769
	TNFα	5.73 (5.25 – 6.64)	5.99 (5.12 – 6.43)	0.919
	IP-10	615.0 (443.3 – 771.8)	661.0 (546.5 – 895.5)	0.500
	IFN-α2a	3.66 (2.26 – 5.16)	3.97 (2.66 – 4.94)	0.880
	IL-18	1135.0 (1023.0 – 1238.8)	980.0 (827.5 – 1219.5)	0.390
	MCP-1	215.0 (145.5 – 260.5)	228.0 (155.5 – 328.0)	0.573
	IL-17A	6.41 (3.72 – 8.16)	6.22 (5.60 – 7.11)	0.850

Table 2. EC4d and BC4d positivity rates in April 2019 versus April 2021. Positivity of EC4d (≥ 15 NET MFI) and BC4d (≥ 61 NET MFI) among clinical samples run prior to the SARS-CoV-2 pandemic (April 2019) and amid the public rollout of SARS-CoV-2 vaccines (April 2021).

	April 2019		April 2021	
CB-CAP Assay	Positivity Ratio	Percentage	Positivity Ratio	Percentage
EC4d (≥15 NET MFI)	548/9057	6.05%	689/11542	5.97%
BC4d (≥61 NET MFI)	393/8571	4.58%	543/11542	4.70%

Background/Purpose: SARS-CoV-2 infection can lead to severe inflammation including increased complement activation (Ma, Kulkarni 2021) and the production of several proinflammatory cytokines. The rapid deployment of novel, effective vaccines against SARS-CoV-2 allow for more in-patient visits across the medical landscape, but little is known about the short-term impact the SARS-CoV-2 vaccines may have on immunological testing. This study examined a mutlianalyte assay panel (MAP), including cell-bound complement activation products (CB-CAPs), as well as levels of cytokines in normal healthy volunteers before and shortly after SARS-CoV-2 vaccination, to explore any impact immunization may have on complement activation, canonical connective-tissue disease markers, or the cytokine milieu.

Methods: Normal healthy volunteers (n = 6; 3 females, 3 males) were tested before and within two weeks (2 subjects each 6-, 11-, and 14-days post-vaccination) of receiving their second SARS-CoV-2 vaccination (Moderna mRNA-1273). Serum C3 and C4 levels were measured using immunoturbidimetry and CB-CAPs were measured from EDTA blood using flow cytometry and expressed as net mean fluorescence intensity (MFI). Autoantibodies were measured by ELISA and anti-dsDNA positivity was confirmed by *Crithidia luciliae* immunofluorescence. Cytokines were measured in plasma or serum by electrochemiluminescence on the Meso Scale Discovery platform. F-tests were performed to describe variance, and p-values were determined by paired, two-tailed t-test.

Results: There were no significant differences between pre (4-22 months prior)- and post-vaccination in the levels of erythrocyte-bound C4d (EC4d), B-cell bound C4d (BC4d), anti-nuclear antibodies (ANA), C3, or C4, as measured by

a 2-tailed equal variance t-test (Figure 1). Accounting for unequal variance found between populations (f-test = 0.02), anti-dsDNA also showed no significant differences pre- and post-vaccination (note: the one anti-dsDNA positive result was not *Crithidia* positive). The CB-CAPs remained well below the positivity threshold of 15 net MFI for EC4d and 61 net MFI for BC4d, regardless of vaccination status (Figure 1). Additionally, levels of inflammatory biomarkers were similar pre- and post-vaccination (Table 1).

Conclusion: Although COVID-19 induces robust inflammation and complement activation, SARS-CoV-2 vaccination does not appear to affect levels of serum complement, complement activation, or cytokine milieu in the 2 weeks post-vaccination. In particular, as erythrocytes circulate for up to 90 days, EC4d can be measured for up to 3 months. If robust complement activation were to occur following vaccination, one might expect increased EC4d in those receiving the SARS-CoV-2 vaccine, thus distorting its diagnostic value. Notably, CB-CAPs positivity rate has remained stable among routinely ordered testing pre-pandemic and post-vaccine rollout time periods (Figure 2). Together, these findings should increase the confidence of any physician ordering a diagnostic MAP containing CB-CAPs even in patients who received the SARS-CoV-2 vaccine.

Disclosure: M. Rudolph, Exagen, Inc, 3, 11; **A. Kammensheidt**, Exagen Inc., 3, 4, 11; **R. Alexander**, Exagen Inc., 3, 11.

Abstract Number: 1087

The Humoral Immunity of mRNA-Based SARS-CoV2 Vaccine in Autoimmune Rheumatic Disease Patients Receiving Immunomodulators

Omar Alsaed, Eman Satti, Bassam Muthanna, Safna Veettil, Hadil Ashour, Einas Alkuwari and Samar Al Emadi, Hamad Medical corporation, Doha, Qatar

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Since the spread of different SARS-CoV2 vaccines over the world, there was an uncertainty of the efficacy and safety of these vaccines in autoimmune rheumatic disease (ARD) patients receiving immunomodulators. Patients with ARD were not included in the vaccines phase 3 trials. Qatar national COVD19 vaccine campaign started in Jan 2021. BNT162b2 vaccine was the first to be introduced followed by mRNA-1273 vaccine.

The aim of this study was to evaluate the humoral immunity response of mRNA-based vaccines in ARD patients receiving immunomodulators.

Methods: SARS-CoV2 infection naïve ARD patients who underwent serological testing for anti-SARS-Cov2 S (Elecsys, Roche) were identified and their electronic medical records were reviewed retrospectively to capture demographic data, underlying ARD and the used immunomodulator agents. We included patients who completed two doses of the vaccine in Qatar and underwent anti-SARS-Cov2 S at least fourteen days post the 2nd dose of the vaccine. The test was considered non-reactive when the titer was zero and poorly reactive when the titer was < 132 U/ml which is the cut off used by American Association of Blood Bank to qualify COVID19 convalescent plasma donor. We ran a descriptive analysis comparing the immunogenic response on each immune modulator used in the cohort.

Medications	Reactive Ab titer > 0 n (90)	Non-reactive Ab titer = 0 n (6)	p value	Reactive Ab titer ≥ 132 n (78)	Poor reactive Ab titer < 132 n (18)	p value
Methotrexate monotherapy	23(25.6%)	0(0)	0.333	22(28.2%)	1(5.6%)	0.063
Methotrexate combination therapy	42(46.7%)	2(33.3%)	0.684	35(44.9%)	9(50%)	0.694
Hydroxychloroquine	16(17.8%)	2(33.3%)	0.313	16(20.5%)	2(11.1%)	0.510
Sulfasalazine	6(6.7%)	0(0)	1.000	6(7.7%)	0(0)	0.590
Leflunomide	3(3.4%)	0(0)	1.000	2(2.6%)	1(5.6%)	0.472
Mycophenolate	0(0)	2(33.3%)	**0.003**	0(0)	2(11.1%)	**0.034**
Anti-TNF alfa	39(43.3%)	0(0)	0.078	31(39.7%)	8(44.4%)	0.714
JAK inhibitors	10(11.1%)	0(0)	1.000	7(9.0%)	3(16.7%)	0.391
Rituximab	12(13.3%)	6(100%)	**0.000**	11(14.1%)	7(38.9%)	**0.015**
Tocilizumab	7(7.8%)	0(0)	1.000	6(7.7%)	1(5,6%)	1.000
Glucocorticoid	5(5.6%)	4(66.7%)	**0.001**	4(5.2%)	5(27.8%)	**0.011**

Ab: Antibody, ARD: Autoimmune Rheumatic Disease

Results: 96 subjects were included in the analysis, 60 (60.2%) were females and median age was 46.7 years (std 12.0). 65.6% were Arab, 22.9% were Asian and 11.5% were from other ethnicities. ARDs distribution was as the following: rheumatoid arthritis 54 (56.3%), axial spondyloarthropathy18 (18.8%), psoriatic arthritis 10 (10.4%), systemic lupus erythematosus 5 (5.2%), vasculitis 3 (3.1%) Sjogren's disease 2 (2.1%) and other ARD 4 (4.1%). In our cohort, the test was non-reactive in 6 patients and poorly reactive in 18 patients. Rituximab, glucocorticoid and mycophenolate were associated significantly with no reaction (p value 0.000, 0.001 and 0.003) and poor reaction (p value 0.015, 0.011 and 0.034), respectively. Methotrexate, hydroxychloroquine, sulfasalazine, leflunomide, anti-TNF alfa, JAK inhibitors and tocilizumab were associated with normal humoral response to mRNA-based SARS-COV 2 vaccines.

Conclusion: The majority of patients on CsDMARDs, anti TNF-alfa, JAK inhibitors and tocilizumab had adequate serologic response to m-RNA based vaccines. Poor vaccine reactivity was mainly associated with Rituximab, glucocorticoid and mycophenolate use. Further analysis in larger matched cohorts is needed to identify the factors associated with poor immune response in this category of patients.

The immunomodulators used in ARD patients stratified according to humoral response post 2 doses of mRNA-based SARS-CoV2 vaccines

Disclosure: O. Alsaed, None; **E. Satti**, None; **B. Muthanna**, None; **S. Veettil**, None; **H. Ashour**, None; **E. Alkuwari**, None; **S. Al Emadi**, None.

Abstract Number: 1088

The Association Between Anti-Type II Collagen Antibodies at the Time of Diagnosis and Recurrence in Relapsing Polychondritis

Osamu Iri, Keisuke Nishimura, Daisuke Waki, Kohei Yo, Ryuta Inaba, Shintaro Yamamoto, Kaoru Mizukawa, Tomohiro Yoshida, Hiroyuki Murabe and Toshihiko Yokota, Department of Endocrinology and Rheumatology, Kurashiki Central Hospital, Kurashiki, Japan

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Serum titers of anti-type II collagen (anti-CII) antibodies were reported to rise at the recurrence of relapsing polychondritis (RP). It remains to be identified whether anti-CII antibodies at the time of diagnosis are risk factors for relapse. The aim of this study is to investigate the association between anti-CII antibodies at diagnosis and relapse.

Methods: We conducted a retrospective study of patients diagnosed with RP in our hospital between April 2006 and June 2020. Relapse was defined as aggravation of manifestations or worsening of imaging findings which require intensified treatments. Anti-CII antibodies were assayed by a clinically certificated ELISA test.

Results: Eighteen patients were included in this study. The median age at diagnosis was 68.2 years (IQR 56.4-72.7 years), and 55.6% were females. The median period of observation was 40.9 months (IQR 20.7-57.1 months). Seven patients had relapses (38.9%). The median time to the first relapse was 161 days (IQR 135-394 days). The anti-CII antibodies were tested in 13 patients. Tracheobronchial involvement and nasal chondritis were more frequent in the relapse group compared to the non-relapse group (71.4% vs 18.2%, p = 0.049; 85.7% vs 9.1%, p = 0.002, respectively). The relapse group had higher levels of anti-CII antibodies at diagnosis [median (IQR) : 66.8 EU/mL(38.9-131.8 EU/mL) vs 14.5 EU/mL(10.7-18.7 EU/mL), p = 0.001] (**Figure 1**). Comparing for initial treatments, the relapse group tended to receive higher dose of prednisolone (median (IQR) 45.0mg (25.0-50.0 mg) vs 30.0mg (1.5-40.0 mg), p = 0.055). Immunosuppressive drugs and biologics were more often used in the relapse group (57.1% vs 0%, p = 0.011). Kaplan-Meier estimates of the relapse-free survival showed the anti-CII antibodies positive group was significantly more likely to relapse than the negative group (Log-rank p = 0.009; HR = 1.017, 95% CI 1.004-1.031) (**Figure 2**).

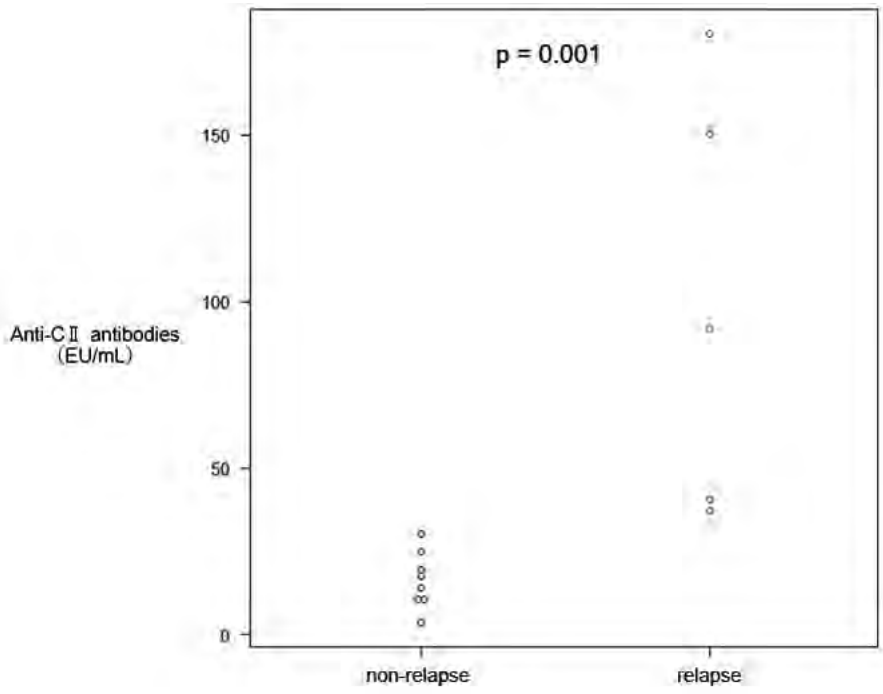


Figure 1. Anti-CII antibody titers of the relapse and non-relapse groups.

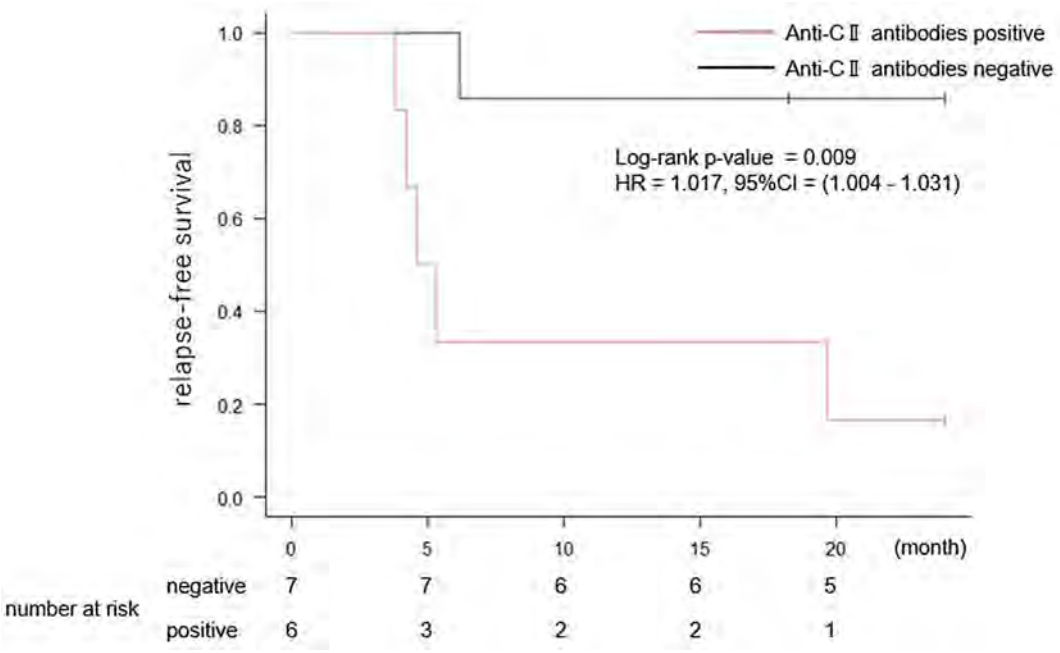


Figure 2. Kaplan-Meier survival curve for relapse in the Anti-CII antibodies positive and negative groups.

Conclusion: High titers of anti-CII antibodies at the time of diagnosis are the risk factors for relapse. This study shows that tracheobronchial involvement may also be a factor associated with relapse. We plan to measure anti-CII antibodies in consistent intervals and discuss whether routine anti-CII antibodies monitoring is useful for predicting future relapse.

Disclosure: O. Iri, None; **K. Nishimura**, None; **D. Waki**, None; **K. Yo**, None; **R. Inaba**, None; **S. Yamamoto**, None; **K. Mizukawa**, None; **T. Yoshida**, None; **H. Murabe**, None; **T. Yokota**, None.

Abstract Number: 1089

Clinical Associations of Anti-Ro52 Antibodies in Patients with Systemic Autoimmune Rheumatic Diseases

Diana Prieto-Peña[1], Belén Atienza-Mateo[2], Miguel Ángel gonzalez-Gay[3] and Ricardo Blanco[4], [1]Hospital Universitario Marqués de Valdecilla, santander, Spain, [2]Group "Research in genetic epidemiology and atherosclerosis of systemic diseases and in bone metabolic diseases of the locomotor system", IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-SSA/Ro antibodies (Abs) can target Ro60 and Ro52 antigens. The presence of anti-Ro60 Abs has been widely described in patients with systemic autoimmune rheumatic diseases (SARDs). However,

	Anti-Ro52+Ro60- (n=11)	Anti-Ro52+Ro60+ (n=27)	Anti-Ro52+Ro60+ with other Abs (n=19)
Age (years), mean ± SD	53.8 ± 18.0*	65.7 ± 10.0	61.7 ± 13.6
Sex (females), n (%)	10 (90.9) *	19 (70.4)	14 (73.7)
Clinical manifestations at anti-Ro52 determination, n (%)			
Arthralgias/arthritis	7 (63.6)	18 (66.7)	14 (73.7)
Raynaud's phenomenon	4 (36.4)	9 (33.3)	9 (47.4)
Myopathy	1 (9.1)	4 (14.8)	2 (10.5)
Final diagnosis, n (%)			
Systemic lupus erythematosus	0 (0)	0 (0)	2 (10.5)
Sjögren's syndrome	1 (9.1)	3 (11.1)	4 (21.1)
Scleroderma	0	1 (3.7)	3 (15.8)
Undifferentiated connective tissue disease	7 (63.6) **	3 (11.1)	3 (15.8)
Overlap myositis	1 (9.1)	7 (25.9)	4 (21.1)
Dermatomyositis	0	1 (3.7)	1 (5.3)
IPAF	0	5 (18.5) **	0
Other systemic inflammatory diseases	0	3 (11.1)	0
Non inflammatory disease	2 (18.2)	4 (14.8)	2 (10.5)
Comorbidities, n (%)			
ILD	1 (9.1) **	11 (40.7)	7 (36.8)
Malignancy	1 (9.1)	5 (18.5)	0 (0.0)

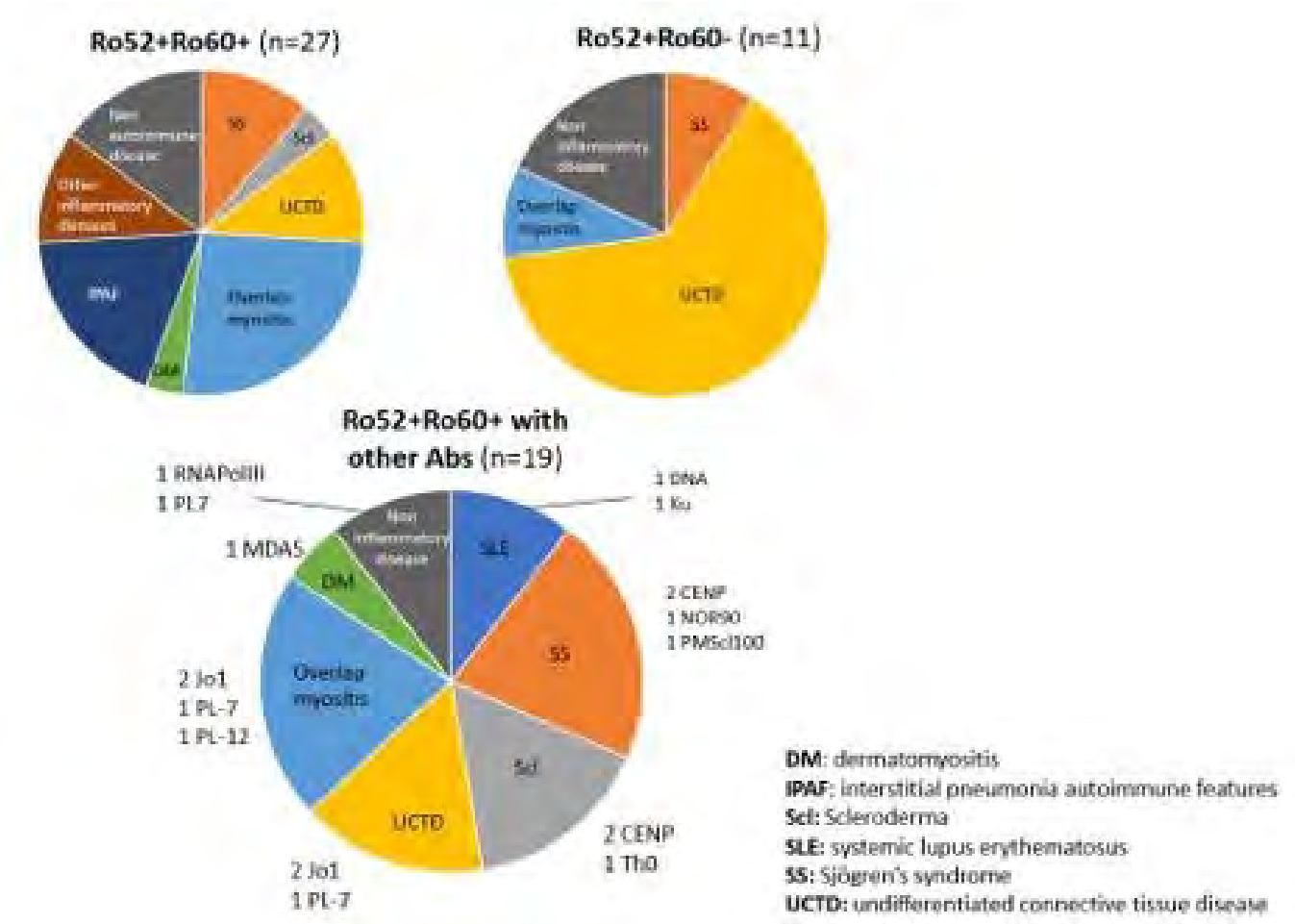
*** p< 0.05** (Ro52+Ro60+ *vs* Ro52+Ro60-)

**** p< 0.05** (Ro52+Ro60+ *vs* Ro52+Ro60- *vs* Ro52+Ro60+ with other Abs)

the clinical implication of anti-Ro52 Abs for the diagnosis and management of SARDs remains unclear. We aimed to assess the clinical associations of anti-Ro52 antibodies in patients with high clinical suspicion of SARDs.

Methods: We retrieved the clinical records of all patients with positive anti-Ro52 Abs tested in our hospital between November 2017 and September 2020. Patients were divided into 3 groups: 1) anti-Ro52+Ro60+ 2) antiRo52+Ro60- 3) antiRo52+Ro60+ with other Abs. A comparative study between groups was performed.

Results: 57 patients (43 women/14 men; mean age 62.1±13.6 years) with antiRo52+ Abs were identified. Final diagnosis were: undifferentiated connective tissue disease (UCTD) (n=13), anti-synthetase/overlap myositis (n=12), Sjögren's syndrome (n=7), interstitial pneumonia with autoimmune features (IPAF) (n=6), scleroderma (n=4), systemic lupus erythematosus (n=2), dermatomyositis (n=2), other systemic inflammatory diseases (n=3). In 8 (14%) patients the diagnosis of inflammatory diseases was finally ruled out. 27 patients were classified in the Ro52+Ro60+ group, 11 in the Ro52+Ro60- group and 19 Ro52+ with other Abs. Patients with Ro52+Ro60- were younger and more often women than patients with Ro52+Ro60+.Interstitial lung disease (ILD) was less frequent in patients with Ro52+Ro60- **(Table)**. Isolated Ro52 Abs were more frequently associated with UCTD, while IPAF was more commonly found in patients with anti-Ro52+Ro60+ Abs **(TABLE and FIGURE)**.



Conclusion: Anti Ro52 Abs determination has clinical implications in the diagnosis of SARDs

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Disclosure: D. Prieto-Peña, None; **B. Atienza-Mateo**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1090

Contribution of Scleroderma/Myositis-Related Antibodies Detected by Immunoblot to the Diagnosis of Systemic Autoimmune Rheumatic Diseases in 134 Patients from a Single Referral Center

Diana Prieto-Peña[1], Belén Atienza-Mateo[2], Miguel Ángel gonzalez-Gay[3], Ricardo Blanco[4] and Marcos Lopez-Hoyos[5], [1]Hospital Universitario Marqués de Valdecilla, santander, Spain, [2]Group "Research in genetic epidemiology and atherosclerosis of systemic diseases and in bone metabolic diseases of the locomotor system", IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [5]Marques de Valdecilla University Hospital-IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

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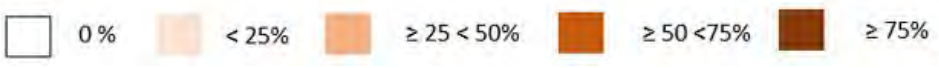
Session Time: 8:30AM–10:30AM

Background/Purpose: Immunoblot assays are increasingly used in clinical practice as part of the diagnostic armamentarium of systemic autoimmune rheumatic diseases (SARDs). Our aim was to assess the contribution of an extended scleroderma/myositis-related antibodies (Ab) determination by immunoblot to the diagnosis of patients with SARDs.

Methods: We reviewed all medical records of patients with positive scleroderma/myositis-related Ab line blot determinations (Euroimmune AG, Lübeck, Germany) in our center from November 2017 to September 2020. These assays were requested due to high suspicion of SARDs in patients presenting with non-specific symptoms.

Results: 134 patients (37men/97women; mean age 59.6 ± 14.8 years) were positive for at least 1 Ab, 25 of them were positive for 2 Abs. Main clinical features at the time of immunoblot requests were: arthralgia/arthritis (n=88), Raynaud's phenomenon (n=59), rash (n=27), sicca syndrome (n=20), myopathy (n=18). During follow-up, 28 patients were diagnosed with undifferentiated connective tissue disease (UCTD), 26 scleroderma, 23 overlap myositis, 18 interstitial pneumonia with autoimmune features (IPAF), 8 other inflammatory diseases, 8 Sjögren's syndrome, 7 systemic lupus erythematosus, 5 dermatomyositis, 1 necrotizing myositis. In 10 patients the diagnosis of SARD was finally ruled out **(Figure)**. Interstitial lung disease (ILD) was present in 50 patients, being particularly frequent in those with anti-PL12, anti-PL7 and anti-MDA5 Abs. Cancer was detected in 9 (6.7%) patients, 6 of them were anti-Ro52 + **(Table)**.

	Mi-2 (n=5)	PL-7 (n=6)	PL-12 (n=4)	Jo-1 (n=6)	MDA5 (n=1)	Ro-52 (n=57)	SRP (n=3)	Scl-70 (n=12)	CENP (n=14)	Th (n=2)	Ku (n=14)	Fibrilarina (n=2)	PM-Scl75/100 (n=23)	NOR90 (n=8)	RNA pol III (n=2)
Dermatomyositis	2 (40)	0	0	0	1 (100)	2 (3.5)	0	0	0	0	0	0	1 (4.3)	0	0
Overlap myositis	1 (20)	5 (83.3)	3 (75)	3 (50)	0	12 (21.1)	0	0	0	0	1 (7.1)	0	3 (13)	0	0
Necrotizing myositis	0	0	0	0	0	0	1 (33.3)	0	0	0	0	0	0	0	0
Systemic lupus erythematosus	0	0	0	0	0	2 (1.7)	0	0	1 (7.1)	0	4 (28.6)	0	2 (8.7)	0	0
Scleroderma	0	0	0	0	0	4 (7.0)	0	9 (75)	10 (71.4)	1 (50)	1 (7.1)	1 (50)	5 (21.7)	1 (12.5)	0
Undifferentiated CTD	1 (20)	0	1 (25)	3 (50)	0	13 (22.8)	0	3 (25)	0	0	4(28.6)	0	5 (21.7)	2 (25)	1 (50)
Sjögren	0	0	0	0	0	7 (12.3)	0	0	2 (14.3)	0	0	1 (50)	1 (4.3)	1(12.5)	0
IPAF	0	0	0	0	0	6 (10.5)	0	0	1 (7.1)	0	4 (28.6)	0	3 (13)	4 (50)	0
Other systemic inflammatory disease	0	0	0	0	0	3 (5.3)	2 (66.7)	0	0	1 (50)	0	0	2 (8.7)	0	0
Non-autoimmune disease	1 (20)	1 (16.7)	0	0	0	8 (14.0)	0	0	0	0	0	0	1(4.3)	0	1 (50)



	Mi-2 (n=5)	PL-7 (n=6)	PL-12 (n=4)	Jo-1 (n=6)	MDA5 (n=1)	antiRo52 (n=57)	SRP (n=3)	Scl-70 (n=12)	CENP (n=14)	Th (n=2)	Ku (n=14)	Fibrilarina (n=2)	PM-Scl75/100 (n=23)	NOR90 (n=8)	RNA pol (n=2)
ILD	0	4 (66.7)	4 (100)	3 (50)	1 (100)	19 (33.3)	0	7 (58.3)	1 (7.1)	0	7 (50)	1 (50)	9 (39.1)	5 (62.5)	0
Cancer	1 (20)	0	0	0	0	6 (10.5)	1 (33.3)	0	0	0	1 (7.1)	0	0	0	0

Conclusion: Immunoblot assays are of great help in the diagnosis of patients with high clinical suspicion of SARDs. While some Abs, such as anti-Ro52, anti-Ku and anti-PMScl75/100, remain to be nonspecific, other Abs including anti-PL12, anti-PL7 or anti-MDA5 are particularly helpful in detecting SARDs patients with associated ILD.

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Abstract Number: 1091

Serum Metabolomic Profiling Identifies Potential Biomarkers in Arthritis in the Elderly

Martha Cedeno[1], Jessica Murillo Saich[1], Roxana Coras[2], Anahy Maria Brandy-Garcia[3], Agueda Prior-Español[4], Lourdes Mateo[5], Melania Martinez-Morillo[5] and Monica Guma[6], [1]University of California San Diego, La Jolla, CA, [2]University of California San Diego/Department of Medicine, Autonomous University of Barcelona, San Diego, CA, [3]Hospital Germans Trias i Pujol, Badalona, Spain, [4]Department of Rheumatology, Germans Trias i Pujol. University Hospital, Badalona, Spain, [5]Department of Rheumatology, Germans Trias i Pujol. University Hospital, Barcelona, Spain, [6]University of California San Diego/San Diego VA Healthcare Service/Department of Medicine, Autonomous University of Barcelona, La Jolla, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Elderly-onset RA (EORA) and polymyalgia rheumatica (PMR) are common rheumatic diseases in the elderly, but their pathogenesis is not yet fully understood. Seronegative EORAneg and PMR have similar clinical characteristics making them difficult to distinguish based on clinical features. The aim of this study was to explore the differences in the serum metabolome using 1H-nuclear magnetic resonance (NMR) to identify potential biomarkers of PMR vs EORAneg.

Methods: ARTIEL (Arthritis in the Elderly) is a cohort that consists of newly diagnosed arthritis in patients older than 60 years. Blood samples were collected at baseline (pre-treatment), along with physician and patient outcome measures throughout a 12-month period. Patients were compared with controls who were random individuals of the same age and gender. A Bruker Avance 700 MHz spectrometer was used to acquire NMR spectra of serum samples. Chenomx NMR suite 8.5 was used for metabolite identification and quantification. IL6 and TNF levels were determined by ELISA. SPSS v.27 and MetaboAnalyst 4.0 were used for statistical and pathway analysis.

Results: From the 66 patients included, 20 were diagnosed with PMR, with an average age of 76.40±4.99, 15% were males, and an average CRP level of 31.56±28.27 mg/dL; 28 patients were diagnosed of EORAneg patients with

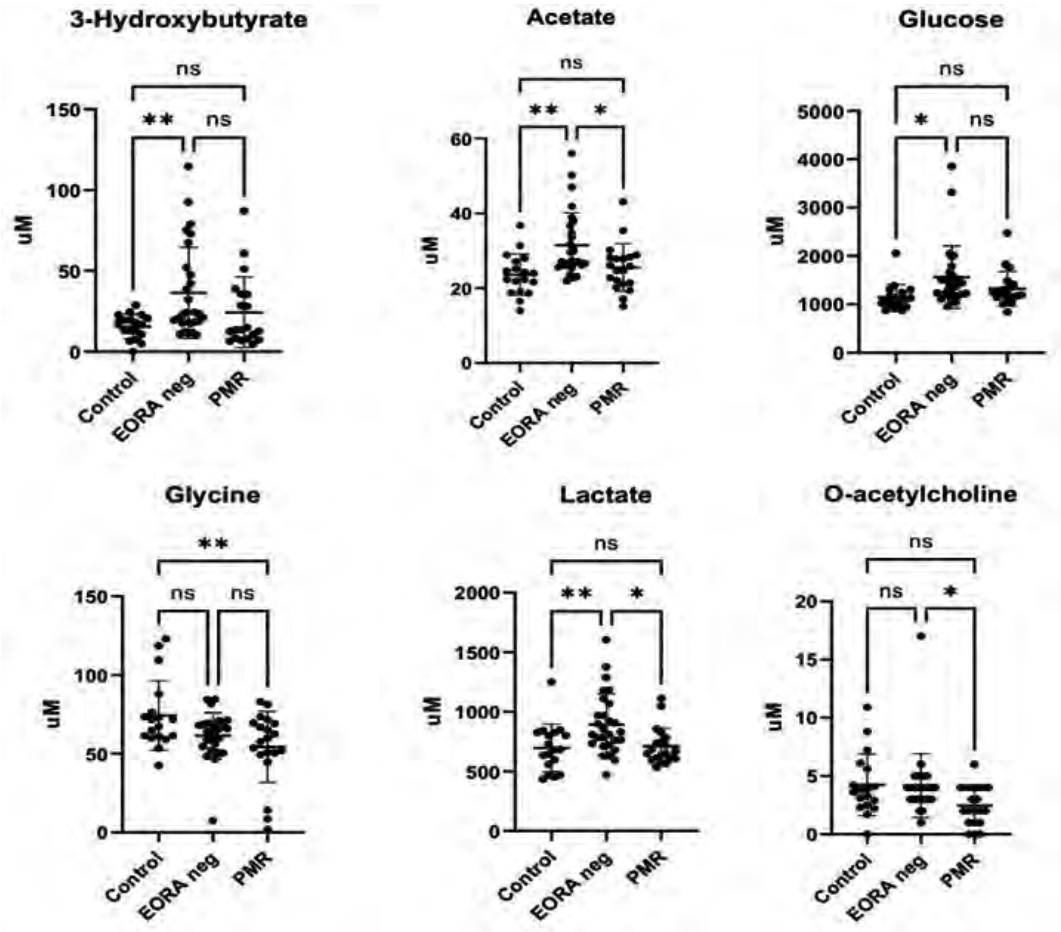


Figure 1. Concentrations of polar metabolites identified with 1H-NMR in control group, elderly-onset seronegative rheumatoid arthritis (EORAneg) and polymyalgia rheumatica (PMR) at baseline. *p<0.05, **p<0.01, ns= not statistically significant.

an average age of 76.75±6.99, 57% males, and an average CRP level of 41.57±52.14 mg/dL; and 18 controls with an average age of 75.39±6.04, 39% males, and an average CRP level of 4.10±6.78 mg/dL. At diagnosis, EORAneg patients had a mean DAS28ESR of 6.21±1.00. One hundred percent of PMR patients reported shoulder pain, and 90% reported pelvic pain. Fifty-eight polar metabolites were identified. 3-Hydroxybutyrate, acetate, glucose, glycine, lactate, and O-acetylcholine were significantly different between the 3 groups. Of these, 3-hydroxybutyrate, acetate, glucose, and lactate were elevated in EORAneg while glycine and O-acetylcholine were lower in PMR compared to control group (Figure 1). Of interest, TNF and IL-6 correlated with different metabolites in PMR and EORAneg suggesting different inflammatory activated pathways (Figure 2). Finally, a logistic regression analysis identified two metabolites, o-acetylcholine and acetate, that contributed to the separation of PMR from EORAneg with 80% sensibility and 96.4% specificity (Figure 3).

Conclusion: EORAneg and PMR have a different serum metabolomic profile that can be used as biomarker to discriminate between both diseases. Further metabolic profiling studies is needed to properly identify significant metabolites in EORAneg vs PMR, and to better understand elements of inflammation pathobiology in these populations.

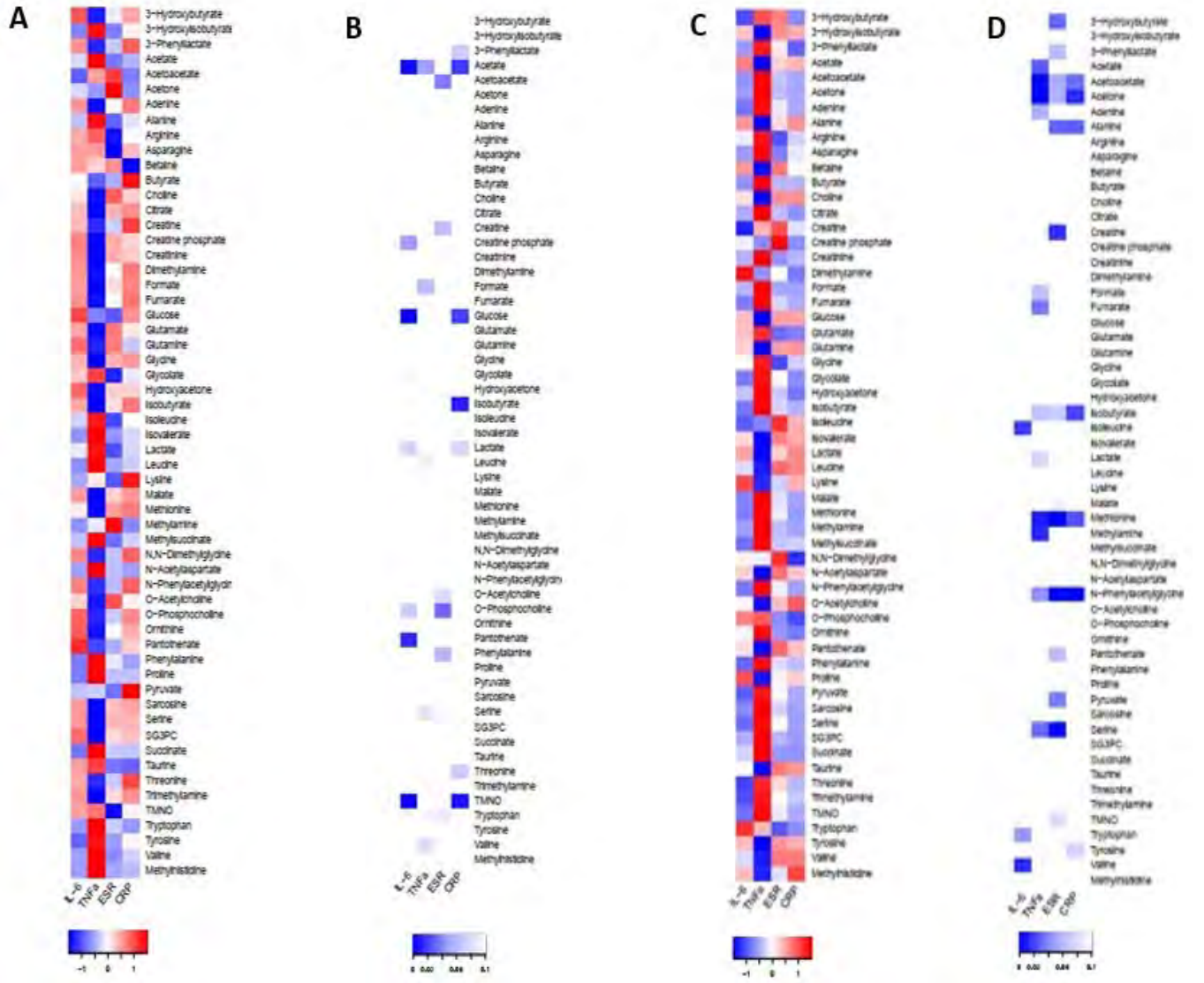
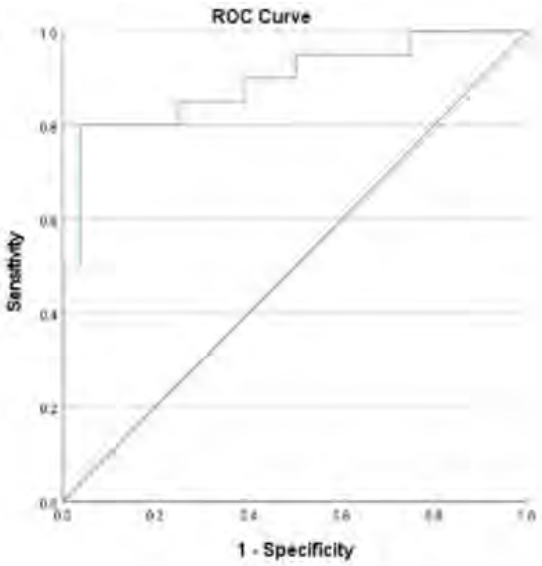


Figure 2. Pearson correlation adjusted by age, gender and BMI (body mass index) at baseline between proinflammatory cytokines and metabolites obtained by 1H-NMR. A) The strength of association of each pair were used to form a cluster heatmap to lend insight into which cytokine were correlated with which group of polar metabolites in patients with PMR or C) EORA neg. B) Correlation significant p-values for PMR or D) EORA neg.

A



B

	B	SE	Wald	Sig	Exp (B)
Acetate	-0.206	0.377	5.881	0.015	0.813
O-acetylcholine	-0.972	0.377	6.66	0.010	0.378
Gender (Female)	-2.571	0.985	6.821	0.009	0.076

Figure 3. A) Receiver operating characteristic curve and B) Binary Logistic regression Model. PMR was consider the principal outcome. The logistic model used significant polar metabolites (p<0.05) and gender. The model showed an area under curve of 0.895 with a sensibility= 80% and specificity= 96.4%; p<0.001.

Disclosure: M. Cedeno, None; **J. Murillo Saich**, None; **R. Coras**, None; **A. Brandy-Garcia**, None; **A. Prior-Español**, None; **L. Mateo**, None; **M. Martinez-Morillo**, None; **M. Guma**, novartis, 5, pfizer, 5, gilled, 5, genentech, 6.

Abstract Number: 1092

Altered Metabolic Pathways in Synovial Fibroblasts of Individuals at Risk of Developing Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Cellular metabolism has been studied in fibroblast-like synoviocytes (FLS) of rheumatoid arthritis (RA) and osteoarthritis (OA) patients and raises the question whether observed metabolic alterations appear in response to chronic inflammation or whether primary changes in cellular metabolism might underlie disease pathogenesis. Previously, we showed that genes involved in lipid metabolism are significantly lower expressed in synovial

tissue from RA-risk individuals that eventually develop RA. Here we investigated whether metabolic changes in FLS are already observed before onset of RA.

Methods: We included individuals with arthralgia who were IgM rheumatoid factor (RF) and/or anti-citrullinated protein antibody (ACPA) positive but without any evidence of arthritis (RA-risk individuals, n=6), RA patients (n=6), OA patients (n=6) and controls without inflammatory disease (n=6). Synovial tissues were collected during orthopedic surgery or individuals underwent mini-arthroscopic synovial tissue sampling of a knee joint. Subsequently, FLS were cultured after synovial tissue digestion. Cellular metabolism was assessed using qPCR, flow cytometry, the XFe96 Seahorse Analyzer and mitochondrial β-oxidation was measured using tritium-labelled oleate.

Results: Real-time analysis of mitochondrial function revealed that basal respiration is significantly lower in FLS from RA-risk individuals and RA patients compared with FLS from controls. When investigating the three main fuel pathways of cellular respiration (glucose, glutamine and fatty acids), basal respiration from all FLS largely depended on fatty acid oxidation, whereas glucose was only highly used by RA FLS. FLS from controls were flexible to switch to another fuel when the other fuel pathways were inhibited, whereas FLS from RA-risk individuals, RA and OA patients were less flexible. When cellular respiration was challenged to maximum capacity, respiration from RA-risk FLS and RA FLS was significantly lower compared with FLS from controls. This was reflected in all three fuel pathways. Based on these data we were able to define the energy profile of our cells. This showed that FLS from controls are relatively more energetic while FLS from RA-risk individuals and RA patients are more quiescent. In addition, mitochondrial β-oxidation was significantly impaired in RA-risk individuals, RA and OA patients compared with FLS from controls. Flow cytometry showed that mitochondrial reactive oxygen species (ROS) production and mitochondrial mass was increased in RA FLS compared with controls.

Conclusion: In this exploratory study, mitochondrial dysfunction and metabolic alterations are already detected in FLS from RA-risk individuals compared with controls, suggesting that these alterations start before clinical manifestation of disease and contribute to disease pathogenesis.

Disclosure: T. de Jong, None; **S. Denis**, None; **P. Tak**, Candel Therapeutics, 4; **R. Houtkooper**, None; **L. van Baarsen**, None.

Abstract Number: 1093

Cardiovascular and Lipid Biomarker Distributions in Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory arthritis (IA) is associated with cardiovascular disease (CVD). Cardiac biomarkers may assist with CVD risk stratification. We aimed to estimate the prevalence, and correlates of abnormal cardiac biomarkers in IA.

Table 1. Baseline characteristics by inflammatory arthritis diagnosis

Variables	Total (N=376)	AS/PsA (N=157)	RA (N=219)	P Value
Female sex	262 (69.7)	81 (51.6)	181 (82.6)	<.001
Age, mean ± SD, years	59.0 ± 10.5	57.0 ± 9.4	60.6 ± 11.0	0.001
Obesity (BMI>30)	131 (35.0)	69 (43.9)	62 (28.6)	0.002
Current/Ever Smoker	167 (46.8)	71 (48.0)	96 (45.9)	0.704
Diabetes Mellitus	33 (8.8)	20 (12.7)	13 (5.9)	0.022
Hypertension	125 (33.2)	68 (43.3)	57 (26.0)	<.001
Dyslipidemia	101 (26.9)	54 (34.4)	47 (21.5)	0.005
Chronic Kidney Disease	2 (0.5)	1 (0.6)	1 (0.5)	1.000
Family History of CVD	95 (25.3)	42 (26.8)	53 (24.2)	0.575
Disease Duration, mean ± SD, years	13.3 ± 12.2	13.7 ± 12.9	13.0 ± 11.8	0.563
Seropositive	155 (72.1)	-	155 (72.1)	-
Erosive Disease	191 (52.8)	89 (64.0)	102 (47.7)	<.001
TJC-68, mean ± SD	2.25 ± 4.04	1.55 ± 3.51	2.75 ± 4.31	0.005
SJC-66, mean ± SD	1.26 ± 2.30	0.6 ± 1.50	1.69 ± 2.66	<.001
PtGA, VAS (0-10cm), mean ± SD	3.38 ± 2.48	3.46 ± 2.53	3.32 ± 2.44	0.591
PhGA, VAS (0-10cm), mean ± SD	2.02 ± 1.97	1.49 ± 1.51	2.40 ± 2.17	<.001
CDAI, mean ± SD	8.2 ± 7.3	6.4 ± 6.0	9.4 ± 8.0	<.001
HAQ, mean ± SD	0.54 ± 0.58	0.51 ± 0.57	0.55 ± 0.59	0.554
VAS Pain, (0-10cm), mean ± SD	3.30 ± 2.50	3.27 ± 2.46	3.32 ± 2.53	0.855
ESR (mm/hr), mean ± SD	18.8 ± 12.8	16.9 ± 12.05	20.2± 13.29	0.014
CRP (mg/L), mean ± SD	5.90 ± 19.9	6.17 ± 20.7	5.71 ± 19.3	0.824
BASDAI, mean ± SD	2.50 ± 3.57	3.80 ± 3.80		-
Current bDMARD	145 (39.0)	68 (43.8)	77 (35.5)	0.143
Current csDMARDs	237 (63.0)	62 (39.5)	175 (79.9)	<.001
Current tsDMARDs	19 (5.1)	0 (0)	19 (8.7)	<.001
Current corticosteroid	21 (5.6)	3 (1.9)	18 (8.2)	0.009
Current NSAID/COXIB	178 (47.3)	68 (43.3)	110 (50.2)	0.185

Comparisons made between RA and PsA/AS group. Values are N (%) unless otherwise indicated. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; bDMARDs, biologic disease modifying antirheumatic drugs; BMI, body mass index; csDMARDs, conventional synthetic disease modifying antirheumatic drugs; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire, HDL-c; high density lipoprotein cholesterol, Lipoprotein A, Lp (a); CDAI, clinical disease activity index; LDL-c, high-sensitivity troponin-T, (hs-TnT); low density lipoprotein cholesterol, NSAID, nonsteroidal anti-inflammatory drug; PhGA, physician global assessment of health; PtGA, patient global assessment of health; SJC-68, swollen joint count 68; TJC-68, tender joint count 66; tsDMARDs, targeted synthetic disease modifying antirheumatic drugs, VAS, visual analog scale;

Table 2. Prevalence of cardiac biomarkers by inflammatory arthritis diagnosis

Variables	Total (N=376)	AS/PsA (N=157)	RA (N=219)	P Value
hs-TnT, mean ± SD	9.45 ± 6.78	9.39 ± 4.12	9.50 ± 8.20	
Abnormal hs-TnT	48 (13.1)	22 (14.2)	26 (12.2)	0.588
NT-proBNP, mean ± SD	66.5 ± 103.5	65.7 ± 93.4	66.9 ± 109.2	
Abnormal NT-proBNP	53 (16.7)	16 (13.6)	37 (18.6)	0.246
Apo B, mean ± SD	0.98 ± 0.42	0.90 ± 0.22	1.03 ± 0.51	
Abnormal Apo B	46 (12.4)	2 (1.3)	44 (20.6)	<.001
Apo A1, mean ± SD	1.58 ± 0.42	1.48 ± 0.28	1.66 ± 0.48	
Abnormal Apo A1	294 (89.6)	131 (94.2)	163 (86.2)	0.018
Lp(a), mean ± SD	25.8 ± 26.7	23.8 ± 22.8	27.2 ± 29.2	
Abnormal Lp(a)	95 (28.6)	40 (28.8)	55 (28.5)	0.956
Total Cholesterol	4.96 ± 1.04	4.99 ± 1.09	4.94 ± 1.01	0.658
LDL-c	2.68 ± 0.86	2.76 ± 0.97	2.63 ± 0.77	0.157
HDL-c	1.58 ± 0.52	1.41 ± 0.47	1.71 ± 0.53	<.001
Non-HDL-c	3.36 ± 0.98	3.57 ± 1.02	3.22 ± 0.93	<.001
Triglyceride	1.55 ± 1.12	1.85 ± 1.20	1.33 ± 1.01	<.001
Cholesterol Ratio, mean ± SD	4.10 ± 31.5	1.22 ± 3.89	6.04 ± 40.5	0.154

Comparisons made between RA and PsA/AS group. Values are N (%) unless otherwise indicated.
AS, ankylosing spondylitis; Apolipoprotein A1, (ApoA1); Apolipoprotein B (ApoB); BNP, N-terminal prohormone BNP; HDL-c; high density lipoprotein cholesterol, high-sensitivity troponin-T, (hs-TnT); Lipoprotein A (LpA), LDL-c, low density lipoprotein cholesterol; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SD, standard deviation

Table 3. Multivariate logistic regression analysis of baseline characteristics for abnormal cardiac biomarkers

	hs-TnT N=320	NT-proBNP N=277	Apo A1 N=285	Apo B N= 322	Lp (a) N=285
RA Diagnosis	0.70 (0.33-1.49)	0.47 (0.18-1.20)	0.33 (0.11-1.02)	**34.2 (4.48-261)**	0.69 (0.33-1.43)
Age, years	**1.12 (1.07-1.16)**	**1.07 (1.03-1.13)**	1.00 (0.97-1.04)	**0.95 (0.91-0.99)**	1.01 (0.98-1.03)
Female sex	**0.25 (0.10-0.63)**	2.53 (0.96-6.65)	**0.14 (0.03-0.72)**	0.74 (0.21-2.62)	**2.76 (1.31-5.81)**
Hypertension	0.83 (0.35-1.97)	1.10 (0.49-2.46)	0.58 (0.22-1.55)	1.77 (0.58-5.43)	0.72 (0.36-1.44)
Diabetes	3.51(0.96-12.7)	0.88 (0.18-4.19)	0.89 (0.06-12.8)	0.70 (0.05-9.22)	1.04 (0.39-2.75)
Dyslipidemia	0.38 (0.11-1.24)	0.64 (0.25-1.66)	1.32 (0.38-4.53)	**3.19 (1.15-8.82)**	1.26 (0.65-2.45)
Current/Ever Smoker	1.05 (0.47-2.35)	1.54 (0.72-3.27)	1.64 (0.70-3.82)	**0.38 (0.16-0.91)**	1.12 (0.65-1.93)
Family History CVD	0.86 (0.32-2.28)	0.60 (0.24-1.53)	0.88 (0.31-2.47)	0.66 (0.24-1.80)	1.00 (0.51-1.97)
Obesity, BMI>30	1.15 (0.48-2.78)	1.56 (0.73-3.33)	**5.38 (1.72-16.8)**	0.39 (0.14-1.10)	1.05 (0.57-1.92)
Disease Duration, years	0.98 (0.95-1.01)	0.99 (0.96-1.02)	1.03 (0.99-1.07)	1.03 (0.99-1.06)	0.98 (0.96-1.01)
CDAI score, mean	1.00 (0.95-1.07)	1.04 (0.98-1.10)	1.01 (0.95-1.07)	1.06 (0.98-1.15)	1.01 (0.97-1.06)
CRP, mg/L	1.01 (0.99-1.02)	0.91 (0.82-1.01)	1.01 (0.99-1.03)	0.99 (0.95-1.03)	0.98 (0.95-1.01)
VAS Pain,mean	1.14 (0.91-1.42)	0.89 (0.76-1.05)	0.89 (0.74-1.07)	1.02 (0.78-1.34)	1.09 (0.93-1.27)
HAQ, mean	1.47 (0.62-3.50)	1.15 (0.53-2.50)	1.66 (0.58-4.76)	0.64 (0.24-1.73)	0.71 (0.34-1.47)
Current NSAID/COXIB	1.25 (0.52-2.99)	0.93 (0.46-1.85)	0.68 (0.29-1.60)	**8.63 (2.91-25.6)**	**0.53 (0.29-0.94)**
Current Corticosteroid	1.48 (0.25-8.65)	0.95 (0.17-5.26)	1.01 (0.18-5.72)	0.07 (0.001-3.73)	1.15 (0.28-4.80)
Current csDMARDs	1.22 (0.52-2.87)	2.76 (1.13-6.75)	**2.94 (1.20-7.22)**	0.76 (0.25-2.33)	0.89 (0.45-1.73)
Current bDMARD or tsDMARD	0.79 (0.37-1.71)	0.81 (0.38-1.74)	0.76 (0.32-1.79)	**3.32 (1.41-7.83)**	0.72 (0.41-1.28)

PsA/AS group is referent. Apolipoprotein A1, (ApoA1); Apolipoprotein B (ApoB); BNP, N-terminal prohormone BNP; HDL-c; high density lipoprotein cholesterol, high-sensitivity troponin-T, (hs-TnT); Lipoprotein A (LpA), LDL-c, low density lipoprotein cholesterol; bDMARDs, biologic disease modifying antirheumatic drugs; BMI, body mass index; csDMARDs, conventional synthetic disease modifying antirheumatic drugs; CRP, C-reactive protein; ESR, HAQ, health assessment questionnaire, CDAI, clinical disease activity index; tsDMARDs, targeted synthetic disease modifying antirheumatic drugs, VAS, visual analog scale

Methods: A cross-sectional study of consecutive patients enrolled in the University of Toronto Cardio-Rheumatology Network from 2017 to 2020 was performed. This is a primary CVD prevention program with structured clinical and laboratory assessments to diagnose and treat CVD. Patients are eligible if they have rheumatoid arthritis (RA) or spondyloarthropathy (SpA, psoriatic arthritis or ankylosing spondylitis), and no documented CVD. We included patients with baseline data for 5 cardiac biomarkers and examined the prevalence of abnormal biomarkers according to site-specific lab cut-offs: high-sensitivity troponin T (hs-TnT) (≥15 ng/L), N-terminal prohormone BNP (NT-proBNP, ≥35 pmol/L or 100 pg/mL), Apolipoprotein A1 (ApoA1, ≤1.96 g/L), Apolipoprotein B (ApoB, ≥1.17g/L or ≥1.46g/L) and Lipoprotein a (Lp(a) ≥9.7mg/dL or ≥30mg/dL). We performed logistic regression to evaluate the association with IA diagnosis and each biomarker, adjusted for demographic, clinical and CVD risk factors.

Results: A total of 376 participants were included. The majority had RA (58%), followed by PsA (33%) and AS (9%). Mean (SD) age of the sample was 59 (10.5) years and 70% were female. Disease activity and acute phase reactants reflected well controlled disease and treatment consisted primarily of csDMARDs (63%) or bioDMARDs (39%) (Table 1). At least 1 CVD risk factor was present in 77% of subjects, most commonly current/ever smoking (47%), obesity (35%), hypertension (33%) or dyslipidemia (27%). Thirteen percent had elevated hs-TnT and 17% had elevated NT-proBNP (Table 2). Abnormal lipid biomarkers occurred in 45%, primarily due to abnormal Apo A1 (90%) and to a lesser degree abnormal Lp (a) levels (29%, Table 2). Subjects with RA were more likely to have abnormalities in NT-proBNP and ApoB, but had more favourable HDL-c, non-HDL-c and triglyceride profiles compared to the PsA/AS group (Table 2). In multivariate analyses, increasing age was significantly associated with abnormal hs-TnT and NT-proBNP but negatively associated with ApoB. Female sex was associated with greater odds for abnormal Lp (a) but lower values of hs-TnT and NT-proBNP (Table 3). No other IA disease-specific or CVD risk factors were consistently associated with cardiac biomarkers (Table 3).

Conclusion: Abnormalities in cardiac and lipid biomarkers are common even in well-controlled IA patients with no known CVD. Additional research is needed to determine if biomarkers may help with CVD risk re-classification beyond traditional clinical risk score approaches. In addition, it will be important to understand whether CVD biomarkers

are responsive to changes in disease activity or particular therapies, which may be another rationale for a treat-to-target approach in IA.

Disclosure: B. Kuriya, None; **S. Akhtari**, None; **M. Movahedi**, None; **J. Udell**, Boehringer-Ingelheim, 1, 5, 6, Sanofi, 1, 5, 6, Bayer, 5, Novartis, 1, 5; **P. Lawler**, Novartis, 2; **P. Harvey**, None; **L. Eder**, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5.

Abstract Number: 1094

Extremely Elevated Erythrocyte Sedimentation Rate Revisited in Rheumatic Diseases: Flare-Up or Infection? Single Centre Retrospective Analysis

Emre Bilgin[1], Zehra Ozsoy[2], Melek Seren Aksun[3], İmdat Eroğlu[3] and Umut Kalyoncu[1], [1]Hacettepe University, Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey, [2]Division of Rheumatology, Department of Internal Medicine, Hacettepe University, Ankara, Turkey, [3]Department of Internal Medicine, Hacettepe University, Ankara, Turkey

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

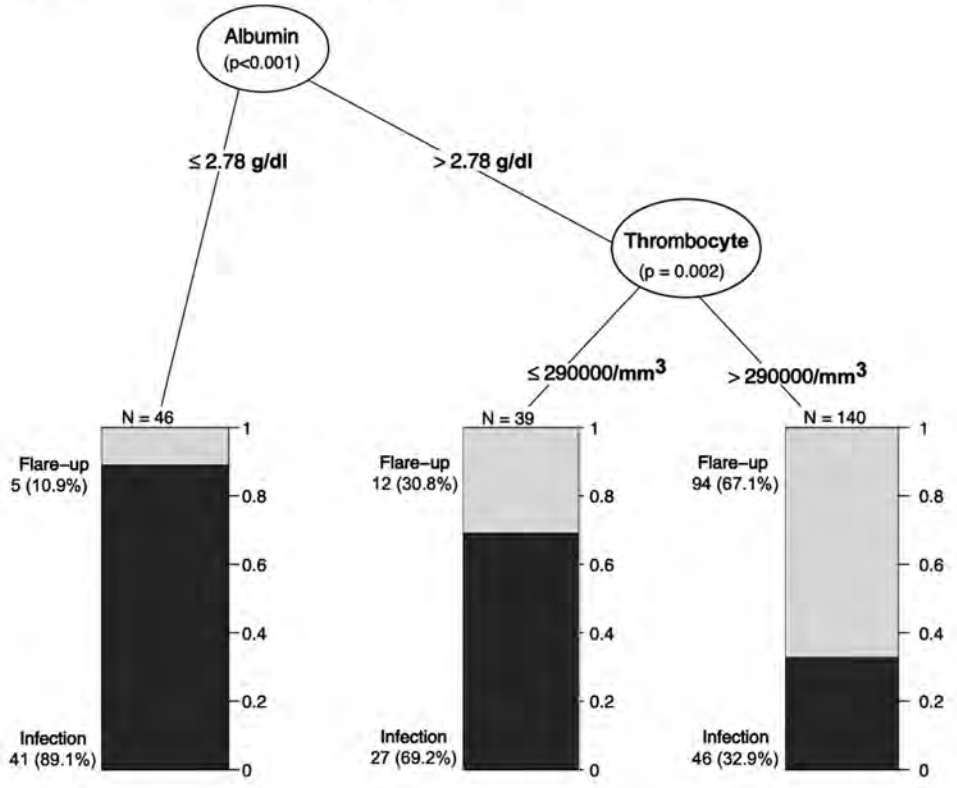
Session Time: 8:30AM–10:30AM

Table. Demographic and laboratory characteristics of study groups

Variable	Patients with disease flare-up (n=111)		Patients with infection (n=114)		p
Female, n(%)	85 (76.6)		63 (55.3)		0.001
Age, mean (SD)	48.1 (17.5)		54.6 (16.7)		0.005
Diagnosis subgroup - Inflammatory arthritis - Vasculitis - Connective tissue disorders	 93 (83.8) 11 (9.9) 7 (6.3)		 65 (57.0) 22 (19.3) 27 (23.7)		<0.001
Hemoglobin (mg/dl)	10.2 (1.3)		10.0 (1.5)		0.43
Leukocyte (/mm^6)	9.4 (3.9)		10.2 (4.4)		0.12
Neutrophil(/mm^6)	6.5 (3.7)		7.8 (4.1)		0.02
Thrombocyte(/mm^6)	441 (178)		350 (152)		<0.001
MCV	76.0 (9.5)		81.6 (8.9)		<0.001
RDW	17.5 (2.7)		17.2 (3.0)		0.45
MPV	7.6 (0.9)		8.0 (1.0)		0.005
	N		N		
AST (IU)	108	24.1 (18.3)	114	30.4 (24.3)	0.03
ALT (IU)	110	22.1 (29.1)	114	29.6 (33.4)	0.07
ALP (IU)	77	103.8 (56.3)	108	133.7 (107.4)	0.026
GGT (IU)	76	49.8 (77.6)	108	66.7 (68.8)	0.12
Creatinine (mg/dl)	108	0.8 (0.6)	114	2.0 (7.8)	0.09
Albumin (g/dl)	108	3.6 (0.6)	114	3.1 (0.7)	<0.001
Total Protein (g/dl)	107	7.2 (0.9)	114	6.7 (1.2)	<0.001
CRP (mg/dl)	110	10.2 (8.6)	114	15.5 (11.2)	<0.001
Fibrinogen (mg/dl)	34	486.0 (186.8)	60	538.4 (188.6)	0.20
Ferritin (microgram/ml)	77	77.4 (119.1)	97	447.3 (1007.7)	0.002

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, ALP: Alkalene phosphatase, CRP: C-reactive protein, GGT: Gamma-glutamyl transferase, MCV: Mean corpuscular volume, MPV: Mean platelet volume, RDW: Red Cell Distribution Width
Data were given as median(minimum-maximum) or n(%), if otherwise specified.

Figure. Decision tree to discriminate patients with flare-up and infection



Background/Purpose: To compare the laboratory characteristics of patients who had rheumatic diseases and presented with extremely elevated ESR (≥100 mm/h) and had either disease flare-up or documented infection and to find factors which may help to differentiate patients with disease flare-up and infection.

Methods: In this retrospective analyses, patients -either inpatient or outpatient- with ESR≥100 mm/h between 2015 and 2020 were identified. Patients with a certain diagnosis of inflammatory rheumatic disease and had either disease flare-up or documented infection were included in the analysis. Flare-up was defined as need of newly prescribed immunosuppressive (IS) agents or increment of dose of the already prescribed IS agents and NOT prescription of any kind of antibiotics. Infection was defined as documentation of possible infective agent via culture or imaging finding AND prescription of any kind of antibiotics. Available laboratory data temporarily nearest to ESR≥100 mm/h were recorded. Decision tree by R (package *party*) was used to construct a clinician-friendly algorithm for the discrimination of disease flare-up and infection by using routine laboratory tests.

Results: Of 311 patients with ESR≥100 mm/h and rheumatic diseases, 225 were included. 111 (49.3%) patients had disease flare-up and 114 (50.7%) patients had infection. In flare-up group, 93 (83.8%) had inflammatory arthritis [57 RA, 31 SPA, 2 JIA, 2 crystal arthritis, 1 adult Still's disease], 11 (9.9%) had vasculitis [5 large-vessel, 4 small-vessel, 2 PMR] , 7 (6.3%) had connective tissue disorder (CTD) [5 SLE, 1 overlap syndrome and 1 SSc]; however, in infection group 65 (57.0%) had inflammatory arthritis [25 RA, 22 SpA, 6 crystal arthritis, 6 FMF, 4 adult Still's disease, 2 JIA], 22 (19.3%) had vasculitis [12 small-vessel, 5 large-vessel vasculitis, 2 PMR, 1 relapsing polychondritis, 1 Behcet's syndrome and 1 PAN] and 27 (23.7%) had CTD [12 SLE, 5 SSc, 3 Sjögren's syndrome, 3 sarcoidosis, 2 myositis, 1 retroperitoneal fibrosis, 1 granulomatous mastitis]. Thrombocyte, MCV, albumin and total protein were significantly lower in infection group, however; neutrophil, MPV, CRP and ferritin were significantly lower in flare-up group (**Table**). Lipids, vitamin B12 and complement levels were similar. In decision tree, serum albumin ≤2.78 g/dl was the

first branch (89.1% for infection vs. 10.9 for flare-up). If serum albumin >2.78 g/dl, thrombocyte ≤290/mm6 was the second branch (thrombocyte count≤290/mm^6; 69.2% for infection vs. 30.8% for flare-up // thrombocyte >290/mm6; 32.9% for infection vs. 67.1% for flare-up) (**Figure**). In multivariable analysis factors were associated with infection over flare-up (reference level): thrombocyte count (per 1/mm^6 increment) (aOR: 0.997 (0.995-0.999)), albumin (per 1 gr/dl increment) (aOR: 0.37 (0.22-0.63)), CRP (1 mg/dl increment) (aOR: 1.044 (1.011-1.044)).

Conclusion: Extremely elevated ESR is an alarming finding for clinicians who follow-up patients with rheumatic diseases. Flare-up of the underlying rheumatic disease and infections should be kept in mind in patients with such presentation. We have generated a simple and clinician-friendly decision tree in which albumin level and thrombocyte count were key elements.

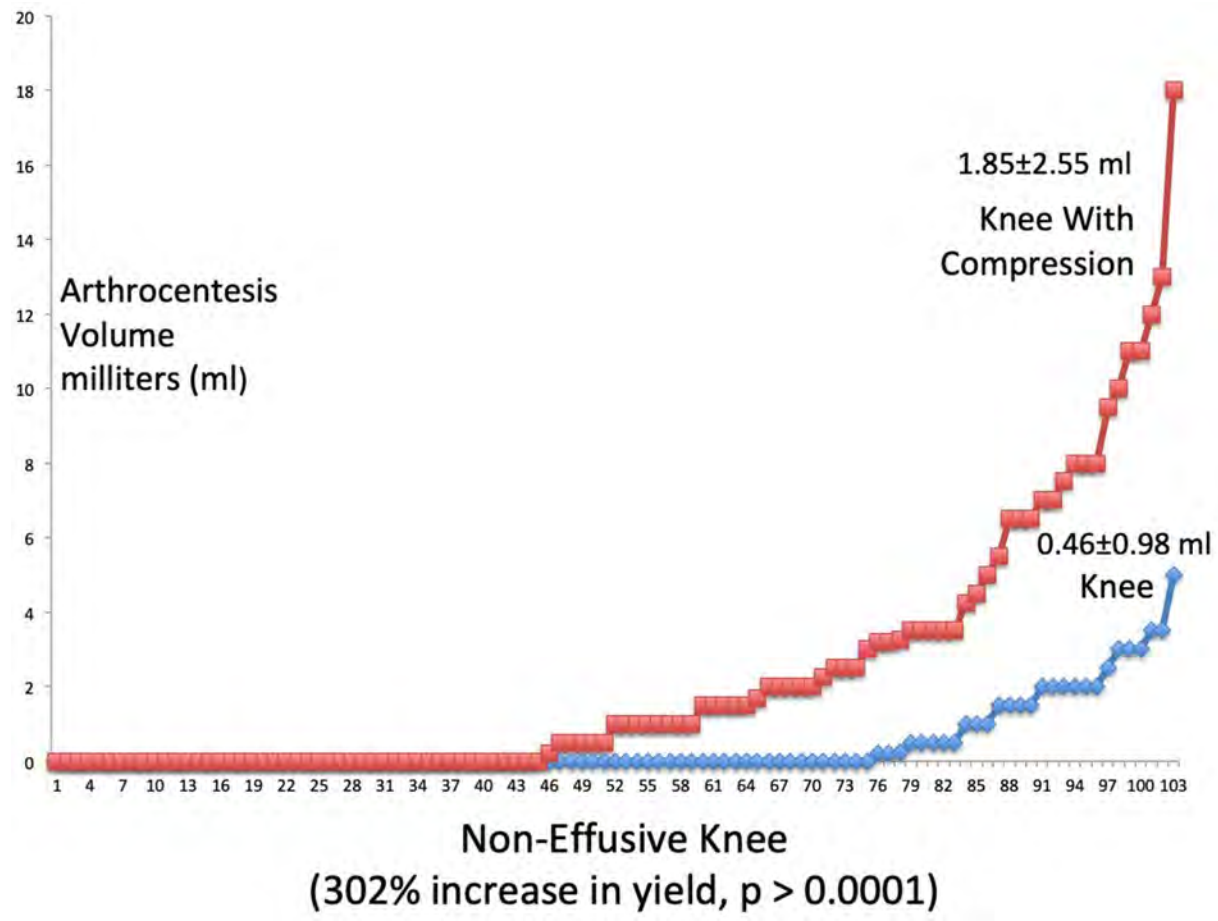
Disclosure: E. Bilgin, None; **Z. Ozsoy**, None; **M. Aksun**, None; . **Eroğlu**, None; **U. Kalyoncu**, None.

Abstract Number: 1095

Improved Arthrocentesis and Fluid Yield of the Non-Effusive Knee Using Pneumatic Compression

Ahsan Iqbal[1], Sumir Brahmbhatt[1], Maheswari Muruganandam[2], David Cisneros[3], Adnan Kiani[2], Fatemeh Farshami[4], Jaren Trost[5], N. Suzanne Emil[2], Sharon Nunez[1] and Wilmer Sibbitt[2], [1]UNM, Albuquerque, NM, [2]University of New Mexico, Albuquerque, NM, [3]University of New Mexico School of Medicine, Albuquerque, NM, [4]University of New Mexico, Albuquerque, MD, [5]Optum, Albuquerque, NM

	No Compression	Compression	95% CI of difference	
Number	103	103	**Where applicable**	P value
Age	60.2±11.6	60.2±11.6.3	CI -3.2 <0< 3.2 0% difference	0.5
Male:Female Ratio	24:79 (67% female)	24:79 (67% female)	0% difference	0.5
Preprocedure Pain	7.3± 1.6	7.3± 1.6	CI -0.44<0< 0.44 0% difference	0.5
Procedure Pain	4.0±2.5	4.0±2.5	CI -0.69<0< 0.69 0% difference	0.5
Post-Procedure Pain	1.6±1.4	1.6±1.4	CI -0.38<0< 0.38 0% difference	0.5
Diagnostic Arthrocentesis ≥ 2 ml	11% (11/103)	37% (38/103)	245% increase	0.00001
Volume for Biomarkers ≥ 0.5 ml	24% (25/103)	55% (57/103)	128% increase	0.00001
Mean Synovial Fluid Yields (ml)	0.46±0.98	1.85±2.55	CI -1.93<-1.39<-0.86 302% increase	0.00001



Non-Effusive Knee arthrocentesis with and without pneumatic compression (302% increase in yield, p > 0.0001)

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
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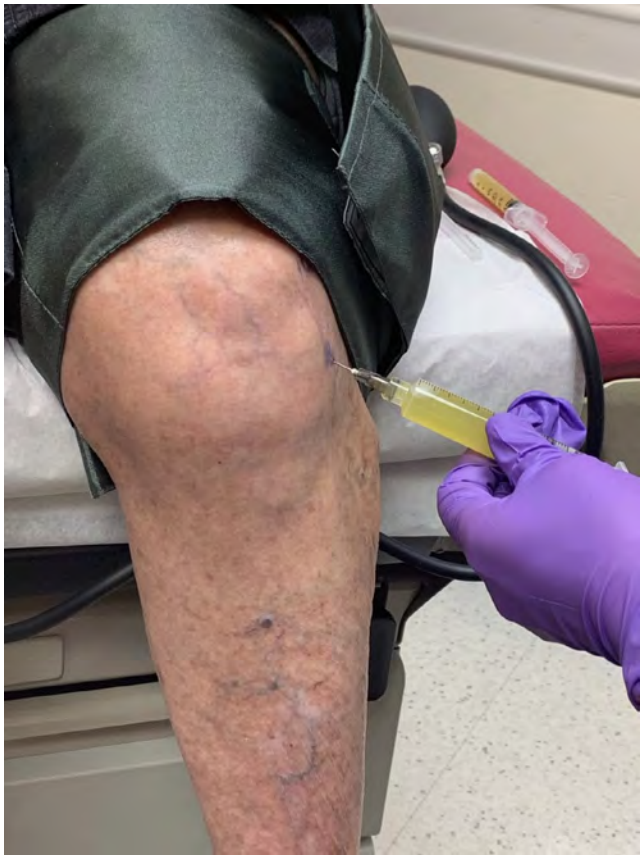
Session Time: 8:30AM–10:30AM

Background/Purpose: Arthrocentesis is critical for diagnosis and therapy of joint disease; however, it is very difficult to obtain diagnostic fluid from an arthritic but clinically non-effusive knee – the so-called "dry tap". In the era of synovial fluid biomarker analysis to diagnose and classify diseases, obtaining at leastsome fluid is of increasing importance.

To use external pneumatic compression on the non-effusive knee to improve arthrocentesis success and synovial fluid yield.

Methods: As a Quality Improvement (QI) Initiative in the Rheumatology Injection Clinic, we instituted standard mechanical compression of the knee during arthrocentesis and determined quality measures before and after. In this IRB approved study conducted from 2018 to 2021, we instituted a modified Arthrocentesis QI program using a flexed knee approach and an inexpensive standard pneumatic thigh blood pressure cuff over the suprapatellar bursa and compared quality measures before and after the procedure.

103 consecutive patients with non-effusive osteoarthritic knees were included in the QI intervention.



Knee aspiration with pneumatic external compression of non effusive knee

Exclusion criteria:

The exclusion of a knee effusion was determined clinically by palpation for suprapatellar bursa distention, ballottement of a floating patella, and fluid shift with asymmetric compression.

Inclusion criteria

1) the presence of no clinically palpable knee effusive,

2) indications for therapeutic-diagnostic joint needle procedure,

3) formal signed consent of the patient to undergo the procedure,

4) knee osteoarthritis.

103 consecutive patients underwent arthrocentesis with the knee in the flexed position with an uninflated thigh blood pressure cuff over the suprapatellar bursa (Figure 1) until fluid return ceased, and then the cuff was inflated to 100 mm Hg and arthrocentesis quality measures were again determined.

Quality Measures:

1) Pain was measured with Visual Analogue Pain Scale,

2) Arthrocentesis success in obtaining at least 2 ml of diagnostic fluid and 0.5 ml for biomarker analysis,

3) Fluid yield in milliliters before and after compression.

Results: Pneumatic compression of the knee markedly improved clinical arthrocentesis success (≥ 2 ml) and sufficient fluid for biomarker analysis (≥ 0.5 ml) while increasing overall synovial fluid yield by 302% (Figure 1, Table 1).
Conclusion:• This study demonstrates consistent improvement in arthrocentesis diagnostic success and synovial fluid yield using external pneumatic compression of the clinically non-effusive knee.

- Compression of the non-effusive knee with an inexpensive standard suprapatellar pneumatic leg blood pressure cuff markedly improves the success and fluid yield of arthrocentesis in the non-effusive knee.
- **Arthrocentesis of the knee with pneumatic compression can be used in all patients who can sit and is especially useful in patients who wish to remain seated or who cannot extend their knee due to flexion contracture, wheelchair confinement, or with pain or severe arthritis.**
- Improving synovial fluid yield from the clinically non-effusive knee will have increasing importance as synovial fluid biomarker analysis is further integrated into the classification schemes of various forms of noninflammatory and inflammatory arthritis.

Disclosure: A. Iqbal, None; **S. Brahmbhatt**, None; **M. Muruganandam**, None; **D. Cisneros**, None; **A. Kiani**, None; **F. Farshami**, None; **J. Trost**, None; **N. Emil**, None; **S. Nunez**, None; **W. Sibbitt**, None.

Abstract Number: 1096

CSF-specific CD8 T Cell Clonal Expansion in Neurosarcoidosis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Neuroinflammation is a severe manifestation of the systemic inflammatory disorders. Sarcoidosis, which leads to neurologic disease in 5-10 % of cases, has traditionally been thought to be driven by CD4 T cells. However, this model has been inferred by studies in pulmonary disease and has not been directly evaluated in the central nervous system (CNS). Here, we evaluated T and B cell clonal expansion in neurosarcoidosis to identify putative antigen-driven T or B cell responses.

Methods: We performed single-cell RNA-sequencing to obtain an unbiased gene expression survey of cerebral spinal fluid (CSF) and blood immune cells in participants with neurosarcoidosis and controls. This analysis allowed quantification, cell type identification, and transcriptional profiling of individual lymphocytes within the inflamed CNS as compared to cells in circulation, along with T cell receptor and B cell receptor sequencing to determine clonotype distribution.

Results: The plurality of CSF cells were CD4 T cells followed by CD8 T cells, with smaller and variable contributions of B cells, NK cells, and myeloid cells. Unexpectedly, B and T cell receptor sequencing revealed robust CD8 T cell clonal expansion specific to the CSF in neurosarcoidosis participants, with minimal CD4 T and B cell clonality. These

CSF-specific CD8 T cells expressed higher levels of CD27 and granzyme K and lower levels of CX3CR1, granzyme B, and granulysin, consistent with reduced cytotoxicity and similar to CD8 T cells seen in uveitis and rheumatoid arthritis. Finally, a core transcriptional signature of CSF-specific CD8 T cells was predominantly composed of interferon-stimulated genes, suggestive of a potential therapeutic target.

Conclusion: These data suggest that neurosarcoidosis may be driven by clonally expanded CD8 T cells that mediate inflammation not via direct cytotoxicity but rather through pro-inflammatory cytokines. As inhibition of interferon signaling with JAK inhibitors has been efficacious in published cases of cutaneous and pulmonary sarcoidosis, this strategy may also be effective in patients with neurologic disease.

Disclosure: M. Paley, None; **B. Baker**, None; **S. Dunham**, None; **N. Linskey**, None; **E. Roberson**, None; **D. Clifford**, None; **W. Yokoyama**, None.

Abstract Number: 1097

Gastrointestinal Malignancies in Sarcoidosis: A Nationwide Analysis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Sarcoidosis is a multisystem disorder that can involve any organ system. It can involve organs like the lungs, skin, eyes, nose, muscles, heart, liver, spleen, bowel, kidney, testes, nerves, lymph nodes, joints, and brain. There has also been some evidence of sarcoidosis causing lymphoma. The prevalence of gastrointestinal (GI) disorders and malignancies have been rarely studied in patients with sarcoidosis. We attempted to answer this retrospectively using the Nationwide Inpatient Sample (NIS) database analysis.

Methods: We queried the 2017 NIS database using ICD-10-CM diagnosis codes to identify all adult patients admitted with a diagnosis of sarcoidosis. We also identified various gastrointestinal disorders and malignancies using ICD-10 codes. Outcomes assessed were association between sarcoidosis and (A) GI disorders and (B) GI malignancies. A multivariate logistic regression was done adjusting the age, gender, comorbidities, insurance status, race and various hospital characteristrics, and comparative analysis was performed between patients with and without sarcoidosis, Odds Ratio (OR) with 95% confidence interval (CI) and p-values were obtained. A p-value of < 0.05 was considered statistically significant for all outcomes. Statistical analysis was performed using STATA software (StataCorp, College Station, Texas).

Results: The 2017 NIS database yielded a total 30.4 million patients, of which 82,060 (mean age 60.03 years and females 61.6%) were identified with a diagnosis of sarcoidosis and the remaining were grouped as non-sarcoidosis. The following GI signs and symptoms were significantly increased in patients with sarcoidosis compared to patients without sarcoidosis: diarrhea (4.79% vs 3.93%, $p < 0.01$), colitis (3.0% vs 2.3%, $p < 0.01$), gastritis (1.9% vs 1.5%, < 0.05), weight loss (1.0% vs 0.5%, $p < 0.01$), dyspepsia (0.6% vs 0.4%, $p < 0.01$), gastroesophageal reflux (28.5% vs 18.6%, $p < 0.01$), diverticulitis (3.1% vs 2.9%, $p < 0.01$), and celiac disease (28.6% vs 18.6%, $p < 0.01$). A somewhat lower prevalence of the following malignancies were noted in patients with sarcoidosis: esophageal cancer (0.06% vs 0.13%, $p < 0.05$), colon cancer (0.4% vs 0.6%, $p < 0.01$), rectal cancer (0.1% vs 0.3%, $p < 0.01$), and pancreatic cancer (0.3% vs 0.4%, $p < 0.01$)

Table 1. Patient Characteristics

	Variable	Sarcoidosis (82,060) N (%)	No Sarcoidosis N(%)	P-value
1.	Female	61.61%	57.73%	<0.01
2.	Mean Age	60.03	57.93	<0.05
3.	***Race***			
	White	46.7%	67.32%	<0.01
	Black	45.71%	15.14%	
	Hispanic	4.15%	11.11%	
	Asian or Pacific Islander	0.88%	2.76%	
	Native American	0.33%	0.62%	
	Other	2.23%	3.06%	
4.	***Charlson comorbidity score***			
	0	15.59%	35.77%	<0.01
	1	21.49%	19.49%	
	2	19.81%	14.49%	
	>3	43.11%	30.25%	
5	***Median income in patient zip code***			
	$1–$38,999	36.11%	30.49%	<0.01
	$39,000–$47,999	24.25%	26.58%	
	$48,000–$62,999	21.64%	23.43%	
	$63,000	18.00%	19.5%	
6.	***Insurance***			
	Medicare	56.82%	49.26%	<0.01
	Medicaid	14.88%	19.16%	
	Private	26.08%	27.56%	
	Uninsured	2.22%	4.02%	
	Hospital Location			
	Rural	7.09%	9.26%	<0.01
	Urban	92.91%	90.74%	
	Hospital size			
	Small	18.92%	20.11%	<0.01
	Medium	27.41%	29.57%	
	Large	53.67%	50.31%	
	Teaching hospital	74.56%	67.71%	

Conclusion: We highlighted a spectrum of GI signs and symptoms which were significantly more prevalent in patients with sarcoidosis. Of these, the most prevalent were gastroesophageal reflux and celiac disease. Interestingly, GI malignancies were significantly less prevalent in patients with sarcoidosis than those without. These results should be evaluated and confirmed in future studies.

Table 2. GI disorders in Sarcoidosis

Disorder	Sarcoidosis	No Sarcoidosis	OR (95% CI)	p-value
Diarrhea	4.79%	3.93%	1.22 (1.14-1.32)	<0.01
Peptic Ulcer	0.6%	0.67%	0.89 (0.72-1.09)	0.27
Colitis	3.00%	2.31%	1.30 (1.19-1.43)	<0.01
Gastritis	1.89%	1.53%	1.23 (1.09-1.38)	<0.01
Weight Loss	0.97%	0.53%	1.83 (1.57-2.13)	<0.01
Nausea/vomiting	2.32%	2.06%	1.12 (1.01-1.25)	<0.05
Constipation	7.24%	5.67%	1.29 (1.21-1.38)	<0.01
Anorexia	0.54%	0.42%	1.28 (1.05-1.57)	<0.05
Hematemesis	0.26%	0.4%	0.65 (0.48-0.88)	<0.01
Rectal bleeding	0.96%	0.90%	1.06 (0.90-1.25)	0.43
Dyspepsia	0.62%	0.42%	1.48 (1.21-1.80)	<0.01
Dysphagia	3.34%	3.11%	1.07 (0.98-1.17)	0.11
Anemia	10.57%	9.26%	1.15 (1.10-1.21)	<0.01
Gastroesophageal Reflux	28.5%	18.6%	1.74 (1.67-1.81)	<0.01
Hypoalbuminemia	0.9%	0.76%	1.19 (1.01-1.42)	<0.05
Diverticulitis	3.1%	2.89%	1.07 (0.97-1.18)	0.13
Celiac Disease	28.62%	18.63%	1.75 (1.68-1.82)	<0.01
Acute Pancreatitis	1.22%	1.44%	0.84 (0.73-0.97)	<0.05
Cholelithiasis	1.83%	1.98%	0.92 (0.82-1.03)	0.17
Cholecystitis	0.32%	0.36%	0.89 (0.68-1.17)	0.44
All GI disorders	51.05%	40.63%	1.52 (1.47-1.57)	<0.01

Table 3. GI malignancies in Sarcoidosis

Cancer	Sarcoidosis	No Sarcoidosis	OR (95% CI)	p-value
Oral cancer	0.067%	0.11%	0.63 (0.35-1.13)	0.12
Esophageal cancer	0.061%	0.13%	0.47 (0.25-0.87)	<0.05
Gastric cancer	0.12%	0.13%	0.91 (0.56-1.46)	0.70
Small bowel cancer	0.03%	0.031%	0.96 (0.40-2.32)	0.94
Colon cancer	0.4%	0.56%	0.71 (0.55-0.92)	<0.05
Rectal cancer	0.12%	0.25%	0.45 (0.28-0.71)	<0.01
Liver cancer	0.12%	0.15%	0.79 (0.49-1.26)	0.32
Pancreatic cancer	0.29%	0.35%	0.82 (0.60-1.11)	0.21

Disclosure: R. Fatima, None; **A. Acharya**, None; **S. Iftikhar**, None; **J. Gekonde**, None.

Abstract Number: 1098

Does Cancer Masquerade as Sarcoidosis?

Daniel Albert, Dartmouth-Hitchcock, Etna, NH

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Several case reports have suggested that cancer can present occultly as a granulomatous inflammatory disease consistent with sarcoidosis. These cases illustrate a problem of potential misdiagnosis leading to adverse outcomes. However, there has not been a study to examine the frequency and circumstances of this issue.

Methods: A retrospective chart review of all the cases of sarcoidosis presenting to Dartmouth-Hitchcock Medical Center from 10/1/2015 to 9/30/2020 were examined for those patients who subsequently developed a malignancy.

Results: Of 1029 individual cases of sarcoidosis 50 patients had a malignancy diagnosed subsequent to the initial determination of sarcoid. 36 of these patients had pulmonary involvement characterized by pulmonary nodules, hilar, paratracheal or mediastinal lymphadenopathy. Of the 14 without pulmonary involvement 2 had CNS, 5 skin, 2 liver, 1 breast, 1 arthritis, 1 inguinal lymphadenopathy and 2 cardiac. 30 of the 50 had biopsy confirmation and the rest imaging consistent with sarcoidosis. 14 of the pulmonary cases had other organ involvement including bone, lymph nodes, skin, pericardial, liver and spleen. Neither of the two CNS cases were confirmed by biopsy and one had a subsequent change of diagnosis to squamous cell of the head and neck. The other had pachymeningitis with elevated CSF ACE levels and no change in diagnosis. Other possible contributing disorders included tuberous sclerosis, Sjogren's Syndrome, Celiac Disease, Crohn's Disease, Lynch Syndrome and Psoriasis. In 36 of the 50 cases the malignancy was unrelated to sarcoidosis primarily breast, thyroid, endometrial, squamous cell, basal cell and melanoma. 7 cases the subsequent diagnosis of cancer might have been related to the therapy for sarcoid including AML after mycophenolate, melanoma after Adalimumab, B cell lymphoma after Adalimumab, CTCL after infliximab and methotrexate, squamous cell and basal cell after methotrexate and adenocarcinoma after methotrexate. In one case treatment for the malignancy (Hodgkin's) probably resulted in the condition labelled sarcoid but was changed to granulomatous disease associated with CVID.7 cases the diagnosis of sarcoidosis appeared to delay the eventual cancer diagnosis by a range of 1 month to 2 years and included cases of Hodgkin's Lymphoma, a MALT tumor, lymphomatoid granulomatosis, squamous cell of the head and neck, seminoma, and CTCL. In one case sarcoidosis delayed the correct diagnosis of MAC by about 2 months. In every case where a malignancy was eventually found the original diagnosis of sarcoidosis was confirmed by biopsy.

Conclusion: Cancer can masquerade as sarcoidosis but it is very rare occurring in 7 of our 1029 (0.7%) cases resulting in a delay in diagnosis usually a matter of months but in 2 cases more than 1 year for seminoma and lymphomatoid granulomatosis. Conversely, immunosuppressive therapy for sarcoid may increase risk for malignancy. In both circumstances clinical vigilance rather than biopsy characteristics is the best guarantee for a good outcome.

Disclosure: D. Albert, None.

Abstract Number: 1099

Characteristics and Outcomes of Myocardial Infarction in Patients with Rheumatoid Arthritis, Systemic Lupus Erythematosus, Systemic Sclerosis, Gout and Osteoarthritis Patients Using the National Inpatient Sample Database from 2002-2018

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with the autoimmune rheumatic disease have an increased risk of acute myocardial infarction (MI). Our study was designed to compare the prevalence, characteristics and in-hospital outcomes among patients with Rheumatoid Arthritis (RA), Systemic lupus erythematosus (SLE), Systemic Sclerosis (SSc), Gout and Osteoarthritis (OA), who developed acute myocardial infarction during 2002- 2018 in a national cohort of US hospitalizations.

Methods: We used the National Inpatient Sample (NIS) database to identify hospitalizations of patients with MI and autoimmune rheumatic diseases including RA, SLE, SSc, Gout. We compared the baseline characteristics, comorbidities, and age-adjusted mortality of patients among the study groups; OA hospitalizations with MI served as a control population. Comparisons of continuous and discrete data were made with ANOVA and the Rao-Schitt chi-square test, respectively. All analyses utilized SAS 9.4 and incorporated the NIS sampling design.

Results: Between 2002- 2018, there was a total of 844,427 MI hospitalizations with RA, SLE, SSc, Gout, and OA (RA: 87,637, SLE: 25,067, SSc: 5,523, Gout: 197,845, and OA: 528,355). Several differences were observed; females were disproportionately higher in SLE, SSc, and RA groups compared to OA (80.6%, 80.3%, 62.6% vs 55%). There was no statistically significant difference in Charlson Comorbidity Index for readmission and mortality among the groups studied. Patients with SLE (60 years; 95% CI: 50 years to 70 years) and SSc (67 years; 95% CI: 58 years to 76 years) had an early age of admission for inpatient hospitalization in comparison to OA (76 years; 95% CI: 66 years to 80 years). The average age of morality is lower in patients with SLE (66 years; 95% CI: 56 years to 76 years) and SSc (72 years; 95% CI: 60 years to 79 years) compared to OA (83 years; 95% CI: 76 years to 89 years). Refer to Table 1 for full characteristics as described above. Inpatient mortality was higher in those admitted with SSc, RA, and SLE in comparison to OA (10.2%, 5.4%, 5.2% vs 4.6%) (Table 2). However, Gout had decreased inpatient mortality compared to OA (4.3% vs 4.6 %) (Table 2).

Conclusion: This is the most updated NIS study comparing the clinical baseline hospitalization characteristics of patients with four autoimmune rheumatic diseases with acute myocardial infarction. Acute MI in SLE and SSc develop at an earlier age compared to other groups. We also observed increased mortality in patients with SSc compared with RA/ SLE/ Gout or OA. There is not much literature on outcomes of MI in patients with SSC and our study demonstrates that this patient group is an independent risk for in-hospital mortality. Therefore, further studies need to be done to evaluate the causes of higher mortality in this group.

Table 1. Clinical characteristics of hospitalized patients with four different systemic rheumatic diseases with myocardial infarction and Osteoarthritis patients with myocardial infarction

Characteristic	RA + MI (N = 87,637)	SLE + MI (N = 25,067)	SSc+ MI (N = 5,523)	Gout + MI (N = 197,845)	OA + MI (N =528,355)	*P*-value
Age at admission, years (Median, IQR)	70 (61,79)	60 (50,70)	67 (58,76)	71 (62,80)	76 (66,84)	< 0.001
Age at mortality, years (Median, IQR)	77 (69,84)	66 (56,76)	72 (60,79)	79 (71,85)	83 (76,89)	< 0.001
Female sex (%)	62.6	80.6	80.3	22.9	55.0	< 0.001
Race (%)						
White	80.9	62.6	76.8	72.2	81.4	
African American	8.5	24.3	11.8	14.4	8.9	< 0.001
Hispanic	6.4	8.3	6.9	5.1	5.8	
Asian	1.5	1.5	1.3	5.4	1.5	
Other	2.3	2.7	2.7	2.6	2.1	
Comorbidities (%)						
Diabetes	30.9	24.3	17.4	44.8	36.3	< 0.001
Chronic obstructive pulmonary disease	10.8	8.1	6.3	7.6	10.5	< 0.001
Hypertension	12.8	10.9	9.3	10.2	15.2	< 0.001
Chronic kidney disease	15.8	21.4	15.2	39.2	21.1	< 0.001
Charlson comorbidity index for readmission (Median, IQR)	13 (6, 24)	15 (7, 26)	13 (6,24)	14 (4, 28)	11 (3, 22)	< 0.001
Charlson comorbidity index for mortality, (Median, IQR)	1 (-1, 8)	2 (-2, 9)	2 (-1, 10)	2 (-2, 9)	1 (-2, 8)	< 0.001

Table 2. Hospital outcomes comparing four different systemic rheumatic diseases and osteoarthritis patients with myocardial infarction

Characteristics	RA+MI	SLE+MI	SSc+ MI	Gout+ MI	OA+MI	p-value
Died (%)	5.4	5.2	10.2	4.3	4.6	<0.001
Cost of index hospitalization, Median (IQR)	15927 (9177-24952)	16502 (9570-25644)	16597 (9596-26598)	16892 (9500-27821)	14527 (8096-23693)	<0.001
Length of Stay, Median (IQR)	3 (2-6)	3 (2-6)	3 (2-6)	3 (2-6)	3 (2-6)	<0.001

RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; SSc: Systemic Sclerosis; OA: Osteoarthritis; MI: Myocardial infarction; IQR: Interquartile range.

Disclosure: S. Gupta, None; **V. thallapally**, None; **S. Aurit**, None; **R. sen**, None; **J. Nahas**, None.

Abstract Number: 1100

Pulmonary Arterial Hypertension in Adult-Onset Still's Disease: A Case Series of 13 Patients

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SESSION INFORMATION

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Background/Purpose: Pulmonary Arterial Hypertension (PAH) is a rare but potentially fatal complication of Adult-Onset Still's Disease (AOSD). To date, only isolated observations have been published. Our objective was to establish the largest case series of AOSD patients with PAH, and to describe their clinical profile, evolution and response to treatments.

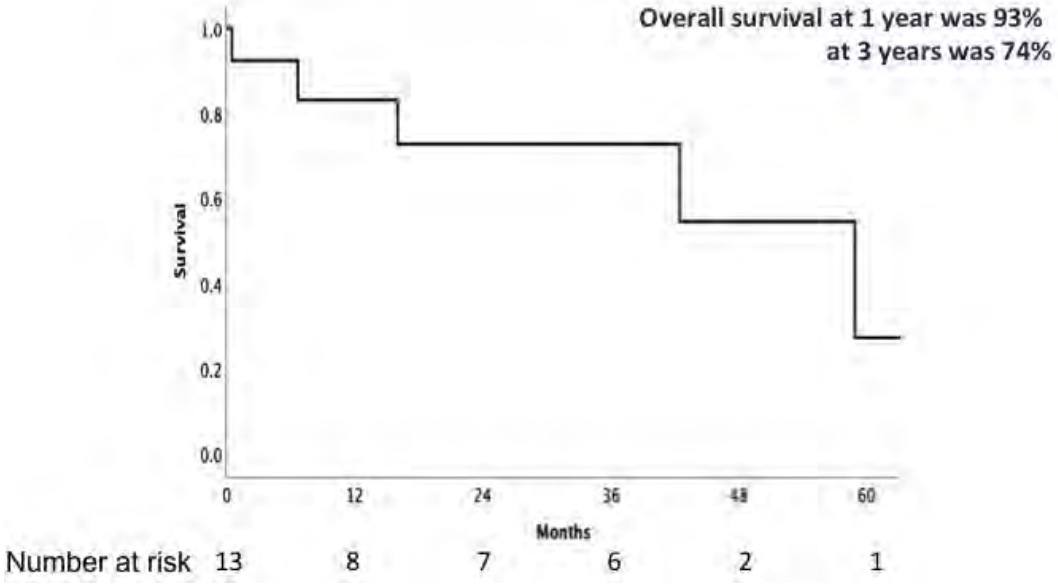
Methods: Cases were retrospectively identified from the French PAH network database and from an online call of the "Club Rhumatismes et Inflammation" (http://www.cri-net.com). To be included, all patients had to fulfil the Yamaguchi or Fautrel criteria for AOSD and PAH had to be confirmed by right heart catheterization. The data were collected using a standardized questionnaire.

Results: Thirteen patients were identified. All cases of PAH occured after the diagnosis of AOSD was made. All were female, the mean age at PAH diagnosis was 32± 12 years, 2 (15%) patients were Caucasian, 6 (46%) from Sub-

Table. Initial PAH therapeutic management

Treatment	*n (%)*
Inotropic therapy	6 (46%)
PAH treatment	10 (77%)
Monotherapy	3
Initial oral dual combination therapy	3
Dual combination therapy including IV prostacyclin	1
Upfront triple combination therapy including IV prostacyclin	3
High-dose corticosteroids	11 (85%)
Interleukin-1 inhibitors initiation	2 (15%)
Interleukin-6 inhibitors initiation	1 (0.7%)
Switch from IL-1 to IL-6 inhibitors	4 (30.7%)

Figure. Overall survival after PAH diagnosis in patients with AOSD



Saharan Africa, 1 (8%) from Asia and 4 (31%) from West Indies. Only 2 (15%) patients were smokers. All patients had a systemic onset of AOSD, 12 had a polycyclic and 1 a chronic articular evolution, and the mean delay between AOSD and PAH diagnosis was 2.9 (range 1.7 -5.4) years. PAH diagnosis was concomitant of AOSD flare in 11 (85%) patients. At PAH diagnosis, patients were receiving the following treatments: 13 (100%) corticosteroids (median dose 12 mg [interquartile range (IQR) 10-20]), 4 (31%) methotrexate, 9 (69%) interleukin (IL)-1 inhibitors (exposure median duration 7.1 months [IQR 4.4-10.1]), none IL-6 inhibitors, 2 (15%) TNF inhibitors. PAH was severe at diagnosis: 2 (15%), 7 (54%) and 4 (31%) patients were in NYHA functional class II, III and IV, respectively, with a median 6-minute walk distance of 289 m [IQR 0-448], a mean pulmonary arterial pressure of 41 ± 12 mmHg, a mean pulmonary arterial occlusion pressure of 6 ± 3 mmHg, a mean cardiac output of 3.9 ± 1.2 L/min, a mean cardiac index of 2.5 ± 0.9 L/min/m^2 and a median pulmonary vascular resistance of 7 Wood Units [IQR 6-11]. The treatment prescribed after PAH diagnosis is detailed in the table. The median follow-up was 34 months [IQR 10-42]. Five patients (38.5 %) died. The haemodynamic response to PAH treatment seemed to be dissociated from the prognosis since three patients died while their haemodynamic had improved or almost normalized. Three patients died during an AOSD flare with disseminated intravascular coagulation. Figure 1 shows the overall survival which was 93% at 1 year and 74% at 3 years.

Conclusion: PAH is a rare but potentially severe complication of AOSD. It affected exclusively women in our case series. AOSD remission should be physicians' objective, since PAH seems to occur when the underlying disease is not controlled.

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Abstract Number: 1101

Atypical Pulmonary Radiographic Findings May Help Identify Patients with Usual Interstitial Pneumonia and Autoimmune Features

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SESSION INFORMATION

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Background/Purpose: Once specific etiologic factors have been ruled out, the majority of patients with chronic interstitial pneumonia (IP) can be classified as idiopathic pulmonary fibrosis (IPF) or as connective tissue autoimmune disease (CTD) associated. Being usual interstitial pneumonia (UIP) the reference radiographic pattern of IPF, a non-UIP pattern is one of the most robust indicators of an alternative diagnosis. In this regard, Fischer's criteria of IP with autoimmune features (IPAF) include either a non-UIP radiographic pattern or the coexistence with alterations at other compartments. However, some patients presenting with UIP could have an autoimmune IP (AIP) and remain unclassified (UAIP). As it has been recently suggested, the involvement of the superior anterior lobe, an exuberant honeycombing and a straight edge between affected and unaffected regions could suggest an AIP diagnosis in patients with UIP. We set a retrospective study to describe the appearance of these atypical UIP signs in our clinic of AIP patients.

Methods: Two radiologists performed independent evaluations of CT scan images from our patients with AIP and an UIP pattern. Concordance was evaluated with kappa index. Epidemiological data, clinical diagnosis and process-associated variables were collected from clinical charts. Comparisons were assessed with non-parametric tests.

Results: Agreement between observer 1 (expert) and observer 2 (trainee) was fair as regards to the identification of the upper anterior lobe sign (p 0.001) and the straight edge ($p < 0.001$), while there was little concordance in the exuberant honeycombing scoring (p 0.7). We subsequently carried out the analysis using observer 1 scoring. There were 9 out of 33 p (27%) showing exuberant honeycombing, 5 p with involvement of the upper anterior lobe (15%) and 2 p with the straight edge sign (6%), irrespectively from the clinical diagnosis. The appearance of at least one of the signs was 62% in the CTD group, 43% in IPAF, and 30% in UAIP. In the UAIP cohort, 2 p had the anterior superior lobe sign. One of them did not fulfil the serological IPAF domain. The second one did not show involvement of other compartments, and had an ACPA titre of 264 IU. The third patient had an exuberant honeycombing, but no additional compartment involvement, along with a > 1/320 ANA titre. The last 2 patients would therefore change classification to IPAF if these signs were taken into account in the classification criteria. On the other hand, 2 patients had high rheumatoid factor but none had the atypical signs and would consequently remain unclassified. There was no association between atypical signs and inflammatory markers, such as glass-grounded opacities or acute phase reactants. Neither was there a relationship between these signs and disease duration time from or the extension of fibrosis. Interestingly, patients with emphysema were more likely to have any of the atypical UIP signs (p 0.047). We did not find associations between these signs and markers of epithelial injury. However, there was an inverse relationship with C'4 (p 0.041).

Conclusion: The new radiographic signs may help characterize a subgroup of patients with AIP, although more studies are necessary.

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Abstract Number: 1102

Comorbidities and Causes of Hospitalizations in a Cohort of IgG4-Related Disease Patients from a Single Center

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SESSION INFORMATION
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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
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Session Time: 8:30AM–10:30AM

Background/Purpose: The frequency and types of comorbidities, causes of hospitalization, and the differences among clinical phenotypes in patients with IgG4-related disease (IgG4-RD) have not been explored thoroughly.

We aimed to disclose the types of comorbidities and causes of hospitalizations and their impact in a cohort of IgG4-RD patients.

Methods: We performed a retrospective study. IgG4-RD patients had to fulfill the Comprehensive Diagnostic Criteria for IgG4-RD and/or the Consensus Statement on Pathology and/or the 2019 ACR/EULAR Classification Criteria for IgG4-RD. Clinical variables, comorbidities and causes of hospitalizations were retrieved from the medical charts in a standardized manner. Patients were classified in clinical phenotypes: Group 1 (pancreato-hepato-biliary), Group 2 (retroperitoneal/aortic), Group 3 (head and neck-limited), Group 4 (Mikulicz/systemic) and Group 5 (undefined). The Charlson Comorbidity Index (CCI) and the Rheumatic Disease Comorbidity Index (RDCI) were calculated at last follow-up.

Table 1. Comorbidities in IgG4-related disease patients

Table 1. Comorbidities in IgG4-related disease patients	
Comorbidity, n (%)	**N = 89**
Type 2 diabetes	8 (9)
Type 3c diabetes	7 (7.9)
Hypertension	24 (27)
Obesity	11 (12.4)
Dyslipidemia	15 (16.9)
Osteoporosis	12 (13.5)
Tobacco use	23 (25.8)
Inflammatory/autoinmune diseases	16 (18)
Atopy	17 (19.1)
History of thrombosis	7 (7.9)
Thyroid disease	12 (13.5)
Malignancies	9 (10.1)

Table 2. Differences among IgG4-related disease phenotypes

	Group 1	Group 2	Group 3	Group 4	Group 5	P
Male, n (%)	17 (70.8)	6 (66.7)	4 (16)	15 (62.5)	5 (71.4)	<0.001
Age, median (IQR), years	51.6 ± 14	39.1 ± 16.8	50.9 ± 19.5	52.2 ± 10.8	42.8 ± 19.2	0.17
Comorbidities, n (%)	23 (95.8)	9 (100)	22 (88)	24 (100)	7 (100)	0.27
Type 2 diabetes, n (%)	9 (37.5)	2 (22.2)	9 (36)	14 (58.3)	0	0.04
Type 3c diabetes, n (%)	4 (16.7)	0	0	4 (16.7)	0	0.11
Hypertension, n (%)	2 (12.5)	3 (33.3)	8 (32)	8 (33.3)	2 (28.6)	0.42
Obesity, n (%)	0	1 (11.1)	6 (24)	2 (8.3)	2 (28.6)	0.03
Dyslipidemia, n (%)	3 (12.5)	1 (11.1)	6 (24)	5 (20.8)	0	0.53
Osteoporosis, n (%)	2 (8.3)	1 (11.1)	7 (28)	2 (8.3)	0	0.22
Tobacco use, n (%)	7 (29.2)	3 (33.3)	4 (16)	8 (33.3)	1 (14.3)	0.59
Autoimmune disease, n (%)	1 (4.2)	2 (22.2)	5 (20)	7 (29.2)	1 (14.3)	0.17
Atopy, n (%)	3 (12.5)	0	5 (20)	9 (37.5)	0	0.06
Thrombosis, n (%)	1 (4.2)	0	0	4 (16.7)	2 (28.6)	0.03
Thyroid disease, n (%)	2 (8.3)	2 (22.2)	4 (16)	4 (16.7)	0	0.69
Malignancy, n (%)	8 (33.3)	2 (22.2)	3 (12)	1 (4.2)	0	0.05
Hospitalization, n (%)	17 (70.8)	5 (55.6)	5 (20)	12 (50)	6 (85.7)	0.001
Relapse, n (%)	11 (64.7)	3 (60)	1 (20)	8 (66.7)	5 (83.3)	0.27
Infection, n (%)	4 (23.5)	2 (40)	3 (60)	4 (33.3)	3 (50)	0.55
Complications of treatment, n (%)	3 (17.6)	1 (20)	0	1 (8.3)	9	0.72
Days of hospitalization, median (IQR)	4 (0-8.5)	4 (0-17)	0	3 (0-14)	13 (7.5-19.5)	0.001
Damage at last follow-up, n (%)	15 (62.5)	4 (44.4)	12 (48)	14 (58.3)	3 (42.9)	0.75
CCI at last follow-up, median (IQR)	3 (1-4)	2 (1-5)	2 (0-4)	3 (2-4)	1 (0-2)	0.56
RDCI at last follow-up, median (IQR)	1 (1-2)	2 (0-4)	1 (0-2)	1 (1-2.5)	0 (0-2)	0.79
Follow-up, median (IQR), months	30.5 (18-64)	34 (26-40)	24 (12-53)	35.5 (19-99)	29 (12.5-36)	0.76

CCI: Charlson Comorbidity Index; IQR: interquartile range; RDCI: Rheumatic Disease Comorbidity Index

Results: We included 89 patients with a mean age at diagnosis of 49.6 ± 16 years, 47 (52.8) were male. Twenty-four (27%) belonged to Group 1, 9 (10.1%) to Group 2, 25 (28.1%) to Group 3, 24 (27%) to Group 4 and 7 (7.9%) to Group 5.

At least one comorbidity was detected in 85 (95.5%) patients (Table 1). Type 2 diabetes was more frequent in Group 4, type 3c diabetes in Group 1 and 4, obesity in group 3 and 5, thrombosis in Group 5 and malignancies in Group 1 (Table 2).

Forty-five (50.6%) patients were hospitalized during follow-up, 22 (24.7%) once, 15 (16.9%) twice and 8 (9%) ≥ 3 times. Causes of first hospitalization (non-exclusive) were: relapse in 28 (62.2%), infection in 16 (35.6), treatment complications in 5 (11.1%) and others in 5 (11.1%). The median days of hospitalization was 1 (IQR 0-11.5). Ten (22.2%) patients were taking prednisone at the time of hospitalization with a median dose of 20 mg (IQR 7.5-45) and 6 (14%) immunosuppressants. Only 4 patients required intensive care unit admission. Hospitalization was more common in patients from Group 1 and 5. Group 5 had the longest days of hospitalization.

The median score of the CCI and RDCI at last follow-up was 3 (IQR 1-4) and 1 (IQR 0-2), respectively. Patients who ever had a hospitalization were more likely to have damage attributed to IgG4-RD at last follow-up (OR 2.8, 95% CI 1.2-6.8, p=0.02). Two patients died during a median follow-up of 30 (IQR 18-63) months.

Conclusion: Comorbidities are very frequent in patients with IgG4-RD and differed according to clinical phenotype. Relapses were a common cause of hospitalization. Hospitalization was more frequent in patients from Group 1 and 5, and they were associated with damage accrual.

Disclosure: D. Faz-Muñoz, None; **E. Martin-Nares**, None; **A. Hernández-Delgado**, None; **G. Hernandez-Molina**, None.

Abstract Number: 1103

Disease Associations with Very High Serum IgG4 Concentrations: A Retrospective Multi-Center Study

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Demographics and clinical characteristics of patients with a serum IgG4 level >5x ULN

	Total Cohort (n = 191)	Stanford Cohort (n = 53)	Mass General Brigham Cohort (n = 138)
Age, median [IQR]	66.0 [54.4, 75.0]	62.2 [44.9, 70.8]	65.1 [57.0, 75.8]
Sex, n (%)			
Female	54 (28.1)	20 (37.7)	34 (24.5)
Male	137 (71.7)	33 (62.3)	104 (75.5)
Race, n (%)			
White	108 (56.5)	18 (34.0)	90 (65.2)
Black	9 (4.7)	2 (3.8)	7 (5.1)
Hispanic	12 (6.3)	10 (18.9)	2 (1.4)
Asian	46 (24.1)	21 (39.6)	25 (18.1)
Unknown	9 (4.7)	1 (1.9)	8 (5.8)
Other	16 (8.4)	10 (18.9)	6 (4.3)
BMI, n (%)			
<25 kg/m^2	25.1 (5.4)	22.0 (2.2)	22.6 (2.1)
25-29.9 kg/m^2	24.3 (2.6)	27.0 (1.3)	26.7 (1.3)
≥30 kg/m^2	32.6 (4.8)	36.5 (5.1)	34.2 (4.2)
Smoking, n (%)			
Never	89 (46.6)	36 (67.9)	62 (44.9)
Former	47 (24.6)	15 (28.3)	35 (25.4)
Current	4 (2.1)	2 (3.8)	2 (1.4)
Unknown	40 (20.4)	0 (0.0)	39 (28.3))
Atopic disease, n (%)	51 (26.6)	22 (41.5)	29 (20.9)
Sinusitis, n (%)	42 (21.9)	14 (26.4)	28 (20.1)
Receiving allergy immunotherapy, n (%)	4 (2.1)	0 (0.0)	4 (2.9)

IgG4 = immunoglobulin G4; ULN = upper limit of normal; IQR = interquartile range; BMI = body mass index.

Table 2. Distribution of patients with a serum IgG4 level >5x ULN by disorder

Disorder	*n* (%)	IgG4 (mg/dL), median [IQR]
Definite IgG4-RD	128 (67.0)	1014.5 [678.5, 1419.9]
Probable IgG4-RD	10 (5.2)	980.3 [807.8, 1207.5]
Atypical IgG4-RD	2 (1.0)	653.2 [609.6, 696.9]
Possible IgG4-RD	4 (2.1)	623.0 [561.5, 824.1]
B cell lymphoma	4 (2.1)	1275 [1213.8, 1489]
B cell leukemia	2 (1.0)	1105.0 [1067.5, 1142.8]
Systemic lupus erythematosus	2 (1.0)	760.0 [756.0, 764.0]
EGPA	3 (1.6)	923.0 [751.3, 1847.2]
Hypereosinophilic syndrome	3 (1.6)	540.0 [511.6, 2702.4]
Histiocytic disease	2 (1.0)	2077.0 [1676, 2478.0]
Unknown	11 (5.8)	923.0 [751.3, 1847.2]
Other*	21 (11.0)	579.0 [534.0, 1834.0]

IgG4 = immunoglobulin G4; ULN = upper limit of normal; IQR = interquartile range; IgG4-RD = IgG4-related disease; EGPA = eosinophilic granulomatosis with polyangiitis.
*Other includes single cases of multiple myeloma, cholangiocarcinoma, food allergies, acute disseminated encephalomyelitis, spondyloenchondrodysplasia with immune dysregulation, POEMS syndrome, cystic fibrosis, MSSA bacteremia and osteomyelitis of the femur, cholangiocarcinoma, T cell lymphoma, bronchiolitis obliterans, postinfectious inflammatory disease, chronic eosinophilic pneumonia, monoclonal gammopathy of undetermined significance, pulmonary mycobacterial infection, sarcoidosis, pediatric autoimmune neuropsychiatric disease associated with Streptococcal infection, lymphadenopathy, small fiber neuropathy

Table 3. Manifestations of IgG4-RD in patients with a serum IgG4 level >5x ULN

IgG4-RD Manifestations	*n* (%)
Number of organs involved, median [IQR]	3 [2,3]
Single-organ involvement	22 (15.3)
Multi-organ involvement	118 (81.9)
Lacrimal gland	48 (33.3)
Salivary gland	71 (49.3)
Orbital	25 (17.4)
Pancreas	72 (50.0)
Biliary	34 (23.6)
Liver	14 (9.7)
Renal	43 (29.9)
Retroperitoneal fibrosis	13 (9.0)
Aorta/large vessel	9 (6.3)

IgG4 = immunoglobulin G4; IgG4-RD = IgG4-related disease; IQR = interquartile range.

Background/Purpose: Serum IgG4 concentrations are used as part of the evaluation for suspected IgG4-related disease (IgG4-RD), but the specificity of this test, especially at very high levels, remains uncertain. Indeed, the ACR/EULAR Classification Criteria for IgG4-RD place high weight on elevated serum IgG4 concentrations; of the 20 points required to be classified as IgG4-RD, 11 are assigned if the patient has an IgG4 concentration ≥ 5x the upper limit of normal (ULN).[1] We sought to evaluate the association of very high serum IgG4 concentrations with a diagnosis of IgG4-RD.

Methods: The data warehouses at two large academic medical centers—Stanford University and Mass General Brigham—were queried for all IgG subclass test results. Patients with any serum IgG4 concentration ≥ 5x the ULN were included. Demographics, medical history, and other laboratory test results of interest were extracted from the electronic medical record of each patient. A diagnosis of IgG4-RD was determined using the ACR/EULAR Classification Criteria for IgG4-RD. The positive predictive value (PPV) of a serum IgG4 concentration ≥ 5x the ULN for the diagnosis of IgG4-RD was estimated. Other conditions associated with very high serum IgG4 concentrations, and specific features of the IgG4-RD patients, were characterized.

Results: Of 34,391 patients with serum IgG subclasses tested, 2,294 (7%) had an elevated serum IgG4 concentration, and 191 (0.6%) had an IgG4 concentration ≥ 5x the ULN. The combined cohort had a median age of 66 years, was predominately male (72%), and was racially diverse (**Table 1**). The PPV of an IgG4 concentration ≥ 5x the ULN for a diagnosis of definite (67%), probable (5%), or atypical (1%) IgG4-RD was 73%. The median [IQR] IgG4 concentration among patients with definite IgG4-RD (*n* = 128) was 1014.5 mg/dL [678.5, 1419.9] (**Table 2**). Other diseases associated with a very elevated serum IgG4 concentration included B cell lymphoma and leukemia, eosinophilic granulomatosis with polyangiitis and other hypereosinophilic syndromes, systemic lupus erythematosus, histiocytic disease, and systemic infections or post-infectious syndromes (**Table 2**). Among IgG4-RD patients with an IgG4 concentration ≥ 5x the ULN, the majority (82%) had multi-organ involvement, with the pancreas (50%), salivary glands (49%), lacrimal glands (33%), and kidneys (30%) being the most commonly involved organs (**Table 3**).

Conclusion: The majority of patients with a serum IgG4 concentration ≥ 5x the ULN in this study had IgG4-RD, with a PPV of 73% for IgG4-RD. These data support the significant weight placed on very elevated serum IgG4 in the IgG4-RD Classification Criteria. However, it is notable that 27% of patients with an IgG4 concentration ≥ 5x the ULN had no identifiable cause or an alternative diagnosis, underscoring the importance of the Classification Criteria's entry and exclusion criteria when evaluating a patient with a very high IgG4 concentration for IgG4-RD. These findings highlight the broad differential to consider when evaluating a patient with a very high IgG4 concentration.

References

1. Wallace ZS, Naden RP, Chari S, et al., Arthritis Rheumatol 72, 7-19 (2020).

Disclosure: M. Baker, Vorso Corp, 2; **C. Cook**, None; **X. Fu**, None; **C. Perugino**, Viela Bio, 2; **J. Stone**, Principia Biopharma Inc, a Sanofi Company, 5, 12, personal fees; **Z. Wallace**, Bristol-Myers Squibb, 5, Principia/Sanofi, 5, Viela Bio, 2, MedPace, 2.

Abstract Number: 1104

Pathogenic *UBA1* Variants in Japanese Patients with Relapsing Polychondritis

Naomi Tsuchida[1], Yosuke Kunishita[2], Yuri Uchiyama[1], Yohei Kirino[3], Kaoru Takase-Minegishi[1], Ryusuke Yoshimi[1], Hideaki Nakajima[1] and Naomichi Matsumoto[1], [1]Yokohama City University Graduate School of Medicine, Yokohama, Japan, [2]Yokohama City University Graduate School of Medicine, Yokohama, Kanagawa, Japan, [3]Yokohama City University, Yokohama, Japan

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Pathogenic somatic variants in the ubiquitin like modifier activating enzyme 1 gene (*UBA1*) were discovered in individuals with systemic inflammation of cartilage, skin, and blood vessels accompanied by hematological abnormalities, named VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, affecting only male patients. Some patients with VEXAS were reported to have a relapsing polychondritis (RP) phenotype. To determine clinical and genetic features of individuals with RP likely caused by pathogenic somatic variants in *UBA1*.

Methods: Fourteen patients with RP who met the Damiani and Levine classification criteria were recruited (12 men, 2 women; median onset age [interquartile range] 72.1 years [67.1–78.0]). Sanger sequencing of *UBA1* was performed using genomic DNA from peripheral blood leukocytes or bone marrow tissue. Droplet digital PCR (ddPCR) and peptide nucleic acid (PNA)-clamping PCR were used to detect low-prevalence somatic variants. Clinical features of the patients were investigated retrospectively. Clinical features were compared pathogenic *UBA1* variant-positive and negative patients. Categorical variables were analyzed using the chi-square test and exact unconditional z-pooled test. Continuous variables were examined using the Mann–Whitney U test. A p-value < 0.0028 (= 0.05/18) was considered statistically significant using Bonferroni's corrected p-value for multiple testing (N=18).

Results: *UBA1* was examined in 13 of the 14 patients; 73% (8/11) of the male patients had somatic *UBA1* variants (c.121A >C, c.121A >G, or c.122T >C resulting in p.Met41Leu, p.Met41Val, or p.Met41Thr, respectively). All the variant-positive patients had systemic symptoms, including a significantly high prevalence of skin lesions. ddPCR detected low-prevalence (0.14%) of somatic variant (c.121A >C) in one female patient, which was subsequently confirmed by PNA-clamping PCR.

Conclusion: Genetic screening for pathogenic *UBA1* variants should be considered in patients with RP, especially male patients with skin lesions.

Table. Clinical features of the 14 patients with relapsing polychondritis and UBA1 variants detected by Sanger sequencing

Patient ID	RP01	RP02	RP03	RP04	RP05	RP07	RP08	RP10	RP11	RP12	RP13	RP14	RP15	RP16
Sex (M, male; F, female)	M†	F†	M†	M†	M†	M	M	F	M	M	M	M	M	M
Age of onset (years)	78.6	93.1	81.1	68.7	71.3	84.2	72.8	43.2	78.5	70.3	66.3	59.9	73.5	66.6
UBA1 variants p.Met41 by Sanger sequencing	c.121A>C: p.Met41Leu	–	c.121A>G: p.Met41Val	c.121A>G/p.Met41Val	c.122T>C: p.Met41Thr	–	–	–	c.121A>C: p.Met41Leu	NA	c.122T>C: p.Met41Thr	–	c.122T>C: p.Met41Thr	c.121A>C: p.Met41Leu
Clinical findings														
Fever	+	–	–	+	+	+	–	+	–	–	+	–	+	+
Skin involvement	+	–	–	+	+	–	–	–	+	+	+	–	+	+
Chondritis*	A*, N, R	N, R*	A, R*	A*, R**	A*, R**	A*	A*	N*, R	A*	A, N	A, N	A*, R	A*	A*
Polyarthritis	–	–	–	+	–	–	+	–	+	–	–	–	+	–
Ocular inflammation	–	–	–	+	–	–	+	–	–	+	+	+	–	+
Audio-vestibular damage	–	–	–	–	–	–	–	–	–	–	+	–	–	–
Macrocytic anemia	+	–	–	+	+	+	–	–	+	+	+	–	+	+
Bone marrow vacuoles	+	NA	NA	+	+	–	NA	NA	+	+	NA	NA	+	+
Others	MDS	–	–	MDS, IP, endocarditis	MDS, DVT, Sweet's syndrome	–	–	–	MDS	MDS	Peritonitis, pericarditis, meningitis	–	–	Arteritis, MDS, DVT
Anti-type II collagen antibody	+	NA	–	–	NA	–	–	+	+	NA	–	+	+	NA
Treatment	PSL	PSL, colchicine	PSL, AZP, colchicine	PSL, MTX, CyA	PSL, AZP, MTX, MZB, ETN	PSL	PSL, IVIg, MTX, IFX, colchicine	PSL, MTX,TAC, TCZ	PSL, AZP, CyA	PSL	PSL, TCZ, colchicine	PSL, POCY	PSL, TCZ	PSL, AZP, TCZ, colchicine

*Chondritis: A, auricular; N, nasal; R, respiratory tract. AZP, azathioprine; CyA, cyclosporine; DVT, deep vein thrombosis; ETN, etanercept; IFX, infliximab; IP, interstitial pneumonia; IVIg, intravenous immunoglobulin; MDS, myelodysplastic syndrome; MTX, methotrexate; MZB, mizoribine; NA, not available; POCY, oral cyclophosphamide; PSL, prednisolone; TAC, tacrolimus; TCZ, tocilizumab; *, confirmed by biopsy; **, confirmed by autopsy; †, deceased.

Disclosure: N. Tsuchida, None; **Y. Kunishita**, None; **Y. Uchiyama**, None; **Y. Kirino**, Chugai, 5, Ono, 5; **K. Takase-Minegishi**, None; **R. Yoshimi**, None; **H. Nakajima**, None; **N. Matsumoto**, None.

Abstract Number: 1105

Discovering Variants in Suspected Monogenic Systemic Inflammatory Disease: An Adult Case Series

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Monogenic systemic inflammatory diseases (MSID) are a heterogeneous group of rare conditions caused by single gene variants leading to immune dysregulation. Diagnostic yield of targeted gene panels in these patients is limited. Whole exome sequencing (WES) has been used in pediatric populations to identify a growing number of genes implicated in MSID. Such approaches to studying MSID in adults are rare in the literature. Here, we have clinically and genetically characterized a case series of adult patients with suspected MSID.

Methods: Our study included 14 adults with suspected MSID and non-diagnostic gene panels, assessed at St Michael's Hospital, Toronto. We excluded patients with inflammation due to non-genetic causes.

Clinical and laboratory data were extracted and entered into a database. Targeted gene (n=31) panel testing on an exome backbone was performed at Genome Diagnostics, SickKids, using paired end sequencing on Illumina HiSeq 2500 platform to an average depth of ~120X following enrichment with the Agilent Clinical Research Exome V1 kit. After obtaining consent, sequence data was analyzed in a research setting using BWA aligner followed by variant calling with GATK, SAMtools, FreeBayes, and Platypus. Annotation was performed using SnpEff, Vcfanno, and custom scripts. Variants were filtered and prioritized using minor allele frequency < 0.01 in gnomAD, in silico prediction tools (CADD, SIFT, Polyphen, Vest3, Revel), conservation, segregation where parental data was available, and associations with known disorders or immunological pathways.

A *definitive* molecular diagnosis was provided if a likely pathogenic or pathogenic variant (as classified by the 2015 American College of Medical Geneticists criteria) was identified in a patient with a fully compatible phenotype. A *probable* diagnosis was defined as a variant of uncertain significance (VUS) in a gene associated with a condition identified in a patient with a compatible phenotype. A *possible* diagnosis was defined as a VUS in a gene involved in immune processes, but without a known associated condition.

Results: The majority of patients were male (64%) and European (57%). Age at study enrollment was between 22-52 years, with 36% having symptom onset before the age of 18. 42% had a family history of an immune-mediated disorder. WES provided one *definite* diagnosis (Aicardi Goutières Syndrome Type I; *TREX1* homozygous deletions) and one *probable* diagnosis (Proteasome Associated Autoinflammatory Syndrome; digenic missense variants in *PSMB4*/*PSMB8*). *Possible* diagnoses were found in eight (57%) patients (VUS's in *STYK1, FAIM3, ARHGAP26, FGD2, IKBKAP, BLK, ASAP1, RRTOR, LILRA6, RNF21)*.

Conclusion: In a series of adults with suspected MSID, exome analysis identified variants leading to a probable or definite diagnosis in 14%, and possible diagnoses in 57% of patients. Our work shows that exome sequencing identifies potential genetic causes of systemic inflammatory disease in patients with negative gene panels. Future studies would include family-based analyses and functional validation of candidate variants. Larger multicenter studies will further define the role of WES in this population.

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Abstract Number: 1106

Phenotypes and Genotypes of NLRP3-AID in Chinese Adult Patients

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: NLRP3-associated autoinflammatory disease (NLRP3-AID, OMIM 606416), previously called cryopyrin-associated periodic syndrome (CAPS), is a spectrum of autosomal dominant inherited diseases associated with NLRP3 gene mutations, leading to the overactivation of NLRP3 inflammasome and the excessive release of interleukin (IL)-1β. NLRP3-AID encompasses three conditions of of increasing severity: familial cold-induced autoinflammatory syndrome (FCAS), Muckle-Wells syndrome (MWS), and chronic infantile neurological cutaneous articular syndrome (CINCA). We aim to report a cohort of Chinese adult NLRP3-AID patients.

Methods: This single-center study included fifteen adult patients diagnosed with NLRP3-AID at Department of Rheumatology, Peking Union Medical College Hospital between July 2015 to September 2020. Demographic informa-

Table 1. Demographic and clinical features of Chinese patients with NLRP3-AID

Patient	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Gender	M	M	M	F	M	F	F	F	M	F	M	F	M	M	M
Age at onset (years)	46	2	2	46	7	37	1	0	10	2	6	6	2	15	40
Age at diagnosis (years)	47	23	31	46	27	42	21	20	22	39	32	45	20	32	52
Diagnostic delay (years)	1	21	29	0	20	5	20	20	12	37	26	39	18	17	12
Family history	-	-	-	-	-	-	+	+	-	+	+	+	-	-	-
NLRP3 variants	Q705K	V72M	T348M	K131R	M116I	P38S	V444I	D303G	T348M	T348M	G328E	A439V	K831T	L632F	V198M
Clinical features															
Fever	+	+	+	+	+	+	+	+	+	+	+	+	+	-	+
Rash	+	+	+	-	-	-	+	+	+	+	+	+	-	+	+
Arthralgia/arthritis	+	+	+	-	+	-	+	+	+	+	+	+	-	+	+
Chest pain	+	-	-	-	+	-	-	-	-	-	-	-	-	-	-
Abdominal pain/ diarrhea	+	-	-	-	+	+	+	-	-	-	-	-	-	-	-
Myalgia	+	+	-	+	+	-	+	-	+	-	+	+	+	-	+
Oral ulcers	-	+	-	-	-	+	+	-	-	-	-	+	+	+	-
Sore throat	-	+	-	-	+	-	-	-	-	-	-	-	+	-	-
Lymphadenopathy	-	-	+	+	-	-	-	-	-	+	-	-	+	-	-
Eyes involvement	-	+	+	-	-	-	-	+	+	+	+	+	-	-	-
Hearing loss	-	-	+	-	+	-	-	+	+	+	+	+	+	+	-
CNS involvement	-	-	+	-	-	-	-	+	+	+	+	+	+	-	-
Treatment															
DMARDs	+	-	-	-	-	-	+	-	-	+	-	-	-	-	+
Glucocorticoids	+	+	+	+	-	-	+	-	-	+	-	-	-	-	+
TNF-α inhibitors	-	-	+	-	+	+	-	+	+	-	-	-	+	+	-

M: male; F: female; DMARDs: diseases modifying antirheumatic drugs.

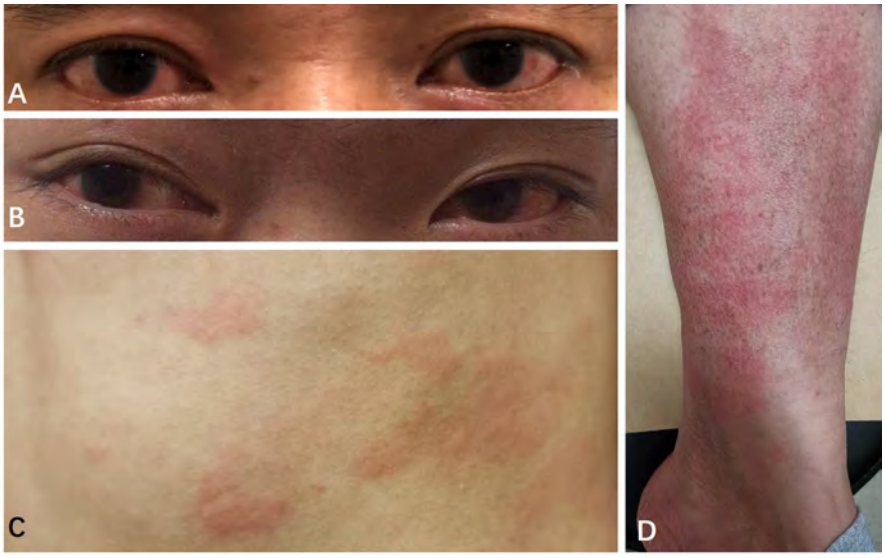

Figure 1. A.&B. Ocular inflammatory manifestations in Patient 9 and Patient 11; C. Erythematous rashes on the trunk of patient 5; D. Papules on the right lower limb of Patient 10.

tion and detailed clinical records were carefully documented and studied. Whole-exome sequencing using next-generation sequencing was performed in each patient.

Results: These 15 patients were all diagnosed as MWS. Of them, the gender ratio of male to female was 3:2. All patients were of Chinese Han ethnicity. The median age of disease onset was 16 (0-46) years old, and adult-onset was observed in 4 patients (26.7%). The median time of diagnosis delay was 20 (0–39) years. 5 patients (33.3%) had positive family history of similar symptoms. The most common clinical manifestations were fever (93.3%), arthritis (80.0%), rash (73.3%), myalgia (66.7%), hearing loss (60.0%) and central nervous system involvement (53.3%). No patient developed renal amyloidosis. Acute phase reactants (CRP 80.3 ±51.0 mg/L and ESR 52 ± 28 mm/h) elevated during flares in all patients and normalized during intervals. Rarely, a 38-year-old female patient presented with positive ANA and antiphospholipid antibodies, which were negative in the other patients. Heterozygous NLRP3 variants confirmed in these patients were T348M (n=3), Q703K, V70M, K131R, M116I, P38S, V444I, D303G, G328E, A439V, K831T, L632F and V198M (n=1, separately). Patients with T348M mutation showed more severe organ damage, including the eyes and the central nervous system. Glucocorticoids were given to 7 patients with partial symptom relief in 6 patients (71.4%). Due to the unavailability of IL-1 inhibitors in China, TNF-α inhibitors (etanercept and adalimumab) were used in 7 patients with effective responses (100%).

Conclusion: We reported a large case series of Chinese adult NLRP3-AID patients. The distinct symptoms of NLRP3-AID patients suggest the heterogeneity of disease. K131R, M116I, P38S, V444 and K831T are identified as novel NLRP3 mutations. These data expanding the clinical phenotype and genotype profile of NLRP3-AID.

Disclosure: N. Wu, None; **D. Wu**, None; **J. Miao**, None; **M. Zhao**, None; **M. Shen**, None.

Abstract Number: 1107

Clinical and Genetic Features of Chinese Adult Patients with Chronic Non-bacterial Osteomyelitis: A Single Center Report

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

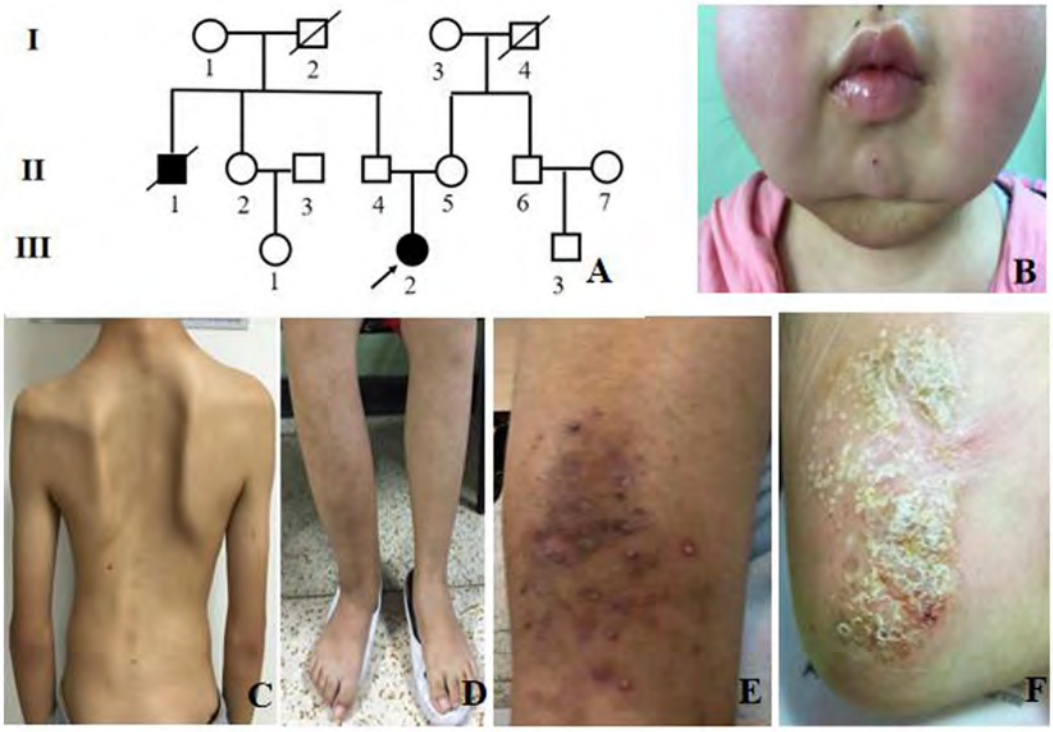

Figure 1. Clinical presentation of CNO patients. A. Pedigree of patient 6. The arrow indicates the proband. Black symbols indicate affected individuals; B. Bilateral mandible involvement; C. Spinal deformity; D. Right tibiofibular deformity; E. Psoriatic rash; F. Plantar pustules.

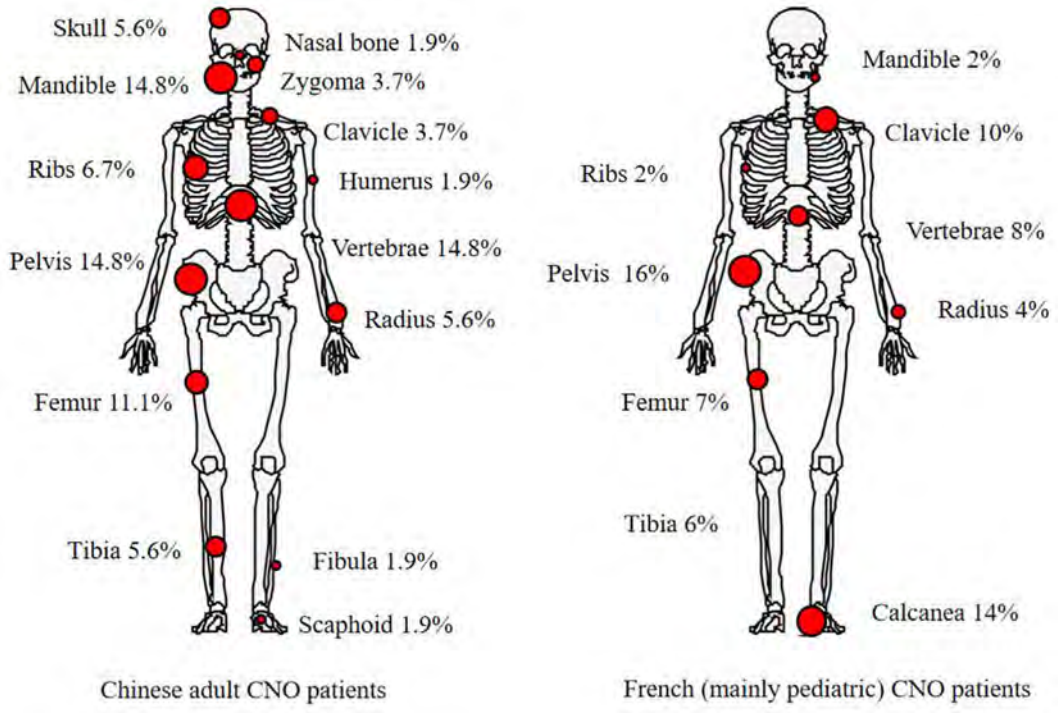

Figure 2. Skeletal involvements of CNO in adult patients compared to those in pediatrics.

Background/Purpose: Chronic non-bacterial osteomyelitis (CNO) is a rare polygenic autoinflammatory bone disease. CNO has been seldom reported in the Chinese population. We aimed to characterize the clinical manifestations and gene variants of Chinese adult patients with CNO.

Characteristics	Our study (n=10)		French cohort[1](n= 178)	
M: F	1: 1		55: 123	
Adult-onset, n (%)	6 (60)		NA	
Age at onset (years)	21 ± 17		10 ± 3	
Diagnosis delay (months, median)	92 ± 78		17 ± 24	
Family history, n (%)	1 (10)		51 (32)	
Bone lesion, n (%)	n=54		n=456	
Skull	3 (5.6)		NA	
Nasal bone	1 (1.9)		NA	
Zygoma	2 (3.7)		NA	
Mandible	8 (14.8)		9 (2)	
Clavicle	2 (3.7)		46 (10)	
Ribs	7 (13)		9 (2)	
Humerus	1 (1.9)		5 (1)	
Radius	3 (5.6)		18 (4)	
Vertebrae	8 (14.8)		36 (8)	
Pelvis	8 (14.8)		73 (16)	
Femur	6 (11.1)		32 (7)	
Tibia	3 (5.6)		27 (6)	
Fibula	1 (1.9)		NA	
Calcanea	0		64 (14)	
Accompanied symptoms, n (%)				
Palmoplantar pustulosis	2 (20)		14 (8)	
IBD	0		6 (3)	
Arthritis	6 (60)		20 (11)	
Elevated ESR, %	90		86	
Elevated CRP, %	90		51	
Elevated ANA, %	10		12	
Positive HLA-B27, %	0		7	
Treatments, n (%)	Use	Response	Use	Response
NSAIDs	7 (70)	4 (57)	193 (97)	126 (73)
Glucocorticoids	3 (30)	2 (67)	14 (8)	NA
DMARDs	7 (70)	5 (71)	35 (20)	10 (10/25, 40)
Bisphosphonate	8 (80)	5 (63)	17 (10)	6 (6/8, 75)
TNFα inhibitors	7 (70)	7 (100)	13 (7)	8 (8/9, 89)

§ : n=159; NA: not available; IBD: Inflammatory bowel disease; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein; ANA: antinuclear antibodies; HLA: human leukocyte antigen; NSAIDs: non-steroid anti-inflammatory drugs; DMARDs: disease-modifying anti-rheumatic drugs; TNF: tumor necrosis factor;

Figure 3. Comparison of clinical features of CNO patients in the Chinese and French cohorts.

Methods: Ten adult patients (≥16 years) were diagnosed and followed up during April 2015 to February 2021, at the Department of Rheumatology, Peking Union Medical College Hospital. Clinical and genetic features of these patients were evaluated and compared with those from the French cohort.

Results: The median age of disease onset was 19 (6-64) years old, and adult-onset was observed in 6 (60%) patients. The mean time of diagnosis delay was 92±78 months. The common symptoms were bone pain (10, 100%), fever (9, 90%), and arthritis (6, 60%). Five patients (50%) had mucocutoneous disorders, manifested as palmoplantar pustulosis, psoriasis, eczema, and apthous stomatitis. In total, there were 54 skeletal lesions, and each patient had no less than 2 lesions. The most frequently affected sites included lower limbs (20.5%), mandible, vertebrae and pelvis (17.5%, separately), followed by ribs (13%), skull, and radius (5.6%, respectively). In contrast, in the French cohort which mainly consisted of pediatric CNO patients, lower limbs and pelvis were the most commonly involved sites. Variants of 3 genes were detected in our study including *COL1A1*, *PSTPIP1* and *LRP5*. A combination therapy containing tumor necrosis factor (TNF) α inhibitors was proved to be effective.

Conclusion: This is the first and largest case series of CNO in Chinese adult patients. CNO should be considered in the differential diagnosis of adult patients with long disease course and recurrent multifocal osteomyelitis of unknown cause. Pathological and etiological examination through bone biopsy is critically helpful. A combination therapy containing TNFα inhibitors is recommended.

Disclosure: M. Zhao, None; **M. Shen**, None; **D. Wu**, None; **K. Yu**, None.

Abstract Number: 1108

More Frequent, Earlier Hip Involvement and Poor Outcome in Spondyloarthritis Associated with Familial Mediterranean Fever

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SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Familial Mediterranean Fever (FMF), an autoinflammatory disease, is characterized by self-limited inflammatory attacks. A significant proportion of patients with FMF experience episodes of acute monoarthritis, however 5 % of patients have chronic arthritis, usually of hips or knees. In this study we aimed to evaluate clinical and laboratory characteristics, genotype/phenotype correlation, outcome and biological DMARD responses in patients with FMF-associated SpA (FMF/SpA) who followed up in our tertiary referral clinic.

Methods: One hundred and twenty-four patients with FMF who fulfilled Tel Hashomer criteria and coexisting SpA were evaluated. After exclusion of 13 patients with missing data, 111 patients included into the analysis. Diagnosis of SpA was made by ASAS and/or modified New York criteria (mNYC). Axial radiographic changes were evaluated and scored according to Bath Ankylosing Spondylitis Radiology Index (BASRI) in plain radiography.

Table 1: Comparison of clinical and laboratory findings of patients between FMF/SpA and SpA control group

Clinical and laboratory variables	FMF/ SpA group (n=111)	Control group (n=216)	p value
Age (years) (mean±SD) (IQR)	43.5±12.3 (18)	43.3±10.6 (17)	0.9
Sex (n, %)			
Male	52 (46.8)	104 (48.1)	0.8
Female	59 (53.2)	112 (51.9)	
Duration of SpA (years) (mean±SD) (IQR)	15.5±9.95 (12.75)	14.9±9.2 (12)	0.6
Age onset of SpA (years) (mean±SD) (IQR)	24.8±10.8 (15)	28.5±8.3 (10)	***0.003 ****
Peripheral arthritis (n, %)	82/107 (76.6)	99/212 (46.7)	***<0.001 (OR:25.96)***
HLA-B27 positivity (n, %)	6/21 (28.6)	105/139 (75.5)	***<0.001 (OR:18.9)***
CRP (mg/dL) (median±SD) (IQR)'	22.2±24.4 (34.7)	8±28.8 (22.5)	***0.003****
ESR (mm/hour) (median±SD) (IQR)'	32±26.3 (32)	32±28.2 (41)	0.8*
Hip involvement (n, %)	60/107 (56.1)	34/189 (18)	***<0.001 (OR:45.7)***
TJR (n, %)	24/103 (23.3)	13/205 (6.3)	***<0.001 (OR:18.7)***
Fulfilling mNYC *(n, %)*	59/90 (65.6)	166 (76.5)	***0.001 (OR:10.9)***
BASRI scores			
BASRI-Hip (median±SD)	2±1.4 (3)	2±1.4 (2.25)	***0.01****
BASRI-Spine (median±SD)	6±2.3 (4)	8±3 (4)	***0.02****
BASRI-total (mean±SD)	8.1±3.2 (5)	8.9±3.8 (6)	0.2
b-DMARD usage (n, %)	69 (62.2)	68 (31.3)	***<0.001 (OR:27.3)***
Anti-TNF usage (n, %)	53 (47.7)	68 (31.3)	***0.005 (OR:7.8)***
Amyloidosis (n, %)	18 (16.2)	5 (2.3)	***<0.001 (OR:20.4)***

Results: One hundred and eleven patients whom 53.2% were female included into the analysis. Mean follow-up time and patient age were 93.6±76.9 (3-324) months, 43.5±12.3 (20-87) years, respectively. Clinical and laboratory characteristics of study participants were summarized in table 1. SpA subtypes were; axial in 23.4%, axial and peripheral in 62.6% and only peripheral in 14% in FMF/SpA group. 56.1% (80.7% bilaterally) of patients had hip involvement, 34.7% knee and 27.7% ankle arthritis. Overall, 23.3% underwent total joint replacement (TJR) in patients with FMF/SpA. Hip involvement and need for TJR were higher in FMF/SpA group compared to control group (table 1).

Table 2: Comparison of clinical and laboratory findings in patients with FMF/SpA according to MEFV gene status

Clinical and laboratory variables	Two copy of MEFV variant (n=56)	One copy of MEFV variant (n=15)	p value	M694V homozygous (n=35)	Others (n=44)	p value
Age (years) (mean±SD) (IQR)	44.6±15.4 (23)	43.3±18.3 (34)	0.8	45.4±13 (21)	41.2±16 (16)	0.8
Sex (n, %) *Male* *Female*	28 (53.2) 28 (46.8)	4 (26.7) 11 (73.3)	0.1	17 (47.2) 19 (44.2)	19 (52.8) 24 (55.8)	0.8
Age onset of FMF (years) (median±SD) (IQR)	11.7±8.5 (9)	13.2±9.4 (16)	0.7*	8.9±6.8 (7)	14.8±8.7 (10)	***0.002****
Age onset of SpA (years) (mean±SD) (IQR)	25.7±12.5 (13)	26.8±8.7 (16)	0.8	25.9±10.8 (17)	24.9±11.8 (14)	0.9
Peripheral arthritis (n, %)	46 (85.2)	8 (61.5)	0.053	29 (82.9)	31 (77.5)	0.6
HLA-B27 positivity (n, %)	5 (33.3)	0	0.5	2 (22.2)	3 (33.3)	0.6
CRP (mg/dL) (median±SD) (IQR)[ı]	28±27.4 (43)	17.9±22.6 (41.1)	0.2*	26.5±26.3 (37.3)	19.6±27.1 (50.8)	0.3*
ESR (mm/hour) (median±SD) [ı] (IQR)	38±28.5 (41)	41±23.3 (42)	0.4*	37.5±26.5 (44)	31±28.9 (33)	0.3*
Hip involvement (n, %)	37 (68.5)	2 (15.4)	***<0.001 (OR:12.2)***	25 (71.4)	18 (45)	***0.02 (OR:5.3)***
TJR (n, %)	15 (27.8)	1 (7.7)	0.1	14 (40)	2 (5)	***<0.001 (OR:13.6)***
Fulfilling mNYC *(n, %)*	36 (73.5)	7 (63.6)	0.5	22 (68.8)	25 (69.4)	0.95
BASRI scores *BASRI-Hip (median±SD) (IQR)* *BASRI-Spine (median±SD)(IQR)* *BASRI-total (mean±SD) (IQR)*	3±1.3 (2) 7±2.2 (3.75) 8.8±2.9 (4)	1.5±1.3 (2) 6±2.8 (4.5) 7.3±4.1 (5.75)	***0.01**** 0.3* 0.2	3±1.1 (2) 7±2.1 (3) 9.2±2.8 (10)	1.5±1.3 (2) 5±2.5 (3.75) 7.4±3.3 (4.75)	***<0.001**** 0.15* ***0.035***
b-DMARD usage (n, %)	42 (75)	8 (53.3)	0.1	29 (80.6)	24 (55.8)	***0.02 (OR:5.4)***
Anti-TNF usage (n, %)	29 (51.8)	7 (46.7)	0.7	21 (58.3)	17 (39.5)	0.096
Anti-IL-1 usage (n, %)	22 (39.3)	2 (13.3)	0.06	15 (41.7)	10 (23.3)	0.08
Amyloidosis (n, %)	14 (25.5)	2 (13.3)	0.3	12 (33.3)	4 (9.5)	***0.009 (OR:6.7)***

While 79 results were available, most frequent MEFV variant was M694V homozygote (44.3%). Hip involvement was higher in patients who had two MEFV variants compared to one copy and M694V homozygous compared to others. Need for TJR was higher in M694V homozygous compared to other MEFV variants. Radiographic sacroiliitis was lower in patients with FMF/SpA compared to control group but similar both in patients who had two MEFV variants compared to one copy and M694V homozygous compared to other MEFV variants. HLA-B27 positivity was lower in patients with FMF/SpA compared to control group (table 2)

Table 3: Comparison of clinical and laboratory features of patients with switchers and no switchers

Variables	Switch		
	Yes	No	p value
Age (mean±SD) (IQR)	48.3±9.1 (13)	43.5±12 (18)	0.2
BASRI score (mean±SD) (IQR)			
Hip score	3±0.7 (1)	2.5±1.5 (3)	0.6*
Spine	5±2.5 (4.5)	6±2.4 (4)	0.3*
Total	8±2.6 (4.5)	8.2±3.6 (6.5)	0.9
Onset age of FMF (mean±SD) (IQR)	11.5±10.1 (5)	14.2±10 (14)	0.5*
Diagnosis age of SpA (mean±SD) (IQR)	33.9±14.7 (22)	29.1±10.5 (14)	0.3
CRP (mg/L) (mean±SD) (IQR)	41.8±25 (38)	28.8±26.3 (33.4)	0.3
Sex (n, %)			
Female (n=33)	8 (24.2)	25 (75.8)	0.07
Male (n=36)	3 (8.3)	33 (91.7)	
Amyloidosis (n, %)			
Yes (n=17)	5 (29.4)	12 (70.6)	0.08
No (n=52)	6 (11.5)	46 (88.5)	
Hip involvement (n, %)			
Yes (n=44)	11 (25)	33 (75)	***0.01 (OR:6.6)***
No (n=22)	0	22 (100)	
Peripheral arthritis (n, %)			
Yes (n=58)	11 (19)	47 (81)	0.2
No (n=8)	0	8 (100)	

Average BASRI hip scores were higher in patients with FMF/SpA compared to SpA only (p=0.01) and also higher both had two MEFV variants compared to one copy (p=0.01) and M694V homozygous compared to other MEFV variants (p< 0.001). Average BASRI-spine scores were higher in patients with SpA compared to FMF/SpA group (p=0.02); but did not differ among various MEFV variants. Average BASRI-total scores did not differ in patients with FMF/SpA and control group and only higher in patients had M694V homozygous compared to other MEFV variants (p=0.035) (table 2).

Conclusion: In our study, hip involvement and need for TJR were associated with MEFV carriage rather than HLA-B27 positivity and higher in patients with FMF/SpA compared to the patients with SpA alone. Our study indicates that the patients with FMF/SpA had more severe disease course including worse outcome and destructive hip involvement than those with SpA alone, especially in patients carrying two copy MEFV variants and M694V homozygous.

SD: standard deviation, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, OR: Odds ratio, TJR: Total joint replacement, mNYC: modifyed New York criteria, b-DMARD: Biological disease modifying antirheumatic drugs Ɨ during the attack free period *Mann Whitney U test

SD: standard deviation, IQR: Interquartile range, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate, OR: Odds ratio, TJR: Total joint replacement, mNYC: modifyed New York criteria, b-DMARD: Biological disease modifying antirheumatic drugs ǂ during the attack free period *Mann Whitney U test

*Mann Whitney U test ǂ According to modified New York Criteria SD: standard deviation, FMF: Familial Mediterranean Fever, SpA: Spondyloarthritis, IQR: Interquartile range, CRP: C reactive protein, OR: Odds ratio, TJR: Total joint replacement, ESRD: End stage renal disease

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Abstract Number: 1109

Comparison of Diagnostic Criteria in Behçet's Disease and Sensitivity in Diagnosing Severe Manifestations

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SESSION INFORMATION

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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

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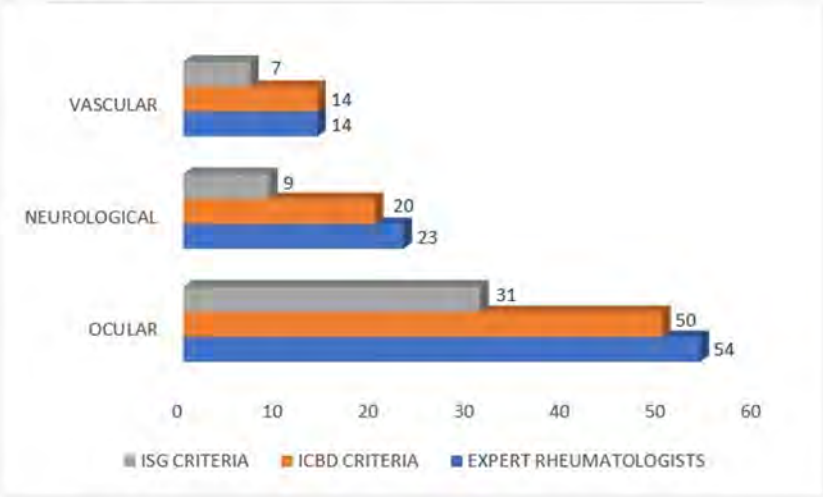
Table: Main clinical features according to different diagnostic criteria. Patients characteristics, data are in n (%)

	Expert rheumatologists (N=120)	ISG criteria (N=59)	ICBD criteria (N=96)
Age, mean years / (SD)	38 (13.8)	35.6 (13)	37 (13)
Gender, men/women, N (%)	62/58 (52.1/47.9)	29/30 (49.1/50.8)	48/48 (50/50)
Oral aphthosis, N (%)	113 (94.2)	59 (100)	94 (97.9)
Genital aphthosis, N (%)	71 (78.5)	46 (78)	71 (74)
Skin manifestations N (%)	76 (63.3)	52 (88.1)	64 (71.6)
Ocular lesions, N (%)	54 (45)	31 (52.5)	50 (52.1)
Joint manifestations, N (%)	78 (65)	38 (64.4)	62 (64.6)
Neurological manifestations, N (%)	23 (19.2)	9 (15.2)	20 (21.1)
Vascular manifestations, N (%)	14 (11.6)	7 (11.9)	14 (14.6)
Gastrointestinal features, N (%)	8 (6.6)	3 (5.1)	5 (5.3)

Figure: Number of patients with vascular, neurological or ocular manifestations diagnosed with BD by different criteria.



Abbreviations: ITRC-ICBD: International Team for the Revision of the International Criteria for BD; **ISG:** International Study Group for Behçet Disease.

Background/Purpose: Behçet disease (BD) is characterized by painful recurrent oral aphthosis genital ulcers and skin lesions. Nevertheless, the major causes of morbidity result from ocular, vascular and neurological involvement. Diagnosis of BD is usually performed according to the International Study Group (ISG*) (Lancet 1990; 335:1078-80).* Recently, criteria proposed by the International Team for the Revision of the International Criteria for BD (ITR-ICBD) have demonstrated a higher sensitivity *(J Eur Acad Dermatology Venereol 2014;28:338-47)*.

The aim of the present study was to assess **a)** the concordance and differences between ISG and ICDB criteria **b)** sensitivity in diagnosing severe manifestations (ocular, vascular and neurological).

Methods: The study included 120 patients diagnosed with definitive or possible BD by expert rheumatologists. They were diagnosed at a well-defined population in Northern Spain between January 1980 and December 2019. The ISG and ICBD diagnostic criteria for BD were applied to all patients and compared among them.

Results: 120 patients (62 men/ 58 women) were studied. Mean age at diagnosis was 37.6±13.8 years. 59 (49.2%) patients fulfilled ISG criteria and 96 (80%) ICBD criteria. Concordance between both criteria was moderate (Kappa 0.41). ICBD criteria diagnosed more patients with neurological (χ^2=49.1, p< 0.01), vascular (χ^2= 56.7, p< 0.01) and ocular manifestations (χ^2=84.4 p< 0.01) **(Figure)**.

Conclusion: ICBD criteria are more likely to diagnose BD and classify more patients with severe manifestations of the disease.

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Abstract Number: 1110

Cryopyrin-associated Periodic Syndromes: GOSH and National Amyloidosis Centre Experience

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Background/Purpose: CAPS is a rare, heterogenous inflammasomopathy associated with gain-of-function mutations in *NLRP3* that encodes cryopyrin. Mutations in NLRP3 result in excessive IL-1ß production that may underlie wide range of symptoms. IL-1 blockade demonstrated complete responses to treatment which has been life-changing in this monogenic inflammasomopathy.

Methods: Patients followed-up in GOSH and NAC specialist CAPS clinics from 2005 to 2021 were identified. Data on following parameters collected: disease subtype, presenting symptoms, CAPS disease activity scores, serum amyloid A (SAA) and CRP levels, MRI brain; and treatment. Descriptive statistical analysis was performed by GraphPad Prism version 9.1.1.

Results: A total of 48 patients [female (n=20, 42 %), male (n=28, 58 %)] with CAPS diagnosis in childhood/adolescence were identified. Median age at disease presentation was 3.50 years (range: 0.20 – 16.23). Disease subtypes were: CINCA (n=4), MWS (n=37), FCAS (n=6), CAPS-like disease (n=1). Two of 6 patients with FCAS harboured *NLRP3* variants of unknown significance (VUS) and were discharged since they ultimately proved asymptomatic after review. Clinical symptoms were recorded, and CAPS disease activity score was calculated in each clinic visit. There was a significant drop in the mean CAPS activity scores between first and last visits (8.66/20 (±2.59), 1.12/20 (±1.29), respectively). Median treatment duration was 5.83 years (range:0.17–15.83). Mutations could not be detected by sanger in 6/48 (12,5 %) patients, although clinical characteristics of CAPS were identified. Two/6 patients had NGS that showed no evidence of mosaicism. The commonest mutation was p.A439V in *NLRP3* gene (19/48), followed by p.V198M (3/48), p.T348M (3/48) and p.R488K (3/48) mutations. CRP and SAA levels were checked prior to treatment and at each clinic visit. 45 of 48 patients (94 %) were on anti-IL1 treatment: 42/45 (93 %) canakinumab, 27 of whom were switched from anakinra; and 3/45 (7 %) on anakinra. Two FCAS patients were discharged from clinic without any treatment, 1 patient with compound heterozygous *IRAK4* mutations in addition to *NLRP3* p.E457D was switched from canakinumab to tocilizumab, with complete clinical and serological response. Median CRP before and after treatment were 5.0 mg/L (range:1.0-83.0) and 5.0 mg/L (range:1.0–51.0). Median SAA before and after treatment were 8.5 mg/L (range:2.4–680.0) and 3.50 mg/L (range:2.0–222.0). Thirteen of 48 (27 %) patients underwent MRI brain due to neurological involvement, mainly due to recurrent headaches, with no abnormalities identified in 9/13 (70 %); whereas 4 patients (3 with CINCA) had changes on their MRI brain. None of the patients experienced deterioration neither in their clinical symptoms nor in their MRI brain scans after starting treatment with anti-IL1.

Conclusion: Anti-IL1 treatment has had a major impact in paediatric patients for the prevention and treatment of CAPS symptoms. Treatment efficacy was observed by improved CAPS clinical disease activity scores; and normalised inflammatory markers. In our cohort, neurological symptoms including sensorineural hearing loss have improved and MRI brain scans have remained stable with anti-IL1 therapies.

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Abstract Number: 1111

Transient Elastography (fibroscan); As a New Non-invasive Diagnostic Method for Detecting Hepatic Involvement of Amyloidosis

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Background/Purpose: Amyloidosis is characterized by accumulation of insoluble fibrils composed of different monomers in extracellular spaces of different organs, and demonstration of deposits by non-invasive methods is important especially for organs difficult to sample. Transient elastography (fibroscan) is a diagnostic method being used to measure liver stiffness (LS) in different chronic liver diseases. We herein aimed to test the place of fibroscan method for detecting increased LS associated with amyloid deposition in patients with amyloidosis.

Methods: Six categories of patients enrolled into this cross-sectional study; AA amyloidosis (AA-a), AL amyloidosis (AL-a), Familial Mediterranean Fever (FMF) patients without amyloidosis, cirrhotic chronic liver disease, non-cirrhotic chronic hepatitis B infection (CHB) and healthy controls (HC). LS assessment by fibroscan were categorized as normal for kPa< 7, significant stiffness for kPa≥7, advanced stiffness for kPa≥9.5 and kPa≥F4 stiffness. FIB-4 and APRI scores were calculated for each patient when they indicated chronic liver disease. Patients with known chronic liver disease and viral hepatitis excluded from amyloidosis and FMF groups.

Results: A total of 165 patients (AA-a, n=65; AL-a, n=15; FMF, n=20; cirrhotic patients, n=16; CHB, n=22; HC, n=27) constituted the study group. Clinical and laboratory features of patients are given in Table 1. Average age was higher in the AL-a group compared to others. Median LS was highest in cirrhotic patients, and it was also higher in AA-a and AL-a patients compared to FMF and HC. Median LS was numerically higher in AL-a compared to AA-a, but it did not reach statistical significance. Median LS was also higher in FMF patients compared to HC. FIB-4 and APRI scores were lower compared to cirrhotic patients in AA-a and AL-a. ALP levels were higher in AA-a and AL-a groups com-

pared to FMF, CHB and HC. FIB-4 and APRI scores, ALP and GGT levels were correlated with LS both in AA-a, AL-a and FMF-AA groups (Table 2). The scores of amyloid depositions were higher in non-FMF-AA-a patients compared to FMF-AA-a. In FMF-AA-a group, median LS, FIB-4 score, GGT, creatinine, cardiac septal wall thickness (CSWT) and frequency of advanced stiffness were higher in patients who had one exon 10 MEFV variant compared to those with two variants. Frequency of advanced and F4 stiffness, GIS involvement and CSWT were lower in M694V homozygous compared to other MEFV variants.

Higher patient age, age at diagnosis of amylodosis, FIB-4 and LS scores, ALP levels, non-FMF causes of AA were associated with hepatic AA amyloid involvement in biopsy-proven patients. A cut-off value 12.05 kPa of LS provided 100% sensitivity and 85.5% specificity (LR=6.9, AUC=0.901, 95% CI 0.81-0.99) for patients with AA-a.

Conclusion: In our single center cohort, we showed a higher median LS by fibroscan in both AL-a and AA-a patients compared to CHB, FMF and HC. Additionally, hepatic amyloid involvement and median LS was higher in non-FMF-AA-a compared to FMF-AA-a, and in FMF-AA-a patients with one exon 10 MEFV variant compared to those with two variants suggesting presence of amyloidogenic genetic factors additional to pathogenic MEFV variants.

p1: comparison of amyloidosis and FMF patients

p2: comparison of amyloidosis and cirrhosis

p3: comparison of amyloidosis and chronic liver disease

p4: comparison of amyloidosis and healthy control

p5: comparison of FMF and healthy control

p6: comparison of AA and AL amyloidosis

* Mann Whitney U test

Table 1: Comparison of liver stiffness and clinical and laboratory parameters between patients with amyloidosis and control groups

	Amyloidosis (n=65)	FMF patients (n=20)	AL myloidosis (n=15)	Cirrhosis (n=16)	Chronic Hepatitis B (non-cirrhotic) (n=22)	Healthy control (n=27)	p¹	p²	p³	p⁴	p⁵	p⁶
Age (years) [mean±SD (median; IQR)]	46.6±12.3 (46; 19)	43.4±11.7 (42.5; 13)	58.1±14.6 (58; 16)	49.8±9.8 (49; 15)	45.5±12 (45; 21)	44.5±16.4 (45; 23)	0.35	0.3	0.8	0.5	0.8	*0.003*
Gender (n, %)												
Male	38 (58.5)	10 (50)	6 (40)	10 (62.5)	13 (59.1)	17 (54.8)	0.5	0.8	0.95	0.7	0.7	0.2
Female	27 (41.5)	10 (50)	9 (60)	6 (37.5)	9 (40.9)	14 (45.2)						
Diabetes Mellitus (n, %)	5 (8.3)	2 (11.1)	2 (13.3)	3 (15)	2 (13.3)	3 (9.7)	0.7	0.6	0.4	0.8	0.9	0.6
Body Mass index (kg/m²) [mean±SD (median; IQR)]	26.1±2.3 (25.7; 1.4)	26.8±4.3 (25.6; 5.4)	25.2±2.4 (24.8; 3.6)	27±3.7 (26.7; 6.7)	26.9±3.9 (25.5; 7.1)	26±4.6 (25.9; 5.7)	0.9	0.4	0.95	0.7	0.7	0.3
Liver stiffness (kPa) [mean±SD (median; IQR)]	10.7±12.9 (6.5; 5.2)	7.04±2.7 (7.2; 4.6)	14.05±12.7 (9.8; 11.6)	28.1±12 (26.7; 21.6)	6.4±3.5 (5.3; 2.8)	4.8±1.4 (4.9; 1.6)	*<0.001**	*<0.001**	*0.028**	*<0.001**	*<0.001**	0.16
Significant stiffness (kPa>7)	31 (47.7)	11 (55)	8 (57.5)	16 (100)	4 (18.2)	2 (6.5)	0.4	*<0.001¹*	*0.012²*	*<0.001³*	*<0.001⁴*	0.6
Advanced stiffness (kPa>9.5)	17 (26.2)	4 (20)	7 (50)	16 (100)	3 (13.6)	0	0.4	*<0.001¹*	0.7	*0.001³*	*0.02⁴*	0.1
F4 stiffness (kPa>12.5)	10 (15.4)	0	5 (35.7)	16 (100)	2 (9.1)	0	0.057	*<0.001¹*	0.4	*0.016⁴*		0.1
FIB-4 score [mean±SD (median; IQR)]	1.4±1.8 (0.97; 0.88)	0.8±0.4 (0.76; 0.56)	1.46±0.75 (1.3; 0.95)	3.5±2.4 (2.5; 3.4)	1.02±0.6 (0.85; 0.8)	0.86±0.75 (0.7; 0.47)	*<0.001**	*<0.001**	0.4*	*0.005**	0.6	0.14
FIB-4 score (>1.45)	18 (27.7)	1 (5.3)	6 (40)	13 (86.7)	4 (20)	3 (11.1)	0.06¹	*<0.001¹*	0.4¹	0.07¹	0.5¹	0.3
FIB-4 score (>3.25)	3 (4.6)	0	0	6 (40)	0	1 (3.7)	0.5	*0.001¹*	0.4	0.7	0.6	
APRI score [mean±SD (median; IQR)]	0.4±0.35 (0.25; 0.17)	0.28±0.14 (0.26; 0.18)	0.8±0.5 (0.24; 0.24)	1.3±1.2 (0.77; 1.25)	0.24±0.11 (0.22; 0.2)	0.2±0.13 (0.16; 0.08)	*<0.001**	*<0.001**	0.3	*0.002**	*0.02**	0.4
Platelet levels (10^3 mcg/L) [mean±SD (median; IQR)]	232±83 (232; 105)	243±54 (234; 93)	209±89 (97-353)	126±56 (117; 77)	246±58 (236; 96)	271±70 (275; 86)	0.6	<0.001	0.5	*0.035*	0.15	0.3
ALT (U/L) [mean±SD (median; IQR)]	25.1±16.6 (19; 17)	36.4±23.2 (28.5; 36.3)	17.5±6.7 (15; 7)	48.3±34.5 (38; 66)	26.4±19.8 (16; 33.8)	22.2±16.2 (17; 12.5)	*0.01**	*0.008**	0.7	0.4	*0.02**	0.15
AST (U/L) [mean±SD (median; IQR)]	25.8±13.9 (20; 17)	24,8±12 (22.5; 17.5)	19.5±10 (8-48)	51.5±39.1 (36; 58)	22±7.9 (20; 13.8)	20±8.4 (18.5; 7.75)	*0.002**	*0,003**	0.5	0.058*	0.08*	0.08*
ALP (U/L) [mean±SD (median; IQR)]	117±61.3 (97; 65.3)	91.5±34.8 (79; 55)	130±81 (103; 54)	115.3±72.2 (79; 126)	78.6±27.8 (76; 38.5)	65.5±16.4 (67; 21.75)	*<0.001**	0.5	*0.002**	*<0.001**	*0.002**	0.7
GGT (U/L) [mean±SD (median; IQR)]	40±91.3 (18; 18)	30.4±30.5 (17; 25.8)	72±113 (24; 61)	41±36.7 (24; 51)	20.7±19 (16; 13.5)	19.1±15.4 (14; 14)	0.074*	0.2	0.2	0.065*	0.3	0.084*

Table 2: Correlation between liver stiffness and clinical and laboratory parameters

	AA amyloidosis		AL Amyloidosis		FMF-AA		Non-FMF-AA	
Variable	**r**	**p value**	**r**	**p value**	**r**	**p value**	**r**	**p value**
Age (years)	***0.354***	***0.004***	0.075	0.7	***0.374***	***0.006***	0.241	0.4
Body mass index (kg/m^2)	-0.046	0.8	-0.06	0.8	0.017	0.9	-0.213	0.5
FIB-4 score	***0.504***	***<0.001***	***0.536***	***0.048***	***0.584***	***<0.001***	0.105	0.7
APRI score	***0.485***	***<0.001***	***0.579***	***0.03***	***0.566***	***<0.001***	0.166	0.6
ALT (U/L)	0.143	0.26	0.09	0.8	0.124	0.4	0.231	0.45
AST (U/L)	***0.341***	***0.006***	***0.542***	***0.046***	***0.329***	***0.02***	0.395	0.2
ALP (U/L)	***0.437***	***<0.001***	***0.645***	***0.013***	***0.322***	***0.024***	***0.799***	***0.001***
GGT (U/L)	***0.506***	***<0.001***	***0.752***	***0.002***	***0.306***	***0.033***	***0.946***	***<0.001***
Onset age of clinical symptoms (years)	***0.303***	***0.043***	NA	NA	***0.313***	***0.049***	0.853	0.066
Duration of underlying disease (years)	0.028	0.85	-0.52	0.067	0.03	0.85	-0.099	0.85
Diagnosis age of amyloidosis (years)	***0.384***	***0.003***	0.17	0.56	***0.391***	***0.007***	0.392	0.2
Duration of amyloidosis (months)	-0.038	0.78	-0.47	0.088	0.062	0.68	-0.256	0.4
Baseline proteinuria (g/day)	-0.083	0.64	0.354	0.2	-0.112	0.6	0.585	0.1
Baseline creatinine (mg/dL)	0.077	0.66	0.27	0.35	0.078	0.7	-0.203	0.6
Current proteinuria (g/day)	-0.052	0.7	***0.655***	***0.02***	-0.055	0.7	0.1	0.8
Current creatinine (mg/dL)	-0.056	0.7	0.35	0.2	-0.086	0.55	-0.026	0.9
Current CRP (mg/L)	-0.068	0.6	0.2	0.5	-0.048	0.74	0.324	0.3
Mean colchicine dose (mg/day)	-0.038	0.8	-	-	0.068	0.64	-	-
Ejection fraction	0.056	0.7	-0.15	0.6	0.126	0.4	-0.241	0.43
Septal wall thickness (mm)	***0.319***	***0.012***	***0.383***	***0.2***	***0.314***	***0.03***	0.365	0.22
Left ventricular wall thickness (cm)	-0.178	0.17	0.184	0.5	0.194	0.2	-0.210	0.5
pro-BNP levels (pg/mL)*	0.226	0.53	0.434	0.072	0.286	0.5	0.268	0.5
Troponin levels (pg/mL)*	0.555	0.2	***0.740***	***0.001***	0.073	0.84	0.401	0.25
Platelet levels (10^3 mcg/L)	-0.141	0.26	-0.19	0.5	-0.192	0.17	-0.089	0.77

Ɨ Fischer's exact test

SD: Standard deviation, IQR: Interquartile range, FMF: Familial Mediterranean Fever, kPa: Kilopascal, FIB-4: Fibrosis-4 index, APRI: AST to platelet ratio index, ALT: Alanine aminotransferase, AST: aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gama glutamyl transferase

*After exclusion of patients had chronic renal failure SD: Standard deviation, IQR: Interquartile range, FMF: Familial Mediterranean Fever, CRP: C-reactive protein, FIB-4: Fibrosis-4 index, APRI: AST to platelet ratio index, ALT: Alanine aminotransferase, AST: Aspartate aminotransferase, ALP: Alkaline phosphatase, GGT: Gama glutamyl transferase

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Abstract Number: 1112

Transient Elastography (Fibroscan) as a Non-Invasive Method for Detecting Amyloid Deposition in Transplanted Kidneys in Patients with AA Amyloidosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Amyloidosis is characterized by accumulation of insoluble fibrils composed of different monomers in extracellular spaces of different organs, and demonstration of deposits by non-invasive methods is important especially for organs difficult to sample. Transient elastography (Fibroscan) is a diagnostic method of measuring liver stiffness (LS) being used in chronic liver diseases.

Table 1: Baseline clinical and laboratory characteristics of study participants

Variables	Amyloidosis (n=19)	Control group (n=16)	p value
Age (years) (median; IQR)	48 (22)	51 (11)	0.4
Gender, male (n, %)	13 (68.4)	11 (68.8)	1
Disease duration (months) (median; IQR)	206 (89)	145 (133)	***0.04***
Duration of renal transplantation (months) (median; IQR)	145 (137)	126 (77)	0.5
Donor age (years) (median; IQR)	46 (20)	56 (28)	0.3
Donor type, alive (n, %)	12 (92.3)	11 (68.8)	0.2
BMI (kg/m^2) (median; IQR)	24.9 (1.2)	28 (5.75)	0.4
DM (n, %)	0	5 (31.3)	***0.013 (OR:6.9)***
Kidney stiffness (kPa) (median; IQR)	15.8 (15.8)	19.8 (34)	0.46
Liver stiffness (kPa) (median; IQR)	5.45 (2.8)	6.1 (4.5)	0.9
Rejection (n, %)	3 (15.8)	5 (33.3)	0.4
Graft loss (n, %)	0	2 (13.3)	0.18
Creatinine (mg/dL)) (median; IQR)	1.4 (0.6)	1.95 (1.8)	***0.015***
CRP (mg/L) (median; IQR)	2.7 (4.4)	1.95 (10.3)	0.6
Proteinuria (g/day) (median; IQR)	3 (15.8)	12 (75)	***<0.001***
Proteinuria (n, %)	0.4 (1.2)	0.9 (2.4)	***0.001 (OR:12.4)***
Hematuria (n, %)	2 (10.5)	2 (12.5)	1

IQR: Interquartile range, BMI: Body mass index, DM: Diabetes mellitus, kPa: kilopascal

Table 2: Comparison of clinical and laboratory features between patients had amyloidosis recurrence and not

Variables	Total	Recurrence -	Recurrence +	p value
Age (years) (median; IQR)	48 (22)	47 (17)	50 (27)	1
Gender, male (n, %)	13 (68.4)	9 (69.2)	4 (66.7)	1
Duration of amyloidosis (months) (median; IQR)	206 (89)	220 (99)	163 (203)	0.08
Onset age of FMF (years) (median; IQR)	5.5 (2)	6 (2)	5 (6)	0.3
Duration of FMF (years) (median; IQR)	41 (20)	41 (14)	45 (24)	0.6
Diagnosis age of FMF (years) (median; IQR)	21 (20)	23.5 (21)	21 (11)	0.6
Diagnosis age of amyloidosis (years) (median; IQR)	28 (17)	27.5 (17)	28 (20)	1
Duration of renal transplantation (months) (median; IQR)	145 (137)	144 (110)	123 (50)	0.7
Donor age (years) (median; IQR)	46 (20)	46 (38)	46 (15)	0.8
Donor gender, male (n, %)	12 (92.3)	4 (30.8)	1 (16.7)	***0.037 (OR:6.6)***
Donor type, alive (n, %)	12 (92.3)	6 (85.7)	6 (100)	1
BMI (kg/m^2) (median; IQR)	24.9 (1.2)	25.3 (3.9)	24.7 (4.4)	0.3
DM (n, %)	0			
Kidney stiffness (kPa) (median; IQR)	15.8 (15.8)	10.9 (7.7)	29.3 (18.9)	***<0.001***
Liver stiffness (kPa) (median; IQR)	5.45 (2.8)	5.4 (2.7)	5.9 (8.9)	0.4
Rejection (n, %)	3 (15.8)	2 (15.4)	1 (16.7)	1
Creatinine (mg/dL) (median; IQR)	1.4 (0.6)	1.4 (0.7)	1.7 (0.5)	0.24
CRP (mg/L) (median; IQR)	2.7 (4.4)	1.3 (4.1)	3.5 (13.9)	0.3
Proteinuria (n, %)	3 (15.8)	1 (7.7)	2 (33.3)	0.2
Proteinuria (g/day) (median; IQR)	0.4 (1.2)			0.4
Hematuria (n, %)	2 (10.5)	1 (7.7)	1 (16.7)	0.6
Pro-BNP (pg/mL) (median; IQR)	769 (1135)	494 (1103)	NA	
Troponin (pg/mL) (median; IQR)	28 (61)	24.2 (28)	NA	
FIB-4 score (median; IQR)	1.04 (1)	1.04 (0.76)	0.87 (1.74)	0.9
<1.45	14 (73.7)	10 (76.9)	4 (66.7)	0.6
>1.45	5 (26.3)	3 (23.1)	2 (33.3)	
<3.25	18 (94.7)	13 (100)	5 (83.3)	0.3
>3.25	1 (5.3)	0	1 (16.7)	
APRI score (median; IQR)	0.24 (0.17)	0.24 (0.12)	0.2 (0.47)	0.9
Platelets (median; IQR)	272 (76)	272 (64.5)	250 (233)	0.9
ALT (U/L) (median; IQR)	20 (12)	20 (8)	23.5 (33)	0.7
AST (U/L) (median; IQR)	20 (13)	22 (12)	17.5 (24)	0.6
ALP (U/L) (median; IQR)	94.5 (49)	93 (38)	101 (116)	0.9
GGT (U/L) (median; IQR)	18 (13)	18 (11)	16.5 (75)	1
CRF at admission (n=15)	14 (93.3)	9 (90)	5 (100)	1
ESRD at admission (n=13)	5 (38.5)	3 (30)	2 (66.7)	0.5
Organ distribution (n, %)				
Liver	0			
GIS (n=17)	7 (41.2)	4 (33.3)	3 (60)	0.6
Heart (n=17)	6 (35.5)	4 (33.3)	2 (40)	0.8
Bone marrow	1 (5.9)			
Thyroid (n=17)	1 (5.9)			
B-DMARD (n, %)	16 (84.2)	10 (76.9)	6 (100)	0.5
Immunosuppressives (n, %)				
CNI	17 (89.5)	13 (100)	4 (66.7)	0.09
m-TOR inhibitors	2 (10.5)	0	2 (33.3)	

IQR: Interquartile range, FMF: Familial Mediterranean Fever, BMI: Body mass index, DM: Diabetes mellitus, kPa: kilopascal, CRF: Chronic renal failure, ESRD: End stage renal disease, GIS: Gastrointestinal system, b-DMARD: Biological disease modifying antirheumatic drug, CNI: Calcineurin inhibitors

We herein aimed to search potential of fibroscan detecting kidney stiffness (KS) associated with amyloid deposition in patients with AA who received kidney transplants.

Methods: Renal transplant recipients (RTR) because of AA amyloidosis-related kidney failure (amyloidosis group; AG) and RTR due to other underlying diseases (control group; CG) enrolled into this study. KS and LS were measured by the same physician blinded to diagnosis. The stiffness results were expressed in kilopascals (kPa). Local ethics committee approval and patient consents were obtained.

Results: Nineteen AG and 16 CG patients included into the study. Baseline clinical and laboratory characteristics of participants are summarized in Table 1. Patient age, gender, body mass index (BMI), donor type, donor gender and donor age, frequency of rejection history and graft loss did not show significant difference between two groups. Frequency of diabetes mellitus (DM), median creatinine and proteinuria, median LS scores were higher in AG group than CG. Although median KS was higher in CG group, the difference was not significant. Baseline clinical and laboratory features were similar in AG patients with recurrent-amyloidosis (n=6) and non-recurrent AG patients (n=13) (Table 2). Median KS score was higher in recurrent compared to non-recurrent AG patients ($p< 0.001$). However median LS did not differ between two groups ($p=0.4$). In multivariate analysis only KS was associated with renal recurrence of AA ($p=0.031$; OR=1.18, 95% CI 1.015-1.362). In ROC analysis, a cut-off value of 24.55 kPa provided 83.3% sensitivity and 92.3% specificity (LR=10.8, AUC=0.936, $p=0.003$). Median KS was higher in patients with a history of rejection both among the patients with AG and CG, but the difference was not significant. Additionally, LS scores were similar between two groups.

In FMF-associated AA, median KS was higher in patients with one MEFV variant compared to those with two variants and tended to be higher in other MEFV variants compared to M694V homozygotes ($p=0.027$ and $p=0.08$, respectively). There was no correlation between the patient age, disease duration, duration of renal transplantation, donor age, BMI, LS, creatinine, CRP, proteinuria, and KS both in patients with AG and CG.

Conclusion: Median KS scores were similar between AG and CG groups; however it was higher in AG patients with recurrent kidney amyloidosis than those without recurrent disease, which may support using the fibroscan method as a useful screening method for establishing AA recurrence. Additionally, higher KS scores in patients with one MEFV variant compared to those with two variants need further studies to be able to identify other yet unidentified amyloidogenic factors.

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Abstract Number: 1113

Validation of the 2019 American College of Rheumatology/European League Against Rheumatism Classification Criteria for IgG4-Related Disease in a Latin American Cohort

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The 2019 ACR/EULAR classification criteria (2019 AECC) for IgG4-related disease (IgG4-RD) have been validated in cohorts mainly composed of Caucasian and Asian patients. Its performance in Latin American patients is not known. We aimed to explore the performance of the 2019 AECC for IgG4-RD in a real-world cohort of Latin American patients.

Methods: We performed a retrospective multicenter study. Participating centers belonged to the Latin American Group for the study of IgG4-RD from Argentina, Chile, Mexico, Peru and Uruguay. Investigators were asked to submit information about patients and mimickers in a standardized fashion. IgG4-RD patients had to fulfill the Comprehensive Diagnostic Criteria for IgG4-RD and/or the Consensus Statement on Pathology. Mimickers were those diseases with overlapping features with IgG4-RD that were evaluated by the investigators. We retrospectively applied the 2019 AECC.

Results: We included 300 patients of which 153 (51%) were male. Mean age was 52 ± 15.3 years. One hundred and eighty (60%) had IgG4-RD and 120 (40%) a mimicker condition. The diagnoses of the mimickers are shown in Table 1.

Table 1. Mimickers

Table 1. Mimickers	
Mimicker conditions, n (%)	**N = 120**
Autoimmune hepatobiliary diseases	16 (13.3)
Sjögren's syndrome	14 (11.7)
Histiocytosis	13 (10.8)
ANCA-associated vasculitis	12 (10)
Idiopathic sclerosing conditions	12 (10)
Chronic pancreatitides	9 (7.5)
Solid malignancies	9 (7.5)
Lymphoma (Hodgkin and non-Hodgkin)	8 (6.7)
Systemic lupus erythematosus	5 (4.2)
Graves' orbitopathy	3 (2.5)
Sarcoidosis	2 (1.7)
Others*	17 (14.2)
Other mimickers: pachymeningitis secondary to systemic autoimmune diseases (2), lymphoid hyperplasia (1), membranoproliferative glomerulonephritis (1), carotid cavernous fistula (1), POEMS syndrome (1), hypereosinohilic syndrome (1), multiple myeloma (1), intersticial pneumonia with autoimmune features (1), organizing pneumonia (1), VEXAS syndrome (1), idiopathic dry eye (1), sclerosing angiomatoid nodular transformation of the spleen (1), immune check point inhibitor-induced hypophysitis and cholangitis (1), lymphocytic hypophysitis (1), lymphocytic dacryoadenitis (1), salivary gland benign tumor (1)	

After applying the 2019 AECC, 180 patients were classified as IgG4-RD (66.7%). Of the 60 false-negative cases (33.3%), 13 did not fulfill the entry criteria; of the remaining 47, 23 fulfilled one exclusion criteria; the remaining 24 did not achieve sufficient inclusion criteria scores.

Fourteen out of the 23 patients fulfilling exclusion criteria were positive for a disease-specific autoantibody, 6 of whom have overlapping autoimmune diseases (2 ANCA-associated vasculitis, 2 systemic sclerosis, 2 rheumatoid arthritis). The other 8 patients had no evidence of another autoimmune disease during follow-up; all of them had multiorgan involvement (median: 6 organs).

The true-positive cases had more involved organs and more frequently an available biopsy and were more likely to be of the Mikulicz/systemic and the proliferative phenotypes (Table 2).

Of the 120 mimickers, 20 (16.7%) did not fulfill the entry criteria, 71 (59.2%) fulfilled at least one exclusion criteria, and the remaining 29 (24.1%) did not achieved a score of 20, resulting in no mimickers fulfilling the 2019 AECC. Four mimickers achieved sufficient inclusion criteria scores (Rosai-Dorfman disease, systemic lupus erythematosus, sarcoidosis, and pancreatic cancer).

Table 2. Comparison of true-positive cases and false-negative cases

Table 2. Comparison of true-positive cases and false-negative cases			
	True positives (n=120)	**False negatives (n=60)**	**P**
Male, n (%)	69 (57.5)	32 (53.3)	0.59
Age at diagnosis, median (IQR), years	53.3 ± 14	50.6 ± 17.5	0.26
Mestizo, n (%)	98 (81.7)	54 (90)	0.14
Caucasian, n (%)	21 (17.5)	5 (8.3)	0.09
CSP, n (%)			
Highly suggestive, n (%)	52 (43.3)	19 (31.7)	0.13
Probable, n (%)	33 (27.5)	17 (28.3)	0.90
Insufficient, n (%)	20 (16.7)	11 (18.3)	0.78
CDC, n (%)			
Definitive, n (%)	53 (44.2)	18 (30)	0.06
Probable, n (%)	32 (26.7)	20 (33.3)	0.35
Possible, n (%)	35 (29.2)	22 (36.7)	0.30
Mono-organic, n (%)	16 (13.3)	18 (30)	0.007
2 involved organs, n (%)	22 (18.3)	15 (25)	0.29
≥ 3 involved organs, n (%)	82 (68.3)	27 (45)	0.003
Number of involved organs, median (IQR)	4 (2-6)	2 (1-4)	0.003
Pancreato-hepato-biliary, n (%)	25 (20.8)	10 (16.7)	0.50
Retroperitoneal/aortic, n (%)	9 (11.7)	7 (11.7)	0.35
Head and neck-limited, n (%)	40 (33.3)	23 (38.3)	0.50
Mikulicz/systemic, n (%)	38 (31.7)	8 (13.3)	0.008
Undefined, n (%)	8 (6.7)	12 (20)	0.007
Proliferative, n (%)	89 (74.2)	36 (60)	0.05
Fibrotic, n (%)	31 (25.8)	24 (40)	0.05
Overlapping systemic autoimmune disease, n (%)	1 (0.8)	6 (10)	0.006
Biopsy, n (%)	106 (88.3)	46 (76.7)	0.04
High IgG4 levels, n (%)	86 (76.8)	38 (66.7)	0.15
Serum IgG4 levels, median (IQR), mg/dL	300.5 (150.5-680)	251 (88-481)	0.17
Inclusion criteria score, median (IQR)	34 (27.5-43.5)	18 (12-32)	<0.001
CDC: Comprehensive diagnostic criteria; CSP: Consensus statement on pathology; IQR: interquartile range			

The performance of the criteria was: sensitivity 66.7%, specificity: 100%, PPV 100%, NPV 66.7%. In a sensitivity analyses where all exclusion criteria were removed the sensitivity increased to 77.8% and the specificity decreased to 96.6%. When only removing the disease-specific autoantibody items, the sensitivity was 73.3% and the specificity 100%.

Conclusion: Application of the 2019 ACR/EULAR classification criteria for IgG4-RD in a real-world Latin American population confirms its high specificity in excluding those without the disease. The sensitivity was lower than the one reported in other cohorts. The presence of concomitant autoimmune diseases and clinically not significant disease-specific autoantibodies excludes a significant number of patients from fulfilling the criteria.

Disclosure: E. Martin-Nares, None; **G. Hernandez-Molina**, None; **D. Baenas**, None; **J. Delgado-de la Mora**, None; **F. Caeiro**, None; **P. Wurmann Kiblisky**, None; **V. Pimentel-Quiroz**, None; **V. Ascuña Valdivia**, None; **D. Faz-Muñoz**, None; **E. Saad**, None; **E. Cairoli**, None; **S. Elgueta Pinochet**, None; **H. Madariaga Charaja**, None; **D. Montante-Montes de Oca**, None; **J. Gallo**, None; **M. Ugarte-Gil**, Pfizer, 5, Janssen, 5; **O. Neira**, None; **P. Burgos**, None; **S. Paira**, None.

Abstract Number: 1114

Pachymeningitis: The Mayo Clinic Experience

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Pachymeningitis is a rare disorder defined by localized or generalized inflammatory thickening of the dura. It can be associated with infections, malignancy, autoimmune disorders, or can be idiopathic. The clinical presentation is dependent on the location of dural involvement and regional structures affected. Typical symptoms include chronic headaches, seizures, facial pain, ataxia, and cranial neuropathies. Case series have reported clinical characteristics and outcomes in patients with pachymeningitis; however, large series are lacking. In our retrospective study, we report the clinical presentation, demographics, etiology, imaging features, laboratory data, treatment, and outcome in 153 patients with pachymeningitis referred to our tertiary care center.

Table 1. Neurologic symptoms of subjects with Pachymeningitis. The top 10 categories by prevalence are shown.

Neurologic Symptoms	N(%)
HEADACHES	103 (67.3%)
HEARING ISSUES	39 (25.5%)
VISUAL CHANGES	39 (25.5%)
OTHERS	31 (20.3%)
DIZZINESS	25 (16.3%)
SENSORY LOSS	22 (14.4%)
NAUSEA	18 (11.8%)
PARESIS	18 (11.8%)
SEIZURES	12 (7.8%)
IMBALANCE	11 (7.2%)

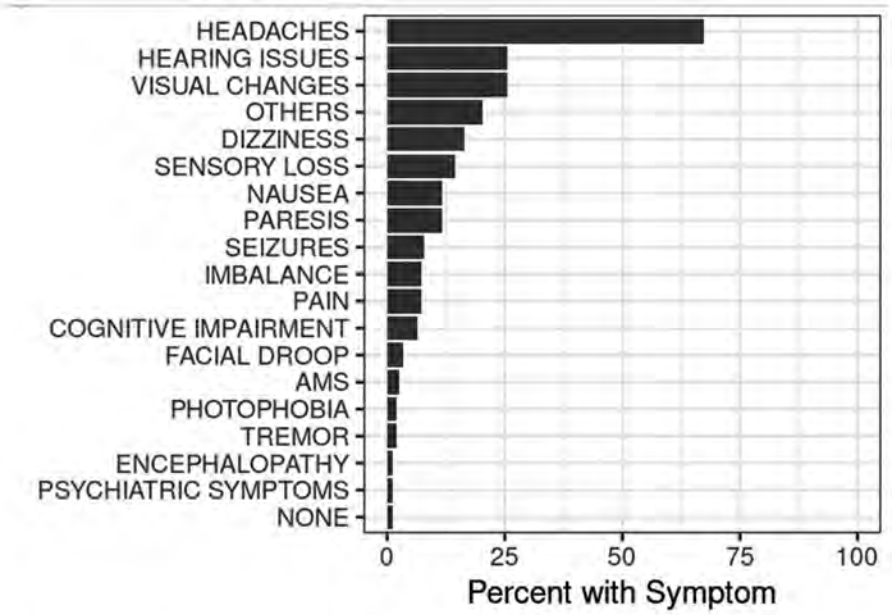

Figure 1. Neurological symptoms of Pachymeningitis.

Table 2. Etiology of Pachymeningitis. The top 10 categories by prevalence are shown.

Etiology	N(%)
IDIOPATHIC	45 (29.4%)
CSF HYPOTENSION SYNDROME/SPONTANEOUS CSF LEAK	29 (19%)
SARCOIDOSIS	19 (12.4%)
INFLAMMATORY UNDETEREMINED	16 (10.5%)
OTHERS	11 (7.2%)
INFECTIOUS	8 (5.2%)
GPA	7 (4.6%)
CANCER	6 (3.9%)
RA	5 (3.3%)
IGG4	5 (3.3%)

Methods: Medical records for all patients with pachymeningitis between 01/01/1990 and 11/01/2019 at our institution were reviewed. Pachymeningitis was defined as focal or diffuse dural thickening or enhancement on magnetic resonance imaging (MRI) of the brain or spinal cord and/or characteristic inflammation on histologic analysis of dura mater tissue samples. Clinical features, laboratory data, radiologic features, pathological findings, and therapeutic data were studied.

Results: 163 cases of potential pachymeningitis were examined, and 10 patients were excluded for not meeting pachymeningitis definition. The cases were 52.3% female (80/153) and 47.7% male (73/153). Mean age at diagnosis was 60 years (range 21 to 87) with mean age at onset of symptoms 58 years (range 17 to 87). Nearly all patients (98.7%) experienced at least one neurological symptom with headache being the most prevalent (N=103/67.3%; Table 1 and Figure 1). CSF analysis via lumbar puncture was performed in 118 patients with opening pressure being high in 19 of 90 patients. Dural thickening and enhancement was more common on MRI than either radiological finding alone, 56.2% versus 3.9% dural thickening alone or 37.9% enhancement alone (without dural thickening). The majority of cases presented with diffuse pachymeningitis on MRI (62.1%). Biopsy of the cranial or spinal parenchyma or meninges was performed in 42.5% (65/153). Etiology of pachymeningitis was idiopathic in 29.4% (45/153). The top 10 categories of etiology by prevalence are shown in Table 2. 60.1% of patients (92/153) received at least one thera-

peutic agent. 51.6% of cases received treatment with corticosteroids. Other treatments depending on etiology of the pachymeningitis included methotrexate, blood patch, antimicrobial therapy, rituximab, and azathioprine with highest prevalence. Complete clinical response and complete initial radiologic response were observed in 12.4% (19/153).

Conclusion: We report the largest series of pachymeningitis patients to date. Etiology may be idiopathic or secondary to infections, malignancy, or autoimmune disorders; therefore, appropriate workup is necessary to guide treatment strategy. Limited number of patients demonstrate complete clinical response.

Disclosure: E. Gilbert, None; **M. Al-Awqati**, None; **T. Gunderson**, None; **F. Berianu**, None.

Abstract Number: 1115

Uveitis and Inflammatory Bowel Disease: Study of 1449 Patients from a Single University Center

Lara Sánchez-Bilbao[1], María José García-García[1], David Martinez-Lopez[1], Iñigo Gonzalez-Mazon[2], Montserrat Rivero-Tirado[1], Beatriz Castro[1], Javier Crespo[1], Miguel Ángel gonzalez-Gay[3] and Ricardo Blanco[4], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]H. U. Marques de Valdecilla, Santander, Spain, [3]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [4]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD), and Ulcerative colitis (UC) are related to Spondyloarthritis (SpA). Ocular manifestations (OM) are well-stablished in axial SpA but not in IBD. It has been classically reported that whereas uveitis with axial SpA is predominantly anterior, unilateral, acute, and non-recurrent; in IBD it is bilateral, posterior, insidious, and chronic.

In a large unselected series of IBD, our aim was to assess **a)** epidemiology and clinical features of uveitis associated to IBD, **b)** to compare patients who developed uveitis and those who did not, and **c)** its relationship with biological treatment used in IBD.

Methods: Study of all consecutive patients from a single University Hospital during the last 40 years with**: a)** IBD (CD and UC), and **b)** uveitis according to Standarization Uveitis Nomenclature (SUN) Working Group. Demographic features, clinical findings, occurrence of other extraintestinal manifestations and treatment were recorded.

Results: We studied 1449 (714 women/735 men) patients with IBD, mean age of 55.2±15.9 years.

Uveitis was present in 23 (1.6 %) (38 eyes) of 1449 IBD patients. The most common pattern of uveitis was typically anterior (n=18; 78.3%), unilateral (n=19; 82.6%), acute (n=19; 82.6%), and non-recurrent (n=12; 52.2%).

The comparative study between patients with and without uveitis showed a significant predominance of women (**TABLE)** in patients with uveitis, as well as erythema nodosum, hidradenitis suppurativa and joint involvement.

TABLE. General features of 1449 patients with IBD with and without uveitis.

	Overall (n=1449)	Uveitis (n=23)	Non uveitis (n=1426)	P
Main general features				
Age, years, mean±SD	55.2±15.9	49.1±14.6	55.2±15.9	0.8
Sex, women/men, n, (% of women)	714 / 735 (49.3)	17 / 6 (73.9)	697 / 729 (48.9)	**0.02***
IBD duration, years, mean±SD	13.2 ± 9.7	17.4 ± 10.2	13.1 ± 8.9	0.08
IBD Severity				
Surgical Interventions, n (%)	289 (19.9)	2 (8.7)	284 (19.9)	0.7
Conventional Immunosuppressive drugs, n (%)	878 (60.6)	14 (60.9)	863 (60.5)	0.5
Biological Therapy, n (%)	384 (26.5)	7 (30.4)	378 (26.5))	0.9
TNFi monoclonal antibodies	384 (26.5)	7 (30.4)	378 (26.5)	0.9
Ustekinumab	27 (1.9)	1 (4.3)	27 (1.9)	0.5
Other	23 (1.6)	1 (4.3)	22 (1.6)	0.3
Extraintestinal manifestations				
Cutaneous manifestations, n (%) (TOTAL)	125 (8.6)	9 (39.1)	121 (8.7)	0.1
Erythema nodosum, n (%)	26 (1.8)	6 (26.1)	24 (1.7)	**0.009***
Pyoderma gangrenosum, n (%)	13 (0.9)	1 (4.3)	13 (0.9)	0.7
Hidradenitis suppurativa, n (%)	2 (0.1)	1 (4.3)	1 (0.1)	**0.0001***
Joint involvement, n (%) (TOTAL)	131 (9)	10 (43.5)	121 (8.5)	**0.0001***
Axial pattern, n (%)	65 (4.5)	4 (17.4)	58 (4.1)	**0.0001***
Peripheral pattern, n (%)	64 (4.4)	4 (17.4)	63 (4.4)	0.9

Regarding IBD severity, in terms of surgical interventions, and conventional and biological immunosuppressive treatments, there were no significant differences.

Conclusion: Although uveitis is more infrequent in IBD than in axial SpA, it is also anterior, unilateral, acute, and non-recurrent in contrast with published data from selected series. Patients with uveitis do not seem to represent more severe phenotype of IBD.

Disclosure: L. Sánchez-Bilbao, None; **M. García-García**, None; **D. Martinez-Lopez**, None; **I. Gonzalez-Mazon**, None; **M. Rivero-Tirado**, None; **B. Castro**, None; **J. Crespo**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1116

Disease Characteristics of Steroid-Induced Spinal Epidural Lipomatosis: A Systematic Review

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Steroid-induced epidural lipomatosis (SEL) is a rare phenomenon causing neuronal compression from adipose tissue deposition in the epidural space. We analyzed the available literature in a systematic review to determine the patient demographics, underlying disease, oral steroid doses, intervention, and outcomes of SEL.

Methods: A comprehensive database search was performed for articles reporting spinal epidural lipomatosis from oral steroid therapy from conception to May 26, 2021. Full-text articles in English language meeting our predefined criteria were analyzed for review (Figure 1).

Results: We included 36 articles for our systematic review including data of 45 patients. The mean age of patients presenting with SEL was 50.1 (27-75) years with male predominance (80.0%). The most common presenting symptom was paraparesis 82.0% (n= 35), followed by back pain 44.4% (n=25). One-third (31.1%) of the patient population had an inflammatory rheumatological indication for chronic steroid therapy. Rheumatoid arthritis was the most common inflammatory disorder in these (57%). The median oral steroid dose was 20.0 (9.75-45.8) mg/day with a median duration of 24.0 (12.0-57.0) months before the diagnosis of SEL. Thoracic spine was affected in 55.8% (n=24), lumbar spine in 34.8% (n=15) and both in 9.3% Laminectomy was performed in 73.3% (n=33) of cases. Case outcomes were variable, however the majority reported recovery to ambulation (65.2%).

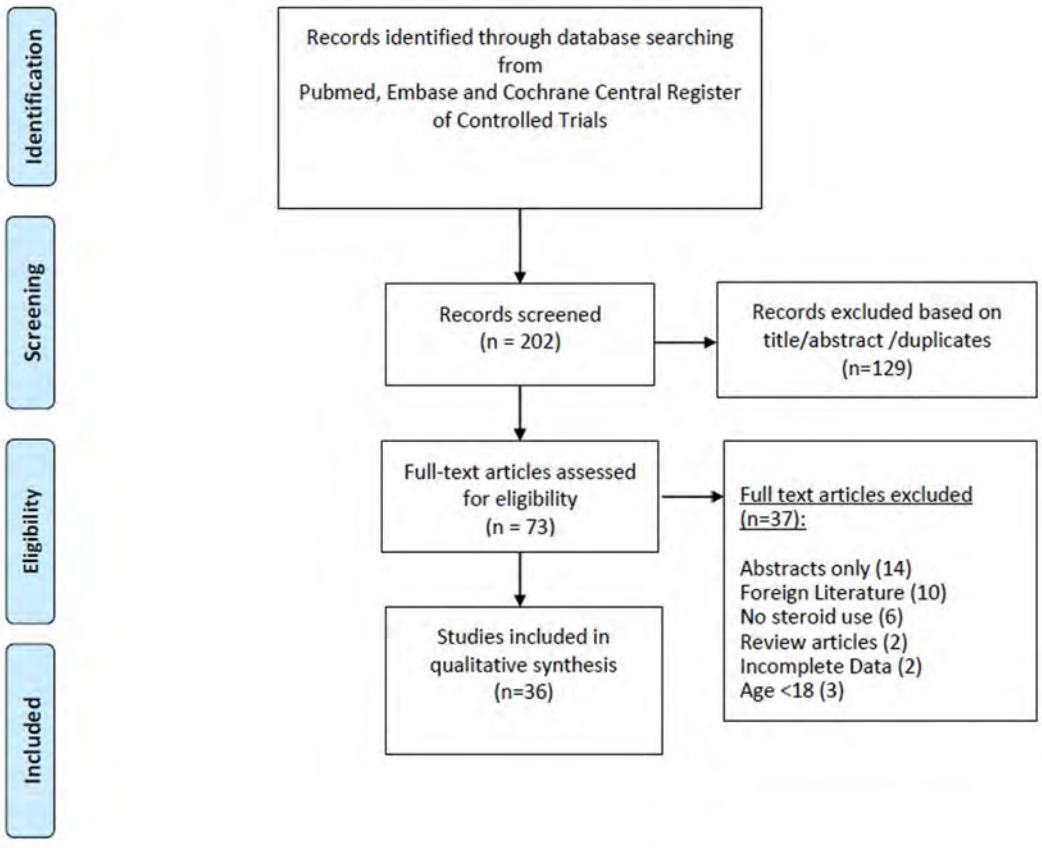


Figure 1. PRISMA flow diagram.

Conclusion: SEL should be considered as a possible etiology for lower limb weakness in patients on chronic oral steroid therapy. Our review highlights this rare association that may further increase the morbidity in patients with underlying rheumatological diseases.

Disclosure: H. Chaudhary, None; **U. Nasir**, None; **K. Syed**, None; **A. Sullivan**, None; **S. Zachariah**, None; **C. Akem-Dimala**, None; **M. Khan**, None; **A. Donato**, None.

Abstract Number: 1117

Ocular Scleral Pathology: Clinical Features and Systemic Treatment in 175 Patients from a Single University Center

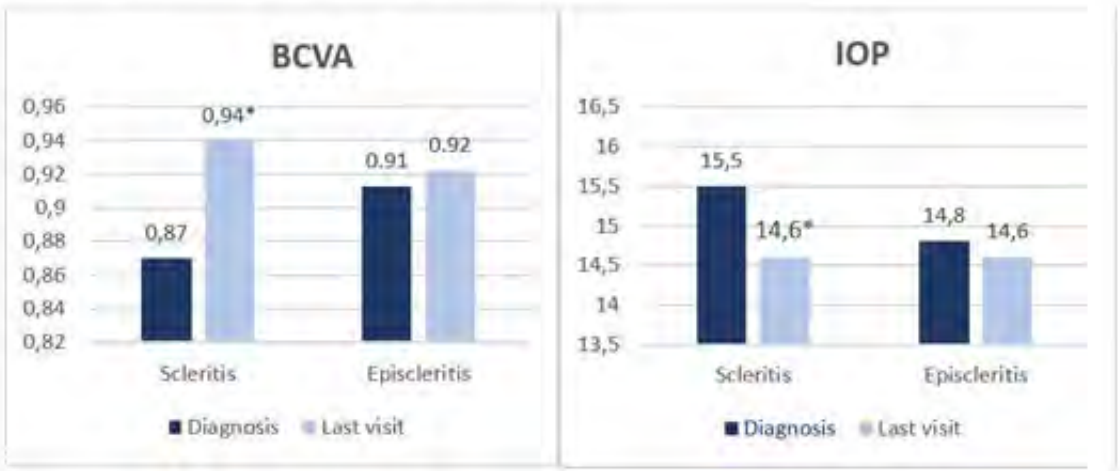
Lara Sánchez-Bilbao[1], Vanesa Calvo-Río[2], José Luis Martin-Varillas[3], Carmen Álvarez-Reguera[1], Alba Herrero-Morant[1], Iñigo Gonzalez-Mazon[4], Rosalia Demetrio-Pablo[1], Miguel Ángel gonzalez-Gay[5] and Ricardo Blanco[2], [1]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain, [3]Hospital Sierrallana, Torrelavega, Spain, [4]H. U. Marques de Valdecilla, Santander, Spain, [5]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

TABLE. Underlying diseases and systemic treatment.

	Overall (n =175)	Episcleritis (n=135)	Scleritis (n=40)	p
Age *(years), mean ± SD*	48.9 ± 14.2	47.8 ± 14.3	52.6 ± 13.9	0.061
Sex *(women), n (%)*	106 (60.6)	81 (60)	25 (62.5)	0.920
UNDERLYING DISEASE				
- Idiopathic, n (%)	81 (46.3)	65 (48.1)	16 (40)	0.364
- Infectious, n (%)	11 (6.3)	7 (5.2)	4 (10)	0.276
- IMID, n (%)	76 (43.4)	57 (42.2)	19 (47.5)	0.563
o Spondyloarthritis	21 (12)	17 (12.6)	4 (10)	0.787
o Crohn's disease	16 (9.1)	14 (10.4)	2 (5)	0.469
o Rheumatoid Arthritis	14 (8)	12 (8.9)	2 (5)	0.740
o Granulomatosis with polyangiits	7 (4)	3 (2.2)	4 (10)	0.080
o Relapsing polychondritis	6 (3.4)	4 (3)	2 (5)	0.621
o Systemic lupus erythematosus	5 (2.9)	2 (1.5)	3 (7.5)	0.079
o Ulcerative colitis	3 (1.7)	2 (1.5)	1 (2.5)	0.796
SYSTEMIC TREATMENT	72 (41.1)	37 (27.4)	35 (87.5)	0.000*
- Systemic glucocorticoids, n (%)	72 (41.1)	37 (27.4)	35 (87.5)	0.000*
- Methotrexate, n (%)	39 (22.3)	17 (12.6)	22 (55)	0.000*
- Non-methotrexatecDMARD, n (%)	35 (20)	24 (17.8)	11 (27.5)	0.177
- TNFibDMARD, n (%)	27 (15.4)	19 (14.1)	8 (20)	0.362
- Non-TNFibDMARD, n (%)	8 (4.6)	5 (3.7)	3 (7.5)	0.386

*p<0,05

FIGURE. BVCA and IOP at diagnosis and last visit.



*p<0,05

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Clinical Features & Diagnostics (1083–1117)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Ocular scleral pathology (OSP) includes episcleritis and scleritis. Episcleritis is generally a benign disease with a self-limited course, while scleritis is a more severe ocular condition. In some severe and refractory cases systemic therapy may be required.

In a wide series with OSP our aim was to assess **a)** underlying diseases and **b)** systemic treatment.

Methods: Study of unselected all consecutive patients studied in a single University Hospital during the last ten years with**: a)** episcleritis and **b)** scleritis diagnosed by clinical features and slit-lamp (Watson and Hayreh criteria). Best corrected visual acuity (BCVA) and intraocular pressure (IOP) were measured at diagnosis and after systemic treatment.

Results: We studied 175 patients (106 women/ 69 men) /212 affected eyes with OSP (episcleritis=135; scleritis=40); mean age 48.9±14.2 years.

OSP was unilateral in 138 (78.9%), recurrent in 74 (42.9%) and chronic in 21 (12%). Most of them were idiopathic (n=81, 46.3%) while associated with IMID were 43.4% **(TABLE).** The most important underlying IMID were spondyloarthritis and inflammatory bowel disease, without significant differences between scleritis and episcleritis. Granulomatosis with polyangiits and systemic lupus erythematosus were more frequent in scleritis, not reaching statistical significance.

Regarding treatment, topical treatment was used in all patients. 41.1% received systemic treatment, including systemic glucocorticoids, cDMARDS and bDMARDs. Systemic glucocorticoids and Methotrexate were used more frequently in scleritis **(TABLE)**. The main indication for biologic therapy was related to underlying IMID in both groups, but 7 bDMARDs in scleritis were indicated for systemic and ocular compromise.

BVCA and IOP improved significantly after systemic treatment in scleritis **(FIGURE)**.

Conclusion: OSP is a relatively frequent entity. It is necessary to exclude an underlying systemic disease to establish correct systemic treatment.

Disclosure: L. Sánchez-Bilbao, None; **V. Calvo-Río**, None; **J. Martin-Varillas**, None; **C. Álvarez-Reguera**, None; **A. Herrero-Morant**, None; **I. Gonzalez-Mazon**, None; **R. Demetrio-Pablo**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1118

The Association of Hand OA with Paid an Unpaid Work Impairment and Related Costs: The Hand Osteoarthritis in Secondary Care Cohort

Sietse Terpstra[1], Lotte van de Stadt[1], Annelies Boonen[2], Frits Rosendaal[1] and Margreet Kloppenburg[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Department of Internal Medicine, Division of Rheumatology, Maastricht University Medical Centre+ (MUMC+), Maastricht, Limburg, Netherlands

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatic musculoskeletal diseases (RMDs) can cause impairment at paid and unpaid work and contributes to societal burden and costs. However, data on this topic concerning hand osteoarthritis (OA) is scarce.

Therefore, we aimed to investigate the association of hand OA with paid and unpaid work participation, as well as socio-demographic and disease characteristics related to productivity loss and societal costs.

Table 1. Characteristics of the HOSTAS population of our present study (n=382)

General patient characteristics	
Age, years	60.9 (8.4)
Sex, women, *n (%)*	320 (84%)
BMI, kg/m²	27.6 (4.9)
Education level, high, *n (%)*	101 (26%)
Hand-specific characteristics	
Fulfilling Altman et al. hand OA criteria, *n (%)*	344 (90%)
Erosive hand OA⁺, *n (%)*	113 (30%)
Symptom duration, years^	0.76 (0.27; 2.65)
AUSCAN hand pain (0-20)	9.4 (4.2)
AUSCAN hand function (0-36)	15.7 (8.2)
Tender joint count (0-30)^	3 (1; 6)
KL ≥ 2 joint count (0–30)^	13 (5; 21)
General burden	
Comorbidities, any comorbidity present, *n (%)*	157 (41%)
Amount of comorbidities^	0 (0; 1)
Work characteristics	
Paid work, *n (%)*	181 (47%)
Hours of paid work per week	25.9 (11.8)
Retired, *n (%)*	117 (31%)
Full work disability, *n (%)*	24 (6.3%)
Full work disability due to hand OA, *n (%)*	16 (4.2%)

Table 2. Outcomes of the Health and Labour Questionnaire in patients having paid work (181 out of 382 patients), concerning the last two weeks

Absence	
Absence due to hand OA, n (%)	13 (7%)
Hours of absence due to hand OA, if any (n=11)	42 (24; 54)
Unproductiveness at work	
Unproductiveness due to hand OA, n (%)	28 (15%)
Hours of unproductiveness due to hand OA, if any (n=28)	4 (2; 6)
Work production loss (= absence + unproductiveness)	
Any work production loss, n (%)	35 (19%)
Hours of work production loss due to hand OA, if any (n=38)	11 (4; 35)
Complaints at work due to hand OA	
Any hinder at work due to hand OA	120 (66%)
Hinder score of paid work complaints (6 - 24)	7 (6; 8)

Numbers represent median (IQR), unless otherwise specified. Abbreviations: OA = osteoarthritis.

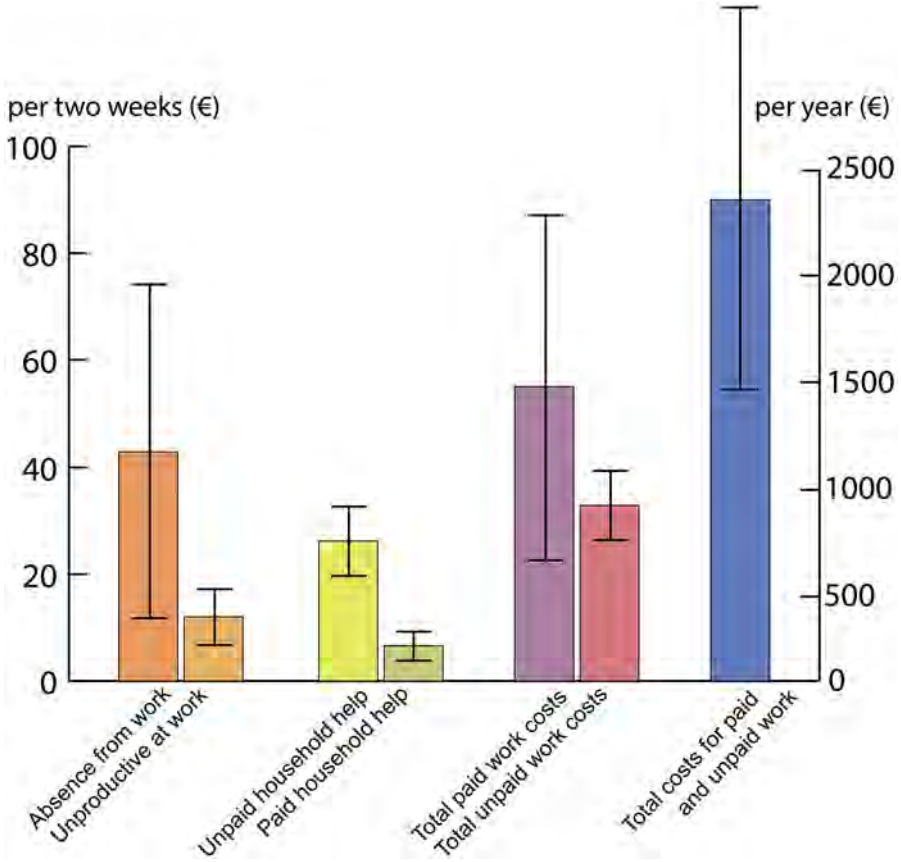


Figure 1. Mean societal costs associated with hand OA per patient in our total cohort, with 95% confidence interval.

Methods: We used data of the Hand OSTeoArthritis in Secondary care (HOSTAS) cohort. A diagnosis of hand OA by the treating rheumatologist was the case definition. Patient and OA characteristics were assessed by validated standardized questionnaires and tests. The Health and Labour Questionnaire (HLQ) was assessed on the last two weeks and related to hand OA for paid work hinder score (6 – 24), production loss while at work and hours of sick leave, as well as unpaid work replacement and hinder score (4 – 16). Self-reported income was collected to estimate income inequality compared to the Dutch age-gender-education matched population without hand OA

Societal costs (€) of paid work were estimated by multiplying number of hours of production lost due to hand OA (while present or absent form work) by the average hourly societal costs of paid work in The Netherlands. Societal costs of unpaid work were estimated by multiplying the hours of unpaid work replaced by others by the Dutch gross

average hourly salary of a household help. Costs were adjusted to 2019 values using consumer price indices. Costs per two weeks were extrapolated to costs per year by a using a conversion factor (26.09).

Results: HLQ data was available for 382 patients (mean age 60.9, 86% women, mean BMI 27.6 and 41% having any comorbidity, **table 1**). Of these persons, 16 (4%) had full work disability due to hand OA, 117 (30%) were retired and 181 (47%) had paid work. Thirteen employed persons (7.2%) reported sick leave due to hand OA, in which case a median of 42 work hours (IQR 24; 54) were lost in the past two weeks (**table 2**). Hinder at work was reported by 120 out of 181 working patients (66%), with a hinder score of 7 (6; 8). Unproductive hours while at work were reported by 28 (15%) patients, with a median of 4 hours (2; 6) in those experiencing unproductive time. Unpaid work hinder score was 8 (7; 10). Replacement of unpaid work was necessary in 180 patients (47%), with a median of 3 hours (2;7) per patient requiring help replaced.

Mean total societal costs per hand OA patient in the cohort (n=382) were estimated €90.00 (95% CI 55.20; 124.81), translating to 2343 euros (1964; 5724) per year (**figure 1**). Furthermore, patients showed a lower yearly and hourly income than a matched general Dutch population aged 55 to 65.

Conclusion: Hand OA is associated with significant hinder in paid and unpaid work participation, which translates in substantial societal costs of lost productivity. Future research should investigate prevention of hand OA sickness, absence and unproductiveness, as well as interventions to adapt the work environment to the hand OA patient.

Disclosure: S. Terpstra, None; **L. van de Stadt**, None; **A. Boonen**, None; **F. Rosendaal**, None; **M. Kloppenburg**, None.

Abstract Number: 1119

Systematic Review of Non-surgical Therapies for Hand Osteoarthritis

Haonan Mi, Christopher Oh and Tanveer Towheed, Queen's University, Kingston, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: This systematic review evaluated all published randomized controlled trials (RCTs) assessing pharmacological and non-pharmacological therapies in patients with hand osteoarthritis (HOA).

Methods: The following electronic data sources were searched from inception to December 2020: MEDLINE, EMBASE, AMED, Clinicaltrials.gov and EBM reviews, including the Cochrane Database of Systematic Reviews (CDSR), Database of Abstracts of Reviews of Effectiveness (DARE), ACP Journal Club, and the Central Cochrane Database. RCTs were included if they evaluated a non-surgical, therapeutic intervention in adult subjects with HOA. The trial must have explicitly stated that a randomized method of allocation to a treatment group was used. RCTs evaluating OA at multiple sites were only included if efficacy data was presented separately for the hand. Exclusion criteria included: RCTs evaluating a surgical therapy, conference proceedings, unpublished RCTs, and non-English RCTs if their English abstracts did not contain sufficient details on trial methodology and outcomes. Study quality was evaluated using the Jadad's scoring checklist. A meta-analysis would be completed if possible.

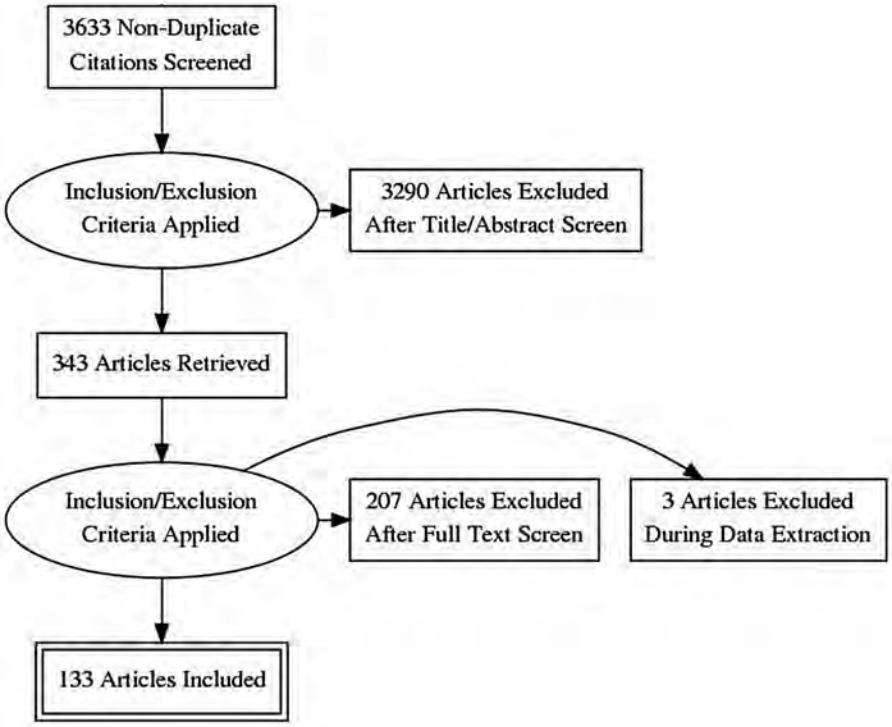


Figure 1. PRISMA diagram summarizing search strategy, study identification and retrieval.

Results: 133 RCTs were analyzed in this systematic review. There was no consistent definition of hand OA used in the RCTs, with most trials (N = 102) not explicitly distinguishing between primary (idiopathic) and secondary OA. Sixty-one RCTs used a validated hand OA classification scheme for study entry, with the most common being the ACR classification criteria (N = 54). Radiographs were taken at baseline in seventy-seven RCTs. Most studies described their methods for randomization, blinding and allocation concealment. However, studies underreported features specific to HOA, such as pattern of joint involvement and number of affected joints. Standardized outcome assessments for pain and function were commonly presented, but measures of other HOA specific outcomes, such as health-related quality of life and patient global assessments, were underreported. The mean Jadad score for all entries was 3.08. Increasing Jadad scores were noted over time. A meta-analysis was not completed due to significant heterogeneity amongst high quality RCTs and limited quantity of data.

The following pharmacologic therapies demonstrated efficacy across multiple RCTs: systemic NSAIDs, topical NSAIDs, intramuscular and intravenous clodronate, topical capsaicin, topical trolamine salicylate, oral chondroitin sulfate. Non-pharmacologic therapies that demonstrated efficacy across multiple studies include splints, joint strengthening exercises, mobilization, paraffin baths and multidisciplinary combined intervention. The remainder of the therapies had mixed or negative results, were compared to other therapies in single studies, or efficacy compared to placebo was only demonstrated in a single study.

Conclusion: HOA is a complex area in which to study the efficacy of therapies. Future trials should consistently report on HOA specific features and outcome assessments to make clinically relevant conclusions about the efficacy of the diverse treatment options available.

Disclosure: H. Mi, None; **C. Oh**, None; **T. Towheed**, Abbvie, 1, 2, 6, Pfizer, 2, UCB, 1, 2, Celltrion, 1, 2, Janssen, 6, Sandoz, 1, 2, 6, Novartis, 1, 2, 6, Amgen, 1, 2, 6.

Abstract Number: 1120

Effectiveness of Stretching and Bracing for the Treatment of Osteoarthritis-associated Joint Contractures Prior to Joint Replacement: A Systematic Review

T Mark Campbell[1], Bahareh Ghaedi[2], Elizabeth Ghogomu[3], Marie Westby[4] and Vivian Welch[5], [1]Elisabeth Bruyere Hospital, Ottawa, ON, Canada, [2]Ottawa Hospital Research Institute, Ottawa, ON, Canada, [3]Bruyere Research Institute, Ottawa, ON, Canada, [4]Centre for Hip Health and Mobility, Vancouver, BC, Canada, [5]Bruyère Research Institute, Ottawa, ON, Canada

SESSION INFORMATION

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Background/Purpose: Many patients with osteoarthritis (OA) develop range of motion (ROM) restrictions in their affected joints (contractures), leading to worse pain and function. OA-related contractures are associated with more rapid progression to arthroplasty, contributing to rising health care costs. Effective treatment guidance for lost ROM in

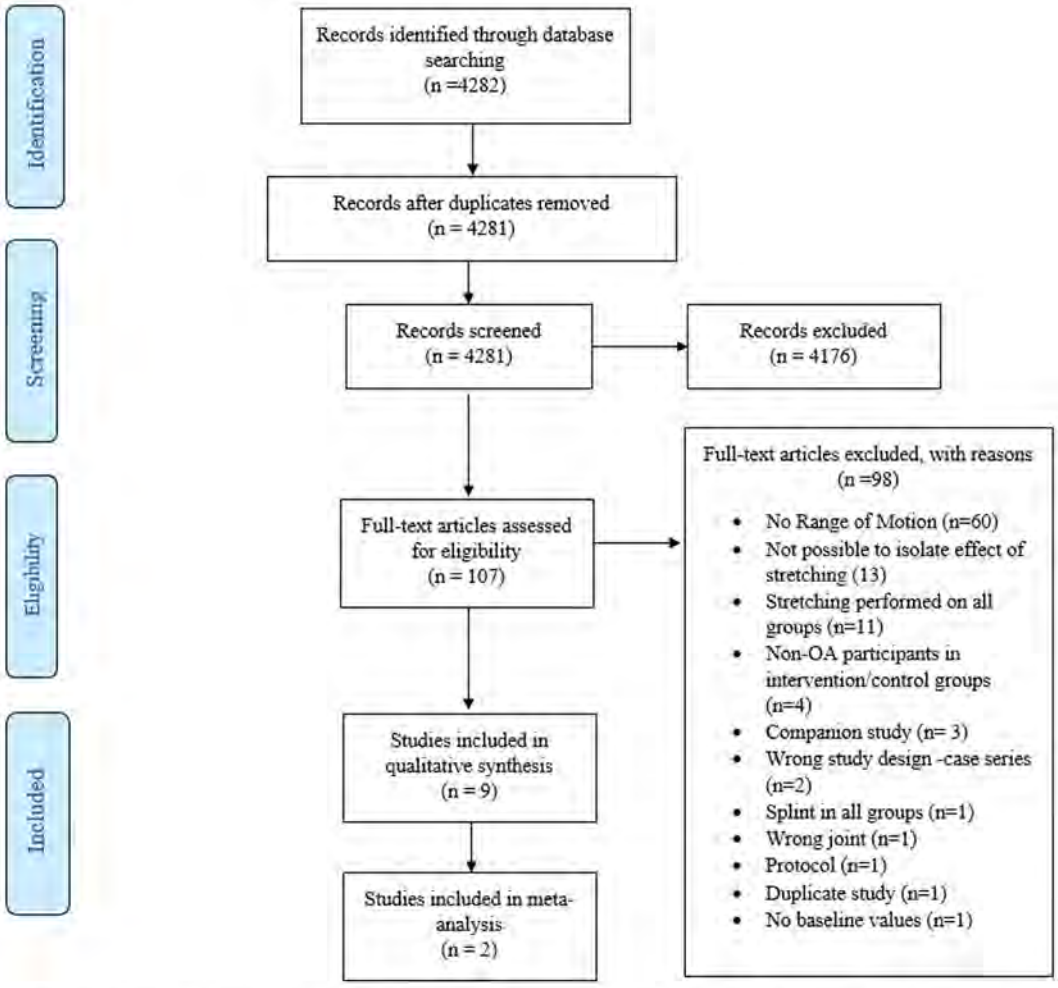

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of search results.

Table 1. Characteristics of Included Studies

Author, Year, Country	Study type	N (% female)	Mean age (years)	Disease duration	OA-affected joint, KL grade	Intervention/Control	Outcome(s) and timepoint(s)
Aoki 2009 Japan	RCT	36 (100)	All = 73.3 ± 5.8	9.8 years ± 7.4	Knee Grade III to IV	Intervention: twice-daily home-based stretching exercises for 3 months - knee flexion assisted by hand while sitting on the floor and knee flexion assisted by hand while prone for 30 seconds, 10 repetitions Control: maintain usual level of physical activity	AROM, PROM Pain during walking (VAS)
Weng 2009 Taiwan	RCT	132 (80)	All = 64.0 ±7.5	4 mo to 9.5 years (mean 42.5 ± 17.6 mo)	Knee Grade II	Intervention: bilateral knee static stretching therapy, then isokinetic strengthening exercises 3x weekly for 8 weeks Control: isokinetic muscular strengthening exercises only	Knee ROM (parameters not specified) Disability (Lequesne Index)
Arazpour 2013 Iran	RCT	24 (63)	Intervention group: 58.75 ± 2.22 Control group: 59.83 ± 2.48		Knee Grade I-II	Intervention: custom knee unloader orthosis to correct varus knee angulation worn for 6 weeks. Control: laterally wedged shoe insoles	Knee ROM (parameters not specified) Pain during walking (VAS) Baseline and 6 weeks
Poulsen 2013 Denmark	RCT	111 (43)	Intervention group = 65.8 ± 8.5 Control group = 65.5 ± 7.3	Intervention group= mean 26 ± 26 mo Control group = mean 32 ± 25 mo	Hip	Intervention: Patient education + Manual therapy - trigger point release, muscular stretching by muscle energy technique and joint manipulation 2x/week for 6 weeks Control: Patient education only	Flexion ROM QoL (HOOS) Baseline, 6 weeks, 3 months and 12 months
Watt 2014 United Kingdom	Non-RCT, internally controlled	26 (88)	All, Median (range) = 63 (51-78)	Median 5.3 (range 0.3-20)	Hand (DIP joints)	Intervention: custom gutter thermoplastic splint for DIP joint worn nightly for 3 months Control: no splint on similarly-affected joint of same participant	Extension ROM Baseline, 3 months and 6 months
Dwyer 2015 United States and South Africa	RCT	78 (63)	Intervention = 62.2 ± 11.8 Control = 60.9 ± 10.3	Intervention = 89.3 (81.4 months) Control = 58.4 (53.4 months);	Knee Grade I-II	Intervention: manual manipulative therapy (joint mobilization and manipulation) + rehabilitation (soft tissue treatment, passive stretches) for 6 sessions over 4 weeks. Control: rehabilitation only.	Flexion, extension ROM WOMAC pain, stiffness, disability 1-, 3-, and 6-months
Aydogdu 2017 Turkey	RCT	54 (85)	Intervention = 52.53 ± 9.68 Control = 51.19 ± 8.94		Knee Grade I-II	Intervention: Daily kinesio-taping on quadriceps and hamstrings with Y-shaped technique for 6 weeks. Control: hot packs, ultrasound, passive stretching, 5 sessions/week for 3 weeks.	Flexion ROM KOOS Pain, Function, Sports and recreation, Symptoms & QoL Baseline and 3 weeks
Estebanez-de-Miguel 2018 Spain and Switzerland	RCT	60 (42)	All = 63 ± 9.7	Intervention group = 31.6 ± 20.8 mo Control group = 26.1 ± 17.1	Hip Grade III	Intervention: high-force mobilization - 3 treatments on alternate days of long-axis distraction mobilization in open packed position. Control: low-force mobilization.	Flexion, extension, external rotation, internal rotation ROM Pain (WOMAC) Pre-post 3 sessions
Mirzaei 2018 Iran	RCT	18 (67)	Intervention = 55.16 ± 4.81 years Control = 54.5 ± 4.23 years		Knee Grade II or III	Intervention: valgus knee brace worn 8 hours/day for 2 weeks Control: lateral wedge insole shoe insole.	Knee ROM (parameters not specified) Pain during walking (VAS) Baseline and 2 weeks

Data not available if not displayed in Table.

AROM: Active ROM; HOOS: Hip disability and osteoarthritis outcome score; KL: Kellgren and Lawrence radiographic grading scale; KOOS: Knee disability and osteoarthritis outcome score; PROM: passive ROM; ROM: range of motion; VAS: Visual analogue scale; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

OA-affected joints is lacking. Our objective is to perform a systematic review and meta-analysis evaluating the effectiveness of stretching and/or bracing protocols on native (non-operated) joint ROM in people with radiographically-diagnosed OA.

Methods: We searched 7 databases CENTRAL, DARE, HTA, Medline, Embase, CINAHL, SCI-EXPANDED and PEDro. We included English-language studies evaluating stretching or bracing in participants with radiographically-

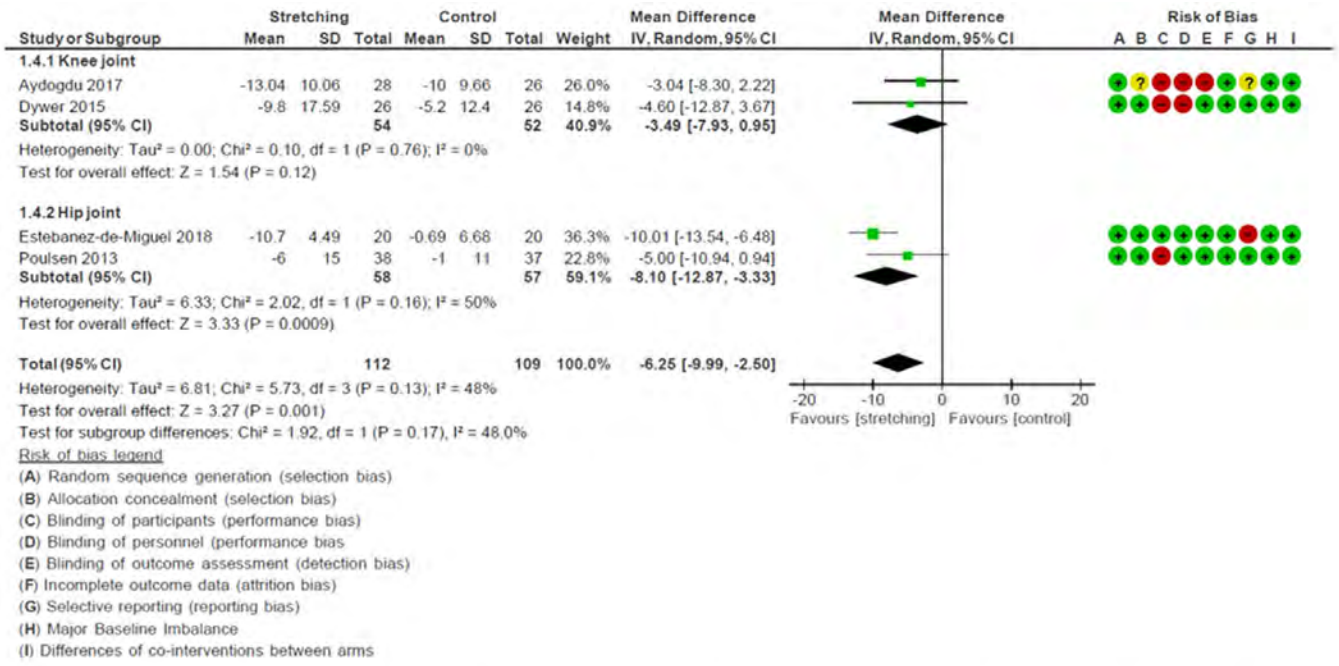

Figure 2. Meta-analysis and risk of bias for RCTs evaluating flexion range of motion following stretching intervention for the knee and hip. While knee flexion remains unchanged, hip flexion improves with stretching. Risk of bias was considered low overall for hip stretch RCTs.

diagnosed OA in any joint, prior to arthroplasty. Two reviewers independently screened titles and abstracts for inclusion and assessed risk of bias in included randomized controlled trials (RCTs) using the Cochrane Risk of Bias tool. Primary outcomes were ROM, pain and adverse events (AEs). A random-effects meta-analysis was performed when appropriate.

Results: We identified 4282 articles through database searching. Eight RCTs and 1 non-RCT met our eligibility criteria and provided adequate data for analysis (Figure 1, Table 1). Of these studies, 5 involved the knee joint, two the hip, and one the hand distal interphalangeal (DIP) joint. Three RCTs found no changes in knee flexion or extension after stretching while 1 reported increased ROM without specifying direction. Meta-analysis (n=2 studies, 1 using long-axis distraction mobilization and 1, manual therapy) showed improvement in hip flexion of 8.1° (95% CI 3.3,12.9°; Figure 2), and 1 RCT reported increased hip extension (7.8°; 95% CI 4.8,10.9°), abduction (6.2°; 95% CI 3.5,8.9), internal (7.6°; 95% CI 4.2,11.1°) and external (6.6°; 95% CI 3.6,9.5°) rotation using manual therapy. In 1 study, mean visual analogue pain reduction in the knee of 2.2 (95% CI –3.3,-1.1). One non-RCT showed that hand DIP joint splinting improved ROM. One study evaluating the hip reported an odds ratio of 4.5 (95% CI 0.9,23.0) for incurring an AE for manual therapy versus control. Risk of bias was generally rated low for studies showing improvement in ROM.

Conclusion: Stretching may be an effective strategy for improving ROM in the hip joint, while knee ROM may be more resistant to treatment. Differences in joint anatomy and biomechanical factors contributing to contractures may play a role in the observed outcomes. Stretching may also help OA-related pain. Stretching and bracing are appropriate conservative treatment options to improve OA outcomes prior to arthroplasty.

Disclosure: T. Campbell, None; **B. Ghaedi**, None; **E. Ghogomu**, None; **M. Westby**, None; **V. Welch**, None.

Abstract Number: 1121

Association of Healthcare Costs and Utilization with Increasing Severity of Pain in Osteoarthritis Patients: An 18-Year Retrospective Study

Jove Graham[1], Tonia Novosat[1], Haiyan Sun[1], Brian Piper[1], Joseph Boscarino[1], Melissa Kern[1], Vanessa Duboski[1], Eric Wright[1], Craig Beck[2], Rebecca Robinson[3], Edward Casey[4], Jerry A. Hall[3] and Patricia Schepman[4], [1]Geisinger, Danville, PA, [2]Pfizer, Inc., London, [3]Eli Lilly and Company, Indianapolis, IN, [4]Pfizer, Inc., New York, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis (OA) is a disease with complex pathogenesis, and it is important to understand a patient's level of severity in order to plan and stage treatment interventions. Prior studies have documented the health and economic burdens of patients with OA compared to those without OA. The goal of our study was to further stratify OA patients based on pain severity and compare healthcare utilization and cost.

Methods: This was a retrospective study using electronic health records and insurance claims from 2001-2018 at Geisinger, an integrated health system in Pennsylvania serving over 500,000 patients per year. Patients age 18 or older were included if they had ≥1 month of insurance coverage and ≥1 numerical pain score (NPS) after receiving a diagnosis code for OA (ICD-9: 715.*, ICD-10 M15-19) on an encounter, problem list, or OA-related procedure (hip/knee replacement, arthroscopy or injection). Pain episodes were defined as periods of time starting with an NPS (mild pain 0-3, moderate 4-6, severe 7-10) and ending when 90 days had elapsed with no new NPS. For each episode, claims were examined for the number of all-cause outpatient visits (OP), emergency department visits (ED) and inpatient days hospitalized (IP), total allowed medical cost, and total allowed pharmacy cost; these were converted to per-member-per-year (PMPY) rates or means. These statistics were compared among mild, moderate and severe pain episodes to look for differences, using generalized linear regression models adjusting for age and sex, with $p < 0.05$ considered statistically significant. Costs were normalized to 2010 US$ based on the Consumer Price Index. Claims containing a diagnosis, procedure, or national drug code related to OA were classified as OA-related and re-analyzed as a subset to examine OA-related utilization and cost.

Results: We identified 92,576 eligible patients with 306,200 pain episodes (43% mild, 32% moderate, 25% severe). For all types of OA-related utilization, moderate and severe pain episodes were associated with significantly higher rates relative to mild pain episodes (OP: 0.84 vs. 1.39 vs. 1.70 visits PMPY for mild, moderate and severe, respectively; ED: 0.13 vs. 0.21 vs. 0.41; IP: 0.10 vs. 0.22 vs. 0.26). All-cause OP and ED utilization also significantly increased with increased pain severity, but IP days did not (OP: 11.09 vs. 11.98 vs. 13.71; ED: 1.05 vs. 1.12 vs. 1.89; IP: 2.77 vs. 2.57 vs. 3.39). Similarly, we observed significant increases in OA-related costs for every category during moderate and severe pain episodes relative to mild pain (pharmacy: $669 vs. $943 vs. $1,207; medical: $1,345 vs. $2,320 vs. $2,429). Increasing pain severity was positively associated with all-cause pharmacy costs, but not all-cause medical costs (pharmacy: $7,729 vs. $9,143 vs. $10,068; medical: $27,571 vs. $22,802 vs. $20,876).

Conclusion: We observed that pain, an important symptom of OA, was strongly associated with patients' OA-related utilization and costs, and to a lesser extent, all-cause utilization and costs. With a better understanding of when and how patients become more expensive and challenging, we can develop better approaches for managing disease burden in the future.

Disclosure: J. Graham, Pfizer Inc., 5, Medtronic Inc., 5, Astra Zeneca, 5; **T. Novosat**, None; **H. Sun**, None; **B. Piper**, Pfizer, 5, Eli Lilly, 5; **J. Boscarino**, Purdue Pharma, 7, Gilead Sciences, 7, Pfizer, 5, Dept. of Defense, 5; **M. Kern**, None; **V. Duboski**, Pfizer, Inc., 5, AstraZeneca, 5; **E. Wright**, None; **C. Beck**, Pfizer Inc, 3, 11; **R. Robinson**, Eli Lilly and Company, 3, 11; **E. Casey**, Pfizer, Inc, 3, 11; **J. Hall**, Eli Lilly & Co, 3, 11; **P. Schepman**, None.

Abstract Number: 1122

Patient-perceived Solutions to the Treatment Barriers in Knee Osteoarthritis: A Qualitative Study from a Diverse Patient Group Including Racial/ethnic Minorities

Jasvinder Singh, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Knee osteoarthritis (OA) has worse outcomes in racial/ethnic minorities. Yet, most of the qualitative studies include primarily Caucasian people with knee OA, with minimal or no representation of racial/ethnic minorities. Therefore, our objective was **t**o examine patient perceived solutions to barriers to treatment of knee OA, in a diverse racial/ethnic group of people.

Methods: Nominal groups were conducted with consecutive patients with knee OA at a medical center clinic, oversampling for African Americans with knee OA. Participants discussed potential solutions and rank-ordered their concerns.

Results: Fourteen nominal groups with 48 knee OA patients were conducted with mean age, 60.6 years (standard deviation, 9.8) and knee OA duration, 7.8 years (sd, 5.4); 25% were men, and 46% were African American. The most frequently cited highly-ranked solutions were as follows:

1. *More Research, New medications/treatments that are more effective and/or safer, and Restoration of the joint cartilage*: Eight of the 14 groups listed this among their top concerns, and nine groups ranked this concern. It received 15% of all votes (43/288).

2. *Early diagnosis*: Two of the 14 groups listed this among their top concerns, and four groups ranked this concern. It received 7% of all votes (20/288). at an earlier stage.

3. *Better and more effective Communication*: Five of the 14 groups listed this among their top concerns, and five ranked this concern. It received 10% of all votes (29/288).

4. *Public and in-clinic patient Education*: Four of the 14 groups listed this among their top concerns, and five ranked this concern. It received 8% of all votes (22/288).

5. *Motivation/behavioral modification*: Four of the 14 groups listed this among their top concerns, and nine ranked this concern. It received 9% of all votes (26/288).

6. *Team Approach*: One of the 14 groups listed this among their top concerns, and four ranked this concern. It received 1% of all votes (2/288).

7. *Personalized medicine*: Six of the 14 groups listed this among their top concerns, and ten ranked this concern. It received 8% of all votes (24/288).

8. *Cheaper and more affordable medications and treatments*: Three of the 14 groups listed this among their top concerns, and four ranked this concern. It received 5% of all votes (15/288).

Conclusion: A diverse group of participants with knee osteoarthritis, including racial/ethnic minorities, identified several solutions to barriers to the effectiveness of current knee OA treatments. These solutions provide new knowledge. These solutions can also lead to the development of future interventions to improve the outcomes of people with knee OA.

Disclosure: J. Singh, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2, Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4.

Abstract Number: 1123

"It's a Dance Between Managing Both [Diabetes and Osteoarthritis]": A Qualitative Study Exploring Perspectives of Persons with Knee Osteoarthritis and Type 2 Diabetes Mellitus on the Impact of Osteoarthritis on Diabetes Management and Daily Life

Lauren King[1], Esther Waugh[1], Crystal McKay[1], Ian Stanaitis[2] and Gillian Hawker[1], [1]University of Toronto, Toronto, ON, Canada, [2]Women's College Hospital, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
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Background/Purpose: The links between osteoarthritis (OA) and other common chronic conditions, such as type 2 diabetes mellitus (T2DM), are increasingly being appreciated in epidemiological studies. However, patient perceptions of the impact of concomitant knee OA on their ability to engage in chronic disease management remains unknown. Using qualitative methods, we sought to explore individuals' experiences living with knee OA and T2DM, with a focus on the impact of OA on T2DM management and daily life.

Methods: Semi-structured telephone interviews were conducted with persons with symptomatic knee OA and T2DM recruited from a hospital-based diabetes clinic and a community OA program (Arthritis Society) in Ontario, Canada. The methodology of qualitative description was used. Interview transcripts were coded by a team of researchers and

data were analysed using thematic analysis to identify major themes. Interviewing stopped after no new themes or subthemes were identified.

Results: Eighteen participants were interviewed: n=9 women, n=9 aged ≥70 years, n=8 urban region, n=9 ≥10 years since diabetes diagnosis, and n=13 ≥10 years since OA diagnosis. Three overarching themes were constructed: 1. *OA impacts diabetes control*: Painful and disabling OA made it difficult for participants to engage in physical activity prescribed for T2DM, and they perceived that lack of physical activity negatively impacted their blood sugar control. Joint pain, and its effect on sleep and emotional health, were also seen to negatively impact blood sugar control. 2. *OA as a health priority due to its effects on quality of life:* Participants, who often had other chronic conditions in addition to T2DM, viewed OA as a health priority. OA-related pain and functional limitations reduced ability to participate in valued activities, e.g., work, and negatively impacted emotional well-being. 3. *Minimization of OA by health professionals and taking personal responsibility for OA care:* Participants perceived a disproportionately greater attention by health professionals to their T2DM compared to their OA. As a result, many participants described being left to coordinate and advocate for their own OA care.

Conclusion: These findings shed light on patients' experiences of living with symptomatic knee OA in the context of T2DM. OA-related pain, functional limitations, poor sleep and mental health were perceived as negatively impacting diabetes control and engagement in daily life activities. While considered important to patients, often these concerns were not being actively addressed by health professionals. Greater recognition by health professionals of the impact of knee OA in persons with T2DM has potential to improve both diabetes care and overall quality of life.

Disclosure: L. King, None; **E. Waugh**, None; **C. McKay**, None; **I. Stanaitis**, None; **G. Hawker**, None.

Abstract Number: 1124

Examining the Relationships Between Treatment and Pain and Physical Function Outcomes in Patients with Osteoarthritis: A Mediation Modeling Approach

Lucy Abraham[1], Robert Dworkin[2], Dennis C. Turk[3], John D. Markman[2], David A. Williams[4], Andrew G Bushmakin[5], Jerry A. Hall[6], David C. Semel[7], Joseph C Cappelleri[5] and Ruoyong Yang[8], [1]Pfizer Ltd., Tadworth, United Kingdom, [2]University of Rochester, Rochester, NY, [3]University of Washington, Seattle, WA, [4]University of Michigan, Ann Arbor, MI, [5]Pfizer Inc, Groton, CT, [6]Eli Lilly and Company, Indianapolis, IN, [7]Pfizer, New York, NY, [8]Pfizer Inc., New York, NY

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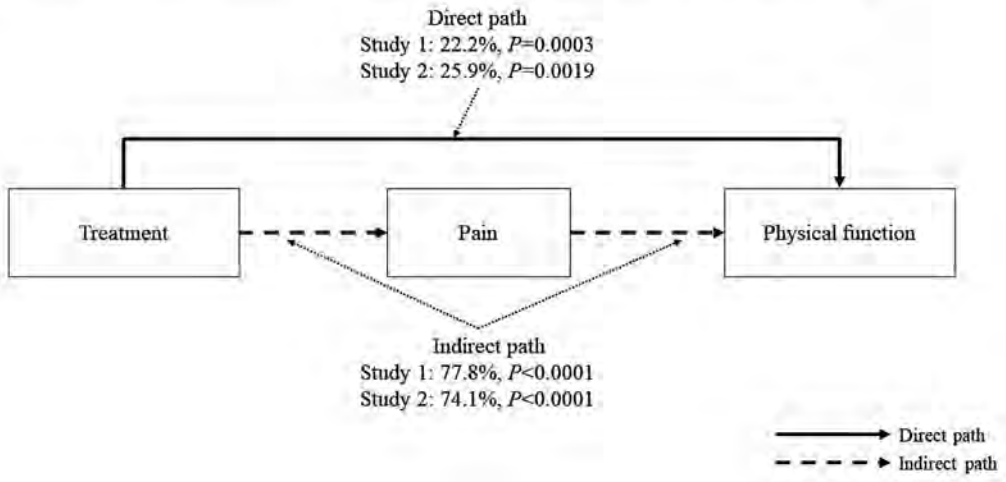
Background/Purpose: To better understand the complex relationships between treatment and pain and physical function (PF) outcomes, we investigated a set of mediation models of osteoarthritis (OA) patients' responses to tanezumab, an antibody against nerve growth factor that is in development for the treatment of OA.

Methods: Data came from two randomized clinical trials of tanezumab (Study 1: NCT02697773, JAMA. 2019;322:37-48 and Study 2: NCT02709486, Ann Rheum Dis. 2020;79:800-810); in both trials tanezumab provided greater pain relief and improvements in PF than placebo in patients with OA (all patients satisfied the American College of Rheumatology criteria for OA). A set of mediation models was used to explore the interrelationships among treatment, PF as measured by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC*) PF scores, and

Figure. Estimated direct and indirect effects (steady-state longitudinal models)



pain (WOMAC Pain scores) as a mediator of the effect of treatment on PF: (a) cross-sectional mediation models, (b) longitudinal mediation models, and (c) pseudo steady-state longitudinal mediation models. The cross-sectional mediation models include the following variables: treatment (tanezumab vs placebo), pain and PF scores (models were assessed separately at weeks 2, 4, 8, 12, 16, or 24). The longitudinal mediation models estimate relationships using data from all weeks simultaneously and include treatment, pain and PF scores at weeks 2, 4, 8, 12, 16, and 24. The longitudinal steady-state mediation model also uses all available data at weeks 2, 4, 8, 12, 16, and 24 with the assumption that relationships among variables in the model are the same at all time points.

*© 1996 Nicholas Bellamy. WOMAC® is a registered trademark of Nicholas Bellamy (CDN, EU, USA).

Results: The results of the cross-sectional and longitudinal mediation models showed that the indirect effect of treatment through pain on PF was stable across time (cross-sectional: 78.8–95.1%, all $P< 0.0001$; longitudinal: 70.5–86.6%, all $P< 0.0001$), indicating that a pseudo steady-state model is appropriate. The results of the longitudinal steady-state mediation models showed that the indirect effect of the treatment on PF was 77.8% in Study 1 and 74.1% in Study 2 ($P< 0.0001$, respectively), while the direct effect of the treatment on PF was 22.2% for Study 1 ($P=0.0003$) and 25.9% for Study 2 ($P=0.0019$) (Figure).

Conclusion: At least 75% of the treatment effect of tanezumab on physical functioning can be explained by the improvements in pain. However, tanezumab has an additional effect on physical functioning (approximately 25%), which is independent of improvements in pain. Research is needed to explain this effect and evaluate additional mediators (e.g., sleep, fatigue, method variance) that may contribute to the observed direct effect.

Disclosure: L. Abraham, Pfizer, 3, 11; **R. Dworkin**, Abide, 1, 2, Acadia, 1, 2, Adynxx, 1, 2, Analgesic Solutions, 1, 2, Aptinyx, 1, 2, Aquinox, 1, 2, Asahi Kasei, 1, 2, Astellas, 1, 2, AstraZeneca, 1, 2, Biogen, 1, 2, Biohaven, 1, 2, Boston Scientific, 1, 2, Braeburn, 1, 2, Cardialen, 1, 2, Celgene, 1, 2, Centrexion, 1, 2, Chromocell, 1, 2, Clexio, 1, 2, Collegium, 1, 2, Concert, 1, 2, Confo, 1, 2, Decibel, 1, 2, Dong-A, 1, 2, Editas, 1, 2, Eli Lilly and Company, 1, 2, Ethismos, 1, 2, Eupraxia, 1, 2, Glenmark, 1, 2, Gloriana, 1, 2, Grace, 1, 2, Hope, 1, 2, Immune, 1, 2, Lotus, 1, 2, Mainstay, 1, 2, Merck, 1, 2, Neumentum, 1, 2, Neurana, 1, 2, NeuroBo, 1, 2, Novaremed, 1, 2, Novartis, 1, 2, Olatec, 1, 2, OliPass, 1, 2, Pfizer, 1, 2, Phosphagenics, 1, 2, Quark, 1, 2, Reckitt Benckiser, 1, 2, Regenacy, 1, 2, Relmada, 1, 2, Sangamo, 1, 2, Sanifit, 1, 2, Scilex, 1, 2, Semnur, 1, 2, SIMR Bio, 1, 2, SK Life Sciences, 1, 2, Sollis, 1, 2, SPRIM, 1, 2, Teva, 1, 2, Theranexus, 1, 2, Trevena, 1, 2, Vertex, 1, 2, Vizuri, 1, 2; **D. Turk**, AccelRx, 2, Eli Lilly and Company, 2, Flexion, 2, GlaxoSmithKline, 2, Pfizer, 2; **J. Markman**, Trigemina, 2, Editas Medicine, 2, Plasma Surgical, 1, 2, Novartis, 1, 12,

Data safety monitoring board, Allergan, 1, 12, Data safety monitoring board, Clexio Biosciences, 1, Flexion Therapeutics, 1, Quark Pharmaceuticals, 1, Quartet Medicine, 1, Collegium Pharmaceutical, 1, Purdue Pharma, 1, Biogen, 1, Aptinyx, 1, Nektar, 1, Grünenthal, 1, Eli Lilly and Company, 1, Depomed, 1, Janssen, 1, Teva Pharmaceutical Industries, 1, KemPharm, 1, Abbott Laboratories, 1, Chromocell, 1, Convergence Pharmaceuticals, 1, Inspirion, 1, Pfizer, 1, Sanofi, 1, Daiichi Sankyo, 1, Trevena, 1; **D. Williams**, Swing Therapeutics, Inc, 2, Community Health Focus Inc, 2; **A. Bushmakin**, Pfizer Inc, 3, 11; **J. Hall**, Eli Lilly & Co, 3, 11; **D. Semel**, Pfizer, 3, 11; **J. Cappelleri**, Pfizer Inc, 3, 11; **R. Yang**, Pfizer Inc., 3, 8, 11.

Abstract Number: 1125

Synovial Perivascular Edema Is Associated with Altered Knee Loading Patterns During Gait in Patients with Medial Compartment-Dominant Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Synovial inflammation and aberrant joint loads are independent risk factors for knee osteoarthritis (OA) incidence and progression. Perivascular edema, the accumulation of fluid around synovial blood vessels

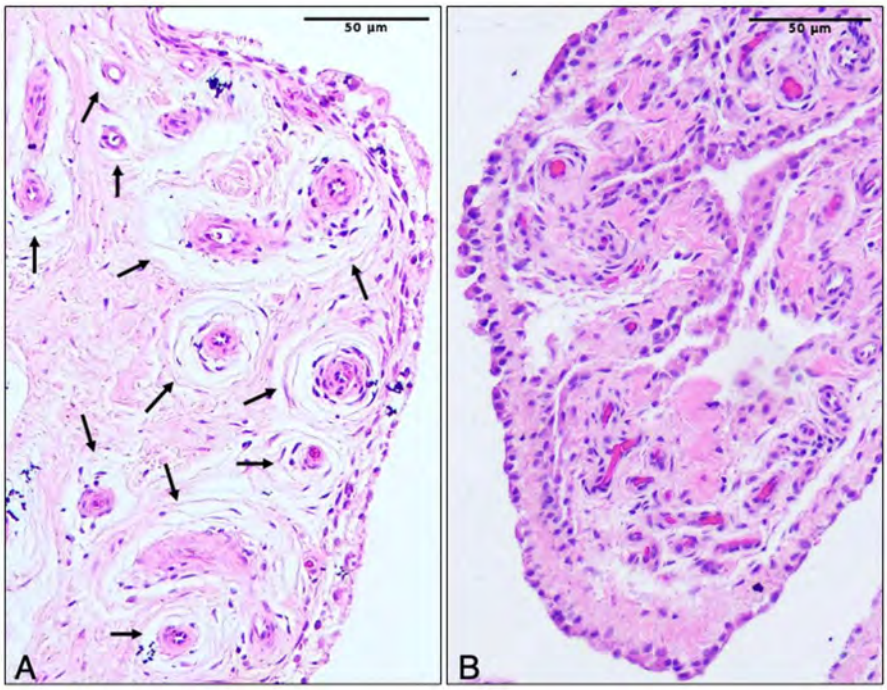

Figure 1. Representative histological images of synovial perivascular edema. Histological evidence of the presence (A) and absence (B) of perivascular edema in synovial biopsies acquired from patients with knee OA. Vessels with perivascular edema are indicated with black arrows.

TABLE 1
Patient Baseline Demographics and Clinical Characteristics ($n = 92$)

Characteristic	Total Cohort ($n = 92$)	Edema ($n = 49$)	No Edema ($n = 43$)
Sex, *n* (%)			
Male	49 (53)	24 (49)	25 (58)
Female	43 (47)	25 (51)	18 (42)
Age, years	66.3 ± 8.5 (41, 85)	64.7 ± 9.9 (41, 85)	68.1 ± 6.2 (53, 80)
BMI, kg/m^2	32.7 ± 5.6 (21.1, 47.2)	32.4 ± 5.8 (21.1, 47.2)	33.1 ± 5.4 (24, 46.3)
Mechanical Axis Angle, degrees	-8.5 ± 4.0 (-18.3, 2)	-8.8 ± 3.9 (-15.2, 0.1)	-8.2 ± 4.2 (-18.3, 2)
Kellgren and Lawrence Grade, *n* (%)			
1	1 (1)	-	1 (2)
2	2 (2)	1 (2)	1 (2)
3	32 (35)	17 (35)	15 (35)
4	57 (62)	31 (63)	26 (61)
Medial OARSI Joint Space Narrowing Grade, *n* (%)			
0	-	-	-
1	4 (4)	1 (2)	3 (7)
2	20 (22)	10 (20)	10 (23)
3	68 (74)	38 (78)	30 (70)
Lateral OARSI Joint Space Narrowing Grade, *n* (%)			
0	53 (59)	31 (64)	22 (52)
1	29 (32)	13 (26)	16 (38)
2	5 (5)	4 (8)	1 (3)
3	4 (4)	1 (2)	3 (7)
Histological Measures of Synovial Inflammation			
Perivascular Edema	0.63 ± 0.56 (0, 2.6)	1.04 ± 0.45 (0.5, 2.6)	0.16 ± 0.17 (0, 0.4)
Synovial Lining Thickness	0.80 ± 0.68 (0, 3)	0.86 ± 0.68 (0, 3)	0.74 ± 0.68 (0, 2.6)
Sub-synovial Infiltration	1.13 ± 0.70 (0, 3)	1.11 ± 0.61 (0, 2.6)	1.15 ± 0.80 (0, 3)
Fibrin Deposition	0.87 ± 0.24 (0.2, 1.4)	0.90 ± 0.21 (0.2, 1.4)	0.84 ± 0.27 (0.2, 1.2)
Vascularization	2.04 ± 0.78 (0, 3)	2.37 ± 0.51 (1.2, 3)	1.64 ± 0.86 (0, 3)
Fibrosis	1.22 ± 0.58 (0, 2.6)	1.21 ± 0.57 (0, 2.6)	1.23 ± 0.60 (0.2, 2.6)

Mean ± SD (minimum, maximum) or n (%)
BMI = body mass index, OARSI = osteoarthritis research society intentional

(Figure 1), is an important component of synovial inflammation in OA. Altered joint loading is hypothesized to contribute to synovial inflammation in OA and may provide sufficient physiological stress to induce perivascular edema. Our objective was to investigate the association between synovial perivascular edema and surrogate measures of knee load during walking in patients with knee OA and medial compartment joint space narrowing.

Methods: Patients undergoing total knee arthroplasty or high tibial osteotomy for symptomatic, radiographic knee OA based on the American College of Rheumatology Classification Criteria, and neutral to varus alignment participated in this cross-sectional study. All participants underwent 3D gait analysis before surgery. Synovial biopsies were obtained intra-operatively for histopathological assessment of perivascular edema (presence/absence). We investigated the association between external knee moments (sagittal, frontal, and transverse planes) and the presence of synovial perivascular edema using a series of multivariate linear regression and polynomial mixed-effects regression models, while adjusting for age, sex, BMI, and gait speed.

Results: Our cohort was composed of 92 patients with complete gait and histopathological data (Table 1). The presence of perivascular edema was associated with lower peak knee flexion moment (β= -7.72 Nm [95%CI -14.18, -1.27]) and greater peak knee extension moment (β= -8.08 Nm [95%CI -15.26, -0.89]). Mixed-effects polynomial regression identified that patients with edema demonstrated higher knee adduction moments between 16-74% of stance (Figure 2A), and lower knee flexion moments from 15-92% of stance (Figure 2B). The largest differences in knee moments during walking between patients with vs. without perivascular edema occurred at 33% of stance for knee adduction (β= 6.87 Nm [95%CI 3.02, 10.72]), and 60% of stance for knee flexion (β = -10.80 [95%CI -16.20, -5.40]).

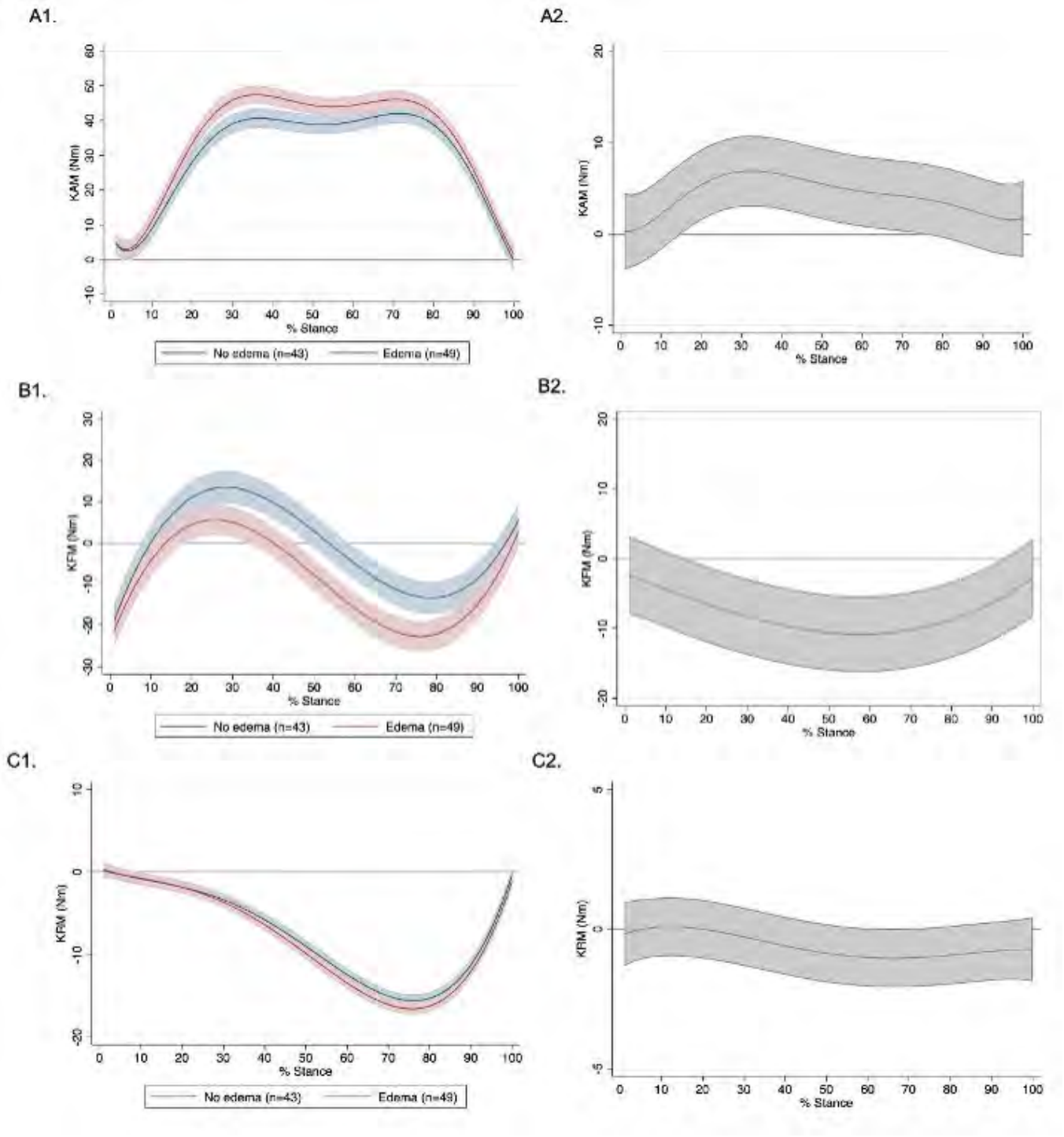

Figure 2. Marginal effects and contrasts for external knee moments over 100% of stance phase in patients with perivascular edema and no perivascular edema. Marginal effect estimates (± 95% CIs) for external knee moments by group are shown in left panels (A1-C1) and marginal contrasts (± 95% CIs) for external knee moments between patients with perivascular edema (n=49) and no perivascular edema (n=43) are shown in the right panels (A2-C2). Separate graphs for A) knee adduction moment (KAM), B) knee flexion-extension moment (KFM), and C) knee external-internal rotation moment (KRM). No perivascular edema is represented in blue and perivascular edema is represented in red. No perivascular edema is the reference group for the marginal contrasts (right panels: A2-C2); therefore, along stance phase, where the 95% CIs no longer includes 0, indicates a significant difference between groups.

Conclusion: Although causal inference is not possible, the association of synovial perivascular edema with increased gait-based proxy measures of knee loading throughout all phases of stance supports the hypothesis that abnormal

joint biomechanics contribute to synovial inflammation in knee OA. Future research is needed to identify direct or indirect mechanisms linking altered joint loading to the development of synovial perivascular edema.

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Abstract Number: 1126

Synovial Cell Dysfunction in Obese Patients May Contribute to Poor Outcomes in Knee Osteoarthritis

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SESSION INFORMATION
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Background/Purpose: Obesity is a major risk factor for poor outcomes in knee osteoarthritis (OA) and may involve both mechanical and physiological stresses on joint tissues. In the synovium, macrophages and fibroblasts are important for maintaining joint homeostasis and adaptive responses to joint stressors. However, the impact of obesity on synovial cellular mechanisms are not well understood. Our objectives were 1) to investigate the association of obesity and synovial histopathological features, and 2) to explore the effect of obesity on synovial cell gene expression in people with knee OA.

Methods: Patients (n=107) diagnosed with clinical knee OA based on the American College of Rheumatology (ACR) criteria were included in this cross-sectional analysis. All patients had severe symptoms and radiographic damage (KL grade 3 or 4), and were undergoing surgery for knee OA. Lateral suprapatellar synovial tissue biopsies were obtained during surgery. Routine synovial histopathology was scored (grade 0-3; None-Severe) in six domains. Multivariate linear regression was used to evaluate the association between median histopathology component scores and BMI, while adjusting for age and sex. Single cells dissociated from whole synovium biopsies were sorted into CD14+ (macrophage/monocyte) and CD90+ (stromal) cell compartments for RNA isolation and sequencing. Quantification of genes was performed in featureCounts and DESeq2 was used to normalize counts. Gene set enrichment was assessed using mSigDB Hallmark gene sets between patients with BMI < 30kg/m^2 (n=7) and BMI >35kg/m^2 (n=6).

Results: Elevated BMI was associated with lower median synovial vascularization (β = -1.35, [95%CI -2.43, -0.27]) and fibrin deposition (β = -3.80, [95%CI -6.98, -0.62]) histopathology scores. In normal to overweight patients (BMI < 30kg/m^2), CD14+ macrophage gene expression showed significant enrichment scores for immune cell signaling (*e.g*. TNF-α signaling, IFN-γ and IFN-α response, IL6/JAK/STAT3 signaling) and cell metabolism pathways (*e.g*. fatty acid metabolism, adipogenesis, oxidative phosphorylation, mTOR signaling). CD90+ stromal cell gene expression also showed significant enrichment scores for response to pro-inflammatory signaling pathways and cell metabolism pathways. In obese patients (BMI >35kg/m^2), synovial macrophage and stromal cell compartments both showed enrichment of cell stress and degenerative pathways (*e.g*. p53 pathway, unfolded protein response, apoptosis, hypoxia, epithelial-mesenchymal transition, hedgehog signaling, Wnt/β-catenin signaling, TGF-β signaling).

Conclusion: Obesity was associated with reduced signs of inflammation in synovial tissues (vascularization and fibrin), and with less inflammatory signaling, impaired cellular metabolism, and greater cellular stress in synovial macrophages and stromal cells. Our results suggest synovial inflammation and vascularization may be adaptive responses to OA-related joint stresses, and that obesity may impair these adaptive synovial processes.

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Abstract Number: 1127

Synovial Fluid Cytokines, Chemokines, and MMPs in Osteoarthritis Patients with Knee Pain Compared to RA Patients and Normal Knees

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SESSION INFORMATION
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Background/Purpose: A major limitation of synovial fluid (SF) biomarker studies in osteoarthritis (OA) has been difficulty in obtaining SF (SF) in patients with small effusions. There is growing evidence that osteoarthritis is not simply a degenerative process but rather cartilage loss is associated with low grade inflammation which can damage chondrocytes and the extra cellular matrix. There is also little information on WBC counts, or the levels of cytokines, MMPs and other proteins in SF from normal knees. To compare differences, a panel of 16 protein biomarkers was measured in knee SF from osteoarthritis (OA) patients, rheumatoid arthritis (RA) patients and normal knees.

Methods: SF was obtained prior to an intra-articular therapeutic injection or a diagnostic arthrocentesis from 21 OA, 27 RA patients as well as 3 normal subjects, using ultrasound (US) guidance and an external pneumatic compression device. All subjects were consented to have remaining SF placed into an IRB approved SF biomarker research protocol. RA patients were categorized as active (n= 20) or controlled (n= 7) disease based upon their SF white blood cell counts (> or < 300 cells/mm^3). Samples were cryopreserved and analyzed by multiplex fluorescent bead assays (Luminex) within 60 minutes of aspiration. Between group differences were identified using ANOVA on log10 transformed concentrations with p values adjusted for multiple testing.

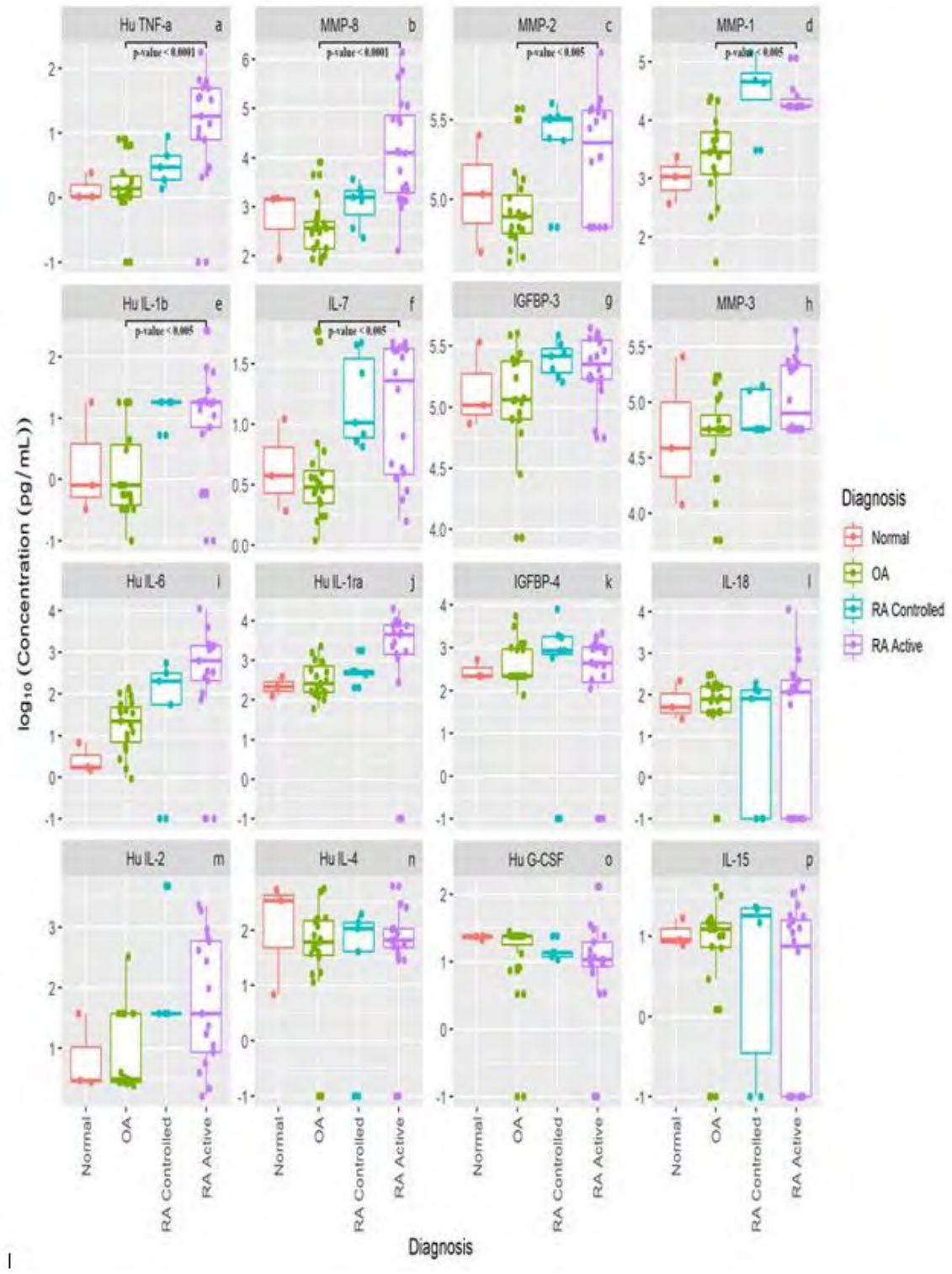
Results: The demographic and clinical features from the 4 groups of subjects are presented in Table 1 including age, gender, BMI, serology, SF WBC counts and drugs taken at the time of knee aspiration. The SF log 10 concentrations of each of these 16 proteins from the 4 groups of subjects are presented in Figure 1. The first 6 panels display p values differences between Active RA and PA patients. Six of the biomarkers were significantly higher in SF from active RA compared to OA (TNF –alpha, IL-1 beta, IL-7, MMP-1, MMP-2, MMP 3) whereas none of the other 10 cytokines, chemokines, MMPs and other proteins (IGFBP-3, MMP-3, IL-6, IL-1ra, IGFBP-4, IL-18, IL-2, IL-4, G-CSF and IL-15) were significantly deferent between OA and Active RA patients. The lack of statistical differences in some of these

	RA active	RA controlled	OA	Normal
Number of Subjects	20	7	21	3
Age Range (years)	33-75	49-78	39-88	44-68
Mean Age	55	63	63	57
Gender (F vs M)	15(75%)/5(25%)	7(100%)/0(0%)	11(52%)/10(48%)	2(66%)/1(33%)
BMI				
Range	20-35	17-37	23-41	21-24
Mean	26	27	30	22
Number on Prednisone, DMARD or Biologic	11 (58%)	6(86%)	2 (9 %)	0
Prednisone	6 (32%)	1 (14%)	0	0
Infliximab	3 (16%)	0	0	0
MTX	2 (11%)	2 (29%)	0	0
HCQ	3 (16%)	3 (43%)	1	0
Rituximab	2 (11%)	1 (14%)	0	0
Tocilizumab	1 (5%)	1 (14%)	0	0
Sulfasalazine	1 (5%)	0	0	0
Etanercept	1 (5%)	0	0	0
Adalimumab	1 (5%)	0	0	0
Golimumab	0	1 (14%)	0	0
+ RF > 14	7 (35%)	6(86%)	ND	ND
+ CCP > 20	10 (50%)	6 (86%)	ND	ND
SF WBC (cells/mm3)				
Range	331-65,000	8-270	0-260	0
Mean	9,620	85	131	0

Demographics and immunomodulatory drug use among patients with OA, RA active, RA controlled and normal subjects

proteins is most likely due to the large variance in levels from several individual patients and possibly due to medications taken at the time of aspiration as listed in Table 1. SF MMP-8 levels was the only protein which correlated with WBC counts ($p < 0.001$).

Conclusion: The fact that only 6 of 16 proteins were significantly higher in SF from Active RA patients compared to those with OA is additional evidence that a pro inflammatory process in OA may lead to further cartilage loss in additional to mechanical factors and genetic predisposition. The results of this small study suggest that normal knee SF may not have any WBCs and that IL 4 as well as other cytokines and even MMPS might be important in maintaining cartilage homeostasis. SF collection using US guidance with external compression combined with a multiplex biomarker panel may help distinguish clinical subtypes and enhance development of disease modifying drugs for OA.



Synovial fluid cytokine, chemokine, MMP and other proteins levels from patients with OA compared to patients with RA active, RA controlled and normal subjects.

Disclosure: R. Meehan, Fidia Pharma USA, 5; **E. Regan**, Fidia Pharma, 5; **E. Hoffman**, Fidia Pharma USA, 5; **M. Wolff**, Fidia, 5; **M. Gill**, fidia pharma USA, 5; **J. Crooks**, Fidia Pharma USA, 5; **P. Parmar**, None; **R. Scheuring**, None; **J. Hill**, None; **k. Pacheco**, None; **V. Knight**, None.

Abstract Number: 1128

Inter-relationships Between Multiple Joint Osteoarthritis and Collagen Biomarkers in Men: The Johnston County Osteoarthritis Project

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Background/Purpose: To determine inter-relationships between blood-based collagen formation and degradation biomarkers and multiple joint osteoarthritis (MJOA) phenotypes in a community-based cohort.

Methods: Data were from Johnston County OA Project participants with baseline (BL, T1/T1*) and follow-up (FU, T2) data, initially selected based on available knee radiographs scored for Kellgren-Lawrence Grade (KLG), and subsequently analyzed for radiographic MJOA outcomes including MJOA-1 (≥1 IP node and ≥2 other sites), MJOA-3 (≥5 joint sites), and MJOA-8 (≥3 joint sites, doi: 10.1016/j.semarthrit.2018.10.001).

Table 1. Description of 3 MJOA types, age, BMI, and biomarkers by clusters derived from multilevel functional principal components analysis among MEN

	Cluster1 *N=109*	Cluster2 *N=43*	Cluster3 *N=64*
MJOA subtypes			
MJOA-1 (N, %)	49 (45%)	15 (35%)	21 (33%)
MJOA-3 (N, %)	57 (52%)	2 (5%)	20 (31%)
MJOA-8 (N, %)	84 (77%)	11 (26%)	37 (58%)
Baseline variables and Biomarker levels (T1)			
Age, years (SD)	66.4 (7.6)	52.3 (3.0)	61.2 (6.3)
BMI, kg/m^2 (SD)	27.7 (2.8)	30.5 (2.5)	36.2 (3.3)
C1M	33.0 (39.9)	29.0 (16.5)	29.7 (17.0)
C2M	0.43 (0.19)	0.43 (0.13)	0.45 (0.26)
C3M	9.2 (3.03)	9.4 (2.1)	9.4 (2.6)
CRPM	7.6 (2.6)	7.1 (2.4)	6.6 (2.5)
PRO-C3	16.0 (13.3)	13.3 (4.6)	14.2 (7.2)
PRO-C6	9.5 (4.2)	9.3 (3.2)	10.6 (9.4)
Col10neo	3349.6 (1153.9)	3616.4(1013.5)	3196.1(919.0)
Biomarker levels at Follow-up (T2)			
C1M	29.8 (16.6)	44.4 (44.6)	31.6 (14.5)
C2M	0.42 (0.17)	0.44 (0.15)	0.45 (0.27)
C3M	9.4 (3.6)	10.5 (3.5)	9.9 (3.6)
CRPM	7.2 (2.9)	7.5 (2.4)	7.2 (2.6)
PRO-C3	17.3 (14.0)	15.9 (13.0)	16.5 (8.1)
PRO-C6	10.1 (4.6)	9.0 (3.7)	12.0 (10.5)
Col10neo	3576.5(1133.6)	3556.4(876.9)	3440.6(1271.0)

MJOA:multiple joint osteoarthritis; BMI:body mass index; MJOA-1: ≥1 IP node and ≥2 other sites; MJOA-3: ≥5 joint sites; MJOA-8: ≥3 joint sites; SD: standard deviation; see text for biomarker definitions.

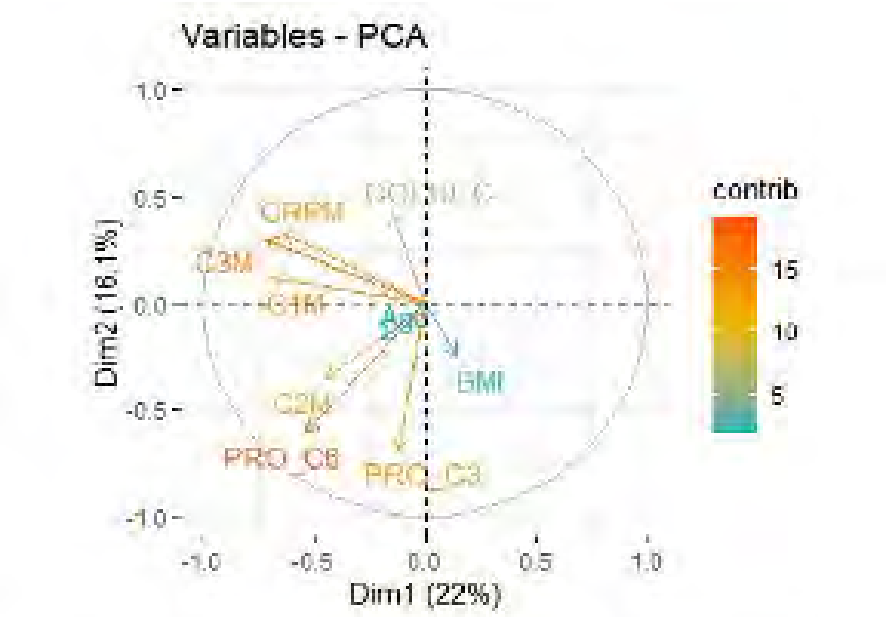

Figure 1. The loadings describe how much each variable contributes to a particular principal component (positive or negative). PC1 (Dim1) and PC2 (Dim2) explain 22% and 16% of variation among participants, respectively.

Serum biomarkers measured included: neo-epitopes of MMP mediated type I, II, and III collagen degradation (C1M, C2M, and C3M, respectively); neo-epitope of MMP-1 and -8 mediated degradation of C-reactive protein (CRPM); N-terminal pro-peptide of C3 (PRO-C3); c-terminal of released C5 domain C6 α3 chain (PRO-C6); and c-terminus of collagen type X release of C10 from cartilage (Col10neo). These represent putative markers of: fibrosis (PRO-C3, -C6); inflammation (C1M, C3M, CRPM); and cartilage degeneration (C2M, Col10neo). Biomarker values were transformed (Box-Cox) and standardized for scale. Multilevel principal component analysis (mPCA) was performed using 7 biomarkers, age, and BMI at BL and FU. Cluster analysis based on PCA-transformed data was used to search for and descriptively analyze MJOA phenotypes.

Results: Results for 225 men are reported; relationships between biomarkers and MJOA were not observed in women (n=503). At BL, C1M, C3M and CRPM clustered together, as did PRO-C3, PRO-C6 and C2M (**Fig 1**); Col10neo was distinct. MPCA identified 3 clusters (**Fig 2**). Cluster 1 had the highest frequencies of MJOA-1, -3, and -8. Cluster 2 had a very low frequency of MJOA-3 and lower frequencies of both MJOA-1 and -8 compared with Cluster 1 (**Table 1** and **Fig 2**). Clusters 2 and 3 demonstrated similar frequencies of MJOA-1. Cluster 3 had intermediate frequencies of MJOA-3 and -8 compared with Clusters 1 and 2.

Men in Cluster 1 were older with a lower BMI compared with the other clusters. This cluster was characterized by higher BL C1M which decreased at FU, higher PRO-C3 at BL and FU, and an increase in Col10neo from BL to FU (i.e., higher but declining inflammation, higher fibrosis, and increasing cartilage degeneration). Men in Cluster 2 were the youngest with intermediate BMI. This cluster had the lowest BL C1M and PRO-C3, which increased at FU; this cluster had the highest C1M at FU (i.e., increasing inflammation). Men in Cluster 3 were of an intermediate age with a much higher BMI. This group had a low BL CRPM and Col10neo, which increased at FU; they also had the highest FU PRO-C6 levels (i.e., low inflammation, increasing cartilage breakdown, and high fibrosis).

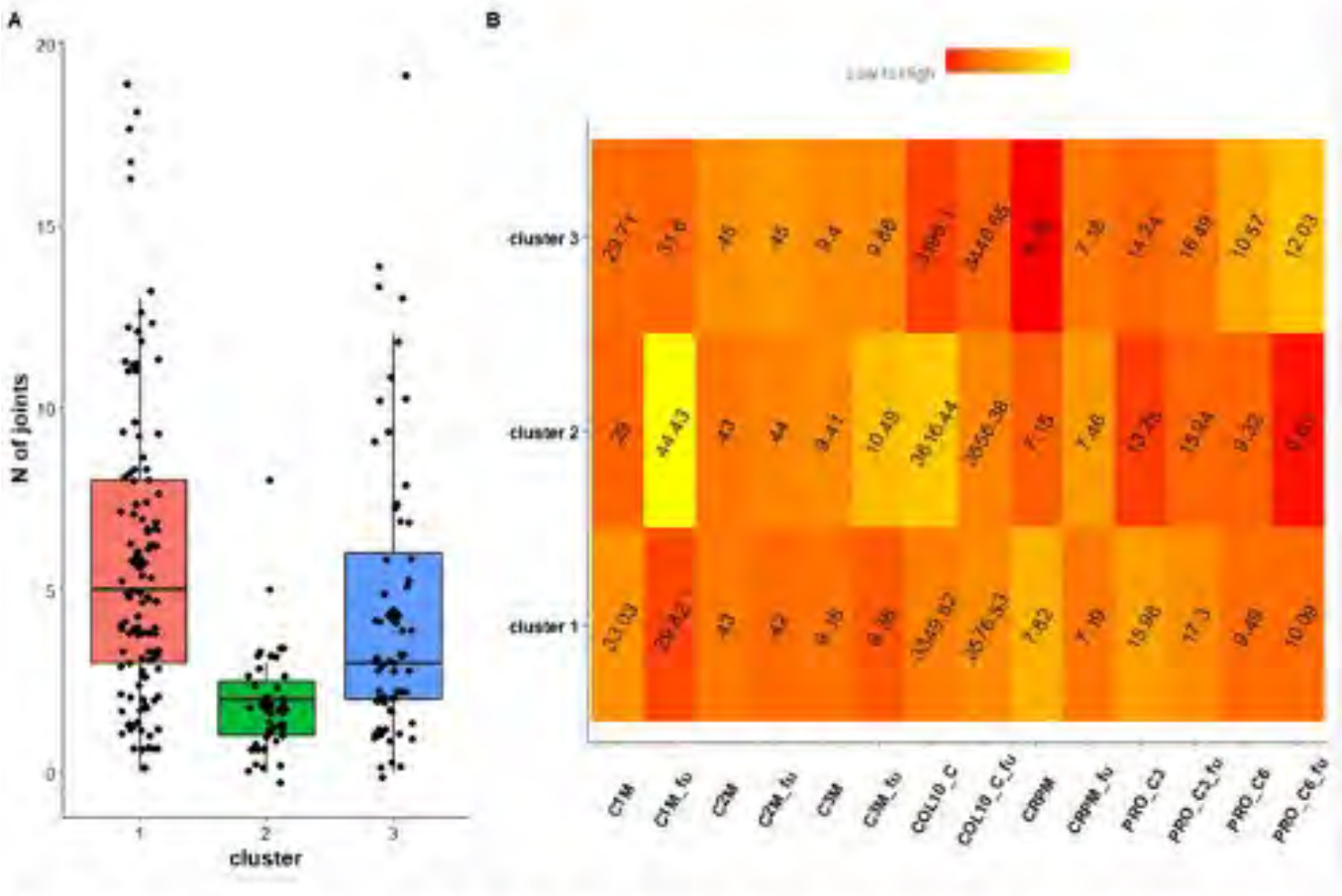

Figure 2. A: Number of joints with OA (KLG>=2) in 225 men from 3 clusters identified by mPCA. The boxplots show the mean (◇) and median (horizontal line drawn within the box); the dots are individual data points. The "whiskers" (the lines extending parallel from the boxes) indicate variability outside the upper and lower quartiles. **B:** heat map showing mean biomarker values in 3 clusters at baseline and follow-up (_fu).

Conclusion: This exploratory analysis utilized combinations of collagen and MMP-mediated degradation biomarkers at 2 time points, identifying clusters in men but not women, characterized by different frequencies of MJOA involvement at FU. This work highlights the importance of sex in OA and may provide novel insights into specific biomarkers and their change in different phenotypes of MJOA.

Disclosure: A. Nelson, Lilly, 1; **L. Arbeeva**, None; **D. Lascelles**, None; **J. Renner**, None; **Y. Golightly**, None; **M. Karsdal**, Nordic Biosciences, 3, 11; **A. Bay-Jensen**, Nordic Biosciences, 3, 11; **R. Loeser**, None.

Abstract Number: 1129

Cost-effectiveness of Weight Loss Interventions Prior to Total Knee Replacement for Patients with Advanced Knee Osteoarthritis and Class III Obesity

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SESSION INFORMATION
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Background/Purpose: Class III obesity, defined by BMI >40kg/m^2, is linked to increased risk of complications post total knee replacement (TKR). This has led to recommendations for weight loss before TKR and even institutional BMI cutoffs for TKR. Surgical and nonsurgical weight loss (NSWL) programs show variable efficacy, but the cost-effectiveness of alternative weight loss interventions prior to TKR has received little study.

Methods: We used the Osteoarthritis Policy Model, a validated widely published microsimulation of knee osteoarthritis (OA), to evaluate the cost-effectiveness of weight loss interventions for patients with advanced knee OA and class III obesity planning to undergo TKR. We considered five strategies: 1) no weight loss intervention, no TKR; 2) immediate TKR; 3) NSWL+TKR; 4) Laparoscopic Sleeve Gastrectomy (LSG)+TKR; 5) Roux-En-Y Gastric Bypass (RYGB)+TKR. In strategies 3-5, patients were evaluated for TKR one year after weight loss intervention start. We followed subjects in the model until death, recording quality-adjusted life years (QALYs) accrued, lifetime medical costs, and TKR utilization. We examined a cohort with WOMAC pain consistent with literature pre-TKR pain (WOMAC Pain (0-100): mean 54, SD 15). We used national databases and published data to estimate weight loss strategy efficacy (initial BMI lost: NSWL 0-20%; LSG 18-38%; RYGB: 23-47%), TKR efficacy (mean WOMAC Pain reduction: 16-38 points, stratified by pre-operative WOMAC pain), surgical costs (LSG $16,099; RYGB $18,042; TKR $18,642-$19,300, stratified by BMI), and costs and risks of complications and mortality attributable to LSG, RYGB, and TKR.

Table. Cost-effectiveness of weight loss interventions prior to TKR in patients with advanced KOA and Class III obesity

Strategy	QALE*	Costs	ICER ($/QALY)	% TKR utilization
No intervention	9.19	$337,010	--	0%
NSWL → TKR	10.03	$358,250	Extended dominance**	91.0%
Immediate TKR	10.05	$358,563	Extended dominance**	99.2%
LSG → TKR	10.86	$381,568	Extended dominance**	85.5%
RYGB → TKR	11.14	$386,139	$25,100	85.4%

*QALE: Quality-adjusted life expectancy
**Extended dominance indicates interventions that have an ICER greater than that of a more effective intervention. An intervention with a higher QALE and a lower ICER is preferred, as there is a greater improvement in QALE with a lower cost per QALY.

In sensitivity analyses we varied: cost of health consequences of class II and III obesity, BMI cutoff and pain thresholds for TKR eligibility, LSG/RYGB pain efficacy, likelihood of complications from LSG/RYGB, and maximum years weight loss is maintained following LSG/RYGB. We discounted costs and QALYs at 3%/year and conducted analysis from a healthcare perspective. We calculated incremental cost-effectiveness ratios (ICERs) as the ratio of change in costs to change in QALYs for competing strategies in 2019 USD.

Results: Among patients with advanced knee OA and class III obesity, undergoing RYGB followed by TKR, if eligible, added 1.95 QALYs and $49,129 in medical costs in comparison to no interventions, resulting in an ICER of $25,100/QALY (Table). All other weight loss interventions were less economically efficient. Weight loss affected TKR usage; the percent of patients undergoing TKR ranged from 99.2% with immediate TKR (< 100% due to contraindications and mortality), 91.0% with NSWL, 85.5% with LSG, and 85.4% with RYGB (Table). ICERs were sensitive to the number of years weight loss was sustained, costs of obesity, LSG complication rates, and LSG/RYGB pain efficacy.

Conclusion: RYGB prior to TKR is a cost-effective strategy for addressing knee pain and obesity in patients with advanced knee OA and Class III obesity. TKR alone and NSWL or LSG prior to TKR are less economically efficient options compared to RYGB prior to TKR.

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Abstract Number: 1130

Osteoarthritis Patients Feel Their Tissue Remodeling

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis (OA) is a chronic disease characterized by pain and disability. Central to the revised FDA guidelines for the approval of a disease modifying OA drug are patient reported outcomes (PROs). There is a need in drug development to understand how biomarkers of tissue remodeling objectively relate to PROs, or even predict changes in PROs. Recently, it was shown that levels of the CRP metabolite (CRPM), but not CRP, with concentrations of above 9 ng/mL were prognostic of knee OA progression assessed by X-ray. Moreover, that 1/3 of OA patients had levels of CRPM like that of RA patients. While several biomarkers of tissue modeling correlate to disease activity score in RA, this information is missing in OA. The joint comprises of multiple connective tissues which consist of collagen such as type I, II, III and IV. Biomarkers have been developed which measures the remodeling of collagens. We hypothesis that such markers may provide the missing link between OA pathology and PROs. We differentiated an OA population in high and low CRPM and investigate the relationship to PROS to serological biomarker of tissue turnover.

Methods: 111 knee OA patients, 62% women, from the placebo arm of a phase III study with knee OA were included: mean (SD) age, 32(10); mean (SD) BMI, 27(4); NSAID users, 32%; and radiographic OA (KL≥2) 68%. PROs were: VAS_{pain} and WOMAC total, pain, stiffness, and function at baseline (BL). 19 healthy individuals were included as refer-

ence. Median (IQR) were 39 (13-69) and 37 (13-52) for BL VAS_{pain} and $WOMAC_{pain}$. Eight serum biomarkers of type I, II, III and IV collagen degradation (C1M, C2M, C3M, C4M) and formation (PRO-C1, PRO-C2, PRO-C3 and PRO-C4) as well as two inflammatory biomarkers CRPM and hsCRP, were assessed. Log2 transformed data was adjusted for race, gender, age, and BMI.

Results: None of the collagen formation or degradation markers were on average higher or lower in OA than healthy controls (adjusted for age, gender, race, and BMI). No correlations between collagen markers and PROs were observed. We confirmed the previous identified cut-off and found an AUC of 0.61 (p=0.078, cut-off of 8.7). In patients with low CRPM: PRO-C2 was positively correlated with VASpain (r=0.53) WOMAC total and pain (r=0.22) and PRO-C4 negatively with WOMACpain (r=-0.26). In patients with high CRPM: PRO-C4 was positively correlated with VASpain (r=0.29), WOMACtotal, pain and stiffness (r=0.28, 0.3 and 0.22). C1M was correlated with VASpain (r=0.20), WOMACtotal, pain, stiffness and function (r=0.32, 0.24, 0.29, 0.30). C2M was negatively correlated with VASpain (r=-0.28), WOMACtotal, pain, stiffness and function (r=-0.49, -0.43, 0.44, -0.43). C3M was also negatively correlated with VASpain (r=-0.44), WOMACtotal, pain, stiffness and function (r=-0.51, -0.42, -0.55, -0.49).

Conclusion: Biomarkers of tissue remodeling did not correlate to PROs in the undifferentiated OA population. In contrast, the two distinct subpopulations of ether low or high CRPM had multiple correlation between tissue turnover and PROs. The data provide the first insights into objective tissue turnover biomarkers and PROs, which is essential for successful drug development, and in the understanding of the processes in the OA joint causing pain.

Disclosure: A. Bay-Jensen, Nordic Biosciences, 3, 11; **Y. He**, None; **C. Thudium**, Nordic Bioscience, 3; **M. Karsdal**, Nordic Bioscience, 3, 11.

Abstract Number: 1131

Interleukin 6 Concentration in Synovial Fluid and Its Clinical Significance

Ivars Veckalns and Anna Mihailova, Riga Stradins University, Riga, Latvia

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory arthritis (IA) treated with disease modifying antirheumatic drugs lead to secondary osteoarthritis (OA) due to inflammation, aging, and other factors. Inflammatory arthritis can start in middle-aged adults with OA. Discrimination between these two conditions can pose a significant challenge, especially when there are no makers for inflammatory arthritis.

Table 1. Primary diagnosis and final diagnosis crosstabulation

			Final diagnosis		Total (%)
			OA	IA	
Primary diagnosis	OA	Count (%)	13 (18.8%)	5 (7.2%)	18 (26.1%)
	IA	Count (%)	20 (29.0%)	31 (44.9%)	51 (73.9%)
Total (%)			33(47.8%)	36 (52.2%)	69 (100%)

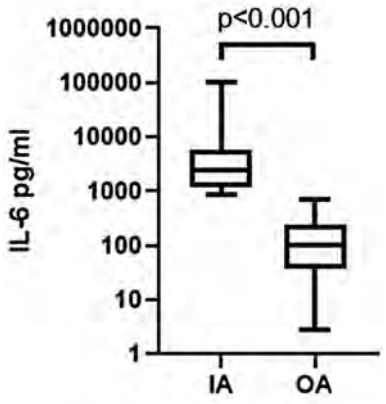

Figure 1. IL-6 concentration comparison in OA and IA patient groups.

The aim is to clarify the importance of IL6 concentration in synovial fluid for treatment purposes.

Methods: Sixty-nine patients with symptomatic swelling of the joints were undergone aspiration of synovial fluid. All patients received intraarticular steroid injections for therapeutic purposes. Then decision about treatment was depended on the IL6 concentration level in synovial fluid. IL6 concentration was determined by immunochemical luminescence method. Patients with low IL6 concentration continued therapy as OA or secondary OA patients with physiotherapy, without DMARD escalation, but high IL6 concentration DMARD treatment was prescribed or adjusted.

Primary diagnosis was made based on classification criteria for certain diseases (RA, PsA, AS, OA), and the conclusion was based on clinical presentation, current lab results, and IL6 level in synovial fluid.

Results: Primarily 51 patients were classified as having IA (AS-1; RA-1; Undifferentiated IA-2; JIA-2; ReA-32; PsA-7; RA-6). 18 patients were classified as having OA. After IL6 analysis 36 patients were re-classified as having IA (Undifferentiated IA-1; JIA-1; ReA-24; PsA-4; RA-6) and 33 patients were re-classified as having OA. Out of these 33 OA patients, 20 patients were previously classified as having IA and 5 patients of the 36 IA patient's group were previously classified as having OA. (Table 1). In 33 OA patients, the median IL6 concentration was 100 pg/ml (IQR 41.0 to 204.0). In 36 IA patients, the median was 2430.5 pg/ml (IQR 1277.0 to 5552.0). The Mann-Whitney U test showed a statistically significant difference ($p< 0.001$) between these two groups. (Figure 1). In the 20 patients, primarily diagnosed as IA and then classified as OA, the median IL6 concentration was 75.1 pg/ml (IQR 38.9 to 169.5). In the five patients, primarily diagnosed as OA and then classified as IA, the median IL6 concentration was 1800 pg/ml (IQR 1394.0 to 7738.0). In this group three patient were without any serological and genetic markers for inflammatory arthritis such as RF, anti-CCP, HLA-B27.

Conclusion: IL6 concentration in synovial fluid is different between IA and OA and may be helpful as an additional factor in the decision-making process.

Disclosure: I. Veckalns, None; **A. Mihailova**, None.

Abstract Number: 1132

Association Between Serum Selenium Level and the Prevalence of Osteoarthritis: Data from the Xiangya Osteoarthritis Study

Ning Wang[1], Mingsheng Xie[1], Chao Zeng[2], Tubao Yang[1], Zidan Yang[1], Yilun Wang[1], Jiatian Li[1], Jian Tian[1], Tuo Yang[1] and Guanghua Lei[1], [1]Central South University, Changsha, China (People's Republic), [2]Central South University, Chang Sha, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Osteoarthritis – Clinical Poster III (1118–1134)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

	Tertiles of serum selenium, μg/L			P for trend
	T1 (≤84.95)	T2 (84.96-99.14)	T3 (≥99.15)	
Knee, hip or hand ROA				
Median of serum selenium level, μg/L	77.98	91.51	107.18	-
Number of events	182	154	133	-
OR [a] (95% CI) [b]	1.00 (reference)	0.69 (0.51, 0.93)	0.56 (0.41, 0.75)	0.0002
OR (95% CI) [c]	1.00 (reference)	0.81 (0.58, 1.14)	0.71 (0.50, 1.00)	0.0485
OR (95% CI) [d]	1.00 (reference)	0.80 (0.57, 1.12)	0.69 (0.49, 0.98)	0.0396
Knee ROA				
Median of serum selenium level, μg/L	77.98	91.51	107.18	-
Number of events	102	97	74	-
OR (95% CI) [b]	1.00 (reference)	0.90 (0.65, 1.25)	0.65 (0.46, 0.92)	0.0134
OR (95% CI) [c]	1.00 (reference)	1.01 (0.70, 1.46)	0.79 (0.54, 1.16)	0.2186
OR (95% CI) [d]	1.00 (reference)	0.99 (0.68, 1.43)	0.76 (0.51, 1.11)	0.1522
Hip ROA				
Median of serum selenium level, μg/L	77.98	91.51	107.18	-
Number of events	19	19	11	-
OR (95% CI) [b]	1.00 (reference)	0.98 (0.51, 1.88)	0.56 (0.26, 1.20)	0.1417
OR (95% CI) [c]	1.00 (reference)	1.11 (0.57, 2.15)	0.68 (0.32, 1.48)	0.3514
OR (95% CI) [d]	1.00 (reference)	1.10 (0.56, 2.14)	0.67 (0.31, 1.45)	0.3231
Hand ROA				
Median of serum selenium level, μg/L	77.98	91.51	107.18	-
Number of events	133	107	94	-
OR (95% CI) [b]	1.00 (reference)	0.69 (0.51, 0.95)	0.59 (0.43, 0.82)	0.0015
OR (95% CI) [c]	1.00 (reference)	0.88 (0.61, 1.25)	0.82 (0.57, 1.18)	0.2947
OR (95% CI) [d]	1.00 (reference)	0.86 (0.60, 1.23)	0.79 (0.55, 1.15)	0.2227

ROA, radiographic osteoarthritis; OR, odds ratio; CI, confidence interval.

[a] This analysis used a logistic regression model to obtain the OR.

[b] Crude OR.

[c] Adjusted for age, gender and body mass index.

[d] Adjusted for age, gender, body mass index, smoking status, alcohol consumption, and educational level.

Table 1. Association between serum selenium levels and radiographic knee, hip or hand ROA (1,032 participants)

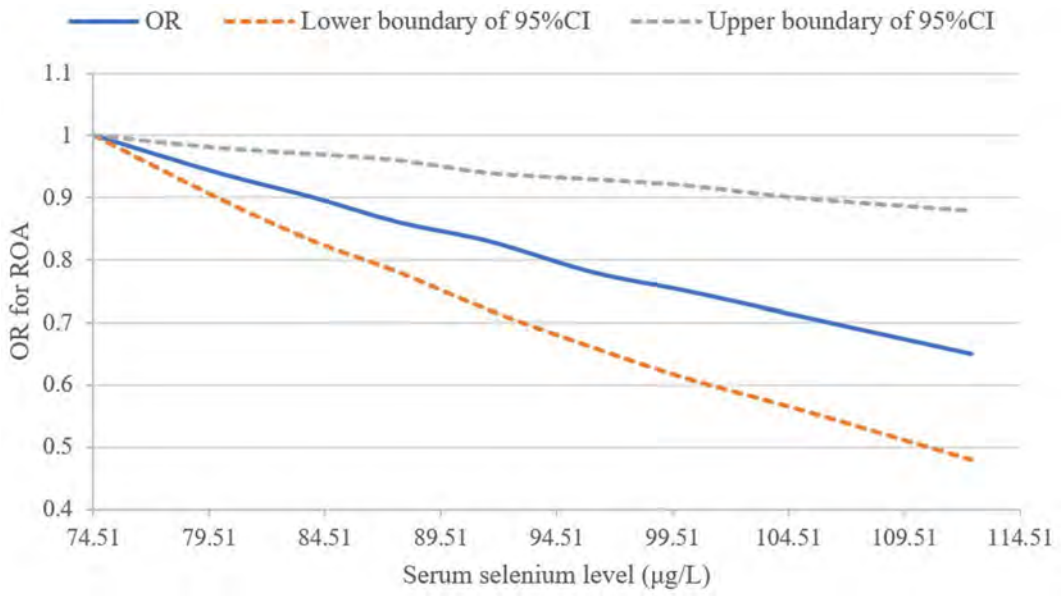

Figure 1. Dose-response relationship between serum selenium level and the odds ratio (OR) for radiographic knee, hand or hip radiographic osteoarthritis (ROA). CI, confidence interval.

Background/Purpose: Selenium plays an indispensable role in the process of antioxidant and antiinflammation. Oxidative stress and inflammation have been hypothesized to be involved in the pathogenesis of cartilage degeneration. We sought to explore the association between serum selenium levels and the prevalence of radiographic osteoarthritis (ROA) in a large population-based study.

Methods: Subjects aged 50 years or older were from the Xiangya Osteoarthritis (XO) Study, a community-based observational study. Serum selenium concentration was measured by inductively coupled plasma-dynamic reaction cell-mass spectrometry. ROA was defined as a Kellgren/Lawrence score ≥ 2 for at least one knee, hip or hand joint. The association between serum selenium levels and ROA were evaluated by conducting logistic and spline regression.

Results: A total of 1,032 participants (women: 52.5%; mean age: 63.1 years; ROA prevalence: 45.4%) were included. Compared with the lowest tertile, odds ratios (ORs) for ROA were 0.69 (95% confidence interval [CI]: 0.51 to 0.93) and 0.56 (95% CI: 0.41 to 0.75) in the second and third tertiles of serum selenium, respectively (P for trend < 0.05) (**Table 1**). Adjusting for potential confounders did not change the results materially. In addition, subjects with lower serum selenium levels had a higher prevalence of OA in a dose-response-relationship manner (P = 0.005) (**Figure 1**).

Conclusion: Subjects with lower levels of serum selenium, even within the normal range, had higher prevalence of ROA in a dose-response relationship manner, suggesting that selenium may have a preventive or therapeutic potential for OA.

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Abstract Number: 1133

The Relation of Serum Urate to Radiographic Knee Osteoarthritis in 2 Cohorts: The ELSA-Brasil MSK and the Original Cohort of the Framingham Heart Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Osteoarthritis – Clinical Poster III (1118–1134)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Hyperuricemia may contribute to the development and/or progression of knee osteoarthritis (OA), based on increased inflammation associated with elevated serum urate (SU). Because hyperuricemia and OA are both associated with obesity, the direction and magnitude of the relation between them need to be thoroughly evaluated, taking the body mass index (BMI) into account. The identification of SU as a modifiable factor in the pathogenesis of OA could lead to the trial use of urate-lowering drugs as potential adjuvant therapy for OA. Therefore, we evaluated the relation of SU to radiographic knee OA (ROA) in two large cohorts unselected for OA, accounting for BMI.

Methods: This was a cross-sectional analysis of the Brazilian Longitudinal Study of Adult Health – Musculoskeletal Study (ELSA-Brasil MSK) cohort, mirroring a previous analysis performed on the original cohort of the Framingham Heart Study (FHS), comparing the results of these two populations. The ELSA-Brasil MSK is an ancillary study of ELSA-Brasil and comprises 2,901 individuals with data on musculoskeletal health at baseline, including knees and hands radiographs. For the present analysis, we selected subjects ≥50 years older. In the ELSA-Brasil MSK, SU was assessed at visit 1 (2008-2010) and ROA at visit 2 (2012-2014); in the FHS, SU was assessed at exams 20 and 21 (1986-1992) and ROA at exam 22 (1990-1994) in original cohort. ROA of each tibiofemoral joint was defined as KL ≥2. SU was categorized as: < 5mg/dL, 5-< 6mg/dL, 6-< 7mg/dL, 7-< 9mg/dL, and ≥9mg/dL. The sex-specific relation of SU to the prevalence of knee ROA was evaluated using logistic regression, adjusted for age and BMI, with generalized estimating equations to account for the correlations of joints within individuals. The same analyses were performed with SU as a continuous variable.

Table 1. Age and body mass index by sex in the two cohorts.

	ELSA-Brasil MSK		Framingham Heart Study original cohort	
	Men N = 972	Women N = 1,124	Men N = 329	Women N = 575
Age, years				
mean (SD)	60.0 (7.1)	59.6 (6.9)	78.8 (4.9)	79.5 (5.4)
range	50 – 78	50 – 79	72 – 99	72 – 101
Body mass index, kg/m²				
mean (SD)	27.0 (4.3)	27.2 (5.0)	25.9 (3.9)	25.0 (4.8)
range	17.3 – 47.9	15.8 – 49.3	18.0 – 43.4	14.0 – 49.6

SD: standard deviation.

Table 2. Relation of serum urate to prevalent radiographic tibiofemoral osteoarthritis.

	N of knees with radiographic OA (%)	Crude OR (95% CI)	Adjusted* OR (95% CI)	P-Value
Serum urate analyzed as categories				
ELSA-Brasil MSK				
Men				
<5 mg/dL	18/236 (7.63)	1.0 (ref)	1.0 (ref)	
5-<6 mg/dL	47/479 (9.81)	1.33 (0.67-2.64)	1.10 (0.55-2.18)	0.792
6-<7 mg/dL	94/574 (16.38)	2.37 (1.25-4.49)	1.71 (0.89-3.27)	0.105
7-<9 mg/dL	77/545 (14.13)	2.00 (1.05-3.84)	1.25 (0.64-2.44)	0.510
≥9 mg/dL	27/108 (25.00)	4.04 (1.84-8.84)	**2.46 (1.09-5.52)**	**0.029**
Women				
<5 mg/dL	159/1230 (12.93)	1.0 (ref)	1.0 (ref)	
5-<6 mg/dL	91/621 (14.65)	1.16 (0.81-1.64)	0.77 (0.53-1.12)	0.179
6-<7 mg/dL	67/287 (23.34)	2.05 (1.37-3.08)	1.22 (0.78-1.88)	0.382
7-<9 mg/dL	29/96 (30.21)	2.89 (1.60-5.24)	1.07 (0.56-2.08)	0.830
≥9 mg/dL	2/8 (25.00)	2.23 (0.29-17.27)	0.95 (0.12-7.34)	0.962
Framingham Heart Study				
Men				
<5 mg/dL	34/165 (20.6)	1.0 (ref)	1.0 (ref)	
5-<6 mg/dL	38/136 (27.9)	1.50 (0.78-2.86)	1.73 (0.88-3.41)	0.114
6-<7 mg/dL	21/128 (16.4)	0.76 (0.37-1.57)	0.88 (0.42-1.83)	0.731
7-<9 mg/dL	23/120 (19.2)	0.92 (0.46-1.82)	0.98 (0.48-2.00)	0.946
≥9 mg/dL	7/16 (43.8)	3.01 (1.16-7.81)	**3.31 (1.28-8.55)**	**0.013**
Women				
<5 mg/dL	112/542 (20.7)	1.0 (ref)	1.0 (ref)	
5-<6 mg/dL	59/208 (28.4)	1.52 (0.96-2.41)	1.31 (0.80-2.14)	0.282
6-<7 mg/dL	39/118 (33.1)	1.90 (1.09-3.29)	1.57 (0.87-2.84)	0.131
7-<9 mg/dL	29/92 (31.5)	1.79 (0.96-3.34)	1.38 (0.67-2.85)	0.377
≥9 mg/dL	4/12 (33.3)	1.92 (0.34-10.70)	1.62 (0.20-13.07)	0.649
Serum urate analyzed continuously				
ELSA-Brasil MSK				
Men	263/1,942 (13.54)	1.23 (1.11-1.37)	**1.12 (1.00-1.26)**	**0.050**
Women	348/2,242 (15.52)	1.33 (1.18-1.50)	1.05 (0.92-1.19)	0.485
Framingham Heart Study				
Men	105/497 (21.1)	1.06 (0.90-1.25)	1.05 (0.88-1.25)	0.576
Women	207/796 (26.0)	1.18 (1.03-1.37)	1.10 (0.93-1.31)	0.268

*Adjusted for age and body mass index. OA: osteoarthritis; OR: odds ratio; CI: confidence interval.

Results: SU and radiographic data were available for 972 men and 1,124 women from the ELSA-Brasil MSK cohort and 329 men and 575 women from the FHS. Of those, 191, 229, 89, and 156 had knee OA, respectively. Age and BMI are shown in Table 1. In both cohorts after adjusting for age and BMI, men with SU ≥ 9 mg/dL had a significantly higher prevalence of knee ROA compared with those with SU < 5 mg/dL: OR 2.46 (CI 1.09-5.52, p=0.029) in the ELSA-Brasil MSK cohort and OR 3.31 (CI 1.28-8.55, p=0.013) in the FHS. In the analyses with SU as a continuous variable, the prevalence of knee ROA among men and women was 1.1 times higher for each mg/dL increment of SU in both cohorts, reaching statistical significance among men from the ELSA-Brasil MSK cohort (Table 2).

Conclusion: There seemed to be a threshold effect of SU to ROA at least among men, although this could not be properly evaluated among women due to the small number of subjects in the female highest stratum of SU.

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01 06 0071.00 RJ). ELSA-Brasil MSK has been supported by CAPES-BR (054/2010), FAPEMIG-BR (APQ-00921-16), and CNPq-BR (42358520169).

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Abstract Number: 1134

Osteoarthritis Risk Is Increased in Patients with Atopic Disease

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Table 1. Baseline characteristics of patients in the Optum cohort.

	Total Cohort (n = 2360247)	Control (n = 2242901)	Asthma (n = 35097)	Atopic Dermatitis (n = 77854)	Asthma and Atopic Dermatitis (n = 4395)
Age in years, mean (SD)	49.6 (15.8)	49.4 (15.9)	53.3 (15.9)	51.4 (15.2)	52.7 (15.4)
Gender, n (%)					
Female	1151625 (48.8)	1080693 (48.2)	21576 (61.5)	46401 (59.6)	2955 (67.2)
Male	1208280 (51.2)	1161880 (51.8)	13518 (38.5)	31442 (40.4)	1440 (32.8)
Unknown	342 (0.0)	328 (0.0)	3 (0.0)	11 (0.0)	0 (0.0)
Race, n (%)					
White	1693183 (71.7)	1604976 (71.6)	25219 (71.9)	59637 (76.6)	3351 (76.2)
Black	216167 (9.2)	207047 (9.2)	3035 (8.6)	5743 (7.4)	342 (7.8)
Asian	114625 (4.9)	109190 (4.9)	1432 (4.1)	3839 (4.9)	164 (3.7)
Hispanic	275190 (11.7)	263609 (11.8)	4678 (13.3)	6473 (8.3)	430 (9.8)
Unknown	61082 (2.6)	58079 (2.6)	733 (2.1)	2162 (2.8)	108 (2.5)
Education, n (%)					
Less than 12th grade	13695 (0.6)	13264 (0.6)	236 (0.7)	172 (0.2)	23 (0.5)
High school diploma	547699 (23.2)	527334 (23.5)	8056 (23.0)	11561 (14.8)	748 (17.0)
Less than bachelor's degree	1292828 (54.8)	1229059 (54.8)	19989 (57.0)	41364 (53.1)	2416 (55.0)
Bachelor's degree or higher	487360 (21.1)	464879 (20.7)	6727 (19.2)	24558 (31.5)	1196 (27.2)
Unknown	8665 (0.4)	8365 (0.4)	89 (0.3)	199 (0.3)	12 (0.3)
Charlson comorbidity score, n (%)					
0-1	2096219 (88.8)	2006137 (89.4)	22820 (65.0)	64140 (82.4)	3122 (71.0)
2-3	186155 (7.9)	168090 (7.5)	7846 (22.4)	9355 (12.0)	864 (19.7)
4-5	45292 (1.9)	39902 (1.8)	2692 (7.7)	2438 (3.1)	260 (5.9)
> 6	32581 (1.4)	28772 (1.3)	1739 (5.0)	1921 (2.5)	149 (3.4)
Years of follow-up, mean (SD)	7.9 (2.5)	7.9 (2.5)	8.2 (2.3)	8.0 (2.3)	9.2 (2.5)
Yearly outpatient visits, mean (SD)	6.3 (8.6)	5.9 (8.3)	12.7 (12.2)	12.5 (11.5)	15.3 (12.7)

SD = standard deviation.

Table 1. Baseline characteristics of patients in the Optum cohort

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Osteoarthritis – Clinical Poster III (1118–1134)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoarthritis (OA) is a highly prevalent disease resulting in joint pain and impaired function. Allergic pathways, including mast cell activation, may play a key role in the pathogenesis of OA.[1] The association between atopic disease and the development of OA is not well understood. The objective of this study was to determine the incidence of OA in patients with atopic disease compared with the general population.

Table 2. Baseline characteristics of patients in the STARR cohort.

	Total Cohort (*n* = 114434)	Control (*n* = 70705)	Asthma (*n* = 11101)	Atopic Dermatitis (*n* = 23855)	Asthma and Atopic Dermatitis (*n* = 8773)
Age in years, mean (SD)	52.4 (16.2)	53.4 (16.4)	54.4 (16.6)	49.8 (15.3)	49.1 (15.4)
Gender, n (%)					
Female	70941 (62.0)	43071 (60.9)	7076 (63.7)	14915 (62.5)	5879 (67.0)
Male	43486 (38.0)	27628 (39.1)	4025 (36.3)	8939 (37.5)	2894 (33.0)
Unknown	7 (0.0)	6 (0.0)	0 (0.0)	1 (0.0)	0 (0.0)
Race, n (%)					
White	67262 (58.8)	42213 (59.7)	7127 (64.2)	12915 (54.1)	5007 (57.1)
Black	4752 (4.2)	2507 (3.5)	688 (6.2)	1037 (4.3)	520 (5.9)
Asian	19754 (17.3)	11557 (16.3)	1268 (11.4)	5373 (22.5)	1556 (17.7)
American Indian/Alaska Native	316 (0.3)	188 (0.3)	33 (0.3)	63 (0.3)	32 (0.4)
Native Hawaiian/Pacific Islander	937 (0.8)	503 (0.7)	97 (0.9)	226 (0.9)	111 (1.3)
Other	14863 (13.0)	9346 (13.2)	1512 (13.6)	2852 (12.0)	1153 (13.1)
Unknown	6550 (5.7)	4391 (6.2)	376 (3.4)	1389 (5.8)	394 (4.5)
Ethnicity, n (%)					
Hispanic	10907 (9.5)	6718 (9.5)	1262 (11.4)	2049 (8.6)	878 (10.0)
Non-Hispanic	93955 (82.1)	57784 (81.7)	9205 (82.9)	19718 (82.7)	7248 (82.6)
Unknown	9572 (8.4)	6203 (8.8)	634 (5.7)	2088 (8.8)	647 (7.4)
Body mass index, n (%)					
< 25 kg/m^2	46953 (41.0)	29221 (41.3)	3982 (35.9)	10594 (44.4)	3156 (36.0)
25 to < 30 kg/m^2	37342 (32.6)	23157 (32.8)	3467 (31.2)	7868 (33.0)	2850 (32.5)
≥ 30 kg/m^2	26796 (23.4)	15449 (21.8)	3552 (32.0)	5078 (21.3)	2717 (31.0)
Unknown	3343 (2.9)	2878 (4.1)	100 (0.9)	315 (1.3)	50 (0.6)
Charlson comorbidity score, n (%)					
0-1	74036 (64.7)	47432 (67.1)	5264 (47.4)	17617 (73.9)	3732 (42.4)
2-3	29242 (25.6)	16688 (23.6)	3990 (35.9)	4510 (18.9)	4054 (46.2)
4-5	7326 (6.4)	4236 (6.0)	1300 (11.7)	1059 (4.4)	731 (8.3)
> 6	3830 (3.3)	2349 (3.3)	547 (4.9)	669 (2.8)	265 (3.0)
Years of follow-up, mean (SD)	9.1 (1.8)	7.8 (1.7)	8.4 (1.8)	8.6 (1.8)	8.7 (1.7)
Yearly outpatient visits, mean (SD)	2.0 (3.9)	1.7 (3.4)	2.2 (4.2)	2.7 (4.2)	3.1 (5.1)

STARR = Stanford Research Repository; SD = standard deviation.

Table 2. Baseline characteristics of patients in the STARR cohort

Table 3. Incidence of osteoarthritis in patients with atopic disease compared to non-atopic control patients.

	Optum Cohort		STARR Cohort	
	Asthma and Atopic Dermatitis (n = 4395)	Control (n = 2360247)	Asthma and Atopic Dermatitis (n = 8773)	Control (n = 70705)
Patients diagnosed with OA, n (%)	1405 (32.0)	306395 (13.7)	1334 (15.2)	6318 (8.9)
Person-years	40339	17718811	76190	552076
IR (95% CI)*	34.8 (33.0-36.7)	17.3 (17.2-17.4)	17.5 (16.6-18.4)	11.4 (11.2-11.7)
OR (95% CI)†	1.84 (1.71-1.97)	1.0	1.54 (1.44-1.65)	1.0

OA = osteoarthritis; *IR = incidence rate per 1,000 person-years; †OR = adjusted odds ratio; 95% CI = 95% confidence interval. Incidence rate 95% CI were estimated using IR +/- 1.96 IR/($n^{0.5}$).

Table 3. Incidence of osteoarthritis in patients with atopic disease compared to non-atopic control patients

Methods: We conducted a retrospective cohort study using claims data from the Optum Clinformatics™ Data Mart and electronic health record data from the Stanford Research Repository (STARR). We included adult patients with more than 5 years of continuous enrollment and excluded patients with preexisting OA or a history of inflammatory arthritis. The exposed group included patients with a diagnosis of incident atopic disease, including asthma and atopic dermatitis. The control group included patients without atopic disease. The primary outcome was the development of OA, defined as two or more ICD-9 or -10 codes for OA separated by seven days or more. In the Optum cohort, the relationship between atopic disease and the development of OA was evaluated using logistic regression, adjusting for age, sex, race/ethnicity, Charlson comorbidity score, education, duration of follow-up, and frequency of outpatient visits. In the STARR cohort, we additionally adjusted for body mass index (BMI), and we were unable to adjust for education.

Results: The Optum cohort included 35,097 patients with asthma, 77,854 patients with atopic dermatitis, 4,395 patients with both asthma and atopic dermatitis, and 2,242,901 control patients without atopic disease (**Table 1**). The STARR cohort included 11,101 patients with asthma, 23,855 patients with atopic dermatitis, 8,773 patients with both asthma and atopic dermatitis, and 70,705 control patients without atopic disease (**Table 2**). There was a higher incidence of OA in patients with asthma (24.7% in Optum; 17.6% in STARR), atopic dermatitis (20.2% in Optum; 15.4% in STARR), and both asthma and atopic dermatitis (32.0% in Optum; 15.2% in STARR) compared to non-atopic control patients (13.7% in Optum; 8.9% in STARR) (**Table 3**). In the Optum cohort, there was an 84% increased risk of developing OA for patients with both asthma and atopic disease compared to non-atopic control patients (adjusted odds ratio (OR) 1.84; 95% CI, 1.71-1.97; p< .001) (**Table 3**). In the STARR cohort, after additionally adjusting for BMI, there was a similarly increased risk of OA in patients with both asthma and atopic dermatitis compared to controls, with an adjusted OR of 1.54 (95% CI, 1.44-1.65; p< 0.001) (**Table 3**).

Conclusion: This study demonstrates an increased incidence of OA in patients with atopic disease compared to the general population. The association between atopic disease and OA is supported by recent observations that mast cells and type II cytokines play important roles in the pathogenesis of OA. Our findings provide further evidence that allergic pathways may contribute to the development of OA, and future interventional studies could consider targeting these pathways for the treatment of OA.

References

1. Wang Q, Lepus CM, Raghu H, et al., Elife 8, (2019).

Disclosure: M. Baker, Vorso Corp, 2; **K. Sheth**, None; **R. Lu**, None; **D. Lu**, None; **E. von Kaeppler**, None; **A. Bhat**, None; **D. Felson**, None; **W. Robinson**, None.

Abstract Number: 1135

Osteoporosis Assessment and Outcomes in Candidates for Liver Transplantation in a Tertiary Center

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: A rapid loss of bone mass and an increase in fractures have been described in the first six months after liver transplantation. This phenomenon occurs in patients with a previous diagnosis of osteoporosis, but also in those with normal bone mass. Several factors, such as corticosteroids and others, may explain the increased risk of fractures. Treatment with bisphosphonates may help halt bone loss, improve lumbar bone mass, and reduce fractures. This study aims to evaluate characteristics, bone health, and risk of fracture of patients included in the liver transplantation pre-assessment at a tertiary center. Also, to ascertain the indication for antiresorptive therapy and the development of bone complications after transplantation.

Methods: A descriptive cross-sectional study of patients enrolled for a multidisciplinary assessment before liver transplantation from February 2019 to March 2021, with a follow-up of 6 and 12 months after transplantation. Sex, age, body mass index (BMI) and alcohol and tobacco consumption were collected. DXA-based osteopenia or osteoporosis diagnoses, the number of bone fragility fractures, and radiographic vertebral fractures were evaluated. FRAX index adapted for the Spanish population was calculated to estimate the 10-year risk of major osteoporotic fracture and hip fracture. Additionally, the indication for antiresorptive treatment and the occurrence of clinical fracture after liver transplantation were registered. Categorical variables are expressed as frequencies and percentages, and continuous variables with normal data distribution, as mean and standard deviation (SD).

	N (%)
NORMAL BONE MINERAL DENSITY (BMD)	19 (19.6%)
OSTEOPENIA by DXA T SCORE -1 to -2,5	57 (58.8%)
OSTEOPOROSIS by DXA T SCORE < -2.5	21 (21.6%)
FRAGILITY FRACTURE	3 (3.1%)
RADIOGRAPHIC VERTEBRAL FRACTURE	15 (15.5%)
OSTEOPOROSIS T SCORE < -2.5 or fragility fracture or radiographic vertebral fracture	30 (30.9%)
FRAX® 10-YEAR RISK ≥ 3% for hip fracture or ≥ **10%** (without BMD) / ≥ **7.5%** (with BMD) **for major osteoporotic fracture***	15 (15.5%)

*Reumatol Clin 2019; 15:188-210.

Results: A total of 97 patients (77.3% men) were included, with a mean age of 60 years (SD 7.5) and a mean BMI of 28.2 kg/m^2 (SD 4.8). 68% were smokers, and 72% had a background of moderate-severe alcohol consumption. 3.1% presented a fragility fracture, and in 15.5%, a vertebral fracture was diagnosed as seen by radiography. 58.8% had osteopenia, and 30.9% osteoporosis by DXA. 91% had a deficiency of 25-OH vitamin D (< 30 ng/ml). The mean 10-year risk of major fracture was 3.9% (SD 3) and 1.6% (SD 2.1) for hip fracture. Lastly, 31 (32.0%) would meet treatment criteria according to FRAX scores, DXA results and background of fragility fractures (**Table**). Adding osteopenia as a criterion for initiating antiresorptive therapy, the number of patients candidates was 75 (77.3%). 66 (68%) finally received treatment (52.6% with IV zoledronate). In the follow-up, 50 received liver transplantation. Twenty-one of them has been followed six months and 17 a year. Two patients have developed a clinical fracture (one case of L2 fracture at five months, and the other a hip fracture at nine months), despite treated at baseline with bisphosphonates.

Conclusion: In this study, many candidates for liver transplantation candidates showed risk factors for the development of fragility fractures, but half of the patients who received antiresorptive drugs would not meet the usual criteria for treatment. Nonetheless, the risk of fracture in the months after transplantation supports the need to optimize bone mineral treatment and to carry out close follow-up.

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Abstract Number: 1136

Risk of Osteoporosis in Patients with Systemic Sclerosis: A Cross-Sectional Analysis of Two European Prospective Cohorts

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with systemic sclerosis (SSc) are at high risk for osteoporosis (OPO) and fragility fractures, although their exact prevalences are unknown. This might be due to traditional risk factors for OPO, such as previous fragility fractures, low BMI, use of glucocorticoids. However, the impact of SSc disease-specific characteristics remains unclear. The aim of this study was to estimate the prevalence of OPO and fragility fractures in a large cohort of SSc patients and to identify risk factors.

Methods: We performed a cross-sectional study involving patients fulfilling ACR/EULAR 2013 SSc classification criteria followed prospectively in two European university hospital cohorts between 2004 and 2020. We used databases prospectively collecting SSc related variables including clinical phenotype, organ involvement, autoantibodies, pulmonary function tests, and biological parameters. Bone health parameters were added retrospectively including bone densitometry (DXA), history of fragility fractures and anti-osteoporotic treatment. OPO was defined by a femoral or

Table 1. Patients Characteristics

	N = 932
Age at visit (years)	59.6 (20.1-90.5)
Disease duration (years)	12.4 (0-79)
Female	782 (83.9%)
Cutaneous diffuse	226 (24.2%)
Modified Rodnan Skin Score	5.95 (0-42)
mRSS > 10	117 (19%)
Smoking, ever	309 (33.2%)
Overlap syndromes	287 (30.8%)
SLE	17 (1.8%)
Sjögren syndrome	119 (12.8%)
Myositis	37 (4%)
Rheumatoid arthritis	73 (7.8%)
Disease features	
Interstitial lung disease	368 (39.5%)
Pulmonary hypertension	108 (11.6%)
Oesophageal involvement	633 (67.9%)
Gut involvement	111 (11.9%)
Renal crisis	16 (1.7%)
Cutaneous features, current or prior	
Telangiectasia	628 (67.4%)
Calcinosis	172 (18.5%)
Digital ulcers	466 (50.0%)
Pitting scars	291 (31.2%)
Auto-antibodies	
Anti-centromere	427 (45.8%)
Anti-topoisomerase I	256 (27.5%)
Anti-RNA Polymerase III	35 (3.8%)
Anti-U1RNP	38 (4.1%)
Anti-PM-Scl	36 (3.9%)
Pulmonary function	
DLCO % predicted	63.7 (9.0-128.0)
DLCO % predicted <80%	684 (73.4%)
DLCO % predicted <60%	335 (35.9%)
DLCO % predicted <40%	91 (9.8%)
TLC % predicted	94.0 (32.0-146)
TLC % predicted <70%	71 (7.6%)
TLC % predicted <50%	12 (1.3%)
New York Hearth Association functional class	
I, II	711 (76.4%)
III, IV	210 (22.5%)
DMARDs	437 (46.9%)
Biologicals	52 (5.6%)
Proton pump inhibitors	605 (64.9%)
Glucocorticoids	388 (41.6%)
Osteoporosis	256 (27.5%)
DXA	350 (37.6%)
Anti-osteoporotic treatment	198 (21.2%)
Main osteoporotic fracture	128 (13.7%)
Fracture, any	183 (19.6%)

BMI: body mass index ; SLE: systemic lupus erythematosus; DXA: dual X-ray absorptiometry ; DLCO: diffusing capacity for carbon monoxide ; TLC: total lung capacity.

lumbar spine T-score below -2.5 and/or history of main osteoporotic fracture and/or prescription of anti-osteoporotic drugs.

Parametric and non-parametric tests were used to compare osteoporotic and non-osteoporotic patients. Odds ratios were calculated for categorical variables. We considered a two-sided significance level of 0.05 for all tests.

Table 2. Univariate analysis

	Osteoporosis N = 275	No-osteoporosis N = 675	Odds ratio [95% CI]	p-value
Age at visit (years)	64.4	57.7		<0.001†
Disease duration (years)	14.6	11.6		0.004‡
Female	85.2%	83.4%		0.517
BMI (kg/m2)	23.9	25.3		0.007‡
Cutaneous diffuse	38.3%	18.8%	2.67 [1.95-3.76]	< 0.001
Modified Rodnan Skin Score	7.45	5.38		< 0.001‡
mRSS > 10	28.3%	15.9%	2.10 [1.48-2.96]	< 0.001
Smoking, ever	27.8%	35.3%	0.71 [0.52-0.97]	0.032
Overlap syndromes	35.4%	30.6%		0.170
SLE	2.8%	1.5%		0.196
Sjögren syndrome	11.8 %	13.8%		0.436
Myositis	6.1 %	3.4%		0.066
Rheumatoid arthritis	11.8%	6.7%	1.85 [1.13-3.03]	0.013
Disease features,				
Interstitial lung disease	57.0%	33.6%	2.61 [1.94-3.52]	< 0.001
Pulmonary hypertension	12.9%	11.1%		0.449
Oesophageal involvement	71.8%	67.9%		0.254
Gut involvement	14.8%	10.8%		0.090
Renal crisis	2.0%	1.6%		0.730
Cutaneous features, current or prior				
Telangiectasia	66.7%	68.1%		0.675
Calcinosis	21.8%	19.0%		0.356
Digital ulcers	50.2%	50.3%		0.979
Pitting scars	30.2%	32.0%		0.583
Auto-antibodies				
Anti-centromere	36.0%	50.4%	0.55 [0.41-0.75]	< 0.001
Anti-topoisomerase I	36.4%	24.4%	1.77 [1.29-2.41]	< 0.001
Anti-RNA Polymerase III	4.3%	3.6%		0.569
Anti-U1RNP	5.5%	3.6%		0.188
Anti-PmScl	3.5 %	4.5%		0.740
Pulmonary function				
DLCO % predicted	58.2	65.8		< 0.001†
DLCO % predicted <80%	83.5%	76.5%	1.55 [1.06-2.29]	0.024
DLCO % predicted <60%	50.8%	33.7%	2.03 [1.50-2.75]	< 0.001
DLCO % predicted <40%	14.5%	8.9%	1.73 [1.10-2.71]	0.016
TLC % predicted	91.3	95.0		0.010†
TLC % predicted <70%	13.1%	7.5%	1.86 [1.13-3.09]	0.014
TLC % predicted <50%	3.7%	0.7%	5.54 [1.65-18.6]	0.005*
New York Hearth Association functional class				
III, IV	32.9%	18.8%	2.13 [1.54-2.94]	< 0.001
DMARDs	62.0%	44.6%	2.02 [1.50-2.74]	< 0.001
Biologicals	9.9%	4.4%	2.41 [1.37-4.24]	0.002
Proton pump inhibitors	78.1%	64.7%	1.94 [1.38-2.74]	< 0.001
Glucocorticoids	63.5%	33.4%	3.48 [2.57-4.70]	< 0.001
CRP (mg/L)	6.1	3.7		0.004‡
Haemoglobin (g/dL)	12.7	13.1		< 0.001†
ESR (mm/1h)	21.7	16.7		< 0.001‡
Serum creatinine (mg/L)	8.2	8.6		0.145‡
Uric acid (mg/L)	48.6	52.0		0.445‡
CPK (IU/L)	105	101		0.052‡
NT-BNP (ng/L)	369	395		< 0.001‡
Ferritin (µg/L)	105	120		0.945‡

Chi square test for all parameters except: * Fisher's exact test, † Student T-test, ‡ Mann-Whitney test.
SLE: Systemic Lupus erythematosus; DXA : dual X-ray absorptiometry ; DLCO: diffusing capacity for carbon monoxide ; TLC: total lung capacity.

Results: Of 932 SSc patients with a mean age of 59.6 years (20.1-90.5). Of the patients 40% had an interstitial lung disease (ILD) and 12% pulmonary hypertension, respectively. Diffuse cutaneous SSc was present in 226 patients (24%); anti-topoisomerase antibodies were detected in 28%. A DXA scan was available in 38% of the patients. The prevalence of osteoporotic fractures and anti-osteoporotic treatments was 14% and 21%, respectively. Overall, 28% of the cohort was identified as having OPO.

Table 2 compares SSc patients with or without OPO. Besides age and low BMI as strong risk factors, the use of proton-pump inhibitors (OR 1.94, 95%CI 1.38-2.74) and glucocorticoids (OR 3.48, 95%CI 2.57-4.70) were statistically associated with OPO. Cutaneous diffuse form (OR 2.67, 95%CI 1.95-3.76), mRSS above 10 (OR 2.10, 95%CI 1.48-2.96), and anti-topoisomerase antibodies (OR 1.77, 95%CI 1.29-2.41) were associated with OPO. ILD (OR 2.61, 95%CI 1.29-2.41) or symptoms such as NYHA III and IV functional classes (OR 2.13, 95%CI 1.54-2.94), were also positively associated with OPO. The ILD severity, estimated through DLCO alteration and restrictive lung disease, was also associated with OPO. We did not identify any significant association between OPO and calcinosis or vasculopathy, nor oesophageal or gut involvement. CRP and ESR levels were significantly higher in the OPO group ($p = 0.004$ and $p < 0.001$, respectively), while haemoglobin levels were significantly lower ($p < 0.001$).

Conclusion: The prevalence of OPO and fragility fractures in patients with SSc was 28% and 20%, respectively. Beyond classical risk factors, our study suggests that disease severity (as reflected by cutaneous subset, organ involvement, autoantibodies and inflammatory markers) was also associated with bone health in SSc patients.

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Abstract Number: 1137

REMS Technology for the Assessment of Bone Health in a Male Population

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: This study aimed to evaluate the diagnostic accuracy of the ultrasound-based densitometric technology called Radiofrequency Echographic Multi Spectrometry (REMS) in the diagnosis of osteoporosis in a population of adult male patients based on lumbar spine scans, compared to Dual-energy X-ray Absorptiometry (DXA), considered as a reference.

Methods: Inclusion criteria were: Caucasian male patients, aged between 30 and 90 years, body mass index (BMI) less than 40 kg/m^2, no significant walking impairments, referral for lumbar spine DXA. Signed informed consent was obtained. The patients underwent a lumbar spine scans with both DXA and REMS.

The correlation between REMS and DXA-measured BMD was expressed by Pearson correlation coefficient. Bland-Altman plot was also obtained. Patients were classified as "with osteoporosis" or "without osteoporosis" on the base of the T-score value using the conventional threshold (-2.5) for both techniques independently. Considering the DXA outcome as reference, the accuracy of the diagnostic classification was assessed as sensitivity, specificity, Cohen's K and 3-classes diagnostic concordance.

Results: Three hundred and thirteen patients were considered, with mean age of 57.7 years (range: 30 to 87 years). The Pearson correlation coefficient between REMS- and DXA-measured BMD values was r=0.92 (r^2=0.85). At Bland-Altman analysis, bias ± 2 standard deviations were -0.002 ± 0.092 g/cm^2.

The agreement in diagnostic classification performed by REMS and by DXA was very high, with a sensitivity of 89.1% and specificity of 90.7%. Cohen's K was 0.71. Considering the 3 diagnostic classes (normal bone, osteopenia, osteoporosis), the diagnostic concordance between technologies was 81.5%.

Conclusion: REMS, applied to the lumbar spine site, is a reliable technology for the diagnosis of osteoporosis in men, thus confirming the diagnostic performance already observed in studies carried out in female populations [1, 2].

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Disclosure: D. Ciardo, None; **P. Pisani**, None; **F. Lombardi**, None; **M. Di Paola**, None; **R. Franchini**, None; **M. Muratore**, None; **F. Conversano**, None; **S. Casciaro**, None.

Abstract Number: 1138

Assessing Trends in Dual Energy X-Ray Absorptiometry (DXA) Utilization Among Medical Providers in the United States

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
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Background/Purpose: The twenty first century has seen falling reimbursement rates for dual energy X-ray absorptiometry (DXA) testing coupled with a rising elderly population in the U.S. The purpose of this study was to assess trends in performing DXA scans among U.S. medical providers and the resulting potential impact of reduced DXA availability on access to care.

Methods: A retrospective review was performed on publicly available data Medicare provider utilization and payment data between 2012 and 2018. Data was accessed from the CMS website and filtered for CPT codes used for reimbursement of DXA testing. This data included information on provider (name and identifier), city, state, zip code, sex, procedure type, location (office-based providers vs hospital-based providers), and provider specialty. Provider zip codes were compared to the Federal Office of Rural Health Policy (FORHP) designation as rural areas.

Results: From 2012-2018 the standardized number of DXA tests per 100,000 women decreased from 5,641 to 4,899 DXA tests per 100,000 women with a nadir of 4,307 DXA tests per 100,000 women in 2015. The number of DXA providers reimbursed located in a rural zip code decreased 41.3% (from 2,945 to 1,728), similar to the relative decrease

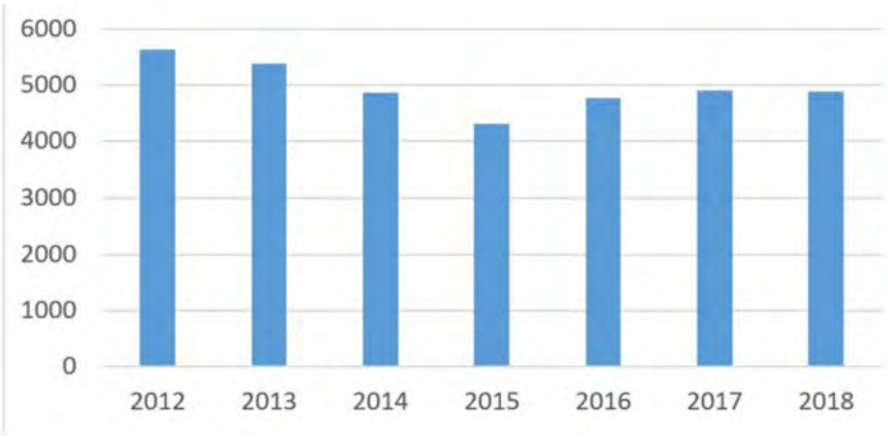

Figure 1. Standardized Number of DXA Scans Per 100,000 Women by Year.

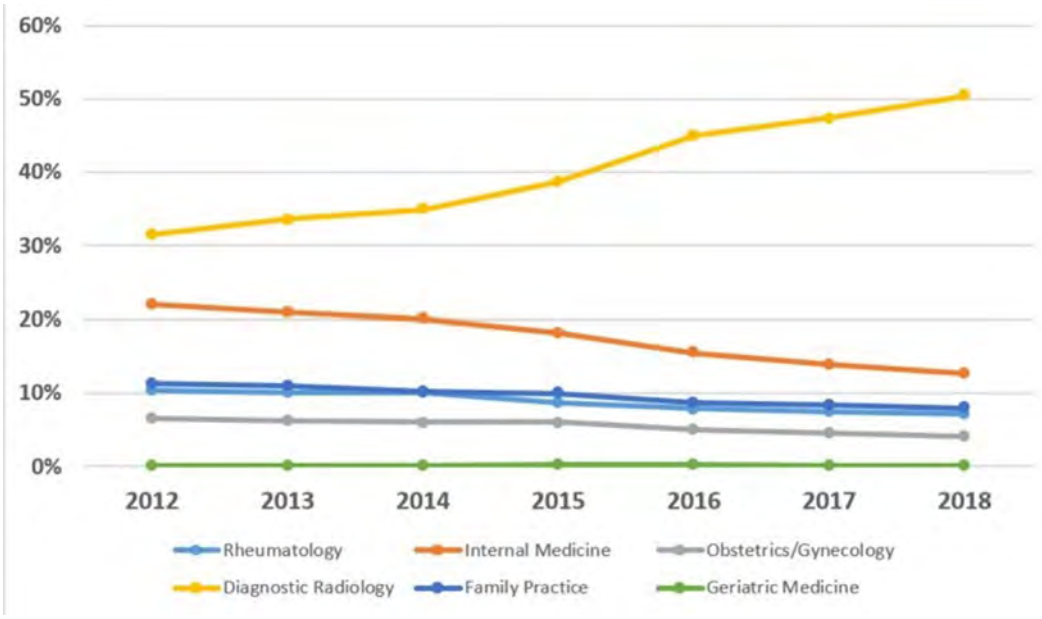

Figure 2. Yearly Trends in Percentages of DXA Testing by Specialty and Year.

in the proportion of rural providers (from 14.2% to 9.0%). The percentage of reimbursed DXA scans performed by rheumatologists decreased from 10.3% to 7.1%, internal medicine from 22.0% to 12.7%, obstetrics/gynecology from 6.5% to 4.2%, and family practice from 11.3% to 8.0%; diagnostic radiology, which are hospital-based providers, increased from 31.6% to 50.4% during the same time period.

Conclusion: The standardized number of DXA tests per 100,000 women Medicare enrollees decreased between 2012 and 2018. During the same time period, the claims for DXA testing for office-based specialties decreased, while the claims for DXA testing performed by diagnostic radiology increased. Both the number and proportion of both rural and primary care providers submitting claims for DXA testing have decreased, leading to likely decreased access to

Specialty	Total, 2012	Standardized	Total, 2018	Standardized
Internal Medicine	328714	1274	188476	620
Diagnostic Radiology	473005	1833	750933	2469
Family Practice	169234	656	118674	390
Obstetrics/Gynecology	97691	379	62229	205
Rheumatology	154573	599	105840	348
Geriatrics	2593	10	1193	4
Orthopedic Surgery	22858	89	11845	39

Table 1. Standardized Yearly DXA Scans Per 100,000 Women by Specialty, 2012-2018. Columns sorted by: Total number of DXA scans in 2012; Number of DXA scans standardized per 100,000 women in 2012; Total number of DXA scans in 2018; Number of DXA scans standardized per 100,000 women in 2018

osteoporosis care among rural residents. With a progressive aging of the population, the access to tools for prevention and treatment of osteoporosis, such as DXA, is key to delivering high-quality osteoporosis care and effectively screening high risk patients.

Disclosure: T. Edgil, None; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **M. Danila**, Boehringer Ingelheim, 5, Amgen, 1, Amgen, 5, AbbVie, 1, Pfizer, 5, Pfizer, 11, Horizon, 5, Novartis, 1, WebMD, 12, writer.

Abstract Number: 1139

Fracture Liaison Service Outcomes at a Southern California County Hospital Highlights Need for Health System Improvements

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
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Background/Purpose: Osteoporosis causes significant morbidity and mortality in the elderly. Despite the benefits of treatment, < 25% of elderly patients who fracture receive treatment. A fracture liaison service (FLS) provides a systematic way to address secondary fracture prevention. An FLS was implemented at our county-affiliated hospital. There is limited data overall on FLS Outcomes at county hospital systems where the majority of patients are indigent, and access to services may be limited. A prior study highlighted worse outcomes in our county population vs a university hospital population. The purpose of this study is to determine the impact of an FLS at a county hospital during its first year of implementation on improving osteoporosis treatment initiation and DXA testing and to identify areas of improvement.

Methods: We performed a retrospective electronic medical chart review on 282 patients diagnosed with osteoporosis based on relevant ICD-10 codes; 144 patients were seen prior to (pre-FLS) and 138 patients seen after (post-FLS) the establishment of an FLS. Age, ethnicity, BMI, calcium and vitamin D supplementation, treatment initiation (with bisphosphonates or biologics), DXA testing, and adherence to outpatient follow-up were collected. We used Pearson's chi-square to test for independence in the demographic and clinical categorical outcome variables while independent samples t-test was used to compare mean differences in the demographic and clinical continuous outcome variables. In the post-FLS group only, we tested treatment initiation, DXA testing, calcium and vitamin D supplementation before admission and after discharge using McNemar's test statistic. We set alpha equal to 0.05 for statistical significance.

Results: The pre-FLS group tended to be slightly younger (p= 0.022) and had a higher percentage of Hispanics (p= 0.021) than the post-FLS group (Table 1). A higher percentage of the post-FLS group was female (76% vs 67%). Smoking and alcohol-use status, and BMI were independent of FLS group status.

No statistically significant differences in mean length of stay, days until next encounter (any) between FLS subgroups were noted (Table 2). While only 14% of FLS patients were seen in Rheumatology clinic, primary care physicians (PCPs) were notified of patient's fracture risk via the FLS. In the post-FLS group, more patients were treated (20 additional patients, p=0.004) and prescribed calcium (66 additional patients, p< 0.001) and vitamin D (66 additional patients, p< 0.001) after discharge in paired outcome analysis (Table 3). No statistically significant changes in DXA orders from pre-admission to post-discharge were noted.

Table 1. Patient Demographic Characteristics by Fracture Liaison Service Group Status, *n*=282

	Patient Group Treated Before Fracture Liaison Service was Established, *n*=144
Age (years), mean ± SD	74.5 ± 11.7
BMI (kg/m^2) mean ± SD	26.7 ± 5.7
Gender, % (*n*)	
Male	33% (47)
Female	67% (97)
Ethnicity, % (*n*)	
Not Hispanic/Latino	63% (91)
Hispanic/Latino	37% (53)
Active Smoker, % (*n*)	
No	81% (116)
Yes	19% (27)
Ever Smoker, % (*n*)	
No	55% (79)
Yes	45% (64)
Ever Alcohol Drinker, % (*n*)	
No	79% (68)
Yes	21% (18)

BMI=Body Mass Index. Percentages are shown by column (Fracture Liaison Service group) and may not add to 100 due to rounding. Based on valid data where missing data varies by characteristic. *p-value based on the chi-square statistic for categorical variables and independent samples t-test for continuous variables, *p-value < 0.05.

Conclusion: Assessment of FLS outcomes highlighted inadequacies in osteoporosis management within the county health system. Interdisciplinary efforts to improve DXA access and PCP awareness of fracture risks are currently underway. Initial efforts have proven successful in increasing the number of patients treated after a fragility fracture in this population.

Table 2. Clinical Characteristics by Fracture Liaison Service Group Status, n=282.

	Patient Group Treated Before Fracture Liaison Service was Established, *n*=144	Patient Group Treated After Fracture Liaison Service was Established, *n*=138	*p*-value[a]
Length of Stay, days, mean ± SD	6.2 ± 12.8	6.2 ± 5.4	0.969
Days Until Next Encounter-Any, mean ± SD	19.2 ± 30.6	19.0 ± 15.0	0.935
Days Until Next Encounter-Outpatient, mean ± SD	18.4 ± 31.2	20.4 ± 16.0	0.533
Albumin, g/dl, mean ± SD	3.3 ± 0.49	3.1 ± 0.60	0.018*
Calcium (corrected), mg/dl, mean ± SD	9.4 ± 0.49	9.2 ± 0.45	<0.001*
Follow-up at Rheumatology Clinic, % (*n*)	0% (0)	14% (19)	0.999
Primary Care Physician in System, % (*n*)	61% (88)	57% (78)	0.434
Osteoporosis Treatment Prior to Fracture, % (*n*)	46% (6)	14% (19)	0.003*
DXA Prior to Admission, % (*n*)	67% (14)	25% (34)	<0.001*
Calcium Supplementation Before Admission, % (*n*)	52% (14)	16% (22)	<0.001*
Adequate Calcium Supplementation, % (*n*)	68% (26)	60% (83)	0.352
Vitamin D Supplementation Before Admission, % (*n*)	60% (22)	23% (31)	<0.001*
Adequate Vitamin D Supplementation, % (*n*)	83% (43)	71% (98)	0.101

For the categorical characteristics, only the "yes" counts and corresponding percentages are shown. Based on valid data where missing data varies by characteristic. *p-value based on the chi-square statistic for categorical variables and independent samples t-test for continuous variables, *p-value < 0.05.

Table 3. Fracture Liaison Service Paired Outcome Measures, *n*=138.

	No, After Discharge	Yes, After Discharge	*p*-value[a]
Osteroporosis Treatment, % (*n*)			
No, Before Admission	83% (99)	17% (20)	0.004*
Yes, Before Admission	26% (5)	74% (14)	
DXA, % (*n*)			
No, Before Admission	80% (83)	20% (21)	0.322
Yes, Before Admission	85% (29)	5% (15)	
Calcium Supplementation, % (*n*)			
No, Before Admission	43% (50)	57% (66)	<0.001*
Yes, Before Admission	9% (2)	91% (20)	
Vitamin D Supplementation, % (*n*)			
No, Before Admission	38% (41)	62% (66)	<0.001*
Yes, Before Admission	7% (2)	93% (29)	

DEXA=Dual-energy X-ray absorptiometry. Percentages add to one-hundred by row. *p-value based on McNemar's test statistic for paired categorical variables, *p-value < 0.05.

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Abstract Number: 1140

Fracture Risk in DXA-Appropriate Patients on Glucocorticoids: Is Everyone Tested According to Screening Guidelines?

Alexandra Chop[1], Rajesh Kupuraju[1], Ruchi Patel[1], Kristen Salava[1], Madhuri Duggirala[1], Aparna Baburaj[1], Andrea Berger[2], Jason Brown[1] and David Bulbin[3], [1]Geisinger Medical Center, Danville, PA, [2]Department of Population Health Sciences, Geisinger Medical Center, Danville, PA, [3]Geisinger Health System, Danville, PA

SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Glucocorticoids are commonly prescribed for a multitude of indications, yet have many side effects, one of which is glucocorticoid induced osteoporosis (GIOP). The 2017 ACR GIOP guidelines were developed to help improve screening and management of osteoporosis for this specific population. In this study, we investigated if patients at a large rural academic center receiving glucocorticoids were appropriately monitored with DXA based on the 2017 ACR screening guidelines.

Methods: Through a retrospective electronic chart review we evaluated patients in a rural tertiary medical center in central Pennsylvania who met specific inclusion criteria: 40 years or older who received a prescription for 2.5mg of a prednisone equivalent ≥ 90 days starting January 1, 2018 – December 31, 2019. Patients that met criteria were reviewed for DXA orders between 2018 – 2020, the department that ordered the steroids, the DXA ordering department,

	Patients n = 673
Patient Age, mean (S.D.)	68.6 (12.3)
Sex, n (%)	
Female	385 (57.2%)
Male	288 (42.8%)
Race, n (%)	
American Indian or Alaska Native	2 (0.3%)
Asian/Pacific Islander	7 (1.0%)
Black or African American	10 (1.5%)
White	654 (97.2%)
Ethnicity, n (%)	
Hispanic/Latino	15 (2.2%)
Not Hispanic/Latino	658 (97.8%)
Mortality, n (%)	
2018	19 (2.8%)
2019	42 (6.2%)
2020	37 (5.5%)
Living as of 12/31/20	575 (85.4%)

Figure 1. Patient demographics

Table A	Steroid Orders		DXA Ordered by Any Department			DXA Completed by Any Department		
Source of Most Recent Steroid Order	n	%	n	%	P-value	n	%	P-value
Endocrinology	19	2.8%	4	21.1%		4	21.1%	
Gastroenterology	12	1.8%	7	58.3%		5	41.7%	
Hem/Onc	39	5.8%	5	12.8%		3	7.7%	
Neurology	13	1.9%	9	69.2%		6	46.2%	
Other	58	8.6%	16	27.6%	0.0004	10	17.2%	0.0033
Primary Care	168	25.0%	59	35.1%		36	21.4%	
Rheumatology	306	45.5%	138	45.1%		104	34.0%	
Surgery	15	2.2%	4	26.7%		4	26.7%	
Pulmonary Medicine	43	6.4%	20	46.5%		15	34.9%	
Total	673		262	38.9%		187	27.8%	

Table B	Steroid Orders		DXA Ordered by Any Department			DXA Completed by Any Department		
Source of Most Recent Steroid Order	n	%	n	%	P-value	n	%	P-value
Rheumatology	306	45.5%	138	45.1%		104	34.0%	
Non-Rheumatology	367	54.5%	124	33.8%	0.0028	83	22.6%	0.0011
Total	673		262	38.9%		187	27.8%	

Figure 2. Table A – source of steroid order by department, if DXA was ordered and completed. Table B – source of steroid order comparing rheumatology vs all other departments combined.

and if a DXA had been completed. Logistic regression models were used to test for overall and pairwise associations between steroid ordering departments and whether DXAs were ordered and whether DXAs were completed.

Results: The total number of charts that met the initial electronic screening criteria was 6022. Of those, 1000 charts were randomly selected for manual review via a computer generated simple random sample. Of those 1000 patients, 673 met the inclusion criteria. Overall, 262 of 673 patients (38.9%) had DXAs ordered in the three-year period and 187 had DXAs completed (27.8%). If the most recent steroid order was from a rheumatology provider, 45.1% of patients had a DXA ordered and 34.0% had a DXA completed. Patients whose steroid was ordered by rheumatology had significantly more DXAs ordered than patients whose steroid orders came from all other departments combined (45.1% vs. 33.8%, p = 0.0028). In pair-wise comparisons against individual departments, patients from rheumatology had more DXA orders than hematology/oncology (45.1% vs 12.8%, p = 0.0005), and primary care (45.1% vs 35.1%, p = 0.0354). There were no statistically significant differences between rheumatology, gastroenterology, neurology, surgery, or pulmonary medicine. Patients whose steroid was ordered by rheumatology had significantly more DXAs completed than patients whose steroid orders came from all other departments combined (34.0% vs. 22.6%, p = 0.0011).

Conclusion: There was significant variability between different specialties in ordering of DXA scans. While the rheumatology department was more compliant with ACR guidelines when all other departments are combined, they still are screening fewer than 50% of patients who meet the ACR guidelines. This demonstrates a care gap in osteoporosis screening in this population. We plan to analyze the remaining 5022 patient charts to determine how many meet criteria for DXA screening and expound on our preliminary results. We also hypothesize that the observed trends in

interdepartmental differences will lead to more robust conclusions when analysis is completed with the full population. Additionally, we intend to implement a medical chart notification that would alert providers to consider DXA screening in appropriate patients.

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Abstract Number: 1141

Factors Associated with Fragility Fracture in Patients with Systemic Mastocytosis: Data from an Inception Cohort in a Single Centre

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Mastocytosis (SM) is a very rare disease (0,5 -1 per 10000 in adults). Most common manifestations are skin related or anaphylaxis, however almost one third of patients may present with concomitant

	Population (N = 17)	Without fragility fracture (N = 13)	With fragility fracture (N=4)	P
Male, n (%)	9 (53%)	7 (54%)	2 (50%)	0.89
Age at first symptoms, years, mean (SD)	37.6 (21.1)	33.0 (20.2)	58.1 (10.1)	0.05
Age at diagnosis, years, mean (SD)	47.7 (21.1)	38.8 (20.9)	59.7 (13.1)	0.08
Ever smoker, n (%)	6 (35%)	4 (30.8%)	2 (50%)	0.48
Alcohol, n (%)	2 (11.76%)	1 (7.69%)	1 (25%)	0.34
BMI, mean (SD)	26.5 (4.3)	25.3 (4.0)	30.6 (2.0)	0.02
BMI<19kg/m2, n (%)	1 (6%)	1 (7%)	0 (0%)	0.56
Cutaneous mastocytosis, n (%)	8 (47%)	5 (38.5%)	3 (75%)	0.20
Anaphylaxia, n (%)	8 (47%)	6 (46.1%)	2 (50%)	0.89
Digestive symptoms, n (%)	8 (47%)	7 (53.5%)	1 (25%)	0.31
Basal serum tryptase >11,4	12 (70.6%)	8 (61.5%)	4 (100%)	0.14
Basal serum tryptase, mean (SD)	20.20 (18.33)	10.68 (20.75)	22.85 (7.64)	0.75
General risk factors for OP present, n (%)	5 (29%)	5 (38.5%)	0 (100%)	0.14
Vitamin D levels, mean (SD)	27.81 (14.72)	12.59 (16.44)	24.35 (7.38)	0.60
PTH levels, mean (SD)	49.29 (24.21)	4.92 (24.62)	46.75 (26.28)	0.81
Femoral T score, mean (SD)	-1.03 (1.22)	-3.82 (1.36)	-1.86 (1.23)	0.12
Lumbar T score, mean (SD)	-1.06 (1.57)	-5.27 (1.36)	-1.95 (2.08)	0.20
Femoral Z score, mean (SD)	-0.34 (1.05)	-1.79 (1.44)	-0.75 (0.65)	0.39
Lumbar Z score, mean (SD)	-0.30 (1.88)	-5,38 (1.57)	-0.67 (2.96)	0.66
FRAX global fracture, mean (SD)	2.27 (2.52)	2.34 (1.57)	6.83 (7.82)	0.11
FRAX hip fracture, mean (SD)	0.23 (1.01)	0.48 (0.27)	2.1 (1.92)	0.18

Table 1. Demographic data, risk associated factors, laboratory test, bone densitometry divided by patients with fragility fracture and patients without fragility fracture.

Patient	Age	Gender	Femoral Neck Bone Mineral Density (gr/cm2)	Localization of Fracture	Severity of Fracture	Time to fracture diagnosis
Patient 1	65	Male	0,714	D6,D8,D10,D11, L1	3 Mild 2 Moderate	2 years prior SM diagnosis
Patient 2	81	Female	0,437	D4,D8,D12, L1	1 Mild 3 Severe	2 years after SM diagnosis
Patient 3	65	Female	0,767	D4,D11	Unknown	2 years prior SM diagnosis
Patient 4	42	Male	0,832	D7,D8,D9,D11,D12, L1,L2,L3,L5	3 Mild 3 Moderate 3 Severe	At time of SM diagnosis

Table 2. Characteristics of Fragility Fracture in four patients with Systemic Mastocytosis

osteoporosis (OP) resulting in fragility fracture (FF) in around 5 -37% of patients. FF affect lumbar spine (LS) more frequently in young men. Alcohol consumption, high serum tryptase level, and low femoral T score have been described as risk factors but there are some discrepancies between studies. [1-2] Our primary objective was to identify factors associated with FF in patients with SM.

Methods: We analysed all consecutive patients attending a multidisciplinary clinic up to April 2021. This clinic has been recently established by experts from Allergy and Rheumatology departments at our Centre, patients with SM diagnosis according to the 2001 WHO criteria are included. We collected demographic data, general risk factors for OP, and clinical characteristics including cutaneous involvement, bone involvement and laboratory data as serum tryptase level. Bone involvement is defined as densitometric OP (T score ≤ - 2.5) or FF. Normally distributed variables are described as means (SD) and dichotomous variables as number and frequencies. Comparison between patients with and without FF is performed using t-test and Chi^2 when needed.

Results: Seventeen patients with SM are included in this preliminary analysis. Four patients (24%) presented a FF, all of them vertebral fractures identified by plain radiographies (most of them multiple, located in dorsal vertebrae). Two men and two women presented FF, they were older versus patients without FF (Table 1), and without general risk factors for OP, including alcohol consumption and tobacco use. All of them have a high basal serum tryptase and most of them presented other MS symptoms (cutaneous, anaphylaxia). FRAX tool was useful in only one patient to predict FF risk. The two men with FF diagnosis do not met criteria for densitometric OP, specific characteristics for these patients are presented in Table 2.

Conclusion: In our cohort of SM, about 25% of patients present FF, in most cases multiple, located in dorsal spine, and without densitometric diagnosis of OP. Our patients are older versus other population described previously in the literature. FRAX may underestimate the risk of FF in patients with SM. We could not identify variables associated to higher risk of FF in this group of patients. SM should always be considered in differential diagnosis in the presence of FF, especially in men with no OP or another risk factor associated.

Disclosure: K. Carpio Astudillo, None; **F. Skrabski**, None; **I. CASTREJON**, None; **J. Alvaro-Gracia**, None; **A. Garcia Prieto**, None; **T. González**, None.

Abstract Number: 1142

For Vulnerable Population Treated at a Community Health Center (CHC), Primary Care Physician (PCP) Turnover Should Be Included in Social Determinants of Health (SDH) on Non-completing Osteoporosis Treatment

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Background/Purpose: Unexplained interruptions in treatment are common among patients with osteoporosis, but it is not well studied how PCP turnover affects incompletion of osteoporosis treatment for the high risk SDH patient population in a CHC setting. We sought to evaluate if provider change, in addition to epidemiologic features and clinical comorbidity, increases risk for the treatment incompletion.

Methods: We defined PCP turnover as a patient having a PCP who has worked at the clinic < 5 years, and treatment incompletion as no treatment or being treated < 3 years with no clear reason for the discontinuation and used Charlson Comorbidity Index (CCI) to assess clinical comorbidity. We used electronic health record (EHR) data from a CHC primary care clinic and identified patients with a diagnosis of osteoporosis who have seen for the last 42 months at the clinic and still alive. The patients who have since established care in another clinic or haven't had a visit for more than 2 years are excluded. The study included 381 patients with 232 identifying as Asian (60.9%), 60 White (15.7%), 59 Black (15.5%), 15 Hispanic (3.9%), 13 Pacific Islanders (3.4%), and other race/ethnicity (0.5%). Average age was 79.9. The study population by sex, preferred language, PCP turnover rate, and CCI score are men(30, 7.9%) vs women(351, 92.1%), Vietnamese(215, 56.4%) vs English(95, 24.9%) vs Spanish(45, 11.8%) vs Cape Verdean Creole(13, 3.4%) vs other language (13, 3.4%), no PCP turnover(228, 59.8%) vs PCP turnover(153, 40.1%), CCI score 1-2(56, 14.7%) vs CCI score 3-4(164, 43%) vs CCI score ≥5 (161, 42.2%).

Results: 25 patients (6.5%) did not complete their osteoporosis treatment. The characteristics of the 25 patients consist of Asian (12, 48%), Black (9, 36%), White (2, 8%), Hispanic (2, 8%) with preferred language of Vietnamese (12, 48%), English (8, 32%), Spanish (3,12%), and Cape Verdean Creole (2, 8%). For PCP turnover, 13 out of 25(52%) patients have not experienced PCP turnover, and 12 patients (48%) have experienced. This cohort's CCI scores are 1-2(3, 20%) vs 3-4(11, 73%) vs ≥ 5(11, 73%). Compared to the patient population at the CHC with osteoporosis diagnoses, relative risk(RR)s for incomplete treatment are ①PCP turnover(RR 1.29, P=0.2) vs no turnover(RR 0.9, P=0.7); ② ethnicity, White (RR 0.54, P=0.3) vs Asian (RR 0.86, P=0.5) vs Black (RR 2.0, P=0.02) vs Hispanic (RR 2.0, P=0.4); ③ language, Vietnamese (RR 0.9, P=0.7) vs Spanish(RR 0.7,P=0.6), vs English (RR 1.2, P=0.5) vs Cape Verdean creole (RR 2.2, P=0.3); ④ CCI score, 1-2(RR 0.84, P=0.7),vs 3-4(RR 1.0, P=1.0)) vs ≥5 (RR 1.0 P=0.9).

Conclusion: Among CHC population of patients with diagnoses with osteoporosis and SDH-related needs, we looked at how PCP turnover, epidemiologic factors and clinical complexity affect treatment incompletion. Patients who experienced PCP turnover are 29% less likely to complete their treatment (RR 1.29). Black and Hispanic population and Cape Verdean Creole speaking patients are at almost doubled risk for treatment incompletion (RR ~2.0). In this study, CCI did not significantly affect Osteoporosis treatment incompletion(R~1.0). These findings highlight the impact of PCP turnover and ethnic difference/language barrier on the incompletion of osteoporosis treatment.

Disclosure: Y. Kim, None; **J. Crosson**, None.

Abstract Number: 1143

Predictors of Engagement in Bone Health Care Among Rural Veterans at Risk for Osteoporosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: A virtual bone health team (BHT) model was implemented to identify, screen, and treat rural Veterans at risk for osteoporosis. This study was conducted to identify social determinants of health and clinical factors associated with osteoporosis screening through enrollment in the BHT clinic and with osteoporosis medication initiation among those with a treatment indication.

Methods: Eligibility for BHT included: ages 50 to 99; enrollment in VA primary care; and either medication, age, or osteoporosis self-assessment tool score- based risk. A cross-sectional cohort design was utilized with a generalized estimating equation (GEE) and logit link function to account for facility-level clustering. Fully saturated and reduced models were fit using backward selection. Given population size and high percentage of medication initiators, contingency tables were constructed, and the Fisher's exact test was performed to understand medication initiation.

Results: The cohort comprised 6985 rural Veterans. Twenty-two percent accepted dual-energy X-ray absorptiometry (DXA) and were male (94%), white (95%), and married (69%), with a mean age of 76 (Table 1). Multivariate models suggest that age, distance from VA services, race, marital status, co-payment, prior fracture, or history of rheumatoid arthritis are significantly associated with DXA acceptance (Table 2). Of those with indication for medication (N=453), most were male and white, with mean age of 77 (Table 3). Few had prior DXA or osteoporosis medication, one-third had prior corticosteroid use. Fisher's exact test results suggest that a history of 2 or more falls in the prior year, current smoking, weight-bearing exercise, and parental history of hip fracture are all associated with osteoporosis medication initiation.

Table 1		
	Enrolled in BHT (N=1508) Percent (N)	Declined Care or Never Responded (N=5477) Percent (N)
Sociodemographic Characteristics		
Age		
50-64	12.33 (186)	8.86 (485)
65-79	57.29 (864)	49.04 (2686)
80-99	30.37 (458)	42.10 (2306)
Distance between Residence and Nearest VAMC		
0 to 40 Miles	12.40 (187)	6.41 (351)
> 40 Miles	87.60 (1321)	93.59 (5126)
Male	94.16 (1420)	93.79 (5137)
Race		
White	94.96 (1432)	92.06 (5042)
American Indian, Alaska Native, Native Hawaiian	0.93 (14)	1.33 (73)
African American	0.53 (8)	0.31 (17)
Asian	0.27 (4)	0.24 (13)
Unknown	3.32 (50)	6.06 (332)
Marital Status		
Married	68.50 (1033)	62.50 (3423)
Single	23.94 (361)	26.40 (1446)
Widowed	7.29 (110)	10.88 (596)
Unknown	0.27 (4)	0.22 (12)
VA Means Category		
Copayment Exempt	53.45 (806)	54.28 (2973)
Copayment Required	26.99 (407)	30.42 (1666)
Unknown	19.56 (295)	15.30 (838)
Pre-Existing Clinical		
DXA	2.92 (44)	2.92 (160)
Osteoporosis Medication	1.19 (18)	2.76 (151)
Any Fracture (Hip, Pelvis, Rib, Vertebral or Wrist)	0.13 (2)	0.57 (31)
Androgen Deprivation therapy	1.66 (25)	2.41 (132)
Corticosteroid Medication Use	31.63 (477)	30.64 (1678)
Back Pain	15.90 (240)	13.24 (725)
Rheumatoid Arthritis	0.66 (10)	0.93 (51)
Osteoporosis	1.79 (27)	2.23 (122)
Parkinson's Disease	1.19 (18)	1.15 (63)
Comorbidity Index (Mean,SD)	2.44 (4.97)	2.83 (5.53)
Number of Primary Care Encounters During Previous Year		
0	30.04 (453)	31.09 (1703)
1+	69.96 (1055)	68.91 (3774)

Sociodemographic and Clinical Characteristics of Eligible Veterans by Decision to Enroll

Conclusion: The BHT model facilitated DXA for rural Veterans at their nearest VA or non-VA facility, but cost and travel remain barriers to DXA in addition to other social determinants of health such marital status, race, and gender. Some known osteoporosis risk factors were associated with lower acceptance of DXA. Age, distance, marital status, and race were not associated with medication initiation, while the proportion of rural Veterans with a history of falls or smoking was greater for those who initiated medication. Further efforts are needed to gain insight into how clini-

Baseline Variables	Fully Saturated Model OR (95% CI)	p	Reduced Model OR (95% CI)	p
Age (ref: 50 to 64)				
65 to 79	0.87 (0.72-1.06)	0.17	0.89 (0.73-1.10)	0.30
80 to 99	0.55 (0.42-0.71)	<0.01	0.57 (0.45-0.72)	<0.01
Distance between residence and nearest VAMC				
>40 miles	0.54 (0.43-0.67)	<0.01	0.54 (0.43-0.68)	<0.01
Female	0.80 (0.58-1.11)	0.18		
Race (ref: white)				
African American	1.23 (0.52-2.94)	0.64	1.19 (0.51-2.82)	0.69
All other	0.59 (0.45-0.78)	<0.01	0.60 (0.46-0.77)	<0.01
Marital status (ref: married)				
Single	0.73 (0.60-0.90)	<0.01	0.72 (0.57-0.91)	<0.01
Widowed	0.70 (0.58-0.84)	<0.01	0.69 (0.56-0.84)	<0.01
Unknown	1.11 (0.39-3.11)	0.85	1.11 (0.38-3.25)	0.85
VA means category (ref: copayment required)				
Copayment exempt	1.13 (1.03-1.25)	0.01	1.13 (1.02-1.25)	0.02
Unknown	1.39 (1.19-1.62)	<0.01	1.33 (1.06-1.66)	0.01
Any fracture (hip, pelvis, rib, vertebral or wrist)	0.25 (0.12-0.50)	<0.01	0.24 (0.10-0.56)	<0.01
Androgen deprivation therapy	0.63 (0.40-0.99)	0.05		
Corticosteroid medication use	1.02 (0.87-1.21)	0.78		
Rheumatoid arthritis	0.65 (0.49-0.87)	<0.01	0.67 (0.51-0.90)	<0.01
Parkinson's disease	1.12 (0.67-1.88)	0.67		
Comorbidity index	0.99 (0.98-1.00)	0.18		
At least 1 primary care encounter during previous year (ref=none)	1.20 (0.74-1.95)	0.46		

Multivariate Logistic Regression Model Predicting BHT Enrollment

cal and social factors impact perception of risk and how health care systems can incorporate social determinant of health and clinical predictors of bone health care engagement to improve bone health care delivery across a variety of contexts.

Table 3

	Medication Indicated (N=453) Percent (N)	
	Initiate (N=407)	Decline (N=46)
Sociodemographic Characteristics		
Age		
50-64	5.65 (23)	4.35(2)
65-79	48.65 (198)	60.87 (28)
80-99	45.70 (186)	34.78 (16)
Distance between Residence and Nearest VAMC		
0 to 40 Miles	7.86 (32)	8.70 (4)
> 40 Miles	92.14 (375)	91.30 (42)
Male	96.56 (393)	93.48 (43)
Race		
White	95.82 (390)	95.65 (44)
American Indian, Alaska Native, Native Hawaiian	0.74 (3)	0 (0)
Black	0 (0)	0 (0)
Asian	0.25 (1)	0 (0)
Unknown	3.19 (13)	4.35 (2)
Marital Status		
Married	66.09 (269)	73.91 (34)
Single	24.57 (100)	17.39 (8)
Widowed	8.60 (35)	8.70 (4)
Unknown	0.74 (3)	0 (0)
VA Means Category		
Copayment Exempt	56.02 (228)	52.17 (24)
Copayment Required	27.27 (111)	28.26 (13)
Unknown	16.71 (68)	19.57 (9)
Pre-Existing Clinical		
Prior DXA	4.91 (20)	8.70 (4)
Prior Osteoporosis Medication	1.72 (7)	6.52 (3)
Prior Androgen Deprivation therapy	1.23 (5)	0 (0)
Prior Corticosteroid Medication Use	32.19 (131)	34.78 (16)
Parkinson's Disease	1.97 (8)	0(0)
Rheumatoid Arthritis	1.47 (6)	0 (0)
Comorbidity Index (Mean, SD)	3.06 (5.37)	3.28 (5.39)
Number of Primary Care Encounters During Previous Year		
0	28.50 (116)	19.57 (9)
1+	71.50 (291)	80.43 (37)
Clinic Evaluation		
Parental History of Hip Fracture	97.30 (396)	89.13 (41)
Prior History of Smoking	38.82 (158)	32.61 (15)
Weight Bearing Exercise	94.35 (384)	78.26 (36)
History of Falls	18.67 (76)	2.17 (1)
Diagnosis		
Osteopenia with Low Fracture Risk	0.49 (2)	2.17 (1)
Osteopenia with High Fracture Risk	57.49 (234)	45.65 (21)
Osteoporosis by DXA	36.12 (147)	46.65 (21)
Osteoporosis by Clinical Factors	9.83 (40)	6.52 (3)

Veteran Characteristics by Response to Treatment Recommendations for Those Enrolled in BHT

Disclosure: K. Miller, None; **K. McCoy**, None; **C. Richards**, None; **A. Seaman**, None; **S. Solimeo**, None.

Abstract Number: 1144

Underestimation of the Fracture Risk by the FRAX Formula in Chronic Glucocorticoid Users: A 10-year Longitudinal Validation Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: To compare the actual fracture incidence over 10 years in a longitudinal cohort of patients using glucocorticoids (GCs) with the risk prediction from FRAX (fracture risk assessment tool).

Methods: Adult patients who attended our out-patient rheumatology clinics between 2007 and 2009 who had underlying rheumatic diseases requiring prednisolone treatment (≥5mg/day) and had a DXA scan performed were included. The predicted rates of major osteoporotic and hip fractures were estimated using FRAX (China database) based on the clinical data at the time of DXA, with adjustment when daily dose of prednisolone ≥7.5mg according to the ACR recommendation. The actual observed incidence of symptomatic vertebral and non-vertebral fractures at 10 years (in years 2017-2019) follow-up was retrieved by medical record review and compared with the estimated rates by FRAX. Factors associated with symptomatic clinical fractures at 10 years were studied by logistic regression.

Results: 89 patients were studied (age 49.3±8.8 years at DXA examination; 98% women). The underlying rheumatic diseases were systemic lupus erythematosus (69%), rheumatoid arthritis (17%) and others (14%). The mean daily dose of prednisolone at baseline was 7.7±6.5mg (38% patients had daily dose ≥7.5mg). History of personal fracture was present in 4(4.5%) patients and 22% of female patients had menopause before the age of 45 years. The mean body mass index (BMI) was 23.5±3.3kg/m^2 (4.5% ≤18kg/m^2). Osteoporosis (bone mineral density [BMD] T score ≤-2.5) of the hip, femoral neck and lumbar spine occurred at a frequency of 11.2%, 13.5% and 25.8%, respectively at baseline (32% at any of the 3 sites). 30(34%) patients received anti-osteoporotic treatment (oral bisphosphonates in 25, raloxifene in 3 and denosumab in 2 patients). The estimated mean 10-year risk of major osteoporotic and hip fractures using the BMD data and other risk factors in the FRAX formula, adjusted for prednisolone dose, was 4.3% and 1.0%, respectively. After a follow-up of 10 years, one patient had a hip fracture, 3 patients had humerus fractures and 9 patients had symptomatic vertebral fractures. The actual observed major osteoporotic and hip fracture incidence was 14.6% and 1.1%, respectively (0.146 and 0.011 per 10 patient-years). The observed major clinical fracture rate was significantly higher than that estimated by FRAX (14.6% vs 4.3%; p=0.04). Logistic regression revealed that the only factor independently associated with major clinical fracture at 10 years was BMD T score ≤-2.5 at spine, hip or femoral neck at baseline (OR7.11[1.73-29.2]; p=0.007). Age, prednisolone daily dose, BMI, history of fracture, chronic smoking, having underlying SLE vs not and early menopause were not significantly associated with new clinical fractures.

Conclusion: Despite adjustment for prednisolone dosage, the FRAX formula underestimates the major clinical fracture risk in patients using long-term GCs. The deleterious effect of GCs on bone quality, high proportion of SLE patients, disease activity and use of additional doses of GCs and other immunosuppressive drugs during follow-up are among the contributing factors for this underestimation.

Disclosure: C. Mok, None; **L. Ho**, None; **S. TSE**, None; **K. Chan**, None.

Abstract Number: 1145

Prevalence of and Risk Factors for Vertebral Fractures and Low Bone Mass Density Among Women Aging with HIV in Peru

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)

Session Type: Poster Session C

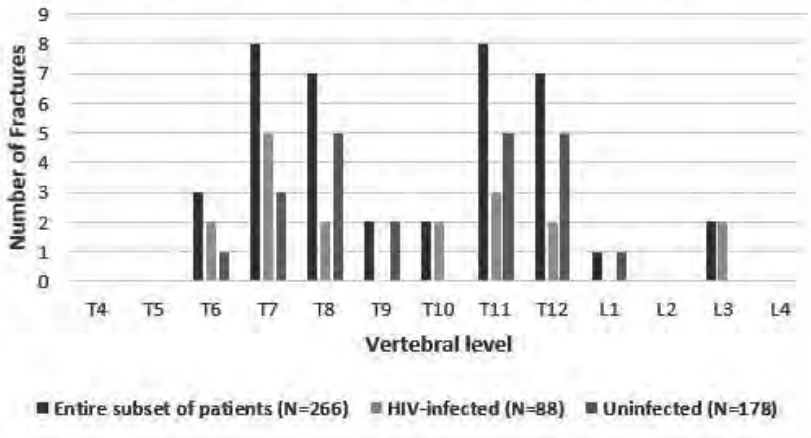
Session Time: 8:30AM–10:30AM

Background/Purpose: Few studies in Latin America and the Caribbean have evaluated osteoporosis and fracture epidemiology among populations at increased risk for secondary osteoporosis, such as women with HIV. We aimed to explore the prevalence of vertebral fracture (VF) and low bone mineral density (BMD) among women aging with HIV in Peru, in order to identify risk factors for osteoporosis and fracture in this population.

Methods: We enrolled HIV-infected and uninfected women aged ≥40 years from a large HIV clinic in Lima, Peru between October 2019 and March 2020. All participants completed a survey regarding sociodemographic, clinical and fracture-associated risk factors, and obtained a dual X-ray absorptiometry (DXA) scan to assess BMD at the lumbar spine, femoral neck and total hip. A subset of patients also obtained lateral thoracolumbar X-rays. Presence of VF was determined using the Genant semiquantitative method. Linear and logistic regression analyses were used to model associations between key risk factors and BMD at each site.

Results: A total of 104 HIV-infected and 212 uninfected women were enrolled with a mean age of 52.4±8.2 and 56.4±8.8 years ($p< 0.001$) and BMI of 26.4±5.1 and 27.6±4.1 kg/m^2 ($p=0.03$), respectively. Among postmenopausal women (257/316, 81.3%), 26.3% of HIV-infected and 25.9% of uninfected had osteoporosis. Among the subset of 88 HIV-infected and 178 HIV-uninfected who obtained thoracolumbar x-rays, 12.5% and 6.2% respectively had at least one VF. Both of these comparisons were not statistically significant. The mean 10-year FRAX risk of major osteo-

Figure. Counts of fracture by vertebral level



porotic fracture and hip fracture was 2.65% and 0.59% among women with HIV. Based on DXA and the FRAX score, 22/104 HIV-infected women met criteria for osteoporosis treatment according to national guidelines, however, none were on treatment. Unadjusted logistic regression analysis among the pre and postmenopausal HIV-infected showed that age ($p< 0.001$), postmenopausal status ($p=0.04$) and years of antiretroviral therapy ($p=0.05$) were predictors for lower BMD. Adjusted linear regression analysis showed that BMD was negatively correlated with older age and positively correlated to higher BMI.

Conclusion: In this study, HIV-infected women had increased VF prevalence compared to the slightly older uninfected group. Age and BMI were independent predictors for BMD at the lumbar spine, hip and femoral neck among women with HIV, and there was a treatment gap among osteoporosis diagnosed women. Larger prospective studies are needed in this region to identify individuals at risk for fracture and to inform prevention guidelines.

Disclosure: D. Cabrera, None; **M. Cornejo**, None; **R. Slotkin**, None; **Y. Pinedo**, None; **W. Yu**, None; **W. Guan**, None; **P. Garcia**, None; **E. Hsieh**, None.

Abstract Number: 1146

Study of Vertebral and Femur Fracture Prevalence and Scanographic Bone Attenuation Coefficient of the First Lumbar Vertebra in an Academic Hospital Setting

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with osteoporosis are prone to suffer fragility fractures leading to an increased risk of future fractures. Detection of osteoporosis has been led by dual energy-ray absorptiometry (DEXA) as the gold standard. However, in acute fracture incidents, DEXA imaging is typically unavailable, and treatment is often delayed. In recent years scanographic bone attenuation coefficient of the first (SBAC-L1) on incidental computed tomography (CT) scans of the lumbar spine has been utilized as an alternative assessment of bone density. In particular, SBAC-L1 $\leq$ 145 HU correlates with osteoporotic bone density on DEXA imaging.

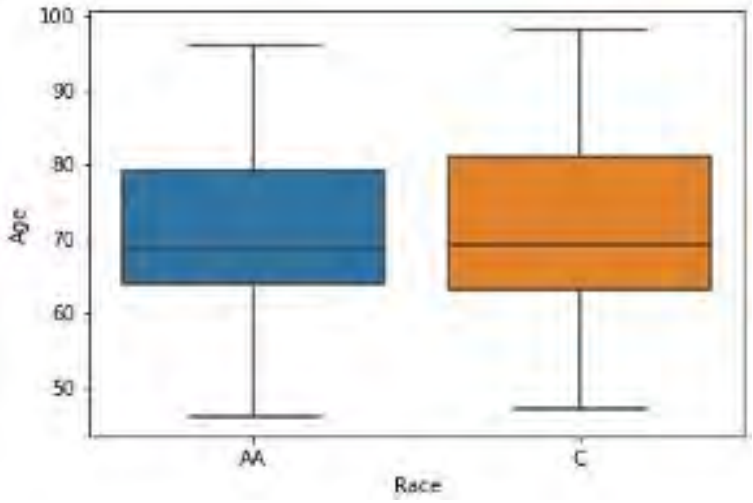
This study aims to assess the SBAC-L1 in HU of incidental CT scans in patients presenting with vertebra or femur fragility fractures in an academic hospital as it relates to osteoporosis.

Methods: We conducted a retrospective chart review of patients aged $\geq$ 45 admitted to an academic hospital for active vertebral or femur fracture between 1/1/2017- 1/31/2019, excluding traumatic and pathological fractures. Measurement of SBAC-L1 in HU was obtained on incidental CT scan imaging. Sex, race, prior and post diagnoses of osteoporosis, prior and post DEXA scan orders, use of calcium, vitamin D, and steroids were abstracted.

Results: There were 297 patients with vertebral or femur fractures from 1/1/2017- 1/31/2019. Of 297 patients, 85 deemed appropriate after excluding pathological, traumatic fractures, and lack of CT scan on the admission for fracture.

	Total Patients [n=85]	Caucasian Patients [n=67]	AA Patients [n=16]	Male Patients [n=31]	Female Patients [n=54]
SBAC- L1 Average ± SD (HU)	100.4 ± 46.5	99.4 ± 44.1	122.1 ± 49.9	97.4 ± 44.3	106.3 ± 47.2
Patients with SBAC- L1 ≤ 145 HU	70	58	10	26	44
Patients with SBAC- L1 > 145 HU	15	9	6	5	10
Vertebral Fractures	57	47	8	19	38
Femur Fractures	28	20	8	12	16
Age Average	71.7	72	70.9	74	70.4
Prior diagnosis of osteoporosis	16	15	1	2	14
Post diagnosis of osteoporosis	6	2	2	2	4
Calcium	20	16	2	2	18
Vitamin D	26	23	1	6	20
Osteoporosis medication	9	8	0	0	9
Steroid use	5	4	1	2	3
DEXA prior	13	12	1	0	13
DEXA after	7	4	1	2	5

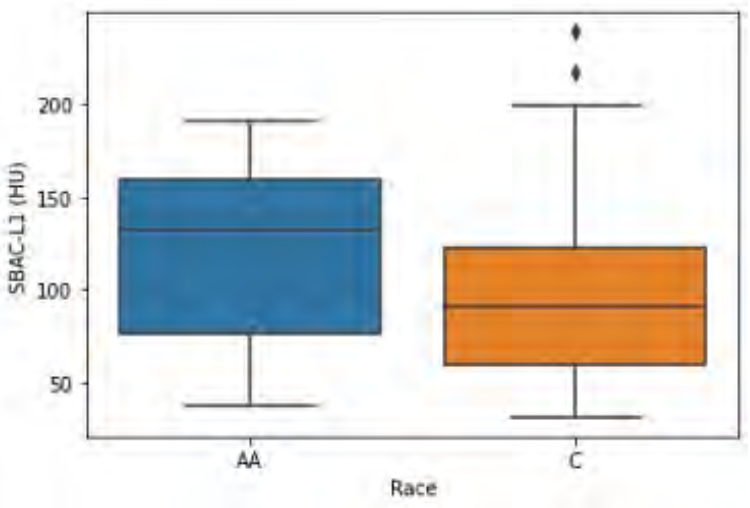
Study Characteristics



Comparison in Age for African American (AA) patients and Caucasian (C) patients

Average SBAC-L1 for all patients was 100.4 ± standard deviation (SD) of 46.5 HU. 82% of all patients had SBAC-L1 ≤ 145 HU. Caucasian patients had a lower average SBAC-L1 [99.4 HU] than African American (AA) patients [122.1 HU]. More Caucasian [n=15] had prior diagnoses of osteoporosis than AA [n=2]. Caucasian patients were prescribed Calcium and Vitamin D more often [n=39] than AA [n=3]. DEXA scan orders were placed more often in Caucasian patients [n=4] than AA patients [n=1]. Osteoporosis medications were prescribed more often in Caucasian patients [n=8] than AA patients [n=0].

Male average SBAC-L1 was 97.4 HU compared to females at 106.3 HU. Females were prescribed calcium and vitamin D more often [n=38] than males [n=8]. DEXA scan orders were placed more frequently in females [n=5] than males [n=2]. Osteoporosis medications were prescribed more often in females [n=9] than male patients [n=0].



SBAC- L1 (HU) in African American (AA) and Caucasian (C) races

Conclusion: 70 of 85 patients with incidental fragility fractures exhibited SBAC-L1 ≤ 145 HU. This is consistent with osteoporotic bone density on DEXA imaging supporting the use of SBAC-L1 measurement to corroborate the diagnosis osteoporosis. SBAC-L1 ≤ 145 HU can be utilized to increase inpatient diagnostic confidence of osteoporosis in the setting of acute fragility fractures to allow initiation of treatment prior to awaiting outpatient DEXA imaging.

The results here also highlight health disparities present among African Americans and males of all races when considering bone health.

Disclosure: Z. Vaghaiwalla, None; **P. Wasserman**, None; **G. Kaeley**, Novartis, 2.

Abstract Number: 1147

Therapeutic Inertia and Low Patient Compliance: Major Contributors to Low Treatment Rates in Patients with Osteoporosis with Clinical Vertebral Compression Fractures

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SESSION INFORMATION
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Background/Purpose: Treatment rates with pharmacologic therapy after osteoporotic vertebral fracture are very low in the United States. Underlying causes of these low treatment rates are poorly understood. Poor communication between acute care teams and primary care providers (PCP), a lack of acknowledgement of vertebral compression fracture as an osteoporotic fragility fracture by PCPs, and a reluctance by patients to start therapy due to concerns regarding side effects have been proposed as possible driving factors. The objective of this study was to define major underlying causes of low treatment rates of osteoporosis in patients with clinical vertebral fractures in our community.

Methods: Medical records of 862 patients seen for new-onset clinical vertebral fractures were retrospectively analyzed to determine if a diagnosis of osteoporosis was recognized by the PCP and if appropriate pharmacotherapy was initiated by the PCP once a diagnosis of osteoporosis was recognized. Subsequent PCP visit records were analyzed to determine if patients started therapy once prescribed.

Results: Total of 862 patients were seen at our health system for new clinical vertebral fractures in the year 2020. A majority of these patients (615 =71%) were seen by their PCP for clinic follow-up within six months of the fracture. PCPs recognized occurrence of clinical vertebral compression fracture in the interim and diagnosed patients with osteoporosis in most cases, (595 patients =96%). However, less than half of these patients (254=40%) were started on pharmacologic treatment for osteoporosis by their PCP. Of the patients that were prescribed this treatment, less than half (105 =41%) decided to proceed with this treatment resulting in an overall treatment rate of around 12 percent at six months of follow up.

Conclusion: Despite regular identification of vertebral compression fractures, therapeutic inertia by PCPs and low compliance by patients were the most important factors contributing to low treatment rates for osteoporosis after these clinical vertebral fractures were identified in this population.

Disclosure: S. Malaty, None; **P. Sidhu**, None; **R. Sharer**, None; **S. Kim**, None.

Abstract Number: 1148

Prevalence and Risk Factors of Insufficiency Fractures of the Foot and Ankle Joint in Rheumatic and Musculoskeletal Diseases

Bjoern Buehring[1], Nadine Al-Azem[1], Ioana Andreica[1], David Kiefer[2], Uta Kiltz[1], Styliani Tsiami[1], Xenofon Baraliakos[1] and Juergen Braun[1], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany, [2]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Essen, Germany

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Unlike fragility fractures, high-trauma and insufficiency fractures (IF) are not classically considered osteoporotic fractures. Patients with rheumatic and musculoskeletal diseases (RMD), especially those with rheumatoid arthritis (RA), are at increased risk of IF due to factors associated with reduced bone quality including chronic inflammation, medication, and altered biomechanics. IF frequently occur in ankle joints and feet. These fractures are often not detected in conventional radiographs, magnetic resonance imaging (MRI) is thought to be more sensitive.

The aim of this study was (i) to determine the frequency of IF in symptomatic ankles and feet of patients presenting to a tertiary hospital, to (ii) identify possible risk factors and (iii) to compare the IF detection rate of radiographs and MRI.

Methods: Using a retrospective study design, data of patients who had undergone MRI scans of the ankle/foot region between 2016 and 2018 were analyzed. Patients with IF were matched with 2 control subjects based on sex, age, and diagnosis and pertinent data was extracted from their medical records. Statistical analyses included T tests, chi-square tests, and regression analyses.

Patient demographics

		Group			
		Insufficieny fracture (A)		Control (B)	
		Column N %	Mean	Column N %	Mean
Sex	female	82,9%		80,8%	
	male	17,1%		19,2%	
Age (years)			58,59		57,72
BMI			28,03		29,67 A
Illness	RA	42,6%		46,3%	
	PsoA	16,3%		18,8%	
	other CIRD	21,7%		19,7%	
	non-CIRD	19,4%		15,3%	
Current glucocorticoids	yes	48,1%		44,5%	
	no	51,9%		55,5%	
MTX	yes	42,6% B		27,9%	
	no	57,4%		72,1% A	
Smoking	yes	37,2% B		23,1%	
	no	62,8%		76,9% A	
Osteoporosis	yes	42,6% B		16,2%	
	no	57,4%		83,8% A	
Lowest T-score			-1,78		-1,20 A
History of fracture	yes	34,9% B		8,8%	
	no	65,1%		91,2% A	

Results are based on two-sided tests. For each significant pair, the key of the category with the smaller column proportion appears in the category with the larger column proportion.
Significance level for upper case letters (A, B, C): ,05 [1]

1. Tests are adjusted for all pairwise comparisons within a row of each innermost subtable using the Bonferroni correction.

Patient demographics BMI - body mass index, RA - rheumatoid arthritis, PsoA - psoriatic arthritis, CIRD - chronic inflammatory rheumatic disease, MTX - methotraxate

Results: In a total of 1471 foot and 281 ankle joint MRIs, 129 (7.4%) IF were detected. The mean age of patients with IF was 59 years, 82.9% were women. Among patients with IF 80,6% had a chronic inflammatory rheumatic disease (CIRD) which was significantly more frequent than non-CIRD diseases (19,4%, p< 0,001). Potential risk factors for IF were: low bone density indicative of osteoporosis (IF 42.6% vs. controls 16.2%, p< 0.001), history of previous fracture

(34.9% vs. 8.6%, p< 0.001), smoking (37.3% vs. 23.1%, p=0.005) and current methotrexate (MTX) therapy (42.6% vs. 27.9%, p=0.005). Of the 96 (74.4%) IF patients who also had x-rays of the ankle/foot region, 24 (25%) had an IF diagnosis in the x-ray report.

Conclusion: With a frequency of 7.4%, IF are a relatively common cause of foot/ankle pain in patients with RMD who underwent MRI after presenting to a tertiary rheumatology hospital. Risk factors for IF largely corresponded to established risk factors for osteoporosis. The potential negative influence of MTX needs further research. Future studies should investigate whether the occurrence of IF represents an indication for anti-osteoporotic therapy and whether such treatment improves fracture healing and lowers the risk of future fractures.

Disclosure: B. Buehring, None; **N. Al-Azem**, None; **I. Andreica**, None; **D. Kiefer**, None; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **S. Tsiami**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5.

Abstract Number: 1149

Efficacy of Alendronate for Prevention of New Fractures and Vertebral Deformities in Patients with Rheumatologic Disorders on Chronic Glucocorticoid Therapy: A Systematic Review and Meta-analysis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Osteoporosis & Metabolic Bone Disease – Basic & Clinical Science Poster (1135–1149)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Glucocorticoids are commonly used in patients with rheumatologic conditions including but not limited to Rheumatoid Arthritis, Polymyalgia Rheumatica, Systemic Lupus Erythematous and so on. There is increased rate of bone resorption after the first few months of initiating glucocorticoid therapy. The risk of bone fractures increase before a decrease in bone mineral density is observed. One of the most common side effects include new fractures and vertebral deformities. Interventions to reduce the risk of fractures involve the use of Alendronate. Alendronate is a bisphosphonate that works by inhibiting the osteoclast mediated bone resorption. It is important to study the benefit of Alendronate on fractures and vertebral deformities in patients who are on long term steroid therapy.

Methods: We conducted a systematic review and meta-analysis of studies that investigated the efficacy of Alendronate for prevention of new fractures and vertebral deformities. We performed a comprehensive search of PubMed/MEDLINE, Embase, and the Cochrane Central Register of Controlled Trials from 2006-2016. We considered randomized control trials. We excluded abstracts, animal studies, case reports, reviews, editorials, cohort studies, case-

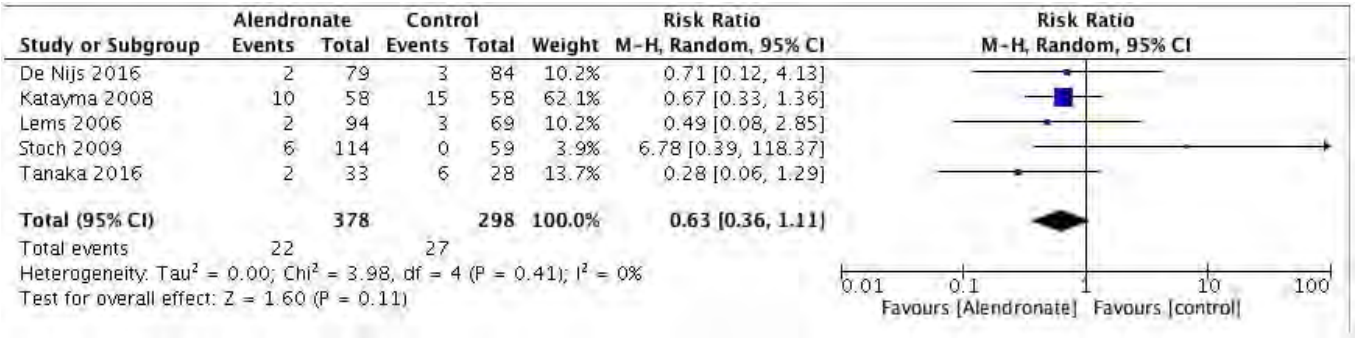

Figure 1.1 Forest plot - Rates of fracture when using Alendronate versus Control.

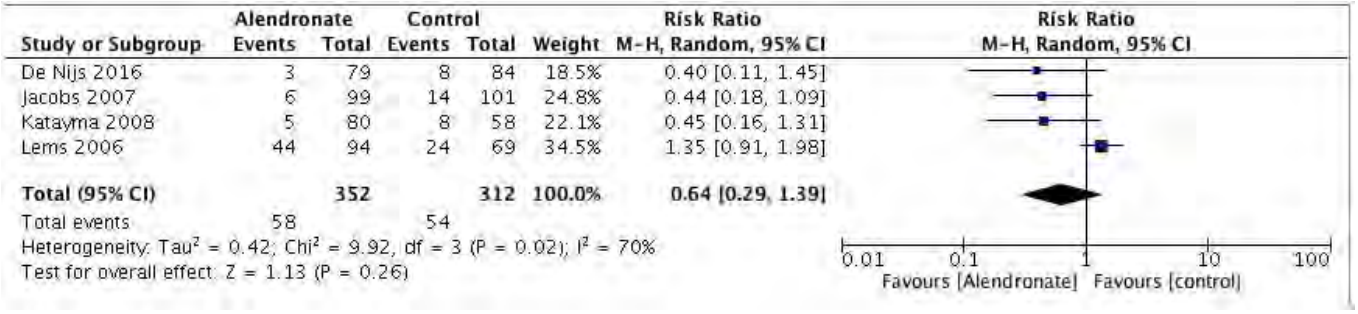

Figure 1.2. Forest Plot- Rate of Vertebral Deformities in Patients with Alendronate versus Control.

control studies, case series and letters to editors. From each study, we collected the number of patients who received Alendronate and other forms of bone protective measures including vitamin D and calcium. The primary outcome was the rate of new fractures. The secondary outcome was rate of vertebral deformities. The random-effects model was used to calculate the risk ratios (RR), mean differences (MD), and confidence intervals (CI). A p value < 0.05 was considered statistically significant. Heterogeneity was assessed using the Higgins I^2 index.

Results: Six randomized control involving 898 patients were included in the meta analysis. Five studies showed that there was no significant difference in the rate of new fractures between the Alendronate group in comparison to the control group (5.8% vs. 9.06% ;RR 0.63, 95% CI 0.36-1.11, p=0.11, I^2 = 0%). Four studies were analyzed to assess for new vertebral deformities in patients receiving Alendronate versus control. There was no significant difference between the rate of vertebral deformities between the two groups (16.5% vs. 1.6%; RR 0.64, 95% CI 0.29-1.39, p=0.26, I^2 = 70%).

Conclusion: Our meta-analysis demonstrated that the use of Alendronate versus control in patients with rheumatologic conditions on chronic prednisone therapy, did not display any significant reduction in new fractures and vertebral deformities. Further randomized control trials with larger sample sizes are needed to confirm our findings.

Disclosure: S. Iftikhar, None; **W. Khokher**, None; **A. Acharya**, None; **J. Gekonde**, None; **N. Kesireddy**, None; **R. Fatima**, None; **N. Altorok**, None.

Abstract Number: 1150

Use of Energy Conversation Strategies as a Result of the Fatigue Management Education for Individuals with Systemic Sclerosis (FAME-iSS)

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Education/Community Programs Poster (1150–1152)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue remains an understudied symptom of systemic sclerosis (SSc). For other diagnoses, increasing the use of energy conservation strategies, especially pacing. has been associated with reduction in fatigue. The purpose of this ongoing study is to understand the use of energy conservation strategies after participation in a new program, Fatigue and Activity Management Education for Individuals with Systemic Sclerosis (FAME-iSS).

Methods: Adult participants were recruited from the Scleroderma Foundation chapters to participate in a 6-week, virtual, occupational therapist-led group program focused on SSc-related fatigue. Eligible participants had a minimum score reflecting moderate to high fatigue experienced, severity, and distress (scales: 1-10). At baseline, participants completed a demographic questionnaire, the Self-Efficacy for Performing Energy Conservation Strategies Assessment (SEPESCA) to measure their confidence in their ability to use energy conservation strategies. At post-intervention and 3-month follow-up, participants also completed the Energy Conservation Strategies Survey to identify use and effectiveness of 14 energy conservation strategies (e.g. changing body positions, planning and prioritizing, communicating needs) and a qualitative interview to contextualize their responses. Descriptive statistics were analyzed; medians and ranges for assessment scores are reported.

Results: Preliminary analysis includes four participants (75% White women; 51.8±12.1 years old) with established SSc (disease duration= 12±8.0 years). All participants completed 100% of FAME-iSS sessions. At post-intervention, all energy conservation strategies were being used by at least 50% of participants, and 7/14 strategies were being used by 75% of participants. Participants perceived effectiveness of strategies as high [8 (3-10)]. The most common cited reason for not adopting a new strategy after the intervention was that it was already in use (17/21 items; 81%). At 3-month follow-up, 11/14 strategies were used by at least 50% of participants, and 5/14 strategies were used by 75% of participants. Perceived effectiveness slightly decreased [7 (2-10)]. While not statistically significant, participants trended toward improved self-efficacy scores for energy conservation strategies (baseline: 8.3 (5.4-8.0); post-intervention: 9.2 (8.3-9.2); 3-month follow-up: 9.6 (4.4-10)]. Participants qualitatively reported that FAME-iSS led to the sharing of new fatigue management strategies and increased attention to their daily activities.

Conclusion: Despite longer disease duration and familiarization with self-management strategies, participants with SSc experienced persistent and disruptive fatigue symptoms. Following completion of FAME-iSS, participants with established SSc adopted new behaviors that they perceived to effectively reduce fatigue. A second round of the intervention is in progress to diversify the participant sample and continue assessing the relationship between FAME-iSS, energy conservation strategies, and quality of life constructs.

Disclosure: J. Poole, None; **D. Connolly**, None; **K. Carandang**, None.

Abstract Number: 1151

Experiences and Finding Meaning Among Latin Americans Living with Lupus: Learning from Social Media Narratives by Patients and Their Social Network

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Table 1. Patients' Experiences of Living with Lupus

Theme	Subtheme	Quote
Lived Experiences	Before & after lupus	*"I have this disease too, and it makes me sad that I used to be very active, and now it's tough for me to do my activities. I have systemic lupus erythematosus and other health issues that come with it. I follow my treatment faithfully. Five years in remission, ten years since the diagnosis. It took a lot of work, but I made it. I've gone through several stages over the years, from fear, anguish, uncertainty, and finally acceptance."*
		"It hits you hard at first, and it's a condition they don't know much about, but I've learned to stop seeing it as my enemy, and little by little, I've been learning to live with lupus. It's true that it's not easy, but it's also true that if you follow the recommendations, change your lifestyle a bit and take care of yourself, you can lead a reasonably normal life."
	Good and bad days: Fluctuation and uncertainty	*"I've had lupus for eight years. I've gone through highs and lows; up until now, I'm fine, and I can say that I've fought it off twice. It's not just any disease; you suffer a lot, you can't lead a normal life like before, you can't have a good quality of life, but I fall, and I get back up again to keep going for my children. The only advice I can give is that you need to push forward without turning back and that you need to become friend with the disease because that's how you can overcome everything that lupus, "THE WOLF THAT ATTACKS YOU," deals you."*
		"There are days when I have lots of energy and other days when the pain in my legs and joints doesn't let up–that's when I think I can't take it anymore. I'm a very positive person, but there are days the pain is overwhelming, and you don't want to get out of bed, and it's depressing, and worst of all, people think it's not that big of a deal."
	The bodily experience of lupus	*"I went through some really tough times; in my case, it [lupus] affected everything, the only thing it didn't affect were my kidneys; I went through a lot, my lupus was pretty aggressive, all my hair fell out."*
		"It's an immune disorder; in other words, the person's own body is attacking itself; it's painful, there are times when it shows up on your face, you can have intense swelling in your legs or feet; other times it attacks the brain, it swells, and that's where it all ends."
	The invisibility of lupus	*"Some people think I'm pretending to be sick, not to work when I feel weak or get dizzy spells out of nowhere. Some people don't understand what I'm going through because they're not in my shoes. I hope these people go through what I'm going through; sooner or later, everything that goes around comes around in this life."*
		"I feel so alone; my husband says there's nothing wrong with me... Dozens of studies have proven otherwise, but I think he's already fed up with me."
	Hope	*"I've had SLE for almost 30 years, now in remission; it affected my nervous system, joints, sight, hearing, and skin. I can hardly walk, the nerves on my left side are damaged. I have very bad days, those days I try to beat the disease, and when they're not so bad, I try to enjoy those days to the fullest. I think without a doubt that my faith in GOD and the support of my family, my husband, and daughters, are what give me strength on the worst days to hope against hope that I'll be better."*

All quotes were extracted from public comments written in Spanish. Quotes were further translated to English by one of the authors (IPB) and independently proofread by a native English-speaker women with a diagnosis of lupus, and a native English-speaker physician (EC) who is fluent in Spanish.

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Patient Education/Community Programs Poster (1150–1152)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: SLE disproportionately affects Latin Americans, and outcomes are worse amongst them compared to non-minority populations. Understanding patients' views of living with SLE is critical to provide proper care and inform culturally competent self-care education programs. However, little is known about illness experiences and perspectives among Latin Americans with lupus. This qualitative study describes the lived experiences and perceived meanings regarding lupus, which have been shared by Latin American patients and their relatives on an open Facebook page.

Methods: Let's Talk About Lupus (*Hablemos de Lupus*) is a public Facebook page that provides reliable and culturally competent education to Spanish speakers living with lupus. Launched in May 2017, the page has gathered nearly 100,000 followers by May 2021. Users often share their stories, questions, and thoughts organically with peers and a team of rheumatologist educators. For this study, we used the Facepager application to extract de-identified narratives posted as a reaction to the most popular resources published within the first 2 years (6 animated videos and 6 patients' testimonials). We conducted a thematic analysis using ATLAS.ti v8, with further triangulation to verify concordance and aid in an interpretative medical anthropology framework.

Table 2. Meanings of Living with Lupus

Theme	Subtheme	Quote
Religious & spiritual thoughts	Grateful to God	*"My life [goal of living] with lupus is to enjoy the moments when I'm well, and I thank God and life for one more day; sometimes, I fall into the deepest darkness, and it seems impossible to move forward. God, the universe, life, gives me another chance, and I am thankful for every moment of my life!!!!!."*
		"... I have lupus; they've just diagnosed it... It was a really difficult process for me; my life changed entirely overnight, but thanks to Jehovah God, who has given me strength and trust in Him, right now I'm doing very well; I lead a normal life, I'm still working, taking my treatment as I should and am grateful to Jehovah God for one more day of life."
	Lupus control by God	*"I've had this disease for over ten years; it's become a part of me, and I have so much faith in God that I feel healthy because only He has control of everything. [I] Put this disease in His hands, and you'll see that everything will be better... I don't even take treatment anymore."*
Metaphors	The purple butterfly	*"Not long ago at night, a dark butterfly stopped at my window. One just like the butterfly my friends with lupus put on their logos and posters to indicate that there, under that poster or inside the purple butterfly T-shirt, there is a survivor (because that's what you do when you have lupus) who wants to go on, who's strong, who loves and dances and runs even if her body and science tell her that she can no longer do so. Well, let's say that sometimes I'm like this, a bit, like the dark butterfly who has lost her way, who turns and turns until she lands on someone's leg asking for help because, in confusion, she doesn't remember and feels that she has nothing left but to trust... She'll just readjust and then go on with her flight, and we have to keep being happy and live each day as if it were the last, so seize the day, keep fighting warrior, butterfly."*
	Not belonging	*"I have that "curse" sometimes it [the disease] punishes me a lot, sometimes it lets up... you have to push through day to day!!!"*
	Bellicose discourse	*"Today I feel strong, with the attitude of an implacable warrior, yearning for victories, every battle won strengthens my spirit. I continue the struggle; every day, I learn to endure it with hope and attitude."*
Heredity	Genetic/ hereditary disease	*"No one in my town knew how to take care of my brothers. I lost three of them and my mother when I was five. Ours is genetic. But I came to the capital [city] and with [the help of] immunologists and different studies, and controls you can have a good life..."*
Experience by Family & Friends	Compassion	*"As a mother, I can tell you that it's horrible to see your daughter with this condition since there's no cure, and I have nothing but admiration for my daughter; she hardly complains at all and has been sick."*

All quotes were extracted from public comments written in Spanish. Quotes were further translated to English by one of the authors (IPB) and independently proofread by a native English-speaker women with a diagnosis of lupus, and a native English-speaker physician (EC) who is fluent in Spanish.

Results: We analyzed 1717 independent comments. Five core themes emerged: lived experiences of lupus (Table 1), religious/spiritual thoughts, lupus metaphors, lupus heredity, and family/friends' experiences (Table 2). Being diagnosed with lupus is perceived as a life-changing event. The fluctuating course of the disease causes uncertainty among patients, and the perception of invisibility within the patient's social circle generates feelings of being misunderstood. Faith and spiritual thoughts are used to cope with living with lupus. Patients use metaphors to communicate the disease's meaning and their lived experiences (e.g., the purple butterfly, not belonging, a hidden enemy, and bellicose discourse). The lupus experience extends to the family, and relatives are negatively impacted by their loved one's suffering.

Conclusion: Latin American patients experience lupus as an unpredictable condition that brings about suffering trajectories to patients, relatives, and friends. Inheriting lupus is a concern shared by patients and families. Patients use metaphoric language to foster empathy and sympathy within their social context. Metaphors are also used to overcome the challenges in communicating the illness experience, which many perceive as an 'invisible illness.' Religion is as important as medical treatment in coping with the disease. These findings can be used to improve physician-patient communication and public health campaigns to serve Latin Americans with lupus.

Disclosure: T. Colmenares-Roa, None; **A. Gastelum-Strozzi**, None; **E. Crosley**, None; **Y. Fuentes-Silva**, None; **C. Reategui-Sokolova**, Jannsen, 5; **C. Elera-Fitzcarrald**, None; **S. Ibañez**, None; **E. Cairoli**, None; **B. Pons-Estel**, Janssen, 5, Glaxo Smith Kline, 6; **I. Peláez-Ballestas**, None; **C. Drenkard**, GSK, 1, 5.

Abstract Number: 1152

A Follow-Up Evaluation of a Longstanding Telephone Peer Counseling Service for People with Systemic Lupus Erythematosus and Their Loved Ones

Priscilla Toral, Roberta Horton and Jillian Rose, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Education/Community Programs Poster (1150–1152)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: With technology rapidly evolving, studies still reinforce the value of telephone peer support for people living with chronic illness. A follow-up evaluation was conducted with participants of a national phone peer counseling service. Ongoing since 1988, this service provides emotional support & education for people with SLE & their loved ones. The program's evolution has been presented at prior ACR meetings, including the psychosocial impact of the service on the volunteers themselves.

Methods: A 62-item online survey, with Likert scale & open-ended questions was administered to callers who used the service for > 6 months during 2020-2021.The survey assessed overall satisfaction & impact, including the relationship/satisfaction with the peer counselor match. Other areas assessed included specific changes in feelings & actions taken as a result of the service.

Results: Of 43 users outreached to, 29 (67%) completed the survey. Most (89%) respondents were female, 28% identified as Black/African-American, 40% White, 23% Hispanic & 20% some other race. Callers' ages ranged from 30-80 with 78% ages 30-59. 52% were employed/self-employed & 19% were unable to work. All respondents had SLE mean year since diagnosis was 12.

Almost all (93%) identified emotional support & coping/SLE management as their initial reasons for calling. When asked about initial expectations of their counselor, callers shared “to gain information & receive emotional support.” Most callers (86%) agreed these expectations were met. When asked how their peer counselor met these expectations, participants shared: “non-judgmental & knowledgeable about SLE”. About half (45%) had > 12 calls with their peer counselor; 97% were very satisfied/satisfied with their match.

Regarding coping, 82% indicated they have coped better with their SLE since using the service & 74% agreed they had a better understanding of SLE. When asked about depression, 59% reported feeling less depressed since joining the service with most callers (81%) crediting the service for this change. Regarding anxiety, 70% reported feeling less anxious since using the service with 74% attributing this to the program. Most (89%) reported feeling less isolated with 78% crediting this to the service.

Over half (60%) indicated their communication with their doctor improved since using the service & 73% attributed this to the program. When asked about the single most helpful part of using the service responses included: “being connected to someone with lived experience with SLE” & “the consistency of the counselor & supervisor.” Almost all (96%) would recommend the service & 92% indicated they are very satisfied/satisfied with the service overall.

Conclusion: Despite limitations of a small sample size, results indicate ongoing satisfaction & positive impact, with slight increases since last evaluation in overall service satisfaction & peer match. Results point to the continued benefit of an accessible telephone support service that connects people with SLE & their loved ones to trained peers. The study highlights further opportunities for research on the impact of phone peer model programs, as traditional in person support forums are limited due to the pandemic.

Disclosure: P. Toral, None; **R. Horton**, None; **J. Rose**, None.

Abstract Number: 1153

The Influence of Companions on a Patient’s Decision to Transition to a Biosimilar: A Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Involving patients in treatment decisions is commonplace in healthcare, but patients are frequently accompanied by a support person (companion). Companions are often actively involved in medical consultations, yet their impact on decisions to change medications is unknown. This study aimed to examine the influence of companions on a patient’s decision to transition to a biosimilar.

Methods: Seventy-nine patients with rheumatic diseases taking an originator biologic who regularly attend clinical appointments with a companion were randomized to receive a video explanation alone or with their usual companion. The video explanation included information on the hypothetical transition to a biosimilar and was presented by the same physician to ensure consistency. The information included the manufacturing process, efficacy, safety, and cost

benefits of biosimilars. Patients who received the explanation with their companion had some time to discuss the information before making a decision. After receiving the explanation, participants reported their willingness to transition, risk perceptions, difficulty understanding and received social support. Decisional conflict (uncertainty about the decision) and satisfaction with the decision were also measured.

Results: Companions did not influence decisions to transition to biosimilars, with accompanied (n = 21, 53%) and unaccompanied (n = 22, 56%) patients reporting similar willingness to transition (p = 0.73). There was also no significant difference between accompanied and unaccompanied patients' cognitive risk perceptions (mean (SD) 45.9 (23.4) vs. 43.9 (26.8), p = 0.72) or affective risk perceptions (54.7 (29.3) vs. 46.5 (30.9), p = 0.23). Unaccompanied patients reported finding it easier to understand the explanation compared to accompanied patients (8.2 (1.9) vs. 6.9 (2.4), p = 0.006). Accompanied patients also thought it was more important to receive information with companions than unaccompanied patients (8.3 (2.6) vs. 6.8 (3.2), p = 0.023). Companions did not impact decision satisfaction (p = 0.12) or decisional conflict (p = 0.86). Receiving emotional, but not practical support, was associated with less decisional conflict in accompanied patients (β = -0.63, p = 0.038).

Conclusion: The presence of companions does not influence risk perceptions or decisions about transitioning to biosimilars but may impact patients' reporting of their ability to understand treatment explanations.

Disclosure: C. Gasteiger, None; **K. Groom**, None; **M. Lobo**, None; **U. Scholz**, None; **K. Petrie**, None; **N. Dalbeth**, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5.

Abstract Number: 1154

What Do Patients Know About Biosimilars and How Satisfied Are They with the Educational Process? - A Systematic Comparison Between Rheumatologists and Nurse Specialists, Including Effects of Multiswitching

Sabina Gall, **Uta Kiltz**, Tanja Kobylinski, Ioana Andreica, Kristina Vaupel, Xenofon Baraliakos and Jürgen Braun, Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The market share of biosimilars (bsDMARDs) is steadily growing, not only in rheumatologic care. Although data on efficacy, efficiency and safety have been generated in the last years, not much is known about patients' views on bsDMARDs and also the experience with multiple switching in a non-medical switch scenario is limited. The aim of this project was to study differences in patient satisfaction after education by rheumatologists or nurse specialists, and to learn more about patients' knowledge and their view on biosimilars.

Methods: The non-medical switch to adalimumab MSB 11022 was taken as an opportunity to study patients' knowledge and views on bsDMARDs and their satisfaction with the information they had received on this subject. Adult patients of a tertiary hospital with chronic inflammatory rheumatic diseases (CIRD) such as rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA) were included in this randomised controlled trial after obtaining informed consent and followed up for 3 months. Patients with other serious diseases and language problems

Table 1. Patient and disease characteristics of both groups

Variables*	RLC (n=40)			NLC (n=62)			P-Value
Sex, male, n (%)	25 (62.5%)			31 (50%)			0.215
Age, years	48.7 (13.3)			48.8(13.9)			0.996
Rheumatoid Arthritis, n (%)	10 (25%)			16(25.8%)			0.927
Axial Spondyloarthritis, n (%)	25 (62.5%)			36 (58.1%)			0.656
Psoriasis arthritis, n (%)	5 (12.5%)			10 (16.1%)			0.613
Disease Duration, years	10.5 (9,2)			9.4 (10,9)			0.574
Number of previous bDMARDs	1.4 (1)			1.5 (0.7)			0.452
Assessments*	**Baseline**	**Follow-up**	**Difference Follow-up -Baseline**	**Baseline**	**Follow-up**	**Difference Follow-up -Baseline**	**P-Value**
DAS28	2 (0.9)	2.4 (0.9)	0.2 (0.7)	1.3 (1)	1 (0.7)	0.2 (0.7)	0.884
HAQ	0.9 (0.7)	1.1 (0.5)	0.08 (0.3)	1.1 (0.4)	0.8 (0.6)	0.1 (0.4)	0.714
BASFI	3.3 (2.7)	2.9 (2.5)	0.3 (0.9)	3.9 (2.5)	3.6 (2.6)	0.3 (1.7)	0.844
ASDAS	1.9 (1)	1.9 (0.8)	0.1 (0.7)	2.1 (0.9)	2 (0.8)	0.01 (0.5)	0.271
Patient Satisfaction							
LSQ-General (1-5)#	3.7 (0.7)	3.6 (0.6)	0.7 (1.5)	3.7 (0.6)	3.7(0.7)	1.0 (1.6)	0.302
LSQ-Information (1-5)	3.6 (0.5)	3.6 (0.5)	0.5 (1.5)	3.6 (0.5)	3.4 (0.5)	1.0 (1.5)	0.156
LSQ-Empathy (1-5)	3.5 (0.6)	3.5 (0.6)	0.6 (1.5)	3.7 (0.6)	3.4 (0.4)	1.0 (1.6)	0.231
LSQ-Technical (1-5)	3.7 (0.5)	4.0 (0.6)	1.2 (1.7)	4.2 (0.6)	3.8 (0.6)	1.4 (1.7)	0.070
LSQ-Attitude (1-5)	3.7 (0.7)	3.8 (0.5)	0.6 (1.5)	3.9 (0.6)	3.8 (0.6)	0.9 (1.6)	0.333
LSQ-Access (1-5)	3.7 (0.6)	3.7 (0.7)	0.6 (1.5)	3.7 (0.7)	3.9 (0.6)	0.8 (1.8)	0.494
LSQ-Overall (1-5)	3.7 (0.5)	3.8 (0.4)	0.6 (1.5)	3.7 (0.5)	3.6 (0.4)	0.9 (1.5)	0.320
LSQ-General (1-5)#	3.7 (0.7)	3.6 (0.6)	0.7 (1.5)	3.7 (0.6)	3.7(0.7)	1.0 (1.6)	0.302
LSQ-Information (1-5)	3.6 (0.5)	3.6 (0.5)	0.5 (1.5)	3.6 (0.5)	3.4 (0.5)	1.0 (1.5)	0.156

NLC = nurse led clinic; RLC = rheumatologist led clinic
* values are mean (SD)
# values of 1 indicate dissatisfaction

were excluded. Patients were randomized into two groups using block randomization: Group 1: educational process by nurse specialist (nurse led clinic (NLC)), Group 2: educational process by rheumatologist (rheumatologist led clinic (RLC)). Standard assessments using validated outcome parameters for disease activity and physical function were used. Patient's satisfaction with care was assessed by the Leeds Satisfaction Questionnaire (LSQ) which contains items on 5 subscales: provision of information, empathy with and attitude to the patient, access to and continuity with

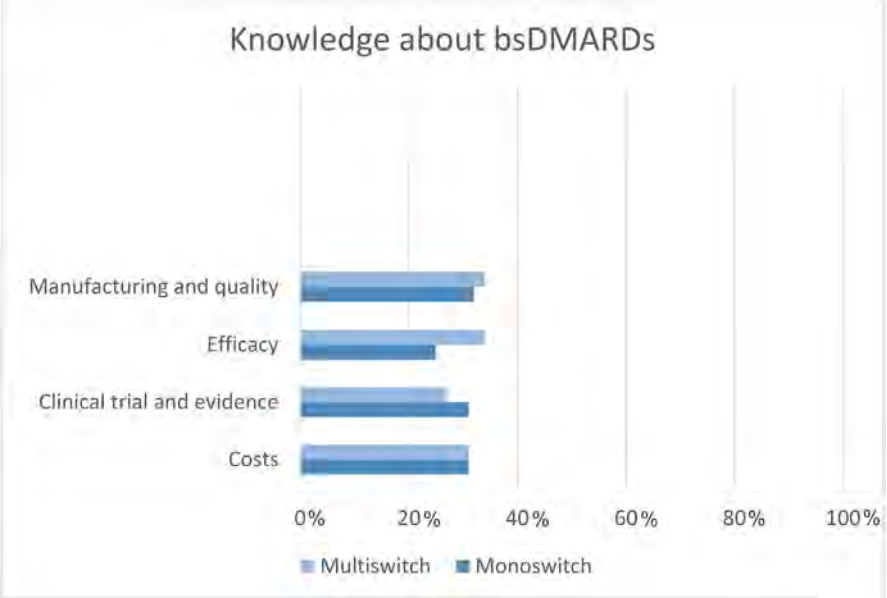

Figure 1. Knowledge about bsDMARDs. bsDMARDs: biosimilar disease-modifying anti-rheumatic drugs.

the care giver, technical competence and a general satisfaction scale. A structured questionnaire was used to assess patient's knowledge of the manufacturing, effectiveness and safety, acceptance and cost of bsDMARDS.

Results: A total of 102 patients were included, 40 (39.2%) by the rheumatologist and 62 (60.8%) were seen by the nurse specialist. Fifty patients (49%) had undergone one and 52 multiple switches (51%). Patient demographics, disease characteristics and the results including patients' knowledge about bsDMARDs and satisfaction with the information process are shown in Table 1. Scores of disease activity and physical function obtained at week 12 remained unchanged for 3 months. Less than one third of patients was able to correctly answer questions about manufacturing, efficacy and safety, approval and costs of bsDMARDs (Fig.1). Patients were generally satisfied with care irrespective of whether information about bsDMARDs and switching had been given by the nurse or the rheumatologist.

Conclusion: This study shows that the satisfaction and the outcomes of patients informed on bsDMARDs by a nurse were not different from information provided by the rheumatologist. Multiswitching did not lead to reduced satisfaction with care in patients on bsDMARDs, and the number of switches did not have a negative impact on patients' satisfaction. However, patients' knowledge on bsDMARDs was limited.

Disclosure: S. Gall, None; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **T. Kobylinski**, None; **I. Andreica**, None; **K. Vaupel**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **J. Braun**, Abbvie, 2, 5, 6, Amgen, 2, 5, 6, Celltrion, 2, 5, 6, Chugai, 2, 5, 6, Medac, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, BMS, 2, 5, 6, Boehringer, 2, 5, 6, Celgene, 2, 5, 6, Centocor, 2, 5, 6, Mundipharma, 2, 5, 6, Sanofi-Aventis, 2, 5, 6, Eli Lilly, 2, 5, 6, EBEWE Pharma, 2, 6.

Abstract Number: 1155

Pregnancy Experiences and Unmet Needs for Women of Childbearing Age with Chronic Rheumatic Disease in China

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Recent European research on patients with chronic rheumatic diseases (CRDs) revealed that women of childbearing age (WoCBA) have many fears and misconceptions about their journey to the motherhood. It is critical for patients to obtain accurate information around their disease management. However, there is limited related research in China. This study aimed to understand pregnancy experiences and unmet needs for WoCBA with CRD in China.

Table 1. Medication discontinuation and changes in disease severity during pregnancy and postpartum

Medication (monotherapy or combination) discontinuation		Numbers (%) of patients discontinued medication
csDMARDs	**Patients base**	**110**
	Never discontinue	20 (18.18%)
	Partially discontinue	16 (14.55%)
	Completely discontinue	74 (67.27%)
Biologic agents	**Patients base**	**30**
	Never discontinue	4 (13.33%)
	Partially discontinue	0
	Completely discontinue	26 (86.67%)
Change in disease severity		**Numbers (%) of patients**
Disease condition during pregnancy	**Patients base**	**157**
	Improved a lot	37 (23.57%)
	Improved a little	36 (22.93%)
	Stayed the same	50 (31.85%)
	Worsened a little	27 (17.20%)
	Worsened a lot	7 (4.46%)
Disease condition after childbirth	**Patients base (delivered a child)**	**149**
	Improved a lot	8 (5.37%)
	Improved a little	17 (11.41%)
	Stayed the same	25 (16.78%)
	Worsened a little	59 (39.60%)
	Worsened a lot	40 (26.85%)

Methods: A cross-sectional online survey was sent to a sample of WoCBA (18-49 years old) drawn from the Chinese Rheumatism Data Center 2019 with physician-diagnosed as moderate or severe CRD (RA AS and PsA). This study was approved by Ethics Committee of Peking Union Medical College Hospital.

Results: Total 1037 WoCBA patients were involved. 157 patients were diagnosed with CRD before pregnancy. Of which 110 and 30 patients took csDMARDs and bDMARDs (TNFi) before the index pregnancy, respectively. During their whole pregnancy, 74 (67.27%) and 26 (86.67%) patients discontinued medications completely, respectively (Table 1). The most common reason for stopping medication was that patients were concerned about the adverse effect of medications on their fetus. Of all the 157 patients, 34 and 99 patients reported that the symptoms worsened during pregnancy and postpartum respectively. Of 157 patients, 19.11% reported that they received inconsistent medication advice from rheumatologists and obstetricians during pregnancy, and 17.83% did not receive any advice.

Conclusion: Our survey indicates that women with CRDs have a wide range of unmet information and needs in relation to pregnancy in China. There is a strong need to reach a multi-disciplinary consensus on treatment recommendations to ensure that WoCBA can obtain consistent advice through all their journey to motherhood.

Disclosure: x. tian, None; **y. fang**, None.

Abstract Number: 1156

Impact of Treatment Experience on Patient Preferences and Disease Burden in Psoriatic Arthritis: Results from a Rheumatology Patient Research Registry

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: To optimize patient-provider shared decision-making, it is important to understand patients' experience with psoriatic arthritis (PsA) and its treatment, including how treatment experience may impact their preferences. We evaluated PsA symptom burden, the most important impacts of disease, and therapy preferences based on past biologic disease-modifying antirheumatic drug (bDMARD) experience among PsA patients from the ArthritisPower registry.

Methods: A cross-sectional, web-based survey was developed and administered to adults with a self-reported diagnosis of PsA recruited from a United States rheumatology patient-centered research registry, ArthritisPower. Object case best-worst scaling (BWS) was used to evaluate the relative burden of 11 PsA symptoms and the relative importance of improvement in 9 PsA-related disease impacts. BWS data were analyzed using a random parameters logit model stratified by past bDMARD experience. Additional survey questions and analyses assessed the impact of prior treatment experience on patients' experience with methotrexate (MTX) and preference for mode of treatment administration as well as overall treatment satisfaction.

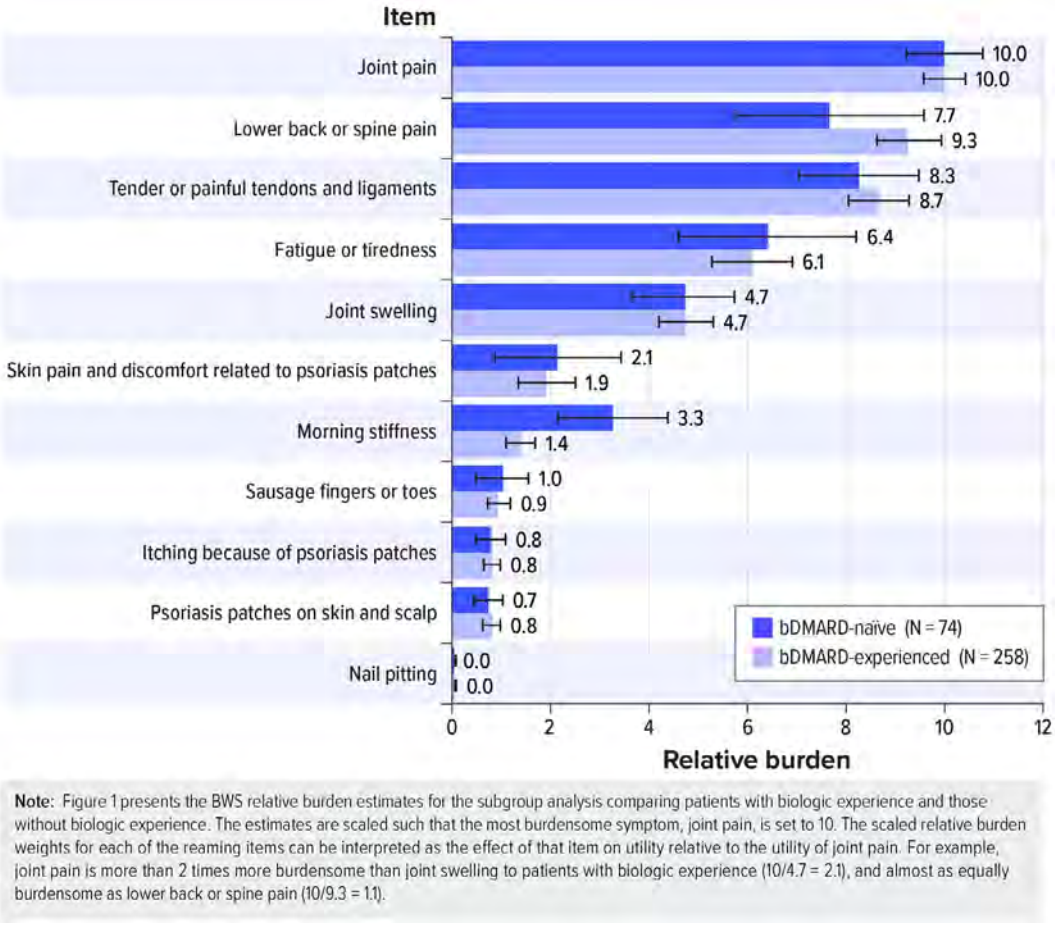

Figure 1. Relative Burden of PsA Symptoms by Biologic Treatment Experience.

Results: Among 332 respondents, 74 (22.3%) were bDMARD-naïve and 258 (77.7%) were bDMARD-experienced. In both groups, musculoskeletal pain-related symptoms were reported as most bothersome while the least bothersome symptoms were psoriasis-related (Figure 1). Patients who were bDMARD-naïve rated morning stiffness as more bothersome than bDMARD-experienced patients. The ability to perform physical activities was reported as the most important disease impact to improve by both groups, while bDMARD-naïve patients rated improvement in sleep quality as more important compared to bDMARD-experienced patients (Figure 2). Among patients with MTX experience, a similar proportion of bDMARD-naïve patients (40%) and bDMARD-experienced patients (34%) were satisfied with MTX. A significantly greater proportion of bDMARD-naïve patients felt that mode of administration was an important factor when deciding to start a new therapy compared to bDMARD-experienced patients (57% vs. 42%, $p< 0.05$). When asked to choose among four different ways of taking their PsA medication (oral once or twice per day, injection every 2 weeks or every month), a once daily oral tablet was the most commonly chosen mode by both bDMARD-naïve (39%) and -experienced patients (38%). Overall satisfaction with current treatment was higher among patients taking an advanced therapy (bDMARDs or tofacitinib) compared with those taking conventional DMARDs only (72% vs 39%, $p< 0.05$).

Conclusion: Among patients with PsA, musculoskeletal pain-related symptoms were ranked as most bothersome, and improvements in physical function were ranked as most important, regardless of bDMARD treatment experience. Though mode of administration was rated as more important among bDMARD-naïve patients, both bDMARD-naïve and -experienced patients preferred a once daily oral route of administration. These findings may serve to optimize patient-provider treatment discussion and decision making across PsA patient populations.

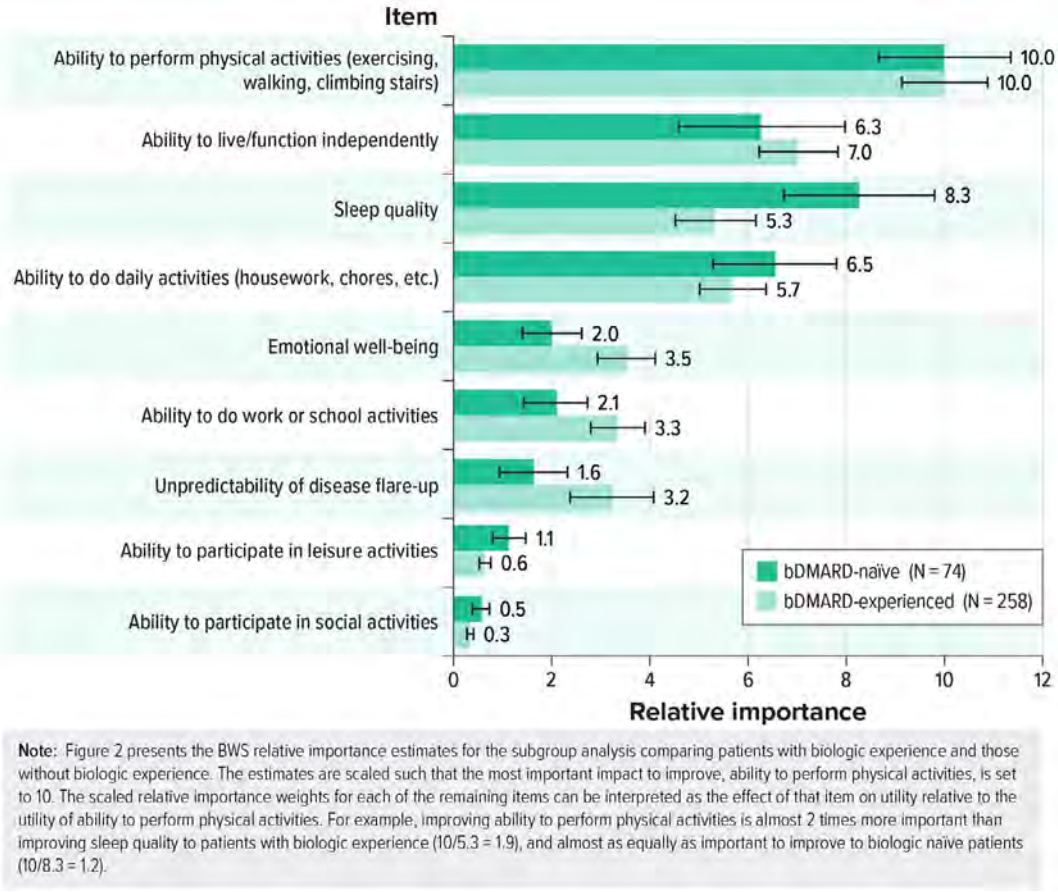

Figure 2. Relative Importance of Improving PsA Disease Impacts by Biologic Treatment Experience.

Disclosure: J. Walsh, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5; **K. Myers**, RTI Health Solutions, 3; **C. Mansfield**, RTI Health Solutions, 3; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **P. Nash**, Janssen, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Novartis, 2, 5, 6, Eli Lilly, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Sanofi, 2, 5, 6, Merck, 2, 5, 6, UCB, 2, 5, 6, Gilead/Galapagos, 2, 5, 6, Celgene, 2, 5, 6, Samsung, 2, 5, 6; **C. Leach**, RTI Health Solutions, 3; **W. Nowell**, Global Healthy Living Foundation, 3, AbbVie, 5, Amgen, 5, Eli Lilly, 5; **K. Gavigan**, Global Healthy Living Foundation, 3; **P. Zueger**, AbbVie, 3, 11; **E. McDearmon-Blondell**, AbbVie, 3, 11; **A. Ogdie-Beatty**, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2.

Abstract Number: 1157

Patient Perspective on the Non Medical Switch of Originator to Its Biosimilar in Inflammatory Arthritis Using a Social Media Survey

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SESSION INFORMATION

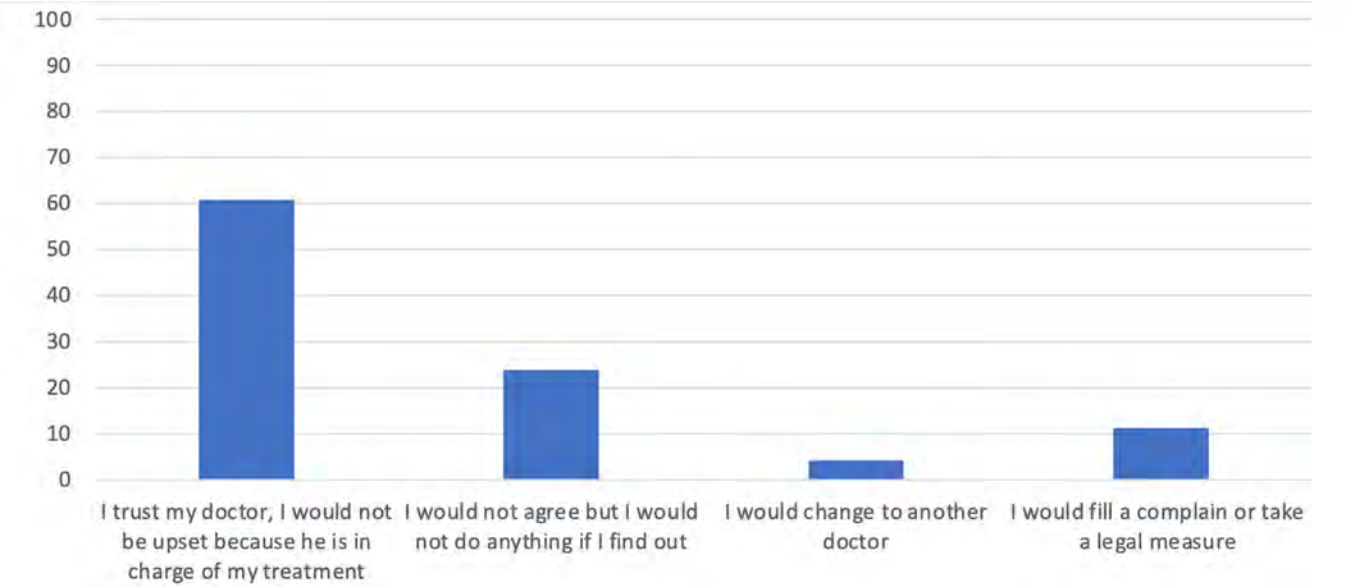
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The use of biosimilars instead of its originator is a controversial subject with many implications. It is considered that a non medical switch should not occur and that pts and physicians must be involved in the decision of choosing the adequate medication.

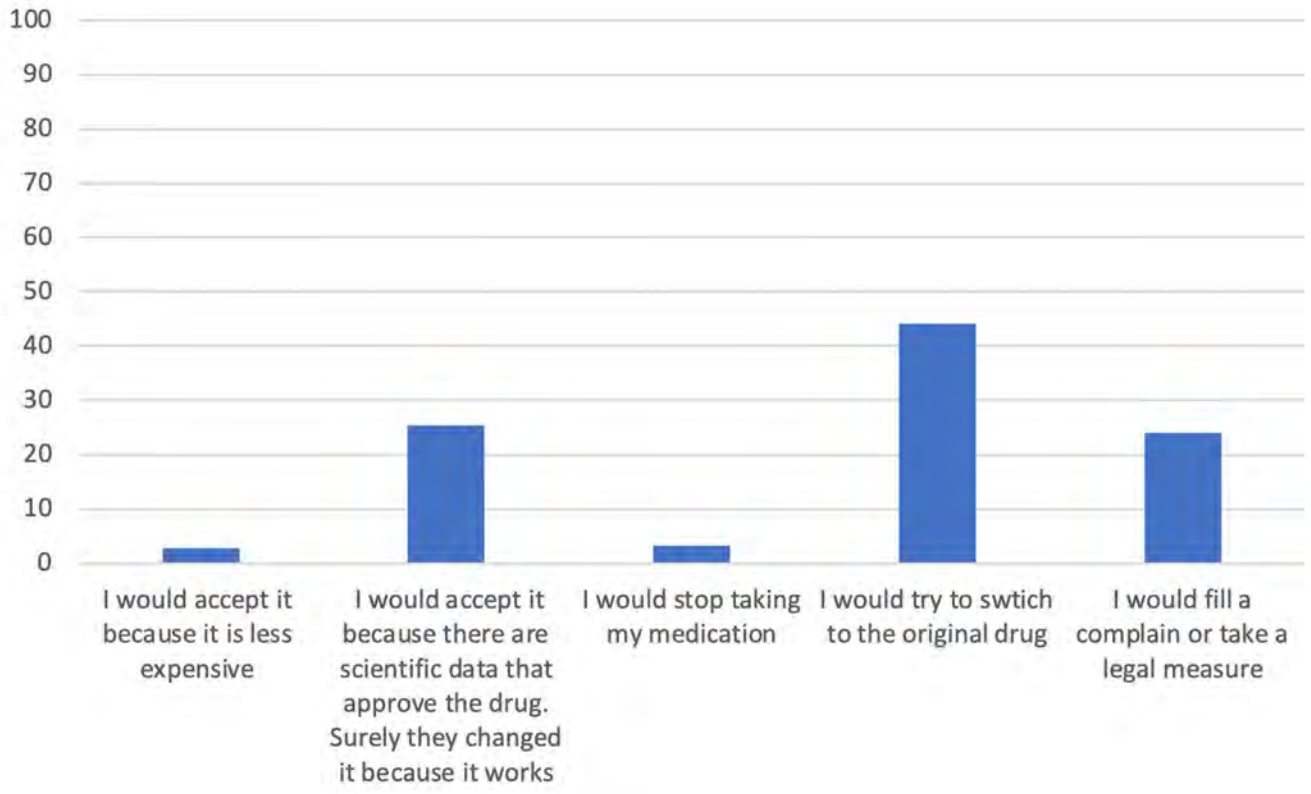
Methods: A social media survey via The Mexican Foundation for Rheumatic Patients (FUMERAC) (Facebook [FB] and Twitter) was conducted in Mexico from November 2020 to January 2021. An opening question to ascertain the consent Pts were eligible if they were >18 years of age and if they had any inflammatory or non inflammatory rheumatic condition and the use of biologics/biosimilars was not mandatory.

Results: A total of 165 pts completed the survey. 81% were women and 79% had high school or higher education. The most frequent diagnoses were RA (56.4%), AS (13.9%), PsA (11.5%) and Lupus (9.1%). DMARD monotherapy was the most common treatment representing 30% of pts. 57% reported prior or current use of biologics. Sixty four percent of pts had never heard the term biosimilar. 38% would accept the change from an originator to its biosimilar if the opinion of the patient and physician was taken into account. 24% of pts would take a legal measure or file a complaint if a NMS was to happen. The subjects asked to pts in order to reduce their inconformity were: treatment effectiveness (65.5%), adverse effects (60%), reason for change (54.4%), treatment duration (29%) and other pts experience (19.3%)

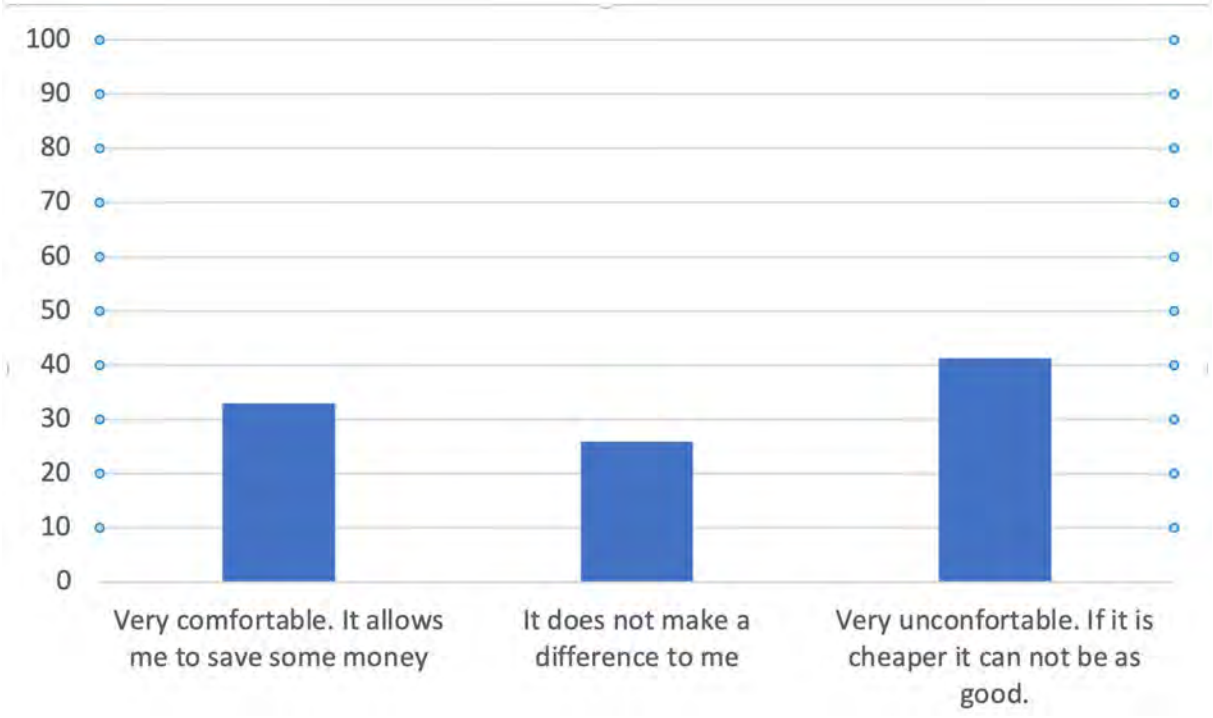
Conclusion: In Mexico the concept of biosimilars is barely known. Most of patients (76%) would not take any measure if they where changed from an originator to its biosimilar. There is still a great amount of confidence from the pts to their physician regarding the management of their medications.



What would you think if your physician changed your originator to its biosimilar without asking nor explaining you?



What would you think if your pharmacist or health insurance policy changed your medication to its biosimilar without informing you or your physician?



Do you think changing your biologic drug to its more economic biosimilar can have a consequence?

Disclosure: D. Vega Morales, None; **A. Garza-Alpirez**, None; **C. Díaz-Garza**, None.

Abstract Number: 1158

Resistance of Patients with Rheumatoid Arthritis to Changing Therapy: A 15-year Follow-up

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Background/Purpose: Treatment options for rheumatoid arthritis (RA) have increased dramatically over the past 15 years. The objective of this study was to investigate whether willingness to change treatment and reasons for not changing have shifted by repeating a pivotal study questionnaire 15 years later.[1]

Methods: Data are from participants with RA enrolled in FORWARD, The National Databank for Rheumatic Diseases, a longitudinal registry of individuals with rheumatic diseases. Patients answered 9 questions on treatment satisfaction and preferences in 2006 (Y06) and/or 2021 (Y21). Questions included an overall assessment of likelihood to change therapy (Q1, "As long as I don't get worse I wouldn't want to change my arthritis medications," rated as true-false)

Table 1. Treatment predictors and preference for not changing therapy

	Questionnaire 2006 (Y06)				Questionnaire 2021 (Y21)			
	Responses according to whether question 1, "As long as I don't get worse I wouldn't want to change my arthritis medications," was answered "true" or "false"							
Questions	% n=6283	TRUE* 64%	FALSE* 36%	% difference§ (true-false)	% n=1632	TRUE* 50.9%	FALSE* 49.1%	% difference§ (true-false)
2. I don't need new medications because I am satisfied with the control I have over my arthritis.	53.2	73.44	17.25	56.1 (54.1 - 58.2)	36.6	56.83	15.62	41.2 (37.3 - 45.1)
3. I don't want the risk of side effects that might come from taking new medications.	72.4	87.13	46.00	41.1 (38.6 - 43.7)	42.7	61.06	23.62	37.4 (32.7 - 42.1)
4. I want to follow my doctor's suggestions, and my doctor thinks I don't need to change medications.	71.3	84.39	47.93	36.4 (34.1 -38.7)	38.1	54.27	21.53	32.7 28.5 - 36.8)
5. I am concerned that new treatments might not work as well and that I might lose control of my arthritis.	67.9	80.74	45.29	35.4 (33.0 - 37.8)	42.3	57.06	26.91	30.0 (24.7 - 35.4)
6. I don't think there are medications currently available that are better than the medications I am using now.	66.2	75.83	48.59	27.1 (24.6 - 29.7)	36.3	46.73	25.53	21.1 (16.4 - 25.8)
7. I don't want to take treatments that require injections or IVs.	35.9	41.75	25.40	16.3 (14.0 -18.5)	16.4	21.09	11.49	9.8 (5.8 - 13.7)
8. I can't afford the cost of new medications.	54.8	45.71	37.89	7.9 (5.2 - 10.5)	28.8	30.14	26.37	3.6 (-0.05 -12.2)
9. Getting approval from my insurance company and the hassle of tests and medical visits for new drugs are important problems for me.	54.8	56.04	52.22	3.8 (1.5 - 6.1)	29.1	33.70	24.34	9.3 (4.8 - 13.7)

§The greater the difference, the stronger the association with unwillingness to change.

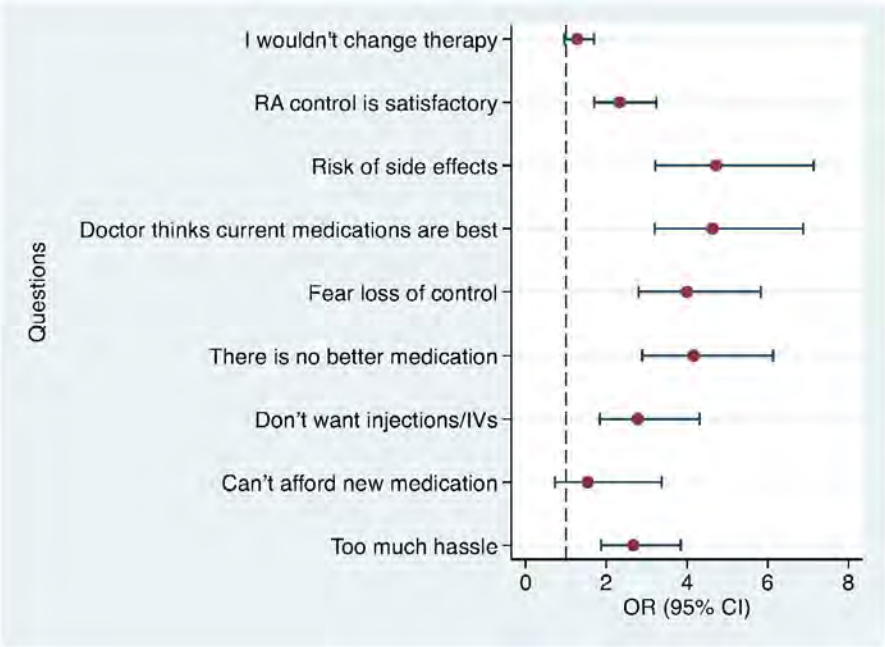

Figure 1. Odds (95% CI) of being unwilling to change medications at Y21 if unwilling to change at Y06.

Table 2. Multivariable predictors of unwillingness to change therapy outcome in overall and paired samples

	Overall		Paired subset	
	Y06	Y21	Y06	Y21
n	6206	1625	442	
RA control is satisfactory	6.80**	3.51**	5.55**	3.55**
Risk of side effects	4.39**	2.86**	2.72**	3.20**
Doctor preference	1.86**	2.22**	2.20**	2.56**
Fear loss of control	1.90**	1.87**	3.32**	1.58
Can't afford	1.32**	1.15	1.15	0.70
There is nothing better	1.38**	1.25	0.84	1.92*
Don't want injections	1.08	1.25	1.27	1.39
Too much hassle	0.83*	1.03	1.22	1.59
Age, per 10 years	1.02	1.11	0.90	0.98
Male sex	1.04	1.06	0.74	1.03
Married	1.21*	1.03	0.80	0.95
College graduate	0.79**	1.22	0.89	1.44
Total income, per US$10K	0.94**	0.96*	1.04	0.95
Employed	0.87	1.06	0.86	0.85
RA duration, years	1.00	1.00	0.99	0.99
Prior no. of DMARDs	1.02	0.99	0.94	0.97
Current bDMARD use	0.82*	1.22	1.10	1.32
Current prednisone use	0.92	0.91	0.94	0.92
Current MTX use	1.15*	0.88	0.85	0.81
VAS pain (0–10)	0.95**	0.94*	0.99	0.95
HAQ (0–3)	1.02	0.90	0.92	1.08

Tabled values are odds ratios. *p<0.05; **p<0.01.

and 8 (Q2-Q9) evaluating reasons for (un)willingness to change (Table 1). Paired McNemar tests were performed in the subset who answered the questionnaire at both Y06 and Y21 to estimate the likelihood of willingness to change therapy at Y21 based on response at Y06. Logistic regression was used to identify predictors at both time points of responses to Q1.

Results: In 2006, 6282 responders had a mean age of 63 years, 17 years RA duration, and exposure to 3 (IQR 2-5) DMARDs. As of April 2021, 1632 responders had a mean age of 66 years, 24 years RA duration, and exposure to 4 (IQR 3-5) DMARDs. Overall for Y06, 64% did not want to change therapy as long as their condition didn't get worse, compared with 51% from Y21. However, when looking at responses of those who completed both Y06 and Y21 questionnaires (n=442), there were no significant differences in willingness to change therapy. The primary reasons for unwillingness to change therapy over time (Y06 vs Y21) were as follows: satisfaction with medication (53% vs 37%), risk of side effects (72% vs 43%), and doctor recommendation (71% vs 38%) (Table 1). In the paired group, those who provided a reason for not changing in Y21 (eg, side effects) were more likely to have provided the same reason in Y06 (eg, 4.7-fold increase for side effects; Figure 1). Predictors of unwillingness to change therapy in Y06 and Y21 included the following: satisfactory control of RA, risk of side effects, fearing loss of control, doctor thinking current medications were best, and lower levels of pain (Table 2). Predictors related to cost or insurance were associated with unwillingness to change in Y06, but not in Y21.

Conclusion: While the overall proportion of respondents who were unwilling to change therapies was lower in 2021 than in 2006, analysis of those who responded to both questionnaires showed little change. In addition, the major reasons given for not wanting to change therapies did not change from 2006 to 2021, although cost and hassle with insurance companies were no longer significant predictors in 2021. Further data are needed to understand whether the correlation between (un)willingness to change treatments and disease activity and clinical outcomes has evolved over time.

Reference

1. Wolfe F, Michaud K. *Arthritis Rheum* 2007;56(7):2135-42.

Disclosure: K. Michaud, None; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Diseases, 3; **V. Jasion**, AbbVie, 3, 11; **H. Budlong**, AbbVie, 3, 11; **J. Suboticki**, AbbVie, 3, 11; **F. Wolfe**, None; **P. Katz**, None.

Abstract Number: 1159

Improving Healthcare Transition Implementation: Recommendations from Young Patients with Rheumatic Conditions

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
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Background/Purpose: Implementation of structured healthcare transition processes remains elusive for most US rheumatology clinics (Johnson et al., 2021). Although research studies have proposed models and best practices for decades, barriers to successful healthcare transition persist, such as systemic procedures and rheumatologists' lack of time and resources (Chira et al., 2014; Zisman et al., 2019). In this study, we identified adolescent and young adult (AYA) patients' recommendations about how to deliver healthcare transition and examined their openness to various methods of implementation.

Methods: Participants aged 16-28 years old with a self-reported diagnosis of a rheumatic condition were recruited from patient organizations and social media. This mixed methods study used a two-phase exploratory sequential design. In phase one, experienced researchers led 90-minute focus groups to elicit AYAs' reactions to principles and resources of the Six Core Elements of Healthcare Transition™ (Sabbagh et al., 2018). Audio transcripts were analyzed using rapid analysis to develop a quantitative survey and later using in-depth content analysis. In phase two, an online quantitative survey was distributed to understand AYAs' willingness to engage in various healthcare transition modalities. Descriptive statistics were performed using SAS v9.4

Results: In phase one, 39 AYAs (20.8 ± 2.9 years old; 82.1% female; 92.3% White; 48.7% using pediatric rheumatology services; 84.6% arthritis) participated in 7 focus groups. Participants discussed the need for a systematic educational care plan that is purposefully introduced and reinforced within regular healthcare encounters. Participants suggested techniques to increase the effectiveness of transition-related discussions, such as pairing transitional skills with developmental milestones and acknowledging the role of parents/caregivers. While AYAs emphasized that rheumatologists ideally should be part of this process, they also provided ideas for how to structure transition education using other team members or outside time-limited rheumatology appointments. In phase two, 137 AYAs (22.9 ± 3.3 years old; 89.1% female; 75.0% White; 19.0% see pediatric-only rheumatologist; 50.4% lupus) completed the quantitative survey. Most participants reported that to learn transition skills, they would be likely or very likely to engage in programs provided by a provider outside of their regular rheumatologist (81.8%); via a patient portal (77.2%), additional telehealth appointment (74.5%), additional in-person appointment (66.4%); or in a group setting (65.7%).

Conclusion: AYA patients desired structured opportunities to discuss transition skills with multidisciplinary health care team members in the clinic and beyond. Results suggest potential for collaborations with community providers or organizations outside of the traditional healthcare system. Incorporating AYAs' expertise and preferences into the refinement of healthcare transition models may improve the feasibility of implementation and uptake by patients.

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Abstract Number: 1160

Evaluation of HCQ Side Effects in New and Prevalent Users over a 20 Year Period Using a Large Database

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SESSION INFORMATION

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Table 1. Baseline characteristics of prevalent and incident HCQ users by diagnoses. * Incident HCQ users were defined as new users (no HCQ use documented in a prior questionnaire) or having a 6-month maximum HCQ duration prior to FORWARD entry. Prevalent HCQ users were any user irrespective of duration of HCQ treatment. Baseline is defined as the phase preceding HCQ initiation or the first observation in the study if duration HCQ≤6 months. For prevalent users the definition is the latter

	Incident HCQ users*			Prevalent HCQ user*		
Mean (sd) or %	**RA (n=4872)**	**SLE (n=498)**	**Other dx (n=315)**	**RA (n=10897)**	**SLE (n=1549)**	**Other dx (n=572)**
Age	58.9 (13.3)	49.9 (13.9)	52.5 (15.1)	57.8 (14.4)	48.5 (14.4)	51.9 (14.0)
% Female	81.4	91.6	86.6	82.6	92.8	87.9
Education level (years)	13.5 (2.4)	14.2 (2.4)	14.4 (2.3)	13.8 (2.4)	14.2 (2.4)	14.7 (2.2)
Annual household income (1000USD)	48.5 (31.6)	54.3 (34.7)	62.2 (35.5)	50.7 (31.8)	53.9 (33.9)	64.0 (34.9)
% Non-hispanic White Caucasian	87.8	70.1	92.7	88.8	71.8	91.2
% Married	67.8	61.3	71.0	68.8	62.8	70.4
Comorbidity index (0-9)	1.7 (1.6)	2.2 (1.8)	1.7 (1.6)	1.7 (1.6)	2.4 (1.8)	1.8 (1.6)
Disease duration (years)	11.3 (10.9)	12.1 (9.9)	8.2 (9.1)	12.1 (10.8)	13.2 (10.6)	9.0 (9.5)
HAQ (0-3)	1.0 (0.7)	0.8 (0.7)	0.7 (0.7)	1.0 (0.7)	0.8 (0.7)	0.7 (0.7)
Patient activity score (0-10)	3.6 (2.2)	3.4 (2.3)	3.1 (2.1)	3.6 (2.2)	3.5 (2.3)	3.2 (2.2)
SF-36 PCS	36.5 (11.0)	37.2 (11.3)	38.6 (10.8)	36.4 (10.9)	36.8 (11.3)	38.5 (11.4)
SF-36 MCS	48.6 (11.6)	44.6 (11.7)	47.9 (10.8)	48.4 (11.6)	44.4 (11.7)	47.8 (10.9)
Pain (0-10)	3.9 (2.8)	3.9 (2.9)	3.7 (2.8)	4.0 (2.8)	4.0 (2.9)	3.9 (2.9)
Global severity (0-10)	3.7 (2.5)	3.9 (2.5)	3.7 (2.5)	3.7 (2.5)	3.9 (2.5)	3.7 (2.5)
Lifetime bDmards count	0.5 (0.8)	0.2 (0.7)	0.2 (0.5)	0.6 (1.0)	0.2 (0.7)	0.2 (0.6)
Lifetime csDmards count	2.5 (1.3)	1.7 (1.1)	1.5 (0.8)	2.7 (1.4)	1.9 (1.1)	1.7 (0.9)
Mono therapy HCQ	26.7	62.3	63.8	25.9	59.4	63.3
HCQ + csDmards	47.6	31.9	25.4	46.7	35.3	26.8
HCQ + bDmards	25.7	5.8	10.8	27.4	5.3	10.0

Session Time: 8:30AM–10:30AM

Background/Purpose: Despite being used for more than 70 years as a conventional (cs) DMARD, very little is known about the overall side effect (SE) profile of hydroxychloroquine (HCQ). In 2020 HCQ became well-known due to the COVID 19 pandemic. We set out to understand the patient-reported side effect of HCQ use in adults with RA, SLE, and other RMDs (excluding Osteoarthritis and Fibromyalgia).

Methods: Data provided by participants in the Forward Databank observational registry from 1999 through 2020. HCQ use was measured at enrollment and every 6 months with follow up questionnaires. Incident HCQ users were defined as new users (no HCQ use documented in a prior questionnaire) or having a 6-month maximum HCQ dura-

Table 2. HCQ use and experience of side effects due to HCQ of the last side effect (multiple infections)

Diagnosis:	RA		SLE		Other	
Incidence rates Per 1000 patients	Pt-yrs (f)	IR (95% CI)	Pt-yrs (f)	IR (95% CI)	Pt-yrs (f)	IR (95% CI)
Any SE	28445.9 (1470)	51.7 (49.1-54.4)	4487.1 (252)	56.2 (49.6-63.5)	1058.5 (79)	74.6 (59.9 – 93.0)
Mono HCQ	6679.0 (481)	72.0 (65.9 -78.7)	2559.2 (157)	61.3 (52.5 – 71.7)	684.3 (62)	90.6 (70.6 – 116.2)
HCQ + csDmards	10907.0 (603)	55.3 (51.0 –59.9)	1465.6 (81)	55.3 (44.5 – 68.7)	247.4 (11)	44.5 (24.6– 80.4)
HCQ + bDmards	8592.2 (374)	43.5 (39.3 -48.2)	257.8 (13)	50.4 (29.3 – 86.8)	96.0 (5)	52.1 (21.7 – 125.2)
SE stopping HCQ	573	20.1 (18.6 –21.9)	79	17.6 (14.1 –21.9)	24	22.7 (15.2 – 33.8)
Mono HCQ	6679.0 (149)	22.3 (19.0 – 26.2)	2559.2 (42)	16.4 (12.1 – 22.2)	836.2 (19)	23.4 (14.3 – 38.2)
HCQ + csDmards	10907.0 (245)	22.5 (19.8 – 25.5)	1777.6 (33)	21.8 (15.4 – 30.9)	304.4 (8)	24.3 (10.9 – 54.0)
HCQ + bDmards	8592.2 (176)	20.5 (17.7 – 23.7)	318.5 (5)	19.4 (8.1 – 46.6)	128.5 (2)	22.7 (15.2 – 33.8)
SE causing hospitalization	10	0.35 (0.19 -0.65)	5	1.11 (0.46-2.70)	0	–

tion prior to FORWARD entry. Prevalent HCQ users were any user irrespective of duration of HCQ treatment. These questionnaires asked about all SEs to medications, including severity of side effect, certainty of medication as cause of side effect, and affected body systems. We analyzed incident rates of side effects overall and by HCQ categorical use: monotherapy, HCQ with concomitant use of another csDMARD, or HCQ with concomitant use of a biologic (b) DMARD or targeted synthetic (ts) DMARD.

Results: Overall, 5,685 patients were included in the initiator group and 13,018 patients were included in the prevalent group, with the majority of patients taking HCQ for RA and SLE. In both the initiator and prevalent cohorts, the majority of patients with RA were on HCQ and another DMARD. In the other RMD and SLE groups, the majority of patients were on HCQ monotherapy. Eighty four percent of patients taking HCQ for any cause did not experience any side effects in both initiator and prevalent groups. Sixteen percent of all RA patients, 16.5% of SLE and 18% of other RMD patients noted a side effect from HCQ in the initiator group, vs 16.2% of RA, 18.8% of SLE and 17.5% of other RMD noted in the prevalent group. Of those patients, 55% in the RA, 41% in the SLE and 39.3% in the other RMD groups discontinued the medication in the initiator group, with very similar results noted in the prevalent group. Hospitalization secondary to a hydroxychloroquine side effect was observed in 1% of RA patients, 2.5% of SLE patients and no patients with other RMDs in the initiator group vs 1% of RA, 2.8% of SLE and no patients with other RMD's noted in the prevalent group. In both the prevalent and initiator groups, the predominant last reported side effects in annualized incidence rates per 1000 patient-years were gastrointestinal (GI; e.g., nausea, diarrhea, 12.35 prevalent, 12.84 initiator), integumentary (e.g., rash, itching, 7.61, 8.6), and ocular (e.g., visual disturbance, 8.54, 7.42), respectively over all 3 disease groups.

Conclusion: This is the largest study of its kind conducted that reviews patient reported side effects over a 20-year period. Our findings confirm the overall low incidence of reported serious side effects from short and long- term hydroxychloroquine use for the treatment of SLE, RA and other RMDs.

Disclosure: D. Meyler, None; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Diseases, 3; **A. Erickson**, None; **P. Katz**, None; **K. Michaud**, None.

Abstract Number: 1161

Patient Preferences for Hydroxychloroquine in Systemic Lupus (SLE)

Jennifer Dollinger[1], Celline Brasil[1], Marcus Wong[1], Glen Hazlewood[2], Ryan Dollinger[1], Wendy Singer[3], Christian Pineau[4], Evelyne Vinet[5], Ann Clarke[2], Jennifer Lee[1] and **Sasha Bernatsky**[4], [1]Research Institute of the McGill University Health Centre, Montréal, QC, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]McGill University Health Centre, Montréal, QC, Canada, [4]McGill University, Montréal, QC, Canada, [5]McGill University Health Centre, Mont Royal, QC, Canada

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Background/Purpose: Although hydroxychloroquine (HCQ) has been shown to reduce SLE flares, concerns exist regarding side effects from long-term use. Very little information is available on patient preferences regarding decisions to continue, lower, or stop the drug. To address these knowledge gaps, we evaluated patient experiences and preferences for HCQ therapy and qualitatively assessed themes underlying these preferences.

Methods: Telephone interviews were conducted with patients recruited from two Canadian SLE clinical cohorts. The interviews were conducted in English and French using a standardized script. The interview recordings were transcribed, and French transcripts were translated to English. Two reviewers conducted a thematic analysis by individually generating codebooks and mutually ruling out discrepancies.

Results: We completed a thematic analysis of 42 interviews. The majority (N=38, 90%) of subjects were female. Average age was 55.7 (SD 13.0) and most subjects (N=32, 76%) were Caucasian; the rest were Black (N=4, 10%), Asian (N=4, 10%) and other races/ethnicities (N=2, 5%). Concepts emerging from interviews centred around past experiences with dose changes, who (patient/physician) makes those decisions, and current patient preferences (Table 1). Over the course of SLE, 35.7% of patients had stopped and 52.4% had lowered HCQ. Most decisions were made by physicians, but almost a fourth of patients had made a decision to lower or stop HCQ without communicating with their doctor. Though most patients preferred their dose at status quo (to avoid flares), over a third were interested in lowering, stopping, or increasing HCQ. Themes around preferences included SLE control, trust in the provider's

Table 1. Concepts discussed during the interviews

	% of patients (N=42)
Past experiences*	
Never changed HCQ dose	28.6%
Lowered HCQ	52.4%
Stopped HCQ temporarily	26.2%
Stopped HCQ permanently	9.5%
Decision-maker	
Physician +/- patient	76.2%
Patient alone	23.8%
Current preferences	
Status quo	54.7%
Lower HCQ dose	23.8%
Stop HCQ	9.5%
Augment HCQ dose	4.8%
Do not know/no preference	7.1%

*Categories are not mutually exclusive.

Table 2. Themes around preferences

Themes	Quote examples
SLE control	"[I wouldn't change the dose]. Anytime I get any medication change, I usually get flare-ups." (Female, 63 years) "If there would be a way to stop taking the medication, I would like to. If there's no risk, if it's good of course, I would stop." (Patient, 34)
Trust in the provider's decision	"I have been staying on [HCQ] mainly because I have great trust and a great relationship with doctor Y… [who] is very intelligent and very up to date." (Female, 69 years) "If the doctor said that I should change my dose, I would." (Male, 81)
Management of other medications	"I am trying to lower the dose of prednisone, and [HCQ] allows me to have my lupus under control." (Female, 36 years) "If I [didn't have] to take prednisone, I would consider lowering [my dose]." (Female, 36)
HCQ safety	"I am a little concerned about heart and vision issues long-term. I was quite eager to get off of [HCQ]." (Female, 69 years) "[I wouldn't change the dose]. I've never had any side effects. It always went well." (Female, 46 years)
HCQ effectiveness	"I don't see any improvements pain wise. I don't think [HCQ] helps. I would prefer to stop it altogether." (Female, 42) "[On HCQ], I think my [symptoms] are lessened. My major problems are less frequent and controlled." (Female, 62)

Table 3. Preferences according to patient characteristics

Characteristics	Preferences			
	Status quo	Lower dose	Stop HCQ	Other*
Sex				
Female (n=38)	57.9%	21.1%	10.5%	10.5%
Male (n=4)	25.0%	50.0%	0	25.0%
Race/ethnicity				
Caucasians (n=32)	50.0%	25.0%	12.5%	12.5%
Non-Caucasians (n=10)	80.0%	10.0%	0	10.0%
Age				
Youngest (n=10)	60.0%	20.0%	20.0%	0
Oldest (n=10)	30.0%	30.0%	10.0%	30.0%
Language				
English (n=32)	59.4%	21.9%	9.4%	9.4%
French (n=10)	40.0%	30.0%	10.0%	20.0%
SLE clinic				
Montreal (n=32)	53.1%	25.0%	6.3%	15.6%
Calgary (n=10)	60.0%	20.0%	20.0%	0
SLE duration				
Shortest (n=10)	50.0%	50.0%	0	0
Longest (n=10)	60.0%	10.0%	10.0%	20.0%

*Includes augmenting the dose or not knowing what their preferences are.

decisions, management of other medications, HCQ safety, and HCQ effectiveness (Table 2). We observed some differences in preferences across patient characteristics (Table 3). A higher proportion of non-Caucasians (80% vs 50% of Caucasians) and of the 10 youngest patients (60% vs 30% of the 10 oldest patients) preferred maintaining their current dose. Concerns about toxicities emerged in the interviews (Table 2). A limitation of our study is that most of our patients had long-established disease, with only about 10% having more recent-onset disease.
Conclusion: In this sample, most patients preferred maintaining their current HCQ dose to avoid SLE flares. However, concerns about toxicities emerged in the interviews, and several patients would prefer decreasing or stopping treatment, but respected physician recommendations. Awareness of these results may help patients and physicians navigate shared decision making. Studies like ours could also contribute to making SLE treatment guidelines more patient-centred and personalized.

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Abstract Number: 1162

Exploring Cannabis Use and Perspectives Among Psoriatic Disease Patients

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Background/Purpose: We aimed to assess the correlation between cannabis use and psoriatic disease severity, health-related quality of life, pain, and psychosocial outcomes in psoriasis without arthritis (PsC) and psoriatic arthritis (PsA) patients.

Methods: PsC and PsA patients enrolled in the International Psoriasis and Arthritis Research Team (IPART) program were surveyed on cannabis use and were asked to provide a serum and urine sample. Demographic and clinical variables were compared between users and non-users using Student's t-test or Mann-Whitney U test for continuous variables, and chi-square or Fisher's exact test for categorical variables.

Results: Of 151 respondents, 30.5% reported current cannabis use within the last year. Compared to non-users, cannabis users were younger ($P = 0.008$), had a shorter PsA duration ($P = 0.024$), and poorer mental health as measured by the SF-36 ($P = 0.046$). Other measures of health-related quality of life and pain were comparable between the groups. Cannabis users felt more hesitant inquiring about cannabis with healthcare professionals prior to its legalization ($P = 0.017$), but were more likely to want cannabis information from their healthcare providers than non-users ($P < 0.001$). Respondents' primary perceived benefits of cannabis use were aid in sleep and arthritis pain relief. Only patients who were taking cannabis had THC detected in the urine. Serum concentrations of IL-23 were significantly

elevated in cannabis non-users (P = 0.0026) (Table). There were no other significant differences in concentrations of measured analytes between the groups.

Table 5: Median (IQR) of urine THC and serum biomarker concentrations compared between cannabis users (n=34) and non-users (n=65)

Variable	Users (n=34)	Non-Users (n=65)	*P*-value
Urine THC (ng/ml)[§]	19.7 (147.9)	0 (0)	< 0.001
INF-gamma (pg/ml)[§]	13.9 (72.8)	46.0 (155.4)	0.26
IL-10 (pg/ml)[§]	0.5 (0)	0.5 (0.3)	0.17
IL-23 (pg/ml)[§]	39.8 (52)	65.3 (408.8)	0.0026
IL-6 (pg/ml)[§]	1.3 (1.7)	1.4 (1.2)	0.46
TNF-alpha (pg/ml)[§]	2.2 (4.7)	2.9 (5.4)	0.26

[§]Median (IQR) Mann-Whitney U test

Conclusion: This study shows that 30.5% of 151 patients used cannabis within the past year and 54.3% of users reported use of cannabis for arthritis pain relief. Knowledge of the patient demographics of cannabis users can help guide clinicians in counselling patients and aid in the development educational materials to promote responsible use.

Disclosure: J. Tsang, None; **O. Silverberg**, None; **R. Machhar**, None; **R. Pollock**, None; **M. Sutton**, None; **D. Pereira**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **C. Rosen**, None.

Abstract Number: 1163

Patients' Insights About Hydroxychloroquine, and Patient-Recommended Strategies to Target Nonadherence

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is the cornerstone of SLE therapy as it improves damage-free survival in all SLE patients. Yet, in new users, as few as 17% of SLE patients took HCQ as recommended for a year increasing risk of poor SLE outcomes and early death. Moreover, Black patients and those from disadvantaged backgrounds have a 2-fold higher HCQ nonadherence rate, which contributes to worse SLE outcomes and health disparities. This highlights that diverse SLE patients could have different perspectives about HCQ and unique barriers to adherence. Yet, most adherence interventions lack diverse patients' insights or tailored strategies addressing their unique challenges with HCQ. Therefore, using qualitative descriptive analysis we aimed to examine diverse SLE patients' perspectives on: insights and priorities about HCQ adherence, and the most valuable and actionable adherence strategies.

Methods: We recruited 11 patients with SLE from Madison (28% non-White; 17% living in poverty) and Milwaukee, Wisconsin (56% non-White; 40% living in poverty) who were identified with a history of nonadherence or actively struggling with taking HCQ. We used purposeful sampling to recruit diverse SLE patients (e.g., age, sex, race/ethnici-

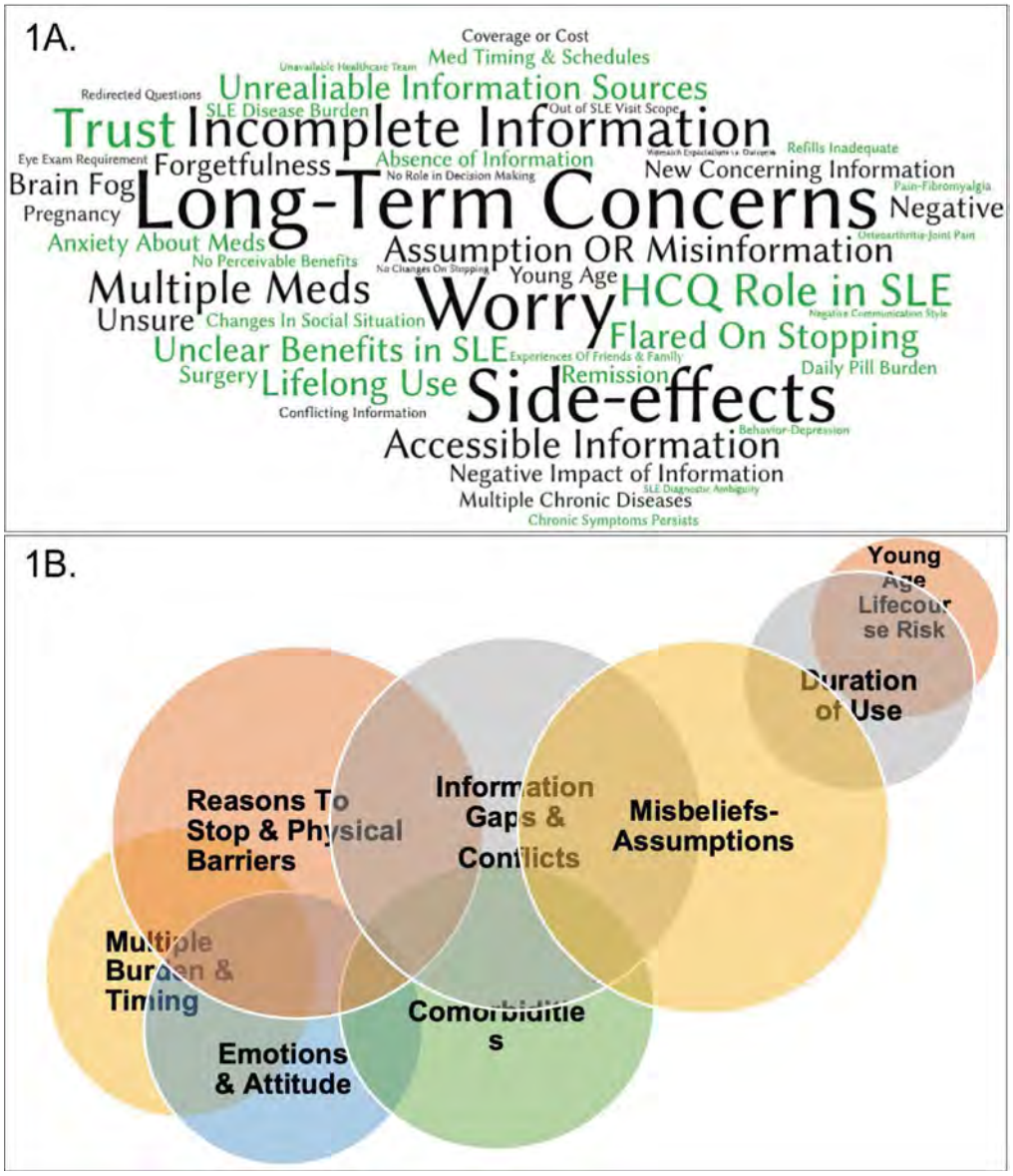

Figure 1. 1A. Patient perspectives and insights about HCQ. The size of the word/phrase matches the listed frequency. 1B. Conceptual scheme showing inter-relationships between themes from analysis of patients' insights about HCQ adherence during four 90-minute focus group meetings (n=11 patients). Note that the size of circles reflects frequency of each theme and the overlap area between circles represents the frequency when both themes were referenced within a quote.

ty, social challenges identified by using social determinants of health documented in the EHR.). Using four 90-minute semi-structured focus groups, facilitators first asked patients to share their perspectives on HCQ, insights and concerns about HCQ that lead to reduced adherence. Next, patients participated in discussing and prioritizing strategies to address their concerns and improve their adherence. All meetings were audio-recorded and transcribed. Using content analysis, we analyzed transcripts from each meeting.

Table 1. Eight Themes Highlighting Patients' Insights And Concerns About HCQ

Themes*	Sub-Categories For Each Theme**	Illustrative Quotes (1-3)
Information gaps & conflicts about medication	Incomplete med information	"Nobody told me that I could take both HCQ doses together. If I would have known, I would not have missed so many HCQ doses."
	Unreliable sources	"I had to go to the internet, which is not a great place to get information!"
	Negative impact of information	"I read drowsiness as a side-effect from HCQ. It was very concerning."
	Absence of information	"My providers did not talk with about what to expect, med response. I never knew if my symptoms from med or lupus."
	Concerning or conflicting information	"I saw on the med source that HCQ is an anti-malarial drug. I freaked out."
Reasons for stopping or physical barriers	Side effects	"I had extremely bad nausea with the medication, I had to stop for few days." "I get hair loss from HCQ." "I get upset stomach every time I take it."
	Multiple meds	"I have to take 8 different meds at 3 different times. I work 3 shifts a day. Sometimes I forget taking the morning doses, but then I wonder if I can take it with the afternoon pills or not."
	Unclear benefits in lupus & lack of perceivable benefits	"What does HCQ do for me or my disease?", "I have not noticed much difference with HCQ." "prednisone helps, but I cant say the same for HCQ."
	Forgetfulness	"Lupus affects memory and causes overwhelming fatigue. I sleep often to ease off some of my symptoms and when I wake up, I forget if I took HCQ or not."
	Changes in social situation	"I was in between providers and I could not get medications as prescribed. It was overwhelming." "I lost insurance, I could not afford HCQ"
	Cost or refills inadequate	"I was in between insurance, I could not get my meds and ended up in the hospital." "I am not sure why we cannot get 90-day fill and several refills."
Misbeliefs-Assumptions	Long-term concerns about HCQ	"I am worried about losing vision with HCQ use", "I am worried about the long-term side effects from this medication on my organs and eyes.", "Dark urine, concerns me if HCQ is affecting my kidneys."
	Assumption-Misinformation	"I got cataracts, I have increased power of my glasses. This is HCQ related, got to be.", "As I undergo regular urine tests, I am concerned about kidney or other organ damage from HCQ.", "I have more blemishes after starting HCQ."
	Unclear HCQ role in lupus	"I think I get confused about HCQ and SLE, not sure how long it will be in their system, what exactly it is doing, and how it is helping."
Emotions & attitude	Worry	"I am worried about losing vision with HCQ use", "Will HCQ be safe for long-term use, I need more reassurance."
	Negative or unsure	"I started having several allergic reactions. I did not know what it really was coming from.", "When I started HCQ, my hair fell off. I was not sure if it was HCQ or something else."
	Experiences of family or friends	"It was hard for me to start HCQ, as my mother had suffered from muscle weakness after taking HCQ."
Comorbidities	Multiple chronic diseases	"I need to know if HCQ could interact with my other chronic diseases?", "My fatigue and pain is still there. I am not sure if HCQ is working or not."
	Brain fog-cognitive issues	"I often forget taking my HCQ doses due to brain fog."
	SLE disease burden	"I had severe disease and my SLE led to kidney disease, blood clots, skin rashes, and heart disease. I take several medications. It is overwhelming."
Medication Burden & Timing	Med schedules & daily pill burden	"My medication timing and schedules are skewed. If I miss a medication then it is very hard for me to pick back up.", " I stopped HCQ as it was honestly hard to keep up with the medications at different times of the day."
	Anxiety about meds	"I find it annoying to take 1.5 tabs a day. I am worried if this will change medication effects.", "I am worried if my eyesight changes are related or not."
Duration of Use	Lifelong use	"I was distraught with the idea that I have to take a medication for the rest life."
Young Age	Life course Risk	"The idea of taking a medication for the rest of my life was unsettling."

**Themes arranged from most common to least common listed frequency. **Only top key sub-categories for each theme shown.*

Results: Eleven patients participated in focus group meetings (attendance - 100% meetings 1-3, 90% 4th meeting); 60% were age ≤ 40 years, 10% male, 40% had disease duration ≤5 years, 70% were non-White, 40% with social challenges, 50% Milwaukee area, and 40% had severe CNS or renal SLE.

"Long-term concerns" and "worry", and "side-effects from HCQ" were the most frequently mentioned words or phrases during the initial focus group meeting where patients shared their perspectives and insights about HCQ (Figure 1A). Qualitative analysis identified eight themes regarding adherence based on patients' discussions about their insights and concerns about HCQ; sub-analysis revealed inter-relationships schematically shown in Figure 1B. The most commonly coded themes and subcategories are in Table 1. Finally, we categorized all patient-suggested strategies, which were ranked by patients from most valuable to least valuable in addressing underlying concerns and barriers in the real world (Table 2).

Table 2. Six Themes Highlighting Patient-Suggested & Ranked Strategies To Address Patient Concerns & Barriers

Themes*	Sub-Categories For Each Theme**	Illustrative Quotes (1-3)
Motivators (People, situations, things that motivate taking meds)	Positive med response	"After taking HCQ, I get less easily tired and have energy. I think HCQ response motivates me to take my medication."
	Fear of disease or hospitalization	"I take my medications, I don't want to be admitted again with SLE flare." "I do not want flares, so I take it." "I just want to feel normal so I take HCQ."
	Knowledge about HCQ role	"I was taking I think you know it did help, you know contribute to helping my body be remission" "I think it reduces flare-ups and pain, and prevents damage."
	Dialogue with healthcare team about concerns or side effects	"I was in remission and I stopped taking HCQ. It was hard for me to talk with my doctor but I did discuss with my rheumatologist about my concerns and if I need to start it or if we can monitor for now."
	Family support	"I take meds regularly so that I feel less tired and I can play with my daughter.", "My husband accepted my disease so, I accepted it as well."
	Better SLE labs	"I think the biggest thing for me was really, you know, seeing the positive test results knowing that you know, these medications were actually doing something good."
Filling Information Gaps & Resolving Conflicts	Validating information sources	"I think people have to be cautious with social media sites because even on lupus sites, people are commenting, but we have to be careful because they're not professionals and they're just giving their opinion."
	Positive impact of information	"I got diagnosed at a young age. I wanted to have kids, and was concerned with medications. My doctor said that HCQ will not be an issue. It alleviated my stress."
	Complete Adequate Med Information	"My rheumatologist and my pharmacist they work together and they kind of give me all med details, like take meds with food, take omeprazole on empty stomach."
Facilitators (Strategies that facilitate taking meds)	Personalization of strategies	"I have different alarm tunes for different meds scheduled to be taken at different time of the day." "I leave pillbox lid open so that I remember to take the med." "I keep meds need toothbrush so that I take it in the morning.", "I keep water near my pillbox."
	Attentive, knowledgeable & resourceful Healthcare team	"My rheumatologist told me that it would be the best option for me to see a lupus specialist, and he would not send me if he was not confident that I would be in good hands. He was right, things have been smooth. I owed him a bit of gratitude for this."
	Increased awareness/knowledge about lupus and meds	"There was some correlation between taking meds and me feeling better." "So, basically it came down to the lesser of two evils, med is a lot less bad than disease."
	Easier schedules	"I was told to take meds at the end of the day, I take HCQ as the last thing after I crawl into my bed. Works for me", "I was told to take both tablets together, so much easy."
	Reassurance on safety	"I would like my healthcare team to reassure me that HCQ is safe and the long-term use would not affect my organs."
	Connectivity through EMR & multidisciplinary clinics	"I pick up my medications if I've got questions, I message and their response is right there.", "I like the one-stop clinic, if I need a nephrologist or pharmacist or a social worker - they have it, its easy!"
Physical & personal reminders	Personalize reminders	"I have different alarm tunes for different meds throughout the day." "I leave pillbox lid open so that I remember to take the med." "I keep meds near toothbrush so that I take it in morning.", "I keep water near my pillbox to remind me to take meds."
	Simple strategies	"Taking both tablets together." "Using a pillbox."
	Reinforcement (using 2 reminders)	"I have a pillbox and I always have an alarm on my phone."
Improving clinician-patient & team communication	Attentive provider & focus on patient	"My rheumatologist makes sure I get my eyes checked regularly so they can kind of look at those results and make sure that they're [eyes] ok."
	Non-judgmental & positive communication	"I think, if the clinicians starts with open questions like what's going on? Any stress? Can I help? It would help patients to open up."
	Acting Promptly & Advocacy for patients	During shortage, my rheumatologist acted very quickly and got me adequate med supplies.
	Team engagement	"Both times I was pregnant and was high risk pregnancy. I think my OB and my rheumatologist were talking a lot"
	Tailored patient relevant details	"I only take questions to medical professionals as they know me and they tailor discussions pertaining to me and my lupus."
Building rapport & trust	Trust	"I trust my caregiver and their knowledge and experience, I think building that trust is very important for all lupus patients."
	Personal link with healthcare team	"We had that relationship, when he [rheumatologist] could just look at me and say you're not feeling good today right?"

**Themes ranked from most valuable to least valuable by patients. **Only top key sub-categories for each theme shown.*

Conclusion: Our study provide new insights regarding inter-related themes and insights about HCQ adherence, and patient-suggested and prioritized strategies will be most valuable for future interventions. Our study brings diverse patient voices to redesign adherence intervention in SLE by using a multifaceted patient-insight informed approach and patient-recommended strategies.

Disclosure: S. Garg, None; **B. Chewning**, None; **N. Kaitz**, None; **S. Gomez**, None; **C. Bartels**, Pfizer, Independent Grants for Learning and Change, 5.

Abstract Number: 1164

A Survey of Treatment Satisfaction with Intravenous Immunoglobulin Among Patients with Inflammatory Myositis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Intravenous Immunoglobulin (IVIg) is used to treat rheumatic conditions such as Inflammatory Myositis. Subcutaneous Immunoglobulin (SCIg) is an alternative route of administering Immunoglobulin. Studies have demonstrated that home-based SCIg therapies are cost-effective with similar outcomes and less adverse events compared to IVIg. To date, there have been no studies that have investigated patient satisfaction with respect to IVIg use in myositis. Our objective was to characterize patient satisfaction regarding IVIg in the treatment of their myositis, and to explore their perceptions of SCIg and interest in transitioning to SCIg.

Methods: Adult patients (age 18+) receiving IVIg for Inflammatory Myositis at a Tertiary Centre in Ottawa, Canada were approached and provided informed consent to participate. An adaptation of the validated Treatment Satisfaction Questionnaire for Medication (TSQM) was administered to collect data on patient satisfaction of IVIg across 4 domains (effectiveness, convenience, side effect burden, and global satisfaction) and to gauge interest in SCIg. Data was collected using a 5 or 7-point Likert scale. Results were anonymized and summarized descriptively with means reported. Ethics approval was obtained from the Ottawa Health Science Network Research Ethics Board.

Results: Indications for IVIg included Dermatomyositis (50%), Polymyositis (12.5%), Anti-Synthetase Syndrome (12.5%), and other Inflammatory Myositis (25%). 50% of participants had received IVIg for more than 3 years, 37.5% had received for less than 1 year, and 12.5% had received for 1-3 years. On average, participants were satisfied with the effectiveness of IVIg (5.6/7). Participants were somewhat dissatisfied with the convenience (4.7/7) but satisfied with the ease of planning when treatments occur (5.6/7). 87.5% of participants had experienced side effects including headache (75%), fatigue (37.5%), nausea (25%), chills (25%), and cramps (12.5%). Side effects were rated as somewhat bothersome. Overall, participants were somewhat dissatisfied with their experience of IVIg (4.9/7). Scores across all 4 domains were similar regardless of diagnosis or treatment duration. 87.5% of participants had not heard about SCIg previously. Participants were somewhat uncomfortable with the idea of SCIg (4/7) with 37.5% citing lack of knowledge. 37.5% were willing to switch to SCIg, 12.5% were not, and 50% were unsure. Those willing to switch to SCIg had on average received IVIg for a shorter duration.

Conclusion: Our results suggest that participants are satisfied with the effectiveness of IVIg in treating their myositis but somewhat dissatisfied with the convenience. This discrepancy has been previously reported in other diseases treated with IVIg, with the inconvenience being attributed to the frequency and duration of infusion appointments. We hypothesize that inconvenience, in addition to somewhat bothersome side effects, may be driving down the global satisfaction score in our study. SCIg may offer a solution to the inconvenience of IVIg, though unfamiliarity with SCIg

may be a barrier to patient buy-in. Further patient education on SCIg as a treatment option in Inflammatory Myositis is required.

Disclosure: A. Zhou, None; **N. Maltez**, None; **C. Ivory**, None.

Abstract Number: 1165

"What Matters": Patient and Clinician Perspectives in Psoriatic Arthritis Care

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SESSION INFORMATION

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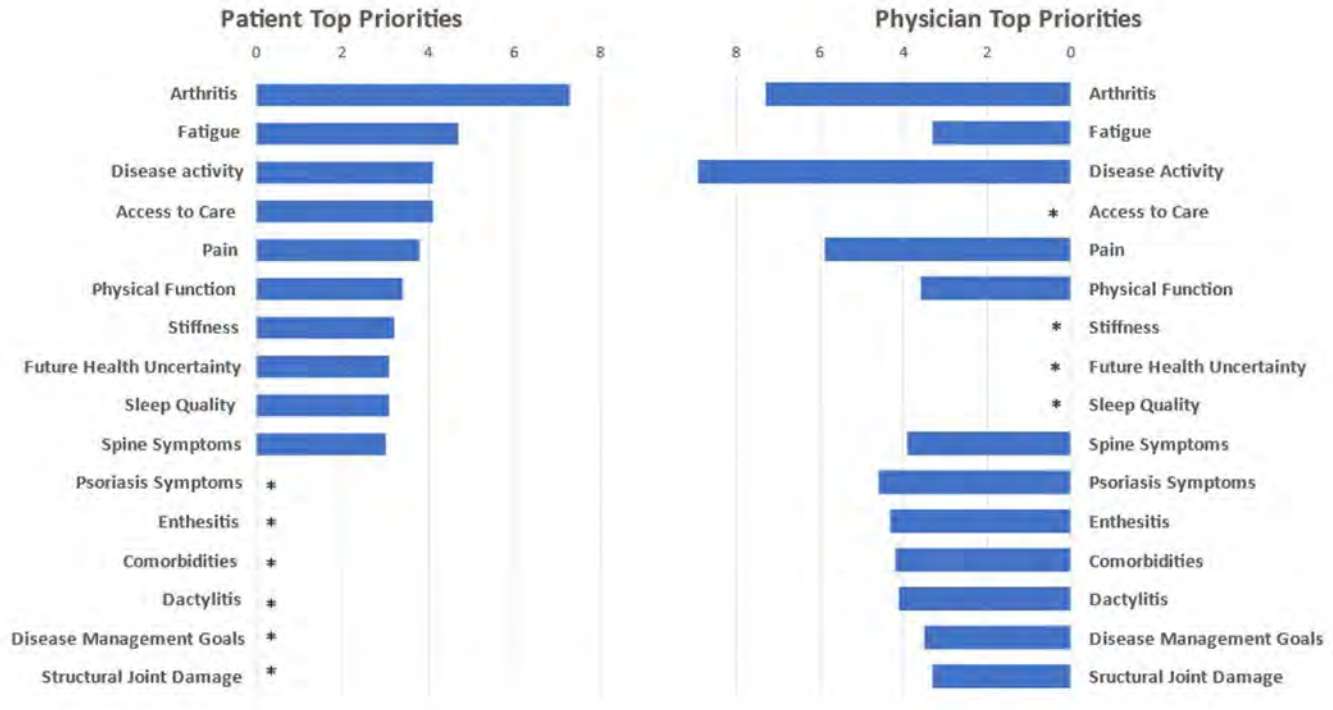
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Figure 1. Top Patient and Physician Priorities



*Not in set of highest ranked items for that group

Background/Purpose: Recent psoriatic arthritis (PsA) treatment recommendations (1), highlight the importance of shared decision making; this ideally requires the clinician understands "what matters" to each patient regarding their disease. Concurrently, patient research partners have been incorporated into projects for the OMERACT core domain set (2) and measures of physical function and (health related) quality of life (3). However, less is known about the similarities and differences between patient and clinician perspectives regarding "what matters" in routine clinical care.

Methods: A comprehensive list of items describing the PsA patient experience was generated in medical anthropologist-designed (CH) peer-to-peer discussions in 4 patient focus groups across the United States (Seattle, Cleveland, Washington, DC). These items were combined with those from the GRAPPA-OMERACT PsA Outcomes patient-physician consensus project (2). A PsA physician and patient steering committee reviewed and revised the list with additional topics considered to be of importance. The final list of 51 items went through a 3 round Delphi process starting with 53 PsA patients and a 2 round Delphi with 13 PsA expert rheumatologists. In each round, participants rated each item for level of importance out of 100 total points.

Results: Top priority items for each group are depicted in Figure 1. Both patients and physicians rated 'Arthritis -Joint pain and swelling' in the top two. Five additional items were included for both groups but with different scores; all related to disease manifestations or physical consequences. 10 items received disparate priority between groups. In this set, patients included two unique items: access to care and future health uncertainty. Other items affecting everyday function were noted. Physician priorities included specific disease manifestations and physical/functional outcomes, and the topic of "disease management goals", focusing on patient-physician communication regarding a treatment plan.

Conclusion: Patients and physicians were in consensus that arthritis disease activity, pain and fatigue are key features of the patient's experience of PsA. Differences appeared in other domains; physicians ranked clinical domains such as enthesitis, dactylitis, and skin disease more highly, patients considered items such as access to care, future health uncertainty and sleep quality to be most important. This study highlights the need for physicians to ask and address "what matters" with patients and to educate patients about potential differences in physicians' areas of concern to optimize shared decision making.

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3. Gossec L, de Wit M, Kiltz U, et al. A patient-derived and patient-reported outcome measure for assessing psoriatic arthritis: elaboration and preliminary validation of the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire, a 13-country EULAR initiative. Ann Rheum Dis 2014;73: 1012–9.

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Abstract Number: 1166

Marijuana Use Amongst Rheumatology Patients: It's More Common Than Rheumatologists Believe

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Background/Purpose: With the legalization of marijuana in many states, rheumatologists are having increased inquiries from patients regarding marijuana use in addition to their pain regimen. There are few studies to guide recom-

Table 1. Patient Survey Demographics

Measure	*n*	%
Sex		
Male	10	26
Female	29	64
Age (Average ± SD)	52 ± 14	
Rheumatologic Diagnosis		
Inflammatory Arthritis	22	49
Systemic Lupus Erythematous	4	9
Fibromyalgia	7	16
Osteoarthritis	7	16
Other	5	11
Education Level		
Less than a College Degree	22	49
College Degree or more	23	51
Ethnicity		
Caucasian	17	38
African American	15	33
Hispanic	10	22
Other	3	7
Employment Status		
Full Time	24	53
Part Time	8	18
Unemployed	9	20
Disability	4	9
Pain Frequency		
Never	4	9
Monthy	7	16
Weekly	13	30
Daily	19	44
Pain Severity Scale 1-10 (Average ± SD)	6 ± 3	

Table 2. Marijuana Preferences Survey Results

Measure	*n*	%
Marijuana Use		
Never	20	44
>1 Year Ago	9	20
Within the Last Year	6	13
Within the Last Month	4	9
Within the Last Week	6	13
Frequency of Marijuana Use		
Daily	4	18
Weekly	7	32
Monthly	4	18
Yearly	7	32
Reason for Marijuana Use (Multiple Answers Accepted)		
Stress/Anxiety	13	31
Sleep Issues	10	24
Pain Issues	15	36
Recreationally	4	10
Pain and Marijuana Use		
Marijuana helped Pain	17	81
Marijuana did not effect Pain	4	19
Marijuana worsened Pain	0	0
Marijuana and Pain Medication Use		
Marijuana decreased use of pain medications	13	65
Marijuana did not decrease the use of pain medications	7	35
Marijuana and Sleep Issues		
Marijuana helped Sleep	20	95
Marijuana did not effect Sleep	0	0
Marijuana worsened Sleep	1	5
Marijuana and Anxiety/Stress		
Marijuana helped Anxiety/Stress	15	79
Marijuana did not effect Stress/Anxiety	3	16
Marijuana worsened Stress/Anxiety	1	5
Interest in Marijuana (if not using)		
Yes	13	57
No	4	17
Yes, but would like more information	6	26

mendations, and those that exist have mixed findings (Hauser, Journal of Pain 2017). Providers need to understand the prevalence of marijuana use among patients and their views regarding its use so that patients can be guided appropriately. This study assesses rheumatology patients' and rheumatologists' perspectives on marijuana use at an urban academic medical clinic.

Methods: Randomly selected patients from an academic rheumatology clinic were consented and enrolled to complete an IRB approved survey. An anonymous survey was given to rheumatology physicians in the same clinic to evaluate their perspectives on marijuana use. Quantitative statistics were used to analyze the data.

Table 3. Rheumatology Provider Responses

Rheumatology Provider Responses (N=12)

Measure	*n*	%
Estimated Percentage of Patients that Use Marijuana		
Less than 20 Percent	8	67
20 to 50 Percent	4	33
Over 50 Percent	0	0
Age of Patients that Use Marijuana (Multiple Answers Accepted)		
Less than 40 years old	8	57
Over 40 years old	6	43
Helpful to have Medical Marijuana Use in EMR		
Yes	10	83
No	2	17

Results: Forty-five patients completed the survey. Their demographics and pain assessment are in Table 1. Of the survey responses, 57% of patient had tried marijuana, with 50% using it weekly. Marijuana use was greater in patients over the age of 40 (p=0.05) and in those with a pain score greater than 6 (65%, p=0.01). Patients with no college degree used marijuana more than those with at least a college degree (p=0.02). Of marijuana users, 81% of patients stated that marijuana decreased their pain; 65% reported a decrease in pain medication use. There was no association between marijuana use and ethnicity, diagnosis, or employment status. The majority, 57%, of non-marijuana users were interested in trying it. Table 2 includes patient responses to the survey.

The results of the rheumatologists' survey are in Table 3. The physician survey found that 66.7% of the rheumatologists believed less than 20% of their patients were using marijuana and a majority felt that younger patients (less than 40) were more likely to use marijuana. Most rheumatologists felt that adding marijuana use to the electronic medical record would be helpful.

Conclusion: At an academic medical center, marijuana use was more common than providers expected and interestingly, more common in older patients. A majority of the patients who were not using marijuana, were interested in trying it. Given that marijuana use is increasing and may now even exceed tobacco use in many practices, it is important to ask about this in all patients. These results also highlight the need for high quality studies on the safety and effects of marijuana use in patients with rheumatic diseases.

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Abstract Number: 1167

Rheumatoid Arthritis Patients' Treatment Goals Relate to Disease Activity and Rheumatology Experiences

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SESSION INFORMATION

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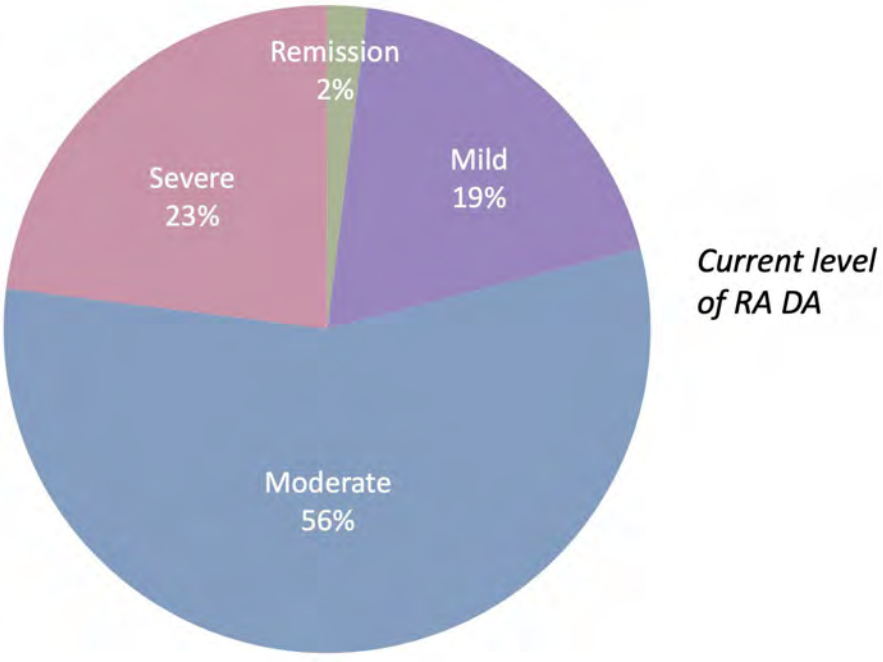
Background/Purpose: Shared decision making and treat to target are recognized guidelines to treat Rheumatoid Arthritis (RA). We previously reported associations of shared treatment goal discussions to greater disease activity (DA) improvement and satisfaction with rheumatology care. Further, only 37% of RA patients surveyed recall having shared goal discussions with providers. Building on our previous reports, we aimed to gain insight to the nature of patient treatment goals and their role in RA management.

Methods: An anonymous online questionnaire was presented in 2019 on a secure survey system. Participants were U.S. residents ≥18 years of age with a self-reported RA diagnosis by a medical professional. They responded to questions on demographics, RA disease activity, diagnosis and DMARD history, improvement from treatment, and

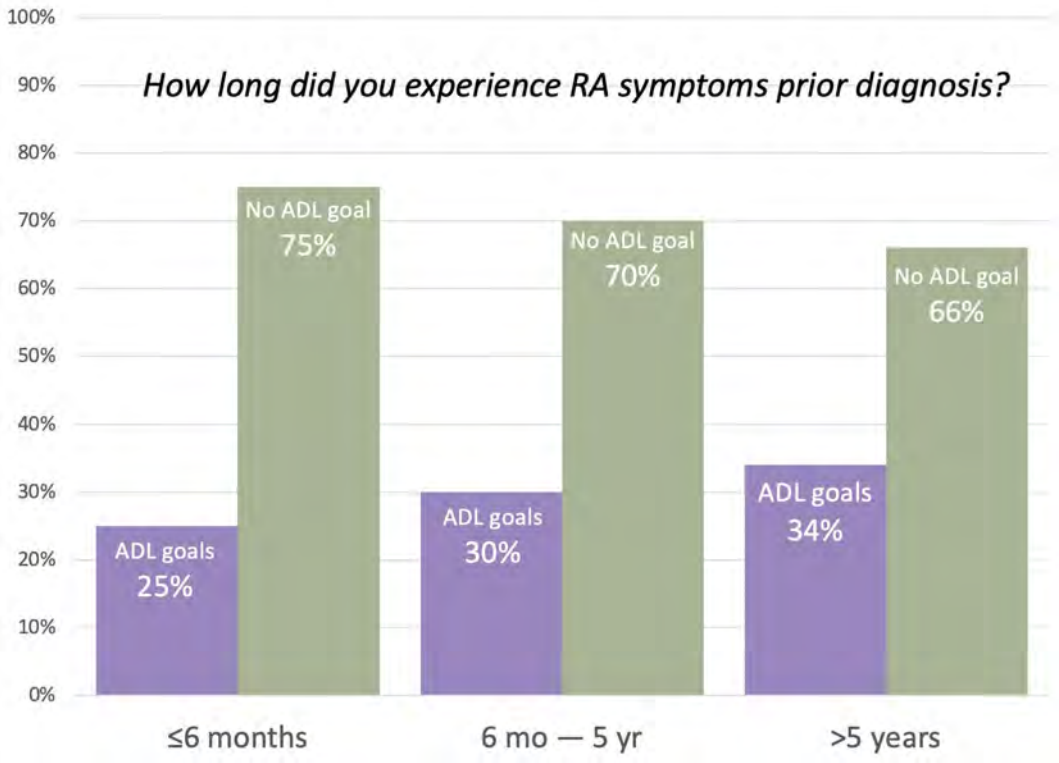
Parameter	Pain	Stop dz progress	Function: ADL	Function: Active	Function: Lifestyle
Current DA	Higher	Lower	Higher	Lower	Lower
Goal discussions	*	More likely	More likely	More likely	More likely
Remission	Less	More	Less	More	Less
No treatment plan	More likely	More likely	Less likely	More likely	Less likely
Time to treatment	Longer	Longer	Longer	Shorter	Shorter
Patient satisfaction	Less	*	Less	Higher	*
# DMARDs tried	More	More	*	Fewer	*

* No clear trend

Parameters that associate with patients' top RA treatment goals With certain parameters, particular RA treatment goals are more likely.



RA Patients Whose Treatment Goals Are Related to Pain: Figure 1. Respondents describing their RA treatment goals using "pain" (or a synonym for pain) are divided by their replies to the question "What is your current level of RA DA?"



Frequency of ADL Goals by Time Before RA Diagnosis: Figure 2. Patients describing their RA treatment goals as relating to activities of daily living (ADLs) were asked how long they had RA symptoms prior to diagnosis.

RA treatment goals. Patients' treatment goals were thematically coded and verified for reliability by a team using qualitative content analysis. If >1 goal was conveyed, both were coded; "To be able to do daily activities without so much pain" mentioned both ADL and pain goals.

Results: The questionnaire was completed by 907 RA patients (90% women, 10% men), with 58 (11) years mean (SD) age and 11 (10) years since diagnosis. In response to the question "What are your goals for RA treatment?", 95% recorded responses (n=861). Fifteen themes were identified, 8 of them present in ≥20% of respondents. Major themes were *function* 59%, *pain* 53%, *stopping disease progression* 30%, *extra-articular disease effects* 26%, *medication* 21%, *communication with providers* 21%, *remission* 20%, and *less disease activity* 20%. Function goals included 3 subthemes: *activities of daily living* (ADL) 31%, *lifestyle* 18%, and *being active* 10%. Subthemes in extra-articular goals included *constitutional health* 17%, *overall health* 5%, and *organ involvement* 4%. Minor themes included *very modest goals* 7%, *nontraditional medicine* 4%, *understanding* 3%, *story but no goal* 2%, *cure* 1%, *hopelessness* 1%, and *hope* 0.7%. Major themes associated with DA levels, time to treatment, shared goal discussions, and presence of treatment plans. Higher DA associated with goals related to pain or ADL; lower DA related to goals of lifestyle, being active, and stopping disease progression. Examples of typical treatment goals: "Significant pain reduction"; "Limit joint damage"; "Able to maintain all independence."

Conclusion: This RA patient survey found previously unreported themes in patients' treatment goals, which associated with aspects of rheumatology care such as presence of a treatment plan or a shared goal discussion as well as RA disease activity. Our study is unique in coding patient treatment goals by common themes. Further research should seek greater understanding of patient treatment goals and investigate their significance in RA outcomes.

Disclosure: K. O'Neill, None; **P. Sinicrope**, None; **K. Marks**, None; **E. Myasoedova**, None; **C. Crowson**, None; **J. Davis**, Pfizer, 5.

Abstract Number: 1168

Barriers to Effectiveness of Non-surgical Treatments for Knee Osteoarthritis in a Diverse Racial/Ethnic Population: A Nominal Group Qualitative Study

Jasvinder Singh, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Knee osteoarthritis (OA) has worse outcome in racial/ethnic minorities, who also have more severe pain, disability and worse outcomes. However, most qualitative studies include primarily Caucasian people with knee OA. Therefore, our objective was **t**o examine patient experience, views and opinions of reasons for why the current knee OA treatments are not working for them in a diverse racial/ethnic group of people.

Methods: Nominal groups were conducted with consecutive clinic patients with knee OA at a medical center, oversampling African Americans. Patients discussed and rank-ordered their concerns.

Results: Fourteen nominal groups with 48 knee OA patients were conducted with mean age, 60.6 years (standard deviation, 9.8) and knee OA duration, 7.8 years (sd, 5.4); 25% were men, and 46% were African American. The most frequently cited highly-ranked concerns, divided into 3 categories as follows:

A. Medication-related: (1) side effects (9 groups); (2) limited efficacy (9 groups); (3) medication not targeting underlying disease; (4) lack of personalized medication use; and (5) temporary benefit;

B. Exercise/Physical therapy related: (1) exacerbation of joint pain (8 groups); (2) difficulty in doing exercises (6 groups); (3) lack of motivation (8 groups); (4) technical challenges/lack of personalized exercise regimens (1 group); (5) cost (3 groups); and

C. Weight loss related: (1) difficulty in achieving weight loss (7 groups); (2) motivation (2 groups); and (3) limited efficacy for symptom improvement (1 group).

Conclusion: Participants with knee osteoarthritis, consisting of a diverse racial/ethnic representation, identified several barriers to the effectiveness of current knee OA treatments. This new knowledge provides insights for making the current treatment options potentially more usable and/or more effective. Given the significant consequences of knee OA, limited/no disease-modifying drugs this strategy can potentially improve clinical care and patient outcomes.

Disclosure: J. Singh, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2, Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4.

Abstract Number: 1169

Patient Preferences for Outcome Measures for a Pragmatic Knee Osteoarthritis (OA) Clinical Trial: Results of a Cross-Sectional Patient Survey That Included Racial/Ethnic Minorities

Jasvinder Singh, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster III: Patient Preferences (1153–1169)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Many effective treatments are available for knee osteoarthritis (OA), however comparative effectiveness research (CER) of various treatments to each other is limited. One of the key challenges to conducting knee OA trials is the choice of primary trial outcome, that is sensitive to change and is relevant to patients as the key stakeholders. Therefore, we conducted a cross-sectional study to examine the outcomes most relevant to patients with knee OA in a sample that included racial/Ethnic minorities.

Methods: We enrolled consecutive patients with a clinical diagnosis of knee OA at a tertiary medical center clinic, oversampling for African Americans with knee OA, during regular clinic visit. Participants ranked various knee OA outcomes in response to the question: "How important is the assessment of the following outcomes in a study of people with knee osteoarthritis?"

Results: In a pilot study of 58 people with knee OA (mean age, 57 years; 72% female; 69% White) at regular clinic visits, the respondents ranked the following outcomes as extremely, very or moderately important for this study: knee pain (95%); function (86%); sleep (87%); fatigue (92%); patient acceptable symptom state (89%); social participation (77%); anxiety/depression (86%). Only 37% of patients were satisfied or very satisfied with current knee OA treatment.

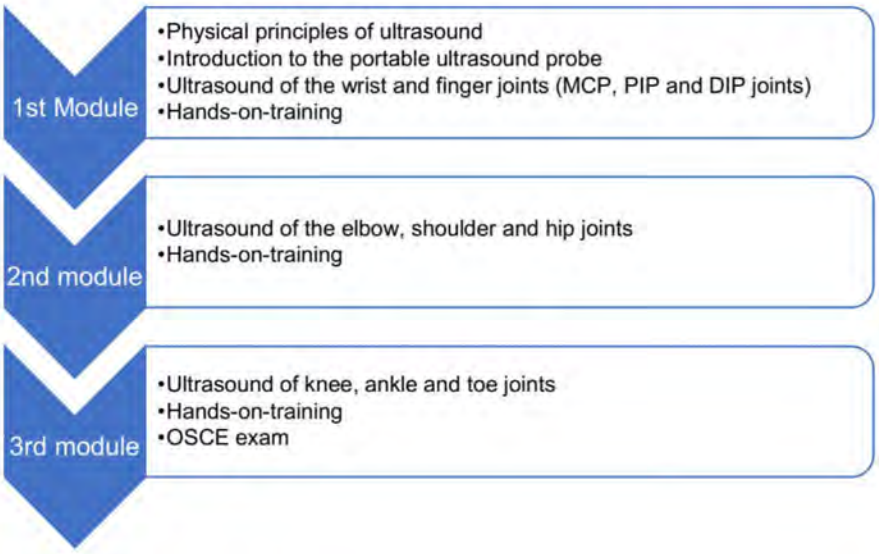
Conclusion: This patient-focused study identified that a large group of patients were unsatisfied with current knee OA treatments. The chosen study outcomes reflect a range of components and outcomes important to patients and other key stakeholders. Identification of patient-relevant and patient-important study outcomes will make outcome selection practical for a pragmatic clinical trial.

Disclosure: J. Singh, Crealta/Horizon, 2, Medisys, 2, Fidia, 2, PK Med, 2, Two labs Inc, 2, Adept Field Solutions, 2, Clinical Care options, 2, Clearview healthcare partners, 2, Putnam associates, 2, Focus forward, 2, Navigant consulting, 2, Spherix, 2, MedIQ, 2, Jupiter Life Science, 2, UBM LLC, 2, Trio Health, 2, Medscape, 2, WebMD, 2, Practice Point communications, 2, the National Institutes of Health, 2, the American College of Rheumatology, 2, TPT Global Tech, 11, Vaxart pharmaceuticals, 11, Charlotte's Web Holdings, Inc., 11, Amarin pharmaceuticals, 11, Viking pharmaceuticals, 11, Moderna pharmaceuticals, 11, speaker's bureau of Simply Speaking, 6, member of the executive of Outcomes Measures in Rheumatology, 4.

Abstract Number: 1170

Establishment and Validation of a Didactic Musculoskeletal Ultrasound Course for Dermatologists Using an Innovative Handheld Ultrasound System

Jakub Grobelski[1], Florian Recker[2], Pantelis Karakostas[1], Dagmar Wilsmann-Theis[3], Wolfgang Hartung[4], Peter Brossart[5] and **Valentin Schäfer**[1], [1]Clinic of Internal Medicine III, Oncology, Haematology, Rheumatology and Clinical Immunology, University Hospital Bonn, Bonn, Germany, [2]Centre for Obstetrics and Gynecology, University Hospital Bonn, Bonn, Germany, [3]Department for Dermatology and Allery, University Hospital Bonn, Bonn, Germany, [4]Department of Rheumatology and Clinical Immunology, Asklepios Clinic, Bad Abbach, Germany, [5]Department of Internal Medicine III, Oncology, Hematology and Rheumatology, University Hospital Bonn, Bonn, Germany



Graphic 1. Ultrasound Course Module Structure

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: In the early detection of arthritis, such as psoriatic arthritis, ultrasound (US) of painful joints plays an important role in diagnosis. Pathological findings can be missed during clinical examination, especially if conducted by physicians who are not trained. Furthermore several publications undermine the importance of early psoriatic arthritis detection in psoriasis patients and the key role of the dermatologists in this process. The objective of this study was to examine a pilot musculoskeletal ultrasound (MSUS) course designed specifically for dermatologists.

Methods: To assess the degree of US expertise of the participants, a questionnaire was conducted before the course. The course concept covered only the most important US sections of all joints and focused on the detection of joint effusion and hyperperfusion. The course consisted of 3 modules and was carried out over 6 months. Graphic 1 shows the modular course concept. A portable US system in combination with a tablet was provided, to enable practice between the courses. The final teaching evaluation was carried out as an objective structured clinical examination (OSCE)(5) consisting of 3 stations, each representing 1 of the course modules. Graphic 2 shows exemplary the course teaching sessions. According to the following grade scoring system, the performance rating was checked: < 60 % failed, ≥ 60 - < 70 % sufficient, ≥ 70% - < 80 % satisfying, ≥ 80% - < 90 % good, ≥ 90 % very good.

Results: Twelve dermatologists participated. The mean age of our cohort was 39 years (SD ± 9.99 years) with 9 females (75 %). Eight were specialists in dermatology in mean for 11.4 years (SD ± 11 years). Four were assistant physicians practicing dermatology in mean for 3.06 years (SD ± 0.97 years).

The survey revealed no prior knowledge of MSUS. The overall mean score of all participants in the OSCE was 21.86 (SD ± 2.12) (87.44%) out of a total of 25 points resulting in a good grade. There was no statistically significant difference between the assistant physicians and the specialists in dermatology regarding the OSCE results. Table 1 shows the OSCE results.

Graphic 2. Practical exercises during the course

Table 1. Objective structured clinical examination results for all three stations in mean Module 1: representing the first OSCE station, Module 2: representing the second OSCE station, Module 3: representing the third OSCE station, overall: the mean result for all OSCE modules

Module	Mean absolute	Standard Deviation	Confidence Interval	Mean percentage	Standard Deviation	Confidence Interval	Grade
1	18.92	+/- 3.07	16.97-20.87	75.67 %	+/-12.27%	67.87-83.46 %	Sufficient
2	23.83	+/-0.99	23.21-24.46	95.33 %	+/-3.94 %	92.83-97.84 %	Very good
3	22.83	+/-0.37	22.60-23.07	91.33 %	+/-1.49 %	90.39-92.28 %	Very good
overall	21.86	+/-2.12	16.59-27.13	87.44 %	+/-8.49 %	66.36-108.53 %	Good

Conclusion: The innovative teaching concept MUDE was able to demonstrate, that it is appropriate for the training of dermatologists in MSUS, independently of their age, experience in dermatology and US.

Disclosure: J. Grobelski, None; **F. Recker**, None; **P. Karakostas**, None; **D. Wilsmann-Theis**, None; **W. Hartung**, None; **P. Brossart**, None; **V. Schäfer**, None.

Abstract Number: 1171

Needs Assessment of a Rheumatology Curriculum for Internal Medicine Residents

Laura Arneson[1], Biana Modilevsky[2], Kaitlin Lima[1], Sarah Fantus[1] and Anisha Dua[3], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]Swedish Hospital, NorthShore University HealthSystem, Chicago, IL, [3]Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The rheumatology workforce faces a shortage in the decade ahead. Internal Medicine (IM) residents comprise the pipeline of physicians who will care for rheumatology patients in general medicine, rheumatology, and other specialties. However, many IM residencies lack formal training on rheumatologic diseases. This needs assessment investigated IM residents' interest, competence, and preferred format of learning rheumatology topics. Results will guide the development of a curriculum to enhance rheumatology teaching for medicine trainees.

Methods: The study population consisted of IM residents at a university hospital (Program A, n=116) and a community hospital (Program B, n= 23). Residents' objective knowledge of rheumatology was assessed via In-Training Exam (ITE) scores from 2020. Their confidence and interest in clinical rheumatology was assessed through an anonymous survey. The survey queried residents' confidence in and interest in learning about six skills: conducting a rheumatology review of systems, performing a large joint exam, performing a small joint exam, ordering appropriate labs for

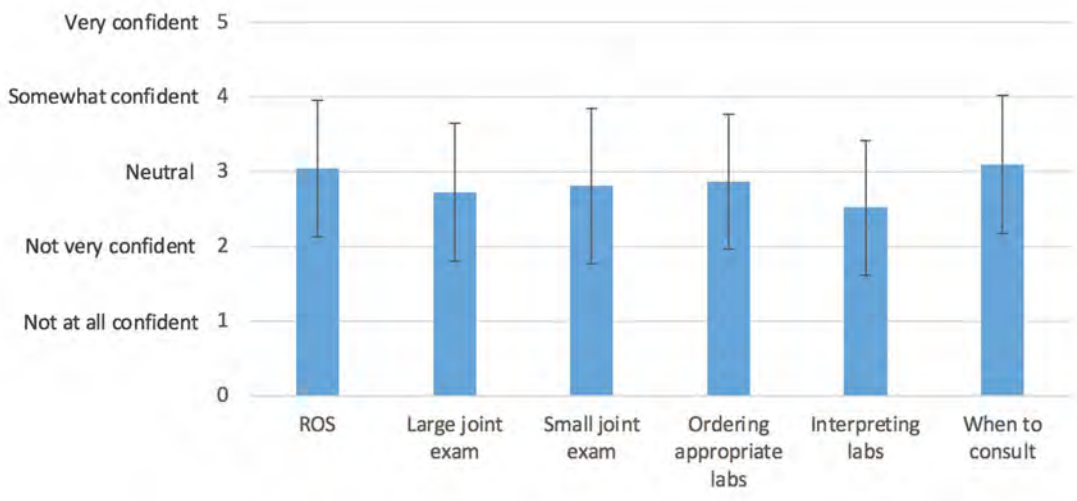


Figure 1. Residents' confidence in rheumatology skills (n=73). Average scores on a 5-point Likert scale are presented, with error bars indicating one standard deviation.

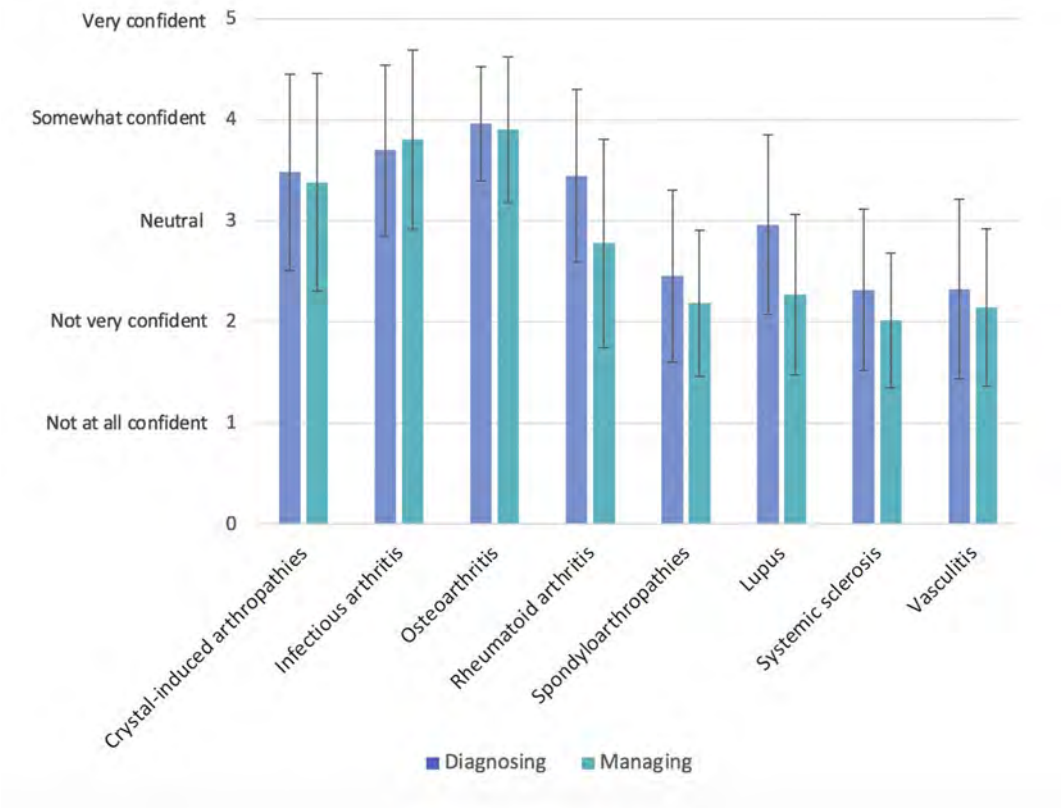


Figure 2. Residents' confidence in diagnosing (left bar) and managing (right bar) rheumatologic conditions (n=73). Average scores on a 5-point Likert scale are presented, with error bars indicating one standard deviation.

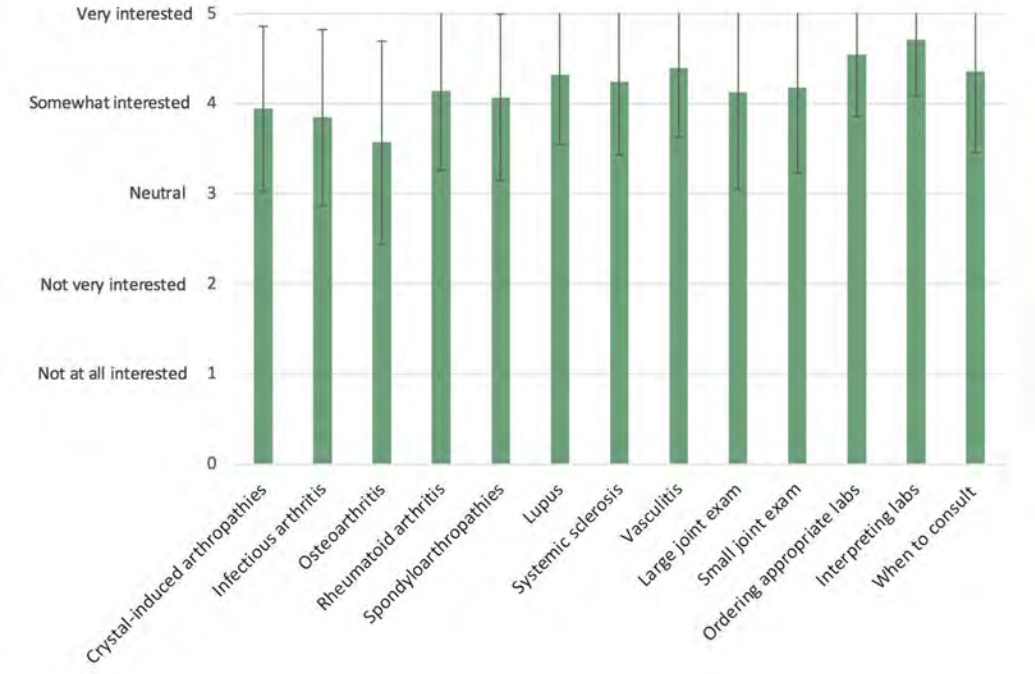


Figure 3. Residents' interest in learning about rheumatology topics (n=72). Average scores on a 5-point Likert scale are presented, with error bars indicating one standard deviation.

autoimmune diseases, interpreting labs for autoimmune diseases, and deciding when to consult rheumatology. It also assessed residents' confidence in diagnosing and managing, and interest in learning about, eight rheumatologic disease categories: crystal-induced arthropathies, infectious arthritis, osteoarthritis, rheumatoid arthritis, spondyloarthropathies, lupus, systemic sclerosis, and vasculitis. Survey questions were presented on five-point Likert scales.

Results: On the 2020 ITE, rheumatology was the subspecialty with the lowest average score for residents nationwide (59%), at Program A (60%), and tied for lowest at Program B (48%). Surveys were completed by 53/116 (46%) of residents at Program A and 20/23 (87%) of residents at Program B. Responses were similar between Program A and B across all questions, and are presented as aggregate scores. Average interest in learning about rheumatology was 3.8/5, between "neutral" and "somewhat interested." Average rating of the amount of rheumatology training received in residency was 2.3/5, between "somewhat inadequate" and "neutral." Confidence in rheumatology skills is presented in Figure 1. Confidence in diagnosing and managing specific rheumatologic conditions is presented in Figure 2. Interest in learning about rheumatology topics is presented in Figure 3. Topics for which residents expressed lowest confidence and highest interest included: ordering and interpreting labs for autoimmune diseases, lupus, vasculitis, and systemic sclerosis. Residents identified noon conference and online self-paced modules as the preferred curriculum formats.

Conclusion: IM residents at both programs demonstrated objective deficits in rheumatology knowledge on the ITE, as well as self-reported need and interest in more rheumatology training. ITE scores and our survey results highlight the urgent need to better address rheumatology training for IM residents nationwide. The study team is developing a series of noon conference sessions for IM residents on the topics identified above, to be recorded and archived for future use.

Disclosure: L. Arneson, None; **B. Modilevsky**, None; **K. Lima**, None; **S. Fantus**, None; **A. Dua**, Abbvie, 1, 2, 6, Novartis, 2, Chemocentryx, 2.

Abstract Number: 1172

Podcast-Based Learning, a Valuable Tool for Learning Rheumatology

Akrithi Udupa[1], Sophia Weinmann[2] and David Leverenz[3], [1]Duke University Hospital, Durham, NC, [2]Duke University Medical Center, Durham, NC, [3]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The onset of the COVID-19 pandemic disrupted the delivery of medical education to trainees, compelling educators to utilize virtual learning platforms. The purpose of this project is to assess the educational value, accessibility, and impact of podcast-based learning as a complementary learning tool for medical trainees rotating on an inpatient rheumatology service at a single academic institution.

Methods: From July 2020 to April 2021, medical trainees (physician assistant student, medical students, residents) rotating on an inpatient rheumatology consult service were given access to a podcast comprised of educational conversations between a fellow and an attending on various topics in Rheumatology, stored on a password protected server. All podcast episodes were less than 25 minutes in length. Access statistics from the server included "previews" (when a trainee listened to an episode directly on the server) and "downloads" (when a trainee downloaded

Table 1. Podcast episode engagement among survey respondents and direct access stats from the podcast server

Podcast episode	Survey respondents	Direct access statistics*	
	n (%)	Previews (n)	Downloads (n)
Systemic Lupus Erythematosus	18 (90%)	51	43
Myositis Part 1	14 (70%)	65	43
Myositis Part 2	8 (40%)	NA†	NA†
Arthrocentesis	8 (40%)	14	19
Giant Cell Arteritis	13 (65%)	43	23
Gout Part 1	10 (50%)	16	13
Gout Part 2	9 (45%)	16	17

Table Notes:
*Trainees could preview or download each episode multiple times, therefore percentages could not be calculated.
†Access statistics were not available for these episodes.

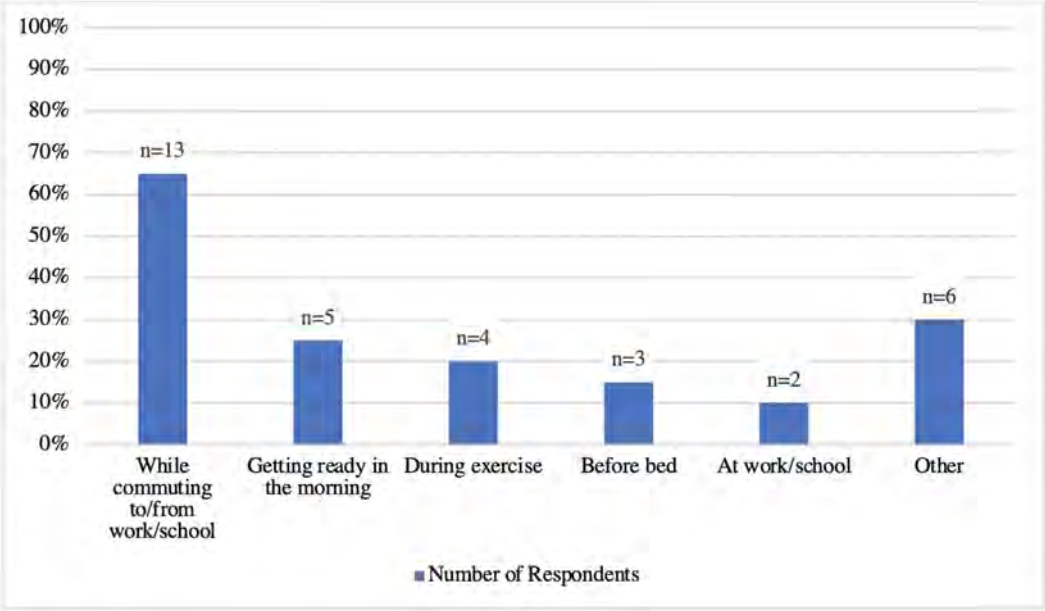


Figure 1. Number of survey respondents who reported listening to the podcast at particular times.

an episode to a device). Participants were surveyed on prior podcast listening, engagement with the rheumatology podcast intervention, perceptions of the podcast's appropriateness of educational content, learning, enjoyment, accessibility, and direct impact on clinical care of rheumatic patients. Data were examined using descriptive statistics.

Table 2. Survey results among 20 respondents regarding podcast educational content, enjoyment, impact, and accessibility.

	Strongly Disagree n (%)	Disagree n (%)	Agree n (%)	Strongly Agree n (%)
The educational content in the podcasts was appropriate for my level of training	1 (5%)	0 (0%)	6 (30%)	13 (65%)
I enjoyed listening to the podcasts	1 (5%)	0 (0%)	4 (20%)	15 (75%)
I learned a lot from the podcasts	1 (5%)	0 (0%)	6 (30%)	13 (65%)
Listening to the podcasts directly changed my approach to evaluation, diagnosis and treatment of patients with rheumatic disease	1 (5%)	0 (0%)	8 (40%)	11 (55%)
It was easy to access and listen to the podcasts	0 (0%)	6 (30%)	2 (10%)	12 (60%)

Results: Of the 41 trainees who received a survey, 20 (48.87%) responded, including 1 physician assistant student, 7 medical students, 5 interns, 3 second-year internal medicine residents, and 4 third-year residents. Prior to this study, 7/20 (35%) spent greater than two hours per week listening to podcasts on any topic and 2/20 (10%) did not listen to any podcasts. Regarding the rheumatology podcast intervention, all respondents reported listening to at least one podcast episode, 12/20 (60%) listened to at least half of the episodes, and 5/20 (25%) listened to all episodes. As shown in Table 1, more than half the respondents listened to episodes on systemic lupus erythematosus, myositis (part 1), and giant cell arteritis; these episodes also received the most "previews" and "downloads" from the podcast server. The preferred podcast episode length was between 10 and 30 minutes for 17/20 (85%) of respondents. As shown in Figure 1, respondents most often played the podcast while commuting to and from school or work (n = 13, 65%). As shown in Table 2, 19/20 (95%) respondents agreed or strongly agreed that the educational content of the podcast was appropriate for level of training, enjoyable and educational, and directly impacted their approach to evaluating, diagnosing, and treating patients with rheumatic disease. Although 14/20 (70%) agreed or strongly agreed that the podcast was easily accessible, 6/20 (30%) disagreed with this statement.

Conclusion: Medical education podcasts are emerging as a supplementary learning tool at all stages of training. Our study demonstrates that medical trainees voluntarily listened to our Rheumatology podcast and the majority of survey respondents found the podcast to be educational, enjoyable, and impactful for rheumatology patient care. Reported difficulty with playing the podcast on the server emphasizes the importance of accessibility in successful podcast learning.

Disclosure: A. Udupa, None; **S. Weinmann**, None; **D. Leverenz**, Pfizer, 5.

Abstract Number: 1173

Bringing Reproductive Health Guidelines into Fellowship Training: A National Survey of Adult and Pediatric Rheumatology Fellows and Program Directors to Assess Educational Need and Inform Curriculum Development

Megan Clowse[1], Stacy Ardoin[2], Elise Berlan[2], Kristine Carandang[3], Kate Chiseri[4], Arthur Kavanaugh[5], Whitney White[6], Kelly Wise[7], Andrew Wong[8] and Michael Battistone[9], [1]Duke University, Chapel Hill, NC, [2]Nationwide Children's Hospital, Columbus, OH, [3]Independent, San Diego, CA, [4]American College of Rheumatology, Atlanta, GA, [5]University of California San Diego, La Jolla, CA, [6]Birmingham VA Medical Center, Birmingham, AL, [7]Nationwide Children's Hospital, Hilliard, OH, [8]Olive View-UCLA Medical Center, Sylmar, CA, [9]Salt Lake City VA, Salt Lake City, UT

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Professional Education Poster (1170–1195)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: In 2020, the American College of Rheumatology (ACR) published clinical practice guidelines addressing reproductive health for patients with rheumatic diseases. The guidelines are the culmination of a 5-year, multi-specialty, interprofessional effort, now known as the Reproductive Health Initiative (RHI). The 2-fold purpose of this study was to (Part I) design national surveys of rheumatology fellows and fellowship program directors (PDs) to inform development of curricula and programs relating to RHI guidelines, and to examine evidence of validity of these surveys using Messick's framework prior to (Part II) future implementation of an ACR sponsored national survey project, coordinated through the Committee on Training and Workforce.

Methods:

Content

Table 1. Expert Review Ratings - Fellows Survey

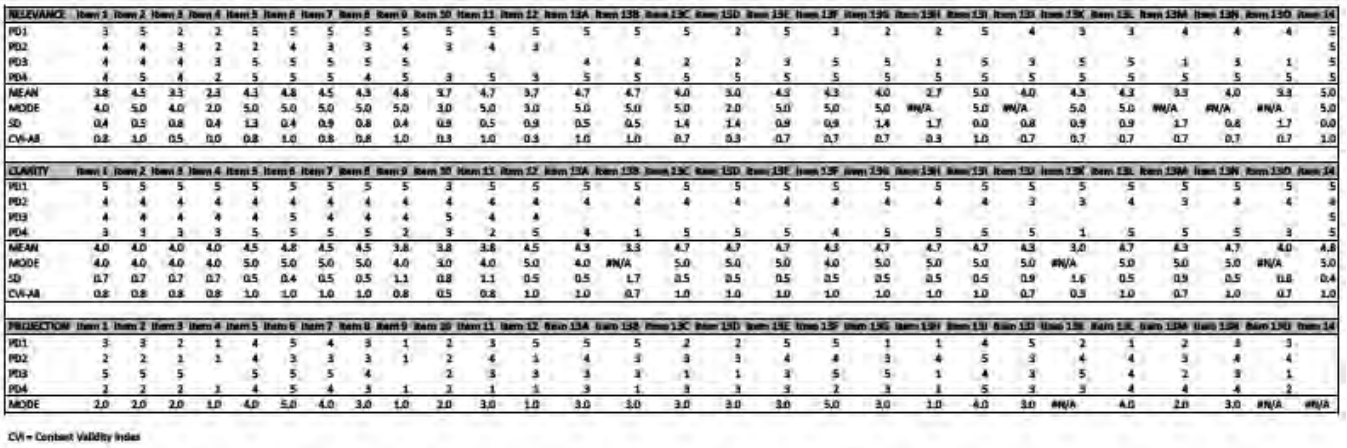
RELEVANCE	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12A	Item 12B	Item 12C	Item 12D	Item 12E	Item 12F	Item 12G	Item 12H	Item 12I	Item 12J	Item 12K	Item 12L	Item 12M	Item 12N	Item 12O	Item 13
RF1	5	3	2	1	4	5	4	5	4	4	1	5	3	5	3	5	2	1	1	5	3	4		5	5	4	4
RF2	4	5	3	3	5	5	4	5	5	4	3																5
RF3	5	5	2	4	4	4	2	4	4	4	3																2
RF4	5	5	5	4	5	5	5	5	5	5	3	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
RF5	5	5	4	2	4	5	4	4	3	3	2	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	4
MEAN	4.4	4.6	3.2	2.8	4.4	4.8	3.8	4.6	4.2	4.0	2.4	5.0	4.3	5.0	4.3	5.0	4.0	3.7	3.7	5.0	4.3	4.7	5.0	5.0	5.0	4.7	4.0
MODE	5.0	5.0	2.0	4.0	4.0	5.0	4.0	5.0	4.0	4.0	3.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	4.0
SD	0.8	0.8	1.2	1.2	0.5	0.4	1.0	0.5	0.7	0.6	0.8	0.0	0.9	0.0	0.9	0.0	1.4	1.9	1.9	0.0	0.9	0.5	0.0	0.0	0.0	0.5	1.1
CVI	0.8	0.8	0.4	0.4	1.0	1.0	0.8	1.0	0.8	0.8	0.0	1.0	0.7	1.0	0.7	1.0	0.7	0.7	0.7	1.0	0.7	1.0	1.0	1.0	1.0	1.0	0.8

CLARITY	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12A	Item 12B	Item 12C	Item 12D	Item 12E	Item 12F	Item 12G	Item 12H	Item 12I	Item 12J	Item 12K	Item 12L	Item 12M	Item 12N	Item 12O	Item 13
RF1	5	5	5	5	5	5	5	5	5	5	5																4
RF2	3	5	5	5	5	5	5	5	5	5	5																5
RF3	4	4	4	4	4	4	4	4	4	4	4																4
RF4	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
RF5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5	5
MEAN	4.4	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	4.8	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	4.8
MODE	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0	5.0
SD	0.8	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.5
CVI	0.8	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0	1.0

PROJECTION	Item 1	Item 2	Item 3	Item 4	Item 5	Item 6	Item 7	Item 8	Item 9	Item 10	Item 11	Item 12A	Item 12B	Item 12C	Item 12D	Item 12E	Item 12F	Item 12G	Item 12H	Item 12I	Item 12J	Item 12K	Item 12L	Item 12M	Item 12N	Item 12O	Item 13
RF1	4	4	3	2	4	4	4	5	2	2	1	3	4	3	5	5	2	2	1	5	3	4	5	5	5	3	
RF2	4	4	4	3	4	5	4	5	1	2	5																
RF3	4	4	3	2	3	3	3	5	2	1	2																
RF4	3	3	3	1	4	5	4	5	1	2	1	5	2	5	4	4	1	3	1	1	4	5	3	3	2	1	
RF5	3	3	2	2	4	5	4	5	1	1	1	5	4	3	2	4	2	1	1	5	4	4	1	3	3	2	
MODE	4.00	4.00	3.00	2.00	4.00	5.00	4.00	5.00	1.00	2.00	1.00	5.00	4.00	3.00	#N/A	4.00	2.00	#N/A	1.00	5.00	4.00	4.00	#N/A	3.00	#N/A	#N/A	#N/A

CVI = Content Validity Index

Table 2. Expert Review Ratings - Program Directors Survey



CVI = Content Validity Index

Constructs of interest were defined through literature review and refined by reflective critique from 8 RHI members, facilitated by a former PD working with a member of the ACR administrative staff. A panel of 9 outside expert reviewers (5 rheumatology fellows and 4 PDs) evaluated survey items for relevance to the constructs and clarity of communication. Descriptive statistical analyses of ratings were performed, and content validity index (CVI) for each item was calculated. Items with CVI < 0.7 were discarded.

Response Process

Cognitive interviewing, consisting of "think aloud interviewing" in which a participant was asked to verbalize their understanding of items through paraphrase, was used to clarify the mental model emerging through survey use.

Results: The construct of interest was defined as "interest in curriculum", and was considered separately for fellows and PDs. Both fellow and PD constructs were conceptualized as 4 dimensions: 1) **confidence** in the current curriculum relating to RHI guidelines; 2) **personal interest** in the topic; 3) **opinions of the importance** of the topic; and 4) **interest in a range of learning materials and educational experiences**. Initial surveys consisted of 27 items for fellows and 28 items for PDs. Expert review ratings are shown in Table 1 (fellow survey) and Table 2 (PD survey), and led to discarding 9 items for fellows and 6 items for PDs; 5 of these were corresponding questions shared across the 2 surveys. Cognitive interviewing suggested that fellows considered questions relating to their level of interest in reproductive health as connecting to a sense of ownership or responsibility for addressing these issues. Final versions of the surveys consisted of 18 items for fellows and 22 items for PDs and are being sent to 753 fellows and 179 program directors representing adult and pediatric rheumatology fellowships.

Conclusion: Validity evidence from content and response process sources support national distribution of the surveys to rheumatology fellows and fellowship PDs. Data collected through (Part II) this ACR sponsored national survey will be of value to educational leaders in developing curricula and programs to improve reproductive health for patients with rheumatic disease.

Disclosure: M. Clowse, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5; **S. Ardoin**, Aurinia, 2, American Board of Pediatrics, 4, Childhood Arthritis and Rheumatology Research Alliance, 4; **E. Berlan**, None; **K. Carandang**, None; **K. Chiseri**, None; **A. Kavanaugh**, AbbVie, 5, 12, Expert advice, Amgen, 5, 12, Expert advice, Bristol Myers Squibb, 5, 12, Expert advice, Janssen, 5, 12, Expert advice, Pfizer, 5, 12, Expert advice, UCB, 5, 12, Expert advice, AstraZeneca, 5, 12, Expert advice, Celgene, 5, 12, Expert advice, Roche, 5, 12, Expert advice, Novartis, 5; **W. White**, Abbvie, 6; **K. Wise**, None; **A. Wong**, None; **M. Battistone**, None.

Abstract Number: 1174

Teaching and Reproducibility of a Pediatric Musculoskeletal Ultrasound Scoring System

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Localized musculoskeletal ultrasound (MSUS) examination is used in adult rheumatology clinics and has been shown to be a valid and feasible method for assessing joint inflammation in rheumatoid arthritis. Pediatric MSUS continues to be an evolving topic of research within the field, with ongoing standardization of protocol and scoring systems. The purpose of this study is to determine the time and resources necessary to reliably train pediatric MSUS sonographers of differing specialties and levels of expertise to reliably utilize a recently proposed 12-joint MSUS scoring protocol in children.

Methods: Physicians of varying degrees of MSUS experience were recruited, including a second-year pediatric rheumatology fellow, a third-year pediatric rheumatology fellow, a pediatric rheumatologist, a pediatric radiology fellow, and a pediatric radiology attending with expertise in musculoskeletal imaging. The group then underwent educational and calibration exercises led by a pediatric rheumatology attending with expertise in musculoskeletal ultrasound,

Table 1. Intraclass correlation between scorers using a pre-existing pediatric musculoskeletal scoring system.

	B-Mode		PD	
Joint/Tendon Area	ICC	Lower CI – Upper CI	ICC	Lower CI - Upper CI
Anterior Elbow	0.93*	0.89 – 0.95*	0.88*	0.77 - 0.94*
Posterior Elbow	0.93*	0.89 - 0.95*	0.77	0.61 - 0.87
Distal Radioulnar Joint	0.87*	0.78 - 0.92*	0.93*	0.87 - 0.96*
Dorsal Medial - Wrist	0.86*	0.80 - 0.90*	0.96*	0.94 - 0.97*
Dorsal Ulnar – Wrist	0.80	0.65 - 0.89	0.90	0.71 - 0.97
Tendons – Wrist	0.74	0.58 - 0.84	0.66	0.35 - 0.84
Talonavicular joint	0.66	0.41 - 0.82	0.91	0.8 - 0.96
Midline Tibiotalar Joint	0.92*	0.88 - 0.95*	0.87*	0.75 - 0.93*
Lateral Tibiotalar Joint	0.86*	0.74 - 0.93	-**	
Medial Tibiotalar Joint	0.82	0.67 - 0.91	-**	
Medial Subtalar Joint	0.77	0.63 - 0.86	0.83	0.59 - 0.94
Lateral Subtalar Joint	0.73	0.57 - 0.84	-**	
Tendons – Ankle	0.53	0.26 - 0.73	0.55	0.1 - 0.81

*Desired reliability attained. **Insufficient data to assess.

detailing the normal anatomy and pathologic variations related to arthritis of the elbow, metacarpal-phalangeal joint, wrist, knee, and ankle in B-mode and power doppler (PD) – mode. The scoring system is based on a semiquantitative scale with grading from 0-3 (0 being normal, 3 being severe pathology), utilizing both B- and PD-mode images. Each participant then scored ultrasound images from an image bank including B- and PD-mode of each joint of varying pathology. The inter-rater reliability, using the intraclass correlation (ICC), was assessed, with a goal of 0.75 or higher for the lower CI for each joint.

Results: A 26- to 39-minute educational and calibration exercise was performed for each selected joint. Participants then completed a reliability exercise for each joint (Table 1). There was good to excellent interrater reliability for the anterior elbow B-mode and PD-mode, posterior elbow B-mode, distal radioulnar joint B-mode and PD-mode, dorsal medial view of the wrist B-mode and PD-mode, talonavicular joint PD-mode, and midline tibiotalar joint B-mode and PD-mode. The remainder of the joint and tendon views demonstrated need for improvement, when considering the goal of 0.75 or higher for the lower CI. At the time of submission, the results for the knee scoring are pending, and there are ongoing training activities looking to improve the reliability of this diverse group. Repeat calibration and scoring exercises will continue to occur until excellent reliability is reached for all views/joints in this group.

Conclusion: Undergoing a single round of educational and calibration sessions facilitated the upskill of a diverse group of academic pediatric ultrasonographers, who demonstrated good to excellent interrater reliability for some joints using a recently proposed pediatric 12-joint MSUS scoring system. There is need for continued improvement in reproducibility and interrater reliability, perhaps via repeated interactive educational and calibration exercises.

Disclosure: Y. Esteban, None; **J. Rodriguez-Smith**, None; **M. Tominna**, None; **A. Meyers**, None; **M. Henrickson**, None; **A. Cassedy**, None; **T. Ting**, None; **P. Vega-Fernandez**, None.

Abstract Number: 1175

Best Practice Guidelines for Telehealth in Rheumatology: An Initiative by the Arab League of Associations for Rheumatology

Nelly Ziade[1], Ihsane Hmamouchi[2], Lina El Kibbi[3], Melissa Daou[4], Nizar Abdulateef[5], Fatemah Abutiban[6], Bassel Elzorkany[7], Khalid Al Naqbi[8], Wafa Hamdi[9], Chafia Dahou-Makhloufi[10], Samar Al Emadi[11], Hussein Halabi[12], Radouane Niamane[13], Mervat Eissa[7], Manal El Rakawi[14], Sima Abu Al Saoud[15], Soad Hashad[16] and Basel Masri[17], [1]Rheumatology Department, Saint-Joseph Medical University and Hotel-Dieu de France Hospital, Beirut, Lebanon, [2]Rheumatology Unit, Temara Hospital, Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, [3]Specialized Medical Center, Riyadh, Saudi Arabia, [4]Faculty of Medicine, Saint-Joseph Medical University, Beirut, Lebanon, Beirut, Lebanon, [5]Rheumatology Unit, Department of Medicine, College of Medicine, University of Baghdad, Baghdad, Iraq, [6]Rheumatology Unit, Department of Medicine, Jaber Alahmed Alsabah Hospital, Kuwait City, Kuwait, [7]Cairo University, Cairo, Egypt, Cairo, Egypt, [8]Al Ain Hospital, AL AIN, United Arab Emirates, [9]Rheumatology Department, Kassab Institute of Orthopedics, UR17SP04, Faculty of Medicine of Tunis, Tunis El Manar University, Tunis, Tunisia, [10]Rheumatology Department, Mohamed Lamine Debaghine University Hospital, Bab El Oued, Algiers, Algeria, [11]Hamad medical corporation, Doha, Qatar, [12]King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia, [13]Department of Rheumatology, Military Hospital Avicenne, University Cadi Ayyad, Marrakesh, Morocco, [14]Rheumatology Department, Douera Hospital, Faculty of Medicine, Saad Dahlab, Blida, Algeria, [15]Makassed Hospital, East Jerusalem, Palestine, East Jerusalem, Palestinian Territories, [16]Tripoli Children Hospital, Tripoli, Libya / The University of Tripoli, Libya, Tripoli, Libya, [17]Jordan Hospital, Amman, Jordan

SESSION INFORMATION

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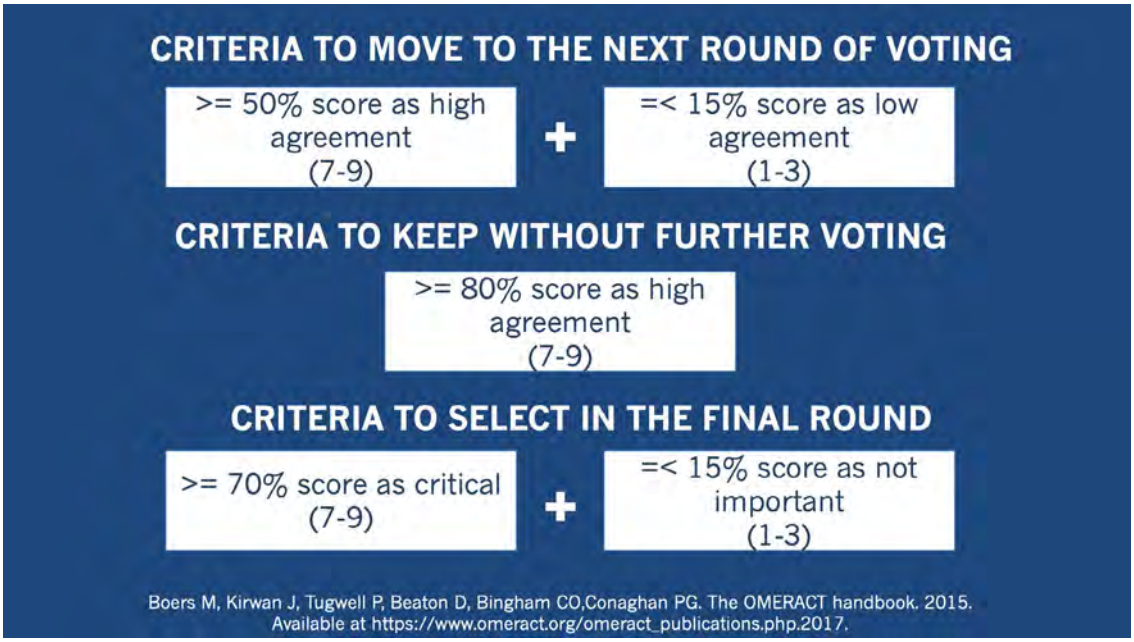

Figure 1. Criteria for selecting statements for final Best Practice Guidelines.

Background/Purpose: The need for telehealth is increasing and will undeniably play a role in the field of health care services, even beyond the COVID-19 era. Best practice guidelines (BPG) are required as they add credibility, standardize approaches, decrease liability and facilitate reimbursement. The objectives of this project were to: (1) develop BPG for the use of Telehealth In Rheumatology in the Arab region (TIROL) and (2) identify the barriers and facilitators of telehealth.

Methods: The BPG were developed under the umbrella of the Arab League of Associations for Rheumatology (ArLAR), in line with the Appraisal of Guidelines for REsearch & Evaluation (AGREE II) instrument. A computerized literature search of four sources (PubMED, American College of Rheumatology (ACR), American Telemedicine Association and World Health Organization) was performed. Guidelines and statements were drafted by a core steering committee, and levels of evidence were indicated according to the Oxford Centre for Evidence-Based Medicine. The draft was reviewed by the ArLAR scientific committee, a law firm advisor and an ACR telemedicine expert. A multidisciplinary task force, including 18 rheumatologists (from the Arab Adult Arthritis Awareness (AAAA) group and ArLAR advisors), 2 patients with rheumatic diseases, 2 regulators and payers from 15 Arab countries was convened and assessed the BPG using 3 rounds of voting by modified Delphi process. Task force members reported their level of agreement and were able to give qualitative comments. The first two Delphi rounds were performed through live online meetings and the last round used asynchronous voting through the Surveylet platform. All votes were anonymous and weighted equally. The criteria for moving from one Delphi round to another and for selecting the final statement was guided by the OMERACT recommendations **(Figure 1)**. The voting on barriers and facilitators was done by one round of anonymous voting using ranking by importance.

Results: The steering committee formulated 4 General Principles and 12 Statements in line with the literature search. All 22 (100 %) task force members participated to each of the 3 rounds. The final BPG are presented in **Table 1**. A consensus of > 80 % was achieved for all statements by the end of round 3. A teleconsultation was defined specifically for the purpose of these guidelines. The possibility of choice of telehealth was highlighted with a particular emphasis on patient's confidentiality, medical information security, rheumatologist's clinical judgment and jurisdictional

Table 1. General Principles and Best Practice Guidelines statements for Telehealth in Rheumatology

General Principles		Level of Evidence*	Consensus** (%)	Level of Agreement*** Arithmetic Mean (SD)/ Median
A Definition of a teleconsultation	A rheumatology teleconsultation is a synchronous exchange of medical information‡ between a patient and a rheumatologist via audio or audio-visual electronic communication, to improve the patient's health status.	5	100	8.14 (0.77) 8
B Access and Continuity of Care	Telehealth may improve the access and continuity of care for patients with rheumatic diseases who are home-bound, live in remote areas or under-served communities, or who need to adhere to social distancing restrictions.	3	100	8.41 (0.80) 9
C Improving disease outcomes	Telehealth can help some patients adhere to the management plan and this is likely to improve disease outcomes in some selected disease states.	2	86.36	7.86 (1.21) 8
D Quality of medical care	Rheumatologists need to use professional experience and judgment to assess whether telehealth is suitable in each situation.	5	95.45	8.14 (0.89) 8
Best Practice Statements				
1 Informed consent	Before the teleconsultation visit, an informed consent should be obtained from the patient, in writing or verbally; it should include an explanation, in a simple language, of the benefits and risks of telehealth encounters, as well as the conditions under which telehealth services may be terminated and a referral made to in-person care.	5	90.91	7.86 (1.28) 8
2 Confidentiality	The use of telehealth services must ensure the patient's information security and confidentiality.	5	100	8.82 (0.50) 9
3 Documentation	The provision of telehealth services should be well documented in the patient's file, similarly to any in-person medical visit. The decision to assess the patient remotely should be justified and recorded in the patient's file.	5	100	8.77 (0.43) 9
4 Shared decision and choice	The choice of using telehealth services should be based on a shared decision between the patient and the physician. Patients should have a choice of their provider of medical teleconsultation.	5	100	8.36 (0.73) 8.5
5 Patient's physical examination	Some parts of the physical exam might be performed remotely, like inspection and evaluation of the range of motion. The patient should be instructed on how to be prepared for a remote physical exam, using appropriate educational material.	2	90,91	7.77 (1.02) 8
6 Patient-reported outcomes	In some chronic rheumatic diseases, the use of patient-reported outcomes by means of self-completed questionnaires adapted for telehealth can help the physician make informed clinical decisions and improve the quality of care.	3	100	7.73 (0.77) 8
7 Safe Prescription	The prescription should be transmitted in a safe and confidential manner to the patient with a particular attention to avoiding abuse ((of opioids and narcotics' prescriptions in particular).	5	95.45	8.05 (0.90) 8
8 Fees and reimbursement	The teleconsultation is subject to medical fees and reimbursement similarly to the in-person visit. Any fees should be set before the teleconsultation.	5	100	8.45 (0.60) 8.5
9 Ethical considerations	Telehealth practice should conform to the same professional ethics that govern in-person care and comply with local jurisdictional laws and regulations of the physician's location.	5	100	8.59 9 (0.60)
10 Rheumatologist training	The rheumatologists are encouraged to receive proper training through seminars, workshops, and conferences to familiarize with the advantages and disadvantages of telehealth and to acquire strategies about the most productive approach to remote medical care.	5	95.45	8.18 (1.05) 8.5
11 Technical infrastructure and equity	The technical infrastructure should be improved for patients and physicians to enable an efficient and equitable access to telehealth services across the countries and in vulnerable populations.	5	100	8.41 (0.73) 9
12 Research	Local and regional research projects to assess the implementation of telehealth and the resulting disease outcomes in the Arab region are strongly encouraged.	5	95.45	8.32 (1.04) 9

* *Level of Evidence: according to* the Oxford Centre for Evidence-Based Medicine
***Consensus : % with score ≥ 80%*
*** *Level of agreement from 1 to 9, with 9 being the highest agreement.*
‡Exchange of medical information includes medical history, physical exam, review of paraclinical results and final prescription.

Table 2. Top Physician- and Patient-related Barriers- and Facilitators to Telehealth in Rheumatology in the Arab region

Choice Rank	Top Physician-related Barriers to Telehealth in Rheumatology in the Arab region
1	Concern about the quality of care (impossible to do a complete clinical exam, lack of non-verbal communication, patient distraction during the visit).
2	External technical difficulties such as poor internet connection or suitable equipment.
3	Internal technical difficulties such as lack of familiarity with e-Health, and lack of trained staff.
4	Lack of motivation (lack of reimbursement).
5	Absence of legal framework: inter-country licensure laws, need for credentialing at multiple sites, and liability concerns.

Choice Rank	Top Physician-related Facilitators to Telehealth in Rheumatology in the Arab region
1	Lack of alternatives when social distancing measures are needed.
2	Better time management, reducing crowded waiting rooms and waiting lists.
3	Less appointment cancellation and no-shows.
4	Better quality of care for close monitoring of chronic diseases.
5	Efficient triage of patients.

Choice Rank	Top Patient-related Barriers to Telehealth in Rheumatology in the Arab region
1	Concern about the quality of care or proper communication
2	Internal technical difficulties such as lack of familiarity with technology.
3	External technical difficulties such as poor internet connection or unsuitable equipment.
4	Resistance to change.
5	Lack of motivation or unclear benefit (patient lives near the healthcare facility, elderly patient with more spare time).

Choice Rank	Top Patient-related Facilitators to Telehealth in Rheumatology in the Arab region
1	Increased access to care and/or possibility to obtain specialist medical opinion from remotely based expert physicians.
2	Lack of alternatives when social distancing measures are needed.
3	Less travel costs.
4	Quick communication and reassurance from the physician.
5	Better time management.

laws and regulations of each country. **Table 2** shows the results of the top 5 Physician- and Patient-related barriers- and facilitators ranked by importance.

Conclusion: These BPG were developed to provide rheumatologists with a series of strategies about the most reliable, productive, and rational approaches to practice telehealth in the rheumatology clinic. Rheumatologists will also need to use their professional experience and judgment to assess whether telehealth is suitable in each situation while ensuring that the services provided are in compliance with the laws and regulations of their respective countri es.

Disclosure: N. Ziade, None; **I. Hmamouchi**, None; **L. El Kibbi**, None; **M. Daou**, None; **N. Abdulateef**, None; **F. Abutiban**, None; **B. Elzorkany**, None; **K. Al Naqbi**, None; **W. Hamdi**, None; **C. Dahou-Makhloufi**, None; **S. Al Emadi**, None; **H. Halabi**, None; **R. Niamane**, None; **M. Eissa**, None; **M. El Rakawi**, None; **S. Abu Al Saoud**, None; **S. Hashad**, None; **B. Masri**, None.

Abstract Number: 1176

Experience from TheMednet: Online Rheumatology Physician Social Network

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Background/Purpose: Expert opinion is valuable in clinical rheumatology practice, especially given the rapid expansion of medical information and limitations of existing data to guide evidence-based medical decision making. However, organized, effective, and accurate platforms for exchange of knowledge among physicians are often lacking. TheMednet is an electronic portal that allows for dissemination of expert knowledge and opinions in a searchable, private, and moderated question and answer format. Originally established in Oncology in 2014, involving over 12,000 US oncologists, we sought to establish the feasibility of this platform among rheumatologists.

Methods: TheMednet was piloted in Rheumatology starting in July 2020. Questions were posted by registered rheumatologists via an 'Ask Question' button. Questions were then reviewed and revised by a team of physician editors and sent to appropriate content experts in Rheumatology. Expert responses were reviewed for accuracy. Rheumatologist engagement was measured in question and citation clicks, logins, and searches.

Results: From 7/2020 to 5/2021, 837 rheumatologists registered to theMednet (35% academic physicians, 58% community physicians, and 7% rheumatology fellows) from 87 institutions. Three hundred and fifteen questions were asked (Figure 1). Two-hundred and fifty-nine questions were approved by a team of editors, and 234 questions were answered by 103 experts (80% academic practice, 20% community practice). Expert geographic locations are detailed in Figure 2. Expert answers included 210 citations to published literature. The most common question topics by the number of views included rheumatoid arthritis (20%), vasculitis (20%), systemic lupus erythematosus (16%), general rheumatology (16%), and myositis (6%). Top 10 most viewed questions are shown in Figure 3. Approximate-

Figure 1: Type of Practice Distribution among Rheumatologists on TheMednet

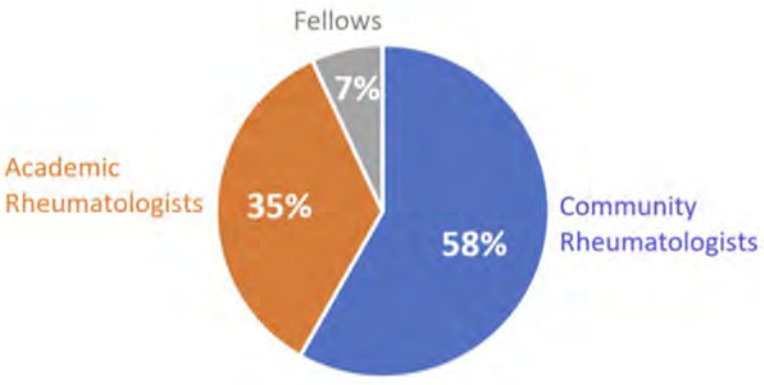

Figure 2: Geographic Distribution of TheMednet Experts in Rheumatology

Figure 3: Top 10 Most Viewed Rheumatology Questions on TheMednet

Views	Question
508	What is your initial treatment of choice in patients with RA and associated interstitial lung disease?
413	Are you recommending the mRNA COVID-19 vaccines to your patients with immune mediated inflammatory diseases?
299	Do you routinely check G6PD level prior to initiation of hydroxychloroquine?
286	How do you counsel rheumatic patients on DMARD therapy about COVID-19 vaccination?
274	What is your threshold for number of alcoholic drinks per week before reconsidering prescribing methotrexate/leflunomide?
273	How do you manage patients who are Hepatitis B core antibody positive/surface antigen negative and starting a biologic DMARD (other than rituximab)?
269	How long do you continue steroid-sparing agents such as tocilizumab for GCA once the disease is in remission off steroids?
264	What is your approach to a patient with an isolated positive rheumatoid factor, negative anti-CCP antibody, and no clinical or imaging evidence of rheumatoid arthritis?
258	Which ANCA vasculitis patients are better candidates for cyclophosphamide rather than rituximab?
255	What do you use to treat uveitis refractory to conventional synthetic DMARDs and TNF inhibitors?

ly 45% of registered rheumatologists were active each month. Over 24,000 question and answer views have been registered to date.

Conclusion: TheMednet is becoming a widely used and effective platform for academic and community rheumatologists to engage in an online network, providing insight on clinical practice and exchanging viewpoints on difficult management decisions. Future initiatives include expansion of the platform to enable exchange of information between rheumatologists and other specialists such as dermatologists, pulmonologists, and ophthalmologists who share in the management of patients with complex, multi-system rheumatic diseases.

Disclosure: Y. Afinogenova, None; **M. Maheswaranathan**, None; **N. Housri**, Mednet, Inc, 3; **S. Fantus**, None.

Abstract Number: 1177

Assessing Resident Needs and Faculty Perceptions for Rheumatology Curriculum Development

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Background/Purpose: The goal of rheumatology rotation during internal medicine (IM) residency is to develop competency in work-up and treatment of common rheumatological conditions. IM residents spend less time in rheumatology compared to other subspecialties, necessitating a well-structured curriculum tailored towards resident needs and various clinical settings. In this study, we aimed to identify resident learning needs and preferences during inpatient and outpatient rheumatology rotations to improve the curriculum.

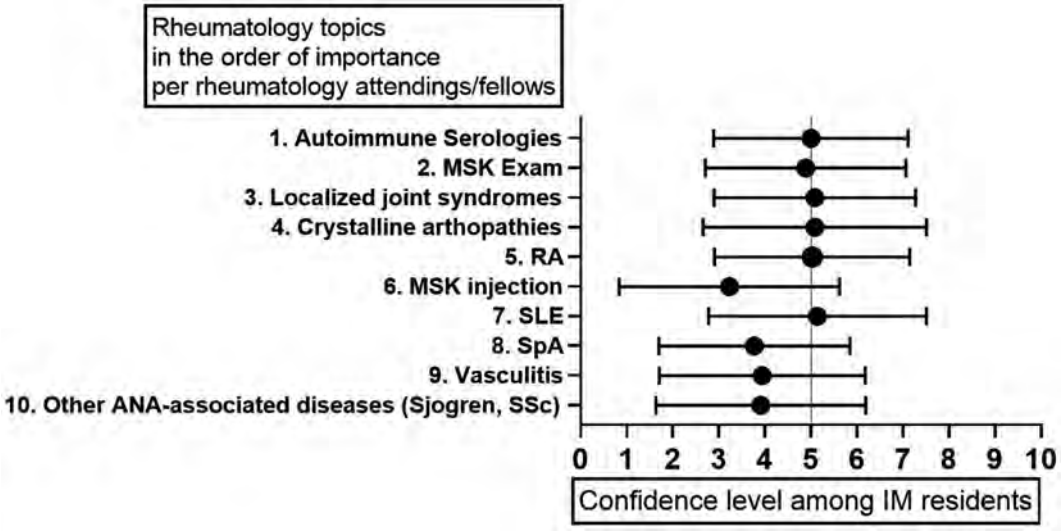


Figure 1. Most important rheumatology topics to learn during rheumatology rotation per rheumatology faculty/fellows and confidence level among residents for each topic [median with IQR].

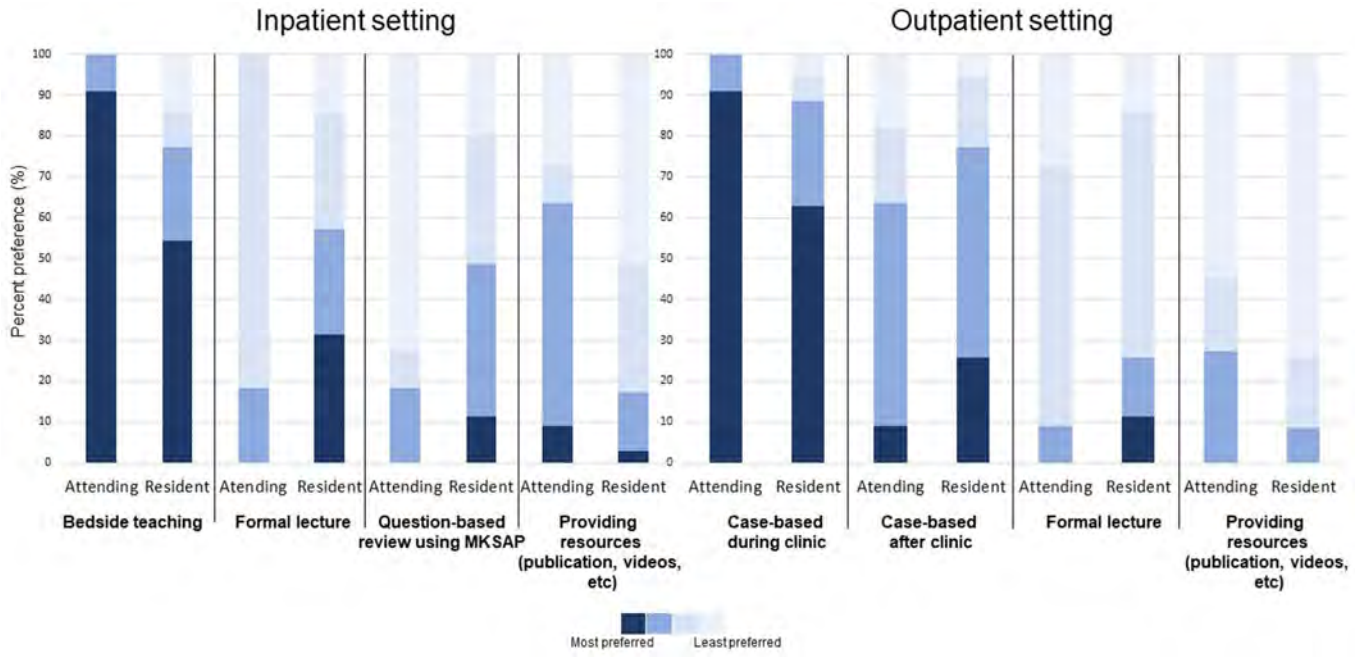


Figure 2. Preferred learning/teaching modalities for rheumatology faculty/fellows and medicine residents in inpatient and outpatient settings.

Methods: We distributed surveys to all the current IM residents at the IM Residency Program and rheumatology faculty/fellows in the Section of Rheumatology via email. Rheumatology faculty/fellows were asked to rank 10 rheumatology topics based on the importance. The resident survey assessed confidence in caring for patients with rheumatologic condition in inpatient and outpatient settings on a 10-point Likert scale. Both resident and attending/fellow surveys assessed respondent to rank their preferred learning modality in inpatient and outpatient settings. No validated instruments were available for these purposes; therefore, we created the surveys used in this study.

Results: Out of 13 rheumatology faculty/fellows, 11 (7/4; 84%) completed the survey. Out of 124 residents, 35 (28.2%) including 8 PGY-1, 13 PGY-2, 10 PGY-3, 3 PGY-4 and 1 PGY-5 completed the survey. Among respondents, 37% had rheumatology rotation in medical school and 66% in residency. Four residents (11%) were interested in rheumatology fellowship, and majority (77%) had interest in learning more about rheumatology.

The most important topics to learn during rheumatology rotation per faculty/fellows were knowing when to order and how to interpret autoimmune serologies, followed by musculoskeletal exam and crystalline arthritis (Figure 1). Median confidence level [IQR] among residents for caring for patients with rheumatological conditions was 6 [3.6-7.5] for inpatient and 5 [3.7-6.5] for outpatient settings (10 being very confident). Topics with least reported confidence included joint injections, spondyloarthritis, and other ANA-associated disorders.

Among attendings/fellows, the most preferred outpatient teaching modality was case-based and least preferred was directing trainees to relevant resources. On the inpatient side, directing to relevant resources was the 2nd most preferred modality after bedside teaching (Figure 2). Among residents, the most preferred learning modality was bedside/case-based learning (54-63%) and the least preferred was being directed to resources for self-learning (51-74%) in both settings. Formal lectures were preferred more by residents than attendings/fellows in both settings.

Conclusion: This study showed that average confidence level of residents for most rheumatology topics was moderate (5 out of 10). There was a high degree of concordance between residents and rheumatology faculty/fellows for their preferred education modality in outpatient setting, whereas discordance existed on inpatient setting. Being

directed to relevant resources for self-learning was not preferred among residents, while faculty/fellows preferred this option commonly in the inpatient setting.

Disclosure: L. He, None; **K. Ko**, E.R. Squibb & Sons, L.L.C., 12, Education and Food/Beverage, EMD Serono, 5, GlaxoSmithKlein(GSK), 1, 12, Food and Beverage, Janssen, 5, 12, Food and Beverage; **L. Quimson**, None; **D. Leverenz**, Pfizer, 5; **S. Martin**, None; **D. Saygin**, None.

Abstract Number: 1178

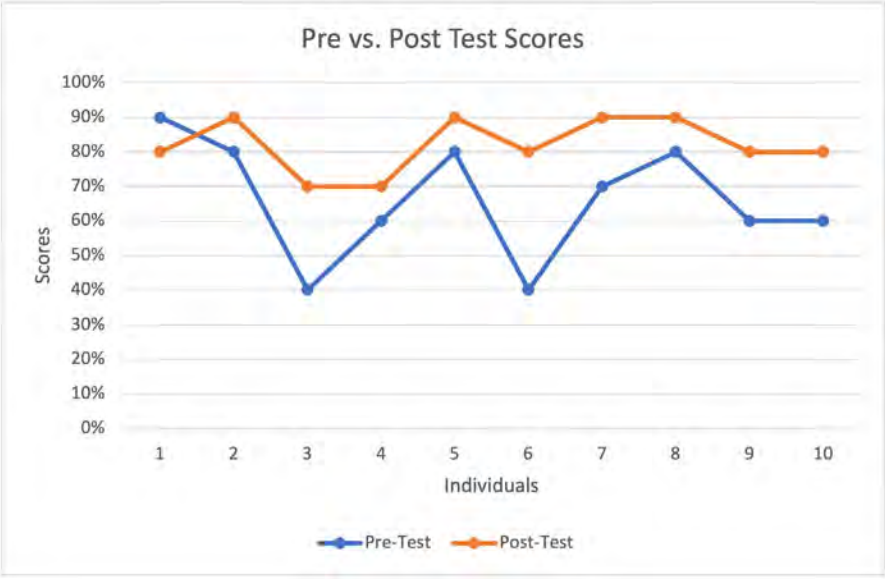
Implementation of a Dermatologic Manifestations of Connective Tissue Disease Learning Module Including All Skin Tones and Social Determinants of Health for Medical Students: A Pilot Study

Mavra Masood, Fnu Nutan, Julia Nunley and Beth Rubinstein, Virginia Commonwealth University, Richmond, VA

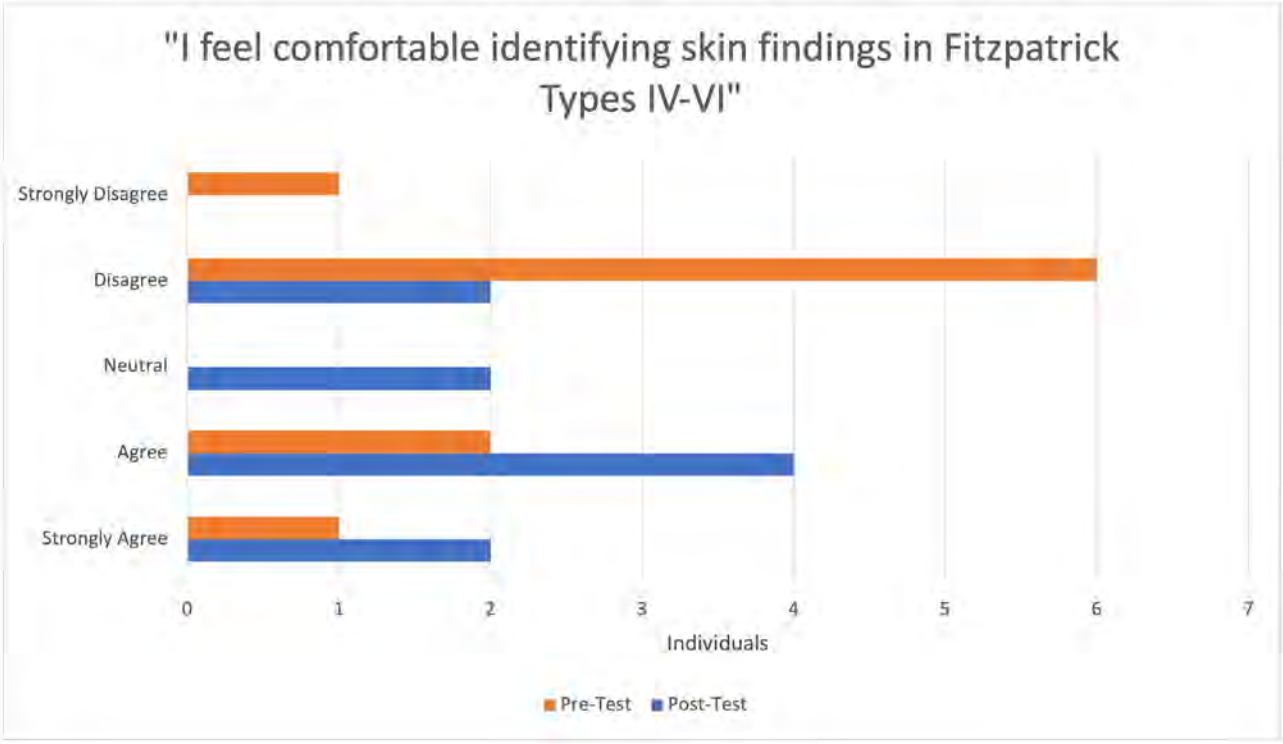
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: There is a dearth of resources for medical students on identifying skin findings of autoimmune disorders in skin of color. Considering how several rheumatologic diseases disproportionally affect communities of color and can present with dermatologic findings, an opportunity arises to address a gap. The lack of materials educating future physicians has significant repercussions on delivering care equitably to an increasingly diverse US population.

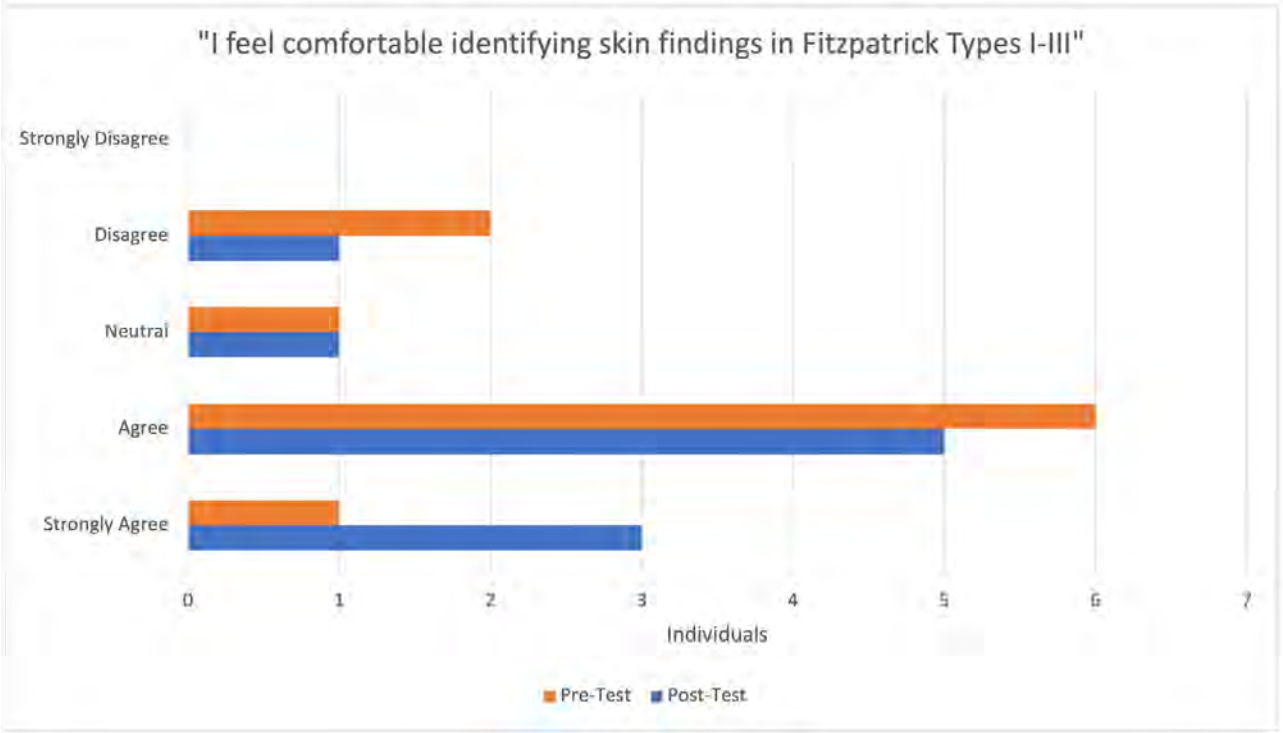
We sought to create a brief module that addresses dermatologic findings in connective tissue disease (CTD) in all skin tones for medical students. Our purpose was to assess whether this module would 1) increase learner comfort



Pre vs. Post Test Module Completion Scores



Pre vs. Post Test comfort level scores with identifying skin findings in Fitzpatrick types IV-VI



Pre vs. Post Test comfort level scores with identifying skin findings in Fitzpatrick types I-III

in identifying dermatologic findings in all skin tones and 2) increase learner knowledge of appropriate workup and lab findings in CTD.

Methods: The study was conducted at our institution's medical school. We developed a PowerPoint-slide based module with pre- and post-tests with three fictional patient scenarios detailing systemic lupus erythematosus, dermatomyositis, and systemic sclerosis. Second through fourth year medical students were asked to complete our module. The pre-test was done immediately prior to the module and the post-test immediately following completion of the module. The test included ten questions evaluating lab and physical exam findings in CTD as well as six questions assessing learner comfort with identifying physical exam findings. De-identified data was collected and stored on a cloud-based program, then analyzed using a paired two tailed student's t-test.

Results: A total of ten medical students completed the pilot module with the pre-test and post-test. Five of the trainees were rising third-year students, four were rising fourth-year students, and one was a rising second-year student. Baseline mean pre-test scores were 66% correct and the mean post-test score was 82%. Completion of the CTD module led to significant improvement from pre- to post-test scores with a mean improvement of 16.20% (P-Value = 0.00456). 80% of students in the post test had at least a 1-point increase in comfort level (i.e., neutral to agree) of identifying skin findings in Fitzpatrick types IV-VI (medium to very dark brown skin tones) and 50% of students had a 1-point increase in comfort level of identifying skin findings in all skin types.

Conclusion: Our pilot study suggests that implementing a CTD module as a part of the medical school rheumatology curriculum results in immediate improvement in medical knowledge and comfort with identifying physical exam findings in Fitzpatrick types IV-VI. Additionally, all students answered, "strongly agree" with this statement: "It is important to learn about how social determinants of health affect outcomes." This suggests that students are interested in learning about the social implications affecting patients as they are treated for their disease. Re-testing after 12 months to evaluate knowledge retention as well as implementing a photo quiz at the end of the module to assess objective improvement are future directions. This module will be implemented as a part of a larger curriculum serving to educate learners on dermatologic manifestations of rheumatologic disease for our students.

Disclosure: M. Masood, None; **F. Nutan**, None; **J. Nunley**, None; **B. Rubinstein**, None.

Abstract Number: 1179

Determining Faculty vs. Fellow Preferences for ROSCE Milestone Assessments; Is It Time for a Change in Needs Assessment?

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Professional Education Poster (1170–1195)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The Pennsylvania Rheumatology Objective Structured Clinical Examination (ROSCE) is an annual assessment of rheumatology fellows' skills in different standardized patient (SP) encounters involving a variety of topics related to communication issues. We previously mapped our ROSCE assessment tools to align with Accreditation Council of Graduate Medical Education (ACGME) internal medicine subspecialty milestones in 2018. In 2020, we conducted our ROSCE entirely online. Seventeen trainees from 8 rheumatology programs in the region participated in 6 SP scenarios and were observed by faculty raters. We aim to better tailor our cases and evaluation forms to address milestones of greatest utility to participants. In this study, we surveyed 2020 ROSCE fellow partici-

Milestone	Description
ICS1	**Avoiding jargon; talking on a patient level with patients and their caregivers**
MK2	**Diagnostic testing accuracy review and interpretation**
PBLI1	Working with teams to improve patient care
PC1	**Gathers and synthesizes essential information to define a complaint**
PC3	**Formulate a comprehensive action plan**
PC4	**Discussion of treatment based upon a patient's own unique needs**
PROF2	Exhibits integrity and ethical behavior
PROF4	Professional interactions with patients, peers and staff
SBP1	Recognizes system error and tries to fix it
SBP2	**Transitions patients across systems**
SBP3	Advocates for cost effective care, understands barriers to cost effective care

Table 1. Milestones presented in the survey; items in **bold** are represented in the ROSCE

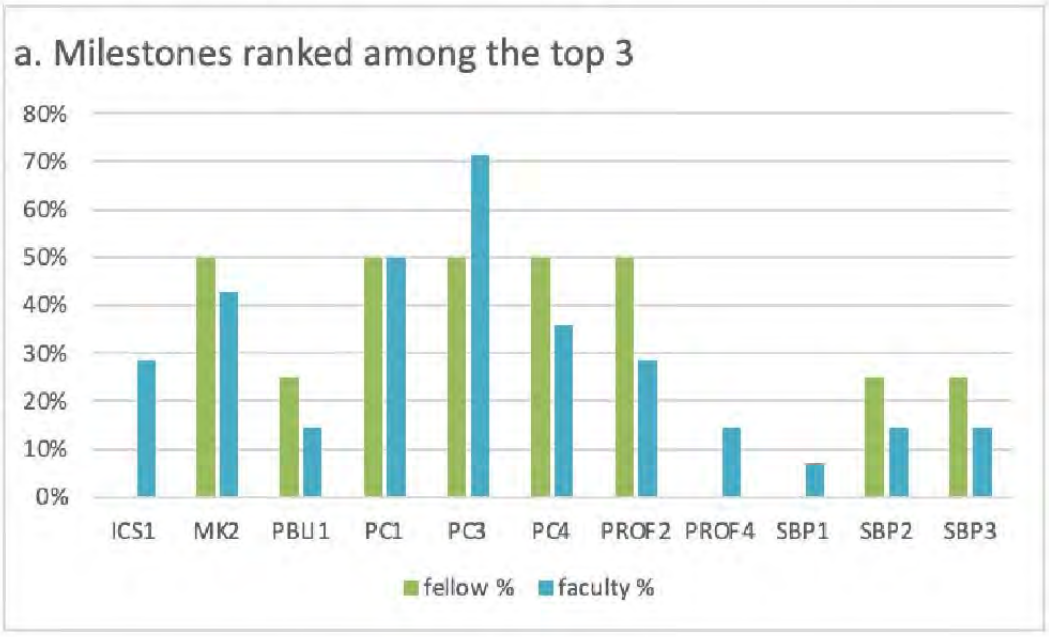
pants and program directors (PDs) regarding their perceptions of the most important competencies for rheumatology fellows to master in order to become excellent clinical rheumatologists.

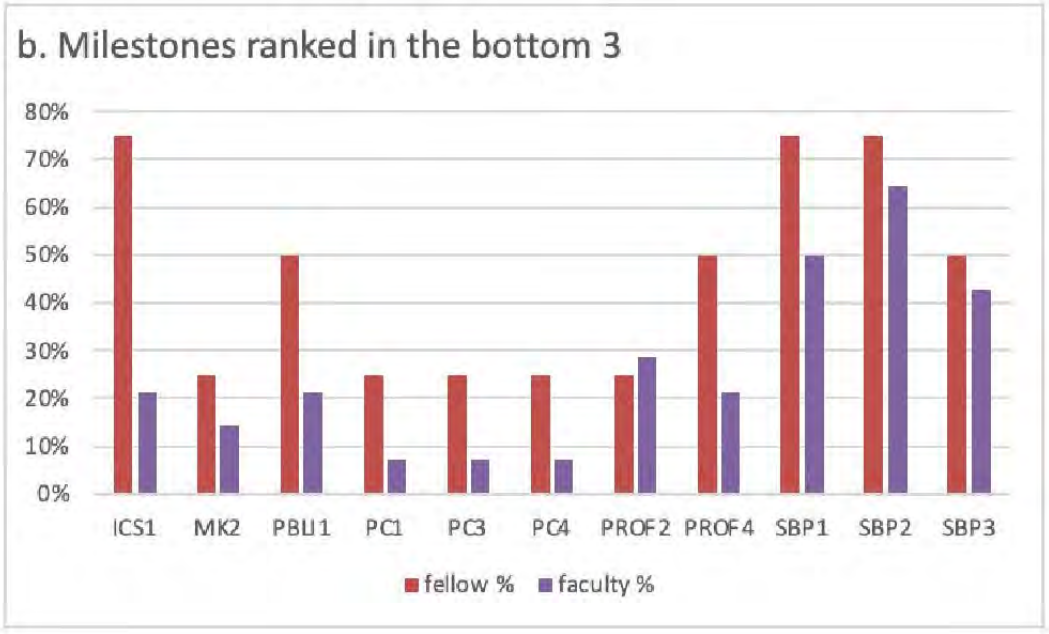
Methods: We created an online survey using survey monkey asking participants to rank 11 ACGME subspecialty milestones in order of their perceived importance to attaining clinical excellence in rheumatology (Table 1). Content validity was determined by consensus of 5 rheumatology fellowship PDs and key clinical faculty. Participants were invited via email; all 2020 ROSCE fellow participants and regional PDs were invited to respond. Milestones rated in the top 3 and bottom 3 for both faculty and fellows are reported in aggregate. We also mapped our 2020 ROSCE evaluation questions to current ACGME subspecialty milestones.

Results: Five fellow participants and 9 PDs completed the survey (response rate 29% and 56%, respectively). Results were similar for faculty and fellows, with MK2, PC1, PC3, PC4, and PROF2 ranked in the top 3 by at least 25% of both groups (Figure 1a), addressing test interpretation, history-taking, forming a plan, therapeutics, and ethical behavior. Conversely, milestones ranked more frequently in the lowest 3 related to jargon use, system error recognition, transitions across health systems, and cost-effective care (Figure 1b). The 2020 ROSCE evaluation questions included 39 Likert scale questions (in addition to narrative comments) (Table 1). All milestones rated as important by faculty and fellows are represented in evaluations except PROF2.

Conclusion: We surveyed rheumatology faculty and fellows to gauge their perceptions of the most important areas to assess in the ROSCE. We observed a low response rate among fellows, possibly due to survey fatigue. In general, faculty and fellow preferences aligned with respect to "top" and "bottom" ranked milestones, though numbers were small. Nearly all top-ranked milestones, dealing predominantly with patient care, are addressed in our ROSCE cases and evaluations, suggesting that it is well-suited to address these areas. PROF2, addressing ethical conduct, was reported to be of high importance but was not included in prior ROSCE cases. We aim to further tailor our ROSCE cases and evaluations to align with these preference needs, thus providing more meaningful information to PDs and fellows for formative feedback.

Figure 1. Faculty and fellow survey rankings of the top 3 (a) and bottom 3 (b) milestones by importance





Disclosure: S. Banks, None; **S. Malkana**, None; **A. Jayatilleke**, None.

Abstract Number: 1180

Better Websites, Better Match: Assessing Quality of Rheumatology Fellowship Websites

Hiral Patel[1], D. Benjamin Riffe[1] and Rachel Wolfe[2], [1]Wake Forest School of Medicine, Winston Salem, NC, [2]Wake Forest Baptist Health, Winston-Salem, NC

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The internet has become an indispensable tool for residency and fellowship recruitment. Prospective applicants rely on publicly available information to learn about the application process and each program. A previous study has shown that applicants considered an easily navigated website important to their application decision-making process.[1] We evaluated adult rheumatology fellowship websites for accessibility and content

Table 1. Quality of content of rheumatology fellowship websites

Domain	N	%
Accessibility		
Functional website	120	96.00%
Social media links on the website	14	11.20%
Overview		
Program Description	117	93.60%
Coordinator's Information	106	84.80%
Director's Name	106	84.80%
Program Address	93	74.40%
Phone Number	105	84.00%
Email Address	106	84.80%
Name of Current Fellows	80	64.00%
Current Fellow's Residency Information	64	51.20%
Name of Past Fellow	46	36.80%
Faculty	104	83.20%
Salary	70	56.00%
Application Process		
Application ID/Program number	14	11.20%
Application Requirement	89	71.20%
Number of Letters of Recommendation Required	63	50.40%
Application Deadlines	29	23.20%
Education		
Didactics	109	87.20%
Journal Clubs	105	84.00%
Schedule	96	76.80%
Teaching Responsibility	40	32.00%
Research Encouraged or Required	110	88.00%
Previous Research Performed at the Institution	46	36.80%
Call Responsibility	10	8.00%
Conference	102	81.60%
Ultrasound Curriculum	92	73.60%
Diversity		
Specific Text Regarding Diversity, Representation, and Minority in Reference to Fellows	25	20.00%
Link to/Descriptions of Diversity Resources	27	21.60%
Organization Dedicated to Diversity	30	24.00%
Overall Completeness (>70%)	29	23.20%

regarding program overview, application process, education, and diversity. The aims of the study are two-fold: to assess each Rheumatology Fellowship program's website for content completeness and to elucidate the specific areas on each program's websites that need to be updated to aid applicants in making informed decisions regarding their training options.

Methods: The American Medical Association Fellowship and Residency Electronic Interactive Database (FREIDA) was used to obtain a complete list of Accreditation Council for Graduate Medical Education (ACGME) accredited adult Rheumatology Fellowships. Information regarding accessibility of the websites, description of the program, application process, fellow education and diversity was collected from the publicly available websites with in a month period from January 4th – February 1st, 2021. Information within the five domains was analyzed via descriptive analysis.

Results: Only 23.2 % (N= 29/125) websites were >= 70.0% completed and 20.8% of websites were lacking more than 50% of the content (Table 1). Links to social media accounts were present on 11.2% of websites. Websites were lacking information regarding current program director (15.0%), names of current rheumatology fellows (36.0%), and previous research done at the institution (63.2%). Only 20.0% (N=25) of the program websites mentioned specific text regarding diversity in reference to their fellows and recruitment process.

Conclusion: The findings of our study reveal that rheumatology fellowship websites differ substantially in the details and amount of content they contain. Websites lack essential information such as program's director's name, current fellow's names, and educational programing each program offers. Most strikingly, the majority of the websites do not include specific text regarding diversity. Given the importance of healthcare organizations striving to improve diversity, equity, and inclusion within medicine, showcasing current efforts of each program on the website is vital. Rheumatology fellowship websites need to be revamped to promote what each program has to offer and to provide accurate and updated information to the future fellowship applicants, especially in the age of virtual recruitment. We hope that this study motivates institutions to keep the content of their fellowship program website well maintained and up to date to provide applicants with the most accurate information and to allow a better program-to-applicant match.

References

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Disclosure: H. Patel, None; **D. Riffe**, None; **R. Wolfe**, None.

Abstract Number: 1181

Self Directed Learning Among Internal Medicine Residents: Incorporating a New Teaching Module on Calcium Pyrophosphate Deposition in the Rheumatology Curriculum

Bassel Bou Dargham, Abhishek Nandan, Beth Rubinstein and Stamatina Danielides, Virginia Commonwealth University, Richmond, VA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)

Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Medical knowledge is evolving at a fast pace, and it is important for medical students and residents to develop self-directed learning skills that will help them apply evidence-based medicine (EBM) in their clinical practice. As future practicing physicians, they should be able to incorporate new literature and updated guidelines into everyday clinical decisions. For that reason, there is a huge emphasis on introducing self-directed learning into undergraduate and medical school curriculums. In fact, the Liaison Committee on Medical Education (LCME) now requires medical schools to engage their students in self-directed learning activities. In this study, we aim to develop an interactive module that briefly covers important concepts and treatment guidelines on a specific topic. We will then assess learners' knowledge acquisition and their ability to apply these concepts in their clinical decision making.

Methods: The study was conducted at Virginia Commonwealth University Health Systems (VCUHS). We developed a module on calcium pyrophosphate deposition (CPPD), and internal medicine residents were asked to complete it as part of their rheumatology rotation. The module included a pre-test, followed by a PowerPoint presentation with case scenarios and interactive questions. Learners were then asked to solve a post-test immediately after finishing the presentation. Same questions were included in both tests, and they were presented in the same order. This process did not include directed learning methods. Data was analyzed using a student's t-test. We compared pre and post-test mean scores for every participant, and further analyzed the percentage of learners answering each question correctly before and after the completing the module (Figure 1).

Results: A total of 10 internal medicine residents completed our pilot module and filled the pre and post-tests. 8 learners were 2nd year internal medicine residents, and 2 learners were 3rd year residents. The tests were comprised of

A: Percentage of learners with a correct answer on each question before and after completing the module; B: Total score (out of 100) of pre and post-tests among different learners.

10 multiple choice questions including 3 case scenarios and 3 EBM questions. There was a significant improvement among learners when comparing their pre and post-test mean scores (30% increase in mean scores with $p< 0.0001$). We also compared the number of learners answering each question correctly in the pre and post-tests. Overall, the percentage of learners choosing the correct answer significantly increased in the post test ($p< 0.0001$). Improvement was mainly noticed in case scenarios (Q8 and Q10), and EBM based concepts (Q2 and Q3).

Conclusion: This study suggests that integrating self-directed learning modules in the rheumatology curriculum of our internal medicine residency program can help residents improve their knowledge base and comfort level with EBM and case-based concepts. The next step is to include medical students rotating on our rheumatology rotation into the participating pool of learners, with the hope that it could be integrated into their own curriculum. A larger group analysis of multiple modules will help develop a comprehensive learning course for all our rotating medical students and residents.

Disclosure: B. Dargham, None; **A. Nandan**, None; **B. Rubinstein**, None; **S. Danielides**, None.

Abstract Number: 1182

Pilot Health Literacy Curriculum Addressing Skills and Content Knowledge for Adult and Pediatric Rheumatology Fellows

Gabriel Tarshish[1], Heather Archer-Dyer[2], Pablo Joo[3], Dawn Wahezi[4], Tamara Tanner[5], Rhonda Acholonu[4], Tamar Rubinstein[6] and Irene Blanco[7], [1]Children's Hospital at Montefiore, New York, NY, [2]Albert Einstein College of Medicine, Bronx, NY, [3]UC Riverside School of Medicine, Riverside, CA, [4]Children's Hospital at Montefiore, Bronx, NY, [5]Montefiore Medical Center, Bronx, NY, [6]Albert Einstein College of Medicine, White Plains, NY, [7]Albert Einstein College of Medicine, Cresskill, NJ

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: 36% of adults in the US have a basic to below basic level of health literacy. Studies show that limited health literacy (LHL) has deleterious effects on patient outcomes and act as a contributing case to health disparities across all of medicine, including rheumatology. Despite the prevalence of LHL, there is a lack of education on this topic for medical trainees. Therefore, we designed a module focused on LHL in patients with rheumatic diseases with an overall goal to help pediatric and adult rheumatology fellows build a foundational knowledge and toolkit addressing LHL in the clinical setting.

Methods: This module was piloted with fellows from the adult and pediatric rheumatology programs from Montefiore and NYU Medical Centers, NY, NY. Participants provided signed consent and pre-course and post-course evaluations were completed anonymously. The evaluations identified changes in the learners' knowledge base, clinical comfort level, and likelihood to integrate these interventions into their practice. The post-course evaluation also elicited feedback of the course. The teaching module consisted of: (1) video of a poor patient-provider interaction to allow for introspection, (2) formal didactic presentation, (3) role play scenario for fellows to practice skills using LHL checklist, (4) exercises to evaluate patient education materials.

Results: The session was held in May 2021 with 7 adult and pediatric rheumatology fellows. 4 fellows were 2nd years and the average age of the participant was 33.7y. Racial and ethic make up of the fellows was broad and 3 of 7

fellows were international medical school graduates. While 6 of 7 fellows had been taught the Teach-back Method (a common technique to assess understanding), 4 of 7 had not received formal education on health literacy. In addition, 5 of 7 fellows had never evaluated distributed patient materials to ensure appropriate reading level. All fellows felt that a patient's LHL impacted treatment plans. Nevertheless, only 2 fellows "agreed" that LHL was regularly discussed with faculty in clinical settings; where 4 of 7 fellows were "neutral" or "disagreed" that faculty were equipped to discuss the issue. After the module, all 7 fellows "agreed" or "strongly agreed" that LHL and the strategies to mitigate it were presented effectively. 6 of 7 "agreed" or "strongly agreed" that LHL should be incorporated into rheumatology education and 5 of 7 "agreed" or "strongly agreed" that faculty would benefit from this module. All 7 of the fellows "plan to modify their practice" based on this content of this module. Several quotations from feedback include: *"[I] never realized what a high reading level some of the information we give to patients can really be*". "*This is a really useful pertinent module*".

Conclusion: Participants reported increased skills in addressing LHL in their practice. Data from this study will help guide improvements to the module with plans to incorporate learner feedback into subsequent teaching sessions. The long-term goal of this work is to design a module that can be used by fellowships broadly to improve health literacy assessments leading to interventions as a means to improve overall health outcomes particularly in LHL who are at risk for disparate care.

Disclosure: G. Tarshish, None; **H. Archer-Dyer**, None; **P. Joo**, None; **D. Wahezi**, None; **T. Tanner**, None; **R. Acholonu**, None; **T. Rubinstein**, None; **I. Blanco**, None.

Abstract Number: 1183

Efficacy of Rapid Transition of a Musculoskeletal/Rheumatology/ Dermatology Course to Online Learning During COVID-19 Pandemic

Elise Belilos and **Megan Bader**, NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic created unprecedented challenges for medical students and faculty with the abrupt transition to online learning in March 2020. At NYU Long Island School of Medicine (LISOM), a new accelerated 3-year primary care medical school, this transition occurred during the charter class's five-week Musculoskeletal/Rheumatology/Dermatology (MSK/Rheum/Derm) course. The core components of LISOM's curriculum, including didactic lectures and longitudinal courses in problem-based learning (PBL), health systems science (HSS), practice of medicine (POM), anatomy/histology/pathology/radiology (M4), and ethics, were rapidly restructured to be delivered either through prerecorded sessions (released in the afternoon on the day prior to the scheduled time) or live classes hosted virtually on WebEx.

Methods: A survey was designed on Qualtrics and distributed to second-year NYU LISOM students. Students could then voluntarily and anonymously opt to participate. All participant information was de-identified. Questions explored the students' perceived efficacy of various components of the MSK/Rheum/Derm curriculum including prerecorded lectures, Q&A sessions, case-based activities, exam review sessions, and longitudinal courses.

Results: 79% (N=19/24) of students in NYU LISOM's charter class participated in this survey. 84% of students rated prerecorded lectures as "extremely" or "very" effective and 89% of students felt that they learned as much from prerecorded lectures as in-person lectures. 52% of students began watching prerecorded lectures prior to their scheduled time and another 37% watched them during the scheduled time. Dedicated Q&A sessions addressing each lecture topic were largely underutilized by students, with 84% students attending < 5 sessions. In spite of this, 89% of students agreed that they were able to have all questions arising from lectures answered. Students felt that problem-based learning (PBL) was the most effective longitudinal course during online learning, with 79% of students rating it as 'extremely' or 'very' effective. Students also felt that MSK/Rheum/Derm lecture material was highly integrated with PBL, M4, and POM. The most difficult subjects to learn virtually were anatomy and histology (M4). Students cited the most effective M4 sessions included prerecorded lectures and the use of 3D modeling. One of the notable challenges of online learning was the development of strong student-faculty relationships with 89% of students indicating that they did not get to know the faculty well. A clear benefit of online learning was the increased flexibility and autonomy to pursue individual study styles with 100% of students agreeing that they had more time for independent study.

Conclusion: To our knowledge, the rapid and successful conversion of the entire MSK/Rheum/Derm curriculum to virtual learning at NYU LISOM during the COVID-19 pandemic was the first of its kind in that it was accomplished within a framework of a unique, compressed 3-year primary care medical school curriculum and is a viable model for remote online rheumatology learning in the setting of a public health emergency.

Disclosure: E. Belilos, None; **M. Bader**, None.

Abstract Number: 1184

Voluntary Online Gout Module: Housestaff Utilization and Efficacy

Sarah Tarplin[1], Susan Kroop[2] and **Catherine Deffendall**[2], [1]Vanderbilt Universty Medical Center, nashville, TN, [2]Vanderbilt University, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: All Internal Medicine (IM) physicians should be competent in gout diagnosis and management. The purpose of this study is to assess learner engagement with a voluntary online gout diagnosis and management curriculum and to assess the impact on their knowledge and skills in the treatment of patients with gout.

Methods: We developed an online interactive module, comprised of clinical vignettes related to the diagnosis and management of gout for IM residents (hereafter described as trainees). The curriculum was published via QuizTime and delivered to trainees during their two-week outpatient or elective rheumatology rotation. QuizTime is an online platform created at Vanderbilt University Medical Center that delivers to learners one teaching quiz question at a set interval (1-2 questions per day) via an email or text link. Learners click the link and are taken to the platform with the clinical vignette quiz and possible answers. If a learner selects a correct response, they are directed to a screen confirming the correct choice and a detailed explanation. If an incorrect answer is chosen, the correct response is displayed along with the same explanation and an option to reengage with the question for up to 48 hours to reinforce new knowledge. Thus, QuizTime employs spaced interval learning and "test-enhanced learning" to reinforce concepts. The module is a supplement to standard teaching including attending clinics with preceptors, suggested readings and core IM didactics.

Half of the trainees received access to the module while the control group received standard teaching only. Pre and post rotation assessments were distributed to all trainees rotating on rheumatology and were used to compare gout knowledge between the two groups. This study was IRB exempt as it involved normal educational practices that was unlikely to adversely impact learners.

Results: Nine trainees received standard teaching in addition to access to the QuizTime Module. Ten trainees were assigned to the control teaching group. Of the nine that received access, only five answered any questions (56%). The five trainees that interacted with the module answered between 1 and 5 out of the 18 questions (2.8 to 5.6%). Three of these five trainees read any explanations (up to 50% of the questions they answered). None of the trainees that were given access to the QuizTime module took the post rotation assessments at the time of abstract submission limiting the evaluation of efficacy of the curriculum.

Conclusion: Approximately half of IM housestaff rotating on Rheumatology accessed a voluntary, online, quiz-based learning module on gout. Of the trainees that engaged with the module, very few questions were answered (2.8 to 5.6%). Data on the efficacy of the curriculum is limited by poor engagement with pre and post assessments. It is disappointing that so few engaged with a voluntary curriculum. This may be due to lack of interest in the topic, competition for housestaff time and attention, feeling that current teaching is sufficient for gout management and/or difficulty engaging with the QuizTime platform. Further study and data collection of knowledge retention is ongoing.

Disclosure: S. Tarplin, None; **S. Kroop**, None; **C. Deffendall**, None.

Abstract Number: 1185

A New Virtual Reality: Needs Assessment and Gains in Current Trainees Experience with a Novel Video-Based Post Rheumatology Rotation Intervention

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
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Background/Purpose: Though trainees see patients at varying stages of their diagnostic course on subspecialty electives, there is often no organized opportunity for residents to follow these patients after the elective has ended. Furthermore, the lack of longitudinal follow-up on subspecialty cases may hamper the educational experience of trainees and future interest in a particular area. There is paucity of literature on strategies to foster trainee experience including increasing continuity in care (Francis, Journal of Graduate Medical Education, 2018). Herein we present preliminary results of needs assessment and virtual systematic intervention in a rheumatology elective. This intervention was designed and implemented to bolster education and continuity in an asynchronous format after the elective concluded.

Methods: Informed consent was obtained from all rotating residents in the rheumatology elective from August 2020 to April 2021. Residents completed a pre-intervention survey for needs assessment delineating current perceptions of continuity, level of exposure in their subspecialty clinics, and willingness to participate in the follow-up intervention.

Participating residents chose a patient case they had seen while on the elective to discuss at a scheduled virtual meeting 4-6 weeks following the end of their elective with a rheumatology faculty member. Participating residents completed a post-intervention survey assessing their satisfaction, changes in perception and medical knowledge, and impact on their choice of subspecialty as a career option. Descriptive statistics and one-sided Fisher exact test were undertaken.

Results: Of the 49 residents that completed the needs assessment pre-survey, 85.7% stated they never had structured continuity in their subspecialty clinics, 75.5% were interested in a structured way to follow-up patients, and 77.6% were open to the intervention. Twenty-six residents completed the intervention and post-survey, which revealed 69.2% of residents felt the intervention added to their medical knowledge and clinical experience with 26.9% felt it helped somewhat; 65.4% of the residents believed this intervention created a positive change in perception of this subspecialty rotation while none noted a negative assessment of the intervention. All trainees (n=7) that noted a positive change in perception of the subspecialty clinic following the intervention, also reported an increased consideration for rheumatology as a career ($p < 0.05$)**Conclusion:** Needs assessment confirmed there is lack of structured programs to provide trainees with longitudinal follow-up on patient encounters seen in a rheumatology elective. There was a high level of interest in an asynchronous intervention strategy to improve longitudinal learning that resulted in increased continuity, medical knowledge, clinical experience, and consideration for the subspecialty as a career. This novel intervention maximizes the use of experiential learning trainees have within their rheumatology rotation even after it has concluded; continuing such measures in the future may enhance subspecialty ambulatory training as the realm of virtual learning continues to be an integrated part of education for trainees.

Disclosure: A. Purohit, None; **C. Hawkins**, None; **M. Jolly**, Rush University, 10, AURINIA, 1; **S. Khandelwal**, None.

Abstract Number: 1186

The Kardashian Index of Rheumatology Program Directors: Comparing Scholarly Activity and Twitter Use of Rheumatology Fellowship Program Directors in the United States

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SESSION INFORMATION
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Background/Purpose: Social media has changed the way we communicate and disseminate information. Program directors (PDs) can use social media to boost visibility for professional networking, collaboration, program promotion, recruitment, and medical education at a global scale. Major rheumatology conferences, such as American College of Rheumatology, are beginning to employ social media ambassadors and hashtags to engage followers. Tweets© have been used to discuss findings published in manuscripts, enhancing peer and patient engagement. Increased social media publicity allows researchers to discover useful citations which they may have missed. The Kardashian index (K-index) can be used to study the correlation between the number of citations for a physician and the number of followers they have on Twitter©. The goal of this study was to analyze the presence and use of Twitter© by rheumatology PDs in the United States (US).

Methods: The Accreditation Council for Graduate Medical Education website was accessed to obtain a list of accredited rheumatology fellowships in the US and all PDs were included. Demographic data, publications, citations and h index were collected using publicly available sources: program websites, Doximity©, Healthgrades© and Scopus©. A Twitter-based search was conducted to collect numbers of followers. The K-index = Ft/F, Ft is the number of followers a physician has on Twitter©, and F is the number of followers a physician should have based on the that physician's number of citations (C). The F factor = 43.3 $(C)^{0.32}$. Nonparametric statistics including Mann-Whitney U and Kruskal-Wallis tests were used to compare differences between groups.

Results: A total of 121 PDs were included. The average age was 52.69±9.17 years, 61 (50.4%) were females, 33 had Twitter© accounts, 11 had more than 100 followers and 10 had less than 10 followers. Active followers ranged from 0 to 1964. The mean±standard deviation (median) number of publications, citations and h-index for PDs were 31.98±45.47 (14), 1344.21±3035.96 (384) and 11.94±13.05 (8). There was no statistical difference between male and female PDs as well as between American and international medical graduates with regards to the distribution of publications (p=0.108; p=0.261), citations (p=0.204; p=0.367) and h-index (p=0.12; =0.337). Their average K-index was 0.864 (SD = 1.75) with a range from 0 to 7.72. There was no significant difference between male and female PDs with Twitter© on their K-index (MW U = 103.00, p = 0.287) or based on location of training (MW U = 108.50, p = 0.434).

Conclusion: A higher K-index suggests a physician may be over celebrated due to his/her active presence on social media. Physicians with a K-index > 5 are considered to be "Kardashians" of the academic world. As only 1 PD had an index > 5, we observed that with most PDs, the Kardashian phenomenon does not exist. Lack of social media presence represents an underutilized resource for PDs, as having an active professional Twitter© account can be used for program highlights, networking and professional advancement.

Disclosure: A. Khanna, None; **K. Gopalakrishnan**, None; **D. Czarny**, None; **B. Quigley**, None; **A. Kwiatkowski**, None.

Abstract Number: 1187

Is Your Program Website Optimized for Recruitment? An Evaluation of Rheumatology Fellowship Program Websites

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Background/Purpose: A program's website is a helpful source of information for a prospective applicant whose decision on where to apply is influenced by the data provided on the internet. During the pandemic, as the applicants were unable to physically visit desired programs, there was an increased reliance on information gathered virtually to make crucial decisions. The purpose of this study was to assess the helpfulness of information provided on program websites for prospective applicants.

Methods: The Accreditation Council for Graduate Medical Education website was accessed to obtain a list of all accredited rheumatology fellowships in the United States (US). Publicly available program websites were accessed

via a Google© search to collect data on presence or absence of 10 categories of recruitment and education related content relevant to applicants. Chi-Square tests were used to compare differences between regional groups and p-value of < 0.05 was considered significant.

Results: As of May 2021, 122 accredited programs were identified and all had functional websites. The program director's description and content was provided for 44.6%, while 71.1% provided the coordinator's information and contact. Research opportunities (59.5%), details about current fellows (52.9%) and educational curriculum (52.9%), were among the most frequently described features. Visa offers (39.6%), number of fellows (38.8%), international medical graduates' acceptance (38.0%), salary or benefits (33.9%), Doctor of Osteopathic Medicine acceptance (29.8%), fellow yearly schedule (17.4%), board pass rate (6.6%) and interview day itinerary (5.0%) were the least frequently described features. Regional differences were examined between 5 areas of the country: the Northeast (n = 36), South (n= 41), Midwest (n =25), Mountain (n= 5), and Pacific (n= 14). Salary was more frequently listed in the Pacific states while curriculum was more commonly listed in the Mountain states, although the Mountain states were least likely to list benefits.

Conclusion: Despite the value that a program's website could provide to applicants when making decisions during the application process, this study revealed there is a lack sufficient, relevant, and standardized information. Improving the content, accessibility and uniformity across all rheumatology websites will reduce inappropriate applications, attract the most suitable applicants, reduce the amount of email inquiries, and could also lessen the financial burden for applicant's applying out of state. Fellowship programs could expand upon the content included, particularly with respect to providing contact information, board pass rates, types of visas offered, schedules and interview day itineraries.

Disclosure: T. Ajayi, None; **A. Khanna**, None; **B. Quigley**, None; **A. Kwiatkowski**, None.

Abstract Number: 1188

Sifting Through Complexity in a Methodological Manner: Identifying Key Items in Teaching Lupus to Medical Students Through Consensus

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Background/Purpose: Creating a curriculum for teaching lupus to medical students is a challenge given the complexities and nuances of this systemic disease. Because lupus spans multiple complex systems, educators outside of rheumatology hold stake in determining what elements of lupus a graduating medical student should be familiar with; this adds further complexity to curricular design. Unfortunately, the literature offers little guidance. The aim of this study is to use consensus methodology involving various stakeholders to identify key lupus curricular items that medical students should learn about during their four year education.

Methods: 86 faculty and housestaff members from the University of Utah (UU) were invited to participate in a 3 step Delphi consensus process. Housestaff members included 3 Rheumatology fellows and 3 Internal Medicine chief

Table 1. List of Identified Key Items meeting >80% Total Group Consensus

Item	Identified Items Meeting >80% Total Group Consensus
	Definitions
1	Recall the definition of autoimmunity
2	Recall the definition of innate and adaptive immunity*
	Pathophysiology
3	Identify SLE as an autoimmune disease
4	Identify SLE as a systemic disease
	Clinical Features
5	Identify mucocutaneous features of SLE
6	Identify discoid lupus
7	Identify that pleurisy is a feature of SLE
8	Identify that inflammatory arthritis is a feature of SLE
9	List SLE as part of a differential for neurological and psychiatric pathology
10	Identify features of lupus nephritis clinically
11	Identify serositis as a clinical feature of SLE including pleuritis, pericarditis, and peritonitis*
12	Identify pulmonary manifestations of SLE including DAH, ILD, thromboembolic disease*
13	Discuss anti-phospholipid antibody syndrome as a component of SLE including features of hypercoagulability and pregnancy complications*
	Lab Abnormalities
14	Identify autoimmune hemolysis as a feature of SLE
15	Identify leukopenia as a feature of SLE
16	Identify thrombocytopenia as a feature of SLE
17	Name ANA as a screening test for SLE
18	Name DSDNA and Smith as specific antibodies for SLE
19	Identify hypocomplementemia as feature of SLE
20	Identify ANA as a screening test and not a diagnostic test (i.e., +ANA without lupus/rheumatic disease symptoms)*
21	Understand ANA is not specific for diagnosis*
22	Correctly identify patients who should be tested for SLE (should receive an ANA test)*
23	Identify the utility of dsDNA and Smith Ab in evaluation for SLE*
24	Identify that antiphospholipid antibody syndrome can overlap with SLE*
25	Identify the utility of urine analysis and urine protein in evaluating/screening of lupus nephritis*
	Treatment
26	Identify hydroxychloroquine as a treatment for SLE
27	Identify immunosuppression as a treatment for SLE
28	Recognize the use of prednisone as a treatment and describe potential side effects, including CV risk*
	Epidemiology*
29	Identify the sex and age associations with SLE prevalence*
30	Identify ethnic association with SLE prevalence*
	Morbidity and Mortality*
31	Recognize life threatening SLE complications, such as nephritis or catastrophic anti-phospholipid syndrome*
32	Identify the risk of arterial/venous clots and need for APS testing in SLE patients with blood clots and miscarriages*

* Additional items proposed by consensus group

residents. Step 1 involved reviewing the 21 current items in the UU medical school curriculum and requesting suggestions for additional items. In step 2, each participant rated every item's importance to be included in the medical school curriculum using a 5-point Likert scale (1 = not at all important; 5 = extremely important). In the 3rd step, participants were given the group's mean and mode rating for each item, reminded of their own initial rating, and asked to make a final 5-point rating. Individual responses to each step remained anonymous. After the final step, items rated ≥4 ("very important" or "extremely important") by at least 80% of participants were retained; these identified items defined the set of lupus curricular elements representing the consensus of the group.

Results: 44 participants accepted the invitation to join our consensus project (51%); 31 participants completed all steps (37% of invited members, 70% of accepted participants). The majority were rheumatologists (16, 52%), 4

Table 2. List of Additional Key Items recommended by >80% Rheumatologists within Total Consensus Group

Item	Additional Items Recommended by >80% of Rheumatologists within total Consensus Group
	Clinical features
1	Identify features of lupus nephritis histo-pathologically
2	Understand Libman-Sacks endocarditis as well as other cardiac manifestation of lupus*
3	Describe neurological and psychiatric presentations of SLE*
4	Discuss common causes of drug-induced lupus*
5	Understand the difference between classification versus diagnostic criteria*
	Lab abnormalities
6	Identify antiphospholipid antibodies such as lupus anticoagulant, anticardiolipin, beta-2 glycoprotein*
	Treatment
7	Identify the role for steroid sparing agents*
	Morbidity and Mortality
8	Identify relation of sex, age, ethnic, economic differences to lupus severity*
9	Identify increased risk for certain co-morbidities in patients with SLE, such as CAD, CVA, cervical cancer, thrombotic events/DVT/PE, pulmonary hypertension and osteoporosis*

* Additional items proposed by consensus group

participants were from internal medicine, and 11 participants were medical school educators (6 of these medical educators also had internal medicine backgrounds).

In step 1, 61 items were added as suggestions to the curriculum leading to a total of 82 items to be rated. The consensus process eliminated 50 items, leaving 32 in the final list of identified important key teaching elements for lupus (see Table 1). In a post-hoc analysis of ratings provided by rheumatologists within the larger consensus group, 9 additional elements were identified though these did not meet total group consensus (see Table 2).

Conclusion: Using a systematic consensus exercise, a diverse group of educators participating in the lupus consensus project identified key teaching items to prioritize during medical school education. The next steps will include developing learning objectives mapped to these identified items in the development of curriculum to educate medical students about lupus.

Disclosure: J. Thomas, None; **M. Battistone**, None; **K. Register**, None; **A. Barker**, None.

Abstract Number: 1189

Ultrasound Online: A Novel Approach to Teaching Rheumatology Focused Musculoskeletal Ultrasonography to Resident Physicians in Training

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SESSION INFORMATION

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Session Title: Professional Education Poster (1170–1195)
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Background/Purpose: Musculoskeletal point of care ultrasound (MSK POCUS) can assess for joint effusions, synovitis and crystalline arthropathy and is increasingly utilized by generalists working in various clinical settings. Generalists are able to perform focused ultrasound (US) exams to answer specific clinical questions with accuracy similar

Table 1

Question	Pretest Correct (%)	Posttest Correct (%)
Which probe position shown is most likely to show a knee effusion if one is present?	N/A	4/4 (100%)
Drag each image to the corresponding pathology label.	0/4 (0%)	4/4 (100%)
In musculoskeletal ultrasound, anisotropy is most likely to be encountered in which tissue type?	1/4 (25%)	3/4 (75%)
Which of the following can be reliably detected with ultrasound used by an experienced operator?	1/4 (25%)	1/4 (25%)

to that of experts after brief instruction, although it is estimated that 2/3 of internal medicine (IM) programs lack a formal US curriculum. At our institution, a 2-week POCUS elective is available for IM residents, however MSK POCUS has not been formally incorporated. A needs assessment survey of residents who previously completed the POCUS elective found that 92% of residents wanted to learn POCUS to assess for joint inflammation or crystalline arthropathy. As the onset of the COVID-19 pandemic necessitated physical distancing, an online electronic learning (eLearn) module was developed to train residents to acquire and interpret MSK POCUS images of the knee. Here we present preliminary results of this model of MSK POCUS instruction for teaching IM residents.

Methods: Three high yield US views of the knee were chosen for their ability to show pathology and ease in demonstrating transducer placement pictorially including the suprapatellar long and short axis views with the knee in neutral position (for joint effusion and synovial thickening) and suprapatellar short axis view with the knee in maximal flexion (for crystalline arthropathy and osteoarthritis changes). The module was developed in Adobe Captivate, hosted on the institution's learning management system (LMS) and made available to residents in the POCUS elective. US images in each view showing normal anatomic landmarks were coupled with graphics to show transducer placement. Common pathology in each view was shown in interactive exercises. US physics, pertinent artifacts, and indications for use were reviewed. To reinforce learning, the module featured interactive elements including simulated transducer placement and point-and-click structure identification items as well as traditional quizzing elements such as drag and drop and matching exercises to provide immediate feedback to learners. Results of a pre and post test were exported to the LMS.

Results: Four residents completed the module between February and May 2021 and serve as a validation cohort. Post-test data show 100% of participants were able to identify correct transducer placement for the highest yield US view to assess for knee effusion and were also able to accurately identify images showing effusion, OA, the double contour sign of gout, and chondrocalcinosis (Table 1).

Conclusion: We present a novel eLearn module to teach targeted MSK POCUS of the knee to IM residents within the context of an existing POCUS elective. The module was effective in teaching appropriate transducer placement and image interpretation in a validation cohort. Future work will assess effects on image acquisition with observed scanning sessions after module completion, demonstrate effect in increasing MSK POCUS utilization among residents over time, and expand this model to additional joint regions and to pediatric subjects.

Disclosure: A. Long, None; **B. Marston**, None; **H. Rahimi**, None; **N. Madsen**, Pfizer, 2, Abbvie, 2; **W. Novak**, None.

Abstract Number: 1190

Rheumatology Continuing Professional Development for Primary Care Providers: A Systematic Review

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Background/Purpose: The 2015 workforce study conducted by the American College of Rheumatology estimated that in 2030, the United States (US) alone will have a shortage of about 4,700 rheumatologists. As such, primary care providers (PCPs) may find themselves taking the initial steps to diagnose and treat some rheumatologic disorders. PCPs can participate in rheumatology-focused continuing professional development (CPD), which may help mitigate this shortfall. However, there is no recent synthesis of the literature describing these initiatives or their efficacy. This risks the use of suboptimal instructional methods and missed opportunities for providers.

Methods: The authors conducted a systematic review of CPD in rheumatology for primary care. PubMed, Embase, Web of Science, ERIC, CINAHL, PsycINFO were systematically searched by a medical librarian. Studies were limited to those performed in the US and Canada. Studies prior to 1995 were excluded to allow the authors to build on a previous review published that year. An extraction form, including the Medical Education Research Study Quality Instrument, was created through an iterative process and applied to the included articles.

Results: 725 studies were retrieved, of which 9 met inclusion criteria. Preliminary results showed that CPD was directed more at non-inflammatory arthritis than inflammatory arthritis. Additionally, 4 studies at least partially focused on teaching arthrocentesis. Autoimmune diseases were underrepresented; rheumatoid arthritis was discussed in 4 studies and an additional study discussed rheumatologic topics more broadly.

In rheumatology CPD, the underrepresentation of autoimmune disease may contribute to questions in diagnosing and referring patients to rheumatology further accentuating the shortfall of rheumatologists. Newer research tended to include multi-component approaches that combine strategies (such as didactics and active learning), whereas older research was less focused on interactive learning modalities. This is consistent with a move towards more active learning in CPD. Cost considerations are important in CPD, though few articles discuss it. Though e-learning is increasing in popularity, identified interventions were predominantly face-to-face with few examples of e-learning. E-learning may continue to evolve, particularly given the impact of COVID-19 on education.

Conclusion: Rheumatology CPD is moving towards more interactive teaching methods and is typically conducted in person through virtual options in rheumatology CPD should be explored to improve access to CPD. Autoimmune disease is an uncommon topic in CPD and may be an area for future expansion.

Disclosure: R. Robbins, None; **J. Maciuba**, None; **L. Maggio**, None; **A. Samuel**, None.

Abstract Number: 1191

Introduction of a Joint Injection and Ultrasound Workshop for Internal Medicine Trainees

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Background/Purpose: There is increasing interest in procedural training at all levels of medical education. While point of care ultrasound (POCUS) and joint injection are not specific requirements of Internal Medicine (IM) training curricula, they are at times included. The aim of this study was to assess the feasibility of an integrated approach to delivering musculoskeletal (MSK) POCUS and joint injection education to Internal Medicine trainees.

Methods: A pilot workshop for IM trainees was created. The workshop consisted of pre-session materials (videos and step-by-step guides to both ultrasound of the knee and knee aspiration and injection), a pre- and post-session knowledge check consisting of two identical multi-sectional cases involving the use of POCUS and joint aspiration/injection in a clinical context and three, 30-minute hands-on small groups sessions on 1: knee ultrasound, 2: knee aspiration and injection and 3: data interpretation/clinical context. Paired t-test was used to compare the pre- and post-session knowledge check scores with a value $p< 0.05$ deemed significant. In addition, post-workshop, feedback in the form of a five-point Likert scale (1 = not at all, 5 = extremely) on each component of the workshop and free text comments were solicitated from participants.

Results: Sixteen IM trainees participated in the pilot workshop (7 Post-Graduate Year (PGY)-1, 4 PGY-2, 4 PGY-3, 1 PGY-4). Eleven subjects had improvement in their test scores after the workshop, three scored the same pre- and post-workshop and one had a lower score post-workshop (Figure 1). The mean test score increased from 5.5 pre-workshop to 7.3 post-workshop ($p=0.001$). Feedback from the group was overall positive with the majority rating

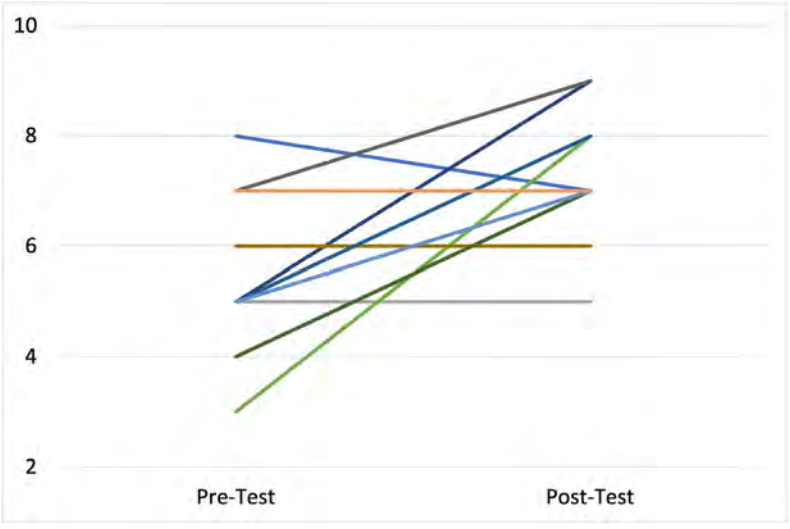

Figure 1. Scores for pre-test cases and post-test cases.

Table 1. Post-workshop feedback (%)

Helpfulness	Pre-session materials	Ultrasound	Aspiration/injection	Data interpretation
Extremely	33	73	53	33
Very	47	27	40	53
Moderately	20	0	7	13
Slightly	0	0	0	0
Not at all	0	0	0	0

each distinct aspect of the workshop either extremely or very useful (Table 1). The three most common feedback comments included 1: obtaining models for different joints in addition to the knee 2: more time to practice MSK POCUS and 3: more examples of pathological states.

Conclusion: An integrated workshop combining ultrasound, aspiration and injection of the knee joint in combination with education around the clinical use and context of these procedures was feasible. In addition, participants found the workshop valuable, leading to increased knowledge post-workshop. Future work is planned to expand this workshop to an entire IM residency program.

Disclosure: L. Milla, None; **D. Lindstrom**, None; **E. Gkrouzman**, None; **J. Subramanian**, None; **E. Murphy**, None; **J. Cheah**, None.

Abstract Number: 1192

Palliative Care for the Rheumatologist: An Educational and Patient Care Intervention

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SESSION INFORMATION
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Background/Purpose: Patients with advanced systemic rheumatic diseases such as systemic sclerosis, inflammatory myositis and vasculitis often have a high burden of symptoms and limited life expectancy. However, these patients have limited access to palliative care. The results of a survey sent out by the Canadian Rheumatology Association revealed that rheumatologists self-report discomfort with, and inadequate knowledge of, palliative care topics including how to engage in advance care planning and goals of care (ACP and GOC) conversations suggesting a gap in training. This study assesses the impact of an education session designed for rheumatologists and trainees.

Methods: A group of rheumatologists and trainees participated in a didactic session and hands on practice with standardized patients based on a structured ACP and GOC Conversation Guide. A post-workshop survey assessed participants' practice patterns and the workshop's impact on participants' comfort with these conversations. Results were analyzed using descriptive statistics.

Results: 12 rheumatology faculty and trainees participated in the workshop and 8 completed the post-workshop survey. Of the participants who completed the survey, 63% (n=5) reported that 5% or more of inpatients that they cared for had advanced rheumatologic diseases with significant functional limitation and/or an estimated prognosis of less than 1 year. 88% (n=7) felt that the workshop was useful to their clinical practices. 75% (n=6) reported that they will be more comfortable in engaging in goals of care conversations with patients following the workshop. 63% (n=5) reported that the workshop raised awareness of the importance of palliative care for patients with life-limiting systemic rheumatic diseases. 63% (n=5) reported that the insights acquired will facilitate challenging aspects of patient care.

Conclusion: We piloted and evaluated a rheumatology-specific advance care planning and goals of care conversation training module delivered to rheumatology residents and faculty. Preliminary results point to participants' increased comfort with these conversations and increased awareness of palliative care's role for patients with end-stage rheumatologic conditions. Further study on a larger scale is required to better assess the value of such educational interventions, and their long-term impact on promoting interdisciplinary models of care for patients with life-limiting rheumatic diseases.

Disclosure: A. Saltman, None; **C. Serapio**, None; **R. Colman**, None; **L. Steinberg**, None.

Abstract Number: 1193

Musculoskeletal Ultrasound Instruction in US and Canadian Pediatric Rheumatology Fellowship Programs

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Background/Purpose: Musculoskeletal ultrasound (MSUS) has value in the evaluation of both pediatric and adult rheumatic diseases. It is taught by at least 94% of adult rheumatology fellowship programs based on a 2017 survey. The objective of the present study is to assess the current teaching of MSUS in Canadian and American pediatric rheumatology fellowship training programs, including surveying the teaching methods being employed.

Methods: A core group of pediatric and adult rheumatologists with at least 5 years of experience in medical education and/or in ultrasound convened to develop a survey that assessed for faculty training in ultrasound, access to equipment, financial support for faculty training and equipment, curricular implementation including educational resources, teaching and assessment of competency in ultrasound. Qualtricsâ was utilized to distribute the survey through email to program directors using an anonymous link, with a follow up email sent in two weeks to non-responders. A list of fellowship programs in the USA (36) and Canada (3) were obtained through the American Medical Association Freida™ Online Residency Program Database and the Royal College of Physicians and Surgeons' Canadian Accreditation of Residency Education (CanEra) website, respectively.

Table 1. Characteristics of Pediatric Rheumatology Fellowship Programs, Faculty Descriptors, *(n=27)*

	n (%)[a]
Respondent Role (indicate all that apply)	
Program Director (PD)	**23 (85%)**
PD & Lead US Faculty, Key Clinical Faculty	2 (7%)
PD & Division Director	3 (11%)
Other	**4 (15%)**
Lead US Faculty, Key Clinical Faculty	3 (11%)
Lead US Faculty, Non-Key Clinical Faculty	3 (4%)
Number of Fellows & Frequency At Which Selected	
1 per year	14 (52%)
2 per year	8 (30%)
3 per year	1 (4%)
1 per 3 years	4 (15%)
Currently Offer Training in MSUS	
No	4 (15%)
No, but we are currently developing a curriculum	3 (11%)
Yes, we have peds only training in these various formats	9 (33%)
Yes, we have both adult and peds training in these various formats	6 (22%)
Yes, we are invited to participate in US training with the adult rheumatology fellowship	5 (19%)
Faculty That Teaches US	
Pediatric rheumatology only	10 (37%)
Adult rheumatology only	4 (15%)
Both pediatric and adult rheumatology	6 (22%)
Rheumatology and other subspecialties	2 (7%)
Other subspecialties (radiology, sports medicine)	2 (7%)
No response	3 (11%)
At Least One Faculty Member Competent in Performing and Teaching US	
Yes	17 (63%)
No	2 (7%)
No, none in pediatric rheumatology, rely on another subspecialty faculty	5 (19%)
No response	3 (11%)
Number of Faculty Who Have Obtained US Training	
One	7 (26%)
Two	4 (15%)
Three or more	6 (22%)
None in pediatric rheumatology, rely on another subspecialty faculty	6 (22%)
None in pediatric rheumatology or in another subspecialty faculty	1 (4%)
No response	3 (11%)
Number of Advanced US Practitioners in Program	
None	23 (85%)
No response	4 (15%)

US=Musculoskeletal Ultrasound. Percentages may not add to one-hundred due to rounding.

We list the cross-sectional descriptive frequencies and percentages to summarize the data provided by the 27 respondents who completed the survey by May 24, 2021.

Results: We garnered a 69% response rate thus far, with 27 responses. Majority of the survey respondents self-identified as program directors [23 (85%)] (Table 1). 20 (74%) respondents affirmed that their programs offered some level of MSUS training but the majority (17, 63%) surveyed did not have a formal MSUS curriculum. 12 (44%) indicated that they have 1-2 faculty members that actively teach MSUS to fellows. Most programs covered normal and abnormal sonoanatomy, image optimization and knobology, US guided procedures, and documentation and billing as content; and utilized various teaching methods (Table 2). Most programs also did not name any formal assessment methods of proficiency but did cite the use of direct observation and feedback, and use of procedure logs.

Table 2. Characteristics of Pediatric Rheumatology Fellowship Programs, Teaching and Evaluation, *(n=27)*

	n (%)[a]
Years of US Experience for Lead US Faculty	
Two to three	4 (15%)
Four to five	2 (7%)
More than five	11 (41%)
No response	10 (37%)
Number of Faculty Certified in US	
None	10 (37%)
One	8 (30%)
Two	2 (7%)
Three or more	4 (15%)
Missing	3 (11%)
Number of Faculty Actively Teaching US to Fellows	
None	10 (37%)
One	7 (26%)
Two	5 (19%)
Three or more	2 (7%)
No response	3 (11%)
Formal US Curriculum in Use	
No, none	17 (63%)
Yes, we are using our own	3 (11%)
Yes, we are using adult rheumatology's (adjusted for multi-response)	2 (7%)
Yes, we are using our own and adult rheumatology's	1 (4%)
Yes, we are using ACR's	2 (7%)
No response	2 (7%)
Average Number of Credentialing-Eligible Scans Performed in One Year	
Less than 50	8 (30%)
50 to 100	2 (7%)
No response	17 (63%)
US Teaching Methods (multi-response)	
Didactic lectures	11
Reading assignments (books, journal articles)	8
Workshop/non-patient care-related practice scanning sessions	9
Hands-on teaching as part of patient care in a clinic	14
Cadaver-based teaching	3
USSONAR fellowship program	11
Online materials (eg. websites with videos)	7
Off-site conferences (i.e. fellows sent to courses)	4
Conferences (Journal Club, Clinical Conf, Research Conf, M&M Conf)	2
Other	5
US Evaluation Methods (multi-response)	
Direct observation and feedback at time of scanning	9
Checklist of knowledge and skills fellows are expected to master	1
Multiple-choice exam	1
Procedure or case logs of scans	2
We don't do any formal assessments	13
Other	3

US=Musculoskeletal Ultrasound. Percentages may not add to one-hundred due to rounding.

The highest ranked barrier identified was “inadequate time or clinic space to perform MSUS in clinic” with 14 votes for it as a minor barrier and 10 votes for it as a major barrier and accounting for 89% of the total respondent ratings (Table 3). “Inadequate number of faculty to teach” [22 (82%)], and “lack of time or clinic space to include MSUS in clinics and didactics” [21 (78%)] were the next highly rated minor or major barriers.

Conclusion: Out of 27 responses, 85% of Canadian and American pediatric rheumatology fellowship programs are teaching MSUS to fellows. Competency assessment methods are needed. Barriers related to curricular integration include needing faculty who can teach and having the time and space to perform MSUS and include MSUS in clinic teaching and didactics. Further faculty development not only to inculcate MSUS skill sets but also to gain MSUS teaching and assessment skill sets and curriculum development are needed.

Table 3. Perceived Barriers to Complete Curricular Integration in Pediatric Rheumatology Fellowship Programs, *n=27* (%)[a]

	Not a Barrier	Minor Barrier	Major Barrier
Lack of ease of access to equipment	15 (56%)	7 (26%)	5 (19%)
Inadequate number of faculty to teach	5 (19%)	8 (30%)	14 (52%)
Lack of faculty/division leadership interest	15 (56%)	7 (26%)	5 (19%)
Lack of faculty interest to learn	12 (44%)	10 (37%)	5 (19%)
Lack of interest by fellows to learn	14 (52%)	10 (37%)	3 (11%)
Lack of funding to train faculty	13 (48%)	7 (26%)	7 (26%)
Lack of faculty proficiency to teach MSUS	13 (48%)	7 (26%)	7 (26%)
Lack of funding to train fellows	12 (44%)	10 (37%)	5 (19%)
Lack of fellow time (already full curriculum)	10 (37%)	10 (37%)	7 (26%)
Political pushback by other specialties	20 (74%)	6 (22%)	1 (4%)
Inability to bill for scans	19 (70%)	6 (22%)	2 (7%)
Inadequate reimbursement for scans	17 (63%)	9 (33%)	1 (4%)
Inadequate time or clinic space to perform MSUS in clinic	3 (11%)	14 (52%)	10 (37%)
Inadequate credentialing tools	18 (67%)	4 (15%)	5 (19%)
Lack of time or clinic space to include MSUS in clinics and didactics	6 (22%)	12 (44%)	9 (33%)

[a]Counts sum across rows and percentages may not add to one-hundred due to rounding.

Disclosure: C. Lin, None; **E. Oberle**, None; **M. Curran**, None; **J. Roth**, None; **P. Vega-Fernandez**, None; **D. De-Ranieri**, None; **T. Ting**, None; **H. Benham**, None; **L. Salto**, None; **K. Torralba**, GlaxoSmithKline, 12, Clinical Trials Support, UCB, 2, Exagen, 2, Aurinia Pharmaceuticals, 2, Ultrasound School of North American Rheumatologists (SUSONAR) Southern California Rheumatology Society (SCRS), 4, Janssen, 12, Support for educational programs, Radius Health, 12, Support for educational programs, Amgen, 12, Support for educational programs, Novartis, 2, 12, Clinical Trials Support, Pfizer, 12, Support for educational programs, AstraZeneca, 12, Clinical Trials Support.

Abstract Number: 1194

A Module on Large Vessel Vasculitis for Learners in Rheumatology

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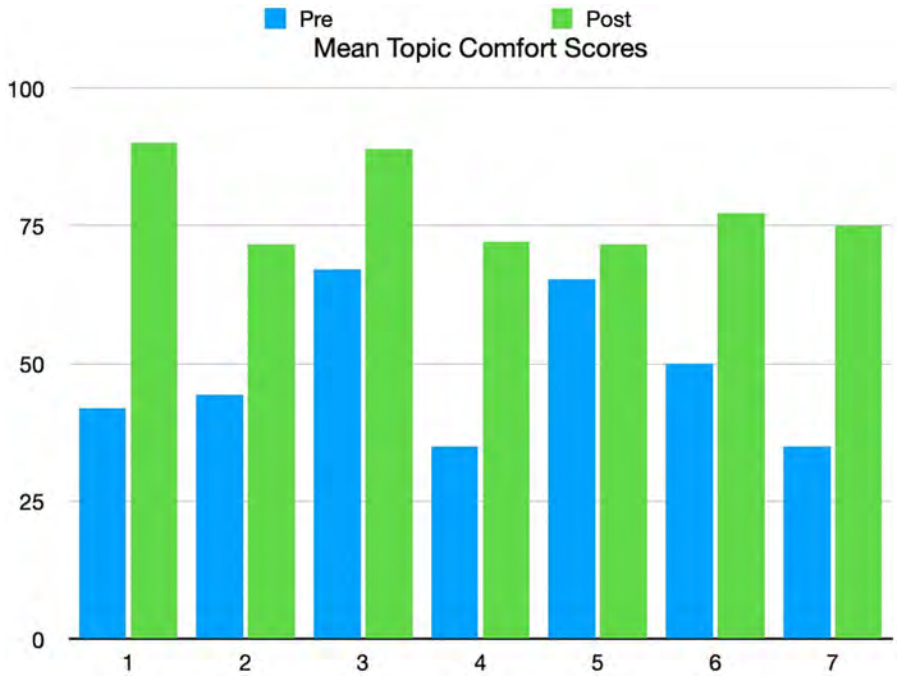
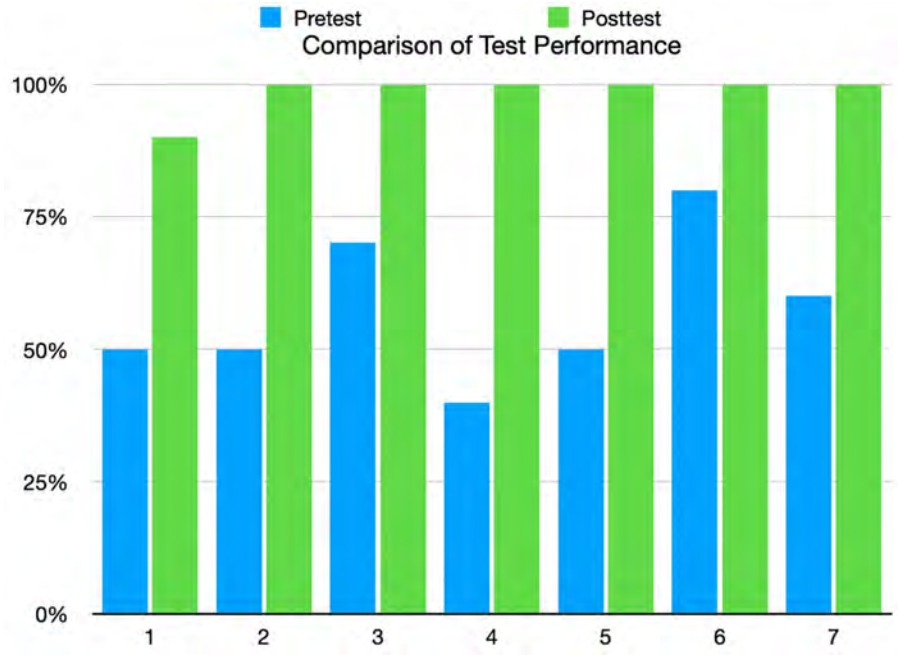
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Professional Education Poster (1170–1195)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Of the rheumatic disorders that learners are expected to know, the vasculitides are among the hardest to grasp. Their pathogenesis is not well-established, they have many overlapping clinical features and they are rarely encountered in general medical practice. Additionally, the consequences of missed diagnosis and delayed treatment can be catastrophic. Therefore, "vasculitis" is a frequently requested topic for teaching from rotating learners. There also have been important advancements in diagnostic methods, guidelines and available treatments that our rotating learners should know about but may not yet have encountered in training.

This module focused on large vessel vasculitis (LVV), namely giant cell arteritis (GCA) and Takayasu arteritis (TAK). It is part of a larger module-based Rheumatology curriculum undergoing development at Virginia Commonwealth University School of Medicine (VCU SOM). The primary goal of this module is to provide learners with a short, effective



Results of each participant's topic comfort rating before and after completing the educational content.



Results of each participant's test scores before and after completing the educational content.

learning tool to improve their understanding of the clinical features, diagnostic methods and treatment options of LVV in preparation for the cases they may encounter on tests and in clinical practice.

Methods: The study was conducted at VCU SOM. A brief slide-based topic overview was created using Apple Keynote that succinctly covered GCA and TAK. Slides contained high yield characteristics of the background, presentation, exam findings, diagnosis and treatment of these disorders. A test was created and administered for self-assessment and data collection via a secure online, cloud-based program. The test included 10 multiple choice

questions to assess knowledge of the clinical presentations, preferred diagnostic techniques and treatment for LVV. A brief topic comfort survey was also created to compare the learner's confidence in the material before and after the module. Learners rated their confidence in three domains on a scale 1-100 (clinical features, exam findings, diagnostic modalities). Learners were asked to take the test and survey just prior to proceeding with the topic overview and again upon completion of the content. Data were analyzed using the unpaired *t*-test.

Results: Seven participants completed the module. Learners reported a greater degree of confidence after completing the module compared to baseline (mean topic comfort scores of 78.1 and 48.4, respectively; improvement of 29.7 points, 16.9 — 42.5, $p = 0.0003$). This corresponded with significant improvement in test performance—mean pretest score was 57.1%, compared with mean posttest score of 98.6% (improvement of 41.5%, 29.6% — 53.2%, $p = < 0.0001$).

Conclusion: While sample size was small, the results show that this module helped learners significantly improve confidence in their knowledge of large vessel vasculitis, which corresponded with significant improvement in test score performance. Plans for future study involve testing participants again after one month to assess the durability of these effects.

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Abstract Number: 1195

NLP-Based Clustering Methods Can Efficiently Categorize Scientific Abstracts for Medical Conferences

Jeffrey Curtis[1], yujie Su[2], Fenglong Xie[2], cassie Clinton[2], Janet Pope[3], Vivian Bykerk[4], Kenneth Saag[2], Josef Smolen[5], Dan Furst[6] and Lauren Davis[7], [1]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Western Ontario, London, ON, Canada, [4]Division of Rheumatology, Hospital for Special Surgery, New York City, NY, [5]Medical University of Vienna, Vienna, Austria, [6]University of California Los Angeles, Los Angeles, CA, [7]American College of Rheumatology, Atlanta, GA

SESSION INFORMATION
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Expanding scientific discovery has resulted in increased challenges to organize and categorize medical knowledge. Dozens or hundreds of abstracts are submitted each year to more than 40 American College of Rheumatology (ACR) Convergence Annual Meeting Abstract Submission Categories. Numerous ACR abstract review teams then are charged to group similar types of abstracts into the many poster and oral sessions (i.e. subcategories), to be presented across Convergence meeting days. This manual process of grouping relies on subject matter expertise to identify similar content across abstracts and is exceedingly time consuming. We developed and implemented an automated approach to sub-categorize similar abstracts within each ACR Abstract Submission Category to increase the efficiency of the grouping process.

Table: Results from Method Used to Subcategorize 2020 ACR Convergence Abstracts using Clustering Algorithm with Natural Language Processing

ACR Convergence Abstract Category	# of abstracts to be sub-categorized	Results: # of clusters, and abstracts/cluster			
		# of clusters	Median	Min	Max
33: Rheumatoid arthritis – Diagnosis, manifestations, outcomes	136	13	10	8	12
34: Rheumatoid arthritis – Treatments	142	14	10	7	14
36: Spondyloarthritis - Diagnosis, manifestations, outcomes	133	11	12	9	16
36: Spondyloarthritis – Treatments	129	12	10	6	18
38: SLE - Diagnosis, manifestations, outcomes	136	12	11	8	14
39: SLE – Treatments	58	6	9	8	12
30: Pediatric Rheumatology – Clinical	106	11	10	7	12
Total # of Abstracts; Median # Clusters, and # Abstracts/Cluster	**840**	**12**	**10**	**8**	**14**

Methods: The corpus of all accepted abstracts to seven of the largest 2020 ACR Convergence Abstract Categories was parsed and processed using natural language processing (NLP) tools from the National Library of Medicine. After filtering stop words, parsing the data, and applying n-grams for tokenization, a bag of words approach was used to identify all terms and multi-word concepts in both the title and body of all abstracts. We counted term and concept frequencies, weighted by the inverse of their frequency across all abstracts. Concepts also were tagged with their semantic type using UMLS. K-means clustering was used to derive abstract category subclusters, optimizing the cluster convergence criterion (CCC) metric to identify the optimal number of subclusters (i.e. abstract session subcategories). An iterative, automated approach subsequently was applied that required the clustering algorithm to select the next number of clusters (also based on the CCC) if the first solution did not meet constraints defined by varying parameters on the size of the subcategories (i.e. min/max number of clusters, and the min/max number of abstracts per cluster).

Results: A total of 840 abstracts distributed across 7 ACR 2020 Convergence categories were analyzed and yielded 156,778 unique concepts derived from 24,990 unique terms. For each of the 7 Abstract Submission Categories and with no constraints applied, the method yielded 6 – 14 subcategory clusters. The min and max number of abstracts per cluster subcategory ranged from 6 - 18 (Table). Applying additional constraints on both the number of clusters and min/max number of abstracts per cluster yielded convergence within 1-4 iterations.

Conclusion: Clustering methods combined with NLP tools has the ability to greatly reduce the time spent by ACR Convergence meeting review teams and has applicability to other scientific meetings to automatically subgroup abstracts into sessions or to pre-categorize them as a basis for further manual refinement.

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Abstract Number: 1196

Morning Stiffness Already Associates with Systemic Inflammation and Subclinical Joint Inflammation in the Pre-RA Phase of Arthralgia

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Morning stiffness (MS) is characteristic for Rheumatoid Arthritis (RA) and associates with markers of systemic and local inflammation in RA-patients. In patients with arthralgia, MS is a cardinal symptom to recognize arthralgia at-risk for RA-development (i.e. clinically suspect arthralgia, CSA). In CSA, MS is also assumed to reflect inflammation, but this has never been studied. Therefore we aimed to study whether MS in CSA-patients is associated with systemic- and subclinical joint-inflammation.

Methods: 575 patients presenting with CSA underwent laboratory investigations and contrast-enhanced 1.5T-MRI of hand and forefoot (scored according to the RAMRIS-method). Associations of MS (duration ≥60 minutes) with presence of subclinical synovitis, tenosynovitis and osteitis with increased CRP (≥5 mg/L) were determined with logistic regression. Additionally, the effect of MS-duration (≥30, ≥60, ≥120 minutes) was studied.

Results: The mean age of the study population was 44 years (SD 13), 439 patients (76%) were female, median tender joint count (TJC68) was 5 (IQR 2-10), and 79 (14%) patients were ACPA-positive. 195 (34%) CSA-patients experienced MS. These patients more often had subclinical synovitis (34% versus 21%, OR 1.95 (95%CI 1.32-2.87)), subclinical tenosynovitis (36% versus 26%, OR 1.59 (1.10-2.31)) and increased CRP (31% versus 19%, OR 1.93 (1.30-2.88)) than patients without MS. In multivariable analyses, subclinical synovitis (OR 1.77 (1.16-2.69)) and CRP (OR 1.78 (1.17-2.69)) remained independently associated with MS. In CSA-patients who later developed RA, and thus in retrospect were 'pre-RA' at time of CSA, MS was more strongly associated with subclinical synovitis (OR 2.56 (1.04-6.52)) and CRP (OR 3.86 (1.45-10.24)). Furthermore, associations increased with longer MS-durations.

Conclusion: Inflammation indeed contributes to MS, already in the CSA-phase that preceded clinical arthritis. These results increase understanding of MS when assessing arthralgia in clinical practice.

Disclosure: D. Krijbolder, None; **F. Wouters**, None; **E. van Mulligen**, None; **A. van der Helm-van Mil**, None.

Abstract Number: 1197

Periodontal Status Before Diagnosis in Patients with Rheumatoid Arthritis Predicts Cumulative Disease Activity in Years After Treatment Inititation

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Transversal cohort studies demonstrated a possible association between periodontal disease (PD) and rheumatoid arthritis (RA). However it is unknown how this association evolves during the disease course. In this study we aimed to compare the severity of PD in RA patients versus non-RA healthy controls prior to clinical diagnosis of RA and thereafter. Additionally, the correlation was analyzed between RA disease activity and PD severity and progression in the same period.

Methods: Data (retrospective with a follow-up of 10 years) of 98 RA patients from general practices and matched healthy control patients from the University Dental College were analyzed. Medical files and dental treatment records were evaluated. PD was analyzed via radiographic assessment using the new periodontal classification system from 2017. Primary outcome measures were the severity and extent of periodontitis (Stage and Grade) and the RA disease activity (DAS28, cumulative DAS28-score). Secondary analytes were gender, year of birth and age at diagnosis, smoking habits, frequency of dental visits for check-up, frequency and duration of periodontal debridement and the presence of rheumatoid factor (RF) and anti-cyclic citrullinated protein antibodies (Anti-CCP). Statistical analyses were performed with IBM SPSS Statistic 25. Depending on the variables Chi-Square Test, Mann-Whitney U Test, Wilcoxon Signed Rank Test, Spearman Correlation and ANOVA were used.

Results: More RA patients had severe periodontitis (stage III/IV) compared to matched healthy controls. The fraction of RA patients with severe PD increased 23% before diagnosis to 43% 5-10 years after diagnosis. The largest part of these patients developed a severe PD with a moderate risk/rate of progression. The proportion of patients that regularly visited the dentist increased from 70% before diagnosis to 80% for patients with mild PD and 94% of patients with severe PD 5-10 years after diagnosis. Development of PD did not differ between sexes or between seronegative and seropositive RA. Patients with severe PD and patients with a high risk of PD progression before RA diagnosis had a higher cumulative DAS28-score than patients with mild PD in the first 7 years after RA treatment initiation.

Conclusion: PD occurs in a proportion of RA patients before diagnosis and in an increasing proportion of patients in the years after diagnosis. PD is associated with decreased response to anti-rheumatic treatment in the years after diagnosis. A proportion of RA patients with radiographic PD infrequently undergoes dental follow up for PD treatment, especially in the years before RA diagnosis.

Disclosure: A. Plachokova, None; **J. Hadisurya**, None; **J. van Bergen**, None; **R. Thurlings**, None.

Abstract Number: 1198

Ultrasonography of the Median Nerve in Patients with Rheumatoid Arthritis Under Suspicion of Carpal Tunnel Syndrome

Styliani Tsiami[1], Efthymia Ntasiou[2], Christos Krogias[2], Ralf Gold[2], Jürgen Braun[1], Michael Sarholz[3] and Xenofon Baraliakos[1], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany, [2]St. Josef-Hospital, Bochum and Ruhr-University Bochum, Germany, Bochum, Germany, [3]Klinik fuer Rheumatologie, St. Marien-Hospital Vreden, Vreden, Germany

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Carpal tunnel syndrome (CTS) is the most common nerve compression syndrome and a common extra-articular manifestation of rheumatoid arthritis (RA). Different causes of CTS are known, among them inflammatory and non-inflammatory pathologies. Electroneurography (ENG) of the median nerve, the method of choice to diagnose CTS, measures impairment of nerve conduction velocity without explaining its underlying cause. However, because the electrical stimulation is often not well tolerated, ENG results may come out inconclusive. Using greyscale ultrasonography (GS-US) provides anatomic information including a structural representation of the carpal tunnel. The aim of this study is to investigate the performance of nerve GS-US in the diagnosis of CTS in patients with RA.

Methods: Consecutive patients with active RA under suspicion of CTS presenting to a large rheumatologic center were included. Both hands were examined by an experienced neurologist including ENG and a GS-US (ML linear probe with 6-15 Hz) of the median nerve. An established grading system for ENG (1), and an established system for GS-US based on cut-offs for the nerve cross sectional area (CSA) [mild: 0,11-0,13cm², moderate: 0,14-0,15 cm², severe: > 0,15 cm² CTS (2)] were used. In addition, the Boston Carpal Tunnel Syndrome Questionnaire (BCTSQ) was used to assess CTS symptoms (3).

Results: Both hands of 58 patients with active RA (n=116) and clinical suspicion of CTS (in 38 cases bilaterally) were included. After clinical examination, CTS was suspicious in 96 hands (82.8%), and 59 of all hands had a final diagnosis of CTS (50.9%). Of the latter, 43 hands (72.9%) had a positive ENG and 16 (27.1%) a positive GS-US finding only, while 30 hands (50.8%) were positive in both examinations.

There was a good correlation of the cross-sectional area (CSA) as well as the CSA-ratio to the ENG findings: the larger the CSA, the more severe was the CTS as assessed by ENG (Spearman's rho=0.554; p< 0.001). The more severe

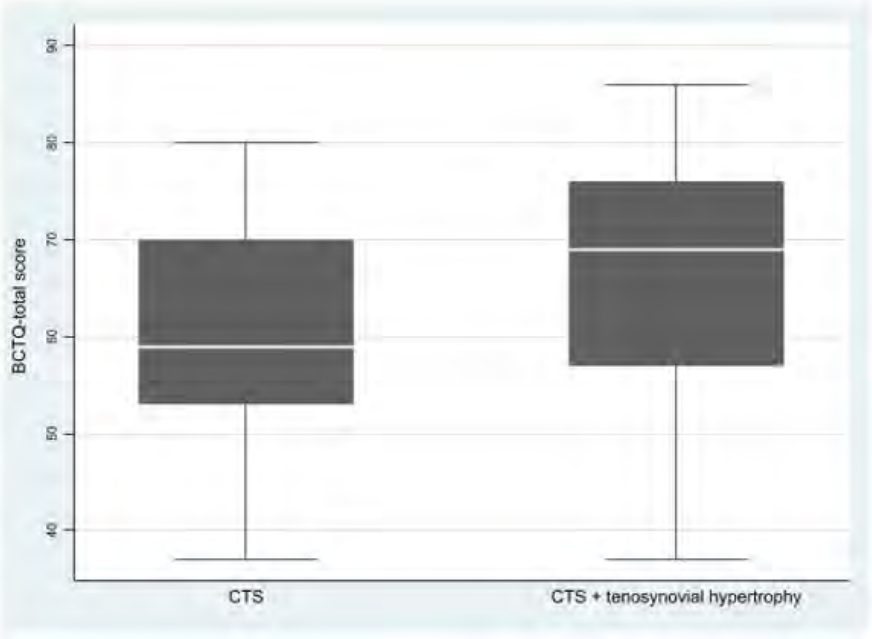

Figure. BCTSQ scores in patients with diagnosis of CTS and absence or presence of RA-related tenosynovial hypertrophy.

the GS-US findings of CTS were, the more definite were the distal motor latency (Spearman's rho=0.554; p< 0.001) and sensible nerve conduction velocity of the median nerve (Spearman's rho=-0.5411; p< 0.001).

In the 46 hands positive in GS-US, tenosynovial hypertrophy of the flexor tendons was detected in 19 hands (41.3%), 7 of which (36.8%) also showed an additional cystic mass. In these 19 patients, clinical complains were more severely present than in patients with non-inflammatory CTS, as assessed by the BCTSQ with a total score of 68.8±13.4 vs. 59.3±13.7, respectively (p=0.007).

Conclusion: In patients with active RA and clinical complains of CTS, ultrasound examinations provide additional information about inflammation which is helpful for a diagnosis of CTS. Thus, ENG and nerve GS-US should be used complementary for a diagnostic workup of CTS in RA patients with a suspicion of CTS. Power-Doppler may further improve the diagnostic performance of GS-US.

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Abstract Number: 1199

Ultrasound in Clinically Suspect Arthralgia: The Role of Power Doppler to Predict Rheumatoid Arthritis Development

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: It is of great importance to identify patients with clinically suspect arthralgia (CSA) who will develop rheumatoid arthritis (RA) or other inflammatory arthritis (IA) because an early diagnosis and initiation of DMARD therapy of these patients is associated with better long term outcomes. Thus, a prompt detection of inflammation and identification of predictors factors of RA is desirable. Our objective is to determine the usefulness of power Doppler (PD) ultrasound (US) to predict RA development in patients with CSA.

Methods: Retrospective analysis of a US unit cohort over a one-year period. Patients with CSA and no previous diagnosis of IA were included for analysis. All underwent bilateral US examination of hands and/or feet according to

Table 1. Predictive factors to rheumatoid arthritis: univariate and multivariate analysis.

		Total n= 110	RA n= 14 (12.7%)	Non-RA n=96 (87.3%)	p	OR*
Age		53.6 ± 15.6	60.4±12.5	52.6±14.6	0.061	1.038 (0.98-1.1)
Sex	Female	80 (72.7%)	10 (71.4%)	70 (72.9%)	0.566	
Smoking n= 87	Non smoker	45 (51.7%)	5 (41.7%)	40 (53.3%)		
	Smoker	34 (39.1%)	5 (41.7%)	29 (38.7%)	0.565	
	Former smoker	8 (9.2%)	2 (16.7%)	6 (8%)		
Extension	Monoarticular	12 (10.9%)	0 (0%)	12 (12.5%)		
	Oligoarticular	22 (20%)	3 (21.4%)	19 (19.8%)	0.372	
	Polyarticular	76 (69.1%)	11 (78.6%)	65 (67.7%)		
Time (months) from symptoms onset		11.7 ± 9.9	9.5±7.6	12±10.2	0.284	
ESR (mm/h)		24.7 ± 18.2	35.1±28.4	23.1 ±15.8	**0.02**	1.006 (0.97-1.04)
CRP (mg/dL)		1.1 ± 3.1	1.8±2.2	0.9± 3.2	0.329	
ANA		15 (13.6%)	1 (7.1%)	14 (14.6%)	0.352	
RF (IU/mL)		39.1 ± 230.5	34±60.7	39.9±246.7	0.647	
ACPA (IU/mL)		98.1 ± 331.2	462±693.4	30.2±127.6	**<0.001**	**1.004 (1-1.007)**
PD US findings		38 (34.5%)	14 (100%)	24 (25%)	**<0.001**	**13.1 (1.07-161.04)**
GS US findings		47 (42.7%)	14 (100%)	34 (35.4%)	**<0.001**	2.7 (0.21-35.08)

*Multivariate analysis: odds ratio with confidence intervals analysis done if P < 0.2 in univariate analysis.

Table 2. GS and PD US findings of patients with CSA

		Grey Scale findings 47 (42.7%)	Power Doppler findings 38 (34.5%)
		Synovitis	
Hands		**31 (28.2%)**	**25 (22.7%)**
	Wrist	28 (25.5%)	20 (18.2%)
	MCP	19 (17.3%)	16 (14.5%)
	PIP	4 (3.6%)	2 (1.8%)
Feet		**16 (14.5%)**	**8 (7.2%)**
	Ankle	5 (4.5%)	4 (3.6%)
	Tarsal joints	3 (2.7%)	3 (2.7%)
	MTP	9 (8.2%)	2 (1.8%)
		Tenosynovitis	
Hands		**13 (11.8%)**	**10 (9.1%)**
	2nd, 3rd, 4th or 5th flexor	7 (6.4%)	5 (4.5%)
	4th extensor	1 (0.9%)	0 (0%)
	6th extensor	6 (5.5%)	6 (5.5%)
Feet		**4 (3.6%)**	**4 (3.6%)**
	Tibialis anterior	0 (0%)	0 (0%)
	Posterior tibialis	3 (2.7%)	3 (2.7%)
	Peroneus	1 (0.9%)	1 (0.9%)
		Erosions	
Total		**9 (8.2%)**	-
Hand		**6 (5.4%)**	
Feet		3 (2.7%)	-

the EULAR guidelines. All US examinations were performed by the same rheumatologist, unaware of the physical exam by the referring rheumatologist. The presence of synovitis and tenosynovitis was assessed on a semiquantitative scale (0-3) for gray scale (GS) and PD, respectively. Active US inflammation was defined as synovitis and/or tenosynovitis with PD signal grade ≥1 at any location. RA diagnosis according to clinician criteria 6 months after the US examination was checked. Univariate and multivariate logistic regression models were employed to investigate possible predictive factors of RA development.

Results: A total of 110 CSA patients (80 females, mean age 53.6 years) were included for analysis., Baseline characteristics of the patients with and without development of RA are shown in Table 1. US active inflammation was

present in 38 (34.5%) patients (28.2% showed PD synovitis and 19.1% PD tenosynovitis) (Table 2). After 6 months of follow up, 14 (36.8%) of the patients with US active inflammation at baseline evolved toward RA, while none of the patients without PD findings (p< 0.01) had the same evolution. In those patients who evolved to RA, the presence of GS and PD findings at US examination were significantly higher at baseline versus those who did not (100% vs 35.4%, p >0.001 and 100% vs 25%, p >0.001, respectively). Higher ACPA levels, but not RF, were also found to be associated with RA development (462±693.4 vs 30.2±127.6, p< 0.001). In the multivariate analysis, only ACPA (OR 1.004; 95%CI 1-1.007) and the presence of PD US findings at baseline (OR 13.1; CI 1.07-161.04) were found to be independent predictive factors of an evolution towards RA.

Conclusion: US is able to detect features of subclinical inflammation in CSA patients. Both ACPA and the presence of PD findings at baseline US assessment are independent predictors of RA development in CSA patients.

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Abstract Number: 1200

Predicting Progression to RA in Patients with Seropositive Arthralgia

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic inflammatory condition often associated with joint destruction, disability, and reduced life expectancy. Before RA diagnosis, some patients may present with seropositive arthralgia characterised by pain and/or stiffness without any clinical evidence of inflammation.

Seropositive arthralgia patients RA defined as joint pain without swelling, positive anti-citrullinated peptide antibodies (ACPA) or IgM rheumatoid factor (RF) are 'at risk' of developing RA. In this study we examine the knee arthroscopy and synovial biopsy features of 'at risk' patients for evidence of subclinical inflammation and assess its ability to predict progression to RA.

Methods: Seropositive arthralgia patients underwent needle arthroscopy and synovial biopsy of a knee joint. . The degree of synovitis and vascularity were recorded on a 0-100mm visual analogue scale. The synovium was examined by routine histology of H&E staining. Patients were followed up at regular intervals (3 months, 6 months and1 year) with a clinical assessment and laboratory investigations to evaluate if they developed RA according to the ACR/EULAR 2010 criteria.

Table 1. Baseline demographics and scope data

Demographic		
Female gender, n (%)		31 (67.4)
Age, mean (S.D.) years		57 (14.2)
Risk factors		
ACPA, positive n(%)		41 (89.1)
RF, positive, n(%)		40 (86.9)
ACPA and RF positive, n(%)		35 (76)
Smoking status		
Current smoker, n(%)		11 (23.9)
Ex-smoker n(%)		12 (26.1)
Family history of RA, n(%)		15 (32.6)
Disease Characteristics	At presentation (T0)	
Symptoms Onset		
Gradual > 1 week, n (%)		36 (78.3)
Subacute <1 week n(%)		10 (21.7)
Knee pain at presentation, n(%)		23 (50)
	At presentation (T0)	At scope (T1)
CRP, median (IQR)	3 (1-5.5)	4 (2-8.2)
TJC, median (IQR)	0 (0-1)	1 (0-4.25)
SJC, median (IQR)	0 (0-0)	0 (0-2.5)
Scope Data	At scope (T1)	
Scope DAS28-CRP, mean (S.D)		3.13 (1.39)
Scope vascularity mean (S.D.)		52.17 (23.84)
Scope synovitis mean (S.D.)		48.78 (24.72)
Features of synovial inflammation		14 (30.40)
Synovial hyperplasia, n(%)		3 (6.53)
Vascular proliferation, n(%)		5 (10.87)
Inflammatory infiltrate, n(%)		

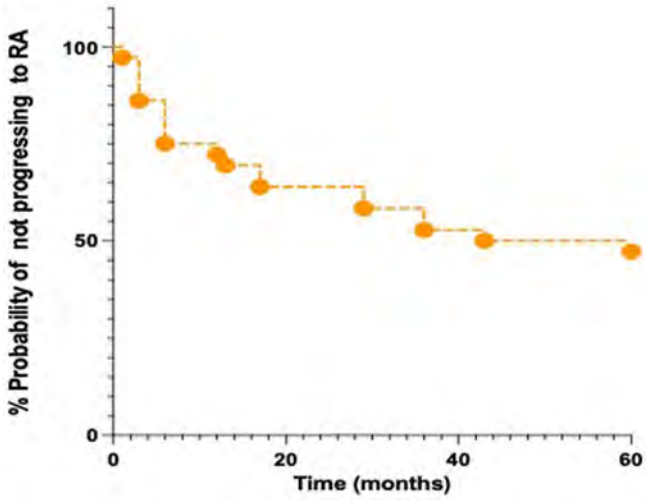

Figure 1. Kaplin-Meier Curve of the timeline of patients converting to RA.

Results: A total of 46 patients were recruited, 78% developed RA. X length of follow up. Patient demographics are outlined in Table 1. Family history, smoking and early morning stiffness were not predictive of developing RA. A statistically significant correlation was found between ACPA levels of >340 and the development of RA (P=.03). A synovitis or vascularity score of greater than 50% at arthroscopy significantly correlated with RA development (P=.04; P=.002,

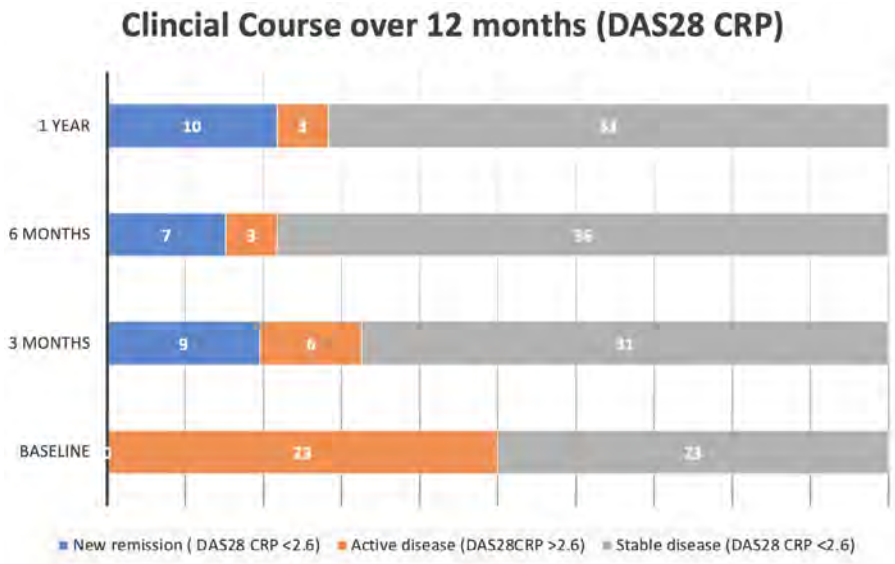

Figure 2. Clinical course over 12 months from scope (T1).

respectively). If a patient had both synovitis and vascularity score of 50%, it was strongly associated with progression to RA (P< .001).

If treated with conventional synthetic(cs) DMARDs for arthralgia, the median time for developing RA was 12 months compared to 3 months in those who did not receive treatment. Figure 1 outlines time to developing RA. The clinical course of the patients over 12 months is outlined in Figure 2.

Conclusion: Seropositive arthralgia patients 'At risk' of developing RA demonstrate >50% macroscopic synovitis or vascularity score at knee arthroscopy. ACPA titre > 340 is associated with progression and csDMARD treatment may delay, but not prevent, onset of RA .

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Abstract Number: 1201

Younger Age and Smoking Status Are Associated with Delayed Diagnosis of Rheumatoid Arthritis in a U.S. Veteran Population

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Baseline Characteristics of Patients with Early vs Delayed Diagnosis of RA

	< 6 mo. (n = 485)	≥ 6 mo. + <5 yrs. (n = 969)	p
Male Gender (%)	428 (88.08)	850 (88.80)	0.69
Positive Family History (%)	144 (32.4)	295 (33.5)	0.72
Current Tobacco Use (%)	108 (22.74%)	272 (28.63%)	0.04
Former Tobacco Use (%)	256 (53.89%)	488 (51.37%)	
Never Tobacco Use (%)	111 (23.37%)	190 (20.00%)	
Mean Time to Diagnosis (days)	86.7	595.2	<0.01
Mean Age at Diagnosis (years)	56.5	53.7	<0.01
Education > 12 years	233 (52.01%)	443 (49.55%)	0.40
Race, non-white	104 (21.49%)	210 (21.69%)	0.93
Positive RF* (%)	330 (73.4)	655 (75.5)	0.96
Positive CCP*	331 (75.7)	655 (75.6)	0.94
CRP >1mg/L (%)	283 (64.8)	563 (64.8)	0.99

**Positivity defined by manufacturer cut-off*

Table 2. Baseline and 2-year Disease Activity Measures of Patients with Early vs Delayed Diagnosis

Disease Activity Measures	< 6 mo. (IQR)	n/excluded	≥ 6 mo. + <5 yrs. (IQR)	n/excluded	p
Initial TJC	5 (10)	177 / 12	4 (10)	237 / 10	0.47
2-year TJC	1 (4)	231 / 6	1 (6)	325 / 11	0.17
Initial SJC	4 (7)	177 / 12	4 (7)	237 / 10	0.35
2-year SJC	0 (3)	231 / 6	1 (4)	325 / 11	0.28
Initial Rapid 3	10.6 (9.6)	173 / 16	9.5 (9.3)	223 / 24	0.25
2-year Rapid 3	7 (7.9)	215 / 22	9.3 (9.1)	289 / 47	<0.01
Initial CDAI	20 (19.8)	137 / 52	18.8 (18.7)	178 / 69	0.59
2-year CDAI	7.5 (10.6)	188 / 49	10.5 (17.7)	252 / 84	0.00
Initial DAS28 CRP	3.6 (2.2)	156 / 33	3.4 (2.1)	201 / 46	0.18
2-year DAS28 CRP	2.5 (1.6)	197 / 40	2.8 (2.1)	261 / 75	0.34
Initial DAS28 ESR	4 (2.2)	163 / 26	3.8 (2.1)	216 / 31	0.10
2-year DAS28 ESR	2.8 (2.0)	211 / 26	2.9 (2.1)	280 / 56	0.03

Background/Purpose: RA is a complex multisystem disease, which, untreated, results in debilitating joint damage, excess morbidity, and premature mortality. Previous research has demonstrated an association between early treatment and improved outcomes; however, there is often a delay between symptom onset and diagnosis. We investigated the demographic and clinical features associated with delay in RA diagnosis and the impact of delayed diagnosis on disease activity in U.S. Veterans.

Methods: We studied patients in the Veterans Affairs Rheumatoid Arthritis (VARA) registry which prospectively captures RA disease activity and severity measures from 12 VA Medical Centers. We included patients who reported a date of symptom onset within 5 years of RA diagnosis to avoid bias related to inaccurate recall. Patient demographics, date of symptom onset and diagnosis (collected by self-report at the time of enrollment); and the results of RF, Anti-CCP, CRP, and tender and swollen joint counts were extracted from the registry. Disease activity measures at

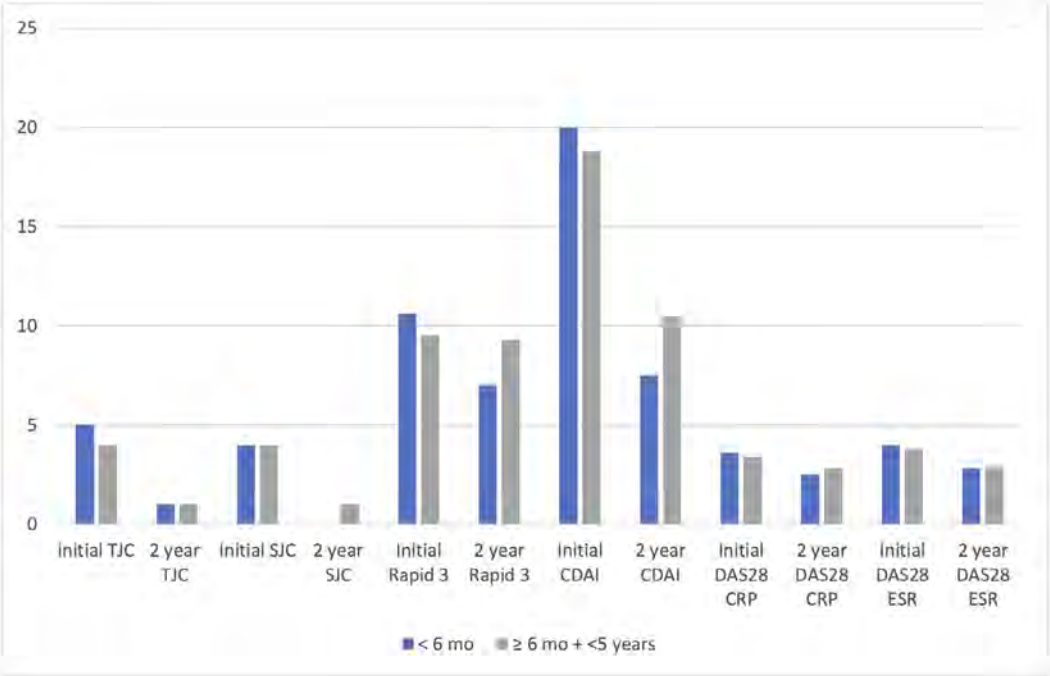

Figure 1. Baseline and 2-year Disease Activity Measures in Early vs Delayed Diagnosis.

enrollment, and 2-years after diagnosis, for RAPID3, CDAI, DAS28ESR and DAS28CRP were calculated. Early diagnosis was defined as diagnosis within 6 months of symptom onset. The relationship between pre-hypothesized study variables and the time to diagnosis was evaluated using contingency analysis and Kruskal-Wallis or Wilcoxon tests for non-normative data. Two-year post-diagnosis disease activity scores were averaged to estimate influence of a delay in diagnosis on subsequent disease control.

Results: At the time of the study there were 2,996 patients eligible for the study and 1,454 were included. The primary reasons for exclusion were patients unable to recall symptom onset date (1,169) and diagnosis date that was greater than 5 years after onset date (373). Of those included, 485 veterans were diagnosed within 6 months and 969 were diagnosed between 6 months and 5 years. Delayed diagnosis was associated with younger age, 53.7 years vs 56.2 years. (Table 1) Those with delayed diagnosis also had higher rates of current smoking. There were no significant differences in terms of family history of RA, education level, or race. No difference was noted in enrollment TJC, SJC, CRP, disease activity scores or rates of RF or CCP positivity. TJC and SJC also did not differ between groups at 2 years, however, there were lower median RAPID3 and CDAI scores in the early diagnosis group, as well as a larger change from baseline scores. No statistical difference was noted in the DAS28CRP scores at 2 years while the DAS-28ESR slightly favored the early group.

Conclusion: In this veteran cohort, where the model of access to care is substantially different from typical U.S. healthcare systems, traditional predictors of delay in RA diagnosis (older age, race, and education level) were not noted to contribute. While 2-year post diagnosis TJC and SJC were not different between the groups, differences in RAPID3 and CDAI suggest that earlier diagnosis may result in better long-term patient-reported outcomes. Additional research is needed to understand why younger age and smoking might lead to delayed diagnosis.

Disclosure: S. Taylor, None; **B. England**, Boehringer-Ingelheim, 2; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **B. Sauer**, None; **J. Richards**, None.

Abstract Number: 1202

Widespread but Not Regional Non-articular Pain Influences Patient and Rheumatologist Reported Change in Clinical Disease Activity Index Scores over Time - Implications for Using Patient Ratings in Telehealth – a Study from the Canadian Early Arthritis Cohort

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: During the COVID pandemic assessments of RA disease activity (DA) have relied on virtual assessments by patient report. It is unknown whether non-articular pain might influence these. We sought to determine if patient reported Non-Articular Pain (NAP) by body pain diagram (BPD) influences the agreement of change in

Table 1: Baseline characteristics of 210 Patients Stratified by Non-Articular Pain and Pattern by Body Pain Diagram Reported at 6 Months

Variable [Mean (SD) or Frequency (%)]	No pain (N=122)	Regional pain (N=65)	Widespread pain (N=23)
Socio-Demographic & lifestyle			
Age (years)	56 (14)	59 (12)	58 (14)
Female	80 (66%)	50 (77%)	19 (83%)
Education > high school	89 (73%)	40 (62%)	14 (61%)
Current Smoker	16 (13%)	6 (9%)	6 (26%)
Obese BMI (≥ 30)	32 (28%)	19 (32%)	9 (43%)
Rheumatic Disease Comorbidity Index (0-9)	1.0 (1.3)	1.6 (1.4)	1.5 (1.3)
RA Characteristics			
Meet RA criteria	97 (80%)	52 (80%)	15 (65%)
ACPA+/ RF+ (%)	63% / 57%	71% / 68%	55% / 52%
TJC (28) / SJC (28) (MD reported)	9 (7) / 9 (6)	9 (6) / 8 (5)	8 (6) / 7 (5)
TJC (28) / SJC (28) (PT reported)	10 (7) / 6 (7)	11 (8) / 8 (7)	10 (6) / 7 (8)
MD Global (0-10)	5.6 (2.4)	5.3 (2.1)	5.3 (2.5)
Patient Global (0-10)	5.0 (2.8)	4.7 (2.9)	6.6 (2.4)
MD-CDAI	28.6 (14.7)	26.1 (11.5)	27.3 (14.0)
PT-CDAI	27.4 (15.0)	28.9 (14.6)	29.2 (13.7)
RA Medication at Baseline			
Non-MTX csDMARD (excluding biologics)	68 (56%)	40 (62%)	12 (52%)
MTX use (+/- csDMARDs)	100 (82%)	47 (72%)	18 (78%)
Biologics or JAK Inhibitors	3 (2%)	1 (2%)	0 (0%)
Oral Glucocorticoids	26 (21%)	17 (26%)	8 (35%)

Table 2: Comparison of MD-CDAI and PT-CDAI scores from 3M and 6M Visits in patients stratified by Uncontrolled or Controlled Disease Activity and grouped as reporting no NAP, Regional or Widespread Pain at 6M

Patient Groups	Disease Activity	MD-CDAI 3M	PT-CDAI 3M	MD-CDAI 6M	PT-CDAI 6M
No NAP Pain (N=122)	Uncontrolled	61 (50%)	61 (50%)	37 (30%)	51 (42%)
	Controlled	61 (50%)	61 (50%)	85 (70%)	71 (58%)
	Kappa (95% CI)	0.57 (0.43, 0.72)		0.61 (0.47, 0.76)	
Regional Pain (N=65)	Uncontrolled	36 (55%)	43 (66%)	28 (43%)	34 (52%)
	Controlled	29 (45%)	22 (34%)	37 (57%)	31 (48%)
	Kappa (95% CI)	0.65 (0.47, 0.83)		0.63 (0.45, 0.82)	
Widespread Pain (N=23)	Uncontrolled	14 (61%)	19 (83%)	12 (52%)	17 (74%)
	Controlled	9 (39%)	4 (17%)	11 (48%)	6 (26%)
	Kappa (95% CI)	0.49 (0.16, 0.836)		0.38 (0.04, 0.72)	

Controlled Disease activity based on MD CDAI score of ≤ 10 at 6 months

Table 3: Change in MD and PT CDAI Scores between 3M and 6M timepoints in Patients Grouped by Non-Articular Pain at 6 months

NAP Group (N=210)	Difference in MD CDAI	Difference in PT CDAI	Difference in Change Scores
No NAP (N=122)	4.5 (9.3)	2.0 (10.3)	2.5 (9.5)
ICC (95% CI)		**0.51 (0.37, 0.63)**	
Regional pain (N=65)	3.6 (12.5)	1.8 (11.7)	1.8 (9.9)
ICC (95% CI)		**0.66 (0.49, 0.77)**	
Widespread pain (N=23)	1.1 (10.3)	1.30 (12.9)	-0.2 (14.5)
ICC (95% CI)		**0.25 (-0.17, 0.59)**	

clinical disease activity index (CDAI) scores over 3 months as rated by rheumatologist (MD) and patient (PT), comparing a previously validated PT CDAI and the standard MD CDAI. We hypothesized agreement would be similar for PT- and MD- CDAI ratings in patients without NAP or regional NAP (RP) but would be worse in patients with widespread NAP (WSP).

Methods: Data were from patients with early RA (Symptoms < 1 year) who were enrolled in CATCH between Mar 2017 and Mar 2021. All had complete data at 3- and 6- month (M) visits to calculate MD- and PT- CDAI scores. Patients had to have completed a BPD at each visit. Patients were classified as having regional RP (1 or 2 regions of pain on BPD), or WSP (3 or more regions of pain on BPD) at their 6M Visit. In CATCH MDs and patients separately identify tender/painful and swollen joints using a 28-joint count homunculus, and both report global assessments (GA) (NRS 0-10) at each visit. The PTCDAI score was the sum of PT-rated TJC28, SJC28, MDGA and PTGA (0-76). We compared PT and MD CDAI scores at 3M and 6M visits in all patients and in subgroups based on presence of and type of NAP. We then compared change in MD and PT CDAI scores between 3M to 6M visits stratified by NAP report and further stratified by disease activity control between 3M and 6M defining controlled as low disease activity or remission (LDA/REM) using a standard cut point of ≤ 10 by MD CDAI at 6M and active uncontrolled disease activity (high or moderate disease activity (HDA/MDA)). Simple Kappa and one way ICC were used to assess agreement for categorical and continuous measures.

Results: The sample included 210 participants with a mean (SD) age of 57 (13), symptom duration of 5.3 (2.8); 80% met RA criteria, 81% were white, 65%/60% were ACPA/RF positive. At 6 months 58% reported no NAP, 31% Regional Pain and 12% Widespread Pain. Patients with any NAP were older, mostly female, with more comorbidities, and higher PT CDAI scores compared to MD CDAI scores. More pts with WSP smoked and received glucocorticoids (Table 1). Agreement between PT and MD CDAI scores at 3M and 6M single time points, regardless of DA control was high for patients without NAP and with RP, but lower for patients reporting WSP (Table 2). Agreement for the change in MD and PT CDAI scores between 3M and 6M visits was high-moderate to high for pts without NAP, and RP but low for pts with WSP (Table 3).

Conclusion: PT CDAI scores at single time points, and the difference in scores between 3- and 6- month visits, were similar to MD CDAI scores for patients without NAP or with regional pain with good agreement, but agreement was poor for patients with WSP. These data suggest using caution in interpreting a PTCDAI in patients with a competing widespread pain disorder. It is possible regional NAP may represent RA-related inflammation such as tendinitis and may explain why agreement is still high in PT- and MD- CDAI scores.

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Abstract Number: 1203

A Change in a Patient Informed Clinical Disease Activity Index (PTCDAI) Is Similar to Their Rheumatologists CDAI When Following Patients with Early RA in the Canadian Early Arthritis Cohort (CATCH) Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Comparison of Overall Change in MD CDAI and PT CDAI scores between the 3 and 6 month follow up visits in 937 participants with complete data

Visit Month	3M	6 M	Change between 3M and 6M
MD CDAI	11.9 (10.9)	9.2 (9.7)	2.7 (10.3)
PT CDAI	15.2 (13.2)	13.1 (12.6)	2.2 (11.9)
ICC (95% CI)	0.65 (0.61, 0.68)	0.65 (0.61, 0.69)	0.59 (0.55, 0.63)

CDAI Scores are mean (SD). Scores and change in scores were compared using one-way random effects, single measure intraclass correlation coefficient (ICC) (95%CI)

Table 2: Mean differences of change in MD and PT CDAI disease activity ratings from 3M to 6M, stratified by change in disease control over 3 months

Disease Activity	Improved to Controlled			Worsened to Active			Remained Active			Remained Controlled		
MD-PT Δ differences	(N=184; 20%)			(N=84; 9%)			(N=227; 24%)			(N=442; 47%)		
	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD
MD CDAI	14.1	(12.7,15.4)	9.2	-12.2	(-14.1, -10.3)	8.8	2.2	(0.8, 3.6)	11.1	1.0	(0.7, 1.3)	3.5
PtCDAI	11.1	(9.5, 12.7)	11.1	-11	(-13.9, -8.1)	13.3	1.3	(-0.4, 3.0)	13.2	1.2	(0.5, 1.9)	7.8
MD-PT CDAI	3.0	(1.3, 4.7)	11.5	-1.2	(-3.7, 1.4)	11.7	0.9	(-0.7, 2.6)	12.7	-0.2	(-0.8, 0.4)	6.8

Change in Disease activity Control: defined as Improved (HDA/MDA to REM/LDA), Worsened (REM/LDA to MDA/HDA), No change remaining active (in HDA/MDA) or remaining controlled (REM/LDA) at both visits

Table 3: Agreement for differences between MD and Patients 3M to 6M Change Scores showing the ICC (95% CI) stratified by changes in control of disease activity in RA

	Improved to Controlled Disease	Worsened to Active Disease	Remained in Active Disease	Remained in Controlled Disease
Difference in MD – PT CDAI 3M to 6M Change Scores	0.34 (0.20, 0.46)	0.46 (0.28, 0.61)	0.45 (0.34, 0.55)	0.36 (0.28, 0.44)

One-way random effects, single measure ICC (95%CI) measures shown, Stratifications of change in disease activity states as controlled (REM/LDA) or uncontrolled (MDA/HDA) disease activity

Background/Purpose: The Clinical Disease Activity Index (CDAI) is a frequently used composite measure by rheumatologists (MD) in routine care used to guide target-based treatment decisions. During the COVID19 pandemic treatment decisions were made during telemedicine visits relying on patient (pt) reports. Virtual care will likely be used in future. We previously showed high agreement between MD- and PT- CDAI scores and control of disease activity (score ≤10) suggesting the PTCDAI can inform if a pt has achieved RA treatment targets. Our goal here was to determine if change scores in a proposed PTCDAI between 3M and 6M visits were similar to those of the reference MD CDAI, amongst patients with differing changes of disease activity to further assess the validity of a PTCDAI for use in virtual care. We hypothesized that differences between MD and PT CDAI change scores over 3 months will be similar whether or not patients remain in controlled/uncontrolled disease activity or not.

Methods: Data were from 937 pts with new onset inflammatory arthritis (Symptoms < 1 year) meeting criteria or MD diagnosis of RA, enrolled between Nov 2011 and July 2020 into the Canadian early ArThritis CoHort (CATCH) study. Eligible pts were all treated for RA and had complete data at 3- and 6- month (M) visits to calculate both CDAI scores. MDs and PTs independently rated 28-tender/painful and 28-swollen joint counts (TJC28/SJC28) using a homunculus, and provided respective global assessments (GA) (NRS 0-10). The PTCDAI score was the sum of Pt rated TJC28, SJC28, MDGA and PtGA (0-76). Changes in MD-CDAI and PT-CDAI scores were compared between 3M and 6M visits. The MD-CDAI cut point of ≤10 was used to identify pts with controlled [remission/low DA (REM/ LDA)] vs. uncontrolled (active) [high/moderate DA (MDA/HDA)] RA. Descriptive statistics were used to summarize and compare 3M and 6M change measures. A simple kappa or one-way, random effects, single measure ICC was used to assess agreement of change.

Results: At baseline, 937 pts had a mean (SD) age of 56 (15), symptoms of 5.5 (2.9) (mos), comorbidity score 1.2 (1.3); 70% were female, 81% white, 14% smokers, 30% BMI ≥ 30, 80% met RA criteria, 65%/60% ACPA+/RF+. CDAI scores were: MD CDAI 25.0 (14.1), PtCDAI 27.5 (15.9). All were treated with csDMARDs (73% methotrexate). There was high agreement between change in either CDAI (Table1). The change in MD- and PT-CDAI scores from 3M to 6M, stratified by a change or not in disease control were numerically similar and as clinically expected (Table 2). Agreement between MD and Pt CDAI change scores over 3M to 6M was moderate across disease control strata. As disease state improved or worsened, or when disease remained active, ratings of change in MD and PT-CDAI were well aligned but there was more variability in change ratings as disease activity improved, with patients rating less improvement than the MDs (Table 3).

Conclusion: These data provide additional evidence for the reliability of change in PTCDAI scores between 2 visits and warrant evaluation of the PT CDAI in future studies of outcomes for use in virtual care and telemedicine.

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Abstract Number: 1204

CXCL13 Outranges DAS28CRP and CRP as Predictor of Long-term Radiographic Status in Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: In a cohort of early rheumatoid arthritis (eRA) patients, we recently showed that early and aggressive treatment led to remission and limited erosive progression at 11 years. Anti-citrullinated protein antibody (ACPA), a high degree of inflammation (DAS28crp) and MRI bone marrow oedema predicted long term radiographic progression at 11 years (Scand J Rheumatol 2018, 48: 1-8). In this cohort, we investigated plasma levels of CXCL13, and its ability to predict radiographic joint destruction.

Methods: In a post-hoc study, a serial set of plasma samples was obtained from the investigator-initiated CIMESTRA study (n=117). CXCL13 was measured at baseline and after 1 year. Patients were characterized and monitored by C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), Disease Activity Score in 28 joint (DAS28), swollen joint count in 28 joints (SJC28), health assessment questionnaire (HAQ) and global visual analogue scales (VAS). IgM-rheumatoid factor (IgM-RF) and ACPA status was recorded at baseline. Cumulative dose of glucocorticoid injections was recorded. Radiographic status and progression were assessed by total Sharp Score (TSS) at baseline and 11 years. Data were analysed using Wilcoxon matched pairs-signed rank test (Median (25-75 percentile), multivariate regression analysis (coefficient +/- standard error), Spearman correlation (rho) and ROC curves, determining the threshold for radiographic damage as a score of 5, applicable for TSS and deltaTSS.

Results: In eRA patients, plasma levels of CXCL13 were increased (60 pg/ml (39-102) and decreased after one year of treatment (31 pg/ml (23-49) ($p< 0.0001$). By Spearman correlation analyses, baseline levels of CXCL13 were associated with CRP (0.50), ESR (0.49), ACPA (0.39), IgM-RF (0.38), VAS Global (0.27), HAQ (0.38), and DAS28CRP (0.27), all $p< 0.05$.

In a multivariate regression analysis, adjusting for smoking status, age, gender, ACPA status, CRP, number of glucocorticoid injections, SJC28 and ESR, baseline CXCL13 was associated with both TSS (0.11 +/- 0.04, p=0.004) and deltaTSS (0.07 +/- 0.03, p=0.042) after 11 years of treatment (Figure 1). The predictive value of baseline CXCL13 for

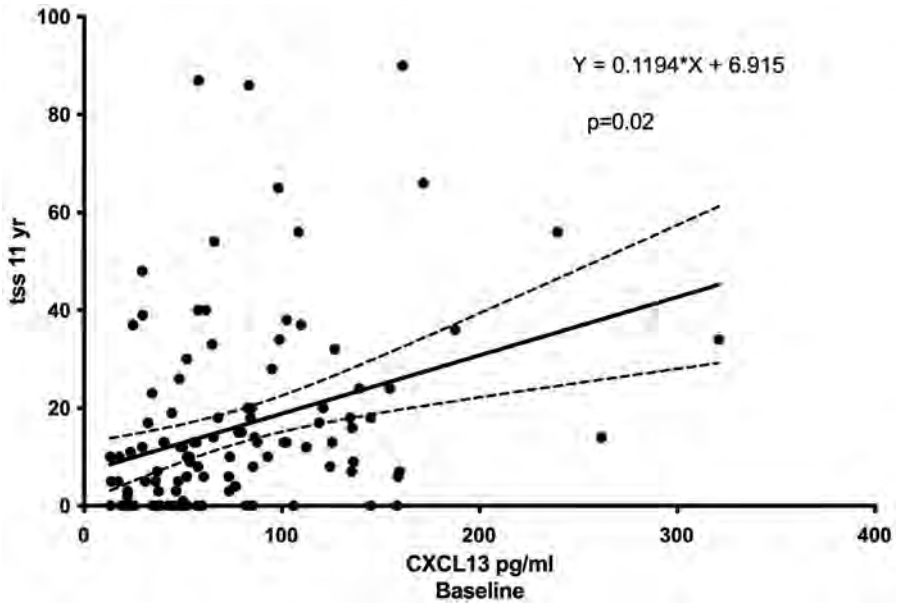
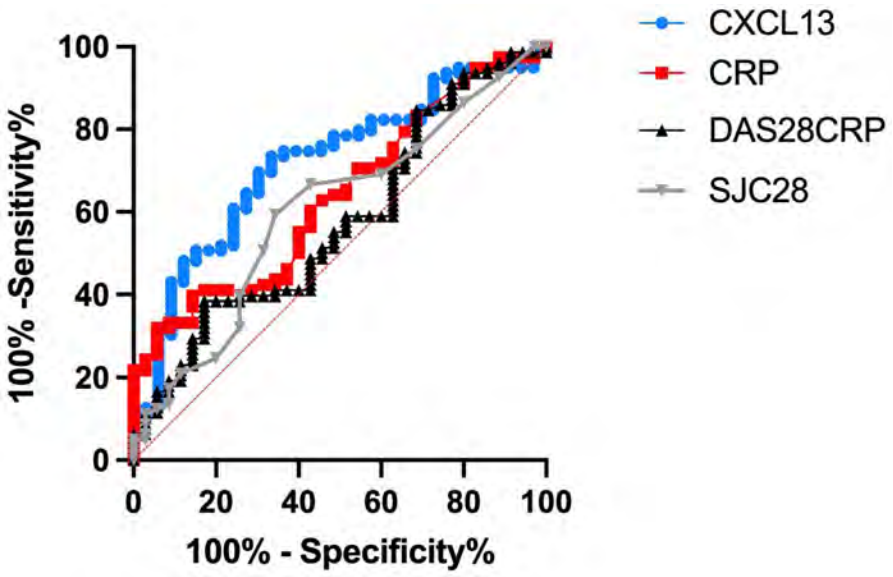


Figure 1. Plot of baseline CXCL13 and TSS after 11 years of treatment.



ROC curves of CXCL13, CRP, DAS28CRP and SJC28 predicting TSS above 5 after 11 years of treatment. A TSS score of 5 or above is considered as significant radiographic progression, as this accounts for one destroyed joint.

TSS >5 at 11 years was illustrated in the ROC curve with an area under curve (AUC) of 0.72, p< 0.001 (Figure 2). AUC for DAS28CRP was: 0.58, p=0.2, for CRP: 0.64, p=0.02 and for ACPA: 0.59, p=0.34. Based on the ROC curve, selecting the highest possible sensitivity and specificity of both 70%, CXCL13 levels above 53 pg/ml predicted significant radiographic destruction after 11 years with a likelihood ratio of 2.3.

Numbers of glucocorticoid injections did not differ between patients with an 11-year TSS< 5 and TSS >5.

A similar analysis was done for baseline CXCL13 and deltaTSS at 11 years, also supporting a predictive value of baseline CXCL13 for radiographic progression (AUC=0.62, p=0.03).

Conclusion: Predicting long-term radiographic destruction in patients with newly diagnosed RA remains challenging. Here, we suggest plasma CXCL13 as a reliable marker of long-term disease severity in RA, especially predicting significant radiographic destruction after more than 10 years of treatment.

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Abstract Number: 1205

Predictors of Discordance Between Patient and Physician Global Assessment in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: The patient's global assessment (PGA) and physician global assessment (PhGA) are important outcomes and commonly used in rheumatoid arthritis (RA) clinical practice. Both measures are included as a part of activity indices and core sets. Up to half of patients have been reported to have discordant results between the two measurements, depending on the cut-off value. PGA was usually higher than PhGA. Understanding the reasons of this discrepancy might be important to decide treatment strategy. We aim to evaluate frequency and predictors of discordance between PGA and PhGA in patients with RA.

Methods: Two hundred-thirty three consecutive RA patients were recruited to this single center cross-sectional study. All participants met the ACR 2010 classification criteria. Demographics, clinical parameters and laboratory

Table 1. Demographics and disease characteristics of study groups

Variables	Discordance ≥30 mm (n:35)	Discordance <30 mm (n:198)	P
Age, mean (SD)	56.7 (12.2)	56.4 (11.1)	0.763
Female gender, n (%)	24 (68.6)	161 (81.3)	0.086
Disease duration, years mean (SD)	9.0 (8.6)	10.4 (8.6)	0.244
Smoking ever, n (%)	19 (54.3)	84 (43.3)	0.229
Body mass index, mean (SD)	27.8 (4.5)	28.3 (5.4)	0.827
PGA (0-100 mm), mean (SD)	73.2 (15.9)	41.5 (24.6)	**<0.001**
PhGA (0-100 mm), mean (SD)	25.7 (14.8)	26.6 (20.5)	0.929
VAS pain (0-100 mm), mean (SD)	59.5 (26.8)	45.0 (28.0)	**0.003**
TJC, mean (SD)	1.8 (2.4)	3.9 (4.7)	**0.041**
SJC, mean (SD)	0.2 (0.5)	1.0 (2.4)	**0.037**
ESR (mm/h), mean (SD)	27.4 (18.7)	30.1 (10.2)	0.328
CRP (mg/L), mean (SD)	4.0 (8.1)	10.2 (15.8)	**0.020**
HAQ, mean (SD)	1.0 (0.9)	1.3 (1.0)	0.625
DAS28 CRP, mean (SD)	2.9 (0.9)	3.0 (1.3)	0.677
CDAI			
Remission, n (%)	1 (2.9)	37 (18.7)	**0.025**
Low disease activity, n (%)	16 (45.7)	75 (37.9)	
Moderate disease activity, n (%)	17 (48.6)	64 (32.3)	
High disease activity, n (%)	1 (2.9)	22 (11.1)	
Treatment			
Methotrexate, n (%)	24 (68.6)	112 (56.6)	0.184
Leflunomide, n (%)	11 (31.4)	58 (29.4)	0.813
Corticosteroid, n (%)	26 (74.3)	127 (64.1)	0.244
Biologic drugs, n (%)	5 (14.3)	47 (23.9)	0.211

Table 2. Correlation analyses results with PGA, PhGA and ΔPhGA-PGA

Variables	PGA		PhGA		ΔPhGA-PGA	
	r	*p*	*r*	*p*	*r*	*p*
Age	0.021	0.748	-.006	0.922	-.053	0.413
Disease duration	0.012	0.856	0.030	0.651	0.018	0.787
BMI	0.010	0.877	0.010	0.877	-.027	0.689
TJC	**0.447**	**<0.001**	**0.666**	**<0.001**	0.048	0.460
SJC	**0.300**	**<0.001**	**0.580**	**<0.001**	**0.252**	**<0.001**
VAS Pain	**0.706**	**<0.001**	**0.677**	**<0.001**	**-.370**	**<0.001**
ESR	0.054	0.406	0.097	0.140	0.007	0.917
CRP	0.064	0.328	**0.184**	**0.005**	0.073	0.266
CDAI	**0.775**	**<0.001**	**0.893**	**<0.001**	**-.206**	**0.001**

Table 3. Predictors of discordance between PGA and PhGA

Variables	Univariable Analyses			Multivariable Analyses		
	OR	95 % CI	p	OR	95 % CI	p
Gender (Male vs Female)	1.9	0.89-4.4	0.090	**2.8**	**1.1-6.9**	**0.020**
TJC (Absent vs Present)	1.6	0.80-3.5	0.164	1.9	0.77-4.6	0.158
SJC (Absent vs Present)	2.4	0.90-6.6	0.076	2.2	0.74-6.9	0.147
VAS pain (≥40mm vs <40 mm)	2.9	1.09-7.9	0.032	**4.4**	**1.4-13.0**	**0.007**
CRP (<5.0 mg/L vs ≥5.0 mg/L)	2.7	1.1-6.2	0.019	**3.0**	**1.2-7.7**	**0.019**

data were collected by using a structured form. Tender (TJC) and swollen joint count (SJC) was assessed by the same rheumatologist. Disease activity was evaluated by using clinical disease activity index (CDAI) and disease activity score 28 -C-reactive protein (DAS28-CRP). PGA, PhGA and pain were measured on a visual analog scale (VAS) ranging between 0 to 100 mm. Discordance was defined as more than 30 mm differences between PGA and PhGA. Spearman correlation and logistic regression analyses were used for association and predictors of discordance. In the multivariable model, we used independent variables which were found to have a p value of < 0.20 in univariate analyses.

Results: One hundred eighty-five (79.3 %) of the 233 patients were female, and the mean age was 56.7 ± 11.4 years. The frequency of discordance was found 15% (35/233) cut-off for ≥30 mm and 59.7% (139/233) for ≥20 mm. Age and gender were found similar in patient with or without discordance and the other demographics and clinical characteristics were summarized in table 1. Patients with discordant assessments had less tender and swollen joint count with less pain score on VAS. And also, discordance was found lower in remission and high disease activity group according to the CDAI. Difference between PGA and PhGA had been shown positively correlated with pain VAS but negatively with SJC and CDAI (Table 2). In multivariable model, male sex, having higher pain VAS and normal CRP levels were found to be predictors of discordance on PGA and PhGA (Table 3).

Conclusion: Discordance between patient and physician was more common in the absence of objective findings such as TJC, SJC and CRP. However male sex, higher VAS pain and normal level of CRP might independently predict disagreement. The majority of the problem was observed in patients with low and moderate disease activity. This can be affected the treatment decision of physician.

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Abstract Number: 1206

Serum Levels of Total IgA Anti-cyclic Citrullinated Protein Antibodies Predict 11-year Radiographic Outcome in Early Rheumatoid Arthritis

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SESSION INFORMATION

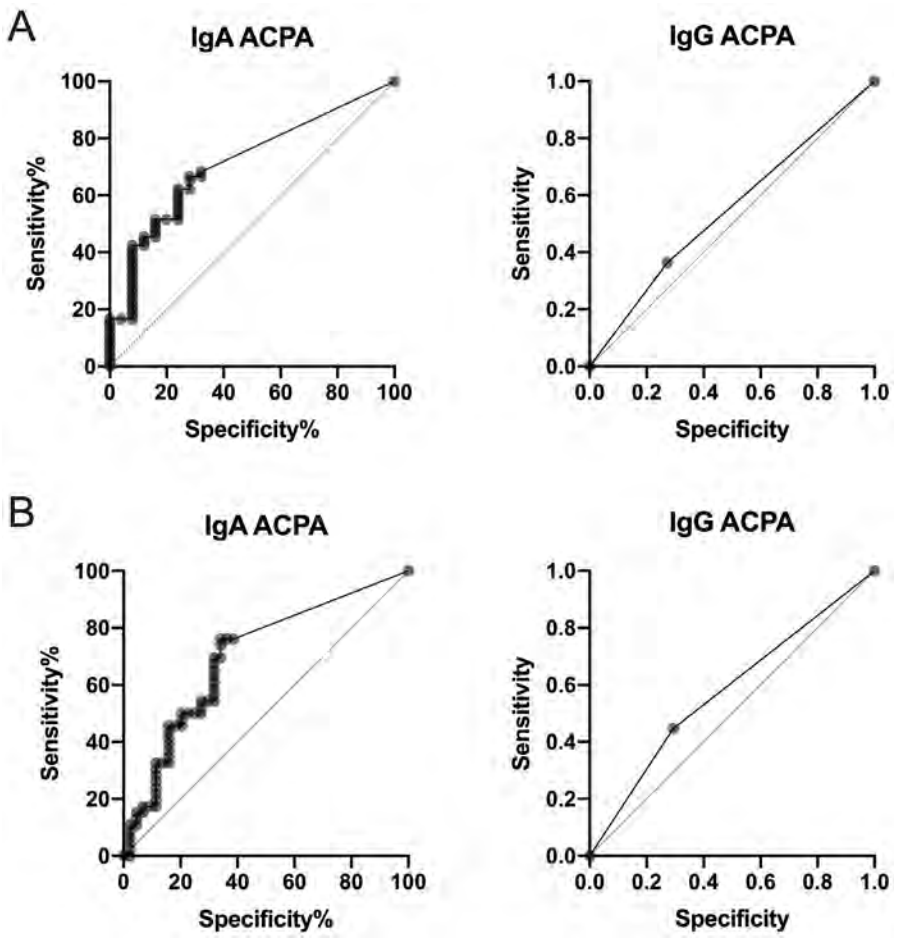
Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by polyarticular synovitis and frequent occurrence of autoantibodies, playing a central role in disease progression. Anti-citrullinated peptide antibodies (ACPA) are as-



ROC curves showing sensitivity vs specificity for IgA ACPA and IgG ACPA. Panel A shows data from TSS, and panel B shows data from ΔTSS. A cut-off value for no radiographic changes was set to 5.

sociated with periodontitis, smoking and upper respiratory tract infections, suggesting a breach of tolerance on mucosal surfaces. Early and aggressive treatment is important to limit long-term disease severity in RA, and seropositivity for APCA IgG is generally considered to be associated with a more aggressive disease. Here, we report the seroprevalence of ACPA IgA and its subtypes in patients with early (e), untreated RA and their association with long-term radiographic outcome.

Methods: The patients (n=121) included in this post hoc analysis participated in the investigator-initiated, double-blinded, placebo-controlled CIMESTRA study were treated with methotrexate and intraarticular glucocorticoids cyclosporin according to a treat-to-target protocol (Scand J Rheumatol 2018, 48: 1-8). Patient characteristics, IgM rheumatoid factor (IgM-RF) and IgG ACPA were recorded at baseline. Disease activity parameters included C-reactive protein (CRP), health assessment questionnaire (HAQ) and visual analogue scale (VAS), Disease Activity Score in 28 joints (DAS28) and swollen joint count in 28 joints (SJC28). Furthermore, structural joint damage was assessed with van der Heijde modified Total Sharp Score (TSS). All parameters were assessed at baseline and after 2 and 11 years. Total IgA, IgA1 and IgA2 ACPA were measured by ELISA at baseline and after 2 years. Statistical analyses and graphs were done using Prism 9 (GraphPad, Software). Correlations were tested using Spearman's rho (ρ).

Results: At baseline and after two years' treatment, total IgA, IgA1 and IgA2 ACPA were detectable in serum. Levels did not differ between baseline and 2 years. Baseline levels of ACPA IgA was associated to: IgG ACPA ($\rho = 0.62$), IgM rheumatoid factor ($\rho = 0.37$), gender ($\rho = 0.24$) and tender joints ($\rho = -0.20$), all p-values < 0.05. We considered a change in TSS ≥ 5 as significant radiographic progression. Using this cutoff, high baseline levels of total serum IgA (AUC = 0.71, $p = 0.002$) and IgA1 ACPA (AUC = 0.65, $p = 0.03$) predicted increased radiographic changes after 11 years, while IgA2 did not ($p = 0.12$). High baseline levels of total serum IgA (AUC = 0.70, $p = 0.001$) or IgA1 ACPA (AUC = 0.64, $p = 0.026$) also predicted high ΔTSS score (> 5). By contrast, total serum IgG ACPA did not predict a worsening of neither TSS ($p = 0.67$) nor ΔTSS ($p = 0.37$) after 11 years (Figure 1).

Conclusion: Our study confirms a role for IgA ACPA in patients with eRA and indicate that seropositivity for IgA ACPA is associated with a poor 11-year radiographic outcome in patients with eRA as measured by TSS. ACPA IgA and IgA1 are superior to ACPA IgG in predicting long-term rapid radiographic progression suggesting that there is a potential clinical gain by measuring ACPA IgA-subclasses in patients with eRA.

Disclosure: E. Rasmussen, None; **L. Thiele**, None; **K. Stengaard-Pedersen**, None; **M. Hetland**, Biogen, 2, 5, 6, Celltrion, 2, 6, Janssen Biologics B.V, 2, 6, MSD, 2, 6, Pfizer, 2, 5, 6, Samsung Bioepis, 2, 6, AbbVie, 5, BMS, 5, Eli Lilly Denmark A/S, 5, 12, personal fees, Lundbeck Fond, 5, Roche, 5, Sandoz, 5, Novartis, 5, Merck, 5, Orion Pharma, 12, personal fees, Medac, 6; **K. Horslev-Petersen**, None; **P. Junker**, None; **M. Ostergaard**, AbbVie, 2, 5, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Novartis, 2, 5, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Hospira, 2, 6, Janssen, 2, 6, Merck, 2, 5, 6, Novo, 2, 6, Orion, 2, 6, Pfizer Inc, 2, 6, Regeneron, 2, 6, Roche, 2, 6, UCB, 2, 6, GSK, 2, 6, Mundipharma, 2, 6, Schering-Plough, 2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **A. Hansen**, None; **M. Hvid**, None; **B. Deleuran**, None; **S. Greisen**, None.

Abstract Number: 1207

A Systematic Review Looking at the Relationship Between Serum Calprotectin and Ultrasound Parameters in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Serum Calprotectin level has been shown to correlate with disease activity, ultrasound (US) parameters, treatment response and clinical remission in rheumatoid arthritis (RA). The purpose of this study is to systematically review the existing literature on the relationship of calprotectin and ultrasound parameters in RA.

Methods: RA studies reporting serum calprotectin levels and US parameters published between 1 January 1988 to 26 December 2020 were included. A literature search was performed on Medline, Embase, CINAHL and Cochrane which yielded a total of 93 articles. After removing duplicates, screening remaining articles and selecting for full-texts, 11 articles were identified by 2 independent reviewers (Figure 1).

Results: A summary of the studies is shown in tables 1 and 2. Ten studies have shown associations between US findings and calprotectin levels in RA patients, seven of which used Spearman's correlation coefficient to show significant correlation between US power doppler (PD) and grey scale (GS) scores with calprotectin. When examining calprotectin in the context of treatment, calprotectin was shown to have a weak but significant correlation with US scores before and after treatment in Jonsson 2017 6. In patients monitored over their course of treatment with bDMARDs, (Nordal 2017 4) the strongest correlation was found between calprotectin and US sum scores at baseline. Calprotectin had the strongest correlation with US sum scores among patients started on etanercept and rituximab.

Figure 1. PRISMA chart

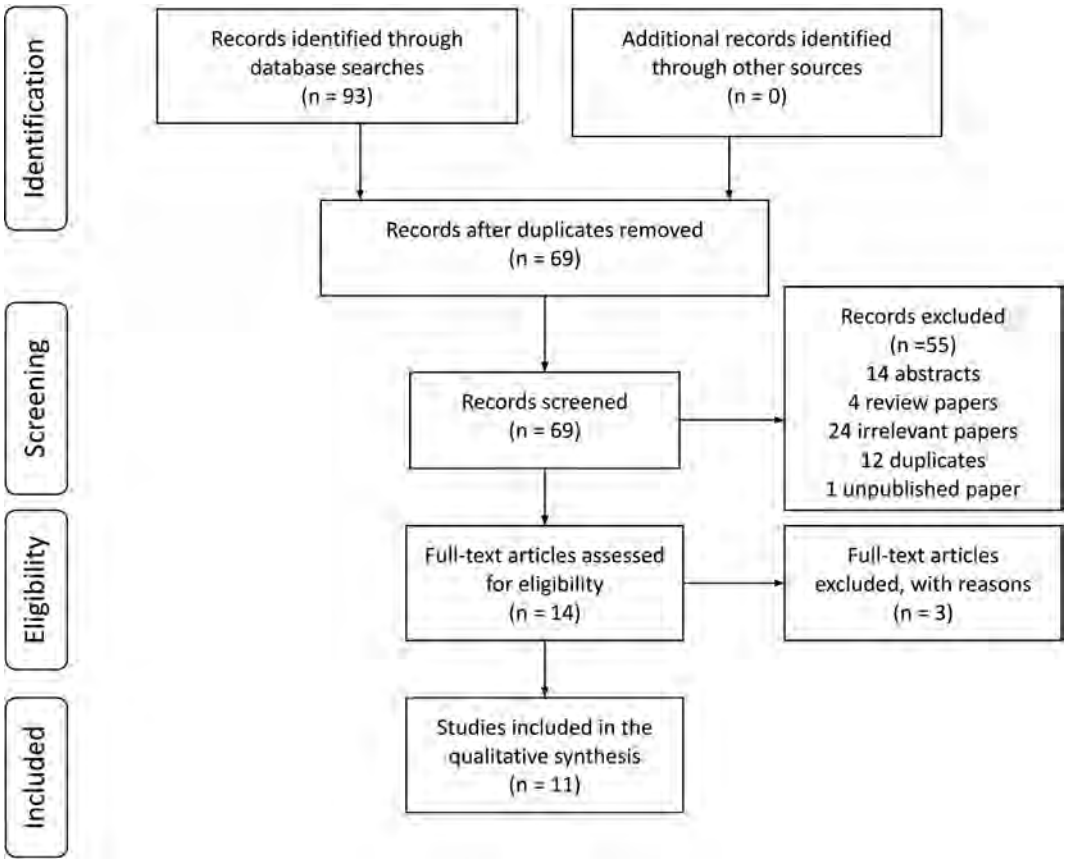

Table 1. Study Characteristics

Study	Year	Study Design	n	Inclusion/Exclusion Criteria	Sample	Ultrasound for Synovitis	Results
Jarlborg et al[1]	2020	CC	969	NR	Serum	4-point scale GS score of +/= 10 or PD score >/= 1 for 22 joints constitute positive SONAR score	Calprotectin (R2 = 0.10, p < 0.001) were associated with elevated USPD scores. Calprotectin could better predict positive SONAR score in disease duration <5 years with AUC 0.72 (95% CI 0.73-0.83) vs AUC 0.65 (95% CI 0.57-0.73) in all patients.
Sakellariou et al[2]	2019	CS	78	Include: -Fulfil CASPAR criteria -Present at EAC of IRCCS Policlinico San Matteo Foundation, Pavia -Present before May 2014 -Morning stiffness >30mins, swelling of 3 or more joints, positive squeeze test	Serum	4-point scale GS and PD >0, pre-specified GS and PD>1 in case of frequent low grade US abnormalities in healthy subjects defined as synovitis: with overall scores of 0 to 36 from sum of single sites	In regression analysis, calprotectin did not predict GS or PD score (R2 0.037, p=0.139 for GS; R2 0.017, p=0.319 for PD).
Nordal et al[3]	2017	Cohort	141	On bDMARD	Plasma Serum	4-point scale 36 joints and 4 tendon sheaths	At baseline, plasma and serum calprotectin showed significant correlation with sum GS. (Plasma = 0.59, p<0.001; serum calprotectin = 0.43, p<0.001). In concordance with sum PD score, plasma = 0.62, p<0.001 and serum = 0.46, p<0.001.
Nordal et al[4]	2017	CS	141	NR	Serum	4-point scale 36 joints and 4 tendon sheaths Weighting of joint according to method of Lansbury	Spearman rank coefficient correlation of serum calprotectin and US parameters at baseline showed strongest association, with 0.59 for sum GS scores, 0.62 for sum PD scores.
Mansour et al[5]	2017	CC	44	NR	Plasma	4-point scale	ANOVA analysis showed US B-mode scores had a statistically significant positive correlation with serum calprotectin levels in RA patients, with F test = 8.050 (p < 0.001).
Jonsson et al[6]	2017	CS	215	Include: -Fulfil ACR/EULAR criteria -DMARD-naïve with indication for DMARD therapy	Plasma	4-point scale 32 joints Ultrasound remission defined as no PD signal in any examined joint	Calprotectin was weakly to moderately correlated with ultrasound scores before treatment onset (US GS = 0.46, p<0.001; US PD = 0.42, p<0.001) and after 12 months of treatment (US GS = 0.20, p<0.01; US PD = 0.27, p<0.001).
Hurnakova et al[7]	2017	CS	150	NR	Serum	4-point scale Modified German US7 score	Calprotectin was significantly correlated with GS (r = 0.379, p<0.001) and PD synovitis scores (r = 0.419, p<0.001).
Inciarte-Mundo et al[8]	2016	CS	42	Exclude: DAS28-ESR >3.2	Serum	4-point scale Active synovitis defined as PD signal in any examined synovial tissue and SH grade >/=2	Calprotectin positively correlated with ultrasound scores (all r coefficients >0.50 in RA). Calprotectin had an AUC of 0.826 in predicting PDUS synovitis.
Hurnakova et al[9]	2016	CC	70	NR	Serum	4-point scale Modified German US7 score Ultrasound remission defined as GS 0-1 AND PD = 0.	Calprotectin correctly distinguished ultrasound remission (AUC DAS28-ESR = 0.692; AUC DAS28-CRP = 0.712) from subclinical activity in 70% of patients.
Hurnakova et al[10]	2015	CS	37	NR	Serum	4-point scale Modified German US7 score	Calprotectin was significantly associated with GS (r = 0.359, p < 0.05) and PD synovitis scores (r = 0.497, p < 0.005).
Hammer et al[11]	2011	Cohort	20	NR	Plasma	4-point scale 78 joints and 56 tendonn/tendon groups	Calprotectin had the highest correlation coefficients with the total BM and PD sum scores (median (range) 0.59 (0.37 to 0.76) for BM and 0.56 (0.38 to 0.72) for PD) as well as the highest Standardised Response Mean (0.84 at one month).

CC = case control, CS = cross sectional, NR = not reported, GS = grey scale, PD = power doppler, SH = synovial hypertrophy.

[1]Jarlborg, M., Courvoisier, D. S., Lamacchia, C., Martinez Prat, L., Mahler, M., ... Nissen, M. J. (2020). Serum calprotectin: a promising biomarker in rheumatoid arthritis and axial spondyloarthritis. Arthritis Research & Therapy, 22(1). doi:10.1186/s13075-020-02190-3

[2]Sakellariou G., Lorenzini G., Vitolo B., Gomarasca M., Faraldi M., Capogni R., Boffi G., Montecucco C. (2019) Serum calprotectin as a marker of ultrasound-detected synovitis in early psoriatic and rheumatoid arthritis: results from a cross-sectional retrospective study. Clin Exp Rheumatol. 2019 May-Jun;37(3):429-436. Epub 2018 Oct 8. PMID: 30299248.

[3]Nordal, H. H., Fagerhol, M. K., Halse, A.-K., & Hammer, H. B. (2017). Calprotectin (S100A8/A9) should preferably be measured in EDTA-plasma: results from a longitudinal study of patients with rheumatoid arthritis. Scandinavian Journal of Clinical and Laboratory Investigation, 78(1-2), 102–108. doi:10.1080/00365513.2017.1419371

[4]Nordal, H. H., Brokstad, K. A., Solheim, M., Halse, A.-K., Kvien, T. K., & Hammer, H. B. (2017). Calprotectin (S100A8/A9) has the strongest association with ultrasound-detected synovitis and predicts response to biologic treatment: results from a longitudinal study of patients with established rheumatoid arthritis. Arthritis Research & Therapy, 19(1). doi:10.1186/s13075-016-1201-0

[5]Mansour, H. E., Abdulrhman, M. A., Mahkadar, S. A., El Maliah, R., Abura, N., Hamed, F., & Farouh Khalil, A. A. (2017). Serum Calprotectin in Rheumatoid Arthritis: A Promising Diagnostic Marker, How Far is it Related to Activity and Sonographic Findings? Journal of Medical Ultrasound, 25(1), 40–46. doi:10.1016/j.jmu.2016.11.001

[6]Jonsson, M. K., Sundlisæter, N. P., Nordal, H. H., Hammer, H. B., Aga, A.-B., Ohm, I. C., ... Haavardsholm, E. A. (2017). Calprotectin as a marker of inflammation in patients with early rheumatoid arthritis. Annals of the Rheumatic Diseases, 76(12), 2031–2037. doi:10.1136/annrheumdis-2017-211695

[7]Hurnakova, J., Hulejova, H., Zavada, J., Hanova, P., Komarc, M., Mann, H., ... Senolt, L. (2017). Relationship between serum calprotectin (S100A8/9) and clinical, laboratory and ultrasound parameters of disease activity in rheumatoid arthritis: A large cohort study. PLOS ONE, 12(8). e0183420. doi:10.1371/journal.pone.0183420

[8]Inciarte-Mundo, J., Ramirez, J., Hernández, M. V., Ruiz-Esquide, V., Cuervo, A., Cabrera-Villalba, S. P., ... Sanmartí, R. (2016). Calprotectin and TNF trough serum levels identify power Doppler ultrasound synovitis in rheumatoid arthritis and psoriatic arthritis patients in remission or with low disease activity. Arthritis Research & Therapy, 18(1). doi:10.1186/s13075-016-1032-z

[9]Hurnakova, J., Hulejova, H., Zavada, J., Komarc, M., Hanova, P., Klein, M., ... Senolt, L. (2016). Serum Calprotectin Discriminates Subclinical Disease Activity from Ultrasound-Defined Remission in Patients with Rheumatoid Arthritis in Clinical Remission. PLOS ONE, 11(11), e0165498. doi.10.1371/journal.pone.0165498

[10]Hurnakova, J., Zavada, J., Hanova, P., Hulejova, H., Klein, M., Mann, H., ... Senolt, L. (2015). Serum calprotectin (S100A8/9): an independent predictor of ultrasound synovitis in patients with rheumatoid arthritis. Arthritis Research & Therapy, 17(1). doi:10.1186/s13075-015-0764-5

[11]Hammer, H., Fagerhol, M. K., Wien, T., & Kvien, T. K. (2011). The soluble biomarker calprotectin (a S100 protein) is associated to ultrasonographic synovitis scores and is sensitive to change in patients with rheumatoid arthritis treated with adalimumab. Arthritis Research & Therapy, 13(5), R178. doi:10.1186/ar3503

Table 2. Patient characteristics

Study	Age (in years)	Sex, M/F	Disease Duration reported	RF+	ACPA+
Jarlborg et al[1]	Mean 57.6	250/719	Mean 10.9 years	672	606
Sakellariou et al[2]	Mean 51.9	22/56	Mean symptoms 134 days	31	24
Nordal et al[3]	Mean 54	27/114	Mean 6.8 years	100	109
Nordal et al[4]	Mean 54	27/114	Mean 6.8 years	100	109
Mansour et al[5]	Mean 50.773	10/34	NR	NR	23
Jonsson et al[6]	Mean 50.9	83/132	Mean 5.8 months	153	177
Hurnakova et al[7]	Mean 55	32/128	Mean 6.4 years	92	90
Inciarte-Mundo et al[8]	Mean 63.5	8/34	Median 15.5 years	NR	NR
Hurnakova et al[9]	Mean 56.7	19/51	NR	42	44
Hurnakova et al[10]	Mean 53.56	13/24	NR	21	22
Hammer et al[11]	Median 53	5/15	Mean 7.5 years	14	NR

refer to table 1 legend

When calprotectin was evaluated in its utility for defining ultrasound remission, it was found to be superior in its ability to distinguish ultrasound-defined active synovitis (UdAS) and non-UdAS compared to C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) Inciarte-Mundo 20168. Hurnakova 20169 also showed its ability to distinguish between patients in US remission and those with subclinical US disease activity. There was a significantly lower median calprotectin levels in patients with US remission at 1, 3 and 12-month interval. Additionally, Jalborg 20201 reported calprotectin could better predict positive SONAR score in patients with disease progression of less than 5 years [AUC 0.72 (95% CI 0.73-0.83) in all patients compared to AUC 0.65 (95% CI 0.57-0.73) in disease duration less than 5 years]

Sakellariou 2019 was the only study which showed no significant correlation between calprotectin levels and US PD and GS scores. In this study, calprotectin level was also unable to predict ultrasound synovitis2. Finally, Nordal 20173 analyzed plasma and serum calprotectin levels and showed a stronger correlation between plasma calprotectin and US parameters when compared to serum calprotectin.

Conclusion: The majority of studies found that calprotectin correlates with ultrasound synovitis in RA patients; some of which found that calprotectin was a better biomarker compared to traditionally used biomarkers such as ESR and CRP. Calprotectin was also found to be an independent predictor of ultrasound synovitis and was able to distinguish those in ultrasound remission from subclinical synovitis. This suggest that there is a role for serum calprotectin to help define a deeper remission state in RA.

Disclosure: A. Low, None; **F. Lim**, None; **M. Ma**, None.

Abstract Number: 1208

Composite Articular Index Including Acute Phase Reactants Should Not Be Used in Patients with Rheumatoid Arthritis Treated with Il6 Inhibitors but May Be Useful in Those Receiving Jak Inhibitors: Ultrasound Evidence

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SESSION INFORMATION
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Background/Purpose: IL6 inhibitors (IL6i) have a dramatic effect on the reduction of C reactive protein (CRP) that does not always correlate with a significant improvement in synovial inflammation in rheumatoid arthritis (RA). Measurement of inflammatory activity with composite articular indices including acute phase reactants (APR) in RA patients treated with IL6i is considered inadequate. Since Jak inhibitors (Jaki) also affect IL6 activity, the performance of these indices in correctly assessing disease activity has been questioned. Joint ultrasound is not included in the composite indices used in RA but is widely used in clinical practice and has a greater sensitivity than clinical exam in detecting active synovitis.

To compare inflammatory activity measured by joint ultrasound with the composite disease activity indices and APR in patients with RA treated with IL6i or Jaki.

Methods: Observational, cross-sectional study in consecutive RA patients (ACR/EULAR 2010) treated with IL6i (tocilizumab, sarilumab) or Jaki (tofacitinib, baricitinib). We evaluated demographic and serologic (autoantibodies, ESR, ultrasensitive (us) CRP) data, composite disease activity indices (DAS28, SDAI, CDAI, RAPID3), HAQ and therapies. Joint ultrasound of both hands was evaluated and graded according to Szudlarek's(1). A synovial hypertrophy (SH) score, power Doppler ultrasound (PDUS) and a total score (SH+PDUS) was obtained. A definition of active synovitis

Table 1: Patient characteristics by therapeutic group (1)

	IL-6 inhibitors (n=42)	JAK inhibitors (n=21)	Total (n=63)	P value
DEMOGRAPHIC VARIABLES				
Age	59.9 (34.0-79.4)	52.4 (26.4-84.7)	58.6 (26.4-84.7)	0.145
Female, n (%)	39 (92.9)	19 (90.5)	58 (92.1)	1
Seropositive (CCP o RF), n (%)	37 /88.1)	20 (92.5)	57 (90.5)	0.654
CCP, n (%)	34 (91.9)	19 (95.0)	53 (93.0)	1
FR, n (%)	31 (83.8)	17 (85.0)	48 (84.2)	1
Erosive disease, n (%)	34 (81.0)	13 (61.9)	47 (74.6)	0.102
Disease duration (years)	15.7 (3.47-37.5)	12.09 (0.2-34.3)	14.4 (0.18-37.51)	**0.040**
Previous biologic treatments	1 (0-4)	1 (0-7)	1 (0-7)	0.89
CONCOMITANT TREATMENT				
Treatment duration (months)	43.8 (7.9-139.9)	9.9 (2.9-77.7)	29.7 (2.9-139.9)	**<0.001**
Concomitant prednisone treatment, n (%)	17 (40.5)	12 (57.1)	29 (46.0)	0.211
Equivalent dose (mg)	2.5 (1.25-10)	5 (1.25-10)	2.5 (1.25-10)	0.586
Concomitant NSAID treatment, n (%)	13 (31.0)	2 (9.5)	15 (23.8)	0.60
Concomitant csDMARD treatment, n (%)	18 (42.9)	11 (52.4)	29 (46.0)	0.475
CLINICAL EVALUATION AND PATIENT-REPORTED RESULTS				
TJC28	2 (0-20)	3 (0.25)	2 (0-25)	0.591
SJC28	1 (0-7)	1 (0-9)	1 (0-9)	0.580
PGA	4 (0-8.5)	4 (0-7.5)	4 (0-8.5)	0.321
PhGA	3 (0-7)	3 (0-7)	3 (0-7)	0.111
VAS pain	3 (0-8)	4 (0-7.5)	3 (0-8)	0.433
DAS28	2.349 (0.970-5.06)	3.439 (1.502-7.294)	2.842 (0.970-7.294)	**0.002**
CDAI	8.5 (0-31)	13 (0-41)	10 (0-41)	0.240
SDAI	8.9 (0.40-31.40)	13.40 (0.40-42.91)	10.40 (0.40-42.91)	0.231
HAQ	0.88 (0.0-2.88)	0.75 (0.0-2.275)	0.88 (0.0-2.88)	0.421
Rapid3	8.6 (0-25.50)	9.0 (1-18)	8.7 (0-25.50)	0.560

developed was considered (SH ≥ 2 plus PD ≥1)(2). We compared the variables between IL6i and Jaki patients. Spearman`s correlation test was used to correlate ultrasound scores and clinical and laboratory parameters.

Results: We included 63 patients (92.1% female, median age 58.6 years, median disease duration 14.4 years, 93% seropositive (RF and/or ACPA). 42 patients were treated with IL6i and 21 with Jaki. Therapy duration was significantly lower in Jaki patients. No significant differences were observed in activity indices, although DAS28 was higher in Jaki patients. No significant between-group differences were observed in ultrasound scores [Table 1].

Active ultrasound synovitis (AUS) (SH ≥ 2 plus PD ≥ 1) in ≥ 1 joint was achieved by 30 IL6i patients and 16 Jaki patients (71% vs. 76% respectively). IL6i patients with AUS had a higher SJC and PhGA score than those without. Jaki patients with AUS had higher SJC, PhGA and usCRP (Table 2).

In IL6i patients, the total ultrasound score significantly correlated only with the SJC28 (r=0.605; p< 0.001) and PhGA (r=0.392; p=0.011), although the CDAI showed a non-significant trend (r=0.279 p=0.07), which was significant when evaluating the PD score (r=0.320; p=0.039). The total ultrasound score in Jaki patients significantly correlated

Table 1: Patient characteristics by therapeutic group (2)

LABORATORY TESTS				
PCRus mg/dL	0.04 (0.0-1.63)	0.16 (0.01-1.38)	1.38 (0.040-1.63)	**0.007**
CRPus <0.1mg/dL, n (%)	34 (81.0)	9 (42.9)	43 (68.3)	**0.002**
ESR	5 (2-14)	16 (6-140)	7 (2-140)	**<0.001**
Hemoglobin g/L	143 (100-168)	125 (100-148)	139 (100-168)	<0.001
ULTRASOUND INDICES				
SH score	4 (0-18)	4 (0-28)	4 (0-28)	0.352
PD score	3.5 (0-18)	3 (0-27)	3 (0-27)	0.825
SH+PD	8 (0-35)	7 (0-55)	8 (0-55)	0.534

assessment; VAS visual analogue scale SH: synovial hypertrophy on ultrasound: PD power Doppler signal on ultrasound. Data expressed as medians and (ranges)

Table 2. Patient characteristics by therapeutic and ultrasound activity group

	IL-6 inhibitors (n=42)			**JAK inhibitors (n=21)**		
	No active ultrasound synovitis (n=12)	Active ultrasound synovitis (n=30)	P value	No active ultrasound synovitis (n=5)	Active ultrasound synovitis (n=16)	P value
TJC28	0.5 (0-15)	2 (0-20)	0.153	3 (0-9)	1.5 (0-25)	0.398
SJC28	0 (0-1)	1 (0-7)	<0.001	0 (0-1)	2 (0-9)	0.075
PGA	3 (0-8.5)	4 (0-6)	0.773	2.5 (2-7)	4.75 (0-7.5)	0.398
PhGA	1 (0-4)	3 (0-7)	0.017	1 (0-3)	4 (0-7)	0.011
VAS pain	2 (0-8)	3.5 (0-8)	0.752	2.5 (2 -7)	4.5 (0-7.5)	0.398
DAS28	2.074 (0.970-4.827)	2.537 (0.970-5.064)	0.146	3.216 (1.534-4.787)	3.780 (1.502-7.293)	0.313
CDAI	6.5 (0-25)	10 (0-31)	0.052	6 (3-20)	14 (0-41)	0.313
SDAI	6.9 (0.4-25.4)	10.40 (0.40-31.40)	0.052	6.4 (3.4-20.4)	14.475 (0.40-42.91)	0.313
HAQ	1.0 (0-2.88)	0.88 (0-2.38)	0.967	0 (0-1.13)	0.879 (0-2.75)	0.032
Rapid3	1 (0-2.88)	9.1 (0-21)	0.752	5.30 (4.5-17.70)	10.25 (1-18)	0.968
PCRus mg/dL	0.03 (0-0.34)	0.04 (0-1.63)	0.417	0.02 (0.01-0.04)	0.42 (0.02-1.38)	0.001
ESR	5 (3-14)	5.50 (2-14)	0.923	14 (6-15)	20.50 (7-140)	0.062
Hemoglobin g/L	141.5 (100-157)	144.5 (111-168)	0.179	126 (110-139)	124.5 (100-148)	0.968
ULTRASOUND INDICES						
SH score	0 (0-2)	6 (2-18)	<0.001	2 (0-3)	6.5 (2-28)	0.002
PD score	0 (0-1)	4 (1-18)	<0.001	0 (0-0)	5 (1-27)	<0.001
SH+PD	0 (0-2)	10 (3-35)	<0.001	2 (0-3)	12.5 (4-55)	<0.001

TJC: tender joint count; SJC: swollen joint count; PGA: patient global assessment PhGA: physician global assessment; VAS visual analogue scale SH: synovial hypertrophy on ultrasound: PD power Doppler signal on ultrasound. Data expressed as medians and (ranges)

with SJC28(r=0.777; p=0.000), PhGA (r=0.728; p=0.000), usCRP (r=0.533; p=0.013) ESR (r=0.692; p=0.001), CDAI (r=0.536; p=0.012), SDAI (r=0.538; p=0.012) and DAS28 (r=0.568; p=0.007).

Conclusion: The composite activity index and APR reflect the inflammatory status, evaluated by ultrasound in RA patients treated with Jakinibs but not in those treated with IL6i.

1. Arthritis Rheum 2003;48:995-62.

2. Arthritis Res Ther 2016,18-160.

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Abstract Number: 1209

Plasma Calprotectin as a Biomarker of Active Synovitis in Rheumatoid Arthritis: A Clinical and Ultrasound Study in Patients Treated with Il6 and JAK Inhibitors

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: IL6 inhibitors (IL6i) have a dramatic effect on acute phase reactants (AFR) such as C reactive protein (CRP) in rheumatoid arthritis (RA). However, CRP serum levels do not correlate with inflammatory activity in RA patients under IL6i therapy. JAK inhibitors (JAKi) also partly inhibit IL6 signaling. Calprotectin is a protein that correlates closely with inflammatory activity and may be a biomarker that accurately reflects the disease status in IL6i and JAKi treated RA patients.

Methods: Cross-sectional study in RA patients (ACR/EULAR 2010) treated with IL6i (tocilizumab, sarilumab) or JAKi (tofacitinib, baricitinib). Demographic, serological data (autoantibodies, ESR, ultrasensitive CRP (usCRP), composite activity indices (DAS28, SDAI, CDAI, RAPID3), disability (HAQ) and therapy were evaluated. Plasma calprotectin levels were measured by ELISA (CALPROLAB ALP Menarini). Hand ultrasound was studied to calculate synovial hypertrophy (SH), power Doppler signal (PD) score and total ultrasound activity score (SH+PD) graded according to Szudlarek's(1) . We compared plasma calprotectin and clinical and ultrasound variables in patients receiving IL6i and JAKi using Spearman's correlation test.

Table 1. Patient characteristics by therapeutic group.

	Group 1: IL-6 inhibitors (n=52)	Group 2: JAK inhibitors (n=26)	Total (n=78)	p Value
DEMOGRAPHIC VARIABLES				
Age	60.5 (34.0-80.5)	53.6 (26.4-84.7)	58.9 (26.4-84.7)	0.49
Female, n (%)	47 (90.4)	24 (92.3%)	71 (91.0)	1
Seropositive (CCP or FR), n (%)	44 (84.6)	25 (96.2)	69 (88.5)	0.25
CCP, n (%)	39 (88.6)	23 (92)	62 (89.9)	1
RF, n (%)	36 (81.8)	22 (88)	58 (84.1)	0.73
Erosive, n (%)	40 (76.9)	17 (65.4)	57 (73.1)	0.28
Disease duration (years)	15.50 (3.7-52)	12.56 (0.2-34.3)	14.52 (0.2-52.0)	0.12
Number of previous biologics	1 (0-4)	1 (0-7)	1 (0-7)	0.73
CONCOMITANT TREATMENT				
Treatment duration (months)	41.8 (7.9-139.9)	10.3 (2.9-77.7)	30.9 (2.9-139.9)	<0.001
Concomitant prednisone treatment, n (%)	24 (46.2)	15 (57.7)	39 (50)	0.34
Equivalent dose (mg/day)	2.5 (1.25-10)	5 (1.25-10)	2.5 (1.25-10)	0.25
Concomitant NSAIDs treatment, n (%)	14 (26.9)	6 (23.1)	20 (25.6)	0.71
Concomitant csDMARD, n (%)	22 (42.3)	14 (53.8)	36 (46.2)	0.34
CLINICAL ASSESSMENT AND PATIENT-REPORTED RESULTS				
TJC28	1.5 (0-20)	3 (0-25)	2 (0-25)	0.33
SJC28	1 (0-7)	1 (0-9)	1 (0-9)	0.24
PGA	4 (0-8.5)	4.25 (0-9.5)	4 (0-9.5)	0.12
PhGA	3 (0-7)	3 (0-7)	3 (0-7.0)	0.08
VAS pain	3 (0-8)	4 (0-9)	3 (0-9.0)	0.13
DAS28	2.26 (0.77-5.06)	3.78 (1.5-7.29)	2.75 (0.77-7.23)	<0.0001
CDAI	8.5 (0-31.0)	12.50 (0-41)	9 (0-41)	0.08
SDAI	8.9 (0.4-31.4)	13.31 (0.4-42.91)	9.59 (0.4-42.41)	0.06
HAQ	0.94 (0-8)	0.88 (0-2.75)	0.88 (0-8)	0.41
RAPID3	8.6 (0-25.50)	9 (1-18.3)	8.70 (0-25.50)	0.39
LABORATORY				
Calprotectin (µg/ml)	0.36 (0.12-2.39)	0.65 (0.19-5.51)	0.43 (0.12-5.51)	0.084
CRPus mg/dL	0.04 (0-1.63)	0.11 (0.01-1.38)	0.04 (0-1.63)	0.001
ESR	5 (2-25)	15.50 (6-140)	7.0 (2-140)	<0.001
Hemoglobin g/L	143 (100-170)	128.00 (100-148)	139 (100-170)	<0.001
ULTRASOUND INDICES				
	(n=42)	(n=21)	(n=63)	
SH score	4 (0-18)	4 (0-28)	4 (0-28)	0.420
PD score	3.5 (0-18)	3 (0-27)	4 (0-28)	0.92
SH+PD (total score)	8 (0-35)	7 (0-55)	8 (0-55)	0.63

TJC: tender joint count; SJC: swollen joint count; PGA: patient global assessment PhGA: physician global assessment; VAS visual analogue scale SH: synovial hypertrophy on ultrasound: PD power Doppler signal on ultrasound. Data expressed as median and (ranges)

Results: We included 78 patients (91% female, median age 58.9 years, median RA duration 14.5 years, 88.5% seropositive (RF and/or ACPA). Fifty two patients were treated with IL6i and 26 with JAKi [Table 1]. Ultrasound studies were made in 63 patients (42 receiving IL6i and 21 JAKi).

No significant between-group differences were observed in the TJC28, SJC28, CDAI, SDAI, and HAQ. DAS28 was higher in JAKi patients. There were no differences in ultrasound scores. The median (range) of plasma calprotectin was 0.36 µg/ml (0.12-2.39) in IL6i patients and 0.65 µg/ml (0.19-5.51) in JAKi patients (p=0.083) [Table 1].

In IL6i patients, plasma calprotectin weakly correlated with SJC28 but not with composite activity indices or with AFR (usCRP or ESR), although there was a significant correlation with all ultrasound scores (SH, PD and SH+PD) that

Tabla 2 Correlation between calprotectin and clinical, laboratory and ultrasound activity parameters				
	IL6 inhibitors (n=52)		JAK inhibitors (n=26)	
	rho	P value	rho	P value
TJC28	0.063	0.662	-0.252	0.225
SJCI28	.289*	0.04	0.288	0.163
PGA	0.149	0.297	0.029	0.892
PhGA	0.238	0.096	0.218	0.296
VAS pain	0.203	0.153	0.054	0.796
usCRP mg/dL	0.191	0.178	.552**	0.004
ESR	0.054	0.708	0.309	0.133
Hemoglobin	0.24	0.09	0.186	0.373
CDAI	0.168	0.239	0.087	0.68
SDAI	0.172	0.228	0.098	0.64
DAS28	0.157	0.271	0.132	0.529
HAQ	0.201	0.158	0.143	0.494
RAPID3	0.115	0.42	0.114	0.587
SH	.391*	0.01	.630**	0.002
PD	.349*	0.023	.703**	0
SH+PD	.383*	0.012	.700**	0

Rho: Spearman's correlation coefficient

was not found with usCRP or ESR. In JAKi patients, calprotectin showed a non-significant trend to correlation with TJC28, and a high correlation with all ultrasound scores (SH, PD and SH +PD) and usCRP levels, but not with activity indices [Table2].

Classification according to CDAI ≤10 vs. CDAI >10 showed no significant differences in calprotectin values: median (range) 0.33µg/ml (0.14-5.51) vs 0.59 µg/ml (0.12-5.50) p= 0.121). Classification according to ultrasound activity (ultrasound synovitis (SH ≥ 2 + PD≥1) in ≥ 1 joint showed -higher calprotectin levels in patients with ultrasound synovitis: median 0.70 µg/ml (0.18-5.03) vs 0.29 µg/ml (0.19-0.69) p< 0.001).

Conclusion: Plasma calprotectin in patients with low-moderate disease activity treated with IL6i or JAKi did not identify patients according to the degree of inflammation measured by the composite activity indices. However, in both groups and specially in patients treated with JAKi, calprotectin was related to ultrasound synovitis scores. Plasma calprotectin might be a biomarker of active synovitis in these patients.

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Abstract Number: 1210

Frequency of Anterior Atlanto-Axial Subluxation in Patients with Rheumatoid Arthritis

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Table 1. Sociodemographic and RA characteristics

	N = 295
Age (years), mean (SD)	54.4 (12.3)
Women, n (%)	253 (85.8)
Occupation, n (%) (n= 261)	108 (41.4)
Disease duration in months, median (IQR)	80 (43-120)
Erosive disease, n (%) (n=277)	166 (59.9)
Extra-articular manifestations, n (%)	163 (55.2)
ESR, median (IQR) (n=225)	25 (14-40)
CRP (mg/dl), median (IQR) (n=228)	1 (0.3-5.5)
RF positivity, n (%) (n=291)	270 (92.8)
ACPA positivity, n (%) (n=225)	186 (82.7)
DAS28, median (IQR)	3.6 (2.5-4.6)
SDAI, median (IQR)	12 (5.2-21.3)
CDAI, median (IQR)	9 (3-17)
HAQ, median (IQR)	0.8 (0.3-1.4)

*__ESR__= Erythrocyte Sedimentation Rate; **CRP=** C-Reactive Protein; **RF=** Rheumatoid Factor; **ACPA=** Anti-Citrullinated Protein/Peptide Antibodies; **DAS28=** Disease Activity Score-28; **SDAI=** Simplified Disease Activity Index; **CDAI=** Clinical Disease Activity Index; **HAQ=** Health Assessment Questionnaire; **IQR=** Interquartile range; **SD**= Standard deviation.

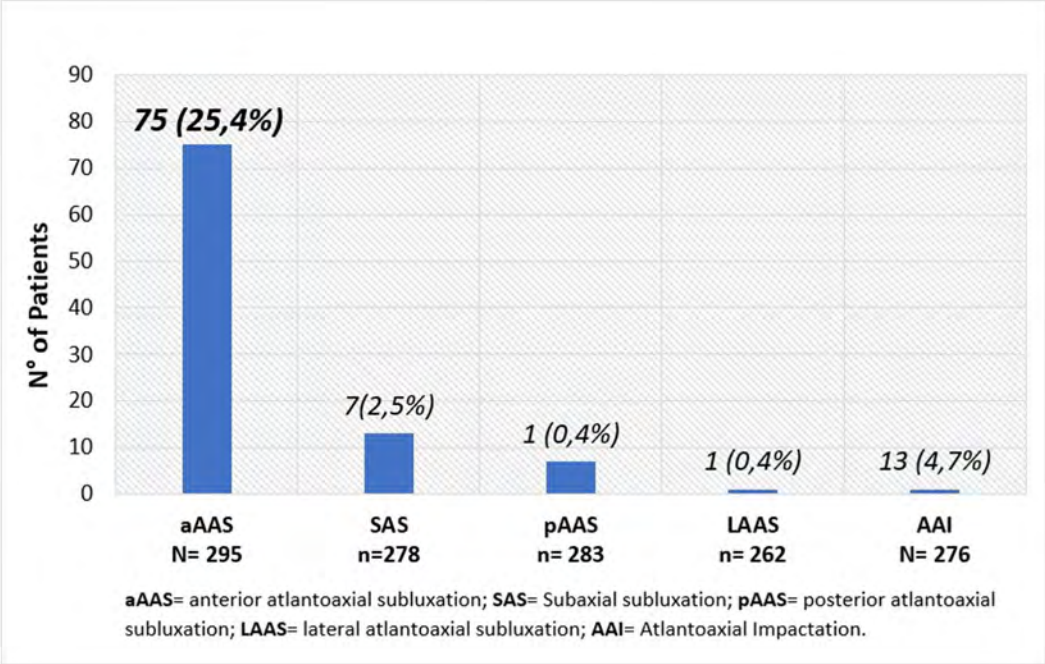

Figure 1. Frecuency of cervical spine involvement.

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: According to some series, cervical spine is the second most affected region in Rheumatoid arthritis (RA). Cervical involvement was reported in 80% of RA patients, being anterior Atlanto-Axial subluxation (aAAS) the most frequent one. Other less frequent types are Subaxial Subluxation (SAS), posterior Atlanto-Axial subluxation (pAAS), lateral Atlanto-Axial subluxation (LAAS) and Atlanto-Axial impaction (AAI). The aim of this study was to describe the frequency of aAAS in a cohort of patients with RA and to evaluate its association with demographic and disease characteristics.

Methods: Multicenter, observational, cross-sectional, descriptive, and analytical study. Patients ≥ 18 years old with diagnosis of RA (ACR-EULAR 2010) and at least one flexion lateral cervical spine radiograph were included. aAAS was defined when anterior Atlanto-Axial distance (aAAD) was ≥ 3mm. The other forms of cervical spine involvement were also reported. All the radiographs were assessed by 3 experienced rheumatologists. Statistical analysis: Descriptive statistics was done. Sociodemographic and disease characteristics of patients with and without aAAS were compared using Student's T test, Chi2 and Fisher's exact test. The aAAD was assessed according to disease characteristics, symptom presence, and disease duration at the time of diagnosis of the aAAS using Spearman correlation, Student's T test, Kruskal Wallis and Wilcoxon test.

Results: A total of 295 patients from 13 centers were included. Sociodemographic and RA characteristics are shown in Table 1. The frequency of aAAS was 25.4% and the average aAAD 4.5 mm (SD 2.4). Their frequency and that of the other types of cervical spine involvement can be observed in **figure 1**. The median disease duration at the time of diagnosis of aAAS was 128 months (IQR 82.5-196). The most frequent reported symptom was radicular pain in 20% of patients, and 6% of them required surgical intervention. Patients with aAAS had longer disease duration (119 months [45-174] vs 76 [43-102] months, $p < 0.05$) and higher frequency of extra-articular manifestations (97.3% vs.

40.9%, p < 0.001). The frequency of pAAS was much higher in the group with aAAS (8.6% vs. 0.5%, p < 0.001). In patients with aAAS, the median of the aAAD was higher in symptomatic patients (5 mm [IQR 3.7-6.5] vs 3 mm [IQR 3-5], p=0.011), and it was particularly associated with radicular pain (5 mm [IQR 4-7] vs 3 mm [IQR 3-5], p=0.009).

Conclusion: The frequency of aAAS in this cohort of RA patients was 25.4%. The prevalence of pAAS was much higher in the group with aAAS. The aAAD was greater than 5 mm in patients with neurological symptoms (especially with radicular pain).

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Abstract Number: 1211

Evaluation of the Cervical Involvement Frequency and Associated Risk Factors in Patients with Rheumatoid Arthritis

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Table 1. Demographics and clinical features of study groups

Variables	With aAAS N:25	Without aAAS N:215	P value
Age, mean (SD)	56.0 (13.8)	56.4 (11.1)	0.68
Female gender, n (%)	20 (80)	171 (79.5)	0.95
Disease duration, years mean (SD)	16.9 (11.5)	9.4 (7.8)	**0.001**
Smoking ever, n (%)	12 (48)	93 (44.1)	0.70
Body mass index, mean (SD)	26.4 (4.9)	28.5 (5.3)	0.40
Neck pain, n (%)	16 (66)	102 (49)	0.10
Joint restriction, n (%)	16 (64)	41 (19.1)	**<0.001**
Erosions in hand or foot radiographs, n (%)	76 (35.3)	17 (68)	**0.002**
History of joint prostheses, n (%)	8 (32)	20 (9.3)	**<0.001**
Osteoporosis, n (%)	7 (28)	43 (20)	0.35
Presence of at least one comorbidity, n (%)	15 (60)	150 (69.8)	0.32
RF or anti-CCP positivity, n (%)	23 (92)	180 (83.7)	0.39
Disease activity measures			
TJC, median (IQR)	1 (4)	2 (6)	0.15
SJC, median (IQR)	0 (1)	0 (1)	0.66
ESR (mm/h), mean (SD)	33.4 (16.5)	29.3 (16)	0.10
CRP (mg/L), mean (SD)	15.6 (18.9)	8.5 (14)	0.09
DAS28-CRP, mean (SD)	3.1 (1.3)	2.9 (1.1)	0.62
CDAI, mean (SD)	12.1 (9.7)	10.1 (6.0)	0.59
HAQ, mean (SD)	1.2 (0.7)	1.1 (1.54)	0.27
Current treatment			
Methotrexate, n (%)	12 (48)	128 (59.5)	0.27
Leflunomide, n (%)	10 (40)	62 (29)	0.26
Corticosteroid, n (%)	20 (80)	139 (64.7)	0.13
Biologic drugs, n (%)	8 (32)	44 (20.6)	0.19

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

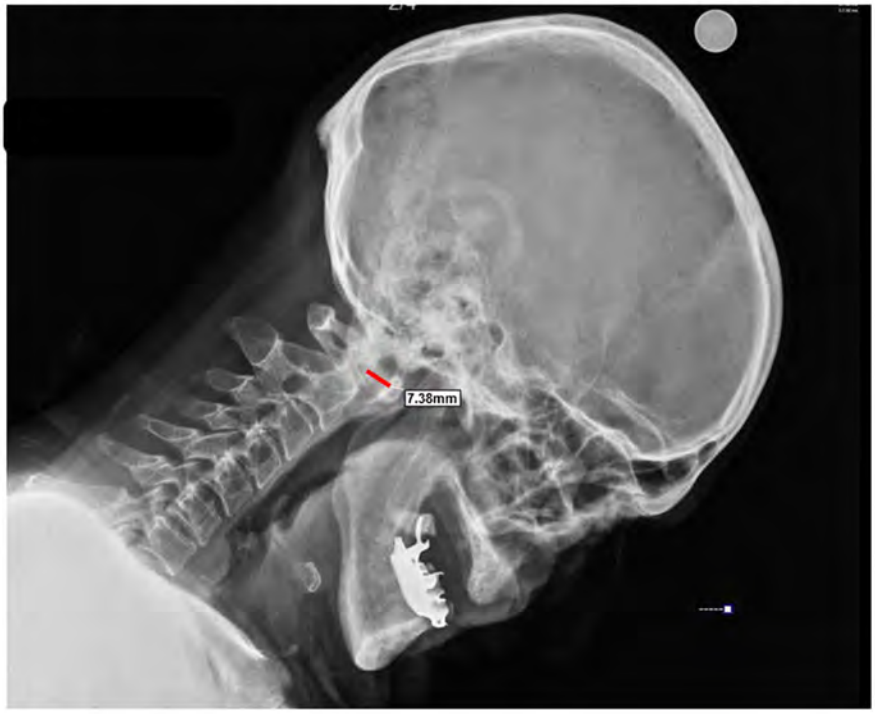
Background/Purpose: Spinal involvement in Rheumatoid arthritis (RA) is limited to the upper region of the cervical spine which leads to cervical spine instability (CSI); anterior atlantoaxial subluxation (aAAS), vertical subluxation (VS), and subaxial subluxation (SAS). In this study, we aimed to evaluate the frequency of cervical involvement and the associated risk factors in patients with RA.

Methods: Two hundred-forty RA patients were recruited consecutively in this single center cross-sectional study. All participants met the ACR 2010 classification criteria. Demographics, laboratory data, patient and physician reported outcomes were collected using by a structured form. Tender and swollen joint count was assessed by the same rheumatologist. Radiographs of the cervical spine were obtained in flexion, extension, neutral position of the neck at the same visit. The presence of erosions on the hand and foot radiographs in the last year was also assessed. A diagnosis of aAAS was based on the distance between the anterior aspect of the dens and, the posterior aspect of the anterior arch of the atlas was > 3 mm during flexion (Figure 1). Vertical subluxation was recorded as present if the tip of the odontoid peg lay more than 4.5 mm above the line described by McGregor. SAS is diagnosed if a vertebra

Table 2. Evaluation of risk factors of AAS

	Univariable analyses			Multivariable analyses		
Variables	**OR**	**95 % CI**	**P value**	**OR**	**95 % CI**	**P value**
Disease duration, years (≥10 vs <10)	**2.92**	**1.2 - 7.0**	**0.017**	1.4	.52 - 3.9	0.49
Joint restriction	**7.5**	**3.1- 18.2**	**<0.001**	**5.8**	**2.1 - 16**	**0.001**
Erosions in hand or foot radiographs	**3.7**	**1.5 - 9.0**	**0.004**	1.3	.47 - 4.0	0.55
History of joint prostheses	**4.5**	**1.7 - 11.9**	**0.002**	**3.6**	**1.2 - 10.5**	**0.019**

Figure1. Measurement of aAAS on the cervical lateral flexion graph.



has moved 3 mm or more in relation to the next vertebra when measured from the posterior line of the vertebral bodies. All cervical spine radiographs were evaluated separately by two readers blinded to all clinical data of patients at the end of the study. There was very good agreement between the two readers [interobserver reliability: intraclass correlation coefficent (ICC) for GA: 0.88 (95% CI: 0.43 - 0.97), ICC for HC:0.80 (95% CI: 0.14 - 0.95); intraobserver reliability: ICC:0.89 (95 % CI: 0.47-0.97)].

Results: One hundred ninety-one (79.6 %) of the 240 patients were female, and the mean age was 56.4 ± 11.4 years with a mean of 10.2 ± 8.5 years of mean disease duration. Two hundred and three (84.6 %) of the participants were seropositive (RF or anti CCP) and erosion was detected in 93 patients' hand or foot radiographs. aAAS was reported in 25 (10.4 %) patients. Only one patient had combination of aAAS and VS. We could not detect any SAS. Age and gender were found similar in patient with or without aAAS and the other demographics and clinical characteristics were summarized in table 1. One in three patients with aAAS had no neck pain. Biologic drugs treatment and presence of osteoporosis was more common in the aAAS group but not reach a statistical difference (32% vs 20%, p:0.19; 28% vs 20%, p:0.37, respectively). Patient with aAAS had longer disease duration, more frequently erosion, joint restriction and history of joint prostheses (Tablo1 and 2). In the multivariate regression model, joint restriction [OR: 5.8 (95% CI: 2.1-16.0)], and history of joint prostheses [OR:3.6 (95% CI: 1.2-10.5)] was found independently predictors of the presence of aAAS.

Conclusion: aAAS was found the most common cervical involvement type in RA in this study. Longer disease duration, presence of erosion, joint restriction and prostheses was associated with aAAS. Even if there is no neck pain, cervical involvement should be kept in mind especially in the established disease.

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Abstract Number: 1212

Prediction of 1-Year Intravenous Abatacept Retention in Patients with RA Using Novel Machine Learning Techniques: Directionality and Importance of Predictors

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

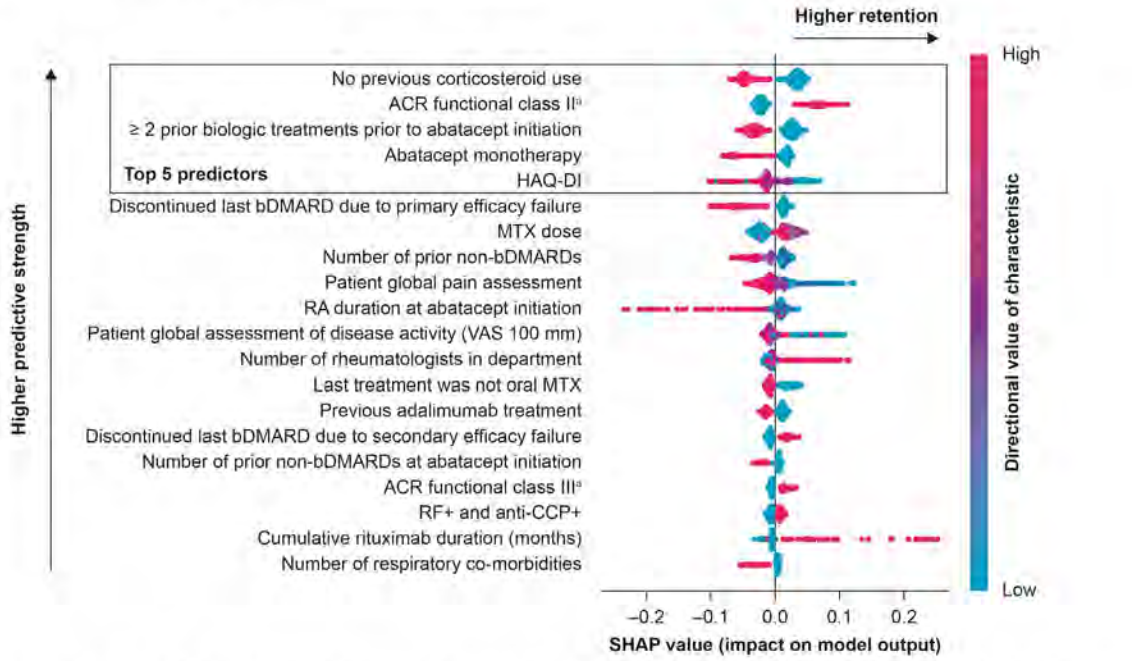
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: In the ACTION study (NCT02109666), previous multivariable Cox proportional-hazards regression models showed that predictors of 1-year retention to intravenous abatacept treatment included: patient

Figure 1. Overall variable importance in ACTION, using SHAP



The box highlights the 5 most important predictors of retention. Colors indicate the value of the variable: pink represents higher and blue represents lower. The bulges in the plot indicate more patients with that value; each dot represents a single patient. Higher SHAP values indicate a higher likelihood of retention.
[a]Compared with other ACR functional classes.
bDMARD, biologic DMARD; HAQ-DI, HAQ-disability index; SHAP, SHapley Additive exPlanations.

global pain assessment, country, reason for stopping last biologic, number of prior biologic treatments, abatacept monotherapy, RF/anti-CCP status, previous neoplasms, psychiatric disorders, and cardiac disorders.[1] Machine learning techniques, using the gradient-boosting model, identified additional predictors of abatacept retention in patients with moderate-to-severe RA enrolled in ACTION; however, the analysis did not show whether the variables predicted reduced or increased retention (directionality).[2] The objective of this analysis was to assess the clinical importance and directionality of each patient demographic or disease characteristic for predicting retention.

Methods: The gradient-boosting model was used to identify predictors of abatacept retention at 1 year in the ACTION study.[2] Retention was defined as treatment for > 365 days or ≤ 365 days in patients who achieved remission or major clinical response (using EULAR response criteria, based on DAS28). This analysis expanded on the previous model, adding SHapley Additive exPlanations (SHAP), a mathematical framework, to show how important each characteristic was for predicting abatacept retention. Higher SHAP values indicate a higher likelihood of retention. Every characteristic's contribution in the model's prediction (except country) was computed for each data point to capture the impact of each individual characteristic. This enabled interpretation for level of importance and directionality at a patient level.

Results: Using data from 2350 patients enrolled in ACTION (May 2008 to December 2013), the mean abatacept retention rate at 1 year was 59.3% (n = 1393). **Figure 1** shows how important each characteristic was for predicting retention. Lower treatment retention was predicted by no previous corticosteroid use, ≥ 2 prior biologic treatments prior to abatacept initiation, abatacept monotherapy, and a higher HAQ-disability index score at baseline, whereas higher treatment retention was predicted by ACR functional class II (vs functional classes I, III, and IV).

Conclusion: Adding SHAP to the gradient-boosting model allowed for a more clinically relevant analysis to be performed, showing how the identified variables impacted retention, either positively or negatively. The most important

baseline characteristics that were predictive of abatacept retention at 1 year were no previous corticosteroid use, which was associated with lower patient retention in the study, and ACR functional class II, which was associated with higher retention. Machine learning offers an innovative and complementary approach to biostatistics and could be used to identify treatment response predictors at an individual patient level, leading to a more personalized treatment approach.

References

1. Alten R, et al. *RMD Open* 2017;3:e000538.
2. Alten R, et al. Presented at the virtual ACR Convergence 2020; November 5–9, 2020. Poster 1745.
Medical writing: Claire Line, PhD (Caudex), funded by Bristol Myers Squibb

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Disclosure: R. Alten, Abbvie, 1, Amgen, 1, Biogen, 1, Galapagos, 1, Gilead, 1, Janssen, 1, Lilly, 1, Novartis, 1, Pfizer, 1, Roche, 1, BMS, 1, Celltrion, 1; **C. Behar**, Bristol Myers Squibb, 2; **C. Boileau**, Excelya, 2; **P. Merckaert**, None; **E. Afari**, None; **V. Vannier-Moreau**, Bristol Myers Squibb, 3; **A. Ohayon**, Bristol Myers Squibb, 3; **S. Connolly**, Bristol Myers Squibb, 3, 11; **A. Najm**, UCB, 1, Bristol-Meyers Squibb, 1, 6, Novartis, 5; **P. Juge**, Bristol Myers Squibb, 2, Boehringer Ingelheim, 6, AstraZeneca, 6; **G. Liu**, Bristol Myers Squibb, 3; **A. Rai**, AMGEN INC, 3, 11, Bristol Myers Squibb, 3, 11, GENMAB, 11; **Y. Elbez**, Bristol Myers Squibb, 2; **K. Lozenski**, Bristol Myers Squibb, 3.

Abstract Number: 1213

Persisting Pain in Rheumatoid Arthritis – an Essential yet Underrated Challenge

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Pain is the symptom with the most significant impact on patients' lives in rheumatoid arthritis (RA), whereas 17% of German RA patients report severe pain [1, 2]. Although RA patients may no longer report pain due to an articular, inflammatory origin, neuropathic pain (NP) may compromise anti-rheumatic treatment success as well.

The data-analysis presented aimed to investigate the proportion of RA patients with persisting pain and suggest clinical practice implications given specified patient-reported outcomes.

Methods: The PAIN-CONTROL study is a prospective, non-interventional, multicenter study in specialized rheumatology centers across Germany. Patients had to fulfill these inclusion criteria: 2010 ACR/EULAR classification criteria for RA, disease duration < 8 yrs, Disease Activity Index 28 (DAS28) ≥ 3.2, SJC ≥ 3, CRP above the reference range, and a visual analog scale (VAS, 0-100) pain rating ≥ 50. Eligible subjects had to be scheduled for initiation or escalation of anti-inflammatory treatment. At wk 24, clinical outcomes were evaluated, and subjects were allocated to three subgroups: Group 1 (reference): DAS28 improvement > 1.2 or DAS28 ≤ 3.2, VAS pain < 50; group 2

Table 1. Disease-related and patient-reported outcomes of the PAIN-CONTROL study (preliminary data analysis)

	Week 0	Week 24				Week 48		
	Total sample (N = 263)	Reference (N = 133)	Non-responders (N = 58)	Persisting pain (N = 72)	N(missing)/ N(total)	Reference/ Non-responders	Persisting pain (N = 51)	N(missing)/ N(total)
DAS28(CRP) (mean ± SD)	5.3 ± 0.8	2.0 ± 0.5	4.9 ± 1.1	3.4 ± 1.0	53/263 (20.2%)	-	2.9 ± 1.2	10/51 (19.6%)
PD-Q ≥ 19 n (%)	68 (25.9%)	9 (6.8%)	15 (25.9%)	18 (25.0%)	76/263 (28.9%)	-	10 (19.6%)	14/51 (27.5%)
RAID ≤ 2 n (%)	8 (3.0%)	65 (48.9%)	2 (3.4%)	6 (8.3%)	24/263 (9.1%)	-	12 (23.5%)	1/51 (2.0%)
PHQ-9 ≥ 10 n (%)	86 (32.7%)	8 (6.0%)	12 (20.7%)	10 (13.9%)	27/263 (10.3%)	-	7 (13.7%)	1/51 (2.0%)

(non-responders): DAS28 improvement ≤ 1.2 or DAS28 > 3.2 with or without alleviation of pain; group 3 (persisting pain): DAS28 improvement > 1.2 or DAS28 ≤ 3.2, VAS pain ≥ 50. For subjects in groups 1 and 2, the study ended at wk 24, subjects in group 3 continued until wk 48. This descriptive, interim analysis includes subjects having completed the study until Sept. 30th 2020, and informs about subjects classified as having NP by a painDETECT questionnaire (PDQ) score of ≥ 19. The attainment of a patient acceptable symptom state (i.e., Rheumatoid Arthritis Impact of Disease (RAID-PASS) score ≤ 2), and the proportion of patients with moderate depressive symptoms or worse according to the Patient Health Questionnaire 9 (i.e., PHQ-9 ≥ 10) were specified as secondary outcomes of interest. Descriptive results are presented as mean±SD or n (%), respectively.

Results: Sample characteristics (N=263) at baseline were as follows: Age 57.6 ± 13.0 yrs, disease duration 2.4 ± 2.6yrs, DAS28(CRP) 5.3 ± 0.8 with 174(66.2%) female subjects. At wk 24, the proportion of subjects who tested positive for NP in group 3 (persisting pain) was similar to group 2 (non-responder), (N=18; 25.0%) vs. (N=15; 25.9%). The number of patients with NP in group 3 decreased until wk 48, (N=10; 19.6%). Between wks 24 and 48, the number of subjects in group 3 attaining RAID-PASS increased from N=6 (8.3%) to N=12 (23.5%). Simultaneously, their DAS28(CRP) decreased from 3.4 ± 1.0 to 2.9 ± 1.2, respectively. During this period of the study, the proportion of patients in group 3 with moderate depressive symptoms or worse hardly changed (wk 24: 10(13.9%), wk 48: 7(13.7%)). For details see table 1.

Conclusion: NP is a frequent underrated challenge in RA patients either not responding to anti-inflammatory treatment or patients with persisting pain. These patient groups are likely to benefit from a multi-disciplinary treatment approach, including tailored pain management.

1. Bischoff S et al. Annual Report - National Database, 2012, DRFZ, Germany

2. Gossec L et al. Ann Rheum Dis. 2009 Nov;68(11):1680–5

Disclosure: C. Baerwald, Abbvie, 1, 2, 5, 6; **E. Stemmler**, Abbvie, 3, 11; **S. Gnuechtel**, Abbvie, 3, 11; **K. Birkner**, Abbvie, 3, 11; **C. Holland**, AbbVie, 3, 11; **B. Fritz**, Abbvie, 3, 11; **D. Adolf**, StatConsult, 3, 11; **R. Baron**, Abbvie, 2, 6.

Abstract Number: 1214

Examining the Relationship Between Shared Epitope, ACPA Seropositivity, and Real-World Drug Effectiveness in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The shared epitope (SE) is an amino acid sequence motif coded by several HLA-DRB1 alleles that are overrepresented among people with rheumatoid arthritis (RA). SE-positivity is associated with the production of anti-citrullinated protein antibodies (ACPA), RA risk, and possibly a more severe disease course. Recent studies showed ACPA positivity to be associated with a significantly greater response to abatacept treatment. Given these prior observations, the purpose of this study was to determine if there is an association between SE status, ACPA status, and the effectiveness of drugs used to treat RA in a real-world setting.

Methods: Data were provided by participants with RA in FORWARD, The National Databank for Rheumatic Diseases, that had known SE and ACPA status. FORWARD participants complete comprehensive questionnaires every six months that include information on medication use and health status. Inclusion criteria required initiation of a TNFi, abatacept, or JAKi during the study period. These individuals had a baseline observation (prior to medication start) and a follow up observation (after medication start) approximately six months later. Descriptive statistics were calculated by drug exposure group for each SE/ACPA cohort. Change in patient activity scale II (PAS-II; a composite index composed of HAQ-II and visual analog scales for pain and patient global) scores between baseline and follow up was calculated and classified as improved (≥1 point improvement), no change (within 1 point), or worsened (≥1 point worsening). Adjusted linear regression models were generated for each medication group to determine the relationship between SE/ACPA group and change in PAS-II, using the SE–/ACPA– group as the reference. For models with a significant relationship between SE/ACPA group and change in PAS-II, an additional model was created using the SE+/ACPA+ group as reference.

Results: Baseline characteristics of the 404 included participants are presented in Table 1 (200 TNFi, 122 abatacept, and 82 JAKi initiators) and the distribution of participants by medication group and by SE/ACPA status is presented in Figure 1. In models for TNFi and JAKi, there was no significant relationship between SE/ACPA status and change in PAS-II (Table 2). Among abatacept initiators, the two ACPA+ groups were more likely to experience an improved PAS-II score compared to the SE–/ACPA– group (B [95% CI] for SE–/ACPA+ : 1.6 (0.6, 2.6), p=0.002; for SE+/ACPA+: 1.3 [0.6, 2.1], p=0.001) and the two ACPA– groups were more likely to experience a worsened PAS-II score compared to the SE+/ACPA+ group (for SE–/ACPA–: -1.3 [-2.1, -0.6], p=0.001; for SE+/ACPA–: -0.7 [-1.4, 0], p=0.050). Change in PAS-II did not vary significantly by SE status.

Table 1. Baseline characteristics by medication initiator group.

	TNFi	Abatacept	JAKi
	n = 200	n = 122	n = 82
Participant Characteristics			
Age (years)	58.1 (11.8)	59.8 (11.0)	59.6 (8.4)
Female, %	90.5	91.8	91.5
White, %	94.0	93.4	95.1
Hx smoking, %	37.5	44.3	39.0
BMI (kg/m²)	29.1 (6.9)	29.8 (7.0)	27.5 (6.6)
Disease duration (years)	13.7 (11.4)	17.6 (13.9)	17.0 (11.9)
RDCI, 0-9	2.1 (1.6)	2.7 (1.9)	2.5 (1.9)
Hx DMARD count	4.1 (2.3)	5.5 (2.4)	6.0 (2.4)
Laboratory Measures			
SE positive, %	69.5	68.9	67.1
ACPA positive, %	54.0	59.8	46.3
RF positive, %	50.0	50.0	41.5
CRP high (≥0.8 mg/dL), %	18.0	14.8	12.2
SE / ACPA Group			
SE- / ACPA -, %	19.0	18.0	25.6
SE- / ACPA+, %	11.5	13.1	7.3
SE+ / ACPA-, %	27.0	22.1	28.1
SE+ / ACPA+, %	42.5	46.7	39.0
Patient-Reported Outcomes			
Baseline PAS-II, 0-10	3.6 (1.9)	4.2 (1.9)	4.0 (2.0)
Follow up PAS-II, 0-10	3.4 (2.0)	3.9 (2.0)	3.8 (2.1)

Values are mean (standard deviation) unless otherwise specified.

TNFi=tumor necrosis factor inhibitor; JAKi=Janus kinase inhibitor; BMI=body mass index; RDCI=Rheumatic Disease Comorbidity Index; SE=shared epitope; ACPA=anti-citrullinated protein antibodies; RF=rheumatoid factor; CRP=C-reactive protein; PAS-II=Patient Activity Scale II.

Conclusion: Using a US-wide, real-world registry, we observed a greater improvement in patient reported RA disease activity after initiation of abatacept in ACPA+ individuals. Neither SE status nor ACPA status predict response to TNF or JAKi, suggesting that the predictive value of ACPA is more specific to abatacept users. This provides early evidence that ACPA status, rather than correlative SE status, may be the stronger predictor of abatacept response among individuals with RA.

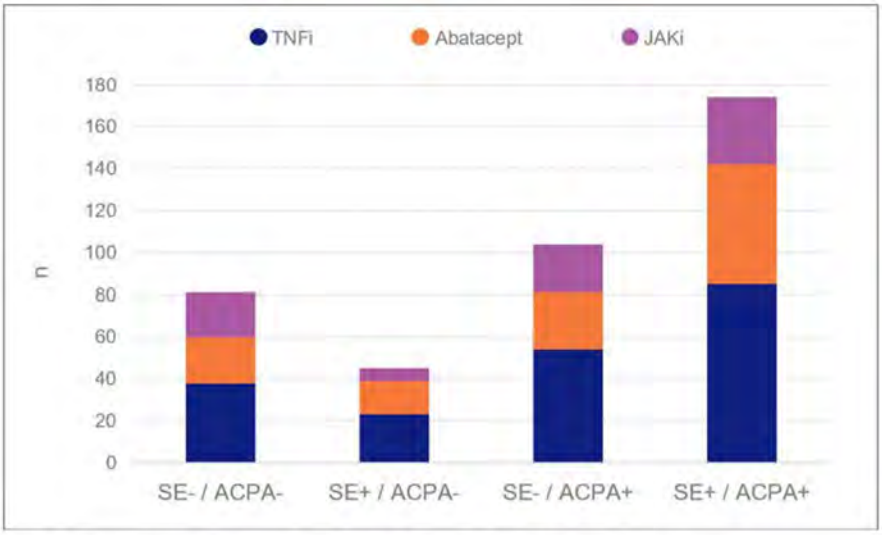

Figure 1. Distribution of participants by medication group and by SE/ACPA status.

Table 2. Linear regression models by medication group for change in PAS-II between baseline and follow up.

	TNFi n=200		Abatacept n=122				JAKi n=82	
	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p	B (95% CI)	p
SE- / ACPA-	reference	-	reference	-	-1.31 (-2.05, -0.56)	0.001	reference	-
SE- / ACPA+	0.51 (-0.23, 1.26)	0.177	1.61 (0.61, 2.60)	0.002	0.30 (-0.57, 1.17)	0.494	-0.22 (-1.94, 1.50)	0.798
SE+ / ACPA-	0.15 (-0.44, 0.74)	0.621	0.60 (-0.25, 1.46)	0.163	-0.70 (-1.41, 0.001)	0.050	0.09 (-1.08, 1.27)	0.877
SE+ / ACPA+	0.24 (-0.30, 0.79)	0.381	1.31 (0.56, 2.05)	0.001	reference	-	0.12 (-0.96, 1.20)	0.825

Model was adjusted for age, sex, race/ethnicity, history of smoking, date, disease duration, BMI, prednisone use, methotrexate use, biologic use, RDCI, and baseline PAS-II score. Positive values indicate improvement, and negative values indicate a worsening in PAS-II score.

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Abstract Number: 1215

Development of a Multivariable Prediction Model for Treatment Response to Etanercept in a Multi-centre Cohort of Patients with Established RA

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Table 1. Baseline statistics for the covariates used in the different models. % in brackets indicate the percentage of missing data for this covariate

Variable \DAS Type	CRP		ESR	
Sample Size (N)	778	-	693	-
Good / Moderate / Poor	310 / 320 / 148	-	228 / 322 / 143	-
% Cases	19.02%	-	20.63%	-
mean SJC (std)	8.8445 (±5.2)	-	8.6479 (±5.15)	-
mean TJC (std)	14.6877 (±6.74)	-	14.5137 (±6.81)	-
mean CRP (std)	19.0739 (±25.07)	-	-	-
mean ESR (std)	-	-	30.2554 (±24.46)	-
mean GHVAS (std)	74.7429 (±17.79)	-	74.7633 (±17.54)	-
mean HEIGHT (std)	164.3806 (±12)	[16.58%]	164.4378 (±12.27)	[15.3%]
mean WEIGHT (std)	78.1844 (±20.01)	[5.91%]	78.0837 (±18.91)	[5.19%]
mean AGEONSET (std)	47.3330 (±13.86)	[1.29%]	47.5377 (±13.77)	[1.01%]
mean DISDUR (std)	9.9401 (±10.35)	[1.29%]	9.9188 (±10.42)	[1.01%]
mean HAQ (std)	1.6085 (±0.65)	[12.85%]	1.6305 (±0.66)	[15.44%]
mean HAD-Anxiety (std)	8.0868 (±4.54)	[15.55%]	7.9947 (±4.49)	[18.04%]
mean HAD-Depression (std)	7.3841 (±4.02)	[15.68%]	7.3298 (±4.11)	[18.18%]
Concurrent DMARD (% Yes)	81.49%	[1.54%]	81.53%	[1.88%]
SEX (% Female)	78.66%	-	78.21%	-
SERO Positive (% Yes)	77.89%	[7.2%]	78.07%	[5.63%]
FIRSTBIO (% Yes)	90.62%	[0.9%]	90.76%	[1.15%]

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: RA patients who respond inadequately to first-line DMARDs usually progress to a biologic DMARD. Treatment response to both DMARDs and biologics is heterogeneous within RA patients. Choosing the right treatment early is vital, but prediction models from the literature are largely based on complex biomarkers such as genetics. Here, we develop a prediction model, using only clinical baseline covariates, to predict 3-month treatment response to the commonly used anti-TNF-α drug Etanercept (ETN).

Methods: Using data from the Biologics in RA Genetics and Genomics Study Syndicate (BRAGGSS), we identified patients treated with ETN or biosimilars. Patients were included for analysis if they had complete data to calculate a Disease Activity Score of 28 Joints (DAS28) at baseline and 3 months. DAS28 was then used to calculate EULAR response groups. We retained patients with complete baseline data as poor-responders if they stopped treatment early due to inefficacy. We created two datasets, containing all samples with complete CRP (N = 778), and ESR data (N = 693), respectively. Samples with complete CRP and ESR data, appear in both datasets. Multivariable logistic regression models were fitted using baseline clinical covariates, to differentiate poor (y = 1) from good and moderate (y = 0) responders at 3 months. Table 1 shows the baseline statistics of the covariates included in the models, for both created datasets. Multiple imputation by chained equations was used to impute missing data, and models

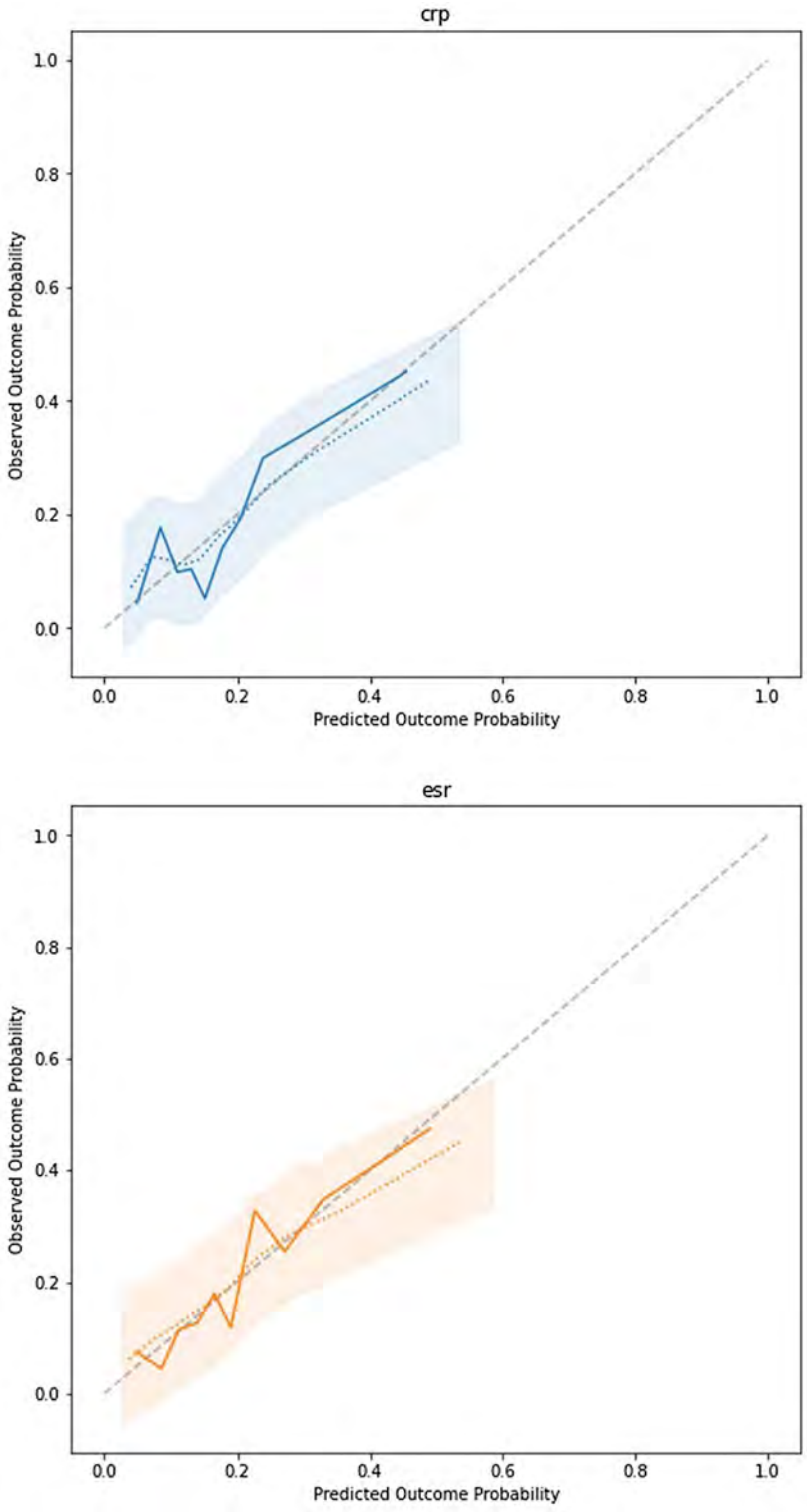

Figure 1. Calibration curves for the fitted models. The dotted line and shaded area represent the average bootstrap calibration curve and its standard deviation.

were internally validated via bootstrapping. We report model discrimination as measured by the area under the ROC curve (AUC), and model calibration via the calibration slope. Model parameters are described using β coefficients and odds-ratios (ORs).

Table 2. Model parameters and their respective odds ratio (OR)

	CRP		ESR	
	β	OR	β	OR
Intercept	1.2956	-	2.7053	-
SJC	-0.0547	0.95	-0.0631	0.94
TJC	0.0088	1.01	-0.0118	0.99
CRP	-0.0079	0.99	-	-
ESR	-	-	-0.0165	0.98
GHVAS	-0.0183	0.98	0.0191	0.98
HEIGHT	-0.0080	0.99	-0.0126	0.99
WEIGHT	-0.0009	1	0.0028	1
AGEONSET	0.0107	1.01	0.0121	1.01
DISDUR	-0.0137	0.99	-0.0157	0.98
HAQ	0.8930	2.44	0.8528	2.35
HAD-Anxiety	0.0331	1.03	0.0023	1
HAD-Depression	-0.0563	0.95	-0.0640	0.94
Concurrent DMARD	-0.1158	0.89	-0.5053	0.60
SEX	-0.2045	0.82	0.0602	1.06
SERO Positive	-0.3835	0.68	-0.0906	0.91
FIRSTBIO	-0.7991	0.45	-0.7278	0.48

Results: Both models are well calibrated with moderate discriminatory ability. Adjusted for optimism, the CRP model achieves an AUC of 0.658 (IQR 0.655-0.66), with a calibration slope of 0.767 (IQR 0.753-0.781). The ESR model shows a slightly higher AUC of 0.671 (IQR 0.67-0.672), with a marginally worse calibration slope of 0.759 (IQR 0.751-0.767). The calibration curve (figure 1) shows predictions are accurate, but that the models rarely predict high probabilities of poor response, which helps explain the moderate AUCs. Model parameters are mostly similar across the two models, and show HAQ to have the biggest impact, with β coefficients of 0.893 (OR 2.44) and 0.8528 (OR 2.35). Additionally, if this is their first biologic treatment, a patient's odds of having a poor response are significantly reduced (OR 0.45 and 0.48 for CRP and ESR, respectively).

Conclusion: Though competitive with existing genetic models from the literature, clinical features alone have insufficient discriminatory ability to predict response to ETN. These models serve as a baseline to investigate and evaluate the use of more complex models incorporating biomarkers to further improve prediction of treatment outcomes in RA. All model parameters are provided (see table 2) to facilitate external validation as well as the further development required to create models that can eventually inform treatment decisions.

Disclosure: M. Stadler, None; **S. Ling**, None; **N. Nair**, None; **J. Isaacs**, None; **K. Hyrich**, Abbvie, 6, Pfizer, 5, BMS, 5; **A. Morgan**, Roche, 5, Kiniska, 5, AstraZeneca, 2; **A. Wilson**, None; **D. Plant**, None; **A. Barton**, None; **J. Bowes**, None.

Abstract Number: 1216

Evidence of a Tendency for Localized Recurrence of Arthritis in Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Local inflammation may cause synovial fibroblasts to become sensitized, resulting in higher susceptibility to arthritis. Longitudinal assessment of joint involvement in rheumatoid arthritis (RA) might show if clinical arthritis tends to recur in the same joints.

Methods: Data from the BeSt study were used, a treat-to-target (disease activity score ≤2.4) study in 508 newly diagnosed RA (ACR 1987 criteria) patients. During 10 years, three-monthly 68-joint assessments (swelling yes/no and Ritchie Articular Index) were done by trained nurses.

We analyzed the association between local joint swelling at baseline and later swelling of the same joint using a multilevel mixed-effects logistic regression model, adjusted for joint location and for timepoint, with joints clustered within patients. A sensitivity analysis was done for the 25% joints that were most often swollen in the study population (MCP 1-3, PIP 2-3, wrists and MTP 2-4).A permutation test was performed to assess if over time joint swelling was better predicted (indicated by a p-value of < 0.05) by baseline swelling of the same joint than by baseline swelling of randomly selected other joints. This was repeated for the joints that were most often swollen.

The association between baseline joint swelling and the number of joint swelling episodes during follow-up was evaluated using a multilevel Poisson regression model, adjusted for joint location and follow-up duration, clustered within patients.

All models were repeated to account for missing data in two ways. First, all missing joint evaluations until end of follow-up were regarded as not swollen. Second, last observation was carried forward for one missing time point if the joint evaluation (swelling yes/no) at the time point before a missing evaluation was the same as at a subsequent time point after the missing evaluation.

Results: At baseline, 8,137/34,423 (24%) assessed joints were scored as swollen. Swelling recurred at least once in 46% of the joints with baseline swelling. Baseline swelling was significantly associated with swelling in the same joint during follow-up (odds ratio 2.37, 95% CI 2.30-2.43, $p< 0.001$). This association also was found in the 25% most swollen joints (OR 2.11, 95% CI 2.03 to 2.19, $p< 0.001$). Local joint swelling (in all joints and in the most susceptible joints) was better predicted by baseline swelling of that particular joint than by baseline swelling of other joints

(p< 0.001). Baseline joint swelling was also predictive for the number of joint swelling episodes in that joint during follow-up (incidence rate ratio 1.48, 95% CI 1.37 to 1.59, p< 0.001). When accounted for missing data, using the two different methods described before, all models showed similar results.

Conclusion: In RA patients treated to target DAS ≤ 2.4, joint swelling tends to recur locally in the joints swollen at presentation. This suggests that local factors influence the manifestation of joint inflammation over time and might indicate that joints that are swollen at disease onset may require additional monitoring and treatment.

Disclosure: S. Heckert, None; **S. Bergstra**, Pfizer, 5; **X. Matthijssen**, None; **Y. Goekoop-Ruiterman**, None; **F. Fodili**, None; **S. ten Wolde**, None; **C. Allaart**, Dutch College of Health Insurances, 5, Schering-Plough BV, 5, Centocor Inc., 5, Eli Lilly, 5; **T. Huizinga**, None.

Abstract Number: 1217

Discontinuation Rate of Tofacitinib Is Similar When Compared to TNF Inhibitors in Rheumatoid Arthritis Patients: Pooled Data from Two Rheumatoid Arthritis Registries in Canada

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Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as the first or an alternative option to biologic disease- modifying antirheumatic drugs (bDMARDs), including tumor necrosis factor inhibitors (TNFi). The similarity in retention of TNFi and TOFA was previously reported separately by the Ontario Best Practices Research Initiative (OBRI) and the Quebec cohort RHUMADATA. To increase the study power, we propose to evaluate the discontinuation rate (due to any reason) of TNFi compared to TOFA, using pooled data from both these registries.

Methods: RA patients enrolled in the OBRI and RHUMADATA initiating their TOFA or TNFi between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Time to discontinuation was assessed using adjusted Kaplan-Meier (KM) survival and Cox regression models. To deal with confounding by indication, we estimated propensity scores for covariates with a standard difference greater than 0.1. Models were then adjusted using stratification and inverse probability of treatment weight (IPTW) methods. Multiple imputation (Imputation by Chained Equation method, N=20) was used to deal with missing data for covariates at treatment initiation.

Results: A total of 1318 patients initiated TNFi (n=825) or TOFA (n=493) with mean (SD) disease duration of 8.9 (9.3) and 13.0 (10.1) years, respectively. In the TNFi group, 78.8% were female and mean age (SD) at treatment initiation was 57.6 (12.6) years. In the TOFA group, 84.6% were female and mean (SD) age at treatment initiation was 59.5 (11.5) years. The TNFi group was less likely to have prior biologic use (33.9%) than the TOFA group (66.9%). At treatment initiation, the mean (SD) CDAI was significantly (p< 0.05) lower in the TNFi group [20.0 (11.7)] compared to the

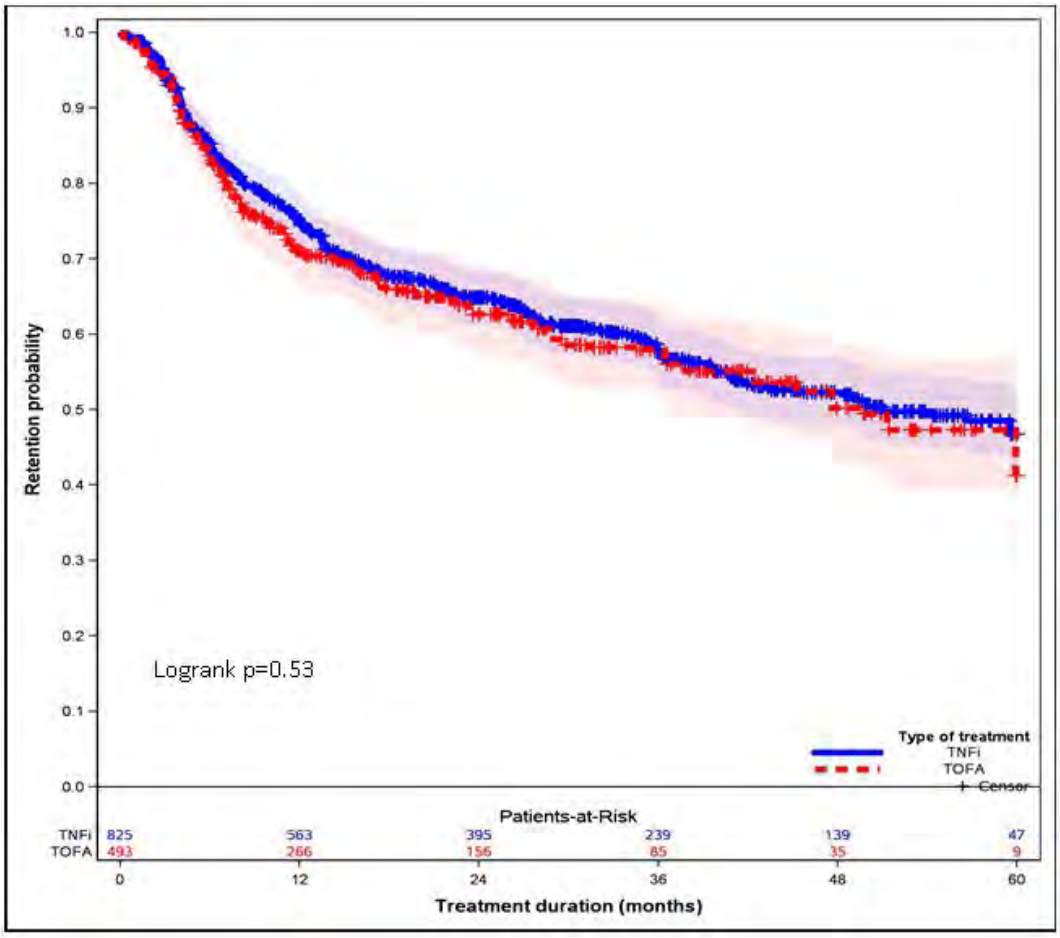

Figure 1. Propensity Score Weighted (IPTW) Survival Curves was performed using one imputed dataset.

TOFA group [22.1(12.4)]. Physical function measured by HAQ-DI was also significantly lower ($p< 0.05$) in the TNFi compared to the TOFA group (1.2 vs.1.3).

Over a mean follow-up of 23.2 months, discontinuation was reported in 309 (37.5%) and 182 (36.9%) of all TNFi and TOFA patients, respectively. After adjusting for propensity score deciles across 20 imputed datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 0.96, 95% CI: 0.78-1.18; p=0.69). The results were similar for two propensity adjustment methods. Figure 1 shows IPTW adjusted KM survival curves comparing discontinuation rates in patients treated with TNFi and TOFA.

Conclusion: In this pooled real -world data study, we found that TNFi and TOFA retention is similar in patients with RA. In the next step we will analysis the data for specific reasons of discontinuation. We will also repeat analysis comparing discontinuation in the first users versus those after one or more biologic failure.

Disclosure: M. Movahedi, None; **D. Choquette**, AbbVie, 2, 5, Amgen, 2, 5, Celltrion, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 2, 5, Sanofi, 2, 5, Teva Pharmaceuticals, 2, Gilead Sciences, 2; **L. Coupal**, None; **A. Cesta**, None; **X. Li**, None; **E. Keystone**, AbbVie, 2, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb Company, 2, Celltrion, 2, Gilead Sciences, 2, F. Hoffmann-La Roche, 2, 6, Janssen, 2, 6, Eli Lilly, 2, Merck, 2, 5, 6, Myriad Autoimmune, 2, Novartis, 6, Pfizer Inc, 2, 5, 6, PuraPharm, 5, Sandoz, 2, Sanofi-Genzyme, 2, 6, Samsung Bioepis, 2; **C. Bombardier**, AbbVie, 2, 5, 6, Amgen, 5, BGP Pharma ULC, 1, 6, Gilead, 5, GSK, 1, 6, Janssen, 2, 5, 6, Lilly Pharmaceuticals, 5, Medreleaf/ Aurora, 5, Merck, 1, 2, 5, 6, Pfizer Pharmaceuticals, 1, 5, Sandoz, 5, Samsung Bioepis, 2, 6.

Abstract Number: 1218

Unsupervised Clustering Identifies Unique Subsets of Patients in a Racially and Ethnically Diverse Rheumatoid Arthritis Cohort

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Background/Purpose: Single biomarkers have limited utility to date in guiding clinical care in RA. There is growing interest in applying machine learning algorithms to combine demographic, clinical, and biomarker data to better identify and stratify RA patient outcomes. We aimed to determine if unsupervised machine learning methods can be employed in a racially and ethnically diverse RA cohort to identify clusters of patients with different disease activity trajectories, as measured by DAS28ESR.

Methods: Data are derived from the longitudinal, observational University of California, San Francisco RA Cohort from years 2011-2018. Along with routine labs, medication use and disease activity assessments, a multiple biomarker of disease activity (MBDA) panel was obtained at each clinical encounter. The MBDA measures 12 unique serum biomarkers. All observations were collapsed to create a cross-sectional dataset before clustering. Missing data were imputed using multiple imputation with chained equations. Data were standardized in preparation for clustering. Patient clusters were identified by unsupervised K-prototype clustering. Longitudinal disease activity (DAS28ESR) trajectories and 95%CIs were plotted for each cluster. Lasso regression was used to identify biomarkers independently associated with DAS28ESR within the whole cohort and by cluster.

Results: Three distinct clusters were identified in our dataset. Cluster 1 (C1) was our smallest cluster (N=56, 20%), with the oldest age (59±14.4), highest proportion of Hispanic/Latino participants (n=43, 77%), the longest disease duration (11.4±8.9) and highest proportion of biological DMARD exposure (N=41, 73%) (Table 1). C1 also had the highest disease activity measured by DAS28ESR of 5.4±0.8. C2 and C3 both had 109 (40%) participants with similar ages 55.2±12.5 and 54.0±14.0, respectively. C3 had the highest proportion of Asian participants of the clusters (N=91, 33%) and the highest BMI of the cohort at 31.8±7.4. Notably, C2 had the lowest DAS28ESR of 3.2±0.7 (Figure 1). C1 had the highest mean DAS28ESR trajectory over time, whereas C3 had high disease activity that decreased over time. C2 had the lowest disease activity throughout the observation period. CRP and matrix metalproteinase-3 (MMP3) both had significant positive associations with DAS28ESR in our lasso regression model of the whole cohort (Table 2). No significant biomarker associations with DAS28ESR were found in C1. IL-6 had a negative association with DAS28ESR in C2 whereas IL-6 had a positive association and TNF-receptor inhibitor had a negative association with DAS28ESR in C3.

Conclusion: Using machine learning methods, we identified 3 clusters of patients in a racially and ethnically diverse longitudinal RA cohort. Each cluster had distinct disease activity trajectories and biomarker associations. This project demonstrated that machine learning methods can be applied to a moderate size RA cohort. Future work will be focused on evaluating baseline data to predict disease activity overtime and validating our findings in an external cohort.

Table 1. Demographics and clinical characteristics of the RA cohort by cluster.

	Cluster 1 (N=56, 20%)	Cluster 2 (N=109, 40%)	Cluster 3 (N=109, 40%)	Overall (N=274)
Age (years)	59.0 ± 14.4	55.2 ± 12.5	54.0 ± 14.0	55.5 ± 13.6
Female	48 (86%)	90 (83%)	96 (88%)	234 (85%)
Race/Ethnicity				
-Asian	9 (16%)	36 (33%)	46 (42.2%)	91 (33%)
-Black	2 (4%)	5 (5%)	16 (14.7%)	23 (8%)
-Hispanic/Latino	43 (77%)	58 (53%)	36 (33.0%)	137 (50%)
-Other	1 (2%)	2 (2%)	5 (4.6%)	8 (3%)
-White	1 (2%)	8 (7%)	6 (5.5%)	15 (6%)
RF	54 (96%)	103 (95%)	102 (94%)	259 (95%)
ACPA	52 (93%)	100 (92%)	98 (90%)	250 (91%)
Disease Duration	11.4 ± 8.9	7.6 ± 6.8	6.1 ± 7.0	7.8 ± 7.6
csDMARD exposed[a]	53 (95%)	103 (95%)	101 (93%)	257 (94%)
csDMARD use[b]	0.7 ± 0.3	0.7 ± 0.3	0.6 ± 0.3	0.6 ± 0.3
bDMARD exposed[a]	41 (73%)	53 (49%)	59 (54%)	153 (56%)
bDMARD use[b]	0.3 ± 0.3	0.3 ± 0.3	0.2 ± 0.3	0.3 ± 0.3
Prednisone Dose	7.5 ± 3.3	6.4 ± 4.3	6.1 ± 2.3	6.5 ± 3.5
Body Mass Index	29.2 ± 6.2	27.7 ± 5.9	31.8 ± 7.4	29.6 ± 6.9
DAS28ESR	5.4 ± 0.8	3.2 ± 0.7	4.4 ± 0.8	4.1 ± 1.1

-RF: rheumatoid factor; ACPA: anti-citrullinated protein antibody; csDMARD: conventional synthetic disease modifying antirheumatic drug; bDMARD: biologic disease modifying antirheumatic drug; DAS28ESR: disease activity score-28-erythrocyte sedimentation rate.
[a]-Ever used during the observation time.
[b]-Proportion of visits reporting use.

Figure 1. DAS28ESR trajectory plots with 95%CIs for the whole cohort and by cluster.

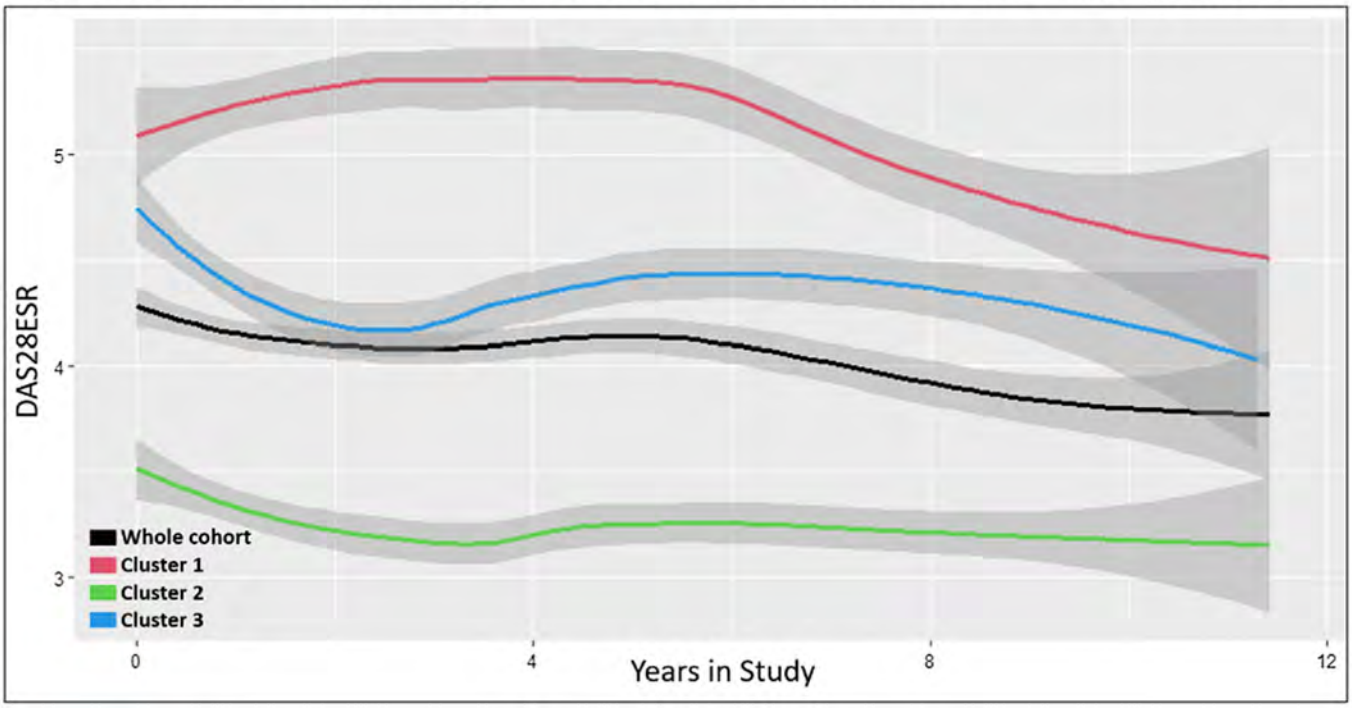

Table 3. Biomarkers independently associated (p<0.05) with DAS28ESR determined by Lasso regression. Values listed per standard deviation of biomarker.

	Cluster 1	Cluster 2	Cluster 3	Overall
IL6	--	-0.12	3.10	--
CRP	--	--	--	0.23
MMP3	--	--	--	0.14
TNFRI	--	--	-0.43	--

-IL6: interleukin-6; CRP: c-reactive protein; MMP3: matrix metalloproteinase-3; TNFRI: tumor necrosis factor receptor inhibitor.

Disclosure: G. Lui, None; **N. Singh**, None; **J. Andrews**, None; **J. Graf**, None; **K. Wysham**, None.

Abstract Number: 1219

Machine Learning Based Prediction Model for Responses of bDMARDs in Patients with Rheumatoid Arthritis and Ankylosing Spondylitis

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SESSION INFORMATION
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Background/Purpose: Few studies on rheumatoid arthritis (RA) have generated machine learning models to predict biologic disease-modifying antirheumatic drugs (bDMARDs) responses; however, these studies included insufficient analysis on important features. Moreover, machine learning is yet to be used to predict bDMARD responses in ankylosing spondylitis (AS). Thus, in this study, machine learning was used to predict such responses in RA and AS patients.

Methods: Data were retrieved from the Korean College of Rheumatology Biologics therapy (KOBIO) registry. The number of RA and AS patients in the training dataset were 625 and 611, respectively. We prepared independent test datasets that did not participate in any process of generating machine learning models. Baseline clinical characteristics were used as input features. Responders were defined as those who met the ACR 20% improvement response criteria (ACR20) and ASAS 20% improvement response criteria (ASAS20) in RA and AS, respectively, at the first follow-up. Multiple machine learning methods, including random forest (RF), were used to generate models to predict bDMARD responses, and we compared them with the logistic regression model.

Results: The RF model had superior prediction performance to logistic regression model (accuracy: 0.726 [95% confidence interval (CI): 0.725–0.730] vs. 0.689 [0.606–0.717], area under curve (AUC) of the receiver operating characteristic curve (ROC) 0.638 [0.576–0.658] vs. 0.565 [0.493–0.605], F1 score 0.841 [0.837–0.843] vs. 0.803 [0.732–0.828], AUC of the precision-recall curve 0.808 [0.763–0.829] vs. 0.754 [0.714–0.789]) with independent test datasets in patients with RA (Figure 1). However, machine learning and logistic regression exhibited similar prediction performance in AS patients. Furthermore, the patient self-reporting scales, which are patient global assessment of disease

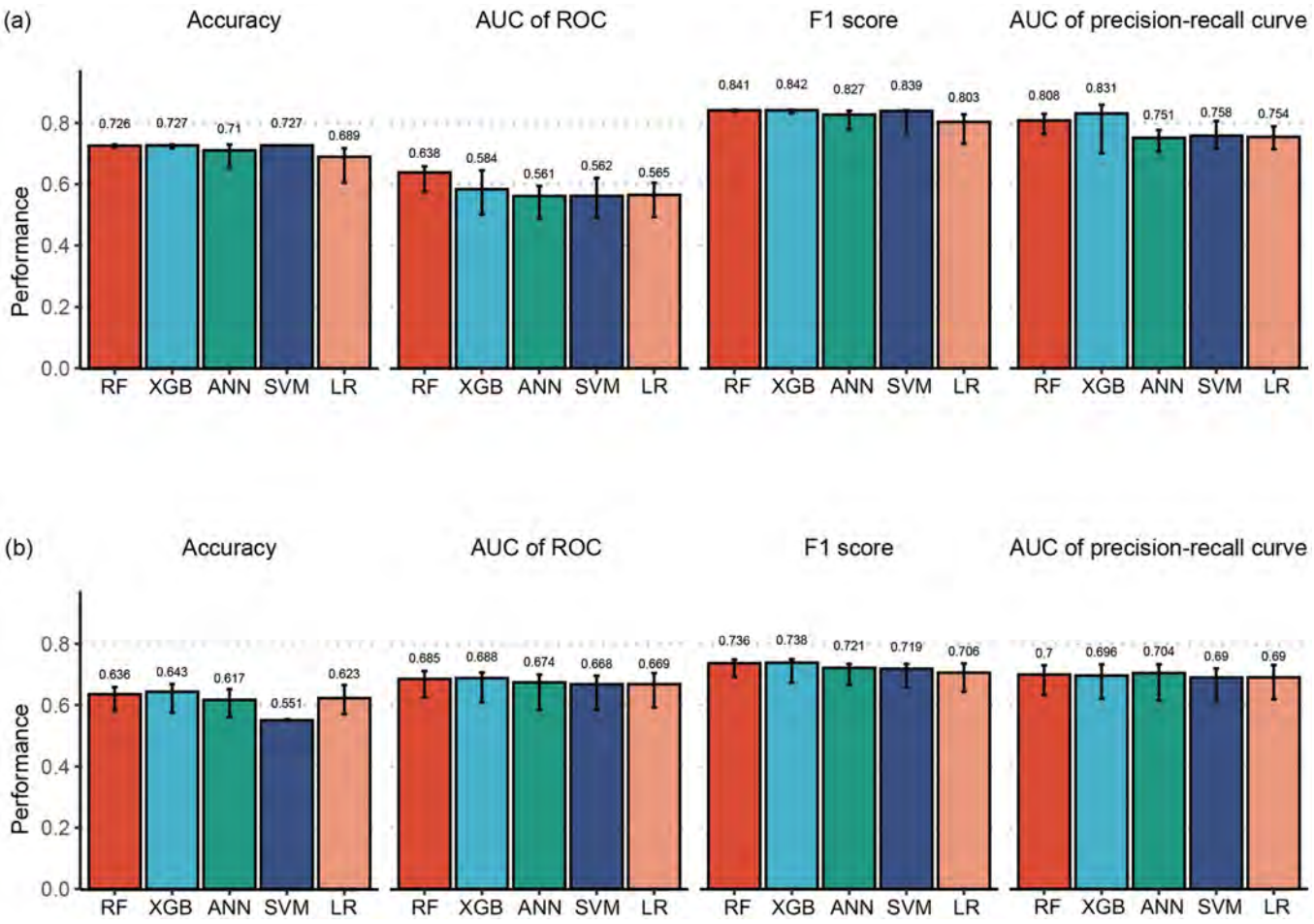

Figure 1. Performances of models trained using various methods (RF, XGBoost, ANN, SVM, and logistic regression) with independent test dataset, in terms of accuracy, AUC of the ROC curve, F1 score, and AUC of the precision-recall curve. (a) RA patients. (b) AS patients. RF, random forest; XGBoost, extreme gradient boosting; ANN, artificial neural network; SVM, support vector machine; LR, logistic regression.

activity (PtGA) in RA and Bath Ankylosing Spondylitis Functional Index (BASFI) in AS, were revealed as the most important features in both diseases (Figure 2).

Conclusion: RF exhibited superior prediction performance for responses of bDMARDs to a conventional statistical method, i.e., logistic regression, in RA patients. In contrast, despite the comparable size of the dataset, machine learning did not outperform in AS patients. The most important features of both diseases, according to feature importance analysis were patient self-reporting scales.

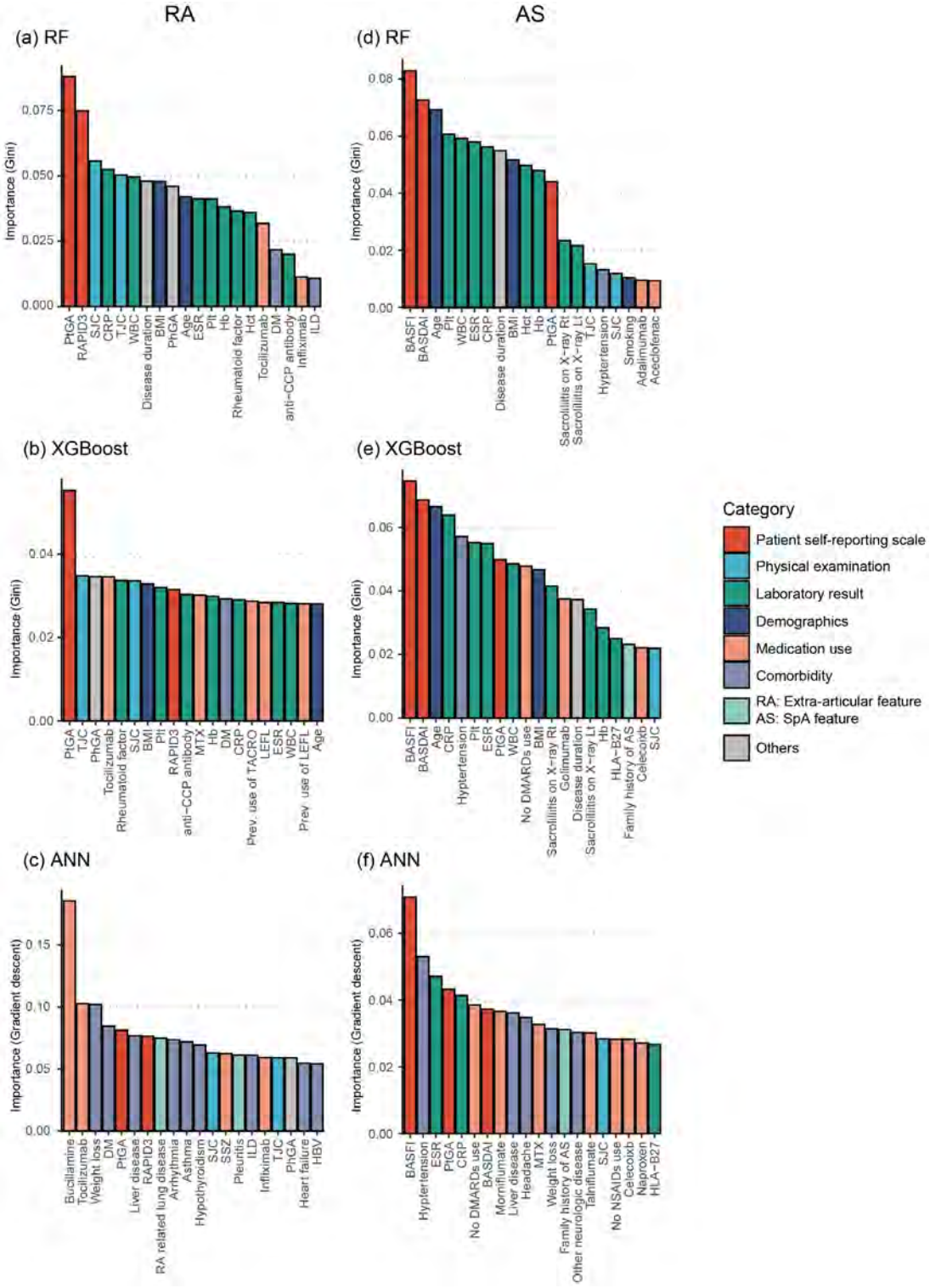

Figure 2. Result of feature importance analysis from the best performing models of each machine learning method. The X-axis represents the input clinical features. The Y-axis represents the feature importance score calculated using the Gini importance or risk backpropagation methods in RF/XGBoost and ANN, respectively. The color of columns represents the categories in which the feature was included. Top 20 important features are shown in figures. Feature importance of (a) RF model, (b) XGBoost model, and (c) ANN model in patients with RA. Feature importance of (d) RF model, (e) XGBoost model, and (f) ANN model in patients with AS. WBC, white cell count; BMI, body mass index; Plt, platelet; Hb, hemoglobin; Hct, hematocrit; DM, diabetes mellitus; anti-CCP, anti-cyclic citrullinated protein; ILD, interstitial lung disease; MTX, methotrexate; TACRO, tacrolimus; LEFL, leflunomide; SSZ, sulfasalazine.

Disclosure: S. Lee, None; **S. Kang**, None; **Y. Eun**, None; **H. Kim**, None; **J. Lee**, None; **E. Koh**, None; **H. Cha**, None.

Abstract Number: 1220

Identification of Underlying Disease Domains by Longitudinal Latent Factor Analysis for Secukinumab Treated Patients in Psoriatic Arthritis and Rheumatoid Arthritis Trials

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SESSION INFORMATION
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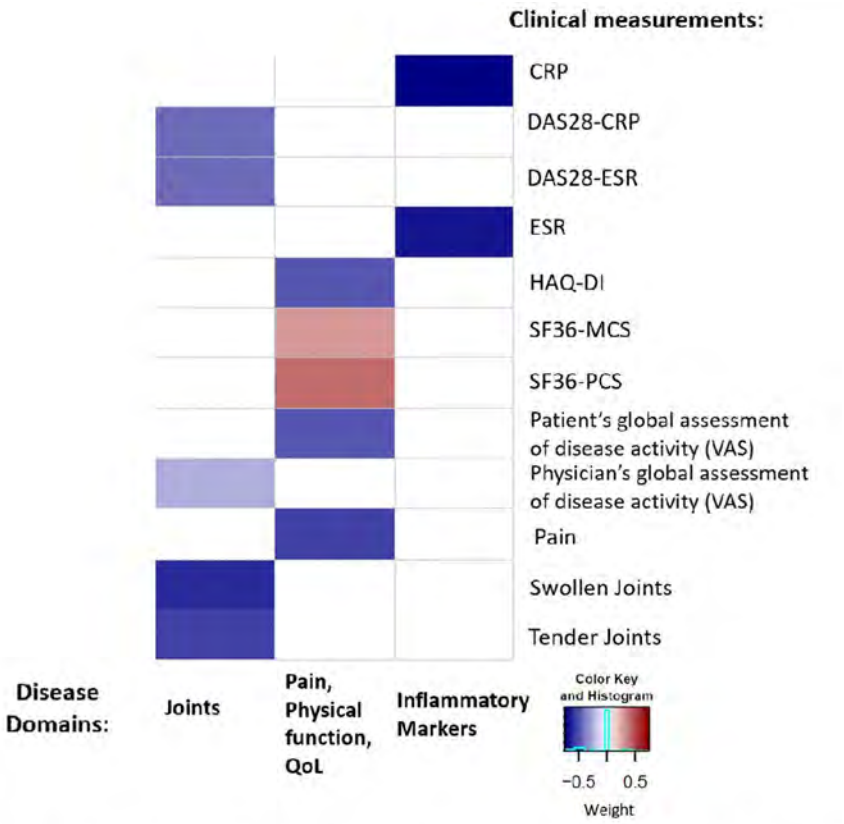
Background/Purpose: Secukinumab is a fully monoclonal antibody approved for the treatment of several related autoinflammatory diseases, including psoriasis, psoriatic arthritis (PsA) and ankylosing spondylitis.[1] While a single clinical endpoint may be chosen to evaluate treatment effect, the natural extension of this sets out to capture a clinical trial's entire longitudinal response profile, made up of multifaceted signs and symptoms. The objective of this analysis is to characterize disease progression and treatment response to secukinumab, across a wide range of clinical variables, thereby complementing traditional analyses of standard endpoints in PsA and rheumatoid arthritis (RA).

Methods: A novel longitudinal latent factor approach was developed and applied across PsA and RA indications. The method identifies underlying (latent) factors that quantify the contribution of each clinical variable to the major sources (axes) of variation in patient response.[2] More importantly, it bundles several clinical endpoints into a small number of concise clinical domains that jointly characterize disease progression. Data from three Phase II RA studies, three Phase III RA studies, and six Phase III PsA studies were pooled, yielding a dataset of 4906 patients; 3464 treated with secukinumab and 1442 treated with placebo. Twelve efficacy endpoints were analyzed up to Week 16 including joint stiffness or swelling, pain, patient-reported outcomes, and alterations in inflammatory markers and quality of life.

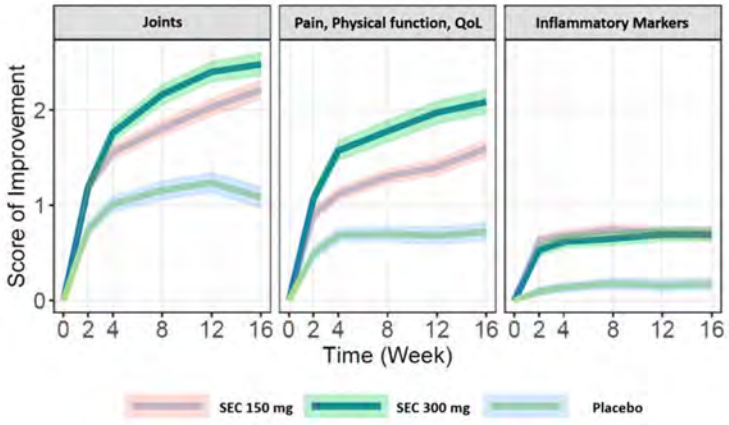
Results: The method summarized the 12 efficacy endpoints in three succinct disease domains, each with a distinct clinical interpretation and role in a multi-dimensional remission [3,4] concept (**Figure 1**). The first disease domain focuses on joint-related symptoms; the second on pain, patient's disease global assessment, and quality of life; and the third on inflammatory laboratory markers. Together, these three disease domains explain three quarters of the variability in the data across both diseases. **Figure 2** displays the trajectory of these latent factors over time. All three disease domains show a numerical separation and greater effect over placebo, with the third separating from placebo as early as Week 4.

Conclusion: The longitudinal latent factor method provided insights into key clinical variables that impact on underlying disease progression and led to better characterization of treatment response. This application has the potential to enhance our understanding of existing composite endpoint methods, as well as to catalyze the development of novel and more robust clinical endpoints.



The heat map depicts the relative weights of efficacy measurement in the disease domains. The color intensity represents the absolute weight of each measurement in a disease domain. The blue color in the histogram represents a negative weight, i.e. the factor tends to increase/improve as that clinical measurement decreases. The red color denotes positive weight, i.e. the factor tends to increase/improve as that clinical measurement increases.

CRP, C-reactive protein; DAS, disease activity score; ESR, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, mental component score; PCS, Physical component score; SF-36, 36-Item Short Form Survey; VAS, visual analogue scale; QoL, quality of life



Longitudinal responses for each treatment arm (curves) in each disease domain (panels). SEC 150mg represents pooled data for treatment regimens of Secukinumab 150 mg s.c and Secukinumab i.v. (10 mg/kg)-150mg. Each panel depicts the trajectory of improvement of the latent factor at each disease domain over time. Each line represents the mean response of each treatment in induction stage from baseline to Week 16. The color band represents the 95% confidence interval of response in each treatment. SEC, secukinumab; QoL, Quality of life.

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Heatmap illustrating the relative weights of measurements in disease domains
Score of response in disease domain stratified by treatment

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Abstract Number: 1221

Association of Neutrophil Lymphocyte and Platelet Lymphocyte Ratios with Joint Inflammation in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Prediction, Biomarkers, & Treatment Response (1196–1222)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: It can be challenging to determine whether rheumatoid arthritis (RA) patients who require arthroplasty have ongoing inflammation, in addition to damage in the affected joint on clinical exam. C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), neutrophil-lymphocyte (NLR) and platelet-lymphocyte ratios (PLR) are all blood biomarkers that have been reported to associate with disease activity.

Table 1. Multivariate ordered logistic regression predicting SLI in all RA patients

	OR	SE	P>|t|	95% Confidence Interval
CRP	1.18	0.102	0.055	(0.997, 1.399)
ESR	**1.02**	**0.008**	**0.035**	**(1.00, 1.03)**
PLR	**1.003**	**0.002**	**0.050**	**(0.9999, 1.007)**
Removed from model as insignificant (p>0.1): DAS28-ESR, SJC, TJC, MD global, NLR				
*bold values significant p<0.05; OR=odds ratio; SE=standard error; CRP = C Reactive Protein; ESR = erythrocyte sedimentation rate; NLR = neutrophil lymphocyte ratio; PLR = platelet lymphocyte ratio; TJC = tender joint count; SJC = swollen joint count				

Table 1. Multivariate ordered logistic regression predicting SLI in all RA patients

	OR	SE	P>|z|	95% Confidence Interval
TJC	0.941	0.030	0.056	(0.885, 1.002)
ESR	**1.025**	**0.011**	**0.016**	**(1.005, 1.046)**
MD Global	1.221	0.135	0.071	(0.983, 1.516)
PLR	**1.006**	**0.003**	**0.044**	**(1.0002, 1.011)**
Removed from model as insignificant (p>0.100): NLR, DAS28-ESR, SJC, CRP				
*bold values significant p<0.05; OR=odds ratio; SE=standard error; ESR = erythrocyte sedimentation rate; NLR = neutrophil lymphocyte ratio; PLR = platelet lymphocyte ratio; TJC = tender joint count; SJC = swollen joint count				

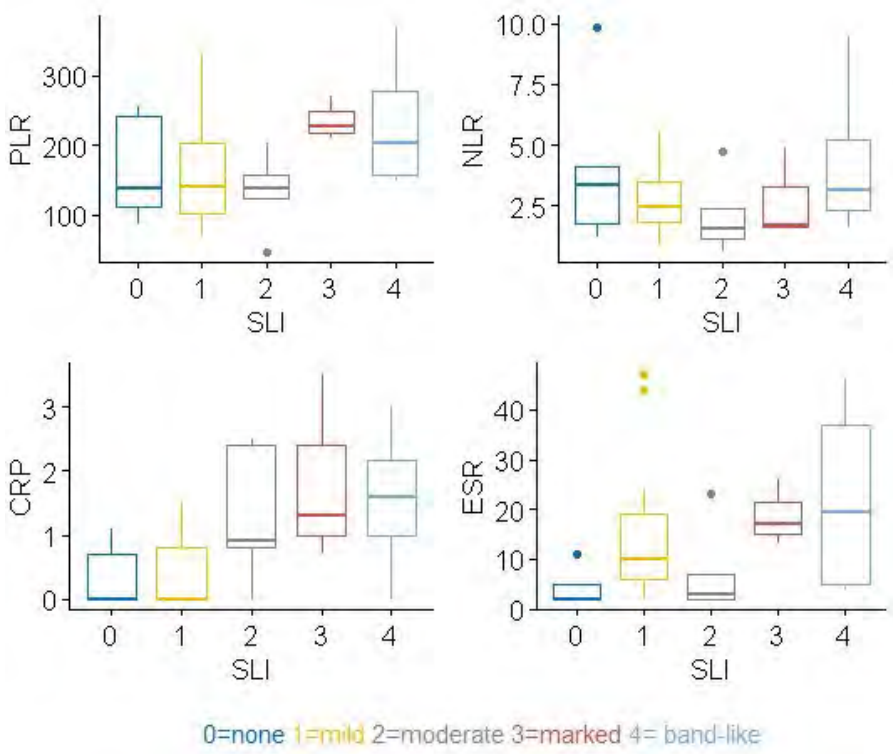

Figure 1. Blood biomarkers by SLI in RA patients with DAS<3.2 not on GCs.

Methods: 239 patients meeting ACR/EULAR 1987 and/or 2010 RA criteria and 162 OA patients were recruited prior to elective total hip, knee, elbow, or shoulder arthroplasty. Disease characteristics and blood samples were collected pre-operatively. Hematoxylin and eosin (H&E) stains of the synovium were prepared and scored by a pathologist. Mann-Whitney and Kruskal Wallis tests were used to compare biomarkers among groups. Stata's backward stepwise regression and multivariable ordered logistic regression was performed to predict synovial lymphocytic inflammation on (1) 239 RA patients, (2) 146 RA patients not on GCs, and (3) 52 RA patients with low disease activity (DAS28-ESR< 3.2).

Results: RA patients (median [IQR] = 159.6 [103.1]) had higher PLR than OA patients (median [IQR] = 138.9[76.5]) (p< 0.001). RA patients (median [IQR] = 2.73 [2.34]) also had a slightly higher NLR compared to OA patients (median [IQR] = 2.45[1.90]) (p=0.052). Additionally, RA patients on glucocorticoids (GCs) had higher NLR (p< 0.001) and PLR (p=0.04) than those not on GCs. In all models predicting SLI in RA, PLR was significantly associated with SLI but not DAS28-ESR or CDAI **(Table 1 and Table 2)**. Patients with DAS28-ESR< 3.2 and high SLI had higher PLR (p=0.01) and CRP (p=0.02) **(Figure 1)** than those with low SLI. PLR was not associated with SLI in OA patients.

Conclusion: Platelet lymphocyte ratio is associated with synovial lymphocytic inflammation in rheumatoid arthritis patients of all disease activity levels. This suggests that inexpensive, routinely performed blood tests may be a useful blood biomarker of RA synovial inflammation, including subclinical synovitis.

Disclosure: D. Pearce-Fisher, Pfizer, 11; **D. Orange**, MedImmune, 2, Pfizer, 2; **B. Mehta**, Novartis, 1, 6; **D. Jannat-Khah**, Cytodyn, 12, own shares of stock, Walgreens, 12, Own stock shares, AstraZeneca, 12, own stock shares, GW Pharmaceuticals, 12, stock ownership; **S. Goodman**, UCB, 1, NOvartis, 5.

Abstract Number: 1222

Drug Response Is Associated with Changes in Specific MicroRNAs in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Background/Purpose: MicroRNAs are markers and mediators of disease and drug response. Prior studies have proposed several miRNAs for prediction of drug response or monitoring drug effect in patients with RA. Our objective was to determine if baseline or change in concentrations of these plasma miRNAs are associated with clinical response to several key disease modifying antirheumatic drugs (DMARDS): methotrexate, adalimumab and tocilizumab.

Methods: We developed a list of candidate miRNAs which are associated with response to a DMARD based on literature: let-7a-5p, let-7b-5p, miR-126-3p, miR-132-3p, miR-146a-5p, miR-16-5p, miR-22-3p, miR-223a-3p, miR-23a-3p, miR-24-3p, and miR-27-3p. Candidate miRNAs were measured in plasma from 70 patients with RA in the TETRAD repository before and 6-months after starting a new DMARD by qPCR. The miRNA concentration was determined from a standard dilution curve of a known DNA mimic concentration. MiRNAs were log2 transformed due to skewness. The relationship between change in miRNA concentration and DAS28-ESR before versus after DMARD was assessed by Spearman correlation and using a two-step linear regression with 6-month DAS28-ESR as the outcome and baseline DAS28-ESR and the log2-transformed residualized miRNA as predictors. The residualized miRNA reflects the baseline adjusted miRNA at 6-months, thus enabling adjustment for both baseline miRNA and DAS28-ESR in the final analysis. The predictive capacity of the baseline concentrations of miRNAs adjusted for baseline DAS28-ESR to predict DAS28-ESR at 6 months was assessed by linear regression. Pathway analysis of the miRNA predicted targets was performed using MSigDB Reactome gene sets.

Table 1. Clinical characteristics of all patients with rheumatoid arthritis initiating methotrexate, adalimumab, or tocilizumab

	all RA (n= 70)	Methotrexate (n = 24)	Adalimumab (n = 23)	Tocilizumab (n = 23)
Age, years	54 (45, 62)	54 (45, 56)	54 (46, 63)	53 (46, 63)
Race, # Caucasian	56 (80)	18 (75)	18 (78)	20 (87)
Gender, # female	57 (81)	18 (75)	19 (83)	20 (87)
Disease duration, years	4.24 (0.34, 12.10)	0.19 (0.08, 1.20)	5.19 (1.81, 10.91)	12.65 (4.80, 21.88)
CCP, # positive	42 (60)	17 (71)	11 (48)	14 (61)
RF, # positive	43 (61)	15 (62)	12 (52)	16 (70)
Baseline DAS28-ESR, units	4.91 (3.61, 5.62)	4.78 (3.34, 5.43)	4.99 (3.78, 5.97)	4.89 (3.69, 5.92)
Concomitant MTX, # yes	30 (43)	-	19(83)	11(48)
Concomitant corticosteroids, # yes	37(65)	13 (87)	12 (60)	12 (55)
EULAR response, # yes	51 (73)	16 (67)	16 (70)	19 (83)

Data presented at median (interquartile range) or number (%). Disease duration= time since symptom onset. CCP= anti-cyclic citrullinated peptide antibody. RF= rheumatoid factor. DAS28-ESR= disease activity based on 28 joints and erythrocyte sedimentation rate. MTX= methotrexate. EULAR= European League Against Rheumatism. EULAR response= moderate to good.

Table 2. Relationship between change in log2_miRNA with change in DAS28-ESR between baseline and 6-months after initiation of new DMARD

	Spearman Rho (comparing change in miRNA and change in DAS28-ESR)	Baseline adjusted P*
let-7a-5p	-0.20	0.02
let-7b-5p	-0.28	0.004
miR-126-3p	-0.18	0.049
miR-132-3p	-0.15	0.38
miR-146a-5p	-0.19	0.04
miR-16-5p	-0.23	0.02
miR-22-3p	-0.17	0.03
miR-223a-3p	-0.10	0.26
miR-23a-3p	-0.18	0.12
miR-24-3p	-0.23	0.07
miR-27-3p	-0.13	0.26

Adjusted P value is the result of the residualized miRNA analyses which adjust for baseline miRNA concentrations and baseline DAS28-ESR scores.

Results: The 70 patients with RA had a median age of 54 years; 80% were Caucasian, 81% were female, median baseline DAS28-ESR was 4.91 units; after 6-months 73% had a moderate to good EULAR response (Table 1). Increasing plasma concentrations between baseline and 6-months of six of the miRNAs (let-7a-5p, let-7b-5p, miR-126-3p, miR-146a-5p, miR-16-5p, and miR-22-3p) were significantly associated with decreasing DAS28-ESR after 6-months of new DMARD treatment in the residualized miRNA analyses (Table 2, all $p< 0.05$), although mean miRNA concentrations did not significantly change before versus after treatment. There was no significant interaction based on the DMARD initiated (all $p >0.2$), and baseline miRNA concentrations did not predict drug response (all $p >0.05$). Pathway analysis demonstrated that the six miRNAs which are associated with change in DAS28-ESR are predicted

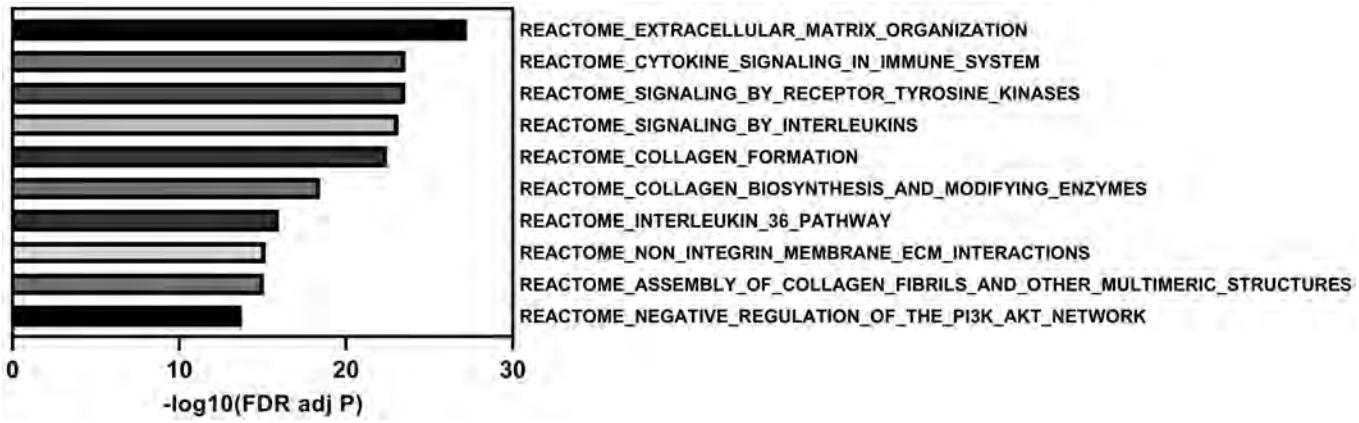


Figure. Reactome pathways which are significantly enriched among miRNA predicted targets.

to target pertinent functions like cytokine signaling, and signaling by receptor tyrosine kinases (Figure), which could contribute to drug response.

Conclusion: Increasing concentrations of six of the eleven miRNAs were significantly associated with greater improvement in RA disease activity 6-months after starting a new DMARD. Pathway analysis demonstrates that these miRNAs, while being markers of drug response may play a direct role in resolution of inflammation. Further studies will be needed to confirm this.

Disclosure: Q. Wu, None; **S. Chen**, None; **F. Ye**, None; **J. Solus**, None; **S. Bridges, Jr**., None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **C. Stein**, None; **M. Ormseth**, None.

Abstract Number: 1223

A Multinational, Prospective, Observational Study in Patients with Rheumatoid Arthritis Receiving Baricitinib, Targeted Synthetic or Biologic Disease-Modifying Therapies: 6-Month Effectiveness and Patient Reported Outcome Data from the European Cohort

Gerd Burmester[1], Bruno Fautrel[2], **Rieke Alten**[3], Marco Matucci-Cerinic[4], Jean hugues Salmon[5], Thorsten Holzkaemper[6], Inmaculada de la Torre[7], Pedro Lopez-Romero[8], Walid Fakhouri[8] and Anja Gentzel-Jorczyk[8], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Pitié Salpêtrière Hospital, APHP, Sorbonne Université, Paris, France, [3]Schlosspark-Klinik University, Berlin, Germany, [4]University of Florence, Florence, Italy, [5]Rheumatology, CHU Maison blanche, Reims, Reims, France, [6]Eli Lilly and Company, Bad Homburg, Germany, [7]Eli Lilly and Company, Alcobendas, Spain, [8]Eli Lilly and Company, Indianapolis, IN

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib (BARI) is a JAK1/2 inhibitor approved for the treatment of adults with moderately to severely active rheumatoid arthritis (RA) and the treatment of adult atopic dermatitis in Europe and Japan.

RA-BE-REAL is a 3-year, prospective, observational study of adult RA patients (pts) evaluating adherence to treatment in clinical practice.

The purpose of this abstract is to report the proportion of European pts with RA that discontinue treatment following 3- and 6-months (M) of either BARI, biologic (b)DMARDs or any other targeted synthetic (ts)DMARDs (b/ tsDMARDs) after starting that treatment for the first time. To report the percentage of pts achieving remission and low disease activity (LDA) based on Clinical Disease Activity Index (CDAI) at 6M. To assess changes from baseline in CDAI and to describe changes in patient reported outcomes (PROs) related to quality of life, pain, and physical functioning at 6M.

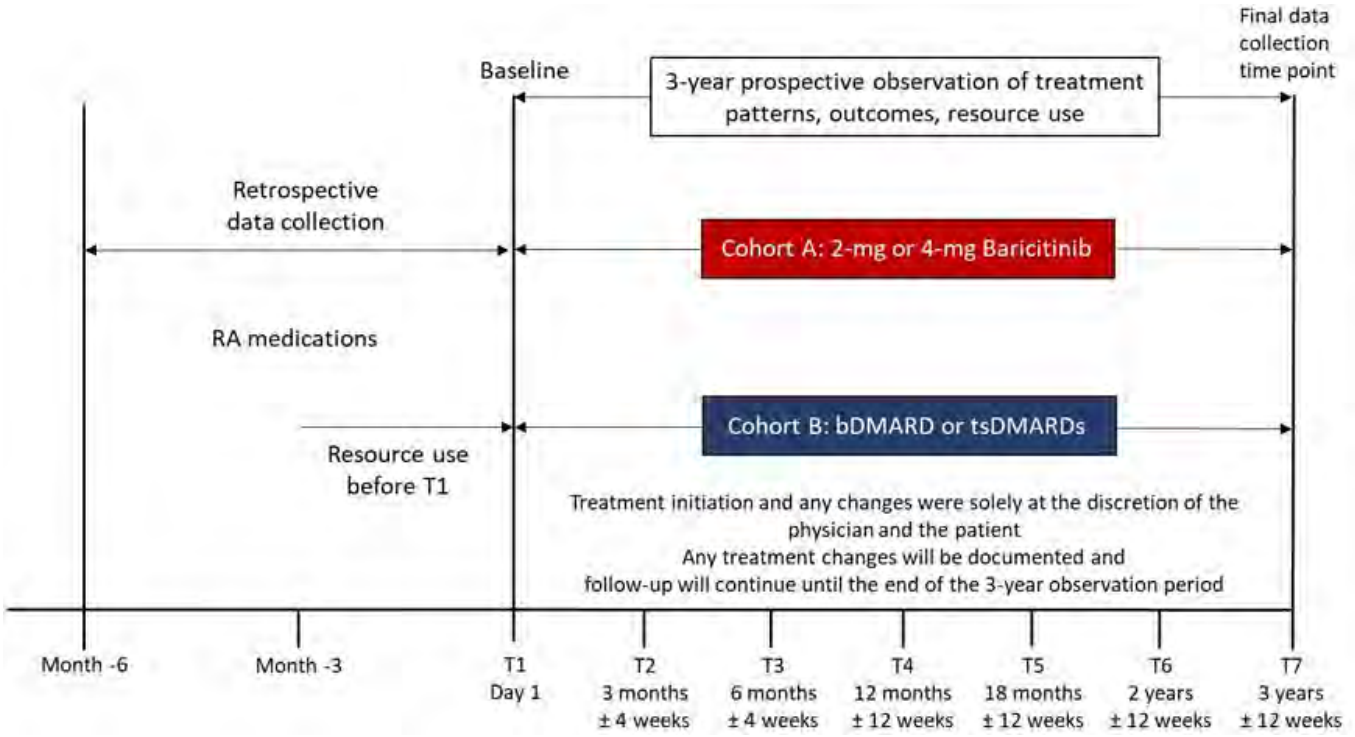
Methods: The primary endpoint is the discontinuation rate of initial RA treatment for all causes (excluding sustained clinical response) over a 24M period. Two pt cohorts are assessed: cohort A, started treatment with BARI (2mg or 4mg), and cohort B, any biologic or any other tsDMARD (Fig. 1). Treatment initiation and changes are at the discretion of the pt or physician. In this interim analysis we report descriptive baseline, 3M and 6M data.

Results: Between October 2018 and March 2020, 1074 adult RA pts were enrolled from France, Germany, Italy, Spain, and UK. At time of enrollment 50.9% of pts in cohort A and 31.2% of pts in cohort B commenced treatment as a monotherapy (Table 1). A similar proportion of pts in cohort A (52/392 pts; 13.3%) and cohort B (59/425; 13.9%) discontinued treatment at 3M. At 6M pts in cohort A (63/336; 18.8%) were less likely to have discontinued their initial RA treatment than pts in cohort B (93/370; 25.1%) (Fig.2A). At 6M a higher percentage of cohort A pts had achieved CDAI remission (cohort A; 25.6%, cohort B; 18.5%) (Fig.2B). Pts in cohort A experienced a greater decrease in disease activity as assessed by CDAI with a mean reduction in disease activity scores of -13.9 (-11.8 for pts in cohort B) (Table 2). With respect to PROs, a similar improvement from baseline in HAQ-DI, pain (VAS), and EQ-5D-5L scores was observed for both cohorts (Table 2).

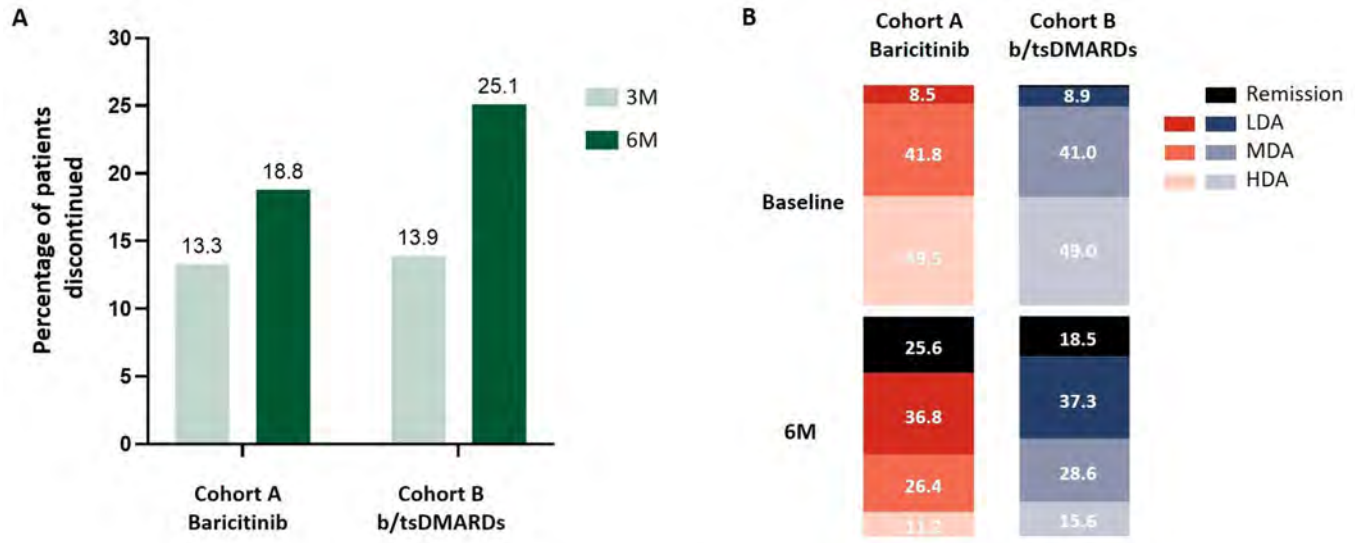
	Cohort A Baricitinib (n=509)	Cohort B b/tsDMARDs (n=565)
Concomitant use of csDMARDs n (%)		
with any csDMARD	250 (49.1)	389 (68.8)
as a monotherapy	259 (50.9)	176 (31.2)
Age in years (SD)	59.1 (13.2)	57.0 (13.9)
Disease duration in years (SD)	10.0 (9.1)	8.9 (9.6)
Oral GCCs at time of enrollment n (%)		
Yes	218 (42.8)	249 (44.1)
No	291 (57.2)	316 (55.9)
b/tsDMARDs treatment any time before enrollment n (%)		
Naive	245 (48.1)	344 (60.9)
1 b/tsDMARD	67 (13.2)	57 (10.1)
2 b/tsDMARDs	110 (21.6)	79 (14.0)
>2 b/tsDMARDs	87 (17.1)	85 (15.0)

Data presented side-by-side for descriptive purposes only. csDMARD; conventional synthetic disease-modifying antirheumatic drugs, GCCs; glucocorticoids, SD; standard deviation

Conclusion: Overall, these observational study results highlight that pts receiving baricitinib are less likely to discontinue treatment and more likely to achieve remission than pts receiving a biologic or any other tsDMARDs.



Study Design. Participants entered cohort A or B based on their treatment decision for BARI or another b/tsDMARD, pts in each cohort were with/without concomitant csDMARDs.



Footnote: M; months, LDA; low disease activity, MDA; moderate disease activity, HDA; high disease activity. Values are presented as a percentage of the population.

A. Percentage of pts that discontinued initial RA treatment at 3M and 6M, B. Percentage of pts in cohort A and cohort B achieving remission and LDA status at 6M.

	Cohort A Baricitinib			Cohort B b/tsDMARDs		
	Baseline mean (SD)	6M mean (SD)	CFB (SD)	Baseline mean (SD)	6M mean (SD)	CFB (SD)
CDAI	24.0 (11.7)	10.0 (9.5)	-13.9 (12.5)	23.8 (12.4)	11.8 (10.4)	-11.8 (13.2)
SJC	5.2 (4.8)	1.5 (2.7)	-3.7 (4.7)	4.7 (4.9)	1.6 (2.9)	-2.8 (4.9)
TJC	7.3 (6.1)	2.6 (4.2)	-4.7 (6.0)	7.8 (6.5)	3.5 (5.0)	-4.0 (6.5)
PhGA	5.6 (2.0)	2.4 (2.2)	-3.1 (2.5)	5.5 (2.1)	2.8 (2.3)	-2.8 (2.7)
PGA	5.9 (2.3)	3.6 (2.7)	-2.3 (2.9)	5.8 (2.4)	3.8 (2.5)	-2.2 (3.0)
HAQ-DI	1.4 (0.7)	1.0 (0.8)	-0.4 (0.6)	1.3 (0.7)	1.0 (0.7)	-0.3 (0.6)
Pain (VAS)	58.9 (23.1)	34.5 (27.1)	-22.4 (28.6)	56.4 (24.3)	35.8 (25.7)	-21.5 (29.3)
EQ-5D-5L	0.5 (0.3)	0.7 (0.2)	0.1 (0.2)	0.5 (0.3)	0.7 (0.2)	0.1 (0.3)

Data presented side-by-side for descriptive purposes only. b/tsDMARDs; biologic/targeted synthetic disease modifying anti-rheumatic drugs, M; month, CFB; change from baseline, CDAI; clinical disease activity index, SJC; swollen joint count, TJC; tender joint count, PhGA; physician global assessment of disease activity, PGA; patient global assessment of disease activity, HAQ-DI; health assessment questionnaire disability index, VAS; visual analog scale, EQ-5D-5L; European quality of life 5 dimensions 5 levels

Observed means (baseline, 6M) and change from baseline in clinical characteristics for pts enrolled in RA-BE-REAL.

Disclosure: G. Burmester, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **R. Alten**, Abbvie, 1, Amgen, 1, Biogen, 1, Galapagos, 1, Gilead, 1, Janssen, 1, Lilly, 1, Novartis, 1, Pfizer, 1, Roche, 1, BMS, 1, Celltrion, 1; **M. Matucci-Cerinic**, Merck, 5, 6, Actelion, 5, 6, Janssen, 6, Eli Lilly and Company, 6, Biogen, 6; **J. Salmon**, None; **T. Holzkaemper**, Eli Lilly, 3, 12, Shareholder; **I. de la Torre**, Eli Lilly and Company, 3, 11; **P. Lopez-Romero**, Eli Lilly and Company, 3, 11; **W. Fakhouri**, Eli Lilly and Company, 3, 11; **A. Gentzel-Jorczyk**, Eli Lilly and Company, 3, 11.

Abstract Number: 1224

Low CD39 Expression on B Cells Predicts the Occurrence of Anti-Drug Antibodies in RA Patients Treated with Rituximab

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SESSION INFORMATION

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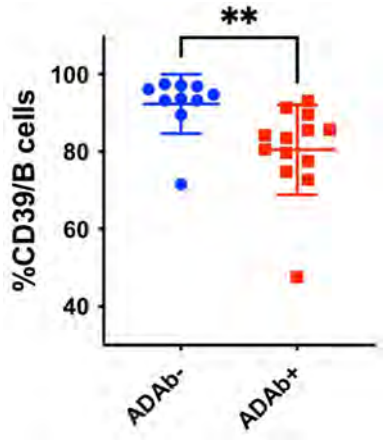

Background/Purpose: Anti-Drug antibodies (ADAb) are well studied and have an impact on response to treatment with monoclonal anti-TNF biologics. Rituximab treatment has an important immunogenic potential as it is a chimeric antibody. Most recent studies on biosimilars have identified low rates of ADAb among rituximab-treated patients without impact on treatment efficacy. The lack of sensitivity in the detection of ADAb might explain discrepancies between TNFi and rituximab. Methotrexate has been associated with less occurrence of ADAb when co-administered with adalimumab. CD73 and CD39 are ectoenzyme involved in the pathway of adenosine production, a known mechanism of action of methotrexate. The objective of this study was to characterize if CD39 and CD73 expression on B cells was a predictor of occurrence of ADAb in a population of RA patients treated with rituximab.

Methods: ABIRISK is an IMI-2 European consortium designed to identify predictors of ADAb among rheumatoid arthritis (RA) patients and inflammatory bowel disease (IBD) patients. Prospective assessment of ADAb was performed using sensitive technique based on Meso Scale diffusion. Response to rituximab was assessed at 6 months using delta DAS 28. Patient's PBMCs at baseline were assessed for B cell lineage markers and CD73 and CD39 using flow cytometry.

Results: Among the 23 analyzed RA patients treated with rituximab, 13 became ADAb+ and 10 remained ADAb negative. There was no difference in the proportion of patients with concomitant methotrexate in both groups with 77 % and 80% in ADAb+ and ADAb- respectively. B cells lineage markers did not vary between patients' groups. Baseline levels of CD73 expression on B cells were similar among patients who later became ADAB+ or negative. At baseline lower levels of CD39 expression on B cells was significantly predictive of the future appearance of ADAb (see figure). There was a trend of correlation between pre-treatment CD39 expression levels and delta DAS 28 at 6 months indicating a potential diminished response to treatment in patients with lower CD39 expression (p= 0,059).

Conclusion: Pre-treatment lower CD39 expression levels on B cells is predictive of the future appearance of ADAb directed against rituximab in RA patients. CD 39 levels trended to negatively correlate with less treatment efficacy. Since the number of patients co-treated with methotrexate is not significantly different between ADAb+ and ADAb- patients, we might hypothesize that the level of CD39 accounts for the occurrence of ADAb. This suggests that the level of adenosine that might be modulated by methotrexate or by the level of CD39 expression may impact the occurrence of anti-rituximab antibodies in RA patients.

Disclosure: S. Bitoun, None; **B. Ly**, None; **S. Hässler**, None; **A. Paoletti**, None; **A. Gleizes**, None; **S. Hacein-Bey**, None; **P. Bröet**, None; **M. Pallardy**, Glycovax, 2, Pierre-Fabre, 2, Servier, 2; **X. Mariette**, GlaxoSmithKline, 2, BMS, 2, Servier, 2, Janssen, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 1225

Baseline Extracellular Matrix Biomarkers Predict Abatacept Treatment Response in MTX-Naive, ACPA+ Patients with Early RA

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Predictive biomarkers reflecting RA processes and treatment (tmt) efficacy are urgently needed to inform medical options. Markers of bone remodeling and extracellular matrix (ECM) turnover may serve as disease-relevant, surrogate biomarkers indicative of synovial joint pathophysiology.[1,2] We evaluated baseline (BL) correlations of biomarkers with disease activity (DA), their predictive value for efficacy, and pharmacodynamic (PD) changes during subcutaneous (SC) abatacept (ABA) tmt in a phase 3b study in MTX-naive, ACPA+ patients (pts) with early RA (AVERT-2; NCT02504268).[3]

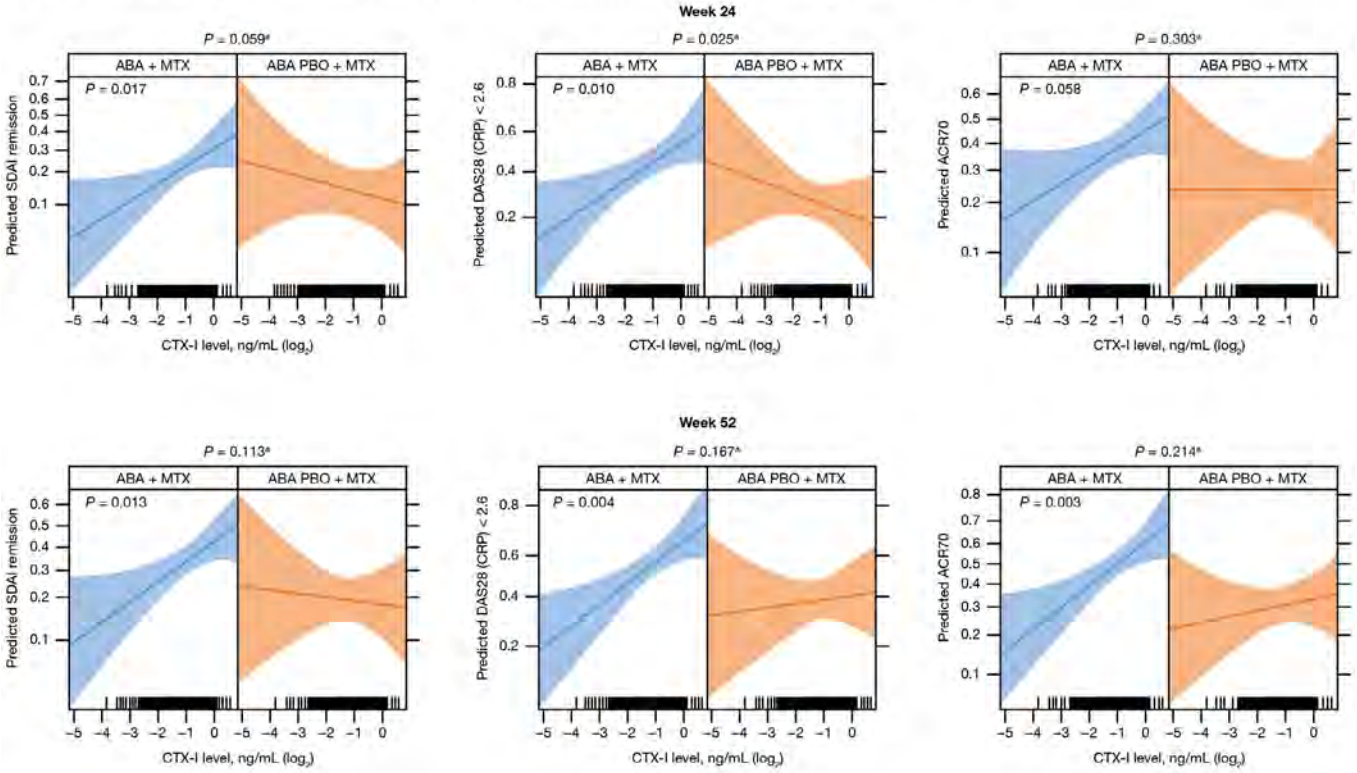
Methods: Pts with early RA (ACR/EULAR 2010)[4] were randomized to SC ABA 125 mg QW or SC ABA placebo (PBO) both with oral MTX for 56 weeks (wks). A subgroup of the overall population (intention-to-treat) was included. Linear correlations were assessed using BL levels of 8 ECM serum biomarkers (Nordic Biosciences) including MMP-mediated degradation products of type III and IV collagen (C3M, C4M), neo-epitope of MMP-mediated degradation of CRP (CRPM), and neo-epitope of cathepsin-mediated degradation of type I collagen (CTX-I), with DA measures.

Table 1. Baseline characteristics in the overall (ITT) population and the ECM biomarker subgroup by treatment arm

	ITT population			ECM biomarker subgroup		
	Abatacept + MTX (n = 451)	Abatacept placebo + MTX (n = 301)	*P* value	Abatacept + MTX (n = 330)	Abatacept placebo + MTX (n = 205)	*P* value
Age, mean (SD)	49 (13)	49 (14)	0.69	48 (13)	47 (14)	0.52
Sex, female, n (%)	349 (77)	243 (81)	0.31	266 (81)	171 (83)	0.48
Race, n (%)						
Asian	77 (17)	52 (17)	0.99	61 (18)	41 (20)	0.96
Black	20 (4)	15 (5)		13 (4)	9 (4)	
Other	39 (9)	25 (8)		31 (9)	19 (9)	
White	315 (70)	209 (69)		225 (68)	136 (66)	
SDAI, mean (SD)	38 (14)	39 (14)	0.25	39 (14)	39 (14)	0.87

ECM, extracellular matrix; ITT, intention to treat; SD, standard deviation; SDAI, Simplified Disease Activity Index.

Figure 1. Probability of achieving efficacy outcomes at weeks 24 and 52 with ABA + MTX or ABA PBO + MTX as predicted by baseline CTX-I level



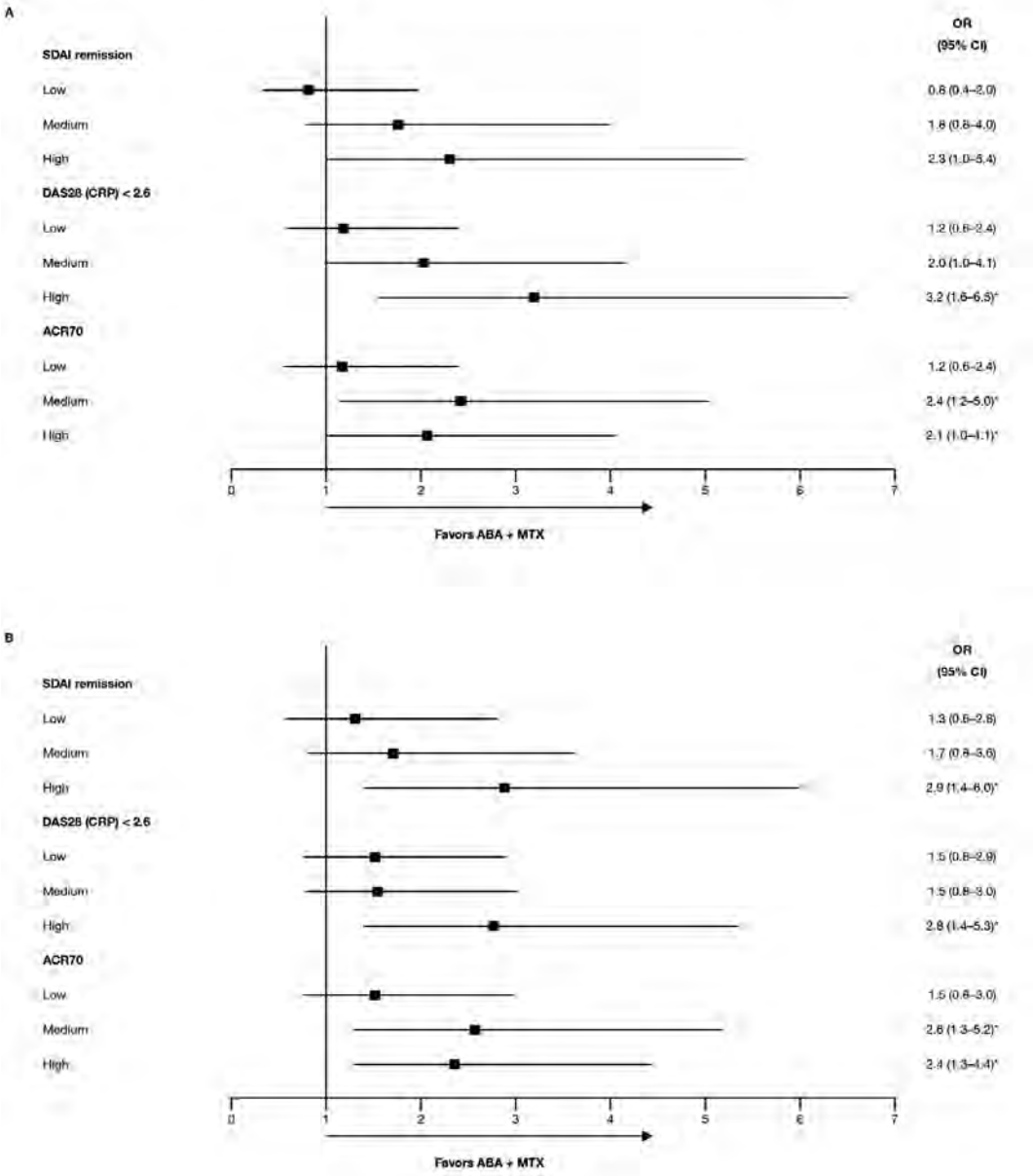
Age, baseline SDAI, and baseline erosion score were used as covariates.
A total of 8 biomarkers were tested: C3M: neo-epitope of MMP-9 mediated degradation of type III collagen; C4G: neo-epitope of granzyme B mediated degradation of type IV collagen; C4M: neo-epitope of MMP-2, -9, and -12 mediated degradation of type IV collagen α1 chain; CPa9-HNE: neo-epitope of human neutrophil elastase (HNE) mediated degradation of calprotectin; CTX-I: neo-epitope of cathepsin-mediated degradation of type I collagen; CRPM: neo-epitope of MMP-1 and -8 mediated degradation of CRP; N-MID: N-MID osteocalcin; VICM: neo-epitope of MMP-2, -8, and trypsin mediated degradation of citrullinated vimentin.
[a]Interaction effect for ABA + MTX versus ABA PBO + MTX.
ABA, abatacept; PBO, placebo; SDAI, Simplified Disease Activity Index.

Logistic regression predictive models were used to evaluate BL bone remodeling markers in predicting clinical efficacy (SDAI remission, DAS28 [CRP] < 2.6, ACR70) at wks 24 and 52 with biomarker levels defined as a continuous variable or categorically (low, medium, high tertiles). For biomarkers with data at wks 24 and 52, PD changes were assessed using a linear mixed-effects model with repeated measures.

Results: BL pt characteristics were similar between the overall population and the ECM biomarker subgroup, and across tmt arms (**Table 1**). BL biomarker levels were generally similar between tmt arms. Of biomarkers tested, BL C3M, C4M, and CRPM showed greatest correlations with BL DA measures; CTX-I showed weak correlation with BL DA. Probability of wk 24 and 52 efficacy as predicted by BL CTX-I showed differential response between ABA + MTX and ABA PBO + MTX tmt arms at both time points (**Figure 1**). This was not seen with BL CRP (data not shown). Categorical analysis showed greater tmt differences for ABA + MTX vs ABA PBO + MTX in pts with medium/high vs low BL CTX-I (**Figure 2**). PD analysis showed significant tmt differences in adjusted change from BL in C3M and C4M (wk 24 and 52) and CRPM (wk 24) with ABA + MTX vs ABA PBO + MTX (data not shown).

Conclusion: In ACPA+ pts with early RA, BL levels of cartilage biomarker CTX-I predicted differential SDAI remission or DAS28 (CRP) < 2.6 with abatacept + MTX vs abatacept PBO + MTX, with higher levels of CTX-I associated with a greater probability of achieving efficacy endpoints for abatacept + MTX; this relationship was not observed with abatacept PBO + MTX. Tmt differences were greatest in pts with medium/high BL CTX-I levels. Significant PD effects of abatacept tmt on C3M, C4M, and CRPM were seen. Additional studies of BL CTX-I as a predictive biomarker of abatacept tmt response are warranted.

Figure 2. Treatment differences in efficacy outcomes at (A) week 24 and (B) week 52 by baseline CTX-I levels (low, medium, high)



Low, medium, and high CTX-I categories are based on tertiles T1 (n = 178, 0.028–0.324 ng/mL), T2 (n = 177, 0.325–0.525 ng/mL), and T3 (n = 178, 0.526–1.570 ng/mL), respectively. Age, baseline SDAI, and baseline erosion score were used as covariates.
*$P < 0.05$ for comparison of ABA + MTX versus ABA PBO + MTX.
ABA, abatacept; CI, confidence interval; CTX-I, neo-epitope of cathepsin-mediated degradation of type I collagen; OR, odds ratio; PBO, placebo; SDAI, Simplified Disease Activity Index.

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3. Emery P, et al. *Arthritis Rheum* 2018;70:abs563.
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Abstract Number: 1226

The Neuro-QOL Upper Extremity Function Scale: New Opportunities to More Reliably and Precisely Measure Self-reported Hand Function and Self-care Activities in People with RA

Susan Bartlett[1], Orit Schieir[2], Marie-France Valois[1], Janet Pope[3], Gilles Boire[4], Edward Keystone[5], Diane Tin[6], Carter Thorne[7], Carol Hitchon[8], Louis Bessette[9], Glen Hazlewood[10], Vivian Bykerk[11] and CATCH Investigators[12], [1]McGill University, Montréal, QC, Canada, [2]Canadian Early Arthritis Cohort Study, Montréal, QC, Canada, [3]University of Western Ontario, London, ON, Canada, [4]Universite de Sherbrooke, Sherbrooke, QC, Canada, [5]Keystone Consulting Enterprises Inc., Toronto, ON, Canada, [6]The Arthritis Program Research Group, Newmarket, ON, Canada, [7]Southlake Regional Health Centre, Newmarket, ON, Canada, [8]University of Manitoba, Winnipeg, MB, Canada, [9]Centre de l'Ostoporose et de Rhumatologie de Qubec, Québec City, QC, Canada, [10]University of Calgary, Calgary, AB, Canada, [11]Hospital for Special Surgery, New York, NY, [12]Canadian Early Arthritis Cohort Investigators, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: RA is an inflammatory disease that results in pain and loss of function, especially in the hands and wrists. Brief self-assessment tools that can reliably and precisely quantify hand/wrist function are needed to assess inflammatory activity when a physical exam is not feasible and to capture day-to-day experience of living with RA. Neuro-QoL is part of the PROMIS family of self-report measures created using a patient-centred approach and IRT methodology. The Neuro-Qol Upper Extremity Function (UEF) scale measures ability across fine motor and ADLs involving digital, manual and reach-related function and self-care. Little is known about its performance in RA. Our goal was to evaluate the validity and responsiveness of the 8-item Neuro-QoL UEF in adults with RA and compare its performance with legacy measures of physical function. We hypothesized scores would be strongly (r >0.7) associated with MHAQ, MD-HAQ, and PROMIS PF, and moderately (r=0.4 to 0.7) with symptoms, disease activity, and QoL indicators, and be responsive to change in disease activity and PF.

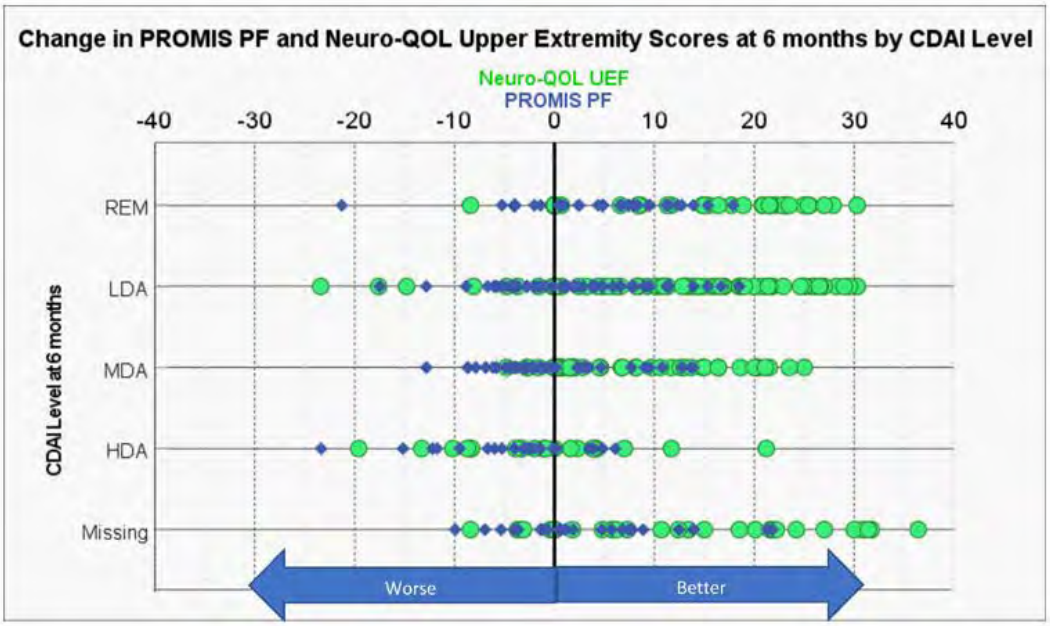
Methods: Data were from the 0 and 6-month visits of adults with early RA (symptoms < 1 yr) enrolled in the Canadian Early Arthritis Cohort, a prospective real-world study at 16 sites across Canada. Participants completed the Neuro-QoL UEF, MHAQ, MDHAQ, PROMIS-29, and PT Global at each visit. Rheumatologists recorded joint counts and

Table 1. Summary statistics of physical function and RA disease activity indices at 6 months

	Mean	SD	Mdn	25%	75%	(Min, Max)
Physical Function						
Neuro-Qol UEF	46.5	9.7	53.8	37.5	53.8	(21.8, 53.8)
MHAQ (0-3)	0.29	0.43	0.13	0.00	0.38	(0.00, 2.25)
MD-HAQ (0-10)	1.39	1.64	0.70	0.00	2.00	(0.00, 8.00)
PROMIS-PF	46.4	8.5	46.2	39.5	56.0	(23.3, 56.0)
RA Disease Activity						
CDAI	9.3	9.9	6.0	3.0	13.0	(0.0, 56.0)
SDAI	10.7	10.9	6.8	3.1	15.2	(0.0, 57.0)
Patient Global	3.0	2.5	3	1	5	(0, 10)
MD Global	1.8	2.2	1	0	3	(0, 9)
Swollen Joints (28)	2.1	3.7	0	0	2	(0, 20)
Tender Joints (28)	2.4	3.9	1	0	3	(0, 24)

Table 2. Mean scores (95% CI) at 6 months by CDAI level

	REM	LDA	MDA	HAD
NeuroQol UEF	52.8 (51.8, 53.7)	48.1 (46.6, 49.7)	42.0 (39.4, 44.6)	33.8 (30.5, 37.1)
MHAQ (0-3)	0.05 (0.02, 0.09)	0.19 (0.14, 0.24)	0.45 (0.34, 0.57)	0.90 (0.63, 1.17)
MD-HAQ (0-10)	0.31 (0.17, 0.46)	1.11 (0.90, 1.32)	2.15 (1.71, 2.59)	3.56 (2.56, 4.56)
PROMIS-PF	52.8 (51.4, 54.2)	46.8 (45.3, 48.2)	42.3 (40.4, 44.2)	38.0 (34.4, 41.6)



MD Global. To evaluate content validity, we examined descriptive statistics across CDAI disease activity levels, and Pearson correlations between the Neuro-QOL UEF, legacy measures, CRP & ESR. Responsiveness was assessed by correlating change scores from visits 0-6 between Neuro-QoL UEF, disease activity and legacy PF scores.

Results: The 262 participants were mostly white (83%) women (71%) with a mean (SD) age of 55 (13). Summary statistics at 6-months are shown in Table 1. Neuro-QOL UEF was moderately-strongly correlated with MHAQ, MDH-AQ, PROMIS-PF (|r|=0.63-0.75) and moderately correlated with pain and stiffness, (|r|=0.59, -0.64), and CDAI, SDAI,

Patient & MD Global, TJ & SJ (|r|=0.39-0.58). Neuro-QOL UEF was moderately correlated with PROMIS QoL domains Pain, Fatigue, Anxiety, Depression, Sleep & Participation (|r|=0.39-0.60).

Neuro-QOL scores decreased in a dose-response manner across worsening CDAI DA states reflecting increasing impairment (Table 2). Persons with HDA reported the highest disability, scoring nearly 0.5 SD lower on the Neuro-QoL UEF than PROMIS PF. Change from baseline to 6 months in Neuro-QoL UEF was moderately correlated with changes in PROMIS PF, MHAQ, Patient Global, and CDAI (|r|=0.44-0.65). The mean change and range from 0-6 months in Neuro-QoL was significantly larger than in PROMIS (8.9 [95% CI 7.5, 10.4] vs. 5.4 [95% CI 4.4, 6.4])(see Figure).

Conclusion: Clinicians, researchers, and patients benefit from practical self-report tools that reliably and precisely monitor hand function in RA. Results offer initial evidence of validity and responsiveness and support use of Neuro-QoL UEF to self-assess inflammatory activity in the hands and day-to-day experiences of living with RA.

Disclosure: S. Bartlett, Merck Canada, 2, 6, Pfizer Canada, 2, 6, Janssen Canada, 2, 6, PROMIS Health Organization, 4, American Thoracic Society, 4, Arthritis Health Professionals Association, 4, UCB, 1, RAND Corporation, 1; **O. Schieir**, None; **M. Valois**, None; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **G. Boire**, Abbvie, 1, 6, 7, BMS, 6, 7, Janssen, 1, 5, 6, Eli Lilly, 1, 7, Amgen, 7, Novartis, 6, 7, Pfizer, 7, Sandoz, 6, 7, Viatris, 1, 6, Samsung Bioepis, 1; **E. Keystone**, AbbVie, 2, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb Company, 2, Celltrion, 2, Gilead Sciences, 2, F. Hoffmann-La Roche, 2, 6, Janssen, 2, 6, Eli Lilly, 2, Merck, 2, 5, 6, Myriad Autoimmune, 2, Novartis, 6, Pfizer Inc, 2, 5, 6, PuraPharm, 5, Sandoz, 2, Sanofi-Genzyme, 2, 6, Samsung Bioepis, 2; **D. Tin**, None; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **C. Hitchon**, Pfizer, 5, UCB Canada, 5; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **G. Hazlewood**, None; **V. Bykerk**, Amgen Inc., 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **C. Investigators**, None.

Abstract Number: 1227

Clinical Predictors of Response to Methotrexate in Patients with Rheumatoid Arthritis: A Machine Learning Approach Using Clinical Trial Data

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Methotrexate (MTX) is the preferred initial disease-modifying drug (DMARD) for rheumatoid arthritis (RA). However, up to 50% of patients respond inadequately to MTX. Clinically useful predictors that effectively identify patients with RA who are likely to respond to MTX are lacking. We aimed to identify clinical predictors of response to MTX among DMARD-naïve patients with RA using machine learning methods.

Methods: Using the resources of the Clinical Study Data Request Consortium (CSDR) we identified 14 randomized clinical trials (RCT) involving 3,003 patients with RA who were randomized to MTX monotherapy or placebo plus MTX. Data were accessed through the Vivli Center for Global Clinical Research Data. Studies with available Disease Activity Score with 28-joint count (DAS28) at baseline, 12 and 24 weeks were included, resulting in exclusion of one RCT. Patients on prior conventional or biologic DMARDs were excluded. Latent class mixed modeling of response to MTX was applied. Patient groups with similar trajectories were compared by pretreatment baseline characteristics: socio-demographics (age, sex, race), baseline DAS28 with erythrocyte sedimentation rate [ESR] and its individual parameters, C-reactive protein, 66 swollen joint count (SJC66), 68 tender joint count (TJC68), RA duration, baseline use of glucocorticoids, health assessment questionnaire [HAQ] score, and serologic status (positive for rheumatoid factor [RF] or anticitrullinated protein antibodies [ACPA]). Proximity imputation was used to impute missing values. Lasso analysis and random forests were used to identify predictors of MTX treatment response. RCT study indicators were included in the model to adjust for heterogeneity among studies.

Results: A total of 1,478 DMARD-naïve patients from 13 RCTs were included. Mean age 50.5 years, 79% female, 84% RF positive, 87% ACPA positive, median RA duration 1.9 years, mean baseline DAS28-ESR 6.7, mean baseline HAQ 1.6. We identified 3 trajectory groups of response to MTX based on mean change in DAS28-ESR between baseline and 24 weeks: Class 1, “responders”, >1.2 unit change per 3 months; Class 2 and 3 “non-responders” < 1.2 unit change per 3 months in each. Using Lasso methods, RA duration, baseline DAS28-ESR, ESR, CRP, SJC66, age, and patient global assessment of disease activity (PtGA) were important predictors of response to MTX. The discrimination of responders from non-responders was acceptable: area under the curve (AUC) 0.70. Concordantly, using Random forests, the top five predictors of response to MTX were baseline DAS28-ESR, RA duration, SJC66, TJC68 and PtGA (AUC 0.69). Sex, race, HAQ score, seropositivity and use of glucocorticoids were not predictive of response to treatment with MTX.

Conclusion: Several baseline clinical characteristics, including DAS28-ESR, RA duration, PtGA, SJC66 were predictive of response to MTX and should be considered during the decision-making when initiating MTX in DMARD-naïve patients with RA.

Acknowledgment: This abstract is based on research using data from data contributors UCB and Roche that has been made available through Vivli, Inc. Vivli is not in any way responsible for, the contents of this publication.

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Abstract Number: 1228

Predicting RA Remission with Subcutaneous Abatacept Treatment in the Real-world Setting

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SESSION INFORMATION

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Session Type: Poster Session C

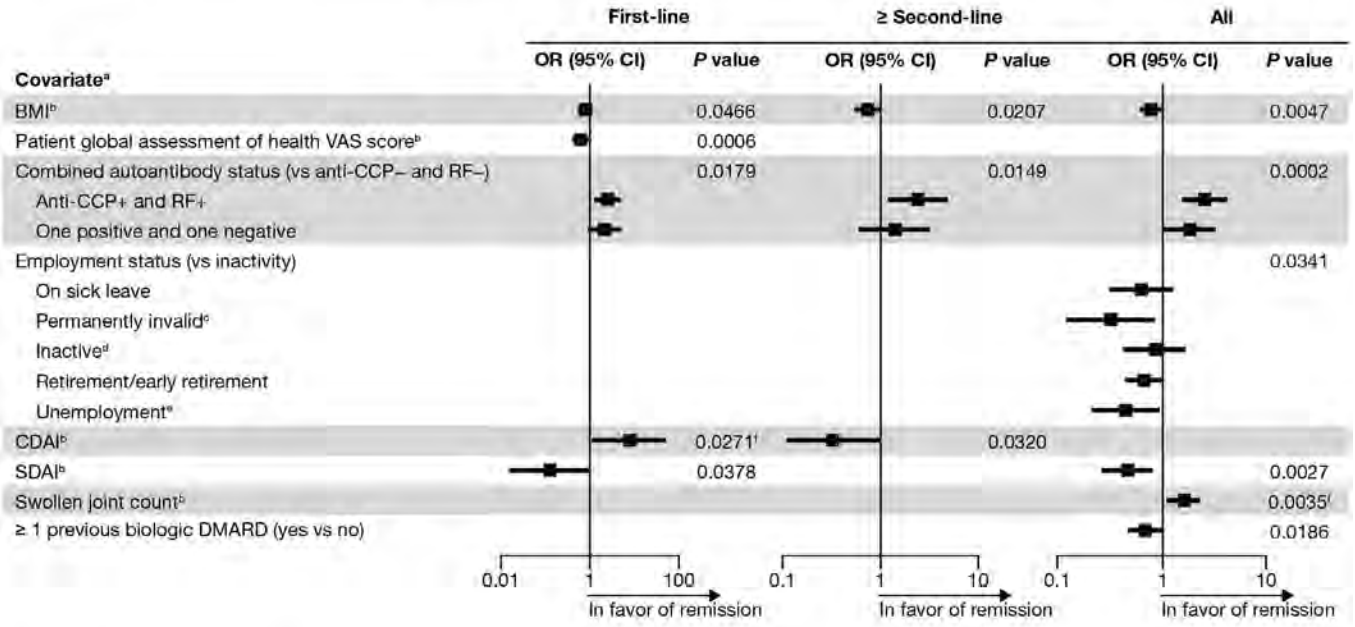
Session Time: 8:30AM–10:30AM

Background/Purpose: A treat-to-target approach for RA management is recommended, with the aim of achieving remission.[1,2] The Abatacept SubCutaneOus in Routine clinical practicE (ASCORE; NCT02090556) study assessed efficacy and safety of subcutaneous (SC) abatacept for the treatment of patients with moderate-to-severe active RA; month 12 retention and clinical response rates were better in patients receiving abatacept as a first- versus later-line biologic (b)DMARD.[3] This post hoc analysis of ASCORE investigated the association of baseline variables with the achievement of DAS28 (CRP), Simplified Disease Activity Index (SDAI), and Clinical Disease Activity Index (CDAI) remission following treatment with SC abatacept in patients with RA.

Methods: Patients from ASCORE (recruited between February 2013 and April 2017) who initiated SC abatacept 125 mg once weekly were included. Analysis of baseline factors predictive of DAS28 (CRP; < 2.6), SDAI (≤ 3.3), and CDAI (≤ 2.8) remission at month 12 was conducted by treatment line (first- and ≥ second-line) and in the overall population. Variables found to be significant ($P < 0.2$) in univariate logistic regression analysis were selected as covariates in a multivariate backward elimination logistic regression model. Odds ratios (95% confidence intervals) and *P* values were calculated. Standardized values were used for the continuous baseline predictors.

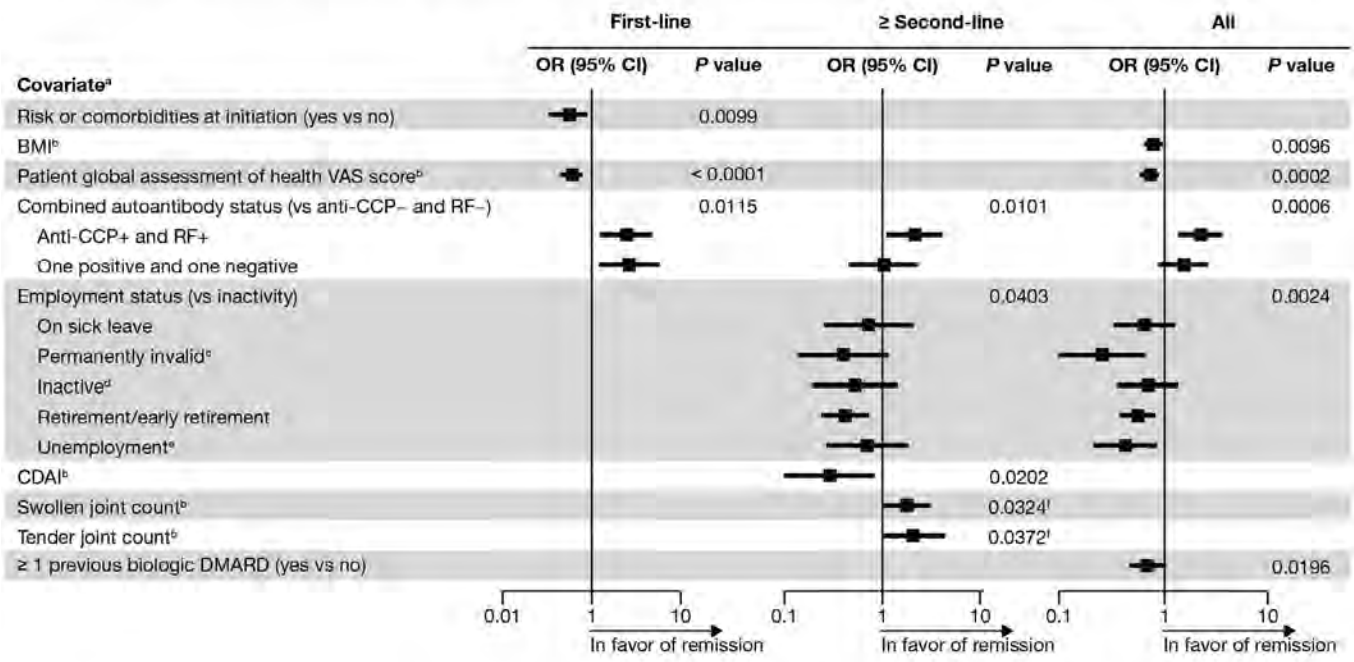
Results: Overall, 2892 patients were included (first-line, n = 1198; ≥ second-line, n = 1694). Baseline mean (standard deviation) age was 57.7 (12.7) years, BMI was 27.2 (5.8) kg/m^2, and HAQ-disability index (DI) score was 1.4 (0.7); 78.6% were female, 61.7% were double seropositive (RF+ and ACPA+), and 18.6% were either RF+ or ACPA+. For patients treated with abatacept as first-line therapy, double/single seropositivity (vs negativity) was a predictor of

Figure 1. Odds ratios of baseline variables for the prediction of CDAI-defined remission in patients with RA



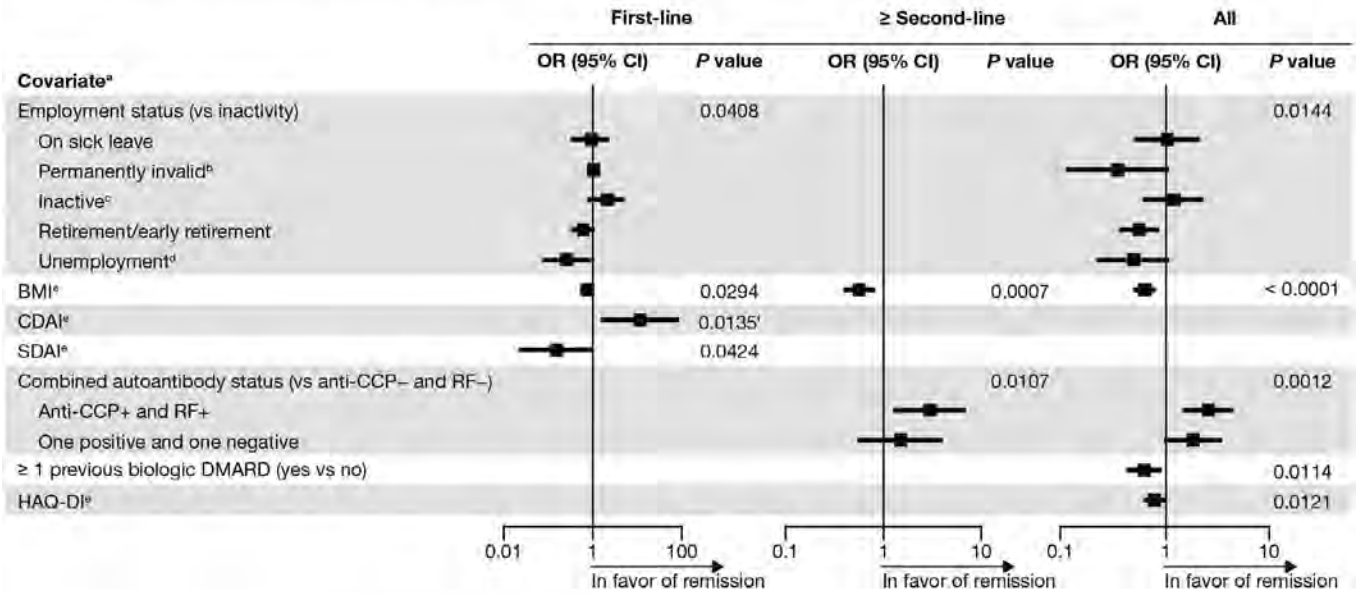
All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission however the OR varied by individual countries; [b]Continuous variables were standardized prior to multivariate analysis; [c]Related or not related to RA; [d]Voluntarily not in employment; [e]Including looking for a position; [f]Inverted directionality versus univariate analysis due to interaction between variables in the multivariate model.
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; SDAI, Simplified Disease Activity Index; VAS, visual analog scale.

Figure 2. Odds ratios of baseline variables for the prediction of SDAI-defined remission in patients with RA



All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission however the OR varied by individual countries; [b]Continuous variables were standardized prior to multivariate analysis; [c]Related or not related to RA; [d]Voluntarily not in employment; [e]Including looking for a position; [f]Inverted directionality versus univariate analysis due to interaction between variables in the multivariate model.
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; SDAI, Simplified Disease Activity Index; VAS, visual analog scale.

Figure 3. Odds ratios of baseline variables for the prediction of DAS28 (CRP)–defined remission in patients with RA



All variables with $P \leq 0.05$ are shown.
[a]Overall, country was shown to impact remission however the OR varied by individual countries; [b]Related or not related to RA; [c]Voluntarily not in employment; [d]Including looking for a position; [e]Continuous variables were standardized prior to multivariate analysis; [f]Inverted directionality versus univariate analysis due to interaction between variables in the multivariate model.
CDAI, Clinical Disease Activity Index; CI, confidence interval; HAQ-DI, HAQ-disability index; OR, odds ratio; SDAI, Simplified Disease Activity Index.

CDAI (**Figure 1**) and SDAI remission (**Figure 2**). For patients treated with abatacept as ≥ second-line therapy, double seropositivity (vs negativity) was a predictor of DAS28 (CRP) (**Figure 3**), SDAI, and CDAI remission. For the overall population, double/single seropositivity (vs negativity) was a predictor of DAS28 (CRP), SDAI, and CDAI remission. Active (vs inactive) employment status, low BMI, no previous bDMARD use, and low HAQ-DI were predictive of achieving remission in the overall population.

Conclusion: In this post hoc analysis of the real-world ASCORE study, several baseline characteristics were associated with remission in patients with RA treated with SC abatacept. Patients with seropositive RA, no previous bDMARD use, low HAQ-DI, and low BMI at baseline were more likely to achieve remission when treated with abatacept. Seropositivity was associated with remission regardless of abatacept treatment line. Early identification of patients with seropositive RA may facilitate a precision medicine approach to treatment.

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Abstract Number: 1229

Does BMI Influence the Efficacy of Subcutaneous or Intravenous Abatacept in Patients with RA in Routine Clinical Practice? A Post Hoc Analysis of Two Real-world Observational Studies

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: BMI has been shown to affect treatment response and may influence the development of optimal individualized treatment plans in patients with RA.[1] The extent to which treatment response is influenced by BMI varies across biologic DMARDs and may be associated with mechanism of action.[1] We evaluated the impact of BMI on disease activity scores in patients receiving intravenous (IV) or subcutaneous (SC) abatacept as reported in the real-world AbataCepT In rOutiNe clinical practice (ACTION)[2] and Abatacept SubCutaneOus in Routine Clinical PracticE (ASCORE)[3] studies in order to determine the impact of BMI on abatacept efficacy.

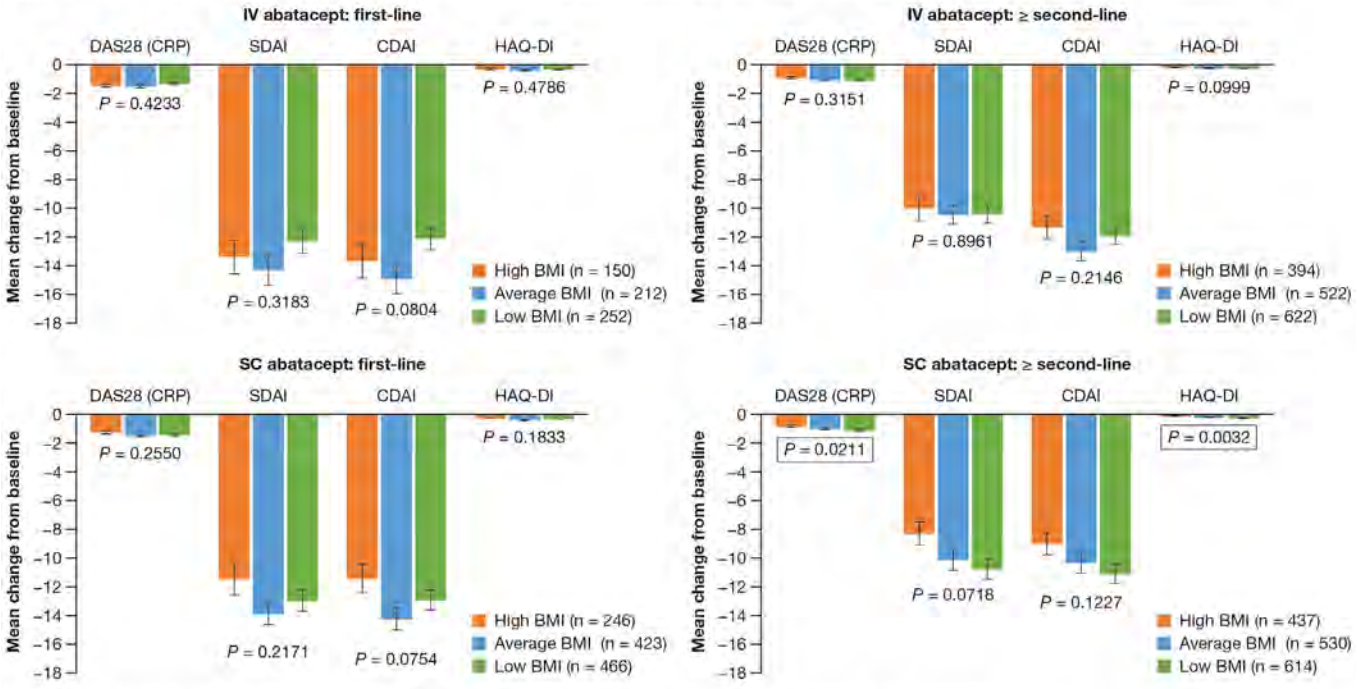
Methods: ACTION (NCT02109666) and ASCORE (NCT02090556) were international observational studies of patients with moderate-to-severe RA receiving IV (body weight–adjusted dosing) or SC (fixed dosing at 125 mg once weekly) abatacept, respectively, over 2 years.[2,3] In this post hoc analysis, patients were stratified by baseline BMI (high, ≥ 30 kg/m^2; average, 25–< 30 kg/m^2; low, < 25 kg/m^2); patients were also stratified by abatacept treatment

Table 1. Baseline disease activity scores (all patients)

	IV abatacept			SC abatacept		
	High BMI (n = 544)	Average BMI (n = 734)	Low BMI (n = 874)	High BMI (n = 683)	Average BMI (n = 953)	Low BMI (n = 1080)
DAS28 (CRP)	5.12 (1.05)	4.95 (1.10)	4.82 (1.13)	4.92 (1.10)	4.70 (1.17)	4.51 (1.16)
SDAI	32.43 (12.93)	31.07 (13.17)	29.40 (12.91)	29.67 (12.78)	27.64 (12.99)	26.36 (12.42)
CDAI	30.82 (12.51)	29.40 (12.54)	27.52 (11.94)	28.24 (12.45)	26.25 (12.42)	25.00 (11.87)
HAQ-DI	1.59 (0.65)	1.46 (0.69)	1.37 (0.67)	1.61 (0.69)	1.37 (0.72)	1.24 (0.72)

Data are presented as mean (SD). BMI groups are defined as high, ≥ 30 kg/m^2; average, 25–< 30 kg/m^2, and low, < 25 kg/m^2.
CDAI, Clinical Disease Activity Index; HAQ-DI, HAQ-disability index; IV, intravenous; SC, subcutaneous; SD, standard deviation; SDAI, Simplified Disease Activity Index.

Figure 1. Mean change from baseline disease activity at 12 months in patients receiving IV or SC abatacept by treatment line



BMI groups are defined as high, ≥ 30 kg/m^2; average, 25–< 30 kg/m^2; and low, < 25 kg/m^2. Patients with missing data for baseline BMI are excluded.
Last observation carried forward imputation method was applied for missing data. *P* value is from an ANOVA test comparing the three BMI groups.
CDAI, Clinical Disease Activity Index; HAQ-DI, HAQ-disability index; IV, intravenous; SC, subcutaneous; SDAI, Simplified Disease Activity Index; SE, standard error.

line (first-line; ≥ second line; all patients). Assessments were performed at month (M)6 and M12 and included mean (standard error) change from baseline in DAS28 (CRP), Clinical Disease Activity Index, Simplified Disease Activity Index, and HAQ-disability index (DI) scores. A last observation carried forward imputation method was applied for missing data. Differences between the three BMI categories were assessed using ANOVA test.

Results: 4868 patients were evaluated. Patient numbers and baseline disease activity scores were similar across BMI groups in both studies. Most patients had low BMI at baseline (**Table 1**). In patients receiving IV abatacept, there were no significant M12 differences across BMI groups for mean change from baseline across all measures of disease activity and physical function (HAQ-DI) in both treatment lines (**Figure 1**). In patients receiving SC abatacept, there were no significant M12 differences across BMI groups for mean change from baseline across all measures of disease activity and HAQ-DI in the first-line treatment group. However, in the ≥ second-line treatment group, significant differences across BMI groups were recorded for DAS28 (CRP) (P = 0.0211) and HAQ-DI scores (P = 0.0032).

Conclusion: BMI status did not significantly impact clinical efficacy in patients treated with IV abatacept. There were no significant differences between BMI categories for patients receiving IV abatacept as first- or ≥ second-line therapy. For SC abatacept, no significant differences across BMI groups were seen in the first-line group, but significant differences were seen in for DAS28 (CRP) and HAQ-DI scores in the ≥ second-line group. While results from clinical trials have shown that BMI has no impact on abatacept clinical efficacy, BMI was shown to significantly impact clinical responses in patients receiving abatacept as ≥ second- line therapy in a real-world observational setting.

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3. Alten R, et al. *Ann Rheum Dis* 2019;78(Suppl 2):A1639.
Medical writing: Lindsay Craik (Caudex), funded by Bristol Myers Squibb

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Abstract Number: 1230

Impact of Serologic Status on Clinical Responses to Upadacitinib or Abatacept in Patients with Rheumatoid Arthritis and Prior Inadequate Response to Biologic DMARDs: Sub-Group Analysis from the Phase 3 SELECT-CHOICE Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Table: Clinical Responses with UPA 15 mg or ABA in RA Patients Across Serologic Status Sub-Groups at Weeks 12 and 24

		RF+ and ACPA+ (n=390)		RF+ and/or ACPA+ (n=492)		RF- and ACPA- (n=120)	
		UPA n=189	ABA n=201	UPA n=242	ABA n=250	UPA n=61	ABA n=59
Proportion of Patients (%) (NRI)†							
ACR20	Wk 12	81.0*	71.1	78.9*	70.8	62.3	47.5
	Wk 24	83.6	77.6	81.8	77.2	67.2	59.3
ACR50	Wk 12	50.8*	39.8	51.2**	39.6	26.2*	11.9
	Wk 24	63.5*	53.2	63.2*	53.6	44.3	32.2
ACR70	Wk 12	23.3	15.9	24.0*	15.2	11.5	6.8
	Wk 24	39.2*	27.9	40.5**	28.0	24.6	20.3
DAS28(CRP) ≤3.2	Wk 12	54.0***	33.8	54.1***	33.2	32.8**	10.2
	Wk 24	64.6**	49.3	64.9**	50.4	54.1	37.3
DAS28(CRP) <2.6	Wk 12	31.7***	16.9	33.1***	15.2	18.0*	5.1
	Wk 24	46.0**	33.3	47.5***	32.8	39.3	25.4
CDAI ≤10	Wk 12	42.3	39.3	43.0	38.8	32.8*	16.9
	Wk 24	58.7	54.7	60.3	56.0	50.8	33.9
CDAI ≤2.8	Wk 12	9.5*	3.5	9.9**	3.2	1.6	0
	Wk 24	23.3*	14.4	23.1**	14.0	11.5	11.9
Mean Change from Baseline (MI)‡							
HAQ-DI	Wk 12	-0.76***	-0.57	-0.73***	-0.54	-0.45	-0.32
	Wk 24	-0.89**	-0.73	-0.84**	-0.69	-0.52	-0.49
Patient's Assessment of Pain	Wk 12	-38.45*	-32.81	-38.05**	-32.38	-23.98	-16.72
	Wk 24	-42.80	-39.15	-42.48	-38.66	-32.30	-29.16
FACIT-F	Wk 12	11.15	9.45	10.72	9.31	6.95	4.91
	Wk 24	11.96	11.17	11.42	10.85	7.45	8.16

ABA, abatacept; ACPA, anti-cyclic citrullinated peptide antibodies; ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology response criteria; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score based on C-Reactive Protein; FACIT-F, Functional Assessment of Chronic Illness Therapy - Fatigue scale; HAQ-DI, Health Assessment Questionnaire - Disability Index; MI, multiple imputation; NRI, non-responder imputation; RA, rheumatoid arthritis; RF, rheumatoid factor; UPA, upadacitinib

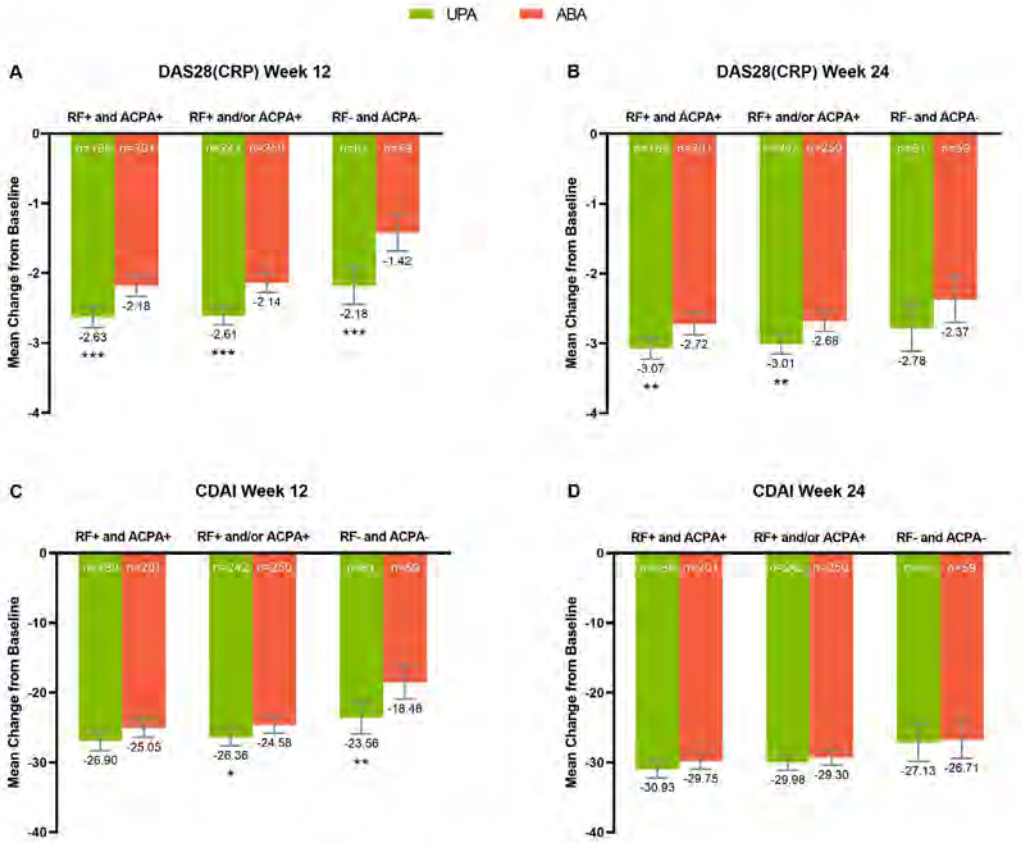
*P<0.05; **P<0.01; ***P<0.001 UPA vs. ABA; nominal P-values are presented and were not adjusted for multiple comparisons
†NRI was used for missing data for categorical endpoints
‡MI was used for missing data for continuous endpoints

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: In patients with RA who had a prior inadequate response or intolerance to biologic DMARDs, the oral Janus kinase inhibitor, upadacitinib (UPA), demonstrated superiority in change from baseline in DAS28(CRP) and DAS28(CRP)< 2.6 at week 12 and improved responses across additional endpoints compared to abatacept (ABA) in the phase 3 SELECT-CHOICE study.[1] Seropositive patients have been reported to respond better to treatment than seronegative patients;[2] therefore, the objective of this sub-group analysis was to evaluate clinical responses with UPA versus ABA among RA patients based on serologic status.

Methods: In SELECT-CHOICE (24-week, phase 3, double-blind, controlled trial), RA patients were randomized to oral UPA (15 mg once daily) or intravenous (IV) ABA (at day 1 and weeks 2, 4, 8, 12, 16, and 20; < 60 kg, 500 mg; 60-100 kg, 750 mg; >100 kg, 1000 mg).[1] UPA patients also received IV placebo and ABA patients also received oral placebo. All patients continued stable background conventional synthetic DMARDs. Starting at week 12, background RA medications were adjusted or added if patients did not experience ≥20% improvement compared to baseline in tender and swollen joint counts at two consecutive visits. For this sub-group analysis, patients were categorized as follows: RF+ and ACPA+, RF+ and/or ACPA+, and RF- and ACPA-. Mean change from baseline in DAS28(CRP), Clinical Disease Activity Index (CDAI), ACR responses, HAQ-DI, patient's assessment of pain, and Functional Assessment

Figure: Mean Change from Baseline in DAS28(CRP) and CDAI with UPA 15 mg or ABA Across Serologic Status Sub-Groups at Weeks 12 (A, C) and 24 (B, D)†



ABA, abatacept; ACPA, anti-cyclic citrullinated peptide antibodies; CDAI, Clinical Disease Activity Index; DAS28(CRP), 28-joint Disease Activity Score based on C-Reactive Protein; RF, rheumatoid factor; UPA, upadacitinib

*P<0.05; **P<0.01; ***P<0.001 UPA vs. ABA; nominal P-values are presented and were not adjusted for multiple comparisons
†Multiple imputation was used for missing data; LS means with 95% confidence intervals are shown

of Chronic Illness Therapy - Fatigue scale (FACIT-F) were evaluated at weeks 12 and 24. Statistical inference was conducted using Chi-square tests or analysis of covariance (ANCOVA) with non-responder imputation or multiple imputation used for missing data and nominal *P*-values shown.

Results: Of the total population (N=612), the majority of patients were seropositive for RF and/or ACPA at baseline (80.4%) (**Table**). Most patients were female (~80%), ~55 years old, and one-third had previously experienced ≥2 biologic DMARDs. Mean change from baseline in DAS28(CRP) and CDAI were numerically higher with UPA vs ABA at weeks 12 and 24 across all sub-groups (**Figure**). Regardless of serologic status, UPA demonstrated numerically higher responses vs ABA for ACR 20/50/70 and proportions of patients in low disease activity and remission at both timepoints (**Table**). Mean change from baseline in the HAQ-DI and the patient's assessment of pain was numerically higher with UPA compared to ABA across all sub-groups and timepoints. Clinical responses were generally numerically higher at week 24 compared to week 12, and for the seropositive groups compared to the seronegative group, with both UPA and ABA.

Conclusion: Across serologic statuses, clinical responses with UPA 15 mg vs ABA were numerically higher at weeks 12 and 24 among RA patients with prior inadequate response or intolerance to biologic DMARDs. In addition, clinical responses were numerically higher for seropositive patients compared to seronegative patients across all endpoints assessed, although the seronegative group had a smaller sample size in this post-hoc analysis.

References

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2. Sokolove J, et al. *Ann Rheum Dis*. 2016;75:709-14

Disclosure: A. Rubbert-Roth, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 2, 6, Roche, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sanofi, 2, 6, Amgen, 2, 6, Novartis, 2, 6; **J. Sparks**, Bristol-Myers Squibb, 2, Gilead, 2, Inova Diagnostics, 2, Optum, 2, Pfizer, 2; **A. Constantin**, AbbVie, 2, 6, BMS, 2, 6, Galapagos, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **R. Xavier**, Abbvie, 2, Janssen, 2, UCB, 2, Pfizer, 2, Novartis, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2; **Y. Song**, AbbVie, 3, 11; **J. Suboticki**, AbbVie, 3, 11; **R. Fleischmann**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GSK, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc., 2, 5, Sanofi-Aventis, 2, 5, UCB, 2, 5, Boehringer Ingelheim, 5, Celgene, 5, Genentech, 5, Regeneron, 5, Roche, 5.

Abstract Number: 1231

Consistent Impact of Autoantibody Enrichment Across All ACR Core Measures in Early Rheumatoid Arthritis Treated with Abatacept: Data from a Large Pooled Analysis of 4 Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Biomarkers play an important role in RA and can help guide treatment decisions. Previous studies have suggested differential treatment efficacy of abatacept (ABA) in patients with biomarker-seropositive RA,[1–4] including differential treatment impact of ABA on ACR20/50/70 among patients with SeroPositive Early & Active RA (SPEAR) in historic randomized controlled trials (RCTs).[5] In this study, we analyzed clinical outcomes among patients with SPEAR and non-SPEAR to understand the differential treatment impact of ABA on each ACR core measure.

Methods: Individual patient data (IPD) from 2087 patients in 4 phase 3, early RA ABA RCTs (AGREE [NCT00122382], AMPLE [NCT00929864], AVERT [NCT01142726], AVERT-2 [NCT02504268]) were pooled. Patients were classified as SPEAR at baseline if they: 1) were RF+ and ≥ 3 times the upper limit of normal on an anti-CCP test (ACPA+), 2) had a disease duration ≤ 12 months, and 3) had DAS28 (CRP) ≥ 3.2. Patients were treated with either ABA (monotherapy or with MTX) or a comparator (MTX or adalimumab + MTX). Outcomes of interest included mean change from baseline to week 24 in ACR core measures (e.g., HAQ-DI score, CRP value, patient global assessment). IPD mixed-effects regressions for each outcome used trial fixed effects, baseline measures of the outcome, and SPEAR status as covariates in the ABA-treated population. In the analysis of the full population, treatment type was added as well as an interaction term of treatment type and SPEAR status. Sensitivity analyses using an alternative SPEAR definition restricted to criterion 1 were also conducted.

Table 1. Baseline characteristics and ACR core measures at baseline and week 24

	All patients	Patients with SPEAR		Patients with non-SPEAR	
		Abatacept	Comparators[a]	Abatacept	Comparators[a]
	N = 2087	n = 784	n = 544	n = 385	n = 374
Trial, n (%)					
AGREE	492 (23.6)	177 (22.6)	155 (28.5)	68 (17.7)	92 (24.6)
AMPLE	509 (24.4)	45 (5.7)	41 (7.5)	206 (53.5)	217 (58.0)
AVERT	339 (16.2)	157 (20.0)	79 (14.5)	68 (17.76)	35 (9.4)
AVERT-2	747 (35.8)	405 (51.7)	269 (49.5)	43 (11.2)	30 (8.0)
Demographics					
Age, mean (SD), years	49.3 (12.9)	48.6 (12.5)	49.2 (13.5)	49.4 (12.6)	50.6 (12.9)
Female, %	79.3	77.2	77.9	81.3	83.4
Race, n (%)					
Asian	206 (9.9)	104 (13.3)	71 (13.1)	19 (4.9)	12 (3.2)
Black	118 (5.7)	35 (4.5)	32 (5.9)	30 (7.8)	21 (5.6)
Other	146 (7.0)	52 (6.6)	27 (5.0)	32 (8.3)	35 (9.4)
White	1,617 (77.5)	593 (75.6)	414 (76.1)	304 (79.0)	306 (81.8)
Disease characteristics					
Disease duration, mean (SD), months	8.5 (12.5)	2.4 (2.8)	2.4 (2.9)	19.9 (15.9)	18.3 (15.1)
RF positive, %	91.0	100	100	74.2	76.1
Anti-CCP positive, %	81.8	100	100	52.2	47.3
DAS28 (CRP), mean (SD)	5.71 (1.13)	5.68 (1.09)	5.76 (1.08)	5.72 (1.19)	5.66 (1.20)
ACR core measures – baseline, mean (SD)					
HAQ-DI score	1.56 (0.69)	1.56 (0.68)	1.59 (0.70)	1.55 (0.69)	1.54 (0.68)
Patient global assessment	62.93 (22.71)	64.01 (22.38)	62.43 (23.23)	62.77 (22.47)	61.59 (22.88)
Physician global assessment	63.12 (19.28)	63.85 (19.02)	64.52 (19.55)	61.50 (18.76)	61.20 (19.75)
Pain visual analog scale	65.09 (22.12)	65.03 (22.34)	64.59 (21.84)	65.06 (22.04)	66.01 (22.19)
CRP value, mg/dL	2.16 (3.09)	2.22 (2.85)	2.45 (3.73)	1.85 (2.42)	1.92 (3.15)
Tender joint count - 68	25.08 (14.85)	23.70 (14.35)	24.68 (13.86)	27.08 (16.01)	26.50 (15.74)
Swollen joint count - 66	16.77 (10.76)	15.87 (10.39)	16.49 (10.05)	17.91 (11.93)	17.90 (11.11)
ACR core measures – week 24, mean (SD)[b]					
HAQ-DI score	0.82 (0.66)	0.71 (0.63)	0.88 (0.65)	0.85 (0.68)	0.92 (0.69)
Patient global assessment	30.28 (22.90)	26.82 (22.08)	33.66 (22.22)	30.19 (22.80)	32.83 (24.70)
Physician global assessment	19.11 (17.61)	16.36 (16.52)	22.33 (18.01)	18.50 (17.11)	20.92 (18.83)
Pain visual analog scale	30.42 (23.56)	26.31 (21.84)	34.27 (23.83)	29.93 (22.87)	34.11 (25.91)
CRP value, mg/dL	0.73 (1.22)	0.56 (1.14)	0.92 (1.36)	0.77 (1.10)	0.80 (1.27)
Tender joint count - 68	8.76 (11.21)	6.84 (9.66)	9.92 (11.40)	9.75 (12.80)	10.09 (11.68)
Swollen joint count - 66	5.00 (7.31)	3.61 (5.45)	6.06 (8.12)	5.44 (8.65)	5.94 (7.52)

[a]Comparators included MTX and adalimumab + MTX.

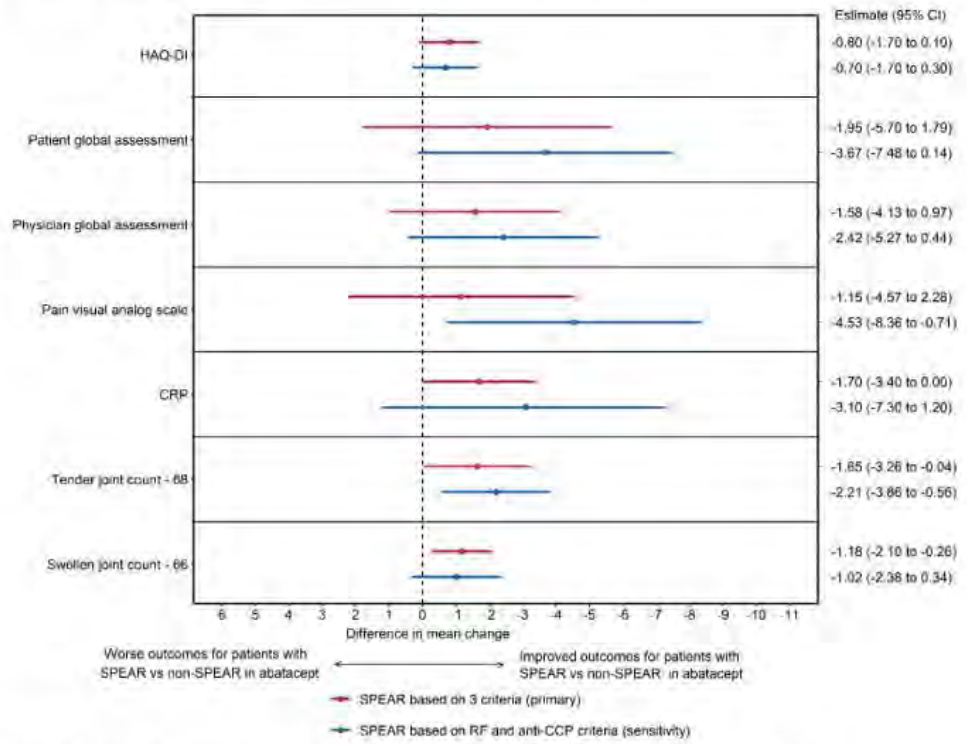
[b]All patients (N = 2057); patients with SPEAR on abatacept (n = 773); patients with SPEAR on comparators (n = 531); patients with non-SPEAR on abatacept (n = 383); patients with non-SPEAR on comparators (n = 370).

SPEAR, SeroPositive Early & Active RA.

Results: A total of 1328 (64%) SPEAR and 759 (36%) non-SPEAR were included. For patients with non-SPEAR, around half were RF+ and three-quarters were ACPA+, while DAS28 (CRP) was high for all patients (**Table 1**). Among ABA-treated patients, outcomes were more favorable for patients with SPEAR compared to patients with non-SPEAR across all outcomes, either statistically or directionally (**Figure 1**). The differences in outcomes between patients with SPEAR vs non-SPEAR were larger for ABA than for comparators across all outcomes with the exceptions of HAQ-DI and pain, where the differences continued to be directionally favorable for ABA (**Figure 2**). The results were consistent in the sensitivity analysis.

Conclusion: This study compared clinical outcomes of patients with enriched autoantibody biomarkers and early RA (SPEAR) to patients with non-SPEAR and found a differential treatment impact of abatacept across all ACR core measures in the RCTs analyzed. These findings corroborate prior studies and further suggest that the differential treatment impact of abatacept is not limited to a subset of core measures but affects all dimensions including laboratory values, joint counts, functional status, patient reported outcomes, and physician global assessment.

Figure 1. Comparison of mean change from baseline to week 24 in ACR core measures between SPEAR vs non-SPEAR groups among patients receiving abatacept



HAQ-DI and CRP were rescaled to 0.1 points and mg/10ml, respectively, for visual clarity.

ABA, abatacept; SPEAR, SeroPositive Early & Active RA.

Patients were classified as SPEAR at baseline if they: 1) were RF+ and $\geq$ 3 times the upper limit of normal on an anti-CCP test (ACPA+), 2) had a disease duration $\leq$ 12 months, and 3) had DAS28 (CRP) $\geq$ 3.2.

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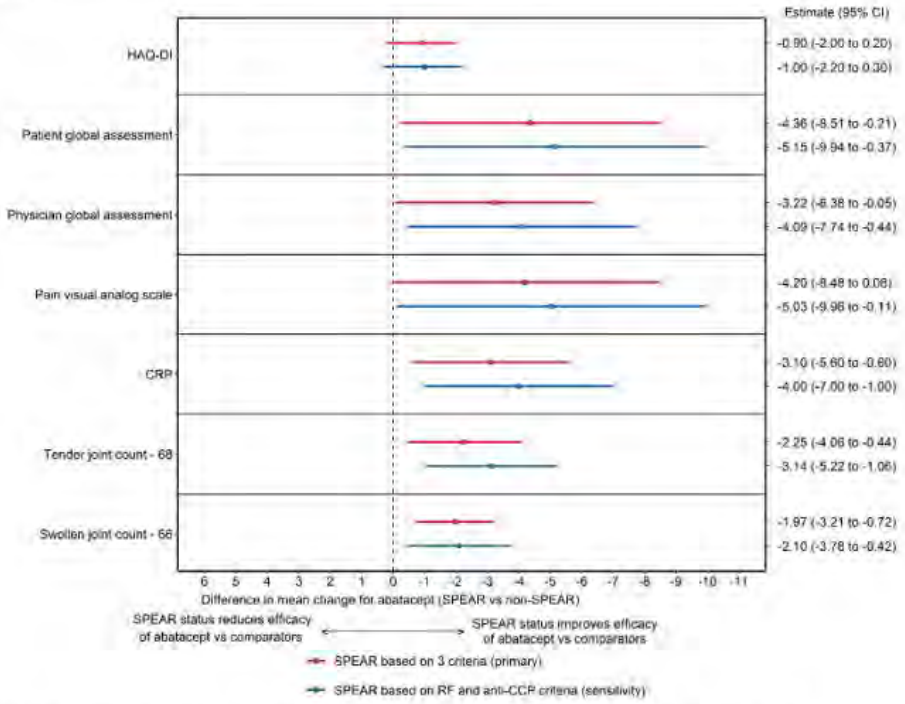
Editorial support: Danielle Johnson (Caudex), funded by Bristol Myers Squibb

Figure 2. Modification of ABA vs comparator efficacy for mean change from baseline to week 24 in ACR core measures by SPEAR status



HAQ-DI and CRP were rescaled to 0.1 points and mg/10mL, respectively, for visual clarity.

Comparators included MTX and adalimumab + MTX.

ABA, abatacept; SPEAR, SeroPositive Early & Active RA.

Patients were classified as SPEAR at baseline if they: 1) were RF+ and ≥ 3 times the upper limit of normal on an anti-CCP test (ACPA+), 2) had a disease duration ≤ 12 months, and 3) had DAS28 (CRP) ≥ 3.2.

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Abstract Number: 1232

Synovial Tissue Lymphoid Aggregates Are Associated with Response to Rituximab Therapy in Rheumatoid Arthritis Patients

Matthew Turk[1], Candice Low[2], Carl Orr[3], Richard Conway[4], Kieran Murray[5], Ursula Fearon[6] and Douglas Veale[7], [1]St. Vincents University Hospital, Dublin, Ireland, [2]St. Vincent's University Hospital, Dublin, Ireland, [3]St Vincent's Hospital, Dublin, Ireland, [4]St. James's University Hospital, Dublin, Ireland, [5]Saint Vincent's University Hospital, Dublin, Ireland, [6]Trinity College Dublin, Dublin, Ireland, [7]University College Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Activated B lymphocytes and plasma cells are implicated in the pathogenesis of rheumatoid arthritis (RA). The anti-CD20 monoclonal antibody therapy (Rituximab) is an effective therapy in some RA patients. The goal of this study was to evaluate the clinical and laboratory factors associated with long-term responses to Rituximab therapy in patients with RA.

Methods: One hundred and fourteen RA patients received Rituximab (1g doses x 2, 2 weeks apart), at a single centre, between 2003-2016. Prior to treatment, arthroscopy and synovial biopsy was performed on patients in this cohort who had active knee arthritis. Demographic, clinical and outcome data were collected prospectively and immunohistology was subsequently performed on synovial tissue biopsies. Clinical and laboratory outcomes were evaluated using linear and binary logistic regression.

Results: The median (IQR) disease duration was 13.5 (7, 24.3) years. The number of prior csDMARDs was 1 (0, 2), and biologic DMARD was 1 (0, 2). Rituximab monotherapy was used in 34 patients, while 80 patients received rituximab-csDMARD combination therapy. Forty-four patients underwent an arthroscopy and synovial biopsy prior to treatment. Synovial tissue lymphoid aggregates (LA) were observed in 21 subjects, of which 17 (81%) showed complete or partial remission in response to treatment with Rituximab. The presence of LA was significantly associated with remission in these patients treated with rituximab (p=0.007, OR=7.286 [1.737-30.555]). A significant association was also shown between LA and CD138 plasma cell staining in the synovial biopsies ($p< 1.0x10^{-4}$, OR=22.667 [3.979-129.119]). 73% of patients were female, 85% were rheumatoid factor (RF) positive, 64% anti-citrullinated protein antibody (ACPA) positive, 59% double positive, and 11% seronegative. Rituximab treatment follow-up time had a median (IQR) of 3.1 (1.8, 6.1) years and median number of treatment courses was 3 (2, 5). Sixty-eight patients (60%) reached sustained remission, while 14 (12%) were primary non-responders, 25 (22%) were secondary non-responders, and 7 (6%) stopped due to adverse events. Twenty-six of the 68 patients in remission (38%) received Rituximab monotherapy and 42/68 (62%) received combination therapy with a csDMARD. Twenty-four of 39 (62%) biologic naïve patients achieved remission on treatment with rituximab. There was no significant association between any other clinical or laboratory markers and remission in patients treated with rituximab.

Conclusion: These data show significant evidence for lymphoid aggregates as a predictive marker for response to treatment with rituximab. Rituximab is an effective long-term treatment for RA, with high remission rates that are associated with synovial lymphoid aggregates.

Disclosure: M. Turk, None; **C. Low**, None; **C. Orr**, None; **R. Conway**, Janssen, 6, Sanofi, 6, Roche, 6, Abbvie, 6; **K. Murray**, None; **U. Fearon**, Abbvie, 1, 5, 6, BMS, 1, Pfizer, 1, 5, Janssen, 5, Eli Lilly, 5, UCB, 5, GSK, 6; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6.

Abstract Number: 1233

Physician and Patient Reported Effectiveness Outcomes Are Similar in Tofacitinib and TNF Inhibitors in Rheumatoid Arthritis Patients: Data from a Rheumatoid Arthritis Registry in Canada

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
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Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment as an alternative option to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi). We aimed to evaluate physician and patient reported effectiveness outcomes in TNFi compared to TOFA, using real-world data from the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (Adalimumab, Certolizumab, Etanercept, Golimumab, Infliximab, and Biosimilars) between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Patients were required to have physician and patient reported effectiveness outcomes data available at treatment initiation and 6-month (± 2 months) follow-up. These included clinical disease activity index (CDAI), rheumatoid arthritis disease activity index (RADAI), HAQ-DI, sleep problem, and anxiety/depression scores. Multiple imputation (Imputation Chained Equation, N=20) was used to deal with missing data for covariates at treatment initiation. To deal with confounding by indication, we estimated propensity scores for covariates with an absolute standard difference greater than 0.1 between the two treatment groups.

Results: A total of 419 patients were included. Of those, 226 were initiating a TNFi and 193 TOFA, and had a mean (SD) disease duration of 8.0 (8.7) and 12.6 (9.6) years, respectively. In the TNFi group, 81.9% were female and mean age (SD) at treatment initiation was 56.6 (13.4) years. In the TOFA group, 85% were female and mean (SD) age at treatment initiation was 60.3 (11.2) years. The TNFi group was less likely to have prior biologic use (21.7%) compared to the TOFA group (67.9%). At treatment initiation, physical function measured by HAQ-DI was significantly lower in TNFi compared to the TOFA group (1.2 vs.1.4).

The rate of CDAI LDA/remission at 6 months was 33.6% and 26.4% in TNFi and TOFA group, respectively. The generalized linear mixed models (GLMM) adjusting for propensity score quantile, showed that there was no significant difference in CDAI LDA/remission (ORs: 0.85, 95% CI: 0.51, 1.43), RADAI (β-coefficient: 0.48, 95% CI: -0.18, 1.14), HAQ-DI (β-coefficient: -0.01, 95% CI: -0.18, 0.16), sleep problems (β-coefficient: -0.25, 95% CI: -0.95, 0.45), and anxiety/depression scores (β-coefficient: 0.12, 95% CI: -0.35, 0.58) between the two treatment groups (TOFA used as reference).

Conclusion: In this real-world data study, we found that, physician and patient reported effectiveness outcomes are similar in the TNFi and TOFA groups 6 months after treatment initiation in patients with RA.

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Abstract Number: 1234

Routine Assessment of Patient Index Data 3 (RAPID3) in Patients with Rheumatoid Arthritis Treated with Long-Term Upadacitinib Therapy

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Routine Assessment of Patient Index Data 3 (RAPID3) is a pooled index of 3 patient-reported measures: patient global assessment, pain, and physical function. RAPID3 was shown to correlate with other composite measures of disease activity[1] and is recommended by the American College of Rheumatology for use in clinical practice.[2] The objective of this analysis was to evaluate the impact of upadacitinib (UPA) versus comparators on RAPID3 over 60 weeks, as well as the correlation of RAPID3 scores with other disease measures in the UPA phase 3 SELECT clinical program.

Methods: This post hoc analysis included placebo-controlled (SELECT-NEXT, -BEYOND, and -COMPARE) and active comparator-controlled (SELECT-EARLY, -MONOTHERAPY, and -COMPARE) trials. Patients received UPA as monotherapy or in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs). Mean change from baseline in RAPID3 and the proportion of patients reporting RAPID3 remission (≤3), low (LDA, >3 to ≤6), moderate (MDA, >6 to ≤12), and high disease activity (HDA, >12) were assessed. Correlations between absolute scores for RAPID3 and Clinical Disease Activity Index (CDAI), Simplified Disease Activity Index (SDAI), and 28-joint Disease Activity Score with C-reactive protein (DAS28[CRP]) were assessed using Spearman correlation coefficients. All data are as observed.

Results: A total of 661, 498, 648, 1629, and 945 patients were included from SELECT-NEXT, -BEYOND, -MONOTHERAPY, -COMPARE, and -EARLY. At baseline, the majority of patients across all studies were in RAPID3 HDA (mean baseline RAPID3 [across all studies], 17.2–19.2) (**Table** and **Figure**). Improvements from baseline in RAPID3 were observed with UPA 15 mg and 30 mg through Week 60, with numerically greater improvements observed with UPA compared with active comparators (**Table**). Across studies, mean improvements in RAPID3 exceeded the minimal clinically important difference (MCID) with UPA and adalimumab (ADA) treatment (MCID=3.8[3]). By Week 60, approximately one-half of UPA-treated patients were in RAPID3 remission or LDA, with only 10–25% remaining in HDA, except for the more refractory population in SELECT-BEYOND, in which ~38% of patients remained in

Table Change from BL in RAPID3 at Week 60 (as observed)

Phase 3 study	Group	n[a]	Mean (SD) BL score	Mean (SD) change from BL[b]
SELECT-EARLY[c] (MTX-naïve)	MTX	236	18.5 (5.6)	−9.6 (7.5)
	UPA 15 mg QD	269	18.9 (5.6)	−12.0 (7.6)
	UPA 30 mg QD	253	18.2 (5.6)	−13.4 (7.2)
SELECT-NEXT (csDMARD-IR)	UPA 15 mg QD	172	17.7 (5.1)	−11.1 (7.3)
	UPA 30 mg QD	172	17.6 (5.3)	−10.4 (6.8)
SELECT-MONOTHERAPY (MTX-IR)	UPA 15 mg QD	172	17.4 (5.8)	−9.6 (7.4)
	UPA 30 mg QD	180	17.2 (5.9)	−10.6 (7.2)
SELECT-COMPARE[c] (MTX-IR)	UPA 15 mg QD	552	18.5 (5.5)	−10.2 (7.1)
	ADA 40 mg EOW	264	18.7 (5.4)	−8.8 (6.7)
SELECT-BEYOND (bDMARD-IR)	UPA 15 mg QD	133	19.2 (5.1)	−8.6 (6.8)
	UPA 30 mg QD	118	18.5 (5.3)	−9.3 (7.3)

b, biologic; BL, baseline; EOW, every other week; IR, inadequate response; MTX, methotrexate; QD, once daily; SD, standard deviation

[a]Number of patients with RAPID3 values at both BL and Week 60. [b]Negative values indicate improvement from BL. [c]Observed data include patients rescued to UPA and/or ADA; treatment effect may include both the randomized and switch treatments in these patients

HDA (**Figure**). RAPID3 scores moderately to strongly correlated with CDAI (ρ=0.69–0.83), SDAI (ρ=0.69–0.82), and DAS28(CRP) (ρ=0.58–0.77), across all studies, at Week 60 (all $p< 0.001$).

Conclusion: UPA, as monotherapy or in combination with csDMARDs, was associated with improvements in patient-reported disease activity, pain, and physical function, as assessed by RAPID3 over 60 weeks in the phase 3 SELECT clinical program. RAPID3 continues to be an important tool in clinical practice to assess disease activity, as it was shown to correlate to other disease activity measures and allows for rapid scoring.

References

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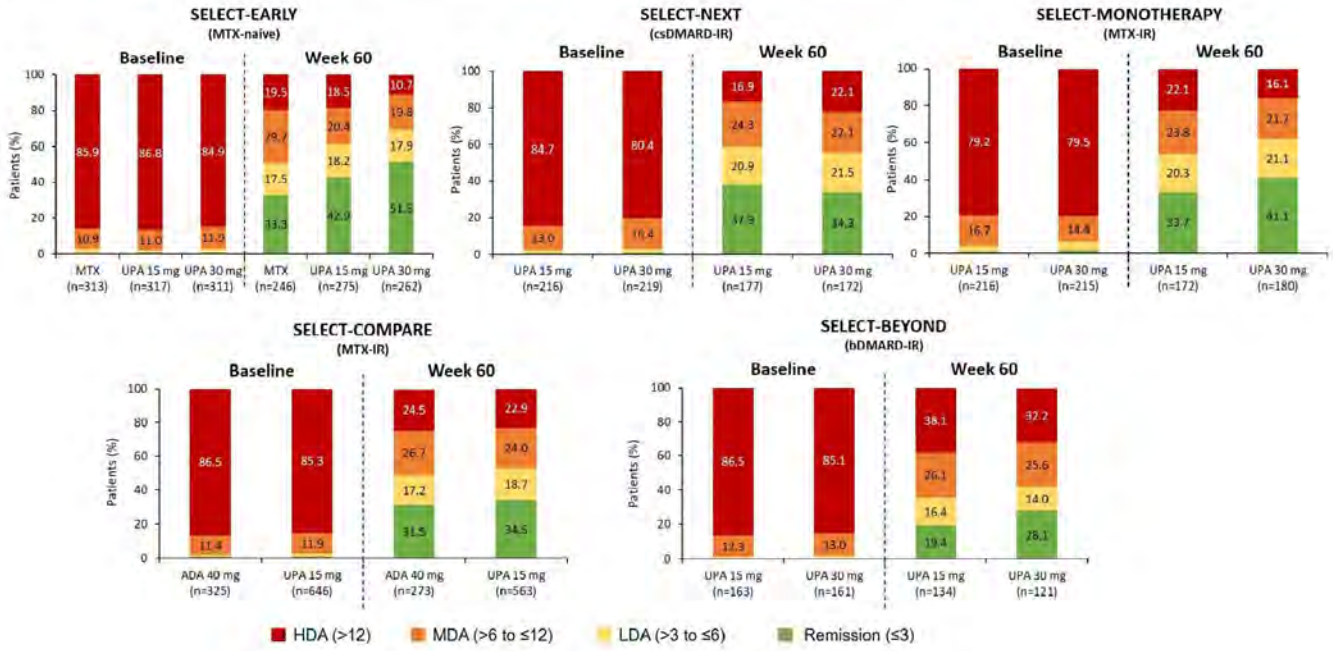
Figure Proportion of patients in RAPID3 remission, LDA, MDA, and HDA at BL and Week 60 (as observed)



ADA, adalimumab; bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; HDA, high disease activity; IR, inadequate response; LDA, low disease activity; MDA, moderate disease activity; MTX, methotrexate; RAPID3, Routine Assessment of Patient Index Data 3; UPA, upadacitinib

Disclosure: M. Bergman, AbbVie, 2, 6, Amgen Inc., 6, Novartis, 2, 6, Pfizer, 2, 6, Sanofi, 2, 6, Bristol Myers Squibb, 2, Celgene, 2, Genentech, 2, Janssen, 2, Merck, 2, Johnson & Johnson, 11, Sandoz, 1, GSK, 6, Scipher, 2; **M. Buch**, AbbVie, 2, 5, 6, Gilead Sciences, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Roche, 2, 5, Sanofi, 2, 5, 6; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 6, Novartis, 6, YL Biologics, 6, Bristol-Myers Squibb, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi-kasei, 5, 6, GSK, 2, 6, Mitsubishi-Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Ayumi, 2, Taisho, 2; **G. Citera**, AbbVie, 2, 5, Eli Lilly, 2, Genzyme, 2, Pfizer Inc, 2, Sanofi-Genzyme, 2, 5, Amgen, 2, 5, Gema, 2, 5, Novartis, 2, 5; **S. Bahlas**, None; **E. Wong**, AbbVie, 2, 5, Chugai, 2, 5, Novartis, 2, 5, UCB, 5, Eli Lilly, 2, MSD, 2, Pfizer, 2, Roche, 2; **Y. Song**, AbbVie, 3, 11; **N. Tundia**, AbbVie, 3, 11; **J. Suboticki**, AbbVie, 3, 11; **V. Strand**, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2.

Abstract Number: 1235

Treatment Effect of Baricitinib on Fatigue: Mediation Analysis Results from Two Phase 3 Trials

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SESSION INFORMATION

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Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue is very common in rheumatoid arthritis (RA) and impairs patient quality of life. Baricitinib (BARI) improved fatigue, pain and other patient-reported outcomes (PROs) in patients with active RA and an inadequate response (IR) to conventional synthetic DMARDs (csDMARDs), or to ≥1 tumor necrosis factor inhibitors or other biological DMARDs (bDMARDs).[1-3] The aim of the current analysis was to investigate the effects of BARI on fatigue that are influenced by disease activity and those that are independent of disease activity in patients from the RA-BEAM and RA-BEACON trials.

Methods: Data were analyzed from two phase 3 studies, RA-BEAM (NCT01710358, methotrexate (MTX)-IR patients) and RA-BEACON (NCT01721044, bDMARD-IR patients). All trial patients had a diagnosis of adult-onset RA as defined by the ACR/EULAR 2010 Criteria for the Classification of RA.[4] Fatigue was assessed by the Functional Assessment of Chronic Illness Therapy-Fatigue scale (FACIT-F). In a mediation analysis, the dependent variable was the change from baseline to week 12, 16, 20 or 24 for FACIT-F. The treatment (BARI 4-mg vs. placebo (PBO) or adalimumab (ADA) vs. PBO) was the independent variable. Changes in Clinical Disease Activity Index (CDAI) from baseline to week 12, 16, 20 or 24 were used as the mediator variables. The total treatment effect on fatigue over PBO that can be accounted for by changes in CDAI is the "indirect" or mediation effect; whereas the total treatment effect that cannot be accounted for by the mediation effect is the "direct" effect. The random-intercept cross-lagged panel model (RI-CLPM) was applied for mediation analysis.[5]

Results: In MTX-IR patients (RA-BEAM trial), disease activity-mediated effect accounted for 50-60% of the fatigue improvement in both BARI 4-mg and ADA over PBO. The total effect, direct effect (i.e., those not associated with disease activity), and mediation effect of treatment on fatigue relief continuously increased in BARI 4-mg group from Week 12 to Week 24 (Table 1). Additionally, the total effect and mediation effect of BARI 4-mg over PBO on FACIT-F were numerically greater than that of ADA over PBO from Week 12 to 24. The direct fatigue relief effect of BARI 4-mg over placebo was significant starting Week 16, but that of ADA was not. In bDMARD-IR patients (RA-BEACON trial), about 20-30% of the effects of BARI 4-mg on FACIT-F were independent of disease activity.

Table 1: Mediation analysis results from RA-BEAM.

RA-BEAM	Week 12		Week 16		Week 20		Week 24	
	ADA vs PBO	BARI 4 mg vs PBO	ADA vs PBO	BARI 4 mg vs PBO	ADA vs PBO	BARI 4 mg vs PBO	ADA vs PBO	BARI 4 mg vs PBO
Direct effect (%) p-value	1.271 (46.85%) 0.062	1.044 (36.68%) 0.100	1.061 (39.81%) 0.123	1.381 (42.95%) 0.030	0.737 (30.84%) 0.301	1.459 (42.60%) 0.026	1.371 (41.51%) 0.061	1.564 (41.46%) 0.018
Indirect effect mediated by CDAI (%) p-value	1.442 (53.15%) <0.001	1.802 (63.32%) <0.001	1.604 (60.19%) <0.001	1.833 (57.01%) <0.001	1.653 (69.16%) <0.001	1.966 (57.40%) <0.001	1.931 (58.49%) <0.001	2.208 (58.54%) <0.001
Total effect (95% CI)	2.713 (1.30, 4.13)	2.846 (1.56, 4.13)	2.665 (1.21, 4.12)	3.215 (1.90,4.53)	2.390 (0.90,3.88)	3.425 (2.09,4.76)	3.303 (1.77,4.83)	3.772 (2.42,5.13)
p-Value	<0.001	<0.001	<0.001	<0.001	0.002	<0.001	<0.001	<0.001

Abbreviations: ADA= Adalimumab, BARI=baricitinib, CDAI= Clinical Disease Activity Index, CIs= confidence intervals. Direct effect=the treatment effect that cannot be accounted by the indirect/mediation effect, indirect effect= The treatment effect on fatigue over PBO that was mediated/influenced by CDAI control. PBO=placebo.

Table 2: Mediation analysis for baricitinib versus placebo in RA-BEACON

RA-BEACON	Week 12	Week 16	Week 20	Week 24
Direct effect (%)	0.564 (19.41%)	1.208 (31.61%)	1.360 (36.63%)	1.093 (31.98%)
p value	(0.588)	(0.224)	(0.180)	(0.294)
Indirect effect mediated by CDAI (%)	2.341 (80.59%)	2.614 (68.39%)	2.352 (63.35%)	2.325 (68.02%)
	<0.001	<0.001	<0.001	<0.001
Total effect	2.905	3.822	3.713	3.418
(95% CI)	(0.73, 5.08)	(1.73, 5.91)	(1.56, 5.87)	(1.15, 5.69)
p-Value	0.009	<0.001	<0.001	0.003

Abbreviations: CDAI= Clinical Disease Activity Index, CIs=confidence intervals, Direct effect=the treatment effect that cannot be accounted by the indirect/mediation effect, indirect effect= The treatment effect on fatigue over PBO that was mediated/influenced by CDAI control.

Conclusion: Irrespective of being MTX-IR or bDMARD-IR, BARI 4-mg had a proportion of effects on fatigue that were independent of disease activity in patients with active RA. The direct fatigue relief effect of BARI 4-mg over placebo was significant starting Week 16, whereas that of ADA was not.

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Abstract Number: 1236

Pain in Patients with Rheumatoid Arthritis Who Did or Did Not Achieve Treatment Response Based on Improvement in Swollen Joints with Baricitinib Clinical Trials

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib (BARI) is a Janus kinase (JAK)1/JAK2 inhibitor which provides improvements to clinical signs, symptoms, and patient-reported outcomes (PROs) in patients with rheumatoid arthritis (RA), with a notable effect on pain.[1,2,3] Pain in RA is multifactorial, with inflammation being an important, but not exclusive, cause.

Methods: Data for these analyses were derived from the Phase 3 study RA-BEAM (NCT01710358). Changes in pain from baseline to week (W)12 and W24 were evaluated using a 0-100 mm visual analog scale. To assess the relationship between pain and inflammation, results were compared between patients receiving BARI 4-mg + MTX and those receiving adalimumab (ADA) + MTX in both patients who achieved ≥ 50% improvement in swollen joint count (SJC) and those who did not at W12 and W24. At each visit, the analysis of covariance (ANCOVA) model was applied which includes the change from baseline of pain as the response variable and baseline pain, region, baseline joint erosion status, treatment, SJC 50% improvement subgroup and the interaction of treatment and subgroup as the explanatory variables. *P*-values were calculated for both treatment comparisons and the interaction term and were not adjusted for multiplicity.

Results: Consistent with previously reported clinical efficacy, most patients achieved SJC 50% improvement when treated with BARI + MTX (365/487, 74.9%) and ADA + MTX (228/330, 69.1%) at W12. For patients who did not achieve 50% improvement in SJC at W12, those treated with BARI 4-mg + MTX reported significantly greater improvements in pain (-24.3 vs -13.4, $p< 0.001$) than ADA + MTX (Fig 1A). This difference was not observed consistently in the group achieving SJC 50% (Fig 1B). The significant interaction test ($p=0.008$) between treatment and subgroup defined by SJC 50% improvement at W12 implies a differential effect of BARI on pain not associated with the improvement in inflammation. A similar trend was found at W24 (Fig 2). Additionally, at W12, the magnitude of pain reduction difference between BARI + MTX and ADA + MTX in the groups achieving or not achieving SJC 20% improvement was directionally similar to results using SJC 50% as the threshold, but this analysis is limited by small sample size in the non-responder group.

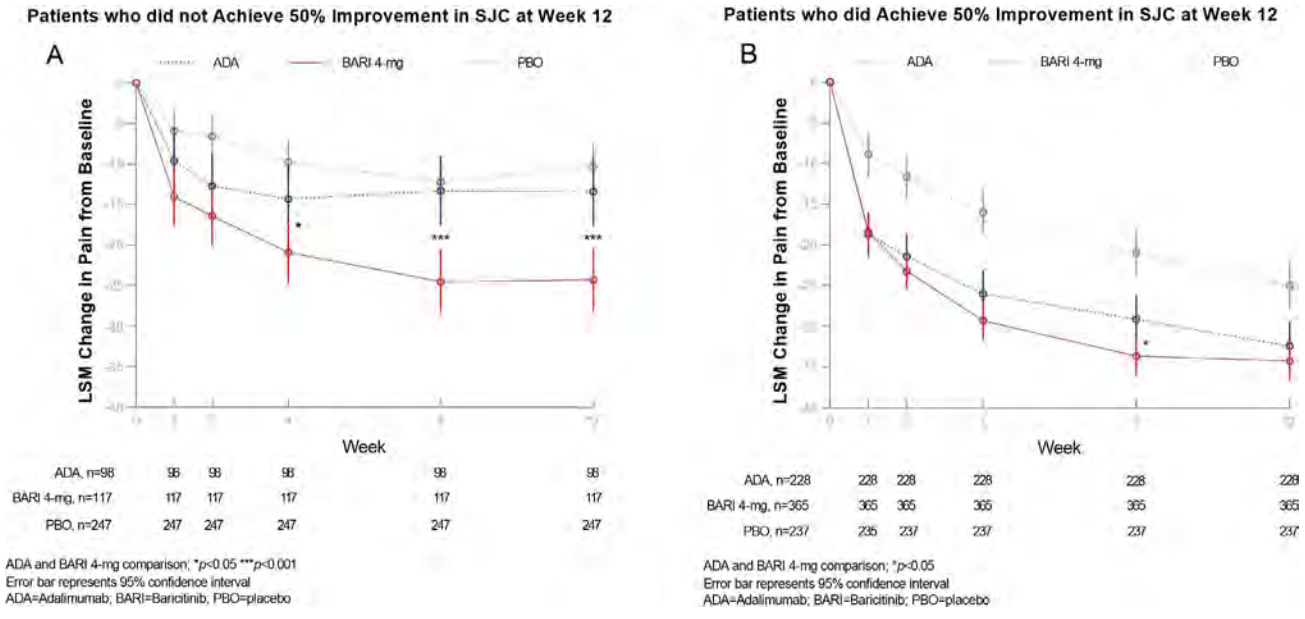

Figure 1. Least Square Mean Change in Pain Score from Baseline to Week 12.

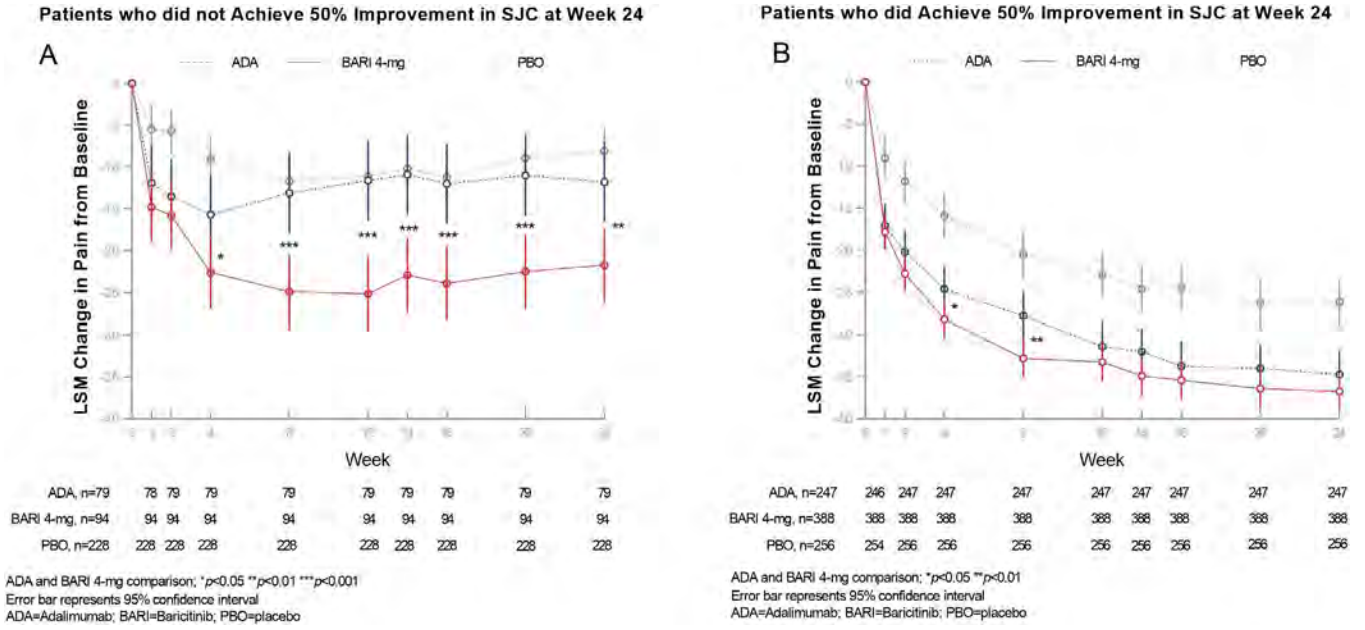

Figure 2. Least Square Mean Change in Pain Score from Baseline to Week 24.

Conclusion: BARI 4-mg + MTX treatment provided superior pain relief compared to ADA + MTX in patients with RA who did not achieve ≥ 50% improvement in SJC at W12 and W24. These results may point toward a differential effect of BARI on pain mediated outside of the inflammatory pathway.

References

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Abstract Number: 1237

Predictors of Response: Baseline Characteristics and Early Treatment Responses Associated with Achievement of Remission and Low Disease Activity Among Upadacitinib-Treated Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

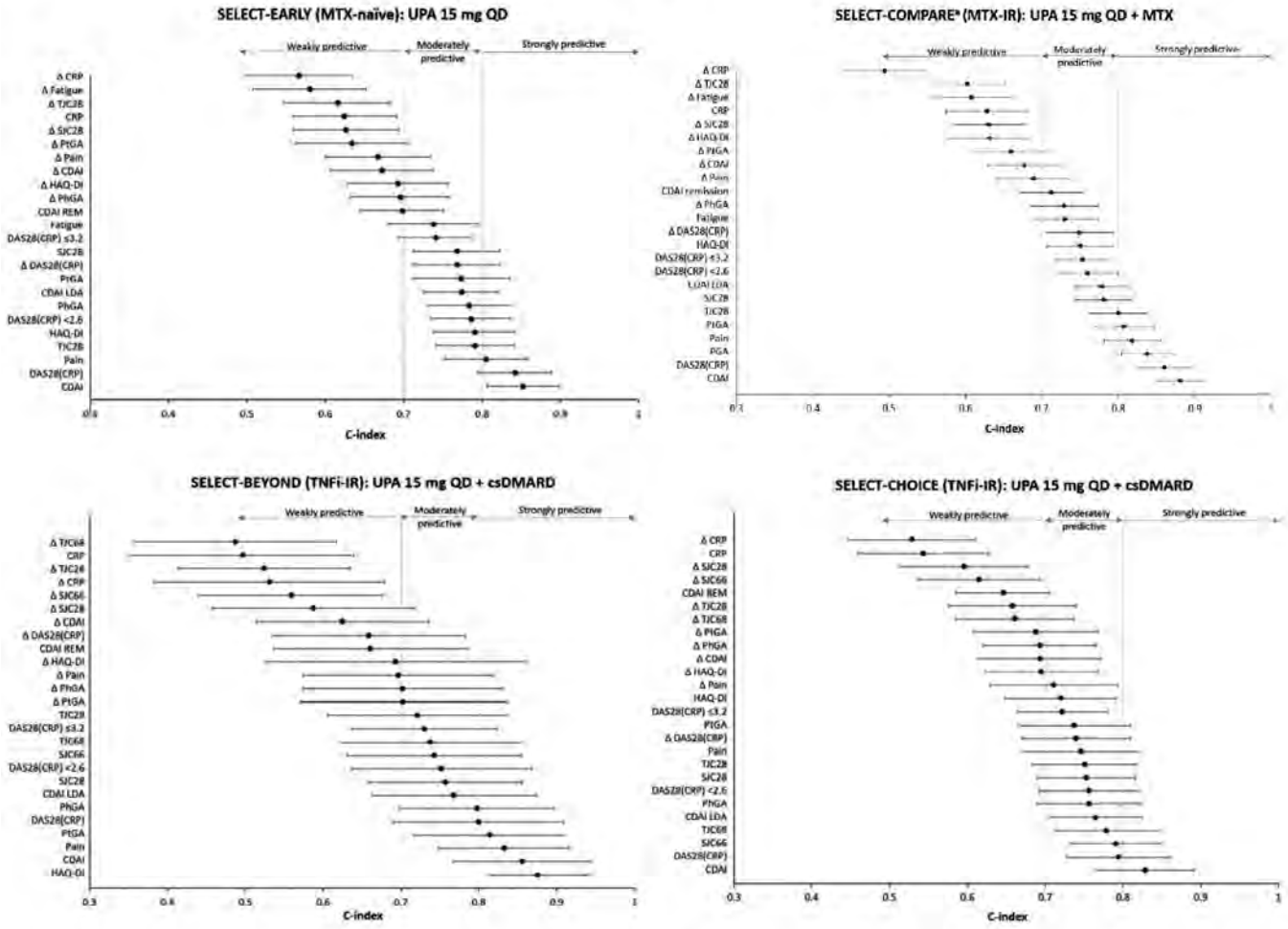
Background/Purpose: Early prediction of response to treatment with upadacitinib (UPA) 15 mg once daily (QD) could help optimize therapy in patients (pts) with RA.[1-4] The objective of this analysis was to identify baseline (BL) characteristics or Week (Wk) 12 disease activity measures that may predict the achievement of remission (REM) or low disease activity (LDA) at 6 months in pts with RA.

Table Achievement of CDAI LDA and REM at Wk 24/26[a]

	SELECT-EARLY	SELECT-COMPARE	SELECT-BEYOND	SELECT-CHOICE
Patient population	MTX-naïve	MTX-IR	TNFi-IR	TNFi-IR
Treatment	UPA 15 mg monotherapy (n=317)	UPA 15 mg + MTX (n=651)	UPA 15 mg + csDMARD (n=146)	UPA 15 mg + csDMARD (n=263)
Efficacy at Wk 24/26[a], n (%)				
CDAI REM (≤2.8)	90 (28.4)	150 (23.0)	16 (11.0)	60 (22.8)
CDAI LDA (≤10)	178 (56.2)	343 (52.7)	73 (50.0)	154 (58.6)

[a] Wk 26 for SELECT-COMPARE only

Figure Wk 12 predictors[a] for CDAI remission at Wk 24/26[b]



[a]Determined by a univariate logistic regression model. C-statistics provide a C-index value from 0.5 (chance prediction) to 1 (perfect prediction). Error bars indicate 95% CI. [b]Wk 26 for SELECT-COMPARE only.
CRP, C-reactive protein; DAS28(CRP), Disease Activity Score in 28 joints using C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; PhGA, Physician Global Assessment; PtGA, Patients Global Assessment; SJC28/66, swollen joint count in 28/66 joints; TJC28/68, tender joint count in 28/68 joints.

Methods: This ad hoc analysis included pts randomized to UPA 15 mg QD, as monotherapy in MTX-naïve pts (SELECT-EARLY) or in combination with conventional synthetic DMARDs (csDMARDs), in pts with inadequate response (IR) to MTX (SELECT-COMPARE) or ≥1 tumor necrosis factor inhibitors (TNFis) (SELECT-BEYOND and SELECT-CHOICE). Association of BL characteristics (age, disease duration, prior/concomitant treatments, C-reactive protein [CRP], seropositivity, and disease activity) and Wk 12 disease activity parameters with achievement of Clinical Disease Activity Index (CDAI) REM (≤2.8) or LDA (≤10) at Wk 24 (or Wk 26 in SELECT-COMPARE) was assessed by concordance statistics (C-statistics), or area under the receiver operator characteristic curve. C-index values and 95% confidence intervals were calculated by fitting a univariate logistic regression model for: demographic and BL characteristics, Wk 12 disease activity measures, and change from BL at Wk 12 in disease activity measures. A multivariate logistic regression with stepwise model selection was also performed. Proportion of pts achieving Wk 24/26 CDAI REM/LDA was stratified by ≥50% improvement from BL in swollen and/or tender joint count in 66/68 joints (SJC66/TJC68).

Results: A total of 1377 pts were included. Across the 4 studies, CDAI REM and LDA were achieved in 11.0–28.4% and 50.0–58.6% of pts, respectively (**Table**). BL demographics and disease characteristics were weakly predictive

(C-index < 0.70) of Wk 24/26 CDAI REM (C-index 0.49–0.69) or LDA (C-index 0.47–0.65), except for BL disability index of HAQ (HAQ-DI) in SELECT-BEYOND, which was moderately predictive of CDAI REM (C-index 0.73). Changes from BL in disease activity measures at Wk 12 were weakly or moderately predictive of Wk 24/26 CDAI REM (**Figure**) or LDA. CDAI value at Wk 12 was strongly predictive (C-index >0.80) of Wk 24/26 CDAI REM or LDA. Disease Activity Score in 28 joints using CRP and pain at Wk 12 were strongly predictive of Wk 24/26 CDAI REM (except in SELECT-CHOICE). Physician's global assessment at Wk 12 was the only common predictor in multivariate regression models for CDAI REM/LDA at Wk 24/26 across studies. Greater proportion of pts achieving ≥50% improvement in SJC66 and TJC68 at Wk 12 achieved CDAI REM (16.5–37.8% vs 0–9.4%) or LDA (66.0–72.8% vs 20.9–35.7%) at Wk 24/26 than those who did not.

Conclusion: BL characteristics did not strongly predict response to UPA, but composite disease activity scores at Wk 12 predicted Wk 24/26 REM/LDA with UPA 15 mg QD across MTX-naïve, MTX-IR, and TNFi-IR pts. ≥50% improvement in SJC/TJC at Wk 12 was also associated with Wk 24/26 REM/LDA.

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Abstract Number: 1238

Low Patient Global Assessment of Disease Activity and Negative Rheumatoid Factor Are Strongly Associated with Likelihood of Maintaining Remission Following Tapering of Therapy in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: According to ACR and EULAR recommendations, patients with rheumatoid arthritis (RA) who persist in remission (REM) should consider tapering RA therapy. Identification of clinical factors that are associated with a patient remaining in REM following tapering is of value. Since low disease activity (LDA) is an acceptable disease state, we utilized multivariate logistic regression to assess baseline (BL) factors associated with remaining in REM or LDA during methotrexate (MTX) monotherapy, etanercept (ETN) monotherapy, or combination therapy (combo).

Methods: SEAM-RA was a phase 3, multicenter, randomized withdrawal, double-blind, controlled study in patients with RA on MTX + ETN (combo) who had very good disease control for 6 months prior to study entry. If REM (primary endpoint, Simplified Disease Activity Index [SDAI] ≤3.3) was sustained through a 24-week open-label period, patients then entered a 48-week, double-blind period and were randomized 2:2:1 to receive MTX monotherapy, ETN monotherapy, or combo therapy. We evaluated >60 covariates in a step-wise approach to identify BL factors associated with REM or LDA at the end of 48 weeks without disease-worsening. A *P* value of ≤0.25 was required to enter the regression model, and covariates remained in the multivariate model if $P \leq 0.15$ or if commonly of clinical interest in studying RA. Interaction terms for all covariates per treatment arm were also assessed during variable selection to

Table 1. Multivariate logistic regression estimates for SDAI REM or LDA

BL Factor	Parameter Estimate (SE)	Odds Ratio [95% CI]	*P* Value
Intercept	2.28 (3.81)	–[a]	0.55
PtGA (0-100)	-0.07 (0.03)	0.93 [0.88, 0.99]	0.012
CRP (mg/L)	-0.07 (0.03)	0.93 [0.87, 0.99]	0.033
ETN duration prior to enrollment, years	0.11 (0.06)	1.12 [1.03, 1.25]	0.044
Treatment group			0.054*
ETN vs MTX	8.84 (5.14)	–[a]	0.086
Combo vs MTX	-3.99 (5.27)	–[a]	0.449
RF-positive vs -negative	-0.78 (0.43)	0.46 [0.20, 1.07]	0.071
Anti-CCP-positive vs -negative	0.35 (0.44)	1.41 [0.60, 3.36]	0.43
BMI ≥30 vs <30 kg/m^2	-0.47 (0.34)	0.63 [0.32, 1.22]	0.17
Blood urea nitrogen (mmol/L)	0.18 (0.11)	1.20 [0.98, 1.48]	0.080
PhGA (0-100)	-0.09 (0.05)	0.92 [0.83, 1.02]	0.097
MTX duration prior to enrollment, years	-0.06 (0.04)	0.94 [0.88, 1.01]	0.10
Duration of RA ≤5 years vs >5 years	1.66 (0.57)	–[a]	0.003
Treatment by RA duration interaction			0.041*
ETN x RA duration of RA ≤5 years	-1.95 (0.78)	–[a]	0.012
Combo x RA duration of RA ≤5, years	-1.15 (0.92)	–[a]	0.21
Mg (mg/dL)	-1.73 (1.72)	–[a]	0.31
Treatment by Mg interaction			0.052*
ETN x Mg	-3.25 (2.38)	–[a]	0.17
Combo x Mg	2.68 (2.45)	–[a]	0.27

[a]Odds ratios for covariates that have interactions with others are evaluated in Table 2. **P* value based on Wald joint test. BL = baseline; BMI = body mass index; CCP = cyclic citrullinated peptide; Combo = MTX + ETN; CRP = C-reactive protein; ETN = etanercept; Mg = magnesium; MTX = methotrexate; PhGA = Physician Global Assessment of Disease Activity; PtGA = Patient Global Assessment of Disease Activity; RA = rheumatoid arthritis; RF = rheumatoid factor; SDAI = Simplified Disease Activity Index.

Table 2. Odds Ratios for SDAI REM or LDA for Covariates With Varying Magnitudes of Association Dependent on Treatment

BL Factor	Odds Ratio [95% CI]		
	MTX	ETN	Combo
1 unit (mg/dL) increase of Mg	0.18 [0.01, 5.14]	0.01* [<0.001, 0.18]	2.58 [0.08, 79.55]
0.1 unit (mg/dL) increase of Mg	0.84 [0.60, 1.18]	0.61* [0.50, 0.84]	1.10 [0.78, 1.55]
≤5 years with RA vs >5 years	5.28* [1.73, 16.05]	0.75 [0.24, 2.33]	1.67 [0.37, 7.63]

BL Factor	≤5 Years RA Odds Ratio [95% CI]	>5 Years RA Odds Ratio [95% CI]
ETN vs MTX at 1.6 mg/dL Mg	5.41 [0.33, 89.31]	38.09* [2.49, 583.16]
Combo vs MTX at 1.6 mg/dL Mg	0.43 [0.02, 8.70]	1.34 [0.08, 22.01]
ETN vs MTX at 2.1 mg/dL Mg	1.07 [0.31, 3.64]	7.51* [2.92, 19.29]
Combo vs MTX at 2.1 mg/dL Mg	1.63 [0.38, 7.03]	5.13* [1.72, 15.31]
ETN vs MTX at 2.6 mg/dL Mg	0.21 [0.02, 2.45]	1.48 [0.15, 14.54]
Combo vs MTX at 2.6 mg/dL Mg	6.21 [0.46, 83.49]	19.58* [1.64, 233.11]

*Significant at the level of $P<0.05$. BL = baseline; Combo = MTX + ETN; ETN = etanercept; LDA = low disease activity; Mg = magnesium; MTX = methotrexate; RA = rheumatoid arthritis; REM = remission; SDAI = Simplified Disease Activity Index.

consider varying magnitudes of association by treatment arm. Score selection with best subset was used to confirm the model.

Results: In total, 253 patients with RA were included in the analysis. BL rheumatoid factor (RF) and Patient Global Assessment of Disease Activity (PtGA) showed strong association with SDAI REM or LDA (Table 1). After adjusting for other factors, patients with a 1-point higher PtGA (0-100 scale) at BL were 0.93 times more likely to maintain SDAI REM/LDA at Week 48. RF-positive patients were less than half as likely (OR, 0.46) as RF-negative patients to remain in REM/LDA at Week 48. Longer RA duration in the MTX arm and shorter duration of ETN treatment strongly decreased the odds of SDAI REM/LDA (Tables 1 and 2). An association was also found between lower CRP at BL and REM/LDA (Table 1). There was a trend for non-obese patients to be more likely to remain in REM than obese patients, although significance was not achieved. In addition, MTX and ETN patients with higher magnesium levels at BL had lower odds of maintaining REM/LDA, with an especially strong association within ETN monotherapy (Table 2). The area under the curve for the receiver operating characteristic of the model was 0.78.

Conclusion: These findings indicate patients with overall lower disease activity are more likely to remain in SDAI REM/LDA after tapering RA therapy. RF-negative status and lower PtGA scores in particular were strongly associated with likelihood of remaining in REM/LDA with MTX or ETN monotherapy. The role of magnesium in disease control warrants further exploration.

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Abstract Number: 1239

Differences in Patient-Reported Outcomes Between Those Who Stay in Remission and Those Who Have Disease-Worsening Following Therapy Withdrawal in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with RA in remission (REM) may experience disease-worsening (DW) following therapy change or withdrawal. The change in patient-reported outcomes (PROs) after therapy withdrawal has not been well described. This analysis examined PRO changes in RA patients in REM at baseline from a clinical trial enacting medication withdrawal.

Methods: SEAM-RA was a phase 3, multicenter, randomized withdrawal, double-blind controlled study in patients with RA on methotrexate (MTX) + etanercept (ETN) (combo) who were in REM (Simplified Disease Activity Index [SDAI] ≤3.3). After randomization to either MTX or ETN withdrawal, patients who experienced an SDAI score >11 at any time following randomization or SDAI >3.3 and ≤11 during 2 consecutive visits ≥2 weeks apart or on ≥3 separate visits were considered to have DW. Patients with DW resumed or continued MTX + ETN (rescue therapy). Patient Global Assessment of Disease Activity (PtGA), Patient Assessment of Joint Pain (PtJP), Health Assessment Questionnaire-Disability Index (HAQ-DI), and the 36-item Short-Form Health Survey (SF-36) were administered at baseline and Weeks 24 and 48 and also at Weeks 12 and 36 for PtGA and PtJP. Over the 48-week period, PROs were

Table 1. Cumulative Proportion of Patients Whose Patient- and Physician-Reported Outcome Scores Worsened Over 48 Weeks

Change From Baseline in Outcome Score	DW (N = 121) n/N (%)	REM (N = 132) n/N (%)
PtGA		
≥20	76/121 (62.8)	21/131 (16.0)
>10	90/121 (74.4)	36/131 (27.5)
PtJP		
≥20	70/121 (57.9)	18/131 (13.7)
>10	89/121 (73.6)	42/131 (32.1)
PhGA		
≥20	59/121 (48.8)	6/131 (4.6)
>10	80/121 (66.1)	24/131 (18.3)
HAQ-DI		
≥0.35	54/120 (45.0)	31/130 (23.8)
SF-36 MCS		
≤−2.5	69/120 (57.5)	58/130 (44.6)
SF-36 PCS		
≤−2.5	82/120 (68.3)	62/130 (47.7)

PtGA, PtJP, and PhGA on a 0–100 scale. Differences between DW and non-DW groups were significant at the level of $P<0.0001$ for all outcome measures. n = number of patients reporting worsening reaching MCID (≥20 or >10); N = number of patients with non-missing data; MCS = Mental Component Summary; PCS = Physical Component Summary.

Table 2. Cumulative Proportion of DW Patients Whose PtGA, PtJP, and PhGA Scores Worsened and Subsequently Improved by Receipt of Rescue Therapy Over 48 Weeks

Change From PRO Worsening Point, n/N (%)	Patients Receiving Rescue Therapy	Patients Not Receiving Rescue Therapy
PtGA		
≥20[a]	45/62 (72.6)	1/14 (7.1)
>10[b]	64/73 (87.7)	1/17 (5.9)
PtJP		
≥20[a]	47/57 (82.5)	0/13 (0.0)
>10[b]	59/73 (80.8)	0/16 (0.0)
PhGA		
≥20[a]	43/51 (84.3)	0/8 (0.0)
>10[b]	56/65 (86.2)	0/15 (0.0)

[a]Improvement defined as change from the first time of worsening ≥MCID up to an improvement of ≤−20.
[b]Improvement defined as change from the first time of worsening ≥MCID up to an improvement of <−10.
PtGA, PtJP, and PhGA on a 0–100 scale. MCID = minimal clinically important difference.

Table 3. Proportion of Patients Whose Week 48 PROs Did Not Worsen More Than an MCID

Change from Baseline in PRO Score, n/N (%)	DW (N = 121)	REM (N = 132)
PtGA		
≥20	82/105 (78.1)	115/121 (95.0)
>10	72/105 (68.6)	106/121 (87.6)
PtJP		
≥20	85/105 (81.0)	115/121 (95.0)
>10	71/105 (67.6)	105/121 (86.8)
PhGA		
≥20	97/105 (92.4)	119/120 (99.2)
>10	89/105 (84.8)	114/120 (95.0)

PtGA, PtJP, and PhGA on a 0–100 scale. Data are observed cases.

evaluated by a change (worsening or improvement) greater than the minimal clinically important difference (MCID) for the instrument/domain. We present cumulative data for patients with PRO change ≥MCID from baseline. Among these patients experiencing DW, we also present improvement after time of worsening.

Results: Of 253 enrolled patients, 132 maintained REM and 121 experienced DW. A greater proportion of DW than REM patients had worse PtGA scores at a ≥20-point change from baseline (62.8% vs 16.0%) and at a >10-point change from baseline (74.4% vs 27.5%) (Table 1). This pattern also was observed for PtJP and Physician Global Assessment of Disease Activity (PhGA) (Table 1). Median time to PtGA worsening >MCID (>10) was 169 days in DW patients and was shorter than median time to overall DW (198 days in the MTX group, not evaluable due to cumulative probability of DW always < 50% in the ETN and combo groups). A higher percentage of patients in DW vs REM deteriorated >MCID on the HAQ-DI (≥0.35) (45.0% vs 23.8%), SF-36 Mental Component Summary (≤–2.5) (57.5% vs 44.6%), and SF-36 Physical Component Summary (≤–2.5) (68.3% vs 47.7%) scores (Table 1). Among DW patients with a ≥20-point change from baseline in PtGA and PtJP, a greater proportion of those who received rescue therapy improved their scores than those who did not receive rescue therapy (72.6% vs 7.1% and 82.5 vs 0.0%, respectively) (Table 2). At Week 48, a higher proportion of REM vs DW patients were closer to their baseline values (< MCID) for PtGA (95.0% vs 78.1%) (Table 3); similar trends were observed for PtJP and PhGA.

Conclusion: Patients who experience a loss of REM also experience deterioration in their patient-reported global health assessment and additional joint pain. The changes in patient outcomes are experienced by more DW patients than those remaining in REM. Median time to PtGA worsening more than an MCID is shorter than median time to

overall DW. DW patients who receive rescue therapy can regain their outcomes, but to a lesser extent than those remaining in REM.

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Abstract Number: 1240

Biomarker Driven Dissection of Inflammation Modulatory Effects of Upadacitinib versus Abatacept in Patients with Active Rheumatoid Arthritis Refractory to Biologic DMARDs

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SESSION INFORMATION
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Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: In patients with active rheumatoid arthritis (RA) refractory to biologic DMARDs (bDMARD-IR), a phase 3, double-blind and active-controlled study (SELECT-CHOICE) demonstrated that upadacitinib (UPA) 15 mg QD was superior to abatacept (ABA) IV in driving change from baseline in DAS28-CRP and achievement of clinical remission at week 12.[1] The objective of this analysis was to compare the effects of UPA versus ABA on inflammatory biomarkers in bDMARD-IR RA patients, and to assess the dynamic relationship of such biomarkers with disease activity.

Methods: A subset of patients was randomly selected from the SELECT-CHOICE study cohort that consented sample collection for exploratory research (UPA: n = 99; ABA: n = 100). Plasma biomarker levels were assessed at baseline, week 2 and week 12 using the *Olink Explore 384 Inflammation* panel. Change from baseline was expressed as $\log_2$ fold change ($\log_2$FC). A Repeated Measure Mixed Linear Model identified biomarkers differentially modulated from baseline. Statistical tests were corrected for multiple comparison using the Benjamini – Hochberg False Discovery Rate (FDR) method. Downstream biological effects were predicted with Ingenuity Pathway Analysis. Responders in this analysis were defined by achieving DAS28-CRP Low Disease Activity (≤3.2) at week 12.

Results: Overall, 58 out of 368 biomarkers assessed were significantly modulated by UPA or ABA at week 12 (Table 1). Compared to ABA, treatment with UPA resulted in faster and broader modulation of inflammatory mediators implicated in RA pathogenesis in bDMARD-IR RA patients. Predictive analysis of downstream biological processes showed overlapped inhibitory effects by UPA and ABA on lymphocytes, myeloid cells, antigen presenting cells, and phagocyte activities, indicating a functional convergence of UPA and ABA mechanisms of action (MOA). IL-6, CCL7,

Table 1. Significantly modulated biomarkers by UPA or ABA in the bDMARD-IR RA patients

PROTEIN	LSMean Log2 FC from BL			
	ABA		UPA	
	Week 2	Week 12	Week 2	Week 12
AGER	0.01	0.10*	0.20***	0.32****
ANGPTL2	-0.01	-0.07	-0.22***	-0.30****
ATP5IF1	0.02	-0.49*	-0.07	-0.25
AXIN1	-0.05	-0.33*	-0.03	-0.10
CCL7	-0.10	-0.45****	-0.52****	-0.76****
CCL13	-0.06	-0.21*	-0.43****	-0.55****
CCL17	-0.38**	-0.39**	0.09	0.11
CCL21	-0.14*	-0.15*	-0.32****	-0.36****
CCL26	-0.13	-0.14	-0.45****	-0.48****
CD160	-0.02	0.02	-0.36****	-0.33****
CSF1	-0.10*	-0.11*	-0.34****	-0.34****
CSF3	-0.01	-0.02	0.30**	0.45****
CST7	-0.17	-0.24*	-0.44****	-0.38***
CXCL1	-0.08	-0.31*	-0.14	-0.11
CXCL3	-0.14	-0.46*	-0.08	-0.15
CXCL9	-0.38*	-0.36*	-0.59***	-0.19
CXCL10	-0.31*	-0.25*	-0.69****	-0.32*
DAPP1	-0.07	-0.55*	-0.01	-0.41
DBNL	0.05	-0.42*	-0.12	-0.21
EGF	-0.06	-0.48*	-0.16	-0.22
EPCAM	-0.01	0.08	0.32**	0.38***
EPO	0.01	0.03	0.58****	0.94****
FASLG	0.00	0.01	-0.40****	-0.39****
FCRL6	-0.06	-0.02	-0.44****	-0.37****
GAL	0.07	0.14*	0.31****	0.47****
GOPC	-0.03	-0.38*	-0.05	-0.20
HCLS1	-0.01	-0.35*	-0.02	-0.11
HPCAL1	-0.04	-0.33*	-0.04	-0.21
HSD11B1	0.02	0.05	0.21****	0.28****
IFNG	-0.42	-0.13	0.43	1.31****
IL6	-0.22	-0.88***	-0.84***	-1.12****
IL10	-0.46***	-0.63****	-0.20	0.10
IL15	0.01	0.03	0.44****	0.53****
IL12B	-0.30***	-0.26**	-0.16*	-0.07
ITGA11	0.03	0.19**	0.26****	0.38****
KLRD1	-0.08	-0.08	-0.53****	-0.39****
LAT	-0.03	-0.37*	-0.10	-0.29
MANF	-0.06	-0.66*	-0.18	-0.40
MGLL	-0.05	-0.41*	-0.05	-0.24
MGMT	-0.02	-0.46*	0.00	-0.17
MLN	-0.22*	-0.27*	-0.35***	-0.39***
MMP1	-0.15	-0.51****	-0.30*	-0.42**
MPIG6B	-0.02	-0.44*	-0.11	-0.28
MZB1	-0.13*	-0.31****	-0.31****	-0.52****
NCK2	-0.04	-0.36*	0.01	-0.17
NCR1	-0.08	-0.06	-0.51****	-0.48****
OSM	-0.22	-0.19	-0.39*	-0.28
PDGFB	-0.01	-0.37*	-0.11	-0.30
PDLIM7	-0.06	-0.47*	-0.09	-0.15
PLA2G4A	-0.03	-0.37*	-0.11	-0.20
PLXNA4	-0.06	-0.33*	-0.01	-0.18
PNLIPRP2	-0.06	-0.06	0.26*	0.30*
PTPN6	-0.03	-0.48*	-0.10	-0.29
RAB6A	-0.06	-0.06	0.23**	0.36****
SH2D1A	-0.10	-0.31*	-0.19	-0.24
SIGLEC1	-0.05	-0.03	-0.40****	-0.45****
SKAP2	-0.07	-0.51*	-0.14	-0.20
TIMP3	-0.09	-0.37*	-0.17	-0.22
TNF	-0.32*	-0.59****	-0.27*	-0.45***

* = FDR < 0.01, ** = FDR < 0.0001, *** = FDR < 0.000001, **** = FDR < 0.00000001

CSF1 and HSD11B1 were identified as DAS28-CRP-related biomarkers in this analysis. The levels of IL-6, CCL7, CSF1, and HSD11B1 significantly correlated with DAS28-CRP at the baseline, and the changes in these biomarkers significantly correlated with changes in DAS28-CRP at week 12. UPA had significantly greater modulation effects on IL-6, CCL7, CSF1 and HSD11B1 compared to ABA; these were more profound in responders than in non-responders.

Conclusion: The results of inflammatory biomarker modulation by UPA and ABA treatment demonstrates their MOA in bDMARD-IR RA patients, consistent with previous findings.[2,3] The more profound modulation of DAS28-CRP-related biomarkers by UPA may provide a mechanistic rationale for the superior efficacy of UPA compared to ABA, which warrants further investigation.

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Abstract Number: 1241

Comparison of the Effects of Upadacitinib Monotherapy with MTX on Protein Biomarkers in MTX-Naïve and MTX-Inadequate Responders in Patients with Active Rheumatoid Arthritis: Results from the SELECT-EARLY and SELECT-MONOTHERAPY Phase 3 Studies

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SESSION INFORMATION
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Background/Purpose: In MTX-naïve patients (SELECT-EARLY/M13-545 Phase 3 study) UPA 15 mg QD monotherapy (UPA Mono) demonstrated significant and clinically meaningful improvements in RA signs and symptoms vs MTX.[1] In MTX-IR patients (SELECT-MONOTHERAPY/M15-555 Phase 3 study), switching to UPA Mono showed significant improvements in RA signs and symptoms versus continuing MTX.[2] These study populations offer excellent opportunities to dissect disease and therapeutic mechanisms using biomarker analysis. The objective of this analysis was to compare the biological activity of MTX and UPA Mono in MTX-naïve and MTX-IR RA patients, via evaluation of circulating protein biomarkers related to inflammation compared with clinical disease activity.

Methods: Patients from the SELECT-EARLY (MTX, n = 96; UPA 15 mg QD, n = 96) and SELECT-MONOTHERAPY (MTX, n = 79; UPA 15 mg QD, n = 99) studies were randomly selected from the subsets of patients with available plasma samples. The levels of 92 inflammation related proteins were analyzed using the Olink platform; change from baseline in protein levels were expressed as Log_2 Fold Change; a Repeated Measure Mixed Linear Model identified proteins differentially modulated by MTX and UPA compared to Baseline. Pathway analysis was performed with Ingenuity Pathway Analysis.

Results: In MTX-naïve RA patients, both UPA Mono and MTX modulated a broad range of protein biomarkers associated with key pathways implicated in RA pathogenesis. UPA Mono had a faster onset of effect than MTX (Table 1) determined by impact on protein biomarker levels. Moreover, UPA Mono had a more profound effect on biomarkers that are significantly associated with baseline disease activity measures. In MTX-IR RA patients, only UPA Mono exerted significant effects on a subset of the biomarkers identified above, whereas continued treatment with MTX had no measured effect. Pathway analysis indicated that in MTX-naïve RA Patients, UPA Mono and MTX were predicted to elicit similar effects on adaptive, innate immune cells and on non-immune bone, connective tissue, and angiogenesis related pathways; but UPA Mono did so faster than MTX. In MTX-IR RA patients, only UPA Mono was predicted to affect those pathways, although to a lesser extent than in MTX-naïve RA patients.

Conclusion: UPA Mono exerted significant effects on protein biomarkers in both MTX-naïve and MTX-IR patients, whereas MTX did so only in MTX-naïve patients. The more profound and rapid effects of UPA Mono in MTX-naïve

Table 1. Overview of Biomarkers Modulated by UPA or MTX

	Relative Change From Baseline								Correlation: BL pBM x BL DAS28CRP	
	SELECT-EARLY (MTX-Naïve)				SELECT-MONO (MTX-IR)				SELECT-EARLY	SELECT-MONO
	MTX		UPA Mono		MTX		UPA Mono			
Protein Biomarker	EARLY LSMean Log2 FC	LATE LSMean Log2 FC	EARLY LSMean Log2 FC	LATE LSMean Log2 FC	EARLY LSMean Log2 FC	LATE LSMean Log2 FC	EARLY LSMean Log2 FC	LATE LSMean Log2 FC	Pearson's r	Pearson's r
AXIN1	-0.18	-0.56**	-0.24	-0.41	0.06	0.41	0.01	-0.05	0.08	-0.13
CASP8	-0.02	-0.21	-0.15	-0.26**	-0.05	0.03	0.13	0.07	0.12	-0.03
CCL7*	-0.10	-0.57****	-0.53****	-0.96****	-0.04	-0.02	-0.37****	-0.49****	0.33****	0.18*
CCL11	-0.01	0.01	0.28****	0.33****	-0.06	0.01	0.26****	0.41****	-0.14	-0.08
CCL13	-0.07	-0.28**	-0.27**	-0.36****	-0.09	0.11	-0.28**	-0.19	0.15	-0.06
CCL19	-0.06	-0.19**	-0.54****	-0.72****	0.07	0.07	-0.56****	-0.69****	0.01	0.03
CCL20	-0.08	-0.26**	0.07	-0.15	0.01	0.00	0.10	0.04	0.17	0.11
CCL23*	-0.04	-0.20****	-0.32****	-0.47****	-0.02	-0.05	-0.18***	-0.27****	0.25**	0.15*
CCL25	0.02	0.07	0.19****	0.23****	0.04	0.06	0.18****	0.29****	-0.01	0.01
CD274	-0.10	-0.16**	-0.18**	-0.28****	-0.03	0.09	-0.09	-0.08	0.23*	0.03
CD8A	-0.08	-0.15**	-0.10	-0.29****	-0.01	0.00	-0.06	-0.05	-0.04	0.08
CSF1*	-0.01	-0.10***	-0.21****	-0.29****	0.03	0.02	-0.15****	-0.17****	0.27***	0.22***
CX3CL1	0.07	0.11**	0.20****	0.32****	0.06	0.06	0.30****	0.35****	-0.07	0.06
CXCL6	-0.12	-0.26*	0.07	-0.04	-0.06	0.20	0.09	0.14	0.11	-0.13
CXCL8	-0.06	-0.37****	0.07	-0.11	-0.01	0.05	0.22*	0.09	0.21*	0.08
CXCL9	-0.06	-0.40****	-0.57****	-0.75****	0.03	0.07	-0.37***	-0.20	0.18*	0.17*
CXCL10*	-0.16	-0.52****	-0.63****	-0.77****	0.04	0.09	-0.47****	-0.35**	0.28****	0.18*
CXCL11	-0.06	-0.27**	-0.45****	-0.69****	-0.02	0.22	-0.42***	-0.30**	0.20*	0.00
DNER	0.00	0.06*	0.13****	0.25****	0.01	0.02	0.15****	0.26****	-0.19*	-0.15*
FGF19	-0.02	-0.03	0.34**	0.42****	0.01	-0.06	0.29*	0.32**	-0.02	-0.04
FLT3LG	0.12	0.14**	0.29****	0.41****	0.14**	0.04	0.15**	0.34****	-0.05	0.05
IFNG	0.20	0.53***	0.70****	0.67****	0.09	0.31	0.49**	0.66****	-0.11	0.03
IL5	-0.12	-0.29***	-0.04	-0.16	0.01	0.02	0.04	0.03	0.15	-0.06
IL6*	-0.27	-1.32****	-0.96****	-1.85****	-0.01	-0.29	-0.46***	-1.00****	0.35****	0.31****
IL7	-0.14	-0.27**	-0.08	-0.24**	-0.07	0.14	-0.04	-0.06	0.20*	-0.06
KITLG*	0.05	0.14***	0.22****	0.39****	0.01	-0.03	0.21****	0.29****	-0.25**	-0.11
LIF*	-0.12	-0.34****	-0.15**	-0.40****	0.01	0.01	-0.09*	-0.17****	0.33****	0.13
MMP1*	-0.01	-0.51****	-0.49****	-1.00****	-0.03	0.04	-0.41****	-0.50****	0.28****	0.18*
NTF3	-0.10	-0.08	0.21**	0.32****	0.08	0.11	0.14**	0.13*	-0.05	0.00
OSM	-0.23	-0.39***	-0.35***	-0.41***	-0.16	-0.11	-0.18	-0.32**	-0.03	0.10
S100A12*	-0.11	-0.85****	-0.02	-1.24****	-0.05	-0.18	0.15	-0.54****	0.37****	0.14
SIRT2	-0.13	-0.51**	-0.24	-0.40	-0.03	0.32	0.07	0.08	0.07	-0.12
SULT1A1	0.01	-0.35**	-0.12	-0.22	-0.02	0.12	0.18	0.09	0.04	-0.12
TNFRSF9	-0.02	-0.14***	-0.21****	-0.42****	0.05	0.04	-0.13**	-0.24****	0.15	0.17*
TNFSF11	-0.01	-0.16**	-0.05	-0.33****	0.03	-0.03	-0.05	-0.26****	0.00	0.05
TNFSF14	-0.13	-0.41****	-0.35***	-0.48****	-0.02	0.09	-0.09	-0.21	0.18*	0.04
VEGFA	-0.10	-0.28****	-0.16**	-0.27****	-0.01	0.02	-0.03	-0.01	0.22*	0.12
* = FDR < 0.01, ** - FDR < 0.0001, *** = FDR < 0.000001, **** = FDR < 0.00000001										

patients provide a possible mechanism for the superior clinical efficacy of UPA Mono over MTX. Overall, treatment with UPA monotherapy resulted in the normalization of key pathways associated with the pathobiology of RA in both MTX-naïve and MTX-IR patients, consistent with our previous observations on the effect of UPA in combination with csDMARDs in csDMARD-IR RA patients.[3,4]

References

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Abstract Number: 1242

Sex Differences in Treatment Response to Three Different Biological Treatments and Corticosteroids in Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

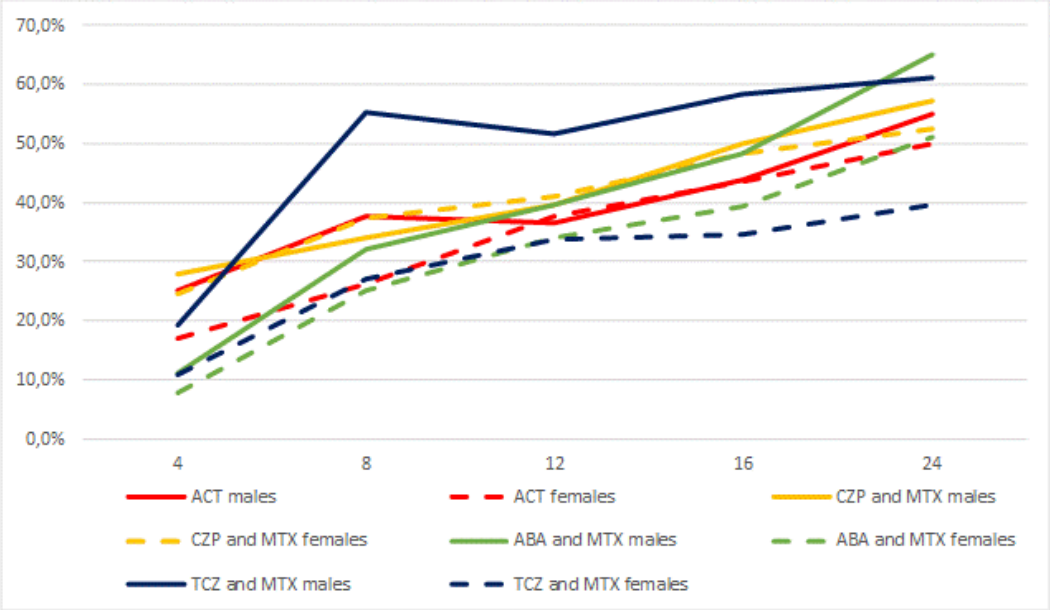
Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: To investigate sex differences in clinical response to three different biological treatments in combination with methotrexate (MTX) versus MTX plus corticosteroids (active conventional treatment; ACT), in early RA. We hypothesized that men and women differ in their response to one or several treatments.

Methods: DMARD-naïve patients with symptom duration < 2 years, moderate to severe disease activity (DAS28-CRP >3.2) and RF or ACPA positivity, or increased CRP (≥10 mg/L) were randomized in the phase IV NORD-STAR trial (NCT01491815) on 1:1:1:1 ratio, stratified by country, sex and ACPA status to 1)ACT; 2)certolizumab pegol (CPZ); 3)abatacept (ABA); 4)tocilizumab (TCZ)[1]. Remission outcomes were analyzed with longitudinal logistic generalized estimating equations analysis. The model included treatment, time (4, 8, 12, 16, and 24 weeks) and sex. The primary and secondary clinical results of the trial after 24 weeks have been published[1]. For this sub-study, the co-primary

Figure 1 Crude clinical disease activity index (CDAI) remission rates over 24 weeks in percentage



ACT=active conventional treatment (methotrexate and corticosteroids); CZP=certolizumab pegol; ABA=abatacept; TCZ=tocilizumab; MTX=methotrexate

outcomes were differences in clinical disease activity index remission (CDAI≤2.8) over 24 weeks and at 24 weeks with ACT as the reference. Sex differences were assessed by interaction terms (males vs. females within each treatment comparison).

Results: This study included all 812 patients in the NORD-STAR trial (251 men and 561 women). The mean age was 56.5 (SD 14.0) and 53.2 (SD 15.0) years in males and females, respectively. Corresponding baseline DAS28-CRP was 5.0 (SD 1.0) and 5.0 (SD 1.1) and CDAI 27.5 (SD 11.6) and 28.1 (SD 12.0).

The crude CDAI remission rates at 24 weeks were 55.0% in males and 50.0% in females for ACT, 57.1% and 52.4% for CZP, 65.0% and 51.1% for ABA and 61.1% and 39.6% for TCZ (Figure 1). The analyses were adjusted for the stratification variables, age, BMI and DAS28-CRP at baseline. Using ACT as the reference, the adjusted overall odds ratios (OR) for achieving CDAI remission (95% confidence intervals, CI) with CZP were 1.26 (0.73-2.19) and 1.26 (0.88-1.81) in males and females, respectively, with ABA 1.25 (0.74-2.13) and 0.86 (0.60-1.24) and with TCZ 1.70 (1.01-2.87) and 0.76 (0.51-1.13). Corresponding odds ratios at 24 weeks with CZP were 1.41 (0.62-3.18) and 1.12 (0.66-1.89), with ABA 2.19 (0.96-4.97) and 1.04 (0.62-1.73) and with TCZ 1.54 (0.68-3.49) and 0.66 (0.38-1.14). For the primary and several secondary outcomes, women responded significantly poorer than men to TCZ compared with ACT (Table 1).

The percentage of males and females who experienced at least one adverse event with ACT was 85.7% and 86.1%, respectively, with CZP 82.5% and 82.7%, with ABA 70.3% and 84.3% and with TCZ 93.2% and 96.0%. The percentage of men and women who stopped treatment early with ACT was 6.3% and 11.1%, respectively, with CZP 12.5% and 10.8%, with ABA 6.3% and 5.0% and with TCZ 6.8% and 14.0%.

Conclusion: After 24 weeks, higher remission rates were observed in men than in women for all four treatment arms, suggesting that this generalized sex difference is related to the disease itself rather than to the treatments. In contrast, a distinctly lower treatment response was seen in female patients treated with tocilizumab versus conventional treatment, suggesting a sex-effect that is specific for IL-6 blockade.

Table 1 Adjusted remission and response outcomes over 24 weeks, at 12 and 24 weeks. Values are odds ratios (95% confidence intervals) with active conventional treatment (methotrexate plus corticosteroids) as the reference

Parameter	Sex	CZP+MTX versus ACT	ABA+MTX versus ACT	TCZ+MTX versus ACT
CDAI remission				
Over 24 weeks	males	1.26 (0.73-2.19); p=0.41	1.25 (0.74-2.13); p=0.41	**1.70 (1.01-2.87); p=0.046****
	females	1.26 (0.88-1.81); p=0.22	0.86 (0.60-1.24); p=0.43	**0.76 (0.51-1.13); p=0.17**
at week 12	males	1.32 (0.60-2.90); p=0.49	1.51 (0.71-3.23); p=0.29	**2.31 (1.09-4.89); p=0.03****
	females	1.13 (0.68-1.89); p=0.63	0.81 (0.48-1.39); p=0.45	**0.88 (0.52-1.51); p=0.65**
at week 24	males	1.41 (0.62-3.18); p=0.41	2.19 (0.96-4.97); p=0.06	**1.54 (0.68-3.49); p=0.30***
	females	1.12 (0.66-1.89); p=0.68	1.04 (0.62-1.73); p=0.89	**0.66 (0.38-1.14); p=0.13**
DAS28-CRP remission				
Over 24 weeks	males	1.45 (0.84-2.50); p=0.18	0.82 (0.49-1.39); p=0.47	**1.99 (1.16-3.40); p=0.01***
	females	1.07 (0.75-1.52); p=0.71	0.82 (0.58-1.17); p=0.27	**1.06 (0.73-1.55); p=0.76**
at week 12	males	**2.28 (0.98-5.31); p=0.06***	1.01 (0.47-2.14); p=0.99	3.17 (1.39-7.25); p=0.006
	females	**0.95 (0.56-1.61); p=0.86**	0.91 (0.53-1.54); p=0.71	1.58 (0.93-2.70); p=0.09
at week 24	males	0.88 (0.36-2.16); p=0.78	1.26 (0.51-3.10); p=0.62	1.53 (0.59-3.96); p=0.38
	females	1.41 (0.77-2.56); p=0.26	1.02 (0.59-1.78); p=0.94	0.73 (0.41-1.27); p=0.28
SDAI remission				
Over 24 weeks	males	1.38 (0.79-2.40); p=0.26	1.25 (0.73-2.13); p=0.41	**1.85 (1.09-3.14); p=0.02****
	females	1.28 (0.89-1.86); p=0.18	0.88 (0.61-1.27); p=0.50	**0.81 (0.55-1.20); p=0.31**
at week 12	males	1.80 (0.81-4.00); p=0.15	1.63 (0.76-3.50); p=0.21	**2.86 (1.34-6.10); p=0.006****
	females	1.15 (0.69-1.92); p=0.59	0.82 (0.49-1.40); p=0.47	**0.98 (0.57-1.67); p=0.93**
at week 24	males	1.63 (0.72-3.67); p=0.24	**2.35 (1.04-5.32); p=0.04***	**1.91 (0.85-4.30); p=0.12****
	females	1.22 (0.72-2.06); p=0.46	**0.98 (0.59-1.63); p=0.94**	**0.68 (0.40-1.18); p=0.17**
EULAR good response				
Over 24 weeks	males	1.42 (0.75-2.68); p=0.28	0.71 (0.41-1.23); p=0.22	1.73 (0.95-3.13); p=0.07
	females	1.36 (0.95-1.95); p=0.09	0.92 (0.65-1.31); p=0.66	1.16 (0.79-1.69); p=0.44
at week 12	males	1.31 (0.55-3.15); p=0.54	0.98 (0.42-2.27); p=0.96	2.63 (0.96-7.22); p=0.06
	females	1.58 (0.90-2.77); p=0.12	1.14 (0.66-1.98); p=0.63	1.64 (0.92-2.90); p=0.09
at week 24	males	0.83 (0.29-2.37); p=0.73	1.04 (0.36-3.00); p=0.95	2.60 (0.63-10.66); p=0.19
	females	1.86 (0.95-3.63); p=0.07	1.50 (0.80-2.78); p=0.20	0.92 (0.50-1.68); p=0.78

****p-value interaction <0.05; *p-value interaction <0.10.** Asterixes indicate a significant difference in the odds ratios between males and females within a treatment; CDAI=clinical disease activity index; DAS28-CRP= disease activity score of 28 joints (C-reactive protein based); SDAI= simple disease activity index; EULAR= European League Against Rheumatism; CZP= certolizumab pegol; ABA= abatacept; TCZ= tocilizumab; ACT= active conventional treatment (methotrexate plus corticosteroids); MTX=methotrexate

References

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2, 6, Takeda, 2, 6, Wyeth, 2, 6, Centocor, 2, 5, 6; **T. Uhlig**, None; **G. Grondal**, None; **K. Hørslev-Petersen**, None; **M. Heiberg**, Roche, 6; **T. Sokka-Isler**, AbbVie, 2, Amgen, 2, BMS, 2, Celgene, 2, DiaGraphIT, 2, Medac, 2, MSD, 2, Novartis Healthcare, 2, Orionpharma, 2, Pfizer, 2, Roche, 2, Sandoz, 2, UCB, 2; **J. Twisk**, None; **I. van der Horst-Bruinsma**, None.

Abstract Number: 1243

Real World Validation of a Rule to Predict Response to Sarilumab in Patients with Rheumatoid Arthritis: Analysis from the RISE Registry

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Accurately identifying patients who may respond better to a specific drug or mechanism of action could improve rational selection of medications to optimize clinical response, reduce irreversible damage, and ameliorate long term outcomes. Using a machine learning approach, previous work using data from clinical trials has found that patients with positive ACPA status (ACPA+) and CRP >12.3 mg/L responded better to sarilumab than patients who did not meet this criterion. However, the average disease activity and CRP levels for most patients initiating sarilumab in real-world settings is often lower than in clinical trials. Therefore, we validated the stratification rule in a national real-world rheumatology based electronic health record (EHR) registry. We hypothesized that sarilumab initiators who are rule-positive (seropositive [RF, ACPA] with CRP levels >12.3 mg/L) are more likely to achieve treatment targets compared with rule-negative patients.

Methods: Using 2017–2020 ACR's Rheumatology Informatics System for Effectiveness (RISE) registry, we identified sarilumab initiators who had ≥1 prescription of sarilumab on or after 5/22/2017 (FDA approval date). The first prescription date was the index date. Eligible patients were required to be 18 years of age, ≥1 rheumatologist diagnosis for RA prior to index, clinical disease activity index (CDAI) >10 within 30 days prior to or 7 days after index, with CRP value within 90 days prior to index, and ≥1 CDAI within 6 ± 3 months after index. Based on the CDAI and CRP levels at the index date, we categorized the cohort into 4 groups, 1) Seropositive and CRP >12.3 mg/L, 2) Seropositive and CRP ≤12.3 mg/L, 3) Seronegative and CRP >12.3 mg/L, 4) Seronegative and CRP ≤12.3 mg/L. Logistic regression models were used to compare the odds of achieving CDAI low disease activity (LDA) or Remission (CDAI < 10), and MCID (minimum clinical important difference; CDAI improvement ≥12 if baseline CDAI >22 or CDAI ≥6 if baseline 10< CDAI < 22) between rule positive and negative patients. Sensitivity analyses using CRP >5 mg/L (rather than 12.3 mg/L) as the rule positive cutoff point were also conducted.

Results: We identified 205 sarilumab users who met all required inclusion and exclusion criteria. Baseline demographic and clinical characteristics are shown in **Table 1**; most characteristics of these patients were equally distributed across the four groups, except that seropositive patients were more likely to be of black race and less likely to have previous Janus kinase inhibitor use. Logistic regression showed that compared with rule negative patients, rule positive patients were more likely to reach LDA/remission and MCID (**Table 2**). The mean difference in Δ CDAI

Table 1. Baseline Demographic and Clinical Characteristics

		Group 1	Group 2	Group 3	Group 4	P-Value
Number of Patients	N	53	91	11	50	.
Age	Mean ± SD	54.47 (11.67)	53.62 (8.72)	49.09 (10.23)	54.36 (12.01)	0.1614
Sex	Male	7 (13.2)	18 (19.8)	3 (27.3)	11 (22.0)	0.5805
	Female	46 (86.8)	73 (80.2)	8 (72.7)	39 (78.0)	.
Race	Black	10 (18.9)	5 (5.5)	0 (0.0)	0 (0.0)	.
	White	32 (60.4)	62 (68.1)	10 (90.9)	39 (78.0)	0.0066
	Other/ missing	11 (20.8)	24 (26.4)	1 (9.1)	11 (22.0)	.
CDAI at index date	Mean ± (SD)	25.50 (13.37)	25.03 (10.94)	31.05 (15.94)	25.31 (9.49)	0.6140
CDAI category at index date	Moderate	27 (50.9)	47 (51.6)	4 (36.4)	20 (40.0)	.
	High	26 (49.1)	44 (48.4)	7 (63.6)	30 (60.0)	0.4693
cDMARD at 1-year baseline	Yes	35 (66.0)	63 (69.2)	4 (36.4)	35 (70.0)	0.1675
	No	18 (34.0)	28 (30.8)	7 (63.6)	15 (30.0)	.
MTX at 1-year baseline	Yes	28 (52.8)	39 (42.9)	2 (18.2)	21 (42.0)	0.1902
	No	25 (47.2)	52 (57.1)	9 (81.8)	29 (58.0)	.
Baseline csDMARD (excluding MTX)	Yes	18 (34.0)	37 (40.7)	4 (36.4)	20 (40.0)	0.8720
	No	35 (66.0)	54 (59.3)	7 (63.6)	30 (60.0)	.
History of TNFi	Yes	40 (75.5)	67 (73.6)	9 (81.8)	39 (78.0)	0.9018
	No	13 (24.5)	24 (26.4)	2 (18.2)	11 (22.0)	.
History of JAKi	Yes	18 (34.0)	41 (45.1)	7 (63.6)	30 (60.0)	0.0397
	No	35 (66.0)	50 (54.9)	4 (36.4)	20 (40.0)	.
History of non-TNF agents	Yes	22 (41.5)	46 (50.5)	7 (63.6)	33 (66.0)	0.0760
	No	31 (58.5)	45 (49.5)	4 (36.4)	17 (34.0)	.
RX of oral steroid at 1-year baseline	Yes	36 (67.9)	63 (69.2)	9 (81.8)	27 (54.0)	0.1785
	No	17 (32.1)	28 (30.8)	2 (18.2)	23 (46.0)	.
RX of opioid at 1-year baseline	Yes	11 (20.8)	16 (17.6)	3 (27.3)	14 (28.0)	0.5115
	No	42 (79.2)	75 (82.4)	8 (72.7)	36 (72.0)	.
RF	Positive	23 (43.4)	44 (48.4)	0 (0.0)	0 (0.0)	0
	Negative	0 (0.0)	10 (11.0)	5 (45.5)	23 (46.0)	.
	Missing	30 (56.6)	37 (40.7)	6 (54.5)	27 (54.0)	.
CRP at index date (-90 to 0 day)	Mean ± SD	33.47 (29.16)	2.68 (3.32)	26.92 (19.13)	3.39 (3.37)	0

All the numbers in the table are n (%) unless indicated otherwise.
Group 1: Seropositive and CRP >12.3 mg/L,
Group 2: Seropositive and CRP ≤12.3 mg/L,
Group 3: Seronegative and CRP >12.3 mg/L,
Group 4: Seronegative and CRP ≤12.3 mg/L.
Seropositive patients were defined as those with a history of anti-CCP positive status or RF positive status or any ICD-10 diagnosis code of M05.
CDAI, clinical disease activity index; csDMARD, conventional synthetic DMARD; ICD, International Classification of Diseases; JAKi, Janus kinase inhibitors; RX, prescription; TNFi, tumor necrosis factor inhibitors.

between rule positive and rule negative patients was 1–4 units (p=0.16). Results from sensitivity analyses (CRP >5 mg/L) yielded a better response in rule positive patients as in the main analysis.

Conclusion: Patients with seropositive status and elevated CRP (>12.3 mg/L, or >5 mg/L) had a better response to sarilumab compared with patients who did not meet these two criteria in real-world settings. Seropositivity seemed to be a stronger driver for response in this data set and validation of an optimal CRP cutoff may require more data.

Table 2. Outcomes at 24 Weeks in Sarilumab Treated Patients

Proportion of patients that achieved primary and secondary outcomes, n (%)					
Outcome		**Group 1**	**Group 2**	**Group 3**	**Group 4**
CDAI LDA[a]	Yes	20 (37.7)	30 (33.0)	2 (18.2)	12 (24.0)
	No	33 (62.3)	61 (67.0)	9 (81.8)	38 (76.0)
CDAI remission[a]	Yes	5 (9.4)	2 (2.2)	0 (0.0)	0 (0.0)
	No	48 (90.6)	89 (97.8)	11 (100.0)	50 (100.0)
CDAI MCID[b]	Yes	20 (37.7)	35 (38.5)	2 (18.2)	16 (32.0)
	No	33 (62.3)	56 (61.5)	9 (81.8)	34 (68.0)
Change in CDAI	Mean ± SD	−8.19 (13.85)	−7.40 (13.83)	−5.77 (18.74)	−4.40 (11.94)

Odds Ratio Estimates			
Effect	**Odds Ratio**	**95% Wald Confidence Limits**	
CDAI LDA[a]			
Group 2 versus Group 1	0.773	0.354	1.687
Group 3 versus Group 1	0.369	0.065	2.082
Group 4 versus Group 1	0.504	0.195	1.302
CDAI MCID[b]			
Group 2 versus Group 1	1.217	0.500	2.963
Group 3 versus Group 1	0.095	0.010	0.880
Group 4 versus Group 1	0.832	0.295	2.348

Group 1: Seropositive and CRP >12.3 mg/L,
Group 2: Seropositive and CRP ≤12.3 mg/L,
Group 3: Seronegative and CRP >12.3 mg/L,
Group 4: Seronegative and CRP ≤12.3 mg/L.
Seropositive patients were defined as ever anti-CCP positive or RF positive or ever have any ICD-10 diagnosis code of M05.
[a]CDAI <10.
[b]CDAI improvement ≥12 if baseline CDAI >22 or CDAI ≥6 if baseline 10<CDAI <22.
CDAI, clinical disease activity index; ICD, International Classification of Diseases; LDA, low disease activity; MCID, minimum clinical important difference.

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Abstract Number: 1244

Mindfulness-Based Stress Reduction (MBSR) to Improve Patient-Related Outcomes (PROs) in Patients with Rheumatoid Arthritis in Clinical Remission but Elevated Negative PROs: A Pragmatic Pilot Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Many patients with controlled rheumatoid arthritis (RA) continue to report high levels of disease activity (PGA), as well as other disturbing patient-related outcomes (PROs), such as depression and anxiety. Aiming to improve PGA and PROs in a pragmatic pilot study, Mindfulness-Based Stress Reduction (MBSR), an eight-week non-pharmacological approach, was offered to patients with controlled RA but elevated negative PROs.

Methods: Patients in clinical remission on stable treatment at their regular visit were referred to research assistants to determine their interest in the study. Recruitment strategies (Table 1) were based either on elevated Center for Epidemiologic Studies Depression scale (CES-D) scores or on a differenre ≥2/10 (Delta) between PGA and Physician General Assessment (EGA). Patients were evaluated 1-4 weeks before MBSR and 6 and 12 months after MBSR's end. Scores were compared between baseline and 6 and 12 months. Differences within and between groups were calculated with linear mixed regression models for continuous outcomes or with generalized estimating equation for dichotomic outcomes. Some participants were interviewed about their experience after the 6-month assessment to complete a qualitative evaluation.

Results: Out of 325 tagged patients, 224 were identified as candidates by rheumatologists, 67 were proposed MBSR, 39 (58%) agreed to participate, 31 took part to 1 of 4 MBSR groups provided over 18 months, and 28 (42%) completed both the baseline and the 6- and/or 12-month evaluation (Table 2). Timing (day vs evening), frequency of the group meetings, distance from home, severe depression, extremes of age and comorbidities were examples of barriers to participation.

Results showed a significant improvement from baseline to 12 months post-MBSR for depression (CES-D; estimate (95% CI)=(-9.21 (-13.96 to -4.41), p=0.004), anxiety (GAD-7; -3.18 (-5.15 to -1.22), p=0.004), emotional coping (-5.18

Table 1. Inclusion and exclusion criteria

	Groups with criteria
Inclusion criteria (both required):	
1. ≥18 year-old patient with DMARD- and/or biologic-treated RA (meeting 1987/2010 ACR classification criteria) and stable arthritis treatment for at least 3 months (expected to be stable over the following months)	All groups
2. ≤2/66 SJC Both ≤2/66 SJC and CRP ≤8 mg/L	First group Other groups
3. CES-D score ≥16 CES-D score ≥16 and/or Δ(PGA – EGA) ≥2cm	First group Other groups
Exclusion criteria (both required):	
1. Inability to consent (e.g. not fluent in French, dementia) or to participate in groups at pre-specified times (e.g. travel difficulties or distance);	All groups
2. Active vasculitis	All groups
3. Untreated active bipolar disease, severe depression with suicidality risk, or psychosis, as determined upon chart review or during patient encounters	All groups

DMARD: Disease Modifying Anti-Rheumatic Drugs, SJC=swollen joint count, CRP: C-reactive protein, CES-D: Center for Epidemiologic Studies Depression scale, PGA: Patient global assessment, EGA: Evaluator Global Assessment of activity

Table 2. Patient characteristics at baseline

	Baseline	
	n	Value
Age (years), mean ± SD	28	61.8 ± 13.6
Women, n (%)	28	24 (85.7)
Disease duration (years), median (IQR)	28	9.8 (4.7-12.5)
Seropositive status, n (%)	26	15 (53.6)
Body mass index (kg/m2), mean ± SD	28	27 ± 5.6
Education (number of years), mean ± SD	28	12.9 ± 3.2
Caucasian, n (%)	28	27 (96.4)
Marital status, n (%)		
Married/living with a partner	28	18 (64.3)
Divorced/separated		4 (14.3)
Single		3 (10.7)
Widowed		3 (10.7)
Treatments		
Biologic, n (%)	28	10 (35.7)
Methotrexate, n (%)	28	17 (60.7)
Sulfasalazine, n (%)	28	4 (14.3)
Hydroxychloroquine, n (%)	28	19 (67.9)
Leflunomide, n (%)	28	6 (21.4)
Prednisone, n (%)	28	0 (0)
Non-steroidal anti-inflammatory drug, n (%)	28	3 (10.7)
Antidepressants, n (%)	28	7 (25.0)

SD: Standard deviation, IQR: Interquartile range (25th-75th percentiles)

(-7.82 to -2.53), p=0.004), sleep (-2.06 (-3.12 to -0.99), p=0.004) and function (M-HAQ; -0.28 (-0.43 to -0.12), p=0.009) (Table 3). At baseline, PGA was significantly correlated with function (r=0.54) but not depression (r=0.18) or anxiety (r=0.19). At 6 months, PGA showed a higher correlation with function (r=0.72) and became significantly correlated with depression (r=0.60) and anxiety (r=0.44). Emotional coping strategy was the only one significantly modified by MBSR; this maladaptive approach to illness is critical to quality of life. Qualitative interviews at 6 months in 10 patients indicated persistent subjective patient benefits including integration of MBSR techniques and effective coping strategies into daily life.

Conclusion: Offering MBSR to RA patients with high negative PROs is both feasible and helpful. MBSR had lasting benefits on outcomes that are important to patients, particularly anxiety, depression, and function. MBSR helped empower patients to practice self-management and enabled them to use fewer emotional coping strategies. MBSR did not appear to improve PGA, despite PGA correlations with function, depression, and anxiety at 6 months. The reasons for this apparent PGA disconnect require further studies.

Table 3. Evolution of outcomes over time

Table 3. Evolution of outcomes over time

	Baseline (n=28)	6 months (n=25)	12 months (n=19)	Global p-value	Adjusted p-value
CES-D	18.9 ± 11.2	12.3 ± 9.8	9.3 ± 8.7	**<0.001**	**0.004**
CES-D ≥ 16, n (%)	19 (67.9)	9 (36.0)	2 (11.8)	**0.002**	**0.007**
Beck Depression Inventory	16.2 ± 11.8	10.4 ± 9.7	10.4 ± 10.0	**<0.001**	**0.004**
GAD-7 Anxiety	7.7 ± 5.3	4.5 ± 3.6	3.7 ± 4.5	**0.001**	**0.004**
M-HAQ (0-3)	0.9 ± 0.8	0.8 ± 0.8	0.7 ± 0.8	**0.003**	**0.009**
M-HAQ ≥ 1, n (%)	16 (57.1)	9 (32.1)	6 (26.1)	**0.047**	0.104
Morning stiffness duration (min)	53.2 ± 107.8	33.0 ± 54.2	41.1 ± 94.8	0.410	0.586
Swollen joint count, 68 joints	0.2 ± 0.7	0.1 ± 0.4	0.5 ± 0.9	0.133	0.242
Tender joint count, 66 joints	2.0 ± 4.3	1.7 ± 4.6	1.1 ± 1.4	0.656	0.729
Patient global assessment (PGA;0-10)	3.4 ± 2.1	2.9 ± 2.4	3.3 ± 3.0	0.465	0.620
Evaluator global assessment (EGA; 0-10)	0.3 ± 0.6	0.7 ± 1.0	1.2 ± 2.0	**0.047**	0.104
Delta (PGA – EGA)	3.1 ± 2.0	2.3 ± 2.6	2.1 ± 3.2	0.076	0.152
C-reactive protein, mg/L	2.9 ± 2.7	3.4 ± 4.5	3.9 ± 4.3	0.593	0.729
SDAI	9.0 ± 6.4	8.7 ± 8.0	9.0 ± 5.8	0.862	0.907
Sleep quality (0-10; 10 being the worst)	5.1 ± 2.7	4.1 ± 3.3	2.9 ± 2.9	**0.001**	**0.004**
Pain (0-10; 10 being the worst)	4.1 ± 2.4	3.4 ± 2.7	3.9 ± 3.1	0.369	0.568
CHIP Distraction (8-40)	26.0 ± 6.4	26.9 ± 6.5	26.7 ± 6.2	0.639	0.729
CHIP Palliative (8-40)	25.0 ± 5.5	25.3 ± 5.5	24.7 ± 8.3	0.926	0.926
CHIP Instrumental (8-40)	29.8 ± 5.8	28.4 ± 5.6	27.9 ± 6.3	0.281	0.468
CHIP Emotional (8-40)	23.3 ± 7.0	21.3 ± 8.6	18.6 ± 6.5	**<0.001**	**0.004**

CES-D: Center for Epidemiologic Studies Depression scale; GAD7: General Anxiety Disorder-7; M-HAQ: Modified Health Assessment Questionnaire; SDAI: Simple Disease Activity Index; CHIP: Coping with Health Injuries and Perturbations

All variables are presented as mean ± standard deviation, except for dichotomic variables presented as n (%). Global p-values were calculated with linear mixed regression models for continuous outcomes or with generalized estimating equation for dichotomic outcomes. p-values were adjusted using False discovery rate correction.

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Abstract Number: 1245

Characteristics of RA Patients Treated with JAK Inhibitors Before versus After VTE Warnings: Results of a Real-World Multicentric Study

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SESSION INFORMATION

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Background/Purpose: In recent decades, the therapeutic arsenal in RA has dramatically expanded. Baricitinib (BARI) and Tofacitinib (TOFA) were the first JAK inhibitors (JAKi) to be recommended for moderate-to-severe RA after conventional synthetic DMARD failure. Several alerts have arisen concerning an increased risk of veinous thromboembolism (VTE) with these drugs. In May 2019, the European Medicines Agency (EMA) sent a warning about an interim post-marketing analysis revealing a significant increase in the number of VTE with TOFA at the dose of 10 mg twice daily. The first objective of this study was to compare the characteristics of patients initiating a JAKi before versus after EMA's warning to determine if use restrictions were currently applied in daily practice. The second objective was to compare the persistence of BARI and TOFA in real-world.

Table 1. Baseline characteristics according to molecules before and after propensity score-matching

	Before propensity score-matching			After propensity score-matching		
Parameters	**Baricitinib** n = 155	**Tofacitinib** n = 77	**ASD (%)**	**Baricitinib** n = 116	**Tofacitinib** n = 70	**ASD (%)**
Women	118 (76.1)	51 (66.2)	21.7	82 (70.8)	49 (69.6)	2.7
Age (years), mean ± SD	59.6 ± 14.2	56.7 ± 13.4	20.9	58.7 ± 15.3	57.6 ± 13.1	7.8
BMI (kg/m²), mean ± SD	27.0 ± 6.3	27.0 ± 6.8	4.2	26.8 ± 6.6	27.0 ± 6.5	3.0
Smoking status			31.5			14.3
Non-smoker	94 (60.7)	33 (43.4)		60 (51.2)	32 (46.1)	
Former smoker	31 (20.1)	19 (24.9)		28 (23.9)	18 (24.9)	
Current smoker	30 (19.2)	24 (31.7)		28 (24.5)	20 (29.0)	
RA duration (years), median (IQR)	11 (4 to 20)	11 (6 to 19)	10.1*	12 (6 to 20)	12 (5 to 19)	3.0*
Seropositivity status			21.7			8.5
RF + / ACPA +	123 (79.4)	55 (70.6)		89 (76.6)	53 (75.6)	
RF + / ACPA -	11 (7.1)	8 (10.6)		10 (8.3)	7 (9.3)	
RF - / ACPA +	8 (5.2)	7 (9.5)		7 (6.4)	4 (6.3)	
RF - / ACPA -	13 (8.4)	7 (9.2)		10 (8.8)	6 (8.9)	
Erosion	106 (68.6)	58 (75.7)	15.7	86 (74.3)	53 (75.7)	3.3
Baseline CRP (mg/L), median (IQR)	7.0 (1.1 to 25.6)	9.9 (2.6 to 27.0)	12.5*	7.7 (1.8 to 26.8)	10.0 (2.7 to 27.2)	4.0*
Prior bDMARD			27.7			7.8
Naïve (0)	23 (14.8)	7 (9.1)		12 (10.7)	7 (10.0)	
1 or 2	50 (32.3)	34 (44.2)		45 (38.8)	29 (42.0)	
3 or more	82 (52.9)	36 (46.8)		59 (50.6)	34 (48.0)	
Concomitant csDMARD	62 (38.7)	29 (37.4)	5.5	43 (37.1)	27 (38.7)	3.4

Values are numbers (%) unless otherwise stated. Values were calculated after handling missing data using a multiple imputation procedure (m=10). * ASD calculated on log transformed data. Abbreviations: ACPA = anti-citrullinated protein antibody; ASD = absolute standardized difference; bDMARD = biological disease-modifying antirheumatic drug; BMI = body mass index; CRP = C-reactive protein; csDMARD = conventional synthetic disease-modifying antirheumatic drug; IQR = interquartile range; RA = rheumatoid arthritis; RF = rheumatoid factor; SD = standard deviation.

Table 2. Comparison of the baseline characteristics of patients according to JAKi initiation before versus after May 2019

	Before May 2019 n = 161	After May 2019 n = 71	P-value
Age (years), mean ± SD	59.1 ± 13.6	57.5 ± 14.8	0.40
BMI (kg/m²)[1], mean ± SD	27.4 ± 6.2	26.0 ± 5.1	0.17
Smoking status			0.65
Non-smoker	62/110 (56.4)	22/43 (51.2)	
Former smoker	25/110 (22.7)	9/43 (20.9)	
Current smoker	23/110 (20.9)	12/43 (27.9)	
Personal history of DVT	10/161 (6.2)	1/71 (1.4)	0.18
Personal history of PE	7/161 (4.3)	2/71 (2.8)	0.73
Neoplastic history	12/161 (7.5)	5/71 (7.0)	0.91

Values are no./total no. (%) unless otherwise stated. [1] 71 missing values (n=42 vs. 29)
Abbreviations: BMI = body mass index; DVT = deep veinous thrombosis; PE = pulmonary embolism; SD = standard deviation.

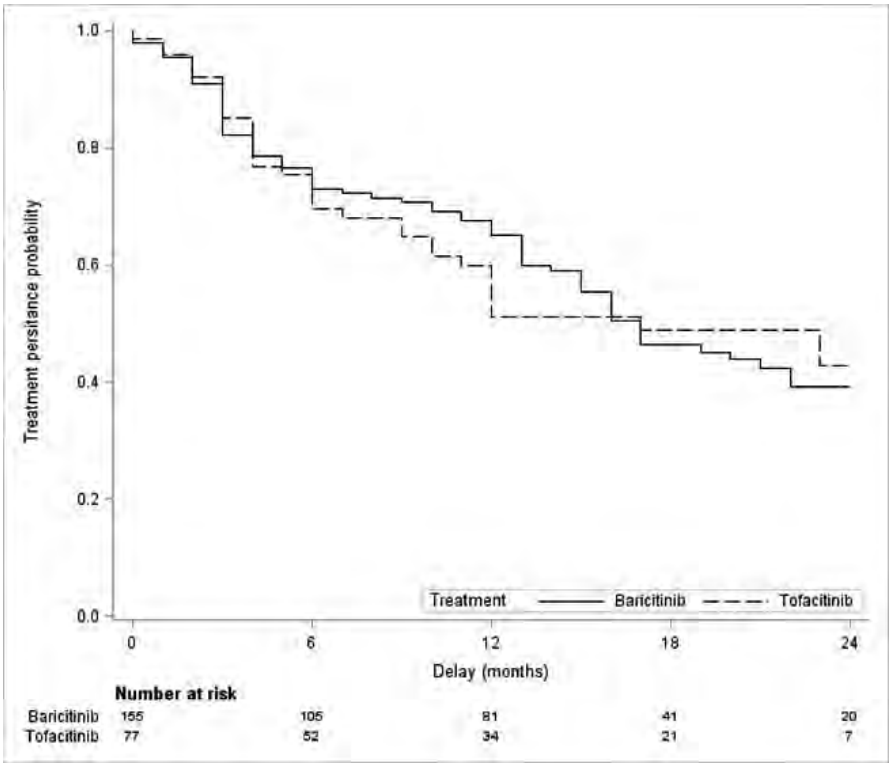

Figure 1. Two-year follow-up treatment persistence with Baricitinib (BARI) and Tofacitinib (TOFA).

Methods: A retrospective multicentric cohort study was conducted. Patients with RA were included if they fulfilled the 2010 ACR/EULAR RA classification criteria and initiated BARI or TOFA between October 2017 and September 2020. Patients were JAKi-naïve. Patient characteristics regarding VTE risk factors were compared between the two periods (before and after May 2019) by using pre-specified statistical tests. Comparison of persistence was assessed by using pre-specified propensity-score methods.

Results: 232 patients were included: 155 with BARI and 77 with TOFA (**Table 1**). Mean age was 59.6±14.2 years old for BARI and 56.7±13.4 years old for TOFA. Median duration of RA was 11 years (IQR, 4 to 20). The proportion of bDMARD-naïve patients was 14.8% with BARI and 9.1% with TOFA. Combination with a csDMARD was reported in 38.7 % (BARI) and 37.4 % (TOFA) of patients. The baseline characteristics of patients regarding VTE risk factors were not statistically different when JAKi was initiated before versus after EMA's warnings although a trend towards a lower proportion of thromboembolic personal history was observed (**Table 2**). The overall median persistence was 17 months (IQR, 13 to 22). Persistence rate at 2 years was 39.3% (BARI) and 42.8% (TOFA) with no significant difference between the two drugs in the propensity score analysis: hazard ratio 0.96; 95% Confidence Interval: 0.52 to 1.74; p=0.89 (**Figure 1**). BARI and TOFA were discontinued due to inefficacy in 64% and 60% of cases, respectively. Both drugs were discontinued due to an adverse event in 30.7% (BARI) and 31.4% (TOFA) of cases. 5 VTE events occurred during our study, 4 with BARI, 1 with TOFA. 4/5 events occurred in patients who initiated JAKi before May 2019. There has been no incident neoplasia nor myocardial infarction reported.

Conclusion: In conclusion, our study revealed that EMA's warnings have not significantly changed RA patient characteristics initiating a JAKi. BARI and TOFA have a similar persistence in our study. The tolerance profile is consistent with post-marketing and real-world data. VTE risk remains a concern in current practice. This study provides additional data and is a hot topic pending the publication of the ORAL-surveillance study (NCT02092467). Monitoring of new marketed JAKi will help understand if there are specific efficacy and safety profiles among JAKi according to the selectively targeted Janus Kinases.

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Abstract Number: 1246

The Effect of Tocilizumab on miR-146a-5p and EMMPRIN/CD147 in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: Angiogenesis is an important contributor to the development of rheumatoid arthritis (RA). Tocilizumab (TCZ), an anti-IL-6 receptor antibody used in the treatment of RA patients, has been shown to exert anti-inflammatory effects. However, its effects on angiogenesis are not fully elucidated, and the molecular mechanisms regulating this effect are unknown.

We aimed to evaluate the expression levels of several microRNA molecules and the concentrations of pro- and anti-angiogenic factors in sera of RA patients before and after the initiation of TCZ treatment and to explore the mechanisms of TCZ action in an *in vitro* co-culture system.

Methods: Sera from 40 RA patients before and 4 months after the initiation of TCZ treatment were collected. Using commercial ELISA kits, the concentrations of the pro-angiogenic factors EMMPRIN, VEGF, MMP-9, IL-6, NGAL, and of the anti-angiogenic factors endostatin and thrombospondin-1 (Tsp-1) were measured, as were the expression levels of microRNA molecules miR-16-5p, miR-21-5p, miR-132-3p, miR-146a-5p, miR-150-5p, miR-155-5p, miR-203a-3p, miR-221-3p, and miR-323a-3p. In vitro, the levels of secreted EMMPRIN, VEGF MMP-9 and Tsp-1 were measured in a co-culture system of HT1080 fibroblasts and U937 monocytes with and without addition of anti-EMMPRIN blocking antibody.

Results: The mean age of RA patients was 57.5±11.1 years, 33 (82.5%) females, mean disease duration 7.7±5.6 years. Of these patients, 25/40 (62.5%) were classified as "responders" based on EULAR criteria.

Statistically significant reduction in the level of EMMPRIN/CD147 ($p=0.035$), without significant changes in serum levels of MMP-9, VEGF, MMP-3, MMP-7 and of the anti-angiogenic factors Tsp-1 and endostatin were found 4 months after TCZ treatment. The ratio between EMMPRIN and Tsp-1 calculated for each patient 4 months after initiating TCZ decreased significantly ($p=0.031$), most notably in responding patients versus non-responders ($p=0.033$), while the levels of VEGF, MMP-9, Tsp-1, and EMMPRIN were unchanged. Of microRNA, only miR-146a-5p and miR-150-5p levels were significantly increased after 4 months of TCZ treatment relative to treatment initiation ($p=0.0178$, $p=0.0028$ respectively), with no difference noted in microRNA levels between patients considered responders and non-responders to TCZ.

In vitro, the accumulation of EMMRPIN, VEGF and MMP-9 in the supernatants was increased by co-culturing the HT1080 fibroblasts and the U937 monocytes ($p< 0.05$, $p< 0.05$, $P< 0.001$ respectively), while the accumulation of the anti-angiogenic factor thrombospondin-1 (Tsp-1) ($p< 0.001$) and the expression levels of miR-146a-5p were reduced ($p< 0.001$). Transfection of the miR-146-5p mimic reduced EMMPRIN, VEGF and MMP-9 levels by 1.3, 2.3 and 2.2-fold, respectively ($p< 0.05$).

Adding anti-EMMPRIN antibody to the co-culture reduced the accumulation of VEGF and MMP-9 in the supernatants by 1.8 and 1.4, respectively ($p< 0.05$).

Conclusion: Our findings implicate miR-146a-5p in the regulation of EMMPRIN and suggest that TCZ affects angiogenesis through its effects on EMMRPIN and miR-146a-5p.

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Abstract Number: 1247

Plasma Cell-free DNA Is a Useful Biomarker for Tocilizumab Therapy in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Endogenous DNA derived from nuclei is released into the blood circulation as cell-free DNA (cfDNA) following cell damage or death. cfDNA is associated with various pathological conditions. In patients with rheumatoid arthritis (RA), cfDNA levels in peripheral blood and synovial fluid are increased. In addition, cfDNA induces joint inflammation via Toll-like receptor 9 (TLR9) pathways both *in vitro* (Dong C, et al. Front Immunol 2020) and *in vivo* (Liang H, et al. Nat Commun 2018). We have previously reported that the amounts of cfDNA released from synovial cells in RA are significantly suppressed with tocilizumab treatment *in vitro*, although they remain unchanged with etanercept (Hashimoto N, et al. ACR 2016 Annual Meeting). This study aimed to evaluate the clinical significance of cfDNA in RA treated with biological disease-modifying antirheumatic drugs (bDMARDs), specifically tocilizumab and tumor necrosis factor inhibitor (TNF-I).

Methods: We enrolled 126 patients with RA who initiated treatment with bDMARDs, including 72 with tocilizumab and 54 with TNF-I (10 with etanercept, 7 with adalimumab, 22 with certolizumab pegol, and 15 with golimumab).

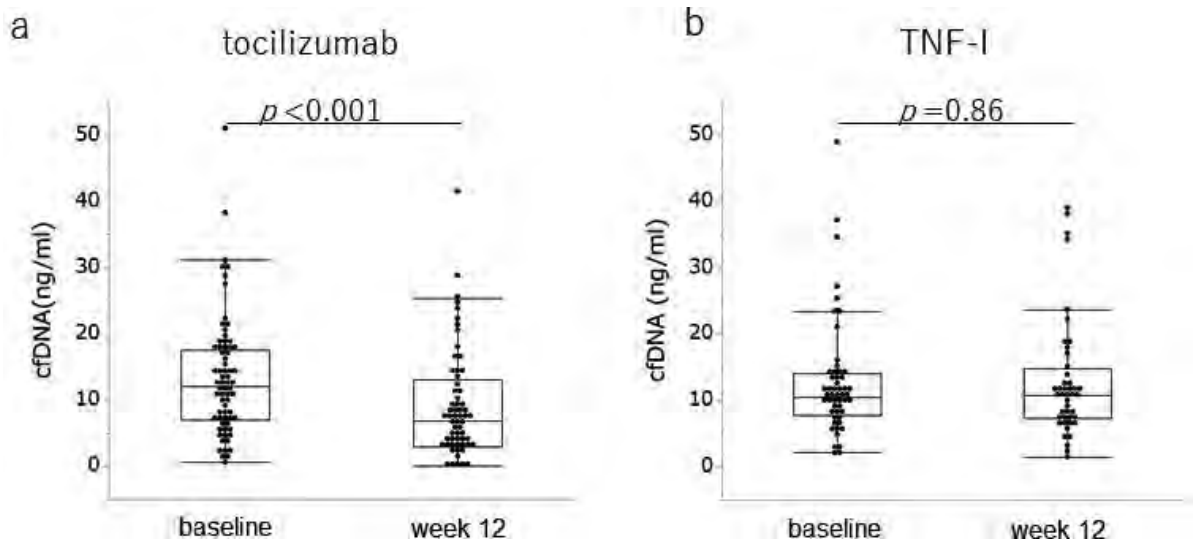

Figure1. cfDNA levels at baseline and week 12 with tocilizumab therapy (a) and with TNF-I (b).

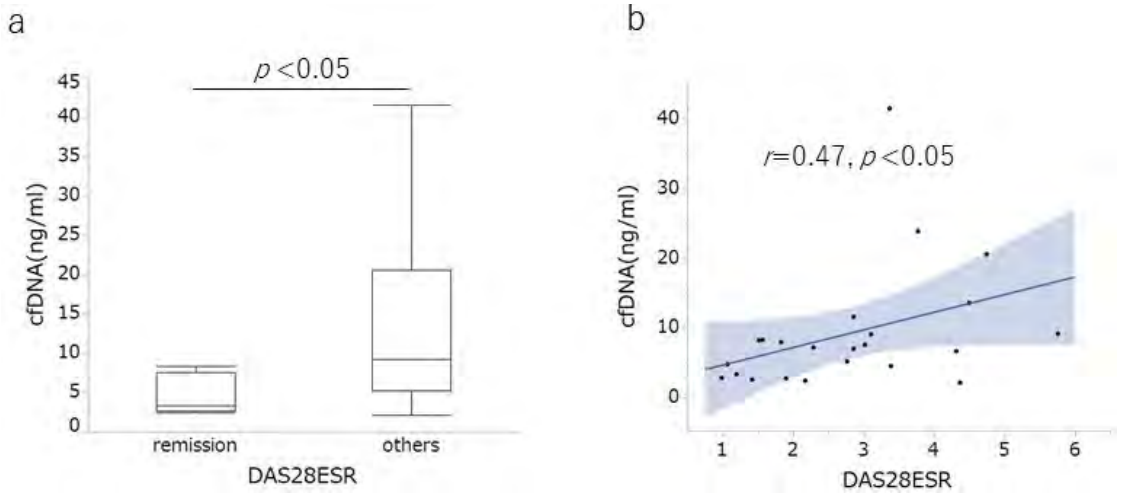

Figure 2. cfDNA levels and DASESR in the biological treatment-naïve patients with tocilizumab therapy. (a) cfDNA levels in DAS28ESR remission patients and others at week 12. (b) Correlation between cfDNA and DAS28ESR at week 12.

Plasma cfDNA levels were measured at baseline, week 4, and week 12 using quantitative polymerase chain reaction (qPCR) assays. Disease activity was also evaluated at the same timepoint, using the disease activity score 28 erythrocyte sedimentation rate (DAS28ESR).

Results: The DAS28ESR at baseline was not different between those who received tocilizumab and TNF-I (median [interquartile range, IQR]: 5.22 [4.35–6.49] and 4.91 [3.92–5.79], respectively), and it was significantly improved in both biological groups at week 12 (median [IQR]: 2.86 [1.82–4.01] and 3.34 [2.74–3.67], respectively). However, cfDNA levels in plasma were significantly decreased with tocilizumab at week 12, but not with TNF-I (Figure. 1). In particular, in the biological treatment-naïve patients with tocilizumab at week 12, cfDNA levels were significantly lower in patients with DAS28ESR remission than those in others (median [IQR]: 3.37 ng/mL [2.69–7.59] and 9.18 ng/mL [5.22–20.6], p< 0.05, respectively) (Figure.2a) and correlated with the DAS28ESR (r=0.47, p< 0.05) (Figure.2b). Meanwhile, there was no difference between remission and others in the biological treatment-naïve patients with TNF-I (median [IQR]: 8.49 ng/mL [7.03–16.4] and 11.2 ng/mL [7.50–18.1], p=0.26, respectively), with no association with the DAS28ESR (r=0.15, p=0.42).

Conclusion: Tocilizumab reduced cfDNA levels in patients with RA, like that in the *in vitro* study. Plasma cfDNA is a possible biomarker for tocilizumab therapy in biological treatment-naïve patients. In addition, tocilizumab may suppress inflammation via the TLR9 pathway by decreasing cfDNA levels.

Disclosure: T. Hashimoto, None; **Y. Yokoyama**, None; **T. Yoshikawa**, None; **T. Furukawa**, None; **N. Azuma**, None; **A. Hashiramoto**, None; **K. Matsui**, None.

Abstract Number: 1248

Adjusted Analyses of the Benefits of Autoantibody Enrichment on Efficacy Outcomes in Early RA, from a Pooled Analysis of 4 Abatacept RCTs

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies have found differential treatment efficacy of abatacept (ABA) for the treatment of RA based on biomarker-seropositivity.[1-4] An earlier study found a differential treatment impact of ABA among SeroPositive Early & Active RA (SPEAR) patients in historic randomized controlled trials (RCTs).[5] In this study, we add to this evidence and test the robustness of the differential treatment impact of ABA among patients with SPEAR to adjustment for patient characteristics.

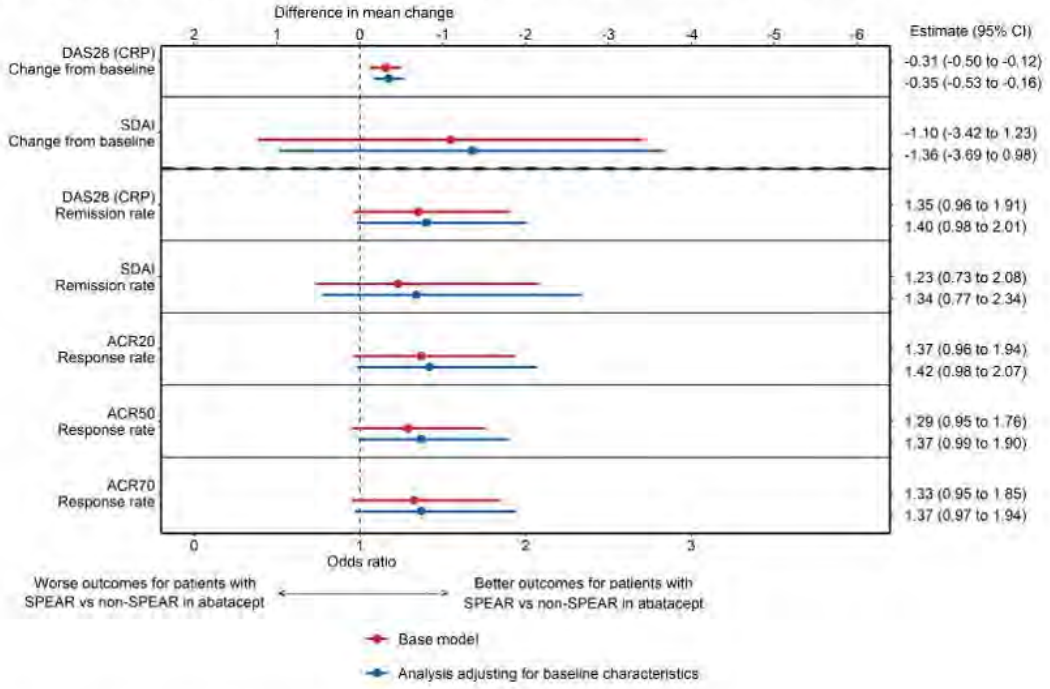
Table 1. Baseline characteristics

	All patients	Abatacept		Comparators[a]	
		Patients with SPEAR	Patients with non-SPEAR	Patients with SPEAR	Patients with non-SPEAR
	N = 2087	n = 784	n = 385	n = 544	n = 374
Trial, n (%)					
AGREE	492 (23.6)	177 (22.6)	68 (17.7)	155 (28.5)	92 (24.6)
AMPLE	509 (24.4)	45 (5.7)	206 (53.5)	41 (7.5)	217 (58.0)
AVERT	339 (16.2)	157 (20.0)	68 (17.76)	79 (14.5)	35 (9.4)
AVERT-2	747 (35.8)	405 (51.7)	43 (11.2)	269 (49.5)	30 (8.0)
Demographics & Disease characteristics					
Age, mean (SD), years	49.3 (12.9)	48.6 (12.5)	49.4 (12.6)	49.2 (13.5)	50.6 (12.9)
Female, (%)	79.3	77.2	81.3	77.9	83.4
Race, n (%)					
Asian	206 (9.9)	104 (13.3)	19 (4.9)	71 (13.1)	12 (3.2)
Black	118 (5.7)	35 (4.5)	30 (7.8)	32 (5.9)	21 (5.6)
Other	146 (7.0)	52 (6.6)	32 (8.3)	27 (5.0)	35 (9.4)
White	1,617 (77.5)	593 (75.6)	304 (79.0)	414 (76.1)	306 (81.8)
Disease duration, mean (SD), months	8.5 (12.5	2.4 (2.8	19.9 (15.9	2.4 (2.9	18.3 (15.1
RF positive, %	91.0	100	74.2	100	76.1
Anti-CCP positive, %	81.8	100	52.2	100	47.3
DAS28 (CRP), mean (SD)	5.71 (1.13)	5.68 (1.09)	5.72 (1.19)	5.76 (1.08)	5.66 (1.20)
CRP Value, mean (SD), mg/dl	2.16 (3.09)	2.22 (2.85)	1.85 (2.42)	2.45 (3.73)	1.92 (3.15)

[a]Comparators included MTX and adalimumab + MTX.

SPEAR, SeroPositive Early & Active RA.

Figure 1. Comparison of SPEAR vs non-SPEAR groups among patients receiving abatacept



SPEAR, SeroPositive Early & Active RA.

Comparators included MTX and adalimumab + MTX.

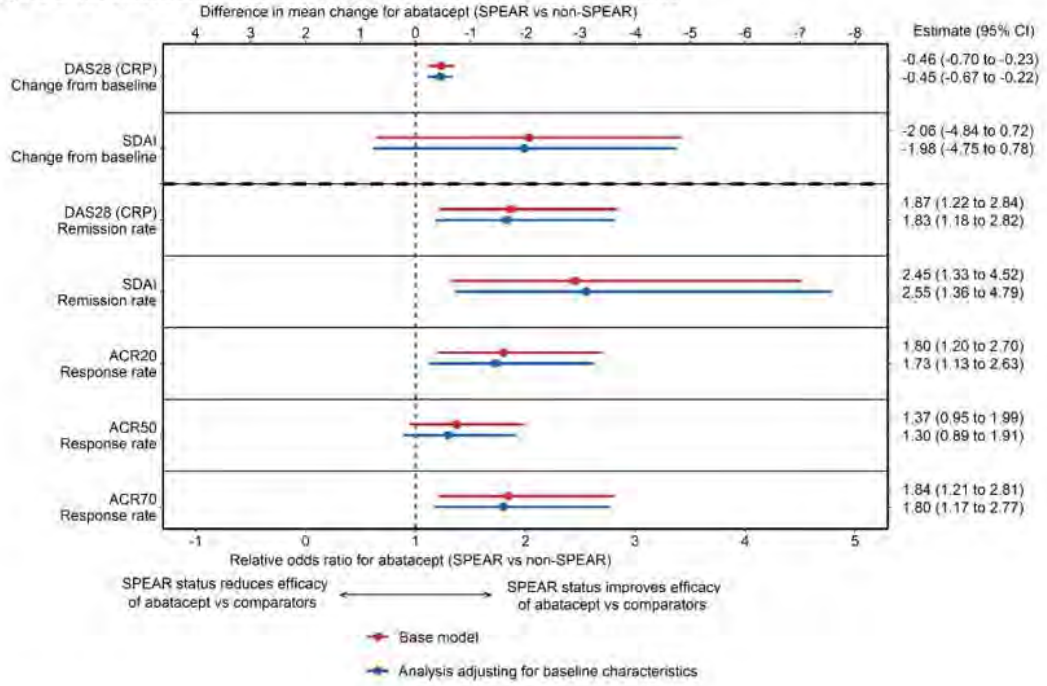
The base model included trial fixed effects, SPEAR status, baseline measures of the outcome (for DAS28-CRP or SDAI outcomes), and treatment type and an interaction between treatment type and SPEAR status (when analyzing the full population).

The analysis adjusting for baseline characteristics included baseline demographics (age, gender, race (White, Non-White), region (North America, Europe, Other)) and baseline ACR core measures as covariates.

Methods: Pooled patient data from 2087 patients from 4 phase 3, early-RA ABA RCTs (AGREE [NCT00122382], AMPLE [NCT00929864], AVERT [NCT01142726], AVERT-2 [NCT02504268]) were analyzed. Patients were defined as SPEAR if they satisfied the following baseline criteria: 1) RF+ and ≥ 3 times the upper limit of normal on an anti-CCP test (ACPA+), 2) disease duration ≤ 12 months, and 3) DAS28 (CRP) ≥ 3.2. Outcomes included DAS28-CRP and SDAI mean change from baseline to week 24 and remission (< 2.6 or ≤3.3, respectively), and ACR 20/50/70 at week 24. Patients were treated with either ABA (monotherapy or ABA+MTX) or a comparator (MTX or adalimumab + MTX). Analyses were conducted separately among ABA-treated patients (comparing SPEAR vs non-SPEAR) and the full population (estimating how the efficacy of ABA vs comparators is modified by SPEAR status). For each outcome, two separate analyses were conducted: the base model included trial fixed effects, SPEAR status, baseline measures of the outcome (for DAS28-CRP or SDAI outcomes), and treatment type and an interaction between treatment type and SPEAR status (when analyzing the full population). In a further adjusted model, baseline demographics (age, gender, race (White, Non-White), region (North America, Europe, Other)) and baseline ACR core measures were added as covariates. Sensitivity analyses defining SPEAR status using only ACPA+ and RF+ were conducted.

Results: This study analyzed 1328 (64%) SPEAR and 759 (36%) non-SPEAR patients. Roughly half of patients with non-SPEAR were RF+ and three-quarters ACPA+; while all patients had high DAS28 (CRP) (**Table 1**). The estimated differential treatment efficacy of ABA among SPEAR patients for both analyses - improved outcomes for ABA-treated SPEAR patients vs non-SPEAR patients, and improved relative efficacy for ABA vs comparators among SPEAR patients vs non-SPEAR patients - was robust to including additional baseline characteristics across all outcomes, with only small changes to effect sizes and precision (**Figures 1 & 2**). Findings were consistent in sensitivity analyses.

Figure 2. Modification of ABA vs comparator efficacy by SPEAR status



SPEAR, SeroPositive Early & Active RA.

Comparators included MTX and adalimumab + MTX.

The base model included trial fixed effects, SPEAR status, baseline measures of the outcome (for DAS28-CRP or SDAI outcomes), and treatment type and an interaction between treatment type and SPEAR status (when analyzing the full population).

The analysis adjusting for baseline characteristics included baseline demographics (age, gender, race (White, Non-White), region (North America, Europe, Other)) and baseline ACR core measures as covariates.

Conclusion: This analysis compared clinical outcomes of RA patients with enriched autoantibody biomarkers and early disease stage (SPEAR) to non-SPEAR, and found that the differential efficacy of ABA was robust to adjustment for baseline demographics and disease status.

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Disclosure: J. Pope, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **S. Park**, Bristol Myers Squibb, 3; **M. Fillbrunn**, None; **K. Lozenski**, Bristol Myers Squibb, 3; **V. Khaychuk**, Bristol Myers Squibb, 3; **K. Michaud**, None; **J. Signorovitch**, Analysis Group, Inc., 3; **H. Lane**, None; **H. Nguyen**, None; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6.

Abstract Number: 1249

In Rheumatoid Arthritis, Inhibition of the Lactate Monocarboxylate Transporters-1, and -4 in Pathological Fibroblast-Like Synoviocytes Led to Decreased ChemokineProduction

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Pathological subsets of fibroblast-like synoviocytes (FLS) have recently been identified as key players in the aggravation of both persistent joint inflammation and destruction in rheumatoid arthritis (RA). In RA, these FLS are considered responsible for the acidification of the synovial fluid through local lactate production and secretion. Lactate transporters such as monocarboxylate transporter-1 (MCT1) and -4 (MCT4) are upregulated on FLS in RA. This facilitates a local build-up of lactate that influence cells in their vicinity. Inhibiting MCT4 in CIA mice led to amelioration of arthritis. In this study, we hypothesized that pathological FLS could be directly targeted by MCT inhibitors to decrease their cytokine production. We investigated the effect of therapeutically inhibiting MCT-1 and -4 in human pathological RA FLS cultures.

Methods: Synovial fluid derived FLS (SF-FLS) were isolated from the synovial fluid of patients with RA (n=6) and evaluated at passage 4, and compared with normal healthy dermal fibroblasts (NHDF). These cells were analyzed by flow cytometry for expression of the surface proteins CD34, CD45, thymocyte differentiation antigen-1 (Thy-1) and podoplanin (PDPN) and additionally evaluated by light microscopy. Subsequently, they were cultured with or without added INFg or TNFa (both 10 ng/mL) and a specific inhibitor of MCT-1 (AZD3965; 1 μM) or MCT-4 (syrosingopine; 10 μM) for 24 hours. The supernatants were analyzed with an Iscus microdialyzer and ELISA.

Results: The homogeneous subpopulations of unstimulated L/D^{neg}+$CD45^{neg}$ FLS, isolated from the synovial fluid, were positive for both Thy-1 and PDPN [94.6%, (79.9-97.4]). Without stimulation, RA SF-FLS showed substantial lactate secretion [2.567 mmol/L, (2.113-3.020)] with a factor of 1.2 more than healthy dermal fibroblasts. These levels did not increase significantly after the cells were stimulated with either INFγ or TNFα. Unstimulated pathological FLS also secreted substantial amounts of MCP-1 [2107 pg/mL, (98-4117)], elevated by a factor of >12 compared with healthy dermal fibroblasts (n=3) ($p< 0.05$). Furthermore, the levels between lactate and MCP-1 in the supernatant showed a significant positive correlation [rho = 0.89, (0.27-0,99)] ($p< 0.02$). Only when the MCT inhibitors were combined, a significant reduction in lactate secretion was detected after 24 hours. This was seen in unstimulated ($p< 0.05$) and INFγ stimulated cells ($p< 0.05$) but not after TNFα stimulation (ns) of FLS cultures. Concomitantly we detected a decrease in MCP-1 production in pathological FLS by a factor of 0.8 (0.6-0.9) ($p< 0.05$). This reduction in MCP-1 secretion was not seen if the cells were pre-stimulated with either INFγ or TNFα prior to MCT inhibition. The reduction in both lactate and MCP-1 levels were not detectable in the NHDF cultures.

Conclusion: In pathological RA FLS the production of lactate and MCP-1 were strongly correlated and blocking the transport of lactate across the cellular membrane in these cells let to decreased chemokine production. Overall, this

human in vitro study supports that targeting metabolic lactate-transporters could be a useful and promising therapeutic strategy in RA, directly affecting pathological FLS.

Disclosure: M. Nielsen, None; **M. Aspari**, None; **K. Frommer**, None; **M. Hvid**, None; **T. Kragstrup**, Pfizer, 6, Bristol-Myers Squibb, 1, 6, Eli Lilly, 6, Novartis, 6, UCB, 6, Abbvie, 6, Gilead, 1, IBIO TECH ApS, 8; **B. Deleuran**, None.

Abstract Number: 1250

Abatacept and Other DMARDs Have Common Transcriptomic Effects on RA Synovial Tissue

Clément TRIAILLE[1], Tatiana SOKOLOVA[1], Gaëlle TILMAN[1], Laurent MERIC de BELLEFON[2], Christine GALANT[3], Patrick DUREZ[4], Bernard LAUWERYS[5] and Nisha LIMAYE[6], [1]Pôle de pathologies rhumatismales systémiques et inflammatoires, Institut de Recherche Expérimentale et Clinique, Université catholique de Louvain, Brussels, Belgium, [2]Service de Rhumatologie, Cliniques Universitaires Saint-Luc, Brussels, Belgium, [3]Service d'Anatomie Pathologique, Cliniques Universitaires Saint-Luc, Brussels, Belgium, [4]Pôle de Recherche en Rhumatologie, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium, [5]UCB Pharma, Brussels, Belgium, [6]Genetics of Autoimmune Diseases and Cancer, de Duve Institute, Université catholique de Louvain, Brussels, Belgium

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Our goal was to assess histological and transcriptomic effects of Abatacept (ABA) on RA synovium, and to compare them with previously published data obtained by our group using the same study design on other DMARDs: Tocilizumab (TCZ), Rituximab (RTX), Methotrexate (MTX) and Adalimumab (ADA).

Methods: Synovial tissue was obtained using ultrasound-guided biopsy from affected joints before (W0) and 16 weeks (W16) after treatment with subcutaneous Abatacept 125mg per week on a MTX background. Paraffin-sections were stained for CD3, CD20 and CD68 and scored by a pathologist for T cell, B cell and macrophage infiltration. Transcriptional profiling was performed using GeneChip Human Genome U133 Plus 2.0 arrays (Affymetrix), and analyzed on Genespring GX (Agilent). Pathway analyses were performed on Genespring GX, Metascape and EnrichR. Protein-Protein Interaction (PPI) networks were generated on STRING.

Results: 14 RA patients were included (female: 9, ACPA/RF positive: 8, erosive disease: 12, median disease duration in years (± SD): 11.7 (± 8.1), median DAS28CRP (± SD): 4.78 (± 1.11)). Median DAS28CRP significantly decreased between W0 and W16, as did US GS score. Evaluation of histological slides (n=11 pairs of samples) showed no significant effect of Abatacept on T cell, B cell or macrophage infiltration. Gene expression analysis (n=10 pairs of samples) identified 304 transcripts differentially expressed (129 downregulated, 175 upregulated) between W0 and W16 (FC≥1.5 and $p< 0.05$, paired Mann-Whitney). Downregulated genes were significantly enriched for immune processes and included several key T cell regulatory genes (*IL2RA, CD28, IL7, IL7R*), strongly overlapping with data from previous studies on TCZ (n= 12 pairs), RTX (n=12 pairs), MTX (n=8 pairs) and ADA (n=8 pairs). Thus, each treatment shares 31 to 48% of its downregulated genes with the others, with genes downregulated by at least three involved in key RA-associated pathways such as *leukocyte activation*, *NF-kappa B signaling*, *TNF signaling and JAK-STAT signaling*. Given their seemingly overlapping effects, data were pooled across these studies, markedly improving power thanks to their paired-design. This revealed that genes downregulated by DMARDs (n=573, Benjamini-Hochberg corrected p-value< 0.05, paired Mann-Whitney) were significantly enriched for both *T cell* and *myeloid leukocyte activation* pathways. Interestingly, DMARDs seem to have a coordinate effect on the two pathways (correlation of

mean Log_2FC: r=0.8558, p< 0.0001), with a stronger impact (Log_2FC_{W16-W0}) in good responders to therapy (n=17) as compared to moderate (n=20) and to non-responders (n=13) (p< 0.0001, Mann-Whitney). Finally, Transcription Factor enrichment and PPI network analyses point to a central role for molecules including JAK/STATs as mediators of all studied therapies.

Conclusion: We provide evidence that the effects of five DMARDs on RA synovium culminate in the same pathways (namely, *T cell* and *myeloid leukocyte activation*). This confirms previous studies suggesting the existence of common mediators downstream of DMARDs, independent of their primary targets, and suggests attractive new therapeutic targets.

Disclosure: C. TRIAILLE, None; **T. SOKOLOVA**, None; **G. TILMAN**, None; **L. MERIC de BELLEFON**, None; **C. GALANT**, None; **P. DUREZ**, Bristol-Myers Squibb, 6, Sanofi, 6, Eli Lilly, 6, Celltrion, 6; **B. LAUWERYS**, UCB Pharma, 3; **N. LIMAYE**, None.

Abstract Number: 1251

Serum B Cell Activating Factor Reflects Good EULAR Response to TNF Inhibition in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The latest breakthroughs in the pathophysiology of rheumatoid arthritis (RA) highlighted the activation of B cells as a trigger of the joint flare initiation and therefore, implicated a central role for B cells in RA pathogenesis. B cell activating factor (BAFF) is essential for B cell activation, differentiation and survival. The main objective of this study was to investigate the role of BAFF in the progression of rheumatoid arthritis during treatment with TNF inhibitors (TNFi) and its association with treatment response.

Methods: This was a prospective study including 158 patients with RA initiated at the first TNFi and followed-up for 6 months (m). Disease activity was assessed using the Disease Activity Score 28 (DAS28) at baseline and 6m of treatment. Clinical response at 6m of treatment was defined according to the EULAR criteria for good responders. BAFF concentration was measured in serum samples collected at baseline and 6m. Associations between the EULAR response at 6m and clinical/serological variables were evaluated using univariable and multivariable logistic regression models. Receiver operating characteristic (ROC) analysis was performed to determine the optimal threshold of serum BAFF concentration portending EULAR response at 6m of TNFi treatment, determined as the highest Youden index.

Results: After 6m of TNFi treatment, 38/158 (24%) of patients attained good EULAR response (GR). These patients had lower body mass index (BMI) (p=0.02), lower baseline DAS28 (p=0.02) and lower serum BAFF concentration at baseline and at 6m compared with patients who did not attain GR. To further investigate the role of BAFF, the cohort was stratified by anti-citrullinated protein antibody (ACPA) seropositivity. 134 (85%) patients were ACPA positive and 24 (15%) were seronegative. After 6m of TNFi treatment, seropositive patients who attained GR had lower serum BAFF concentration compared with patients who did not attain GR (median [IQR]: 793 [712-956] pg/mL vs. 955 [808-1176] pg/mL; p=0.006) (Figure 1). However, there were no differences in ACPA negative patients (Table 1). Therefore, the optimal threshold value for serum BAFF concentration associated with GR at 6m of TNFi treatment was evaluated in seropositive patients. Serum BAFF< 968 pg/mL at 6m represented the concentration likely to best discriminate between GR and non-GR at 6m of TNFi treatment (AUC: 0.67; 95% CI: 0.56-0.78; p=0.009; sensitivity: 50%, specificity: 81%; PPV: 89%, NPV: 35%), yielding a positive likelihood

Table 1. Patient characteristics. The table shows mean±SD, median (IQR) or absolute number (percentage) for patients included (n=158). The results are stratified by ACPA positivity. Statistically significant differences between good responders and non-responders are indicated as p<0.05 (*) or p<0.01 (**). ACPA, anti-citrullinated peptide antibody; BAFF, B cell activating factor; csDMARDs, conventional synthetic disease-modifying anti-rheumatic drugs; DAS28, disease activity score-28; MTX, methotrexate; OD, other csDMARDs; RF, rheumatoid factor; TNFi, tumour necrosis factor inhibitor

	All (n=158)			ACPA negative (n=24)			ACPA positive (n=134)		
Patient characteristics	**Pooled**	**EULAR NR (n=120; 76%)**	**EULAR GR (n=38; 24%)**	**Pooled**	**EULAR NR (n=16; 67%)**	**EULAR GR (n=8; 33%)**	**Pooled**	**EULAR NR (n=104; 78%)**	**EULAR GR (n=30; 22%)**
Age (years)	54±14	54±14	55±16	51±14	50±12	54±17	55±14	55±14	55±16
Female	130 (82)	96 (80)	34 (89)	21 (87)	14 (87)	7 (87)	109 (81)	82 (79)	27 (90)
Disease duration (years)	8 (4-13)	9 (4-14)	7 (4-11)	7 (2-12)	8 (4-11)	3 (1-14)	8 (4-13)	9 (4-14)	7 (5-11)
RF positive	126 (80)	97 (81)	29 (76)	9 (37)	5 (31)	4 (50)	117 (87)	92 (88)	25 (83)
ACPA positive	134 (85)	104 (87)	30 (79)	0 (0)	0 (0)	0 (0)	134 (100)	104 (100)	30 (100)
Smokers	74 (47)	57 (47)	17 (45)	12 (50)	8 (50)	40 (50)	62 (46)	49 (47)	13 (43)
Body mass index (kg/m²)	25.2 (21.8-29.7)	24.2 (22.7-26.2)	23.6 (21.4-26.2) (*)	25.4 (23.3-28.0)	26.7 (23.9-29.3)	23.4 (20.1-26.4)	24.8 (21.6-30.3)	26.2 (21.8-30.4)	23.8 (21.5-26.3)
Baseline DAS28	5.1±1.3	5.2±1.4	4.8±0.8 (*)	4.6±1.0	4.6±1.1	4.6±0.9	5.2±1.3	5.4±1.4	4.9±0.8 (*)
Previous TNFi	18 (11)	16 (13)	2 (5)	5 (21)	4 (25)	1 (12)	13 (10)	12 (11)	1 (4)
Concomitant csDMARDs	144 (91)	108 (90)	36 (95)	21 (87)	14 (87)	7 (87)	123 (92)	94 (90)	29 (97)
MTX [±OD]	104 (66)	78 (65)	26 (68)	14 (58)	8 (50)	6 (75)	90 (67)	70 (67)	20 (67)
MTX dose (mg/week)	20 (15-25)	20 (15-25)	20 (12.5-22.5)	20.0 (16.9-23.1)	20 (20-25)	18.7 (15.0-20.6)	20 (12.5-25)	20 (15-25)	20 (12.5-22.5)
Only OD	40 (25)	30 (25)	10 (26)	7 (29)	6 (37)	1 (12)	33 (25)	24 (23)	9 (30)
Prednisone use	83 (52)	66 (55)	17 (45)	13 (54)	10 (62)	3 (37)	70 (52)	56 (54)	14 (47)
Prednisone dose (mg/day)	5.0 (0.0-5.0)	5.0 (0.0-5.0)	0.0 (0.0-5.0)	5.0 (0.0-5.0)	5.0 (2.5-6.2)	0.0 (0.0-5.0) (*)	5.0 (0.0-5.0)	5.0 (0.0-5.0)	0.0 (0.0-5.0)
Baseline serum BAFF (pg/mL)	844 (686-1054)	866 (701-1060)	754 (622-922) (*)	792 (708-963)	792 (732-963)	756 (625-989)	846 (681-1060)	876 (684-1120)	754 (622-891)
Serum BAFF at 6m (pg/mL)	890 (722-1074)	917 (792-1044)	793 (715-956) (*)	799 (700-992)	856 (697-992)	758 (715-1090)	903 (776-1104)	955 (808-1176)	793 (712-956) (**)

ratio of 2.7 (Figure 2). Then, a logistic regression analysis adjusted by patient characteristics with p-value≤0.1 in univariable analysis (disease duration, BMI and baseline DAS28) was performed. We found that a serum BAFF< 968 pg/mL at 6m was significantly and independently associated with GR attainment in seropositive patients (OR: 5.28; 95% CI: 1.72-16.17; p=0.004).

Conclusion: Our results show that serum BAFF concentrations reflect clinical response to TNFi after 6m of treament, mainly in ACPA positive patients. These results suggest that BAFF may be considered a biomarker of clinical response to TNFi in patients with RA.

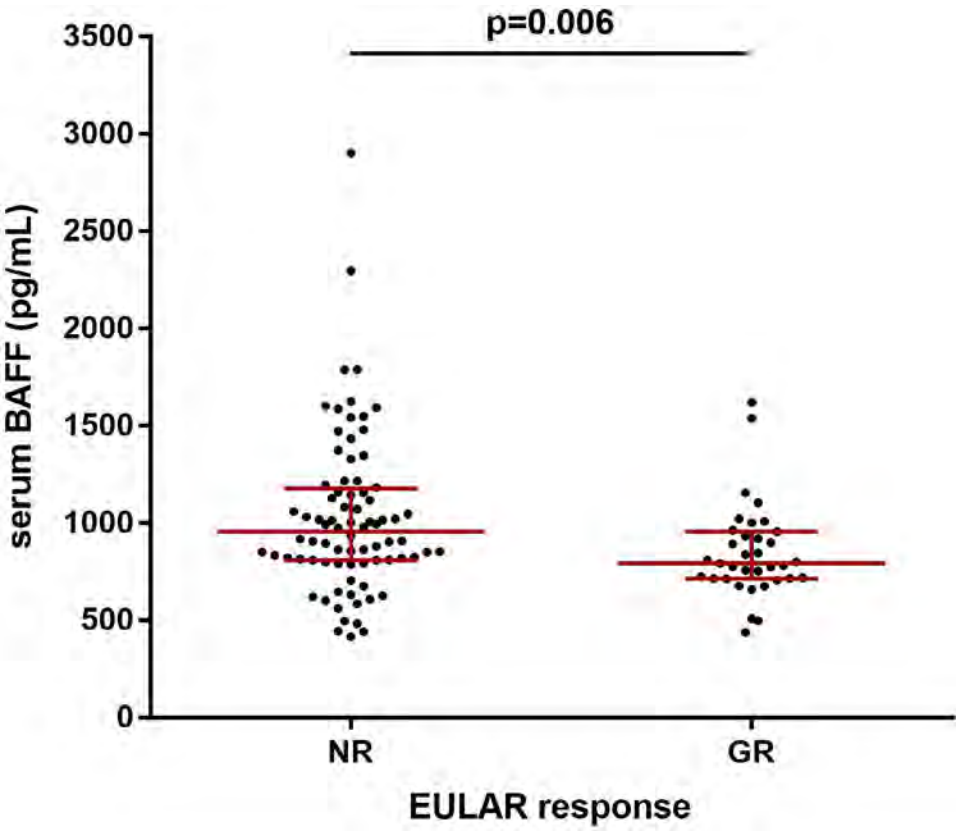

Figure 1. Serum BAFF concentration (median [IQR]) stratified by EULAR response at 6 months of TNFi treatment in seropositive patients.

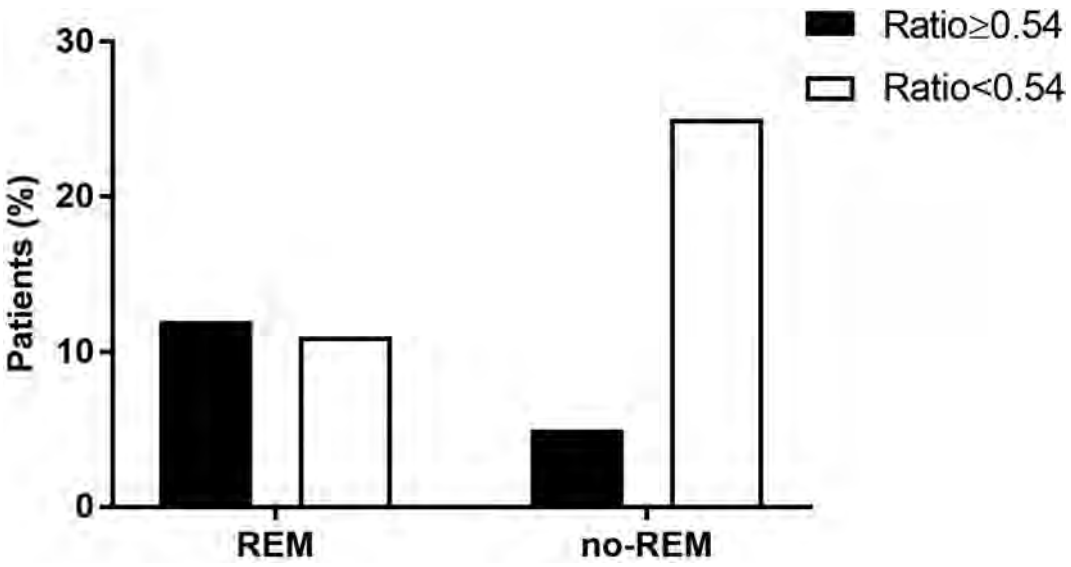

Figure 2. EULAR response at 6 months of TNFi according the serum BAFF concentration threshold.

Disclosure: B. Hernandez-Breijo, None; **I. Parodis**, Amgen, Elli Lilly and Company, and Gilead Sciences., 5, 6, GlaxoSmithKline and Novartis., 5, 6; **C. Plasencia-Rodríguez**, None; **M. Díaz-Almirón**, None; **A. Martínez-Feito**, None; **M. Novella-Navarro**, None; **D. Pascual-Salcedo**, None; **A. Balsa**, BMS, 5, 6, Gebro Pharma, 5, Pfizer, 5, 6, Roche, 5, 6, UCB, 5, 6, Novartis, 5, 6, Abbvie, 6, MSD, 6, Lilly, 6, Nordic, 6, Galapagos, 6, Gilead, 6, Sandoz, 6.

Abstract Number: 1252

Discontinuation of TNFi Treatment Among Rheumatoid Arthritis Patients with a Molecular Signature of Non-response to Tumor Necrosis Factor-α Inhibitor Therapies

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: A 23-feature blood-based molecular signature response classifier[1] (MSRC) identifies rheumatoid arthritis (RA) patients who are unlikely to respond to tumor necrosis factor-α inhibitor (TNFi) therapies. This study evaluated treatment outcomes over a 12-month period among patients prescribed TNFi therapies as a first targeted treatment and stratified according to MSRC results.

Methods: RA patients (N=175)[1] from the CERTAIN study[2] were followed 12-months following initiation of TNFi therapy. The MSRC evaluated patient gene expression data, anti-CCP and clinical metrics (sex, BMI, patient global assessment) prior to starting TNFi therapy to predict which patients were unlikely to respond to TNFi therapies. Prescription choices, response to therapies, and time on TNFi were assessed at 6, 9 and 12 months following TNFi treatment initiation. Response was measured using the ACR50 criteria.

Results: Relative to those without a molecular signature of non-response to TNFi therapies (n=93), a larger proportion of patients with high (n=26) and very high (n=47) signature of non-response discontinued their first TNFi therapy within the 12-month monitoring period (29.1% vs 42.3% and 59.6%, respectively). When a reason for discontinuation was provided, 63.6% reported issues with efficacy and 22.7% reported safety concerns. Predicted inadequate responders who did not reach ACR50 spent an average of 279 days (interquartile range 200-370) receiving TNFi therapy. Disease activity measures (DAS28-CRP, clinical disease activity index [CDAI], tender joint count and swollen joint counts) assessed at 6, 9 and 12 months following TNFi treatment initiation indicated less improvement from baseline among predicted inadequate responders compared to patients without a molecular signature of inadequate response. Among the 22 patients with more than one reported treatment cycle none (0/6) of the twelve PrismRA predicted inadequate responders achieved an ACR50 response to a second cycle TNFi therapy; however, 33% (2/6) achieved an ACR50 response to a non-TNFi treatment.

Conclusion: The molecular signature predictive of inadequate response to TNFi correlated with more discontinuation to TNFi therapy by 12 months, mostly due to lack of effectiveness; and despite this inactivity patients remained on TNFi treatment for 279 days on average.

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Disclosure: J. Curtis, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **J. Kremer**, CoreEvitas, 2, 8, Pfizer, 6, BMS, 2; **D. Pappas**, Sanofi, 2, Abbvie, 2, Gtech Roche Hellas, 2, Novartis, 2, CorEvitas, 3, 4, 11; **L. Zhang**, Scipher, 3, 11; **E. Connolly-Strong**, Scipher, 3, 11; **J. Withers**, Johanna Withers, 3, 11; **V. Akmae**, Scipher, 3, 11; **A. Saleh**, Scipher, 3, 11.

Abstract Number: 1253

Acupuncture in Rheumatoid Arthritis Activity

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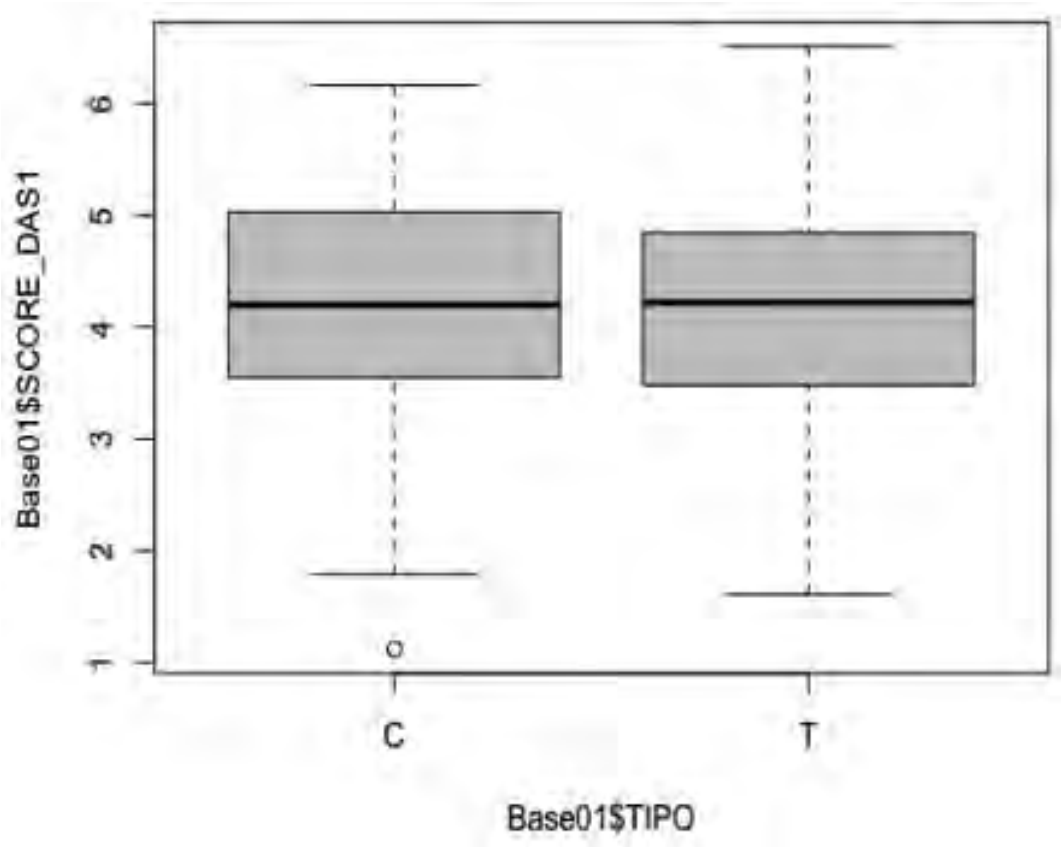
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: High activity rates of Rheumatoid Arthritis (RA) lead to an increased risk of mortality. RA patients have a high incidence of comorbidities, associated with the chronic inflammatory process, with joint inflammation and deformity, loss of functional capacity and quality of life. Although over time it is difficult to sustain low disease activity/remission rates, associated with a decrease in functional disability and therefore a better quality of life, reaching these goals in a timely manner leads to better functional and quality of life outcomes for patients (1). The objective of the study was to investigate the effect of acupuncture, combined with the pharmacological treatment instituted, on RA activity, through DAS28-CRP.

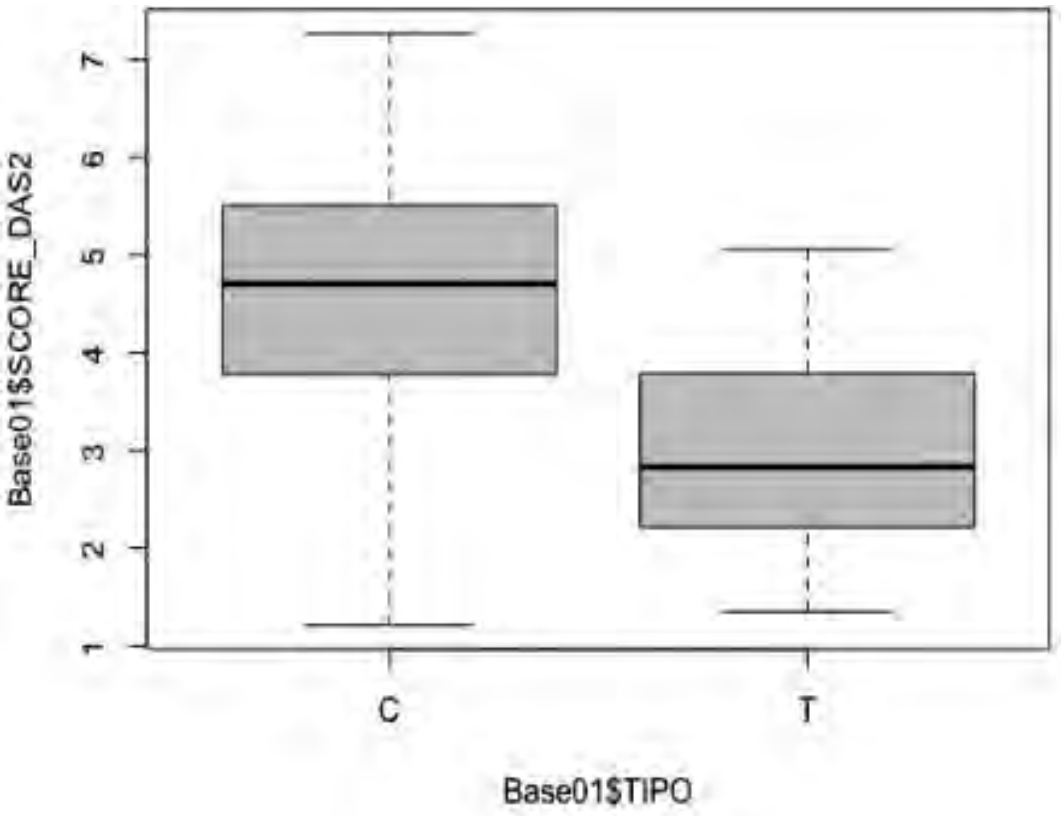
1 Scott IC, Ibrahim F, Panayi G, Cope AP, Garrood T, Vincent A, et al. The frequency of remission and low disease activity in patients with rheumatoid arthritis, and their ability to identify people with low disability and normal quality of life. *Seminars in Arthritis and Rheumatism* 49 (2019) 20-26

Methods: Randomized, prospective and controlled experimental study. Patients were submitted one acupuncture session per week for 8 consecutive weeks, with DAS28-CRP evaluation immediately before the 1st acupuncture session and another evaluation one week after the last acupuncture session. The 101 patients were randomly assigned to an Experimental Group (EG), submitted to acupuncture (n=50) and Control Group (CG), not submitted to acupuncture (n=51). All maintained pharmacological treatment in progress, not initiating any another pharmacological and/or non-pharmacological treatment during the present study.

Results: The results obtained in the first evaluation were similar between the study groups, with no significant differences that allow them to be distinguished from each other, mean (4,129 versus 4,245) and median (4,220 versus 4,200), classifying them as EG and CG, respectively, with moderate activity, defined by DAS28-CRP. In the evaluation carried out after treatment with acupuncture for EG patients, it was obtained through the DAS28-CRP score, mean (2,993) and median (4,541). CG patients, in the last evaluation, presented different and very significant results, namely the mean (4,541) and median (4,705). According to the definition by DAS28-CRP, after treatment with acupuncture, the EG decreased the disease activity index, defining itself with low activity, in contrast to the CG that maintained



Graph 1. Boxplot DAS28-CRP scores: 1st Review Experimental Group and Control Group.



Graph 2. Boxplot DAS28-CRP scores: 2nd Review Experimental Group and Control Group.

values very close to those of the first evaluation, with a moderate disease activity index. This statistical evidence is graphically explained in Graph 1 and Graph 2.

Conclusion: The effect of acupuncture was evident in patients whose treatment was combined with the pharmacological treatment already in place. The decrease in the DAS28-CRP score was clearly visible, and it's possible to inform that acupuncture, when combined with treatment already underway, allows to decrease RA activity. Thus, acupuncture may be a non-pharmacological intervention to start early, when diagnosing RA, as a way of managing and treating the disease, based on the individual needs of each patient.

Disclosure: D. Seixas, None; **F. Farinha**, None; **M. Pacheco da Fonte**, None; **M. Laranjeira**, None; **M. Rua**, None.

Abstract Number: 1254

The Role of Regulatory T Cells (CD4+CD25+FOXP3) in Methotrexate Unresponsiveness in a Cohort of Naive Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic immune-mediated heterogenous disease characterized by a defect in the compartment of regulatory CD4+Foxp3+ T cells (Treg) which are essential for maintenance of self-tolerance and exert a suppressive effect. The first-line anchor drug for RA is low-dose methotrexate (MTX). However, 46% of RA patients started on MTX therapy discontinue treatment by 3 years and our ability to predict who will experience a good response versus non response remains very limited. Accordingly, the aim of the present study was to evaluate the role of (CD4+ CD25+ FOXP3) regulatory T cells in MTX unresponsiveness in naïve RA patients and to examine their correlation with the traditional clinical and serological markers of disease activity.

Methods: Fifty random early untreated RA patients diagnosed according to the ACR/EULAR 2010 criteria of RA, naïve to disease-modifying anti-rheumatic drugs (DMARDS) were enrolled. Information on disease duration, disease activity, presence and duration of morning stiffness, articular and extra articular complaints, smoking habits and comorbidities was recorded. The British version of the Health Assessment Questionnaire (HAQ) was performed to assess functional status. Disease activity with DAS-28 activity score was calculated for all patients. Peripheral blood (CD4+ CD25+ FOXP3) Tregs were determined in all RA patients before and after MTX treatment using multi-color flow cytometry. All patients received MTX monotherapy at a dose of 15 to 20 mg/week, maintained for at least four weeks before peripheral blood collection. Patients were stratified according to their response to MTX therapy into two groups: **Unresponsive:** (UR-MTX), treated with MTX by a dose of ≥ 15mg/week for at least 6 months and still presented active disease (DAS28 >4.0) and **Responsive:** (R-MTX), treated with MTX by a dose of ≥ 15mg/week for at least 6 months and presented remission (DAS28 < 3.0) using the EULAR response criteria.

Results: Six months after MTX monotherapy, 30 patients were classified as responders and 20 as non-responders. The mean value of CD4+ CD25+ FOXP3 Treg cells % was significantly higher in the (R-MTX) group; 0.63 ± 0.57, than in the (UR-MTX) group; 0.18 ± 0.14, p< 0.001. In the (R-MTX) group, the absolute change of (CD4+ CD25+ FOXP3)

Tregs % was inversely correlated to DAS-28 score (r_s = -0.652, p< 0.001), ESR (r_s = -0.654, p< 0.001), CRP (r_s = -0.840, p< 0.001), VAS (r_s = -0.550, p=0.002), and HAQ score. (r_s = -0.548, p=0.002), but directly correlated to serum Hb levels (r_s = 0.535, p=0.002).

Conclusion: MTX responsiveness is directly related to the expansion of (CD4+ CD25+ FOXP3) Tregs % after 6 months of MTX monotherapy, likely via the ADO/A2aR pathway. The absolute change of Tregs % correlates inversely with disease activity in responsive patients, which suggests an important role of (CD4+ CD25+ FOXP3) Treg cells in the pathogenesis of disease activity and flares. Our data also suggest that, low expression of (CD4+ CD25+ FOXP3) Treg cells after 6 months of MTX monotherapy, could be a biomarker for predicting unresponsiveness to MTX in RA patients.

Disclosure: A. Abou-Raya, None; **D. ELHallous**, None; **M. Ossama**, None; **N. Farahat**, None; **M. Khaled**, None; **S. Abou-Raya**, None.

Abstract Number: 1255

A Molecular Signature Response Classifier Predicts the Likelihood of Non-response to TNF Inhibitor Therapies in RA at 3 Months

Stanley Cohen[1], Theodore Mellors[2], Lixia Zhang[3], Alex Jones[3], Erin Connolly-Strong[4], Dimitrios Pappas[5], Joel Kremer[6], Johanna Withers[3] and Viatcheslav Akmae[3], [1]Metroplex Clinical Research Center, Dallas, TX, [2]Scipher Medicine, Waltham, TX, [3]Scipher Medicine, Waltham, MA, [4]Scipher Medicine, Austin, TX, [5]CorEvitas, LLC, Waltham, MA, [6]Albany Medical College, Latham, NY

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Most people with rheumatoid arthritis (RA) are prescribed a TNF inhibitor (TNFi) as their first targeted therapy. A blood-based molecular signature response classifier (MSRC) was shown to predict inadequate response to TNFi therapies, before treatment initiation.[1] Identification of likely inadequate responders has the potential to reduce the time spent on trial-and-error approaches for treatment selection. Incorporating this test into clinical workflows could result in improved patient outcomes, reduced patient burden and potentially reduced disease progression.[2,3] In a treat-to-target treatment approach, 3-months post treatment initiation is an important decision point for assessment of response;[4] therefore, further validation of the MSRC at timepoints earlier than 6 months are warranted.

Methods: The MSRC uses data collected at baseline before starting targeted therapy, including gene expression features, laboratory tests (anti-CCP) and clinical metrics (sex, BMI, patient global assessment) to determine if patients have a molecular signature predictive of inadequate response to TNFi. The MSRC was used to evaluate RA patients (N=96) from the CERTAIN study[5] who were initiating a TNFi as their first targeted therapy. None of these patients were included in previous MSRC validation studies, and only baseline and 3-month follow-up visit data were available. MSRC prediction of inadequate response were compared to treatment response, ACR50, reported at 3 months. Odds ratios and area under the receiver operating characteristic curve (AUC) were used to evaluate the ability of the MSRC test to predict inadequate response to TNFi therapy at 3 months.

Results: Of the 96 RA patients described in Table 1, 51.0% (49/96) had a molecular signature of non-response. An ACR50 response at 3 months to a TNFi therapy was observed in 20.8% (20/96) of patients. Patients were stratified

Table 1. Patient demographics

Characteristic	RA patients (N = 96)
Age, median (SD)	54 (13.7%)
Female, n (%)	74 (77.1%)
CCP positive, n (%)	57 (59.3%)
RF positive, n (%)	57 (59.3%)
TNFi use, n (%)	
Adalimumab	38 (39.6%)
Etanercept	26 (27.1%)
Infliximab	18 (18.8%)
Certolizumab pegol	11 (11.5%)
Golimumab	3 (3.1%)

according to detection of a molecular signature of non-response to TNFi therapy with an AUC of 0.63. Patients with a molecular signature of non-response were 3 times less likely to satisfy the ACR50 response criterium at 3 months compared to patients lacking the molecular signature (odds ratio 3.0, 95% confidence interval 1.1-8.8).

Conclusion: The MSRC identified RA patients who did not fulfill the ACR50 response criteria to TNFi therapies by 3 months post-treatment initiation. Minimal response to treatment at 3 months is indicative of poor treatment response targets at later timepoints.[6,7] Thus, MSRC test results received prior to treatment could support targeted therapy treatment selection in treat-to-target management strategies.

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Disclosure: S. Cohen, Amgen Inc, 1, 2, 5, AbbVie, 1, 2, 5, Pfizer, 1, 2, 5, Genentech, 1, 2, 5, Eli Lilly, 1, 2, 5, Gilead, 1, 2, 5; **T. Mellors**, Scipher, 3, 11; **L. Zhang**, Scipher, 3, 11; **A. Jones**, Scipher, 3, 11; **E. Connolly-Strong**, Scipher, 3, 11; **D. Pappas**, Sanofi, 2, Abbvie, 2, Gtech Roche Hellas, 2, Novartis, 2, CorEvitas, 3, 4, 11; **J. Kremer**, CoreEvitas, 2, 8, Pfizer, 6, BMS, 2; **J. Withers**, Scipher, 3, 11; **V. Akmae**, Scipher, 3, 11.

Abstract Number: 1256

Factors Associated with the Use of Biologic Disease-modifying Antirheumatic Drugs in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: RA – Treatments Poster II: PROs, Biomarkers, & Systemic Inflammation (1223–1256)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune inflammatory disease characterized by polyarthritis of small and large joints. RA is the second most common type of autoimmune arthritis. RA treatment has been revolutionized by the development of biologic disease-modifying antirheumatic drugs (bDMARDs), which are increasingly used after the introduction of biosimilar products. This study evaluates the association between biologic DMARDs use and the social demographic characteristics of the RA patient population and assesses changes in biologic DMARDs utilization in the RA patient population after biosimilars market entry.

Methods: In this retrospective analysis of Medical Expenditure Panel Survey (MEPS) data from 2010 to 2018, the study population includes RA patients diagnosed using the International Classification of Disease. Logistic regression will be conducted to measure the association between biologic DMARD use and the study population's social demographic characteristics. Linear regression will also be used to assess changes in biologic DMARDs utilization in the RA patient population after biosimilars market entry.

Results: A total of 1620 patients were diagnosed with RA in 2010-2015, of which 72% of RA patients were females, and 28% were males. Most patients were aged 45-70 years (63.3%) with a mean±SD age of 58.5±15.2 and a range of 6 to 85 years old. RA patients were predominantly white (61.2%) and non-Hispanic (78.7%). Private and public health insurance covered 41% and 52% of the patient population, respectively, and 7% were uninsured. bDMARDs were used by 20% and cDMARDs by 80% of the patients. Methotrexate, among cDMARDs, was the drug more often prescribed. Adalimumab and etanercept, among bDMARDs, had a similar percentage of prescriptions. The results of the regression analyses will be also presented.

Conclusion: Biologic disease-modifying antirheumatic drugs play a crucial role in managing and treating rheumatoid arthritis. Thus, it is essential for clinicians, healthcare providers, and policy-makers to understand the association of the social demographic characteristics of RA patients and the utilization of DMARDs to improve RA patients' outcomes.

Disclosure: R. Hosseini, None; **S. fawaz**, None; **E. Seoane-Vazquez**, None.

Abstract Number: 1257

Improvements in Abnormal Laboratory Tests Are Associated with Clinical Outcomes in Patients with Active Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Laboratory tests are routine in the management of SLE. In clinical trial endpoints, data from laboratory tests contribute to responder status, but this is captured using discrete thresholds rather than continuous data. We investigated whether the trajectory of abnormal laboratory tests in patients with active SLE, measured as continuous data, corresponds with conventional measures of clinical improvement.

Methods: We used clinical and laboratory data from a large multinational prospectively followed longitudinal cohort. Eligible patients had active disease (SLEDAI-2K ≥6), and at least one abnormal routine laboratory test (haemoglobin, white cell count, lymphocytes, platelets, ESR, albumin, C3, C4, anti-dsDNA, and urine protein, red cells or white cells), at a visit designated as baseline. At 12 months thereafter, for each laboratory test we classified improvement from individual patient baselines as complete response (CR; 100% improvement i.e. restoration to normal range), partial response (PR; ≥ 20-< 100% improvement) or no response (NR; < 20% improvement)) and assessed associations with a range of improvement outcomes: modified SLE responder index (omitting BILAG criteria) (mSRI4), physician global assessment (PGA) improvement ≥ 0.3, attainment of lupus low disease activity state (LLDAS (Golder, 2019)), SLE flare index (SFI) and SLICC/ACR damage index accrual (SDI increase >0), using logistic regression.

Results: 1,525 patients were included, with separate subsets for each individual abnormal laboratory test. Most patients were female (93%), Asian (88%) and had established SLE. Associations (odds ratios, 95% confidence inter-

vals and significance) of laboratory variable CR and PR with clinical outcomes at 12 months are shown in Figure 1. Improvement in proteinuria, albumin, haemoglobin, ESR and platelets had the strongest associations with clinical improvement measures, including increased odds of LLDAS attainment and protection against damage accrual. In contrast, serology was associated only with the less stringent outcomes of PGA improvement and mSRI4. White cell count and lymphocytes had the weakest associations with improvement measures. Although CR had stronger associations, PR of certain laboratory tests also conferred benefit.

Laboratory test and definition of abnormal	Laboratory test improvement at 12 months	Modified SRI4	Improved PGA ≥0.3	Presence of flare (SFI)	LLDAS attainment	Damage accrual (increased SDI)
Urine protein >0.5g/day n=443	CR (≥100%) n=191	**21.6** (12.2-38.5)	**9.21** (5.45-15.6)	**0.11** (0.06-0.21)	**50.9** (15.6-165)	**0.26** (0.12-0.56)
	PR (≥20-<100%) n=116	**2.29** (1.33-3.97)	**4.70** (2.68-8.25)	**0.53** (0.32-0.89)	**3.41** (0.88-13.2)	**0.57** (0.28-1.17)
Urine red cells >5/high power field n=346	CR (≥100%) n=183	**5.99** (3.25-11.0)	**3.21** (1.85-5.57)	**0.29** (0.16-0.53)	**4.57** (2.14-9.76)	**0.85** (0.40-1.80)
	PR (≥20-<100%) n=114	**2.49** (1.37-4.53)	**2.53** (1.40-4.57)	**0.35** (0.18-0.68)	**2.04** (0.89-4.69)	**0.73** (0.31-1.73)
Albumin <35g/L n=367	CR (≥100%) n=236	**3.45** (1.97-6.06)	**4.20** (2.38-7.44)	**0.38** (0.21-0.68)	**7.53** (2.64-21.5)	**0.39** (0.20-0.75)
	PR (≥20-<100%) n=57	**2.73** (1.33-5.61)	**2.05** (0.99-4.31)	**0.76** (0.36-1.62)	**4.07** (1.22-13.6)	**0.48** 0.20-1.17)
Haemoglobin <110mg/dL n=383	CR (≥100%) n=198	**2.49** (1.55-4.02)	**3.05** (1.87-4.99)	**0.72** (0.42-1.22)	**1.89** (1.09-3.31)	**0.42** (0.23-0.78)
	PR (≥20-<100%) n=68	**1.93** (1.05-3.57)	**2.44** (1.31-4.55)	**0.82** (0.41-1.63)	**1.00** (0.46-2.14)	**0.72** (0.33-1.55)
ESR >20mm/hr n=628	CR (≥100%) n=197	**1.52** (1.04-2.22)	**1.27** (0.87-1.86)	**0.60** (0.38-0.95)	**1.46** (0.97-2.20)	**0.53** (0.30-0.94)
	PR (≥20-<100%) n=184	**1.71** (1.16-2.52)	**1.43** (0.97-2.11)	**0.84** (0.54-1.31)	**1.11** (0.72-1.69)	**0.98** (0.58-1.64)
Platelets <150 x 10^9/L n=216	CR (≥100%) n=132	**2.60** (1.29-5.24)	**2.22** (1.10-4.48)	**1.18** (0.53-2.65)	**3.82** (1.27-11.5)	**0.48** (0.21-1.10)
	PR (≥20-<100%) n=37	**1.84** (0.76-4.48)	**1.62** (0.66-3.97)	**0.86** (0.29-2.54)	**2.35** (0.63-8.80)	**0.53** (0.18-1.61)
C3 <0.8g/L n=726	CR (≥100%) n=238	**3.07** (2.14-4.39)	**1.79** (1.26-2.55)	**0.66** (0.44-0.99)	**1.34** (0.92-1.96)	**1.15** (0.53-1.71)
	PR (≥20-<100%) n=187	**1.99** (1.37-2.88)	**2.19** (1.50-3.19)	**0.67** (0.43-1.04)	**1.00** (0.66-1.52)	**0.95** (0.53-1.71)
C4 <0.16g/L n=623	CR (≥100%) n=173	**2.20** (1.49-3.26)	**1.93** (1.31-2.85)	**0.67** (0.41-1.09)	**0.82** (0.54-1.25)	**1.01** (0.55-1.86)
	PR (≥20-<100%) n=160	**1.83** (1.23-2.71)	**1.54** (1.04-2.29)	**1.15** (0.73-1.79)	**0.63** (0.40-0.98)	**1.02** (0.55-1.92)
Anti-dsDNA >upper limit normal n=738	CR (≥100%) n=161	**3.37** (2.25-5.05)	**1.28** (0.87-1.88)	**0.75** (0.47-1.20)	**1.56** (1.03-2.36)	**1.02** (0.54-1.93)
	PR (≥20-<100%) n=242	**1.89** (1.35-2.65)	**1.39** (0.99-1.94)	**0.81** (0.54-1.22)	**1.33** (0.92-1.93)	**1.23** (0.72-2.10)
Urine white cells >5/high power field n=382	CR (≥100%) n=187	**3.97** (2.08-7.61)	**1.20** (0.58-1.13)	**0.47** (0.25-0.87)	**2.17** (1.07-4.37)	**1.11** (0.45-2.76)
	PR (≥20-<100%) n=94	**1.39** (0.72-2.70)	**0.59** (0.30-1.13)	**0.54** (0.27-1.10)	**1.22** (0.55-2.72)	**0.90** (0.32-2.57)
White cell count <4 x 10^9/L n=339	CR (≥100%) n=228	**1.16** (0.66-2.04)	**1.09** (0.62-1.94)	**1.30** (0.69-2.44)	**1.11** (0.59-2.08)	**1.76** (0.70-6.82)
	PR (≥20-<100%) n=45	**1.67** (0.76-3.70)	**1.68** (0.76-3.69)	**0.39** (0.13-1.16)	**1.59** (0.68-3.71)	**2.22** (0.73-6.82)
Lymphocytes <1.5 x 10^9/L n=833	CR (≥100%) n=222	**1.11** (0.80-1.55)	**0.93** (0.66-1.30)	**0.72** (0.49-1.06)	**1.43** (0.98-2.1)	**0.90** (0.54-1.50)
	PR (≥20-<100%) n=206	**1.32** (0.94-1.85)	**1.37** (0.97-1.92)	**0.67** (0.45-1.00)	**1.33** (0.91-1.94)	**0.70** (0.40-1.23)

Odds ratio (95% CI) | p>0.1 | p=0.05-1.0 | p<0.05

Figure 1. Associations of partial and complete improvement in abnormal laboratory tests between baseline and 12 months, and corresponding clinical improvement outcomes.

Conclusion: Improvements in abnormal laboratory tests were predictive of clinical outcomes at 12 months, with a discrepancy between tests currently incorporated in clinical trial endpoints, such as serology, and those with the strongest associations with clinical outcomes. Associations with improved clinical outcomes were associated with improvement thresholds less stringent than complete resolution for some tests. The selection, weighting and threshold-based use of laboratory tests in lupus trial endpoints should be revised.

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Abstract Number: 1258

Measurement of Specific Organ Domains in Lupus Randomised Controlled Trials

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Randomised controlled trials (RCTs) in SLE typically adopt composite responder definitions as primary efficacy endpoints, however outcomes within individual organ domains are also important to understand in order to infer the efficacy profile of a new treatment. The aim of this study was to evaluate how, and how consistently, organ-specific disease activity and therapeutic responses have been measured and reported in lupus RCTs.

Methods: We conducted a scoping review in accordance with the Johanna Briggs Institute Guidance and 2018 PRISMA statement. We systematically searched MEDLINE, EMBASE, Cochrane registry and clinicaltrials.gov. Eligible studies were RCTs investigating efficacy of an immune-directed drug therapy in active SLE, published January 2000-March 2021, excluding studies limited to lupus nephritis. Data items for each eligible RCT were general study/patient characteristics, and clinician-reported outcome measures of organ-specific disease activity at baseline and

treatment response definitions at the primary endpoint. Data were extracted independently in duplicate into a pre-established form and summarised descriptively.

Results: A total of 34 RCTs were included (PRISMA diagram, Figure 1). Nine non-renal organ domains were measured using a limited number of instruments. Table 1 summarises the frequency of organ-specific involvement at baseline, and different response definitions used, across the RCTs. Study populations had a high, although variable, frequency of baseline musculoskeletal and mucocutaneous activity and low but also variable representation of other domains. Definitions of organ-specific responses were inconsistent, even within individual instruments. Response in most organ domains were evaluated using BILAG and SLEDAI components but meaningful comparison between treatment arms was limited by small subgroups analysed in post-hoc fashion. Outcome measures using Cutaneous Lupus Erythematosus Disease Area and Severity Index activity scores (CLASI-A) and joint counts (tender, swollen and/or active) were also commonly used, including within pre-specified organ-specific endpoints, which discriminated between treatment arms in some studies.

Conclusion: Mucocutaneous and musculoskeletal manifestations predominate in SLE RCTs. Organ-specific outcome measures are commonly reported, but definitions of involvement and response are inconsistent between trials. Research into the development of new outcome measures for key organ domains, and validation and comparison of response definitions using existing instruments is needed, to facilitate evaluation of the efficacy of novel therapies and ensure the validity, consistency, and comparability of individual organ responses within and between trials.

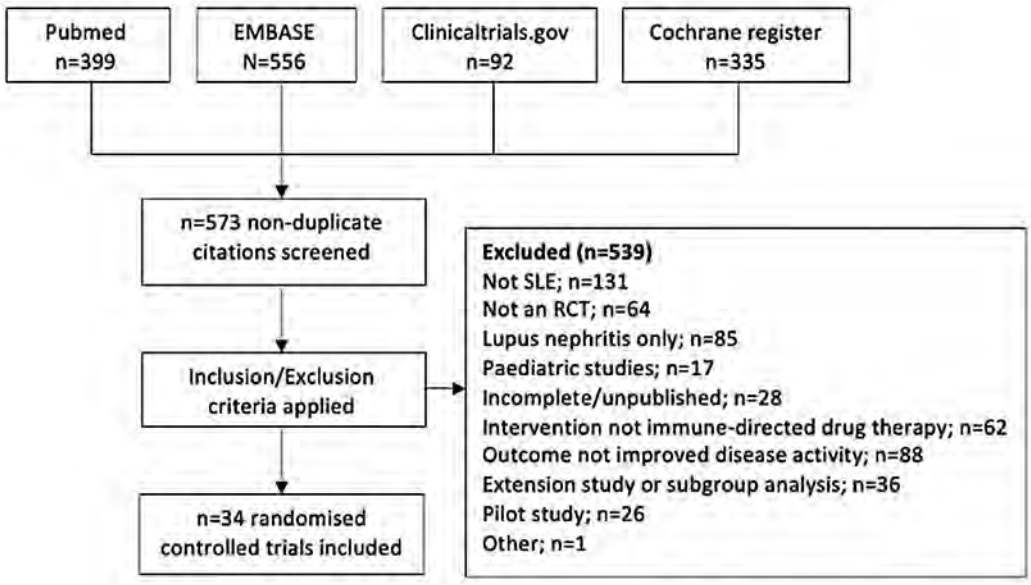

Figure 1. PRISMA diagram demonstrating study selection.

Table 1. Definition and rates of organ-specific activity and treatment responses in the included RCTs, according to instruments employed in at least one study

Domain	Instrument	Rates of organ involvement	Response definitions
Muco-cutaneous	SLEDAI	Mucocutaneous SLEDAI (11 studies): 82-96%	Reduction in score from mucocutaneous items (7 studies)
	BILAG	BILAG A/B (14 studies): 49-86% BILAG A (5 studies): 15-33%; B (4 studies): 57-72%	Reduction in mucocutaneous letter grade from A/B (5 studies) Reduction in mucocutaneous letter grade from A/B/C (1 study) Resolution in mucocutaneous letter grade to BILAG D (2 studies)
	CLASI-A	Mean CLASI-A (8 studies): 3.8-13.6	Reduction ≥50% from baseline ≥10 (4 studies) Reduction ≥50% from baseline ≥4 (1 study) Reduction ≥4 from baseline ≥10 (1 study) Difference in mean change from baseline (3 studies)
Musculo-skeletal	SLEDAI	Musculoskeletal SLEDAI (12 studies): 59-96%	Reduction in score from musculoskeletal items (6 studies)
	BILAG	BILAG A/B (14 studies): 27-98% BILAG A (5 studies): 9-32%; B (4 studies): 51-63%	Reduction in musculoskeletal letter grade from A/B (5 studies) Resolution in musculoskeletal letter grade to BILAG D (2 studies)
	Joint count	Mean 28-SJC (8 studies): 2.7-8.6 Mean 28-TJC (8 studies): 7.3-20.1 Mean 28-active joint count (2 studies): 6.8-7.9	Reduction ≥50% in TJC and SJC from baseline ≥6 (1 study) Reduction ≥50% in TJC and SJC from baseline ≥8 (3 studies) Reduction ≥50% in TJC and SJC from baseline ≥4 (1 study) Difference in mean change in TJC from baseline (3 studies) Difference in mean change in SJC from baseline (3 studies) Difference in mean change in active joints from baseline (3 studies)
Haematologic	SLEDAI	Haematological SLEDAI (10 studies): 5-13%	Reduction in score from haematological items (6 studies)
	BILAG	BILAG A/B (10 studies): 0-24% BILAG A (4 studies): 0-2%; B (3 studies): 0-22%	Reduction in haematological letter grade from A/B (5 studies) Resolution in haematological letter grade to BILAG D (1 study)
Cardio-Respiratory	SLEDAI	Cardio-respiratory SLEDAI (8 studies): 1-9%	Reduction in score from cardio-respiratory items (5 studies)
	BILAG	BILAG A/B (10 studies): 0-29% BILAG A (4 studies): 0-19%; B (3 studies): 3-18%	Reduction in cardio-respiratory letter grade from A/B (5 studies) Resolution in cardio-respiratory letter grade to BILAG D (2 studies)
Neurologic	SLEDAI	Neurological SLEDAI (9 studies): 0-3%	Reduction in score from neurological items (5 studies)
	BILAG	BILAG A/B (10 studies): 0-16% BILAG A (4 studies): 0-7%; B (3 studies): 0-10%	Reduction in cardio-respiratory letter grade from A/B (5 studies) Resolution in cardio-respiratory letter grade to BILAG D (2 studies)
Vasculitis	SLEDAI	Vasculitis SLEDAI (11 studies): 3-13%	Reduction in score from vasculitis item (5 studies)
	BILAG	BILAG A/B (5 studies): 9-15%	Reduction in vasculitis letter grade from A/B (5 studies)
Gastro-intestinal	BILAG	BILAG A/B (5 studies): 0-3% BILAG A (3 studies): 0-1%; B (2 studies): 0-1%	Reduction in gastrointestinal letter grade from A/B (2 studies)
Ophthalmic	BILAG	BILAG A/B (5 studies): 0-1% BILAG A (3 studies): <1%; B (2 studies): <1%	Reduction in ophthalmic letter grade from A/B (2 studies)
Constitutional	SLEDAI	Constitutional SLEDAI (7 studies): 1-12%	Reduction in score from constitutional item (4 studies)
	BILAG	BILAG A/B (9 studies): 2-42% BILAG A (3 studies): 0-10%; B (2 studies): 2-32%	Reduction in constitutional letter grade from A/B (5 studies) Resolution in constitutional letter grade to BILAG D (2 studies) Reduction in constitutional letter grade from A/B/C (1 study)

Abbreviations: BILAG, British Isles Lupus Assessment Group; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity score; SLEDAI; SLE disease activity index; SJC, swollen joint count; TJC, tender joint count; ^Active joint count = both tender and swollen

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Association of SLE Responder Index (SRI) Attainment and Long-term Clinical Outcomes

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SESSION INFORMATION

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Background/Purpose: The SLE Responder Index (SRI) is a composite responder definition employed as a clinical trial endpoint in SLE. Despite its widespread adoption, recent discrepant trial results have questioned its performance as an efficacy endpoint, and there is limited validation of the SRI against long-term clinical outcomes. The aim of this study was to investigate longitudinal associations of SRI attainment with key clinical outcomes.

Methods: We used data from a large multi-centre longitudinal SLE cohort. Eligible patients had active disease (SLEDAI-2K ≥6) at a visit designated as baseline. Attainment of a modified version of the SLE Responder Index (mSRI; excluding BILAG criteria) defined as a reduction in SLEDAI-2k ≥4 with no worsening in physician global assessment (PGA) ≥0.3 was determined at 1-year intervals from baseline (up to 5 years). The associations between mSRI attainment and a range of clinical outcomes (longitudinal disease activity, steroid use, flare, damage accrual, attainment of lupus low disease activity state (LLDAS (Golder 2019)), clinical remission on therapy (CROT (van Vollenhoven 2017)) and mortality) were determined using univariable linear and logistic regression.

Results: A total of 2,024 patients had an eligible baseline visit. Baseline characteristics are summarised in Table 1. mSRI response was attained by 55.5% of patients at 1 year, with similar rates (54-57%) at subsequent annual visits. Associations of mSRI response with clinical outcomes were similar at each of the annual time points; Table 2 presents results at years 1, 3 and 5 post baseline. Attainment of mSRI was associated with significantly lower disease activity over follow-up.

Table 1. Baseline characteristics (n=2024)

Baseline characteristic	Median (interquartile range) or n (%)
Age at enrolment	37 (28, 47)
Age at diagnosis	27 (21, 37)
Female	1868 (92.3%)
Asian ethnicity	1783 (88.4%)
SLEDAI-2K score	8.0 (6.0, 10.0)
Physician global assessment (PGA)	1.0 (0.5, 1.5)
Prednisolone (mg/day)	7.5 (5.0, 15)
Mild/moderate flare	871 (45.3%)
Severe flare	331 (17.2%)
SLICC-ACR damage index (SDI) >0	777 (41.8%)

Table 2. Associations between mSRI attainment and clinical outcomes at follow up years 1, 3 and 5

Outcome	Year 1 (n=1567)			Year 3 (n=936)			Year 5 (n=522)		
	mSRI responder			mSRI responder			mSRI responder		
	No n=671	Yes n=838	RC or OR p-value	No n=399	Yes n=472	RC or OR p-value	No n=213	Yes n=282	RC or OR p-value
SLEDAI-2K	7.4 (3.6)	2.8 (2.5)	**-4.55 p<0.001**	7.0 (3.7)	2.5 (2.1)	**-4.46 p<0.001**	6.4 (3.0)	2.5 (2.2)	**-3.93 p<0.001**
Time-adjusted mean SLEDAI-2K	6.7 (2.8)	5.2 (2.9)	**-1.48 p<0.001**	6.0 (2.5)	4.5 (2.5)	**-1.46 p<0.001**	5.7 (2.4)	4.6 (2.3)	**-1.17 p<0.001**
Physician global assessment (PGA)	0.9 (0.6)	0.5 (0.5)	**-0.39 p<0.001**	0.9 (0.6)	0.4 (0.4)	**-0.47 p<0.001**	0.8 (0.5)	0.3 (0.3)	**-0.42 p<0.001**
Time-adjusted mean PGA score	0.8 (0.5)	0.7 (0.5)	**-0.12 p<0.001**	0.8 (0.5)	0.6 (0.4)	**-0.14 p<0.001**	0.7 (0.4)	0.6 (0.3)	**-0.15 p<0.001**
Prednisolone dose (mg/day)	10.4 (28.3)	5.9 (5.1)	**-4.57 p<0.001**	8.1 (8.3)	5.9 (23.1)	-2.18 p=0.076	7.7 (10.6)	4.6 (4.8)	**-3.16 p<0.001**
Time-adjusted mean prednisolone dose	9.1 (9.8)	9.2 (7.1)	0.03 p=0.938	8.3 (12.2)	7.3 (5.3)	-1.03 p=0.098	7.6 (5.5)	7.2 (6.8)	-0.46 p=0.423
SELENA-SLEDAI flare mild/moderate (ever)	408 (61%)	477 (57%)	1.51 p=0.128	265 (67%)	341 (73%)	1.33 p=0.057	158 (75%)	221 (78%)	1.22 p=0.364
SELENA-SLEDAI flare severe (ever)	223 (33%)	248 (30%)	1.42 p=0.13	172 (44%)	226 (49%)	1.19 p=0.202	110 (53%)	158 (57%)	1.18 p=0.38
Damage accrual after baseline visit (SDI)	68 (10%)	65 (8%)	2.94 p=0.106	101 (26%)	92 (20%)	**0.71 p=0.037**	74 (36%)	86 (31%)	0.82 p=0.32
Lups low disease activity state (LLDAS) (ever)	203 (30%)	525 (63%)	**2.16 p<0.001**	245 (62%)	366 (79%)	**2.24 p<0.001**	141 (67%)	243 (86%)	**3.14 p<0.001**
Clinical remission on therapy (CROT)	138 (21%)	362 (43%)	**5.37 p<0.001**	184 (47%)	167 (29%)	**2.36 p<0.001**	123 (59%)	216 (77%)	**2.31 p<0.001**
Death	0 (0%)	2 (0.2%)	N/A	0 (0%)	0 (0%)	N/A	1 (0.5%)	0 (0%)	N/A

Note patients with unknown PGA were excluded when defining mSRI responder status

Damage accrued in 9% of patients at 1 year and 32% by 5 years, with rates numerically lower in mSRI responders at all time points (significant at years 2 and 3). mSRI response was also significantly associated with attainment of LLDAS and clinical remission on therapy. Prednisolone doses at follow-up visits were consistently lower in the mSRI responder group, but time-adjusted mean dose had no significant differences. mSRI response was not associated with significant protection against flare. There were insufficient deaths for meaningful between-group comparison.

Conclusion: In a longitudinal cohort of SLE patients with baseline SLEDAI ≥6, attainment of a modified SRI responder index at annual visits up to 5 years was associated with clinical benefit including lower disease activity, reduced damage accrual and higher attainment of treat-to-target endpoints.

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Abstract Number: 1260

Factors That Impact Medication Adherence in Hospitalized Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease, characterized by episodes of flares, often involving multiple organ systems. Medication nonadherence remains a significant problem, reported by 43% to 75% of patients with one third self-discontinuing treatment after 5 years. Medication nonadherence has been linked to increased morbidity and hospital readmission. In addition to known predictors of nonadherence, including low socioeconomic status and side effects of medications, we hypothesized that pill burden, medical/psychiatric comorbidities and patient beliefs also play a role. Using survey methodology, our study examines factors that impact medication adherence among hospitalized patients with SLE. By characterizing these factors qualitatively and quantitatively, we hope to identify ways to decrease barriers to nonadherence.

Methods: This study was approved by the local Institutional Review Board. Hospitalized patients with SLE were identified and invited to participate. Demographics, education level, employment, insurance status, and self-reported outpatient medication use were obtained by patient interview. Patient-reported medication use was compared to outpatient prescriptions from the medical record to determine pill burden and adherence. Qualitative information was collected on beliefs surrounding medications and the presence of family and community support. Patients were

instructed to complete the STOFHLA health literacy questionnaire. Two-sample t-tests for continuous variables and Fisher's exact test for categorical measures were performed as appropriate.

Results: 20 patients with SLE met eligibility criteria and consented to participate. Most of our patients were black (n=18, 90%) and all were female, with a mean age of 36.4 ± 15.3. In his cohort, 55% of patients reported lack of medication adherence within 2 weeks of hospitalization. Nonadherent patients were more likely to have 3 or more additional medical/psychiatric comorbidities ($p< 0.01$). Nonadherent patients were also more likely to report that taking their medication was a hassle or inconvenience ($p< 0.05$). Factors such as age, employment, insurance status, or self-reported presence of family and/or community support were not significantly associated with adherence. There was no statistical difference in hospital length of stay (7.4 vs. 8.1 days) or pill burden per week (135 vs. 123 pills/week) between adherent and nonadherent patients. Health literacy, as measured by the STOFHLA, was not significantly different between adherent and nonadherent patients.

Conclusion: Within this predominantly African American female cohort of patients with SLE, there was high pill burden and prevalence of medication nonadherence prior to hospitalization. Despite the small sample size, this ongoing study provides insight into barriers important to patients and modifiable risk factors that healthcare providers can target when treating patients with SLE and addressing nonadherence.

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The Impact of Remission and Low Disease Activity Attainment on Health-related Quality of Life in Two Phase III Clinical Trials of Belimumab in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Health-related quality of life (HRQoL) is considered one of the most important outcomes in clinical trials of systemic lupus erythematosus (SLE), along with reduction in disease activity and safety. We studied the duration and consecutiveness of remission or low disease activity throughout a 52-week long period on standard therapy plus belimumab or placebo in relation to HRQoL outcome.

Methods: We analysed pooled 52-week data from the BLISS-52 (N=865) and BLISS-76 (N=819) phase III trials. We determined remission using the prevailing Definitions of Remission in SLE (DORIS) definition (1) and low disease activity using the Lupus Low Disease Activity State (LLDAS) (2). Remission required clinical (c)SLEDAI-2K=0, PhGA (0–3) <0.5, and prednisone ≤5 mg/day. LLDAS required SLEDAI-2K ≤4, PhGA (0–3) ≤1, and prednisone ≤7.5 mg/day. HRQoL was measured with the SF-36 physical and mental component summary (PCS and MCS), and EQ-5D-3L. Minimal clinically important difference (MCID) at week 52 for PCS and MCS was set to 2.5, and for EQ-5D-3L utility index to 0.040. Associations were assessed using quantile regression analysis. Adjustments for demographics, disease duration, organ damage and baseline status were incorporated.

Results: The minimum cumulative attainment of remission to achieve a benefit in PCS ≥MCID at week 52 was four visits (corresponding to 16 weeks) (β=0.63), while 7 visits (28 weeks) were required for MCS differences ≥MCID (β=0.37). Correspondingly, 9 visits in LLDAS (36 weeks) were required for achieving differences ≥MCID in both PCS (b=0.28) and MCS (β=0.29). Table 1 shows 95% confidence intervals and p values. When analysing the impact of sustained remission and LLDAS, four consecutive visits in remission (16 weeks) were required for PCS ≥MCID (b=0.70), whereas six visits (24 weeks) were required for MCS ≥MCID (b=0.46). Sustained LLDAS for nine consecutive visits (36 weeks) was needed for PCS and MCS ≥MCID (b=0.31 and 0.31, respectively). For EQ-5D ≥MCID to be reached, a cumulative total of seven visits (28 weeks) in remission (b=0.006), or eight visits (32 weeks) in LLDAS (b=0.005) was required, whereas if sustained, remission for six visits (24 weeks; b=0.008) or LLDAS for seven visits (28 weeks; b=0.006) were sufficient.

Conclusion: Attainment of remission or LLDAS in the BLISS-52 and BLISS-76 trials of belimumab was associated with improved HRQoL. Less time was required in remission than in LLDAS to achieve clinically important differences in multiple HRQoL aspects. Clinically important differences in HRQoL required shorter total time if the remission or LLDAS was sustained. Clinically important differences in mental aspects of HRQoL required longer time in remission than physical aspects. The impact of cumulative and sustained remission or LLDAS on HRQoL adds evidence on the clinical importance of these treat-to-target endpoints.

Associations with:	PCS β (95% CI) P value	MCS β (95% CI) P value	EQ-5D β (95% CI) P value
≥2 cumulative visits in remission	0.63 (4 visits) (0.31–0.95) P<0.001	0.37 (7 visits) (0.12–0.62) P=0.004	0.006 (7 visits) (0.002–0.010) P=0.002
≥2 cumulative visits in LLDAS	0.28 (9 visits) (0.13–0.43) P<0.001	0.29 (9 visits) (0.10–0.47) P=0.002	0.005 (8 visits) (0.003–0.007) P<0.001
≥2 consecutive visits in remission	0.70 (4 visits) (0.33–1.08) P<0.001	0.46 (6 visits) (0.20–0.71) P<0.001	0.008 (6 visits) (0.003–0.012) P<0.001
≥2 consecutive visits in LLDAS	0.31 (9 visits) (0.11–0.51) P=0.002	0.31 (9 visits) (0.09–0.53) P=0.007	0.006 (7 visits) (0.004–0.009) P<0.001

References

1) van Vollenhoven R. et al. Ann Rheum Dis. 2017
2) Franklyn K. et al. Ann Rheum Dis. 2016

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Abstract Number: 1262

Fish Oil Supplementation and Pro-inflammatory and Pro-Resolving Lipid Mediators in Patients with and Without Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Omega-3 fatty acid-derived "specialized pro-resolving mediators" (SPM) are low-abundance lipid mediators (LM) central to inflammation resolution. In this cross-sectional study, we investigated whether fish oil (FO) supplementation was associated with pro-inflammatory and pro-resolving LM in SLE patients compared to matched non-SLE controls.

Methods: Within the Mass General Brigham Biobank, we identified 16 patients with SLE taking FO, who were matched by age, sex, and race to 16 patients without SLE taking FO. Another 16 patients with SLE not taking FO were matched on the same factors to 16 non-SLE patients not taking FO. Demographic and clinical data were obtained by medical record review (**Table 1**). Targeted liquid chromatography-tandem spectroscopy was performed on plasma to quantify 27 omega-3-derived LM, identified with >6 diagnostic ions by tandem mass spectrometry (MS-MS). Multivariable linear analyses examined whether SLE, FO, and the interaction between SLE and FO were associated with LM levels (log-transformed to improve normality), adjusting for smoking status, body mass index and medications. In SLE case-only analyses, we additionally adjusted for C-reactive protein or erythrocyte sedimentation rate (normal/elevated), anti-double stranded DNA (dsDNA positive/negative), C3 and C4 (normal/low), and presence of lupus nephritis. We adjusted for multiple comparisons using a False Discovery Rate (FDR) with a cut-off of 0.05. For missing data, we used multiple imputation.

Table 1. Baseline characteristics of SLE patients and age, sex, and race matched controls				
Characteristic	**Not taking Fish Oil**		**Taking Fish Oil**	
	SLE (n=16)	**Matched controls (n=16)**	**SLE (n=16)**	**Matched controls (n=16)**
Age, mean (SD)	43.97 (10.81)	43.30 (10.27)	43.26 (10.59)	43.41 (10.28)
Sex, female, %	16 (100.0)	16 (100.0)	16 (100.0)	16 (100.0)
Race, %				
White	13 (81.25)	14 (87.50)	14 (87.50)	15 (93.75)
Non-white	2 (12.50)	2 (12.50)	1 (6.25)	1 (6.25)
Missing	1 (6.25)	0 (0.00)	1 (6.25)	0 (0.00)
Smoking, %				
Current	2 (12.50)	0 (0.00)	0 (0.00)	2 (13.33)
Past	4 (25.00)	4 (25.00)	2 (12.50)	2 (13.33)
Never	10 (62.50)	10 (62.50)	14 (87.50)	11 (73.33)
Unknown	0 (0.00)	2 (12.50)	0 (0.00)	1 (0.06)
BMI, kg/m^2, mean (SD)	28.36 (7.38)	26.12 (7.40)	24.78 (3.75)	27.46 (5.64)
Statin use[1], %	2 (12.50)	0 (0.00)	0 (0.00)	0 (0.00)
Current prednisone use, %	3 (18.75)	0 (0.00)	3 (18.75)	1 (6.25)
HCQ use, %	12 (75.00)	0 (0.00)	15 (93.75)	0 (0.00)
Other immunosuppressant medication use[2], %	2 (12.50)	2 (12.50)	1 (6.25)	0 (0.00)
Elevated CRP or ESR, %	4 (28.57)		7 (46.67)	
Positive anti-dsDNA, %	2 (13.33)		7 (43.75)	
Hypocomplementemia, %	4 (30.77)		6 (42.86)	
Lupus Nephritis, %	1 (6.25)		4 (25.00)	

Abbreviations: BMI, body mass index; HCQ, hydroxychloroquine; SD, standard deviation; SLE, systemic lupus erythematosus

1. Pravastatin, atorvastatin, lovastatin, rosuvastatin, simvastatin
2. Methotrexate, leflunomide, sulfasalazine, cyclophosphamide, cyclosporine, mycophenolate mofetil, etanercept, adalimumab, rituximab, infliximab, belimumab, tofacitinib, tocilizumab

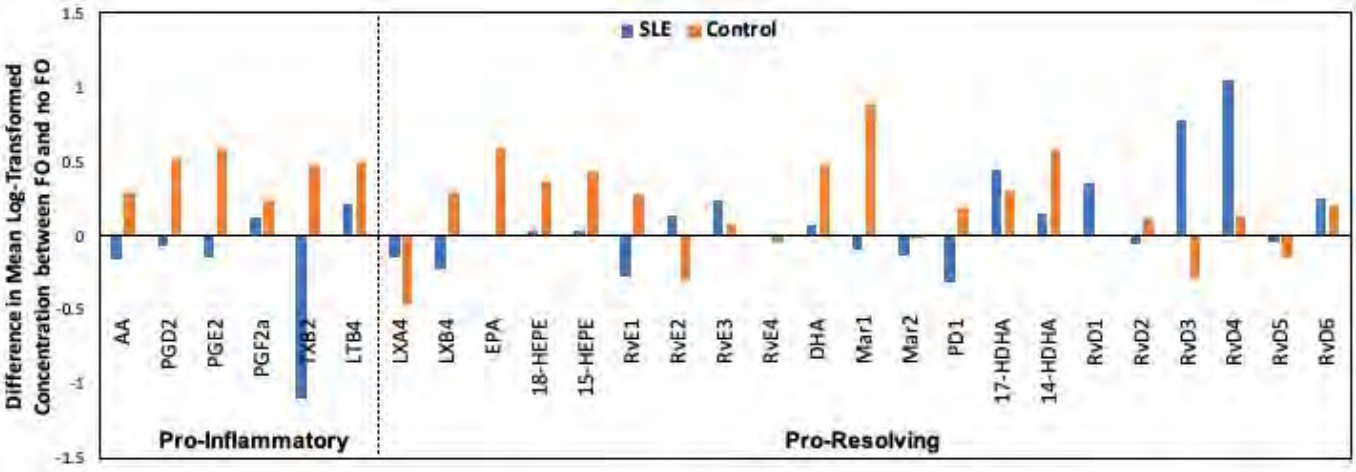

Figure 1. Difference in mean log-transformed Omega-3 fatty acid derived lipid concentration between taking vs. not taking fish oil supplementation among SLE and controls. No statistically significant differences were found after adjustment for multiple comparisons was performed using false discovery rate of 0.05. Abbreviations: LTB4, Leukotriene B4; LXA4, Lipoxin A4; LXB4, Lipoxin B4; MaR1-2, maresin 1-2; PGD2, Prostaglandin D2; PGE2, Prostaglandin E2; PGF2a, Prostaglandin F2 alpha; TXB2, Thromboxane B2; PD1, protectin D1; RvD1-6, resolvin D-6; RvE1-4, resolvin E1-4; 14-HDHA, 14-hydroxy-docosahexaenoic acid; 15-HEPE, 15-hydroxyeicosapentaenoic acid; 17-HDHA, 17-hydroxy-docosahexaenoic acid; 18-HEPE, 18-hydroxyeicosapentaenoic acid.

Results: Among SLE patients, lower levels of arachidonic acid (AA) and most (60%) of its pro-inflammatory derivatives were observed in those taking vs. not taking FO, whereas, among the controls, higher levels of AA and all of its pro-inflammatory derivatives were observed in those taking vs. not taking FO (**Figure 1**). However, after adjustment for multiple comparisons, there were no significant differences for any LM between SLE compared to matched controls, taking or not taking FO. Among controls, taking FO was associated with higher levels of eicosapentaenoic acid (adjusted ß coefficient 0.67 (95% CI: 0.28-1.07), FDR = 0.04) (**Table 2**). Taking FO was not associated with SPM levels among SLE patients even after adjusting for markers of disease activity. The interaction between SLE and FO was not statistically significant.

Conclusion: In this cross-sectional study, FO supplementation among SLE patients was not significantly associated with higher levels of several pro-resolving SPMs. This may be related to a higher level of inflammatory burden in SLE patients at baseline, reduced ability to biosynthesize SPMs, or failure to take regular and adequate doses of FO. As FO preparations and doses were not controlled in this observational study, further larger controlled studies should pursue these observations.

Table 2. Effects of dietary fish oil supplements on Omega-3 Fatty Acid derived Lipid Mediators, adjusted for smoking, BMI, medications (prednisone, immunomodulators, and statins) and markers of SLE disease activity (for SLE cases only)

	Lipid	Among SLE taking FO (n=16) vs. not taking FO(n=16)			Among Control Subjects taking FO (n=16) vs. not taking FO (n=16)		
		β coef. (95%CI)	Unadj. p-values	FDR	β coef. (95%CI)	Unadj. p-values	FDR
Pro-Inflammatory	AA	-0.13 (-0.49-0.23)	0.47	0.99	0.32 (-0.07-0.71)	0.10	0.34
	PGD2	-0.14 (-0.82-0.54)	0.67	0.99	0.56 (-0.05-1.16)	0.07	0.32
	PGE2	0.12 (-1.08-1.33)	0.83	0.99	0.60 (-0.04-1.24)	0.07	0.32
	PGF2a	0.01 (-1.43-1.45)	0.99	0.99	0.53 (-0.47-1.52)	0.29	0.52
	TXB2	-0.68 (-2.34-0.98)	0.40	0.99	0.39 (-0.74-1.52)	0.49	0.76
	LTB4	0.56 (-0.28-1.41)	0.18	0.99	0.51 (-0.07-1.09)	0.08	0.32
Pro-Resolving	LXA4	-0.01 (-0.79-0.77)	0.98	0.99	-0.53 (-1.53-0.47)	0.29	0.52
	LXB4	-0.56 (-1.41-0.28)	0.18	0.99	0.32 (-0.65-1.29)	0.51	0.76
	EPA	-0.07 (-0.620.48)	0.80	0.99	**0.67 (0.28-1.07)**	**<0.01**	**0.04**
	18-HEPE	0.20 (-0.60-1.00)	0.61	0.99	0.42 (-0.26-1.11)	0.21	0.52
	15-HEPE	0.12 (-0.48-0.73)	0.68	0.99	0.42 (-0.24-1.07)	0.20	0.52
	RvE1	-0.23 (-0.92-0.47)	0.51	0.99	0.08 (-0.50-0.67)	0.77	0.96
	RvE2	-0.11 (-0.71-0.48)	0.70	0.99	-0.47 (-1.36-0.42)	0.29	0.52
	RvE3	-0.02 (-0.70-0.65)	0.95	0.99	0.08 (-0.73-0.88)	0.85	0.96
	RvE4	-0.13 (-1.24-0.97)	0.80	0.99	-0.06 (-1.13-1.01)	0.91	0.96
	DHA	0.08 (-0.35-0.50)	0.72	0.99	0.54 (0.10-0.99)	0.02	0.12
	MaR1	0.09 (-0.56-0.74)	0.78	0.99	**1.04 (0.32-1.76)**	**0.01**	**0.05**
	MaR2	-0.18 (-0.53-0.17)	0.29	0.99	-0.00 (-0.28-0.27)	0.97	0.97
	PD1	0.08 (-0.91-1.07)	0.87	0.99	0.19 (-0.74-1.12)	0.68	0.92
	17-HDHA	0.61 (-0.69-1.92)	0.34	0.99	0.07 (-0.88-1.03)	0.88	0.96
	14-HDHA	0.07 (-0.86-1.00)	0.88	0.99	**0.59 (0.19-0.99)**	**0.01**	**0.05**
	RvD1	0.72 (-0.65-2.08)	0.28	0.99	-0.47 (-1.34-0.41)	0.28	0.52
	RvD2	0.11 (-0.79-1.00)	0.81	0.99	0.20 (-0.13-0.52)	0.22	0.52
	RvD3	0.89 (-0.77-2.55)	0.27	0.99	0.23 (-0.92-1.39)	0.68	0.92
	RvD4	0.82 (-0.55-2.20)	0.23	0.99	0.05 (-1.03-1.13)	0.92	0.96
	RvD5	-0.29 (-1.02-0.44)	0.42	0.99	-0.10 (-0.90-0.70)	0.80	0.96
	RvD6	0.01 (-1.60-1.62)	0.99	0.99	0.56 (-0.67-1.78)	0.36	0.60

Bolded when p<0.05 adjusted for multiple comparisons using false discovery rate. Abbreviations: LTB_4, Leukotriene B_4; LXA4, Lipoxin A_4; LXB_4, Lipoxin B_4; MaR1-2, maresin 1-2; PGD_2, Prostaglandin D_2; PGE_2, Prostaglandin E_2; PGF2a, Prostaglandin F2 alpha; TXB_2, Thromboxane B_2; PD1, protectin D1; RvD1-6, resolvin D-6; RvE1-4, resolvin E1-4; Unadj., unadjusted; 14-HDHA, 14-hydroxy-docosahexaenoic acid; 15-HEPE, 15-hydroxyeicosapentaenoic acid; 17-HDHA, 17-hydroxy-docosahexaenoic acid; 18-HEPE, 18-hydroxyeicosapentaenoic acid.

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Abstract Number: 1263

Treatment of Pediatric Lupus Is Associated with Significant Re-Organization of B Cell Chromatin

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) may be triggered by gene-environment interactions. Data remain scarce on how epigenetic variance contributes to disease risk in pediatric SLE (pSLE). Our objectives were to identify differences in chromatin architecture in treatment-naïve pSLE compared to healthy children (HC) and pSLE patients after induction therapy.

Methods: We used assays for transposase-accessible chromatin-sequencing (ATACseq) in 8 pSLE patients pre- and post-induction therapy and 5 HC to investigate whether regions of open chromatin unique to pSLE patients demonstrate enrichment for transcriptional regulators, using standard computational approaches and a false discovery rate of < 0.05.

Results: The mean age of onset was 13.75 (range 7-17) years in pSLE, and mean SLEDAI was 12.8 (range 6-24). We identified 245 differentially accessible regions (DAR) around peaks unique to treatment-naïve pSLE patients, of which over 50% appear to be more accessible in pSLE than HC, and are located more than 100kb from the nearest transcription start site (nTSS), implying transcription factors (TF) may be acting on distal enhancers to regulate transcription. pSLE DAR were enriched for enhancer marks. In DAR encompassing TF binding sites, pSLE samples, but not HC, were enriched for disease-associated single nucleotide polymorphisms (SNPs) previously identified in lupus genome-wide association studies. Variant calling within DAR found 3864 genes belonging to 129 different biologic processes, including cellular activation in immune response and responses to external stimuli. In contrast, over 80% of peaks unique to pSLE patients post-induction therapy are located distal to nTSS. Induction therapy for pSLE patients included corticosteroids in all patients, cyclophosphamide in 5, and mycophenolate in 3. DAR from pSLE patients post-induction therapy were not enriched for enhancers or disease-associated SNPs.

Conclusion: We demonstrate an epigenetically-distinct profile in pSLE B cells when compared to HC, indicating pSLE B cells are predisposed for disease development. Pathways of significance analyses identified immunologic pathways important in the pro-inflammatory response in treatment-naïve pSLE patients. These pathways were absent in analyses from the same pSLE patients post-induction therapy. Thus, increased chromatin accessibility in genomic regions controlling activation of inflammatory and immune responses suggest transcriptional dysregulation of key players in immune cell activation plays an important role in pathogenesis of SLE. Treatment with corticosteroids and immunosuppressive medication changes this epigenetic profile, making pathways responsible for inflammation and B cell activation less accessible.

Disclosure: J. Hui-Yuen, None; **K. Jiang**, None; **S. Malkiel**, None; **B. Diamond**, ISD, 2, nextcure, 2, J5J, 2, astlia, 2, dbv, 2, cyxone, 2; **J. Jarvis**, None.

Abstract Number: 1264

Racial Differences in Chronic Glucocorticoid Use in Patients with SLE: A Cross Sectional Study

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
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Background/Purpose: Black patients with systemic lupus erythematosus (SLE) face higher rates of morbidity and mortality compared to White patients. Long-term glucocorticoid use has been associated with worse health outcomes among patients with SLE. We sought to quantify chronic glucocorticoid use among Black and White patients with SLE within a prospective registry.

Methods: Using a registry at a large academic institution, we compared chronic glucocorticoid use among participants with SLE that self-identify as Black or White race. SLE was defined by either Systemic Lupus International Collaborating Clinics or American College of Rheumatology criteria. At the time of registry enrollment, demographic and disease specific variables, including age, sex, Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2k), hospitalization in the year before registry enrollment, disability status, and current SLE-related medications were captured. Chronic glucocorticoid utilization was defined as both documentation of current glucocorticoid use by participant self-report and physician documentation of steroid use as part of SLE treatment at the time of registry enrollment. Multivariable logistic regression of race and chronic glucocorticoid use was performed, adjusting for covariates exhibiting a bivariate association with chronic glucocorticoid use at significance level $p < 0.10$.

Results: 114 White participants (mean age 45; standard deviation (SD) 15) and 59 Black participants (mean age 42; SD 14) were analyzed. White participants had mean SLEDAI-2K score of 3.7 (SD 5.2). Black participants had mean SLEDAI-2K scores of 6.3 (SD 6.0). Among Black participants, 43 (72%) utilized glucocorticoids compared to White participants 39 (34%) (unadjusted odds ratio (OR) 5.17; 95% confidence interval (CI) 2.59-10.33). We did not observe differences between unadjusted hydroxychloroquine (OR 0.69; 95% CI 0.28-1.65) or conventional disease-modifying anti-rheumatic drug (cDMARD) (OR 1.07; 95% CI 0.57-2.01) utilization among Black and White participants. SLEDAI-2K, disability, recent hospitalization, and past or present hydroxychloroquine or cDMARD use were included in a logistic regression model. Adjusting for covariates, Black participants were more likely to be on glucocorticoids (adjusted OR 5.69; 95% CI 2.17-14.96); p=0.0004).

Conclusion: Adjusting for disease activity and other medications, Black patients had greater exposure to chronic glucocorticoids than White patients in a prospective SLE registry while cDMARD use remained the same. These patients may face increased glucocorticoid-related morbidity, which could contribute significantly to long-term health outcomes and utilization of health care resources. Future research in larger, more diverse registries should be conducted to further characterize patterns of glucocorticoid use.

Table 1. Demographics of White and Black participants in the SLE registry.

Variable	White (N = 114)	Black (N = 59)
Mean age (years; standard deviation)	45 (15)	42 (14)
Hispanic ethnicity (N, %)	8 (7%)	2 (3%)
Currently disabled (N, %)[a]	23 (21%)	16 (31%)
Medical insurance type		
Medicaid	7 (6%)	19 (32%)
Medicare	24 (21%)	14 (24%)
Private	71 (62%)	22 (37%)
None	0 (0%)	3 (3%)
Other	3 (3%)	0 (0%)
Missing	9 (8%)	1 (2%)
Annual Income		
<$25,000	24 (41%)	28 (47%)
$25,000 – $75,000	44 (39%)	17 (29%)
>$75,000	28 (25%)	3 (5%)
Student	5 (4%)	2 (3%)
Missing	13 (11%)	9 (15%)
Total SLEDAI-2K[b] (mean, SD)	3.7 (5.2)	6.3 (8.0)
+Total SLEDAI-2K[b] ≥ 6 (N, %)	23 (20%)	32 (54%)
Hospitalized in the past year (N, %)[a]	20 (20%)	20 (37%)
Median SLE medications (median, interquartile range)[a]	2 (1-3)	2 (2-3)

[a]Indicates missing data: Disabled N = 161; Hospitalized N = 152; Median medications N = 168

[b]SLEDAI-2K stands for systemic lupus erythematosus disease activity index 2000

Table 2. Current SLE medication use among White and Black participants

Medication	White (n = 114)	Black (n = 59)	P-value[a]	Odds ratio (95% confidence interval)
Chronic oral corticosteroids	39 (34%)	43 (73%)	**< 0.0001**	5.17 (2.59-10.33)
NSAIDs[b]	35 (31%)	20 (34%)	0.62	1.19 (0.51-2.33)
Hydroxychloroquine	100 (88%)	49 (83%)	0.40	0.69 (0.28-1.65)
Conventional DMARDs[c,d]	58 (51%)	31 (53%)	0.84	1.07 (0.57-2.01)
Biologic DMARDs[e]	8 (7%)	3 (5%)	0.75[f]	0.71 (0.18-2.78)

[a] All statistical tests performed utilized Pearson's Chi Squared Test except where indicated
[b] NSAIDs stands for non-steroidal anti-inflammatory drugs
[c] DMARD stands for disease-modifying anti-rheumatic drug
[d] Conventional DMARDs consist of methotrexate, azathioprine, mycophenolate leflunomide, cyclophosphamide
[e] Biologic DMARDs consist of rituximab, belimumab
[f] Fischer's Exact Test

Table 3. Multivariable logistic regression of odds of chronic glucocorticoid use among White and Black participants in the SLE registry. Independent variables include race, hospitalization in the last year, total SLEDAI-2K dichotomized at 6, disability, no current or prior hydroxychloroquine, and current or prior conventional disease-modifying anti-rheumatic drugs (methotrexate, azathioprine, mycophenolate, leflunomide, cyclophosphamide). Odds ratios and significance are Wald based.

Variable	Estimate	Odd ratio (95% confidence interval)	P-value
Intercept	-2.51		<0.0001
Race (Black)	1.74	5.69 (2.17-14.96)	0.0004
Hospitalization	-0.52	0.60 (0.21-1.69)	0.33
Total SLEDAI-2K[a] ≥ 6	1.73	5.66 (1.93-16.56)	0.002
Disabled	1.34	3.81 (1.45-10.07)	0.007
Never used hydroxychloroquine	1.24	3.44 (0.59-19.33)	0.17
Ever used cDMARD[b]	1.75	5.76 (2.20-15.04)	0.0004

Overall model p-value <0.0001; Overall model N = 145

[a]SLEDAI-2K stands for systemic lupus erythematosus disease activity index 2000

[b]cDMARD stands for conventional disease-modifying anti-rheumatic drug (methotrexate, azathioprine, mycophenolate, leflunomide, cyclophosphamide)

Disclosure: J. Sullivan, None; **E. Littlejohn**, Aurinia Pharmaceuticals, 6.

Abstract Number: 1265

Paradoxical Effect of Vitamin D on Bone Mineral Density in SLE

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
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Background/Purpose: Osteoporosis with fractures is consistently one of the top three items in the SLICC/ACR Damage Index in cohort studies internationally. As vitamin D insufficiency and deficiency are common in SLE, we asked whether 25(OH) vitamin D levels were associated with bone mineral density.

Methods: We took the first DXA scan after the first 25(OH) vitamin D blood level measurement. 1099 SLE patients (meeting SLICC or EULAR/ACR classification criteria) had a DXA scan done after a 25(OH) vitamin D measurement. We examined bone mineral density in two ways: 1) binary – osteoporosis or not; and 2) continuous variable of lumbar spine t-score.

Table 1. Association of Patient Demographic Variables with Osteoporosis

	Osteoporosis	
	N (%)	**p-value**
SEX		0.8559
Female	76/1012 (7.5%)	
Male	7/87 (8%)	
ETHNICITY		0.7401
African American	38/459 (8.3%)	
Other	8/111 (7.2%)	
Caucasian	37/529 (7%)	
EVER SMOKING		0.0037
Never	45/748 (6%)	
Ever	38/345 (11%)	
EDUCATION		0.056
<=12 yrs	31/309 (10%)	
>12 yrs	52/784 (6.6%)	
HOUSEHOLD INCOME		0.2511
<$30000	27/279 (9.7%)	
$30-$65k	26/327 (8%)	
$ 65K+	30/472 (6.4%)	
INSURANCE		0.1144
None	3/19 (15.8%)	
Medical Assistance	19/189 (10.1%)	
Private	60/886 (6.8%)	

Table 2. Association Between 25(OH) Vitamin D Level and Lumbar Spine Bone Density

	Osteoporosis			Spine t-score (continuous)		
	n (%)	OR (95% CI)	p-value	mean (SD)	mean estimate	p-value
First Vitamin D level						
1.<10	8/66 (12.1%)	2.51 (0.99, 6.37)	0.0532	-0.59 (1.34)	-0.21 (-0.59, 0.16)	0.2633
2.10-<20	20/220 (9.1%)	1.8 (0.89, 3.65)	0.1044	-0.39 (1.44)	-0.08 (-0.32, 0.17)	0.544
3.20-<30	16/257 (6.2%)	1.22 (0.59, 2.54)	0.5947	-0.53 (1.27)	-0.19 (-0.42, 0.05)	0.1159
4.30-<40	15/278 (5.4%)	1.00 (Ref)	Ref	-0.38 (1.38)	0 (Ref)	Ref
5.40-<50	18/175 (10.3%)	2.01 (0.98, 4.14)	0.0563	-0.61 (1.27)	-0.29 (-0.55, -0.03)	0.0289
6.50-<60	2/55 (3.6%)	0.71 (0.16, 3.24)	0.6616	-0.42 (1.52)	-0.13 (-0.52, 0.27)	0.536
7.>=60	4/48 (8.3%)	1.54 (0.48, 4.88)	0.4673	-0.88 (1.43)	-0.48 (-0.9, -0.06)	0.024
Mean Vitamin D levels prior to the DXA scan						
1.<10	2/21 (9.5%)	1.87 (0.4, 8.87)	0.4288	-0.25 (1.27)	-0.15 (-0.76, 0.45)	0.6214
2.10-<20	13/118 (11%)	2.48 (1.16, 5.3)	0.0191	-0.55 (1.52)	-0.22 (-0.5, 0.07)	0.1428
3.20-<30	23/236 (9.7%)	1.96 (1.03, 3.74)	0.0408	-0.6 (1.28)	-0.31 (-0.53, -0.08)	0.0081
4.30-<40	18/343 (5.2%)	1.00 (Ref)	Ref	-0.29 (1.35)	0 (Ref)	Ref
5.40-<50	18/263 (6.8%)	1.29 (0.65, 2.55)	0.4669	-0.54 (1.35)	-0.23 (-0.45, -0.01)	0.0381
6.50-<60	8/78 (10.3%)	1.86 (0.77, 4.51)	0.1687	-0.74 (1.42)	-0.43 (-0.76, -0.09)	0.013
7.>=60	1/40 (2.5%)	0.45 (0.06, 3.47)	0.442	-0.69 (1.15)	-0.43 (-0.87, 0.02)	0.0621
Most recent past vitamin D level prior to DXA scan						
1.<10	2/22 (9.1%)	2.26 (0.47, 10.97)	0.311	-0.22 (1.38)	-0.08 (-0.67, 0.5)	0.7863
2.10-<20	10/103 (9.7%)	2.5 (1.05, 5.95)	0.0377	-0.54 (1.51)	-0.35 (-0.66, -0.05)	0.0243
3.20-<30	25/219 (11.4%)	2.77 (1.39, 5.52)	0.0038	-0.65 (1.33)	-0.46 (-0.7, -0.23)	0.0001
4.30-<40	14/285 (4.9%)	1.00 (Ref)	Ref	-0.2 (1.35)	0 (Ref)	Ref
5.40-<50	10/205 (4.9%)	0.97 (0.42, 2.23)	0.9352	-0.54 (1.32)	-0.32 (-0.56, -0.08)	0.01
6.50-<60	10/118 (8.5%)	1.59 (0.68, 3.74)	0.2832	-0.77 (1.25)	-0.55 (-0.84, -0.26)	0.0002
7.>=60	6/93 (6.5%)	1.32 (0.49, 3.55)	0.5879	-0.53 (1.33)	-0.33 (-0.65, -0.02)	0.037

Results: 1012 (92%) were female, 459 (42%) were African American, 529 (48%) were Caucasian. The mean age at their DXA scan after vitamin D level measurement was 45 years (SD=13.1). There were 83 patients with spine t-score < =-2.5. Table 1 shows demographic variables and their association with osteoporosis. Smoking was strongly associated. Next we looked at the first 25(OH) vitamin D, the mean, and most recent levels versus both osteoporosis AND the lumbar spine t-score (Table 2). These analyses showed a U-shaped relationship centered at 25(OH) vitamin D levels of 30-40. Both lower levels and some higher levels were associated with osteoporosis and with lower lumbar spine t-scores.

Conclusion: Vitamin D has a surprisingly paradoxical relationship to bone health in SLE. The Ideal 25(OH) vitamin D level appears to be 30-40 ng/mL. Vitamin D is not truly a "vitamin" but should be considered a sterol hormone, which may contribute to its complicated role in bone health. As 40 ng/mL is also the ideal level for renal lupus, this appears to be the best 25(OH) vitamin D target in SLE management.

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Abstract Number: 1266

Quality of Life Measures and Physical Activity in Childhood Systemic Lupus Erythematosus

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SESSION INFORMATION

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Background/Purpose: Childhood systemic lupus erythematosus (cSLE) is a life-long disease with significant morbidity and mortality, and with associated significant impact on health-related quality of life (HRQOL). Prior research has shown that SLE patients' physical activity level is lower than that of healthy individuals. Increased physical activity is associated with improved wellbeing in SLE.There is a paucity of literature examining relationship between physical activity and HRQOL in cSLE. We sought to describe the physical activity and determine the relationship between exercise, SLE activity and treatment modalities and HRQOL in cSLE. To our knowledge, this is the first study investigating the relationship between the Physical Activity Questionnaire (PAQ) and Simple Measure of the Impact of Lupus Erythematosus in Youngsters (SMILEY) total scores (both used in our study).

Methods: Children < 18 years of age with SLE and their parents were enrolled and completed corresponding child and parent SMILEY reports, and the PAQ for Children (PAQ-C) or Adolescents (PAQ-A). Through retrospective chart review we assessed disease activity (SLE Disease Activity Index). Descriptive statistics as well as Pearson's correlation coefficients were performed with the data obtained, with the patients stratified into two cohorts of lower and higher levels of physical activity (PAQ score < 2 and ≥ 2) and based off the average PAQ score of 2, with median PAQ score of 1.8 (range 1.0- 4.7). We utilized a conservative estimate of PAQ scoring, with previous studies identifying normative PAQ scores in a healthy pediatric population ranges between a minimum of 2.7-2.9 based on age and gender, respectively.

Results: Forty-four children and their parents were enrolled; clinical data, SMILEY and PAQ-C or PAQ-A scores of cSLE subjects were evaluated. The most frequently reported exercise modality was walking (61.4%), with mean frequency of 3.7 ± 1.8 days/week, and a median of 3.5 days/week. Running was the second most frequent exercise reported (54.5%), with mean frequency of 3.1 ± 2.0 days/ week, and a median of 1.5 days/week. Our patients had an overall lower frequency of Cyclophosphamide use and higher frequency of Mycophenolate and Rituximab use. Patients with hypocomplementemia at diagnosis, current prednisone use, Class IV/V lupus nephritis, and Cyclophosphamide use had a higher proclivity towards less activity (PAQ score < 2). There was a mild correlation between SMILEY total score and PAQ [cSMILEY and PAQ (Pearson correlation=0.2), and pSMILEY scores (Pearson correlation=0.3; p=0.05*)]*. cSLE patients with PAQ≥ 2 had higher child and parent SMILEY scores but the difference was not statistically significant. There was a strong correlation between child and parent-SMILEY scores (Pearson correlation=0.7; p= < .00001).

Conclusion: Patients with cSLE prefer walking followed by running. cSLE patients with higher physical activity appeared to have better HRQOL, lower steroid use, and less cyclophosphamide use. We need larger samples to un-

Table 1. Characteristics of SMILEY Participants stratified by PAQ scores. This table depicts the patient demographics, clinical features and management of enrolled pediatric systemic lupus erythematosus patients for patients with PAQ scores < 2 and ≥2

Demographics	**Our cohort (n=44)**	**Lower physical activity [PAQ Scores < 2] (n=23)**	**Higher physical activity [PAQ Scores ≥ 2] (n=21)**
Female	*36* (82%)	*19* (83%)	*17* (81%)
Male	*8* (18%)	*4* (17%)	*4* (19%)
Age, mean ± SD (median, range)	15.2 ± 2.2 (16.0, 7-18)	15.7 ± 1.86 (16.0, 8-18)	14.6 ± 2.4 (15.0, 7-17)
Race			
Caucasian	*18* (41%)	*9* (39%)	*9* (43%)
African American	*21* (48%)	*13* (57%)	*9* (43%)
Asian	*5* (11%)	*1* (4%)	*2* (10%)
Other		*0*	*1 (5%)*
Disease Characteristics			
SLE Disease duration in years, mean ± SD (median, range)	1.6 ± 2.6 (1.0, 0-8)	2.3 ± 2.5 (1.0, 0-8)	1.6 ± 2.1 (0.5, 0-8)
SLEDAI, mean ± SD (median, range)	3.1 ± 3.3 (2.0, 0-13)	3.17 ± 3.2 (2.0, 0-10)	3.0 ± 3.6 (2.0, 0-13)
SLEDAI, ≥12	*2* (5%)	*0*	*2* (10%)
Class IV/V Lupus Nephritis	*15* (34%)	*9* (39%)	*6* (29%)
Neuro-psychiatric	*5* (11%)	*3* (13%)	*2* (10%)
Mean C- SMILEY Score ± SD	64.0 ± 16.9	61.0 ± 17.2	68.0 ± 17.2
Mean P- SMILEY Score ± SD	61.0 ± 16.2	58.0 ± 15.9	65.0 ± 16.1
Medication (current use)			
Prednisone	*31* (71%)	*18* (78%)	*12* (57%)
High dose Prednisone (≥15 mg daily)	*15* (34%)	*8* (35%)	*7* (33%)
Mycophenolate mofetil	*25* (57%)	*14* (61%)	*12* (57%)
Azathioprine	*3* (7%)	*3* (13%)	*0*
Plaquenil	*42* (96%)	*22* (96%)	*20* (95%)
Cyclophosphamide	*12* (27%)	*8* (35%)	*4* (19%)
Rituximab	*5* (11%)	*3* (13%)	*2* (10%)
Biomarkers at diagnosis			
Anti-dsDNA	*25* (57%)	*13* (57%)	*12* (57%)
Anti-Smith	*11* (25%)	*5* (22%)	*7* (33%)
Low C3/C4	*15* (34%)	*9* (39%)	*6* (29%)
Arthritis	*22* (50%)	*9* (39%)	*11* (52%)
Serositis	*13* (30%)	*7* (30%)	*5* (24%)
Cytopenia	*28* (64%)	*14* (61%)	*13* (62%)
Rash	*28* (64%)	*12* (52%)	*13* (62%)

[i] Values depicted as n (percentage)

derstand the prognostic value of activity levels and the extent to which increasing physical activity through exercise might be linked to improvements in HRQOL in this vulnerable population.

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Abstract Number: 1267

Frailty and Emergency Department Utilization in Systemic Lupus Erythematosus: An Administrative Claims Data Analysis

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SESSION INFORMATION

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Background/Purpose: Emergency department (ED) utilization is associated with worse quality of care and health-related quality of life (HRQoL) in systemic lupus erythematosus (SLE). While frailty is a risk factor for adverse health outcomes in SLE, whether frailty is a risk factor for ED utilization in SLE is unknown. We aimed to study frailty prevalence in adults with SLE < 65 years of age compared to age- and gender-matched comparators without systemic rheumatic disease (SRD) using two validated claims-based frailty indices (CFIs) [1-2] and to assess the risk of ED utilization in frail patients with and without SLE, as well as in frail patients without SRD, compared to non-frail patients without SRD.

Methods: We conducted a longitudinal study using the Centers for Medicare and Medicaid Services Medicaid subset of the Truven Health MarketScan dataset from 2011-2016. We identified patients with SLE 18-65 years of age by ≥3 ICD-9 CM codes for SLE (710.0) ≥30 days apart during the baseline period (2011), as well as age- and gender-matched non-SRD comparators [1:4]. Baseline frailty status was determined using two CFIs validated by Segal et al. and Kim et al. [1-2]. We identified patients who were frail according to one ("frail discordant") or both ("frail concordant") CFIs or non-frail according to both CFIs. Agreement between CFIs was evaluated with a kappa statistic. During the follow-up period (2012-2016), we examined the risk of ED utilization in the following groups: non-frail patients without SRD (referent), non-frail with SLE, frail concordant and discordant without SRD, and frail concordant and discordant with SLE. Cox proportional hazard models were calculated, adjusting for baseline hydroxychloroquine, glucocorticoid, and immunosuppressive medication use.

Results: We identified 2262 patients with SLE and 9048 matched comparators without SRD (Table 1). Baseline frailty prevalence in patients with SLE was higher than in patients without SRD according to each CFI (Segal's definition: 38.3% versus 21.6%; Kim's definition: 50.4% versus 18.6%), with moderate agreement between CFIs (κ=0.47, p< 0.0001). 28.8% of patients with SLE and 11.6% of comparators without SRD were frail according to both CFIs (Table 1). Patients with SLE who were frail concordant were older and less commonly on hydroxychloroquine and immunosuppressive medication at baseline than non-frail patients with SLE (Table 1). Compared to non-frail patients without SRD, non-frail patients with SLE had a 2.1 times higher hazard of ED utilization (Table 2). Frail patients with SLE, using either frailty definition, had a 3.4 times higher hazard of ED utilization than non-frail patients without SRD (Table 2).

Table 1. Baseline sociodemographic features and SLE-related medication use in frail and non-frail patients with SLE and non-systemic rheumatic disease (SRD) comparators

	Patients with SLE (N=2262)		Non-SRD comparators (N=9048)	
N (%), unless otherwise specified	Frail* (N=651)	Non-frail** (N=904)	Frail* (N=1050)	Non-frail** (N=6458)
Age in years, mean (SD)	50.8 (8.0)	35.2 (9.5)	54.3 (5.8)	37.2 (10.1)
Female	610 (93.7)	842 (93.1)	982 (93.6)	578 (91.2)
Race				
Black or African American	354 (54.4)	447 (49.5)	324 (38.6)	1817 (28.1)
White	216 (33.2)	320 (35.4)	595 (56.7)	3723 (57.7)
Other	42 (6.5)	62 (6.9)	66 (6.3)	481 (7.5)
Unknown	39 (6.0)	28 (3.1)	19 (1.8)	245 (3.8)
Hydroxychloroquine use	239 (36.7)	544 (60.2)	0 (0)	10 (0.15)
Glucocorticoid use	367 (56.4)	548 (60.6)	768 (11.9)	768 (11.9)
Immunosuppressive medication use	119 (18.3)	335 (37.1)	3 (0.5)	21 (0.33)

*Frail according to both claims frailty indices.
**Non-frail according to both claims frailty indices.

Table 2. Hazard of emergency department visits according to baseline frailty status and presence of SLE from 2011 to 2016

Patient group	Unadjusted hazard ratio (95% confidence interval)	Adjusted† hazard ratio (95% confidence interval)
Non-frail* non-SRD**	Referent group	Referent group
Non-frail SLE	2.0 (1.8-2.3)	2.1 (1.8-2.4)
Frail concordant‡ SLE	3.6 (3.1-4.0)	3.4 (2.9-3.9)
Frail discordant‡‡ SLE	3.5 (3.1-4.0)	3.4 (2.9-3.9)
Frail concordant‡ non-SRD**	2.3 (2.0-2.5)	2.1 (1.9-2.4)
Frail discordant‡‡ non-SRD**	1.7 (1.5-1.9)	1.7 (1.5-1.8)

*Non-frail according to both claims frailty indices.
**Non-systemic rheumatic disease.
‡Frail according to both claims frailty indices.
‡‡Frail according to one claims frailty index.
†Adjusted for baseline hydroxychloroquine, glucocorticoid, and immunosuppressive medication use.

Conclusion: Frailty prevalence in young and mid-aged patients with SLE exceeded that in age- and gender-matched patients without SRD in this sample of Medicaid beneficiaries. Both SLE and frailty appear to be associated with a higher hazard of ED visits. Frailty may identify a subset of patients with SLE at increased risk of ED utilization and serve as a novel target for interventions to improve HRQoL in SLE.

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Disclosure: S. Lieber, None; **I. Navarro-Milln**, sobi, 6; **M. Nahid**, None; **M. Rajan**, None; **S. Sattui**, None; **L. Mandl**, Regeneron Pharmaceuticals, 5.

Abstract Number: 1268

Predicting Adverse Pregnancy Outcomes in Women with Systemic Lupus Erythematosus: A Comparison of Machine Learning Methods

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Nearly 20% of pregnancies in patients with Systemic lupus erythematosus (SLE) result in an adverse pregnancy outcome (APO); early identification of women with SLE who are at high risk of APO is vital. We previously derived a risk model for APO using logistic regression and data from the PROMISSE Study, a large multi-center, multi-ethnic/racial study of APO in women with mild/moderate SLE and/or aPL. While this highly interpretable regression model showed promising predictive performance, we sought to determine if novel and increasingly popular machine learning (ML) approaches would enhance APO risk prediction using all available predictors and potential complex relationships such as interactions or higher order terms. We compared logistic regression modeling to LASSO, a regression approach that handles high-dimensionality and correlated predictors through shrinkage of estimated coefficients, as well as several "black box" ML algorithms. ML techniques are well-suited to high-dimensional data, require no variable selection, and unlike regression-based approaches are able to explore complex relationships without explicit input by the user.

Methods: We used the original PROMISSE data (41 predictor variables from 385 subjects) with APO (71/385, 18.4%) defined as preterm delivery due to placental insufficiency or preeclampsia, fetal or neonatal death, or fetal growth restriction. Logistic regression with stepwise selection (LR-S) was compared to LASSO, random forest (RF), neural network (NN) with 2 hidden neurons, support vector machines with RBF kernel (SVM_{RBF}), and gradient boosting (GB). To summarize discrimination we present cross-validated area under the receiver operating curve (AUC), along with sensitivity (Sn) and specificity (Sp) at an optimal cut-point.

Results: Regression based classifiers confirmed the predictors of APO identified in our previously reported model: non-white race, use of anti-hypertensive medication, low platelets, SLE disease activity, lupus anticoagulant (LAC) +, and high diastolic blood pressure (DBP). RF additionally revealed two novel interaction variables that increased APO risk: LAC+ with anti-b2GPI IgM, high DBP with low C3. LR-S and LASSO were observed to have similar overall discrimination (AUC=0.75 vs. 0.77) but LASSO had higher sensitivity (Sn=0.71 vs. 0.65). ML classifiers RF and SVM_{RBF} had similar good performance (AUC=0.77-0.78), while NN and GB were inferior.

Table 1: Summary of 5x10 fold cross-validation results

Model	*AUC*	*sensitivity*	*specificity*
LR-S	0.75	0.65	0.78
LASSO	0.77	0.71	0.75
NN	0.71	0.70	0.61
RF	0.77	0.77	0.78
GB	0.72	0.72	0.72
SVM-RBF	0.78	0.78	0.73

Conclusion: Several popular ML algorithms did not provide meaningful improvements to the previously identified model for APO prediction. The strong relative performance of regression-based models with this large and well-characterized clinical data set is notable as these models are highly interpretable, well-understood, and generally require fewer variables to generate a risk prediction. New clinical and laboratory markers may improve predictions in the future.

Disclosure: M. Fazzari, None; **M. Guerra**, None; **J. Salmon**, UCB, 1, 5, BMS, 1, Aurinia, 1; **M. Kim**, None.

Abstract Number: 1269

The Burden of Systemic Lupus Erythematosus Patients in the United States – Evidence from the Medical Expenditure Panel Survey (2016-2018)

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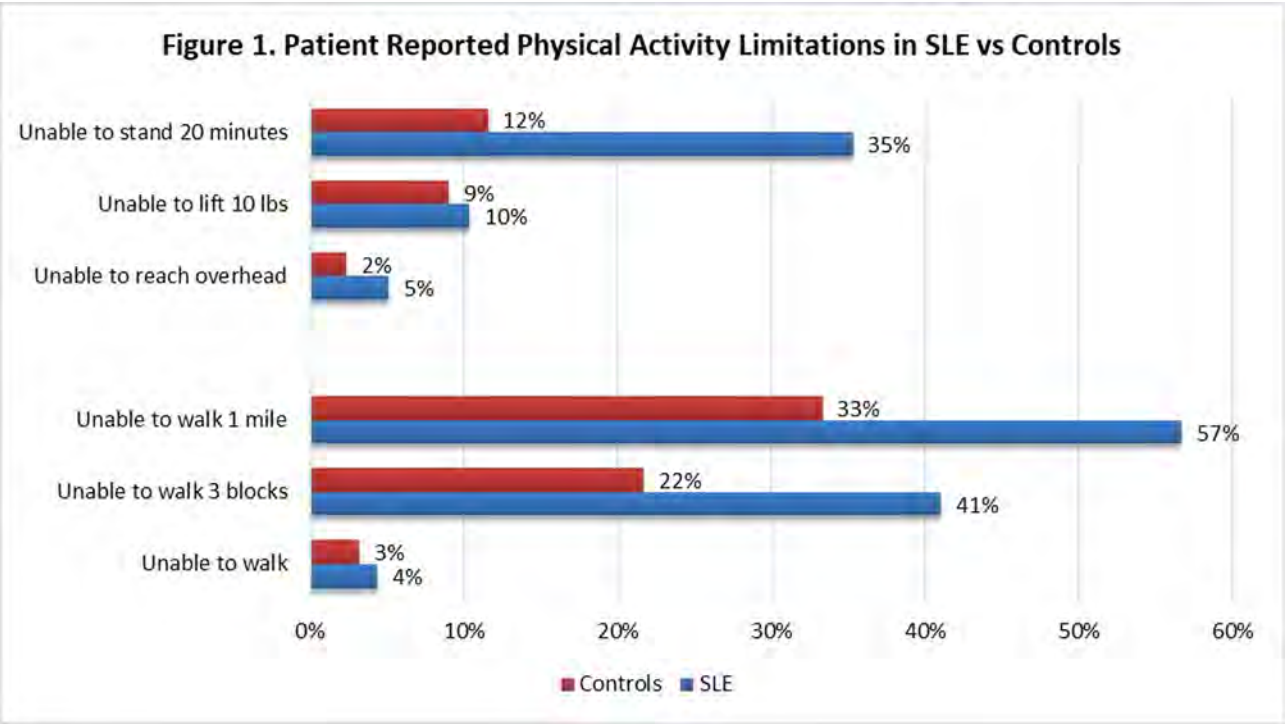
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Due to the heterogeneity of systemic lupus erythematosus (SLE), clinical characteristics, quality of life (QOL), social determinant of health (SDOH), health care utilization (HRU), and cost are important metrics in evaluation of treatment efficacy. Our study sought to use a generalizable real-world data source to characterize SLE patient characteristics compared to the general population.

Methods: We analyzed 2016 - 2018 Medical Expenditure Panel Surveys (MEPS). MEPS is an annual survey designed to represent the US civilian non-institutionalized population. SLE patients were identified using ICD-10 M32 and had to have either/or SLE-related medication and rheumatologist visit. A non-SLE (referent) cohort from the general MEPS population was 1:5 matched using matching without replacement to SLE patients on index year, age, gender, and geographic region. Data were pooled across all three years. Continuous variables and proportions were compared with t-tests or Chi-square tests, respectively. Logistic models were used to evaluate the odds ratio (OR) of SLE vs controls for HRU and QOL outcomes. Generalized linear models (GLM) were used to assess mean cost differences



comparing adults with SLE to controls. The 95% confidence intervals (CI) were reported for all models adjusted for race, payer, and key comorbidities.

Results: 154 (0.16%) respondents among 96,996 adults who reported annual data in MEPS met our criteria for SLE. After applying weights to generate nationally representative estimates, SLE adults were more likely to be publicly insured (35% vs. 18%), have lower median family income ($46,925 vs. $70,624), and higher unemployment (50%

Table 1. Weighted annualized all-cause HCRU data in SLE compared to the control population

	SLE (n=490,385)		Controls (n=2,625,427)		*p*-value
	n	%	n	%	
Patients with office-based provider visits, n (%)	479,099	97.7%	2,155,953	82.1%	<0.0001
Patients with outpatient events,[a] n (%)	218,658	44.6%	572,117	21.8%	<0.0001
Patients with ER events, n (%)	152,821	31.2%	416,862	15.9%	<0.0001
Patients with inpatient events, n (%)	81,920	16.7%	300,095	11.4%	<0.0001
	Mean	SE	Mean	SE	*p*-value
Number of office-based provider visits	18.3	1.7	10.4	0.5	<0.0001
Number of outpatient events	5.6	1.2	2.2	0.1	0.0059
Number of ER events	2.5	0.1	1.4	0.0	<0.0001
Number of inpatient events	1.7	0.1	1.3	0.0	<0.0001

Table 2. Weighted annualized all-cause cost in SLE compared to the control population

	SLE (n=490,385)		Controls (n=2,625,427)		*p*-value
	Mean	SD	Mean	SD	
Total healthcare expense	**$17,270**	$1,762	$8,350	$868	<0.0001
Total prescription expense	**$4,512**	$510	$1,952	$547	0.0007

vs. 34%); however, education level did not differ compared to the non-SLE cohort. Comorbidities were significantly higher in SLE vs. non-SLE adults, including joint pain (63% vs. 33%), arthritis (61% vs 29%), hypertension (39% vs 26%), asthma (27% vs. 13%) and heart disease (24% vs. 8%). 17% percent of SLE respondents reported they were "unable to work due to illness/disabled" compared to only 3% of non-SLE adults. More SLE adults reported "delaying getting necessary care" (14% vs. 5%) and "unable to pay family medical bills" (16% vs. 5%) than the non-SLE cohort. The adjusted odds ratio of "pain limited work" was significantly higher in SLE adults vs. controls (2.5 (95% CI: 1.4,4.3)). Adults with SLE were significantly more likely to report perceived poorer physical and mental health, including a higher OR of depression (2.1 (95% CI: 1.3, 3.3)). SLE adult had a higher HRU of outpatient and ER visits with approximately twice as many annual visits. All-cause healthcare and prescription expenses were significantly higher in SLE adults compared to non-SLE patients ($17,270 vs $8,350 and $4,512 vs $1,952 respectively).

Conclusion: This study characterizes adults with SLE compared to the general non-SLE population in a nationally representative weighted data source. Overall, comorbidity, QOL, HRU and cost burden was higher in SLE compared to non-SLE adults. It is essential to understand both direct and indirect factors in HRU and cost, including patient experience, to make treatment recommendations and decrease disease burden.

Disclosure: S. Grabich, AstraZeneca, 2; **E. Farrelly**, AstraZeneca, 2; **R. Ortmann**, AstraZeneca, 3; **M. Pollack**, AstraZeneca, LP., 3; **S. Sze-jung Wu**, AstraZeneca, 3.

Abstract Number: 1270

Disease Severity and Healthcare Costs Associated with Chronic Kidney Disease in Patients with Systemic Lupus Erythematosus

Shirley Huang[1], Amy Guisinger[2], Carlyne Averell[1] and **Christopher Bell**[1], [1]GlaxoSmithKline, Research Triangle Park, NC, [2]US Value, Evidence and Outcomes, GlaxoSmithKline, Research Triangle Park, NC

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE), occurring in approximately 40% of SLE patients (pts) and often resulting in the development of chronic kidney disease (CKD) and permanent kidney damage.[1] CKD is categorized by progressive disease stages (1-5) based on kidney biopsy, ultimately resulting in end-stage kidney disease (Stage 5). While healthcare costs of CKD by stage for broad CKD populations have been quantified,[2,3] few studies have examined CKD costs among SLE pts. This study described and compared disease severity and healthcare costs for SLE pts with and without CKD in the United States of America.

Methods: A retrospective analysis (GSK Study 217378) was conducted using claims data from the Optum Research Database. Adults who had ≥2 outpatient medical claims or ≥1 inpatient claim for SLE from January 1, 2018, to December 31, 2018 (identification period), were assessed. During the identification period, SLE pts with CKD were identified based on ≥1 CKD International Classification diagnosis code and were subsequently categorized based on their highest diagnosed CKD stage (date of highest CKD stage=index). SLE pts without CKD were required to have no CKD diagnoses (date of their first SLE diagnosis=index). Pts' characteristics and disease severity were assessed for

the baseline period (12 months pre index). Healthcare costs (in 2019 US$) were assessed for the observation period (January 1, 2019, to December 31, 2019) for SLE pts with CKD (overall and by CKD stage) and SLE pts without CKD.

Results: A total of 2666 SLE patients with CKD and 9488 SLE patients without CKD met study criteria. Patients were mostly female (CKD: 86.6%; no CKD: 91.1%) with a mean (standard deviation, SD) age of 63.9 (14.1) (CKD) and 57.8 (14.5) (no CKD) years. During the baseline period, SLE patients with CKD had greater disease activity than SLE patients without CKD (moderate-severe disease: 93.9% vs 66.4%; ≥1 flare of any severity: 96.5% vs 92.0%; mean [SD] number of flares: 5.9 [3.1] vs 4.7 [2.8]). Also, 4.1% of SLE patients with CKD had evidence of biopsy versus 0.2% of SLE patients without CKD, and 76.9% had LN versus 3.0% of SLE patients without CKD. During the observation period, mean (SD) annual healthcare costs were substantially higher for SLE patients with CKD versus those without CKD ($59,956 [100,785] vs $31,652 [57,781]). In addition, costs increased with advancing stages of CKD, from $36,417 ($56,028) (Stage 1) to $152,169 ($177,656) (Stage 5) (**Figure**).

Conclusion: SLE patients with CKD had more severe disease and incurred higher annual healthcare costs compared with SLE patients without CKD. Among SLE patients with CKD, healthcare costs increased with each CKD stage progression. These results demonstrate the substantial burden of CKD in patients with SLE and highlight the need to manage SLE to prevent progression to CKD.

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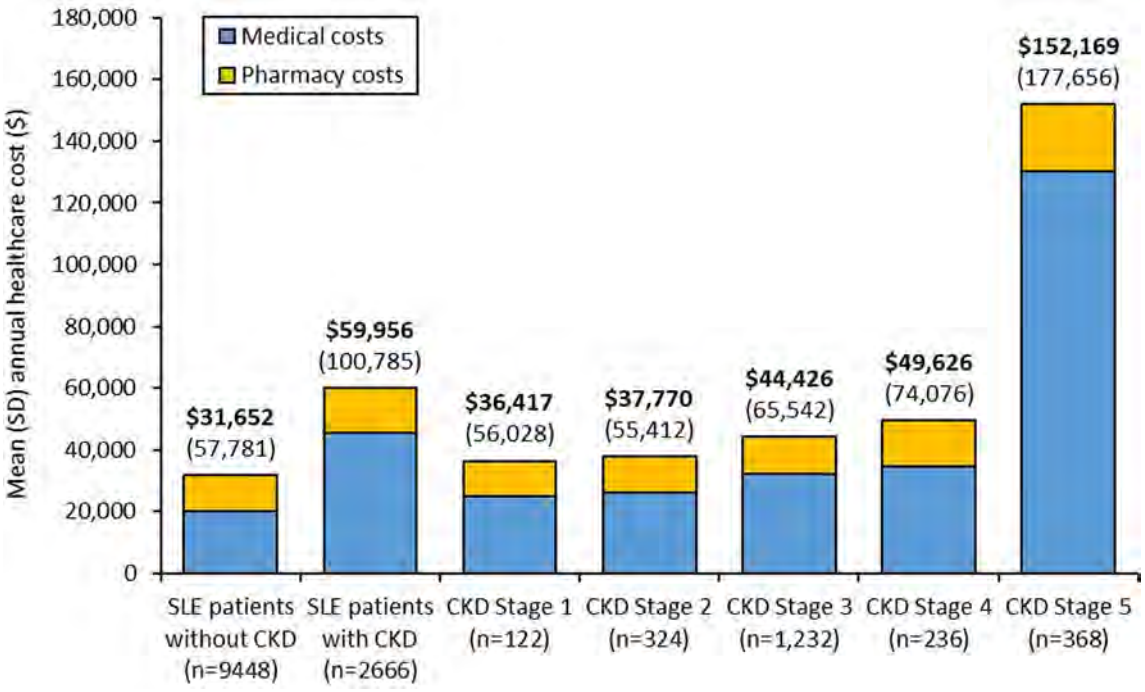

Annual healthcare cost per patient among SLE patients with and without CKD

Disclosure: S. Huang, GlaxoSmithKline, 3, 11; **A. Guisinger**, GlaxoSmithKline, 3; **C. Averell**, GlaxoSmithKline, 3, 8, 11; **C. Bell**, GlaxoSmithKline, 3, 11.

Abstract Number: 1271

Healthcare Resource Utilization and Costs Associated with Systemic Lupus Erythematosus After Diagnosis of End-Stage Kidney Disease: Evidence from Two United States Databases

Shirley Huang[1], Amy Guisinger[2] and **Christopher Bell**[1], [1]GlaxoSmithKline, Research Triangle Park, NC, [2]US Value, Evidence and Outcomes, GlaxoSmithKline, Research Triangle Park, NC

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Approximately 40% of patients with systemic lupus erythematosus (SLE) develop lupus nephritis (LN), of whom up to 20% may progress to end-stage kidney disease (ESKD).[1] Despite this substantial clinical burden, data on healthcare resource utilization (HCRU) and healthcare costs of ESKD among patients with SLE are limited. This study describes HCRU and costs for patients with SLE in the 12 months after ESKD diagnosis in the United States (US).

Methods: This was a retrospective analysis (GSK Study 215295) of two US administrative claims databases (IBM MarketScan [DB#1]; Optum Research Database [DB#2]), conducted between March 2011 and December 2019. The study population comprised adults with SLE who were newly diagnosed with ESKD between March 1, 2012, and December 31, 2018 (diagnosis based on International Classification of Disease [ICD-9/10] diagnosis codes for SLE and ESKD). HCRU and costs (2019 US Dollars) were reported for patients with 12-month continuous enrolment post ESKD diagnosis.

Results: Overall, 1356 and 425 patients with SLE and ESKD were identified in DB#1 and DB#2, respectively. Mean (standard deviation, SD) age was 46.7 (12.32) years (DB#1) and 46.3 (13.95) years (DB#2), and the majority of patients were female (DB#1: 81.8%, DB#2: 79.3%). A total of 805 (DB#1) and 261 (DB#2) patients had 12-month continuous enrollment post-ESKD diagnosis. The mean (SD) annual cost post-ESKD diagnosis was $179,914 ($272,011) (DB#1) and $160,284 ($200,000) (DB#2). Mean (SD) costs were greatest at 1 month post-ESKD diagnosis and stabilized thereafter (**Figure**). In the 12 months following ESKD diagnosis, HCRU was similar across databases: 97.9% (DB#1)

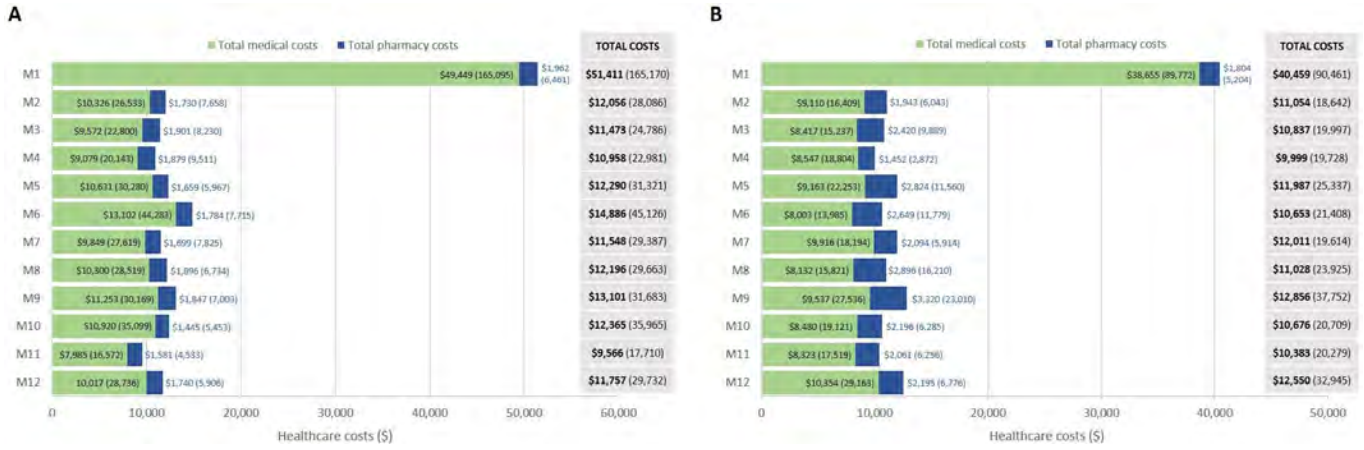

Figure. Mean (SD) healthcare costs (in 2019 US dollars) within 12 months following ESKD diagnosis. A. DB#1 (N=805), B. DB#2 (N=261).

Table 1. HCRU within 12 months following ESKD diagnosis

All-cause HCRU, n (%)	DB#1 (N=805)	DB#2 (N=261)
Any visit	805 (100.0%)	261 (100.0%)
Ambulatory	804 (99.9%)	255 (97.7%)
Physician office	788 (97.9%)	251 (96.2%)
Outpatient	747 (92.8%)	234 (89.7%)
Inpatient	553 (68.7%)	186 (71.3%)
Emergency room	383 (47.6%)	144 (55.2%)
Other*	644 (80.0%)	226 (86.6%)
Pharmacy fills	702 (87.2%)	258 (98.9%)

*Other includes ambulance, assisted living facilities, comprehensive rehabilitation facilities, custodial care facilities, hospice/home care services, intermediate care facilities, psychiatric facilities, and skilled nursing facilities

Table 2. SLE-related medications within 12 months following ESKD diagnosis

Medications, n (%)	DB#1 (N=805)	DB#2 (N=261)
Antimalarials	318 (39.5%)	110 (42.2%)
Oral corticosteroids	522 (64.8%)	194 (74.3%)
Immunosuppressants	416 (51.7%)	153 (58.6%)
Methotrexate	15 (1.9%)	4 (1.5%)
Mycophenolate	276 (34.3%)	94 (36.0%)
Cyclophosphamide	52 (6.5%)	26 (10.0%)
Azathioprine	72 (8.9%)	32 (12.3%)
Cyclosporine	27 (3.4%)	7 (2.7%)
Tacrolimus	143 (17.8%)	45 (17.2%)
Biologics	55 (6.8%)	12 (4.6%)
Rituximab	40 (5.0%)	7 (2.7%)
Belimumab	15 (1.9%)	6 (2.3%)

and 96.2% (DB#2) of patients had at least one physician office visit, 68.7% (DB#1) and 71.3% (DB#2) had an inpatient visit, and 47.6% (DB#1) and 55.2% (DB#2) had an emergency room visit (**Table 1**). SLE-related medications in the 12 months post-ESKD diagnosis included oral corticosteroids (DB#1: 64.8%, DB#2: 74.3%), immunosuppressants (DB#1: 51.7%, DB#2: 58.6%), antimalarials (DB#1: 39.5%, DB#2: 42.2%), and biologics (DB#1: 6.8%, DB#2: 4.6%) (**Table 2**).

Conclusion: Patients with SLE and newly diagnosed with ESKD had high healthcare costs and utilization 12 months post-ESKD diagnosis. Study results reflect the considerable clinical and economic burden associated with newly diagnosed ESKD among patients with SLE.

Funding: GSK

Reference: 1. Menez SP, *et al. Rev Recent Clin Trials* 2018;13:105–13

Disclosure: S. Huang, GlaxoSmithKline, 3, 11; **A. Guisinger**, GlaxoSmithKline, 3; **C. Bell**, GlaxoSmithKline, 3, 11.

Abstract Number: 1272

Characterizing Patient and Physician Perceptions of Systemic Lupus Erythematosus (SLE) Disease Burden Using Traditional Rheumatoid Arthritis Outcomes Measures

Christopher Bell[1], Shirley Huang[1], Meg Wang[2], Maral DerSarkissian[2], Mei Sheng Duh[2], Bhavna Dhillon[3], Carlyne Averell[1], Bernie Rubin[1] and Daniel Wallace[4], [1]GlaxoSmithKline, Research Triangle Park, NC, [2]Analysis Group, Boston, MA, [3]United Rheumatology, Hauppauge, NY, [4]Cedars-Sinai, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: SLE is a chronic, autoimmune disease affecting multiple organ systems, and characterized by fluctuating disease activity. Many SLE disease measures may be impractical for routine clinical practice due to administrative burden and delay in scoring while awaiting laboratory results. Patients may also feel discouraged if their laboratory results indicate improvement while their physical/mental well-being has not improved. Rheumatoid arthritis (RA)–specific disease measures are widely used to assess patients with RA. This study evaluated the use of RA disease measures among patients with SLE in United Rheumatology's community-based physician network in the United States.

Methods: A retrospective, observational analysis (GSK Study 213818) was conducted using the United Rheumatology Normalized Integrated Community Evidence (UR NICE) electronic medical records database. Patients ≥5 years of age diagnosed with SLE (≥1 encounter with an SLE International Classification of Disease-9 or 10 code) between January 1, 2010 and December 31, 2014 were assessed (date of first SLE diagnosis = index date). At least 5 years of clinical activity post-index was required. Patient characteristics were reported at index date, and certain RA disease measures were assessed during a 5-year follow-up period (Patient/Physician Global Assessment [PtGA/PGA]; Pain Index; tender/swollen joint counts [TJC/SJC]; Health Assessment Questionnaire [HAQ]; Routine Assessment of Patient Index Data 3 [RAPID3]), as counts and percentages, or means and standard deviations.

Results: Overall, 5990 patients with SLE and 5 years' follow-up met the inclusion criteria (20–59 years of age, 73.8%; female, 91.8%; commercial insurance, 63.7%; comorbid RA post-index, 9–11%) (**Table 1**). The most frequently used RA assessments included: Pain Index; TJC/SJC; HAQ, PtGA; PGA; and RAPID3. In Year 1, use of RA measures ranged from 2.0% for PGA to 36.1% for Pain Index; use increased in Year 5 (ranging from 20.0% for PGA to 59.2% for Pain Index). Across the 5-year follow-up period, mean PtGA scores were consistently higher (indicating greater

Table 1. Patient characteristics (N=5990)

Categories	
Age at index, years, n (%)	
5–19	157 (2.6)
20–39	1469 (24.5)
40–59	2951 (49.3)
60+	1413 (23.6)
Female, n (%)	5490 (91.8)
Race, n (%)	
Patients with known race	4062 (67.8)
Caucasian	2822 (69.5)
Black African ancestry	954 (23.5)
Insurance type at index, n (%)	
Commercial	3815 (63.7)
Medicaid	141 (2.4)
Medicare	2034 (34.0)
Comorbid RA diagnosis post-index, n (%)	
Year 1	631 (10.5)
Year 2	562 (9.4)
Year 3	561 (9.4)
Year 4	545 (9.1)
Year 5	540 (9.0)
Cumulative Year 1–5	870 (14.5)

Table 2. RA outcome measures for patients with SLE during the 5-year follow-up period (N=5990)

RA outcome measures	Year 1	Year 2	Year 3	Year 4	Year 5
Patient Global Assessment,* n (%)	565 (9.4)	709 (11.8)	1006 (16.8)	1409 (23.5)	2098 (35.0)
Mean (SD) score	4.9 (2.6)	4.4 (2.7)	4.3 (2.8)	4.2 (2.7)	4.2 (2.7)
Physician Global Assessment,* n (%)	119 (2.0)	222 (3.7)	471 (7.9)	802 (13.4)	1199 (20.0)
Mean (SD) score	2.4 (2.2)	1.8 (2.1)	2.3 (2.2)	2.4 (2.1)	2.5 (2.4)
Pain Index,* n (%)	2163 (36.1)	2282 (38.1)	2528 (42.2)	2907 (48.5)	3548 (59.2)
Mean (SD) score	4.2 (2.7)	4.1 (2.7)	4.1 (2.7)	4.1 (2.7)	4.1 (2.7)
Swollen Joint Count,† n (%)	1310 (21.9)	1270 (21.2)	1391 (23.2)	1523 (25.4)	1752 (29.2)
Mean (SD)	1.1 (3.0)	0.9 (2.7)	1.1 (2.9)	1.1 (2.8)	0.9 (2.7)
Tender Joint Count,† n (%)	1287 (21.5)	1233 (20.6)	1344 (22.4)	1481 (24.7)	1729 (28.9)
Mean (SD)	3.5 (5.3)	3.3 (5.2)	3.4 (5.4)	3.3 (5.3)	3.2 (5.0)
Health Assessment Questionnaire,* n (%)	971 (16.2)	958 (16.0)	1101 (18.4)	1445 (24.1)	2285 (38.1)
Mean (SD) score	1.5 (1.8)	1.7 (1.8)	1.9 (1.8)	1.9 (1.8)	2.0 (1.9)
Routine Assessment of Patient Index Data 3,* n (%)	517 (8.6)	649 (10.8)	929 (15.5)	1291 (21.6)	1959 (32.7)
Mean (SD) score	4.3 (2.2)	3.9 (2.3)	3.8 (2.3)	3.6 (2.2)	3.7 (2.3)
Remission or low disease activity, n (%)	93 (18.0)	167 (25.7)	256 (27.6)	392 (30.4)	546 (27.9)

*Scale: 0–10, where higher scores indicate higher level of disease activity.

†Scale: 0–28, where higher scores indicate higher level of disease activity.

disease activity) than PGA scores. Mean scores for Pain Index and TJC/SJC were relatively stable throughout the 5-year period (Pain Index, 4.1 to 4.2; SJC, 0.9 to 1.1; TJC, 3.2 to 3.5). Similar findings were observed for HAQ and RAPID3 (HAQ: 1.5 to 2.0; RAPID3: 3.6 to 4.3). However, the proportion of patients classified as in remission or low disease activity by RAPID3 increased over the 5-year period (Year 1, 18.0%; Year 5, 27.9%) (**Table 2**).

Conclusion: RA disease measures were used, albeit infrequently, to assess patients with SLE in a rheumatology physician network. PtGA scores consistently indicated greater disease activity than the PGA scores, which may correspond to the discordance of Pain Index and TJC/SJC results over the 5-year period. Further research is needed to better understand the utility of various RA assessments for evaluating patients with SLE. However, they may ultimately represent an efficient approach to measuring patient outcomes and improving care.

Funding: GSK

Disclosure: C. Bell, GlaxoSmithKline, 3, 11; **S. Huang**, GlaxoSmithKline, 3, 11; **M. Wang**, GlaxoSmithKline, 5; **M. DerSarkissian**, GlaxoSmithKline, 5; **M. Duh**, GlaxoSmithKline, 5; **B. Dhillon**, None; **C. Averell**, GlaxoSmithKline, 3, 8, 11; **B. Rubin**, GlaxoSmithKline, 3, 8, 11; **D. Wallace**, GlaxoSmithKline, 2, 6, Eli Lilly and Company, 2, 6, AstraZeneca, 2, 6, Aurunia, 2, 6, EMD Serono, 2.

Abstract Number: 1273

A 12-week Aerobic Exercise Training Program in Women with Systemic Lupus Erythematosus (SLE) Improves Fatigue, Mitochondrial Dysfunction and Associated Interferon Gene Signature

Sarfaraz Hasni[1], Marquis Chapman[2], Rebekah Feng[1], Anam Ahmad[1], Sarthak Gupta[3], Mohammad Naqi[1], Adam Munday[1], Shajia Lu[1], Massimo Gadina[2], Zerai Manna[1], Xiaobai Li[4], Yinghui Shi[1], Kalyani Mishra-Thakur[1], Michael Davis[5], Jun Chu[3], Elaine Poncio[6], Yenealem Temesgen-Oyelakin[7], Jonathan Martinez[1], Zoe Morris[1], Isabel Ochoa[6], Shuichiro Nakabo[8], Bart Drinkard[1], Gayle McCrossin[1], Marybeth Stockman[1], Mariana Kaplan[1], Leorey Saligan[1], Randall Keyser[9], Leighton Chan[1] and Lisa Chin[1], [1]National Institutes of Health, Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [3]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [4]Clinical Center, National Institutes of Health, Bethesda, MD, [5]NIAMS, Bethesda, MD, [6]NIH/NIAMS, Bethesda, MD, [7]National Institutes of Health (NIH), Bethesda, MD, [8]NIAMS/NIH, Bethesda, MD, [9]George Mason University, Bethesda

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue in SLE patients is ubiquitous and is reported as one of the most debilitating symptoms. Yet mechanisms underlying the pathophysiology of SLE-related fatigue are not well understood. Data from our group and others have shown that fatigue is independent of SLE disease activity. One mechanism proposed to explain fatigue is impairment in mitochondrial metabolism. Impaired mitochondrial metabolism lead to abnormal T-cell activation and effector function contributing to immune dysregulation. Type I IFN were shown to downregulate mitochondria-derived genes and metabolic pathways causing increased apoptosis of $CD8^+$ T-cells contributing to SLE pathogenesis. Regulation of mitochondrial transmembrane potential ($\Delta\psi m$) and blocking mammalian target of rapamycin (mTOR) in T-cells was shown to improve SLE disease activity and fatigue. The purpose of this study is to characterize the responses to an aerobic exercise program in SLE patients and to understand mechanisms underlying fatigue.

Methods: Sixteen female SLE patients with SELENA-SLEDAI < 4 that self-reported the presence of significant fatigue (Fatigue Severity Scale=FSS > 3) were enrolled in a supervised, aerobic exercise training program of treadmill exercise for 30 minutes, thrice a week for 12 weeks. The primary outcome measure was the time to reach the anaerobic threshold(tAT) during a cardiopulmonary exercise test (CPET). Secondary outcomes included 10 Minute

Walk Test (10MWT) distance, and self-reported changes in fatigue and health related quality of life from the FSS and the Patient-Reported Outcomes Measurement Information System (PROMIS) scores, respectively. Extracellular flux studies were done to measure mitochondrial dysfunction (MiD) by Oxygen Consumption Rate (OCR) / ExtraCellular Acidification Rate (ECAR) ratio before and after administering mitochondrial respiratory inhibitors and interferon stimulated genes (ISGs) signature by nanostring.

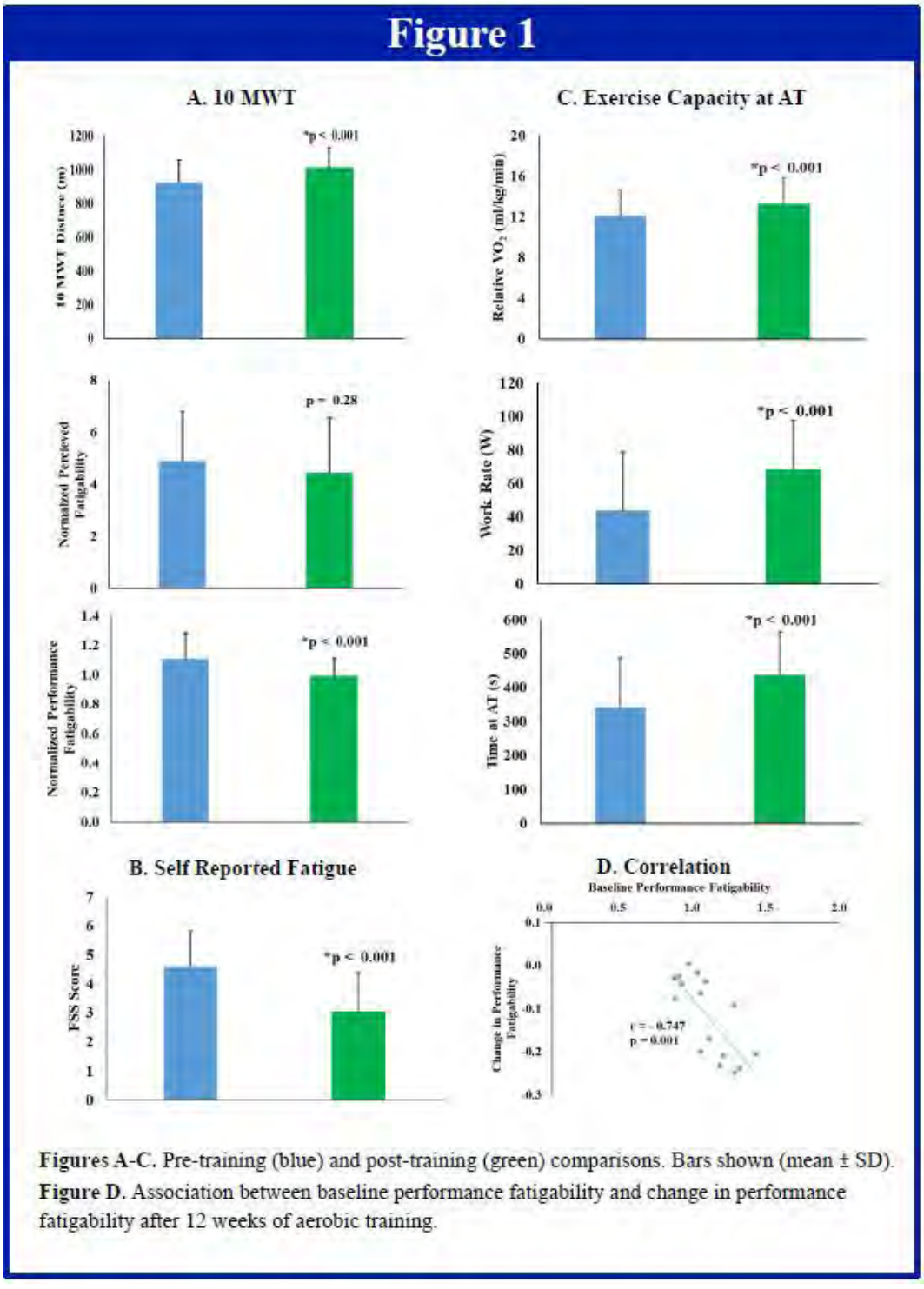

Figure 1. Pre-Exercise and post-exercise of Anaerobic Threshold(AT), 10MWT, FSS, and.

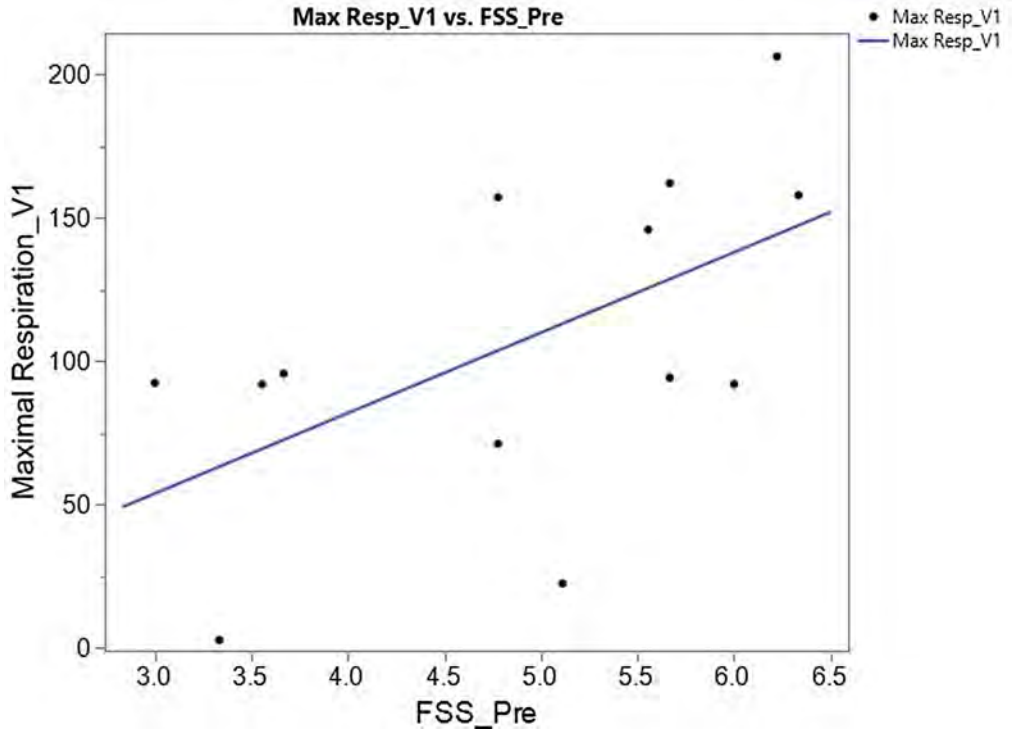

Figure 2. FSS correlates with mitochondrial maximal respiration. r = 0.59, p =0.03.

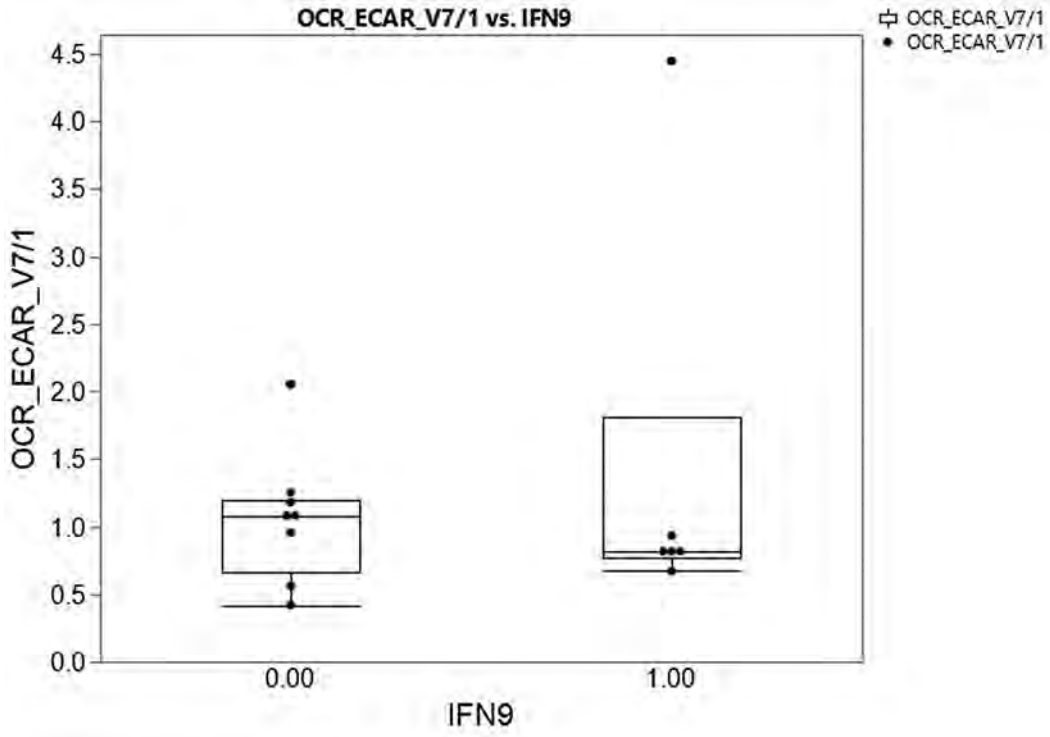

Figure 3. The 9 patients with improved IFN signature had higher increases in OCR/ECAR ratio from V1 to V7. V7-V1 indicates the difference in values between the 2 timepoints. V7/V1 indicates the ratio. p = 0.013.

Results: The mean ±SD age of subjects was 42.0 (± 10.3) years with the duration of disease 9.1 (± 6.5) years, 8/16 (50%) of subjects were Hispanic. The baseline SELENA-SLEDAI and FSS scores were mean (±SD)1.4 (± 1.9) and 4.6 (± 1.2) respectively. There were significant improvements in tAT ($p< 0.001$), 10 MWT ($p< 0.001$), total FSS score($p< 0.0001$), and most of the PROMIS domains(Figure 1). The disease activity remained unchanged throughout the study. The pre and post-exercise decrease in FSS scores correlated with increases in OCR/ECAR ratio ($r=-0.59$, $p=0.03$) (Figure 2). A subset of subjects (9/16) had significant reductions in post-exercise ISGs expression ($p=0.007$) accompanied by a significant increase in OCR/ECAR ratio ($p=0.013$)(Figure3).

Conclusion: In this study a 12- week exercise program resulted in significant improvements in physiological reserve and self-reported fatigue. Fatigue correlated with MiD which improved with exercise. The ISGs scores improved with a corresponding improvement in MiD. Larger studies are needed to confirm the role of MiD in the pathogenesis and its therapeutic targeting in management of fatigue in SLE.

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Abstract Number: 1274

Severe Flares Are Associated with a Poorer Health-Related Quality of Life (HRQoL) in Systemic Lupus Erythematosus (SLE) Patients

Manuel Ugarte-Gil[1], Rocio Gamboa-Cardenas[2], Cristina Reategui-Sokolova[3], Victor Pimentel-Quiroz[1], Mariela Medina[4], Claudia Elera-Fitzcarrald[2], Francisco Zevallos[4], Cesar Pastor-Asurza[5], Federico Zazzetti[6], Chetan Karyekar[7], Risto Perich-Campos[5] and Graciela Alarcn[8], [1]Hospital Guillermo Almenara Irigoyen, Essalud/Universidad Científica del Sur, Lima, Peru, [2]Universidad Cientifica del Sur/Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, [3]Hospital Guillermo Almenara Irigoyen, Lima, Peru, [4]Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, [5]Universidad Nacional Mayor de San Marcos/Hospital Guillermo Almenara Irigoyen. EsSalud, Lima, Peru, [6]Medical Affairs, Jan-Cil Argentina, Buenos Aires, Argentina, [7]Janssen R&D, Spring House, PA, [8]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Flares in SLE patients, regardless of their severity, have been associated with damage accrual. However, their impact on HRQoL has not been fully evaluated. In fact, disease activity is only minimally associated with HRQoL. The aim of this study is to determine the association between flares and HRQoL.

Methods: Patients from the Almenara Lupus Cohort were included. Visits occurring between December 2015 and February 2020 were included. Flares were defined as an increase on the SLEDAI-2K of at least 4 points; severe flares were those with a final SLEDAI-2K higher than 11 and mild-moderate flares all the others. HRQoL was measured using the LupusQoL. Univariable and multivariable generalized estimating regression equations were performed, adjusting for possible confounders. Confounders were determined at one visit whereas the outcome was determined on the subsequent visit; flares were determined based on the variation of the SLEDAI-2K between these visits.

Table 1: Association between flares and health-related quality of life. Multivariable models

	Physical health		Pain		Planning		Intimate relationship		Burden to others		Emotional health		Body image		Fatigue	
	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value	B (SE)	p value
Flares																
Severe	-7.0 (4.5)	0.117	**-11.9 (5.0)**	**0.018**	**-9.8 (4.4)**	**0.027**	-5.3 (9.9)	0.590	-10.4 (6.9)	0.133	**-9.3 (4.3)**	**0.030**	-10.8 (6.5)	0.097	**-6.4 (3.0)**	**0.031**
Mild-moderate	2.3 (1.7)	0.183	-1.9 (2.0)	0.355	-1.8 (1.8)	0.330	-2.4 (2.8)	0.388	-2.3 (2.6)	0.365	3.1 (1.8)	0.085	3.7 (2.8)	0.177	-0.4 (1.8)	0.858
No flares	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Male gender	3.5 (2.1)	0.094	**4.9 (2.3)**	**0.038**	3.4 (2.3)	0.145	9.7 (4.7)	0.037	1.0 (3.2)	0.744	2.1 (2.5)	0.404	2.5 (3.6)	0.487	3.4 (2.4)	0.168
Age at diagnosis, years	**-0.1 (0.0)**	**0.001**	**-0.1 (0.1)**	**0.006**	-0.1 (0.0)	0.064	-0.4 (0.1)	<0.001	0.0 (0.1)	0.699	0.0 (0.0)	0.332	0.0 (0.1)	0.708	0.0 (0.0)	0.749
Socio economic status																
High	3.3 (2.1)	0.108	4.4 (2.4)	0.071	4.2 (2.2)	0.054	6.9 (4.4)	0.112	-1.5 (2.7)	0.579	2.0 (2.0)	0.324	1.0 (3.2)	0.759	-0.2 (2.2)	0.934
Medium	2.1 (1.7)	0.228	2.6 (2.1)	0.204	0.7 (1.8)	0.721	2.0 (3.7)	0.576	0.6 (2.4)	0.783	0.0 (1.8)	0.999	-1.4 (2.9)	0.617	0.5 (1.8)	0.783
Low	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Educational level, years	-0.1 (0.2)	0.677	-0.1 (0.3)	0.611	-0.1 (0.2)	0.801	0.0 (0.6)	0.966	0.2 (0.3)	0.522	0.2 (0.3)	0.355	0.7 (0.4)	0.075	0.4 (0.3)	0.113
Disease duration	0.0 (0.1)	0.620	0.0 (0.1)	0.961	0.1 (0.1)	0.281	0.0 (0.1)	0.906	0.2 (0.1)	0.029	0.0 (0.1)	0.611	0.2 (0.1)	0.194	0.1 (0.1)	0.172
SDI	**-1.2 (0.4)**	**0.002**	**-1.1 (0.5)**	**0.016**	-0.8 (0.4)	0.059	-0.7 (0.8)	0.380	-0.7 (0.6)	0.214	-0.3 (0.4)	0.402	-0.9 (0.7)	0.206	-0.3 (0.4)	0.370
Prednisone, mg/d	**-0.1 (0.0)**	**<0.001**	**-0.1 (0.0)**	**0.029**	**-0.1 (0.0)**	**0.002**	**-0.1 (0.1)**	**0.016**	**-0.1 (0.1)**	**0.010**	0.0 (0.0)	0.538	0.0 (0.0)	0.719	**-0.1 (0.0)**	**0.013**
Antimalarial use																
Current	-1.4 (2.5)	0.571	1.1 (4.0)	0.777	-1.6 (2.5)	0.535	-5.8 (3.6)	0.108	**-6.8 (2.4)**	**0.005**	-2.0 (3.3)	0.547	4.9 (7.1)	0.497	-1.4 (2.2)	0.519
Past	-0.6 (2.9)	0.836	2.5 (4.3)	0.572	0.1 (2.8)	0.979	-2.3 (5.1)	0.648	**-6.9 (3.1)**	**0.028**	0.3 (3.8)	0.935	2.5 (7.5)	0.736	-1.3 (2.6)	0.633
Never	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Immunosuppressive drugs use																
Current	-0.9 (1.1)	0.470	-1.8 (1.4)	0.194	-1.5 (1.4)	0.286	-1.4 (2.7)	0.605	-0.6 (2.0)	0.771	1.4 (1.4)	0.265	0.3 (2.4)	0.903	1.7 (1.5)	0.237
Past	1-1 (1.4)	0.446	0.8 (1.7)	0.640	0.4 (1.6)	0.792	-1.5 (3.4)	0.670	-1.8 (2.3)	0.426	2.1 (1.6)	0.181	1.1 (2.8)	0.703	**4.2 (1.6)**	**0.010**
Never	Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.		Ref.	
Same domain of LupusQoL	0.7 (0.0)	<0.001	0.6 (0.0)	<0.001	0.6 (0.0)	<0.001	0.5 (0.0)	<0.001	0.6 (0.0)	<0.001	0.6 (0.0)	<0.001	0.5 (0.0)	<0.001	0.7 (0.0)	<0.001

SE: Standard error of the estimate. SDI: SLICC/ACR damage index

Results: Two hundred and seventy-seven patients were included; 256 (92.4%) were female, mean age at diagnosis was 36.0 (SD: 13.3) and a mean disease duration at baseline was 9.1 (SD: 7.1) years. Patients had mean of 4.8 (SD: 1.9) visits and a mean follow-up of 2.7 (1.1) years. Out of 1098 visits, 115 (10.5%) flares were defined, 17 were severe and 98 mild-moderate. After adjustment for possible confounders, only severe flares were associated with a poorer HRQoL in pain, planning, emotional health and fatigue (table 1).

Conclusion: Severe flares, but not mild-moderate flares are associated with poorer HRQoL.

Disclosure: M. Ugarte-Gil, Pfizer, 5, Janssen, 5; **R. Gamboa-Cardenas**, None; **C. Reategui-Sokolova**, Jannsen, 5; **V. Pimentel-Quiroz**, None; **M. Medina**, None; **C. Elera-Fitzcarrald**, None; **F. Zevallos**, None; **C. Pastor-Asurza**, None; **F. Zazzetti**, Janssen, 3; **C. Karyekar**, Janssen Global Services, LLC, 3, 11; **R. Perich-Campos**, None; **G. Alarcn**, None.

Abstract Number: 1275

Digital Solution for Collection of Patient-reported Outcome Measures in Patients with Systemic Lupus Erythematosus: A Randomised, Crossover, Agreement Study

Line Uhrenholt[1], Simone Høstgaard[2], Julie Pedersen[2], Robin Christensen[3], Lene Dreyer[1], Henrik Leffers[4], Peter C Taylor[5], Vibeke Strand[6], Sren Jacobsen[4], Anne Voss[7], Jon Gregersen[8] and Salome Kristensen[1], [1]Department of Rheumatology, Aalborg University Hospital, Aalborg, Denmark, [2]Department of Clinical Medicine, Aalborg University, Aalborg, Denmark, [3]Section for Biostatistics and Evidence-Based Research, the Parker Institute, Bispebjerg and Frederiksberg Hospital, Copenhagen & Research Unit of Rheumatology, Department of Clinical Research, University of Southern Denmark, Copenhagen, Denmark, [4]Copenhagen Lupus and Vasculitis Clinic, Centre for Rheumatology and Spine Diseases, Copenhagen University Hospital, Rigshospitalet, Copenhagen, Denmark, [5]University of Oxford, Oxford, United Kingdom, [6]Stanford University School of Medicine, Portola Valley, CA, [7]Department of Rheumatology, Odense University Hospital, Odense C, Denmark, [8]Department of Nephrology, Aalborg University Hospital, Aalborg, Denmark, Aalborg, Denmark

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Patient-reported outcome measures (PROMs) provide the physician with an important insight into the patients' perception of lupus disease activity. Technology and the widespread use of digital platforms have made it possible for patients to access and respond to disease specific PROMs from home using their own device.

This study aims to assess agreement in various PROMs, with Systemic Lupus Erythematosus Activity Questionnaire (SLAQ) global health as primary outcome, between a web application (app) on the patient's own smartphone/tablet and an outpatient touchscreen among patients with SLE.

Methods: The study was a randomised, crossover, agreement trial (NCT04411407). Patients diagnosed with SLE for ≥ 12 months was assessed for eligibility. Participants were randomised in a 1:1 ratio to: 1) Group web app → touch-screen i.e. PROMs answered on the web app and after a "washout period" on the outpatient touchscreen or 2) Group touchscreen → web app i.e. vice versa. The "washout period" was pre-specified to be one to two days to minimise recall bias. Agreement between the two device types was assessed using mixed linear models.

Results: In total, 34 patients were enrolled as visualised in **Figure 1**.

An excellent agreement for SLAQ global health between the two device types was observed, visualised in the Bland-Altman plot (**Figure 2**). Mean difference in SLAQ global health between the two device types was -0.21, (95% confidence interval [95% CI]: -0.65 to 0.23) (**Table 1**); thus, equivalence was demonstrated as the 95%CI was within the pre-specified equivalence margin of ± 0.75. Furthermore, equivalence was proven for all other PROMs except Visual Analogue Scale (VAS) global health. However, the observed difference in VAS global health is within the limits of the pre-specified minimum clinically important difference (MCID); thus, not anticipated to have any clinical relevance.

Thirty-one (91.2%) patients preferred the DANBIO web app over the outpatient touchscreen.

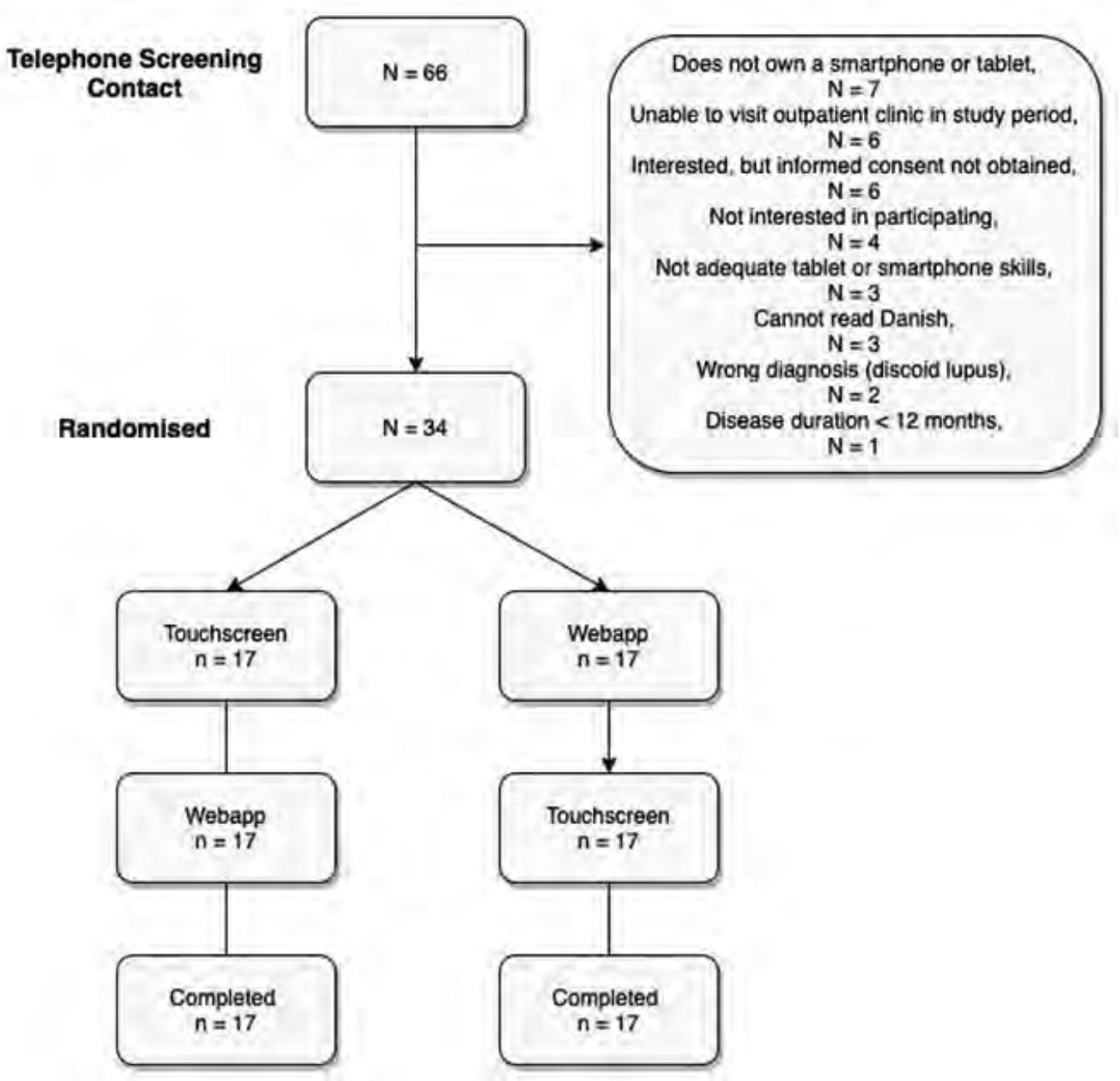

Figure 1. Flow diagram of patient recruitment.

Conclusion: To our knowledge, equivalence between two electronic device types has not previously been demonstrated for a collection of various PROMs among patients with SLE. A very high patient preference for the web app was observed. Implementation of the device is expected to be of great value for patients with SLE; thereby, improving management of their disease.

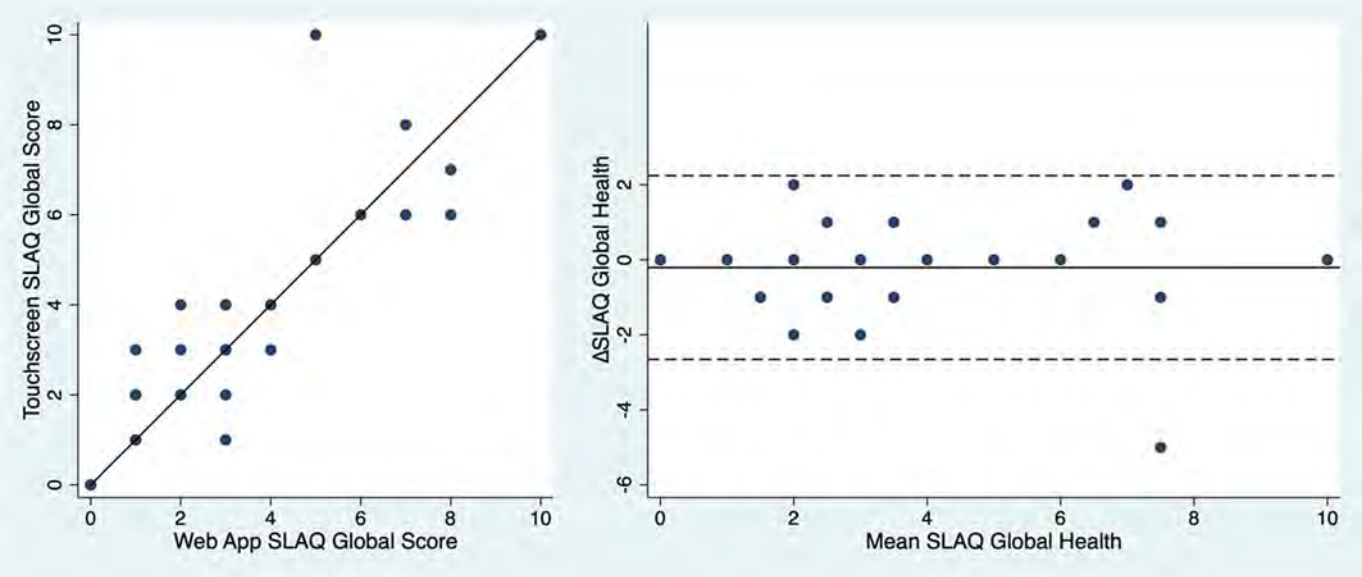

Figure 2. Bland-Altman plot on SLAQ global health registered on the two device types.

Table 2. Comparison between intervention groups for all PROMs

	Group Web App→ Touchscreen				Group Touchscreen → Web App				Difference	
	Web App		*Touchscreen*		*Touchscreen*		*Web App*		*Web App - Touchscreen*	
Outcome	***Mean***	***SE***	***Mean***	***SE***	***Mean***	***SE***	***Mean***	***SE***	***Mean difference***	***95% CI***
Primary outcome										
SLAQ global health (0-10)	2.9	0.7	3.3	0.7	3.4	0.7	3.3	0.7	-0.21	-0.65 to 0.23
Secondary outcomes										
SLAQ symptom score (0-24)	9.3	1.3	9.7	1.3	11.5	1.3	10.8	1.3	-0.56	-1.10 to -0.01
SLAQ total score (0-44)	10.2	1.8	10.0	1.8	12.2	1.8	10.8	1.8	-0.61	-1.45 to 0.22
SLAQ flare "No Flare", n (%)	11/17	64.7%	11/17	64.7%	12/17	70.6%	11/17	64.7%	28/34 (82.3%)[a]	p = 0.766[b]
HAQ-DI (0-3)	0.41	0.08	0.41	0.08	0.38	0.08	0.42	0.08	0.02	-0.01 to 0.05
VAS pain (0-100 mm)	19.7	4.5	19.3	4.5	26.6	4.5	30.1	4.5	2.0	-0.85 to 4.85
VAS fatigue (0-100 mm)	51.9	4.6	52.8	4.6	41.4	4.6	41.7	4.6	-0.3	-3.80 to 3.15
VAS global (0-100 mm)	33.3	4.1	26.0	4.1	30.6	4.1	28.7	4.1	2.7	-1.18 to 6.53
PASS "Yes", n (%)	12/17	70.6%	15/17	88.2%	12/17	70.6%	14/17	82.4%	25/34 (73.5%)[c]	p = 0.739
Anchoring question (-3 to 3)	-0.06	0.24	0.06	0.24	0.00	0.24	-0.24	0.24	-0.18	-0.46 to 0.11

SE: standard error, CI: confidence interval, SLAQ: Systemic Lupus Activity Questionnaire, n: number, HAQ-DI: Health Assessment Questionnaire disability index, VAS: Visual Analogue Scale. ***Missing values: none.***

[a]: Number and percentage of patients with no change in SLAQ flare score between the two device types i.e. SLAQ flare difference = 0.

[b]: Chi-Square test was used to assess if a significant difference in SLAQ flare score between the two device types was observed.

[c]: Number and percentage of patients with no change in PASS score between the two device types i.e. PASS difference = 0.

[d]: McNemar's test was used to assess a possible difference in PASS score between the two device types was observed.

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Abstract Number: 1276

Predictors of Remission (on and off Treatment) and Lupus Low Disease Activity State (LLDAS) in Systemic Lupus Erythematosus (SLE): Data from a Multinational, Multicenter SLICC (Systemic Lupus International Collaborating Clinics) Cohort

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Remission and LLDAS have been proposed as the goals for the treatment of SLE patients. However, the predictors of each state remain unknown. The aim of this study was to determine predictors of remission and LLDAS.

Methods: We studied patients from a long-term longitudinal multinational, multiethnic SLE inception cohort followed for a mean of 6.5 years; eligible patients were those completing at least two annual visits. Three outcomes were established: 1. Remission off treatment, defined as a SLEDAI-2K (excluding serology) =0, without prednisone (PDN) and immunosuppressive drugs (IS). 2. Remission on treatment, defined as a SLEDAI-2K (excluding serology) =0, PDN≤5

mg/d and maintenance IS drugs (based on the 2017 DORIS definition). 3. LLDAS, defined as a SLEDAI-2K≤4 with no activity in major organ systems, with no new features of lupus disease activity compared to the previous assessment, PDN≤7.5 mg/d and maintenance IS drugs (based on the Asia Pacific Lupus Consortium definition). Antimalarials were allowed in all groups. Possible predictors included were sex, age at diagnosis, ethnicity, educational level, SLEDAI-2K at cohort entry, disease duration at baseline, highest PDN dose before baseline, number of methylprednisolone (MP) IV pulses as well as mean dose per pulse before baseline. Antimalarial use and the SLICC/ACR damage index (SDI) were time-dependent covariates. Three outcome groups were defined after exclusion of patients who had already achieved the outcome at baseline. Univariable and multivariable interval-censored survival regression models for each outcome (stepwise selection procedure, including age at diagnosis and sex in all models) were used. Alternative models including SLEDAI-2K's domains instead of the global score were performed.

Results: Remission off treatment was achieved in 367 of 1243 patients (29.5%), remission on treatment in 749 of 1185 patients (63.2%), and LLDAS in 833 of 1151 patients (72.4%). Non-Caucasian ethnicity (in particular African) as well as a higher SLEDAI-2K scores and glucocorticoid (GC) dose (oral PDN as well as MP pulses) were associated with a lower probability of achieving these states. Older age at diagnosis and antimalarial use during the follow-up period were associated with a higher probability of remission on treatment and LLDAS. Disease duration at baseline was associated with a lower probability of remission off treatment. Sex, educational level, and the SDI were not associated with any of these states. These data are summarized in Table 1. In the alternative models, the SLEDAI-2K domains associated with a lower probability of achieving at least one of the outcomes were mucocutaneous (all outcomes), renal (remission off treatment and LLDAS), fever (remission off treatment) and musculoskeletal and neurological (LLDAS).

Conclusion: Older age at diagnosis and antimalarial use during follow-up were associated with a higher probability of achieving these treatment goals; on the other hand, non-Caucasian ethnicity (in particular African), a higher

Table 1: Predictors of Remission (off and on) Treatment and LLDAS*

	Remission off treatment N=1243	Remission on treatment N=1185	LLDAS N=1151
	HR (CI95%)	HR (CI95%)	HR (CI95%)
Male sex	0.705 (0.471-1.054)	0.835(0.645-1.082)	0.925 (0.736-1.162)
Age at diagnosis	1.008 (0.999-1.016)	1.008 (1.002-1.014)	1.007 (1.001-1.013)
Ethnicity			
Caucasian, US	Ref	Ref.	Ref.
Caucasian, other	0.925 (0.679-1.261)	1.115 (0.906-1.373)	1.182 (0.951-1.470)
African	0.676 (0.476-0.961)	0.689 (0.538-0881)	0.722 (0.571-0.913)
Asian	0.645 (0.443-0.938)	0.838 (0.648-1.085)	1.066 (0.839-1.354)
Hispanic	0.474 (0.323-0.698)	0.968 (0.768-1.219)	0.928 (0.748-1.152)
Other	0.818 (0.439-1.526)	1.001 (0.611-1.641)	0.9782 (0.593-1.592)
SLEDAI-2K			
<=4	Ref.	Ref.	Ref.
5-10	0.725 (0.567-0.928)	0.759 (0.640-0.899)	0.651 (0.553-0.766)
>10	0.496 (0.344-0.714)	0.746 (0.611-0.911)	0.635 (0.524-0.770)
Disease duration at baseline	0.583 (0.420-0.807)		
Highest PDN dose before baseline, mg/day			
<=5	Ref.	Ref.	Ref.
5-10	0.400 (0.266-0.602)	0.673 (0.489-0.925)	0.565 (0.406-0.786)
10-30	0.288 (0.212-0.392)	0.506 (0.407-0.629)	0.405 (0.324-0.505)
>30	0.373 (0.282-0.493)	0.596 (0.484-0.734)	0.517 (0.421-0.635)
MP pulses, mean dose/pulse, g.	0.084 (0.014-0.515)	0.477 (0.306-0.744)	0.559 (0.360-0.869)
Antimalarials use		1.305 (1.102-1.545)	1.318 (1.121-1.549)

LLDAS: Low lupus disease activity state, SLEDAI-2K: systemic lupus erythematosus disease activity index 2000, SDI: SLICC/ACR damage index. PDN: prednisone, MP: Methyl prednisolone. *Only variables which remained in the models were included.

SLEDAI-2K, a longer disease duration at baseline and a higher dose of GC (PDN or MP pulses) early in the course of the disease were associated with a lower probability of achieving these treatment goals.

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Abstract Number: 1277

Patient Perspectives on Two Distinct Patterns of Type 2 SLE Symptoms

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

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Background/Purpose: The Type 1 & 2 SLE Model was developed to better characterize the signs and symptoms of SLE. Type 1 SLE consists of inflammatory manifestations like arthritis, nephritis, and rashes; Type 2 SLE includes symptoms of fatigue, myalgia, mood disturbance, and cognitive dysfunction. In this study, we explored patient experiences living with Type 2 SLE symptoms.

Methods: Semi-structured in-depth interviews were conducted among adult participants meeting ACR or SLICC criteria for SLE. Participants were purposefully selected for age, race, sex, and nephritis history. All interviews were audio-recorded and transcribed. Data were analyzed through episode profile analysis. Two rheumatologists and a lupus researcher independently read transcripts, summarized patterns of Type 1 & 2 SLE symptoms described by participants, and identified broader themes about the relationship between Type 1 & 2 SLE symptoms. Through this process, two patterns of Type 2 SLE symptoms were identified. The two patterns were then descriptively compared.

Results: We interviewed 42 patients with SLE (93% female, 52% Black, mean age 45 years, mean disease duration 15 years). All but two participants reported experiencing Type 2 SLE symptoms at some point during their disease course.

Type 2 SLE Pattern: Two patterns of Type 2 SLE were identified: intermittent or resolving (n=18) and persistent or pervasive (n=24). Patients with intermittent Type 2 often experience Type 2 symptoms in tandem with or as a result of Type 1 symptoms. In these patients, Type 2 symptoms improve and are often not present when Type 1 disease is inactive, leaving these patients feeling generally well. In contrast, patients with persistent Type 2 experience Type 2 symptoms regardless of Type 1 symptoms. For these patients, Type 2 symptoms are always present, although the severity may fluctuate.

Demographics: Compared to patients with persistent Type 2, patients with intermittent Type 2 were typically younger (39 vs. 50 years old) and more often Black (67% vs. 42%).

Self-Reported Symptoms during Disease Course: A majority of participants in both groups reported they had experienced brain fog and depression, and all but two participants reported experiencing fatigue. Almost all had experienced traditional lupus symptoms of joint pain, hair loss, and rash. Participants in the persistent Type 2 group were more likely to describe experiencing anxiety, muscle pain, and widespread pain.

Clinical Criteria: Almost all participants met musculoskeletal and mucocutaneous SLE criteria. However, more patients with intermittent Type 2 met renal, hematologic, and immunologic criteria.

Conclusion: Almost all patients in our study experienced Type 2 symptoms, and we found two unique patterns of Type 2 SLE: intermittent and persistent. Patients with intermittent Type 2 SLE have more internal SLE manifestations and feel generally well when Type 1 is inactive. Patients with persistent Type 2 always experience Type 2 symptoms despite inactive Type 1. We hypothesize some degree of Type 2 symptoms in each group might be inflammation-driven; however, the persistence of Type 2 in one group suggests different underlying pathophysiology.

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Clinical Outcomes in a Cohort of Puerto Ricans with Systemic Lupus Erythematosus After SARS CoV-2 Infection

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The coronavirus disease 2019 (COVID-19) pandemic is of particular concern for people with autoimmune rheumatic diseases and for those who are immunosuppressed given the risk for complications during and after the acute infection. Some studies on SLE have been reported, but most have evaluated the clinical manifestations, complications, and outcomes of COVID-19 rather than the impact on lupus. As seen for other viral infections, COVID-19 could induce an exacerbation of lupus. Therefore, we studied the short- and mid-term clinical outcomes after COVID-19 in a cohort of lupus patients.

Methods: A cohort of adult Puerto Ricans with SLE (per 1997 American College of Rheumatology classification criteria) was studied from March 2020 to May 2021. Demographic parameters, COVID-19 manifestations, SLE manifestations, disease activity (per Systemic Lupus Erythematosus Disease Activity Index ([SLEDAI]), disease damage (per Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index [SDI]), pharmacologic treatment, SLE exacerbations, emergency room (ER) visits, and hospitalizations were ascertained. SARS CoV-2 infection was confirmed by polymerase chain reaction test. The proportion of COVID-19 cases was compared to the entire population of Puerto Rico per data provided by the Department of Health.

Results: Of the entire SLE cohort (n=337), 18 patients (5.3%) had COVID-19. During the same study period, 3.7% of the adult population of Puerto Rico had COVID-19, but this was not statistically different from that observed for SLE patients (p=0.11). The mean (standard deviation [SD]) age of SLE patients that had COVID-19 was 43.7 (8.9) years; 94.4% were female. Except for one patient who had COVID-19 pneumonia requiring hospitalization and oxygen therapy, the rest had mild symptoms (77.8%) or were asymptomatic (22.2%). The main COVID-19 manifestations were anosmia (50.0%), myalgias (50.0%), polyarthralgia (35.7%), headaches (35.7%), fever (22.6%), and fatigue (22.6%). At the time of COVID-19, patients had mean (SD) SLEDAI and SDI scores of 0.7 (0.3) and 1.0 (1.1), respectively, and were receiving therapy with hydroxychloroquine (72.2%), corticosteroids (66.7%), mycophenolate mofetil (50.0%), tacrolimus (11.1%), and azathioprine (11.1%). Patients were followed for a mean (SD) period of 6.8 (2.8) months. During the follow-up, none had disease exacerbations, ER visits, hospitalizations, or worsening of disease activity or damage accrual.

Conclusion: In this group of Puerto Ricans with SLE, 5.3% had COVID-19. All patients had low disease activity or were in clinical remission at the time of infection. After a mean follow-up of nearly 7 months after infection, none had disease exacerbations or damage accrual. This study suggests that COVID-19 does not have a negative impact in the short and mid-term clinical outcomes of these patients.

Disclosure: A. González-Meléndez, None; **L. Vilá**, None.

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Impact of Active Lupus Nephritis in Patient-Reported Outcomes from a Latin American, Multicenter Lupus Cohort

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SESSION INFORMATION

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multiple and heterogeneous clinical manifestations that may negatively affect these patients' quality of life (QoL) and their levels of activity and productivity, despite overall progress in treatment of the disease. The aim of this study is to assess lupus quality of life (LupusQol) and work productivity and activity impairment (WPAI) of daily life in a SLE multicenter Latin American cohort (GLADEL 2.0, *Grupo Latino Americano De Estudio del Lupus*) among patients with active lupus nephritis (LN) versus those without LN (never) and/or currently inactive LN.

Methods: The GLADEL 2.0 cohort enrolled SLE patients >18 years of age, from three different subsets: Group I: SLE patients, without renal involvement (never); Group II: SLE patients with prevalent renal involvement (at any time during their disease course), currently inactive; Group III: SLE patients with prevalent or incident renal involvement, currently

Table 1. Demographic and Clinical Characteristics of SLE Patients from the GLADEL 2.0 Cohort

	Total (n=849)	Group I LN never (n=344)	Group II Inactive LN (n=205)	Groups III Active LN (n=300)	p_value
Female n(%)	755 (88.93)	316 (91.86)	184 (89.76)	255 (85.00)	0.020
Age, yrs*median (IQR)*	37 (29-47)	40 (31-49)	39 (32-49)	31 (26-39)	< 0.001
Disease duration, months *median (IQR)*	88.5 (40-159.8)	94 (51-161)	135 (74-208)	52 (22-123)	0.009
Education level, yrs *median (IQR)*	12 (11-16)	12 (11-16)	13 (11-16)	12 (11-16)	0.266
Ethnic group n(%)					0.014*
Caucasian	209 (24.62)	100 (29.07)	57 (27.8)	52 (17.33)	
Mestizo	562 (66.20)	212 (61.63)	131 (63.9)	219 (73.00)	
Amerindio	7 (0.82)	4 (1.16)	2 (0.98)	1 (0.33)	
Afro-Latin American	66 (7.77)	26 (7.56)	13 (6.34)	27 (9.00)	
Socioeconomic status n(%)					0.010*
High/High-middle	199 (23.44)	83 (24.13)	66 (32.2)	50 (16.67)	
Middle	301 (35.45)	122 (35.47)	66 (32.2)	113 (37.67)	
Middle-low/Low	345 (40.64)	136 (39.54)	73 (35.6)	136 (45.33)	
Employment status, n(%)					< 0.001
Full time job	335 (39.46)	144 (41.86)	94 (45.85)	97(32.33)	
Part time job	106 (12.49)	42 (12.21)	26 (12.68)	38(12.67)	
Unemployed	120 (14.13)	56 (16.28)	19 (9.27)	45(15.0)	
Unemployed (due to SLE)	140 (16.49)	44 (12.79)	30 (14.63)	66(22.0)	
Student	78 (9.19)	26 (7.56)	14 (6.83)	38(12.67)	
Retired	41 (4.83)	25 (7.27)	12 (5.85)	4(1.33)	
Comorbidities , n(%)	300 (35.34)	93 (27)	90 (44)	117 (39.0)	< 0.001
SLEDAI*median (IQR)*	4 (0-10)	2 (0-6)	2 (0-4)	12 (8-18)	<0.001
SDI*median (IQR)*	0 (0-1)	0 (0-1)	0 (0-2)	0 (0-1)	0.019
Anti- dsDNA antibodies n(%)	647 (76.20)	219 (64.22)	163 (79.51)	265 (88.93)	< 0.001
Hypocomplementemia (C3, C4, CH50) n(%)	687 (80.92)	240 (69.77)	170 (82.93)	277 (92.33)	<0.001
Treatment n(%)					
Oral Glucocorticoids n(%)	599 (70.55)	205 (59.59)	120 (58.54)	274 (91.33)	<0.001
Intravenous Glucocorticoids n(%)	115 (13.55)	13 (3.78)	8 (3.9)	94 (31.33)	<0.001
Antimalarials n(%)	653 (76.91)	268 (77.91)	164 (80)	221 (73.67)	0.739
Immunosuppressors[1] n (%)	545 (64.19)	193 (56.1)	137 (66.83)	215 (71.67)	<0.001

PGA: Physician Global Assessment. SLEDAI-2k: Systemic Lupus Erythematosus Disease Activity Index. SDI: damage with the SLICC/ACR Damage Index. Immunosuppressors1: Mycophenolate, Methotrexate, Azathioprine, Oral Cyclophosphamide, Intravenous Cyclophosphamide, Tacrolimus, Ciclosporin A.

Table 2. LupusQol Responses by Domain in the GLADEL 2.0 Cohort Patients from the Different Groups

LupusQol Domain n (%)	Total 836 (98.47)	Group I LN never 338 (98.26)	Group II Inactive LN 204 (99.51)	Groups III Active LN 294 (98.0)	p_value
Physical Health n (%)	715 (85.53)	289 (85.50)	157 (76.96)	269 (91.5)	<0.001
Pain n (%)	575 (68.78)	235 (69.53)	114 (55.88)	226 (76.87)	<0.001
Planning n (%)	545 (65.19)	212 (62.72)	104 (50.98)	229 (77.89)	<0.001
Intimate Relationshipn n (%)	402 (48.09)	163 (48.22)	78 (38.24)	161 (54.76)	0.001
Burden to others n (%)	743 (88.88)	296 (87.57)	165 (80.88)	282 (95.92)	<0.001
Emotional Health n (%)	733 (87.68)	293 (86.69)	160 (78.43)	280 (95.24)	<0.001
Body Image n (%)	601 (71.89)	241 (71.30)	128 (62.75)	232 (78.91)	<0.001
Fatigue n (%)	731 (87.44)	293 (86.69)	164 (80.39)	274 (93.20)	<0.001
Lupus QoL questions within each domain were categorized as: never or present at different degree					

Lupus QoL questions within each domain were categorized as: never or present at different degree Percentages reflect positive responses (i.e., present) on the QOL questions

Table 3. Evaluation of Work Productivity with the WPAI in GLADEL 2.0 Cohort Patients from the Different Groups

WPAI n (%)	Total 795 (93.64)	Group I LN never 324 (94.19)	Group II Inactive LN 200 (97.56)	Groups III Active LN 271 (90.33)	p_value
Question 1 *Currently employed, n (%)*	357 (44.91)	144 (44.44)	105 (52.50)	108 (39.85)	0.024
Question 5* *Degree health affected productivity while working, median (IQR)*	2 (0-5)	1.5 (0-4.25)	0 (0-3)	4 (0-7)	<0.001
Question 6* *Degree health affected regular activities, median (IQR)*	4 (0-6)	3 (0-6)	1.5 (0-5)	5 (2.25-8)	<0.001
*Questions 5 and 6 measures a scale from 0 to 10 being 10 the highest involvement					

*Questions 5 and 6 measures a scale from 0 to 10 being 10 the highest involvement

active. Disease activity was ascertained with the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2k) and the Physician Global Assessment (PGA) and damage with the SLICC/ACR Damage Index (SDI). The differences in the baseline Lupus QoL (questions were categorized as never or present at different degree) and WPAI-Lupus [Questions 1 (Currently employed), 5 (Degree health affected productivity while working) and 6 (Degree health affected regular activities)] were analyzed among these three groups. We particularly were interested in examining in more detail Question 6 of the WPAI, that focus on activities of daily living and which is answered by everybody regardless of

whether they are working or not. Numeric variables are reported as medians (interquartile ranges IQR) and compared using Wilcoxon test; categorical variables are reported as frequencies (percentages) and compared using Chi-square or Fisher test, as appropriate. To evaluate the impact of active versus inactive LN in WPAI (Question 6), a multivariate analysis (MV) was adjusted for possible confounders such as: sex, age, socioeconomic level, ethnicity, education, activity and damage in a negative binomial model.

Results: A total of 849 patients with a diagnosis of SLE were included; 344 in Group I, 205 in Group II and 300 in Group III. Their main sociodemographic and clinical features are shown in Table 1. Patients with active LN (group III) had a higher proportion of male patients, were younger at diagnosis, had a shorter disease duration and higher SLEDAI and PGA scores. This group of patients also presented greater impact in all LupusQoL domains (Table 2) and in the WPAI (Table 3). Moreover, the MV analysis for Question 6 of the WPAI demonstrate a significant higher degree health regular activities impairment and active LN after adjusting for confounders (p=0.02) (Data not shown).

Conclusion: In this cohort, we have shown that active LN significantly affects the patients' QoL especially in their physical health, emotional health, body image and fatigue. In addition, an impact in work productivity and activity impairment was observed in this group.

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Generation of Evidence Supporting the Content Validity of SF-36, Lupus-Qol, and FACIT-Fatigue, and Newly Developed Patient-reported Outcome (PRO) Symptom Items to Address Conceptual Gaps for Use in Patient with Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is an autoimmune disease characterized by inflammation of the kidneys, a severe manifestation of systemic lupus erythematosus (SLE) that occurs in approximately 50% of SLE patients. To evaluate treatment benefit effectively, it is critical that patient-reported outcome (PRO) measures are fit-for-purpose and have strong evidence of content validity in the specific context of use, to serve as trial endpoints and support product label claims. SF-36, Lupus-QoL, and FACIT-Fatigue are commonly used clinical trial endpoints in SLE populations, with demonstrated evidence of content validity in this population. Similar evidence of their content validity in an LN population is lacking. A prior qualitative literature and online blog review and concept elicitation interviews with LN patients identified key symptoms (i.e., skin rash, joint pain, joint stiffness, and swelling of the legs/feet) and symptom properties (i.e., severity) not adequately assessed by these three PRO measures. Novel PRO symptom severity items were developed to address conceptual gaps. This study aimed to evaluate the content validity of SF-36, Lupus-QoL, FACIT-Fatigue, and novel PRO items in a sample of LN patients.

Methods: Qualitative, semi-structured, telephone cognitive interviews were conducted with 20 US adult patients with a diagnosis of LN. To evaluate the content validity of the existing PRO measures, participants' understanding and relevance of the concepts to their experience of LN was assessed. Participants completed the novel PRO items using a 'think aloud' process. Questioning explored understanding and relevance of item wording, instructions, different recall periods (24-hour vs 7-day), and response scales (numeric rating scale (NRS) vs verbal response scale). Interviews were conducted in two rounds to allow for modifications to novel PRO items and subsequent re-testing. Qualitative analysis of verbatim interview transcripts was performed.

Results: Symptom and impact concepts assessed by SF-36, Lupus-QoL, and FACIT-Fatigue were well understood, with most considered relevant by the majority of participants asked. Symptoms assessed by the novel PRO items were considered relevant to most participants. Participant feedback informed modifications to the novel PRO items and instructions to improve clarity and understanding between rounds. Each iteration of the item wording and instructions were understood and interpreted consistently by all participants asked. The selected 7-day recall period and NRS in the final iteration of the PRO items were understood, relevant, and appropriately endorsed.

Conclusion: Findings support the content validity of the symptom and impact concepts assessed by SF-36, Lupus-QoL, FACIT-Fatigue in LN patients, providing evidence of their suitability as supportive efficacy endpoints in LN randomized controlled trials. Content validity evidence was also generated for the novel PRO items in LN patients, supporting their suitability to address conceptual gaps in existing PRO measures. Further research is required to establish the psychometric validity of the novel PRO items in a LN population.

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Abstract Number: 1281

Longitudinal Association of Baseline Frailty with Patient-Reported Outcome Measures

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SESSION INFORMATION
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Background/Purpose: Frailty has been associated with disability and mortality in systemic lupus erythematosus (SLE). While frailty is known to be associated with worse patient-reported outcome measures (PROMs) cross-sectionally, the extent to which frailty, particularly the self-reported FRAIL scale (FS) [1], predicts poor health-related quality of life (HRQoL) longitudinally in SLE is not well understood. We aimed to assess the association of baseline frailty according to two validated metrics, the FS and the Fried phenotype (FP) [2], with PROMs at 1 year in a single center prospective cohort of women with SLE.

Methods: Women 18 to 70 years old with SLE validated according to the 1997 Update of the 1982 American College of Rheumatology Revised Classification Criteria and mild or moderate disease activity were identified prospectively at a single center. Multiple measures were obtained at baseline and 1 year, including frailty (FS, an entirely self-reported instrument, and the FP, including objective and self-reported components); physician-reported disease activity and damage; and PROMs (including Patient-Reported Outcomes Measurement Information System (PROMIS) computerized adaptive tests and Valued Life Activities (VLA) self-reported disability). Differences between frail and non-frail participants according to each frailty metric were evaluated using Fisher's exact or Wilcoxon rank sum tests and the association of baseline frailty with disability (as defined by the upper quartile of VLA scores) at 1 year using logistic regression.

Results: Of 72 women enrolled at baseline, 1-year follow-up data were available for 51 women (71%). Among these 51 women, 24% and 16% were frail at baseline according to the FS and the FP, respectively (Table 1). Frail women had greater disease damage at baseline than non-frail women (FS: $p< 0.01$; FP: $p=0.02$); compared to non-frail women, frail women according to the FS had lesser educational attainment ($p=0.05$) while frail women according to the FP were more often Black or African American ($p< 0.01$), had greater comorbidity burden ($p=0.04$), and were more commonly smokers over their lifetime ($p=0.04$) (Table 1). Women who were frail at baseline had worse PROMIS measures related to mobility (FS and FP: $p< 0.01$), physical function (FS and FP: $p< 0.01$), pain interference (FS: $p< 0.01$; FP: $p=0.01$), and fatigue (FS: $p< 0.01$; FP: $p=0.02$) and greater VLA disability (FS and FP: $p< 0.01$) at 1 year than women who were not frail at baseline (Table 2). Baseline frailty according to either metric was not associated with VLA disability at 1 year (FS: Odds ratio (OR) 2.1, 95% confidence interval (CI) 0.5-8.9; FP: OR 4.0, 95% CI 0.8-19.5).

Conclusion: Women with SLE who were frail at baseline had worse HRQoL at 1 year than non-frail women. Baseline frailty was not longitudinally associated with self-reported disability at 1 year according to either frailty metric in this small sample of women with SLE. Longitudinal follow-up is underway to determine whether frailty status trajectory may be a more informative predictor of self-reported disability.

Table 1. Baseline characteristics of women with SLE by frailty classification

Characteristic (Median and interquartile range unless otherwise specified)	FRAIL Scale (N=51)			Fried Definition (N=51)		
	Non-frail (N=39)	Frail (N=12)	p-value	Non-frail (N=43)	Frail (N=8)	p-value
Age (years)	46.0 [28.0, 58.0]	55.0 [39.5, 64.0]	0.07	46.0 [31.0, 59.0]	56.0 [36.0, 64.0]	0.15
Race, N (%) Asian Black or African American White Other or declined to state	 2 (5.3) 13 (34.2) 12 (31.6) 11 (29.0)	 0 (0) 5 (41.7) 4 (33.3) 3 (25.0)	1.00	 2 (4.7) 11 (25.6) 17 (35.4) 12 (25.0)	 0 (0) 7 (100.0) 0 (0) 0 (0)	<0.01
Ethnicity, N (%) Hispanic Non-Hispanic	 9 (24.3) 28 (75.7)	 4 (33.3) 8 (66.7)	0.71	 13.0 (31.0) 29 (69.1)	 0 (0) 7 (100.0)	0.17
Educational attainment High school or less Some college College Graduate or professional school	 2 (5.1) 10 (25.6) 17 (43.6) 10 (25.6)	 5 (41.7) 2 (16.7) 3 (25.0) 2 (16.7)	0.05	 6 (14.0) 9 (20.9) 17 (39.5) 11 (25.6)	 1 (12.5) 3 (37.5) 3 (37.5) 1 (12.5)	0.83
SLE disease duration (years)	13.0 [6.0, 20.0]	15.5 [11.5, 30.0]	0.09	13.0 [6.0, 25.0]	14.0 [11.5, 16.5]	0.78
SELENA-SLEDAI* score	2.0 [0, 4.0]	4.0 [2.0, 6.5]	0.21	4.0 [1.0, 4.0]	1.0 [0, 7.5]	0.67
SLICC/ACR Damage Index** score	0 [0, 1.0]	2.0 [1.5, 4.0]	<0.01	0 [0, 2.0]	3.0 [1.0, 4.5]	0.02
Charlson Comorbidity Index	3.0 [1.0, 3.0]	3.0 [2.0, 4.5]	0.30	3.0 [1.0, 3.0]	3.5 [2.5, 6.0]	0.04
Current prednisone dose (milligrams)	5.0 [3.5, 7.8]	5.0 [3.0, 5.0]	0.34	5.0 [4.0, 7.5]	5.0 [3.0, 5.0]	0.51
Ever smoking, N (%)	6 (15.4)	4 (33.3)	0.22	6 (14.0)	4 (50.0)	0.04
Self-reported fibromyalgia, N (%)	6 (15.4)	3 (25.0)	0.42	7 (16.3)	2 (25.0)	0.62

*SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Scores range from 0-105, with higher scores indicating greater disease activity.

**SLICC/ACR Damage Index: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index. Scores range from 0-46, with higher scores indicating greater damage.

Table 2. Patient-reported outcome measures among women with SLE by frailty classification at 1 year

Characteristic (Median and interquartile range)	FRAIL scale (N=51)			Fried definition (N=51)		
	Non-frail (N=39)	Frail (N=12)	p-value	Non-frail (N=43)	Frail (N=8)	p-value
PROMIS* measure						
Mobility	46.0 [41.7, 49.7]	36.2 [33.0, 7.9]	<0.01	45.2 [40.2, 49.3]	34.6 [32.6, 38.1]	<0.01
Physical function	44.6 [38.9, 47.4]	34.3 [26.9, 35.5]	<0.01	43.5 [37.7, 47.4]	33.5 [27.8, 35.5]	<0.01
Pain behavior	56.3 [47.7, 58.8]	60.5 [55.4, 63.4]	0.02	56.3 [50.2, 59.6]	59.1 [57.9, 61.5]	0.09
Pain interference	56.0 [46.6, 61.1]	62.7 [59.9, 65.2]	<0.01	56.1 [48.9, 61.5]	63.1 [60.3, 63.9]	0.01
Fatigue	55.4 [47.4, 63.3]	64.0 [60.8, 67.9]	<0.01	56.3 [50.6, 64.0]	65.9 [57.6, 70.0]	0.02
Depression	46.1 [38.9, 58.8]	54.1 [42.3, 57.5]	0.47	49.5 [43.6, 58.8]	42.0 [36.8, 55.8]	0.30
Anxiety	52.9 [43.9, 63.3]	53.5 [43.6, 59.8]	0.97	52.9 [45.7, 59.7]	45.9 [42.0, 61.6]	0.50
Valued Life Activities† disability	0.5 [0.1, 1.0]	1.1 [0.9, 1.4]	<0.01	0.6 [0.1, 1.0]	1.0 [1.0, 1.5]	<0.01

*PROMIS: Patient Reported Outcome Measurement Information System. Scored using a T score metric, with 50 representing the population mean and a difference of 5 considered clinically significant.
†Valued Life Activities: Scores range from 0-3, with higher scores indicating greater disability.

References

1. Morley J et al. J Nutr Health Aging 2012. 16:601-8.
2. Bandeen-Roche K et al. J Gerontol A Biol Sci Med Sci 2006. 61:262-6.

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Abstract Number: 1282

Classification of Disease Activity and Damage in Cutaneous Lupus

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Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
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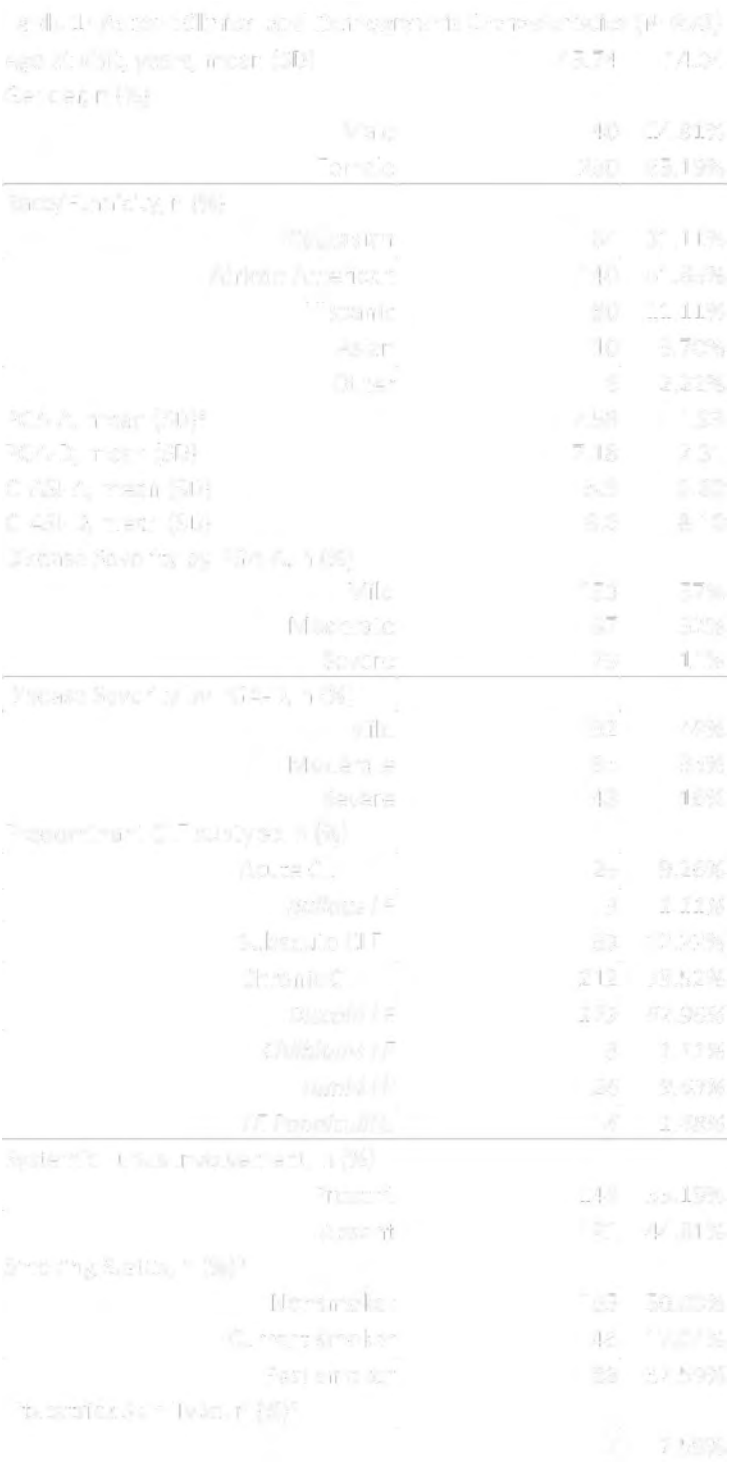
Background/Purpose: The Cutaneous Lupus Disease Area and Severity Index (CLASI) can quantify disease activity and damage in Cutaneous Lupus Erythematosus (CLE). Classification of CLASI scores provides standardized clinical context for patients and providers. A prior study used a small patient cohort to classify CLASI activity (CLASI-A) scores into mild, moderate and severe categories, but was limited by small sample size.[1] The objectives of the present study were to classify both CLASI-A and CLASI damage (CLASI-D) scores into mild, moderate, and severe categories using a large, heterogeneous cohort of CLE patients, and determine risk factors for different categories of activity and damage.

Table 1. Patient Clinical and Demographic Characteristics (N=270)



Methods: This was a single-center, cross-sectional study involving patients seen in the outpatient dermatology clinics at University of Texas Southwestern and Parkland Health and Hospital System from April 2009 to January 2020. Table 1 shows demographic and clinical features of participants. Skin severity measurements including CLASI and Physicians' Global Assessment (PGA) of Activity and Damage were scored for all patients. The anchoring outcome measure was the PGA-A and PGA-D, which classified patients into mild, moderate, and severe categories for sub-

Table 2. Percent sensitivity, specificity, and correctly classified for CLASI category ranges

		Sensitivity (%)	Specificity (%)	Correctly Classified (%)
New Disease Activity Category Ranges	Mild (0-6)	96	68	80
	Moderate (7-14)	49	93	78
	Severe (15-70)	72	96	70
Previous Disease Activity Category Ranges[a]	Mild (0-9)	99	44	70
	Moderate (10-20)	26	91	59
	Severe (21-70)	38	99	85
Disease Damage Category Ranges	Mild (0-5)	86	96	95
	Moderate (6-16)	73	83	69
	Severe (17-56)	65	90	56

[a] Klein R, Moghadam-Kia S, LoMonico J, et al. Development of the CLASI as a tool to measure disease severity and responsiveness to therapy in cutaneous lupus erythematosus. Arch Dermatol. 2011;147(2):203-208. doi:10.1001/archdermatol.2010.435

Figure 1: Characteristics associated with different categories of activity and damage.

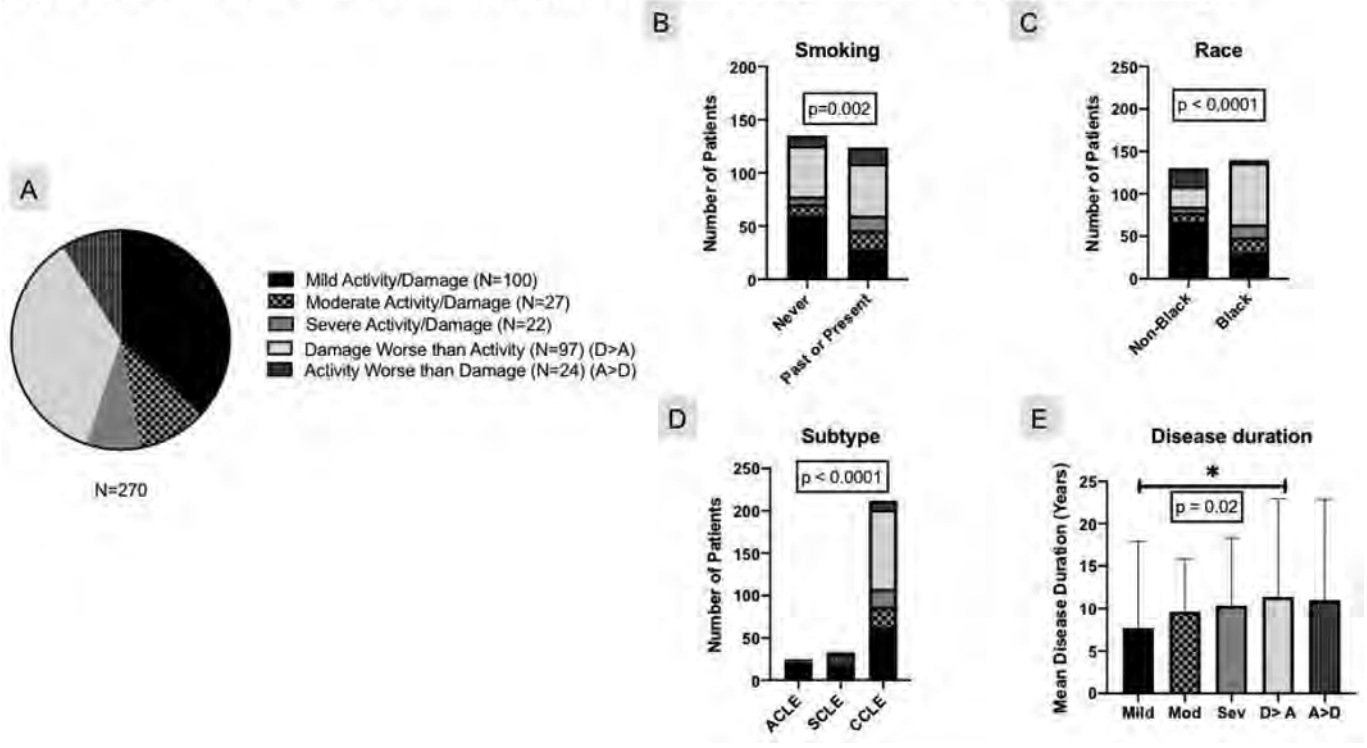


Figure 1. Characteristics associated with different categories of activity and damage.

sequent analysis with CLASI scores. Severity strata were evaluated using receiver operating characteristics (ROC) curves. Skindex-29+3 scores were collected to evaluate patient quality of life.

Results: 270 patients with CLE (**Table 1**) met recruitment criteria. CLASI-A scores of 0-6, 7-14, and 15-70 corresponded to mild, moderate, and severe disease activity. These performed better than previously published strata[1] by sensitivity,

specificity, and percent correctly classified (**Table 2**). CLASI-D scores of 0-5, 6-16, and 17-56 corresponded to mild, moderate, and severe disease damage. Patients had significantly more impaired quality of life with more severe categories of both activity and damage ($p< 0.0001$). About half (55%) of patients had matching disease activity and damage categories, with the other half having discrepant categories. Smoking ($p=0.002$), race ($p< 0.0001$), CLE subtype ($p< 0.0001$), and disease duration ($p=0.02$) were factors that were significantly different amongst the groups of activity and damage (**Figure 1**). Black race, chronic CLE, and longer disease duration were associated with disease damage disproportionately worse than disease activity. Smoking was associated with worsening severity of both activity and damage.

Conclusion: CLASI-A and CLASI-D scores can be classified into mild, moderate, and severe categories with high specificity and sensitivity using a large, diverse cohort. This will allow providers to have greater context of disease severity using CLASI scores for prognostic, clinical, and research use. Future studies across multiple cohorts will help validate these ranges.

Reference: 1. Klein R, Moghadam-Kia S, LoMonico J et al. Development of the CLASI as a tool to measure disease severity and responsiveness to therapy in cutaneous lupus erythematosus. Arch Dermatol 2011; 147:203-208. doi:10.1001/archdermatol.2010.435

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Abstract Number: 1283

Reduction in Glucocorticoid Use in Patients with Systemic Lupus Erythematosus Treated with Belimumab: A Large Pooled Analysis of 5 Placebo-Controlled Studies

Karen Costenbader[1], Yoshiyuki Abe[2], Laurent Arnaud[3], George Bertsias[4], Norma Lynn Fox[5], Mathew Gibb[6], Anne Hammer[5], Alexa Meara[7], Holly Quasny[8], David Roth[5] and Tania Gonzalez-Rivera[5], [1]Brigham and Women's Hospital, Belmont, MA, [2]Juntendo University School of Medicine, Tokyo, Japan, [3]Department of Rheumatology, French National Reference Center for Autoimmune Diseases (CRMR RESO), Strasbourg, France, [4]Rheumatology, Clinical Immunology and Allergy, University of Crete School of Medicine, Heraklion, Greece, [5]GlaxoSmithKline, Collegeville, PA, [6]Veramed Ltd., Twickenham, United Kingdom, [7]Ohio State University Wexner Medical Center, Columbus, OH, [8]GlaxoSmithKline, Research Triangle Park, NC

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Glucocorticoids (GC) play an important role in rapid systemic lupus erythematosus (SLE) symptom relief. However, chronic GC use increases organ damage risk; and treatment recommendations are to minimize/discontinue GC use when clinically possible.[1] Belimumab (BEL) is a disease-modifying SLE treatment that demonstrated a consistent efficacy profile in 4 Phase 3 trials.[2–5] This study analyzed pooled SLE data to assess whether GC reduction occurred more rapidly in patients (pts) randomized to BEL versus placebo (PBO).

Methods: Belimumab Summary of Lupus Efficacy (Be-SLE) analyzed data from 5 double-blind, PBO-controlled BEL studies in SLE: BLISS-76, BLISS-52, BLISS-NEA, BLISS-SC, and EMBRACE. The analysis compared BEL (10 mg/

kg intravenous [IV] or 200 mg subcutaneous [SC]) versus PBO (IV and SC) pooled data, collected every 4 weeks from baseline to Week 52. Although GC tapering was recommended for pts responding well to treatment, GC adjustments were at the investigator's discretion. GC use was converted to prednisone-equivalent dose (mg/day). A ≥25% GC reduction from baseline to ≤7.5 mg/day at Week 52 was a key GC endpoint in all trials. Odds ratios (OR) and 95% confidence intervals (CI) for GC dose changes were calculated using a logistic regression model with covariates of treatment, study, baseline GC dose, and (SELENA-SLEDAI score (≤9 versus ≥10).

Results: The analysis included 1869 and 1217 pts receiving BEL and PBO, respectively. Most pts were female (94.4%), with a median age of 36.0 years (range 18–77 years); baseline demographics and disease characteristics were balanced between groups. Most pts (BEL 88.2% [n=1648]; PBO 88.7% [n=1079]) received GC at baseline; mean baseline GC dose for BEL and PBO was 12.3 and 12.2 mg/day, respectively. A ≥25% GC reduction from baseline to ≤7.5 mg/day during Week 40 through Week 52 was achieved by 16.9% (n=202) of BEL recipients versus 11.9% (n=91) of PBO patients (OR: 1.52 [95% CI: 1.16–1.99], p=0.0024).

At Week 52, 33.9% of pts receiving BEL had a GC decrease from baseline, versus 27.4% with PBO (OR: 1.41 [95% CI: 1.18–1.70], p=0.0002; **Figure**). Conversely, 11.1% and 16.2% of BEL and PBO pts had a GC increase, respectively (OR: 0.65 [95% CI: 0.52–0.81], p=0.0001; **Figure**). Statistically significant differences in GC use between BEL and PBO were observed as early as Week 12 for *"any increase in GCs*," and by Week 24 for *"any decrease in GC"* (**Figure**). Mean (standard deviation) cumulative GC dose over 1 year was 4495 mg (4018.8) with BEL and 5096 mg (5641.6) with PBO (p=0.024 by analysis of covariance).

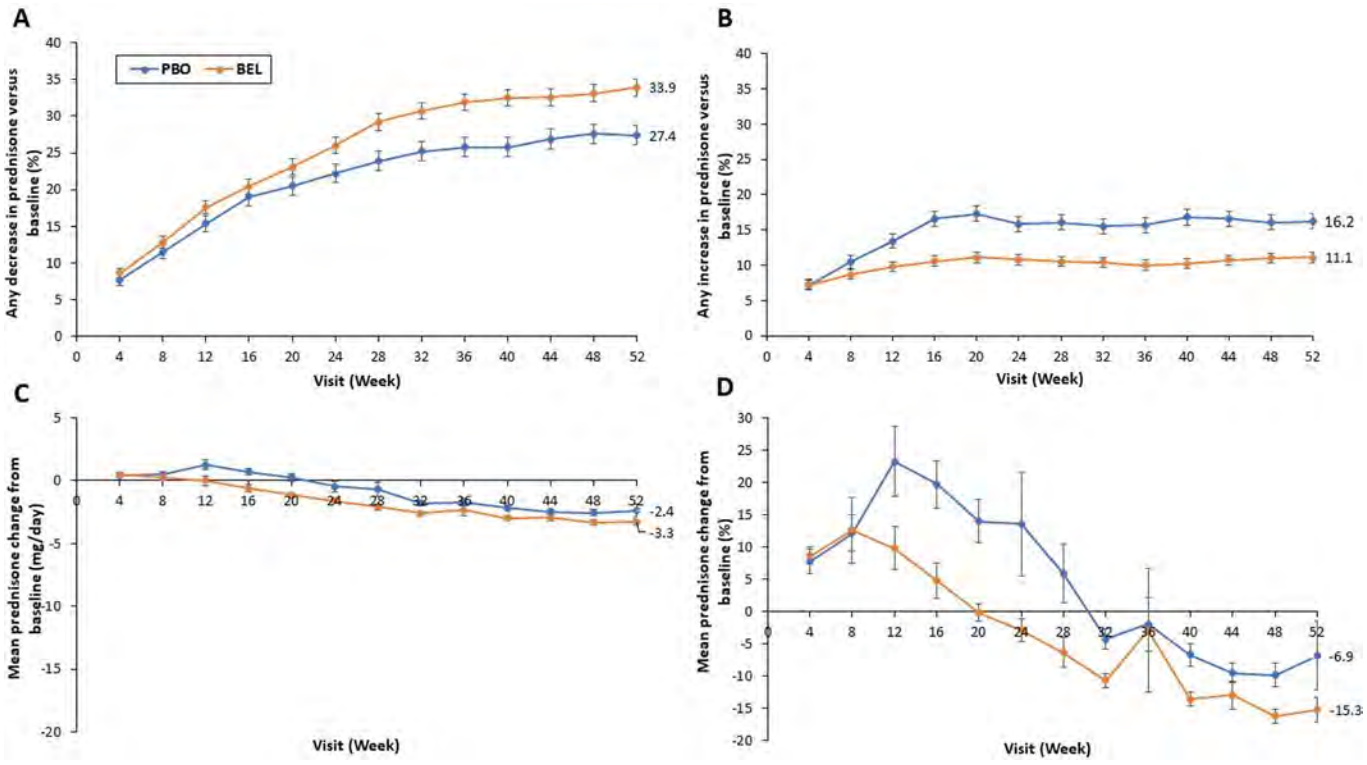

Figure. Percentage of pts with a decrease in GC dose compared with baselinea at each visit (A), percentage of pts with an increase in GC dose compared with baselineb at each visit (B), mean change from baselineb in GC dose (mg/day) at each visit (C); mean percentage change from baselinea in GC dose at each visit (D) Error bars represent the standard error. Numerical values shown represent data at Week 52. aAnalysis of pts receiving GCs at baseline bAnalysis of all pts, including those receiving GCs at baseline.

Conclusion: BEL was associated with significantly greater reductions in GC dose from baseline, and a lower cumulative GC dose over 1 year versus PBO. GC reductions with BEL occurred early in the 52-week treatment period despite no forced taper in the original studies. These data further support the role of BEL as a GC-sparing treatment in SLE management.

Funding: GSK

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Abstract Number: 1284

One Third of Lupus Nephritis Patients Classified as Complete Responders Continue to Accrue Progressive Renal Damage Despite Resolution of Proteinuria

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Up to 40% of individuals with lupus nephritis (LN) develop chronic kidney disease (CKD). Biopsy studies have revealed that patients with SLE can have active class III, IV, or V LN even in the absence of proteinuria or an abnormal glomerular filtration rate (GFR). We hypothesized that some patients with LN might be classified as treatment responders based on proteinuria, yet continue to accrue kidney damage. We sought to characterize early CKD in LN, and assessed the ability of traditional prognostic features, such as renal biopsy class and resolution of proteinuria, to identify patients likely to accrue progressive renal damage.

Methods: We conducted a single center retrospective study of SLE patients diagnosed with their first episode of biopsy-proven class III, IV, and/or V LN (n = 37). Participants with fewer than five years of clinical follow-up data were excluded, as were participants diagnosed with LN before 2004, so as to reflect modern outcomes. For each participant, eGFR calculated by CKD-EPI was graphed over time from date of renal biopsy to five years thereafter. Participants were divided into those with progressive GFR loss (GFR slope < -5 mL/min/1.73 m^2 per year) versus

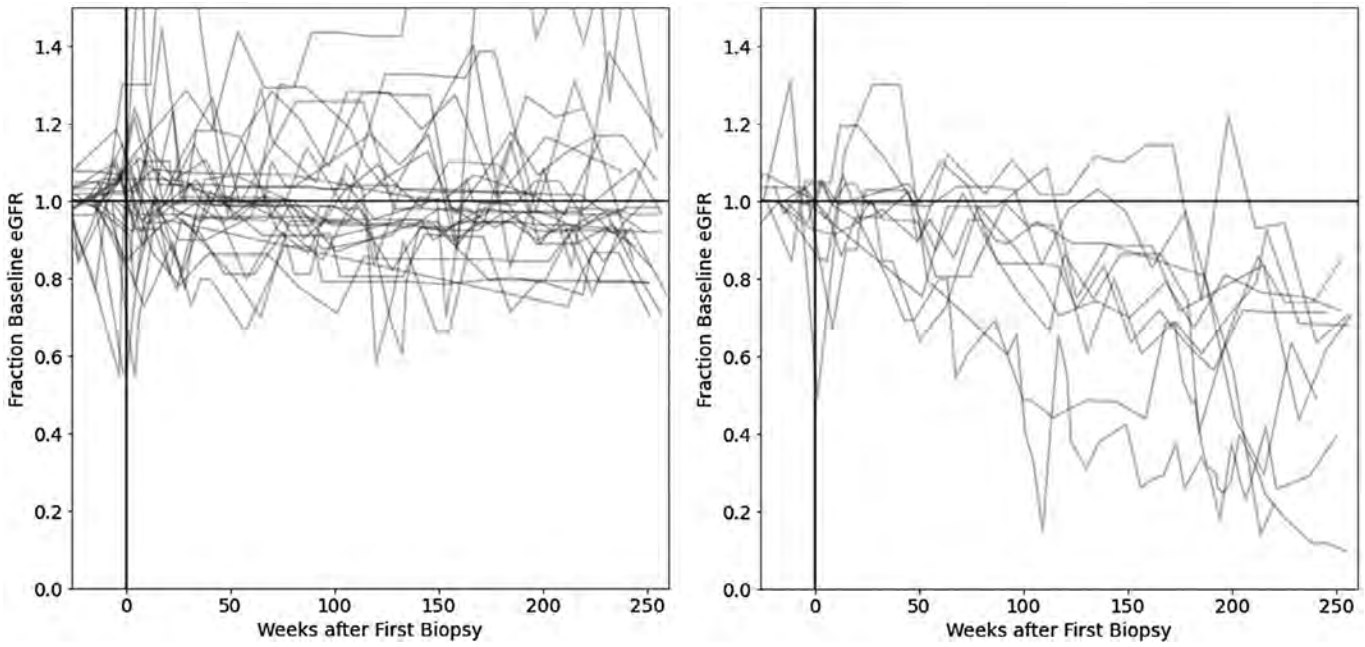

Figure 1. GFR trajectories of participants who maintained a stable GFR (left panel; n = 26) versus those who progressively lost GFR (right panel; n = 11). Each line represents the GFR values for one participant over time. To facilitate comparison between participant trajectories, GFR values were normalized to each participant's pre-LN baseline GFR.

Table 1. Baseline or other early characteristics of the GFR trajectory groups. Unless otherwise noted, average values are shown

Baseline Characteristic	GFR Trajectory Group		P Value
	Stable (n = 26)	Decline (n = 11)	
Sex, female	77%	91%	0.65
Race, black	77%	55%	0.24
Age at biopsy, years	31.9	37.7	0.14
BMI	26.7	28.5	0.34
Baseline GFR, mL/min/1.73 m^2	111	115	0.77
Urine protein (semi-quant), median	2+	2+	1.0
LN class, any proliferative	77%	82%	1.0
Activity index, median*	5	4	0.47
Chronicity index, median*	3	2	0.41
dsDNA, positive	69%	82%	0.69
C3	76	71	0.60
C4	14	11	0.37
RVVT >40	23%	10%	0.65
IgG aCL, positive	4%	0%	1.0
IgM aCL, positive	0%	0%	1.0
IgA aCL, positive	4%	0%	1.0
Hydroxychloroquine use at time of biopsy	89%	82%	0.62
Maximum prednisone dose, mg/kg	0.30	0.31	0.89
Induction therapy, MMF	77%	82%	1.0
ACEi or ARB use	50%	46%	1.0
History of hypertension**	31%	36%	1.0
History of diabetes**	0%	0%	1.0

* Activity and chronicity indices were available for 20 participants
** Prior to diagnosis of LN. No patients developed diabetes within the first year after biopsy.

Table 2. Response status (based on proteinuria < 500 mg/mg) at one year versus GFR trajectory group. Resolution of proteinuria at one year did not associate with ultimate GFR trajectory (p = 1.0). Response status could not be calculated for two participants in the stable GFR group (excluded from this table) due to missing clinical information at one year

Response Status at One Year	GFR Trajectory Group		
	Stable	Decline	
Responder	12	6	33% with GFR decline
Non-responder	12	5	29% with GFR decline
	50% classified as responders	55% classified as responders	

those who maintained a stable GFR (GFR slope not meeting the above threshold). Baseline demographics, renal biopsy features, immunologic status, treatment regimen, and comorbidities were compared between GFR trajectory groups using the Student's t-test, Wilcoxon rank-sum test, or Fisher's exact test as appropriate. Finally, proteinuria was assessed at one year after renal biopsy, and participants were classified as complete responders if urine protein was < 500 mg/mg at this time.

Results: Among these participants diagnosed with their first episode of LN, 30% (n = 11) accrued progressive renal damage despite standard of care therapy over the first five years following renal biopsy (**Figure 1**). There were no significant differences in baseline characteristics between GFR trajectory groups, including no association between progressive GFR loss and renal biopsy class, chronicity index, prednisone dosage, induction regimen, ACE inhibitor or ARB initiation, or prevalence of pre-existing hypertension or diabetes (**Table 1**). Likewise, resolution of proteinuria at one year did not differentiate between GFR trajectory groups (**Table 2**). Notably, 55% of participants with progressive GFR loss (n = 6 of 11) would be classified as complete responders based on < 500 mg/mg urine protein at one year after biopsy, and 33% (n = 6 of 18) of complete responders based on this urine protein threshold continued to accrue renal damage.

Conclusion: We have identified an understudied category of patients with LN who accrue progressive renal damage despite apparent response to standard of care therapy. Roughly half of the participants in this study with a worrisome GFR trajectory would be misleadingly classified as complete responders at one year based on resolution of proteinuria. These findings indicate that definitions of LN treatment response based on proteinuria can fail to identify patients who continue to accrue renal damage despite treatment. Better definitions and biomarkers of response are needed to improve long-term renal outcomes and trial design.

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Abstract Number: 1285

Major Determinants of Prolonged Remission in Systemic Lupus Erythematosus: Retrospective Study over a 41-Year Period

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Disease activity is a major determinant of mortality whereas prolonged remission contributes to improving health outcomes in SLE patients (pts). Remission is thus a key target, however, different definitions have been used.

Our aim was to investigate predictors of sustained complete remission for at least 3 and 5 years.

Methods: Retrospective observational study from Jan.1978-Dec.2019. Pts attending the Lupus Clinic in a tertiary care hospital for a period of at least three years. All pts fulfilled either the 1997 update of the 1982 American College of Rheumatology (ACR) revised criteria for classification of SLE or the 2019 EULAR/ACR criteria. To be included in the study, pts had to have been attending the clinic at least once a year. At each visit, disease activity was assessed using the BILAG index (also sensitive to detect flares) and blood test were done.

Complete remission (CR) was defined as no clinical activity (BILAG score C, D or E only), taking no steroids or immunosuppressants (antimalarials were permitted) and no serological activity (normal dsDNA antibodies and C3 levels) for a minimum of 3 consecutive years. Pts were **serologically active clinically quiescent (SACQ)** if there was no clinical activity, but an active serological profile (low C3 and/or high dsDNA) for at least 3 consecutive years; and in **serological remission (SR)** if there was no serological activity but persistent clinical activity (BILAG score A or B and/or treatment with steroids or immunosuppressive drugs) for at least 3 consecutive years. Pts not meeting the remission definitions were included in a **no-remission group**.

After testing for normality, we compared continuous numerical variables with Kruskal-Wallis test. For categorical variables, we compared groups using Pearson's chi-squared test. Kaplan-Meier curves were used to investigate cumulative survival. Pts were censored if they were lost to follow-up or reached the end of the study. Cox regression analysis was performed to investigate predictors of sustained remission. For continuous numerical variables showing a significant result, we used ROC curves to find a cut-off for each variable. All variables with a significant result in univariable analysis were included in the multivariable model. Statistical significance for P value < 0.05.

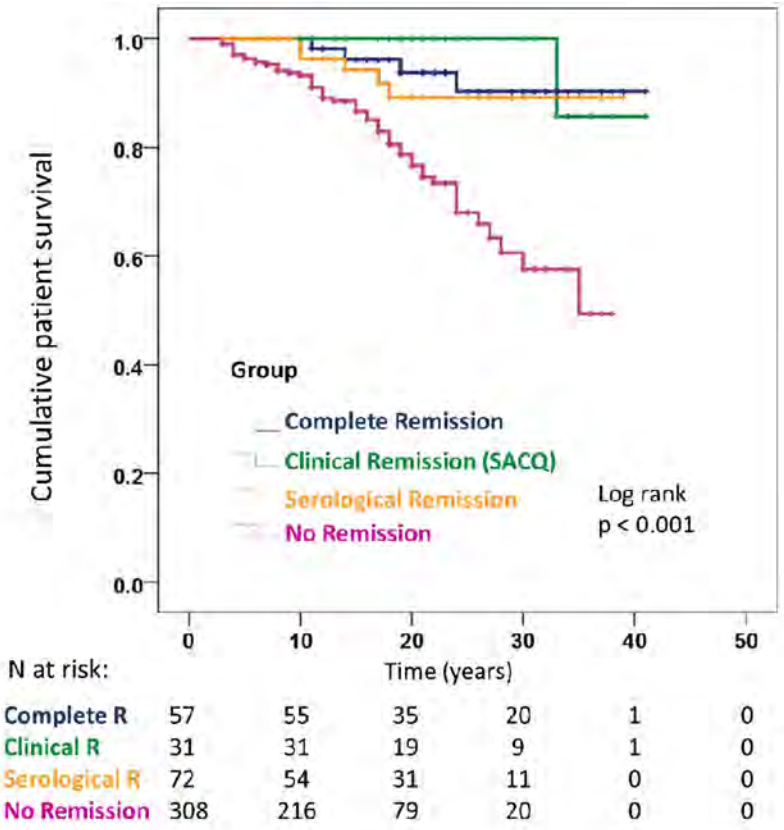
Results: 564 pts included. 15% achieved CR; 7% SACQ; 15% SR. 63% attained no remission.

Table 1. Comparison between patients who achieved different levels of sustained remission (at least 3 years) and no remission

	Total	Complete remission	Clinical remission (SACQ)	Serological remission	No remission	P
Total, N (%)	564 (100)	86 (15)	38 (7)	85 (15)	355 (63)	
Females, N (%)	528 (92)	78 (91)	36 (95)	79 (93)	327 (92)	0.878
Ethnicity						
White, N (%)	305 (54)	66 (77)	26 (68)	36 (42)	177 (50)	
Black, N (%)	112 (20)	6 (7)	7 (18)	17 (20)	82 (23)	
Subcontinent, N (%)	68 (12)	10 (12)	2 (5)	17 (20)	39 (11)	<0.001
Asian, N (%)	32 (6)	2 (2)	1 (3)	6 (6)	24 (7)	
Other, N (%)	47 (8)	2 (2)	2 (5)	10 (12)	33 (9)	
Age SLE diagnosis(y), median (IQR)	27 (17)	32.5 (20)	30 (19)	27 (16)	26 (17)	<0.001
Time follow-up since SLE diagnosis(y), median (IQR)	14.5 (13)	21 (18)	22.5 (17)	17 (18)	13 (11)	<0.001
Duration of remission(y), median (IQR)	7 (8)	9 (10)	7.5 (5)	6 (6)	N/A	0.121
Organ/system involvement						
Mucocutaneous, N (%)	496 (88)	80 (93)	34 (90)	80 (94)	302 (85)	0.046
Musculoskeletal, N (%)	519 (92)	83 (97)	36 (95)	78 (92)	322 (91)	0.309
Renal, N (%)	200 (36)	13 (15)	8 (21)	36 (42)	143 (40)	<0.001
Serositis or cardiopulmonary, N (%)	222 (39)	25 (29)	13 (34)	33 (39)	151 (43)	0.125
Neurological, N (%)	94 (17)	10 (12)	3 (8)	23 (27)	58 (16)	0.016
Haemolytic anaemia or ITP, N (%)	53 (10)	8 (9)	3 (8)	7 (8)	35 (10)	0.945
Gastrointestinal, N (%)	11 (2)	0	1 (3)	3 (4)	7 (2)	0.405
Associated conditions/overlap						
Antiphospholipid Syndrome, N (%)	56 (10)	3 (4)	7 (18)	11 (13)	35 (10)	0.048
Sjogren's syndrome, N (%)	76 (14)	15 (17)	8 (21)	15 (18)	38 (11)	0.084
Myositis	19 (3)	1 (1)	3 (8)	3 (4)	12 (3)	0.298
Rheumatoid arthritis	26 (5)	2 (2)	0	9 (11)	15 (4)	0.020
Deaths, N (%)	65 (14)	4 (7)	1 (3)	5 (7)	55 (18)	0.007

SLE: Systemic Lupus Erythematosus; y: years; IQR: interquartile range; ITP: immune thrombocytopenia. The p value refers to the comparison between the 4 groups (except in duration of remission - only 3 groups).

Pts who did not reach any kind of sustained remission died significantly earlier ($p < 0.001$). Cumulative survival figures at 5, 10, 20 and 30 years were 100, 100, 94 and 90%, respectively, for pts who achieved CR and 96, 93, 77 and 58%, respectively, for pts in the no-remission group.



	N total	N deaths	Cumulative survival %			
			5 y	10 y	20 y	30 y
Total	468	65	98	95	84	75
Complete Remission	57	4	100	100	94	90
Clinical Remission	31	1	100	100	100	100
Serological Remission	72	5	100	96	89	89
No remission	308	55	96	93	77	58

Figure 1. Kaplan-Meier curves showing cumulative patient survival in patients who reached different levels of sustained remission (for at least 3 years).

Significant predictors of CR were white ethnicity, adjusted hazard ratio (HR) 2.16 [95% CI 1.30-3.59] p=0.003; older age at diagnosis (>32-years), HR 1.92 [1.24-2.97] p=0.003; absence of renal involvement, HR 2.55 [1.39-4.67] p=0.002; and no concomitant antiphospholipid syndrome (APS), HR 4.92 [1.55-15.59] p=0.007.

Conclusion: Pts not achieving any kind of sustained remission have a higher risk of early mortality. White ethnicity, older age at diagnosis, absence of renal involvement and of APS were significantly associated with CR.

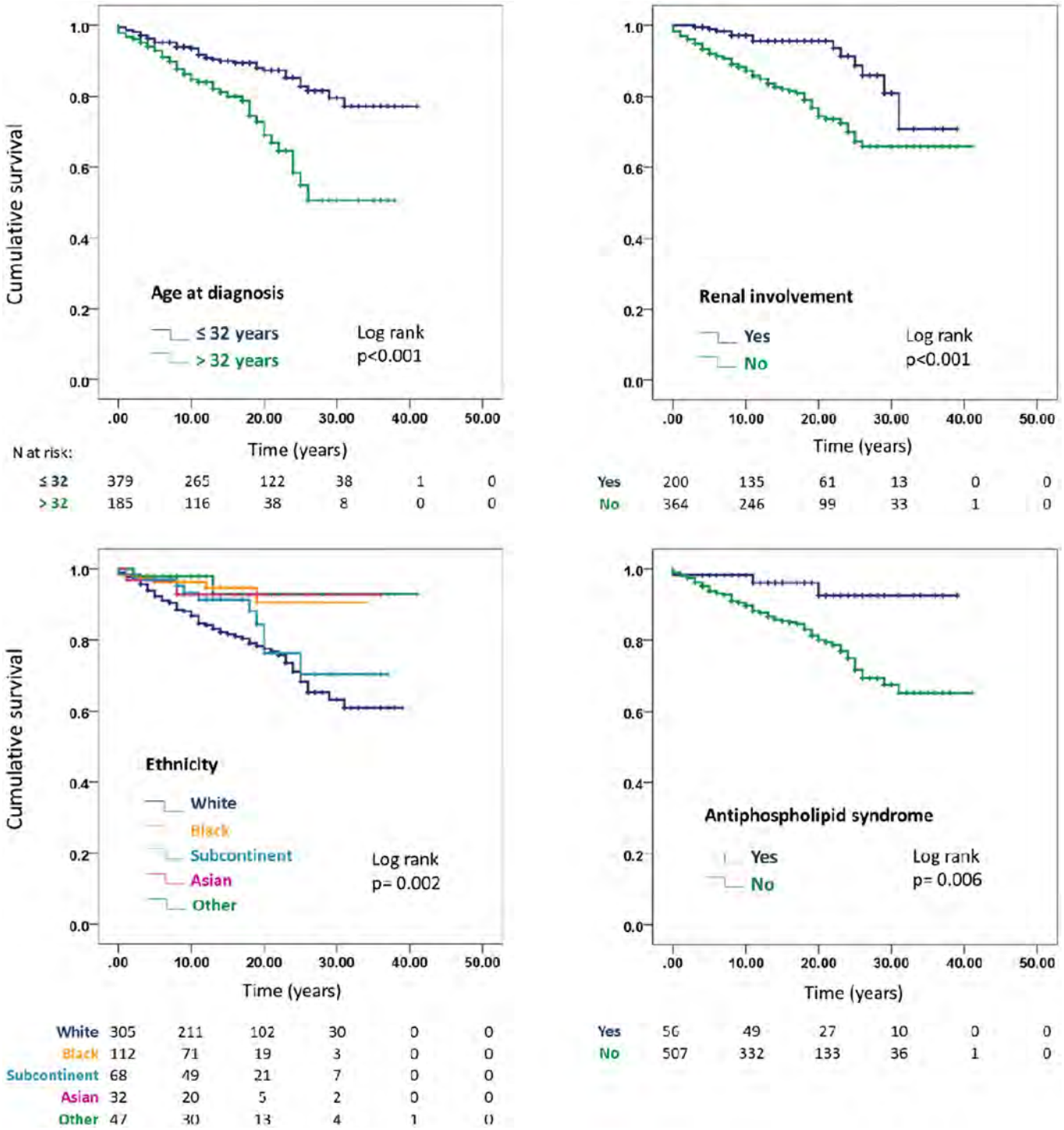


Figure 2. Kaplan-Meier curves showing cumulative survival free of complete sustained remission (at least 3 years), in different groups of patients, after the diagnosis of SLE.

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Abstract Number: 1286

Twenty-Year Trends in Systemic Lupus Erythematosus All–Cause Mortality in Mexico: A Nationwide Health Registry

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Marked regional variation in systemic lupus erythematosus (SLE) mortality may be due to different spectra of local environmental factors. There have been no large population-based studies of SLE mortality trends in Mexico. The aim of this study was to assess mortality trends in adults with SLE using a nationwide health registry.

Methods: Data came from the Dynamic Cubes of the General Direction of Health Information from 1998-2017 for mortality. In patients aged ≥ 15 years, SLE as the principal cause of death was defined according to the International Classification of Diseases (ICD)-10 code M32 and was classified by sex and age. Information was provided by the National Institute of Statistics, Geography and Informatics on mortality in the general population during the study period. Joinpoint trend analyses of annual age-standardized mortality rates (ASMR) (Table) for SLE patients and non-SLE people were carried out.

Results: From 1998 through 2017, we identified 11,449 SLE deaths and 9,911, 323 non-SLE deaths. The mean age of deaths for SLE was 37 years. The proportion of deaths among women was higher for SLE than for non-SLE. Over this period, SLE ASMR increased more than non-SLE ASMR, with a 53.8% cumulative increase in the ratio of SLE to non-SLE.

Whereas the non-SLE ASMR remained relatively stable throughout the 20 years (either overall or by sex), the SLE ASMR significantly increased between 1998 and 2008 (annual percentage change of 6.4 [95% CI 4.7 to 8.0]), decreased not significantly between 2008 and 2011 and not significantly increased there after. Similar pattern was seen for women with SLE and for men with SLE an increased between 2003 to 2017 was identified. Both women and men had large cumulative increase in the ratio of the SLE to the non-SLE ASMR (73.8% and 191.3%, respectively). Moreover, of the 11,449 deaths, 445 (3.8%) were in geographical areas where ≥ 40% of the population is indigenous, 6552 (57.6%) in areas with ≥ 5,000 indigenous inhabitants, and 4452 (38.6%) occurred in areas with no or very small indigenous inhabitants.

Conclusion: SLE mortality rates have increased since 1998 and remain high compared with non-SLE mortality: significant sex disparities persist.

The same method was used to calculate ASMR for all years from 1998 to 2017 and for all subpopulation based con sex.

Direct age standardization calculation for SLE mortality in Mexico female population for 2017

Age group	SLE deaths, n	General population, n	Age-Specific SLE crude mortality per 100,000 inhabitants	Standard Population (Year 2010), n	Expected Deaths, n
15-24 y	119	10859477	1.10	10585058	115.99
25-34 y	131	10147490	1.29	9026969	116.53
35-44 y	160	8902838	1.80	7987153	143.54
45-54 y	114	7219520	1.58	5766206	91.05
55-64 y	87	4998172	1.74	3665627	63.81
65-74 y	37	2867228	1.29	2222033	28.67
75+ y	22	1940245	1.13	1514009	17.17
All	670	46934970	1.42	40767055	576.77

Disclosure: C. Mendoza-Pinto, None; **I. Etchegaray-Morales**, None; **M. García-Carrasco**, None; **P. Munguía-Realpozo**, None; **S. Méndez-Martínez**, None.

Abstract Number: 1287

Association of Limited Health Literacy with Patient-Provider Communication in Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: Low health literacy is common among US adults, including patients with SLE, and is associated with higher disease activity and worse patient-reported outcomes. The complex nature of managing lupus puts SLE patients with low health literacy at even greater risk of poor outcomes. Limited health literacy has also been associated with worse patient-provider communication in other chronic diseases, though this has not been evaluated in SLE. Our study aimed to explore the relationship between health literacy and patient-provider communication in patients with SLE.

Methods: Patients with SLE meeting ACR/SLICC criteria were recruited from a university lupus clinic. Patient-provider communication data, as measured by the Interpersonal Processes of Care (IPC-29) survey, with a 0-5 range, were collected 7/2018-1/2019. On the IPC-29 survey, we considered a difference of ≥ 0.5 points by median score as clinically significant for each individual question. Health literacy was assessed using the Newest Vital Sign (NVS), a validated 6-item measure of reading comprehension and numeracy; limited health literacy was defined as NVS < 4. The NVS was administered from 9/2020-2/2021 during routine clinic visits and over video call. We compared charac-

teristics median IPC-29 scores between limited and adequate health literacy groups by descriptive statistics, and we stratified the IPC-29 domains by race.

Results: The study included 58 SLE patients (48% white, 48% Black, 5% Hispanic). Median age was 41 years; 97% were female, 59% had at least a college education, and 57% had Medicare or Medicaid, and 45% were on disability. 26% of our cohort was found to have limited health literacy.

Compared to adequate health literacy, those with limited health literacy were more likely to be Black, have Medicare/Medicaid, be on disability, have less than a college education, and have an annual income of ≤$50,000. Patients with limited health literacy were more likely to rate their providers as speaking too quickly, using difficult words, not finding out concerns, and not involving the patient in treatment decisions (Table 1).

Non-Black patients with limited health literacy reported lower provider eliciting of patient concerns, higher discrimination and worse physician compassion and respect compared to those with adequate health literacy. On the other hand, among Black patients, those with limited health literacy reported lower patient-centered decision making (Table 2).

Conclusion: Our results show that low health literacy is common, affecting 1 in 4 patients with SLE. While we did not find major differences in overall perceived communication based on level of health literacy, there were some notable differences in the eliciting concerns, patient-centered decision-making, and compassionate/re-

Table 1: Interpersonal Processes of Care (IPC-29) survey results by Health Literacy group

Interpersonal Processes of Care Domain	Total Median (IQR)	Limited Health Literacy	Adequate Health Literacy	p-value
Hurried Communication	1.2 (1.0-1.6)	1.4 (1-2)	1.2 (1.0-1.4)	0.4
• How often did doctors speak too fast?	1 (1-2)	**2 (1-3)**	**1 (1-2)**	
• How often did doctors use words that were hard to understand?	1 (1-2)	**2 (1-3)**	**1 (1-2)**	
Elicited Concerns, Responded	5 (4.3-5)	4.8 (4-5)	5 (4.7-5)	0.6
• How often did doctors really find out what your concerns were?	5 (4-5)	**4.5 (4-5)**	**5 (4-5)**	
Explained Results and Medications	4.75 (4.25-5)	4.9 (4.25-5)	4.75 (4.25-5)	0.8
Patient-Centered Decision Making	4.5 (3.5-5)	4.25 (3-4.75)	4.5 (3.5-5)	0.4
• How often did you and your doctors work out a treatment plan together?	5 (4-5)	**4 (4-5)**	**5 (4-5)**	
• If there were treatment choices, how often did doctors ask if you would like to help decide your treatment?	5 (4-5)	**4 (3-5)**	**5 (4-5)**	
Compassionate, Respectful	5 (4.2-5)	5 (4-5)	5 (4.2-5)	0.9
Discrimination	1 (1-1)	1 (1-1)	1 (1-1)	0.3
Disrespectful Office Staff	1 (1-1)	1 (1-1)	1 (1-1)	0.7

• Questions are included if they demonstrated a difference of ≥ 0.5 points by median score between limited vs adequate health literacy groups.

Table 2: Interpersonal Processes of Care (IPC-29) survey stratified by race

IPC Domain	Total	Limited HL	Adequate HL
Hurried Communication			
Non-Black	1.2 (1-1.4)	1.4 (1.1-2.2)	1.2 (1-1.4)
Black	1.4 (1-2.2)	1.4 (1-2)	1.2 (1-2.2)
Elicited Concerns, Responded			
Non-Black	5 (4.7-5)	**4 (4-5)**	**5 (4.7-5)**
Black	5 (4.3-5)	5 (4.3-5)	5 (4.3-5)
Explained Results and Medications			
Non-Black	4.5 (4-5)	4.5 (4.3-5)	4.5 (3.8-5)
Black	5 (4.25-5)	5 (4.3-5)	4.9 (4.4-5)
Patient-Centered Decision Making			
Non-Black	4.5 (4-5)	4.5 (4-5)	4.5 (3.5-5)
Black	4.4 (3-5)	**4.1 (3-4.8)**	**4.6 (3.1-5)**
Compassionate, Respectful			
Non-Black	5 (4.2-5)	**4 (4-5)**	**5 (4.4-5)**
Black	5 (4.1-5)	5 (4.3-5)	4.9 (4-5)
Discrimination			
Non-Black	1 (1-1)	**1.5 (1-1.8)**	**1 (1-1)**
Black	1 (1-1)	1 (1-1)	1 (1-1)
Disrespectful Office Staff			
Non-Black	1 (1-1)	1 (1-2)	1 (1-1)
Black	1 (1-1)	1 (1-1)	1 (1-1)

spectful sub-domains by race. Our results suggest that avoiding fast speech and increasing patient involvement in decision making may be important in improving the patient-provider relationship, especially for those with low health literacy.

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Abstract Number: 1288

First Year Infection Risk in SLE Patients Treated with Rituximab versus Standard of Care Treatment: Results from the British Isles Lupus Assessment Group Biologics Registry (BILAG-BR)

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Individuals with systemic lupus erythematosus (SLE) have an increased risk of infection compared to the general population. We aimed to assess the early risk of infection following rituximab therapy in a large national biologics register.

Methods: Patients receiving rituximab (RTX) or standard of care (SoC) treatment recruited to the UK national SLE biologics registry (2010-21) were included. Demographic, clinical and laboratory data were recorded at recruitment

Table 1. Baseline characteristics of patients receiving rituximab and standard of care treatment

Characteristic	RTX cohort	SoC cohort	p value
Gender, n (%)			
Female	442 (90)	107 (90)	
Male	48(10)	12 (10)	0.90
BMI* (IQR)	26 (22-30)	26 (22-30)	0.90
Ethnicity, n (%)			
White Caucasian	415 (58.0)	87 (55.0)	
Black	112 (15.6)	26 (16.3)	
Asian	148 (20.7)	36 (22.5)	
Other	41 (5.7)	10 (6.3)	
Age*, years (IQR)	41 (31-51)	44 (35-54)	0.90
Disease duration*, years, (IQR)	**4.2 (1.6-10.1)**	**1.8 (0.39-10.1)**	**0.04**
Serology (ever), n (%)			
dsDNA antibody positive	466 (64.9)	96 (61.9)	0.48
Low complement, n (%)	504 (69.7)	97 (64.2)	0.19
Serum IgG g/L*, (IQR)	**12.3 (8.9-16.3)**	**15.3 (10.2-20.4)**	**0.024**
Antimalarials	673 (87.7)	136 (81.9)	0.05
Mycophenolate	**563 (73.8)**	**33 (19.9)**	**<0.0001**
Azathioprine	**448 (58.7)**	**66 (39.8)**	**<0.0001**
Cyclophosphamide	**211 (27.7)**	**22 (13.3)**	**<0.0001**
Other immunosuppressants	**115 (15.0)**	**10 (6.0)**	**0.002**
Number of previous IS medications			
0-1	264 (34.4)	124 (74.7)	
2-3	438 (57.1)	38 (22.9)	
4-5	**65 (8.5)**	**4 (2.4)**	**<0.0001**
Background maintenance oral steroid dose (mg)*, (IQR)	**10 (5-15)**	**12.5 (5-25)**	**<0.0001**
Current smoking	198 (40.5)	37 (31.6)	0.08
Baseline comorbidities			
Chronic kidney disease	132 (18.9)	34 (22.4)	0.33
Ischaemic heart disease	22 (3.0)	1 (0.6)	0.09
Diabetes	42 (5.8)	7 (4.4)	0.51
Stroke	33 (4.5)	6 (3.8)	0.69
Asthma/COPD	100 (13.6)	11 (6.9)	**0.02**
Chronic liver disease	34 (4.7)	4 (2.6)	0.24
Previous cancer	65 (10.2)	11 (8.0)	0.42
Hypertension	203 (27.9)	35 (22.4)	0.17
Number of comorbidities* (IQR)	1 (0-1)	0 (0-1)	0.24

*Median. Abbreviations – RTX, rituximab; SoC, standard of care; IQR, interquartile range; BMI, body mass index; IS, immunosuppressant; COPD, chronic obstructive pulmonary disease.

Table 2. Clinical characteristics and their association with infection risk in rituximab treated patients

	Univariate		Adjusted for age and gender	
	OR (95% CI)	p value	OR (95% CI)	p value
Age	0.99 (0.97-1.01)	0.621	-	-
Sex	1.18 (0.90-1.55)	0.222	-	-
BMI	1.00 (0.96-1.05)	0.832	1.00 (0.94-1.06)	0.921
Disease duration	1.00 (0.95-1.05)	0.994	1.00 (0.95-1.07)	0.894
IgG <6.0 g/L at baseline	**2.23 (1.09-4.54)**	**0.001**	**2.35 (1.06-5.18)**	**0.035**
IgM <2.0 g/L at baseline	12.3 (0.63-2.53)	0.520	1.23 (0.52-2.85)	0.650
Diabetes	1.66 (0.73-3.81)	0.230	2.14 (0.80-5.73)	0.130
CKD	**2.25 (1.13-4.46)**	**0.020**	1.98 (0.89-4.40)	0.090
Asthma/COPD	1.64 (0.82-3.29)	0.160	2.05 (0.94-4.42)	0.068
Smoking	0.87 (0.45-1.70)	0.692	0.91 (0.46-1.80)	0.793
Number of comorbidities	**1.27 (1.07-1.50)**	**0.007**	**1.34 (1.08-1.65)**	**0.006**
Previous cyclophosphamide	1.42 (0.80-2.50)	0.227	1.00 (0.50-2.03)	0.990
Current antimalarial use	1.22 (0.75-2.01)	0.423	0.94 (0.52-1.69)	0.838
Background maintenance oral steroid dose	**1.03 (1.00-1.06)**	**0.009**	**1.05 (1.01-1.08)**	**0.004**
IV steroid pulse at time of recruitment	0.98 (0.77-1.25)	0.866	0.87 (0.59-1.29)	0.492

Abbreviations – OR, odds ratio; BMI, CI, confidence interval; body mass index; Ig, immunoglobulin; CKD, chronic kidney disease; IV, intravenous.

and during follow up. Information relating to infection and mortality were collected from study centres and the UK Office for National Statistics in the first 12-months after treatment initiation. Serious infections were defined as those requiring intravenous antibiotic treatment, hospital admission, resulting in disability or death.

Statistical analysis was performed using Stata (v14). Baseline variables were compared using Chi-squared or Mann-Whitney U tests. A logistic regression model adjusted for age and sex was used to test the association of baseline variables with serious infection within the first year.

Results: We included 931 patients (764 RTX and 167 SoC). In the SoC arm, commonest prescribed recent therapies included mycophenolate (n=126, 75%), azathioprine (n=46, 28%) and/or cyclophosphamide (n=38, 23%).

Baseline characteristics were similar between the two groups but RTX patients had a longer disease duration, higher number of previous immunosuppressants, more obstructive airways disease and lower maintenance steroid dose and baseline serum IgG (Table 1). In the first year following treatment initiation, 259 infections were reported in 143 (15%) patients, including 106 (41%) serious infections. In the RTX group, 127 (17%) individuals reported an infection compared to 16 (10%) in the SoC group, *p=0.022*. There was no difference in the number of serious infections between groups, 58 (8%) and 10 (6%) patients in RTX and SoC groups respectively, *p=0.471*. Recurrent serious infections occurred in 21 (2%) patients and were not significantly different between RTX and SoC groups (2.5% Vs 1.2%, *p=0.309*).

After adjusting for age and gender in the RTX group, number of comorbidities (OR 1.34 95% CI 1.08-1.65), maintenance steroid dose (OR 1.05 CI 1.01-1.08) and hypogammaglobulinaemia (IgG < 6.0 g/L) (OR 2.35, 95%CI 1.06-5.18) were associated with increased risk of infection (Table 2).

The commonest sites of serious infection were respiratory (n=24, 23%), bone/soft tissue (n=14, 13%), ENT (n=11, 10%) and urinary tract (n=8, 8%). One RTX-treated individual died of an infection (sepsis) within a year of treatment initiation.

Conclusion: RTX-treated SLE patients do not demonstrate an increased risk of serious infections compared to those on SoC treatment. Baseline hypogammaglobulinaemia, higher number of comorbidities and usual oral steroid dose correlate with infection risk in RTX-treated patients.

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Abstract Number: 1289

Patients Enrolled in the Accelerating Medicines Partnership (AMP) RA/SLE Network with Isolated Renal Disease Report Minimal Quality of Life Impairment on PROMIS-29 Compared to Patients with Extrarenal Symptoms

Philip Carlucci[1], Jessica Li[2], Heather Gold[3], Kristina Deonaraine[1], Andrea Fava[2], Jill Buyon[4], Judith James[5], Chaim Putterman[6], Deepak Rao[7], Betty Diamond[8], Derek Fine[2], Jose Monroy-Trujillo[2], Kristin Haag[9], Accelerating Medicines Partership (AMP) RA/SLE Network[10], H. Michael Belmont[4], Sean Connery[11], Fernanda Payan-Schober[12], Richard Furie[13], Celine Berthier[14], Maria Dall'Era[15], Kerry Cho[16], Diane Kamen[17], Kenneth Kalunian[18], The Accelerating Medicines Parternship In SLE Network[19], Peter Izmirly[1] and Michelle Petri[20], [1]New York University School of Medicine, New York, NY, [2]Johns Hopkins University, Baltimore, MD, [3]NYU Grossman School of Medicine, New York, NY, [4]NYU School of Medicine, New York, NY, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Albert Einstein College of Medicine, Bronx, NY, [7]Brigham and Women's Hospital, Boston, MA, [8]Northwell Health, Manhasset, NY, [9]Johns Hopkins School of Medicine, Baltimore, MD, [10]Brigham and Women's Hospital, Everett, MA, [11]Texas Tech University Health Sciences Center, Texas, TX, [12]Texas Tech University Health Sciences Center, El Paso, TX, [13]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [14]University of Michigan, Ann Arbor, MI, [15]University of California San Francisco, Corte Madera, CA, [16]University of California San Francisco, San Francisco, CA, [17]Medical University of South Carolina, Charleston, SC, [18]UC San Diego, La Jolla, CA, [19]Multiple Institutions, Multiple Cities, [20]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis can occur as an isolated component of disease activity or be accompanied by diverse extrarenal symptoms that can adversely affect a patient's quality of life (QOL). Whether renal disease absent other activity is sufficient to decrease QOL is unknown. A lack of reported QOL impairment may place patients at risk for delayed diagnosis of nephritis or medication noncompliance yet nephritis trials have largely neglected QOL. As such, this study leveraged the multi-center multi-racial Accelerating Medicines Partnership (AMP) lupus nephritis cohort to assess QOL measured by PROMIS-29.

Methods: Patients (n=182) fulfilling ACR or SLICC criteria for SLE with a uPCR ≥ .5 and biopsy Class III, IV, V, or mixed were consecutively enrolled in AMP at the time of renal biopsy and clinical history, PROMIS-29, and disease activity as assessed by the hybrid SELENA-SLEDAI were recorded. Patients were determined to have extrarenal clinical activity if, after excluding all laboratory parameters from the SLEDAI, the score remained ≥ 1. Raw PROMIS-29 scores were transformed to t-scores with the mean of 50 ± 10 representing the US population and a difference of 5 points considered clinically meaningful. PROMIS-29 physical and mental health summary scores were calculated according to published formulas.

Results: Forty-three percent of patients (n=78) had extrarenal clinical manifestations including vasculitis (4%), arthritis (39%), rash (45%), alopecia (42%), mucosal ulcers (13%), pleurisy (12%), pericarditis (8%), and fever (4%). Patients with isolated renal disease (n=104, 57%) did not have PROMIS-29 scores that differed clinically from the US population whereas patients with extrarenal disease reported deficits in physical functioning, fatigue, social functioning, and pain (Table 1). Patients with extrarenal disease had significantly lower physical health summary scores compared to patients with isolated disease (median [IQR]: 40.31 [35.79, 47.02] p< 0.001 vs. 48.6 [40.14, 57.08]) and significantly lower mental health summary scores (44.12 [38.63, 51.39], p=0.024 vs. 48.67 [40.51, 55.07]). Female and African American patients and those with nephrotic range proteinuria or undergoing first biopsy had significantly lower physical health summary scores, but mental health summary scores did not differ by these variables. Patients on greater than 20 mg of prednisone had both significantly lower physical and mental health summary scores compared to those on lower doses. PROMIS-29 scores did not differ by low complements, anti-dsDNA, or anti-Ro antibodies. Stepwise multivariable linear regression analysis demonstrated that the association between extrarenal disease and lower PROMIS-29 summary scores was primarily driven by arthritis and independent of potential confounders (Tables 2 and 3).

Table 1. PROMIS-29 scores among patients with isolated renal vs extrarenal disease.

Category	Isolated Renal n=104	Extrarenal n=78	P-value
Physical functioning <	48.3 [40.5-57.0]	41.2 [36.7-48.3]	**<0.0001**
Anxiety >	53.7 [40.3-59.5]	51.2 [40.3-59.5]	0.87
Depression >	45.0 [41.0-55.7]	45.0 [41.0-57.3]	0.88
Fatigue >	53.1 [46.0-62.2]	57.9 [48.6-64.6]	**0.009**
Sleep >	54.3 [48.9-57.9]	54.3 [48.4-59.8]	0.80
Social functioning <	51.9 [44.2-64.2]	44.2 [42.3-51.9]	**0.002**
Pain >	55.6 [41.6-61.2]	61.2 [55.6-66.6]	**0.0002**
Pain intensity >	3.0 [1.0-5.8]	6.0 [3.0-8.0]	**<0.0001**

Results are presented as median [IQR], Mann-Whitney U test of significance
< lower scores indicate worse outcome
> higher scores indicate worse outcome

Table 2. Stepwise multivariable linear regression analysis of extrarenal manifestations and PROMIS-29 physical health summary scores

	Physical health summary scores <	
Predictors	**Estimate (95% CI)**	**p-value**
Arthritis (yes vs. no)	-8.68 (-12.32 ,-5.03)	**<.0001**
Rash (yes vs. no)	-2.24 (-5.65 ,1.17)	0.196
Prednisone>20mg	-4.68 (-7.4 ,-1.97)	**0.0008**
Sex: female	-3.05 (-6.5 ,0.4)	0.0827

< lower scores indicate worse outcome

Table 3. Stepwise multivariable linear regression analysis of extrarenal manifestations and PROMIS-29 mental health summary scores

	Mental health summary scores <	
Predictors	**Estimate (95% CI)**	**p-value**
Arthritis (yes vs. no)	-5.93 (-9.47 ,-2.38)	**0.0012**
Rash (yes vs. no)	-1.9 (-5.29 ,1.49)	0.2699
Prednisone>20mg	-2.39 (-5.11 ,0.33)	0.0848
Non-Hispanic Caucasian	-4.13 (-7.76 ,-0.49)	**0.0266**

< lower scores indicate worse outcome

Conclusion: The majority of patients had isolated renal disease and report a QOL similar to that of the general population. In contrast, those with extrarenal manifestations report significantly worse QOL outcomes. These results reinforce the critical importance of routine laboratory surveillance and medication compliance for nephritis even in patients with seemingly quiescent clinical disease.

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Abstract Number: 1290

Validation of a Novel Lupus Multivariable Outcome Score as an Outcome Measure for Systemtic Lupus Erythematosus Trials

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Development of effective new Systemic Lupus Erythematosus (SLE) treatments requires a validated responder index responsive to clinically meaningful change and relevant to clinical practice. To address this challenge, we have recently developed a new Lupus Multivariable Outcome Score (LuMOS) to optimize discrimination between outcomes of actively treated patients *versus* those randomized to placebo [1]. We now report on external validation of LuMOS in two independent SLE clinical trials.

Methods: Validation was carried out in the Illuminate trials used to evaluate tabalumab (TB) in SLE. All participants in both Illuminate 1 and 2 clinical trials met the ACR classification criteria for SLE and all were included in our analyses. To adapt LuMOS for use with laboratory results assessed on different platforms than used in the trials of belimumab employed to generate the original LuMOS outcome score [1], we calculated a standardized score using z-score transformation. For validation, in each of the Illuminate trials, we calculated LuMOS scores at week 52 for all participants receiving either placebo or one of 2 dosage regimens of TB. Cohen D Effect Size (ES), with 95% confidence intervals (CI), assessed the ability of LuMOS to discriminate between outcomes in active treatment groups *versus* placebo, and compared it with SRI-5 responder index used in the trials.

Results: LuMOS using standardized z-score transformed laboratory data worked comparably to the original LuMOS model in the original data from the belimumab trials and was then applied to the Illuminate data sets. LuMOS-based ES for both TB groups in both trials indicated highly significant ($p < 0.0001$), moderately strong treatment effects (ES

Table 1

Trial	Group (n)	**LuMOS: Effect Size (95% CI)**	**SRI-5: Effect Size (95% CI)**
ILLUMINATE-1	TB-q4weeks (n=378)	**0.44 (0.30; 0.59)**	**0.13 (- 0.02; + 0.27)**
ILLUMINATE-1	TB-q2weeks (n=381)	**0.42 (0.27; 0.56)**	**0.05 (- 0.09; + 0.20)**
ILLUMINATE-2	TB-q4weeks (n=376)	**0.54 (0.39; 0.68)**	**0.15 (+0.01; +0.30)**
ILLUMINATE-2	TB-q2weeks (n=372)	**0.69 (0.53; 0.83)**	**0.23 (+0.08; +0.37)**

Comparison of Effect Sizes of LuMOS vs. SRI-5 for discrimination between TB-treated and placebo groups n Illuminate-1/-2 trials

>0.4), in contrast to weak effects (ES< 0.25) based on SRI-5, that were statistically *non*-significant for Illuminate-1, as reflected by the 95% CI's that included 0 (Table).

Conclusion: LuMOS improves the ability to detect statistically significant treatment effects. Further validation in SLE trials of non-B cell directed treatments is necessary to document utility as an outcome measure independent of drug mechanism.

[1] Abrahamowicz et al. *Arthritis Rheumatol*. 2018;70:1450-58.

Disclosure: M. Abrahamowicz, None; **P. Lipsky**, Horizon, 2.

Abstract Number: 1291

Risk of Bleeding-related Complications After Kidney Biopsy in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
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Background/Purpose: Kidney biopsy is essential for the diagnosis and classification of lupus nephritis in patients with systemic lupus erythematosus (SLE). Even though the risk of bleeding-related complications is not low in such patients, data on the risk of percutaneous kidney biopsy in SLE patients are limited. Thus, we investigated the rate of bleeding-related complications and examined the risk factors for complications of kidney biopsy in patients with SLE.

Methods: We retrospectively reviewed the medical records of SLE patients who underwent ultrasound-guided percutaneous kidney biopsy between 2002 and 2020 at a tertiary referral center. Major complications included bleeding events that required interventions (e.g., blood transfusion, angiographic embolization, surgery) after biopsy. Minor complications included hematoma, oozing at the biopsy site, and passing hematuria without a need for intervention. Statistical analysis with a multivariate logistic regression model was performed to identify the risk factors associated with complications.

Results: In a total of 165 SLE patients, the rate of overall bleeding-related complication after kidney biopsy was 25% (major: 8%, minor: 17%). In terms of the details of major complications, 86% (12/14) of patients needed a blood transfusion alone without embolization or surgery, and the remaining two patients needed embolization for bleeding control. Patients with any kind of complication had a significantly lower platelet level than did those without complications (p< 0.001). Univariate analysis showed that the levels of hemoglobin (OR 0.81; 95% CI, 0.66–0.99), platelet (OR 0.99; 95% CI, 0.99–1.00), aPTT (OR 1.05; 95% CI, 1.00–1.11), and proteinuria (OR 1.00; 95% CI, 1.00–1.00) were significantly associated with the risk of complications. Multivariate analysis revealed that low platelet count (OR 0.99; 95% CI, 0.98–0.99) was significantly associated with the risk of bleeding-related complications after kidney biopsy.

Conclusion: Percutaneous kidney biopsy was accompanied by the risk of bleeding-related complications, although the majority of events did not require vascular intervention for bleeding control. Low levels of platelet counts had a significantly increased risk of complications after kidney biopsy in patients with SLE.

Table 1. Clinical and laboratory characteristics of SLE patients with and without complication after kidney biopsy

Characteristics	Complication group (n=42)	Non-complication group (n=123)	p-value
(1) Clinical features			
Age at biopsy, mean (SD)	37.26 (14.39)	37.80 (14.14)	0.802
Female gender, n (%)	35 (83.3)	107 (87.0)	0.608
BMI, mean (SD)	21.86 (3.26)	22.96 (3.64)	0.085
Hypertension, n (%)	14 (33.3)	39 (31.7)	0.850
Diabetes Mellitus, n (%)	3 (7.1)	2 (1.6)	0.105
sBP at biopsy, mean (SD)	121.93 (19.49)	123.23 (16.45)	0.455
(2) Laboratory data			
Hemoglobin, mean (SD)	10.05 (1.68)	10.72 (1.86)	0.015
Platelet, mean (SD)	157.05 (71.08)	209.25 (83.08)	<0.001
PT INR, mean (SD)	1.01 (0.14)	0.98 (0.17)	0.208
aPTT, mean (SD)	30.57 (9.56)	27.44 (6.21)	0.064
Creatinine, mean (SD)	1.07 (0.80)	0.98 (1.13)	0.352
eGFR, mean (SD)	85.92 (40.71)	93.79 (42.33)	0.384
C3, mean (SD)	49.48 (28.90)	59.42 (29.53)	0.049
C4, mean (SD)	10.56 (7.99)	11.90 (9.98)	0.591
dsDNA, mean (SD)	274.23 (487.47)	506.87 (1003.52)	0.738
Proteinuria, mean (SD)	3156.14 (2602.73)	2262.45 (1897.26)	0.118
ESR, mean (SD)	30.06 (24.70)	33.85 (24.79)	0.392
Lupus anticoagulant, n (%)	11 (26.2)	36 (29.3)	0.843
ACA, n (%)	13 (31.0)	29 (23.6)	0.412
B2–GPI, n (%)	9 (21.4)	20 (16.3)	0.484
(3) Medications			
Warfarin, n (%)	2 (4.8)	5 (4.1)	1.000
Antiplatelet, n (%)	1 (2.4)	3 (2.4)	1.000
ACEi/ARB, n (%)	13 (31.0)	42 (34.1)	0.850
Prednisone, n (%)	26 (61.9)	90 (73.2)	0.176
Prednisone dose, mean (SD)	22.19 (26.66)	19.93 (21.96)	0.860
(4) ISN/RPS classification			
Class 3–4, n (%)	24 (57.1)	71 (57.7)	1.000
Class 5, n (%)	13 (31.0)	27 (22.0)	0.297
Others, n (%)	5 (11.9)	25 (20.3)	0.256

BMI: body mass index; sBP: systolic blood pressure; PT INR : prothrombin time international normalized ratio; aPTT: activated partial thromboplastin time; eGFR: estimated glomerular filtration rate; C3/C4: complement 3/4ESR: eryth-

rocyte sedimentation rate; ACA: anticentromere antibody; B2-GPI: Beta-2-glycoprotein I antibody ACEi/ARB: angiotensin converting enzyme inhibitor/angiotensin receptor blocker ISN/RPS: International Society of Nephrology and Renal Pathology Society

Table 2. Logistic analysis for the risk factors of complications after kidney biopsy in SLE patients

	Univariable			Multivariable		
Parameter	OR	95% CI	p value	adjusted OR	95% CI	p value
(1) Clinical features						
sBP at biopsy	0.996	0.975–1.016	0.672			
(2) Laboratory data						
Hemoglobin	0.810	0.661–0.992	0.041	0.860	0.690–1.072	0.180
Platelet	0.991	0.986–0.996	0.001	0.994	0.988–0.999	0.022
PT INR	2.256	0.314–16.208	0.419			
aPTT	1.057	1.006–1.110	0.028	1.030	0.979–1.083	0.256
eGFR	0.995	0.987–1.004	0.293			
C3	0.988	0.975–1.001	0.063			
Proteinuria	1.000	1.000–1.000	0.022	1.000	1.000–1.000	0.053
ESR	0.994	0.979–1.008	0.391			
Lupus anticoagulant	1.166	0.529–2.569	0.703			
ACA	0.688	0.317–1.494	0.345			
B2–GPI	0.712	0.296–1.715	0.449			
(3) Medications						
Prednisone	1.678	0.801–3.516	0.170			

sBP: systolic blood pressure; PT INR : prothrombin time international normalized ratio; aPTT: activated partial thromboplastin time; eGFR: estimated glomerular filtration rate; C3: complement 3 ESR: erythrocyte sedimentation rate; ACA: anticentromere antibody; B2-GPI: Beta-2-glycoprotein I antibody

Disclosure: E. Kang, None; **J. Oh**, None; **S. Ahn**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None; **S. Hong**, None.

Abstract Number: 1292

Systemic Lupus Erythematous Readmissions Has Reduced in the Last Decade in the United States: A 9- year Longitudinal Study of the Nationwide Readmission Database

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Longitudinal data on trends of Systemic Lupus Erythematous (SLE) readmissions is scarce. Our study aims to study trends of 30-day readmissions of patients admitted for SLE flare in the United States (US) from 2010-2018. We also aim to highlight the most common reasons for 30-day readmissions of patients admitted for SLE flare in the last decade.

Methods: Data were obtained from the Nationwide Readmission Database (NRD). NRD includes nested and weighted discharge data stratified in clusters to produce national estimates. We performed a retrospective 9-year longitudinal trend analysis of NRD 2010 – 2018 databases. Every other year was sampled during the study period. We searched for index hospitalizations for patients aged ≥ 18 years with "principal" diagnosis of SLE using ICD 9 & 10 codes ("7100" & "M32" respectively) for the corresponding year. The principal diagnosis is the main reason for hospitalization, hence index hospitalizations with SLE as the principal diagnosis are defined as SLE flare hospital-

Table 1. Characteristics and longitudinal trends of 30-day readmissions following index hospitalization for Systemic Lupus Erythematous flare Abbreviations: Readmit: Readmissions, d, days, LOS: Hospital length of stay, Cost: total hospital cost, CCI: Charlson comorbidity index score, USD: United States dollars, yr: years SLE: Systemic Lupus Erythematous, AKI: Acute kidney injury, UTI: Urinary tract infection. p-value <0.05 is statistically significant. *We included hospitalizations with a "principal" diagnosis of SLE. **Readmission cost for each year was adjusted for inflation using 2018 US dollars according to the medical expenditure panel survey-based factor for hospital care

Variables	2010	2012	2014	2016	2018	Adjusted p-trend
No. of Index hosp. discharged alive *	9705	9430	9033	8132	8063	
Readmit Proportion, %	20.3	20.6	19	22.5	17.6	0.009
Readmit Mean Age, yr	37.4	36.2	38.2	37.3	36.9	0.483
Readmit Female, %	86.5	87	87.3	85.9	84.2	0.287
Readmit mortality, %	2.5	1.6	2.8	1.5	2	0.317
Readmit Mean LOS, d	6.7	6.4	6.4	6	6	0.045
Readmit Mean Cost**, USD	15,843	15,609	15,420	13,974	14,619	0.052
Readmit CCI, %						<0.0001
0-2	57.8	57.7	54.8	50.8	45.7	
≥3	42.2	42.3	45.2	49.3	54.4	
Most common reasons for Readmit						
	SLE	SLE	SLE	SLE Glomerulonephritis	SLE Glomerulonephritis	
	Pneumonia	Pneumonia	Pneumonia	SLE, unspecified	SLE, unspecified	
	Sepsis	Sepsis	Sepsis	Sepsis	Sepsis	
	AKI	Chest pain	AKI	AKI	AKI	
	UTI	UTI	Pericardial disease	SLE with unspecified organ or system involvement	SLE with unspecified organ or system involvement	

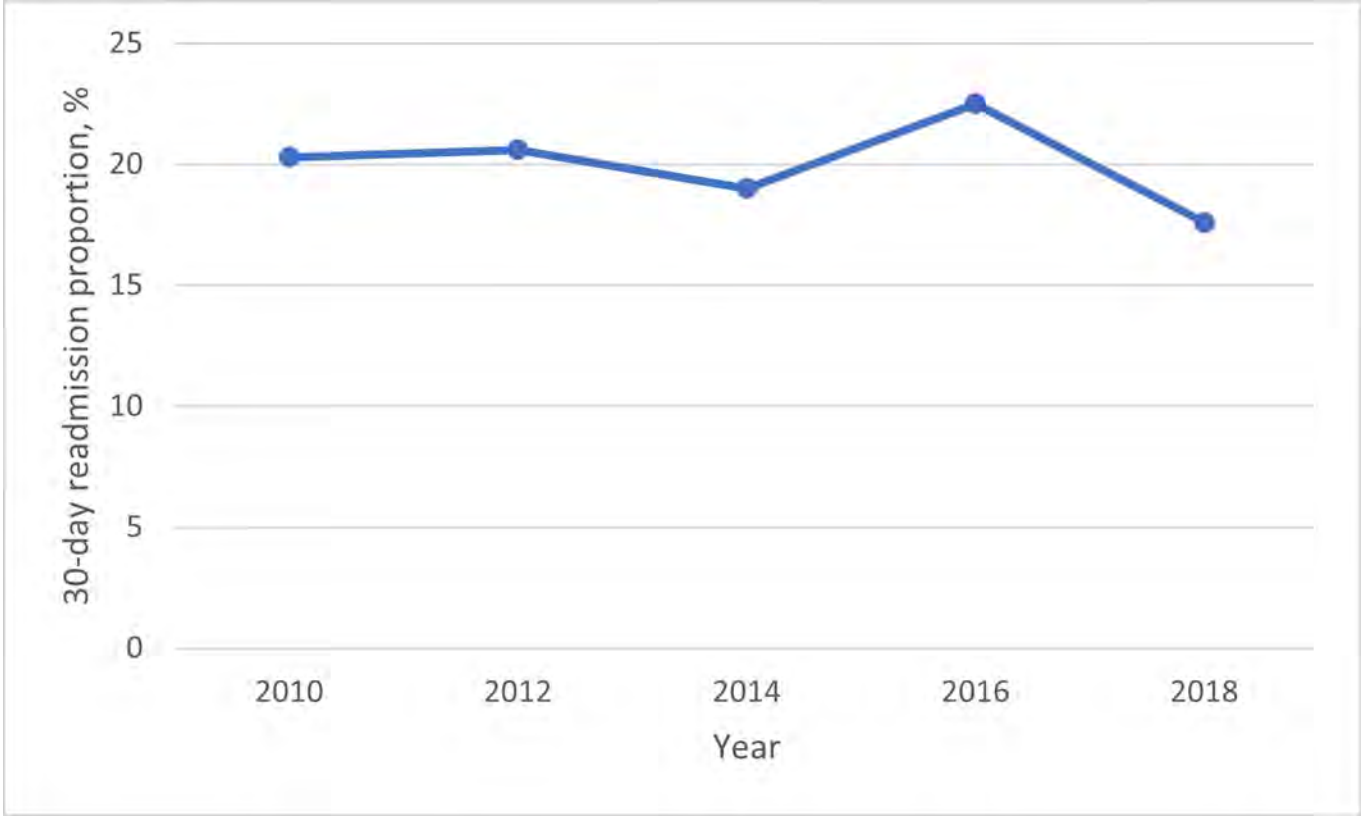

Figure 1. Proportion of 30-day readmissions following index admission for SLE flare from 2010-2018.

izations. Elective and traumatic readmissions were excluded. The 5 most common principal diagnoses or reasons for readmissions for each sampled year were highlighted. Multivariable logistic and linear regression analyses were used to calculate adjusted p-trend for categorical and continuous outcomes, respectively. We adjusted for change in demographics and Charlson comorbidity index (CCI) score over the years. Analysis was performed using STATA, 16.

Results: 30-day readmissions following admissions for SLE flare decreased from 20.3% in 2010 to 17.6% in 2018 (adjusted p-trend=0.009). See Figure 1. Readmission mortality reduced from 2.5% to 2% (adjusted p-trend=0.317, hospital length of stay (LOS) reduced from 6.7 days to 6 days (adjusted p-trend=0.045), and total hospital cost reduced from $15,843 to $14,619 (adjusted p-trend=0.052) from 2010 to 2018. Proportion of readmissions with CCI score ≥3 increased from 42.2% to 54.4% (adjusted p-trend< 0.0001) during the study period. SLE, sepsis and infections were common reasons for 30-day readmissions across the years (table 1).

Conclusion: About 1 in 5 SLE flare admission results in 30-day readmission. 30-day readmissions following hospitalization for SLE flares have reduced in the last decade. Although readmission LOS reduced, CCI score has increased over time. Decreasing readmission rates over time may reflect improved discharge care and outpatient flare management. Infection control strategies are important in reducing 30-day readmissions following admissions for SLE flare.

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Abstract Number: 1293

Studying Clusters of Patients with SLE According to Cognitive Function, Self-reported Outcomes, Disease Activity, and Clusters Dynamic over 1 Year

Ambika Gupta[1], Sindhu Johnson[2], Jiandong Su[3], Kathleen Bingham[4], Andrea Knight[5], Juan Diaz-Martinez[6], Mahta Kakvan[3], Maria Tartaglia[3], Lesley Ruttan[4], Joan Wither[3], May Choi[7], Marvin Fritzler[8], Dennisse Bonilla[3], Dorcas Beaton[9], Patricia Katz[10], Robin Green[3] and Zahi Touma[1], [1]University of Toronto, Mississauga, ON, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]University Health Network, Toronto, ON, Canada, [4]University of Toronto, University Health Network, Toronto, ON, Canada, [5]Hospital for Sick Children, Toronto, ON, Canada, [6]UHN, Toronto, ON, Canada, [7]Brigham and Women's Hospital | University of Calgary, Calgary, AB, Canada, [8]University of Calgary, Calgary, AB, Canada, [9]Institute for Work & Health, Toronto, ON, Canada, [10]University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) has a high prevalence of cognitive impairment (CI) (38% (95% confidence interval: 33-43%)). Patient reported outcomes (PROs) capture patient perceptions of their health condition, mood, health related quality of life (HRQoL) and other aspects. We aimed to determine if self-reported fatigue, anxiety, depression, perceived deficits questionnaire (PDQ-20), HRQoL, disease activity scores and cognitive neuro-battery (NB) cluster into distinct groups in SLE patients. We assessed if patients changed clusters at 1 year of follow-up.

Methods: This is a retrospective analysis of consecutive consenting patients, aged 18-65 years, who attended a single center (Jul 2016 – Mar 2019) and completed baseline and 1 year follow-up visits. Patients completed a comprehensive NB evaluating six cognitive domains: manual motor speed and dexterity, simple attention and processing, visual spatial construction, verbal fluency, learning and memory (verbal and visuospatial) and executive function. We derived a total score for the NB. Patients completed the Beck anxiety, Beck depression, fatigue severity score (FSS), Short Form Health Survey (SF-36) physical (PCS) and mental scores (MCS), and the PDQ-20 (subjective cognitive function). Disease activity was assessed by SLEDAI-2K. Ward's method was used for clustering and Principal Component Analysis (PCA) was used to confirm the number of clusters. Clusters were grouped based on symptom intensity, defined as those that had high, medium, and low PROs scores relative to one another. We assessed the stability and movement of clusters at 1 year. Stability was assessed with kappa statistic.

Results: 142 patients were included, 89.4% comprised of females. The mean age and SLE duration at enrolment were 43.1 ± 12.1 and 15.3 ± 10.1 years, respectively.

Three clusters were found: **Cluster 1** had low symptom intensity, **Cluster 2** had moderate symptom intensity and **Cluster 3** had high symptom intensity (**Figure 1**). In Cluster 3, the most severe scores for fatigue, depression, anxiety, PDQ-20, and SF-36 MCS were found. NB scores in Cluster 3 were similar to Cluster 2. SLEDAI-2K was similar in Clusters 1 and 3 and more active in Cluster 2.

At 1 year follow-up, 49% of patients (69/142) remained in their baseline cluster; a fair agreement of stability (Kappa statistic 0.35;95% confidence interval 23.0-47.3) was found. Cluster 1 had the highest stability (77% of patients stayed in the same cluster), followed by Cluster 3 (51%) and Cluster 2 had the lowest stability (3%; Table 1). A minor-

ity of patients from Cluster 1 moved to Cluster 3 (19%). In Cluster 3, a larger number moved to Cluster 2 (40%) and less to Cluster 1 (9%).

Conclusion: Three distinct clusters of symptom intensity were defined by PCA in SLE patients in association with cognitive function with Cluster 3 displaying the highest symptom severity and worse cognitive function versus Cluster 1 having the lowest symptom burden and better cognitive function. Patients remained in the same cluster at one year, particularly in Cluster 1 and Cluster 3, and there was a low tendency to move between these two Clusters.

Figure 1. Clusters plotted against eight measurements, demonstrating symptom severity.

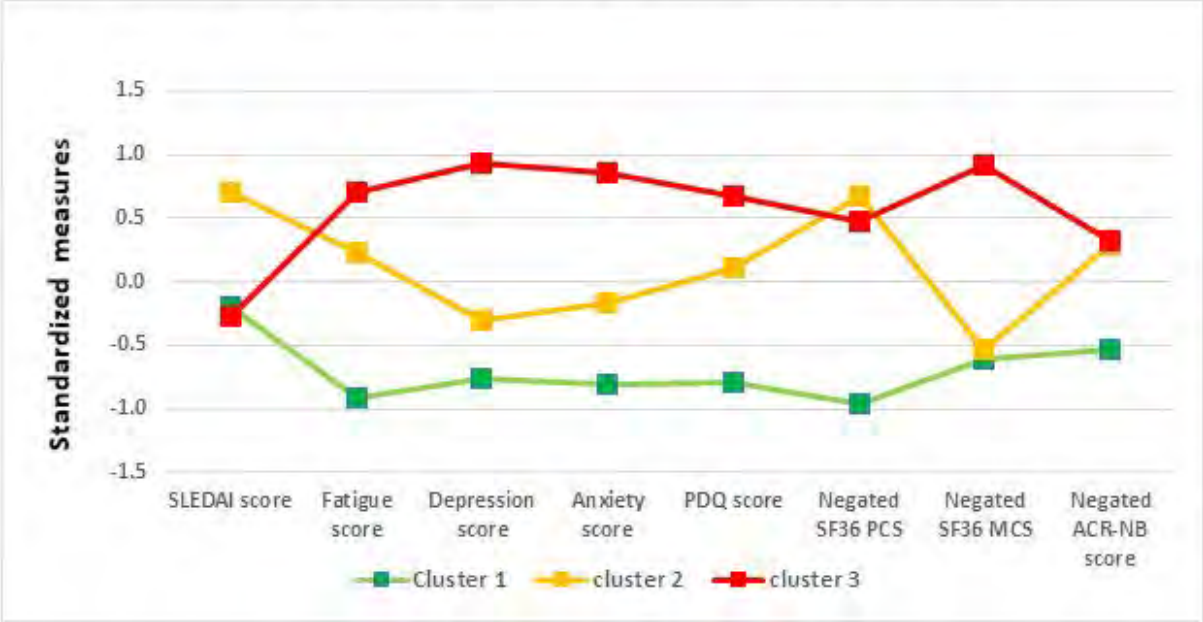

Table 1. Stability and dynamic of clusters at baseline compared to at year 1

Baseline Clusters	Clusters on follow up at year 1		
	Cluster 1 Patients' numbers (%)	Cluster 2 Patients' numbers (%)	Cluster 3 Patients' numbers (%)
Cluster 1	**40 (77%)**	2 (4%)	10 (19%)
Cluster 2	10 (28%)	**1 (3%)**	24 (69%)
Cluster 3	5 (9%)	22 (40%)	**28 (51%)**

Interpretation for the table: e.g. In Cluster 1, 77% of patients remained in this cluster at year 1 while 4% moved to Cluster 2 and 19% to Cluster 3.

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Abstract Number: 1294

Predictors of BILAG-based Outcomes in Patients with SLE: Analysis from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort and MASTERPLANS Consortium

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Several novel SLE therapies are in development. Precision medicine aims to improve treatment practices and real-world outcomes. Certain factors, however, will likely reflect overall good outcomes even with current standard of care (SOC). Such factors need to be considered when assessing treatment-specific response markers in trials of novel therapies. Using an international SLE cohort, we aimed to identify factors associated with attaining favourable response states in SLE.

Methods: Patients were recruited into an international inception SLE cohort from 11 countries. To mimic a trial setting, we selected patients at the first visit in which they fulfilled a definition of active disease, comparable to a level reflecting entry to a clinical trial using 'classic' BILAG i.e. >=1 BILAG A and/or >= 2 BILAG B scores.

The first visit where the BILAG criteria were met was classified as their baseline visit. We examined the rates of, and factors associated with achieving outcomes at 12 months namely, 'Major Clinical Response' (MCR, defined as reduction to BILAG C in all domains, steroid dose of < = 7.5mg & SLEDAI < = 4) and 'Improvement' (defined as reduction to < = 1B score in previously active organs & no new BILAG A/B, stable or reduced steroid dose & no increase in SLEDAI). Univariate and multi-variate logistic regression with Least Absolute Shrinkage and Selection Operator (LASSO) and cross-validation in randomly split samples were used to build prediction models. Variables were ranked by the percentage of times selected by LASSO.

Results: In total, 924 patients (51% of the cohort) met criteria for active disease, including 820 (89%) women. The median [IQR] age and SLE disease duration were 30.6 [23.2 - 41.3] and 0.34 [0.12 - 0.71] years respectively. Common

Table 1. Univariate odds ratios for predictors of major clinical response (selected by LASSO in >=50% of the prediction models) in the active disease cohort

Predictors	Point of Reference	Odds Ratio	95% Confidence Interval
Anti-malarial use	yes vs. no	2.273	1.406 – 3.676
Hypertension	yes vs. no	0.573	0.371 – 0.884
Low C3 or C4	yes vs. no	0.481	0.310 – 0.746
Number of BILAG A or B	>= 2 vs. 1	0.439	0.288 – 0.668
Haematology (BILAG)	A or B vs. C, D or E	0.617	0.404 – 0.941
SLEDAI	1-unit increase	0.884	0.844 – 0.926
Oral steroid dose	Moderate (>7.5 -30mg/day) vs. low (<= 7.5mg/day)	0.327	0.174 – 0.617
Immunosuppressant use	yes vs. no	0.441	0.292 – 0.668

BILAG-2004 organ systems for which patients scored an A or B were renal (n = 480, 52%), haematological (n = 406, 44%), musculoskeletal (n = 335, 36%) and mucocutaneous (n = 317, 34%).

Outcome data at 12 months were available in 759 (82%) patients; MCR and Improvement were achieved in 114 (15%) and 261 (34%) respectively. Factors associated with a higher or lower probability of achieving MCR (selected by LASSO in >= 50% of the prediction models) are shown in Table 1.

Factors associated with a lower probability of achieving improvement in the active disease cohort were residence in Mexico (versus Canada), Hispanic and African (versus Caucasian) race/ethnicity, immunosuppressant use, low C3 or C4 and a higher SLEDAI score.

Conclusion: In active SLE receiving SOC, several factors are associated with the likelihood of achieving MCR and Improvement. Such factors are important to consider, potentially as stratification or minimisation factors, when designing clinical trials or precision medicine studies. Imbalances in geography, demographics, disease characteristics or background therapy may influence the interpretation of such trials.

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Abstract Number: 1295

Belimumab Reduces Severe Flares in Systemic Lupus Erythematosus Across Multiple Patient Subgroups: Results of a Large Integrated Analysis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Belimumab (BEL) is a disease-modifying systemic lupus erythematosus (SLE) treatment that inhibits B-lymphocyte stimulator. BEL has demonstrated a consistent efficacy profile across 4 pivotal Phase 3 trials[1-4] and has improved renal outcomes in active LN and reduced SLE organ damage progression[5,6]. In 2011, BEL became the first biologic approved for SLE treatment in the USA[7] with additional approvals in >70 countries. Severe flares in SLE are linked to poor long-term outcomes and increased healthcare resource utilization[8]. BEL has been shown to decrease severe flare risk[2]; however, data are lacking for specific patient (pt) subgroups. This analysis evaluated the role of BEL in preventing severe flares across a large pooled population as well as by subgroups.

Methods: The Belimumab Summary of Lupus Efficacy (Be-SLE) analysis assessed data from 5 double-blind, placebo (PBO)-controlled BEL studies: BLISS-76, BLISS-52, BLISS-NEA, BLISS-SC, and EMBRACE. Data from pts receiving BEL (10 mg/kg intravenously or 200 mg subcutaneously) were compared with PBO; both groups received also standard therapy (ST). Data were collected every 4 weeks from baseline until Week 52. Severe flare was defined using the Safety of Estrogens in Lupus Erythematosus National Assessment (SELENA)-SLE Disease Activity Index (SLEDAI) flare index. The number of pts and time to first severe flare (days) were determined for both groups. Time to first severe flare was evaluated by the following subgroups: SLE International Collaborating Clinics (SLICC)/American College of Rheumatology (ACR) Damage Index (SDI) score, disease duration, anti-double stranded deoxyribonucleic acid (dsDNA), serum levels of C3 and C4 proteins, steroid use, and immunosuppressant use. Hazard ratios (HR) for severe flare risk between groups were calculated using Cox proportional hazards model, adjusted for study and baseline SELENA-SLEDAI score.

Results: The analysis included 1869 pts receiving BEL and 1217 pts receiving PBO. Mean age (~37 years) and percentage of females (~94%) were similar between treatment groups. Over 52 weeks, 13.8% (n=258) of pts receiving BEL had severe flares versus 22.2% (n=270) of pts receiving PBO. BEL yielded a 39% reduction in the risk of severe flares versus PBO (HR: 0.61; 95% confidence interval [CI]: 0.51, 0.72). BEL also consistently reduced the risk of severe flares versus PBO across various pt subgroups (**Figure**); risk reductions appeared greater in pts with anti-dsDNA+ and ≥C3/C4, or SDI=0.

Conclusion: Pts receiving BEL had a reduced risk of severe flares versus pts receiving PBO. Some subgroups had greater risk reduction; these pts in particular may benefit from BEL. These results reinforce the advantage of BEL in ST in the treatment of SLE.

Funding: GSK

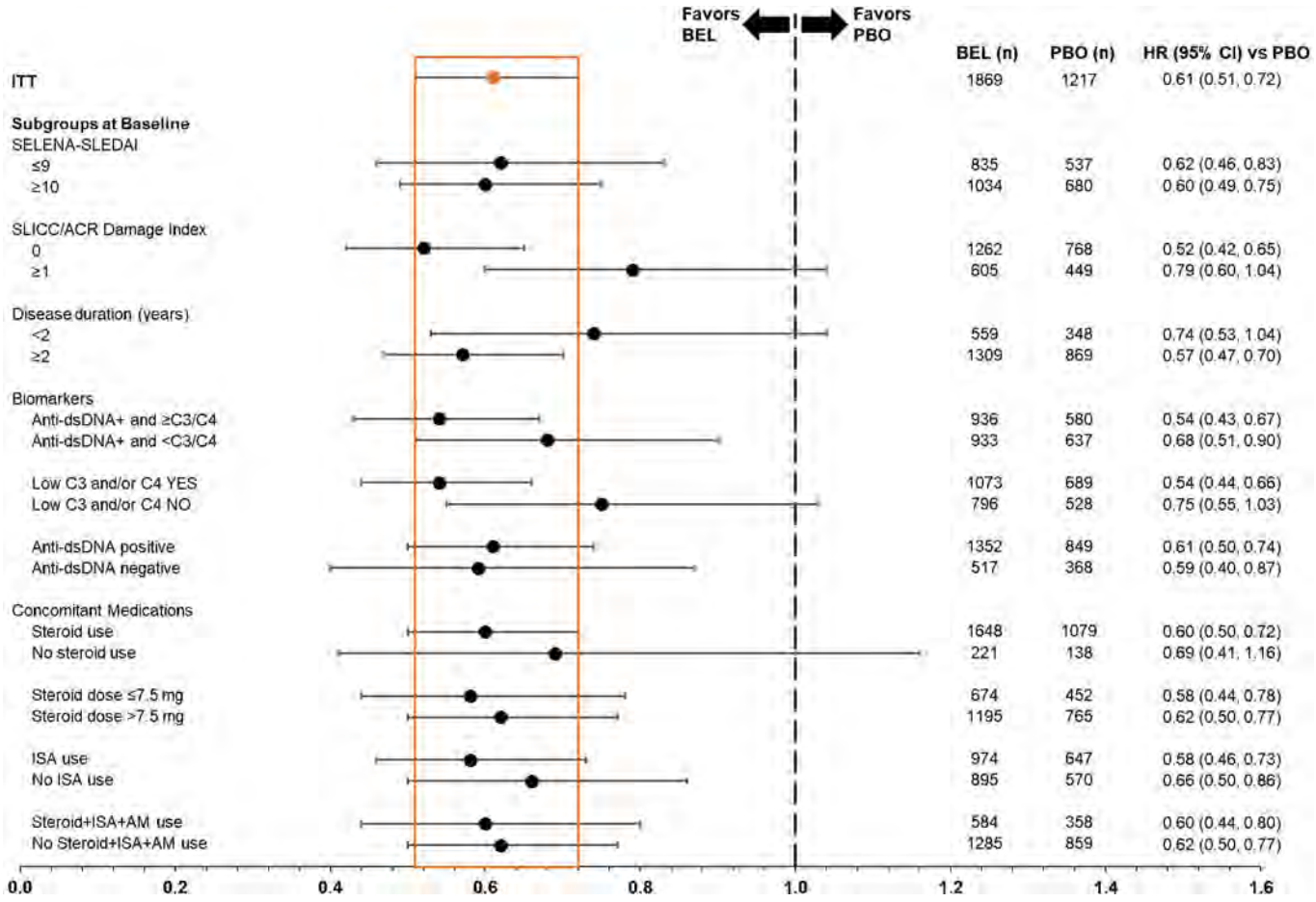

Figure Risk of severe flares HR for BEL versus PBO for various pt characteristic subgroups AM, antimalarial; ISA, immunosuppressant The orange box denotes the 95% CI for the overall (intention-to-treat) HR.

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Abstract Number: 1296

Mortality and Survival in Argentinian Lupus Patients: A Multicenter Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The mortality in lupus patients is 2–3 times higher than the general population. However, survival in these patients has improved significantly and it is currently 95% at 5 years according to several studies. Since the last 20 years, there are no new reports on this issue in Argentina. Objetive: To analyze the factors associated with mortality, survival and causes of death in SLE patients.

Methods: Ten rheumatology argentinian centers participated in this longitudinal - multicenter study. Patients with SLE (ACR 1997 and / or SLICC 2012 criteria) with a minimum follow-up of 6 months between january 2008 and december 2018 were included. Demographic, clinical, laboratory, therapeutic variables (treatments received during the evolution of the disease and within 60 days prior to death or last control); mortality, causes of death and survival at 5, 10 and 20 years were evaluated. Statistical analysis: descriptive statistics, Kaplan-Meier survival curves and Cox regression model.

Results: Three hundred and eighty two patients were included; 90% women and 82% mestizos. Mean disease duration was 4.1 ± 6.7 years. Mean age was 37.2 ± 12.7 years, SLEDAI 3.2 ± 4.2 and SLICC 1.2 ± 1.9 at the last control or death. During the evolution the main manifestations were: mucocutaneous (90.6%), osteoarticular (76%), hematological (55.2%) and renal (55%) involvement. Ninety two percent of the patients received treatment with hydroxychloroquine (HCQ), for an average time of 53 ± 59 months, 43% methylprednisolone pulses, 38% cyclophosphamide and 28% mycophenolate.

Mortality rate was 12% (95% CI [8-15]) and the causes of death were: Infections (27), cardiovascular disease (6), SLE activity (3), catastrophic antiphospholipid syndrome (2) and other causes (8). According to Cox regression models, the variables that increased the risk of death significantly were: renal involvement (RR 3.3), cardiac involvement (RR 2.7), central nervous system involvement (RR 2.1), arterial thrombosis (RR 2.3), hyperlipemia (RR 2.4), number of infections (RR 1.2) and last SLEDAI (1.1). Osteoarticular involvement had a protective effect on the risk of death in all of them.

The use of hydroxychloroquine for more than 36 months decreased the risk of death in this cohort (40%, p= 0.03) and was a mortality protection factor (RR 0.4). Cyclophosphamide was a risk factor for death (RR 5.2).Prednisone was not associated with mortality (p NS).

Patients who died from infection had less disease duration (Me 2.25 years) than those who died due to cardiovascular causes (Me 10 years) or SLE activity (Me 15 years), p= 0.017. In this cohort, survival was 93% at 5 years, 88% at 10 years and 72% at 20 years.

Conclusion: Mortality in argentinian lupus patients was 12% and infection was the main cause of death. The use of HCQ decreased the risk of death.

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Abstract Number: 1297

Factors Associated with Employment and Work Disability in Patients with SLE: A Nested Case-control Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease that can affect multiple organ systems and can vary in its manifestations between individuals. SLE can range in severity, resulting in some patients being unable to continue working while others can remain employed.

The purpose of this study is to analyze and compare factors including SLE disease activity between work disabled and employed patients with SLE to elucidate variables associated with unemployment.

Methods: This is a cross-sectional study focused on the status of last employment reported in the data on 1110 adult SLE patients followed at a single centre where 746 patients were categorized as “Employed” and 364 as “Unemployed” (work disability or Sick Leave). In the employed group, 478 patients were matched to 297 patients in the unemployed group by 2:1 matching. Patients were matched on gender, inception status (whether patient was first seen at clinic within 12 months of SLE diagnosis), disease duration at last visit (+/- 3 years), ethnicity (Caucasian or non-Caucasian) and highest education level obtained. Associations between variables and employment status were assessed using univariate and multivariate conditional logistic regressions in a nested case-control study. Greedy matching algorithm was used to assemble the cases and controls. Patients’ characteristics were compared by paired t-test and McNemar’s test in matched cohorts, and a conditional logistic regression was performed to examine patients’ demographics, last five years’ disease activity, organ damage, disease burdens and treatment to the last em-

Table 1: Patient characteristic data of the Unemployed and Employed groups

Variable in the last 5 years	Value	Unemployed (N=297)	Employed (N=478)	P-value
Inception Patients	Yes (%)	122 (41.1%)	194 (40.6%)	N/A[1]
Gender	Female	273 (91.9%)	445 (93.1)	N/A[1]
	Male	24 (8.1%)	33 (6.9%)	
Ethnicity	Black	65 (21.9%)	66 (13.8%)	N/A[1]
	Caucasian	173 (58.2%)	269 (56.3%)	
	Chinese	20 (6.7%)	62 (13.0%)	
	Filipino	12 (4.0%)	31 (6.5%)	
	Others	27 (9.1%)	50 (10.5%)	
Age at SLE Diagnosis	Mean ± SD	32.3 ± 12.0	27.7 ± 11.1	<0.0001[2]
Disease duration in years at last visit	Mean ± SD	17.2 ± 10.4	16.2 ± 9.8	N/A[1]
Education at last visit	<Grade 8	8 (2.7%)	0 (0.0%)	N/A[1]
	Grade 8	20 (6.7%)	16 (3.3%)	
	High school graduate	77 (25.9%)	114 (23.8%)	
	College	114 (38.4%)	149 (31.2%)	
	University	78 (26.3%)	199 (41.6%)	
Adjusted mean SLEDAI	Mean ± SD	4.4 ± 3.8	3.5 ± 3.3	<0.0001
Adjusted mean SLEDAI-2KG	Mean ± SD	6.1 ± 4.9	4.7 ± 4.3	<0.0001
Last SDI	Mean ± SD	2.4 ± 2.3	0.9 ± 1.4	<0.0001
Myocardial infarction	Yes (%)	23 (7.7%)	13 (2.7%)	0.0005
Stroke	Yes (%)	29 (9.8%)	15 (3.1%)	0.0002
Fibromyalgia	Yes (%)	114 (38.4%)	71 (14.9%)	<0.0001
Hypertension[3]	Yes (%)	217 (73.1%)	269 (56.3%)	<0.0001
Dyslipidemia[4]	Yes (%)	215 (72.4%)	256 (53.6%)	<0.0001
Cumulative dose of glucocorticoids (grams)	Mean ± SD	28.0 ± 46.5	14.0 ± 25.0	<0.0001
Average dose while on glucocorticoids within last five years in the clinic (mg/day)	Mean ± SD	8.5 ± 8.8	5.3 ± 6.7	<0.0001

[1] Variables were matched and hence were not compared

[2] Variable was not matched

[3] Hypertension defined as blood pressure ≥140/90 mmHg or treated with antihypertensives

[4] Dyslipidemia defined as abnormal total cholesterol or Low-density Lipoprotein levels or treated with antidyslipidemic agents

Table 2: Univariate and multivariate conditional logistic regression analyses to assess the association with unemployment

	Univariate Conditional Logistic Regression				Multivariable Conditional Logistic Regression With SLEDAI-2K + Glucocorticoids				Multivariable Conditional Logistic Regression With SLEDAI-2KG			
Independent	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	Pr > Chi-Square	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	Pr > Chi-Square	Odds Ratio Estimate	Lower 95% Confidence Limit for Odds Ratio	Upper 95% Confidence Limit for Odds Ratio	Pr > Chi-Square
Age at SLE diagnosis	1.04	1.03	1.06	<0.0001	1.04	1.02	1.06	0.0002	1.04	1.02	1.06	0.0001
Adjusted Mean SLEDAI in last five years	1.08	1.04	1.13	0.0004	1.06	1.00	1.12	0.07				
Adjusted Mean SLEDAI-2KG in last five years	1.09	1.05	1.13	<0.0001					1.07	1.03	1.12	0.002
Last SDI score	1.60	1.43	1.79	<0.0001	1.58	1.39	1.79	<0.0001	1.59	1.40	1.80	<0.0001
Myocardial infarction within last five years	2.80	1.41	5.58	0.0033								
History of stroke within last five years	3.08	1.61	5.88	0.0007								
Fibromyalgia within last five years	3.47	2.42	4.96	<0.0001	3.88	2.54	5.94	<0.0001	3.84	2.52	5.86	<0.0001
Hypertension[1] within last five years	2.09	1.52	2.89	<0.0001								
Dyslipidemia[2] within last five years	2.26	1.62	3.14	<0.0001								
Cumulative dose of glucocorticoids within last five years in the clinic (grams)	1.13	1.13	1.14	<0.0001	1.07	1.06	1.08	0.044				
Average dose while on glucocorticoids within last five years in the clinic (mg/day)	1.07	1.04	1.09	<0.0001								

[1] Hypertension defined as blood pressure ≥140/90 mmHg or treated with antihypertensive

[2] Dyslipidemia defined as abnormal total cholesterol or Low-density Lipoprotein levels or treated with antidyslipidemic agents

ployment status. Step-down variable selection method was adopted in the multivariable model building with Akaike Information Criterion (AIC) used as the model fitting statistics.

Results: The demographics of 775 patients were represented in Table 1. Patients in the unemployed group showed significantly greater disease activity (higher adjusted mean SLEDAI-2K and SLEDAI-K Glucocorticoid index (SLEDAI-2KG) in the past five years and greater damage by SDI). Patients were also found to have a significantly higher prevalence of myocardial infarction, stroke, fibromyalgia, hypertension, and higher daily and cumulative glucocorticoid use. In the multivariable analysis (Table 2), age at SLE diagnosis (OR, 95% CI: 1.04,1.02-1.06), adjusted mean SLEDAI-2KG in past five years (OR, 95% CI: 1.07, 1.03-1.12), SDI (OR, 95% CI: 1.59, 1.40-1.80) and prevalence of fibromyalgia (OR, 95% CI: 3.84, 2.52, 5.86) were associated with the increased risk of unemployment. We conducted additional modeling where adjusted mean SLEDAI-2KG was substituted by adjusted mean SLEDAI-2K and cumulative glucocorticoid dose in the past five years, and the results were similar to the previous model.

Conclusion: High disease activity, damage and use of glucocorticoids were associated with an increased likelihood of patients being unemployed. Similarly, fibromyalgia was strongly associated with a patient being unemployed. Employment status may be improved by better control of SLE disease activity and management of fibromyalgia and other risk factors.

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Abstract Number: 1298

Clinical Characteristics of Patients with Pre-pubertal Onset SLE and Disease Outcome Throughout Puberty: A Multicenter North American Longitudinal Study

Martha Rodriguez[1], Kiana Rachele Johnson[2] and Kathleen O'Neil[1], [1]Riley Hospital for Children at Indiana University, Indianapolis, IN, [2]East Tennessee state University, Johnson, TN

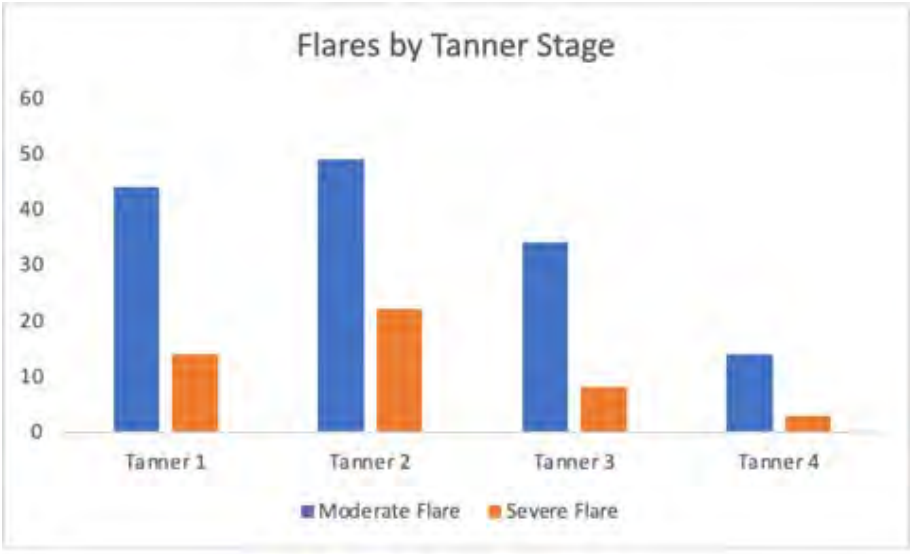
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Pediatric Onset SLE is associated with higher disease activity and higher risk of damage. There is limited information on prepubertal patients with SLE and how disease activity varies throughout puberty. With the increasing life expectancy and yet subsequent cumulative damage it is paramount to characterize the clinical manifestations, disease activity, organ damage and quality of life in these patients. The aims of this study are to describe the clinical characteristics, disease activity pattern, frequency and classification of flares and organ damage of patients with prepubertal onset SLE and to evaluate the association of disease outcome as they relate to pubertal progress and hormonal changes.

Methods: This database represents 63 subjects (51 girls and 12 boys) from 12 CARRA sites followed every 3 months from late pre-puberty through completion of maturation process or study completion. Collected data included comprehensive medical history, physical examination findings, Tanner stage, SLEDAI-2k activity scores and MD-global assessments. Analytes measured in serum: Sex *Hormones* – Prolactin, estradiol, testosterone; adipose derived hormones *Adipokines* – leptin, adiponectin, resistin, visfatin. Flares were determined by SELENA-SLEDAI flare index. Two generalized estimating equations were calculated using SLEDAI and PGA as predictors in two different models. Multivariable models were adjusted for possible confounders.

Results: A total of 484 follow-up visits were included. Mean length of study involvement was 21 months. Arthritis, hematologic and renal manifestations were predominant among this group of subjects. Results of the of GEE analysis of hormones predicting disease activity indicated the main effects of adiponectin (Wald $c^2 = 14.25$, $p < .001$) and estradiol (Wald $c^2 = 6.04$, $p < .01$) significantly predicted disease activity as measured by the SLEDAI. Interactions between Tanner stage and adiponectin (Wald $c^2 = 22.64$, $p< .001$) and Tanner stage and Estradiol (Wald $c^2 = 7.187$, $p< .001$) predicted disease activity as indicated by higher SLEDAI scores. In our second model, the main effects of leptin (Wald $c^2 = 8.14$, $p < .01$), adiponectin (Wald $c^2 = 15.88$, $p < .001$), visfatin (Wald $c^2 = 9.61$, $p < .001$), and progesterone (Wald $c^2 = 12.64$, $p < .001$) predicted disease activity as indicated by PGA scores.

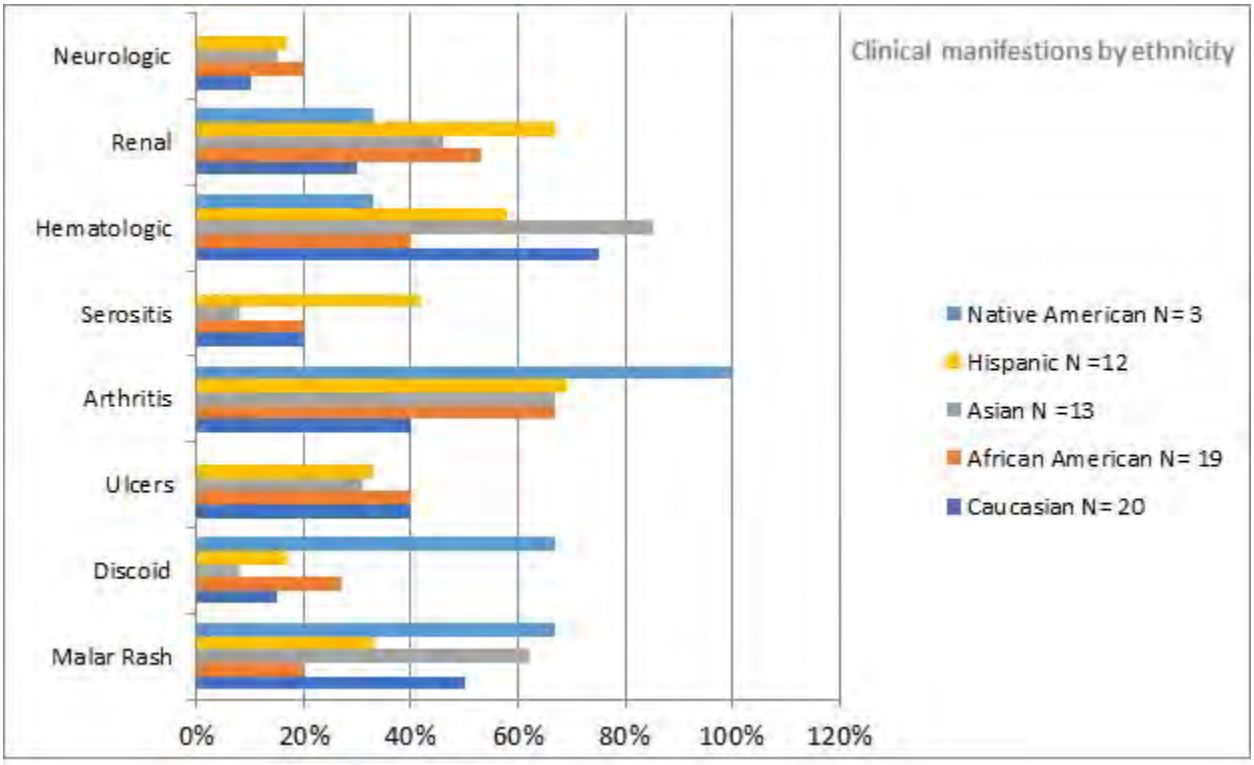
Conclusion: The activity level of SLE and risk of disease flare rise as soon as the first signs of puberty are apparent, a time referred to as the start of Tanner 2. Changes of adiponectin and estradiol significantly predicted disease activity as measured by the SLEDAI. Disease activity and flare risk declined once the child was sexually mature. Treatment algorithms based on these factors may help to improve long-term outcomes in childhood SLE.



Flares vs Tanner Stages

SLEDAI model	Wald χ^2	p-value
Adiponectin	14.25,	$p < .001$
Estradiol	6.04	$p < .01$
Tanner stage X adiponectin	22.64	$p < .001$
Tanner stage X Estradiol	7.187	$p < .001$
PGA Model		
leptin	8.14	$p < .01$
adiponectin	15.88	$p < .001$
visfatin	9.61	$p < .001$
progesterone	12.64	$p < .001$
tanner stage X leptin	16.47	$p < .001$
tanner stage X adiponectin	17.85	$p < .001$
tanner stage X visfatin	19.65	$p < .001$
tanner stage X progesterone	8.23	$p < .05$

SLEDAI PGA models



Clinical manifestations by ethnicity

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Abstract Number: 1299

Longitudinal Patterns of Response to Standard of Care Therapy for Lupus Nephritis: Data from the Accelerating Medicines Partnership Lupus Network

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Response Rates in AMP LN

N = 121	Baseline	Wk 12	Wk 26	Wk 52
CR	0	16	28	34
% CR	0.0%	13.2%	23.1%	28.1%
PR	0	19	24	28
CR and PR	0	35	52	62
% CR and PR	0.0%	28.9%	43.0%	51.2%

Figure 1. Heat Map Displaying Longitudinal CR and PR Responses in AMP LN

Background/Purpose: The Accelerating Medicines Partnership (AMP) Lupus Network was established with the goal of applying novel technologies to the interrogation of blood and tissue samples from patients with lupus nephritis (LN). In contrast to global LN clinical trials, the AMP LN cohort affords an opportunity to generate outcome data representative of a US multicenter multi-ethnic real-world experience. In this analysis, the AMP clinical dataset was investigated to determine the percentages of patients who attained prespecified definitions of partial or complete responses at 52 weeks. In addition, incorporation of response rates at weeks 12 and 26 to the analysis provided longitudinal patterns of response to standard of care.

Methods: Patients with LN who were undergoing kidney biopsies as part of standard of care were eligible to enroll in the AMP LN study. Response definitions were only applied to cases whose baseline spot urine protein/creatinine (UPCR) ratios were > 1.0. Complete response (CR) required: 1) UPCR < 0.5; and 2) normal creatinine (< 1.3 mg/dL) or, if abnormal at baseline, < 125% of baseline; and 3) prednisone < 10 mg/day at the time of the study visit. Partial response required: 1) >50% reduction in UPCR without meeting UPCR criterion for CR; and 2) normal creatinine (< 1.3 mg/dL) or, if abnormal, < 125% of baseline; and 3) prednisone dose < 15 mg/day at the time of the study visit. Patients who did not achieve a CR or PR at the specific timepoints were considered non-responders (NR). Only patients with renal biopsies that demonstrated ISN/RPS classes III, IV, V or combined III or IV with V and data available at all four timepoints (baseline, weeks 12, 26 and 52) were included in this analysis. Cross-sectional and longitudinal analyses of responses were performed, and heat maps were generated to graphically display response patterns.

Results: Data on 121 patients with LN enrolled in AMP were included in this analysis. Cross-sectional response rates at 52 weeks were: CR: 28.1%; PR: 23.1%; NR: 48.8% (Table 1). Response rates at weeks 12 and 26 are additionally displayed in Table 1, and Figure 1 is a heat map demonstrating longitudinal responses of our patients. All patients were considered NR at baseline. Only 7.4% of patients had week 12 CR responses sustained through week 52, whereas 19% had attained PR or CR at all 3 visits. An additional 14.9% achieved a PR or CR at 26 weeks which was sustained at 52 weeks. Overall, 36.4% of patients were NR at all time points.

Conclusion: Clinical data from the AMP Lupus Network revealed rates of 52-week CR and PR that were consistent with placebo response data from recently conducted LN trials. Low sustained CR rates not only underscore the need for more efficacious therapies but highlight how critically important it is to understand the molecular pathways that are associated with response and non-response.

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Abstract Number: 1300

Effect of Time in Clinical Remission on Damage Accrual in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

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Session Time: 8:30AM–10:30AM

Background/Purpose: We have previously shown that prolonged clinical remission for ≥10 years is associated with significantly less damage accrual in inception patients with systemic lupus erythematosus (SLE)[1]. However, most lupus patients (approximately 70%) will follow a relapsing-remitting disease course pattern with greatly varying duration of remission over time. The aim of the present study was to assess the optimal duration of clinical remission in inception lupus patients and investigate its effect on damage accrual.

Methods: Inception SLE patients (time from diagnosis to first clinic visit ≤18 months) with at least 10 years of follow-up who had a relapsing-remitting pattern (≥2 distinct clinical flares over that decade) were retrieved from our long-term longitudinal database. Optimal duration of remission during the first decade of disease for the outcome of new damage accrual was established from a Logistic regression analysis (Receiver Operating Characteristic curve, ROC). Subsequently, subjects were divided into two groups according to the optimal remission duration (defined as clinical SLEDAI-2K=0 regardless of therapy). Groups were compared for percentage of patients with new damage accrual at 10 years, mean Damage Index, atherosclerotic vascular events (AVEs), osteonecrosis, osteoporosis and cumulative glucocorticoid dose. Outcomes were compared by Student's t-test for mean values and Chi-Square test for binary variables.

Results: Two hundred patients were retrieved. Remission duration of 7.1 years yielded the best threshold based on the ROC analysis using Youden index as the selection criterion (specificity 82%, sensitivity 33%). Patients were divided into groups A (time in remission ≤7.1 years) and B (>7.1 years). Patients in group A had significantly less mucocutaneous involvement; there were no significant differences regarding the other demographic, clinical, immunological and therapeutic variables at baseline (Table 1). Outcomes are shown in Table 2. Group B received significantly less glucocorticoids than group A and accrued significantly less damage. Osteoporosis was significantly less frequent in these patients. The prevalence of atherosclerotic vascular events and osteonecrosis was also less although insignificantly.

Conclusion: Among inception patients with SLE, clinical remission of at least 7.1 years is associated with significantly less damage over 10 years than shorter remission. While the difference in AVEs was not statistically significant, this comorbidity usually manifests later in disease course.

Table 1. Demographic, clinical, immunological and therapeutic characteristics at baseline

VARIABLE	Group A N=149	Group B N=51	*p*
Age (y)	35.2 ± 13.3	35.5 ± 14.1	0.872
Females (n, %)	134 (89.9%)	46 (90.2%)	0.957
Blacks	19 (12.8%)	6 (11.8%)	0.841
Caucasians (n, %)	106 (71.1%)	34 (66.7%)	
Chinese (n, %)	10 (6.7%)	5 (9.8%)	
Others (n, %)	14 (9.4%)	6 (11.8%)	
SLEDAI-2K	9.9 ± 7.9	8.8 ± 8.1	0.382
CNS involvement	23 (15.4%)	5 (9.8%)	0.317
Renal involvement (n, %)	36 (24.2%)	8 (15.7%)	0.207
MSK involvement	33 (22.1%)	13 (25.5%)	0.624
Skin involvement	87 (58.4%)	19 (37.3%)	0.009
Serositis (pleuritis / pericarditis)	19 (12.8%)	4 (7.8%)	0.343
Hematological involvement	14 (9.4%)	5 (9.8%)	0.932
Anti-dsDNA positive	68 (45.6%)	28 (54.9%)	0.253
Low C3/C4	75 (50.3%)	25 (49%)	0.871
Lupus anticoagulant	31 (23.3%)	11 (23.9%)	0.934
Anticardiolipin antibodies	14 (17.9%)	7 (21.9%)	0.634
Current Smoker	25 (16.8%)	12 (24.5%)	0.23
Glucocorticoids	110 (73.8%)	39 (76.5%)	0.708
Prednisone dose (mg/day)	33.6 ± 22.4	29.1 ± 19.7	0.268
Antimalarials	72 (48.3%)	27 (52.9%)	0.569
Immunosuppressives	36 (24.2%)	15 (29.4%)	0.458
Anticoagulation / Antiplatelets	5 (3.4%)	5 (9.8%)	0.068

Table 2. Outcomes at 10 years

VARIABLE	Group A N=149	Group B N=51	*p*
New damage accrual (n, %)	92 (61.7%)	23 (45.1%)	0.038
New damage definitely/possibly related to glucocorticoids (n, %)	61 (40.9%)	16 (31.4%)	0.226
New damage not related to glucocorticoids (n, %)	57 (38.3%)	11 (21.6%)	0.03
SDI	1.3 ± 1.4	0.8 ± 1.0	0.037
AVEs	15 (10.1%)	4 (7.8%)	0.64
Osteonecrosis	23 (15.4%)	7 (13.7%)	0.768
Osteoporosis	19 (12.8%)	0 (0%)	0.017
Cumulative prednisone dose (g)	28.3 ± 18.5	19.1 ± 15.3	0.003

Disclosure: K. Tselios, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **J. Su**, None; **M. Urowitz**, GlaxoSmithKline, 2, 5, 6, UCB, 2, Lilly, 6, AstraZeneca, 2.

Abstract Number: 1301

Early Increase in Circulating Memory B Cells Portends Clinical Response to Treatment in Pooled Data from Three Phase III Trials of Belimumab

Ioannis Parodis[1], Alvaro Gomez[2], Julius Lindblom[2], Alexander Borg[2], Sharzad Emamikia[2] and Mariele gatto[3], [1]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden and Department of Rheumatology, Faculty of Medicine and Health, Örebro University, Örebro, Sweden, [2]Division of Rheumatology, Department of Medicine Solna, Karolinska Institutet, Karolinska University Hospital, Stockholm, Sweden, [3]Department of Rheumatology, University of Padua, Padua, Italy

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Belimumab blocks soluble B cell activating factor (BAFF) and is the only to date approved targeted treatment for systemic lupus erythematosus (SLE). Identification of biological predictors of response occurring earlier upon treatment would provide measurable tools to improve patient monitoring and stratification according to likelihood of response. We investigated early changes in B lymphocyte subsets in relation to response to standard therapy plus belimumab or placebo given to patients with active SLE and mainly musculoskeletal and mucocutaneous symptoms.

Methods: We analyzed pooled data from belimumab phase III clinical trials including BLISS-76 (N=819) and BLISS-SC (N=836); in addition, 60 patients from the BLISS North-East Asia trial were included in the analysis. B lymphocyte subsets were determined with flow cytometry. Treatment response was assessed using the composite measure SLE Responder Index 4 (SRI-4), defined as decrease in SLEDAI by ≥4 points, no worsening in the physician's global assessment by >30% and no new British Lupus Isles Assessment Group (BILAG) index (≥1 A or ≥2 B), at week 52. Additionally, persistence of SRI-4 through week 52 was evaluated. We investigated B cell changes relative to baseline using logistic or proportional hazards regression analysis, as appropriate.

Results: We found an association between an early expansion of $CD19^+CD20^+CD27^+$ memory B cells from baseline through week 8 and attainment of SRI-4 response at week 52 (OR: 1.5; 95% CI: 1.18–1.89; P=0.001), or for relative increases >10% (OR: 1.5; 95% CI: 1.17–1.83; P=0.001). Expansion above this threshold of 10% was also associated with increased probability or shorter time to achieve SRI-4 response that was maintained through week 52 (HR: 1.4; 95% CI: 1.15–1.61; P< 0.001). Notably, belimumab treatment (any dose) yielded an 11.5-fold increased probability of memory B cell expansion through week 8 compared with placebo (95% CI: 8.74–15.02; P< 0.001). No association with SRI-4 response was observed for early changes in $CD19^+CD20^+$ B cells, $CD19^+CD20^+CD27^-$ naïve B cells, $CD19^+CD20^+CD69^+$ activated B cells, $CD19^+CD20^-CD27^{bright}$ short-lived plasma cells, $CD19^+CD20^-CD138^+$ long-lived plasma cells, or $CD19^+CD38^{bright}CD27^{bright}$ SLE-associated plasma cells.

Conclusion: Early increases in memory B cells through the first 8 weeks of therapy, mainly driven by belimumab, portended good and sustained clinical response within one year from treatment initiation. Early immunological changes preceding the clinical outcome and may prove useful in early evaluation of belimumab therapy.

Disclosure: I. Parodis, Amgen, Elli Lilly and Company, and Gilead Sciences., 5, 6, GlaxoSmithKline and Novartis., 5, 6; **A. Gomez**, None; **J. Lindblom**, None; **A. Borg**, None; **S. Emamikia**, None; **M. gatto**, None.

Abstract Number: 1302

Year-3 Observational Follow-up of Belimumab Safety (Mortality and Malignancies) in Patients with SLE Who Completed a Phase 4, 52-Week, Randomized, Double-Blind Placebo-Controlled Safety Study

Saira Sheikh[1], Cheng-Chung Wei[2], Dana Tegzova[3], William Stohl[4], Ricardo Acayaba de Toledo[5], Tamara Mucenic[6], Mauricio Abello Banfi[7], Kathleen Maksimowicz-McKinnon[8], Carlos Abud-Mendoza[9], Sandra Navarra[10], Mercedes Garcia[11], Ignacio Garcia-De La Torre[12], Regina Kurrasch[13], Sofia Fernandes[14], Julia Harris[15], Saima Muzaffar[14], Norma Lynn Fox[13], Andrew Liu[16], Holly Quasny[17] and David Roth[13], [1]University of North Carolina Thurston Arthritis Research Center, and Department of Medicine, Division of Rheumatology, Allergy and Immunology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, [2]Institute of Medicine, Chung Shan Medical University; Graduate Institute of Integrated Medicine, China Medical University, Taichung, Taiwan (Republic of China), [3]Institute of Rheumatology, Prague, Czech Republic, [4]University of Southern California Keck School of Medicine, Los Angeles, CA, [5]Faculdade de Medicina de São José do Rio Preto, São José do Rio Preto, Brazil, [6]Hospital Moinhos de Vento, Porto Alegre, Brazil, [7]Centro Integral de Reumatología del Caribe, Barranquilla, Colombia, [8]Henry Ford Hospital, Wayne State University, Detroit, MI, [9]Hospital Central "Dr Ignacio Morones Prieto", Unidad Regional de Reumatología y Osteoporosis, Hospital Central and Facultad de Medicina de la Universidad Autónoma de San Luis Potosí, San Luis Potosí, Mexico, [10]University of Santo Tomas Hospital, Manila, Philippines, [11]Hospital Interzonal General de Agudos José de San Martín, La Plata, Argentina, [12]Centro de Estudios de Investigación Básica y Clínica, S.C., Guadalajara, Mexico, [13]GlaxoSmithKline, Collegeville, PA, [14]GlaxoSmithKline, Stevenage, Hertfordshire, United Kingdom, [15]GlaxoSmithKline, Uxbridge, United Kingdom, [16]GlaxoSmithKline, Brentford, United Kingdom, [17]GlaxoSmithKline, Research Triangle Park, NC

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Table 1. Year-1, Year-2 and Year-3 post-treatment* follow-up mortality and new primary malignancy rates by study treatment during Year 1

	BEL Year-1 treatment group	PBO Year-1 treatment group	Total
Year-1 (as-treated) population	**N=2002**	**N=2001**	**N=4003**
Year-1 deaths, n (%)	13 (0.65)	22 (1.10)	35 (0.87)
Year-1 new primary malignancies, n (%)	9 (0.45)	10 (0.50)	19 (0.47)
Year-2 (as-treated in Year 1) population (off-study treatment)	**N=1694**	**N=1670**	**N=3364**
Year-2 deaths, n (%)	9 (0.53)	21 (1.26)	30 (0.89)
Year-2 new primary malignancies, n (%)	3 (0.18)	7 (0.42)	10 (0.30)
Year-3 (as-treated in Year 1) population (off-study treatment)	**N=1647**	**N=1619**	**N=3266**
Year-3 deaths by MedDRA SOC, n (%)	9 (0.55)	17 (1.05)	26 (0.80)
Infections/infestations	3 (0.18)	3 (0.19)	6 (0.18)
Cardiac disorders	0	4 (0.25)	4 (0.12)
General disorders/administration site conditions	1 (0.06)	3 (0.19)	4 (0.12)
Musculoskeletal/connective tissue disorders	1 (0.06)	3 (0.19)	4 (0.12)
Respiratory/thoracic/mediastinal disorders	0	2 (0.12)	2 (0.06)
Gastrointestinal disorders	1 (0.06)	0	1 (0.03)
Hepatobiliary disorders	1 (0.06)	0	1 (0.03)
Neoplasms	1 (0.06)	0	1 (0.03)
Vascular disorders	1 (0.06)	0	1 (0.03)
Nervous system disorders	0	1 (0.06)	1 (0.03)
Uncoded	0	1 (0.06)	1 (0.03)
Year-3 new primary malignancies (neoplasms) by MedDRA SOC, n (%)	8 (0.49)	9 (0.56)	17 (0.52)

*Patients in the post-treatment follow-up period are no longer receiving study treatment.

MedDRA, Medical Dictionary for Regulatory Activities; SOC, system organ class.

Background/Purpose: Belimumab (BEL) is a recombinant IgG1λ monoclonal antibody that is approved for treatment of systemic lupus erythematosus (SLE). Although clinical studies of BEL have demonstrated a favorable benefit–risk profile, varying incidence rates of mortality and adverse events of special interest, including malignancies, warrant further consideration. The Belimumab Assessment of Safety in SLE (BASE) placebo- (PBO)-controlled trial was conducted to assess long-term safety following BEL exposure.[1]

Methods: This was a post-treatment follow-up of the Phase 4, double-blind BASE study (GSK Study BEL115467; NCT01705977).[1] A total of 4003 adults with active, autoantibody positive SLE received BEL (10 mg/kg IV) or PBO, plus standard therapy (ST) for 48 weeks. Following the treatment period, patients entered a Year 2–5 follow-up period in which they received physician-directed ST. All patients were contacted annually by telephone, including patients who discontinued treatment during the study. Mortality and new primary malignancies (including nonmelanoma skin cancer [NMSC]) were the only endpoints collected and rates were summarised. We present the data for the Year-3 follow-up by treatment received during the 52-week double-blind treatment period (Year 1).

Results: Baseline characteristics at the start of the 52-week treatment for the Year-3 follow-up population (N=3266) were similar to those of the Year-1 double-blind study population (N=4003). By the Year-3 follow-up, cumulatively 12.0% and 10.9% of patients in the original BEL and PBO Year-1 treatment groups had received BEL as part of physician-directed care, respectively. In total (for both treatment groups), crude mortality rates were similar across Year 1 (0.87%), Year 2 (0.89%), and Year 3 (0.80%), whilst crude malignancy rates for Year 3 (0.52%) were numerically higher than Year 2 (0.30%), but similar to Year 1 (0.47%) (**Table 1**). Mortality and malignancy rates were lower in the BEL versus PBO Year-1 treatment group. Cumulative rates are shown in **Table 2**.

Table 2. Cumulative deaths and new primary malignancies by follow-up year

	BEL Year-1 treatment group N=2002	PBO Year-1 treatment group N=2001	Total N=4003
Cumulative deaths by Year 1, n (%)	13 (0.65)	22 (1.10)	35 (0.87)
Incidence rate per 100 patient years	0.66	1.11	
Cumulative deaths by Year-2 follow-up*, n (%)	22 (1.10)	43 (2.15)	65 (1.62)
Incidence rate per 100 patient years	0.60	1.18	0.89
Cumulative deaths by Year-3 follow-up*, n (%)	31 (1.55)	60 (3.00)	91 (2.27)
Incidence rate per 100 patient years	0.58	1.14	0.86
Cumulative new primary malignancies by Year 1, n (%)	9 (0.45)	10 (0.50)	19 (0.47)
Incidence rate per 100 patient years for malignancies (excluding NMSC)†	0.25	0.35	
Incidence rate per 100 patient years for NMSC†	0.20	0.15	
Cumulative new primary malignancies by Year-2 follow-up*, n (%)	12 (0.60)	17 (0.85)	29 (0.72)
Incidence rate per 100 patient years	0.34	0.48	0.41
Cumulative new primary malignancies by Year-3 follow-up*, n (%)	20 (1.00)	25 (1.25)	45 (1.12)
Incidence rate per 100 patient years	0.39	0.49	0.44

*Year-2 and Year-3 follow-up populations were off-study treatment; †As summarized for Year 1.

Conclusion: Post-treatment follow-up results in Year 3 from BASE, the largest study of patients with SLE to date, provide continued support for the safety profile of BEL and remained consistent with the Year-2 follow-up data. No new safety concerns for BEL were identified in patients with active, autoantibody-positive SLE receiving ST.

Funding: GSK

References:

[1]Sheikh SZ, et al. *Lancet Rheum* 2020 (ePub ahead of print) doi.org/10.1016/S2665-9913(20)30355-6

Disclosure: S. Sheikh, Pfizer, 5, GlaxoSmithKline, 2, 5; **C. Wei**, Abbvie, 2, 5, Amgen, 5, Astellas, 5, BMS, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Gilead, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, TSH Biopharm, 2, Chugai, 2, Eisai, 2, Pfizer, 2, Sanofi-Aventis, 2, Sun, 5; **D. Tegzova**, None; **W. Stohl**, Gilead, 5, Pfizer, 5, GlaxoSmithKline, 2, 5; **R. Acayaba de Toledo**, Pfizer, 5, AbbVie, 2, 5, 6, Novartis, 2, 5, 6, GSK, 5, UCB, 2, 5, 6, Roche, 5, 6, Janssen, 5, 6; **T. Mucenic**, GSK, 5, Janssen, 5, 6, Roche, 5, 6, Eli Lilly, 5, Gilead, 5, UCB, 5, Novartis, 6, BMS, 6, AbbVie, 6, Pfizer, 6; **M. Abello Banfi**, None; **K. Maksimowicz-McKinnon**, Chemocentryx, 1; **C. Abud-Mendoza**, Lilly, 6, GlaxoSmithKline, 6, Pfizer, 6; **S. Navarra**, Biogen, 2, Boehringer Ingelheim, 6, Pfizer, 6, Novartis, 6, Johnson & Johnson, 6; **M. Garcia**, GSK, 6, Janssen, 6, Pfizer, 6; **I. Garcia-De La Torre**, None; **R. Kurrasch**, GlaxoSmithKline, 3, 8, 11; **S. Fernandes**, GlaxoSmithKline, 3, 8, 11; **J. Harris**, GlaxoSmithKline, 3, 8, 11; **S. Muzaffar**, GlaxoSmithKline, 3, 8, 11; **N. Fox**, GlaxoSmithKline, 3, 8, 11; **A. Liu**, GlaxoSmithKline, 3, 8, 11; **H. Quasny**, GlaxoSmithKline, 3, 8, 11; **D. Roth**, GlaxoSmithKline, 3, 8, 11.

Abstract Number: 1303

Associations Between Early Changes in Circulating B Cell Subsets and Severe Flare in Systemic Lupus Erythematosus – Results from Three Phase III Trials of Belimumab

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Outcomes (1257–1303)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Belimumab is the only approved targeted treatment for systemic lupus erythematosus (SLE). Identification of early predictors of response or non-response to therapy is imperative to optimize surveillance and decision-making. We studied early changes in B cell subsets in relation to flare during standard therapy plus belimumab or placebo given to patients with active SLE within the frame of three phase III clinical trials of belimumab.

Methods: We analyzed pooled 52-week data from BLISS-76 (N=819), BLISS-SC (N=836), and BLISS North-East Asia (N=60). B cell subsets were determined with flow cytometry. Severe flare was evaluated according to the SELENA-SLEDAI Flare Index every fourth week. We investigated B cell changes relative to baseline using proportional hazards regression analysis.

Results: Early decreases in $CD19^+CD20^-CD138^+$ long-lived (HR: 0.7; 95% CI: 0.56–0.98; P=0.034) and $CD19^+CD38^{bright}CD27^{bright}$ SLE-associated plasma cells (HR: 0.7; 95% CI: 0.50–0.87; P=0.003) from baseline through week 24 were negatively associated with the development of a severe flare during the study period, i.e. through week 52 from treatment initiation. A similar trend was seen for decreases in naïve $CD19^+CD20^+CD27^-$ B cells (HR: 0.7; 95% CI: 0.56–1.00; P=0.051). No such association was observed for early changes in the total $CD19^+CD20^+$ B cell pool, or in $CD19^+CD20^+CD27^+$ memory B cells, $CD19^+CD20^+CD69^+$ activated B cells, $CD19^+CD20^+CD138^+$ cells or $CD19^+CD20^-CD27^{bright}$ short-lived plasma cells. The association with $CD19^+CD38^{bright}CD27^{bright}$ SLE-associated plasma cells held true for patients treated with belimumab (any dose) (HR: 0.7; 95% CI: 0.47–0.97; P=0.032) but not placebo, while placebo receivers showing reductions in $CD19^+CD20^-CD138^+$ long-lived plasma cells displayed a lower probability to flare (HR: 0.6; 95% CI: 0.38–0.87; P=0.009).

Conclusion: Early decreases in long-lived circulating plasma cells were negatively associated with severe flares in patients with active SLE treated with standard immunosuppression with or without add-on belimumab, while reductions in circulating $CD19^+CD38^{bright}CD27^{bright}$ SLE-associated plasma cells may prove a useful early biological marker of favorable response to belimumab therapy.

Disclosure: I. Parodis, Amgen, Elli Lilly and Company, and Gilead Sciences., 5, 6, GlaxoSmithKline and Novartis., 5, 6; **A. Gomez**, None; **J. Lindblom**, None; **A. Borg**, None; **S. Emamikia**, None; **M. gatto**, None.

Abstract Number: 1304

Increased Risk of Vertebral Fracture Among Patients with Psoriatic Arthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Increased risk of vertebral fracture (VF) has been documented in several autoimmune diseases as a result of excessive inflammatory burden and use of corticosteroids. The risk is well-established in several autoimmune diseases with high inflammatory burden such as rheumatoid arthritis and systemic lupus erythematosus. However, the risk among patients with autoimmune diseases of less inflammatory burden, including psoriatic arthritis (PsA), is unclear.

Methods: Potentially eligible studies were identified from MEDLINE and EMBASE database from inception to December 2020 using search strategy that comprised of terms for “Psoriatic Arthritis” and “Vertebral Fracture”. Eligible study must be cohort study that consists of one cohort of patients with PsA and another cohort of comparators without PsA. Then, the study must investigate for the prevalence of VF in both groups. Odds ratio (OR) with 95% confidence intervals (95% CIs) comparing prevalent VF between the groups or sufficient raw data to calculate this OR must be provided. Point estimates with standard errors were retrieved from each study and were combined together using the generic inverse variance method. Funnel plot was used to assess for the presence of publication bias.

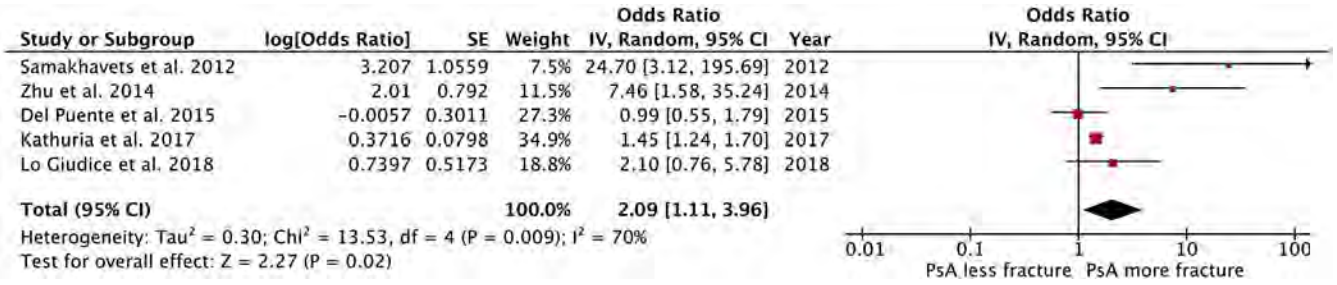

Figure 1. Forest plot of this meta-analysis.

Results: A total of 26,090 articles were identified. After two rounds of independent review by three investigators, five cohort studies met the eligibility criteria and were included into the meta-analysis. PsA is significantly associated with VF with the pooled odds ratio of 2.09 (95% CI, 1.11 – 3.96; I^2 70%) (Figure 1). The funnel plot was fairly symmetric and was not suggestive of publication bias.

Conclusion: This systematic review and meta-analysis found a significantly increased risk of prevalent VF among patients with PsA.

Disclosure: P. Ungprasert, None; **N. Charoenngam**, None; **B. Ponvilawan**, None; **J. Thongpiya**, None; **P. Yingchoncharoen**, None.

Abstract Number: 1305

Undiagnosed Depression in Axial Spondyloarthropathy and the Negative Impact on Patient Outcomes: Results of a Screening Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Previous research in axial spondyloarthropathy(axSpA) has shown this population to have a high prevalence of depression. This co-morbidity has been previously shown to impact disease activity in patients with rheumatic disease.

The purpose of this study was to screen for early signs of depression using two validated tools, the Patient Health Questionaire-9 (PHQ-9) and the Hospital Anxiety and Depression Scale for depression (HADs-D) in patients with known axSpA.

Methods: AxSpA patients attending the Rheumatology department in St James' Hospital between February and October 2020 were invited to take a self-administered survey which included the PHQ-9 and the HADs-D. Scores from the HADs-D yielded a numerical result which was then categorised as normal, borderline or abnormal. PHQ-9 numerical results were categorised as normal, mild, moderate, moderate/severe or severe. Patients with a known

diagnosis of depression were excluded. In addition to baseline demographics, patient reported outcomes from the clinic visit were also recorded.

Data analysis was performed using IBM SPSS version 26. Continuous variables were recorded as means, categorical variables as frequencies with percentages. A one-way analysis of variance analysis (ANOVA) was used to determine significance of variation in outcomes between patient outcomes as determined by the HADs-D and PHQ-9. A p-value of < 0.05 was deemed significant. Informed consent was obtained prior to participation. Approval for this study was received from the St James'/Tallaght Hospital Joint Ethics Committee.

Results: In total 71 axSpA patients took part in the survey. The population was 70.4%(50) males and 29.5%(21) female, with an average age 47.9 years and mean disease duration 19.7 years (mean outcomes: BASDAI 4.08, BASFI

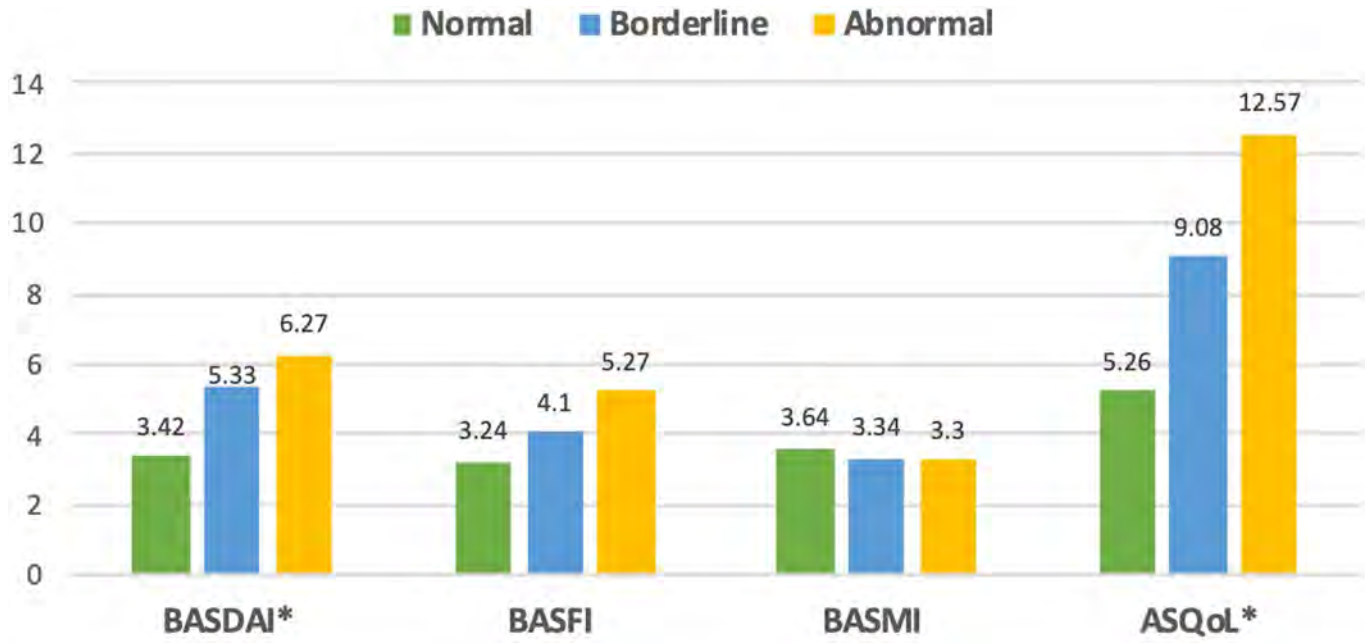

Figure 1. Patient outcomes by HADs-D scores (*indicates significant differences at the p<0.05 level).

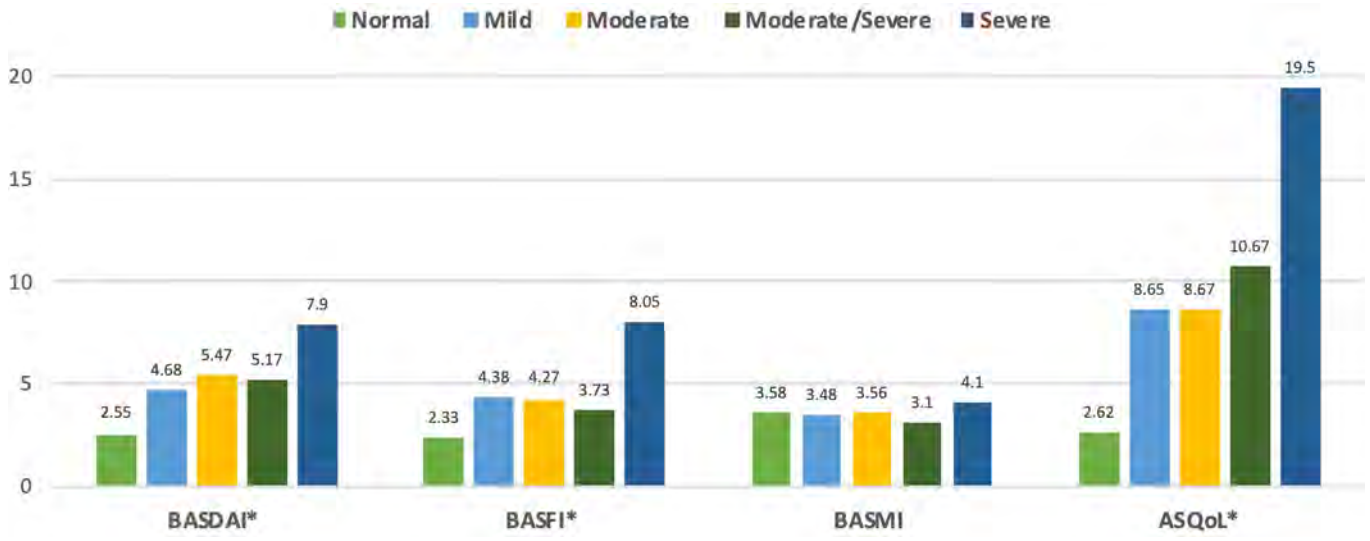

Figure 2. Patient outcomes by PHQ-9 scores (*indicates significant differences between normal, mild and severe groups at the p<0.05 level).

3.62, BASMI 3.54, ASQoL 6.79). Overall, 7 (9.9%) participants recorded abnormal HADs-D scores, while 17 (23.9%) recorded moderate to severe PHQ-9 scores indicative of underlying depression. AxSpA females had higher mean HADs-D scores (7.5 vs 4.8, p=0.01) than males, with abnormal scores in 19%(4) of females and 6% (3) of males. No significant differences were found in PHQ-9 scores between genders.

Analysis revealed significantly worse BASDAI (6.27 vs 3.42, p< 0.01) and AQoL scores (12.57 vs 5.26, p< 0.01) in axSpA patients with abnormal compared to normal HADs-D scores (figure 1). No significant differences were noted in BASFI, BASMI or baseline demographics. A similar pattern was noted on analysis of PHQ-9 scores, with significantly worse BASDAI (7.9 vs 2.55, p< 0.01), BASFI (8.05 vs 2.33, p< 0.01) and ASQoL (19.5 vs 2.62, p< 0.01) noted in those scoring as severe compared to normal (figure 2). No significant differences were detected in BASMI scores or baseline demographics.

Conclusion: A high percentage of axSpA patients recorded high HADs-D and PHQ-9 scores concerning for undiagnosed depression. These patients were noted to have significantly worse disease activity and quality of life as compared to patients with normal scores. Clinicians treating axSpA should consider actively screening for depression in this population.

Disclosure: S. Maguire, Gilead, 5; **P. Gallagher**, None; **F. O'Shea**, None.

Abstract Number: 1306

Clinical and Imaging Characteristics of Spondyloarthritis Among Crohn's Disease Patients

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Inflammatory bowel disease (IBD) affects up to 1.3% of the population and is associated with musculoskeletal manifestations including spondyloarthritis (SpA). Axial SpA (axSpA) is estimated to occur in 3-10% of IBD patients, but variation in imaging modalities and diagnostic criteria may underestimate the prevalence. Early recognition and identification of inflammatory changes on imaging can influence treatment that can alleviate symptoms, prevent radiographic progression, and improve quality of life. The aim of this study is to determine the prevalence of inflammatory changes on imaging in the Crohn's disease (CD) population utilizing routine magnetic resonance enterography (MRE) or magnetic resonance imaging (MRI) and to identify patient characteristics that can assist in early recognition of axSpA.

Methods: This is a retrospective chart review of patients with a diagnosis of CD at our institution between 2014 and 2020. Inclusion criteria included patients with CD, 18 years of age or older, with MRE or MRI pelvis studies available for review. Exclusion criteria included patients with ulcerative colitis, less than 18 years of age, and those without imaging. Images were reviewed by a blinded radiologist using the Assessment of Spondyloarthritis international Society criteria including abnormal enhancement on T1- weighted fat-saturated images and bone marrow edema on T2-weighted fat-saturated images as well as inflammatory structural lesions such as fat deposits, erosions, sclerosis,

Table. Patient characteristics and medical history. BMI: Body mass index; CD: Crohn's Disease; B1p: nonstricturing perianal disease; B2p: stricturing perianal disease; B3p: penetrating perianal disease

Characteristic	All patients (n = 48)	No imaging abnormalities (n=36)	Imaging abnormalities (n = 12)	Imaging abnormalities with back pain (n =4)	Imaging abnormalities without back pain (n = 8)
Age	35 (29, 15)	36 (28, 46)	35 (30, 41)	33 (26, 48)	36 (32, 41)
Female	28 (58%)	19 (53%)	9 (75%)	2 (50%)	7 (88%)
White Race	45 (94%)	34 (94%)	11 (92%)	3 (75%)	8 (100%)
BMI	26 (23, 31)	26 (23, 30)	28 (24, 33)	31 (28, 33)	26 (25, 29)
Medical History					
CD Montreal Classification					
Age at diagnosis					
A1, ≤ 16	9 (19%)	10 (28%)	0 (0%)	0 (0%)	0 (0%)
A2, 17-39	31 (66%)	19 (53%)	100%	4 (100%)	8 (100%)
A3, ≥ 40	7 (15%)	7 (19%)	0%	0 (0%)	0 (0%)
Location					
L1, ileal	16 (35%)	10 (28%)	6 (50%)	2 (50%)	4 (50%)
L2, colonic	4 (9%)	3 (9%)	2 (17%)	1 (25%)	1 (13%)
L3, ileocolonic	25 (54%)	21 (60%)	4 (33%)	1 (25%)	3 (38%)
L4, isolated upper disease	1 (2%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)
Behavior					
B1, nonstricturing	11 (23%)	9 (25%)	2 (17%)	1 (25%)	1 (13%)
B2, stricturing	17 (36%)	12 (33%)	6 (50%)	3 (75%)	3 (38%)
B3, penetrating	5 (11%)	3 (8%)	2 (17%)	0 (0%)	2 (25%)
Perianal disease					
B1p	6 (13%)	5 (14%)	1 (8%)	0 (0%)	1 (13%)
B2p	2 (6%)	3 (8%)	0 (0%)	0 (0%)	0 (0%)
B3p	5 (11%)	4 (11%)	1 (8%)	0 (0%)	1 (13%)
Inflammatory arthritis	6 (13%)	5 (14%)	1 (8%)	0 (0%)	1 (13%)
Uveitis	1 (2%)	0 (0%)	1 (8%)	0 (0%)	1 (13%)
Ankylosing spondylitis	2 (4%)	1 (2.8%)	1 (8%)	0 (0%)	1 (13%)
Psoriasis	2 (4%)	2 (6%)	0 (0%)	0 (0%)	0 (0%)
Psoriatic arthritis	1 (2%)	1 (3%)	0 (0%)	0 (0%)	0 (0%)
Smoking history					
Never	33 (69%)	25 (69%)	8 (67%)	3 (75%)	5 (63%)
Former	15 (31%)	11 (31%)	4 (33%)	1 (25%)	3 (37%)
Current	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Family History					
Crohn's disease	10 (21%)	7 (19%)	3 (25%)	1 (25%)	2 (25%)
Ulcerative colitis	8 (17%)	7 (19%)	1 (8%)	0 (0%)	1 (13%)
Rheumatoid arthritis	3 (6%)	1 (2%)	2 (17%)	0 (0%)	2 (25%)

Values expressed as median (interquartile range) or (percentage)

or ankylosis. Demographics, medical history, medications, and labs at the time of imaging were recorded. Patients were assessed by a questionnaire for rheumatologic symptoms including inflammatory back pain and peripheral joint manifestations.

Results: 48 patients met the inclusion criteria. 41 had MREs and 7 had MRIs of the pelvis. 12 patients (25%) were identified with imaging abnormalities, all of which were found on MREs. 7 had structural lesions indicating prior inflammation and 5 were noted to have abnormal enhancement or bone marrow edema in the sacroiliac joints. From the 12 patients with imaging abnormalities, 8 (67%) were asymptomatic with no reported back pain or stiffness, 9 (75%) were female, 8 (67%) had stricturing or penetrating CD (Table). 3 patients (25%) were seeing a rheumatologist. From all the patients surveyed, 13 (30%) reported back pain, 26 (59%) reported previous joint pain or swelling, 13 (30%) had previous entire digit swelling, and 16 (36%) reported previous heel pain.

Conclusion: This study reveals that among Crohn's disease patients at our institution, the prevalence of abnormal sacroiliac joint findings on MRE and MRI is 25%. Majority of these patients did not report back pain, were female, and had intestinal complications of CD. Only 25% were following with a rheumatologist. Asymptomatic or subclinical axSpA in Crohn's disease patients remains under diagnosed and our study suggests that MREs should be routinely evaluated for musculoskeletal abnormalities. Furthermore, female sex and sticturing or penetrating CD may be risk factors for axSpA. Patients with these characteristics should be formally evaluated for the presence of inflammatory back pain as part of their clinical care.

Disclosure: L. Quimson, None; **N. Oren**, None; **C. Burns**, None; **R. Jan**, None.

Abstract Number: 1307

Uveitis in Spondyloarthritis Patients. Is There Any Specific Clinical Picture?

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Uveitis is the most frequent extra-musculoskeletal manifestation in Spondyloarhtritis (SpA). Moreover, up to 50% of patients with an acute episode of uveitis develop recurrent anterior uveitis. Recently, the prevalence of history of uveitis reported in ASAS perSPA study (PERipheral involvement in SpondyloArthritis) was similar in axial and peripheral SpA (21.6% and 17.3%, respectively). However, it is not well known whether the clinical characteristics of patients with uveitis and recurrent uveitis differ between patients with axial and peripheral SpA. The primary objective was to compare the clinical characteristics of axial and peripheral SpA patients who have ever suffered from uveitis. Secondary objective was to compare the clinical characteristics of axial and peripheral SpA patients with a single episode of uveitis versus SpA patients with recurrent uveitis.

Methods: This is a post-hoc analysis of the ASAS-PerSpA study which included 3465 patients with SpA, 2910 patients fulfilling ASAS axSpA criteria and 555 patients fulfilling peripheral ASAS criteria. Recurrent uveitis was defined as the presence of 2 or more episodes of uveitis ever. Univariable and multivariable binary logistic regression analyses were conducted to identify factors associated with the presence of uveitis ever and the presence of recurrent uveitis.

Results: In the multivariable analysis, the presence of uveitis was significantly associated with the presence of HLA-B27 and disease duration, OR 2.88 (CI95% 2.15 - 3.91) and OR 1.05 (CI95% 1.04 - 1.06) respectively. Furthermore, the presence of inflammatory bowel disease ever is increased in patients with uveitis, OR 1.60 (CI95% 1.04 - 2.44). Nevertheless, the presence of psoriasis is decreased in patients with uveitis, OR 0.43 (CI95% 0.31 - 0.59). Patients from Latin America region were more likely to present uveitis in comparison with European patients, OR 1.42 (CI95% 1.02 - 1.94). Importantly, the presence of uveitis was not significantly different in patients with axSpA

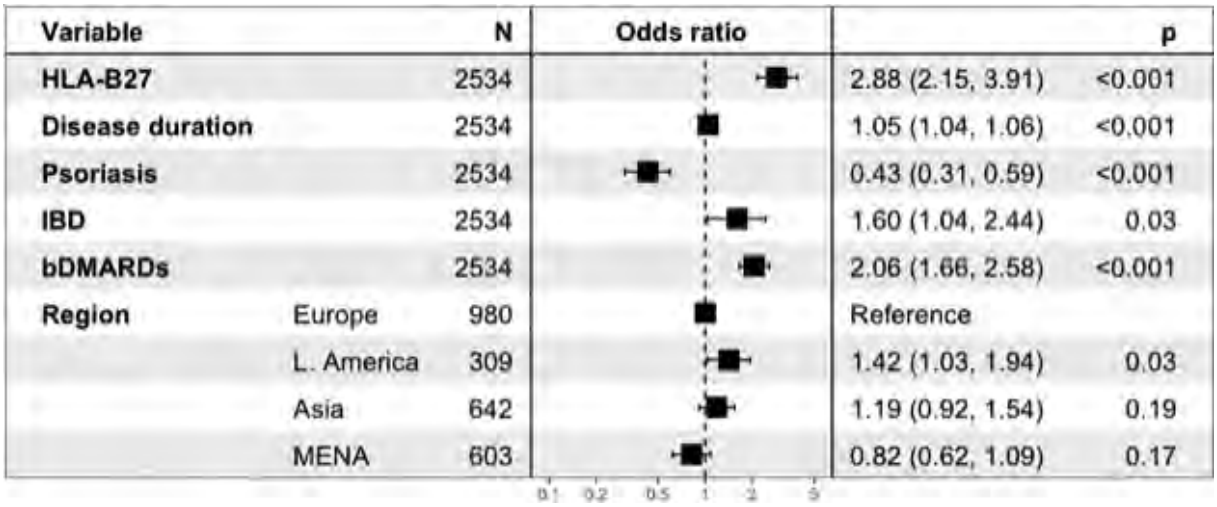

Figure 1. Multivariable analysis of 2534 patients with Spondyloarthritis to identify factors associated with the presence of uveitis ever. IBD, inflammatory bowel disease; HLA-B27, human leucocyte antigen B27; bDMARDs, biological disease-modifying antirheumatic drugs.

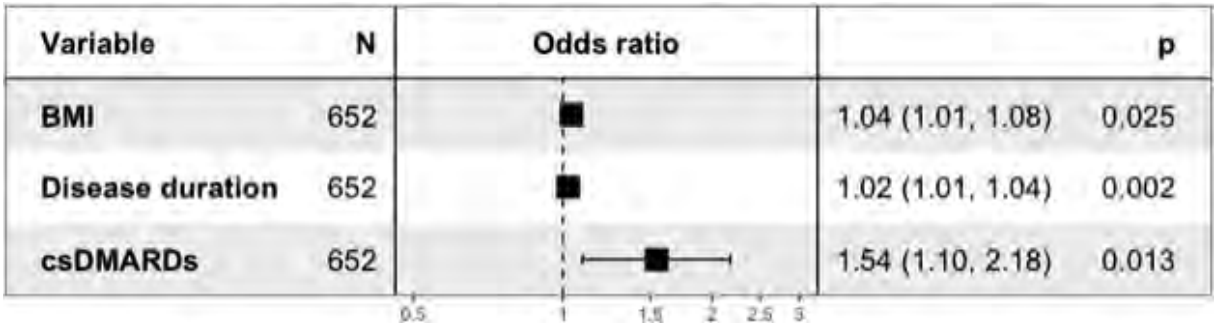

Figure 2. Multivariable analysis of 2534 patients with Spondyloarthritis to identify factors associated with the presence of recurrent uveitis. BMI, body mass index; csDMARDs, conventional synthetic disease-modifying antirheumatic drugs.

as compared to patients with pSpA (Figure 1). One the other hand, only disease duration and body mass index (BMI) was significantly associated with the presence of recurrent uveitis, OR 1.04 (CI95% 1.01-1.08) and OR 1.02 (CI95% 1.01-1.04) (Figure 2).

Conclusion: The prevalence of uveitis was not significantly higher in patients with axSpA as compared to patients with pSpA. HLA-B27 positivity is associated with the presence of uveitis, but not with recurrent uveitis in SpA patients. Hence, further biomarkers are needed to identify patients at risk of recurrent uveitis

Disclosure: M. LLOP VILALTELLA, Novartis, 6; **M. moreno**, UCB, 6, Abbvie, 2, 6, Novartis, 2, 6; **M. Arévalo**, Abbvie, 6, Gebro Pharma, 6; **J. Gratacós**, Pfizer, 2, 6, MSD, 2, 6, Abbvie, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Lilly, 2, 6, Celgene, 2, 6; **M. Dougados**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **C. López Medina**, None.

Abstract Number: 1308

Higher Prevalence of Echocardiographic Abnormalities in Psoriatic Arthritis and Rheumatoid Arthritis Patients Compared to Controls

Alejandra Rodriguez-Romero, **Jose Azpiri-Lopez**, Dionicio Galarza-Delgado, Iris Colunga-Pedraza, Natalia Guajardo-Jauregui, Julieta Loya-Acosta, Alejandro Meza-Garza, Jesus Cardenas-de La Garza, Salvador Lugo-Perez, Catalina Andrade-Vazquez and Alan De Leon-Yañez, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory arthropathy associated with cardiovascular abnormalities. The echocardiography is a non-invasive tool useful in the detection of cardiac abnormalities, which may be the only manifestation of cardiac involvement preceding a global dysfunction. However, echocardiographic differences between PsA patients, rheumatoid arthritis (RA) patients, and controls have not yet been well described. Therefore our objective was to analyze the echocardiographic parameters in PsA patients and to compare them with RA patients and controls.

Methods: This case-control study included thirty-six patients (nineteen in each group), aged 40-75 years, with PsA and RA who fulfilled the CASPAR (Classification criteria for Psoriatic Arthritis) and ACR/EULAR 2010 classification criteria, respectively, matched by age, gender and comorbidities with nineteen healthy controls. Exclusion criteria were a poor echocardiographic window, patients with a previous atherosclerotic cardiovascular disease (ischemic heart disease, cerebrovascular accident or peripheral arterial disease), and pregnancy. A Transthoracic echocardiogram was performed and reviewed by 2 board-certified cardiologists, in all study subjects. Comparisons were done with X^2, Kruskall Wallis or ANOVA.

Results: There were not any statistically significant differences found in the demographic characteristics (Table 1). When comparing echocardiographic findings a statistically significant difference was found in the prevalence of di-

Table 1. Comparison of demographic characteristics between patients with PsA, RA and controls.

	PsA (n=19)	RA (n=19)	Controls (n=19)	*p-value*
Age, years ± SD	54.7 ± 7.7	55.4 ± 9.9	55.3 ± 5.9	NS
Female, n (%)	11 (57.9)	11 (57.9)	11 (57.9)	NS
Diabetes Mellitus, n (%)	4 (21.1)	3 (15.8)	2 (10.5)	NS
Hypertension, n (%)	10 (52.6)	8 (42.1)	7 (36.8)	NS
Dyslipidemia, n (%)	10 (52.6)	4 (21.1)	7 (36.8)	NS
Active smoking, n (%)	4 (21.1)	2 (10.5)	5 (26.3)	NS
Disease duration, years (p25-p75)	6 (4-14)	7 (5-18)	-	NS
DAS28-CRP, mean ± SD	2.2 ± 0.8	3.1 ± .8	-	**0.003**

NS, non-significant; DAS28-CRP, disease activity score using 28 joints and C reactive protein.

Table 2. Comparison of echocardiographic findings between patients with PsA, RA and controls.

Echocardiographic findigs	PsA (n=19)	RA (n=19)	Controls (n=19)	*p-value*
Diastolic dysfunction, n (%)	10 (52.6)	10 (52.6)	1 (5.3)	**0.002**
LV mass index, g/m^2 (p25-p75)	78.9 (55.9-86.9)	73.7 (61.0-85.7)	69.5 (52.0-98.7)	**NS**
LVEF, ± mean SD	62.3 ± 6.1	59.7 ± 8.6	62.9 ± 6.1	NS
TAPSE, cm ± SD	21.8 ± 2.7	22.4 ± 2.7	23.7 ± 3.1	NS
Mild aortic regurgitation, n (%)	5 (26.3)	4 (21.1)	1 (5.3)	NS
Mild mitral regurgitation, n (%)	16 (84.2)	10 (52.6)	2 (10.5)	**<0.001**
Mild pulmonary regurgitation, n (%)	13 (68.4)	2 (10.5)	0 (0)	**<0.001**
Mild tricuspid regurgitation, n (%)	15 (83.3)	13 (76.5)	11 (57.9)	NS
LV geometry alterations, n (%)	13 (68.4)	12 (63.2)	4 (21.1)	**0.006**
Concentric remodeling, n (%)	12 (63.2)	10 (52.6)	4 (21.1)	**0.025**

LV, left ventricular; LVEF, left ventricular ejection fraction; TAPSE, tricuspid annular plane systolic excursion.

astolic dysfunction, being more prevalent in PsA and RA patients compared with controls (52.6% vs 52.6% vs 5.3%, *p=0.002),* likewise the presence of mild mitral valve regurgitation was higher (84.2% vs 53.6% vs 10.5%, *p=0.001*) and mild pulmonary valve regurgitation (68.4% vs 10.5% vs 0%, *p=0.001*). Prevalence of abnormal left ventricular geometry was higher in PsA and RA patients than controls (68.4% vs 63.2% vs 21.1%, *p=0.006)*. Results are shown in Table 2.

Conclusion: This study shows the high prevalence of echocardiographic alterations in PsA patients compared to the general population, of the same magnitude as patients with RA. We emphasize the value of an echocardiogram for a complete cardiovascular evaluation and early detection of cardiac abnormalities in these patients.

Disclosure: A. Rodriguez-Romero, None; **J. Azpiri-Lopez**, None; **D. Galarza-Delgado**, None; **I. Colunga-Pedraza**, None; **N. Guajardo-Jauregui**, None; **J. Loya-Acosta**, None; **A. Meza-Garza**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **C. Andrade-Vazquez**, None; **A. De Leon-Yañez**, None.

Abstract Number: 1309

Impact of the Number of Comorbidities on the Outcome Measures and on the Retention Rate of the First Anti-TNF in Patients with Ankylosing Spondylitis: Two-year Follow-up REGISPONSER-AS

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: a) To evaluate the impact of the number of comorbidities on the outcome measures after two years of follow-up in patients with ankylosing spondylitis (AS) and b) to determine whether the number of comorbidities influences the retention rate to the first anti-TNF alpha.

Methods: Observational and prospective study during 2 years of follow-up that includes a subgroup of 749 patients with AS (REGISPONSER-AS) from the REGISPONSER study (Spanish Rheumatology Spondyloarthritis Registry). The patients were divided into three groups according to the number of comorbidities at baseline (0, 1 or ³2 comorbidities). The Patient Reported Outcomes (PROs) evaluated were the Global VAS, BASDAI, ASDAS, BASFI and the mental and physical components from the SF12 questionnaire. Linear regression models were performed using the PROs as the dependent variable and the three groups of patients according to their comorbidities as the explanatory variable. Since disease duration may influence both the number of comorbidities and the PROs, additional models adjusting for this variable were explored. After that, the impact of the number of comorbidities on PROs over two years of follow-up was evaluated using mixed models for repeated measures (MMRM) adjusting for disease duration. Finally, we compared the retention rate to the first anti-TNF alpha across the three groups of patients using a Kaplan-Meier curve and a Log-rank test.

Results: 749 patients were included (mean age 48.37 ± 12.2 years, of which 75.3% were men). The association between the number of comorbidities and the PROs is shown in Table 1. We found that patients with 2 or more comorbidities showed an increase (b coefficient) in all PROs compared with patients without comorbidities. The impact of the number of comorbidities on the PROs after two years of follow-up is shown in Figure 1. In general, patients with two or more comorbidities showed higher scores during the two years of follow-up in Global VAS, BASDAI, ASDAS, BASFI and worse levels of the physical component from the SF12.

Table 1. Association of the number of comorbidities with PROs

	Global VAS		BASDAI		ASDAS	
	Crude β (95%CI)	β (95%CI) adjusted for disease duration	Crude β (95%CI)	β (95% CI) adjusted for disease duration	Crude β (95%CI)	β (95%CI) adjusted for disease duration
1 comorbidity vs. 0 comorbidities	0.21 (-0.07 to 0.49)	0.15 (-0.14 to 0.43)	0.03 (-0.43 to 0.48)	-0.01 (-0.46 to 0.45)	0.09 (-0.08 to 0.25)	0.06 (-0.11 o 0.23)
2 or more comorbidities vs. 0 comorbidities	0.78 (0.52 to 1.05)	0.63 (0.35 to 0.91)	1.12 (0.69 to 1.56)	1.04 (0.59 to 1.50)	0.49 (0.33 to 0.64)	0.42 (0.26 to 0.58)
	BASFI		SF12 Physical component		SF12 Mental component	
	Crude β (95%CI)	β (95%CI) adjusted for disease duration	Crude β (95%CI)	β (95%CI) adjusted for disease duration	Crude β (95%CI)	β (95%CI) adjusted for disease duration
1 comorbidity vs. 0 comorbidities	0.59 (0.20 to 0.98)	0.41 (0.02 to 0.80)	-1.27 (-2.40 to -0.13)	-1.09 (-2.24 to 0.05)	0.32 (-0.98 to 1.63)	0.13 (-1.19 to 1.45)
2 or more comorbidities vs. 0 comorbidities	1.68 (1.31 to 2.05)	1.25 (0.87 to 1.64)	-2.23 (-3.33 to -1.14)	-1.70 (-2.83 to -0.56)	1.52 (0.26 to 2.78)	1.08 (-0.23 to 2.39)

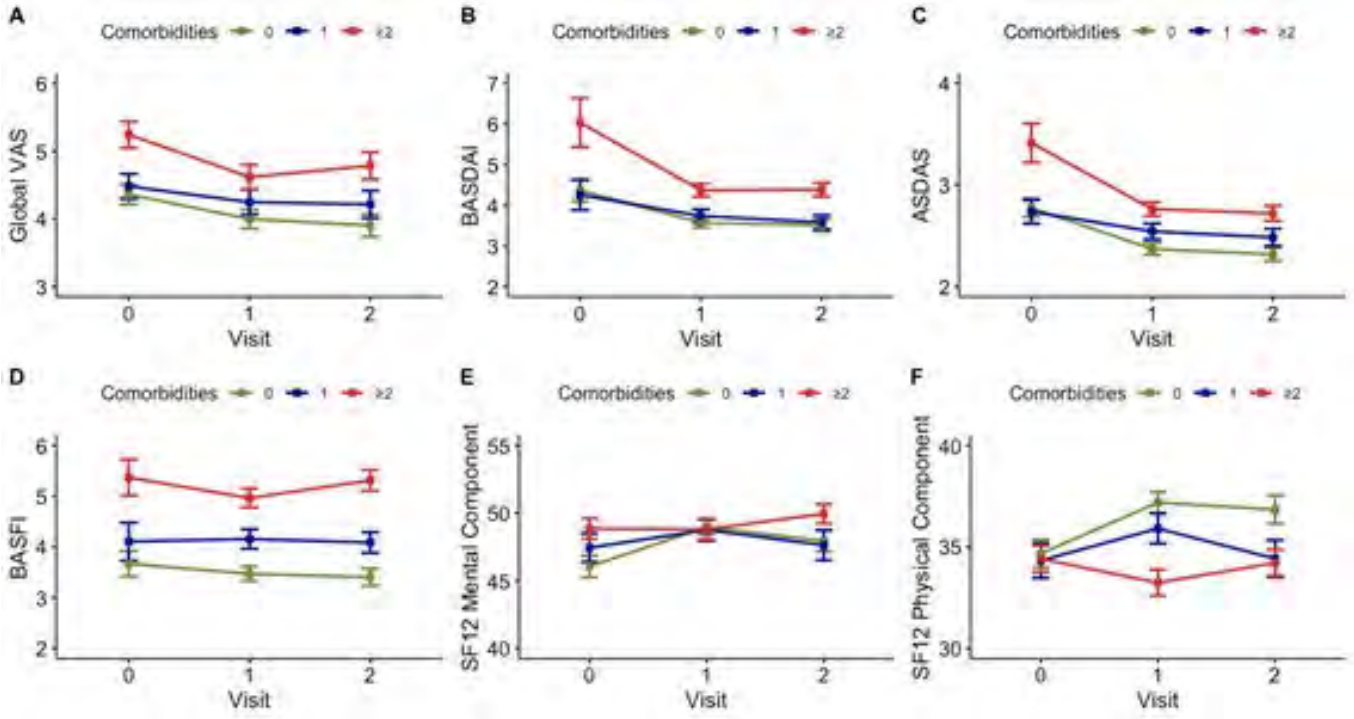

Figure 1. Impact of the number of comorbidities on PROs over two years of follow-up.

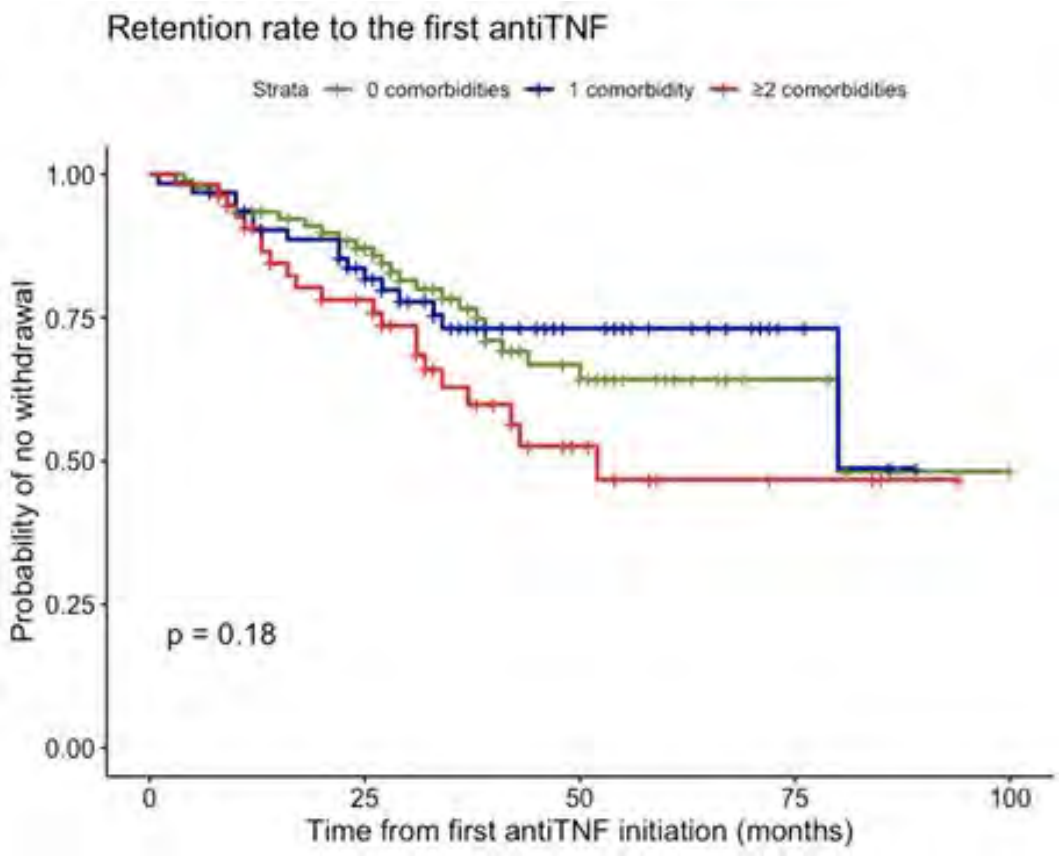

Figure 2. Impact of the number of comorbidities on the adherence to the first TNF-alpha blocker.

The impact of the number of comorbidities on the retention rate of the first anti-TNF is shown in Figure 2. We found a higher probability of discontinuation of the first anti-TNF in patients with 2 or more comorbidities compared with the other two groups (38.2% vs. 26.6% vs. 25.4% for 2 or more comorbidities, 0 and 1 comorbidity, respectively), although these differences were not significant (Log-rank test: p-value = 0.180).

Conclusion: In patients with AS, the presence of 2 or more comorbidities was associated with poorer scores on the outcome measures after two years of follow-up, in comparison with patients without comorbidities. Despite the three groups showed a similar use of anti-TNF alpha, a greater tendency of discontinuation of the first anti-TNF was observed in patients with 2 or more comorbidities.

Disclosure: M. Puche Larrubia, None; **M. Ladehesa-Pineda**, None; **P. Font**, None; **A. Escudero Contreras**, None; **E. Collantes-Estevez**, None; **C. López Medina**, None.

Abstract Number: 1310

Clinical Characteristics of Patients with SpA and Concomitant IBD: Results from the ASAS PerSpA Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: A recent study reports that gut inflammation is linked to degree of bone marrow edema in sacroiliac joints in patients with axial spondyloarthritis (SpA). SpA patients with concomitant inflammatory bowel disease (IBD) typically have more severe disease requiring aggressive treatment. However, the clinical characteristics of SpA patients with IBD has not been shown in a large cohort and there are few descriptions of regional differences.

Table 1. Clinical Characteristics of SpA patients with IBD

	SpA patients with IBD	SpA patients without IBD	p.value
n	287	4178	
Male	155 (54.0)	2569 (61.5)	**0.014**
Age at study visit, yrs	45.0 [34.0, 56.0]	44.0 [33.0, 55.0]	0.22
Smoking ever	118 (41.1)	1786 (42.7)	0.63
Diagnostic delay, yrs	5.1 [1.3, 12.0]	2.9 [0.6, 9.0]	**<0.001**
HLA B27 positive among measured	68 (37.2)	1998 (68.0)	**<0.001**
Family history of SpA	97 (33.8)	1435 (34.3)	0.9
Family history of IBD	42 (14.6)	96 (2.3)	**<0.001**
Inflammatory back pain	229 (79.8)	3093 (74.0)	**0.036**
Radiographic sacroiliitis	163 (56.8)	2354 (56.3)	0.93
Sacroiliitis on MRI among tested (n/tested patients, %)	130/194 (67.0)	1687/2614 (64.5)	0.54
Axial ASAS criteria	195 (67.9)	2715 (65.0)	0.34
Peripheral ASAS criteria	23 (8.0)	532 (12.7)	**0.024**
Peripheral arthritis: Ever present	169 (58.9)	2372 (56.8)	0.52
As first symptom	40 (13.9)	945 (22.6)	**0.001**
Enthesitis: Ever present	139 (48.4)	2051 (49.1)	0.88
As first symptom	25 (8.7)	462 (11.1)	0.26
Dactylitis: Ever present	26 (9.1)	659 (15.8)	**0.003**
As first symptom	3 (1.0)	110 (2.6)	0.12
Psoriasis: Ever present	38 (13.2)	1321 (31.6)	**<0.001**
As first symptom	13 (4.5)	851 (20.4)	**<0.001**
Uveitis: Ever present	59 (20.6)	703 (16.8)	0.12
As first symptom	10 (3.5)	182 (4.4)	0.65
Comcomitant fibromyalgia	27 (9.4)	373 (8.9)	0.87
CRP elevation	191 (66.6)	2766 (66.2)	0.96
Patient Global Assesment	4.0 [2.0, 7.0]	4.0 [2.0, 7.0]	0.84
ASDAS-CRP	2.4 [1.7, 3.2]	2.5 [1.6, 3.3]	0.59
BASDAI	3.6 [1.8, 5.6]	3.6 [1.8, 5.8]	1
BASFI	2.8 [0.8, 5.0]	2.3 [0.6, 4.9]	0.24
ASAS HI	6.4 [3.0, 11.0]	6.0 [3.0, 10.0]	0.2
csDMARDs (Ever)	254 (88.5)	2733 (65.4)	**<0.001**
bDMARDs (Ever)	211 (73.5)	2436 (58.3)	**<0.001**

Values are expressed as n (%) or median [IQR] unless otherwise indicated.

The purpose of this study is to clarify the clinical characteristics of SpA patients with IBD compared to those SpA patients without IBD. In addition, we aim to determine the phenotype of patients given a definitive diagnosis of IBD-associated SpA by their treating rheumatologist.

Methods: Using ASAS-PerSpA data, an observational study, we analyzed information on demographics and disease characteristics, dichotomizing patients by IBD status. SpA patients with IBD were further categorized by region; Japan, non-Japan Asia, and non-Asian countries. SpA patients with IBD were also categorized as IBD-associated SpA or other SpA with IBD by their rheumatologists.

Results: Among 4465 SpA patients included in the study, 287 were identified with IBD. Compared to those without IBD, SpA patients with IBD were less likely male (54.0 vs 61.5%) and more likely to have experienced diagnostic delay (5.1 vs 2.9 years) (Table 1). SpA patients with IBD had lower prevalence of positive HLA-B27 (37.2% vs 68.0%) and less dactylitis (9.1% vs 15.8%) despite similar rates of other peripheral signs. Disease activity, radiographic sacroiliitis and inflammation on MRI were similar in the two groups. csDMARDs and bDMARDs use was higher in SpA patients with IBD.

With respect to regional differences, SpA patients with IBD was more common in Japan than in both non-Japan Asia and non-Asian countries (13.2, 1.7 and 7.1%, respectively). SpA patients with IBD in Japan experienced more diagnostic delay (12.8, 0.3 and 5.0 years, respectively), had lower prevalence of positive HLA-B27 (0, 81.8 and 36.2%, respectively) and less axial symptom (inflammatory back pain: 57.7, 84.6 and 81.9%, radiographic sacroiliitis: 23.1,46.2 and 60.9%, sacroiliitis on MRI: 33.3, 83.3 and 71.3%, respectively).

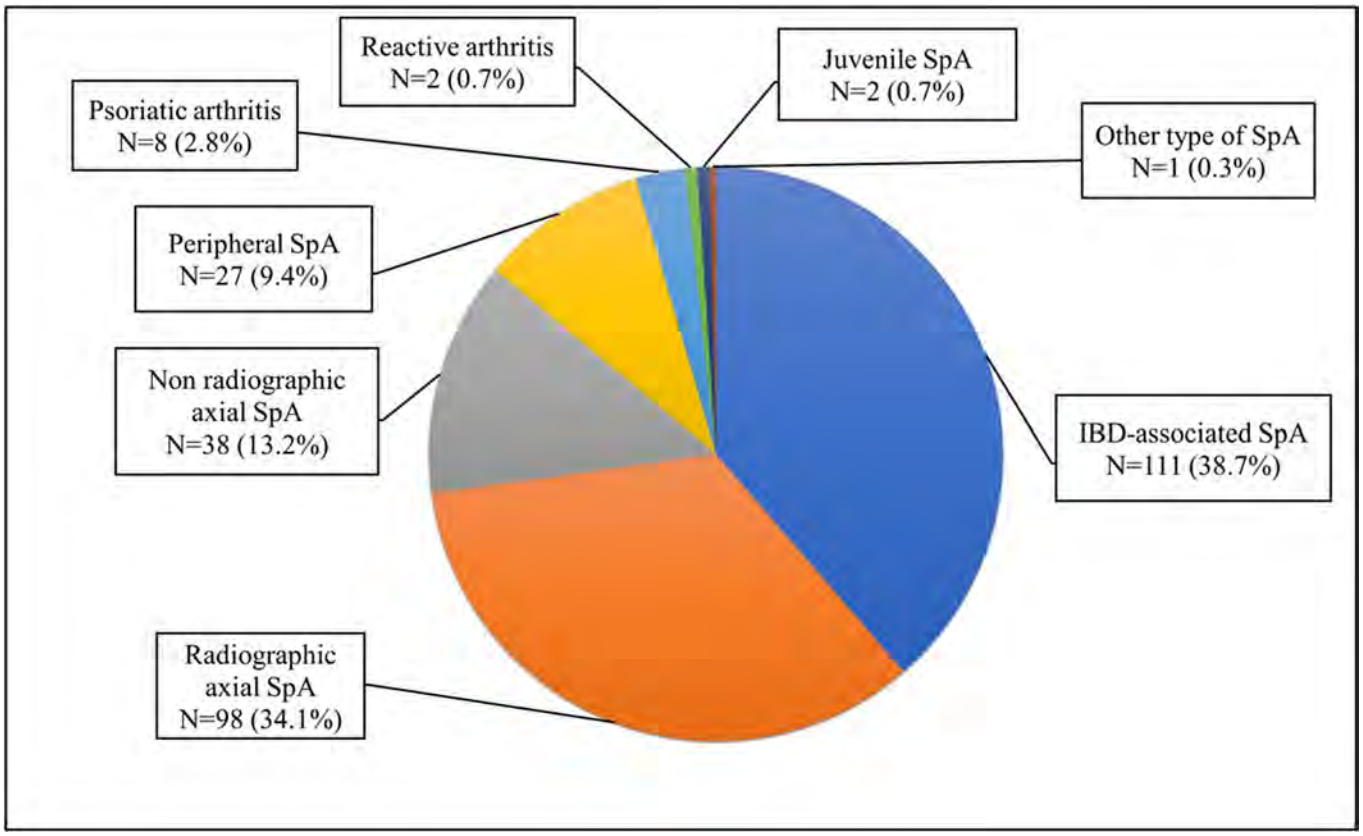

Figure 1. Final clinical diagnosis of SpA patients with IBD patients by rheumatologists. (N=287).

Table 2. Clinical Characteristics of IBD-associated SpA compared to other SpA patients with IBD

	IBD-associated SpA patients	Other SpA patients with IBD	p.value
n	111	176	
Male	59 (53.2)	96 (54.5)	0.91
Age at study visit, yrs	48.0 [34.5, 58.5]	44.0 [34.0, 53.0]	0.13
Smoking ever	45 (40.5)	73 (41.5)	0.97
Diagnostic delay, yrs	5.9 [1.4, 14.2]	5.1 [1.2, 11.6]	0.39
HLA B27 positive among measured	11 (19.3)	57 (45.2)	**0.001**
Family history of SpA	27 (24.3)	70 (39.8)	**0.01**
Family history of IBD	14 (12.6)	28 (15.9)	0.55
Inflammatory back pain	74 (66.7)	155 (88.1)	**<0.001**
Radiographic sacroiliitis	50 (45.0)	113 (64.2)	**0.002**
Sacroiliitis on MRI among tested (n/tested patients, %)	37/67 (55.2)	93/127 (73.2)	**0.018**
Axial ASAS criteria	57 (51.4)	138 (78.4)	**<0.001**
Peripheral ASAS criteria	14 (12.6)	9 (5.1)	**0.027**
Peripheral arthritis: Ever present	77 (69.4)	92 (52.3)	**0.006**
As first symptom	14 (12.6)	26 (14.8)	0.73
Oligoarticular	47 (42.3)	49 (27.8)	**0.016**
Enthesitis: Ever present	56 (50.5)	83 (47.2)	0.67
As first symptom	11 (9.9)	14 (8.0)	0.72
Dactylitis: Ever present	10 (9.0)	16 (9.1)	1
As first symptom	1 (0.9)	2 (1.1)	1
IBD: Ever present	111 (100.0)	176 (100.0)	NA
As first symptom	70 (63.1)	44 (25.0)	**<0.001**
Specific treatment	105 (94.6)	133 (75.6)	**<0.001**
Psoriasis: Ever present	4 (3.6)	34 (19.3)	**<0.001**
As first symptom	1 (0.9)	12 (6.8)	**0.019**
Uveitis: Ever present	18 (16.2)	41 (23.3)	0.2
As first symptom	4 (3.6)	6 (3.4)	1
Comcomitant fibromyalgia	7 (6.3)	20 (11.4)	0.21
CRP elevation	60 (54.1)	131 (74.4)	**0.001**
Patient Global Assesment	4.0 [2.0, 6.0]	5.0 [2.0, 7.0]	0.21
ASDAS-CRP	2.3 [1.6, 2.9]	2.6 [1.7, 3.4]	0.11
BASDAI	3.2 [1.7, 5.3]	3.8 [2.2, 6.0]	0.15
BASFI	2.2 [0.3, 4.6]	3.0 [1.1, 5.6]	**0.044**
ASAS HI	6.0 [3.0, 10.1]	7.0 [3.0, 11.3]	0.18
csDMARDs (Ever)	108 (97.3)	146 (83.0)	**<0.001**
bDMARDs (Ever)	74 (66.7)	137 (77.8)	0.051

Values are expressed as n (%) or median [IQR] unless otherwise indicated.

SpA patients with IBD were categorized by rheumatologists into their respective clinical diagnoses, of which 111 were diagnosed with IBD-associated SpA (Figure 1). IBD-associated SpA patients, compared to those diagnosed as primarily SpA patients with IBD but not IBD-associated SpA, had lower prevalence of both HLA-B27 (19.3 vs 45.2%) and family history of SpA (24.3 vs 39.8%) (Table 2). IBD-associated SpA patients had fewer axial symptom and signs, and were more likely to have peripheral arthritis - especially oligoarthritis. In IBD-associated SpA patients, IBD appears more often as the first symptom of SpA, and IBD-specific treatment was needed more frequently. csDMARDs use was higher in IBD-associated SpA.

Conclusion: SpA patients with IBD required more specific treatments than those without IBD. In SpA patients with IBD, rheumatologists tended to diagnose IBD-associated SpA in those without axial signs but with peripheral signs, and those with IBD as the initial symptom and requiring IBD-specific treatment.

Disclosure: K. Ono, a, 1; **M. Kishimoto**, AbbVie, 2, 6, Amgen-Astellas BioPharma, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, BMS, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, Teijin Pharma, 2, 6, UCB Pharma, 2, 6; **G. Deshpande**, None; **S. Fukui**, None; **S. Kawaai**, None; **H. Sawada**, None; **M. Matsuura**, Janssen Pharmaceutical K.K., 2, 6, Takeda Pharmaceutical Co. Ltd., 2, 6, AbbVie GK, 2, 6, Mitsubishi Tanabe Pharma Corporation, 2, 6, Kyorin Pharmaceutical Co. Ltd., 2, 6, Mochida Pharmaceutical Co., Ltd., 2, 6, JIMRO Co., 2, 6, Nippon Kayaku Co. Ltd., 2, 6, Mylan EPD G.K., 2, 6, Aspen Japan Co. Ltd., 2, 6; **V. Rios Rodriguez**, None; **F. Proft**, Novartis, 1, 5, 6, Eli Lilly and Company, 1, 5, UCB, 1, 5, 6, AbbVie, 1, 6, Amgen, 1, 6, Bristol-Myers Squibb, 1, 6, Hexal, 1, 6, MSD, 1, 6, Pfizer, 1, 6, Roche, 1, 6; **K. Tada**, None; **N. Tamura**, AbbVie Japan GK, 6, Bristol-Myers Squibb Co. Ltd, 6, Chugai Pharmaceutical Co. Ltd, 6, Eisai Co. Ltd, 6, Eli Lilly Japan K.K, 6, Glaxo Smith Kline K.K., 6, Janssen Pharmaceutical K.K., 6, Mitsubishi-Tanabe Pharma Co., 6, Novartis Pharma K.K, 6; **Y. Taniguchi**, None; **A. Hirata**, None; **H. Kameda**, Asahi-Kasei, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 5, 6, Chugai, 5, 6, Mitsubishi-Tanabe, 5, 6, Astellas, 2, Eli Lilly, 2, 6, Pfizer, 6, Eisai, 5, 6, Gilead Sciences, 2, Janssen, 2, 6, Sanofi, 2, UCB, 2; **S. Tsuji**, None; **Y. Kaneko**, None; **H. Dobashi**, None; **T. Okano**, None; **Y. Haji**, None; **A. Morita**, None; **A. Asahina**, Sun Pharmaceutical Industries, Inc., 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Celgene, 5, 6, Eisai, 5, 6, Kyowa Kirin, 5, 6, LEO Pharma, 5, 6, Maruho, 5, 6, Mitsubishi Tanabe Pharma, 5, 6, Taiho Pharma, 5, 6, Torii Pharmaceutical, 5, 6, UCB, 5, 6, Eli Lilly Japan, 5, 6; **M. Okada**, AbbVie, 2, Eli Lilly, 2, AbbVie Japan, 6, Eli Lilly and Company, 6, Ono Pharmaceutical, 6; **Y. Komagata**, None; **C. López Medina**, None; **A. Molto**, None; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **M. Dougados**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Merck, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Roche, 2, 5, UCB, 2, 5; **T. Hisamatsu**, Alfresa Pharma Co., Ltd., 5, Mitsubishi Tanabe Pharma Corporation, 2, 5, 6, EA Pharma Co., Ltd., 2, 5, 6, AbbVie GK, 2, 5, 6, JIMRO Co., Ltd., 2, 5, 6, Zeria Pharmaceutical Co., Ltd., 5, Daiichi-Sankyo, 5, Nippon Kayaku Co., Ltd., 5, Pfizer Inc., 2, 5, 6, Mochida Pharmaceutical Co., Ltd., 2, 5, 6, Celgene K.K., 2, 6, Kyorin Pharmaceutical Co. Ltd., 2, 5, 6, Janssen Pharmaceutical K.K., 2, 6, Takeda Pharmaceutical Co., Ltd., 2, 5, 6; **T. Tomita**, None; **S. Kaname**, None.

Abstract Number: 1311

De Novo Psoriasis Can Be Reported at Any Timepoint in Early Axial Spondyloarthritis: An Analysis of 6 Years of Follow-up of the DESIR Cohort

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

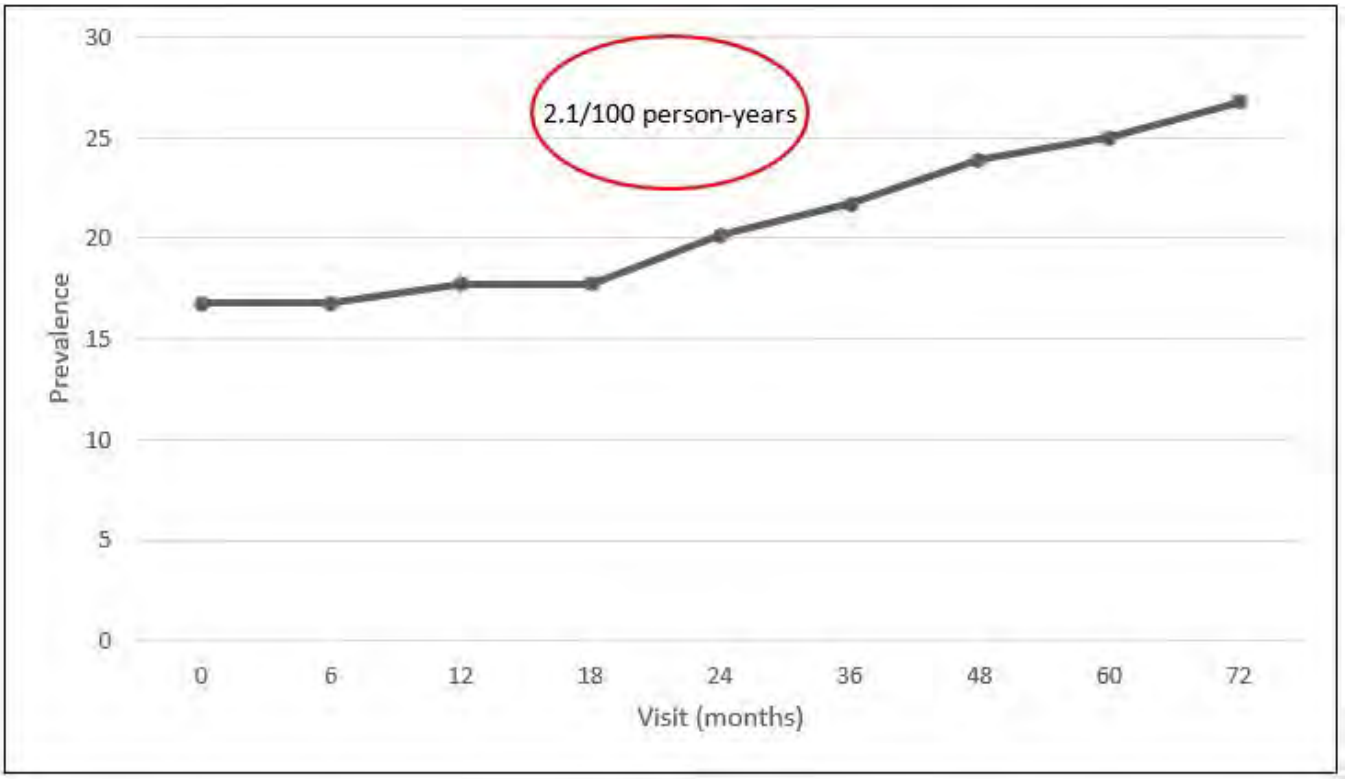
Background/Purpose: Psoriasis is a frequent extra-articular manifestation in axial spondyloarthritis (axSpA) with a prevalence in established axSpA around 9% and consequences on the disease course. In recent axSpA, prevalence and consequences of psoriasis are unclear.

The objectives were to determine the prevalence and the impact of psoriasis in recent axSpA over 6 years of follow-up.

Methods: This was an analysis of the first 6 years of the French prospective cohort DESIR (NCT01648907) which recruited adult patients with inflammatory back pain for less than 3 years suggestive of SpA(4). Psoriasis was recorded at baseline and at each visit (once or twice per year) through the rheumatologist's reporting. Functional assessment (HAQ-AS, BASFI) and disease activity were assessed at each time point. Cumulative prevalence of psoriasis at each time point and cumulative incidence were calculated. Baseline characteristics associated with cumulative psoriasis were assessed by univariable analysis. Patients with versus without psoriasis were compared at 5 years for sacroiliac and spine SPARCC inflammatory score and at 6 years, for HAQ-AS, BASFI, ASDAS-CRP and MASES enthesitis index, in univariable then multivariable analysis adjusted on demographic variables and baseline values of each score. Patients with complete data for ASDAS-CRP at 6 years were included in this analysis. There was no imputation of missing data.

Results: After 6 years, 589/708 (83.2%) patients were followed-up: mean age 40.5±8.7 years, 45.8% men. The cumulative prevalence of psoriasis increased from 99/589 (16.8%) at baseline to 158/589 (26.8%) at 6 years (Figure), leading to an incidence of 2.1/100 patient-years. As expected, patients with psoriasis had more peripheral arthritis and a higher BMI at baseline. After 6 years of follow-up, for 343 patients with complete data, there was no significant impact of psoriasis on functional capacity (BASFI, HAQ), on disease activity (similar ASDAS-CRP score), enthesitis or MRI.

Conclusion: Psoriasis is frequent in early axSpA and is often concomitant to the diagnosis of axSpA. Over 6 years of follow-up, de novo psoriasis may be detected at any time point, necessitating regular work-ups. In this analysis, outcomes did not appear worse for patients with psoriasis than without. Further research to explore impact of psoriasis on axSpA is needed.



Cumulative prevalence and incidence of psoriasis in 589 axial SpA patients over 6 years of follow-up

Disclosure: F. LUCASSON, None; **P. Richette**, AbbVie, 1, 6, Amgen, 1, 6, Celgene, 1, 6, Janssen, 1, 6, Eli Lilly, 1, 6, MSD, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **k. aouad**, None; **A. RUYSSEN-WITRAND**, None; **D. Wendling**, None; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **L. Gossec**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1312

What Is the Optimal Screening Strategy for Early Recognition of Spondyloarthritis in Patients with Acute Anterior Uveitis?

Judith Rademacher[1], Hanna Müllner[2], Dominika Pohlmann[3], Valeria Rios Rodriguez[1], Fabian Proft[1], Mikhail Protopopov[1], Susanne Lüders[4], Burkhard Muche[5], Laura Spiller[1], Anne-Katrin Weber[2], Sabrina Sron[2], Hildrun Haibel[6], Uwe Pleyer[3] and Denis Poddubnyy[7], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin; Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin; Department of Ophthalmology, Berlin, Germany, [4]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, Berlin, Germany, [5]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Berlin, Germany, [6]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [7]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The diagnostic delay remains long in patients with spondyloarthritis (SpA), thus effective screening/referral strategies for early recognition are needed. Up to 40% of patients presenting with acute anterior uveitis (AAU) have an undiagnosed SpA [1]. The Dublin Uveitis Evaluation tool (DUET) was presented as a referral tool for ophthalmologists [1]. The objective of this study was to compare the performance of the DUET with a screening strategy based on the Assessment of SpondyloArthritis International Society (ASAS) referral recommendations in AAU patients (figure, [2]).

[1] Haroon M, et al. Ann Rheum Dis 2015;74:1990-5.

[2] Poddubnyy D, et al. Ann Rheum Dis 2015;74:1483-7.

Methods: A total of 207 consecutive patients with non-infectious AAU seen in the ophthalmology clinic and ophthalmological private practices were included, 189 of them completed a standardized rheumatological examination in the specialized center including imaging of sacroiliac joints (MRI performed in 185 patients, X-rays performed in 116 patients) allowing for a definite conclusion on the presence/absence of SpA. The sensitivity, specificity and positive predictive value of both referral tools were calculated. Mann Whitney U and Fisher's exact tests were used for comparison between AAU patients with and without SpA.

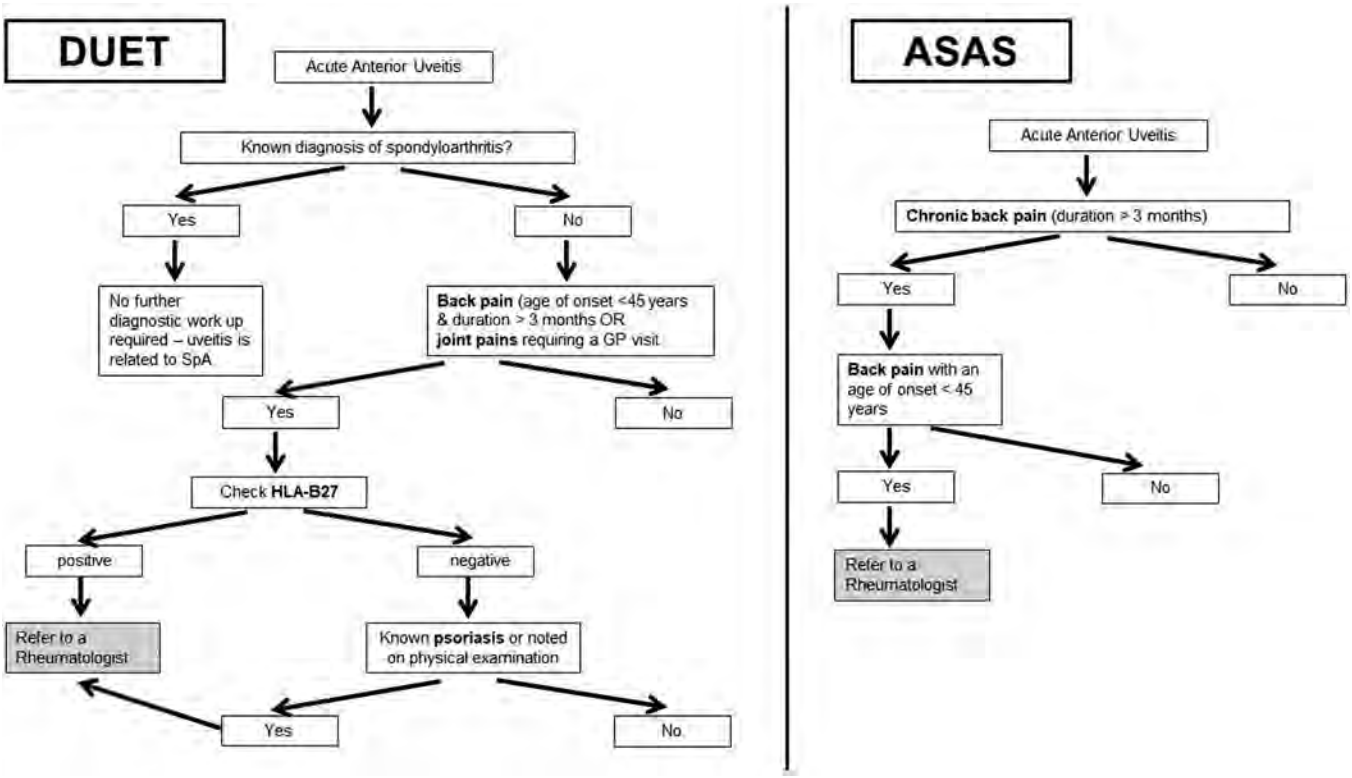


Figure: DUET and ASAS referral tool, modified after [1,2].

Table 1. Demographic and clinical parameters of the 189 included patients with acute anterior uveitis with and without spondyloarthritis (SpA). * Mann Whitney U test for numerical and Fisher's exact test for categorical variables. Mean is given for numerical variables together with standard deviation (SD)

	All	SpA	No SpA	p value*
Number (%)	189	105 (55.6%)	84 (44.4%)	
Age in years	40.8 (12.3)	42.1 (11.8)	39.3 (12.8)	0.087
Male sex (%)	103 (54.5%)	67 (63.8%)	36 (42.9%)	**0.005**
Uveitis				
Unilateral uveitis (including alternating eyes, %)	162/188 (86.2%)	95/104 (91.3%)	67 (79.8%)	**0.032**
Recurrent uveitis (%)	129 (68.3%)	72 (68.6%)	57 (67.9%)	1.000
Synechia current (%)	22/119 (18.5%)	13/68 (19.1%)	9/51 (17.6%)	1.000
Back pain				
Back pain ever (%)	177 (93.7%)	100 (95.2%)	77 (91.7%)	0.376
Current back pain (last week) (%)	129 (68.3%)	79 (75.2%)	50 (59.5%)	**0.028**
Duration of back pain in years (SD)	12.6 (10.3)	14.0 (10.7)	10.7 (9.4)	**0.024**
Age of onset of back pain <45 years	163 (86.2%)	94 (89.5%)	69 (82.1%)	0.202
Chronic back pain (>3months)	150 (79.4%)	85 (81.0%)	65 (77.4%)	0.590
Inflammatory Back Pain	103/188 (54.8%)	67/104 (64.4%)	36/84 (42.9%)	**0.003**
Disase activity parameters				
Physician Global Assessment VAS (SD)	3.1 (2.5)	3.5 (2.5)	2.6 (2.3)	**0.006**
Patient Global Assessment VAS (SD)	3.5 (3.1)	4.0 (3.2)	2.8 (2.8)	**0.006**
BASDAI (SD)	3.1 (2.0)	3.3 (2.2)	2.8 (1.7)	0.153
BASFI (SD)	1.7 (3.0)	2.2 (3.7)	1.0 (1.4)	0.002
ASDAS-CRP (SD)	2.0 (0.9)	2.2 (1.0)	1.7 (0.7)	**0.001**
ASDAS-ESR (SD)	2.0 (1.0)	2.2 (1.0)	1.7 (0.8)	**0.000**
Clinical Examination				
Modified Schober test (in cm, (SD))	4.2 (2.0)	3.9 (1.8)	4.7 (2.0)	**0.002**
Lateral flexion (right side, cm, (SD))	16.6 (5.8)	15.8 (6.3)	17.6 (4.9)	**0.035**
Lateral flexion (left side, cm, (SD))	16.6 (5.7)	16.0 (6.1)	17.2 (5.0)	0.244
Laboratory Parameters				
C-reactive protein (in mg/l, (SD))	4.5 (8.7)	5.9 (10.4)	2.7 (5.5)	**0.000**
ESR (in mm/h, (SD))	14.7 (14.1)	17.7 (16.3)	11.0 (9.8)	**0.001**
HLA-B27 positivity (%)	153 (81.0%)	97 (92.4%)	56 (66.7%)	**0.000**
SpA Features (ever)				
Previous diagnosis of SpA (%)	33 (17.5%)	30 (28.6%)	3 (3.6%)	**0.000**
Psoriasis (%)	17 (9.0%)	16 (15.2%)	1 (1.2%)	**0.001**
Inflammatory bowel disease (%)	5 (2.6%)	5 (4.8%)	0	0.067
Peripheral arthritis (%)	53 (28.0%)	36 (34.3%)	17 (20.2%)	**0.035**
Dactylitis (%)	6 (3.2%)	4 (3.8%)	2 (2.4%)	0.690
Enthesitis (%)	40 (21.2%)	27 (25.7%)	13 (15.5%)	0.107
Referral Tools				
ASAS Tool positive (%)	143/180 (79.4%)	83/97 (85.6%)	60/83 (72.3%)	**0.041**
ASAS Tool for unknown SpA (%)	112/148 (75.7%)	55/68 (80.9%)	57/80 (71.3%)	0.185
DUET positive (%)	129/180 (71.7%)	80/97 (82.5%)	49/83 (59.0%)	**0.001**
DUET for unknown SpA (%)	99/148 (66.9%)	52/68 (76.5%)	47/80 (58.8%)	**0.024**

Table 2. Performance of referral tools in all patients (N=180) and only patients without a previously diagnosed spondyloarthritis (N=148): Dublin Uveitis Evaluation Tool (DUET) versus an adaption of the Assessment of SpondyloArthritis International Society referral tool (ASAS)

	ASAS, n/N (%)	DUET, n/N (%)	ASAS, patients without a known diagnosis of SpA, n/N (%)	DUET, patients without a known diagnosis of SpA, n/N (%)
Sensitivity	83/97 (85.6%)	80/97 (82.5%)	55/68 (80.9%)	52/68 (76.5%)
Specificity	23/83 (27.7%)	34/83 (41.0%)	23/80 (28.8%)	33/80 (41.3%)
Positive predictive value	83/143 (58.0%)	80/129 (62.0%)	55/112 (49.1%)	52/99 (52.5%)
Prevalence of SpA	97/180 (53.9%)		68/148 (45.9%)	

Results: Out of the 189 AAU patients, 105 (56%) were diagnosed with SpA: the majority of them (n=100, 95%) had predominantly axial SpA, 5 patients solely peripheral SpA. 33 of the included 189 patients had a previous external diagnosis of SpA, however, in three out of them SpA was excluded after rheumatologist evaluation as part of the study.

Patients with underlying SpA were more often male, HLA-B27 positive and had predominantly unilateral uveitis (table 1). Though back pain was frequent in the overall study population, back pain present at inclusion as well as inflammatory back pain were significantly more prevalent in the AAU patients with SpA. Moreover, SpA patients had higher disease activity parameters and elevated inflammatory markers (both CRP and ESR) as well as reduced spinal mobility compared to patients without SpA. Patients with SpA presented more frequently with psoriasis and peripheral arthritis.

The ASAS referral tool showed a higher sensitivity (86% vs. 83%) but a lower specificity (28% vs. 41%) compared to the DUET. The positive predictive value was 58% for the ASAS tool and 62% for the DUET (table 2). Similar performances were observed when analyzing only patients without a known diagnosis of SpA (table 2).

Conclusion: We revealed a high prevalence of undiagnosed SpA in patients with acute anterior uveitis. As anticipated, the DUET strategy also including psoriasis and HLA-B27 positivity showed higher specificity for recognition of SpA than the ASAS referral tool focusing on back pain, which showed a higher sensitivity. Given the high prevalence of SpA in AAU patients, we recommend referring all AAU patients with relevant back pain for a rheumatologic evaluation.

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Abstract Number: 1313

The Impact of Comorbidities on Patients with Axial Spondyloarthritis: A Cluster Analysis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous study using cluster analysis technique analyzed the association between comorbidities and various outcome measures in patients with axial spondyloarthritis (axSpA). Due to the cross-sectional nature of the study, however, prognostic information about each group were not provided. Using the data retrieved from Korean College of Rheumatology Biologics (KOBIO) registry, which includes longitudinal data of axSpA patients using anti-TNF agents, this study aims to perform cluster analysis to differentiate axSpA patients in terms of comorbidities and to examine the differential treatment outcomes of these groups.

Methods: Clinical characteristics and demographic data of axSpA patients in KOBIO registry were analyzed using an agglomerative hierarchical cluster analysis. The optimum number of clusters was determined by the pseudo-F statistic. After clustering, baseline clinical characteristics and treatment outcomes were compared between isolated axSpA and classified comorbidity groups using multivariable linear models and mixed linear models, respectively.

Results: 1,207 patients were included in the study. At least one comorbidity was seen in 464 (38%) axSpA patients. Compared with those with isolated axSpA, patients with comorbidity were older, longer disease duration, and reported higher patient global assessment of disease activity (PtGA, $p = 0.019$), and BASFI ($p < 0.001$), but did not have significantly different BASDAI, ESR, and CRP levels (Table 1). The most common comorbidities were hypertension (14.4%), hyperlipidemia (13.0%), and obesity (4.5%). The hierarchical cluster analysis classified patients in 21 groups. We combined clusters 17-21 for further evaluation due to the small size of clusters (< 5 patients). In multivariable linear models for baseline clinical characteristics, we found that patients in the hypothyroidism, asthma, and headache clusters reported poorer PtGA, BASDAI, or BASFI, and the weight loss cluster had higher level of CRP, compared with patients with isolated axSpA even after adjustment of patient demographic data (Table 2). After 1-year treatment of anti-TNF agents, the patients in the hypothyroidism and weight loss clusters decreased greater amounts of BASDAI and BASFI scores and ESR/CRP levels, respectively, compared with patients with isolated axSpA (Table 3). However, the degree of improvement in asthma and headache clusters, which had higher disease activities at baseline, was similar with isolated axSpA. Therefore, they still had higher disease activity scores at the 1-year follow-up.

Conclusion: Comorbidity could affect the treatment outcomes in patients with axSpA in certain subgroups. Thus, we should also pay attention to the comorbidities when treating axSpA.

Table 1. Patient and disease characteristics according to the presence or absence of comorbidities

	Isolated axSpA	axSpA with comorbidities	p
n	743	464	
Age at baseline (years)	35.19 (11.90)	44.41 (13.05)	**<0.001**
BMI (kg/m^2)	22.85 (2.80)	24.69 (4.02)	**<0.001**
Disease duration (years)	3.41 (4.93)	4.58 (5.98)	**<0.001**
Male sex	571 (76.9)	350 (75.4)	0.621
csDMARDs use	77 (10.4)	49 (10.6)	0.99
NSAIDs use	645 (86.8)	399 (86.0)	0.75
HLA-B27 positivity	675 (90.8)	416 (89.7)	0.56
Inflammatory back pain	634 (85.3)	388 (83.6)	0.472
Sacroiliitis on X-rays	659 (88.7)	424 (91.4)	0.162
Good response to NSAIDs	270 (36.3)	156 (33.6)	0.368
Family history	95 (12.8)	60 (12.9)	>0.999
Smoking	350 (47.1)	236 (50.9)	0.226
Current extra-axial SpA features at baseline			
Peripheral arthritis	210 (28.3)	174 (37.5)	**0.001**
Enthesitis	129 (17.4)	75 (16.2)	0.644
Uveitis	60 (8.1)	47 (10.1)	0.264
Dactylitis	18 (2.4)	16 (3.4)	0.385
Psoriasis	19 (2.6)	13 (2.8)	0.942
IBD	10 (1.3)	4 (0.9)	0.626
History of extra-axial SpA features			
Peripheral arthritis	251 (33.8)	195 (42.0)	**0.005**
Enthesitis	154 (20.7)	92 (19.8)	0.761
Uveitis	142 (19.1)	115 (24.8)	**0.023**
Dactylitis	11 (1.5)	15 (3.2)	0.066
Psoriasis	16 (2.2)	13 (2.8)	0.601
IBD	9 (1.2)	5 (1.1)	>0.999
Disease outcome measures at baseline			
PtGA	6.27 (2.04)	6.56 (2.10)	0.019
CRP (mg/dL)	2.25 (2.92)	2.30 (2.94)	0.775
ESR (mm/h)	37.34 (29.37)	38.60 (31.08)	0.477
BASDAI	5.94 (1.88)	6.13 (1.93)	0.088
BASFI	3.32 (2.55)	3.87 (2.61)	<0.001

Data are shown in mean (SD) or number (%).
BMI, body mass index; csDMARDs, conventional synthetic disease modifying anti-rheumatic drugs; NSAIDs, non-steroidal anti-inflammatory drugs; HLA, human leukocyte antigen; SpA, spondyloarthritis; IBD, inflammatory bowel disease; PtGA, patient global assessment of disease activity; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index.

Table 2. Comparing each cluster to patients with isolated axSpA (i.e. no comorbidity) using multivariable linear models for each baseline clinical outcome measure as the dependent variable, and cluster as a dummy independent variable

Cluster/description		PtGA	BASDAI	BASFI	ESR	CRP
2	isolated axSpA	Reference	Reference	Reference	Reference	Reference
1	Hyperlipidemia	-0.204 (-0.634 - 0.226)	0.03 (-0.367 - 0.428)	0.359 (-0.173 - 0.891)	-5.401 (-11.536 - 0.734)	-0.216 (-0.821 - 0.388)
3	Obesity	0.038 (-0.67 - 0.746)	-0.242 (-0.896 - 0.412)	0.254 (-0.622 - 1.131)	2.955 (-7.149 - 13.059)	0.227 (-0.769 - 1.222)
4	HTN	-0.048 (-0.514 - 0.419)	-0.275 (-0.707 - 0.156)	-0.312 (-0.89 - 0.266)	-1.574 (-8.238 - 5.09)	-0.067 (-0.724 - 0.59)
5	DM	0.179 (-0.51 - 0.868)	0.048 (-0.589 - 0.685)	0.051 (-0.802 - 0.904)	9.081 (-0.756 - 18.917)	0.948 (-0.021 - 1.917)
6	Liver ds	-1.014 (-2.817 - 0.788)	-0.599 (-2.264 - 1.067)	0.053 (-2.179 - 2.285)	1.05 (-24.683 - 26.783)	-0.582 (-3.118 - 1.954)
7	Depression	0.368 (-0.798 - 1.534)	0.559 (-0.519 - 1.637)	0.56 (-0.884 - 2.004)	-12.586 (-29.235 - 4.062)	-0.349 (-1.99 - 1.291)
8	Osteoporosis	0.17 (-0.581 - 0.92)	0.14 (-0.554 - 0.833)	0.352 (-0.577 - 1.281)	-3.455 (-14.167 - 7.257)	-0.429 (-1.485 - 0.626)
9	Malignancy	0.206 (-0.82 - 1.232)	0.359 (-0.589 - 1.307)	0.316 (-0.954 - 1.587)	-2.033 (-16.68 - 12.615)	0.833 (-0.611 - 2.276)
10	Hypothyroidism	**1.637 (0.199 - 3.075)†**	**2.36 (1.031 - 3.689)†**	**2.943 (1.162 - 4.724)†**	-3.475 (-24.004 - 17.055)	-0.048 (-2.071 - 1.975)
11	Weight loss	0.96 (-0.685 - 2.605)	0.807 (-0.713 - 2.327)	1.594 (-0.443 - 3.631)	17.926 (-5.562 - 41.414)	**3.456 (1.141 - 5.77)†**
12	IHD	0.067 (-1.165 - 1.299)	0.622 (-0.517 - 1.76)	-0.229 (-1.754 - 1.297)	13.613 (-3.977 - 31.203)	1.084 (-0.65 - 2.817)
13	HBV	0.153 (-0.829 - 1.135)	-0.057 (-0.964 - 0.851)	0.027 (-1.189 - 1.244)	10.166 (-3.856 - 24.188)	0.813 (-0.569 - 2.195)
14	Peptic ulcer	0.177 (-0.753 - 1.106)	-0.118 (-0.977 - 0.741)	-0.403 (-1.554 - 0.748)	1.566 (-11.704 - 14.837)	-0.154 (-1.462 - 1.154)
15	Asthma	**2.026 (0.379 - 3.672)†**	1.381 (-0.14 - 2.903)	1.167 (-0.872 - 3.205)	13.458 (-10.048 - 36.964)	0.607 (-1.709 - 2.924)
16	Headache	**1.19 (0.486 - 1.894)†**	**0.96 (0.309 - 1.61)†**	0.246 (-0.625 - 1.118)	-0.026 (-10.074 - 10.023)	0.433 (-0.557 - 1.423)
17-21	Micellaneous	-0.134 (-1.31 - 1.042)	-0.229 (-1.316 - 0.858)	0.811 (-0.646 - 2.267)	**-17.908 (-34.699 - -1.118)†**	-1.197 (-2.852 - 0.457)

† p-value < 0.05

Table 3. Comparing each cluster to patients with isolated axSpA (i.e. no comorbidity) using multivariable linear mixed models for each treatment outcome measure at 1-year follow-up as the dependent variable

Cluster/description		PtGA	BASDAI	BASFI	ESR	CRP
2	isolated axSpA	Reference	Reference	Reference	Reference	Reference
1	Hyperlipidemia	0.382 (-0.171 - 0.934)	0.058 (-0.455 - 0.572)	-0.216 (-0.711 - 0.278)	5.404 (-0.515 - 11.322)	0.221 (-0.399 - 0.84)
3	Obesity	0.233 (-0.57 - 1.036)	0.098 (-0.648 - 0.844)	-0.078 (-0.811 - 0.656)	**9.005 (0.481 - 17.529)†**	0.358 (-0.553 - 1.269)
4	HTN	0.349 (-0.244 - 0.942)	0.544 (-0.007 - 1.095)	0.393 (-0.138 - 0.924)	3.76 (-2.536 - 10.056)	0.007 (-0.649 - 0.663)
5	DM	0.355 (-0.544 - 1.254)	0.399 (-0.416 - 1.214)	0.307 (-0.498 - 1.111)	-2.109 (-11.511 - 7.294)	-0.27 (-1.262 - 0.723)
6	Liver ds	0.882 (-1.792 - 3.556)	0.066 (-2.419 - 2.551)	-0.055 (-2.447 - 2.337)	-2.791 (-28.473 - 22.891)	0.961 (-1.91 - 3.832)
7	Depression	0.465 (-1.087 - 2.018)	-0.176 (-1.618 - 1.267)	-0.08 (-1.469 - 1.309)	8.442 (-8.213 - 25.098)	0.571 (-1.169 - 2.312)
8	Osteoporosis	0.188 (-0.79 - 1.167)	0.211 (-0.698 - 1.12)	-0.08 (-0.955 - 0.795)	2.287 (-8.205 - 12.779)	0.09 (-0.979 - 1.158)
9	Malignancy	-0.118 (-1.466 - 1.23)	-0.353 (-1.606 - 0.9)	-0.399 (-1.605 - 0.807)	-3.016 (-17.478 - 11.446)	-0.778 (-2.226 - 0.67)
10	Hypothyroidism	-1.243 (-3.139 - 0.653)	**-2.147 (-3.908 - -0.385)†**	**-2.38 (-4.076 - -0.684)†**	2.234 (-18.11 - 22.578)	-0.087 (-2.123 - 1.95)
11	Weight loss	-0.618 (-2.804 - 1.568)	-0.901 (-2.932 - 1.131)	-1.93 (-3.886 - 0.026)	**-26.891 (-50.351 - -3.431)†**	**-4.197 (-6.544 - -1.849)†**
12	IHD	0.2 (-1.42 - 1.82)	0.02 (-1.485 - 1.526)	0.975 (-0.475 - 2.424)	-8.027 (-25.411 - 9.357)	-0.345 (-2.169 - 1.479)
13	HBV	0.007 (-1.341 - 1.355)	-0.034 (-1.287 - 1.218)	-0.186 (-1.392 - 1.02)	-11.391 (-25.43 - 2.649)	-1.062 (-2.557 - 0.432)
14	Peptic ulcer	-0.197 (-1.437 - 1.042)	0.118 (-1.033 - 1.27)	0.425 (-0.684 - 1.534)	-3.759 (-17.057 - 9.538)	-0.044 (-1.45 - 1.363)
15	Asthma	0.049 (-2.138 - 2.235)	0.833 (-1.199 - 2.864)	0.254 (-1.702 - 2.209)	-1.058 (-24.517 - 22.402)	2.018 (-0.552 - 4.589)
16	Headache	-0.103 (-1.052 - 0.846)	0.169 (-0.713 - 1.051)	0.463 (-0.387 - 1.312)	0.344 (-9.693 - 10.382)	-0.046 (-1.132 - 1.04)
17-21	Micellaneous	1.291 (-0.329 - 2.911)	0.575 (-0.931 - 2.08)	0.366 (-1.084 - 1.815)	12.776 (-3.879 - 29.431)	0.742 (-0.925 - 2.41)

† p-value < 0.05

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Abstract Number: 1314

Predictive Factors for the Development Acute Anterior Uveitis Attacks in Patients with Axial Spondyloarthritis; The Results of a Longitudinal Analysis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory rheumatic disease mainly affecting sacroiliac joints and spine. Peripheral arthritis, dactylitis and enthesitis may also occur. Acute anterior uveitis (AAU) is the most frequent extra musculo-skeletal manifestation of axSpA which may lead to severe functional impairment. Moreover, an AAU attack can be the presenting symptom that may lead to diagnosis of axSpA. However, there is limited data regarding the factors predicting the development of AAU attacks in patients with axSpA.

Purpose: To examine the factors associated with the AAU attacks in patients with axSpA in a longitudinal axSpA cohort.

Methods: In total 469 axSpA patients (272 [58%] male; 297 [63%] with AS and 172 [36%] with non-radiographic (nr)-axSpA) who have followed up to three years were included in this observational study. Baseline disease characteristics and follow-up data including the development of AAU attacks, concurrent disease activity, serum CRP levels, usage of conventional synthetic and biological disease modifying anti-rheumatic drugs (cs-DMARD, bDMARD) were collected on 3, 6, 12, 24 and 36th months. The longitudinal relationship between AAU attacks (dependent) and potential predictive factors (independent) tested by using generalized estimating equations (GEE) which is a technique for longitudinal data analysis allowing the use of all available data even deviated from normality.

Results: Overall, 99 (%21) of 469 patients had experienced at least one AAU attack (77 [78%] on history and 31 of them also in follow up, 11 patients [11%] presented with AAU in their first visits and 11 have developed their first AAU attacks on follow up) (Table 1). In total 89 AAU attacks were observed during follow up (35 attacks on presentation, 10 attacks at 3nd month, 4 attacks at 6th month, 12 attacks at 12ndmonth, 16 attacks at 24th month and 12 attacks at 36th months of follow up). At baseline patients with the AAU history were older (p=0.001), had more peripheral arthritis (p< 0.001), higher BASMI score (p=0.007), and higher serum CRP levels (p=0.016). Those patients with a positive AAU history have been also using cs- and bDMARD more commonly. Univariate longitudinal analysis revealed that the development of AAU attacks was significantly associated with the history of AAU, male gender, the presence of extraspinal involvement, concomitant cs-DMARD usage, BASDAI scores, ASDAS-CRP, and PGA of disease activity. However, multivariate analysis showed that the presence of AAU history and concurrent disease activity assessed by BASDAI were the only independent determinants of the development of AAU attacks in axSpA patients (Table 2).

Table 1. Baseline characteristics of axSpA patients with and without history of uveitis

	All group N=469	Patients with a history of AAU N=77	Patients without a history of AAU N=392	*p*
Age, years median (IQR)	43 (18)	47.5 (18)	42 (16)	**0.001**
Sex, male, %	58	54.5	58.7	0.53
HLA-B27 positivity, %	60.5	66.7	59.4	0.38
The presence of extraspinal involvement history (arthritis or dactylitis or enthesitis)	58.5	70.8	56.1	**0.021**
Peripheral arthritis, %	32.6	51.4	28.9	**<0.001**
Enthesitis, %	47.5	51.7	46.8	0.57
Dactylitis, %	3.1	1.4	3.4	0.71
Psoriasis, %	4.3	5.2	4.3	1
Inflammatory bowel disease, %	3.3	5.1	3	0.42
BASDAI (0 to 10), median (IQR)	4 (3)	3.3 (3.4)	3.6 (3.1)	0.22
BASFI (0 to 10), median (IQR)	2.8 (4.2)	2.1 (4)	2.4 (3.6)	0.65
BASMI (0 to 10), median (IQR)	2 (3)	3 (3)	2 (3)	**0.007**
CRP (mg/dl), median (IQR)	1 (8)	4 (8)	1 (4.3)	**0.016**
PGA of disease activity (0 to 100), median (IQR)	40 (40)	35 (50)	40 (40)	0.36
Current cs-DMARD use, %	25.8	45.2	22	**<0.001**
Current bDMARD use, %	67	45.5	30.6	**0.007**

Conclusion: Our results showed that AAU attacks were significantly higher in axSpA patients who had history of AAU and higher disease activity. Moreover, the presence of AAU might have an impact on treatment in axSpA patients.

Table 2. The factors assosiated with uveitis attacks in patients with axSpA

		Model 1	
	B	95%CI	*p*
BASDAI	-0.332	-0.619; -0.45	***0.023***
History of AAU	2.873	1.914; 3.832	***<0.001***
History of extraspinal involvement	-0.518	-1.650; 0.614	*0.37*
PGA	0.001	-0.017; 0.019	*0.90*
Concomitant cs-DMARD use	0.891	-0.222; 2.003	*0.18*
Male sex	-0.587	-1.555; 0.381	*0.23*

Disclosure: H. Cinaklı, None; **E. Ediboglu**, None; **E. Otman Akat**, None; **D. Solmaz**, Roche, 6, Farmanova, 6, Pfizer, 6, Lilly, 6; **G. Alp**, None; **E. Erpek**, None; **S. Gücenmez**, None; **M. Ozmen**, None; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6.

Abstract Number: 1315

The Best Cardiovascular Risk Algorithm to Predict the Presence of Carotid Plaque in Psoriatic Arthritis Patients

Natalia Guajardo-Jauregui, **Iris Colunga-Pedraza**, Jose Azpiri-Lopez, Dionicio Galarza-Delgado, Alejandra Rodriguez-Romero, Diana Flores-Alvarado, Julieta Loya-Acosta, Alejandro Meza-Garza, Jesus Cardenas-de La Garza, Salvador Lugo-Perez and Jessica Castillo-Treviño, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic inflammation in psoriatic arthritis (PsA) patients accelerates the process of atherosclerosis; this increases the risk of presenting a major cardiovascular (CV) event than the general population. The carotid ultrasound (US), a non-invasive diagnostic tool, has the ability of detecting subclinical atherosclerosis, but it is not available to all patients.

The aim of this study was to determine which is the best CV risk (CVR) algorithm to predict the presence of carotid plaque (CP) in PsA patients.

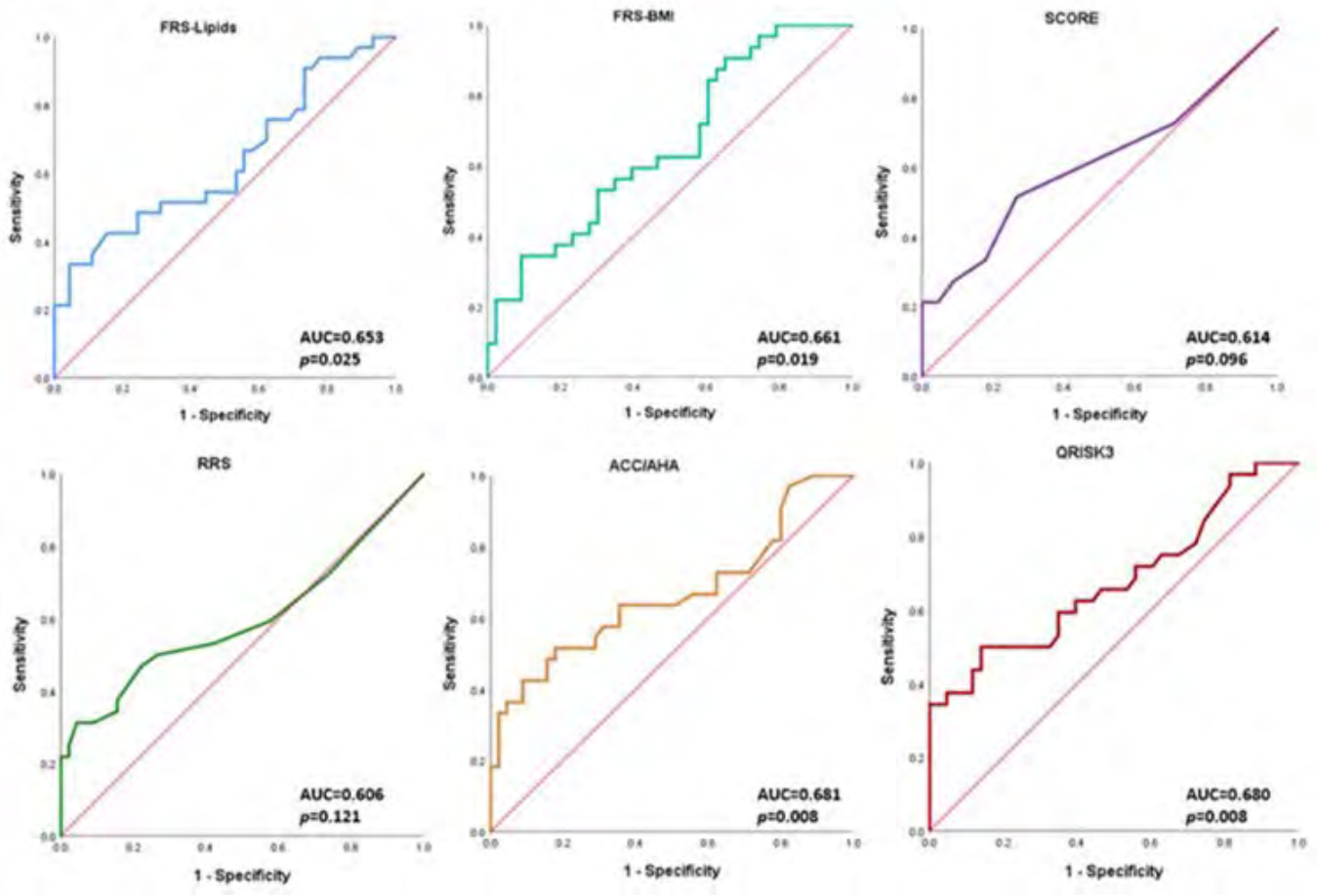
Methods: This was a cross-sectional and observational study. A total of 78 patients aged 40-75 years, who fulfilled the 2006 CASPAR classification criteria for PsA were included. The CVR of each patient was assessed by six different CVR algorithms, including: Framingham Risk Score (FRS)-lipids, FRS-body mass index (FRS-BMI), American College of Cardiology and American Heart Association (ACC/AHA) Risk Algorithm, Systematic Coronary Risk Evaluation (SCORE), QRISK3 and Reynolds Risk Score (RRS). A carotid US was performed in all study subjects to identify the presence of CP. A ROC-curve analysis was done to establish the cut-off points of each algorithm to predict the presence of CP, calculating sensitivity, specificity and area under the curve (AUC) to determine the discriminative capacity. A p-value < 0.05 was considered statistically significant.

Table 1. ROC curve analysis of the cardiovascular risk algorithms.

Cardiovascular risk algorithms (cut-off points)	AUC	CI 95%		p	Sensitivity	Specificity	Likelihood ratio	
		Inferior limit	Superior limit				+	-
FRS-lipids (11.55)	0.653	0.523	0.783	**0.025**	51.5%	68.9%	1.66	0.70
FRS-BMI (13.8)	0.661	0.536	0.786	**0.019**	59.4%	60.5%	1.50	0.67
SCORE (1.5)	0.614	0.478	0.750	0.096	-	-		
RRS (3.5)	0.606	0.467	0.745	0.121	-	-		
ACC/AHA (4.8)	0.681	0.551	0.812	**0.008**	63.6%	64.4%	1.79	0.56
QRISK3 (5.15)	0.680	0.551	0.810	**0.008**	62.5%	60.5%	1.58	0.62

AUC, area under the curve; FRS, Framingham Risk Score; BMI, body mass index; SCORE, Systematic Coronary Risk Evaluation; RRS, Reynolds Risk Score; ACC/AHA, American College of Cardiology and American Heart Association.

Figure 1. ROC-curve of the six cardiovascular algorithms.



Results: Most patients were women (55.1%) with a mean age of 53.46 (±10.86) years. The prevalence of CP was 42.3%. Four of the six CVR algorithms showed the capacity of predicting CP in PsA patients. FRS-lipids showed an AUC 0.653 (0.523-0.783), p=0.025, a cut-off point ≥11.55, a sensitivity of 51.5% and specificity of 68.9%. FRS-BMI showed an AUC 0.661 (0.536-0.786), p=0.019, a cut-off point ≥13.8, sensitivity of 59.4% and specificity of 60.5%. ACC/AHA showed an AUC 0.681 (0.551-0.812), p=0.008, a cut-off point ≥4.8, sensitivity of 63.6% and specificity of 64.4%. QRISK3 showed an AUC 0.680 (0.551-0.810), p=0.008, a cut-off point ≥5.15, sensitivity of 62.5% and specificity of 60.5% (Table 1, Figure 1).

Conclusion: The best CVR algorithm to predict CP in PsA patients was the ACC/AHA risk score. However, there is a need of lower cut-off points to have the capacity of identifying patients classified in the low-moderate risk, according to these algorithms, with subclinical atherosclerosis, who would benefit from an opportune treatment.

Disclosure: N. Guajardo-Jauregui, None; **I. Colunga-Pedraza**, None; **J. Azpiri-Lopez**, None; **D. Galarza-Delgado**, None; **A. Rodriguez-Romero**, None; **D. Flores-Alvarado**, None; **J. Loya-Acosta**, None; **A. Meza-Garza**, None; **J. Cardenas-de La Garza**, None; **S. Lugo-Perez**, None; **J. Castillo-Treviño**, None.

Abstract Number: 1316

Vitamin D Deficiency and Disease Activity in Patients with Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: There are increasing data about vitamin D immunomodulatory potential in different rheumatologic disorders. Deficiency of vitamin D is frequent in patients with spondyloarthritis (SpA) but studies about the role of vitamin D in disease activity and functional impairment are controversial. This study aims to assess whether vitamin D deficiency is associated with increased disease activity and functional impairment in patients with SpA.

Methods: Our cross-sectional study included patients with SpA according to Assessment of Spondyloarthritis International Society classification criteria. All study patients were treated with biologic disease-modifying antirheumatic drug (bDMARD). Disease activity was assessed using Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) and functional impairment using Bath Ankylosing Spondylitis Functional Index (BASFI). Serum 25-hydroxyvitamin D [25(OH)D] levels were measured in SpA patients after 6 months of bDMARD therapy. Vitamin D deficiency was defined as 25(OH)D< 30ng/mL. Vitamin D deficient patients were compared with non-deficient patients using Student's t-test for Gaussian.

Results: We included 190 patients with axial and peripheral SpA, 98 were females (51.6%) and 41 current smokers (21.6%). Mean age was 42.7±12.1 and mean disease duration 8.0±9.1 years. Non-steroidal anti-inflammatory drugs were used by 102 patients (53.7%). Seventy patients (36.8%) were treated with conventional syntheticDMARDs and all patients were on bDMARD therapy (189 patients with tumor necrosis factor inhibitors and one with interleukin-17 inhibitor. The mean concentration of 25(OH)D was 27.2±13.4 ng/ml and 118 patients (62.1%) had 25(OH)D levels below the recommended threshold (< 30 ng/ml). Vitamin D supplementation was used by 75 patients (39.5%). Sub-

Table 1: Differences in BASDAI, ASDAS e BASFI in SpA patients with (<30 ng/ml) and without (≥30 ng/mL) vitamin D deficiency

25(OH)D concentration ng/mL	BASDAI (mean±SD)	ASDAS (mean±SD)	BASFI (mean±SD)
<30	4.28±2.41	2.48±1.01	4.82±2.97
≥30	3.16±2.23	2.09±1.00	3.41±2.51
* Student's t-test	p= 0.007*	p= 0.02*	p=0.004*

groups analysis of SpA patients with low 25(OH)D concentration (< 30ng/ml) compared to higher 25(OH)D concentration show that mean BASDAI (4.28 vs 3.16), ASDAS (2.48 vs 2.09) and BASFI (4.82 vs 3.41) were all significantly higher in patients deficient for vitamin D (p< 0,05).

Conclusion: The group of patients with vitamin D deficiency has significantly higher levels of activity and functional impairment than the group of patients with normal vitamin D concentration. According to these data vitamin D can therefore play an immunomodulating and anti-inflammatory role and can be considered a co-adjuvant in the treatment of these patients.

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Abstract Number: 1317

Impairment of Memory in Axial Spondyloarthritis?

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: There is certain evidence that neuropsychiatric changes occur in systemic lupus(1) and rheumatoid arthritis (2). However, there is little knowledge about possible cognitive changes in axial spondyloarthritis (axSpA). The aim of this study ist to evaluate patients with axial spondyloarthritis regarding cognitive impairments.

Methods: 101 consecutive patients with axial spondyloarthritis attending two rheumatology practices were routinely evaluated by different rheumatologists and underwent a computer-based memory and attention test (MAT) described elsewhere (3, 4). The results of short-term memory and working memory were analyzed compared with an age-, sex- and education-matched control group of healthy subjects.

Results: Patients' characteristics are displayed in table 1. Patients with axSpA revealed a decreased working memory (table 2) as analysed by Wilcoxon signed-rank test (table 3).

Conclusion: The MAT computerized testing is a highly feasible test and was well accepted by patients. It showed a clinically meaningful decrease in working memory in patients with axial spondyloarthritis. Further work-up is required to characterise possible causes or associations of this cognitive impairment.

Table 1. Patients' characteristics

	n	%	Mean	SD	Median	25% Quantile	75% Quantile
Age	101	100	51,1	11,6	52	42	60
Age (female)	48	47,5	52,6	11,7	54	44,5	61
Age (male)	53	52,5	49,8	11,5	51	41	57
< 13 years formal education	47	46,5					
≥ 13 years formal education	54	53,5					
Disease duration (years)	101	100	13,7	11,7	12	4	21
Disease duration (female, years)	48	47,5	11,6	9,9	9	4	17,2
Disease duration (male, years)	53	52,5	15,5	12,9	15	5	23
BASDAI	92	91,1	3,7	1,7	3,8	2,4	5
BASFI	91	90,1	3	2,4	2,3	1,2	4,5
BASMI	75	74,3	1,9	2,3	1	0	3
ASDAS	98	97	2,3	0,8	2,3	1,8	2,8

Controll Group	n	%	Mean	SD	Median	25% Quantile	75% Quantile
Working Memory (Score)	101	100	13,7	2,3	15	13	15
Shortterm Memory (Score)	101	100	12,8	3	15	12	15
Axial Spondyloarthritis							
Working Memory (Score)	101	100	12	5,3	15	10	15
Shortterm Memory (Score)	101	100	13,1	3,6	15	13	15

Working Memory and short term memory test results. Patients with spondyloarthritis and an age-, sex, and education-matched controll group.

	Δ mean	Δ SD	Δ median	Δ 25% Quantile	Δ 75% Quantile	V	p-value	r
Working Memory	-1,644	5,946	0	-5	1	539,5	0,006	-0,24
Shortterm Memory	0,317	4,798	0	0	3	1075	0,351	-0,08

Wilcoxon signed-rank test revealed a clinically relevant and signficant difference in working memory between patients and controll group.

Disclosure: S. Kleinert, Novartis, 5, Abbvie, 1, Siemens Healthineers, 1, Sanofi, 11; **F. Schuch**, Abbvie, 1, 6, Novartis, 1, 6, Lilly, 1, Gilead, 1, 6; **P. Rapp**, None; **M. Ronneberger**, None; **J. Wendler**, Janssen Cilag, 1, 6, Roche Pharma, 1, 6; **P. Sternad**, None; **F. Popp**, None; **P. Bartz-Bazzanella**, None; **C. Von der Decken**, None; **K. Karberg**, None; **G. Gauler**, Lilly, 1, Abbvie, 1, 6, Gilead, 6, Novartis, 6; **P. Wurth**, None; **S. Späthling-Mestekemper**, None; **C. Kuhn**, None; **M. Englbrecht**, None; **W. Vorbrüggen**, None; **G. Adler**, None; **M. Welcker**, Abbvie, 2, 5, 6, Actelion, 5, Aescu, 6, Amgen, 6, Biogen, 6, BMS, 2, 6, Berlin Chemie, 6, Celgene, 2, Galapagos, 2, 5, Gilead, 2, 5, GSK, 2, 5, 6, Hexal, 5, 6, Janssen, 6, Medac, 2, 6, MSD, 6, Mundipharma, 6, Mylan, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 6, Riemser, 6, Sanofi, 2, 6, UCB, 2, 5, 6.

Abstract Number: 1318

Interplay Between Covid-19 and Spondyloarthritis or Its Treatment

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The Covid-19 pandemic has been especially challenging for patients with inflammatory diseases including spondyloarthritis (SpA). Patients with rheumatic and musculoskeletal diseases (RMDs) remain at an increased risk of morbidity and mortality from vaccine preventable infections, often as a result of disease activity, comorbidities, and immunosuppressive medication.[1] Susceptibility and severity of Covid-19 was addressed with an online survey of patients with a diagnosis of SpA established by a physician.

Methods: We conducted a web-based survey of SpA distributed to approximately 40,000 individuals (mostly in North America) who had registered with the Spondylitis Association of America. Additional surveys were distributed based on lists provided by the Axial Spondyloarthritis International Federation (ASIF). The survey was translated into 15 additional languages to accommodate ASIF members.

Results: Responses from 4723 subjects with SpA and 450 household contacts of these subjects. Most from the US (64.9%), Canada (8%), and the rest from 72 other countries. 63% of the were female. Median age was male 54 and females 49. Several forms of SpA were identified, with 83.5% as ankylosing spondylitis. Respondents reported being exposed to Covid-19 (19.6%) with 384 (8.2%) reported being infected. Of those infected 295 had a confirmatory positive test. Table 1 indicates that none of the treatments appeared to affect the likelihood to develop Covid-19 or the subjective rating of the severity of Covid-19. Some classes of medications such as anti-malarials and JAK inhibitors were not commonly used by the respondents so the statistical meaning of the results could be confounded by the limited size of the database. Patients with SpA were not statistically significantly different from household controls.

Conclusion: Based on survey results, SpA does not affect susceptibility or severity of Covid-19. Medications commonly used to treat spondyloarthritis do not affect susceptibility or severity of Covid-19.

We cannot exclude confounding because patients taking certain medications such as a biologic might exercise greater care to socially distance and minimize exposure.

	C19 cases	Person-months	Rate ratio	lower	upper	p-value*	Mean severity	SD	p-value**
No Med	14	1937.7	1.00	NA	NA	NA	4.14	2.25	NA
MTX	31	3671.4	1.17	0.62	2.20	0.641	5.19	2.27	0.160
HCQ	5	941	0.74	0.26	2.04	0.579	5.40	2.30	0.327
Prednisone	12	2271.9	0.73	0.34	1.58	0.432	5.18	2.18	0.256
Sulfasalazine	29	2598.7	1.54	0.82	2.92	0.181	4.41	2.01	0.705
Anti-TNF	135	14856.9	1.26	0.73	2.18	0.423	4.75	2.40	0.353
NSAID	155	15708.7	1.37	0.79	2.36	0.261	4.72	2.32	0.370
Anti-IL17	27	2985	1.25	0.66	2.39	0.504	4.44	2.24	0.695
JAK inhibitor	6	439.7	1.89	0.73	4.91	0.210	6.20	2.28	0.126

Analysis of medication usage and the susceptibility and severity of Covid-19 * Wald test; ** t-test against No Med. Rate ratio is calculated relative to patients taking no medication. Mean severity is the subjective severity of Covid-19 infection using a one (most mild) to ten (most severe) scale. Abbreviations: C19=Covid-19; SD=standard deviation; MTX=methotrexate; HCQ=hydroxychloroquine; TNF=tumor necrosis factor; NSAID=nonsteroidal anti-inflammatory drug; JAK=janus kinase; No Med=no medication for spondyloarthritis.

Disclosure: R. Howard, AbbVie, 11, Amgen, 11, Bristol-Myers Squibb, 11, GSK, 11, Johnson & Johnson, 11, Lilly, 11, Merck, 11, Novartis, 11, Pfizer, 11, Teva, 11, GSK, 2, Novartis, 2, UCB, 11; **M. Weisman**, Novartis, 2, Gilead, 2, GSK, 2, UCB, 2; **H. Hamilton**, None; **C. Shafer**, None; **E. Aslanyan**, None; **J. Reveille**, UCB, 1, Eli Lilly, 1, Eli Lilly, 5, Novartis, 1; **K. Winthrop**, Pfizer, 2, 5, Bristol-Myers Squibb, 2, 5, UCB Pharma, 2, 5, AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Glaxo-SmithKline, 2, Regeneron, 2, Sanofi, 2; **D. Choi**, None; **K. Ogle**, None; **S. Siegel**, Insmed, 2; **E. Papaspyru**, None; **D. Grims**, None; **J. Rosenbaum**, AbbVie, 2, UCB, 2, Novartis, 2, Gilead, 2, Corvus, 2, Roivant, 2, Revolo, 2, Neoleukin, 2, Affibody, 2, Santen, 2, Celgene, 2, Bristol Myers, 2, Pfizer, 5, Horizon, 5, UpToDate, 9.

Abstract Number: 1319

Cardiovascular Risk Reclassification According to Six Traditional Cardiovascular Risk Algorithms and a Carotid Ultrasound in Psoriatic Arthritis Patients

Natalia Guajardo-Jauregui, **Iris Colunga-Pedraza**, Jose Azpiri-Lopez, Dionicio Galarza-Delgado, Alejandra Rodriguez-Romero, Diana Flores-Alvarado, Alejandro Meza-Garza, Julieta Loya-Acosta, Jesus Cardenas-de La Garza, Salvador Lugo-Perez, Octavio Ilizaliturri-Guerra, Gisela Garcia-Arellano and Jessica Castillo-Treviño, Hospital Universitario "Dr Jose E. Gonzalez", Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with psoriatic arthritis (PsA) have a higher risk of developing a cardiovascular (CV) event than the general population. This could be attributed to a higher prevalence of traditional CV risk (CVR) factors and to disease characteristics such as systemic inflammation. There are multiple algorithms to estimate the CVR for the general population, however there is not one for PsA patients.

The aim of this study was to compare the CVR reclassification using six CVR algorithms and a carotid ultrasound (US) in PsA patients and controls.

Methods: This was a cross-sectional, observational, and comparative study. A total of 75 patients aged 40-75 years old, who fulfilled the 2006 CASPAR criteria and 75 controls without PsA matched by age (±5 years), gender and comorbidities were recruited for this study. Initially CVR was evaluated according to six CVR algorithms, including Framingham Risk Score (FRS)-lipids, FRS-body mass index (BMI), American College of Cardiology and American Heart Association (ACC/AHA) Risk Algorithm, Systematic Coronary Risk Evaluation (SCORE), QRISK3 and Reynolds Risk Score (RRS). Posteriorly a carotid US was performed in all subjects to identify the presence of subclinical atherosclerosis, defined as the presence of carotid plaque (CP) or an increased carotid intima media thickness (cIMT) which was considered as a value ≥0.8mm. CP was defined as a cIMT ≥1.2mm or a focal narrowing of the surrounding lumen ≥0.5mm. Patients with presence of CP but classified in the low-moderate risk by the CVR algorithms were re-classified to a higher risk category. Distribution was evaluated with the Kolmogorov-Smirnov test. Comparisons were done using χ^2 test for qualitative variables, and Student's t test and Mann-Whitney's U test for quantitative variables. A p-value < 0.05 was considered statistically significant.

Results: Mean age was 53.89 ± 10.59 in PsA patients and 54.25 ± 7.08 in the control group (p=0.807), 57.3% were women in both groups. There were no significant differences in traditional CVR factors between PsA patients and controls. A difference was found in the presence of CP, being more prevalent in PsA patients (44.0% vs 26.7%, p=0.026) and in the presence of subclinical atherosclerosis overall (52.0% vs 34.7%, p=0.032) (Table 1). When comparing the CVR reclassification to a higher risk category a difference was found in five of the six CVR algorithms. The reclassification was more prevalent in PsA patients: 29.3% vs 13.3%, p=0.017 with FRS-lipids; 26.7% vs 10.7%, p=0.012 with FRS-BMI; 40.0% vs 21.3%, p=0.013 with SCORE; 33.3% vs 17.3%, p=0.024 with QRISK3; and 36.0% vs 21.3%, p=0.047 with RRS (Table 2).

Table 1. Demographic characteristics and ultrasound findings.

	PsA (n=75)	Controls (n=75)	*p-value*
Age years, mean ± DE	53.89 ± 10.59	54.25 ± 7.08	NS
Female gender, n (%)	43 (57.3)	43 (57.3)	NS
T2DM, n (%)	16 (21.3)	15 (20.0)	NS
HTN, n (%)	28 (37.3)	21 (28.0)	NS
Dyslipidemia, n (%)	33 (44.0)	28 (37.3)	NS
Obesity, n (%)	31 (41.3)	32 (42.7)	NS
Active smoking, n (%)	14 (18.7)	18 (24.0)	NS
BMI kg/m^2, median (p25-p75)	29.32 (26.23-32.03)	28.9 (25.4-33.5)	NS
Disease duration years, median (p25-p75)	5.0 (3.0-10.0)	-	-
DAPSA, median (p25-p75)	12.6 (5.3-22.9)	-	-
Carotid ultrasound findings			
Carotid plaque, n (%)	33 (44.0)	20 (26.7)	**0.026**
cIMT ≥0.8mm, n (%)	14 (18.7)	9 (12.0)	NS
Subclinical atherosclerosis, n (%)	39 (52.0)	26 (34.7)	**0.032**

PsA, psoriatic arthritis; NS, not significant; T2DM, type 2 diabetes mellitus; HTN, hypertension; BMI, body mass index; DAPSA, disease activity for psoriatic arthritis; cIMT, carotid intima media thickness.

Conclusion: The CVR algorithms underestimate de real CVR of PsA patients. This could be attributed to the fact that these algorithms do not include disease characteristics that can affect the CV prognosis of PsA patients. For this reason, a carotid US should be done to correctly classify the CVR of PsA patients and identify those who would benefit from an opportune treatment.

Table 2. Cardiovascular risk reclassification.

	PsA (n=75)	Controls (n=75)	*p-value*
FRS-lipids			
Reclassification, n (%)	22 (29.3)	10 (13.3)	**0.017**
Low risk, n (%)	16 (21.3)	3 (4.0)	**0.001**
Moderate risk, n (%)	6 (8.0)	7 (9.3)	NS
FRS-BMI			
Reclassification, n (%)	20 (26.7)	8 (10.7)	**0.012**
Low risk, n (%)	13 (17.3)	3 (4.0)	**0.008**
Moderate risk, n (%)	7 (9.3)	5 (6.7)	NS
SCORE			
Reclassification, n (%)	30 (40.0)	16 (21.3)	**0.013**
Low risk, n (%)	9 (12.0)	1 (1.3)	**0.009**
Moderate risk, n (%)	17 (22.7)	11 (14.7)	NS
High risk, n (%)	4 (5.3)	4 (5.3)	NS
ACC/AHA algorithm			
Reclassification, n (%)	23 (30.7)	13 (17.3)	0.056
Low risk, n (%)	17 (22.7)	10 (13.3)	NS
Moderate risk, n (%)	6 (8.0)	3 (4.0)	NS
RRS			
Reclassification, n (%)	27 (36.0)	16 (21.3)	**0.047**
Low risk, n (%)	17 (22.7)	7 (9.3)	**0.026**
Moderate risk, n (%)	10 (13.3)	9 (12.0)	NS
QRISK3			
Reclassification, n (%)	25 (33.3)	13 (17.3)	**0.024**
Low risk, n (%)	19 (25.3)	9 (12.0)	**0.036**
Moderate risk, n (%)	6 (8.0)	4 (5.3)	NS

PsA, psoriatic arthritis; NS, not significant; FRS, Framingham Risk Score; BMI, body mass index; SCORE, Systematic Coronary Risk Evaluation; ACC/AHA, American College of Cardiology and American Heart Association; RRS, Reynolds Risk Score.

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Abstract Number: 1320

Obesity and Its Associations with Clinical Manifestations and Disease Burden of Patients with Spondyloarthritis: An Ancillary Study from the ASAS-perSpA Project

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Demographics, patient characteristics, and differences between the groups

	Total	Divided by current BMI (BMI_c)			
		Normal weight	Overweight	Obese	p
Number of patients	4465	1976	1539	934	
Diagnosis					< 0.001[1]
Axial SpA	2711 (60.9%)	1272 (64.4%)	962 (62.5%)	477 (51.1%)	
Juvenile SpA and others	111 (2.5%)	63 (3.2%)	37 (2.4%)	11 (1.2%)	
Peripheral SpA	431 (9.7%)	210 (10.6%)	120 (7.8%)	101 (10.8%)	
Psoriatic arthritis	1028 (23.1%)	337 (17.1%)	367 (23.8%)	324 (34.7%)	
Age, years with Mean (SD)	44.4 (14.0)	40.5 (14.4)	46.5 (13.1)	49.0 (12.3)	< 0.001[1]
Sex, male ratio with %	2715 (61.0%)	1199 (60.7%)	1024 (66.5%)	492 (52.7%)	< 0.001[2]
Education					< 0.001[2]
<Primary school	735 (16.5%)	245 (12.4%)	284 (18.5%)	206 (22.1%)	
Secondary	1903 (42.8%)	808 (40.9%)	660 (42.9%)	435 (46.6%)	
University	1809 (40.7%)	923 (46.7%)	594 (38.6%)	292 (31.3%)	
Disease duration, years with Mean (SD)	12.4 (10.5)	15.6 (11.6)	16.4 (11.9)	14.3 (11.3)	< 0.001[1]
Ever-smoker, yes (%)	1895 (42.6%)	755 (38.2%)	715 (46.5%)	425 (45.5%)	< 0.001[2]
Inflammatory back pain, yes (%)	3310 (75.3%)	1532 (78.6%)	1150 (75.5%)	628 (67.8%)	< 0.001[2]
Sacroiliitis ever					
X-ray	2511 (60.6%)	713 (38.4%)	547 (37.9%)	374 (44.4%)	0.004[2]
MRI	1813 (64.8%)	859 (67.2%)	612 (65.0%)	342 (59.0%)	0.003[2]
Enthesitis, yes (%)	1979 (44.5%)	867 (43.9%)	668 (43.4%)	444 (47.5%)	0.103[2]
Psoriasis, yes (%)	1204 (27.1%)	413 (20.9%)	430 (27.9%)	361 (38.7%)	< 0.001[2]
Uveitis, yes (%)	706 (16.0%)	306 (15.6%)	254 (16.6%)	146 (15.7%)	0.704[2]
CRP, mg/dL with Median (Q1-Q3)	4.0 (1.0, 11.0)	3.0 (1.0, 11.0)	4.0 (1.0, 10.0)	7.0 (3.0, 13)	< 0.001[1]
Fatigue, BASDAI-Q1 with Mean (SD)	4.6 (2.8)	4.2 (2.7)	4.6 (2.8)	5.3 (2.8)	< 0.001[1]
BASDAI, Mean (SD)	3.9 (2.4	3.5 (2.3)	3.9 (2.4)	4.6 (2.5)	< 0.001[1]
ASDAS-CRP	2.5 (1.1)	2.4 (1.1)	2.5 (1.1)	2.9 (1.1)	< 0.001[1]
Fibromyalgia, doctor opinion, yes (%)	397 (8.9%)	116 (5.9%)	136 (8.8%)	145 (15.5%)	< 0.001[2]
Fibromyalgia, FIRST with Mean (SD)	2.3 (2.0)	2.0 (1.9)	2.4 (2.0)	2.9 (2.0)	< 0.001[1]
Ongoing NSAID, yes (%)	3016 (67.8%)	1362 (68.9%)	1028 (66.8%)	626 (67.0%)	< 0.001[2]
Ongoing cDMARDs, yes (%)	1624 (36.4%)	698 (15.6%)	554 (12.4%)	392 (8.8%)	< 0.001[2]
Ongoing glucocorticoids, yes (%)	499 (11.2%)	221 (11.2%)	167 (10.9%)	111 (11.9%)	0.731[2]

[1] Pearson's Chi-squared test, [2] Kruskal-Wallis rank sum test

SpA: Spondyloarthritis, BASDAI: Bath ankylosing spondylitis disease activity index, ASDAS: Ankylosing Spondylitis Disease Activity Score, FIRST: Fibromyalgia Rapid Screening Tool, NSAID: Non-steroidal anti-inflammatory drugs, cDMARDs: conventional disease-modifying antirheumatic drugs

Background/Purpose: Obese patients with spondyloarthritis (SpA) had more functional limitations, higher subjective disease activity, fewer benefits of exercise, and showed less response to drug therapy. This study aims to explore the relationship of obesity with clinical manifestations and disease burden including biologic/targeted DMARD (btDMARD) burden, SpA-related surgery burden, labor loss, and patient-reported health status.

Methods: An ancillary analysis of ASAS-PerSpA cross-sectional study from 24 participating countries. The ASAS-PerSpA study included the data of diagnosis, demographics, disease duration, clinical manifestations (ie, inflammatory back pain, sacroiliitis, enthesitis, psoriasis, uveitis, fatigue, and fibromyalgia assessment), disease activity, ongoing treatment and treatment history (ie, ongoing btDMARDs use, ever btDMARDs use, number of btDMARDs kinds ever-prescribed, number of btDMARD discontinuation, and the reasons for discontinuation), SpA-related surgery (ie, spinal vertebrectomy, total hip replacement, peripheral joint surgery), work productivity and activity impairment (WPAI) questionnaire, ASAS Health Index (ASAS-HI), Bath Ankylosing Spondylitis Functional Index (BASFI), and global wellbeing (on a visual analog scale). In addition to the current BMI (BMI_c), the 20-year-old BMI (BMI_{20}) data were also noted. Patients were divided into three groups according to the BMI_c and comparisons between the obese patients ($BMI_c \geq 30$ kg/m^2), overweights ($BMI_c \geq 25$ to < 30 kg/m^2), and normal weights ($BMI_c < 25$ kg/m^2) were performed

Table 2. Burden associations with the current BMI

Burden		Normal weight	Overweight	Obese	p	$p^{adj\ (N\text{-}OW)}$	$p^{adj\ (N\text{-}Ob)}$
btDMARDs	Ongoing btDMARDs use	835 (42.3%)	725 (47.2%)	457 (48.9%)	<0.001[1]	0.12	0.01
	Patients ever use btDMARDs	981 (49.6%)	819 (53.2%)	538 (57.6%)	<0.001[1]	0.40	<0.001
	btDMARDs kind ever-prescribed						
	Median (Q1, Q3)	1 (1.0, 2.0)	1 (1.0, 2.0)	1 (1.0, 2.0)	<0.001[1]	0.10	<0.001
	Mean (SD)	1.4 (0.8)	1.5 (0.9)	1.6 (1.0)			
	Number discontinued, Mean (SD)	0.6 (0.9)	0.6 (0.9)	0.8 (1.0)	<0.001[1]		
	Reasons for discontinuation						
	Side/adverse effects, Mean (SD)	0.1 (0.4)	0.1 (0.4)	0.1 (0.4)	0.442[1]	*	*
	Inefficacy, Mean (SD)	0.3 (0.7)	0.4 (0.7)	0.5 (0.9)	<0.001[1]	*	*
	Other, Mean (SD)	0.2 (0.4)	0.1 (0.4)	0.2 (0.4)	0.059[1]	*	*
SpA-related surgery	Patients underwent SpA-related surgery	111 (5.6%)	73 (4.8%)	64 (6.8%)	0.085	*	*
	Spinal vertebrotomy	22 (1.1%)	17 (1.1%)	13 (1.4%)	0.775[1]	*	*
	Total hip replacement	59 (3.0%)	41 (2.7%)	31 (3.3%)	0.640[1]	*	*
	Total schoulder replacement	2 (0.1%)	3 (0.2%)	3 (0.3%)	-	*	*
	Peripheral joint surgery	28 (1.4%)	12 (0.8%)	17 (1.8%)	0.064[1]	*	*
Labor loss (WPAI)	Currently employed	1165 (59.0%)	950 (61.7%)	470 (50.3%)	0.064[1]		
	Work time missed, Mean (SD)	8.9 (23.2)	9.6 (24.1)	13.0 (28.2)	0.562[1]		
	Overall work impairment Mean (SD)	30.8 (30.5)	32.7 (31.9)	38.9 (33.4)	0.027[1]	<0.001	<0.001
Patient reported health	ASAS-HI, Mean (SD)	6.1 (4.6)	6.6 (4.5)	7.7 (4.5)	<0.001[2]	<0.001	<0.001
	BASFI, Mean (SD)	2.5 (2.5)	3.1 (2.6)	3.9 (2.7)	<0.001[2]	<0.001	<0.001
	Global wellbeing (VAS), Mean (SD)	4.1 (2.7)	4.3 (2.7)	5.0 (2.6)	<0.001[2]	<0.001	<0.001

p: for the comparisons between three groups ([1]Pearson's Chi-squared test, [2]Kruskal-Wallis rank sum test)
$p^{adj\ (N\text{-}OW)}$: for the adjusted comparisons between normal weights and overweight's by correcting sex, disease duration, and smoking
$p^{adj\ (N\text{-}Ob)}$: for the adjusted comparisons between normal weights and obeses by correcting sex, disease duration, and smoking
btDMARD: Biologic or targeted disease-modifying anti-rheumatic drugs, SpA: Spondyloarthritis, WPAI: Work productivity and activity impairment questionnaire, ASAS-HI: Assessment of spondyloarthritis international society health index, BASFI: Bath ankylosing spondylitis functional index, VAS: Visual analog scale
**The count of data is not sufficient for statistical model construction*

Table 3. Burden associations with the 20-year-old BMI (

Burden		Normal weight	Overweight	Obese	p	$p^{adj\ (N\text{-}OW)}$	$p^{adj\ (N\text{-}Ob)}$
btDMARDs	Ongoing btDMARDs use	1479 (43.7%)	379 (48.9%)	130 (54.6%)	<0.001[1]	0.02	<0.001
	Patients ever use btDMARDs	1727 (51.0%)	437 (56.4%)	143 (60.1%)	<0.001[1]	0.01	<0.001
	btDMARDs kind ever prescribed						
	Median (Q1, Q3)	1 (1.0, 2.0)	1 (1.0, 2.0)	1 (1.0, 2.0)	0.022[1]	0.94	<0.001
	Mean (SD)	1.5 (0.9)	1.5 (0.8)	1.7 (1.2)			
	Number discontinued, Mean (SD)	0.6 (0.9)	0.6 (0.9)	0.8 (1.2)	0.278[1]	*	*
	Reasons for discontinuation					*	*
	Side/adverse effects, Mean (SD)	0.1 (0.4)	0.1 (0.4)	0.2 (0.4)	0.136[1]	*	*
	Inefficacy, Mean (SD)	0.4 (0.8)	0.3 (0.6)	0.6 (1.1)	0.009[1]	*	*
	Other, Mean (SD)	0.1 (0.4)	0.2 (0.5)	0.1 (0.3)	0.003[1]	*	*
SpA-related surgery	Patients underwent SpA-related surgery	196 (4.8%)	38 (4.9%)	13 (5.5%)	<0.001[1]	*	*
	Spinal vertebrotomy	39 (1.2%)	8 (1.0%)	4 (1.7%)	0.714[1]	*	*
	Total hip replacement	107 (3.2%)	19 (2.5%)	5 (2.1%)	0.412[1]	*	*
	Total shoulder replacement	5 (0.1%)	3 (0.4%)	0 (0.0%)	-	*	*
	Peripheral joint surgery	45 (1.3%)	8 (1.0%)	4 (1.7%)	0.695[1]	*	*
Labor loss (WPAI)	Currently employed	1992 (58.9%)	453(58.5%)	119 (50.0%)	0.027[1]		
	Work time missed, Mean (SD)	8.9 (23.2)	9.6 (24.1)	13.0 (28.2)	0.562[1]		
	Overall work impairment Mean (SD)	30.8 (30.5)	32.7 (31.9)	38.9 (33.4)	0.027[1]	0.09	0.01
Patient reported health	ASAS-HI, Mean (SD)	6.1 (4.6)	6.6 (4.5)	7.7 (4.5)	<0.001[2]	0.03	<0.001
	BASFI, Mean (SD)	2.5 (2.5)	3.1 (2.6)	3.9 (2.7)	<0.001[2]	<0.001	<0.001
	Global wellbeing (VAS), Mean (SD)	4.1 (2.7)	4.3 (2.7)	5.0 (2.6)	<0.001[2]	0.02	<0.001

p: for the comparisons between three groups ([1]Pearson's Chi-squared test, [2]Kruskal-Wallis rank sum test)
$p^{adj\ (N\text{-}OW)}$: for the adjusted comparisons between normal weights and overweights by correcting sex, disease duration, and smoking
$p^{adj\ (N\text{-}Ob)}$: for the adjusted comparisons between normal weights and obeses by correcting sex, disease duration, and smoking
btDMARD: Biologic or targeted disease-modifying anti-rheumatic drugs, SpA: Spondyloarthritis, WPAI: Work productivity and activity impairment questionnaire, ASAS-HI: Assessment of spondyloarthritis international society health index, BASFI: Bath ankylosing spondylitis functional index, VAS: Visual analog scale
**The count of data is not sufficient for statistical model construction.*

for the above-mentioned parameters. In addition, the same population was also divided into different three groups according to their BMI_{20} and they have compared again in themselves.

Results: A total of 4449 patients with the BMI_c values were included. The mean age was 44.4 (SD 14.0) and 61.0% were male. The mean disease duration was 14.3 (SD 11.3) years and 42.6% of them were ever-smokers. Demographics and patient characteristics were demonstrated in Table 1. Comparisons of the disease burden according to the BMI_c (Table2) and BMI_{20} (Table 3) documented the statistical significances between the groups.

Conclusion: Obesity is related to a biological (or targeted) therapy burden, labor loss, and worse patient-reported health status.

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Abstract Number: 1321

Uveitis in Patients with Psoriatic Arthritis – a Database Analysis

Nizar Hijaze[1], Tal Gazitt[2], Amir Haddad[3], Muna Elias[4], Idit Lavi[4], Ilan Feldhamer[5], Arnon Dov Cohen[5], Shaul Sar[4], Oren Tomkins Netzr[4] and Devy Zisman[4], [1]Carmel medical centre, Tamra, Israel, [2]Carmel Hospital, Haifa, Israel, [3]Carmel Medical Centre, Haifa, Israel, [4]Carmel Medical Center, Haifa, Israel, [5]Clalit Health Services, Tel Aviv, Israel

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) belongs to the group of spondyloarthropathies in which uveitis is an associated disease . The prevalence of uveitis among PsA patients especially in the era of biologic treatment is not well established.

Methods: A retrospective database study was conducted on 6,147 adult PsA patients who were newly diagnosed with PsA between January 1, 2005 (start date) and 31 December 2020 (end date) with date of diagnosis considered the index date compared to 23,999 randomly selected control subjects matched for age, sex, ethnicity, and index date. Both groups were followed from the index date until the first episode of uveitis, death, or end of follow-up, whichever came first. Demographic variables, smoking status, socioeconomic status (SES), body mass index (BMI), presence of selected chronic comorbidities, and medication use including conventional and biologic disease-modifying anti-rheumatic drugs (c/b DMARD) were extracted in both groups.

Descriptive statistics was applied as appropriate. Marginal model with robust covariant estimate counting for the matching was used to estimate the crude and adjusted hazard ratio (HR) for the association between PsA and uveitis. Within the group of PsA patients, Cox proportional hazard regression time dependent models were used to calculate the risk of uveitis given demographic variables, SES, smoking, selected comorbidities, and c/bDMARD. All tests were 2-sided; p values of ≤ 0.05 were considered statistically significant.

Results: PsA cohort consisted of 53.1% females with mean age of 51.75±15.39. In the PsA group, 107 patients (1.7%) were diagnosed with uveitis, compared to 187 patients (0.8%) in the control group ($p< 0.0001$, HR 2.25, CI 1.78-2.86). Compared to the control group with uveitis, patients with PsA and uveitis were more often female (64.5% vs 51.9% p=0.036), of a younger age (54.49±16.2 vs 58.89±14.8, p=0.02).

Within the PsA group, patients with uveitis had a previous history of uveitis (HR 33.56 CI 20.76- 54.25), and were more often treated with cDMARDS (83.2% vs 67.1%, $p< 0.0001$), monoclonal anti-Tumor Necrosis Factor-a (anti-TNF-a) agents (68.2% vs 38.6%, $p< 0.0001$) and etanercept (37.4% vs 20.8%, $p< 0.0001$). No difference in uveitis occurrence was noted regarding treatment with anti-IL-17 or anti IL12/23 agents or with regards to demographic characteristics and comorbidities.

No difference in uveitis occurrence was noted regarding treatment with anti-IL-17 or anti IL12/23 agents or with regards to demographic characteristics and comorbidities.

Conclusion: The hazard ratio for uveitis was significantly higher in the PsA group relative to the general population. A high index of suspicion for uveitis is warranted in PsA patients with previous episode of uveitis. Uveitis was reported in patients treated with TNFα blockers irrespective of their mode of action.

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Abstract Number: 1322

Body Mass Index (BMI) Underestimates Obesity in Females with Axial Spondyloarthropathy

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Worldwide prevalence of obesity has been steadily increasing, despite public health campaigns to raise awareness. In axial spondyloarthropathy (axSpA) obesity has been shown to be associated with higher levels of disease activity and decreased response to treatment. The waist to hip ratio (WtHpR) is a tool to screen for abdominal obesity. Abdominal deposition of adipose tissue is associated with increased risk of cardiovascular disease, type II diabetes and premature death. Abdominal obesity is more common in males, with females more prone to gluteal-femoral fat deposition. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data of axSpA patients in Ireland. The aim of this study was to capture the prevalence of abdominal obesity in a large cohort of axSpA patients and assess for variation in prevalence between sexes.

Methods: Participants were analysed on the basis of gender and presence of obesity by BMI and WtHpR. Obesity was defined by body mass index (BMI) with a result of >30 categorised as obese as per CDC definitions. Abdominal obesity was assessed by WtHpR and defined as per WHO guidelines (table 1). Categorical variables were tested for statistical significance with a chi^2 test for independence, while continuous variables were tested with an independent t-test or Mann Whitney U test. A Spearman's correlation analysis was run to assess the strength of association between BMI and WtHpR. A p-value of < 0.05 was deemed significant. IBM SPSS version 26 was used for statistical analysis.

Table 1. Waist to Height Ratio definitions for Abdominal Obesity as per the World Health Organisation (WHO) guidelines

	Males	Females
Normal	< 0.9	< 0.8
Overweight	0.9-0.99	0.8-0.84
Obese	> 1.0	> 0.85

Table 2. Assessment of Obesity by Sex

	Males	Females	p value
n	77.7% (538)	22.3% (154)	
Weight (kg)	84.98	72.76	*<0.01*
BMI (kg/m²)	28.08	27.69	*0.45*
Underweight	0.9% (5)	0.06% (1)	*0.49*
Normal Weight	29.2% (157)	36.4% (56)	
Overweight	39.2% (211)	34.4% (53)	
Obese	29.9% (161)	28.6% (44)	
Waist Circumference (cm)	97.43	90.03	*<0.01*
Hip Circumference (cm)	102.11	101.27	*0.56*
Waist to Hip Ratio	0.956	0.890	*<0.01*
Normal Weight	23.8% (128)	17.5% (27)	*<0.01*
Overweight	46.3% (249)	14.3% (22)	
Obese	29.9% (161)	68.2% (105)	

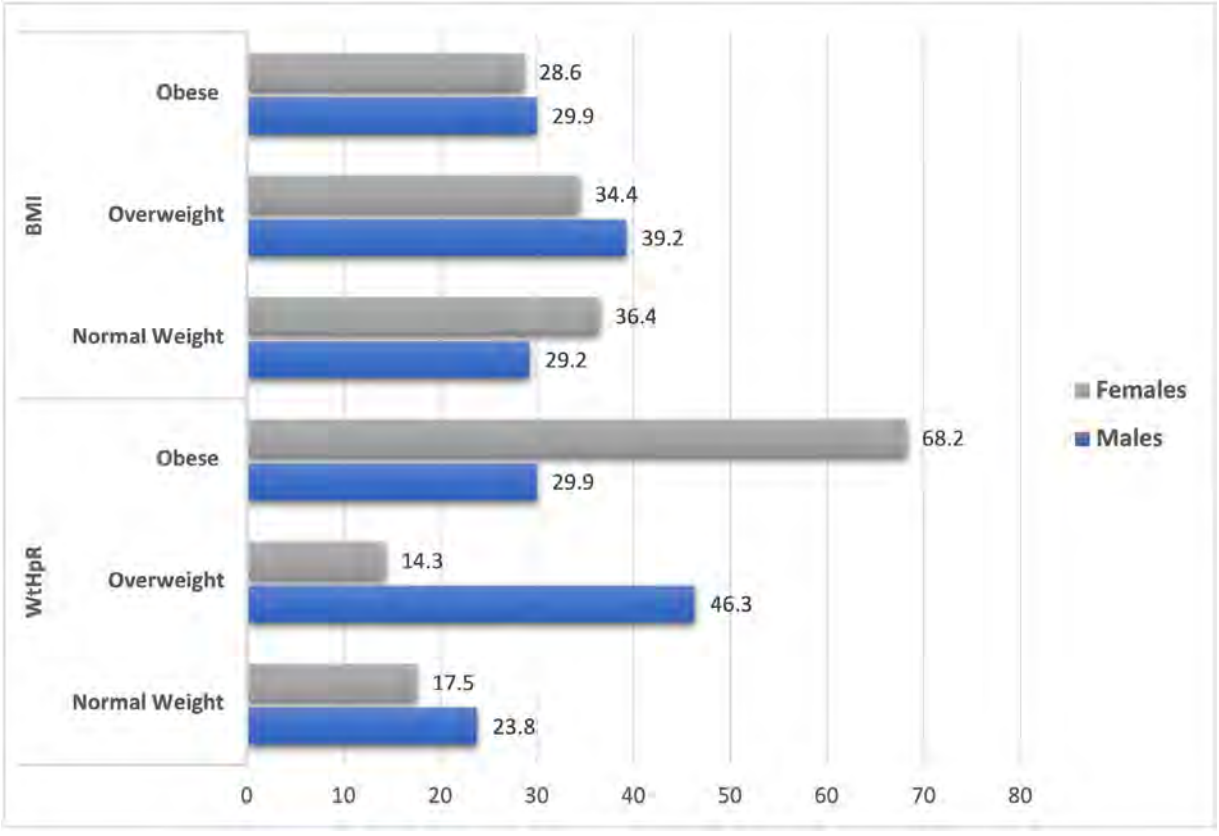

Figure 1. Prevalence of Obesity (%) in AxSpA as detected by Body Mass Index (BMI) and Waist to Hip Ratio (WtHpR) within each sex.

Results: At the time of analysis, physical measurements were available on 692 patients in the ASRI made up of 96.2% (666) Caucasians with 22.3% (154) females and 77.7% (538) males. The average age was 45.9 years with a mean disease duration of 18.8 years (mean scores: BASDAI 4.09, BASFI 3.71, BASMI 3.99, HAQ 0.54, ASQoL 6.72). 80.9% (560) of patients had radiographic sacroiliitis while 49.1% (340) had sacroiliitis on MRI.

Overall 29.5% (215) patients were obese based on BMI results, while 37.5% (274) were centrally obese as per the WtHpR. Analysis on the basis of sex revealed no significant variation in mean BMI (28.1 vs 27.7, p=0.45) or prevalence of obesity as assessed by BMI (29.9% vs 28.6%, p=0.49) between males and females (table 2). As expected, analysis of WtHpR revealed higher mean ratios in males compared to females (0.96 vs 0.89, p< 0.01), however there was a significantly higher prevalence of abdominal obesity in females (29.9% vs 68.2%, p< 0.01) (figure 1).

A moderate positive correlation was detected between BMI and WtHpR (r_s =0.454, p< 0.01). When cases were analysed within each sex the correlation was noted to be stronger in males than females (r_s = 0.543 vs 0.304, p< 0.01).

Conclusion: There is a high prevalence of abdominal obesity as assessed by WtHpR in axSpA, especially in females with axSpA. BMI can underestimate obesity in axSpA women, as the association between BMI and WtHpR is stronger in axSpA males. Use of WtHpR should be considered when screening for obesity in axSpA.

Disclosure: S. Maguire, Gilead, 5; **W. Fiona**, None; **P. Gallagher**, None; **F. O'Shea**, None.

Abstract Number: 1323

Uveitis in 406 Patients with Psoriatic Arthritis: Epidemiology, Clinical Characteristics and Relationship with Biological Treatment. Study of a Single University Center

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Uveitis is the most common ocular manifestation of psoriatic arthritis (PsA). It has been described that uveitis in PsA tends to be insidious, chronic, posterior and bilateral onset, unlike uveitis in spondyloarthritis (SpA), which tends to be of sudden onset, acute course, unilateral and recurring. The use of TNF inhibitory agents (TNFi), especially monoclonal antibodies, has been shown to be effective in the prevention and treatment of refractory non-infectious uveitis.

In a large unselected series of patients with PsA, our objectives were to evaluate a) the epidemiology and clinical characteristics of uveitis associated with PsA, b) the differences between patients with and without uveitis and c)the relationship of uveitis with the biological treatment used.

Methods: Cross-sectional study of patients with PsA from a single referral hospital. They were classified according to the CASPAR criteria. Those with ocular manifestations were evaluated by expert ophthalmologists for the presence of uveitis. Demographic characteristics, clinical findings, complementary tests, presence of other extra-articular manifestations and treatment used were recorded.

Results: We studied 406 (202 women/204 men) patients with PsA; mean age of 46.3±12.3 years. The mean duration of the disease was 9.9±8.2 years.

Uveitis was observed in 20 of 406 (4.9%) patients (12 women/8 men); mean age of 43.1±14.5 years). Uveitis was characterized by being of acute onset (100%), anterior (80%), unilateral (80%) and recurrent (50%).

The comparison between patients with PsA who developed uveitis and those who did not is shown in the Table. The patients who present uveitis were characterized by a higher frequency of HLA-B27 (45%), sacroiliitis on MRI (25%) and ocular surface pathology (10%). The result of PsAID (Psoriatic Arthritis Impact of Disease) (median 5.9 [IQR 2.1-6.8]) and the BASFI index (Bath Ankylosing Spondylitis Functional Index) (median 4 [IQR 1.6-5]) was higher in patients with PsA and uveitis.

Table. General features of 406 patients with PsA. Comparison between patients with and without uveitis

	Overall (n=406)	Uveitis (n=20)	Non uveitis (n=386)	p value
Main general features				
Age, years, mean±SD	46.3±12.3	43.1±14.5	46.5±12.2	0.225
Sex, women/men, N, (% of women)	202/204(49.8)	12/8(60)	218/168(56.5)	0.757
HLA-B27 positive, N (%)	38(9.4)	9(45)	29(7.5)	**0.000***
PsA duration, years, mean±SD	9.9±8.2	12.7±9.2	9.8±8.2	0.129
PsA Characteristics				
Axial pattern, N (%)	48(11.8)	4(20)	44(11.4)	0.277
Peripheral pattern, N (%)	236(58.1)	12(60)	224(58)	0.862
Mixed pattern, N (%)	122(30.1)	4(20)	118(30.6)	0.315
PsA Scores				
BASDAI, mean ± SD	2.7±2.6	3.1±1.3	2.6±2.6	0.492
BASFI, median [IQR]	1.2 [0.0 – 4.0]	4.0 [1.6 - 5.0]	1.0 [0.0 – 3.5]	**0.01***
PsAID, median [IQR]	1.4 [0.0 – 3.5]	5.9 [2.1 – 6.8]	1.25 [0.0 – 3.0]	**0.001***
DAPSA >4, N (%)	65(16)	6(30)	59(15.3)	0.11
Radiological features				
Sacroiliitis on MRI, N (%)	37(9.1)	5(25)	32(8.3)	**0.027***
Other extraarticular manifestations				
Inflammatory bowel disease, N (%)	21(5.2)	2(10)	19(4.9)	0.277
Ocular surface pathology, N (%)	5(1.2)	2(10)	3(0.8)	**0.021***
Previous treatments				
Etanercept	31(7.6)	1(5)	30(7.8)	0.999
TNFi monoclonal antibodies	160(39.4)	12(60)	148(38.3)	0.053
Secukinumab	48(11.8)	1(5)	47(12.2)	0.158
Other	41(10.1)	1(5)	40(10.4)	0.708

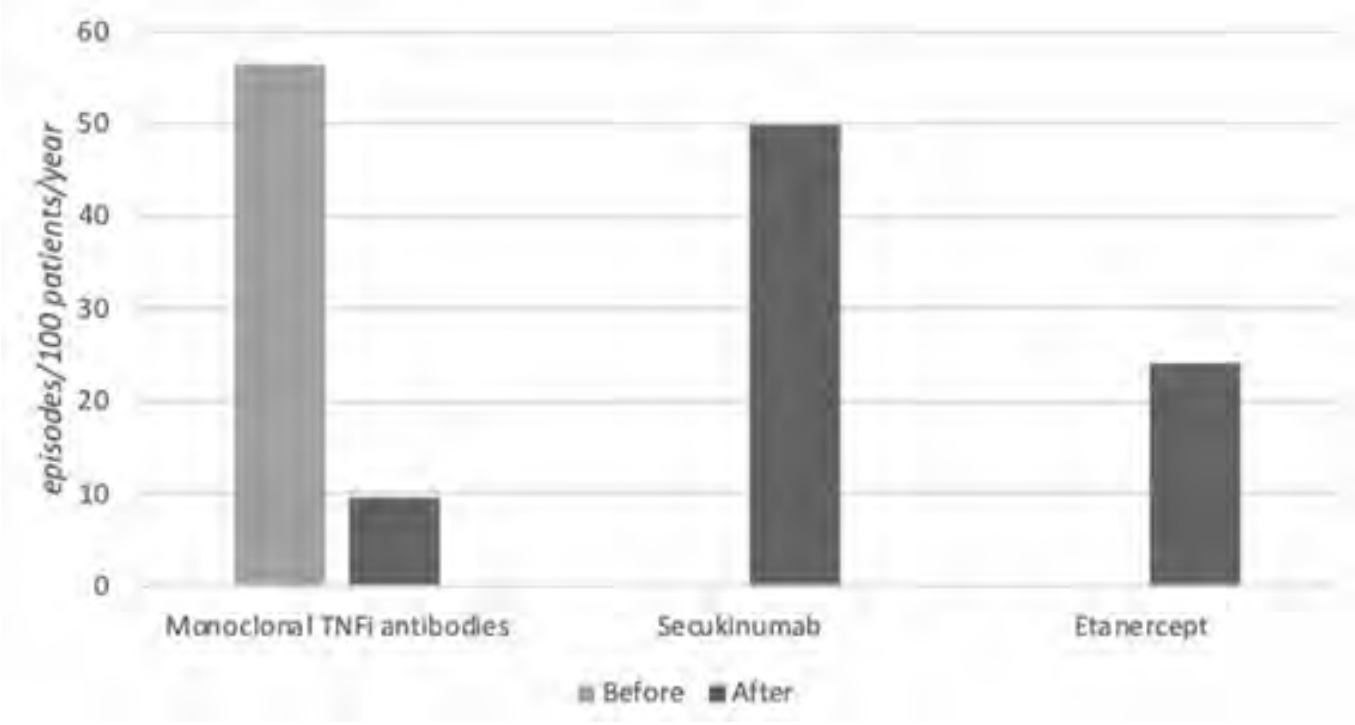

Figure. Uveitis incidence rate before and after biological therapy.

The incidence of uveitis prior to treatment with monoclonal antibodies TNFi and ETN was 56.3 and 6.03 episodes/ 100 patients/year respectively (Figure). Once the treatment was established, the incidence of uveitis in patients with monoclonal antibodies TNFi became 9.4 episodes/ 100 patients/ year while in those treated with ETN and SECU was 24.2 and 50 episodes/100 patients/year respectively.

Conclusion: In our study, the prevalence of uveitis in patients with PsA was 4.9%. The pattern was similar to that observed in axSpA with acute onset and anterior and unilateral pattern. Patients who developed uveitis more frequently presented HLA-B27 positivity, sacroiliitis in MRI and ocular surface pathology, in addition to a higher PsAID score and the BASFI index. The uveitis rate decreased with the monoclonal antibodies TNFi, while an increase was recorded with ETN or SECU.

Disclosure: A. de Vicente Delmás, None; **L. Sánchez-Bilbao**, None; **V. Calvo-Río**, None; **D. Martinez-Lopez**, None; **A. Herrero-Morant**, None; **E. Galindez-Agirregoikoa**, None; **I. Gonzalez-Mazon**, None; **N. Barroso García**, None; **N. PALMOU FONTANA**, Novartis, 5, GSK, 6, Amgen, 6, Sanofi, 6; **R. Blanco**, Brystol Myers Squibb, 6; **M. gonzalez-Gay**, None.

Abstract Number: 1324

Uveitis in 301 Patients with Axial Spondyloarthritis of a Single University Center: Epidemiology, Clinical Features and Biological Treatment

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Uveitis is the most common extra-articular manifestation of axial spondyloarthritis (axSpA). It is characterized by sudden onset, acute, anterior and unilateral. The most widely used biological drugs for its treatment are TNF inhibitors (TNFi), especially monoclonal antibodies.

Our objectives were to evaluate a) epidemiological and clinical characteristics of patients with axSpA and uveitis, and b) the biological treatment received.

Methods: Cross-sectional study of patients with axSpA from a single referral hospital. They were diagnosed of axSpA according to the ASAS criteria. Demographic characteristics, clinical findings including extra-articular manifestations, and the treatment used were recorded. Those with ocular manifestations were evaluated by expert ophthalmologists for diagnosis and characterization of uveitis.

Results: We studied 301 patients with axSpA, 72.1% of them met New York criteria for Ankylosing Spondylitis (AS) and the remaining 27.9% met ASAS criteria for non-radiographic axSpA (nr-axSpA). 59.1% were male and the mean age was 52.16± 12.50 years. At the time of the study, 44 patients (14.6%) had developed at least one episode of uveitis (36 AS and 8 nr-axSpA). The uveitis pattern was anterior and acute (AAU) in all cases and 93% presented unilateral involvement.

The comparison of baseline characteristics between patients with axSpA with and without uveitis is shown in the Table. The group of patients with uveitis showed a higher delay in diagnosis (median [IQR]: 8.5[1-21] Vs 4[1-10], p=0.08) and a higher prevalence of HLA-B27 (84.1% Vs 59.5%, p=0.002).No differences were found in the other clinical characteristics collected (presence of peripheral arthritis, enthesitis and dactylitis throughout the disease, or BASDAI, BASFI or BASMI values at the time of the study). The presence of other extra-articular manifestations was also comparable in patients with and without AAU.

17 (38.6%) patients with AAU were treated with TNFi agents versus 115(44.7%) patients without AAU, with no differences between the diferents agents used. In both groups, the most widely used TNFi agents were Adalimumab,

Table. General baseline characteristics of 301 patients with axSpA.Comparison between patients with and without uveitis

	Overall (n= 301)	Uveitis (n=44)	Non uveitis (n= 257)	p
Main general features				
Age, years, mean ± SD	52.16±12.50	53.34±10.37	51.96±12.84	0.221
Sex, men/women, N, (% of women)	179/122(40.5)	25/19(43.2)	154/103(40.2)	0.713
HLA-B27 positive, N (%)	190(63.1)	37(84.1)	153(59.5)	**0.002**
Delayed axSpA diagnosis, years, median [IQR]	4[1-10]	8.5[1-21]	4[1-10]	**0.008**
axSpA Characteristics				
AS, N (%)	217(72.1)	36(81.8%)	181(70.4%)	0.081
nr-axSpA, N (%)	84(27.9)	8(18.2)	76(29.6)	0.081
Peripheral arthritis, N (%)	96(31.9)	12(27.3)	84(32.7)	0.477
Enthesitis, N (%)	108(35.9)	14(31.8)	94(36.6)	0.334
Dactylitis, N (%)	17(5.6)	3(6.8)	14(5.4)	0.465
Hip affectation, N (%)	20(6.6)	3(6.8)	17(6.6)	0.583
Scores				
BASDAI, mean ± SD	3.81±2.26	3.62±2.42	3.84±2.18	0.603
BASFI, mean ± SD	3.61±2.46	3.23±2.65	3.67±2.43	0.238
BASMI, mean ± SD	2.79±1.76	2.74±1.54	2.80±1.80	0.943
Other extraarticular manifestations				
Inflammatory bowel disease, N (%)	22(7.3)	2(4.5)	20(7.8)	0.348
Psoriasis, N (%)	35(11.6)	6(13.6)	29(11.3)	0.405
Treatment				
Adalimumab, N (%)	64(21.3)	6(13.6)	58(22.6)	0.125
Infliximab, N (%)	34(11.3)	6(13.6)	28(10.9)	0.376
Certolizumab pegol, N (%)	5(1.7)	0	5(1.9)	0.451
Golimumab, N (%)	16(5.3)	2(4.5)	14(5.4)	0.577
Etanercept, N (%)	13(4.3)	3(6.8)	10(3.9)	0.292

which received 13.6% and 22.6% (p=0.125) of patients with and without AAU, and Infliximab used in 13.6% and 10.9% (p=0.376) respectively. No differences were observed in the use of Etanercept.

Conclusion: In our series, 14.6% of the patients with axSpA had developed at least one episode of uveitis at the time of the study. Uveitis in patients with axSpA was anterior and acute in all cases and unilateral in 93%. Patients who developed AAU were characterized by a higher delay in diagosis and a higher prevalence of HLA-B27. No differences were found in the TNFi agents used in patients with and without AAU.

Disclosure: A. de Vicente Delmás, None; **I. Gonzalez-Mazon**, None; **J. Rueda-Gotor**, None; **A. Herrero-Morant**, None; **N. Barroso García**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1325

Osteoporosis in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Osteoporosis (OP) is a frequently underestimated comorbidity in immune-mediated inflammatory diseases (IMIDs). Its association with IMIDs is worse characterized in Psoriatic Arthritis (PsA) than in rheumatoid arthritis (RA). The objective of the study was determine the densitometric values in lumbar spine (LS) and femoral neck (FN) of our cohort of PsA patients to estimate the frequency of OP and analyze the factors associated with a lower bone mineral density (BMD).

Methods: Cross-sectional study in patients (pts) with PsA from a monographic consultation of recent-onset PsA who were invited to perform a DXA densitometry (GELunar Prodigy®). SPSS25 was used for statistical analysis.

Results: 155 PsA pts was screened with DXA. Osteopenia was observed in 84/155 (54.2%) pts: femoral neck (FN) in 74/155 (47,7%) pts and lumbar spine (LS) in 51/152 (33,5%) pts (3 pts could not have lumbar spine determination by previous surgery). OP was observed in 19 (12.3%) pts: LS in 11/152 (7.2%), and FN in 11/155 (7.1%) pts. The

	Osteopenia			Osteoporosis (OP)			Femoral OP		
Characteristics /Coefficients	Beta	t	p	Beta	t	p	Beta	t	p
Sex	-0,10	-0,77	0,44	-0,07	-0,52	0,60	0,06	0,48	0,63
Axial involvement	0,03	0,22	0,83	-0,07	-0,55	0,59	0,03	0,26	0,80
Steroids	-0,09	-0,69	0,49	0,02	0,14	0,89	-0,06	-0,52	0,60
Overweight	0,06	0,51	0,61	0,06	-0,50	0,62	-0,08	-0,80	0,42
Diabetes Mellitus	0,13	0,93	0,36	0,08	0,59	0,55	0,23	1,87	0,66
HBP	0,11	0,76	0,45	0,06	0,39	0,70	0,20	1,50	0,14
Hyperlipidemia	-0,14	-1,01	0,32	-0,04	-0,29	0,77	-0,06	-0,52	0,60
Hyperuricemia	-0,04	-0,32	0,75	-0,26	-1,94	0,06	-0,37	-3,21	0,002
25OHD3 < 20ng/dl	0,03	0,23	0,82	0,07	0,53	0,60	0,14	1,22	0,23
Age DMO (year)	0,37	2,64	0,01	0,15	1,02	0,31	0,10	0,78	0,44
Disease evolution (years)	0,26	2,05	0,04	0,12	0,92	0,36	-0,05	-0,40	0,69
Ischemic heart disease	0,05	0,39	0,70	0,29	2,08	0,42	0,38	3,17	0,002

mean (SD) age at DXA was 47.1 (12.9) years (y). The mean evolution time was 10.2y (6.2) from diagnosis to DXA; median 9y (6;13). OP, in general, and FN OP, were associated with age, but not with the average evolution time of PsA: OP 55.3y (10.0) vs 45.9y (12.8) (p=0.003) and NF OP 58.5y (10.2) vs 46.2y (12.7), (p=0.002). LS OP was not associated with any of the parameters studied. LS osteopenia was more frequent in women 32/76 (42.1%) than men 19/76 (25%) [OR 1,515 (1,020;2,249); p=0.026]. Hyperuricemic pts were less likely to have vertebral osteopenia (OR 2.525 (1.027;6.205) than non-hyperuricemic. Inflammatory bowel disease (IBD) was associated with LS osteopenia [OR 8.511 (0.926;78.247), p=0.044]. FN OP was more frequent in males 9/79 (11.4%) than females 2/76 (2.6%) OR=4.75 (0.99; 22.8) p(fisher)=0.057. We found association of FN OP with axial involvement [OR 3.882 (1.115;13.518); p=0.024], hypertension [OR 9,9 (2,055;47,689); p< 0.001], ischemic heart disease (IHD) [OR 7.657 (1.914;30.630), p< 0.001] and vitamin D deficiency (< 20ng/dl) [26/75 (16,8%) pts; OR 8.727 (0.921;82.691), p=0.046, but not with the rest of the PsA domains, comorbidities or cardiovascular risk factors (CVRF). Femoral osteopenia was only associated with hypertension but more weakly than FN OP. We found no association between the presence of OP and current or previous treatments. Pts who received DMARDs had a lower tendency to present osteopenia [OR 3.28 (0.98; 10.96), p=0.04]. Forty-three pts had received steroids, 141 DMARDs, 129 conventional syinthetic-DMARDs (122 methotrexate), 69 biological-DMARDs with a total of 119 cycles (mainly, TNFi) and 20 targeted synthetic-DMARDs. In the multivariate analysis, we found a positive correlation with OP and IHD (OR= 2.08; 0.42) as in femoral OP (OR=3.17; 0.002), and negative with hyperuricemia (p=0.002). Osteopenia is associated with age (OR=2.64; 0.01), axial involvement and time of disease evolution (not significant).

Conclusion: In our cohort, OP is more frequent in men, it is associated with age despite the time of evolution of the disease. Femoral OP is more frequent in patients with axial involvement, hypertension, heart ischemic disease and vitamin D deficiency.

Disclosure: S. Rojas Herrera, None; **I. Braña Abascal**, None; **M. Priego Fernanddez-Martos**, None; **D. Fernandez Lozano**, None; **L. Chaves Chaparro**, None; **R. Veroz Gonzalez**, None; **J. Aznar Sanchez**, None; **E. Chamizo Carmona**, None.

Abstract Number: 1326

Epidemiology of Comorbidities in an Incident Psoriasis Cohort: A Population-Based Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriasis, a chronic immune-mediated skin disease affecting 2-4% of the US population, is increasingly recognized as a *systemic inflammatory disorder* associated with cardiometabolic and other comorbidities. Additionally, psoriasis frequently precedes the development of psoriatic arthritis (PsA) and among patients with psoriasis, certain comorbidities may be risk factors for development of PsA. The objectives of this study were to: 1) investigate the prevalence of comorbidities in an *incident* cohort of psoriasis patients compared to age- and

sex-matched controls, and 2) compare the prevalence of comorbidities in mild psoriasis with moderate to severe psoriasis at diagnosis.

Methods: A population-based incidence cohort of psoriasis subjects ≥18 years of age and first diagnosed between 2000 and 2010 was identified. Complete medical records of all potential psoriasis subjects were reviewed, and psoriasis was defined as a confirmatory diagnosis in the medical record, either by a dermatologist or a physician's

Table. Prevalence of 44 comorbidities in patients without and with psoriasis and in mild psoriasis compared to moderate/severe psoriasis at psoriasis incidence date. (* SMD of >0.1 signifies potentially meaningful difference)

	No Psoriasis (N=849)	Psoriasis (N=817)	*SMD PsO vs no PsO	Mild (N=120)	Moderate to Severe (N=561)	*SD mild vs mod/severe PsO
Alcohol abuse	16 (1.9%)	29 (3.5%)	-0.10	3 (2.5%)	19 (3.4%)	-0.05
Anemia	40 (4.7%)	32 (3.9%)	0.04	4 (3.3%)	19 (3.4%)	-0.01
Anxiety	57 (6.7%)	63 (7.7%)	-0.04	9 (7.5%)	45 (8.0%)	-0.02
Arrhythmias	36 (4.2%)	36 (4.4%)	-0.01	6 (5.0%)	21 (3.7%)	0.06
Asthma	35 (4.1%)	40 (4.9%)	-0.04	3 (2.5%)	34 (6.1%)	-0.18
Back disorders	123 (14.5%)	124 (15.2%)	-0.02	18 (15.0%)	86 (15.3%)	-0.01
Bipolar disease	3 (0.4%)	7 (0.9%)	-0.06	1 (0.8%)	5 (0.9%)	-0.01
Coronary artery disease	55 (6.5%)	45 (5.5%)	0.04	7 (5.8%)	30 (5.3%)	0.02
Cancer	29 (3.4%)	30 (3.7%)	-0.02	5 (4.2%)	16 (2.9%)	0.07
Heart failure	10 (1.2%)	13 (1.6%)	-0.03	1 (0.8%)	6 (1.1%)	-0.03
Chronic obstructive Pulmonary disease	13 (1.5%)	22 (2.7%)	-0.08	3 (2.5%)	12 (2.1%)	0.03
Dementia	2 (0.2%)	0 (0.0%)	0.06	0 (0.0%)	0 (0.0%)	0
Depression	110 (13.0%)	122 (14.9%)	-0.05	18 (15.0%)	89 (15.9%)	-0.02
Diverticulitis	17 (2.0%)	13 (1.6%)	0.03	2 (1.7%)	11 (2.0%)	-0.02
Diabetes mellitus	56 (6.6%)	68 (8.3%)	-0.06	9 (7.5%)	46 (8.2%)	-0.03
Drug abuse	7 (0.8%)	12 (1.5%)	-0.07	1 (0.8%)	8 (1.4%)	-0.06
Fibromyalgia	11 (1.3%)	22 (2.7%)	-0.10	5 (4.2%)	17 (3.0%)	0.06
Gastroesophageal reflux disease	45 (5.3%)	42 (5.1%)	0.01	5 (4.2%)	35 (6.2%)	-0.09
Gout	7 (0.8%)	5 (0.6%)	0.02	0 (0.0%)	5 (0.9%)	-0.13
Gynecologic (females)	93 (20.9%)	103 (24.2%)	-0.08	24 (34.3%)	73 (25.5%)	0.19
Headache	60 (7.1%)	51 (6.2%)	0.04	6 (5.0%)	35 (6.2%)	-0.05
Hearing loss	33 (3.9%)	26 (3.2%)	0.04	3 (2.5%)	18 (3.2%)	-0.04
Hypertension	152 (17.9%)	191 (23.4%)		30 (25.0%)	136 (24.2%)	
Hyperlipidemia	192 (22.6%)	173 (21.2%)	0.03	31 (25.8%)	126 (22.5%)	0.08
Hyperplasia (males)	18 (4.5%)	10 (2.6%)	0.10	0 (0.0%)	8 (2.9%)	-0.24
Hypothyroid disorder	49 (5.8%)	63 (7.7%)	-0.08	11 (9.2%)	45 (8.0%)	0.04
Interstitial lung disease	1 (0.1%)	2 (0.2%)	-0.03	0 (0.0%)	2 (0.4%)	-0.09
Liver disease	12 (1.4%)	15 (1.8%)	-0.03	4 (3.3%)	7 (1.2%)	0.14
Neuropathy	30 (3.5%)	34 (4.2%)	-0.04	4 (3.3%)	25 (4.5%)	-0.06
Osteoarthritis	60 (7.1%)	61 (7.5%)	-0.02	10 (8.3%)	41 (7.3%)	0.04
Obesity	54 (6.4%)	58 (7.1%)	-0.03	11 (9.2%)	40 (7.1%)	0.08
Osteoporosis	19 (2.2%)	19 (2.3%)	-0.01	1 (0.8%)	13 (2.3%)	-0.12
Parkinson	3 (0.4%)	0 (0.0%)	0.09	0 (0.0%)	0 (0.0%)	0
Post-traumatic stress disorder	3 (0.4%)	3 (0.4%)	0.00	0 (0.0%)	2 (0.4%)	-0.09
Peptic ulcer disease	1 (0.1%)	3 (0.4%)	-0.06	0 (0.0%)	3 (0.5%)	-0.10
Pulmonary disease	7 (0.8%)	6 (0.7%)	0.01	0 (0.0%)	5 (0.9%)	-0.13
Peripheral vascular disease	16 (1.9%)	13 (1.6%)	0.02	1 (0.8%)	6 (1.1%)	-0.03
Renal disease	13 (1.5%)	8 (1.0%)	0.05	0 (0.0%)	6 (1.1%)	-0.15
Sleep disorder	38 (4.5%)	43 (5.3%)	-0.04	5 (4.2%)	31 (5.5%)	-0.06
Stroke	22 (2.6%)	10 (1.2%)	0.10	1 (0.8%)	6 (1.1%)	-0.03
Urinary disorders	4 (0.5%)	14 (1.7%)	-0.12	4 (3.3%)	8 (1.4%)	0.13
Valvular disease	23 (2.7%)	18 (2.2%)	0.03	2 (1.7%)	10 (1.8%)	-0.01
Vision loss	97 (11.4%)	95 (11.6%)	-0.01	11 (9.2%)	68 (12.1%)	-0.09
Total Comorbidities			0.866			1.000
0	318 (37.5%)	290 (35.5%)		34 (28.3%)	200 (35.7%)	
1	156 (18.4%)	165 (20.2%)		27 (22.5%)	110 (19.6%)	
2	126 (14.8%)	100 (12.2%)		22 (18.3%)	61 (10.9%)	
3	75 (8.8%)	58 (7.1%)		12 (10.0%)	40 (7.1%)	
4	65 (7.7%)	60 (7.3%)		10 (8.3%)	42 (7.5%)	
5-9	95 (11.2%)	130 (15.9%)		14 (11.7%)	100 (17.8%)	
10+	14 (1.6%)	14 (1.7%)		1 (0.8%)	8 (1.4%)	

description of the lesions, or a skin biopsy if available. In doubtful cases, medical records were reviewed by a dermatologist. Severity of psoriasis was defined based on the body surface area involved, sites involved, and requirement for phototherapy or systemic therapy. Incident psoriasis cases were age-, and sex-matched to subjects from the same population. Diagnosis codes (≥2 codes at least 30 days apart) within a five-year lookback period were used to determine the presence of comorbidities; at least one year of available medical history was required. Comorbidities were defined using 44 categories (England et al. Ann Rheum Dis. 2021). Standardized differences were calculated to examine differences between psoriasis and controls, and between mild and moderate to severe psoriasis subjects.

Results: There were 871 incident cases of psoriasis from 2000-2010. Excluding those with < 1 year of prior medical history, 817 psoriasis patients were analyzed, with a mean age of 45.7(SD=16.9) years and 52% females; severity of psoriasis ranking was available for 681 (83.4%). At incidence, 35.5, 20.2, 12.2, 7.1, 7.3, 15.9, and 1.7% of the psoriasis patients had 0, 1, 2, 3, 4, 5-9, and ≥10 England comorbidities. There was no substantial difference in the prevalence of the comorbidities between newly diagnosed psoriasis patients and controls (Table). Similarly, few comorbidities were meaningfully different (SMD >0.1) among subjects with mild psoriasis at diagnosis compared to those with moderate to severe psoriasis at diagnosis (Table).

Conclusion: In this population-based cohort of incident psoriasis, there were no substantial differences in the prevalence of comorbidities (including cardiometabolic) between newly diagnosed psoriasis and the general population. Comorbidities may develop over the course of psoriatic disease with no apparent differences at psoriasis diagnosis. Further studies to examine the trajectory of comorbidities in this incident psoriasis cohort are planned.

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Abstract Number: 1327

Impact of BMI on Treatment Response Among PsA Patients Initiating TNF Inhibitors, IL17 Inhibitors and Oral Small Molecules

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Obesity is associated with poor response to treatment in patients with psoriatic arthritis (PsA), however, available data are mostly focused on tumor necrosis factor inhibitor (TNFi) initiators with only a few studies that have examined this association with initiators of other therapies. There are even fewer studies with patient reported outcome (PRO) measures as the outcomes of interest in PsA treatment. The clinical Disease Activity Index for

Table 1. Baseline Characteristics Overall and by BMI Category. Normal weight (BMI 19 to <25 kg/m2), Overweight (BMI 25 to <30 kg/m2), Obese (BMI ≥30 kg/m2)

Characteristics	Overall (n=310)	Normal Weight (n=79)	Overweight (n=99)	Obese (n=126)
Age, yrs, mean (SD)	51.8 (13.5)	52.2 (14.8)	53.2 (13.2)	49.8 (12.2)
Female Sex, n (%)	174 (56.1)	40 (50.6)	48 (48.5)	80 (63.5)
Patients with elevated CRP, n (%)	62 (25.3)	10 (15.9)	11 (14.3)	41 (41)
Patients ever fulfilled ASAS axial SpA criteria, n (%)	46 (15.7)	18 (23.7)	15 (15.2)	13 (11.6)
Body Surface Area %, mean (SD)	1.3 (3.4)	1.2 (3.9)	0.7 (1.7)	1.9 (4.1)
CDAPSA score (range 0-154), mean (SD)	17.3 (12.7)	18.7 (13.3)	16.3 (13.8)	17.3 (11.5)
RAPID3 Score (range 0-30), mean (SD)	10.9 (5.8)	11.5 (6.3)	9.7 (5.7)	11.5 (5.5)
PSAID Score (range 0-10), mean (SD)	3.6 (2.2)	3.7 (2.1)	3.2 (2.1)	3.8 (2.2)
Swollen joint count (range 0-28), mean (SD)	2.6 (3.7)	2.4 (3.1)	2.8 (4.6)	2.6 (3.4)
Tender joint count (range 0-38), mean (SD)	5.8 (7.2)	6.9 (8.4)	5.5 (7.1)	5.4 (6.6)
Leeds Enthesitis index (range 0-6), mean (SD)	0.7 (1.1)	0.8 (1.2)	0.5 (0.96)	0.7 (1.1)
Leeds Dactylitis Index, mean (SD)	0.2 (1.1)	0.2 (0.6)	0.2 (1.4)	0.3 (1.1)
BASDAI Score (range 0-10), mean (SD)	4.7 (2.3)	4.9 (2.2)	4.4 (2.5)	4.9 (2.1)
HAQDI (range 0-3), mean (SD)	0.7 (0.6)	0.7 (0.5)	0.7 (0.7)	0.7 (0.5)
PROMIS10 Mental Health T score, mean (SD)	46.4 (10.5)	48.2 (11.9)	47.8 (10.9)	44.5 (9.1)
PROMIS10 Physical Health T score, mean (SD)	42 (8.1)	42.7 (8.9)	43.8 (8.7)	40.3 (6.9)
PROMIS Depression T score, mean (SD)	61.2 (9.6)	60.7 (9.9)	59.2 (10.9)	62.6 (8.0)
PROMIS Fatigue T score, mean (SD)	56.9 (9.9)	56.4 (10.2)	54.9 (11.1)	58.3 (8.4)
MDHAQ (range 0-3), mean (SD)	2.1 (1.6)	2.1 (1.5)	1.7 (1.6)	2.2 (1.6)
Patient Global (range 0-10), mean (SD)	4.1 (2.4)	4.2 (2.6)	3.8 (2.4)	4.4 (2.3)
MD Global (range 0-10), mean (SD)	4.3 (2)	4.2 (2.0)	4.4 (2.2)	4.4 (1.9)
MD Global Joint (range 0-10), mean (SD)	3.4 (2)	3.4 (2.0)	3.6 (2.2)	3.1 (1.9)
Patient Pain (range 0-10), mean (SD)	4.7 (2.6)	5.1 (2.8)	4.2 (2.5)	4.9 (2.5)
Number of patients starting TNF, n (%)	136 (43.9)	31 (39.2)	47 (47.5)	55 (43.6)
Number of patients starting IL17, n (%)	55 (17.7)	12 (15.2)	16 (16.2)	27 (21.4)
Number of patients starting OSM, n (%)	103 (33.2)	19 (24.1)	40 (40.4)	42 (33.3)

Psoriatic Arthritis (cDAPSA) is a composite measure of disease activity in PsA and the, Routine Assessment of Patient Index Data 3 (RAPID3) and Psoriatic Arthritis Impact of Disease (PsAID) are PROs used in PsA. We examined the association of obesity with change in cDAPSA, RAPID3, PsAID among patients with PsA initiating TNFi, interleukin 17 inhibitors (IL17i) and oral small molecules (OSM).

Methods: Patients with PsA were enrolled in the Psoriatic Arthritis Research Consortium longitudinal cohort study in the US between 2016-2020, initiated therapy with either TNFi, IL17i or OSM and completed at least one follow up visit. Treatment response was assessed by change in cDAPSA, RAPID3, or PsAID. Patients were stratified based on body mass index category (normal weight = BMI 19 to < 25 kg/m^2, overweight = BMI 25 to < 30 kg/m^2, obese = BMI ≥ 30 kg/m^2). Baseline characteristics were reported descriptively. BMI category and its association with change in the outcomes of interest was examined in univariable and age-and-sex adjusted linear regression models.

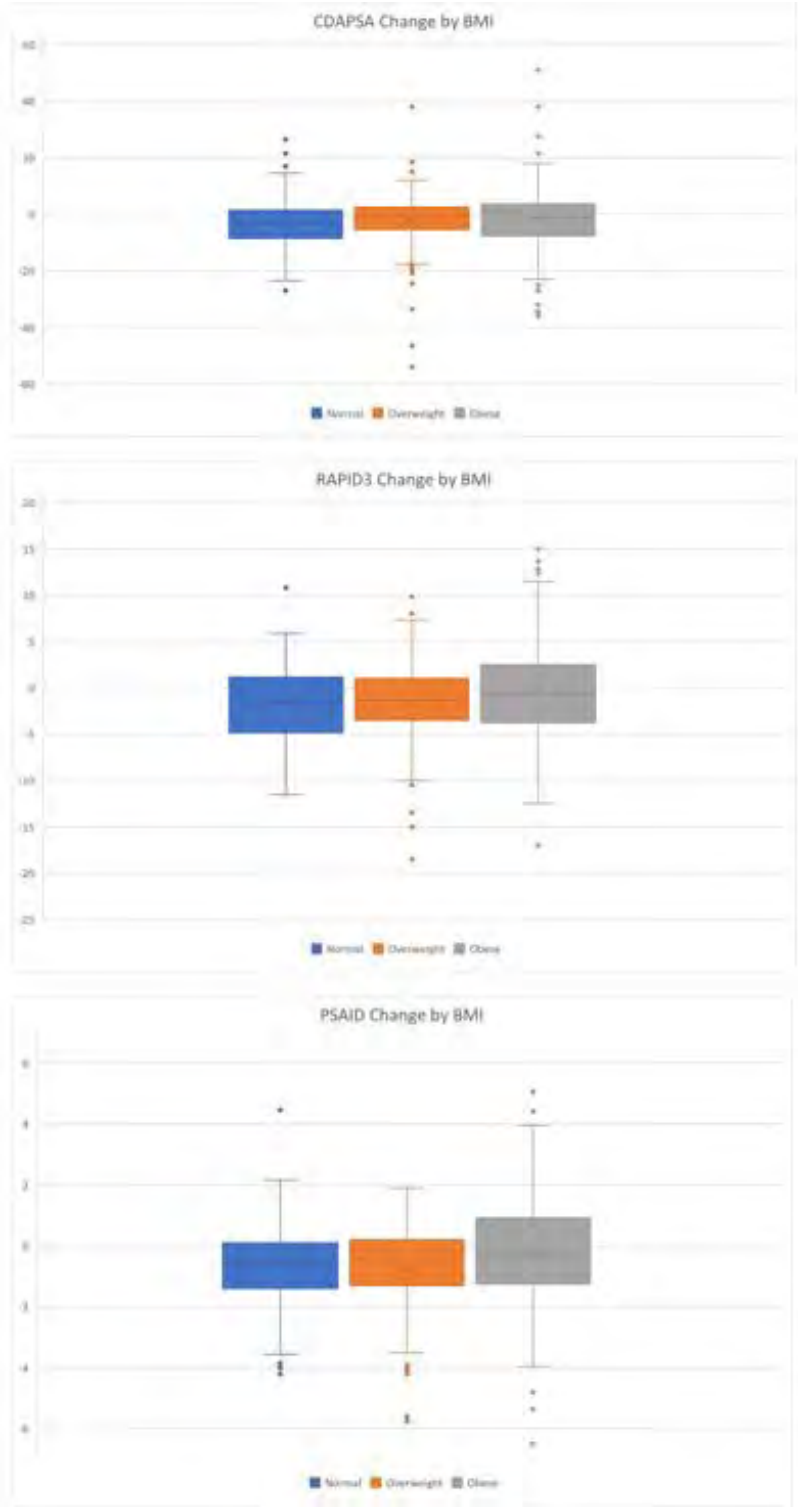

Figure 1. Change in Patient Reported Outcomes by BMI Category. The mean change in cDAPSA was lowest among obese patients (-2.91 (SD 9.56) in normal BMI, -2.29 (SD 11.48) in overweight BMI, and -1.42 (SD 12.33) in obese BMI, p value 0.38). The mean change in RAPID3 was lowest among obese patients (-1.53 (SD 4.50) in normal BMI, -1.69 (SD 4.47) in overweight BMI, and -0.26 (SD 5.46) in obese BMI, p value 0.12). The mean change in PsAID was lowest among obese patients (-0.58 (SD 1.48) in normal weight BMI, -0.72 (SD 1.47) in overweight BMI, and -0.17 (SD 1.98) in obese BMI, p value 0.24).

Table 2. Univariate and Age/Sex Adjusted Linear Regression Analysis. Beta-coefficients are interpreted as the difference in change in the outcome among the overweight group compared to the normal weight group and the obese group compared to the normal weight group. In other words, a beta-coefficient of 1.48 means that the obese group had 1.48 units less improvement than the normal BMI group (as the normal group was negative (improved), the obese group improved less). Abbreviations: TNFi = tumor necrosis factor inhibitor; IL17*i* = interleukin 17 inhibitor; OSM = oral small molecule

Treatment Category	BMI Category	CDAPSA		RAPID3		PSAID	
		Unadjusted	Age/Sex Adjusted	Unadjusted	Age/Sex Adjusted	Unadjusted	Age/Sex Adjusted
Overall	Normal (n=79)	Ref	Ref	Ref	Ref	Ref	Ref
	Overweight (n=99)	0.62 (-2.77-4.00)	0.65 (-2.73-4.03)	-0.16 (-1.61-1.30)	-0.16 (-1.61-1.30)	-0.13 (-0.64-0.37)	-0.14 (-0.64-0.37)
	Obese (n=126)	1.48 (-1.73-4.70)	1.24 (-2.00-4.48)	1.27 (-0.11-2.66)	1.19 (-0.20-2.59)	0.41 (-0.07-0.89)	0.41 (-0.07-0.90)
TNFi	Normal (n=31)	Ref	Ref	Ref	Ref	Ref	Ref
	Overweight (n=47)	-1.58 (-7.59-4.42)	-1.28 (-7.41-4.86)	-0.64 (-3.20-1.91)	-0.50 (-3.09-2.09)	-0.05 (-0.90-0.80)	-0.06 (-0.92-0.81)
	Obese (n=55)	1.31 (-4.52-7.14)	1.13 (-4.77-7.04)	1.55 (-0.93-4.02)	1.48 (-1.01-3.97)	0.74 (-0.09-1.56)	0.75 (-0.08-1.58)
IL17i	Normal (n=12)	Ref	Ref	Ref	Ref	Ref	Ref
	Overweight (n=16)	0.58 (-8.62-9.79)	1.36 (-8.63-11.34)	-0.10 (-3.34-3.14)	-0.52 (-4.01-2.96)	-0.46 (-1.58-0.67)	-0.54 (-1.77-0.69)
	Obese (n=27)	-1.81 (-10.17-6.55)	-0.64 (-9.95-8.67)	0.65 (-2.29-3.59)	0.35 (-2.90-3.60)	0.46 (-0.56-1.48)	0.39 (-0.76-1.53)
OSM	Normal (n=19)	Ref	Ref	Ref	Ref	Ref	Ref
	Overweight (n=40)	-4.28 (-11.04-2.49)	-4.10 (-10.96-2.76)	-1.74 (-4.21-0.72)	-1.54 (4.01-0.92)	-0.41 (-1.25-0.43)	-0.41 (-1.26-0.44)
	Obese (n=42)	-2.75 (-9.47-3.96)	-2.86 (-9.66-3.94)	-1.02 (-3.47-1.42)	-1.07 (-3.52-1.37)	0.12 (-0.71-0.96)	0.16 (-0.68-1.00)

Results: A total of 310 patients were included in the analysis. The mean age of patients was 52 and 56% were female. At baseline, the mean cDAPSA was 17.3 (SD 12.7), the mean PsAID was 3.6 (SD 2.2), the mean RAPID3 was 10.9 (SD 5.8). Baseline scores were overall similar when stratified by BMI category (**Table 1**). The mean change in cDAPSA was lowest among obese patients (-2.91 (SD 9.56) in normal BMI, -2.29 (SD 11.48) in overweight BMI, and -1.42 (SD 12.33) in obese BMI). The mean change in RAPID3 was lowest among obese patients (-1.53 (SD 4.50) in normal BMI, -1.69 (SD 4.47) in overweight BMI, and -0.26 (SD 5.46) in obese BMI). The mean change in PsAID was lowest among obese patients (-0.58 (SD 1.48) in normal weight BMI, -0.72 (SD 1.47) in overweight BMI, and -0.17 (SD 1.98) in obese BMI) (**Figure 1**). These differences were not statistically significant, potentially due to sample size. In unadjusted and age-and-sex adjusted analyses (**Table 2**), compared to the normal BMI category, obese patients had less improvement in cDAPSA, RAPID3 and PsAID. Similar numerical reduction in improvement was also found in the TNFi initiators although there was not a stepwise decrease in improvement with increasing BMI in IL17*i* nor OSM initiators.

Conclusion: The mean change in the selected outcome measures (cDAPSA, RAPID3, PsAID) was lowest among obese patients compared to the other BMI categories. Interestingly, this pattern was observed primarily among TNFi initiators as opposed to OSM or IL17i initiators.

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Abstract Number: 1328

Assessment of Microvascular Involvement in Psoriatic Arthritis by Nailfold Capillaroscopy

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes III: Comorbidities, Extra-muskuloskeletal Manifestations, & Related Conditions (1304–1328)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Capillaroscopy has gained increasing importance in the microvascular assessment of rheumatic diseases (1). Increased cardiovascular risk has been observed in psoriatic arthritis (PsA) (2). Recent data suggest microvascular involvement (3). Few studies have analyzed capillaroscopic anomalies in PsA. No specific capillaroscopic pattern has yet been identified (4-6). Conditions that can affect the nail bed vasculature were not always excluded. The objective of this study was to determine capillaroscopic abnormalities in patients with PsA with no cardiovascular risk factors or other conditions that could interfere with nailfold capillaroscopy results.

Methods: We conducted a cross-sectional study on 13 patients diagnosed with PsA according to CASPAR Classification criteria. We excluded all patients with concomitant cardiovascular risk factors or conditions known to alter the nail bed capillaries including concomitant cardiovascular risk factors, coexistent connective tissue disorder, primary or secondary Raynaud's phenomenon, chronic kidney disease, current malignancy, pregnancy or lactation and vasoactive or anticoagulant therapies. Patient characteristics and disease activity score (DAPSA) were collected. Main outcome was the presence of any capillaroscopic abnormality on nailfold capillaroscopy performed by the same physician. Association with disease duration and activity was tested using Chi Square test for categorical variables and Mann-Whitney U test for continuous variables.

Results: Mean (+/-SD) age was 46 years +/- 13.5, mean disease duration 17 years +/- 15.2; 54.0% were men. None of the patients had distal interphalangeal joint involvement, mean DAPSA score was 23.36 +/- 19.5. 70,0% had cutaneous psoriasis and 54.0% had ungual involvement. All patients had capillaroscopic abnormalities (figure 1). The 3 most common findings were: tortuosity (84.6%, mean of 4 tortuous loops for a density of 8 loops/mm), reduced capillary density (50.0%, mean density of 8 +/- 1 loops/mm) and microhaemorrhages (38.5%). Less frequent findings were perivascular oedema (30.8%), ramifications (15.4%), dilated loops (15.4%), and visibility of subpapillary plexus (15.4%). We a small study population, we were unable to document statistical association between capillaroscopic findings and disease duration ($p < 0.4$) or DAPSA ($p < 0.42$).

Conclusion: PsA patients exhibit capillaroscopic abnormalities characterized by the presence of tortuosity, reduced capillary density and microhaemorrhages, independent from potential conditions that may alter the nailfold capillaries. Larger studies are needed to identify specific capillaroscopic patterns in PsA and to reflect on the prognostic value of our findings.

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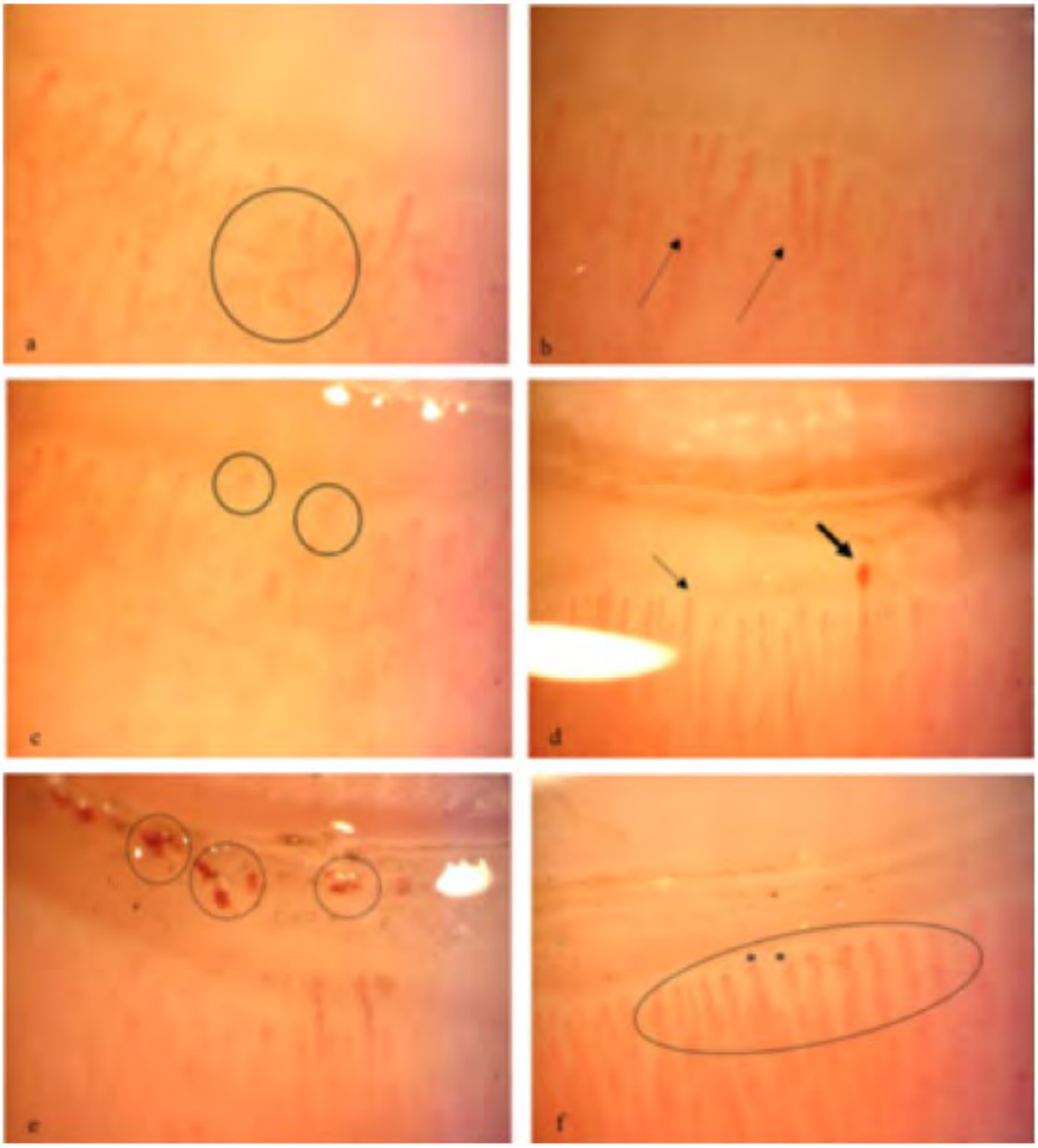

Figure 1. Nailfold capillaroscopic abnormalities in patients with psoriatic arthritis. a) Visibility of subpapillary plexus highlighted in the circled area. b) Long arrows point to tortuous loops. c) Circled areas highlight perivascular edema. d) Bold arrow points to a microhemorrhage. Normal arrow points to a tortuous loop. e) Circled areas highlight multiple microhemorrhages. f) Circled area shows many tortuous loops.

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Abstract Number: 1329

Guselkumab (TREMFYA®) Maintains Resolution of Dactylitis and Enthesitis in Patients with Active Psoriatic Arthritis: Results Through 2 Years from a Phase 3 Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), a selective inhibitor of IL-23, significantly improved the diverse manifestations of active psoriatic arthritis (PsA), including dactylitis and enthesitis, in the DISCOVER (D)-1 & 2 trials of

Table 1. Frequency and severity of dactylitis and enthesitis at baseline

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO	Total
Pts, N	245	248	246	739
Pts with dactylitis, N	121	111	99	331
Pts with enthesitis (+/+)[a,b]	95 (78.5)	82 (73.9)	81 (81.8)	258 (77.9)
Pts with enthesitis LEI score=1[a]	23 (24.7)	22 (26.8)	15 (19.0)	60 (23.6)
Pts with enthesitis LEI score =2[a]	19 (20.4)	23 (28.0)	19 (24.1)	61 (24.0)
Pts with enthesitis LEI score ≥3[a]	51 (54.8)	37 (45.1)	45 (57.0)	133 (52.4)
Pts without dactylitis , N	124	137	146	407
Pts with enthesitis (-/+)[a,b]	75 (60.5)	76 (55.5)	97 (66.4)	248 (60.9)
Pts with enthesitis LEI score =1[a]	18 (24.7)	19 (25.3)	26 (27.1)	63 (25.8)
Pts with enthesitis LEI score =2[a]	19 (26.0)	22 (29.3)	32 (33.3)	73 (29.9)
Pts with enthesitis LEI score ≥3[a]	36 (49.3)	34 (45.3)	38 (39.6)	108 (44.3)
Pts with Enthesitis, N[c]	170	158	178	506
Pts with dactylitis (+/+)[a]	95 (55.9)	82 (51.9)	81 (45.5)	258 (51.0)
Pts without Enthesitis, N	75	90	67	232
Pts with dactylitis (-/+)[a]	26 (34.7)	29 (32.2)	18 (26.9)	73 (31.5)

[a]Data presented as N (%); [b]4 pts with LEI score missing; [c]8 pts with LEI score missing; +/+ represent pts with both enthesitis and dactylitis; -/+ represents pts without dactylitis with enthesitis or pts without enthesitis with dactylitis

Table 2. LS mean change from baseline over time in dactylitis and LEI scores in pts with manifestation at baseline

	GUS 100 mg Q4W	GUS 100 mg Q8W	PBO → GUS 100 mg Q4W
Dactylitis score (0-60)			
Pts, N	121	111	99
Week 24[a]	-5.9 (-6.7, -5.0)	-6.0 (-6.8, -5.1)	-4.0 (-5.0, -3.1)
Week 52[a]	-6.5 (-7.2, -5.8)	-7.2 (-7.9, -6.5)	-6.9 (-7.6, -6.2)
Week 100[a]	-6.5 (-7.1, -5.8)	-7.5 (-8.1, -6.8)	-6.9 (-7.6, -6.2)
LEI Score (1-6)			
Pts, N	170	158	178
Week 24[a]	-1.5 (-1.8, -1.3)	-1.6 (-1.8, -1.4)	-1.0 (-1.3, -0.8)
Week 52[a]	-1.8 (-2.0, -1.6)	-1.9 (-2.1, -1.7)	-2.0 (-2.2, -1.8)
Week 100[a]	-1.9 (-2.1, -1.7)	-2.1 (-2.3, -1.8)	-2.1 (-2.3, -1.9)

[a]Results are LS Mean (95% confidence interval [CI]) change; LS mean change determined by ANCOVA; missing data was imputed as no change for pts who discontinued treatment and using multiple imputation for remaining missing data

patients (pts) with active PsA[1,2], with maintenance of response rates through 1 year.[3,4] Dactylitis and enthesitis, extra-articular manifestations of PsA, can be difficult to treat and cause significant disease burden.[5,6] Here, we evaluated the ability of GUS to provide long-term resolution of dactylitis and enthesitis in pts with PsA through 2 years of D-2.

Methods: D-2 biologic-naïve pts with active PsA were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO). At W24, PBO pts crossed over to GUS Q4W. Independent assessors evaluated dactylitis (total score: 0-60) and enthesitis (Leeds Enthesitis Index [LEI]; total score 0-6). These post-hoc analyses assessed baseline (BL) frequency and severity of enthesitis in pts with dactylitis and dactylitis frequency in pts with enthesitis. Post-baseline, changes in dactylitis and LEI scores over time (least squares [LS] mean changes; analysis of covariance [ANCOVA]) and rates of resolution of dactylitis and enthesitis (Chi square correlation test) were determined among pts with these manifestations at BL (missing data imputed as no change/response).

Results: At BL, more D-2 pts had enthesitis (68%) than dactylitis (45%). At BL 78% of pts with dactylitis vs 61% without dactylitis had enthesitis and 51% of pts with enthesitis vs 32% without enthesitis had dactylitis. Among pts with enthesitis at BL, a higher percentage of total pts with dactylitis had severe enthesitis with LEI score ≥3 (52%) versus pts without dactylitis (44%) (Table 1). Among those with the condition at BL, rates of resolution of dactylitis (57% [Q4W], 64% [Q8W]) and enthesitis (44% [Q4W], 54% [Q8W]) at W24 increased through W52 (dactylitis, 74% [Q4W], 78% [Q8W]; enthesitis, 57% [Q4W], 61% [Q8W]) and were maintained at W100 (dactylitis, 72% [Q4W], 83% [Q8W]; enthesitis, 62% [Q4W], 70% [Q8W]). Consistent results were observed when evaluating mean changes in dactylitis and LEI scores and also in pts who crossed over from PBO to GUS Q4W at W24 (Table 2). In pts with both dactylitis and enthesitis at BL, GUS-treated pts showed significant correlations between resolution of enthesitis and dactylitis at W24 ($p=0.004$), W52 ($p< 0.001$) and W100 ($p=0.039$), with nearly 90% of pts with enthesitis resolution also achieving dactylitis resolution at W52 and W100 (Figure).

Conclusion: Pts with PsA often present with concurrent enthesitis and dactylitis, both of which can be recalcitrant to treatment. GUS resolved enthesitis and dactylitis in substantial proportions of pts through W100. GUS-treated pts who achieved enthesitis resolution were more likely to achieve dactylitis resolution and vice versa.

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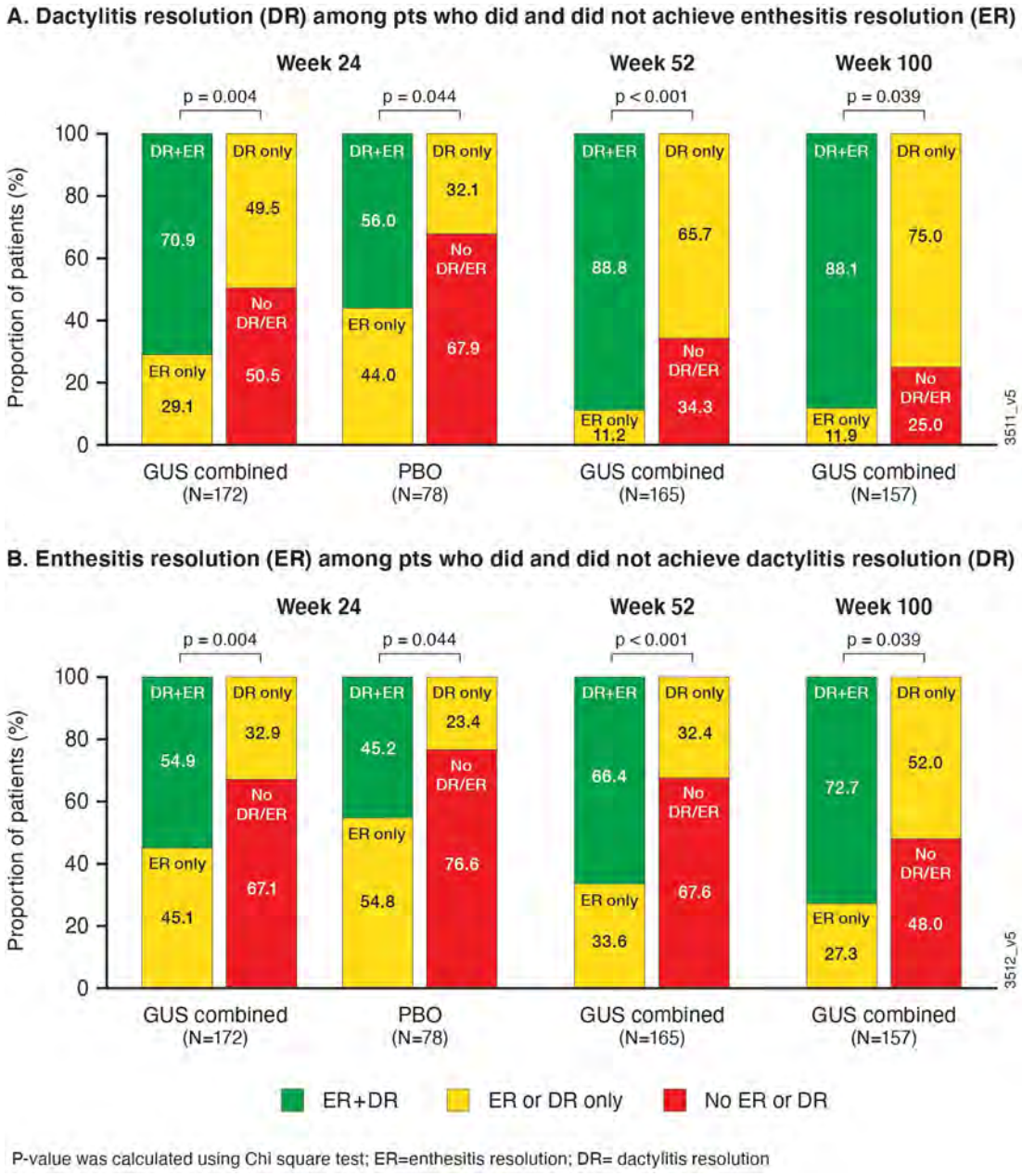

P-value was calculated using Chi square test; ER=enthesitis resolution; DR= dactylitis resolution

Figure. Correlation analysis between resolution of enthesitis and dactylitis over time among pts with enthesitis and dactylitis at baseline.

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Disclosure: P. Rahman, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos,

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Abstract Number: 1330

Effect of Guselkumab (TREMFYA®), a Selective IL-23p19 Inhibitor, on Axial-Related Endpoints in Patients with Active PsA: Results from a Phase 3, Randomized, Double-blind, Placebo-controlled Study Through 2 Years

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), a selective IL-23p19 inhibitor, resulted in greater mean improvements in BASDAI scores vs placebo (PBO) at W24 among patients (pts) with active PsA and investigator-confirmed sacroiliitis in pooled post hoc analyses of data from two phase 3 trials, DISCOVER-1&2. Improvements in these symptoms of axial involvement were maintained through 1 year.[1]We aimed to further assess maintenance of GUS effect on symptoms of axial involvement among biologic-naïve PsA pts with investigator-confirmed sacroiliitis through 2 years of DISCOVER-2.

Methods: In this phase 3, double-blind, PBO-controlled study, 739 bio-naïve pts with active PsA (≥5 swollen joints, ≥5 tender joints, CRP ≥0.6mg/dL despite standard therapies) were randomized 1:1:1 and treated with GUS 100 mg every 4 weeks (Q4W; n=245), GUS 100 mg at W0, W4, then Q8W (n=248), or PBO (n=246), with PBOàGUS 100 mg Q4W at W24. Pts identified by the investigator as having axial symptoms and sacroiliitis (prior X-ray or MRI, or pelvic X-ray at screening) were evaluated. Efficacy was assessed by change in BASDAI, modified BASDAI (mBASDAI, excluding Q3 [peripheral joint pain]), and BASDAI Q2 (Spinal Pain) scores and proportions of pts achieving BASDAI 50 response, Spinal Pain score ≤2, and AS Disease Activity Score (ASDAS) responses through W100. Through W24, pts who met treatment failure criteria or had missing data were considered nonresponders or to have no change from baseline. After W24, missing data were imputed as nonresponse for binary endpoints or no change from baseline for

continuous endpoints (nonresponder imputation [NRI]). Axial-related outcomes were also summarized by HLA-B27 status (+/-) among 149 pts with available data.

Results: 246 pts had sacroiliitis confirmed by the investigator. Baseline characteristics were similar across treatment groups (62% male; mean age 44.4 years); mean BASDAI scores ranged from 6.5-6.6. At W24, LSmean/mean changes in BASDAI (-2.4/-2.6) and ASDAS (-1.3/-1.5) scores were greater in GUS than PBO-treated pts. Mean changes from baseline were maintained through W100 in GUS-treated pts for BASDAI (-3.1), Spinal Pain (-3.1), mBASDAI (-3.1), and ASDAS (-1.7) scores. Similar response patterns were observed for BASDAI 50 response rates among GUS-treated pts (W24 38-40%; W100 49-54%). At W24, GUS-treated pts had higher response rates for achievement of ASDAS inactive disease, major improvement, and clinically important improvement vs. PBO; response rates (NRI) were maintained, or in some cases further increased, at 2 years. Consistent results were observed for achievement of ASDAS LDA and Spinal Pain score ≤2 (data not shown). GUS-related improvements in axial symptoms through W100 were generally consistent across pts who were HLA-B27+/- (data not shown).

Conclusion: In bio-naive pts with active PsA and investigator-confirmed sacroiliitis, GUS provided durable improvements in axial symptoms through W100, with substantial proportions of pts achieving and maintaining clinically meaningful improvements.

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Table. Axial symptom assessments through W100 in PsA pts with investigator-confirmed sacroiliitis in DISCOVER-2 (NRI)

	GUS Q4W N=82	GUS Q8W N=68	PBO→GUS Q4W N=96
Change in BASDAI score			
W24, LS mean (95% CI)	-2.5 (-2.9, -2.0)	-2.4 (-3.0, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.0)	-2.6 (2.4)	-1.4 (2.4)
W52, mean (SD)	-2.9 (2.3)	-2.7 (2.5)	-2.9 (2.6)
W100, mean (SD)	-3.0 (2.3)	-3.1 (2.6)	-3.3 (2.6)
Change in mBASDAI (excludes Q#3) score			
W24, LS mean (95% CI)	-2.4 (-2.9, -1.9)	-2.4 (-2.9, -1.8)	-1.2 (-1.7, -0.7)
Mean (SD)	-2.5 (2.1)	-2.6 (2.5)	-1.3 (2.3)
W52, mean (SD)	-2.7 (2.6)	-2.6 (2.5)	-2.9 (2.4)
W100, mean (SD)	-3.3 (2.6)	-3.1 (2.6)	-3.0 (2.4)
Change in Spinal Pain (BASDAI Q#2) score			
W24, LS mean (95% CI)	-2.2 (-2.7, -1.7)	-2.3 (-2.9, -1.7)	-0.9 (-1.5, -0.4)
Mean (SD)	-2.3 (2.6)	-2.5 (2.8)	-1.1 (2.5)
W52, mean (SD)	-2.6 (2.7)	-2.5 (2.7)	-2.5 (2.7)
W100, mean (SD)	-2.8 (2.7)	-3.1 (2.8)	-3.0 (2.8)
Change in ASDAS score			
W24, LS mean (95% CI)	-1.3 (-1.6, -1.1)	-1.3 (-1.6, -1.1)	-0.6 (-0.8, -0.4)
Mean (SD)	-1.4 (1.0)	-1.5 (1.2)	-0.7 (1.1)
W52, mean (SD)	-1.5 (1.1)	-1.5 (1.3)	-1.5 (1.3)
W100, mean (SD)	-1.6 (1.2)	-1.7 (1.2)	-1.6 (1.2)

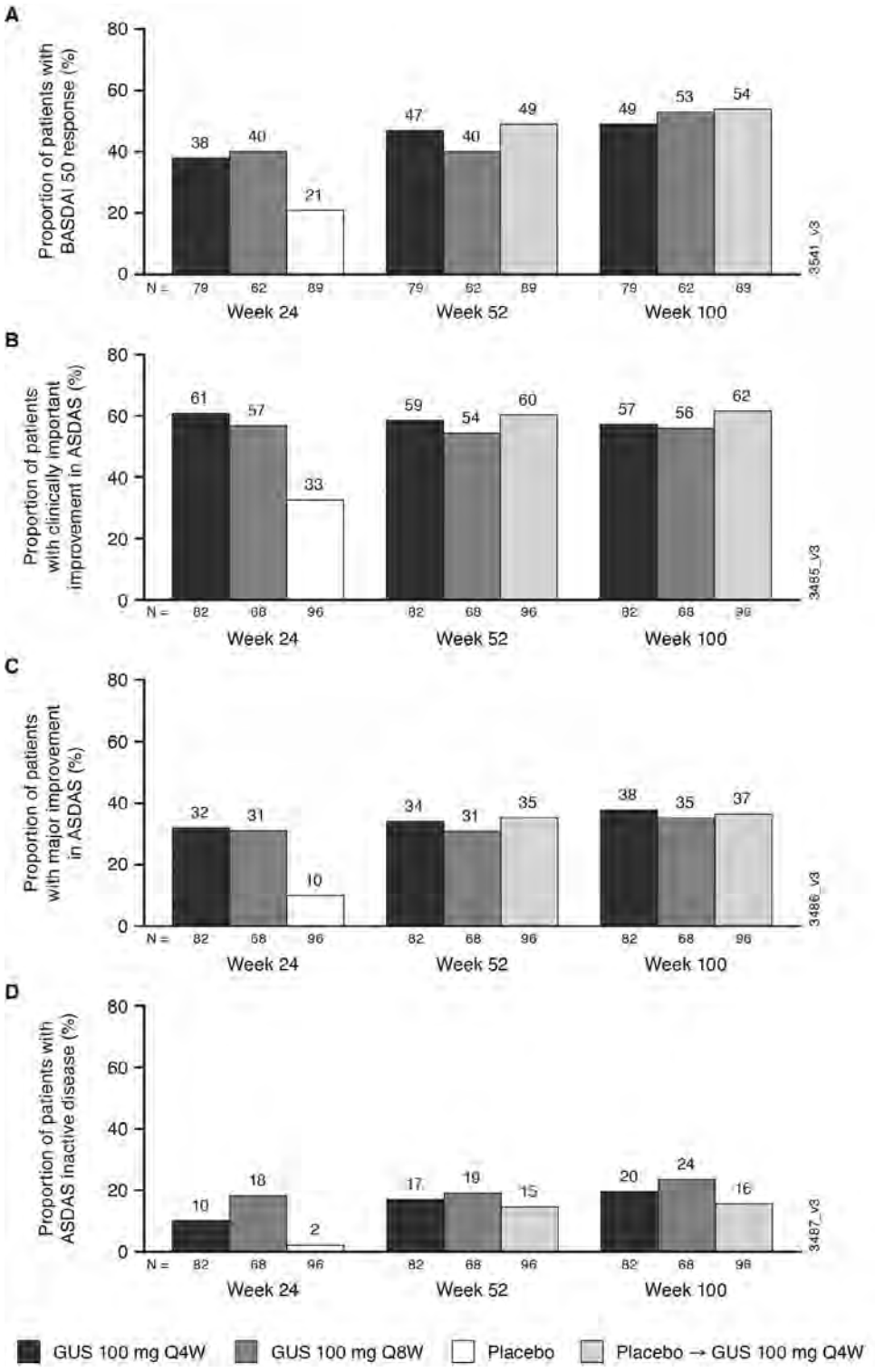

Figure. Proportion of PsA patients with investigator-confirmed sacroiliitis achieving BASDAI 50 response (A), and ASDAS clinically important improvement (decrease ≥1.1) (B), major improvement (decrease ≥2.0) (C), and inactive disease (<1.3) (D) through W100 (NRI).

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Abstract Number: 1331

Guselkumab (TREMFYA®) Improves Anemia in Patients with Active Psoriatic Arthritis: Results from Two Phase 3 Randomized Controlled Clinical Trials

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Anemia related to systemic inflammation can be an important feature of psoriatic arthritis (PsA). Hemoglobin (Hgb) levels have been shown to be inversely related to disease activity in other rheumatic diseases.[1,2] This post hoc analysis assessed the effect of guselkumab (GUS), a selective IL-23p19 inhibitor, on anemia in the pooled Phase 3 DISCOVER-1 & -2 trials.

Methods: 1120 patients (pts) with active PsA, biologic naïve (except ~30% of DISCOVER-1 pts who had received 1-2 TNF inhibitors), were randomized and treated with SC GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or placebo (PBO, with crossover to GUS 100 mg Q4W at W24). Treatment was given for 1 yr (DISCOVER-1) or 2 yrs (DISCOVER-2). Mean Hgb levels and number (%) of pts with anemia (Hgb < 13.5 g/dL males [M]; < 12.0 g/dL females [F]) were assessed by treatment group through 1 yr. A logistic regression model estimated odds ratios (ORs) and 95% CI for achieving anemia resolution (i.e., anemia at baseline [BL] but not W24). The binary endpoint was anemia responder status at W24 (Y/N); predictors examined included age, sex, swollen/tender joint count, and C-reactive protein (CRP).

Results: The analyses included 1074 pts (96% of pooled study population; 564 M and 510 F). At BL, ~24% of M (N=136) and F (N=120) pts were anemic. Pts with anemia at BL had, on average, more swollen & tender joints, systemic inflammation (CRP), and fatigue (assessed via Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] score) than pts without anemia (Table). For both GUS treatment groups, mean Hgb levels increased from BL through W52 for M and F, particularly among pts who were anemic at BL (Fig 1). For PBO pts, mean Hgb levels were unchanged from BL through W24; however, following PBO®GUS switch at W24, they increased to levels similar to GUS-randomized pts at W52 (Fig 1). Consistently, the proportions of M and F meeting criteria for anemia decreased over time (Fig 2), with M exhibiting a more rapid response (data not shown). Pts with anemia at BL but not at W24 (anemia resolution) comprised more M and had shorter duration of PsA and lower CRP levels at BL than pts with unresolved anemia at W24 (Table). Logistic regression analyses confirmed that F (OR [95% CI]: 0.37 [0.21, 0.65]) and pts with higher BL CRP levels (0.53 [0.41,0.69]) were significantly less likely to achieve anemia resolution at W24 than M and pts with lower BL CRP, respectively. Importantly, pts with anemia resolution (N=112) appeared to exhibit better outcomes at W24 than pts with unresolved anemia (N=136), with numerically fewer mean (SD) swollen (4.8 [6.76] vs 6.2 [8.01]) and tender (10.7 [11.07] vs 12.5 (11.89]) joints, less systemic inflammation (CRP 0.8 [0.92] vs 2.3 [2.73]), and less fatigue (FACIT-F 37.4 [10.60] vs 33.0 [10.45]).

Conclusion: In both M and F pts with active PsA, GUS treatment through 1 yr increased Hgb levels and lessened the prevalence of anemia. Anemia resolution with GUS use, which was more likely in M and pts with lower CRP levels at BL, was associated with improved clinical status relative to pts with persistent anemia.

References

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Table. Pt Characteristics by BL Anemia Status and Anemia Responder Status

	Anemia at BL		Anemia Resolution[a]	
	No	Yes	No	Yes
Number of Pts	**818**	**256**	**136**	**112**
Female, %	47.7%	46.9%	52.2%	37.5%
Male, %	52.3%	53.1%	47.8%	62.5%
PsA disease duration (yrs)	5.6 (5.94)	6.4 (5.93)	7.4 (6.92)	5.2 (4.23)
Age (yrs)	46.9 (11.35)	45.5 (12.09)	45.2 (12.01)	45.7 (12.26)
Swollen joint count (0-66)	10.9 (6.75)	13.0 (9.09)	13.2 (8.77)	13.0 (9.77)
Tender joint count (0-68)	19.8 (12.91)	22.4 (13.24)	22.5 (13.11)	22.2 (13.70)
CRP (mg/dL)	1.3 (1.61)	3.2 (3.26)	3.3 (3.21)	3.1 (3.37)
FACIT-F (0-52)	30.4 (9.79)[b]	28.7 (10.09)	27.2 (9.83)	30.7 (10.15)

Reported as mean (SD) unless otherwise stated.
[a]Resolution=anemia at BL and no anemia at W24.
[b]N=817.

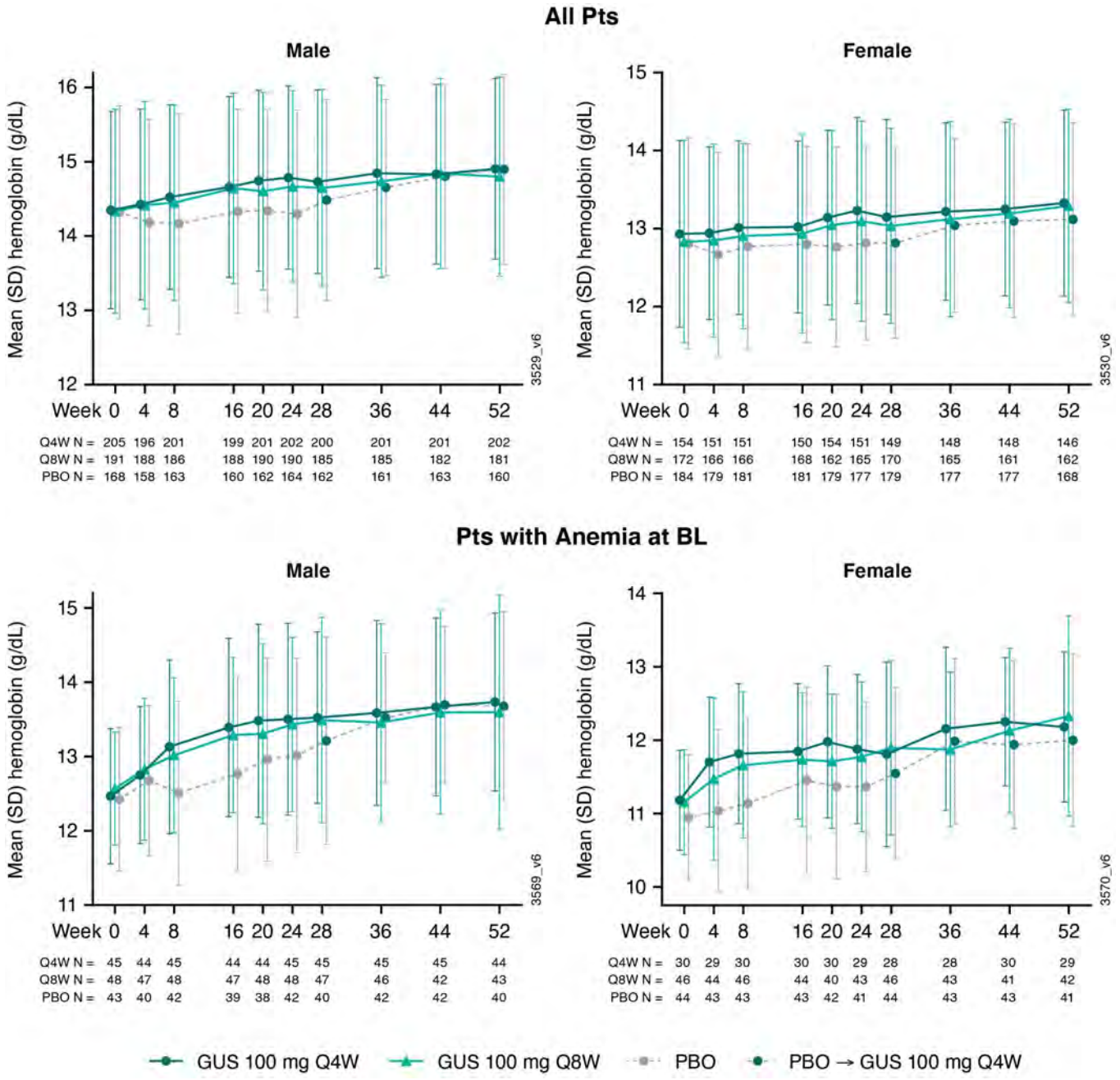

Figure 1. Hgb Levels by Sex Through W52.

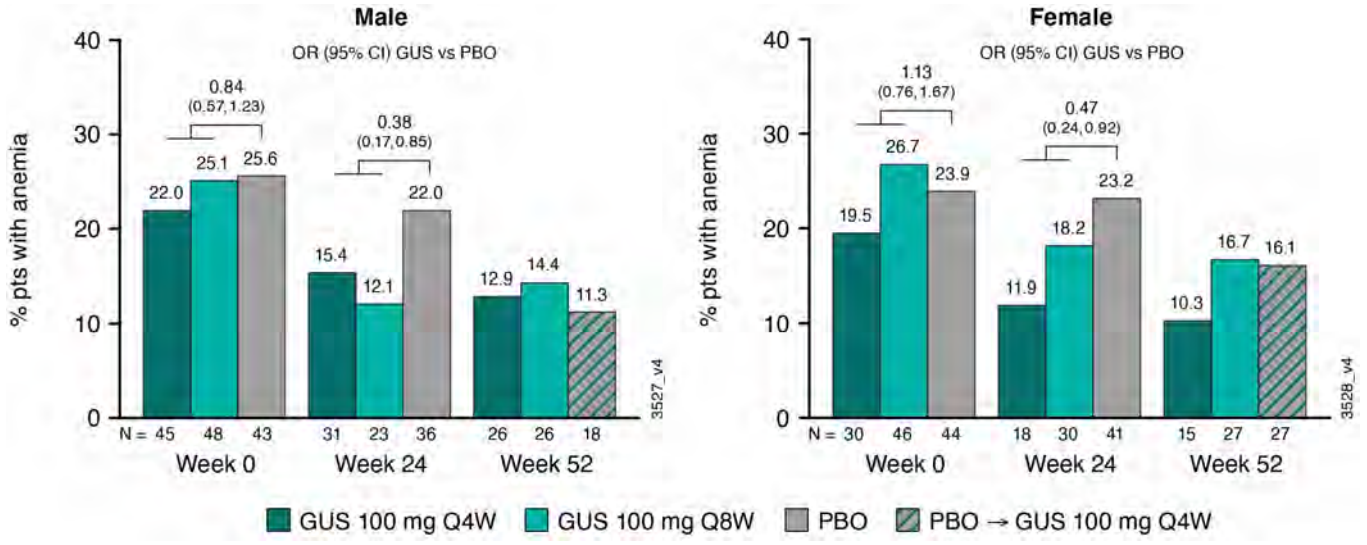

Figure 2. Proportion of Pts With Anemia by Sex and Treatment Group Through W52.

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Abstract Number: 1332

Validation of the PROMIS-29 Profile in Patients with Active Psoriatic Arthritis Using Data from a Phase 3, Randomized, Placebo-Controlled Study Evaluating Guselkumab (TREMFYA®)

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: It is important to assess symptoms of pain, fatigue, anxiety, depression, sleep disturbance, and impaired physical function in patients (pts) with psoriatic arthritis (PsA), as these symptoms are common and can negatively affect health-related quality of life (HRQoL).[1] The Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) Profile is a generic health outcomes instrument that is validated in several general and disease-specific populations[2] but not in PsA. Here we validate PROMIS-29 Profile psychometric properties using data from the global DISCOVER-1 Phase 3 study of guselkumab vs placebo in 381 pts with active PsA (≥3 swollen & ≥3 tender joints; C-reactive protein ≥0.3 mg/dL; 31% had prior TNF inhibitor exposure) and inadequate response to standard therapies.

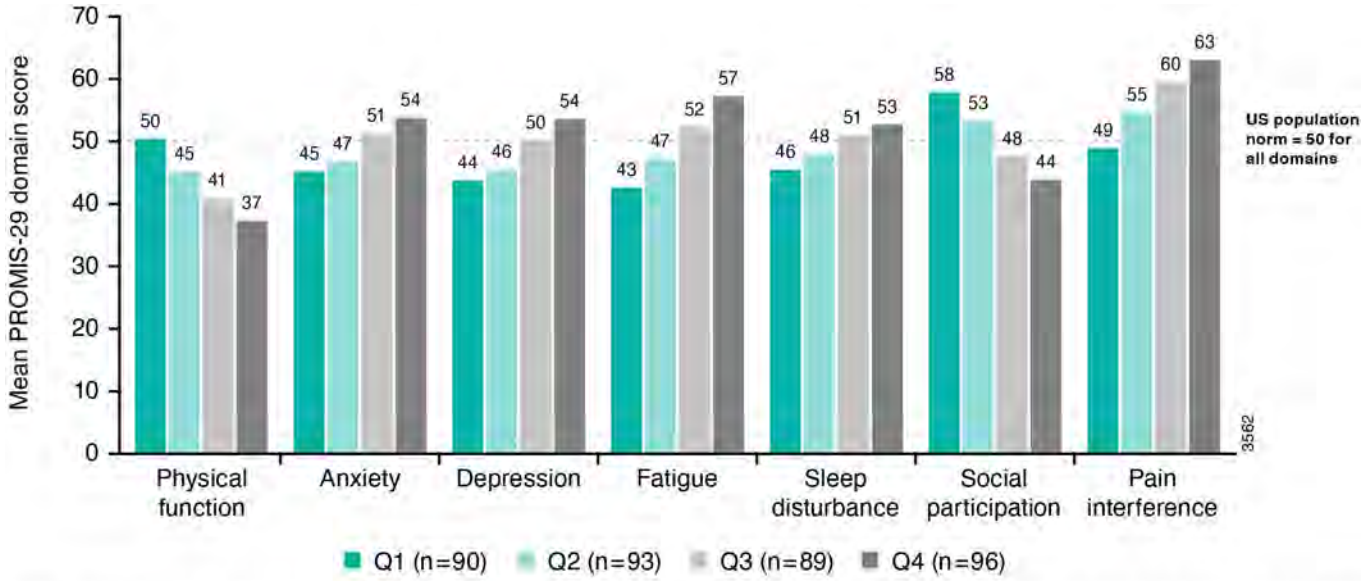
Methods: The PROMIS-29 Profile contains 4 items for each of 7 domains (physical function, anxiety, depression, fatigue, sleep disturbance, social participation, pain interference; 28 items scored on 5-point Likert scale) and 1 pain intensity item (0-10 visual analog scale). Raw scores are converted to standard T-scores, with norms based on a general US population mean=50 and SD=10; changes ≥5 points are considered clinically meaningful. PROMIS-29 validation assessments included convergent and discriminant analyses based on Spearman's correlation (r_s) with 36-item Short Form Health Survey (SF-36) domain scores (r_s < 0.4=weak, 0.4-< 0.6=moderate, 0.6-1.0=strong correlation); known-groups validity of mean T-scores by the anchor variable of Patient Global Assessment Disease (PGAD) quartile scores at Week (W) 24; and test-retest reliability based on intra-class correlation (ICC) between PROMIS-29 scores at baseline/W16/W24 in pts with stable (change within ±10) PGAD (ICC ≥0.7=acceptable). Analyses were conducted using observed data, combining pts across treatment groups.

Results: The strongest correlations (r_s >0.8) between PROMIS-29 and SF-36 domains were observed for concepts that are similar for both instruments (eg, pain interference and pain intensity vs bodily pain; physical function vs physical function; fatigue vs vitality); correlations were weak (r_s < 0.4) for dissimilar domains (Table 1). Mean T-scores across subgroups defined by PGAD quartiles at W24 were significantly different for all PROMIS-29 domains, indicating known-groups validity (Figure). ICCs of test-retest reliability in pts with stable (change within ±10) PGAD at W16

Table 1. Spearman's correlation between PROMIS-29 domains and SF-36 subdomains and component scores

	SF-36 subdomains†								Component scores†	
PROMIS-29 domains*,†	Physical function	Vitality	Bodily pain	Role-physical	Social function	Mental health	Role-emotional	General health	PCS	MCS
Physical function‡	**0.88**	0.66	0.77	0.78	0.67	0.46	0.48	0.55	**0.85**	0.39
Fatigue**	-0.62	**-0.83**	-0.67	-0.67	-0.75	-0.68	-0.57	-0.57	-0.60	-0.68
Pain interference**	-0.79	-0.73	**-0.86**	-0.80	-0.73	-0.55	-0.50	-0.59	**-0.83**	-0.49
Pain intensity**	-0.72	-0.65	**-0.85**	-0.69	-0.59	-0.46	-0.45	-0.55	-0.78	-0.39
Social participation‡	0.72	0.76	0.73	0.76	0.78	0.60	0.58	0.60	0.72	0.59
Anxiety**	-0.33	-0.52	-0.40	-0.40	-0.56	-0.71	-0.66	-0.40	-0.23	-0.72
Depression**	-0.40	-0.59	-0.48	-0.48	-0.62	-0.72	-0.66	-0.49	-0.33	-0.74
Sleep disturbance**	-0.39	-0.61	-0.43	-0.43	-0.47	-0.61	-0.47	-0.42	-0.34	-0.58

*p<0.0001 for all correlations.
†For SF-36, higher score represents better health. For PROMIS-29, higher scores in anxiety, depression, fatigue, sleep disturbance, and pain interference indicate more severe symptoms; higher physical function and social participation scores indicate better health outcomes.
‡Positive values indicate correlations between improvements in each SF-36 subdomain and improved physical function and social participation, respectively, on the PROMIS-29.
**Negative values indicate correlations between improvements in each SF-36 subdomain and less anxiety, depression, fatigue, sleep disturbance, pain interference, and pain intensity, respectively, on the PROMIS-29.
Green=strong correlations (r_s=0.6-1.0); yellow=moderate correlation (r_s=0.4-<0.6); red=weak correlation (r_s<0.4). **Bold**=strongest correlations (r_s=>0.8).
MCS=mental component summary; PCS=physical component summary.



p<0.0001 for all PROMIS-29 domains vs PGAD quartile, indicating lower PGAD scores were associated with better physical function and social participation, and less anxiety, depression, fatigue, sleep disturbance, and pain interference.
PROMIS-29: Lower scores in anxiety, depression, fatigue, pain interference, and sleep disturbance indicate less severe symptoms; higher scores in physical function and social participation indicate better health outcomes. Mean general US population norm score=50 for all domains.
PGAD: 0-100 mm VAS scored from left (excellent) to right (poor); Q1, 0 to ≤18; Q2, 19 to ≤39; Q3, 40 to ≤62; Q4, 63 to 100. Higher PGAD quartiles represent greater disease activity or a worse state of global health.

Figure. Mean PROMIS-29 Domain T-Scores by PGAD Quartile at W24.

Table 2. Test-retest reliability among pts with stable PGAD (change within ±10 points) over time

	Stable PGAD from baseline to W16 (n=108)			Stable PGAD from baseline to W24 (n=100)		
Mean (SD) PROMIS-29 T-scores	**Baseline**	**W16**	**ICC (95% CI)**	**Baseline**	**W24**	**ICC (95% CI)**
Physical function	39.9 (6.8)	39.8 (6.6)	0.85 (0.79, 0.89)	40.6 (7.2)	40.3 (7.5)	0.83 (0.75, 0.88)
Anxiety	50.7 (9.1)	50.4 (8.9)	0.66 (0.55, 0.76)	52.3 (9.8)	52.7 (10.4)	0.66 (0.54, 0.76)
Depression	49.7 (8.4)	50.1 (8.4)	0.73 (0.63, 0.81)	51.0 (9.0)	52.1 (9.6)	0.68 (0.56, 0.77)
Fatigue	53.3 (9.5)	52.3 (9.3)	0.79 (0.71, 0.85)	54.0 (9.9)	54.5 (11.1)	0.75 (0.65, 0.82)
Sleep disturbance	51.5 (6.9)	50.1 (7.8)	0.68 (0.58, 0.78)	53.6 (7.0)	52.2 (8.1)	0.70 (0.60, 0.79)
Social participation	47.1 (8.7)	47.6 (8.1)	0.62 (0.50, 0.73)	47.0 (8.3)	46.5 (8.3)	0.67 (0.55, 0.77)
Pain interference	60.8 (6.2)	59.9 (6.4)	0.83 (0.77, 0.88)	60.7 (6.8)	60.4 (7.1)	0.84 (0.78, 0.89)
Pain intensity (0-10 VAS)	6.17 (1.8)	6.01 (1.9)	0.79 (0.71, 0.85)	6.21 (1.9)	6.08 (2.0)	0.75 (0.66, 0.83)

Intra-class correlation ≥0.7=acceptable.
CI, confidence interval; VAS, visual analog scale.

and W24 were generally ≥0.7, indicating PROMIS-29 results are reproducible when no change has occurred (Table 2). Mean (SD) PROMIS-29 T-score changes from baseline to W24 were sensitive to PGAD changes in disease severity. In pts with PGAD improvements of 21-30 and 31-40 points, respectively, absolute mean changes across PROMIS-29 domains ranged from 2.7 (anxiety) to 5.4 (pain interference) and 3.1 (sleep disturbance) to 6.6 (pain interference), respectively, from baseline to W24.

Conclusion: This analysis confirms the reliability and validity of the PROMIS-29 Profile to assess HRQoL in pts with active PsA, as well as the responsiveness of this instrument for detecting change.

References

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Disclosure: A. Orbai, AbbVie, 5, Eli Lilly, 2, 5, Celgene, 5, Novartis, 2, 5, Janssen, 2, 5, Horizon, 5, Pfizer, 2, UCB, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Neuhold**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Liu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Liu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11.

Abstract Number: 1333

Guselkumab (TREMFYA®) Provides Consistent and Durable Pain Improvement in Patients with Active Psoriatic Arthritis: Results of 2 Phase 3, Randomized, Controlled Clinical Trials

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), a targeted inhibitor of IL-23p19, demonstrated significant efficacy v placebo (PBO) in achieving ACR20 response at week (W) 24 in patients (pts) with active PsA in 2 Phase 3 trials, DISCOVER-1 & 2.[1,2] Pts with PsA report pain relief as a priority for treatment.[3] We conducted post hoc analyses to further assess GUS effect on pt-reported pain across outcome measures and maintenance of pain relief with up to 2 years (yr) of GUS.

Methods: DISCOVER-1 (1 yr) included 381 pts with active PsA despite standard therapies, including 1-2 TNF inhibitors in 31% of pts. DISCOVER-2 (2 yr) included 739 biologic-naïve pts with active PsA. In both studies, pts were randomized (1:1:1) to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W at W24 (PBO→Q4W). Pts rated pain using a 0-10 VAS (Pt Pain) as part of ACR, Disease Activity in Psoriatic Arthritis, and Minimal Disease Activity response criteria and reported Bodily Pain intensity over the past 4 W via the 36-Item Short-Form Health Survey (SF-36) question 21 (0-5). Pts with spondylitis and peripheral arthritis at

Table 1. Observed Mean (SD) Change from Baseline in Pain Scores, TJC, and SJC at W24, W52, and W100 in DISCOVER-2

	W24			W52			W100		
	GUS Q4W	GUS Q8W	PBO	GUS Q4W	GUS Q8W	PBO→Q4W	GUS Q4W	GUS Q8W	PBO→Q4W
Pt Pain (0-10),* N	240	243	243	229	234	231	220	224	215
	-2.39 (2.35)	-2.53 (2.47)	-1.08 (2.42)	-2.89 (2.68)	-3.20 (2.56)	-2.75 (2.66)	-3.52 (2.62)	-3.69 (2.63)	-3.41 (2.58)
Spinal Pain (0-10),† N	80	65	92	79	64	88	76	61	82
	-2.26 (2.57)	-2.54 (2.70)	-1.13 (2.48)	-2.74 (2.63)	-2.67 (2.71)	-2.65 (2.69)	-3.11 (2.67)	-3.44 (2.71)	-3.37 (2.66)
Joint Pain (0-10),* N	80	65	92	79	64	88	76	61	82
	-2.88 (2.17)	-2.90 (2.68)	-1.40 (2.91)	-3.32 (2.27)	-3.21 (2.76)	-3.42 (2.92)	-3.54 (2.35)	-3.61 (2.77)	-3.80 (2.95)
SF-36 (Q21; 0-5), N	240	243	242	229	234	230	220	224	214
	-0.99 (1.03)	-1.03 (1.12)	-0.50 (1.11)	-1.18 (1.33)	-1.29 (1.17)	-1.10 (1.16)	-1.39 (1.25)	-1.47 (1.38)	-1.36 (1.27)
TJC (0-68), N	240	243	243	228	234	231	220	224	213
	-11.85 (9.88)	-10.37 (9.49)	-7.26 (11.15)	-15.04 (10.51)	-13.44 (10.03)	-14.15 (11.39)	-16.37 (10.70)	-15.27 (11.10)	-16.29 (11.27)
SJC (0-66), N	240	243	243	228	234	231	220	224	213
	-8.77 (5.46)	-8.14 (6.07)	-6.44 (7.20)	-10.38 (6.17)	-9.56 (6.28)	-10.17 (6.79)	-10.83 (6.66)	-10.20 (6.88)	-10.58 (6.15)

ACR=American College of Rheumatology; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; DAPSA=Disease Activity in Psoriatic Arthritis; GUS=guselkumab; MDA=minimal disease activity; PBO=placebo; pt=patient; Q=question; QxW=every x weeks; SD=standard deviation; SF-36=36-Item Short-Form Survey; SJC=swollen joint count; TJC=tender joint count; VAS=visual analog scale; W=week

*ACR, DAPSA, MDA: VAS 0-10; †BASDAI: VAS 0-10

baseline (BL) rated their Spinal and Joint Pain (0-10) as part of BASDAI. Pain data were evaluated for observed mean change, percent improvement from BL, and proportion of pts achieving ≥20% or ≥50% improvement in Pt Pain (non-responder imputation [NRI]). Percent improvement from BL in tender (TJC; 0-68) and swollen (SJC; 0-66) joint counts, determined by independent assessors, was determined to evaluate consistency of improvements in pt-reported v physician-derived pain measures.

Results: In DISCOVER-2, mean BL Bodily Pain (range across groups: 4.4-4.5), Pt Pain (6.2-6.3), Spinal Pain (6.5-6.7), Joint Pain (6.3-6.8), SJC (11.7-12.9) & TJC (19.8-22.4) indicated moderate pain and disease activity at study outset. GUS-treated pts reported ~2x the improvement in Pt Pain, Spinal Pain, Joint Pain & Bodily Pain intensity at W24 v PBO; GUS improvements were maintained or further increased at W52 & W100. PBO→Q4W pts had similar improvements in pain as GUS-randomized pts (Table 1, Figure). Pt-reported pain appeared more sensitive to treatment effect, with larger differences in percent improvement v PBO, than physician-reported TJC/SJC at W24 (Figure); further research is warranted. While patterns were consistent, pain improved to a lesser degree than TJC/SJC, suggesting other causative factors. Consistent results were seen in DISCOVER-1 through 1 yr (data not shown). Among 748 GUS-treated pts across DISCOVER-1 & 2, substantial proportions achieved meaningful improvement in Pt Pain at early time points: 32% (W4) and 48% (W8) achieved ≥20% improvement; 28% (W12) and 33% (W16) achieved ≥50% improvement. At W24, 63% and 39% reported ≥20% and ≥50% pain improvement (Table 2).

Conclusion: GUS provided consistent and durable improvements in pt-reported pain across several measures. Pt-reported pain as an early and sensitive indicator of treatment effect in pts with active PsA and other factors underlying pain merit further evaluation.

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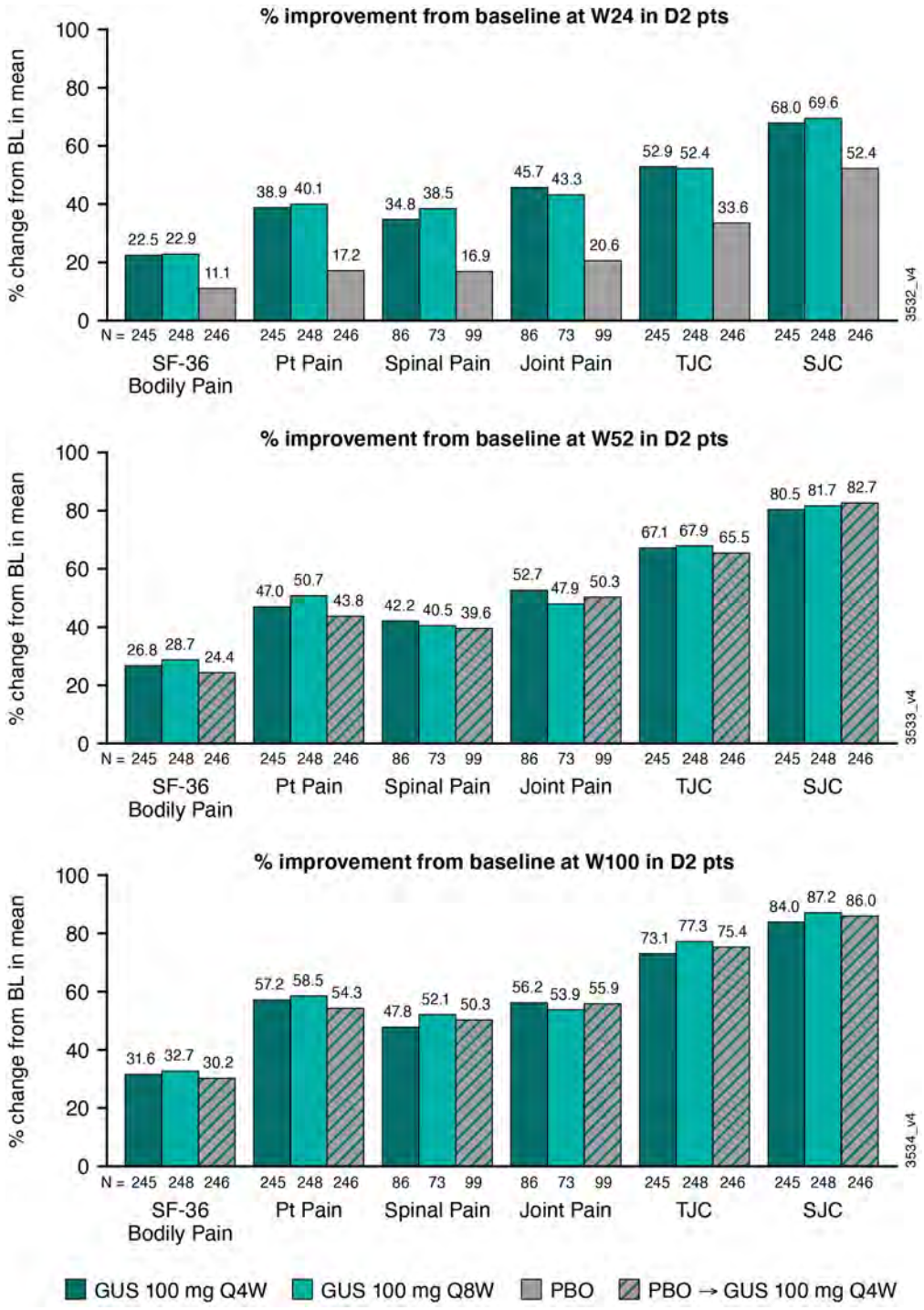

Figure. Percent Improvement from Baseline in Pt-Reported Pain Scores and Physician-Reported TJC and SJC in DISCOVER-2 Pts.

Table 2. Proportion of Guselkumab (Q4W+Q8W) Randomized Pts Pooled Across DISCOVER-1 & 2 (N=748) Reporting ≥20% or ≥50% Improvement in Pt Pain Through W24 (NRI)

	W4	W8	W12	W16	W20	W24
≥20% Improvement in Pt Pain, %	32.4	47.9	54.7	57.8	61.4	63.4
≥50% Improvement in Pt Pain, %	10.4	19.3	28.1	32.6	36.5	39.2
NRI=nonresponder imputation; pt=patient; QxW=every x weeks; W=week						

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Abstract Number: 1334

How Does Gender Affect Secukinumab Treatment Outcomes and Retention Rates in Patients with Psoriatic Arthritis? – Real World Data from a German Observational Study

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SESSION INFORMATION

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Background/Purpose: Gender disparities in PsA can affect natural course of disease, clinical presentation and response to medication[1]. The German non-interventional study AQUILA provides real-world data on the influence of gender of patients with psoriatic arthritis (PsA) on therapeutic effectiveness and retention rate under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A.The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate secukinumab treatment outcomes on disease activity, depressive mood and retention rate depending on the gender of PsA patients.

Methods: AQUILA is an ongoing, multi-center study including more than 3000 patients with active PsA or ankylosing spondylitis. Patients were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. Data was collected on impact of disease (Psoriatic Arthritis Impact of Disease - 12 items, PsAID-12 score), skin disease activity (Psoriasis Area and Severity Index, PASI), joint counts and severity of depressive mood (Beck´s Depression Inventory version II, BDI-II), in addition to patient´s global assessment (PGA). Moreo-

Table 1. Overview of baseline characteristics in PsA patients depending on gender

Demographics*	Male (N=531)	Female (N=747)
Age, years	51.9 (11.6)	53.1 (11.2)
BMI, kg/m²	29.1 (4.9)	29.0 (6.4)
BMI >25 to ≤30 kg/m², n (%)	219 (42.8)	211 (29.5)
BMI >30 kg/m², n (%)	188 (36.7)	285 (39.8)
Smoker, n (%)	103 (19.4)	196 (26.2)
PsAID-12	4.8 (2.2)	5.3 (2.2)
PGA	4.9 (2.6)	5.6 (2.4)
PASI	6.8 (9.8)	7.0 (11.1)
Tender joint counts	6.8 (7.9)	7.3 (7.4)
Swollen joint counts	3.7 (5.3)	3.7 (5.0)
BDI-II	10.2 (8.8)	13.0 (9.4)
Medication prior to secukinumab initiation, n (%):		
NSAID	290 (54.6)	467 (62.5)
csDMARD	460 (86.6)	678 (90.8)
b-bsDMARD	299 (56.3)	477 (63.9)
*variables given as mean (SD)		

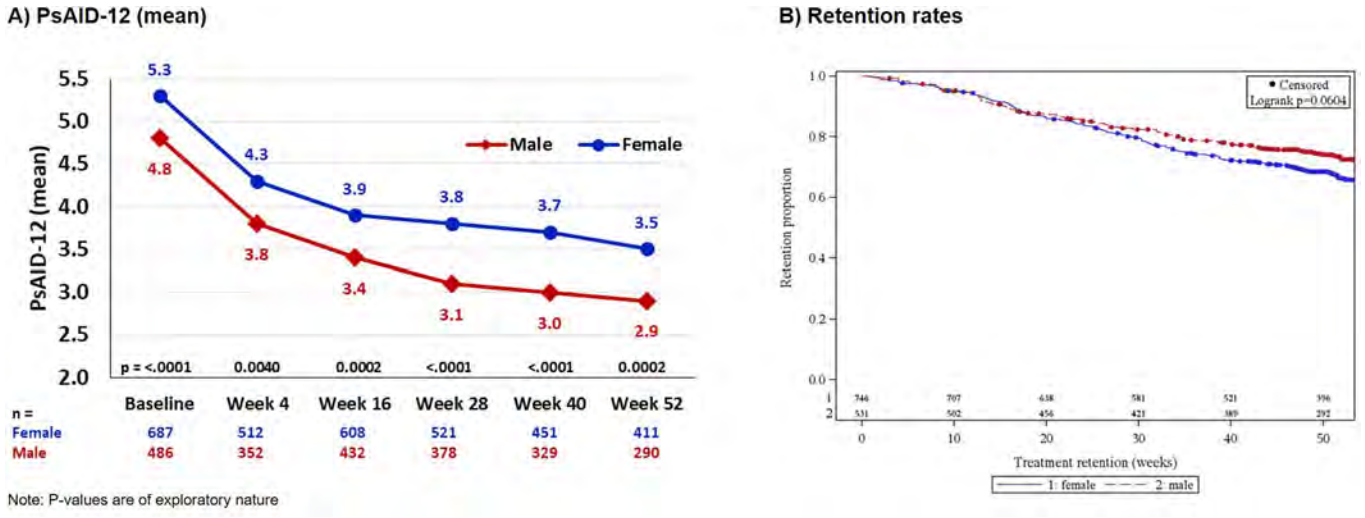

Figure 1. Impact of disease and treatment retention in PsA patients stratified by gender.

ver, retention rates (time from study inclusion until premature secukinumab treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on the subgroups of male and female PsA patients.

Results: At BL, 1278 PsA patients were included: 41.5% (n=531) male and 58.5% (n=747) female. Demographic data (Table 1) of male and female PsA patients differed most obviously regarding proportion of overweight patients, smokers, pretreatment with nonsteroidal anti-inflammatory drugs (NSAIDs) and biologicals/biosimilars (b-bsDMARDs).

Mean PsAID-12 values over time were higher in women; nevertheless, PsAID-12 improved comparably for both genders from BL to week 52 (♂: 4.8 at BL to 2.9 at w52, ♀: 5.3 at BL to 3.5 at w52, Figure 1A). This was similar to the course of improvements for mean PGA across genders (♂: 4.9 at BL to 3.0 at w52, ♀: 5.6 at BL to 3.5 at w52). In terms of PASI scores, both BL mean values and improvements over time were similar across genders (♂: 6.8 at BL to 1.9 at w52, ♀: 7.0 at BL to 1.0 at w52). Mean joint counts (tender/swollen) also improved similarly (♂: 6.8/3.7 at BL to 3.1/0.9 at w52, ♀: 7.3/3.7 at BL to 2.8/0.9 at w52). Over time, male patients showed overall reduced BDI-II values;

nevertheless, BDI-II reductions were comparable across the genders (♂: 10.2 at BL to 8.1 at w52, ♀: 13.0 at BL to 10.6 at w52). Secukinumab treatment retention rate for men was (not significantly) higher than for women (Figure 1B).

Conclusion: In a real-world setting, secukinumab improved disease activity and depressive mood of PsA patients in both men and women. Women showed overall higher burden of disease. Altogether, this interim analysis shows that secukinumab is an effective treatment up to 52 weeks with high treatment retention rates in real-world setting, irrespective of gender.

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Brandt-Jrgens**, Abbvie, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, Novartis, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, UCB, 2, 6, BMS, 2, 6, Janssen, 2, 6, Medac, 2, 6; **P. Kästner**, Chugai, 2, Novartis, 2; **E. Riechers**, AbbVie, 2, 5, Chugai, 2, 5, Eli Lilly, 5, Janssen, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 5, UCB, 2, 5; **D. Peterlik**, Novartis, 3; **H. Tony**, AbbVie, 2, Astra-Zeneca, 2, BMS, 2, Chugai, 2, Janssen, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, Roche, 2, Sanofi, 2.

Abstract Number: 1335

Guselkumab Provides Sustained Domain-Specific and Comprehensive Efficacy as Assessed Using Composite Endpoints in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS) is a human monoclonal antibody specific to the p19-subunit of interleukin-23. GUS significantly improved signs and symptoms of PsA through Week 24, and improvements were maintained through Week 52 in the phase 3 DISCOVER-1[1] and DISCOVER-2[2] studies. This study assessed GUS efficacy through Week 52 in DISCOVER-1&-2 using composite indices.

Methods: Adult patients enrolled had active PsA despite standard therapies. Patients in DISCOVER-1 had ≥3 swollen and ≥3 tender joints and C-reactive protein (CRP) ≥0.3 mg/dL; in DISCOVER-2, patients had ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. 31% of DISCOVER-1 patients received 1-2 prior tumor necrosis factor inhibitors; DISCOVER-2 patients were biologic-naïve. Patients were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week 0, Week 4, then every 8 weeks (Q8W); or placebo (PBO); PBO patients crossed over to GUS 100 mg Q4W at Week 24. Composite endpoints pooled across the two studies were: Disease Activity Index for Pso-

Table. Pooled response rates for DISCOVER-1 and DISCOVER-2 randomized and treated patients.

	DISCOVER-1&2		
	GUS Q4W	GUS Q8W	PBO --> GUS Q4W[1]
Randomized and treated patients, n	373	375	372
PASDAS[2] LDA			
Wk 24	27.9%**	30.1%**	8.9%
Wk 52	45.3%	41.9%	36.8%
MDA[3]			
Wk 24	22.8%**	24.3%**	7.8%
Wk 52	35.9%	30.7%	28.2%
DAPSA[4] Remission			
Wk 24	10.2%**	8.3%**	2.2%
Wk 52	18.2%	17.6%	11.0%
VLDA[3]			
Wk 24	27.9%**	30.1%**	8.9%
Wk 52	45.3%	41.9%	36.8%

Data reported as proportions of patients, %. Unadjusted p values at Wk24 vs PBO: *p<0.05; **p<0.001.

[1] Patients randomized to PBO crossed over to GUS Q4W at Wk24.

[2] PASDAS is derived from Pt global assessment of arthritis and psoriasis (0-100), Physician global assessment (0-100), swollen joint count (0-66), tender joint count (0-68), CRP (mg/L), Leeds enthesitis index score, tender dactylitis count, and the 36-item Short-Form Health Survey Physical Component Summary score. PASDAS LDA ≤3.2.

[3] MDA is 5/7 criteria met; VLDA is 7/7 criteria met: tender joint count ≤1, swollen joint count ≤1, Psoriasis Activity and Severity Index ≤1, Pt assessment of pain ≤15 (0-100), Pt global assessment of disease activity ≤20 (0-100), Health Assessment Questionnaire-Disability Index score ≤0.5, Tender entheseal points ≤1.

[4] DAPSA Remission: score ≤4 (definition in figure legend).

CRP, C-reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; GUS, guselkumab; MDA, Minimal Disease Activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; Pt, patient; Q4W, every 4 weeks; Q8W, every 8 weeks; VLDA, Very Low Disease Activity; Wk, week.

riatic Arthritis (DAPSA), Psoriatic Arthritis Disease Activity Score (PASDAS), Minimal Disease Activity (MDA), and Very Low Disease Activity (VLDA). GUS versus PBO comparisons through Week 24 employed a Cochran-Mantel-Haenszel test with baseline stratification factors or Fisher's exact test; no treatment group comparisons were performed beyond Week 24. P-values were not adjusted for multiplicity. From Week 24 -Week 52, patients with missing data were considered nonresponders (>90% of patients completed study treatment through Week 52).

Results: In randomized and treated patients from DISCOVER-1 (N=381) and DISCOVER-2 (N=739), pooled baseline characteristics were generally well-balanced across treatment groups and reflected active disease. Differences in response rates between GUS Q4W or Q8W and PBO were seen as early as Week 8 and increased over time through Week 24. In patients continuing GUS Q4W or Q8W, respectively, post-Week 24 response rates associated with these composite indices continued to increase through Week 52, at which time they were 54.2% and 52.5% for DAPSA LDA, 45.3% and 41.9% for PASDAS LDA, 35.9% and 30.7% for MDA, 18.2% and 17.6% for DAPSA remission, and 13.1% and 14.4% for VLDA, with no discernable difference between the GUS Q4W and Q8W dosing regimens (Table and Fig). After PBO patients crossed over to GUS Q4W at Week 24, response rates increased through Week 52.

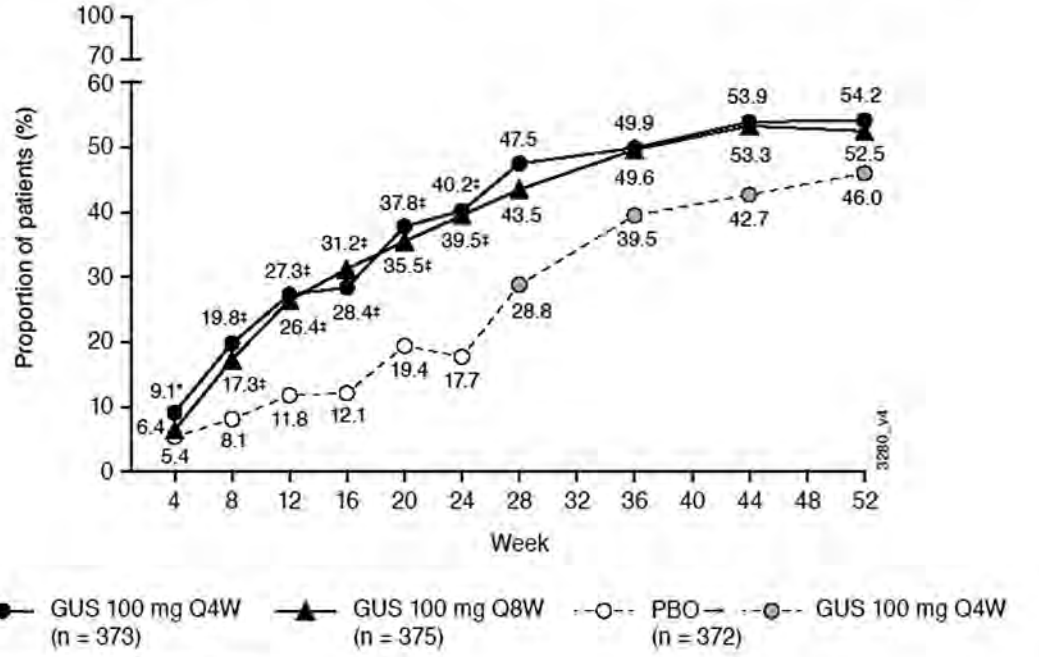
Conclusion: GUS 100 mg Q4W and Q8W provided robust and sustained benefits to patients with active PsA across multiple domains, indicating that GUS may provide an alternative treatment option for the diverse manifestations of PsA.

References

[1]Ritchlin CT, et al. *RMD Open*. 2021;7(1):e001457

[2]McInnes IB, et al. *Arthritis Rheumatol*. 2021;73(4):604-616

Figure. Proportions of Pooled DISCOVER-1 and DISCOVER-2 Patients Achieving DAPSA LDA[a] Through Week 52.



Missing data imputed as nonresponse.

*, +, ‡ $p < 0.05$. 0.01, 0.001, respectively, vs placebo. Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

[a] The DAPSA score is derived from tender joint count (0–68), swollen joint count (0–66), CRP (mg/dL), patient assessment of pain (0–10 cm VAS), and patient global assessment of disease activity (arthritis, 0–10 cm VAS). DAPSA LDA: ≤14. DAPSA Remission: ≤4.

DAPSA, Disease Activity Index for Psoriatic Arthritis; GUS, guselkumab; LDA, Low Disease Activity; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks

Disclosure: L. Coates, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **L. Gossec**, Galapagos, 5, Sandoz, 5, Sanofi, 5, AbbVie, 2, Amgen, 2, 5, Bristol Myers Squibb, 2, Biogen, 2, Celgene, 2, Eli Lilly, 2, 5, Gilead, 2, Janssen, 2, 5, Novartis, 2, Pfizer, 2, 5, Samsung Bioepis, 2, Sanofi-Aventis, 2, UCB, 2; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Karyekar**, Janssen Global Services, LLC, 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Noel**, Janssen Global Services, LLC, 3, 12, Owns stock in Johnson & Johnson; **Y. Jiang**, Cytel, Inc., providing statistical support (funded by Janssen), 3; **S. Sheng**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Wang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1336

Efficacy and Safety of Guselkumab, a Monoclonal Antibody Specific to the p19-Subunit of Interleukin-23, Through 2 Years: Results from a Phase 3, Randomized, Double-blind, Placebo-controlled Study Conducted in Biologic-naïve Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), an anti-IL-23p19-subunit mAb dosed every 4 or 8 weeks (Q4W or Q8W), demonstrated efficacy for joint and skin symptoms, inhibition of structural damage progression (Q4W), and safety vs placebo (PBO) through Week (W) 24 of phase 3, double-blind, PBO-controlled trial in biologic-naïve patients with PsA (DISCOVER-2).[1] Favorable benefit-risk was also seen through 1 year.[2] This study assessed GUS efficacy and safety through 2 years.

Methods: Biologic-naïve adults with active PsA (≥5 swollen joint count [SJC] + ≥5 tender joint count [TJC]; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24. Clinical efficacy (ACR/PASI/IGA/HAQ-DI) was assessed in the modified intention to treat (mITT) population through W100 with missing data imputation (nonresponse for categorical endpoints; no change/multiple imputation for continuous endpoints). Observed PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52, W100 (or at discontinuation [d/c]) and adverse events (AEs) through W112 were collected.

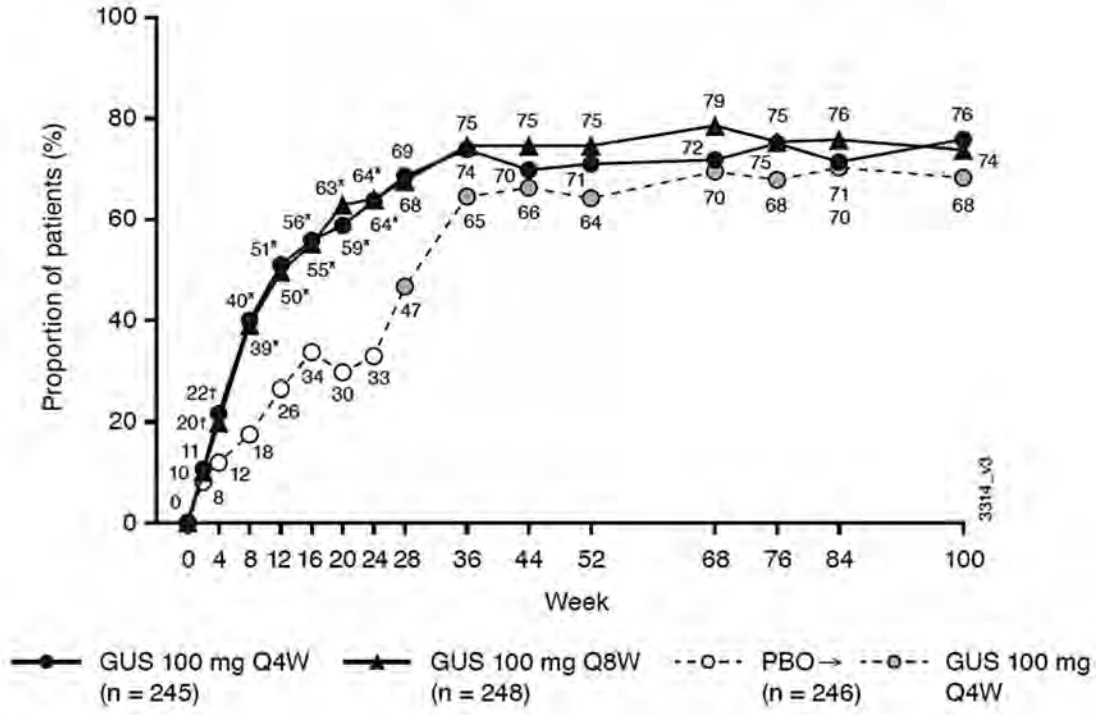
Table: Efficacy Through W100 (NRI)

Data are %	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
	W24	W52	W100	W24	W52	W100	W24	W52	W100
Analysis set, n	245			248			246		
ACR 50	33	46	56	32	48	55	14	41	48
ACR 70	13	26	35	19	28	36	4	18	30
BL HAQ-DI ≥0.35, n	228			228			236		
Improvement ≥0.35[a]	56	59	63	50	58	64	31	48	56
BL ≥3% BSA psoriasis + IGA ≥2, n	184			176			183		
IGA0/1	69	80	76	71	74	72	19	79	77
PASI75	78	87	83	79	86	82	23	83	80
PASI90	61	77	74	69	74	70	10	72	77
PASI100	45	58	59	46	53	53	3	52	61

[a]≥0.35 improvement among patients with HAQ-DI ≥0.35 at baseline

ACR, American College of Rheumatology; BL, Baseline; BSA, body surface area; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire Disability Index; IGA, Investigator Global Assessment; NRI, nonresponder imputation; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week.

Figure. ACR 20 Response Through W100 (NRI)
(Note: Patients randomized to PBO crossed over to GUS 100 mg Q4W at W24)



*p ≤ 0.001; †p < 0.05

ACR, American College of Rheumatology; GUS, guselkumab; NRI, nonresponder imputation; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week.

Results: 712/739 (96%) randomized patients continued study agent at W24; 687/739 (93%) continued at W52; 652/739 (88%) completed W100. ACR20 response rates in the mITT population continued to increase after W24, and at W100 were 76% for Q4W and 74% for Q8W (Fig). Similar response patterns were seen for ACR50/70, HAQ-DI and PASI90/100 (Table), and IGA0/1 and PASI75 response rates were consistent through W100 in patients randomized to Q4W and Q8W; W100 data for PBO→Q4W patients were consistent with patients treated with Q4W and Q8W (Table). GUS improvements in SF-36 PCS/MCS at W52 also persisted through W100 (data not shown). Low rates of radiographic progression (as measured by PsA-modified vdH-S scores) were observed during W52-W100 for Q4W (n=227; 0.75) and Q8W (n=232; 0.46). In the PBO→Q4W group (n=228), radiographic progression was 1.12 during W0-W24 (while on PBO), 0.51 during W24-W100 (while on Q4W), and 0.13 during W52-W100. Through W112, the incidences of AEs, serious AEs (SAEs), AEs leading to d/c, infections, serious infections, and injection site reactions were generally consistent with the PBO-controlled period and through 1 year. Of the patients in Q4W (n=245), Q8W (n=248), and PBO→Q4W (n=238) groups, 9%, 9% and 7% had ≥1 SAE; 2%, 3% and 3% had ≥1 serious infection; 2 Q8W patients (fungal esophagitis, disseminated herpes zoster) and 1 PBO→Q4W patient (listeria meningitis) had opportunistic infections; 1 PBO→Q4W patient died (road traffic accident); 1 PBO-randomized patient had IBD; no patient had anaphylactic or serum sickness reaction, or active TB.

Conclusion: In biologic-naïve PsA patients, GUS improvements in joint and skin symptoms, physical function, and low rates of radiographic progression persisted through 2 years. GUS safety in PsA through 2 years was comparable with safety at 6 months and 1 year, similar between Q4W and Q8W, and consistent with GUS safety in psoriasis.

Reference

[1]Mease PJ. *Lancet*. 2020;395:1126-36.
[2]McInnes IB. *Arthritis Rheumatol*. 2021;73:604-616.

Disclosure: I. McInnes, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **A. Gottlieb**, Boehringer Ingelheim, 1, 2, 5, Incyte, 1, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, UCB, 1, 2, 5, Xbiotech, 1, 2, 5, Bristol Myers Squibb, 1, 2, LEO Pharma, 1, 2, AnaptysBio, 1, 2, Avotres, 1, 2, Eli Lilly, 1, 2, Pfizer, 1, 2, Beiersdorf, 1, 2, Sun Pharmaceuticals, 1, 2, 5, Dermavant, 1, 2, GlaxoSmithKline, 1, 2; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Sheng**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Jiang**, Cytel, Inc., providing statistical support (funded by Janssen), 3; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas, 2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1337

Long-Term Safety Data for IL-12/23 Inhibitor (Ustekinumab) or Tumor Necrosis Factor Inhibitor in Patients with Psoriatic Arthritis from a Real-World Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriasis and PsA are associated with multiple comorbidities such as cardiovascular disease and metabolic syndrome. These comorbidities may render patients prone to developing adverse events (AEs) during treatment. In contrast to randomized controlled trials (RCT), patients with comorbidities frequently receive biologic treatment in real life, and long-term safety profiles may differ from RCT findings. Here, we analyze the long-term safety of biologic treatments from the real-world PsABio study, including the influence of baseline comorbidities on treatment effects.

Methods: PsABio (NCT02627768) was a multinational, observational study in patients with PsA prescribed either ustekinumab (UST, an IL-12/23 inhibitor) or a TNF inhibitor (TNFi) as 1st, 2nd or 3rd line treatment. The safety set included all patients with baseline and any available follow-up data. The frequency of new AEs or aggravation of existing comorbidities was analyzed during 6-monthly follow-up periods until study end at a maximum of 3 years (36 ± 3 months) of follow-up. AEs were summarized for all treatments that started prior to the AE and included events that occurred within a 91-day period (risk window) after treatment stop. All neoplasm events, excluding the ones occurring within 12 months of treatment start, are included irrespective of when they occurred after treatment stop.

Results: Safety data exist for 494 patients treated with UST and 557 treated with TNFi during the 36-month study period (this includes patients who switched from one treatment to the other). Baseline characteristics, treatment data and comorbidities are presented in **Table 1**. The UST group were older, had more comorbidities (especially cardiometabolic disease) and later line of bDMARD treatment vs the TNFi group, who had higher MTX use. UST-treated patients were followed for a total of 991.3 patient-years (PY), and TNFi-treated patients for 1232.9 PY; the mean follow-up time per patient for the UST group was 2.0 (±1.0) years vs 2.2 (±0.9) years for the TNFi group. At least one

Table 1. Baseline demographics, treatment characteristics and comorbidities of patients with PsA treated with ustekinumab and TNFi

Mean [95% CI]	UST (n=439)	TNFi (n=456)
Age, years (SD)	51.0 (12.4) [49.9 ; 52.1]	48.5 (12.5) [47.4 ; 49.6]
Female, n (%)	258 (56.2%) [51.5 ; 60.8]	257 (54.1%) [49.5 ; 58.7]
BMI, kg/m² (SD)	28.5 (6.1) [27.9 ; 29.1]	27.7 (5.4) [27.2 ; 28.2]
Disease duration (time since initial diagnosis), years (SD)	7.4 (8.1) [6.7 ; 8.2]	6.2 (6.6) [5.6 ; 6.8]
csDMARD exposure, n (%)		
Ongoing exposure at baseline	183 (39.9%) [35.4 ; 44.5]	263 (55.4%) [50.8 ; 59.9]
Methotrexate exposure ongoing at baseline	139 (30.3%) [26.1 ; 34.7]	201 (42.3%) [37.8 ; 46.9]
Other treatment exposure ongoing at baseline, n (%)		
NSAIDs	246 (53.6%) [48.9 ; 58.2]	323 (68.0%) [63.6 ; 72.2]
Steroids	149 (32.5%) [28.2 ; 37.0]	163 (34.3%) [30.1 ; 38.8]
Line of bDMARD treatment, n (%)		
First-line	210 (45.8%) [41.1 ; 50.4]	262 (55.2%) [50.6 ; 59.7]
Second-line	154 (33.6%) [29.2 ; 38.1]	156 (32.8%) [28.6 ; 37.3]
Third-line	95 (20.7%) [17.1 ; 24.7]	57 (12.0%) [9.2 ; 15.3]
Concurrent comorbidities, n (%)	308 (67.1) [62.6 ; 71.4]	272 (57.3) [52.7 ; 61.8]
Cardiometabolic disease and obesity*	75 (16.3) [13.1 ; 20.0]	64 (13.5) [10.5 ; 16.9]
Gastrointestinal disease	40 (8.7) [16.3 ; 11.7]	40 (8.4) [6.1 ; 11.3]
Depression	44 (9.6) [7.1 ; 12.7]	32 (6.7) [4.7 ; 9.4]
Anxiety or panic disorders	19 (4.1) [2.5 ; 6.4]	19 (4.0) [2.4 ; 6.2]
Neurological disease	6 (1.3) [0.5 ; 2.8]	2 (0.4) [0.1 ; 1.5]
Malignancies	9 (2.0) [0.9 ; 3.7]	8 (1.7) [0.7 ; 3.3]
Chronic hepatitis	10 (2.2) [1.0 ; 4.0]	1 (0.2) [0.0 ; 1.2]
Non-alcoholic fatty liver disease	21 (4.6) [2.9 ; 6.9]	14 (2.9) [1.6 ; 4.9]
Chronic obstructive pulmonary disease	10 (2.2) [1.0 ; 4.0]	11 (2.3) [1.2 ; 4.1]

35 patients in the UST group and 82 in the TNFi group received the drugs later over the course of the study.

*Hypertension, myocardial infarction, angina pectoris, congestive heart failure, stroke or transient ischemic attack, peripheral vascular disease, hyperlipidemia, type 1 or 2 diabetes plus BMI >30 kg/m².

BMI, body mass index; bDMARD, biologic DMARD; CI, confidence interval; SD, standard deviation; csDMARD, conventional synthetic DMARD; TNFi, TNF inhibitor; UST, ustekinumab.

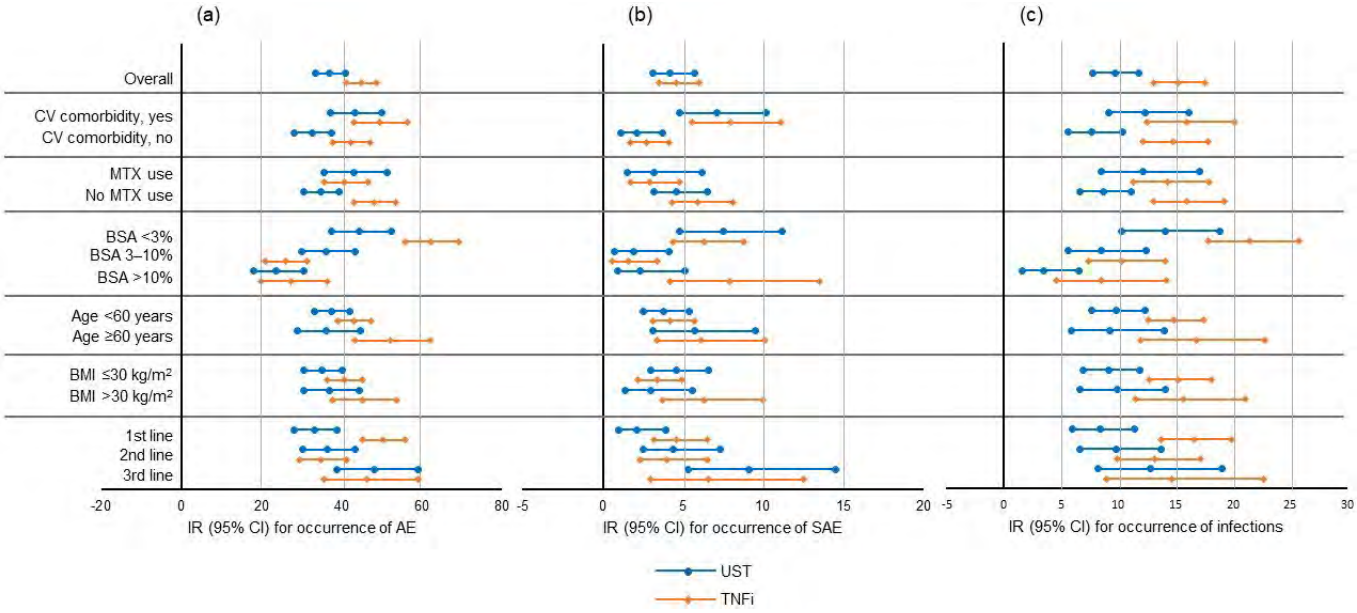


Figure 1. Exposure-adjusted incidence rate per 100 PY at risk (95% CI) for the occurrence of: (a) adverse events; (b) serious adverse events; and (c) infections in patients receiving UST and TNFi in the PsABio study. AE, adverse event; BMI, body mass index; BSA, body surface area; CI, confidence interval; CV, cardiovascular; IR, incidence rate; PY, patient-year; SAE, serious adverse event; TNFi, TNF inhibitor; UST, ustekinumab.

(non-neoplasm) AE was recorded in 34.6% of UST and 39.7% of TNFi-treated patients, with 6.3% and 7.2%, respectively, recording at least 1 serious AE (SAE). Malignancies were recorded in 3 (0.6%) UST (colon cancer, malignant neoplasm of eye, and prostate cancer) and 4 (0.7%) TNFi (bladder neoplasm, colon cancer, malignant urinary tract neoplasm, and squamous cell carcinoma of skin) patients. In the subgroup analysis by baseline characteristics and comorbidities, UST-treated patients generally tended to have a lower risk of clinically relevant AEs vs TNFi-treated patients in several subgroups (**Figure 1a**). The risk of infections was also lower with UST vs TNFi for the overall group and for several subgroups (**Figure 1c**). No clinically relevant differences were detected for SAEs (**Figure 1b**).

Conclusion: The PsABio study demonstrated an acceptable long-term safety profile of treatment with UST and TNFi in patients with PsA in a real-world setting.

Disclosure: S. Siebert, AbbVie, 5, 6, Biogen, 6, Amgen (previously Celgene), 5, 6, Bristol Myers Squibb, 5, Boehringer-Ingelheim, 5, Novartis, 5, 6, UCB, 5, 6, Janssen, 1, 5, 6, GlaxoSmithKline, 5; **P. Bergmans**, Janssen, 3, Johnson & Johnson, 11; **K. de Vlam**, Amgen, 6, 7, AbbVie, 6, Celgene, 2, 5, 6, Eli Lilly, 2, Johnson & Johnson, 2, Novartis, 2, 6, Galapagos, 2, 7, UCB, 2, 6, 7; **E. Gremese**, AbbVie, 2, 6, UCB, 2, 6, Pfizer, 2, 6, Janssen, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, Novartis, 2, 6; **B. Joven-Ibáñez**, AbbVie, 6, 12, Participant in clinical trials, Celgene, 2, 6, Janssen, 2, 6, 12, Participant in clinical trials, Novartis, 2, 6, 12, Participant in clinical trials, MSD, 6, Pfizer, 6, UCB, 2, Lilly, 12, Participant in clinical trials; **T. Korotaeva**, Pfizer, 2, 6, UCB, 2, 6, MSD, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Novartis-Sandoz, 2, 6, BIOCAD, 2, 6, AbbVie, 2, 6, Lilly, 2, 6, Amgen, 2, 6; **W. Noël**, Janssen, 3, 11; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5; **P. Sfikakis**, Actelion, 2, Pfizer, 2, 5, Genesis, 2, MSD, 2, UCB, 2, Boehringer Ingelheim, 2, 5, Enorasis, 2, Farmaserv-Lilly, 2, Gilead, 2, AbbVie, 2, 5, Novartis, 2, Roche, 5, Faran, 5, Amgen, 5, Janssen, 5, Celgene, 2, 5, Lilly, 2, 5; **E. Theander**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **L. Gossec**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1338

Bimekizumab in Patients with Psoriatic Arthritis: 3-Year Results for Overall and Tumor Necrosis Factor Inhibitor (TNFi)-Naïve Populations from a Phase 2b Open-Label Extension Study

Philip Mease[1], Atul Deodhar[2], Joseph Merola[3], Iain McInnes[4], Deepak Assudani[5], Rajan Bajracharya[5], Jason Coarse[6], Barbara Ink[7] and Georg Schett[8], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [2]Oregon Health & Science University, Portland, OR, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [4]University of Glasgow, School of Medicine, Glasgow, Scotland, United Kingdom, [5]UCB Pharma, Slough, United Kingdom, [6]UCB Pharma, Raleigh, NC, [7]UCB Celltech, Slough, UK, Slough, United Kingdom, [8]Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits interleukin (IL)-17F and IL-17A, and has demonstrated clinical improvements in joint and skin outcomes up to 152 weeks (wks) and an acceptable safety profile in patients (pts) with active psoriatic arthritis (PsA).[1,2] We report the long-term efficacy and safety of BKZ treatment up to 3 years in the overall BKZ-treated population and TNFi-naïve (n) pts from a phase 2b dose-ranging study (BE ACTIVE; NCT02969525) and its open-label extension (OLE; NCT03347110).

Methods: BE ACTIVE and OLE study designs have been described previously.[1,2] Pts who completed 48 wks of BKZ treatment without meeting withdrawal criteria were eligible for OLE entry. All OLE pts received BKZ 160 mg every 4 wks after completing BKZ 160 mg or 320 mg in BE ACTIVE. Data are presented from Wk 48 to 152 for all BKZ-treated pts and the TNFi-n (defined as biologic DMARD-naïve) subgroup. Pre-planned subgroup analyses of efficacy outcomes are reported for the full analysis set (FAS; pts who received ≥1 dose BKZ with a valid primary efficacy variable measurement at baseline [BL]): ACR criteria 20/50/70; resolution of dactylitis (in pts with BL Leeds Dactylitis Index >0) or enthesitis (in pts with BL Maastricht Ankylosing Spondylitis Enthesitis Score >0); Psoriasis Area and Severity Index (PASI)100 (in pts with BL body surface area ≥3%); dual achievement of ACR50+PASI100; and minimal/very low disease activity (MDA/VLDA) in PsA. Treatment-emergent adverse events (TEAEs) are reported for the safety set (SS; pts who received ≥1 dose BKZ in BE ACTIVE).

Results: In BE ACTIVE, 206 pts were randomized at BL and 184 were enrolled in the OLE.[1,2] Of pts randomized at BL, 167 were TNFi-n. Over half of TNFi-n pts achieved ACR50 at Wks 48/152 (58.7/52.7% non-responder imputation [NRI]; 63.6/69.8% observed case [OC]; **Table 1; Figure 1**). At Wk 152, the majority of TNFi-n pts had resolution of dactylitis (70.2% NRI; 100.0% OC) and enthesitis (60.7% NRI; 80.6% OC). The proportion of TNFi-n pts with PASI100 at Wks 48/152 was high (63.3/58.7% NRI; 68.3/74.4% OC). At Wk 152, a large proportion of TNFi-n pts had dual achievement of ACR50+PASI100 (46.8% NRI; 60.0% OC). The proportions of TNFi-n pts achieving MDA/VLDA at Wk 152 were 52.1%/31.1% NRI, respectively; 69.0%/41.3% OC, respectively (**Table 1; Figure 1**).

Over 152 wks, the exposure-adjusted incidence rate per 100 pt-years for all BKZ-treated pts was 4.1 for serious TEAEs, 0.7 for serious infections and 4.6 for *Candida* infections (**Table 2**). One event was adjudicated by an independent committee as inflammatory bowel disease (microscopic colitis). All *Candida* infections were localized, mild/moderate

Table 1. Further efficacy outcomes up to 3 years

Efficacy (FAS)	Overall BKZ (N=206)		TNFi-n (N=167)	
	NRI n (%)	OC n/N (%)	NRI n (%)	OC n/N (%)
ACR20				
Wk 48	149 (72.3)	149/191 (78.0)	121 (72.5)	121/154 (78.6)
Wk 152	132 (64.1)	132/157 (84.1)	108 (64.7)	108/126 (85.7)
ACR50				
Wk 48	118 (57.3)	118/191 (61.8)	98 (58.7)	98/154 (63.6)
Wk 152	109 (52.9)	109/157 (69.4)	88 (52.7)	88/126 (69.8)
ACR70				
Wk 48	82 (39.8)	82/191 (42.9)	67 (40.1)	67/154 (43.5)
Wk 152	81 (39.3)	81/157 (51.6)	67 (40.1)	67/126 (53.2)
Dactylitis resolution [a]				
Wk 48	45 (76.3)	45/50 (90.0)	37 (78.7)	37/40 (92.5)
Wk 152	42 (71.2)	42/42 (100.0)	33 (70.2)	33/33 (100.0)
Enthesitis resolution [b]				
Wk 48	61 (57.0)	61/98 (62.2)	49 (55.1)	49/80 (61.3)
Wk 152	67 (62.6)	67/83 (80.7)	54 (60.7)	54/67 (80.6)
PASI100 [c]				
Wk 48	88 (64.2)	88/127 (69.3)	69 (63.3)	69/101 (68.3)
Wk 152	79 (57.7)	79/107 (73.8)	64 (58.7)	64/86 (74.4)
ACR50+PASI100 [c]				
Wk 48	63 (46.0)	63/127 (49.6)	54 (49.5)	54/101 (53.5)
Wk 152	63 (46.0)	63/106 (59.4)	51 (46.8)	51/85 (60.0)
MDA				
Wk 48	105 (51.0)	105/191 (55.0)	87 (52.1)	87/154 (56.5)
Wk 152	106 (51.5)	106/157 (67.5)	87 (52.1)	87/126 (69.0)
VLDA				
Wk 48	54 (26.2)	54/191 (28.3)	48 (28.7)	48/154 (31.2)
Wk 152	62 (30.1)	62/157 (39.5)	52 (31.1)	52/126 (41.3)

Full analysis set. All patients received BKZ 160 mg during the OLE (Wks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE. [a] in the subset of overall BKZ or TNFi-n patients with BL LDI >0, NRI: N=59 or 47, respectively; [b] in the subset of overall BKZ or TNFi-n patients with BL MASES >0, NRI: N=107 or 89, respectively; [c] in the subset of overall BKZ or TNFi-n patients with BL BSA ≥3%, NRI: N=137 or 109, respectively. BKZ: bimekizumab; BL: baseline; BSA: body surface area; DMARD: disease-modifying antirheumatic drugs; FAS: full analysis set; LDI: Leeds Dactylitis Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PASI: Psoriasis Area and Severity Index; TNFi-n: tumor necrosis factor inhibitor (biologic DMARD) naïve; VLDA: very low disease activity; wk: week.

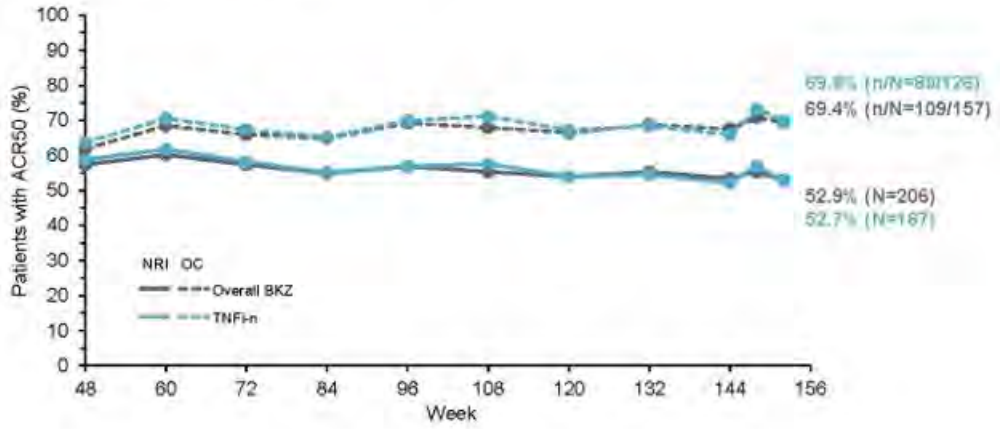
and resolved with appropriate antifungal therapy (the majority were oral candidiasis). Overall, 17 pts (8.3%) discontinued study treatment due to TEAEs.

Conclusion: High thresholds of disease control were achieved by >50% of TNFi-n pts treated with BKZ up to 3 years, reflected in long-term improvements in joint and skin outcomes. The safety profile of BKZ up to 3 years in pts with PsA reflects previous observations.[1,2]

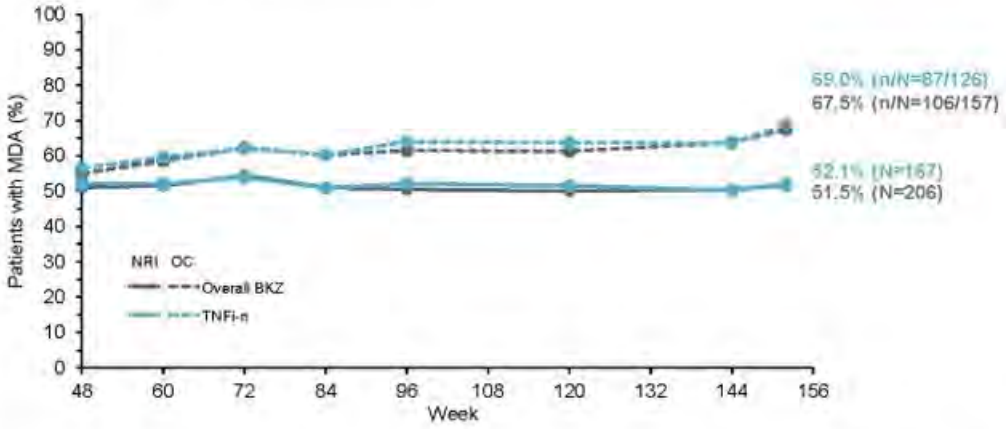
References: 1. Ritchlin CT. Lancet 2020;395:427–40; **2**. McInnes IB. Ann Rheum Dis 2020;79:1153–4.

Figure 1.

A) ACR50 responders up to 3 years



B) MDA responders up to 3 years [a]



[a] Data for Wks 108/132/148 not included as not all components of MDA were collected. NRI and OC data shown for all timepoints from Wks 48–152. All patients received BKZ 160 mg during the OLE (Wks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE. BKZ: bimekizumab; DMARD: disease-modifying antirheumatic drugs; MDA: minimal disease activity; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; TNFi-n: tumor necrosis factor inhibitor (biologic DMARD) naïve; wk: week.

Table 2. Safety outcomes up to 3 years

Safety (SS) **n (%) [EAIR/100 PY]**	**Overall BKZ (N=206) [a]**
Any TEAE	184 (89.3) [126.4]
Serious TEAEs [b]	22 (10.7) [4.1]
Severe TEAEs [c]	14 (6.8) [2.5]
Permanent discontinuation of drug due to TEAEs	17 (8.3) [3.0]
Drug-related TEAEs	97 (47.1) [26.4]
Deaths	0
TEAEs of special monitoring	
Serious infections	4 (1.9) [0.7]
Infections and infestations	47 (22.8) [9.7]
Candida infections [d]	24 (11.7) [4.6]
Oral candidiasis [e]	19 (9.2) [3.5]
Increases in hepatic enzymes [f]	
ALT increased [g]	13 (6.3) [2.4]
AST increased [g]	10 (4.9) [1.8]
Hepatic enzyme increased [g]	4 (1.9) [0.7]
Adjudicated MACE	0
Malignancies [h]	1 (0.5) [0.2]
Adjudicated IBD [i]	1 (0.5) [0.2]
Injection site reactions	3 (1.5) [0.5]
Suicidal ideation and behavior [j]	1 (0.5) [0.2]

Safety set. All patients received BKZ 160 mg during the OLE (Weeks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE. No anaphylactic reactions, major adverse cardiac events or deaths were reported. [a] Results of patients who received BKZ in the full safety set; TEAEs from time on placebo are not included, including two patients who completed placebo treatment but did not continue in the study; [b] serious TEAEs met at least one of the following criteria: death; life-threatening; significant or persistent disability/incapacity; congenital anomaly/birth defect; initial inpatient hospitalization or prolongation of hospitalization; important medical event that, based upon appropriate medical judgment, may jeopardize the patient and may require medical or surgical intervention to prevent one of the other outcomes listed in the definition of serious; [c] severe defined as the subject is unable to work normally or to carry out his/her usual activities, or the AE is of definite clinical consequence; [d] all fungal infections were localized, not systemic; [e] all oral candidiasis TEAEs were mild to moderate, none of the cases were serious; [f] no cases of Hy's law were reported; [g] preferred term; [h] malignant melanoma in situ; [i] microscopic colitis; [j] during dose-blind phase; patient was withdrawn.[1] AE: adverse event; ALT: alanine aminotransferase; AST: aspartate aminotransferase; BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; IBD: inflammatory bowel disease; MACE: major adverse cardiovascular event; OLE: open-label extension; PY: patient-years; SS: safety set; TEAE: treatment-emergent adverse event.

Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **J. Merola**, AbbVie, 2, Biogen, 2, Bristol Myers Squibb, 2, Dermavant, 2, Eli Lilly, 2, 5, Janssen, 2, Novartis, 2, Pfizer, 2, UCB Pharma, 2, Amgen, 2, 5, Sanofi, 2, Regeneron, 2, Leo Pharma, 2; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **D. Assudani**, UCB Pharma, 3; **R. Bajracharya**, UCB Pharma, 3; **J. Coarse**, UCB Pharma, 3; **B. Ink**, GSK, 11, UCB Pharma, 3, 11; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6.

Abstract Number: 1339

Treatment Persistence Was Similar at 3 Years in Patients with Psoriatic Arthritis Treated with Ustekinumab (STELARA®) or a Tumor Necrosis Factor Inhibitor in a Prospective Real-World Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Several options exist in the treatment of PsA, but data on long-term persistence are rare. Here, we assess long-term persistence with ustekinumab (UST) or TNF inhibitor (TNFi) in patients treated for PsA in the real world.

Methods: PsABio (NCT02627768) was a multinational, observational study in patients with PsA treated with 1st, 2nd, or 3rd line UST or a TNFi. Here we present drug persistence, one of the primary outcomes. All patients with baseline and post-baseline effectiveness data up to the complete study duration (3 years ± 3 months), including those who switched/stopped initial treatment, were analyzed. Persistence of UST and TNFi is presented as Kaplan-Meier (KM) curves and compared between cohorts using Cox regression analysis, including propensity score (PS) to adjust for baseline imbalanced covariates. Factors including concomitant MTX use and skin involvement were added to the Cox model to investigate their effect on the PS-adjusted treatment effect. Hazard ratios (HR) including 95% confidence intervals (CI) are presented.

Results: Baseline characteristics, treatment data, and comorbidities potentially influencing persistence showed imbalance between treatment groups, especially with treatment line (21% of patients in the UST group were on 3rd-line treatment vs 12% in the TNFi group) and comorbidities (67% in UST vs 57% in the TNFi group) (**Table 1**). Of 439 and 456 patients who started UST and TNFi, respectively, 42% and 41% stayed on their first treatment up to Month 36. Mean duration of initial treatment line was 24.7 (95% CI: 23.5 ; 25.8) months for UST and 24.1 (95% CI: 22.9 ; 25.3) months for TNFi-treated patients. Reasons for stopping/switching were related to safety and tolerability in 17% (UST) and 24% (TNFi) patients, and effectiveness in 83% (UST) and 76% (TNFi) patients.

Unadjusted KM graphs are shown in **Figure 1a–c**. Similar to findings from the 1-year persistence analysis (1), the estimates demonstrated similar drug persistence between UST and TNFi (**Figure 1a**). As expected, 1st-line biologic treatment was associated with longer treatment persistence than other lines. After PS adjustment for baseline imbalances, the risk of stopping/switching was similar for UST vs TNFi; HR 0.94 (0.75 ; 1.16). In patients with severe psoriasis (body surface area >10%), risk of stopping/switching was lower for UST vs TNFi; HR 0.55 (0.32 ; 0.98); a similar effect was seen for treatment with UST monotherapy vs TNFi monotherapy (without MTX); HR 0.75 (0.57 ; 0.98). This points to the importance of treatment persistence, next to concomitant therapy, when there is skin involvement.

Table 1. Baseline demographics, clinical characteristics and comorbidities of PsA patients treated with ustekinumab and TNFi

Mean [95% CI]	UST (n=439)	TNFi (n=456)
Age, years (SD)	51.1 (12.5) [49.9; 52.2]	48.5 (12.6) [47.3; 49.6]
Female, n (%)	247 (56.3%) [51.5; 61.0]	248 (54.4%) [49.7; 59.0]
BMI, kg/m² (SD)	28.6 (6.2) [27.9; 29.2]	27.8 (5.3) [27.2; 28.3]
Time since initial diagnosis, years (SD)	7.5 (8.1) [6.7; 8.3]	6.2 (6.6) [5.6; 6.9]
sDMARD exposure, n (%)		
Previous exposure	385 (87.7%) [84.3; 90.6]	422 (92.5%) [89.7; 94.8]
Ongoing exposure at baseline	175 (39.9%) [35.3; 44.6]	252 (55.3%) [50.6; 59.9]
Methotrexate exposure ongoing at baseline	132 (30.1%) [25.8; 34.6]	193 (42.3%) [37.7; 47.0]
Other treatment exposure ongoing at baseline, n (%)		
NSAIDs	240 (54.7%) [49.9; 54.9]	313 (68.6%) [64.2; 72.9]
Steroids	144 (32.8%) [28.4; 37.4]	156 (34.2%) [29.9; 38.8]
Line of bDMARD treatment, n (%)		
First-line	210 (45.8%) [41.1; 50.4]	262 (55.2%) [50.6; 59.7]
Second-line	154 (33.6%) [29.2; 38.1]	156 (32.8%) [28.6; 37.3]
Third-line	95 (20.7%) [17.1; 24.7]	57 (12.0%) [9.2; 15.3]
Concurrent comorbidities, n (%)	295 (67.2) [62.6; 71.6]	261 (57.2) [52.6; 61.8]
Cardiometabolic disease and obesity*	72 (16.4) [13.1; 20.2]	61 (13.4) [10.4; 16.8]
Gastrointestinal disease	40 (9.1) [6.6; 12.2]	40 (8.8) [6.3; 11.8]
Depression	41 (9.3) [6.8; 12.5]	29 (6.4) [4.3; 9.0]
Anxiety or panic disorders	18 (4.1) [2.4; 6.4]	18 (3.9) [2.4; 6.2]
Neurological disease	6 (1.4) [0.5; 3.0]	2 (0.4) [0.1; 1.6]
Malignancies	9 (2.1) [0.9; 3.9]	6 (1.3) [0.5; 2.8]
Chronic hepatitis	10 (2.3) [1.1; 4.1]	1 (0.2) [0.0; 1.2]
Non-alcoholic fatty liver disease	18 (4.1) [2.4; 6.4]	13 (2.9) [1.5; 4.8]
Chronic obstructive pulmonary disease	9 (2.1) [0.9; 3.9]	11 (2.4) [1.2; 4.3]

*Hypertension, myocardial infarction, congestive heart failure, stroke or transient ischemic attack, peripheral vascular disease, hyperlipidemia, type 1 or 2 diabetes or angina pectoris.

BMI, body mass index; bDMARD, biologic DMARD; CI, confidence interval; SD, standard deviation; sDMARD, synthetic DMARD; TNFi, TNF inhibitor; UST, ustekinumab.

Conclusion: In the prospectively followed PsABio study across Europe, slightly more than 40% of PsA patients stayed on UST or TNFi for 3 years or more. After correction for baseline differences, the risk of stopping/switching treatment over 3 years was similar for UST and TNFi, with better persistence for UST vs TNFi in the subgroup of patients with severe psoriasis and in those receiving the biologic DMARD without MTX. Both drug classes offer interesting options for the treatment of PsA.

Reference

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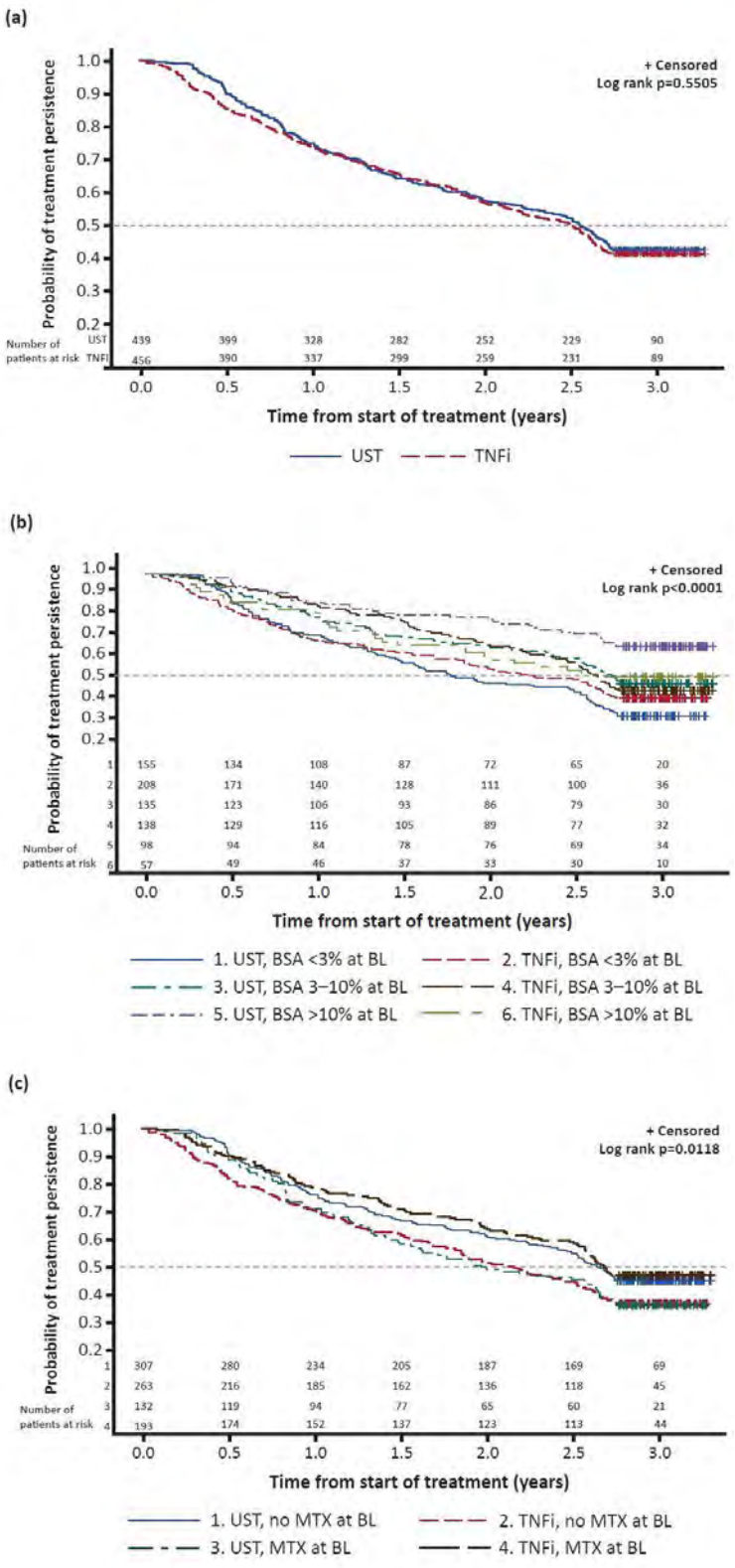

Figure 1. Kaplan-Meier graphs showing treatment persistence by (a) UST vs TNFi; (b) bDMARD and extent of skin involvement at baseline; (c) bDMARD and presence/absence of MTX at baseline. Dotted line indicates median survival. The curves becoming flat after 2.5 years is due to some patients prematurely stopping the study. bDMARD, biologic DMARD; BL, baseline; BSA, body surface area; TNFi, TNF inhibitor; UST, ustekinumab.

Disclosure: L. Gossec, Galapagos, 5, Sandoz, 5, Sanofi, 5, AbbVie, 2, Amgen, 2, 5, Bristol Myers Squibb, 2, Biogen, 2, Celgene, 2, Eli Lilly, 2, 5, Gilead, 2, Janssen, 2, 5, Novartis, 2, Pfizer, 2, 5, Samsung Bioepis, 2, Sanofi-Aventis, 2, UCB, 2; **S. Siebert**, AbbVie, 5, 6, Biogen, 6, Amgen (previously Celgene), 5, 6, Bristol Myers Squibb, 5, Boehringer-Ingelheim, 5, Novartis, 5, 6, UCB, 5, 6, Janssen, 1, 5, 6, GlaxoSmithKline, 5; **P. Bergmans**, Janssen, 3, Johnson & Johnson, 11; **K. de Vlam**, Amgen, 6, 7, AbbVie, 6, Celgene, 2, 5, 6, Eli Lilly, 2, Johnson & Johnson, 2, Novartis, 2, 6, Galapagos, 2, 7, UCB, 2, 6, 7; **E. Gremese**, AbbVie, 2, 6, UCB, 2, 6, Pfizer, 2, 6, Janssen, 2, 6, Boehringer Ingelheim, 2, 6, Celgene, 2, 6, Novartis, 2, 6; **B. Joven-Ibáñez**, AbbVie, 6, 12, Participant in clinical trials, Celgene, 2, 6, Janssen, 2, 6, 12, Participant in clinical trials, Novartis, 2, 6, 12, Participant in clinical trials, MSD, 6, Pfizer, 6, UCB, 2, Lilly, 12, Participant in clinical trials; **T. Korotaeva**, Pfizer, 2, 6, UCB, 2, 6, MSD, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Novartis-Sandoz, 2, 6, BIOCAD, 2, 6, AbbVie, 2, 6, Lilly, 2, 6, Amgen, 2, 6; **W. Noël**, Janssen, 3, 11; **M. Nurmohamed**, Pfizer, 2, 5, 6, AbbVie, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, MSD, 2, 5, 6, Mundipharma, 2, 5, 6, UCB, 2, 5, 6, Janssen, 2, 5, 6, Menarini, 2, 5, 6, Lilly, 2, 5, 6, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Gilead/Galapagos, 2, 5; **P. Sfikakis**, Actelion, 2, Pfizer, 2, 5, Genesis, 2, MSD, 2, UCB, 2, Boehringer Ingelheim, 2, 5, Enorasis, 2, Farmaserv-Lilly, 2, Gilead, 2, AbbVie, 2, 5, Novartis, 2, Roche, 5, Faran, 5, Amgen, 5, Janssen, 5, Celgene, 2, 5, Lilly, 2, 5; **E. Theander**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1340

Upadacitinib Effects on Entheseal Domain in Psoriatic Arthritis Patients – a Pooled "post-hoc" Analysis from Two Phase III Studies (Select PsA 1 and 2)

Fabrizio Cantini[1], Antonio Marchesoni[2], Francesca Marando[3], Giuliana Gualberti[3], Lucia Novelli[3], Giacomo Curradi[3], Erin McDearmon-Blondell[4], Tianming Gao[5] and **Carlo Salvarani**[6], [1]Department of Rheumatology, Azienda USL Toscana Centro, Hospital of Prato, Prato, Italy, [2]Dipartimento di Reumatologia, ASST Gaetano Pini-CTO, Milano, Italy, [3]AbbVie, Rome, Italy, [4]AbbVie Inc., Elmhurst, IL, [5]AbbVie Inc., North Chicago, IL, [6]Unità Operativa di Reumatologia, Azienda USL-IRCCS di Reggio Emilia, Italy, Reggio Emilia, Italy

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Reaching control or improvement on enthesitis domain in psoriatic arthritis (PsA) is challenging, and it continues to be a priority for patients (pts) and rheumatologists. Upadacitinib (UPA) has demonstrated efficacy across key manifestations, including enthesitis, in pts with active PsA with inadequate response to non-biologic or biologic DMARDs from the SELECT-PsA Clinical trials program[1,2]. The objective of this analysis was to further estimate UPA 15 mg qd effects on enthesitis using different assessment tools through 56 weeks (W).

Methods: The SELECT-PsA 1 and 2 primary results were described elsewhere[1,2]. For the purpose of this analysis, the UPA 15 mg arms were pooled from the two studies to 56W (continuous UPA), the PBO arms to W24 and the PBO to UPA 15 arms from 24W to 56W.

Enthesitis resolution was assessed as proportion of pts achieving LEI =0 and/or SPARCC=0 at each timepoint for patients with LEI >0 or SPARCC > 0 at baseline (BL). Change from BL in LEI and SPARCC scores was also assessed at each timepoint. Residual enthesitis sites and maintenance of an enthesitis-free state were assessed through 56W. Non-responder imputation was used for binary endpoints and mixed-effect model repeated measures (MMRM) for continuous endpoints.

Results: Pooled population comprised 639 UPA 15 mg pts and 635 PBO pts. A significantly greater improvement in LEI and SPARCC scores (change from baseline) was observed with UPA 15 mg QD vs PBO as early as 12W to 24W, (nominal P< 0.0001; Figure 1) and results were either sustained or increased through 56W. A higher proportion of pts treated with UPA in comparison to PBO achieved complete resolution of enthesitis as assessed with LEI=0 or SPARCC=0 (nominal P<0.0001, **Figure 2)** and "LEI + SPARCC=0" (nominal p=0.0003 at 12W and p< 0.0001 at 16W / 24W). Resolution of enthesitis was sustained or increased through 56W, particularly in the continuous UPA 15 mg arm. Maintenance rate of an enthesitis-free state after LEI resolution at week 24 for UPA 15 mg continuous arm was: 84.2% at 36W, 80.2% at 56W, and with 72.3% remaining in remission at both 36W and 56W. Similarly, SPARCC assessment showed a 81.4% maintenance rate at 36W, 78.2% at 56 W, and 69.5% at both 36 W and 56W. For partial responders (pts experiencing a reduction in LEI or SPARCC but not achieving enthesitis resolution at 24W), UPA 15 mg still showed improvement over placebo for all components of LEI (or SPARCC) at 24W, with no specific refractory sites identified (Figure 3). For subjects with LEI=0 at baseline, Upa 15 mg also showed higher proportion of prevention of enthesitis versus placebo up to 24W, (between 12W and 24W the proportion of pts with LEI=0 for UPA ranged from 84.7% to 80.1% while for PBO ranged from 76% to 58.8%; nominal p< 0.05).

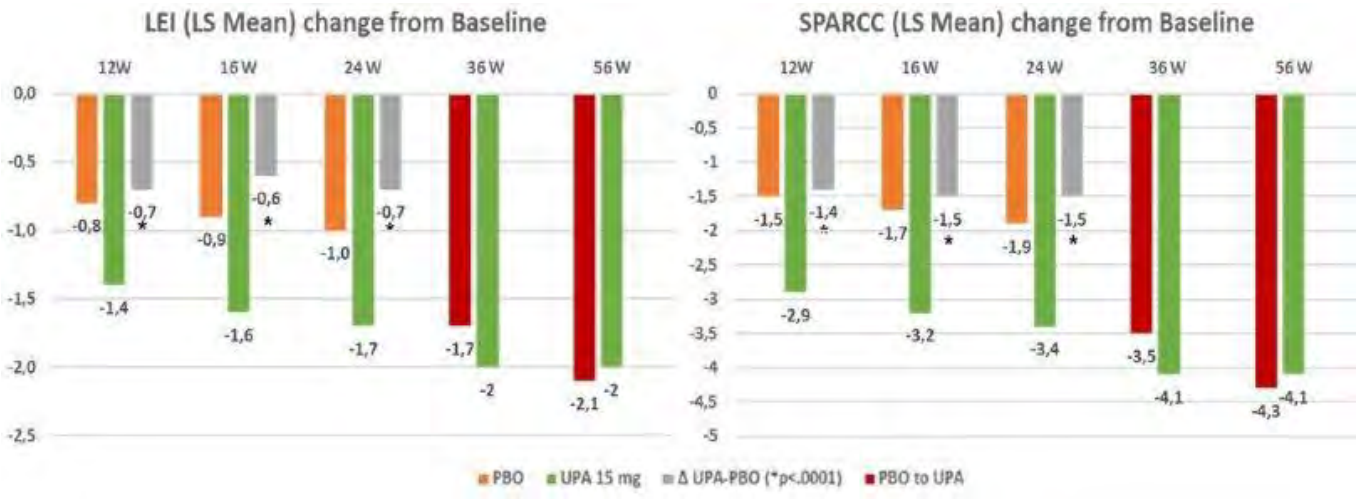

Figure 1. Change from BL in LEI/SPARCC by Visit and Treatment among subjects with BL values>0.

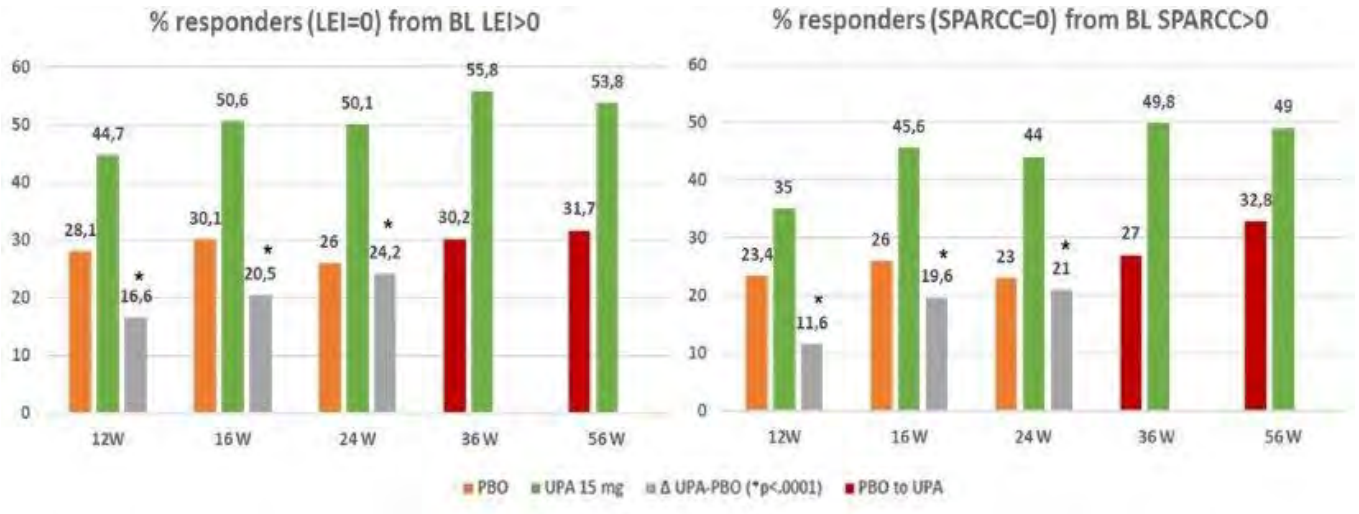

Figure 2. Proportion of Subjects Achieving Resolution of Enthesitis (LEI / SPARCC = 0) by Visit & Treatment among subjects with BL values>0.

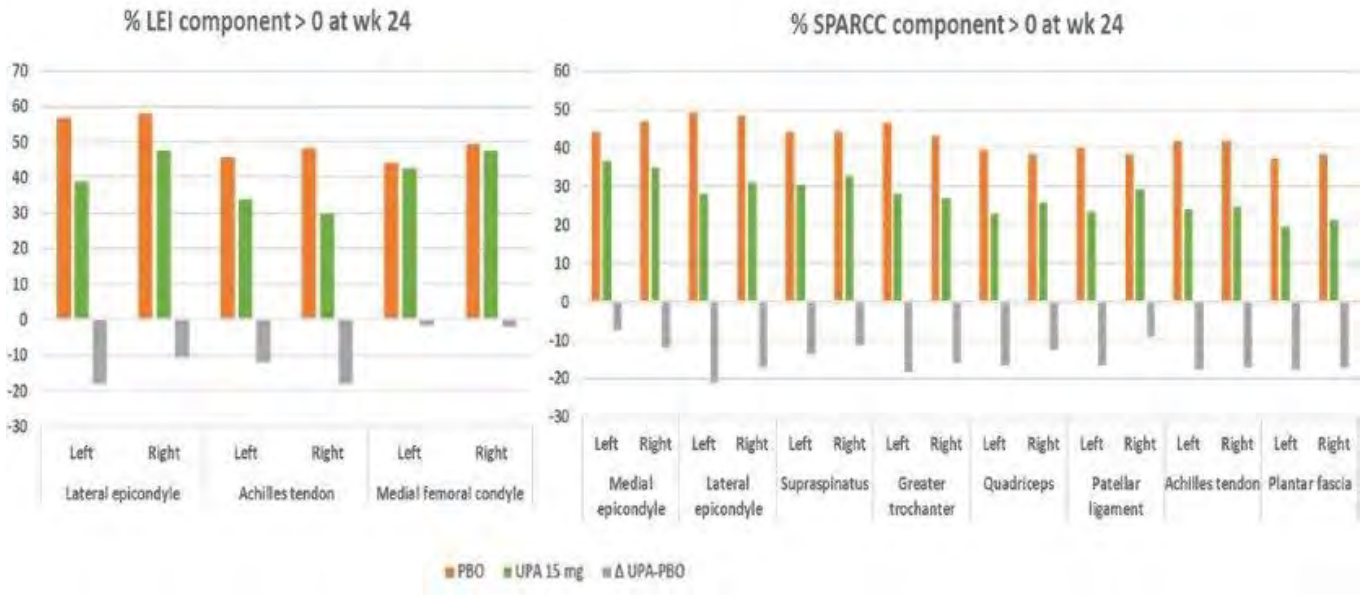

Figure 3. Residual Enthesitis sites at 24W among Subjects Not Achieving Full Resolution.

Conclusion: In pts with active PsA who had inadequate response to non-biologic or biologic DMARDs, UPA 15 mg achieved a rapid and comprehensive impact on enthesitis, across individual entheseal sites and with a high rate of maintenance of an enthesitic free state after resolution.

Disclosure: F. Cantini, Eli-Lilly, Novartis, Janssen, Pfizer, Abbvie, 6; **A. Marchesoni**, Abbvie, Pfizer, MSD, UCB, Novartis, Eli Lilly, and Janssen, 6; **F. Marando**, AbbVie, 3, 11; **G. Gualberti**, AbbVie, 3, 11; **L. Novelli**, AbbVie, 3, 11; **G. Curradi**, AbbVie, 3, 11; **E. McDearmon-Blondell**, AbbVie, 3, 11; **T. Gao**, AbbVie, 3, 11; **C. Salvarani**, Abbvie, Pfizer, MSD, Novartis, and Eli Lilly, 6.

Abstract Number: 1341

Ixekizumab Shows a Pattern of Pain Improvement in Patients with and Without Measurable Inflammation in Psoriatic Arthritis

Kurt de Vlam[1], Gaia Gallo[2], Philip Mease[3], Proton Rahman[4], Venkatesh Krishnan[2], David Sandoval[2], Chen Yen Lin[2], Danting Zhu[2], Rebecca Bolce[2] and Philip Conaghan[5], [1]University Hospitals Leuven, Leuven, Belgium, [2]Eli Lilly and Company, Indianapolis, IN, [3]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [4]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The efficacy of ixekizumab (IXE) and adalimumab (ADA) in patients with psoriatic arthritis (PsA) has been previously reported using ACR 50 and Psoriasis Area and Severity Index (PASI) 100 responses.[1,2] To minimize confounding effects, in this analysis we assessed the efficacy of either IXE or ADA monotherapy on reduction of pain beyond measurable inflammation in patients with active PsA and with low C-reactive protein (CRP) (< 5mg/L) at baseline.

Methods: SPIRIT-H2H (NCT03151551) was a 52 week (W), multicenter, randomized, open-label, parallel-group, assessor-blinded study evaluating the efficacy and safety of IXE vs ADA.[1] Participants were randomized (1:1) to approved-label dosing of IXE or ADA. This post-hoc analysis included only patients treated with IXE or ADA as monotherapy and with low CRP (< 5mg/L) at baseline. Changes in joint pain were measured using PsA Patient's Assessment of Pain Visual Analog Scale (VAS). We stratified patients into four categories by two measures of inflammation:

1. Sustained low inflammation either by
   a CRP < 5 mg/L during W4-24 or
   b ≥ 50% improvement in swollen joint count (SJC) during W8-24.
2. Fluctuating inflammation either by
   a CRP ≥ 5 mg/L at least once between W4-24 or
   b < 50% improvement in SJC at least once between W8-24.

Results: Ninety-five monotherapy patients with a CRP < 5mg/L at baseline were included in this analysis. Baseline characteristics were similar between both treatment arms. In patients with fluctuating inflammation as measured by CRP, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated

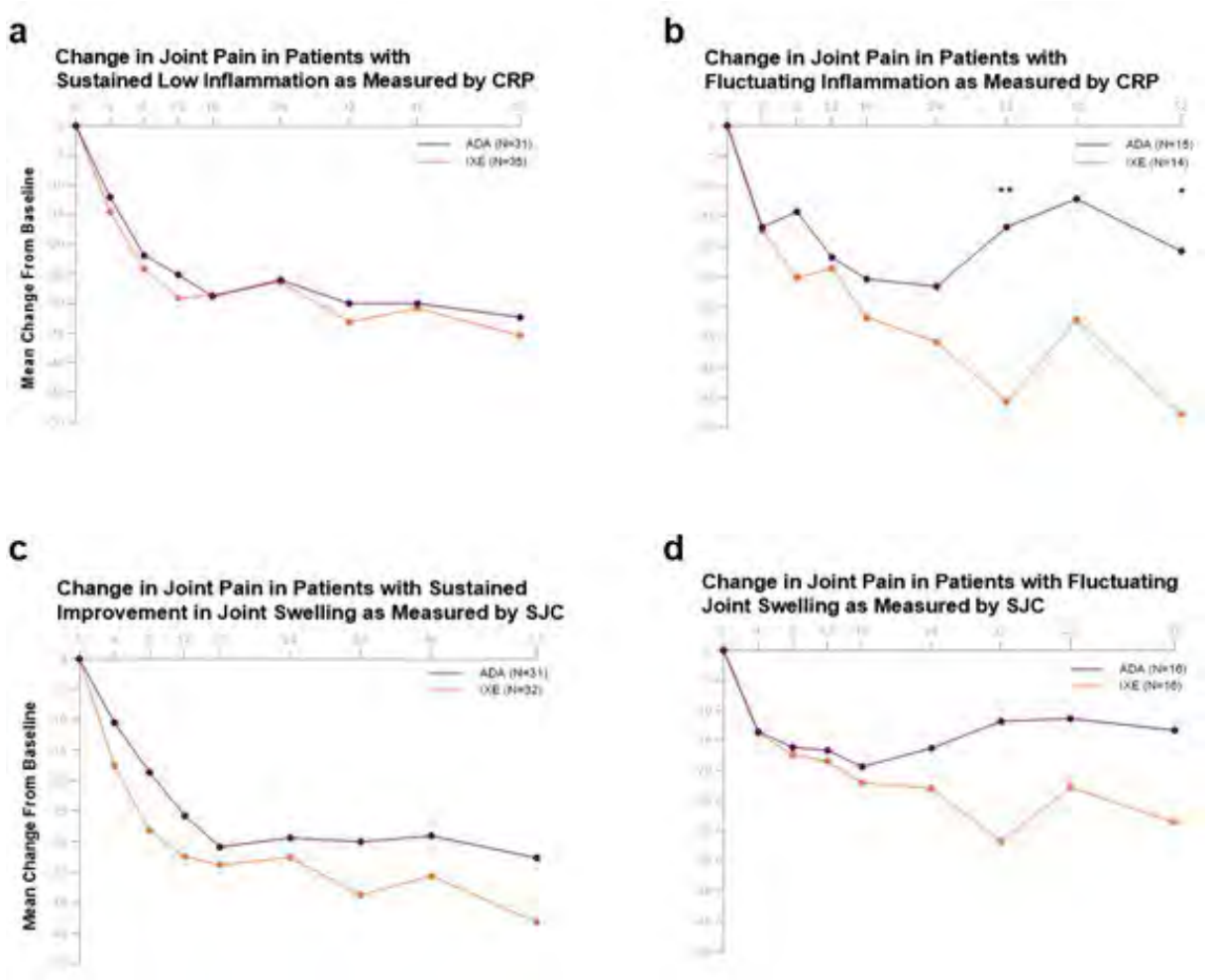

Figure 1. All patients had low baseline CRP (CRP < 5mg/L) and were treated with IXE or ADA as monotherapy. (a) Change in joint pain from baseline of patients with sustained low inflammation measured by CRP in IXE and ADA treatment groups. (b) Change in joint pain from baseline of patients with fluctuating inflammation measured by CRP in IXE and ADA treatment groups. (c) Change in joint pain from baseline of patients with sustained improvement in SJC in IXE and ADA treatment groups. (d) Change in joint pain from baseline of patients with fluctuating improvement in SJC in IXE and ADA treatment groups. *p value ≤ 0.05, **p value ≤ 0.01. Some patients were excluded from analysis due to missingness at visits.

patients at W16 (IXE: -31.64, ADA: -25.33, Figure 1b) that was sustained up to W52 (IXE: -47.69, ADA: -20.67, Figure 1b). There was significance in favor of IXE at W32 (p = 0.0045) and W52 (p = 0.0288, Figure 1b). In patients with sustained low inflammation as measured by CRP, there was no difference in improvement in joint pain between IXE and ADA-treated patients (Figure1a). In patients with sustained improvement in joint swelling as assessed by SJC, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated patients from W4 (IXE: -17.47, ADA: -10.42, Figure 1c) that was sustained through W52 (IXE: -43.16, ADA: -32.62, Figure 1c). In patients with fluctuating improvement in joint swelling as assessed by SJC, IXE-treated patients demonstrated a numerically greater mean improvement in joint pain VAS vs ADA-treated patients from W16 (IXE: -22.00, ADA: -19.31, Figure 1d) that was sustained through W52 (IXE: -28.57, ADA: -13.27, Figure 1d).

Conclusion: This analysis suggests a different pattern of pain improvement in patients with low baseline CRP treated with IXE or ADA monotherapy, with a favorable pain reduction outcome for IXE-treated patients, even when inflammation is fluctuating as measured by CRP or SJC improvement. This analysis supports the hypothesis that IXE improves joint pain in PsA patients with and without measurable inflammation.

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Disclosure: K. de Vlam, Amgen, 6, 7, AbbVie, 6, Celgene, 2, 5, 6, Eli Lilly, 2, Johnson & Johnson, 2, Novartis, 2, 6, Galapagos, 2, 7, UCB, 2, 6, 7; **G. Gallo**, Eli Lilly and Company, 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **V. Krishnan**, Eli Lilly and Company, 3, 11; **D. Sandoval**, Eli Lilly and Company, 3; **C. Lin**, Eli Lilly and Company, 3, 11; **D. Zhu**, Eli Lilly and Company, 3; **R. Bolce**, Eli Lilly and Company, 3, 11; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6.

Abstract Number: 1342

Low Incidence of Gastrointestinal-related and Overall Serious Adverse Events Among Guselkumab-treated Patients: Pooled Analyses of VOYAGE 1 & 2 and DISCOVER 1 & 2 Through 1-Year

Philip Mease[1], Peter Foley[2], Kristian Reich[3], Jerry Bagel[4], Mark Lebwohl[5], Ya-Wen Yang[6], May Shawi[7], Megan Miller[8], Alexa Kollmeier[9], Elizabeth Hsia[8], Xie Xu[8], Miwa Izutsu[10], Paraneedharan Ramachandran[10], Shihong Sheng[8], Yin You[8], Philip S Helliwell[11] and Wolf-Henning Boehncke[12], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [2]University of Melbourne, Carlton, Australia, [3]University Medical Center Hamburg-Eppendorf, Hamburg, Germany, [4]Psoriasis Treatment Center of Central New Jersey, Department of Dermatology, East Windsor, NJ, USA, East Windsor, NJ, [5]Icahn School of Medicine at Mount Sinai, New York, NY, [6]Janssen Global Services, LLC, Horsham, PA, [7]Janssen Immunology Global Commercial Strategy Organization, Toronto, ON, Canada, [8]Janssen Research & Development, LLC, Spring House, PA, [9]Janssen Research & Development, LLC, La Jolla, CA, [10]Janssen Research & Development, LLC, Immunology, Spring House, PA, [11]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [12]Geneva University Hospitals, Geneva, Switzerland

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), an anti-interleukin (IL)-23p19-subunit mAb, demonstrated efficacy in VOYAGE (VOY) 1&2 patients (pts) with moderate to severe plaque psoriasis (PsO)[1,2] and in DISCOVER (DISC) 1&2 pts with active PsA.[3,4] IL-17 inhibitors used to treat PsO and PsA have been associated with exacerbation or new onset of IBD.[5] We evaluated the incidence of gastrointestinal (GI)-related and overall serious adverse events (SAEs) from pooled safety data through 1-year of GUS 100 mg treatment from the phase 3 VOY 1&2 and DISC 1&2 trials.

Methods: Using pooled safety data from VOY 1&2 PsO and DISC 1&2 PsA trials, GI-related SAEs were identified using the Medical Dictionary for Regulatory Activities (MedDRA) system-organ class "GI disorders". Pts with a previous history of IBD were not excluded; IBD history was collected at baseline in DISC 1&2. Rates of overall and GI-related SAEs were calculated as the number of SAEs per 100 pt-years (PY) of follow-up (95% confidence intervals). Data are presented for the placebo (PBO)-controlled period (VOY 1&2: Weeks [W] 0-16; DISC 1&2: W0-24) and through 1-year (VOY 1&2: through W48; DISC 1: through W60, DISC 2: through W52). Events of uveitis and opportunistic infections were also analyzed.

Results: Through the PBO-controlled period, the overall rates of GI-related SAEs per 100 PY for pooled VOY 1&2 were: PBO 0.78 (0.02, 4.34), GUS every (q) 8w 0; and for pooled DISC 1&2: PBO 0.58 (0.01, 3.23), GUS q8w 0.58 (0.01, 3.21), GUS q4w 0. The GI-related SAEs included: VOY 1&2, gastrointestinal hemorrhage (PBO; n=1); and DISC 1&2, IBD (PBO; n=1) and mechanical ileus (GUS q8w; n=1). Through 1-year, overall rates of GI-related SAEs for VOY 1&2 were: combined GUS group (GUS q8w + PBO→GUS) 0.51 (0.17, 1.20); and for DISC 1&2: GUS q8w 0.52 (0.06, 1.88), GUS q4w 0, combined GUS group (GUS q8w + GUS q4w + PBO→GUS) 0.21 (0.02, 0.74). The GI-related SAEs in the combined GUS group for pooled VOY 1&2 included: gastritis, hemorrhoids, inguinal hernia, pancreatitis, and umbilical hernia (0.10/100 PY [0.00, 0.57]; n=1 for each); and in the combined GUS group for pooled DISC 1&2: mechanical ileus and pancreatitis chronic (0.10/100 PY [0.00, 0.57]; n=1 for each). Overall, no cases of exacerbation or new onset of IBD were reported in GUS-treated pts, including 2 pts with a prior history of IBD in DISC 1&2 (total PY of follow-up for the combined GUS groups in VOY and DISC were 974 and 973, respectively). Through the PBO-controlled period, rates of overall SAEs for GUS-treated pts were comparable to PBO-pts and SAE rates remained low through 1-year of follow-up in VOY 1&2 and DISC 1&2. No cases of uveitis, opportunistic infections, or tuberculosis were reported in GUS-treated pts through 1-year.

Conclusion: Through 1-year of follow-up with GUS treatment in pooled VOY 1&2 and DISC 1&2, GI-related SAE rates were low. There were no reported cases of uveitis, opportunistic infections, or new onset/exacerbation of IBD in GUS-treated pts. No new safety concerns were identified through 1-year.

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Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6,

Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Foley**, AbbVie, 1, 5, 6, 12, Travel grants, Amgen, 1, 5, Celgene, 1, 5, 6, Aslan, 1, 5, Janssen, 1, 2, 5, 6, 12, Travel grants, Leo Pharma, 1, 2, 5, 6, 12, Travel grants, Eli Lilly, 1, 2, 5, 6, 12, Travel grants, Merck, 1, 2, 5, 6, 12, Travel grants, Novartis, 1, 2, 5, 6, 12, Travel grants, Pfizer, 1, 2, 5, 6, 12, Travel grants, Sanofi, 2, 5, 12, Travel grants, Sun Pharma, 1, 2, 5, 12, Travel grants, AstraZeneca, 5, Arcutis, 5, Boehringer Ingelheim, 2, Hexima, 5, UCB Pharma, 2, 5, Valeant, 5, 6, Bristol Myers Squibb, 1, 2, 5, Celtaxsys, 5, CSL, 5, Cutanea, 5, Dermira, 5, Galderma, 1, 5, 6, Genentech, 5, GlaxoSmithKline, 1, 5, 6, Regeneron, 5, Reistone, 5, Roche, 2, 5, 6, 12, Travel grants; **K. Reich**, AbbVie, 1, 5, 6, Amgen, 1, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, UCB Pharma, 1, 5, Affibody, 1, 5, Almirall, 1, 5, 6, Boehringer Ingelheim, 1, 5, Bristol Myers Squibb, 1, 5, 6, Celgene, 1, 5, 6, Forward Pharma, 1, 5, Galderma, 1, 5, Kyowa Kirin, 1, 5, Leo Pharma, 1, 5, 6, Eli Lilly, 1, 5, 6, Medac, 1, 5, 6, Ocean Pharma, 1, 5, Sanofi, 1, 5, 6, MoonLake Immunotherapeutics, 3; **J. Bagel**, AbbVie, 2, 5, 6, Amgen, 2, 5, Arcutis Biotherapeutics, 5, Boehringer Ingelheim, 5, Bristol Myers Squibb, 5, Celgene Corporation, 2, 5, 6, Corrona, LLC, 5, Dermavant Sciences, LTD, 5, Dermira/UCB, 5, Eli Lilly and Company, 2, 5, 6, Glenmark Pharmaceuticals Ltd, 5, Janssen Biotech, 2, 5, 6, Kadmon Corporation, 5, Leo Pharma, 2, 5, Lycera Corp, 5, Menlo Therapeutics, 5, Novartis, 2, 5, 6, Pfizer, 5, Regeneron Pharmaceuticals, 5, Sun Pharmaceutical Industries Ltd, 2, 5, Taro Pharmaceutical Industries Ltd, 5, Valeant Pharmaceuticals, 2, 5; **M. Lebwohl**, Aditum Bio, 2, Abbvie, 5, Allergan, 2, Almirall, 2, Amgen, 5, Arcutis, Inc., 2, 5, Avotres Therapeutics, 2, BirchBioMed Inc., 2, BMD skincare, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Cara Therapeutics, 2, Castle Biosciences, 2, CorEvitas, LLC, 2, Dermavant Sciences, 2, 5, Evelo, 2, Eli Lilly, 5, Evommune, 2, 5, Facilitate International Dermatologic Education, 2, Foundation for Research and Education in Dermatology, 2, Inozyme Pharma, 2, Kyowa Kirin, 2, Leo Pharmaceutucals, 2, 5, Meiji Seika Pharma, 2, Incyte, 5, Janssen, 5, Menlo, 2, Mitsubishi, 2, Neuroderm, 2, Ortho Dermatologics, 5, Pfizer, 2, 5, Promius/Dr. Reddy's Laboratories, 2, Serono, 2, Theravance, 2, Verrica, 2, UCB, 5; **Y. Yang**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Miller**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Izutsu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **P. Ramachandran**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Sheng**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. You**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **W. Boehncke**, Leo, 2, 6, Pfizer, 5, Abbvie, 2, 6, Almirall, 2, 6, Celgene, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6.

Abstract Number: 1343

Guselkumab Treatment Modulates Core Psoriatic Arthritis Gene Expression in Two Phase 3 Clinical Trials (DISCOVER-1 and -2)

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

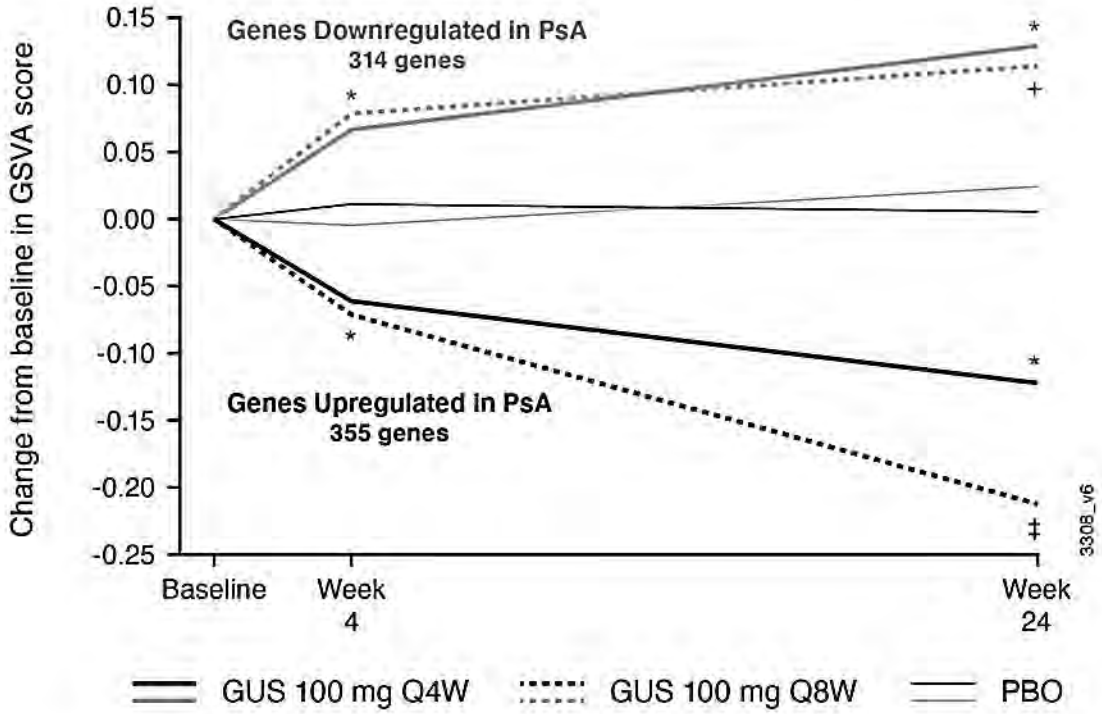
Background/Purpose: Guselkumab (GUS), an anti-IL-23 p19-subunit monoclonal antibody, demonstrated efficacy vs placebo (PBO) in reducing signs and symptoms of PsA in the phase-3 DISCOVER-1 & -2 studies.[1,2] This study evaluated gene expression in the blood of PsA patients (pts) in DISCOVER-1 & -2 and the impact of GUS on the expression of these genes.

Table. Top DEGs derived from PsA vs healthy whole blood transcriptomes

Upregulated in PsA				Downregulated in PsA			
Gene	logFC	logCPM	FDR	Gene	logFC	logCPM	FDR
ADGRG7	**5.92**	-0.90	0.02101	AK8	-1.36	-1.06	1.61E-07
ADAMTS2	**4.06**	0.82	0.006466	FTCD	-1.48	-1.74	1.67E-05
PGF	**3.21**	-0.68	0.006466	GPR15	-1.54	1.81	1.67E-05
PCSK9	**3.21**	-2.96	0.023872	CHRM3	-1.54	-2.62	9.6E-08
OLAH	**2.76**	0.75	0.004539	RFPL4AL1	-1.69	-3.34	0.009738
MAOA	**2.55**	-0.26	0.005463	SPACA3	-1.85	-3.23	0.000216
SLC2A14	**2.30**	0.59	0.022594	VANGL2	-1.95	-1.79	9.6E-08
MMP1	**2.25**	-1.16	0.004745	RFPL4A	-2.04	-1.28	0.004539
DAAM2	**2.12**	4.31	0.024628	GLYATL2	-2.77	-2.78	1.93E-15
				BCAR1	-3.13	-2.58	6.24E-26

Bold indicates positive change.
CPM, counts per million; DEGs, differentially expressed genes; FC, fold change; FDR, false discovery rate.

Figure. Change from baseline in median GSVA scores for upregulated and downregulated genes in PsA for GUS and PBO treatment arms from DISCOVER-1 and 2.



*, +, ‡ $p \leq 0.05, 0.01, 0.001$, respectively. Wilcox test performed between GUS (Q4W, dashed line; Q8W, solid line) and PBO.

GSVA, gene set variation analysis; GUS, guselkumab; PBO, placebo; PsA, psoriatic arthritis; Q4W, every 4 weeks; Q8W, every 8 weeks.

Methods: Pts were treated with GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week (W) 0, W4, then Q8W; or matching PBO. Whole transcriptome profiling by RNA-sequencing was performed using the Novaseq platform on blood samples obtained from a subset of 673 pts with PsA at baseline across the 2 DISCOVER studies, as well as from 21 demographically (age, sex, ethnicity) matched healthy controls procured independently of the clinical program. A subgroup (N=227), selected based on having baseline characteristics (demographics, disease activity, medication use) representative of the overall cross-study PsA population, also had serial blood samples (W0/W4/W24) evaluated. Significance of differentially expressed genes (DEGs) between PsA and healthy controls was defined by a false discovery rate < 0.05 based on a log-linear model using edgeR. Top genes were defined by significance and |logFC| >1. For cell type analysis, genes that changed with GUS treatment were tested for enrichment using Cibersort. Gene enrichment scores were calculated using Gene Set Variation Analysis.

Results: To define disease genes, we compared genes at baseline in pts with active PsA vs healthy control whole blood transcriptomes and detected 355 upregulated and 314 downregulated (top genes shown in Table), defined here as core disease genes. Upregulated genes were largely related to neutrophils, monocytes, macrophages, and extracellular matrix, whereas downregulated genes were related to T cells. The upregulated disease genes were significantly decreased and the downregulated disease genes were significantly increased by GUS treatment vs PBO at W4 and W24 (Figure). Upon stratification by ACR 20 response, changes in core disease gene expression from W0 were statistically significant among responders, but not in nonresponders, at W4 and W24 (data not shown). We then performed the second differential expression analysis comparing baseline to W4 and W24 for both PBO and GUS treatment arms to define genes that changed with treatment over time. At W4 and W24, we found many DEGs from baseline with GUS treatment and none with PBO. These included genes related to B-, T-, NK-, and plasma cells (increased by GUS) and neutrophils, monocytes, eosinophils, and macrophages (decreased by GUS), suggestive of a partial normalization of immune cell composition in whole blood.

Conclusion: Using whole transcriptome profiling, we detected DEGs in blood samples obtained from PsA pts vs healthy controls, suggesting a dysregulation of immune cell profiles in PsA. The majority of these disease-associated genes were modulated by GUS, with directionality toward a normalization of whole blood transcriptomic signatures.

1. Deodhar A et al. *Lancet*. 2020;395:1115
2. Mease P et al. *Lancet*. 2020;395:1126

Disclosure: S. Siebert, AbbVie, 5, 6, Biogen, 6, Amgen (previously Celgene), 5, 6, Bristol Myers Squibb, 5, Boehringer-Ingelheim, 5, Novartis, 5, 6, UCB, 5, 6, Janssen, 1, 5, 6, GlaxoSmithKline, 5; **K. Sweet**, Janssen Research and Development, LLC, 3, 11; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Q. Song**, Janssen Research and Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Miron**, Janssen Research and Development, LLC, (a subsidiary of Johnson & Johnson), 3, 11.

Abstract Number: 1344

Impact of Achieving Minimal Disease Activity on Patient-Reported Outcome Measures and Disease Activity Among Patients with Psoriatic Arthritis Treated with Biologic and Targeted Synthetic DMARDs

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Minimal disease activity (MDA) is a common goal for disease control when managing PsA. The aim of this study was to assess the association between MDA achievement and disease activity/patient-reported outcome measures (PROMs) after 6 months of biologic DMARD (bDMARD) or targeted synthetic DMARD (tsDMARD) therapy among PsA patients.

Methods: This study included patients with PsA enrolled in CorEvitas' prospective, multicenter, observational PsA/SpA Registry, who had not attained MDA, were initiating bDMARD or tsDMARD therapy at baseline, and had a 6-month follow-up visit (3/2013-3/2021). MDA was achieved at follow up if ≥5 of the following was met: tender joint count 68 ≤1, swollen joint count 66 ≤1, body surface area ≤3%, patient's assessment of pain ≤15 (0-100 VAS), patient's global assessment of disease activity ≤20 (0-100 VAS), HAQ-Disability Index ≤0.5, or Leeds Enthesitis Index ≤1. Baseline patient characteristics of MDA achievers and non-achievers were compared with t-tests and chi-square tests. Relative risk (RR) of achieving minimal clinically important difference (MCID) for PROMs and clinically meaningful improvements in disease activity components was estimated by Poisson generalized linear models adjusted for the baseline PROM or baseline disease activity component. RRs of maintaining or switching the initiated therapy by 6 months were calculated to determine the association with MDA achievement.

Results: MDA was achieved by 22.8% (285/1251) of patients 6 months after initiating bDMARD (n=987) or tsDMARD (n=264) therapy for PsA. Most baseline characteristics were similar between MDA achievers and non-achievers; however, those who achieved MDA tended to be younger with shorter duration of disease and were less likely to be female, obese, or have a history of depression (**Table 1**). DMARD therapy at initiation was similar between MDA achievers and non-achievers, except that more achievers were bDMARD-naïve at baseline (**Table 1**). Patients who achieved MDA were more likely to maintain the initiated bDMARD (RR =1.3, 95% CI 1.2-1.5) or tsDMARD (RR =1.4, 95% CI 1.1-1.8) therapy and less likely to switch from the initiated bDMARD (RR=0.5, 95% CI 0.3-0.7) and tsDMARD (RR=0.6, 95% CI 0.4-1.1) therapy (**Figure 1**). MDA achievement was associated with higher probability of achieving MDA components and MCID in PROMs at 6 months (**Figure 2**).

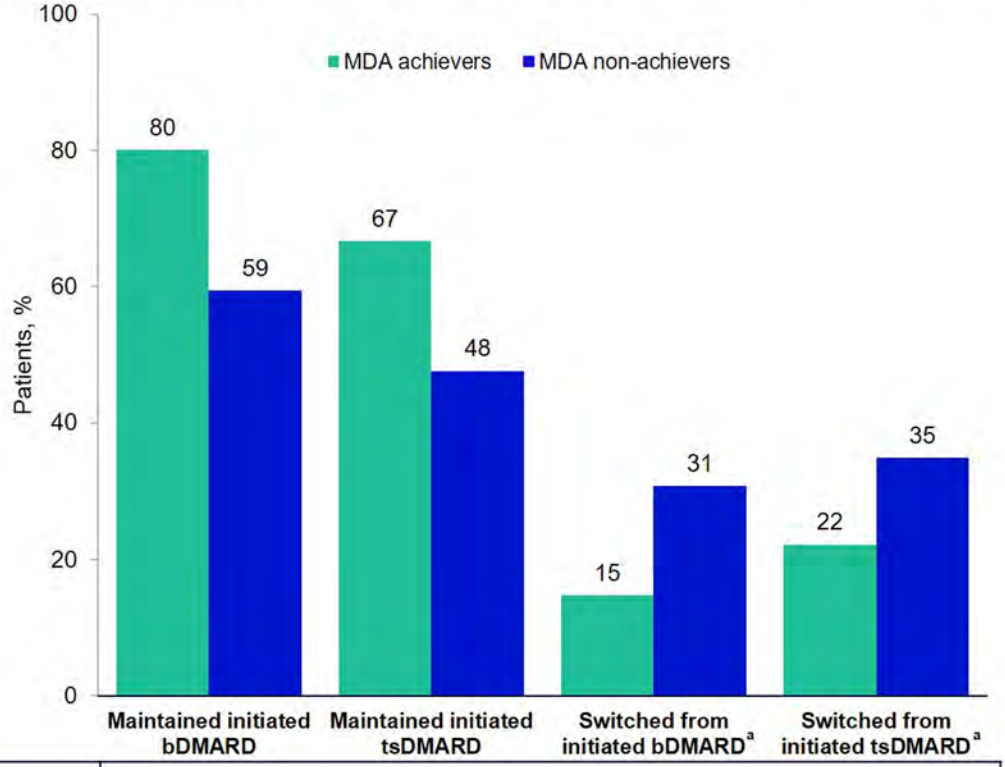
Conclusion: In this real-world study, MDA achievement was associated with a higher probability of achieving clinically meaningful improvements in disease activity and PROMs, suggesting MDA as a viable target endpoint for disease control. Patients who achieved MDA were also more likely to be persistent on b/tsDMARD therapy. This data underscores the importance of utilizing MDA in clinical practice in order to achieve optimal outcomes for patients.

Table 1. Baseline demographics and clinical characteristics among patients with PsA who initiated biologic or targeted synthetic DMARD treatment, by MDA achievement at 6 months follow-up

Demographic and health characteristics	MDA Status: Achievers N=285	MDA Status: Non-Achievers N=966	*P*-value[a]
Age, [years], mean ± SD	52.3 ± 13.2	53.9 ± 11.9	0.05
Female, n (%)	142 (50.0)	594 (61.6)	<0.001
White, n (%)	257 (90.2)	891 (92.2)	0.27
BMI category, n (%)			0.02
Underweight/normal weight	41 (14.5)	95 (10.1)	
Overweight	78 (27.7)	219 (23.2)	
Obese	163 (57.8)	628 (66.7)	
History of depression, n (%)	36 (12.6)	239 (24.7)	<0.001
Clinical characteristics			
Duration since PsA diagnosis [years], mean ± SD	5.9 ± 7.2	7.0 ± 7.8	0.04
Duration since PsA symptoms [years], mean ± SD	8.3 ± 9.0	10.9 ± 9.7	<0.001
BSA >3% affected, n (%)	106 (37.2)	383 (39.6)	0.46
Presence of enthesitis, n (%)	77 (27.0)	371 (38.4)	<0.001
Presence of dactylitis, n (%)	80 (28.1)	154 (15.9)	<0.001
DMARD treatment initiated at baseline[b]			
bDMARD, n (%)	231 (81)	756 (78)	0.31
Monotherapy	146 (63)	435 (58)	0.07
Naïve	129 (45)	289 (30)	<0.001
tsDMARD, n (%)	54 (19)	210 (22)	0.31
Monotherapy	26 (58)	121 (58)	0.12
Naïve	235 (83)	747 (77)	0.06

[a]*P*-values for differences between MDA groups were calculated using student t-test for estimated difference of means for continuous measures and chi-squared test for differences in distribution of categorical variables. [b]Monotherapy and naïve DMARD treatment groups are overlapping. bDMARD, biologic DMARD; BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; MDA, minimal disease activity; SD, standard deviation; tsDMARD, targeted synthetic DMARD.

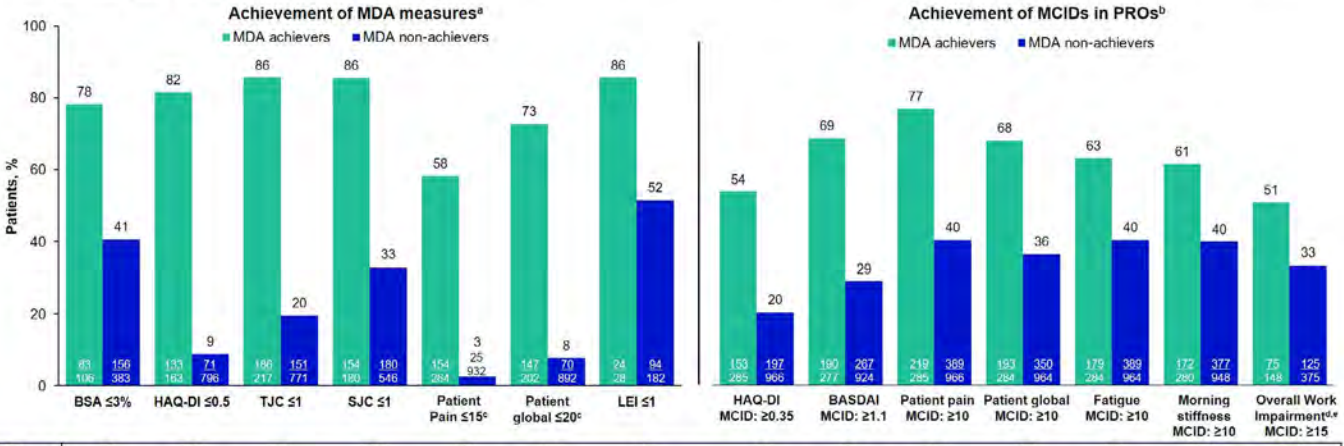
Figure 1. Treatment patterns and relative risk of switching or maintaining therapy in MDA achievers versus non-achievers at 6-month follow-up[a]



	Maintained initiated bDMARD	Maintained initiated tsDMARD	Switched from initiated bDMARD[a]	Switched from initiated tsDMARD[a]
RR[b] (95% CI)	1.3 (1.2, 1.5)	1.4 (1.1, 1.8)	0.5 (0.3, 0.7)	0.6 (0.4, 1.1)
P-value[c]	<0.001	0.005	<0.001	0.100

[a]Switching is defined as evidence of discontinuation of initiated therapy and initiation of a new therapy within the 6-month follow-up. [b]Relative risk estimates from the Poisson generalized linear model, with MDA non-achieving group as reference. [c]*P*-value is testing whether the relative risk of maintaining or switching from initiated therapy at six months for the MDA achievers is different from 1.0. bDMARD, biologic DMARD; MDA, minimal disease activity; tsDMARD, targeted synthetic DMARD.

Figure 2. Proportions of patients and relative risk of achieving MDA component threshold or MCID in PROMs among MDA achievers versus non-achievers at 6-month follow-up



	BSA ≤3%	HAQ-DI ≤0.5	TJC ≤1	SJC ≤1	Patient Pain ≤15[c]	Patient global ≤20[c]	LEI ≤1	HAQ-DI MCID: ≥0.35	BASDAI MCID: ≥1.1	Patient pain MCID: ≥10	Patient global MCID: ≥10	Fatigue MCID: ≥10	Morning stiffness MCID: ≥10	Overall Work Impairment[d,e] MCID: ≥15
RR[f] (95% CI)	1.9 (1.6, 2.2)	6.6 (5.1, 8.6)	3.9 (3.4, 4.6)	2.5 (2.2, 2.9)	19.5 (12.8, 29.7)	8.4 (6.5, 10.9)	1.5 (1.2, 1.8)	4.2 (3.6, 5.0)	3.3 (2.9, 3.7)	2.4 (2.1, 2.6)	2.5 (2.3, 2.9)	2.2 (1.9, 2.4)	1.7 (1.6, 2.0)	2.0 (1.6, 2.4)
P-value[g]	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001

[a]Analysis was limited to patients who did not meet MDA criteria at baseline. [b]MCID values are the minimum point reductions from baseline that are considered clinically meaningful. [c]Measured using a 100-point visual analog scale. [d]MCID for overall work impairment is a percent increase from baseline. [e]Overall work impairment was only determined for those who reported employment at baseline. [f]Relative risk estimates determined from a Poisson generalized linear model, with MDA not-achieving group as reference. [g]*P*-value is testing whether the relative risk of maintaining or switching from initiated therapy at six months for the MDA achievers is different from 1.0. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; HAQ-DI, The Health Assessment Questionnaire Disability Index; MCID, minimal clinically important difference; LEI, Leeds enthesitis index; MDA, minimal disease activity; PRO, patient-reported outcome; SJC, swollen joint count; TJC, tender joint count.

Disclosure: A. Ogdie, Amgen, 2, AbbVie, 2, 11, BMS, 2, Celgene, 2, CorEvitas, 2, Gilead, 2, Janssen, 2, Lilly, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer, 2, 5, Novartis, 2, 5; **R. McLean**, CorEvitas, 3; **M. Marchese**, CorEvitas, 3; **T. Blachley**, CorEvitas, 3; **L. Anatale-Tardiff**, CorEvitas, 3; **C. Saffore**, AbbVie, 3, 11; **K. Douglas**, AbbVie, 3, 11; **D. Quach**, AbbVie, 3; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1345

Long-Term Safety and Effectiveness of Upadacitinib in Patients with Psoriatic Arthritis: Results at 56 Weeks from the SELECT-PsA 1 Study

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Background/Purpose: In the SELECT-PsA 1 study, through 24 weeks (wks), once daily upadacitinib 15 mg (UPA15) and 30 mg (UPA30) showed improvements in musculoskeletal symptoms, psoriasis, physical function, pain, fatigue, and quality of life, as well as inhibition of radiographic progression in patients (pts) with psoriatic arthritis (PsA) and inadequate response or intolerance to ≥1 non-biologic disease-modifying antirheumatic drug (DMARD).[1] This analysis reports the efficacy and safety of UPA vs adalimumab (ADA) up to 56 wks from the ongoing long-term extension of SELECT-PsA 1.

Methods: Pts received UPA15 or UPA30, ADA 40mg every other wk for 56 wks, or PBO through wk 24 switched thereafter to either UPA15 or UPA30 until wk 56. Efficacy endpoints as listed and defined in the **Table** were analyzed at wk 56. Results for binary endpoints are based on non-responder imputation analysis; treatments were compared using the Cochran-Mantel-Haenszel test. Results for non-radiographic continuous endpoints are based on mixed model repeated measures model based on as observed data. Radiographic endpoints were analyzed based on linear extrapolation. Treatment-emergent adverse events (TEAEs) per 100 pt years (PY) were summarized for pts who received ≥1 dose of study drug.

Results: Of 1704 pts who received ≥1 dose of study drug, 1419 (83.2%) completed 56 wks of treatment on study drug. Across all treatment groups, the proportions of pts who had achieved ACR20/50/70, MDA, PASI75/90/100, resolution of enthesitis, and resolution of dactylitis were maintained or further improved from wk 24[1] through wk 56; these proportions were generally greater for pts originally randomized to UPA vs ADA (**Table**). At wk 56, mean change

Table. Efficacy Endpoints at Week 56

Endpoint	PBO → UPA15	PBO → UPA30	UPA15	UPA30	ADA
ACR20, %	73.0	74.1	74.4	74.7#	68.5
ACR50, %	54.5	60.4	59.7*	60.5#	51.3
ACR70, %	29.9	35.8	40.6*	43.7#	31.2
Minimal Disease Activity, %	29.4	35.8	44.8	47.3#	39.6
PASI75[a], %	58.3	60.2	65.4	63.3	61.1
PASI90[a], %	41.7	53.7	49.1	49.5	46.9
PASI100[a], %	22.3	38.9	34.6	39.5	31.3
Resolution of enthesitis by Leeds Enthesitis Index[b], %	38.1	45.5	59.3	58.1	54.0
Resolution of dactylitis by Leeds Dactylitis Index[c], %	47.7	59.0	75.0	74.8	74.0
Δ from BL in Bath Ankylosing Spondylitis Disease Activity Index[d]	-3.1	-3.1	-3.3	-3.2	-2.8
Δ from BL in modified total Sharp/van der Heijde Score (mTSS)	0.44[e]		-0.05†	0.02‡	-0.06

* and †, p≤0.05; for UPA15 vs ADA and PBO, respectively; # and ‡, p≤0.05; for UPA30 vs ADA and PBO, respectively.

[a] for pts with psoriasis affecting ≥3% of body surface area at BL. [b] for pts with LEI >0 at BL. [c] for pts with LDI >0 at BL. [d] for pts with psoriatic spondylitis at BL. [e]pooled PBO.

ACR20/50/70, ≥20%/50%/70% improvement in American College of Rheumatology criteria; ADA, adalimumab; BL, baseline; PASI75/90/100, ≥75%/90%/100% improvement in Psoriasis Area and Severity Index; PBO, placebo; pts, patients; UPA, upadacitinib.

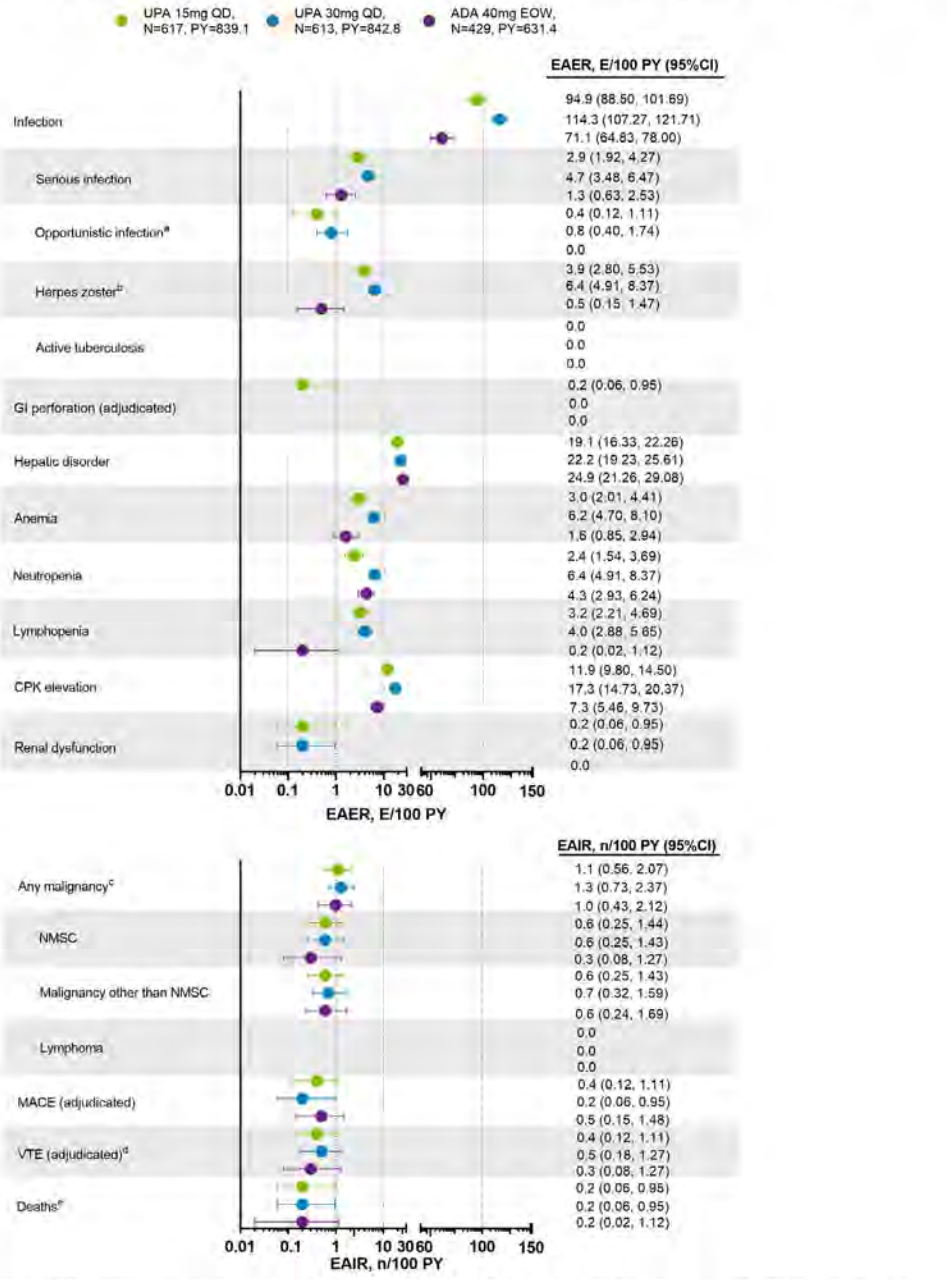
from BL in mTSS was similar with UPA15, UPA30, and ADA. Improvements in pts who switched from PBO to UPA were generally similar to those originally randomized to UPA at wk 56. Through wk 56, the rates of TEAEs and serious AEs, including serious infections, were similar in the UPA15 and ADA arms and higher with UPA30 (**Figure**). The rate of herpes zoster was higher with UPA vs ADA in a dose-dependent manner. Malignancies were reported at similar rates among all treatment groups. Adjudicated venous thromboembolic events and major adverse cardiovascular events were reported in all groups with comparable rates. Two deaths were reported with UPA15, 2 with UPA30, and 1 with ADA; 1 death was reported with PBO during the 24-wk PBO-controlled period.

Conclusion: Efficacy responses were maintained or further improved with UPA15 and UPA30 over 56 wks and were numerically higher for pts originally randomized to UPA vs ADA. The inhibition of radiographic progression was maintained at wk 56 and was similar with UPA and ADA. At wk 56, improvements in efficacy were observed in pts who switched from PBO to UPA. No new safety findings were observed with longer exposure to UPA.

References

1. McInnes IB et al. *Ann Rheum Dis*, 2020; 79:12.

Figure. Exposure-adjusted Event and Incidence Rates of Treatment-emergent AEs Through Week 56



ADA, adalimumab; AE, adverse event; CI, confidence interval; CPK, creatine phosphokinase; EAER, exposure-adjusted event rate; EAIR, exposure-adjusted incidence rate; EOW, every other week; GI, gastrointestinal; MACE, major adverse cardiovascular events (defined as non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death); NMSC, non-melanoma skin cancer; PY, patient years; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolism (defined as deep vein thrombosis [DVT] and pulmonary embolism [PE]).

[a] Opportunistic infections excluding tuberculosis and herpes zoster. UPA15: one event each of candida urethritis, bronchopulmonary aspergillosis, and oral fungal infection; UPA30: one event each of cytomegalovirus infection, oropharyngeal candidiasis, and pneumocystis jirovecii pneumonia; and four events of oral fungal infection.

[b] Herpes zoster; most events were mild or moderate in severity, limited to 1-2 dermatomes, and did not lead to study drug discontinuation.

[c] UPA15: 4 basal cell carcinomas, 2 squamous cell carcinoma of skin, and 1 event each of endometrial adenocarcinoma, lung adenocarcinoma, lung cancer metastatic, malignant melanoma, and neuroendocrine carcinoma; UPA30: 2 basal cell carcinomas, 2 squamous cell carcinoma of skin, and 1 event each of adenocarcinoma of colon, Bowen's disease, breast cancer, clear cell renal cell carcinoma, invasive breast carcinoma, lung adenocarcinoma, and plasma cell myeloma); ADA: 2 basal cell carcinomas, and 1 event each of colon cancer metastatic, ovarian cancer, pancreatic carcinoma metastatic, and uterine cancer.

[d] 10 VTEs were reported in 9 patients. UPA15: 1 DVT, 1 PE, 1 pt had had concurrent DVT and PE; UPA30: 1 DVT, 3 PEs; ADA: 2 DVTs

[e] Deaths: UPA15: 1 due to metastatic lung cancer and 1 due to lower respiratory tract infection; UPA30: 1 due to corona virus infection and 1 due to interstitial lung disease; ADA: traffic accident. One death was reported in the placebo group during the 24-week placebo-controlled period in a patient who was driving and experienced an unspecified emergency.

Disclosure: I. McInnes, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **K. Kato**, AbbVie, 3, 11; **M. Magrey**, AbbVie, 2, 5, UCB Pharma, 5, Novartis, 2, Eli Lilly, 2, Pfizer, 2, Amgen, 5; **J. Merola**, AbbVie, 2, Arena, 2, Biogen, 2, Dermavant Sciences, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer Inc, 2, Sun Pharma, 2, UCB Pharma, 2, Avotres Inc, 2, Celgene, 2, EMD Serono, 2, Regeneron, 2, Sanofi, 2, Leo Pharma, 2, Merck, 2, Bristol-Myers Squibb, 2; **M. Kishimoto**, AbbVie, 2, Amgen-Astellas BioPharma, 2, Asahi-Kasei Pharma, 2, Ayumi Pharma, 2, BMS, 2, Celgene, 2, Chugai, 2, Daiichi-Sankyo, 2, Eisai, 2, Eli Lilly, 2, Gilead, 2, Janssen, 2, Kyowa Kirin, 2, Novartis,

2, Ono Pharma, 2, Pfizer, 2, Tanabe-Mitsubishi, 2, Teijin Pharma, 2, UCB Pharma, 2; **C. Pacheco Tena**, Eli Lilly, 5, 6, AbbVie, 5, 6, Roche, 5, 6, Pfizer, 5, 6, Janssen, 5, 6, Astra-Zeneca, 5, 6, UCB, 5, 6, Gilead, 5, 6, R-Pharm, 5, 6, Sanofi Regeneron, 5, 6; **D. Haaland**, AbbVie, 2, 5, 6, Adiga Life Sciences, 5, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Can-Fite BioPharma, 5, Celgene, 5, Eli Lilly, 5, 6, Gilead, 5, GlaxoSmithKline, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Regeneron, 5, Sanofi, 2, 5, 6, UCB, 2, 5, 6, AstraZeneca, 6, Merck, 6, Takeda, 2, 6, Roche, 2, 6; **L. Chen**, AbbVie, 3, 11; **Y. Duan**, AbbVie, 11; **P. Zueger**, AbbVie, 3, 11; **J. Liu**, AbbVie, 3, 11; **R. Lippe**, AbbVie, 3, 11; **A. Pangan**, AbbVie, 3, 11; **F. Behrens**, Chugai, 5, 6, AbbVie, 6, Amgen, 6, GlaxoSmithKline, 5, Janssen, 5, 6, Pfizer, 5, 6, Roche, 5, 6, Boehringer Ingelheim, 6, Celgene, 6, Eli Lilly, 6, Merck, 6, Novartis, 6, Sanofi, 6, UCB, 6.

Abstract Number: 1346

Comparable Safety Profile of Guselkumab in Psoriatic Arthritis and Psoriasis: Results from Phase 3 Trials Through 1 Year

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: DISCOVER 1&2 (PsA) and VOYAGE 1&2 (psoriasis [PsO]) are Phase 3 trials of guselkumab (GUS). Here we compared safety results through up to 1 year of GUS in PsA and PsO patients.

Methods: In DISCOVER 1&2, 1120 patients with active PsA despite standard therapy were treated. Most patients were biologic-naïve; ~30% in DISCOVER 1 had previous exposure to 1-2 TNFi. Concomitant MTX (57%), oral corticosteroids (17%), and NSAIDs (64%) were permitted. Patients were randomized to subcutaneous (SC) GUS 100 mg at week (W) 0, W4, then every 8 weeks (Q8W); GUS 100 mg Q4W; or placebo (PBO). At W24, PBO patients were switched to GUS 100 mg Q4W. In VOYAGE 1&2, in which concomitant MTX use was prohibited, 1245 patients with moderate to severe PsO were treated and randomized to SC GUS 100 mg at W0, W4, W12, then Q8W; or PBO at W0, W4, W12, with crossover to GUS at W16, W20, then Q8W. Adverse events (AEs) and laboratory parameters, analyzed by National Cancer Institute-Common Terminology Criteria for AEs [NCI-CTCAE] toxicity grades, were summarized through the PBO-controlled periods and 1 year.

Results: Safety profiles were generally consistent across the GUS PsO and PsA clinical programs (Table). Time-adjusted incidence rates for numbers of AEs, serious AEs, serious infections, malignancy, major adverse cardiovascular events and AEs leading to discontinuation were generally similar between PsO and PsA. No cases of anaphylaxis or opportunistic infections were reported. Proportions of patients with decreased neutrophil counts and

Treatment-Emergent AEs During PBO-controlled Period and Through 1 Year: VOYAGE & DISCOVER Trials									
	Pooled VOYAGE 1&2			Pooled DISCOVER 1&2					
Time Period	W0-16		Through 1 Year	W0-24[b]			Through 1 Year		
(N=)	PBO (422)	GUS Q8W (823)	Combined GUS[a] (1221)	PBO[c] (372)	GUS Q8W (375)	GUS Q4W (373)	GUS Q8W (375)	GUS Q4W (373)	Combined GUS[†] (1100)
Total pt-yrs of follow-up	128	255	974	173	173	172	384	385	973
Incidence/100 pt-yrs (95% CI)[d]									
AEs	317 (287,349)	330 (308,353)	259 (249, 270)	219 (198,243)	256 (232,281)	221 (200, 245)	218 (203,233)	177 (164,191)	191 (182, 199)
SAEs	5 (2, 10)	6 (4, 10)	6 (5, 8)	9 (5, 15)	4 (2, 8)	5 (2, 10)	6 (4, 9)	4 (2, 7)	6 (4, 7)
AEs leading to study agent discontinuation	3 (0.9, 8)	4 (2, 8)	2 (2, 4)	4 (2, 8)	3 (1, 7)	7 (4, 12)	2 (1, 4)	4 (2, 6)	3 (2, 5)
Infections	86 (71, 104)	98 (86, 111)	98 (92, 104)	58 (48,71)	58 (47, 71)	63 (51, 76)	58 (50, 66)	53 (46, 61)	55 (50, 60)
Serious Infections	0. 8 (0, 4)	0.4 (0, 2)	1 (0.5, 2)	4 (2, 8)	0.6 (0, 3)	2 (0.4, 5)	2 (0.6, 3)	1 (0, 2)	2 (0.9, 3)
All Malignancy	0 (0,2)	0.4 (0,2)	1 (0.4, 2)	0.6 (0, 3)	1 (0, 4)	0 (0, 2)	0.5 (0, 2)	0 (0, 0. 8)	0 (0,1)
MACE	0 (0, 2)	0.4 (0, 2)	0.4 (0, 1)	0.6 (0, 3)	0 (0, 2)	0.6 (0, 3)	0 (0, 0.8)	0.3 (0, 1.4)	0.1 (0, 0.6)
% pts with ≥1 injection site reaction	3.1	4.5	5.0	0.3	1.3	1.1	1.6	2.4	1.7

[a]Placebo crossover patients were included in the combined GUS column after crossover to GUS
[b]For all patients who discontinued study treatment early with the last dose of PBO/GUS prior to W24 and who did not receive any PBO/GUS at or after Wk24, all data including the final safety follow-up visit collected through 1 year were included
[c]For patients in PBO group who switched to GUS due to cross-over or inadvertently, only data prior to first administration of GUS were included.
[d]CI based on an exact method assuming observed number of events follows a Poisson distribution
AE, adverse event; CI, confidence interval; GUS, guselkumab; MACE, major adverse cardiovascular events; PBO, placebo; pt, patient; Q4W, every 4 weeks; Q8W, every 8 weeks; SAE, serious adverse event; W, week; yrs, years

elevations in hepatic transaminases were slightly higher in PsA versus PsO. These abnormalities were mostly of NCI-CTCAE Grade 1 or 2 (< lower limit of normal-1000/mm^3 for neutrophils; < 5.0 x upper limit of normal for aspartate transaminase/alanine aminotransferase [AST/ALT]), generally transient, required no medical interventions, resolved spontaneously, and did not lead to interruption or discontinuation of treatment. Through 1 year, proportions of patients with ALT/AST elevations in PsA trials were slightly higher for GUS Q4W than Q8W and in patients with versus without baseline MTX use.

Conclusion: The GUS safety profile was generally consistent in PsA and PsO GUS-treated patients through 1 year of the DISCOVER and VOYAGE trials.

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Abstract Number: 1347

Ixekizumab Efficacy in Patients with Psoriatic Arthritis Presenting with Symptoms Indicative of Axial Involvement

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Many patients with psoriatic arthritis (PsA) experience back pain and stiffness indicative of axial involvement [1]. The prevalence of axial involvement varies between 25-70% [2]. Ixekizumab (IXE), a monoclonal antibody with high affinity for IL17-A, has been studied in Phase 3 trials in patients with PsA (SPIRIT-P1 [Biologic-naïve; NCT01695239] and SPIRIT-P2 [Inadequate response or intolerant to 1 or 2 TNF inhibitors (TNFi); NCT02349295]) [3] [4]. The objective of this analysis was to determine the efficacy of IXE up to 52 weeks (Wks) in reducing axial symptoms and improving quality of life in patients with active PsA presenting with symptoms indicative of axial involvement.

Methods: This post-hoc analysis included data from two subpopulations of patients with PsA (pooled SPIRIT-P1 and -P2). Symptoms indicative of axial involvement were defined as Bath Ankylosing Spondylitis Disease Activity Index

Table. Baseline values and change from baseline (mBOCF) in the overall analysis population at Wks 16, 24 and 52 for BASDAI and ASDAS related endpoints in patients with PsA and axial pain. Data presented as mean (SD) unless otherwise specified. ‡p<0.001 vs PBO

	PBO (N=151)		IXE Q4W (N=162)		
Baseline values	**Wk 0**		**Wk 0**		
BASDAI	6.7 (1.4)		6.6 (1.3)		
Q2	7.0 (1.7)		6.7 (1.7)		
Q5	7.3 (1.5)		7.3 (1.5)		
Q6	5.8 (2.7)		5.5 (2.7)		
mBASDAI	6.7 (1.4)		6.6 (1.3)		
ASDAS	3.7 (0.8)		3.6 (0.9)		
SF-36 PCS	29.9 (7.4)		30.0 (8.4)		
Outcome measures	**Wk 16**	**Wk 24**	**Wk 16**	**Wk 24**	**Wk 52**
ASDAS	-0.4 (0.8)	-0.4 (0.8)	-1.2 (1.2)‡	-1.3 (1.2)‡	-1.4 (1.2)
BASDAI50, n (%)	16 (11)	12 (8)	51 (32)‡	61 (38)‡	64 (40)
mBASDAI	-1.0 (1.7)	-1.0 (1.7)	-2.1 (2.1)‡	-2.4 (2.3)‡	-2.7 (2.1)
SF-36 PCS	1.9 (7.3)	2.0 (6.9)	5.8 (8.8)‡	6.8 (9.9)‡	8.8 (9.5)

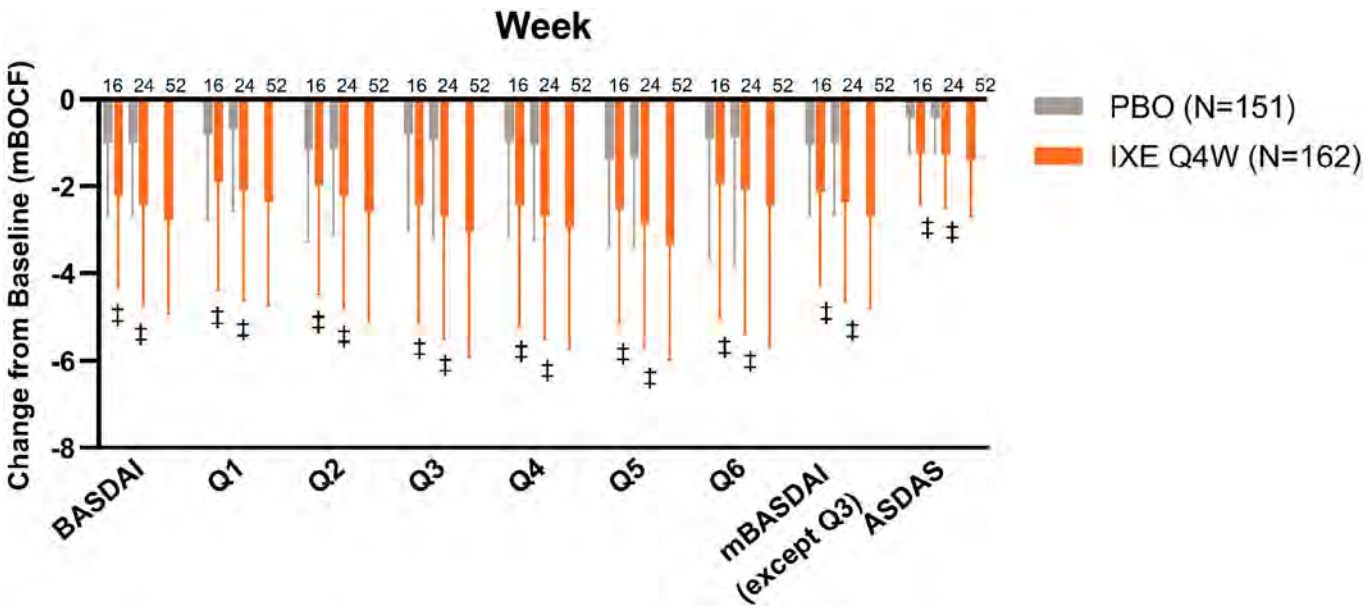

Figure. Change from baseline (mBOCF) in BASDAI and ASDAS related endpoints in patients with PsA and axial pain in the overall analysis population. Data presented as mean (SD). ‡p<0.001 vs PBO.

(BASDAI) Q2 (back pain) ≥4, and an average of Q5 + Q6 (intensity and duration of morning stiffness in the spine) ≥4 at baseline. Patients included in the sensitivity analysis subgroup 1 were, in addition to the above-mentioned criteria, < 45 years of age, while patients included in sensitivity analysis subgroup 2 were aged < 45 but had also elevated C-reactive protein (CRP) (> 5 mg/l) at baseline. Efficacy of IXE was analysed using BASDAI questions, total BASDAI, mBASDAI (without Q3), and Ankylosing Spondylitis Disease Activity Score (ASDAS) change from baseline, as well as

BASDAI50 response and Short-Form-36 physical component summary (SF-36 PCS) improvement, at Wks 16, 24 and 52. Treatment comparison was done using logistic regression for BASDAI50, and analysis of covariance (ANCOVA) model for other endpoints. Missing data for binary and continuous endpoints were imputed by non-responder imputation and modified baseline carried forward (mBOCF), respectively.

Results: A total of 313 patients (placebo (PBO), N=151; IXE Q4W, N=162) met the overall analysis inclusion criteria. Baseline values for BASDAI and ASDAS related endpoints were balanced across treatment arms (Table). Improvement in axial symptoms were significantly greater in patients treated with IXE compared to PBO at Wks 16 and 24 (Figure). Improvement in quality of life (QoL) measures (SF-36 PCS) were also significantly greater in patients treated with IXE compared to PBO at Wks 16 and 24 (Table). Similar results were observed for patients < 45 years, and in patients < 45 years with CRP > 5 mg/l at baseline (sensitivity analysis, data not shown).

Conclusion: IXE is effective in reducing axial symptoms and improving QoL in patients with active PsA presenting with symptoms indicative of axial involvement.

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2. Feld J. Nat Rev Rheumatol. 2018;14
3. Orbai A. Clin Exp Rheumatol. 2020[online]
4. Genovese MC. Rheumatol. 2018;57(11)

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Abstract Number: 1348

Predictors for Achievement of Low Disease Activity at Week 56 in Patients with Psoriatic Arthritis Who Received Upadacitinib 15 Mg Once Daily: Pooled Analysis of Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Upadacitinib (UPA) 15 mg once daily (QD) has demonstrated efficacy and safety in patients with psoriatic arthritis (PsA) for up to 56 weeks in the Phase 3 SELECT-PsA 1 and 2 trials.[1,2] This post hoc analysis of these studies explored the association of baseline characteristics and short-term responses with achievement of minimal disease activity (MDA) and Disease Activity Index for Psoriatic Arthritis (DAPSA) low disease activity (LDA).

Methods: Data were pooled from patients with prior inadequate response or intolerance to ≥1 non-biologic (b) DMARDs (SELECT-PsA 1) or ≥1 bDMARDs (SELECT-PsA 2) originally randomized to UPA 15 mg QD. Logistic re-

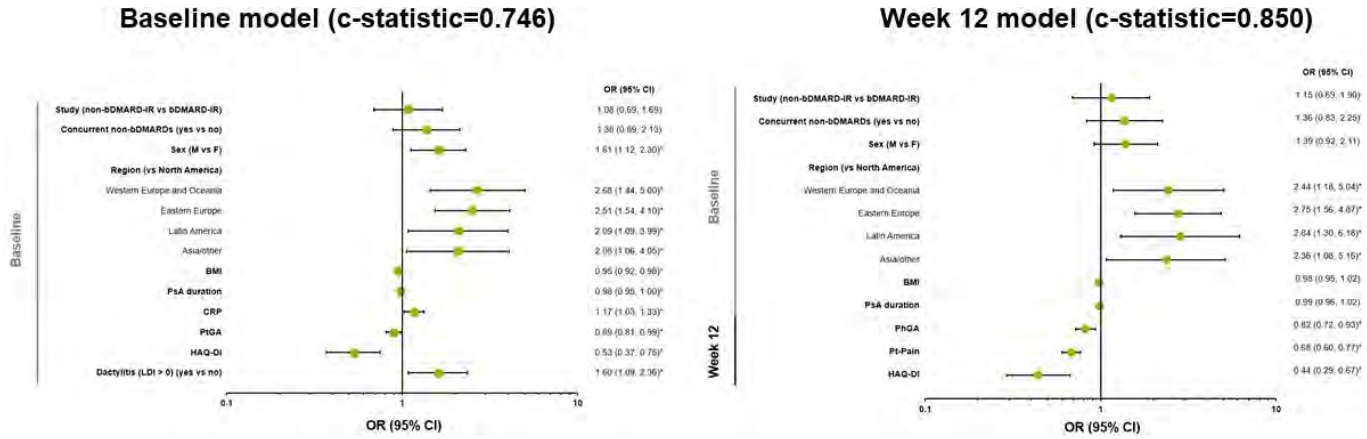

Figure 1. Predictors of Achievement of MDA at Week 56 with Upadacitinib 15 mg – Evaluated Simultaneously. *p<0.05. c-statistics: 0.6 indicates a fair model, 0.7 indicates a good model, and 0.8 indicates a strong model. Non-responder imputation was used for MDA at Week 56. bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; F, female; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate responder; LDI, Leeds Dactylitis Index; M, male; MDA, minimal disease activity; OR, odds ratio; PhGA, Physician's Global Assessment; PsA, psoriatic arthritis; PtGA, Patient's Global Assessment; Pt-Pain, Patient's Assessment of Pain.

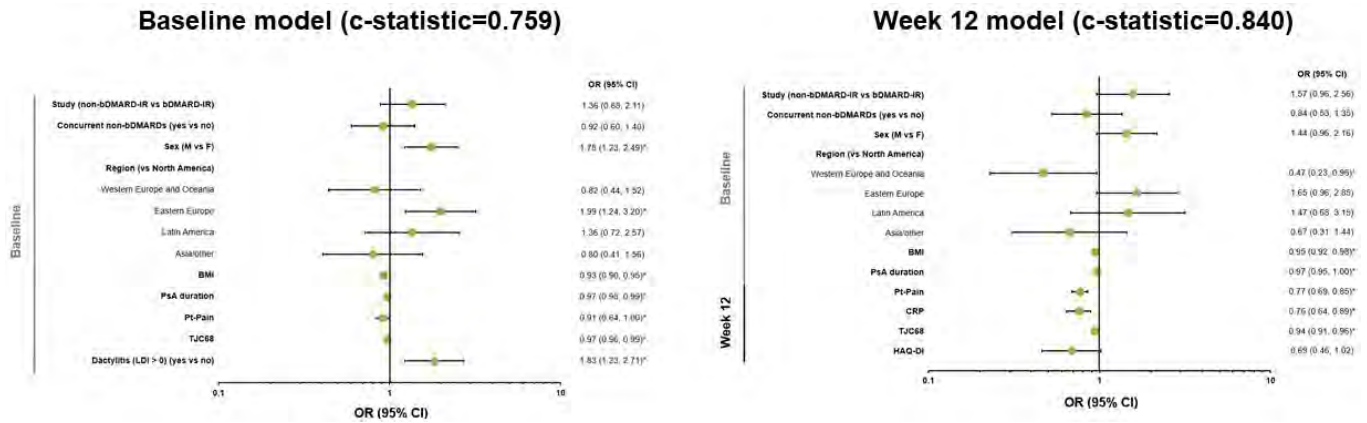

Figure 2. Predictors of Achievement of DAPSA LDA at Week 56 with Upadacitinib 15 mg – Evaluated Simultaneously. *p<0.05. c-statistics: 0.6 indicates a fair model, 0.7 indicates a good model, and 0.8 indicates a strong model. Non-responder imputation was used for DAPSA LDA at Week 56. bDMARD, biologic disease-modifying antirheumatic drug; BMI, body mass index; CI, confidence interval; CRP, C-reactive protein; DAPSA, Disease Activity Index for Psoriatic Arthritis; F, female; HAQ-DI, Health Assessment Questionnaire-Disability Index; IR, inadequate responder; LDA, low disease activity; LDI, Leeds Dactylitis Index; M, male; OR, odds ratio; PsA, psoriatic arthritis; Pt-Pain, Patient's Assessment of Pain; TJC68, tender joint count in 68 joints.

gression models were used to assess the association between baseline characteristics and short-term (Week 12) responses with achieving MDA or DAPSA LDA at 56 weeks, sustained MDA (MDA at Weeks 36 and 56), or sustained DAPSA LDA (DAPSA LDA at Weeks 36, 44, and 56). Each predictor was evaluated separately in an initial model that included effects for study and concurrent non-bDMARD use. Odds ratios and concordance (c-)statistics were used to determine the predictive accuracy. Statistically significant predictors were then evaluated simultaneously using stepwise logistic regression with the Akaike Information Criterion for model-building.

Results: Of 640 patients included in the analysis, 40% and 47% achieved MDA and DAPSA LDA, respectively, at 56 weeks. Evaluated separately, younger age, sex (male), geographic region, lower weight, lower body mass index, the presence of dactylitis or enthesitis, and lower scores of Patient's Assessment of Pain (Pt-Pain), Patient's Global Assessment (PtGA), tender joint count in 68 joints, and Health Assessment Questionnaire-Disability Index (HAQ-DI) were significant baseline predictors for achieving MDA and DAPSA LDA at Week 56. Lower Pt-Pain (Weeks 12–24) and PtGA (Weeks 16–24) scores were strongly predictive (c-statistics >0.8) of achieving MDA at Week 56, and both measures (from Week 8) were moderately predictive (c-statistics >0.7) of achieving DAPSA LDA. Evaluated simultaneously with several baseline characteristics, lower Pt-Pain and HAQ-DI scores at Week 12 were included in models strongly predictive of achieving MDA (c-statistic=0.850; **Figure 1**) and DAPSA LDA (c-statistic=0.840; **Figure 2**) at Week 56. For each 1-point increase in Pt-Pain or HAQ-DI scores at Week 12 (after adjusting for other effects in the model), patients were less likely to achieve MDA (by 32% or 56%, respectively) or DAPSA LDA (by 23% or 31%, respectively) at Week 56. Predictors for achieving sustained MDA and sustained DAPSA LDA were generally similar to those identified for achieving MDA and DAPSA LDA, respectively.

Conclusion: In patients with PsA receiving UPA 15 mg, baseline characteristics and early responses strongly predicted achievement of MDA or DAPSA LDA at Week 56. This may guide considerations of treatment targets in clinical trials and encourage physicians to further optimize treatment of their patients in clinical practice.

1. McInnes IB, et al. Ann Rheum Dis 2020;79:16–7.

2. Mease PJ, et al. Rheumatol Ther 2021 [Epub ahead of print].

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Abstract Number: 1349

Joint-specific Responses to Tofacitinib and Adalimumab in Patients with Psoriatic Arthritis: Post Hoc Analysis of a Phase 3 Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

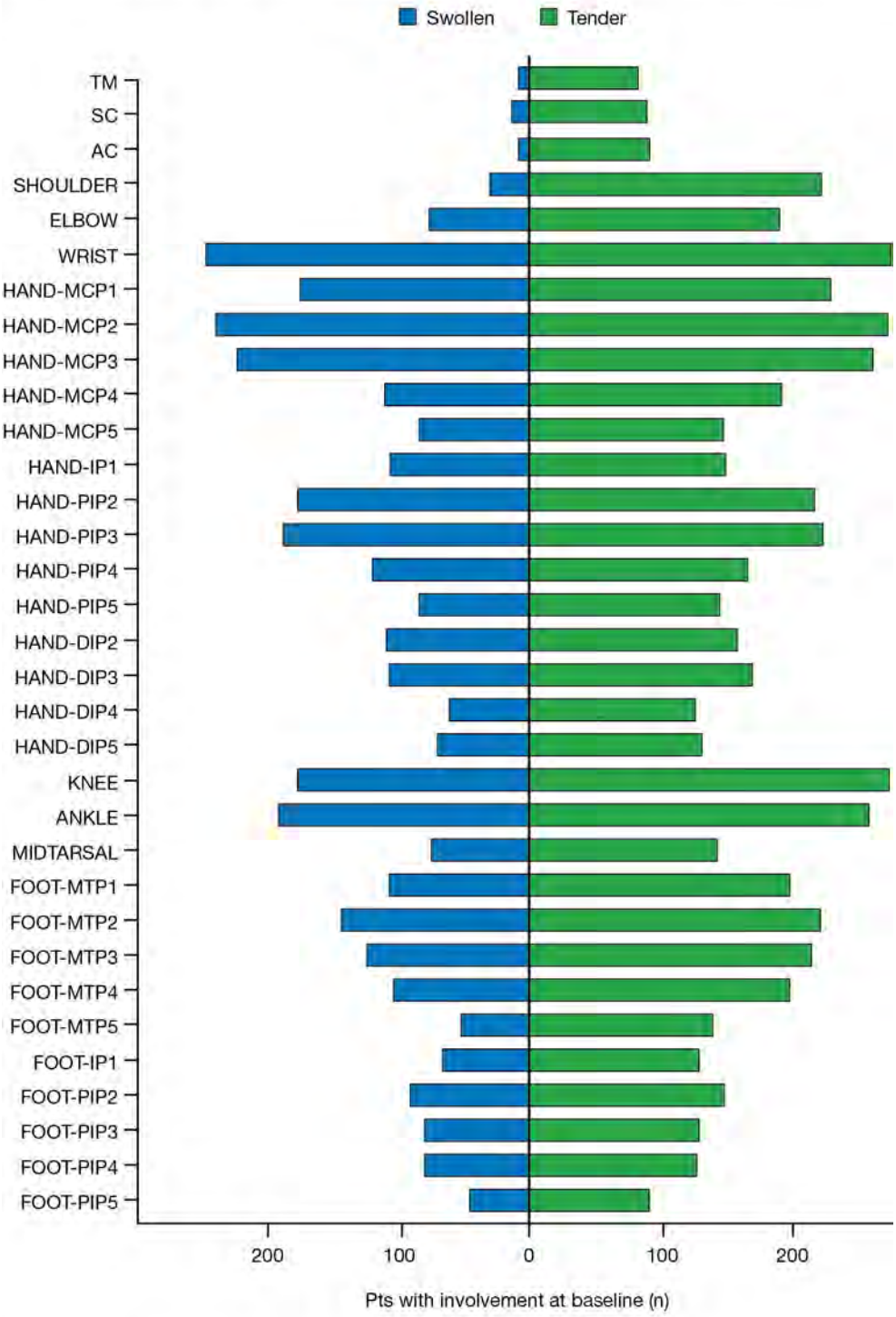
Background/Purpose: Peripheral joint involvement in PsA varies. In RA, varied joint involvement may reflect site-specific differences in stromal cell transcriptome, including Janus kinase-signal transducer and activator of transcription (JAK-STAT). Tofacitinib, an oral JAK inhibitor for the treatment of PsA, has been associated with improvements in peripheral arthritis.[1] Data on joint-specific responses in patients (pts) with PsA are sparse.[2] This analysis describes patterns of peripheral joint involvement and response to tofacitinib or adalimumab (ADA) treatment in pts with active PsA.

Methods: This post hoc analysis used data from OPAL Broaden (12 months; NCT01877668; N=422). Pts with PsA received tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, ADA 40 mg subcutaneous injection every 2 weeks, or placebo (PBO) switching to tofacitinib 5 or 10 mg BID at Month (M)3; all pts received a single background conventional synthetic DMARD (75–88% of pts received MTX).[1] OPAL Broaden was not designed to test non-inferiority/superiority between tofacitinib and ADA. Data at M3, 6, and 12 were included. A paired joint pathology score (PJPS), the sum of bilateral swollen/tender joint counts ranging from 0 (neither side swollen/tender) to 4 (both swollen and tender), was calculated. Percent change from baseline (%Δ) in PJPS for each joint and absolute differences in mean PJPS for each tofacitinib dose and PBO switch group at M3, 6, and 12 vs ADA were displayed as descriptive heat maps. Joint damage at M12 in the hand PIP, MCP, and wrist joints, and foot (IP and MTP joints), was assessed using components of the modified total Sharp score (mTSS). Statistical comparison of radiographic PJPS (rPJPS), derived from bilateral mTSS in each joint group, was performed using a mixed-effects model for repeated measurements.

Results: The baseline distribution of involved joints was typical for PsA (Fig 1).[2] At M3, %ΔPJPS (improvement) was greater in joints below the knee with PBO. At M12, greater reductions in PJPS were observed with tofacitinib or ADA in the wrist, radial MCPs, and hand PIPs vs other joints (Fig 2a). At M12, greater reductions in PJPS were observed with ADA vs tofacitinib in the hand DIPs, and in the hand PIPs and feet (especially PIPs) with tofacitinib vs ADA (Fig 2b). Despite no major numeric differences in %ΔrPJPS with tofacitinib vs ADA, greater radiographic progression in the feet was observed at M12 in pts switching from PBO to tofacitinib 10 mg BID at M3, vs ADA ($p < 0.05$) (Fig 2c). Various limitations preclude comparisons between tofacitinib and ADA.

Conclusion: We provide descriptive data on joint-level responses in pts with PsA receiving tofacitinib or ADA, and further evidence of a possible proximal/distal response gradient in MTX-treated arthritis.[3] No consistent joint response patterns were observed with tofacitinib or ADA. A 3-month delay in advanced therapy initiation may result in radiographic progression in the feet.

Figure 1. Total number of pts with specific joint involvement at baseline in OPAL Broaden (N=422)



N represents the number of pts with baseline PJPS > 0 for a given joint

AC, acromioclavicular; PJPS, paired joint pathology score; SC, sternoclavicular

1. Mease P et al. N Engl J Med 2017; 377: 1537-50.
2. Stekhoven D et al. Clin Rheumatol 2017; 36: 2035-43.
3. Frank-Bertoncelj M et al. Arthritis Rheumatol 2019; 71 (Suppl 10): Abs 1388.

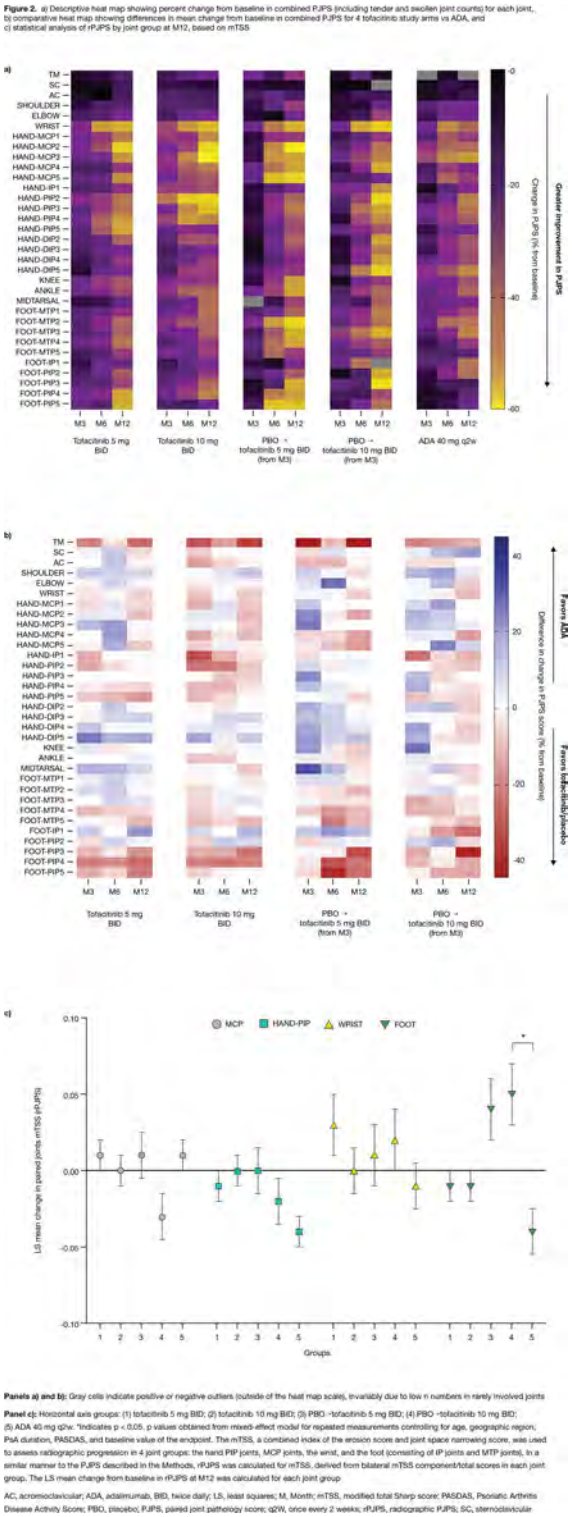


Figure 2. a) Descriptive heat map showing percent change from baseline in combined PJPS (including tender and swollen joint counts) for each joint, b) comparative heat map showing differences in mean change from baseline in combined PJPS for 4 tofacitinib study arms vs ADA, and c) statistical analysis of rPJPS by joint group at M12, based on mTSS

Panels a) and b): Gray cells indicate positive or negative outliers (outside of the heat map scale), invariably due to low n numbers in rarely involved joints

Panel c): Horizontal axis groups: (1) tofacitinib 5 mg BID; (2) tofacitinib 10 mg BID; (3) PBO →tofacitinib 5 mg BID; (4) PBO →tofacitinib 10 mg BID; (5) ADA 40 mg q2w. *Indicates $p < 0.05$. p values obtained from mixed-effect model for repeated measurements controlling for age, geographic region, PsA duration, PASDAS, and baseline value of the endpoint. The mTSS, a combined index of the erosion score and joint space narrowing score, was used to assess radiographic progression in 4 joint groups: the hand PIP joints, MCP joints, the wrist, and the foot (consisting of IP joints and MTP joints), in a similar manner to the PJPS described in the Methods. rPJPS was calculated for mTSS, derived from bilateral mTSS component/total scores in each joint group. The LS mean change from baseline in rPJPS at M12 was calculated for each joint group

AC, acromioclavicular; ADA, adalimumab, BID, twice daily; LS, least squares; M, Month; mTSS, modified total Sharp score; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; PJPS, paired joint pathology score; q2W, once every 2 weeks; rPJPS, radiographic PJPS; SC, sternoclavicular

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Abstract Number: 1350

Sustained Improvement in Physical Function, Disease Impact and Health-Related Quality of Life in Patients with Psoriatic Arthritis Treated with Bimekizumab: 3-Year Results from a Phase 2b Open-Label Extension Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Bimekizumab (BKZ) is a monoclonal IgG1 antibody that selectively inhibits both interleukin (IL)-17F and IL-17A, and has demonstrated clinical improvements in joint and skin outcomes up to 152 weeks (wks) with an acceptable safety profile in patients (pts) with active psoriatic arthritis (PsA).[1,2] Achievement of low disease activity in pts with PsA has been associated with improvements in pt-reported health-related quality of life (HRQoL).[3] To report long-term impact of BKZ treatment, up to 3 years, on pt-reported outcome (PRO) measures from a phase 2b dose-ranging study (BE ACTIVE; NCT02969525) and its open-label extension (OLE; NCT03347110).

Methods: BE ACTIVE and OLE study designs have been described previously.[1,2] Pts who completed 48 wks of BKZ treatment without meeting withdrawal criteria were eligible for OLE entry. All OLE pts received BKZ 160 mg every 4 wks. Data are presented from BE ACTIVE baseline (BL) and at Wks 48 and 152. PROs reported (full analysis set [FAS]): 9-item Psoriatic Arthritis Impact of Disease (PsAID-9) individual domains (change from BL [CfB]) and Patient Acceptable Symptom State (PASS [score≤4]),[4] Health Assessment Questionnaire Disability Index (HAQ-DI) Minimal Clinically Important Difference (MCID; ≥0.35 decrease from BL), CfB in Short Form-36 (SF-36) individual domains, CfB in SF-36 Physical and Mental Component Summaries (PCS/MCS), and CfB in Patient's Assessment of Arthritis Pain (PtAAP) visual analogue scale (VAS). In addition to observed case (OC) data, we report results with non-responder imputation (NRI) or multiple imputation (MI; based on the missing at random assumption).

Results: Of 206 randomized pts at BL in BE ACTIVE, 66.5% had psoriasis body surface area ≥3%, 18.9% had prior tumor necrosis factor inhibitor exposure, and 63.6% received concomitant methotrexate. Mean BL PRO scores were

Table 1. Baseline demographics and disease characteristics

	BKZ 160 mg → 160 mg OLE [a] (n=124)	BKZ 320 mg → 160 mg OLE [b] (n=82)	Total (N=206)
Age (years), mean (SD)	50.5 (12.6)	47.4 (12.0)	49.3 (12.4)
Sex (female), n (%)	69 (55.6)	32 (39.0)	101 (49.0)
Weight (kg), mean (SD)	83.8 (18.4)	88.5 (18.5)	85.7 (18.5)
TJC, mean (SD)	20.6 (14.3)	23.3 (15.9)	21.6 (15.0)
SJC, mean (SD)	10.9 (7.5)	12.5 (9.5)	11.5 (8.4)
hs-CRP (mg/L), median (min–max)	5.7 (0.1–99.9)	5.9 (0.3–85.2)	5.9 (0.1–99.9)
Psoriasis BSA ≥3%, n (%)	79 (63.7)	58 (70.7)	137 (66.5)
Dactylitis, n (%)	34 (27.4)	25 (30.5)	59 (28.6)
Enthesitis, n (%)	65 (52.4)	42 (51.2)	107 (51.9)
Prior TNFi therapy, n (%)	23 (18.5)	16 (19.5)	39 (18.9)
Concomitant MTX, n (%)	75 (60.5)	56 (68.3)	131 (63.6)
Baseline PRO scores, mean (SD)			
PsAID-9	4.5 (1.9)	4.9 (2.0)	4.6 (1.9)
HAQ-DI	1.0 (0.6)	1.0 (0.6)	1.0 (0.6)
SF-36 PCS	37.0 (9.1)	36.0 (9.0)	36.6 (9.1)
SF-36 MCS	56.0 (8.6)	55.4 (9.1)	55.8 (8.7)
PtAAP	50.8 (22.7)	54.3 (23.4)	52.2 (23.0)
Baseline PsAID-9 PASS, n (%)	45 (36.3)	26 (31.7)	71 (34.5)

comparable across dose groups in BE ACTIVE (**Table 1**). At Wks 48/152, the proportions of patients who achieved PsAID-9 PASS (NRI) were 74.2–76.8%/63.7–67.1%; the proportions of patients who achieved HAQ-DI MCID (NRI) were 47.6–53.7%/42.7–45.1% (**Figure 1A–D**). All PsAID-9 domains and the majority of the 8 SF-36 domains improved from BL to Wks 48 and 152, including measures of fatigue and bodily pain. SF-36 PCS improved from BL to Wks 48 and 152 and SF-36 MCS remained within the normal range from BL, as expected (**Figure 1E–F; Table 2**). Pts showed sustained improvements in pain by mean CfB in PtAAP VAS score at Wk 48 (between –26.8 and –34.7; MI) and Wk 152 (between –31.3 and –33.0; MI) (**Figure 1G**). There were no clear differences between pts who completed either BKZ 160 mg or BKZ 320 mg in BE ACTIVE prior to receiving BKZ 160 mg in the OLE.

Conclusion: BKZ treatment is associated with sustained improvements in PRO measures of disease impact up to 3 years, including in pain and fatigue. Furthermore, BKZ treatment is associated with substantial and durable improvements in measures of overall physical function and HRQoL up to 3 years.

References: 1. Ritchlin CT. Lancet 2020;395:427–40; **2**. McInnes IB. Ann Rheum Dis 2020;79:1153–4; **3**. Gossec L. Ann Rheum Dis 2020;79:1687; **4**. Gossec L. Ann Rheum Dis 2014;73:1012–9.

Full analysis set. All patients received BKZ 160 mg during the OLE (Wks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE: [a] Includes pts within the indicated analysis set from the dose-response, double-blind period who were subsequently re-randomized to 160 mg, or [b] pts who received 320 mg during the dose-blind periods; all pts

Table 2. Baseline and change from baseline in PsAID-9 domains and SF-36 domains (multiple imputation)

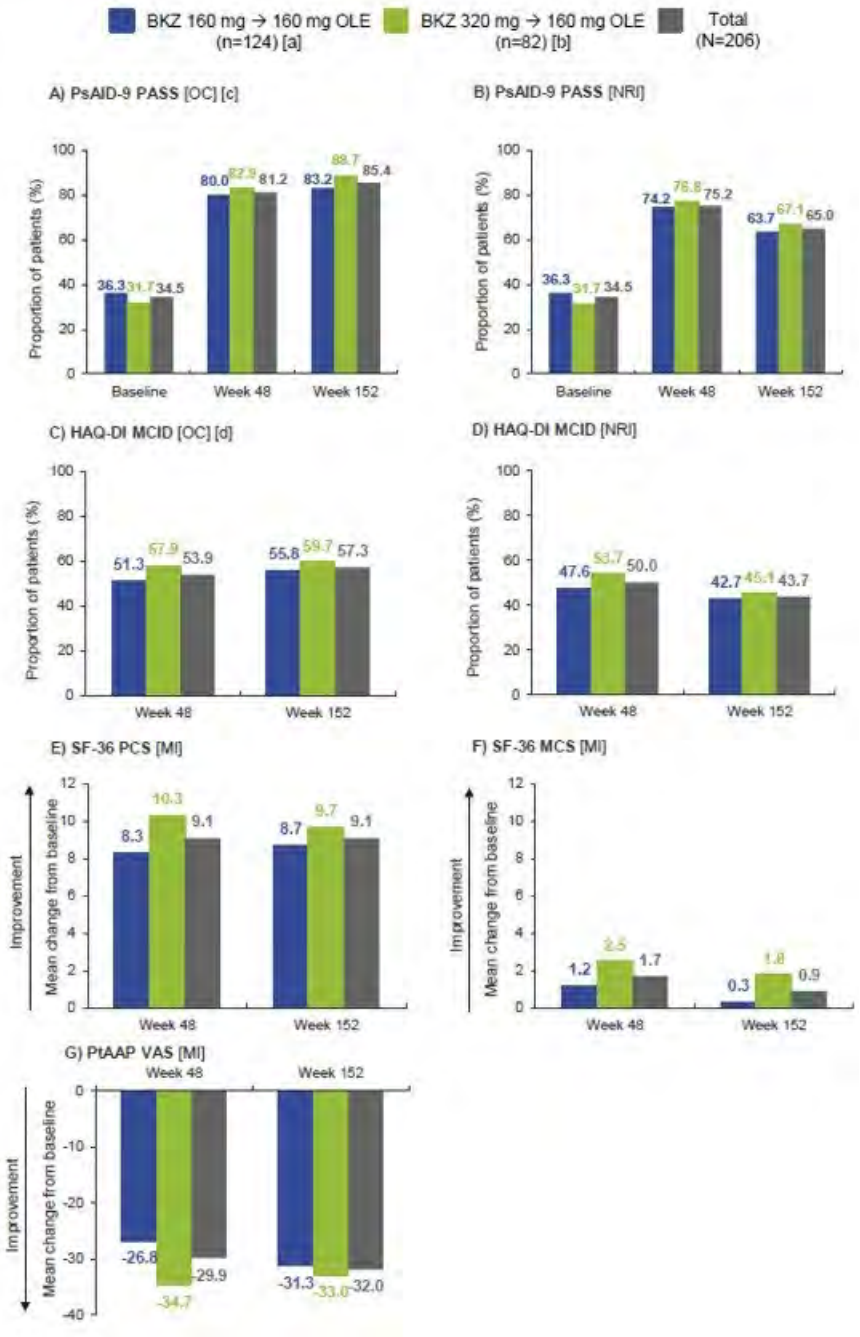
		Wk	BKZ 160 mg → 160 mg OLE [a] (n=124)	BKZ 320 mg → 160 mg OLE [b] (n=82)	Total (N=206)
PsAID-9, mean (SE)					
Pain	Absolute value	0	5.6 (0.2)	5.9 (0.2)	5.7 (0.1)
	CfB	48	−2.7 (0.2)	−3.2 (0.3)	−2.9 (0.2)
		152	−3.2 (0.2)	−3.3 (0.3)	−3.3 (0.2)
Fatigue	Absolute value	0	5.0 (0.2)	5.3 (0.3)	5.1 (0.2)
	CfB	48	−2.2 (0.2)	−2.7 (0.3)	−2.4 (0.2)
		152	−2.5 (0.2)	−2.9 (0.3)	−2.7 (0.2)
Skin problems	Absolute value	0	4.7 (0.2)	4.9 (0.3)	4.8 (0.2)
	CfB	48	−2.9 (0.3)	−3.2 (0.3)	−3.0 (0.2)
		152	−2.7 (0.3)	−3.0 (0.4)	−2.8 (0.2)
Work and/or leisure activities	Absolute value	0	4.6 (0.2)	5.1 (0.3)	4.8 (0.2)
	CfB	48	−2.4 (0.2)	−3.0 (0.3)	−2.6 (0.2)
		152	−2.6 (0.2)	−3.0 (0.3)	−2.8 (0.2)
Functional capacity	Absolute value	0	4.7 (0.2)	5.0 (0.3)	4.9 (0.2)
	CfB	48	−2.5 (0.2)	−2.9 (0.3)	−2.6 (0.2)
		152	−2.6 (0.2)	−2.9 (0.3)	−2.7 (0.2)
Discomfort	Absolute value	0	4.4 (0.2)	4.6 (0.3)	4.5 (0.2)
	CfB	48	−2.4 (0.3)	−2.7 (0.3)	−2.5 (0.2)
		152	−2.5 (0.2)	−2.7 (0.3)	−2.6 (0.2)
Sleep disturbance	Absolute value	0	3.6 (0.3)	4.2 (0.3)	3.9 (0.2)
	CfB	48	−1.7 (0.2)	−2.2 (0.4)	−1.9 (0.2)
		152	−1.7 (0.3)	−2.6 (0.3)	−2.1 (0.2)
Coping	Absolute value	0	3.8 (0.2)	4.5 (0.3)	4.1 (0.2)
	CfB	48	−2.0 (0.2)	−2.6 (0.3)	−2.3 (0.2)
		152	−1.9 (0.2)	−2.9 (0.3)	−2.3 (0.2)
Anxiety, fear and uncertainty	Absolute value	0	2.4 (0.2)	2.6 (0.3)	2.5 (0.2)
	CfB	48	−1.0 (0.2)	−1.3 (0.3)	−1.1 (0.2)
		152	−0.9 (0.2)	−1.0 (0.3)	−1.0 (0.2)
SF-36, mean (SE)					
Bodily pain	Absolute value	0	38.4 (0.7)	37.4 (0.9)	38.0 (0.5)
	CfB	48	9.6 (0.9)	12.4 (1.2)	10.7 (0.7)
		152	11.0 (1.0)	11.5 (1.3)	11.2 (0.8)
General health	Absolute value	0	43.1 (0.8)	40.9 (1.0)	42.2 (0.6)
	CfB	48	4.1 (0.7)	6.9 (1.0)	5.2 (0.6)
		152	3.3 (0.8)	4.3 (1.1)	3.7 (0.7)
Mental health	Absolute value	0	51.9 (0.8)	52.0 (1.0)	52.0 (0.6)
	CfB	48	2.9 (0.8)	4.3 (1.1)	3.5 (0.6)
		152	2.4 (0.8)	3.5 (1.2)	2.8 (0.7)
Physical functioning	Absolute value	0	41.0 (0.8)	40.4 (1.0)	40.8 (0.7)
	CfB	48	6.2 (0.8)	8.4 (1.0)	7.1 (0.6)
		152	6.9 (0.9)	8.2 (1.1)	7.4 (0.7)
Role emotional	Absolute value	0	52.4 (0.6)	51.3 (0.9)	52.0 (0.5)
	CfB	48	1.5 (0.6)	2.9 (0.9)	2.0 (0.5)
		152	0.8 (0.6)	2.0 (1.0)	1.3 (0.5)
Role physical	Absolute value	0	41.7 (0.8)	41.6 (1.0)	41.6 (0.6)
	CfB	48	6.3 (0.8)	6.9 (1.0)	6.6 (0.6)
		152	5.9 (0.9)	6.7 (1.1)	6.2 (0.7)
Vitality	Absolute value	0	50.2 (0.8)	48.9 (1.1)	49.7 (0.7)
	CfB	48	4.7 (0.8)	8.6 (1.2)	6.3 (0.7)
		152	5.1 (0.9)	7.6 (1.2)	6.1 (0.7)
Social functioning	Absolute value	0	48.7 (0.8)	48.1 (1.1)	48.5 (0.7)
	CfB	48	4.6 (0.8)	4.9 (1.2)	4.8 (0.7)
		152	3.8 (0.9)	5.2 (1.1)	4.3 (0.7)

received 160 mg during the open-label extension. Lower HAQ-DI scores correspond to better performance of daily activities; Higher SF-36 scores indicate better pt HRQoL; Lower PsAID-9 scores correspond to lower impact of disease on pt QoL; Lower PtAAP VAS scores indicate less pain. BKZ: bimekizumab; BSA: body surface area; HAQ-DI: Health Assessment Questionnaire Disability Index; hs-CRP: high sensitivity C-reactive protein; MTX: methotrexate; OLE: open-label extension; PASS: Patient Acceptable Symptom State; PRO: patient-reported outcome; PsAID-9: Psoriatic Arthritis Impact of Disease-9; PtAAP: Patient's Assessment of Arthritis Pain; pts: patients; (HR)QoL: (health-related) quality of life; SD: standard deviation; SF-36 MCS: Short Form-36 Mental Component Summary; SF-36 PCS:

Short Form-36 Physical Component Summary; SJC: swollen joint count; TJC: tender joint count; TNF: tumor necrosis factor; VAS: visual analogue scale; wk: week.

Full analysis set. All patients received BKZ 160 mg during the OLE (Wks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE: [a] Includes pts within the indicated analysis set from the dose-response, double-blind period who were subsequently re-randomized to 160 mg, or [b] pts who received 320 mg during the dose-blind periods; all pts received 160 mg during the open-label extension. Higher SF-36 scores indicate better pt HRQoL; Lower PsAID-9 scores correspond to lower impact of disease on pt QoL. Missing data were imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random. BKZ: bimekizumab; BL: baseline; CfB: change from Baseline;

Figure 1. Patient-reported outcomes for up to 3 years of BKZ treatment



OLE: open-label extension; PsAID-9: Psoriatic Arthritis Impact of Disease-9; pts: patients; (HR)QoL: (health-related) quality of life; SE: standard error; SF-36: Short Form-36; wk: week.

Full analysis set. All patients received BKZ 160 mg during the OLE (Wks 48–152) after completing BKZ 160 mg or 320 mg in BE ACTIVE: [a] Includes pts within the indicated analysis set from the dose-response, double-blind period who were subsequently re-randomized to 160 mg, or [b] pts who received 320 mg during the dose-blind periods; all pts received 160 mg during the open-label extension; [c] OC baseline [160 mg/320 mg/Total]: n=124/82/206, respectively; Wk 48 [160 mg/320 mg/Total]: n=115/76/191, respectively; Wk 152 [160 mg/320 mg/Total]: n=95/62/157, respectively; [d] OC Wk 48 [160 mg/320 mg/Total]: n=115/76/191, respectively; Wk 152 [160 mg/320 mg/Total]: n=95/62/157, respectively. Higher SF-36 scores indicate better pt HRQoL; Lower PtAAP VAS scores indicate less pain. BKZ: bimekizumab; HAQ-DI: Health Assessment Questionnaire Disability Index; MCID: minimal clinically important difference; MI: multiple imputation; NRI: non-responder imputation; OC: observed case; OLE: open-label extension; PASS: Patient Acceptable Symptom State; PsAID-9: Psoriatic Arthritis Impact of Disease-9; PtAAP: Patient's Assessment of Arthritis Pain; pts: patients; (HR)QoL: (health-related) quality of life; SF-36 MCS: Short Form-36 Mental Component Summary; SF-36 PCS: Short Form-36 Physical Component Summary; VAS: visual analogue scale; wk: week.

Disclosure: L. Gossec, Galapagos, 5, Sandoz, 5, Sanofi, 5, AbbVie, 2, Amgen, 2, 5, Bristol Myers Squibb, 2, Biogen, 2, Celgene, 2, Eli Lilly, 2, 5, Gilead, 2, Janssen, 2, 5, Novartis, 2, Pfizer, 2, 5, Samsung Bioepis, 2, Sanofi-Aventis, 2, UCB, 2; **A. Asahina**, AbbVie, 5, 6, Celgene, 5, 6, Eisai, 5, 6, Eli Lilly, 5, 6, Janssen, 5, 6, Kyowa Kirin, 5, 6, Leo Pharma, 5, 6, Maruho, 5, 6, Mitsubishi Pharma, 5, 6, Sun Pharma, 5, 6, Taiho Pharma, 5, 6, Torii Pharmaceutical, 5, 6, UCB Pharma, 5, 6; **A. Gottlieb**, Boehringer Ingelheim, 1, 2, 5, Incyte, 1, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, UCB, 1, 2, 5, Xbiotech, 1, 2, 5, Bristol Myers Squibb, 1, 2, LEO Pharma, 1, 2, AnaptysBio, 1, 2, Avotres, 1, 2, Eli Lilly, 1, 2, Pfizer, 1, 2, Beiersdorf, 1, 2, Sun Pharmaceuticals, 1, 2, 5, Dermavant, 1, 2, GlaxoSmithKline, 1, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **B. Ink**, GSK, 11, UCB Pharma, 3, 11; **D. Assudani**, UCB Pharma, 3; **J. Coarse**, UCB Pharma, 3; **S. Hellot**, UCB Pharma, 3; **J. Eells**, UCB Pharma, 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1351

The Impact of Skin Involvement and Depression on Patient Acceptable Symptom State in Patients with Psoriatic Arthritis and Psoriasis: Results from a Multinational Survey

Alexis Ogdie-Beatty[1], Joseph Merola[2], Pascal Richette[3], Sven Richter[4], Shauna Jardon[5], Lihua Tang[4] and William Tillett[6], [1]University of Pennsylvania, Philadelphia, PA, [2]Harvard Medical School, Brigham and Women's Hospital, Boston, MA, [3]Lariboisiere Hospital, Paris, France, [4]Amgen Inc., Thousand Oaks, CA, [5]Amgen Inc., Gilbert, AZ, [6]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

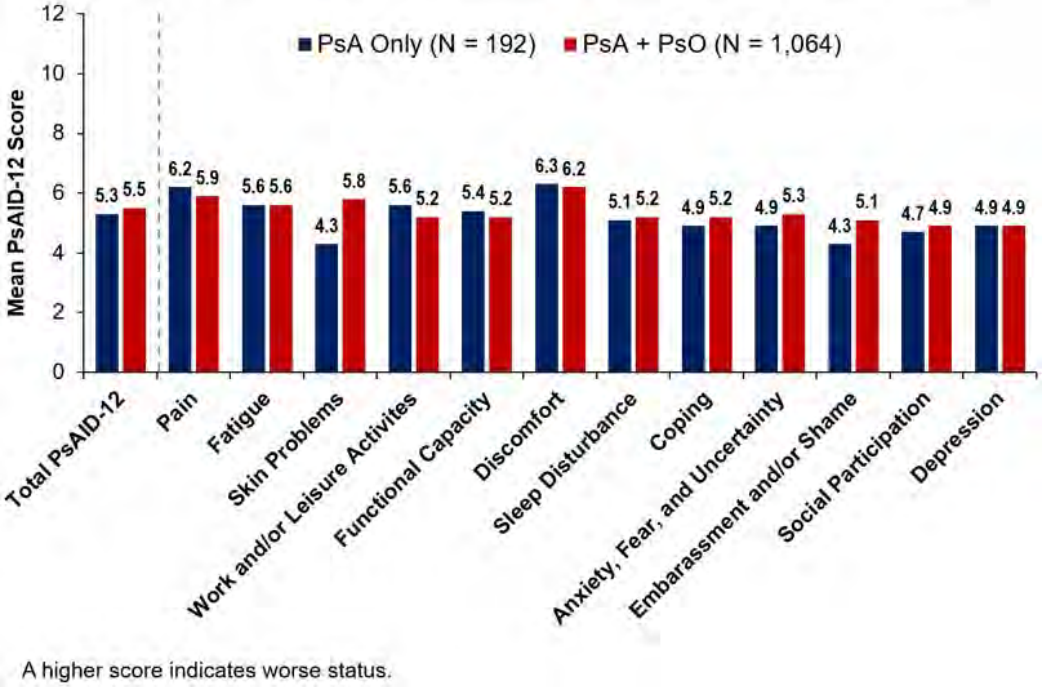
Background/Purpose: Depression, a common comorbidity in patients with psoriasis (PsO) and PsA, has been shown to be independently associated with Psoriatic Arthritis Impact of Disease (PsAID-12) scores. We investigated how

much active PsO and a positive 2-item Patient Health Questionnaire (PHQ-2) depression screen impacted PsAID-12 scores in patients with PsA in the Understanding Psoriatic Disease Leveraging Insights for Treatment (UPLIFT) survey.

Methods: UPLIFT was a multinational Web-based survey conducted in 2020 in adults who reported ever being diagnosed by a healthcare provider (HCP) with PsA and/or PsO. For patients with PsA, we report PsAID-12 total and domain scores and Patient Acceptable Symptom State (PASS) achievement (PsAID-12 ≤4) according to the presence of active PsO and depression status. A PHQ-2 score ≥3 indicates a positive screen for depression.

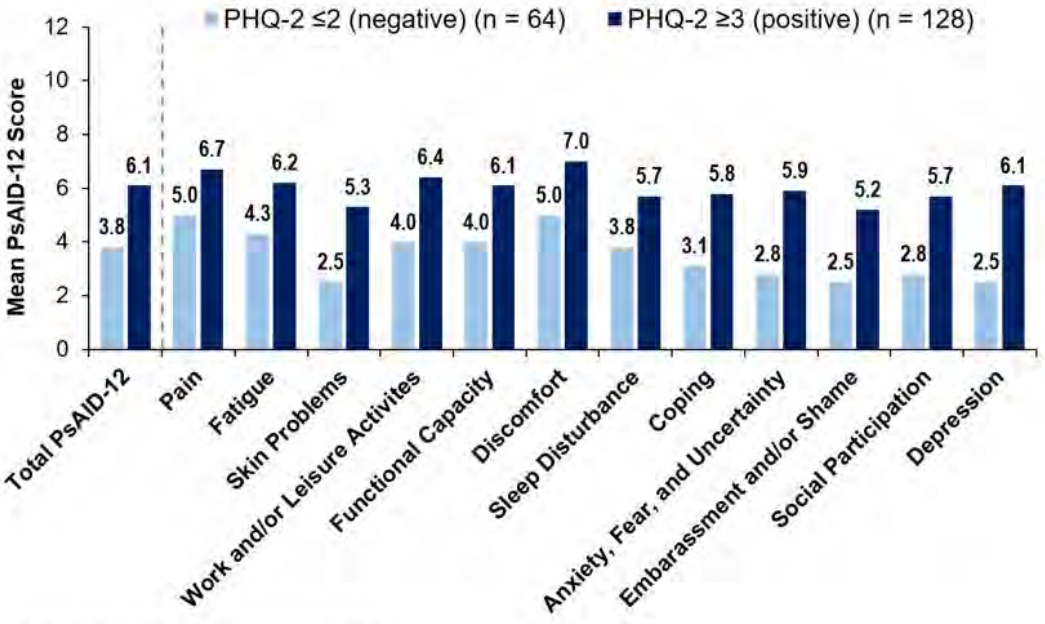
Results: Of the 3,806 patient survey respondents, 1,256 reported HCP-diagnosed PsA, of which 1,064 had HCP-diagnosed PsA + active PsO and 192 had PsA only. In patients with PsA + PsO, enthesitis (44.5%), dactylitis (47.0%), and polyarthritis (59.8%) were more prevalent than in patients with PsA without active PsO (37.5%, 37.5%, and 36.5%, respectively). More patients with PsA + PsO vs PsA only had a history of patient-reported HCP-diagnosed comorbidities, including depression (42.7% vs 26.6%), cancer (30.7% vs 21.4%), heart disease (23.1% vs 13.5%), hypertension (44.0% vs 33.3%), liver disease (21.0% vs 12.5%), and inflammatory bowel disease (25.5% vs 14.1%). Despite differences in comorbidity burden, mean total PsAID-12 scores (Figure 1) and rates of PASS achievement (25.0% vs 26.9%) were similar in patients with PsA only and PsA + PsO. Mean individual PsAID-12 domain scores were generally similar between groups; however, impact of "skin problems" and "embarrassment and/or shame" was more pronounced for the PsA + PsO group (Figure 1). A total of 67% of PsA only and 66% PsA + PsO patients had a PHQ-2 ≥3. Patients with PHQ-2 ≥3 had higher PsAID-12 scores, indicating worse health status, regardless of whether they had active PsO. Fewer patients with PHQ-2 ≥3 achieved PASS (PsA: 10.9%, PsA + PsO: 10.7%) compared with those who screened negative for depression (PsA: 53.1%, PsA + PsO 58.8%). Similarly, higher PsAID-12 domain scores were reported in patients with PsA with PHQ-2 ≥3 vs those with PHQ-2 ≤2 (Figure 2) and to a greater extent in those with PsA + PsO (Figure 3). The greatest differences between groups were observed in domains of "work and/or leisure activities," "coping," "anxiety, fear, and uncertainty," "embarrassment and/or shame," and "social participation."

Figure 1. Total PsAID-12 and Domain Scores in Patients With PsA and PsA + PsO



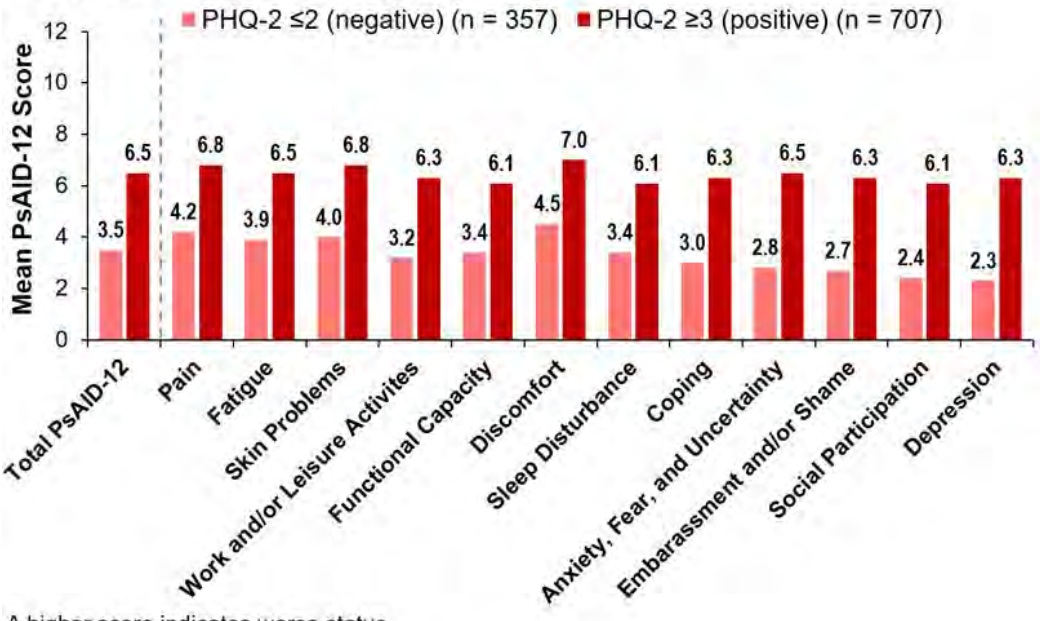
A higher score indicates worse status.

Figure 2. Total PsAID-12 and Domain Scores in Patients With PsA According to PHQ-2 Screening Status



A higher score indicates worse status.

Figure 3. Total PsAID-12 and Domain Scores in Patients With PsA + PsO According to PHQ-2 Screening Status



A higher score indicates worse status.

Conclusion: For patients with PsA in UPLIFT, active PsO was associated with generally more active disease and a higher prevalence of comorbidities, including depression. Having a positive PHQ-2 screen for depression was associated with overall disease impact as measured by PsAID.

Disclosure: A. Ogdie-Beatty, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to

University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2; **J. Merola**, AbbVie, 2, Arena, 2, Biogen, 2, Dermavant Sciences, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2, Pfizer Inc, 2, Sun Pharma, 2, UCB Pharma, 2, Avotres Inc, 2, Celgene, 2, EMD Serono, 2, Regeneron, 2, Sanofi, 2, Leo Pharma, 2, Merck, 2, Bristol-Myers Squibb, 2; **P. Richette**, AbbVie, 1, 6, Amgen, 1, 6, Celgene, 1, 6, Janssen, 1, 6, Eli Lilly, 1, 6, MSD, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **S. Richter**, Amgen Inc., 3, 11; **S. Jardon**, Amgen Inc., 3, 11; **L. Tang**, Amgen Inc., 3, 11; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2.

Abstract Number: 1352

Deucravacitinib Efficacy in Psoriatic Arthritis (PsA) by Baseline DMARD Use: Exploratory Analysis from a Phase 2 Study

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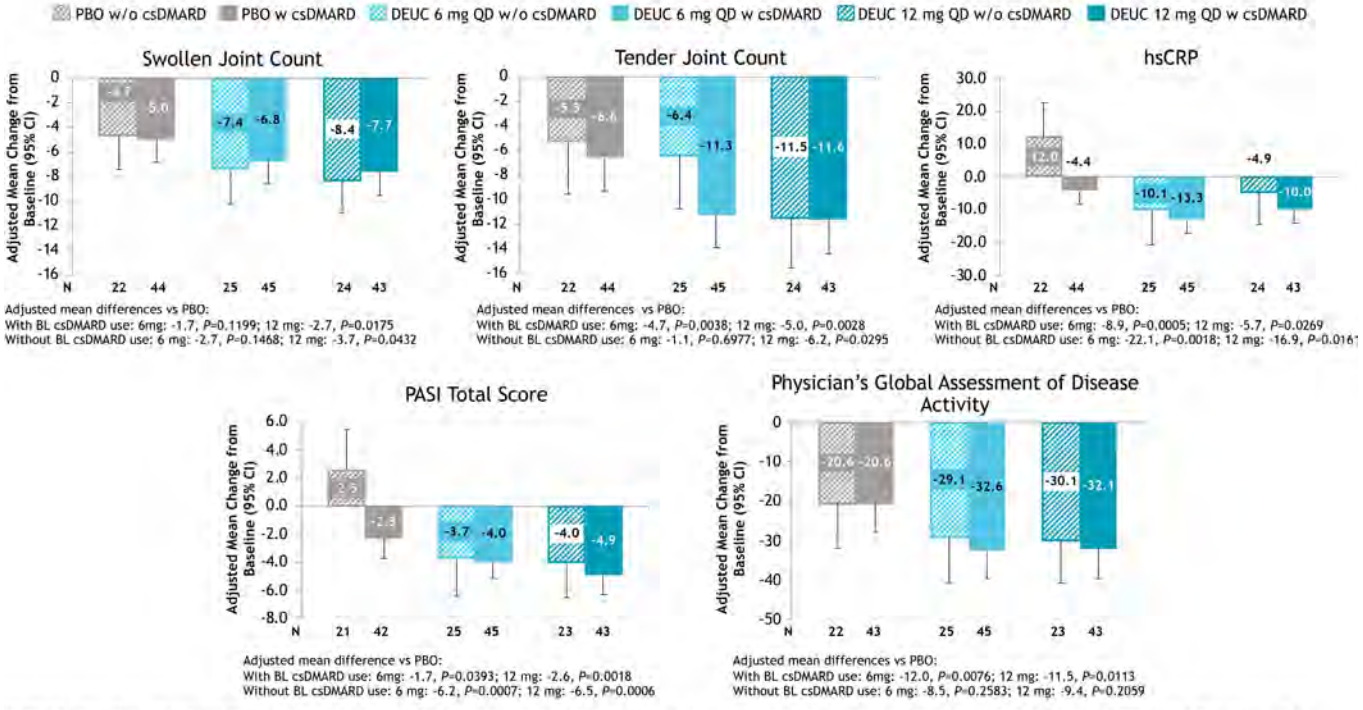
SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

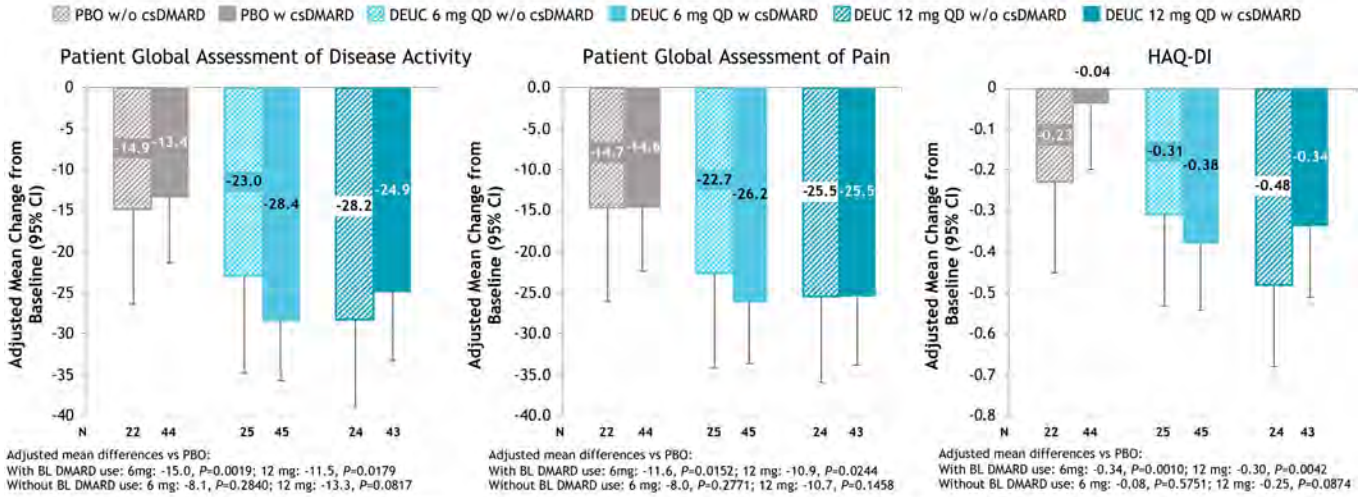
Background/Purpose: PsA presents with heterogeneous clinical manifestations including joint pain, enthesitis, dactylitis, and skin and nail lesions. Treatment guidelines recommend that PsA patients (pts) who do not adequately respond to conventional synthetic DMARDs (csDMARDs) can initiate treatment with targeted synthetic DMARDs with or without background use of csDMARDs. Deucravacitinib is a novel, oral, selective inhibitor of tyrosine kinase

Figure 1: Adjusted Mean Change from Baseline at Week 16 by csDMARD Use: Clinical Measures



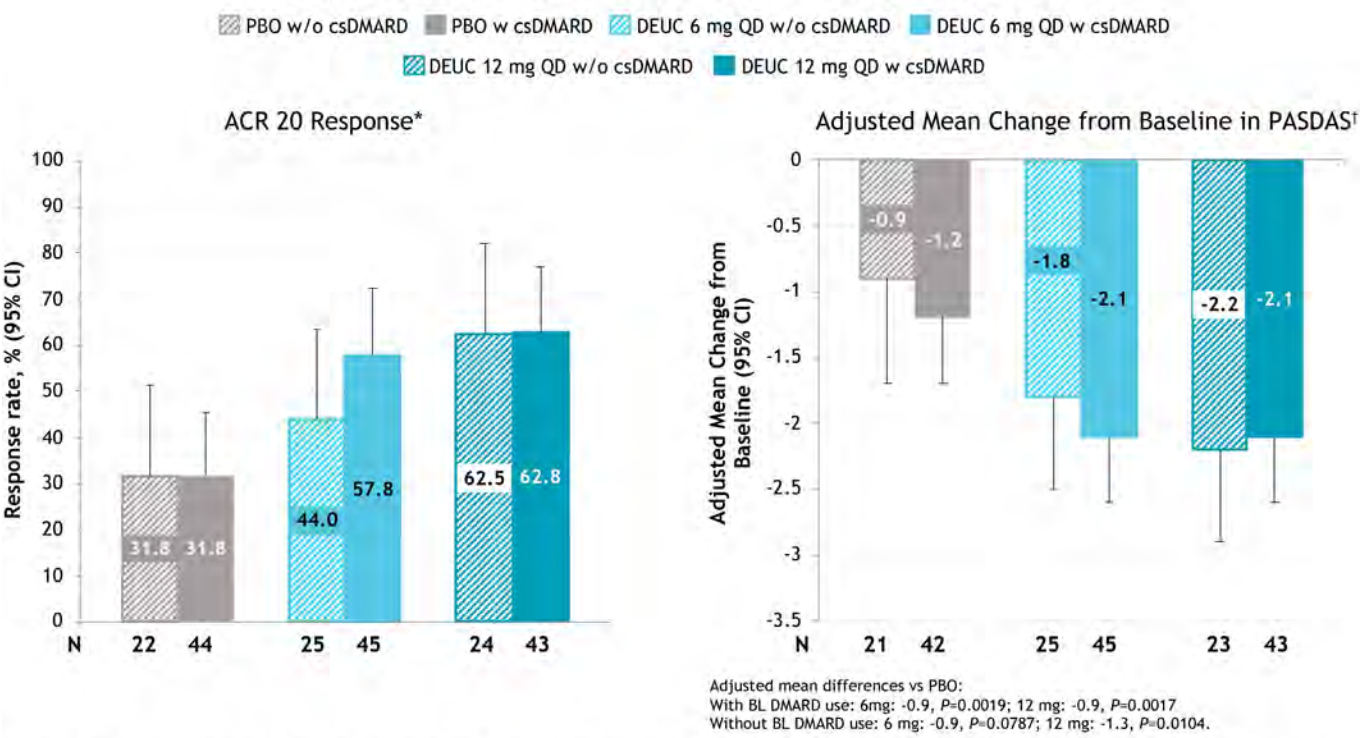
Modified baseline observation carried forward was used to impute missing data. Adjusted means, 95% CI, and p-values from an analysis of covariance model with factors for body weight and TNFi use and the baseline value as covariate. BL, baseline; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DEUC, deucravacitinib; hsCRP, high-sensitivity C-reactive protein; PASI, Psoriasis Area Severity Index; PBO, placebo; QD, daily.

Figure 2: Adjusted Mean Change from Baseline at Week 16 by csDMARD Use: Patient-Reported Outcomes



Modified baseline observation carried forward was used to impute missing data. Adjusted means, 95% CI, and p-values from an analysis of covariance model with factors for body weight and TNFi use and the baseline value as covariate. BL, baseline; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DEUC, deucravacitinib; HAQ-DI, Health Assessment Questionnaire Disability Index; PBO, placebo; QD, daily.

Figure 3: Composite Measures at Week 16 by csDMARD Use



*Analyses were performed using NRI for patients with missing data. †Modified baseline observation carried forward was used to impute missing data. Adjusted means, 95% CI, and p-values from an analysis of covariance model with factors for body weight and TNFi use and the baseline value as covariate. ACR, American College of Rheumatology; csDMARD, conventional synthetic disease-modifying antirheumatic drug; DEUC, deucravacitinib; NRI, non-responder imputation; PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; QD, daily.

2 (TYK2) with a unique mechanism of action distinct from other kinase inhibitors. It binds to the TYK2 regulatory domain and allosterically inhibits the enzyme, thereby suppressing signaling of key cytokines (eg, IL-23) involved in the pathogenesis of PsA. In a Phase 2 trial in pts with active PsA, the primary endpoint, ACR 20 response at Week (Wk) 16, was met and the results showed that deucravacitinib was efficacious and well tolerated versus placebo (PBO).[1] This analysis further evaluated improvements with deucravacitinib in the Phase 2 trial in PsA pts treated with and without background csDMARDs.

Methods: This 1-year, randomized, double-blind, placebo-controlled, multicenter Phase 2 trial (NCT03881059) enrolled pts who had a PsA diagnosis for ≥6 months, fulfilled Classification Criteria for Psoriatic Arthritis (CASPAR) at screening, had active joint disease (≥3 tender and ≥3 swollen joints), a high-sensitivity CRP level of ≥3 mg/L, and ≥1 plaque psoriasis lesion (≥2 cm). Pts either failed or were intolerant to ≥1 NSAID, corticosteroid, csDMARD, and/or 1 TNF inhibitor (TNFi; up to 30%). Pts were randomized 1:1:1 to deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. A post hoc subgroup analysis in pts with and without background csDMARD use assessed improvements in select clinical outcomes (ACR 20 response, and change from baseline in ACR components, Psoriasis Area and Severity Index total score, and Psoriatic Arthritis Disease Activity Score) at Wk 16.

Results: Baseline demographics, clinical characteristics, and disease activity were generally similar among pts with and without background csDMARD use. At baseline, background csDMARD use was 64.3%, 64.2%, and 66.7% in the deucravacitinib 6 mg QD, 12 mg QD, and PBO groups, respectively. Among pts on csDMARDs at baseline, 77.8%, 86%, and 88.6%, respectively, were being treated with methotrexate. Pts with and without background csDMARD use showed similar improvements at Wk 16 with deucravacitinib treatment vs PBO on most clinical measures (**Figure 1**), pt-reported outcomes (**Figure 2**), and composite measures (**Figure 3**). No clinically relevant differences in adverse events (AEs) were observed in pts with or without background csDMARD use.

Conclusion: These analyses demonstrate that the efficacy of deucravacitinib for the treatment of PsA was similar in pts with and without background csDMARD use. The AE profile of deucravacitinib treatment with and without csDMARD use was consistent with findings from the overall Phase 2 PsA trial population.

Reference: 1. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

Disclosure: A. Deodhar, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **M. Nowak**, Bristol Myers Squibb, 3, 11; **J. Ye**, Bristol Myers Squibb, 3, 11; **T. Lehman**, Bristol Myers Squibb, 3, 11; **L. Wei**, Bristol Myers Squibb, 3, 11; **S. Banerjee**, Bristol Myers Squibb, 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1353

Whole Blood Transcriptional Changes Following Treatment with Filgotinib in Patients with Psoriatic Arthritis

Dafna Gladman[1], Yihua Liu[2], Oh Kyu Yoon[2], Mona Trivedi[2], René Galien[3], Robin Besuyen[4], Vlad Malkov[2], Angie Hertz[2] and Vinod Chandran[1], [1]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [2]Gilead Sciences, Foster City, CA, [3]Galapagos NV, Romainvulle, France, [4]Galapagos BV, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

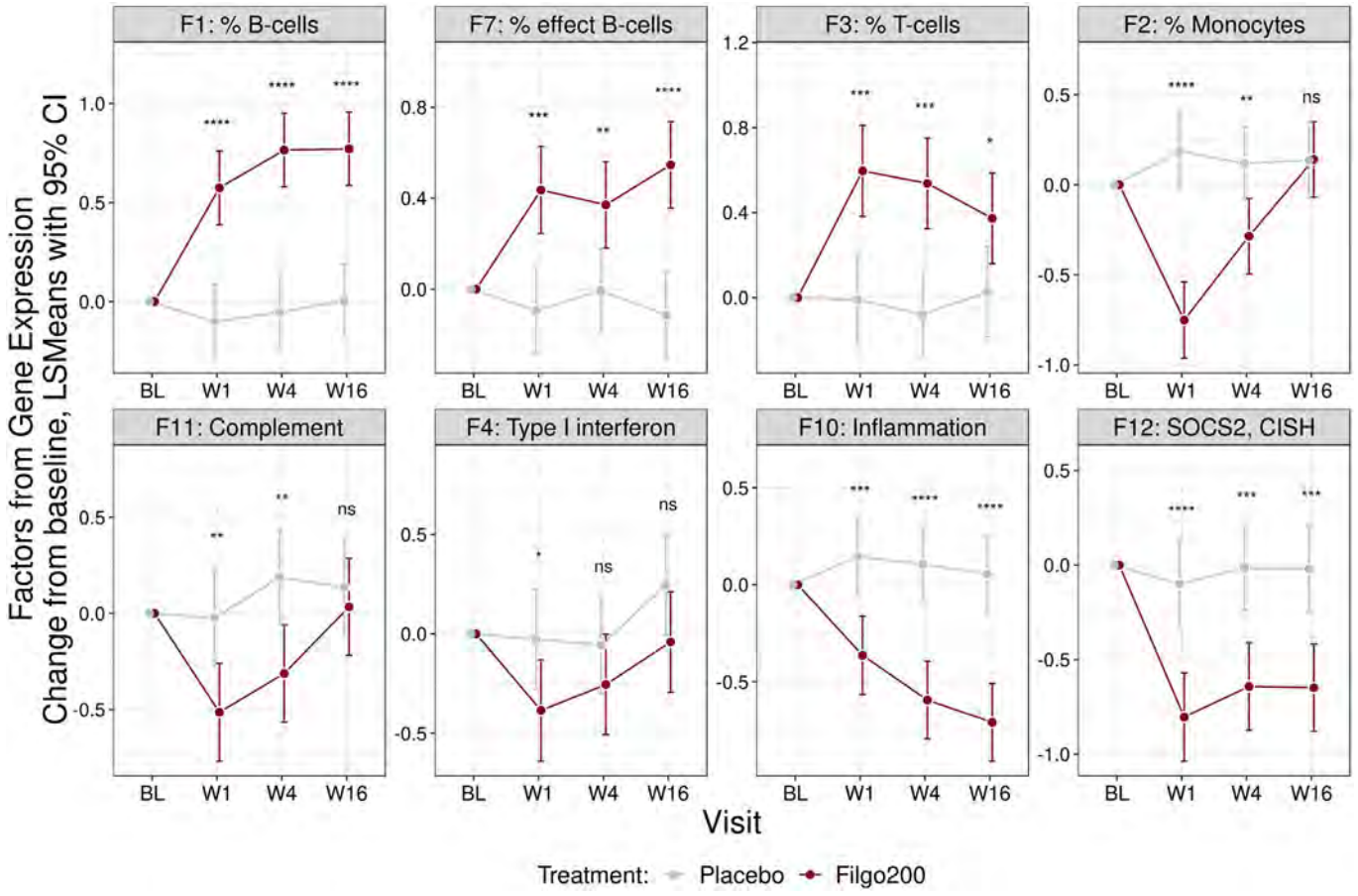


Figure 1. Pharmacodynamic gene expression changes observed during 16 weeks of treatment with FIL or PBO. Exploratory Factor Analysis was performed using the union of gene signatures (FIL vs PBO) at BL and Weeks 1, 4 and 16. Eight derived factors showed significant changes with FIL treatment as compared to PBO with FDR<0.05. Changes in circulating cell composition (Factor 1: % B cells, Factor 7: % Effector B cells, Factor 3: % T cells, Factor 2: % Monocytes) and changes in transcriptional pathways (Factor 11: Complement, Factor 4: Type I Interferon, Factor 10: Inflammation, Factor 12: SOCS2,CISH) were observed. * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$, **** $p \leq 0.0001$.

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory autoimmune disease characterized by musculoskeletal and skin inflammation. Selective inhibition of Janus kinase 1 (JAK1) has the potential to simultaneously block multiple inflammatory pathways and alleviate pathology. In the recently completed EQUATOR study, filgotinib (FIL), a preferentially JAK1 selective inhibitor, showed significant improvements in clinical signs and symptoms of PsA versus placebo.[1] In this study, whole-blood RNA-Seq data analysis was performed to evaluate the impact of FIL on gene expression and biological pathways in the EQUATOR study.

Methods: EQUATOR (Clinicaltrials.gov identifier: NCT03101670) was a phase 2 double-blind, placebo (PBO)-controlled study in 131 patients with active moderate-to-severe PsA and insufficient response or intolerance to ≥1 conventional synthetic DMARD. Patients were randomized 1:1 to receive FIL 200 mg or PBO orally once daily for 16 weeks. Whole blood samples from patients were collected at baseline and weeks 1, 4 and 16. Illumina TruSeq Stranded mRNA was generated for 452 samples from 121 patients. Gene-level quantification of RNA-seq counts and transcripts/million was conducted using Salmon (v0.8.2, and gencode GRCh38.p7 v25). Pathway analysis was performed using single sample gene set enrichment analysis based on Hallmark 50 pathways (v7.0) from the MSigDB. Treatment effect was evaluated using differential expression analysis by limma. Twelve factors were extracted from the union of genes significantly affected by FIL treatment compared to PBO at either week 1, 4 or 16. An effect of FIL on Factor scores was evaluated with mixed effect linear models for repeated measures.

Results: At baseline, Spearman rank correlation analyses showed a number of inflammation-associated genes and immune related Hallmark 50 pathways significantly correlated with CRP, Disease Activity in Psoriatic Arthritis score (DAPSA) and patient reported pain. Several of these pathways were decreased with FIL treatment including IL6_JAK_STAT3 and Inflammatory Response. Differential gene expression analysis comparing PBO-corrected samples from FIL-treated patients revealed significant changes in individual gene expression across weeks 1, 4 and 16 such as downregulation of the CRP-associated gene FAM20A and the JAK-STAT pathway members SOCS2 and CISH.

The pharmacodynamic effects of FIL can be described by changes in 8 factors derived from latent variables resulting from Exploratory Factor Analysis (Figure 1). These factors are split into two distinct categories: changes in circulating cell composition (% total B cells, % effector B cells, % T cells, % monocytes) and changes in transcriptional pathways (Complement, Type I Interferon, Inflammation, SOCS2/CISH).

Conclusion: Treatment with FIL rapidly downregulates inflammatory and immune pathways associated with PsA disease activity as a result of changes in inflammatory gene expression and alterations in circulating cellular composition.

Reference

1. Mease P, Coates LC, Helliwell PS, et al. *Lancet.* 2018;392(10162):2378-2387.

Disclosure: D. Gladman, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **Y. Liu**, Gilead Sciences, 3, 11; **O. Yoon**, Gilead Sciences, 3, 11; **M. Trivedi**, Gilead Sciences, 3, 11; **R. Galien**, Galapagos NV, 3, 11, 12, Warrant holder; **R. Besuyen**, Galapagos, 3, 11; **V. Malkov**, Gilead Sciences, 3, 11; **A. Hertz**, Gilead Sciences, 3, 11; **V. Chandran**, Abbvie, 1, 2, 5, Amgen, 1, 2, 5, Eli Lilly, 1, 2, 5, BMS, 2, 5, Janssen, 1, 2, 5, Novartis, 1, 2, 5, Pfizer, 1, 2, 5, AstraZeneca, 12, Spousal employment, Celgene, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 1354

Differences in Real-World Patient Characteristics of 8921 Patients with Psoriasis with and Without Comorbid Psoriatic Arthritis Using the UK BADBIR Database

William Tillett[1], Alexis Ogdie[2], Patricia Gorecki[3] and Alun Passey[4], [1]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]University of Pennsylvania, Philadelphia, PA, [3]Janssen Medical Affairs, London, United Kingdom, [4]Janssen Real World Evidence, HEMAR EMEA, High Wycombe, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis (PsO) and multiple comorbidities.[1] Approximately one-third of patients with PsO develop PsA during the course of their disease.[2] As patient cohorts included in randomized clinical trials are not necessarily representative of the real world, registry data can complement information gained on patient characteristics and disease outcomes.[1,3] The British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR) is one such registry for patients

with plaque PsO, with PsA being one of the comorbidities recorded at patient enrollment. The primary objective of this study was to evaluate baseline characteristics and comorbidities in patients with PsO with and without a PsA diagnosis using the BADBIR database. The hypothesis was that patients with both diseases have a higher likelihood of being diagnosed with additional comorbid conditions vs. those with PsO alone.

Methods: This was a retrospective observational study using two cohorts of BADBIR data (i.e. adult patients with PsO either receiving ustekinumab [UST] as their biologic treatment or receiving conventional systemic anti-psoriatic medication [conventional systemic]). Comparisons were made between comorbid PsA and PsO alone patients in each cohort at baseline, additionally stratifying by biologic experience in the UST treatment group. Baseline characteristics of interest were evaluated, including body mass index, smoking, and employment status, as well as comorbidities (i.e. diabetes, hypertension, myocardial infarction, and depression). Strength of association between variables was measured by odds ratio, and 95% confidence intervals were generated; two-sided p-values were obtained by Fisher's exact test.

Results: Patient counts in each cohort were as follows: UST without PsA, n=2697; UST with PsA, n=590; conventional systemic without PsA, n=5105; conventional systemic with PsA, n=529. Patients with PsO and a PsA diagnosis had a higher prevalence of diabetes, obesity, and hypertension across both conventional systemic and UST cohorts vs. PsO alone (Table 1). Similarly, inability to work was notably higher in patients with PsO and comorbid PsA vs. PsO alone (Figure 1). Patients with PsO and comorbid PsA receiving UST were more likely to have a diagnosis of depression than those receiving conventional systemic treatment (Table 1).

Table 1. Prevalence odds ratio of baseline characteristics of patients with PsO treated with either UST or a conventional systemic agent. Odds ratios and 95% CIs are shown for the prevalence of each patient baseline characteristic in the PsO with comorbid PsA group vs. the prevalence in the PsO alone group. *Obesity is defined as a BMI ≥30 kg/m2. BMI, body mass index; CI, confidence interval; PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab

Baseline variable	Treatment cohort	Odds ratio	95% CI
Ability to work	UST	0.27	0.21–0.35
	Conventional systemic	0.49	0.37–0.65
Smoking	UST	0.94	0.76–1.17
	Conventional systemic	0.72	0.58–0.89
Depression	UST	1.54	1.25–1.88
	Conventional systemic	1.14	0.91–1.42
Obesity*	UST	1.34	1.11–1.62
	Conventional systemic	1.21	1.01–1.46
Diabetes	UST	1.45	1.10–1.89
	Conventional systemic	1.51	1.11–2.04
Hypertension	UST	1.54	1.26–1.87
	Conventional systemic	1.30	1.03–1.62
Myocardial infarction	UST	1.67	0.98–2.76
	Conventional systemic	1.17	0.56–2.21

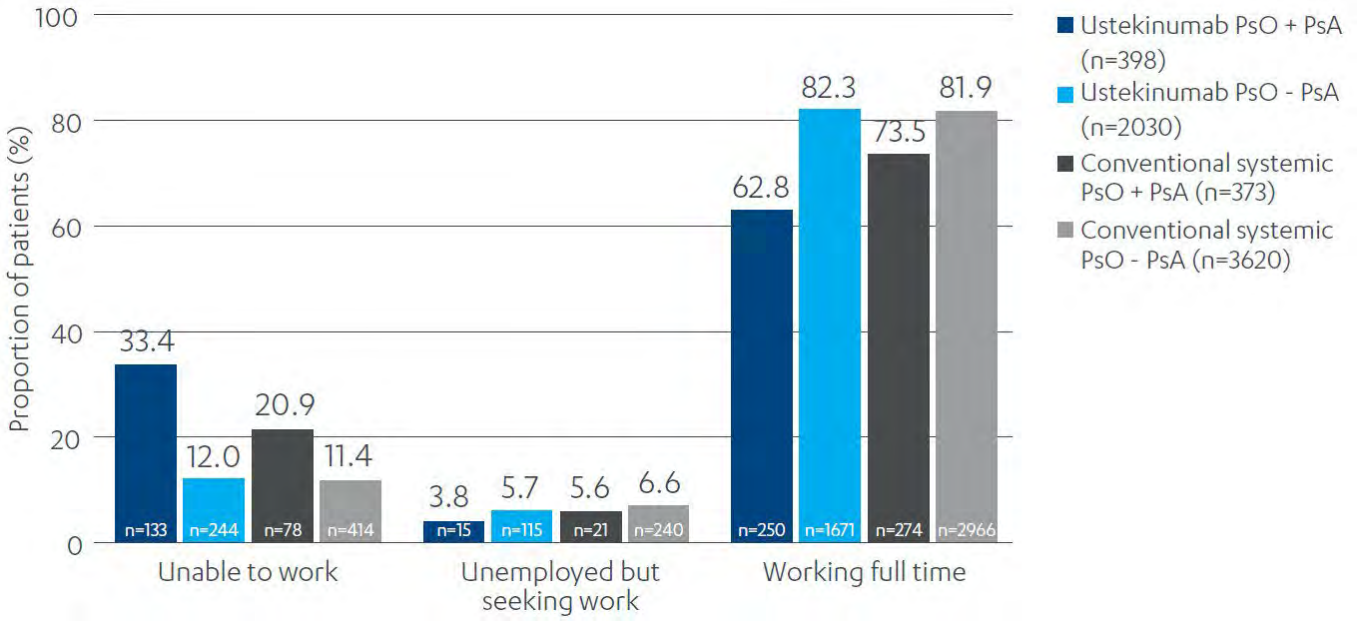


Figure 1. Employment status of patients with PsO by presence of comorbid PsA and treatment type. PsA, psoriatic arthritis; PsO, psoriasis.

Conclusion: These results indicate that the prevalence of obesity, diabetes, hypertension, and inability to work was higher in patients with PsO and comorbid PsA vs. PsO alone. Depression was also more prevalent in patients with PsO and comorbid PsA receiving biologic treatment vs. those receiving conventional systemics. These results potentially indicate a higher inflammatory and quality-of-life burden in patients with PsO and comorbid PsA, highlighting the need for adequate patient assessment and follow-up to ensure a best possible holistic patient management approach.

References: 1. Shah et al. *RMD Open* 2017;3:e000588; 2. Coates et al. *Lancet* 2015;386:2489–98; 3. Mason et al. *JAMA Dermatol* 2018;154:581–8.

Disclosure: W. Tillett, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **A. Ogdie**, Amgen, 2, 5, AbbVie, 2, BMS, 2, Celgene, 2, Gilead, 2, Lilly, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5; **P. Gorecki**, Janssen, 3; **A. Passey**, Janssen, 3.

Abstract Number: 1355

Psoriatic Arthritis Incidence Among Patients Receiving Biologic Medications for Psoriasis; A Nested Case Control Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The objective of this study was to investigate the effect of biological treatments for psoriasis on the incidence of psoriatic arthritis.

Methods: A retrospective cohort study using the electronic medical records of a large health maintenance organization. Patients who had received biological treatment for psoriasis and were not diagnosed with psoriatic arthritis before or at the time of biologic treatment initiation were included. Controls were matched by age at diagnosis, gender, time until treatment initiation, maximum BMI and smoking. The groups were different in most characteristics. Hence,

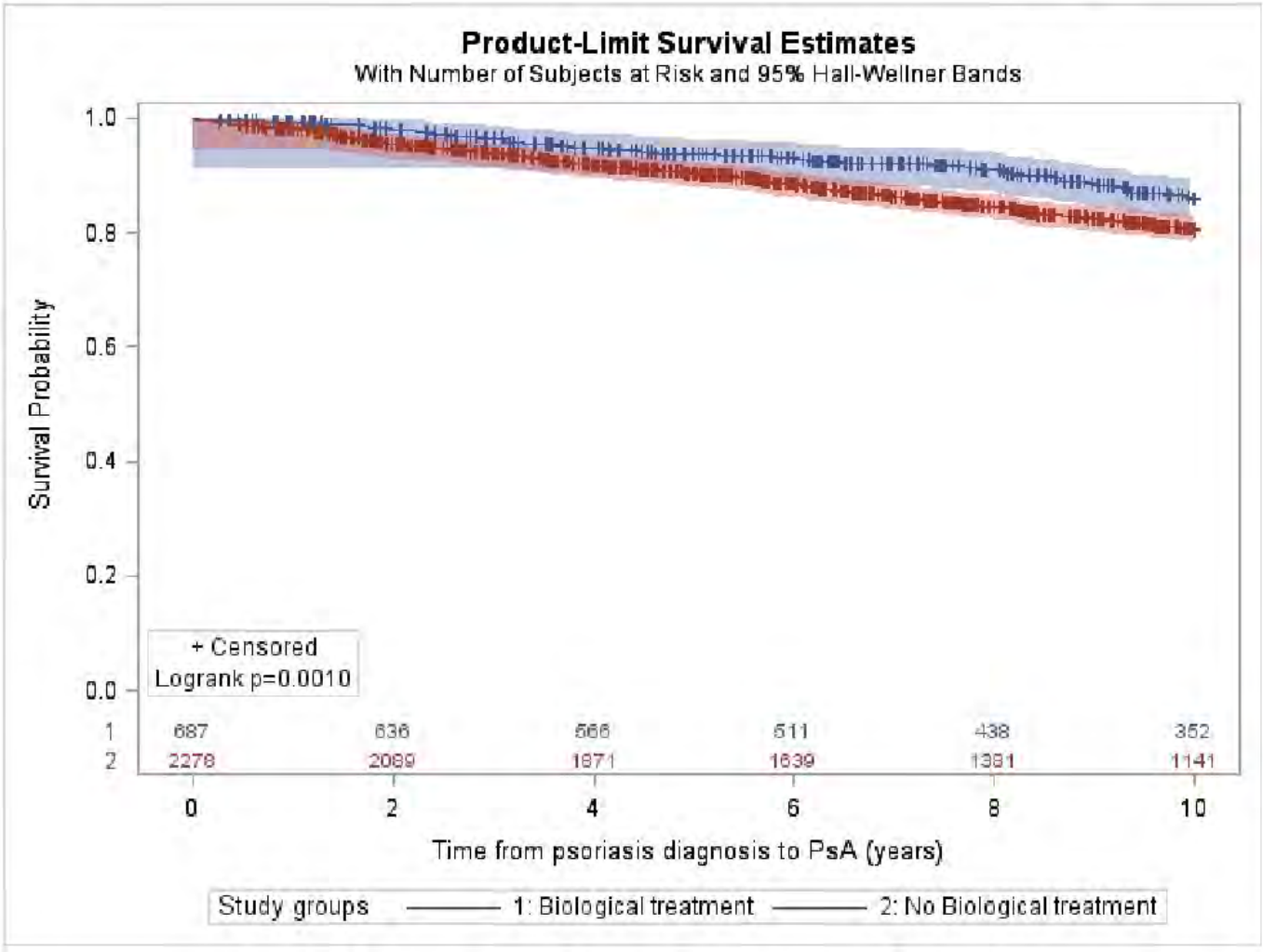
Table 1. comparisons between the study groups

	No biological treatment N=2278	Biological treatment N=687	P-value
Age at psoriasis diagnosis	46.72 (15.74) [48.1, 1.74-88.83]	35.25 (15.09) [33.3, 0.97-86.68]	<.0001
Age at psoriasis diagnosis grouped			<.0001
0-18	104 (4.57%)	80 (11.64%)	
18-25	127 (5.58%)	101 (14.7%)	
25-35	294 (12.91%)	202 (29.4%)	
35-45	438 (19.23%)	120 (17.47%)	
45-55	596 (26.16%)	107 (15.57%)	
55-65	442 (19.4%)	57 (8.3%)	
65-75	218 (9.57%)	16 (2.33%)	
75+	59 (2.59%)	4 (0.58%)	
Gender - female	837 (36.74%)	244 (35.52%)	0.5584
#BMI measures‡	10.7 (10.8) [8, 1-135]	8.9 (9.5) [6, 1-72]	<.0001
Maximum BMI (Kg/m²)‡	30.25 (6.4) [29.3, 14.3-60]	29.5 (6.78) [28.7, 13.9-58.2]	0.0032
mean BMI (Kg/m²)‡	28 (5.3) [27.4, 14.3-49.4]	27.4 (5.8) [27, 12.9-47]	0.0038
BMI≥30 (Kg/m²)‡	976 (44.94%)	277 (41.04%)	0.0747
Smoking‡			0.0845
Currently or in the past	1206 (53.79%)	335 (50%)	
Never	1036 (46.21%)	335 (50%)	
Time between diagnosis and treatment (years)	2.7 (2.8) [1.6, 0-9.5]	3.8 (3) [3.4, 0-9.5]	<.0001
Time between diagnosis and treatment (years)			<.0001
0-1	941 (41.31%)	174 (25.33%)	
1-3	499 (21.91%)	145 (21.11%)	
3-6	448 (19.67%)	169 (24.6%)	
6+	390 (17.12%)	199 (28.97%)	
Diagnosis year			0.0001
1998-2004	917 (40.25%)	218 (31.73%)	
2005-2011	708 (31.08%)	227 (33.04%)	
2012-2020	653 (28.67%)	242 (35.23%)	
Follow-up time (years)	7.6 (3.1) [10, 0-10]	7.8 (3) [10, 0-10]	0.4292
PsA in 10 years	374 (16.4%)	76 (11.1%)	0.0006

Continuous variables are presented with mean (standard deviation) [median, range].

Figure 1- Kaplan-Meier curve

Kaplan-Meier curves comparing PsA incidence in 10 years among patients with and without biological treatment.



a propensity score matching was implemented. The groups were compared via log rank test and a multivariable Cox regression.

Results: Overall, 1326 cases were included; 663 patients that had received biological treatment and 663 that had not. The Kaplan-Meier curve for the propensity score matched groups reflected a statistically significant increased risk for PsA among the control group compared to the biological treatment group. The results of the multivariable Cox regression showed that the control group had a significantly higher risk for PsA compared to the biological treatment group (adjusted HR=1.39; 95%CI: 1.03-1.87).

Conclusion: This study demonstrates a statistically and clinically significant lower risk for developing PsA among patients with psoriasis that receive biologic medications. The results suggest considering treatment with biologic medications in patients that present with significant risk factors for PsA at an earlier stage of treatment.

Table 2. Multivariable Cox regression of the propensity score matching table

	Adj.HR	95%CI		P-value
		Low	Up	
No biological treatment	1.39	1.03	1.87	0.0295
Age at diagnosis	1.02	1.01	1.03	<.0001
Gender - female	1.80	1.34	2.42	<.0001
Time till start treatment	0.86	0.81	0.91	<.0001
Diagnosis period				
1998-2004	0.47	0.31	0.71	0.0003
2005-2011	0.43	0.29	0.61	<.0001
2012-2020	1			

Adj.HR = adjusted hazard ratio

Disclosure: I. Sagy, None; **Y. Shalev Rosenthal**, None; **N. Schwartz**, None; **L. Pavlovsky**, None.

Abstract Number: 1356

Effects of TNF-α versus Secukinumab on Active Ultrasound Confirmed Enthesitis in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Enthesitis is an important aspect of disease in PsA and its clinical assessment has problems in terms of sensitivity and overlap with alternative co-morbid conditions. Imaging has emerged as the preferred option to assess enthesitis and research has demonstrated that those with persistent active US entheseal disease are at risk of progressive articular damage. There is limited data to help clinicians select the most appropriate biologic therapy for PsA patients. We wanted to assess the response on active US confirmed enthesitis to different forms of biologic therapy to study its utility in making more informed decisions and correlate clinical and imaging data.

Methods: The MAdrid Sonographic Enthesitis Index (MASEI) score assesses both chronic and active entheseal disease and is validated for use in SpA. The MASEI score was modified to count only the active elementary lesions (ActiveMASEI) which include hypoechogenicity, bursitis, tendon thickness and active power doppler signal at 12 entheses sites. This was a prospective observational study and to be included patients had to be aged ≥ 18 years, fulfil the classification criteria for PSA (CASPAR) and due to commence on their first biologic therapy. The trained

Table 1. Baseline characteristics as per class of biologic treatment. All variables with SD unless stated and assessed per group by an Independent T test apart from sex which was by Fisher's Exact Test

Patient Characteristic n=80	Overall	IL-17i (n=24)	TNFi (n= 56)	p-value (<0.05 in bold)
Baseline Characteristics				
Age, years	45.29 (12.74)	46.04 (10.33)	44.96 (13.72)	0.70
Sex, (n)%				0.23
Male	38 (47.5)	14	24	
Female	42 (52.5)	10	32	
BMI kg/m^2	28.99 (5.57)	29.63 (4.99)	28.70 (5.83)	0.47
Duration of from PsA diagnosis, years	7.97 (7.38)	7.21 (7.49)	8.29 (7.38)	0.56
Concomitant csDMARD n (%) .	38 (51.3)	7 (29.2)	31 (55.4)	0.10
Methotrexate n (%)	29 (36.3)	7 (29.2)	22 (39.3)	0.73
Baseline Disease scores				
Tender Joint count	12.43 (11.78)	11.04 (10.63)	13.02 (12.28)	0.47
Swollen Joint count	4.29 (5.11)	4.42 (5.60)	4.23 (4.94)	0.89
PASI	3.10 (4.13)	4.35 (3.86)	2.56 (4.15)	0.07
Patients Global assessment of disease activity VAS mm	58.36 (23.16)	55.83 (22.97)	59.45 (23.36)	0.53
Patients Global assessment of pain VAS mm	61.71 (22.84)	56.88 (19.99)	63.79 (23.82)	0.19
LEI /6	1.18 (1.35)	1.29 (1.04)	1.13 (1.47)	0.57
SPARCC enthesitis index /16	2.84 (2.30)	2.71 (1.83)	2.89 (2.50)	0.71
BASDAI score	6.51 (2.09)	6.32 (2.08)	6.59 (2.11)	0.61
Dactylitis score /20	0.66 (1.41)	0.75 (1.68)	0.63 (1.29)	0.75
NAPSI fingernails /80 n = 65	9.90 (11.45)	13.05 (14.24)	8.59 (9.97)	0.22
HAQ-DI	1.26 (0.68)	1.24 (0.75)	1.27 (0.66)	0.84
DLQI	6.51 (6.61)	9.96 (7.29)	5.04 (5.76)	**0.01**
CRP mg/L	6.80 (11.81)	5.41 (11.22)	7.39 (12.10)	0.48
DAS-28	3.57 (1.20)	3.41 (1.23)	3.65 (1.89)	0.43
DAPSA	29.42 (17.81)	27.30 (16.97)	30.33 (18.24)	0.48
Baseline ultrasound score				
ActiveMASEI /64	11.73 (7.01)	10.83 (5.44)	12.11 (7.60)	0.40

sonographer was blinded to all clinical findings and treatment choice prior to scanning. All patients were rescanned at 16 weeks of treatment as per their first review by the same investigator blinded to treatment and clinical outcomes.

Results: In total 80 patients were enrolled. All patients received the licensed dosing with 24 patients commenced on secukinumab (150mg n =18, 300mg n = 6) and 56 on TNFi (Adalimumab n = 50, certolizumab pegol n =4 and etanercept n = 2). 75 patients completed the study (Secukinumab n = 23 and TNFi n= 52). Baseline characteristics are as per Table 1 and were broadly similar for either class of biologic apart from the baseline DLQI (Skin questionnaire) score. The average age was 45.29 yrs (12.74) and 42 (52.5%) participants were female.

Table 2. Change in clinical outcomes from baseline after 16 weeks of treatment. Outcomes assessed with an independent t test apart from PsARC and MDA criteria which used a Chi square test

Outcome n = 75 unless stated	IL-17i (n = 23)	TNFi (n = 52)	P-value (< 0.05 in bold)
Tender Joint count	3.96 (8.01)	5.29 (7.19)	0.48
Swollen Joint count	2.61 (4.55)	2.65 (4.10)	0.97
PASI	3.44 (3.50)	1.03 (2.30)	**0.001**
Patients Global assessment of disease activity VAS mm	23.52 (26.91)	23.06 (28.89)	0.95
Patients Global assessment of pain VAS mm	22.39 (20.16)	23.73 (26.63)	0.83
LEI	0.61 (1.16)	0.27 (1.16)	0.25
SPARCC enthesitis index	1.39 (1.88)	1.11 (2.00)	0.58
BASDAI score	2.13 (2.18)	2.25 (2.19)	0.83
Dactylitis score /20	0.61 (1.37)	0.56 (1.16)	0.87
NAPSI fingernails /80 n = 60	8.74 (11.70) n=19	4.56 (7.46) n=41	0.10
HAQ-DI	0.30 (0.58)	0.32 (0.53)	0.90
DLQI	5.57 (7.52)	1.35 (4.18)	**0.005**
CRP mg/L n= 73	3.23 (11.46)	2.30 (13.88)	0.78
DAS-28 n = 73	0.98 (1.03)	1.01 (1.056)	0.89
DAPSA n =73	11.50 (13.30)	12.97 (12.93)	0.66
Achieved MDA (%)	10 (43.5)	21 (40.4)	0.81
PsARC response achieved (%)	16 (69.6)	41 (78.8)	0.40

The mean ActiveMASEI score reduction was 4.37 (5.31) with TNFi compared with 2.22 (3.01) for secukinumab which was significant (-2.148(-4.080, -0.216) p = 0.030). The Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC) correlated with the baseline ActiveMASEI score as per Spearman's Rank (rs = 0.23 p = 0.04) and a change in SPARCC significantly correlated with a change in ActiveMASEI (rs =0.30 p = 0.01). This was not seen with the Leeds Enthesitis Index (LEI) score at baseline or with change (rs= 0.07 p = 0.51 and rs =0.14 p = 0.23 respectively). Clinical outcomes are noted in table 2 and apart from a significant reduction in regards to the PASI and DLQI

score with Secukinumab versus TNFi (3.44 (3.50) vs 1.03 (2.30) p = 0.001 and 5.57 (7.52) vs 1.35 (4.18) p = 0.005 respectively) similar findings were seen for both classes of biologic therapy.

Conclusion: In this study we have compared the effect on active US confirmed enthesitis between different forms of biologic therapy for PsA. We have demonstrated superiority of TNFi versus secukinumab in regards to active entheseal disease. The SPARCC score correlated with baseline active entheseal US disease and with change in response to treatment highlighting it ability to capture active entheseal disease.

Disclosure: A. Elliott, NOVARTIS, 6, LILLY, 6; **G. Wright**, None; **A. Pendleton**, None; **M. Rooney**, None.

Abstract Number: 1357

Clinical and Molecular Profiles Determining Cardiovascular Risk in Psoriatic Arthritis: Specific Response to Apremilast and Methotrexate

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: 1) to evaluate clinical and subclinical markers of cardiovascular (CV) disease risk and its relationship with inflammation, disease activity and metabolic comorbidities in PsA patients and 2) to identify clinical and molecular profiles that could distinguish patients who may be benefit from the positive effects of PDE-4 inhibitor on CV risk.

Methods: Design: 1) Cross-sectional study including 100 PsA patients and 100 healthy donors (HDs) and 2) Longitudinal study including 45 patients treated with the PDE-4 inhibitor, Apremilast (n = 15), Methotrexate (MTX) (n = 15) alone or in combination (n = 15), evaluated at baseline and after 6 months of treatment. CV risk factors and clinical characteristics were recorded. Levels of 92 proteins mainly related to CV disease were evaluated in plasma by "Olink Proteomics" technology. The mRNA expression of CV-related proteins was analyzed in peripheral mononuclear cells (PBMCs). Cluster analyses were performed to identify specific clinical and molecular profiles of patients. ROC curve analyses were also performed to recognize biomarkers of disease activity, insulin resistance (IR) and therapeutic response.

Results: PsA patients showed a higher prevalence of metabolic alterations such as, obesity (30%) and IR (45%) compared to HDs. Metabolic complications were associated with disease activity and higher acute phase reactants. Specifically, IR state was related to a persistent inflammatory status (c-reactive protein) during the 5-years prior to

this study. Thirty-six CV-related proteins were altered in the plasma of PsA patients and associated with clinical parameters such as disease activity, acute phase reactants, body surface area affected by psoriasis and the presence of onychopathy. Biomarkers of IR (MMP-3, CD-163 and FABP-4) and disease activity (GAL-3 and FABP-4) were identified by ROC analyses. Two clusters of PsA patients were identified depend on the clinical and molecular profiles which showed different therapeutic responses to Apremilast and MTX. Thus, the cluster 2 which included patients with higher prevalence of CV risk factors and increased CV-related proteins in plasma showed a better response with Apremilast compared to MTX. In these patients, PDE-4 inhibitor reduced disease activity in parallel with body mass index and IR state. Likewise, biomarkers of therapeutic response to Apremilast were recognized (CD-163, LTBR and CNTN-1) with high sensitivity and specificity.

Conclusion: 1) Metabolic alterations in PsA are associated with disease activity and persistence of inflammatory profile; 2) Subclinical CV risk biomarkers in PsA is related to clinical characteristics where CD-163 could play an important role; 3) PsA patients with a specific clinical and molecular profile showed better response to therapy with Apremilast and 4) circulating plasma levels of CD-163, LTBR and CNTN-1 could be useful as biomarkers of therapeutic response to Apremilast.

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Abstract Number: 1358

Clusters of Psoriatic Arthritis Patients at Baseline Based on Different Ultrasound Detected Synovitis: Exploratory Analysis from a Phase III Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is characterized by inflammation of synovial membranes and entheseal sites leading to pain, structural damage, impairment of physical function and quality of life.[1 2] ULTIMATE

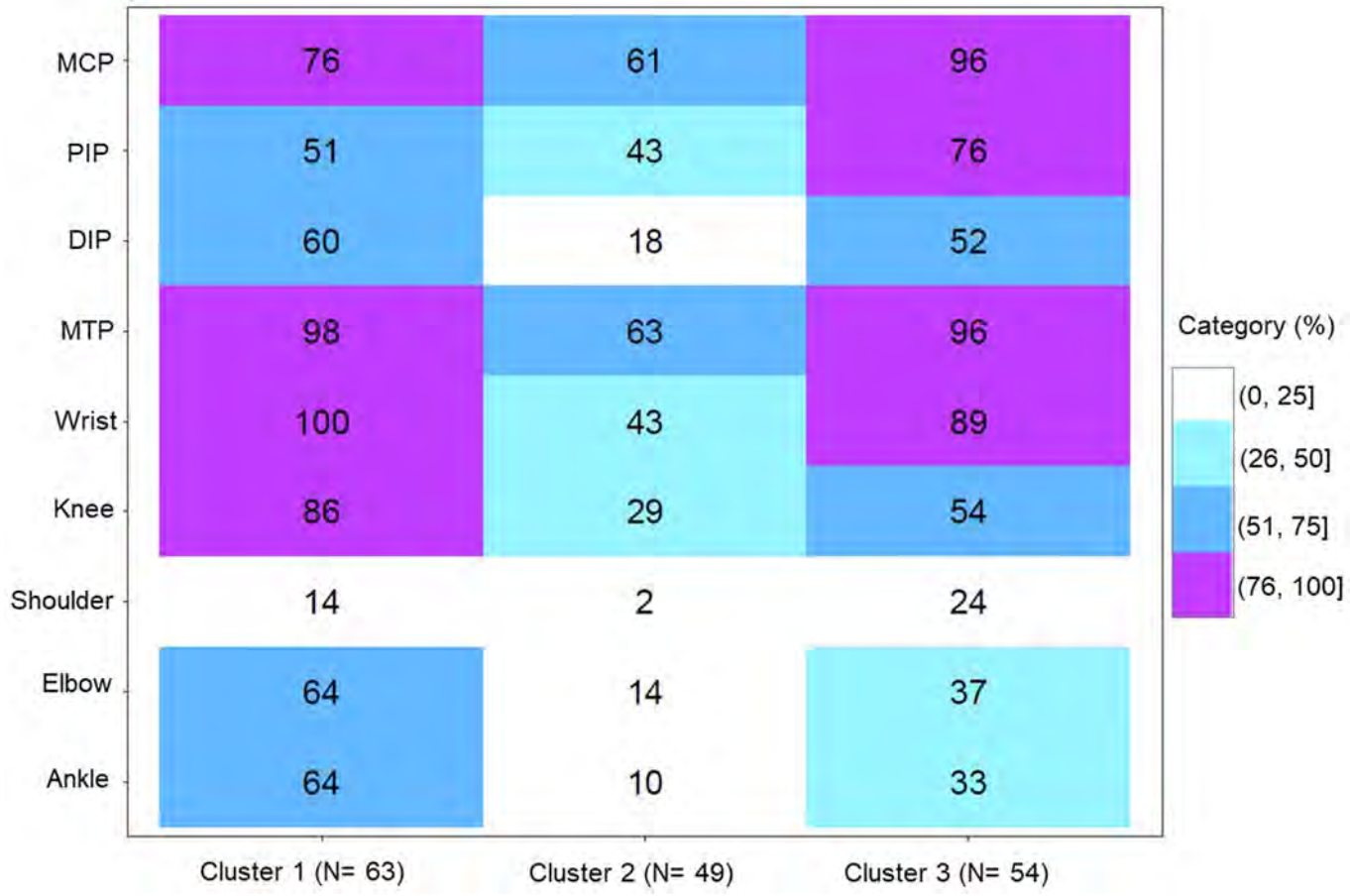

Figure 1. Heat map reporting the distribution of ultrasound detected synovitis for each cluster. Ultrasound detected synovitis was defined as PDUS ≥ 1 DIP, distal interphalangeal; MCP, metacarpophalangeal; MTP, metatarsophalangeal; PIP, proximal interphalangeal.

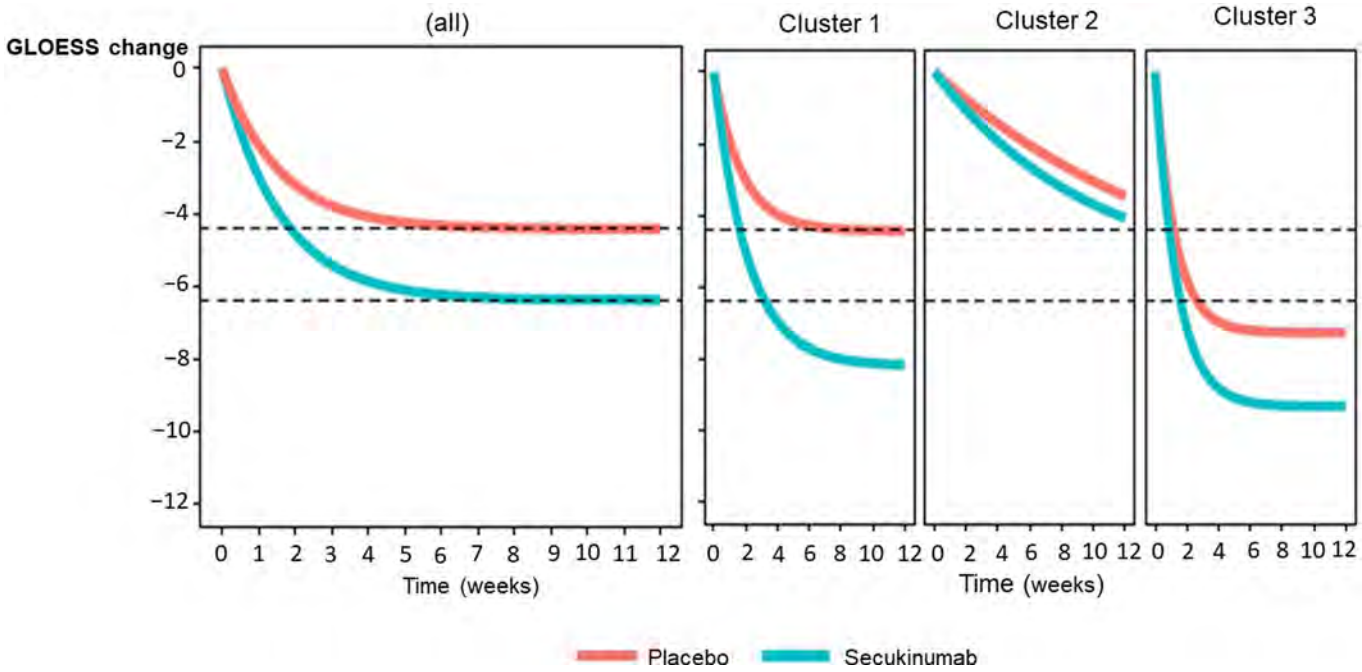

Figure 2. Non linear mixed model for change in GLOESS from baseline to week 12 by US cluster and treatment. GLOESS, global EULAR-OMERACT synovitis score; US, ultrasound.

Table. Main Baseline Clinical Characteristics of Ultrasound Clusters

Table. Main Baseline Clinical Characteristics of Ultrasound Clusters			
Characteristics, mean (SD) unless otherwise specified	**Cluster 1 (N=63)**	**Cluster 2 (N=49)**	**Cluster 3 (N=54)**
Clinical Characteristics			
Tender joint count (out of 78 joints)	12 (8)	12 (8)	17 (13)
Swollen joint count (out of 76 joints)	8 (5)	8 (6)	12 (11)
SPARCC enthesitis index	5 (3)	4 (3)	4 (3)
Patient VAS psoriatic arthritis pain	54 (24)	60 (22)	63 (20)
Patient global assessment of disease activity (VAS)	58 (26)	59 (21)	62 (20)
HAQ-DI score	1 (1)	1 (1)	1 (1)
Physician's global assessment of disease activity (VAS)	54 (22)	52 (14)	56 (21)
C- reactive protein levels mg/dl	9 (13)	12 (16)	13 (18)
Ultrasound Characteristics			
OMERACT enthesitis score definition1	6 (4)	5 (4)	6 (5)
GLOESS Power Doppler Ultrasound	29 (11)	10 (6)	35 (18)
GLOESS synovial hypertrophy	29 (11)	10 (6)	34 (18)
GLOESS Power Doppler	4 (4)	5 (3)	13 (10)
Number of synovitis GLOESS joints	11 (4)	4 (2)	13 (4)

GLOESS, Global EULAR-OMERACT synovitis score; HAQ-DI, Health Assessment Questionnaire-Disability Index; OMERACT, Outcome Measures in Rheumatology; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada Index; VAS, visual analogue scale.

Global OMERACT (PDUS) enthesitis score (definition 1) ranges from 0-48 and is the sum of the B-Mode (0 = absence, 1 = presence) and PD signal across 12 enthesitis sites.

(NCT02662985) was the first large, randomized, double-blind, placebo-controlled phase IIIb study in PsA, using the Global OMERACT EULAR Synovitis Score (GLOESS), an ultrasound score at patient level, to demonstrate that secukinumab (SEC) rapidly and significantly decreased synovitis.[2] However, little is known about the heterogeneity of PsA related to the distribution of ultrasound detected synovitis in PsA and its impact on treatment response. We report exploratory analyses to identify clusters of patients (pts) based on baseline ultrasound distribution and severity of synovitis [power doppler and greyscale alone and combined power doppler ultrasound (PDUS)] and their longitudinal treatment trajectory with SEC versus Placebo over 12 weeks.

Methods: ULTIMATE was a 52-week study with a 12-week double-blind, placebo-controlled period followed by 12-week open-label (OL) treatment and 6-month OL extension period. Factor analysis and clustering methods were applied post hoc to identify groups of PsA pts with similar baseline composite PDUS-detected synovitis characteristics. Aggregation of baseline demographics, clinical and ultrasound characteristics were explored through cluster analysis using descriptive statistics. Nonlinear mixed models for change in GLOESS (primary endpoint of the study) from baseline to Week 12 across clusters were used to explore the treatment difference between SEC and placebo up to Week 12.

Results: The baseline demographics, clinical and ultrasound characteristics have been reported previously.[3] One hundred and sixty-six pts could be categorized in 3 different clusters (N1=63, N2=49 and N3=54) at baseline. The heatmap in **Figure 1** shows the differences in the distribution of PDUS-detected synovitis at the joint level across the 3 clusters. The baseline ultrasound characteristics showed higher disease activity, more severe synovitis and enthesitis in clusters 3 and 1 vs. cluster 2 (**Table**). Cluster 3 showed a trend toward increased clinical activity (TJC, SJC, pain and PGA VAS). The longitudinal trajectories of the 3 clusters up to Week 12 showed a treatment difference in favor of SEC, compared with placebo, in clusters 3 and 1 but not in cluster 2 (**Figure 2**).

Conclusion: The cluster analysis in the ULTIMATE trial highlights the heterogeneity of PsA. Interestingly, only clusters 1 and 3, with evidence of higher amounts of PDUS-detected inflammation had disease activity that responded to secukinumab treatment. Ultrasound may help in identifying different levels of inflammation of synovitis and enthesitis at tissue level in patients with similar clinical phenotype and could support a more rigorous selection of patients with active disease in future clinical trials.

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2. D'Agostino M-A, et al. *Arthritis Rheumatol* 2020;72 (suppl 10)
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Disclosure: M. D'Agostino, Sanofi, 2, 6, Novartis, 2, 6, BMS, 2, 6, Janssen, 2, 6, Celgene, 2, 6, Roche, 2, 6, AbbVie, 2, 6, UCB, 2, 6, Eli Lilly, 2, 6; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6; **C. Gaillez**, Novartis Pharma AG, 3, 11, BMS, 11; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **E. Naredo**, AbbVie, 6, Roche, 6, BMS, 6, Pfizer, 6, UCB, 6, Lilly, 5, 6, Novartis, 6, Janssen, 6, Celgene GmbH, 6; **P. Carron**, UCB, 2, 5, 6, Merck Sharp Dohme, 2, 5, 6, Pfizer, 2, 5, 6, Novartis, 2, 6, Bristol Myers Squibb, 2, 6, AbbVie, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Celgene Corporation, 2, 6; **R. Burgos-Vargas**, None; **P. Mandl**, MSD, 5, 6, Celgene, 5, 6, Lilly, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6; **J. Rosa**, Abbvie, 6, Pfizer, 6, Lilly, 6, Janssen, 6, Novartis, 6, BMS, 6; **M. Boers**, BMS, 2, Pfizer, 2, GSK, 2, Novartis, 2; **P. Goyanka**, Novartis, 3; **W. Bao**, Novartis, 3; **D. Demanse**, Novartis, 3, 11.

Abstract Number: 1359

Risk of Respiratory Tract Infections with Biologic and Targeted Synthetic Antirheumatic Agents in Psoriatic Arthritis: A Systematic Review and Network Meta-analysis

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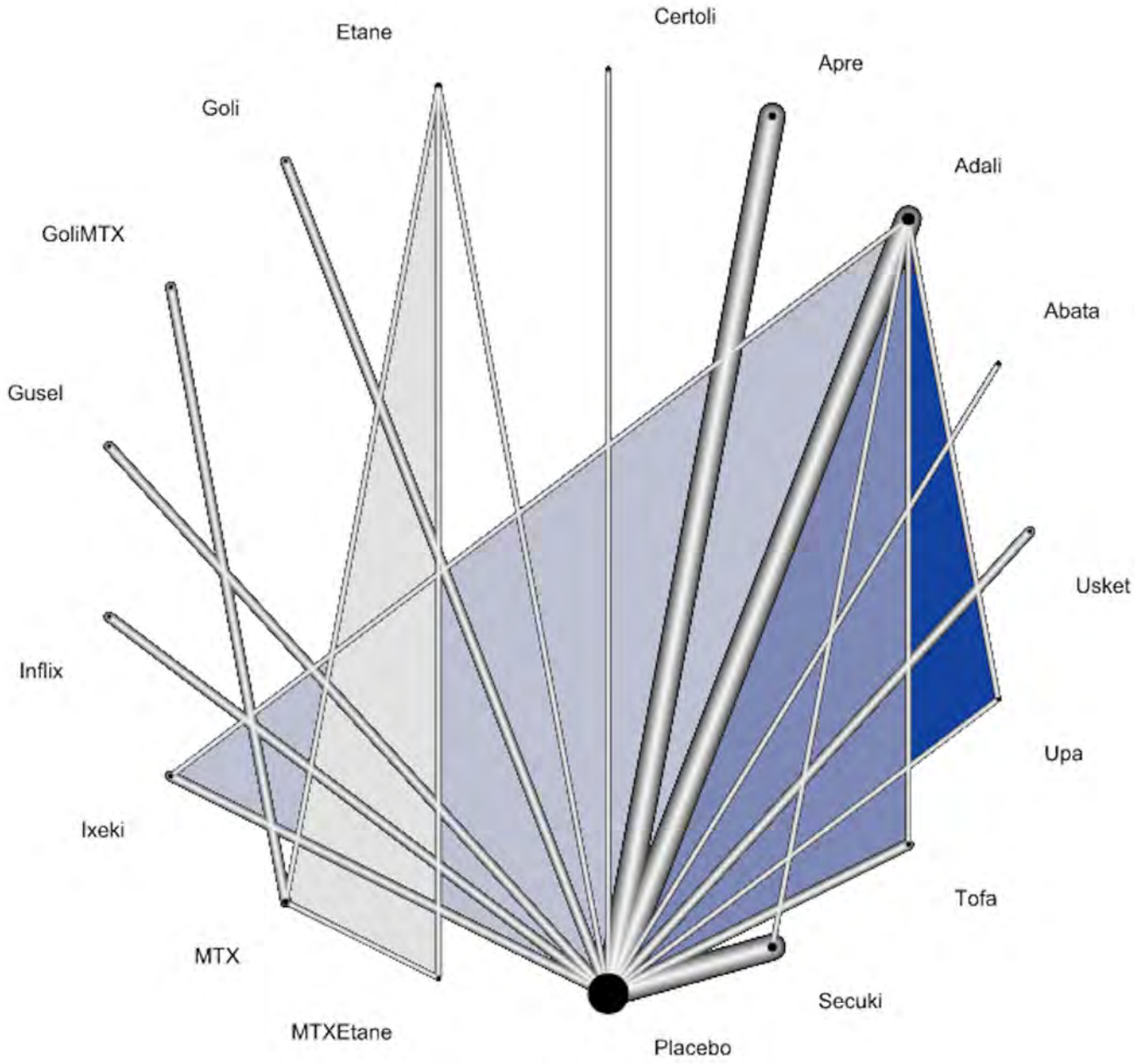
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: A variety of biologic and targeted synthetic disease modifying antirheumatic agents have been widely used among patients with psoriatic arthritis (PsA). Due to the lack of head-to-head comparison trials, the comparative risk of respiratory tract infections (RTIs) among these available agents remains unclear, however. Consequently, a network meta-analysis (NMA) was used to address this knowledge gap, and we sought to investigate the comparative risk of RTIs with different biologic and targeted synthetic disease modifying antirheumatic agents in PsA.



Abata (Rank 1)																	
0.40 (0.24, 0.69)	Adali (Rank 11)																
0.36 (0.17, 0.74)	0.73 (0.51, 1.05)	Apre (Rank 17)															
0.34 (0.15, 0.79)	0.71 (0.41, 1.21)	0.97 (0.54, 1.72)	Certoli (Rank 16)														
0.69 (0.28, 1.70)	1.41 (0.74, 2.68)	1.93 (0.98, 3.77)	1.99 (0.91, 4.38)	Etane (Rank 3)													
0.38 (0.19, 0.86)	0.78 (0.41, 1.50)	1.07 (0.54, 2.11)	1.11 (0.50, 2.44)	0.56 (0.23, 1.32)	Goli (Rank 14)												
0.68 (0.14, 2.07)	1.12 (0.36, 3.89)	1.53 (0.47, 5.01)	1.58 (0.40, 5.54)	0.80 (0.30, 2.11)	1.43 (0.39, 5.26)	GoliMTX (Rank 8)											
0.42 (0.19, 0.92)	0.87 (0.55, 1.36)	1.19 (0.73, 1.93)	1.23 (0.65, 2.31)	0.62 (0.30, 1.27)	1.11 (0.53, 2.29)	0.77 (0.23, 2.61)	Gusel (Rank 13)										
0.71 (0.30, 1.68)	1.40 (0.82, 2.39)	2.00 (1.09, 3.67)	2.07 (1.00, 4.29)	1.04 (0.46, 2.33)	1.87 (0.82, 4.21)	1.31 (0.37, 4.64)	1.69 (0.67, 3.25)	Inflix (Rank 2)									
0.50 (0.23, 1.08)	1.03 (0.67, 1.57)	1.41 (0.88, 2.30)	1.45 (0.77, 2.75)	0.73 (0.35, 1.51)	1.31 (0.63, 2.73)	0.92 (0.27, 3.10)	1.19 (0.66, 2.09)	0.70 (0.36, 1.36)	Ixeki (Rank 10)								
0.65 (0.25, 1.73)	1.34 (0.84, 2.80)	1.83 (0.95, 3.92)	1.89 (0.80, 4.49)	0.95 (0.68, 1.37)	1.71 (0.67, 4.35)	1.19 (0.48, 2.99)	1.54 (0.69, 3.47)	0.91 (0.38, 2.21)	1.30 (0.58, 2.99)	MTX (Rank 4)							
0.53 (0.20, 1.41)	1.09 (0.52, 2.28)	1.49 (0.70, 3.19)	1.55 (0.65, 3.65)	0.78 (0.54, 1.11)	1.39 (0.59, 3.55)	0.97 (0.37, 2.58)	1.26 (0.56, 2.83)	0.75 (0.31, 1.80)	1.06 (0.47, 2.38)	0.82 (0.57, 1.16)	MTXEtane (Rank 9)						
0.56 (0.29, 1.10)	1.15 (0.93, 1.43)	1.58 (1.18, 2.11)	1.64 (1.00, 2.68)	0.82 (0.49, 1.51)	1.48 (0.82, 2.73)	1.03 (0.33, 3.26)	1.33 (0.90, 1.98)	0.79 (0.49, 1.34)	1.12 (0.79, 1.67)	0.86 (0.43, 1.75)	1.06 (0.52, 2.14)	Placebo (Rank 5)					
0.58 (0.28, 1.14)	1.19 (0.93, 1.44)	1.64 (1.11, 2.23)	1.64 (0.96, 2.80)	0.82 (0.43, 1.58)	1.48 (0.78, 2.82)	1.03 (0.32, 3.32)	1.34 (0.89, 2.08)	0.79 (0.45, 1.39)	1.13 (0.73, 1.74)	0.87 (0.42, 1.81)	1.06 (0.51, 2.20)	1.00 (0.82, 1.22)	Secuki (Rank 7)				
0.36 (0.16, 0.83)	0.74 (0.44, 1.24)	1.01 (0.56, 1.80)	1.04 (0.52, 2.11)	0.52 (0.24, 1.15)	0.94 (0.43, 2.06)	0.68 (0.19, 2.51)	0.85 (0.45, 1.61)	0.50 (0.24, 1.05)	0.72 (0.35, 1.52)	0.55 (0.23, 1.31)	0.68 (0.28, 1.80)	0.64 (0.39, 1.05)	0.64 (0.37, 1.09)	Tofa (Rank 15)			
0.45 (0.22, 0.93)	0.92 (0.69, 1.23)	1.26 (0.83, 1.90)	1.30 (0.73, 2.32)	0.65 (0.33, 1.28)	1.18 (0.62, 2.32)	0.85 (0.25, 2.89)	1.06 (0.62, 1.79)	0.63 (0.34, 1.15)	0.90 (0.55, 1.50)	0.69 (0.32, 1.49)	0.84 (0.38, 1.87)	0.80 (0.58, 1.07)	0.80 (0.57, 1.12)	1.25 (0.71, 2.21)	Upa (Rank 13)		
0.58 (0.26, 1.30)	1.29 (0.71, 2.01)	1.64 (0.84, 2.80)	1.69 (0.80, 3.39)	0.85 (0.39, 1.80)	1.53 (0.71, 3.32)	1.07 (0.31, 3.65)	1.38 (0.75, 2.68)	0.82 (0.42, 1.68)	1.16 (0.63, 2.16)	0.90 (0.38, 2.10)	1.10 (0.47, 2.58)	1.04 (0.66, 1.66)	1.04 (0.62, 1.79)	1.62 (0.82, 3.23)	1.30 (0.75, 2.27)	Usket (Rank 6)	

Methods: Medline, PubMed, Embase, Scopus, Cochrane Central, and clinicaltrials.gov were searched to identify phase 3 and 4 randomized clinical trials (RCTs) that reported safety outcomes of biologic and targeted synthetic disease modifying antirheumatic agents in PsA. Outcome of interest was occurrence of respiratory tract infection(s) within on-treatment or placebo-controlled duration. Mixed treatment comparisons were computed using NMA within

the frequentist framework. Fixed effect models were used due to sparse direct evidence and open network. Effect estimates were expressed as odds ratio (OR) with their 95% confidence intervals (CIs). P-scores were calculated to establish relative rankings of different treatment options. A sensitivity analysis was conducted using Bayesian NMA approach. All statistical analyses were conducted in R (v 4.0.2).

Results: A total of 33 RCTs were included in this systematic review. A total of 32 RCTs with 14,974 patients, and 17 unique treatment arms were included in the NMA and one RCT did not report any RTI events was excluded [see Figure 1.] Mixed treatment comparisons showed that abatacept (P-score 0.92) ranked as the best (lowest likelihood of RTIs) treatment compared to adalimumab (OR 0.49; 95% CI 0.24-0.99), apremilast (OR 0.36; 95% CI 0.17-0.74), certolizumab (OR 0.34; 95% CI 0.15-0.79), golimumab (OR 0.38; 95% CI 0.15-0.95), guselkumab (OR 0.42; 95% CI 0.19-0.92), tofacitinib (OR 0.36; 95% CI 0.16-0.83), and upadacitinib (OR 0.45; 95% CI 0.22-0.93). Apremilast ranked the lowest with increased likelihood of RTIs compared to infliximab (OR 2.00; 95% CI 1.09-3.67), and secukinumab (OR 1.58; 95% CI 1.11-2.25). However, no other significant differences were observed across different biologic and targeted synthetic disease modifying antirheumatic agents [Figure 2]. The results were consistent with Bayesian NMA.

Conclusion: Abatacept may have a lower risk of RTIs when used for treatment of PsA. Further analyses are warranted to assess the severity and type of RTIs associated with these treatments.

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Abstract Number: 1360

Ultrasound Demonstrates Continued Improvement in Psoriatic Arthritis Synovitis and Enthesitis with Secukinumab: 52-week Results from a Phase III Study

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SESSION INFORMATION

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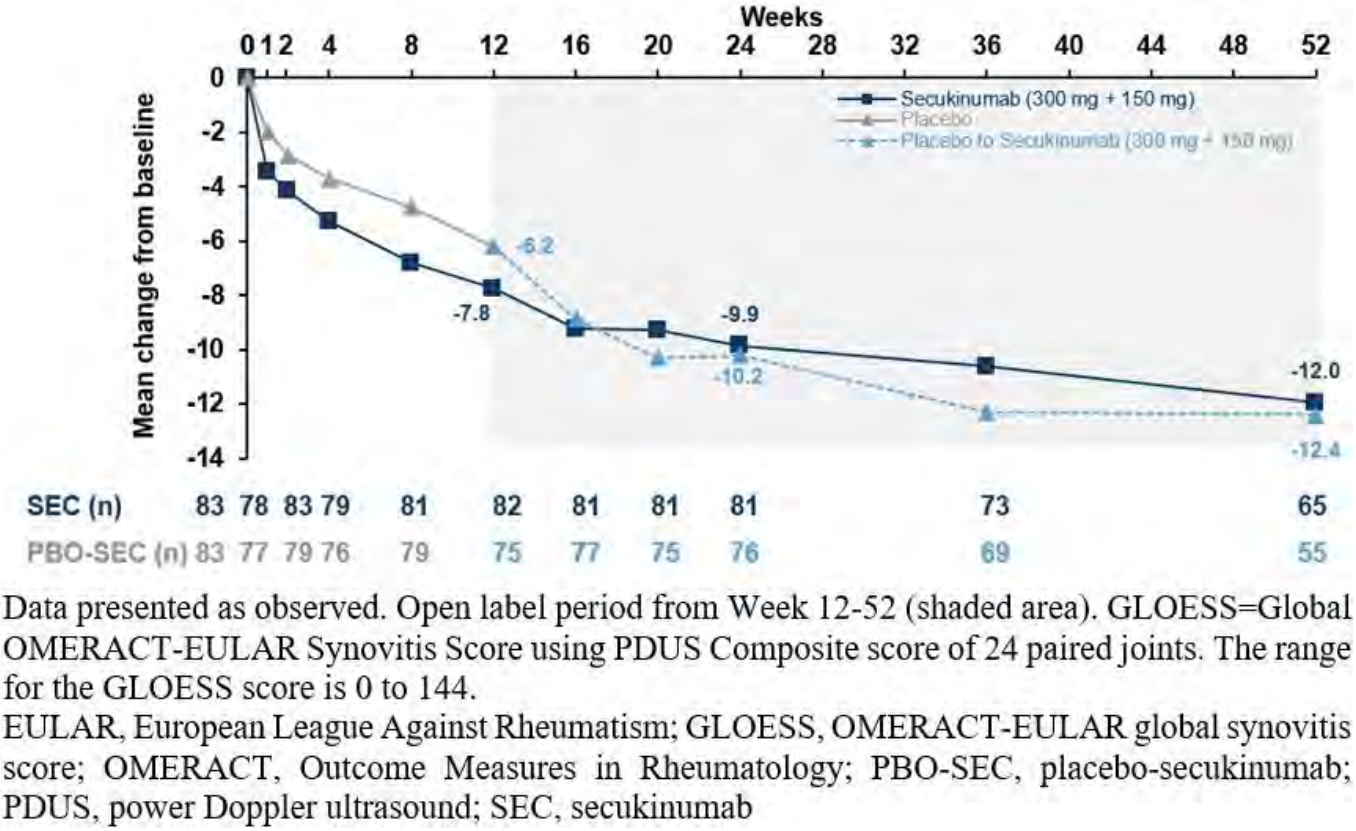
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM



Data presented as observed. Open label period from Week 12-52 (shaded area). GLOESS=Global OMERACT-EULAR Synovitis Score using PDUS Composite score of 24 paired joints. The range for the GLOESS score is 0 to 144.
EULAR, European League Against Rheumatism; GLOESS, OMERACT-EULAR global synovitis score; OMERACT, Outcome Measures in Rheumatology; PBO-SEC, placebo-secukinumab; PDUS, power Doppler ultrasound; SEC, secukinumab

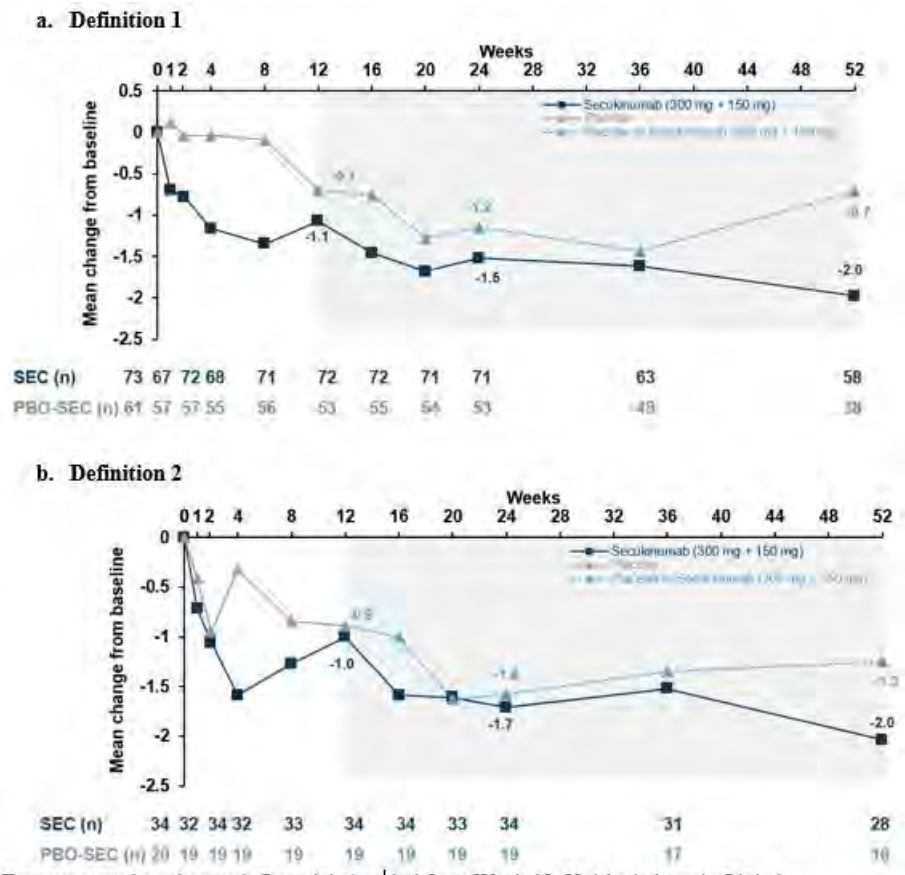
Figure 1. Mean change from baseline in GLOESS by treatment up to Week 52.

Background/Purpose: Power Doppler ultrasound (PDUS) is a sensitive non-invasive imaging tool to visualize a wide range of articular and periarticular inflammation in psoriatic arthritis (PsA).[1,2] ULTIMATE (NCT02662985) is the first large RCT that used ultrasound with Global OMERACT ultrasound synovitis score (GLOESS) as the primary endpoint, to demonstrate early benefits of secukinumab on synovitis in patients with PsA through 12 weeks.[3] Here we report the responsiveness of ultrasound on synovitis and enthesitis, clinical efficacy, and safety of secukinumab up to 52 weeks.

Methods: This was a 52-week study with a 12-week double-blind placebo-controlled treatment followed by 12-week open-label treatment and 6-month open-label extension treatment in all patients. Detailed study design and eligibility criteria have been reported previously.[3,4] Synovitis and ultrasound enthesitis response were measured by GLOESS and Global OMERACT enthesitis Score (Definitions 1 and 2)[4] at patient level, respectively. Other assessments across key PsA manifestations of joints (ACR responses), enthesitis, (SPARCC), skin (PASI responses), dactylitis (LDI) and physical function (HAQ-DI) were also evaluated. Data are presented as observed.

Results: A total of 166 patients were enrolled, of which 90% (75/83) of secukinumab and 83% (69/83) of placebo-secukinumab participants completed 52 weeks. A continued improvement in GLOESS was observed in both secukinumab and placebo-secukinumab group after switch to active therapy at Week 12 through Week 52 (**Figure 1**). A similar trend of improvement in Global OMERACT enthesitis score (Definition 1 and 2) was observed up to 52 weeks in both groups (**Figure 2**). Sustained clinical response rates were observed across multiple facets of disease and physical function up to 52 weeks in both secukinumab and placebo-secukinumab groups (**Table**). There were no new or unexpected safety findings.

Conclusion: ULTIMATE demonstrated the responsiveness of ultrasound on both synovitis and enthesitis outcomes in PsA supporting its use in clinical trials, and confirmed the rapid and continued benefits of secukinumab through 52



Data presented as observed. Open label period from Week 12-52 (shaded area). Global OMERACT (PDUS) enthesitis score Definition 1 ranges from 0-48 and is the sum of the B-Mode (0 = absence, 1 = presence) and PD signal across 12 enthesitis sites; Definition 2 ranges from 0-36 and is the sum of the PD signal across 12 sites. At each time point, only patients with a value at both baseline and that time point are included. Only patients with positive values (>0 at baseline) were included.
EULAR, European League Against Rheumatism; GLOESS, OMERACT-EULAR global synovitis score; N, total number of randomized patients; n, number of evaluable patients; OMERACT, Outcome Measures in Rheumatology; PBO-SEC, placebo-secukinumab; PDUS, power Doppler ultrasound; SEC, secukinumab

Figure 2. Mean change from baseline Global OMERACT enthesitis score up to Week 52.

weeks. Sustained efficacy was also observed across key clinical PsA manifestations with a safety profile consistent with previous reports.

References

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2. Uson J, et al. *Rheumatol Clin* 2018;14:27–35
3. D'Agostino MA, et al. *Arthritis Rheumatol* 2020;72 (suppl 10)
4. Boers M et al. *Ann Rheum Dis* 2021;80:314

Table. Clinical efficacy outcomes at Week 52 (Extension period)

	Secukinumab (300 mg + 150 mg; N = 83)	**Placebo-Secukinumab (N = 83)**
Responders, %		
ACR20	89	84
ACR50	68	72
ACR70	48	47
PASI 90*	59	74
PASI 100*	55	48
Resolution of dactylitis (LDI=0)	89	92
Change from baseline, mean (SD)		
SPARCC enthesitis index	–3.0 (2.3)	–3.6 (3.4)
HAQ-DI	–0.8 (0.6)	–0.7 (0.6)

*PASI response was calculated for patients with BSA ≥3 %. At Week 52, m for ACR were 65 and 57, PASI were 22 and 23, and LDI were 18 and 13 for secukinumab and placebo-secukinumab group, respectively.
ACR, American College of Rheumatology; BSA, Body Surface Area; HAQ-DI, Health Assessment Questionnaire Disability Index; LDI, Leeds Dactylitis Index; N, number of randomized patients, m, number of evaluable patients; PASI, Psoriasis Area and Severity Index; SD, standard deviation; SPARCC; Spondyloarthritis research consortium of Canada - enthesitis index.

Disclosure: M. D'Agostino, Sanofi, 2, 6, Novartis, 2, 6, BMS, 2, 6, Janssen, 2, 6, Celgene, 2, 6, Roche, 2, 6, AbbVie, 2, 6, UCB, 2, 6, Eli Lilly, 2, 6; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6; **C. Gaillez**, Novartis Pharma AG, 3, 11, BMS, 11; **C. Guerrero**, None; **P. HANOVA**, None; **T. Cazenave**, None; **M. Stoenoiu**, AbbVie, 2, 5, 6, UCB, 2, 5, 6, Pfizer, 2, 5, 6, MSD, 2, 5, 6, Roche, 2, 5, 6; **M. Backhaus**, BMS, 2, 5, 6, AbbVie, 2, 5, 6, Gilead, 2, 5, 6, Jonsson, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6; **G. Mouterde**, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6; **M. Boers**, BMS, 2, Novartis, 2, GSK, 2, Pfizer, 2; **A. Duggan**, Novartis, 3; **P. Goyanka**, Novartis, 3; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6.

Abstract Number: 1361

Impact of Intermediate Treatment Interruption on Secukinumab Efficacy in Patients with Active Psoriatic Arthritis and Ankylosing Spondylitis: Interim Analysis Results from the SERENA Study

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SESSION INFORMATION

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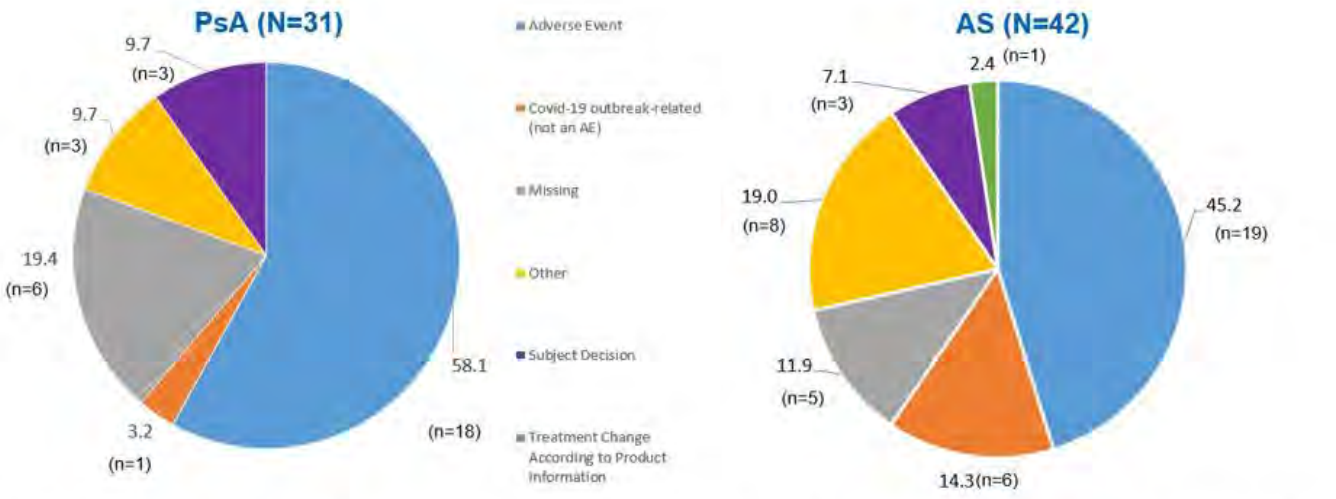
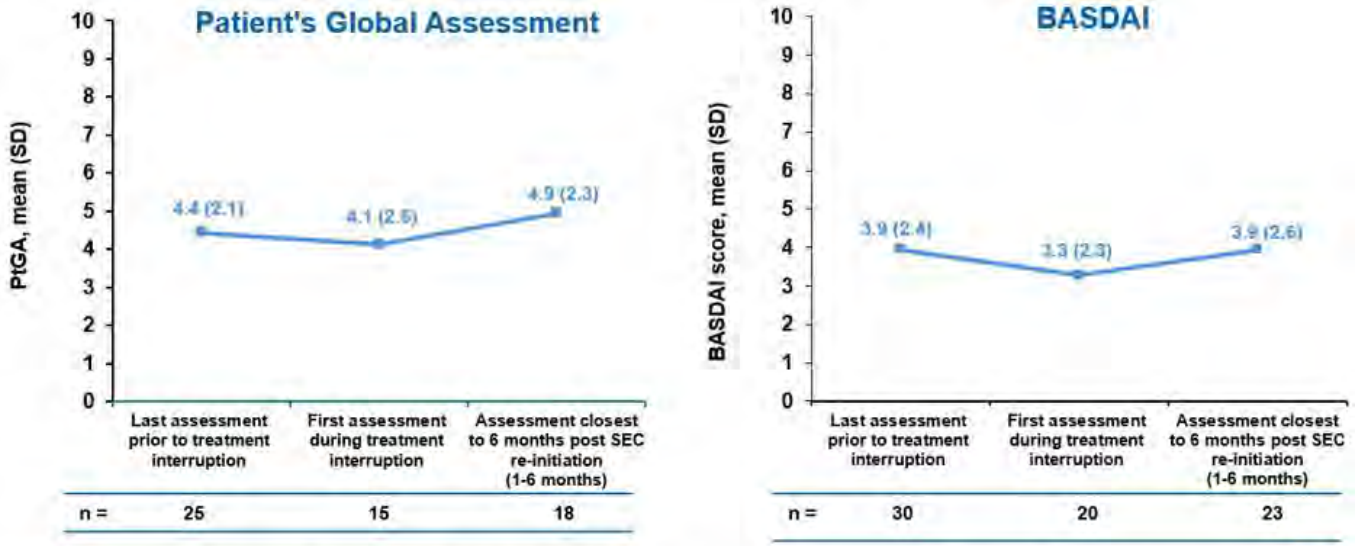
Session Time: 8:30AM–10:30AM

Background/Purpose: Secukinumab (SEC) has demonstrated long-lasting efficacy and a favorable safety profile in patients (pts) with psoriatic arthritis (PsA) and ankylosing spondylitis (AS) across Phase 3 trials.[1, 2] SERENA is an ongoing, longitudinal, observational study in more than 2900 pts with moderate to severe psoriasis, active PsA, and AS conducted at 438 sites across Europe with an expected duration of up to 5 years.[3] Here we report data on impact of intermediate treatment interruption on SEC effectiveness in pts with active PsA or AS from the SERENA study.



If a patient had more than one treatment interruption then the interruption with the longest duration was included.
AE, adverse event; AS, ankylosing spondylitis; PsA, psoriatic arthritis; n, number of patients with non-missing data; N, number of subjects with treatment interruption.

Figure 1. Reasons for a secukinumab treatment interruption in PsA and AS patients.



If a patient had more than one intermediate treatment interruption, then the interruption with 1. Assessments in all of the temporal periods (prior/during/post the intermediate treatment interruption) and 2. The longest duration, was included.
AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; n, number of patients with non-missing data; PtGA, patient's global assessment; SD, standard deviation; SEC, secukinumab.

Figure 2. Patient's Global Assessment and BASDAI score before the treatment interruption, during the treatment interruption and post re-initiation in AS patients.

Methods: This interim analysis included data for 534 PsA and 470 AS pts enrolled in the study between Oct 2016 and Oct 2018 and followed up for at least 2 years. Pts (aged ≥18 years) with active PsA or AS were required to have received at least 16 weeks of SEC treatment before enrolment in the study. A treatment interruption was defined as interruption of SEC therapy for at least 3 months between the last injection and re-initiation. Effectiveness assessments included swollen and tender joint count in PsA pts, and Pt Global Assessment (PtGA) and BASDAI score in AS pts before and during treatment interruption and post SEC re-initiation. Pts with assessments in at least two of the time periods were included. The last assessment prior to the intermediate treatment interruption was used as baseline. The assessment closest to 6 months after re-initiation was considered as post SEC re-initiation assessment.

Results: A total of 31 PsA (5.8%) pts and 42 (8.9%) AS pts had an intermediate treatment interruption since initiation of SEC treatment. The mean (SD) duration of treatment interruption was 24.8 (16.4) and 26.4 (22.9) weeks for PsA and AS pts, respectively. The mean (SD) duration of SEC treatment before the treatment interruption was 86.8 (50.3) and 90.2 (46.9) weeks, and after the treatment interruption was 73.6 (44.4) and 63.2 (46.8) weeks. The most commonly reported reasons included adverse events (AEs) reported in 18 (58.1%) PsA and 19 (45.2%) AS pts, pt decision reported in 3 (9.7%) PsA and 3 (7.1%) AS pts, and COVID-19 outbreak-related reasons reported in 1 (3.2%) PsA and 6 (14.3%) AS pts (**Figure 1**). More than 80% of PsA pts and 76% of AS pts, reinitiated SEC without a loading phase after the treatment interruption. The swollen and tender joint count increased in PsA pts from the last assessment prior to the treatment interruption [1.3 (1.0) and 7.2 (11.4); n=6] to the first assessment during the treatment interruption [4.0 (1.4) and 16.5 (19.1); n=2], and gradually decreased post SEC re-initiation [0.4 (0.5) and 2.0 (0.7); n=5]. PtGA and BASDAI remained stable in AS pts from the last assessment prior to the treatment interruption to the first assessment during the treatment interruption and after SEC re-initiation (**Figure 2**).

Conclusion: SEC intermediate treatment interruption occurred due to a variety of reasons in the real-world setting mainly due to AEs and pt decision. The majority of pts re-initiated SEC treatment without a loading phase. No notable impact of the intermediate treatment interruption was observed on the effectiveness of SEC.

References

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2. Pavelka K, et al. *Arthritis Res Ther*. 2017;19(1):285
3. Kiltz, U et al. *Adv Ther* 2020; 37:2865–83

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Abstract Number: 1362

No Change in Bone Marrow Edema of the Sacroiliac Joints and Spine After High Intensity Interval Training in PsA

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Physical activity is recommended for patients with psoriatic arthritis (PsA) especially due to the high prevalence of overweight/obesity, and the risk of comorbidities such as CVD and metabolic syndrome. Further, physical exercise may be beneficial regarding disease activity in patients with arthritis. However, in PsA there is a potential risk of increased disease activity including worsening of enthesitis after physical exercise due to mechanical strain.

The primary aim of this study was to measure the effect of high intensity interval training (HIIT) on bone marrow edema (BME) in MRI of the sacroiliac joints (SIJ) and spine as an objective measure of inflammation. Secondly, we aimed to observe whether there was an association between BME and disease activity markers at baseline.

Methods: 41 PsA patients satisfying CASPAR criteria were recruited from clinics to a randomized clinical trial. The intervention group (N=21) performed HIIT, defined as 4 times 4 minutes training at 85-95% of maximum heart rate on a stationary bicycle 2-3 times a week for 11 weeks. The control group (N=20) was instructed not to change their pre-study physical exercise habits during the study. Patients underwent MRI of the SIJ and spine at baseline, and, at average 13 (range: 8 – 26) days after completion of the intervention. MRI was scored for BME according to the

Table 1. Baseline characteristics of the patients with psoriatic arthritis in the intervention and control groups

	Intervention (n= 21)	Control (n= 20)
Age, years mean (SD)	51.6 (9.1)	44.4 (12.9)
Female, n (%)	17 (81)	12 (60)
HLA-B27 positive, n (%)	4 (19)	3 (15)
hs-CRP, median (IQR) mg/liter	1.8 (23.6)	2.2 (28.6)
DAPSA68 categories, n		
1 remission	1	2
2 low	7	5
3 moderate	9	12
4 high	4	1
Pain, mean (SD) 0-100 mm VAS	40.5 (21.6)	36.0 (21.2)
PGA, mean (SD) 0-100 mm VAS	43.6 (24.2)	42.4 (20.7)
ASDAS-CRP, mean (SD)	2.3 (1.0)	2.1 (0.9)
SPARCC enthesitis index, median (IQR)	4 (12)	2.5 (5)
SIJ-BME-SPARCC, median (IQR)	0 (4)	0 (14)
SIJ-BME-SPARCC, n		
<2	16	15
≥2	5	5
Spine-BME-SPARCC, median (IQR)	4 (39)	4 (36)
Spine-BME-SPARCC, n		
<2	8	7
≤2 – 10	7	9
>10	6	4

Hs-CRP = high-sensitivity C-reactive protein
IQR = interquartile range
DAPSA68 = Disease Activity index for Psoriatic Arthritis of 66/68 joints
DAPSA68 categories: 1. Remission (0-4) 2. Low (5-14) 3. Moderate (15-28) 4. High (>28)
PGA = patient's global assessment
ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score using the CRP level.
SPARCC enthesitis index = Spondyloarthritis Research Consortium of Canada enthesitis index (0-16)
SIJ-BME-SPARCC = SPARCC index of sacroiliac joint bone marrow edema (0-72, remission<2)
Spine-BME- SPARCC = SPARCC index of spine bone marrow edema (0-108, remission<2)

Spondylarthritis Research Consortium of Canada (SPARCC). The minimal important change is 2,5 and 5 in SPARCC BME score for SIJ and spine, respectively. Logistic regression analysis was performed to calculate the odds ratio (OR) with 95% CI for worsening in SPARCC-BME for both SIJ and spine between HIIT and control groups. Disease activity markers like HS-CRP, Dapsa68, Pain, ASDAS-CRP and SPARCC enthesitis index assessed at baseline were compared with SPARCC BME scores for SIJ and spine using linear regression and Mann-Whitney test.

Results: The included patients had a low to moderate disease activity measured by Dapsa68 and ASDAS-CRP (table 1). There was no difference in change of SPARCC-BME in SIJ and spine between the two groups with an OR of 0.56 (95 % CI 0.05 to 6.81) and 1.19 (95 % CI 0.07 to 20.54) for SIJ and spine, respectively, for worsening comparing the HIIT with the control group. At baseline, there was an inverse association between SPARCC enthesitis index and SPARCC-BME of SIJ with a mean difference of -2.34 (95% CI -4.53 to -0.15). The results were confirmed by a Mann-Whitney test (p-value 0.02). There was no association between other disease activity markers and SPARCC-BME of SIJ and spine at baseline.

Conclusion: The risk of increased BME in SIJ and spine as an objective marker of inflammation after 11 weeks of HIIT was not higher in the HIIT group compared to controls in a cohort of PsA patients with low to moderate disease activity. Of interest, the degree of baseline BME in SIJ was inversely associated with the subjectively measured burden of enthesitis. The results support that physical exercise does not cause objective signs of increased disease activity in PsA.

Disclosure: R. Thomsen, None; **T. Nilsen**, None; **M. Hoff**, None; **G. Haugeberg**, None; **A. Kavanaugh**, AbbVie, 5, 12, Expert advice, Amgen, 5, 12, Expert advice, Bristol Myers Squibb, 5, 12, Expert advice, Janssen, 5, 12, Expert advice, Pfizer, 5, 12, Expert advice, UCB, 5, 12, Expert advice, AstraZeneca, 5, 12, Expert advice, Celgene, 5, 12, Expert advice, Roche, 5, 12, Expert advice, Novartis, 5.

Abstract Number: 1363

Identification of PsA Phenotypes with Machine Learning Analytics Using Data from a Phase 3 Clinical Trial Program of Guselkumab in a Bio-naïve Population of Patients with PsA

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster II: Psoriatic Arthritis I (1329–1363)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is mainly described based on the individual domains or clinical components of the disease.[1,2] The aim of this *post hoc* analysis was to identify hypothesis-free clusters of phenotypes according to patients' clinical features and characteristics at baseline (BL) using data from the guselkumab Phase 3 DISCOVER-1 and -2 clinical trials of patients with PsA.

Figure 1. Examples of unsupervised machine learning-identified Clusters, 1 and 7.

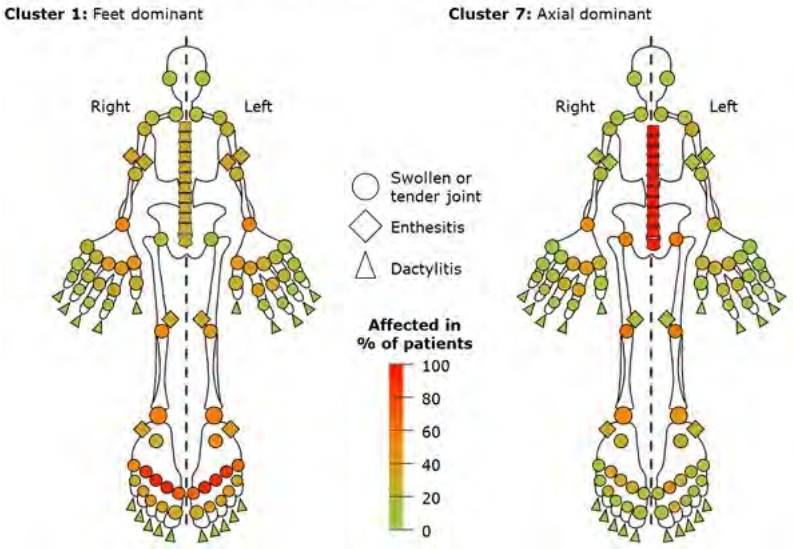


Table 1. Baseline characteristics of PsA phenotype clusters.

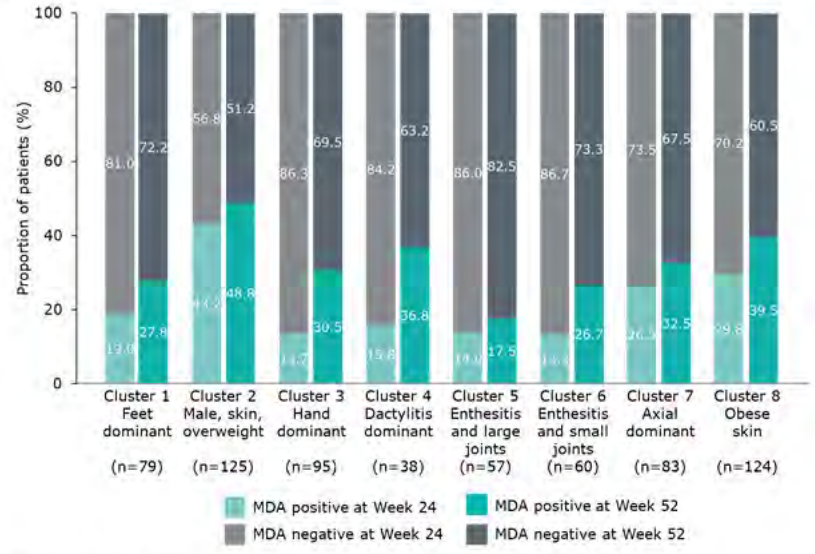
	Cluster 1 Feet dominant	Cluster 2 Male, skin, overweight	Cluster 3 Hand dominant	Cluster 4 Dactylitis dominant	Cluster 5 Enthesitis and large joints	Cluster 6 Enthesitis and small joints	Cluster 7 Axial dominant	Cluster 8 Obese, skin
Number of randomized and treated patients	79	125	95	38	57	60	83	124
Age, years	45.8 (10.4)	45.8 (13.2)	48.9 (11.8)	44.8 (12.3)	43.6 (13.3)	45.8 (11.6)	43.8 (10.4)	47.5 (11.1)
Female	54.4	20.0	60.0	26.3	64.9	41.7	36.1	61.3
BMI, kg/m²	29.3 (5.4)	27.4 (3.6)	29.3 (6.1)	26.9 (4.6)	28.6 (7.5)	29.0 (6.2)	28.4 (6.9)	32.1 (6.5)
CRP, mg/dL	1.7 (1.8)	1.7 (2.0)	1.4 (2.3)	2.5 (2.8)	1.7 (1.9)	1.7 (1.8)	2.2 (3.1)	1.5 (1.8)
Disease duration, years	5.0 (5.3)	5.1 (4.8)	5.8 (6.5)	6.1 (5.5)	6.8 (7.6)	6.1 (5.6)	4.7 (4.6)	5.2 (6.7)
SJC, 0–66	13.2 (7.1)	8.2 (3.8)	15.0 (8.0)	18.0 (10.1)	10.1 (5.1)	17.5 (11.8)	9.0 (4.2)	8.8 (3.9)
TJC, 0–68	23.4 (10.1)	12.8 (5.9)	26.0 (12.0)	30.6 (15.3)	23.2 (12.6)	37.5 (18.6)	14.6 (6.5)	12.7 (5.2)
BSA, %	12.6 (19.4)	20.7 (19.8)	14.8 (19.5)	29.7 (26.4)	14.6 (21.6)	14.5 (18.4)	15.2 (19.4)	14.4 (15.7)
BSA >3%	63.3	86.4	76.6	100.0	61.4	72.9	81.9	90.3
BSA >10%	36.7	63.2	43.6	71.1	36.8	42.4	41.0	44.4
Dactylitis %	48.1	30.4	42.1	100.0	36.8	53.3	49.4	31.5
Dactylitis score	3.0 (4.8)	1.4 (3.2)	2.7 (4.8)	27.5 (12.3)	2.3 (5.2)	3.9 (6.8)	2.2 (2.9)	1.3 (2.5)
Enthesitis %	70.9	49.6	58.9	81.6	96.5	73.3	69.9	45.2
LEI score	2.0 (1.7)	1.0 (1.3)	1.7 (1.8)	2.9 (1.9)	4.2 (1.6)	2.7 (2.3)	1.3 (1.2)	1.0 (1.3)
Current smoker	16.5	23.2	13.7	18.4	12.3	23.3	13.3	21.8

Data shown are mean (SD) or %. White cells indicate differentiating features of individual clusters. BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; LEI, Leeds Enthesitis Index; PsA, psoriatic arthritis; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count.

Methods: Data from bio-naïve patients with active PsA treated with guselkumab 100 mg either every 4 or 8 weeks in DISCOVER-1 and -2 were retrospectively analyzed. Non-negative matrix factorization was applied as an unsupervised machine learning technique to identify clusters of PsA phenotypes, with BL characteristics and clinical observations as input features. Clusters are described here according to their characteristics and clinical features, including the relation to achievement of minimal disease activity (MDA) at Weeks 24 and 52 (W24; W52).

Results: Data from 661 bio-naïve patients were pooled. Eight distinct clusters of PsA phenotypes were identified. **Cluster 1** was characterized by a high frequency of lower limb involvement, notably foot/ankle, and the lowest rates of severe skin involvement (Figure 1). **Cluster 2** was characterized by high skin involvement, the lowest proportion of females, and the highest proportion of overweight patients (70% body mass index [BMI] 25–< 30). **Cluster 3** was

Figure 2. MDA response to guselkumab 100 mg (pooled Q4W and Q8W) at Week 24 and Week 52 by PsA phenotype clusters.



MDA, minimal disease activity; PsA, psoriatic arthritis; Q4W, every 4 weeks; Q8W, every 8 weeks.

characterized by a high burden of disease in the hands/wrists. **Cluster 4**, the smallest cluster, was distinguished by the highest degree of dactylitis involvement; second highest proportion of male patients; and the highest proportion of patients with ≥3% body surface area (BSA) psoriasis involvement. **Cluster 5** was differentiated based on the highest proportion of patients with enthesitis at BL. Large joint involvement was also common in this cluster. **Cluster 6** was characterized by a high level of involvement of small joints in the hands and feet, but a low mean dactylitis score. Presence of nail involvement (78%) and enthesitis at BL were also common in this cluster. **Cluster 7** was characterized by axial involvement at BL (100%); nearly one-half of patients with dactylitis, two thirds with enthesitis and the majority with BSA ≥3% at BL (Figure 1). **Cluster 8** was characterized by low rates of joint involvement, high rates of more extensive skin involvement, and the highest proportion of obese patients (67% with BMI >30; Table 1). MDA response rates at W24 and W52 were highest in **Cluster 2** and lowest in **Cluster 5**. **Clusters 3** and **4** were characterized by low MDA response rates at W24 that increased at W52 (Figure 2).

Conclusion: Unsupervised machine learning was able to identify 8 clusters of PsA phenotypes with significant differences in demographic and clinical features, including patterns of involvement of joint, skin/nail, dactylitis, and enthesitis manifestations as well as MDA responses. These clusters seem to differ in their initial vs. later responses to guselkumab. Further analysis will clarify which MDA domains play a role in this response kinetics.

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2. Gossec L *et al. Ann Rheum Dis* 2012; 71: 4–12.

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Abstract Number: 1364

Autologous Hematopoietic Stem Cell (HSC) Transplantation for Systemic Sclerosis, North American Registry: Updated Outcomes and the Impact of CD34+ HSC Enrichment

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Autologous hematopoietic stem cell transplantation (AHSCT) is now established as a preferred standard of care treatment for patients with severe scleroderma with internal organ involvement (SSc). Two large randomized clinical trials of AHSCT vs. monthly cyclophosphamide (CYC) used CD34+ HSC enrichment to deplete immune cells from the autologous peripheral blood stem cell (PBSC) graft. One trial used total body irradiation (TBI)/CYC/anti-thymocyte globulin (ATG) conditioning regimen[1], the other used CYC/ATG (no TBI)[2]. After these trials, due to reporting issues, many SSc patients given HSCT received unmanipulated PBSC (no CD34+ enrichment). We sought to (1) update the outcomes of AHSCT for SSc in North America in a larger contemporary cohort and (2) examine the importance of patient factors and transplant regimens for overall survival (OS) and progression free survival (PFS).

Methods: A questionnaire for SSc-specific health status before and after AHSCT was created for patients reported to the Center for International Blood & Marrow Transplantation Research. Participating HSCT/rheumatology sites completed questionnaires for each SSc patient transplanted between 2000 to 2020, by conducting medical records review/ telephone interviews in early/mid-2021. Health status, physical function, toxicities, DMARD use and major medical events were recorded. Event endpoints included time to death, initiation of unplanned DMARD, organ failure/ transplant, supplemental oxygen, new diagnosis of pulmonary arterial hypertension, enteral feeding tube, total parenteral nutrition, or subsequent HSCT.

Results: 104 patients with SSc were reported to the registry and provided SSc-specific health data. All patients had skin involvement, 56% with lung, 29% lung with other organ, 3% with kidney/GI, and 13% with skin only SSc.

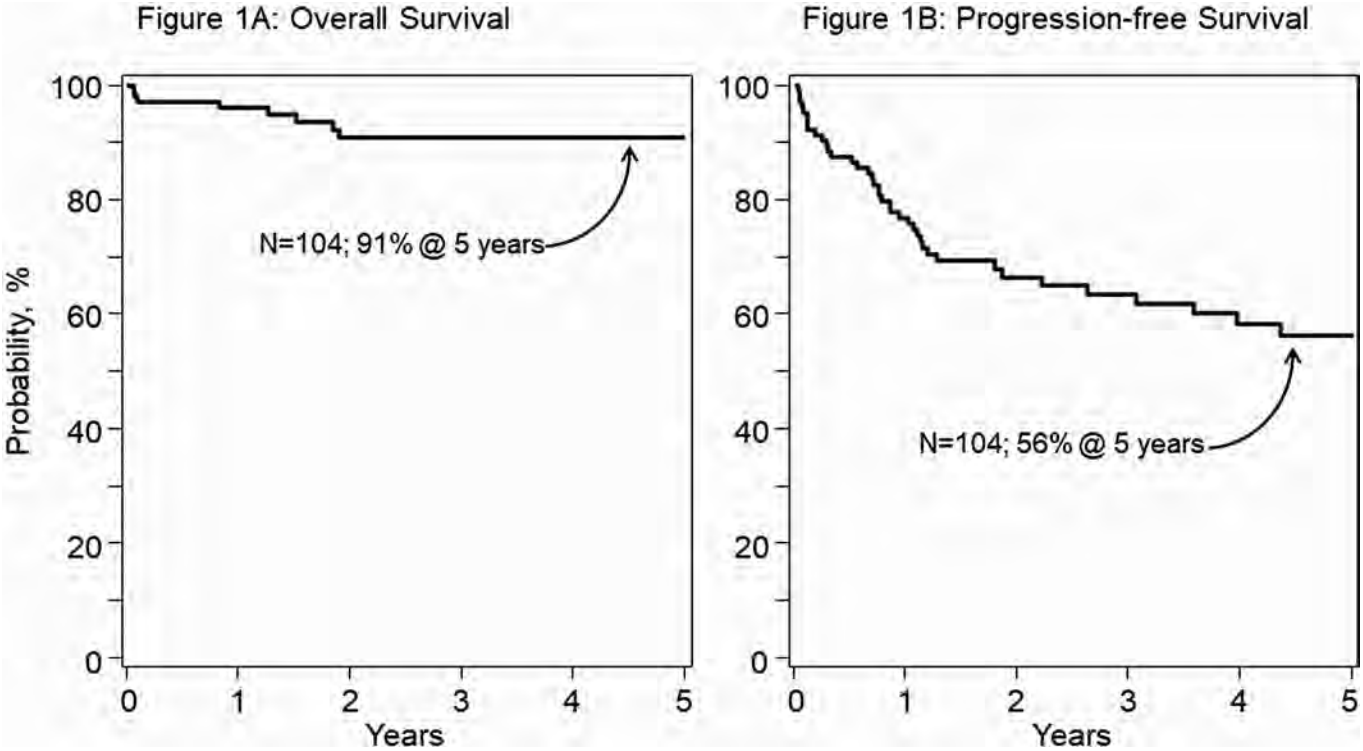

Figure 1. A. 5-year overall survival (OS) for 104 SSc registry patients with AHSCT between 2000 and 2020. B. Corresponding progression-free survival (PFS). Kaplan-Meier (KM) estimate.

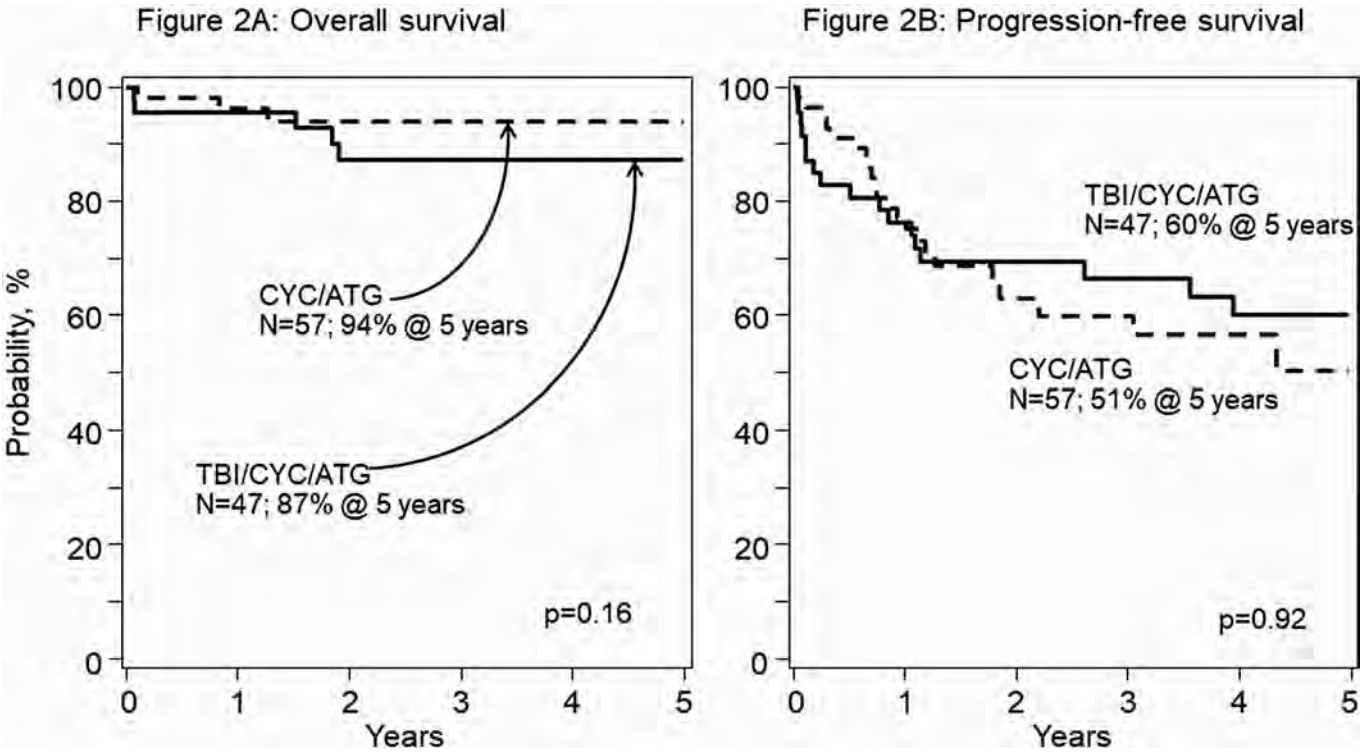

Figure 2. A. 5-yr. OS after AHSCT for SSc, non-randomized, registry patients conditioned with TBI/CYC/ATG vs. CYC/ATG, 87% and 94%, P= 0.16. B. Corresponding 5-yr. PFS, 60% and 51%, P=0.92, log-rank test.

Conditioning with TBI/CYC/ATG was in 45%, CYC/ATG was in 55%. CD34+ enrichment of PBSC was used in 39%, 61% without enrichment. 64% had AHSCT between 2015 to 2020. Median follow-up was 41 (range, 5-222) months.

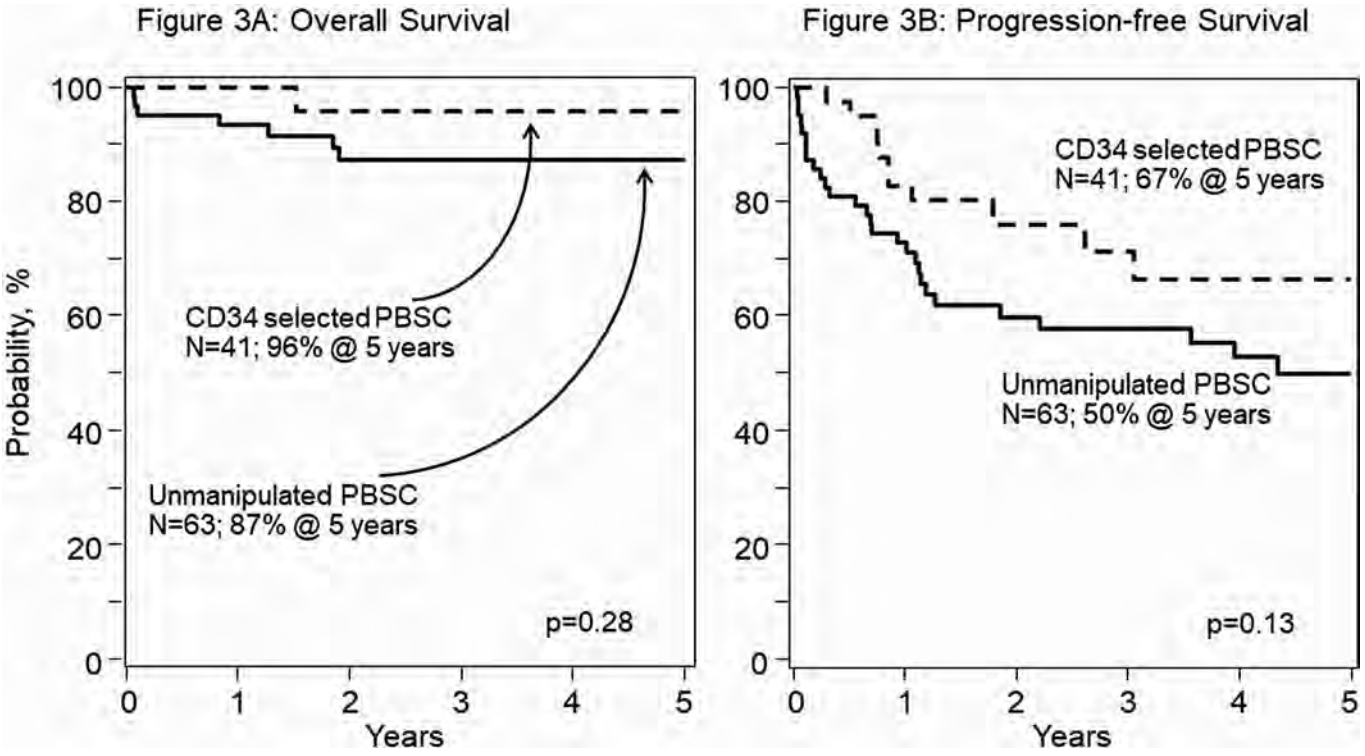

Figure 3. A. 5-yr. OS after AHSCT for SSc, non-randomized, registry patients with PBSC CD34+ enriched vs. unmanipulated, 96% and 87%, P=0.28. B. Corresponding 5- yr. PFS 67% and 50%, P=0.13, log-rank test.

Median age at AHSCT was 48 (range, 14-74) years (yr). For the entire cohort of 104 patients (Figure1), the 5-yr OS was 91%, (95% confidence interval, 84-95). The 5-yr PFS was 56% (45-67). Figure2, the 5-yr OS with TBI/CYC/ATG was 87% (75-96) and CYC/ATG 94% (86-99) (P-value = 0.16). The corresponding 5-yr PFS were 60% (45-75) and 51% (33-68) (P = 0.92). Figure3, the 5-yr. OS for the cohort given CD34+ enriched PBSC was 96% (85-100) and unmanipulated PBSC was 87% (77-95) (P = 0.28). The 5-yr. corresponding PFS were 67% (49-83) and 50% (36-64) (P = 0.13). ATG source (horse vs. rabbit) did not affect OS/PFS. Age, examined as a predictor for OS/PFS, was not significant. In multivariate analysis, no tested covariates were significant for OS or PFS.

Conclusion: The OS and PFS benefit of AHSCT for patients with severe SSc was confirmed in this 5-year retrospective, real-world, non-randomized analysis and was independent of the patient factors or transplant regimens analyzed. While the data suggested use of CD34+ enrichment of PBSC for AHSCT improved PFS for SSc patients, study of a larger cohort for a longer time is needed to evaluate significance.

References [1]Sullivan, NEJM 2018; 378:35-47 [2]van Laar, JAMA 2014; 311:2490-98

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Abstract Number: 1365

Release of High-Mobility Group Box-1 After an Raynaud's Attack Potentially Leads to Fibroblast Activation and Interferon-γ Induced Protein-10 Production in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Raynaud's Phenomenon (RP) leading to repetitive ischaemia and reperfusion (IR) stress, is the first recognisable sign of systemic sclerosis (SSc). Although RP has been linked to SSc aetiology, direct observations substantiating this are scarce. High-mobility group box-1 (HMGB1) is a nuclear factor released by necrotic cells, of which serum levels may rise quickly after IR injury in other diseases. IR injury promotes interferon (IFN) inducible

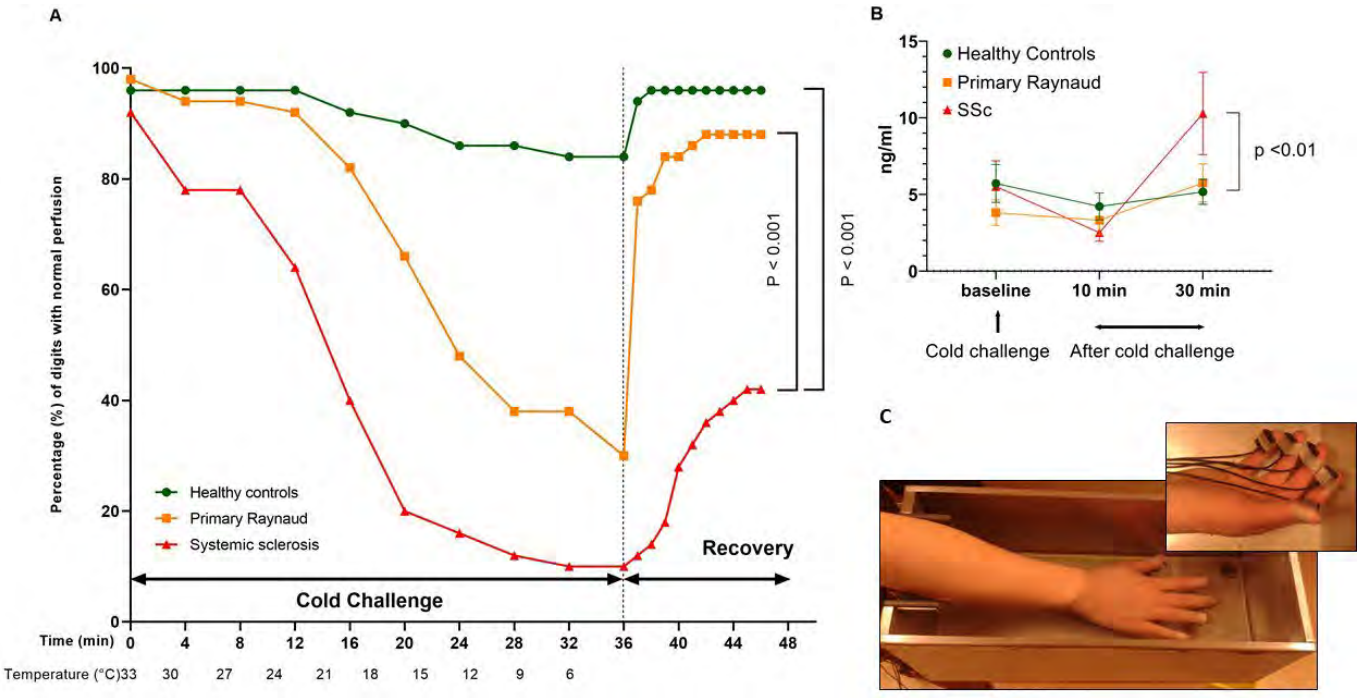

Figure 1. Cold challenge in patients with SSc, primary RP and healthy controls showing effects on fingers perfusion (Figure 1a). The hand is gradually cooled from 33 to 6 degrees Celsius within 36 minutes, and rewarmed at ambient temperature (22 degrees Celsius) to assesses recovery of perfusion. In Figure 1b the effect of the cold challenge is shown on levels of HMGB1. Figure 1c shows that hand is submerged in water to perform the cold challenge, and digital perfusion is measured by photoplethysmography.

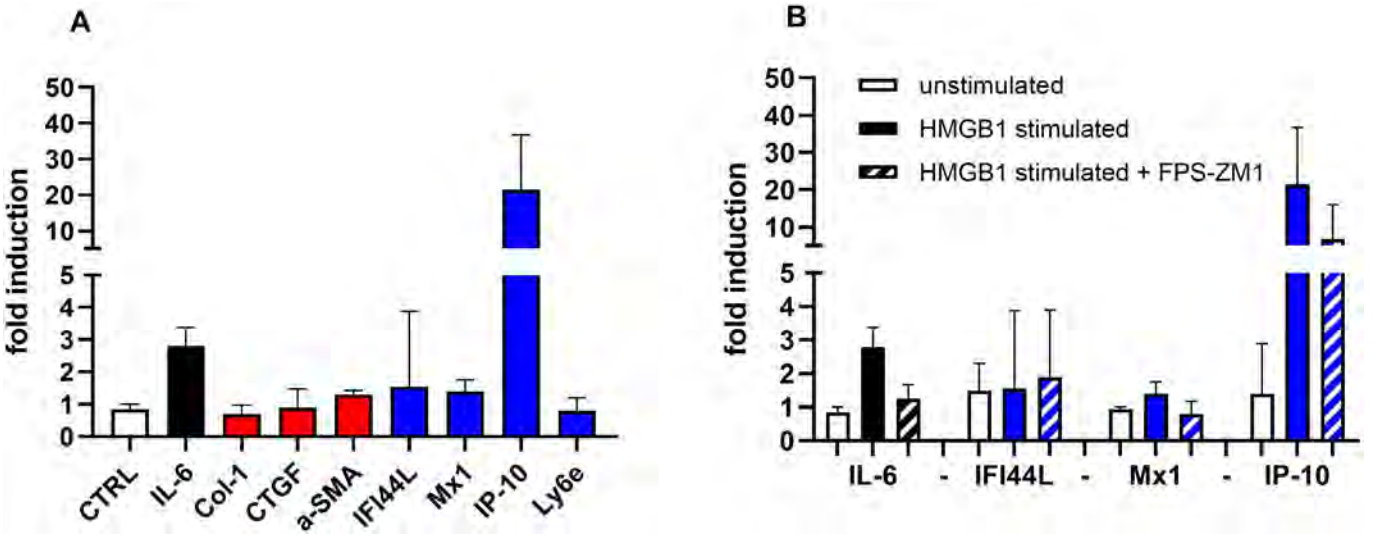

Figure 2. In vitro stimulation of dermal fibroblast with HMGB1. Figure 2a shows induction of inflammatory (black), profibrotic (red), and IFN genes (blue), and negative control (white). Fig 2b shows the RAGE inhibitor FPS-ZM1 on IL-6 (black) and IFN genes (blue).

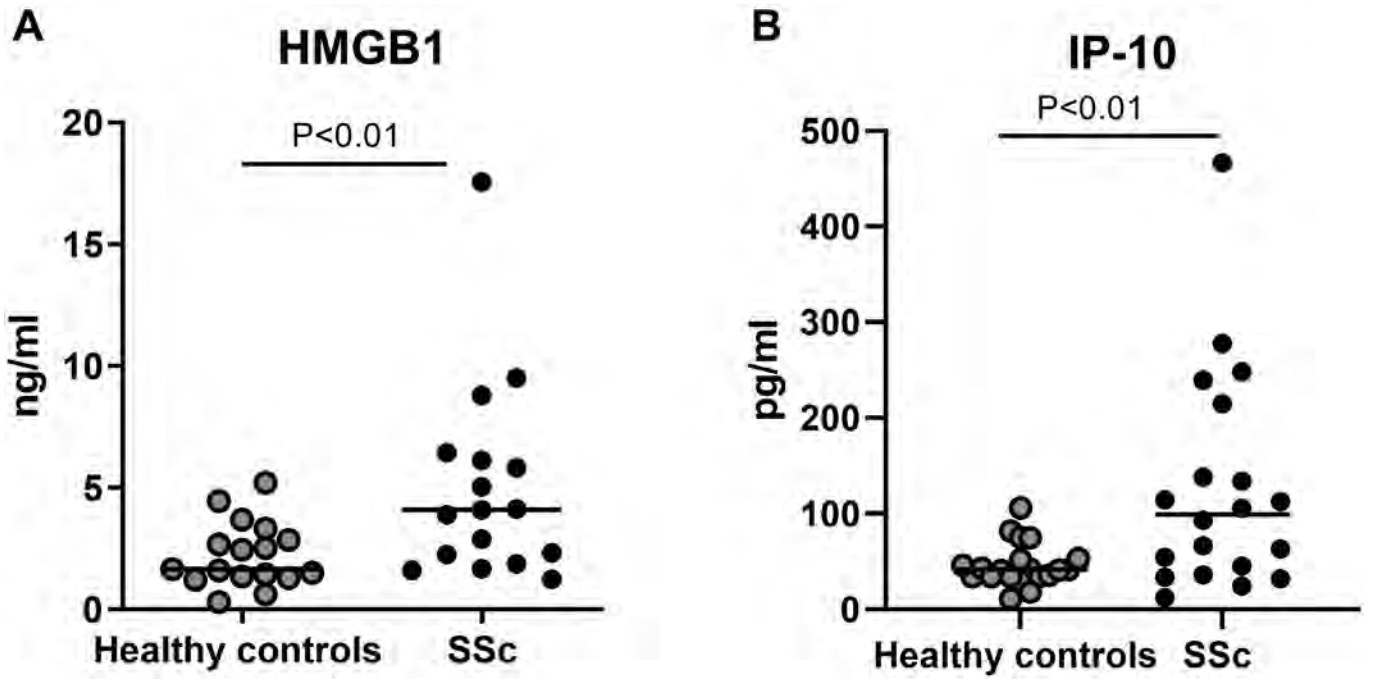

Figure 3. Serum levels of HMGB1 (Figure 3a) and IP-10 (Figure 3b) in patients with SSc compared with age and sex matched healthy controls.

genes, which have been implicated in SSc pathophysiology. Since HMGB1 can signal through the receptor for advanced glycation endproducts (RAGE), we investigated whether an RP attack promotes release of HMGB1, leading to fibroblast activation and upregulation of IFN- inducible genes in a translational study.

Methods: A cold challenge was performed to simulate an RP attack in patients with SSc (N=10, age 56.2 ± 11.5 years), primary RP (N=10, age 47.8 ± 16.2, 8), and healthy controls (N=10, age 29.9 ± 2.7). We measured levels of HMGB1 and IFN gamma-induced Protein 10 (IP-10) before, 10 and 30 min after cold challenge in blood drawn from ipsilateral forearm. Digital perfusion was assessed by photoplethysmography. For studying *in vitro* effects of HMGB1, healthy human dermal fibroblasts were stimulated with HMGB1 or TGF-β1 as control. Inflammatory (Interleukin-6 [IL-6]) genes, profibrotic (type 1 collagen [Col1], α-smooth muscle actin [α-SMA]), connective tissue growth factor

[CTGF]) genes, and IFN-inducible genes (IFN α-induced44L [IFI144L], Myxovirus resistance protein 1 [Mx1], Lymphocyte antigen 6 complex, locus E [LY6E];, and IP-10) were measured by RT-PCR. RAGE signalling was determined by preincubation with its inhibitor FPS-ZM1. Differentiation to myofibroblasts was assessed by staining of α-SMA. In an independent cohort, sera were obtained from 20 patients with SSc (age 50 (44–54) years, 13 female) and 20 age- and sex-matched healthy controls (53 (47–63), 13) to determine HMGB1 and IP-10 levels.

Results: During cold challenge, finger perfusion was reduced in SSc and recovered slower than in primary RP and healthy controls (Figure 1a). HMGB1 increased significantly 30 min after cold challenge in SSc compared to healthy controls, but not to primary RP (Figure 1b). IP-10 remained stable. I*n vitro* stimulation of fibroblasts with HMGB1 resulted in 20-fold increase in mRNA expression of IP-10, while IL-6 increased 3-fold. Col1, α-SMA, IFI144L, Mx1, and LY6E did not change (fig 2a). IP-10 expression was inhibited by 50% by preincubation with FPS-ZM1 (fig 2b). TGF-β1 stimulation promoted IL-6 and CTGF, without effects on IFN gene expression. HMGB1 stimulation induced myofibroblast differentiation and formation of α-SMA fibers. Both HMGB1 and IP-10 were significantly higher in patients with SSc compared to healthy controls (fig 3).

Conclusion: In this translational study, we show for the first time that an RP attack in patients with SSc leads to release of HMGB1. *In vitro*, HMGB1 induces IFN regulated gene expression in fibroblasts, especially interferon-γ inducible IP-10, at least in part in a RAGE dependent manner. This potentially links HMGB1 release following an RP attack to IFN inducible proteins as putative sequential steps leading to disease progression in SSc.

Disclosure: I. Atzeni, None; **Y. Al-Adwi**, None; **B. Doornbos-van der Meer**, None; **A. Eman Abdulle**, None; **A. Van Roon**, None; **A. Stel**, None; **H. Van Goor**, None; **A. Smit**, None; **J. Westra**, None; **D. Mulder**, None.

Abstract Number: 1366

The Use of Lipid-Lowering Agents in Systemic Sclerosis: Is There a Relationship with Prevalence of Digital Ulcers and Overall Survival?

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Digital ulcers (DU) are common in systemic sclerosis (SSc). Vasodilator therapies have limited benefit in prevention and promoting healing. Lipid-lowering agents (LLAs) such as statins reduce endothelial damage, increase vasodilation, and in small studies prevent new DU. This study examined whether LLAs have an impact on the prevalence of DU and overall survival in patients with SSc.

Methods: Data collected prospectively from the Australian Scleroderma Cohort Study between 2008 and 2020 included patient demographics, the presence of DU, vasodilator therapies, SSc manifestations and other vascular comorbidities. LLA use was defined as use of a LLA on two consecutive annual reviews. Multivariate longitudinal logistic modelling was used to assess associations with DU and a Kaplan-Meier (K-M) curve and multivariate cox proportional hazard modelling were used to assess survival by LLA use.

Variable	Odds Ratio	p-value	95% CI
Ever had lipid lowering agents over 2 consecutive reviews	1.06	0.766	0.74 - 1.52
Diffuse disease Limited disease	3.40 1.00	<0.001	2.40 - 4.81
PAH	1.98	0.008	1.20 - 3.27
PVD	5.21	<0.001	2.46 - 11.02
CCA	2.62	<0.001	1.90 - 3.64
PDE-5 inhibitor	2.00	0.004	1.25 - 3.20
Iloprost	9.78	<0.001	5.28 - 18.11
IHD	0.80	0.369	0.49 - 1.31
Age at non-RP symptom onset	0.97	<0.001	0.96 - 0.98

Table 1. Multivariate logistic analysis of associations with digital ulcers

Results: Among 1485 patients, 323 patients (21.8%) had used a LLA. Patients in the LLA group were older at the onset of the first non-Raynaud's symptom than patients in the non-LLA group (51.6 years *vs* 44.8 years, p = 0.001) and were more likely to have the anti-centromere antibody, interstitial lung disease, pulmonary arterial hypertension (PAH) and to have used calcium channel blockers. In a multivariate analysis (Table 1), the odds of ever having a DU were increased in males, patients with the diffuse subtype of SSc, pulmonary arterial hypertension (PAH) and those who received calcium channel blockers and vasodilators for PAH. Patients with peripheral vascular disease (PVD) were much more likely to have DU with an OR 5.21 (p = < 0.001; CI 2.46-11.02). There was a protective effect of older age, likely explained by survivor bias. There was no association of DU with LLA or other cardiovascular disease. In a multivariate model, LLA use was associated with reduced all-cause mortality (HR 0.60, p < 0.002, 95% CI 0.44-0.83). Patients with disease duration of less than 4 years receiving LLAs had worse survival than those not taking LLAs, with a hazard ratio of 2.41 (p = 0.002, 95% CI 1.38 – 4.20) but not when adjusted for age and gender.

Conclusion: DU prevalence was not influenced by LLA use but was strongly associated with PVD. While DU are traditionally considered to be related to local vasoconstriction and microvascular disease, macrovascular disease may also be an aetiological factor. LLA use was associated with reduced all-cause mortality but did not improve survival in patients with incident SSc who have the highest mortality early in the disease.

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Abstract Number: 1367

Associations of Esophageal Dysmotility Patterns with Extra-intestinal Features in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: The gastrointestinal (GI) tract is the most commonly affected internal organ in systemic sclerosis (SSc). SSc GI disease is heterogeneous, with some patients experiencing only mild acid reflux, while others progress to severe GI disease requiring total parenteral nutrition to sustain life.[1–3] As our understanding of disease pathogenesis is poor and risk stratification tools in SSc GI disease are limited, we sought to determine whether distinct types of esophageal dysfunction associate with specific clinical phenotypes and outcomes in SSc.

Methods: Patients in the Scleroderma Center Research Registry who had high resolution esophageal manometry (HRM) studies completed in our hospital system as part of their clinical care between 2011 and 2020 were identified through our Precision Medicine Analytics Platform. Data from the manometry reports were downloaded, abstracted, and merged with existing demographic, clinical and serologic data that had been collected longitudinally from 1991-2020 as part of our Center's Research Registry. Associations between esophageal abnormalities identified on manometry [absent contractility (AC), ineffective esophageal motility (IEM), hypotensive LES (hypoLES)] and patient demographics, clinical characteristics, and autoantibody profiles were examined.

Results: Ninety-five patients with SSc had HRM data. Of these patients, 67 patients (71%) had AC (44 patients with only AC, 23 patients with AC and a hypoLES), 17 patients (18%) had IEM (3 with a hypoLES), and 11 patients (12%) had normal studies. Median disease duration in patients with AC was 12 years (6-23) and in patients with IEM was 19 years (10-22). The presence of AC was significantly associated with diffuse cutaneous disease (36% vs. 14%; p=0.05), more severe cardiac involvement (Medsger score >1; 41% vs. 19%; p=0.04), and more severe Raynaud's phenomenon (Medsger score >1; 57% vs. 29%, p=0.01). AC was seen in 100% of the patients in the study that died (14/14, p< 0.01). Among patients with AC, 21% died, whereas none of the patients without AC died (p< 0.01). Interestingly, 93% (15/16) of Ro52 positive patients had AC (p=0.06). These findings were not seen in patients with IEM.

Conclusion: In patients with SSc who are referred for manometry, the presence of AC, but not IEM, is strongly associated with a severe clinical phenotype and a high risk of death. Further prospective studies are needed to assess the prevalence of AC in early disease, the timing of its onset relative to other end organ complications, and its rate of progression among patients with SSc.

References

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Table 1. Characteristics of patients with systemic sclerosis in the cohort

Clinical and demographic features	
Age, years, mean (SD)	56 (10)
Disease duration, years, median (IQR)	14 (6-23)
Race, % (n)	
White	80 (76/95)
Black	14 (13/95)
Other	6 (6/95)
Gender	
Female sex, % (n)	87.4 (83/95)
SSc Type	
Diffuse cutaneous disease, % (n)	29.5 (28/95)
Myopathy, % (n)	25.3 (24/95)
Muscle involvement (>1), % (n)	2.13 (2/93)
Cardiac involvement (>1), % (n)	34.4 (31/90)
Gastrointestinal severity (>1), % (n)	85.3 (81/95)
Raynaud's severity (>1), % (n)	47.9 (45/94)
Lung involvement (>1), % (n)	82.6 (73/88)
Tendon friction rubs, % (n)	10.6 (10/94)
Sicca, % (n)	85.3 (81/95)
Death, % (n)	14.7 (14/95)
Time from Manometry to death, years, median (range)	3.1 (0.7-8.2)
Pulmonary function parameters	
Low FVC, (<70% pred.), % (n)	52.7 (50/94)
Low DLCO, (<60% pred.), % (n)	52.7 (50/94)
High RVSP by echo (>40 mmHg), % (n)	36 (9/25)
Antibodies	
Centromere, % (n)	40 (30/75)
Scl70 (i.e. Topoisomerase-1), % (n)	24.0 (18/75)
RNA polymerase-3, % (n)	4.1 (3/75)
Ro52, % (n)	21.3 (16/75)
Fibrillarin, % (n)	1 (1/75)
ThTo, % (n)	1.4 (1/75)
Ku, % (n)	1.4 (1/75)
PMScl, % (n)	0 (0/75)

FVC: Forced vital capacity. DLCO: Diffusing capacity of lung for carbon monoxide. RVSP: Right ventricular systolic pressure. Reduced FVC defined as <70% predicted. Reduced DLCO defined as <60% predicted. Elevated RVSP by TTE defined as >40 mm Hg. Severity of organ involvement was determined based on Medsger severity scores definitions [3] Significance determined by Fisher's exact test if sample size =5 or chi-squared test if sample size >5.

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Table 2. Association of characteristics of the SSc patients in the cohort with abnormal high-resolution esophageal manometry results

Clinical and demographic features	AC	No AC	P-value	IEM	No IEM	P-value	Hypotensive LES	No hypotensive LES	P-value
Age at first symptoms, mean (SD)	56 (10)	55 (11)	0.45	55 (7)	56 (11)	0.62	56 (10)	56 (10)	0.87
Disease duration from 1st symptoms to baseline visit, median (IQR)	12 (6-23)	17 (7-23)	0.85	19 (10-22)	12 (6-23)	0.39	11 (7-27)	14 (5-22)	0.53
Race/Ethnicity									
White, % (n)	82 (55/67)	82 (23/28)	1.00	76 (13/17)	83 (65/78)	0.50	89 (23/26)	79 (54/68)	0.38
Gender									
Female sex, % (n)	85 (57/67)	93 (26/28)	0.50	94 (16/18)	87 (67/78)	0.69	85 (22/26)	90 (61/68)	0.49
SSc Type									
Diffuse cutaneous disease, % (n)	**36 (24/67)**	**14 (4/28)**	**0.05**	18 (3/17)	32 (25/78)	0.38	**50 (13/26)**	**21 (14/68)**	**<0.01**
Gastrointestinal severity (>1), % (n)	90 (60/67)	75 (21/28)	0.07	82 (14/17)	86 (67/78)	0.71	96 (25/26)	81 (55/68)	0.10
Cardiac involvement (>1), % (n)	**41 (26/63)**	**19 (5/27)**	**0.04**	19 (3/16)	38 (28/74)	0.25	**56 (14/25)**	**25 (16/64)**	**<0.01**
Myopathy, % (n)	25 (17/67)	25 (7/28)	0.97	29 (5/17)	24 (19/78)	0.76	31 (8/26)	24 (16/68)	0.47
Muscle involvement (>1) % (n)	0 (0/66)	7 (2/27)	0.08	**13 (2/16)**	**0 (0/77)**	**0.03**	0 (0/24)	3 (2/68)	1.00
Tendon friction rubs, % (n)	12 (8/67)	7 (2/27)	0.72	12 (2/17)	10 (8/77)	1.00	19 (5/26)	6 (4/67)	0.11
Sicca, % (n)	88 (59/67)	79 (22/28)	0.23	71 (12/17)	89 (69/78)	0.12	89 (23/26)	84 (57/68)	0.75
Raynaud's severity (>1), % (n)	**57 (38/67)**	**29 (8/28)**	**0.01**	35 (6/17)	51 (40/78)	0.23	62 (16/26)	43 (29/68)	0.10
Lung involvement (>1), % (n)	84 (53/63)	80 (20/25)	0.76	80 (12/15)	84 (61/73)	0.72	92 (23/25)	79 (49/62)	0.21
Death, % (n)	**21 (14/67)**	**0 (0/28)**	**<0.01**	0 (0/17)	18 (14/78)	0.07	12 (3/26)	15 (10/68)	1.00
Pulmonary function parameters									
Reduced FVC, % (n)	53 (35/66)	54 (15/28)	0.96	59 (10/17)	52 (40/77)	0.61	54 (14/26)	52 (35/67)	0.89
Reduced DLCO, % (n)	59 (39/66)	39 (11/28)	0.08	41 (7/17)	56 (43/77)	0.27	54 (14/26)	52 (35/67)	0.89
Elevated RVSP by TTE, % (n)	39 (7/18)	29 (2/7)	1.00	40 (2/5)	35 (7/20)	1.00	50 (3/6)	32 (6/19)	0.63
Antibodies, % (n)									
Scl-70	27 (15/56)	16 (3/19)	0.54	25 (3/12)	24 (15/63)	1.00	30 (7/23)	22 (11/51)	0.41
Centromere	34 (19/56)	58 (11/19)	0.07	50 (6/12)	38 (24/63)	0.44	35 (8/23)	43 (22/51)	0.50
Fibrillarin	2 (1/56)	0 (0/19)	1.00	0 (0/12)	2 (1/63)	1.00	4 (1/23)	0 (0/51)	0.31
RNA polymerase-III	5 (3/56)	0 (0/19)	0.57	0 (0/12)	5 (3/63)	1.00	0 (0/23)	4 (2/51)	1.00
Ro52	27 (15/56)	5 (1/19)	0.06	8 (1/12)	24 (15/63)	0.44	26 (6/23)	20 (10/51)	0.53
ThTo	2 (1/56)	0 (0/19)	1.00	0 (0/12)	2 (1/63)	1.00	4 (1/23)	0 (0/51)	0.31
Ku	2 (1/56)	0 (0/19)	1.00	0 (0/12)	2 (1/63)	1.00	0 (0/23)	2 (1/51)	1.00

AC: Absent contractility. IEM: Ineffective esophageal motility. LES: Lower esophageal sphincter. SD: Standard deviation. IQR: Interquartile range. SSc: Systemic sclerosis. RP: Raynaud's phenomenon. FVC: Forced vital capacity. DLCO: Diffusing capacity of lung for carbon monoxide. RVSP: Right ventricular systolic pressure. TTE: transthoracic echocardiogram. Scl-70: topoisomerase 1 antibody. Reduced FVC defined as <70% predicted. Reduced DLCO defined as <60% predicted. Elevated RVSP by TTE defined as >40 mm Hg. Severity of organ involvement was determined based on Medsger severity scores definitions.[3] Significance determined by Fisher's exact test if sample size =5 or chi-squared test if sample size >5.

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Abstract Number: 1368

Characterising Exercise Capacity in Systemic Sclerosis Using Cardiac Magnetic Resonance Imaging, Skeletal Muscle Imaging and Cardiopulmonary Exercise Testing

Laura Ross[1], Benedict Costello[2], Dylan Hansen[3], Anniina Lindqvist[2], Zoe Brown[4], Andrew Burns[4], David Prior[4], Wendy Stevens[4], Marcus Pianta[4], Warren Perera[4], Andre La Gerche[2] and Mandana Nikpour[1], [1]University of Melbourne at St Vincent's Hospital, Melbourne, Australia, [2]Baker Heart and Diabetes Institute, Melbourne, Australia, [3]St. Vincent's Hospital Melbourne, Victoria, Australia, Adelaide, Australia, [4]St Vincent's Hospital, Melbourne, Australia

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Impaired exercise capacity contributes to functional impairment, negatively impacting individuals' quality of life. Functional impairment is notable from early in the disease course of systemic sclerosis (SSc).[1] Routine investigations such as pulmonary function tests (PFT) and echocardiography (TTE) often fail to adequately

Table 1. Baseline demographics n=33

Age (years, mean, SD)	55.39 (7.60)	*Cardiopulmonary exercise test results (n=33)*	
Female (n, %)	24 (72.73%)	Peak VO_2 (L/min) (median, IQR)	1.18 (1.04-1.35)
Limited / Diffuse (n, %)	13 (39.39%) / 20 (60.61%)	Peak VO_2 (mL/kg/min) (mean, SD)	19.11 (5.01)
Disease duration (years, median, IQR)	10.17 (2.32-12.36)	Peak VO_2 <14.0 (n, %)	3 (9.09)
Disease onset < 4 years (n, %)	14 (42.42%)	Peak VO_2, % predicted (mean, SD)	70.18 (18.98)
Body Mass Index (kg/m^2, mean, SD)	25.04 (4.45)	VE/VCO_2 (median, IQR)	29.6 (26-35)
Current smoking (n, %)	2 (11.11%)	VE/VCO_2 >35 (n, %)	7 (21.21)
Hypertension (n, %)	3 (9.09%)	Peak workload (median, IQR)	96 (55-122)
Type II diabetes (n, %)	2 (6.06%)	RER >1.15 (n, %)	33 (100%)
Anti-centromere positive (n, %)	8 (24.24%)	Peak heart rate (mean, SD)	161 (14.1)
Scl70 positive (n, %)	12 (36.36%)	% predicted heart rate (mean, SD)*	111.45 (10.15)
RNA polymerase III positive (n, %)	5 (15.15%)	Heart rate recovery ≤12 beats at 1 min (n, %)	2 (6.06%)
Modified Rodnan skin score (median, IQR)	10 (3-19)	Peak systolic blood pressure (mmHg) (mean, SD)	184.27 (24.96)
Digital ulcers (n, %)	17 (51.52%)	*Cardiac MRI results (n=31)*	
Interstitial lung disease (n, %)	10 (30.30%)	LV ejection fraction (%) (mean, SD)	64.39 (6.37)
ILD currently requiring treatment	5 (15.15%)	LV end diastolic volume (mL) (median, IQR)	119 (106-147)
FVC (% predicted, median, IQR)	91 (79-98)	LV GLS (%) (mean, SD)	-16.68 (2.31)
DLCO (% predicted, median, IQR)	97.25 (72.32-106.50)	LV mass (median, IQR)	100 (86-115)
Inflammatory arthritis (n, %)	19 (57.58%)	RV ejection fraction (%) (mean, SD)	52.52 (5.74)
Myositis* (n, %)	2 (6.06%)	RV end diastolic volume (mL) (mean, SD)	139.26 (30.69)
Creatine kinase (median, IQR)	86 (69.5-110)	Native T1 time (ShMOLLI) (ms) (median, IQR)	1221.60 (1194.60-1252.90)
CRP (median, IQR)	5 (4-7)	ECV (ShMOLLi) (%) (mean, SD)	30.61 (2.55)
ESR (median, IQR)	15 (11-24.5)	Late gadolinium enhancement (n, %)	9 (30%)
Haemoglobin (g/L, mean, SD)	129.48 (11.71)	Native T2 time (FLASH) (ms) (mean, SD)	42.48 (3.74)
Transthoracic echocardiogram results (n=33)		*Skeletal muscle MRI results n=32*	
LV ejection fraction (%, mean, SD))	59.39 (4.47)	Muscle oedema (n, %)	12 (37.50%)
Average LV GLS (%, mean, SD)	-19.42 (2.48)	Fatty muscle infiltration (n, %)	5 (15.62%)
LV end diastolic volume (mL, mean, SD)	86.05 (17.26)	Muscle atrophy (n, %)	1 (3.13%)
LV end systolic volume (mL, median, IQR)	33 (29.2-37.2)		
LAVi (mL/m^2, mean, SD)	32.76 (7.45)		
Average E/e' (mean, SD)	7.96 (2.11)		
RVSP (mmHg, mean, SD)	27.92 (4.07)		

*Myositis previously diagnosed by muscle biopsy or typical MRI findings with elevated CK and/or ESR and CRP.

Abbreviations: CRP: C-reactive protein; DLCO: diffusing capacity of the lung for carbon monoxide, ESR: erythrocyte sedimentation rate; FLASH: fast angle low shot; GLS: global longitudinal strain; ILD: interstitial lung disease; IQR: interquartile range; LV: left ventricle; MRI: magnetic resonance imaging; ml: millilitre; ms: millisecond; RER: respiratory exchange ratio; RV: right ventricle; SASHA: saturated recovery single-shot acquisition; SBP: systolic blood pressure; Scl70: anti-topoisomerase antibody; SD: standard deviation; ShMOLLI: shortened modified look locker; VE/VCO_2: minute ventilation / carbon dioxide production slope; VO_2: oxygen consumption

Table 2. Regression analysis of clinical characteristics associated with peak oxygen consumption (% predicted)

Clinical variable	Coefficient	p value (95% CI)	Clinical variable	Coefficient	p value (95% CI)
Age	0.14	p=0.76 (-0.77-1.05)	*Transthoracic echocardiogram*		
Disease duration	0.11	p=0.81 (-0.86-1.09)	LVEF	0.92	p=0.228 (-0.60-2.43)
mRSS	-0.99	p=0.001 (-1.52- -0.47)	LV GLS	-2.86	p=0.03 (-5.39- -0.32)
Digital ulcers	-13.60	p=0.04 (-26.36- -0.84)	LAVi	-0.89	p=0.047 (-1.76- -0.01)
Inflammatory arthritis	-3.53	p=0.61 (-17.32-10.26)	RVSP	-1.45	p=0.105 (-3.23-0.33)
ILD requiring treatment	-17.19	p=0.06 (-35.21- 0.84)	Indeterminate diastolic function	-22.29	p=0.01 (-37.36- -7.21)
ESR	-0.36	P=0.130 (-0.84-0.11)	*Cardiac magnetic resonance imaging*		
CRP	-0.90	p=0.196 (-2.30-0.49)	LVEF	1.10	p=0.032 (0.10-2.10)
CK	0.04	p=0.228 (-0.03-0.10)	LV GLS	-4.14	p=0.003 (-6.76- -1.51)
Haemoglobin	0.18	p=0.542 (-0.41-0.77)	Late gadolinium enhancement	-13.43	p=0.06 (-27.43-0.57)
Treatment			Native T1 time (ShMOLLI)	-0.28	p<0.001 (-0.42- -0.13)
Current prednisolone	-15.95	p=0.02 (-29.25- -2.66)	Native T2 time (FLASH)	-1.73	p=0.049 (-3.45- -0.01)
Current immunosuppression	-13.11	p=0.045 (-25.94 - -0.29)	*Skeletal muscle magnetic resonance imaging*		
Current statin	-0.19	p=0.989 (-28.88-28.49)	T2 hyperintensity	-17.06	p=0.01 (-29.86- -4.26)
Respiratory function			Fatty muscle infiltration	-18.48	p=0.045 (-36.55- -0.42)
FVC	0.45	p=0.01 (0.14-0.76)	Muscle atrophy	4.55	p=0.819 (-35.76-44.86)
DLCO	0.66	p=0.319 (-0.67-1.98)			

Abbreviations: CK: creatine kinase; CRP: C-reactive protein; DLCO: diffuse capacity for carbon monoxide; ESR: erythrocyte sedimentation rate; FVC: forced vital capacity; LAVi: left atrial volume index; LVEF: left ejection fraction; LV GLS: left ventricular global longitudinal strain; MRI: magnetic resonance imaging; mRSS: modified Rodnan Skin score; RVSP: right ventricular systolic pressure; ShMOLLI: shortened modified look locker

account for the symptom burden reported by patients.[2]Cardiopulmonary exercise testing (CPET) is the gold standard test for aerobic capacity. We sought to quantify the degree of exercise impairment in SSc using CPET and correlate disease manifestations, cardiac and pulmonary function and skeletal muscle abnormalities to peak VO_2. Our aim was to understand the disease specific features that contribute to impaired aerobic fitness in SSc.

Methods: Thirty four patients who all fulfilled 2013 ACR/EULAR criteria for SSc were recruited. Participants underwent PFT, TTE, cardiac MRI with mapping sequences, skeletal muscle MRI and CPET. No participant had a history of myocarditis, pulmonary arterial hypertension, ischaemic heart disease, valvular heart disease or renal impairment. Using logistic and linear regression analysis we analysed the SSc manifestations and imaging features associated with peak VO_2.

Results: Baseline characteristics of patients are listed in Table 1. We detected significant exercise impairment; mean % predicted peak VO_2 70.18 ± 18.98%. Diffuse myocardial fibrosis was a near universal finding with 30/31 patients having elevated native T1 times, including in those patients with early limited disease and no known SSc internal organ involvement. Nine (30%) patients had areas of late gadolinium enhancement. There was evidence of diffuse

myocardial oedema, with elevated T2 mapping times recorded. Skeletal muscle oedema was highly prevalent; 12 (37.50%) of participants had T2 hyperintensity on MRI. Skeletal muscle T2 hyperintensity was not associated with creatine kinase (p=0.94), ESR (p=0.79) or CRP (p=0.56).

Conclusion: Patients with SSc commonly have profoundly limited exercise capacity. This impairment is multifactorial; subclinical cardiac and skeletal muscle involvement and impaired lung function are significantly associated with reduced peak VO_2 in SSc. So-called subclinical organ involvement has negative physiological sequelae and contribute to global functional impairment. Future work is required to establish whether aerobic capacity in SSc can be improved by treatment of specific disease features or with exercise therapy.

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2. Baron M, Sutton E, Hudson M, et al. The relationship of dyspnoea to function and quality of life in systemic sclerosis. Ann Rheum Dis 2008;67:644

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Abstract Number: 1369

Adipose Tissue-Derived Stromal Vascular Fraction Plus Fat Grafts for Hand Therapy in Patients with Systemic Sclerosis. a Randomized Controlled Clinical Trial

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Adipose tissue-derived Stromal Vascular Fraction (ADSVF) has been proposed as regenerative treatment for hand deformities and digital ulcer healing in patients with Systemic Sclerosis (SSc). We aimed to evaluate its regenerative properties after local injection of autologous ADSVF in the hands of these patients.

Methods: This was an open-label, monocentric, randomized controlled study, approved by our local IRB and registered at clinicaltrials.gov (NCT04387825). Twenty patients diagnosed with SSc and moderate to severe hand contractures according to the Medsger's severity scale and/or digital tip ischemic ulcers (distal to PIP joints) with more than 30 days of evolution despite medical treatment, were enrolled and assigned to the experimental or control group. Both groups continued standard medical treatment. Autologous ADSVF was obtained by liposuction and then by enzymatic digestion in the experimental group. This group received ADSVF plus fat micrografts injection into the right hand. Digital oximetry, pain, Raynaud phenomenon (RP), digital ulcer healing (DUH) time, range of motion (ROM), vascular density of the nail bed, cell surface markers, hand function, and quality of life scores were evaluated in both

groups. The follow-up period was 168 days. Continuous variables were expressed as median with 95% confidence intervals. The differences between before and after the intervention were analyzed with the Wilcoxon range test, and the differences between the control and experimental groups at 0 and 168 days were analyzed with the Mann–Whitney U test. The range of total viable nucleated cells in the ADSVF was $167.5x10^6$, with viability of 82% or higher. Stem cell markers into the ADSVF were: CD34+ 4.72% , CD45+ 43.9%, CD44+ 36.3%, CD73+ 6.18 %, CD90+ 34.4 %, CD105+ 7.27%, HLA-DR 12.1%, Stromal cells 4.05%.

Results: At 168 days of follow-up there were significant improvements in pain level (p= 0.02) and DUH (p= 0.003) only in the experimental group. We also found increased active ROM of the MCP joints in the treated hand of the experimental group, while the non-treated hand MCP joint ROM decreased significantly. Raynaud phenomenon improved in both groups. There were no changes in disease activity or severity, nailfold capillaroscopy pattern, mobility or hand function between both treatment groups. One patient in the experimental group reported transient hand edema that solved within 7 days.

Conclusion: ADSVF local injection is safe and well tolerated in SSc patients. This therapeutic method may improve pain and time to digital ulcer healing in patients with severe joint contractures and refractory digital ulcers.

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Abstract Number: 1370

Complement Factor D and Factor H Represent Disease and Severity Biomarkers for Systemic Sclerosis Associated Pulmonary Arterial Hypertension (SSc-PAH)

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Pulmonary arterial hypertension (PAH) is a severe vascular complication of systemic sclerosis (SSc) and a major cause of mortality. Despite significant advances in the treatment of PAH, the pathogenesis of SSc-PAH is not well understood. Our previous work has shown that serum levels of complement factor D (fD, adipsin), a critical regulator of complement alternative pathway (AP) activation and amplification loop engagement, is associated with limited cutaneous SSc and SSc-PAH. Here we assessed the levels of complement cascade proteins utilizing a well-characterized cohort of SSc-PAH to investigate the possible role of complement components as biomarkers for disease development and progression.

Table 1. Plasma levels of 11 complement components in SSc-PAH, SSc patients without PAH, healthy controls and patients with psoriatic arthritis are represented as mean and standard deviation (S.D.). Comparisons of all SSc-PAH (n= 156) vs all controls (n=100) and SSc-PAH vs SSc without PAH are shown with corresponding ANOVA p-value

Plasma Complement Component	SSc-PAH (n=156)		Healthy Control (n=40)		SSc no PAH (n=33)		Psoriatic Arthritis (n=27)		SSc-PAH vs all Controls	SSc-PAH vs SSc no PAH
	Mean	S.D.	Mean	S.D.	Mean	S.D.	Mean	S.D.	p-value	p-value
C1q	108.6	27.5	84.9	17.5	115.0	37.2	102.3	16.6	**0.012**	0.360
C2	10.3	7.8	15.2	18.8	6.2	4.9	45.0	92.3	0.055	**0.0003**
C3	158.4	103.8	750.9	349.4	131.6	53.4	494.0	397.3	**<0.0001**	**0.034**
C4	133.9	32.3	141.8	28.8	120.6	28.6	190.6	58.0	**0.010**	**0.022**
C5	81.0	19.7	66.0	17	65.1	18.9	86.1	21.2	**0.0002**	**<0.0001**
Factor B	139.0	74.1	131.0	39.4	225.3	312.	171.4	29.2	0.085	0.130
Factor D	2.3	1.3	0.9	0.3	1.2	0.71	1.1	0.4	**<0.0001**	**<0.0001**
Factor H	195.5	31.6	203.2	40.1	182.6	47.1	282.6	83.1	**0.003**	0.140
Factor I	30.9	5.8	30.4	8.2	28.7	7.7	33.2	8.5	0.705	0.114
MBL	0.8	0.7	0.6	0.7	0.8	0.8	0.9	0.7	0.298	0.818
Properdin	17.7	3.7	19.2	4.7	17.7	5.2	24.6	4.5	**0.0002**	0.941

Methods: We evaluated 156 SSc-PAH patients from the PAH Biobank (www.pahbiobank.org), 33 SSc without PAH, 27 patients with psoriatic arthritis (PsA) and 40 healthy controls. Patients with interstitial lung disease were excluded from the SSc-PAH group. Plasma levels of complement components (C1q, C2, C3, C4, C5, fB, fD, fI, fH, Properdin and Mannose binding lectin) were assessed by Luminex at Exsera Biolabs, a CAP/CLIA certified laboratory. Associations between complement levels and clinical data in SSc-PAH (including NYHA functional status, 6-minute walk test, and hemodynamic data) were assessed and were corrected for age, sex, race, disease duration, obesity, smoking and scleroderma subtype. ANOVA was used to determine differences between serum complement levels across groups. Multiple logistic regression analysis was performed to characterize associations.

Results: Four out of 11 complement components (fD, C1q, C3, C5) were significantly dysregulated in SSc-PAH patients compared to healthy controls ($p< 0.0001$). Logistic regression analysis using these eleven markers revealed that C3, C5, fB and fH were able to distinguish SSc-PAH from all of the control groups. When comparing SSc-PAH to SSc without PAH, we found that fD, C2, C3, C4 and C5 were markedly and specifically elevated in SSc-PAH. Within the SSc-PAH cohort, a number of complement factors were significantly associated with markers of disease severity including VO2 (fH OR=1.03, p=0.02 and C3 OR=0.982, p=0.01), NYHA functional status (fB OR=1.063 $p< 0.001$, fH OR=0.964 p=0.03, fI OR=0.699 p=0.001, C2 OR=0.786 p=0.001), right atrial pressure (fD OR=0.320, p=0.001 and MBL OR=3.593, p=0.01), cardiac index (fH OR=1.048, p=0.008), cardiac output (fH OR=0.028, $p< 0.0001$) and mortality at follow-up (fH OR=0.975, p=0.014).

Conclusion: Factor D and other complement components are significantly altered in patients with SSc-PAH compared to controls. Factor H demonstrates potential utility as a marker of severity across multiple outcomes. These findings suggest that the alternative complement cascade plays a critical role in SSc-PAH pathogenesis and can potentially serve as a biomarker to inform diagnosis and prognosis.

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Abstract Number: 1371

Symptom Management in Systemic Sclerosis: A Pilot Study of a Web-based Intervention Using Peer-Health Coaches

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: People with systemic sclerosis (SSc) have a high burden of chronic symptoms that have dramatic effects on function and quality of life. Fatigue, along with pain, sleep disturbance, and physical limitations, affects the ability to fulfill life roles. Unfortunately, relevant interventions that can help people with SSc learn skills to manage fatigue and co-occurring symptoms and to improve wellbeing are not currently available in clinical care and are urgently needed. This pilot study examined feasibility and preliminary effects of a web-based intervention called the Resilience-Based Energy Management Program to Enhance Wellbeing (RENEW) intervention.

Methods: Participants with SSc and had access to a reliable, internet-connected device were enrolled. The study design was a one arm, pretest-posttest trial. The intervention involved 12 weeks of working on health goals based on online modules. Trained "peer" health coaches, who also had an SSc diagnosis, assisted in establishing goals and checking on progress during regular calls (10 over the study). We examined feasibility metrics (recruitment/retention rates, and coach call participation), symptom outcomes, patient global impression of change (PGIC), and end-of-program feedback. Outcomes were assessed at baseline, mid-treatment (6 weeks) and 12 weeks, including PROMIS29 and perceived self-efficacy to manage the condition. Participant characteristics and feasibility metrics were analyzed using descriptive statistics. One-way repeated-measures analysis of variance (ANOVA) was used to analyze changes in outcomes over time. SPSS 24.0 was used for analyses, and statistical significance was set at $p < 0.05$.

Results: Twenty-two participants consented, 21 completed baseline questionnaires; of these, 19 (90%) completed 12-week questionnaires. Participants had a mean age of 54 ± 11 years, (range 25 - 67), 64% were female, and 90% were White (Table 1). Of the 21 participants, 43% had diffuse SSc, 48% had limited SSc, and 9% had overlap. Mean health coach call participation was 9 calls ± 1.1. Among completers of the program, 13 (68.4%) rated overall quality of this program as excellent and 6 (31.6%) rated as good. 72% of participants reported moderate to great improvements on the PGIC. Over the 12 weeks, significant improvements were not shown in symptoms (Table 2), however, 50% of participants had improvements from baseline in sleep disturbance and 44% had improvements in anxiety, pain interference, and fatigue. A significant improvement was found in perceived self-efficacy in medications management ($p = 0.01$). Although perceived informational support increased, results did not reach statistical significance ($p = 0.08$). 95% of people (18/19) felt the program helped them stay positive; 89% said it improved their mood. Participants reported that health coaching was important to them and 63% said talking to someone with their condition was what they liked best.

Conclusion: A 12-week program addressing SSc symptom management with peer health coaches was feasible to deliver and was positively viewed by patients. Health coaching by trained peers was particularly valuable to patients.

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Abstract Number: 1372

Outcomes and Risk Factors for Respiratory Failure in Patients with Scleroderma Associated with ILD

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Scleroderma is associated with underlying ILD. About 48% those with diffuse cutaneous SSc and 26% of those with limited cutaneous SSc were found to have ILD on HRCT based on prior literature. The most common cause of mortality in Scleroderma has shifted from renal crisis to pulmonary diagnoses. In our study, we aim to identify the risk factors and outcomes of acute respiratory failure in patients with underlying ILD and Scleroderma.

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. This database is the largest collection of inpatient admission data in the USA. It is a nationally representative sample of 20% of hospitalizations from approximately 1000 hospitals. The NIS was searched for hospitalizations in 2016, 2017 and 2018 containing ICD-10 for acute respiratory failure codes with J96 as principal diagnosis and underlying Scleroderma associated with ILD as secondary diagnoses with codes M34.81, J84 and J98.4. Using STATA software, the total number of discharges, age, race, length of stay (LOS), mortality and total hospital charges were recorded. A univariate logistic regression analysis was used to calculate unadjusted odds ratios (ORs) for a principal diagnosis of acute respiratory failure. All variables with p-values < 0.2 were included in a multivariate logistic regression model. P-values < 0.05 were considered significant in the multivariate analysis.

Results: A total number of 1,274 patients with underlying Scleroderma-ILD were hospitalized for acute respiratory failure in 2016, 2017 and 2018. Characteristics of patients with acute respiratory failure and underlying Scleroderma *vs* all other adult hospitalizations are displayed in table 1. When compared to the reference group, females were 81% *vs* 57%. Mean age was 61 yrs *vs* 57 yrs Caucasians formed 55% *vs* 67%, followed by African Americans 24% *vs* 15%. 125 (9%) patients underwent BAL *vs* 0.6%. Mean LOS was 7.25 days *vs* 4.74 days, mean total charge of hospitalization was $90,547 *vs* $53,572. Inpatient mortality was 14% *vs* 2%. The following were found to be significant risk factors for acute respiratory failure among scleroderma ILD patients in multivariate analysis: pneumonia OR 5.0, Heart failure OR 4.8, female sex OR 3.6, PE OR 2.6, white race OR 0.6, Quartile 1 of income status based on zip code OR 0.6 and smoking OR 0.3

Conclusion: This analysis represents the largest sample to-date to assess the incidence, mortality, and risk factors for development of acute respiratory failure among Scleroderma patients with ILD. Results show slightly higher mean

Table 1- Descriptive data of patients admitted with acute respiratory failure and underlying Scleroderma-ILD

Hospitalization characteristics	Acute Respiratory failure from SSc-ILD (n=1274)	Non-SSc ILD hospitalizations (n= 90,878,286)	P-value
Women, number (%)	1,045 (81%)	52468697 (57%)	<0.0001
Age, mean in years	61	57	<0.0001
Number (%) hospitalizations by age			
Age 18-40 years	65 (5%)	21950081 (24%)	<0.0001
Age 40-60 years	500 (39%)	21700952 (23%)	<0.0001
Age 60-80 years	610 (47%)	32359091 (35%)	<0.0001
Age > 80 years	100 (7%)	14868162 (16%)	<0.0001
Race (%)			
A) White	55%	67%	<0.0001
B) African American	24%	15%	<0.0001
C) Hispanic	12%	11%	0.518
D) Asian or Pacific Islander	2%	2%	0.4
E) Native American	1%	0.6%	0.251
F) Other	3%	3%	0.821
Bronchoscopy done, number (%)	125 (9%)	619515 (0.6%)	<0.0001
Length of stay, mean days	7.25	4.74	<0.0001
Total charges, mean	$90,547	$53,572	<0.0001
Inpatient mortality, number (%)	180 (14%)	2,020,154 (2%)	<0.0001

age in this group compared to the reference group. The cost of hospitalization and inpatient mortality are also noted to be significantly higher. Female sex, pneumonia, PE, and heart failure are risk factors for acute respiratory failure. This study emphasizes that Scleroderma-ILD patients have high inpatient mortality. Prompt recognition of respiratory distress and pro-active management of above risk factors should be studied as means to improve inpatient scleroderma outcomes.

Table 2 – Univariate screen of risk factors associated with acute respiratory failure in Scleroderma-ILD

Demographic variables	Odds ratio	P-value	95% CI	
Age	1.01	<0.001	1.00	1.01
Female sex	3.32	<0.001	2.40	4.60
Race: a) White	0.60	<0.001	0.46	0.77
b) African American	1.76	<0.001	1.31	2.36
c) Hispanic	1.15	0.52	0.76	1.74
d) Asian /Pacific Islander	0.73	0.49	0.30	1.78
e) Native American	1.95	0.25	0.62	6.08
f) Other race	1.08	0.82	0.54	2.18
Income Quartile 1*	0.72	0.03	0.54	0.97
Income Quartile 2*	1.02	0.91	0.76	1.36
Income Quartile 3*	1.11	0.50	0.83	1.48
Income Quartile 4*	1.29	0.09	0.96	1.74
Pneumonia infection	6.04	<0.001	3.72	9.80
History of cocaine use	0.29	0.21	0.04	2.04
History of smoking	0.28	<0.001	0.15	0.50
History of Pulmonary embolism	3.83	0.001	1.71	8.60
History of heart failure	4.50	<0.001	3.52	5.76

*Quartile descriptions as of NIS 2018:

Quartile 1 income $	Quartile 2 income $	Quartile 3 income $	Quartile 4 income $
1 - 45,999	46,000 - 58,999	59,000 - 78,999	79,000+

Table 3 – Multivariate screen of risk factors associated with acute respiratory failure in Scleroderma-ILD

Variables	Odds Ratio	p-value	[95% Conf.	Interval]
Age	1.00	0.46	0.99	1.00
History of pneumonia	5.08	<0.0001	3.06	8.44
History of smoking	0.34	0.001	0.18	0.64
Female sex	3.69	<0.0001	2.62	5.19
History of PE	2.68	0.03	1.10	6.56
History of heart failure	4.86	<0.0001	3.49	6.77
Race- white	0.63	0.005	0.46	0.87
Race- African American	1.33	0.14	0.91	1.95
Income Quartile 1	0.62	0.01	0.43	0.90
Income Quartile 4	1.17	0.40	0.81	1.68

Disclosure: S. Kambhatla, None; **A. Manadan**, None; **A. Trang**, None.

Abstract Number: 1373

Paraoxonase-1: Potential Novel Marker of Disease Extent and Activity in Systemic Sclerosis

Suzanne Kafaja[1], Isela Valera[2], Yossra Suliman[3], Mohamed Alemam[4], Rosha Mamita[5], Jennifer Wang[5], Ani Shahbazian[6], Philip Clements[7] and Christina Charles-Schoeman[6], [1]University of California Los Angeles Division of Rheumatology, Los Angeles, CA, [2]Florida Universtity- College of Health and Human Sciences, Talahhasse, FL, [3]Department of Clinical Pathology, Qena Faculty of Medicine, Assiut, Egypt, [4]Department of Pathology< Qena Faculty of Medicine, South Valley University,, Assiut, Egypt, [5]University of California Los Angeles, Los Angeles, CA, [6]Department of Medicine, University of California, Los Angeles, Los Angeles, CA, [7]University of California Los Angeles School of Medicine, Department of Rhemumatology, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Our understanding of the pathogenesis of systemic sclerosis (SSc) continues to evolve. Oxidative stress has been implicated in the pathophysiology of disease, but minimal work has investigated specific markers and mechanisms for oxidative stress in SSc. Paraoxonase-1 is a major HDL-associated protein, which metabolizes pro-inflammatory, oxidized lipids. In the current work, we evaluated the paraoxonase (PON), lactonase

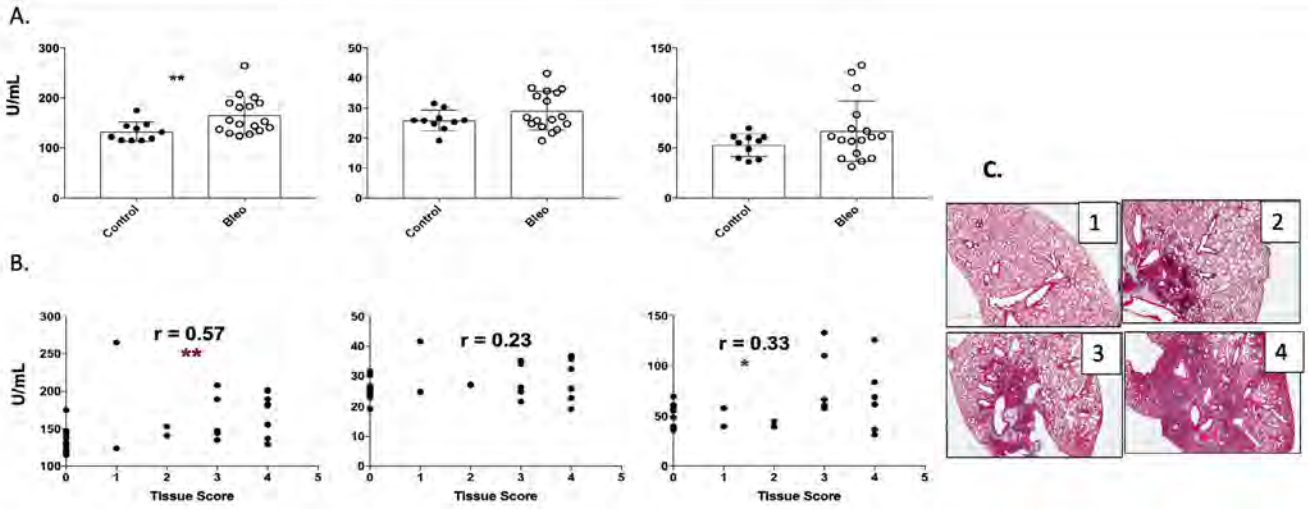

Figure-1: PON-1 activity in Bleo and PBS treated mice and correlation with lung tissue severity. A) Peripheral blood from 17 bleomycin-treated and 10 PBS -treated mice (CTRL) was evaluated for ARES, LAC and PON activity in U/ml. (B) Lung tissue were stained for Masson's Trichrome and assessed for fibrosis severity using a modified Ashcroft score, a numerical fibrosis scoring scale. A score of 0 indicates no fibrosis, 1 minimal, 2 mild, 3 moderate, and 4 severe fibrosis . Sample of lung tissue severity scoring is denoted in panel C. Each symbol represents data from an animal. *p<0.05, ** p<0.01, *** p <0.001.

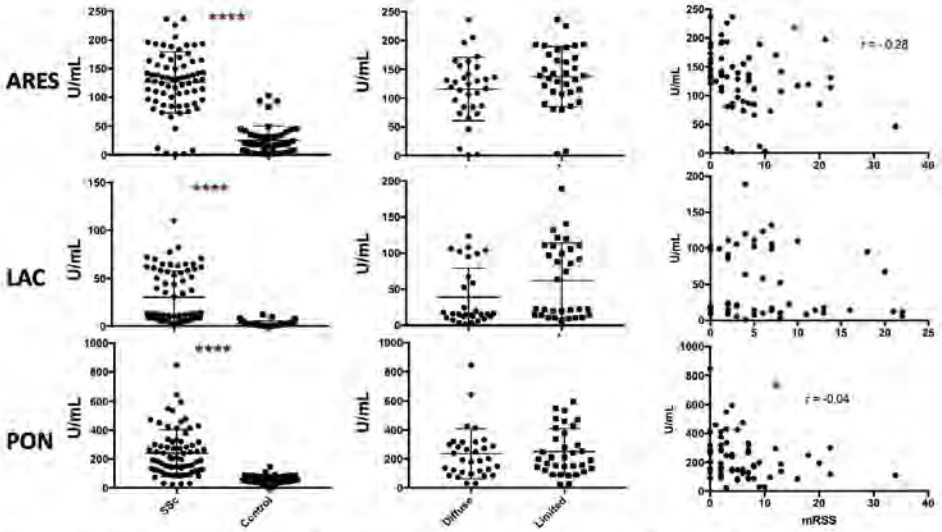

Figure-2: Detection of PON-1 activity in peripheral blood of controls and SSc patients and its correlation with disease type and skin severity score. Panel 1 -PON-1 activity (in U/ml) as denoted by ARES, LAC and PON in 50 controls as well as 72 SSc patients . Each symbol represents data from a patient. Panel 2- represent PON-1 activity in diffuse (dcSSc) as well as limited SSc (dcSSc). Panel 3- represents PON-1 activity in (U/ml)and its correlation with skin disease severity represented by modified Rodnan Skin Score, (ranging from 0-51). A score of 0 indicates no fibrosis, and 51 severe fibrosis . *p<0.05, ** p<0.01, *** p <0.001, **** p <0.0001.

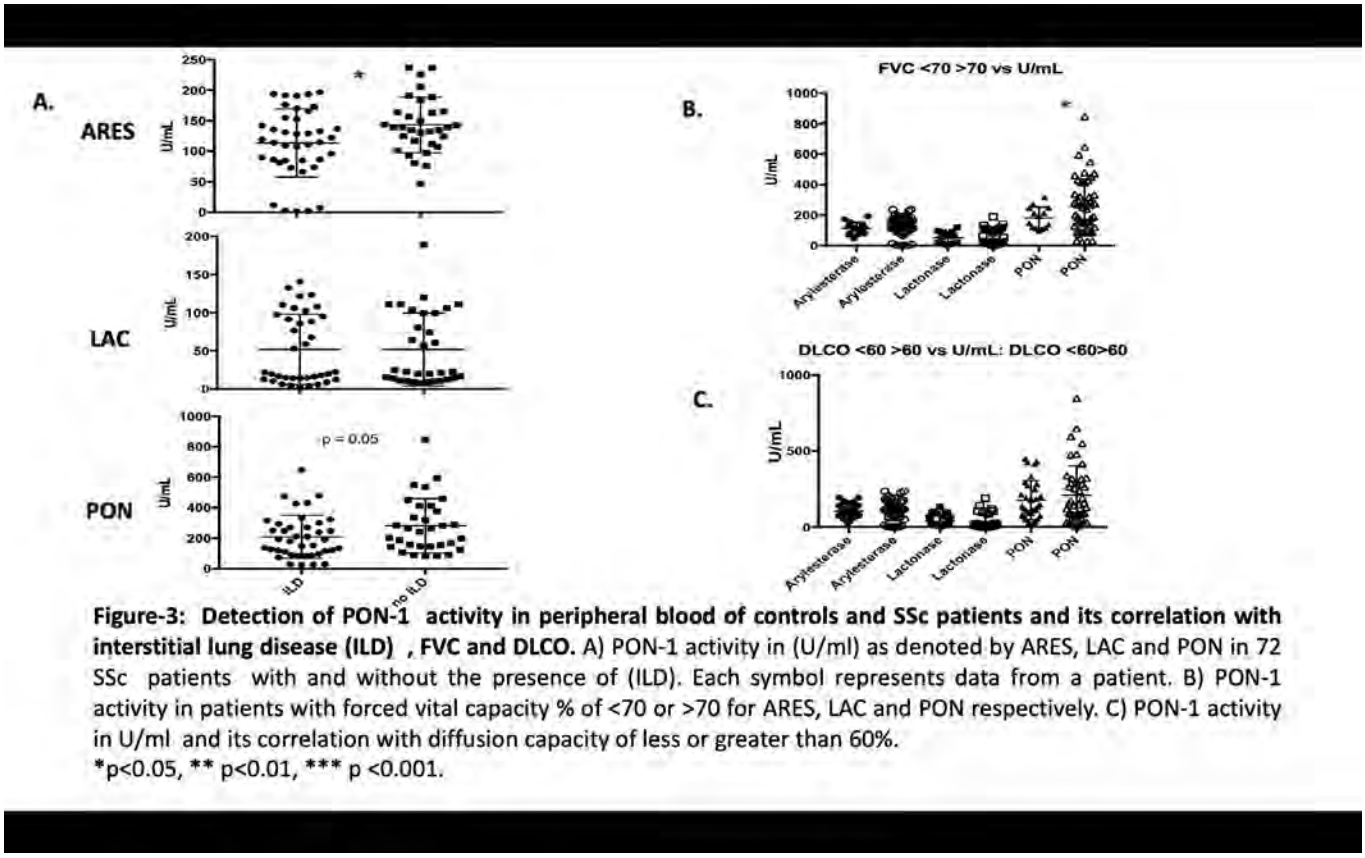

Figure-3: Detection of PON-1 activity in peripheral blood of controls and SSc patients and its correlation with interstitial lung disease (ILD) , FVC and DLCO. A) PON-1 activity in (U/ml) as denoted by ARES, LAC and PON in 72 SSc patients with and without the presence of (ILD). Each symbol represents data from a patient. B) PON-1 activity in patients with forced vital capacity % of <70 or >70 for ARES, LAC and PON respectively. C) PON-1 activity in U/ml and its correlation with diffusion capacity of less or greater than 60%.
*p<0.05, ** p<0.01, *** p <0.001.

(LAC), and arylesterase (ARES) activities of PON1 in both a murine model of SSc and human samples, assessing their correlation with the extent of SSc manifestations and severity.

Methods: We assessed PON, ARES and LAC activities in the murine model of SSc using Black 6 (B6) mice. To induce fibrosis, mice age 8-10 weeks were anesthetized with intraperitoneal ketamine (then treated via oropharyngeal installation with bleomycin (Bleo) or PBS. We assessed Masson's trichrome-stained lung sections using a modified Ashcroft score, a numerical fibrosis scoring scale. A score of 0 indicates no fibrosis, 1 minimal, 2 mild, 3 moderate, and 4 severe fibrosis. PON1 activities were also evaluated in serum samples from 72 SSc patients (pts) meeting the ACR/EULAR 2013 SSc criteria and 50 healthy controls (CTRL). We assessed associations of PON, ARES and LAC activities with disease manifestations including interstitial lung disease (ILD), in both humans and mice (histopathological), vascular disease (pulmonary arterial hypertension (PAH) as well as skin severity (modified Rodnan Skin Score (mRSS). PON1 activities were measured in mouse and human serum samples as described previously using paraoxon (PON), phenylacetate (ARES), and dihydrocoumarin (LAC) as substrates.

Results: Clinical patient characteristics include: 32 (44%) with diffuse SSc (dcSSc) , age (mean , range in years) (56 , 20-85) SSc and (48, 18-65) CTRL; gender,19.4% male (SSc) 18% male (CTRL); active skin ulcers 17 (25.7%); interstitial lung disease (ILD) 40 (55%) pts; (PAH) 23 (31%) pts.

In the murine model of SSc, serum PON1 activities were greater in bleo-treated mice when compared to PBS. Higher ARES , PON and LAC activities correlated with greater tissue severity scores (with r^2 of 0.57 ($p < 0.001$), 0.33 ($p < 0.05$) and 0.23 (p =ns) respectively) (Figure 1). In human data, mean ARES and LAC activities were higher in SSc compared to CTRL (66.43 ± 3.29 SSc patients vs 13.31 ± 1.91 CTRL) $p < 0.0001$. ARES and LAC activities were lower in patients with dcSSc compared to limited (lcSSc). No significant differences were noted in PON activity between dcSSc and lcSSc pts. Moreover, lower levels of ARES and PON significantly correlated with higher skin scores: mRSS correla-

tions: ARES (r^2= 0.08, $p < 0.05$) and PON (r^2= 0.06, $p < 0.04$), (Figure2. Interestingly, lower activities of ARES, LAC, and PON were noted in patients with ILD, (figure 3).

Conclusion: Markers of oxidative stress measured by PON1 activities associate with disease severity in both SSc patients and a murine model of SSc. Further work is warranted and ongoing to examine the role of PON1 as a disease marker and mechanism in the pathogenesis of SSc and SSc-associated ILD.

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Abstract Number: 1374

A Deep Neural Network Classifier to Identify Inflammatory Systemic Sclerosis Patients from Histological Images

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) patients can be divided into four molecular subsets (inflammatory, fibroproliferative, limited and normal-like) identifiable with gene expression in skin and peripheral blood cells (PBCs). The inflammatory subset typically associated with the presence of inflammatory lymphocyte and innate immune cell infiltrates. SSc participants assigned to the inflammatory subset showed significant improvement in the Abatacept Systemic SclErosis Trial (ASSET). In order to provide a fast and more accessible inflammatory subset predictor, we trained a deep neural network to identify these participants using the images of immunohistochemically (IHC)-stained skin biopsies.

Methods: 164 whole-slide microscopy images were obtained from the ASSET clinical trial. Molecular-subset labels for each whole-slide image were obtained using a previously reported support vector machine (SVM) classifier applied to paired gene expression profiles from the same skin biopsy. A blinded rheumatologist (RL) scored the extent of inflammation and fibrosis in each biopsy. Images were split into training, validation, and test set (70%/15%/15%) with a focus on predicting the inflammatory subset. Small patches were generated using a sliding-window approach and used to train a convolutional neural network (CNN) to infer the subset of the given biopsy. Spearman correlations between predicted probabilities and clinical inflammation scores were examined to validate our model.

Results: A CNN was trained and validated on small patches generated from 140 whole-slide images. The model was evaluated using a hold-out test set of 24 whole-slide images. The final model identifies participants with inflammatory gene signature with 83.33% accuracy (F1-score of 0.75) when data sets are split-by-patient, and 91.30% accuracy (F1-score of 0.9) when data sets are split-by-biopsy. Visualization of patches and predicted decisive regions provided insights on important cell types contributing to the molecular subsets. Areas of the image important for inflammatory subset prediction were identified and visualized. The predicted inflammatory probabilities were significantly correlated with clinical inflammation scores, as assessed by RL.

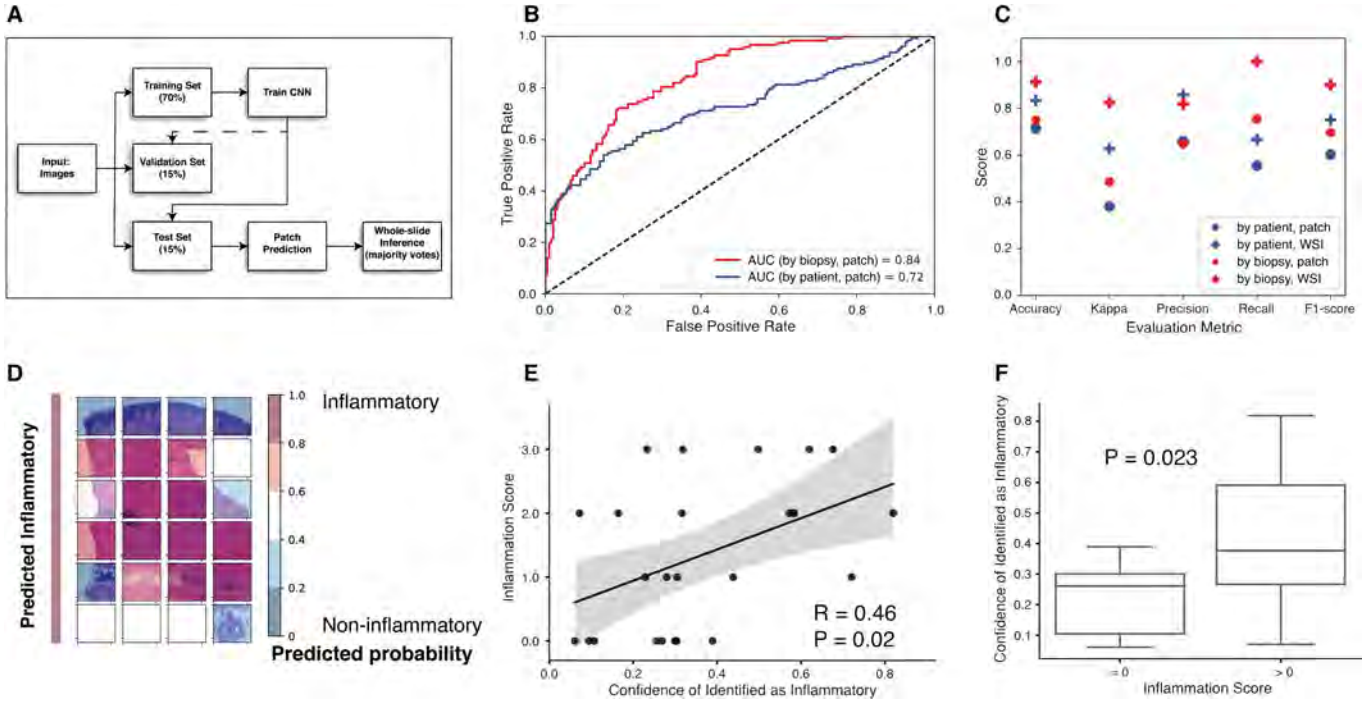

Figure 1. (A) Schematic depiction of the dataset partitioning. (B) Receiver operating characteristic (ROC) curves and their area under the curves (AUCs) on the test set. (C) Models' performance on the test set for models trained on splitting by patient or by biopsy datasets, patch-based and post aggregation whole-slide level. (D) Visualization of patches in a representative true inflammatory slide by overlapping a colored heatmap based on predicted probability. (E) Correlation of confidence scores for prediction as inflammatory subset and clinical inflammation scores. (F) Whole-slide images with inflammation showed significantly higher confidence scores for prediction as inflammatory subset.

Conclusion: We trained a CNN that classifies SSc patients into the inflammatory molecular subset using standard IHC images of skin biopsies. This provides a method that is less costly than genomic assays to identify these individuals and can be applied to evaluate retrospective data where genomic data were not collected but for paraffin embedded blocks or IHC-stained images are available.

Disclosure: Y. Yuan, None; **R. Lafyatis**, Bristol Meyers Squibb, 2, 5, Formation, 2, 5, Corbus, 5, Moderna, 5, Regeneron, 5, Pfizer, 5, Kiniksa, 5, Sanofi, 2, Merck, 2, Genentech/Roche, 2, Acceleron, 2, Boehringer-Ingelheim, 2; **J. Gudjonsson**, Almirall, 5, Eli Lilly, 5, BMS, 5; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **M. Whitfield**, Celdara Medical, LLC, 2, 5, 8, 12, Scientific Founder, Bristol Myers Squibb, 2, 5, 6, Acceleron, 2, Corbus Pharmaceuticals, 2, 6, Abbvie, 6, Kadmon, 6.

Abstract Number: 1375

Improvement in Overall Survival, Skin Fibrosis and Lung Function with Autologous Hematopoietic Stem Cell Transplantation in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a chronic disease characterized by vasculopathy, inflammation and fibrosis. Rheumatologists have limited options to effectively treat rapidly progressive disease. There is an important unmet medical need for disease modifying therapy for patients with SSc. Autologous hematopoietic stem cell transplantation (AHSCT) has been shown in randomized controlled trials and is well recognized to be an effective treatment for rapidly progressive SSc. However, there is a paucity of data pertaining to its performance as compared to real-world routine clinical practice. The objective of this study was to evaluate the effectiveness of AHSCT for SSc compared to conventional care used in routine clinical practice.

Methods: SSc patients from France who underwent AHSCT were compared to SSc patients who met criteria for AHSCT (as defined in the ASTIS trial[1]) but received conventional care in Canada. The primary outcome was overall survival. Secondary outcomes included modified Rodnan skin score (mRSS), forced vital capacity (FVC) and diffusion capacity for carbon monoxide (DLCO). Baseline characteristics were compared using descriptive statistics. Overall survival for both groups was estimated by constructing Kaplan-Meier survival curves based on time to death. Measures of mRSS, FVC and DLCO were compared using linear regression models. Analyses were adjusted for baseline scores and incorporated stabilized inverse probability of treatment weights to account for confounding by indication. Propensity scores were estimated using logistic regression.

Results: 41 SSc patients who underwent AHSCT and 85 patients treated with conventional care were compared. Baseline characteristics are delineated in Table 1. Mean mRSS was 25.0 (10.5) in the AHSCT group and 27.0 (8.0) in the conventional care group. Mean FVC and DLCO were 78.9 (17.5) and 55.2 (15.5) in the AHSCT group and 79.0 (20.2) and 62.0 (19.6) in the conventional care group, respectively. AHSCT was associated with improvement in overall survival (log-rank p=0.115; Figure 1). In follow-up, the mRSS was lower with AHSCT compared to conventional care: 7.25 point between group difference at 12 months (p=< 0.001), 6.41 points at 24 months (p=< 0.001) and 4.48 points at 36 months (p=< 0.001). There was no statistically significant difference in FVC between groups at 12 months but at 24 months, AHSCT was associated with a higher FVC (between group difference of 9.22 (p=< 0.001)) but a lower DLCO (between group difference of -3.43 (p=0.002)).

Conclusion: The present study provides crucial real-world long-term data pertaining to key clinical outcomes to support the use of AHSCT in patients with SSc.

Table 1: Baseline characteristics

	AHSCT *n / mean (SD)* (n=41)	Conventional Care *n / mean (SD)* (n=85)	Missing Data AHCST	Missing Data Conventional Care
Sex (% female)	27 (65.9%)	64 (75.3%)	0	0
Age	44.7 (13.3)	53.5 (11.6)	0	0
Disease duration (months)	30.6 (18.5)	19.5 (11.1)	0	0
BMI (kg/m^2)	23.4 (4.0)	24.9 (5.1)	0	2
Modified Rodnan Skin Score	25.0 (10.5)	27.0 (8.0)	1	0
Smoking			4	3
Never smoker	25 (67.6%)	36 (43.9%)		
Past smoker	8 (21.6%)	39 (47.6%)		
Current smoker	4 (10.8%)	7 (8.5%)		
Interstitial lung disease (% present)	38 (92.7%)	55 (64.7%)	3	7
FVC	78.9 (17.5)	79.0 (20.2)	4	5
DLCO	55.2 (15.5)	62.0 (19.6)	0	12
Pulmonary artery pressure (mmHg)	31.0 (9.1)	35.0 (13.9)	0	30
Left ventricular ejection fraction			2	11
> 50%	38 (100%)	76 (97.4%)		
45-49%	0	2 (2.6%)		
Creatinine (umol/L)	62.4 (12.8)	90.3 (48.1)	0	6
ESR (mm/h)	42.8 (24.8)	34.4 (27.8)	17	14
Hemoglobin (g/L)	126.2 (11.8)	118.2 (19.8)	0	1
Serologies				
ACA (+)	1 (2.6%)	10 (13.5%)	1	11
ATA (+)	26 (65.0%)	20 (27.0%)	0	10
ANA (+)	27 (65.8%)	64 (75.3%)	0	0

Table 1. Baseline characteristics

1. Van Laar, J. M. et al. Autologous hematopoietic stem cell transplantation vs intravenous pulse cyclophosphamide in diffuse cutaneous systemic sclerosis: a randomized clinical trial. JAMA J. Am. Med. Assoc. **311,** 2490-2498 (2014).

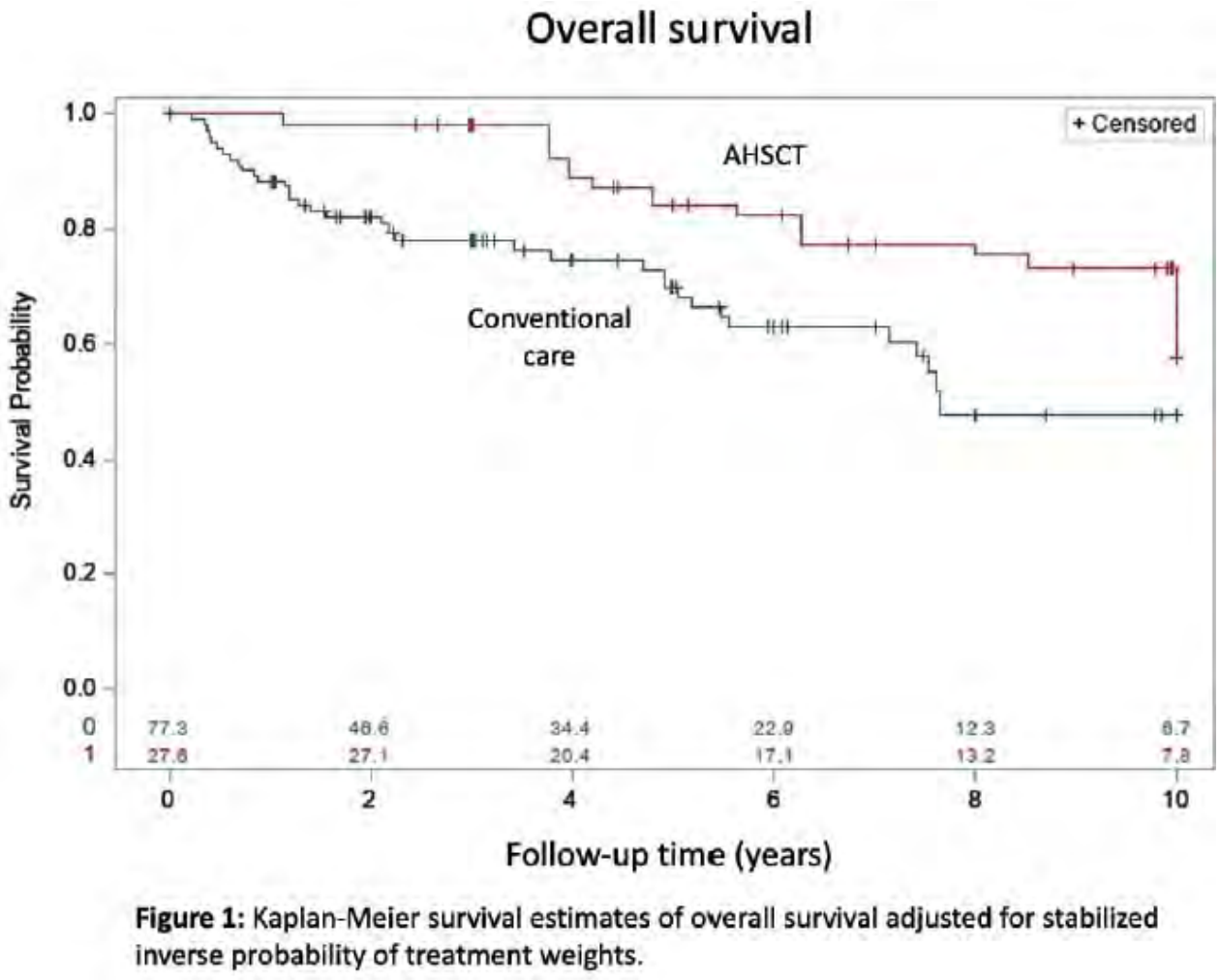

Figure 1: Kaplan-Meier survival estimates of overall survival adjusted for stabilized inverse probability of treatment weights.

Figure 1. Kaplan-Meier survival estimates of overall survival adjusted for stabilized inverse probability of treatment weights.

Disclosure: N. Maltez, None; **M. Wang**, None; **G. Wells**, None; **P. Tugwell**, None; **M. Baron**, None; **Z. Marjanovic**, None; **P. Lansiaux**, None; **D. Farge**, None; **M. Hudson**, None.

Abstract Number: 1376

Outcome Reporting in Systemic Sclerosis-Related Digital Ulcers: A Scoping Review

Michael Hughes[1], Nancy Maltez[2], Edith Brown[3], Virginia Hickey[4], Heiyoung Park[5], Beverley Shea[2], John Pauling[6], Susanna Proudman[7], Peter Merkel[8] and Ariane Herrick[9], [1]Tameside and Glossop Integrated NHS Foundation Trust, Manchester, United Kingdom, [2]University of Ottawa, Ottawa, ON, Canada, [3]n/a, Manchester, United Kingdom, [4]n/a, Adelaide, Australia, [5]5. National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, [6]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [7]University of Adelaide, Medindie, Australia, [8]University of Pennsylvania, Philadelphia, PA, [9]University of Manchester, Salford, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Domains and outcome instruments/measurements used in clinical research studying digital ulcers in systemic sclerosis

Domain	Outcome (number of studies)	Instrument or Measurement (number of studies)
DU Burden	Digital ulcer count/number (23)	Net ulcer burden/number of ulcers (17) Number of new ulcers (11)
	Digital ulcer improvement (20)	Ulcer healing (prevalence or number) (10) Ulcer measurement (7) All ulcers healed (6) Healing of cardinal ulcer (3) Time to healing of digital ulcer (2)
	Digital ulcer complications (7)	Ulcer infection (5) Gangrene (3) Need for hospitalization (3) Need for surgical intervention (2) New vasodilator therapy (2) Need for analgesia (2) Ulcer inflammation (2)
	Global digital ulcer assessment (2)	Clinician opinion (2) Patient opinion (1)
DU Impact	Function (10)	Scleroderma Health Assessment Questionnaire (7) Health Assessment Questionnaire Disability Index (6) Cochin hand function scale (4) McMaster-Toronto arthritis patient preference disability questionnaire (2) Hand mobility in scleroderma (1) Hand disability in systemic sclerosis-digital ulcers (1) Hand functional index (1) Scleroderma functional index (1) Kapandji score (1)
	Pain (6)	Visual analogue scale (6) Short-form McGill pain questionnaire (1)
	Health-related quality of life (4)	36-item short form survey (3) Hospital anxiety and depression scale (2) Pittsburgh sleep quality index (1)
Special tests	Microvascular assessment (4)	Laser speckle contrast analysis (2) Laser Doppler perfusion imaging (2)
	Histopathology (1)	Wound biopsies (with measurement of vascular endothelial growth factor and endothelin-1 type A receptor autoantibodies) (1)

Background/Purpose: Digital ulcers (DUs) are a major cause of pain and disability in patients with systemic sclerosis (SSc). Despite the availability of a range of treatment approaches including drug therapies, DUs are often slow to heal, and many patients experience recurrent digital ulceration. Assessment of DU burden is hugely challenging in both clinical practice and clinical trials resulting in a major barrier to the development of new and optimized treatment approaches for DUs. The aim of this scoping review of the literature was to evaluate the domains of illness studied, and the range of instruments and outcome measures used in clinical studies of DUs in patients with SSc.

Methods: Embase, MEDLINE and Cochrane Central Register of Controlled Trials were searched for all articles written in the English language relating to SSc-associated DUs. Two reviewers (MH & NM) independently screened the abstracts. A minimum of 15 participants for DU imaging-derived studies and 25 participants for questionnaire-based studies was required for inclusion. Basic laboratory and genetic studies, and studies of pediatric/juvenile SSc were excluded. There was no limitation by intervention, comparator, or study setting. All primary and secondary outcomes measured and instruments used in each study were recorded along with the study characteristics, including date of publication, sample size, interventions, and study types.

Results: A total of 4869 manuscripts was identified with 1126 duplicates excluded. Of the remaining 3743 abstracts, 123 were eligible for full-text review, and 40 were included in the final analysis. Most studies were either randomized controlled trials (n=13) or non-randomized prospective (n=12) or retrospective (n=8) studies. There was wide variation in the sample sizes of the intervention/actively studied (n=8 to 1439) and comparator (n=9 to 186) arms of the studies. Active interventions included oral/intravenous drugs therapies (n=25), topical/local treatments (n=4), and surgical interventions (n=2).

Domains and instruments/measurements used to study DUs in SSc are presented in **Table 1**. Half the studies assessed either the count/number of DUS (n=23) or improvement in DU (n=20). Functional impact of DUs was examined in 25% (n=10) of studies assessed. Other outcomes were related to complications of DU (n=7), pain (n=6), health-related quality of life (n=4), microvascular assessment/pathophysiology (n=4), or global DU assessment (n=2). For each outcome, there was significant heterogeneity regarding the types and number of instruments/measurements used within and between studies (**Table 1**).

Conclusion: This review identified a broad range of disease-related domains and associated outcome instruments/measurements used to study SSc-DUs, including in randomized clinical trials. There has been significant heterogeneity in outcomes used by investigators to study the impact of SSc-DUs.

These data will inform the ongoing work of the OMERACT Vascular Disease in Systemic Sclerosis Working Group to define a core set of disease domains to capture the burden of SSc-DUs.

Disclosure: M. Hughes, Actelion Pharmaceuticals, 6, Eli Lilly, 6, Pfizer, 6; **N. Maltez**, None; **E. Brown**, None; **V. Hickey**, None; **H. Park**, None; **B. Shea**, None; **J. Pauling**, None; **S. Proudman**, Boehringer-Ingelheim, 1, Janssen, 1, Gossamer, 1, Janssen, 5; **P. Merkel**, Pfizer, 2, Abbvie, 2, Astra Zeneca, 2, 5, Biogen, 2, BMS, 2, 5, Boeringher-Ingelheim, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 2, Jannsen, 2, Kiniksa, 2, Magenta, 2, Sparrow, 2, Talaris, 2; **A. Herrick**, None.

Abstract Number: 1377

Assessment of Autoantibodies and Clinical Associations in SSc Patients with ANA Positivity & Negative for Prototypic Autoantibodies

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a clinically heterogenous disease typically characterized by a positive ANA (ANA+), and prototypical antibodies including anti-centromere, anti-topoisomerase, and anti-RNA polymerase III antibodies which each carry specific clinical associations. A subset of SSc patients, however, lack these prototypic SSc related autoantibodies (triple negative), and have been poorly characterized largely due to lack of clinical testing for additional autoantibodies. The purpose of this study was to identify the prevalence of autoantibodies present in ANA+ triple negative patients and assess their clinical correlations.

Methods: Patients with ANA+ and triple negative for prototypic SSc associated antibodies were selected from the scleroderma biorepositories at University of Rochester (UR) and Northwestern University (NU). Demographic and clinical data was obtained to identify specific disease outcomes and associations. Sera were screened for ANA by indirect immunofluorescence testing on HEp-20-10 slides with respect to the intensity, pattern, and titer through EUROPattern microscope. Autoantibody identification was performed using the EUROLINE SSc and Autoimmune Inflammatory Myopathies profiles (EUROIMMUN, Lubeck, Germany).

Results: Of the 280 SSc patient sera queried from UR and NU, 57 were identified as ANA+ and triple negative using clinical testing, and 40 were confirmed to have this status after EUROLINE testing. Of these 40 patients, 53% had limited cutaneous SSc, 83% of patients were female, 75% Caucasian, mean age 53 ± 14.5 years, with disease duration 9 ± 9.7 years. Patients had an average MRSS 7.6 ± 6.8, 19 (47.5%) patients had digital ulcers, 24 (60%) had interstitial lung disease (ILD) with an average FVC of 79 ± 20.6 percent predicted and DLCO 62 ± 19.5 percent predicted, and 6 (15%) had pulmonary hypertension. Of the ANA patterns, the majority of patients had mixed speckled/nucleolar patterns (42.5%) or speckled (30%). Of 29 autoantibodies tested, the most prevalent were Ro-52 (50%), Th/To (40%), MDA5 (35%), SAE1 (27.5%), PM-75 (25%), fibrillarin (25%) (Table 1). Ro-52 was associated with ILD (RR 2.67, 95% C.I. 1.51-5.29, p< 0.001) and elevated CK (RR 2.64, 95% C.I. 1.11-6.96, p< 0.05), PM-75 was associated with digital ulcers (RR 2.18, 95% C.I. 1.17-3.85, p< 0.05), and Mi-2b was associated with increased MRSS (RR 4.00, 95% C.I. 1.25-11.75. p< 0.05).

Conclusion: Patients defined as ANA+ triple negative have equal prevalence of lcSSc and dcSSc, and high prevalence of digital ulcers and ILD. These patients have a variety of autoantibodies which are not typically clinically assessed, and each has important clinical associations, particularly Ro-52 which is present in 50% of patients and strongly associated with ILD. ANA+ triple negative represents a unique and heterogenous patient population which should be further characterized in larger SSc cohorts.

Table 2. Antibody prevalence as measured by immunoblot. Prevalence of scleroderma and myositis specific antibodies in the ANA positive triple negative cohort, antibodies with a prevalence <10% are not shown. Associations with clinical variables (interstitial lung disease (ILD), pulmonary arterial hypertension (PAH), modified rodnan skin score (MRSS), creatine kinase (CK), and digital ulcers) were ascertained using a Fisher's exact test. Percentage prevalence of each clinical feature is calculated based on antibody prevalence. Statistically significant results (p<0.05) are highlighted

Antibody	Confirmed Triple Negative (n=40)	ILD			PAH			MRSS >12			CK (>145)			Digital ulcers		
		n (%)	RR (95% CI)	p-value	n (%)	RR (95% CI)	p-value	n (%)	RR (95% CI)	p-value	n (%)	RR (95% CI)	p-value	n (%)	RR (95% CI)	p-value
Ro-52	20 (50)	**17 (85)**	**2.67 (1.51 - 5.29)**	**0.0007**	6 (30)	2.00 (0.63 - 6.63)	0.45	4 (20)	1 (0.30 - 3.25)	>0.99	**10 (50)**	**2.64 (1.11 - 6.96)**	**0.04**	11 (55)	1.37 (0.71 - 2.74)	0.53
Th/To	16 (40)	10 (63)	1.07 (0.61 - 1.77)	>0.99	3 (19)	0.75 (0.22 - 2.32)	0.72	2 (13)	0.5 (0.12- 1.85)	0.44	7 (44)	1.33 (0.59 - 2.96)	0.51	7 (44)	0.87 (0.42 - 1.67)	0.75
MDA5	14 (35)	8 (57)	1.11 (0.59 - 1.88)	0.76	2 (14)	0.53 (1.33 - 1.86)	0.45	4 (29)	1.86 (0.57 - 5.88)	0.42	4 (29)	0.6 (0.23 - 1.40)	0.31	8 (57)	1.35 (0.68 - 2.52)	0.51
SAE1	11 (27.5)	6 (55)	1.00 (0.48 - 1.71)	>0.99	1 (9)	0.33 (0.05 - 1.61)	0.4	2 (18)	0.88 (0.22 - 3.10)	>0.99	3 (27)	0.68 (0.23 - 1.66)	0.7	6 (55)	1.22 (0.57 - 2.25)	0.73
Fibrillarin	10 (25)	3 (30)	0.51 (0.18 - 1.12)	0.16	1 (10)	0.37 (0.06 - 1.80)	0.4	2 (20)	1.00 (0.25 - 3.46)	>0.99	5 (50)	1.39 (0.58 - 2.95)	0.47	6 (60)	1.38 (0.66 - 2.52)	0.47
PM75	10 (25)	6 (60)	1.10 (0.54 - 1.84)	>0.99	1 (10)	0.37 (0.06 - 1.80)	0.4	2 (20)	1.00 (0.25 - 3.50)	>0.99	4 (40)	1.00 (0.38 - 2.22)	>0.99	**8 (80)**	**2.18 (1.17 - 3.85)**	**0.03**
Ku	9 (22.5)	7 (78)	1.46 (0.80 - 2.29)	0.26	4 (44)	2.76 (0.91 - 7.58)	0.17	2 (22)	1.15 (0.28 to 3.90)	>0.99	4 (44)	1.60 (0.63 - 3.29)	0.4	3 (33)	0.65 (0.22 - 1.43)	0.46
PM100	9 (22.5)	7 (78)	1.46 (0.80 - 2.29	0.26	2 (22)	0.98 (0.25 - 3.21)	>0.99	2 (22)	1.15 (0.28 - 3.90)	>0.99	5 (56)	1.60 (0.68 - 3.34)	0.43	6 (67)	1.59 (0.77 - 2.82)	0.26
Mi-2b	8 (20)	5 (63)	1.17 (0.52 - 1.85)	>0.99	3 (38)	2.00 (0.61 - 5.58)	0.35	**4 (50)**	**4.00 (1.25 - 11.75)**	**0.04**	2 (25)	0.67 (0.18 - 1.78)	0.68	5 (63)	1.43 (0.65 - 2.56)	0.44
CN-1A	7 (17.5)	5 (71)	1.28 (0.61 - 2.03)	0.68	1 (14)	0.59 (0.10 - 2.61)	>0.99	2 (29)	1.57 (0.39 - 5.11)	0.61	3 (43)	1.09 (0.37 - 2.45)	>0.99	5 (71)	1.68 (0.78 - 2.92)	0.23
SRP	7 (17.5)	6 (86)	1.57 (0.84 - 2.37)	0.21	1 (14)	0.59 (0.10 - 2.61)	>0.99	1 (14)	0.67 (0.11 - 3.06)	>0.99	4 (57)	1.93 (0.78 - 3.81)	0.19	4 (57)	1.26 (0.51 - 2.32)	0.69
NXP2	5 (12.5)	4 (80)	1.40 (0.63 - 2.13)	0.63	1 (20)	0.87 (0.15 - 3.50)	>0.99	1 (20)	1.00 (0.17 - 4.14)	>0.99	1 (20)	0.46 (0.08 - 1.66)	0.63	4 (80)	1.87 (0.82 - 3.10)	0.17

Disclosure: K. Kruzer, None; **R. Marangoni**, None; **I. Heckler**, None; **A. Elhage**, None; **V. John**, None; **M. Hinchcliff**, None; **M. Carns**, None; **K. Aren**, None; **A. Wielgosz**, None; **M. Nuzzo**, None; **I. Venkataraman**, None; **B. Korman**, None.

Abstract Number: 1378

Presence of Anti-RNA Polymerase 3 Antibody in Systemic Sclerosis, Renal Disease, Malignancy and ILD from a Single Academic Center Cohort

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Clinical and laboratory characteristics of patients with RNApol3 positivity. Descriptive statistics used for age and gender are Mean(SD) and Number(%)

	Characteristics	Yes	No	p-value
Systemic Sclerosis		52	80	
	Age	54.4 (12.8)	52.3 (18.2)	0.432
	Female	43 (82.7%)	55 (68.8%)	0.103
	RNAPol3			<0.001 *
	-Mean (SD)	73.6 (48)	35.1 (19.6)	
	-Median (IQR)	56 (85)	29 (19.5)	
	-Range	(21, 178)	(20, 127)	
Renal Insufficiency		19	113	
	Age	59.8 (14.1)	52 (16.4)	0.039 *
	Female	13 (68.4%)	85 (75.2%)	0.574
	RNAPol3			0.037 *
	-Mean (SD)	73 (49.8)	46.4 (35.2)	
	-Median (IQR)	54 (84)	32 (25)	
	-Range	(21, 178)	(20, 162)	
Malignancy		12	120	
	Age	63 (12.6)	52.2 (16.3)	0.015 *
	Female	8 (66.7%)	90 (75%)	0.505
	RNAPol3			0.511
	-Mean (SD)	52 (42.3)	50.1 (38.3)	
	-Median (IQR)	31.5 (48)	33.5 (30.5)	
	-Range	(20, 127)	(20, 178)	
Interstitial Lung Disease		47	85	
	Age	59.9 (15.1)	49.4 (15.7)	<0.001 *
	Female	30 (63.8%)	68 (80%)	0.061
	RNAPol3			0.404
	-Mean (SD)	53.1 (39)	48.7 (38.4)	
	-Median (IQR)	34 (41)	33 (28)	
	-Range	(20, 162)	(20, 178)	

*Statistically significant, SD = Standard Deviation, IQR = Interquartile Range

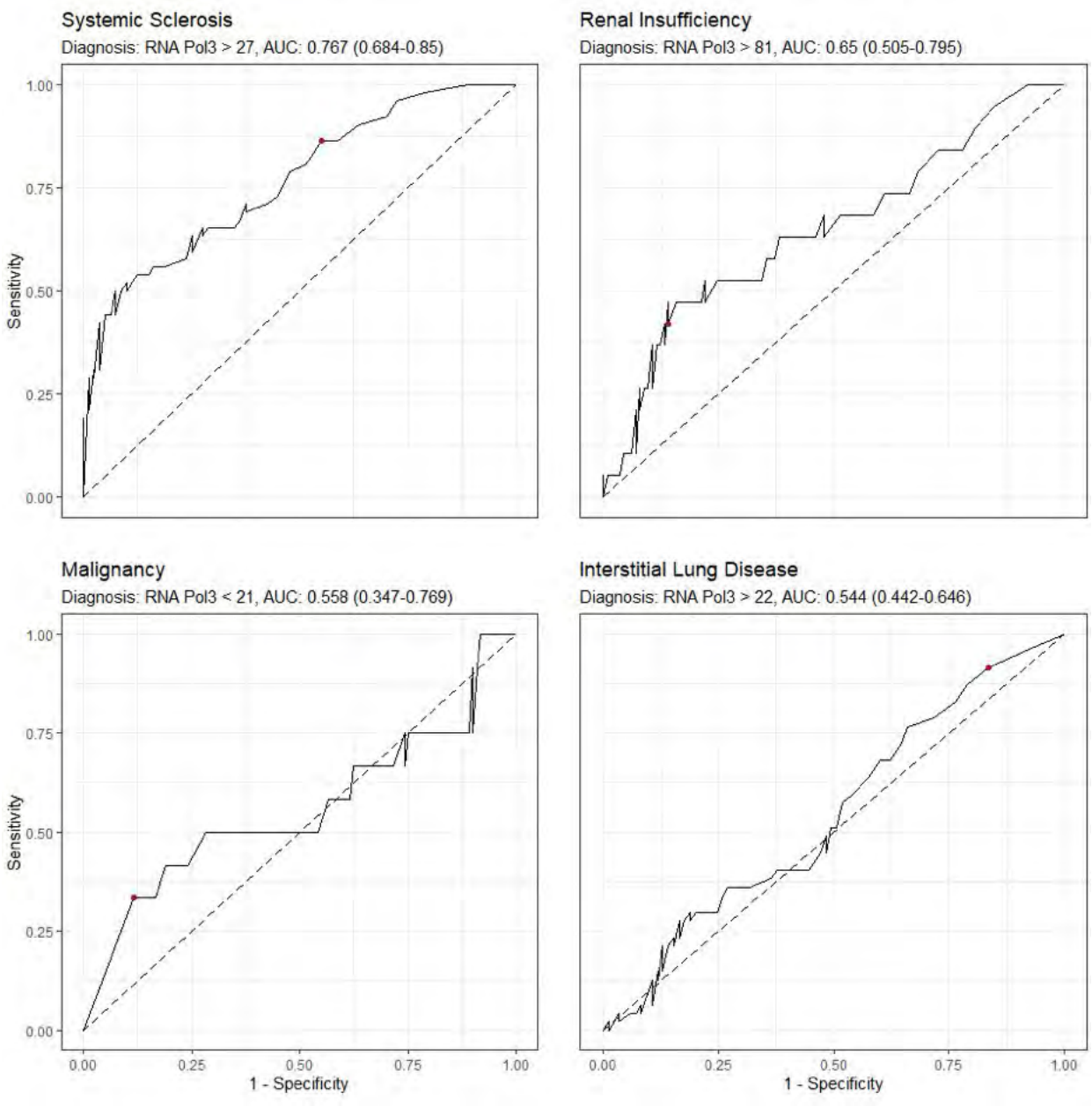

Figure 1. ROC curves and AUCs with 95% CIs (DeLong method). The red dots refer to the false positive rate (FPR) and true positive rate (TPR) of the optimal cutpoint.

Background/Purpose: Autoantibodies are included in the disease classification criteria for systemic sclerosis (SSc). Our group previously reported the level of topoisomerase autoantibody as an important factor for disease classification (Tebo, et al, J. Rheumatology, 46(4) 440-442, 2019). This project analyzed the level of anti-RNA polymerase 3 (RNApol3) antibodies in a cohort of patients assessed for autoimmune disease at a large academic institution.

Methods: 1555 patients were assessed for autoimmune disease under IRB #00029507. RNApol3 antibody positivity (≥20 units) was detected in 132 patients. Two investigators manually reviewed the clinical records for these patients and recorded age, sex, disease classification and disease features. The statistical hypothesis testing methods for age, gender, and RNApol3 are Student's t-test, Fisher's exact test and Wilcoxon rank-sum test, respectively.

Results: Among the 132 patients with a positive RNApol3 antibody, 80 did not meet classification criteria for SSc at the time of the assessment (Table 1). The 52 patients that did meet criteria for SSc had a higher level of RNApol3 antibody, with an optimal cut-off level of 27 units (Figure 1). Age and sex were not significantly different in the two groups of RNApol3 antibody positive patients with and without SSc. In the SSc patient population, age and RNApol3 level >81 units was significantly correlated with the presence of renal insufficiency (Figure 1). The presence of malignancy and ILD was significantly correlated to age but not level of RNApol3 antibody.

Conclusion: Our study supports that the level RNApol3 antibody may be important in classification criteria for SSc. Similarly, in the SSc cohort of patients with a positive RNApol3 antibody, the level may correlate with renal insufficiency. Our study did not find that the level of RNApol3 antibody correlated with ILD or malignancy.

Disclosure: M. Kirkpatrick, None; **J. Lee**, None; **A. Tebo**, None; **H. Li**, None; **y. zhang**, None; **T. Frech**, None.

Abstract Number: 1379

Serum Levels of the Soluble Receptor for Advanced Glycation Endproducts Are Prospectively Associated with Pulmonary Arterial Hypertension in Systemic Sclerosis

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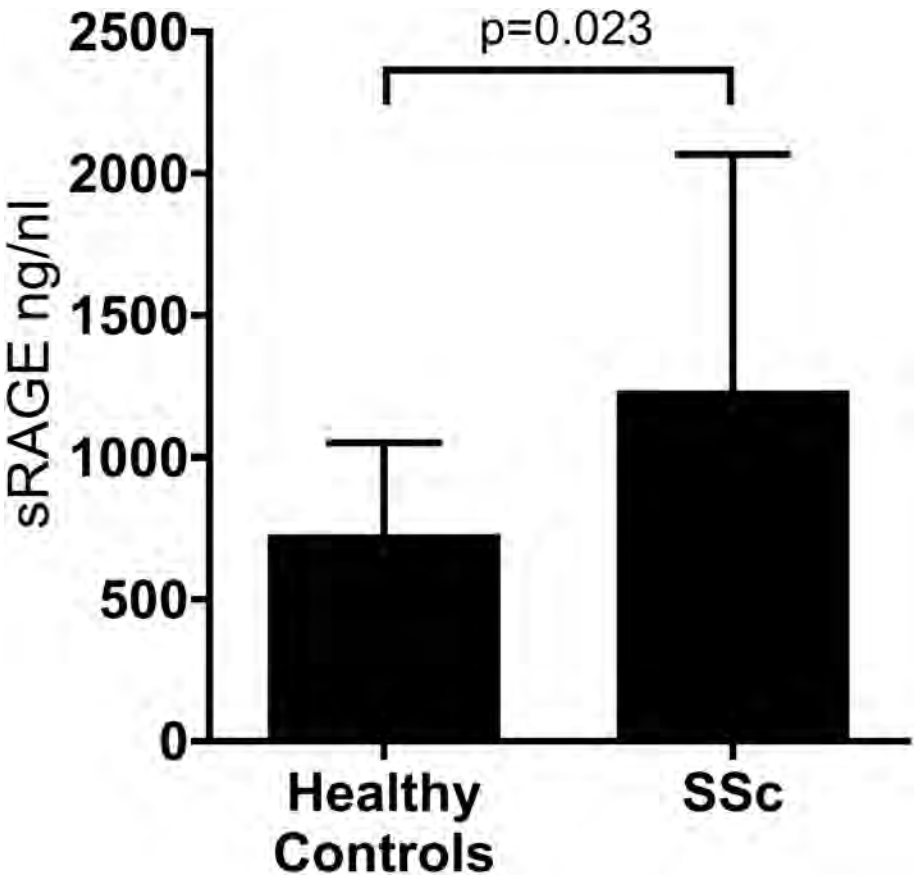

Figure 1. Serum sRAGE levels in patients with SSc compared with age- and sex matched healthy controls.

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) and pulmonary arterial hypertension (PAH) are the leading causes of death in Systemic Sclerosis (SSc). Markers for early detection of these pulmonary complications are urgently needed. The receptor for advanced glycation endproducts (RAGE) is highly expressed in lung tissue. RAGE is involved in cell-matrix adhesion, proliferation and migration of alveolar epithelial cells, and remodeling of pulmonary vasculature. Therefore, we aimed to investigate soluble RAGE (sRAGE) in its association with current and future incidence of SSc-related pulmonary complications.

Methods: In a case-control study, sRAGE levels in 20 patient with SSc (age 51 (44-58) years, 13 female, disease duration since first non-RP 2 (1-8) years, 50% lung involvement, 40% gastrointestinal involvement) were compared with 20 age- and sex matched healthy controls (age 52 (45-62) years, 14 female). Subsequently, sRAGE was measured in an independent retrospective cohort of 188 patients with SSc (64 years (55-72), 145 female, 60% ACA positive, 89%

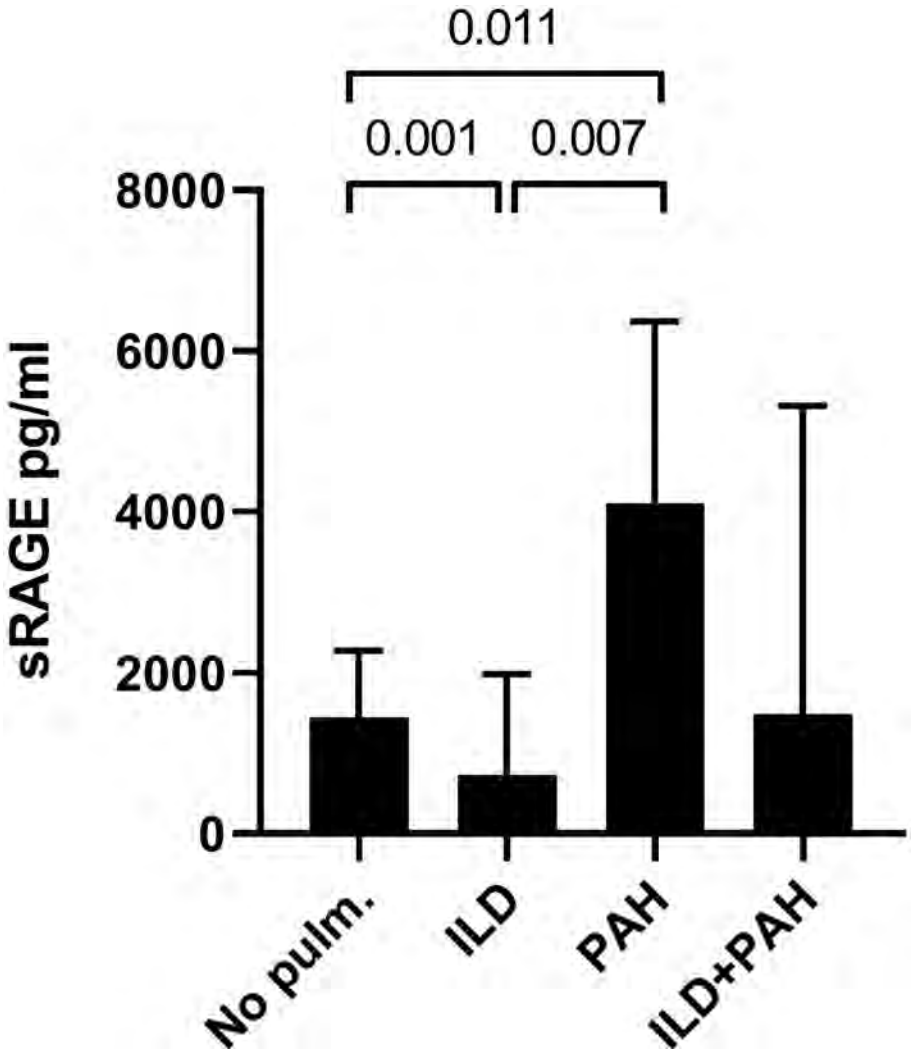

Figure 2. Serum sRAGE levels in patients with SSc in a retrospective cohort. Patients are divided into group of baseline presence of pulmonary complications. No pulm. indicates that ILD and PAH were not present clinically. ILD+PAH indicated that these patients had ILD as wel as PAH at baseline.

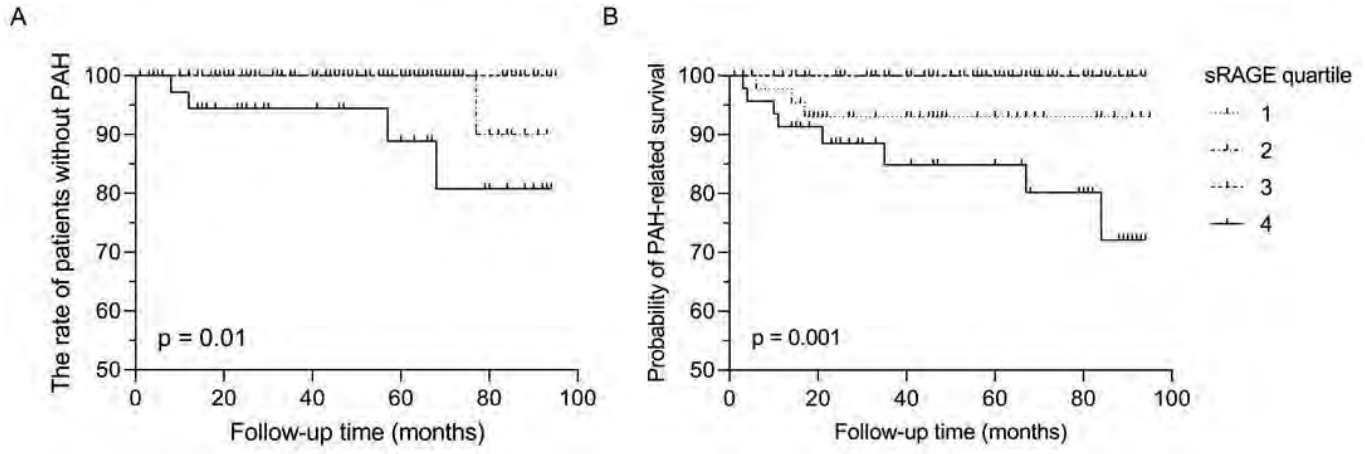

Figure 3. Kaplan-Meier survical curves of sRAGE quartiles. Fig 3a shows the association of sRAGE with the delepoment of SSc-PAH in those without pulmonary involvement at baseline. Fig 3b shows the association of sRAGE with mortality related to PAH. P value was calculated by log-rank test.

limited SSc, 83% sclerodactyly, 53% history of pitting scars or digital ulcers, 74% telangiectasia, 36% calcinosis cutis, 68% gastrointestinal involvement) who were followed for the long-term occurrence of pulmonary events and mortality. Levels of sRAGE were measured by an enzyme-linked immunosorbent assay in serum.

Results: Serum sRAGE levels were significantly higher in patients with SSc compared with controls (Figure 1). In the second cohort, levels of sRAGE were significantly lower (median 735.0 pg/ml [IQR 525.5-1988.5], p = 0.001) in SSc-ILD (n=41) and higher in SSc-PAH (n=12; 4099.0 pg/ml [936.3-6365.3], p = 0.011) compared to patients without pulmonary involvement at baseline (n=124; 1444.5 pg/ml [966.8-2276.0]). sRAGE levels in patients who had ILD as wel as PAH at baseline (n=11) did not differ significantly from those without pulmonary involvement (Figure 2). Regression analyses revealed that sRAGE levels were positively associated with the presence of SSc-PAH ($p < 0.001$), ACA serology ($p < 0.001$), and sclerodactyly ($p = 0.017$), independent of age, gender, ILD, COPD, use of vasodilators, or immunosuppression. Lung involvement developed in 13% (4% PAH after median time of 57 (10-73) months and 9% ILD after median time of 31 (15-57) months) of the patients without baseline lung involvement. sRAGE levels > 4th quartile were associated with the incidence of PAH (log-rank p = 0.01, Figure 3a) and PAH-related mortality (p = 0.001,Figure 3b). However, low sRAGE levels were not associated with ILD occurrence (p = 0.713) or ILD-specific mortality.

Conclusion: This is the first study to demonstrate that serum sRAGE levels are increased in patients with SSc, with significantly lower levels in SSc-ILD and higher levels in SSc-PAH. The association with PAH was independent of potential confounders. Importantly, high sRAGE levels in patients without baseline lung involvement were prospectively associated with the incidence of PAH and PAH-related mortality in SSc, potentially indicating it's role as a predictor for SSc-PAH and a putative future therapeutic target for early interventions.

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Abstract Number: 1380

Quality of Life in Patients with Scleroderma Associated Calcinosis Cutis: A Cross-Sectional Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Calcinosis cutis (CC) can commonly affect patients with systemic sclerosis (SSc), which is often painful, resulting in functional impairment and morbidity. A radiographic scoring system called SCTC (Scleroderma Clinical Trials Consortium) hand score[1] was developed, which assesses the severity of hand calcinosis in patients with SSc. We aimed to use this scoring system and quality of life measures via patient-reported outcomes (PRO) to assess hand calcinosis in patients with SSc.

Methods: We screened 1104 adult patient charts for diagnosis of SSc and CC based on ICD-10 codes. Diagnosis of SSc was confirmed as per 2013 ACR/EULAR classification criteria, whereas the diagnosis of CC was established as per clinical diagnosis, radiographic evidence, or biopsy. Patients with an overlap syndrome were excluded. Data on patient demographics, serology, and clinical manifestations were collected. SCTC hand score was calculated on patients with available hand radiographs. Patients were invited to participate in a survey utilizing validated, SSc-specific PRO tools. The survey questionnaire included standardized tools such as pain visual analog scale, Scleroderma Health Assessment Questionnaire Disability Index (S-HAQ-DI), Mawdsley Calcinosis Questionnaire (MCQ), and Cochin Hand Function Scale (CHFS). Each survey computed a total score for each PRO tool.

Results: Our cohort included 19 patients with SSc and CC, of which 17 patients had CC in their fingers; 17 patients had hand radiographs available from which SCTC hand scores were calculated. Baseline demographics, disease manifestations, and serology are shown in Table 1. Means, medians, and standard deviations for total scores for each PRO tool were computed, and each total score was regressed against the patient's SCTC Hand Score, the statistical summary of which is shown in Table 2. In the case of each PRO tool, the total score for a single patient with an SCTC Hand Score of 755 was an extremely influential response. Regressions were run with and without this patient. There were no significant correlations ($P < .05$) between any of the total scores and SCTC Hand Scores using data from all patients. However, when the influential data point was removed, there was a significant correlation between SCTC Hand Scores and S-HAQ-DI and CHFS total scores. A significant correlation was also found between SCTC Hand Scores and the number of calcinotic digital ulcers. These correlations are shown in Figure 1.

Conclusion: Our study shows a significant correlation between SCTC hand scores and S-HAQ-DI, CHFS, and the number of calcinotic digital ulcers. A higher SCTC hand score may predict a higher likelihood of developing calcinotic ulcers. No significant correlation between SCTC hand scores and MCQ could relate to non-accountability for psychological aspects of CC in SCTC hand scores, highlighting the limitation of using SCTC hand scores alone to assess the quality of life in SSc patients with CC.

Table 1. Baseline demographics, disease manifestations and serology

	Total (N=19)
Gender	
Female	17 (89.5)
Male	2 (10.5)
Race	
Caucasian	15 (78.9)
African American	1 (5.3)
Hispanic	1 (5.3)
Other	2 (10.5)
Serology	
Anti-Scl 70 antibody	2 (10.5)
Anti-centromere antibody	4 (21.1)
RNA polymerase III antibody	6 (31.6)
Anti PM-Scl antibody	2 (10.5)
Other	5 (26.3)
Type of Systemic Sclerosis (SSc)	
Limited	14 (73.7)
Diffuse	5 (26.3)
Onset	
Age at diagnosis of SSc	48.8±12.6
Age at onset of Raynaud's	44.9±12.3
Clinical manifestations	
Sclerodactyly	18 (94.7)
Raynaud's phenomenon	19 (100.0)
Soft tissue contractures	8 (42.1)
Telangiectasias	15 (78.9)
Digital ulcers/ pitting	16 (84.2)
Acro osteolysis	5 (26.3)
Arthralgias	19 (100.0)
Swelling of extremities	6 (31.6)
Anatomical location of calcinosis	
Hands	11 (57.9)
Fingers	17 (89.5)
Feet	5 (26.3)
Trunk	2 (10.5)
Extremity	9 (47.4)
Multiple sites	5 (26.3)
Sequalae of calcinosis	
Infection from calcinosis site	10 (52.6)
Extruding material from calcinosis	15 (78.9)
Mode of diagnosis of calcinosis	
Visual appearance	16 (84.2)
Imaging	19 (100.0)
Biopsy	4 (21.5)
Prior treatment of calcinosis	
Sodium thiosulfate	4 (21.1)
Calcium channel blocker	12 (63.2)
Colchicine	3 (15.8)
Minocycline	1 (5.3)
IVIG	2 (10.5)
Surgery	8 (42.1)
Quantification of hand calcinosis	
SCTC hand score	142.1±200.6

Reference

1. Chung L, Valenzuela A, Fiorentino D, et al. Validation of a Novel Radiographic Scoring System for Calcinosis Affecting the Hands of Patients with Systemic Sclerosis. Arthritis Care Res (Hoboken). 2014 Aug 22

Table 2. Patient-reported outcomes

Table 2: Statistical Summary for Total Scores *					
	Summary Statistics			Regression Summary**	
Total Scores	Mean	Median	Std. Dev.	P-Value	R-Square
S-HAQ-DI	0.7	0.4	0.6	.024	.31
Mawdsley Calcinosis Questionnaire	67.5	52	42.1	.13	.16
Cochin Hand Function Scale	37.4	30	19.8	.003	.48

*This statistical summary is after excluding data point of single patient with SCTC hand score of 755

**Total scores from each questionnaire/scale were regressed against patient's SCTC Hand score

S-HAQ-DI: Scleroderma Health Assessment Questionnaire Disability Index

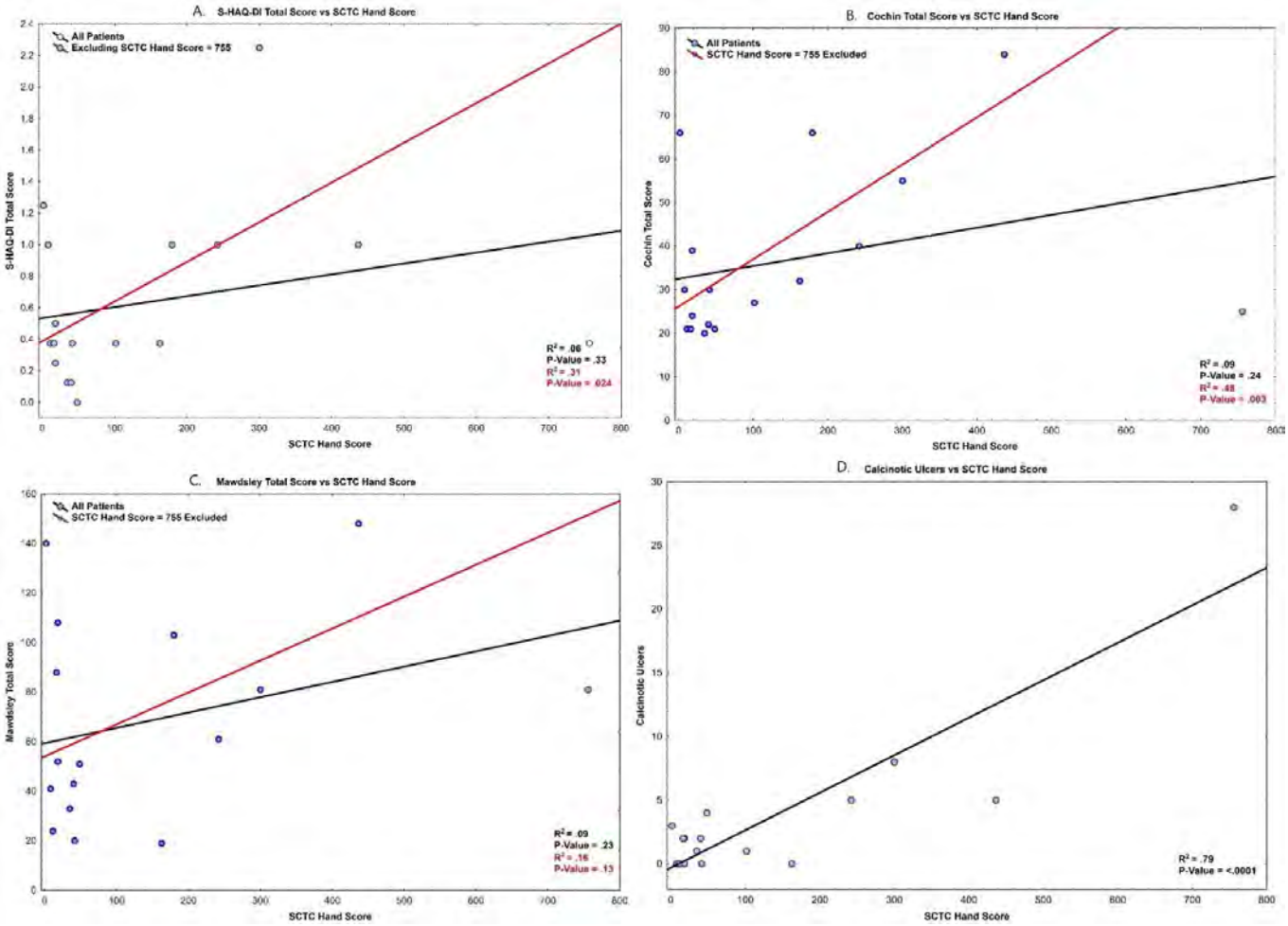

Figure 1.

Disclosure: A. Patel, None; **M. Grewal**, None; **R. Butler**, None; **S. Chatterjee**, None.

Abstract Number: 1381

Chemokines CCL2 and CCL17 as Potential Serum Biomarkers for Interstitial Lung Disease in Systemic Sclerosis

Imon Barua[1], Håvard Fretheim[2], Hilde Jenssen Bjørkekjær[3], Henriette Didriksen[4], Oyvind Midtvedt[2], Trond Mogens AAløkken[2], Torhild Garen[5], Oyvind Molberg[6], John Belperio[7] and Anna-Maria Hoffmann-Vold[1], [1]Department of Rheumatology, Oslo University Hospital, Oslo, Norway, [2]Oslo University Hospital, Oslo, Norway, [3]Department of Rheumatology, Sørlandet sykehus HF, Kristiansand, Norway, [4]Oslo University Hospital, Moss, Norway, [5]Department of Rheumatology, Oslo University Hospital, Oslo, Nepal, [6]Oslo University Hospital, Oslo, Nepal, [7]University of California Los Angeles Interstitial Lung Disease Center, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) carries high risk for progressive interstitial lung disease (ILD). Several anti-inflammatory therapies have been used to treat SSc-ILD and recently the first antifibrotic therapy has been approved. Personalized treatment strategies are largely missing to date and it is unclear, which patients to treat with which treatment approach. The two chemokines, CCL2 (MCP-1) and CCL17 (TARC) have been shown to be markers of inflammation and fibrosis, respectively. The aim of this study was to examine associations between ILD characteristics and serum levels of CCL2 and CCL17 in a large and unselected SSc cohort with complete data sets on pulmonary function and lung fibrosis extent on HRCT.

Methods: Sera from the prospective Oslo University Hospital SSc cohort (n=371) and healthy blood donor controls (HC; n=100) were analyzed for CCL2 and CCL17 by multiplex assays. CCL2 and CCL17 levels were defined as high or low using 95% CI in HC sera as cut-off values. Paired pulmonary function tests and HRCT images were obtained at baseline and follow-up. All patients in the SSc cohort met the 2013 ACR/EULAR classification criteria. ILD was diagnosed on HRCT and categorized by the extent of lung fibrosis as limited (1-10%) or extensive (>10%) ILD by semi-quantitative assessment. Descriptive statistics were applied.

Results: Of all 371 patients, 212 (57%) had available levels for circulating CCL2 and CCL17. These levels were significantly increased in SSc compared to HC (Figure). High levels of CCL17 (>700 pg/ml) and CCL2 (>1000pg/ml) were identified in 43/254 (17%) and 84/471 (18%) of the SSc patients, respectively (Table). High levels of both CCL17 and CCL2 were associated with lower FVC at baseline and a higher extent of lung fibrosis on HRCT (Table). Of those with high CCL2 and CCL17, 67% had extensive lung fibrosis on HRCT. Categorization of ILD into no ILD, limited or extensive ILD showed a numerical association between high CCL17 levels and the extent of fibrosis (Table).

Conclusion: In this explorative SSc cohort study, high levels of both CCL2 and CCL17 were associated with more severe ILD, potentially mirroring ongoing inflammatory and fibrotic processes, which may have an implication on treatment choices for SSc-ILD.

Table 1. Demographics and clinical findings in the SSc cohort stratified by level of CCL2 and CCL17

	All patients (N=371)	Low CCL2 and CCL17	High CCL17	High CCL2	High CCL2 and CCL17
SSc patients, n (%)	371	94 (44.3)	75 (35.4)	34 (16)	9 (4.2)
Age at onset, years (SD)	51 (15.5)	48 (15.7)	55 (14.1)	48 (13.5)	50 (14.8)
Male, n (%)	59(15.9)	16(17.0)	16(21.3)	4(11.8)	2(22.2)
Anti-centromere Ab, n (%)	212(57.1)	53 (56.3)	26 (34.6)	16 (47.0)	2 (22.2)
Anti-topoisomerase antibodies, n (%)	211(56,9)	10 (10.6)	17 (22.9)	10 (29.4)	1 (11.1)
Baseline FVC, % (SD)	95.4 (19.7)	98.9 (2.0)	93.8 (2.4)	90.5 (3.7)	77.1 (4.6)
Baseline DLCO, % (SD)	65.0(19.3)	67.3(19.7)	61.4(17.8)	64.3(19.6)	45.7(18.4)
mRSS (SD)	206(55.5)	7.2(7.2)	13.3(11.6)	9.6(8.9)	11.44(12.4)
Digital ulcers (%)	205(55.3)	44 (46.8)	30 (40)	21 (61.7)	5 (55.6)
Lung fibrosis on HRCT, n (%)	206(55.5)	91(44.2)	72(35.0)	34(16.5)	9(4.4)
No fibrosis, n (%)	84(40.8)	49 (53.8)	25 (34.7)	10 (29.4)	0 (0)
<10% fibrosis, n (%)	76(36.9)	27 (29.7)	29 (40.3)	17 (50.0)	3 (33.3)
>10%fibrosis, n (%)	46(22.9)	15 (16.5)	18 (25)	7 (20.6)	6 (66.7)

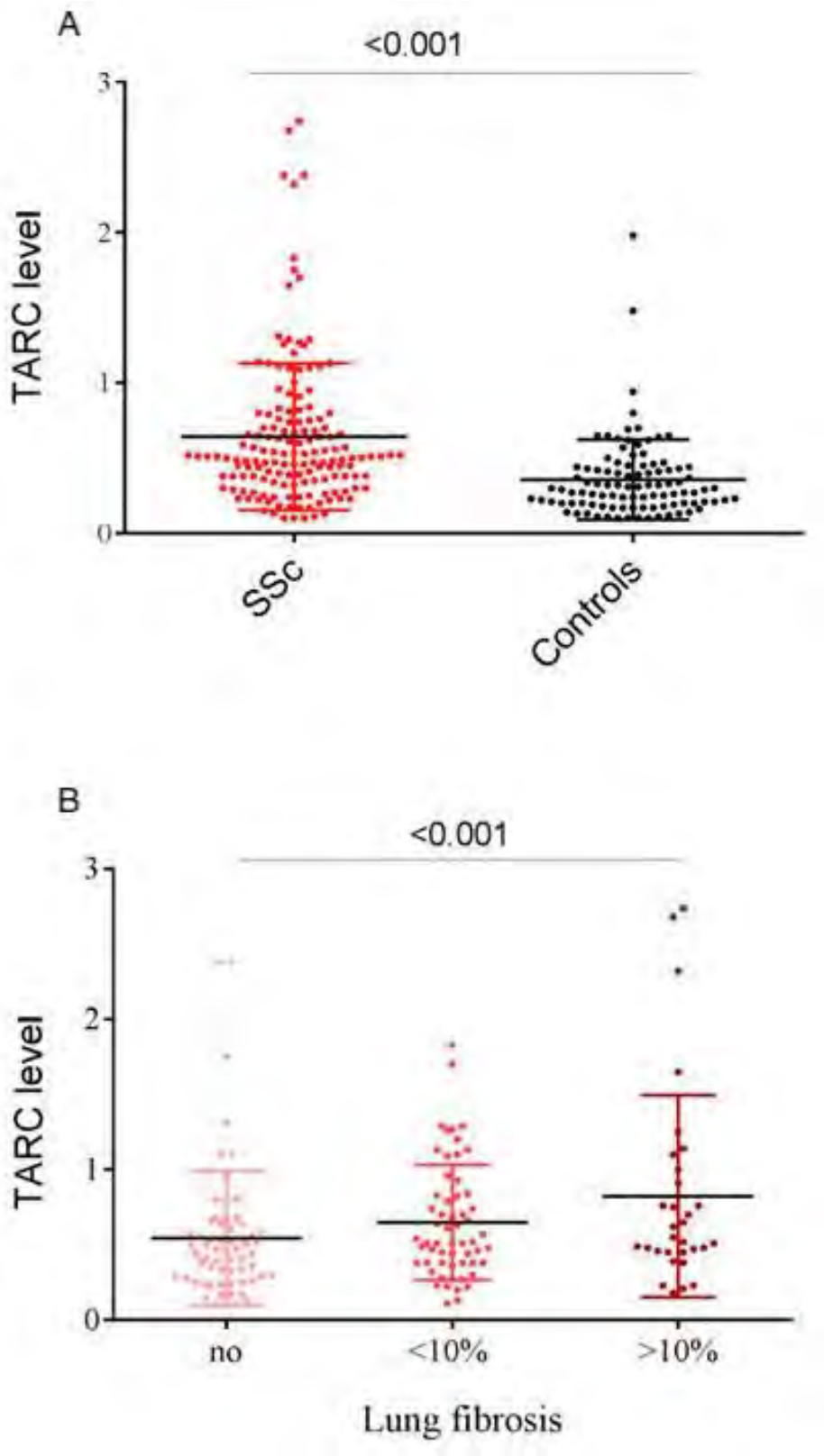

Figure 1. CCL17(TARC) levels and extent of lung fibrosis.

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Abstract Number: 1382

Survey on Treatment Practices in Subclinical Interstitial Lung Disease in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of mortality in systemic sclerosis (SSc). Early detection and treatment of SSc-ILD may lead to improved outcomes, however no formal recommendation exists to guide management in subclinical SSc-ILD. We undertook an international survey to understand current screening and treatment practices in subclinical SSc-ILD.

Methods: An electronic REDCap survey was distributed to 611 general rheumatologists, 348 national and international SSc experts, 285 respirologists and 15 experts in ILD.

Results: Up until April 8th, 2021, 178 participants responded to the survey, including 131 (76%) general rheumatologists and 32 (19%) respirologists. The estimated response rate was 23% among general rheumatologists, 25% among SSc experts, 8% among respirologists and 23% among ILD experts. The majority saw SSc-ILD patients at least monthly (79%) and had been in practice for at least 5 years (80%).

Overall, 59% of respondents reported routinely ordering HRCTs in all newly diagnosed SSc patients, whereas 40% ordered HRCTs only in the presence of symptoms, crackles or abnormal pulmonary function tests or chest X-ray (35%) and/or in the presence of risk factors for severe or progressive ILD (17%). There was significant regional heterogeneity in screening practices, with HRCTs being routinely ordered by 48% (40/84) in North America, 83% (29/35) in Europe, 70% (7/10) in Asia, 40% (2/5) in Australia and 100% (4/4) in Latin America.

Six-minute walk tests (6MWT) were ordered by 34% of respondents in the baseline evaluation of subclinical SSc-ILD, and more frequently by respirologists (72%) than general rheumatologists (24%). 6MWT were more rarely used in the routine follow-up of SSc-ILD (33%), with most (57%) respondents using 6MWT only if there was disease progression. Factors that influenced 6MWT use included access/availability, symptoms, pulmonary function tests and extent of ILD on CT, risk factors for progressive ILD, suspicion of hypoxemia on ambulation or concomitant pulmonary hypertension, and presence of other SSc manifestations that could affect test validity (including severe Raynaud, skin or musculoskeletal disease).

Nearly half (47%) of participants responded that they would not treat subclinical lung disease, 17% would treat and 36% responded that it would depend. Factors that would influence their decision included risk factors for progressive lung disease, other SSc manifestations requiring treatment (e.g. progressive/diffuse skin disease, myositis), disease trajectory over close follow-up, comorbidities/life expectancy, discussions with the treating respirologist, and shared decision-making with the patient regarding risks and benefits. The majority (75%) of respirologists would not treat subclinical lung disease.

Conclusion: There is considerable variability in screening and treatment practices in subclinical SSc-ILD. Further studies are required to define the impact of screening and treatment strategies on clinical outcomes in subclinical SSc-ILD, including controlled trials.

Disclosure: S. Hoa, None; **M. Baron**, None; **M. Hudson**, None.

Abstract Number: 1383

Prediction of Digital Ulcers in Patients with Systemic Sclerosis Based on the Use of Platelet Inhibitors and Other Parameters - A EUSTAR Study on Derivation and Validation of a Clinical Prediction Model

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Digital ulcers (DUs) affect half of the patients with systemic sclerosis (SSc) and can be complicated by gangrene and amputation. Platelets are known to be activated in SSc, therefore, platelet inhibitors might represent a therapeutic option in the management of DUs. However, until now, there is no clinical study to assess the importance of platelet inhibitors in the occurrence of DUs in patients with SSc. The aim of the study was to develop and validate a prediction model for the occurrence of DUs in patients with SSc based on platelet inhibitors and other parameters.

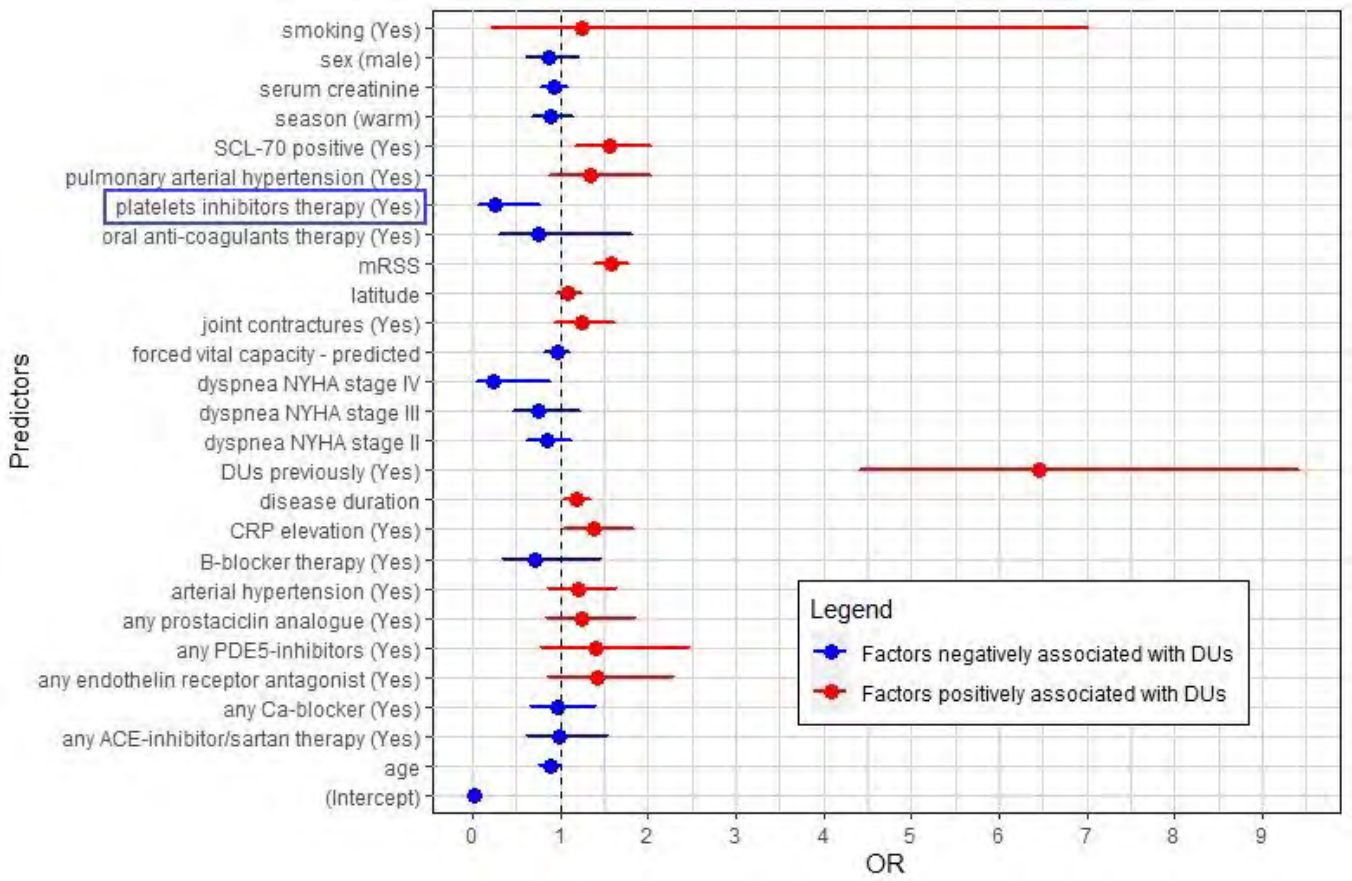

Figure 1. Forest plot displaying the OR of the logistic classification model.

Methods: This study used prospectively collected data from the European Scleroderma Trials and Research group (EUSTAR) registry. Patients fulfilling the 2013 ACR/EULAR SSc classification criteria with complete longitudinal data on the presence of DUs and platelet inhibitors were included in the analysis. Multiple imputation using a *random forest* algorithm was implemented to handle missing values.

The dataset, containing the information of the last follow-up visit of every patient, was split into a derivation cohort (patients recorded before 2017-01-01 in the EUSTAR registry) and validation cohort (patients recorded after 2017-01-01). To investigate the response for the binary dependent variable of DUs, binary logistic regression was implemented to develop a prediction in the derivation cohort and to validate it using ROC analysis and calibration plots to address discrimination and calibration, respectively.

Results: Of 3,710 patients (14.6% males, 67.8% limited cutaneous SSc, median age 56.97 years, median disease duration 8.94 years), 486 had current DUs at the baseline and 150 were exposed to platelet inhibitors. At the follow-up visit (median follow-up time 1.03 years) 487 had current DUs and 90 remained exposed to platelet inhibitors.

Factors associated with absence or presence of DUs at the next follow-up visit are shown in *figure 1*. This confirmed the risk factors for the presence of DUs identified by previous studies.

The discrimination ability of the model evaluated by ROC curve analysis showed an AUC = 80.8% (95% CI = [78.7% to 83.0%]) for the derivation cohort (2,827 patients) and AUC = 83.4% (95% CI = [80.0% to 86.8%]) for the validation cohort (883 patients), respectively, corresponding to an acceptable discrimination (*figure 2*). The calibration plots revealed an adequate calibration of the model (*figure 3*).

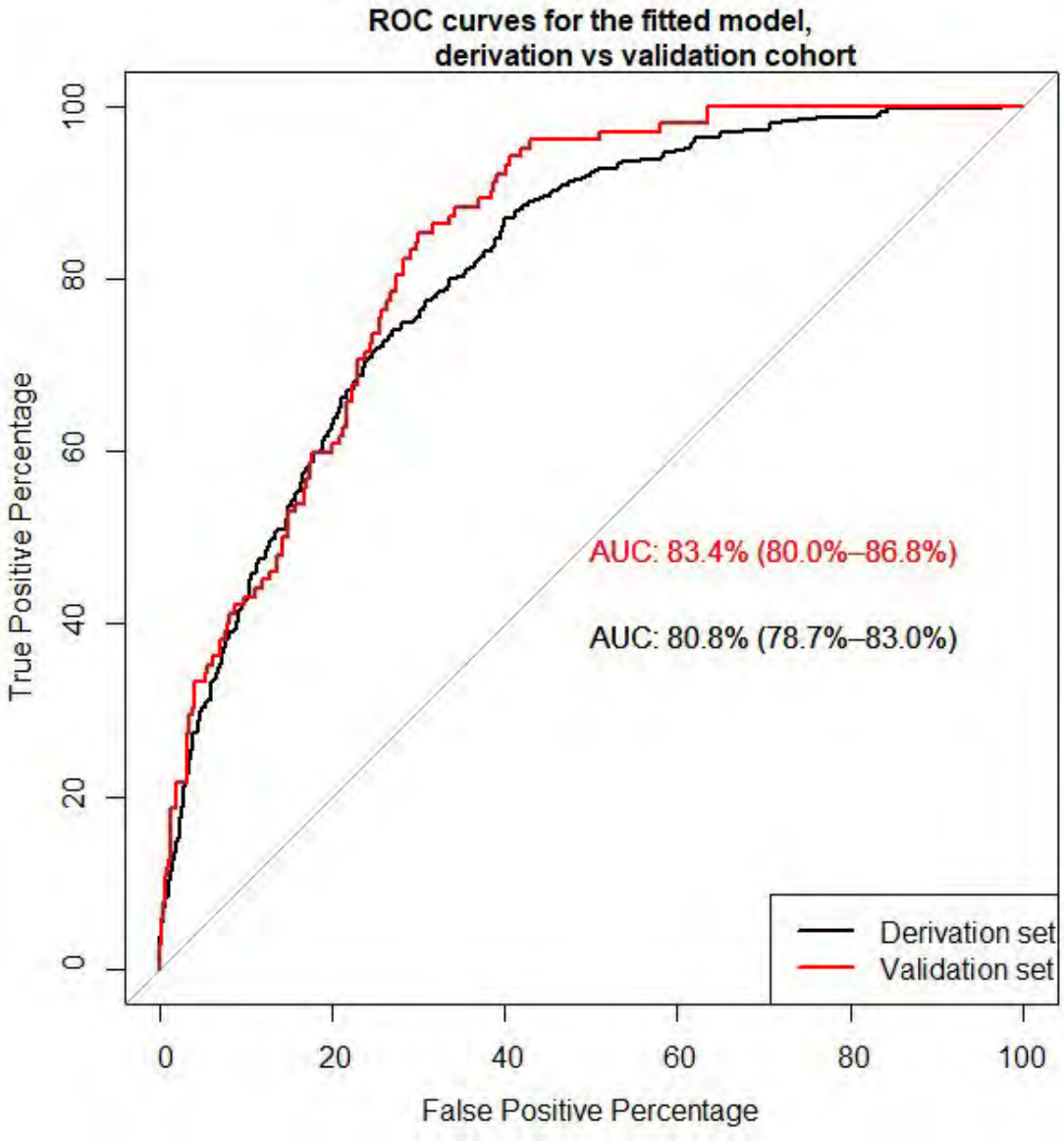

Figure 2. ROC curves displaying the discrimination ability of the fitted model in the derivation and validation cohort, respectively.

Amongst other predictive factors, our model revealed that exposure to platelet inhibitors is associated with a reduced odds ratio of DUs occurrence at the next follow up visit (OR = 0.25, 95%CI [0.07-0.77]).

Conclusion: Our model shows good discrimination and adequate calibration for the difficult task of predicting the occurrence of DUs at a one-year follow up visit. Use of platelet inhibitors was among the factors predicting lower probability of DUs occurrence at follow-up.

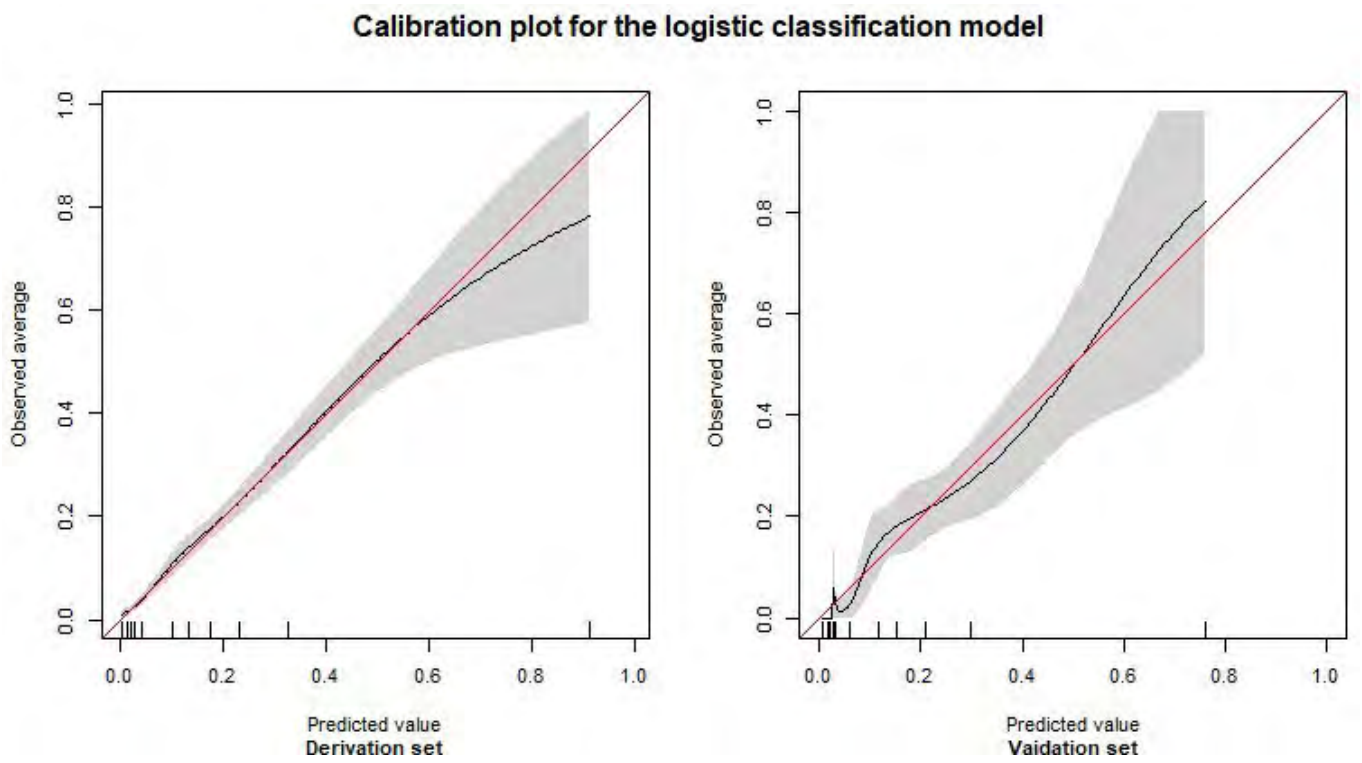

Figure 3. Calibration plots for the logistic classification model - the figure shows the calibration plot of the model in the derivation cohort (left side) and in the validation cohort (right). On the X-axis, the model's predicted probability of the occurrence of DUs is plotted against the observed risk of presence of DUs on the Y-axis (0 = absence of DUs, 1 = presence of DUs). The red line represents perfect prediction, meaning that the predicted risk is exactly the same as the observed risk across the whole range. Ideally, the lines obtained should lie exactly on top of the red line.

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Abstract Number: 1384

A Genomic Meta-Analysis of Clinical Variables and Association with Intrinsic Molecular Subsets in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Four intrinsic molecular subsets (Inflammatory, Fibroproliferative, Limited, Normal-like) have been identified in systemic sclerosis (SSc) that may have different clinical associations. To test this hypothesis we

Table 1. Clinical and Demographic Variables of the Discovery Cohort

Discovery Cohort (n=311)	**Inflammatory** (n=117)	**Fibroproliferative** (n=105)	**Normal-like** (n=85)	**Limited** (n=5)
Age – Mean (SD)	52.92 (11.22)	47.41 (11.06)	49.50 (12.46)	60.6 (4.62)
Sex – no.				
Female	88	66	67	5
Male	16	29	13	0
Race – no.				
White	58	41	35	4
Black	7	13	4	1
Asian	3	2	0	0
Other/Unknown	49	49	46	0
Ethnicity – no.				
Hispanic or Latino	4	6	7	0
Non-Hispanic or Non-Latino	27	18	19	0
Unknown	86	81	58	5
Clinical Subtype – no.				
Diffuse	103	79	50	0
Limited	14	26	34	5

Table 2. Clinical and Demographic Variables of ASSET Validation Cohort

Validation Cohort (n=84)	**Inflammatory** (n=33)	**Fibroproliferative** (n=18)	**Normal-like** (n=33)	**Limited** (n=0)
Age – Mean (SD)	53.21 (10.18)	46.56 (14.96)	51.0 (13.41)	-
Sex – no.				
Female	24	9	29	-
Male	9	9	4	-
Race – no.				
White	32	11	28	-
Black	1	5	1	-
Asian	1	3	2	-
Other/Unknown	0	0	2	-
Ethnicity – no.				-
Hispanic or Latino	3	2	5	-
Non-Hispanic or Non-Latino	30	15	28	-
Unknown/Undisclosed	0	1	0	-
Clinical Subtype – no.				
Diffuse	33	18	33	-
Limited	-	-	-	-

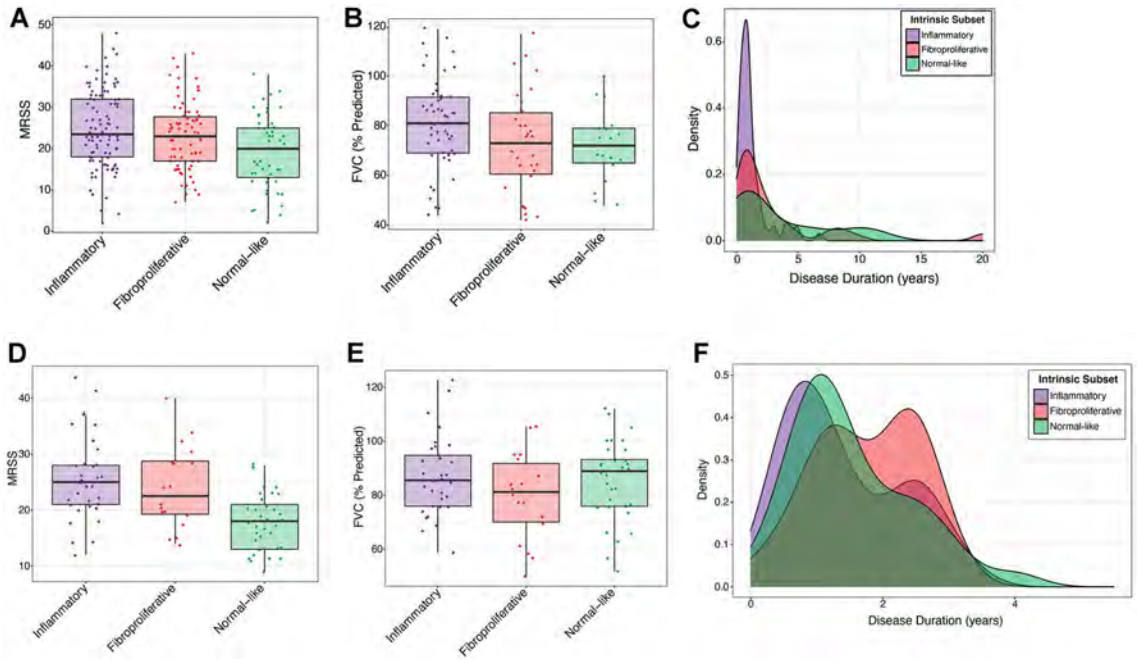

Figure 1. Measures of phenotypic severity in dcSSc patients of the discovery (A-C) and validation cohorts (D-F) stratified by intrinsic subset. Differences in MRSS (A, D), FVC (B, E) and disease duration (C, F) are shown.

investigated associations between baseline clinical demographics and intrinsic subsets in a meta-analysis of 14 gene expression datasets for 395 individuals with SSc.

Methods: Publicly available gene expression data measured in skin for 311 independent SSc patients were classified into the intrinsic molecular subsets using a previously trained machine learning classifier. Data from 84 independent participants from the ASSET trial was used as a validation cohort. Normalized RPKM values from skin were similarly classified into the intrinsic gene expression subsets. Patient clinical and demographic data were collected for each cohort from original publications or from individual investigators. Associations were tested using Fisher's Exact Test and Tukey's pairwise comparisons.

Results: The majority of the SSc patients in this analysis were white (50.74%), female (69.49%), and classified as dcSSc (70.96%). Males were 2.5 - 4x as likely to be fibroproliferative than females in discovery (p=0.0046) and validation cohorts (p=0.015). Females and males were equally likely to be classified as inflammatory, normal-like, or limited. SSc patients who identified as African-American/Black were 2.5x more likely to be classified as fibroproliferative compared to White/Caucasian patients in both discovery (p=0.0378) and validation cohorts (p=0.0062). SSc patients who identify as White or Caucasian were more likely to be classified as inflammatory or normal-like (p=0.0037). Patients sera positive for RNA pol I (p< 0.0001) and RNA pol III (p=0.0001) autoantibodies were enriched in the inflammatory subset, while Scl-70 was enriched in the fibroproliferative subset, but did not reach statistical significance. There were statistically significant differences in modified Rodnan skin score (mRSS). Inflammatory and fibroproliferative subsets had higher average mRSS relative to normal-like (p=0.0027). There was no difference between the average mRSS for inflammatory (avg=24.67) and fibroproliferative (avg=23.13) individuals. Patients in the fibroproliferative and normal-like subsets on average had a trend toward lower %FVC. We identified a statistically significant difference in average disease duration between the inflammatory, fibroproliferative, and normal-like intrinsic subsets (p=8.8E-4). Patients in the inflammatory subset had the shortest disease duration, which was lower than both the fibroproliferative subset (p=0.0073) and the normal-like subset (p=0.0042).

Conclusion: We found multiple significant associations between demographic and clinical variables with intrinsic subsets. By leveraging data from multiple studies, we increased statistical power and validated these associations. These findings identify may have clinical implications for identifying treatments more likely to work in certain SSc populations. This difference in temporal distributions may reflect chronological stages of fibrosis.

Disclosure: J. Franks, None; **D. Toledo**, None; **V. Martyanov**, Celdara Medical LLC, 3; **Y. Wang**, None; **S. Huang**, None; **T. Wood**, Celdara Medical LLC, 2; **C. Spino**, None; **R. Domsic**, None; **M. Hinchcliff**, None; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **M. Whitfield**, Celdara Medical, LLC, 2, 5, 8, 12, Scientific Founder, Bristol Myers Squibb, 2, 5, 6, Acceleron, 2, Corbus Pharmaceuticals, 2, 6, Abbvie, 6, Kadmon, 6.

Abstract Number: 1385

Overall Survival in Patients with Systemic Autoimmune Diseases Following Lung or Heart-Lung Transplantation at a Single High-Volume Academic Transplant Center: A Comparative Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Lung manifestations of systemic autoimmune diseases are a frequent cause of early death. For many patients, current treatments cannot arrest the inexorable progression to end-stage lung disease. Lung transplantation can be life-saving, but many transplant centers withhold this option from patients with systemic autoimmune diseases due to concerns that extrapulmonary manifestations and immune abnormalities could lead to additional post-transplant risks. Additional data on lung transplant experience in patients with systemic autoimmune diseases are needed to clarify risks and benefits in this population.

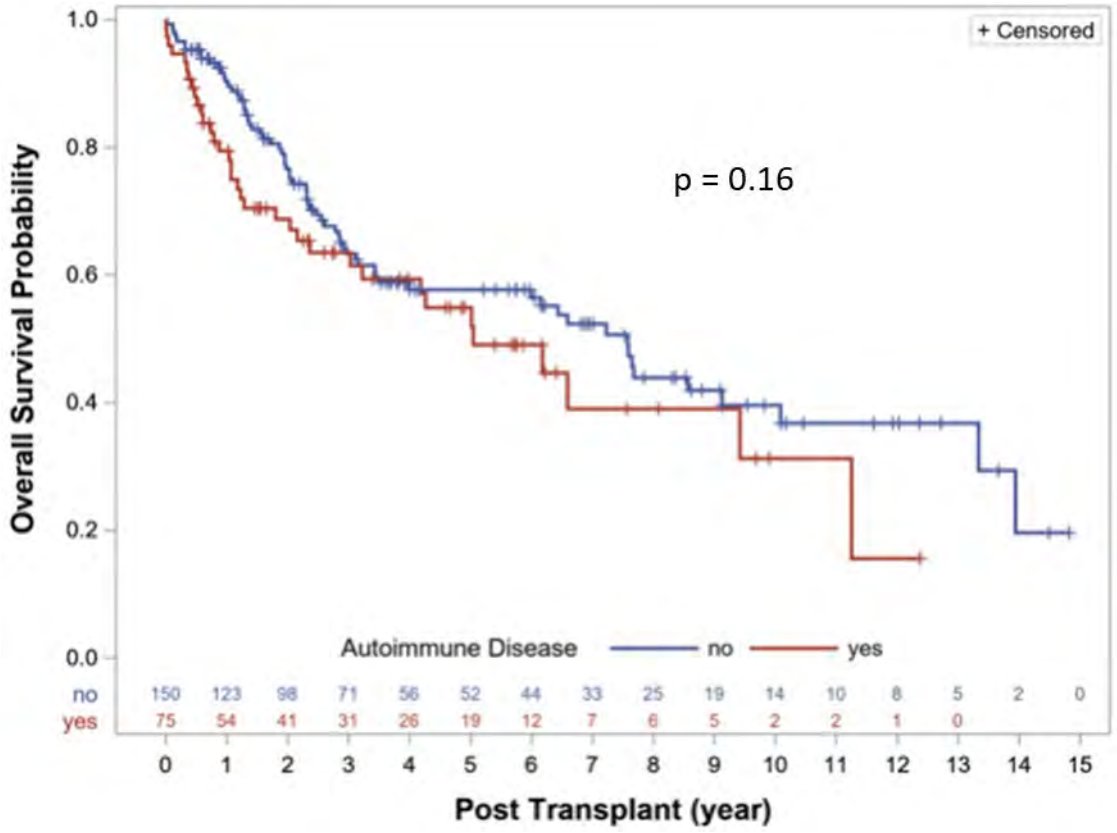
Methods: We conducted a retrospective cohort study of patients undergoing lung or heart-lung transplant at Stanford University between January 1, 2005 and January 1, 2020. Patients whose lung disease was attributed to a systemic autoimmune disease were identified from among this population based on ICD-9 or ICD-10 coding followed by verification that patients fulfilled classification criteria specific to their disease by medical record review. Patients were matched 1:2 to controls without autoimmune diseases according to their age, gender, year of transplantation, indication for transplantation (interstitial lung disease vs. pulmonary hypertension) and type of transplant procedure (single lung, double lung, heart-lung). We compared overall survival in those with and without autoimmune diseases using Kaplan-Meier curves by log-rank test. We used multivariable Cox proportional hazard regression to estimate the hazard ratios (HR) and 95% confidence intervals (CI) for overall survival following transplant accounting for the variables described above.

Population Characteristics	Autoimmune	Non-Autoimmune
Age (average)	55	55
Gender (% Female)	51%	61%
Autoimmune Disease (total)	75	--
Rheumatoid arthritis	17	--
Systemic sclerosis	16	--
Sarcoidosis	15	--
Idiopathic inflammatory myositis	14	--
Sjogren's syndrome	8	--
Mixed connective tissues disease	4	--
Systemic lupus erythematosus	1	--
Transplant Indication		
Interstitial lung disease	52	116
PAH / ILD-PH	23	36
Transplant Procedure		
Single lung transplant	6	14
Double lung transplant	64	134
Heart-lung transplant	5	4

Basic population characteristics of patients who underwent lung transplantation for end-stage lung disease due to their underlying systemic autoimmune disease compared to matching patients without systemic autoimmune diseases

Results: In total, 75 lung or heart-lung transplant patients with systemic autoimmune diseases were identified, including 17 with rheumatoid arthritis, 16 with systemic sclerosis, 15 with sarcoidosis, 14 with idiopathic inflammatory myositis, eight with Sjogren's syndrome, four with mixed connective tissue disease, and one with systemic lupus erythematosus. These patients were matched to 152 patients without autoimmune diseases. One-year and five-year survival was 79.4% and 54.9% in patients with autoimmune diseases and 90.3% and 57.7% in the matched cohort (p=0.16). The hazard ratio for overall survival following transplant favored patients without autoimmune diseases but was not significantly different from those with autoimmune diseases (unadjusted HR 1.29, 95% CI [0.80 – 2.08] p-value 0.31, adjusted HR 1.24, 95% CI [0.71 – 2.18] p=0.45).

Conclusion: Patients with systemic autoimmune disease fared as well after lung or heart-lung transplantation as patients without systemic causes of end-stage lung disease. These data continue to provide support for lung transplantation as a life-saving option for well-qualified patients with systemic autoimmune diseases.



Kaplan-Meier survival curves comparing post-lung transplant survival in patients with systemic autoimmune diseases (red) versus those without (blue)

Disclosure: J. Melehani, None; **S. Li**, None; **J. Mooney**, Genentech/Roche, 2, Boehringer Ingelheim, 2; **L. Chung**, Boerhinger Ingelheim, 1, 5, 6, Genentech, 2, Eicos, 1, Reata, 1.

Abstract Number: 1386

Measurement of TIMP-1 in Pulmonary Vessels May Be a Novel Marker of Reflecting mPAP in CTD-PH

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: CTD is a disease with immune abnormalities which could alter normal cytokine profile. CTD-PH has a different pathogenesis from that of iPAH, and immunosuppressive therapy is effective. These facts suggest that the two PH conditions have different pathologies related to pulmonary artery inflammation. Various cytokine abnormalities have also been reported to be involved in the pathogenesis of CTD-PH. However, the relationship between these cytokine abnormalities and pulmonary artery pressure has not been fully elucidated.

To clarify the relationship between cytokines and mean pulmonary artery pressure by analysis of the cytokine profile in PH patients including CTD-PH. In addition, we will clarify the differences in cytokine profiles between CTD-PH and iPAH.

Methods: Patients who underwent RHC for PH diagnosis at our hospital from 2015 to 2020 years were included in the study. Right heart catheterization and left heart catheterization were tried, and pre- and post-pulmonary sera were collected to measure cytokines. The target cytokines were TIMP-1, MCP-1, IL-17 and IL-21, IL-12p70 and IL-6, which were measured by ELISA (ABCAM UK, Ella simple plex USA). The relationship between the measured cytokine profiles and hemodynamic parameters was compared.

Results: 21 CTD patients (SSc 12 cases, MCTD 7cases, SLE 2 cases) and 13 non-CTD patients were subjected to be analyzed cytokines in pulmonary vessels . As previously reported, there was a positive correlation between serum IL-6 level and mPAP (mean pulmonary arterial pressure) in all our patients, but not observed in CTD patients(Figure1.). Furthermore, serum TIMP-1 level showed a significant correlation with mPAP in all patients. Additionally, this correlation was observed more remarkable in CTD patients compared to non CTD patients (Figure 2.). In addition among CTD patients, serum MCP-1, IL-6, and TIMP-1 level in SSc-PH cases tend to be higher than those in those of non SSc CTD-PH. Serum IL-12p70 and IL-17 level were lower in SSc- PH compared that non SSc CTD-PH. In some CTD cases who were investigated before and after PH treatment, serum IL-17, IL-21, and TIMP-1 level were decreased along with improvement of pulmonary vascular hemodynamics.

Conclusion: The cytokine profile of pulmonary capillaries reflected hemodynamics, the significance of which was different in CTD-PH and iPAH. Measurement of IL-17, IL-21, and TIMP-1 in pulmonary vessels may be useful for diagnosis, monitoring, and evaluation of therapeutic effects in CTD-PH.

Disclosure: S. Nakashima, None; **K. Ishikawa**, None; **K. Ueeda**, None; **T. Kameda**, None; **H. Shimada**, None; **R. Wakiya**, None; **M. mai**, None; **M. Kato**, None; **T. Miyagi**, None; **K. Sugihara**, None; **R. Semba**, None; **M. Mizusaki**, None; **H. Dobashi**, None.

Abstract Number: 1387

Macrovascular Dysfunction and Its Clinical Implication in Systemic Sclerosis

Devender Bairwa[1], Chengappa Kavadichanda[2], sanket Shah[3], Anoop Mathew[1], saikumar dunga[3], Aishwarya Gopal[3], Molly Mary Thabah[1] and VirSingh Negi[1], [1]Jawaharlal Institute of Postgraduate Medical Education and Research (JIPMER), Puducherry, India, [2]JIPMER, Pondicherry, India, [3]Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Microvascular dysfunction is a key and determining feature of scleroderma (SSc). But contrary to earlier belief there is emerging evidence to suggest co-occurrence of macrovascular dysfunction. The clinical

implication of macrovascular dysfunction in SSc is unknown and its correlation with microvascular dysfunction is inconclusive. Therefore the objectives of this study were to assess the prevalence and clinical impact of macrovascular dysfunction in a cohort of SSc. To study the correlation between macrovascular dysfunction as assessed by percent change in flow mediated vasodilation (FMD) of brachial artery and microvascular dysfunction as assessed by nail fold capillaroscopy (NFC) findings in SSc.

Methods: Cross-sectional comparative study enrolled SSc patients (n=59) and age & gender matched healthy controls (n=64). FMD change was calculated using standard USG probe (6 MHz) in right brachial diameter from the average of 3 consecutive end diastolic frames. NFC was performed using portable nail fold capillary microscope at 800X magnification. Clinical features of SSc were compared between SSc patients with and without macrovascular dysfunction.

Results: SSc had significantly ($p < 0.001$) lower FMD change (median-4.54, IQR 3.13-8.82) compared to healthy controls (median – 10.30, IQR 8.33-13.16). Two out of every three SSc patients 43/59 (66.2%) had impaired FMD. We replicated significantly (p-value< 0.0001) lower capillary density (median – 3.19, IQR 2.38-3.94) in SSc compared to healthy controls (median – 7.56, IQR 7.06-8.0) (Table 01). Impairment in FMD was not associated with Raynaud's phenomenon, digital gangrene, digital ulcer, acro-osteolysis or pulmonary hypertension suggesting need for a prospective study to identify the implications (Table 02). Magnitude of NFC findings and FMD changes did not corelate with the impairment in FMD among SSc patients (Figure 01)

Table 1. Comparison of parameters between the SSc patients with healthy controls (*P value < 0.001)

Parameters	SSc patients (n=59)	Healthy controls (n=64)
	Frequency (percentage) / median (interquartile range)	
FMD changes		
FMD % change*	4.54 (3.13-8.82)	10.30 (8.33-13.16)
Impaired FMD (Δ FMD <8.33)	43/59 (66.2%)	-
NFC changes		
Number of capillaries *	51 (38-63)	121 (113-128)
Average capillary density *	3.19 (2.38-3.94)	7.56 (7.06-8)
Disorganized architecture (%) *	37.5 (12.5-37.5)	0
Abnormal (%) *	36.11 (14.03-55.26)	0
Enlarged (%) *	10.63 (2.94-23.68)	0
Giant (%) *	21.05 (0-45.45)	0
Microhemorrhages (%)*	6.25 (0-12.5)	0
Neoangiogenesis (%) *	3.85 (0-20)	0
Avascular area (%) *	50 (31.25- 75)	0

Table 2. comparison of macrovascular complication between SSc patients with or without impaired FMD

Parameters	SSc patients with impaired FMD (n=43)	SSc patients with normal FMD (n=16)	P value
Age in years (median, IQR)	37 (28-46)	40 (26-46.5)	0.595
Disease subtype			0/686
Diffuse SSc	21/43 (48.8%)	08/16 (50%)	
Limited SSc	14/43 (32.6%)	06/16 (37.5%)	
SSc sine scleroderma	07/43 (16.3%)	01/16 (6.3%)	
Overlap with myositis	01/43 (1.7%	01/16 (6.3%)	
Disease duration in years (median, IQR)	5 (03-10)	5 (03-8.5)	0.791
Scl-70 positivity	27/43 (62.7%)	13/16 (81.3%)	0.454
NFC pattern			0.254
Normal	01/43 (02.3%)	02/16 (12.5%)	
Early	07/43 (16.3%)	02/16 (12.5%)	
Active	19/43 (44.2%)	09/16 (56.3%)	
Late	16/43 (37.2%)	03/16 (18.8%)	
Raynaud's phenomenon	33/43 (76.7%)	12/16 (75%)	1.0
Digital pitting	20/43 (46.5%)	08/16 (50%)	1.0
Fingertip ulcer	03/43 (07%)	05/16 (31.3%)	0.028
Fingertip gangrene	01/43 (2.3%)	01/16 (6.3%)	0.472
Fingertip infection	01/43 (2.3%)	02/16 (12.5%)	0.176
Acro-osteolysis	04/43 (9.3%)	04/16 (25%)	0.194
Ulcer elsewhere	04/43 (9.3%)	00/16 (0%)	0.566
Pulmonary Hypertension	08/43 (18.6%)	05/16 (31.3%)	0.311

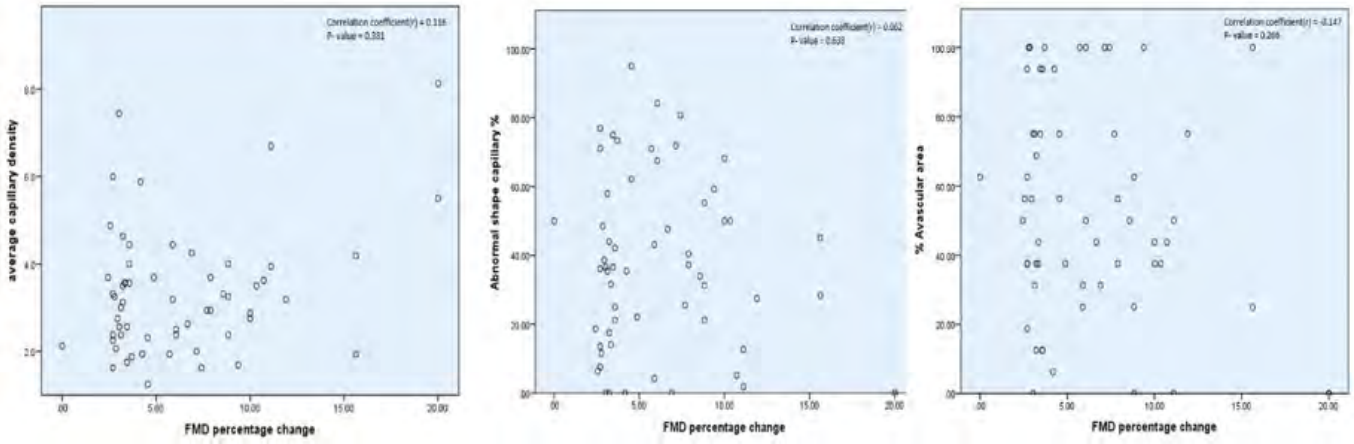

Figure 1. Correlation of FMD percent change with (a) average capillary density (b) abnormal capillaries and (c) % avascular area.

Conclusion: About 2/3rd of patients with SSc have macrovascular complications but their clinical implications may need long term prospective follow up. Macrovascular and microvascular dysfunction appears to be independent of each other in SSc.

Disclosure: D. Bairwa, None; **C. Kavadichanda**, None; **s. Shah**, None; **A. Mathew**, None; **s. dunga**, None; **A. Gopal**, None; **M. Thabah**, None; **V. Negi**, None.

Abstract Number: 1388

Heterogeneity of Primary and Secondary Peristalsis in Systemic Sclerosis: A New Model of Scleroderma Esophagus

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Although esophageal dysmotility is common in systemic sclerosis (SSc), little is known regarding the pathophysiology of the motor abnormalities driving reflux severity and dysphagia. This study aimed to assess primary and secondary peristalsis in SSc using a complementary approach focused on High-resolution manometry (HRM) and functional luminal imaging probe (FLIP) Panometry to provide a more comprehensive assessment of esophageal motility.

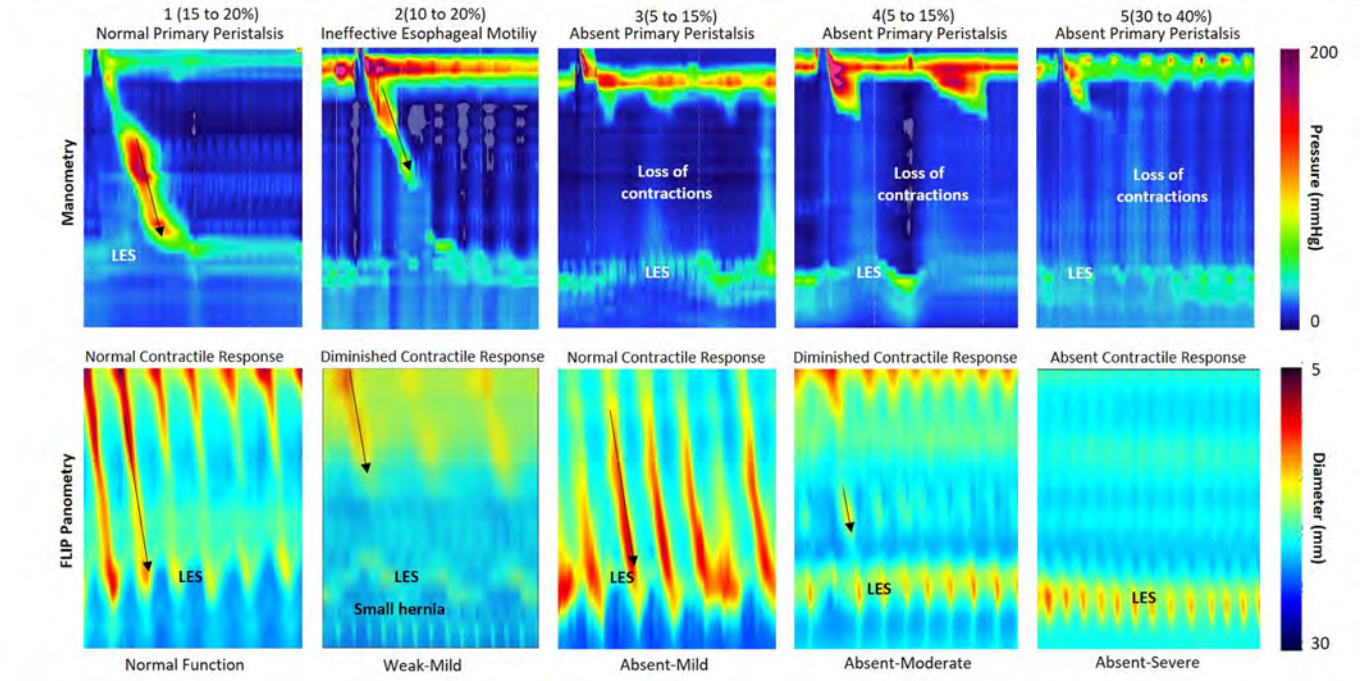
Methods: We performed simultaneous HRM and FLIP Panometry in 33 patients with SSc (28F, ages 38 to 77). Secondary peristalsis, i.e. contractile responses (CR), was classified on FLIP Panometry by presence and pattern of contractility as normal (NCR), borderline (BCR), impaired/disordered (IDCR), absent (ACR), or spastic-reactive (SRCR). Primary peristalsis on HRM was assessed according to the Chicago Classification. EGJ-distensibility index (EGJ-DI) was measured in all patients during FLIP-Panometry as a marker of LES function/opening.

Results: We were able to obtain complete data in 32 subjects as one patient had a sensor malfunction on FLIP. The manometric diagnoses were: Absent Contractility- 18 (56%); Ineffective Esophageal Motility- 7 (22%); Normal motility- 7 (22%). SSc patients also had heterogeneity in terms of secondary peristalsis with 38% (n=12) of patients having ACR, 38% (n=12) having IDCR, 19% (n=6) having BCR and 15% (n=5) having normal. The median (IQR) EGJ-DI was 5.8 mm^2/mmHg (4.8-10.1) mm^2/mmHg; 10/32 (31%) of the SSc patients had an EGJ-DI >8.0 mm^2/mmHg and all 32 patients had an EGJ-DI >2.0 mm^2/mmHg. Of the 18 patients that had absent contractility on HRIM; 11 (61%) patients had ACR, 5 (28%) had IDCR and 2 (11%) had BCR. Of the 7 patients with IEM, 1 patient had ACR, 1 patient had NCR and 5 had IDCR. All of the patients with Normal peristalsis had NCR or BCR. Based on these observations, a three tiered classification describing the relationship between findings on HRM and FLIP-Panometry is described in the Figure.

Conclusion: This was the first study to assess combined HRM and FLIP–Panometry in a cohort of SSc patients. Our results support heterogeneity in both primary and secondary peristalsis and a hierarchal classification scheme which can more accurately describe abnormalities of bolus transit.

Patients are defined by peristaltic function on manometry (top panels) and contractile response to volumetric distention (bottom panels). Each pair of Manometric and FLIP Panometric images can be combined to create specific subtypes [Normal, Weak, Absent] /stages [Mild, Moderate, Severe]. Examples are noted in the 5 panels: 1) SSc with Normal Esophageal Function, 2) SSc Esophagus with IEM and borderline or diminished function on FLIP, 3) Absent Contractility with Normal Contractile Response, 4) SSC esophagus with impaired contractile response and 5) SSc with aperistalsis on manometry and an absent contractile response to volumetric distention.

This model has the capacity to define disease progression along the neurogenic and myogenic pathway in extreme detail to provide a timeline for our translation assessment of molecular targets and biomarkers. Additionally, this assessment may uncover distinct phenotypes beyond the classic progression to aperistalsis and that may have varying levels of neurogenic dysfunction . LES- Lower esophageal sphincter



Subtypes of Esophageal Function in SSc defined by combined manometry/FLIP-panometry.

Disclosure: J. Pandolfino, Medtronic, 1, 2, 5, 6, 9, 10, Diversatek, 2, 5, Takeda, 2, 6; **H. Perlman**, Kiniksa, 1, 2; **M. Hinchcliff**, None; **M. Carns**, None; **J. Pandolfino**, Medtronic, 2, 5, 6, 9, 10, Diversatek, 2, 5, Takeda, 2, 6; **J. Pandolfino**, None; **C. Correia**, Boehringer Ingelheim, 2, 6; **J. Pandolfino**, Medtronic, 1, 2, 5, 6, 9, 10, Diversatek, 2, 5, Takeda, 2, 6.

Abstract Number: 1389

Subclinical ILD Is Frequent and Progresses Across Different Connective Tissue Diseases

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II (1364–1390)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Clinical characteristics, demographics and outcome of CTD without ILD, and with subclinical and clinical ILD

	No ILD (n=227)	Subclinical ILD (n=67)	Clinical ILD (n=231)
Age, y (SD)	50 (15.4)	51 (14.4)	52 (15.3)
Male sex, n (%)	89 (39)	22 (33)	111 (48)
Deceased, n (%)	50 (22)	12 (18)	91 (39)
Observation period, y median (range)	13.7 (18.6)	13.9 (17.9)	11.5 (17.1)
FVC% (SD)	97 (18.6)	99 (17.9)	81 (20.9)
FVC decline% (SD)	-0.70 (11.1)	-0.81 (16.5)	-1.61 (15.9)
DLCO% (SD)	73 (19.4)	73 (16.9)	55 (17.4)
Extent of ILD% (SD)	0 (0)	2.3 (1.5)	19.3 (16.8)
ILD progression% (SD)	0.08 (1.0)	3.1 (6.2)	3.6 (9.9)
ILD progressors, n (%)	3 (2)	20 (38)	72 (51)

Background/Purpose: Based on the argument that symptoms-define-disease, physicians commonly apply the terms pre-clinical or sub-clinical disease to describe patients with disease-related findings, but no accompanying symptoms. For patients with connective tissue disease associated interstitial lung disease (CTD-ILD), the term sub-clinical applies frequently to patients with mild ILD changes on HRCT, within normal range functional capacity and no respiratory symptoms. Previous work in systemic sclerosis (SSc)-ILD did however show that patients with even minor extent of ILD at baseline often progressed and had increased mortality risk; indicating that it is not appropriate to define these patients as “subclinical”. The objective of this study was to to identify the prevalence of subclinical ILD across CTD diagnoses, and assess the rate of progression of lung fibrosis compared to CTD without ILD and with clinical ILD.

Methods: All CTD patients, including SSc, anti-syntethase syndrome (ASS) and mixed connective tissue disease (MCTD) from the Oslo University Hospital diagnosed before 2015 assessed for the presence of ILD by HRCT were included. 2015 was chosen to secure an observation time of at least 5 years from ILD diagnosis to study end on 01.01.2021 or time of death. All patients fulfilled the respective CTD classification criteria. Subclinical ILD was defined as an ILD extent < 5% by semi-quantitative assessment at baseline HRCT, preserved lung function with a forced vital capacity (FVC) >80%predicted and no respiratory symptoms. Clinical ILD was defined as >5% extent of ILD or < 5% extent of ILD on HRCT with respiratory symtoms or FVC< 80%. The outcome was progression of lung fibrosis assessed on HRCT at follow up. Vital status was available in all patients and mortality assessed. Descriptive statistical analyses were conducted and time to progressive event determined by Kaplan-Meier estimates.

Results: We identified 525 CTD patients, including 296 SSc, 135 MCTD and 94 ASS patients assessed for ILD. Of these, 227 (43%) had no ILD, 67 (13%) subclinical and 231 (44%) clinical ILD (Table). Of the 67 subclinical ILD patients, 45 (15%) had SSc, 13 (10%) MCTD and 9 (10%) ASS. Over a median time of 4.5 years between baseline and follow up HRCT, 95/395 (24%) showed lung fibrosis progression, including 72 (26%) SSc and 23 (19%) MCTD patients. Disease progression was frequently present in both subclinical ILD (38%) and clinical ILD (51%) patients (Figure). Age, gender, underlying CTD and baseline lung function were not predictive for lung fibrosis progression. The events were too low for multivariable regression analyses. After a median observational period of 12 years, 153 (29%) of the patients died. The 1-, 5- and 10-year survival rates in no ILD, subclinical and clinical ILD were 97%/97%/99%, 88%/91%/82% and 82%/85%/68% (p< 0.001), respectively.

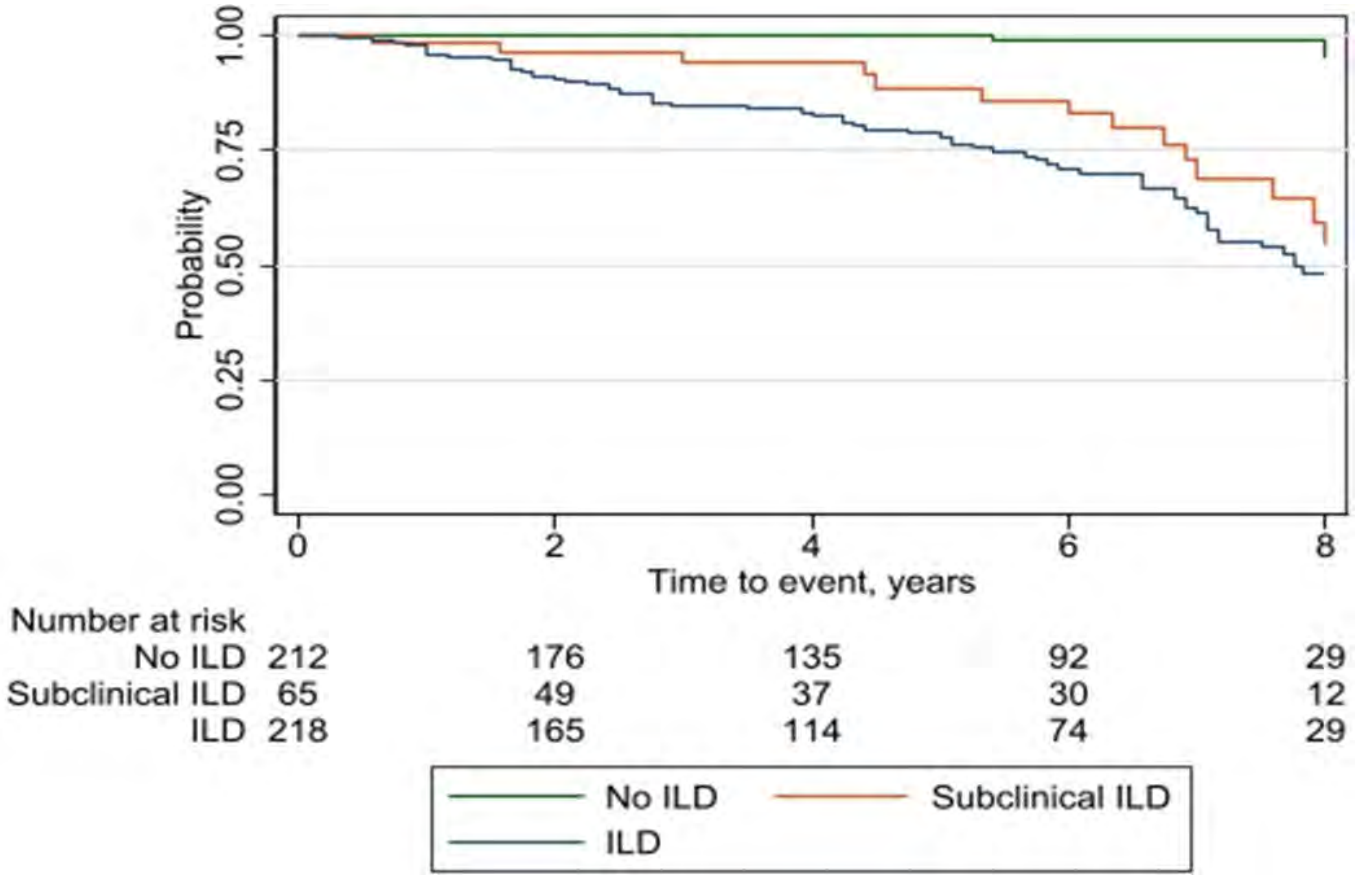

Figure 1. Time to progressive event.

Conclusion: Subclinical ILD is frequently present across CTDs and progresses over time in a substantial subgroup of patients, comparable to patients with clinical ILD. Our findings question the terms sub- and preclinical ILD, which may potentially lead to to a suboptimal "watchful waiting management strategy".

Disclosure: A. Hoffmann-Vold, Actelion, 1, 2, 6, Arxx Therapeutics, 1, 2, Bayer, 5, Boehringer Ingelheim, 1, 2, 5, 6, Lilly, 6, Medscape, 2, 6, Merck Sharp & Dohme, 6, Roche, 6; **H. Andersson**, None; **S. Reiseter**, None; **H. Fretheim**, Bayer, 12, Dr. Fretheim reports grants from Norwegian Women's Public Health Association, during the conduct of the study; personal fees from Bayer and travel bursaries from Actelion and GlaxoSmithKline, outside the submitted work; ., Actelion, 12, Travel bursaries from Actelion, GlaxoSmithKline, 12, travel bursaries GlaxoSmithKline, outside the submitted work;; **I. Barua**, None; **T. Garen**, None; . **Midtvedt**, None; **R. Gunnarsson**, None; **M. Durheim**, Boehringer Ingelheim, 2, 5, 6, 12, Spouse is a BI employee, Roche, 2, 6; **T. AAløkken**, None; . **Molberg**, None.

Abstract Number: 1390

A 5% Increase in Interstitial Lung Disease at 1-Year Follow-up Is Associated with Long-Term ILD Progression in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
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Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: The clinical course of interstitial lung disease (ILD) in systemic sclerosis (SSc) is highly variable. Some patients experience a progressive decline in lung function while others remain stable. SSc patients with ILD may be monitored for progression by high-resolution computed tomography (HRCT), pulmonary function studies (PFT), or both, to determine i) need for therapy, or ii) stability on therapy. However, the percent change in ILD over time that constitutes significant progression on HRCT remains unclear. Additionally, whether short-term change in ILD% is associated with an increased risk for long-term ILD progression (traditionally defined as a reduction in forced vital capacity (FVC) on PFT of ≥10% predicted from baseline) is unknown. Small increases in ILD% on short-term follow-up HRCT scans may not be easily recognized due to high interrater variability in grading of the severity and extent of ILD on serial HRCT. The purpose of this study is to evaluate whether rate of change in interstitial lung abnormalities measured by quantitative CT (QCT) associates with long-term ILD progression.

Methods: All patients meeting the 2013 ACR/EULAR Classification Criteria for SSc and seen between 2007 and 2019 at our institution were identified. Subjects were eligible for inclusion in this initial proof of concept study if they had a baseline HRCT ± 2 yrs of SSc diagnosis, a follow-up HRCT within 12 months ± 6 months of baseline HRCT, and had ≥5% total ILD on baseline HRCT. Additionally, subjects were required to have a baseline PFT ± 6 months of baseline HRCT, and at least one or more PFTs after the 12-month follow-up HRCT. Subjects were excluded if the eligible HRCT scans showed pulmonary edema secondary to heart failure, pleural effusions, malignancy, or infection. HRCTs were analyzed using CALIPER (Computed Aided Lung Informatics for Pathology Evaluation and Rating) QCT software, and all parenchymal (e.g. ground glass opacities (GGO), reticular densities (RD), honeycombing (HC)) and vascular features (pulmonary vascular related structures: PVRS) were quantified and normalized by total lung volume. Total ILD% is the summation of GGO%, RD%, and HC%. ILD progression was defined as a decline in FVC of ≥10% predicted from baseline PFT. The association between rate of change in quantitative parenchymal and vascular features and ILD progression was determined using Cox models.

Results: 36 subjects (75% female; mean age 60 yrs [SD 8.4]) were analyzed. Most had limited cutaneous SSc (75%) and had no current or prior history of smoking (69%). Median time under observation was 3.3 yrs (IQR 1.4, 4.6). A

Table 1. Univariable association between 12-month change in CALIPER parameters and ILD progression by PFT, adjusting for age, sex, and diffuse SSc.

CALIPER parameters	HR (95% CI)	p-value
GGO% per 5% increase	2.64 (0.99-7.03)	0.052
RD% per 1% increase	1.09 (0.58-2.04)	0.79
Honeycomb% per 0.001% increase	1.10 (0.99-1.24)	0.07
ILD% per 5% increase	2.53 (1.02-6.23)	0.044
PVRS% per 1% increase	5.49 (1.11-27.24)	0.037

Baseline HRCT to next follow-up HRCT (median 0.8 years; IQR 0.5-1.4 years)

total of 8/34 subjects (24%) met ILD progression endpoint. A 5% increase in total ILD conferred a 2.5-fold increase in risk of ILD progression (HR: 2.53, 95% CI 1.02-6.23) (Table 1). A 1% increase in PVRS was associated with a 5-fold increase in risk of ILD progression (HR: 5.49, 95% CI 1.11-27.24).

Conclusion: QCT detects changes in parenchymal and vascular features on 1-year follow-up HRCT that may otherwise be too small to consistently detect and characterize by visual assessment, yet are early radiomic biomarkers of long-term disease progression risk. The utility of QCT in the evaluation and follow-up of SSc-ILD warrants further study.

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Abstract Number: 1391

Rituximab Is Superior to Placebo in Polymyalgia Rheumatica Patients: A Double Blind Randomized Controlled Proof of Principle Trial

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Time: 8:30AM–10:30AM

Background/Purpose: Corticosteroids remain the cornerstone of polymyalgia rheumatica treatment, but their use has several disadvantages such as long treatment duration and glucocorticoid-related adverse events.[1,2] Data on evidence based effective glucocorticoid-sparing agents are negative or absent.[2]

Because B-cells may be involved in the pathogenesis of polymyalgia rheumatica, we evaluated the efficacy of rituximab in polymyalgia rheumatica.

Methods: In a 21-week double-blind placebo controlled exploratory study, 47 polymyalgia rheumatica patients (recently diagnosed n=38 / relapsing on prednisolone ≥7.5mg/day n=9) fulfilling the 2012 EULAR/ACR criteria, were randomized 1:1 to intravenous rituximab 1 x 1000 mg (n=23) or placebo (n=24), with a 17-week long glucocorticoid co-treatment. Primary outcome was glucocorticoid-free remission at week 21. Secondary outcomes were glucocorticoid ≤5mg/day and adverse events. Several post-hoc analyses were done for robustness of results.

Results: Glucocorticoid-free remission was achieved in 48% (rituximab) versus 21% (placebo), one-sided 95%-CI 4% to 100%; p=0.049, and glucocorticoid ≤5mg/day in 100% versus 54% (one sided 95%-CI 20% to 100%; p=0.005). Post-hoc analysis showed efficacy mainly in recently diagnosed patients: glucocorticoid-free remission in 58% versus 21% (one-sided 95%-CI 10% to 100%; p=0.02); glucocorticoid ≤5mg/day in 100% versus 47% (one-sided 95%-CI 29 to 100%; p< 0.001). No significant differences were observed regarding other outcomes (table 1), except for less morning stiffness after rituximab.

Conclusion: Rituximab is superior to placebo in combination with 17-week glucocorticoid-treatment to achieve glucocorticoid free remission in polymyalgia rheumatica. The largest effect was seen in recently diagnosed polymyalgia rheumatica patients (funding: Sint Maartenskliniek; Dutch trial number NL7414).

Table 1. Outcomes at week 21*

	Rituximab (n=23)	Placebo (n=24)	Difference, one sided 95%-CI	One sided p-value
Cumulative glucocorticoid dose in mg	*1356 (151)*	*1406 (189)*	-50 (- — to 34)	0.16
Median CRP in mg/l (median, IQR) ‡	3 (1 to 5)	2 (1 to 12) [21]		
Change from baseline (median, IQR)	- 1.5 (-9 to 2) [22]	- 5 (-13 to 0)[21]	3.5 (CI NA)	0.16
Mean ESR in mm/hour	19 (11) [21]	16 (13) [22]		
Change from baseline	-7 (25) [21]	-12 (19) [21]	5 (- — to 17)	0.79
Relapsing patients during follow-up – no (%)†	7 (30)	8 (33)	-1 (- 100 to 20)	0.54
Median PMR-AS	5.5 (2.1 to 10)	11.7 (4.0 to 18.7)		
Change from baseline	-13.8 (2.9)	-3.8 (3.6)	-10 (- — to -2.2)	0.02
Morning stiffness in minutes (median, IQR)	5 (0 to 30)	30 (9 to 90)		
Change from baseline (median, IQR)	-60 (-120 to -5)	-20 (-60 to 0)	-40 (CI NA)	0.02
			Rate ratio RTX vs placebo (95% CI)	
Any adverse event §	136	148	0.96 (0.8 to —)	
Serious adverse event(s) ††	1	0		
Infections ‡ ‡	15	8	1.96 (1.0 to —)	
Infusion related complaints ¶	10	3	3.47 (1.3 to —)	

* Values are means, SD, unless specified otherwise. Numbers of observations is indicated between brackets [ ]. No correction for type I error.

† Judged by research physician

‡ Wilcoxon rank sum (Mann-Whitney) test

§ All adverse events that occurred during the study period were included in the analyses. Adverse events numbers are number of events, not number of patients with events. Safety outcomes were compared by chi-squared test (cumulative incidences). No correction for type I error was performed. All adverse events were graded according to Common Terminology Criteria for Adverse Events version 5.0, grade range 0–5;higher scores indicate worse events.

†† was A pulmonary embolism occurred in one patient

‡ ‡ Labelled by the research physician. No serious infections ≥ grade 3 occurred.

¶ Labelled by research physician. No serious infusion related complaints ≥ grade 3 occurred.

CRP denotes C-reactive protein, IQR interquartile range, NA not applicable, ESR erythrocyte sedimentation rate, CI confidence interval, PMR-AS polymyalgia rheumatica activity score, RTX rituximab

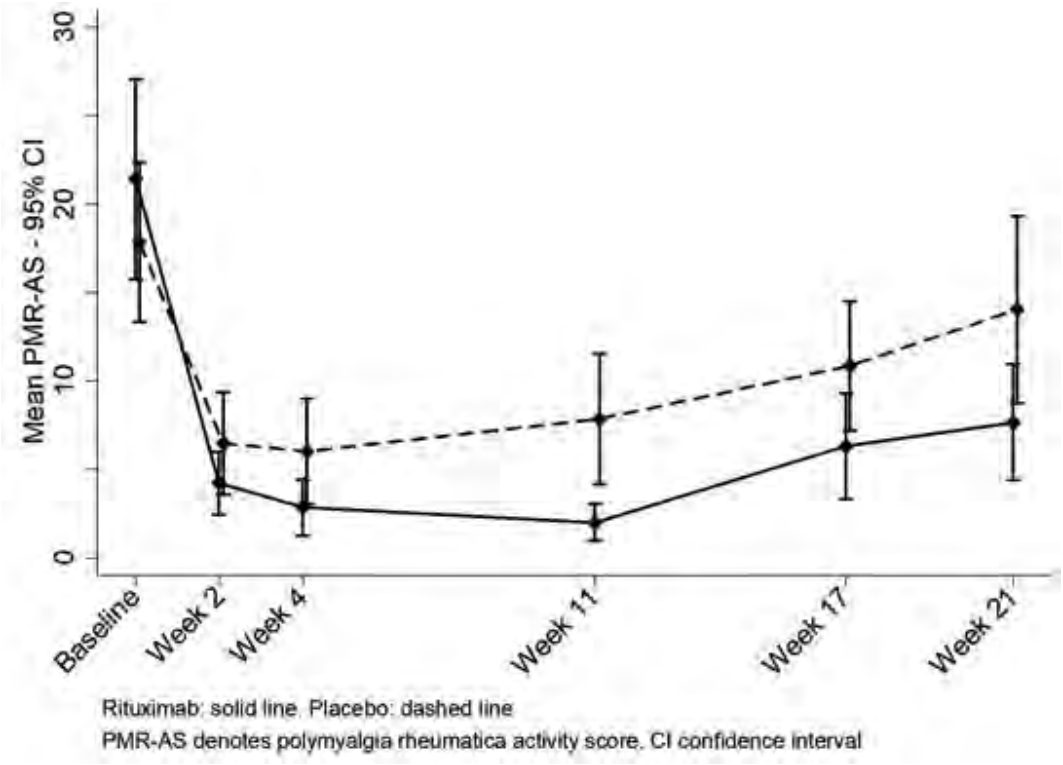

Figure 1. Mean Polymyalgia Rheumatica Activity Score at each visit.

Disclosure: D. Marsman, None; **N. den Broeder**, None; **F. van den Hoogen**, None; **A. den Broeder**, Amgen, 12, Expert witness fee adalimumab biosimilar litigation, Galapagos, 12, Congress invitation, Sanofi, 12, Congress invitation, Abbvie, 12, Editorial work education, Novartis, 12, Editorial work education, Abbvie, 5, Pfizer, 5, Lilly, 5, Novartis, 5, Sanofi, 5; **A. van der Maas**, None.

Abstract Number: 1392

Assessment of a Patient Self-Report Frailty Tool in Patients with Polymyalgia Rheumatica

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

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Background/Purpose: Frailty, a syndrome characterized by decreased physiologic reserve, is associated with chronic inflammation. We have shown a high prevalence of frailty in patients with polymyalgia rheumatica (PMR) using the Fried criteria (FC), the gold standard frailty phenotypic instrument[1]. However, the FC is not practical to use at point of care. The Frail scale (FS), an easy-to-use self-report frailty instrument, has not been evaluated in patients with PMR.

Table 1. Frequency of frailty components for each classification and categorization

FRAIL scale		Fried frailty criteria	
Component	**Participants (N = 41), %**	**Component**	**Participants (N = 41), %**
Fatigue	16 (39%)	Weight loss	10 (24%)
Resistance	11 (27%)	Exhaustion	17 (41%)
Ambulation	0 (0%)	Inactivity	6 (15%)
Illnesses	10 (24%)	Slowness	1 (2%)
Loss of Weight	9 (22%)	Weakness	21 (51%)
Overall			
Robust	14 (34%)	Robust (0 criteria)	10 (24%)
Pre-frail	22 (54%)	Pre-frail (1-2 criteria)	24 (59%)
Frail	5 (12%)	Frail (≥3 criteria)	7 (17%)

Table 2. Baseline characteristics by frailty classification as classified by FRAIL scale

Characteristic	Robust N = 14	Pre-fail N= 22	Frail N = 5	p-value
Age, years, median [IQR]	71.3 (65.2,74.9)	75.4 (67.1, 79.1)	75.8 (72.5, 78.5)	0.20
Sex, female, n (%)	7(50%)	8 (36%)	5 (100%)	0.04
Race, n (%) White/Caucasian Asian Other	 14 (100%) 0 (0%) 0 (0%)	 20 (90%) 1 (5%) 1 (5%)	 4 (80%) 0 (0%) 1 (20%)	0.43
Ethnicity, n (%) Hispanic Non-Hispanic	 0 (0%) 14 (100%)	 1 (5%) 21 (95%)	 1 (20%) 4 (80%)	0.29
Education, n (%) High school/GED or less Some college College Graduate/advanced professional degree	 0 (0%) 0 (0%) 3 (21%) 11 (79%)	 1 (5%) 2 (9%) 6 (27%) 13 (59%)	 1 (20%) 0 (0%) 2 (40%) 2 (40%)	0.61
Smoking, ever, n (%)	7 (50%)	10 (45%)	4 (80%)	0.51
Alcohol use, ever, n (%)	12 (86%)	18 (82%)	5 (100%)	0.37
Charlson Comorbidity Index, median [IQR]	1 (1, 1)	2 (1, 3)	1 (1, 3)	0.03
Number of daily medications taken, median [IQR]	4 (3, 5)	5 (3, 7)	5 (2, 8)	0.34
Duration of disease, days, median [IQR]	134.5 (75, 273)	111.5 (49, 239)	181 (131, 280)	0.50
PMR-AS score, median [IQR]	1.3 (.7, 4.3)	2.1 (.7, 4.8)	3.9 (2.4, 5.5)	0.54
C-reactive protein at diagnosis, (mg/dl) median [IQR]	2.7 (1.0, 3.7)	2.89 (1.4, 5.1)	8.41 (3.9, 8.7)	0.06
Erythrocyte Sedimentation Rate at diagnosis, (mm/hr), median [IQR]	40 (30, 52)	49.5 (33, 84)	75 (39, 81)	0.38
C-reactive protein at baseline, (mg/dl) median [IQR]	0.7 (0.7, 0.7)	0.7 (0.5, 0.7)	0.7 (0.7, 0.8)	0.13
Erythrocyte Sedimentation Rate at baseline, (mm/hr), median [IQR]	5 (2, 8)	11 (3, 19)	19 (14, 19)	0.05
Glucocorticoid dose (mg/day), median [IQR]	5.5 (3, 7.5)	6.5 (4, 12)	7.5 (7, 7.5)	0.45
Glucocorticoid exposure duration, days, median [IQR]	121 (70, 250)	97 (34, 237)	188 (131, 280)	0.33
Steroid sparing agent use, n (%)*	0 (0%)	3 (15%)	0 (%)	1.00
Body mass index (BMI), kg/m^2, median [IQR]	25.8 (23.9, 27.3)	26.4 (23.9, 29.3)	28.3 (24.3, 30.1)	0.80

*Steroid sparing agents such as methotrexate, hydroxychloroquine, tocilizumab. PMR-AS = Polymyalgia Rheumatica Activity Score
†Prednisone equivalent in mg/day.

The objectives of this study were to evaluate the prevalence of frailty using the FS, to compare its performance with the FC, and to describe the association of frailty with health-related quality of life (HRQoL) in patients with PMR.

Methods: Patients with PMR who fulfilled 2012 EULAR/ACR Provisional Classification Criteria at time of diagnosis, ≤ 12 months from diagnosis and on active treatment with glucocorticoids were recruited from a single center. Disease activity was measured with the PMR-activity score. Comorbidity burden was measured by the Charlson Comorbidity Index (CCI). Frailty and pre-frailty were defined according to FC and the FS[2]. HRQoL was assessed using global Patient-Reported Outcomes Measurement Information System (PROMIS) computerized adaptive tests. Sarcopenia

Table 3. Health-related Quality of Life, Sarcopenia and Disability by frailty classification

	FRAIL scale				Fried frailty criteria			
	Robust n =14	Pre-frail n = 22	Frail n = 5	p-value	Robust N = 10	Pre-frail N= 24	Frail N =7	p-value
PROMIS Domain*								
Anxiety	51.0 (44.3, 52.1)	51.2 (49.2, 52.8)	59.9 (55.9, 66.4)†	**0.02**	52.0 (49, 53.5)	50.8 (46.7, 52.1)	55.9 (51.2, 61.5)†	0.12
Anger	47.5 (45.2, 49.9)	49.6 (42.1, 52.4)	51.5 (46.3, 54.9)	0.48	48.2 (44.3, 52.3)	47.5 (42.1, 52)	50.15 (47.8, 54.7)	0.42
Depression	47.5 (45.95, 49.4)	48.2 (43.8, 50.4)	53.1 (41.4, 58.2)	0.63	48.2 (46.9, 50.8)	46.1 (42.6, 49.9)	48.95 (48.2, 57.6)	0.21
Fatigue	42.3 (38.7, 48.5)	48.5 (47.9, 54.4)	59.3 (48.6, 61.5)†	**0.02**	48.5 (38.2, 52.8)	48.5 (45.1, 50.7)	53.3 (48.5, 60.5)	0.33
Pain behavior	35.3 (35.3, 52.0)	51.8 (35.3, 55.9)	57.5 (54.3, 59.6)†	**0.04**	51.3 (35.3, 57.5)	35.3 (35.3, 52.6)	57.5 (56.3, 58.8)†	**0.01**
Pain interference	42.7 (38.7, 48.6)	48.4 (38.7, 55.2)	57.5 (55.1, 61.7)†	**0.02**	46.6 (38.7, 54.3)	46.6 (38.7, 52.6)	57.6 (55.8, 60.3)†	**<0.01**
Physical function	53.7 (46.5, 55.75)	46.8 (41.8, 53.1)	36.3 (34.2, 39.6)†	**0.01**	53.7 (41.4, 55.2)	48.5 (43.5, 53.7)	39.55 (35.7, 46.8)†	0.06
Satisfaction with social role	57.1 (49.9, 63.4)	50.8 (45.1, 58.1)	52.1 (40.2, 58.4)	0.22	52.4 (47.4, 64.6)	54.0 (45.8, 60.2)	49.05 (45.8, 58.3)	0.39
Cognitive	49.4 (45.8, 61.4)	49.8 (46.7, 58.4)	47.2 (42.7, 59.2)	0.91	52.3 (49.1, 60.7)	49.3 (45.8, 54.4)	47.15 (41.5, 68)	0.50
Sarcopenia, n (%)	0 (0%)	7 (32%)	0 (0%)	**0.02**	1 (10%)	5 (21%)	1 (14%)	0.85
Disability								
Dependence in ADLs, n (%)	3 (21%)	3 (14%)	0 (0%)	0.70	3 (30%)	3 (13%)	0 (0%)	0.27
Dependence in IADLs, n (%)	0 (0%)	2 (9%)	0 (0%)	0.62	0 (0%)	2 (8%)	0 (0%)	1.00

*Presented as t-scores, median (interquartile range).
†5 points are considered a minimally clinical important difference. **Sarcopenia defined following the EWGSOP2 recommendations.
ADL = activities of daily living assessed by Katz Index; IADL = instrumental activities of daily living assed by Lawton scale

was assessed by DXA. Fisher's exact test, chi-square tests and Kruskal-Wallis tests were used to describe differences among groups as appropriate. Frailty according to FC and FS were compared using a Spearman correlation.

Results: 41 patients completed a baseline visit. 12% and 17% of patients were frail, and 54% and 59% were pre-frail according to the FS and FC, respectively (Table 1). There was a strong correlation between the FRAIL scale and the Fried frailty criteria ($r = 0.71$, $p < 0.05$). Based on the FS, there were significant differences in the sex and CCI among frail, pre-frail, and robust patients ($p = 0.03$) (Table 2). Although non-significant, frail patients had higher CRP at diagnosis and ESR at study visit. According to both definitions, frail patients had more pain behavior (FS: p=0.04; FC: p=0.01) and pain interference (FS: p=0.02; FC: p< 0.01) (Table 3). Additionally, according to FS, frail patients also had more fatigue (p=0.02) and anxiety (p=0.02), and worse physical function (p=0.01). Pre-frail patients, according to FS, had more sarcopenia (p=0.02). There were no differences in disability according to either definition.

Conclusion: There was a higher prevalence of frailty and pre-frailty in this cohort of patients with PMR. Despite similar disease duration, comorbidity burden, and dose of glucocorticoids, frail patients with PMR had statistically significant and clinically meaningful worse HRQoL. There was a strong correlation between self-reported frailty and a standard frailty measure suggesting the use of the FS as a simple frailty screening tool for patients with PMR in clinical practice.

References

< !1. Sattui SE, et al. Arthritis Rheumatol. 2020; 72 (suppl 10).
< !2. Morley JE et al. J Nutr Health Aging 2012;16:601.

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Abstract Number: 1393

All-cause Mortality in a Hospital Ascertained Cohort with Giant Cell Arteritis: A Longitudinal Population-level Data Linkage Cohort Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Giant Cell Arteritis (GCA) is the most common primary vasculitis in high income countries and ischemic complications of GCA include blindness and stroke. The impact of GCA on mortality is unclear, with conflicting evidence as to whether mortality is increased. We utilized whole-population linked health data to investigate all-cause mortality and the contributing causes of death of hospitalised GCA patients compared to matched hospital controls.

Methods: All hospital presentations with GCA from 1980 to 2015 were identified. Each patient (n=1,802) was propensity score matched with hospital-based controls (n=3,945). Data from the from the Death Registrations database were used to determine all-cause and contributing causes of mortality. The association between GCA and mortality was assessed using Cox regression models. Standardized mortality ratios (SMR) were produced for the GCA cohort compared to the general population of Western Australia.

Results: GCA patients had increased unadjusted (HR 1.58, 95% CI 1.46, 1.71; P< 0.001), and multivariable-adjusted risk of mortality (aHR 1.13, 95%CI 1.04, 1.23; P< 0.001) compared to controls. GCA patients requiring hospital care had an increased likelihood of mortality compared to the general population for up to ten years, most pronounced in the first year (SMR 2.67, 95%CI 2.30, 3.10; p< 0.001). Adjusting for age, sex and IA status, people with GCA had an increased likelihood of 18-year deaths related to diseases of the musculoskeletal, connective tissue and subcutaneous system diseases (excluding GCA); diseases of the eye and adnexa; diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism; diseases of the genitourinary system; certain infectious and parasitic diseases; diseases of the digestive system; endocrine, nutritional and metabolic diseases; diseases of the respiratory system; diseases of the circulatory system. Adjusting for age, sex and IA status, people with GCA had a decreased likelihood of 18-year deaths related to neoplasm and diseases of the central nervous system.

Conclusion: Western Australians presenting to hospital with GCA from 1980 to 2015 had increased mortality compared to matched controls. The increased risk of death is likely related to both the disease, and complications of steroid therapies; both more efficacious and less harmful therapies are required to reduce mortality in GCA.

Disclosure: H. Keen, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **W. Raymond**, None; **S. Lester**, None; **D. Preen**, None; **C. Inderjeeth**, None; **C. Hill**, None; **J. Nossent**, None.

Abstract Number: 1394

Vascular Ultrasound for Giant Cell Arteritis: An Effective Diagnostic Modality for a Fast Track Clinic in the United States

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of large vessel vasculitis. Prompt diagnosis and treatment of GCA is vital to prevent vision loss. The European League Against Rheumatism (EULAR) recommends ultrasound as the preferred imaging modality for GCA, and in subjects with positive imaging findings and a high clinical suspicion, diagnosis can be made without temporal artery biopsy (TAB). Fast track clinics (FTC) evolved in European countries to diagnose GCA through the use of ultrasound. However, the American College of Rheumatology (ACR) does not yet endorse the use of ultrasound for diagnosis, and FTCs in the United States are still relatively new. We present the results of the largest cohort of subjects reported to date referred to a United States FTC for the diagnosis of GCA.

Methods: Subjects referred to the FTC from November, 2017 – April 2021 were triaged by an attending rheumatologist who arranged for urgent rheumatology consultation and ultrasound and/or TAB. A protocolized ultrasound for the evaluation of GCA was performed by a trained vascular sonographer. The first 43 subjects referred to the FTC received both TAB and ultrasound. After demonstrating concordance between ultrasound and TAB, in subsequent referrals TAB was not performed in the setting of high clinical suspicion for GCA and positive ultrasound, or low suspicion for GCA and negative ultrasound. Ultrasound was considered positive for GCA if there was a halo sign with compression in the temporal arteries or if intima-media thickness (IMT) was increased in the large vessels.

Results: 209 subjects were referred to the FTC for ultrasound evaluation. 166 referrals were for evaluation of suspected new onset GCA, 16 were to evaluate for recurrent GCA, 18 were to evaluate concern for extracranial large vessel vasculitis, and 1 was to evaluate refractory PMR. The median time from referral to ultrasound was 1 day, with subjects on prednisone for 2 days prior to ultrasound. The time from referral to TAB was 7 days. 63 subjects were diagnosed with GCA. 209 subjects underwent ultrasound for GCA, and 51 were positive for GCA. Of the 51 positive ultrasounds, 25 had a positive halo sign and 35 had increased IMT of a large vessel. 69 subjects underwent TAB, and 9 were positive for GCA. Only one subject had a positive TAB and negative ultrasound, after IV methylprednisolone. Ultrasound identified evidence of vasculitis in 12 of 59 subjects with negative TAB. 10 subjects were diagnosed with GCA on clinical grounds alone despite negative TAB and/or ultrasound. 7 subjects diagnosed with GCA had permanent vision loss at the time of referral to the FTC. No subjects developed permanent vision loss following referral to the FTC. 3 subjects diagnosed with GCA died.

Table 1. describes baseline clinical characteristics and outcomes. Median (IQR) reported for continuous variables. Abbreviations: FTC, fast track clinic; GCA, giant cell arteritis; IQR, interquartile range; TAB, temporal artery biopsy

	Fast Track Ultrasound N=209 (IQR)
Clinical Characteristics Age, years	69 (23)
Female	146
ESR (mm/h)	40 (51)
CRP (mg/L)	18 (46)
Reasons for Ultrasound Suspected GCA	166
Recurrent/known GCA	16
Eval of LVV	18
Refractory PMR	1
Fast Track Clinic Outcomes Time from FTC referral to US, days	1 (2) N=159
Time from FTC activation to rheumatology evaluation, days	1 (2) N=131
Time on prednisone prior to ultrasound, days	2 (0) N=127
Time on prednisone prior to TAB, days	7 (5) N=59
Positive ultrasound (temporal arteries and large vessels)	51 N=209
Positive temporal artery biopsy	9 N=69
Clinical Outcomes Diagnosed as GCA	63 N=193
Transient visual complaints in subjects with GCA	43
Permanent visual loss in subjects with GCA	7
Death in subjects with GCA	3

Conclusion: This FTC in the United States used ultrasound to successfully facilitate the diagnosis of GCA. Subjects received ultrasound rapidly following referral to the FTC and received prednisone for a short duration prior to ultrasound. Ultrasound frequently identified evidence of vasculitis in subjects with negative TAB.

Disclosure: C. Oshinsky, None; **A. Bays**, Genentech, 5, Abbvie, 5; **I. Sacksen**, None; **E. Jernberg**, None; **E. zierler**, None; **A. Diamantopoulos**, Sanofi, 1; **S. Pollock**, None.

Abstract Number: 1395

Utility and Validity of the Southend Pretest Probability Score (SPTPS) in a Giant Cell Arteritis Fast Track Clinic: Analysis in a Spanish Cohort of 297 Patients

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SESSION INFORMATION

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Background/Purpose: The implementation of fast track clinics (FTC) has enabled quick diagnosis and reduced the blindness rate of giant cell arteritis (GCA). Recently, the Southend Pre Test Probability Score (SPTPS) has been proposed, which allows establishing a probability of having GCA and validating the results of imaging before deciding to perform other diagnostic tests. Since this score has only been tested in the cohort from which it originated, we believe that it should be validated in other populations. The objective is to evaluate the validity of the SPTPS and its usefulness in our population.

Methods: Demographic, clinical and laboratory data of the patients referred to the GCA-FTC of La Paz University Hospital (Madrid, Spain) between 2016 and 2020 were retrospectively collected. Those for which insufficient data were available were excluded. SPTPS was calculated in all included patients. All had undergone color Doppler ultrasound (CDUS) of the temporal arteries and large vessels (axillary, subclavian and carotid arteries). The definitive diagnosis was established according to the physician's criteria, based on clinical features, CDUS -and other imaging tests or biopsy according to physician criteria- and evolution, after a minimum follow-up of 6 months. The quartiles to stratify the risk of GCA, the ROC curve and the validity of the SPTPS in our cohort were calculated.

Results: A total of 297 patients were included, of which 97 (32.7%) were diagnosed with GCA. Their characteristics are shown in table 1. The mean value of SPTPS was 9.9 ± 3.6 and it area under the curve 0.787 (95% confidence interval: 0.731-0.843) (image 1). The mean SPTPS in the GCA group was 12.4 ± 3.6 and 8.7 ± 3.1 in the non-GCA group ($p < 0.005$). The SPTPS results showed a value of 10 at the 50th percentile and 12 at the 75th percentile. Therefore, we classified as low risk (LR) the value of SPTPS < 10, intermediate risk (IR) 10-12, and high risk (HR) > 12. The category of HR included 47 patients with GCA (48.5%) and only 20 non-GCA patients (10%), showing a specificity of 90%, sensitivity 48.4%, positive predictive value (PPV) 70% and negative predictive value (NPV) 78%. The IR category included 32 patients with GCA (33%) and 63 non-GCA (31.5%) (specificity 68.5-83%). And the LR category, 18 with GCA (18.5%) and 117 non-GCA (58.5%). A SPTPS ≥ 10 (that is, IR or RA), showed a sensitivity of 81.4%, specificity of 58.5% and NPV of 86.6%. The cut-off ≥7 (equivalent to p25) showed a sensitivity of 95% and a NPV of 90%, while the cut-off ≥14 had a specificity of 95.5% (table 2). There were 51 cases with a score < 7, of which 5 had GCA; the majority had a pattern of extracranial involvement (3 out of 5), which represented 20% of all cases with this pattern. Despite this trend, no statistically significant differences were observed in the SPTPS value between the different patterns of involvement (cranial, mixed, extracranial).

Table 1. Demographic, clinical and laboratory characteristics included in the SPTPS of the patients in our cohort

	TOTAL (n = 297)	GCA (n = 97)	Non-GCA (n = 200)
Age (years)	Mean: 75.4 ± 9.6 ≤ 49: 4 (1.3%) 50-60: 22 (7.4%) 61-65: 25 (8.4%) ≥ 66: 246 (82.8%)	Mean: 77.3 ± 7.9 ≤ 49: 0 (0%) 50-60: 2 (2.1%) 61-65: 7 (7.2%) ≥ 66: 88 (90.7%)	Mean: 74.4 ± 10.2 ≤ 49: 4 (2%) 50-60: 20 (10%) 61-65: 18 (9%) ≥ 66: 158 (79%)
Sex	Female: 205 (69%) Male: 92 (31%)	Female: 53 (54.6%) Male: 44 (45.4%)	Female: 152 (76%) Male: 48 (24%)
Onset of symptoms (weeks)	< 6: 119 (40.1%) 6-12: 58 (19.5%) 12-24: 34 (11.4%) > 24: 77 (25.9%)	< 6: 38 (39.2%) 6-12: 25 (25.8%) 12-24: 15 (15.5%) > 24: 14 (14.4%)	< 6: 81 (40.5%) 6-12: 33 (16.5%) 12-24: 19 (9.5%) > 24: 63 (31.5%)
CRP (mg/L)	Mean: 40.4 ± 52.6 0-5: 82 (27.6%) 6-10: 37 (12.5%) 11-25: 47 (15.8%) ≥ 25: 119 (40.1%)	Mean: 63.3 ± 58.1 0-5: 9 (9.3%) 6-10: 10 (10.3%) 11-25: 12 (12.4%) ≥ 25: 63 (64.9%)	Mean: 28.9 ± 45.6 0-5: 73 (36.5%) 6-10: 27 (13.5%) 11-25: 35 (17.5%) ≥ 25: 56 (28%)
Headache	175 (58.9%)	71 (73.2%)	104 (52%)
Polymyalgia rheumatica	113 (38%)	47 (48.5%)	66 (33%)
Constitutional symptoms	Single: 58 (19.5%) Combination: 14 (4.7%) Total: 73 (24.6%)	Single: 28 (28.9%) Combination: 6 (6.2%) Total: 35 (36.1%)	Single: 30 (15%) Combination: 8 (4%) Total: 38 (19%)
Ischaemic symptoms	89 (30%)	40 (41.2%)	48 (24%)
Visual signs	24 (8.1%)	12 (12.4%)	12 (6%)
Temporal artery abnormality	Tenderness: 21 (7.1%) Thickening: 13 (4.4%) Pulse loss: 7 (2.4%) Total: 41 (13.9%)	Tenderness: 9 (9.3%) Thickening: 9 (9.3%) Pulse loss: 5 (5.2%) Total: 23 (23.8%)	Tenderness: 12 (6%) Thickening: 4 (2%) Pulse loss: 2 (1%) Total: 17 (8.5%)
Extracranial artery abnormality	Thickening: 1 (0.3%) Bruit: 1 (0.3%) Pulse loss: 3 (1%) Total: 4 (1.3%)	Thickening: 1 (1%) Bruit: 1 (1%) Pulse loss: 3 (3.1%) Total: 4 (4.1%)	Thickening: 0 (0%) Bruit: 0 (0%) Pulse loss: 0 (0%) Total: 0 (0%)
Cranial nerve palsy	3 (1%)	1 (1%)	2 (1%)
Alternative diagnosis	Infection: 31 (10.4%) Cancer: 23 (7.7%) Systemic rheumatic disease: 41 (13.8%) Head and neck pathology: 10 (3.4%) Other: 17 (5.7%) Total: 96 (32.3%)	Infection: 5 (5.2%) Cancer: 13 (13.4%) Systemic rheumatic disease: 9 (9.3%) Head and neck pathology: 1 (1%) Other: 3 (3.1%) Total: 19 (19.6%)	Infection: 26 (13%) Cancer: 10 (5%) Systemic rheumatic disease: 32 (16%) Head and neck pathology: 9 (4.5%) Other: 14 (7%) Total: 77 (38.5%)

Conclusion: The SPTPS is useful to stratify patients referred to GCA-FTC. A score ≥14 is associated with a very high probability of having GCA and a value < 7 with a very low probability. However, although there were no statistically significant differences, 20% of the patients with extracranial GCA had an SPTPS < 7, so this test may not be able to discriminate well this subtype of the disease.

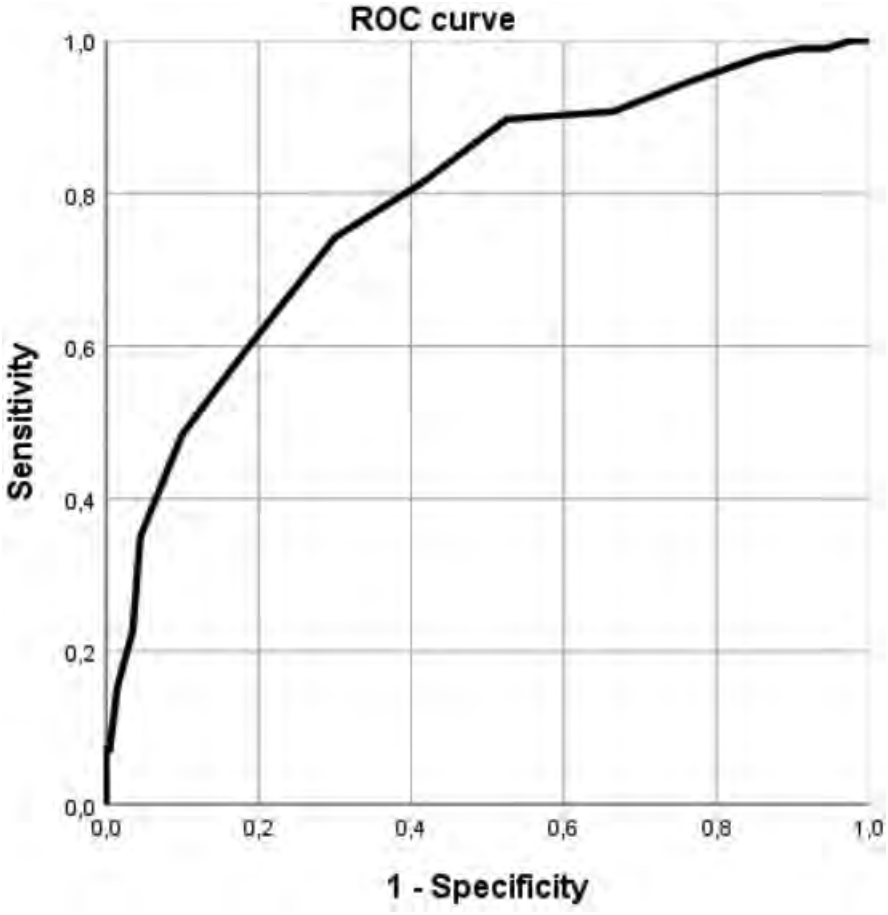

Image 1. SPTPS ROC curve in our population.

Table 2. Sensitivity and specificity of the different SPTPS cut-off points in our cohort

Cut-off	Sensitivity	1 - Specificity
-1,00	1,000	1,000
,50	1,000	,995
1,50	1,000	,990
2,50	1,000	,975
3,50	,990	,945
4,50	,990	,910
5,50	,979	,860
6,50	,948	,770
7,50	,907	,665
8,50	,897	,525
9,50	,814	,415
10,50	,742	,300
11,50	,577	,170
12,50	,485	,100
13,50	,351	,045
14,50	,227	,035
15,50	,155	,015
16,50	,072	,005
17,50	,072	0,000
18,50	,062	0,000
19,50	,052	0,000
20,50	,041	0,000
21,50	,021	0,000
23,00	0,000	0,000

Disclosure: E. Fernández-Fernández, None; **I. Monjo**, Roche, 2, 6, UCB, 6, Gedeon Richter, 6, Novartis, 6; **E. De Miguel**, Roche, 6, 12, Paid instructor, Abbvie, 2, 5, 6, Novartis, 2, 5, 6, 12, Paid instructor, Pfizer, 2, 5, 6, MSD, 6, BMS, 6, UCB, 6, Grunental, 6, Janssen, 6, 12, Paid instructor, Sanofi, 6, Galapagos, 2.

Abstract Number: 1396

Baricitinib in Relapsing Giant Cell Arteritis: A Prospective Open-Label Single-Institution Study

Matthew Koster[1], Cynthia Crowson[2], Rachel Giblon[1], Ali Duarte-Garcia[1], Jane Jaquith[1], Cornelia M. Weyand[1] and Kenneth Warrington[3], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN, [3]Mayo Clinic, Rochester, Minnesota

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Pre-clinical giant cell arteritis (GCA) mouse models have demonstrated effective suppression of arterial wall lesional T-cells through inhibition of Janus kinase 3 (JAK3) and JAK1. However, the use of JAK inhibition in patients with GCA has not been formerly investigated.

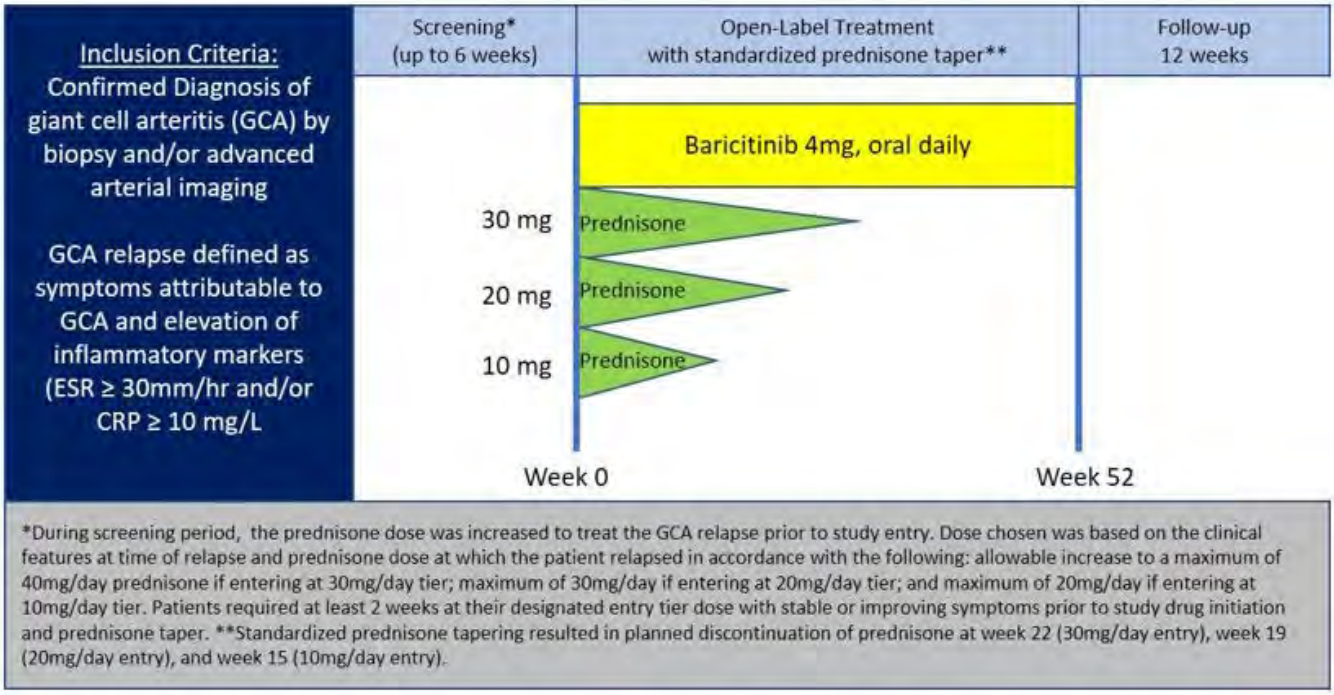

Figure 1. Study Schema.

Table 1. Characteristics at giant cell arteritis diagnosis and relapse prior to study entry

Characteristic	GCA diagnosis (N=15)	Relapse prior to study entry (N=15)
Headache	11 (73)	6 (40)
Scalp tenderness	10 (67)	3 (20)
Jaw claudication	7 (47)	1 (7)
Visual Ischemia	4 (27)	0 (0)
Limb claudication	1 (7)	0 (0)
Polymyalgia rheumatica	4 (47)	8 (53)
Constitutional symptoms	11 (73)	8 (53)
New or worse large vessel vasculitis on arterial imaging	5 (33)	4 (27)
Method of diagnosis		—
TAB (+) / Imaging (+)	5 (33)	
TAB (+) / Imaging (-) or ND	5 (33)	
TAB (-) or ND / Imaging (+)	5 (33)	
TAB, temporal artery biopsy; ND, not done		

Methods: We performed a prospective, open-label, pilot study of baricitinib (4mg/day) in patients with relapsing GCA. The primary outcome was the frequency of adverse events and serious adverse events at week 52. Secondary outcomes included relapse at week 24 and week 52, change in pre-enrollment erythrocyte sedimentation rate (ESR)

Table 2. Study Outcomes

Outcome	Pre-baricitinib relapse	Week 0	Week 24	P-value	Week 52	p-value
Prednisone dose, mg/day**	---	20 (10,30)	0 (0, 0)[γ]	<0.001[ε]	0 (0, 0)	<0.001[ε]
ESR, mm/h*	36.1 (19.3)	10.3 (7.6)	21.1 (29.2)	0.005[ψ]	18.4 (29.8)	0.04[ψ]
CRP mg/L*	22.8 (7.7)	5.2 (3.7)	7.2 (16.9)	0.006[ϕ]	4.0 (3.0)	<0.001[ϕ]
BVAS**	2 (1, 3)	---	0 (0, 0)	<0.001[ϕ]	0 (0, 0)	<0.001[ϕ]
Patient global assessment*	---	22.4 (21.6)	8.6 (12.9)[γ]	0.04[ε]	7.1 (9.1)	<0.007[ε]
Stopped glucocorticoids	---	---	14/14 (100%)	---	13/14 (93%)	---
Relapse on study drug	---	---	1/14 (7%)	---	1/14 (7%)	---

*mean(SD), **median(IQR)
[ϕ]Comparison pre-baricitinib relapse value to week 24; [ψ]comparison pre-baricitinib relapse value to week 52
[γ]Comparison week 0 value to week 24; [ε]comparison week 0 value to week 52

and C-reactive protein (CRP) to week 24 and week 52, and comparison of glucocorticoid dose at enrollment to week 24 and week 52. The study schema is outlined in Figure 1.

Results: 15 patients were enrolled in the study (11, 73% female) with a mean(SD) age at entry 72.4(7.2) years, median (IQR) duration of GCA of 9 (7, 21) months, and median of 1 (1, 2) prior relapse. Treatments prior to study entry included: glucocorticoids (15, 100%); methotrexate (2, 13%); cyclophosphamide (1, 7%); sirukumab (1, 7%). Characteristics at GCA diagnosis and at relapse prior to study entry are listed in Table 1. Four (27%) patients entered the study on prednisone 30mg/day, 6 (40%) at 20 mg/day, and 5 (33%) at 10mg/day. One patient with baseline chronic kidney disease had a decline in renal function below study threshold for continuation and was withdrawn at week 8. The remaining 14 patients completed 52 weeks of baricitinib. At week 52, 14/15 (93%) patients had at least one adverse event recorded with the most frequent events including: infection not requiring antibiotics (n=8), infection requiring antibiotics (n=5), nausea (n=6), leg swelling (n=2), fatigue (n=2), diarrhea (n=1), abdominal pain (n=1). Two patients contracted COVID-19 during the study, both with mild symptoms, neither hospitalized. Only one patient had a serious adverse event during the study (transient thrombocytopenia attributed to concomitant use of antimicrobial therapy).

Study outcomes are highlighted in Table 2. ESR and CRP were significantly lower at week 24 and week 52 compared to pre-enrollment values. Patient global assessment at week 0 was also significantly improved at both week 24 and week 52. Only 1 of 14 (7%) patients relapsed during the study (same patient at week 24 and week 52) The remaining 13 patients achieved steroid discontinuation and remained in disease remission during the duration of the 52-week study. Among patients completing the study, 4/14 (29%) flared during the 12-week follow up period after baricitinib discontinuation.

Conclusion: In this proof of concept study, baricitinib at a dose of 4mg/day appeared both safe and effective in the management of patients with relapsing GCA. Larger randomized clinical trials are needed to determine the utility of JAK inhibition in GCA.

Disclosure: M. Koster, None; **C. Crowson**, None; **R. Giblon**, None; **A. Duarte-Garcia**, None; **J. Jaquith**, None; **C. Weyand**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5.

Abstract Number: 1397

Treatment of Giant Cell Arteritis with Tocilizumab: A Retrospective Cohort Study of 119 Patients

jigisha rakholiya[1], Matthew Koster[1], Hannah Langenfeld[1], Cynthia Crowson[2], Andy Abril[3], Pankaj Bansal[4], Lester Mertz[5], Alicia Rodriguez Pla[6], Rahul Sehgal[4], Benjamin Wang[7] and Kenneth Warrington[8], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN, [3]Mayo Clinic, Ponte Vedra Beach, FL, [4]Mayo Clinic, Eau Claire, WI, [5]Mayo Clinic Arizona, Scottsdale, AZ, [6]Mayo Clinic in Arizona, Scottsdale, AZ, [7]Mayo Clinic, Jacksonville, FL, [8]Mayo Clinic, Rochester, Minnesota

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Giant cell arteritis (GCA) is an inflammatory condition of medium- and large-sized arteries. Prospective clinical trials have demonstrated the efficacy of tocilizumab (TCZ) for treatment of patients with GCA.

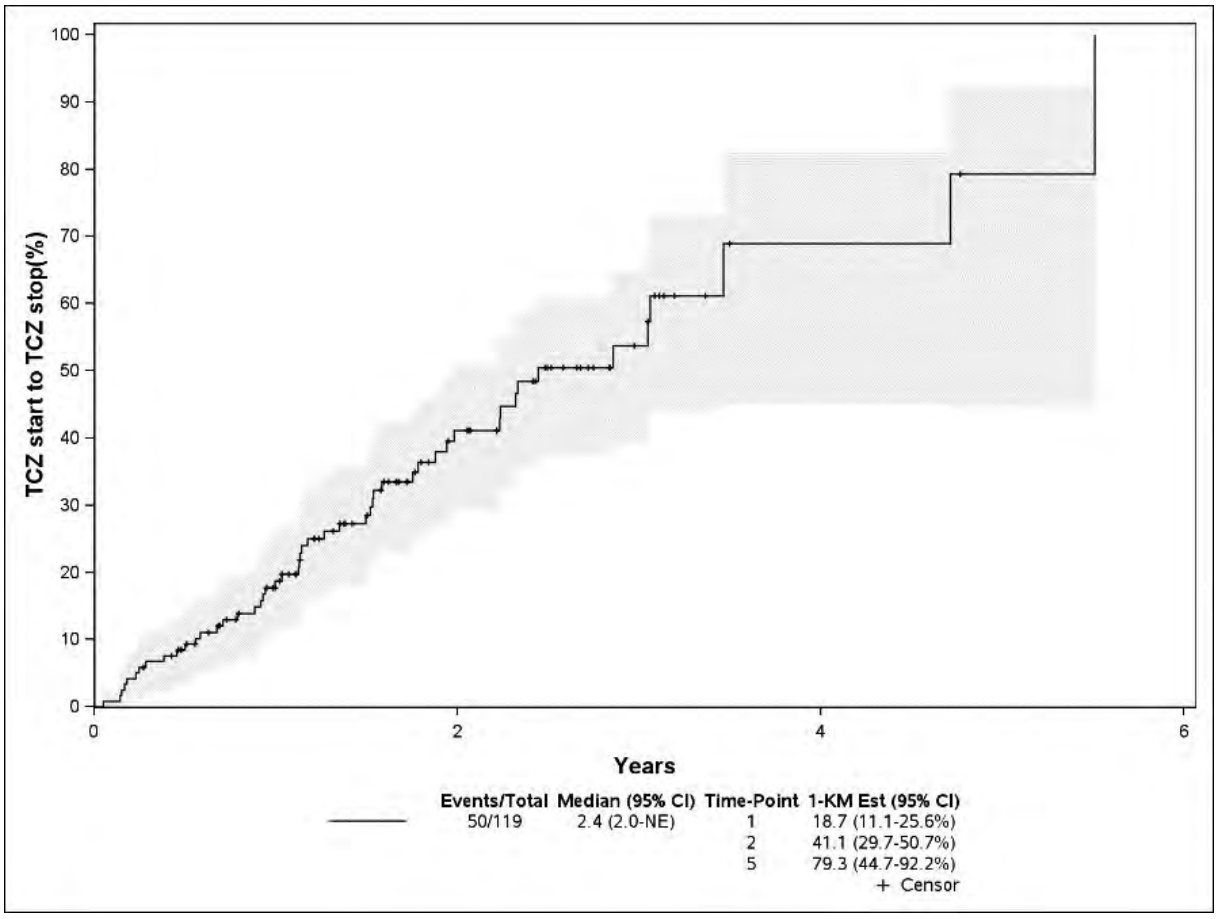

Image 1. Time from TCZ start to TCZ discontinuation.

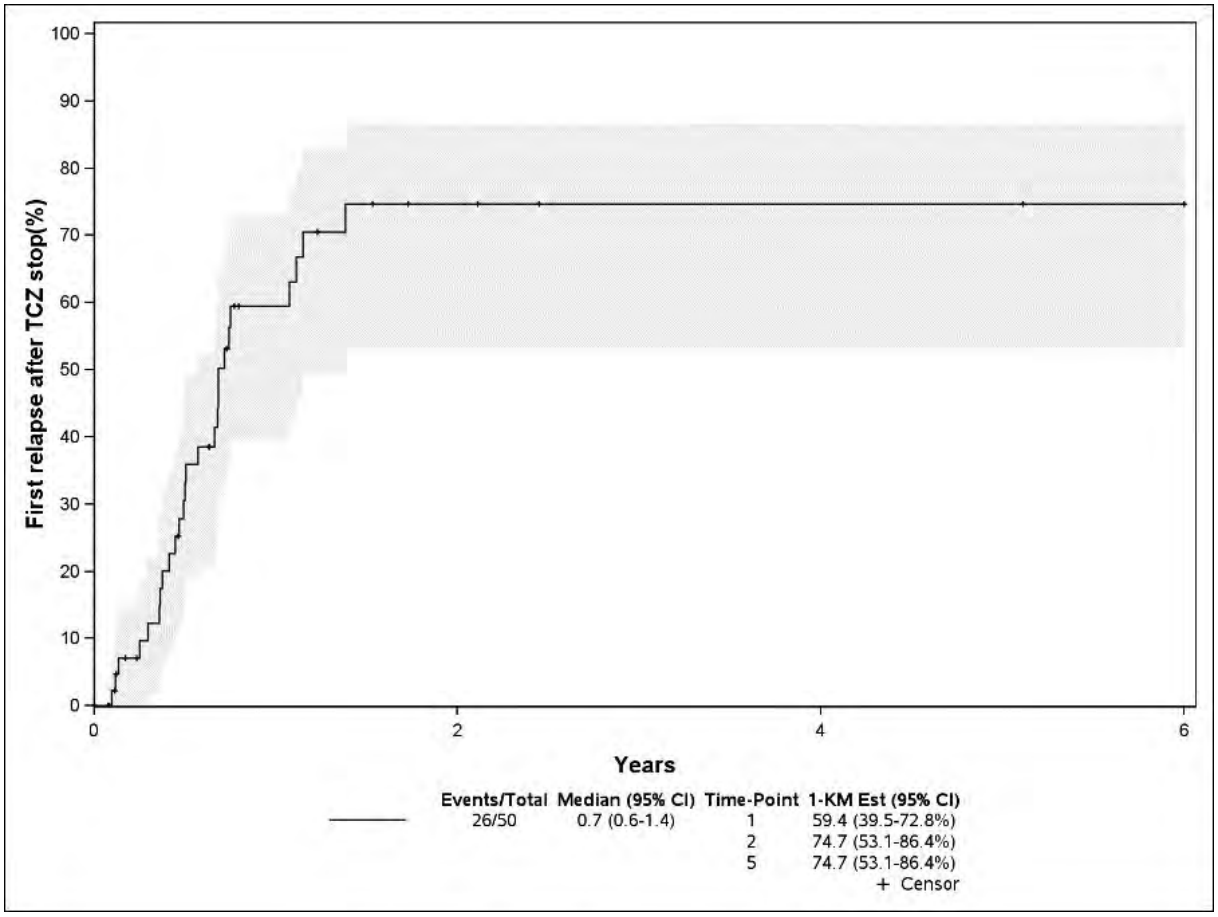

Figure 2. Time to first relapse after TCZ stop.

However, there is a limited data on the use of TCZ in routine clinical practice. The objective of the study was to evaluate the efficacy and safety of TCZ in a retrospective cohort study of patients with GCA treated with TCZ.

Methods: Patients with GCA treated with TCZ at 4 clinical centers of a single tertiary care institution (2000-2020) were identified. The diagnosis of GCA was confirmed by arterial biopsy, large vessel imaging, or clinical diagnosis meeting ACR classification criteria and physician diagnosis. Patient demographics, clinical presentation, laboratory studies, treatment course and adverse events were abstracted from the medical record; only patients with at least 6 months of follow-up after TCZ initiation were included. Kaplan-Meier methods were used to estimate time to TCZ discontinuation and first relapse after discontinuation. Poisson regression models were used to compare relapse rates before and after TCZ initiation.

Table 1. Main outcome variables

	At TCZ initiation	At TCZ discontinuation/last follow up visit
Prednisone dose, mean (SD) mg/day	31 (19)	3.8 (6.6)
ESR, mean (SD) mm/hour	22 (20)	5.9 (9.2)
CRP, mean (SD) mg/L	19.1 (25)	5.4 (16.6)
Relapse rate per year	0.77	0.44

Results: The study included 119 patients [61% female; mean(SD) age at GCA diagnosis 70.3(8.2) years]. The majority of patients (89%) had a biopsy-proven and/or imaging-based diagnosis of GCA, while 13(11%) had a clinical diagnosis of GCA. In addition to glucocorticoids, 40(34%) patients received other immunosuppressive agents prior to TCZ. The method of initial TCZ administration was subcutaneous (162mg/ml) weekly in 48(41%), subcutaneous every other week in 20(17%), monthly 4mg/kg infusions in 34(29%), monthly 8mg/kg infusions in 14(12%) and non-standard dosing in 3 remaining patients. The median(IQR) duration from GCA diagnosis to TCZ initiation was 4.8(1.2-22.0) months. The median(IQR) duration of TCZ treatment was 18(11-28) months. The mean(SD) dose of prednisone at TCZ initiation was 31(19) mg/day and was reduced to a mean(SD) dose of 3.8(6.6) mg/day at TCZ discontinuation/last follow-up visit. The relapse rate per year decreased 43% from 0.77 to 0.44 after the initiation of TCZ (RR=0.57; 95% CI: 0.44-0.75; p< 0.001). The mean(SD) ESR and CRP decreased from 22(20) mm/hour to 6(9.2) mm/hour and from 19.1(25) mg/L to 5.4(16.6) mg/L, respectively from TCZ initiation to TCZ discontinuation/last follow-up visit. At 2 years of follow-up, 67% of patients had discontinued glucocorticoids. At last follow up, 50 patients had discontinued TCZ, only 16 of which were due to adverse events. The median time to TCZ discontinuation was 2.4 years. The most common adverse events were infections and cytopenias. While on TCZ, 1 patient developed new onset vision loss related to GCA and 1 patient, without history of diverticulitis, had bowel perforation. Among those discontinuing TCZ, 61% had relapsed at least once by 1 year after discontinuation.

Conclusion: TCZ use significantly reduced relapse rate and prednisone dosage. Patients tolerated long-term use with only 13% discontinuing due to adverse events. However, the high relapse rate after discontinuation indicates that ongoing use may be required beyond two years to maintain remission.

Disclosure: j. rakholiya, None; **M. Koster**, None; **H. Langenfeld**, None; **C. Crowson**, None; **A. Abril**, None; **P. Bansal**, None; **L. Mertz**, None; **A. Rodriguez Pla**, None; **R. Sehgal**, None; **B. Wang**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5.

Abstract Number: 1398

Adrenal Insufficiency After Glucocorticoid Treatment of Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Adrenal insufficiency is frequently neglected and underappreciated complication of systemic glucocorticoid therapy. We aimed to evaluate the prevalence of glucocorticoid induced adrenal insufficiency in giant cell arteritis (GCA).

Methods: We analysed adrenal function data in a cohort of GCA patients (51 (67.1%) females, median (IQR) age 72.9 (66.3-77.4) years) in whom a discontinuation of methylprednisolone therapy was planned. Adrenal function was tested by Corticotropin (Synacthen®) stimulation test (CST). To perform the CST, methylprednisolone was substituted with hydrocortisone (20mg qd in three divided doses) for one to four weeks before the test. Adrenal insufficiency was defined as cortisol level < 450 nmol/l measured 30 minutes after the corticotropin injection; additionally, the result of

the CST was defined as borderline when the cortisol level 30 minutes after corticotropin injection was between 450 nmol/l and 500 nmol/l.

Results: Adrenal function was tested in 76 GCA patients before definite methylprednisolone withdrawal (after a median 13.5 (12.9 – 24.6) months of glucocorticoid therapy). The mean (SD) methylprednisolone dose, prior to substitution with hydrocortisone and subsequent CST, was 3.7 (0.9) mg. Adrenal insufficiency was detected in 37/76 patients (48.7%); additionally, 10/76 patients (13.2%) had a borderline CST result. Twenty-two patients with either adrenal insufficiency or borderline CST result, had a repeated CST after a median (IQR) 11.6 (8.1; 13.3) months. Adrenal insufficiency persisted in 12/22 (54.5%) patients and was borderline in one patient (4.5%). In 9/22 (40.9%) patients adrenal function recovered meanwhile. A third CST was performed in 6/13 patients with abnormal second CST after median (IQR) 8.3 (6.9; 12.6) months. Adrenal function recovered in one patient, while insufficiency persisted in the remaining 5 patients.

Conclusion: Adrenal insufficiency is frequent and potentially long-lasting glucocorticoid induced adverse event in GCA patients.

Disclosure: A. Hocevar, None; **R. Jese**, None; **J. Kramaric**, None; **M. Tomšič**, None; **Z. Rotar**, None.

Abstract Number: 1399

Validation of a Giant Cell Arteritis Probability Score

Charlie Oshinsky[1], Alison Bays[1], Ingeborg Sacksen[2], Elizabeth Jernberg[3], Eugene zierler[1], Andreas Diamantopoulos[4] and Scott Pollock[1], [1]University of Washington, Seattle, WA, [2]University of Washington, Bellingham, WA, [3]Virginia Mason Medical Center, Seattle, WA, [4]Akerhus University Hospital, Brum, Norway

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

Background/Purpose: Giant cell arteritis (GCA) is the most common large vessel vasculitis. Failure to rapidly diagnose and treat patients with GCA can result in irreversible blindness. The American College of Rheumatology (ACR) developed classification criteria for GCA in 1990. However, these criteria are neither sensitive nor specific. Furthermore, these criteria do not provide a mechanism to quickly risk stratify referrals for GCA as the criteria rely in part on temporal artery biopsy (TAB) results, often not available at the time of referral. Triage, early treatment, and diagnosis would benefit from a GCA probability score. Laskou et al produced the GCA Probability Score (GCAPS) in 2019, which was subsequently used by Sebastian et al to successfully risk-stratify referrals to the Southend fast track clinic (FTC). However, this probability score requires further external validation. We report the results externally validating this probability score from our ultrasound-based FTC in the United States.

Methods: We included subjects referred to the FTC from November 2017 – December 2020. Only subjects with complete data to calculate the probability score were included. Subjects deemed very low risk were not offered an ultrasound for GCA and were not included in this study. All subjects evaluated by rheumatology received an ultrasound for GCA. Subjects received TAB at the discretion of the rheumatologist. A probability score was calculated as defined by Laskou et al, and compared to the low (< 9), intermediate (9-12), and high risk (>12) probability score thresholds as defined by Sebastian et al. Diagnosis of GCA was also compared to the ACR 1990 classification of GCA criteria. A subject was determined to have GCA if this was deemed the most likely diagnosis 6 months after initial presentation.

N	121
Age Median (IQR)	69 (19)
Female (%)	83 (68.6%)
Duration of symptoms (%)	
• >24 weeks	11 (9.1%)
• 12-24 weeks	6 (5.0%)
• 6-12 weeks	10 (8.3%)
• <6 weeks	94 (77.7%)
CRP Median (IQR)	20.7 (44.5)
Headache (%)	91 (75.2%)
PMR	32 (26.4%)
Constitutional	42 (34.7%)
Jaw claudication	18 (14.9%)
Vision symptoms	41 (33.9%)
Vision loss from AION, CRAO, RAPD, field loss	9 (7.4%)
Temporal artery abnormality on exam	28 (23.1%)
Extra-cranial artery abnormality on exam	0 (0%)
Cranial nerve palsy	3 (2.5%)
Known alternative at time or referral (infection, malignancy, systemic rheumatic disease, head and neck pathology, other)	15 (12.4%)
Probability score Median (IQR)	12 (6)
ACR>=3	51 (42.1%)
Ultrasound positive	27 (22.3%)
Diagnosed as GCA	42 (34.7%)

Clinical characteristics and outcomes of subjects evaluated by the fast track clinic for giant cell arteritis.

Results: 166 subjects were referred to the FTC for suspected GCA during the specified time period. 121 had complete data to calculate the probability score (Table 1). 42 subjects were diagnosed with GCA. The median (interquartile range) probability score in the group diagnosed with GCA was 15 (5.75), in those not diagnosed with GCA was 11 (5), and the difference in probability score between the two groups was statistically significant (p=< 0.001). 3/27 subjects with low risk probability score, 12/42 subjects with intermediate risk probability score, and 27/52 subjects with high risk probability score were diagnosed with GCA. The low risk probability threshold was 92.9% sensitive and 30.4% specific (Table 2) for GCA. Of the low risk subjects diagnosed with GCA, one had a negative ultrasound for GCA and other diagnoses are being considered, one subject had negative TAB and ultrasound and was diagnosed based on clinical suspicion, and one subject had evidence of extra-cranial large vessel vasculitis on ultrasound. The high risk probability threshold was 64.3 sensitive and 68.4 specific. The 1990 ACR Classification of GCA Criteria were 52.4% sensitivity and 63.3% specific. Ultrasound was 62.5% sensitive and 97.3% specific.

	Sensitivity	Specificity
ACR criteria	52.38%	63.29%
Vascular ultrasound	62.50%	97.26%
Low Risk probability score	92.86%	30.38%
High risk probability score	64.29%	68.36%

Sensitivity and specificity of diagnostic and screening modalities for GCA.

Conclusion: In our cohort, the low risk probability score was sensitive, but not 100% sensitive, for GCA, and may serve as a reasonable screening tool. The high risk probability score threshold was not specific.

Disclosure: C. Oshinsky, None; **A. Bays**, Genentech, 5, Abbvie, 5; **I. Sacksen**, None; **E. Jernberg**, None; **E. zierler**, None; **A. Diamantopoulos**, Sanofi, 1; **S. Pollock**, None.

Abstract Number: 1400

Analyses of Plasma Inflammatory Proteins Reveal Biomarkers Predictive of Subsequent Development of Giant Cell Arteritis; A Nested Case-Control Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies have demonstrated that metabolic factors may predispose to giant cell arteritis (GCA). The purpose of this study was to investigate the relation between biomarkers of inflammation in biobank samples and subsequent development of GCA.

Methods: Participants in a population-based cohort established in 1991-1996 who were subsequently diagnosed with GCA were identified through register linkage and validated in a structured process. GCA-free controls, matched for sex, year of birth, and year of inclusion, were selected from the study cohort. Plasma samples from cases and controls that had been obtained at inclusion were analyzed using the OLINK proteomics inflammation panel, which measures 92 inflammatory proteins, and provides arbitrary values based on log2 normalized quantification. Variables with a skewed distribution were log transformed, and Z-scores for all proteins were included in conditional logistic regression models with GCA case/control status as the dependent variable. Analyses were pre-designated as hypothesis-driven or hypothesis-generating. A priori hypotheses were formulated for 8 biomarkers. For these, Holm's correction of p-values was applied to account for multiple testing. In the hypothesis-generating part of the study, principal component analysis was used to identify groups of proteins that explain the variance in the pro-

teome. Within components selected based on Eigenvalues, proteins with a factor loading of >0.50 were investigated as potential predictors of GCA. All analyses were stratified by quartile of time from inclusion to GCA diagnosis among the cases.

Results: A total of 94 cases with a confirmed incident diagnosis of GCA (82 % female; 64 % biopsy positive, mean age at diagnosis 73.6 years) were identified and had preserved plasma samples. The median time from inclusion to diagnosis was 11.9 years (range 0.3-19.1). Among biomarkers with a priori hypotheses, IFN-g was positively associated with GCA (odds ratio (OR) 1.52; 95% confidence interval (CI) 1.00-2.30). However, none of the associations in this subset reached statistical significance after correction for multiple testing (Table 1). Of 37 biomarkers with factor loading >0.5 within 6 principal components with Eigenvalues >2.5, 8 were significantly associated with development of GCA (Table 2). Among these, higher levels of IFN-g (OR 2.37; 95% CI 1.14-4.92) and MCP3 (OR 4.27; 95% CI 1.26-14.53) were particularly associated with increased risk of GCA in the subset sampled < 8.5 years before diagnosis. Several other proteins known to be important for T cell function were also associated with GCA in these analyses, e.g. CXCL9, IL-2, CD40 and CCL25 (Table 2).

Table 1 – Relation between plasma biomarkers with a priori hypothesis and development of GCA, overall and stratified for time from inclusion to diagnosis, conditional logistic regression.

	All			**Quartile 1** (0.3-8.5 years)			**Quartile 2** (8.5-11.9 years)			**Quartile 3** (11.9-15.5 years)			**Quartile 4** (15.5-19.1 years)		
	OR (CI)	*P*	*P* (corr)	OR (CI)	*P*	*P* (corr)	OR (CI)	*P*	*P* (corr)	OR (CI)	*P*	*P* (corr)	OR (CI)	*P*	*P* (corr)
IFN-γ	**1.5 (1.0-2.3)**	**0.048**	0.38	**2.4 (1.1-4.9)**	**0.021**	0.17	1.7 (0.8-3.8)	0.18	1.00	1.1 (0.4-3.1)	0.87	1.00	0.6 (0.2-1.8)	0.35	1.00
IL-6	0.9 (0.6-1.4)	0.67	1.00	1.37 (0.6-2.9)	0.41	1.00	1.2 (0.3-4.2)	0.83	1.00	1.4 (0.6-3.6)	0.43	1.00	**0.4 (0.2-1.0)**	**0.038**	0.27
CXCL-10	1.5 (0.9-2.5)	0.10	0.71	**3.3 (1.0-11)**	**0.045**	0.27	2.1 (0.8-5.4)	0.12	0.82	0.82 (0.3-2.1)	0.69	1.00	0.9 (0.3-2.8)	0.85	1.00
CXCL-11	1.4 (0.9-2.2)	0.14	0.82	2.2 (0.8-5.6)	0.95	0.95	**2.6 (1.0-6.6)**	0.04	0.43	0.6 (0.2-1.3)	0.20	1.00	1.4 (0.5-3.6)	0.54	1.00
Caspace-8	0.9 (0.5-1.5)	0.68	1.00	1.4 (0.5-4.0)	0.57	0.57	1.4 (0.6-3.0)	0.42	1.00	1.0 (0.3-3.8)	0.99	1.00	**0.1 (0-0.7)**	**0.016**	0.13
FGF-21	1.0 (0.7-1.5)	0.85	1.00	1.60 (0.7-3.8)	0.28	0.29	0.9 (0.4-1.9)	0.70	1.00	0.7 (0.4-1.3)	0.25	1.00	1.7 (0.7-4.0)	0.22	1.00
PD-L1	1.3 (0.9-2.0)	0.22	1.00	**3.9 (1.1-14)**	**0.037**	0.26	0.74 (0.4-1.5)	0.40	1.00	0.9 (0.3-3.1)	0.86	1.00	2.6 (0.6-12)	0.22	1.00
LIF	1.2 (0.8-1.8)	0.44	1.00	1.2 (0.6-2.2)	0.64	0.64	0.6 (0.2-1.6)	0.35	1.00	1.6 (0.7-3.6)	0.30	1.00	1.6 (0.6-4.6)	0.34	1.00

Odds ratios (OR) per standard deviation with 95 % confidence intervals (CI). P-values with and without Holm's correction for multiple testing

Table 2 – Biomarkers from the hypothesis generating analysis with significant overall association with GCA, stratified for time from inclusion to diagnosis; conditional logistic regression

	All	Quartile 1 (0.3-8.5 years)	Quartile 2 (8.5-11.9 years)	Quartile 3 (11.9-15.5 years)	Quartile 4 (15.5-19.1 years)
	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)	OR (95 % CI)
IFN-γ	**1.52 (1.00-2.30)**	**2.37 (1.14-4.92)**	1.72 (0.78-3.77)	1.09 (0.39-3.06)	0.60 (0.21-1.75)
MCP3	**2.01 (1.24-3.25)**	**3.74 (1.26-11.07)**	2.31 (0.94-5.64)	1.15 (0.41-3.20)	1.44 (0.51-4.02)
CXCL9	**2.17 (1.31-3.59)**	2.22 (0.82-5.98)	**5.67 (1.83-17.56)**	1.00 (0.42-2.39)	1.92 (0.48-7.77)
IL-2	**1.52 (1.02-2.27)**	1.65 (0.83-3.28)	1.23 (0.49-3.10)	1.09 (0.37-3.21)	1.82 (0.88-3.80)
SCF	**1.84 (1.20-2.82)**	1.93 (0.81-4.59)	**3.43 (1.35-8.76)**	0.52 (0.19-1.44)	2.36 (0.99-5.61)
IL-10RB	**1.63 (1.01-2.61)**	2.40 (0.92-6.24)	1.94 (0.74-5.09)	1.21 (0.49-3.02)	1.18 (0.43-3.24)
CD40	**1.66 (1.02-2.70)**	**4.27 (1.26-14.53)**	0.78 (0.34-1.80	1.10 (0.49-2.48)	**8.17 (1.74-38.25)**
CCL25	**1.67 (1.04-2.67)**	1.35 (0.03-73.52)	2.52 (0.90-7.04)	0.91 (0.34-2.44)	1.46 (0.52-4.14)

Odds ratios (OR) per standard deviation with 95 % confidence intervals (CI).

Conclusion: In this nested-case control study, elevated IFN-g levels were found years prior to diagnosis in cases who were subsequently diagnosed with GCA, although we cannot exclude that this finding is due to multiple testing. Principal component analysis revealed that several T cell related proteins that explain a major part of the variance in the proteome were associated with subsequent GCA, suggesting that T cell activation may precede the clinical onset of GCA.

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Abstract Number: 1401

Utility of CRP and ESR in the Assessment of Giant Cell Arteritis Relapse in a Phase 2 Trial of Mavrilimumab

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Although giant cell arteritis (GCA) relapse is mostly defined by the recurrence of GCA signs/symptoms, in patients treated only with glucocorticoids, the C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR) help clinicians assess disease activity. Tocilizumab directly inhibits IL-6-driven acute-phase reactant synthesis in the liver rendering ESR and CRP unreliable for monitoring of disease relapse. Mavrilimumab (MAV), a GM-CSF receptor α inhibitor currently under study for GCA,[1] downregulates inflammation upstream of IL-6. Therefore, we hypothesized that MAV would not interfere with the utility of CRP and ESR in monitoring disease activity.

In this study we analyzed the relationship between CRP/ESR and clinical disease activity in GCA patients treated with MAV.

Methods: New-onset and relapsing GCA patients with active disease were recruited. Glucocorticoid-induced remission (no GCA symptoms and CRP < 1 mg/dL or ESR < 20 mm/hr) was required by baseline. Patients were randomized 3:2 to MAV 150 mg or placebo (PBO) subcutaneously every 2 weeks (wks) plus a protocol-defined 26-wk prednisone taper. The primary efficacy endpoint was time to relapse by Wk 26. Relapse (adjudicated) was defined as recurrent GCA signs/symptoms, and/or new/worsening vasculitis on imaging and concurrent CRP ≥1 mg/dL and/or ESR ≥30 mm/hr. CRP and ESR were measured periodically during the trial. This post hoc analysis assessed the CRP and ESR levels from randomization through Wk 26 in patients with and without relapse by treatment arm.

Results: A total of 70 patients were enrolled (MAV, N=42; PBO, N=28). Relapses occurred in 8 (19.1%) and 13 (46.4%) patients in the MAV and PBO groups, respectively. Unequivocal GCA symptoms were present in 20/21 patients with relapse. In the patient without unequivocal GCA symptoms, flare was determined based on worsening vasculitis by imaging. CRP or ESR were elevated at the time of relapse in all cases regardless of treatment arm (Table). Among 34 MAV recipients without relapse, 47.1% had at least one elevated ESR and 29.4% had at least one elevated CRP value. Among 15 PBO recipients without relapse, 66.7% had at least one elevated ESR and 73.3% had at least one

Table. CRP and ESR levels in patients with or without GCA relapse

Assessment§	Mavrilimumab + Pred-26 N=42	Placebo + Pred-26 N=28	Mavrilimumab + Pred-26 N=42	Placebo + Pred-26 N=28
	With Relapse		Without Relapse	
# of patients	19.1% (8)	46.4% (13)	81.0% (34)‡	53.6% (15)‖
Elevated CRP* or ESR†	**100.0% (8)**	**100.0% (13)**	**58.8% (20)**	**93.3% (14)**
Elevated CRP*	87.5% (7)	76.9% (10)	29.4% (10)	73.3% (11)
Median (interquartile range) mg/dL**	1.8 (1.4 – 6.3)	1.8 (1.2 – 2.8)	2.6 (1.8 – 3.0)	2.0 (1.5 – 3.4)
Elevated ESR†	75.0% (6)	69.2% (9)	47.1% (16)	66.7% (10)
Median (interquartile range) mm/hr**	40 (33 - 73)	49 (33 - 51)	42 (34 - 62)	54 (42 - 59)

§% (#), except where indicated otherwise.
*CRP ≥ 1 mg/dL. Any patient with at least one CRP ≥ 1 mg/dL at any visit from randomization to Wk 26 were included for this analysis.
†ESR ≥ 30 mm/hr. Any patient with at least one ESR ≥ 30 mm/hr at any visit from randomization to Wk 26 were included for this analysis.
‡Four mavrilimumab recipients had self-limited, equivocal symptomatology without concurrent CRP or ESR elevation; all 4 completed the prespecified prednisone taper by Wk 26 without need for rescue glucocorticoids, so relapse was not confirmed. Three of the four patients had asymptomatic CRP or ESR elevation at another timepoint during the study.
‖One placebo-treated patient developed chronic anemia, unexplained weight loss, and elevated ESR at Wk 24, which was assessed by the investigator as relapse but was not confirmed by adjudication because of the absence of unequivocal GCA symptoms or positive imaging. PET-CT showed increased vascular FDG uptake in this patient at Wk 30.
**For patients with relapse, CRP/ESR levels were those associated with the relapse. For patients without relapse, CRP/ESR levels were the maximum value measured from randomization to Wk 26. Local CRP/ESR measurements were used; if local CRP was not available, central measurements were used.
Pred-26 = 26-week prednisone taper

elevated CRP value. Overall, at least one elevated inflammatory marker (ESR or CRP) measurement was observed in 58.8% and 93.3% of patients receiving MAV and PBO, respectively (nominal p-values: 0.03 for ESR/CRP; < 0.01 for CRP; 0.32 for ESR).

Conclusion: The observed association of CRP and ESR elevation with recurrent GCA signs/symptoms supports the feasibility of a stringent definition of relapse (i.e., characteristic clinical manifestations plus increased inflammatory markers) in GCA clinical trials. The frequency and magnitude of CRP and ESR elevations at relapse were similar in both treatment groups, indicating that CRP and ESR retain their clinical value under GM-CSF blockade therapy. Transient CRP and ESR elevation without relapse, indicating possible subclinical activity, occurred more often in PBO recipients.

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Abstract Number: 1402

Clinical, Laboratory and Imaging Outcomes in Tocilizumab-Treated Patients with Large Vessel-Giant Cell Arteritis According to Early Onset Therapy

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SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

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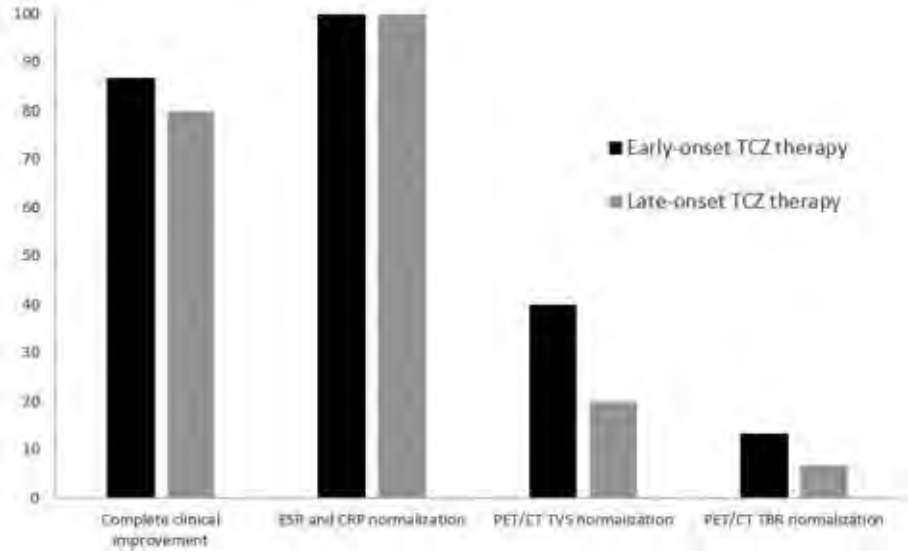
Session Time: 8:30AM–10:30AM

Background/Purpose: Tocilizumab (TCZ) has shown efficacy in large vessel vasculitis (LVV)-Giant Cell Arteritis (LVV-GCA) **(1-2)**. ^{18}F-fluodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) is useful to assess LVV disease activity **(3-5)**. It is unknown if early treatment with TCZ may have an influence on clinical, laboratory and imaging outcomes. Our aim was to assess clinical, laboratory and PET/CT activity improvement in LVV-GCA patients treated with TCZ according to the time from disease diagnosis to TCZ onset.

Methods: Comparative single-center study of 30 LVV-GCA patients treated with TCZ who were divided into 2 groups depending on the time of onset of TCZ: **a)** early onset (≤ 6 months; n=15) and **b)** late onset (> 6 months; n=15). All patients had a baseline and a follow-up PET/CT scan. Complete clinical improvement and normalization of laboratory markers (CRP ≤0.5mg/dL and/or ESR ≤ 20 mm/1st hour) was assessed. For imaging evaluation, normalization of total visual score (TVS) was considered when TVS = 0 and normalization of semiquantitative activity if the target to background ratio (TBR) at the thoracic aorta was < 1.34.

	Early-onset TCZ therapy (n= 15)	Late-onset TCZ therapy (n=15)	p
General features			
Age (years), mean ± SD	65.8 ± 9.9	65.5 ± 10.1	0.94
Sex (female), n (%)	11 (73.3)	13 (86.7)	0.65
GCA evolution before TCZ onset, median [IQR]	2.0 [1.0-5.0]	18.0 [9.0-34.0]	**< 0.01**
Laboratory			
ESR (mm/1st hour), mean ± SD	34.7 ± 26.3	30.8 ± 28.7	0.70
CRP (mg/dL), median [IQR]	1.1 [0.6-2.3]	0.8 [1.8 -2.5]	0.28
Prednisone dose (mg/day), mean ± SD	10.0 [5.9-15.0]	5.0 [5.0-7.5]	**0.01**
TCZ therapy			
Intravenous, n (%)	10 (66.7)	11(73.3)	0.99
Combined with MTX, n(%)	6 (40)	8 (53.3)	0.46
PET /CT activity			
TBR at thoracic aorta	1.86 ± 0.69	1.54 ± 0.18	0.09
TVS	7.0 [4.0-9.0]	3.0 [2.0-5.0]	**< 0.01**
Complete clinical improvement, n (%)	13 (86.7)	12 (80)	0.99
Normalization of ESR and CRP, n (%)	15 (100)	15 (100)	0.99
PET/CT improvement			
Complete TBR normalization	6 (40)	3 (20)	0.23
Complete TVS normalization	2 (13.3)	1 (6.7)	0.54

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TBR: target-to-background ratio. * Normalization of TBR was considered when TBR < 1.34. ** Normalization of TVS was considered when TVS=0.



Results: 30 patients were included (24 women/6 men); mean age 65.7± 9.8 years. Patients in the TCZ early-onset group were receiving higher doses of prednisone (10.0[5.9-15.0] vs 5.0 [5.0-7.5] mg/day; p< 0.01) and had higher TVS scores (7.0 [4.0-9.0] vs 3.0 [2.0-5.0]; p< 0.01) at baseline (**Table**). Following TCZ initiation, after a mean of 10.8±3.7 months, most patients achieved complete clinical improvement and normalization of ESR and CRP in both groups. Uncoupling with imaging outcomes was observed in both groups. Although non-significant statistical differences were observed, complete TBR normalization (TBR < 1.34) and complete TVS normalization (TVS=0) tended to be more frequent in the group ofpatients who received early-onset TCZ therapy (**Figure**).

Conclusion: TCZ was effective in patients with LVV-GCA regardless the time from disease diagnosis to TCZ onset. However, complete normalization of vascular activity in PET/CT scans tended to occur more likely in patients who receive early-onset TCZ therapy within the first 6 months of the disease.

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Abstract Number: 1403

Giant Cell Arteritis Subtypes: Data from the ARTESER Registry

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

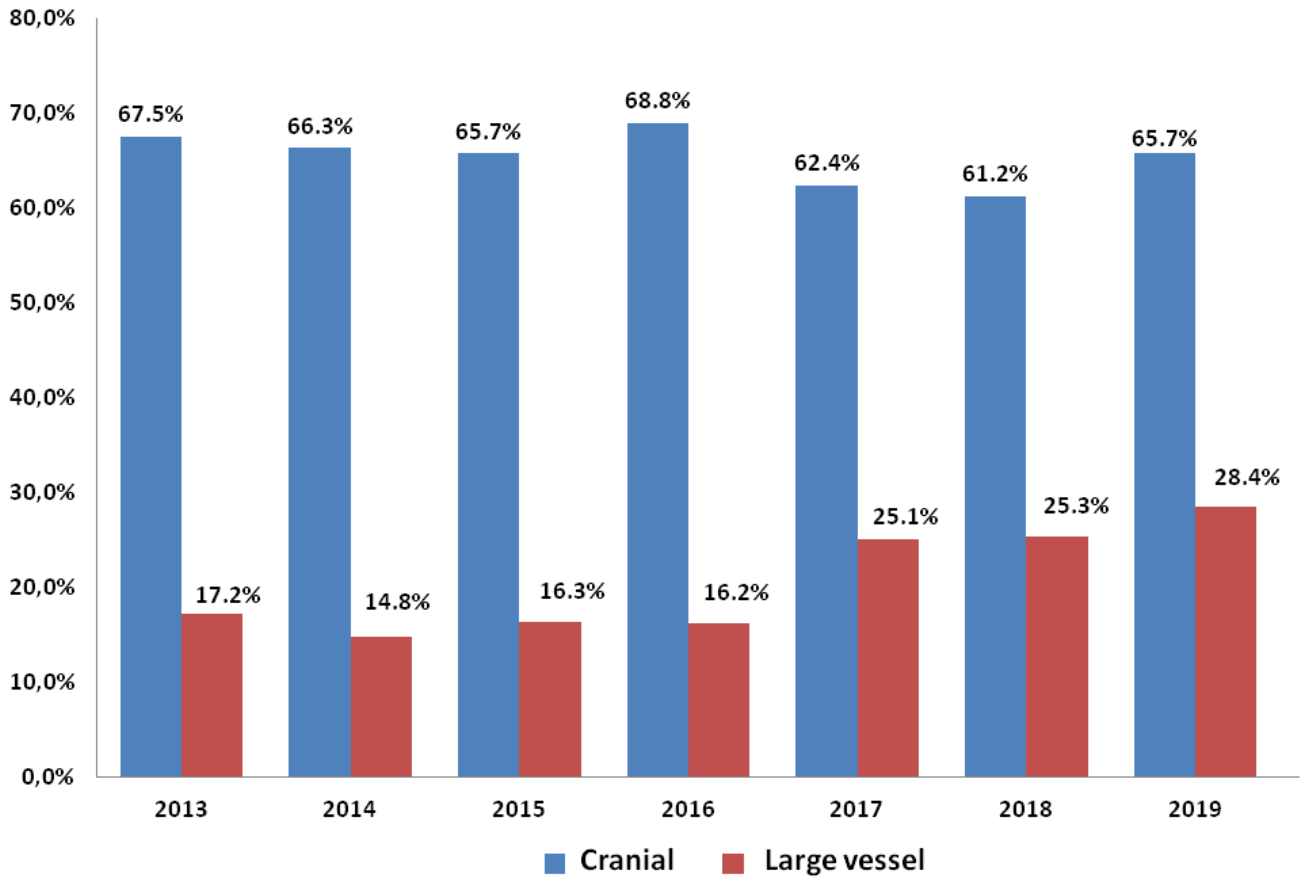
Session Time: 8:30AM–10:30AM

Background/Purpose: Giant cell arteritis (GCA) is the most common systemic vasculitis over 50 years of age. Classically, GCA was assimilated with the involvement of the temporal arteries and a biopsy of these arteries (TAB) was used for its diagnosis. Although the risk of developing aortic aneurysms and large vessel involvement in this disease was well known, the study of the large vessels was not included in the standard diagnosis process. Nowadays, with the incorporation of imaging techniques, the diagnosis of GCA extracranial forms is more and more frequent. The objective of this study was to determine the frequency of cranial and extracranial vessel involvement in our population with GCA.

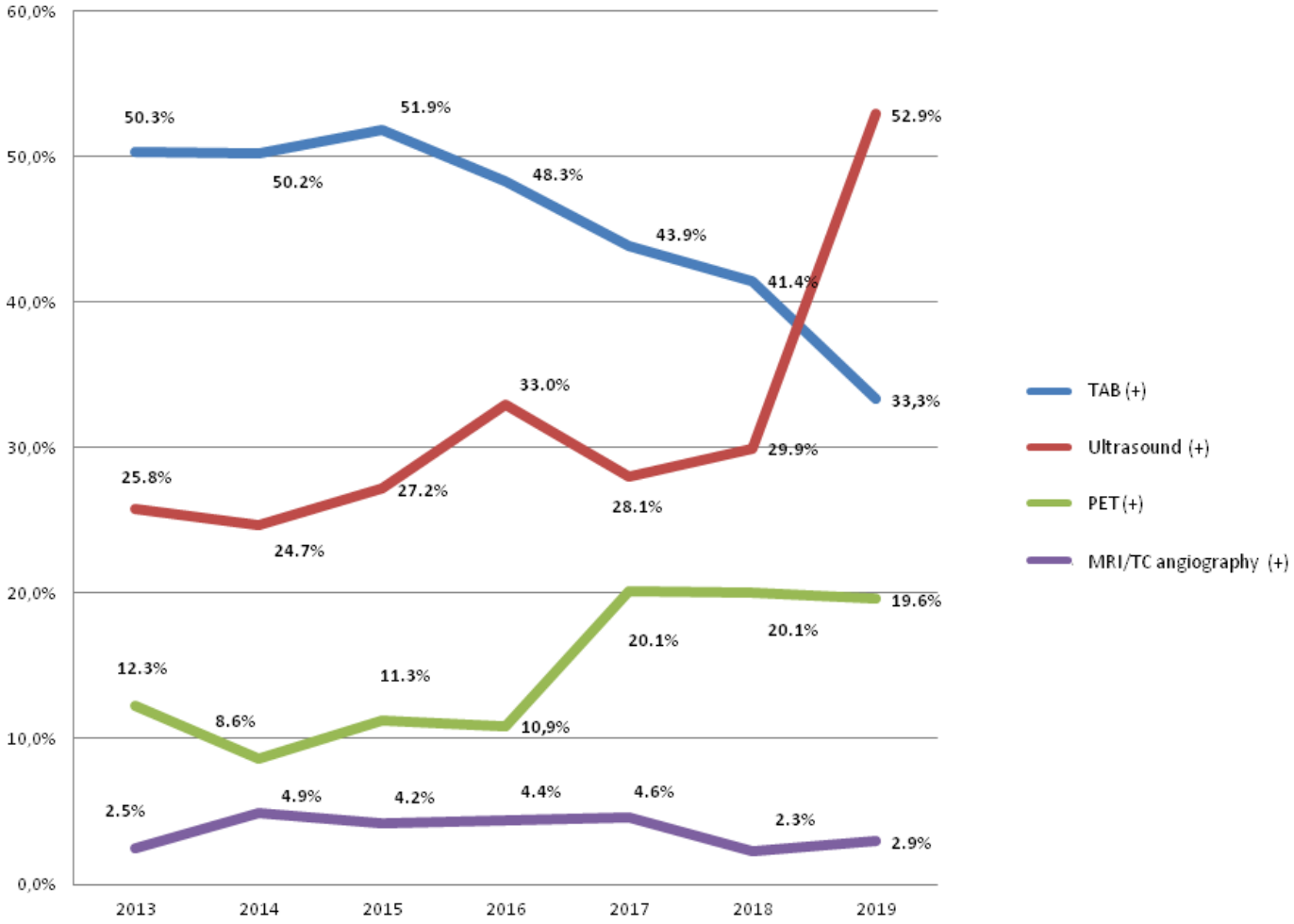
Methods: ARTESER is a multicenter observational retrospective study promoted by the Spanish Society of Rheumatology with 26 participating centers and in which patients diagnosed with GCA between June 1 2013 and March 29 2019 were included. The gold standard for the diagnosis of the disease was the opinion of the responsible physician according to the clinical, analytical, imaging and TAB data available. This analysis includes the data collected from TAB and imaging (ultrasound, PET, and MRI/CT-angiography) as support to classify the patient as having a cranial and/or extracranial GCA subtype.

Results: 1675 patients with GCA were included. Mean age ± SD was 76.9 ± 8.1 years and gender distribution was 1178 (70.3%) women and 497 (29.7%) men. From the data collected, it was found that 1091 patients had cranial involvement, 331 extracranial involvement and 170 patients had mixed involvement (cranial and extracranial). The Figure 1 shows how the frequency of extracranial involvement has increased in recent years, coinciding with the increase of the use of imaging tests in diagnosis. The Figure 2 shows how the ultrasound diagnosis increased from 25.8% in 2013 to 52.9% in 2019, and PET increased from 12.3% in 2013 to 19.6% in 2019. TAB was performed in the 46.3% of the patients and contributed to the diagnosis of cranial forms. Since imaging tests were not performed in all patients, and that the increase in their use is directly related with the increase in the diagnosis of forms with extracranial large vessel involvement, it is likely that the frequency of large vessel GCA increases by the next years. As a limitation, it should be noted that the subtype of vascular involvement was not detailed in 253 patients.

Conclusion: The forms with cranial involvement are the most frequent in GCA. The diagnosis of large vessel GCA has increased in recent years in direct relation to the increase in the diagnostic use of imaging tests. The diagnosis of extracranial vessel involvement it is likely to increase in the coming years.



Evolution of GCA subtypes cranial and extracranial along the time



GCA: Temporal evolution of diagnostic tests

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Lower Frequency of Comorbidities Prior to Onset of Giant Cell Arteritis; A Population-based Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Advancing age, female sex and white race are well-known risk factors for development of giant cell arteritis (GCA). Recent studies suggest that certain metabolic features such as lower fasting blood glucose (FBG) may predispose to GCA. However, risk factors for development of GCA remain incompletely understood. We aimed to assess the frequency of comorbidities and metabolic risk factors at, and prior to, onset of GCA.

Methods: We conducted a retrospective case-control study of patients diagnosed with incident GCA in a geographically defined population from 01/01/2000 till 12/31/2019. Two age- and sex-matched controls were identified for every GCA case and assigned an index date corresponding to the incidence date of GCA. Twenty-five chronic conditions from either the Charlson, Elixhauser, or Rheumatic Disease Comorbidity Index were identified using ICD-9 diag-

Table 1. Demographic and comorbidities using ICD-9 Coding among GCA cases and controls

Table 1: Demographics and Comorbidities using ICD-9 coding among GCA cases and controls				
	At index date		At 5-year prior to index date	
	Cases (N=129)	Controls (N=253)	Cases (N=117)	Controls (N=226)
Demographics				
Age, Mean (SD)	77.1 (8.1)	77.0 (8.1)	72.1 (8.2)	71.5 (8.2)
Females, n (%)	96 (74.4)	190 (75.1)	88 (75.2)	171 (75.7)
Non-Hispanic White, n (%)	127 (98.4)	241 (95.3)	115 (98.3)	216 (95.6)
Comorbidities, n (%)				
Alcohol Abuse	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Deficiency Anemias	**19 (14.7)***	**20 (7.9)***	2 (1.7)	15 (6.6)
Cancer	7 (5.4)	15 (5.9)	8 (6.8)	12 (5.3)
Congestive Heart Failure	9 (7.0)	19 (7.5)	4 (3.4)	9 (4.0)
Coagulopathy	0 (0.0)	3 (1.2)	0 (0.0)	4 (1.8)
Dementia	1 (0.8)	3 (1.2)	0 (0.0)	1 (0.4)
Depression	6 (4.7)	9 (3.6)	2 (1.7)	10 (4.4)
Diabetes Mellitus	**7 (5.4)***	**43 (17.0)***	**2 (1.7)***	**30 (13.3)***
Drug Use	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Fracture of leg, hip, or spine	1 (0.8)	8 (3.2)	0 (0.0)	3 (1.3)
Human Immunodeficiency Virus	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Hypertension	54 (41.9)	115 (45.5)	**32 (27.4)***	**101 (44.7)***
Hypothyroidism	21 (16.3)	30 (11.9)	11 (9.4)	31 (13.7)
Liver Disease	0 (0.0)	2 (0.8)	0 (0.0)	3 (1.3)
Metastatic Cancer	0 (0.0)	4 (1.6)	0 (0.0)	2 (0.9)
Myocardial Infarction	3 (2.3)	10 (4.0)	1 (0.9)	8 (3.5)
Other Neurological Disorders	10 (7.8)	16 (6.3)	4 (3.4)	5 (2.2)
Paralysis	1 (0.8)	1 (0.4)	0 (0.0)	1 (0.4)
Pulmonary Circulation Disorders	2 (1.6)	2 (0.8)	1 (0.9)	0 (0.0)
Psychoses	2 (1.6)	7 (2.8)	1 (0.9)	7 (3.1)
Chronic Pulmonary Disease	10 (7.8)	17 (6.7)	4 (3.4)	16 (7.1)
Peripheral Vascular Disease	13 (10.1)	14 (5.5)	3 (2.6)	5 (2.2)
Renal Failure	4 (3.1)	9 (3.6)	1 (0.9)	6 (2.7)
Stroke	11 (8.5)	15 (5.9)	2 (1.7)	8 (3.5)
Valvular Disease	13 (10.1)	14 (5.5)	6 (5.1)	11 (4.9)
Total Comorbidities, Mean (SD)	1.5 (1.7)	1.5 (1.6)	**0.7 (1.0)***	**1.3 (1.4)***
***p-value<0.05**				

Table 2. Clinical and laboratory data of GCA cases and controls at incidence, 5-years and 10-years prior

Table 2: Clinical and laboratory data of GCA cases and controls at incidence, 5-years, and 10-years prior

	At index date		At 5-years prior to index date		At 10-years prior to index date	
	Cases (N=129) *Median (Q1, Q3)*	Controls (N=253) *Median (Q1, Q3)*	Cases (N=117) *Median (Q1, Q3)*	Controls (N=226) *Median (Q1, Q3)*	Cases (N=117) *Median (Q1, Q3)*	Controls (N=226) *Median (Q1, Q3)*
Systolic BP (mm Hg)	128 (121, 140)	130 (120, 140)	132 (120, 142)	130 (120, 140)	132 (122, 144)	132 (124, 148)
Diastolic BP (mm Hg)	70 (62, 76)	70 (62, 78)	74 (66, 80)	72 (66, 80)	75 (70, 83)	78 (70, 84)
Height (cm)	163.0 (156.2, 168.9)	162.0 (157.0, 168.5)	162.8 (156.2, 169.3)	162.5 (157.9, 168.0)	162.8 (156.2, 170.1)	162.6 (158.5, 167.6)
Weight (kg)	**67.5 (57.3, 79.2)***	**73.3 (62.3, 83.4)***	**70.9 (61.5, 81.0)***	**73.3 (62.4, 86.9)***	70.8 (61.7, 81.4)	74.0 (63.9, 85.9)
Body Mass Index (kg/m²)	**25.1 (23.0, 28.4)***	**27.7 (24.4, 30.9)***	**25.8 (23.1, 29.9)***	**27.7 (24.0, 31.7)***	26.0 (23.4, 30.1)	27.8 (24.4, 31.1)
Hemoglobin (gm/dL)	**12.0 (11.2, 13.1)***	**13.4 (12.2, 14.4)***	13.5 (12.8, 14.1)	13.5 (12.6, 14.3)	13.3 (12.7, 14.2)	13.7 (12.8, 14.6)
Leukocytes(x10^9/L)	**9.4 (7.7, 11.3)***	**6.8 (5.5, 8.2)***	6.3 (5.3, 8.1)	6.3 (5.4, 7.7)	6.3 (5.6, 7.6)	6.1 (5.2, 7.2)
Platelets (x10^9/L	**352.5 (261.0, 459.8)***	**223.0 (192.0, 274.8)***	225.0 (198.0, 264.0)	225.0 (188.0, 271.0)	236.5 (205.0, 268.5)	227.0 (191.0, 263.0)
TSH levels (mIU/L)	2.0 (1.3, 3.1)	2.0 (1.2, 3.0)	2.1 (1.5, 3.4)	1.9 (1.0, 2.9)	2.3 (1.5, 3.8)	2.0 (1.2, 3.0)
Fasting Blood Glucose (mg/dL)	104.0 (94.8, 114.0)	103.0 (93.0, 114.5)	**96.0 (90.0, 102.5)***	**104.0 (93.8, 117.3)***	**93.0 (88.8, 101.3)***	**98.0 (93.0, 111.5)***
Creatinine (mg/dL)	0.9 (0.7, 1.0)	1.0 (0.8, 1.2)	**0.9 (0.8, 1.1)***	**1.0 (0.9, 1.2)***	0.9 (0.9, 1.1)	1.0 (0.9, 1.1)
Total cholesterol (mg/dL)	181.0 (154.5, 207.5)	185.0 (157.0, 213.0)	**211.0 (187.0, 234.5)***	**201.0 (177.5, 221.0)***	204.5 (181.3, 231.5)	207.5 (181.5, 239.0)
High density lipoprotein (HDL) mg/dL	59.0 (48.0, 70.0)	54.0 (44.0, 66.0)	**62.0 (52.0, 74.5)***	**57.0 (45.0, 67.0)***	60.5 (49.3, 72.0)	57.0 (45.5, 71.0)
Low density lipoprotein (LDL) mg/dL	95.0 (77.0, 121.0)	98.5 (78.0, 119.8)	**123.0 (97.0, 139.5)***	**112.5 (88.0, 129.3)***	112.0 (98.0, 138.5)	122.0 (91.0, 141.0)
Triglycerides (mg/dl)	101.0 (78.0, 158.0)	121.0 (87.0, 167.0)	107.0 (90.0, 167.5)	132.0 (93.0, 183.0)	109.0 (73.0, 183.0)	127.0 (95.8, 166.8)

*p-value <0.05

nosis codes within a two-year lookback period; 2 or more codes ≥30 days apart were used to define a comorbidity. Prevalence of comorbidities, clinical and laboratory data among cases and controls were compared at incidence date and 5 years prior. Subjects with less than one year of diagnosis history were excluded from each analysis. Medical records of all subjects were manually abstracted for comorbidities and laboratory data at incidence date, at 5 years, and at 10 years prior to incidence date. Comparisons were performed using Chi square, Fisher exact, or t-tests.

Results: The cohort included 129 patients with GCA (74% female, mean age at diagnosis 77 years) and 253 controls (Table 1). At GCA incidence/index date, the prevalence of diabetes mellitus (DM) was lower in patients with GCA (5% vs 17%; p=0.001) while that of other comorbidities was similar in cases and controls. At 5 years prior to incidence/index date, cases had a lower prevalence of DM (2% vs 13%; p< 0.001) and hypertension (HTN) (27% vs 45%; p=0.002) as compared to controls. The mean number (SD) of comorbidities at 5 years prior to incidence/index date was lower [0.7 (1.0)] in cases than controls [1.3 (1.4)] (p< 0.001) (Table 1).

Moreover, at 5 years prior to incidence/index date, cases had a significantly lower median FBG (96 vs 104 mg/dL; p < 0.001) and body mass index (BMI) (25.8 vs 27.7 kg/m^2; p-value=0.019) as compared to controls. At 10 years prior to the incidence/index date, the median FBG among cases was also lower (93 vs 98 mg/dL; p=0.002), although BMI was not significantly different at this time point. On the other hand, total cholesterol (median 211 vs 201 mg/dL; p=0.036), low-density lipoprotein (123 vs 112 mg/dL; p=0.043), and high-density lipoprotein (62 vs 57 mg/dL; p=0.032) were higher among cases compared with controls at 5 years prior to incidence/index date, and no different at 10 years prior. (Table 2).

Conclusion: Development of GCA was associated with a lower prevalence of DM and HTN, and lower total number of comorbidities, at 5 years prior to incidence date. FBG and BMI were also lower among individuals who later developed GCA, suggesting that metabolic factors influence the risk of GCA. Future studies to elucidate the pathomechanisms underlying these observations are warranted.

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Effectiveness of Tocilizumab in Cranial and Extracranial Phenotypes of Giant Cell Arteritis: Multicenter Study of 471 Cases

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SESSION INFORMATION

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Background/Purpose: Giant cell arteritis (GCA) may be divided into cranial, and extracranial GCA phenotypes. Tocilizumab (TCZ) has shown efficacy and safety in GCA.

Our aim was to compare the efficacy of TCZ in cranial and extracranial phenotypes of GCA.

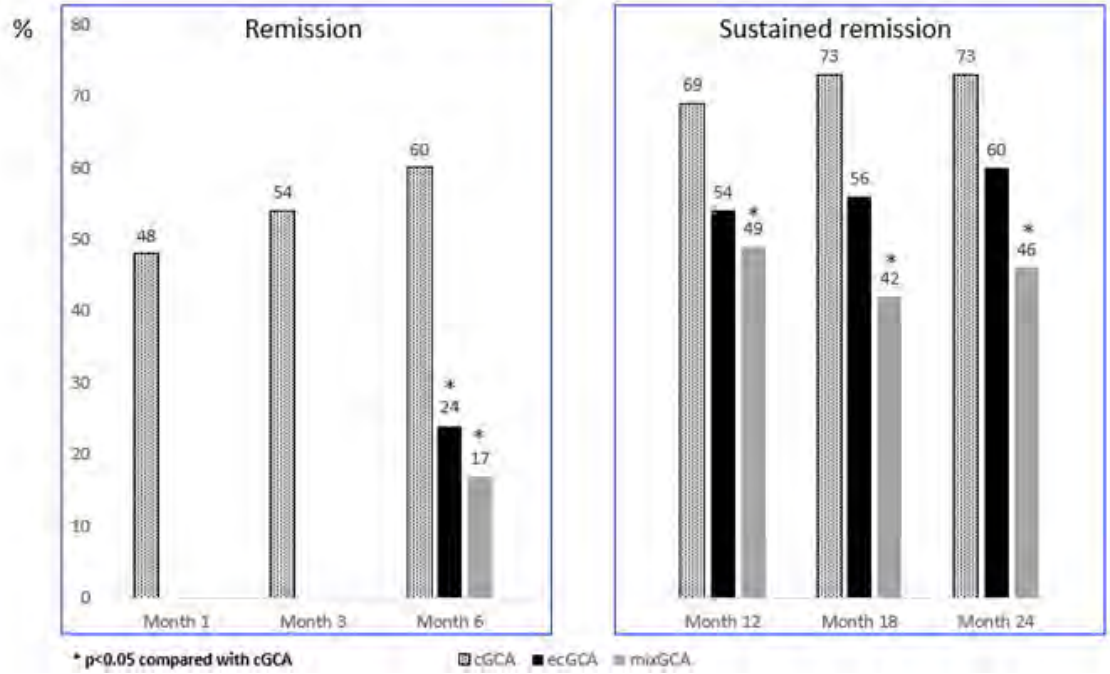
Methods: Multicenter observational study of 471 patients with GCA treated with TCZ. Patients were divided into 3 groups: **a)** exclusively cranial involvement (cGCA), **b)** exclusively extracranial involvement (ecGCA) and **c)** mixed involvement (mixGCA). GCA was diagnosed by: **a)** ACR criteria and/or **b)** temporal artery biopsy and/or **c)** imaging

TABLE. Main features of the 471 GCA patients at TCZ onset.

	Overall (n=471)	cGCA (n=217)	ecGCA (n=80)	mixGCA (n=174)	Cranial vs Extracranial GCA p
Main features					
Age at TCZ onset, years, mean± SD	74±9	76±8	68±10	73±8	**0.000***
Sex, women/men, n (% women)	342/129 (73)	156/61 (72)	60/20 (75)	126/48 (72)	0.699
Time from diagnosis to TCZ onset (months, median [IQR]	6 [2-18]	5 [2-17]	5 [2-15.5]	9 [3-24]	0.699
Biopsy-proven GCA, n (%)	201 (43)	122 (56)	0 (0)	79 (45)	**0.000***
Systemic manifestations at TCZ onset, n (%)					
Fever, n (%)	57 (12)	24 (11)	10 (12)	23 (13)	0.919
Constitutional syndrome, n (%)	175 (37)	64 (29)	34 (43)	77 (44)	0.057
PmR, n (%)	284 (60)	122 (56)	54 (68)	108 (62)	0.145
Ischemic manifestations at TCZ onset, n (%)					
Visual involvement, n (%)	81 (17)	58 (27)	0 (0)	23 (13)	**0.000***
Headache, n (%)	259 (55)	159 (73)	0 (0)	100 (57)	**0.000***
Jaw claudication, n (%)	112 (24)	76 (35)	0 (0)	36 (21)	**0.000***
Acute phase reactants					
ESR, mm/1st hour, median [IQR]	32 [12-57]	30 [9-60]	32.5 [14-53]	28 [14-53]	0.438
CRP, mg/dL, median [IQR]	1.5 [0.5-3.4]	1.2 [0.3-3.8]	1.4 [0.5-2.3]	1.5 [0.6-3.5]	0.733
Prednisone dose at TCZ onset, mean ± SD	20 [10-40]	30 [15-45]	15 [10-25]	20 [10-30]	**0.000***
TCZmono/TCZcombo, n (% TCZ mono)	353/118 (75)	176/41 (81)	51/29 (64)	126/48 (72)	**0.003***
Follow-up (months), mean ± SD	25.3±21.7	24.5±19.6	26.4±21.4	25.8±24.2	0.613

Abbreviations: CRP: C-reactive protein; ESR: erythrocyte sedimentation rate, GCA: giant cell arteritis, IQR: interquartile range, PmR: polymyalgia rheumatica; SD: standard deviation, TCZcombo: tocilizumab in combination with synthetic immunosuppressants (besides corticosteroids), TCZmono: tocilizumab in monotherapy (besides corticosteroids)

FIGURE. Remission and sustained remission of ecGCA and mixGCA according to EULAR recommendations. In the first 3 months we only could assess cGCA because in most patients with ecGCA and mixGCA a control imaging test was not performed.



tests. Remission and sustained remission were defined according to EULAR definitions. In ecGCA and mixGCA we also assessed improvement (complete or partial) by imaging techniques.

Results: We studied 471 patients (342 women/129 men; mean age: 74±9 years). **TABLE** shows the main characteristics of the 3 groups. Remission at 6 months was observed in a higher number of patients with cGCA, as well as the sustained remission at 12, 18 and 24 months **(FIGURE)**. Partial/complete improvement by imaging techniques at 6, 12, 18 and 24 months was 67%/17%, 58%/19%, 63%/16% and 56%/33%, respectively in ecGCA, and 81%/12%, 57%/29%, 85%/11% and 73%/13% in mixGCA.

Conclusion: TCZ seems to be more effective in the cGCA phenotype. Improvement by imaging techniques was partial and rarely complete in ecGCA and mixGCA.

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Abstract Number: 1406

Incidence and General Clinical Features of Giant Cell Arteritis in the ARTESER Multicenter Study

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Table 1. Incidence rate by age groups and sex from June 2013 to March 2019 (x 100,000 inhabitants ≥50 years)

Table 1. Incidence rate by age groups and sex from June 2013 to March 2019 (x 100,000 inhabitants =50 years)						
	Men		Women		Total	
Age group	N	Incidence rate (95% CI)	N	Incidence rate(95% CI)	N	Incidence rate (95% CI)
From 50 to 54	6	1.58 (1.38-1.79)	7	1.92 (1.62-2.22)	13	1.71 (1.53-1.88)
From 55 to 59	11	3.54 (3.11-3.97)	28	8.69 (7.90-9.47)	39	5.95 (5.50-6.39)
From 60 to 64	25	8.70 (8.11-9.28)	49	17.08 (15.90-18.25)	74	12.61 (11.95-13.28)
From 65 to 69	49	19.96 (18.65-21.27)	123	46.96 (44.86-49.06)	172	32.98 (31.74-34.21)
From 70 to 74	73	36.64 (34.29-38.98)	203	89.17 (85.89-92.44)	276	62.51 (60.50-64.52)
From 75 to 79	121	80.62 (76.70-84.54)	283	150.22 (145.74-154.69)	404	115.36 (112.41-118.30)
From 80 to 84	121	100.31 (96.11-104.51)	290	158.84 (153.65-164.02)	411	130.12 (126.71-133.54)
From 85 to 89	74	110.98 (103.94-118.02)	146	120.11 (114.86-125.36)	220	112.59 (108.48-116.71)
90 and up	17	55.17 (49.08-61.25)	49	65.28 (59.97-70.59)	66	59.63 (55.60-63.66)
TOTAL	**497**	**27.77 (27.19-28.35)**	**1178**	**57.87 (57.05-58.69)**	**1675**	**42.67 (40.62-44.71)**

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Epidemiological information on Giant Cell Arteritis (GCA) comes mainly from the Scandinavian countries of northern Europe, which show a higher incidence than the countries of southern Europe. GCA clinical manifestations can be divided into cranial, extracranial, and general syndrome.

In a large series of GCA from Spain, we studied **a)** the incidence of GCA, **b)** clinical manifestations, and **c)** comorbidities at the time of disease diagnosis.

Methods: ARTESER is a retrospective epidemiological observational study of GCA promoted by the Spanish Society of Rheumatology in which 26 hospitals participate. The inclusion criteria were: all new patients diagnosed with GCA by a) ACR criteria, b) positive diagnostic test (temporal artery biopsy, temporal artery ultrasound or other relevant imaging techniques) and/or c) investigator's clinical judgment. The patient recruitment period ranged from June 1, 2013 to March 29, 2019. The overall incidence of GCA per 100,000 people ≥50 years for the whole period and the mean annual incidence were evaluated. The clinical variables were collected by reviewing the patient's medical history.

Results: 1675 patients were included. The average annual incidence rate was 7.42 (95% CI: 6.57-8.27). All the cases were older than 50 years, and the age group with the highest incidence was that of 80 to 84 years, where it reached a value of 130.12 (95% CI: 126.71-133.54). The mean annual incidence is higher in women than in men 10.06 (95% CI: 8.7-11.5) vs 4.83 (95% CI 3.8- 5.9) (**Table 1**).

The description of the population is shown in **Table 2**, the mean age at diagnosis was 76.9±8.1 years, 1178 (70.3%) were women. ACR criteria were met by 1400 (83.6%) patients and an objective diagnostic test by 1258 (75.1%). The

Table 2. General characteristics, comorbidities and clinical manifestations

Table 2. General characteristics, comorbidities and clinical manifestations			
Demographic and general data	**Men**	**Women**	**Total**
Gender, n (%)	497 (29.7)	1178 (70.3)	1675
Race, n (%)			
Caucasian	494 (99.4)	1168 (99.2)	1662 (99.2)
African	0 (0.0)	1 (0.1)	1 (0.1)
Latin American	2 (0.4)	9 (0.8)	11 (0.7)
Others	1 (0.2)	0 (0.0)	1 (0.1)
Age at diagnosis, years, mean (SD)	76.9 (8.3)	76.9 (8.0)	76.9 (8.1)
Age at onset of symptoms, years, mean (SD)	76.7 (8.3)	76.7 (8.1)	76.7 (8.2)
Time between symptoms and diagnosis, years, mean (SD)	2.5 (4.5)	3.1 (6.1)	2.9 (5.7)
GCA diagnosis, n (%)			
ACR criteria	400 (80,5)	1000 (84,9)	1400 (83,6)
Objective tests	384 (77,3)	874 (74,2)	1258 (75,1)
Temporal artery biopsy (Positive)	240 (48.3)	536 (45.5)	776 (46.3)
Temporary arterial ultrasound (Positive)	169 (34.0)	313 (26.6)	482 (28.8)
Other relevant imaging tests	138 (27.8)	290 (24.6)	428 (25.6)
Clinical diagnosis	24 (4.8)	38 (3.2)	62 (3.7)
Comorbidities at diagnosis			
Arterial hypertension, n (%)	330 (66.8)	749 (63.7)	1079 (64.6)
Diabetes Mellitus, n (%)	134 (27.2)	217 (18.6)	351 (21.1)
Dyslipidemia, n (%)	238 (48.3)	563 (47.9)	801 (48.0)
Osteoporosis, n (%)	22 (4.5)	260 (22.3)	282 (17.0)
Tobacco consumption, n (%)			
Former smoker	63 (13.4)	69 (6.3)	132 (8.4)
Smoker	216 (46.0)	84 (7.7)	300 (19.1)
Never been a smoker	191 (40.6)	944 (86.1)	1135 (72.4)
Obesity (>30 BMI), n (%)	34 (7.0)	115 (9.8)	149 (9.0)
Alcohol consumption, n (%)	93 (18.9)	26 (2.2)	119 (7.1)
Cardiovascular disease, n (%)	163 (33.1)	204 (17.4)	367 (22.0)
Chronic renal failure, n (%)	55 (11.2)	112 (9.6)	167 (10.0)
Neoplasms, n (%)	95 (19.3)	109 (9.3)	204 (12.3)
Cranial clinical manifestations			
New-onset headache, n (%)	382 (76.9)	955 (81.1)	1337 (79.9)
Temporal artery pulse sensitivity or decrease, n (%)	231 (46.5)	593 (50.4)	824 (49.2)
Scalp hypersensitivity, n (%)	127 (25.6)	324 (27.5)	451 (26.9)
Visual Clinic, n (%)	194 (39.0)	411 (34.9)	605 (36.1)
Mandibular claudication, n (%)	172 (34.6)	425 (36.1)	597 (35.7)
Facial pain, n (%)	55 (11.1)	158 (13.4)	213 (12.7)
Vertigo, n (%)	38 (7.6)	89 (7.6)	127 (7.6)
Ischemic and / or hemorrhagic stroke, n (%)	25 (5.0)	38 (3.2)	63 (3.8)
Dysphagia, n (%)	25 (5.0)	31 (2.6)	56 (3.3)
Hearing loss, n (%)	16 (3.2)	29 (2.5)	45 (2.7)
Transient ischemic attack, n (%)	13 (2.6)	19 (1.6)	32 (1.9)
Extracranial			
Polymyalgia rheumatica, n (%)	178 (35.8)	521 (44.3)	699 (41.8)
Lower limb claudication, n (%)	53 (10.7)	104 (8.8)	157 (9.4)
Claudication of upper limbs, n (%)	38 (7.6)	114 (9.7)	152 (9.1)
Peripheral synovitis, n (%)	27 (5.5)	59 (5.1)	86 (5.2)
General syndrome			
Asthenia, n (%)	239 (48.1)	634 (53.9)	873 (52.2)
Anorexia, n (%)	180 (36.2)	428 (36.4)	608 (36.3)
Weight loss, n (%)	174 (35.0)	367 (31.2)	541 (32.3)
Low-grade fever or fever, n (%)	113 (22.7)	254 (21.6)	367 (21.9)
Analysis at diagnosis			
Erythrocyte sedimentation rate mm/h, years, mean (SD)	72.3 (34.7)	77.4 (33.0)	75.9 (33.6)
Hemoglobin, g/dl, years, mean (SD);	12.3 (1.8)	11.6 (1.5)	11.9 (1.6)
Platelets, x 10^2/L, years, mean (SD)	302.3 (144.3)	337.0 (192.5)	326.6 (180.0)
Alkaline phosphatase, IU/L, years, mean (SD)	109.8 (92.6)	112.3 (97.3)	111.5 (95.9)
Alanine transaminase, IU/L, years, mean (SD)	24.6 (18.9)	21.4 (21.8)	22.4 (21.0)
Aspartate transaminase, IU/L, years, mean (SD)	23.0 (15.7)	21.5 (17.5)	21.9 (17.0)

more frequent comorbidity was arterial hypertension (n=1079; 64.6%), followed by dyslipidemia (n=801, 48%). The predominant cranial manifestation was headache, (n= 1337; 79.9%) and 605 patients experienced visual symptoms (36.1%). Polymyalgia rheumatica (n=699; 41.8%) and asthenia (n=837; 52.2%) were the most frequent extracranial and general syndrome manifestation, respectively. Regarding laboratory parameters, the most characteristic data was the increase of ESR (75.9±33.6 mm/1st h).

Conclusion: The mean annual incidence of GCA in Spain, 7.42 (95% CI: 6.57-8.27), is lower than that of the Scandinavian countries. It is higher in people older than 80 years. Cranial manifestations constituted the most clinical features. The most frequent clinical manifestations are cranial. Up to a third of patients had visual manifestations.

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Abstract Number: 1407

Characterization of Synovial Fluid T Cells in Polymyalgia Rheumatica: Implication of Th1 and Tc1 Effector Memory Profiles

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: Polymyalgia Rheumatica (PMR) is a common rheumatic inflammatory disease in the elderly. PMR is characterized by synovial inflammation of (peri)articular structures in the shoulders and hips. Patients are treated with glucocorticoids. Targeted treatments are lacking since little is known about the synovial pathobiology of PMR. We aim to investigate the phenotype and function of various T cell subsets in blood and synovial fluid of patients with PMR.

Methods: Blood samples were obtained from 18 newly diagnosed PMR patients before treatment, and 36 age- and sex-matched healthy controls. In addition, paired blood and bursal synovial fluid (subacromial-subdeltoid bursa, subscapular bursa) or tenosynovial fluid (biceps long head) samples were collected from 9 patients with active PMR. The following T cell subsets were identified by flow cytometry: T naive (CD45RO-CCR7+), central memory (CD45RO+CCR7+), effector memory (CD45RO+CCR7-), effector memory re-expressing CD45RA (CD45RO-CCR7-) cells and CD28null senescent cells. Expression of intracellular cytokines (IL-17A, IFN-γ, IL-4) was determined at 4 hours after stimulation with PMA/calcium ionophore.

Results: The frequencies of all major T cell subsets were similar in the blood of patients with PMR and healthy controls. Synovial fluid of patients with PMR was enriched with effector memory CD4+ and CD8+ T cells, whereas the

percentage of CD28null senescent CD8+ T cells was lower in the synovial fluid than in blood. Synovial fluid T cells demonstrated a capacity to produce IFN-γ rather than IL-17 or IL-4.

Conclusion: Synovial fluid T cells in PMR show a non-senescent effector memory phenotype with the capacity to produce IFN-γ, a Th1/Tc1 type cytokine. Our study provides first insights into T cell populations at the site of inflammation in patients with PMR.

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Abstract Number: 1408

Treatment of Giant Cell Arteritis in the ARTESER Multicenter Study of 1675 Patients

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

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Background/Purpose: Glucocorticoids (GC) are the mainstay therapy in Giant Cell Arteritis (GCA), initially at high doses (40-60 mg/day) followed by gradual glucocorticoid tapering. This treatment, especially in older patients, is associated with numerous adverse effects (AE). In addition, there are frequent relapses. Therefore, conventional synthetic immunosuppressants such as methotrexate (MTX), leflunomide, azathioprine, cyclophosphamide or my-

cophenolate, have been used with controversial results. Studies with biological immunosuppressants, such as TNFi have been ineffective; in contrast, tocilizumab (TCZ) has obtained positive results and was approved for the treatment of GCA.

In the ARTESER study we describe **a)** treatment with GC, synthetic or biological immunosuppressants and concomitant treatments; **b)** AE of CG; and **c)** evolution.

Methods: ARTESER is a retrospective observational study sponsored by the Spanish Society of Rheumatology. 26 Spanish centers participated and all new patients diagnosed with GCA from June 1, 2013 to March 29, 2019 were included. Data on GC and immunosuppressants were collected at the beginning and during the follow-up of GCA patients. For the calculation of the cumulative dose of GC, an application was developed that, by including the periods of time, dose and type of GC received during follow-up, performs the automatic calculation in mg of prednisone.

Results: Of the 1675 patients included, GC treatment was adequately recorded in 1650 patients **(Table 1)**. All received oral treatment, being prednisone the most frequently drug used (N=1602, 97.09%). In addition, 426 (25.82%) patients received at least one iv pulse of methylprednisolone, being the 1000 mg regimen the most frequent (n=217; 50.9%). The total mean duration of GC treatment was 22.65 months. The mean cumulative dose per patient at the end of follow-up was 8514.98 mg of prednisone.

The most prescribed concomitant treatment at the time of diagnosis of GCA was calcium (n=1281, 76.9%), vitamin D (n=1258, 75.6%) and bisphosphonates (n=831, 50.1%). The most widely used immunosuppressant was MTX both at diagnosis (n=165; 9.9%) and during follow-up (n=532; 31.8%), followed by TCZ, at diagnosis (22; 1.3%) and at follow-up (153; 9.1%).

AE with GC were described in 393 patients (23.8%), highlighting serious infections (n=67; 10.03%) followed by diabetes mellitus (n=63; 9.43%), steroid myopathy (n=53; 7.9%), vertebral fractures (n=47; 7.04%), non-vertebral fractures (n=36; 5.39%), heart failure (n=36; 5.39%), arterial hypertension (n=34; 5.09%) and neuropsychiatric alterations (n=27; 4.04%).

During the follow-up, 334 (19.9%) patients had relapses, 532 (31.8%) were hospitalized on some occasion, and 142 patients (8.48%) died. The main cause of death were infections (n=44; 30.99%), neoplasms (n=23; 16.2%), cardiovascular (n=15; 10.56%), and cerebrovascular (n=10; 7.04%).

Table 1. Corticosteroid treatment

Table 1. Corticosteroid treatment	
Patients taking oral corticosteroid	1650
Prednisone, n (%)	1602 (97.09)
Methylprednisolone, n (%)	164 (9.94)
Deflazacort, n (%)	64 (3.88)
Patients receiving intravenous corticosteroid, n (%)	426 (25.82)
Patients receiving pulses n (%)	426
125 mg pulse	52 (12.2)
250 mg pulse	65 (15.3)
500 mg pulse	130 (30.5)
1000 mg pulse	217 (50.9)
Mean duration of steroid treatment, mean (SD)	22.65 (17.36)
Mean cumulative dose at the end of follow-up per patient, mg of prednisone, mean (SD)	8514.98 (6570.21)

Table 2. Immunosuppressant and concomitant treatments

Table 2. Patients with immunosuppressive treatment at diagnosis *(no more than 30 days have passed between the diagnosis of GCA and the start of treatment)*	
Methotrexate, n (%)	165 (9.9)
Leflunomide, n (%)	2 (0.1)
Azathioprine, n (%)	3 (0.2)
Cyclophosphamide, n (%)	7 (0.4)
Mycophenolate, n (%)	1 (0.1)
Tocilizumab, n (%)	22 (1.3)
Patients with immunosuppressive treatment during follow-up	
Methotrexate, n (%)	532 (31.8)
Leflunomide, n (%)	19 (1.2)
Azathioprine, n (%)	26 (1.5)
Cyclophosphamide, n (%)	10 (0.6)
Mycophenolate, n (%)	10 (0.6)
Tocilizumab, n (%)	153 (9.1)
Patients with treatments concomitant to diagnosis	
Aspirin prior to diagnosis, n (%)	313 (18.8)
Aspirin initiation after diagnosis, n (%)	585 (35.4)
Calcium initiation after diagnosis, n (%)	1281 (76.9)
Initiation of Vitamin D after diagnosis, n (%)	1258 (75.6)
Bisphosphonate initiation after diagnosis, n (%)	831 (50.1)

Conclusion: The main treatment for GCA was oral GC, which were required for almost two years on average, in a quarter of patients associated with IV pulses. The cumulative steroid dose was high as well as the side effects. MTX was the most widely used immunosuppressant and TCZ was prescribed in 10%. Relapses and admissions at the hospital were relatively frequent.

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Clinical Features at Disease Onset of Different Subsets of Large-vessel-giant Cell Arteritis in a Monocentric Cohort of 100 Patients

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Giant Cell Arteritis (GCA) is the most frequent systemic vasculitis in patients older than 50 years involving medium-sized and large arteries. Inflammation of the extracranial branches of the carotid artery gives rise to the classic symptoms of GCA. However, GCA involves also the aorta and its major branches in almost two-thirds of patients (1,2). Large vessel involvement leads to a different atypical clinical picture which can be challenging to diagnose (3). More information on clinical presentation and vessel involvement in large-vessel GCA are needed to better diagnose it. The aim of this study is to analyze a large cohort of GCA comparing patients with large-vessel involvement to patients with classical cranial disease.

Methods: 100 consecutive patients with a clinical diagnosis of GCA were enrolled in this retrospective study. All patients were older than 50 years of age, met the ACR criteria for GCA (4) or had a positive temporal artery biopsy or evidence of large vessel vasculitis at FDG-PET/CT scan.

Results: Based on vascular involvement, patients were classified into three group: 61 patients with only cranial arteritis (C-GCA), 16 patients with only extracranial large vessel vasculitis (LV-GCA) and 23 patients with both cranial and large vessel involvement (LV-C-GCA).

	GCA (n: 100)	C-GCA (n: 61)	LV-C-GCA (n: 23)	LV-GCA (n: 16)	*p*
Age: median (IQR)	76 (67-79)	75 (71-80)	74 (69-77)	63 (59-72)	0.001
Female	68 (68%)	38 (62%)	17 (74%)	13 (81%)	0.276
Male	32 (32%)	23 (38%)	6 (26%)	3 (19%)	0.276
Time between symptom onset and diagnosis (weeks)	8 (4-20)	4 (3-12)	12 (4-16)	20 (16-82)	<0.001
Cranial symptoms (overall)	84 (84%)	61 (100%)	23 (100%)	0 (0%)	<0.001
New temporal headache	77 (77%)	58 (95%)	19 (83%)	0 (0%)	<0.001
Visual symptoms	39 (39%)	34 (56%)	5 (22%)	0 (0%)	<0.001
Jaw or tongue claudication	35 (35%)	27 (44%)	8 (35%)	0 (0%)	0.004
Fever	48 (48%)	23 (38%)	14 (61%)	11 (69%)	0.032
Fatigue	75 (75%)	40 (66%)	21 (91%)	14 (88%)	0.023
Weight loss	52 (52%)	28 (46%)	13 (57%)	11 (69%)	0.235
Polymyalgia rheumatica	43 (43%)	27 (44%)	13 (57%)	3 (19%)	0.061
Arm or leg claudication	5 (5%)	0 (0%)	4 (17%)	1 (6%)	0.005
CRP (C-reactive protein)	83 (45-127)	77 (39-115)	89 (50-134)	95 (20-124)	0.461
ESR (erythrocyte sedimentation rate)	72 (47-96)	70 (46-88)	75 (28-105)	66 (44-91)	0.711
Cranial arteries	84 (84%)	61 (100%)	23 (100%)	0 (0%)	<0.001
Carotid arteries	19 (19%)	0 (0%)	12 (52%)	7 (44%)	<0.001
Subclavian and upper limb arteries	21 (21%)	0 (0%)	10 (43%)	11 (69%)	<0.001
Thoracic aorta	29 (29%)	0 (0%)	15 (65%)	14 (88%)	<0.001
Abdominal aorta	21 (21%)	0 (0%)	10 (43%)	11 (69%)	<0.001
Iliac and inferior limb arteries	10 (10%)	0 (0%)	6 (26%)	4 (25%)	<0.001

Compared to C-GCA, patients with large vessel involvement (LV-GCA and LV-C-GCA) were younger and more frequently women, and the difference was further significant for patients with isolated LV-GCA. Patients with isolated LV-GCA had also the longer duration of symptoms at GCA diagnosis [LV-GCA 20(16-82) vs LV-C-GCA 12(4-16) vs C-GCA 4(3-12) weeks; p< 0.001]. Systemic symptoms, as fever and fatigue, were associated with large vessel involvement, both in LV-GCA and LV-C-GCA groups. Polymyalgia rheumatica was equally reported in all three groups and no significant differences were found in inflammatory markers levels according to vessel involvement. In patients with large vessels involvement (LV-GCA and LV-C-GCA) thoracic aorta, subclavian arteries and abdominal aorta were the most frequently involved arteries.

Conclusion: GCA is not a single entity but includes several patterns of disease. Female gender, younger age and systemic symptoms are associated with large vessel involvement, regardless the presence or absence of cranial symptoms. The different clinical manifestations of large vessel GCA lead to a longer time to diagnosis if compared to C-GCA. For these reasons, in patients with the aforementioned characteristics, a large vessel involvement should be considered in order to reduce the time to diagnosis.

1: De Boysson H, et al. Clin Exp Rheumatol 2019; 2: Prieto-González S, et al. Ann Rheum Dis 2012; 3: Muratore F, et al. Rheumatol 2015; 4: Hunder GG, et al. Arthritis Rheum 1990

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Predictors of Relapse in Giant-Cell Arteritis: A Retrospective Single Center Analysis

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SESSION INFORMATION
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Background/Purpose: Giant Cell Arteritis (GCA) is the most common systemic vasculitis in North America, typically affecting Caucasian female adults over 50 years of age. Flares and relapses requiring increased and prolonged steroidal medication remains a common trend in patients with GCA. The adverse effects of steroid therapy, and the morbidity and mortality associated with relapsing GCA, is well described however, predictors of relapse remains an understudied area.

Methods: A retrospective chart analysis was performed on 400 patients with an associated ICD10 code diagnosis of GCA seen at Loma Linda University Health from 2013 to 2020. 60 patients were identified with confirmed diagnosis of GCA based on either a positive temporal artery biopsy or meeting the ACR 1990 GCA classification criteria confirmed by a Rheumatologist. We used Pearson's chi-square to test for independence between demographic, clinical categorical variables, and relapse status. We then used logistic regression to model the relapse binary outcome regressed on permanent vision loss, new onset headache, fever, anterior ischemic optic neuritis, abnormal vascular ultrasound, and pulse steroid as predictor variables. We set alpha equal to 0.05 for statistical significance.

Table 1. Demographic and Comorbid Conditions

	All	Relapse, n=37	No Relapse, n=23	*p*-value[a]
Gender, % (*n*)				
Male	14	16.2% (6)	34.8% (8)	0.098
Female	46	83.8% (31)	65.2% (15)	
BMI, kg/m^2, mean ± SD	60	29.35 ± 7.37	27.19 ± 6.62	0.606
Age, years, mean ± SD	60	71.62 ± 10.32	71.35 ± 10.29	0.97
Ethnicity, % (*n*)				
Caucasian	31	59.5% (22)	39.1% (9)	
Asian	6	10.8% (4)	8.7% (2)	
African American/Black	5	8.1% (3)	8.7% (2)	
Hispanic/Latino	18	21.6% (8)	43.5% (10)	
Delay in treatment >3 months	4	8.1% (3)	4.3% (1)	0.57
Comorbid Conditions at Diagnosis				
Cerebrovascular Accident	7	85.7% (6)	14.3% (1)	0.154
Coronary Artery Disease	20	70% (14)	30% (6)	0.311
Hyperlipidemia	29	75.9% (22)	24.1% (7)	0.029
Diabetes Mellitus	29	75.9% (22)	24.1% (7)	0.029
Hypertension	44	63.6% (28)	36.4% (16)	0.603
Anticoagulation Use	8	62.5% (5)	37.5% (3)	0.989
History of Smoking	20	65%(13)	61.5% (24)	0.79
Obesity	21	71.4% (15)	28.6% (6)	0.25

Percentages are estimated across rows and may not add to one-hundred due to rounding.

[a]*p*-value based on the chi-square statistic for categorical variables. Data shown for rows displays only yes category values.

Results: A total of 60 patients were included, of which 46 were female, with an average age of 71 years old and BMI of 28. In our cohort, relapse was defined as an increase in prednisone dose by ≥10 mg for at least two weeks within the first 12 months of GCA diagnosis.

Overall, Caucasians had a higher rate of relapse when compared to other ethnicities, other demographic information was similar between the two groups (Table 1). We found that Hyperlipidemia (HLD), Diabetes Mellitus (DM), and the use of pulse steroids were not independent of relapse status. Those with HLD were more likely to relapse compared to those without HLD (p=0.029). The same outcomes were seen in DM (Table 1). We noted that a higher proportion of patients who relapsed were also those who did not receive pulse steroids (p=0.039) (Table 3). Furthermore, the use of pulse steroids at the time of diagnosis decreased the odds of relapse in this group of patients [OR 0.325 (95% CI 0.110, 0.961)].

Those in the relapse group also had a higher proportion of Cerebrovascular Accidents, Coronary Artery Disease, Hypertension, Obesity, elevated creatinine, and were on anticoagulation treatment at the time of diagnosis. A higher proportion of the relapse group presented with new onset headache, jaw claudication, scalp ischemia, facial pain/ trigeminal neuralgia, and fever (Table 1). In addition, this group were more likely to have been diagnosed via positive temporal artery biopsy (Table 3).

Table 2. Initial Presentation, Laboratory, and Imaging data

	All	Relapse, n=37	No Relapse, n=23	*p*-value[a]
Initial Presentation at Diagnosis				
New Onset headache	52	61.5% (32)	38.5% (20)	0.96
Abnormal Temporal Artery	19	57.9% (11)	42.1% (8)	0.682
Scalp Ischemia	9	77.8% (7)	22.2% (2)	0.26
Facial Pain/Trigeminal neuralgia	23	65.2% (15)	34.8% (8)	0.69
Jaw Claudication	22	63.6% (14)	36.4% (8)	0.811
PMR symptoms	39	56.4% (22)	43.6% (17)	0.254
Unintentional Weight Loss	13	61.5% (8)	38.5% (5)	0.96
Fever (T>100.4)	16	75% (12)	25% (4)	0.2
Anterior Ischemic Optic Neuritis	21	52.4% (11)	47.6% (10)	0.31
Permanent Vision Loss	22	59.1% (13)	40.9% (9)	0.75
Transient Vision Changes	20	65% (13)	35% (7)	0.71
Laboratory Data at Presentation				
Elevated ESR	50	58% (29)	42% (21)	0.361
Elevated CRP	51	56.9% (29)	43.1% (22)	0.099
Elevated Creatinine	6	83.3% (5)	16.7% (1)	0.25
Elevated IL6	12	58.3% (7)	41.7% (5)	0.831
Elevated Liver function tests	9	55.6% (5)	44.4% (4)	0.68
Elevated Alkaline Phosphatase	4	25% (1)	75% (3)	0.19
Anemia	11	36.4% (4)	63.6% (7)	0.06
Elevated Platelet count	5	60% (3)	40% (2)	0.94
Elevated WBC count	12	41.7% (5)	58.3% (7)	0.11
Imaging				
Main Aortic Branch Stenosis on CT	7	42.9% (3)	57.1% (4)	0.28
Temporal/Axillary Ultrasound				
Positive Halo Sign	6	50% (3)	50% (3)	0.54
Negative	54	63% (34)	37% (20)	

Percentages are estimated across rows and may not add to one-hundred due to rounding.
[a]*p*-value based on the chi-square statistic for categorical variables. Data shown for rows displays only yes category values not complete chi-square table.

Conclusion: In our cohort, we found patients with comorbidities such as HLD and DM, as well as patients who did not receive pulse steroids were more likely to relapse within the first 12 months of GCA diagnosis. A few clinical manifestations at the time of diagnosis were associated with higher rates of relapse. Our findings suggest certain clinical manifestations and patient comorbidities may provide meaningful insight in relapse prediction. Larger scale studies are required to replicate our findings.

Table 3. Modality of Diagnosis, Steroid use

	All	Relapse, n=37	No Relapse, n=23	*p*-value[a]
Modality of Diagnosis				
Clinical	39	56.4% (22)	43.6% (17)	0.25
Biopsy	21	71.4% (15)	28.6% (6)	
Pulse Steroids				
Yes	29	48.3% (14)	51.7% (15)	0.039
No	31	74.2% (23)	25.8% (8)	

Percentages are estimated across rows and may not add to one-hundred due to rounding.

[a]*p*-value based on the chi-square statistic for categorical variables.

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Decreased Use of Ultrasound Fast-track Pathways of Giant Cell Arteritis Due to COVID-19 Pandemic: A Potential Risk for Permanent Visual Loss

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Background/Purpose: The implementation of ultrasound (US) fast-track pathways (FTP), aiming at an early diagnosis of giant cell arteritis (GCA), has led to a decrease in permanent vision loss. However, the COVID-19 pandemic lock-down has had a negative impact in GCA patients, leading to a decline in referral rates of patients accompanied by cases with delayed presentation and vision loss.

The aim of our analysis was to assess the rate of US examinations included in our FTP and the rate of permanent visual loss due to GCA since the COVID-19 pandemic.

Methods: Retrospective observational study including patients referred to our US FTP for evaluation of possible GCA over a 16-month period. Visual loss due to anterior ischemic optic neuropathy (AION) confirmed by ophthalmology evaluation was checked. The gold standard for GCA diagnosis was the clinical confirmation after 6-months of follow-up. We compared the 8-month pre- and post- COVID-19 outbreak periods (July 2019 to February 2020 and March 2020 to October 2020).

Results: Since the beginning of the COVID-19 pandemic, 31 patients were referred to the FTP compared with 50 patients in the previous 8-months (38% reduction), although the service was regularly operating. The number of newly GCA diagnosis during the COVID-19 pandemic remained similar, although the percentage over the total examinations was higher (45.2% vs 22%; p=0.028). We found no notable differences in clinical referral patterns. However, it is note-

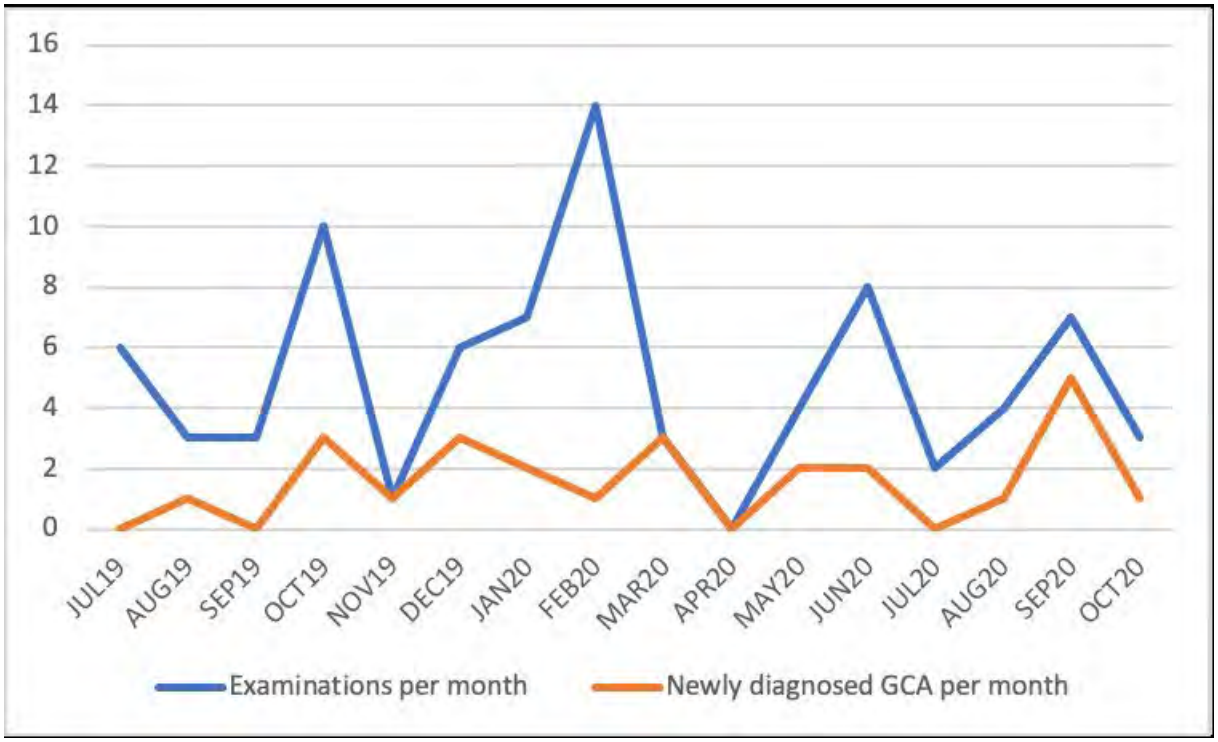

Figure 1. Number of patients evaluated in the fast-track pathway and number of newly GCA diagnosis over the study period.

worthy that 2 patients presented with AION during the COVID-19 pandemic, while noN AION in the previous period, although these differences were not statistically significant (p=0.14). During confinement, patients referred to the FTP presented higher C-reactive protein (7.6 vs 3.4 mg/dL; p=0.008), erythrocyte sedimentation rate (73.9 vs 45.7mm/h; p=0.02), platelets (342.1 vs 254.1 10^9/L; p=0.001) and lower hemoglobin levels (11.7 vs 12.8 g/dL; p=0.019). We found that the halo and compression sign were more frequently found during the COVID-19 pandemic (38.7 vs 16%; p=0.021 and 25.8 vs 10%; p=0.06, respectively). It is also worth highlighting a higher proportion of positive temporal artery biopsy during the COVID-19 pandemic (50% vs 33% p=0.049).

Conclusion: Our data shows a reduction in utilization of GCA FTP since the COVID-19 outbreak and an increase of possibly preventable AION. US FTP has demonstrated to be useful in the reduction of permanent vision loss (1,4), so an impaired use of this tool may lead to worse outcomes. Our results go in line and confirm previous work that noticed a reduction in the requests for FTP assessments by May 2020 (3) . Although a higher proportion of patients referred to the FTP had GCA, the number of newly diagnosed GCA remained similar before and after the COVID-19 outbreak, in contrast with other studies that observed an increased number of GCA after the COVID-19 outbreak(5,6).

Our study highlights the potential risks of COVID-19 lockdown in the reduced referral of suspected GCA patients, the occurrence of permanent visual loss, and the need for maintaining urgent access to FTP during the COVID-19 pandemic

Table 1. Clinical, laboratory and ultrasound findings of patients referred to the fast-track clinic for suspected GCA before and after lockdown.

	Total n=81	8 months period previous to lockdown (July 2019 – February 2020) n=50	8 months period after lockdown (March 2020 – October 2020) n=31	p
Age, mean (SD)	74.1 (11.2)	75 (10.8)	72.7 (11.8)	0.394
Female, n (%)	25 (30.9%)	18 (36%)	7 (22.6%)	0.204
Baseline use of steroids, n (%)	37 (46.3%)	26 (53.1%)	11 (35.5%)	0.124
Temporal artery biopsy positive n=16, no. of patients	5 (31.3%)	1 (11.1%)	4 (57.1%)	0.049
^{18}F-FDG-PET/CT positive n=23, no. of patients	10 (43.5%)	3 (33.3%)	7 (50%)	0.669
Fulfilling 1990 GCA criteria, no. of patients	18 (22.2%)	10 (20%)	8 (25.8%)	0.541
PMR diagnosis before US examination, no. of patients	27 (33.3%)	20 (40%)	7 (22.6%)	0.106
Headache, no. of patients	35 (43.2%)	26 (52%)	9 (29%)	0.043
Scalp tenderness, no. of patients	5 (6.2%)	4 (8%)	1 (3.2%)	0.386
Jaw claudication, no. of patients	12 (14.8%)	7 (14%)	5 (16.1%)	0.793
Visual symptoms, no. of patients	14 (17.3%)	8 (16%)	6 (19.1%)	0.698
Fever, no. of patients	10 (12.3%)	5 (10%)	5 (16.1%)	0.415
Myalgias, no. of patients	40 (49.4%)	24 (48%)	16 (51.6%)	0.752
AION, no. of patients	2 (2.5%)	0 (0%)	2 (6.5%)	0.14
Abnormal TA clinical examination, no. of patients	5 (6.2%)	4 (8%)	1 (3.2%)	0.386
CRP (mg/dL), mean (SD)	5(6.2)	3.4 (5.1)	7.6 (7.1)	0.008
ESR (mm/h), mean (SD)	56.2 (34.7)	45.7 (30.5)	73.9 (34.5)	0.002
Hemoglobin (g/dL), mean (SD)	12.5 (±1.8)	12.8 (±1.6)	11.7 (±1.9)	0.019
Platelets 10^9/L, mean (SD)	283.8 (±113.7)	254.1 (±91.3)	342.1 (±131.6)	0.001
Positive US findings, no. of patients	23 (28.4%)	11 (22%)	12 (38.7%)	0.115
Temporal artery positive US findings, no. of patients	15 (18.5%)	8 (16%)	7 (22.6%)	0.459
Axillary or subclavian positive US findings, no. of patients	13 (16%)	6 (12%)	7 (22.6%)	0.207
Temporal artery + axillary or subclavian positive US findings, no. of patients	5 (6.2%)	3 (6%)	2 (6.5%)	0.935
Halo sign positive, no. of patients	20 (24.7%)	8 (16%)	12 (38.7%)	0.021
Compression signs positive, no. of patients	13 (16%)	5 (10%)	8 (25.8%)	0.06
GCA clinical diagnosis, no. of patients	25 (30.9%)	11 (22%)	14 (45.2%)	0.028

AION: anterior ischemic optic neuropathy; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; FDG: fluorodeoxyglucose; GCA: giant cell arteritis; PET: positron emission tomography; PMR: polymyalgia rheumatica; SD: standard deviation; TA: Temporal artery; US: ultrasound;

Table 1. Clinical, laboratory and ultrasound findings of patients referred to the fast-track clinic for suspected GCA before and after lockdown

Disclosure: F. Montero, None; **J. Molina**, None; **I. CASTREJON**, None; **J. Martínez Barrio**, None; **J. Nieto**, None; **J. Alvaro-Gracia**, None.

Abstract Number: 1412

Effectiveness of Tocilizumab in the Visual Involvement of Giant Cell Arteritis: Multicenter Study of 471 Patients of Clinical Practice

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: One of the most feared complications of giant cell arteritis (GCA) is visual affection. Tocilizumab (TCZ) has demonstrated efficacy and safety in GCA. However, data on visual affection with TCZ are scarce and sometimes contradictory.

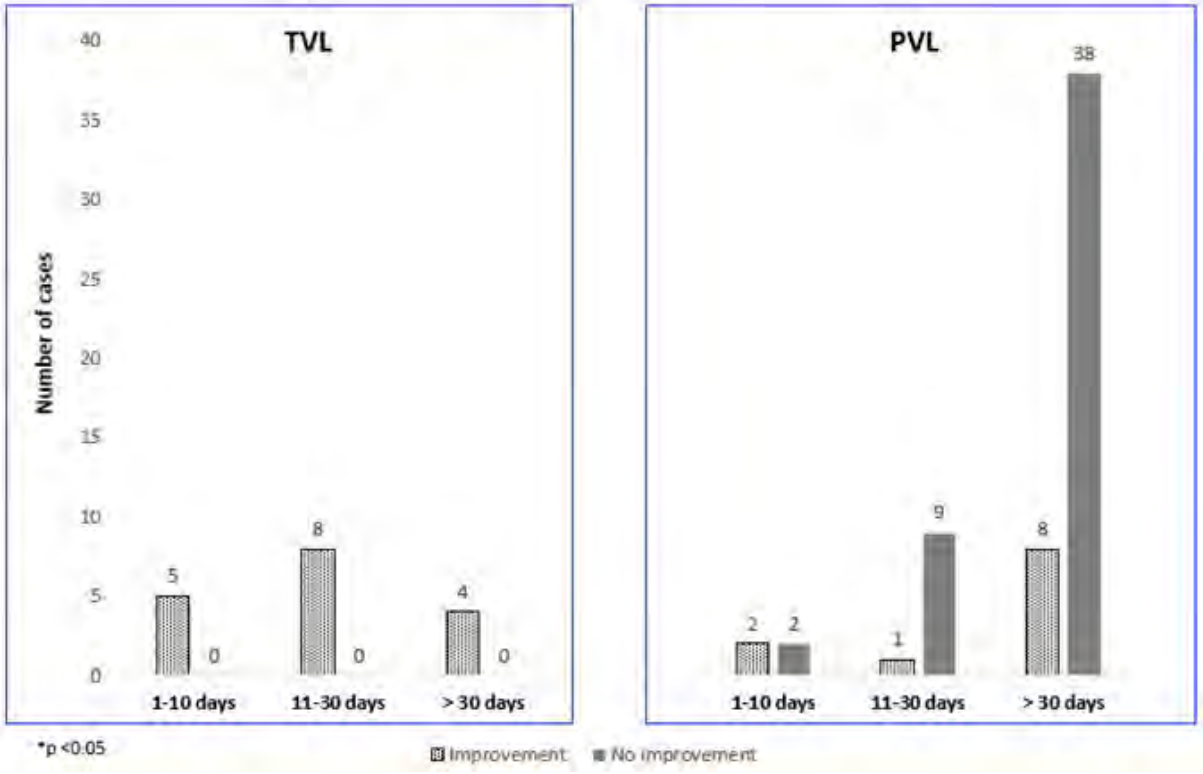
Our objectives were to evaluate the efficacy of TCZ in **a)**preventing the onset of new visual manifestations, and **b)**improving visual symptoms when present.

TABLE. Main features of 471 GCA patients at TCZ onset.

	Overall N= 471	GCA with visual involvement (n= 122)	GCA without visual involvement (n=349)	p
General features				
Age (mean±SD)	74±9	76±8	73±9	**0.000**
Women/Men (% of women)	342/129 (73)	77/45 (63)	265/84 (76)	**0.006**
Time from GCA diagnosis to TCZ onset (months), median [IQR]	6 [2-18]	5 [1-12]	7 [2-22]	0.088
Positive TAB, n (%)	201 (43)	55 (45)	146 (42)	0.53
Ischemic manifestations				
Visual involvement, n (%)	81 (17)	81 (66)	0 (0)	**0.000**
Headache, n (%)	259 (55)	92 (75)	167 (48)	**0.000**
Jaw claudication, n (%)	112 (24)	49 (40)	63 (18)	**0.000**
Systemic manifestations				
Fever, n (%)	57 (12)	10 (9)	47 (13)	0.12
Constitutional syndrome, n (%)	175 (37)	43 (35)	132 (38)	0.55
PmR, n (%)	284 (60)	66 (54)	218 (62)	0.094
Acute phase reactants				
ESR, mm/1 hour, median [ICR]	32 [12-57]	34 [15-67]	30 [11-54]	0.22
CRP (mg/dL), median [ICR]	1.5 [0.5-3.4]	1.5 [0.4-4.7]	1.4 [0.5-3.0]	**0.042**
Prednisone dose, mg/day, mean±SD	20 [10-40]	30 [15-45]	20 [10-30]	**0.000**

Abbreviations: GCA: giant cell arteritis, SD: standard deviation, TCZ: Tocilizumab, IQR: interquartile range, TAB: temporal artery biopsy, PmR: polymyalgia rheumatica, ESR: erythrocyte sedimentation rate, CRP: C-reactive protein.

FIGURE. Effectiveness of TCZ in GCA patients with TVL and PVL



Methods: Multicenter observational study of 471 patients with GCA treated with TCZ of clinical practice. Patients were diagnosed with GCA according to **a)**ACR criteria, and/or **b)**temporal artery biopsy, and/or **c)**imaging techniques.

Patients were divided into 2 groups: **a)**with visual involvement at some time during the disease, and **b)**without visual involvement. Visual manifestations were classified as: **a)**transient visual loss (TVL) (amaurosis fugax), **b)**permanent

visual loss (PVL) (more than 24 hours) (partial or complete; unilateral or bilateral), **c)**diplopia, and **d)**blurred vision. According to the duration between the onset of visual symptoms and the onset of TCZ we have considered **a)**1-10 days, **b)**11-30 days, and **c)**more than 30 days.

Results: We studied 471 (342 women/ 129 men; mean age: 74 ± 9 years). Visual manifestations at any time of the disease were observed in 122 (26%) patients. In 81 of them visual manifestations were present at TCZ onset, while the remaining 41 patients had had a complete recovery previously to TCZ. The main GCA features of patients with and without visual involvement are shown in **TABLE**. Patients with visual involvement were older, with other ischemic complications, and required higher doses of corticosteroids.

After starting TCZ, no patient developed new visual involvement. At TCZ onset, 81 patients had the following visual manifestations: PVL (n= 60; unilateral/bilateral: 48/12), TVL (n= 17; unilateral/bilateral: 11/6), diplopia (n=2) and blurred vision (n=2).

None of the patients with TVL had new episodes after initiation of TCZ, while 11 out of 60 patients with PVL experienced some improvement **(FIGURE)**. The two patients with diplopia and one of the two patients with blurred vision improved.

Conclusion: TCZ seems to prevent the appearance of new ocular manifestations. When they are present, TCZ may improve totally TVL and partially PVL.

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Abstract Number: 1413

Tocilizumab in Combination with 8 Weeks of Prednisone for Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Even with the use of tocilizumab (TCZ), significant glucocorticoid exposure (usually ³ 6 months) continues to be an important problem in giant cell arteritis (GCA). Therefore, we evaluated the efficacy and safety of TCZ in combination with 2 months of prednisone in a group of patients with GCA.

Methods: We conducted a prospective, single arm, open-label study of TCZ in combination with 2 months of prednisone for new-onset and relapsing GCA patients with active disease. GCA diagnosis required confirmation by temporal artery biopsy or vascular imaging. Active disease was defined as presence of cranial or polymyalgia rheumatica symptoms needing treatment within 6 weeks of baseline. All patients received TCZ 162 mg subcutaneously every week for 12 months and an 8-week prednisone taper starting between 20 mg and 60 mg daily. The primary endpoint, sustained prednisone-free remission, was defined as absence of relapse from induction of remission up to week 52 while adhering to the prednisone taper. Relapse was defined as recurrence of symptoms of GCA requiring treatment intensification, regardless of erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels. Safety was also evaluated.

Results: Between 11/2018 and 11/2020 we enrolled 30 patients (mean age 74 years, 60% female, 97% Caucasian, 57% new-onset disease, 77% temporal artery biopsy-proven, 47% imaging-proven) (Table 1). The mean ESR and CRP at screening were 50.3 mm/hour and 53.2 mg/L, respectively. At this moment, 22 patients have completed the study treatment protocol and 8 patients have yet to reach week 52 (mean follow up 35 weeks). Here we report the outcomes of the 22 patients that have completed the study. The initial prednisone dose in this group was 60 mg (n

Table 1 shows patient baseline characteristics

	GCA patients (n = 30)
Age, years: mean (SD)	74 (8.0)
Female sex	18 (60.0)
White race	29 (96.7)
New onset disease	17 (56.7)
Biopsy-proven disease	23 (76.7)
Imaging-proven disease	14 (46.7)
Cranial signs or symptoms	26 (86.7)
PMR symptoms	19 (63.3)
ESR, mm/hour: mean (SD)	50.3 (21.9)
CRP, mg/L: mean (SD)	53.2 (45.8)

Values represent number and (%) unless otherwise specified.
SD, standard deviation; PMR, polymyalgia rheumatica;
ESR, erythrocyte sedimentation rate; CRP, C-reactive protein.

Table 2 shows outcomes for the 22 patients who have completed the treatment protocol to date

	GCA patients (n = 22)
Efficacy	
Sustained, prednisone-free remission by week 52	18 (81.8)
Cumulative prednisone dose (mg) at week 52, mean (SD)	1,037 (367)
Relapse	4 (18.2)
Time to relapse, weeks: mean (SD)	20.5 (15.9)
Clinical manifestations at relapse	
Headaches	2 out of 4 patients
Scalp tenderness	2 out of 4 patients
PMR symptoms	2 out of 4 patients
Safety	
Serious adverse events	4 (18.2)
Cellulitis	1 (4.5)
Cholecystitis	1 (4.5)
COVID-19	1 (4.5)
Fragility fracture	1 (4.5)

Values represent number and (%) unless otherwise specified. SD, standard deviation; PMR, polymyalgia rheumatica.

= 6), 40 mg (n = 7), 30 mg (n = 4), and 20 mg (n = 5). All patients entered remission within 4 weeks of baseline. The primary endpoint was achieved by 18 (82%) patients (Table 2). The mean (SD) cumulative prednisone dose in these 18 patients was 1,037 (367) mg. After a mean period of 20.5 weeks, 4 (18%) patients relapsed (Table 2). All relapses occurred after the completion of the prednisone taper. Overall, 4 (18%) participants developed a serious adverse event (Table 2). No cases of vision loss occurred during the study.

Conclusion: Pending the final analysis of this pilot study, the results presented here suggest that 12 months of TCZ in combination with 8 weeks of prednisone could be efficacious for maintaining disease remission in patients with GCA. Confirmation of these findings in a randomized controlled trial is required.

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Abstract Number: 1414

The Current State of Expedited Referral Systems Incorporating Vasculitis Ultrasound for the Diagnosis of Giant Cell Arteritis in Rheumatology Practices in the United States

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Background/Purpose: Expedited referral systems or "fast-track" clinics incorporating vasculitis ultrasound (VUS) into the evaluation of patients with suspected giant cell arteritis (GCA) have shown reduced complications, such as blindness and inappropriate use of prednisone. EULAR guidelines recommend VUS as an initial diagnostic modality in GCA. The use of VUS for GCA diagnosis in the United States has been limited to date. We report the current state of fast-track clinics that include VUS in the diagnosis of GCA at several academic institutions and 1 large private practice in the United States, on behalf of USSONAR.

Methods: A 31-item survey questionnaire was sent via Qualtrics® to the lead clinic director of 6 practices using VUS in the diagnosis of GCA within an expedited referral system. The survey included 31 questions (Qs) with the following domains: 1) general identifying data (3 Qs), 2) clinical evaluation of GCA patients (3 Qs), 3) VUS utilization, acquisition, interpretation (8 Qs), 4) interdisciplinary collaboration (4 Qs), 5) systems-based effectiveness; support for GCA referral system (9 Qs), 6) utilization of other imaging modalities (4 Qs).

Results: Survey respondents included 5 academic institutions: Massachusetts General Hospital (MGH), University of Washington (UW), Brigham and Women's Hospital (BWH), Loma Linda University (LLU), and University of California-Los Angeles (UCLA); and 1 large private practice Arthritis and Rheumatism Associates PC, Wheaton MD (ARA). VUS acquisition and interpretation varied by institution. At 2 centers (MGH, UCLA), VUS images were obtained and interpreted by a vasculitis specialist. At 3 centers (MGH, LLU, ARA), a vasculitis specialist referred patients to a VUS-trained rheumatologist for acquisition and interpretation. At 2 centers (UW, BWH), vasculitis specialists referred patients to US technicians trained in VUS; images were interpreted by a vascular surgeon with verification by a VUS-trained rheumatologist (UW), or a vascular medicine specialist (BWH). VUS evaluation for GCA occurred within 48 hours at all centers. The majority of referred patients had clinically high suspicion of GCA; some referrals were deemed inappropriate, e.g. headache only. A multidisciplinary collaborative approach to the evaluation and management of LVV was employed by most centers; EM, ENT, neurology, and plastic, vascular and general surgery were the most common collaborators. Three institutions co-led the expedited referral system with primary care or one or more specialties. Most rheumatologists managed the cases post-diagnosis, except for one institution (LLU) where there was co-management with ophthalmology. Additional imaging was utilized in some cases despite a positive VUS to ascertain other non-cranial large-vessel involvement and possible inclusion in clinical research (MGH, ARA). A temporal artery biopsy was obtained if VUS was positive (UCLA, LLU), or negative/indeterminate based on clinical scenario (ARA, UW, BWH, MGH).

Conclusion: VUS in GCA is currently implemented in different ways in few institutions in the United States. There is a need for further training and systems-based changes to support the development of fast-track clinics in the United States.

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Abstract Number: 1415

Temporal Artery Biopsy Reports Can Be Accurately Classified by Artificial Intelligence

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SESSION INFORMATION

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Background/Purpose: Studies of giant cell arteritis (GCA) rely on classifying temporal artery biopsies (TABs), the gold-standard diagnostic test. However, these results exist as free text, rather than discrete classifications stored in databases or tables. Automated phenotyping using TAB reports in the electronic medical record (EMR) can streamline GCA studies.

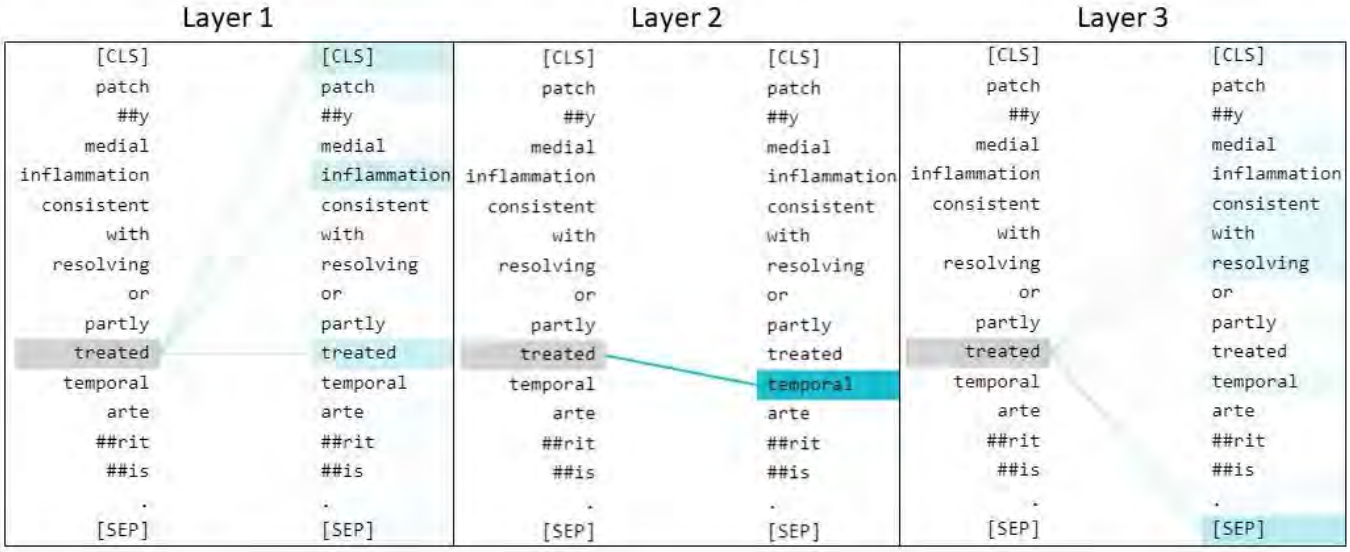
Methods: TAB reports from a single centre (Centre A) between January 2011 and November 2020 were manually classified according to the presence or absence of 4 features: intimal hyperplasia, adventitial inflammation, giant cells, and whether the TAB was diagnostic for GCA. The body of the biopsy reports was extracted using regular expressions, and the dataset was split into training (70%) and validation (30%) sets. All models were trained from a pre-trained DistilBERT (1) architecture, using the Transformers Python library (2) after text tokenization using a pre-trained tokenizer. This architecture is a light-weight neural network that uses multihead attention to learn word meaning from textual context (see figure 1). Summary statistics for Centre A are reported on the validation set, which was held out from model training. The models were then tested on an external cohort of TABs from another centre (Centre B), which were processed in an identical manner. Finally, the data from both centres was pooled, with the single centre method used to train and test a new model. Model performance was assessed with the area under the receiver operating characteristic (AUC).

Results: 161 TAB reports from Centre A were included in the study, comprising 41 patients with GCA. The most uncommon histopathological feature was adventitial inflammation, occurring in just 23 of 161 patients (14%). Within the validation dataset, the model had excellent discrimination of GCA cases (AUC 0.991), and of most histopathological features (table 1). Testing the same model on Centre B (220 TAB reports, 35 cases of GCA), there was a drop in discrimination of GCA cases (AUC 0.930), although performance on adventitial inflammation improved. The model

Table 1: Area under the receiver operating characteristic curve by biopsy feature, model and validation dataset

	Model Trained on Centre A (70% train set)		Model Trained on Centres A + B (70% train set)
	Centre A (30% validation set)	Centre B (full dataset)	Centres A + B (30% validation set)
GCA	0.991	0.930	0.995
Intimal hyperplasia	0.919	0.935	0.957
Adventitial inflammation	0.833	0.949	0.954
Giant cells	0.985	0.967	0.994

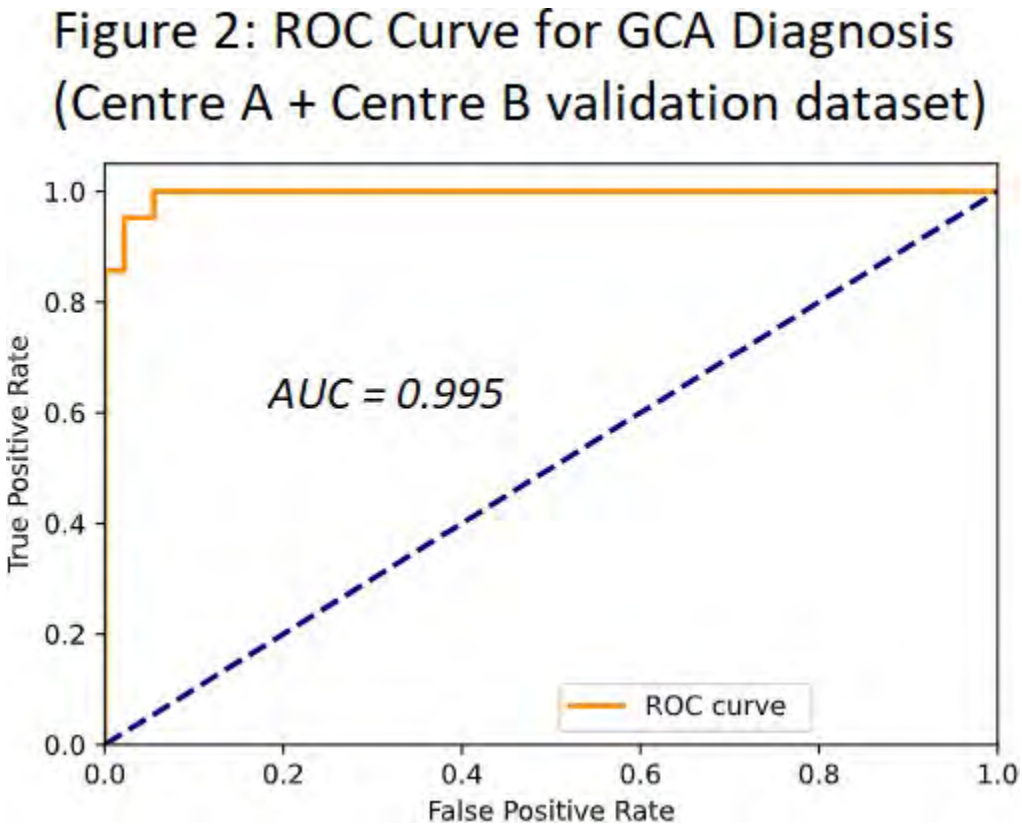
Figure 1: Model Attention Layers



Note: interrogating 3 layers of the attention maps shows the words and phrases that attend to the word "treated" in order to derive their meaning. "Inflammation", "temporal" and "consistent with resolving" all attend to the word "treated" in these layers.

trained on the pooled dataset had improved performance on all four tasks, with almost perfect accuracy for discriminating GCA cases (see figure 2).

Conclusion: Machine learning algorithms can accurately classify TAB reports according to histopathological features. These algorithms are robust to changes in language between centres, but performance is improved with larger datasets. In practice, this could streamline studies of GCA by reducing the need for manual review of biopsy reports.



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Disclosure: C. McMaster, None; **V. Yang**, None; **B. Sutu**, None; **S. Oon**, Janssen, 6; **G. Ngian**, None; **I. Wicks**, Kiniksa, 2, CSL, 2, 10; **R. Buchanan**, None; **D. Liew**, None.

Abstract Number: 1416

Dysregulated Glucose Metabolism and Dyslipidemia in GCA and PMR Patients at Diagnosis

Idil Esen[1], Philip Therkildsen[2], Berit Dalsgaard Nielsen[2], Anna van 't Ende[1], Annemieke Boots[1], Peter Heeringa[1], Ellen-Margrethe Hauge[2], Elisabeth Brouwer[1] and Yannick van Sleen[3], [1]University Medical Center Groningen, Groningen, Netherlands, [2]Aarhus University Hospital, Aarhus, Denmark, [3]University of Groningen, Groningen, Netherlands

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Table 1. Patient characteristics, laboratory tests, comorbidities and intoxications are shown. NA: not applicable.****<0.0001, ***<0.001 corresponds to difference between GPS and Lifelines cohorts

	General population (Lifelines)	GCA (GPS)	PMR (GPS)	GCA (Aarhus)	PMR (Aarhus)
N (total)	48263	50	44	52	25
Age in years, mean± SD	60±7.8	**71±8.2**	**73±7.7**	68±6.9	68±7.7
Female, n (%)	27289 (56.5)	35 (70)	26 (59)	32 (61)	13(52)
Physical measurements					
BMI, mean± SD	27±4.1	25±3.9	27±4.7	24±3.6	27±3.5
Systolic BP (mmHg), mean± SD	131±16.9	138±24.4	141±16.9	135±20.5	143±23.1
Diastolic BP (mmHg) mean± SD	76±9.5	75±9.7	82±7.4	77±10.8	83±21.6
Laboratory measurements					
HbA1c (mmol/mol), mean± SD	39±5.5	**44±7.4****	43±8.5	43±8.3	40±4.8
Glucose (mmol/L), mean± SD	5.3±0.9	**6.5±1.3****	**6.2±1.3**	NA	NA
Triglycerides (mmol/L), mean± SD	1.3±0.8	1.1±0.4	1.1±0.4	1±0.3	1±0.4
Cholesterol(mmol/L), mean± SD	5.5±1.0	**3.9±0.8****	5±0.9	4±1.0	5±0.7
HDL (mmol/L), mean± SD	1.5±0.4	**1.2±0.4*****	1.5±0.4	1±0.4	**1±0.3**
LDL (mmol/L), mean± SD	3.5±0.9	**2.3±0.6****	2.9±0.8	2±1.0	3±0.6

Background/Purpose: Giant cell arteritis (GCA) is the large and medium vasculitis that affects elderly people GCA frequently overlaps with polymyalgia rheumatica (PMR). PMR is a common rheumatic disease and it affects the proximal large joints in the shoulders and hips. Long-term glucocorticoids (GCs) administration is the main treatment option for GCA and PMR patients. However, GCs lead to GC-related adverse events including hypercholesterolemia, hypertension, diabetes mellitus, cataract, and infections. Therefore, new treatment options is required. Previous studies suggest a negative association between metabolic features cholesterol, blood glucose) and a BMI in the development of GCA. However, data are limited. In this study, we aimed to investigate the metabolic features, BMI in two independent GCA/PMR cohorts and elaborate the prevalence of comorbidities in GCA/PMR patients at the time of diagnosis and during treatment to stratify patients.

Methods: This study included two independent cohorts from Aarhus and Groningen (GPS cohort). The GPS cohort included 50 GCA and 44 PMR patients. As a background population, 50-93 years old participant of Lifelines cohort study was included. In addition, 52 GCA and 25 PMR patients from the Aarhus cohort were included. Baseline characteristics of GCA/PMR patients from the GPS cohort were compared with general population and patients in the Aarhus cohort. Patients in the GPS cohort were prospectively followed with visits at 3 months, 1, 2, 3, 4 and 5 years. Laboratory measurements, comorbidities (diabetes mellitus, hypercholesterolemia, hypertension, obesity and cataract) were assessed at every visit.

Results: In contrast to previous literature, higher HbA1c and glucose levels and lower LDL, HDL and cholesterol were detected in GCA patients than in general population. This suggested a dysregulation in lipid and glucose metabolism in GCA patients. Aarhus cohort was comparable with GPS cohort. Next, association of comorbidities with acute-phase markers at the time of diagnosis was investigated. GCA patients with cataract had reduced CRP and ESR whereas higher ESR was observed in PMR patients with cataract compared to patients without cataract. Analysis of GC treatment effect on comorbidities revealed a significant increase in diabetes and cataract in GCA patients, mainly after 3 months and 5 years, respectively, compared to baseline. BMI significantly increased 1, 4 years and 5 years after GC treatment initiation. Additionally, frequency of obese patients increased after 5years of GC usage in GCA patients.

Conclusion: Here we show that a disturbance in glucose and lipid metabolism in newly-diagnosed GCA patients. GC treatment resulted in the development of comorbidities and BMI in GCA patients, emphasizing the need for improved GC-sparing treatment options.

Disclosure: I. Esen, None; **P. Therkildsen**, None; **B. Dalsgaard Nielsen**, None; **A. van 't Ende**, None; **A. Boots**, None; **P. Heeringa**, None; **E. Hauge**, AbbVie, 6, Sanofi, 6, Sobi, 6, SynACT Pharma, 6, Novo Nordic Foundation, 5, Roche, 5, Novartis, 5; **E. Brouwer**, Roche, 2, 6; **Y. van Sleen**, None.

Abstract Number: 1417

Machine Learning Enhances the Identification of GCA from Its Mimics Based on Clinical Factors

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)
Session Type: Poster Session C
Session Time: 8:30AM–10:30AM

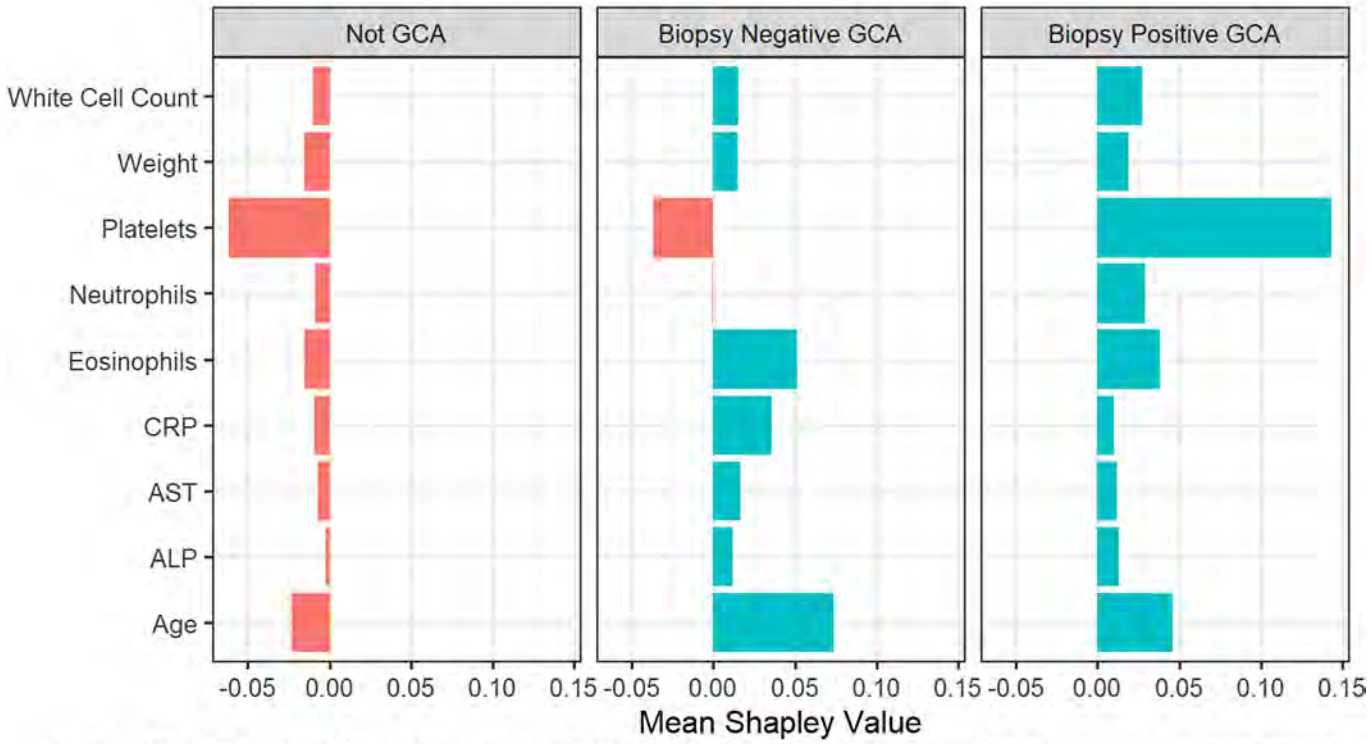
Background/Purpose: To determine whether an eventual diagnosis of giant cell arteritis in both temporal artery biopsy positive and negative patients can be identified using prospective clinical factors, either through direct identification or machine learning techniques.

Methods: All patients at a single center who underwent temporal artery biopsy between January 2011 and November 2020 with accessible progress notes were included. Final diagnosis was determined from the documented clinical disease course after a minimum of one year, and was ascertained from the medical record by two assessors, with arbitration by a third assessor for cases of disagreement. Models were trained to distinguish GCA from mimics, with further comparisons performed on the subgroups of biopsy-positive and biopsy-negative GCA. Variables considered included pathology, clinical and demographic features (Table 1). Missing variables were imputed using k-nearest neighbours and the minority class was upsampled using SMOTE(1). After hyperparameter tuning, random forest models were fitted to the data(2), using 50-repeated 5-fold cross-validation to determine the out-of-sample area under the receiver operating characteristic (AUC). To assess individual variable contribution to model predictions, Shapley scores were calculated and compared between the three groups(3).

Results: During the study period, 194 patients underwent temporal artery biopsy (130 not GCA, 19 biopsy-negative GCA, 45 biopsy-positive GCA). The mean AUC of the random forest classifier was 0.726 (95% CI 0.715 - 0.737), with an overall classification accuracy of 70.4%. The Shapley scores demonstrate that, whilst the platelet count strongly predicts biopsy-positive GCA, the model must rely on a variety of other variables to predict biopsy-negative GCA. In particular, the eosinophil count, patient age, and liver function tests were discriminators of biopsy-negative GCA (Figure 1). The presence of an elevated eosinophil count or elevated aspartate aminotransferase distinguishes GCA mimics from biopsy-negative GCA (Figure 2).

Conclusion: Platelets, eosinophils, age, and ALT assist in differentiating biopsy-negative GCA, but discriminating GCA from mimics is best performed by machine learning models. In particular, the more difficult cases of biopsy-negative GCA may be distinguishable using models that use both positive markers of GCA diagnosis and vari-

Figure 1: Top Ranking Model Variables



Note: variables with the highest Shapley scores were selected. The absolute value of the Shapley score represents its contribution to the model prediciton. Positive scores indicate variables that predict GCA. Negative scores indicate variables that predict not GCA.

Figure 2: Eosinophil Count and ALT by Diagnosis

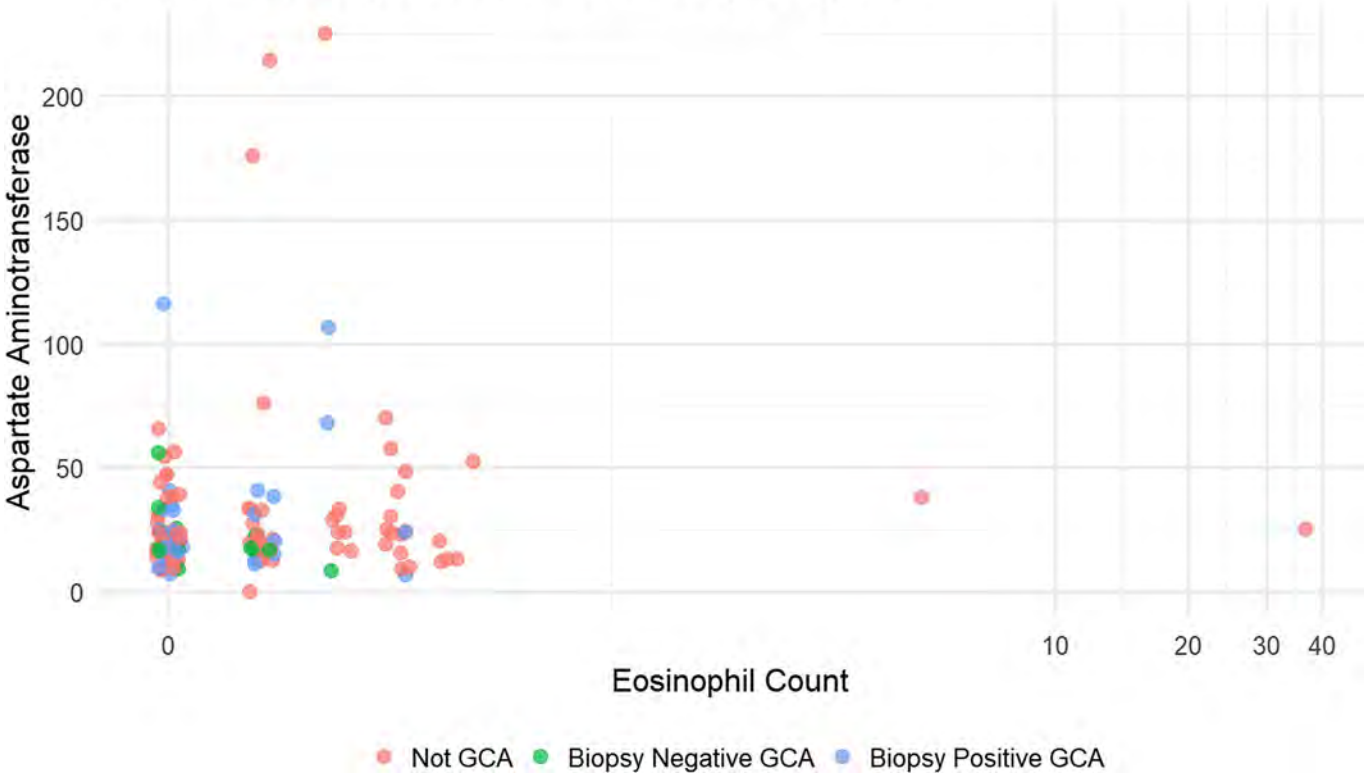


Table 1: Variables included in the machine learning model.

Age (years)	PMR (yes or no)
Sex (M or F)	Gout (yes or no)
Interpreter required (yes or no)	Migraine (yes or no)
Time from symptom onset (weeks)	Depression (yes or no)
Headache (yes or no)	Opioid use (yes or no)
Fatigue (yes or no)	Hemoglobin
Diplopia (yes or no)	White Cell Count
Amaurosis fugax (yes or no)	Platelet Count
Loss of vision (yes or no)	Neutrophil Count
Shoulder pain (yes or no)	Lymphocyte Count
Jaw pain (yes or no)	Monocyte Count
Limb pain (yes or no)	Eosinophil Count
Fever (yes or no)	Erythrocyte Sedimentation Rate
Temporal Artery tenderness (yes or no)	C-Reactive Protein
TA pulse (present or absent)	Albumin
Weight (kg)	Aspartate Aminotransferase (AST)
Heart Rate (BPM)	Alanine Aminotransferase (ALT)
Mechanical pain (yes or no)	Gamma-Glutamyl Transferase (GGT)
Inflammatory arthritis (yes or no)	Alkaline Phosphatase (ALP)

ables that predict GCA mimics. Predictive models should therefore be developed on datasets that consider both predictors of GCA and its mimics.

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Disclosure: C. McMaster, None; **V. Yang**, None; **R. Buchanan**, None; **D. Liew**, None.

Abstract Number: 1418

Patient Reported Outcomes on Quality of Life in Patients with Giant Cell Arteritis and Polymyalgia Rheumatica

Yannick van Sleen[1], Kornelis van der Geest[2], Annemieke Boots[2], Maria Sandovici[2] and Elisabeth Brouwer[2], [1]University of Groningen, Groningen, Netherlands, [2]University Medical Center Groningen, Groningen, Netherlands

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

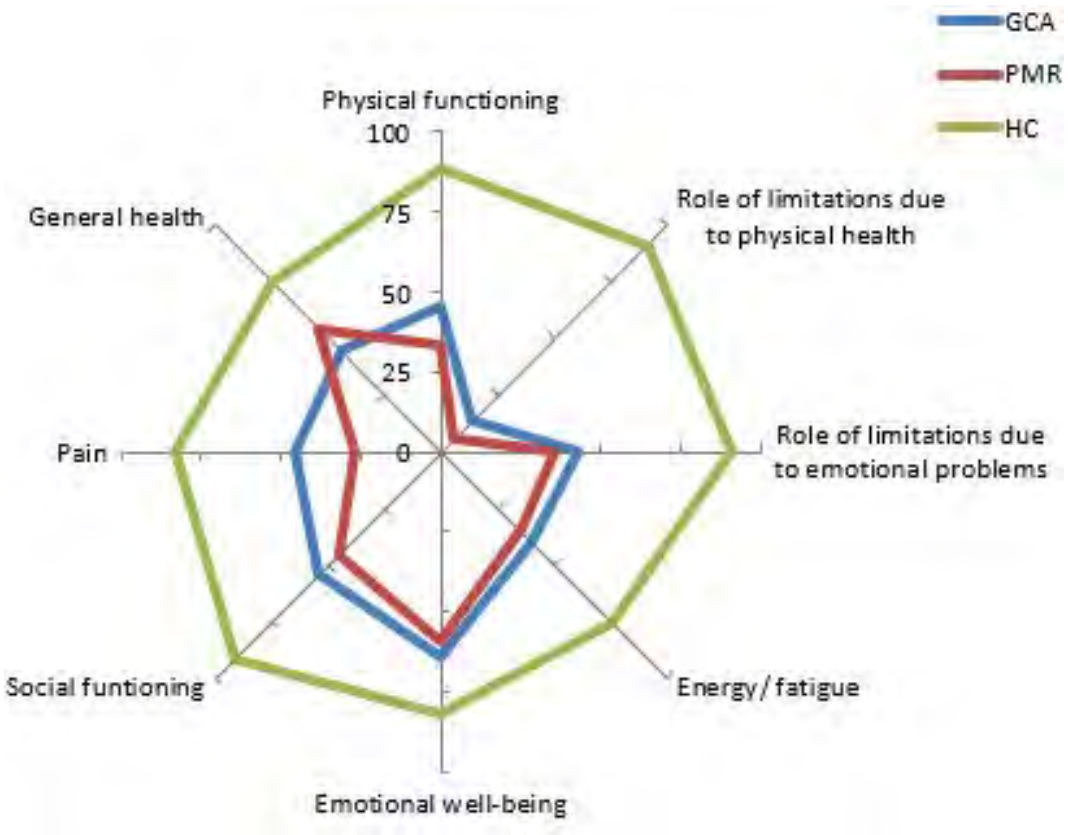


Figure 1. Scores of the eight domains of the SF-36 at baseline in GCA and PMR patients. Data are compared to age- and sex-matched HCs. Scores range from 0-100; a score of 100 indicates the most healthy outcome.

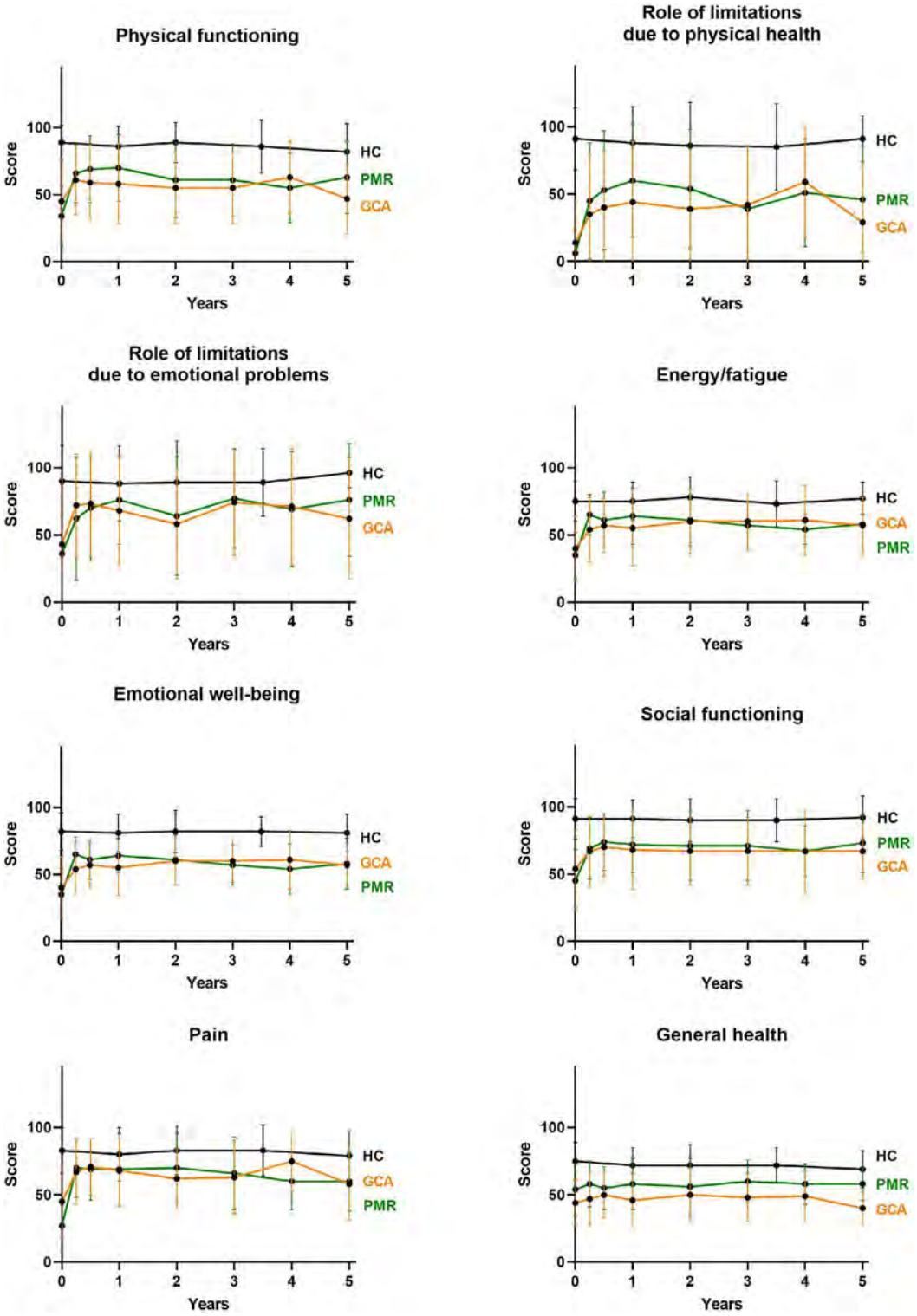


Figure 2. Scores of the eight domains of the SF-36 throughout the disease course in GCA and PMR patients. Data are compared to age- and sex-matched HCs.

Background/Purpose: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) are often overlapping inflammatory diseases that occur in people older than 50 years. Both diseases can affect the quality of life, due to the burden of vascular inflammation and ischemia-related symptoms (GCA), joint symptoms (PMR) and systemic symptoms (GCA and PMR), in addition to the side-effects of long-term treatment with glucocorticoids. We hypothesized that

GCA and PMR have both short- and long-term impact on the quality of life. We therefore documented patient reported outcomes (PROs) on the quality of life in GCA and PMR patients for five years.

Methods: We followed treatment-naïve GCA (n=44) and PMR (n=40) patients since diagnosis for up to five years. At each visit, PROs were recorded by the Groningen Frailty Indicator (GFI), the Health Assessment Questionnaire-Disability Index (HAQ-DI) and the Short Form (SF)-36. Data were compared with age- and sex-matched healthy controls (HCs) that were also followed for up to five years.

Results: At diagnosis, both GCA and PMR patients reported significantly worse on each PRO compared to HCs. On each of the eight domains of the SF-36, patients scored substantially lower than HCs, with PMR patients scoring slightly worse than GCA patients (Figure 1). Initiation of GC treatment rapidly improved PROs, however, scores either never recovered to HC values (GFI, SF-36 (Figure 2)) or increased again after two years (HAQ-DI).

Conclusion: GCA and PMR patients experience both short-term and long-term impact on their quality of life, likely caused by both the disease and its treatment. Future studies should document whether a direct start of additional treatment such as methotrexate or tocilizumab substantially improve PROs in these patients.

Disclosure: Y. van Sleen, None; **K. van der Geest**, Roche, 6; **A. Boots**, None; **M. Sandovici**, None; **E. Brouwer**, Roche, 2, 6.

Abstract Number: 1419

Development and Validation of a Patient Reported Outcome Measure for Giant Cell Arteritis

Mwidimi Ndosi[1], Celia Almeida[2], Jill Dawson[3], Emma Dures[2], Rosemary Greenwood[4], Catherine Guly[5], Sarah Mackie[6], Alison Bromhead[4], Steve Stern[4] and Joanna Robson[2], [1]University of the West of England, Bristol, Filton, United Kingdom, [2]UWE Bristol, Bristol, United Kingdom, [3]University of Oxford, Oxford, [4]University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, United Kingdom, [5]University Hospitals Bristol and Weston NHS Foundation Trust, Bristol, [6]School of Medicine, University of Leeds, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I: Giant Cell Arteritis & Polymyalgia Rheumatica (1391–1419)

Session Type: Poster Session C

Session Time: 8:30AM–10:30AM

Background/Purpose: Giant cell arteritis (GCA) causes inflammation of the blood vessels of the head and neck and can cause visual loss and large vessel vasculitis. Patients suffer severe headaches, pain around the scalp and jaw and musculoskeletal symptoms. Treatment includes high dose glucocorticoids, to control symptoms and protect sight.

The aim of this study was to produce a validated disease-specific PROM for patients with GCA, to capture the impact of GCA and its treatment on health-related quality of life

Methods: This was a large cross-sectional survey including patients with clinician-confirmed GCA (cranial, visual loss and large vessel vasculitis) from the UK. Participants with a diagnosis date within the last three years OR flare of disease within the last year were recruited, to enrich the sample of participants with active disease. An underpinning

Table 1. Fit statistics for each of the four domains GCA-PROM

Domain	Location	Standard error	Fit Residuals	Chi Square	DF	p-value
Acute symptoms (8 items)	0.270	0.017	2.807	3.346	6	0.764
Activities of daily living (7 items)	-0.047	0.010	-1.969	9.336	6	0.156
Psychological (7 items)	-0.208	0.013	-0.421	4.271	6	0.640
Participation (8 items)	-0.016	0.011	-1.828	8.267	6	0.219

Table 2. Convergent validity of the four domains with EQ5D-5L and CATPRO5

Correlation with EQ5D		
Domain	**Spearman's Correlation coefficient**	**p-value**
Acute symptoms	-0.631	<0.001
Activities of daily living	-0.729	<0.001
Psychological	-0.648	<0.001
Participation	-0.735	<0.001
Total score	-0.778	<0.001
Correlation with CAT-PRO5		
Acute symptoms	0.551	<0.001
Activities of daily living	0.557	<0.001
Psychological	0.442	<0.001
Participation	0.490	<0.001
Total score	0.556	<0.001

qualitative study and cognitive testing developed 40 candidate items each with a 5-point Likert scale [1]. Patients completed this 40-item draft GCA-PROM alongside EQ5D-5L, CAT-PRO5 and self-report disease activity and steroid usage.

The statistical analysis aimed at determining the construct validity with Rasch models and factor analysis performed iteratively. Items were fitted to the Rasch model to determine its construct validity, reliability, unidimensionality and statistical sufficiency of the total score from the scale. Factor analysis was used to establishing factor structure. Item reduction decisions were be based on clinical importance, lack of fit to the Rasch model, and redundancy.

Further evidence of validity was tested by comparing the scores of the newly validated GCA-PROM (i) in participants who self-identify as having 'active disease' versus patients 'in remission' (known groups validity) (ii) with scores derived from EQ5D-5L and CAT-PRO5 (convergent validity).

Results: The validation sample comprised 426 patients, with a mean (SD) age of 74.2 (7.2), 327 (76%) had cranial GCA and 285 (67%) were female.

The initial analysis of the 40 items, resulted in a lack of fit to the Rasch model and led to the deletion of 10 items. Of the remaining items, 22/30 displayed disordered thresholds necessitating collapsing two categories (very mild and mild) resulting into a 4-response category structure which improved the thresholds.

Four factors (domains) were identified: Acute symptoms (8 items), Activities of daily living (7 items), Psychological (7 items) and participation (8 items). The four domains were analysed as 'super-items' and shown to fit the Rasch model. Table 1 presents item parameters for each of the 4 domains (non-significant Chi-Square probabilities indicate fit to the Rasch model).

The overall scale had an adequate fit to the Rasch model: $X^2 = 25.219$, DF=24, p=0.394 including reliability PSI=0.828. The raw-to-linear transformation scale was calibrated to enable parametric analyses if desired.

Each domain was shown to have known-groups validity and correlation with EQ5D-5L and CAT-PRO5 (Rs) ranging between 0.4.42 and 0.778 (Table 2).

Conclusion: The final 30-item GCA-PROM with 4 domains is a robust measure of health-related quality of life in people with GCA. Further work will explore its use in clinical trials and practice.

Disclosure: M. Ndosi, None; **C. Almeida**, None; **J. Dawson**, None; **E. Dures**, None; **R. Greenwood**, None; **C. Guly**, None; **S. Mackie**, Roche, 2, Sanofi, 2, UK Medical Research Council (MRC) TARGET Partnership Grant (MR/N011775/1/MRC_/Medical Research Council/United Kingdom), 5, UK National Institute for Health Research (NIHR) Leeds Biomedical Research Centre, 5; **A. Bromhead**, None; **S. Stern**, None; **J. Robson**, None.

Abstract Number: 1420

Evaluation of SARS-CoV-2 Vaccine Response in a Multi-Racial/Ethnic Cohort of Patients with Systemic Lupus Erythematosus

Peter Izmirly[1], Mimi Kim[2], Marie Samanovic-Golden[3], Ruth Fernandez Ruiz[4], Sharon Ohana[3], Alexis Engel[5], Kristina Deonaraine[1], Mala Masson[4], Xianhong Xie[6], Amber Cornelius[4], Ramin Herati[4], Rebecca Haberman[4], Jose Scher[1], Allison Guttmann[3], Rebecca Blank[7], Ben Plotz[3], Mayce Haj-Ali[4], Brittany Banbury[3], Sara Stream[8], Ghadeer Hasan[3], Gary Ho[3], Paula Rackoff[7], Ashira Blazer[3], H. Michael Belmont[3], Amit Saxena[3], Mark Mulligan[4], Robert Clancy[4] and Jill Buyon[3], [1]New York University School of Medicine, New York, NY, [2]Albert Einstein College of Medicine, Larchmont, NY, [3]NYU School of Medicine, New York, NY, [4]NYU Grossman School of Medicine, New York, NY, [5]NYU Langone Health, New Yok, NY, [6]Department of Epidemiology and Public Health, Albert Einstein College of Medicine, Bronx, NY, [7]New York University, New York, NY, [8]NYU Langone Health, New York, NY

SESSION INFORMATION

Session Date: Monday, November 8, 2021

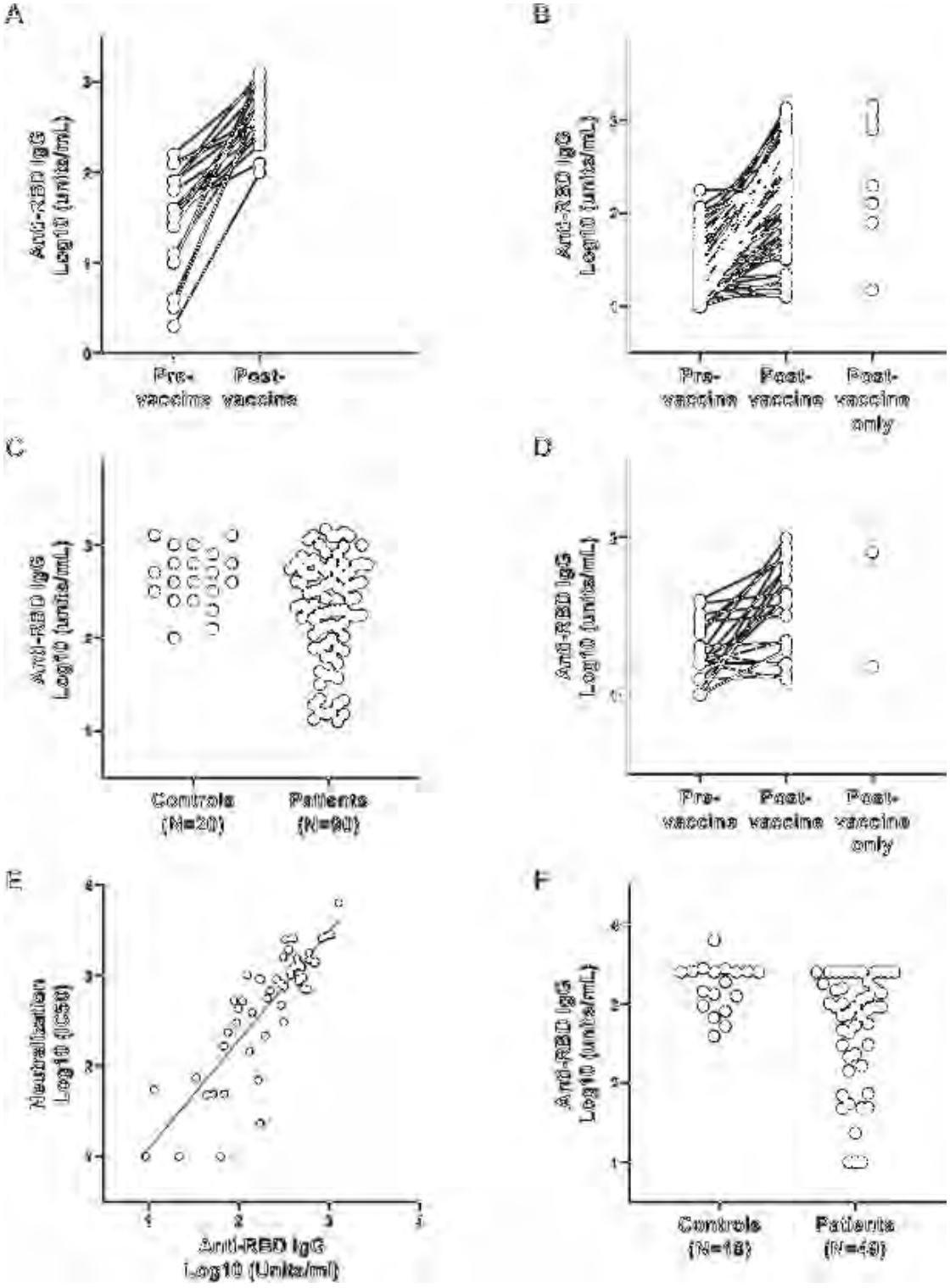
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: COVID-19 Vaccine Experience & Translational Science (1420–1423)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Since the Phase 3 clinical studies of all three COVID-19 vaccines excluded patients on immunosuppressants or immune-modifying drugs within 6 months of enrollment, data on SLE is virtually absent. Given the potential of disease flares following immunization, there has been hesitancy for vaccination in patients with rheumatic diseases, including those with SLE. Accordingly, this study was initiated to evaluate seroreactivity and disease flares after COVID-19 vaccination in a multi-ethnic/racial cohort of patients with SLE.

Methods: 90 patients from the NYU Lupus cohort and 20 healthy controls who received a complete COVID-19 vaccine schedule were included. IgG seroreactivity to the SARS-CoV-2 Spike receptor-binding domain (RBD) measured by ELISA and SARS-CoV-2 microneutralization assay were used to evaluate B cell responses, and IFN-γ production



to assess T cell responses as measured by ELISpot. Disease activity was measured by the hybrid SLE disease activity index (SLEDAI) and flares assigned by the SELENA/SLEDAI flare index.

Results: Overall, the mean titers of post-vaccine antibody levels were lower in SLE patients compared to controls (Figure 1). Specifically, 26 (29%) patients generated IgG antibody responses to the SARS-CoV-2 Spike RBD that fell below that of the lowest response obtained for the controls (≤100) (Table 1). Factors in the SLE patients which significantly associated with poor responses in bivariate analysis included prednisone use in combination with at least 1

Table 1: Demographic and Medications of the Low Responders

Age	Gender	Race	Ethnicity	Vaccine type	Medications
39	Male	White	Hispanic	PFIZER	HCQ, MMF, Obinutuzumab
71	Female	Other	Hispanic	PFIZER	MTX, Abatacept
57	Female	White	Non-Hispanic	PFIZER	HCQ, Belimumab
57	Female	Asian	Non-Hispanic	PFIZER	Prednisone 4mg, HCQ, MTX, Adalimumab
39	Male	White	Hispanic	MODERNA	HCQ, RTX
61	Female	Other	Hispanic	PFIZER	HCQ, MMF
42	Female	White	Hispanic	PFIZER	HCQ, Tacrolimus, RTX
38	Female	Asian	Non-Hispanic	PFIZER	Prednisone 5mg, Mycophenolic acid, Tacrolimus
59	Female	White	Hispanic	PFIZER	Prednisone 5mg, HCQ
62	Male	White	Non-Hispanic	PFIZER	HCQ, Belimumab
46	Female	White	Hispanic	MODERNA	Prednisone 5mg, HCQ, MMF
54	Female	Asian	Non-Hispanic	PFIZER	HCQ
49	Female	Black	Non-Hispanic	PFIZER	Prednisone 3mg, MMF, Belimumab
55	Female	White	Hispanic	J&J	Prednisone 5mg, HCQ, Mycophenolic acid
53	Female	White	Non-Hispanic	PFIZER	MMF
35	Female	Black	Non-Hispanic	MODERNA	HCQ, AZA, Belimumab
66	Female	White	Hispanic	MODERNA	Prednisone 5mg
72	Female	Asian	Non-Hispanic	J&J	None
44	Female	Asian	Non-Hispanic	MODERNA	HCQ
47	Female	Black	Non-Hispanic	PFIZER	Prednisone 10mg, HCQ, MMF
40	Male	Asian	Non-Hispanic	PFIZER	Prednisone 5mg, HCQ, MMF
27	Female	White	Non-Hispanic	J&J	HCQ, MMF
29	Female	Asian	Non-Hispanic	PFIZER	Prednisone 2.5mg, HCQ, MMF
41	Female	Other	Non-Hispanic	MODERNA	Prednisone 20mg, MMF
28	Female	Other	Hispanic	MODERNA	HCQ
28	Male	Other	Non-Hispanic	J&J	Prednisone 10mg, MTX

MTX=Methotrexate, MMF=mycophenolate mofetil, HCQ=hydroxychloroquine, RTX=Rituximab

immunosuppressant (p=0.049), a combination of two immunosuppressants (p=0.01), prednisone use (p=0.021), mycophenolate mofetil or mycophenolic acid use (p=0.001), receiving the Jansen/Johnson & Johnson vaccine (p=0.04) and a normal anti-dsDNA level prior to vaccination (p=0.03); only antimalarial use associated with a positive response (p< 0.0001). A logistic regression model of predictors of ELISA response >100 among SLE patients showed that taking antimalarials or no medications [OR 11.8 (95%CI 2.9, 48.5, p=0.0006)], and elevated anti-dsDNA prior to vaccination [OR 7.8 (95%CI 2.9, 48.5, p=0.0047)] are independent predictors of vaccine response. IgG seroreactivity to the SARS-CoV-2 Spike RBD strongly correlated with the SARS-CoV-2 microneutralization assay (R=0.81; p< 0.0001,

Table 2: Flares Post Vaccination

Flare Severity	Flare Type	Flare Details	Timing of Flare	Vaccine Type	Treatment
Mild/moderate	Pleuritis	Recurrent mild pleuritis	After first dose	Pfizer	No treatment
Mild/moderate	Arthritis	Recurrent mild joint pain and swelling	After second dose	Pfizer	No treatment
Mild/moderate	Renal	Recurrent proteinuria. Urine Protein/Creatinine Ratio increased from 0.8 to 1.4	After second dose	Pfizer	Rituximab/Tacrolimus changed to Voclosporin
Mild/moderate	Oral ulcers	Recurrent oral ulcers. Patient had been off of Benlysta for 3 months	After second dose	Moderna	No treatment
Mild/moderate	Pericarditis	New presumed pericarditis, EKG negative. Resolved with naproxen	After second dose (two weeks)	Pfizer	Naproxen
Severe	Arthritis	Recurrent arthritis	After second dose	Moderna	Methotrexate
Mild/moderate	Thrombocytopenia	Recurrent thrombocytopenia within patient's range	After second dose	Pfizer	No treatment
Mild/moderate	Arthritis	New mild joint pain and swelling	After second dose	Pfizer	No treatment
Mild/moderate*	Thrombocytopenia	Recurrent thrombocytopenia	After second dose	Pfizer	No treatment
Other Notables Events:					
Non-SLE related	COPD/Asthma Flare		After second dose	Pfizer	Treated in ER with steroids, then released

*Patient with SLE/APLS and ESRD was admitted 13 days after second dose of vaccine. The patient had her anticoagulation temporarily held for a procedure presented with shortness of breath found to have superior vena cava syndrome. The patient had a prolonged hospital course complicated by bleeding and sepsis and was transitioned to hospice care and died 50 days after second dose

Figure 1) and correlated with the ELISpot (R=0.57; p=0.0135). In a subset of patients with poor antibody responses, IFN-γ production was likewise diminished. In aggregate, there was no change in post-vaccination SLEDAI scores compared to those measured pre-vaccination. Only 11% of patients were considered to have post vaccination disease flares; 1% severe (further details in Table 2).

Conclusion: In a multi-ethnic/racial study of SLE patients nearly 30% had a low response to the COVID-19 vaccine. Having a normal anti-dsDNA and taking any medications other than antimalarials independently associated with a decreased vaccine response. Reassuringly, disease flares were rare. While minimal protective levels remain unknown, these data suggest protocol development to assess efficacy of booster vaccination.

Disclosure: P. Izmirly, Momenta/Janssen, 1; **M. Kim**, None; **M. Samanovic-Golden**, None; **R. Fernandez Ruiz**, None; **S. Ohana**, None; **A. Engel**, None; **K. Deonaraine**, None; **M. Masson**, None; **X. Xie**, None; **A. Cornelius**, None; **R. Herati**, CareDx, 5; **R. Haberman**, Janssen, 1; **J. Scher**, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, AbbVie, 2, Sanofi, 2, Kaleido, 2, UCB, 2; **A. Guttmann**, None; **R. Blank**, None; **B. Plotz**, None; **M. Haj-Ali**, None; **B. Banbury**, None; **S. Stream**, None; **G. Hasan**, None; **G. Ho**, None; **P. Rackoff**, None; **A. Blazer**, Glaxo Smith Kline, 1, 2, Novartis, 1; **H. Belmont**, None; **A. Saxena**, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Glaxo Smith Kline, 1, Kezar Life Sciences, 1, Astra Zeneca, 1, Jannsen, 1; **M. Mulligan**, Meissa Vaccines, 1, Eli Lilly, 5, Pfizer, 5, Sanofi, 5; **R. Clancy**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2.

Abstract Number: 1421

Efficacy and Tolerance of Vaccination Against COVID-19 in Patients with Systemic Lupus Erythematosus: The International VACOLUP Study

Renaud Felten[1], Lou KAWKA[2], Maxime DUBOIS[2], Manuel Ugarte-Gil[3], Yurilis Fuentes-Silva[4], Matteo PIGA[5] and Laurent Arnaud[1], [1]Department of Rheumatology, French National Reference Center for Autoimmune Diseases (CRMR RESO), Strasbourg, France, [2]National Reference Center for Rare East South-West Autoimmune Systemic Diseases RESO, Strasbourg University Hospitals, Strasbourg, France, [3]Hospital Guillermo Almenara Irigoyen, Essalud/Universidad Científica del Sur, Lima, Peru, [4]Division of Rheumatology, Complejo Hospitalario Universitario Ruiz y Páez, Universidad de Oriente, Ciudad Bolívar, Centro Nacional de Enfermedades Reumáticas, Ciudad Bolívar, Venezuela, [5]Department of Medical Science and Public Health, University of Cagliari, Cagliary, Italy

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: COVID-19 Vaccine Experience & Translational Science (1420–1423)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: Both efficacy and safety data regarding COVID vaccines in systemic lupus erythematosus (SLE) are lacking. We conducted the international Vaccination Against COvid in systemic LUPus study (VACOLUP) to evaluate the efficacy and tolerance of the vaccination against SARS-CoV-2 (COVID-19) in SLE. Our main objective was to describe the tolerance of SARS-CoV-2 vaccination in SLE patients, and to assess the risk of post-vaccination flare.

Methods: VACOLUP was designed as a cross-sectional study which consisted of 43 web-based questions. The study took place from March 22, 2021 to May 17, 2021. Main study outcomes included: demographical characteristics; history of COVID-19; history of vaccination against SARS-CoV-2 and tolerance. Self-reported side-effects, medically-confirmed lupus flare or COVID-19 after vaccination were analyzed.

Results: The study included 696 participants (669 [96.1%] women and 27 [3.9%] men), with a median age of 42 years [IQR: 34-51]), from 29 countries. Side-effects were reported by 316 patients (45.4%) after the first dose of COVID-19 vaccine and 181 (52.8%) of those who received a second dose of vaccine. There was no difference in the occurrence of side effects according to gender (p=0.11), age (p=0.08) or by mechanism of action (mRNA vaccines versus others, p=0.69). The type and intensity of side effects are shown in figure 1, being minor or moderate in intensity (i.e., with no consequence on the ability to perform daily tasks) in more than 80% of cases. Taking into account all vaccine doses together (n=1039), side effects required a medical consultation in 81 cases (7.8%), an emergency consultation in 14 cases (1.3%) and an hospitalization in 5 cases (0.5%), including 4 for the occurrence of a SLE flare. A total of 21 patients (3.0%) reported a medically-confirmed lupus flare, typically with predominant musculoskeletal symptoms

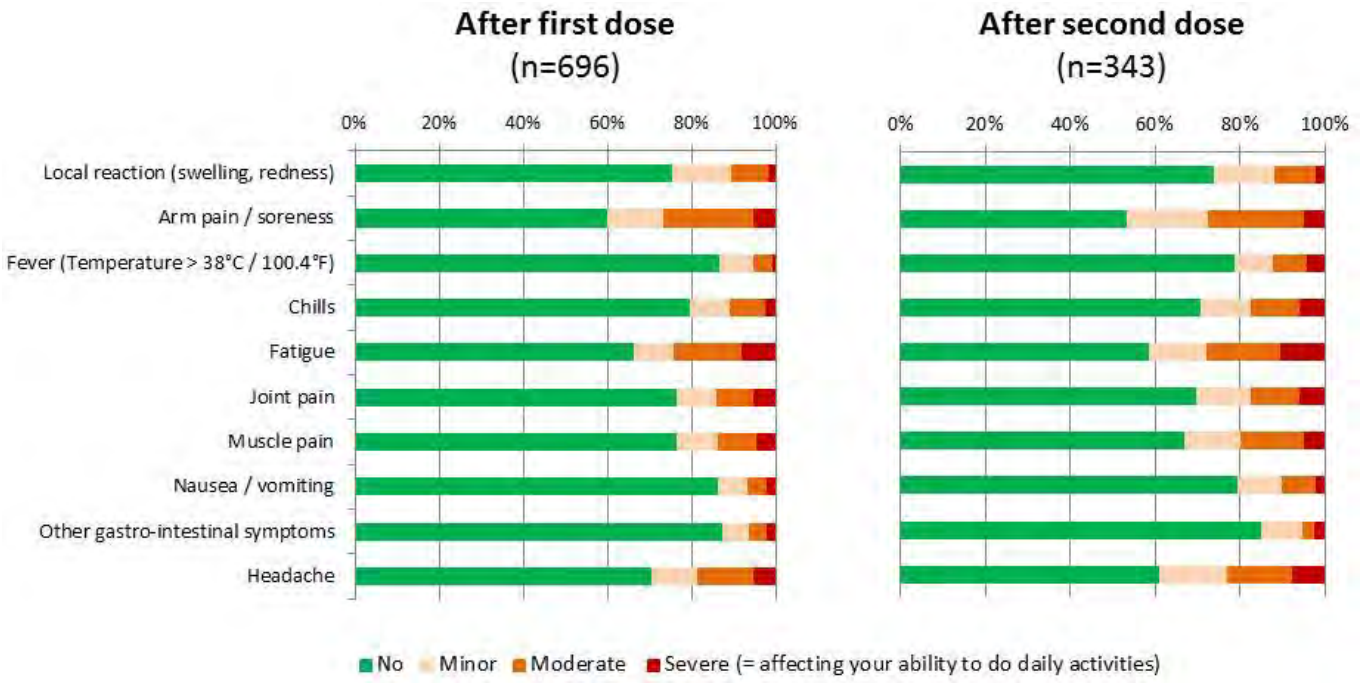


Figure 1. Type and intensity of side effects after COVID-19 vaccination Cumulative plot showing the proportion of minor, moderate and severe reaction for each adverse event (as self-reported by patients, with severe manifestations defined as affecting the ability to do daily activity).

(90.5%) and fatigue (85.7%). Of note these symptoms were reported to occur after a median delay of 3 days (IQR: 0-29) following COVID-19 vaccination. This led to a change in lupus treatment in 15/21 cases.

Conclusion: Side effects are common but minor or moderate in 80% of the cases. Only 21 (3.0%) self-reported a medically confirmed SLE flare. These flares were mainly represented by musculoskeletal symptoms (90.5%) and fatigue (85.7%) and occurred early after COVID-19 vaccination, suggesting it might be difficult to distinguish between lupus flares and common side-effects of vaccination in SLE patients. Disseminating these reassuring data should therefore help clinicians to increase vaccine coverage in SLE patients.

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Abstract Number: 1422

Urinary CD163 Predicts Proliferative Lupus Nephritis in SLE Patients with Proteinuria: A Practical Liquid Biopsy Approach

Andrea Fava[1], Jessica Li[1], Daniel Goldman[2], Jose Monroy-Trujillo[1], Mohamed G. Atta[1], Derek Fine[1], Jill Buyon[3], Joel Guthridge[4], Judith James[4], Michelle Petri[2] and Accelerating Medicines Partership (AMP) RA/SLE Network[5], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]NYU School of Medicine, New York, NY, [4]Oklahoma Medical Research Foundation, Oklahoma City, OK, [5]Brigham and Women's Hospital, Everett, MA

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: COVID-19 Vaccine Experience & Translational Science (1420–1423)

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Session Time: 9:00AM–10:00AM

Background/Purpose: Diagnosis of lupus nephritis (LN) relies on a kidney biopsy obtained in SLE with proteinuria. Delayed access to kidney biopsies may delay diagnosis and treatment, and can be limited by rapid access to biopsy, antithrombotic and anticoagulation treatments, thrombocytopenia, and in resource poor settings. Here, we employed urine proteomics to develop a non-invasive biomarker to predict proliferative LN.

Methods: We quantified 1200 biomarkers (Kiloplex, RayBiotech) in urine samples collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy in SLE patients with proteinuria > 500mg/d and compared their abundance between patients with or without a subsequent biopsy with proliferative LN (ISN class III or IV ± V). Prospective urine proteomic profiles were obtained in patients with class III, IV, or V at baseline and week 12, 24, or 52.

Results: A total of 237 patients were included: 138 (58%) with proliferative LN, 57 (24%) pure membranous LN, 21 (9%) ISN class I or II LN, 9 (4%) ISN class VI, and 12 (5%) did not have LN. Forty urinary proteins were differentially abundant in patients with proliferative LN, topped by CD163 (**Figure 1**). Urinary CD163 (uCD163) was significantly elevated in proliferative LN compared to all other groups (**Figure 2**). Longitudinal analysis revealed that uCD163 selectively declined in patients that achieved renal response at 12 months (**Figure 3**).

Conclusion: Urinary CD163, a cleaved M2c macrophage receptor, can help to identify proliferative LN in SLE patients with proteinuria. Noninvasive monitoring of uCD163 may lead to early diagnosis and treatment of proliferative LN, thus reducing irreversible kidney damage.

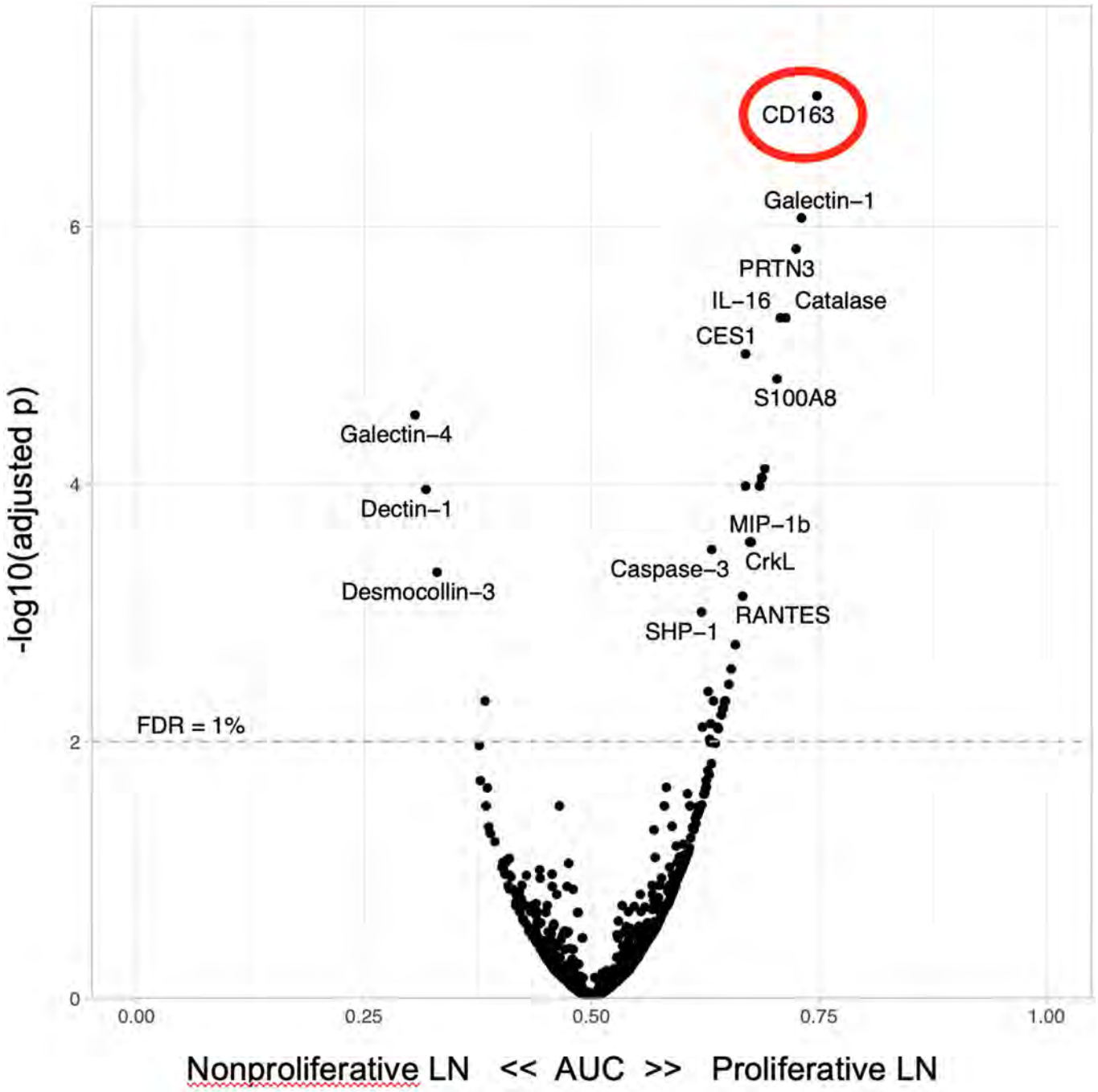


Figure 1. Urine proteomics to identify candidate biomarkers for proliferative LN. Volcano plot displaying the power of 1200 urinary proteins to discriminate proliferative from nonproliferative LN. Area under the curve (AUC), adjusted p values are shown, and a false discovery rate (FDR) of 1% threshold are shown.

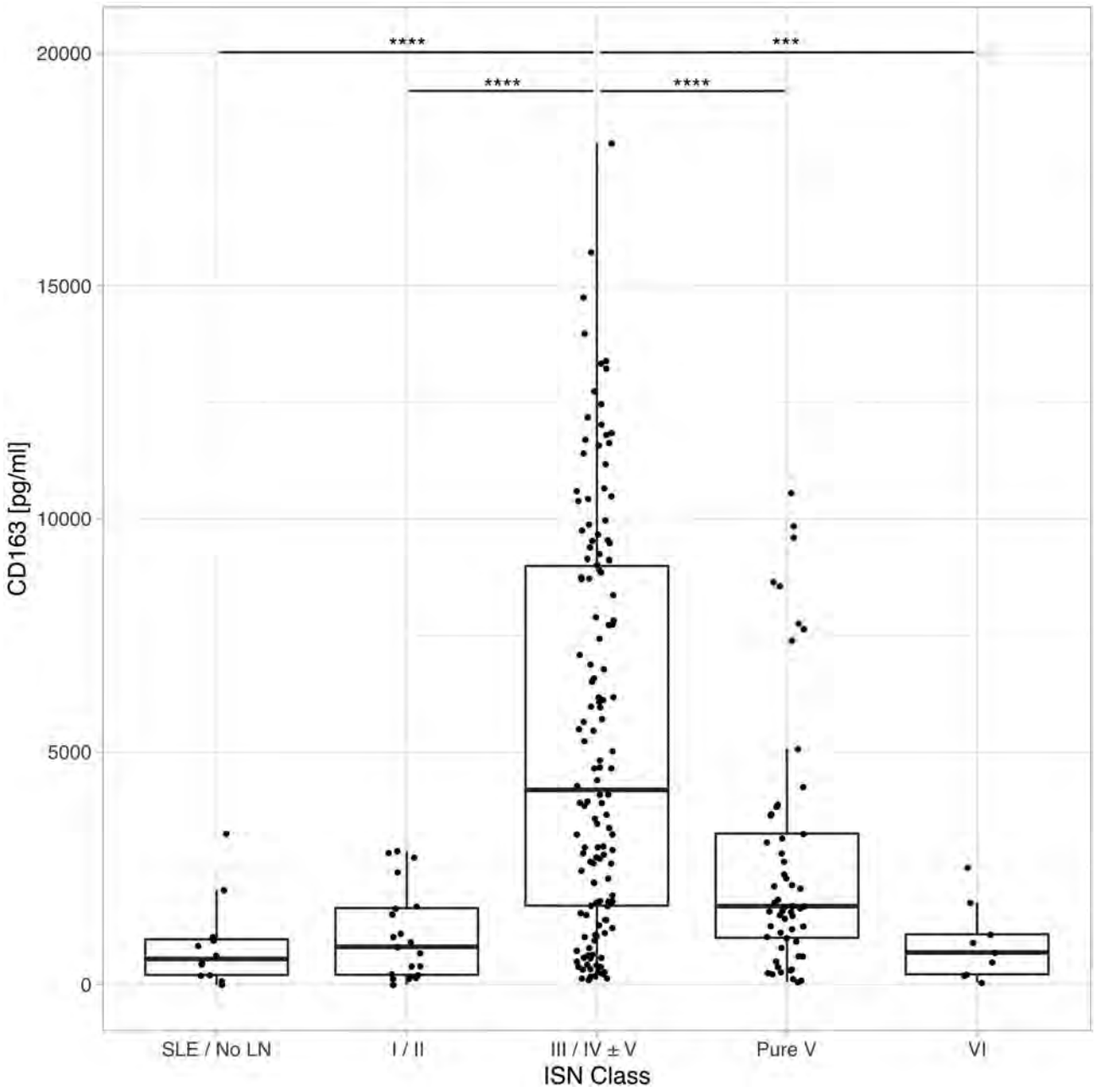


Figure 2. uCD163 is significantly elevated in proliferative LN. Scatter and boxplots displaying the concentration of uCD163 according to LN ISN class (n=237). ANOVA p<10-9; Tuckey post-hoc p values are reported (*** p<0.01, **** p<0.001).

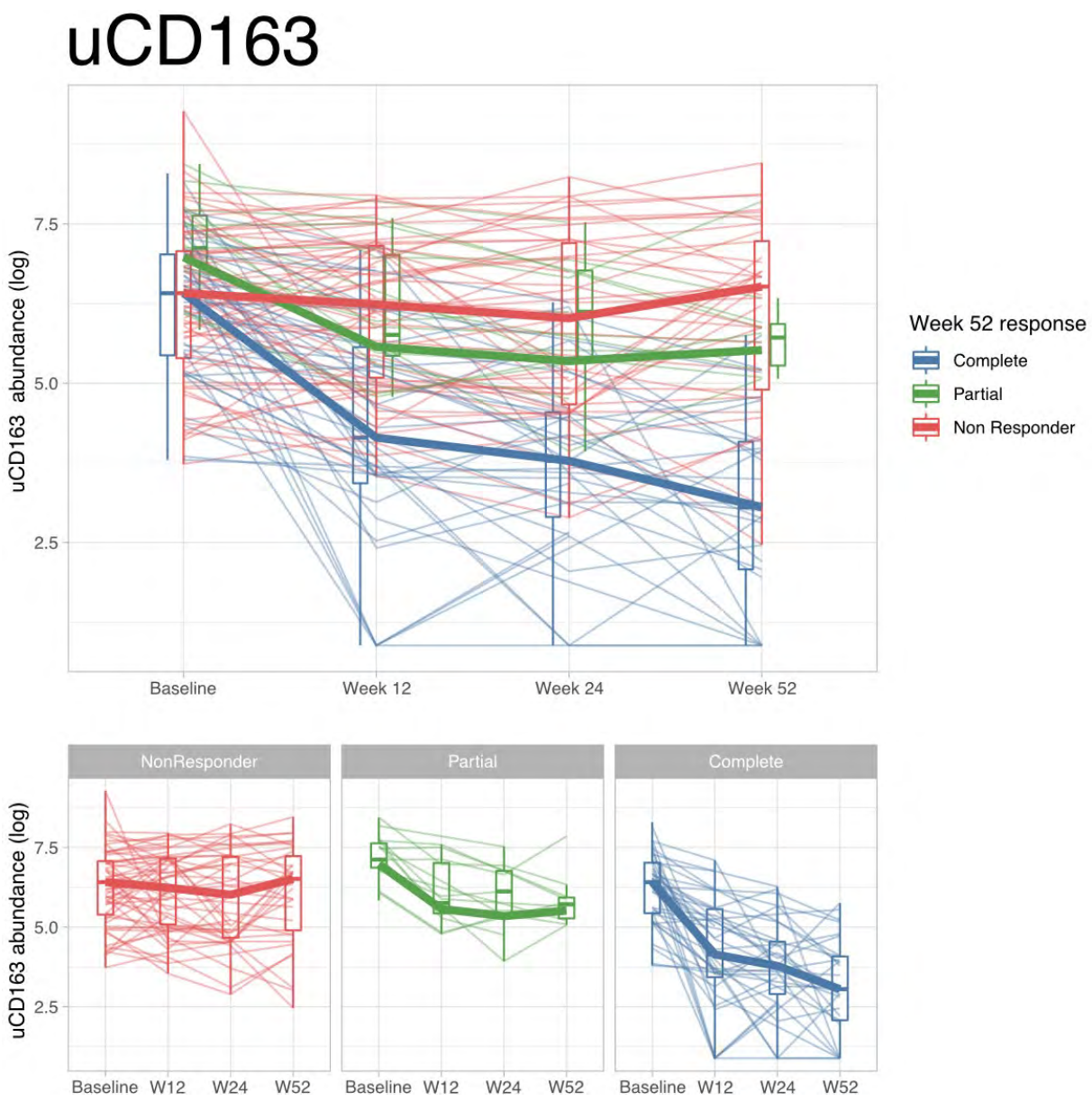


Figure 3. Urinary CD163 declined in treatment responders. Longitudinal trajectories of uCD163 in patients with class III, IV, or V LN (n=351) according to their response status. Thick lines connect the medians at each time point. Response was defined at 52 weeks from renal biopsy (Response was defined at 52 weeks from renal biopsy (Complete, urine pr/cr (UPCR) <0.5, serum creatinine <125% of baseline, prednisone < or equal to 10mg/day; Partial, UPCR < 50% from baseline but >0.5, same creatinine requirement but prednisone allowed to 15 mg; Non responder, not meeting previous definitions).

Disclosure: A. Fava, None; **J. Li**, None; **D. Goldman**, None; **J. Monroy-Trujillo**, None; **M. Atta**, None; **D. Fine**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **J. Guthridge**, None; **J. James**, Progentec Diagnostics, Inc., 2; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **A. (AMP) RA/SLE Network**, None.

Abstract Number: 1423

Ability of Soluble Immune Mediators and SLE-associated Autoantibody Specificities to Forecast Transition to Classified SLE and Inform a Lupus Classification Risk Immune Index

Melissa Munroe[1], Rufei Lu[2], Timothy Gross[1], George Tsokos[3], Michael Keith[4], John Harley[5] and Judith James[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, OUHSC, Oklahoma City, OK, [3]BIDMC, Boston, MA, [4]Inova, Arlington, VA, [5]US Department of Veterans Affairs Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes I: COVID-19 Vaccine Experience & Translational Science (1420–1423)

Session Type: Abstract Session

Session Time: 9:00AM–10:00AM

Background/Purpose: SLE is a chronic autoimmune disease driven by immune dysregulation. We have previously identified patterns of disordered immunity present prior to and concurrent with the accrual of SLE-associated autoantibodies (AutoAbs) and classification criteria (Munroe et al. Ann Rheum Dis. 2016; Lu et al. J. Autoimmun. 2016). This study seeks to determine the feasibility of an immune mediator-informed Lupus Classification Risk Immune Index (LCRII) to distinguish patients who transition to classified SLE.

Methods: Sera from 84 SLE cases with serial specimens spanning from time points prior to 1997 ACR classification criteria through SLE classification (≥ 4 criteria; average timespan= 6.0 years) and matched healthy individuals (Ctrl) were obtained from the Department of Defense Serum Repository. Demographic, therapeutic, and ACR classification criteria were extracted from medical records. A modified version of the recent SLE Risk Probability Index (SLERPI; C. Adamichou et al. Ann. Rheum. Dis. 2021) was adapted to the 1997 ACR classification criteria (excluding alopecia, complement, and interstitial lung disease components). Samples were tested for SLE-associated AutoAbs, including dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, and RNP, and 32 soluble immune mediators, including cytokines, chemokines, and soluble receptors. The LCRII is the sum of log-transformed, standardized immune mediators, weighted by the Spearman r correlation coefficient of mediator levels vs. the number of SLE-associated AutoAbs present and correlates with number ACR criteria present (Spearman r = 0.456, $p< 0.0001$) and mSLERPI (Spearman r = 0.463, $p< 0.0001$).

Results: Unlike ACR classification criteria and mSLERPI, future SLE patients could be identified in the absence of classification criteria (Pre-Criteria) using the LCRII informed by 32 immune mediators (LCRII-32, **Fig 1**). Of 32 mediators assessed, after correcting for multiple comparison (Bonferroni $p\leq 0.0016$), 9 were elevated during the Pre-Criteria phase compared to matched Ctrl, including adaptive mediators IL-12p70, IFN-γ, IL-4, IL-5, IL-17A, TGF-β, chemokines IP-10 and MCP-3, and plasminogen activator inhibitor-1 (PAI-1). Informing the LCRII with these 9 mediators (LCRII-9) did not reduce the ability of the LCRII to distinguish future SLE patients in the Pre-Criteria and AutoAb negative phases of SLE development (**Fig 1**). Overall, the LCRII-9 more clearly identified individuals by classification and AutoAb status (**Fig 2**). On average, future SLE patients met their first clinical criterion 6.4 months before reaching disease classification. In addition to the immunologic criterion, LCRII-32 and select informative mediator levels were altered in initial univariate analyses with select clinical features, including photosensitivity, serositis, and renal criteria (**Fig 3**). Neither hydroxychloriquine nor steroid use at/after SLE classification impacted the LCRII.

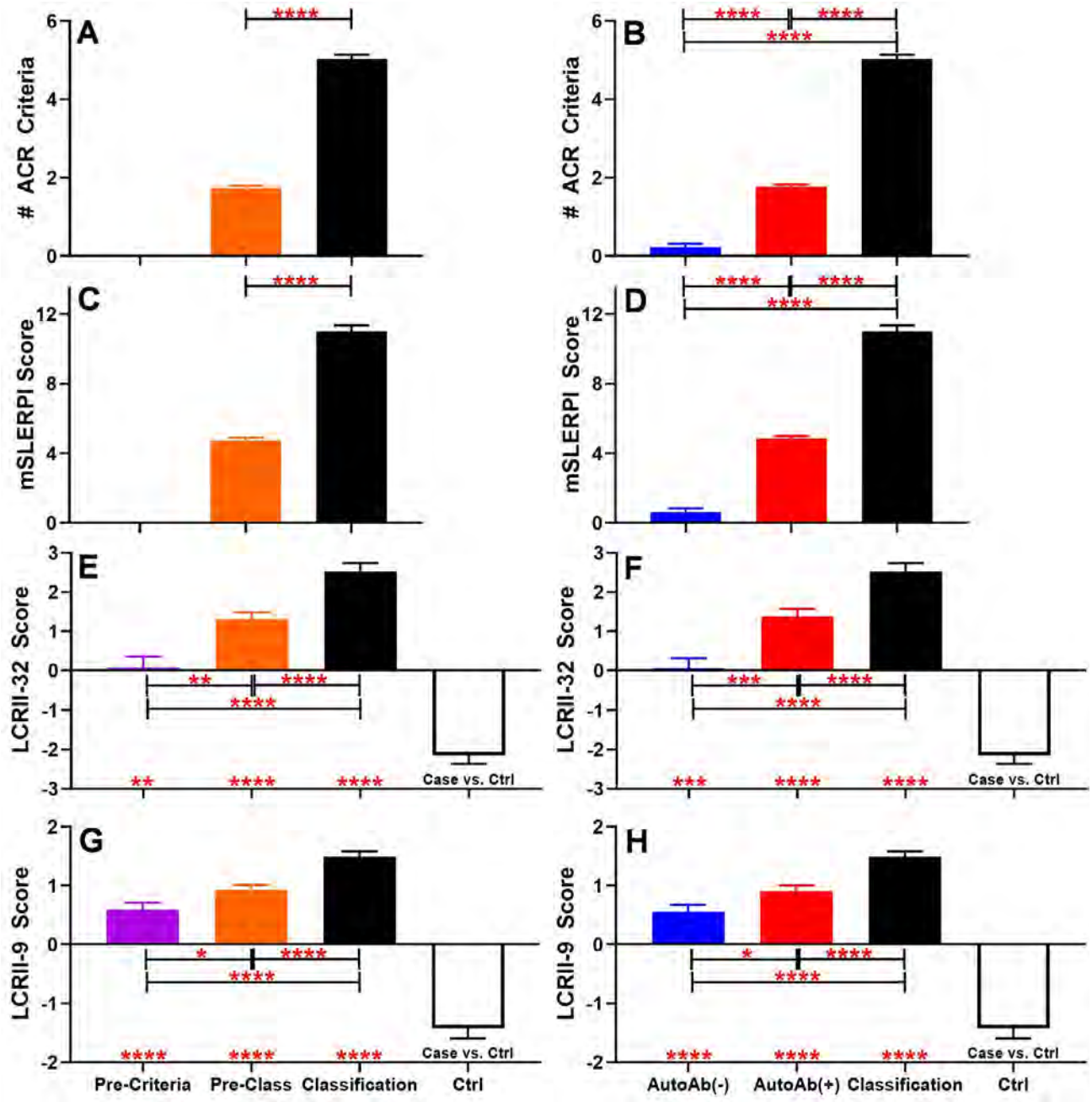
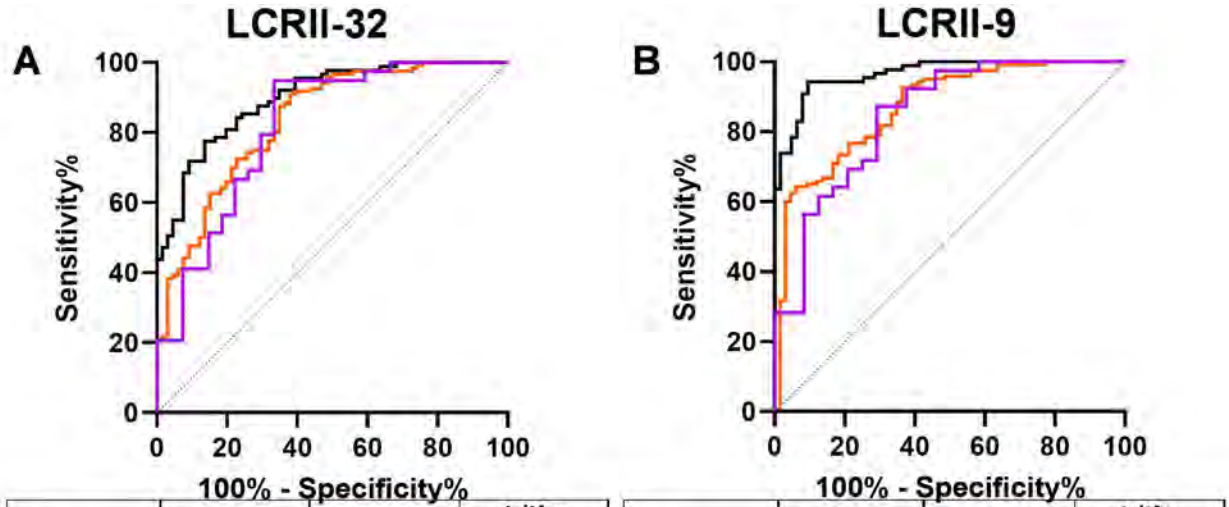


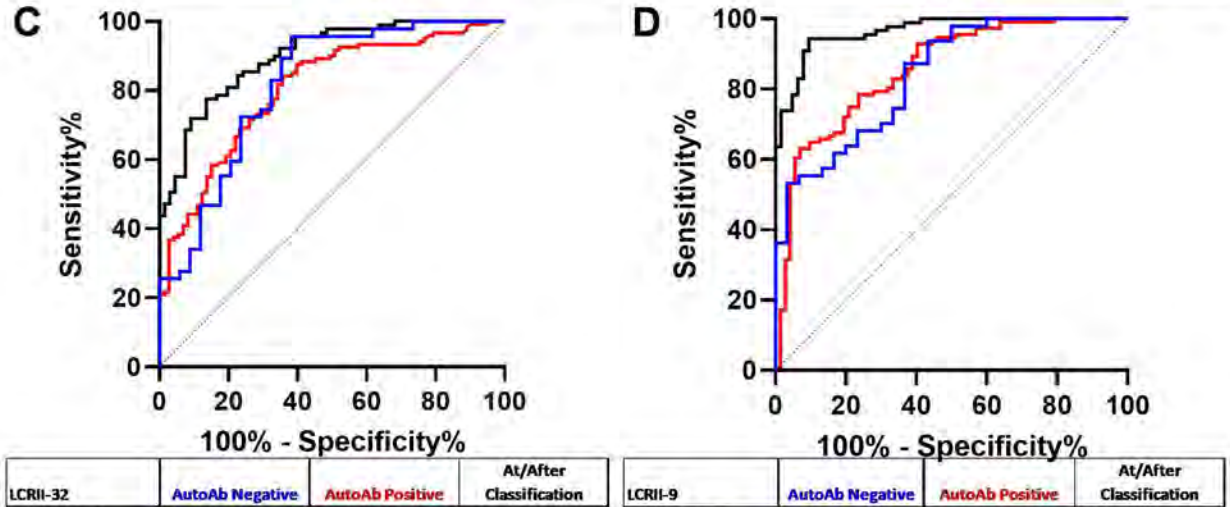
Fig. 1 Comparison of # of ACR criteria (**A-B**) vs. a modified SLE Risk Probability Index (mSLERPI, **C-D**) vs. a Lupus Classification Risk Immune Index (LCRII) informed by 32 (LCRII-32, **E-F**) or 9 (LCRII-9, **G-H**) mediators. Future SLE patients were compared by SLE classification status (prior to meeting ACR criteria [Pre-Criteria] vs. Pre-Classification vs. At/After Classification (Classification) in **A,C,E,G**) or by AutoAb status (absence (AutoAb[-]) vs. presence (AutoAb[+] of SLE-associated AutoAb specificities vs. Classification in **B, D, F, H**). LCRII-32 and LCRII-9 also contain SLE classification or AutoAb status comparisons to sex/race/age/time of sample procurement-matched healthy controls (Case vs. Ctrl comparisons along x-axis in **E-H**). Data are presented as mean ± SEM. *$p<0.05$, **$p<0.01$, ***$p<0.001$, **$p<0.0001$ Kruskal-Wallis test with Dunn's multiple comparison.

Conclusion: Clinically notable components of immunological profiles may help elucidate disease pathogenesis and help identify individuals at risk for developing SLE for clinical monitoring, early intervention, and enrollment in prevention trials.



LCRII-32	Pre-Criteria	Pre-Classification	At/After Classification
AUC (95% CI)	0.817 (0.708, 0.926)	0.835 (0.774, 0.895)	0.898 (0.852, 0.945)
p-value	*<0.0001*	*<0.0001*	*<0.0001*
Odds Ratio (95% CI)	6.3 (1.4, 28.9)	7.9 (4.0, 16.0)	15.2 (6.5, 33.0)
p-value	*0.0122*	<0.0001	<0.0001
Sensitivity	0.33	0.70	0.88
Specificity	0.93	0.77	0.68
PPV	0.89	0.84	0.79
NPV	0.44	0.59	0.81

LCRII-9	Pre-Criteria	Pre-Classification	At/After Classification
AUC (95% CI)	0.846 (0.745, 0.947)	0.870 (0.817, 0.923)	0.965 (0.941, 0.990)
p-value	*<0.0001*	*<0.0001*	*<0.0001*
Odds Ratio (95% CI)	6.8 (2.0, 20.8)	9.6 (4.8, 18.9)	67.9 (20.5, 217.4)
p-value	*0.0008*	<0.0001	<0.0001
Sensitivity	0.69	0.78	0.97
Specificity	0.75	0.73	0.70
PPV	0.81	0.83	0.81
NPV	0.60	0.65	0.94



LCRII-32	AutoAb Negative	AutoAb Positive	At/After Classification
AUC (95% CI)	0.815 (0.718, 0.912)	0.803 (0.741, 0.866)	0.898 (0.852, 0.945)
p-value	*<0.0001*	*<0.0001*	*<0.0001*
Odds Ratio (95% CI)	6.6 (2.0, 19.2)	6.6 (3.3, 12.4)	15.2 (6.5, 33.0)
p-value	*0.0008*	<0.0001	<0.0001
Sensitivity	0.47	0.67	0.70
Specificity	0.88	0.77	0.68
PPV	0.84	0.82	0.79
NPV	0.55	0.58	0.81

LCRII-9	AutoAb Negative	AutoAb Positive	At/After Classification
AUC (95% CI)	0.840 (0.752, 0.927)	0.856 (0.800, 0.911)	0.965 (0.941, 0.990)
p-value	*<0.0001*	*<0.0001*	*<0.0001*
Odds Ratio (95% CI)	5.5 (2.1, 15.1)	8.3 (4.3, 16.0)	67.9 (20.5, 217.4)
p-value	*0.0009*	<0.0001	<0.0001
Sensitivity	0.70	0.79	0.97
Specificity	0.70	0.68	0.70
PPV	0.78	0.79	0.81
NPV	0.60	0.68	0.94

Fig. 2 Performance of LCRII-32 (**A, C**) and LCRII-9 (**B, D**) at assessing risk of transition to classified SLE by classification status (**A-B**) or the absence/presence of SLE-associated AutoAb specificities (**C-D**) prior to reaching SLE classification as determined by receiver operating characteristic curve analysis (graphs represent area under the curve [AUC] and Fisher's exact test (positive vs. negative LCRII score in cases vs. controls at selected time points).

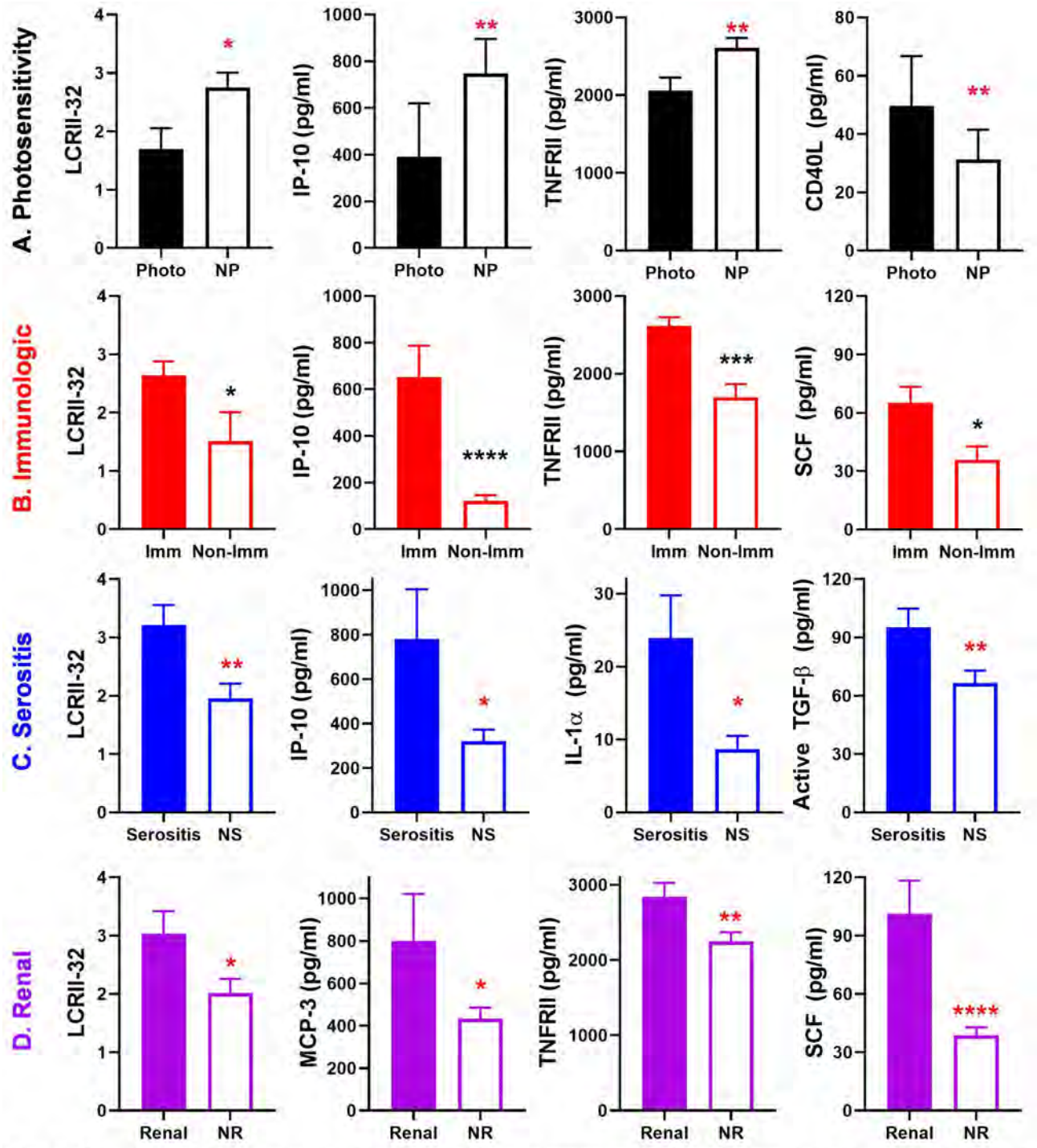


Fig. 3 LCRII-32 and select soluble mediators distinguish cases by ACR classification criteria at/after patients have reached SLE classification, including photosensitivity (**A**), immunologic (**B**), serositis (**C**), and renal (**D**) classification criteria. Data are presented as mean ± SEM. *$p<0.05$, **$p<0.01$, ***$p<0.001$, ****$p<0.0001$ Mann-Whitney test.

Disclosure: M. Munroe, Progentec Diagnostics, Inc., 5, 10, 12, Salary Support; **R. Lu**, None; **T. Gross**, None; **G. Tsokos**, None; **M. Keith**, None; **J. Harley**, Now Diagnostics, Inc., 4, 8, 11, University of Pittsburgh, 6, Glaxo Smith Kline, 2, Montagna Symposium, 6, Shenzhen Rheumatology Hospital & Symposium, 6, International Lupus Genetics Conferences, Seoul, South Korea, 6, National Academy of Sciences, 1, 6; **J. James**, Progentec Diagnostics, Inc., 2.

Abstract Number: 1424

Secukinumab Treatment in Children and Adolescents with Enthesitis-related Arthritis and Juvenile Psoriatic Arthritis: Efficacy and Safety Results from a Phase 3 Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Plenary III (1424–1429)

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Session Time: 10:30AM–12:00PM

Background/Purpose: Enthesitis-related arthritis (ERA) and juvenile psoriatic arthritis (JPsA) are two conditions that represent pediatric correlates of axial spondyloarthritis (axSpA) and adult psoriatic arthritis (PsA), respectively.[1,2] Secukinumab (SEC) has demonstrated efficacy and safety in adult patients (pts) with PsA, ankylosing spondylitis and non-radiographic axSpA.[3-5] This study evaluated efficacy and safety of SEC using a randomized double-blind placebo controlled flare prevention design in pts with active ERA and JPsA.

Methods: Pts (aged 2 to < 18 years) classified as ERA or JPsA according to ILAR criteria of ≥ 6 months duration with active disease were included. The 2-year study consisted of open-label (OL) s.c. SEC (75/150 mg in pts < 50/ ≥ 50 kg) treatment at baseline (BL), and at Weeks (Wk) 1, 2, 3, 4, 8 and 12 in treatment-period (TP) 1. Responders who achieved at least JIA ACR 30 response at Wk 12 were randomized into the double-blinded TP2 to continue SEC or placebo (PBO) every four wks until a disease flare, or up to Wk 100. The primary endpoint was the time to flare in TP2; key secondary endpoints included JIA ACR 30/50/70/90/100, inactive disease, juvenile arthritis disease activity score (JADAS), enthesitis and active joint counts, and safety. Analysis of time to flare in TP2 included the proportion of pts with disease flare, Kaplan-Meier estimate of median days for time to flare, hazard ratio estimate, and stratified log-rank test *P*-value. Intent-to-treat (ITT) analysis using non-responder imputation (NRI) and as observed analysis were performed for JIA ACR 30/50/70/90/100 responses and inactive disease.

Results: 86/97 (88.7%) screened pts were enrolled in TP1 (mean age, 13.1 years; female, 33.7%; ERA, n=52; JPsA, n=34) with a mean JADAS-27 score of 15.1 and enthesitis count of 2.6 at BL. At Wk 12, 75/83 (90.4%) pts achieved JIA ACR 30 and entered TP2. There were 21 flares in PBO treated and 10 flares in SEC treated pts during TP2. The primary endpoint was met as, compared to PBO, SEC treated pts had a significantly longer time to flare, resulting

Efficacy Outcomes, %	TP1 (Wk 12)	TP2			
	SEC (N=86)	SEC (N=37)	95% CI	PBO (N=38)	95% CI
JIA ACR 30	87.2	54.1	37.1, 70.2	39.5	24.5, 56.5
JIA ACR 50	83.7	51.4	34.7, 67.8	39.5	24.5, 56.5
JIA ACR 70	67.4	51.4	34.7, 67.8	39.5	24.5, 56.5
JIA ACR 90	38.4	43.2	27.5, 60.4	39.5	24.5, 56.5
JIA ACR 100	24.4	37.8	22.9, 55.2	36.8	22.3, 54.0
Inactive disease[#]	34.9	40.5	25.2, 57.8	36.8	22.3, 54.0
JADAS-27, mean change from BL (SD)	−10.5 (7.2)	−13.3 (8.0)	NA	−12.9 (5.9)	NA
Enthesitis count, mean change from BL (SD)	−1.8 (2.3)	−2.1 (2.0)	NA	−1.9 (1.2)	NA
Active joint count, mean change from BL (SD)	−6.3 (7.2)	−6.8 (5.3)	NA	−5.5 (3.3)	NA

[#]Inactive disease: Definition adapted from JIA ACR criteria of Wallace et al., 2011. N=36 for SEC at the end of TP2
NRI data (ITT population) for binary variables, and as observed data for continuous variables presented for TP1 and TP2
N, total number of patients in the treatment group; NA, not available

in a 72% reduced flare risk (HR: 0.28; 95% CI: 0.13–0.63; $P< 0.001$). JIA ACR responses, disease activity, enthesitis count and joints with active arthritis are reported in the **Table**. There were minor differences between the ITT and as observed analysis in JIA ACR responses and inactive disease in TP1. Improvement in the JADAS-27 score was observed in pts in both the ERA and JPsA categories (**Figure**). Rates of adverse events (AEs; 91.7% vs 92.1%) and serious AEs (14.6% vs 10.5%) in the SEC and PBO groups were comparable in the entire TP. No new safety signals were observed in pts receiving SEC (injection site reaction, n=1; overall pt-years =141.5).

Conclusion: In children and adolescents with ERA and JPsA, efficacy of SEC was demonstrated with a significantly longer time to flare vs PBO with sustained improvement of signs and symptoms up to Wk 104. Efficacy was observed in both ERA and JPsA pts along with a favorable safety profile.

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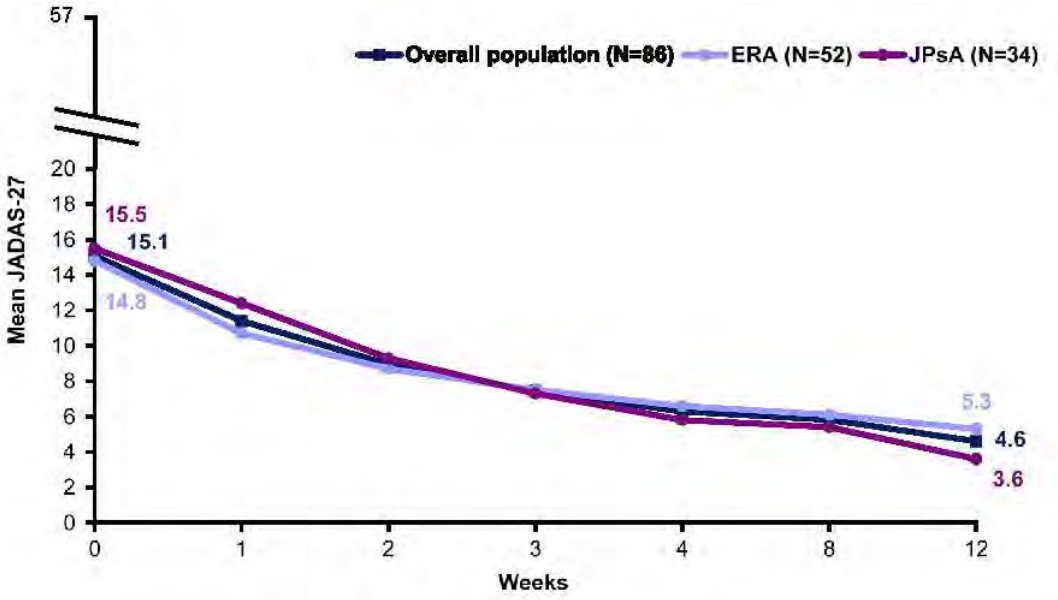
Efficacy of secukinumab at the end of Treatment Periods 1 and 2 (Key secondary endpoints) as per ITT and NRI imputation for JIA ACR evaluation/inactive disease and as observed for continuous variables



Week	1	2	3	4	8	12
Overall (n)	84	85	86	86	86	83
ERA (n1)	50	51	52	52	52	51
JPsA (n2)	34	34	34	34	34	32

N, number of patients in the full analysis set 1, by JIA category; n, number of patients who satisfy the evaluation criteria in the respective group.

Improvement in JADAS-27 in the overall population, and ERA and JPsA categories in treatment period 1

Disclosure: H. Brunner, Novartis, 6, Pfizer, 6, Roche, 6, GlaxoSmithKline, 6, Abbvie, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Biogen, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, AstraZeneca-Mediimmune, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Boehringer, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, BMS, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Celgene, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Eli Lilly, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, EMD Serono, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Idorsia, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Cerocor, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner

without any commitment to third parties, F.Hoffman-La Roche, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Merck, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Novartis, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Sanofi, 12, Contributions to employer (Cincinatti Children's Hospital) *NOTE: This funding has been reinvested for the research activities of the hospital in a fully independent manner without any commitment to third parties, Aurina, 2; **I. Foeldvari**, Novartis, 4; **E. Alexeeva**, Novartis, 6, Pfizer, 6, Sanofi, 6, MSD, 6, Amgen, 6, Eli Lilly, 6, Roche, 6; **N. Ayaz**, None; **I. Calvo Penads**, Sobi, 2, 6, Novartis, 2, 6, Abbvie, 2, 6, GlaxoSmithKline, 2, 6, Pfizer, 2, 6, Amgen, 2, 6, Clementia, 2, 6; **O. Kasapcopur**, None; **V. Chasnyk**, Pfizer, 5, Novartis, 5, Amgen, 5, Elli Lilly, 5, Bristol Myers Squibb, 5, GlaxoSmithKline, 5, Roche, 5; **M. Hufnagel**, None; **Z. Zuber**, None; **G. Schulert**, Novartis, 6; **S. Ozen**, None; **A. Popov**, None; **A. Ramanan**, Roche, 6, Sobi, 6, Eli Lilly, 6, UCB, 6, Novartis, 6; **C. Scott**, None; **B. Sozeri**, Novartis, 6; **E. Zholobova**, Abbvie, 6, Pfizer, 6, Roche, 6; **X. Zhu**, Novartis, 3, 11; **S. Whelan**, Novartis, 3, 11; **L. Pricop**, Novartis, 3, 11; **A. Ravelli**, Abbvie, 2, 6, BMS, 2, 6, Pfizer, 2, 6, Hoffmann-La Roche, 2, 6, Novartis, 2, 6, Centocor, 2, 6, Anjelini Holding, 2, 6, Reckitt Benckiser, 2, 6; **A. Martini**, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Abbvie, 2, 6, EMD Serono, 2, 6; **D. Lovell**, Bristol Myers Squibb, 12, PI, Abatacept, Juvenile Idiopathic Arthritis, AstraZeneca Pharm, 2, Boehringer Ingleheim, 2, GSK, 2, Hoffman LaRoche, 2, Janssen, 12, Co-PI of overall studies of IV and sub-Q Golimumab in JIA, NIH / NIAMS, 12, R01 AR074098-01A1, NIH / NICHD, 12, NIH / R01 HD 089928-01A1, Novartis, 2, Pfizer, 3, Roche, 12, PI, Tociluzumab, Juvenile Idiopathic Arthritis, UBC, 2; **N. Ruperto**, Ablynx, 2, 6, Amgen, 2, 6, Astrazeneca-Medimmune, 2, 6, Aurinia, 2, 6, Bayer, 2, 6, Bristol Myers and Squibb, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Cambridge Healthcare Research (CHR, 2, 6, Celgene, 2, 6, Domain therapeutic, 2, 6, Eli-Lilly, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, EMD Serono, 2, 6, Glaxo Smith and Kline, 2, 6, Idorsia, 2, 6, Janssen, 2, 6, Novartis, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Pfizer, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, Sobi, 2, 6, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties, UCB, 2, 6, F Hoffmann-La Roche, 12, The IRCCS IGG, where NR works as full-time public employee has received contributions, this has been reinvested for research activities of the hospital in a fully independent manner, without any commitment with third parties.

Abstract Number: 1425

Voclosporin for Lupus Nephritis: Interim Analysis of the AURORA 2 Extension Study

Amit Saxena[1], Christopher Mela[2] and Antonia Coeshall[3], [1]NYU School of Medicine, New York, NY, [2]Aurinia Pharmaceuticals Inc., Victoria, BC, Canada, [3]Aurinia Pharmaceuticals Inc., Rockville

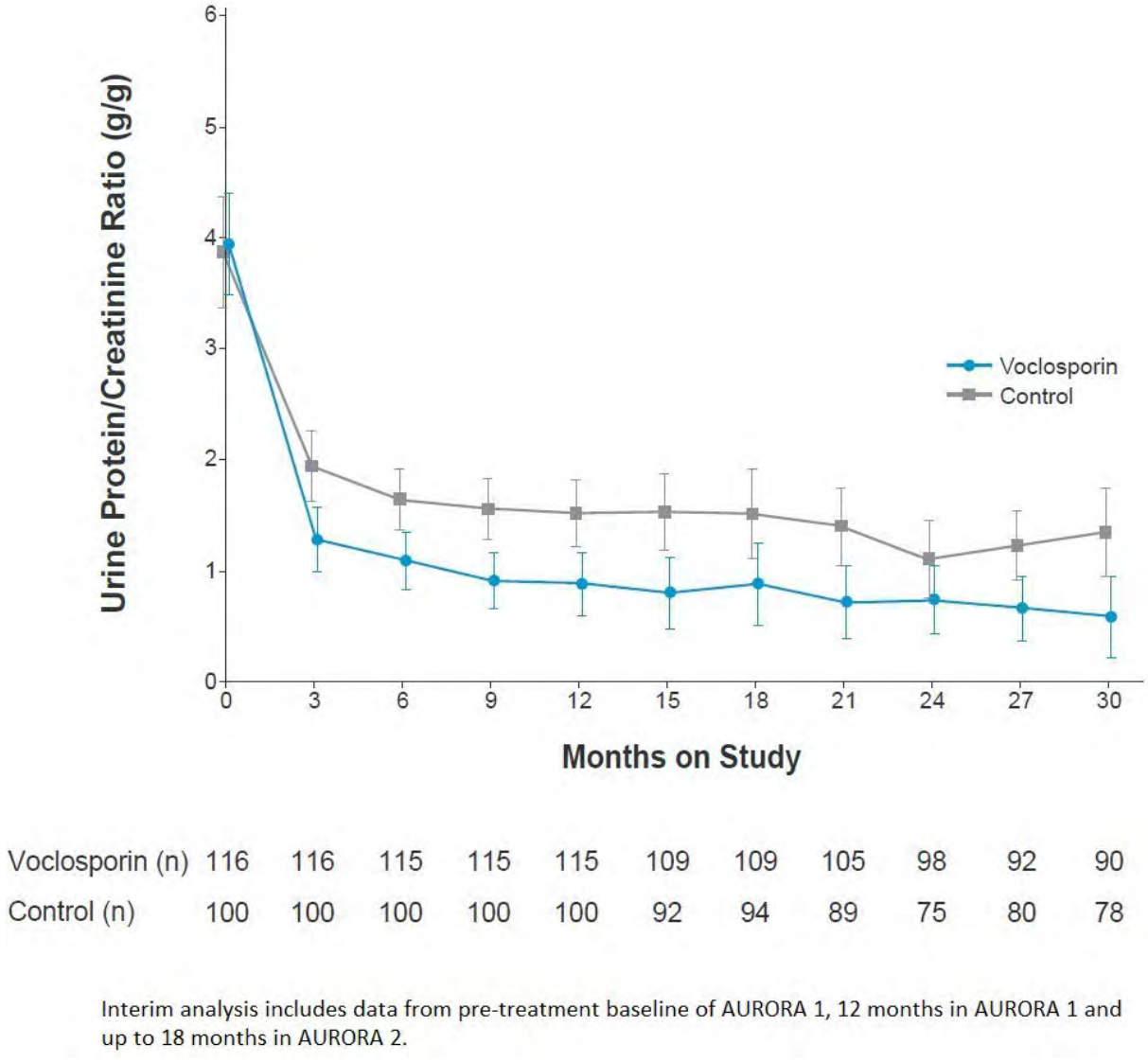
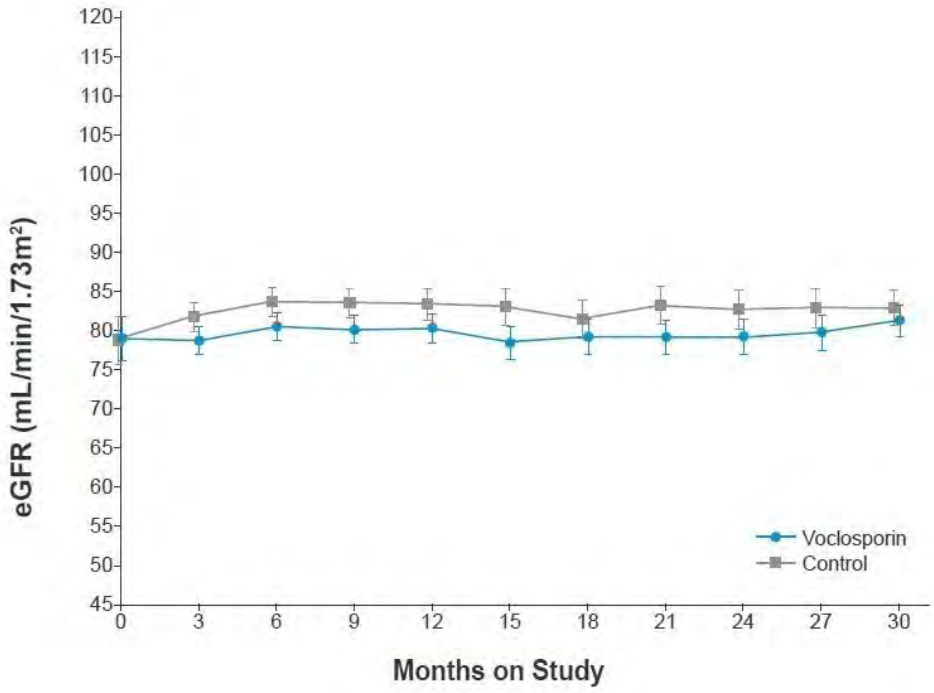


Figure 1. UPCR Over Time.

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Plenary III (1424–1429)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: Voclosporin, a novel calcineurin inhibitor (CNI), has been tested successfully in 2 pivotal trials in adult patients with lupus nephritis (LN). Previously reported results from the Phase 3 AURORA 1 and Phase 2 AURA-LV studies showed that compared with mycophenolate mofetil (MMF) and low-dose steroids alone, the addition of voclosporin significantly increased the renal response rate and reduced proteinuria, as measured by urine protein creatinine ratio (UPCR), in patients with LN at 48 weeks in AURA-LV and 52 weeks in AURORA 1.

Methods: Here we report on the second interim analysis of the ongoing 2-year, blinded, controlled extension study, AURORA 2, with exposure up to 30 months (12 months from AURORA 1 and up to an additional 18 months in AURORA 2). All patients enrolled in AURORA 1 had a diagnosis of systemic lupus erythematosus according to the ACR



Voclosporin (n)	116	116	116	116	116	112	111	105	97	92	90
Control (n)	100	100	100	100	100	96	95	89	75	78	76

Renal function assessed with corrected eGFR (Chronic Kidney Disease Epidemiology Collaboration equation) using a prespecified ceiling of 90 mL/min/1.73 m². Interim analysis includes data from pre-treatment baseline of AURORA 1, 12 months in AURORA 1 and up to 18 months in AURORA 2.

Figure 2. eGFR Over Time.

criteria and biopsy-proven LN; patients completing AURORA 1 were eligible to continue in AURORA 2 with the same randomized treatment of voclosporin (23.7 mg BID) or placebo, in combination with MMF (1 g BID) and low-dose oral steroids. UPCR and estimated glomerular filtration rate (eGFR) were evaluated. In total, 116 patients in the voclosporin arm and 100 patients in the control arm enrolled in the extension study; 90 and 78 patients, respectively, had received 30 months of total treatment as of this interim analysis.

Results: Mean UPCR at pre-treatment (AURORA 1) baseline was 3.94 mg/mg in the voclosporin arm (n=116) and 3.87 mg/mg in the control arm (n=100). The LS mean change in UPCR from pre-treatment baseline to month 30 was -3.32 mg/mg for the voclosporin arm (n=90) and -2.55 mg/mg for the control arm (n=78; Figure 1). There was a small, expected and early decrease in mean eGFR in the voclosporin arm in the first 4 weeks of treatment in AURORA 1, after which eGFR remained stable through month 30 (Figure 2). There were no unexpected new adverse events reported in patients who continued voclosporin treatment compared to control-treated patients. A total of 6 and 10 patients in the voclosporin and control arms reported events of coronavirus (COVID-19) infection, with 2 and 6 patients, respectively, reporting serious coronavirus infections.

Conclusion: Patients in the voclosporin treatment arm maintained meaningful reductions in proteinuria with no change in mean eGFR at 30 months of treatment. Additional AURORA 2 efficacy and safety data will be provided at the conclusion of the study.

Disclosure: A. Saxena, Bristol Myers Squibb, 1, Eli Lilly and Company, 1, Glaxo Smith Kline, 1, Kezar Life Sciences, 1, Astra Zeneca, 1, Jannsen, 1; **C. Mela**, Aurinia Pharmaceuticals Inc., 3, 11; **A. Coeshall**, Aurinia Pharmaceuticals Inc., 3, 11.

Abstract Number: 1426

Genotype and Transfusion Dependence Predicts Mortality in VEXAS Syndrome, a Newly Described Disease with Overlap Inflammatory and Hematologic Features

Marcela Ferrada[1], Sinisa Savic[2], Hugh Alessi[3], Daniela Ospina[4], Lorena Wilson[5], Wendy Goodspeed[6], Tannaz Kermani[7], Kenneth Warrington[8], Matthew Koster[8], Bhavisha Patel[9], Patrycja Hoffmann[10], James Poulter[11], Rachel Tattersall[12], Amanda Ombrello[1], Christopher Duncan[13], Elspeth Payne[14], Karoline Krause[15], Hanna Bonnekoh[16], Daniel Kastner[17], Peter Grayson[18] and David Beck[1], [1]National Institutes of Health, Bethesda, MD, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, Leeds, United Kingdom, [3]National Institutes of Health, Bethesda, Maryland, [4]NIH/NHGRI, Bethesda, MD, [5]National Institutes of Health, Silver Spring, MD, [6]National Institutes of Health (NIH), Bethesda, MD, [7]University of California Los Angeles, Los Angeles, CA, [8]Mayo Clinic, Rochester, MN, [9]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Bethesda, MD, [10]National Institutes of Health, Vienna, VA, [11]University of Leeds, Leeds, United Kingdom, [12]Sheffield Teaching Hospitals NHS Foundation, Sheffield, United Kingdom, [13]Translational and Clinical Research institute, Immunity and Inflammation Theme, Newcastle, United Kingdom, [14]University College London, Cancer Institute, London, United Kingdom, [15]Department of Dermatology and Allergy, Charité, Berlin, Germany, [16]Department of Dermatology and Allergy, Charité, Berlin, United Kingdom, [17]National Human Genome Research Institute, Bethesda, MD, [18]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Plenary III (1424–1429)

Session Type: Plenary Session

Session Time: 10:30AM–12:00PM

Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a newly defined disease cause by myeloid-restricted somatic mutations in blood. Missense mutations at codon 41 of *UBA1* comprise almost all cases of VEXAS and lead to amino acid substitutions of a methionine for either a threonine, valine, or leucine. Reduced translation of the UBA1b isoform and loss of cellular ubiquitylation contribute to severe inflammation. Median survival and predictors of mortality in VEXAS have not been defined and may be essential to guide management.

Methods: Patients referred to two centers for possible VEXAS were included if Sanger sequencing confirmed disease-associated variants in *UBA1*. Kaplan-Meier was used to estimate median survival. Difference in survival was compared by genotype using the logrank test. Cox proportional hazard regression was used to identify associations between clinical features of disease (age at disease onset, thromboembolic disease, pulmonary infiltrates), transfusion dependance, genotype, and mortality. In vitro expression systems were used to study associations between genetic variants and UBA1b isoform expression.

Results: 73 patients with genetically-confirmed VEXAS syndrome were included. Median age at disease onset was 66 years (range 40-85). All patients were male and white. All patients were treated with glucocorticoids.

Prior to genetic testing, the most common clinically assigned diagnosis was relapsing polychondritis (53%), myelodysplastic syndrome (35%), or Sweet syndrome (20%). The most common variants at methionine 41 were threonine

Figure 1 A

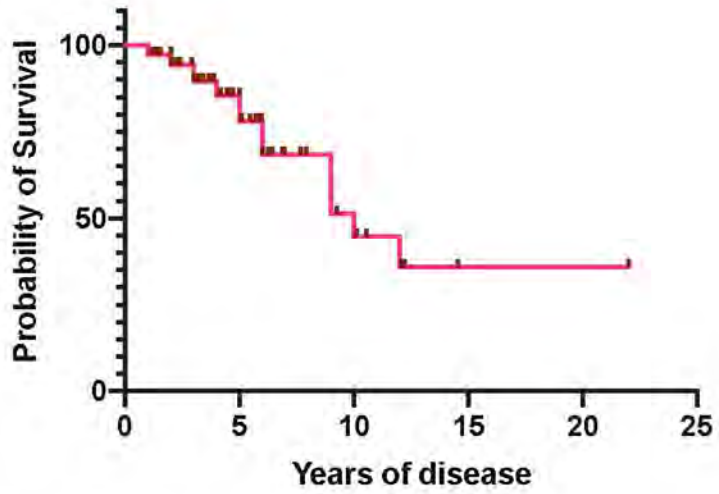
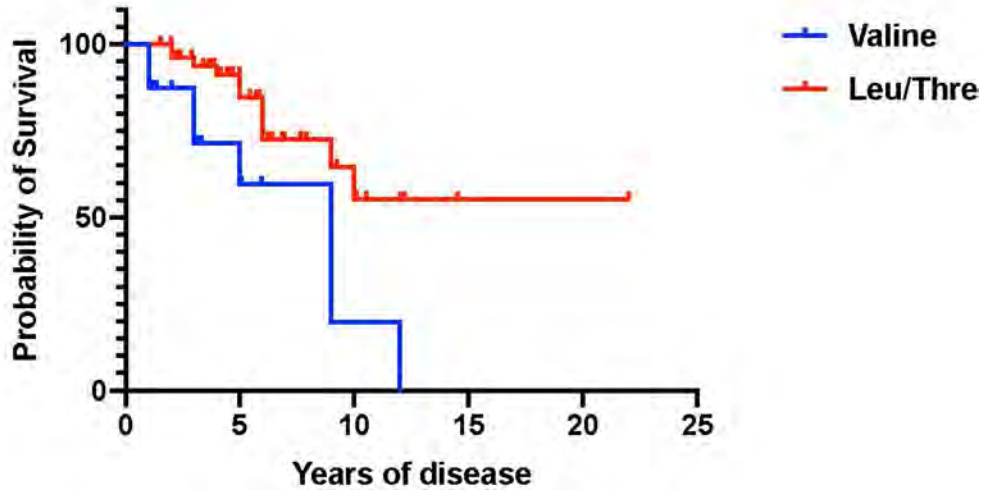


Figure 1 B



(p.Met41Thr) = 42, valine (p.Met41Val) = 16, and leucine (p.Met41Leu) = 11. Four patients had variants outside of codon 41 and were excluded from further analysis.

The overall mortality was 27%. Median survival from symptom onset was 10 years **(Figure 1A)**. Death was more common in patients with the valine variant (50%) compared to patients with leucine (18%) or threonine (22%). Median survival of patients with the valine variant was 9 years and was significantly shorter compared to patients with other variants ($p < 0.01$, **Figure 1B)**. In multivariable Cox regression, there were two independent predictors of mortality; patients with the valine variant and patients who became transfusion dependent had 3.84x (95% CI 1.50-9.81, $p=0.01$) and 3.48x (95%CI 1.28-9.49, $p < 0.005$) increased risk of death respectively. No other clinical features were associated with mortality. Translation of the UBA1b isoform was reduced in p.Met41Val compared to p.Met41Leu or p.Met41Thr.

Conclusion: A relationship between genotype, bone marrow failure, and survival is seen in patients with the VEXAS syndrome. While mortality rate is high in VEXAS, patients who become transfusion dependent and have a valine amino acid substitution at codon 41 have the highest risk for death. In vitro expression systems provide a mechanistic basis for the genotype specific mortality. Given the high mortality rate and lack of effective medical treatments,

patients with VEXAS should be considered for bone marrow transplantation, with particular focus on patients with risk factors for increased mortality.

Disclosure: M. Ferrada, None; **S. Savic**, None; **H. Alessi**, None; **D. Ospina**, None; **L. Wilson**, None; **W. Goodspeed**, None; **T. Kermani**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **M. Koster**, None; **B. Patel**, None; **P. Hoffmann**, None; **J. Poulter**, None; **R. Tattersall**, UCB, 6; **A. Ombrello**, None; **C. Duncan**, None; **E. Payne**, None; **K. Krause**, None; **H. Bonnekoh**, Novartis, 1, Sanofi-Aventis, 6; **D. Kastner**, None; **P. Grayson**, None; **D. Beck**, None.

Abstract Number: 1427

Reduction of Cardiovascular Disease and Mortality versus Risk of New Onset Diabetes with Statin Use in Patients with Rheumatoid Arthritis

Gulsen Ozen[1], Sophie Dell'Aniello[2], Sofia Pedro[3], Kaleb Michaud[4] and Samy Suissa[5], [1]University of Nebraska Medical Center, Bellevue, NE, [2]Center for Clinical Epidemiology, Lady Davis Research Institute - Jewish General Hospital, Montréal, QC, Canada, [3]Forward, The National Databank for Rheumatic Diseases, Wichita, KS, [4]University of Nebraska Medical Center, Omaha, NE, [5]Center for Clinical Epidemiology, Lady Davis Research Institute - Jewish General Hospital;Depts of Epidemiology and Biostatistics and of Medicine, McGill University, Montréal, QC, Canada

SESSION INFORMATION
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Session Title: Plenary III (1424–1429)
Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: The risks of death and of type 2 diabetes mellitus (T2DM) are increased in RA mainly due to inflammation mediated accelerated cardiovascular disease (CVD) and insulin resistance. In the general population, statins reduce CVD and mortality with a slight increase in T2DM risk. We aimed to assess CVD and mortality benefits and T2DM risk with statins in RA patients.

Methods: We conducted a prevalent new-user cohort study within the UK Clinical Practice Research Datalink, the Hospital Episode Statistics [HES] and Office of National Statistics [ONS] databases. The cohort included individuals ≥18 years old who had a 1st diagnosis of RA and ≥1 DMARD use with no alternative diagnoses and ≥1 year baseline data between 1989 and 2018. Patients with prior DM and no HES/ONS linkage were excluded for T2DM and CVD/mortality cohorts, respectively. Statin initiators were matched with non-users (1:2) on the time-conditional propensity score (TCPS) that included age, sex, BMI, smoking, alcohol, joint surgeries, prior CVD, hypertension, rheumatic diseases comorbidity index, osteoporosis/fractures, cancer, thyroid, chronic liver, kidney, lung and other heart diseases, healthcare utilization, DMARDs, glucocorticoids, NSAIDs, and CVD medications (DM and ethnicity for CVD/mortality). The subjects were followed up for the outcomes of CVD (myocardial infarction, stroke, hospitalized heart failure, CVD death), all-cause mortality and T2DM (diagnostic codes or prescription of antidiabetics). The risk of outcomes was estimated using Cox proportional hazards with adjustment for deciles of TCPS and imbalanced patient characteristics after matching.

Results: The study included 1768 statin initiators and 3528 non-users for CVD/mortality; 3608 statin initiators and 7208 non-users for T2DM (*Figure*). Baseline characteristics of the statin initiators and non-users in the matched cohort were balanced except for DM, some medications and prior cerebrovascular disease (*Table 1*). Among 1768 statin initiators and 3528 non-users, 63 vs. 340 CVD (3.0/100 person-years [PY] vs. 2.7/100 PY) and 62 vs. 525 deaths (2.7/100 PY vs. 4.1/100 PY) occurred, respectively (*Table 2)*. Incident T2DM was noted in 128 of 3608 statin initiators (3.0/100 PY) and 518 of 7208 non-users (2.0/100 PY). Statin initiation was associated with 32% (HR=0.68, 95% CI

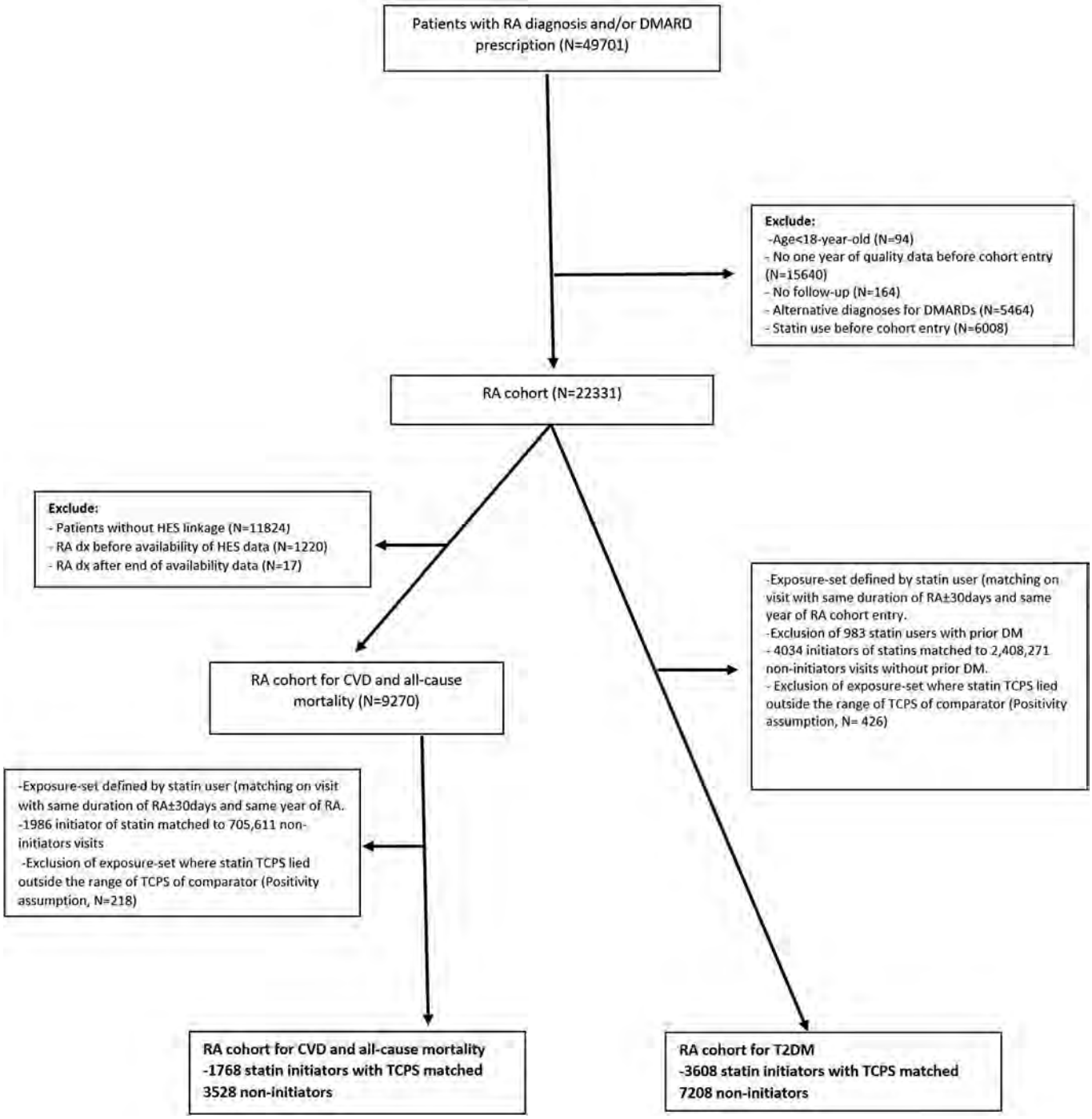

Figure. Overview of the study design and cohort creation for outcomes of cardiovascular disease (CVD), all-cause mortality and type 2 diabetes mellitus (T2DM).

0.51-0.90) reduction in CVD, 54% (HR=0.46, 95% CI 0.35-0.60) reduction in all-cause mortality, and 33% increase in T2DM (HR= 1.33, 95% CI 1.09-1.63) risks. Number needed to treat (NNT) to prevent a CVD and mortality in 1-year was 102 and 42, respectively. Number needed to harm (NNH) for a new T2DM was 127. Patients with and without prior CVD had similar CVD (36% vs. 34%) and mortality (62% vs. 54%) reduction with statins (*Table 2*).

Conclusion: Statins are associated with important reductions in CVD and mortality in both primary and secondary CVD prevention, with a modest increase in T2DM risk in RA patients. The resulting NNT/NNH suggest that CVD/mortality benefits of statins outweigh T2DM risk.

Table 1. Baseline characteristics of propensity score matched cohorts

Variables	TCPS-Matched cohort for CVD			TCPS-Matched cohort for T2DM		
	Statin initiators, N=1768	Comparators, N=3528	Standardized difference	Statin initiators, N= 3608	Comparators, N=7208	Standardized difference
Age at cohort entry, mean (SD)	65.7 (10.5)	64.4 (11.2)	**0.118**	66.0 (10.1)	64.9 (10.4)	**0.102**
Female, n (%)	1173 (66.3)	2434 (69.0)	-0.057	2379 (65.9)	4937 (68.5)	-0.054
Time with RA, years (mean [SD])	4.3 (3.4)	4.3 (3.3)	0.008	5.2 (4.2)	5.2 (4.2)	0.005
Smoking status, n (%)						
Smoker	1104 (62.4)	2111 (59.8)	0.054	2207 (61.2)	4271 (59.3)	0.039
Non-smoker	532 (30.1)	1151 (32.6)	-0.055	1111 (30.8)	2425 (33.6)	-0.061
Missing	132 (7.5)	266 (7.5)	0.003	290 (8.0)	512 (7.1)	0.035
Body mass index (BMI), kg/m2						
<18.5	25 (1.4)	50 (1.4)	0.000	52 (1.4)	111 (1.5)	-0.008
18.5-24.9	364 (20.6)	789 (22.4)	-0.043	854 (23.7)	1765 (24.5)	-0.019
25-29.9	512 (29.0)	1025 (29.1)	-0.002	1091 (30.2)	2132 (29.6)	0.014
30-34.9	325 (18.4)	583 (16.5)	0.049	564 (15.6)	1101 (15.3)	0.010
35+	184 (10.4)	311 (8.8)	0.054	274 (7.6)	537 (7.5)	0.005
Missing	358 (20.2)	770 (21.8)	-0.039	773 (21.4)	1562 (21.7)	-0.006
Disease modifying antirheumatic drugs (DMARDs)						
Methotrexate	1105 (62.5)	2267 (64.3)	-0.036	2144 (59.4)	4301 (59.7)	-0.005
Biologic DMARDs	9 (0.5)	29 (0.8)	-0.038	32 (0.9)	76 (1.1)	-0.017
Other synthetic DMARDs	1156 (65.4)	2249 (63.7)	0.034	2411 (66.8)	4771 (66.2)	0.013
Teflunomide	170 (9.6)	293 (8.3)	0.046	366 (10.1)	643 (8.9)	0.042
Sulfasalazine	753 (42.6)	1414 (40.1)	0.051	1617 (44.8)	3070 (42.6)	0.045
Antimalarial	454 (25.7)	916 (26.0)	-0.007	872 (24.2)	1808 (25.1)	-0.021
Azathioprine	53 (3.0)	113 (3.2)	-0.012	117 (3.2)	230 (3.2)	0.003
Cyclosporine	18 (1.0)	29 (0.8)	0.021	36 (1.0)	58 (0.8)	0.020
Rheumatic diseases comorbidity index (RDCI)						
0	1021 (57.7)	2000 (56.7)	0.021	2119 (58.7)	4229 (58.7)	0.001
1	360 (20.4)	772 (21.9)	-0.037	701 (19.4)	1512 (21.0)	-0.039
2+	387 (21.9)	756 (21.4)	0.011	788 (21.8)	1467 (20.4)	0.036
Medications in the year prior to cohort entry						
ACEi/ARBs	619 (35.0)	955 (27.1)	**0.172**	1160 (32.2)	1943 (27.0)	**0.114**
Beta blockers	449 (25.4)	735 (20.8)	**0.108**	948 (26.3)	1568 (21.8)	**0.106**
Thiazide diuretics	473 (26.8)	765 (21.7)	**0.119**	914 (25.3)	1580 (21.9)	0.080
Non-statin antilipidemics	13 (0.7)	14 (0.4)	0.045	32 (0.9)	33 (0.5)	0.053
Aspirin	486 (27.5)	676 (19.2)	**0.198**	1055 (29.2)	1531 (21.2)	**0.185**
Glucocorticoids	984 (55.7)	1951 (55.3)	0.007	1857 (51.5)	3719 (51.6)	-0.003
Hydroxychloroquine	453 (25.6)	915 (25.9)	-0.007	871 (24.1)	1808 (25.1)	-0.022
NSAIDs	1460 (83.1)	2977 (84.4)	-0.035	2949 (81.7)	5939 (82.4)	-0.017
Diabetes treatment	211 (11.9)	143 (4.1)	**0.294**	-	-	-
Comorbidities in the year prior to cohort entry						
Ischemic coronary heart disease	97 (5.5)	127 (3.6)	0.091	74 (2.1)	79 (1.1)	0.077
Cerebrovascular events	78 (4.4)	90 (2.6)	**0.102**	115 (3.2)	115 (1.6)	**0.104**
Peripheral vascular disease	18 (1.0)	24 (0.7)	0.037	18 (0.5)	23 (0.3)	0.028
Heart failure	74 (1.4)	36 (1.0)	0.031	46 (1.3)	62 (0.9)	0.040
Atrial fibrillation	38 (2.1)	50 (1.4)	0.055	71 (2.0)	128 (1.8)	0.014
Hypertension	346 (19.6)	660 (18.7)	0.022	720 (20.0)	1424 (19.8)	0.005
COPD - Asthma	264 (14.9)	510 (14.5)	0.013	527 (14.6)	1091 (15.1)	-0.015
Chronic kidney diseases (stage 3-)	54 (3.1)	100 (2.8)	0.013	143 (4.0)	261 (3.6)	0.018
Chronic liver diseases	5	6 (0.2)	0.013	7 (0.2)	23 (0.3)	-0.025
Cancer	41 (2.3)	84 (2.4)	-0.004	67 (1.9)	109 (1.5)	0.027
Osteoporosis	429 (24.3)	799 (22.6)	0.038	910 (25.2)	1694 (23.5)	0.040
Fragility fracture	20 (1.1)	39 (1.1)	0.002	29 (0.8)	72 (1.0)	-0.021
Thyroid disease	207 (11.7)	395 (11.2)	0.016	437 (12.1)	826 (11.5)	0.020
Diabetes	350 (19.8)	445 (12.6)	**0.196**	-	-	-
Joint Surgery	24 (1.4)	54 (1.5)	-0.015	52 (1.4)	107 (1.5)	-0.004
Number of GP visits in the year prior to cohort entry						
0-8	308 (17.4)	603 (17.1)	0.009	709 (19.7)	1318 (18.3)	0.035
9-14	401 (22.7)	868 (24.6)	-0.045	818 (22.7)	1786 (24.8)	-0.050
15-22	485 (27.4)	1004 (28.5)	-0.023	929 (25.7)	1984 (27.5)	-0.040
23+	574 (32.5)	1053 (29.8)	0.057	1152 (31.9)	2120 (29.4)	0.055

TCPS= Time-conditioned propensity score; CVD= Cardiovascular disease; T2DM= Type 2 diabetes mellitus; RA= Rheumatoid arthritis; ACEi/ARB= Angiotensin converting enzyme inhibitor/ Angiotensin receptor blocker; NSAIDs= Nonsteroidal anti inflammatory drugs; COPD= Chronic obstructive pulmonary disease; GP= General practitioner.

Table 2. Association between statin initiation and CVD, all-cause mortality and T2DM

Outcomes	N events/N exposure	Person-years	IR per 100 pt-years	Crude HR	Adjusted HR* (95% CI)	Adjusted HR** (95% CI)
CVD						
Entire cohort						
Non-users	340/3528	12676	2.7	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	63/1768	2118	3.0	1.02	**0.74 (0.56 - 0.97)**	**0.68 (0.51 - 0.90)**
Men						
Non-users	135/1094	3659	3.7	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	28/595	742	3.8	1.01	0.79 (0.52 - 1.21)	0.79 (0.51 - 1.21)
Women						
Non-users	205/2434	9017	2.3	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	35/1173	1376	2.5	0.98	0.70 (0.48 - 1.01)	**0.59 (0.40 - 0.87)**
History of CVD						
Non-users	81/253	471	17.2	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	32/208	286	11.2	0.61	0.67 (0.44 - 1.02)	**0.64 (0.41 - 0.99)**
No history of CVD						
Non-users	259/3275	12205	2.1	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	31/1560	1832	1.7	0.84	0.72 (0.49 - 1.05)	**0.66 (0.45 - 0.97)**
All-cause mortality						
Entire cohort						
Non-users	525/3528	12767	4.1	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	62/1768	2211	2.8	0.65	**0.49 (0.37 - 0.64)**	**0.46 (0.35 - 0.60)**
Men						
Non-users	188/1094	3680	5.1	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	30/595	788	3.8	0.72	0.59 (0.40 - 0.88)	**0.56 (0.38 - 0.84)**
Women						
Non-users	337/2434	9088	3.7	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	32/1173	1424	2.2	0.58	0.43 (0.29 - 0.62)	**0.39 (0.27 - 0.57)**
History of CVD						
Non-users	100/253	505	19.8	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	26/208	343	7.6	0.37	0.38 (0.25 - 0.60)	**0.38 (0.24 - 0.60)**
No history of CVD						
Non-users	425/3275	12263	3.5	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	36/1560	1868	1.9	0.57	0.50 (0.35 - 0.71)	**0.46 (0.33 - 0.65)**
T2DM						
Entire cohort						
Non-users	518/7208	26490	2.0	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	128/3608	4335	3.0	1.44	**1.34 (1.09 - 1.63)**	**1.33 (1.09 - 1.63)**
Men						
Non-users	159/2271	7570	2.1	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	36/1229	1457	2.5	1.07	1.03 (0.71 - 1.49)	1.03 (0.71 - 1.50)
Women						
Non-users	359/4937	18920	1.9	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	92/2379	2878	3.2	1.65	1.52 (1.20 - 1.93)	**1.52 (1.20 - 1.92)**
History of CVD						
Non-users	22/331	745	3.0	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiator	17/277	416	4.1	1.31	1.32 (0.66 - 2.63)	1.19 (0.59 - 2.41)
No history of CVD						
Non-users	496/6877	25745	1.9	1.00	1.00 (Reference)	1.00 (Reference)
Statin initiators	111/3331	3919	2.8	1.40	1.33 (1.08 - 1.65)	**1.32 (1.07 - 1.64)**

*adjusted for age, male, deciles of PS

**adjusted for age, male, deciles of PS, aspirin, beta-blockers, ACEI/ARBs, cerebrovascular disease, thiazides diuretics and diabetes (the latter two only for CVD and mortality), due to being imbalanced in TCPS matching.

CVD= *Cardiovascular disease;* T2DM= Type 2 diabetes mellitus; IR= Incidence rate; HR= Hazard ratio; CVD= Cardiovascular disease

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Abstract Number: 1428

Association Between Ongoing Glucocorticoid Use and Major Adverse Cardiovascular Events Among Veterans with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Plenary III (1424–1429)

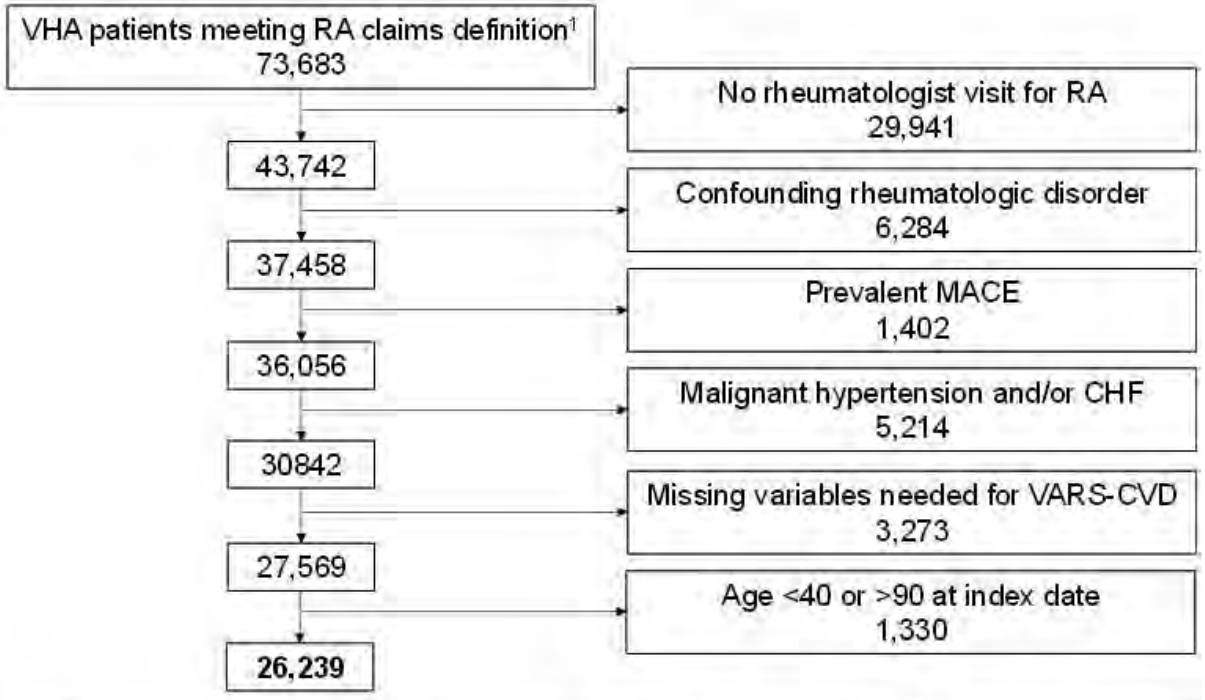
Session Type: Plenary Session

Session Time: 10:30AM–12:00PM

Background/Purpose: A third of RA patients use long-term glucocorticoids (GCs) despite a known dose-dependent association with major adverse cardiovascular (CV) events (MACE). Prior work suggests long-term GC use is common among RA patients with MACE risk factors. We know little about the incremental effect of ongoing GC use on MACE risk in RA patients.

Methods: In this retrospective cohort study, we used national VA administrative data to identify RA patients with ≥1 rheumatology visit during 2013-2018. We defined the index date as the first rheumatology visit in this period after

Figure 1: Data Attrition diagram



[1]Either 1) ≥2 RA outpatient diagnosis codes within >7 but <365 days and ≥1 DMARD dispensed within a year or 2) ≥1 outpatient rheumatologist visit for RA and ≥1 DMARD dispensed within a year

Table 1: Baseline characteristics by MACE risk

	Overall cohort 26,239	Low MACE risk* 5,504	Medium MACE risk* 14,751	High MACE risk* 5,984
Demographics				
Age in years, mean (SD)	63.9 (9.9)	52.8 (6.9)	64.2 (6.9)	73.4 (8.1)
Male, N (%)	22,261 (85%)	2,700 (49%)	13,712 (93%)	5,849 (98%)
Years of follow-up after index date, median (IQR)	4.9 (2.5-5.8)	4.4 (2.2-5.7)	5.1 (2.7-5.8)	5.0 (2.5-5.8)
Health status over lookback period[1]				
Estimated 5-year MACE risk per VARS-CVD, median (IQR)	5.7 (3.4-8.7)	1.8 (1.1-2.4)	5.7 (4.4-7.1)	11.5 (10.1-13.7)
Adjusted Elixhauser count**, median (IQR)	2 (1-3)	2 (1-3)	2 (1-3)	2 (1-4)
Systolic blood pressure in mmHg, mean (SD)	132.9 (15.1)	124.6 (12.0)	132.5 (13.7)	141.6 (16.3)
Diabetes, N (%)	6,799 (26%)	467 (9%)	3,472 (24%)	2,860 (48%)
Smoking history, N (%)	11,406 (44%)	1,330 (24%)	6,590 (45%)	3,486 (58%)
Total cholesterol in mg/dL, mean (SD)	174.8 (36.8)	185.1 (36.2)	172.6 (36.3)	170.7 (36.9)
HDL cholesterol in mg/dL, mean (SD)	47.7 (14.8)	52.9 (16.4)	47.1 (14.4)	44.1 (12.8)
Healthcare utilization				
All office visits/past year, median (IQR)	10 (6-17)	10 (6-18)	10 (6-17)	10 (6-17)
Unique outpatient prescriptions/past year, median (IQR)	10 (6-15)	9 (5-14)	10 (6-15)	10 (7-15)
Emergency department visits/past year, median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	0 (0-1)
RA status				
Methotrexate use/past year (y/n), N(%)	11395 (43%)	2300 (42%)	6530 (44%)	2565 (43%)
Biologic use/past year (y/n), N (%)	7331 (28%)	1410 (26%)	4347 (29%)	1574 (26%)
Rheumatology clinic visits/past year, median (IQR)	2 (1-3)	2 (0-3)	2 (1-3)	2 (0-3)
Glucocorticoid (GC) use				
90-days GC use, year prior to index date, N(%)	4590 (18%)	763 (14%)	2721 (19%)	1106 (19%)
90-days GC use, first year of study period, N(%)	6056 (23%)	1053 (19%)	3562 (24%)	1441 (24%)
GC duration (days), first year of study period, mean (SD)	60.7 (102.9)	49.8 (92.3)	63.8 (105.5)	63.3 (105.0)
MACE				
≥1 MACE during study period, N(%)	837 (3.2%)	65 (1.2%)	477 (3.2%)	295 (4.9%)

[1]Patients with any MACE event or congestive heart failure during the lookback period were excluded from the cohort
MACE: Major adverse cardiovascular events; HDL = high density lipoprotein
* Veterans' Affairs Risk Score for Cardiovascular Disease (VARS-CV) score <3%, 3-9%, and >9%, respectively
** Exclude RA, diabetes, hypertension, CHF

meeting RA diagnostic criteria. We excluded patients < 40 or >90 years and those with other rheumatologic disorders, prior MACE, or congestive heart failure during a lookback period of up to 5 years (Figure 1). We used pharmacy dispensing data to calculate days' supply of GC (exposure), and claims to identify incident MACE (outcome). We defined MACE as any of acute myocardial infarction, stroke, transient ischemic attack, cardiac arrest, or coronary revascularization. We used multilevel logistic regression to evaluate the association between days' supply of GC dispensed in a 6-month period, and the lagged outcome of incident MACE in the following 6-month period. Patients

Table 2: Multilevel logistic regression showing association between days' supply of GC over a 6-month period and incident MACE in the following 6 months

25,630 patients 217,093 observations	Unadjusted odds ratio OR	95% CI	P value
Days' supply GC (per 30 days increase)	**1.151**	**1.12-1.19**	**<0.0001**
VARS-CV score (per 5% increase)	**1.547**	**1.44-1.67**	**<0.0001**
	Model 1*		
Days' supply GC	**1.150**	**1.11-1.19**	**<0.0001**
VARS-CV score	**1.533**	**1.42-1.65**	**<0.0001**
	Model 2**		
Days' supply GC	**1.14**	**1.10-1.19**	**<0.0001**
VARS score	**1.55**	**1.38-1.71**	**<0.0001**

MTX = methotrexate
* Model 1 adjusted for VARS-CV score only
**Model 2 adjusted for 5 baseline covariates: VARS-CV score, sex, number of office visits in year prior to index date, modified Elixhauser count (excluding RA, diabetes, hypertension, and CHF] in year prior to index date, and use of >90 days of GC in the year prior to index date) and 2 time-varying covariates updated every 6 months: methotrexate use and biologic use

were censored after their first MACE event. We adjusted for baseline covariates including demographics, healthcare utilization, and long-term GC use (>90 days), and time-varying covariates including methotrexate and biologic use. We also adjusted for baseline MACE risk using the Veteran's Affairs Risk Score for CV Disease (VARS-CV), developed to recalibrate the ACC/AHA risk calculator for the Veteran population. The algorithm uses medical and pharmacy claims, vital signs, and lab results to calculate a continuous risk prediction estimate, but can also categorize 5-year MACE risk as low (< 3%), medium (3-9%) or high (>9%) using cut points from the ACC/AHA algorithm.

Results: Among 26,239 patients, median 5-year MACE risk by VARS-CV at baseline was 5.7% (IQR 3.4-8.7); 5,984 patients (23%) had high MACE risk (Table 1). Twenty-three percent of patients overall, and 24% with high MACE risk, received ≥90 days of GCs during Year 1 of followup. Incident MACE occurred in 3.2% of patients overall, and 4.9% of patients with high MACE risk. Median (IQR) time to incident MACE was 25 (12-44) months. After adjustment for the covariates above, ach additional 30 days of GC use in a 6-month period was associated with a 1.14 (95% CI 1.10-1.19) increase in odds of MACE in the following 6-month period (Table 2).

Conclusion: In this national RA cohort, 30 days of GC use in a 6-month period was associated with a 14% increase in odds of MACE over the subsequent 6 months. This association was independent of baseline CV, risk, prior long-term GC exposure, and claims-based markers of RA severity such as biologic use. Future work should be directed towards evaluating the effect of persistent GC use on rates of additional MACE events among those who have experienced prior MACE, and examining how baseline MACE risk impacts the relative effect of GC use on incident MACE.

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ALPN-303, an Enhanced, Potent Dual BAFF/APRIL Antagonist Engineered by Directed Evolution for the Treatment of Systemic Lupus Erythematosus (SLE) and Other B Cell-Related Diseases

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SESSION INFORMATION
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Session Type: Plenary Session
Session Time: 10:30AM–12:00PM

Background/Purpose: B cell activating factor (BAFF) and a proliferation inducing ligand (APRIL) are TNF superfamily members that bind TACI (transmembrane activator and CAML interactor), BCMA (B cell maturation antigen), and/or BAFF-R on B cells and together support B cell development, differentiation, and survival. Their co-neutralization dramatically reduces B cell survival and function, including antibody (Ab) production, whereas inhibition of either BAFF or APRIL alone mediates relatively modest effects. ALPN-303 is an Fc fusion protein of a human TACI variant TNFR domain engineered by directed evolution (**Figure 1**). It mediates significantly improved combined BAFF and

APRIL inhibition *in vitro* and enhanced pharmacokinetic (PK) and immunomodulatory properties *in vivo,* as compared to wild-type (WT) TACI-Fc molecules. B cell targeting therapies like the WT TACI-Fc fusions atacicept and telitacicept have demonstrated promising clinical potential in B cell-related diseases like SLE. ALPN-303, with enhanced inhibitory activity against BAFF & APRIL, may further improve clinical outcomes.

Methods: Variant TNFR domains (vTD) of TACI that exhibit enhanced affinity for BAFF and APRIL as compared to WT TACI were identified using our directed evolution platform (**Figure 1**). The most potent variant TACI domain identified was fused to a human IgG Fc to generate the therapeutic candidate ALPN-303. ALPN-303 was evaluated for functional activity: 1) *in vitro* in human lymphocyte assays and in a Jurkat/NF-κB reporter cell line transduced with TACI, 2) in mouse KLH immunization models, 3) in the mouse collagen-induced arthritis model, 4) in the bm12àBL/6

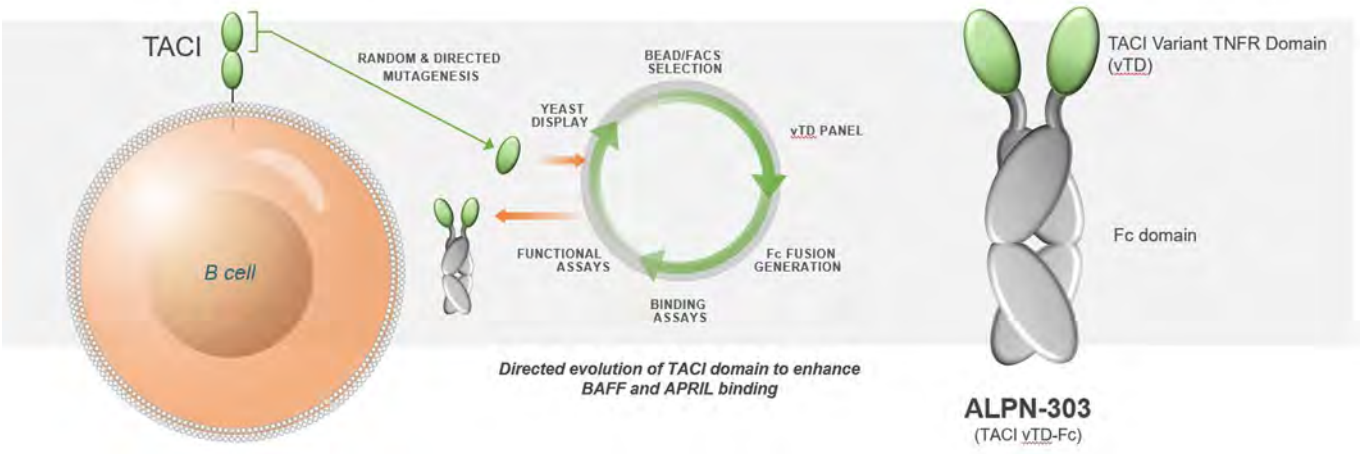
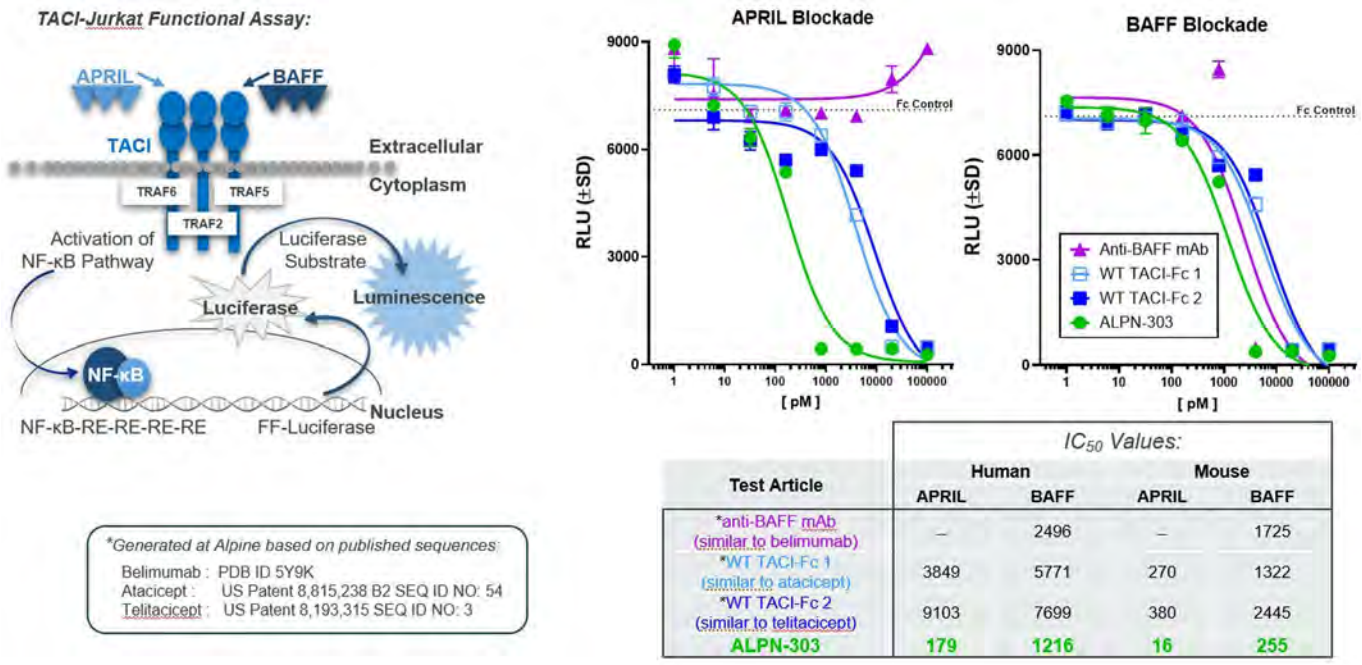


Figure 1. ALPN-303 is a modified TACI-Fc fusion protein generated via directed evolution that mediates enhanced BAFF and APRIL inhibition vs. WT TACI-Fc.



Test Article	IC_{50} Values: Human APRIL	Human BAFF	Mouse APRIL	Mouse BAFF
*anti-BAFF mAb (similar to belimumab)	–	2496	–	1725
*WT TACI-Fc 1 (similar to atacicept)	3849	5771	270	1322
*WT TACI-Fc 2 (similar to telitacicept)	9103	7699	380	2445
ALPN-303	**179**	**1216**	**16**	**255**

Figure 2. ALPN-303 neutralizes APRIL and BAFF activity more potently than WT TACI-Fc in a cell-based reporter assay.

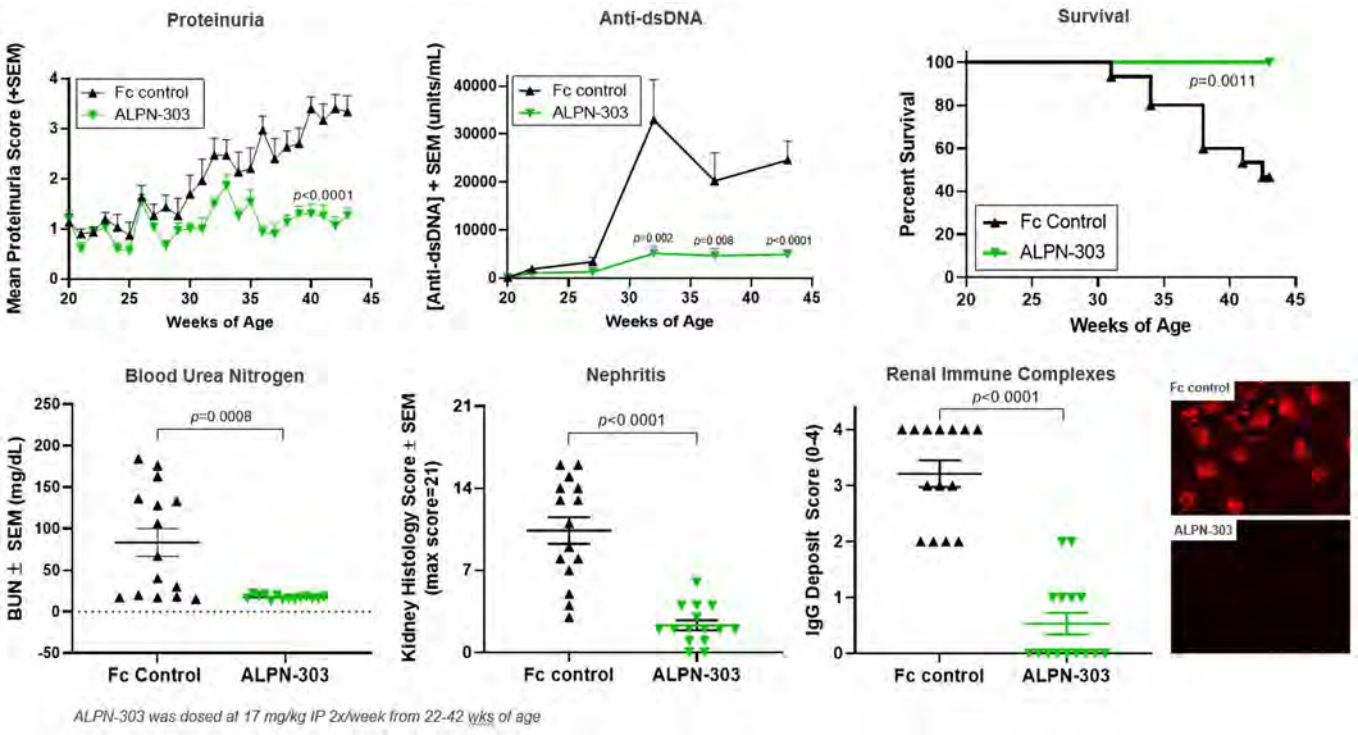


Figure 3. ALPN-303 suppresses disease in the (NZBxNZW)F1 spontaneous lupus model.

induced model of lupus, 5) in the (NZBxNZW)F_1 spontaneous mouse model of lupus, and 6) in preclinical PK/pharmacodynamic studies.

Results: ALPN-303 inhibited BAFF- and APRIL-mediated signaling *in vitro* in human lymphocyte and TACI$^+$ Jurkat assays (**Figure 2**), with significantly lower IC_{50} values than WT TACI-Fc and anti-BAFF Ab comparators. In all mouse models evaluated, administration of ALPN-303 rapidly and significantly reduced key lymphocyte subsets including plasma cells and follicular T helper cells. Furthermore, treatment with ALPN-303 significantly decreased titers of antigen-specific antibodies in immunized mice and in induced disease models, and potently suppressed anti-dsDNA autoAbs, blood urea nitrogen levels, proteinuria, glomerular IgG deposition, and nephritis in the spontaneous NZB/W lupus model (**Figure 3**). Following single dose administration to cynomolgus monkeys, ALPN-303 exhibited higher overall serum exposure and notably enhanced suppression of serum immunoglobulins IgA, IgM, and IgG as compared to WT TACI-Fc treatment.

Conclusion: Directed evolution of TNFR domains has successfully facilitated the development of the novel immunomodulator ALPN-303, a potent BAFF/APRIL antagonist that consistently demonstrates encouraging immunomodulatory activity and efficacy *in vitro* and *in vivo*, superior in preclinical studies to anti-BAFF Abs and WT TACI-Fc. ALPN-303 may thus be an attractive development candidate for the treatment of multiple autoimmune and inflammatory diseases. Preclinical development to enable clinical trials has been initiated.

Disclosure: S. Dillon, Alpine Immune Sciences, 2, 10, 11; **L. Evans**, Alpine Immune Sciences, 3, 10, 11; **K. Lewis**, Alpine Immune Sciences, 3, 10, 11; **J. Yang**, Alpine Immune Sciences, 3, 10, 11; **M. Rixon**, Alpine Immune Sciences, 3, 10, 11; **J. Kuijper**, Alpine Immune Sciences, 3, 10, 11; **D. Demonte**, Alpine Immune Sciences, 3, 10, 11; **J. Bhandari**, Alpine Immune Sciences, 3, 11; **S. Levin**, Alpine Immune Sciences, 3, 10, 11; **K. Kleist**, Alpine Immune Sciences, 3, 11; **S. Mudri**, Alpine Immune Sciences, 3, 11; **S. Bort**, Alpine Immune Sciences, 3, 11; **D. Ardourel**, Alpine Immune Sciences, 3, 11; **M. Seaberg**, Alpine Immune Sciences, 3, 11; **N. Wang**, Alpine Immune Sciences, 3, 11; **C. Gudgeon**, Alpine Immune Sciences, 3, 11; **R. Sanderson**, Alpine Immune Sciences, 3, 11; **M. Wolfson**, Alpine Immune

Sciences, 3, 10, 11; **J. Hillson**, Alpine Immune Sciences, 3, 11; **P. Holland**, Alpine Immune Sciences, 3, 11; **S. Peng**, Alpine Immune Sciences, 3, 4, 10, 11.

Abstract Number: 1430

Autoantibodies Stabilize Neutrophil Extracellular Traps in COVID-19

Yu Zuo[1], Srilakshmi Yalavarthi[1], Sherwin Navaz[1], Claire Hoy[1], Alyssa Harbaugh[1], Kelsey Gockman[1], Melanie Zuo[1], Jacqueline Madison[1], Hui Shi[1], Yogendra Kanthi[2] and Jason Knight[1], [1]University of Michigan, Ann Arbor, MI, [2]NHLBI, NIH, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Innate Immunity (1430–1433)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: The release of neutrophil extracellular traps (NETs) by hyperactive neutrophils is recognized to play an important role in the thromboinflammatory milieu inherent to severe presentations of COVID-19. At the same time, a variety of functional autoantibodies have been observed in individuals with severe COVID-19 where they likely contribute to immunopathology. Work by our group and others has found that many hospitalized COVID-19 patients develop antiphospholipid antibodies similar to those found in antiphospholipid syndrome (APS). Patients with APS (as well as lupus and ANCA-associated vasculitis) have also been reported to develop autoantibodies targeting NETs, which impair NET clearance and activate complement. Here, we aimed to determine the extent to which autoantibodies might target NETs in COVID-19 and, if detected, to elucidate their clinical associations and potential functions.

Methods: NETs were solubilized and coated onto ELISA plates. We then measured IgG and IgM global anti-NET activity in 328 individuals hospitalized with COVID-19 alongside 48 healthy controls. The ability of COVID sera and purified anti-NET antibodies to protect NETs from degradation was determined. We assessed complement deposition on NETs by immunofluorescence microscopy.

Results: We found elevated levels of anti-NET IgG and IgM in patients with COVID-19 as compared with healthy controls ($p< 0.0001$ for both IgG and IgM) (Figure 1A-B). Using a cutoff of 2 standard deviations above the control mean, 27% of patients were positive for anti-NET IgG and 60% for anti-NET IgM. There was a strong interrelationship between anti-NET IgG and anti-NET IgM ($r=0.4$, $p< 0.0001$). High anti-NET antibody levels associated with circulating markers of NETs. Specifically, anti-NET IgG and IgM levels were positively correlated with myeloperoxidase-DNA complexes (IgG $r=0.31$, $p< 0.0001$; IgM $r=0.41$, $p< 0.0001$) and calprotectin (IgG $r=0.33$, $p< 0.0001$; IgM $r=0.34$, $p< 0.0001$). Clinically, anti-NET antibodies tracked with impaired oxygenation efficiency defined as SpO_2/FiO_2 ratio (IgG $r=-0.17$, $p=0.018$; IgM $r=-0.30$, $p< 0.0001$) and elevated levels of circulating D-dimer (IgG $r=0.33$, $p< 0.0001$; IgM $r=0.19$, $p=0.0012$). Furthermore, patients who required mechanical ventilation had higher levels of anti-NET antibodies than those who did not require oxygen supplementation (IgG $p=0.0013$; IgM $p< 0.0001$). Mechanistically, levels of anti-NET IgG in particular demonstrated a negative correlation with the NET degradation potential of COVID sera (Figure 1C), while purified IgG from high anti-NET sera impaired the ability of DNases in healthy serum to degrade NETs (Figure 1D). As compared with low anti-NET COVID sera, high anti-NET sera also more efficiently deposited complement C3d on NETs (Figure 2).

Conclusion: In summary, these data reveal high levels of anti-NET antibodies in many individuals hospitalized with COVID-19, where they track with NETs themselves and also disease severity. It is likely that these antibodies impair

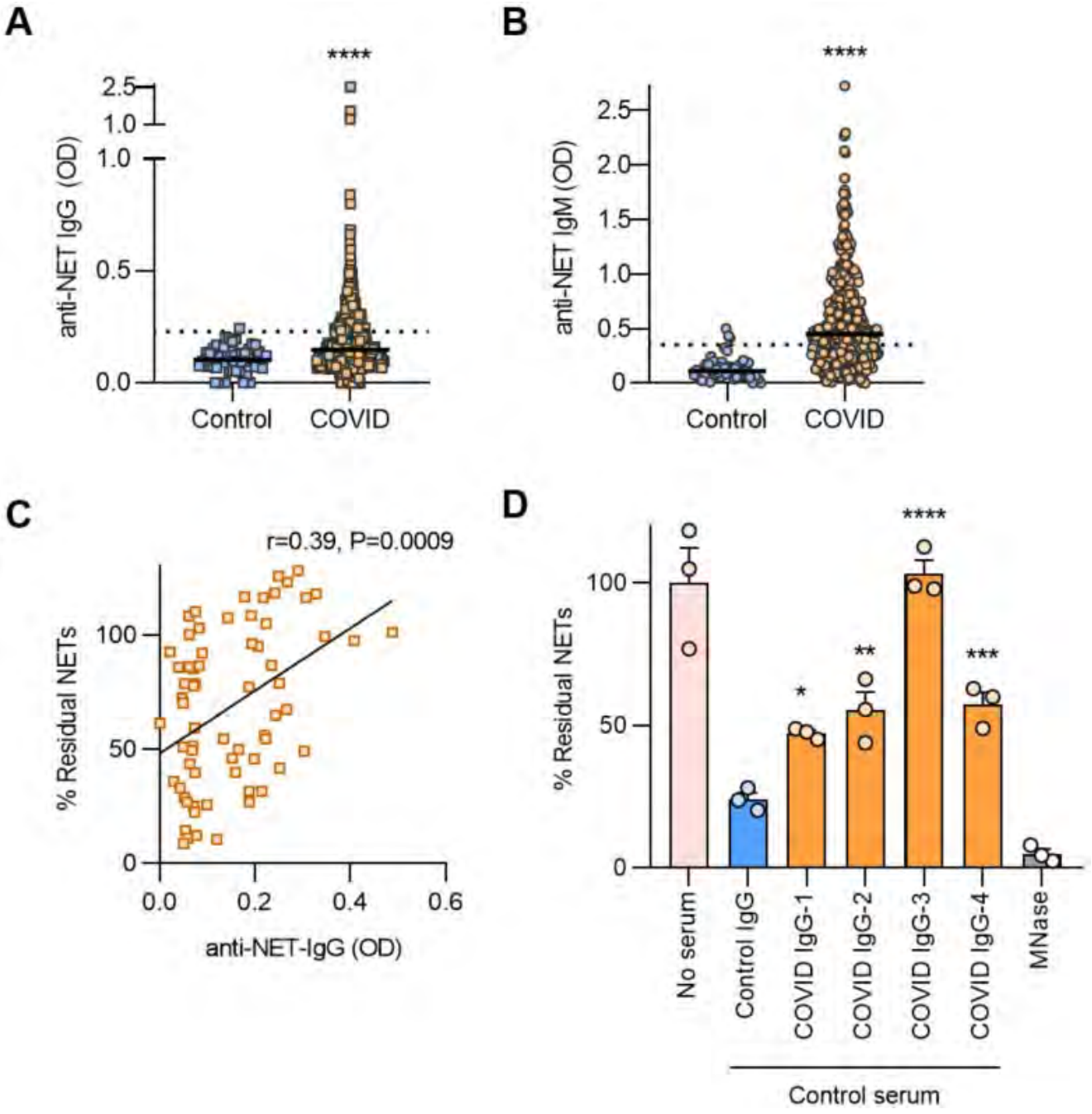


Figure 1. A-B, Anti-NET IgG/M levels were compared by Mann-Whitney test; ****p<0.0001. Dotted lines indicate positive threshold set at 2 standard deviations above the control mean. C, Freshly-induced NETs were incubated with sera from COVID-19 patients. After 90 minutes, percent residual NETs were determined. Correlation with anti-NET IgG was determined by Spearman's method. D, Freshly-induced NETs were incubated with control serum supplemented with either purified IgG from COVID patients or controls, and percent residual NETs were determined after 90 minutes. COVID IgG was compared to control by one-way ANOVA; *p<0.05, **p<0.01, ***p<0.001, and ****p<0.0001.

NET clearance and potentiate complement activation, which may together conspire to potentiate SARS-CoV-2-mediated thromboinflammation.

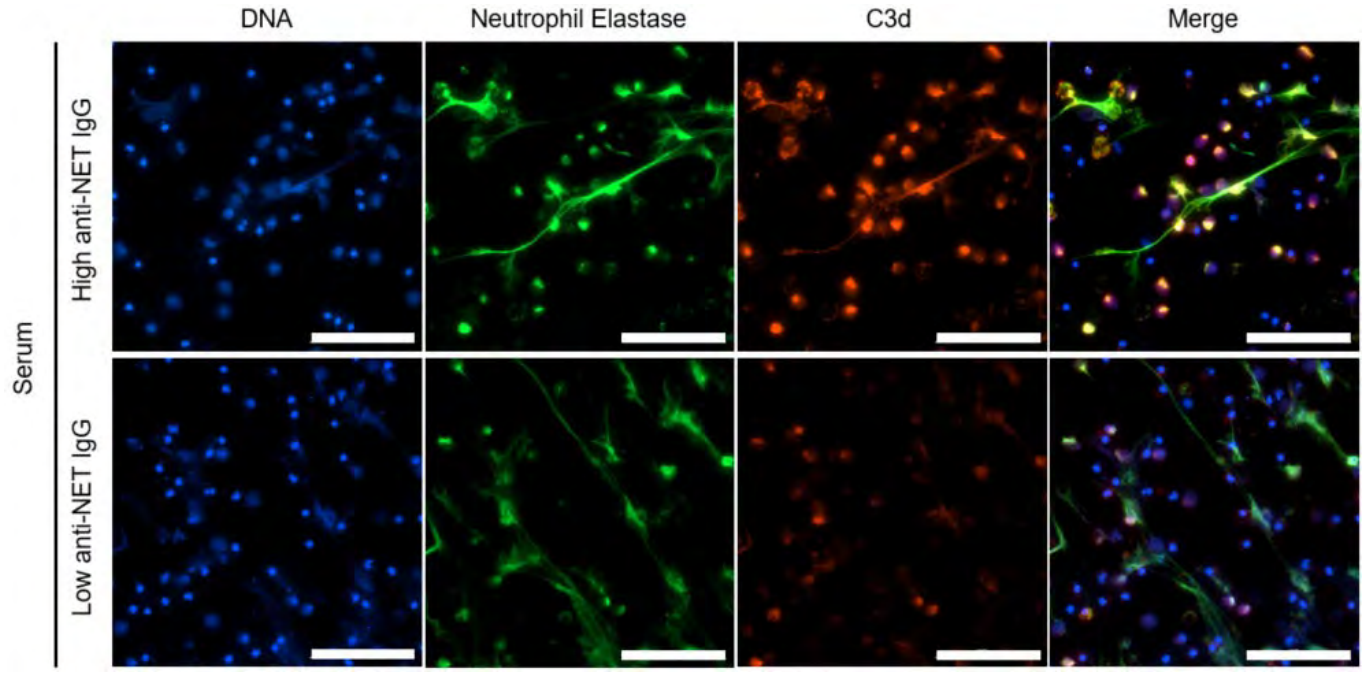


Figure 2. Control neutrophils were stimulated with PMA to generate NETs. After fixation with paraformaldehyde, NETs were incubated with sera from patients with high (top panels) or low (bottom panels) anti-NET IgG; scale bars=100 microns.

Disclosure: Y. Zuo, None; **S. Yalavarthi**, None; **S. Navaz**, None; **C. Hoy**, None; **A. Harbaugh**, None; **K. Gockman**, None; **M. Zuo**, None; **J. Madison**, None; **H. Shi**, None; **Y. Kanthi**, None; **J. Knight**, None.

Abstract Number: 1431

Human TLR8 Leads to Fatal Anemia Due to Ineffective Erythropoiesis in Bone Marrow Erythroblastic Islands in Murine SLE

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Innate Immunity (1430–1433)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: There are multiple causes of anemia in SLE including hemolysis, inflammation, renal insufficiency and, more rarely, microangiopathy, hemophagocytosis and bone marrow insufficiency. One cause of anemia in SLE is impaired bone marrow erythropoiesis, possibly mediated by inflammatory cytokines such as TNF or Type I interferon, or by autoantibodies. Because innate immune mechanisms are associated with anemia, here we studied the effect of TLR7 and TLR8 overexpression on SLE related anemia in an animal model in which we introduced human TLR8. Mouse and human TLR7 and human TLR8 recognize ssRNA but human TLR7 and TLR8 differ with respect to their cellular locations and the type of RNA they recognize.

Methods: Sle1.Yaa mice expressing 1-2 copies of huTLR8 as a BAC transgene (huTR8.tg) were generated and followed clinically. HuTLR8 DNA copy number and mRNA expression was confirmed by qDigital and qRT-PCR respec-

tively. Serum autoantibodies were assessed over time. Spleen weights were assessed and splenocytes, renal and bone marrow cells were characterized by flow cytometric analysis. Mammalian erythropoiesis occurs within anatomic niches, erythroblastic islands (EBIs), where erythroblast maturation occurs by close interaction with a central macrophage. EBIs from both bone marrow and spleen were characterized by multispectral imaging flow cytometry and isolated for single cell RNA sequencing (scRNAseq) analysis.

Results: HuTLR8.tg SLE1.Yaa males expressing 2 copies of huTLR8 showed accelerated mortality by 4 months of age compared with >9 months in Sle1.Yaa and homozygous huTLR8.tg C57BL/6.Yaa controls. Complete blood counts in male SLE1.Yaa.huTLR8 mice identified severe anemia as the cause of death. This phenotype first became evident at >12 weeks of age, required both the Sle1 and Yaa loci, as well as the huTLR8 transgene and was more common and severe in huTLR8tg homozygotes. Flow cytometric analyses revealed ineffective erythropoiesis with a block at the transition from the CFU-E to proerythroblast stage. Single cell RNASeq showed that this was associated with an inflammatory phenotype in erythroblastic island central macrophages with a downregulation in adhesion and phagocytic receptors. Compensatory stress erythropoiesis in the spleen was associated with vast expansion of red pulp macrophages with phagocytic properties and fatal anemia was associated with a decrease in red blood cell (RBC) half-life, suggesting that excessive RBC phagocytosis eventually exceeds the capability of stress erythropoiesis to replace the RBC mass.

Conclusion: These data implicate huTLR8 innate inflammatory signals and the presence of auto-antibodies in defective bone marrow hematopoiesis, resulting in an altered phenotype of bone marrow EBI-associated central macrophages consequently reducing erythroid output. Furthermore, loss of mature cells through increased phagocytosis of red cells results in a fatal anemia phenotype. Further elucidating how dysregulated TLR8 signaling disrupts homeostasis of the bone marrow niche is crucial to better understand the role of this TLR in autoimmunity and will facilitate more precise therapeutic targeting.

Disclosure: N. Maria, None; **J. Papoin**, None; **C. Raparia**, None; **Z. Sun**, None; **S. Martinez**, None; **W. Zhang**, RenalytixAI, 1, 9; **L. Blanc**, None; **A. Davidson**, None.

Abstract Number: 1432

Modulation of Auto-Inflammation with a Novel Selective Cyclic GMP-AMP Synthase (cGAS) Inhibitor in a *Trex1*$^{-/-}$ Model

Kelly Pike[1], Alexandre Caron[1], Emilie Bérubé[1], Ramsay Beveridge[1], Marc-Oliver Boily[2], Jason Burch[1], Valerie Dumais[1], Nadine Fradet[1], Samuel Gaudreault[1], Daniel McKay[1], Marianne Raymond[1], Eleftheria Seliniotakis[1], Daniel Sietsema[3], Alexander Skeldon[1], Miguel St.-Onge[1], Li Wang[3] and Michael Crackower[4], [1]Ventus Therapeutics, Montréal, QC, Canada, [2]Ventus Therapeutics, Monreal, QC, Canada, [3]Ventus Therapeutics, Boston, MA, [4]Ventus Therapeutics, Boston, QC, Canada

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Innate Immunity (1430–1433)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Serum titers of anti-type II collagen (anti-CII) antibodies were reported to rise at the recurrence of relapsing polychondritis (RP). It remains to be identified whether anti-CII antibodies at the time of diagnosis are risk factors for relapse. The aim of this study is to investigate the association between anti-CII antibodies at diagnosis and relapse.

Methods: We conducted a retrospective study of patients diagnosed with RP in our hospital between April 2006 and June 2020. Relapse was defined as aggravation of manifestations or worsening of imaging findings which require intensified treatments. Anti-CII antibodies were assayed by a clinically certificated ELISA test.

Results: Eighteen patients were included in this study. The median age at diagnosis was 68.2 years (IQR 56.4-72.7 years), and 55.6% were females. The median period of observation was 40.9 months (IQR 20.7-57.1 months). Seven patients had relapses (38.9%). The median time to the first relapse was 161 days (IQR 135-394 days). The anti-CII antibodies were tested in 13 patients. Tracheobronchial involvement and nasal chondritis were more frequent in the relapse group compared to the non-relapse group (71.4% vs 18.2%, p = 0.049; 85.7% vs 9.1%, p = 0.002, respectively). The relapse group had higher levels of anti-CII antibodies at diagnosis [median (IQR) : 66.8 EU/mL(38.9-131.8 EU/mL) vs 14.5 EU/mL(10.7-18.7 EU/mL), p = 0.001] (**Figure 1**). Comparing for initial treatments, the relapse group tended to receive higher dose of prednisolone (median (IQR) 45.0mg (25.0-50.0 mg) vs 30.0mg (1.5-40.0 mg), p = 0.055). Immunosuppressive drugs and biologics were more often used in the relapse group (57.1% vs 0%, p = 0.011). Kaplan-Meier estimates of the relapse-free survival showed the anti-CII antibodies positive group was significantly more likely to relapse than the negative group (Log-rank p = 0.009; HR = 1.017, 95% CI 1.004-1.031) (**Figure 2**).

Conclusion: High titers of anti-CII antibodies at the time of diagnosis are the risk factors for relapse. This study shows that tracheobronchial involvement may also be a factor associated with relapse. We plan to measure anti-CII antibodies in consistent intervals and discuss whether routine anti-CII antibodies monitoring is useful for predicting future relapse.

Disclosure: K. Pike, None; **A. Caron**, None; **E. Bérubé**, None; **R. Beveridge**, None; **M. Boily**, None; **J. Burch**, None; **V. Dumais**, None; **N. Fradet**, None; **S. Gaudreault**, None; **D. McKay**, None; **M. Raymond**, None; **E. Seliniotakis**, None; **D. Sietsema**, None; **A. Skeldon**, None; **M. St.-Onge**, None; **L. Wang**, None; **M. Crackower**, None.

Abstract Number: 1433

Endothelium-protective, Histone-neutralizing Properties of the Polyanionic Agent Defibrotide

Hui Shi[1], Alex Gandhi[1], Stephanie Smith[1], Qiuyu Wang[1], Diane Chiang[1], Srilakshmi Yalavarthi[1], Ramadan Ali[2], Chao Liu[1], Gautam Sule[1], Eliza Pei-Suen Tsou[1], Yu Zuo[1], Yogendra Kanthi[3], Jiandie Lin[1], James Morrissey[1] and Jason Knight[1], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ann Arobr, MI, [3]NHLBI, NIH, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Innate Immunity (1430–1433)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Neutrophil-mediated activation of the endothelium plays a role in the pathogenesis of diverse disease states ranging from autoimmunity to cancer to COVID-19. Neutralization of cationic proteins (such as neutrophil extracellular trap/**NET**-derived histones) with polyanionic compounds has been suggested as a strategy for protecting the endothelium from such insults. Here, we investigated the role of the FDA-approved agent defibrotide (a pleotropic mixture of oligonucleotides) in engaging histones and blocking their pathological effects on endothelium.

Methods: Human umbilical vein endothelial cells (**HUVECs**) and human microvascular endothelial cells (**HMVECs**) were cultured with purified NETs or histone H4. Cell activation was determined by specific gene expression (e.g., E-selectin), neutrophil adhesion, enzymatic activity of tissue factor, and RNA sequencing. Cell viability was tested

by staining with crystal violet and annexin V. Surface plasmon resonance was used to verify molecular interactions. Thrombosis was modeled in mice via stenosis of the inferior vena cava.

Results: HUVECs and HMVECs were treated with NETs (1 μg DNA content/ml) in the presence or absence of defibrotide (10 μg/ml) for 4 hours. Defibrotide significantly ($p < 0.0001$) mitigated NET-mediated upregulation of E-selectin (30% reduction), ICAM-1 (70%), and VCAM-1 (60%). Calcein-AM-labeled neutrophils adhered 10-times more strongly to NET-activated endothelial cells, an effect that was reduced by 50% in the presence of defibrotide ($p < 0.01$). NET-mediated tissue factor upregulation was also significantly reduced by defibrotide, whether measured by gene expression or enzymatic activity. Network analysis of upregulated genes in NET-stimulated endothelial cells revealed an inflammatory signature highlighted by meta groups such as the TNF and NF-κB signaling pathways, which were downregulated by defibrotide. Narrowing the focus from polymolecular NETs to specific NET components, a strong interaction between histone H4 and defibrotide was confirmed by surface plasmon resonance (K_D 53.5 nM). Purified histone H4 (25 μg/ml) increased expression of E-selectin and ICAM-1 by endothelial cells, effects that were completely abolished by defibrotide. Furthermore, defibrotide markedly protected the viability of endothelial cells over a 24-hour period of exposure to histone H4 (100 μg/ml). Notably, histone H4-mediated cell death was on the spectrum of pyroptosis with increased IL-1β and cleavage of gasdermin D (both inhibited by defibrotide). Finally, in a mouse model of thrombosis, injection of histones (10 mg/kg) markedly increased thrombus accretion at 24 hours (mean thrombus weight 8 mg vs. 2 mg), with thrombus weight returned to baseline by infusion of 150 mg/kg defibrotide at the time of histone injection. Notably, soluble E-selectin tracked closely with thrombus accretion, as did infiltration of thrombus leukocytes.

Conclusion: These data provide insights into the potential role of polyanionic compounds in protecting the endothelium from thromboinflammation with potential implications for myriad NET- and histone-accelerated disease states.

Disclosure: H. Shi, None; **A. Gandhi**, None; **S. Smith**, None; **Q. Wang**, None; **D. Chiang**, None; **S. Yalavarthi**, None; **R. Ali**, None; **C. Liu**, None; **G. Sule**, None; **E. Tsou**, None; **Y. Zuo**, None; **Y. Kanthi**, None; **J. Lin**, None; **J. Morrissey**, None; **J. Knight**, None.

Abstract Number: 1434

Multiomic Study of Skin, Peripheral Blood and Serum: Is Serum Proteome a Reflection of Disease Process at the End-Organ Level in Systemic Sclerosis?

Victor Farutin[1], Elma Kurtagic[2], Joel Pradines[3], Ishan Capila[3], Maureen Mayes[4], Minghua Wu[5], Anthony Manning[3] and Shervin Assassi[6], [1]Janssen R&D, LLC, Watertown, MA, [2]Janssen R&D, LLC, Cambridge, [3]Momenta Pharmaceuticals, Inc., Cambridge, MA, [4]Division of Rheumatology and Clinical Immunogenetics, University of Texas McGovern Medical School, Houston, TX, [5]University of Texas Health Science Center at Houston, Houston, TX, [6]University of Texas McGovern Medical School at Houston, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (1434–1437)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Discovery of biomarkers in systemic sclerosis (SSc) represents an unmet clinical need. Samples from prominently affected fibrotic end-organs such as lung and skin are not readily available whereas serum proteins are assessed during routine clinical care. However, it is unclear to what extent serum proteins reflect the

molecular dysregulations of peripheral blood cells (PBCs) or affected end-organs. This study describes multiomic comparative analysis of SSc serum proteomic profile as well as gene expression analysis of PBC and skin biopsies in concurrently collected samples from SSc patients and healthy controls.

Methods: Global gene expression profiling on Illumina HumanHT-12 BeadChip was carried out in skin and PBC samples obtained from 49 patients and 25 unaffected controls. Levels of 911 proteins were determined in concurrently collected serum samples with Olink Proximity Extension Assay (PEA) technology.

Results: SSc serum profile revealed an upregulation of proteins involved in pro-fibrotic, homing and extravasation, as well as extracellular matrix components/modulators. Notably, several soluble receptor proteins such as EGFR, ERBB2, ERBB3, VEGFR2, TGFBR3, and PDGF-Rα were downregulated. Thirty-nine proteins correlated with severity of SSc skin disease as assessed by modified Rodnan Skin Score (mRSS) (FDR< 5%). There was a significant correlation between direction of differential expression of serum proteins in SSc vs. control comparison and their association with mRSS (ρ=0.59, permutation p< 0.0001) (Figure 1). Correlative analysis of differences between SSc patients and healthy controls among the three datasets demonstrated that:

1) The differential expression of serum protein in SSc vs. control comparison significantly correlated with the differential expression of corresponding transcripts in skin but not in PBCs (p=0.014 vs. p=0.24) (Fig 2A).

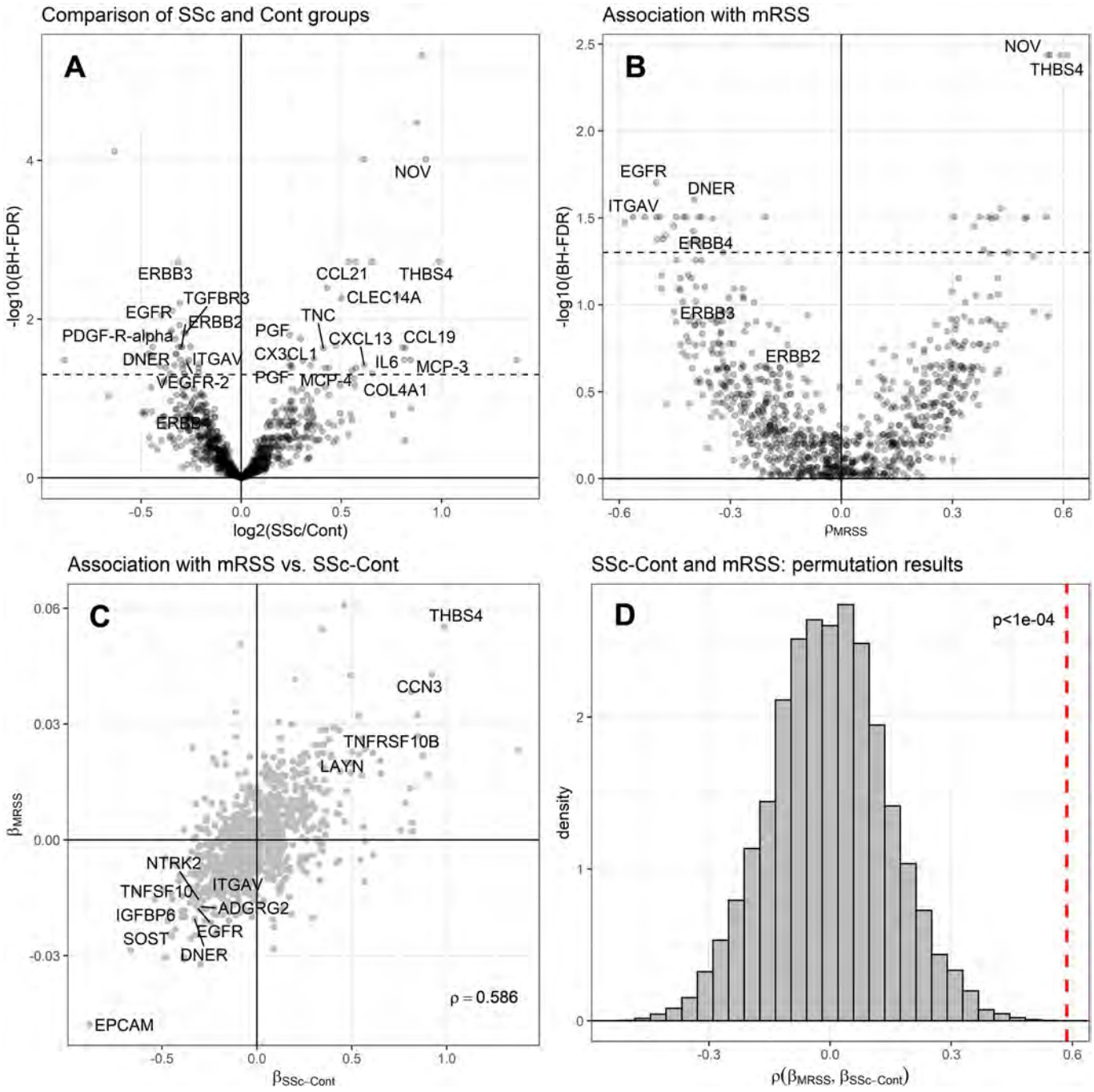
2) The differentially expressed serum proteins represented more significant Well-Associated-Proteins (WAP) (Pradines et al. PMC7046299) in the skin than in PBC gene expression dataset, as demonstrated by lower WAP scores in the skin tissue (Figure 2B).

3) The assessment of the concordance of between-sample similarities at the entire dataset level revealed that the molecular profile of serum proteins and skin gene expression data were significantly concordant in SSc patients but not in healthy controls. On the contrary, the concordance of similarities between serum protein and PBC gene expression profiles was most pronounced in healthy controls and notably reduced in patients, suggesting disruption of correlation between the serum proteome and PBC transcriptome in SSc patients, contrary to healthy controls due to spill-over effect from skin. (Fig 3).

Conclusion: In this first multiomic cross-comparison of SSc serum proteins, PBC transcriptome and skin transcriptome in concurrently collected samples, the serum protein profile correlated more closely with molecular dysregulations of skin than PBCs, supporting the notion that it might serve as a reflection of disease severity at the end-organ level.

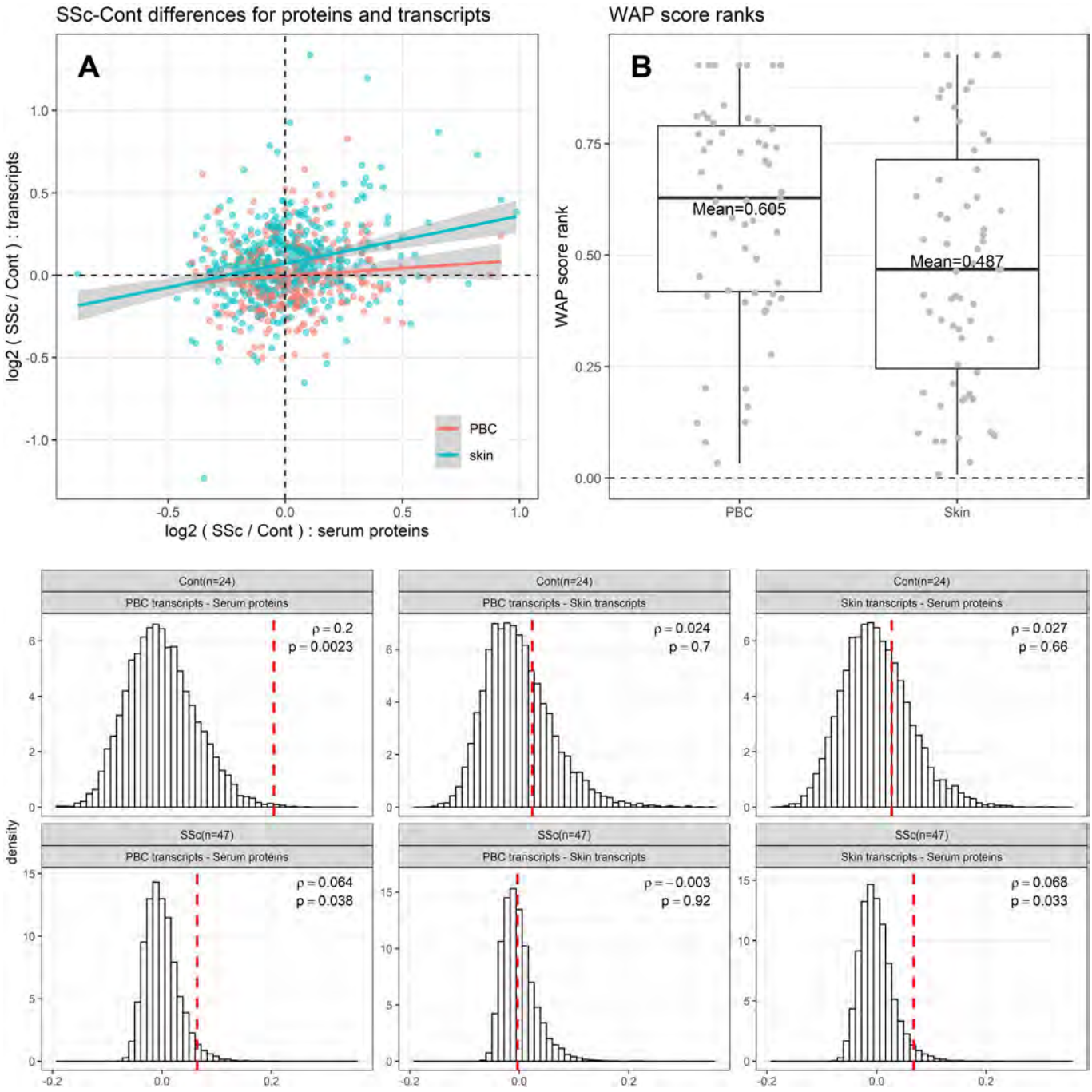
Serum proteins associations with disease and mRSS: a) Volcano plot of SSc-Cont differences; b) Volcano plot of correlation with mRSS in SSc patients; c) Scatterplot of serum proteins associations with mRSS vs. SSc-Cont differences; d) Permutation-based significance of the correlation between serum protein associations with mRSS and SSc-Cont differences. Vertical red dashes in panel d) indicate observed correlation between mRSS and disease effects on serum proteome; histogram represents distribution of such correlations obtained for randomly permuted sample annotation. Text labels in panel c) indicate proteins associated at BH-FDR<5% both with mRSS and disease.

SSc-Cont differences for the serum proteins are significantly associated with SSc-Cont differences in skin: a) SSc-Cont differences are positively correlated between serum proteins and corresponding skin transcripts; b) WAP score ranks of differentially expressed serum proteins for SSc-Cont differences in skin and in PBC (lower values of rank represent more significant WAPs). The WAP ranking is generated based on prior knowledge in the form of protein-protein interaction networks.



Concordance of between samples similarities (as Spearman correlations) for each pairwise combination of the three datasets: serum proteins, PBC transcripts and skin transcripts. Top row displays results for healthy controls, bottom row – for SSc patients. Mantel test results (vertical red dashes represent the observed concordance of between sample similarities for the actual mapping of samples to subjects) are compared to their corresponding null distributions (obtained by randomly permuting assignment of samples to subjects in each dataset).

Disclosure: V. Farutin, Janssen Pharmaceutical Companies of Johnson & Johnson, 3, 11, Momenta Pharmaceuticals, Inc., 3, 11; **E. Kurtagic**, Johnson & Johnson, 3, 11; **J. Pradines**, Takeda Pharmaceuticals, 3; **I. Capila**, Johnson and Johnson, 12, Share holding, Momenta Pharmaceuticals, 12, Share holding; **M. Mayes**, Actelion Pharma, 1, Mitsubishi-Tanabe, 1, Corbus Pharma, 5, Boehringer-Ingelheim, 1, 5, Eicos, 1, 5, Galapagos Pharma, 1, 5; **M. Wu**,



None; **A. Manning**, None; **S. Assassi**, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2.

Abstract Number: 1435

Identification of Distinct Fibroblast Populations in Systemic Sclerosis 3D Skin Tissues with Single Cell Omics

Noelle Kosarek[1], Heetaek Yang[2], Fred W. Kolling[3], Tamar Abel[4], Mengqi Huang[5], Avi Smith[6], Jonathan Garlick[6], Patricia A. Pioli[2] and Michael L. Whitfield[7], [1]Dartmouth Geisel School of Medicine, Hartford, VT, [2]Geisel School of Medicine, Hanover, NH, [3]Centers for Quantitative Biology, Hanover, [4]Geisel School of Medicine, West Lebanon, NH, [5]University of Pittsburgh, Pittsburgh, PA, [6]Tufts University School of Dental Medicine, Boston, MA, [7]Geisel School of Medicine, Lebanon, NH

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (1434–1437)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disease characterized by skin and internal organ fibrosis, vascular abnormalities, and autoantibody formation. Single cell genomics studies have identified multiple fibroblasts populations in normal and fibrotic skin *in vivo*. Here we report a 3D skin-like tissue that reproduces multiple fibroblasts populations similar to those observed in human skin *in vivo*.

Methods: We have developed *in vitro* 3D skin-like tissues that reproduce phenotypic and molecular aspects of SSc. Two different types of 3D tissues were analyzed including a self-assembly (SA) tissue with only fibroblasts and a skin equivalent (saSE) tissue constructed with fibroblasts, keratinocytes, macrophages, and plasma isolated from donors. SA or saSE 3D skin-like tissues were seeded with either SSc-derived or control cells; the same cells were seeded into 2D culture in parallel. 3D skin-like tissues were dissociated into single cell suspensions and processed using the 10X genomics platform. Single cell RNA-sequencing (scRNA-seq) of the saSE tissues yielded expression profiles for 15,921 SSc and 31,632 control cells, the SA tissue model included expression profiles for 27,217 SSc and 26,415 control cells, 2D cells in cultures included 36,419 SSc and 26,991 control cells.

Results: scRNA-seq was performed to compare cells grown in 2D cultures to 3D SA, and saSE tissues. The most complex model, the saSE model, exhibited four distinct fibroblasts populations that parallel those observed in normal-human skin (Figure 1A). Analysis of fibroblasts grown in 2D culture showed the least diversity, consisting of only two fibroblast subsets. Fibroblast subsets in the more complex saSE tissue model were characterized by greater expression of mediators implicated in SSc pathogenesis. Fibroblast subpopulations were named by their top two differentially expressed genes and are referred to as “Fibroblast VEGFA, STC1”, “Fibroblast APOE, CDF”, “Fibroblast LUM, TPM1”, and “Fibroblast MMP2, PTGDS”. The “Fibroblast LUM, TPM1” cluster was marked by expression of collagen genes, notably COL1A1 and COL3A1, that are over-expressed in SSc (Figure 1B). Gene set enrichment analysis (GSEA) of each fibroblast subpopulation demonstrated upregulation of TGFβ signaling in clusters “Fibroblast LUM, TPM1” and “Fibroblast VEGFA, STC1”. IL2-STAT5 signaling, Hypoxia, and PI3K signaling were also reported as differentially-expressed pathways among these fibroblast subpopulations. Comparison to scRNA-seq data from human skin biopsies shows parallel populations of fibroblasts highly expressing APOE, PTGDS, and LUM.

Conclusion: We have used scRNA-seq to capture fibroblasts diversity in a fabricated 3D human skin model that recapitulates SSc dermal fibrosis. We identified four fibroblast subsets with potential roles in SSc. GSEA demonstrated that each of these populations is characterized by distinct signaling pathway activation. These fibroblast subsets likely make unique contributions to underlying SSc pathology and may represent targetable cell types for therapeutic intervention in 3D skin models that more closely approximate the human condition.

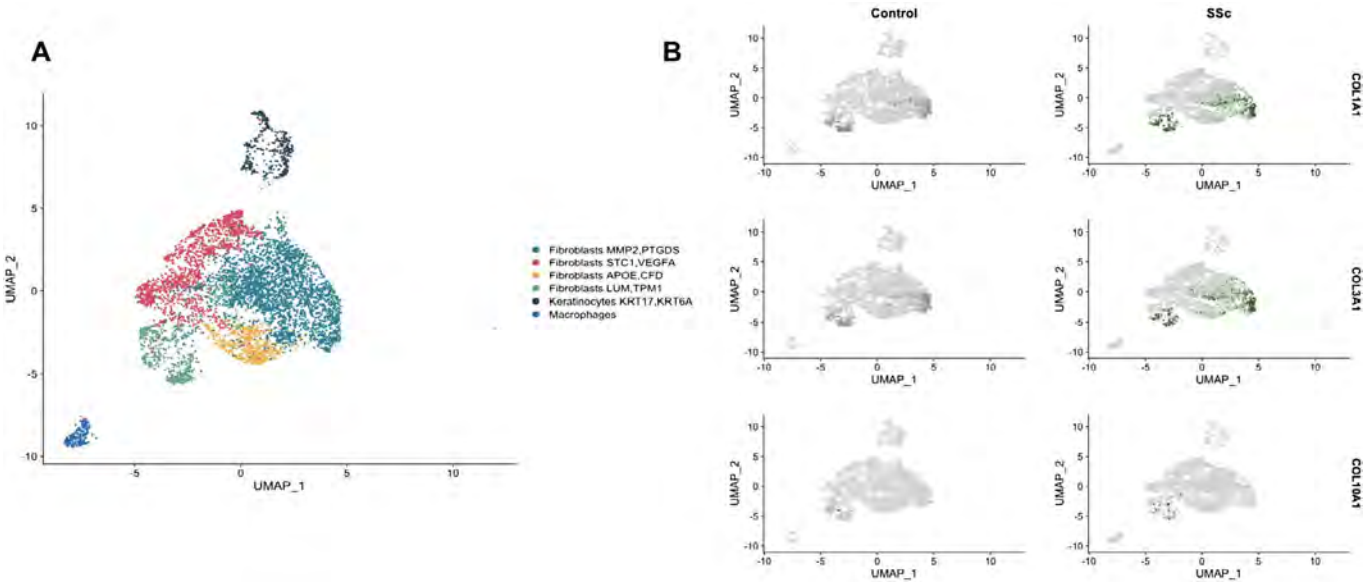


Figure 1. A. The saSE model system revealed four distinct fibroblast populations expressing biologically and pathologically relevant genes. We also identified a small populations of macrophages and keratinocytes. B. Differential gene expression between SSc and healthy control samples revealed upregulation of collagen genes COL1A1, COL3A1, and COL10A1 in SSc samples. This differential activation of fibroblasts is likely contributing to SSc pathogenesis.

Disclosure: N. Kosarek, None; **H. Yang**, None; **F. Kolling**, None; **T. Abel**, None; **M. Huang**, None; **A. Smith**, None; **J. Garlick**, None; **P. Pioli**, None; **M. Whitfield**, Celdara Medical, 2, 5, 8, 12, Scientific Founder.

Abstract Number: 1436

Expanded PD-1^{hi} CXCR5^{-} HLA-DR^{+} T Cells Is Associated with Interstitial Lung Disease in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (1434–1437)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Interstitial lung disease (ILD) is the major cause of morbidity and mortality in systemic sclerosis (SSc), yet there are few biomarkers to identify pathologic immune activation. T cells play a key role in initiating and promoting lung injury in SSc. Recent reports have indicated that circulating PD-1^{+} CXCR5^{+} T follicular helper cells (Tfh) and PD-1^{hi} CXCR5^{-} T peripheral helper cells (Tph) are expanded in SSc patients. Tfh and Tph cells are B cell-helper T cells that can display variable expression of ICOS and/or HLA-DR. Here we have evaluated both the frequency and phenotype of PD-1^{hi} cells in the peripheral blood of SSc patients, and assessed association with ILD.

Methods: We immunophenotyped blood T cells using a 39-marker mass cytometry panel. Peripheral blood mononuclear cells were collected from SSc patients (n=82) and age matched non-inflammatory controls (n=18). Patient samples were analyzed in barcoded batches with each one randomized to include both healthy controls and SSc

patients with varying lung disease. Data was analyzed by biaxial gating in FlowJo and by FlowSOM dimensional reduction and clustering. Comparisons between SSc patient samples and healthy controls were performed using Mann-Whitney *U* test with Bonferroni correction. Association between expanded cell population and lung disease metrics was assessed by Spearman correlation.

Results: In this cohort, the frequencies of Tph (PD-1^{hi} CXCR5^{-}) and Tfh (PD-1^{hi} CXCR5^{+}) CD4 T cells were not increased in SSc patients compared to healthy controls. However, tSNE visualization of PD-1hiCXCR5- cells revealed substantial heterogeneity in expression of ICOS and HLA-DR within this subset. A detailed cytometric analysis of expression of the markers in the cytometry panel on these cell subsets identified upregulation of HLA-DR and CD38 expression on PD-1^{hi} CXCR5^{-} cells from SSc patients compared to controls (Bonferroni adjusted p< 0.05) (Figure 1A). Biaxial gating confirmed the significant expansion of a specific CD4 T cell population with a PD-1^{hi} CXCR5^{-} ICOS^{-} HLA-DR^{+} phenotype, which was significantly increased in SSc patients compared to healthy controls (0.22% vs. 0.12%, p=0.003) (Figure 1B). This subset was also expanded in patients with SSc-ILD when compared with those

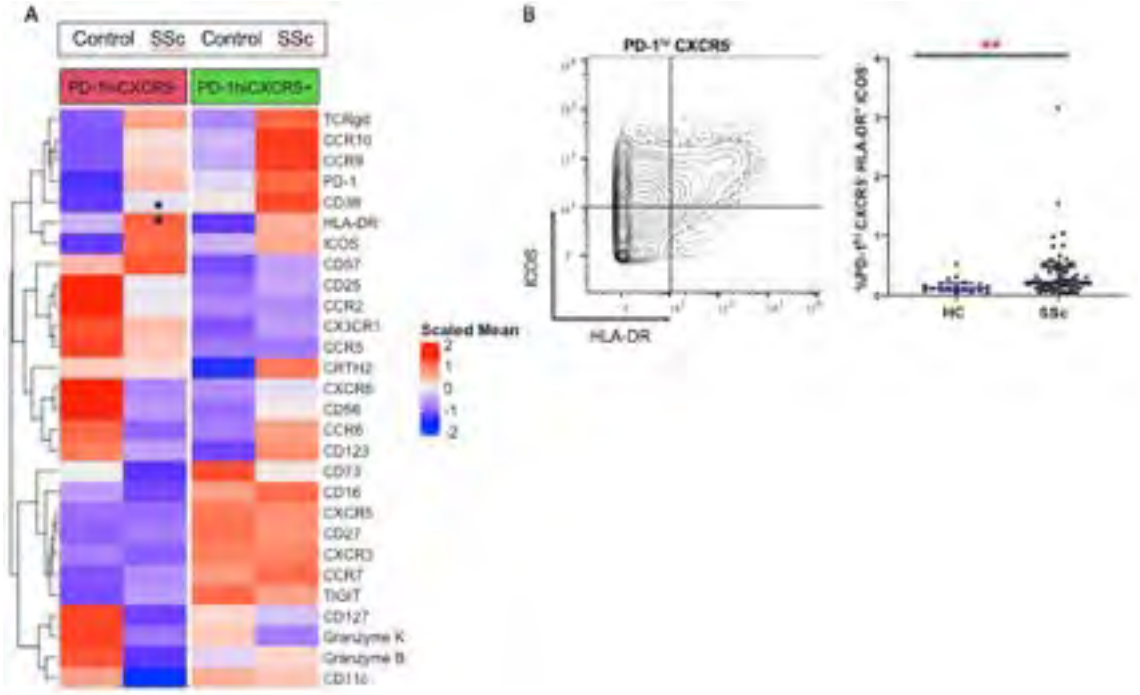

Figure 1. Altered cytometric phenotype of circulating PD-1hi CXCR5- cells in SSc patients. (A) Heatmap of row-normalized expression of cytometry markers on indicated subsets. * indicates markers (HLA-DR, CD38) that are significantly upregulated on PD-1hiCXCR5- cells in SSc compared to controls (Bonferroni adjusted p<0.05). (B) Biaxial gating of ICOS and HLA-DR expression on PD-1hi CXCR5- memory CD4 T cells. Frequency of PD-1hi CXCR5- HLA-DR+ ICOS- T cells was increased in SSc patients compared to controls (Mann-Whitney test p=.003).

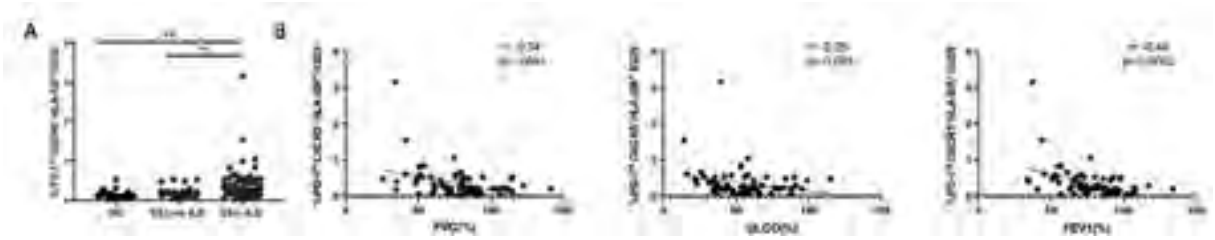

Figure 2. Association of CD4 T cell subset with ILD (A) Frequency of CD4+ T cells with PD-1hi CXCR5- HLA-DR+ ICOS- phenotype in SSc patients with ILD compared to controls and SSc patients without ILD (* p=0.017, ** p=0.001). (B) Correlation of PD-1hi CXCR5- HLA-DR+ ICOS- CD4+ T cells with FVCpp, DLCOpp and FEV1pp (pp=percent predicted). Spearman correlation statistics shown.

without ILD (p=0.02) and healthy controls (HC) (p=0.001) (Figure 2A). Further, the frequency of this CD4 T cells was increased in SSc subjects with more severe ILD (p= 0.017). Consistent with this observation, the frequency of PD-1^{hi} CXCR5^{-} ICOS^{-} HLA-DR^{+} CD4^{+} cells in SSc patients showed an inverse correlation with multiple metrics of pulmonary function, including forced vital capacity % predicted (FVCpp, r= -0.34, p=.0043), diffusing capacity for carbon monoxide (DLCO, r= -0.25, p=0.038) and forced expiratory volume 1 % predicted (FEV1pp, r=-0.44, p=0.0002) (Figure 2B).

Conclusion: High dimensional CyTOF analysis conducted in this cohort of SSc patients highlighted a specific expanded CD4+ T cell population (PD-1^{hi} CXCR5^{-} HLA-DR^{+} ICOS^{-}) that is significantly associated with presence and severity of lung disease. Further studies will evaluate whether this marker can predict the rate of decline of lung function in SSc-ILD, a critically needed tool in the care of patients with SSc.

Disclosure: M. Elahee, None; **A. Mueller**, None; **R. Wang**, None; **Y. Cao**, None; **A. Fava**, None; **P. Dellaripa**, None; **F. Boin**, None; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6.

Abstract Number: 1437

Fat and Fibrosis: A Novel Developmental Gene in Systemic Sclerosis

Nancy Wareing[1], Brian Skaug[2], Minghua Wu[3], Scott Collum[1], Cory Wilson[1], Lucy Revercomb[4], Marka Lyons[5], Weizhen Bi[6], Tingting Mills[1], Julio Charles[5], Shervin Assassi[1] and Harry Karmouty-Quintana[1], [1]University of Texas McGovern Medical School at Houston, Houston, TX, [2]University of Texas McGovern Medical School Houston, Houston, TX, [3]University of Texas Health Science Center at Houston, Houston, TX, [4]Rice University, Houston, TX, [5]Division of Rheumatology, University of Texas McGovern Medical School at Houston, Houston, TX, [6]McGovern Medical School at UTHealth, Houston, TX

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Systemic Sclerosis & Related Disorders – Basic Science (1434–1437)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Early loss of skin-associated adipose tissue and concomitant replacement by extracellular matrix is a hallmark of systemic sclerosis (SSc). However, the contribution of adipose tissue to SSc pathogenesis remains poorly understood. In murine models of skin fibrosis, lipid-laden adipocytes acquire features of migratory myofibroblasts.[1] This adipocyte-to-myofibroblast transition offers up a promising suggests a mechanism for direct contribution of skin-associated adipose tissue to the early SSc skin phenotype. The developmental gene sine oculis homeobox homolog 1 (*SIX1*) is known to regulate cell fate and transdifferentiation in disease. We hypothesize that elevated *SIX1* promotes adipocyte-to-myofibroblast transition, thus contributing to loss of adipose tissue and progression of fibrosis in SSc.

Methods: Skin *SIX1* expression levels were identified by RNA sequencing and DNA microarray in the PRESS and GENISOS cohorts, respectively. All patients satisfied ACR classification criteria for SSc. Clinical correlations between *SIX1* were assessed by Spearman's rank-order and Pearson's correlation for continuous variables. Cellular localization of SIX1 was confirmed in patient and mouse skin samples by single molecule *in situ* hybridization. Ubiquitous genetic deletion of Six1 in eight-week-old mice was achieved using the tamoxifen-inducible Cre recombinase-loxp system. Immunofluorescent staining of collagen 6 (the primary collagen in fat tissue) was quantified as percent positive signal within the dermal adipose.

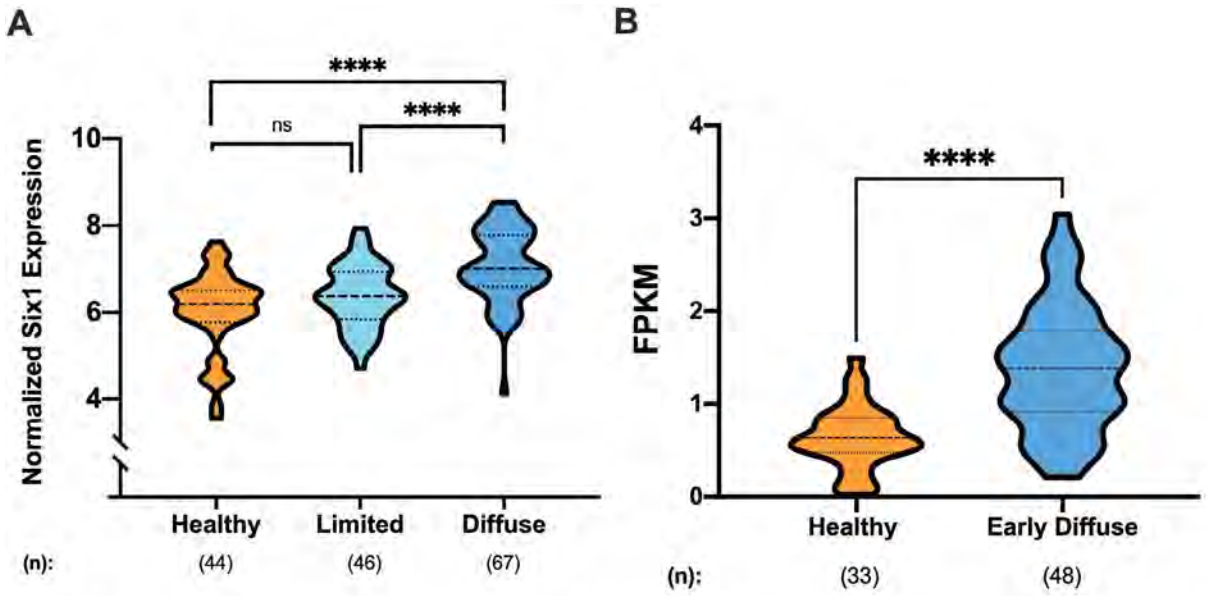

Figure 1. *SIX1* transcript is elevated in SSc versus healthy skin. *SIX1* expression in skin biopsies from SSc patients at the baseline visit, compared to age- sex- and race-matched controls. **A)** Gene expression by DNA microarray from patients in the Genetics Versus Environment in Scleroderma Outcome Studies (GENISOS) cohort. Statistics by non-parametric one-way ANOVA with multple comparisons. **B)** Expression profiling by RNA-sequencing in patients in the Prospective Registry for Early Systemic Sclerosis (PRESS) cohort. FPKM = fragments per kilobase million. Statistics by Welch's two-tailed t-test. ns = non- significant. ****p<0.0001.

Figure 1. SIX1 transcript is elevated in SSc versus healthy skin.

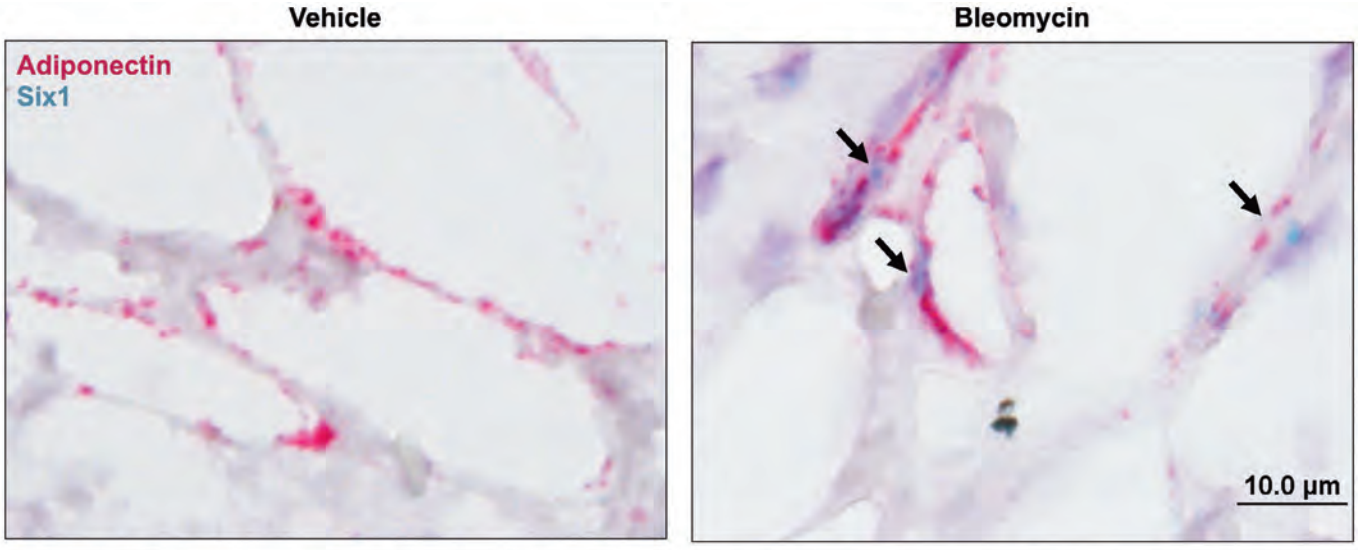

Figure 2. *Six1* is overexpressed in dermal adipocytes of bleomycin-treated mouse skin. *Six1* and *Adiponectin* mature transcript expression as detected by single molecule *in situ* hybridization after 7 days of subcutaneous bleomycin or vehicle (PBS). Arrows indicate double positive cells within the dermal adipose layer.

Figure 2. Six1 is overexpressed in dermal adipocytes of bleomycin-treated mouse skin.

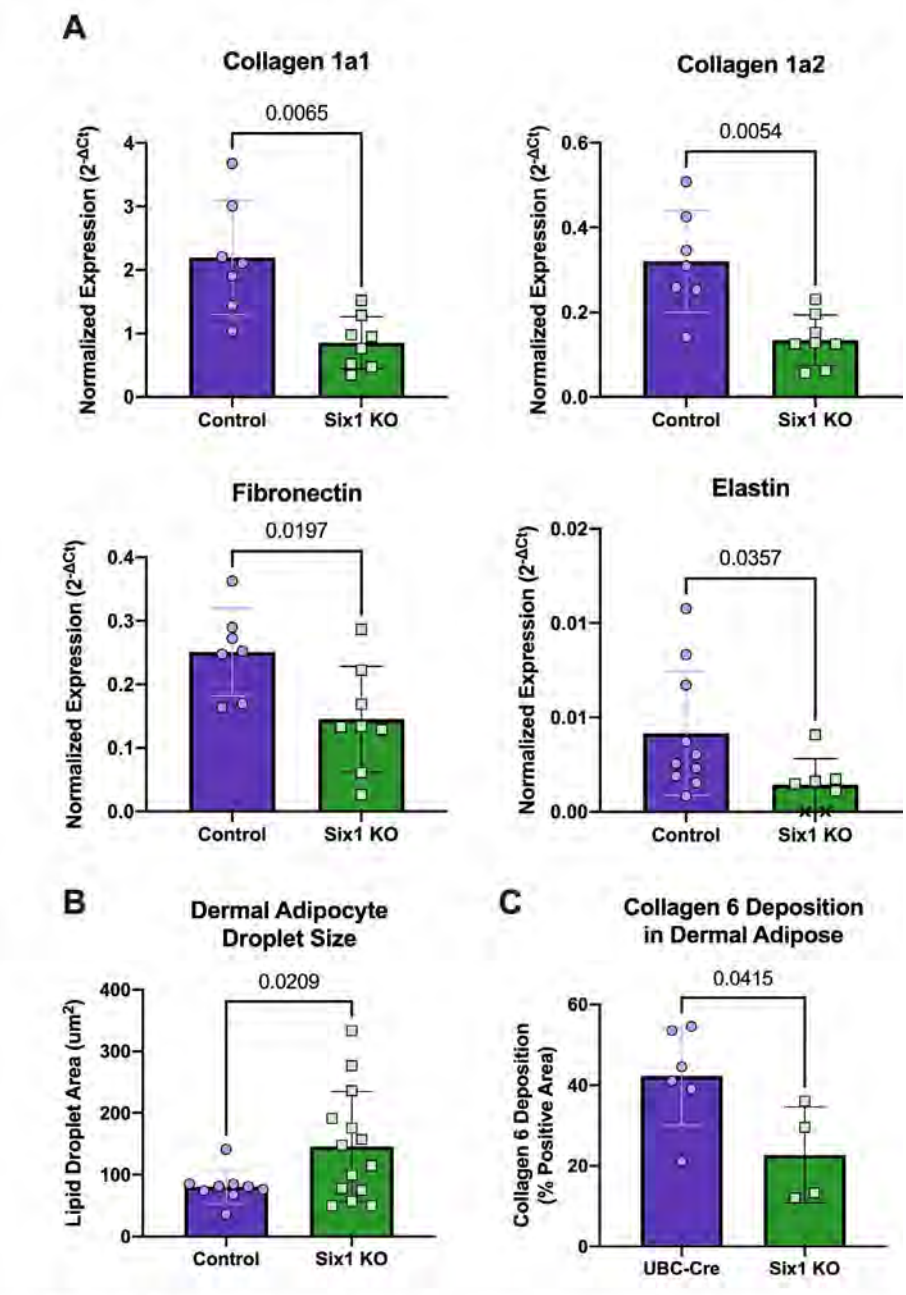

Figure 3. *Six1* depletion reduces fibrotic gene signature, lipoatrophy and dermal adipose collagen deposition in bleomycin-challenged mouse skin. A) Gene expression as measured by RT-qPCR. Raw Ct values were normalized to 18s rRNA. x = undetectable. **B)** Average droplet area of 100 dermal adipocytes per mouse. **C)** Percent of dermal adipose layer positive for collagen 6 staining by immunofluorescent staining.

Figure 3. Six1 depletion reduces fibrotic gene signature, lipoatrophy and dermal adipose collagen deposition in bleomycin-challenged mouse skin.

Results: *SIX1* was upregulated in the affected skin of patients in the GENISOS and PRESS cohorts (**Fig 1A & 1B, respectively**) at the time of enrollment. Baseline *SIX1* expression positively correlated with baseline modified Rodnan Skin Score ($r = 0.37$, $p < 0.0001$) and local skin score ($r = 0.38$, $p < 0.0001$). In dcSSc patients, *SIX1* negatively correlated with disease duration at the time of enrollment ($r = -0.28$, $p=0.022$). *SIX1* strongly correlated with a subcutaneous adipose gene expression signature in two independent cohorts and lipolysis-associated molecular pathways,

supporting a driving role of *SIX1* in adipocyte dysfunction. *Six1* was overexpressed early in dermal adipocytes of the subcutaneous bleomycin murine model of skin fibrosis (**Figure 2**). When challenged with bleomycin, inducible *Six1*-deficient mice (*Six1* KO) demonstrated lower fibrotic gene expression compared to control mice (**Figure 3A**). *Six1* KO mice were protected against lipoatrophy (**Figure 3B**) and collagen 6 deposition within the dermal fat (**Figure 3C**).

Conclusion: We concluded that *SIX1* is elevated in skin-associated fat of SSc patients, and enriched in early diffuse disease. Higher *SIX1* expression was associated with worsened skin fibrosis in baseline samples. Inhibiting *SIX1* can protect against atrophy of dermal fat and increased fibrotic responses in models of SSc-like skin fibrosis. Developmental genes that become activated during disease are ideal candidate targets for new therapeutics, as these genes are lowly expressed in healthy adult tissues, thus dramatically reducing the likelihood of off-target effects. Our findings support further investigation into *SIX1* as a feasible drug molecular target for SSc.

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Abstract Number: 1438

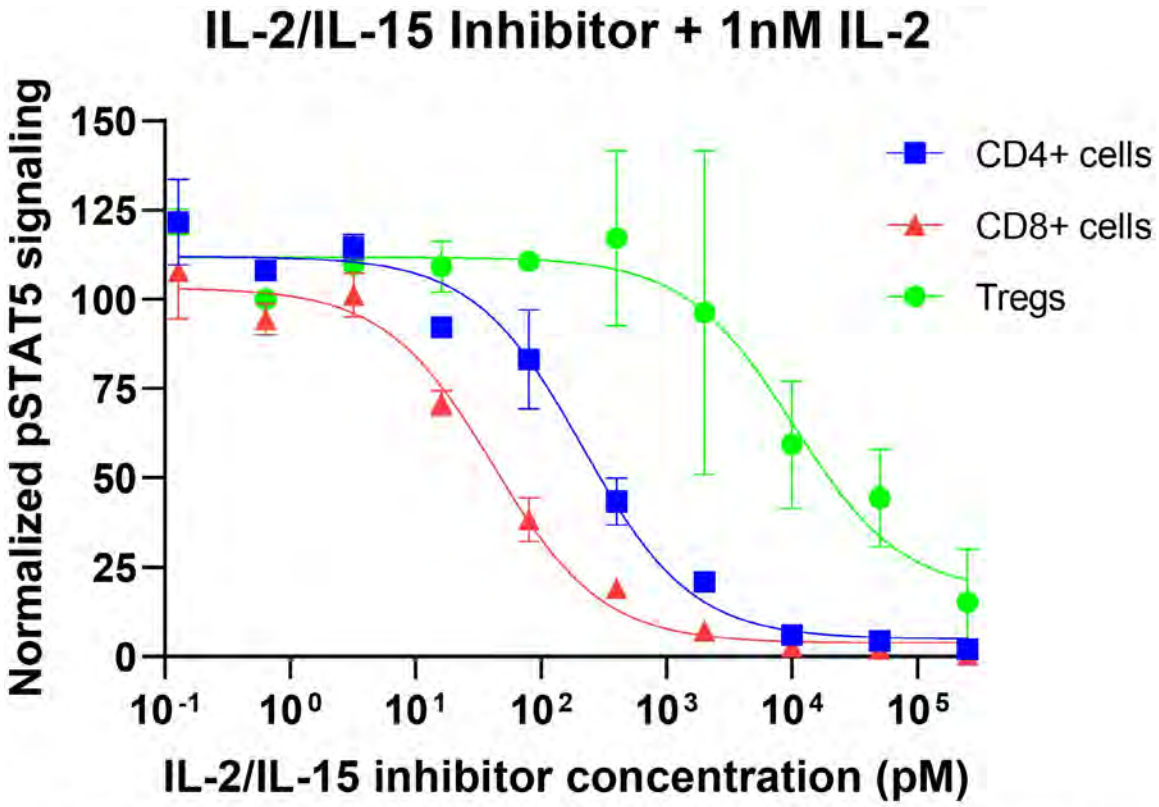
Development of a Computationally Designed, Hyperstable Dual Inhibitor of the IL-2 and IL-15 Receptors: A Novel Therapeutic Candidate for Inflammatory Conditions

Renan Vergara[1], Alex Chen[1], Jerry Chen[1], Marianne Riley[1], Luis Blancas-Mejia[1], Christie Mortales[1], Tania Berrocal[1], Tanu Priya[1], Marsha Mason[1], Kevin Yu[1], Olga Sharapova[1], Jorgen Nelson[1], Alfredo Quijano-Rubio[1], Thomas Linsky[1], **Ryan Swanson**[1] and Daniel-Adriano Silva[2], [1]Neoleukin Therapeutics, Inc., Seattle, WA, [2]Formerly of Neoleukin Therapeutics, Inc., Seattle, WA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Cytokines & Cell Trafficking (1438–1441)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: T cell mediated pathology is central to many forms of autoimmunity, and cytokines perform critical inflammatory functions during this process. IL-2 and IL-15 are well studied common gamma chain cytokine family members that sharply augment T and NK cell function. Antagonizing both pathways with a single molecule is an attractive therapeutic strategy, especially if the IL-2 function in suppressive Tregs can be spared. Using our computational design platform coupled with directed evolution, we created a de novo IL-2/IL-15 inhibitor that has high affinity for IL-2 receptor beta (IL2RB) with no detectable IL-2 receptor gamma (IL2RG) binding, resulting in an inhibitor that antagonizes both the IL-2 and IL-15 pathways. Further computational engineering strategies were performed to improve the inhibitor's thermodynamic stability in low pH environments and increase its resistance to proteases. The resulting therapeutic candidate has potential clinical applications that are differentiated from other related biological therapies, enabling local routes of administration and sparing Treg function.

Methods: Computationally derived binding profiles against IL2RB and IL2RG were determined via biolayer interferometry. Protein stability was addressed in the pH range 2.0-8.0 by thermal and/or chaotropic denaturation assays using spectroscopic techniques. Proteolytic resistance was separately assessed by mass spectrometry. Therapeutic candidates with high affinity for IL2RB and hyperstable biophysical properties were assessed for functional



	CD4+ cells	CD8+ cells	Tregs
IC_{50} (pM)	215	42	10,265

Figure 1. An IL-2/IL-15 dual inhibitor blocks human CD4+ and CD8+ T cell pSTAT5 signaling at concentrations where Tregs demonstrate 100% pSTAT5 signaling (best-fit values).

antagonism of IL-2 and IL-15 signaling via pSTAT5 flow cytometric analysis of human T and NK cell subsets. In vivo,biophysical properties were assessed by inhibitor quantification in the GI tract of orally dosed mice, and biological anti-inflammatory activity was assessed using a murine delayed-type hypersensitivity (DTH) model.

Results: We report development of a *de novo* IL-2/IL-15 inhibitor with higher affinity for IL2RB compared to wild type IL-2 (K_D < 1nM) and undetectable IL2RG binding via Octet biolayer interferometry. This molecule inhibits IL-2 pSTAT5 signaling in human pan T cells with single digit nM IC_{50} potency, while Treg cells are still able to utilize IL-2 through pSTAT5 signaling at those concentrations (Figure 1). In vitro, this therapeutic candidate shows better thermodynamic properties at pH 2 and > 10-fold increase in protease resistance compared to a parental agonist molecule. Systemically administered, the IL-2/IL-15 dual inhibitor blocked DTH swelling in mice with statistical significance; orally administered, it retained receptor binding activity in the intestines, demonstrating robust resistance to denaturation and degradation.

Conclusion: Computational design enabled development of a potent, hyperstable inhibitor of both the IL-2 and IL-15 pathways. These biophysical properties may enable novel therapeutic strategies for inflammatory and autoimmune diseases. Furthermore, these results demonstrate that de novo protein design can be readily applied to adjust receptor specificity and affinity to achieve the binding and functional therapeutic profile of interest.

Disclosure: R. Vergara, Neoleukin Therapeutics, Inc., 3, 11; **A. Chen**, Neoleukin Therapeutics, Inc., 3, 11; **J. Chen**, Neoleukin Therapeutics, Inc., 3, 11; **M. Riley**, Neoleukin Therapeutics, Inc., 3, 11; **L. Blancas-Mejia**, Neoleukin Therapeutics, 3, 11; **C. Mortales**, Neoleukin Therapeutics, Inc., 3, 11; **T. Berrocal**, Neoleukin Therapeutics, Inc., 3; **T. Priya**, Neoleukin Therapeutics, Inc., 3, 11; **M. Mason**, Neoleukin Therapeutics, Inc., 3; **K. Yu**, Neoleukin Therapeutics, Inc., 3; **O. Sharapova**, Neoleukin Therapeutics, Inc., 3, 11; **J. Nelson**, Neoleukin Therapeutics, Inc., 3, 11; **A. Quijano-Rubio**, Neoleukin Therapeutics, Inc., 3, 11; **T. Linsky**, Neoleukin Therapeutics, Inc., 3; **R. Swanson**, Neoleukin Therapeutics, Inc., 3; **D. Silva**, Neoleukin Therapeutics, Inc., 2, 11.

Abstract Number: 1439

Inhibitors of Endogenous Reverse Transcriptases Suppress *in Vitro* Type I Interferon Responses and *in Vivo* Antigen-specific T Cell Responses

Nafeeza Hafeez, Jimmy Zhong, Jared Steranka, Margit Hagel, Greg Bisacchi, Donna Romero, Rosana Kapeller, Dennis Zaller and **Wenyan Miao**, Rome Therapeutics, Cambridge, MA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Cytokines & Cell Trafficking (1438–1441)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Transposable elements (TEs) are mobile DNA elements that can replicate and move from one position to another within the host genome. Through co-evolution, TEs in the human genome have developed complex relationships with the host to regulate a variety of cellular functions. TEs are largely silent in healthy adult cells but are reactivated and transcribed in certain disease states, such as cancer, autoimmunity, and neurodegeneration. Class I TEs are retrotransposons that have mobilized throughout the genome via reverse transcription of RNA intermediates. In humans, there are two Class I TEs that encode functional endogenous reverse transcriptases (RTs), LINE-1 and HERV-K. The DNA and RNA products from TE reactivation and reverse transcription are potential source of nucleic acid that are recognized by pattern recognition receptors, such as cGAS, that sense these nucleic acids and trigger proinflammatory responses during sterile inflammation. We tested inhibitors of these endogenous RTs for their ability to block immune responses.

Methods: We generated recombinant reverse transcriptases of LINE-1 and HERV-K and developed biochemical reverse transcriptase assays. We engineered a reporter cell line to measure LINE-1 retrotranposition in cells. Utilizing these assays, we discovered potent LINE-1 RT nucleoside reverse transcriptase inhibitors (NRTIs) with a range of potencies against HERV-K RT. These inhibitors were characterized *in vitro* for their impact on interferon responses in immune cells and *in vivo* on antigen-specific T cell responses in mice.

Results: Compound A is a potent inhibitor of LINE-1 RT and a weak inhibitor of HERV-K RT. In enzymatic assays, its active tri-phosphorylated form has an IC_{50} of 0.006 μM and 6.4 μM against LINE-1 and HERV-K RT, respectively. Compound A demonstrated excellent potency in the cell-based LINE-1 retrotransposition assay with IC_{50} of 0.12 μM. To characterize the impact of the NRTIs on immune responses, we used Decitabine to induce LINE-1 and HERV-K expression in TREX-1 knock out THP-1 cells, and subsequently measured the effect of NRTIs on TE-induced type I interferon responses. Compound A effectively inhibited this response with IC_{50} of 0.05 μM. We investigated the *in vivo* activity and mechanism of action of Compound A in a murine model of MOG peptide-induced T cell responses. Mice were immunized with MOG_{35-55}, 10 days later cells from draining lymph nodes were collected and cultured with

MOG_{35-55}. At 40 mg/kg oral dosing, Compound A suppressed antigen specific T cell proliferation and reduced IL-17A, TNFa and IFNg production.

Conclusion: We used biochemical and cell-based assays to identify potent endogenous RT inhibitors. These inhibitors suppressed *in vitro* repeat element-induced type I interferon responses in monocytic cells and attenuated *in vivo* antigen-specific T cell responses. These data demonstrate the potential of endogenous RT inhibitors to modulate host immune responses for therapeutic benefit in autoimmune/inflammatory diseases.

Disclosure: N. Hafeez, None; **J. Zhong**, None; **J. Steranka**, None; **M. Hagel**, None; **G. Bisacchi**, None; **D. Romero**, None; **R. Kapeller**, None; **D. Zaller**, None; **W. Miao**, None.

Abstract Number: 1440

Targeting Endogenous Mesenchymal Stromal Cell Response to Interferong in Sjögren's Syndrome

Sara McCoy, Ilya Gurevic, Maxwell Parker and Jacques Galipeau, University of Wisconsin, Madison, WI

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Cytokines & Cell Trafficking (1438–1441)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Sjögren's syndrome (SS) is a systemic autoimmune disease that is associated with a lymphoma risk 14-fold that of the general population. Greater focal lymphocytic infiltrate of salivary glands (SGs) and high SG IFNg are associated with elevated lymphoma risk. Interestingly, IFNg is also biologically relevant to mesenchymal stromal cells (MSCs), a SG resident cell with unique regenerative and immunoregulatory capacity. In contrast to the role of IFNg in SS, IFNg is considered to promote a beneficial MSC immunomodulatory phenotype. The objective of this study is to define the immunobiology of IFNg-exposed SG MSCs with and without the JAK inhibitor ruxolitinib.

Methods: All SS subjects fulfilled ACR/EULAR criteria. Sicca-control subjects had symptoms of dryness but did not have diagnoses of autoimmune disease or laboratory abnormalities supportive of an autoimmune disease. SG MSCs were isolated from minor salivary gland tissue and frozen for storage. SS SG MSCs were treated with IFNg 10 ng/mL +/- various doses of ruxolitinib. Experimental methods included flow cytometry, RNA-Sequencing, chemokine array, ELISA, and transwell experiments.

Results: We found that the IFNg promoted expression of MSC immunomodulatory surface markers, and this expression was reversed by 1 μM ruxolitinib (Figure 1A-C). Accordingly, we performed RNA-Sequencing on MSCs pretreated with IFNg +/- 1 μM ruxolitinib. RNA-Sequencing of SS and control SG MSCs showed nearly identical responses IFNg inhibition with ruxolitinib (Figure 1D & E). Because several chemokines were highlighted in the RNA-Sequencing results, we performed a chemokine array on conditioned media from SG-MSCs treated with IFNg +/- ruxolitnib and identified candidate chemokines for further investigation (Figure 2A & B). We confirmed the differential expression of CXCL9, CXCL10, CXCL11, CCL2, and CCL7 using ELISA (Figure 2C). We then sought to define the effect of IFNg and ruxolitinib on MSC-induced PBMC migration (Figure 3A). MSCs promote migration alone, but PBMC migration is amplified by pre-treatment of SG-MSCs with IFNg (Figure 3B). Ruxolitinib reverses this increased migration, though not reaching statistical significance (Figure 3C). We determined $CD4^+$ T cells migrate significantly more with IFNg ($p=0.04$) and that neutralizing CXCL9, CXCL10, and CXCL11 attenuated IFNg-induced migration (Figure 3D).

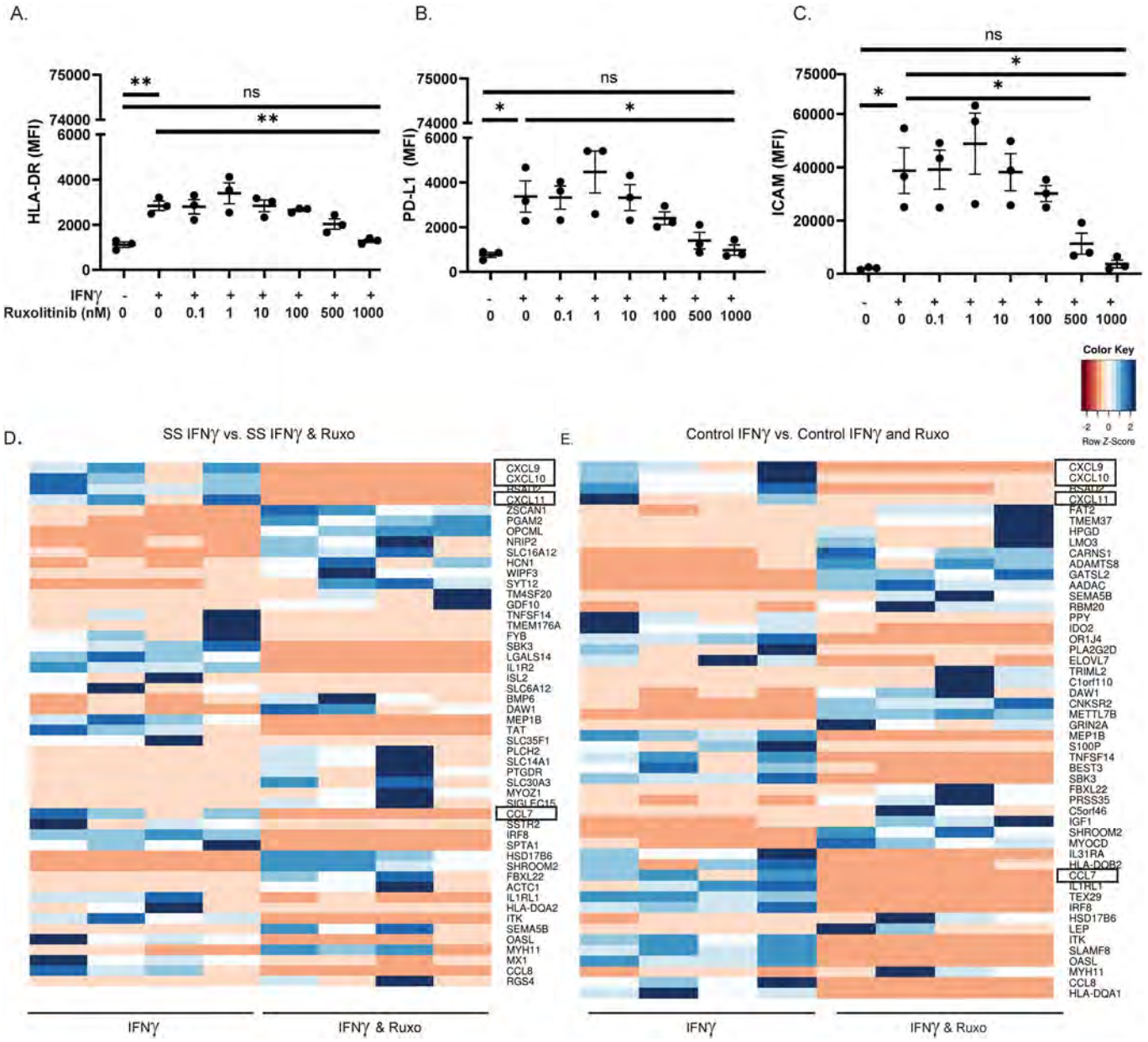


Figure 1. Ruxolitinib reverse IFN**γ**-induced SG-MSC immunomodulatory protein expression and transcript profile. SG-MSCs were treated +/- IFN**γ** for 48 hours +/- ruxolitinib. A-C) Median immunofluorescence intensity (MFI) of MSC immunomodulatory markers HLA-DR, PD-L1, and ICAM (n=3); D-E) Transcriptomic profiling of SS (n=4) and control (n=4) SG-MSCs. Heat maps display the top differentially regulated genes filtered for an adjusted p value of <0.05. Boxes highlight differentially expressed chemokines. .ns=not significant; *=p<.05; **=p<0.01.

Conclusion: These findings establish that ruxolitinib mitigates IFNg-induced expression of immunomodulatory surface markers and chemokines expressed by SG-MSC. Ruxolitinib also reverses IFNg-induced PBMC migration, likely through acting on CXCL9, 10, and 11 to reduce $CD4^+$ T cell migration. Because IFNg is higher in SS than control SGs, we have identified SG MSCs as a plausible pathogenic cell type in SS, promoting $CD4^+$ T cell chemotaxis within SS SGs. Further, we have shown ruxolitinib reverses the effect of IFNg on key chemokine expression, providing a possible therapeutic avenue. Future studies will confirm our findings with *ex vivo* and mouse model studies

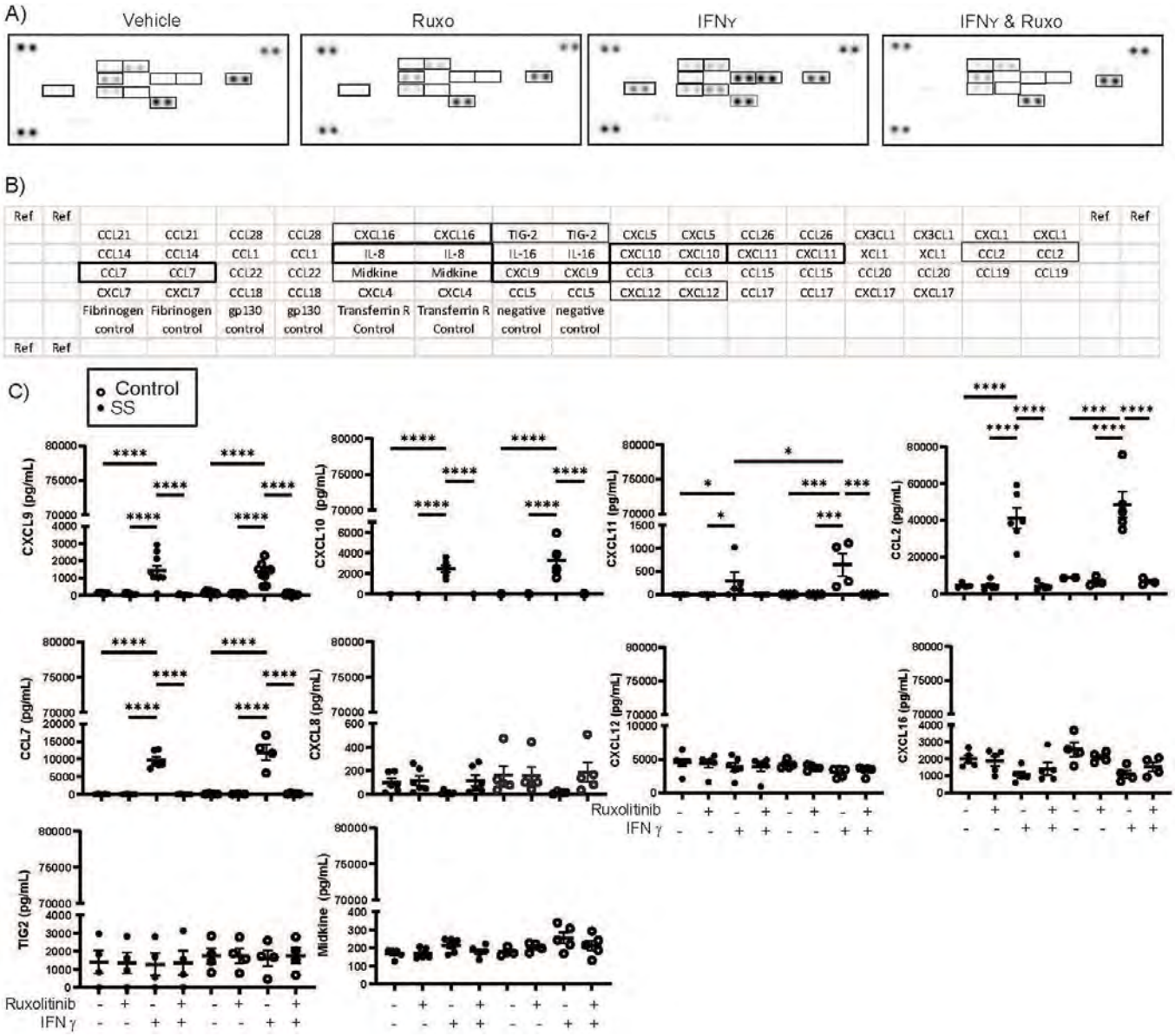


Figure 2. IFN**γ**-induced production of CXCL9, CXCL10, CXCL11, CCL2, & CCL7 in salivary gland MSCs is reversed by ruxolitinib. Salivary gland MSCs were culturedwith IFN**γ** +/- 1000 nM ruxolitinib or vehicle for 48 hours. After 48 hours, conditioned media was collected for further study. Conditioned media was applied to a chemokine array per the manufacturer's specifications. Quantitative analysis using densitometry was performed. ELISA was performed on the conditioned media for each chemokine identified as differentially expressed in the chemokine array per manufacturer's recommendations. A) Images of the chemokine membrane incubated with conditioned media derived from vehicle treated, IFN**γ** treated, ruxolitinib treated, or both IFN**γ** and ruxolitinib-treated salivary gland MSCs; B) Key identifying the layout of the chemokine array; C) Confirmation of the chemokine array was performed using the conditioned media ELISA including CXCL9, CXCL10, CXCL11, CCL2, CCL7, CXCL8, CXCL12, CXCL16, TIG2, and midkine. ELISAs were performed on control (n=5) and SS (n=6) subjects.*=p<0.05; **=p<0.01; ***=p<0.001; ****=p<0.0001.

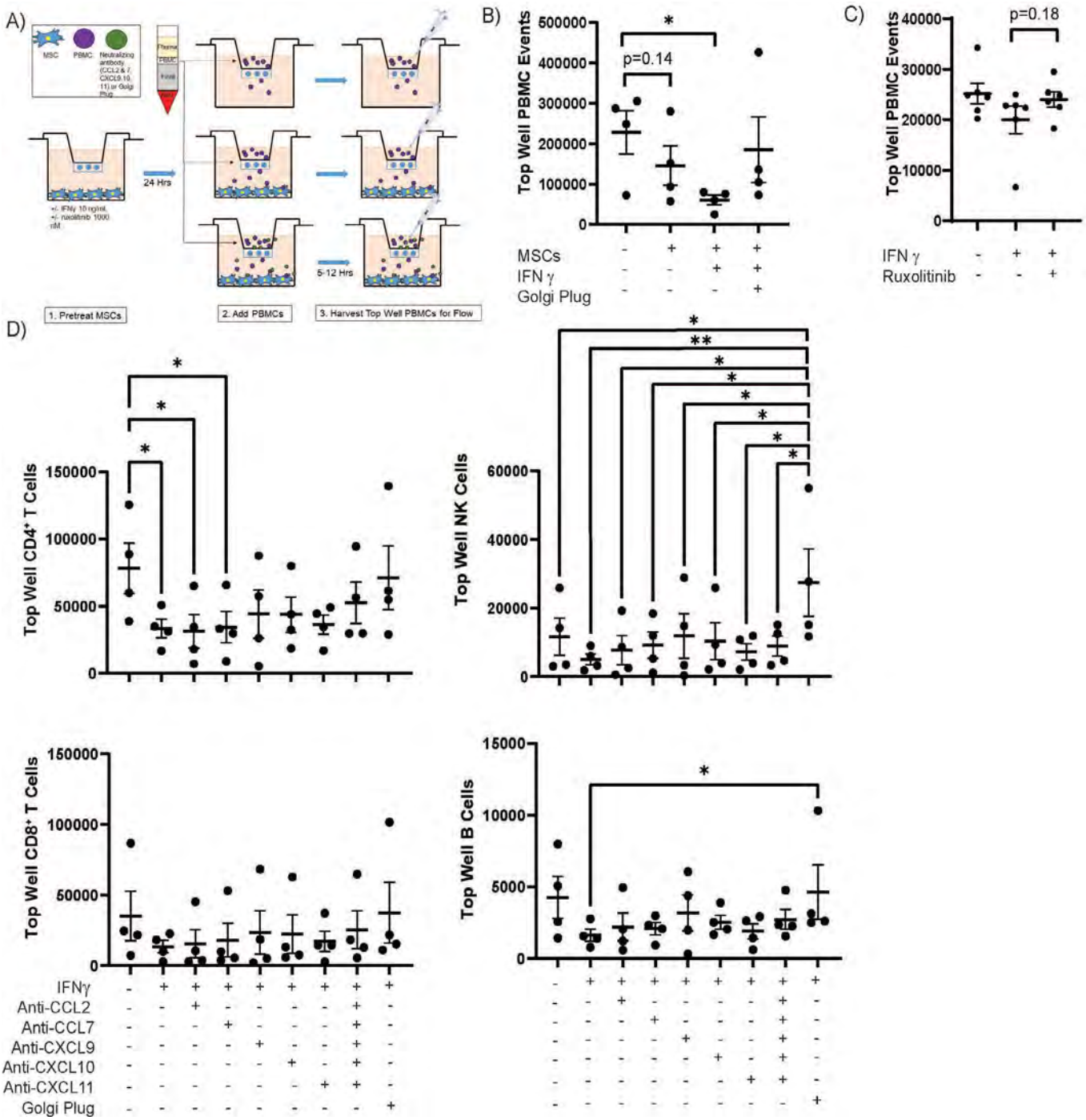


Figure 3. MSCs Promote PBMC Migration, an effect amplified by IFN**γ**. MSCs were plated onto the bottom of a transwell. MSCs were serum starved for 24 hours then treated +/- IFN**γ** or ruxolitinib for another 24 hours. The MSCs were washed well then PBMCs were added into the top well. After 5-12 hours, the cells remaining in the top well were collected, stained, and subjected to flow cytometry. A) Representative figure of the transwell experimental setup; B) MSCs (n=1)were treated with IFN**γ** 10 ng/mLfor 24 hours, washed, then PBMCs (n=4) were added into the top of a five micron transwell system for five hours. IFN**γ** increased PBMC migration across the transwell filter. C) MSCs (n=6) were treated with IFN**γ** 10 ng/mL +/- or 1000 nM ruxolitib for 24 hours, washed, then PBMCs (n=1) were added into the top of an eight micron transwell system for five hours. Ruxolitinib abrogates the pro-migratory effect of IFN**γ**. D) MSCs (n=1) were pre-treated with IFN**γ** then PBMCs (n=4) were added to the top well of a 5 micron transwell system in the presence of neutralizing antibodies or golgi plug. Data were presented as the number of lymphocytes from the top well (cells that did not migrate). CD4+ T cells migrated most robustly in the presence of IFN**γ** and neutralizing antibodies to CXCL9, 10, and 11 reduced migration. A similar less significant trend was seen in CD8+ T cells, B cells, and NK cells. *=p<0.05; **=p<0.01.

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Abstract Number: 1441

Pharmacological Characterization of GLPG3667, a Selective TYK2 Inhibitor for Treatment of Inflammatory Diseases

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Cytokines & Cell Trafficking (1438–1441)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates the signaling from type 1 interferon (IFN), interleukin (IL)-12/IL-23 and the IL-10 family of cytokines. Genetic analyses have indicated an association between TYK2 variants and risk of inflammatory diseases. In addition, clinical data obtained with ustekinumab suggest that compounds that inhibit TYK2 could be potential treatments for inflammatory diseases, notably through inhibition of IL-12 and IL-23 signaling. We describe here GLPG3667, a potent and selective TYK2 inhibitor that is in development as a treatment for inflammatory and autoimmune diseases.

Methods: Potency and selectivity of GLPG3667 on TYK2 was addressed using radioactive and fluorescent biochemical assays. Peripheral blood mononuclear cells (PBMC) and human whole blood assays for various Janus kinase (JAK)-dependent pathways were performed to address GLPG3667 potency and selectivity, using flow cytometry or enzyme-linked immunosorbent assay. GLPG3667 pharmacological activity was demonstrated in a psoriasis mouse model driven by IL-23 (a cytokine that signals through JAK2/TYK2). In healthy human volunteers (HV), pharmacodynamic activity of GLPG3667 was demonstrated by measuring signal transducer and activator of transcription (STAT) phosphorylation using flow cytometry analysis on the IFNα pathway and selectivity described through analysis of IL-2 and granulocyte-macrophage colony-stimulating factor (GM-CSF) pathways. Biological effects of GLPG3667 in humans were assessed using transcriptomic analysis of blood cells after *in vivo* IFNα (1 million IU of IntronA) challenge in healthy HV.

Results: Biochemical assays showed that GLPG3667 displayed nanomolar potency on TYK2 with a selectivity over other JAK kinases >3-fold. In human PBMC, GLPG3667 showed comparable potency on the IFNα and IL-23 pathways (around 50 nM). Selectivity for TYK2 on the IFNα pathway was >14-fold and >19-fold toward the IL-2 and GM-CSF pathways in human PBMC and whole blood, respectively. Dermal ear inflammation in a mouse model of psoriasis driven by IL-23 was prevented by GLPG3667 with a minimal effective dose of 3 mg/kg given orally once daily. This effect was associated with a decrease in neutrophil infiltration and STAT3 phosphorylation at sites of inflammation. In healthy HV, GLPG3667 completely inhibited IFNα-induced STAT1 and STAT3 phosphorylation but did not impact IL-2- and GM-CSF-induced STAT5 phosphorylation. After *in vivo* IFNα challenge, GLPG3667 blocked the induced expression of IFN-response genes.

Conclusion: The TYK2 inhibitor GLPG3667 demonstrated selectivity toward the three other JAK family members in several biochemical, cellular and human whole blood assays *ex vivo* and *in vivo* during a Phase 1 study (NCT04097938)

in healthy HV. Pharmacological effects of GLPG3667 were demonstrated in a mouse model of psoriasis driven by IL-23 and in healthy HV challenged with IFNα. GLPG3667 is in development for the treatment of moderate to severe psoriasis.

Disclosure: R. Blanque, Galapagos SASU, 3, 12, Warrant holder; **K. Shoji**, Galapagos SASU, 3; **M. Jans**, Galapagos NV, 3, 11; **F. Marsais**, Galapagos SASU, 3, 12, Warrant holder; **L. Furio**, Galapagos SASU, 3; **M. Colli**, Galapagos NV, 3; **C. Cottereaux**, Galapagos SASU, 3, 11, 12, Warrant holder; **C. David**, Galapagos SASU, 3, 12, Warrant holder; **N. Houvenaghel**, Galapagos NV, 3, 12, Warrant holder; **I. Parent**, Galapagos SASU, 3, 12, Warrant holder; **A. Van de Water**, Galapagos NV, 3; **L. Perret**, Galapagos SASU, 3, 12, Warrant holder; **S. Alves**, Galapagos SASU, 3, 12, Warrant holder; **D. Amantini**, Galapagos NV, 3; **S. Van der Plas**, Galapagos NV, 3, 11; **R. Galien**, Galapagos NV, 3, 11, 12, Warrant holder.

Abstract Number: 1442

Effectiveness of Cycling JAKi Compared to Switching to bDMARD in Patients Who Failed a First JAKi in an International Collaboration of Registries of Rheumatoid Arthritis Patients (the JAK-pot Study)

Manuel Pombo-Suarez[1], Carlos Sanchez-Piedra[2], Juan J Gomez-Reino[3], Kim Lauper[4], Nevsun Inanc[5], Anja Strangfeld[6], Doreen Huschek[7], Karel Pavelka[8], Eirik Kristianslund[9], Tore Kvien[10], Ziga Rotar[11], Dan Nordström[12], Denis Choquette[13], Ori Elkayam[14], Burkhard Leeb[15], Maria José Santos[16], Kimme Hyrich[17], Lianne Kearsley-Fleet[18], Catalin Codreanu[19], Denis Monguin[20], Delphine Courvoisier[20] and Axel Finckh[21], [1]Rheumatology Service, Hospital Clinico Universitario, Santiago De Compostela, Santiago de Compostela, Spain, [2]Research Unit, Spanish Society of Rheumatology, Madrid, Spain, [3]Hospital Clínico Universitario, Santiago de Compostela, Spain, [4]Geneva University Hospitals, Geneve, Switzerland, [5]Division of Rheumatology, Marmara University, School of Medicine, Istanbul, Turkey, [6]Deutsches Rheuma-Forschungszentrum Berlin, Berlin, Germany, [7]Epidemiology and Health Services Research, German Rheumatism Research Center, Berlin, Germany, Berlin, Germany, [8]Institute of Rheumatology, Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, [9]Division of Rheumatology and Research, Diakonhjemmet Hospital, Oslo, Norway, Oslo, Norway, [10]Diakonhjemmet Hospital, Oslo, Norway, [11]Department of Rheumatology, University Medical Centre Ljubljana, Ljubljana, Slovenia and Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, [12]Division of Internal Medicine and Rheumatology, Helsinki University Hospital, Helsinki, Finland, [13]Institut de Rhumatologie de Montréal, Montréal, QC, Canada, [14]Tel Aviv Medical Center, Tel Aviv, Israel, [15]Karl Landsteiner University for Health Sciences, Krems/Donau, Karl Landsteiner Institute for Clinical Rheumatology, Hollabrunn, Austria, [16]Rheumatology Department, Hospital Garcia de Orta, Almada, Portugal, [17]University of Manchester, Manchester, United Kingdom, [18]Centre for Musculoskeletal Research, University of Manchester, Manchester, United Kingdom, [19]Center of Rheumatic Diseases, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, [20]Division of Rheumatology, Geneva University Hospital, Geneva, Switzerland, [21]University Hospital of Geneva, Geneve - Vesenaz, Switzerland

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: RA – Treatments II: New Findings in Established Therapies (1442–1445)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: With the arrival of new Janus kinase inhibitors (JAKi), with different JAK inhibition profiles, there is the possibility of using a second JAKi in the event of failure to a first JAKi in patients with rheumatoid arthritis (RA). There are no data on the effectiveness of cycling JAKi compared to switching to biologic disease-modifying antirheumatic drug (bDMARD) in patients who have failed a first JAKi. The objective of this study is to compare the effectiveness of cycling JAKi vs switching to bDMARD in a real-world RA population.

Methods: Nested cohort study within an international collaboration of RA registries (data contributed from 14 national registries of the JAK-pot collaboration). We pooled prospectively collected data from RA patients who failed a first JAKi and were subsequently treated with either a second JAKi (JAKi cycling) or with a bDMARD (switching) in routine care. We compared the effectiveness of both strategies in terms of drug retention and in terms of disease activity (DAS28) evolution over 1 year after second treatment initiation. Differences in drug survival rates were assessed by Log Rank Test. DAS28 trajectories were predicted based on an age- and gender-adjusted linear mixed model with a quadratic trend over time.

Results: 708 patients who failed JAKi were included. 154 cycled to a second JAKi and 554 switched to a bDMARD (Table 1). Patients cycling JAKi were older, had longer disease duration, had received more bDMARDs and had longer exposure to first JAKi treatment than switchers to a bDMARD. Monotherapy was more prevalent and discontinuation of the first JAKi was more common for safety reasons than for lack of effectiveness. Cycling and switching strategies showed similar drug survival rates after two years of follow-up (Figure 1). Nevertheless, a non-significant trend emerged where discontinuation was more likely among patients cycling JAKi when reason for stopping the first JAKi was an adverse event, whereas discontinuation was less likely among patients cycling JAKi when reason for stopping the first JAKi was ineffectiveness. DAS28 over time evolved in a similar way between patients cycling JAKi and switching to a bDMARD, with improvements after one year of follow-up (Figure 2).

Conclusion: After failing a first JAKi, cycling JAKi versus switching to a bDMARD appears to have similar effectiveness despite a more difficult to treat patient profile for the patients cycling to JAKi.

Table 1. Baseline characteristics

	JAKi to JAKi (n=154)	JAKi to bDMARD (n=554)	P
Female (%)	135 (87.7)	448 (80.9)	ns
Age, mean (SD)	58.41 (12.43)	54.74 (12.74)	0.002
Disease duration in years, mean (SD)	13.95 (10.52)	11.37 (8.77)	0.002
Seropositive, RF or ACPA, n (%)	105 (74.5)	365 (75.1)	ns
N° of previous bDMARDs, median (IQR)	1.5 (1-3)	1 (0-2)	<0.001
First JAKi: tofacitinib (%)	117 (76.0)	441 (79.6)	ns
Stop reason of first JAKi, n (%)			0.003
Adverse event	42 (27.3)	99 (17.9)	
Lack of efficacy	94 (61.0)	360 (65.0)	
Other	18 (11.7)	95 (17.1)	
Treatment duration of first JAKi in years, mean (SD)	1.38 (1.31)	0.69 (0.72)	<0.001
Concomitant csDMARD (%)	69 (44.8)	349 (63)	<0.001
DAS28, mean (SD)	4.10 (0.98)	4.17 (0.85)	ns

Figure 1. Kaplan-Meier curves of second treatment discontinuation for any reason, both overall and stratified by reasons for discontinuation of first treatment (Log Rank Test analysis)

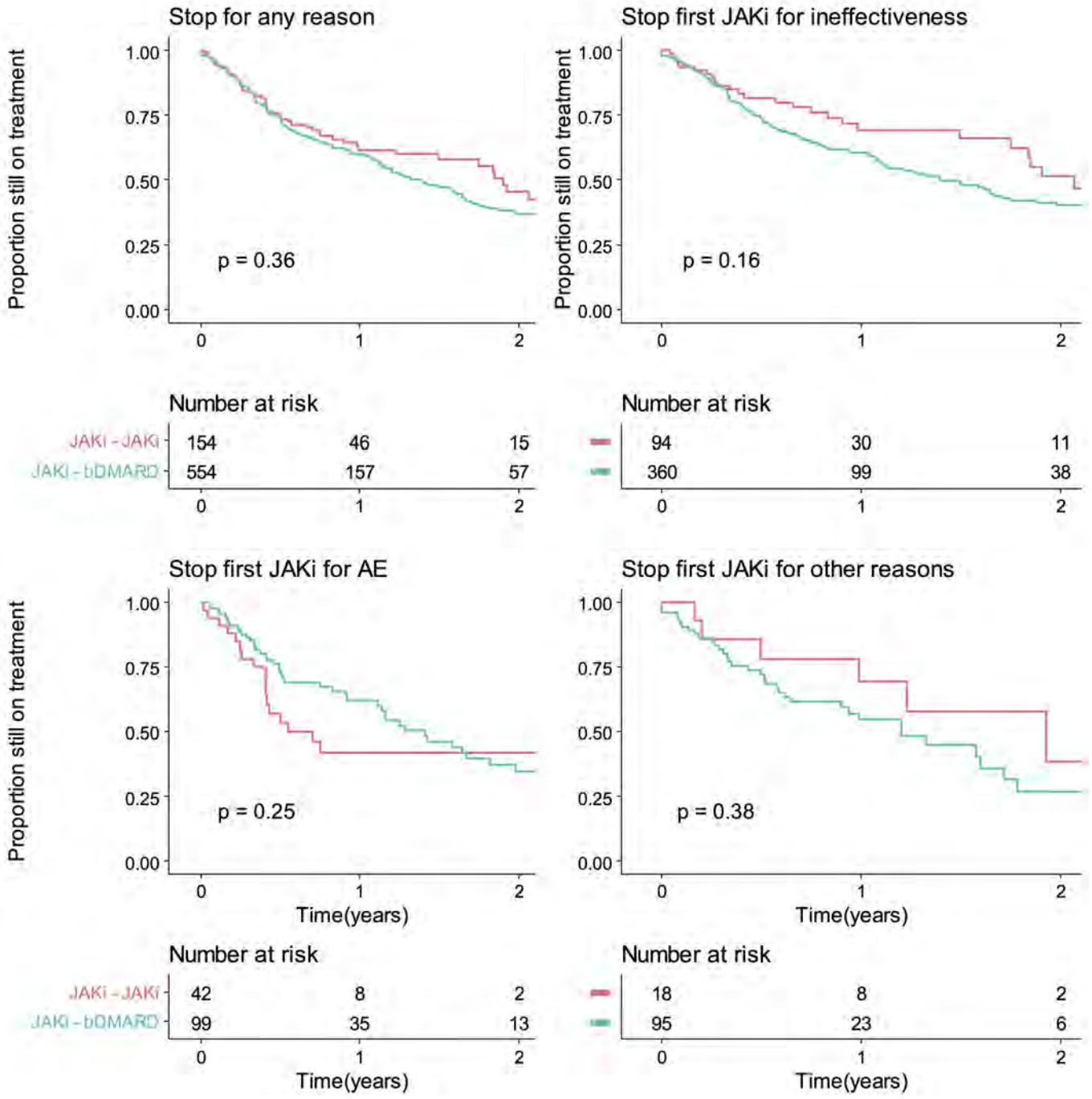
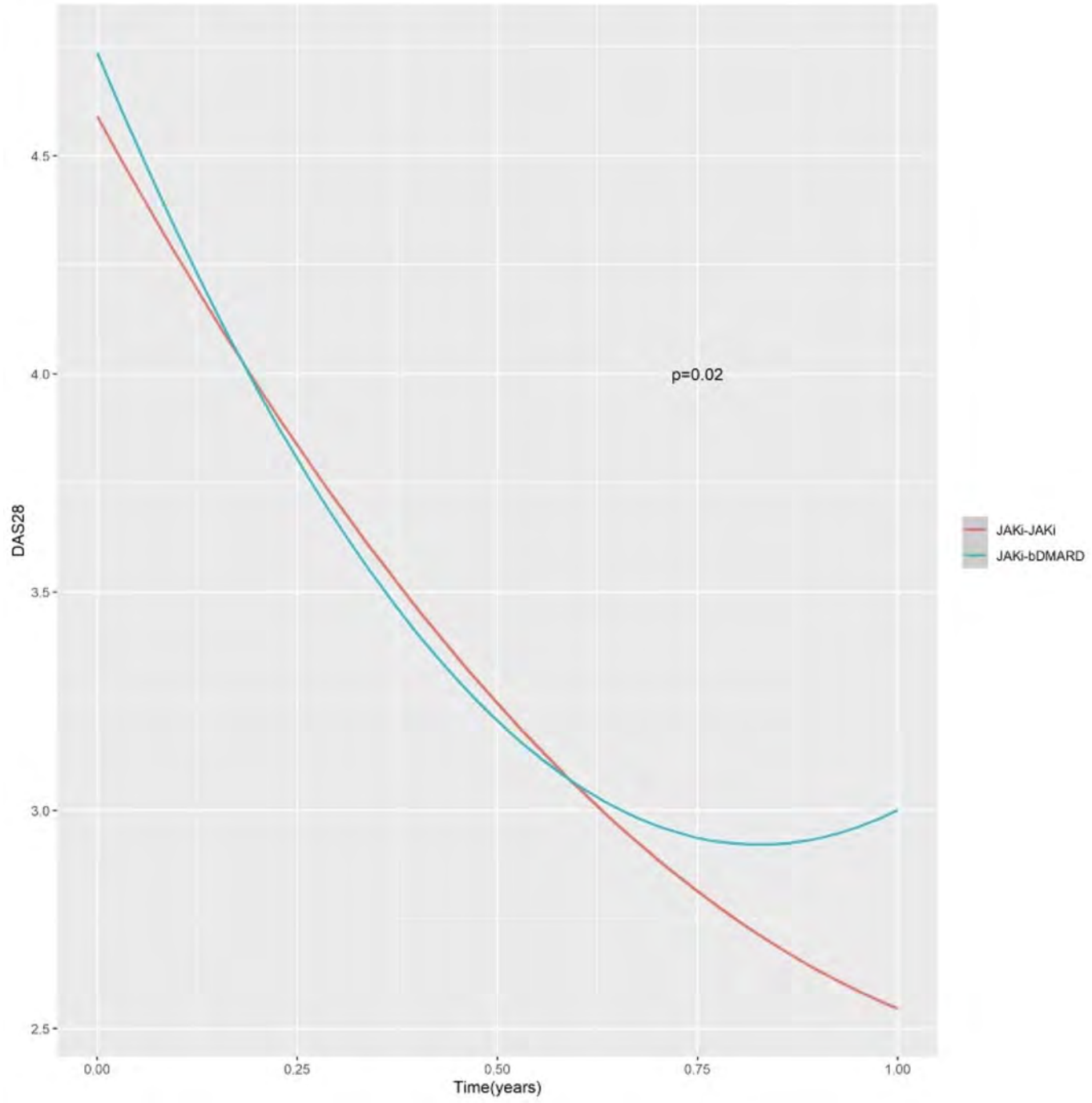


Figure 2. Age- and gender-adjusted DAS28



Disclosure: M. Pombo-Suarez, MSD, 1, SANOFI, 6, Janssen, 6, Lilly, 6; **C. Sanchez-Piedra**, None; **J. Gomez-Reino**, Pfizer Inc, 2, 5, Biogen, 2, 5, Gilead Sciences, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Roche, 2, 5; **K. Lauper**, Gilead Galapagos, 6, Viatris, 6; **N. Inanc**, Abbvie, 6, Lilly, 6, MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Amgen, 6, Celltrion, 6, UCB, 6; **A. Strangfeld**, Pfizer, 6, Roche, 6, MSD, 6, BMS, 6, Abbvie, 6, Celltrion, 6; **D. Huschek**, None; **K. Pavelka**, Abbvie, 6, UCB, 6, MSD, 6, Roche, 6, Pfizer, 6, Eli Lilly, 6, Egis, 6, Biogen, 6, Pfizer, 6; **E. Kristianslund**, None; **T. Kvien**, Biogen, 6, Celltrion, 6, Egis, 6, Eli Lilly, 6, Evapharma, 6, Ewopharma, 6, Gilead, 6, Hikma, 6, Mylan, 6, Oktal, 6, Sandoz, 6, Sanofi, 6, Abbvie, 5, 6, BMS, 5, MSD, 5, Novartis, 5, 6, Pfizer, 5, 6, Amgen, 5, 6, UCB, 5; **Z. Rotar**, Abbvie, 6, Eli Lilly, 6, MSD, 6, Novartis, 6, Pfizer, 6, Roche, 6, Sandoz, 6, UCB, 6; **D. Nordström**, Abbvie, 6, BMS, 6, Lilly, 6, MSD, 6,

Novartis, 6, Pfizer, 6, Roche, 6, UCB, 6, Celgene, 5; **D. Choquette**, AbbVie, 2, 5, Amgen, 2, 5, Celltrion, 2, Eli Lilly, 2, Novartis, 2, 5, Pfizer Inc, 2, 5, Sandoz, 2, 5, Sanofi, 2, 5, Teva Pharmaceuticals, 2, Gilead Sciences, 2; **O. Elkayam**, NOVARTIS, 1, 2, 6, Pfizer, 1, 2, 5, 6, Lilly, 1, 2, 6, Abbvie, 1, 6, BI, 1, 6; **B. Leeb**, Abbvie, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, Janssen-Cilag, 2, Morphosys, 2, Biogen, 2, 6, Novartis, 2, Sandoz, 6, Roche, 6, Grünenthal, 6, Celgene, 6; **M. José Santos**, Abbvie, 6, Novartis, 6, Pfizer, 6, Roche, 6; **K. Hyrich**, Abbvie, 6, Pfizer, 5, BMS, 5; **L. Kearsley-Fleet**, None; **C. Codreanu**, AbbVie, 1, 6, Amgen, 1, 6, Ewopharma, 6, Lilly, 6, Novartis, 1, 6, Pfizer, 1, 6; **D. Monguin**, None; **D. Courvoisier**, Medtalks Switzerland, 6; **A. Finckh**, Eli Lilly, 5, 6, Pfizer Inc, 2, 5, 6, AbbVie, 2, 5, UCB, 2, Roche, 2, Galapagos, 5, MSD, 2, A2 Biotherapeutics, 2, Bristol-Myers Squibb, 2, 5.

Abstract Number: 1443

Long-term Effectiveness of Ultra-Low Doses of Rituximab in Rheumatoid Arthritis

Nathan den Broeder[1], Lise Verhoef[2], Yael De Man[3], Marc Kok[4], Rogier Thurlings[5], Wilfred van der Weele[6], Bart van den Bemt[7], Frank van den Hoogen[8], Aatke van der Maas[9] and Alfons den Broeder[10], [1]Radboud University Medical Centre, Nijmegen, Gelderland, Netherlands, [2]Sint Maartenskliniek, Nijmegen, Netherlands, [3]Ziekenhuisgroep Twente (Hospital Group Twente), Borne, Netherlands, [4]Maasstad Hospital, Rotterdam, Netherlands, [5]Radboud University Medical Centre, Nijmegen, Netherlands, [6]Reade, Amsterdam, Netherlands, [7]Sint Maartenskliniek; Radboud University Medical Center, Ubbergen, Netherlands, [8]Sint Maartenskliniek, Ubbergen, Gelderland, Netherlands, [9]St Maartenskliniek, Nijmegen, Gelderland, Netherlands, [10]Sint Maartenskliniek, Nijmegen, Gelderland, Netherlands

Table 1. Patient characteristics by original randomization. Data are n (%), mean (SD), or median (IQR)

	1000mg (n=24)	500mg (n=48)	200mg (n=46)
Age (years)	65 (9)	64 (11)	64 (12)
Female	15 (63%)	28 (58%)	34 (74%)
Meeting ACR1987 or ACRU/EULAR 2010 RA criteria	22 (92%)	47 (98%)	43 (93%)
Disease duration (years)	14 (9-24)	14 (7-21)	13 (8-20)
RF or ACPA positive	22 (92%)	44 (92%)	40 (87%)
Duration of rituximab use (years)	3.0 (1.6-5.5)	2.0 (1.0-5.5)	3.7 (2.0-5.7)
Concomitant csDMARD	17 (71%)	29 (60%)	27 (59%)
Previous number of b/tsDMARDs used	2 (2-2)	2 (1-3)	2 (1-2)
Previous number of csDMARDs used	3 (1-3)	2 (1-4)	3 (1-3)
Oral GC use at baseline	3 (13%)	8 (17%)	5 (11%)
Baseline DAS28-CRP	2.3 (0.9)	2.3 (0.9)	2.5 (1.1)

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Abstracts: RA – Treatments II: New Findings in Established Therapies (1442–1445)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: The optimal rituximab (RTX) dose for the treatment of rheumatoid arthritis remains unclear. RTX treatment of 1000mg per 6 months and 2000mg per 6 months were shown to be similarly efficacious (1). The REDO trial showed comparable 6-month efficacy of continued treatment with 500mg and 200mg compared to 1000mg, though formal non-inferiority could not be established (2). We followed trial participants for up to 4 years in this extension study to confirm effectiveness of ultra-low doses.

Methods: Patients from the REDO trial were invited to participate in this study. Treatment decisions were left at the discretion of the rheumatologist and patient. Disease activity (DAS28-CRP), and medication use (b/tsDMARD, csDMARD, gluccocorticoids [GC]) were collected from start of the trial to censoring in April 2021. The primary outcome was disease activity, secondary outcomes were RTX persistence, RTX doses and intervals, and use of comedication.

Disease activity was analyzed using a longitudinal mixed model with random intercepts to account for intra-patient correlations, in two ways: 1. By original randomization and stratification factors (RF/ACPA and csDMARD use). 2. By time-varying total RTX dose received in the year preceding each disease activity measurement, adjusted for current csDMARD or GC use, and RF/ACPA. The original DAS28-CRP non-inferiority (NI) margin of 0.6 was used.

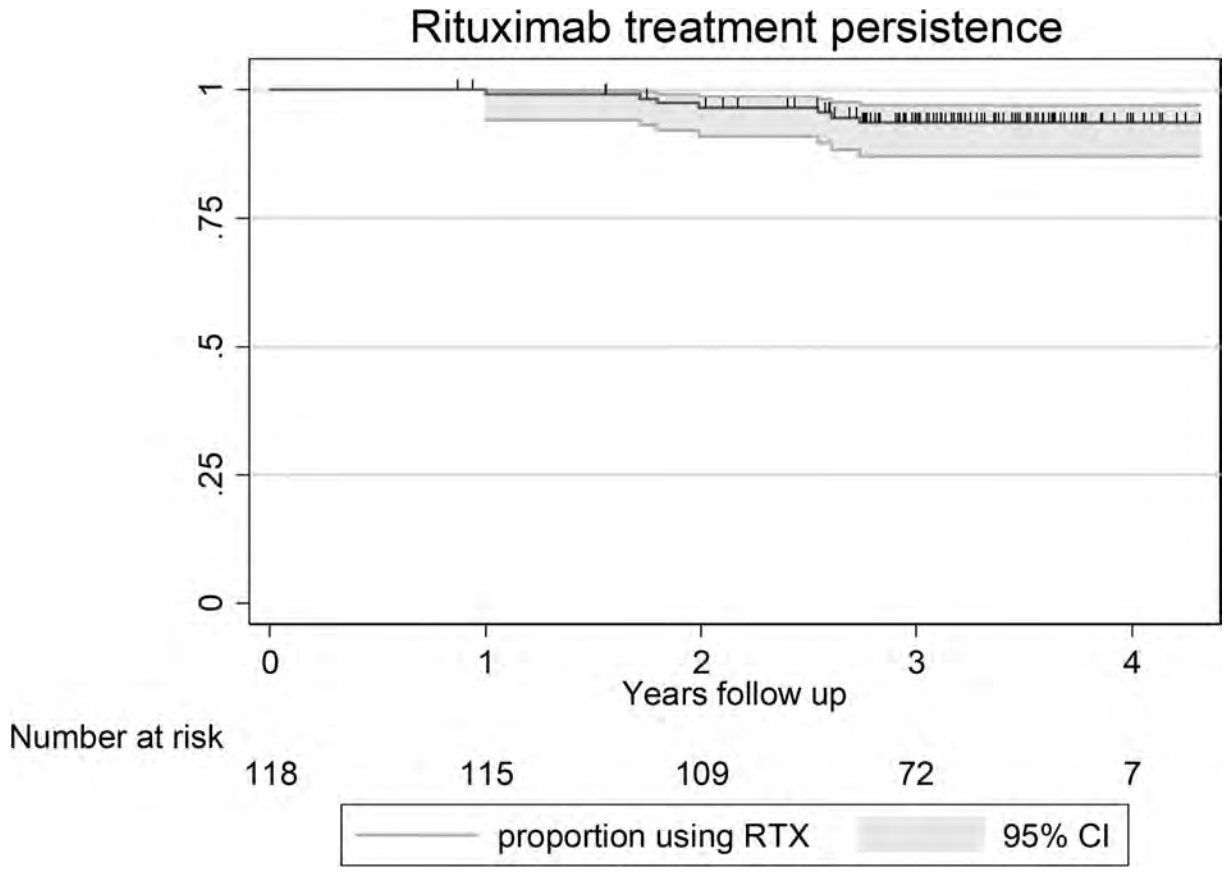


Figure 1. Rituximab treatment persistence during follow up.

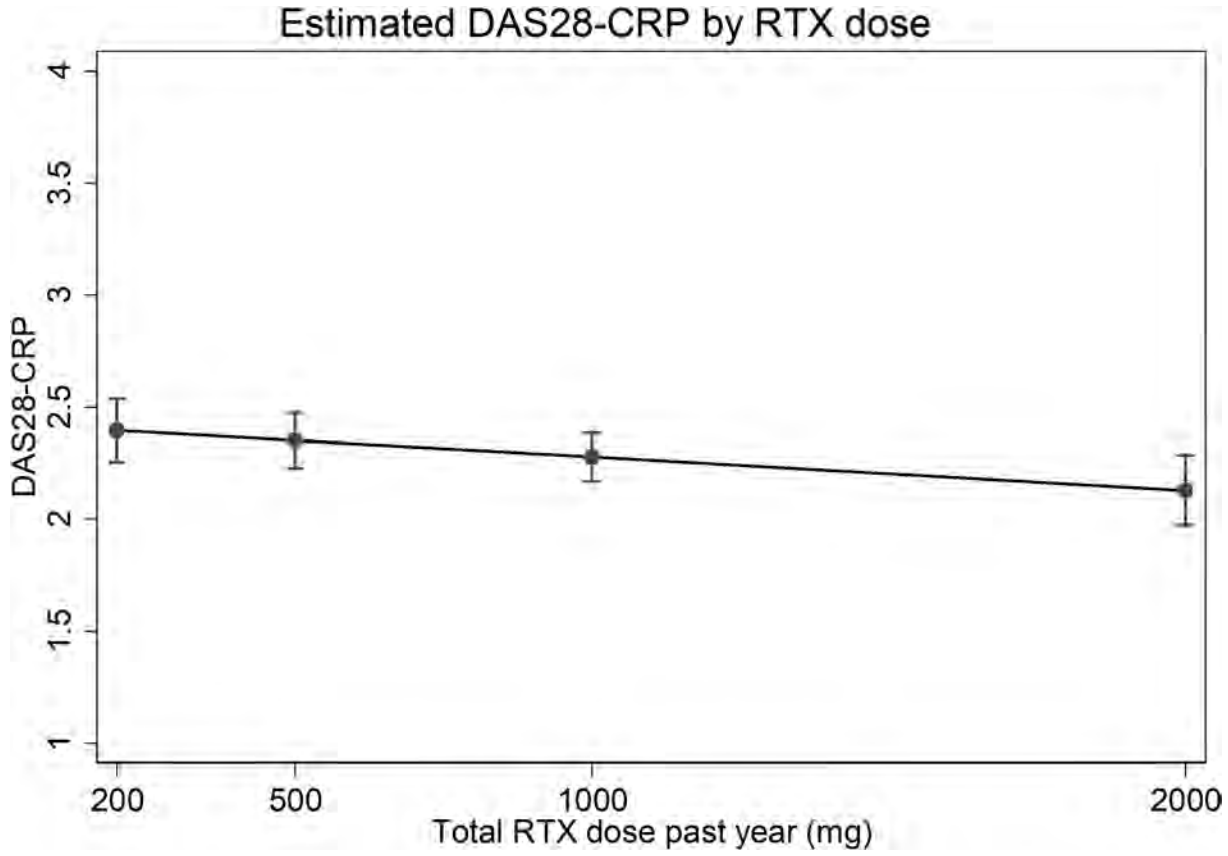


Figure 2. Estimated effect on disease activity of RTX dose in the year preceding disease activity measurement, corrected for RF/ACPA, csDMARD, oral and intramuscular glucocorticoid use.

Results: 118 out of 142 REDO patients were included in current analyses (table 1) Reasons for exclusion were: continuing treatment elsewhere (n=3), no informed consent (n=9) and data yet to be collected in 2 study centers (n=12). Mean follow up was 3.2 years (total of 377 patient-years), with 7 patients switching to another b/tsDMARD (Figure 1) upon which they were censored from disease activity analyses.

Disease activity in both ultra-low dose groups was non-inferior to the 1000mg group, with a mean DAS28-CRP (95% CI) during follow-up of 2.2 (2.0-2.4) in the 1000mg group, 2.2 (2.1-2.4) in the 500mg group and 2.3 (2.2-2.5) in the 200mg group.

Analyzed by received RTX dose, lower RTX dose was significantly associated with a higher DAS28-CRP: 0.15 (95% CI: 0.04-0.26) points higher per 1000mg more RTX (Figure 2). The upper limit for relevant RTX doses was below the prespecified NI margin, excluding a relevant effect of RTX dose on disease activity.

Median (IQR) yearly RTX dose was 978mg (704mg-1425mg). Final RTX dose per infusion was 200mg in 37 patients (31%), 500mg in 47 (40%) and 1000mg in 34 (29%), with a median (IQR) final interval between infusions of 6.0 (5.7-6.5), 6.2 (6.0-7.4) and 6.4 (6.0-9.6) months respectively. The rate of GC injections was 0.38 (95% CI: 0.32-0.44) per patient-year and initiation rate of oral GC was 0.05 (0.03-0.08) per patient-year.

Conclusion: A majority of patients treated with ultra-low dose RTX remained on ultra-low doses for up to 4 years, while disease activity remained low and did not relevantly differ between RTX doses, either according to original randomization or by received dose. Switching to other b/tsDMARDS or use of GC was rarely required.

References

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2. Verhoef LM et al. Lancet Rheumatol. 2019; 1: e145-e153.

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Abstract Number: 1444

Baseline Factors Associated with the Development of Nausea and Alopecia over One Year in Patients Starting Methotrexate for Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: RA – Treatments II: New Findings in Established Therapies (1442–1445)
Session Type: Abstract Session
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Background/Purpose: Methotrexate (MTX) is the first-line treatment in the management of patients with rheumatoid arthritis (RA) due to its good efficacy. However, certain adverse events, such as nausea and alopecia, often create considerable concerns to patients starting the treatment, and could affect their quality of life. This may result in non-adherence to MTX or permanent discontinuation of treatment in the early period following the start of MTX. This study aimed to summarise the prevalence rates nausea and alopecia, and identify baseline factors associated with the development of these adverse events over the first year of MTX treatment.

Methods: The Rheumatoid Arthritis Medication Study (RAMS) is a multi-centre prospective cohort study of patients with RA commencing MTX for the first time. Relevant demographic, clinical and medication related data were collected at baseline (Table). Adverse events were reported at six- and twelve-month follow-ups. The prevalence rates of nausea and alopecia were calculated based on the proportions of patients who reported having an adverse event within one year of follow-up. Multivariable logistic regression analyses were performed to assess the associations between candidate baseline predictors and nausea or alopecia.

Results: A total of 1069 patients with early RA were included in this analysis. The mean age at the start of MTX was 59.2 (SD: 13.5) years, 65.3% were women, and the mean duration of symptom was 7.7 (SD: 5.6) months. Around one third of the patients (31.1%) reported nausea over the first year of treatment with MTX. Alopecia was reported by 83 patients (7.8%).

Women were more likely to report nausea and alopecia compared with men, odds ratios (ORs) were 2.22 (95%CI: 1.59 to 3.11) and 3.93 (95%CI: 2.01 to 7.70), respectively (Table). Older age was associated with decreased odds of reporting nausea, OR 0.97 (95%CI: 0.96 to 0.99). Alcohol consumption was associated with increased odds of

Table. Baseline factors associated with the development of nausea and alopecia

Baseline factors	Nausea (332 events)	Alopecia (83 events)
	Odds ratio (95% confidence interval)	
Demographic and lifestyles		
Age (years)	**0.97 (0.96, 0.99)**	1.00 (0.98, 1.02)
Female sex vs male	**2.22 (1.59, 3.11)**	**3.93 (2.01, 7.70)**
Current vs never smokers	0.97 (0.65, 1.46)	0.89 (0.48, 1.76)
Former vs never smokers	0.93 (0.68, 1.28)	1.05 (0.63, 1.76)
Alcohol consumption, (yes vs no)	**1.44 (1.04, 1.97)**	**1.98 (1.11, 3.53)**
BMI (Kg/m^2)	1.02 (1.00, 1.05)	–
Caffeine intake (cups per day)	1.08 (1.01, 1.14)	–
Disease activity and patient-reported outcomes		
DAS28-CRP	**1.15 (1.02, 1.31)**	0.89 (0.70, 1.12)
HAQ score	1.01 (0.77, 1.32)	**1.64 (1.05, 2.57)**
VAS pain (mm)	1.00 (0.99, 1.01)	1.00 (0.98, 1.01)
BMQ concern scale	**1.06 (1.02, 1.10)**	–
Laboratory tests		
ACPAs positive vs negative	1.14 (0.73, 1.78)	–
RF positive vs negative	0.76 (0.48, 1.19)	1.21 (0.71, 2.06)
eGFR (ml/min/1.73 m^2)	1.00 (0.99, 1.01)	–
Medication related		
MTX starting dose> 15mg per week	0.92 (0.69, 1.22)	1.02 (0.63, 1.63)
Concomitant DMARDs, (yes vs no)	**0.72 (0.50, 1.02)**	**0.62 (0.34, 1.16)**
NSAIDs, (yes vs no)	1.11 (0.82, 1.50)	–

ACPA: Anti-citrullinated protein antibodies; BMI: body mass index; BMQ: Beliefs about Medicines Questionnaire; csDMARDs: conventional synthetic Disease-Modifying Antirheumatic Drugs; DAS28-CRP: disease activity score 28 joint counts; eGFR: estimated glomerular filtration rate; HAQ: health assessment questionnaire; MTX: methotrexate; NSAIDs: non-steroidal anti-inflammatory drugs; RF: rheumatoid factor; VAS: visual analogue scale

developing nausea and alopecia, ORs were 1.44 (95%CI: 1.04 to 1.97) and 1.98 (95%CI: 1.11 to 3.53), respectively. Higher Disease Activity Score and Belief about Medication Questionnaire – Concern scale at baseline were associated with increased odds of nausea. The use of concomitant csDAMRDs with MTX at baseline was associated with less reporting of nausea and alopecia.

Conclusion: Identifying factors associated with adverse event occurrence could help alleviate patients' concerns and improve adherence to MTX. Limiting alcohol consumption may influence the likelihood of developing MTX-related adverse events.

Disclosure: A. Sherbini, None; **J. Gwinnutt**, Bristol Meyers Squibb, 5; **K. Hyrich**, Abbvie, 6, Pfizer, 5, BMS, 5; **S. Verstappen**, Bristol Meyer Squibb, 5, Pfizer, 6.

Abstract Number: 1445

Association Between Baseline Use of Rituximab and COVID-19 Outcomes in Patients with Rheumatoid Arthritis (RA)

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Abstracts: RA – Treatments II: New Findings in Established Therapies (1442–1445)
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Background/Purpose: Patients with Rheumatoid arthritis (RA) are at a potentially increased risk of SARS-CoV-2 infection, and immunosuppressive or biologic drugs used to treat RA might also be associated with a higher risk of infection or worse COVID-19 outcomes. Limited data to date suggest rituximab is associated with worse COVID-19 outcomes. The objective of our study was to evaluate the association between baseline use of rituximab and COVID-19 outcomes among patients with RA using a nationally representative sample of patients.

Methods: Our study sample included patients in the National COVID Cohort Collaborative (N3C), a centralized, harmonized, high-granularity electronic health record repository that is the largest, most representative U.S. cohort of COVID-19 cases and controls to date. N3C includes patient encounters from January 1, 2018 to provide information

Table 1. Baseline characteristics of the cohort

about pre-existing health conditions. We identified patients with RA who had two or more International Classification of Diseases (ICD)-10 codes for RA (M05.X or M06.X), and in sensitivity analyses we defined RA as having one or more than one RA-specific ICD-10 code (a more sensitive, less specific definition). We identified baseline use of DMARDs using the medication tables. Our primary outcomes were: SARS-CoV-2 infection, defined as COVID-19–positive polymerase chain reaction or antigen test, or an ICD-10-CM diagnostic code; and for those with COVID-19 diagnosis,

Table 2. Multivariable-adjusted association of Rituximab and no DMARD use with COVID-19 and COVID-19 outcomes

	SARS-Co-V-2 positivity	Hospitalized	Invasive ventilation	30-day mortality
	Odds ratio (95% Confidence Interval)			
Conventional synthetic DMARD (csDMARDs)	1.0	1.0	1.0	1.0
Rituximab use	0.89 (0.72-1.10)	**2.00 (1.32-3.04)**	**2.60 (1.13-5.70)**	1.98 (0.93-4.25)
No DMARD use	0.60 (0.58-0.64)	**1.60 (1.40-1.80)**	**1.40 (1.07-1.90)**	0.98 (0.78-1.22)
Adjusted for demographics (age, sex, race/ethnicity), Body mass index, US region, Deyo-Charlson comorbidity index [17 medical comorbidities], and smoking status				

hospitalization, invasive ventilation, and 30-day mortality. Multivariable logistic regression models assessed the association of rituximab use with the odds of COVID-19 and associated outcomes compared with the use of conventional synthetic DMARDs (csDMARDs) as the referent category. Analyses were adjusted for demographics, medical comorbidities, smoking status, US region, and body mass index (BMI).

Results: A total of 57,725 patients met our eligibility criteria of which 16,342 were SARS-CoV-2 positive during the study period. Mean (±SD) age of the cohort was 62 (±14.6) years, 75% females, 68% White and 76% were non-smokers (Table 1). 1477 (2.6%) patients were exposed to rituximab prior to their first positive COVID-19 test. Pulmonary disease was seen in 40% of the cohort. In multivariable-adjusted models, compared to the use of csDMARDs, baseline rituximab use was associated with increased odds of hospitalization among those who were diagnosed with COVID-19 (adjusted odds ratio, aOR 2.0, 95% CI 1.3-3), and invasive ventilation (aOR 2.6, 95% CI 1.13-5.7) (Table 2). No DMARD use was also associated with significantly higher odds of hospitalization among those who were diagnosed with COVID-19. Results were similar in sensitivity analyses where RA cohort was defined based on the presence of at least one ICD-10 code for RA (n=80,063).

Conclusion: We leveraged data from a large national repository to study the association between baseline use of DMARDs and various COVID-19 outcomes. Compared to csDMARD use, rituximab use in patients with RA was associated with higher odds of COVID-19 hospitalizations and invasive ventilation. These results stress the need of prioritizing COVID-19 vaccination for RA patients.

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Abstract Number: 1446

Trauma Is Associated with Flares in Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Background/Purpose: Daily psychological stress and trauma exposure with or without symptoms of post-traumatic stress disorder have been linked to an increased risk of SLE onset.[1, 2] Adverse childhood experiences (ACEs) have been linked to worse patient-reported outcomes in SLE, but not to physician-assessed disease activity.[3] This analysis examines the association between experiences of trauma and disease flares in SLE.

Methods: Data are from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort of individuals with rheumatologist-confirmed SLE. Data are collected annually through in-person research visits and structured interviews. The Brief Trauma Index (BTI) was administered to assess the experience of trauma as well as whether the respondent believed they were at risk for serious injury or death, and whether they were actually injured (Table 1). In contrast to ACEs, traumatic events could be in childhood or adulthood, although one question specifically addresses childhood events. The total number of traumatic events, events with perceived danger, and events with injury, as well as the experience of any of these were calculated. Lupus flares over the previous year were self-reported as any flare (FLARE) or whether the respondent visited the doctor or was hospitalized for the flare (DR-FLARE). Cross-sectional analyses examined whether trauma (number of events or any event) was associated with flares. Multivariable analyses examined the role of trauma on the occurrence of flares controlling for age, disease duration, sex, poverty, race/ethnicity, comorbidities, and obesity. Finally, analyses were repeated and stratified by whether the individual reported ACEs. For this analysis, the BTI item on childhood trauma was excluded.

Results: Among the 251 individuals who completed the BTI, mean age was 50 ± 13 years, disease duration 22 ± 11 years, 90% were female, 31% Asian, 23% Hispanic, 33% white non-Hispanic, and 10% African American. 106 (42%) reported FLARE in the past year; 62% of these (n=66) reported DR-FLARE. 83% reported any trauma; excluding the BTI item on serious illness, 77% reported any trauma (Table 1). 64% reported trauma with perceived danger, and 23% with injury. Among those with FLARE and DR-FLARE, the number of all types of events was higher (Table 2). In multivariate analyses, the associations remained significant (Table 3). The association between trauma in adulthood and flares appeared to be stronger among individuals who had previously experienced ACEs (e.g., 0-1 ACEs, odds of DR-FLARE per number of traumatic events = 1.2 [95% CI 0.9, 1.6)] vs. ≥2 ACES 1.7 [1.2, 2.5]).

Conclusion: Individuals with SLE who have experienced trauma during adulthood may be at increased risk for more frequent self-reported flares over time, and the experience of childhood trauma may magnify that risk. Given the high frequency of traumatic experiences, identifying both the mechanisms of these associations and interventions that may reduce the impact of trauma is critical.

Table 1. Frequency of responses to Brief Trauma Index (n=251)			
	Has this ever happened to you?	Did you think your life was in danger or you might be seriously injured?	Were you seriously injured?
	Yes →	Yes	Yes
1. Have you ever served in a war zone, or have you ever served in a noncombat job that exposed you to war-related casualties	2.0% (5)	1.2% (3)	0
2. Have you ever been in a serious car accident or a serious accident at work or somewhere else?	25.5% (64)	17.9% (45)	10.0% (25)
3. Have you ever been in a major natural or technological disaster, such as a fire, earthquake, tornado, hurricane, explosion, or chemical spill?	40.6% (102)	22.7% (57)	0.8% (2)
4. Have you ever had a life-threatening illness such as cancer, a heart attack, leukemia, AIDS, multiple sclerosis, etc.?	47.8% (120)	37.5% (94)	
5. Before age 18, were you ever physically punished or beaten by a parent, caretaker, or teacher so that: you were very frightened or thought you would be injured; or you received bruises, cuts, welts, lumps, or other injuries?	25.9% (65)	12.4% (31)	6.0% (15)
6. Besides what you just told me about, have you ever been attacked, beaten, or mugged by anyone, including friends, family members or strangers?	27.5% (69)	19.1% (48)	8.8% (22)
7. Has anyone ever made or pressured you into having some type of unwanted sexual contact?	32.3% (81)	13.6% (34)	10.0% (25)
8. Have you ever been in any other situation in which you were seriously injured, or have you ever been in any other situation in which you feared you might be seriously injured or killed?	21.1% (53)	7.6% (19)	
9. Has a close family member or friend died violently, for example, in a serious car crash, mugging, or attack?	23.5% (59)		
10. Other than the events you already told me about, have you ever witnessed a situation in which someone was seriously injured or killed, or have you ever witnessed a situation in which you feared someone else would be seriously injured or killed?	27.5% (69)		

1. Roberts A, et al. *Arthritis Rheum.* 2017;69:2162-2169.
2. Feldman CH, et al. J Rheumatol. 2019;46(12):1589-1596.
3. DeQuattro K, et al. *Arthritis Care Res.* 2020;72(525-533).

Table 2. Association of SLE flares and traumatic exposures (bivariate)

	Flare in past year			Flare w/ associated doctor visit or hospitalization in past year		
	No (n=146)	Yes (n=106)	P	No (n=186)	Yes (n=66)	p
Number of events						
All traumatic events	**2.4 ± 2.0**	**3.4 ±2.4**	**.007**	**2.4 ± 1.9**	**3.5 ± 2.7**	**.0034**
All events, excluding health	**2.0 ± 1.9**	**2.8 ± 2.2**	**.003**	**2.0 ± 1.7**	**3.0 ± 2.5**	**.004**
Events with perceived danger	**1.2 ± 1.5**	**1.9 ± 1.8**	**.009**	**1.2 ± 1.5**	**2.1 ± 2.0**	**.0034**
Events with injury	**0.3 ± 0.8**	**0.6 ± 1.1**	**.03**	**0.3 ± 0.8**	**0.7 ± 1.2**	**.02**
Any event in category						
Any traumatic event	82.2 (120)	83.0 (88)	.99	82.8 (154)	81.8 (54)	.85
Any event, excluding health	74.7 (109)	79.3 (84)	.45	76.3 (142)	77.3 (51)	.99
Any event with perceived danger	**57.5 (84)**	**73.6 (78)**	**.01**	**60.8 (113)**	**74.2 (49)**	**.05**
Any event with injury	**15.8 (23)**	**33.0 (35)**	**.002**	**19.4 (36)**	**33.3 (22)**	**.03**

Table 3. Association of SLE flares and trauma (multivariate)

	Flare in past year		Flare w/ associated doctor visit or hospitalization in past year	
	OR (95% CI)	P	OR (95% CI)	p
Number of events				
All traumatic events	**1.31 (1.13, 1.51)**	**.0003**	**1.28 (1.10, 1.49)**	**.0017**
All events, excluding health	**1.35 (1.16, 1.59)**	**.0002**	**1.31 (1.11, 1.55)**	**.0016**
Events with perceived danger	**1.50 (1.24, 1.83)**	**<.0001**	**1.33 (1.10, 1.61)**	**.0029**
Events with injury	**1.75 (1.23, 2.51)**	**.0021**	**1.43 (1.03, 1.97)**	**.03**
Any event in category				
Any traumatic event	0.96 (0.46, 2.02)	.92	0.66 (0.30, 1.51)	.33
Any event, excluding health	1.24 (0.63, 2.42)	.53	0.88 (0.42, 1.86)	.74
Any event with perceived danger	**2.05 (1.12, 3.77)**	**.02**	1.62 (0.81, 3.23)	.17
Any event with injury	**2.44 (1.23, 4.87)**	**.0112**	2.03 (0.97, 4.27)	.06
Controlling for age, disease duration, female, poverty, race/ethnicity, number of comorbidities, and obesity. Analyses controlling for Brief Index of Lupus Damage (BILD) (T4 if available (n=198); T1 if not) did not show any substantive differences.				

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Abstract Number: 1447

Long-Term Effect of Prescription Non-Steroidal Anti-Inflammatory Drug Regular Use on the Risk of a Knee Replacement

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SESSION INFORMATION

Session Date: Monday, November 8, 2021
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Background/Purpose: Non-steroidal anti-inflammatory drugs (NSAIDs) are a primary treatment for osteoarthritis (OA). It is uncertain, however, whether regular use of NSAIDs affects the risk of structural progression and ultimately increase joint replacement risk. Reports suggest that users of analgesics including NSAIDs may experience more progressive structural deterioration than non-users. On the other hand, NSAIDs may reduce intra-articular inflammation sufficiently to minimize potential damage. Whereas regular use of prescription NSAIDs is common in persons with OA, the long-term effects of pain-relieving interventions on structural damage are not fully characterized. Previous studies focused on short-term effects and only compared always-users of NSAIDs with non-users and had limited ability to mitigate confounding by indication. We used a causal inference-based approach, and designed a hypothetical longitudinal trial from observational data to assess the risk of a knee replacement (KR) under various time-varying regimens of regular prescription NSAIDs use.

Methods: We included 8 years of data from the Osteoarthritis Initiative (OAI) cohort, including baseline, 12-, 24-, 36-, 48-, 72-, and 96-month OAI study visits. Study outcome was defined as a KR. Study exposure was defined as the regular use of any prescription NSAIDs, which was determined at every study visit. Study covariates included baseline and time-dependent confounders measured at all OAI visits that included knee pain characterized by the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale. We used targeted learning, a double-robust causal inference-based methodology, to compare the risk of a knee replacement under hypothetical intervention regimens that included comparing no NSAID use in persons with painful knees to a hypothetical regimen of regular NSAIDs use in the same persons and under the same conditions. We examined KR risk for hypothesized NSAIDs initiation at knee pain levels of 7, 10, and 15 on the 0-20 WOMAC scale, compared to no NSAID use at the same pain levels.

Results: Data included 528 KR events (in 9592 knees; 5.5%) in 4796 persons (58.5% female; baseline mean age = 61.2 [SD = 9.2]). The estimated reference risk of a KR event in OAI (i.e., the risk for the no intervention regimen), adjusted for loss to follow-up and death, was 5.9% (95% CI: 5.2%, 6.5%). KR risk increased by 232%, 51%, and 12% when NSAIDs initiation was triggered at WOMAC pain level of 7, 10, and 15, respectively, suggesting an increased risk of KR with NSAID use especially when prescription NSAIDs were initiated at lower knee pain levels. Examining WOMAC pain < 7 was not possible given the rarity of regular NSAID use at this threshold in OAI participants. To adjust for pain severity, we used WOMAC pain score at the annual exam prior to report of regular NSAID use and if pain worsened over the year, triggering NSAID use, our findings may overestimate NSAID risk.

Table 1. Estimated knee-level risk of a knee replacement in the Osteoarthritis Initiative cohort under dynamic intervention regimen of prescription NSAIDs initiation based on a knee pain level.

WOMAC pain score to trigger NSAIDs initiation	Average treatment effect risk ratio (95% CI)
7	2.32 (1.01, 5.35)
10	1.51 (1.25, 1.81)
15	1.12 (1.06, 1.19)

CI: Confidence interval; NSAIDs: Non-steroidal anti-inflammatory drugs; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index.

Conclusion: Our findings suggest that, for the same level of pain, prescription NSAIDs users may experience higher risk of a KR compared to non-users.

Confounders included demographics, body mass index, Kellgren and Lawrence grade, regular use of prescription opioids, WOMAC stiffness and function scores, objective functional performance measures of chair stand time, 20- and 400-meter walk tests, malalignment, Charlson comorbidity index, Center for Epidemiologic Studies Depression (CES-D) scale, Physical Activity Scale for the Elderly (PASE) score, a knee injury, hip pain or stiffness, and a family history of a knee or a hip replacement.

Disclosure: S. Jafarzadeh, Pfizer, 5; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **D. Felson**, None.

Abstract Number: 1448

Virtual Visits versus Face-to-Face Visits for Rheumatoid Arthritis (RA): Comparison of Treat to Target (TTT) Adherence in 18 US Rheumatology Practices

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SESSION INFORMATION

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Background/Purpose: TTT is the recommended paradigm for managing RA according to major rheumatology organizations, however the literature suggests that TTT has not been widely implemented in US rheumatology. In a prior randomized controlled trial, we found that a learning collaborative (LC) was effective for improving implementation of TTT. (1) During the current study, we worked with US rheumatology practices on implementing TTT during 2020-2021 when some visits were conducted face-to-face (F2F) and other visits virtually (VV). These analyses examine differences in adherence with TTT based on whether the visit was F2F or VV.

Figure 1: Adherence with Treat to Target Across All Sites, Comparing Face to Face with Virtual Visits

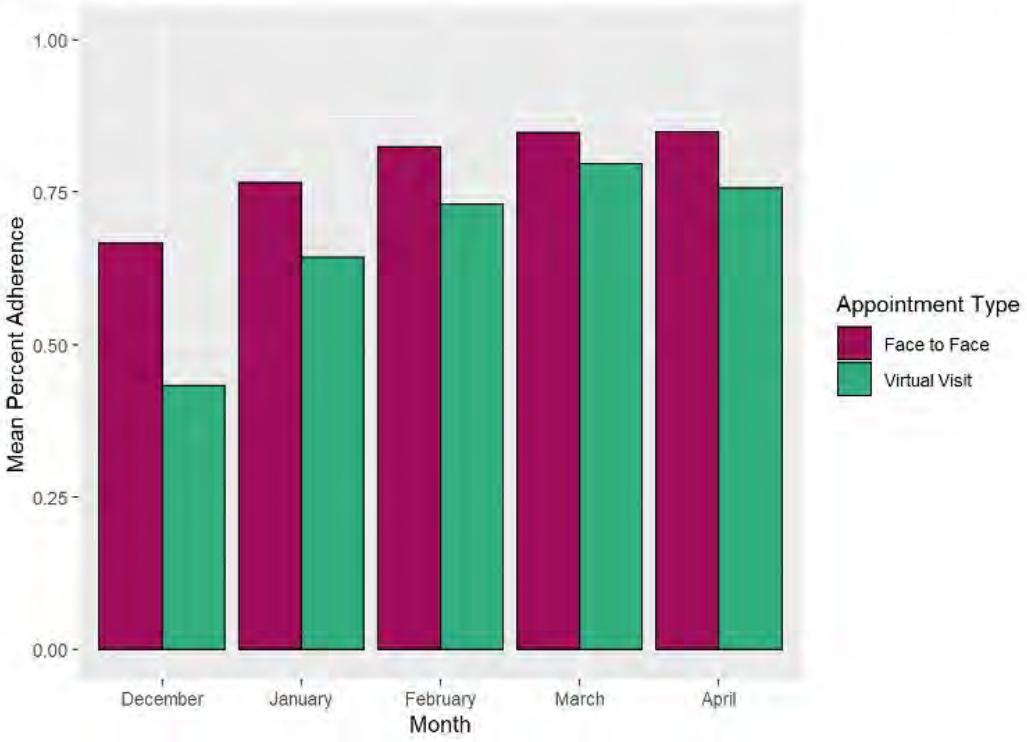

Table 1: Comparison of F2F versus VV and Adherence with Components of Treat to Target

Component of TTT	Face to face	Virtual visit	P-value
Disease activity measure	994 (87.4)	215 (67.8)	<0.0001
Target Noted	914 (80.4)	190 (59.9)	<0.0001
At Target	417 (36.7)	117 (36.9)	0.94
Not at target, change treatment	402 (35.4)	86 (27.1)	0.006
Shared decision making	702 (61.7)	204 (64.4)	0.40

Methods: During 2020-2021, we conducted a virtual Learning Collaborative (LC) for TTT in RA. 18 US-based rheumatology practices and 45 clinicians (MD, DO, NP, PA, RN) were engaged in the LC. The LC was 6 months in duration and each month the practices abstracted data from 20-25 visits with RA patients, focusing on adherence with TTT. Adherence was measured as a percentage of TTT component processes: 1) measure and document disease activity (any standard measure was acceptable), 2) determine a target disease activity, 3) make treatment changes if not at target, and 4) document shared decision-making. We then analyzed TTT adherence overall and by visit type, comparing F2F with VV. Further, VV visits were stratified as telephone or video.

Results: The 18 sites were distributed widely across the US, representing 10 states plus Washington DC, and their locations varied in COVID pandemic policies. During the 6 months, sites entered data on 1826 patient visits: 78% were F2F and 22% were VV. Overall adherence with TTT during the six months improved from a mean of 51% to 84%. Each component process of TTT was compared between F2F and VV visits (see **Table 1**). Over the full follow-up of the LC, there was greater adherence with TTT when visits were F2F (79% adherence) versus VV (65% adherence) ($p < 0.0001$). Documentation of a disease activity measure, a target, and change in treatment if not at target were all more common in the F2F versus VV visits (all $p < 0.05$). Documentation of shared decision making was similar across the

two types of visits. F2F adherence started at 67% whereas VV was 43% ($p < 0.0001$). However, by the last month, F2F was at 85% and VV at 76% ($p = 0.059$) (see **Figure 1**). Of the VV, 43% were conducted by telephone and 57% by video. Comparing overall adherence with TTT across these two types of VVs, there was not difference in overall adherence between video visits and telephone visits, 64.8% and 65.3%, respectively.

Conclusion: Implementing TTT for RA is a challenge, especially during the COVID pandemic. Among 18 US rheumatology practices engaged in implementing TTT, we found that adherence with TTT was slightly worse for VV compared with F2F. However, adherence with TTT improved for both types of patient visits, even during the COVID19 pandemic, and was similar after a six-month learning collaborative.

1. Solomon, D. H., et al. Implementation of Treat-to-Target in Rheumatoid Arthritis Through a Learning Collaborative: Results of a Randomized Controlled Trial. Arthritis Rheumatol 2017;69:1374-1380.

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Abstract Number: 1449

Is Repeat Serum Urate Testing Superior to a Single Test to Predict Incident Gout over Time?

Sarah Stewart[1], Amanda Phipps-Green[2], Gregory Gamble[1], Lisa Stamp[3], William Taylor[4], Tuhina Neogi[5], Tony Merriman[6] and Nicola Dalbeth[1], [1]University of Auckland, Auckland, New Zealand, [2]University of Otago Dunedin, Dunedin, New Zealand, [3]University of Otago, Christchurch, Christchurch, New Zealand, [4]University of Otago Wellington, Auckland, New Zealand, [5]Boston University School of Medicine, Boston, MA, [6]University of Alabama at Birmingham, Dunedin, New Zealand

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Clinical Epidemiology (1446–1451)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Elevated serum urate is the most important risk factor for developing gout. However, in longitudinal cohort studies, a small proportion of people with normal urate levels develop gout and the majority of those with high urate levels do not. These observations may be due to subsequent variations in serum urate over time. It is unclear whether repeated testing of serum urate improves the ability to accurately predict development of gout. This analysis aimed to examine whether single or repeat testing of serum urate more accurately predicts incident gout over time.

Methods: Individual participant data was included from three publicly available cohorts: Atherosclerosis Risk in Communities Study (ARIC), Coronary Artery Risk Development in Young Adults Study (CARDIA), and the original cohort of the Framingham Heart Study (FHS). Data from paired serum urate measures 3-5 years apart, followed by an assessment of gout incidence 5-6 years from the second urate measure were used to calculate the predictive ability of four models of serum urate measurement on incident gout: the first measure, the second measure, the average of the two measures, and the highest of the two measures. Participants with prevalent gout prior to the second measure were excluded. Receiver operator characteristic (ROC) curves and area under the curve (AUC) statistics were computed to compare the four models.

Results: A total of 16,017 participants were included across the three cohorts. Overall, 56% of participants were female, and 80% were European. The mean age of participants at baseline was 49 years. The mean follow-up from the first serum urate test was 9.3 years (range 8.9-10.1 years). Overall, there was a small increase in the mean serum urate between the first and second measures (5.42 mg/dL vs. 5.71 mg/dL, $P< 0.001$) which were a mean (SD) of 3.5 (0.9) years apart, but the first and second measures were highly correlated ($r = 0.81$, $P< 0.001$). No differences were observed in the predictive ability of incident gout between the four measures of serum urate measurement with ROC curve AUC statistics ranging between 0.81 (95% confidence intervals: 0.78-0.84) and 0.84 (95% confidence intervals: 0.81-0.87) (Table).

Conclusion: Repeat serum urate testing is not superior to a single measure of serum urate for prediction of incident gout over approximately one decade. These results may inform the design of longitudinal studies of incident gout, and clinical practice when providing advice to individuals about their risk of developing gout.

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Abstract Number: 1450

Unsupervised Machine Learning Methods to Cluster Comorbidities in a Population-based Cohort of Patients with Rheumatoid Arthritis

Elizabeth Atkinson[1], Tina Gunderson[1], John Davis[1], Elena Myasoedova[1], Vanessa Kronzer[1], Caitrin Coffey[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Abstracts: Clinical Epidemiology (1446–1451)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Comorbidities are common in patients with rheumatoid arthritis (RA), and comorbidity patterns are of interest. We aimed to examine clusters of comorbidities and clusters of patients based on comorbidities using several methods.

Methods: In this retrospective, population-based study, residents of a geographically well-defined area with prevalent RA on 1-1-2015 were identified from a comprehensive medical record linkage system. Diagnostic codes were retrieved for a 5 year period prior to the prevalence date. Using 2 codes at least 30 days apart, the 44 comorbidities described by England et al (ARD 2020) were defined. Unsupervised machine learning methods of interest included ascendant hierarchical clustering, network analysis, partitioning around medoids and latent class analysis. Methodologic considerations include the research question of interest, whether the method is appropriate for categorical data, method assumptions (e.g., some methods assume equal sample size per cluster), the optimal number of clusters, internal validation, stability and biological plausibility.

Results: A total of 1409 patients with prevalent RA (72% female; 92% white; mean age 63.5 years) were studied. Comorbidities were present in 1187 (84%) of the subjects with 5+ comorbidities present in 749 (53%) subjects.

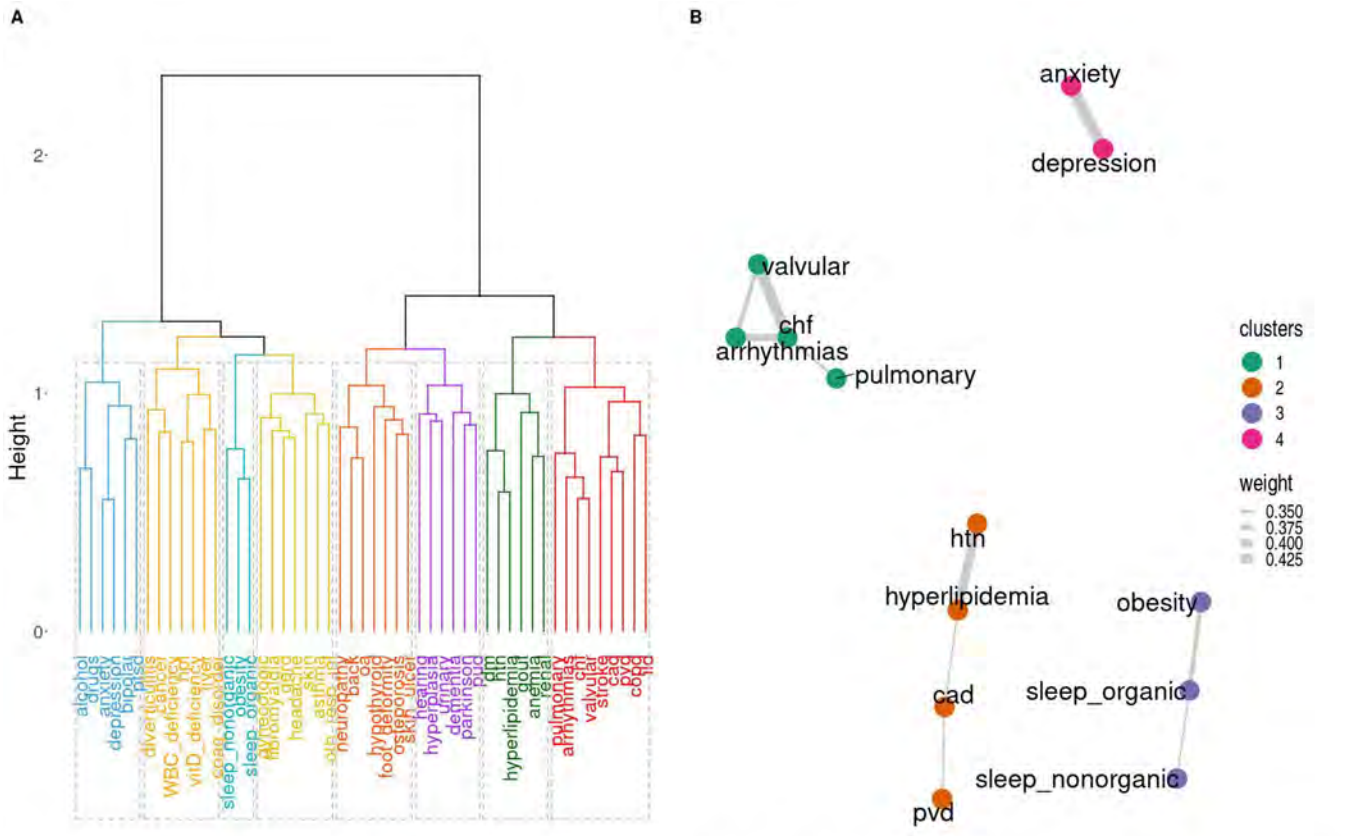

Figure 1. Panel A shows hierarchical clustering of comorbidities using the RA cohort; each color block represents a different cluster. Panel B shows network analysis using the same data. Thicker lines represent a higher correlation between the comorbidities and comorbidities not shown had smaller correlations with other comorbidities.

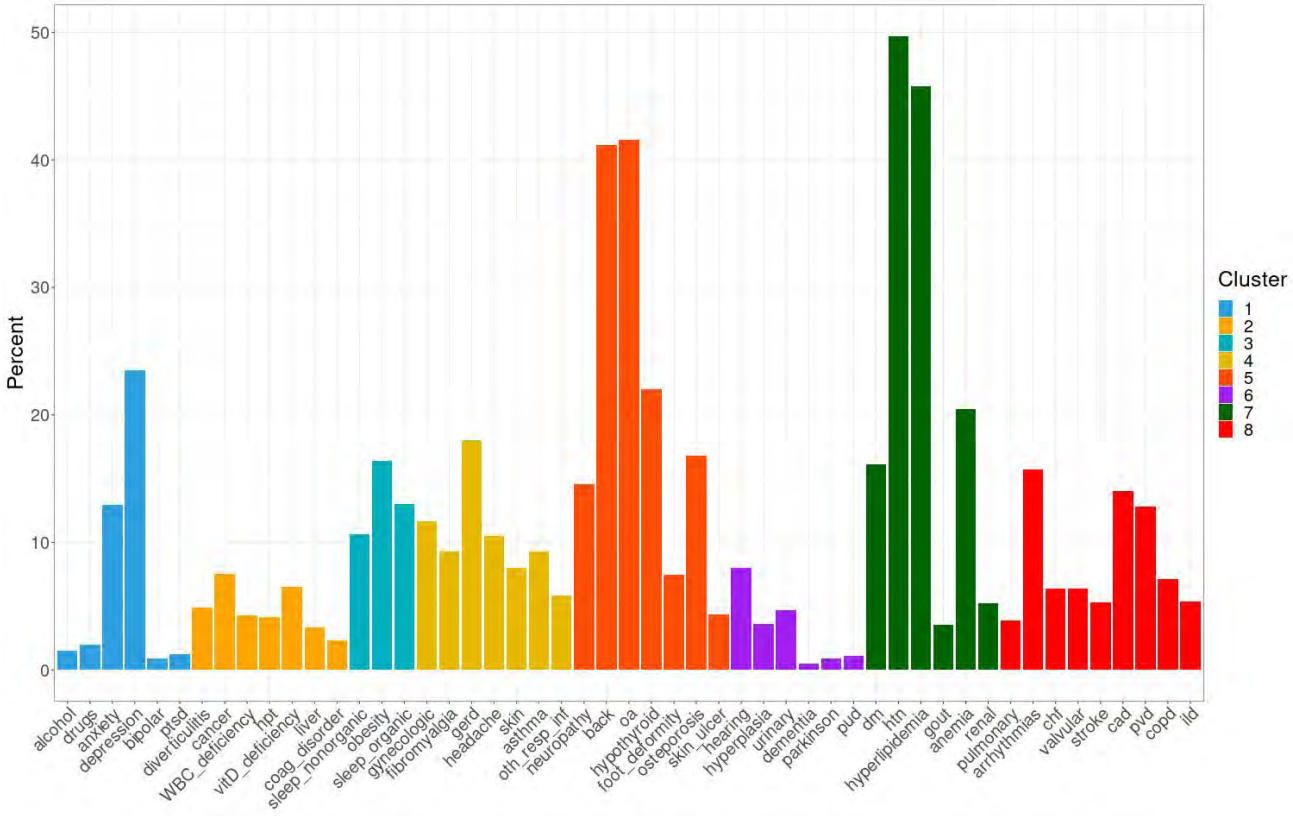

Figure 2: Frequency of comorbidities identified in the RA cohort within the past 5 years, grouped by the clusterd identified in Figure 1

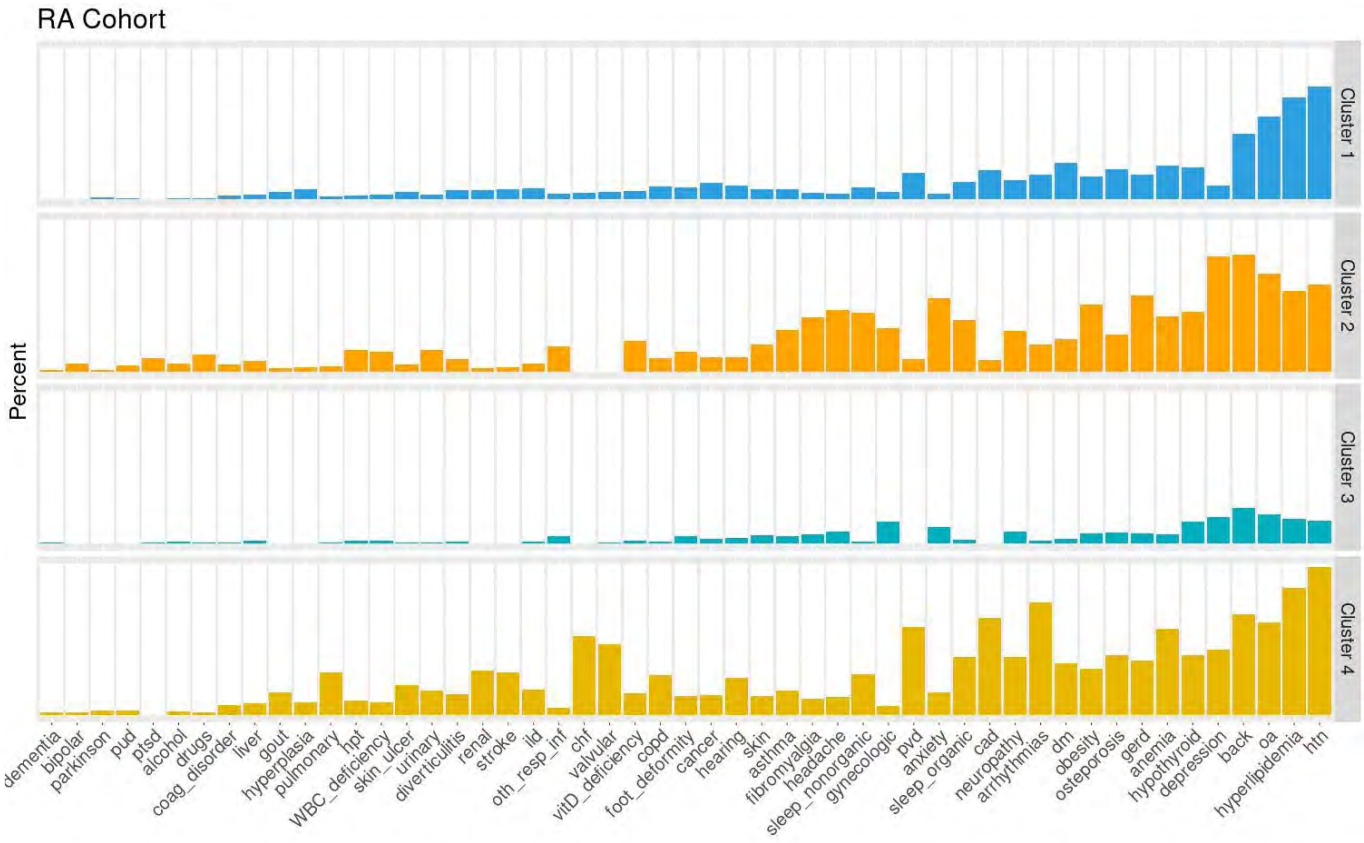

Figure 3: Latent class analysis using the RA cohort where each subject is in a cluster. The comorbidities listed along the horizontal axis are ordered by overall frequency in cohort. Cluster 3 includes subjects with few underlying comorbidities whereas cluster 4 includes subjects with multiple comorbidities.

Clustering of comorbidities using hierarchical clustering methods yielded 8 clusters (Figure 1a) while network analysis (Figure 1b) yielded 4 clusters. In both methods, the clusters were primarily organized around body systems (e.g., cardiovascular, respiratory, mental/behavioral comorbidities) with greater stability between methods for comorbidities with higher prevalence than those that were less common. Figure 2 illustrates the prevalence of each comorbidity within the cohort, grouped according to the clusters identified using the hierarchical approach.

Clustering of patients into subgroups based on comorbidity profiles using partitioning around medoids and latent class analysis yielded groups with no/few comorbidities, many comorbidities, and 2-3 intermediate groups with some comorbidities. Figure 3 shows the prevalence of each comorbidity within the 4 clusters identified using latent class analysis.

Conclusion: Clustering of comorbidities and clustering of patients can provide useful information about multimorbidity patterns in patients with RA. Clustering variables allows for easy application to other cohorts (e.g., non-RA). Clustering of RA subjects primarily created groups of subjects who had varying numbers of comorbidities. Various clustering methods are available, and these methods yield different results. It is important to understand the assumptions of these methods, as well as how to determine the optimal number of clusters for each method. Further research is needed to determine the best methods for identifying comorbidity patterns in RA.

Disclosure: E. Atkinson, None; **T. Gunderson**, None; **J. Davis**, Pfizer, 5; **E. Myasoedova**, None; **V. Kronzer**, None; **C. Coffey**, None; **C. Crowson**, None.

Abstract Number: 1451

Improving Health Outcomes and Social Connectedness Through Virtual Exercise Programs in Community Members with Musculoskeletal Conditions

Titilayo Ologhobo[1], Bertilia Trieu[2], Claudia Zurlini[1], Bonnie McGrath[1], Linda Roberts[1], Vilma Briones[1], Pamela Sanchez-Villagomez[2], Robyn Wiesel[1], Sandra Goldsmith[1] and Laura Robbins[1], [1]Hospital for Special Surgery, New York, NY, [2]Hospital of Special Surgery, New York

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Clinical Epidemiology (1446–1451)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: According to the 2020 American Health Ranking System, 26% of adults are physically inactive with a higher prevalence found in adults ages ≥65 years. Physical inactivity coupled with musculoskeletal conditions can result in poor health outcomes i.e., decreased pain tolerance, weak muscles, and stiff joints. These problems increase with age with nearly 75% of adults ages ≥65 years affected by musculoskeletal diseases. The COVID-19 pandemic resulted in significant disruption to daily living, social interaction, physical activity, and access to healthcare services. Under these conditions, physical inactivity was more prominent resulting to a potential decline of musculoskeletal function and health outcomes. To address these gaps, and ensure continued access to healthcare services, HSS pivoted from onsite to virtual exercise programming.

Methods: In March 2020, during the height of the pandemic, HSS shifted to 60-minute virtual exercise classes (Pilates, Yoga, and T'ai Chi) via Zoom. Our classes were targeted and structured to provide increased opportunity for

physical activity, social interaction with others, and access to programs. We introduced a variety of low-intensity exercises conducted safely at home, increased frequency of exercise classes, and promoted dialogue among participants before classes begin. Program effectiveness was measured using pre/post online surveys assessing sociodemographics, and self-reported health outcomes i.e., pain intensity, pain interference with seven aspects of daily living (ADL), physical functioning, stiffness, fatigue, physical activity, and self-efficacy. A longitudinal analysis was conducted using regression models.

Results: Our virtual exercise classes reached 5,030 community members. Of those assessed (n=287), 61 participants who self-reported having a musculoskeletal condition were mostly females (98%) ages ≥60 years (83%) and Caucasian (88%). Overall, these participants reported a 9% decrease in pain intensity ($p \leq 0.05$), 14% decrease in pain interference with relations with others ($p \leq 0.05$), and 9% decrease in stiffness ($p \leq 0.05$) with every 6-week virtual exercise session. In a sub-sample of participants with self-reported musculoskeletal conditions that participated in classes at least 2x/week (n=17), results revealed a 18% decrease in pain intensity ($p \leq 0.001$), 13% decrease in stiffness ($p \leq 0.001$), 14% decrease in stiffness ($p \leq 0.05$), and decreased pain interference with six ADL - general activity (18%; $p \leq 0.001$), mood (14%; $p \leq 0.05$), walking ability (17%; $p < 0.05$), normal work (16 %; $p \leq 0.01$), sleep (18%; $p \leq 0.05$), and enjoyment of life (18%; $p < 0.01$) with every 6-week virtual exercise session.

Conclusion: Our targeted approach in implementing safe low-intensity virtual exercises proved to be successful. Results indicate that virtual exercise classes were effective in improving health outcomes and fostering social connectedness in participants with musculoskeletal conditions. Amid uncertainties caused by the pandemic, shifting to virtual programming increased overall reach, reduced the negative impact of isolation, and enabled those with musculoskeletal conditions have increased access to effective health programs.

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Abstract Number: 1452

COVID-19 Infection Among Autoimmune/Auto-inflammatory Rheumatic Disease Patients: Data from an Observational Study

Clio Mavragani[1], Athanasios-Dimitrios Bakasis[2], Kyriaki Boki[3], Athanasios Tzioufas[4], Panayiotis Vlachoyiannopoulos[1], Ioanna Stergiou[5], Fotini Skopouli[6] and Haralampos Moutsopoulos[7], [1]National and Kapodistrian University of Athens, Athens, Greece, [2]1 Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, Athens, Greece, [3]3 Rheumatology Unit, Sismanoglio General Hospital, Athens, Greece, Athens, Greece, [4]Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, Athens, Greece, [5]Department of Pathophysiology, School of Medicine, National and Kapodistrian University of Athens, Athens, [6]Department of Nutrition and Clinical Dietetics, Harokopio University of Athens, Athens, Greece, [7]Athens Academy of Athens, Chair Medical Sciences/Immunology, Athens, Greece

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: The impact of COVID-19 infection in patients with autoimmune/auto-inflammatory rheumatic diseases (AARD) under immunomodulatory treatment is not entirely clear and deeper knowledge is of paramount importance during the SARS-CoV-2 pandemic. Whether risk factors as in the general population or the immune dys-

regulation in the context of the underlying AARD per se and/or the immunomodulatory therapy used predispose to a more severe disease course and hospitalization, has to be elucidated.

Methods: In this observational study, demographic data, AARD related features and comorbidities, COVID-19 manifestations and outcome, as well as antibody responses to SARS-CoV-2 were recorded among 77 AARD patients infected by SARS-CoV-2. We next wished to identify risk factors for COVID-19 severity and subsequent hospitalization Analysis of data was performed using univariate and multivariate models.

Results: The majority of patients (68.8%) experienced a mild COVID-19 course. The predominant symptoms were upper respiratory tract symptoms (68.8%), fatigue (58.4%) and low grade fever (45.4%). One out of four patients required hospitalization (23.3%) and the mortality rate was 1.3%. Regarding COVID-19 severity, prior treatment with corticosteroids, mycophenolate mofetil or rituximab was more common in patients who developed a more serious disease course (60.0 vs 29.9%, p=0.003, 40.0 vs 7.5%, p=0.003, 10.0 vs 0.0%, p=0.009, respectively). Among COVID-19 related features, patients with shortness of breath and high-grade fever were more likely to get hospitalized (OR [95%]: 7.06 [1.36–36.57], 12.04 [2.96–48.86]), while anosmia was independently associated with lower hospitalization risk (OR [95%]: 0.09 [0.01–0.99]). When disease related features and comorbidities were considered in multivariate models, older age and lung disease in the context of the AARD were found to be independent predictive factors for hospitalization (OR [95%]: 1.09 [1.03–1.15] and 6.43 [1.11–37.19]).

Conclusion: Though the majority of AARD patients displayed a mild COVID-19 course, certain AARD related features and COVID-19 related manifestations should prompt alertness for the physician to identify patients with AARD at high risk for severe COVID-19 and need for hospitalization.

Disclosure: C. Mavragani, None; **A. Bakasis**, None; **K. Boki**, None; **A. Tzioufas**, None; **P. Vlachoyiannopoulos**, None; **I. Stergiou**, None; **F. Skopouli**, None; **H. Moutsopoulos**, None.

Abstract Number: 1453

Lung Interleukin-33 Is Elevated in Rheumatoid Arthritis-Associated Lung Disease

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: The alarmin interleukin (IL)-33 is a member of the IL-1 cytokine family that is rapidly released from the nucleus of a variety of lung cells upon cellular damage or xenobiotic (including airborne biohazard) exposures. IL-33 has been implicated in rheumatoid arthritis (RA), where increased levels in sera and synovial fluid correlate with disease activity. Moreover, elevated sera and lung IL-33 occur in idiopathic pulmonary fibrosis, a condition that resembles RA-interstitial lung disease. However, IL-33 levels and its role in the pathogenesis of RA-associated lung disease are not known.

Table 1. Characteristics of RA patients and corresponding lung tissue sample.

#	Sex	Age	Disease	Pathology Report
1	M	59	RA-ILD	Patchy and non-specific foci of subpleural fibrosis, chronic cellular bronchiolitis associated fibrosis and chronic interstitial pneumonitis suggestive of usual interstitial pneumonia
2	M	67	RA-ILD	Organizing diffuse alveolar damage, chronic interstitial pneumonia, and patchy foci of significant interstitial fibrosis with honeycomb change and areas of chronic pleuritis
3	F	62	RA-mild disease	Bronchial mucosa with mild chronic inflammation and eosinophils
4	F	49	RA-ILD	Patchy fibrosis with subpleural, paraseptal and peribronchiolar distribution, bronchiectasis, focal lymphoid aggregates
5	F	49	RA-ILD	Fibrovascular pleural adhesion, mild diffuse interstitial lymphoid hyperplasia, patchy non-specific chronic interstitial pneumonitis, chronic cellular bronchiolitis
6	F	60	RA-nodules	Nodules with diffuse interstitial deposition of eosinophilic extracellular materials with multinucleated giant cells on background of chronic inflammation of plasma cells and lymphocytes.
7	M	51	RA-ILD	Focal areas of pleural fibrosis with necrotizing granuloma with peripheral palisading histiocytes[1]
8	M	65	RA-nodules	Nodules of necrotizing granulomatous inflammation
9	F	42	RA-ILD	Mild ground-glass opacity, mild honeycombing, mild air trapping, features more consistent with usual interstitial pneumonia with fibrosis

[1]Evidence of both RA and RA-nodules.

Methods: Formalin-fixed, paraffin-embedded (FFPE) de-identified human lung sections from patients with RA-lung disease (N=9) and normal "control" (N=7) donors (deemed unsuitable for transplant) were obtained from the local institutional IRB-approved biobanks. An animal model combining the collagen-induced arthritis (CIA) and 5 weeks of repetitive inhalation of lipopolysaccharide (LPS, 100 ng) was utilized to obtain lung sections from 4 groups of DBA/1J mice (N=5/group): 1) Sham (saline injection/saline inhalations); 2) CIA (CIA injections/saline inhalations); 3) LPS (saline injections/LPS inhalations); and 4) CIA+LPS. Sections were stained for human or mouse anti-IL-33 and vimentin. Photographs (10 per lung section per patient/mouse) were taken using a Zeiss fluorescent microscope. Integrated densities (the product of area and mean gray value) of each protein were measured as a single color on black background with color thresholds determined by Image J.

Results: Characteristics of patients with RA-associated lung disease and corresponding lung tissue pathology are summarized in **Table 1**. Lung IL-33 expression was strikingly increased in the lung tissues of patients with RA-associated lung disease (5.7-fold), with lesser, but significant, increases in vimentin staining (1.9-fold) ($p=0.0002$ and $p=0.0033$, respectively) relative to control lung tissues (**Figure 1**). In sensitivity analyses excluding 2 subjects with RA-related pulmonary nodules and 1 subject with mild inflammation, IL-33 and vimentin expression remained significantly elevated ($p < 0.01$ for both). In murine modeling studies, lung IL-33 expression was increased with LPS alone (5.3-fold) and CIA+LPS (5.7-fold) vs. Sham ($p < 0.001$) and vs. CIA alone (3.1-fold and 3.4-fold, respectively, p<

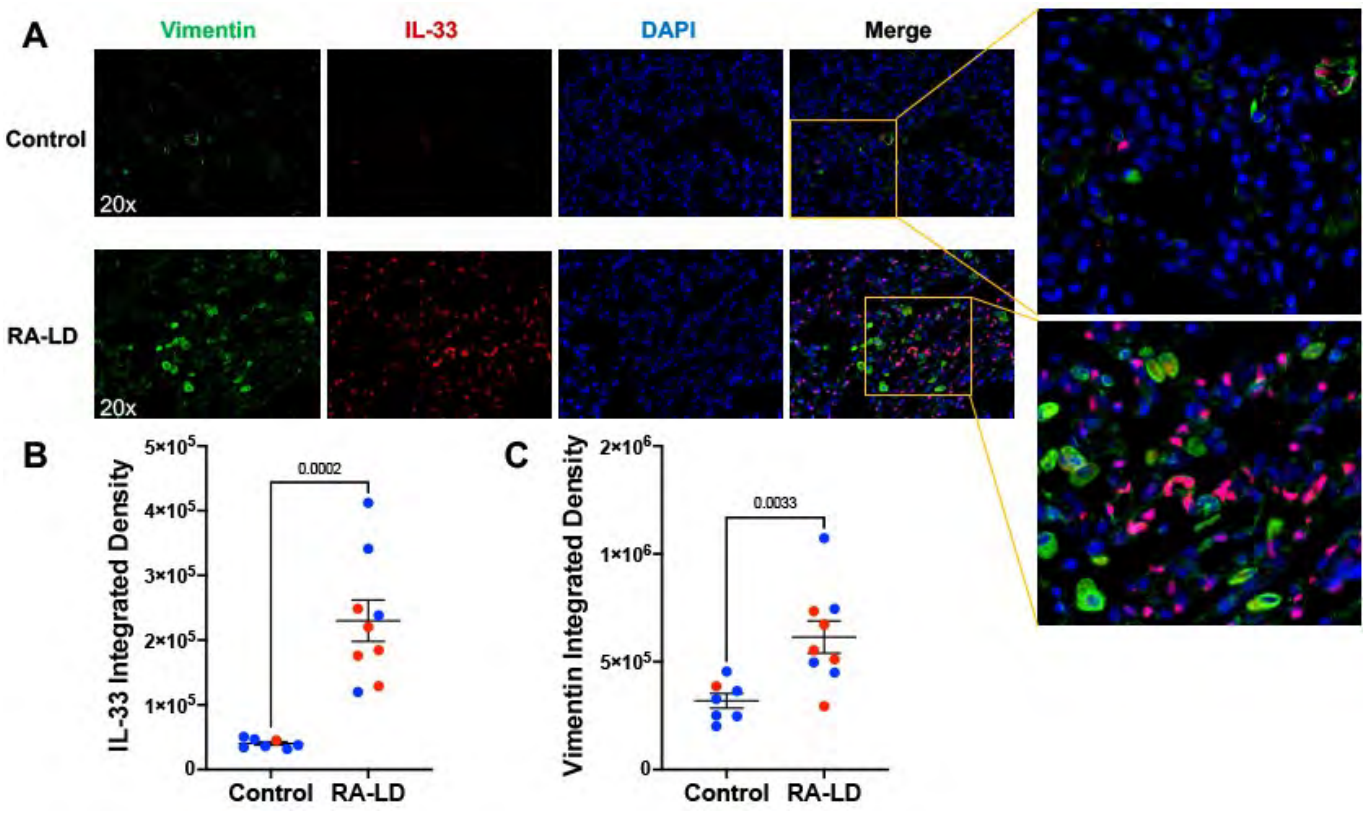

Figure 1. Lung IL-33 and vimentin expression in human tissue sections. Photomicrographs were taken of entire lung section using a Zeiss fluorescent microscope. (A) A representative image of individual and merged stains of IL-33 (red), vimentin (green) and DAPI (blue; nuclei), with a zoomed image of an area from a control subject and patient with RA-LD (RA-associated lung disease). Scatter plots with bar graph for IL-33 (B) and vimentin (C) with p values. Red dots denote females and blue dots denote males in each group.

0.001) with no significant difference between LPS and CIA+LPS (**Figure 2**). Vimentin expression was increased in CIA (2.6-fold, $p< 0.01$), LPS (2.8-fold, $p< 0.05$) and CIA+LPS (3.8-fold, $p< 0.01$) vs. Sham.

Conclusion: This study demonstrates that lung IL-33 expression is increased in patients with RA-associated lung disease. In the combined inhalant LPS+CIA animal modeling studies, lung IL-33 was also elevated, primarily driven by LPS exposure. As clinical studies are underway utilizing anti-IL-33/ST2 pathway antibodies in COPD, this approach could be explored in RA-associated lung disease. Alternatively, IL-33 warrants further investigation as a biomarker to identify patients with RA who are at risk of developing RA-associated lung disease.

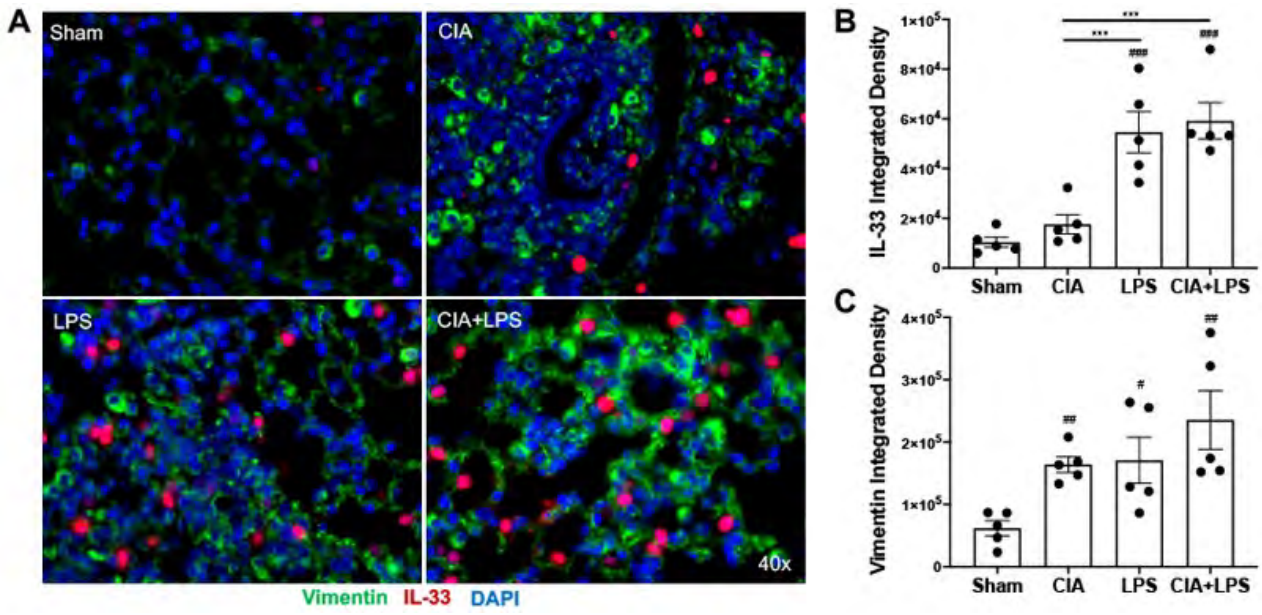

Figure 2. Combined modeling of repetitive lipopolysaccharide (LPS)-induced airway inflammation and collagen-induced arthritis (CIA) demonstrates increases in lung IL-33 expression. Photomicrographs were taken of entire lung section using a Zeiss fluorescent microscope. (A) A representative merged image of all three stains of IL-33 (red), vimentin (green) and DAPI (blue; nuclei) from each murine treatment group. N=5 mice/group. Scatter plots with bar graph for IL-33 (B) and vimentin (C). Statistical differences are shown for treatment groups versus sham (#p<0.05, ##p<0.01, ###p<0.001, ####p<0.0001) and between treatment groups (*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001).

Disclosure: R. Gaurav, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **G. Thiele**, Regeneron, 6; **B. England**, Boehringer-Ingelheim, 2; **M. Wolfe**, None; **K. Bailey**, None; **A. Nelson**, None; **M. Duryee**, None; **D. Romberger**, None; **D. Ascherman**, None; **J. Poole**, None.

Abstract Number: 1454

RHAPSODY: Rilonacept, an IL-1α and IL-1β Trap, Resolves Pericarditis Episodes and Reduces Risk of Recurrence in a Phase 3 Trial of Patients with Recurrent Pericarditis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: Recurrent pericarditis (RP) is an autoinflammatory disease with no FDA-approved therapies. RHAPSODY, a global Phase 3 study, evaluated rilonacept, a once-weekly IL-1α/IL-1β trap, in RP. RHAPSODY data helped support FDA approval of the first therapy for RP.

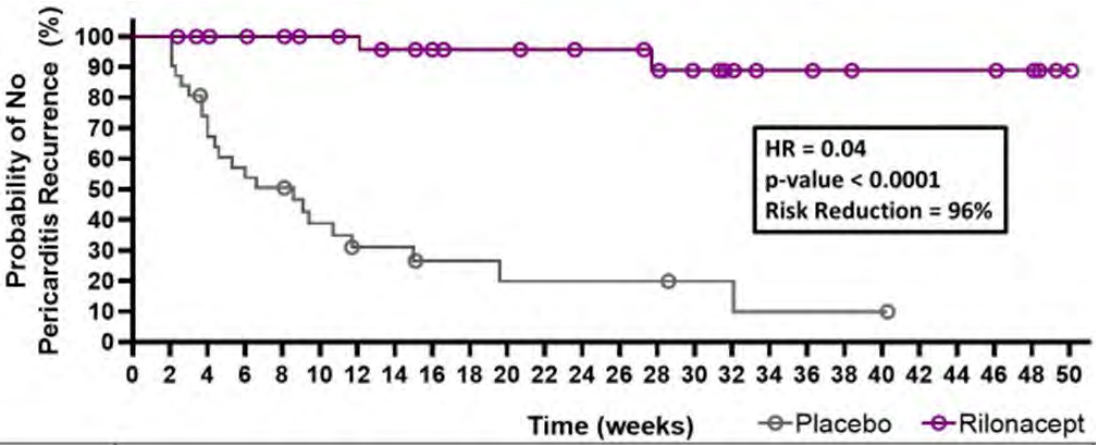
Methods: RHAPSODY was a randomized withdrawal (RW) trial: 86 patients (pts) with acute symptomatic RP, failing standard therapy (NSAIDs, colchicine, and/or corticosteroids [CS]), enrolled in a 12-week single-blind run-in (RI) period: rilonacept (320 mg SC load, 160 mg SC weekly) was administered while background pericarditis medications were discontinued. Clinical responders on rilonacept monotherapy were then randomized 1:1 to placebo or continued rilonacept in an event-driven double-blind RW period. Primary efficacy endpoint: time-to-first adjudicated pericarditis recurrence. Pts experiencing an eligible RP event during RW could receive open-label (OL) bailout rilonacept and remain on study.

Results: Etiology: idiopathic (85%), post-cardiac injury (15%).

Baseline characteristics (mean): disease duration was 2.4 years, with 4.7 lifetime episodes and 4.4 episodes/year.

Qualifying episode: pericarditis medications – NSAIDs (67%), colchicine (80%), and CS (49%). Mean pericarditis pain (11-point NRS scale) was 6.2, and mean C-reactive protein (CRP) was 6.18 mg/dL.

RI: 92% of pts completed RI; medians: time to NRS score ≤2 was 5 days; time to CRP normalization (≤0.5 mg/dL) was 7 days; time to Treatment Response was 5 days; time to monotherapy rilonacept was 7.9 weeks.



	Patients at Risk, n																									Number of Patients with Recurrence* n (%)	Number of Weeks to Recurrence* median (95% CI)
Week	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	
Rilonacept	30	30	28	27	26	24	23	21	20	17	17	16	15	15	13	11	9	7	7	6	5	5	5	5	4	1	2 (6.7)	NE (NE, NE)
Placebo	31	31	22	17	15	10	7	7	4	4	3	3	3	3	3	2	2	1	1	1	1						23 (74.2)	8.6 (4.0, 11.7)

CEC: Clinical Endpoint Committee; NE: not-estimable; HR: hazard ratio;
*First adjudicated pericarditis recurrence

Figure. Time to First CEC-Adjudicated Pericarditis Recurrence.

RW: 25 adjudicated events accrued in 61 randomized pts (Figure). Median time to event: placebo 8.6 wks, rilonacept Not-Estimable due to few events; HR 0.04 (96% risk reduction) ($p < 0.0001$). All 3 major secondary efficacy endpoints (Wk 16) were significant: maintained Clinical Response (rilonacept 81% vs. placebo 20% [p=0.0002]); absent/minimal pericarditis symptoms on 7-point Patient Global Impression of Pericarditis Severity scale (rilonacept 81% vs. placebo 25% [p=0.0006]); % of days with none/minimal pericarditis pain (rilonacept 98% vs. placebo 46% [$p < 0.0001$]).

No subsequent RP events were documented in pts on OL bailout rilonacept. 74 of 75 eligible pts continue OL rilonacept in a long-term extension up to 24 months.

Rilonacept was well-tolerated; 4 discontinuations in RI for AEs; SAEs: rilonacept (n=4), placebo (n=1), none drug-related; 1 withdrawn consent in RW.

Conclusion: Rilonacept (IL-1α/IL-1β trap) provided rapid and sustained reductions in pain and CRP as soon as after the first dose. Rilonacept monotherapy reduced RP event risk by 96% vs placebo. Rilonacept may provide a targeted therapeutic option for patients with RP.

Disclosure: A. Klein, Kiniksa, 1, 5, Sobi, 1, Pfizer, 1; **M. Imazio**, Kiniksa, 1, Sobi, 1; **P. Cremer**, Kiniksa, 5, 12, personal fees, Novartis, 5, Sobi, 12, personal fees; **A. Brucato**, Kiniksa, 12, My institution received funding from Kiniksa as an investigative site to run the study, Sobi, 5, Acarpia, 5; **A. Abbate**, Kiniksa, 5, Olatec, 5, 12, personal fees, Serpin, 5, 12, personal fees, Novartis, 5, 12, personal fees, Novo-Nordisk, 12, personal fees, Cromos Pharma, 12, personal fees, Janssen, 5, 12, personal fees; **F. Fang**, Kiniksa Pharmaceuticals Corp., 3, 11; **A. Insalaco**, None; **M. LeWinter**, Kiniksa, 5, 12, personal fees; **B. Lewis**, Kiniksa, 12, personal fees; **D. Lin**, Regeneron, 12, fees; **S. Luis**, Kiniksa, 1, Sobi, 1, 2, Medtronic, 2; **S. Nicholls**, Kiniksa, 5, 12, personal fees, AstraZeneca, 2, 5, Amgen, 5, Anthera, 2, 5, Eli Lilly, 2, 5, Esperion, 2, 5, Novartis, 5, Cerenis, 5, The Medicines Company, 5, Resverlogix, 2, 5, InfraReDx, 5, Roche, 5, Sanofi-Regeneron, 2, 5, Liposcience, 5, Akcea, 2, Omthera, 2, Merck, 2, Takeda, 2, CSL Behring, 2, Boehringer Ingelheim, 2; **A. Pano**, Kiniksa Pharmaceuticals Corp., 3, 11; **A. Wheeler**, Kiniksa Pharmaceuticals, Ltd., 2; **L. Zou**, Kiniksa Pharmaceuticals Corp., 3, 11; **J. Paolini**, Kiniksa Pharmaceuticals Corp., 2, 10, 11.

Abstract Number: 1455

IL1β mRNA Expressions in Peripheral Blood Mononuclear Cells Increase and May Associate with Cartilage Damage of the Respiratory Tract Probably Through Matrix metalloproteinase-3 Production in Patients with Relapsing Polychondritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: Relapsing polychondritis (RP) is an inflammatory disorder that affects cartilage of ears, nose, joints, and respiratory tract. The inflammation often spreads to eyes, cardiovascular system, inner ears, skin, and CNS. Previous studies of RP disclosed that mononuclear cells migrated into the perichondral tissues and adjacent

chondrocytes produced matrix metalloproteinase (MMP)-3. We found that serum MMP3 concentrations were significantly higher in RP patients, especially in patients with respiratory involvement, than healthy individuals (HI). In the current study, we investigate whether serum MMP3 associate with inflammatory cytokine mRNA expressions of peripheral blood mononuclear cells (PBMC) in RP patients with a focus on the incidence and severity of the complications.

Methods: We obtained sera and PBMC from 30 RP patients and age and gender matched 14 HI. We divided the patients into two subgroups, that is, those with airway involvement (respiratory subgroup, 16 patients) and those without airway involvement (non-respiratory subgroup, 14 patients). We measured mRNA expressions of IL1β, IL6, TNFα, and MMP3, in freshly isolated, 6-hour-cultured, and 24-hour-cultured PBMC. We collected time series data of serum MMP3 and cytokine gene expressions from 6 RP patients (follow-up, mean ± sem., 34 ± 7.0 months) and 6 HI (45 ± 0.2 months).

Results: Inflammatory cytokine mRNA expressions of freshly isolated PBMC were significantly lower in RP patients than those in HI. IL1β and MMP3 mRNA expressions of 24-hour-cultured PBMC were significantly higher in RP patients than those in HI. Serum MMP3 increased significantly in respiratory subgroup compared with those in non-respiratory subgroup. Serum MMP3 and mRNA expressions of IL1β and IL6 showed positive linear correlations in 6-hour- and 24-hour-cultured PBMC of respiratory subgroup, but not those in non-respiratory subgroup. Linear correlations were found between serum MMP3 and PBMC MMP3 mRNA in both respiratory and non-respiratory subgroups. A linear correlation was observed between serum MMP3 and RPDAI in non-respiratory subgroup but not in respiratory subgroup. The time series study suggests that serum MMP3 and IL1β mRNA expressions of 6-hour-cultured PBMC were higher in RP patients than those in HI at least for several years (39 ± 3.7 months).

Conclusion: It is possible that IL1β has a potential to induce efficiently immune responses of RP cartilaginous tissues in the airway tract using MMP3. RPDAI may be more sensitive for the evaluation of disease status in non-respiratory subgroup than that in respiratory subgroup. RP PBMC may have a characteristic for persisting their dysregulated immune responses for a long time.

Disclosure: J. Shimizu, None; **S. Wakisaka**, None; **T. Suzuki**, None; **N. Suzuki**, None.

Abstract Number: 1456

Cannabidiol Treatment in Hand Osteoarthritis and Psoriatic Arthritis - A Randomized, Double-blind Placebo-controlled Trial

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: Medical cannabis is increasing in popularity yet the recent International Association for the Study of Pain presidential task force on cannabis and cannabinoid analgesia found a lack of trials examining canna-

bidiol (CBD) for pain management. We examined CBD as add on analgesic therapy in patients with hand osteoarthritis or psoriatic arthritis.

Methods: Our trial was randomized double-blind and placebo-controlled. Patients received synthetic CBD 20-30mg or placebo daily for 12 weeks. Primary outcome was pain intensity during the last 24 hours (0-100mm); safety outcomes were percentage of patients experiencing adverse events and a characterization of serious adverse events. Exploratory outcomes included change in Pittsburgh Sleep Quality Index (PSQI), Hospital Anxiety and Depression Scale (HADS), Pain Catastrophizing Scale (PCS) and Health Assessment Questionnaire (HAQ-DI)

Results: We recruited and randomized one hundred and thirty-six patients and 129 were included in the primary analysis. Between group difference in pain intensity at 12 weeks was 0.23mm (95%CI -9.41 to 9.90; p = 0.96). 22% patients receiving CBD and 21% receiving placebo experienced a reduction in pain intensity ≥ 30mm p=1. Between group difference for exploratory outcomes: HAQ-DI 0.03 (95%CI-0.11 to 0.18), PSQI -0.71 (95%CI -1.99 to 0.55), HADS depression -0.04 (95%CI -0.79 to 0.70), HADS anxiety -0.69 (95%CI -0.41 to 2.75) and PCS 1.07 (95%CI -1.73 to 3.88)

Conclusion: We found no statistically significant effect of CBD for clinical pain intensity in patients with hand osteoarthritis and psoriatic arthritis compared to placebo and no statistically significant effects regarding sleep quality, scores of depression, anxiety or pain catastrophizing.

Disclosure: J. Vela, None; **S. Kristensen**, None; **L. Dreyer**, BMS, 5, Galderma, 6, Eli Lilly, 6, Janssen, 6; **K. Kjær Petersen**, None; **L. Arendt Nielsen**, None.

Abstract Number: 1457

Clinical Heterogeneity of the VEXAS Syndrome: A Case Series

Matthew Koster[1], Taxiarchis Kourelis[1], Kaaren Reichard[1], Tanaz Kermani[2], David Beck[3], Daniela Ospina Cardona[4], Matthew Samec[1], Abhishek Mangaonkar[1], Kebede Begna[1], Christopher Hook[1], Jennifer Oliveira[1], Samih Nasr[1], Benedict Tiong[5], Mrinal Patnaik[1], Michelle Burke[1], Clement Michet[1] and Kenneth Warrington[6], [1]Mayo Clinic, Rochester, MN, [2]University of California Los Angeles, West Hills, CA, [3]National Institutes of Health, Bethesda, MD, [4]National Institutes of Health, Germantown, MD, [5]University of California Los Angeles Medical Center, Culver City, CA, [6]Mayo Clinic, Rochester, Minnesota

SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: Miscellaneous Rheumatic & Inflammatory Diseases: New Insights into Therapies & Mechanisms of Disease (1452–1457)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome is a recently described myeloid-driven autoinflammatory condition caused by somatic mutations affecting methionine-41 (p.Met41) in the UBA1 gene which encodes the major E1 enzyme which initiates ubiquitylation.[1] The purpose of this study was to describe a series of cases highlighting the clinical features and outcomes of patients with this condition.

Methods: The divisions of rheumatology and hematology at Mayo Clinic, Rochester, Minnesota and the rheumatology division of the University of California, Los Angeles, (UCLA) identified all patients who underwent testing for UBA1 somatic mutations. The National Institutes of Health (NIH) performed testing for somatic mutations of the UBA1 gene, using methods previously described.[1] No patient included in this study was part of the original NIH cohort.[1] Demo-

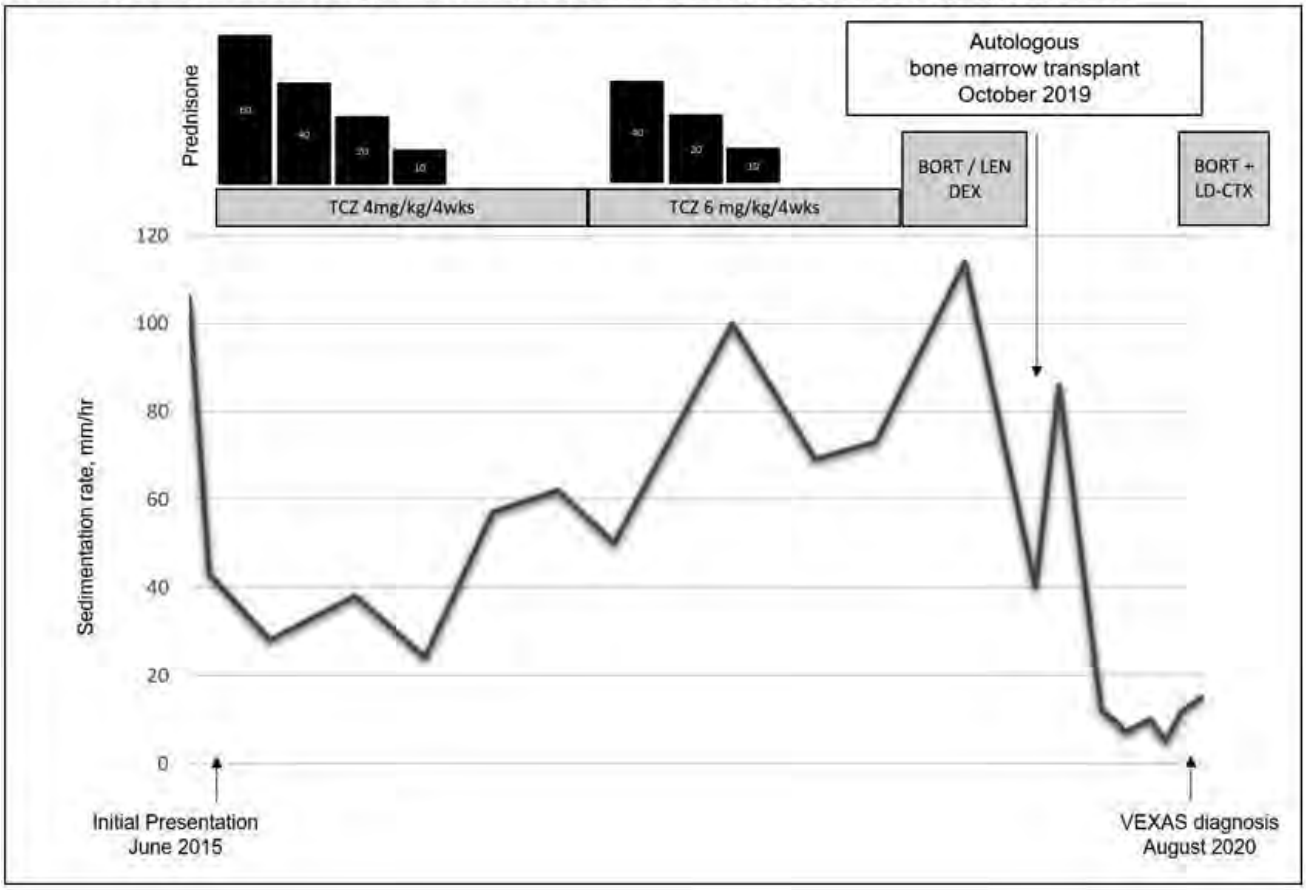
Table 1: Characteristics of patients with VEXAS

Patient	Male	Age Sx / Dx / Death	UBA1 Variant p.Met41	Variant allele frequency*	Const. Sx	Vasculitis*	Ear/nose chondritis	Ocular** inflammation	Inflammatory arthritis	DVT	Macrocytic Anemia	Bone marrow vacuoles	GCs	Coexisting hematologic disorder	Disease modifying agents
1	+	73 / 80 / 80	Val	79.99	+				+		+	+	+		MTX, AZA, MMF, DEC
2	+	70 / 76	Leu	8.98*	+				+		+	+	+	Multiple Myeloma	ANA, TCZ, BORT/LEN/DEX, ASCT, BORT+LD-CTX
3	+	57 / 63	Thr	83.35	+		+	+	+		+	+	+		MTX, MMF, RTX, TCZ, DEC, CYC
4	+	70 / 74	Thr	0.25*	+	+		+	+		+	+	+		RTX, MMF, IFX, TCZ, TOFA, DEC
5	+	72 / 74 / 74	Thr	82.40	+		+	+		+	+	+	+		MTX
6	+	75.5 / 77	Thr	59.76			+	+	+		+	+	+		IFX, TCZ
7	+	66 / 69	Thr	80.43	+	+	+			+	+	N/A	+		MTX, ADA, DAP, TCZ
8	+	64 / 65	Thr	39.61	+	+	+			+	+	+	+	Myelodysplastic syndrome	MTX
9	+	68 / 69	Thr	72.74	+	+				+	+	+	+		MTX
Total N (%) or median (IQR)	9 (100)	70 (65, 72.5) / 74 (67, 76.5)	9 (100)	—	8 (88)	4 (44)	5 (55)	4 (44)	5 (55)	4 (44)	9 (100)	8/8 (100)	9 (100)		

ADA, adalimumab; ANA, anakinra; ASCT, autologous stem cell transplant; AZA, azathioprine; BORT/LEN/DEX, combination treatment with bortezomib/lenalidomide/dexamethasone; Const. Sx, constitutional symptoms (fever, chills, night sweats, weight loss); CYC, cyclosporin; DAP, dapsone; DEC, decitabine; DEX, dexamethasone; DVT, deep vein thrombosis; Dx, diagnosis (VEXAS); GC, glucocorticoids; IFX, infliximab; LD-CTX, low-dose cyclophosphamide MMF, mycophenolate; MTX methotrexate; RTX, rituximab; Sx, symptom onset (VEXAS) TCZ, tocilizumab; TOFA, tofacitinib. *Vasculitis (cutaneous vasculitis patients 4, 7, 8, 9, large-vessel arterial occlusions in patient 9 and renal peritubular capillaritis with low titer positive proteinase 3 antibody in patient 4). **Uveitis (n=2), Episcleritis (n=2). Patient 7 declined bone marrow biopsy.
*Testing for VEXAS was performed in patient 2 following bone marrow transplant and in patient 4 while on hypomethylating agent resulting in lower mutational burden levels with reduced observed variant allele frequencies

Figure 1

Timing of inflammatory response and treatment in patient #2 with VEXAS syndrome undergoing autologous stem cell transplant. TCZ: tocilizumab; BORT, bortezomib; LEN, lenalidomide; DEX, dexamethasone; LD-CTX, low-dose cyclophosphamide.



Pre and Post transplant inflammatory response in patient #2.

graphic information, clinical characteristics, peripheral blood and bone marrow biopsy findings, treatment regimens and outcome were abstracted from direct medical chart review. Continuous data are presented as mean ± standard deviation (SD) or median [interquartile range (IQR) (25th percentile, 75th percentile)] and categorical variables as percentages.

Results: Nine men with somatic mutations in the *UBA1* gene were identified. Clinical features are noted in Table 1. The most frequent variant was p.Met41Thr (7/9, 78%). The median age at VEXAS diagnosis was 74 (67, 76.5) years, and patients had a median duration of symptoms for 4 years prior to diagnosis. Refractory constitutional symptoms (88%), ear/nose chondritis (55%) and inflammatory arthritis (55%) were common clinical features. Vasculitis was noted in four patients (44%). All four patients had cutaneous vasculitis, but additionally one (#4) had evidence of renal peri-tubular capillaritis, one (#8) had type III cryoglobulinemia with digital gangrene and one (#9) had large-vessel vasculitis. All patients had significantly elevated inflammatory markers and macrocytic anemia. Thrombocytopenia was present in 66% at VEXAS diagnosis. Eight patients had bone marrow biopsies performed. All bone marrows were hypercellular and there was vacuolization of the erythroid (100%) and/or myeloid precursors (75%). Glucocorticoids attenuated symptoms at doses ≥ 20 mg/day but no other immunosuppressive agent showed consistent long-term disease control. One patient with co-existing plasma cell myeloma received plasma cell directed therapy (bortezomib, lenalidomide, dexamethasone induction therapy) followed by autologous stem cell transplant resulting in improvement of the inflammatory response, which is a novel finding (Figure 1).

Conclusion: VEXAS syndrome is a clinically heterogenous, treatment-refractory inflammatory condition caused by somatic mutation of the *UBA1* gene. Patients present with overlapping rheumatologic manifestations and persistent hematologic abnormalities. Optimal treatment regimens remain to be defined. The utility of bone marrow transplantation requires further investigation.

References: [1]Beck DB, Ferrada KA, Sikora KA, *et al*. Somatic Mutations in UBA1 and Severe Adult-Onset Autoinflammatory Disease. NEJM 220;383:2628-28.

Disclosure: M. Koster, None; **T. Kourelis**, None; **K. Reichard**, None; **T. Kermani**, None; **D. Beck**, None; **D. Ospina Cardona**, None; **M. Samec**, None; **A. Mangaonkar**, None; **K. Begna**, None; **C. Hook**, None; **J. Oliveira**, None; **S. Nasr**, None; **B. Tiong**, None; **M. Patnaik**, None; **M. Burke**, None; **C. Michet**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5.

Abstract Number: 1458

Sustained Efficacy and Safety of Iberdomide to Week 52 in Patients with Active Systemic Lupus Erythematosus (SLE) in a Phase 2, Randomized, Placebo-Controlled Study

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: SLE – Treatment: New Agents, Old Agents (1458–1463)

Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: We previously reported 24-wk results of a phase 2b trial of iberdomide, a high-affinity cereblon ligand that promotes proteasomal degradation of Ikaros (*IKZF1)* and Aiolos (*IKZF3*), 2 key transcription factors linked to SLE. The study (NCT03161483) met its primary endpoint at wk 24.[1] Results through wk 52 are reported here.

Methods: Adults (N=288) with autoantibody-positive SLE and SLEDAI 2K scores ≥6 were randomized (2:2:1:2) to oral iberdomide (0.45, 0.3, 0.15 mg) or placebo (PBO) daily, added to background lupus therapy. At wk 24, patients (pts) on PBO were re-randomized to iberdomide 0.3 or 0.45 mg, while pts on iberdomide continued their original regimens. Efficacy analyses were based on the intent-to-treat population, including all pts who were randomized at wk 0 and received ≥1 dose of study drug.

Results: 214 (87.0%) pts completed 52 wks. As previously reported, the primary endpoint, SRI-4 response at wk 24, was achieved by 54.3% of pts on iberdomide 0.45 mg vs. 34.9% on PBO (stratified difference, 19.4%; *P*=0.011). At wk 52, the proportions of SRI-4 responders were sustained or improved in all groups originally randomized to iberdomide: 0.45 mg (wk 24: 54.3% vs. wk 52: 51.9%), 0.3 mg (40.2% vs. 52.4%), and 0.15 mg (47.6% vs. 50.0%)

Table 1. Primary and Secondary Efficacy Outcomes at Week 24 and Week 52 (Non-responder Imputation)

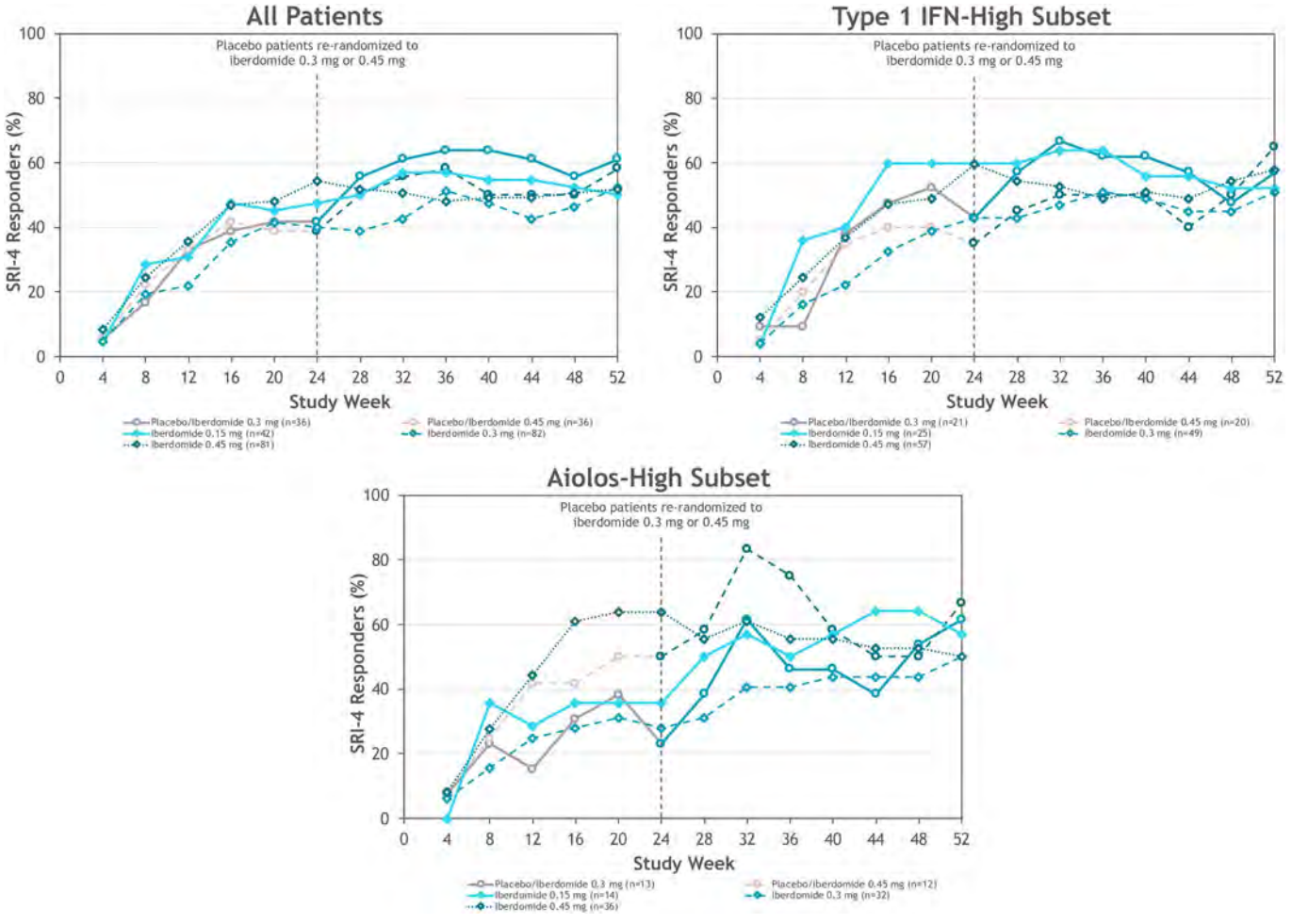
Outcome, n/N (%)	Placebo/Iberdomide 0.3 mg QD (N=36)	Placebo/Iberdomide 0.45 mg QD (N=36)	Iberdomide 0.15 mg QD (N=42)	Iberdomide 0.3 mg QD (N=82)	Iberdomide 0.45 mg QD (N=81)
ITT population					
SRI-4					
Week 24	15/36 (41.7)	14/36 (38.9)	20/42 (47.6)	33/82 (40.2)	44/81 (54.3)
Week 52	22/36 (61.1)	21/36 (58.3)	21/42 (50.0)	43/82 (52.4)	42/81 (51.9)
SRI-6					
Week 24	10/35 (28.6)	7/36 (19.4)	14/42 (33.3)	21/82 (25.6)	29/81 (35.8)
Week 52	15/35 (42.9)	13/36 (36.1)	14/42 (33.3)	29/82 (35.4)	30/81 (37.0)
S2K ≥4-pt improvement from BL					
Week 24	16/36 (44.4)	14/36 (38.9)	20/42 (47.6)	35/82 (42.7)	45/81 (55.6)
Week 52	23/36 (63.9)	21/36 (58.3)	21/42 (50.0)	43/82 (52.4)	43/81 (53.1)
BICLA					
Week 24	13/32 (40.6)	11/26 (42.3)	13/35 (37.1)	20/60 (33.3)	22/59 (37.3)
Week 52	16/32 (50.0)	11/26 (42.3)	15/35 (42.9)	26/60 (43.3)	27/59 (45.8)
PGA (change <0.3 from BL)					
Week 24	31/36 (86.1)	34/36 (94.4)	38/42 (90.5)	60/82 (73.2)	69/81 (85.2)
Week 52	28/36 (77.8)	30/36 (83.3)	31/42 (73.8)	56/82 (68.3)	58/81 (71.6)
FACIT Fatigue, adjusted mean CFB, (95% CI)[a]					
Week 24	4.2 (1.0, 7.4)	3.6 (0.6, 6.7)	2.6 (-0.3, 5.5)	3.1 (0.9, 5.4)	5.1 (3.0, 7.3)
Week 52	5.4 (2.2, 8.6)	4.9 (1.7, 8.0)	3.7 (0.7, 6.8)	4.9 (2.7, 7.2)	8.3 (6.0, 10.5)
CLASI-A, adjusted mean CFB (95% CI) (CLASI ≥8 at BL)[a]					
Week 24	-8.2 (-11.8, -4.7)	-11.0 (-14.1, -7.9)	-9.3 (-11.9, -6.6)	-10.1 (-12.2, -8.0)	-10.5 (-12.4, -8.6)
Week 52	-10.6 (-15.0, -6.3)	-10.4 (-14.3, -6.4)	-12.0 (-15.0, -8.9)	-10.8 (-13.1, -8.4)	-10.3 (-12.6, -8.1)
CLASI-50 (CLASI ≥8 at BL)					
Week 24	4/7 (57.1)	6/9 (66.7)	8/13 (61.5)	13/24 (54.2)	16/24 (66.7)
Week 52	3/7 (42.9)	5/9 (55.6)	10/13 (76.9)	14/24 (58.3)	11/24 (45.8)
SJC, adjusted mean CFB (95% CI) (SJC ≥6 at BL)[a]					
Week 24	-8.9 (-10.2, -7.6)	-9.5 (-10.9, -8.2)	-7.9 (-9.3, -6.5)	-7.8 (-8.8, -6.7)	-8.7 (-9.7, -7.6)
Week 52	-9.6 (-10.3, -8.8)	-9.9 (-10.7, -9.2)	-9.5 (-10.3, -8.8)	-9.5 (-10.1, -8.9)	-9.1 (-9.8, -8.4)
TJC, adjusted mean CFB (95% CI) (TJC ≥6 at BL)[a]					
Week 24	-7.8 (-10.2, -5.5)	-8.7 (-11.1, -6.4)	-5.9 (-8.3, -3.5)	-6.5 (-8.3, -4.8)	-8.3 (-10.0, -6.5)
Week 52	-9.2 (-11.1, -7.3)	-10.0 (-12.0, -8.1)	-8.8 (-10.7, -6.9)	-9.6 (-11.0, -8.1)	-9.3 (-10.8, -7.9)
Aiolos-High Subgroup					
SRI-4					
Week 24	3/13 (23.1)	6/12 (50.0)	5/14 (35.7)	9/32 (28.1)	23/36 (63.9)
Week 52	8/13 (61.5)	8/12 (66.7)	8/14 (57.1)	16/32 (50.0)	18/36 (50.0)
Type 1 IFN-High Subgroup					
SRI-4					
Week 24	9/21 (42.9)	7/20 (35.0)	15/25 (60.0)	21/49 (42.9)	34/57 (59.6)
Week 52	12/21 (57.1)	13/20 (65.0)	13/25 (52.0)	25/49 (51.0)	33/57 (57.9)

[a]Observed cases. BICLA, BILAG-based Combined Lupus Assessment; BILAG, British Isles Lupus Assessment Group; BL, baseline; CFB, change from baseline; CI, confidence interval; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-50, ≥50% improvement in CLASI score; FACIT, Functional Assessment of Chronic Illness Therapy; IFN, interferon; ITT, intent to treat; PGA, Physician's Global Assessment; QD, once daily; SJC, swollen joint count; S2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SRI, SLE Responder Index; TJC, tender joint count

Table 2. Treatment-Emergent Adverse Events

TEAE, n/N (%)/ EAIR[a]	Placebo	Iberdomide 0.15 mg QD	Iberdomide 0.3 mg QD	Iberdomide 0.45 mg QD	Total Iberdomide
Any TEAE					
Weeks 0-24	54/83 (65.1)/ 289.2	31/42 (73.8)/ 324.4	64/82 (78.0)/ 399.5	63/81 (77.8)/ 427.2	158/205 (77.1)/ 391.8
Weeks 0-52	-	34/42 (81.0)/ 233.5	88/117 (75.2)/ 264.5	97/117 (82.9)/ 313.6	219/276 (79.3)/ 278.1
Drug-related TEAE					
Weeks 0-24	24/83 (28.9)/ 80.8	14/42 (33.3)/ 101.8	36/82 (43.9)/ 150.9	32/81 (39.5)/ 122.0	82/205 (40.0)/ 128.4
Weeks 0-52	-	18/42 (42.9)/ 63.8	48/117 (41.0)/ 80.2	50/117 (42.7)/ 77.9	116/276 (42.0)/ 76.2
Serious TEAE					
Weeks 0-24	7/83 (8.4)/ 20.0	3/42 (7.1)/ 16.5	4/82 (4.9)/ 12.4	6/81 (7.4)/ 17.5	13/205 (6.3)/ 15.3
Weeks 0-52	-	4/42 (9.5)/ 10.9	10/117 (8.5)/ 12.2	12/117 (10.3)/ 14.0	26/276 (9.4)/ 12.7
Severe TEAE					
Weeks 0-24	5/83 (6.0)/ 14.1	3/42 (7.1)/16.5	4/82 (4.9)/ 12.4	1/81 (1.2)/2.8	8/205 (3.9)/ 9.3
Weeks 0-52	-	3/42 (7.1)/ 8.0	8/117 (6.8)/ 9.7	3/117 (2.6)/ 3.4	14/276 (5.1)/ 6.7
TEAE leading to drug interruption					
Weeks 0-24	15/83 (18.1)/ 45.6	10/42 (23.8)/ 62.6	14/82 (17.1)/ 48.2	23/81 (28.4)/ 77.8	47/205 (22.9)/ 63.0
Weeks 0-52	-	15/42 (35.7)/ 48.8	22/117 (18.8)/ 30.1	37/117 (31.6)/ 51.6	74/276 (26.8)/ 42.2
TEAE leading to drug withdrawal					
Weeks 0-24	6/83 (7.2)/ 16.8	2/42 (4.8)/ 11.0	11/82 (13.4)/ 35.0	4/81 (4.9)/ 11.5	17/205 (8.3)/ 20.1
Weeks 0-52	-	4/42 (9.5)/ 10.5	13/117 (11.1)/ 15.6	9/117 (7.7)/ 10.1	26/276 (9.4)/ 12.3
TEAE leading to death					
Weeks 0-24	1/83 (1.2)/ 2.8[b]	0	0	0	0
Weeks 0-52	-	0	1/117 (0.9)/ 1.2[c]	0	1/276 (0.4)/ 0.5

[a]EAIR per 100 person-years is 100 times the number of patients with the specific event divided by the total time (in years) at risk.
[b]1 patient on placebo had a pulmonary thromboembolism at week 8.
[c]1 patient on iberdomide 0.3 mg had a sudden cardiac death at week 44.
EAIR, exposure-adjusted incidence rate; QD, once daily; TEAE, treatment-emergent adverse event.



(**Figure**). Of wk 24 SRI-4 responders, response was maintained at ≥70% of the visits through wk 52 by 75.0%, 81.8%, and 70.0% in the 0.45-mg, 0.3-mg, and 0.15-mg groups. Increased proportions of pts attained SRI-4 response after switching from PBO to 0.3 mg (41.7% vs. 61.1%) or from PBO to 0.45 mg (38.9% vs. 58.3%) (**Figure**). In the iberdomide 0.3-mg group and the 2 PBO switching groups, improvements in the proportions meeting SRI-6 and ≥4-point decrease in SLEDAI-2K at wk 52 were observed (**Table 1**). In pts originally randomized to iberdomide, there were trends of increased BICLA responses and improved swollen/tender joint counts at wk 52 (**Table 1**). In the 0.3-mg and 0.45-mg groups, the enhanced SRI-4 responses at wk 24 in the prespecified subsets of pts with Type 1 IFN high signatures at baseline were similar or improved at wk 52 and also achieved by pts switching from PBO to iberdomide (**Figure** and **Table 1**). In Aiolos-high pts at baseline, enhanced responses were observed at wk 52 in the 0.15-mg and 0.3-mg groups and PBO switching groups, but response rates were not sustained in the 0.45-mg group. There were no increases in exposure-adjusted incidence of treatment-emergent adverse events (TEAEs), TEAEs leading to drug interruption or withdrawal, or serious AEs (SAEs) (**Table 2**). Most TEAEs were mild to moderate in severity, the most common being urinary tract infection (14.9%), upper respiratory tract infection (11.2%), and neutropenia (9.8%). Neutropenia was reversible and rarely led to discontinuation (1.4%). One pt on iberdomide (0.3 mg) had an SAE of varicella zoster pneumonia with full recovery.

Conclusion: Iberdomide treatment of pts with SLE was associated with sustained clinical benefits in multiple measures of disease activity up to wk 52. Enhanced clinical responses in pts with IFN-high and Aiolos-high signatures were also observed at 52 wks. Iberdomide was well tolerated with safety data consistent with that reported at wk 24.

Reference

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Abstract Number: 1459

Attainment of the Lupus Low Disease Activity State in Response to Anifrolumab in 2 Phase 3 Trials

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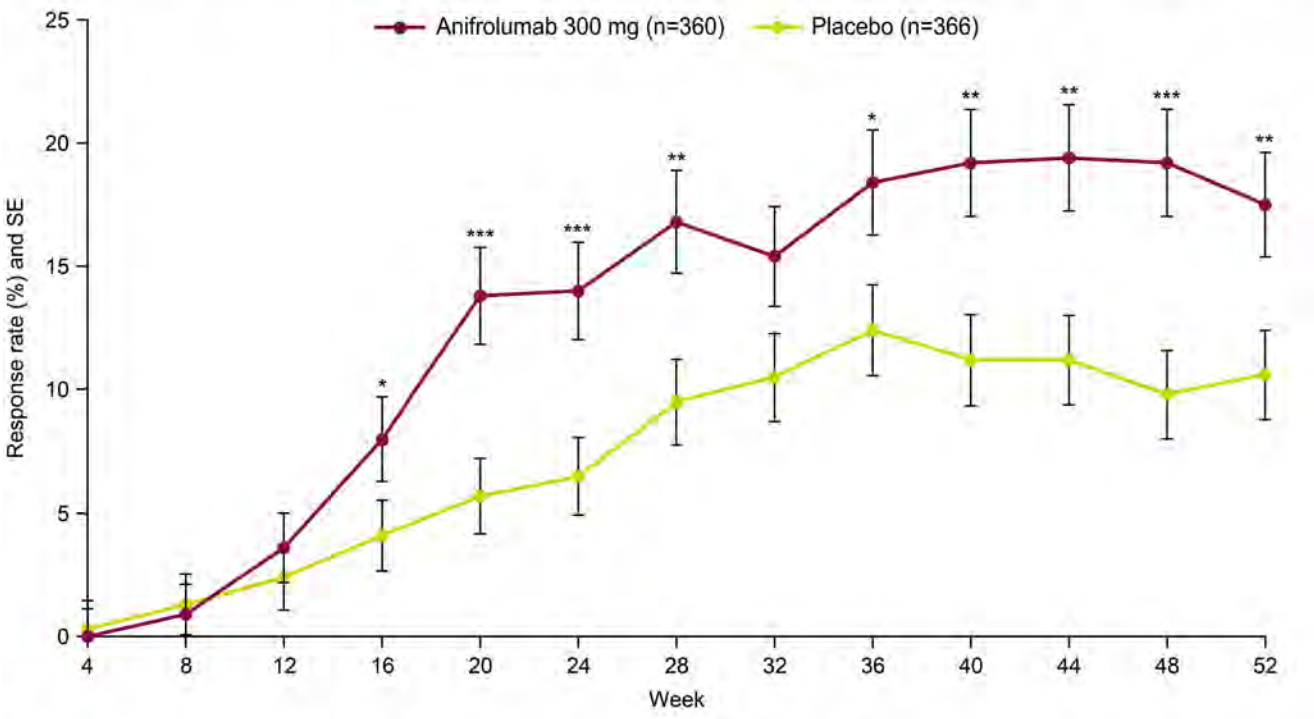
SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: SLE – Treatment: New Agents, Old Agents (1458–1463)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: The Lupus Low Disease Activity State (LLDAS), a treat-to-target (T2T) endpoint for SLE, is prospectively validated as protective from flares and damage accrual.[1] LLDAS attainment is therefore an SLE treatment goal, and was achieved more frequently with active treatment than placebo in 2 SLE phase 2 trials.[2,3] In the TULIP-2 (NCT02446899) phase 3 trial, efficacy of anifrolumab, a type I IFN receptor mAb, was demonstrated using the BILAG–based Combined Lupus Assessment (BICLA) response, and these findings were supported in TULIP-1 (NCT02446912).[4,5] We investigated if anifrolumab treatment was associated with increased LLDAS attainment in pooled TULIP data.

Methods: TULIP-1/2 were randomized, placebo-controlled, 52-week trials of IV anifrolumab (Q4W, 48 weeks) in eligible patients meeting ACR 1997 criteria for SLE with moderate to severe SLE despite standard therapy. Pooled data for the anifrolumab 300 mg and placebo groups were analyzed by time point for LLDAS attainment (defined as all of the following: SLEDAI-2K ≤4 without major organ activity, no new disease activity, Physician's Global Assessment [0–3] ≤1, prednisone or equivalent ≤7.5 mg/day, and well-tolerated standard immunosuppressant dosing[6]). Time to first LLDAS attainment was compared between treatment groups using Cox regression, cumulative time in LLDAS was compared using a Cochran–Mantel–Haenszel approach, and responses were compared using logistic regression. All P-values are nominal.

Results: In an analysis agnostic to treatment group, 114 (13.9%) patients attained LLDAS at Week 52. Of these patients, 102 (89.5%) were also BICLA responders (analysis included the TULIP-1 anifrolumab 150 mg group). Among the 318 BICLA responders at Week 52, 102 (32.0%) attained LLDAS. LLDAS attainment increased across the 52-week trial and was attained earlier with anifrolumab 300 mg than placebo (Figure) (time to first LLDAS, HR 1.76, 95% CI 1.35–2.30, *P*< 0.001). At Week 52, 17.5% of anifrolumab-treated and 10.6% of placebo patients were in LLDAS (OR 1.8, 95% CI 1.2–2.8, P=0.008). More cumulative time (*P*< 0.001) and percentage of time (P < 0.001) was spent

Figure. LLDAS Response Rate by Randomized Treatment in Patients With SLE in the TULIP-1 and TULIP-2 Trials



CMH, Cochran–Mantel–Haenszel; LLDAS, Lupus Low Disease Activity State; SE, standard error.
Responder rates were calculated using a stratified CMH approach, with stratification factors of SLEDAI-2K at screening, Day 1 glucocorticoid dosage, type I IFN gene signature at screening, and study. Nominal *P*-values were calculated using logistic regression with the same factors as for the CMH approach.
*Nominal *P*<0.05; **nominal *P*<0.01; ***nominal *P*<0.001.

in LLDAS by patients receiving anifrolumab than placebo, and cumulative time in LLDAS thresholds of ≥20% (OR 1.8, 95% CI 1.2–2.7, *P*=0.004) and ≥50% (OR 1.9, 95% CI 1.0–3.4, P=0.035) also favored anifrolumab. Anifrolumab-treated patients were more likely to be in sustained LLDAS for ≥3 consecutive visits (18.6% vs 12.5%, OR 1.6, 95% CI 1.1–2.4, *P*=0.024), ≥5 consecutive visits (11.2% vs 7.7%, OR 1.5, 95% CI 0.9–2.6, *P*=0.106), or ≥7 consecutive visits (6.8% vs 2.7%, OR 2.6, 95% CI 1.2–5.6, *P*=0.014).

Conclusion: LLDAS is an attainable T2T endpoint in SLE clinical trials. LLDAS is more stringent than BICLA, but LLDAS attainment is highly coincident with BICLA response. Anifrolumab treatment was associated with earlier, more frequent, more prolonged, and more sustained LLDAS attainment.

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Disclosure: E. Morand, GlaxoSmithKline, 2, 5, 6, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **G. Abreu**, AstraZeneca, 3; **R. Furie**, AstraZeneca, 2; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1460

Lupus Nephritis Renal Responses in Relation to Treatment and Demographics: Observations from a Multi-racial/ethnic Cohort of 159 Patients in the NYU Lupus Registry

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: SLE – Treatment: New Agents, Old Agents (1458–1463)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Lupus nephritis (LN) disproportionately affects racial and ethnic populations. Contreras reported African-American (AA) and Hispanic patients had worse outcomes as compared to patients of European ancestry. ALMS highlighted different responses finding that AA and Hispanics had better response rates with MMF than with cyclophosphamide (CYC) (p=0.033). Reports from Asian nations describe high response rates especially with MMF regimens. The purpose of our study is to determine response rates in relation to treatment and demographics

Methods: Retrospective review of NYU Lupus registry. Patients met ACR/SLICC criteria for LN, had at least one episode of proteinuria (>500 mg spot or 24-hour uPCR), and LN flare after 2012 Epic implementation. Demographics, uPCR, Creatinine (Cr), albumin, C3, C4, anti-DNA levels collected at 0, 12, 24, 52, and 104 weeks for de novo epi-

Table 1. Demographics

TOTAL (N = 159)	Number of patients (%)
RACE	
African ancestry	51 (32%)
Asian ancestry	34 (21%)
European ancestry	74 (47%)
ETHNICITY	
Non-Hispanic	100 (63%)
Hispanic	59 (37%)
GENDER	
Female	138 (87%)
Male	21 (13%)

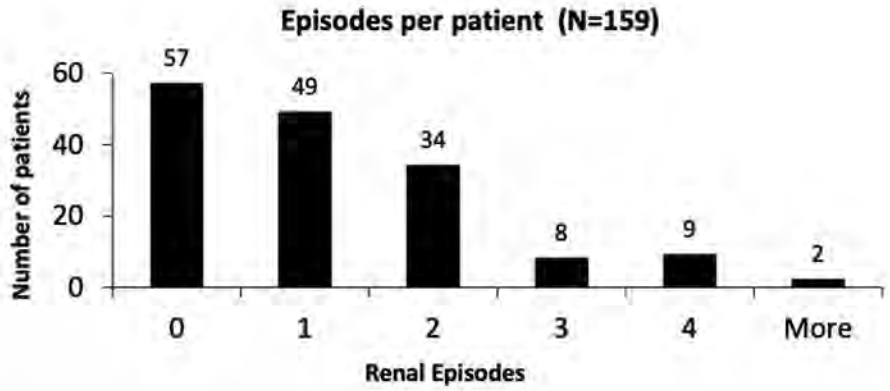

TABLE 1 describes the demographics of the patient population. The graph below is a histogram describing renal episodes per patient. Of the 159 patients, 57 patients only had a de novo episode labeled as 0 on the X-axis. 49 patients had 1 flare, 34 patients had 2 flares, 8 patients had 3 flares, 9 patients had 4 flares, 1 patient had 5 flares, and 1 patient had 6 flares.

sodes and renal flares. De novo episode defined as first episode leading to biopsy followed by change in medication or a clinical note documenting new onset LN accompanied by a change in medication. A renal flare was defined as a prior de novo episode and 1 of 3 conditions: biopsy, episode with change in proteinuria by at least 50%, or a note documenting a renal flare with each scenario required medication change. Responses are complete uPCR $\leq$ 0.5, satisfactory uPCR $\leq$ 0.7, or partial uPCR at least < 50% from baseline and in all 3 cases Cr unchanged or increased < 20%. No response uPCR more than 50% from baseline. Treatment regimens included MMF, CYC, MMF/tacrolimus, RTX, or other. Univariate analysis chi-squared test used to assess for differences in responses by treatment. Multivariable logistic regression (MR) analysis used to assess for differences in responses by gender, race, and ethnicity.

Results: 159 patients with de novo episodes, 188 flare episodes:138(87%) female, 74(47%) European, 51(32%) AA, 34(21%) Asian & Hispanic 59(37%) (Table 1A-B). There was a statistical difference (p= 0.003) in responses by treatment for de novo episodes at 104 weeks, favoring MMF or CYC as opposed to MMF/tacrolimus or RTX/CYC (Fig 1A).

FIGURE 1A. Statistically significant difference in renal response by treatment for 104 Week De Novo Episodes

	Total (N= 55)	Response (N = 44)	No Response (N = 11)	P value
TREATMENT				0.003
MMF	37	30 (81.1%)	7 (18.9%)	
MMF/Tacrolimus	2	1 (50%)	1 (50%)	
CYC	6	6 (100%)	0 (0%)	
RTX/CYC	3	0 (0%)	3 (100%)	
Other	7	7 (100%)	0 (0 %)	

FIGURE 1B. No significant difference in renal responses by treatment for 24-week flares

	Total (N= 145)	Response (N = 74)	No Response (N = 71)	P value
TREATMENT				0.281
MMF	50	26 (52%)	24 (48%)	
MMF/Tacrolimus	11	5 (45.4%)	6 (54.5%)	
CYC	32	16 (50%)	16 (50%)	
RTX/CYC	31	20 (64.5 %)	11 (35.4 %)	
Other	21	7 (33.3 %)	14 (66.6%)	

Figure 1C. No significant difference in renal responses by treatment for 52-week flares

	Total (N= 116)	Response (N = 69)	No Response (N = 47)	P value
TREATMENT				0.908
MMF	45	29 (64.4%)	16 (35.5%)	
MMF/Tacrolimus	10	6 (60%)	4 (40%)	
CYC	19	11 (58%)	8 (42%)	
RTX/CYC	23	12 (52%)	11 (48%)	
Other	19	19 (16.4%)	11 (15.9%)	

Figure 1D. No significant difference in renal responses by treatment for 104-week flares

	Total (N= 52)	Response (N = 92)	No Response (N = 40)	P value
TREATMENT				0.873
MMF	35	17(48.5%)	18 (51.5%)	
MMF/Tacrolimus	9	4 (44.4%)	5 (55.5%)	
CYC	14	6 (42.8%)	8 (57.2%)	
RTX/CYC	21	9 (42.8%)	12 (57.2%)	
Other	13	4 (30.8%)	9 (69.2%)	

There were no differences seen in responses by treatment for any flares occurring 24, 52, or 104 weeks (Fig1b-d). MR analysis demonstrated that patients who received "other" treatments had worse outcomes at 24 weeks as compared to MMF (p=0.004) (Fig2A). Patients who received RTX/CYC had worse outcomes when compared to MMF group at 52 and 104 weeks (p =0.013) (Fig2B-C). AA did not have worse responses when compared to Europeans. Asians had better outcomes when compared to Europeans at 52 and 104 weeks (Fig 2B-C).

Figure 2A.
Renal responses at 24 weeks adjusted for gender, race, and ethnicity

	OR [95% CI OR]	P (logistic)
Gender		
Female	1	Reference group
Male	0.98 [0.43, 2.27]	0.963
Race		
European ancestry	1	Reference group
African ancestry	1.26 [0.58, 2.78]	0.562
Asian ancestry	1.95 [0.80, 4.90]	0.146
Ethnicity		
Non-Hispanic	1	Reference group
Hispanic	1.15 [0.53, 2.54]	0.727
Treatment		
MMF	1	Reference group
MMF/Tacrolimus	0.57 [0.17, 1.83]	0.338
CYC	0.80 [0.37, 1.71]	0.556
RTX/CYC	1.29 [0.57, 3.04]	0.549
Other	0.27 [0.11, 0.64]	0.004

Figure 2B.
Renal responses at 52 weeks adjusted for gender, race, and ethnicity

	OR [95% CI OR]	P (logistic)
Gender		
Female	1	Reference group
Male	1.87 [0.69, 5.76]	0.241
Race		
European ancestry	1	Reference group
African ancestry	1.42 [0.60, 3.41]	0.423
Asian ancestry	5.26 [1.80, 16.92]	0.003
Ethnicity		
Non-Hispanic	1	Reference group
Hispanic	0.98 [0.41, 2.36]	0.969
Treatment		
MMF	1	Reference group
MMF/Tacrolimus	0.69 [0.19, 2.85]	0.58
CYC	0.56 [0.21, 1.56]	0.258
RTX/CYC	0.30 [0.11, 0.77]	0.013
Other	0.40 [0.15, 1.09]	0.071

Figure 2C.
Renal responses at 104 weeks adjusted for gender, race, and ethnicity

	OR [95% CI OR]	P (logistic)
Gender		
Female	1	Reference group
Male	0.51 [0.18, 1.41]	0.193
Race		
European ancestry	1	Reference group
African ancestry	0.75 [0.26, 2.19]	0.59
Asian ancestry	3.50 [1.09, 11.960]	0.039
Ethnicity		
Non-Hispanic	1	Reference group
Hispanic	1.89 [0.66, 5.63]	0.237
Treatment		
MMF	1	Reference group
MMF/Tacrolimus	0.57 [0.14, 2.21]	0.41
CYC	0.72 [0.25, 2.14]	0.547
RTX/CYC	0.37 [0.13, 1.01]	0.056
Other	0.43 [0.14, 1.30]	0.136

Conclusion: Renal responses for de novo episodes were superior with MMF or CYC at 104 weeks compared to MMF/tacrolimus or RTX/CYC explained by treatment resistance when first episode appeared on immunosuppression. There were no differences seen in responses by treatment for any flares. Our findings are inconsistent with previous studies demonstrating that AA and Hispanic patients have worse outcomes when compared to Europeans explained by reliance on MMF as first line therapy and use of rescue options including low dose CYC and RTX. Asian residents of NY metropolitan had better outcomes validating high response rates reported from Asian nations.

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Abstract Number: 1461

Belimumab Improves Renal Responses in Patients with or Without Steroid Pulses During Induction Therapy for Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

Session Title: Abstracts: SLE – Treatment: New Agents, Old Agents (1458–1463)

Session Type: Abstract Session

Session Time: 3:30PM–5:00PM

Background/Purpose: In the BLISS-LN trial (GSK Study BEL114054; NCT01639339), the administration of belimumab (BEL), a B-lymphocyte stimulator antagonist, resulted in improved renal outcomes in patients with active lupus nephritis (LN) compared with standard therapy alone.[1] The aim of this analysis was to evaluate the effects of BEL on renal outcomes in patients with or without intravenous (IV) steroid pulses during induction therapy for LN in the BLISS-LN trial.

Methods: This post hoc analysis assessed patients from the BLISS-LN trial, a Phase 3, randomized, double-blind, 104-week study of adults with active LN. Patients were administered with either IV BEL 10 mg/kg, or placebo (PBO), plus standard therapy that consisted of oral glucocorticoids and either cyclophosphamide (CYC) for induction followed by azathioprine (AZA) for maintenance, or mycophenolate mofetil (MMF) for both induction and maintenance. At the investigator's discretion, 1 to 3 IV pulses of methylprednisolone, 500 to 1000 mg each, could be administered during induction. The primary endpoint was Primary Efficacy Renal Response (PERR=urine protein:creatinine ratio [uPCR] ≤0.7; estimated glomerular filtration rate [eGFR] no more than 20% below preflare value or ≥60 ml/min/1.73 m^2; no rescue therapy) at Week 104. Other endpoints were Complete Renal Response (CRR=uPCR < 0.5; eGFR no more than 10% below preflare value or ≥90 ml/min/1.73 m^2; no rescue therapy) at Week 104, and time to a renal-related event (end-stage kidney disease, doubling of serum creatinine, increased proteinuria and/or impaired renal function, renal disease–related treatment failure) or death. The current analysis compared subgroups of patients who received BEL or PBO with and without IV steroid pulses at induction.

Results: In total, 76 (34.1%) of the 223 patients administered with BEL and 97 (43.5%) of the 223 patients administered with PBO received IV steroid pulses at induction. At Week 104, patients who received BEL, with or without IV steroid pulses at induction, had greater proportions of responders for both PERR and CRR compared with PBO (Table). A higher proportion of patients without, versus those with steroid pulses at induction, achieved PERR and CRR at Week 104, in both BEL and PBO groups. Risk of a renal-related event or death was lower at any time with BEL versus PBO, with or without IV steroid pulses at induction (Table).

Table. Renal outcomes (PERR, CRR, and time to renal-related event or death) at Week 104 by steroid pulse subgroups

	Steroid pulses		No steroid pulses	
	BEL (n=76)	**PBO (n=97)**	**BEL (n=147)**	**PBO (n=126)**
PERR at Week 104, n (%)	29 (38.2)	28 (28.9)	67 (45.6)	44 (34.9)
OR (95% CI) vs PBO	1.56 (0.79, 3.05)		1.59 (0.96, 2.66)	
p-value	0.1979		0.0743	
CRR at Week 104, n (%)	16 (21.1)	17 (17.5)	51 (34.7)	27 (21.4)
OR (95% CI) vs PBO	1.11 (0.50, 2.50)		2.19 (1.24, 3.89)	
p-value	0.7953		0.0071	
Time to renal-event or death, n (%)	12 (15.8)*	30 (30.9)*	23 (15.6)*	33 (26.2)*
HR (95% CI) vs PBO	0.42 (0.21, 0.83)		0.55 (0.32, 0.94)	
p-value	0.0122		0.0286	

OR, 95% CI and p-value are from a logistic regression model run within the subgroup level for the comparison between BEL and PBO with covariates: induction regimen (CYC vs MMF), race (Black vs non-Black), baseline uPCR, and baseline eGFR

HR, 95% CI and p-value are from a Cox proportional hazards model run within the subgroup level for the comparison between BEL and PBO adjusting for induction regimen (CYC vs MMF), race (Black vs non-Black), baseline uPCR, and baseline eGFR

*Number (percentage) of patients reporting the event

CI, confidence interval; HR, hazard ratio; OR, odds ratio

Conclusion: The addition of BEL to standard therapy for the treatment of active LN improved renal outcomes compared with PBO in patients with or without IV steroid pulses during induction therapy. Proportions of responders were generally higher in subgroups that did not receive steroid pulses at induction across both BEL and PBO groups. While one might postulate that those who received IV steroid pulses had more active kidney disease and might have been less responsive to therapy, additional analyses of steroid usage and correlates with LN class and severity are needed to address this question.

Funding: GSK

Role of the Study Sponsor: GSK was involved in study design, collection, analysis and interpretation of data, and publication development.

Reference

[1]Furie R, *et al. N Engl J Med* 2020;383(12):1117–28

Disclosure: R. Furie, GlaxoSmithKline, 2, 5; **F. Houssiau**, GSK, 2, Astra-Zeneca, 2; **L. Lightstone**, Achillion, 2, 6, Alexion, 2, 6, AstraZeneca, 2, 6, Aurinia, 2, 6, BMS, 2, 6, GSK, 2, 6, Kezar Life Sciences, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **X. Yu**, National Natural Science Foundation of China, 5, Baxter, 2, 5, 6, Equipment Grant Program, 5, Wanbang Biopharmaceuticals, 2, 5, 6, AstraZeneca, 2, 5, GSK, 2, 5, Fresenius, 2, 6, Fresenius Kabi, 2, 6, Elsevier, 9, CAN, 9,

People's Medical Publishing House, 9, Kyowa Kirin, 6; **J. Weinmann-Menke**, GSK, 2, 6; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 6, Novartis, 6, YL Biologics, 6, Bristol-Myers Squibb, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi-kasei, 5, 6, GSK, 2, 6, Mitsubishi-Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Ayumi, 2, Taisho, 2; **A. Jones-Leone**, GlaxoSmithKline, 3, 8, 11; **T. Gonzalez-Rivera**, GlaxoSmithKline, 3, 8, 11; **J. Gilbride**, GlaxoSmithKline, 3, 8, 11; **A. Madan**, GlaxoSmithKline, 3, 8, 11; **Y. Green**, GlaxoSmithKline, 3, 8, 11; **D. Roth**, GlaxoSmithKline, 3, 8, 11.

Abstract Number: 1462

Hydroxychloroquine Dose and the Risk of Systemic Lupus Erythematosus Flares

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SESSION INFORMATION
Session Date: Monday, November 8, 2021
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Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Hydroxychloroquine (HCQ) is an important treatment for systemic lupus erythematosus (SLE), known to reduce disease activity and flares. To minimize the risk of toxicity, recent guidelines recommend using HCQ dosages less than 5mg/kg/day, which is less than 400mg/day for many patients. However, the dose needed to prevent lupus flares is unknown. The aim of this study was to determine the association between HCQ dose and the risk of lupus flares.

Methods: We identified a cohort of patients with SLE taking HCQ who met 1997 ACR classification criteria and had at least two rheumatology visits between January 2016 and December 2020. We obtained demographics, anthropometrics, medications, SLE history and disease manifestations, and disease activity (e.g., clinical SLEDAI) assessed at each rheumatology visit. The outcome of interest was SLE flare defined by the revised SELENA-SLEDAI flare index (rSSFI). Among patients who had at least one SLE flare during the study period, we performed a case-crossover study. Each patient's follow up time was divided into case periods, defined by the 6-months prior to each flare, as well as control periods, defined as 6-month periods with no SLE flares (Figure 1). The exposure of interest was HCQ dose, categorized as high-dose (e.g. 400 mg/day) or low-dose (e.g., < 400 mg/day); low-dose was further categorized into < 300 and between 300 and < 400mg. The average HCQ dose was calculated for each case and control period. Conditional logistic regression was used to estimate the odds ratios (ORs) and 95% confidence intervals (CI) s for SLE flare associated with low-dose HCQ use compared with high-dose, and we stratified patients according to body weight. We adjusted for time-varying glucocorticoid use, SLE immunosuppressant use, and clinical SLEDAI score prior to each six-month observation period.

Results: Of 342 patients with SLE who used HCQ, mean age was 46 years, and 87% were female (Table 1). Body weight was below 80kg for 67% of patients, thus 400mg would exceed 5mg/kg/day. 74 patients (22%) received high-dose and low-dose HCQ during the study period, whereas 158 (46%) and 110 (32%) received only high-dose and only low-dose HCQ, respectively. There were 466 total rSSFI SLE flares over 2,176 visits during the study period, including 105 flares among those who received both high-dose and low-dose HCQ. The adjusted OR for SLE flare associated with low-dose HCQ was 2.38 (95% CI 1.24-4.56) (Table 2). For patients weighing less than 80kg/day, a

Table 1. Baseline Characteristics of Hydroxychloroquine Users with Systemic Lupus Erythematosus

Baseline Characteristics*	Overall	Hydroxychloroquine Dose		
		High-dose (400mg/day)	Low-dose (<400mg/day)	High-dose and Low-dose
N	342	158 (46)	110 (32)	74 (22)
Age (y), mean (SD)	45.9 ± 14.8	44.2 ± 13.7	49.1 ± 16.0	44.7 ± 14.5
Female, n (%)	299 (87)	125 (79)	106 (96)	68 (92)
Race/Ethnicity, n (%)				
White	213 (62)	92 (58)	65 (59)	56 (76)
Black	41 (12)	24 (15)	11 (10)	6 (8)
Asian	27 (8)	10 (6)	16 (15)	1 (1)
Hispanic	20 (6)	14 (9)	4 (4)	2 (3)
Other/unknown	51 (15)	26 (16)	15 (14)	10 (14)
Weight (kg), mean (SD)	75.3 ± 20.3	81.9 ± 20.0	66.5 ± 16.1	74.2 ± 21.5
Weight < 80 kg, n (%)	230 (67)	85 (54)	91 (83)	54 (73)
Height (cm), n (%)	163 ± 8.6	165 ± 9.1	161 ± 7.4	163 ± 8.2
SLE Duration (y), mean (SD)	12.2 ± 11.6	10.6 ± 10.1	15.3 ± 14.1	10.8 ± 9.4
SLE Manifestations, n (%)				
Malar Rash	116 (34)	55 (35)	40 (36)	21 (28)
Arthritis	273 (80)	136 (86)	76 (69)	61 (82)
Nephritis	65 (19)	27 (17)	24 (22)	14 (19)
Clinical SLEDAI, mean (SD)	2.6 ± 3.1	2.8 ± 3.3	2.5 ± 3.1	2.1 ± 2.6
SLE Serologies (ever positive), n (%)				
dsDNA antibody	227 (66)	106 (67)	67 (61)	54 (73)
Smith antibody	88 (26)	42 (27)	28 (25)	18 (24)
RNP antibody	121 (35)	57 (36)	39 (35)	25 (34)
SSA antibody	101 (30)	39 (25)	35 (32)	27 (36)
SSB antibody	60 (18)	27 (17)	20 (18)	13 (18)
Hypocomplementemia	139 (41)	64 (41)	48 (43)	27 (36)
Antiphospholipid antibodies	102 (30)	46 (30)	34 (31)	22 (30)
SLE Medications, n (%)				
Glucocorticoids	122 (36)	59 (37)	40 (36)	23 (31)
Oral Immunosuppressant	102 (36)	56 (35)	29 (26)	17 (23)
Belimumab	8 (2)	5 (3)	2 (2)	1 (1)
Rituximab	11 (3)	3 (2)	7 (6)	1 (1)
Cyclophosphamide	4 (1)	2 (1)	2 (2)	0 (0)

*Assessed at the initial visit during the study period. SLE, systemic lupus erythematosus

HCQ dose under 300mg/day was associated with an increased risk of SLE flares. For patients weighing at least 80kg, any HCQ dose under 400mg/day was associated with an increased risk of SLE flares.

Conclusion: Low-dose HCQ use was associated with an increased risk of SLE flares. The risks of toxicity and benefits for preventing SLE flares must be balanced in choosing the optimal HCQ dose.

Table 2. Association of Hydroxychloroquine Dose with Risk of Systemic Lupus Erythematosus Flare

Hydroxychloroquine Dose	SLE Flares	Non-Flares	Unadjusted OR	Adjusted OR*
Overall				
High Dose, 400mg/day	36	139	1.0	1.0
Low Dose, <400mg/day	69	104	2.90 (1.61-5.22)	2.38 (1.24-4.56)
300 to <400mg/day	32	39	3.35 (1.58-7.11)	2.25 (0.93-5.43)
Less than 300 mg/day	37	65	2.54 (1.24-5.21)	2.48 (1.14-5.37)
Body Weight < 80kg				
400mg/day	24	89	1.0	1.0
Low-dose <400mg/day	52	76	2.77 (1.34, 5.75)	2.11 (0.95, 4.66)
300 to <400mg/day	22	31	2.69 (1.05, 6.88)	1.41 (0.46, 4.39)
Less than 300 mg/day	30	45	2.83 (1.21, 6.61)	2.63 (1.05, 6.57)
Body Weight ≥ 80kg				
400mg/day	12	50	1.0	1.0
Low-dose <400mg/day	17	28	3.14 (1.15, 8.57)	8.31 (1.45, 47.50)
300 to <400mg/day	10	8	5.53 (1.50, 20.39)	46.85 (2.30, 954.90)
Less than 300 mg/day	7	20	1.53 (0.39, 6.08)	4.53 (0.72, 28.59)

*Analyses adjusted for prior SLEDAI, glucocorticoid use, and SLE immunosuppressant use

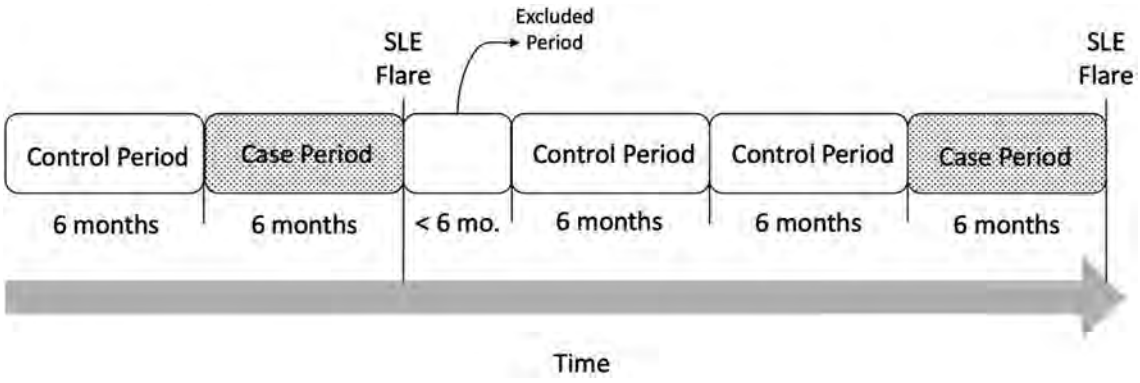

Figure 1. Case-crossover study design. Each patient's follow up time was divided into case periods defined by the 6-months prior to each flare as well as control periods defined as 6-months periods without a SLE flare. Each patient could have multiple case and/or control periods, and control periods could occur before or after case periods. Additional periods shorter than 6 months were excluded from the analysis.

Disclosure: A. Jorge, None; **C. Mancini**, None; **X. Fu**, None; **G. Ho**, None; **Y. Zhang**, None; **K. Costenbader**, Neutrolis, 11, Merck, Exagen, Gilead, 5, Astra Zeneca, Neutrolis, 2; **H. Choi**, None.

Abstract Number: 1463

Use of Telemedicine for Follow-up of Lupus Nephritis in the COVID-19 Outbreak: The 6-month Results of a Randomized Controlled Trial

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SESSION INFORMATION
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Session Title: Abstracts: SLE – Treatment: New Agents, Old Agents (1458–1463)
Session Type: Abstract Session
Session Time: 3:30PM–5:00PM

Background/Purpose: Telemedicine (TM) has been widely advocated and used to follow up patients with rheumatic diseases during the COVID-19 outbreak. However, there is no evidence supporting its use in systemic lupus erythematosus. We aimed to evaluate the short-term patient satisfaction, compliance, disease control and infection risk of TM compared with standard in-person follow-up (FU) for patients with lupus nephritis (LN) during the pandemic.

Methods: This was a single-center open-label randomized controlled study. Consecutive patients followed at the LN clinic were randomized to either TM or standard FU (SF) group in a 1:1 ratio. Patients in the TM group received FU via videoconferencing. SF group patients continued conventional in-person outpatient care. The 6-month data were compared and presented.

Results: From June to December 2020, 122 patients were randomized (TM: 60, SF: 62) and had at least 2 FUs. There were no baseline differences, including SLEDAI-2k and proportion of patients in lupus low disease activity state (LLDAS), between the 2 groups except a higher physician global assessment score (PGA) in the TM group (table). After a mean FU of 19.8±4.5 weeks, the overall patient satisfaction score was higher in the TM group with a significantly shorter waiting time from entering the clinic waiting room (virtual or real) to seeing a rheumatologist (figure). More patients in the TM group had hospitalization (15/60, 25.0% vs 7/62, 11.3%; p=0.049) with higher baseline PGA (OR=1.15, 95% CI 1.07-1.23) being the independent predictor. The proportions of patients remained in LLDAS were similar in the 2 groups (TM: 75.0% vs SF: 74.2%, p=0.919). None of the patients had COVID-19.

Conclusion: TM FU resulted in better patient satisfaction and similar short-term disease control in patients with LN compared to standard care. However, it was associated with more hospitalizations and might need to be complemented by in-person visits especially in patients with higher PGA.

	Overall (n=122)	Telemedicine group (n=60)	Standard follow-up group (n=62)	P-value
Age in years	44.4±11.5	44.1±11.7	44.7±11.5	0.779
Gender: Female	111 (91.0)	55 (91.7)	56 (90.3)	0.796
Disease duration in years	15.1±9.0	16.2±8.7	14.0±9.1	0.115
Nephritis class III, IV or V	108 (88.5)	54 (90.0)	54 (87.1)	0.427
24 hour urine proteinuria in gram	0.51±0.63	0.53±0.60	0.50±0.65	0.712
Current use of prednisolone	112 (91.8)	57 (95.0)	55 (88.7)	0.323
Daily prednisolone dose in mg	5.51±4.21	5.69±4.17	5.34±4.29	0.570
Use of immunosuppressant	90 (73.8)	46 (76.7)	44 (71.0)	0.474
SLEDAI-2K	3.65±2.33	4.00±2.34	3.30±2.29	0.097
PGA	0.56±0.65	0.67±0.69	0.45±0.60	**0.003**
LLDAS	78 (63.9)	36 (60.0)	42(67.7)	0.251
Remission	0 (0)	0 (0)	0 (0)	n/a
Presence of comorbidity	87 (71.3)	40 (66.7)	47 (75.8)	0.264
Number of comorbidity	1.34±1.33	1.45±1.53	1.24±1.11	0.866
SDI	0.93±1.15	1.08±1.28	0.78±0.98	0.243
HAQ-DI	0.23±0.46	0.25±0.47	0.21±0.44	0.571
HADS:				
Anxiety scale	6.07±4.12	6.20±4.19	5.93±4.09	0.720
Depression scale	5.72±4.31	5.73±3.93	5.70±4.68	0.724
LupusQoL score for:				
Physical health	79.1±20.3	78.2±20.3	80.1±20.3	0.534
Pain	81.3±19.3	81.4±19.2	81.2±23.0	0.230
Planning	83.5±18.1	83.2±16.1	83.7±20.0	0.533
Intimate relationship	74.2±27.7	72.4±28.5	75.6±27.3	0.578
Burden to others	74.2±23.2	72.9±20.9	75.5±25.3	0.153
Emotional health	80.5±18.1	79.9±16.6	81.0±19.6	0.487
Body image	77.0±24.1	77.3±20.2	76.6±27.5	0.428
Fatigue	73.7±20.4	73.2±19.8	74.1±21.0	0.665

Data are reported as mean ± SD or number (%). SLEDAI-2k: Systemic Lupus Erythematosus Disease Activity Index 2000; PGA: physician global assessment; LLDAS: lupus low disease activity state; SDI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology (SLICC/ACR) Damage Index; HAQ-DI: Health Assessment Questionnaire Disability Index; and HADS: Hospital Anxiety and Depression Scale.

Table. Baseline clinical data of the recruited patients and comparison between the telemedicine/standard follow-up groups

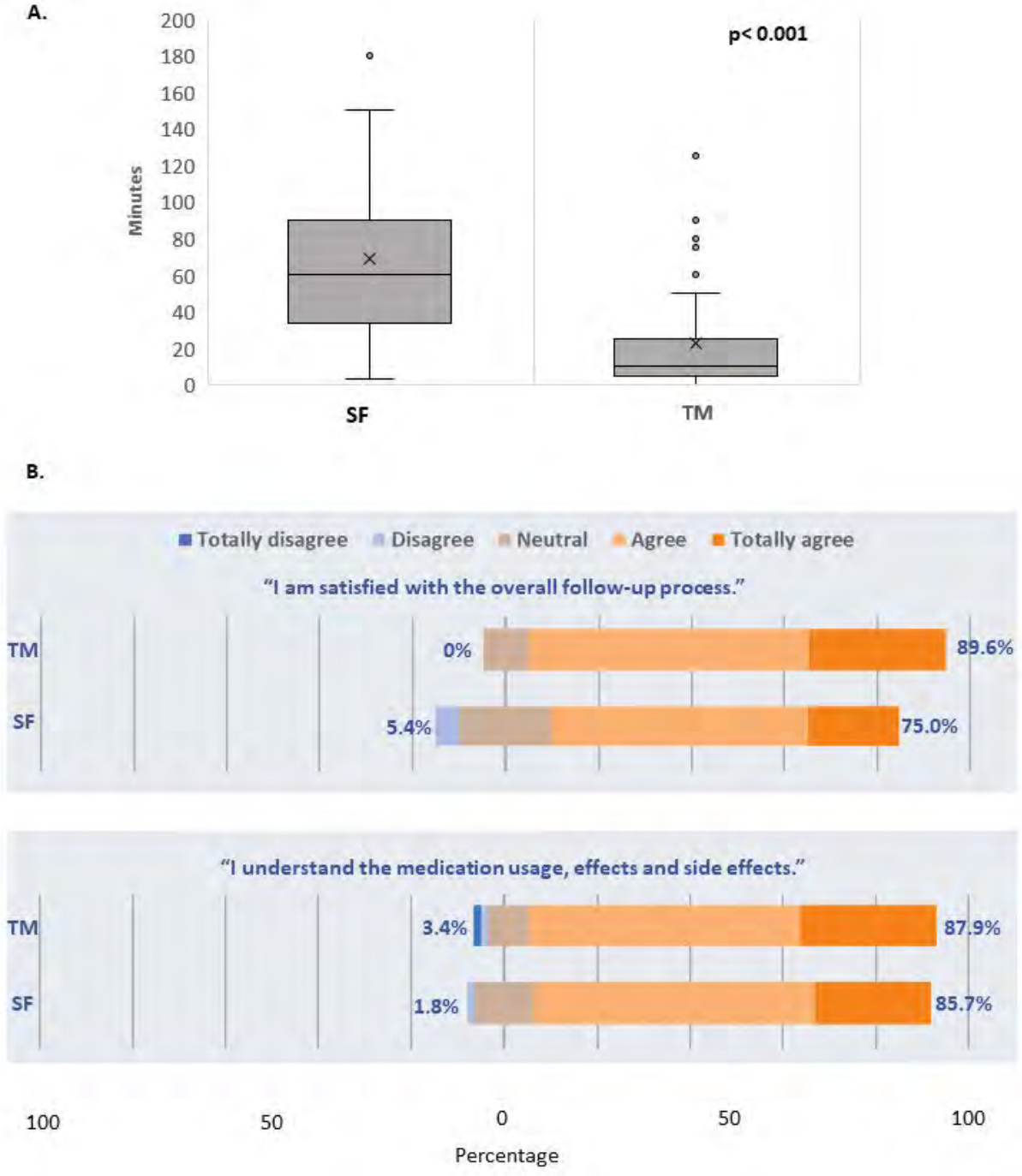

Figure A. Mean waiting time between entering the clinic waiting room (virtual or real) and seeing a rheumatologist. TM = Telemedicine, SF = Standard follow-up. B. Satisfaction scores of patients who used TM) compared to SF. Response is shown as percentage with positive responses on the right. The neutral category was removed when calculating percentages.

Disclosure: h. SO, None; **E. Chow**, None; **I. Cheng**, None; **X. Lau**, None; **T. Li**, None; **C. Szeto**, None; **L. Tam**, Janssen, 2, 5, Pfizer, 2, 5, GlaxoSmithKline, 5, AbbVie, 2, Novartis, 5, Amgen, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, Sanofi, 2.

Abstract Number: 1464

Ambulatory Fetal Heart Rate Monitoring (FHRM) to Surveil Pregnancies at Risk for Congenital Heart Block

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SESSION INFORMATION

Session Date: Monday, November 8, 2021

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Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: Congenital Heart Block (CHB) complicates 2% of anti-Ro/SSA antibody positive pregnancies and carries substantial perinatal morbidity and mortality. Almost all survivors require lifelong pacing. Data suggests the potential of anti-inflammatory treatment of 1° and 2° CHB in preventing progression to immutable complete block. However, the optimal surveillance strategy to detect rapidly transitioning and potentially reversible conduction disease is unknown. This study addresses the feasibility, acceptance and accuracy of the fetal heart rate and rhythm technique (FHRM) in high risk mothers.

Methods: Prospective data from the Surveillance To Prevent AV Block Likely to Occur Quickly (STOP BLOQ) study were leveraged. Mothers referred to the study all had commercially positive anti-Ro/SSA antibodies and were stratified into high and low titers of anti-Ro60 and Ro52 based on a research ELISA which used a threshold cutoff defined as the titer above or below that obtained for 50 mothers with a previous CHB offspring. Mothers with anti-Ro60 or 52 antibodies at or above 1,000 I.U or with a previous CHB offspring, were trained to perform FHRM with an educational video and personal instruction from a pediatric cardiologist. From 17- 25 weeks of gestation, FHRM was completed 3x/day in addition to weekly or biweekly fetal echocardiograms (echo). Mothers texted all FHRM sounds to the study's data coordinating center. For those FHRM deemed abnormal by the mothers, texts were immediately sent to an on call pediatric cardiologist who either reassured if FHRM was normal or referred for emergency fetal echo in < 6 hours if abnormal. Postnatal electrocardiograms were evaluated for CHB.

Results: Fifty-six mothers with commercial anti-Ro/SSA positivity were consented to the study. Of these, 37 (inclusive of 6 with previous CHB) performed FRHM since they had high titer anti-Ro60 (n=8) or 52 antibodies (n=7) or both (n=21), albeit one mother had unexpectedly low titer antibodies to both Ro60 and 52 and a child with incomplete CHB 4 yrs prior to enrollment. In total 3,360 FHRM audiotexts were received during the monitoring period. Of these, 39 recordings from 5 concerned mothers prompted an immediate call with the cardiologist. All but 2 recordings were deemed to be normal based on review of the audiotext alone; the cardiologist requested that the patient send repeat recordings after review as part of re-training and to provide additional reassurance. In the 2 cases an emergency echo was completed in < 6 hrs. In both there were premature atrial contractions which confirmed the mother's perception of the FHRM abnormality. However, there was no evidence of conduction disease. All surveillance echoes were normal. Thus, the overall rate of false positive recordings for the concern of a conduction defect perceived by the mothers was 1.1% (38/3360). There were no cases of CHB at birth.

Conclusion: These data support that FHRM is feasible and accurate. Mothers can be empowered to detect rhythm abnormalities with very few false perceptions thus supporting this technique to substantially enhance the management of anti-Ro/SSA pregnancies.

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Abstract Number: 1465

Trends in Adverse Pregnancy Outcomes Among Women with Systemic Sclerosis in the United States

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SESSION INFORMATION
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Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (1464–1467)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: Autoimmune connective tissue diseases disproportionately affect women of childbearing age. Systemic sclerosis (SSc) is associated with increased risk of adverse pregnancy outcomes (APO). However, changes in obstetric practices may have improved SSc pregnancy outcomes in recent years, as seen for SLE. We sought to examine APO occurrences among women with and without SSc and determine whether APOs have declined over the past 18 years in a large nationwide sample.

Methods: The National Inpatient Sample (NIS) database for years 2000–2017 was used to derive national estimates of delivery-associated hospitalizations. SSc deliveries were identified using ICD codes, excluding those with concurrent SLE or RA. Each SSc hospitalization was matched by age, delivery year, and race to non-SSc hospitalizations from the NIS in a 1:100 ratio. APOs included fetal death, Cesarean delivery, hospital length of stay, preterm birth, intrauterine growth restriction, and hypertensive disorders of pregnancy (preeclampsia, eclampsia, gestational hypertension, and superimposed preeclampsia). All analyses accounted for the complex survey design and sampling weights were applied. Adjusted odds ratios for each APO for the entire study period were calculated from multivariable regression analyses using maternal age, race, diabetes mellitus, and preexisting hypertension as covariates. To compare differences in temporal trends in APOs between SSc and non-SSc deliveries, we pooled data into 6-year intervals and applied logistic or linear regression with an interaction term between SSc (yes vs. no) and year.

Results: From 2000 to 2017, there were 3,740 (95% CI 3,446–4,034) delivery-associated hospitalizations for women with SSc. Mean maternal age at delivery was 30 years. There were significant differences in comorbidities between the SSc and non-SSc groups including pre-existing hypertension, renal disease, and pulmonary hypertension (Table 1). The odds of all APOs during the entire study period were significantly higher in SSc vs. non-SSc deliveries (Table 2). Fetal deaths notably declined in SSc deliveries from 4,896 per 100,000 delivery-related admissions in 2000–2005 to 1,619 per 100,000 in 2012–2017. Difference in trend over time for fetal death was significant (p=0.043) between SSc and non-SSc deliveries, but trends in other APOs were not significantly different (Figure 1).

Table 1. Baseline demographics and clinical characteristics of SSc and non-SSc deliveries*

Variable	SSc (n = 3,740)	Non-SSc (n = 374,035)	P value
Mean age, years (SD)	30.2 (0.2)	30.2 (0.04)	0.8701
Race, n (%)			0.9997
White	1,820 (48.7)	182,955 (48.9)	
Black	468 (12.5)	46,885 (12.5)	
Hispanic	525 (14.0)	51,637 (13.8)	
Asian or Pacific Islander	104 (2.8)	10,118 (2.8)	
Other or Missing	823 (22.0)	82,439 (22.0)	
Clinical comorbidities, n (%)			
Diabetes†	344 (9.2)	28,918 (7.7)	0.1634
Preexisting Hypertension	262 (7.0)	9,218 (2.5)	**<.0001**
Renal Disease‡	35 (0.9)	356 (0.1)	**0.0177**
Pulmonary Hypertension	60 (1.6)	65 (0.02)	**0.0006**
Smoker	211 (5.7)	16,721 (4.5)	0.1601

SSc, systemic sclerosis; SD, standard deviation.

*All values are weighted estimates.

† Includes preexisting and gestational diabetes.

‡ Includes chronic kidney disease and end stage renal disease.

Table 2. Adjusted odds ratios of adverse pregnancy outcomes in SSc and non-SSc deliveries

Pregnancy Outcome	SSc (n = 3,740)	Non-SSc (n= 374,035)	OR* (95% CI)
Fetal deaths per 100,000 admissions, n	2,888	704	**4.00 (2.55–6.27)**
Cesarean section, %	44.4	32	**1.66 (1.44–1.92)**
Preterm birth, %	21.9	9.4	**2.65 (2.23–3.14)**
Hypertensive disorders of pregnancy,† %	15.1	7.9	**1.97 (1.61–2.41)**
IUGR, %	5.5	2.2	**2.45 (1.74–3.45)**
Mean length of stay, days	4.1	2.7	**1.35 (0.98–1.71)‡**

SSc, systemic sclerosis; OR, odds ratio; CI, confidence interval; IUGR, intrauterine growth restriction.

% is given as % of deliveries.

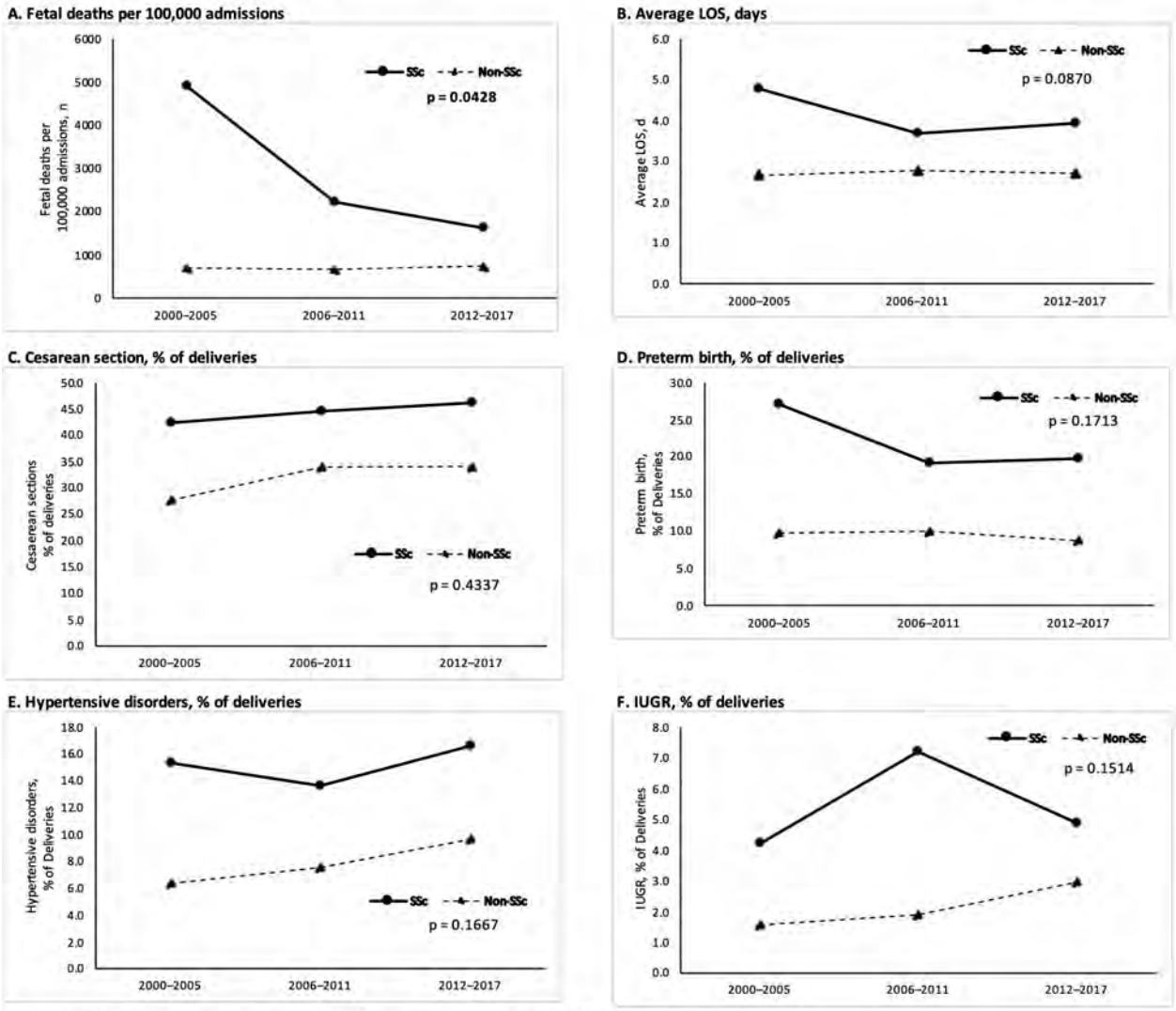
* OR expressed as adjusted odds ratios (95% CI) from multivariable logistic regression analyses except as noted. Covariates included maternal age, race, diabetes mellitus and preexisting hypertension.

† Includes gestational hypertension, preeclampsia, eclampsia, superimposed preeclampsia.

‡ Linear regression expressed as β coefficients (95% CI).

Conclusion: In this large nationwide sample, the risk of fetal death among women with SSc markedly improved over the past 18 years. We focused on delivery-associated hospitalizations rather than all obstetric hospitalizations; therefore, fetal death represents stillbirth, and captures neither miscarriages earlier in pregnancy nor neonatal death. The risk of other APOs remained high in SSc deliveries, and further studies are needed to determine what factors or therapeutics can improve these outcomes.

Figure 1. Temporal trends in adverse pregnancy outcomes in SSc and non-SSc deliveries



P value is for difference in trends. SSc, systemic sclerosis; LOS, length of stay; IUGR, intrauterine growth restriction.

A: Fetal deaths per 100,000 admissions declined among SSc deliveries from 2000–2005 to 2012–2017, with significant difference in trends between SSc and non-SSc deliveries (p=0.0428). **B–F**: There was no significant difference in trends between SSc and non-SSc deliveries for average LOS (**B**) or percentages of Cesarean section (**C**), preterm birth (**D**), hypertensive disorders of pregnancy (**E**), or IUGR (**F**).

Disclosure: Y. Kawano, None; **K. Kolstad**, None; **S. Li**, None; **J. Simard**, None; **L. Chung**, Boerhinger Ingelheim, 1, 5, 6, Eicos, 1, 2, Genentech, 2, Reata, 1.

Abstract Number: 1466

Increased Adverse Maternal Postpartum Outcomes in Systemic Lupus Erythematosus Pregnancies Compared to Controls

April Barnado, Janie Hubbard, Sarah Green and Sarah Osmundson, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION

Session Date: Monday, November 8, 2021
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (1464–1467)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: Studies show increased risks of adverse pregnancy outcomes in SLE patients. Few studies have investigated postpartum outcomes in these patients. Using a large, de-identified electronic health record (EHR), we estimated rates of postpartum infection, blood transfusion, and hospital length of stay and compared them to rates in controls without autoimmune disease. We also assessed for postpartum flares in SLE mothers.

Methods: Using a large, de-identified EHR with over 3.2 million subjects, we identified deliveries to SLE mothers using a validated and published algorithm. This algorithm has a positive predictive value of 90% and uses ≥ 4 SLE ICD-9 or ICD-10-CM codes and ≥ 1 validated, delivery-related codes. We performed chart review to confirm SLE diagnosis by a rheumatologist and focused on SLE deliveries after SLE diagnosis. We assessed for SLE medication use at a postpartum visit between 6 weeks to 3 months after delivery. We identified control mothers without autoimmune disease ICD-9 or ICD-10-CM codes and the same delivery-related codes used to identify SLE deliveries. We then

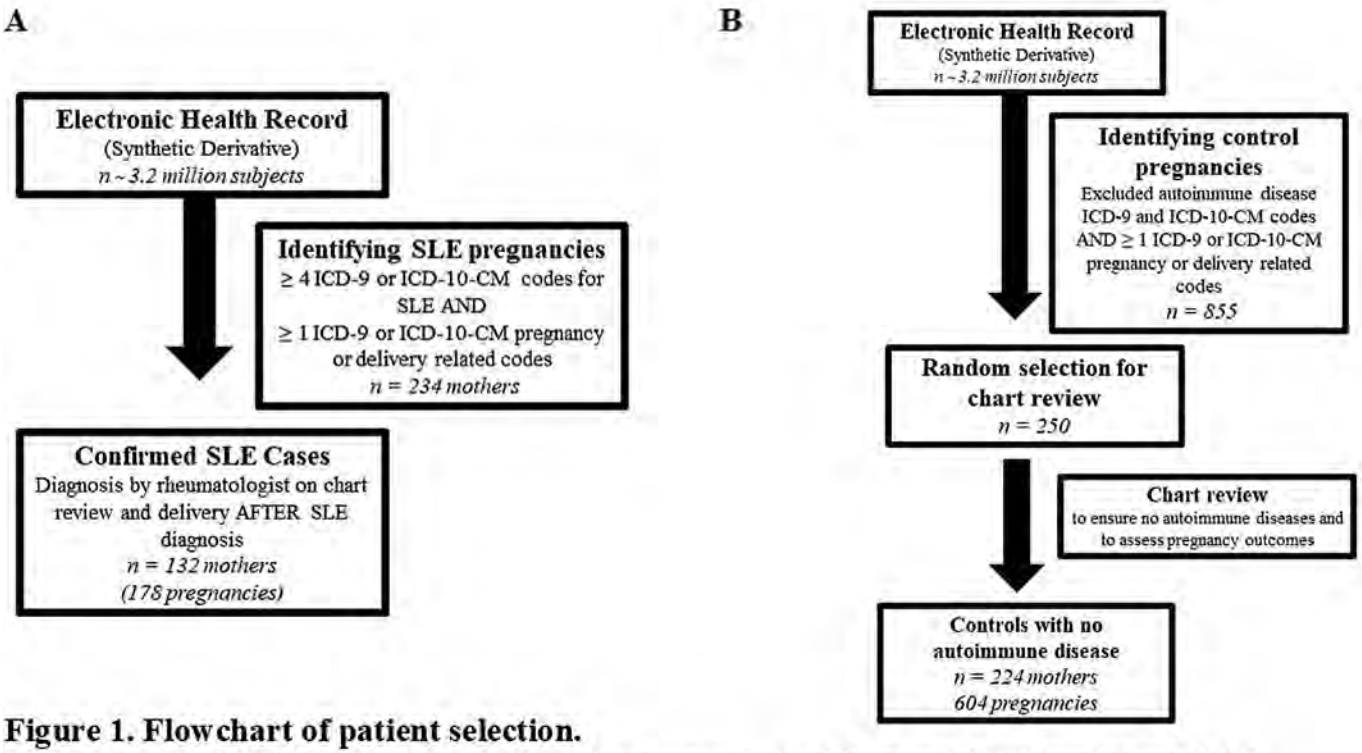


Figure 1. Flowchart of patient selection.
SLE pregnancies (A) were selected from the electronic health record (EHR) using = 4 SLE ICD-9 (710.0) or ICD-10-CM (M32.1 or M32.8 or M32.9) codes while also requiring = 1 ICD-9 or ICD-10-CM pregnancy or delivery related codes. We then required chart review to confirm SLE diagnosis by a rheumatologist and delivery after SLE diagnosis resulting in 132 SLE cases with 178 pregnancies. **Control pregnancies (B)** were selected from the EHR using the same pregnancy or delivery related codes used for the SLE pregnancies along with requiring that controls not have codes for autoimmune diseases. We then chart reviewed a random 250 controls to ensure no autoimmune disease and to assess pregnancy outcomes resulting in 224 mothers with 604 pregnancies.

Table 1. Demographics and postpartum outcomes in SLE cases compared to controls.

Characteristics	SLE deliveries (n = 178)*	Control deliveries (n = 604)*	p value
Mean age at delivery ± standard deviation	27.3 ± 6.0	27.0 ± 6.6	p = 0.67
Race (%)			
White	66%	59%	p = 0.11
Black	30%	38%	
Asian	2%	2%	
Other/Multi-race	2%	1%	
Ethnicity (%)			
Hispanic	5%	11%	p < 0.01
Duration in the EHR** (years) ± standard deviation	13.3 ± 8.3	12.0 ± 7.6	p = 0.18
Postpartum Outcomes			
Blood transfusion any (%)	23/143(16%)	6/350 (2%)	p < 0.001
Platelets	5/143 (4%)	0/350 (0%)	p = 0.01
Red blood cells	18/143 (13%)	6/350 (2%)	p < 0.001
Infection any (%)	30/122 (25%)	13/303 (4%)	p < 0.001
Urinary tract infection	10/122 (8%)	1/291 (0.3%)	p < 0.001
Endometritis	6/122 (5%)	4/302 (1%)	p = 0.03
Surgical site infection	5/122 (4%)	3/303 (1%)	p = 0.03
Pneumonia	4/122 (3%)	4/297 (1%)	p = 0.19
Mastitis	1/122 (1%)	1/290 (0.3%)	p = 0.52
Cellulitis	1/121 (1%)	1/290 (0.3%)	p = 0.52
Length of stay (days) Mean ± standard deviation	4.7 ± 2.8	2.9 ± 1.8	p < 0.001

*n refers to deliveries.

**Duration in the EHR defined as time from first code to last code in the EHR.

randomly selected 250 control mothers for chart review to ensure they did not have autoimmune disease. A flowchart is shown in Figure 1. Postpartum infection was defined as infection documented by a physician from delivery to 6 weeks postpartum. Blood transfusions were assessed during the admission for delivery. SLE flares were defined as the rheumatologist documenting a flare or increase in disease activity in notes from delivery to 6 months postpartum. Length of stay was days from admission to discharge.

Results: We identified 178 pregnancies after SLE diagnosis to 132 SLE mothers and 604 pregnancies to 224 control mothers without autoimmune disease. Our SLE and control mothers had similar mean age at delivery (27.0 ± 6.6 vs. 27.3 ± 6.0, p = 0.67) and a similar racial/ethnic makeup that was predominantly White (66% vs. 59%, p = 0.11) (Table 1). Blood transfusion rates were significantly higher in SLE cases vs. controls (16% vs. 2%, p < 0.001) (Table 1). Postpartum infection rates for any infection were significantly higher in SLE cases vs. controls (25% vs. 4%, p < 0.001). Hospital length of stay was significantly longer in SLE cases vs. controls (4.7 ± 2.8 vs. 2.9 ±1.8, p < 0.001). For

Table 2. Comparison of SLE deliveries with flare vs. no flare postpartum.

SLE patient characteristics	SLE deliveries with a flare (n = 39)	SLE deliveries with NO flare (n = 63)	p value
Demographics			
Mean age at delivery ± standard deviation	28.3 ± 5.6	28.8 ± 5.5	p = 0.61
Race (%)			
White	55%	62%	p = 0.39
Black	42%	32%	
Asian	3%	5%	
Other	0%	1%	
Ethnicity (%)			
Hispanic	10%	8%	p = 0.75
Disease characteristics			
SLE disease duration (years)**	5.6 ± 5.4	6.4 ± 5.3	p = 0.23
Nephritis (%)	36%	37%	p = 0.90
Medication use* (%)**			
Corticosteroids	24/39 (62%)	41/63 (65%)	p = 0.72
Antimalarials	**17/39 (44%)**	**42/63 (67%)**	**p = 0.03**
DMARDs	10/39 (26%)	12/63 (19%)	p = 0.43
No medication	8/39 (21%)	10/63 (16%)	p = 0.55

*n refers to SLE deliveries.
**SLE disease duration defined as time from first SLE billing code in the EHR or date documented by a rheumatology note, whichever came first, to delivery date.
***Medication use was assessed at time of postpartum visit between 6 weeks and 3 months after delivery.

SLE cases, postpartum flare rate was 38%. We compared SLE deliveries with a disease flare vs. deliveries without a flare (Table 2). There were no significant differences in age, race, ethnicity, SLE nephritis, or SLE disease duration. For deliveries without a flare, mothers were more likely to be on antimalarials compared to deliveries with a flare (67% vs. 44%, p = 0.03). Flares were managed by adding or increasing corticosteroids (79%), adding an antimalarial (16%), adding or titrating a DMARD (11%), although 11% had no change to medications.

Conclusion: Our study demonstrates that SLE patients are at an increased risk for adverse postpartum outcomes compared to controls including infections, blood transfusions, and longer lengths of stay. We observed frequent flares postpartum with patients being more likely to flare if not prescribed antimalarials postpartum. This finding emphasizes the importance of antimalarials in the postpartum period to reduce flares.

Disclosure: A. Barnado, None; **J. Hubbard**, None; **S. Green**, None; **S. Osmundson**, None.

Abstract Number: 1467

Determinants of Cervical Cancer Screening Patterns Among Women with Systemic Lupus Erythematosus

Sarah Chung[1], Kimiko Oshima[1], **Jenna Thomason**[1], Michael Singleton[1] and Namrata Singh[2], [1]University of Washington, Seattle, WA, [2]University of Washington, Bellevue, WA

SESSION INFORMATION
Session Date: Monday, November 8, 2021
Session Title: Abstracts: Reproductive Issues in Rheumatic Disorders (1464–1467)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: Women with systemic lupus erythematosus (SLE) are vulnerable to cervical dysplasia. This is due to the persistence of human papillomavirus (HPV) related to immunosuppression and also immune dysregulation inherent to the disease. Thus, routine screening for cervical cancer is important for SLE women. The United States Preventative Services Task Force (USPSTF), American College of Obstetricians and Gynecologists (ACOG), and the American Society of Colposcopy and Cervical Pathology (ASCCP) all provide different recommendations regarding screening intervals. The ASCCP provides the only SLE-specific guidelines, advising more frequent screening in this patient population. The purpose of this study was to investigate the prevalence of up-to-date cervical cancer screening per ASCCP guidelines among SLE women established in our institution's registry program. In addition to identify-

Table 1. Characteristics of study population (n=130).

Age (mean, ±SD)	38 (11.3)
Self-reported race (n, %)	
White	59 (46%)
Black	18 (14%)
American Indian	10 (8%)
Asian/Pacific Islander	31 (24%)
Other	5 (4%)
Unknown	16 (12%)
Primary care provider (n, %)	
Yes	122 (94%)
No	8 (6%)
Gynecology provider (n, %)	
Yes	42 (32%)
No	84 (65%)
Gender of rheumatologist (n, %)	
Male	65 (50%)
Female	65 (50%)
Meets 2019 ACR/EULAR Criteria for SLE (n, %)	
Yes	123 (95%)
No	4 (3%)
Incomplete data	3 (2%)
SLE Disease Activity Index (SLEDAI-2k) score (mean, ±SD)	5.52 (5.3)

ing the organizational recommendations providers most frequently utilize, we aimed to identify SLE disease-specific determinants associated with overdue screening.

Methods: Inclusion criteria were women aged 21-65 years enrolled in our institution's SLE registry program. Data regarding cervical cancer screening status at the time of her last rheumatology clinic visit was obtained by retrospective chart review. Data regarding disease duration, 2019 ACR/EULAR SLE classification criteria, SLEDAI-2k score, SLE damage index (SDI) score, immunosuppressant exposure, and gynecologic history were collected. Descriptive

Table 2. Variables pertaining to healthcare factors, SLE disease characteristics, and medication exposure in patients up-to-date on cervical cancer screening per ASCCP guidelines (n=45), patients up-to-date on cervical cancer screening per ACOG guidelines (n=19), and patients overdue for cervical cancer screening per USTFPF, ACOG, or ASCCP guidelines (n=54) at time of rheumatology office visit. Categorical variables are represented as n (%) unless otherwise stated. Effect size for categorical variables is reported by Cramer's V where V=0.01 represents a small effect size, V=0.3 represents a medium effect size and V=0.5 represents a large effect size. Effect size for continuous variables is reported by η^2, where η^2=0.01 represents a small effect size, η^2=0.06 represents a medium effect size, and η^2>0.14 represents a large effect size.

	ASCCP (n=45)	ACOG (n=19)	Overdue for Screening (n=54)	Effect size
Healthcare factors				
Primary care provider				
Yes	44 (98%)	18 (95%)	49 (91%)	V=0.14
No	1 (2%)	1 (5%)	5 (9%)	
Gynecologist				
Yes	22 (49%)	9 (47%)	8 (15%)	V=0.36
No	22 (49%)	10 (52%)	44 (81%)	
Gender of the rheumatologist				
Male	23 (51%)	8 (42%)	28 (52%)	V=0.07
Female	22 (49%)	11 (58%)	26 (48%)	
Duration of care with rheumatologist				
≥ 1 year	27 (60%)	12 (63%)	30 (56%)	V=0.06
≤ 1 year	18 (40%)	7 (37%)	24 (44%)	
SLE disease characteristics				
Duration of SLE (years), mean (±SD)	9.3 (9.0)	9.0 (6.3)	8.9 (8.6)	η^2 = 0.001 (0, 0.003)
SLEDAI-2k total score, mean (±SD)	6.6 (5.6)	4.4 (4.1)	5.1 (5.1)	η^2 = 0.026 (0, 0.09)
SDI total score, mean (±SD)	0.98 (1.1)	0.37 (0.6)	0.81 (1.1)	η^2 = 0.037 (0, 0.12)
Medication exposure				
Current medication use				
Hydroxychloroquine	43 (96%)	16 (84%)	47 (87%)	V=0.15
Corticosteroids	25 (56%)	6 (32%)	21 (39%)	V=0.19
Methotrexate	6 (13%)	3 (16%)	15 (28%)	V=0.17
Leflunomide	1 2%)	1 (5%)	1 (2%)	V=0.08
Azathioprine	7 (16%)	1 (5%)	2 (4%)	V=0.20
Mycophenolate	23 (51%)	3 (16%)	20 (37%)	V=0.25
Cyclophosphamide	0 (0%)	0 (0%)	1 (2%)	V=0.10
Rituximab	1 (2%)	0 (0%)	2 (4%)	V=0.08
Belimumab	2 (4%)	0 (0%)	1 (2%)	V=0.10
Tacrolimus	4 (9%)	1 (5%)	1 (2%)	V=0.15
Prior medication exposure				
Azathioprine	8 (18%)	3 (16%)	7 (13%)	V=0.06
Mycophenolate	6 (13%)	4 (21%)	3 (6%)	V=0.18
Cyclophosphamide	0 (0%)	0 (0%)	5 (9%)	V=0.23
Rituximab	3 (7%)	1 (5%)	3 (6%)	V=0.02
Belimumab	4 (9%)	0 (0%)	2 (4%)	V=0.15
Tacrolimus	1 (2%)	1 (5%)	2 (4%)	V=0.06

statistics and univariable analyses were performed. Effect sizes were characterized by Cramer's V statistic for categorical variables and by eta squared for continuous variables.

Results: Our study included 130 women with SLE who met eligibility criteria. The mean age (±SD) was 38 (11.3) years, 46% self-reported her race as white (Table 1). 95% met 2019 ACR/EULAR criteria for SLE; mean SLEDAI-2k score (SD) was 5.5 (5.3). 94% had a primary care provider, but only 32% had established with a gynecologist. There were 12 women for whom screening status could not be determined, resulting in a sample size of N=118 for the univariable analysis of correlates of screening status. 45 women were up-to-date with screening per ASCCP guidelines, 19 women per ACOG guidelines, and 54 women were overdue for screening. Patients without a gynecologist were more likely to be overdue for screening. A higher proportion of women screened per ASCCP guidelines were on immunosuppressive medications compared to women screened per ACOG guidelines and those overdue. SLE disease characteristics were not associated with screening patterns (Table 2).

Conclusion: Only half of the women with SLE in our study cohort had guideline-congruent care for cervical cancer screening. A greater proportion of women screened per ASCCP guidelines were on immunosuppressive medications compared to those screened by ACOG guidelines. This study reveals the variety of practice patterns employed for cervical cancer screening in our SLE population and suggests the need for increased awareness among rheumatologists, primary care providers, and gynecologists regarding the ASCCP SLE-specific screening guideline schedules.

Disclosure: S. Chung, None; **K. Oshima**, None; **J. Thomason**, None; **M. Singleton**, None; **N. Singh**, None.

Abstract Number: 1468

Intra-articular (IA) Injection of Empty Large Multilamellar Vesicles Liposomes Reduces Cartilage Degeneration in Rat Osteoarthritis Model

Alison Bendele[1], Jacob Favret[1], Gadi Sarfati[2], Ronny Pinkus[2] and **Roni Wechsler**[2], [1]Bolder BioPATH Inc., Boulder, CO, [2]Moebius Medical LTD, Tel Aviv, Israel

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: A suspension of **empty** large multilamellar vesicles (MLV) liposomes composed of dimyristoylphosphatidylcholine (DMPC) and dipalmitoylphosphatidylcholine (DPPC), is currently under clinical development for symptomatic knee osteoarthritis (OA). *In-vivo* bio-distribution studies and *ex-vivo* wear tests have shown that following IA injection, the MLV liposomes are retained on the cartilage surface, providing lubrication, and leading to a reduction in wear of the cartilage. In a first-in-man study, a single injection of the MLV liposomes was demonstrated to lower pain in knee OA patients for up to 3 months.

Given the lubricating properties, cartilage wear reduction, and pain-lowering effect of the MLV liposomes, we hypothesized that their IA administration may also reduce OA progression.

The purpose of the current study was to evaluate the effects of three consecutive weekly IA injections of the MLV liposomes on cartilage degeneration in a rat surgical model of osteoarthritis.

Methods: Male Lewis rats underwent a unilateral medial meniscal tear (MMT) on study day 0. The rats (n=15 per group) were treated by the IA route on study days 7, 14, and 21 with the liposomes (50ml/knee), a vehicle control or left untreated. At day 28, joints were processed for histological analysis following staining with toluidine blue. Scoring for cartilage degeneration was based on chondrocyte death/loss, proteoglycan (PG) loss, and collagen loss or fibrillation and was measured by ocular micrometer. Substantial Cartilage Degeneration was identified by chondrocyte and proteoglycan loss extending through greater than 50% of the cartilage thickness. Gait analysis was performed at day 24 to confirm expected animal mobility post-surgery.

Results: Weekly IA treatment with the MLV liposomes (5.35 mg/knee) resulted in significant beneficial effects on cartilage damage and collagen degeneration in the rat meniscal-tear–induced model of OA as determined by evaluation of knee histopathology including significant reductions in substantial cartilage degeneration widths (38% reduction), summed cartilage degeneration scores (33%), total joint scores (25-26%), and combined severe to mild collagen degeneration widths (32%) as compared to the vehicle control. The treatment also resulted in significant reductions in subchondral bone sclerosis (16%) and osteophyte scores (16%) as compared to vehicle control rats. Rats treated with the liposomes had a statistically significant increase in synovial inflammation as compared to the vehicle control group with all animals showing minimal to mild synovitis. Animal body weight gain and mobility post-surgery in rats treated with the liposomes did not differ statistically from the vehicle control group.

Conclusion: Weekly IA treatment with the MLV liposomes resulted in significant reduction in cartilage damage and collagen degeneration in a rat model of OA as determined by evaluation of knee histopathology. The minimal to mild synovitis associated with the injected liposomes is expected from IA-injected particulate agents that lodge in the

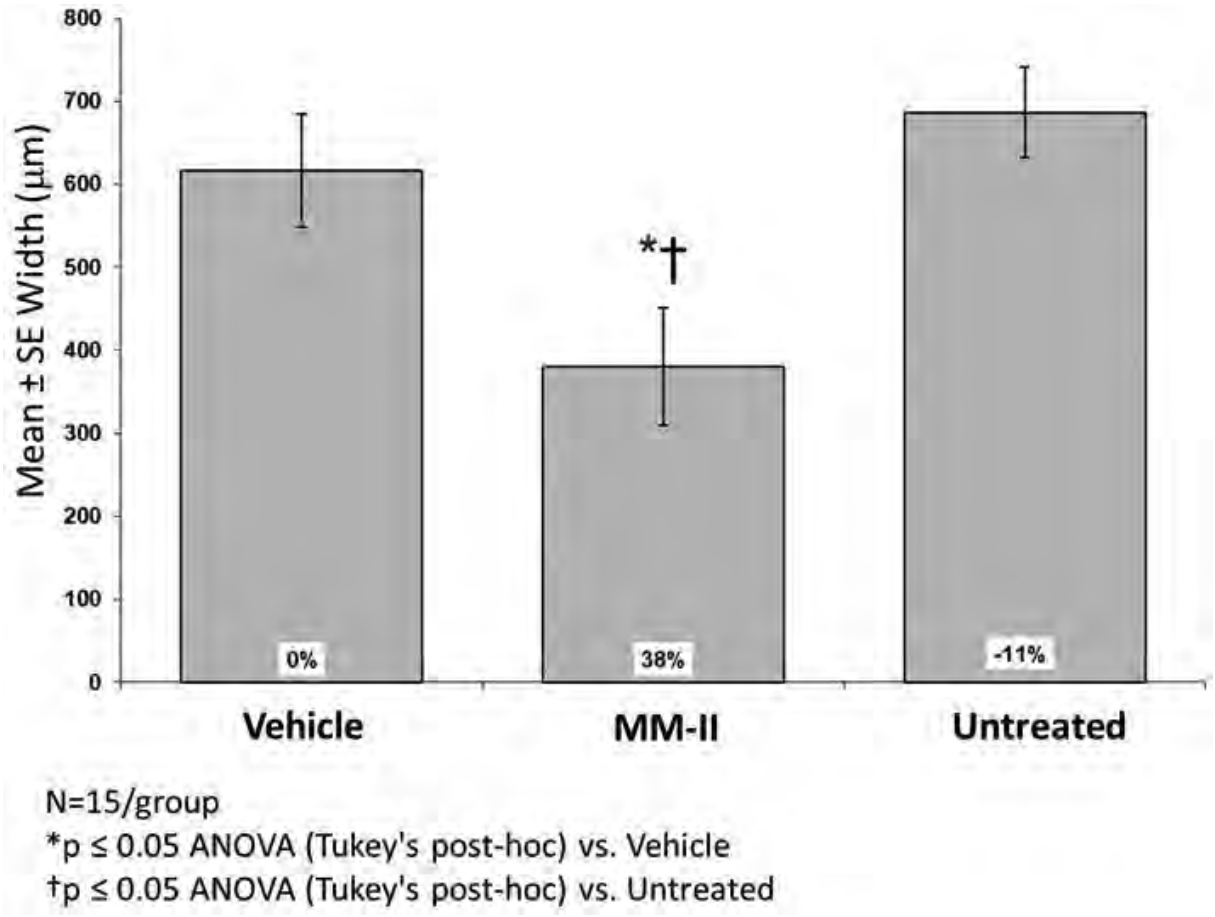


Figure 1. Substantial Tibial Cartilage Degeneration Width.

synovium. The above results indicate that treatment with large DPPC- and DMPC- based MLV liposomes has the potential to be a disease modifying OA therapy.

Disclosure: A. Bendele, Bolder BioPATH, Inc, 7, Bolder BioPATH, Inc, 7; **J. Favret**, Bolder BioPATH, Inc, 7, Bolder BioPATH, Inc, 7; **G. Sarfati**, Moebius Medical, 3; **R. Pinkus**, Moebius Medical LTD, 3; **R. Wechsler**, Moebius Medical LTD, 3.

Abstract Number: 1469

Lorecivivint (SM04690), an Intra-articular, Small-Molecule CLK/DYRK Inhibitor That Modulates the Wnt Pathway, as a Potential Treatment for Meniscal Injuries

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Meniscal injuries are the most common pathology of the knee and are associated with pain, stiffness, and localized swelling. Meniscal damage is a frequent finding on MRI images of knee osteoarthritis (OA).[1] Efforts to repair meniscal damage have been largely unsuccessful and do not prevent the progression of degenerative changes that lead to knee OA.[2] The Wnt signaling pathway has been shown to be regulated during meniscal development,[3] suggesting that manipulation of this pathway may influence the regenerative capacity of the meniscus. Lorecivivint (LOR; SM04690) is an intra-articular (IA), small-molecule CLK/DYRK inhibitor that modulates the Wnt pathway.[4] LOR was evaluated in preclinical studies to determine its protective and anabolic effects in ex vivo explants and in a rat model of chemically induced inflammatory meniscal degeneration.

Methods: Effects of LOR (30 nM) on matrix metalloproteinase (MMP) expression in cultured rat menisci treated with IL-1b were measured by qRT-PCR. In vivo, LOR activity was evaluated in a rat model of monosodium iodoacetate

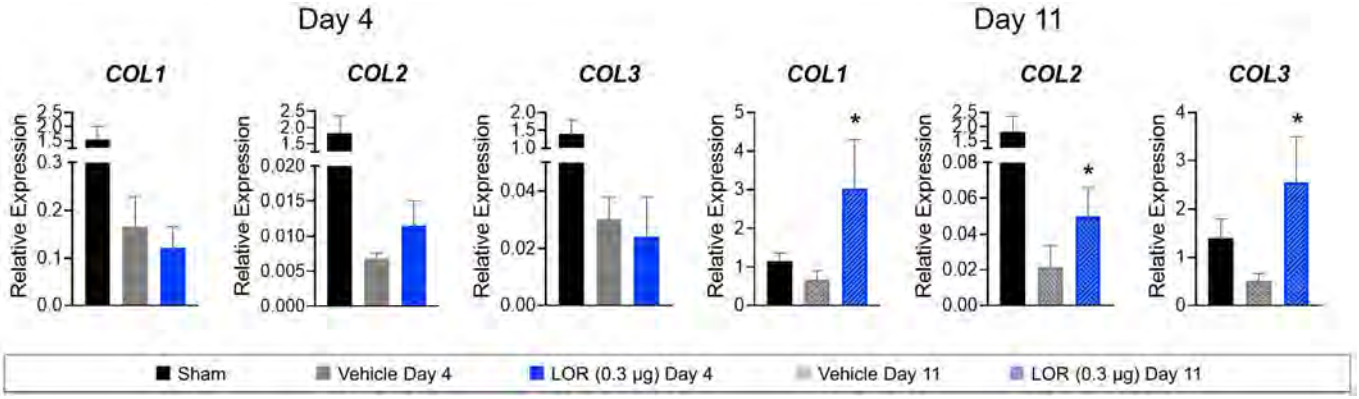

Figure 1. LOR increased collagen gene expression in vivo. A single IA injection of monosodium iodoacetate (MIA; 3 mg) was immediately followed by a single IA injection of LOR (0.3 µg) or vehicle at 10 weeks of age. Knees were harvested on Days 1, 4, and 11 after injection and menisci were isolated. Gene expression was measured by qRT-PCR. N=3, Mean ± SEM, *P<0.05, one-way ANOVA.

(MIA) injection-induced inflammatory meniscal degeneration. A single IA injection of MIA was immediately followed by a single IA injection of LOR (0.3 mg) or vehicle. Knees were harvested on Days 1, 4, and 11 and menisci were isolated. Anti-inflammatory effects were evaluated by qRT-PCR for *TNFA* and *IL6* expression. Meniscal protection was evaluated by qRT-PCR for MMPs and aggrecanase. Anabolic effects were evaluated by qRT-PCR for collagens.

Results: In ex vivo meniscal explants, LOR inhibited expression of *MMP1*, *MMP3*, and *MMP13* compared with DMSO ($P < 0.01$). In vivo, LOR significantly decreased expression of MMPs and aggrecanase ($P < 0.05$) and reduced expression of inflammatory cytokines *TNFA* and *IL6* compared with vehicle in the rat model of inflammatory meniscal degeneration at Day 4 after MIA injection. Additionally, LOR increased expression of collagen types I, II, and III at Day 11 after MIA injection (Figure 1).

Conclusion: LOR exhibited protective effects in the meniscus ex vivo and in vivo by reducing catabolic enzyme expression compared with control. Anti-inflammatory effects of LOR were demonstrated by inhibition of inflammatory cytokine expression. Compared with vehicle, LOR increased collagen expression in vivo, indicating potential meniscal anabolic effects. These data support further investigation of LOR as a potential structure-modifying treatment for meniscal injuries.

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Disclosure: T. Seo, Biosplice Therapeutics, Inc, 3, 11, GNF, 3; **V. Deshmukh**, Biosplice Therapeutics, 3, 11; **Y. Yazici**, Amgen, 2, BMS, 5, Biosplice, 3, 8.

Abstract Number: 1470

Cartilage Epigenetic Changes Induced by Microbial DNA Amplified from Human OA Samples

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Strong links between epigenetic changes, particularly alterations in DNA methylation, have been linked with the onset and progression of knee osteoarthritis (OA); however, the environmental factors driving epigenetic changes within articular tissues have not yet been fully elucidated. We have previously demonstrated that the microbial DNA signatures within human cartilage and shown changes in microbial signatures correlate with primary knee OA progression. In this study, we hypothesized that alterations in microbial DNA may induce epigenetic changes within articular cartilage. To test this, we exposed chondrocyte cell lines *in vitro* to amplified microbial DNA from human OA patients and controls.

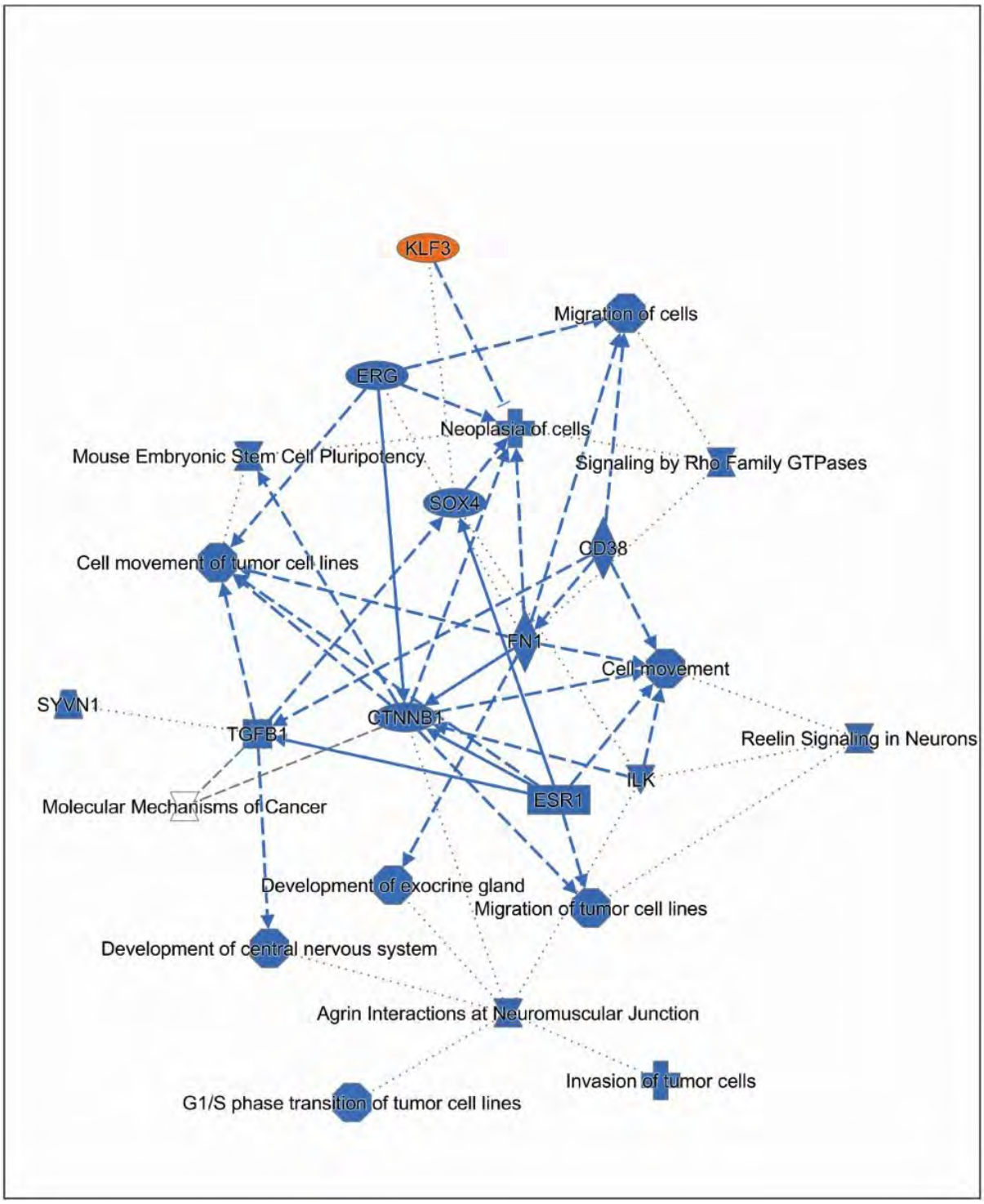

Figure 1. Graphical summary of top pathways and regulators associated with DNA methylation changes induced by exposure of chondrocytes in vitro to microbial DNA amplified from human OA patient cartilage samples.

Methods: Matched discarded cartilage samples from macroscopically eroded (n=4) and intact (n=4) OA specimens were obtained from patients undergoing total knee arthroplasty. Control cartilage samples were obtained from cadaveric control patients. Microbial DNA was isolated using an anti-MBD2 magnetic bead approach and microbial DNA subjected to whole-genome amplification. Twenty micrograms of amplified microbial DNA was added Tc28a2 cells in culture. After a 3-day incubation period, DNA was extracted, treated with sodium bisulfite, and loaded onto Illumina Infinium Methylation EPIC chips .DNA methylation beta values were extracted from raw chip imaging and

processed in R using the ChAMP package. Genes associated with differentially methylated CpG sites were evaluated ontologically using the Ingenuity Pathway Analysis (IPA) software package.

Results: Microbial DNA treatment induced substantial changes in DNA methylation levels. Comparing eroded-OA microbial DNA-treated cells with control microbial DNA-treated cells, we found 1638 differentially methylated CpG sites (DMPs), 1637 hypomethylated in the eroded group, corresponding to 1109 unique genes. No DNA methylation differences were induced when comparing non-OA with intact-OA microbial DNA-treated cells. Comparing eroded-OA to intact-OA, we identified 1275 DMPs, 1274 hypomethylated in the eroded group, corresponding to 881 unique genes. Ontology analysis of differentially methylated genes associated with eroded-OA vs. control microbial DNA treatment revealed numerous OA-related pathways and upstream regulators (**Figure 1**). These include axonal guidance signaling, Rho family GTPases, ERK/MAPK signaling, stem cell pluripotency, and ErbB signaling, among others. Upstream analysis included enrichment in ERG, miR-137 (which regulates ADAMTS5), miR-21 (which targets Gdf5), miR-16 (which targets Smad3), among others.

Conclusion: Herein, we demonstrate that exposure of human chondrocytes *in vitro* to microbial DNA is sufficient to induce widespread epigenetic changes. OA-related epigenetic modifications are identified when cells are treated with microbial DNA extracted from eroded-OA human cartilage samples. These data represent a novel potential mechanism of microbiome-epigenome interaction in the development of OA. Future work should focus on testing whether these findings are replicable *in vivo* and explore the mechanism(s) through which this epigenetic alteration is induced.

Disclosure: V. Izda, None; **C. Dunn**, None; **C. Sturdy**, None; **J. Martin**, None; **C. Velasco**, None; **P. Jacob**, None; **M. Jeffries**, None.

Abstract Number: 1471

Oral Administration of Berberine Limits Post-traumatic Osteoarthritis Development and Associated Pain via AMP-activated Protein Kinase (AMPK) in Mice

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SESSION INFORMATION
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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
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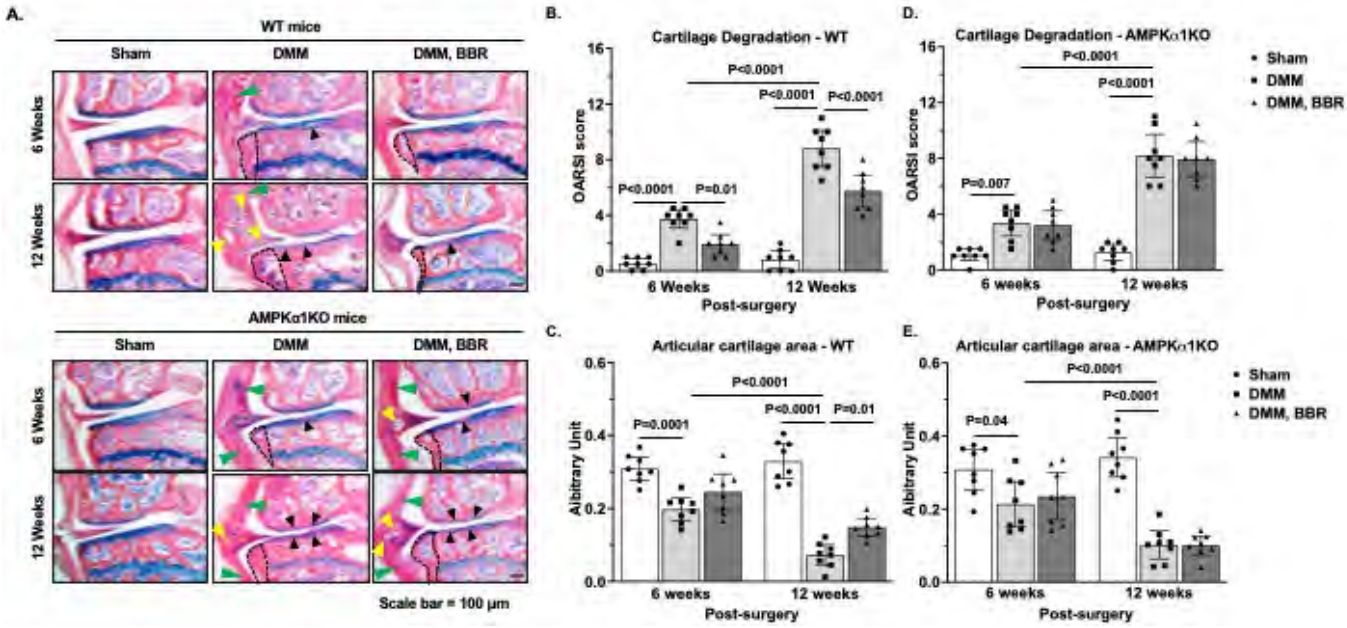
Background/Purpose: AMP-activated protein kinase (AMPK), a master regulator of energy balance and metabolism, is implicated to play an important role in cartilage homeostasis. Berberine is an isoquinoline alkaloid extracted from plants with low toxicity. It has anti-microbial, anti-inflammatory and anti-oxidant properties. The beneficial effect of berberine is mediated through multiple signaling pathways, and activation of AMPK is through to be one of the main actions of berberine. Although berberine exhibits chondroprotective effect, the underlying mechanism is not fully understood. In addition, whether berberine has ability to alleviate OA-associated pain remains unclear. Thus, in this study, we investigated the effect of berberine on OA development and associated pain in mice *in vivo*.

Figure 1. Berberine protected mice from cartilage damage in an AMPK-dependent manner in a post-traumatic OA model in mice.



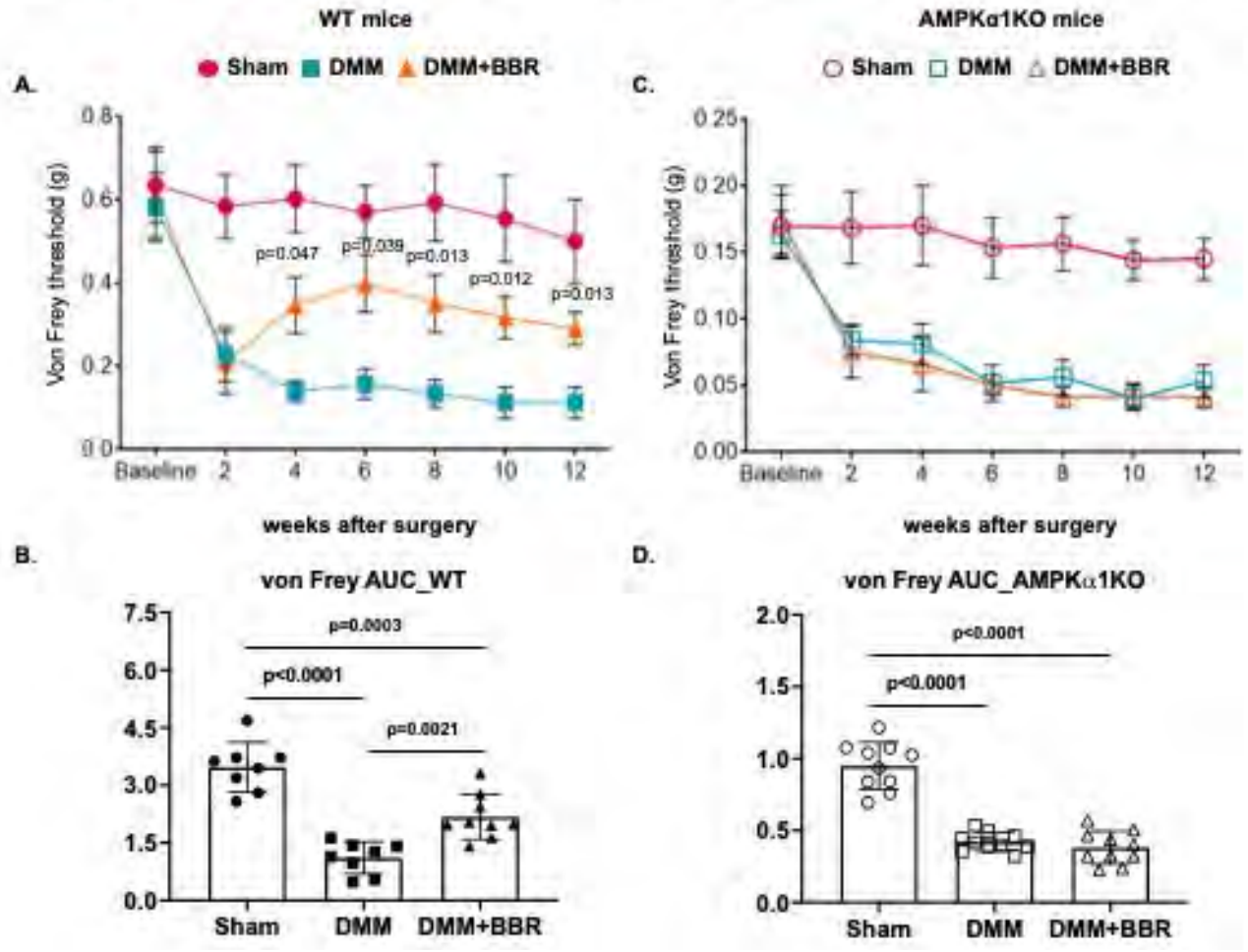
Methods: Human primary knee chondrocytes were included to investigate how AMPK is activated by berberine *in vitro*. Both global knockout (KO) of AMPKa1 and congenic wild type (WT) male mice were subjected to the post-traumatic OA through destabilization of medial meniscus (DMM) surgery. Two weeks after surgery, the mice were divided into two groups with one group receiving berberine chloride daily via drinking water. They were sacrificed at 6 and 12 weeks after surgery. OA severity was assessed by histological analyses of cartilage damage using the OARSI score system. Articular cartilage area of medial tibia plateau was quantified by tracing the Alcian blue-positive staining areas using the OsteoMeasure system. The osteophyte formation was evaluated semi-quantitatively based on both size and maturity of osteophytes. Immunohistochemistry (IHC) analyses were carried out to examine AMPK signaling. Pain behavior was evaluated by von Frey filament test to assess pain sensitivity. The Laboratory Animal Behavior Observation Registration and Analysis System was used to assess spontaneous pain behavior. GraphPad PRISM 8 was used for statistical analyses.

Results: Berberine induced phosphorylation of AMPKa (Thr172) via liver kinase B1 (LKB1), the major upstream kinase of AMPK, in chondrocytes *in vitro*. Both WT and AMPKa1KO exhibited OA phenotype such as cartilage damage, osteophyte formation and associated pain behavior, which progressed from mild to severe at 6 and 12 weeks post DMM surgery, respectively. Berberine treatment significantly reduced severity of OA and attenuated pain in WT but not AMPKa1KO mice, indicating the effect of berberine on chondroprotection and pain alleviation was AMPK-dependent. IHC analysis of WT mice revealed decreased phosphorylation of AMPKa (Thr172) and concomitantly reduced expression of SIRT1 and SIRT3 *in situ* in the DMM knee cartilage, which were significantly reversed by berberine. Stimulation human OA chondrocytes with berberine *in vitro* resulted in increased phosphorylation of AMPKa (Thr172), correlated with increased NAD^+/NADH ratio and expression of NAD^+-dependent SIRT1 and SIRT3, suggesting importance of activation of AMPK signaling in mediating beneficial effect of berberine.

Conclusion: Berberine acts through AMPK to reduce joint structural damage and alleviate pain associated with post-traumatic OA in mice *in vivo*, implicating its OA disease modifying potential.

Both WT and AMPKa1KO mice were subjected to the DMM surgery to induce OA development. Two weeks after the surgery, mice in the treatment group started to receive berberine chloride via drinking water. At 6 and 12 weeks after the DMM surgery, mice were sacrificed and histological analysis of mouse knee sections (A) and assessment of

Figure 2. AMPK mediated the effect of berberine on relieving pain through reduced pain sensitivity in post-traumatic OA.

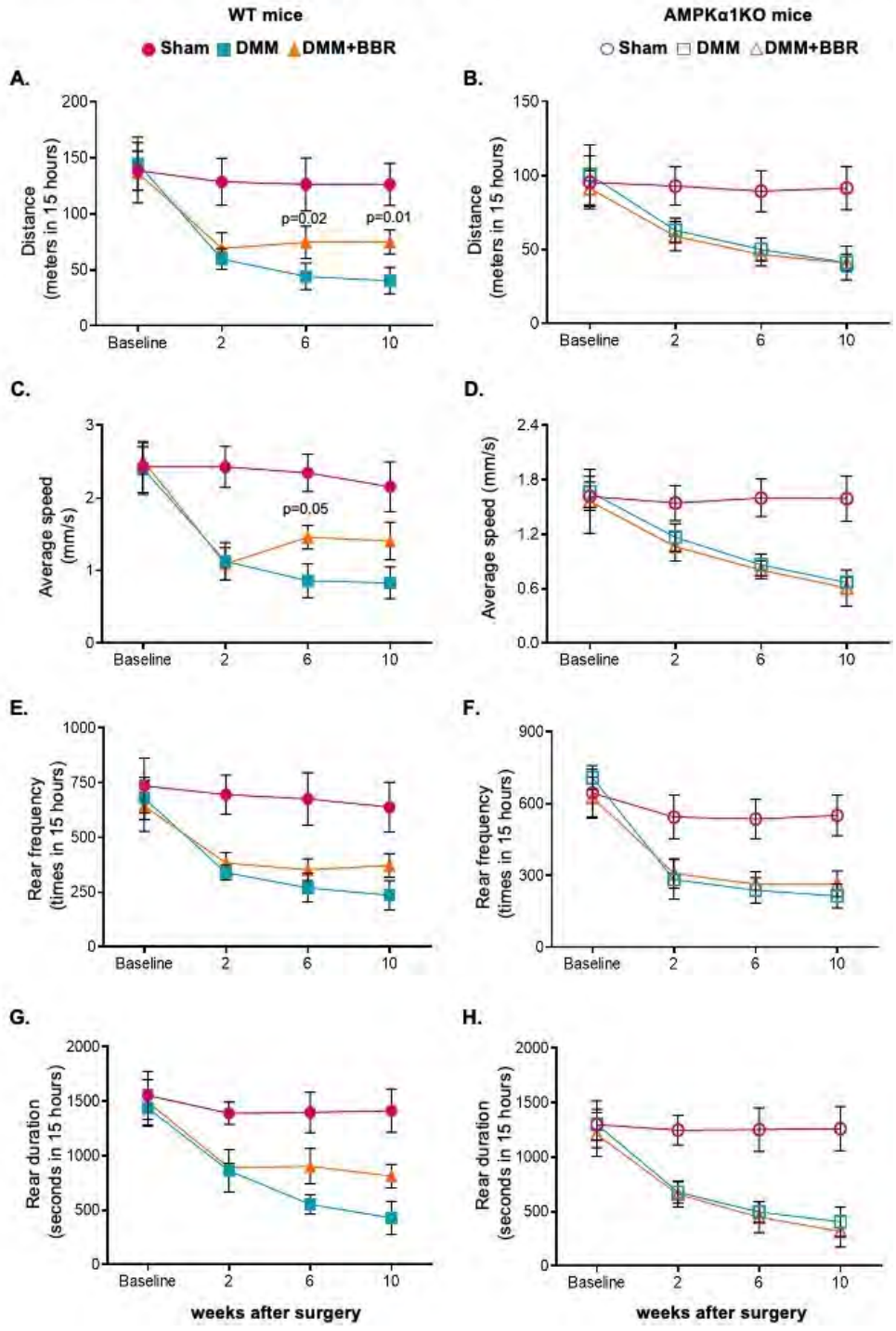


cartilage damage including cartilage degradation (B and D) and cartilage area (C and E) were performed as described in the Methods. Two-way ANOVA with the post-hoc Tukey test was used for statistical analysis in B-E.

The von Frey test was performed to assess pain sensitivity biweekly after DMM surgery (n=8, each group) in WT and AMPKa1 KO mice with and without berberine treatment as described in the Methods. Statistical analysis was conducted using two-way ANOVA with the Tukey post-hoc test.

The LABORAS system was used to evaluate spontaneous pain biweekly after DMM surgery (n=4, each group) in WT and AMPKa1 KO mice with and without berberine treatment as described in the Methods, which included travel distance (A, B), average walking speed (C, D), rear frequency (E, F), and rearing duration (G, H). Statistical analysis was conducted using two-way ANOVA with the Tukey post-hoc test.

Figure 3. AMPK mediated the effect of berberine on relieving pain through improving spontaneous activities in post-traumatic OA.



Disclosure: J. Li, None; **Y. Wang**, None; **D. Chen**, None; **R. Liu Bryan**, None.

Abstract Number: 1472

Characterization and Function of Tumor Necrosis Factor α and Interleukin-6–Induced Osteoclasts in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)

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Session Time: 8:30AM–10:30AM

Background/Purpose: We have previously reported that stimulation of mouse bone marrow–derived macrophages with a combination of tumor necrosis factor α (TNFα) and interleukin-6 (IL-6) induces differentiation of osteoclast-like cells with bone resorption activity (Yokota K *et al*., Arthritis & Rheumatology 2014, 66:121-129). The present study aims to clarify the characterization and function of human TNFα and IL-6–induced osteoclasts using human peripheral blood cells collected from patients with rheumatoid arthritis (RA) or healthy donors. In addition, we also identify the differences in the molecular expression patterns between the novel TNFα and IL-6-induced osteoclasts and conventional RANKL-induced osteoclasts.

Methods: Human peripheral blood monocytes were cultured with a combination of TNFα and IL-6, TNFα alone, IL-6 alone, or RANKL, and their bone resorption ability were evaluated. Expression levels of nuclear factor of activated T cell (NFAT) c1, proinflammatory cytokines, matrix metalloproteinase-3 (MMP-3), and cathepsin K (CTSK) were analyzed. The effects of osteoprotegerin (OPG), NFAT inhibitor, and JAK inhibitor on these osteoclastogenesis were examined. Furthermore, we examined the relationship between the number of TNFα and IL-6–induced osteoclasts or RANKL-induced osteoclasts differentiated from peripheral blood mononuclear cells in patients with RA and the relationship, modified total Sharp score (mTSS) and whole-body bone mineral density (BMD).

Results: Peripheral blood monocytes stimulated with a combination of TNFα and IL-6 showed the ability to absorb bone matrix, which has been supposed to be the function of osteoclasts. The differentiation was not inhibited by the addition of OPG contrary to that of RANKL-induced ones. Stimulation with a combination of TNFα and IL-6 promoted NFATc1 expression, whereas the NFAT and JAK inhibitors prevented this TNFα and IL-6–induced osteoclast formation. Expression levels of *IL-1β*, *TNFα*, and *IL-12p40* were significantly increased in TNFα and IL-6–induced osteoclasts, but not in RANKL-induced osteoclasts. IL-1β up-regulated the differentiation of TNFα and IL-6–induced osteoclasts. The number of TNFα and IL-6–induced osteoclasts from patients with RA positively correlated with the mTSS, whereas RANKL-induced osteoclast numbers negatively correlated with the whole-body BMD of the same patients. The expression levels of *MMP-3* were significantly higher in TNFα and IL-6-induced osteoclasts than in RANKL-induced osteoclasts. Conversely, the expression levels of *CTSK* were significantly higher in RANKL-induced osteoclasts than in TNFα and IL-6-induced osteoclasts.

Conclusion: Our results demonstrate that TNFα and IL-6–induced osteoclasts differentiate via RANKL-independent pathways and may contribute to the joint destruction in the inflammatory arthritis, such as RA.

Disclosure: K. Yokota, None; **K. Sato**, None; **Y. Aizaki**, None; **S. Tanaka**, None; **M. Sekikawa**, None; **N. Kozu**, None; **Y. Kadono**, None; **H. Oda**, None; **T. Mimura**, None.

Abstract Number: 1473

Chaperone-mediated Autophagy Is a Hallmark of Joint Damage in Osteoarthritic Patients

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: In osteoarthritis (OA), defects in Autophagy are evident and precede joint damage. Therefore, identifying hallmarks associated with specific autophagy subtypes could shed light to fundamental mechanisms of joint disease.

Methods: A comparative analysis of 35 autophagy genes was performed from blood from the Prospective OA Cohort of A Coruña (PROCOAC). Non-OA subjects (n=18) and Knee OA subjects (n=18, OA III-IV) were profiled using an autophagy gene expression array. Confirmatory studies were performed in blood from Non-OA subjects (n=30) and Knee-OA subjects (n=30, OA III-IV).

The candidate gene was evaluated in human knee joint tissues (cartilage, meniscus, ligaments, synovium) with different KL grades (KL0, 2, 4) and in both spontaneous aging and surgically-induced OA in mice by IHC. The functional consequences were studied in primary human OA chondrocytes. Autophagy, Chaperone-mediated autophagy (CMA), inflammation, and cellular senescence were analyzing by gene and protein expression. Moreover, oxidative stress and cell death were evaluated by FACS. The contribution of CMA to chondrocyte homeostasis was evaluated by studying the capacity of CMA to restore proteostasis upon autophagy deficiency by siATG5.

Results: 15 autophagy-related genes were significantly downregulated in blood from knee OA patients compared to non-OA patients. No significant upregulation was found for any studied gene, although a trend towards upregulation was found in genes involved in the mTOR pathway. Interestingly, HSP90AA1 and HSPA8, CMA markers involved in stress response and protein folding, were downregulated. Confirmatory studies showed a significant downregulation of MAP1LC3B and HSP90AA1 in blood from knee OA patients. Remarkably, HSP90A was found reduced in femoral cartilage, meniscus and ACL, while in synovial membrane, the expression was found increased. This expression signature was dependent on OA severity. In addition, we observed a decrease of HSP90A with aging and OA in mice. The functional consequences of HSP90AA1 gene silencing are related to an increase in NFkB, MMP13, and p16 expression. Interestingly, LAMP2A, a key CMA marker, and MAP1LC3B expression were upregulated, which

might indicate an early response to maintain homeostasis. On the other hand, LAMP2A protein is decreased upon HSP90AA1 deficiency, while LC3II and p62 were increased, indicating a failure in the autophagy flux that leads to impaired lysosomal degradation. Moreover, p21, p16 and prbS6 were increased, besides increasing mitochondrial ROS production and apoptosis. ATG5 silencing blocks autophagy by reducing LC3II and increasing prbs6, p62, p16 and p21. Interestingly, LAMP2A and HSP90A were found increased, indicating a compensative activation of CMA in response to autophagy defects. These results support that HSP90A has an important role in chondrocyte homeostasis by participating in the cross-talk between CMA and autophagy.

Conclusion: Taking together, we identified HSP90A, a CMA regulator, as critical in chondrocyte homeostasis. These disease mechanisms are relevant in OA and constitute hallmarks potentially useful to prevent OA progression.

Disclosure: I. Lorenzo-Gómez, None; **U. Nogueira-Recalde**, None; **N. Oreiro**, None; **J. pinto**, None; **F. Blanco-García**, None; **B. Caramés**, None.

Abstract Number: 1474

Automatic Detection of Bone Marrow Lesions from Knee MRI Data from the OAI Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Subchondral bone marrow lesions (BMLs) are associated with symptoms and structural progression of knee OA. BMLs are characterized by diffuse hyperintensity on fat suppressed T2-weighted images. BMLs are commonly assessed using semi-quantitative (SQ) scoring systems by expert readers or volume quantification. Automated detection of BMLs using machine learning approaches may help in screening potential participants in clinical trials enriched for fast structural progression.

Methods: The dataset consists of 1,899 knee MRI exams from three sub-studies of the Osteoarthritis Initiative (OAI) with available baseline SQ readings: Foundation for NIH (FNIH) OA biomarker, Pivotal OAI MRI Analysis (POMA) incident radiographic knee OA, and POMA knee replacement. We trained a deep learning model (modified MRNet) using the sagittal intermediate-weighted (IW) fat-suppressed (FS) images. We dichotomized the MOAKS (MRI Osteoarthritis Knee Score) grades into presence or absence categories. The split was done by categorizing grades > 0 as presence and grades = 0 as absence. The whole data were randomly split into a training set (1524 exams) to train the model, a validation set (182 exams) to select the best model, and a test set (193 exams) to evaluate prediction performance. After the deep learning models were trained, we obtained probabilities of the existence of BMLs from IW images on each of 15 subregions in the femur and tibia. The logistic regression model was trained to combine the probabilities of different regions for IW images to output a probability of BMLs status for each subject overall. We utilized the area under the receiver operating characteristic curve (AUC) to assess the model's performance and 95% confidence intervals of AUC to measure the variability of AUC. AUC values range from 0 to 1, with 1 indicating a 100% correct detection.

Table 1. AUC values for the test set

Subregions	AUC
femur medial anterior	0.51
femur lateral anterior	0.89
femur medial central	0.83
femur lateral central	0.86
femur medial posterior	0.59
femur lateral posterior	0.81
tibia sub- spinous	0.77
tibia medial anterior	0.81
tibia lateral anterior	0.83
tibia medial central	0.90
tibia lateral central	0.85
tibia medial posterior	0.83
tibia lateral posterior	0.69
patella medial	0.56
patella lateral	0.90

Results: The highest AUC value for IW images in the test set was 0.90 at two regions (tibia central medial and patella lateral). AUC values ranged from 0.51 to 0.89 in the test set for the other regions, see Table 1. At the subject level, the detection performance of the combined model achieved an AUC value of 0.87 with a 95% confidence interval of [0.82, 0.93].

Conclusion: We have developed and validated a fully automated deep learning framework to detect BMLs from MRI data. After the model had been trained, we applied the trained model to MRI data without MOAKS readings to predict the probability of BMLs status automatically. The prediction performance of detecting BMLs varied among different regions. Our method has some limitations, e.g., the prediction accuracy at the subject level is not as good as the accuracy for the individual subregions. In future studies, we will utilize images from other MRI sequences and additional MOAKS readings to improve our model's performance. Automated classification of diffuse vs cystic BMLs and severity grading will be important in addition.

Disclosure: S. Liu, None; **X. Sun**, None; **F. Roemer**, None; **E. Ashbeck**, EMD Serono, 2; **E. Bedrick**, None; **Z. Li**, None; **A. Guermazi**, Pfizer, MerckSerono, Regeneron, TissueGene, AstraZeneca, Novartis, 2, BICL, 8; **K. Kwoh**, Regeneron, 2, LG Chem, 2, Express Scripts, 2, Abbvie, 12, Principal investigator for pharma sponsored clinical trials, UCB, 12, Principal investigator for pharma sponsored clinical trials, Eicos, 12, Principal investigator for pharma sponsored clinical trials, Cumberland, 12, Principal investigator for pharma sponsored clinical trials, Mitsubishi, 12, Principal investigator for pharma sponsored clinical trials, GSK, 12, Principal investigator for pharma sponsored clinical trials, Kolon TissueGene, 4, Avalor Therapeutics, 4.

Abstract Number: 1475

Long Term Compressive Loading Modulates the Extracellular Matrix Response to Growth Factors in Bovine Cartilage Explants

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Mechanical loading of cartilage is an essential part of the function and maintenance of the joint. Despite the apparent importance of continuous mechanical loading, this factor is rarely considered in cell or tissue models potentially limiting their translatability. The majority of studies that have investigated the impact of mechanical loading on cartilage remodeling have done so in one sitting, investigating the effects of a single loading procedure,

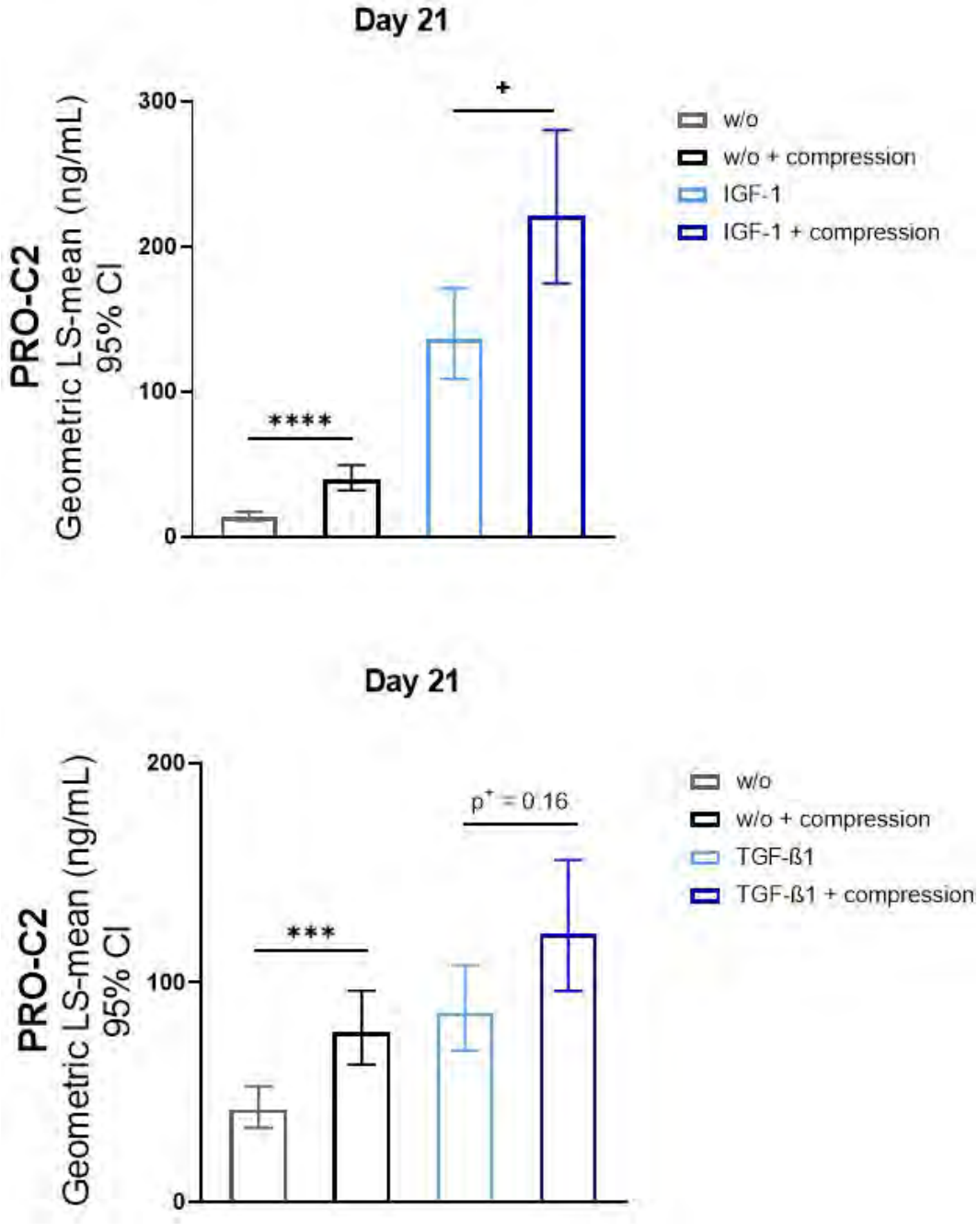

Figure 1. Effect of compression on IGF-1 and TGF-β1 induced cartilage formation.

typically lasting hours or days of duration. Cartilage remodeling has however been described to be augmented when loading procedures are repeated over several days, allowing creep recovery of cartilage to occur between loading procedures. The aim of this study was to elaborate on such regimens of repeated loading and investigate cartilage remodeling when dynamic compression was repeated daily for three weeks.

Methods: Bovine cartilage explants were isolated from the femoral condyles of 1–2-year-old calves. Explants were subjected to 20 minutes of 1 MPa dynamic compressive loading five times a week, with culturing lasting 21 days. The impact of dynamic compression on cartilage remodeling was investigated in presence of growth factors IGF-1 and TGF-β1, as well as SB525334, a TGF-β receptor 1-selective kinase inhibitor. Cartilage remodeling was determined at baseline and once every week by measuring biomarkers for type II collagen formation (PRO-C2) and fibronectin turnover (FBN-C) in the conditioned media from explants. Metabolic activity was likewise determined at baseline and once every week by alamarBlue™.

Results: Daily cyclic loading of bovine cartilage explants increased PRO-C2 and FBN-C levels at day 21 compared to unloaded explants. Treatment with IGF-1 increased PRO-C2, but not FBN-C levels, compared to vehicle, while daily cyclic loading increased both PRO-C2 and FBN-C compared to IGF-1 alone. TGF-β1 increased both PRO-C2 and FBN-C levels compared to vehicle, while no additional effect of daily cyclic loading was observed in explants treated with TGF-β1. Inhibition of SMAD2/3 signaling by SB525334 blocked PRO-C2 and FBN-C release in both naïve and dynamically compressed explants indicating inhibition of both regular and compression induced cartilage formation.

Conclusion: We here show that daily low-grade cyclic compression of cartilage explants increases type II collagen formation. We find that the growth factor IGF-1 work in addition to the anabolic response generated by compression, increasing the overall impact on cartilage formation. Further, TGF-β1 signaling was found to be important for mediating the anabolic effect of mechanical loading in bovine cartilage explants. These data suggest that mechanical loading is important to consider in translational models.

Disclosure: F. Gillesberg, None; **A. Engstrøm**, None; **M. Karsdal**, Nordic Bioscience, 3, 4, 11; **A. Bay-Jensen**, Nordic Biosciences, 3, 11; **C. Thudium**, Nordic Bioscience, 3, 11.

Abstract Number: 1476

Metabolic Reprogramming: Inhibiting Osteoarthritis-induced Expression of the Pyruvate Dehydrogenase Kinase Preserves Mitochondrial Respiration

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SESSION INFORMATION
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Background/Purpose: Osteoarthritis (OA) is the most common degenerative joint disease worldwide, traditionally classified as non-inflammatory. Recently, attention has been drawn to the importance of synovitis in the pathogenesis

of OA. Fibroblast-like synoviocytes (FLS), which maintain structural and dynamic integrity of the joint under physiological conditions, have been proposed to be key factors in joint destruction during OA. Of these, pathogenic THY1- FLS of the synovial lining are assumed to destroy bone and cartilage, whereas THY1+ FLS of the sublining drive synovitis. The latter are classified as invasive proliferative cells characterized by a dominant glucose metabolism. In order to demonstrate inflammation-induced metabolic changes in FLS, we chose mesenchymal stromal cells (MSCs) as a phenotypically indistinguishable, non-activated fibroblast-like control. To identify novel targets for the diagnosis and treatment of OA, we compared human FLS isolated from tibial plateau samples collected during knee arthroplasty for OA with bone marrow-derived MSCs from patients with OA at the transcriptomic, proteomic, and metabolic levels.

Methods: We characterized FLS and MSCs for their multipotency, surface marker pattern, proliferation rate, expression of metabolic-related markers, and mitochondrial function using flow cytometry, immunofluorescence and Seahorse™ technology. Using qPCR and mass spectrometry, we analyzed selected gene and protein expression patterns.

Results: We observed a comparable phenotype of FLS and non-inflamed MSCs with respect to the minimal criteria defining the MSC phenotype. Mapping the distribution of subsets within expanded FLS, we observed >90% THY1+ FLS proliferating faster than non-inflamed MSCs. Global proteome comparison of FLS with MSCs revealed 592 differentially expressed proteins. In detail, we observed no differences between the two cell types with respect to the expression of classical fibroblast markers. When mitochondrial function was analyzed, FLS showed significantly lower basal respiration and ATP production rates but higher spare respiratory capacity and number of mitochondria compared with MSCs. In addition, we identified the pyruvate dehydrogenase kinase (PDK) 3 to be highly expressed in proliferative FLS compared with MSCs. Inhibition of PDKs by dichloroacetate (DCA) significantly increased basal respiration and ATP production rates in FLS but not in MSCs. Finally, DCA significantly reduced the proliferation of FLS compared with untreated FLS controls.

Conclusion: Our data suggest that, although the classical fibroblast markers do not distinguish between non-inflammatory MSCs and THY1+ FLS, the latter have significantly higher expression of PDK isoforms. PDK isoforms are known to inhibit the entry of pyruvate into the tricarboxylic acid cycle, thereby limiting the mitochondrial ATP production, and may play a critical role in the expansion of FLS during OA pathogenesis. Therefore, it is likely, that reprogramming FLS metabolism from glycolysis to mitochondrial respiration by inhibiting PDK isoforms might be a potential new approach to treat OA.

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Abstract Number: 1477

Circulating MicroRNAs in Hand Osteoarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: microRNAs (miRNAs) are small non-coding RNAs that can ignite the degradation of mRNAs or inhibit the protein translation and are therefore essential for several physiological and pathological functions. It is now clear that several miRNAs (e.g. miR-9, miR-140) regulating genes related to OA progression have a significantly different levels of expression in various tissues [1,2]. Under certain circumstances, miRNAs can be released into the body fluids and easily be detected in the blood samples.

The aim of this study was to evaluate circulating miRNAs in patients with hand osteoarthritis (HOA) and healthy individuals. Simultaneously, we studied specific miRNAs in order to differentiate between erosive and non-erosive subsets of the disease.

Methods: Eight patients with HOA (erosive: n=4, 3 females, mean age=63.7±7 yrs; non-erosive: n=4, 3 females, mean age= 62.4±6 yrs) and 4 healthy controls (3 females, mean age=63.5±7 yrs) were included in this study. Firstly, Advance TaqMan low-density assay (TLDA) was performed for the purpose of miRNA high-throughput screening. Differently expressed miRNAs were further verified by real-time qPCR on the validation cohort in 31 patients with hand OA (19 females, mean age=66.2±7 yrs, erosive: n=9, non-erosive: n=10, healthy controls: n=12).

Results: We identified 346 circulating miRNAs in plasma of HOA patients and healthy controls. Out of these, 40 circulating miRNAs were differently expressed in patients with HOA compared to healthy controls. We validated altered expression of 10 miRNAs in patients with HOA compared to healthy controls, e.g. miR-191-5p (3.4 fold), miR-151a-3p (3.4 fold) or miR-222-3p (2.4 fold). None of the miRNA could distinct erosive from a non-erosive subset of the disease.

Conclusion: Extensive profiling of circulating miRNAs revealed several miRNAs that can be associated with HOA and can help to better understand OA pathogenesis.

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Disclosure: A. Pekacova, None; **J. Baloun**, None; **O. Sleglova**, None; **J. Vencovsky**, AbbVie, 1, 6, Boehringer Ingelheim, 2, Eli Lilly, 1, 6, Gilead, 1, Octapharma, 1, Biogen, 6, MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6, Novartis, 6, Werfen, 6; **K. Pavelka**, Abbvie, 6, UCB, 6, MSD, 6, Roche, 6, Pfizer, 6, Eli Lilly, 6, Egis, 6, Biogen, 6, Pfizer, 6; **L. Senolt**, None; **O. Ruzickova**, None.

Abstract Number: 1478

An Orphan Receptor and Osteoarthritis: Mouse Gpr34 Expression in Dorsal Root Ganglia After Partial Meniscectomy

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

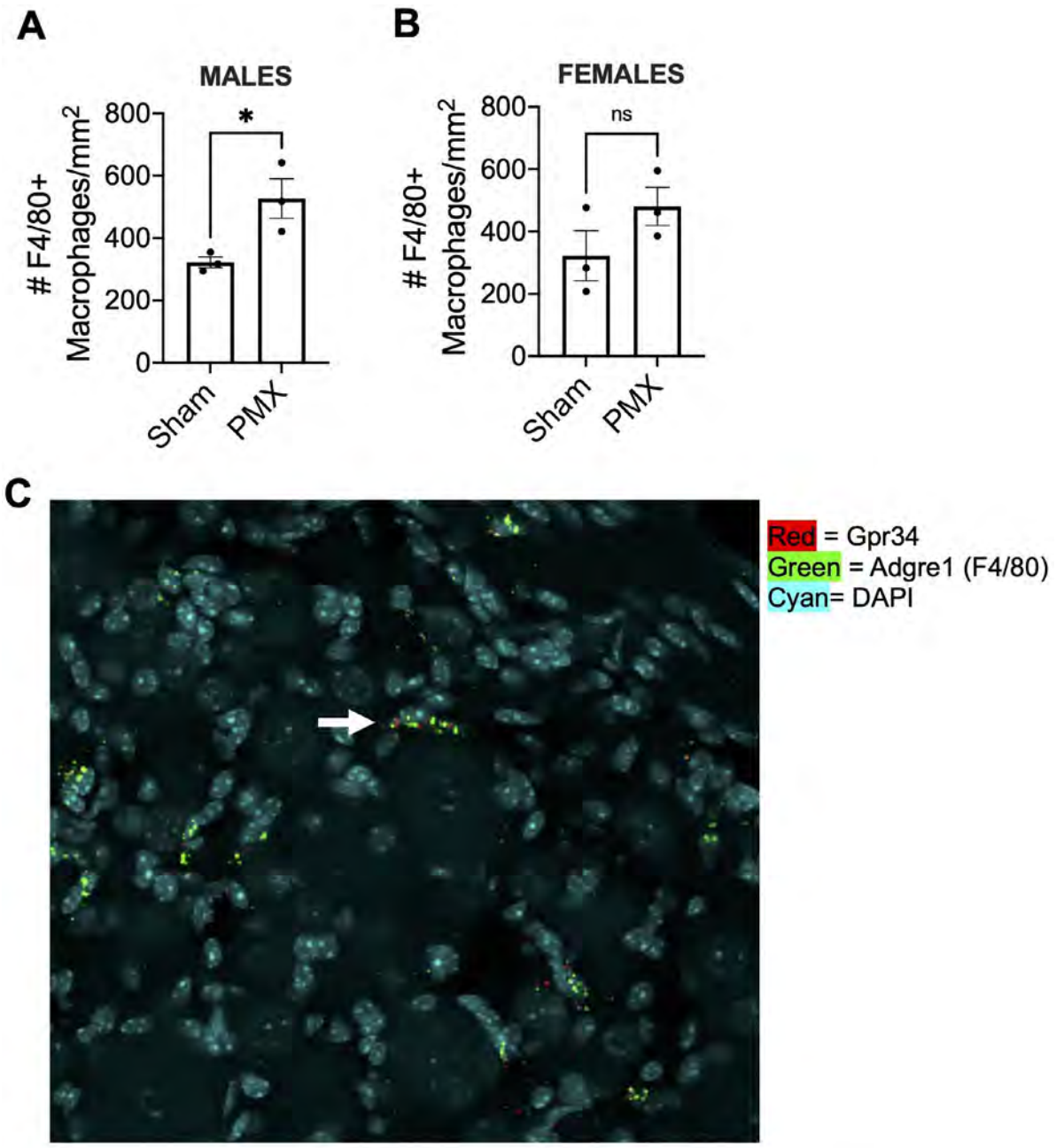

Figure 1. Macrophages (F4/80+Gpr34+) infiltrate the DRG in experimental OA. (A) F4/80+ cells quantified in the ipsilateral L4 mouse DRG of (A) male and (B) female mice 12 weeks after PMX or sham surgery (n=3). (C) RNAscope *in situ* hybridization of *Gpr34* or *Adgre1* (F4/80 gene name) co-stained with DAPI (nuclear stain) on a male PMX L4 DRG tissue sample (60X magnification). Arrow points to co-localization of *Gpr34* and *Adgre1* expression. Statistical analysis by Mann-Whitney t-test. *$p < 0.05$

Background/Purpose: Osteoarthritis (OA) is one of the leading causes of musculoskeletal pain and disability. Worldwide, an estimated 303 million patients have clinically diagnosed OA, with over 14 million new cases emerging annually. Yet, management of OA pain remains poor, and often relies on analgesics with limited efficacy. To identify new analgesic targets, we use molecular biology techniques to study the mechanisms underlying OA pain in mouse models. Single cell RNA-sequencing of mouse dorsal root ganglia (DRG) identified novel molecular targets, including several G-protein coupled receptor (GPCR) genes with specific expression patterns in populations of neuronal and non-neuronal DRG cells. In particular, we found that the rhodopsin class GPCR, *Gpr34*, is specifically expressed by macrophages in the DRG. Given that neuroimmune interactions have been implicated in the development of persistent pain, targets on immune cells infiltrating the DRG may be therapeutically useful. The objective of this study was to investigate expression of *Gpr34* by DRG macrophages in experimental OA, induced by partial meniscectomy (PMX). We have previously shown that both male and female mice develop joint damage and signs of pain behavior in this model by 12 weeks post surgery.

Methods: We performed PMX or sham surgery on 10-week-old male and female mice (n=3 per group). Ipsilateral L4 DRG were collected 12 weeks following surgery, fixed in 4% paraformaldehyde, transferred to 30% sucrose solution for cryoprotection and cryo-sectioned onto slides. RNAscope analysis was completed with probes for mouse Gpr34 and Adgre1 per ACD Bio-Techne Multiplex Fluorescent v2 Assay standard protocol. We evaluated macrophage presence in the DRG via immunofluorescence staining for F4/80, a pan-macrophage marker, as previously described. Final images were processed using a Fluoview FV10i confocal microscope, and quantification was completed via ImageJ software. Briefly, in ImageJ, regions of interest (ROIs) were automatically generated from a set intensity threshold and cell size parameters, and the number of positive cells in 30X image area were counted by a blinded observer.

Results: By immunofluorescence, we observed an increase in the total number of F4/80+ cells in DRGs 12 weeks post PMX compared to sham controls, in both male and female mice (n=3) (Figs. 1A+B). In addition, RNAscope in situ hybridization revealed overlap with *Gpr34* and *Adgre1* (gene name for F4/80) 12 weeks post PMX in male mice, supporting the single cell RNA sequencing data that these cells are indeed macrophages (n=3) (Figure 1C).

Conclusion: This study suggests that macrophages are increased in the DRGs of both male and female mice after PMX, during a time when the mice have developed both joint damage and persistent pain behaviors. Our lab has previously shown that macrophages numbers also increase in DRGs following destabilization of the medial meniscus (DMM), suggesting that these cells may contribute to the development of persistent pain. Moreover, a novel druggable receptor, *Gpr34* is expressed by these macrophages. Future work will examine the contribution of macrophages and *Gpr34* to OA pain, and GPR34 and macrophage gene expression in human DRGs.

Disclosure: D. Thomas, Rheumatology Research Foundation, 5; **T. Geraghty**, NIH NIAMS, 5; **A. Obeidat**, None; **J. Li**, None; **R. Miller**, NIH NIAMS, 5; **A. Malfait**, Pfizer, 2, Eli Lilly, 2, Ceva, 2, AKP, 2, NIH NIAMS, 5, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 1479

CD14, a Toll-like Receptor Co-Factor, Influences Osteoclast Differentiation and Activity, but Does Not Alter Osteoblastic Potential of Bone-Marrow Precursors in Mice

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SESSION INFORMATION

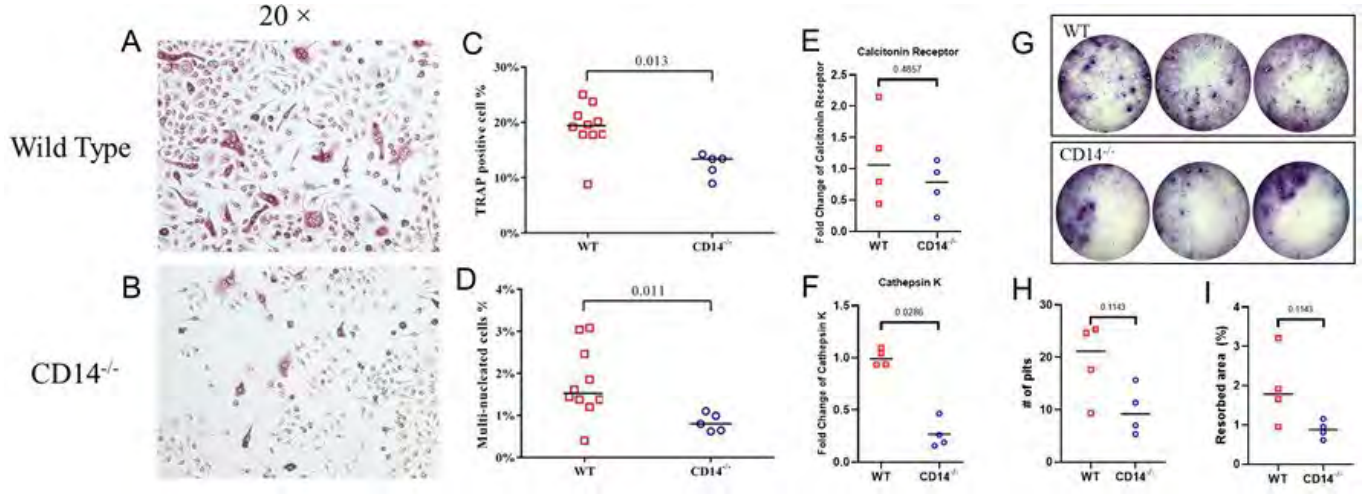
Session Date: Tuesday, November 9, 2021
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster (1468–1479)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Changes in subchondral bone structure (SCB) occur in osteoarthritis (OA), and are visible by imaging as subchondral sclerosis on radiographs, and bone marrow lesions (BMLs) by MRI. These changes are the result of active bone remodeling that occurs in OA. BMLs are correlated with pain in OA patients. We previously demonstrated that bone remodeling was significantly reduced after joint injury in mice deficient in CD14. CD14 enhances Toll-like receptor (TLR) mediated inflammation by acting as a co-receptor for multiple TLRs, increasing TLR sensitivity to damage associated molecular patterns (DAMPS) to activate proinflammatory signaling pathways. Soluble CD14 (sCD14), TLRs, and DAMPs (TLR ligands) are all elevated in OA, and sCD14 has been implicated as a biomarker of symptom and structural severity in OA. Increasing evidence suggests TLR signaling influences bone remodeling as well, through activation of osteoclast precursor cells, but the specific role of CD14 on this process is unknown. Here, we investigate the potential mechanism by which CD14 influences bone remodeling through *in vitro* analysis of osteoclastogenic and osteoblastic potential.

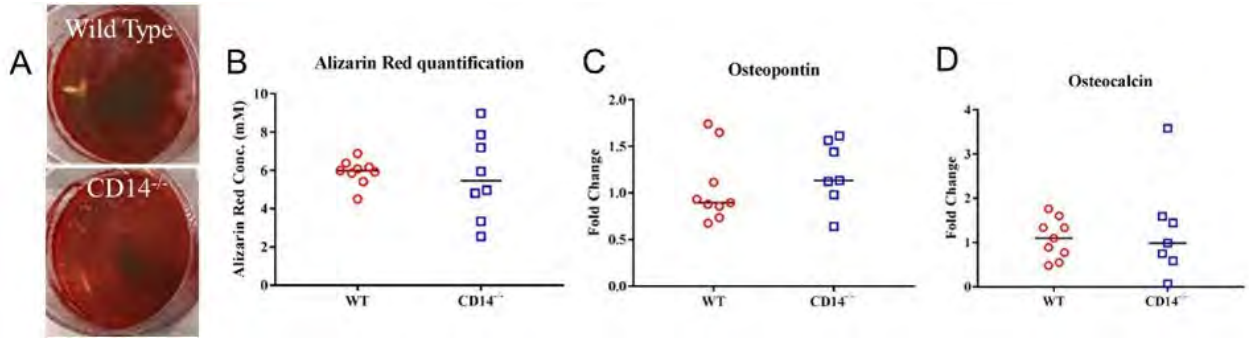
Methods: Bone marrow (BM) hematopoietic and mesenchymal precursors were isolated from long bones of male wild-type C57BL/6 (WT) and CD14-deficient ($CD14^{-/-}$) mice (12 weeks). BM cells flushed from long bones were cultured for 1 day to separate non-adherent from adherent population. Osteoclast differentiation (non-adherent cells) was stimulated by M-CSF and RANKL for 5 days. Osteoblastic cultures (adherent cells) were stimulated with β-glycerophosphate, ascorbic acid, and Dexamethasone for 19 days. Osteoclasts were identified as TRAP-positive multinucleated cells. Osteoclast activity was assessed by resorption assays on bone slices and toluidine blue staining. Osteoblast cultures were stained with Alizarin red to detect mineralization. RT-qPCR analysis was performed to detect mRNA levels of osteoclast (calcitonin receptor/CTR and cathepsin K/Ctsk) and osteoblast (osteopontin/OPN and osteocalcin/BLAP) differentiation markers.

Results: $CD14^{-/-}$ BM cells had reduced number of TRAP positive and multinucleated cells ($p = 0.01$; **Figure 1 A-D**) and reduced Ctsk mRNA ($p = 0.03$; **Figure 1 E&F**), compared to WT. $CD14^{-/-}$ cells showed a 50% reduction in resorption activity compared to WT (**Figure 1 G-I**). No significant differences were observed between strains in osteoblastic potential measured by mineralization and mRNA levels of osteoblastic markers (**Figure 2**).

Conclusion: $CD14^{-/-}$ BM precursor cells have reduced capacity to differentiate into osteoclasts, while osteoblastic potential is retained. This suggests that the reduced capacity of $CD14^{-/-}$ osteoclastic cells may impact bone remodeling in response to joint injury by disrupting the balance between resorption and formation. Future experiments will determine the influence of DAMPs relevant to OA pathogenesis on osteoclastogenesis, and the density of osteoclasts and precursors in SCB after injury. These experiments will lead to a better understanding CD14/ TLR signaling in SCB remodeling following joint injury and OA, and the potential for CD14 blockade to prevent pathologic bone remodeling in disease.



Representative TRAP staining from (A) wild type mice and (B) CD14-/- mice. (C) TRAP positive cells and (D) multinucleated cells quantitated by automated image analysis using ImageJ software. mRNA for CTR (E) and Ctsk (F) quantitated by qPCR. (G) Osteoclast activity was assayed by quantifying the (H) number of resorption pits and (I) resorption area on bone slices stained with toluidine blue.



(A&B) Alizarin Red staining of WT and CD14-/- BMMSCs after differentiation. No differences were observed between strains. This was confirmed by measuring mRNA levels of osteoblastic markers, (C) osteopontin and (D) osteocalcin.

Disclosure: J. Martinez, None; **V. Nguyen**, None; **C. Zhou**, None; **G. Dodge**, None; **C. Scanzello**, None.

Abstract Number: 1480

LncRNA *XIST* Alters the Balance of Peripheral Blood Immune Cells in Systemic Lupus Erythematosus by Regulating the *miR-17-92/OFLM4* and *CEACAM8* Axis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: X-inactive-specific transcript (*XIST*) has been shown to silence linked genes on the X chromosome that may be related to the pathogenesis of systemic lupus erythematosus (SLE) in female patients. However, the function of XIST in SLE at other levels remains unclear. The present study aimed to clarify the correlations between *XIST* expression and SLE clinical features and the contribution of *XIST* to SLE pathogenesis at the transcriptome level.

Methods: Expression of *XIST* in 79 SLE patients and 23 healthy controls was detected by quantitative-polymerase chain reaction. Bioinformatics methods were used to explore the function and regulatory mechanism of *XIST*.

Results: Expression of XIST was significantly upregulated in SLE patients compared with healthy controls (Figure 1A, $p = 0.0043$), and had a high diagnostic value for SLE (Figure 1B, AUC = 0.762, 95% CI: 0.658 to 0.867, $p = 0.000136$). Compared with male patients and older patients, *XIST* was significantly upregulated in female patients (Figure 1C, $p = 0.0162$) and younger patients (Figure 1D, $p = 0.0429$). Moreover, *XIST* was highly expressed in patients with arthralgia (Figure 1E, $p = 0.0222$). Importantly, SLE patients with high expression of XIST tended to have elevated levels of total T cells and CD8+ T cells, but reduced levels of Treg cells and NK cells. Bioinformatics analyses suggested that XIST may regulate the expression of *OLFM4* and *CEACAM8* by acting as a spongy body for *miR-20a*, *miR-92a*, *miR-106a*, and *miR-449a* (Figure 2). Furthermore, *OLFM4* and *CEACAM8* are significantly upregulated in SLE patients and had significant positive correlations with expression of *XIST*.

Conclusion: We propose that *XIST* may alter the balance of peripheral blood immune cells in SLE by acting as a spongy body for the *miR-17-92* cluster and promoting the expression of *OLFM4* and *CEACAM8*, resulting in immune dysregulation and tissue damage in SLE.

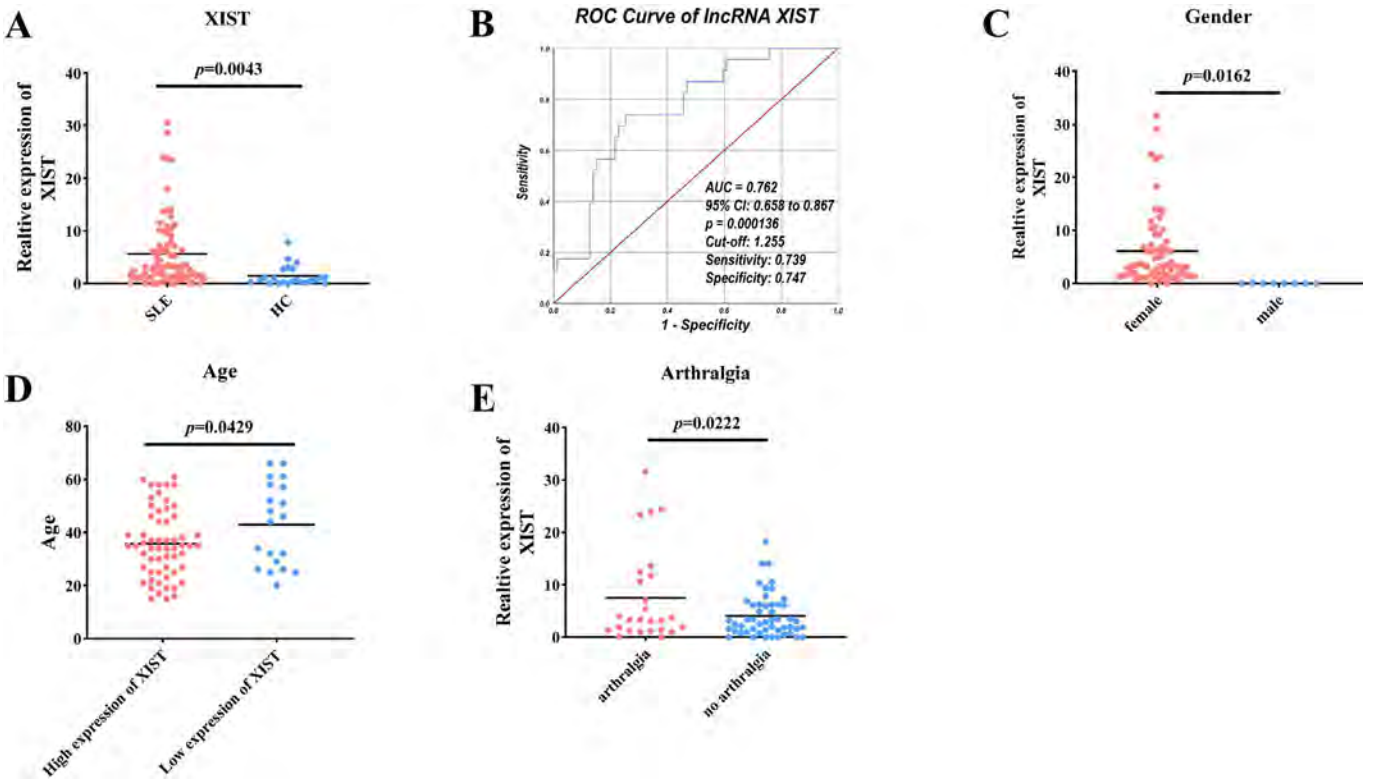

Figure 1. Expression of lncRNA XIST and its diagnostic value for SLE. A. Expression of XIST in SLE patients and healthy controls. B. ROC curves of XIST in the two groups. C and D. XIST is significantly upregulated in female (C) and young (D) patients. E. XIST is highly expressed in patients with arthralgia.

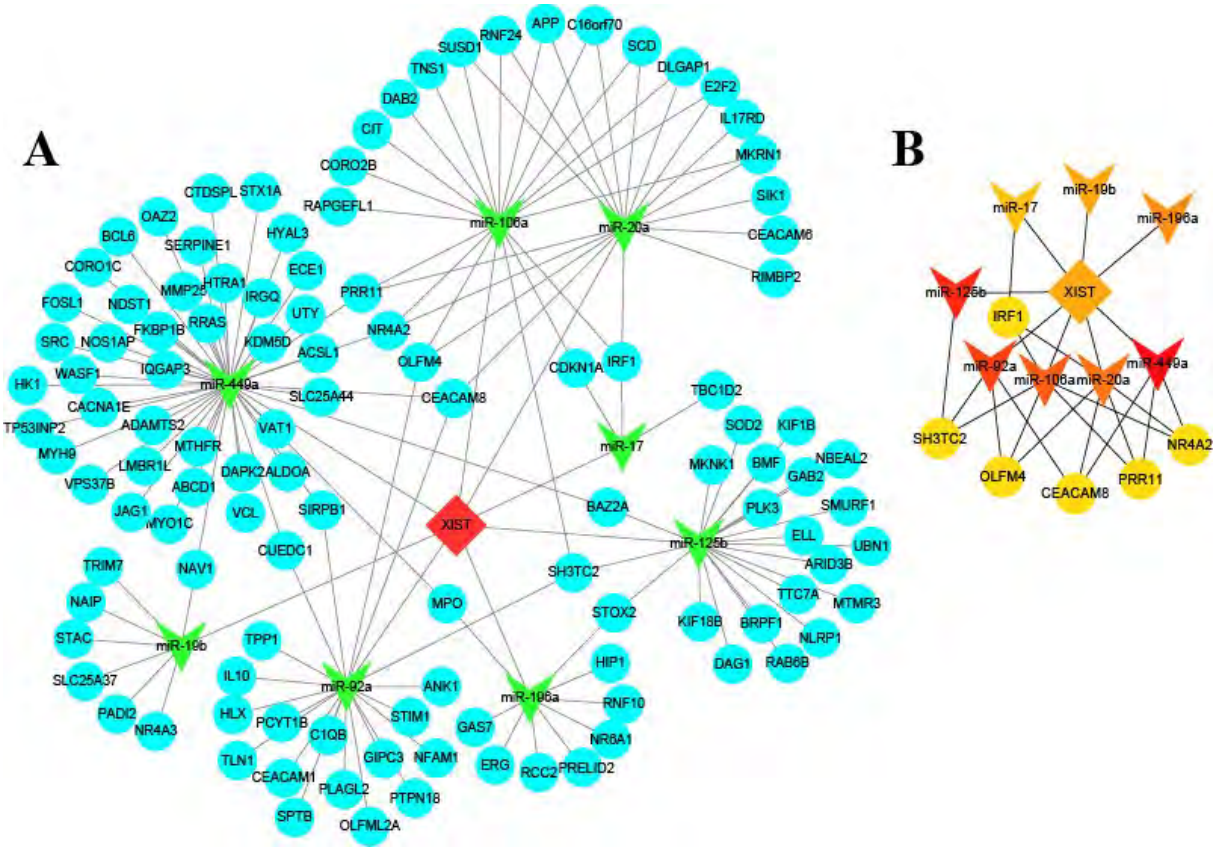

Figure 2. Function and regulatory mechanism of XIST at transcriptome level. A.The ceRNA network was composed of 1 lncRNA, 8 miRNAs, 115 mRNAs, and 150 edges. Each edge represents one interaction between two transcripts. Red diamond, lncRNA; green V, miRNA; sky-blue circle, mRNA. B. Subnetwork of hub transcripts constructed by Cytoscape and its plug-in Cytohubba.

Disclosure: Q. Cheng, None; **M. Chen**, None; **x. Chen**, None; **p. zhang**, None; **h. wu**, None; **y. du**, None.

Abstract Number: 1481

Malondialdehyde-acetaldehyde Antibodies Occur in Systemic Lupus Erythematosus and Associate Specifically with Neuropsychiatric Involvement

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogenous autoimmune disease characterized by a global loss of self-tolerance. Although autoantibodies are an important hallmark of SLE, many autoantibodies are not specific for SLE or for a specific SLE manifestation. Post-translational modifications (PTMs), including citrullination and carbamylation, have been studied extensively in rheumatoid arthritis and antibodies against these PTMs are

Table 1. Prevalence of antibodies against specific post-translational modifications in patients with systemic lupus erythematosus (SLE) and healthy controls

	SLE patients (n = 349)		Healthy controls (n = 108)	
		n, % positive		*n, % positive*
Anti-MAA	35.2 [0 – 428]*	101 (29)	23.0 [0 – 54]	3 (3)
Anti-AGE	111.8 [0 – 1627]*	63 (18)	80.0 [0 – 436]	4 (4)
Anti-CarP	126.3 [0 – 1136]*	49 (14)	34.9 [0 – 1208]	5 (5)
Anti-Cit	3.2 [0 – 201]	22 (6)	3.3 [0 – 32]	3 (3)
Anti-AL	7.8 [0 – 615]	29 (8)	3.8 [0 – 243]	8 (7)
Anti-NT	44.0 [0 - 3510]	17 (5)	9.5 [0 – 3613]	8 (7)

Levels are presented as median [range] * $p \leq 0.0001$

MAA = malondialdehyde-acetaldehyde adduct; AGE = advanced glycation end-product; CarP = carbamylated protein; Cit = citrullinated protein; AL = acetylated protein; NT = nitrated protein.

associated with disease progression. While PTMs have also been detected in SLE patients, studies on the presence of anti-PTM antibodies and the relation to clinical aspects remain limited.

Methods: IgG antibody responses against six PTMs (malondialdehyde-acetaldehyde adducts (MAA), advanced glycation end-products (AGE), carbamylation (CarP), citrullination (Cit), acetylation (AL) and nitration (NT)) were tested using enzyme-linked immunosorbent assays in sera of SLE patients and compared to 108 healthy controls. Serum of SLE patients visiting the neuropsychiatric SLE (NPSLE) clinic of the Leiden University Medical Center between 2007-2019 was used. Levels and positivity of anti-PTM antibodies were correlated with clinical features and SLE manifestations.

Results: 349 patients with SLE were included in this study: 87% female and a mean age of 44 ± 13 years. Anti-MAA, -AGE and -CarP antibodies showed significantly higher positivity in SLE compared to controls, as shown in *Table 1* (all $p \leq 0.0001$). Anti-MAA and anti-AGE antibodies both correlated with clinical and serological measures associated with SLE, including complement consumption (low C3/C4) and Systemic Lupus Erythematosus Disease Activity Index (SLEDAI-2K). Patients with major NPSLE showed higher positivity of anti-MAA antibodies (39 vs 24%, $p = 0.007$) and anti-CarP antibodies (20 vs 11%, $p = 0.042$) compared to patients without NPSLE.

Conclusion: SLE patients have anti-PTM antibodies against MAA, AGE and CarP modified proteins. Interestingly, anti-MAA antibodies clearly associate with major NPSLE, a clinical condition for which virtually no biomarkers exist.

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Abstract Number: 1482

LN Urinary Proteomics Reveals Common Biological Pathways Identified by Distinct Disease Measures

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: LN is a severe consequence of SLE and there is a huge unmet need for discovery of urine protein biomarkers that provide non-invasive surrogates of disease activity and response to therapy. The purpose of this study was to measure protein biomarkers in urine samples from a diverse cohort of LN patients and to assess their correlations with patient demographics and clinical characteristics including the renal measures of estimated glomerular filtration rate (eGFR), SLEDAI-renal (SLEDAI-R) and National Institutes of Health Activity (NIH-AI) and chronicity (NIH-CI) indices

Methods: The demographics and characteristics of the cohort of 112 patients is described in Table 1. All patients fulfilled the 1997 ACR criteria for SLE and all had biopsy-proven LN. Urine samples from patients and 16 healthy donors (HD) were analyzed for 192 proteins by Luminex and 5 by Simoa™. Protein concentrations were normalized to urinary creatinine levels. Log-concentrations of each protein was assessed for correlation with each clinical feature using linear regression adjusted for age, gender, ethnicity, disease duration, and treatment. eGFR was assessed using the cutoff of >60. The Benjamini-Hochberg procedure was used to calculate false discovery rates, with a cut-off of 0.1 used to determine significance. Statistical significance of intersections of protein lists was assessed via permutation. Pathway assessments were conducted using Ingenuity core analysis.

Results: Pre-filtering proteins for LN normalized mean concentrations to be greater than the HD mean + 1.5 SD yielded 97 distinct upregulated proteins. The largest numbers of protein-outcome associations were confounded by age (but not disease duration), gender, and MMF dose. After removing the influence of all confounders, numerous proteins showed statistically significant differential expression with respect to eGFR, SLEDAI-2K, SLEDAI-R, serum C3 and C4, NIH-AI, and NIH-CI. Conversely, no proteins were significantly correlated with LN class, race, or SDI (SLICC/ACR disease Index). The highest numbers of significant proteins were found for eGFR (55 proteins) followed by SLEDAI-R (36) and NIH-AI (20). There was a significant overlap of 11 proteins (Table 2) across these three lists (intersection $p=4.1 \times 10^{-5}$), indicating that these clinical renal measures share common biological processes. Pathway analysis of the 11 common proteins indicated enrichment for functions known to be associated with fatty acid/lipid metabolism, cardiovascular disease, cellular trafficking and immune cell infiltration

Conclusion: By analyzing LN urinary proteomics, we revealed that 3 clinical renal measures: eGFR, SLEDAI-R and NIH-AI are commonly associated with various proteins and pathways, most of which support the emerging importance of renal vascular pathology in LN.

Table 1.

Demographics, treatment and disease characteristics		
Age, years	Median (range)	34.0 (18, 67)
Sex, n (%)	Male	19 (17.0)
Race, n (%)	Asian	18 (16.1)
	Black/African American	7 (6.2)
	American Indian/Alaska Native	2 (1.8)
	Other	35 (31.2)
	Native Hawaiian/Pacific Islander	1 (0.9)
	White	49 (43.8)
Time from initial LN diagnosis, months	Median (range)	8.3 (0, 307)
MMF before randomization, n (%)	Yes	80 (71.4)
MMF Dosage, mg/day	Mean (SD)	1.77 (0.46)
OCS Dosage, n (%)	>20 mg/day	109 (97.3)
OCS Dosage, mg/day	Mean (SD)	22.39 (10.71)
Concomitant ACEI/ARB treatment, n (%)	Yes	81 (72.3)
Baseline 24-hour UPCR, mg/mg, Threshold, n (%)	>3.0	46 (41.1)
Baseline 24-hour UPCR, mg/mg, Continuous	Mean (SD)	3.34 (2.65)
Clinical outcomes		
Baseline eGFR mL/min/1.73m2, Threshold, n (%)	>60	86 (76.8)
Baseline eGFR mL/min/1.73m2, Continuous	Mean (SD)	94.58 (42.86)
LN Class, n (%)	Class II	2 (2.0)
	Class III	22 (21.8)
	Class III and Class V	11 (10.9)
	Class IV	59 (58.4)
	Class IV and Class V	6 (5.9)
	Class V	1 (1.0)
SLEDAI-2K score, Continuous	Mean (SD)	10.76 (4.74)
SLEDAI-R score, Continuous	Mean (SD)	6.11 (3.32)
SDI score, n (%)	0	70 (63.6)
	1	29 (26.4)
	2	9 (8.2)
	3	1 (0.9)
	4	1 (0.9)
NIH Lupus Nephritis Activity Index, n (%)	High (>8)	35 (34.7)
NIH Lupus Nephritis Chronicity Index, n (%)	High (>4)	31 (30.7)
Serum C3, n (%)	Low C3	75 (67.0)
Serum C4, n (%)	Low C4	32 (28.6)

Table 2. 11 urinary proteins which reached statistical significance (false discovery rate <0.1) for association with eGFR, SLEDAI-R and NIH-AI

Urinary Protein
Adiponectin
Alpha-2-Macroglobulin (A2Macro)
Apolipoprotein A-I (Apo A-I)
Apolipoprotein B (Apo B)
Apolipoprotein C-I (Apo C-I)
Apolipoprotein C-III (Apo C-III)
Lactoferrin (LTF)
Neuropilin-1
Omentin
Serum Amyloid P-Component (SAP)
von Willebrand Factor (vWF)

Disclosure: P. Newcombe, AstraZeneca, 3; **M. Ramaswamy**, AstraZeneca, 3; **D. Sinibaldi**, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **F. Jones**, AstraZeneca, 3; **A. Akhgar**, AstraZeneca, 3; **P. Brohawn**, AstraZeneca, 3, 11, Immunocore, 3; **R. Tummala**, AstraZeneca, 3; **W. White**, AstraZeneca, 3, 11.

Abstract Number: 1483

Down-regulation of Hematopoietic Progenitor Kinase 1 by Aberrant Epigenetic Alterations in T Follicular Helper Cells Accounts for Excessive Immunity in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Recently, T follicular helper cells (Tfh cells) have been discovered to be the main $CD4^+$ T cells assisting B cells to produce antibody. Tfh cells are over activated in patients with systemic lupus erythematosus (SLE), consequently lead to excessive immunity. Hematopoietic progenitor kinase 1 (HPK1) negatively regulates T cell-mediated immune responses and TCR signal. This study aims to investigate the roles of HPK1 and the mechanisms that regulate HPK1 expression in SLE Tfh cells.

Methods: Naive $CD4^+$ T cells and B cells were isolated from 30 normal controls and 30 SLE patients. Subsequently naive $CD4^+$ T cells were induced to differentiate into Tfh cells by culturing with anti-CD3 antibody, anti-CD28 antibody, IL-6, IL-12, IL-21, and TGF-β. HPK1 mRNA and protein levels in Tfh cells were measured by quantitative PCR (qPCR) and western blot analysis respectively. The productions of IL-21, BAFF, IFNγ, IL-17A, IgM, IgG1, IgG2, and IgG3 were analyzed using ELISA. Tfh cells proliferation was evaluated with MTT assay. Numbers of histone H3 lysine 27 trimethylation (H3K27me3), H3K27 methyltransferase enhancer of zeste homolog 2 (EZH2), H3K27 demethylase jumonji domain containing 3 (JMJD3), and DNA methyltransferase 3a (DNMT3a) within the HPK1 promoter were determined by chromatin immunoprecipitation (ChIP) combined with qPCR. DNA methylation abundance at the HPK1 promoter was assessed by methylated DNA immunoprecipitation (MeDIP) combined with qPCR.

Results: HPK1 mRNA and protein levels were significantly reduced in SLE Tfh cells, and HPK1 mRNA level negatively correlated with SLE Disease Activity Index (SLEDAI). Knocking down HPK1 with siRNA in normal Tfh cells significantly elevated Tfh cells proliferation and secretions of IL-21, BAFF, IFNγ, IgG1, IgG2, and IgG3. There were no marked alters in IL-17A and IgM productions. The opposite effects were observed in SLE Tfh cells transfected with HPK1 overexpressing plasmid: Tfh cells proliferation and productions of IL-21, BAFF, IFNγ, IgG1, IgG2, and IgG3 were all alleviated. And there were no significant changes in IL-17A and IgM levels. H3K27me3, DNA methylation, and DNMT3a amounts sharply increased at the HPK1 promoter in SLE Tfh cells compared to controls. Moreover, a striking decrease was detected in JMJD3 enrichment, but no marked change in EZH2 number at the HPK1 promoter of Tfh cells from patients with SLE.

Conclusion: Our results suggest for the first time that at the HPK1 promote region of SLE Tfh cells, decreased JMJD3 binding up-regulates H3K27me3 amount, and increased DNMT3a enrichment elevates DNA methylation level. All these factors inhibit expression of HPK1 in SLE Tfh cells, leading to Tfh cells overactivation and B cells overstimulation, subsequently, the onset and progression of SLE.

Disclosure: Q. Zhang, None; **H. Zhang**, None; **Y. Xie**, None.

Abstract Number: 1484

B Cell Intracellular IFNβ as a Unique Cellular Marker for the Development of Lupus Nephritis

Fatima Alduraibi[1], Huma Fatima[1], Winn Chatham[2], Hui-Chen Hsu[1] and John Mountz[1], [1]University of Alabama Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
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Background/Purpose: Our laboratory previously demonstrated a strong association of B cell intracellular interferon beta (IFNβ) with the development of anti-Smith/ribonuclear protein (Sm/RNP), anti-DNA, and lupus nephritis (LN) in African American (AA) systemic lupus erythematosus (SLE) patients. The objective of the present study is to determine if B cell IFNβ can be a unique SLE clinical prognostic marker and if specific histopathologic features of LN can be identified in patients with elevated B cell IFNβ.

Methods: All patients (N=80) met American College of Rheumatology (ACR) 1997 revised SLE criteria, ACR/EULAR classification criteria of SLE or Systemic Lupus International Collaborating Clinics (SLICC) classification criteria were recruited. Demographic, clinical data, and serologic manifestations included creatinine, urine protein/creatinine ratio, anti-DNA, anti-Sm, C3, and C4 were included. Intracellular IFNβ in naïve B cells was analyzed using high dimensional flow cytometry analysis. Isotype specific (IgG and IgM) anti-Sm/RNP and anti-DNA were measured using a standard ELISA method. LN class was defined based on the revised ISN/RPS (2004) criteria and included renal histopathology findings on light, electron microscopy, and immunofluorescence (IF) for IgM, IgG, IgA, C1q, and C3 staining (N=23).

Results: The most common manifestations were arthritis in 68% (n=54), photosensitivity rash in 47% (n=38), LN in 41% (n=33), and oral ulcer in 40% (n=32) of SLE patients. There was a significant positive correlation between naïve B cell IFNβ with race (AA > European American) and LN class (P=0.006, P< 0.0001, respectively). Naïve B cell IFNβ is negatively correlated with photosensitivity (P=0.0451) and oral/nasal ulcer (P=0.0031), and it did not correlate with other symptoms of SLE. Patients with elevated serum anti-Sm (P=0.032 by history; P=0.01 at the time enrollment) and anti-DNA (P=0.013 at the time enrollment) exhibited significantly higher naïve B cell IFNβ. Further, SLE patients with a higher percentage of intracellular IFNβ in naïve B cells also showed a higher serum C3 (P=0.005) and a lower circulating protein/creatinine ratio (P=0.065). Unsupervised ClustVis analysis was used to cluster histologic features associated with B cell intracellular IFNβ into two groups (Figure 1). LN group 1 (n=13) exhibited low activity (1.8±3.9, p=0.0018) and chronicity index (1.5±0.8, p=0.072) with a lower naïve B cell intracellular IFNβ (46±29%, p=0.0041) compere to LN group 2 (n=10) with high activity (5.9±3.8) and chronicity index (3.0±2.1) with a higher naïve B cell intracellular IFNβ (82±20%) (Figure 1). There was a lower incidence of wire loop lesions (p=0.0944), fibrocellular crescents (p=0.0005), fibrous crescents (p=0.0237), endocapillary hypercellularity (p=0.0449), and segmental scaring (p=0.0045) in LN group 1 compared to LN group 2 patients. Immunofluorescence did not show the significance for IgG, IgM, IgA, and C1q, and C3.

Conclusion: Our results suggest that B-cell intracellular IFNβ can be used in combination with other clinical diagnostic markers to identify patients at high risk of developing advanced LN. IFNβ blockade may be developed into individualized therapy for this subset of SLE patients.

Disclosure: F. Alduraibi, None; **H. Fatima**, None; **W. Chatham**, None; **H. Hsu**, None; **J. Mountz**, None.

Abstract Number: 1485

Glycosphingolipids: Potential Urine Biomarkers of Therapeutic Response in Lupus Nephritis

Tammy Nowling, Jessalyn Rodgers, Bethany Wolf, Brian Troyer and Jim Oates, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
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Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is a chronic, immune complex-mediated glomerulonephritis affecting up to 60% of patients with lupus. Progression of the most aggressive forms of LN (proliferative classes III and IV) to end-stage renal failure is ~20% and another ~40% develop chronic kidney disease despite aggressive treatment. Patients that fail to respond continue to accumulate organ damage. Thus, there is a critical need for noninvasive biomarkers

to predict therapeutic response. We previously demonstrated that the glycosphingolipid (GSL) lactosylceramide (LacCer) is elevated in the urine of lupus patients, and preliminary data suggests that GSLs in extracellular vesicles (EVs) in urine are higher prior to treatment in patients that do not respond to treatment. Thus, we compared levels of GSLs in urine EVs in longitudinal samples from LN patients that completely responded (CR) or did not respond (NR) to MMF treatment after one year of treatment.

Methods: EVs were isolated from longitudinal (baseline, and 3 or 12 months post-treatment) urine samples obtained from 59 LN patients (29 CR, 30 NR). All patients met ACR classification for SLE with biopsy-confirmed nephritis (93% with class III or IV LN). Criteria for CR included UPr:UCr < 0.5, normal sCr, inactive urine sediment, UPr:UCr reduced >75%, and eGFR increased >25%. NR criteria included persistent UPr:UCr >3, decreased UPr:UCr < 25%, eGFR decreased >25%, and failure to taper glucocorticoid therapy to < 10 mg/day. GSLs were quantified in the urine EV samples by SFC/MS/MS. Galectin-3 binding protein (G3BP) and gelsolin, identified in a small proteomics screen, were quantified in the urine EV samples or total urine using independent ELISAs. A panel of cytokines and chemokines were measured in total urine samples by a multiplex laser bead array.

Results: All chain lengths of Hexosylceramides (HexCers) were significantly higher ($p< 0.001$) in the baseline EV samples from NR patients (total HexCers, 48.6 ±56.9 pmol/ml/mg UCr) compared to CR patients (total HexCers, 11.7 ± 13.4 pmol/ml/mg UCr). All chain lengths of LacCers were significantly higher ($p< 0.001$) in the baseline EV samples from NR patients (total LacCers, 13.5 ± 10.9 pmol/ml/mg UCr) compared to CR patients (total LacCers, 3.5 ± 4.1 pmol/ml/mg UCr). Gelsolin levels in total urine, but not in urine EVs, were significantly different ($p=0.003$) between NR (574.8 ± 473.3 ng/mg UCr) and CR (178.1 ± 177.9 ng/mg UCr) at baseline. Total urine G3BP levels were significantly higher ($p=0.039$) in NR (282.4 ± 421.4 ng/mg UCr) compared to CR (115.2 ± 146.4 ng/mg UCr). Of the 23 cytokines/chemokines measured in total urine, 18 were detected and all 18 were significantly or showed a trends of higher levels in NR compared to CR.

Conclusion: These results suggest that in general, patients that failed to respond to therapy likely had worse disease prior to starting therapy. Urine EV levels of HexCers and LacCers, along with urinary levels of a panel of proinflammatory factors and clinical measures may be useful in identifying LN patients prior to beginning treatment that are unlikely to respond to conventional therapies.

Disclosure: T. Nowling, None; **J. Rodgers**, None; **B. Wolf**, None; **B. Troyer**, None; **J. Oates**, None.

Abstract Number: 1486

A Novel Requirement for IFNβ1 Signaling for IFNκ Induction in Keratinocytes

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) affects up to 70% of patients with systemic lupus erythematosus (SLE), and type I interferons (IFNs) are important promoters of SLE and CLE. Our previous work identified

IFN-kappa (IFNκ), a keratinocyte-produced type I IFN, as upregulated in non-lesional and lesional lupus skin and a critical regulator for enhanced UVB-mediated cell death in SLE keratinocytes. Importantly, the molecular mechanisms governing regulation of IFNκ expression have been relatively unexplored. Thus, this study sought to identify critical regulators of IFNκ and identified a novel role for IFN beta (IFNβ).

Methods: Human N/TERT keratinocytes were treated with the RNA mimic poly (I:C) or 50 mJ/cm^2 ultraviolet B (UVB), followed by mRNA expression quantification by RT-qPCR in the presence or absence of the JAK1 inhibitor baricitinib (BARI) or a neutralizing antibody to the type I IFN receptor (IFNAR). *IFNB, MYD88, IFNK, STAT1,* and *TMEM173* knockout (KO) keratinocytes were generated using CRISPR/Cas9.

Results: Time courses of poly-IC and UVB treatment revealed a differential expression of IFN genes: IFNβ was upregulated between 3-6 hours and IFNκ was upregulated 24 hours after stimulation. Intriguingly, while the upregulation of IFNβ and IFNκ was inhibited by baricitinib, only IFNκ expression was substantially abrogated by neutralizing antibodies to IFNAR, suggesting that only IFNκ upregulation required type I IFN signaling for induction. This was confirmed using *STAT1* KO keratinocytes which exhibited normal upregulation of *IFNB* but no upregulation of *IFNK* after poly-IC and UVB. The sequential nature of transcription, specifically *IFNB* followed by *IFNK* upregulation with both poly-IC and UVB treatment suggests that IFNβ1 may play a role in regulation of IFNk induction in KC. Indeed, *IFNB1* KO keratinocytes abrogated *IFNK* induction and the downstream IFN-stimulated gene MX1 expression in response to either PolyIC or UVB, suggesting that robust IFN-κ production is dependent on an initial upregulation of *IFNB*.

Conclusion: Collectively, our work describes a novel mechanistic paradigm in keratinocytes in which initial *IFNK* induction in response to PolyIC and UVB is IFNβ1-dependent. Loss of this regulatory dependence in SLE keratinocytes could be an explanation as to why IFNκ is increased in SLE skin. Further experiments to determine if this mechanism is intact or skewed in SLE keratinocytes are ongoing.

Disclosure: B. Xu, None; **Y. Tan**, None; **J. Musai**, None; **W. Swindell**, Sytheon LTD, 2; **M. Sakar**, None; **J. Gudjonsson**, BMS, 5, Eli Lilly, 5, Janssen, 5, Sanofi, 1; **J. Kahlenberg**, astrazeneca, 1, Janssen, 5, Bristol Myers Squibb, 1, 5, q32 Bio, 5, Ventus Therapeutics, 2, Eli Lilly, 1, GlaxoSmithKlein, 1; **G. Hile**, None.

Abstract Number: 1487

Type I Interferon Modulates Langerhans Cell ADAM17 in Lupus to Contribute to Photosensitivity

Thomas Li[1], Keila Veiga[2], Noa Schwartz[3], Jose Lora[4], Yong Liu[4], Ali Jabbari[5], William Shipman[1], Mehdi Rashighi[6], James Krueger[7], Niroshana Anandasabapathy[4], David Oliver[8], Yurii Chinenov[8], Carl Blobel[1] and Theresa Lu[1], [1]Hospital for Special Surgery, New York, NY, [2]New York Medical College, Hawthorne, NY, [3]Albert Einstein College of Medicine/Montefiore Medical Center, New York, NY, [4]Weill Cornell Medicine, New York, NY, [5]University of Iowa, Iowa City, IA, [6]University of Massachusetts Medical School, Worcester, MA, [7]Rockefeller University, New York, NY, [8]David Z. Rosensweig Genomics Research Center, Hospital for Special Surgery, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Photosensitivity is a common feature in the autoimmune disease lupus erythematosus (LE) where patients develop inflammatory skin lesions in response to ultraviolet radiation (UVR). In patients with the sys-

temic form of the disease (SLE), photosensitivity can also be associated with serious flares of systemic disease. As current treatments are limited, mechanistic understanding of photosensitivity can lead to better care and quality of life. We recently showed that Langerhans cells (LCs) limit UVR-induced keratinocyte apoptosis and skin injury via ADAM17-mediated EGFR ligand activation and that reduced LC ADAM17 activity in two lupus models contributed to their photosensitivity. However, what causes LC dysfunction in the lupus models is not known. Type I interferon (IFN-I) is elevated in SLE non-lesional skin, and anifrolumab (anti-IFNAR) showed efficacy in human cutaneous disease, suggesting a pathogenic role for IFN-I in SLE skin. This led us to assess a role for IFN-I in LC ADAM17 dysfunction.

Methods: To assess IFN-I gene signature, microarray of non-lesional skin from human cutaneous LE and RNA sequencing of whole skin from lupus mouse models were performed. To quantify LC ADAM17 activity and expression, flow cytometric-based assays were conducted using human and murine LCs. To evaluate photosensitivity, skin inflammation and cellular infiltrate were measured and characterized using *in vivo* lupus models.

Results: We show that non-lesional skin from human cutaneous LE and photosensitive MRL/lpr and B6.Sle1yaa mice have IFN-I signatures and that IFN-I is sufficient to reduce human and murine LC ADAM17 activity independently of surface ADAM17 levels. IFN-I-induced LC ADAM17 activity defects were abrogated with tofaticinib, a JAK kinase inhibitor approved for rheumatoid arthritis and other inflammatory diseases. We further show that anti-IFNAR1 treatment prior to UVR exposure in lupus models restores LC ADAM17 activity and limits photosensitivity.

Conclusion: Together, our results suggest that LC ADAM17 is dysregulated by the elevated IFN-I associated with disease and IFN-I contributes to LE skin disease, in part, by causing LC dysfunction.

Disclosure: T. Li, None; **K. Veiga**, None; **N. Schwartz**, None; **J. Lora**, None; **Y. Liu**, None; **A. Jabbari**, None; **W. Shipman**, None; **M. Rashighi**, None; **J. Krueger**, Amgen, 2, Boehringer Ingelheim, 2, Bristol Myers Squibb, 2, Dermira, 2, Innovaderm, 2, Janssen, 2, Kadmon, 2, Kineta, 2, Kyowa, 2, LEO Pharma, 2, Lilly, 2, Novartis, 2, Paraxel, 2, Pfizer, 2, Provectus, 2, Regeneron, 2, Vitae, 2; **N. Anandasabapathy**, Veila Biosciences, 2; **D. Oliver**, None; **Y. Chinenov**, None; **C. Blobel**, SciRhom, 1, 2, 5, 8, 10; **T. Lu**, None.

Abstract Number: 1488

Metabolic Alterations of Systemic Lupus Erythematosus NK Cells Determine Response to Anti-CD38 and Anti-SLAMF7 Monoclonal Antibodies

Morgane Humbel, Natalia Fluder, Florence Bellanger, Alice Horisberger, Craig Fenwick, Camillo Ribi and Denis Comte, CHUV, Lausanne, Switzerland

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem inflammatory condition of unknown pathogenesis. We have previously shown that SLE Natural killer (NK) cells are decreased in count and display a dysfunctional cytotoxicity. In addition, engagement of SLAMF7 with elotuzumab and CD38 with daratumumab restores the cytotoxic capacity of SLE NK cells. Furthermore, priming of SLE NK cells with daratumumab promotes the specific destruction of antibody-producing circulating plasma cells (cPC).

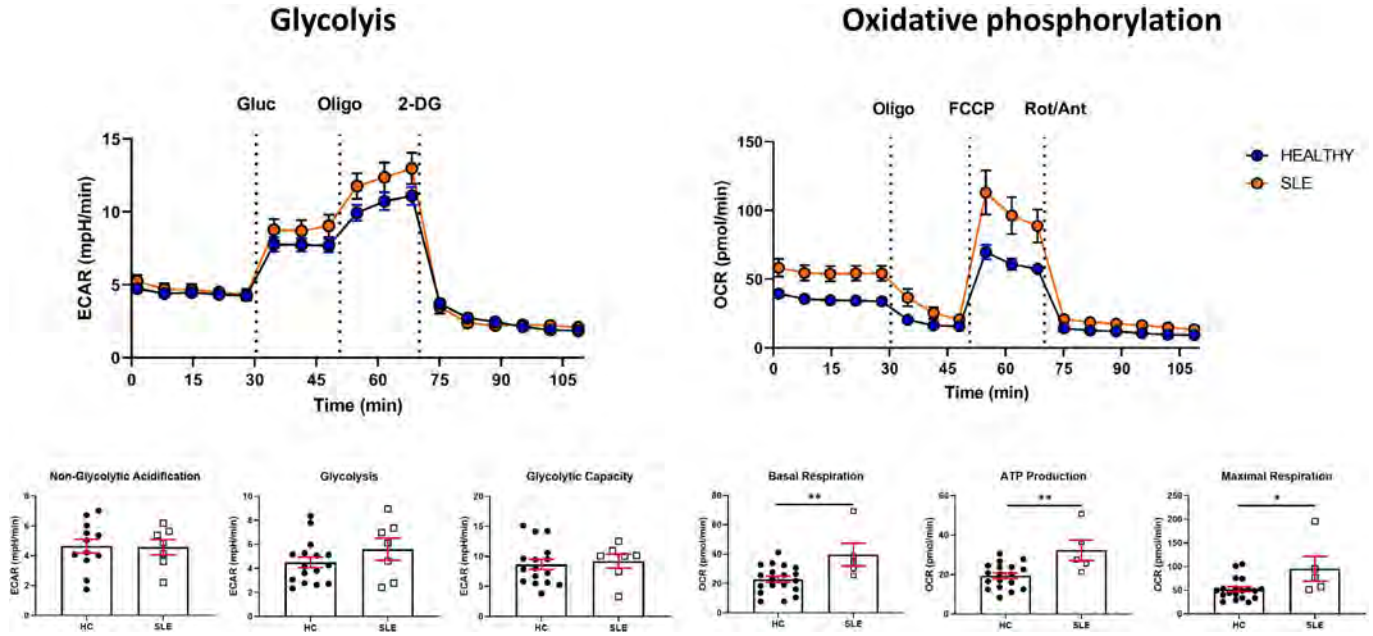

Figure 1. Oxidative phosphorylaation is increased in SLE NK cells. Glycolytic metabolism measured as extracellular acidification rate (ECAR) upon addition of glucose (Gluc), oligomycin (Oligo) and 2-Deoxy-glucose (2-DG) in NK cells of HC (n=13) and SLE (n=7) shows no statistical difference (Welch's T-test, points represent mean±SEM). Oxidative phosphorylation measured as oxygen consumption rate (OCR) upont addition of oligomycin (Oligo), FCCP, rotenone and antimycin-A (Rot/AA) in NK cells of HC (n=19) and SLE (n=9) shows a significatively higher basal respiration, ATP production and maximal respiration in SLE NK cells (Welch's T test, p*<0.003, **p<0.002, ***p<0.001).

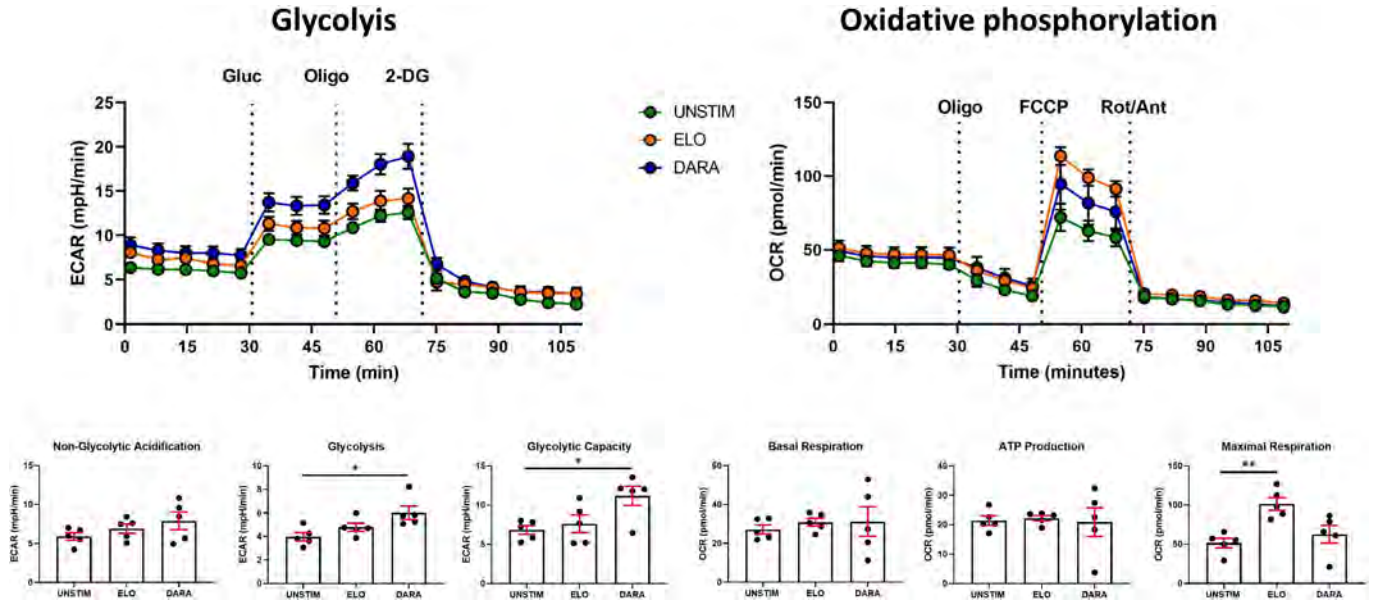

Figure 2. Daratumumab primarily promotes glycolysis and elotuzumab oxidative phosphorylation of NK cells. Stimulation of healthy NK cells with daratumumab significantly promotes glycolysis and glycolytic capacity compared to unstimulated condition (n=5,One-way ANOVA). Stimulation of healthy NK cells with elotuzumab significantly increases the maximal respiration (n=5, One-way ANOVA, p*<0.003, **p<0.002, ***p<0.001).

To deeper understand the alterations that characterize SLE NK cells and the contribution of CD38 and SLAMF7 in their dysfunction, we examined the cellular metabolism of SLE NK cell and how the ligation of daratumumab and elotuzumab influences the major metabolic pathways involved in NK cell activation.

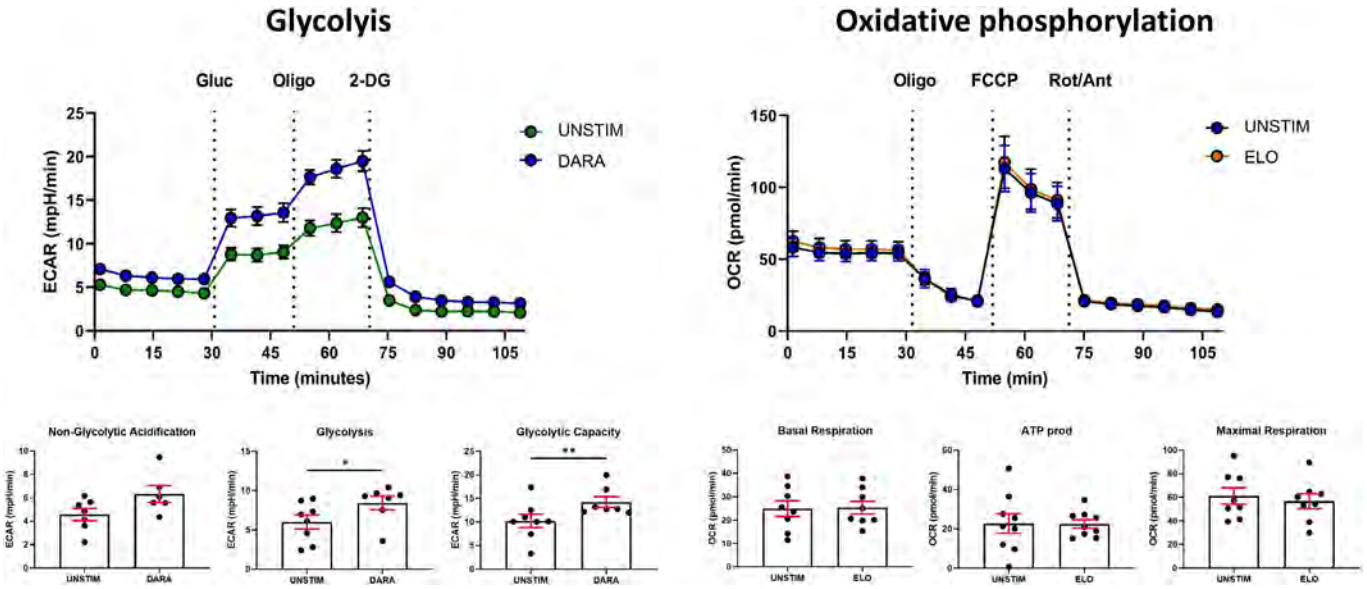

Figure 3. Daratumumab promotes glycolysis but elotuzumab has no effect on oxidative phosphorylation of SLE NK cells. Stimualtion of SLE NK cells with daratumumab significantly increases glycolysis and glycolytic capacity (n=7, Welch's T test), similarly to what was observed on healthy cells. Stimualtion of SLE NK cells with elotuzumab, contrarily to what was observed in healthy cells, has no impact on the oxidative phosphorylation (n=9, Welch's T test, p*<0.003, **p<0.002, ***p<0.001).

Methods: Cryopreserved PBMC from SLE patients and healthy controls were thawed to isolate NK cells by positive selection. Immunometabolism was assessed using XFe96 Seahorse. Analysis of glycolysis was measured by extracellular acidification rate (ECAR) and oxidative phosphorylation by oxidative consumption rate (OCR), after stimulations with mentioned conditions.

Results: We analyzed the cellular metabolic alterations of SLE NK cells. We showed that SLE NK cellular glycolysis is unaltered compared to healthy NK cells, whereas oxidative phosphorylation is increased (Figure1). In addition, the engagement of CD38 with daratumumab and SLAMF7 with elotuzumab activated different metabolic pathways in healthy NK cells: daratumumab primarily enhanced NK cell glycolysis, while elotuzumab increased oxidative phosphorylation (Figure 2). In SLE patients, daratumumab increased NK cell cellular glycolysis and had no significant effect on oxidative phosphorylation, while elotuzumab showed no significant effect on glycolysis or oxidative phosphorylation (Figure 3).

Conclusion: SLE NK cells exhibit abnormally high oxidative phosphorylation, while cellular glycolysis is normal.

Additionally, daratumumab and elotuzumab both enhance the degranulation of SLE NK cells, but only SLE NK cells activated with daratumumab have the ability to kill cPC, thus limiting the production of autoantibodies. This difference is likely explained by the fact that the two antibodies activate NK cells by enhancing two different metabolic pathways. Daratumumab primarily promotes glycolysis, while elotuzumab mainly increases oxidative phosphorylation, which is already abnormally high in SLE NK cells and cannot be increased further.

Disclosure: M. Humbel, None; **N. Fluder**, None; **F. Bellanger**, None; **A. Horisberger**, None; **C. Fenwick**, None; **C. Ribi**, None; **D. Comte**, None.

Abstract Number: 1489

Identification of Mitochondrial Antigens Targeted by Autoantibodies in Systemic Lupus Erythematosus (SLE)

Yann BECKER[1], Jean-Philippe Gagné[2], Anne-Sophie Julien[3], Tania Lévesque[1], Nadine Gougeard[4], Vicente Rubio[4], François-Michel Boisvert[5], Dominique Jean[6], Guy Poirier[2], Paul R Fortin[7] and Éric Boilard[1], [1]Centre de Recherche ARThrite, Université Laval, Québec City, QC, Canada, [2]Centre de Recherche du Centre Hospitalier Universitaire de Québec - Université Laval, Québec City, QC, Canada, [3]Département de mathématiques et statistique, Université Laval, Québec, QC, Canada, [4]Structural Enzymopathology Unit, Instituto de Biomedicina de Valencia, Consejo Superior de Investigaciones Científicas, Valencia, Spain, [5]Department of Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, QC, Canada, [6]Department of Anatomy and Cell Biology, Université de Sherbrooke, Sherbrooke, Canada, [7]CHU de Quebec - Universite Laval, Québec City, QC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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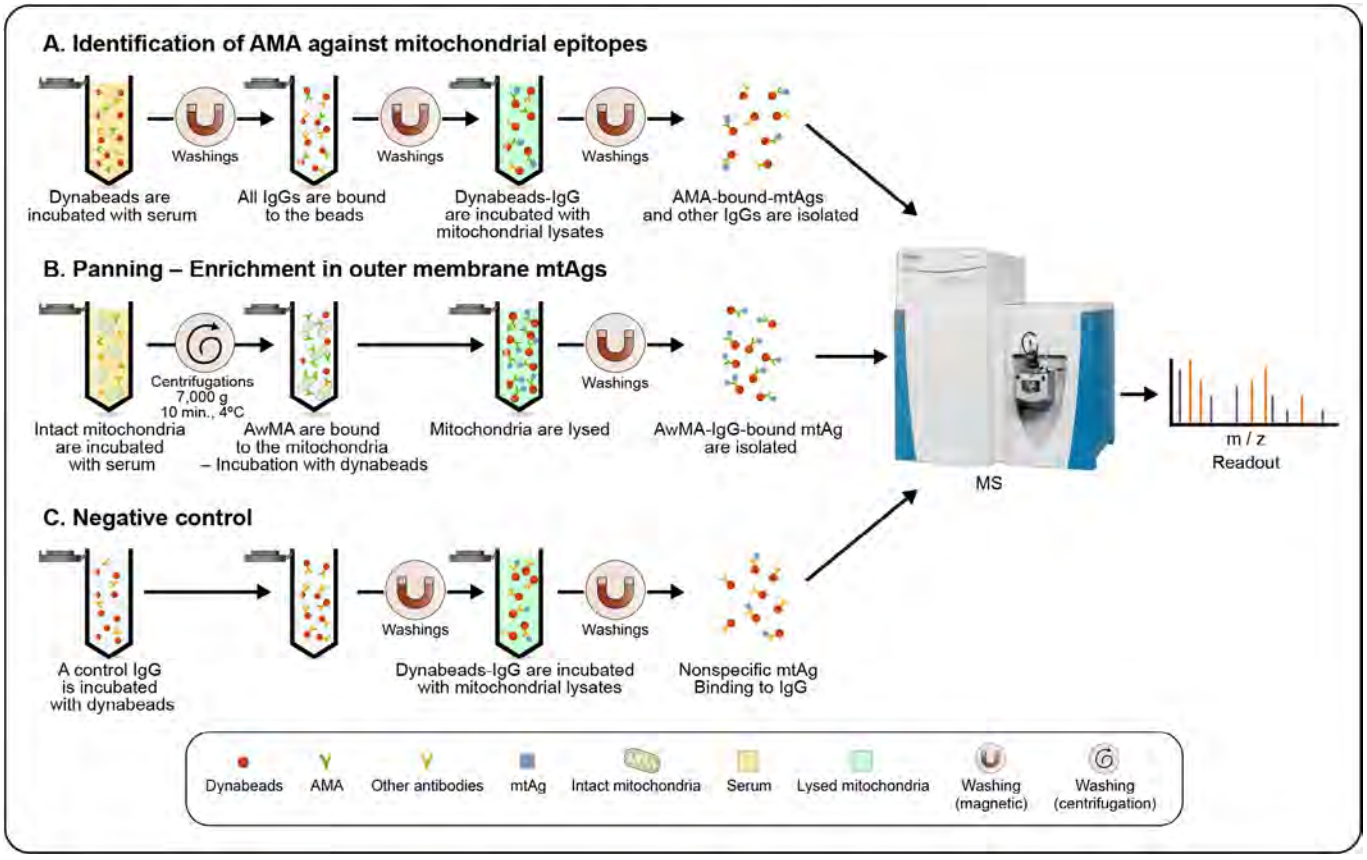

Figure 1. Workflow used for the detection of mitochondrial antigens targeted by anti mitochondrial antibodies in SLE. (a) Antibodies of the IgG subclass are isolated, using Dynabeads®-Protein G, from pooled sera from either 10 healthy donors or 10 SLE patients with high levels of anti-whole mitochondrial IgG (AwMA IgG). Dynabeads®-bound IgG were subsequently incubated with mitochondrial lysates, allowing the affinity purification of mitochondrial antigens (mtAgs) from all sub-localizations. (b) Freshly isolated intact mitochondria were incubated with pooled sera. Mitochondria incubated with AwMA were then lysed and AwMA-IgG isolated with Dynabeads™. (c) An irrelevant monoclonal IgG targeting FcγRIIa – a protein absent from mitochondria, is bound to Dynabeads™ and incubated with mitochondrial lysates in order to identify non-specific binding of mtAgs. For each approach, samples were acquired in triplicate and mtAgs were identified by mass-spectrometry (MS).

Background/Purpose: Mitochondria are organelles that possess several bacterial features such as a double-stranded genome with hypomethylated CpG islets, formylated proteins, and a double membrane composed of cardiolipin. In systemic lupus erythematosus (SLE), mitochondria and their inner components are released into the extracellular space, potentially eliciting a pro-inflammatory response by the immune system. While cardiolipin and mitochondrial DNA (mtDNA) and RNA (mtRNA) are confirmed targets of autoantibodies, antigenic mitochondrial proteins in SLE remain to be identified. Herein, we aim to characterize the antigenic protein repertoire recognized by anti-mitochondrial antibodies in SLE patients.

Methods: SLE (n=87) and healthy controls (n=30) agreed to participate to our systemic autoimmune rheumatic diseases biobank and database. Sociodemographic and disease characteristic variables [e.g., ACR classification criteria, SLEDAI-2K, SLICC/ACR damage index (SDI), comorbidities] as well as serum samples were collected at the time of the inclusion of the patients in the systemic autoimmune rheumatic disease biobank and data repository. The anti-dsDNA, IgGs against anticardiolipin or anti-β_2GPI (i.e., cut-offs of 40 UPL or above the 99th percentile of controls) were measured by ELISA. Lupus anticoagulant assay was performed, following international guidelines for this functional assay. Healthy controls were recruited under the conditions of having no known illnesses and infectious symptoms at the time of the blood draw. Autoantibodies against whole mitochondria (AwMA), mtDNA (AmtDNA) and mtRNA (AmtRNA) were previously assessed. Sera of either 10 healthy donors or 10 SLE patients with high titers of AwMA were pooled and incubated with sources of mitochondrial antigens (**Figure 1**) and IgG were isolated, using Dynabeads-protein G. Identification of mitochondrial proteins associated to IgGs were performed in triplicates by shotgun proteomic analysis. Immunoreactivities to C1qBP and Mfn1 were assessed by direct ELISA. Comparisons

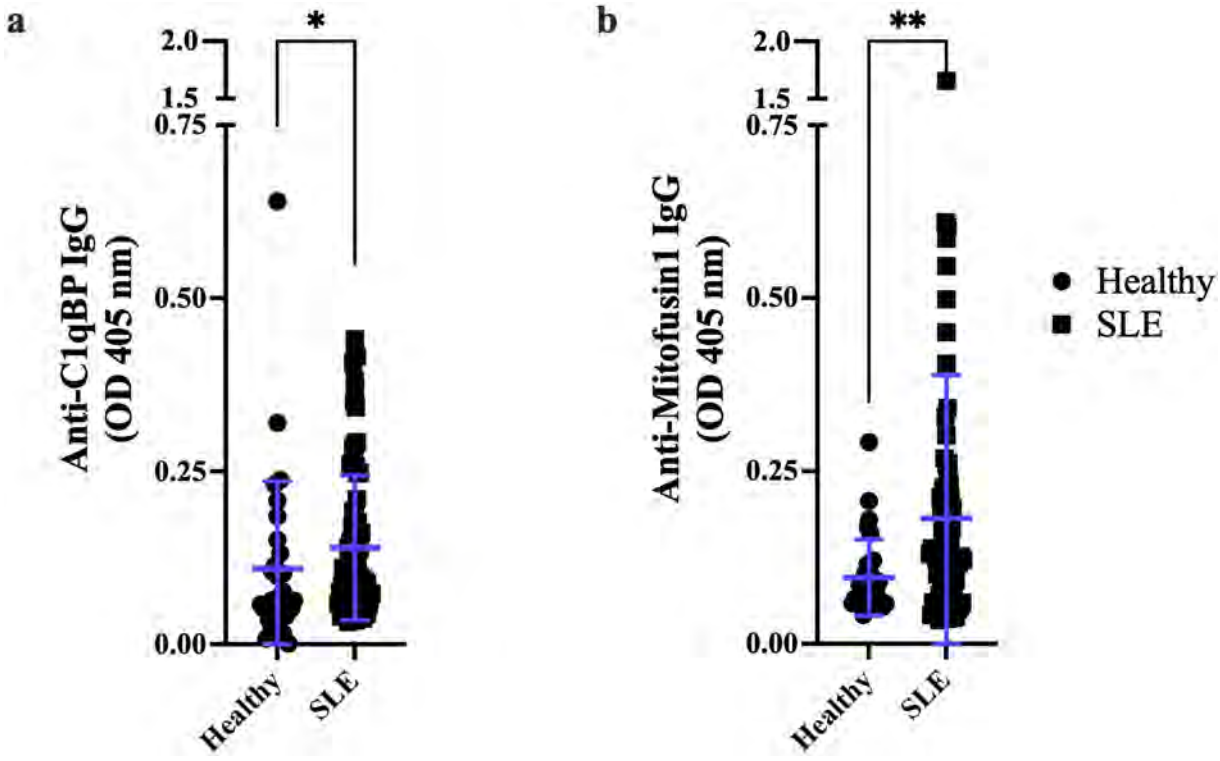

Figure 2. C1qBP and Mfn1 are two surface mtAgs with increased immunoreactivity in SLE. Immunoreactivity against mitochondrial proteins was assessed by direct ELISA. (a) The receptor for the complement component C1q (C1qBP) is a protein stored within the mitochondrion and subsequently dispatched to the cell surface and/or released into the extracellular space. SLE patients display increased levels of IgGs targeting C1qBP, compared with healthy individuals (p=0.0167). (b) Mitofusin 1 (Mfn1) is a protein expressed at the surface of the mitochondrion and is responsible for the fusion of mitochondrial outer membranes; anti Mfn 1 IgG are significantly increased in patients with SLE, compared with healthy donors (p=0.0022). Healthy: n=30, SLE: n=87. Data are mean optical densities read at 405 nm (OD405 nm) ± standard deviation. Wilcoxon-Mann-Whitney test. *: p≤0.05; **: p<0.01.

Table 1. Correlations between anti-C1qBP, anti-Mitofusin 1 and various continuous variables in SLE patients. Correlations presented, herein, for anticardiolipins or anti-β2-GPI were tested for IgGs

			Anti-C1qBP	Anti-Mitofusin 1
Clinical serology	Anticardiolipin antibodies (n = 80)		$r_s = 0.25$ $p = 0.02$	$r_s = 0.45$ $p < 0.0001$
	Anti-β_2 Glycoprotein I (n = 80)		$r_s = 0.12$ $p = 0.28$	$r_s = 0.26$ $p = 0.02$
	Anti-double-stranded DNA (n = 22)		$r_s = 0.11$ $p = 0.63$	$r_s = 0.44$ $p = 0.04$
Anti-mitochondrial antibodies	Anti whole mitochondria (AwMA)	IgG	$r_s = 0.32$ $p = 0.003$	$r_s = 0.65$ $p < 0.0001$
		IgM	$r_s = 0.08$ $p = 0.46$	$r_s = 0.31$ $p = 0.003$
	Anti-mitochondrial DNA (AmtDNA)	IgG	$r_s = 0.23$ $p = 0.03$	$r_s = 0.52$ $p < 0.0001$
		IgM	$r_s = 0.07$ $p = 0.50$	$r_s = 0.24$ $p = 0.03$
	Anti-mitochondrial RNA (AmtRNA)	IgG	$r_s = 0.03$ $p = 0.75$	$r_s = 0.27$ $p = 0.01$
		IgM	$r_s = 0.03$ $p = 0.82$	$r_s = 0.27$ $p = 0.01$

between groups were performed using the Wilcoxon-Mann-Whitney test. Spearman correlations were calculated to see associations between AMA and antibodies assessed in clinical laboratory.

Results: We identified 1345 proteins, 431 of which were associated with the mitochondrial proteome. Autoantibodies to two candidates, namely to the complement component 1 Q subcomponent-binding protein (C1qBP) and mitofusin 1 (Mfn1) were significantly increased in SLE patients compared to healthy individuals (anti-C1qBP: p=0.0167, anti-Mfn1: p=0.0022. **Figure 2**). Patients with positive lupus anticoagulant had increased anti-C1qBP (p=0.049), while anti-Mfn1 levels were increased in patients positive for antiphospholipids (p=0.011). Levels of Anti-Mfn1 were associated with those of IgGs to anticardiolipin (r_s=0.454; p< 0.0001), anti-β_2GPI (r_s=0.261; p=0.019) and anti-dsDNA (r_s=0.443; p=0.039) (**Table 1**).

Conclusion: These results suggest that autoantibodies to C1qBP and Mfn1 are comprised represented within the AMA repertoire in SLE and display different associations with serological criteria in the disease.

Disclosure: Y. BECKER, None; **J. Gagné**, None; **A. Julien**, None; **T. Lévesque**, None; **N. Gougeard**, None; **V. Rubio**, Recordati Rare Diseases, 6, RECKITT BENCKISER HEALTHCARE, S.A., 6; **F. Boisvert**, None; **D. Jean**, None; **G. Poirier**, None; **P. Fortin**, Lilly, 1, AbbVie, 1, AstraZeneca, 1; . **Boilard**, None.

Abstract Number: 1490

Myeloid and B Cell Transcriptional Phenotypes Reveal Race Dependent Differences in Early Autoimmunity

Aleksandra Bylinska, Samantha Slight-Webb, Kevin Thomas, Miles Smith, Susan Macwana, Nicolas Dominguez, Eliza Chakravarty, Joan Merrill, Judith James and Joel Guthridge, Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Early immune events leading to clinical autoimmune disease are complex and the pathways involved remain incompletely defined. Anti-nuclear antibody (ANA) positivity is a feature of several autoimmune diseases; however, up to 20% of healthy women are ANA+, and most will never develop clinical autoimmune disease. We have previously evaluated T cells in healthy ANA+ individuals, and found differences by race. European American (EA) ANA+ subjects, at lower risk for transition to autoimmunity, had T cells with a decreased interferon (IFN) gene signature compared to ANA- healthy and EA SLE patients. T Cells of ANA+ African Americans (AA) had greater expression of IFN and activation markers. The current project evaluated the impact of race on gene expression in B Cells and myeloid cells of healthy ANA - and ANA+ individuals as well as SLE patients.

Methods: scRNA-seq and CITE-seq was performed on healthy EA and AA ANA- (n=12), and ANA+ (n=12) people, and SLE patients (n=12). CD2 depleted peripheral blood mononuclear cells were used to determine B cell and myeloid cell subset frequencies and identify differential gene signatures. Library preparation was done on a 10X Genomics® Chromium instrument and sequencing was completed on Illumina NextSeq. Analyses using Seurat package in R were used to identify and visualize distinct cell clusters, while clusterProfiler was used for gene enrichment and pathway analyses.

Results: Cells from all subjects clustered into 14 unique B cell populations and 6 distinctive myeloid cell populations. IgE+ B cells and several naïve B cell clusters frequencies were elevated in B cells of ANA+ healthy people compared to ANA- controls. Gene enrichment analyses revealed greater neutrophil activation and degranulation in AA ANA+ and SLE patients ($Q < 0.0025$), and greater expression of T cell stimulatory signals (CD52, HLA-Class I and II, ISG) ($Q < 0.00006$) in classical monocytes (CD14+CD16-) than EA subjects. Both EA and AA patients with SLE had gene enrichment in transcription initiation, viral transcription, and protein targeting to the endoplasmic reticulum ($Q < 0.0005$) with modest enrichment found in ANA+ healthy individuals ($Q < 0.01$). EA ANA+ healthy individuals also had enrichment of gene pathways involved in regulation of viral life cycle ($Q=0.01$), regulation of viral entry into the host cell ($Q=0.01$), and negative regulation of the viral process ($Q=0.01$). Expression of these pathways was reduced in SLE patients and not found in AA ANA+ healthy samples. S100 gene expression was increased with disease in both EA and AA SLE patients ($Q < 0.00007$); however, AA ANA+, AA SLE patients ($Q < 0.002$) and even AA ANA- controls ($Q < 0.0007$) had higher expression of genes in the S100 pro-inflammatory family than EA subjects.

Conclusion: In healthy ANA+ individuals, gene expression pathways in myeloid and B cell subsets are altered. Healthy ANA+ African Americans exhibit heightened gene expression in cellular activation pathways and decreases in certain viral regulatory networks, suggesting an ongoing struggle with viral-like stimuli which may enhance their risk for progression to clinical autoimmunity.

Disclosure: A. Bylinska, None; **S. Slight-Webb**, None; **K. Thomas**, None; **M. Smith**, None; **S. Macwana**, None; **N. Dominguez**, None; **E. Chakravarty**, None; **J. Merrill**, GlaxoSmithKline, 2, 5, UCB, 2, AbbVie, 2, EMD Serono, 2, Remegen, 2, Celgene/Bristol Myers Squibb, 2, AstraZeneca, 2, 5, Daiichi Sankyo, 2, Servier, 2, Immupharma, 2, Amgen, 2, Janssen, 2, Lilly, 2, Genentech, 2, Resolve, 2, Alpine, 2, Aurinia, 2, Astellas, 2, Alexion, 2, Provention, 2; **J. James**, Progentec Diagnostics, Inc., 2; **J. Guthridge**, None.

Abstract Number: 1491

Single-cell Analysis of Paired Skin and Blood Samples from Patients with SLE and Cutaneous Lupus Suggests CD16+ DCs Arise from Non-classical Monocytes That Enter Nonlesional Skin, Undergo Type I IFN Education, and Engage in Extensive Crosstalk with Diverse Immune and Stromal Cell Types

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is an incompletely understood autoimmune disease that can occur in isolation or in the context of SLE. CLE is often disfiguring, and no FDA-approved therapies exist. Further, evidence suggests skin inflammation in CLE can provoke systemic autoimmune disease, including precipitating nephritis. Thus, understanding CLE pathogenesis has great potential to alleviate lupus morbidity and even mortality.

Methods: We used single-cell RNA sequencing (scRNA-seq) to investigate cellular transcriptomes in lesional skin, sun-protected nonlesional skin, and peripheral blood mononuclear cell (PBMC) samples from 7 CLE patients. 6 of 7 patients met ACR criteria for SLE. Data were analyzed in combination with control skin biopsies taken from 14 healthy patients and PBMCs from 4 healthy donors using Seurat. Keratinocytes (KCs), melanocytes, eccrine gland

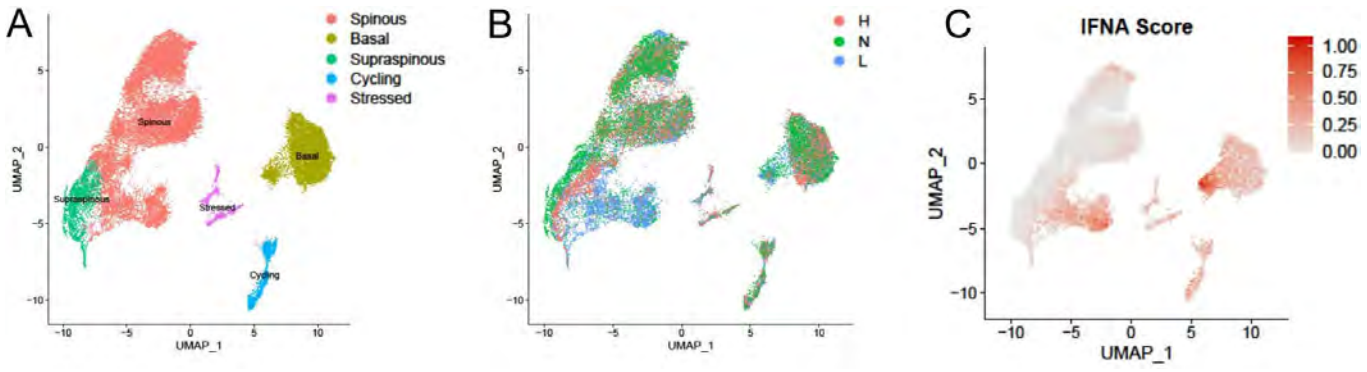

Figure 1. KC sub-clustering. A. KC subsets. B. KCs colored by origin; healthy (H), nonlesional lupus (N), lesional lupus (L) skin. C. KCs colored by IFNα cytokine module scores.

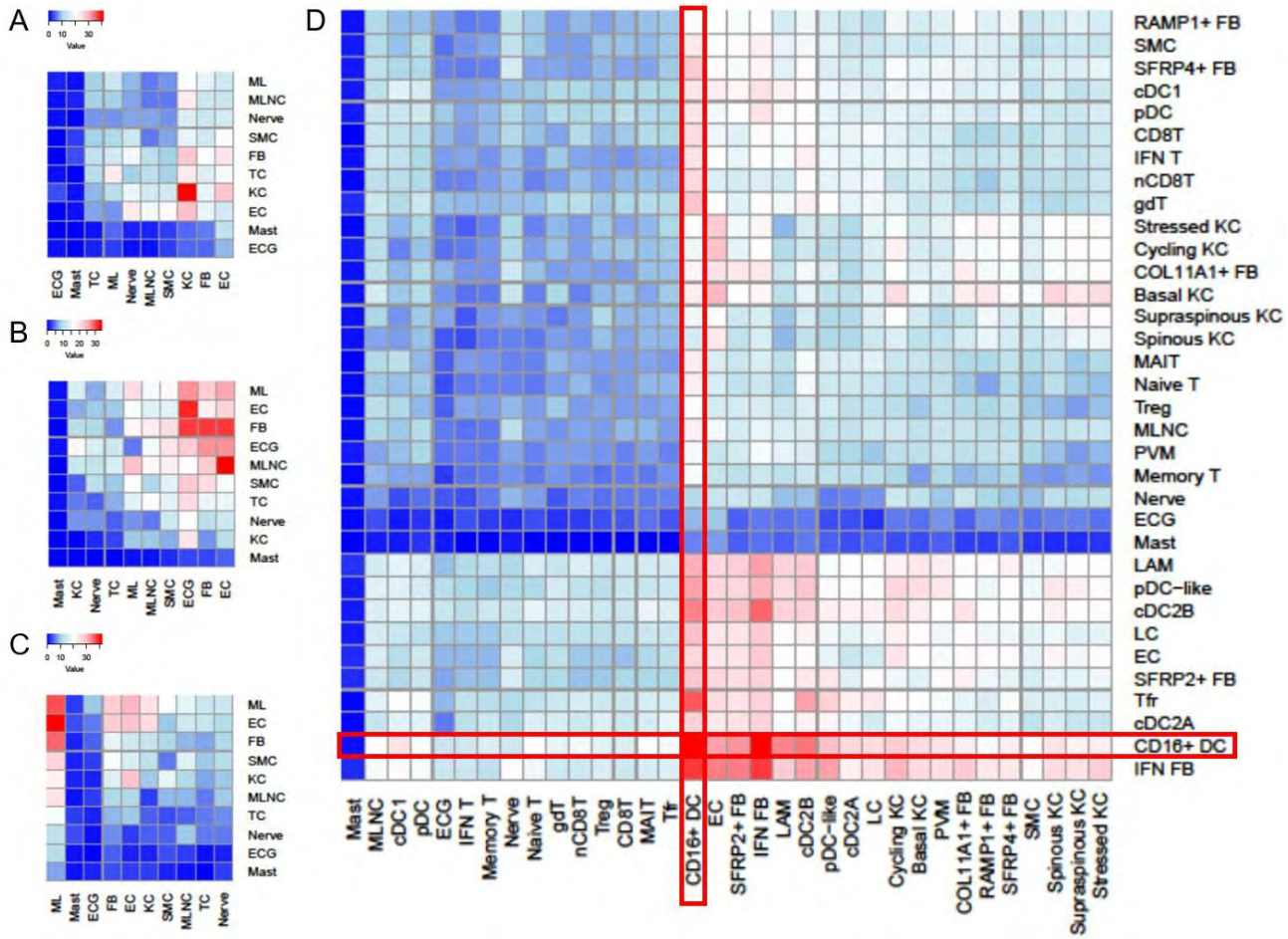

Figure 2. Number of predicted ligand-receptor interactions in skin. Red, more interactions. ML, myeloid cell. MLNC, melanocyte. SMC, smooth muscle cell. TC, T cell. EC, endothelial cell. ECG, eccrine gland. A. Control skin. B. Nonlesional lupus skin. C. Lesional lupus skin. D. Receptor-ligand interactions of detailed cell subsets in the skin.

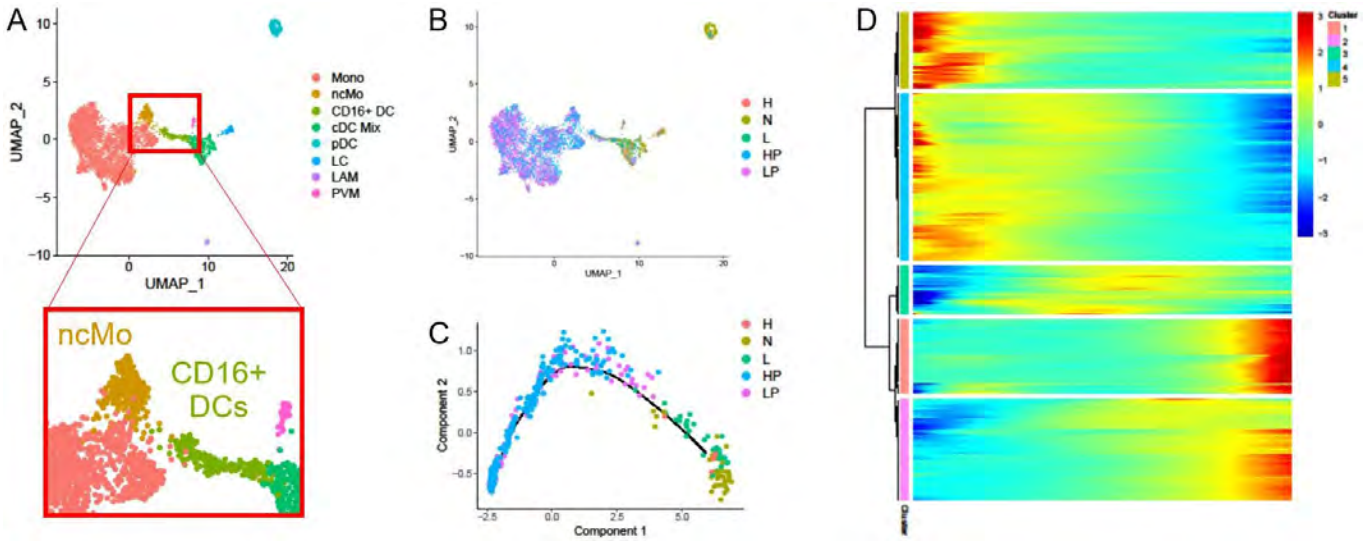

Figure 3. CD16+ DCs may arise from circulating non-classical monocytes (ncMo). A. Myeloid cells from paired skin and PBMC samples colored by subset. Mono, classical monocyte. B. Colored by origin. HP, healthy PBMC. LP, lupus PBMC. C. Pseudotime projection of the transition of ncMo to CD16+ DC. D. Gene markers cluster into five expression patterns across pseudotime.

cells, endothelial cells, fibroblasts (FBs), smooth muscle cells, nerve cells, T cells, myeloid cells, and mast cells were identified. KCs, FBs, T cells, and myeloid cells were sub-clustered and cell subsets annotated. Cytokine module scores were calculated for KCs and FBs using signature genes induced upon treatment of KCs and FBs with panels of cytokines. Cell-cell communication was examined using CellPhoneDB to perform ligand-receptor analysis for select cell subsets. To further investigate cellular interactions, spatial sequencing was performed, and cell signatures derived from scRNA-seq were used to identify the proximity of different cell types in lesional skin from a patient with DLE. Finally, pseudotime analysis was performed on cells bridging the connection between circulating and skin-resident myeloid cells.

Results: Both lesional and nonlesional SLE/CLE KCs showed very strong type I IFN signature scores (**Figure 1**). Lesional and nonlesional SLE/CLE skin exhibited dramatic shifts in cell-cell crosstalk (**Figure 2A-C**); CD16+ DCs were very enriched in CLE lesions relative to control and were among the most active communications both as expressers of ligands (horizontal) and receptors (vertical) even in nonlesional SLE/CLE skin (**Figure 2D**). Spatial transcriptomics demonstrated CD16+ DCs localizing most prominently in the superficial dermis, enabling interaction with KCs. Subclustering of paired circulating and skin myeloid cells revealed CD16+ DCs may arise from non-classical monocytes, with discrete shifts in myeloid cell transcriptional states, including a robust IFN education in the skin, detectable across this transition (**Figure 3**).

Conclusion: Nonlesional skin of patients with SLE and CLE exists in a type I IFN-rich, "prelesional" state. This affects gene transcription in all major cell types present in skin and dramatically alters cell-cell communication. Non-classical monocytes may infiltrate this environment to become CD16+ DCs that engage in crosstalk with diverse cell types as one of the earliest steps in the evolution of CLE lesions.

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Abstract Number: 1492

A Permissive Factor of Anti-Ro+ Mothers of Neonatal Lupus Children Is Linked to Overt SLE Associated with Immunity to a Gut Commensal

Robert Clancy[1], Miranda Marion[2], Hannah Ainsworth[2], Miao Chang[1], Timothy Howard[3], Peter Izmirly[4], Mala Masson[5], Jill Buyon[6] and Carl Langefeld[7], [1]NYU Grossman School of Medicine, New York, NY, [2]Wake Forest University, Winston-Salem, NC, [3]Wake Forest University, Quakertown, NC, [4]New York University School of Medicine, New York, NY, [5]NYU Grossman School Medicine, New York, NY, [6]NYU School of Medicine, New York, NY, [7]Wake Forest University, Winston Salem, NC

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Unknown factors trigger the transition of anti-Ro+ mothers of neonatal lupus (NL) children from preclinical autoimmunity to clinical disease. One candidate may be the gut microbiome with specific taxa serving as environmental triggers contributing to clinical phenotype. We have previously reported differential abundances between anti-Ro+ mothers versus healthy controls (HC), noting a bloom in relative abundance of protective

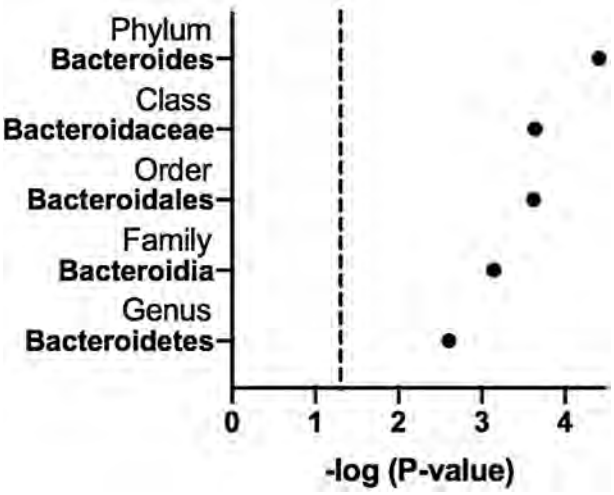

Figure 1. Analysis of the stool genus, Bacteroides, meeting statistical significance (FDR P-value<0.05) using the taxonomic stepdown method.

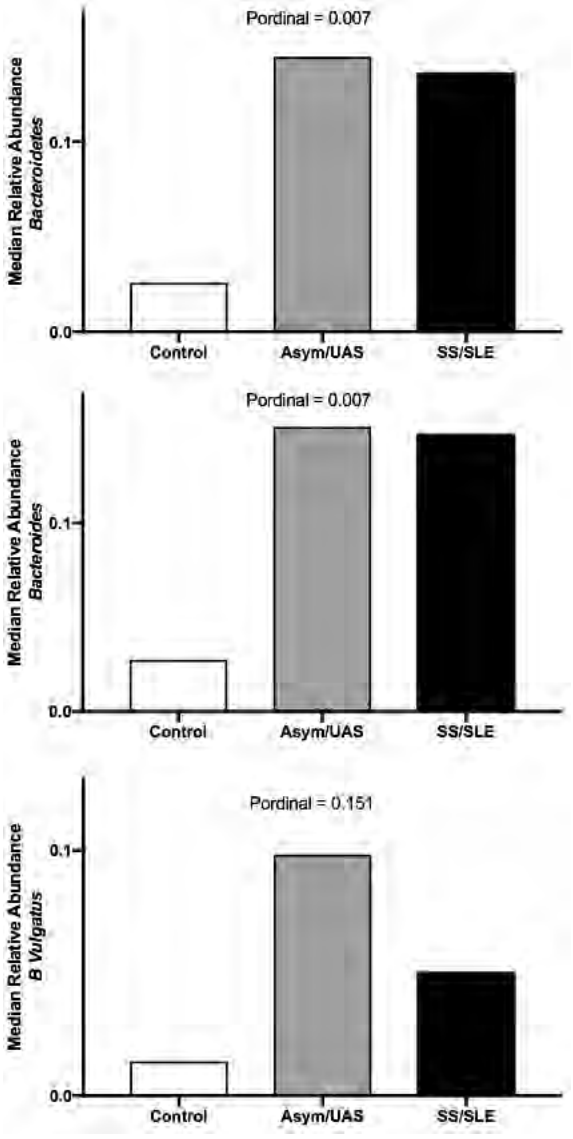

Figure 2. Species does not share ordinal significance, a feature that was evident at family and genus levels.

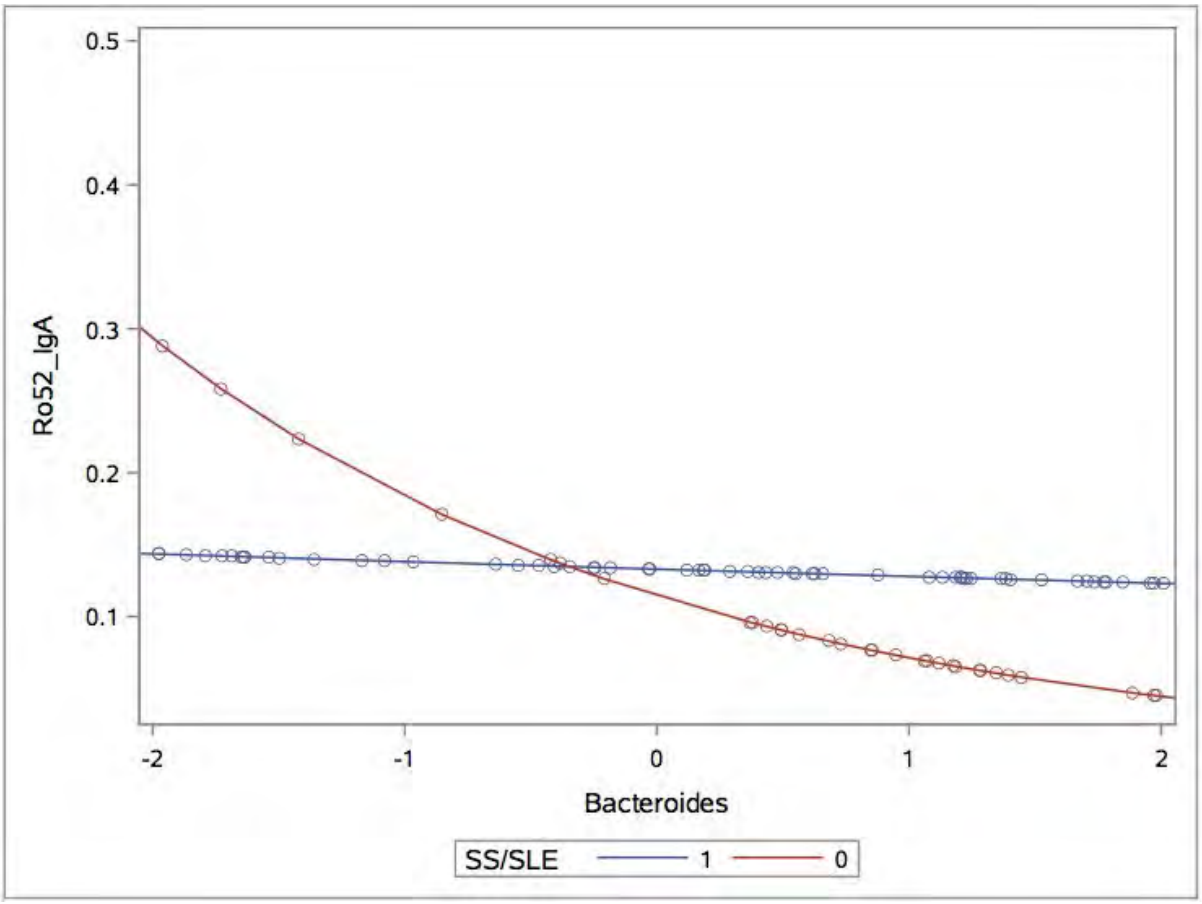

Figure 3. With anti-Ro52 IgA as an outcome, levels of autoantibody decreased with abundance in Asym/UAS subjects (P<0.005).

commensals including the genus *Bacteroides*. This taxon promotes tolerance at the interface of mucosal immunity. This study was initiated to test for associations of abundance of *Bacteroides*, and disease groups and for associations of anti-Ro titers.

Methods: Subjects included 125 RRNL mothers and 23 healthy controls. Stool microbiome of anti-Ro+ women in RRNL (asymptomatic and undifferentiated autoimmune syndrome (Asym/UAS), and SLE, SS, SS/SLE (SS/SLE)), and healthy controls (HC) were processed using 16S ribosomal RNA sequencing and use of a standard informatics pipeline. Tests for differential relative abundances of stool taxa applied compositional data analysis methods, linear models and adjustments for multiple comparisons. Assessments also included titers and specificities of anti-Ro using ELISA.

Results: The relative abundances varied as a function of clinical severity (HC < Asym/UAS < SS/SLE) shown across 13 genera (FDR < 0.05) including *Bacteroides*. Importantly, these ordered differences were maintained through the taxonomic hierarchy to *Bacteroides* (**Figure 1**) with the exception at species level *Bacteroides vulgatus* whereby relative median abundance reported at HC < SS/SLE < Asym/UAS (**Figure 2**), a finding that supported a focus on unique features of Asym/UAS that relate to *Bacteroides.* The initial analysis involved a comparison of Asym/UAS relative to HC. Applying multiple test correction, we observed an association of *Bacteroidetes* (P< 0.0001), as well as taxa at subsequent lower taxonomic levels including *Bacteroides* (P= 2.45 x 10-7), reflecting a higher relative abundance in Asym/UAS relative to HC. A subsequent analysis involved associations of *Bacteroides* relating to anti-Ro autoantibodies. While high titers of anti-Ro60 IgG and IgA as well as anti-Ro52 IgG and IgA titers were present in all NL mothers and absent in HC, there was an association between anti-Ro and *Bacteroides* relative abundance with an observed genus-by-disease interaction (P=0.0045; β=0.43 SE(β)=0.15) for Ro52 IgA levels. Specifically, with anti-Ro

as an outcome, levels were relatively constant for individuals diagnosed with SS/SLE but decreased with abundance in Asym/UAS (P< 0.005, **Figure 3**). These data suggest that the abundance of *Bacteroides* may influence features that are a distinction of SS/SLE such as high levels of autoantibody, which in this study was favored by low abundance of *Bacteroides*.

Conclusion: The data provide intriguing initial evidence that a permissive factor in NL anti-Ro+ mothers which links overt SLE immunity to a gut commensal, *Bacteroides vulgatus*.

Disclosure: R. Clancy, None; **M. Marion**, None; **H. Ainsworth**, None; **M. Chang**, None; **T. Howard**, None; **P. Izmirly**, Momenta/Janssen, 1; **M. Masson**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **C. Langefeld**, None.

Abstract Number: 1493

Association of the Soluble Terminal Complement Complex C5b-9 (sC5b-9) with Urinary Signs of Kidney Disease in a Swiss SLE Cohort

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Few reliable laboratory biomarkers exist to determine disease activity in SLE. The role of the soluble terminal complement complex, sC5b-9, in active SLE has yet to be elucidated. Its proinflammatory effects on a number of cell types, e.g. glomerular mesangial cells, have been reported.

The objective of the study was to correlate clinical activity according to the components of the SLEDAI and PROs with levels of soluble complement proteins and laboratory parameters of standard care. In completion of the preliminary analyses based on 2 consecutive patients' visits that suggested an association of sC5b-9 with haematuria und glomerular dysmorphic erythrocytes[1], we here present the analysis of all 4 visits during the 2-year time period of the study of 127 patients.

Methods:
Study population and design:
Patients fulfilling the ACR criteria were included into the Swiss SLE Cohort Study (SSCS, from the St. Gallen Centre) and were entered consecutively into a prospective observational, cross-sectional study (Oct. 2015 - Jan. 2021). The following parameters were determined at 2-4 clinical visits, at least 6 months apart, and compared with 48 healthy controls (age- and gender-matched):

- clinical disease activity (SELENA-SLEDAI, PGA), PROs (FACIT, SF-36) and SLICC-Damage
- sC5b-9 by ELISA
- a spectrum of routine laboratory of standard care

Statistics:
Independent associations of continuous variables were studied by analysis of covariance (ANCOVA) models, using the general linear model approach. Correlation analyses were performed calculating nonparametric Spearman rank correlation coefficients.

Results: Disease activity in our cross-sectional cohort was generally low (SELENA-SLEDAI 1.7 ± 2.6 (mean ± SD), SLEDAI of > 4 in 8.5% patients, 8.1 ± 3.3 (mean ± SD)). The median age was 48 [interquartile range (IQR) 38–54] years and disease duration 5.3 [IQR 3.8-8.8] years, respectively. Clinical manifestations were mainly hematologic 59%, musculoskeletal 56%, skin 41%, photosensitivity 41%, oral ulcers 37% and renal 15%.

A significant association in line with urinary signs of renal manifestations was found between:
- haematuria (F=2.501, p< 0.0001) and/or increase in glomerular dysmorphic erythrocytes
- (F=1.593, p= 0.039) and sC5b-9
- A significant correlation of proteinuria, albuminuria or pyuria with sC5b-9 could not be detected.

There were further correlations between sC5b-9 and:
- dsDNA antibodies (ab) (r=0.119, p= 0.014), IgG (r=0.181, p< 0.0001), soluble IL-2 receptor (r=0.100, p= 0.042), ESR (r=0.112, p= 0.017), CRP (r=0.223 p< 0.0001), C3a (r=0.317, p< 0.0001), C3 (r= 0.224, p< 0.0001)
- In addition, IgG (F=2.420, p= 0.004) and sIL-2 receptor (F=8.756, p< 0.0001) levels were associated with SELENA-SLEDAI in a multivariate model after adjustment for age, gender, CRP, ESR, levels of dsDNA ab, C3 and C4.

Conclusion: The study showed that sC5b-9 was associated with laboratory parameters of standard care and elevated in our cohort in line with urinary signs of renal manifestation. It may contribute to the pathogenesis of renal glomerular manifestation in SLE and serve as a new marker of active renal disease.

References

1. Arthritis Rheumatol. 2019; 71 (suppl 10) 1176-1178.

Disclosure: K. Schmiedeberg, None; **R. Mueller**, None; **T. Neumann**, None; **I. Pirker**, None; **P. Rein**, None; **C. Ribi**, None; **A. Rubbert-Roth**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 2, 6, Roche, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sanofi, 2, 6, Amgen, 2, 6, Novartis, 2, 6; **M. Kirschfink**, None; **J. Schroeder-Braunstein**, None; **R. Voll**, None; **J. von Kempis**, None.

Abstract Number: 1494

Functional Effects of a Lupus-associated *PRKG1* Variant on the RhoA-ROCK Pathway and Response to Type I Interferon

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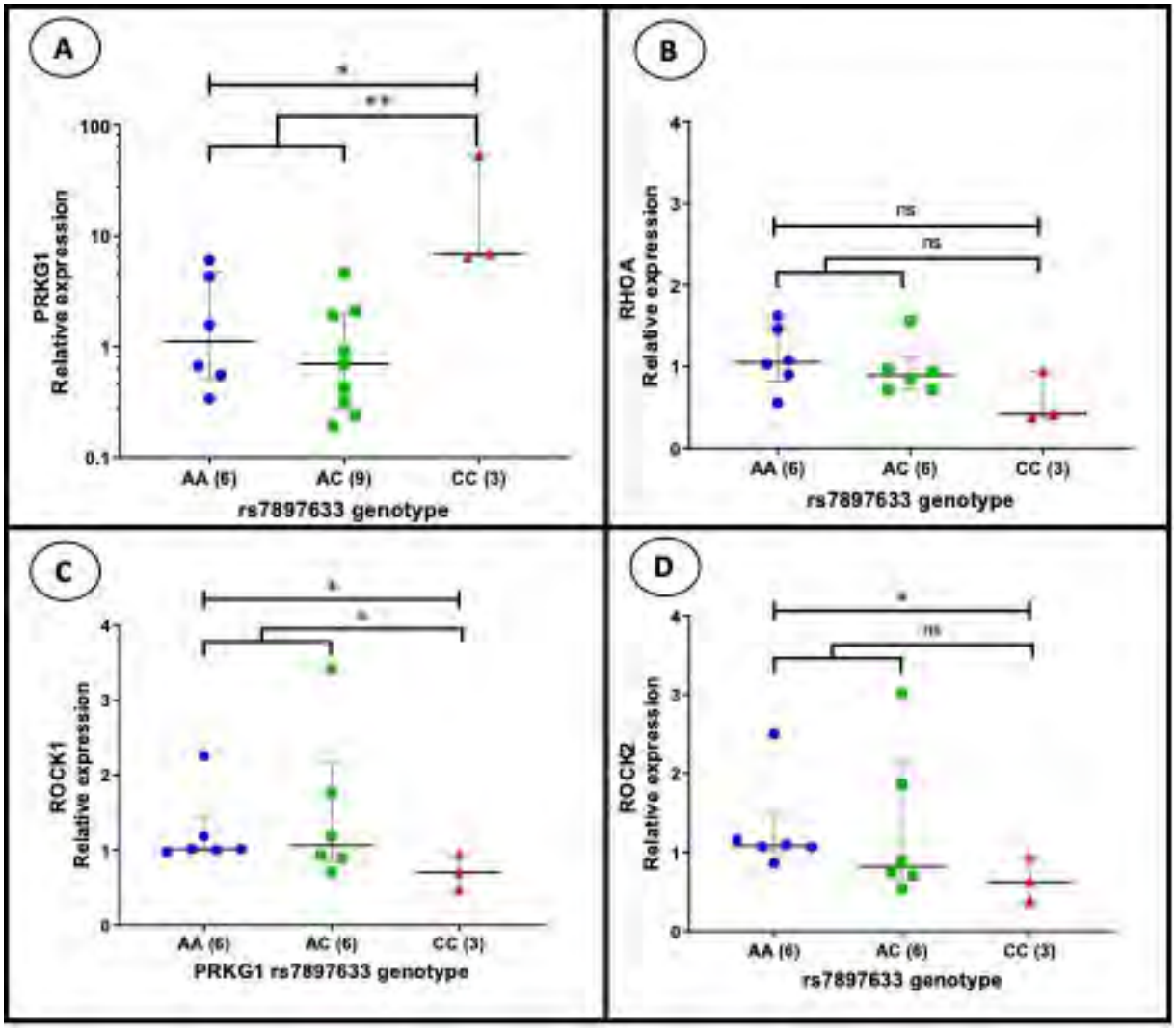

Figure 1. mRNA expression of PRKG1, RHOA, ROCK1 and ROCK2 in B lymphoblastoid cell lines according to the PRKG1 rs7897633 genotype category. (A) PRKG1, (B) RHOA, (C) ROCK1 and (D) ROCK2 mRNA levels are shown for B lymphoblastoid cell lines of different rs7897633 genotypes. Each symbol represents a cell line assessed in duplicate, n = 3 to 9. The median and interquartile ranges are shown. Mann-Whitney U was used to test significant differences for mRNA levels between genotype groups. *p<0.05; **p<0.01; ns=not significant.

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Interferon (IFN)-α contributes to susceptibility and severe manifestations in systemic lupus erythematosus (SLE). The *PRKG1* rs7897633 variant has been previously identified as the top hit in European ancestry patients with SLE and high IFN-α compared to those with low circulating IFN activity. However, the mechanisms by which *PRKG1* polymorphisms impact the immune system remain unknown. *PRKG1* codes for the cGMP-dependent protein kinase I (PKGI). Activation of PKGI leads to VASP phosphorylation, and the inhibition of RhoA and Rho-associated kinases (ROCK). A subgroup of patients with SLE exhibit higher ROCK activity in circulating immune cells compared to healthy controls. ROCK inhibition decreases IFN-α production and ameliorates disease in murine

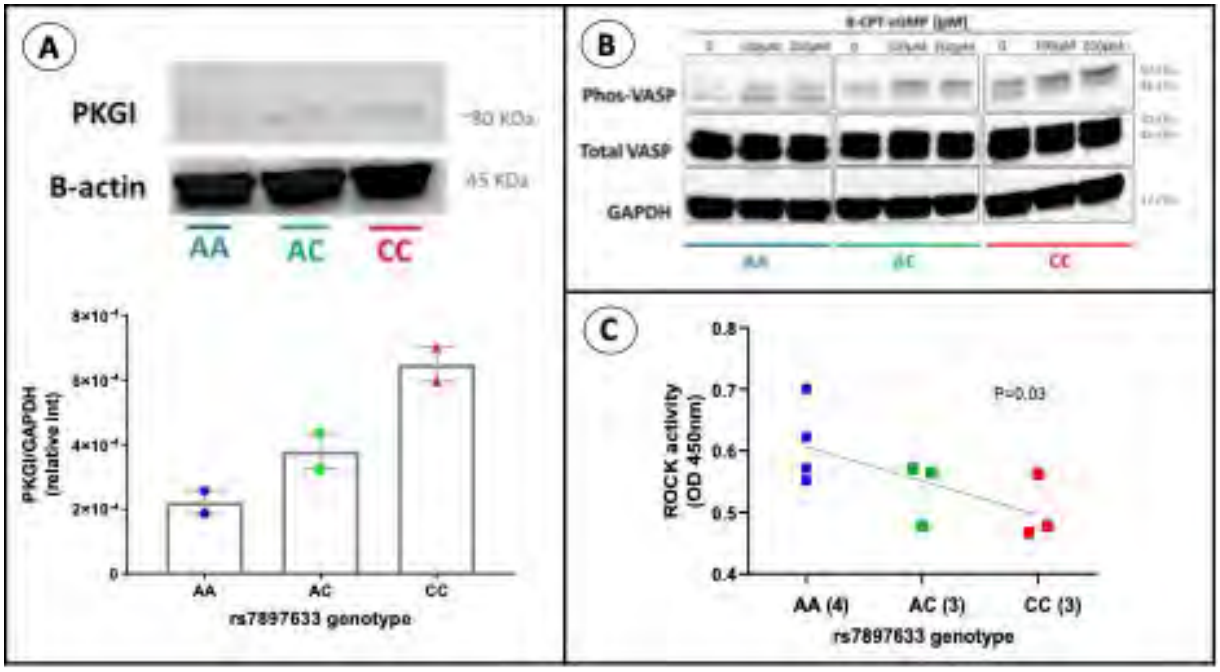

Figure 2. The rs7897633 AA variant is associated with lower PKGI abundance, decreased VASP phosphorylation, and greater baseline ROCK2 activity in B lymphoblastoid cell lines. (A) Representative Western blot analysis comparing PKGI (80 KDa) abundance, normalized for beta-actin (45 KDa), in different rs7897633 genotype categories. (B) Representative Western blot analysis comparing phosphorylated VASP and total VASP (46, 50 KDa) with increasing doses of 8-CPT-cGMP, a PKGI agonist, compared by rs7897633 genotype categories, n=2 (as a surrogate marker of PKGI activity). (C) Baseline ROCK2 activity in cells of different rs7897633 genotypes, with each symbol representing an individual cell line assessed in triplicate, and the P value reflecting the probability of the null hypothesis as compared to a regression line across genotype categories calculated using the sum-of-squares F test, n=3 to 4.

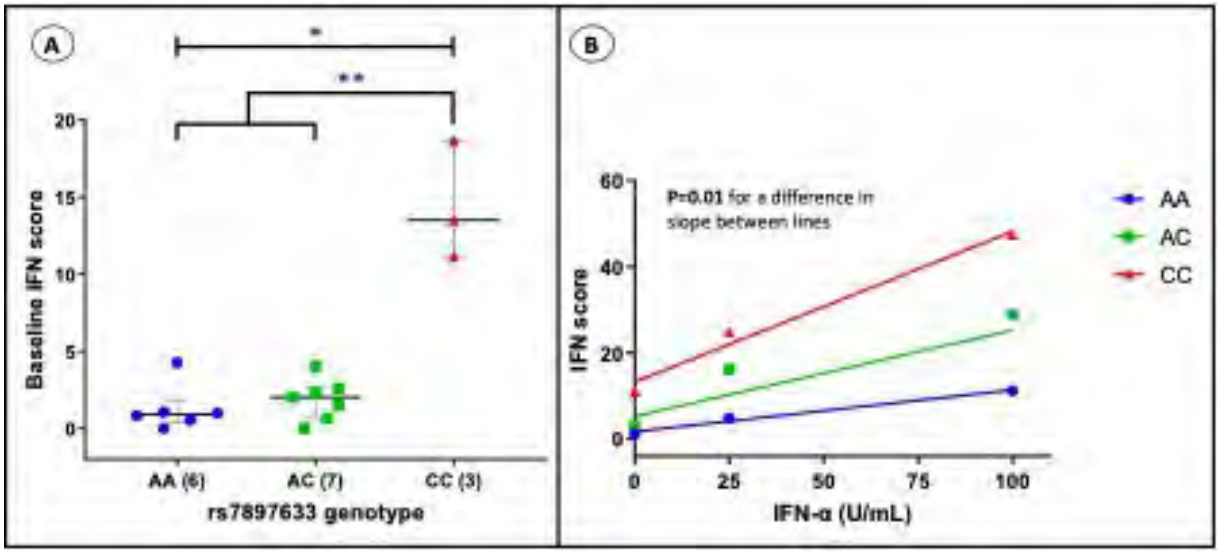

Figure 3. The rs7897633 CC genotype is associated with higher baseline and IFN-induced mRNA expression (as calculated by the interferon score) in B-lymphoblastoid cells. (A) Interferon (IFN) score (calculated from mRNA expression levels of the IFN-stimulated genes MX1, IFIT1, and PKR) at baseline in B-lymphoblastoid cells. Each symbol represents a cell line assessed in duplicate, n=3 to 7. The median and interquartile ranges are shown. Mann-Whitney U was used to test significant differences in IFN scores at baseline between genotype groups. *p<0.05; **p<0.01. (B) Association between rs7897633 genotypes and IFN score in B lymphoblastoid cells treated with increasing doses of IFN**α** (0, 25 U/mL, 100 U/mL). P value reflects the difference in slope between the regression lines of each genotype category, calculated using the sum-of-squares F test, n=2.

models of lupus. Accordingly, we aimed to assess whether the *PRKG1* gene variant was associated with decreased gene expression and activity of *PRKG1*, hyperactivation of the ROCK pathway, and altered response to type I IFN.

Methods: We used B lymphoblastoid cell lines (LCL) derived from healthy subjects of European ancestry (Coriell repositories) homozygous (AA or CC) and heterozygous (AC) at the rs7897633 SNP for all experiments. Gene expression of *PRKG1*, *RHOA*, and *ROCK* was assessed by RT-qPCR using gene-specific primers, normalized by GAPDH, and measured by the $2^{-\Delta\Delta CT}$ method. IFN score at baseline and after treatment of LCL with increasing doses of IFN-α was measured by quantifying 3 canonical IFN-stimulated genes (*IFIT1*, *MX1* and *PKR*) and summing to generate a score reflecting the degree of IFN-induced gene expression in the cells. Abundance of PKGI and VASP phosphorylation (as a surrogate of PKGI activity) were determined by Western blotting at baseline and after treatment with a PKGI agonist. ROCK2 enzymatic activity was performed by a colorimetric assay (Cell Biolabs). Unstimulated and stimulated cells were compared among PRKG1 genotype categories. Statistically significant differences were determined by Mann Whitney U test or sum-of-squares F test, as appropriate.

Results: *PRKG1* expression was lower in the homozygous AA genotype as compared with the homozygous CC genotype in LCL ($p< 0.05$). In contrast, ROCK expression was higher in LCL with the AA rs7897633 genotype ($p< 0.05$). Compared to LCL with the homozygous AA variant of rs7897633, homozygous CC LCL have greater abundance of PKGI, phosphorylated VASP/total VASP ratio in response to a PKGI agonist (indicating increased PKGI activity), and lower baseline ROCK activity (sum-of-squares F test, $p< 0.05$). The IFN score was significantly higher in the homozygous CC allele LCL, both at baseline and with increasing doses of IFN-α, suggesting increased sensitivity to type I IFN ($p< 0.05$).

Conclusion: *PRKG1* AA genotype associates with lower *PRKG1* and higher *ROCK* mRNA expression, decreased PKGI abundance and activity, and greater ROCK baseline activity. In contrast, the rs7897633 CC genotype is associated with increased response to IFNα. Overall, these findings suggest an important role of genetic variation at *PRKG1* in modulating the RhoA-ROCK pathway and regulating response to type I IFNs in LCL, which may have therapeutic implications in patients with SLE.

Disclosure: R. Fernandez Ruiz, None; **J. Shum**, None; **K. Van Buren**, None; **T. Niewold**, None.

Abstract Number: 1495

Multiplexed Profiling of Treatment Naïve Cutaneous Lupus Skin Stratified by Patient Response to Antimalarials

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

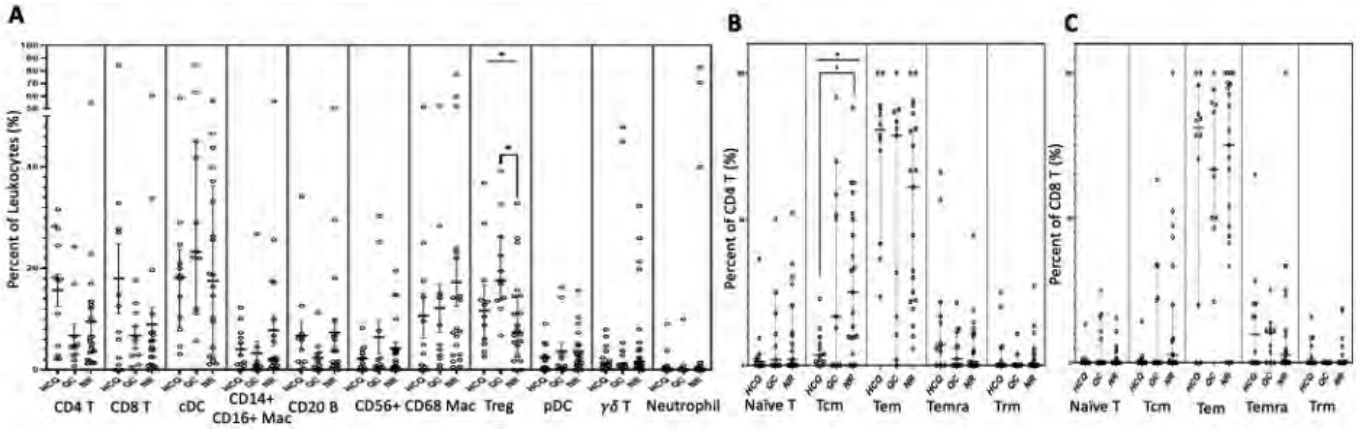

Figure 1. Cell types identified in cutaneous lupus stratified according to patient responses to antimalarials (A). CD4 (B) and CD8 (C) T cell subsets in cutaneous lupus stratified by patient responses to antimalarials.

Background/Purpose: Lupus erythematous (LE) is a systemic autoimmune disease with a variety of cutaneous manifestations. Antimalarials are first-line systemic therapy, yet not all patients respond to hydroxychloroquine (HCQ), quinacrine (QC), or either (NR). Our group has previously shown that QC responders demonstrate increased conventional dendritic cells (cDC) and TNF relative to HCQ responders.

Methods: Here, we investigated the differences between these patients using imaging mass cytometry (IMC), an unbiased multiplexed technique. 12 HCQ, 11 QC, and 20 NR treatment-naïve FFPE samples were stained with two panels consisting of 37 metal-conjugated antibodies and ablated on the Hyperion Imaging System (Fluidigm). Images were segmented using a nuclear staining based algorithm in Visiopharm and imported into histoCAT where single cell mean pixel intensity data was obtained to cluster cells using the Phenograph algorithm. RNA fluorescent *in situ* hybridization (ISH) using RNAscope was performed to confirm certain findings. Kruskal-Wallis, and post-hoc Dunn's tests were performed for cell percentages, and median with IQR are depicted. One-way ANOVA and post-hoc Tukey were performed for normally distributed intracellular markers with mean and SEM shown. Bivariate correlations were determined by Pearson's r.

Results: We identified 12 unique cell types. T cells were then manually gated on CCR7, CD69, and CD45RA to identify effector and memory subsets. NR patients were found to have a decreased percentage of Tregs compared to QC responders ($p< 0.05$) (Figure 1A). There was a significant increase in CD4+ central memory T cells in NR patients compared to HCQ patients ($p< 0.05$) (Figure 1B). We compared epidermal staining and found a significant difference is pNFκB staining between the treatment groups ($p< 0.05$) (Figure 2A). The post hoc test was not significant, but there was a trend towards decreased pNFκB in the QC group compared to both HCQ and NR. In the dermis, HCQ responders had significantly more pJAK3 staining than the QC group ($p< 0.05$) (Figure 2B). QC responders had a higher expression of pSTING and dermal cell IFNκ compared to HCQ responders ($p< 0.05$) (Figure 2A). The total expression of pSTING and IFNκ was found to positively correlate (Figure 3A) and colocalize in the dermis ($p< 0.0001$, $r=0.676$). We identified conventional dendritic cells (cDCs) as the major producers of IFNκ in CLE and found that their production of IFNκ and phosphorylation of STING was also elevated in the QC group compared to HCQ (Figure 3B). Since keratinocytes have been shown to be important producers of IFNκ in CLE, we compared the mean pixel intensity (MPI) of IFNκ in the epidermis to the cDCs and found a higher MPI in cDCs in all treatment groups. We then performed RNA ISH on QC responder biopsies and found CD11c mRNA (ITGAX) and IFNκ mRNA colocalized, suggesting cDCs are producers of IFNκ in CLE. CD14+CD16+/CD68+ macrophages and cDCs were the predominant cell types found to express pSTING and IFNκ.

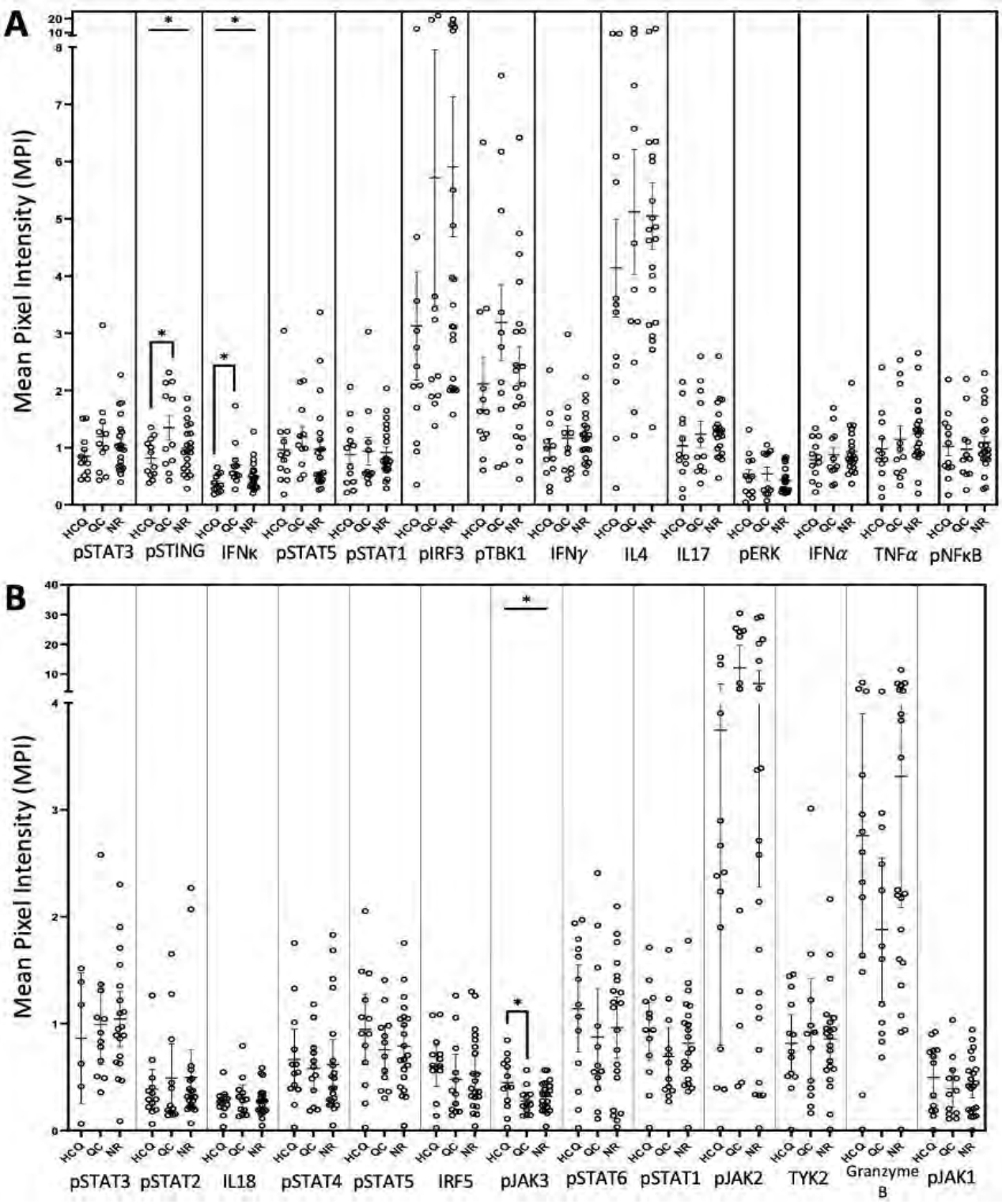

Figure 2. Mean pixel intensities of intracellular cytokines and activated cell signaling pathways in cutaneous lupus erythematosus.

Conclusion: This analysis on treatment naïve biopsies may lead to further discovery of biomarkers that may predict patient response to therapy and direct targeted treatment.

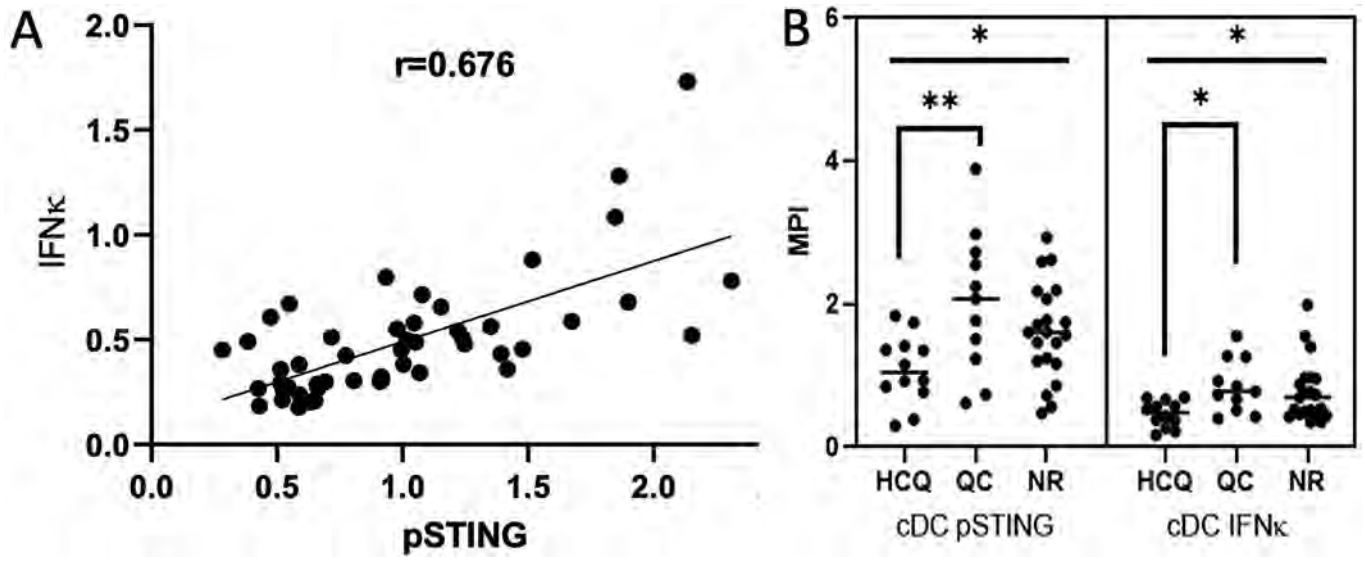

Figure 3. Phosphorylated-STING (pSTING) and interferon kappa are correlated in cutaneous lupus (r=0.676) (A). Conventional dendritic cells (cDCs) express more pSTING (p<0.01) and interferon kappa (p<0.05) in quinacrine (QC) responders (B).

Disclosure: T. Vazquez, None; **J. Patel**, None; **D. Yan**, None; **E. Keyes**, None; **D. Diaz**, None; **Y. Li**, None; **M. Grinnell**, None; **R. Feng**, None; **V. Werth**, Celgene, 5, Resolve, 2, Janssen, 2, 5, Eli Lilly, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Gilead, 2, 5, Amgen, 2, EMD Serono, 2, Viela Bio, 2, 5, Kyowa Kirin, 2, AstraZeneca, 2, AbbVie, 2, GlaxoSmithKline, 2.

Abstract Number: 1496

A Metagenome-wide Association Study Revealed Disease-specific Landscape of the Gut Microbiome of Systemic Lupus Erythematosus in Japanese

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

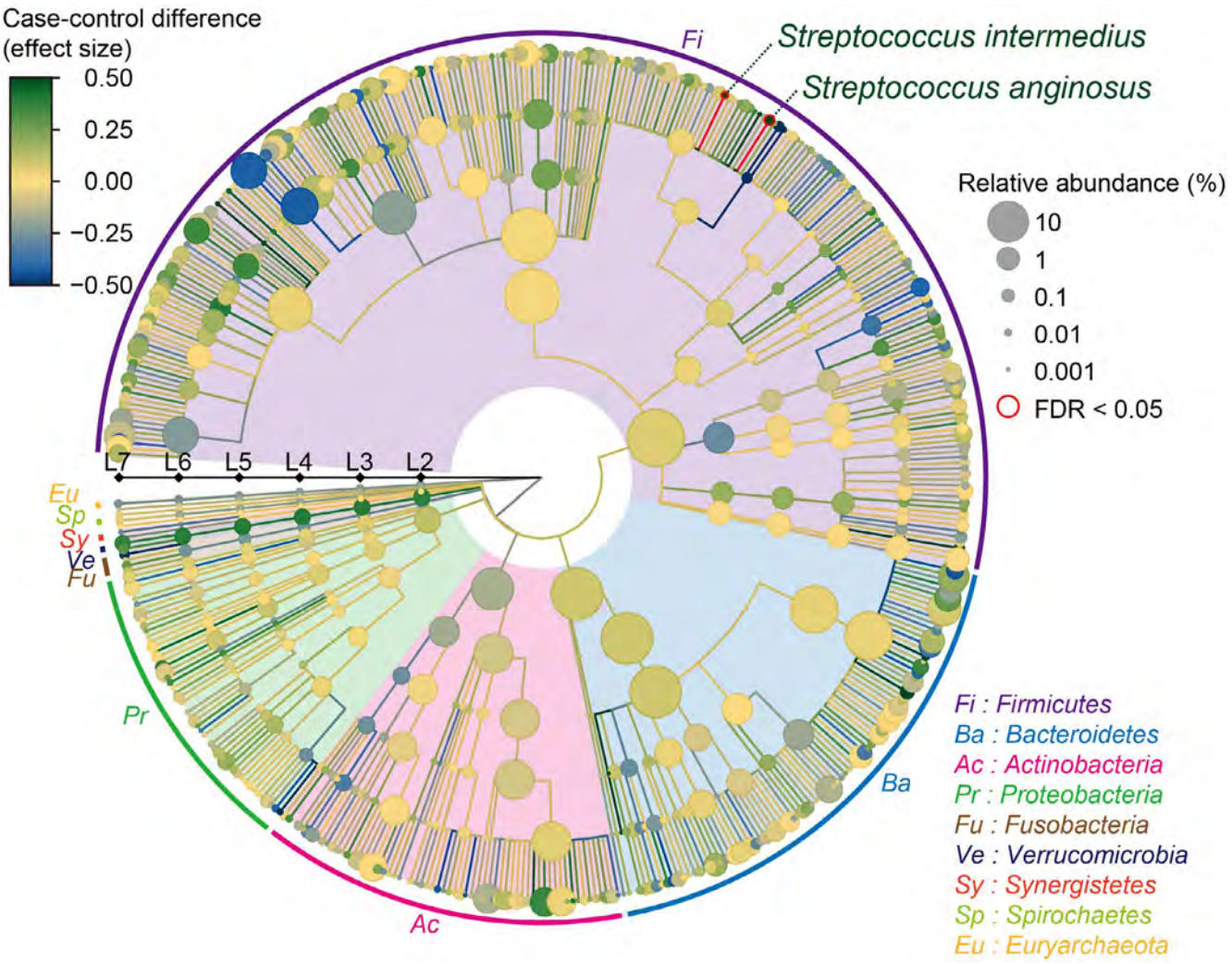
Session Time: 8:30AM–10:30AM

Background/Purpose: Alteration of the gut microbiome has been linked to the pathogenesis of systemic lupus erythematosus (SLE). However, a comprehensive view of the gut microbiome in SLE and its interaction with the host remains to be revealed. This study aimed to reveal SLE-associated changes in the gut microbiome and its interaction

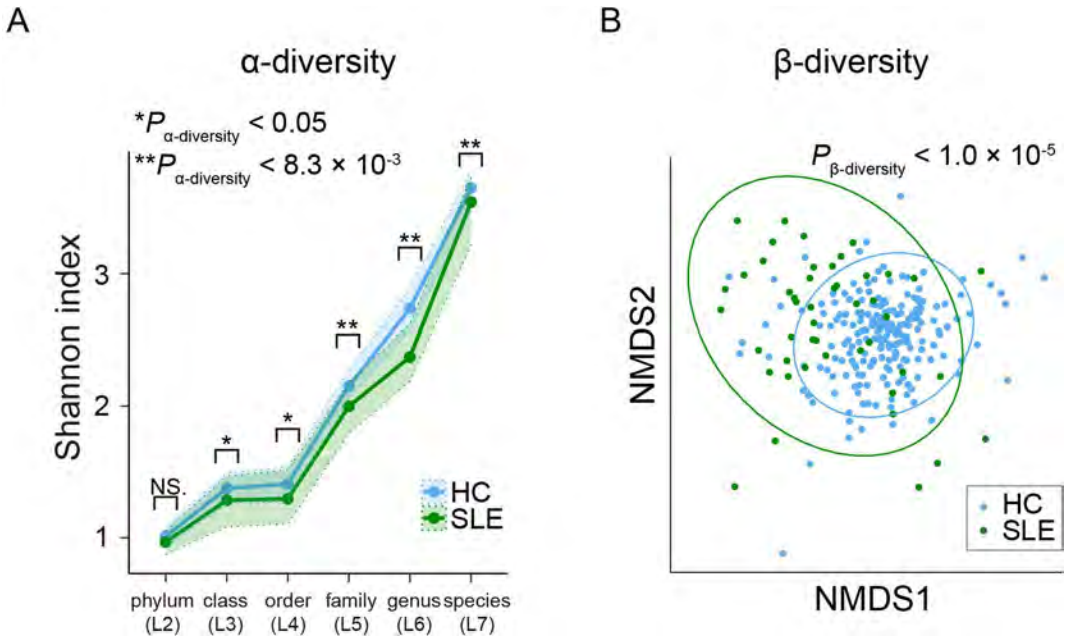
with the host by a comprehensive metagenome-wide association study (MWAS) based on shotgun sequencing followed by integrative analysis.

Methods: We performed a MWAS of SLE based on shotgun sequencing of the gut microbial DNA from Japanese individuals (N_{case} = 47, $N_{control}$ = 203). All of the 47 SLE patients were diagnosed according to the systemic lupus international collaborating clinics classification criteria (SLICC). Our MWAS consisted of three major bioinformatic analytic pipelines (phylogenetic analysis, functional gene analysis and pathway analysis). We integrated the result of the MWAS with the genome-wide association study (GWAS) data and plasma metabolite data.

Results: Via species level phylogenetic analysis, we identified and validated increases of *Streptococcus interdemius* and *Streptococcus anginosus* in the SLE patients (effect size = 0.617 and $P_{microbe} = 3.7 \times 10^{-5}$ for *Streptococcus anginosus*, effect size = 0.579 and $P_{microbe} = 7.5 \times 10^{-5}$ for *Streptococcus intermedius*; Figure 1). Microbial gene analysis revealed increases of the eight *Streptococcus* derived genes including one involved in redox reaction. Additionally, microbial pathways related to sulfur metabolism and flagella assembly were altered in the SLE patients. We identified a pathway level SLE-specific link between the metagenome and the germline genome by comparing the result of the



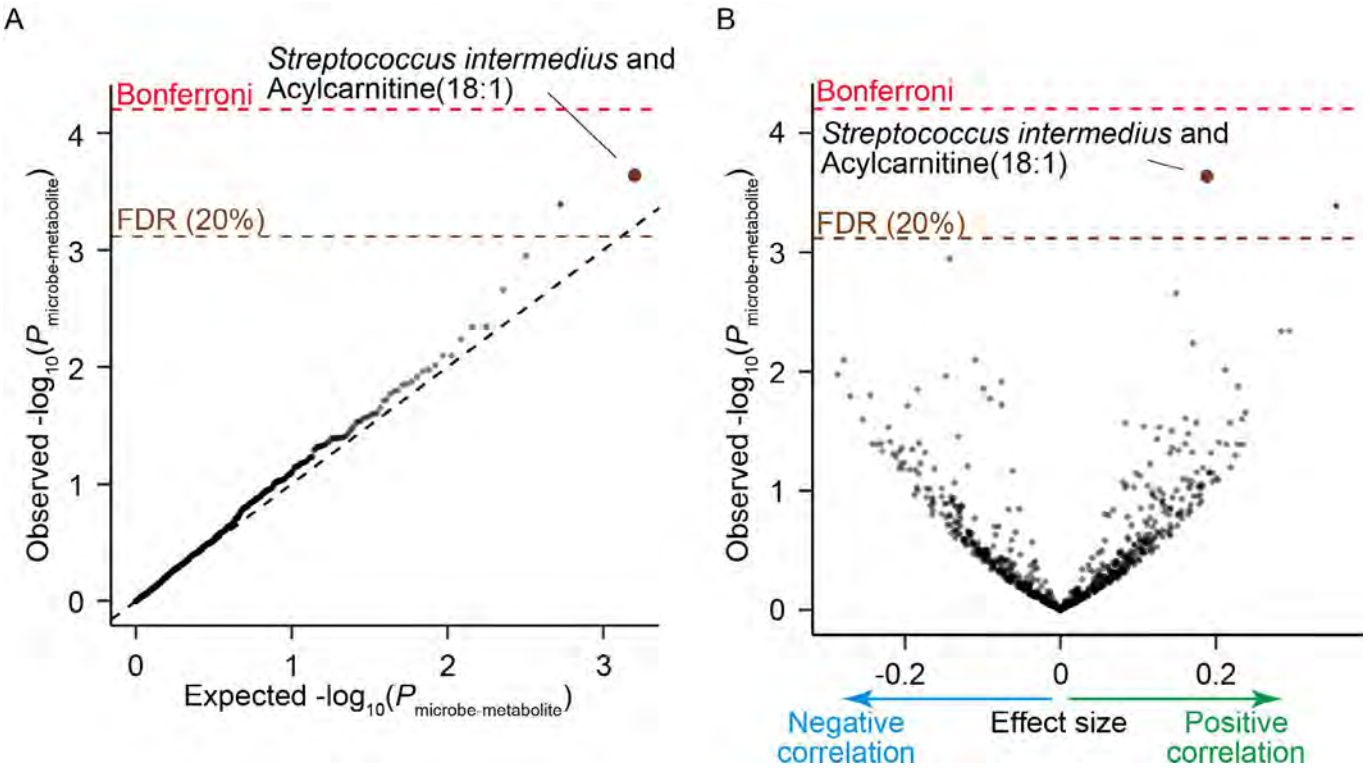
A phylogenetic tree. Levels L2-L7 are from the inside layer to the outside layer. The size and the color of nodes represent relative abundances and effect sizes, respectively. The two clades with significant case-control associations (FDR < 0.05) are outlined in red. FDR, false discovery ratio.



(A) A quantile-quantile plot of the p-values from the microbe-metabolite association analysis. The x-axis indicates log-transformed empirically estimated median P-value. The y-axis indicates observed -log10(P). The diagonal dashed line represents y = x, which corresponds to the null hypothesis. The horizontal red dashed line indicates the Bonferroni-corrected threshold (α = 0.05), and the brown dashed line indicates the FDR threshold (FDR = 0.20) calculated with Benjamini-Hochberg method. The microbe-metabolite pairs with FDR < 0.20 are plotted as brown dots, and the other microbe-metabolite pairs are plotted as black dots. (B) A volcano plot. The x-axis indicates effect sizes in linear regression. The y-axis, horizontal dashed lines and dot colors are the same as in (A). FDR, false discovery rate; HC, healthy control; SLE, systemic lupus erythematosus.

current MWAS and the GWAS of SLE (i.e., MWAS-GWAS interaction). α- and β-diversity analyses provided evidence of dysbiosis in the metagenome of the SLE patients (Figure 2). Microbiome-metabolome association analysis identified positive dosage correlation of acylcarnitine with *Streptococcus intermedius*, an SLE-associated taxon (Figure 3).

Conclusion: Our MWAS followed by integrative analysis revealed SLE-associated changes in the gut microbiome and its interaction with the host, which provided novel insights into the pathogenesis of SLE.



(A) α-diversities of the phylogenetic relative abundance data for the six taxonomic levels. Blue and green dots represent the median Shannon index of the HC and SLE subjects. Upper and lower dashed lines indicate the 1st and 3rd quantile of Shannon index for the HC and SLE subjects. (B) β-diversities of the phylogenetic relative abundance data at the species level. Result of NMDS based on Bray-Curtis distance is represented. Blue and green dots represent the HC and SLE subjects. HC, healthy control; IQR, interquartile range; NMDS, non-metric multidimensional scaling; SLE, systemic lupus erythematosus; *, $P < 0.05$; **, $P < 0.0083$.

Disclosure: Y. Tomofuji, None; **Y. Maeda**, None; **E. Oguro-Igashira**, None; **T. Kishikawa**, None; **K. Yamamoto**, None; **K. Sonehara**, None; **D. Motooka**, None; **Y. Matsumoto**, None; **H. Matsuoka**, None; **M. Yoshimura**, None; **M. Yagita**, None; **T. Nii**, None; **S. Ohshima**, None; **S. Nakamura**, None; **H. Inohara**, None; **K. Takeda**, None; **A. Kumanogoh**, None; **Y. Okada**, None.

Abstract Number: 1497

Kidney Disease in Lupus Patients Is Linked to Monocytes' Aberrant Spliceosome and Altered Expression of IFN-Response Related Genes

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The present study aimed at: 1- Identifying altered SLE monocytes transcriptomic signatures linked to the immune response and its association with clinical features. 2- Evaluating the involvement of those altered molecular profiles in lupus nephropathy. 3- Analyzing mechanistically the impact of spliceosome alterations in the SLE-monocytes activity.

Methods: Sixty SLE patients and forty healthy donors (HD) were included in the study. Infiltration rate of myeloid cells was analyzed in kidney biopsies by Immunohistochemistry. Circulating monocytes were purified from peripheral blood by immune-magnetic selection and both, transcriptome and spliceosome profiling were assessed, respectively, by Nanostring and a microfluidic qPCR array (Fluidigm). Extensive clinical/serological evaluations were also performed. *In vitro* studies involving over/down-expression of splicing machinery components were developed.

Results: Infiltration of CD68+ expressing cells was confirmed in kidney biopsies and associated with parameters of kidney failure (C3/C4, chronic index), highlighting the key role of the myeloid compartment in lupus nephropathy. Gene expression profiling recognized 156 genes differentially expressed in SLE monocytes *vs* HDs, most of them associated with the IFN response. In parallel, the altered expression of 27 components of the splicing machinery (SM) was revealed in SLE-monocytes. Correlation studies demonstrated that the aberrant expression of SM components was linked to both, the altered IFN signature and the plasma inflammatory profile. This altered molecular profile was associated with disease activity, anti-dsDNA positivity and C3/C4 levels. Interestingly, SLE patients with renal disease displayed a simultaneous alteration of both, the IFN and the SM signatures in monocytes, along with an enlarged pro-inflammatory profile in plasma. Logistic regression models integrating the concomitant alteration of SM components and IFNs genes identified lupus nephritis patients with high accuracy. In vitro SLE-serum promoted in DS-monocytes a concomitant deregulation of both, the IFN signature and several SM components. Besides, the over/down-expression of selected SM components in SLE-monocytes reduced the release of inflammatory cytokines and their adhesion capacity.

Conclusion: 1) Monocytes from SLE patients with renal involvement exhibit a remarkable alteration of genes associated with the IFN response, further linked with the aberrant expression of several SM components. 2) Serum SLE promoted the dysregulation in monocytes of both, the IFN and spliceosome signatures, along with an active release of proinflammatory mediators. 3) The modulation of key SM components in monocytes from SLE patients reduce their pro-inflammatory status and migration capacity.

Disclosure: C. Lopez-Pedrera, None; **A. Patiño-Trives**, None; **A. Ibañez-Costa**, None; **M. Luque-Tevar**, None; **I. Arias de la Rosa**, None; **D. Ruiz**, None; **P. Seguí-Azpilicueta**, None; **M. Espinosa**, None; **R. Ortega**, None; **N. Barbarroja**, None; **J. Cataño**, None; **R. Luque**, None; **M. Aguirre**, None; **C. Pérez-Sánchez**, None.

Abstract Number: 1498

Platelet Secreted LGALS3BP Induces a Pro-inflammatory Phenotype in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a complex chronic heterogeneous autoimmune disease, which increases the risk of atherothrombosis. In addition to their well described role in thrombosis and hemostasis, platelets are key mediators of inflammation and have immune effector cell properties. This study was initiated to investigate the role of platelet associated Lectin Galactoside-binding Soluble 3 Binding Protein (LGALS3BP), which binds to macrophage-associated lectin Mac-2, as a mediator of inflammation in SLE and potential biomarker associated with clinical phenotypes.

Methods: RNA transcriptome analysis was performed on platelets isolated from 51 patients with SLE (not taking aspirin or anticoagulants) and 18 age, sex and race/ethnicity matched controls. LGALS3BP protein expression was determined in platelet releasates by ELISA and western blot analysis. Gene and protein expression of LGALS3BP in Megakaryocyte cell line (MEG-01) was investigated upon stimulation with IFN-α. Correlations between circulating serum LGALS3BP and LGALS3BP platelet mRNA and releasates were assessed. Subsequently, correlation analysis

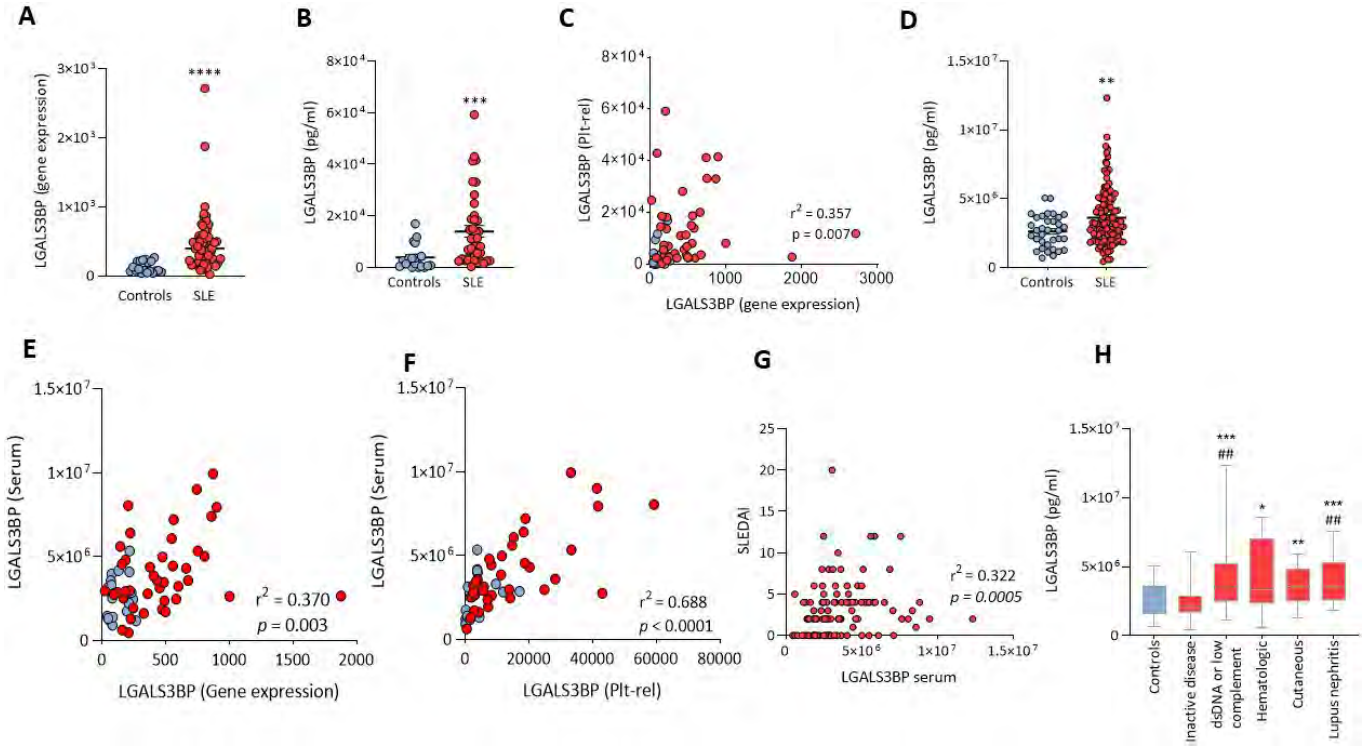


Figure 1. LGALS3BP is highly expressed in SLE and correlates with SELENA SLEDAI hybrid disease activity index A) LGALS3BP gene expression in platelets isolated from 51 patients with SLE and 18 age, sex and race/ethnicity matched controls, determined by RNA sequencing analysis. B) Levels of LGALS3BP measured by LGALS3BP specific ELISA in platelet releasates (plt-rel) of 40 patients with SLE and 20 healthy controls. C) Correlation between the levels of LGALS3BP measured in platelet releasates and platelet LGALS3BP gene expression D) LGALS3BP levels measured by LGALS3BP specific ELISA in serum of 115 patients with SLE and 34 healthy controls. E) Correlation between serum LGALS3BP and Platelet LGALS3BP gene expression F) Correlation between serum LGALS3BP and LGALS3BP in platelet releasates in 36 patients with SLE and 16 healthy controls G) Correlation between serum LGALS3BP levels and SELENA SLEDAI hybrid disease activity index in 115 patients with SLE H) Serum LGALS3BP levels stratified based on clinical phenotypes. Pounds indicate comparison to healthy controls and asterisks to inactive disease All data represent the mean ± s.e.m. and are analyzed by two-sided Student's t-test. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001.

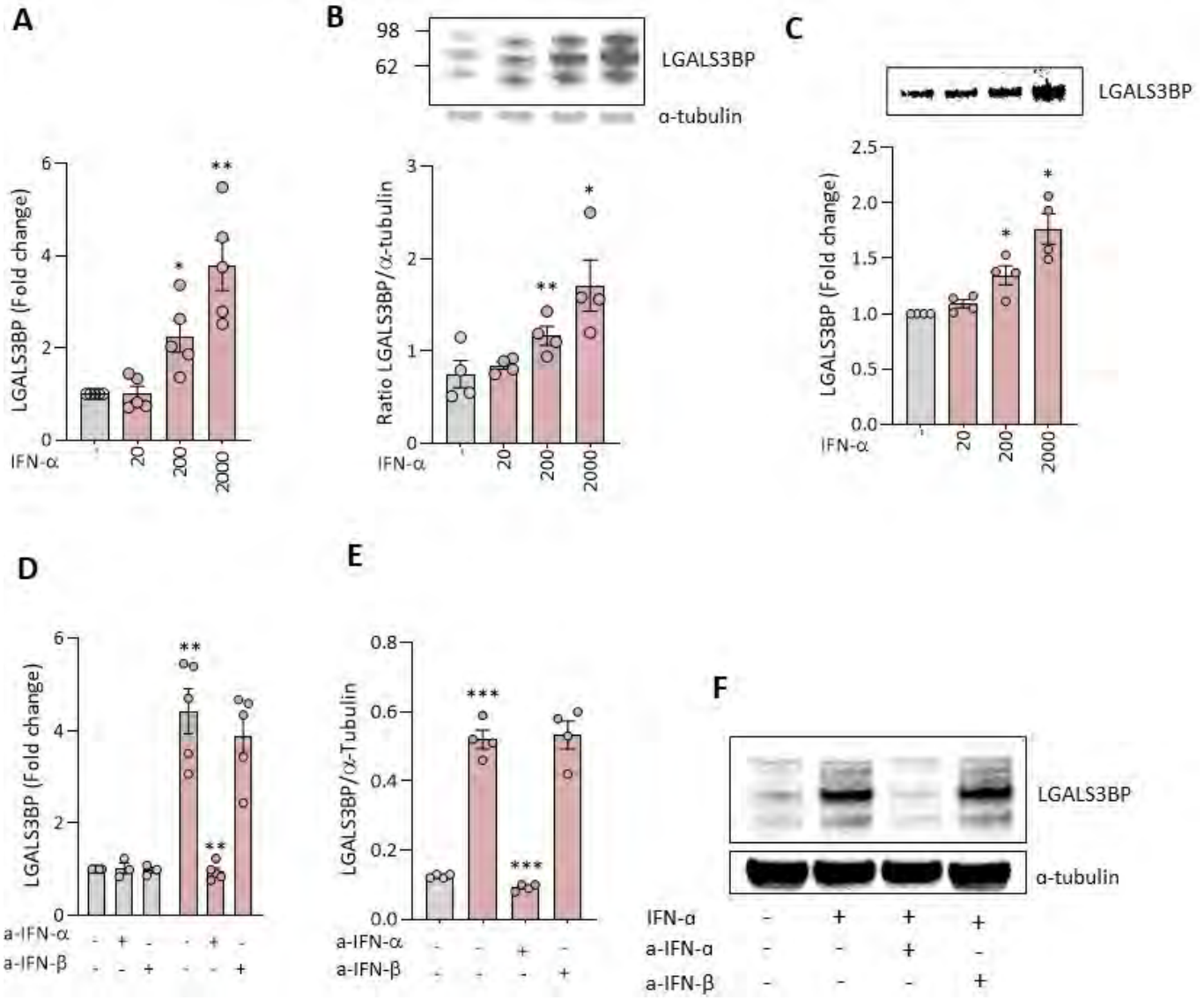


Figure 2. IFN-α induces the expression and the production of LGALS3BP in Megakaryocyte cell line (MEG-01) in a dose dependent manner MEG-01 cells were stimulated or not with 20, 200 and 2000 U/mL IFN-α. After 24h, LGALS3BP gene expression (A) and protein expression in the lysates and supernatants (B and C respectively) were determined by qPCR and western blot analysis. LGALS3BP gene (D) and protein (E and F) expression were quantified using qPCR and western blot in MEG-01 cell lysates after stimulation with 2000 U/mL IFN-α in the presence or absence of neutralizing antibodies against IFN-α and IFN-β All data represent the mean ± s.e.m. and are analyzed by two-sided Student's t-test. *P < 0.05, **P < 0.01, ***P < 0.001.

between clinical features of SLE and circulating serum LGLAS3BP was performed. Finally, the effects of platelets and LGALS3BP on macrophage inflammatory response were studied *in vitro*.

Results: Platelet transcriptome analysis revealed that LGALS3BP was one of the most differentially expressed transcripts in SLE versus matched-healthy controls (Fold change, 3.9, adjusted *P*-value = 2.5×10^{-11}) (**Figure1A**). Consistently, LGALS3BP in platelet releasates was significantly higher in 40 patients with SLE than 20 controls ($p = 0.002$) (**Figure1B**). Platelet LGALS3BP gene and protein expression were highly correlated with circulating LGALRS3BP in serum ($r^2 = 0.370$, $p = 0.003$ and $r^2 = 0.689$, $p < 0.0001$ respectively) (**Figure1E and F**). LGALS3BP measured in serum of 115 patients with SLE correlated with the SELENA SLEDAI hybrid disease activity index ($r^2 = 0.322$, $p = 0.0005$) (**Figure1G**). In particular, higher serum LGALS3BP levels were observed in SLE patients with lupus nephritis compared to those with SLE and inactive disease (P=0.0001) (**Figure1H**). In longitudinal analysis of 22 patients without

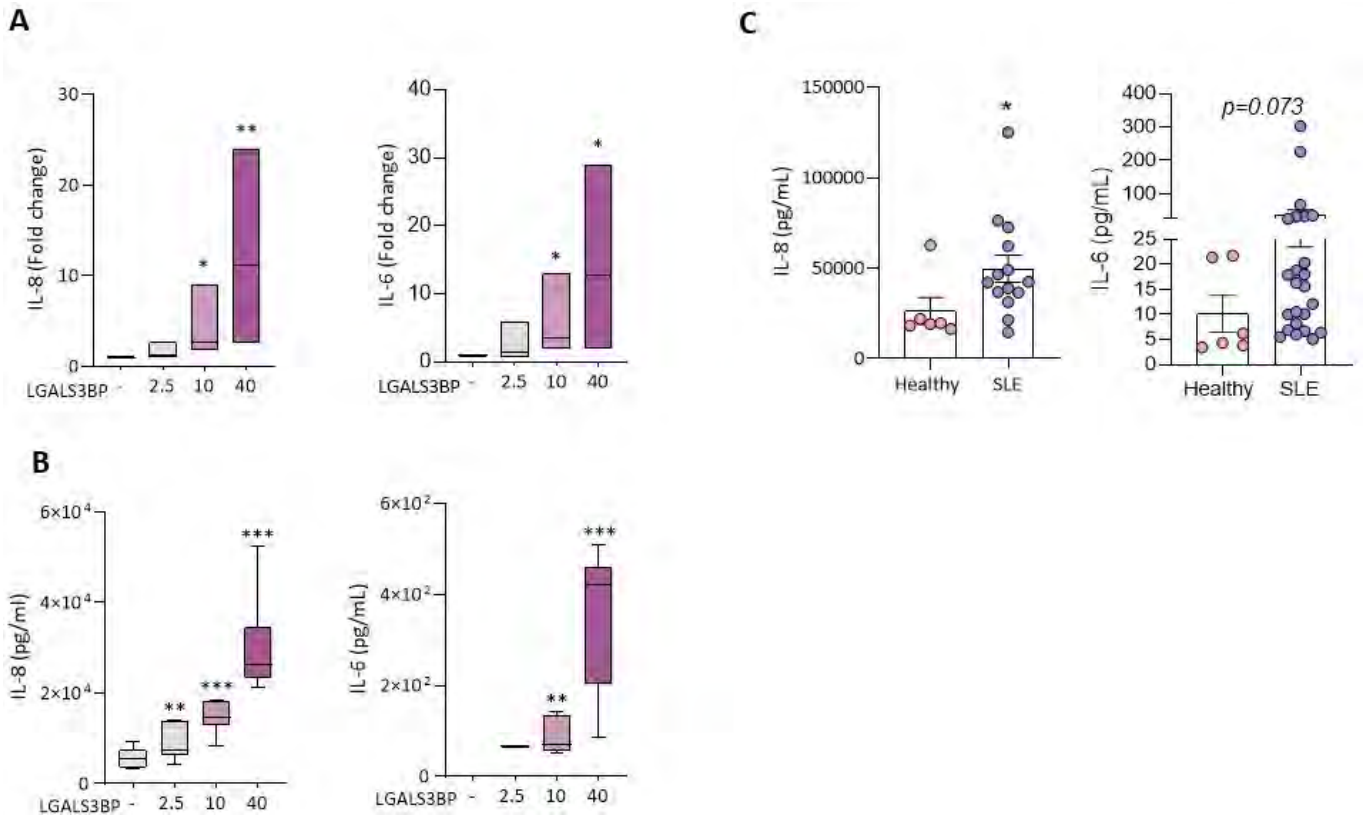


Figure 3. LGALS3BP and platelets from patients with SLE induce production of pro-inflammatory cytokines IL-8 and IL-6 in macrophages Monocytes derived macrophages were cultured for 7 days for differentiation in the presence of macrophage colony stimulating factor (MCSF) After differentiation, cells were either cultured without stimulation or stimulated with increasing concentrations of LGALS3BP (2.5, 10 and 40 μg/mL) for 6h and cytokine gene expression (A) and secretion (B) were determined by qPCR and multiplex beads-based assay respectively. Platelet releasates from patients with SLE or healthy controls were added to macrophages for 24h. IL-8 and IL-6 were measured in the supernatants using multiplex beads-based assay respectively. All data represent the mean ± s.e.m. and are analyzed by two-sided Student's t-test. *P < 0.05, **P < 0.01, ***P < 0.001.

proteinuria at baseline who went on to develop proteinuria over time, circulating plasma LGALS3BP tracked with flares of nephritis (p=0.06). *In vitro*, IFN-α induced the expression and production of LGALS3BP in MEG-01 cells in a dose dependent manner (**Figure2A, B and C**), which was completely inhibited by IFN-α neutralizing antibody (**Figure2D, E and F**). Recombinant LGALS3BP (**Figure 3A and B**) and Platelet releasates from SLE (**Figure 3C**) induced the production of pro-inflammatory cytokines such as IL-8 (p=0.04) and IL-6 (p=0.073) by macrophages.

Conclusion: These data show that platelets isolated from patients with SLE highly express and secrete LGALS3BP which induces a proinflammatory macrophage and is associated with SLE disease clinical phenotype. LGALS3BP may contribute to pathogenesis and serve as a novel biomarker of SLE disease activity.

Disclosure: H. EL Bannoudi, None; **M. Cornwell**, None; **E. Luttrell-Williams**, None; **A. Engel**, None; **C. Rolling**, None; **P. Izmirly**, Momenta/Janssen, 1; **H. Belmont**, Alexion, 6; **K. Ruggles**, None; **R. Clancy**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **J. Berger**, None.

Abstract Number: 1499

Imbalance Between T Follicular Cells and T Regulatory Cells Involved in High Fat-Diet Associated Lupus Development in MRL/lpr Mice

Ronak Patel[1], Therese Posas-Mendoza[2], Juan Meng[3], Xuhua Shi[3], Swathi Dhulipala[4], Chad Hille[2], Linh Hellmers[1], Robert Quinet[5], William Davis[6], Jerald Zakem[7], Chandana Keshavamurthy[1], Zongbing You[3] and Xin Zhang[1], [1]Ochsner, New Orleans, LA, [2]Ochsner Clinic Foundation, New Orleans, LA, [3]Tulane University, New Orleans, LA, [4]Ochsner Clinic Foundation, River Ridge, LA, [5]Ochsner Health, River Ridge, LA, [6]Ochsner Medical Center, New Orleans, LA, [7]Ochsner Health Systems, Metairie, LA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease characterized by persistent inflammation and production of autoantibodies, which deposit within numerous tissues leading to systemic damage. Multiple studies have suggested a link between obesity, metabolic syndrome, and SLE. Our recent data has shown that fat-diet-induced obesity exacerbates lupus symptoms in lupus prone mice, suggesting a unique role of obesity in autoimmune pathogenesis. This study is to probe the role of follicular T helper (Tfh) cells and T regulatory (Treg) cells in fat-diet associated lupus development in MRL/lpr lupus prone mice.

Methods: Forty MRL/lpr mice were fed and grouped in a regular diet (RD, 10% calories from fat) or high fat diet (HFD, 60% calories from fat). Their body weights and skin lesions were recorded weekly. Urine protein was assessed weekly by Bradford assay. Blood was collected monthly for anti-dsDNA antibody and anti-nuclear antibody (ANA) detection. At week 14, mice were euthanized, their spleen were measured and weighed. Kidney and skin biopsy were embedded in paraffin and tissue sections for H&E and PAS staining to detect lupus histopathological lesions and quantified as kidney index and histological skin score. B cells ($CD19^+$), germinal center B cells (GC-B cell, $GL7^+CD19^+$), plasma cells ($CD20^-CD138^+$), Tfh cells ($CD4^+CXCR5^+ICOS^+$), and Treg cells ($CD4^+FoxP3^+$) were examined in splenocytes by flow cytometry and confirmed in the spleen slides using immunofluorescent staining.

Results: The HFD group demonstrated a significant increase in mouse body weight by week 3 and continued until week 14 compared to RD group ($p < 0.05$ to $p < 0.01$). SLE features, such as skin lesions on the dorsum of neck ($p < 0.05$), splenomegaly ($p < 0.05$), and proteinuria developed significantly earlier and more severe in HFD group than RD group. Increased of acute/chronic index of kidney and increased levels of anti-dsDNA antibody were also observed in HFD group. However, ANA level was comparable between HFD group and RD group. At week 14, the Immune cells such as the frequencies of GC-B cells and plasma cells were significantly higher in the spleens of HFD group than RD group ($p < 0.05$). There was no difference in the frequencies of $CD4^+$ and $CD8^+$ T cells in the spleens of HFD group and RD group. Significant increase of Tfh cells and enlarged germinal centers were observed in the spleen of HFD group ($p < 0.05$). The ratio of Tfh/Treg in the spleen of HFD mice was also significantly increased compared to the RD group ($p < 0.05$).

Conclusion: Our results show that high fat diet induced an accelerated and more severe form of lupus development and imbalance of Tfh/Treg cells in MRL/lpr mice. This indicates that HFD affects T cell homeostasis and exacerbates the autoimmunity in lupus development. Modulations of diet or restoring the balance between Tfh and Treg cells may improve both lupus symptoms and outcomes in genetically predisposed SLE patients.

Disclosure: **R. Patel**, None; **T. Posas-Mendoza**, None; **J. Meng**, None; **X. Shi**, None; **S. Dhulipala**, None; **C. Hille**, None; **L. Hellmers**, None; **R. Quinet**, None; **W. Davis**, None; **J. Zakem**, None; **C. Keshavamurthy**, None; **Z. You**, None; **X. Zhang**, None.

Abstract Number: 1500

Expression of Neuropilin-1 Is Significantly Increased in Dendritic Cells and CD4 + T Cells and It Correlates Disease Activity in the Patients with Systemic Lupus Erythematosus

Yunjung Choi[1], Eun-gyeong Lee[1], Yu-Mi Lee[2], Myeung-Su Lee[3], Chang-Hoon Lee[3], Chong Hyuk Chung[3] and **Wan-Hee yoo**[1], [1]Research Institute of Clinical Medicine of Jeonbuk national university-Biomedical Research Institute of Jeonbuk national university hospital, Jeonju, Republic of Korea, [2]Jeonbuk National University Hospital, Jeonju, Republic of Korea, [3]Wonkwang University Hospital, Iksan, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Neuropilin-1 (NRP-1) is a transmembrane glycoprotein that acts as a receptor of class III/IV semaphorins which role in the pathogenesis of autoimmune diseases. The NRP-1 has been studied for its immunomodulatory activity in malignancy, but there have been limited studies on the role of autoimmune inflammatory rheumatic disease, including systemic lupus erythematosus (SLE). This study was aimed to investigate the expression and the clinical implication of NRP-1 in lupus mouse models and patients with SLE.

Methods: The expression of NRP-1 was measured in T cells in spleen and renal tissue and monocyte-induced dendritic cells from control mouse and TLR-7 agonist-induced lupus mouse by flow cytometry, PCR, and immunofluorescence. CD4+ T cells from human peripheral blood were isolated to investigate the expression of NRP-1 in healthy control and the patients with SLE (n=40). In vitro analysis, the activation of the JAK-STAT pathway was examined in monocyte-induced dendritic cells treated with TLR-7 agonists with or without NRP-1 receptor antagonists.

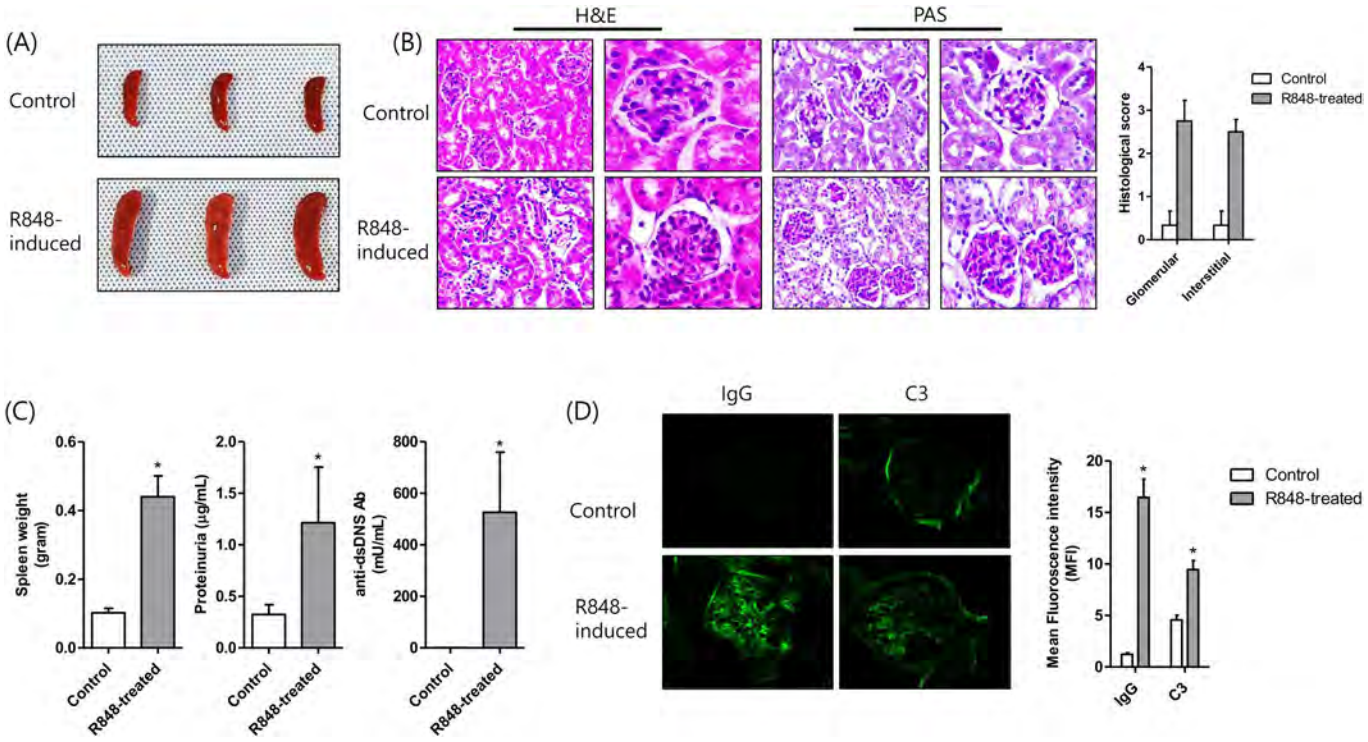
Results: The frequency of NRP-1 positivity in CD4+ T cells in spleen was significantly higher in lupus mouse group compared to vehicle mouse group. The quantitative analysis of NRP-1 fluorescence intensity in the kidney, and monocyte-derived dendritic cells isolated from bone marrow revealed an increased level in the lupus group compared to the control group.

The CD4+ T cells from peripheral blood mononuclear cells in the patients with lupus also showed significantly higher frequency of NRP-1 positive CD4+ T cells than those from healthy controls. Comparing the correlation of the expression of NRP-1 and disease activity with SLEDAI, C3, C4, and anti-DNA antibodies, the significant correlation between NRP-1 and disease activity markers were confirmed.

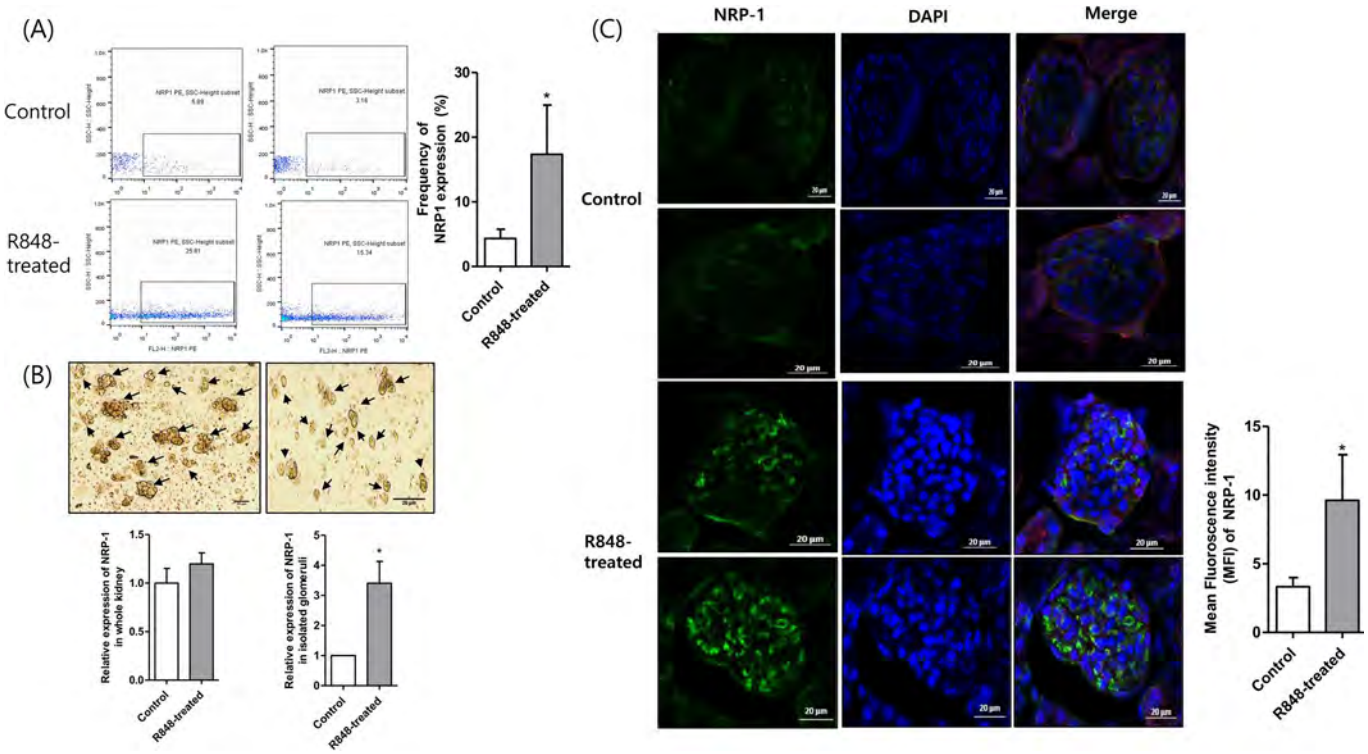
In vitro analysis of monocyte-derived dendritic cells, the phosphorylation of STAT and expression of NRP-1 were enhanced by treatment of TLR7 agonist and these expressions were decreased by co-treatment of EG00229, which is an NRP-1 receptor antagonist.

Conclusion: Our results show that NRP-1 is involved in the phosphorylation of STATs activated by TLR-7 agonists, and the expression of NRP-1 significantly correlates with the disease activity of patients with SLE.

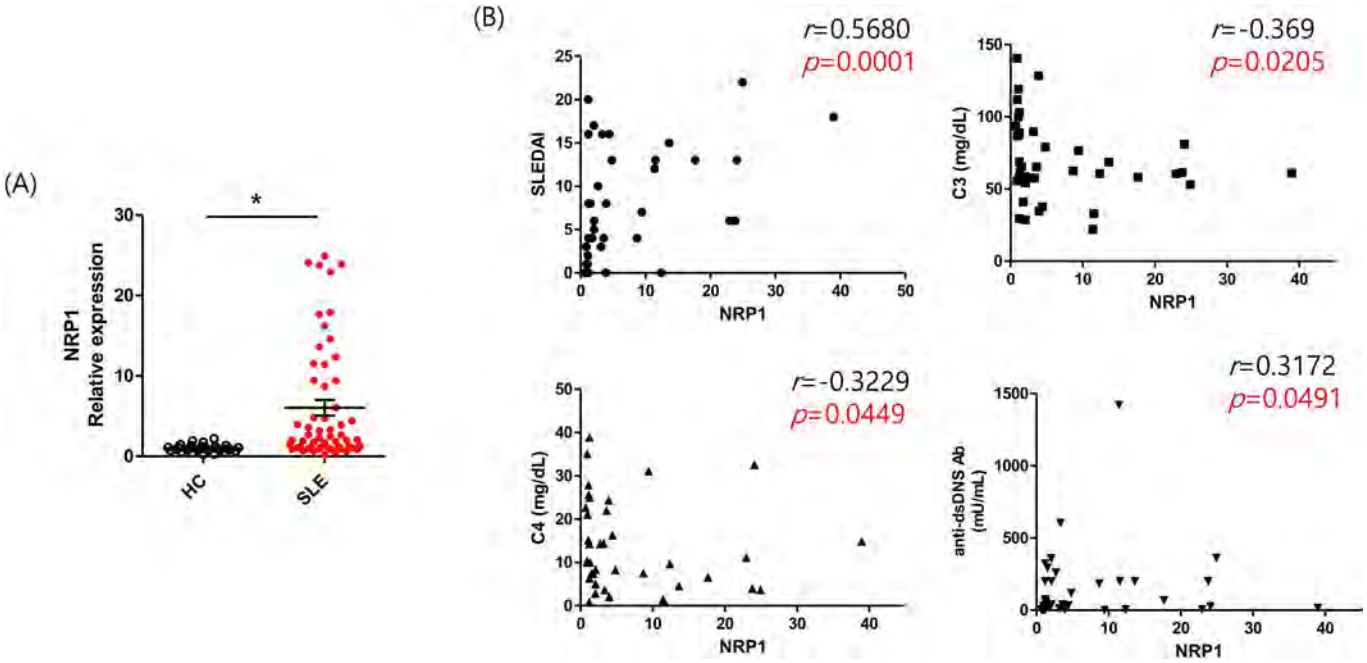
These results indicate the significant contribution of NRP-1 in the pathogenesis of SLE and the potential of targeting NRP-1 for the treatment of SLE.



Toll-Like Receptor 7 agonist-induced lupus model



Upregulated expression of NRP-1 in spleen and kidney of lupus murine model



The correlation of NRP-1 expression and disease activity in the patients with SLE

Disclosure: Y. Choi, None; **E. Lee**, None; **Y. Lee**, None; **M. Lee**, None; **C. Lee**, None; **C. Chung**, None; **W. yoo**, None.

Abstract Number: 1501

Molecular Modelling Predicts **Inhibition** of Functional Effects of Anti-thrombin III on Factor Xa Mediated Complement Activation by Anti-Factor Xa IgG in SLE and APS

Thomas McDonnell[1], Raj Amarnani[2], Valentina Spiteri[2], Carina Spicer[3], Charis Pericleous[4], Bahar Artim-Esen[5], Ian Mackie[1], Marina Botto[4], Anisur Rahman[1] and Ian Giles[1], [1]University College London, London, United Kingdom, [2]University College London, London, [3]Merck, Philadelphia, PA, [4]Imperial College London, London, United Kingdom, [5]Istanbul University School of Medicine, İstanbul, Turkey

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The significance of antibodies directed against activated Factor (FXa) and thrombin (Thr) found in ~40% of patients with Systemic Lupus Erythematosus (SLE) and/or Antiphospholipid Syndrome (APS) has not been determined. FXa and Thr are both co-regulated by antithrombin (AT)III and increasingly implicated in alternative pathways of complement activation. Therefore, we studied the ability of anti-(a)FXa and/or anti-(a)Thr IgG to modulate complement activation in SLE and APS.

Methods: Patients with SLE +/- APS and known aThr and/or aFXa IgG positivity had serial measurements of complement C3 at clinic appointments at University College London Hospital from 2015-19. Affinity purification of aFXa and aThr IgG were performed by passage through heparin/FXa or heparin/Thr and then protein G column. The effect of this IgG upon FXa and Thr mediated C3 and C5 activation was measured by Western Blot. Structural analysis of FXa and Thr was performed by Scalable Molecular Dynamics (NAMD), Visual Molecular Dynamics (VMD) and Discotope

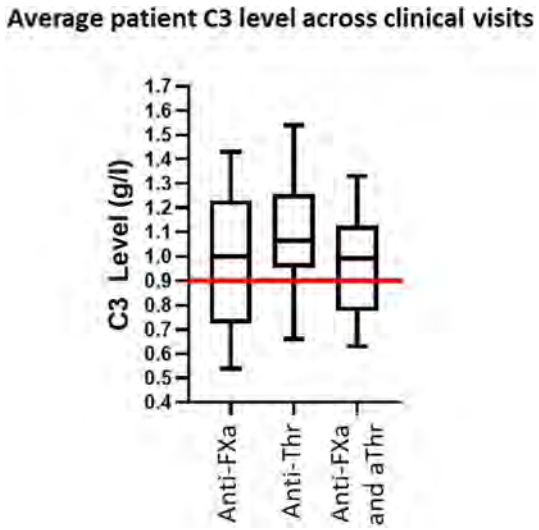


Figure 1. The average C3 level from SLE and APS patients (n=66) across their visits to clinic (2015-2019) demonstrate lower levels of C3 on average for FXa positive patients and double positive (aFXa and aThr) patients compared to aThr alone. The red line indicates clinical cutoff for low C3 levels. This implies the presence of aFXa antibodies may influence the C3 levels of SLE and APS patients.

(v1.1). Predicted sites were modelled onto high resolution crystal structures of the ATIII-FXa and ATIII-Thr complexes and compared with the in-vitro ability of ATIII to regulate aFXa-FXa and aThr-Thr mediated C3/C5 activation.

Results: Longitudinal analysis of 66 patients with SLE (n=5 with APS) from an average of 8.2 (range 1 to 10) visits across 5 years found that patients positive for anti(a)FXa alone (n=16) or in combination with anti(a)Thr IgG (n=26) had lower C3 levels than patients with aThr IgG alone (n=24) (Figure1). We affinity purified IgG from 15 of these patients. aThr IgG increased Thr mediated activation of C3 (x 1.8 fold) and C5 (x3 fold), whilst aFXa IgG increased (x 1.3 fold) C3 activation only. Using *in silico* epitope mapping we identified potential epitopes for binding of aFXa to FXa and aThr to Thr. These studies predicted steric hindrance of binding to ATIII at 2 of 4 potential aFXa IgG epitopes on FXa compared with only 1 of 6 aThr IgG epitopes on Thr. This increased likelihood of steric hinderance of aFXa compared to aThr was confirmed by in-vitro studies whereby ATIII inhibition of Thr-mediated C3 and C5 activation was not affected by aThr IgG, whilst ATIII inhibition of FXa-mediated C3 and C5 activation was abrogated by aFXa IgG.

Conclusion: We propose a novel method of complement regulation in SLE and APS patients whereby aFXa and aThr IgG increase complement activation. Furthermore, we demonstrate that natural inhibition by ATIII is less efficient on FXa-FXa IgG-mediated complement activation compared with the one mediated by Thr-aThr IgG due to proximity of the IgG epitope to the ATIII binding site in FXa but not Thr.

Disclosure: T. McDonnell, None; **R. Amarnani**, None; **V. Spiteri**, None; **C. Spicer**, Merck & Co., Inc., 3; **C. Pericleous**, None; **B. Artim-Esen**, None; **I. Mackie**, None; **M. Botto**, None; **A. Rahman**, Lilly, 6; **I. Giles**, None.

Abstract Number: 1502

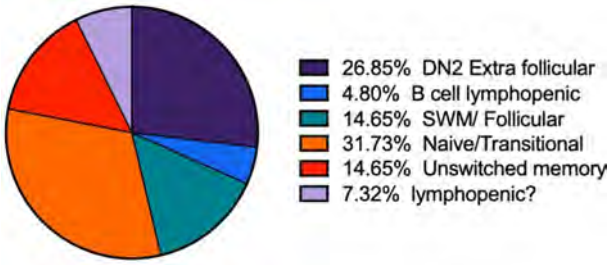
Longitudinal Changes in B Cell Subsets in Patients in the Mesenchymal Stromal Cell Trial in Lupus: Analysis of the First Cohort

Diane Kamen[1], S Sam Lim[2], Scott Jenks[3], Regina Bugrovosky[3], Aisha Hill[3], Chungwen Wei[3], Cristina Drenkard[3], Kenneth Kalunian[4], Ummara Shah[5], Mariko Ishimori[6], Rosalind Ramsey-Goldman[7], Saira Sheikh[8], Mary Alison Mahieu[7], Daniel Wallace[9], Ellen Goldmuntz[10] and **Gary Gilkeson**[1], [1]Medical University of South Carolina, Charleston, SC, [2]Department of Medicine, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, [3]Emory University, Atlanta, GA, [4]UC San Diego, La Jolla, CA, [5]University of Rochester, Rochester, NY, [6]Cedars-Sinai Health System, Los Angeles, CA, [7]Northwestern University, Chicago, IL, [8]University of North Carolina, Chapel Hill, NC, [9]Attune Health, Beverly Hills, CA, [10]National Institutes of Health, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Recent advances allow expanded identification of B cell subtypes of pathogenic potential in lupus. Of particular interest are IgD- CD27- double negative (DN2) B cells and activated naïve B cells (AN). These subsets are expanded in African American women with lupus and are progenitors of autoantibody producing cells. Less is known of these subsets in other ethnicities, their stability over time or their response to treatment. As part of the double-blind placebo controlled trial of mesenchymal stromal cells (MSCs) for treatment of refractory lupus, we assessed B cell phenotypes at week 0, week 4, week 8 and week 24 in patients in the first cohort of participants. To prevent unblinding, we did not determine associations between B cell phenotypes and clinical response during this low dose cohort of the trial.

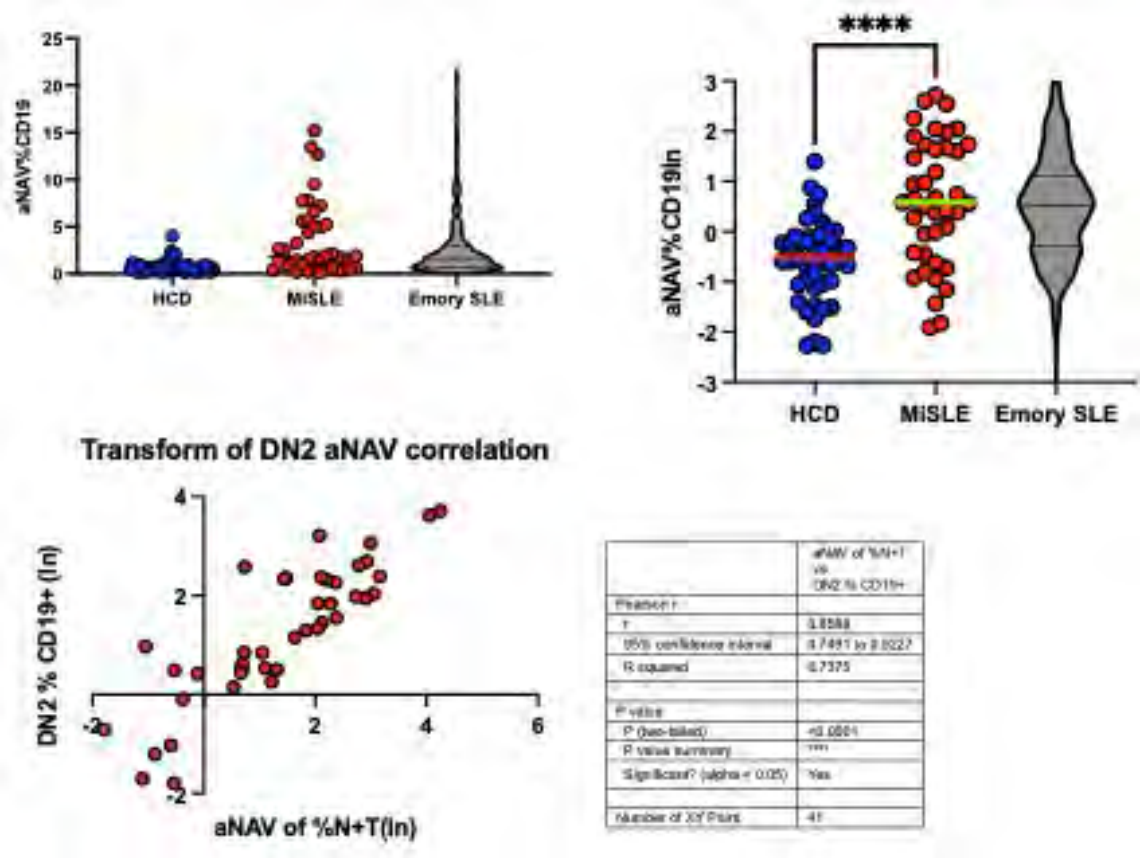
Methods: 41 lupus patients, primarily women (90%) and mixed ethnicities (49% Caucasian, 39% African American, 12% other) were enrolled. They were randomized to receive either $1x10^6$ umbilical cord derived MSCs/kg or placebo



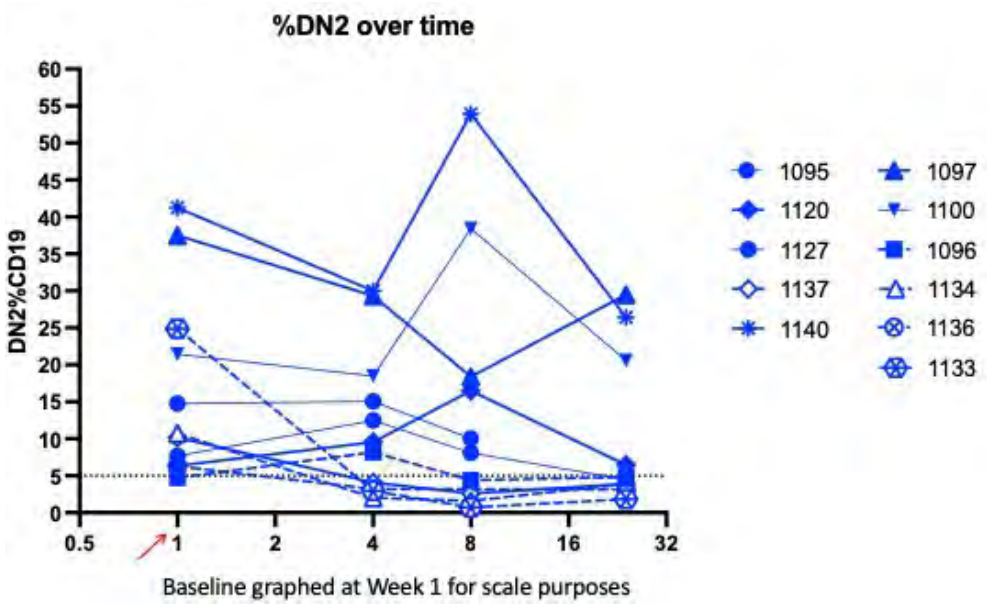
B cell phenotypes at baseline of the 41 patients enrolled into the MSCs in Lupus Erythematosus trial

at a 2/1 ratio. All patients met ACR criteria and had a SLEDAI >6 having failed immunosuppressive therapy. Patients with nephritis were included. Samples for B cell analysis were shipped to Emory for analysis via overnight delivery. Analyses were done by FLOW using 11 color flow. Comparative analyses were done with matched healthy controls and with previously analyzed samples in the Emory lupus cohort.

Results: As expected, there was significant heterogeneity of B cell phenotypes, as demonstrated in Figure 1. with 31.7% expressing a Naïve/Transitional phenotype and 26.9% having a DN2 extrafollicular phenotype. The B cell phenotype remained stable generally, but there were substantial shifts in some patients. Over 50% of lupus study patients had increased numbers of DN2 B cells compared to controls (Figure 2). There was a strong positive correlation between percent of DN2 B cells and AN B cells. Overtime, patients with a very high percentage of DN2 B cells retained this phenotype, where those with a moderate DN2 expansion at baseline, decreased significantly over



Activated naive B cells are expanded in patients with SLE. There is a strong correlation between percentage of activated naive and DN2 B cells in the patients in the trial.



Chronologic changes in DN2 B cells. Data presented is from patients whose baseline % of DN2 B cells was greater than 5%. As noted, patients with very high percentage of DN2 B cells tended to retain this phenotype while those with moderate increased percentage of DN2 B cells, the % DN2 cells trended down over the 24 weeks. Only 1/41 patients had an increased DN2 percentage during the trial period.

time. Patients with low DN2 B cells at baseline retained this phenotype. Unswitched memory B cells were low and remained low compared to controls. There was considerable heterogeneity in switched memory B cells, but no population level differences from controls. Overall naïve B cells were similar between patients and controls, but some patients had very low levels of naïve cells.

Conclusion: These results indicate mixed ethnicity patients from 7 sites in the US, participating in the MSC trial, exhibited considerable B cell phenotypic heterogeneity, though the majority had a B cell Naïve/Transitional or DN2 extrafollicular phenotype. Longitudinal analysis reveals stability of B cell phenotype in many patients, while others have significant changes in B cell phenotype, predominantly due to decreased frequency of DN2 and AN B cells. Further characterization will determine clinical correlates between baseline B cell phenotype and lupus disease phenotype and differences in response to therapy based on initial B cell phenotypes.

Disclosure: D. Kamen, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **S. Jenks**, None; **R. Bugrovosky**, None; **A. Hill**, None; **C. Wei**, None; **C. Drenkard**, GSK, 1, 5; **K. Kalunian**, Amgen, 2, AbbVie, 2, AstraZeneca, 2, Biogen, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Equillium, 2, Genentech/Roche, 2, Gilead, 2, Janssen, 2, Lupus Research, 5, Pfizer, 5, Sanford Consortium, 5, Vielabio, 2, Aurinia, 2, Alliance, 2, Nektar, 2; **U. Shah**, None; **M. Ishimori**, None; **R. Ramsey-Goldman**, None; **S. Sheikh**, None; **M. Mahieu**, None; **D. Wallace**, None; **E. Goldmuntz**, None; **G. Gilkeson**, None.

Abstract Number: 1503

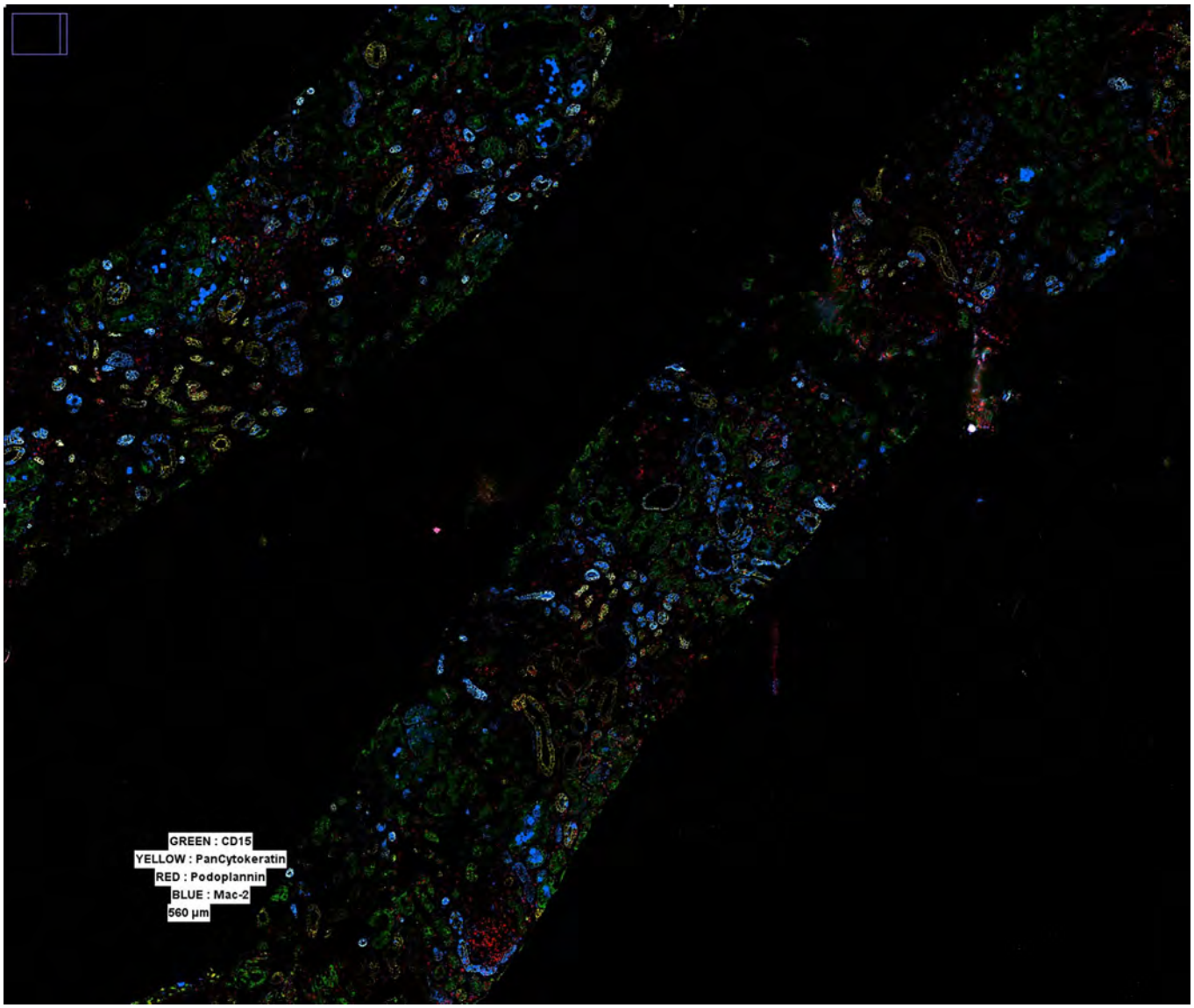
Putting the Pieces on the Board: Mapping SLE Nephritis Biopsies from the Accelerating Medicines Project Using High-Density Immunofluorescence Imaging

Craig Smuda[1], Anna Eichinger[2], Robert Clancy[2], Jill Buyon[3] and Boris Reizis[4], [1]NYU Grossman School of Medic ine, New York, NY, [2]NYU Grossman School of Medicine, New York, NY, [3]NYU School of Medicine, New York, NY, [4]New York University Grossman School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The Accelerating Medicines Project (AMP) has enabled significant increases in understanding of SLE nephritis pathology, providing a profile of dozens of leukocyte subsets within affected kidneys by single-cell RNA sequencing of nephritis biopsies. While these results suggest a complex network of interactions between cell populations during nephritis, the spatial positioning of these cells is lost during the sequencing process. Inferred interactions between the diverse identified cell types would be greatly strengthened by detailed spatial information, placing these cells in context with each other and with the surrounding structures of the kidney.

Methods: In consultation with AMP, we have used CODEX, a multicycle imaging technology allowing for staining of up to 40 targets on a single tissue sample without tissue degradation, to capture preliminary images of the AMP

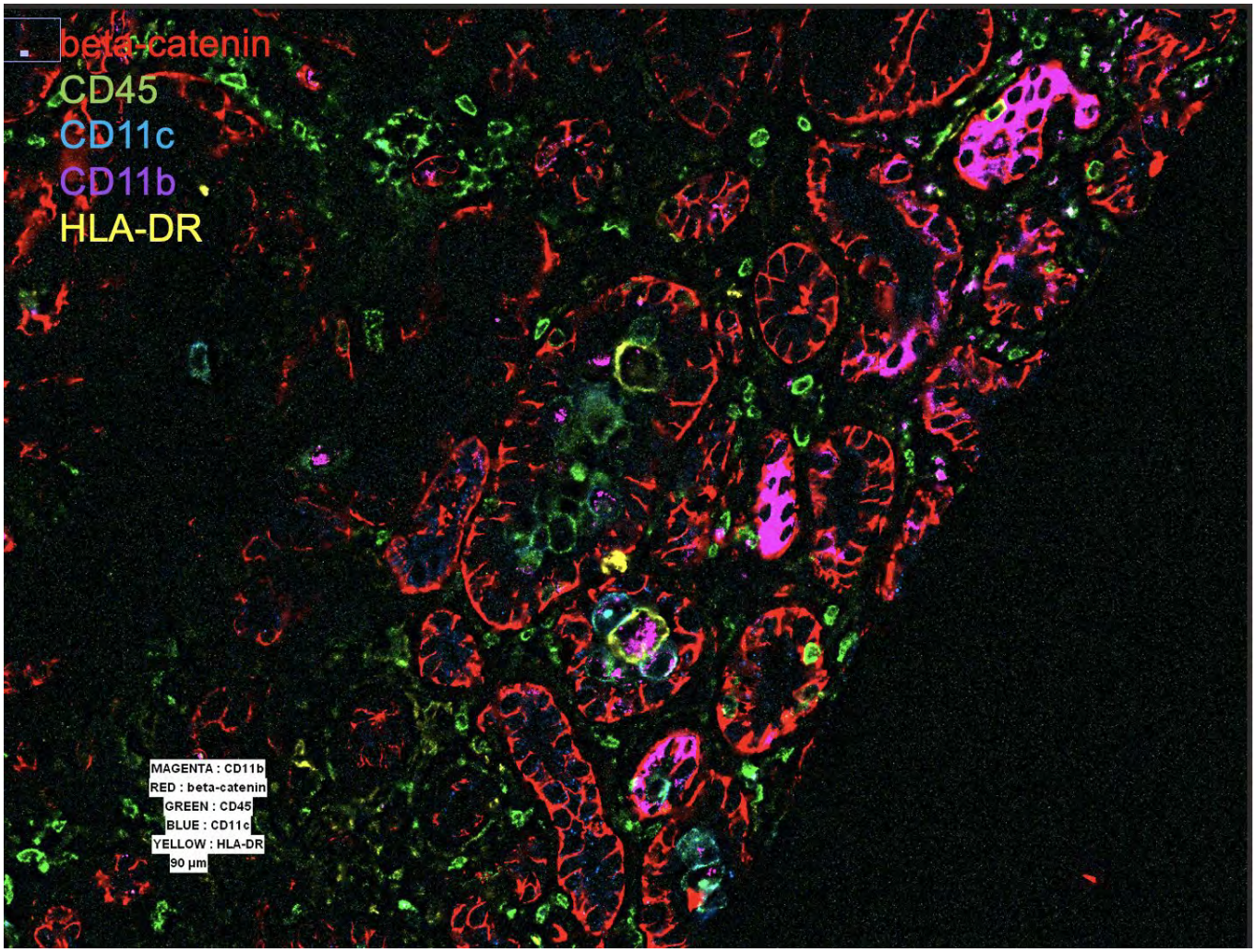


A wide view of a selected biopsy demonstrates ultrastructure via multiple structural markers. Multiple such regions can be captured, allowing for the entirety of a biopsy sample to be imaged. All images shown display only a subset of the overall stained markers due to visual limitations.

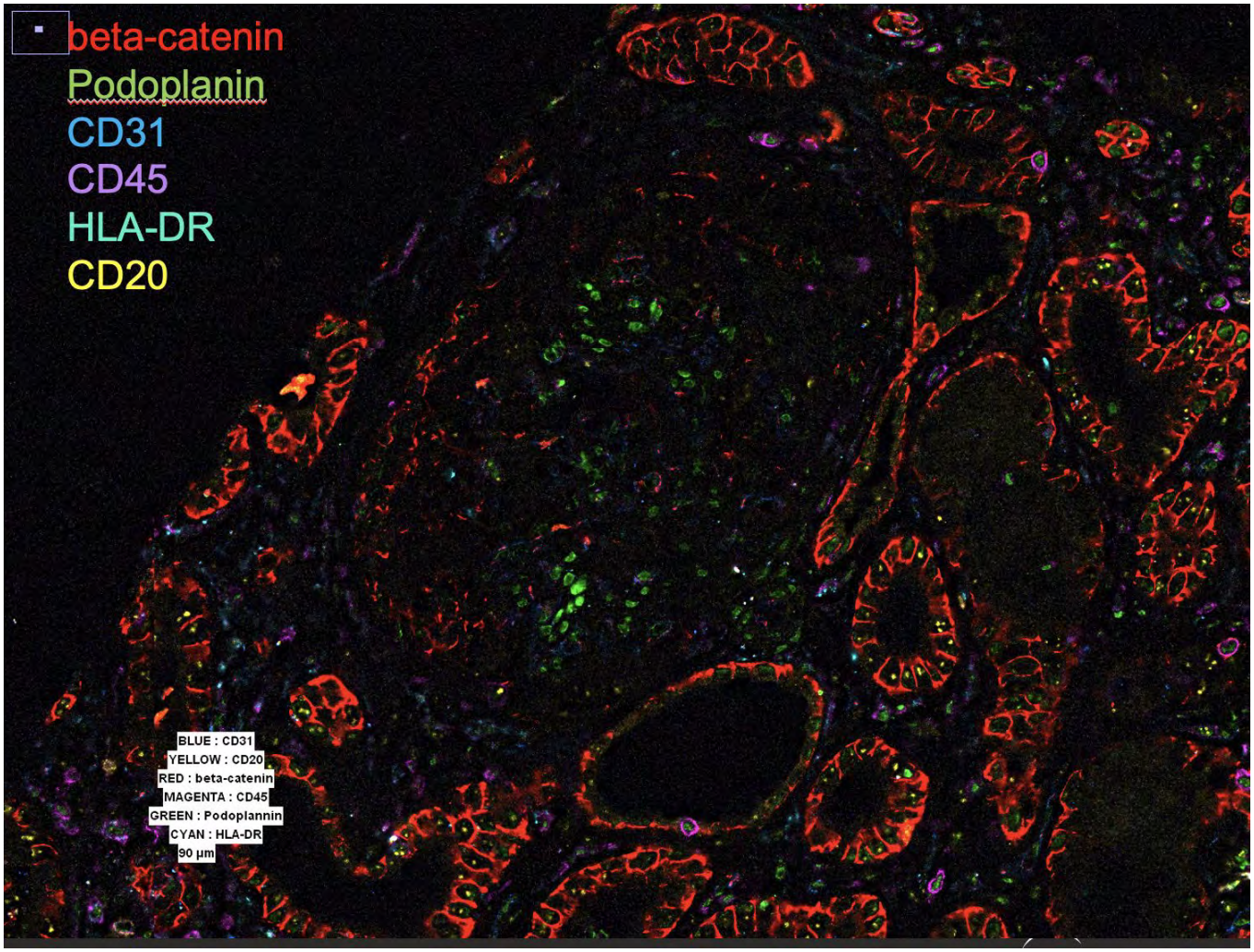
tissue biopsies available at New York University. Extensive antibody screening, sample preparation, optimization of antigen retrieval, and imaging steps are required, which remain under active optimization to allow for imaging the entirety of the AMP biopsy cohort available at the Grossman School of Medicine, which has been fully processed for future staining.

Results: At present we are able to image sixteen targets capturing dense interstitial T and B cell infiltrates, intratubular and interstitial myeloid populations, and sparser glomerular infiltrating cells in our demonstration cohort, with clear imaging of the glomeruli, tubules, and interstitial spaces. Further targets will be added as they are optimized, further allowing subsetting of T, B, and myeloid populations, with the goal of capturing the populations identified previously in single-cell sequencing.

Conclusion: CODEX imaging of renal biopsy samples provides spatial context for prior observations across a range of SLE nephritis samples, with complex interstitial populations found around glomeruli and tubules in active disease. Deeper profiling with expanded antigen targets to enable further sub-population phenotyping and activation states and imaging of the full cohort of biopsies available at NYU will provide a spatial atlas to SLE nephritis and further reveal underlying mechanisms of disease.



Close examination of a tubule reveals diverse infiltrating cells, including CD11c+, CD11b/c+, and sparse CD11b/c+ HLA-DR+ cells. Surrounding interstitial lymphocytes can be seen, which correspond to CD3+ CD4+ T cells (stains not shown).



Periglomerular infiltration, without significant glomerular cellular involvement, is seen in this image. CD20+ B cells and HLA-DR+ cells can be seen in the lower left.

Disclosure: C. Smuda, None; **A. Eichinger**, None; **R. Clancy**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmith-Kline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **B. Reizis**, None.

Abstract Number: 1504

Association Between Anti-RNP Antibodies and Interferon Gene Expression but Not Complement Consumption in SLE

Erika Hubbard[1], David Pisetsky[2] and Peter Lipsky[1], [1]AMPEL BioSolutions, Charlottesville, VA, [2]Duke University Medical Center, Durham, NC

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Anti-nuclear antibodies are important serologic features of SLE and facilitate diagnosis. Anti-double stranded DNA (dsDNA) antibodies are routinely monitored for disease prognosis and are related to complement consumption, with immune complex deposition in the kidneys causing tissue damage. Relatively less is known about autoantibodies against RNA binding proteins (RBP) and about the relationship between either autoantibody and expression of the interferon (IFN) stimulated gene (ISG) signature. Extensive laboratory measurements from 2 clinical trials of tabalumab in SLE (ILLUMINATE 1&2) allowed analysis of the relationships between autoantibody levels, ISG expression, and complement (C) C3 and C4 levels.

Methods: Microarray data from 1620 active (SLEDAI≥6), female SLE patients and accompanying laboratory measurements were analyzed (GSE88884). All patients satisfied ≥4 of the 1997 ACR classification criteria. Gene Set Variation Analysis (GSVA) was carried out to determine enrichment of the ISG signature in each patient. Linear regression analysis was used to determine relationships between ISG GSVA scores and C3 and/or C4 levels as well as autoantibody levels. Unbiased classification and regression trees (CART) were constructed to determine the highest predictors of ISG expression.

Results: Patients were stratified by autoantibody positivity. Comparison of GSVA scores of the core IFN signature, shared by type I and type II IFNs, demonstrated that SLE patients positive for anti-ribonucleoprotein (RNP) antibodies alone had greater enrichment of ISG than those positive for anti-dsDNA alone (Figure 1). Similar results were noted for gene signatures of type I IFN, IFNα2, IFNβ, and IFNγ. In contrast, the TNF gene signature was observed comparably in patients with anti-dsDNA or anti-RNP antibodies and the IL-1 signature was only observed in those with anti-dsDNA. By linear regression, IFN GSVA scores and C3 and C4 levels were significantly, inversely related in patients with anti-dsDNA antibodies but not those with anti-RNP antibodies. Antibody levels correlated with decreased C levels in dsDNA+ patients. Additionally, ISG GSVA scores were increased in anti-dsDNA+ patients with low C3 or C4 compared to anti-dsDNA+ patients with high/normal C, but there was no significant difference in ISG expression in anti-RNP+ patients with the same stratification. CART analysis identified anti-RNP status was the highest predictor of ISG GSVA score. Finally, 56.2% of SLE patients without an ISG signature exhibited autoantibodies, but only 13.7% of SLE patients negative for autoantibodies expressed the ISG signature (Figure 2).

Conclusion: Taken together, these data indicate that anti-RNP antibodies are associated with ISG expression more strongly than anti-dsDNA antibodies, but are not related to the depression of C3 or C4. Furthermore, ISG expression is not required for autoantibody production, but autoantibodies are likely directionally related to the ISG signature.

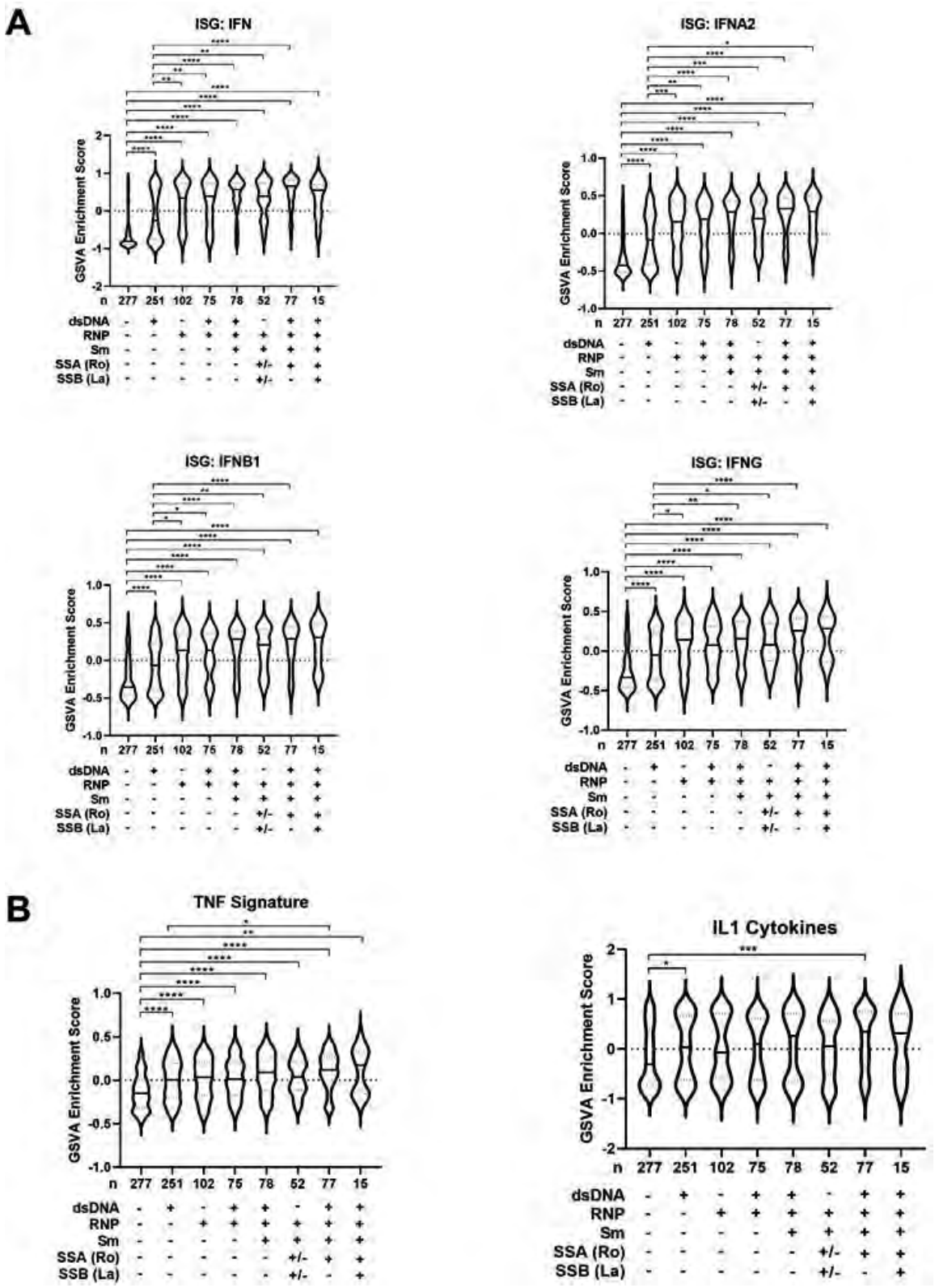


Figure 1. ISG (A) and other inflammatory cytokine (B) enrichment in SLE patients with various autoantibodies. Violin plots display median values of GSVA enrichment (solid lines) and upper and lower quartiles (dashed lines). *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001 by Dunn's multiple comparisons test.

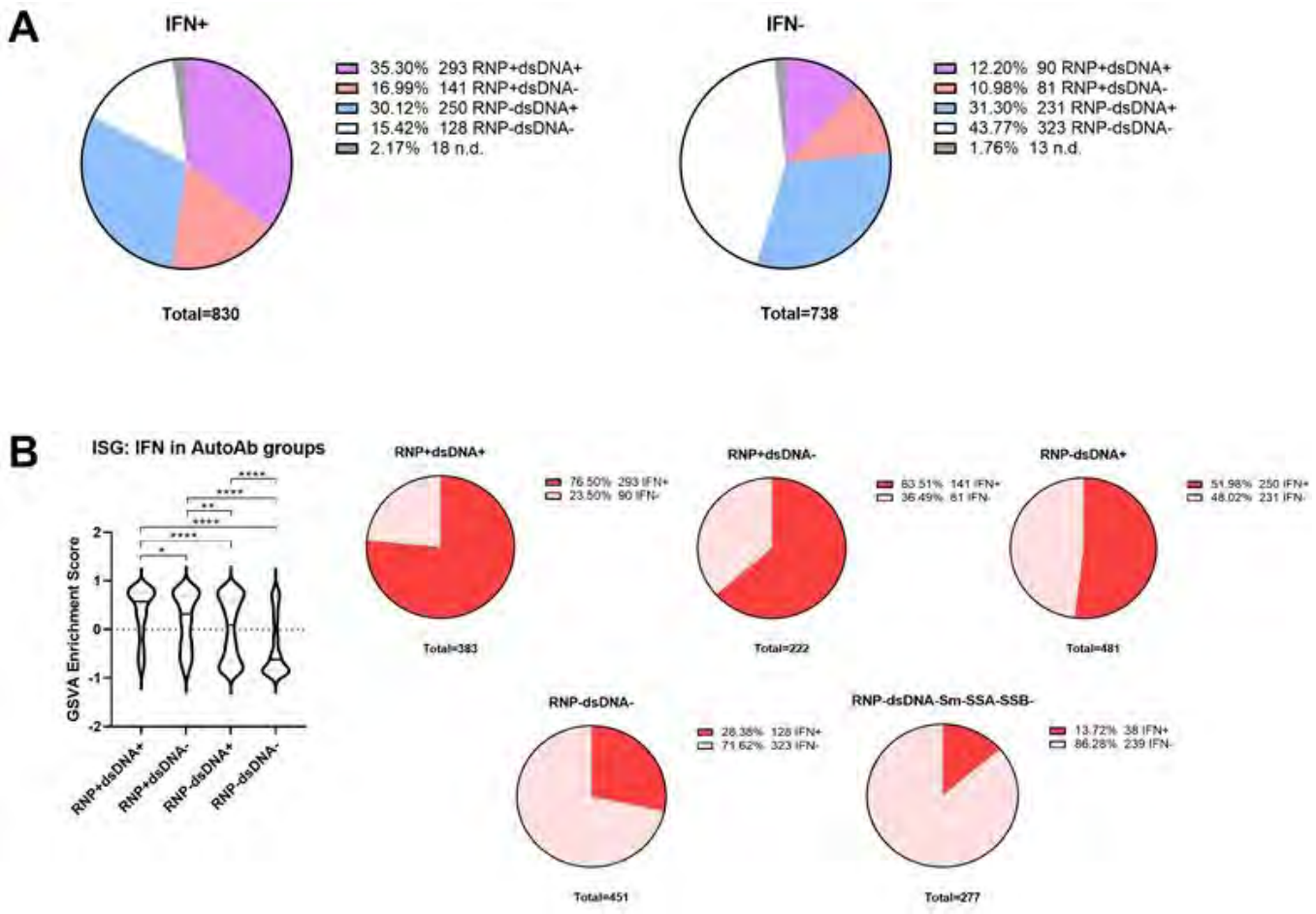


Figure 2. Autoantibody status was examined in IFN+ (GSVA enrichment score>0) and IFN- (GSVA enrichment score<0) SLE patients in (A) whereas IFN status was examined in autoantibody-stratified patients in (B). Dunn's multiple comparisons test determined significant differences in ISG enrichment among the groups displayed by violin plots. n.d.=no data. *p<0.05; **p<0.01; ***p<0.001; ****p<0.0001.

Disclosure: E. Hubbard, None; **D. Pisetsky**, Immunovant, 2; **P. Lipsky**, Horizon, 2.

Abstract Number: 1505

Inflammatory Dendritic Cell and Th17 Polarization in Mouse Model of Lupus Nephritis

Latha Prabha Ganesan[1], Noushin Saljoughian[1], James Turman[1], Murugesan Rajaram[1], Brad Rovin[2], Wael Jarjour[1] and Samir Parikh[2], [1]Ohio State University, Columbus, OH, [2]Ohio State University Wexner Medical Center, Columbus, OH

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: We have recently identified inflammatory dendritic cells (InfDC) in human lupus kidneys. These cells are over expressed in LN patients compared to healthy controls. Knowledge on how the infDC interact with intra-renal T cells and their role in pathogenesis of LN kidney is crucially needed

Methods: We examined infDC and T cells in the kidneys of NZM 2410 (NZM), from proteinuric (prot-NZM) mice (proteinuria ≥300mg/dl) and pre-proteinuric NZM (pre-prot-NZM) mice by Immunofluorescence (IF). To quantitatively assess infDC and various T cells, we analyzed single cell suspensions obtained by enzymatic digestion followed by gentle MACS dissociation from prot-NZM kidneys and pre-prot-NZM kidneys by multi-color flow cytometry using specific markers for infDC and T cells

Results: The immunofluorescence (IF) studies recapitulated the human LN robust infiltration of the infDC marked by FcRγ in the periglomerular and tubulointerstitium in prot-NZM compared to pre-prot-NZM. The infDC were also identified to be in close proximity to CD3+ T cells constant with an immunological synape. Further characterization by IF revealed infDC in mice LN were $FcR\gamma^{+}$, $MHCII^{+}$,$CD11c^{+}$,$CD163^{-}$,$CD11b^{+}$,$Ly6C^{+}$. Interestingly, 2 subtypes of infDC were identified in NZM mice, $FcR\gamma^{+}MHCII^{+}CD11c^{+}$,$CD11b^{+}$ and $FcR\gamma^{+}MHCII^{+}CD11c^{-}$,$CD11b^{+}$ and differentiated by the presence or absence of CD11c. Flow cytometry analysis of T helper cell phenotypes shows that Th17 expression, but not Th1 was upregulated significantly in prot-NZM compared to pre-prot-NZM in parallel to infDC.

Conclusion: 1) Similar to human LN, infDC are abundant in prot-NZM LN kidneys compared to respective pre-prot NZM and healthy control kidneys; 2) infDC synapse with CD3+ T cells in LN kidneys; and 3) Th17 cells, but not Th1 cells, correlate with infDC's expression in LN kidneys. These data suggests that infDC regulate the intra-renal Th17 cell response in LN and contribute to IL-17 mediated kidney injury. Ongoing studies will examine if these infDC are necessary or sufficient to cause LN.

Disclosure: L. Ganesan, None; **N. Saljoughian**, None; **J. Turman**, None; **M. Rajaram**, None; **B. Rovin**, GlaxoSmith-Kline, 2, 5; **W. Jarjour**, None; **S. Parikh**, None.

Abstract Number: 1506

SLAMF6 Compartmentalization Regulates Autoimmune T Cell Responses

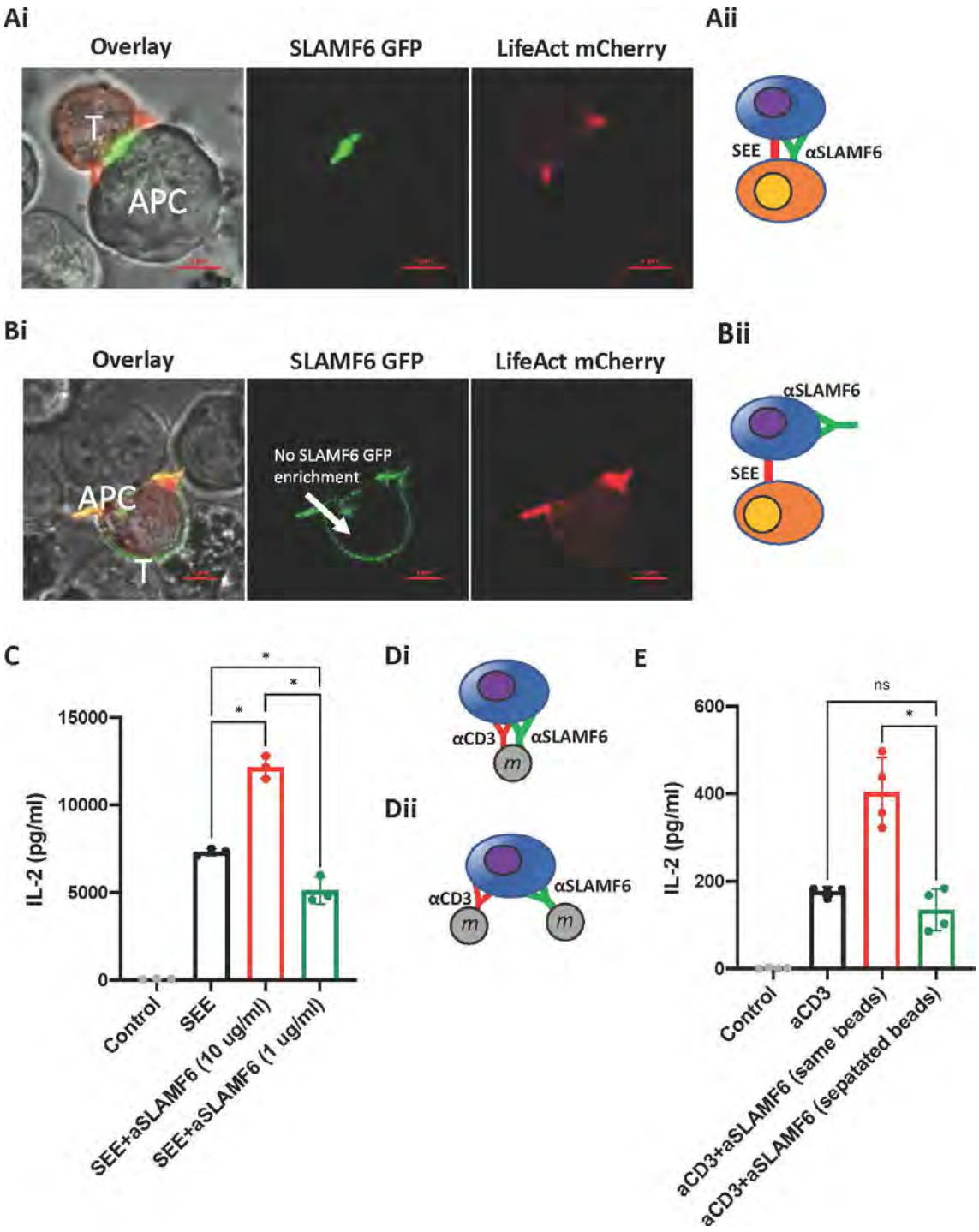
Yevgeniya Gartshteyn[1], Anca Askanase[2] and Adam Mor[3], [1]Columbia University Medical Center, Glen Rock, NJ, [2]Columbia University Medical Center, New York, NY, [3]CUIMC, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Etiology & Pathogenesis Poster (1480–1506)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: T cell activation is initiated by engagement of the T cell receptor (TCR) complex and requires co-receptor signaling. SLAMF6 is a major T cell co-receptor and aberrant signaling downstream this receptor has have been implicated in the pathogenesis of systemic lupus erythematosus (SLE). Moreover, genome association studies in spontaneous murine lupus models of SLE associated SLAMF6 polymorphisms with loss of tolerance, autoantibody production, and susceptibility to SLE.

Accordingly, uncovering the mechanism of SLAMF6 signaling in autoimmune T cells could improve our understanding of the biology of SLE and could have translational therapeutic implications.

Methods: Activation of Jurkat T cells (ATCC) with 1) immobilized anti-CD3 and anti-SLAMF6 allowed for SLAMF6 clustering to the immunological synapse (IS) or 2) immobilized anti-CD3 and soluble anti-SLAMF6 resulted in exclusion of SLAMF6 from the IS. ELISA was used to measure cytokine secretion and CFSE assay to assess T cell proliferation. Co-immuno precipitation of SLAMF6 was performed using a SLAMF6 knock-out cell line that was transduced to express V5-tagged SLAMF6, results were analyzed using protein electrophoresis with immunoblotting and mass spectrometry.



SLAMF6 expression was evaluated in lymphocytes isolated from the peripheral blood of SLE patients with well characterized clinical phenotypes.

Results: Previously we discovered that SLAMF6 clustering is a requirement for its co-stimulatory functions. In the current work, we show that SLAMF6 recruitment to the immunological synapse (IS) is needed to support T cell proliferation and survival. Using confocal microscopy, we also show a direct correlation between SLAMF6 localization within the different compartments of the IS and the ability of this receptor to enhance secretion of multiple cytokines. Mechanistically, and through co-immunoprecipitation experiments, we reveal that SLAMF6 recruits several members of the Src family of kinases to IS, leading to enhance proximal phosphorylation of the TCR complex. Finally, taking

advantage of Tfh cell isolated from patients with active SLE, we show that specific pharmacological interventions that prevent SLAMF6 clustering inhibit TCR signaling and multiple effector functions.

Conclusion: This transitional study advances the understanding of how SLAMF6 contribute to SLE pathogenesis, linking known SLE susceptible genes to specific signaling pathway in autoimmune T cells. Means to manipulate SLAMF6 signaling are promising approaches for novel SLE therapeutics.

Disclosure: Y. Gartshteyn, None; **A. Askanase**, GSK, 2, 5, AstraZeneca, 1, 5, Amgen, 1, Aurinia, 2, Abbvie, 1, Pfizer, 5, Eli Lilly, 5, Idorsia, 5; **A. Mor**, None.

Abstract Number: 1507

Role of CD4+ T Cells in the Pathogenesis of RA: Immunization with Citrullinated T Cell Epitopes Is Sufficient to Induce Immunological and Clinical Manifestations of Arthritis in DR4-Transgenic Mice

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Although the etiology of rheumatoid arthritis (RA) remains unclear, existing research suggests a complex interplay of both genetic and environmental factors. Citrullinated proteins/peptides, and immune responses to them, may lead to the breaching of immunological tolerance, and subsequent disease. While most research to date has focused on the specificity of anti-citrullinated protein antibodies (ACPAs) in RA, the role of T cell responses to citrullinated peptides remains to be further investigated. The aim of this study is to better understand the involvement of T cells in the pathogenesis of the disease, with the ultimate vision of developing therapeutic interventions for RA.

Methods: HLA-DRA/DRB1*0401 transgenic mice were immunized with two subcutaneous injections of 10 citrullinated T-cell epitopes known to bind to DRB1*0401 and derived from proteins implicated in the development of RA. After 1 week, a second boost was performed, either with citrullinated human fibrinogen protein or with an additional dose of the 10 peptides. Two months after, the mice received an intra-articular (IA) boost in the right knee with a mixture containing 5 citrullinated peptides. All immunizations were performed in complete (for the priming injection, CFA) or incomplete (for the subsequent boosts, IFA) Freund's adjuvant.

Results: Within weeks of the initial subcutaneous immunizations, the mice developed T-cell responses that were specific for the citrullinated peptides and not for their native counterparts. Remarkably, the injection of citrullinated T cell epitopes was sufficient to induce the production of ACPA, detectable in the blood by ELISA. In addition, the IA boost led to the manifestation of clinical signs of arthritis: mice injected intra-articularly with citrullinated peptides and IFA showed prolonged articular swelling and systemic inflammation in comparison to the control groups. Such signs were even more pronounced in mice previously treated with the citrullinated human fibrinogen protein.

Conclusion: This study shows that immunization with shared epitope-binding citrullinated peptides is sufficient to induce immunological and clinical signs of RA, by triggering arthritogenic T cell responses. These results provide

direct evidence of the pathogenic contribution of particular peptides to arthritis and of the pivotal role of T cells in the pathogenesis of the disease. Furthermore, these findings also introduce the possibility of using peptide immunotherapy to re-establish immunological tolerance to RA autoantigens.

Disclosure: E. Tonti, None; **B. Duvvuri**, None; **S. Dhar**, None; **D. Haaland**, AbbVie, 2, 5, 6, Adiga Life Sciences, 5, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Can-Fite BioPharma, 5, Celgene, 5, Eli Lilly, 5, 6, Gilead, 5, GlaxoSmith-Kline, 2, 5, 6, Janssen, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Regeneron, 5, Sanofi, 2, 5, 6, UCB, 2, 5, 6, AstraZeneca, 6, Merck, 6, Takeda, 2, 6, Roche, 2, 6; **M. Larche**, Adiga Life Science Inc, 10; **M. Larché**, Adiga Life Sciences Inc, 2, 5, 10, Vaxerna Ltd., 2, 8, Circassia Pharmaceuticals PLC, 8.

Abstract Number: 1508

Decrease of Angiogenic T Cells Associated to the Presence of Interstitial Lung Disease in Patients with Connective Tissue Diseases

Verónica Pulito-Cueto[1], Sara Remuzgo-Martinez[1], Fernanda Genre[1], Belén Atienza-Mateo[2], Victor M. Mora-Cuesta[3], David Iturbe-Fernández[3], Leticia Lera-Gómez[1], Raquel Perez-Fernández[1], Pilar Alonso-Lecue[4], Javier Rodriguez-Carrio[5], Diana Prieto-Peña[6], Virginia Portilla[6], Ricardo BLANCO[7], Alfosno Corrales[6], José M. Cifrián[8], Raquel López-Mejías[1] and Miguel Ángel gonzalez-Gay[9], [1]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Santander, Spain, [2]Group "Research in genetic epidemiology and atherosclerosis of systemic diseases and in bone metabolic diseases of the locomotor system", IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System; Department of Pneumology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [4]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL; Department of Pneumology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [5]Deparment of Functional Biology, Immunology Area, Faculty of Medicine, Universidad de Oviedo, Oviedo, Asturias, Spain., Oviedo, Spain, [6]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL; Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [7]Hospital University Marqués de Valdecilla, Santander, Spain, [8]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL; Department of Pneumology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain, [9]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) is one of the most significant complications of connective tissue diseases (CTD) leading to an increase of the morbidity and mortality in patients with CTD, mainly in those with systemic sclerosis (SSc) and rheumatoid arthritis (RA) [1]. A specific T cell subset termed angiogenic T cells (TAng), implicated in endothelial repair and revascularization, has been involved in the pathogenesis of CTD [2-4]. However, to the best of our knowledge, no information regarding the role of TAng in CTD-ILD$^+$ is available. Accordingly, we aimed to evaluate the role of TAng related to vascular damage in CTD-ILD$^+$.

Methods: This study included 40 patients with CTD-ILD$^+$: 20 RA-ILD$^+$ and 20 SSc-ILD$^+$. Furthermore, three comparative groups were included: 1) 43 patients with CTD-ILD$^-$: 24 RA-ILD$^-$and 19 SSc-ILD$^-$; 2) 21 patients with idiopathic pulmonary fibrosis (IPF); and 3) 20 healthy controls (HC). All subjects were recruited from the Rheumatology and Pneumology de-

partments of Hospital Universitario Marqués de Valdecilla, Santander, Spain. Quantification of TAng was performed from peripheral venous blood by flow cytometry. TAng were considered as triple-positive for CD3, CD31 and CXCR4.

Results: Patients with CTD-ILD$^+$ exhibited a significantly lower TAng frequency than CTD-ILD$^-$ patients ($p< 0.001$). Specifically, RA-ILD$^+$ patients and SSc-ILD$^+$ patients showed a lower frequency of TAng than RA-ILD$^-$ patients and SSc-ILD$^-$ patients, respectively ($p=0.006$ and $p=0.04$, in each case). A decreased TAng frequency was also found in CTD-ILD$^+$ patients when compared with HC ($p< 0.001$), whereas no difference was observed between CTD-ILD$^+$ patients and those with IPF. In addition, a significant increase of TAng frequency was shown in patients with CTD-ILD$^-$ in relation to IPF patients ($p< 0.001$), while no difference was observed between CTD-ILD$^-$ patients and HC.

Conclusion: Our study supports a role of TAng in the vascular damage in CTD-ILD$^+$. Furthermore, our results reveal a decrease of TAng frequency associated to the presence of ILD, both in CTD patients, in particular in those with RA and SSc, and in IPF patients.

References: [1] Expert Rev Clin Immunol 2018;14(1):69-82; [2] Circulation 2007;116(15):1671-82; [3] Ann Rheum Dis 2015 74(5):921-7; [4] PLoS One 2017;12(8):e0183102.

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Disclosure: V. Pulito-Cueto, None; **S. Remuzgo-Martinez**, None; **F. Genre**, None; **B. Atienza-Mateo**, None; **V. Mora-Cuesta**, None; **D. Iturbe-Fernández**, None; **L. Lera-Gómez**, None; **R. Perez-Fernández**, None; **P. Alonso-Lecue**, None; **J. Rodriguez-Carrio**, None; **D. Prieto-Peña**, None; **V. Portilla**, None; **R. BLANCO**, AbbVie, 2, 5, 6, MSD, 2, 5, 6, Roche, 2, 5, 6, Pfizer, 2, 6, Bristol-Myers, 2, 6, Janssen, 2, 6, UCB Pharma, 2, 6, Lilly, 6; **A. Corrales**, None; **J. Cifrián**, None; **R. López-Mejías**, None; **M. gonzalez-Gay**, None.

Abstract Number: 1509

Pharmacological Inhibition of MALT1 Reverses Activation-Induced Metabolic Reprogramming and Ameliorates Autoimmune Pathogenesis in Multiple Animal Models of Chronic Inflammation

Subhabrata Biswas, Mya Steadman, Ynes Helou, Katherine Sellers, Keng Soh, Aditi Chalishazar, Mehmet Badur, Joanna DiSpirito, Brian DeChristopher, John Monroe, Dania Rabah, Barbara Fox and Andy Long, Rheos Medicines, Inc, Cambridge, MA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Current therapies for autoimmune and inflammatory diseases generally target select disease nodes, often failing to produce durable clinical remission. Chronic inflammation is associated with alterations in immune cell metabolism, and it is possible that modulating metabolism may result in more durable responses. Mucosa-associated lymphoid tissue lymphoma translocation protein-1 (MALT1) is a component of the CBM (CARMA/CARD-Bcl10-MALT1) signaling complex that plays a critical role in effector functions of multiple immune cell subsets implicated in autoimmune diseases. While MALT1 is known to regulate NF-kB activation, its role in metabolic reprogramming of immune cells has remained relatively unexplored. We have used allosteric small molecule inhibitors

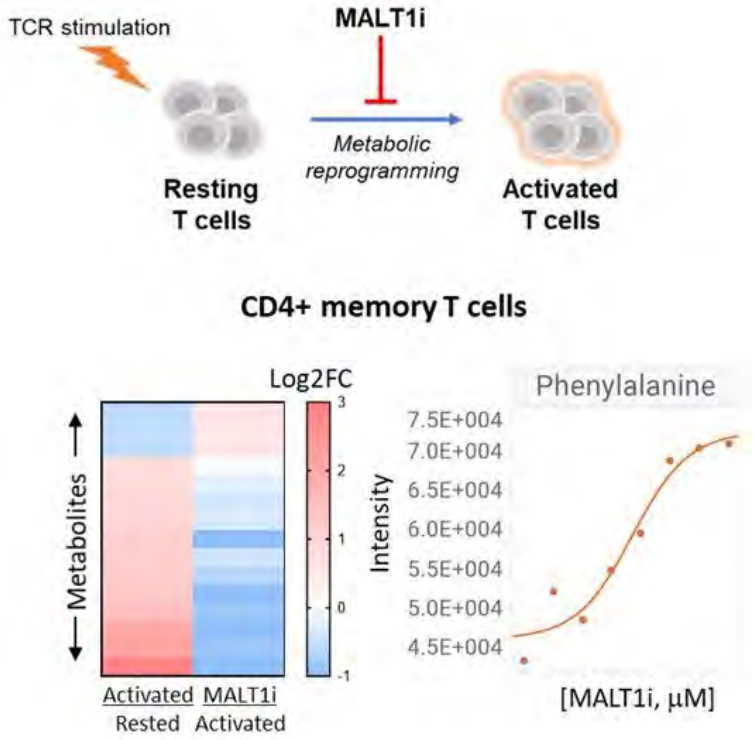

Figure. 1. Effect of MALT1 inhibition on metabolic reprogramming of T-cells. Metabolites were measured from human CD4+CD45RO+ cells 24 hours after stimulation with anti-CD3/CD28/CD2. MALT1 treated cells (MALTi) were preincubated with 5 uM REO-751 for 30 minutes. Dose-dependent effect (0-5 uM MALT1i) on essential amino acids (e.g., Phe) is shown.

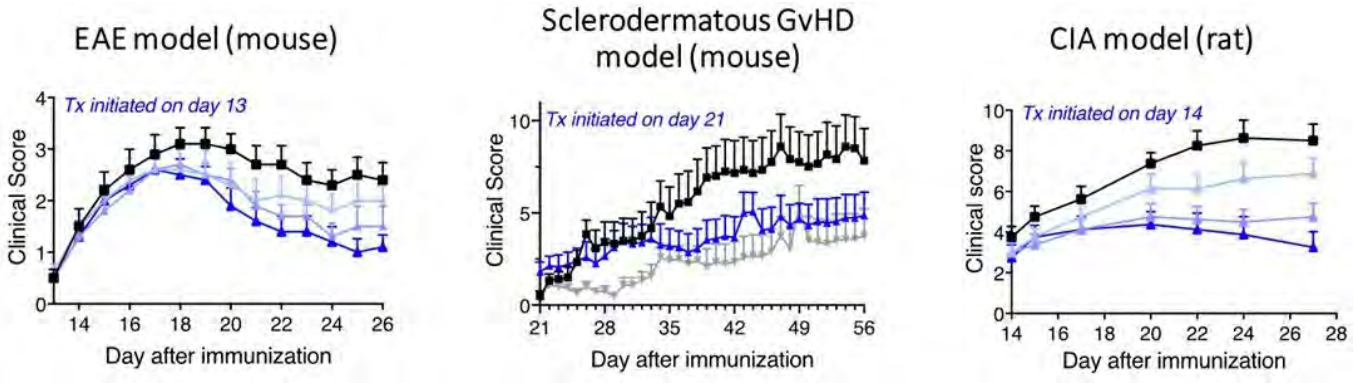

Figure 2. MALT1 inhibition is efficacious in multiple animal models of chronic inflammatory diseases. Black squares represent treatment with vehicle, blue triangles represent different doses (0.1 – 10 mg/kg; 100 mg/kg in scGVHD) of MALT1 inhibitor administered daily via oral route, gray inverted triangles represent Ruxolitinib, a JAK1/2 inhibitor as a comparator. n = 8-15 animals per group.

of MALT1 as tools to evaluate the relationship of MALT1 inhibition to activation-induced metabolic reprogramming with the goal of advancing MALT1 inhibitors as therapeutics for autoimmune disease.

Methods: Activated human memory T-cells, B-cells, macrophages, and whole blood were evaluated for the effect of MALT1 inhibitor on effector cell functions downstream of activation receptors. *In vivo* effects of MALT1 inhibition were evaluated in an anti-CD3 antibody treated mouse model of acute inflammation. Three rodent models of disease (EAE, chronic GVHD and CIA) were employed to evaluate effects of orally administered MALT1 inhibitors on disease activity and metabolite levels. Untargeted metabolomics was performed via LCMS in human memory T-cells and tissues from animal studies.

Results: We identified a common set of metabolite changes that are conserved across multiple immune cell subsets activated via immune tyrosine activated motif (ITAM) containing receptors. This metabolite-based 'activation

signature' was reversed by MALT1 inhibition *in vitro*. In parallel, MALT1 inhibition also decreased proinflammatory cytokine production from the same sets of cells: TCR-activated memory T-cells and immune-complex stimulated macrophages, as well as BCR-induced B-cell proliferation. The metabolic activation signature was also observed *in vivo* in isolated splenocytes from anti-CD3 challenged mice and again was associated with decreased cytokine production. Treatment with MALT1 inhibitors led to disease improvement in a mouse model of sclerodermatous cGVHD, to decrease in disease scores in a TH17-driven EAE model, and to reversal of joint pathology in a rat CIA model. We found that the effect of MALT1 inhibition on disease score coincided with alterations in metabolite levels at sites of inflammation. These data suggest that MALT1-dependent metabolic reprogramming is associated with immune cell activation and disease activity and opens up a new avenue for evaluating the activity of therapeutic agents.

Conclusion: Our results identify MALT1-dependent effects on immune cell metabolism downstream of immune activation and associate those changes with disease activity. Ongoing studies are exploring 1) the role these MALT1-dependent changes in metabolism play in directing the effector function of disease-relevant immune cells and 2) whether metabolic changes may help identify important new biomarkers for disease-associated effector cells.

Disclosure: S. Biswas, Rheos Medicines Inc., 3; **M. Steadman**, Rheos Medicines Inc., 3; **Y. Helou**, Rheos Medicines, 3; **K. Sellers**, Rheos Medicines, 3, Agios, 3; **K. Soh**, Rheos Medicines, 3; **A. Chalishazar**, Rheos Medicines, 3; **M. Badur**, Rheos Medicines, 3, 11; **J. DiSpirito**, Rheos Medicines, 3; **B. DeChristopher**, Rheos Medicines, 3; **J. Monroe**, Rheos Medicines, 2, Rubius Therapeutics, 2, AnaptysBio, 2; **D. Rabah**, Rheos Medicines Inc., 3; **B. Fox**, Merck, 2, 12, Potential milestone payments, Rheos Medicines, 3, 4, 8, 11; **A. Long**, Rheos Medicines, 3.

Abstract Number: 1510

Joint CD8+ Tissue Resident Memory Cell Activation Produces Local Inflammatory Arthritis

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

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Following infection, resident memory CD8+ T cells (T_{RM}) populate tissues as long lived sentinel cells. Their aberrant activation can trigger relapsing inflammation in autoimmune diseases with a strong site- and tissue-specific component such as inflammatory arthritis. Virus specific CD8+ T cells are a recognized component of synovial fluid and synovial biopsies from individuals with autoimmune arthritis. Here, we demonstrate vesicular stomatitis virus encoding ovalbumin (VSV-OVA) specific CD8+ T cells in the mouse knee following resolution of acute infection. With antigen exposure, joint T_{RM} proliferate and recruit additional immune cells preferentially to the site of activation.

Methods: OT1 lymphocytes express a transgenic TCR which recognizes the SIINFEKL peptide of ovalbumin. CD45.1+OT-1 cells are transferred intravascular (i.v.) to CD45.2+ C57BL/6 recipient mice. The next day, recipient mice received 10^6 PFU VSV-OVA i.v. Thirty days after infection, mice receive intra-articular (i.a.) SIINFEKL, PBS alone, or no injection. Knees are fixed, decalcified with EDTA, and frozen. Slides were stained with DAPI, anti-CD45.1, anti-collagen II, streptavidin-PE or streptavidin-C594, anti-B220, anti-Ly6G, and anti-CD4.

Results: Stimulation with SIINFEKL peptide induces proliferation of T_{RM} in target joint but not in opposite joint as demonstrated by both increased OT-1 numbers and their proportion to all cells as identified by DAPI staining

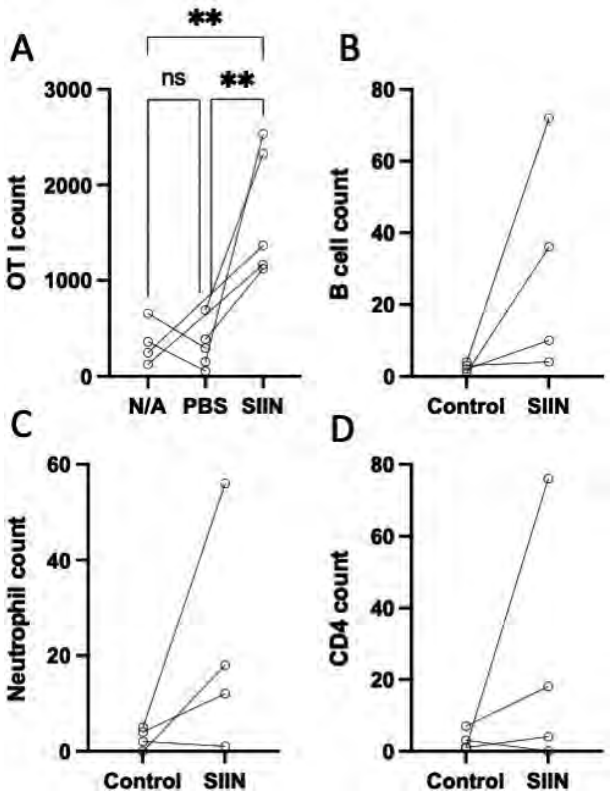

Figure 1. Intra-articular OT-1, B220, Ly6G, and CD4 enumeration. Connecting lines indicate paired knees from same indiivudal mouse. *,p<0.01, ANOVA followed by Tukey's multiple comparison.

(Figure 1A). Increased OT-1 numbers are accompanied by increased B cells, Neutrophils, and CD4 cells within the joint space. (Figure 1B-D).

Conclusion: Following acute infection with VSV-OVA, CD45.1+ donor OT-1 cells populate both joint synovium at a timepoint well past resolution of acute infection. As with T_{RM} at other sites, they proliferate in response to antigenic stimulation and recruit additional inflammatory cells to the joint space.

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

Abstract Number: 1511

Investigation of Antigen Specific CD4$^+$ T Cells in Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) also known as myositis, are rare chronic autoimmune disorders represented by lesions in muscle, skin and lung. One of the most common autoantibodies in myositis, with a prevalence of 25-35%, is the anti Jo-1 autoantibodies, targeting the histidyl-transfer RNA synthetase (HisRS). The presence of autoantibodies in patients along with strong associations with the HLA-DRB1*03:01 genotype, which is responsible to present peptides to activate CD4+ T-cells, suggest the existence of autoantigens being recognized by autoreactive CD4+T-cells. Moreover, we have previously shown that upon stimulation of both peripheral blood mononuclear cells (PBMC) and bronchoalveolar lavage fluid cells (BALF) with HisRS protein and peptides, CD4+ T-cells were activated and produced inflammatory cytokines. Thus, presence of antigen specific autoreactive CD4+T-cells has not been established in myositis yet but there are clear indications about their existence.The main aim of this study is to investigate the HisRS specific CD4+T-cell population using HLA Class II tetramers. HLA Class II tetramer is an important tool for the characterization of specific CD4+T-cells and is being widely used in a large variety of diseases and vaccine studies. These cells are of specific interest to understand autoimmunity and to develop new therapies in autoimmune diseases.

Methods: HLA-DRB1*03/*01 monomers with selected tetanus and HisRS peptides were produced in-house in E.coli system. The peptides of interest were attached to the N-terminus of the HLA β-chain via a flexible peptide linker. HLA-tetramers were assembled using a commercial fluorescently labeled streptavidin. The efficacy of the peptide-HLA tetramers was validated by stimulating PBMC from HLA-matched healthy controls with tetanus peptide. The frequency of tetanus specific CD4+ T-cells were detected at different time points (6,13 and 21 days) from the cultures using tetanus peptide bound HLA-DRB1*03/*01 tetramers. The presence of tetanus specific T-cells was confirmed by the secretion of significantly higher IFNg levels upon re-stimulation of cells with tetanus peptide. HisRS specific CD4+ T-cells were investigated from PBMC of anti-Jo1+ and HLA-DRB1*03/*01 patients using tetramers and surface marker expressions.

Results: Our findings demonstrate the presence of HisRS+CD4+ T-cells in PBMC of Jo-1+ patients (n=4) using two HisRS tetramers with different fluorochromes and activation markers following stimulation with the respective peptide. We are now including more patient samples to confirm our findings, and further support our findings with functionality assays by flow cytometry and ELISA/fluorospot assays.

Conclusion: Myositis is a rare and chronic autoimmune disorder, with no currently available cure. Previous studies indicate the importance of T cells in this disease. However, the phenotype, functionality and role of these cells in the disease pathogenesis has not been fully established. Characterization of this autoreactive T-cell population will help us enhance our understanding of the disease pathogenesis and thus to develop better treatment options.

Disclosure: B. Horuluoglu, None; **A. Galindo-Feria**, None; **K. Chemin**, None; **G. Kozhukh**, None; **A. Dubnovitsky**, None; **V. Malmström**, None; **I. Lundberg**, Corbus Pharmaceutical,, 2, EMD Serono Research & Development Institute, 2, Argenx, 2, Bristol Myers Squibb, 2, Janssen, 2, Kezaar, 2, Octapharma, 1, Orphazyme, 1, Roche, 11, Novartis, 11.

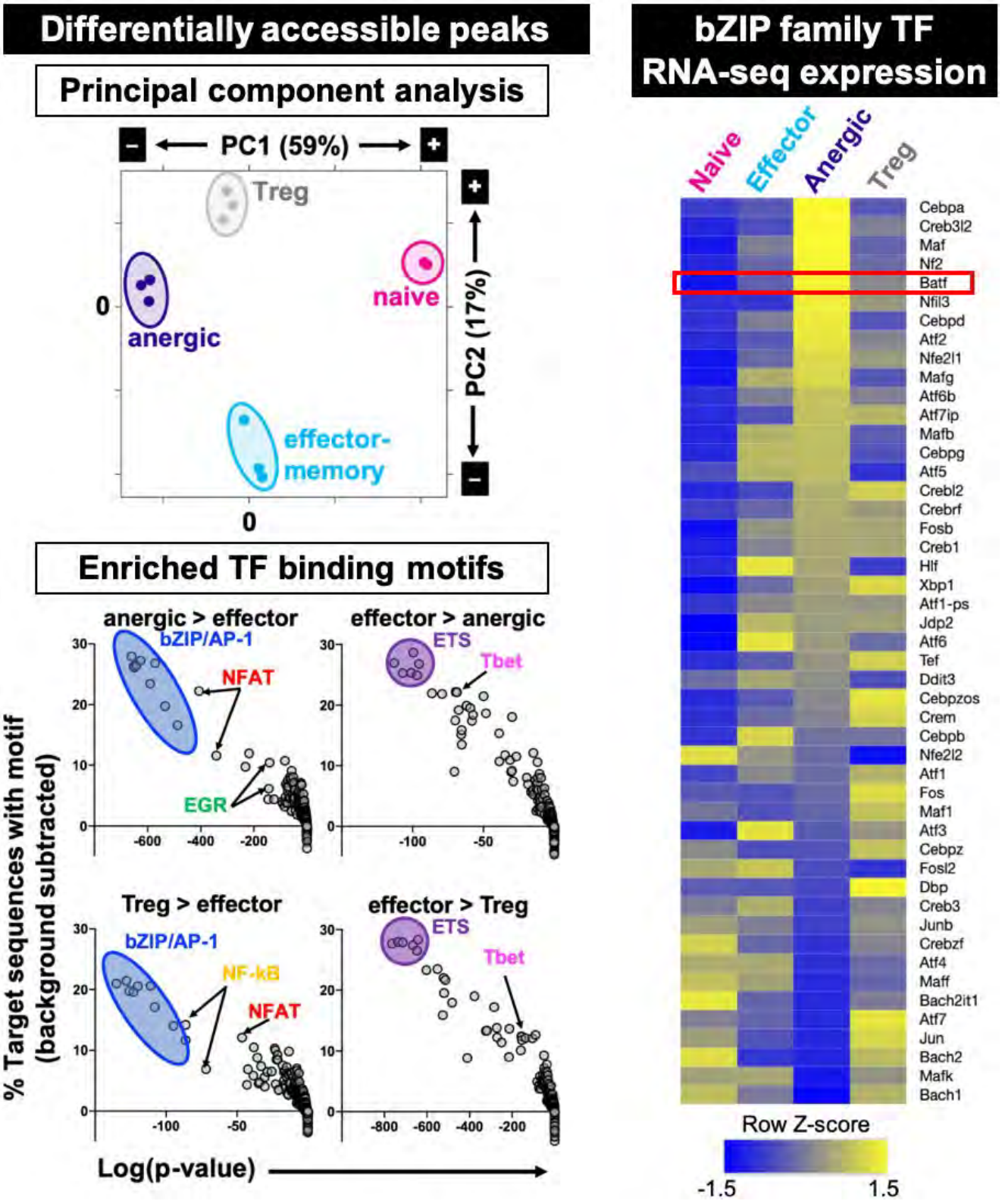
Abstract Number: 1512

Epigenetic and Transcriptional Programs of CD4+ T Cell Anergy

Philip Titcombe, Milagros Silva Morales and Daniel Mueller, University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: T cell tolerance is essential for preventing autoimmune diseases and resolving inflammation. To maintain tolerance, $CD4^+$ T cells recognizing self-antigens in the periphery can exert active suppression as regulatory T cells (Treg) or enter an inactive state known as anergy. Recent evidence suggests that anergy



Anergic T cells exhibit a distinct transcriptional program.

occurs naturally within a subpopulation of polyclonal CD4$^+$ T cells and can generate precursors to Foxp3-expressing Treg cells. We aimed to identify transcription factors (TFs) underlying T cell anergy induction and its potential plasticity.

Methods: Polyclonal CD4$^+$ T cell subsets from untreated C57BL/6 mice were sorted based on previously established markers for downstream sequencing-based interrogation. Anergic CD44^{high} Foxp3$^-$ CD73^{high} FR4^{high} Nrp1$^+$ T cells were compared to effector-memory (CD44^{high} Foxp3$^-$ CD73^{low} FR4^{low}), Treg (Foxp3$^+$ CD25$^+$), and naïve (CD44^{low}) T cell populations. Divided aliquots from the same samples were processed in parallel to generate corresponding bulk RNA-seq and accessible chromatin DNA information. Bioinformatic analyses were applied to identify unique transcriptional networks in the anergic T cell subpopulation. Anergy-enriched TFs were then investigated in an antigen-specific system of tolerization by repeated peptide infusions.

Results: Paired epigenome and transcriptome analysis revealed a unique anergy signature driven by bZIP family (*Batf*, *Cebpa, Nfil3, Maf*), NFAT family (*Nfatc1*), and EGR family (*Egr3*) transcription factors. In response to peptide tolerization, antigen-specific CD4$^+$ T cells from *Batf*-deficient mice demonstrated exaggerated expansion and minimal Foxp3$^+$ Treg cell differentiation.

Conclusion: Our data indicate that a unique transcription factor network, including BATF, generates and maintains peripheral CD4$^+$ T cell anergy

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Disclosure: P. Titcombe, None; **M. Silva Morales**, None; **D. Mueller**, None.

Abstract Number: 1513

Control of T Cell Tolerance by the NR4A Family of Nuclear Receptors

Ryosuke Hiwa[1], **Hailyn Nielsen**[1], James Mueller[1] and Julie Zikherman[2], [1]University of California San Francisco, San Francisco, CA, [2]UCSF Medical Center, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Current therapies for autoimmune disease often lead to treatment-limiting immunosuppression. Selective manipulation of antigen (Ag)-specific immune responses could enhance our therapeutic approach. Targeting members of the NR4A family of nuclear receptors could achieve this as they mediate immune tolerance in Ag-activated lymphocytes. Thymic deletion of multiple – but not individual – NR4A genes (*Nr4a1* and *Nr4a3* > > *Nr4a2*, which is minimally expressed*)* results in deficiency of regulatory T cells (Treg) and a severe inflammatory disease (Fig. 1A-B). Thus, it has been challenging to unmask additional redundant functions of these druggable transcription factors (TFs) in conventional T cells (Tconv). We devised innovative conditional genetic and bone marrow chimera strategies to preserve Treg homeostasis and overcome this obstacle.

Methods: We created mixed radiation bone marrow (BM) chimeras reconstituted with congenically marked CD45.2 *Nr4a1*$^{-/-}$*Nr4a3*$^{-/-}$ (germline double knock-out or gDKO) and CD45.1 wild-type (WT) bone marrow. Control chimeras

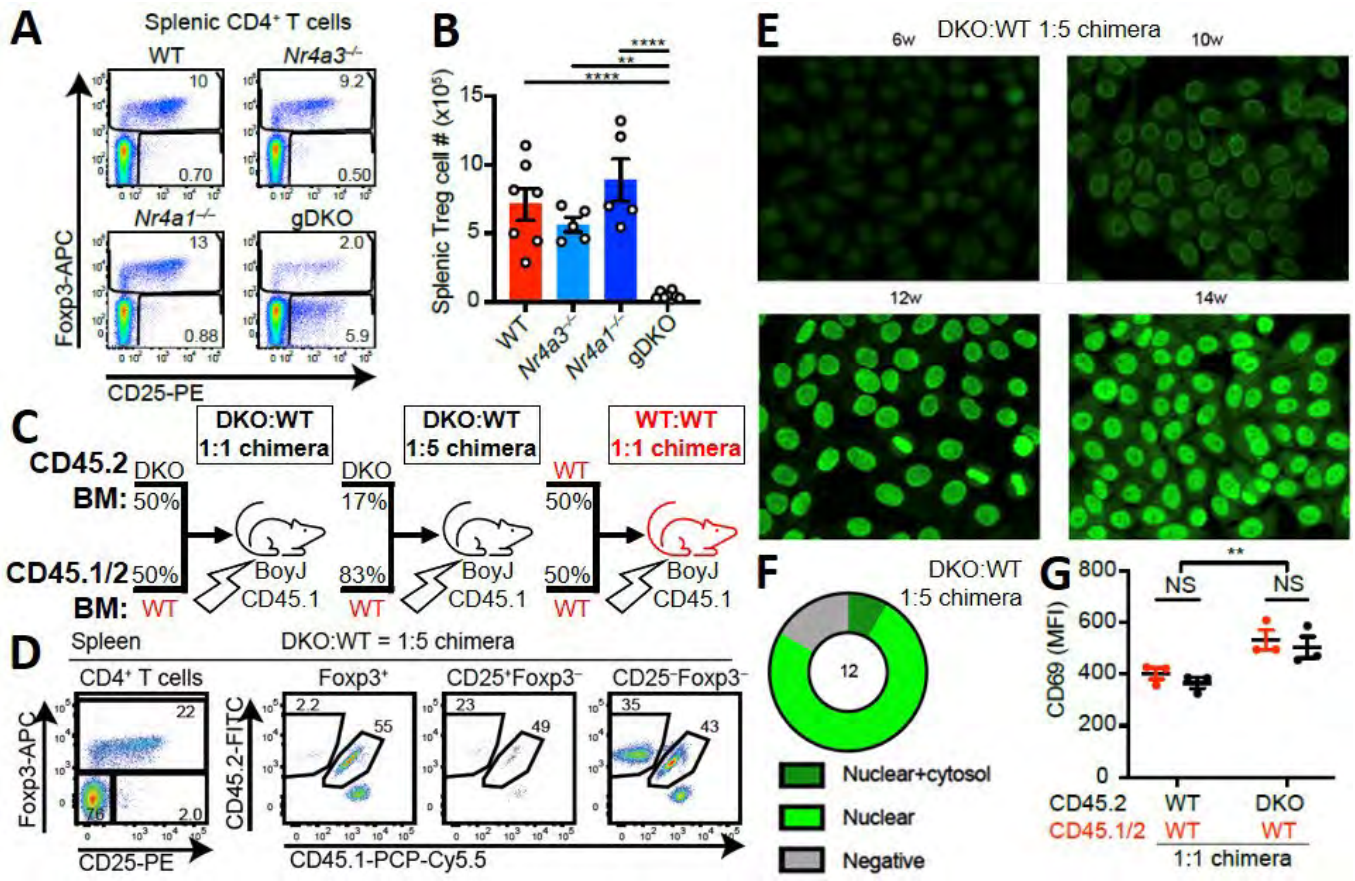


Figure 1. DKO:WT chimeras develop ANA and systemic autoimmunity despite restored Treg homeostasis. A) Representative plots showing loss of Foxp3+ Treg in germline DKO (gDKO) mice. B) Quantification of data from A. C) Schematic of mixed bone marrow chimera design. D) Representative plots from 1:5 DKO:WT chimeras showing reconstitution of Foxp3+ Treg compartment by WT donor cells. E) Representative immunofluorescence images on serum of 1:5 DKO:WT chimeras showing development of ANA in sera between 6-14 weeks post-reconstitution. F) Penetrance and staining pattern of ANA from 1:5 DKO:WT chimeras. G) Both DKO and WT B cells from DKO:WT but not WT:WT chimeras show increased CD69 expression.

were reconstituted with CD45.2 WT and CD45.1 WT BM. We evaluated Tconv and Treg homeostasis and thymic development with conventional methods.

Results: In DKO:WT chimeras, the Treg compartment was reconstituted from largely WT donor cells (Fig. 1D). Despite this, chimeras rapidly developed anti-nuclear autoantibodies (ANA) and evidence of cell-extrinsic polyclonal B cell activation (Fig. 1E-G). CD4 and CD8 single positive (SP) thymocytes accumulate in DKO but not control chimeras, suggesting a profound cell-intrinsic impairment of negative selection of DKO thymocytes (Fig 2A-D). Supporting this, activated caspase-3 expression was reduced in DKO double-positive (DP) thymocytes (Fg 2C-D). In addition, peripheral DKO CD8 T cells with a memory phenotype ($CD44^{hi}$) accumulate in DKO:WT chimeras (Fig 2E-G), but not in CD8-cre $Nr4a1^{fl/fl}$ $Nr4a3^{-/-}$ mice which delete NR4A genes only after thymic selection in the CD8 SP stage (Fig 2H-J). DKO CD4 Tconv cells expressing phenotypic markers of anergy (FR4hiCD73hi) accumulate in these DKO:WT chimeras (Fig. 3A-B), suggesting escape of self-reactive T cells into the periphery. Indeed, these cells indeed exhibit a dampened proximal signaling downstream of the T cell receptor (TCR) (Fig 3C-E). However, these self-reactive DKO CD4 Tconv also exhibit exaggerated IL-2 production (Fig 3F-G), suggesting that *functional* anergy is defective.

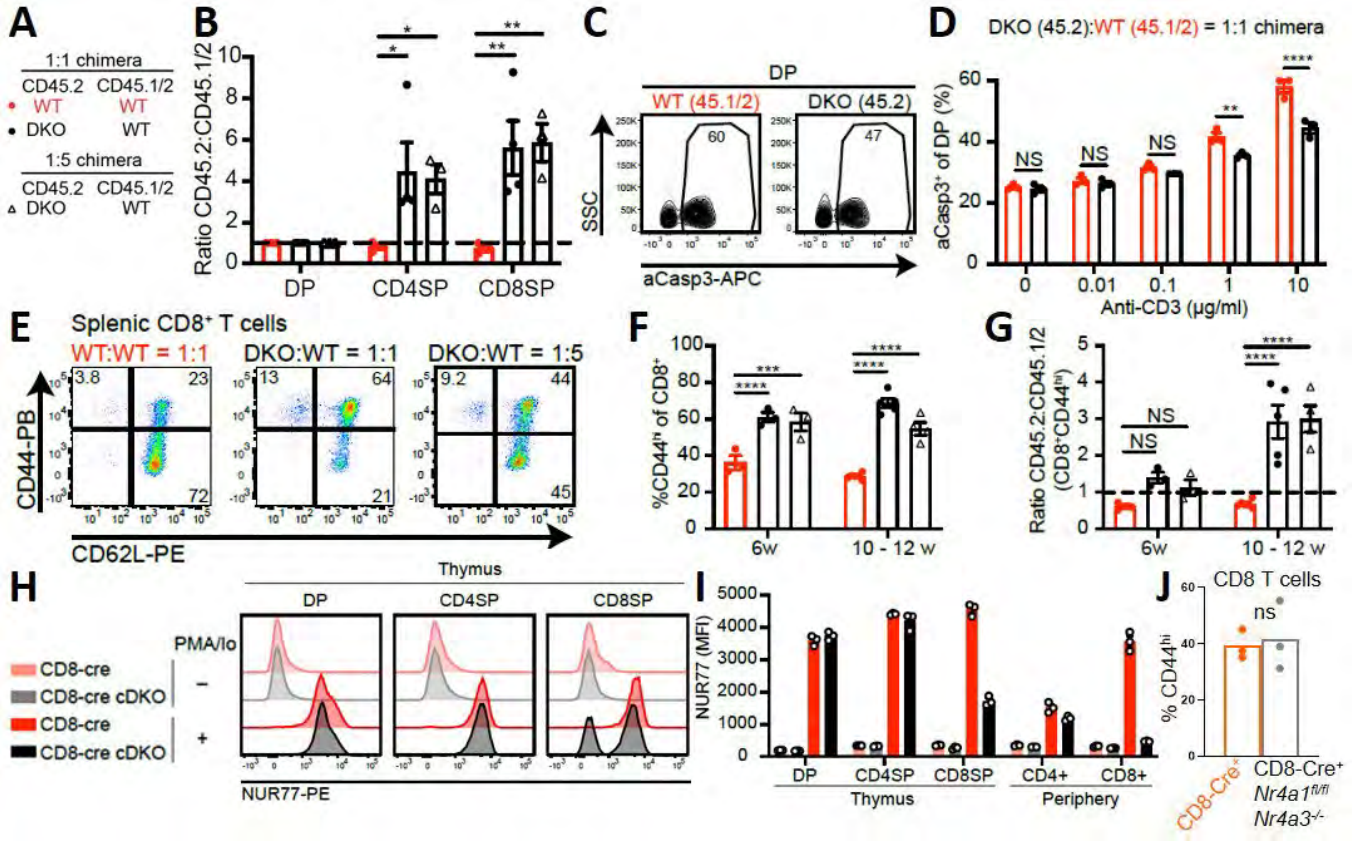


Figure 2. DKO thymocytes have a cell-intrinsic defect in negative selection. A) Key for graphs in B, F, and G. B) Ratio of CD45.2:CD45.1/2 cells among double positive (DP) and CD4 and CD8 single positive (SP) thymocytes normalized to DP. C) Representative plots showing reduced activated caspase-3 expression in DKO DP thymocytes from 1:1 DKO:WT chimeras upon ex vivo stimulation with anti-CD3. D) Quantification of data from C. E) Representative plots showing accumulation of CD44hi CD8 T cells from DKO chimeras. F) Quantification of data from E at 6 or 10-12 weeks post-reconstitution. G) Ratio of CD45.2:CD45.1/2 CD8+CD44hi cells. H) Representative plots showing Nur77 expression in thymocytes from CD8-cre and CD8-cre Nr4a1fl/fl Nr4a3-/- (CD8-cre cDKO) mice. I) Quantification of Nur77 expression in thymocytes (as in H) and splenocytes (key as in H). J) CD8+ CD44hi cells from CD8-cre and CD8-cre cDKO mice.

Conclusion: Together, these data support the unifying hypothesis that NR4A family members play cell-intrinsic, but redundant, roles in both central and peripheral CD4 T cell tolerance. These studies reveal roles for the NR4A family in multiple layered T cell tolerance mechanisms and demonstrate that each is essential to preserve immune homeostasis.

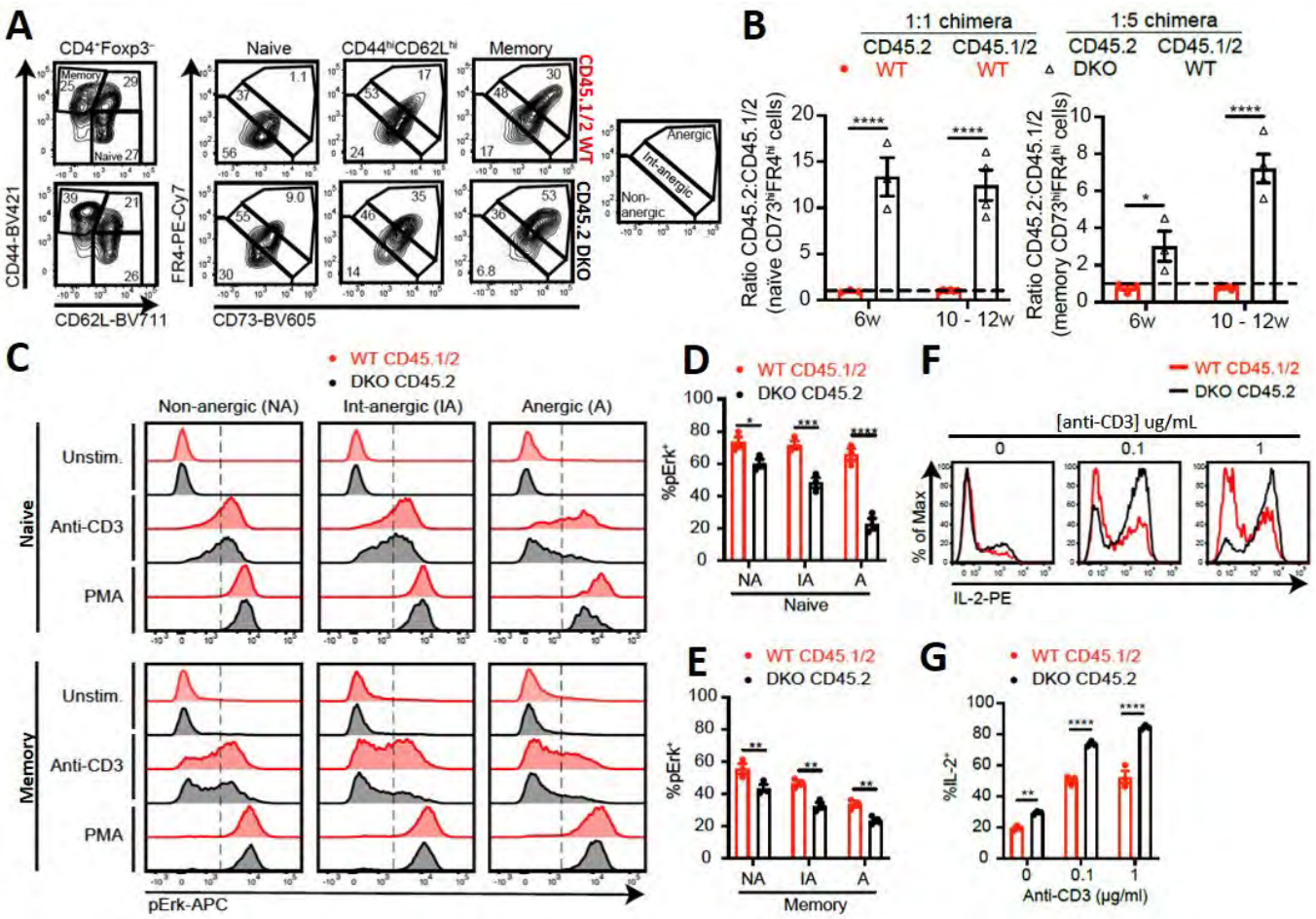


Figure 3. Conventional DKO CD4+ T cells have impaired peripheral tolerance. A) Representative plots from 1:5 DKO:WT chimeras showing gating strategy to identify FR4hiCD73hi anergic phenotype CD4 T cells among naïve and memory compartments. B) Ratio of CD45.2:CD45.1/2 FR4hiCD73hi cells from 1:5 DKO:WT chimeras in naïve (left) and memory (right) compartments 6-12 weeks post-reconstitution. C) Representative histograms showing intracellular phospho-Erk staining after ex vivo stimulation of non-anergic, intermediate anergic, and anergic phenotype cells from 1:5 DKO:WT chimeras in both naïve and memory compartments, gated as depicted in A. D-E) Quantification of data shown in C. F) Intracellular staining for IL-2 after ex vivo stimulation of splenocytes from 1:1 DKO:WT chimeras with anti-CD3 followed by PMA and ionomycin. G) Quantification of data shown in F.

Disclosure: R. Hiwa, None; **H. Nielsen**, None; **J. Mueller**, None; **J. Zikherman**, Walking Fish Therapeutics, 2, 11.

Abstract Number: 1514

Age-related Metabolic Reprogramming of Memory CD4+ T Cells Is Associated with Reactive Oxygen Species-induced Immune Cell Dysfunction

Yuling Chen[1], Pierre-Louis Krau[2], Pelle Löwe[3], Moritz Pfeiffenberger[4], Lisa Ehlers[3], Alexandra Damerau[4], Paula Hoff[3], Frank Buttgereit[5] and **Timo Gaber**[4], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Charit Universittsmedizin Berlin, corporate member of Freie Universitt Berlin, Humboldt-Universitt zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany, [3]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt Universität zu Berlin, Department of Rheumatology and Clinical Immunology, Berlin, Germany, [4]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [5]Charité – Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Inflamm-aging is a sterile, low-grade, chronic systemic inflammatory state characterized by an increase in proinflammatory cytokines involved in the development of most age-related diseases such as cancer, Alzheimer's disease, type 2 diabetes, stroke, cardiovascular disease, and rheumatoid arthritis (RA). Because cellular metabolism modulates T cell function, metabolic changes can be hypothesized to promote the reprogramming of memory CD4+ T cells into senescent CD4+ T cells and contribute to memory CD4+ T cell dysfunction during aging. Therefore, we hypothesized that metabolic reprogramming of CD4+ T cells may be a major factor promoting immune cell dysfunction during aging, contributing to the pathogenesis of age-related diseases such as RA.

Methods: To this end, we analyzed memory CD4+ T cells isolated from PBMCs from young donors (20-32 years) and old donors (52-67 years) using MACSTM technology. Ex vivo memory CD4+ T cells were analyzed using Seahorse™ technology to determine proton efflux rate (PER) as a measure of glycolysis (glycoPER) and oxygen consumption rate (OCR) as a measure of mitochondrial respiration (mitoOCR). Cytokine secretion was measured by flow cytometry and multiplex assay with and without mitotempo, an inhibitor of mitochondrial reactive oxygen species (ROS). Finally, TCR-stimulated proliferation of memory CD4+ T cells was determined by flow cytometry using CSFE and Ki-67 at 3 and 4 days. ROS and mitochondrial activity were analyzed by flow cytometry after 24 h using DCF-DA as well as CellROX Deep Red and Mitotracker.

Results: In a quiescent state, memory CD4+ T cells from elderly individuals demonstrated a decrease in basal glycolysis and compensatory glycolysis, and an increase in the ratio of basal mitoOCR to glycoPER while their mitochondrial profile was equivalent to that of young donors while the number of mitochondria was higher with no increase in steady-state ATP level. In this line and in comparison, to the younger reference group, memory CD4+ T cells from aged donors presented a greater spare respiratory capacity after TCR-activation and a marked increase in intracellular ROS production. Interestingly, we did not observe an impact of aging on memory CD4+ T cell proliferation as determined by CFSE and Ki-67. Although the capacity of intracellular cytokine expression did not differ between the compared groups, the levels of secreted IFN-γ, IP-10, IL-4, IL-6, IL-9, and MCAF were significantly higher in the supernatants of memory CD4+ T cells taken from aged donors but were sensitive to ROS inhibition.

Conclusion: These findings suggest that metabolic reprogramming in human memory CD4+ T cells during aging results in an increased expression of proinflammatory cytokines as a result of ROS production and mitochondrial dysfunction. This process may culminate in T cell dysfunction and thus contribute to the pathogenesis of inflamm-aging and the development of age-related diseases such as rheumatoid arthritis (RA).

Disclosure: Y. Chen, None; **P. Krau**, None; **P. Löwe**, None; **M. Pfeiffenberger**, None; **L. Ehlers**, None; **A. Damerau**, None; **P. Hoff**, None; **F. Buttgereit**, Horizon Therapeutics, 2, 5, Mundipharma, 5, Roche, 1, 5, Pfizer, 1, 5, 6; **T. Gaber**, None.

Abstract Number: 1515

Programmed Cell Death Protein 1 (PD-1)-Expressing CD4+ T Cells Are Expanded in Early Rheumatoid Arthritis and Correlate with Response to Treatment

Katie Williams[1], Annabelle Small[2], Qingxuan Song[3], Suzanne Cole[4], Ling-yang hao[5], William Murray-Brown[6], Susanna Proudman[7], Malcolm Smith[8], Sunil Nagpal[9] and Mihir Wechalekar[10], [1]Flinders University, Adelaide, Australia, [2]Flinders University, Bedford Park, Australia, [3]Janssen Research & Development LLC, Spring House, PA, [4]Janssen Research, Adelaide, Australia, [5]Janssen Research, Philadelphia, PA, [6]GlaxoSmithKline, Adelaide, Australia, [7]University of Adelaide, Medindie, Australia, [8]Flinders Medical Centre, Adelaide, Australia, [9]Janssen Research, Collegeville, PA, [10]Flinders Medical Centre, Bedford Park, Australia

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster (1507–1515)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Programmed death protein 1 (PD-1) expressing T cells, including T follicular and T peripheral helper cells, are expanded in the circulation of individuals with rheumatoid arthritis (RA). Despite this, the origins of these cells and their functional role in RA remain poorly understood. To address this, we sought to investigate the genetic profiles of PD-1-expressing lymphocytes of the peripheral blood and synovial infiltrate of patients with early RA, and to characterise these cells in disease.

Methods: Isolated peripheral blood mononuclear cells (PBMCs) from patients with established RA (n=5) were sorted into $CD4^+/CD8^+$ $PD\text{-}1^{+/-}$ populations by fluorescence activated cell sorting. mRNA was then isolated, converted into cDNA libraries, and subjected to total RNA sequencing using a NextSeq500. In conjunction with this, quantitative reverse-transcription PCR was used to support our findings. Finally, we assessed for alterations in $CD4^+PD\text{-}1^+$ and $CD8^+PD\text{-}1^+$ cell gene expression in synovial tissue (ST) biopsies (n=19) before and after six-month triple disease modifying anti-rheumatic drug (tDMARD) treatment.

Results: Proportions of $CD4^+$ and $CD8^+$ cells were expanded in the early RA synovial tissue (ST) compared with the peripheral blood. Comparisons of the gene signatures between $CD4^+PD\text{-}1^+$ vs. $PD\text{-}1^-$ cells from early RA PBMCs identified significant upregulation of genes involved in the inflammatory response including *IL21*, *CXCL13*, and *c-MAF*, and in pathways including T helper-1 pathways, neuroinflammation signalling, and pathways involved in crosstalk between dendritic cells and natural killer cells. No significant differences in gene signatures between $CD8^+$ $PD\text{-}1^+$ vs. $PD\text{-}1^-$ cells were observed. Additionally, analysis of gene signatures from early RA ST before and after six-month tDMARD treatment revealed down-regulation of the $CD4^+PD\text{-}1^+$ gene signatures (including genes such as *PDCD1*, *CXCL13*, and *CTLA4*) following treatment.

Conclusion: Our study suggests the pathogenic nature of $CD4^+$ PD-1-expressing T cells in RA, and also reveals a mechanism through which tDMARDs exert their effect through influencing T cell populations in the synovial compartment. Furthermore, we identify factors associated with B cell help that are enhanced in the RA ST compared with PBMCs, highlighting the importance of these molecules in driving inflammation within the synovium.

Disclosure: K. Williams, None; **A. Small**, None; **Q. Song**, Janssen Research and Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Cole**, Janssen Research, 3; **L. hao**, Janssen Research, 3; **W. Murray-Brown**, BMS, 3; **S. Proudman**, Boehringer-Ingelheim, 1, Janssen, 1, Gossamer, 1, Janssen, 5; **M. Smith**, None; **S. Nagpal**, None; **M. Wechalekar**, Janssen Research, 5.

Abstract Number: 1516

Clinical Phenotypes and Treatment of Rheumatic Immune-Related Adverse Events from Checkpoint Inhibitors: A Retrospective Cohort of 112 Patients

Tiphaine Lenfant[1], Yuxuan Jin[2], Elizabeth Kirchner[3], Pauline Funchain[2], Jung-Min Song[2], Moshe Ornstein[2], Laura Wood[2], Donald Eicher[2], Rula Hajj-Ali[4], Leonard Calabrese[2] and **Cassandra Calabrese**[5], [1]Institut Mutualiste Montsouris, Paris, France, [2]Cleveland Clinic, Cleveland, OH, [3]CCF, Cleveland, OH, [4]Cleveland Clinic, Hunting Valley, OH, [5]Cleveland Clinic Foundation, Cleveland Heights, OH

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

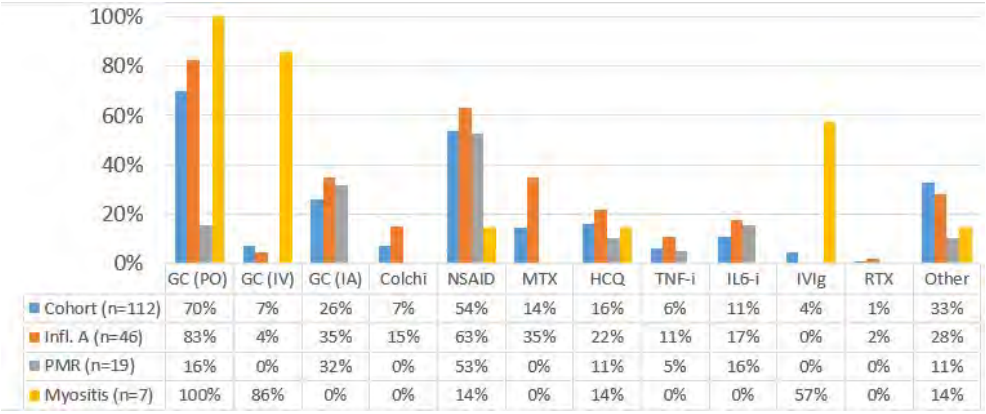
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: To describe a single center cohort of rheumatic immune related adverse events (irAEs) observed in patients treated with checkpoint inhibitor therapy (ICI) and to identify potential risk factors for persistent rheumatic disease activity.

Methods: Patients referred to the Cleveland Clinic Department of Rheumatic and Immunologic Diseases for rheumatic irAE were retrospectively included and assessed via chart review (2015-2020). Persistent rheumatic irAE was defined as still requiring treatment for rheumatic irAE at last follow-up.

Results: A total of 112 patients (median age 60 years) were identified. The most common irAE clinical phenotypes included inflammatory arthritis (IA, n=46), sicca syndrome (n=21), and polymyalgia rheumatica (n=19). In the entire cohort ICI therapy was held temporarily for rheumatic irAE in 15 patients (13%) for toxicity and permanently discontinued in 26 (23%). At last follow-up, rheumatic irAE had resolved in 41 patients (37%), whereas 71 patients still required treatment of rheumatic irAE (median follow-up 15 months, range 5-30 months). Among therapies administered for irAE, glucocorticoids (GC) were most commonly prescribed (n=78, 70%), followed by hydroxychloroquine (16%), methotrexate (14%), and anti-IL-6 agents (11%). Patients with persistent rheumatic irAE activity more frequently received GC (p=0.018) and had IA (p=0.02) compared to patients that had resolution of irAE. In multivariate analysis, IA patients were at higher risk of persistent rheumatic irAE (OR 3.5 [1.3-10], p=0.014). The overall mortality rate was 27% (n=30). Risk factors for mortality included tumor progression (OR 15.3 [4-65], p< 0.001) and continued treatment



	GC (PO)	GC (IV)	GC (IA)	Colchi	NSAID	MTX	HCQ	TNF-i	IL6-i	IVIg	RTX	Other
Cohort (n=112)	70%	7%	26%	7%	54%	14%	16%	6%	11%	4%	1%	33%
Infl. A (n=46)	83%	4%	35%	15%	63%	35%	22%	11%	17%	0%	2%	28%
PMR (n=19)	16%	0%	32%	0%	53%	0%	11%	5%	16%	0%	0%	11%
Myositis (n=7)	100%	86%	0%	0%	14%	0%	14%	0%	0%	57%	0%	14%

Figure 1. Treatment of rheumatic irAEs Colchi: colchicine; GC: glucocorticoids; HCQ: hydroxychloroquine; Infl. A: inflammatory arthritis; IA: intra-articular; IL6-i: interleukin 6 inhibitors; MTX: methotrexate; RTX: rituximab.

with GC at the last follow-up (OR 5.8 [1.5-29], p=0.016). In a survival analysis, continued GC at the end of follow-up was significantly associated with mortality (HR 4.0 [1.3-12], p=0.0001).

Conclusion: In this single-center retrospective cohort of rheumatic irAEs patients, the presence of ICI-related IA was associated with persistent rheumatic disease activity.

Disclosure: T. Lenfant, None; **Y. Jin**, None; **E. Kirchner**, Sanofi, 12, Speaker's training, did not speak for company., Novartis, 1, Janssen, 1; **P. Funchain**, BMS, 5, Pfizer, 5; **J. Song**, None; **M. Ornstein**, Bristol Myers Squibb, 1, 2, 5, Merck, 2, Pfizer, 2, 5; **L. Wood**, Bristol Myers Squibb, 6, EMD Serono, 6, Merck, 6, Pfizer, 6; **D. Eicher**, None; **R. Hajj-Ali**, Novartis, 6, Rockpointe, INC., 6, Projects In Knowledge, 6, UpToDate, 9; **L. Calabrese**, Lilly, 2, BMS, 2, Genentech, 2; **C. Calabrese**, Sanofi-Regeneron, 2, 6.

Abstract Number: 1517

Prevalence of Autoantibodies in Patients with Melanoma Who Develop Rheumatic Immune Related Adverse Events During Treatment with Immune Checkpoint Blockade

Sophia Weinmann[1], Amanda Eudy[2] and David Pisetsky[1], [1]Duke University Medical Center, Durham, NC, [2]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with malignancy who develop rheumatic immune related adverse events (IRAEs) during immune checkpoint blockade (ICB) are commonly autoantibody negative. The change from chemotherapy to ICB as first-line therapy in melanoma could be important since chemotherapy causes cell death of both malignant and healthy cells, potentially increasing exposure of self-antigen. This in turn could lead to autoantibody production against antigens that would not be exposed as frequently without chemotherapy. It is unknown whether the presence of autoantibodies in patients who develop rheumatic IRAEs varies based on prior exposure to chemotherapy. Our hypothesis in this pilot study is that patients with melanoma referred to rheumatology for rheumatic IRAEs from ICB who had prior chemotherapy would have a higher prevalence of autoantibodies compared to those who did not receive chemotherapy.

Methods: A total of 23 patients with melanoma who developed rheumatic IRAEs during treatment with ICB were seen at an academic medical center rheumatology clinic from September 1, 2017 to March 31, 2020. Demographic information, clinical characteristics/type of IRAEs, ICB treatments received including prior chemotherapy, and autoantibody profiles including ANA (indirect immunofluorescence using HEp-2 cell lines) were collected. An ANA titer of 1:40 was considered negative. Differences in ANA positivity between patients who did and did not receive chemotherapy were estimated by Fisher's exact test.

Results: There were 23 patients with melanoma who had a rheumatic IRAE, mean age of 61 years, 52% female and 2 non-white patients, who received single agent ICB (65%) versus combination ICB. Of the 23 total patients, 11 (48%) had 1 or more autoantibodies: 5 (22%) ANAs, 3 (13%) RFs, 2 (9%) Ro/SSA antibodies, 1 (4%) ACPA and 1 (4%) dsDNA. ANA was present in 3/5 patients (60%) who received chemotherapy prior to ICB compared to 2/18 patients (11%)

who did not (p=0.05). The most common rheumatic IRAE was inflammatory arthritis (70%) with 8/11 autoantibody positive, followed by myositis (13%) and PMR (9%).

Conclusion: About half of patients with melanoma who developed rheumatic IRAEs had one or more autoantibody. There was a higher prevalence of autoantibodies, specifically ANA, in patients who received chemotherapy prior to ICB. The majority of autoantibody positive patients developed inflammatory arthritis. Although this is a small pilot, the findings are consistent with the idea that prior chemotherapy, by exposing autoantigens, could influence the risk for autoantibody production and development of rheumatic IRAEs. Larger studies are needed to explore this idea and determine the importance of prior chemotherapy in risk stratification for rheumatic IRAEs.

Disclosure: S. Weinmann, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **D. Pisetsky**, Immunovant, 2.

Abstract Number: 1518

Elucidating Activated Osteoarthritis as an Emerging Immune Checkpoint Inhibitor Toxicity: A Descriptive Observational Study

Pankti Reid[1], David Liew[2], Rajshi Akruwala[3], Anne Bass[4] and Karmela Kim Chan[5], [1]University of Chicago Medical Center, Chicago, IL, [2]Austin Health, Heidelberg, Australia, [3]SUNY Downstate Health Sciences University College of Medicine, Brooklyn, NY, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [5]Hospital for Special Surgery, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICIs) are a type of immunotherapy used for cancer management. ICI toxicities can challenge the ability to safely continue ICI therapy despite its notable clinical benefit. Immune-related inflammatory arthritis (ICI-IA) has been described in literature, but herewith we introduce and characterize post-ICI activated osteoarthritis (ICI-aOA), wherein there is exacerbation of a degenerative arthropathy after ICI initiation.

Methods: We conducted a multi-center, retrospective, observational study of patients with cancer treated with ICIs who experienced worsening of their osteoarthritis after ICI start. The ICI-aOA diagnosis was established by the treating rheumatologist and graded using the CTCAE (Common Terminology Criteria for Adverse Events) V6.0 rubric. RECIST (Response evaluation criteria in solid tumors) V.1.1 (v.4.03) guidelines determined tumor response. Chi-squared testing was used for tests of association and multivariate analysis was conducted using logistic regression analysis.

Results: Of the total 36 patients with ICI-aOA, mean age at time of rheumatology presentation was 66 years (51-81yrs). Most patients had metastatic melanoma (10/36, 28%) and had received a PD1/PDL1 inhibitor monotherapy (31/36, 86%) with 5/36 (14%) combination therapy. Large joint involvement (hip/knee) was noted in 53% (19/36), small joint (CMC, DIP, PIP) 25% (9/36), and spine 14% (5/36). Two-thirds (24/36) suffered multiple joint involvement. Three of 36 (8%) had CTCAE grade≥3, 14 (39%) grade 2 and 19 (53%) grade 1 manifestations. Symptom onset ranged from 6 days to 34 months with median of 5 months after ICI initiation; five patients suffered ICI-aOA after ICI cessation

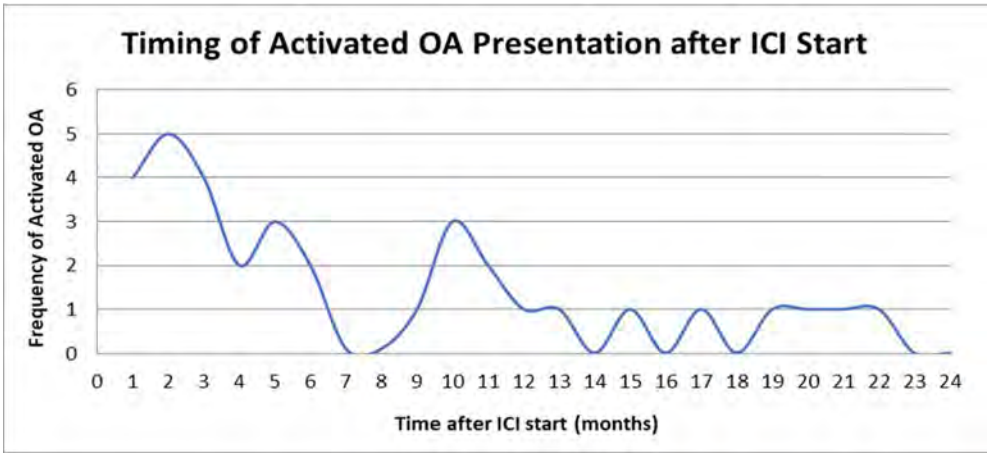


Figure 1. Median onset of ICI-aOA symptoms was 5 months with a wide range from about 6 days to 34 months. Five patients suffered ICI-aOA after ICI cessation (3, 15, 19, 32, 67 weeks after ICI cessation). ICI: Immune-checkpoint inhibitor; aOA: Activated osteoarthritis.

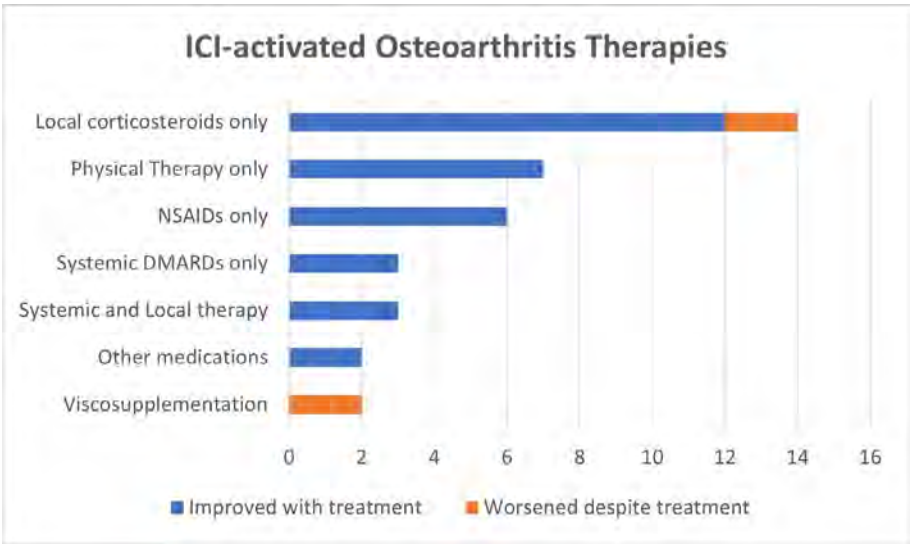


Figure 2. Local therapy was sufficient and successful for majority of the patients. Patients who failed their aOA therapy were all notably patients who had other immune-related adverse events. Systemic DMARDs used included prednisone and hydroxychloroquine. Other medications included acetaminophen and cyclobenzaprine. ICI: Immune-checkpoint inhibitor; NSAIDs: Non-steroidal anti-inflammatory drugs; DMARDs: Disease modifying anti-rheumatic drugs.

(3, 15, 19, 32, 67 weeks after ICI cessation). Most common form of therapy was local corticosteroid injections only (16/36, 44%) followed by NSAIDs only (7/36, 20%) or physical therapy only. Twenty patients (56%) experienced other irAEs, with rheumatic and dermatologic being the most common. All three patients with high-grade ICI-aOA also had another irAE diagnosis at some point after ICI initiation.

Conclusion: We present the first investigation of osteoarthritis exacerbation after cancer immunotherapy. Majority of ICI-aOA cases were low grade and manageable with local therapy or NSAIDs. This demonstrates the importance of early referral to a rheumatologist to facilitate the distinction between ICI-IA from ICI-aOA, the latter of which can be managed with local therapy that will not compromise ICI efficacy.

Disclosure: P. Reid, Co-inventor of a filed patent covering the use of low-dose tocilizumab in viral infections., 10; **D. Liew**, None; **R. Akruwala**, None; **A. Bass**, None; **K. Chan**, None.

Abstract Number: 1519

Concomitant Targeted Therapy with Ongoing Immune Checkpoint Inhibitor (ICI) Therapy for Severe Immune Related Adverse Events (irAEs): Clinical Experience from Two Centers

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Treatment of irAEs is a balance of suppressing irAE-associated hyper-inflammation without inhibiting anti-tumoral effects of ICI. Treatment of grade 3/4 irAEs is most challenging and guidelines from multiple oncology groups recommend holding or permanently discontinuing ICIs and treating with escalating immunosuppression until resolved, followed by switch to conventional anti-cancer therapies. Such strategies are effective for mild and self-limiting irAEs and often allows resumption of ICI after resolution but can be highly problematic for rheumatic irAEs which are often chronic as well as more severe and refractory than non-rheumatic irAEs. For these patients a maintenance regimen of chronic targeted therapy followed by resumption of ICI therapy theoretically may allow ongoing irAE control while sparing the anti-tumoral potential of ICI with select immunomodulation. Unfortunately, the published experience of such combined therapies is extremely limited. We now report our experience of sustained targeted and ICI therapy in 9 patients.

Methods: All patients receiving concomitant biologic therapy and ongoing ICI seen in the Cleveland Clinic Department of Rheumatic and Immunologic Diseases and the Jewish General Hospital Department of Oncology at McGill University were included and retrospectively assessed for efficacy, tolerability, safety and effect on tumor progression.

Results: Nine patients received ICI concurrently with biologic therapy (6 melanoma, 1 gastric carcinoma, 2 renal cell). Three were treated with ipilimumab/nivolumab, 4 with nivolumab and 2 with pembrolizumab. Two of the nivolumab patients had previously received ipilimumab/nivolumab. Five patients had ICI-related inflammatory arthritis, 1 had pre-existing rheumatoid arthritis, and 3 had refractory ICI-related colitis. Three patients received concurrent treatment with adalimumab, 1 tocilizumab, 1 tofactinib and 4 infliximab. Prior to initiation of biologic, ICI was held for irAE in 8, all received systemic glucocorticoids and 3 methotrexate. The average duration of combined treatment with ICI and biologic was 4.5 months (range 1-11 months). irAEs were controlled (low disease activity) in 7/9 while 2/9 had moderate disease activity. Regarding tumor outcomes, 5 patients have stable disease, and 4 had disease progression. There were no adverse events, including serious or opportunistic infections known to be associated with biologic therapy.

Conclusion: This limited experience suggests that combining ongoing targeted therapies with ICI is possible with no clear serious adverse events noted to be directly associated with targeted therapies. The effect of combining such therapies on tumor response remains unclear and will require prospective clinical trials.

Disclosure: C. Calabrese, Sanofi-Regeneron, 2, 6; **K. Esfahani**, BMS, 1, 6, Pfizer, 5, 6, Roche, 1, Sanofi, 6, Ipsen, 6, Merck, 1, 6; **L. Calabrese**, Lilly, 2, BMS, 2, Genentech, 2.

Abstract Number: 1520

Do Specific Rheumatic Autoantibodies Predict Severity or Time to Onset of Immune-related Adverse Events from Checkpoint Inhibitors?

Nilasha Ghosh[1], Deanna Jannat-Khah[2], Karmela Kim Chan[2], Michael Postow[3] and Anne Bass[4], [1]Hospital for Special Surgery, New York, NY, [2]Hospital for Special Surgery, New York, NY, [3]Memorial Sloane Kettering Cancer Center, New York, NY, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICI) are a novel cancer therapeutic that have had a dramatic impact on treating advanced malignancies by enhancing the anti-tumor T cell response. However, the ongoing activation of T cells also cause autoimmune side effects, termed immune-related adverse events (irAE). Autoantibodies are present in many patients with irAE and, in lung cancer patients, autoantibodies have been associated with survival (Toi et al. JAMA Onc 2019). Given the similarity of some irAE to de novo rheumatic diseases, autoantibodies could also serve as biomarkers of organ specific irAE. In this study we asked whether prototypical rheumatological autoantibodies were associated with irAE organ specificity, severity, time or with patient survival.

Methods: This study utilized clinical data and plasma collected from 60 patients enrolled in a prospective phase II clinical trial of two doses of combination ICI (anti-CTLA4/anti-PD1) followed by anti-PD1 monotherapy for the treatment of advanced melanoma (PI Postow). IrAE severity was graded based on Common Terminology Criteria for Adverse Events (CTCAE) guidelines. Plasma was collected, frozen and stored at baseline and week six after treatment initiation, and later thawed and tested for anti-nuclear antibody (ANA), rheumatoid factor (RF) and anti-cyclic citrullinated peptide (CCP) using traditional methods. Characteristics were compared between seropositive and seronegative patients using Chi-square, t-tests and Wilcoxon rank-sum testing. The association of autoantibodies with timing of irAE was analyzed with Kaplan-Meier curves and log-rank testing, as was progression free and overall survival.

Results: **Table 1** highlights the 60 patients included in the study with the mean age (SD) of 60.4 (SD 13.3), 63% male and 85% with stage IV melanoma. Ninety-two percent of patients experienced at least one irAE, with 45% experiencing grade 1-2, or mild irAE, and 46.7% experiencing grade 3-5, or severe irAE. Timing of the first irAE was less than six weeks in 69% of patients, most of which were dermatologic or gastrointestinal. Twenty-eight percent of patients had a baseline antibody (ANA, RF or CCP). There were no significant differences between the seropositive and seronegative patients in severity of irAE or type of irAE, except for thyroid irAE which was more common in the seronegative group (**Table 2**). There were no differences between the two groups in time to first irAE or first severe irAE (**Figure 1**), nor in progression free survival and overall survival.

Conclusion: Our study of melanoma patients did not find any association between ANA, RF and CCP positivity and irAE development, time to first irAE, irAE severity or survival. Seronegative patients were more likely to experience thyroid irAE than seropositive patients. These specific autoantibodies do not appear to be reliable biomarkers for irAE, although other autoantibodies or autoantibody profiles may prove to be more informative.

Table 1. Patient characteristics

Age, mean (SD)	60.4 (13.3)
Sex, male n (%)	38 (63)
Cancer stage, n (%)	
- III	9 (15)
- IV	51 (85)
Melanoma type, n (%)	
- Cutaneous	38 (63.3)
- Uveal	1 (1.7)
- Acral	1 (1.7)
- Mucosal	15 (25)
- Unknown	5 (8.3)
Cycles of ICI received, median [IQR]	5.5 [3, 18.5]
Total number of irAE, median [IQR]	3 [2, 5]
Max irAE grading*, n (%)	
- None	5 (8.3)
- Mild (grade 1-2)	27 (45)
- Severe (grade 3-5)	28 (46.7)
Timing to first irAE, n (%)	
- <6 weeks	38 (63)
- ≥6 weeks	17 (28)
Time to first severe irAE, n (%)	
- <6 weeks	6 (21)
- ≥ 6 weeks	22 (79)
ANA, n (%)	
- Baseline	14 (23.3)
- 6 weeks	14 (23.3)
- Any	19 (31.7)
RF, n (%)	
- Baseline	4 (6.7)
- 6 weeks	4 (6.7)
- Any	6 (10)
CCP, n (%)	
- Baseline	0
- 6 weeks	1 (2)
- Any	1 (2)
Baseline + antibody (%)	17 (28)
Any + antibody (%)	24 (40)

Abbreviations: ICI = immune checkpoint inhibitor, irAE = immune-related adverse event, ANA = anti-nuclear antibody, RF = rheumatoid factor, CCP = cyclic citrullinated peptide

*Grading by Common Terminology Criteria for Adverse Events (CTCAE)

Table 2. Differences between baseline antibody negative and antibody positive patients

	Antibody negative (n=43)	Antibody positive (n=17)	*p-value*
Age, mean (SD)	59.6 (12.3)	62.4 (14.8)	0.71
Sex, male n (%)	18 (42)	4 (24)	0.24
Number of ICI cycles, median [IQR]	5 [3, 19]	6 [3, 10]	0.82
Any irAE experienced, n (%)	41 (95)	14 (82)	0.13
Time to irAE (weeks), median [IQR]	3.7 [1.4, 6.4]	2.8 [1.5, 9]	0.56
Time to irAE, <6 weeks, n (%)	13 (30)	4 (24)	1.00
Severe irAE (grade 3-5*), n (%)	18 (42)	10 (59)	0.26
Total number of irAE, median [IQR]	3 [2, 5]	3 [2, 4]	0.95
Rash/pruritis, n (%)	19 (44)	4 (24)	0.16
Diarrhea/colitis, n (%)	12 (28)	9 (53)	0.08
Myocarditis, n (%)	2 (5)	1 (6)	1.00
Myalgia/myositis, n (%)	5 (12)	1 (6)	0.66
Hepatitis, n (%)	16 (37)	6 (35)	1.00
Thyroid, n (%)	**14 (33)**	**0 (0)**	**0.006**
Arthritis/arthralgia, n (%)	4 (9)	2 (12)	1.00
Sicca, n (%)	7 (16)	1 (6)	0.42
Non-thyroid endocrine[1], n (%)	14 (33)	3 (18)	0.35

Abbreviations: ICI = immune checkpoint inhibitor, irAE = immune-related adverse event, ANA = anti-nuclear antibody, RF = rheumatoid factor, CCP = cyclic citrullinated peptide

*Grading by Common Terminology Criteria for Adverse Events (CTCAE)

[1]Non-thyroid endocrine includes hypophysitis, adrenalitis, diabetes mellitus

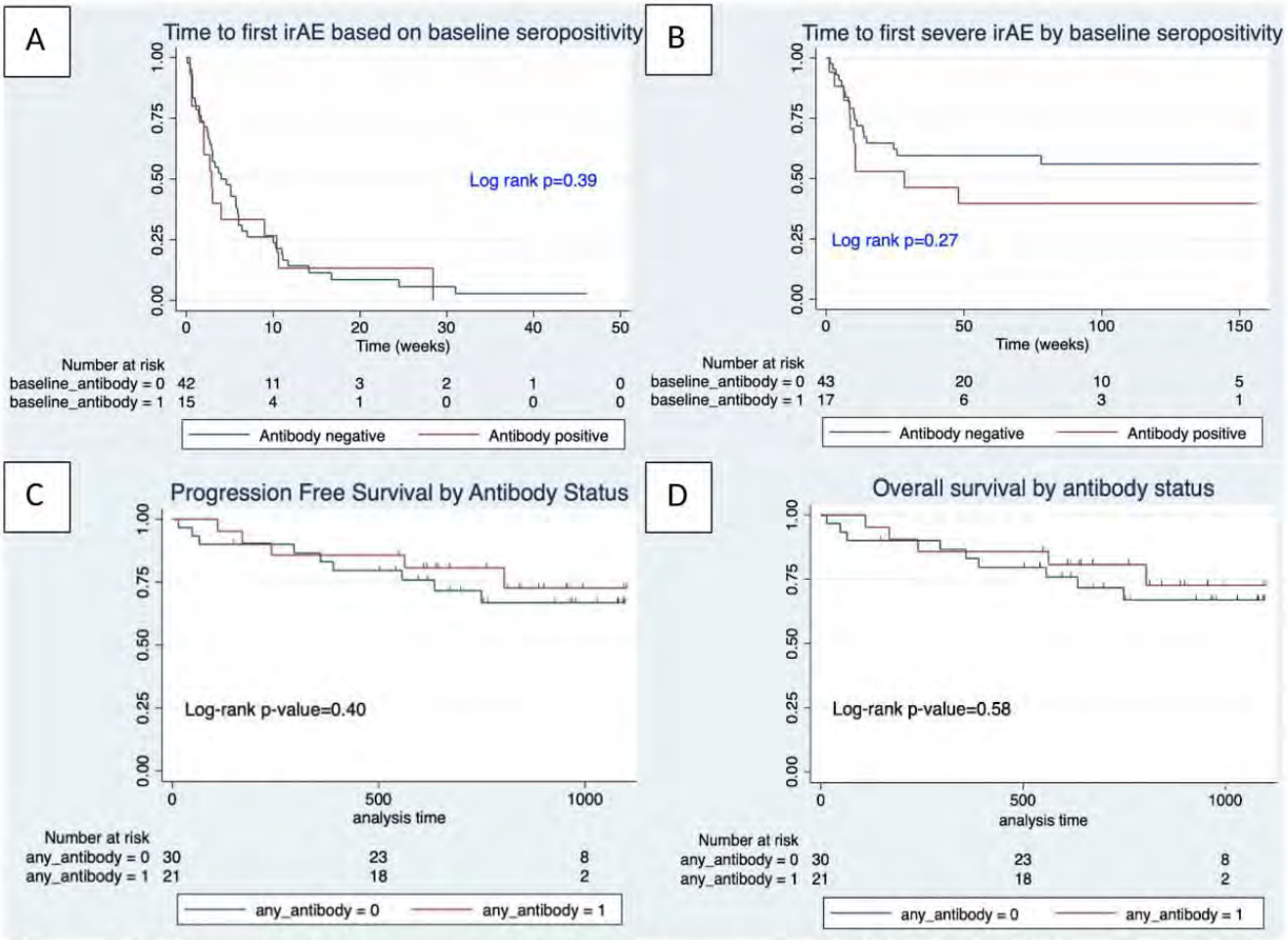

Figure 1. (A) Time to first immune-related adverse event and (B) Time to first *severe* immune-related adverse event stratified by baseline seropositivity; (C) Progression free survival and (D) Overall survival stratified by any seropositivity

Disclosure: N. Ghosh, None; **D. Jannat-Khah**, Cytodyn, 12, own shares of stock, Walgreens, 12, Own stock shares, AstraZeneca, 12, own stock shares, GW Pharmaceuticals, 12, stock ownership; **K. Chan**, None; **M. Postow**, BMS, 2, 5, 6, Merck, 2, 5, 6, Array Biopharma, 2, 5, Novartis, 2, 5, Incyte, 2, NewLink Genetics, 2, Aduro, 2, Eisai, 2, Pfizer, 2, RGenix, 5, AstraZeneca, 5, Infinity, 5; **A. Bass**, None.

Abstract Number: 1521

Autoantibody Microarray Signal Intensities May Predict the Occurrence of Immune-related Adverse Events

Nilasha Ghosh[1], Chengsong Zhu[2], Karmela Kim Chan[3], Michael Postow[4] and Anne Bass[5], [1]Hospital for Special Surgery, New York, NY, [2]UT Southwestern, Dallas, TX, [3]Hospital for Special Surgery, New York, NY, [4]Memorial Sloane Kettering Cancer Center, New York, NY, [5]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Immune checkpoint inhibitors (ICI) are a novel cancer therapeutic that have had a dramatic impact on treating advanced malignancies by enhancing the anti-tumor T cell response. However, the ongoing activation of T cells also cause autoimmune side effects, termed immune-related adverse events (irAE). Given that some irAE draw comparisons to traditional autoimmune diseases, autoantibodies have been proposed as potential biomarkers to predict the occurrence of irAE.

Methods: This study utilized clinical data and plasma collected from 60 patients enrolled in prospective phase II oncologic clinical trial of two doses of combination ICI (anti-CTLA4/anti-PD1) followed by anti-PD1 monotherapy for the treatment of advanced melanoma (PI Postow). Plasma was collected, frozen and stored at baseline and week 6 after treatment initiation. Samples were later thawed and incubated with a 120-autoantigen microarray to identify IgM and IgG autoantibodies commonly associated with autoimmune diseases. Average signal intensities of autoantibodies both at baseline and fold changes between the baseline and week 6 timepoint were compared among patients with vs. without an organ-specific irAE. Student's t test was used to determine if there was a significant difference between average signal intensities for each antibody across toxicity groups, and $\log_2$ fold changes (FC) and p-values were recorded for each antibody. Statistically significant changes in differential expression are noted in the figures as green (negative FC) and red (positive FC) dots. Unsupervised clustering was also performed.

Results: The 60 patients had a mean age (SD) of 60.4 (SD 13.3), 63% male. Ninety-two percent experienced at least one irAE and 63% had their first irAE before 6 weeks. Patients who experienced an organ-specific irAE (e.g. colitis) tended to have fewer autoantibodies at baseline than patients who did not experience that irAE (Figure 1). Additionally, patients who experienced any irAE before 6 weeks had fewer autoantibodies at baseline than those with irAE only after 6 weeks (**Figure 1**). There were essentially no baseline autoantibodies whose presence predicted an organ-

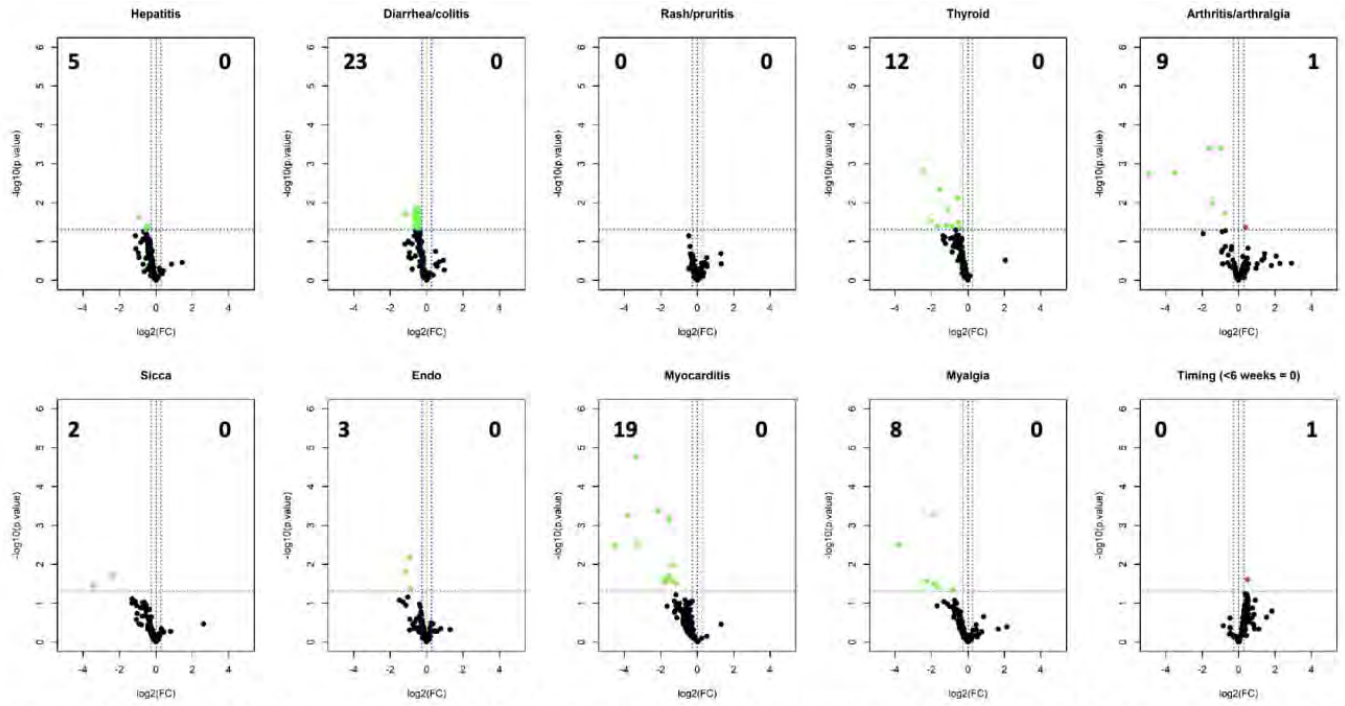

Figure 1. Differential expression of IgG based on organ specific irAE vs non-irAE groupings and late vs. early timing. Dots represent fold changes in autoantibody concentration between the groupings. Those on the left are lower in affected group, those on the right are higher. The dotted line represents a significant fold change with a p-value of 0.05. Black dots = non-significant fold changes, green = lower fold changes in event group, red = higher fold changes in event-group.

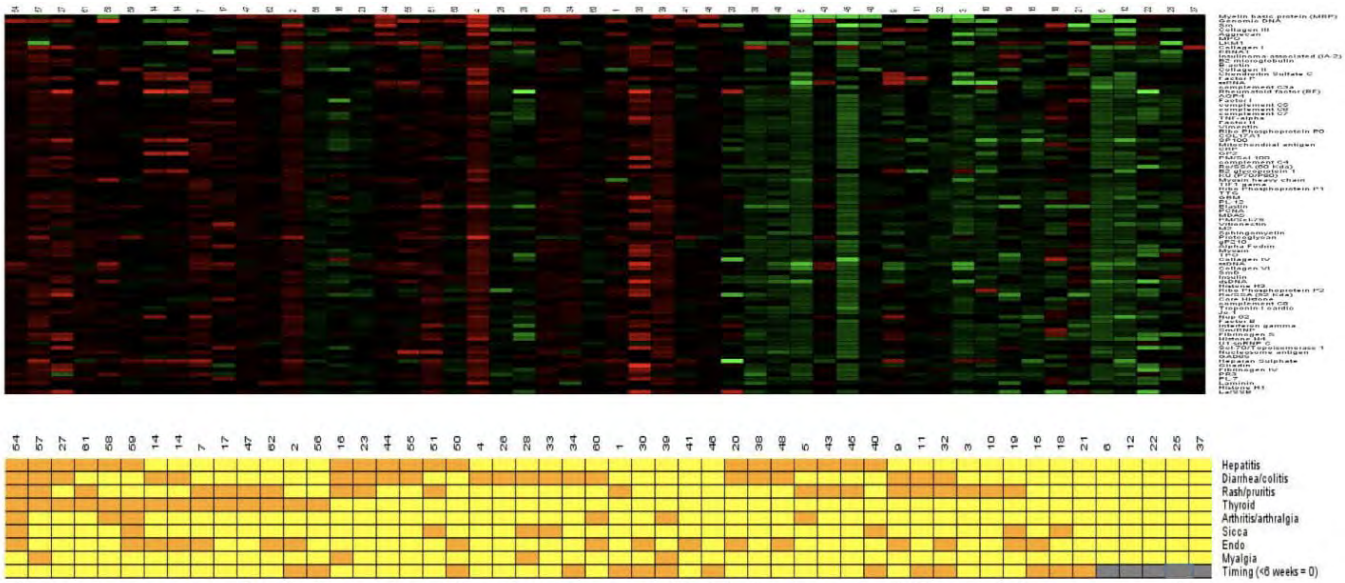

Figure 2. Unsupervised clustering of patient irAE and fold changes in differentially expressed IgM autoantibodies from baseline to 6 weeks (green = negative fold changes, red = positive fold changes)

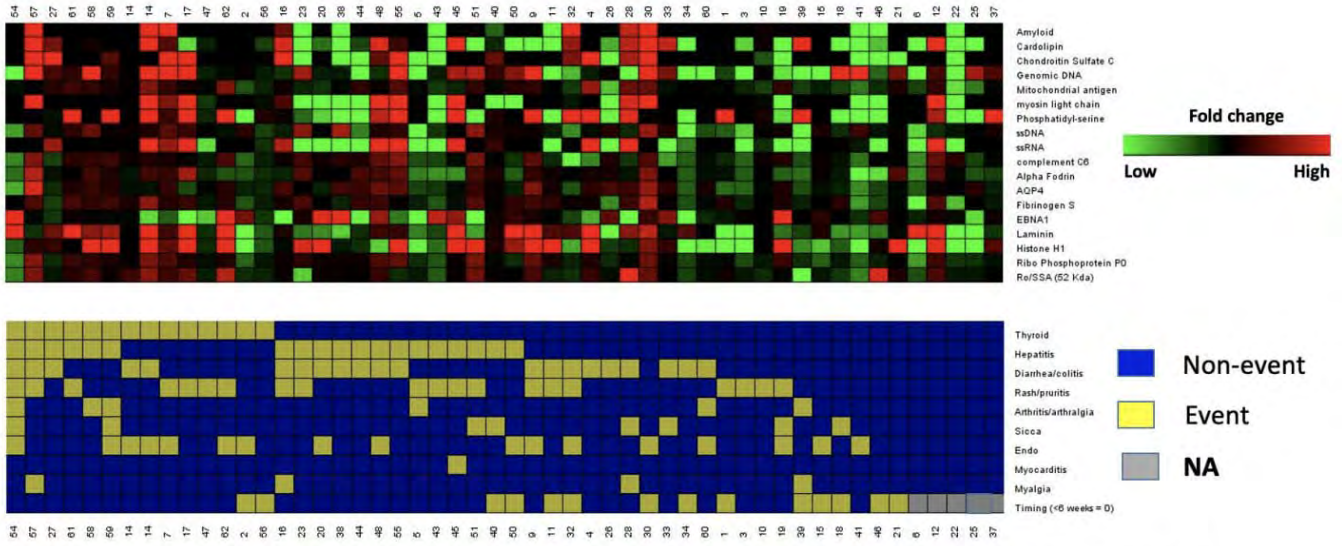

Figure 3. Unsupervised clustering of patient irAE and fold changes in differentially expressed IgG autoantibodies from baseline to 6 weeks

specific irAE. Unsupervised clustering suggested that patients with irAE had a greater fold change in IgM (Figure 2. and IgG (Figure 3. from baseline to 6 weeks than those without irAE, and the same was true for patients who experienced an irAE before compared to after 6 weeks.

Conclusion: A low level of baseline autoantibodies and an increase in autoantibodies after ICI treatment were associated with organ specific irAE. This finding may reflect a skewing toward cellular immunity in these patients prone to irAE rather than a humoral dispensation.

Disclosure: N. Ghosh, None; **C. Zhu**, None; **K. Chan**, None; **M. Postow**, BMS, 2, 5, 6, Merck, 2, 5, 6, Array Biopharma, 2, 5, Novartis, 2, 5, Incyte, 2, NewLink Genetics, 2, Aduro, 2, Eisai, 2, Pfizer, 2, RGenix, 5, AstraZeneca, 5, Infinity, 5; **A. Bass**, None.

Abstract Number: 1522

Potential Predictors of Persistence in Immune Check Point Inhibitor Induced Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Immune Check Point Inhibitors (ICIs) are widely used in Oncology and are associated with multiple autoimmune and systemic inflammatory reactions called immune-related adverse events. We sought to investigate the long-term outcomes of patients who develop ICI induced inflammatory arthritis (IA) and identify potential risk factors associated with IA persistence.

Methods: We conducted a retrospective chart review of patients referred to the rheumatology department for IA associated with ICIs by medical oncology between December 2015 to March 2021 at the Queen Elizabeth Hospital, Birmingham. Information was obtained using clinical records at the baseline visit and 6, 12 and 18 month follow up visits. A qualitative analysis without formal statistical testing was conducted due to the small size of the cohort.

Results: 38 patients were identified. None had pre-existing IA. There was slight male predominance (55.3% Males vs 44.7% Females). Mean age at diagnosis was 65.2 years. Mean Duration of IA was 15.2 months. The knee was the most commonly involved joint (84.2%) at Baseline. Mean baseline CRP was 63.3 mg/L. All patients were ACPA negative, 2 had borderline RF positivity. Mean interval between the first immune checkpoint inhibitor infusion and the onset of the rheumatic adverse events was 6.4 months. ICIs were stopped in 11/38 (28.9%) and temporarily suspended in 5/38 (13.2%) due to IAs. 18/28 (47.3%) required DMARDs and 4/38 (10.5%) were initiated on tumour necrosis factor alpha inhibitors. Persistence at follow up was defined as the presence of clinically assessed synovial swelling and/or ongoing requirement for corticosteroid or DMARD treatment for IA. At 6, 12 and 18 months follow up, 27/34 (79.4%), 16/24 (66.7 %) and 13/23 (56.5%) of patients had persistent IA respectively. Persistence at 6 months follow up was associated with non-smoking status in 18/18 patients (100%), additive course (defined as patients who develop more inflamed joints in addition to the primarily affected joint) in 23/24 patients (95.8 %) and ANA positivity in 19/20 patients (95%). In comparison, all non-persistors had a history of smoking; only one patient had an additive course: 1/24 (4.2%) and only one patient had ANA positivity: 1/20 (5%) in this group. IA was more likely to persist in patients who presented with baseline characteristics such as insidious onset, polyarthritis, symmetrical pattern and, involvement of both small and large joints. Patients with persistent IA had more flares in first six months as compared to non-persistors. Non-persistors had a numerically slightly higher total corticosteroid exposure over the first three months as compared to persistors.

Conclusion: Our findings highlight that ICI-induced IA can become a long term complex disease necessitating management by rheumatology for immunosuppression. Large multicentre cohorts are required to confirm potential risk factors for persistence versus remission.

Disclosure: A. Desai, None; **L. Shadananan**, None; **A. Croft**, None; **L. Pallan**, None; **N. Steven**, None; **B. Fisher**, Novartis, 2, BMS, 1, Janssen, 1, 5, Servier, 2, 5, Galapagos, 2, 5, Roche, 5.

Abstract Number: 1523

Outcomes and Disease Characteristics in Patients with Rheumatoid Arthritis Treated with Immune Checkpoint Inhibitors for Malignancy at a Single Academic Institution

Megan Hansen, Danny Zakria and Douglas Johnson, Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Table 1. Characteristics of patients with RA undergoing ICI treatment at Vanderbilt University Medical Center. n=19

Demographics	
Age, years	73 (35-83)
Sex, female	9 (47.3)
Length of follow up, months	12 (2-37)
Oncologic Characteristics	
Type of Malignancy	
Melanoma	10 (52.6)
Lung Adenocarcinoma	4 (21.1)
SCC	2 (10.5)
SCLC	1 (5.3)
DLBCL	1 (5.3)
Bladder cancer	1 (5.3)
ICI Class	
Anti-PD1	17 (89.5)
Anti-PDL1	1 (5.3)
Anti-CTLA4	1 (5.3)
RA Characteristics	
RF positive	5 (26.3)
CCP positive	5 (26.3)
DMARD during ICI treatment	6 (31.6)
RA active at start of ICI treatment	1 (5.3)
RA treatment at diagnosis	
None	4 (21.1)
HCQ	2 (10.5)
MTX	11 (57.9)
Prednisone	1 (5.3)
Biologic or smDMARD	5 (26.3)
RA treatment at start of ICI	
None	11 (57.9)
HCQ	4 (21.1)
MTX	3 (15.8)
Prednisone	2 (10.5)
Biologic or smDAMRD	0 (0)

Data presented as median (range) or frequency (percentage). ICI: immune checkpoint inhibitor; SCC: squamous cell carcinoma; SCLC: small cell lung cancer; DLBCL: diffuse large B-cell lymphoma; PD1: programmed cell death 1; PDL1: programmed cell death ligand 1; CTLA4: cytotoxic T-lymphocyte-associated protein 4.

Background/Purpose: Since the introduction of the first immune checkpoint inhibitor (ICI) in 2011, they have become widely utilized in the treatment of malignancy. It is well established that patients with autoimmune disease, such as RA, are at risk for flares of their disease when treated with ICIs. However, there is little information available on patients with RA who receive ICIs. This study aims at evaluating RA disease characteristics, outcomes, and treatment in patients with RA who were treated with ICIs at Vanderbilt University Medical Center.

Methods: Patients with RA diagnosed at least one year prior to onset of malignancy receiving ICI therapy were included. Full medical record review was performed. Data collected includes type and stage of malignancy, ICI treatment regimen (anti-PD1, anti-PDL1, and/or anti-CTLA4 therapy), RA serologies, RA disease activity at time of cancer diagnosis and ICI start, RA treatment at the time of cancer diagnosis and ICI start, time on ICI therapy, treatment of RA while receiving ICI, treatment of RA flares, immune-mediated adverse events (IRAEs), and overall cancer survival.

Results: A total of 19 patients treated over the past 10 years were identified (Table 1). The most common cancer represented was melanoma (10 patients). Five patients were RF positive, 5 patients were anti-CCP antibody positive, 2 patients were seronegative, and serologies were unavailable for 10 patients. Only 1 patient had active RA by physician's assessment at time of cancer diagnosis. Fifteen patients were on a DMARD at the time of cancer diagnosis but only 7 remained on a DMARD at the time of ICI initiation. The most commonly continued DMARD was hydroxychloroquine (4) followed by methotrexate (3). Eleven patients had an RA flare (increase in joint pain and/or swelling) with median time to onset of flare of 25 days (range 1 to 185 days) (Table 2). Of the 7 patients on a DMARD at time of ICI start, 4 had RA flares and 3 required glucocorticoids. Ten patients received glucocorticoids for flare (prednisone 10 to 40 mg). Of the 6 seropositive patients, 4 had flares. One of the 2 seronegative patients had a flare and 6 of 11 patients with unknown serologies flared. Six patients had other IRAEs which included hepatitis (2), colitis (2), and pneumonitis (2). Median overall cancer survival was 12 months which includes 11 living patients, some of whom were undergoing active ICI treatment.

Conclusion: Most patients were on DMARDs for RA at the time of cancer diagnosis and all but one were well controlled. However, at the time of ICI start, most patients stopped their DMARDs. Patients with even well-controlled RA can have flares when treated with ICIs. Flares can happen at any time during treatment and risk of flare is not clearly associated with seropositivity. However, most patients stopped or decreased number/dose of immunosuppressive medications when starting ICI therapy which may have contributed to rate of flares. Most flares were treated with

Table 2: Outcomes of patients with RA undergoing treatment with ICI for malignancy. n=19

RA Outcomes	
Flare on ICI	11 (57.9)
Time to flare, days	25 (1-185)
Flare treatment*	
None	1 (9.1)
Prednisone 10 mg	2 (18.2)
Prednisone 15 mg	1 (9.1)
Prednisone 20 mg	3 (27.3)
Prednisone 30 mg	1 (9.1)
Prednisone 40 mg	3 (27.3)
Malignancy Outcomes	
Survival, months	12 (2-37)
Survival at end of study	11 (57.9)
IRAE	6 (31.6)
Colitis	2 (10.5)
Pneumonitis	2 (10.5)
Hepatitis	2 (10.5)

Data presents at frequency (%) or median (range). *n=11. ICI: immune checkpoint inhibitor; IRAE: immune-related adverse event.

prednisone. Only one patient stopped ICI treatment due to RA flare. Prospective studies would be helpful for risk stratification of RA patients receiving ICIs as well as role for DMARDs concomitantly with ICIs.

Disclosure: M. Hansen, None; **D. Zakria**, None; **D. Johnson**, None.

Abstract Number: 1524

COVID-19 Vaccination Rates and Adverse Events Among Patients on Immunosuppressive Therapy in the Rheumatology Clinic Caring for an Underserved Population

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with autoimmune inflammatory rheumatic disease (AIRD) are at a higher risk for serious infections due to a combination of disease related immune dysfunction and the use of immunosuppressive therapy[1]. With the advent of the COVID-19 vaccination, there is an opportunity to protect this vulnerable patient population. However, there is inadequate data regarding vaccination rates, efficacy and vaccine related adverse events in this unique patient population.

The primary aim of this study is to assess the vaccination rates and adverse events among patients who are on immunosuppressive therapy. The secondary aim was to assess disparities in vaccination rates based on gender, age and ethnicity in patients from an underserved population.

Methods: A retrospective cross-sectional study was conducted from 1st January 2021 to April 30th 2021. Patients aged 18 years and older, who were on immunosuppressive therapy (prednisone >=5mg, conventional and biologic DMARDs) presenting to the rheumatology clinic at an academic medical center, were included. Statistical analysis was done using Chi-square and a p-value of < 0.05 was considered statistically significant.

Results: 376 patients met inclusion criteria. 31.65% (119/376) received atleast one COVID-19 vaccine dose, of whom a majority 28.2% (96/376) were fully vaccinated. 69% patients received the Pfizer and 31% received the Moderna vaccine. Vaccine rates (for atleast 1dose) based on age were variable.18-24 years-41.6%; 25-44 years-16.9%, 45-64 years- 32.6% (58/178) and 65 years and above- 53.7% (36/67) ($p< 0.00001$). 31.7% (97/306) women and 31.4% (22/70) men receiving atleast one dose. Racial and ethnic differences in vaccinations did not reach statistical significance. 29.5% African Americans (47/159), 28.8% (39/135) Caucasians, 43.6% (17/39) Hispanics, 33.3% (3/9) Asians and 38.2% (13/34) Other received atleast one vaccine dose.

No major adverse events were reported (Table 1). Only 3 vaccinated patients (1.3%) presented to the ED with presumed post vaccination side effects. Complaints included rash, dizziness and headache. 4 vaccinated patients (1.7%) reported a mild exacerbation of their underlying rheumatologic disease. Only 2 vaccinated patients were diagnosed with COVID-19 infection with one patient having received only the 1st dose. The 2nd patient was found to be COVID-19 + within 3 weeks of receiving the 2nd vaccine.

Adverse events requiring hospital admission	Number of events observed
Anaphylaxis	0
Acute myocardial infraction	0
Stroke	0
Venous thromboembolism	0
Ischemic stroke	0
Hemorrhagic stroke	0
Immune thrombocytopenia	0
Transverse myelitis	0
Myocarditis/pericarditis	0
Encephalitis / myelitis / encephalomyelitis	0
Guillain-Barré syndrome	0
Bell's palsy	0
Multisystem inflammatory system in adults	0

Side effects of COVID vaccinations that required ED visits	Post 1 st dose/2 nd dose	Rheumatological diagnosis
Rash	2 nd dose	RA
Headache and Dizziness	1st dose	RA
Sore throat	1st dose	Sicca syndrome

Patients who reported an exacerbation of autoimmune disease post vaccination	Post 1st/2nd dose	Rheumatological diagnosis	Severity
	2nd dose	RA	Mild
	1st dose	RA	Mild
	1st dose	RA	Mild
	1st dose	Psoriatic arthritis	Mild

Conclusion: Vaccination rates observed in our patient population was comparable to rates in Missouri (MO)- 31.65% v/s 37.3%(MO) and 28.2% v/s 27.4% (MO) for the 1st and 2nd Covid vaccine doses respectively as of April 30th 2021. Severe adverse events were not seen and the vaccine was well tolerated by our patients. Statistically significant differences were not seen based on gender and ethnicity. Age differences were statistically significant with patients aged 65+ being more likely to get vaccinated, which is likely a reflection of preferential vaccine rollout in more vulnerable populations. Vaccine hesitancy or disparity in access was not seen in our patient population based on preliminary data. Our goal is to reassess the data again in 6 - 12 months to identify any vaccination disparities.

Disclosure: S. Gallappaththy, None; **S. Ifteqar**, None; **A. Edrees**, None.

Abstract Number: 1525

Risk Factors for Anti-infliximab Antibody Formation: Results from a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

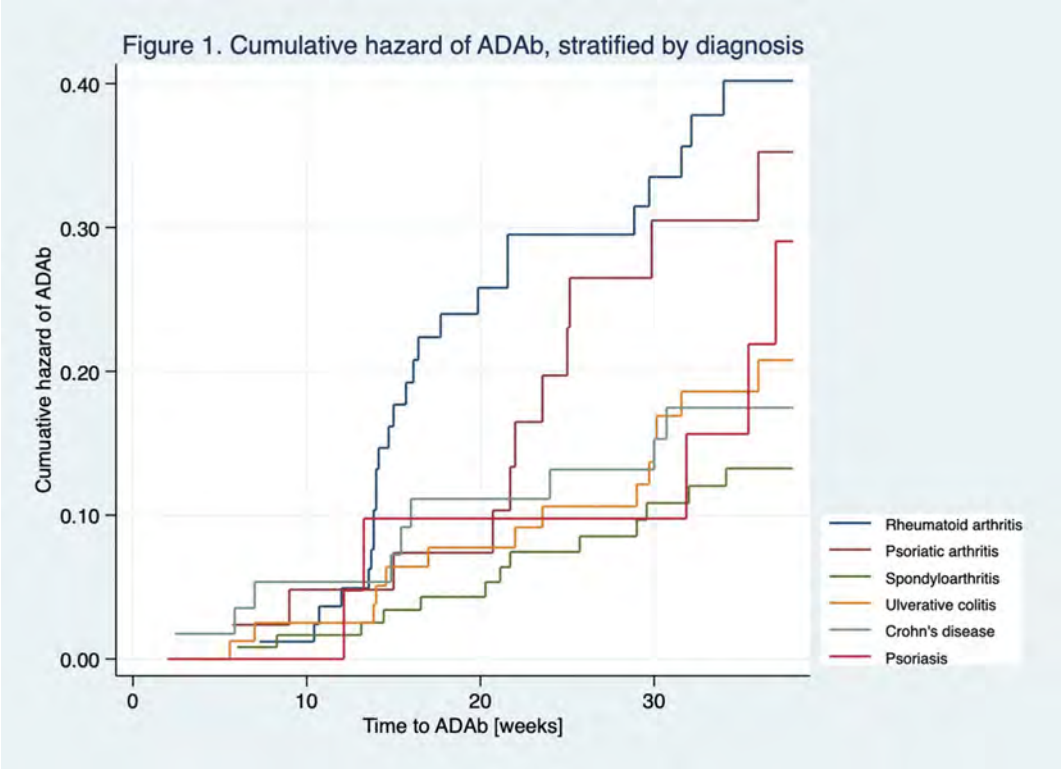
Session Time: 8:30AM–10:30AM

Background/Purpose: Immunogenicity is related to loss of efficacy and safety to TNFα inhibitors and is frequently observed early in the treatment course. The highest rate of anti-drug antibody (ADAb) formation has been reported for infliximab (IFX). Knowledge about risk factors for immunogenicity might contribute to better handling of this problem in clinical practice. The aim of this sub study of the NOR-DRUM A trial (main results recently published in JAMA[1]) was to identify risk factors for ADAb formation during the early phase of infliximab (IFX) treatment.

Table. Risk factors for ADAb formation. Results from logistic regression analyses

	Univariate analyses		Multivariate analyses (Adjusted for diagnosis- disease activity- age and gender)	
	OR	CI	OR	CI
RA	2.2**	1.3-3.8	2.1*	1.1-3.9
SpA	0.4**	0.2-0.8	0.5*	0.2-0.9
Concomitant immunosuppressive therapy*	0.9	0.5-1.4	0.4**	0.2-0.8
Current or former smoking	2.2**	1.3-3.8	1.8*	1.0-3.3
Mean sIFX	0.7***	0.6-0.8	0.7***	0.6-0.8
>11 weeks between infusions	3.9*	1.3-11.9	4.1*	1.2-13.8
IFX dose increment	0.5*	0.3-0.9	0.4**	0.3-0.8
Mean DAS28 (RA and PsA)	1.5*	1.0-2.1	1.5*	1.0-2.3
Mean ESR	1.1***	1.0-1.1	1.1***	1.0-1.1
Mean CRP	1.1**	1.0-1.1	1.1**	1.0-1.1

Results are presented as Odds ratios (OR) with 95% confidence intervals (CI). * p<0.05, ** p<0.01, *** p<0.001. All variables with a P-value <0.25 in univariate analyses were examined in multivariate analyses adjusting for potential confounders. Only variables with a p-value <0.05 are shown. Non-significant variables include other demographic variables and IFX dose. *Included in table despite an unadjusted P-value>0.25 because this variable vas significant in adjusted analysis.



Nelson-Aalen plot showing the cumulative hazard of ADAb for each diagnosis. Each step indicates a new event (ADAb). The slope of the curve indicates the hazard rate.

Methods: 411 patients with immune-mediated inflammatory diseases (84 rheumatoid arthritis (RA), 119 spondyloarthritis (SpA), 45 psoriatic arthritis, 83 ulcerative colitis, 58 Crohn's disease and 22 psoriasis) initiating IFX treatment were included in the 38-week NOR-DRUM A trial and randomised 1:1 to therapeutic drug monitoring or standard IFX therapy.[1] The primary endpoint was clinical remission at week 30. Serum (s) IFX levels and ADAb were measured at each infusion by in-house assays; time-resolved fluorometric assay for sIFX and inhibition assay for ADAb.[1] Possible risk factors for ADAb formation including demographic variables, diagnosis, comedication, disease activity, IFX dose, sIFX and drug holidays, were assessed using logistic regression. Variables with a p-value < 0.25 in univariate analyses were further examined in multivariate analyses adjusting for potential confounders (diagnosis, disease activity, age and gender).

Results: 410 patients with at least one available sIFX measurement were included in the present analyses. 76% were biologic-naive, and 45% (18% of RA patients) used IFX as monotherapy. Patients received a mean IFX dose of 3.2-5.9 mg/kg (RA 3.2 mg/kg). ADAb were detected in 78 (19%) patients. The Table shows variables with a significant association to ADAb formation. Analyses revealed an increased risk of ADAb development in patients with RA (Odds ratio (OR) 2.1, 95% confidence interval (CI) 1.1-3.9) ADAb formation, while SpA had a lower risk (OR 0.5, CI 0.2-0.9) compared to the other diagnoses. These findings were consistent in both univariate- and multivariate analyses. Figure 1 shows the cumulative hazard for ADAb formation according to diagnosis. Other risk factors for ADAb formation (Table) were smoking (OR 1.8, CI 1.0-3.3) and drug holidays of more than 11 weeks (OR 4.1, CI 1.2-13.8). Additionally, the risk of ADAb increased with higher disease activity (OR 1.5, CI 1.0-2.3) and lower sIFX levels (OR 0.7, CI 0.6-0.8). Patients using concomitant immunosuppressive medication (OR 0.4, CI 0.2-0.8), or having one or more IFX dose increments (OR 0.4, CI 0.3-0.8), had a reduced risk of immunogenicity.

Conclusion: This study identified smoking, drug holidays, high disease activity, IFX monotherapy and low sIFX levels as risk factors for ADAb development. Of particular interest, we found that RA patients had an increased risk of ADAb compared to the other immune-mediated inflammatory diseases. Whether this novel finding reflects different underlying disease mechanisms or the fact that RA patients receive a lower IFX dose, is not known and needs to be further explored.

[1] Syversen SW et al. *JAMA*. 2021;325(17):1744–1754.

Disclosure: M. Brun, None; **G. Goll**, AbbVie, 1, 6, Pfizer, 1, 6, Eli Lilly, 6, Novartis, 6, Orion Pharma, 6, Roche, 6, Boehringer Ingelheim, 6, Celltrion, 6, Sandoz, 6; **K. Jørgensen**, Celltrion, 6, AOP Orphan Pharmaceticals, 6, Norgine, 6; **J. Sexton**, None; **J. Gehin**, None; . **Sandanger**, None; **I. Olsen**, None; **R. Klaasen**, None; **D. Warren**, None; **C. Mørk**, Novartis, 6, Leo Pharma, 6, Cellegene, 6, Abbvie, 6, Galderma, 6, UCB, 6; **T. Kvien**, Biogen, 6, Celltrion, 6, Egis, 6, Eli Lilly, 6, Evapharma, 6, Ewopharma, 6, Gilead, 6, Hikma, 6, Mylan, 6, Oktal, 6, Sandoz, 6, Sanofi, 6, Abbvie, 5, 6, BMS, 5, MSD, 5, Novartis, 5, 6, Pfizer, 5, 6, Amgen, 5, 6, UCB, 5; **J. Jahnsen**, None; **N. Bolstad**, None; **E. Haavardsholm**, Pfizer, 6, AbbVie, 2, 6, Celgene, 2, Janssen, 2, Gilead, 2, Eli-Lilly, 2, UCB, 2, 6, Novartis, 12, personal fees; **S. Syversen**, Thermo Fisher, 6.

Abstract Number: 1526

Development of Antinuclear Antibodies and Systemic Lupus Erythematosus in Patients on Tumor Necrosis Factor α Inhibitor Therapy

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Tumor necrosis factor α (TNF-α) inhibitor therapy has been widely used worldwide as a potent immunosuppressant for a variety of rheumatological diseases. Induction of antinuclear antibodies (ANA) and systemic lupus erythematosus (SLE) in patients receiving anti-TNF-α therapy have been previously documented[1]. It is known that up to 15% of healthy individuals have a positive ANA test[2]. In this study we examined the frequency and safety outcomes of ANA and SLE induction following initiation of anti-TNF-α therapy.

Methods: Patients, age >18 years, from January 2012 – December 2020 who were newly prescribed the following TNF-α inhibitor were included in this study: golimumab, cetrolizumab, adalimumab, etanercept, infliximab and inflectra. They were categorized into two groups based on immune fluorescence ANA assay performed either before or after anti-TNF-α therapy was started. The ANA tested cohort was sub-categorized to ANA-positive and ANA-negative result. ANA positive patients were sub-categorized for ANA 'positivity before' or 'positivity after' TNF-α inhibitor start date. Fisher's exact two tailed test and two tailed chi-square was calculated on the GraphPad Prism 9.0 statistical software; two-tailed p values < 0.05 were considered significant.

Results: 2803 patients met inclusion criteria. 1120 were and 1683 were not tested for ANA. Of 1120, 742 had a positive test and 378 had a negative test result. From 742, 508 and 234 had a positive ANA test before and after the initiation of a TNF-α inhibitor, respectively. Percentage developing a positive ANA test following anti-TNF-α was 20.8%

Table 1. Effect of TNF-α inhibitors on the development of ANA and SLE in 2803 patients				
	Before TNF-α Inhibitor	After TNF-α Inhibitor	Chi-square	p value
ANA positive ANA negative	508 2295	742 2061	5.361	P<0.0001
SLE No SLE	83 2720	115 2688	56.38	0.0247

Table 2. Prevalence of ACR & SLICC SLE Criteria in 32 patients with TNF inhibitor-induced SLE	
SLE Criteria	Number (%)
ANA	32 (100)
Anti-dsDNA	2 (6.2)
Anti-Sm	3 (9.3)
Photosensitivity	2 (6.2)
Low complements	3 (9.3)
Alopecia	4 (12.5)
Synovitis	4 (12.5)
Non erosive arthritis	14(43.7)
Malar rash	7 (21.8)
Leukopenia	0 (0)
Thrombocytopenia	2 (6.2)
Acute cutaneous lupus	4 (12.5)
Chronic cutaneous lupus	0 (0)
APLA	5 (15.6)
Oral/nasal ulcers	2 (6.2)
Neurology	1 (3.1)
Lymphopenia	2 (6.2)
Discoid Rash	0 (0)
Serositis	0 (0)
Renal Involvement	0 (0)
Hemolytic Anemia	0 (0)
Direct Coombs Test	0 (0)

Table 3. Outcome of TNF-α inhibitor in 32 SLE induced patients	
Outcome (Number)	Reason (Number)
TNF-α inhibitor discontinued (22)	Subacute erythematous rash (4) Arthritis not improved (13) Diarrhea (1) Bronchitis (1) Injection site reaction (1) Depression (1) History of congestive heart failure (1)
TNF-α inhibitor continued (10)	SLE overlap syndrome (10)

(234/1120). 83 patients had SLE before and 32 developed clinician diagnosed SLE after TNF-α inhibitor. There was a statistically significant difference on the impact on ANA induction and development of SLE (Table 1).

32 patients met ACR or SLICC criteria for SLE (Table 2). Arthritis and synovitis had to be present before TNF-α inhibitor was started in these 32 patients. TNF-α was discontinued in 22 and continued in 10 (Table 3). No life-threatening SLE complications, hospitalizations, or death were noted in patients with TNF-α inhibitor-induced SLE.

Conclusion: The data from our cohort newly prescribed anti-TNF-α therapy demonstrate the autoimmunity which should be carefully monitored for adverse events attributable to the development of SLE. Timely discontinuation, less than a week from identification of TNF-α induced SLE, appears to have prevented serious SLE-related adverse events. Additionally, we show that compared to healthy persons that the prevalence of a positive ANA test is higher in TNF-α treated patients, 15% vs. 20.8%.

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Disclosure: C. Wijewardena, None; **P. Pirinavan**, None; **S. Nasr**, None; **A. Perl**, None.

Abstract Number: 1527

Effect of Rituximab on IgG Levels and Associated Infection Risk in Myositis

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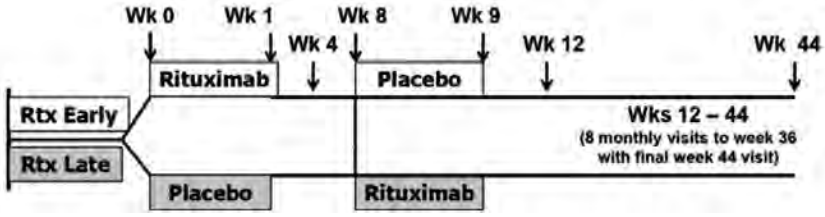
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

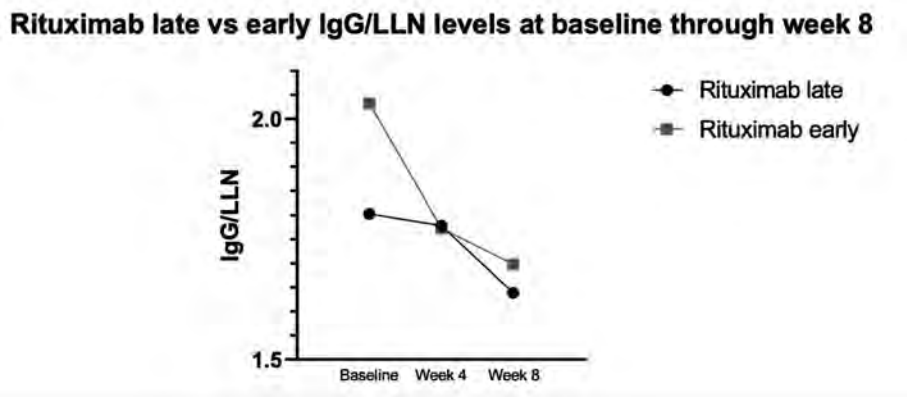
Background/Purpose: Rituximab is an anti-CD20 antibody with therapeutic use in myositis. However, given its B cell depleting mechanism, there is concern regarding its association with hypogammaglobinemia and consequent risk of infection in myositis. We therefore aimed to perform a comprehensive analysis of the effect of rituximab on IgG levels of DM/PM/JDM patients and the association of IgG levels with infections using the Rituximab in Myositis (RIM) study data.

Methods: We retrospectively analyzed data collected in the RIM Trial, which included a rituximab early (RE) and late (RL) group with rituximab administered at weeks 0/1 and at week 8/9, respectively (Figure 1). Serum IgG levels were measured as the ratio of absolute IgG level divided by the lower limit of normal (LLN) for the reference lab. Data were compared for the overall, RL, and RE groups, with/without stratification by disease states that included DM, PM and JDM. IgG levels were compared using a paired t-test. Frequency and duration of abnormally low IgG levels was also evaluated. Associations between the number of infections and IgG levels as well as baseline immunosuppressive drugs were determined using spearman correlation.

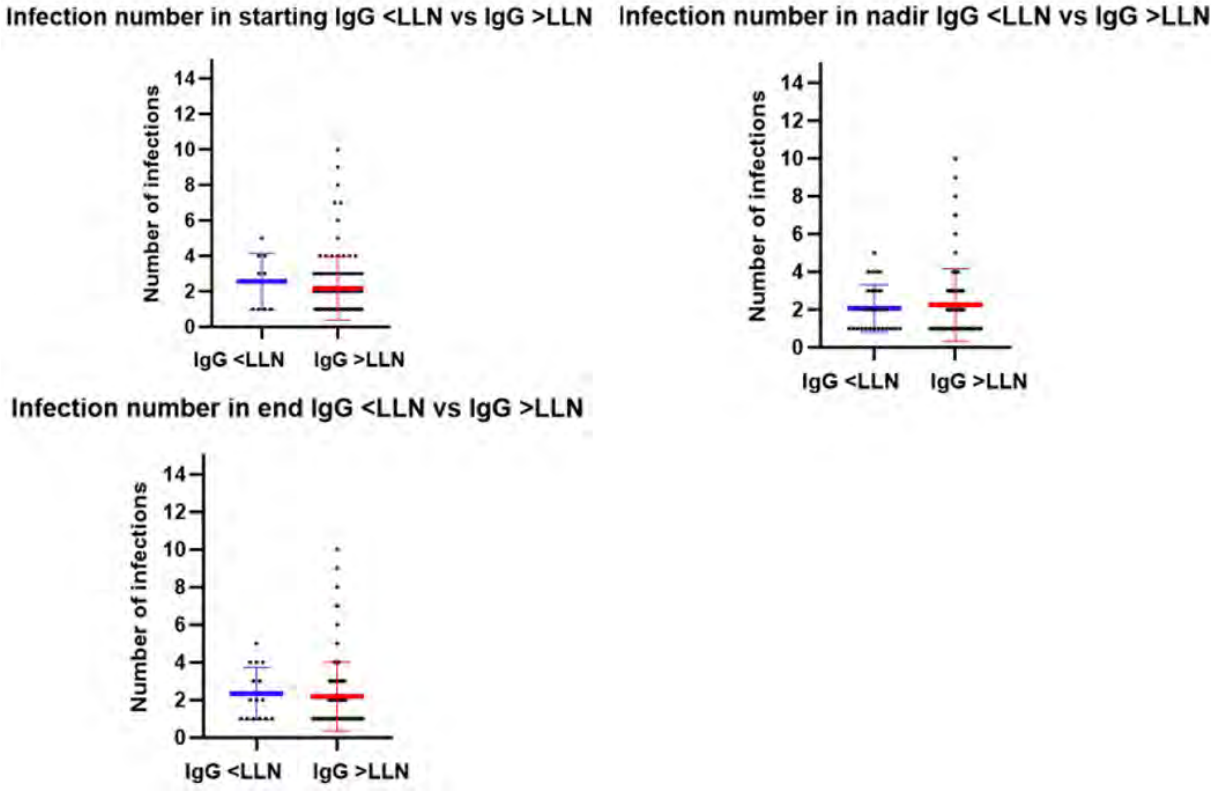
Results: A total of 194 patients (72 DM, 74 PM, 48 JDM) meeting Bohan & Peter criteria were included in this study; with mean age 41 years, 73% female and 71% Caucasian. There was a small, but significant decrease in mean IgG levels (1.9 vs 1.7 xLLN) seen from baseline to week 8, significant only in RE (Early: 2.0 vs. 1.7, p=0.005; Late: 1.8 vs. 1.6, p=0.10) (Figure 2). Nadir IgG levels showed a small but significant decline from baseline levels in both RE and RL; however, end of trial levels were significantly decreased only in RE. Similar trends were seen in subgroup analyses of



Study design of Rituximab in Myositis (RIM) study



Mean IgG/LLN levels for baseline through week 8 for rituximab late vs rituximab early



Infection number by LLN status at baseline, nadir and ending level. Note, plotted lines include mean in middle, SD at top/bottom

adult DM, PM, and JDM; except that end of trial levels were only significantly lower from baseline in DM ($p< 0.0001$), with a non-significant decline in PM ($p=0.110$ and JDM ($p=0.11$).

Despite the small decline in IgG levels, most patients (77%) had IgG levels that remained normal. Amongst 45 (23%) patients with IgG levels below LLN at any time, there were 3 trends: (a) patients with IgG levels below LLN at baseline (n=18); (b) patients with transient decline of IgG levels below LLN (n=14); (c) patients who developed long term decline of IgG levels below LLN (n=13).

Overall, 56.2% patients had infections during the study, with the average number of infections being 2.2 (Figure 3). There was no association between IgG level and number of infections anytime during the trial except in the DM subgroup, where more infections were seen in patients with IgG levels below LLN at baseline (median # infections: 4 vs 2, $p=0.027$). There was no correlation between number of immunosuppressant medications or baseline steroid dose and number of infections.

Conclusion: Rituximab led to a modest, but statistically significant decline in IgG in myositis patients of unclear clinical significance, without clear association between IgG levels and infection except in the DM subgroup with IgG levels below LLN at baseline. These data should provide additional evidence supporting the safety of rituximab in myositis, where most patients' IgG levels remained normal or declined only transiently.

Disclosure: M. Macklin, None; **C. Oddis**, Genentech, 5, Pfizer, 2, Corbus, 5, CSL Behring, 5, EMD Serono, 2, 5; **S. Moghadam-Kia**, None; **D. Ascherman**, None; **R. Aggarwal**, Mallinckrodt, 1, 5, Bristol Myers-Squibb, 2, 5, Pfizer, 2, Genentech, 5, Orphazyme, 1, 2, CSL Behring, 1, 2, AstraZeneca, 2, Kezar, 2, Q32, 2, 5, Alexion, 2, Argenx, 2, Boehringer Ingelheim, 2, Corbus, 2, EMD Serono, 2, 5, Janssen, 2, Kyverna, 2, Octapharma, 1, 2.

Abstract Number: 1528

Clinical Consequences of Hepatitis B Core Antibody Positivity After IVIG Administration

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Immunological Complications of Therapy Poster (1516–1529)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Intravenous immunoglobulin (IVIG) is a blood product created by pooling of donor plasma that is used for a wide range of indications. IVIG is commonly used in the fields of neurology, rheumatology, hematology, and transplant medicine. Previous studies have identified transient positivity of hepatitis B core antibody (HBcAb) after receiving IVIG. This phenomenon signifies a passive transference of HBcAb from IVIG as opposed to a previous exposure to HBV. This study examines the clinical consequences of this concept, including the inappropriate administration of antiviral therapy and the deferment of immunotherapy, such as anti-CD20 monoclonal antibodies, in fear of HBV reactivation.

Methods: Preliminary database search identified patients that were at least 18 years of age, tested HBcAb-positive, and received IVIG between January 2013 through January 2021. After exclusion criteria were applied, retrospective chart review was performed to determine the indication for IVIG, whether patients received antiviral therapy, and whether they received an anti-CD20 monoclonal antibody (rituximab, ocrelizumab, or ofatumumab).

Results: Preliminary search yielded 123 patients that met inclusion and exclusion criteria. Of these 123 patients, 37 (30.1%) tested HBcAb-negative before IVIG, tested HBcAb-positive after IVIG, and had undetectable HBV DNA levels (see Figure 1). Indications for IVIG included pathologies in hematology, immunology, neurology, rheumatology, and transplant medicine (see Figure 2). These patients represent confirmed false-positives for HBcAb. Of these 37 patients, 22 (42.3%) received antiviral therapy (either tenofovir or entecavir). 29 (78.4%) did and 8 (21.6%) did not receive anti-CD20 monoclonal antibody therapy.

Conclusion: This study demonstrates that a significant portion of patients receive unnecessary antiviral therapy due to the passive transfer of HBcAb with IVIG. This leads to an inappropriate utilization of resources and potential expo-

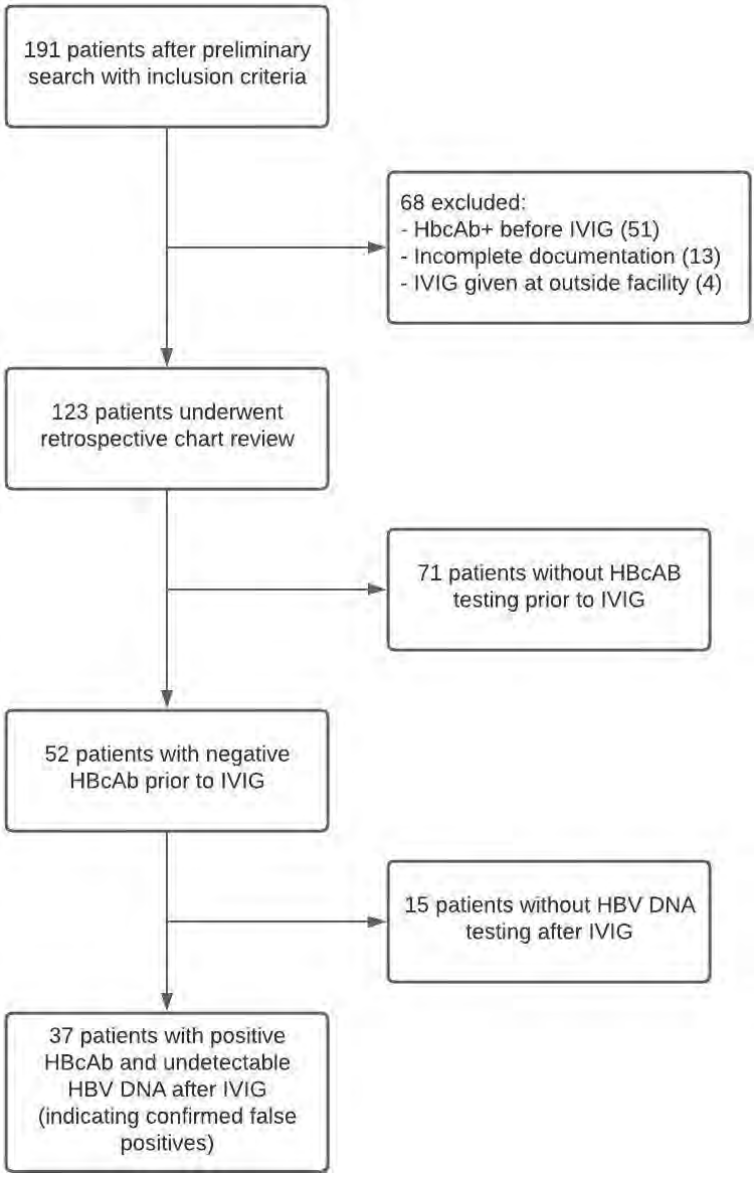

Figure 1. Flowchart of Retrospective Analysis.

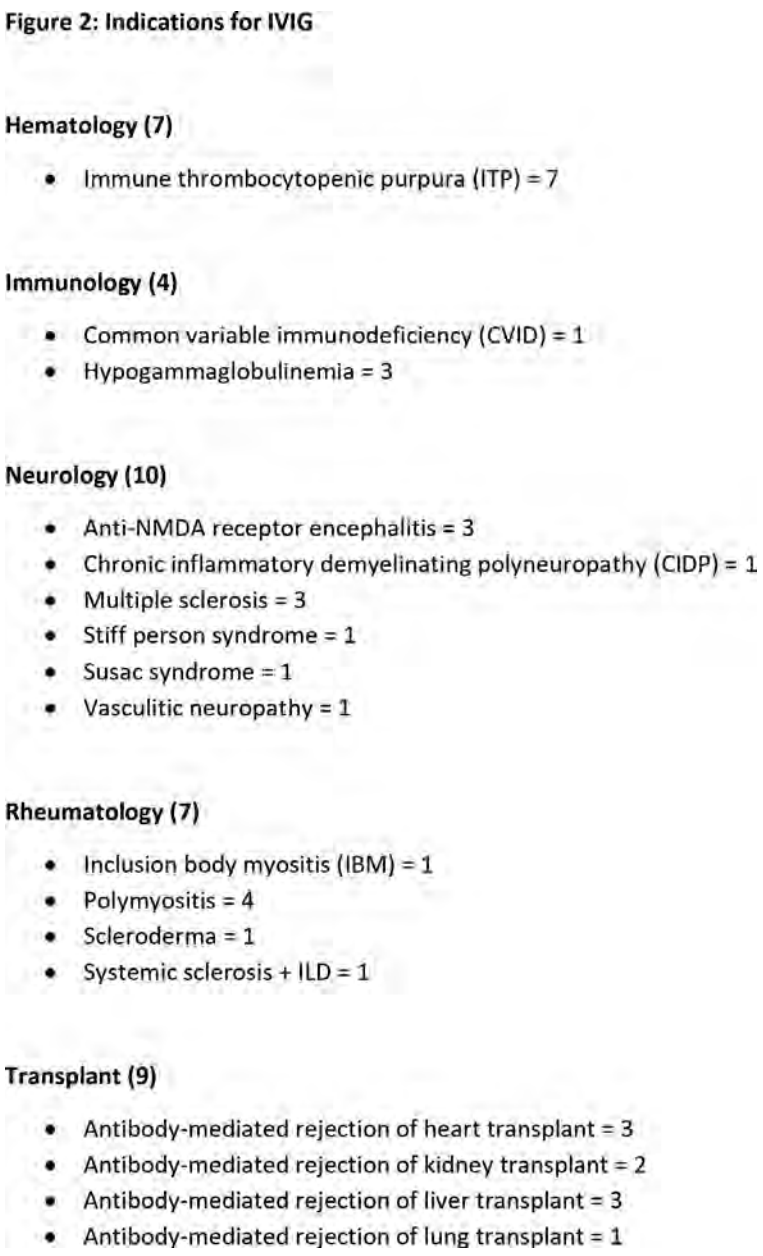

Figure 2. Indications for IVIG.

sure to side effects of the medication. This study also highlights a proportion of patients that do not receive anti-CD20 monoclonal antibody therapy, which may be related to HBcAb-positivity. As previous studies have suggested, HBV testing should be done prior to IVIG administration in order to establish an accurate HBV status for the patient. In doing so, patients may avoid unnecessary prescription of antiviral therapy. Furthermore, physicians would have a clear understanding of the actual risk of HBV reactivation when considering the use of anti-CD20 monoclonal antibodies.

Disclosure: W. West, None; **T. Posas-Mendoza**, None; **J. Zakem**, None; **W. Davis**, None; **R. Quinet**, None.

Abstract Number: 1529

Effectiveness and Safety of Pegloticase with Concomitant Immunomodulatory Therapy

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Immunological Complications of Therapy Poster (1516–1529)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Oral urate-lowering therapy (ULT) is one of the primary treatments for gout. Unfortunately, a proportion of patients with advanced gout are resistant to oral ULT or have severe tophaceous gout. For patients with uncontrolled gout, pegloticase, a recombinant pegylated uricase, is approved by the US Food and Drug Administration (FDA) and has proven efficacy. However, pegloticase use can be limited by immunogenicity as the development of anti-drug antibodies contributes to both loss of efficacy and a higher risk of infusion reactions. Small clinical trials (Khanna, 2021; Boston, 2021) have suggested that concomitant immunomodulatory (IMM) drugs (e.g. mycophenolate moefitil or methotrexate) reduce pegloticase immunogenicity and improve treatment persistence, but real-world evidence is still lacking. Therefore, we evaluated pegloticase persistence and adverse events associated with concomitant IMM drug use in patients with uncontrolled gout.

Methods: We conducted a retrospective cohort and selected patients with procedure code(s) for pegloticase (J2507) using ACR's Rheumatology Informatics System for Effectiveness (RISE) registry from 01/2016 through 06/2020. The first date of pegloticase was defined as the index date. Based on use of the concomitant IMM drug, we identified 2 exposure groups: 1) IMM users (defined as ≥ 1 IMM prescription within ±60days of index); 2) non-IMM users. We

Table 1: Demographic characteristics of the patients stratified by immunomodulatory (IMM) drug use given concomitant to pegloticase

		IMM users N=124	Non-users N=576	All N=700
Characteristics				
Age	Median (25%, 75%)	61.33 (51.46, 73.28)	61.68 (49.90, 72.32)	61.46 (50.22, 72.44)
Male		96 (77.4%)	449 (78.0%)	545 (77.9%)
Race	Asian	15 (12.1%)	29 (5.0%)	44 (6.3%)
	African American	11 (8.9%)	60 (10.4%)	71 (10.1%)
	White	74 (59.7%)	363 (63.0%)	437 (62.4%)
	Unknown	24 (19.4%)	122 (21.5%)	146 (20.9%)
Body Mass Index	Median (25%, 75%)	31.50 (27.30, 37.19)	31.67 (27.28, 36.26)	31.74 (27.28, 36.31)
Ever smoker	Yes	26 (21.0%)	108 (18.8%)	134 (19.1%)
RxRISK category count	Median (25%, 75%)	8.00 (6.00, 11.00)	8.00 (4.00, 11.00)	8.00 (4.00, 11.00)

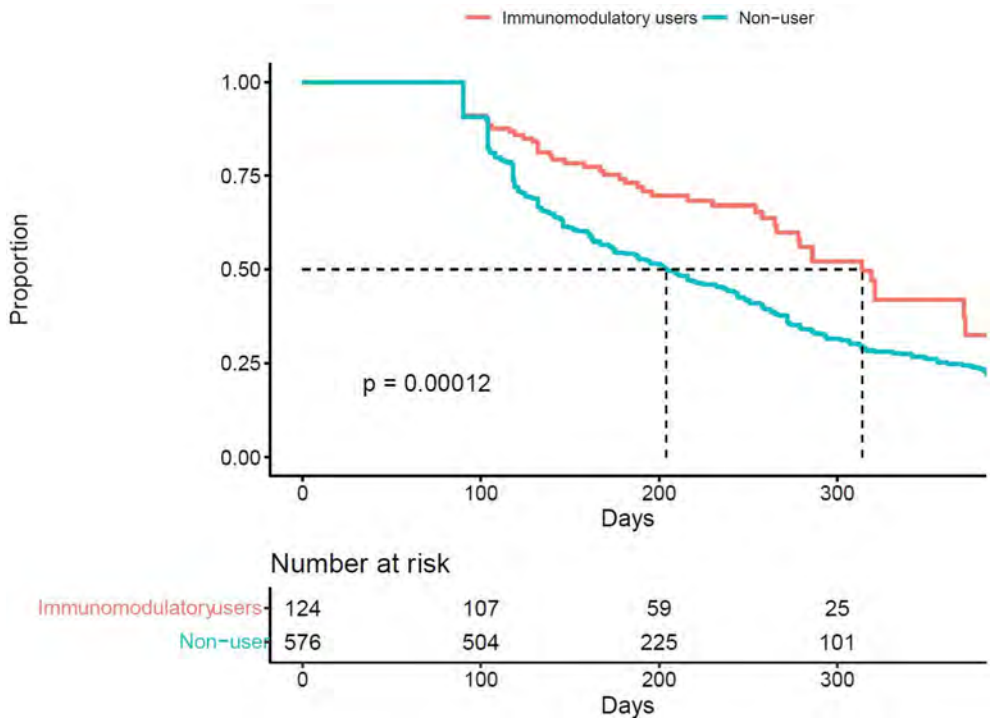

Figure 1. Kaplan-Meier plot for time to discontinuation stratified by immunomodulatory drug use given concomitant to pegloticase.

calculated the proportion of patients who ever achieved the serum urate (sUA) ≤ 6mg/dL and patients who had lab abnormalities (WBC < 3.4; platelets < 135,000; hematocrit [HCT] < 30; ALT or AST ≥1.5X ULN) within 180 days after the index date. Time to pegloticase discontinuation was analyzed using cox regression model controlling for potential confounders including age, sex, race, body mass index (BMI), national area deprivation index (ADI), concurrent medications (Rx), and number of RxRisk categories (a measure of comorbidity based on medications for specific diseases).

Results: We identified 700 pegloticase users with median follow-up of 14 months. Among these, 124 were IMM users and 576 non-users (**Table 1**). For IMM users, the most used IMM medications were methotrexate (79%), followed by azathioprine (12.1%). During follow-up, 90% of patients ever met sUA treatment target. The median number of pegloticase infusions were 7 for IMM drug users and 5 for non-users . Compared to non-users, IMM users were less likely to discontinue pegloticase (**Figure 1**). After adjustment, the hazard ratio of discontinuation of pegloticase associated with concomitant IMM therapy was 0.57 (95% CI: 0.43-0.78). Lab abnormalities were uncommon (< 5%) among pegloticase users, and were not higher in patients also on IMM therapy.

Conclusion: Consistent with small trials, results from this large observational registry suggest that concomitant immunomodulatory drug use improves pegloticase persistence. Rare lab abnormalities suggest no disproportionate toxicity resulting from this strategy.

Disclosure: H. Yun, Pfizer, 5; **B. LaMoreaux**, Horizon Therapeutics, 3, 11; **L. Chen**, None; **S. Ledbetter**, None; **M. Francis-Sedlak**, Horizon Therapeutics plc, 3, 11; **K. Saag**, Arthrosi, 2, Atom Bioscience, 2, Horizon Therapeutics, 2, 5, LG Pharma, 2, Mallinkrodt, 2, SOBI, 2, 5, Takeda, 2, Shanton, 5; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5.

Abstract Number: 1530

Evaluation of the Possible Different Evolution of SARS-CoV-2 Infection with Tumor Necrosis Factor Inhibitors or with Rituximab in Rheumatic Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: To assess whether two different biological therapies (BT), tumor necrosis factor inhibitor (TNFi) and ritixumab (RTX), are related to a different course and severity of SARS-CoV-2 infection in patients with rheumatic diseases.

Methods: Observational and retrospective multicenter study that includes patients under follow-up by the rheumatology services of Hospital La Mancha Centro, Hospital Nª Sª del Prado and Hospital de Tomelloso, and who received some BT from at least 3 months prior to the beginning of the COVID19 pandemic until March 2021. Sociodemographic, clinical and treatment variables were collected through digital medical history, as well as the presence of confirmed SARS-CoV-2 infection (by nasopharyngeal RT-PCR, rapid antigen or antibodies IgG tests) and its posterior evolution. The development of pneumonia and the need for hospital admission, the need for ventilatory support, refractoriness to corticosteroids (CS), absence of development of IgG antibodies against the virus, higher WHO clinical progression scale and the exitus were considered worse evolution and greater severity. These evolution variables were compared between the patients who received TNFi versus others and also between who received RTX versus others.

Results: In the 3 hospitals, a total of 372 patients with rheumatic diseases received BT during follow-up, of which 68 patients (18.3%) had SARS-CoV-2 infection, with a mean age of 54.8±13.8 years (54.4% women and 45.6% men). The most frequent diagnoses were inflammatory spondyloarthropathy (39.7%), rheumatoid arthritis (32.3%) and pso-

Table 1. Patients with BT and SARS-CoV-2. Diagnoses and treatments (n = 68).

Diagnoses		Treatments	
SpA	27 (39.7%)	TNFα inhibitors	45 (66.2%)
RA	22 (32.3%)	Rituximab	9 (13.2%)
PsA	8 (11.8%)	IL17 inhibitors	4 (5.9%)
Vasculitis	5 (7.4%)	Ustekinumab	3 (4.4%)
Systemic Autoinmune disease	3 (4.4%)	JAK inhibitors	3 (4.4%)
Uveitis	2 (2.9%)	Abatacept	2 (2.9%)
Behçet disease	1 (1.5%)	IL6 inhibitors	1 (1.5%)
		Apremilast	1 (1.5%)

** Vasculitis: Granulomatosis withon polyangiitis (n=3), ANCA associated Vasculitis (n=1), Microscopic polyangiitis (n=1); Systemic autoinmune disease: Polymyositis (n=1), Sjögren´s Syndrome (n=1), Mixed connective tissue disease (n=1).*

Table 2. Evolution of SARS-CoV-2 patients; TNFi vs others BT.

Evolution SARS-CoV-2		TNFi	Others BT	
Pneumonia	**No** (n=47; 69.1%)	40 (88.9%)	7 (30.4%)	***p = 0.000***
	Yes (n=21; 30.9%)	5 (11.1%)	16 (69.6%)	
Hospital admission	**No** (n=51; 75%)	41 (91.1%)	10 (43.5%)	***p = 0.000***
	Yes (n=17; 25%)	4 (8.9%)	13 (56.5%)	
Refractory to CS	**No** (n=25; 73.5%)	14 (87.5%)	11 (61.1%)	p = 0.125
	Yes (n=9; 26.5%)	2 (12.5%)	7 (38.9%)	
Ventilatory support	**No** (n=11; 64.7%)	4 (100%)	7 (53.8%)	p = 0.237
	Yes (n=6; 35.3%)	0 (0%)	6 (46.2%)	
Hospitalization (days)		7.5±2.9	12±37.8	***p = 0.045***
WHO scale	**Mild (≤3)** (n=50; 73.5%)	40 (88.9%)	10 (43.5%)	***p = 0.000***
	Moderate (4-5) (n=12; 17.6%)	5 (11.1%)	7 (30.4%)	
	Severe (≥6) (n=6; 8.8%)	0 (0%)	6 (26.1%)	
Exitus	**No** (n=66: 97.1%)	45 (100%)	21 (91.3%)	p = 0.111
	Yes (n=2; 2.9%)	0 (0%)	2 (8.7%)	
IgG+ SARS-CoV2 development	**No** (n=9; 33.3%)	0 (0%)	9 (75%)	***p = 0.000***
	Yes (n=18; 66.7%)	15 (100%)	3 (25%)	

Table 3. Evolution of SARS-CoV-2 patients; RTX vs others BT.

Evolution SARS-CoV-2		RTX	Others BT	
Pneumonia	**No** (n=47; 69.1%)	1 (11.1%)	46 (78%)	***p = 0.000***
	Yes (n=21; 30.9%)	8 (88.9%)	13 (22%)	
Hospital admission	**No** (n=51; 75%)	2 (22.2%)	49 (83.1%)	***p = 0.001***
	Yes (n=17; 25%)	7 (77.8%)	2 (16.9%)	
Refractory to CS	**No** (n=25; 73.5%)	5 (55.6%)	20 (80%)	p = 0.201
	Yes (n=9; 26.5%)	4 (44.4%)	5 (20%)	
Ventilatory support	**No** (n=11; 64.7%)	4 (57.1%)	7 (70%)	p = 0.644
	Yes (n=6; 35.3%)	3 (42.9%)	3 (30%)	
Hospitalization (days)		12.0±37.9	10.5±23.6	p = 0.193
WHO scale	**Mild (≤3)** (n=50; 73.5%)	2 (22.2%)	48 (81.4%)	***p = 0.001***
	Moderate (4-5) (n=12; 17.6%)	4 (44.4%)	8 (13.6%)	
	Severe (≥6) (n=6; 8.8%)	3 (33.3%)	3 (5.1%)	
Exitus	**No** (n=66: 97.1%)	8 (88.9%)	58 (98.3%)	p = 0.249
	Yes (n=2; 2.9%)	1 (11.1%)	1 (1.7%)	
IgG+ SARS-CoV2 development	**No** (n=9; 33.3%)	8 (100%)	1 (5.3%)	***p = 0.000***
	Yes (n=18; 66.7%)	0 (0%)	18 (94.7%)	

riatic arthritis (11.8%), and the BT administered were TNFi (66.2%), RTX (13.2%) and IL17 inhibitors (5.9%) (table 1). The mean time of BT administration was 54.9±46.4 months.

Of the patients infected with SARS-CoV-2, 21 (30.9%) developed pneumonia, 17 (25%) suffered hospital admission and 34 (50%) required some treatment (of which 9 (13.2%) were initially refractory to CS treatment and 6 (8.8%) required ventilatory support). The mean time of hospitalization was 25.1±30.5 days and the mean of the WHO clinical progression scale was 2.8±2.1, with 2 dead patients (2.9%). At the end of the follow-up, 9 patients (13.2%) had not developed IgG antibodies against the virus.

In the group TNFi compared to the others TB, there was a lower percentage of patients who developed pneumonia and hospitalization, had a lower score on the WHO clinical progresión scale and a shorter hospitalization time, with all patients developing SARS-CoV-2 IgG after infection. No patient in this group died (table 2).

In the RTX group there was a higher percentage of SARS-CoV-2 infection (37.5%) than in others (17%); also, the patients with RTX had a higher percentage of development of pneumonia and hospital admission and had a higher score on the WHO scale, with no developing of SARS-CoV-2 IgG during follow-up in any of them. One patient in this group died (table 3).

Conclusion: In our rheumatic patients under treatment with TB there has been a different evolution of the SARS-CoV-2 infection, having been better and less severe in patients with TNFi and worse and more severe in patients with RTX.

Disclosure: S. Sánchez-Fernández, None; **L. Rojas Vargas**, None; **L. Del Olmo Pérez**, None; **P. García Morales**, None; **A. Alía Jiménez**, None; **J. Carrasco Fernández**, None; **S. Masegosa Casanova**, None.

Abstract Number: 1531

New-Onset IgG Autoantibodies in Hospitalized Patients with COVID-19

Sarah Chang[1], Allan Feng[1], Wenzhao Meng[2], **Sokratis Apostolidis**[2], Elisabeth Mack[3], Maja Artandi[1], Linda Barman[1], Kate Bennett[4], Saborni Chakraborty[1], Iris Chang[1], Peggie Cheung[1], Sharon Chinthrajah[1], Shaurya Dhingra[1], Evan Do[1], Amanda Finck[4], Andrew Gaano[4], Reinhard Gessner[5], Heather Giannini[4], Joyce Gonzalez[4], Sarah Greib[3], Margrit Gündisch[3], Alex Hsu[1], Alex Kuo[1], Monali Manohar[1], Rong Mao[1], Indira Neeli[6], Andreas Neubauer[3], Oluwatosin Oniyide[2], Abigail Powell[1], Rajan Puri[1], Harald Renz[3], Jeffrey Schapiro[7], Payton Weidenbacher[1], Rich Wittman[1], Neera Ahuja[1], Ho-Ryun Chung[3], Pras Jagannathan[1], Judith James[8], Peter Kim[1], Nuala Meyer[2], Kari Nadeau[1], Marko Radic[6], William Robinson[9], Upinder Singh[1], Taia Wang[1], John Wherry[4], Chrysanthi Skevaki[3], Eline Luning Prak[4] and Paul Utz[10], [1]Stanford, San Francisco, [2]University of Pennsylvania, Philadelphia, PA, [3]Marburg University, Marburg, Germany, [4]UPenn, Philadelphia, PA, [5]University of Marburg, Marburg, Germany, [6]UTHSC, Memphis, TN, [7]KPNC Regional Laboratory, Berkeley, [8]Oklahoma Medical Research Foundation, Oklahoma City, OK, [9]Stanford University, Palo Alto, CA, [10]Stanford University, Stanford, CA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Coronavirus Disease 2019 (COVID-19), caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), is associated with a wide range of clinical manifestations, including autoimmune features and autoantibody production. Autoantibody production has been implicated in other acute viral infections; however, the extent and breadth of autoantibodies present during acute COVID-19 has been less characterized.

Methods: We developed three different protein arrays to measure hallmark IgG autoantibodies associated with Connective Tissue Diseases (CTDs), Anti-Cytokine Antibodies (ACA), and anti-viral antibody responses in 147 hospitalized COVID-19 patients in three different centers. The CTD autoantibody array included prominent antigens (Figure 1a, left to right) targeted in systemic sclerosis, myositis and overlap syndromes, systemic lupus erythematosus and Sjögren's syndrome, gastrointestinal and endocrine autoimmune disorders, chromatin-associated antigens, and mis-

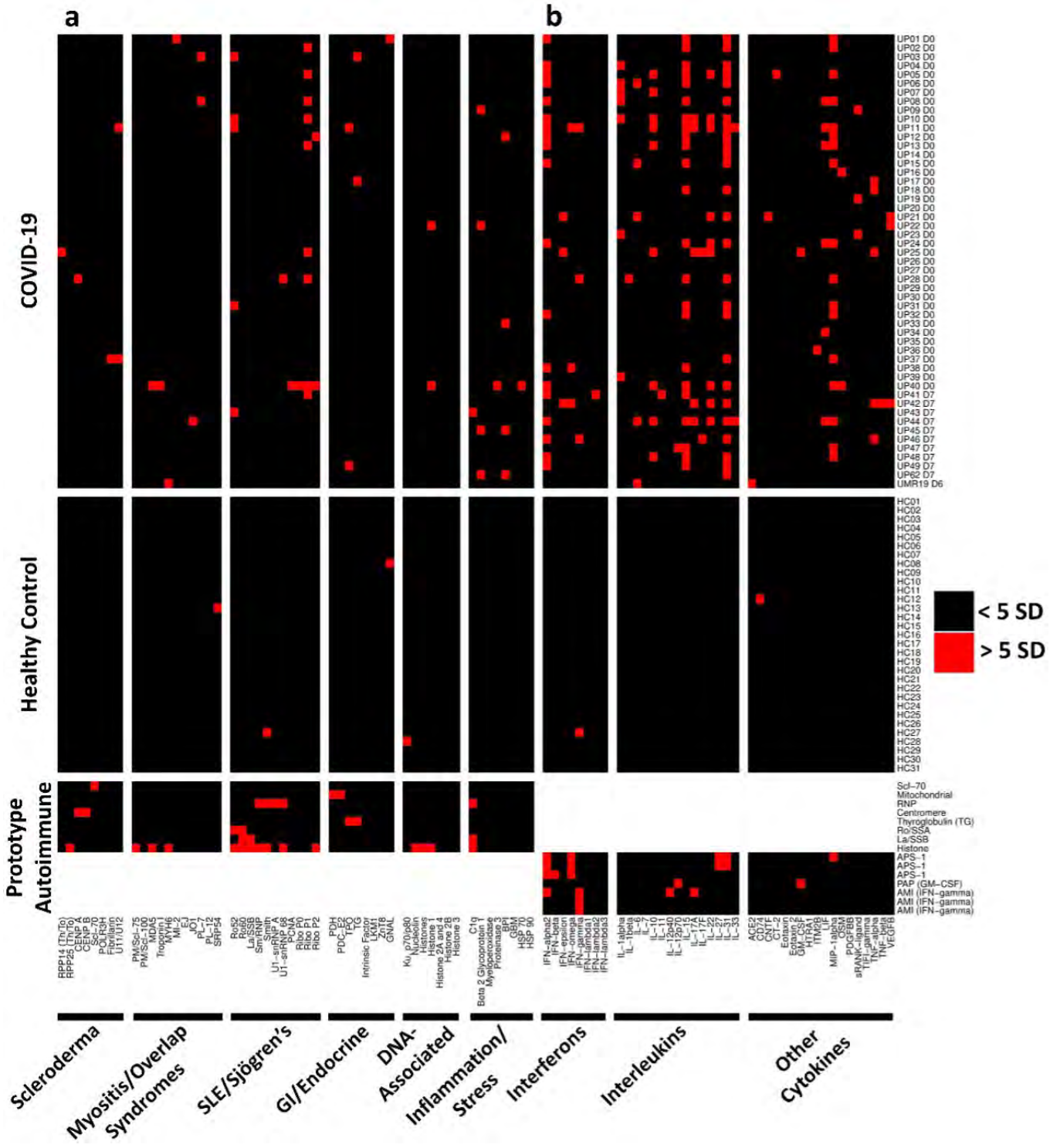

Figure 1.

cellaneous antigens, including proteins targeted in vasculitis. The ACA array included antigens represented within the interferon, interleukin or miscellaneous category (Figure 1b, left to right).

Results: Autoantibodies were identified in 49% of patients, but in < 15% of healthy controls. When present, autoantibodies largely targeted autoantigens associated with rare disorders such as myositis, systemic sclerosis and CTD overlap syndromes. Ribosomal P proteins (P0, P1, and P2) were most prominently targeted (10 of 50 patients, 20%), but were not found in any of the healthy controls. Patients with CTD autoantibodies tended to demonstrate one or a few specificities whereas ACA were more prevalent, and patients often had antibodies to multiple cytokines (Figure 1). Rare patients were identified with IgG antibodies against angiotensin converting enzyme-2 (ACE-2). Longitudinal analysis identified an expansion of autoantigen reactivity in a subset of patients at the second available time point (Figure 2). Focusing our analysis in patients early in their infection course based on spike/RBD antibody seroconversion between consecutive samples, we could identify a subset of CTD autoantibodies and ACAs that developed *de novo* following SARS-CoV-2 infection while others were transient (Figure 3. sequential samples in white boxes that demonstrated *de novo* development of CTD autoantibodies and ACAs). Autoantibodies tracked with longitudinal development of IgG antibodies that recognized SARS-CoV-2 structural proteins such as S1, S2, M, N and a subset of non-structural proteins, but not proteins from influenza, seasonal coronaviruses or other pathogenic viruses.

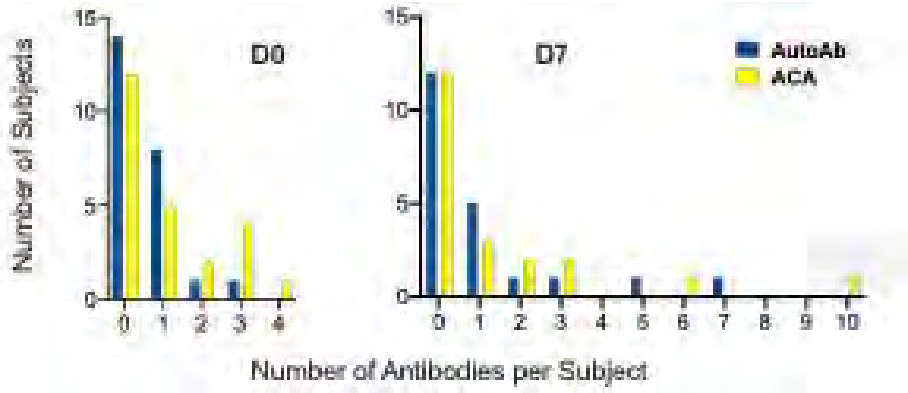

Figure 2.

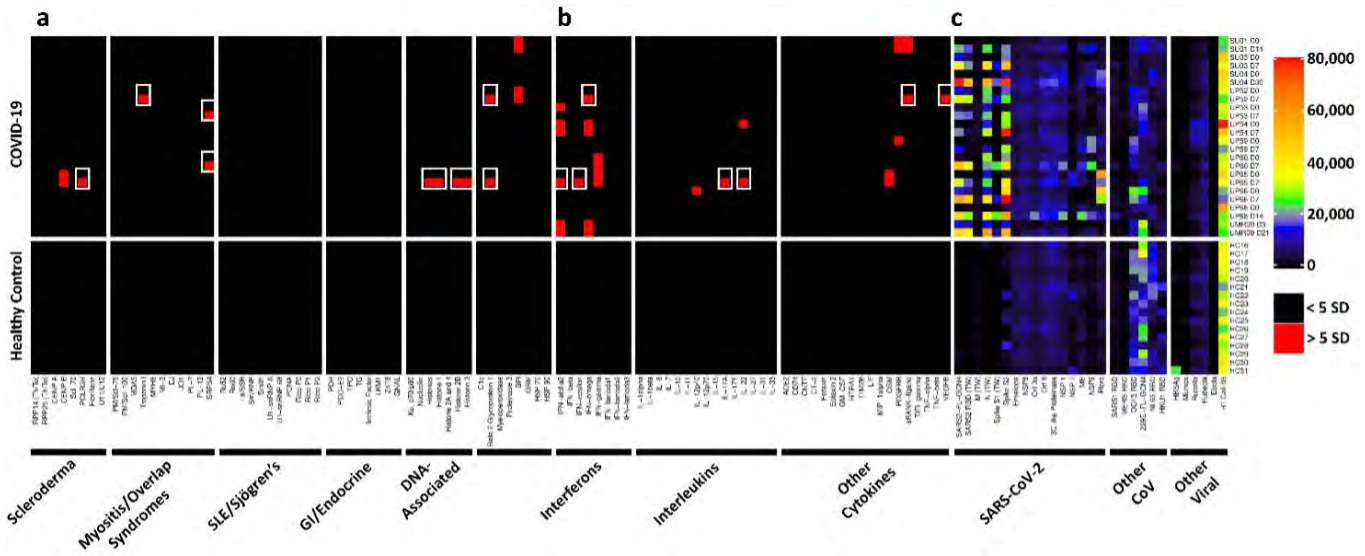

Figure 3.

Conclusion: We conclude that SARS-CoV-2 infection a) is accompanied by increased prevalence of CTD-related autoantibodies and ACAs, b) in a subset of patients causes development of new-onset IgG autoantibodies, and c) that autoantibody development is positively correlated with immune responses to SARS-CoV-2 proteins.

Disclosure: S. Chang, None; **A. Feng**, None; **W. Meng**, None; **S. Apostolidis**, None; **E. Mack**, Roche, 2; **M. Artandi**, None; **L. Barman**, None; **K. Bennett**, None; **S. Chakraborty**, None; **I. Chang**, None; **P. Cheung**, None; **S. Chinthrajah**, CoFAR, 5, Aimmune, 5, DBV Technologies, 5, Astellas, 5, Regeneron, 5, FARE, 5, Alladapt, 1, Genentech, 1, Novartis, 1, Sanofi, 1, Nutricia, 9; **S. Dhingra**, None; **E. Do**, None; **A. Finck**, None; **A. Gaano**, None; **R. Gessner**, None; **H. Giannini**, None; **J. Gonzalez**, None; **S. Greib**, None; **M. Gündisch**, None; **A. Hsu**, None; **A. Kuo**, None; **M. Manohar**, None; **R. Mao**, None; **I. Neeli**, None; **A. Neubauer**, None; **O. Oniyide**, None; **A. Powell**, None; **R. Puri**, None; **H. Renz**, None; **J. Schapiro**, None; **P. Weidenbacher**, None; **R. Wittman**, None; **N. Ahuja**, None; **H. Chung**, None; **P. Jagannathan**, None; **J. James**, Progentec Diagnostics, Inc., 2; **P. Kim**, None; **N. Meyer**, Athersys Inc, 5, Biomarck Inc, 5, Quantum Leap Healthcare Collaborative, 1; **K. Nadeau**, None; **M. Radic**, None; **W. Robinson**, None; **U. Singh**, None; **T. Wang**, None; **J. Wherry**, Merck, 1, 2, Elstar, 1, 2, Janssen, 1, 2, Related Sciences, 1, 2, Synthekine, 1, 2, Surface Oncology, 1, 2, 8, Arsenal Biosciences, 8, Roche/Genentech, 10; **C. Skevaki**, Hycor Biomedical, 2, 5, Thermo Fisher Scientific, 2, 5, Mead Johnson Nutrition, 5, Bencard Allergie, 2; **E. Luning Prak**, Janssen, 5, Roche Diagnostics, 2, 5, Enpicom, 2, Antibody Society, 1, Immune Epitope Database, 4, American Autoimmune Related Diseases Association, 1; **P. Utz**, None.

Abstract Number: 1532

Methotrexate Hampers Immunogenicity to BNT162b2 mRNA COVID-19 Vaccine in Immune-Mediated Inflammatory Disease

Rebecca Haberman[1], Ramin Herati[1], David Simon[2], marie Samanovic[1], Michael Tuen[1], Rebecca Blank[3], Sergei Koralov[1], Raja Atreya[4], Koray Tascilar[5], Joseph Allen[1], Rochelle Castillo[6], Amber Cornelius[1], Paula Rackoff[3], Gary Solomon[7], Samrachana Adhikari[1], Natalie Azar[8], Pamela Rosenthal[9], Peter Izmirly[10], Jonathan Samuels[11], Brian Golden[12], Soumya Reddy[9], Markus Neurath[4], Steven B. Abramson[10], Georg Schett[13], Mark Mulligan[1] and Jose Scher[10], [1]NYU Grossman School of Medicine, New York, NY, [2]Department of Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nrnberg, Erlangen, Germany, [3]New York University, New York, NY, [4]Deutsches Zentrum fur Immuntherapie, FAU Erlangen-Nuremberg and Universitatsklinikum Erlangen, Erlangen, Germany, [5]Friedrich Alexander University of Erlangen Nuremberg, Universitaetsklinikum Erlangen Department of Medicine-3 Rheumatology and Immunology, Erlangen, Germany, [6]NYU Langone Health, New York, NY, [7]NYU Langone School of Medicine, Hartsdale, NY, [8]NYU Langone, New York, NY, [9]NYU School of Medicine, New York, NY, [10]New York University School of Medicine, New York, NY, [11]NYU Langone, Rye Brook, NY, [12]NYU Langone Medical Center - NYU Hospital for Joint Diseases, New York, NY, [13]Universitätsklinikum Erlangen, Department of Internal Medicine 3 – Rheumatology and Immunology, Erlangen, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with immune mediated inflammatory disorders (IMIDs) have an inherently heightened susceptibility to infection and may be considered high risk for developing COVID-19. While data regarding the COVID-19 vaccine's immunogenicity in an immunocompetent adult population is rapidly emerging, the ability of IMID patients to adequately respond to these vaccines is not known. Here, we investigate the humoral and cellular immune response to mRNA COVID-19 vaccines in patients with IMIDs on immunomodulatory treatment

Table 1. Baseline characteristics and spike-specific SARS-CoV-2 antibody titers in the New York Cohort.

Characteristic	Healthy (n = 27)	IMID No MTX* (n = 61)	IMID Yes MTX* (n = 64)	p-value
Age- mean (range, SD)	50.3 (28-78, 12.9)	49.1 (24-79, 14.7)	56.5 (22-81, 13.7)	0.011
Female- n (%)	16 (59.3)	37 (60.7)	49 (76.6)	0.106
Race- n (%)				0.048
White	17 (63.0)	51 (83.6)	51 (79.7)	
Black	1 (3.7)	4 (6.6)	5 (7.8)	
Asian	9 (33.3)	5 (8.2)	6 (9.4)	
Other	0 (0.0)	1 (1.6)	2 (3.1)	
Hispanic ethnicity- n (%)	1 (3.7)	9 (14.8)	11 (17.2)	0.226
Primary IMID - n (%)				0.002
Psoriatic Arthritis or Ankylosing Spondylitis	--	40 (65.6)	22 (34.4)	
Rheumatoid Arthritis	--	16 (26.2)	35 (54.7)	
Other*	--	5 (8.2)	7 (10.9)	
Long term medication- n (%)				
Methotrexate	--	0 (0.0)	64 (100.0)	--
Tumor necrosis factor inhibitor	--	28 (45.9)	31 (48.4)	0.858
Other anti-cytokines/Janus kinase inhibitors	--	24 (39.3)	5 (7.8)	<0.001
Other oral immunomodulators	--	13 (21.3)	11 (17.2)	0.652
Methotrexate dose- mean (SD)	--	--	15.0 (4.9)	
COVID-19 infection prior to vaccination- n (%)	4 (14.8)	9 (14.8)	4 (6.3)	0.247
Days post 1st vaccination- mean (range, SD)	29.0 (4.6)	35.1 (8.1)	34.4 (8.4)	<0.001
Number receiving 2nd vaccination dose- n (%)	27 (100.0)	62 (100.0)	64 (100.0)	1.00
Adequate humoral response#- n (%)	26 (96.3)	56 (91.8)^	48 (75.0)	0.006
Spike-specific SARS-CoV-2 antibody titers - median (range)	107,518 (141-601,185)	130,051 (25-3,529,440)	57,106 (25-1,391,744)	0.167

*IMID denotes immune mediated inflammatory disease, MTX methotrexate.
*Vasculitis, dermatomyositis, adult onset stills disease, sarcoidosis, inflammatory bowel disease, and polymyalgia rheumatica.
#Adequate humoral response defined as greater than 5000 units.
^ Of note, three of the five patients who did not response in the IMID No MTX group were on rituximab.

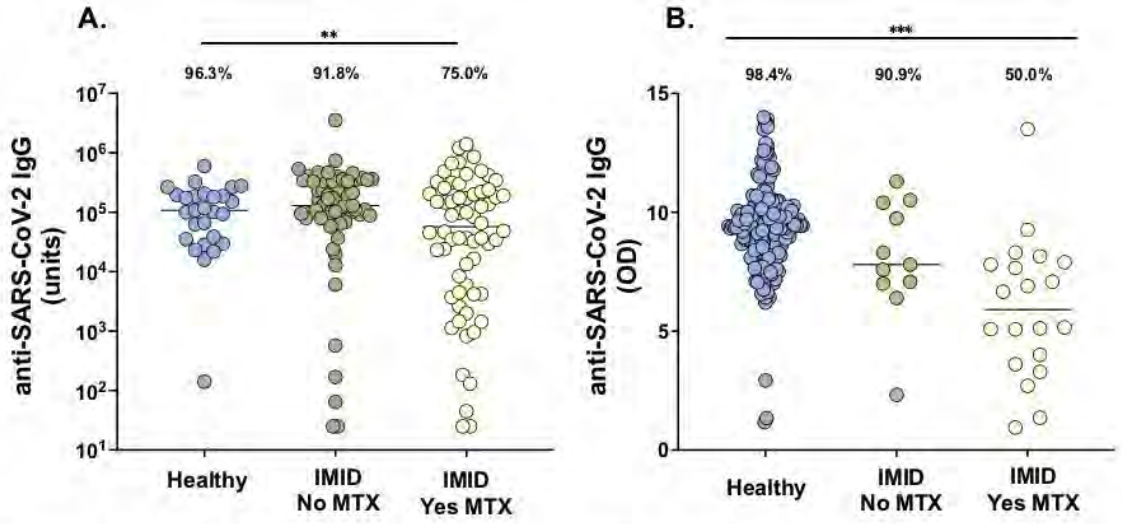

Figure 1. Anti-SARS-CoV-2 IgG levels in cohorts from New York City (A) and Erlangen (B) in healthy participants without immune-mediated inflammatory diseases (IMID; blue), IMID patients not receiving methotrexate (MTX; green), and IMID patients treated with MTX (yellow). Solid lines represent mean titer of each group. For the New York City cohort (A), adequate response is defined as greater than 5000 units and for the Erlangen cohort (B), adequate response is defined as greater than 5.7 (OD450nm), two standard deviations of the mean of controls. Percentages and group comparisons using chi squared test of independence reflect proportion of those achieving an adequate response within each group.
** $p < 0.01$
*** $p < .0001$

Methods: Patients with immune mediated inflammatory disorders (IMIDs) have an inherently heightened susceptibility to infection and may be considered high risk for developing COVID-19. While data regarding the COVID-19 vaccine's immunogenicity in an immunocompetent adult population is rapidly emerging, the ability of IMID patients to adequately respond to these vaccines is not known. Here, we investigate the humoral and cellular immune response to mRNA COVID-19 vaccines in patients with IMIDs on immunomodulatory treatment.

Results: The NY cohort baseline characteristics are found in Table 1. The Erlangen cohort consisted of 182 healthy subjects, 11 subjects with IMID receiving TNFi monotherapy, and 20 subjects with IMID on MTX monotherapy. In both cohorts, healthy individuals and those with IMID not on MTX were similar in age, while those IMID patients receiving MTX were generally older.

In the NY cohort, of the healthy participants, 96.3% demonstrated adequate humoral immune response. Patients with IMID not on MTX achieved a similar rate of high antibody response rate (91.8%), while those on MTX had a lower rate of adequate humoral response (75.0%) (Figure 1A). This remains true even after the exclusion of patients who had evidence of prior COVID-19 infection (*P*= 0.014). Of note, 3 out of the 4 IMID patients receiving rituximab did not produce an adequate response. Similarly, in the Erlangen validation cohort, 98.3% of healthy controls, 90.9% of patients with IMID receiving TNFi monotherapy, and 50.0% receiving MTX monotherapy achieved adequate immunogenicity (Figure 1B). These differences remain significant when combining the cohorts, using a stricter definition of adequate response, and in a subgroup analysis by age.

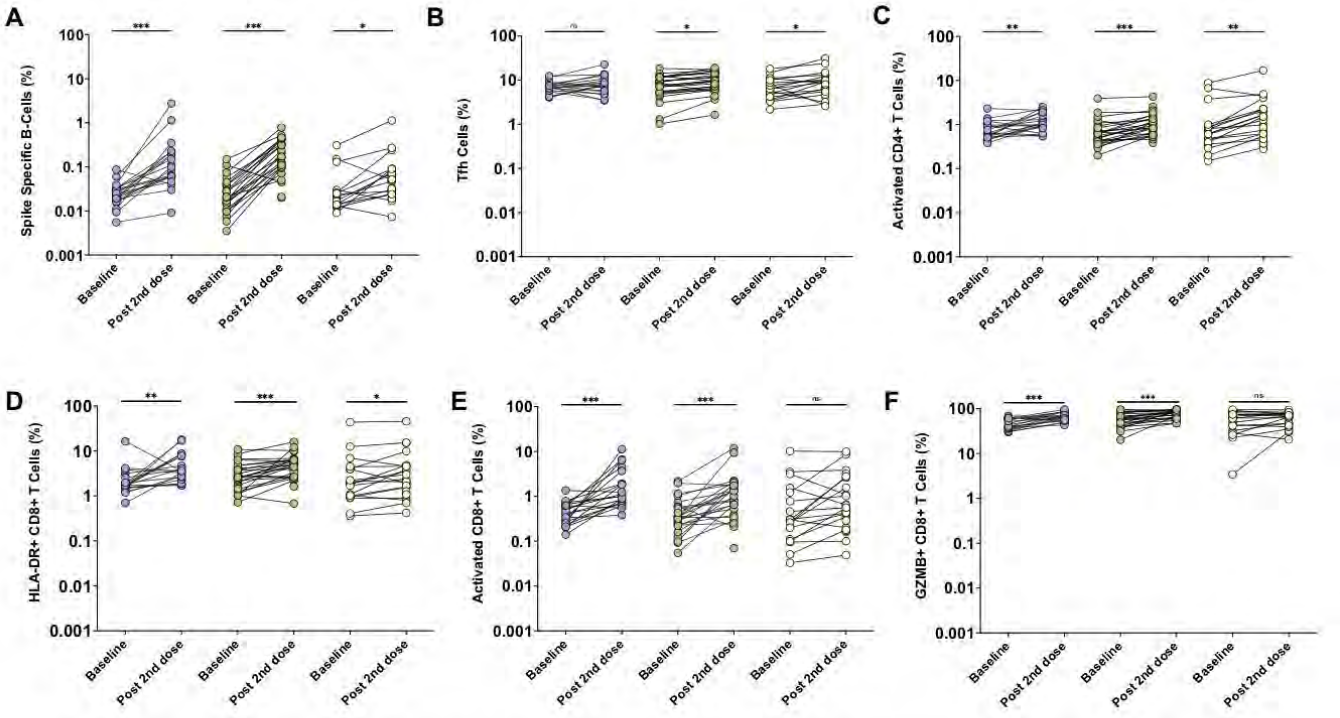

Figure 2. Immune cell populations from the New York City cohort by high-spectral flow in healthy controls (blue, n=20), patients with immune mediate inflammatory disease (IMID) not on methotrexate (MTX; green, n= 24), and patients with IMID on MTX (yellow, n=18), at baseline and post 2nd dose of BNT162b2 mRNA vaccine. Pre- and post- vaccination comparisons were performed using Wilcoxon Signed Rank tests. Y-axes presented as a logarithmic scale.
ns indicated no statistical significance
* p < .05
** p < .01
*** p< .0001

Cellular response was also analyzed in a subgroup of the NY cohort before and after second vaccination. Activated CD8+ T cells (CD8+ T cells expressing Ki67 and CD38) and the granzyme B-producing subset of these activated CD8+ T cells, were induced in immunocompetent adults and those with IMID not on MTX, but not induced in patients receiving MTX (Figure 2).

Conclusion: In two independent cohorts of IMID patients, MTX, a widely used immunomodulator for the treatment of several IMIDs, adversely affected humoral and cellular immune response to COVID-19 mRNA vaccines. Although precise cut offs for immunogenicity that correlate with vaccine efficacy are yet to be established, our findings suggest that different strategies may need to be explored in patients with IMID taking MTX to increase the chances of immunization efficacy against SARS-CoV-2, as has been demonstrated for other viral vaccines.

Disclosure: R. Haberman, Janssen, 1; **R. Herati**, CareDx, 5; **D. Simon**, None; **m. Samanovic**, None; **M. Tuen**, None; **R. Blank**, None; **S. Koralov**, None; **R. Atreya**, None; **K. Tascilar**, None; **J. Allen**, None; **R. Castillo**, None; **A. Cornelius**, None; **P. Rackoff**, None; **G. Solomon**, None; **S. Adhikari**, Johnson and Johnson, 5; **N. Azar**, None; **P. Rosenthal**, None; **P. Izmirly**, Momenta/Janssen, 1; **J. Samuels**, None; **B. Golden**, None; **S. Reddy**, Novartis, 1, Janssen, 1, UCB, 1, Pfizer, 1; **M. Neurath**, None; **S. Abramson**, None; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6; **M. Mulligan**, Meissa Vaccines, 1, Eli Lilly, 5, Pfizer, 5, Sanofi, 5; **J. Scher**, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, AbbVie, 2, Sanofi, 2, Kaleido, 2, UCB, 2.

Abstract Number: 1533

Comparison of Hospitalization and Mortality Rate in Patients with Different Rheumatic Diseases: A Brazilian Registry Cross-Sectional Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has brought uncertainties to the rheumatological practice, and despite the large number of publications to date, many questions remain unanswered. One of the unmet needs is

related to the differential risk among the immune mediated rheumatic diseases (IMRD), mainly related to the severity COVID-19 outcomes.

The aim of this study was to compare COVID-19 outcomes among patients with Systemic Lupus Erythematosus (SLE), Rheumatoid Arthritis (RA) and Spondyloarthritis (SpA) in a cohort of Brazilian patients and the main risk factors associated.

Methods: We performed a cross-sectional analysis from the ReumaCoV-Brasil registry comparing the moderate/ severe forms, including hospitalization, intensive care unit (ICU) admission, mechanical ventilation (MV) and death, in patients with RA, SLE and SpA and COVID-19. COVID-19 diagnosis was defined as clinical symptoms and lab test confirmation (RT-PCR and/ or serology against SARS-CoV-2). Demographic and clinical data, as well as details on COVID-19 management and endpoints were collected on the REDCap database. Specific and international classification criteria were used to define each IMRD of this study. This study was registered at the Brazilian Registry of Clinical Trials—REBEC, RBR-33YTQC.

Results: From May 20th, 2020 to Jan 24th, 2021, a total of 751 patients were included, of whom 317 with SLE (42.2%), 269 with RA (35.8%) and 165 with SpA (22.0%). Most of patients were female (81.6%) with mean age was 46.7 (13.5) years. The main comorbidity was hypertension (36.6%). Regarding the symptoms of COVID-19, patients with RA reported a higher frequency of arthralgia than the other groups (35.3% vs. 23.0% and 21%; p=0.001, respectively) and longer symptoms duration (15.5±10.7 days vs. 12.1±8.8 days and 13.1±9.9 days, p< 0.001, respectively). The COVID-19 endpoints were quite similar among groups, including hospitalization, ICU admission, MV and mortality rate (Table 1). Analyzing the whole group, older age was significantly associated with all outcomes, as well current oral corticosteroids dosage above 10mg/day and cardiopathy. On the other hand, absence of any comorbidity played a protective role for all the outcomes. After multiple adjustments, the risk factors associated with death were age (OR=1.03; 95%CI 1.004-1.09, p=0.027) and have no kidney disease (OR = 0.150; 95%CI 0.04-0.45, p=0.0001) (Figure 1).

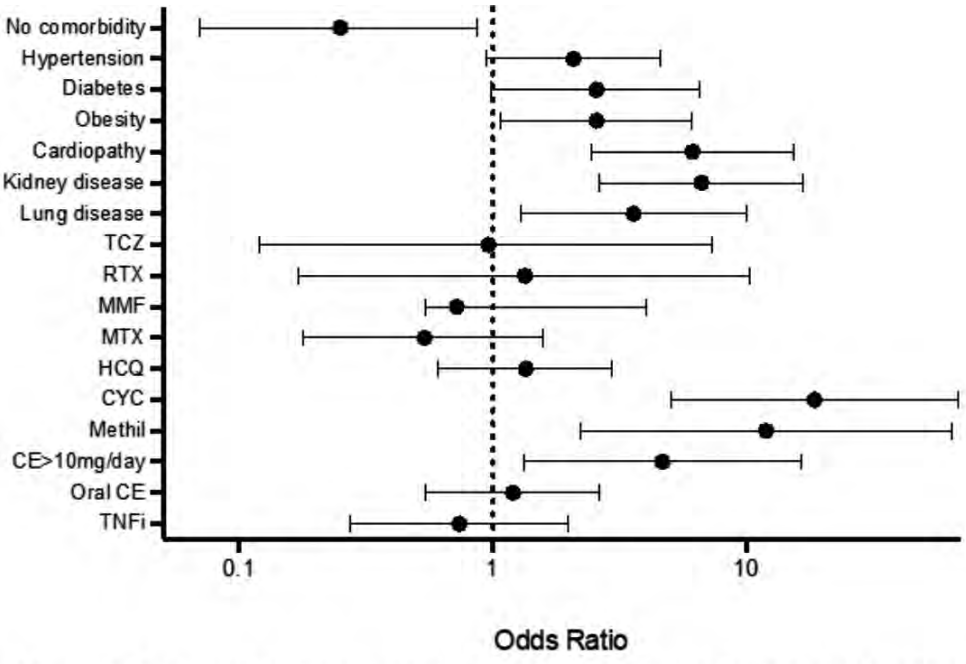

Figure 1: Odds ratio of death associated with comorbidities and medications used to treat rheumatic diseases

TNFi: Tumor necrosis factor inhibitor, TCZ: Tocilizumab, RTX: Rituximab, Methil: Methilprednisolone pulse therapy, CYC: Cyclophosphamide pulse therapy, MMF: Mycophenolate mofetil, MTX: Methotrexate, HCQ: hydroxychloroquine, CE: corticosteroid

Conclusion: Although no differences have been observed regarding COVID-19 outcomes among patients with SLE, RA and SpA, some risk factors associated with death, hospitalization, IUC admission and MV are directly related to DMARDs, particularly current corticosteroids. However, it is important to note that traditional risk factors are more related to unfavorable COVID-19 than underlying IMRD, especially older age and comorbidities.

Disclosure: C. Marques, None; **A. Reis**, None; **A. Kakehasi**, Abbvie, 6, UCB, 6, Pfizer, 6, Sandoz, 6, Boehinger, 6, Amgen, 6, Janssen, 6; **E. Neto**, GlaxoSmithKline (GSK), 6, Novartis, 6, BracePharma, 6; **M. Pinheiro**, AbbVie, 2, Eli Lilly, 2, Janssen, 2, Novartis, 2; **G. Pileggi**, None; **G. Ferreira**, None; **L. Mota**, Janssen, 1, 6, Pfizer, 6, UCB, 6, Abbvie, 6, Boehringer Ingelheim, 6, Sandoz, 6, Amgen, 6, GSK, 1, Lilly, 6; **O. Andre Monticielo**, GSK, 6, GSK, 2; **S. Ribeiro**, None; **F. Omura**, None; **A. Marinho**, None; **F. Ribeiro**, None; **L. Rocha Jr**, None; **A. Martins**, None; **M. Yazbek**, None; **M. Souza**, UCB, 6, AMGEN, 6, SANDOZ, 6, NOVARTIS, 6, ABBVIE, 6, JANSSEN, 6, PFIZER, 6; **N. Sacilotto**, None; **S. Shinjo**, None; **L. Valadares**, None; **A. Silva**, None; **D. de Brito**, None; **V. de Souza**, None; **C. Costa**, None; **S. Studart**, None; **A. Ximenes**, None; **R. Xavier**, Abbvie, 2, Janssen, 2, UCB, 2, Pfizer, 2, Novartis, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2.

Abstract Number: 1534

Severity Factors of Covid-19 Infection in Rheumatic Immune-mediated Inflammatory Diseases: Study in a Single University Hospital

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Severity factors for COVID-19 have been widely studied in the general population. However, the severity factors and characteristics of COVID-19 in patients with rheumatic immune-mediated inflammatory diseases (R-IMID) remain unknown. Our aim was to analyze the severity factors of COVID-19 infection in R-IMID.

Methods: Cross-sectional study in a single University Hospital. We included all consecutive patients with a diagnosis of a R-IMID and a positive test for COVID-19 up to March 31st, 2021. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2. Medical records of 25,367 patients that suffered COVID-19 in our region, and 7,218 with R-IMID from our hospital were reviewed. COVID-19 severity was divided into mild, moderate, severe and critical according to the United States National Institute of Health (NIH) COVID-19 guidelines. Mild/moderate COVID19 was compared to critical.

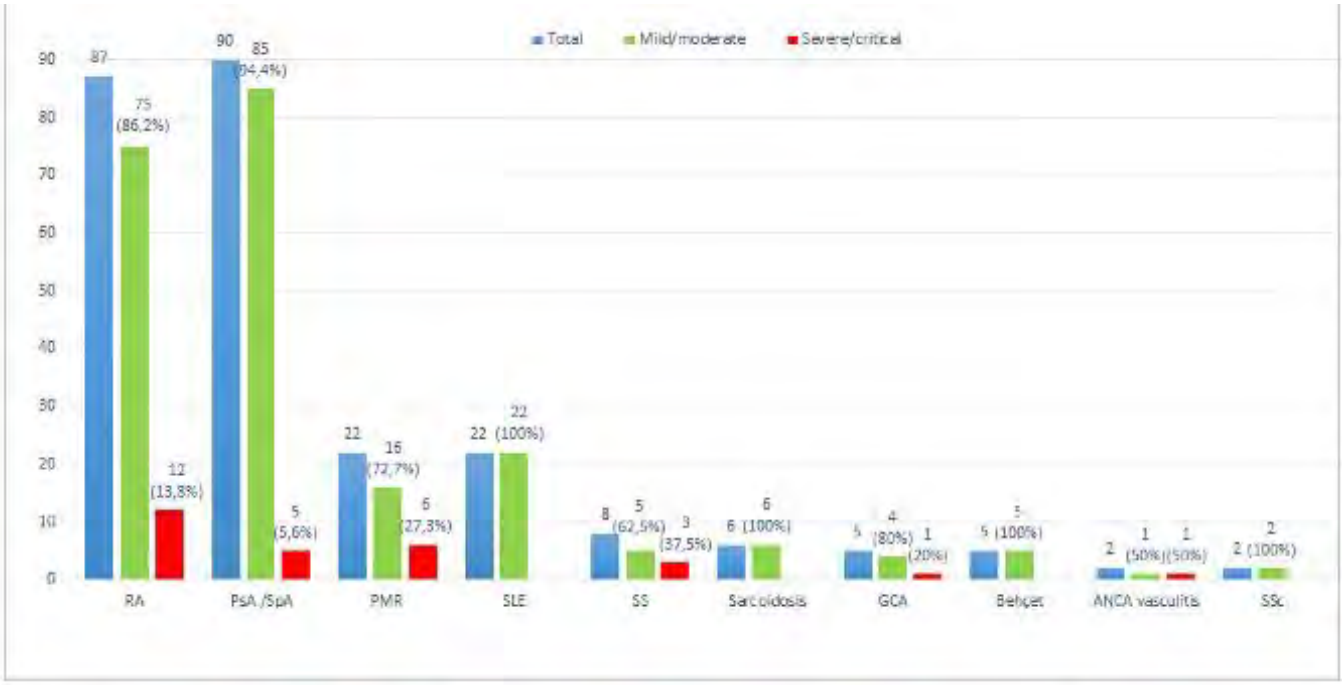
Table. Clinical severity of 274 with R-IMID diagnosed with COVID-19 (analytical findings and Immunosuppressants are at COVID diagnosis)

	Overall N= 274	Mild/Moderate N= 245	Severe/Critical N= 29	Mild/moderate vs severe/critical p
Comorbidities (n,%)				
Hypertension	119 (43.4)	96 (39.2)	23 (79.3)	**0.0001***
Dyslipidemia	119 (43.4)	100 (40.8)	19 (65.5)	**0.02***
Age higher than 65 years	100 (36.5)	75 (30.6)	25 (86.2)	**0.0001***
Obesity	49 (17.9)	42 (17.1)	7 (24.1)	0.5
Diabetes mellitus	36 (13.1)	29 (11.8)	7 (24.1)	0.1
Pulmonary diseases	29 (10.6)	17 (6.9)	12 (41.4)	**0.0001***
Cardiovascular diseases	45 (16.4)	34 (13.9)	11 (37.9)	**0.002***
Chronic kidney diseases	27 (9.9)	18 (7.3)	9 (31)	**0.0002***
Analytical findings (median±IQR)				
Creatinine (mg/dl)	0.91±0.4	0.89±0.38	1.31±0.93	**0.005***
Platelets (x103 /µL)	179±78	205±91	140±152	0.379
Lymphocytes (x103 /µL)	1±1	1.2±0.5	0.6±0.4	**0.007***
D-Dimer (ng/mL)	999±1256	701±753	1333±1578	0.110
Immunosuppressants, n(%)				
Oral GC	77 (28.1)	71 (29)	6 (20.7)	0.47
HCQ	50 (18.2)	47 (19.2)	3 (10.3)	0.36
MTX/Other cDMARDs	62/23 (22.6/8.4)	58/21 (23.7/8.6)	4/2 (13.8/6.9)	0.33/0.96
AZA	6 (2.2)	6 (2.4)	0	0.88
MMF	1 (0.4)	1 (0.4)	0	0.74
TNF inhibitors	31 (11.3)	30 (12.2)	1 (3.4)	0.29
RTX	8 (2.9)	4 (1.6)	4 (13.8)	**0.002***
Other bDMARDs	19 (6.9)	16 (6.5)	3 (10.3)	0.71
JAKINIB	6 (2.2)	5 (2)	1 (3.4)	0.86
COVID-19 therapy, n (%)				
No treatment	208 (75.9)	201 (82)	7 (24.1)	**0.0001***
HCQ	37 (13.5)	25 (10.2)	12 (41.4)	**0.0001***
Systemic GC	30 (10.9)	18 (7.3)	12 (41.4)	**0.0001***
Antivirals	21 (7.7)	13 (5.3)	8 (27.6)	**0.0001***
Anti-IL1/anti-IL6 agents	4 (1.5)	0	4 (13.8)	**0.0001***

AZA: azathioprine, GC: Glucocorticoids, HCQ: Hydroxychloroquine, MM: mycophenolate mofetil. MTX: Methotrexate, RTX: Rituximab *P <0.05

Results: We included 274 patients (185 women/89 men), mean age 59.1±18 years. Most cases were mild to moderate (n=245). The remaining patients presented severe (n=8) or critical (n=21) disease. 17 (6.2%) presented a fatal outcome.

More frequent R-IMID were: Rheumatoid arthritis (RA) (n=87, 31.8%), Axial spondyloarthritis/ Psoriatic arthritis (SpA/PsA) (n=90, 32.8%), Polymyalgia Rheumatica (PMR) (n=22, 8%) and Systemic Lupus Erythematosus (SLE) (n=22, 8%) (**FIGURE**).



GCA: Giant cell arteritis, SLE: Systemic lupus erithematosus, SpA: Axial spondyloarthritis, SS: Sjögren's syndrome, SSc: Systemic scleroderma, PsA: Psoriatic arthritis, RA: Rheumatoid arthritis

Figure. Severity of COVID-19 according to R-IMID. Data between parentheses are the percentage of patients with mild/moderate or severe/critical disease.

Main comorbidities were hypertension (n=119, 43.4%), dyslipidemia (n=119, 43.4%), age higher than 65 years old (n=100, 36.5%), obesity (n=49, 17.9%), cardiovascular disease (n=45, 16.4%), diabetes mellitus (n=36, 13.1%), chronic pulmonary disease (n=29, 10.6%) and chronic kidney disease (n=27, 9.9%).

Comorbidities in R-IMID associated with severe to critical disease ($p< 0.05$) were hypertension, dyslipidemia, age higher than 65 years, previous cardiovascular, kidney or lung disease and PMR.

Rituximab was the only treatment associated with increased severity of COVID-19 ($p <0.05$). Severe/critical compared with mild/moderate disease showed significantly higher levels of serum creatinine, and lower levels of lymphocytes and received more frequently systemic glucocorticoids **(TABLE)**. Tocilizumab and Anakinra were used only in critical patients, 2 cases each.

Conclusion: Although most cases of COVID-19 are mild, it can be a life-threatening disease in patients with R-IMID. Hypertension, dyslipidemia, older age, previous cardiovascular, kidney or lung disease, the use of rituximab and PMR were associated with critical disease.

Disclosure: D. Martinez-Lopez, None; **D. Prieto-Peña**, None; **L. Sánchez-Bilbao**, None; **C. Álvarez-Reguera**, None; **A. Herrero-Morant**, None; **F. Benavides-Villanueva**, None; **C. Corrales-Selaya**, None; **M. Trigueros-Vazquez**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6; **R. Wallmann**, None.

Abstract Number: 1535

Low Incidence and Transient Elevation of Autoantibodies Post mRNA COVID-19 Vaccination

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Recent studies have shown high rates of autoantibody production in patients hospitalized with COVID-19, including antinuclear antibodies (ANA) and antibodies associated with antiphospholipid syndrome. However, the long-term implications of these phenomena remain unknown. Similarly, whether vaccination against SARS-CoV-2 with novel mRNA constructs may lead to an increase in autoantibody production (or clinically evident autoimmunity) is yet to be elucidated. Here, we describe the incidence of ANA seroconversion in a cohort of patients with immune-mediated inflammatory diseases (IMID) after mRNA COVID-19 vaccination.

Methods: As part of the NYU Langone SAGA (Serologic Testing and Genomic Analysis of Autoimmune, Immune-mediated, and Rheumatic patients with COVID-19) cohort, 72 subjects (n=27 healthy controls and n=45 patients with IMID) were assessed for autoantibody production via serum ELISA. Time-points included pre/post COVID-19 infection as well as pre/post mRNA COVID-19 vaccination with time points up to 3 months post initial dose of mRNA vaccine. Spike IgG antibody titers were also assessed by in-house laboratory-based ELISA.

Results: In the SAGA cohort of healthy controls and IMID patients, 12 participants had documented prior COVID-19 infection. Of these, one patient with IMID converted from a negative to a positive ANA. Sixty participants, none of whom had previous COVID-19 infection, completed their 2-dose mRNA COVID-19 vaccination series. The overall incidence of *de novo* ANA positivity in these patients at 4-5 weeks post vaccination was 5% (3/60, 1 healthy control and 2 IMID). In the 3 participants who demonstrated ANA positivity, the healthy control was also Scl-70 positive on an extended autoantibody ELISA panel whereas the other 2 participants were negative for dsDNA, Smith, SS-A, SS-B, Scl-70, CENP, and Jo-1. Further, ANA antibodies were no longer present at the 3-month time point. Four patients (one of whom developed positive ANA) reported a flare of their disease after vaccination. No participant developed clinical manifestations of new autoimmune disease. There was no difference in the level of the SARS-CoV-2 spike IgG antibody response between those who transiently seroconverted after vaccination and those who did not ($p = 0.496$).

Conclusion: In a cohort of healthy controls and patients with IMID, the rate of ANA positivity after COVID-19 mRNA vaccination was low. In patients who developed a positive ANA, this finding was transient, resolving by the 3-month time point. While our findings are reassuring regarding the risk of developing autoimmunity after vaccination, the sample size is small and follow up is limited. Larger, long-term studies are critically needed to better characterize possible autoimmune manifestations after vaccination.

Disclosure: R. Blank, None; **R. Haberman**, Janssen, 1; **R. Castillo**, None; **m. Samanovic**, None; **P. Vasudevanpillai Girija**, None; **P. Rackoff**, None; **G. Solomon**, None; **N. Azar**, None; **P. Rosenthal**, None; **P. Izmirly**, Momenta/Janssen, 1; **J. Samuels**, None; **B. Golden**, None; **S. Reddy**, Novartis, 1, Janssen, 1, UCB, 1, Pfizer, 1; **S. Abramson**, None; **M. Mulligan**, Meissa Vaccines, 1, Eli Lilly, 5, Pfizer, 5, Sanofi, 5; **J. Scher**, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, AbbVie, 2, Sanofi, 2, Kaleido, 2, UCB, 2.

Abstract Number: 1536

Acceptability of Vaccines Against COVID-19 and Other Preventable Infections Among Patients with Rheumatic Disease

Sara Tedeschi[1], Jack Ellrodt[1], Jacklyn Stratton[1], Leah Santacroce[1], Paulette Chandler[1], Ellen Gravallese[2] and Daniel Solomon[3], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA, [3]Brigham and Women's Hospital, Newton, MA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Vaccination against preventable infections is widely recommended for patients with systemic rheumatic disease. The COVID-19 pandemic has highlighted variability in attitudes toward vaccination, particularly with the use of novel vaccine platforms. We studied attitudes toward vaccination against COVID-19 and other preventable infections among patients with systemic rheumatic disease, and compared these against the general population.

Methods: We invited a convenience sample of patients treated for systemic rheumatic disease at an academic medical center in MA to complete a secure web-based survey or paper survey in English or Spanish, 12/2020-4/2021. The survey covered self-reported race and ethnicity, socioeconomic status, rheumatic disease diagnoses and treatments, comorbidities relevant to risk of severe COVID-19, prior infections, prior vaccination, COVID-19 infection, and vaccination against COVID-19. We included survey questions used in the nationwide Harris Poll (2/2021, n=2043 respondents), allowing comparison of responses to the general population. Response frequencies were summarized with descriptive statistics and compared using Chi square tests.

Results: Of 243 participants (25% response rate), mean age was 56 years, 82% were women, 67% White, 16% Asian, 10% Black; 13% identified as Latinx (Table 1). Rheumatoid arthritis (50%), systemic lupus erythematosus (28%), and psoriatic arthritis (13%) were the most common diagnoses. 88% were currently taking an immunomodulator. 30% had previously been hospitalized for any type of infection. 76% worried a lot or somewhat about contracting COVID-19. Attitudes toward vaccination were very favorable, with 92% having received a flu shot in the past year and 84% desiring a COVID-19 vaccine as soon as possible compared to 42% of Harris Poll respondents ($p< 0.001$). Intent to receive a COVID-19 vaccine (yes vs. no/not sure) did not differ by immunomodulator use ($p=0.99$), race ($p=0.16$), or Latinx ethnicity ($p=0.10$) (Table 2). Physician recommendation to receive a vaccine (90%) and desire to avoid infection (70%) were the most common reasons for previously receiving vaccines. Among the 11% of participants that had declined a vaccine in the past, reasons included concerns about possible flare of rheumatic disease, concerns about safety, not believing in getting vaccines, previous adverse reaction to vaccines, and allergy.

Table 1. Characteristics of 243 survey respondents	
Age in years	56.0 (14.5)
Gender	
Man	18.1
Woman	81.5
Transgender	0.4
Race	
White	66.7
Black	10.3
Asian	15.6
Other or choose not to answer	9.5
Latinx[+]	12.5
Primary language	
English	91.8
Spanish	6.6
Other	1.7
Highest level of education[+]	
High school graduate or less	7.4
Some college	16.5
College graduate	34.3
Post-college degree	41.7
Systemic rheumatic disease	
Rheumatoid arthritis	49.8
Systemic lupus erythematosus	27.6
Psoriatic arthritis	13.2
Other**	9.5
Rheumatic disease treatment*	
None	12.4
Conventional synthetic DMARD	60.1
TNF inhibitor	18.5
Other biologic	14.0
JAK inhibitor	9.9
Glucocorticoid	16.5
Self-reported comorbidities	
Cancer	11.9
Lung disease	20.2
Chronic kidney disease	9.9
Coronary artery disease	4.1
Diabetes	9.5
Heart failure	2.9
Hypertension	34.6
Obesity	15.2
Stroke	5.8

Presented as mean (SD) or percent
[+]Data missing for Latinx (n=3), education (n=1)
*Categories not mutually exclusive
** Inflammatory myositis (n=7), scleroderma (n=7), ankylosing spondylitis (n=4), giant cell arteritis (n=4), or polymyalgia rheumatica (n=1)

Conclusion: Vaccine acceptability, including toward COVID-19 vaccines, was high among this population of systemic rheumatic disease patients seen at an academic medical center cohort. Physician recommendation is a key factor for vaccine uptake.

Table 2. Vaccination history and attitudes toward vaccination

	All (N=243)	White (n=159)	Asian (n=38)	Black (n=24)	Latinx (n=30)
Vaccines in general					
Where would you consider yourself on the following spectrum regarding vaccines in general?					
I am strongly against vaccines	0	0	0	0	0
I am pretty much against vaccines	1.7	1.9	2.6	0	0
Neutral	7.9	4.4	7.9	26.1	13.8
I'm pretty much in favor	17.8	17.6	10.5	34.8	17.2
I am very in favor of vaccines	72.7	76.1	79.0	39.1	69.0
Received flu shot last year	92.4	96.1	94.7	82.6	70.0
Previous vaccines (ever)					
Flu	97.5	97.5	100.0	95.8	96.7
Pneumonia	71.2	74.8	68.4	70.8	50.0
Shingles	48.2	50.9	36.8	50.0	36.7
Tdap	51.9	53.5	65.8	41.7	30.0
Yellow fever	7.0	7.5	2.6	8.3	10.0
Hepatitis A	19.8	18.2	31.6	12.5	13.3
Hepatitis B	30.5	30.8	34.2	25.0	20.0
HPV	10.7	10.7	21.1	0	10.0
Reasons for receiving previous vaccines					
Doctor advised me to get it	89.7	93.1	89.5	87.5	80.0
Important for community health	45.3	47.2	57.9	29.2	20.0
Easy to do	36.6	40.3	47.4	8.3	16.7
Wanted to avoid infection	70.4	76.7	76.3	41.7	50.0
International travel	18.1	16.4	21.1	20.8	23.3
Cost covered by health insurance	20.6	17.6	36.8	8.3	13.3
Family encouraged me to get it	7.0	5.7	15.8	4.2	0
Ever declined a vaccine that your doctor recommended for you to get	10.7	7.6	10.5	33.3	10.0
COVID-19 vaccine[+]					
When there is a coronavirus vaccine, will you get vaccinated?					
Yes	91.4	93.1	92.1	79.2	83.3
No	1.7	1.3	2.6	4.2	3.3
Not sure	7.0	5.7	5.3	16.7	13.3
When would you want to get the coronavirus vaccine?					
As soon as possible (ASAP)	84.1	87.3	78.4	69.6	82.8
Within the 1st year but not ASAP	10.0	7.0	21.6	17.4	3.5
Wait until other people have been getting it for at least 1 year	5.9	5.7	0	13.0	13.8
Features of a coronavirus vaccine rated "important" or "very important"					
Safety	95.4	96.2	97.4	91.7	93.1
How well it works	94.9	96.2	94.6	90.9	92.6
Cost to me	27.7	21.8	32.4	47.8	46.2
If I have to stop my medicines	61.5	60.1	56.8	73.9	64.0
Only one (vs. several) dose required	24.7	22.4	8.1	56.5	30.8

Presented as percentages. Data missing for general attitude toward vaccines (n=1), flu shot last year (n=5), timing of COVID vaccine (n=4), vaccine safety (n=2), how well it works (n=7), cost (n=8), stopping medications (n=12), number of doses (n=8)

[+] Survey distribution began before any COVID-19 vaccine had received FDA Emergency Use Authorization

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Abstract Number: 1537

Impact of COVID-19 Infection on Patient-Reported Outcomes in Rheumatic Disease Patients: A Cross Sectional Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The persistence of symptoms following COVID 19 is an area of great interest yet remains poorly understood. Long COVID symptoms are dominated by fatigue (58%) and musculoskeletal pain (19%)1 and thus, of great interest, to know whether patients with rheumatic diseases will experience similar or worse outcomes than the general population. Prior analysis in the current COVID-19 literature lack pre-COVID infection data on these symptoms. This study provides a unique opportunity to examine the change in patient-reported outcomes (PROs) following COVID-19.

Methods: Rheumatic disease patients were evaluated for routine care and completed PROs in 2019 and following documented COVID-19 were included. Patients completed NIH's Patient Reported Outcomes Measurement Information System (PROMIS) Fatigue, Physical Function, Pain Interference, Global Health (mental and physical function), and PHQ-2 or 9 depression scale. Data on potential predictors of worsening PROs were collected including severity of COVID-19 infection, index diagnosis, concomitant therapies and associated high risk comorbidities. Change in PROs was evaluated with paired t-test. Predictors of patients who meaningfully worsened on PROs (≥5 T-score points) following COVID-19 were identified through multivariable logistic regression models.

Results: There were 264 rheumatic disease patients (57yrs (+/-12.9), 203 female (77%)) seen in the outpatient department with 222 (84.1%) patients had a diagnosis of immune mediated disease by a board certified rheumatologist and 42 (15.9%) patients had a non immune mediated disease. Regarding COVID-19 outcomes, 43 (16.3%) were

Table 1. Changes in Patient-Reported Outcomes from Pre- to Post-COVID-19

	PROMIS Fatigue†	PROMIS Pain Interference†	PROMIS Physical Function	PROMIS Global Mental Health	PROMIS Global Physical Health
Number with pre- and post-COVID PRO	N=244	N=243	N=244	N=132	N=139
Pre-COVID score, mean (SD)	53.8 (10.7)	56.7 (9.7)	43.3 (9.4)	47.6 (8.7)	44.7 (9.1)
Days between PRO and COVID-19, mean (SD)	196 (155)	192 (154)	195 (155)	217 (143)	227 (147)
Post-COVID score, mean (SD)	55.2 (10.9)	57.7 (9.7)	42.9 (8.7)	46.7 (9.0)	44.3 (9.9)
Days between COVID-19 and PRO, mean (SD)	87 (65)	88 (67)	87 (65)	93 (70)	92 (68)
Change in score, mean (SD)	+1.32 (7.78)	+0.97 (6.82)	-0.39 (6.79)	-0.84 (5.11)	-0.38 (6.35)
P-value for change*	0.008	0.027	0.37	0.060	0.48
Clinically meaningful worsening‡, n (%)	**62 (25.4%)**	**57 (23.5%)**	**42 (17.2%)**	**24 (18.2%)**	**31 (22.3%)**

*p-value based on paired t-test for change; †Higher scores indicate worse symptoms and positive change indicates worsening; For the other domains, lower scores indicate worse symptoms and negative change indicates worsening; ‡Clinically meaningful worsening defined as 5+ T-score points; SD = standard deviation

hospitalized with 3(1.1%) requiring mechanical ventilation and 10 (3.8%) with pneumonia. Average length of stay was 6 (3,6) days and one patient died 1 (0.4%). PROs were completed a median of 6.5 months prior to COVID, and again median of 3 mo following COVID-19. Patient T-scores worsened on all PROs, but were only significantly worse on the domains of fatigue (mean±sd, 1.32±7.78) and pain interference (0.97±6.82). (Table 1) Meaningful worsening (≥5+ T-score) occurred for 25.4% of patients on PROMIS Fatigue, 23.5% on PROMIS Pain Interference, 17.2% on PROMS Physical Function, 18.2% on Global Mental Health, and 22.3% on Global Physical Health.

Eighty-seven patients completed the PHQ-2 or 9 prior to and following COVID-19. Eighteen patients (20.7%) had moderate/severe depressive symptoms and following COVID-19, depressive symptoms were indicated in only 10 (11.5%), p=.033. A reduction in Global Mental Health was experienced overall but was not significant. There were few predictors of worsening PROs and having better pre-COVID-19 PROs was the most predictive indicator of worsening.

Conclusion: Data from our rheumatology clinic where pre-infection PROs were available demonstrated a surprising modest effect of COVID including relevant domains of pain interference and fatigue compared to baseline. While further analysis is necessary including comparisons to non-rheumatic disease patients, these data suggest that in general patients with rheumatic disease make reasonable recovery following COVID-19 and may not have increased susceptibility to Long COVID-19 sequelae.

1. Lopez-Leon S, Wegman-Ostrosky T, Perelman C, Sepulveda R, Rebolledo PA, Cuapio A, Villapol S. More than 50 Long-term effects of COVID-19: a systematic review and meta-analysis. medRxiv [Preprint]. 2021 Jan 30:2021.01.27.21250617. doi: 10.1101/2021.01.27.21250617. PMID: 33532785; PMCID: PMC7852236.

Disclosure: E. Husni, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2; **C. Calabrese**, Sanofi-Regeneron, 2, 6; **B. Lapin**, None; **E. Kirchner**, Sanofi, 12, Speaker's training, did not speak for company., Novartis, 1, Janssen, 1; **L. Calabrese**, Lilly, 2, BMS, 2, Genentech, 2.

Abstract Number: 1538

Adverse Events After SARS-CoV-2 Vaccination Among Rheumatology Outpatients in New York City

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Vaccination against SARS-CoV-2 is important for patients with systemic rheumatic diseases (SRDs), who may be at increased risk of severe outcomes post-COVID-19 infection. However, as patients with SRDs were not included in vaccine trials, limited data exist on post-vaccine adverse events in the SRD population. We evaluated the prevalence of adverse events post- SARS-CoV-2 vaccination in rheumatology outpatients from New York City.

Methods: We emailed a secure web-based survey on March 5, 2021 to 7,505 patients aged ≥18 years evaluated at least once between 2018-2020 by a rheumatologist at a single Rheumatology Division in New York City. We included

individuals who received at least one vaccine dose. ICD-10-CM codes were used to identify SRD diagnoses. We collected data on sociodemographics, medical comorbidities, and medication use at time of vaccination. Patients were asked to report adverse events defined as "symptoms within 1 week" of receiving each vaccine dose. Patients were asked to report symptoms they did not attribute to an SRD flares, which were reported separately.

Results: As of May 17, 2021, 1852 respondents (24.7% response rate) had received at least one COVID-19 vaccine dose (53.9% Pfizer vaccine, 44.4% Moderna, 1.4% Janssen, 0.3% Astrazeneca). Mean age of respondents was 62.8 [14.2] years; 80% female; 88.6% White; 4.2% Hispanic/Latinx ethnicity). 1173 patients received two vaccine doses and 679 patients received only the first dose. 1076 patients (58.1%) met an ICD-10-CM algorithm for an SRD. Immunosuppressive or immunomodulatory medications were used by 47.6% of individuals at the time of vaccination. Adverse events at the first or second vaccine dose were reported by 1357 (73.3%) individuals, and most commonly included pain at injection site (45.3%), fatigue (38.8%), headache (26.2%), muscle aches (23.1%), sore shoulder (22.2%). 14.4% of respondents reported only local injection site reactions (i.e. pain, swelling, redness, rash) at either vaccine dose. Severe symptoms such as throat closing, wheezing, fainting, chest pain, difficulty breathing, bleeding, and swelling of the eyes, lips or other parts of body were reported by less than 1%. Medications to prevent vaccine side effects were used by 8.4% of patients (Table); after vaccination, only 2 patients (0.1%) required use

Table 1. Baseline Characteristics of 1852 Rheumatology Outpatients Receiving At Least One COVID-19 Vaccination	
Age, Mean (SD)	62.8 (14.2)
Female Sex	1481 (80.0%)
Race	
• American Indian/Alaskan Native/ Native Hawaiian/Other	11 (0.6%)
• Asian/ Indian Subcontinent	57 (3.1%)
• Black	57 (3.1%)
• White	1640 (88.6%)
• Missing	87 (4.7%)
Ethnicity	
• Hispanic/Latinx	78 (4.2%)
• Not hispanic/Latinx	1681 (90.8%)
• Missing	93 (5.0%)
Body Mass Index	
• <25	877 (47.4%)
• 25-29	549 (29.6%)
• 30+	412 (22.2%)
• missing	14 (0.8%)
General Medical Comorbidities*	
• 0	849 (45.8%)
• 1	665 (35.9%)
• 2 or more	338 (18.3%)
Smoking Status	
• Never	1156 (62.4%)
• Ever	541 (29.2%)
• Missing	
Systemic Rheumatic Disease History	1076 (58.1%)
Vaccine Manufacturer	
• Pfizer/BioNTech	999 (53.9%)
• Moderna	822 (44.4%)
• Janssen	26 (1.4%)
• Astrazeneca/Other	5 (0.3%)
Immunomodulatory or Immunosuppressive Medication Use at time of Vaccination	881 (47.6%)
**Comorbidities include any of the following identified by the Centers for Disease Control and Prevention in 2/2021 as being most relevant for COVID-19 risk: Asthma or lung disease, Cancer, Chronic Kidney Disease, Diabetes, Congestive Heart Failure or Myocardial Infarction, Ever smoking, Stroke	

Table 2. Adverse Events Reported by 1852 Rheumatology Outpatients after COVID-19 Vaccination	
Any adverse event	1357 (73.3%)
• Bleeding or bruising	4 (0.2%)
• Chest pain	11 (0.6%)
• Chills	324 (17.5%)
• Difficulty breathing	16 (0.9%)
• Facial drooping	0 (0%)
• Fainting	3 (0.2%)
• Fast heart beat	32 (1.7%)
• Fever	223 (12.0%)
• Flushing/feeling hot	148 (8.0%)
• Hand pain	88 (4.8%)
• Headache	485 (26.2%)
• Hives	6 (0.3%)
• Hoarseness or wheezing	10 (0.5%)
• Itching	75 (4.0%)
• Joint pain	289 (15.6%)
• Lightheaded/fainted	86 (4.6%)
• Muscle aches	428 (23.1%)
• Muscle weakness	101 (5.5%)
• Neck pain	93 (5.0%)
• Nausea/Vomiting	106 (5.7%)
• Hand numbness and/or tingling	41 (2.2%)
• Face numbness and/or tingling	10 (0.5%)
• Numbness and/or tingling in other parts of your body	27 (1.5%)
• Pain at the injection site	839 (45.3%)
• Rash not at the injection site	23 (1.2%)
• Rash at the injection site	57 (3.1%)
• Redness/swelling at the injection site	148 (8.0%)
• Sore shoulder	412 (22.2%)
• Abdominal pain	45 (2.4%)
• Swelling eyes or lips	6 (0.3%)
• Swelling of the lymph nodes in your armpit	39 (2.1%)
• Swelling in other parts of your body	16 (0.9%)
• Tiredness/Fatigue	718 (38.8%)
• Throat Closing	6 (0.3%)
• Other	66 (3.6%)
Duration of Adverse Event	
• <1 day	240 (13.0%)
• 2-7 days	878 (47.4%)
• >1 week	239 (12.9%)
• missing	495 (26.7%)
Medications for prevention of vaccine side effects	
Any Prevention Medication	156 (8.4%)
• Benadryl/Antihistamines	41 (2.2%)
• Corticosteroids	17 (0.9%)
• Acetaminophen	79 (4.3%)
• NSAIDs/CoX-2 inhibitors	49 (2.6%)
• Other	5 (0.3%)
Medications for treatment after vaccine	
Any Post-Vaccine Treatment Medication	551 (29.8%)
• Benadryl or other antihistamines	40 (2.2%)
• Corticosteroids	21 (1.1%)
• Acetaminophen	487 (26.3%)
• NSAIDs/CoX-2 inhibitors	273 (14.7%)
• Other	48 (2.6%)
• Missing	612 (33.0%)

of epinephrine and 21 patients (1.1%) used corticosteroids for symptom relief. 35 patients (1.9%) reported seeking medical attention (i.e. urgent care, ER or hospital) after any vaccination. Typical adverse event duration was 2-7 days (47.4%); 13% experienced symptoms < 1 day, and 13% experienced symptoms >1 week.

Conclusion: Interim data from our cohort demonstrate that 73.3% of rheumatology patients experienced a local or systemic adverse event post-SARS-CoV-2 vaccination, similar to estimates from Pfizer BioNTech vaccine clinical trial data. Symptoms were typically transient (< 7 days) and consisted predominantly of common side effects such as injection site pain, fatigue, headache, and myalgias. Less than 1% of patients experienced more serious post-vaccination events, which is reassuring and may help inform vaccine decision making for rheumatology patients.

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Abstract Number: 1539

High Disease Activity, as Assessed by RAPID3, Increases Risk of Hospitalization and Predicts Lower Chance of Recovery from COVID-19 in a Cohort of Tertiary Care Rheumatology Patients

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
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Background/Purpose: There is a need to understand which patients with rheumatologic diseases may be at highest risk for poor COVID-19 related outcomes so that both physicians and patients can make informed decisions regarding disease management and pandemic-related precautions. Routine assessment of patient index data 3 (RAPID3) is a quick tool to assess disease activity that has been validated in numerous rheumatologic conditions. Here, we evaluate the association between RAPID3 and other comorbidities with COVID-19 related outcomes in a cohort of rheumatology patients treated at an urban academic medical center.

Methods: The department of rheumatology COVID-19 data repository is an IRB approved registry consisting of patients at an academic center with both a COVID-19 diagnosis and a rheumatologic condition. Data collected included demographics, comorbidities, and disease activity as measured by the RAPID3. Chi-square and paired t-tests and logistic regression models were used to analyze associations between demographics, comorbidities, disease activity and COVID-19 hospitalization rates and recovery.

Results: 169 patients with a laboratory confirmed diagnosis of COVID-19 were included. Demographics are summarized in Table 1. The majority of patients had high or moderate pre-COVID-19 RAPID3 scores. In our analysis, increased age, T2DM, HTN, chronic kidney disease (CKD), and high pre-COVID-19 RAPID3 score were associated with higher odds of COVID-19 infection requiring hospitalization (Table 2). High pre-COVID-19 RAPID3 scores were also associated with lower odds of full recovery (Table 3).

Table 1
Demographics of cohort of patients with rheumatologic condition and COVID-19 diagnosis

Rheumatologic Disease	N (% Total)
SLE	43 (24.4%)
RA	52 (30.9%)
Psoriasis	20 (11.9%)
Psoriatic arthritis	6 (3.6%)
Vasculitis	0 (0%)
Sjogren's	5 (3%)
JIA	3 (1.8%)
Other	41 (24.4%)
Sex	N (% Total)
Female	133 (78.7%)
Male	36 (21.3%)
Ethnicity	N (% Total)
Asian	2 (1.2%)
African American	60 (44.6%)
Hispanic	63 (36.7%)
Caucasian	29 (17.5%)
Native	0 (0%)
Other	2 (1.2%)
Refused	3 (1.8%)
BMI	N (% Total)
Underweight / Normal (<18.5 - 24.9)	34 (20.4%)
Overweight (25 - 29.9)	35 (20.9%)
Obese I (30 - 34.9)	31 (18.6%)
Obese II (35 - 39.9)	35 (20.9%)
Obese III (>= 40)	32 (19.2%)
Medical Comorbidities	N (% Total)
T2DM	28 (16.6%)
CHF	14 (8.3%)
HTN	77 (45.6%)
CAD	17 (10.1%)
COPD / asthma	31 (18.3%)
CKD	12 (7.1%)
Pre-COVID RAPID3 score	N (% Total)
High (> 12)	50 (54.9%)
Moderate (6.1 - 12)	19 (20.9%)
Low (3.1 - 6)	10 (11%)
Remission (<= 3)	12 (13.2%)
	N (Mean)
Age	169 (50.5)
BMI	167 (33)

HTN and CKD were associated with higher odds of intensive care (ICU) admission (HTN OR 5.8, CI 1.6-21.1, p 0.007; CKD OR 5.8, CI 1.5-22.1, p 0.02) and intubation (HTN OR 10.9, CI 1.3-89.3, p 0.01; CKD OR 7.8, CI 1.6-36.9, p 0.02). HTN was also associated with an increase in length of stay (14.9 days vs 6.6 days, p 0.01).

Table 2
Association between comorbidities and pre-COVID-19 RAPID3 scores and outpatient versus inpatient management

		Total (N=169)	Outpatient management (N=119)	Inpatient management (N=50)	Odds ratio (95%CI)	P-value
Variable		N (% Total)	N (% Total)	N (% Total)		
Pre-COVID-19 RAPID3	**High (>12)**	**50 (55%)**	**35 (49%)**	**15 (79%)**	**0.25 (0.08-0.83)**	**0.018**
	Other (<= 12)	41 (45%)	37 (51%)	4 (21%)		
T2DM	**Yes**	**28 (17%)**	**12 (10%)**	**16 (32%)**	**0.24 (0.1-0.55)**	**<0.001**
	No	141 (83%)	107 (90%)	34 (68%)		
HTN	**Yes**	**77 (46%)**	**45 (38%)**	**32 (64%)**	**0.34 (0.17-0.68)**	**0.002**
	No	92 (54%)	74 (62%)	18 (36%)		
CKD	**Yes**	**12 (7%)**	**5 (4%)**	**7 (14%)**	**0.27 (0.08-0.9)**	**0.043**
	No	157 (93%)	114 (96%)	43 (86%)		

Table 3
Association between pre-COVID-19 RAPID3 scores and likelihood of recovery

		Total (N=120)	Full Recovery (N=88)	No Full Recovery (N=32)	Odds ratio (95%CI)	P-value
Variable		N (% Total)	N (% Total)	N (% Total)		
Pre-COVID RAPID3 Group	**High (>12)**	**37 (53%)**	**23 (43%)**	**14 (82%)**	**6.09 (1.56-23.72)**	**0.009**
	Other (<=12)	33 (47%)	30 (57%)	3 (18%)		

Conclusion: In this cohort of rheumatology patients, high pre-COVID-19 disease activity, as assessed by RAPID3 scores, was associated with increased odds of COVID-19 infection requiring hospitalization and decreased odds of full recovery. To our knowledge, this is the first study to use an exclusively patient-reported outcome tool to demonstrate the relationship between disease activity and COVID-19 outcomes in patients with rheumatic disease.

Similar to other studies, age, HTN, T2DM, and CKD were associated with severe COVID-19 outcomes. In contrast to previously described cohorts, this group is younger, predominantly female, and consists of a high proportion of Hispanic and Black patients.

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Abstract Number: 1540

Antibody Response After SARS-CoV-2 Infection in Patients with Rheumatic Diseases: A Multicenter, Nationwide Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The development and duration of humoral immunity after SARS-CoV-2 natural infection remains of interest. For the general population, available data suggest a robust immune response, able to protect against reinfection for at least 6-8 months. As for the subgroup of patients with rheumatic and musculoskeletal diseases (RMDs), information is lacking. Considering that immunosuppression might preclude an adequate anti-viral response, we aimed to assess the rate of seroconversion after natural infection in patients with RMDs and to find factors that may influence antibody response.

Methods: Multicenter observational study of patients with RMDs prospectively-followed in the Rheumatic Diseases Portuguese Register – Reuma.pt –in the first 6 months of the pandemic in Portugal – March to September 2020. We included all patients with inflammatory and non-inflammatory RMDs with confirmed (PCR-positive) or suspected COVID-19. Patients were asked to collect a blood sample for antibody testing against SARS-CoV-2 at least 3 months after the resolution of infection. All samples were processed in a single center. IgG antibodies recognizing the SARS-CoV-2 receptor-binding domain (RBD) were quantified using ELISA. Seroconversion was assumed for any titer ≥1:50.

Results: Out of 179 included patients, 79 (44%) performed antibody testing. Of these, 65 (82%) had inflammatory RMDs and 14 (18%) had non-inflammatory RMDs – described in Table 1. Blood samples were collected between days 89 and 331 (median time 237, IQR 125 days) after symptom onset or positive PCR test (if asymptomatic). Seventy (89%) patients had positive IgG antibodies, with a geometric mean titer of 1/1508±4.075 (min 1/100- max 1/25600).

No differences were seen in the seroconversion rate between patients with and without inflammatory RMDs. Disease activity status at the time of the infection also did not influence seroconversion. Although DMARD therapy didn't influence seropositivity, the proportion of patients under TNF inhibitors (TNFi) was numerically higher in patients who did not develop IgG antibodies (33.3% vs 8.6%, p=0.062). Of note, all patients treated with corticosteroids (N=30) and rituximab (N=2) developed antibodies. There was no correlation between sample timing and RBD IgG titers. On multivariate analysis, treatment with TNFi (OR 0.13, 95%CI: 0.02-0.91, p=0.041), and symptomatic COVID-19 (OR 15.1, 95%CI 2.33-98.48; p=0.004) were the only variables independently associated with serological response (Table 2).

Conclusion: Most patients with rheumatic diseases developed IgG antibodies against SARS-CoV-2, with medium-to-high titers detected between 3 to 11 months after natural infection. In this population, treatment with TNFi decreased the odds of seroconversion while symptomatic COVID-19 was associated with a higher likelihood of developing a humoral immune response.

Table 1 – Demographic and clinical data of patients with inflammatory and non-inflammatory RMDs who performed serology

	Inflammatory arthritis[1] N, %	CTD/Vasculitis[2] N, %	Non-inflammatory diseases[3] N, %	Total N, %	p value
N,%	40, 51	25, 32	14, 18	79, 100	
Age (y) Median (IQR)	53 (16)	58 (15)	61 (14)	57 (14)	**0.026**
Female N,%	26, 65	22, 88	13, 93	61, 77	**0.03**
Treatment[4] (N, %)					
Corticosteroids	17, 43	12, 48	1, 7	30, 38	**0.029**
Azathioprine	1, 3	3, 12	0, 0	4, 5	0.150
Hydroxychloroquine	1, 3	11, 44	1, 7	13, 17	**<0.001**
Leflunomide	3, 8	1, 4	0, 0	4, 5	0.522
Mycophenolate	0, 0	1, 4	0, 0	1, 1	0.335
Methotrexate	16, 40	10, 40	1, 7	27, 34	0.063
Sulfassalazine	3, 8	0, 0	0, 0	3, 4	0.219
Belimumab	0, 0	1, 4	0, 0	1, 1	0.335
Rituximab	1, 3	1, 4	0, 0	2, 3	0.735
Tocilizumab	2, 5	0, 0	0, 0	2, 3	0.368
TNF inhibitors	9, 23	0, 0	0, 0	9, 11	**0.007**
Ustekinumab	1, 3	0, 0	0, 0	1, 1	0.610
COVID-19 severity (N, %)					0.425
Asymptomatic[5]	5, 13	3,12	0, 0	8, 10	
Mild[6]	8, 20	2, 8	2, 14	12, 15	
Moderate[7]	21, 53	15, 60	7, 50	43, 54	
Severe[8]	6, 15	4, 16	5, 36	15, 19	
Critical[9]	0, 0	1,4	0,0	1,1	
Timing of serology[10] (days) Median (IQR)	256 (123)	225 (161)	234 (65)	237 (125)	0.543
IgG+ (N,%)	33, 83	23, 92	14, 100	70, 89	0.168
IgG Titers (GM±GSD) (min.-max)	1/1436±3.96 (1/100-1/25600)	1/1367±4.262 (1/100-1/25600)	1/1903±4.327	1/1508±4.075	0.051

1 – Includes rheumatoid arthritis, psoriatic arthritis (PsA), spondyloarthritis other than PsA, RS3PE, undifferentiated arthritis and microcrystalline arthritis, adult onset Still disease. 2 – Includes systemic lupus erythematosus, undifferentiated connective tissue disease, mixed connective tissue disease, systemic sclerosis, Sjögren syndrome, giant cell arteritis, Behçet disease. 3 – Fibromyalgia, osteoarthritis, osteoporosis, Paget bone disease. 4 – treatment before infection; only DMARDs and corticosteroids were considered; 5 – reference for statistical analysis; 6 - symptomatic disease without evidence of pneumonia; 7 - clinical signs of pneumonia but room-air SpO2 ≥ 90%; 8 - hypoxemic pneumonia and/or need for hospitalization; 9 - requiring admission to intensive care unit or death. 10 – relative to symptom onset or first positive PCR test if asymptomatic. CTD – connective tissue diseases; GM: geometric mean; GSD: geometric SD factor; y: years.

Table 2 – Differences between patients who developed IgG antibodies and those who did not and binary logistic regression model for prediction of IgG development

	IgG+ (N, %)	IgG – (N, %)	Univariate analysis (p value)	Multivariate analysis OR (95% CI); p value
N,%	70, 89	9, 11		
Age (y) median (IQR)	58 (14)	48 (21)	0.649	1.01 (0.94-1.07); 0.885
Female, N,%	55, 79	6, 67	0.418	1.09 (0.17-7.10); 0.930
Rheumatic diseases: N,%			0.168	
Inflammatory arthritis[1]	33, 47	7, 78		
CTD/Vasculitis	23, 33	2, 22		
Non-inflammatory	14, 20	0, 0		
Disease activity before infection: N,%			1.000	2.29 (0.18-28.81); 0.521
Remission/low	54, 84	8, 89		
Moderate/high	10, 16	1, 11		
Treatment: N, %				
Corticosteroids	30, 100	0, 0	**0.011**	
Azathioprine	4, 6	0, 0	1.000	
Hydroxychloroquine	12, 17	1, 11	1.000	
Leflunomide	4, 6	0, 0	1.000	
Mycophenolate	1, 1	0, 0	1.000	
Methotrexate	24, 34	3, 33	1.000	
Sulfassalazine	3, 4	0, 0	1.000	
Belimumab	1, 1	0, 0	1.000	
Rituximab	2, 3	0, 0	1.000	
Tocilizumab	2, 3	0, 0	1.000	
TNF inhibitors	6, 9	3, 33	0.062	0.13 (0.02-0.91); **0.041**
Ustekinumab	1, 1	0, 0	1.000	
Comorbidities:				
Hypertension	22, 31	1, 11	0.271	
Diabetes mellitus	5, 7	1, 11	0.528	
Cardiovascular disease[2]	6, 9	1, 11	0.586	
Obesity	21, 30	2, 22	1.000	
COVID-19 severity: (N, %)			**0.007**	
Asymptomatic[3]	4, 6	4, 44		
Mild	11, 16	1, 11		15.15 (2.33-98.48); **0.004**
Moderate	39, 56	4, 44		
Severe	15, 21	0, 0		
Critical	1, 1	0, 0		
Timing from symptoms to sampling (days) Median (IQR)	236 (126)	239 (105)	0.875	

1 –reference for statistical analysis; 2 – includes personal history of heart failure and/or ischemic cardiopathy. 3 - reference for statistical analysis. CTD: connective tissue diseases.

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Abstract Number: 1541

Preliminary Criteria for Macrophage Activation Syndrome Associated with Coronavirus Disease-19

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 runs a severe disease associated with acute respiratory distress syndrome in a subset of patients, and a hyperinflammatory response developing in the second week contributes to the worse outcome. Inflammatory features are mostly compatible with macrophage activation syndrome (MAS) observed in other viral infections despite resulting in milder changes. Early detection and treatment of MAS may be associated with a better outcome. However, available criteria for MAS associated with other causes have not been helpful. To identify distinct features of MAS associated with COVID-19 using a large database enabling to assess of dynamic changes.

Methods: PCR-confirmed hospitalized COVID-19 patients followed between March and September 2020 constituted the discovery set. Patients considered to have findings of MAS by experienced physicians and given anakinra or tocilizumab were classified as the MAS group and the remaining patients as the non-MAS group. The MAS group was then re-grouped as the cases with exact-MAS and borderline-MAS cases by the study group. Clinical and laboratory data including the Ct values of the PCR test were obtained from the database, and dynamic changes were evaluated especially for the first 14 days of the hospitalization. The second set of 162 patients followed between September-December 2020 were used as the replication group to test the preliminary criteria. In the second set, hospitalization rules were changed, and all patients required oxygen support and received dexamethasone 6mg/day or equivalent glucocorticoids. Daily changes were calculated for the laboratory items in MAS, borderline, and non-MAS groups to see the days differentiating the groups, and ROC curves and lower and upper limits (10-90%) of the selected parameters were calculated to determine the cutoff values.

Results: A total of 769 PCR-confirmed hospitalized patients were analysed, and 77 of them were classified as MAS and 83 as borderline MAS patients. There was no statistically significant difference in the baseline viral loads of MAS patients compared to the non-MAS group according to the Ct values. Daily dynamic changes in the MAS group differed from the non- MAS group especially around the 6th day of hospitalization, and more than a twofold increase in ferritin and a 1.5-fold increase in D-dimer levels compared to the baseline values help to define the MAS group.

Table 1. Preliminary Criteria for Macrophage Activation Syndrome Associated with Coronavirus Disease-19

1. Fever (>37.0 °C)
2. Ferritin concentration > 550 ng/mL
3. More than 2 times increase of ferritin concentration within 7 days of disease onset
4. Neutrophil count > 6000 cell/mm3
5. Lymphopenia < 1000 cell/mm3
6. Neutrophil/lymphocyte ratio > 6
7. D-dimer concentration > 1000 ng/ml
8. More than 50% increase of D-dimer concentration within 7 days of disease onset
9. CRP concetration > 50 mg/L
10. LDH concentration > 300 U/L
11. ALT or AST concentration > 50 U/L
12. Procalcitonin concentration < 1.2

1 point for each positive item assessed on Days 5-7

Score calculation: Total points / 12 x 100

Possible MAS ≥45 and Definite MAS ≥60

Twelve items selected for the criteria are given in Table 1 below. The total score of 45 provided 79.6% sensitivity for the MAS (including borderline cases) and 81.3% specificity around days 5 and 6 in the discovery set, and a score of 60 increased the specificity to 94.9% despite a decrease in sensitivity to 40.8%. The same set provided a similar sensitivity (80.3%) in the replication, but a lower specificity (47.4-66% on days 6 to 9) due to a group of control patients with findings of MAS possibly masked by glucocorticoids.

Conclusion: This study defined a set of preliminary criteria using the most relevant items of MAS according to the dynamic changes in the parameters in a group of COVID-19 patients. A score of 45 would be helpful to define a possible MAS group with reasonable sensitivity and specificity to start necessary treatments as early as possible.

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Abstract Number: 1542

Does Adjustment to Dosing and Timing of Immunomodulatory Drugs Impact Immunogenicity of COVID19 Vaccines in Patients with Autoimmune and Inflammatory Rheumatic Disease (AIIRD)?

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Clinical trials leading to approval of the COVID19 vaccines did not include immunocompromised individuals. Concerns have been raised that immunogenicity of the vaccines may be impaired in patients with

AIIRD on immunomodulatory drugs. The ACR COVID-19 Vaccine Clinical Guidance Task Force has suggested that the timing and dosing of certain drugs be modified to optimize vaccine response but acknowledged it was a "living document" that would likely change as additional studies were published. We sought to characterize antibody re-

Table 1. Recommendations regarding adjustment of dosing/timing. *AOCC: Arthritis & Osteoporosis Consultants of the Carolinas, Charlotte, NC 1https://www.rheumatology.org/Portals/0/Files/COVID-19-Vaccine-Clinical-Guidance-Rheumatic-Diseases-Summary.pdf

	ACR[1] (2/8/2021; modified 3/4/2021)	AOCC *(12/20/2020)
methotrexate	*"Hold for 1 week after each of the 2 mRNA vaccine doses, for those with well–controlled disease; no modifications to vaccination timing."*	Reduce dose to 7.5 mg for 2 weeks after each vaccine dose
JAK inhibitors	*"Hold JAKi for 1 week after each vaccine dose; no modifications to vaccination timing."*	Hold 2 days before and for 2 weeks after each vaccine dose
abatacet iv	*"Time vaccine administration so that the first vaccination will occur four weeks after abatacept infusion (i.e. the entire dosing interval) and postpone the subsequent abatacept infusion by one week (i.e. a 5 week gap in total); no medication adjustment for the second vaccine dose."*	Wait 4 weeks after abatacept infusion to receive the first vaccine dose; delay next infusion until 2 weeks after 2nd vaccine dose.
abatacept sc	*"Hold SQ abatacept both one week prior to and one week after the first COVID-19 vaccine dose (only); no interruption around the second vaccine dose."*	Hold abatacept sc 1 week prior and for 2 weeks after each vaccine dose.
rituximab	*"...schedule vaccination so that the vaccine series is initiated approximately 4 weeks prior to next scheduled rituximab cycle; after vaccination, delay RTX2-4 weeks after final vaccine dose, if disease activity allows."*	Wait 4 mos. (Moderna), 4.5 mos. (Pfizer) or 5 mos. (J&J) after last rituximab infusion for 1st vaccine dose; delay next rituximab infusion for 2 weeks after last vaccine dose.

Table 2. Baseline patient characteristics

Gender:	
female	145 (78%)
male	53 (22%)
Median age	61.8 yrs.
Vaccine type:	
Pfizer	145 (74%)
Moderna	48 (23%)
J & J	5 (3%)
Diagnosis: (patient may have more than 1 dx.)	
RA	164 (77%)
PsA	12 (6%)
SLE	9 (5%)
Sjogrens	4 (2%)
IBD	4 (2%)
GPA	4 (2%)
DM/PM	3 (1.5%)
AxSpa, PSS, Behcet's, Still's ds., alopecia, atopic dermatitis, MG	1 each

sponses to the SARS COV-2 spike protein in patients with AIIRD both in those who adjusted and in those who failed to make adjustments to their drug therapy in a real world study.

Methods: We measured SARS CoV2 IgG antibody levels to the receptor-binding domain of the S1 spike antigen using a semi-quantitative assay (Siemens Atellica; QUEST) in patients with AIIRD followed in a single specialty community based practice of 13 providers (AOCC) in Charlotte NC from 3/17 – 5/14/2021. Patients with a prior self-reported history of COVID19 were excluded. All tests were performed by Day 14 or later following BNT162b2 (Pfizer), mRNA -1273 (Moderna) or Ad26COV2.S (Johnson & Johnson) vaccine. We compared the number of antibody positive (Ab+) vs. antibody negative(Ab-) and mean Ab levels in Ab+ patients for those who did or did not make adjustments to dosing/timing of methotrexate (MTX), JAK inhibitors (JAKi), rituximab (RTX) and/or abatacept (ABA). Associations were evaluated using Student's t-test. In 12/2020, our clinic recommended adjustments to the dosing/timing of these drugs that were similar but slightly more stringent than subsequent recommendations in 2/2021 from the ACR Task Force (Table 1).

Results: 198 patients with AIIRD were studied. Baseline characteristics including gender, age, vaccine type and diagnosis are presented in Table 2. Findings related to % of total patients on MTX, JAKi, RTX and ABA with absent antibody response and comparison of antibody response with or without adjustment in dosing and/or timing are presented in Table 3. Only 13% of all patients on RTX and 52 % of all patients on ABA were Ab+. In contrast, fully 91% of patients on JAKi were Ab+ whereas 80% of patients on methotrexate alone were Ab+. Adjustments to the dose of MTX or JAKi did not significantly alter the immunogenicity as measured by IgG antibodies to the S1 spike antigen.

Table 3. Adjustments to drug dosing/timing. IgG antibodies to SARS CoV-2 S1 RBD antigen were measured using a semi-quantitative chemiluminescent immunoassay (Siemens Atelllica IM/Siemens Atellica IM Analyzer; QUEST) in which negative/nonreactive was <1.0, and positive/reactive was reported from 1.00 to 20.00 or > 20.00. https://www.siemens-healthineers.com/en-us/laboratory-diagnostics/assays-by-diseases-conditions/infectious-disease-assays/sars-cov-2-igg-assay

				No adjust		Adjust				
Drug	N	Total without antibody response (Ab-)	Total with antibody response (Ab+)	Ab -	Ab +	Ab-	Ab+	No Adjust mean Ab+	Adjust mean Ab+	P value
methotrexate (all)	110	27 (25%)	83 (75%)	16 (27%)	44 (73%)	11 (22%)	39 (78%)	12.08	10.88	0.437
methotrexate (no bio)	51	10 (20%)	41 (80%)	6 (20%)	24 (80%)	4 (19%)	17 (81%)	12.92	8.79	0.087
JAK inhibitor	23	2 (9%)	21 (91%)	1 (8%)	11 (92%)	1 (9%)	10 (91%)	12.96	13.89	0.137
rituximab	38	33 (87%)	5 (13%)	17 (85%)	3 (15%)	16 (89%)	2 (11%)	5.07	11.28	0.427
abatacept	27	13 (48%)	14 (52%)	5 (45%)	6 (55%)	8 (50%)	8 (50%)	12.62	12.7	0.406
abatacept iv	20	11 (55%)	9 (45%)	4 (67%)	2 (33%)	7 (50%)	7 (50%)	5.4	12.74	0.317
abatacept sc	7	2 (29%)	5 (71%)	1 (25%)	4 (75%)	1 (50%)	1 (50%)	12.51	20.00	

IgG antibodies to SARS CoV-2 S1 RBD antigen were measured using a semi-quantitative chemiluminescent immunoassay (Siemens Atelllica IM/Siemens Atellica IM Analyzer; QUEST) in which negative/nonreactive was <1.0, and positive/reactive was reported from 1.00 to 20.00 or > 20.00 .
https://www.siemens-healthineers.com/en-us/laboratory-diagnostics/assays-by-diseases-conditions/infectious-disease-assays/sars-cov-2-igg-assay

Adjustments to the timing of vaccine in relationship to last RTX dose and last vaccine injection in relation to next RTX infusion failed to increase the likelihood of an antibody response. Adjustments to the timing of ABA (either iv or sc) did not significantly increase antibody response. Limitations to this real world study include a non-randomized design and not measuring potential residual confounders.

Conclusion: Holding JAKi, lowering the dose of MTX or altering the timing of the vaccine in relation to RTX or ABA administration did not alter immunogenicity as measured by SARS CoV2 Abs to the S1 spike antigen. Coupled with additional measure of humoral immune response and T cell function, these findings may provide further guidance for dosing and timing of immunomodulatory therapies in the setting of COVID19 vaccinations in patients with AIIRD.

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Abstract Number: 1543

Epidemiology and Disease Burden of Hospitalized Children with Paediatric Multisystem Inflammatory Syndrome Temporally Associated with SARS-CoV-2 Infection in Canada: A Canadian Pediatric Surveillance Program National Prospective Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: As of May 2021, Canada had reached over 1.3 million confirmed cases of SARS-CoV-2 infection, and over 25,000 deaths. This study identified children in Canada hospitalized with paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 infection (PIMS), also known as multisystem inflammatory syndrome in children (MIS-C), and aimed to 1) Describe clinical and laboratory features at presentation, management, outcomes, and 2) Identify risk factors for intensive care unit (ICU) admission.

Methods: We conducted a national prospective study using the infrastructure of the Canadian Paediatric Surveillance Program (CPSP), a network of >2,800 paediatricians across Canada. Physicians reported cases of hospitalized children who met study criteria from March 2020-May 2021, through a weekly online questionnaire distributed via the CPSP network. Cases were categorized as confirmed MIS-C, presumed MIS-C, and/or confirmed PIMS defined in **Figure 1.** Modified Poisson regression analysis was used to compute adjusted risk ratios (aRR) for ICU risk factors associated with PIMS/MIS-C.

Results: A total of 506 cases of children hospitalized with PIMS/MIS-C were reported during the study period, of which 383 unique cases were included in the primary analysis (161 confirmed MIS-C, 202 presumed MIS-C, and/or 352 confirmed PIMS) with the majority of cases being reported from the provinces of Ontario (44.6%) and Quebec (39.7%). A total of 167/383 (43%) cases had a SARS-CoV-2 link (62.3% close contact, 58.1% positive PCR, 32.3% known positive serology). Of the 216 cases (56%) with no known link, 55/114 with serology results available were negative. Majority were preschool (1-5 years) or school aged (6-12 years), with slight male predominance (57.7%), and were previous healthy (60 (15.7%) with co-morbidities). Median duration of fever was 6 days; 283/383 (74%) had gastrointestinal involvement; more than half had mucocutaneous changes including rash (64.5%), bilateral non-exudative conjunctivitis (62.9%), and changes in lips/oral cavity (58.7%). Laboratory features indicated hyperinflammation (**Table 1**).

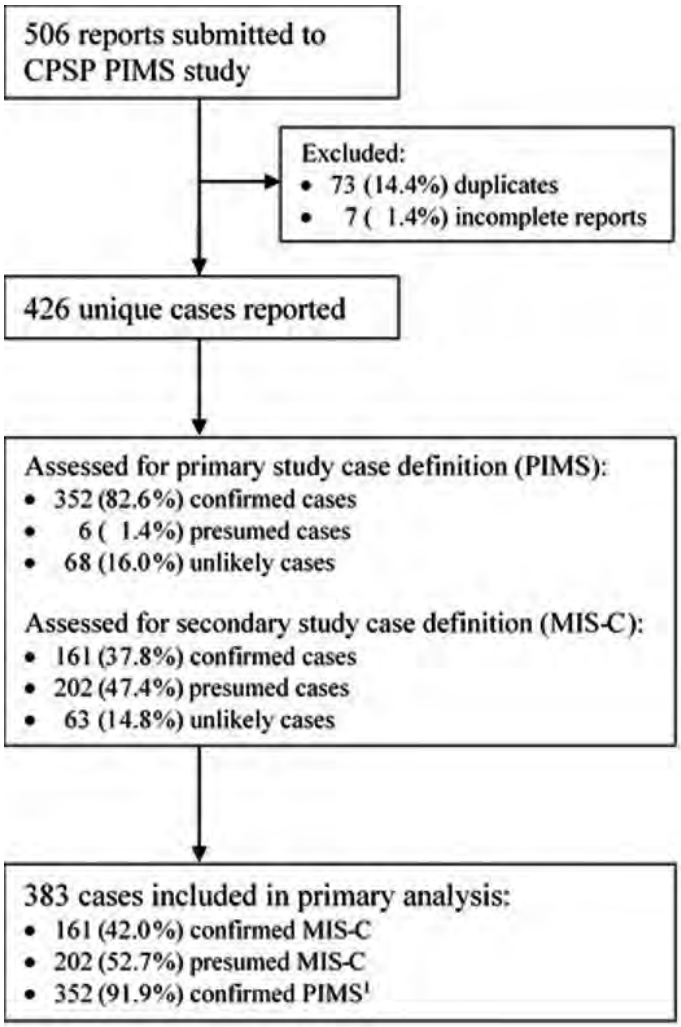

Figure 1. Flow chart of participants meeting the case definitions for MIS-C and PIMS. Confirmed MIS-C: meets MIS-C criteria (adapted by the World Health Organization (WHO))a AND no other cause identified AND SARS-COV-2 link present (defined as a history of positive PCR, rapid test, or serology or close contact with microbiologically confirmed SARS-CoV-2 infection); Presumed MIS-C: same as confirmed MIS-C except no known SARS-CoV-2 link; Confirmed PIMS: meets study criteria (1) fever ≥3 days (2) elevated inflammatory markers (C-reactive protein (CRP) ≥ 30 mg/L, Erythrocyte sedimentation rate (ESR) ≥ 40 mm/h OR Ferritin ≥ 500 µg/L) (3) one or both: features of Kawasaki disease or toxic shock syndrome AND (4) no other cause identified. a https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19 1Of confirmed PIMS cases, 150 also met criteria for confirmed MIS-C, 182 also met criteria for presumed MIS-C, while 20 did not meet criteria for MIS-C. Six cases met criteria for confirmed or presumed MIS-C but not confirmed PIMS.

Table 1. Clinical and laboratory features of children meeting case definitions for MIS-C and PIMS in Canada.

Characteristics	All Cases	SARS-CoV-2 Linkage		p-value[1]
		Absent/Unknown	Present	
Number of MIS-C/PIMS admissions, N	383	216	167	—
Duration of fever (days), median (IQR)	6 (5–8)	7 (5–9)	6 (5–8)	0.014*
Clinical features, n (%)				
Abdominal pain/vomiting/diarrhea	283 (73.9)	141 (65.3)	142 (85.0)	<0.001*
Rash	247 (64.5)	149 (69.0)	98 (58.7)	0.037*
Bilateral bulbar conjunctival injection without exudate	241 (62.9)	135 (62.5)	106 (63.5)	0.845
Changes in lips/oral cavity	225 (58.7)	146 (67.6)	79 (47.3)	<0.001*
Changes in peripheral extremities	181 (47.3)	125 (57.9)	56 (33.5)	<0.001*
Shock/hypotension	125 (32.6)	36 (16.7)	89 (53.3)	<0.001*
Cervical lymphadenopathy >1.5 cm diameter	92 (24.0)	63 (29.2)	29 (17.4)	0.007*
Periungual desquamation	53 (13.8)	41 (19.0)	12 (7.2)	<0.001*
Coagulation dysfunction, n (%)	178 (46.5)	76 (35.2)	102 (61.1)	<0.001*
Laboratory features, median (IQR)				
ALT (peak; U/L)	34 (17–80)	30 (16–86)	37 (19–80)	0.209
Albumin (nadir; µmol/L)	28 (23–34)	31 (26–36)	25 (21–30)	<0.001*
AST (peak; U/L)	46 (34–83)	48 (33–82)	46 (35–94)	0.995
Bilirubin (peak; µmol/L)	7.3 (4.9–13.1)	5.5 (4.0–9.4)	9.7 (6.1–17.8)	<0.001*
CRP (peak; mg/L)	146 (96–219)	118 (77–190)	186 (123–244)	<0.001*
D-dimer (peak; µg/mL)	2.0 (1.2–4.0)	1.9 (1.0–4.0)	2.3 (1.5–4.1)	0.002*
ESR (peak; mm/h)	54 (42–78)	56 (45–81)	50 (38–70)	0.003*
Ferritin (peak; µg/L)	319 (163–672)	206 (119–486)	435 (275–931)	<0.001*
LDH (peak; U/L)	490 (324–820)	566 (341–901)	402 (298–722)	0.008*
Platelet count (nadir during admission; x10^9/L)	208 (134–319)	289 (190–366)	147 (108–204)	<0.001*
Platelet count (peak after admission; x10^9/L)	489 (360–639)	516 (398–689)	436 (295–579)	<0.001*
Sodium (nadir; µmol/L)	134 (132–136)	135 (134–137)	133 (130–136)	<0.001*
Troponin (peak; ng/L)	10 (9–80)	10 (5–12)	56 (10–219)	<0.001*
Elevated laboratory features, n / patients with tests (%)				
ALT > Institutional 'normal' reference	194/344 (56.4)	106/201 (52.7)	88/143 (61.5)	0.105
AST > Institutional 'normal' reference	121/243 (49.8)	69/146 (47.3)	52/97 (53.6)	0.332
Bilirubin > Institutional 'normal' reference	37/152 (24.3)	13/77 (16.9)	24/75 (32.0)	0.030*
CRP ≥ 30 mg/L	371/383 (96.9)	205/216 (94.9)	141/141 (100.0)	0.012*
D-dimer > Institutional 'normal' reference	298/311 (95.8)	155/162 (95.7)	143/149 (96.0)	1.000
ESR ≥ 40 mm/h	235/303 (77.6)	148/181 (81.8)	87/122 (71.3)	0.032*
Ferritin ≥ 500 µg/L	119/360 (33.1)	45/195 (23.1)	74/165 (44.8)	<0.001*
LDH > Institutional 'normal' reference	154/287 (53.7)	89/160 (55.6)	65/127 (51.2)	0.453
Troponin > Institutional 'normal' reference	128/320 (40.0)	29/158 (18.4)	99/162 (61.1)	<0.001*
Radiologic findings, n / patients with imaging (%)				
Abnormal chest x-ray	85/253 (33.6)	28/125 (22.4)	57/128 (44.5)	<0.001*
Abnormal CT scan	22/39 (56.4)	6/17 (35.3)	5/22 (22.7)	0.019*
Abnormal MRI scan	8/18 (44.4)	DNS	DNS	—
Abnormal ultrasound	47/107 (43.9)	22/63 (34.9)	25/44 (56.8)	0.025*

ALT = Alanine aminotransferase test; AST = Aspartate aminotransferase test; CRP = C-reactive protein; ESR = Erythrocyte sedimentation rate; LDH = Lactate dehydrogenase. Asterisks (*) denote p<0.05.

[1]Statistical tests are conducted between children with versus without a SARS-CoV-2 link

Shock/hypotension was reported in 125 (32.6%). There were no deaths. Cardiac involvement with abnormal echocardiograms was reported in 161/366 (44%) including decreased heart function (14.5%), coronary dilatation (9.1%) and aneurysms (13.1%). Almost one third (28.5%) required ICU admission, with 25.1% requiring respiratory/hemodynamic support. For treatment, 235 (61%) received both IVIG and corticosteroids, 111 (29%) received IVIG only, 7 (1.8%) received corticosteroids only, 30 (7.8%) received neither, and 18 (4.7%) received biologics. Risk factors for ICU admission included presence of SARS-CoV-2 link (aRR 2.79, 95% CI 1.79-4.35; $p < 0.001$) and older age groups: school aged (aRR 2.76, 95% CI 1.71-4.46; $p < 0.001$) and adolescents (13-17 years) (aRR 3.00, 95% CI 1.81-4.98; $p < 0.001$); while no association found with sex or comorbidity (**Table 2**).

Conclusion: This national prospective study reports on the largest series of children hospitalized with PIMS/MIS-C in Canada, providing insight on overall severity and at–risk groups that is essential for prompt recognition and management.

Table 2. Poisson regression analysis of predictors of ICU admission.

Characteristics, n (%)	Level of care required		RR	(95% CI)	p-value	aRR	(95% CI)	p-value
	Inpatient ward	Intensive care						
Number of MIS-C/PIMS admissions, N	274	109	—	—	—	—	—	—
Age of child								
Infants (<1 year)	37 (12.5)	5 (4.6)	1.01	0.40–2.55	0.985	1.16	0.48–2.81	0.735
Preschool (1-5 years)	142 (51.8)	19 (17.4)	ref	ref	—	ref	ref	—
School age (6-12 years)	72 (26.3)	60 (55.1)	3.85	2.43–6.12	<0.001*	2.76	1.71–4.46	<0.001*
Adolescents (13-17 years)	23 (8.4)	25 (22.9)	4.41	2.67–7.30	<0.001*	3.00	1.81–4.98	<0.001*
Sex of child								
Female	119 (43.4)	43 (39.4)	ref	ref	—	ref	ref	—
Male	155 (56.6)	66 (60.6)	1.13	0.81–1.56	0.479	1.04	0.78–1.40	0.778
SARS-CoV-2 linkage[1]								
No	190 (69.3)	26 (23.9)	ref	ref	—	ref	ref	—
Yes	84 (30.7)	88 (76.1)	4.13	2.79–6.11	<0.001*	2.79	1.79–4.35	<0.001*
Phase of pandemic								
Wave 1 (Mar–Aug 2020)	102 (37.2)	18 (16.5)	ref	ref	—	ref	ref	—
Wave 2/3 (Sep 2020–May 2021)	172 (62.8)	91 (83.5)	2.31	1.46–3.65	<0.001*	1.19	0.77–1.84	0.431
Any comorbid condition								
No	234 (85.4)	89 (81.7)	ref	ref	—	ref	ref	—
Yes	40 (14.6)	20 (18.3)	1.21	0.81–1.80	0.350	1.06	0.75–1.49	0.760

aRR = Adjusted risk ratio; CI = Confidence interval; RR = Risk ratio. Asterisks (*) denote p<0.05.
[1]SARS-CoV-2 link is defined as a history of positive PCR, rapid test, or serology or close contact with microbiologically confirmed SARS-CoV-2 infection.

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Abstract Number: 1544

Clinical Course and Risk Factors for Severe/Critical COVID-19 in Patients with Rheumatic Diseases – a Multicenter, Nationwide Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Since the beginning of the COVID-19 pandemic, some studies have addressed risk factors for severe forms of the disease in patients with rheumatic diseases. Higher prednisolone doses and rituximab (RTX) have been associated with an increased risk of severe COVID-19, although not consistently. Our main goal was to assess the clinical features and to identify risk factors for severe COVID-19 in patients with rheumatic diseases.

Table 1. Characteristics of patients with COVID-19 *Diagnosis with n≥3 are specified

Rheumatic diagnosis, N (%)	
Inflammatory arthropathies*	111 (62.0)
Rheumatoid arthritis	48 (26.8)
Spondyloarthritis	32 (17.9)
Psoriatic arthritis	20 (11.2)
Crystal-induced arthropathies	4 (2.2)
Polymyalgia rheumatica	3 (1.7)
Connective tissue diseases/Vasculitis*	51 (28.5)
Systemic lupus erythematosus	12 (6.7)
Undifferentiated connective tissue disease	8 (4.5)
Vasculitis	8 (4.5)
Systemic sclerosis	7 (3.9)
Sjögren syndrome	5 (2.8)
Mixed connective tissue disease	3 (1.7)
Non-inflammatory diseases*	17 (9.5)
Osteoarthritis	9 (5.0)
Fibromyalgia	3 (1.7)
Osteoporosis	3 (1.7)
COVID-19 diagnosis, N (%)	
PCR confirmed	170 (95)
Positive Serology	4 (2.2)
Suspected	5 (2.8)
COVID-19 severity, N (%)	
Asymptomatic	17 (9.5)
Mild	29 (16.2)
Moderate	88 (49.2)
Severe	30 (16.8)
Critical	15 (8.4)
COVID-19 Hospitalization care, N (%)	
Hospitalization	45 (25.1)
Low flux oxygen therapy	34 (19.0)
Non-invasive ventilation/high flux oxygen therapy	12 (6.7)
Invasive ventilation	4 (2.2)
COVID-19 treatment, N (%)	
Corticosteroids	19 (10.6)
Hydroxychloroquine	28 (15.6)
Azithromycin	16 (8.9)
Other antibiotic	6 (3.4)
Lopinavir/ritonavir	6 (3.4)
Remdesivir	3 (1.7)
Tocilizumab	1 (0.6)
Intravenous immunoglobulin	1 (0.6)
DMARD modification during COVID-19	
Conventional synthetic DMARD suspension	35/124
Biologic DMARD suspension	21/38
JAK inhibitor suspension	2/2
COVID-19 complications	
Acute respiratory distress syndrome	13 (7.3)
Heart failure	1 (0.6)
Bacterial infection	16 (8.9)
Macrophage activation syndrome	2 (1.1)
Thromboembolic event	1 (0.6)
Acute kidney failure	8 (4.5)
COVID-19 outcome	
Cure	166 (92.7)
Death	10 (5.6)

Methods: Multicenter observational nationwide study of adult patients with rheumatic diseases and confirmed or suspected infection by SARS-CoV-2 prospectively-followed in the Rheumatic Diseases Portuguese Register – Reuma.pt – between march and september 2020. Mild COVID-19 was defined as symptomatic disease without pneumonia; moderate disease if clinical signs of pneumonia without hypoxemia; severe disease as hypoxemic pneumonia and/or need for hospitalization; and critical disease as requiring admission to intensive care unit or death. Clinical features and treatment of patients with mild/moderate vs. severe/critical COVID19 were compared using Pearson Chi-Square, exact Fisher and Mann-Whitney U tests, as adequate. Independent association between demographic, disease-related and treatment-related variables and COVID-19 severity was evaluated through multivariate logistic regression.

Results: We included 179 patients with confirmed (97.2%) or suspected (2.8%) COVID-19 (Table 1). Forty-five (25.1%) patients developed severe/critical disease, requiring hospitalization, and 10 (5.6%) patients died. In the same time frame, the national rate of hospitalization was 8.4% and mortality 2.6%. Most patients reported direct contact with a positive patient (65.9%). Major symptoms reported were cough, fever, malaise, fatigue, myalgia, headache and anosmia (Table 2). Lymphopenia and elevated CRP were the most frequent laboratory abnormalities. Patients with severe/critical disease were older (p< 0.001), had a higher prevalence of arterial hypertension (p=0.001), diabetes (p< 0.001), cardiovascular disease (p=0.007) and chronic kidney disease (p=0.036) (Table 3). Considering inflammatory arthritis as the reference category, patients with CTD/vasculitis (33.3% vs 26.9%, OR 1.69, 95CI 0.787-3.611) and non-inflammatory diseases (17.8% vs 6.7%, OR 3.60, 95CI 1.25-10.39) had a higher probability of severe/critical COVID-19. Regarding therapy, the proportion of patients under RTX was higher in severe/critical COVID-19 patients (11.1% vs 1.5%, OR 8.25, p=0.012). Treatment with TNF inhibitors was associated with less probability of severe/crit-

Table 2. Symptoms and laboratory data in COVID-19 patients

Symptoms, N (%)	
Cough	91 (50.8)
Fever	87 (48.6)
Malaise	81 (45.3)
Fatigue	67 (37.4)
Myalgia	61 (34.1)
Headache	55 (30.7)
Anosmia	55 (30.7)
Dysgeusia	52 (29.1)
Dyspnea	36 (20.1)
Diarrhea	36 (20.1)
Thoracic pain	32 (17.9)
Odynophagia	28 (15.6)
Arthralgia	27 (15.1)
Rhinorrhea	25 (14)
Abdominal pain	16 (8.9)
Vomiting	14 (7.8)
Laboratory abnormalities, n/total N	
Anemia	6/60
Leucopenia	19/60
Lymphopenia	36/60
Thrombocytopenia	6/60
Elevated transaminases	15/59
Elevated C-reactive protein	27/59
High D-dimers	26/38
Low fibrinogen	2/30
Ferritin>2000	4/28
High IL6	1/7

Table 3. Comparison of patients with severe/critical vs mild/moderate COVID-19 *At least 1 comorbidity among arterial hypertension, obesity, diabetes, cardiovascular disease, asthma, chronic obstructive pulmonary disease, chronic kidney disease

	Severe/critical COVID19 (n=45)	Mild/moderate COVID19 (n=134)	Univariate analysis p-value	Multivariate analysis OR (95%CI); p-value)
Female, N (%)	33 (73.3)	104 (77.6)	0,548	0.73 (0.28-1.88); p=0.510
Age, mean±SD, in years	67.8±14.1	52.0±12.6	**<0.001**	**1.09 (1.06-1.13); p<0.001**
Caucasian, N (%)	39 (86.7)	111 (82.8)	0,166	
Rheumatic disease, N (%)			**0,039**	
Non-inflammatory	8 (17.8)	9 (6.7)		2.01 (0.57-7.12); p=0.280
Inflammatory arthropathy	22 (48.9)	89 (66.4)		
CTD and vasculitis	15 (33.3)	36 (26.9)		1.92 (0.76-4.85); p=0.170
Disease duration, median (IQR), in years	9.7 (14.3)	6.5 (10.0)	0,092	
Disease activity before COVID-19, N (%)			0,270	
Remission	18 (40.0)	43 (32.1)		
Low	13 (28.9)	69 (51.5)		
Moderate	5 (11.1)	16 (11.9)		
High	4 (8.9)	6 (4.5)		
Comorbidities, N (%)				
Obesity	11 (24.4)	27 (20.1)	0,534	
Arterial hypertension	21 (46.7)	28 (20.9)	**0,001**	
Diabetes	10 (22.2)	3 (2.2)	**<0.001**	
Cardiovascular disease	8 (17.8)	6 (4.5)	**0,007**	
Chronic kidney disease	4 (8.9)	2 (1.5)	**0,036**	
Cerebrovascular disease	1 (2.2)	5 (3.7)	0,627	
Asthma	2 (4.4)	0 (0.0)	0,062	
Chronic obstructive pulmonary disease	1 (2.2)	5 (3.7)	0,627	
Interstitial lung disease	1 (2.2)	1 (0.7)	0,441	
Hyperuricemia	1 (2.2)	2 (1.5)	0,573	
Ever smoked	9 (20.0)	5 (3.7)	0,741	
Malignancy	4 (8.9)	4 (3.0)	0,111	
Comorbidity index ≥1*	29 (64.4)	48 (35.8)	**0.001**	1.50 (0.65-3.48); p=0.345
Medications prior to COVID				
Corticosteroids	18 (40.0)	53 (39.6)	0,958	
NSAIDs	2 (4.4)	28 (20.9)	**0.010**	
Methotrexate	14 (31.1)	51 (38.1)	0,475	
Sulphasalazine	4 (8.9)	11 (8.2)	0,887	
Leflunomide	2 (4.4)	9 (6.7)	0,733	
Hydroxychloroquine	6 (13.3)	20 (14.9)	0,793	
Azathioprine	1 (2.2)	5 (3.7)	0,627	
Mycophenolate mofetil	0 (0.0)	1 (0.7)	0,561	
JAK inhibitors	0 (0.0)	2 (1.5)	0,410	
TNF inhibitors	1 (2.2)	23 (17.2)	**0,010**	
Tocilizumab	0 (0.0)	5 (3.7)	0,333	
Ustekinumab	0 (0.0)	1 (0.7)	0,561	
Rituximab	5 (11.1)	2 (1.5)	**0.012**	**13.77 (2.23-85.17); p=0.005**
Belimumab	0 (0.0)	1 (0.7)	0,561	

ical COVID-19 (2.2% vs 17%, OR 0.11, p=0.033). Treatment with other DMARDs was not associated with COVID-19 severity. Age (OR 1.09, 95CI 1.06-1.13, p< 0.001) and treatment with RTX (OR 13.77, 95CI 2.23-85.17, p=0.005) were independently associated with severe/critical COVID-19 (Table 3).

Conclusion: Hospitalization and mortality in rheumatic patients was higher than the reported in the general national population for the same time frame, although a reporting bias must be considered. Older age and treatment with RTX were independent risk factors for severe/critical COVID-19 in patients with rheumatic diseases.

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Abstract Number: 1545

Safety of JAK Inhibitor in Patients with Rheumatoid Arthritis Who Developed Reactivation of Herpes Zoster Virus After Receiving JAK Inhibitor

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Janus kinase inhibitor (JAKi) increases the risk of the reactivation of herpes zoster (HZ) virus and may thus be temporarily discontinued in cases of HZ infection. However, the amount of information on the outcomes of JAKi use after an episode of HZ reactivation is insufficient. In this study, we sought to determine the safety of JAKi during or following an HZ reactivation.

Methods: Medical records of all patients (*n* = 417) who received JAKi at a tertiary referral center between August 2015 and May 2021 were retrospectively reviewed. Among them, data from patients who developed HZ reactivation were collected and the clinical outcomes were evaluated for those who continued or resumed JAKi after HZ reactivation.

Results: Of 417 patients who received JAKi, 33 (7.9%) developed HZ reactivation during JAKi treatment (tofacitinib, n = 22; baricitinib, n = 11). The median age of the patients (male, n = 2; female, n = 31) was 61 years (IQR, 53–69); 14 patients received glucocorticoids, and the mean dose of prednisone was 4.0 ± 2.3 mg. The median duration of JAKi administration before HZ reactivation was 11 months (IQR, 4–29). JAKi was continued in 24 (72.7%) patients during the HZ reactivation episode, and 5 (15.2%) patients temporarily discontinued the JAKi and then resumed it after episode of HZ. All patients with HZ reactivation had typical skin lesions, and 3 (9.1%) patients had acute complications such as encephalitis with HZ ophthalmicus. Four (12.1%) patients, including the three patients with complications, permanently discontinued JAKi. Of the 27 patients who were followed up for a median of 12 months (IQR, 5.5–22.5) after the HZ reactivation episode, HZ reactivation recurred in one (3.7%) patient; this patient maintained JAKi treatment for further 18 months, during which additional HZ recurrence was not observed. Two (6.1%) patients had postherpetic neuralgia.

Table 1. Clinical characteristics of the patients who were receiving JAKi at the time of diagnosis of HZ reactivation

	Patients ($n = 33$)
Age (yrs), median (IQR)	61 (53–69)
Female, *n* (%)	31 (93.9)
Disease duration (yrs), median (IQR)	9 (5–16)
BMI (kg/m^2), median (IQR)	24.8 (22.1–26.2)
Diabetes, *n* (%)	3 (9.1)
DAS28-ESR, mean (SD)	3.6 (1.6)
Concomitant MTX use, *n* (%)	22 (66.7)
Weekly MTX dose (mg), mean (SD)	10.0 (3.5)
Concomitant oral GC use, *n* (%)	14 (42.4)
Daily GC dose (mg), mean (SD)*	4.0 (2.3)
Prior bDMARDs use, *n* (%)	22 (66.7)
History of previous HZ, *n* (%)	5 (15.2)
HZ vaccination, *n* (%)	1 (3.0)
JAKi	
Tofacitinib, *n* (%)	22 (66.7)
Baricitinib, *n* (%)	11 (33.3)
HZ onset after JAKi initiation (months), median (IQR)	11 (4–29)

BMI=body mass index. DAS28-ESR=28-joint disease activity score based on ESR. MTX=methotrexate. GC=glucocorticoid. csDMARDs=conventional synthetic disease-modifying antirheumatic drugs. bDMARDs=biologic disease-modifying antirheumatic drugs. JAKi=Janus kinase inhibitor. HZ=herpes zoster.

*Prednisone equivalent.

Table 2. Clinical outcome of the patients after the diagnosis of HZ reactivation

	Patients ($n = 33$)
Acute complications, *n* (%)	3 (9.1)
Encephalitis with HZ ophthalmicus, *n*	1
Ramsay Hunt syndrome (HZ oticus), *n*	1
Sustained neuritis, *n*	1
Postherpetic neuralgia, *n* (%)	2 (6.1)
Continued use of JAKi during HZ reactivation, *n* (%)	24 (72.7)
Resumed JAKi after HZ reactivation, *n* (%)	5 (15.2)
	Patients ($n = 27$)
Follow-up duration after JAKi use, (months), median (IQR)	12 (5.5–22.5)
HZ recurrence after JAKi use, *n* (%)	1 (3.7)

JAKi=Janus kinase inhibitor. HZ=herpes zoster.

Conclusion: JAKi was commonly continued or re-administered in patients with HZ reactivation, and the majority of patients did not experience significant complications or a recurrence of HZ reactivation. Thus, the use of JAKi after HZ reactivation episode may be generally safe and well-tolerated.

Disclosure: W. Choi, None; **S. Ahn**, None; **Y. Kim**, None; **C. Lee**, None; **B. Yoo**, None; **S. Hong**, None.

Abstract Number: 1546

Immune Responses to COVID-19 Vaccines in Patients Using Immunosuppressive Medication for Inflammatory Arthritis - An Observational Study of 1500 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: To assess the strength and duration of the immunological response to COVID-19 vaccines in patients treated with immunosuppressive medication for inflammatory arthritis.

Methods: Adult patients with a clinical diagnosis of rheumatoid arthritis (RA), spondyloartritis (SpA) or psoriatic arthritis (PsA) on treatment with any bDMARD, csDMARD, tsDMARD or prednisolone (> 7,5 mg/day) intending to receive a COVID-19 vaccine and without contraindications for vaccination were eligible for inclusion in this observational study. A cohort of healthy controls consisting of health care workers has also been established. All subjects receive vaccines according to the national corona vaccination program, independent of the current study.

Serum samples have been obtained from participants before the first vaccine dose. Vaccinations and collection of blood samples 2-4 weeks after the second vaccine dose is still ongoing. Further serum samples will be collected for assessment every 3-6 months during the study period of 5 years. Samples are consecutively analysed for antibodies to SARS-CoV-2 using Microsphere Affinity Proteomics (MAP) (1). In order to further elucidate the immune response to COVID-19 vaccines, the T cell response will also be evaluated in a subgroup of patients and controls. Data regarding demographics, immunosuppressive medication and adverse events related to vaccination are recorded. Information regarding vaccination status and potential COVID-19 disease is obtained from relevant national health registers.

Results: From February 15 until May 27 2021, 1713 patients have been enrolled in the study. At present, 1515 patients have received at least one vaccine dose and 130 participants have provided samples for T cell analyses. The distribution of diagnoses and medication in the 1515 patients with at least one vaccine dose is shown in Table 1. 651 patients have received a second vaccine dose and 80 patients have serum samples available for analysis 2-4 weeks after the second vaccine dose. Further analyses of serological and cellular responses are currently ongoing, with first results expected summer of 2021.

Conclusion: Long-term immunosuppressive medication may differentially impact the COVID 19 vaccine response in patients being treated for arthritic diseases. Determining how strong and how long lasting the immune response is in different treatment groups will be crucial in decision-making with regard to adjustments in medication and to assess a possible need for re-vaccination. Further results on serological and cellular responses are expected late summer 2021 and will be of urgent importance to patients, health care systems and decision makers.

Table1. Distribution of diagnoses and medication. Patients may have several diagnoses and use several medications.

	Total	RA	PsA	SpA
All medication	1515	734	377	415
Infliximab	143	40	27	81
Rituximab	74	74	0	0
Etanercept	277	116	66	107
Adalimumab	259	71	68	133
Golimumab	43	13	12	19
Certolizumab Pegol	71	19	31	25
Tocilizumab	28	25	3	0
Abatacept	16	15	1	0
Sekukinumab	15	1	7	9
Baricitinib	21	20	1	0
Tofacitinib	13	12	3	1
Sulphasalazine	33	21	4	10
Leflunomide	14	10	4	0
Prednisolone	126	97	22	7
Methotrexate	758	497	266	64
Methotrexate monotherapy	350	240	122	7
1st vaccine dose	1515	734	377	415
AZD1222	57	25	16	16
mRNA-1273	382	185	93	106
Tozinameran (BNT162)	1076	524	268	293

References

1. Holter JC et al. Proc Natl Acad Sci 2020

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Abstract Number: 1547

Potential Predictors of Outcome for Anakinra Treatment in COVID-19 Patients with Macrophage Activation Syndrome

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Coronavirus Disease 2019 (COVID-19) runs a severe course in a subset of patients with acute respiratory distress syndrome and multiorgan failure, and a hyperinflammatory syndrome compatible with features of macrophage activation syndrome (MAS) contributes to this worse outcome. Glucocorticoids have become standard of care for those requiring oxygen support or mechanical ventilation. More targeted anti-inflammatory treatment with tocilizumab and anakinra have also been shown to be effective, however, more studies are being awaited to clarify the features of patients who would benefit more. We, therefore, investigated characteristics of the patients who received anakinra in a single tertiary referral center.

Methods: The records of hospitalized adult COVID-19 patients between March 2020 and May 2021 were retrospectively analyzed, and those patients diagnosed with MAS and who received anakinra treatment constituted the study group. Diagnosis of COVID-19 was confirmed by RT-PCR or typical findings on computed tomography. Diagnosis of MAS was based on expert opinion and the preliminary criteria developed by the investigators. All laboratory features and clinical findings were recorded using a standard form. Anakinra dose was determined according to the needs of the patients mainly determined by the inflammatory parameters, varying 100-300 mg/day SC to 400-800 mg/day IV.

Results: Out of 1080 COVID-19 patients, 218 (151 male, 67 female, mean age 60.6±15.2) who received anakinra were identified. Among them, 125 (57.3%) patients followed in the ward, 21(9.6%) did not need oxygen treatment during the hospitalization. Sixty-nine (31.6%) patients followed at ICU, 40 of them were intubated, 30 (13.7%) died in ICU. Despite similar baseline values with an exception of lower procalcitonin levels in survivors, dead patients had higher CRP, ferritin, D-dimer, and LDH levels at the anakinra initiation (Table 1). Died patients did not show a significant response in CRP, ferritin, and D-dimer values, and they had even higher ferritin and a 2-fold increase in D-dimer levels on the day of death. Laboratory follow-up studies also revealed an increase in procalcitonin, troponin, transaminase

Table 1. Characteristics of patients treated with anakinra

	Survivors			Died			
	Baseline	Anakinra initiation	Discharge	Baseline	Anakinra initiation	Death	P value
Neutrophil	6.8±4.2	7.6±4.1	6.7±2.8	6.7±4.3	9±5.8	9.7±7.3	0.02
Lymphocyte	0.7±0.4	0.7±0.4	1.3±0.8	0.7±0.3	0.6±0.3	0.9±0.7	0.06
Monocyte	0.4±0.2	0.4±0.2	0.6±0.3	0.4±0.2	0.4±0.3	0.6±0.9	0.03
Platelet	235±101	293±132	337±139	223±115	255±120	210±148	0.03
Ferritin	1209±1094	1374±1446	775±680	997±1063	1560±1208	2606±6784	0.03
D-dimer	2170±4202	1808±2921	1000±1300	1996±3144	2422±2256	5181±5321	0.002
CRP	115±87	87±70	8±19	154±102	132±91	154±126	0.005
LDH	399±157	396±141	270±84	389±238	450±170	583±567	0.005
ALT	41±33	57±62	84±78	38±29	50±63	112±174	0.004
AST	49±50	49±41	36±27	42±26	50±43	218±458	0.005
Procalcitonin	0.3±0.7	0.2±0.3	0.2±1.3	0.7±1.5	0.6±0.9	3.6±4.9	0.005
Troponin	24±67	73±599	26±66	40±57	35±47	132±160	0.55
Creatinine kinase	230±331	139±179	43±43	120±51	166±199	83±35	0.02
Fibrinogen	607±155	601±152	382±122	665±204	660±186	539±164	0.005
Creatinin	1.2±1	1.1±0.7	1.1±1.1	1.3±1.1	1.2±1	1.3±0.7	0.58

Table 2. A separate analysis of the patients followed at the ward, ICU, and those who died.

	Ward			ICU			Died			P-value
	Baseline	Anakinra initiation	Discharge	Baseline	Anakinra initiation	Discharge	Baseline	Anakinra initiation	Death	
Neutrophil	6.4±3.9	7.2±3.8	6.9±2.7	8.8±5	9.2±5.3	5.3±2.7	6.7±4.3	9±5.8	9.7±7.3	0.03
Lymphocyte	0.7±0.4	0.7±0.4	1.3±0.7	0.8±0.5	0.7±0.3	1.4±0.8	0.7±0.3	0.6±0.3	0.9±0.7	0.84
Monocyte	0.4±0.2	0.4±0.2	0.6±0.3	0.3±0.2	0.5±0.3	0.5±0.2	0.4±0.2	0.4±0.3	0.6±0.9	0.03
Platelet	226±93	285±132	346±143	274±128	330±130	298±117	223±115	255±120	210±148	0.08
Ferritin	1213±1143	1333±1304	795±689	1193±871	1554±1963	686±643	997±1063	1560±1208	2606±6784	0.59
D-dimer	1748±2836	1557±2188	965±1374	4009±77557	2091±4912	1150±917	1996±3144	2422±2256	5181±5321	0.005
CRP	114±87	89±72	8±20	118±86	80±64	9±16	154±102	132±91	154±126	0.005
LDH	383±135	385±130	265±84	472±219	442±175	290±83	389±238	450±170	583±567	0.005
ALT	38±29	52±58	89±83	54±45	79±73	62±45	38±29	50±63	112±174	0.004
AST	45±32	47±40	37±29	68±92	59±42	32±14	42±26	50±43	218±458	0.005
Procalcitonin	0.2±0.3	0.2±0.4	0.2±1.4	0.7±1.5	0.2±0.1	0.1±0.2	0.7±1.5	0.6±0.9	3.6±4.9	0.005
Troponin	20±68	73±662	16±41	40±60	74±163	67±118	40±57	35±47	132±160	0.45
Creatinin kinase	219±311	140±183	44±44	428±644	113±110	33±21	120±51	166±199	83±35	0.03
Fibrinogen	603±155	612±145	382±109	623±153	559±173	381±159	665±204	660±186	539±164	0.20
Creatinin	1.2±0.9	1.1±0.8	1.1±1.1	1.2±1.5	0.9±0.3	1.1±0.9	1.3±1.1	1.2±1	1.3±0.7	0.12

levels in dead patients indicating contribution of accompanying secondary infections. A similar pattern was observed when patients followed in the ward and ICU were analyzed separately (Table 2).

Conclusion: Laboratory parameters predicting the outcome of anti-cytokine treatments in the management of hyper-inflammatory response associated with COVID-19 are urgently needed. Analysis of this cohort of patients indicates that earlier use of anakinra treatment in hospitalized patients provides better results, and a decrease in CRP, ferritin, and D-dimer values, as well as an increase in lymphocyte count, are associated with favorable outcomes. Increasing values of D-dimer and troponin during the anakinra treatment were found to be associated with worse outcomes, possibly indicating cardiovascular and thrombotic pathologies not responding well to anakinra.

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Abstract Number: 1548

Q Fever as a Mimicker of Rheumatologic Conditions: A Case Series from Two Tertiary Care Academic Centers in Southern California

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Q fever, an endemic disease in Southern California, is a zoonosis caused by Coxiella burnetii. The infection can present with multiple non-specific acute and chronic manifestations including fever, headache, fatigue, endocarditis, and hepatitis. Q fever is also associated with the presence of elevated inflammatory markers and autoimmune antibodies. This combination of the clinical picture and laboratory features may be misinterpreted for various rheumatologic conditions.

Methods: We evaluated records of patients who were newly diagnosed with Q-fever during an inpatient stay at 2 academic medical centers from 2013 to 2021. Data was collected for all Q fever cases in whom rheumatology was consulted, including demographics, symptoms on admission, comorbidities, labs, imaging, tissue sample obtained, and medical specialties consulted. Inpatient rheumatology consultation reports were reviewed. The reason for the consult, differential diagnosis, the time it took from admission to rheumatology consult, and rheumatology consult to Q fever diagnosis were analyzed.

Table 1. Patient demographics and presenting symptoms of patients diagnosed with Q fever patients who received Rheumatology inpatient consultation (n=8)

Age in years (range)	20-65
Gender	
Male	4 (50%)
Female	4 (50%)
Comorbidities	
Hypertension	4 (50%)
Diabetes	4 (50%)
Hyperlipidemia	3 (37.5%)
Vestibular migraines	1 (12.5%)
Recent COVID infection	1 (12.5%)
Graves' disease	1 (12.5%)
Obesity	1 (12.5%)
CAD, heart failure, Atrial fibrillation	1 (12.5%)
Timing of symptom onset	
Jan-March	5 (62.5%)
April- June	2 (25 %)
July-Sept	1 (12.5 %)
Oct- Dec	0
Animal exposure	
Dog	2 (25 %)
Cow	2 (25 %)
Rat	1 (12.5%)
Cat	1 (12.5%)
Sheep	1 (12.5%)
Goat	1 (12.5%)
Horse	1 (12.5%)
None	1 (12.5%)
Presenting Symptoms	
Fever, chills, myalgia	7 (87.5%)
GI (nausea, vomiting, diarrhea, abdominal pain	5 (62.5%)
Weight loss, night sweats	2 (25%)
Headache	2 (12.5%)
Polyarthralgia	1 (12.5%)
Neck stiffness, confusion	1 (12.5%)

Table 2. Work-up done prior to rheumatology consult, specialties consulted, and abnormal results

Infectious workup		
Blood culture, urine culture, chest X-ray		8 (100%)
Coxiella		8 (100%)
HIV, hepatitis		6 (75%)
COVID		5 (62.5%)
Bartonella, Brucella		6 (75%)
EBV, CMV, HSV		7 (87.5%)
West Nile, VZV		3 (37.5%)
Coccidiodes, Histoplasma, Cryptococcus, Aspergillus		4 (50%)
C.diff, Stool culture, Stool O/P		
Syphilis, gonorrhea, chlamydia		2 (25%)
Malaria, Dengue		
		2 (25%)
ESR, CRP		8 (100 %)
Auto-immune hepatitis workup (anti- microsomal, liver and kidney, anti-smooth muscle, mitochondrial) Ceruloplasmin, alpha-fetoprotein, ferritin		5 (62.5%)
		5 (62.5%)
Lumbar puncture, CSF studies		3 (37.5%)
Rheumatologic serologies		
ANA panel		8 (100%)
Vasculitis panel		5 (62.5%)
RF, CCP		3 (37.5%)
APS		3 (37.5%)
Cryoglobulins		3 (37.5%)
ANA-hep 2, C3, C4		1 (12.5%)
Biopsy		**Findings**
Liver	2 (25 %)	Granulomatous hepatitis with ring granuloma
Skin	1 (12.5 %)	Perivascular, interstitial lymphohistiocytic inflammation, no vasculitis
Lymph node	1 (12.5 %)	Focal granulomatous inflammation with multinucleated giant cell formation
Temporal artery	1 (12.5 %)	No temporal arteritis
Bone marrow	1 (12.5 %)	
Imaging		
CT chest/abdomen/pelvis		3 (37.5%)
CT chest		2 (25%)
CT abdomen		1 (12.5%)
CT head, MRI brain		4 (50%)
Echocardiogram		7 (87.5%)
NM tagged WBC scan		1 (12.5%)
Number of medical specialties consulted		3-6, average 4.6/patient
Abnormal labs/imaging		
Elevated ESR/CRP		8 (100%)
Transaminitis		5 (62.5%)
Splenic infarct		1 (12.5%)
Positive ANA		1 (12.5%)
Positive RF		1 (12.5%)
Positive EBV IgG, CMV IgG, Rubella IgG		1 (12.5%)

ANA– antinuclear antibody; APS- antiphospholipid antibodies; CCP- Cyclic Citrullinated Peptide; RF-rheumatoid factor

Results: From 2013-2021, 23 patients were diagnosed with Q fever during an inpatient stay. Eight patients (34.7%) received rheumatology consultation prior to their Q fever diagnosis. Majority of the patients (62.5%) had symptom onset during the first quarter of the year, 75% of patients had exposure to cattle, sheep, goat, or rats, 37.5% had do-

Table 3. Details on rheumatology consultation, differentials, and workup

	Reason for rheumatology referral	Rheumatology Differentials	Labs and/additional consults requested by rheumatology	Imaging requested by rheumatology	Admit to Q fever diagnosis (in days)	Rheum consults to Q fever diagnosis (in days)
Case 1	FUO, elevated inflammatory markers	Infection, malignancy, Vasculitis, Behcet's, AOSD, Sarcoidosis	ANA panel, C3, C4, MPO, PR3, Vasculitis panel, Cryoglobulins, RF, CCP	CTA chest	10	6
Case 2	FUO, elevated inflammatory markers	AOSD, autoimmune hepatitis	ANA, APS, Vasculitis panel, Cryoglobulin, ANCA, Immunoglobulins, Genetic testing for fever syndromes	none	10	5
Case 3	FUO, elevated inflammatory markers	Autoimmune/auto-inflammatory, infection, malignancy, AOSD	Ferritin, ESR, CRP daily, ANA-hep 2, C3, C4	CT chest	11	6
Case 4	GCA evaluation	GCA	Temporal artery biopsy, ENT, Ophthalmology consult	CTA chest, MRI orbit	6	7
Case 5	FUO, elevated inflammatory markers, positive RF	Infection vs malignancy vs sJIA	Consider GI eval for IBD	None	7	1
Case 6	FUO, positive ANA	Infection, malignancy, AOSD, autoinflammatory syndromes	Ferritin, SSA, SSB, RF, CCP, auto-inflammatory gene panel (MEFV, MVK, TNFRSF1A)	None	13	6
Case 7	FUO, headaches, hepatitis, positive ANA	Aortitis, Autoimmune hepatitis, AOSD	ANCA, ANA hep 2, IgG4, liver biopsy, Ferritin, ESR, CRP, Cryoglobins	CTA chest, XR hands	12	3
Case 8	Sarcoidosis evaluation	Neurosarcoidosis, Pulmonary sarcoid, Autoimmune hepatitis, CNS vasculitis	TB quantiferon, ACE, Lysozyme, Vit D, Lumbar puncture, ANCA	MRI brain, cardiac MRI	16	13

ACE – angiotensin converting enzyme; ANA – antinuclear antibody; ANCA- Antineutrophil Cytoplasmic Antibodies; AOSD – adult-onset still's disease; APS- antiphospholipid antibodies; CCP- Cyclic Citrullinated Peptide; FUO –fever of unknown origin; GCA- giant cell arteritis; MPO- myeloperoxidase; PR3-proteinase 3; RF – rheumatoid factor; sJIA- Systemic juvenile idiopathic arthritis

mestic pet exposure, and 1 patient did not report any known animal exposure. Almost all (87.5%) patients had fever and flu-like symptoms, with 63% having GI symptoms. All patients had extensive infectious workup done. All patients had elevated inflammatory markers, and 63% with abnormal liver enzymes. One patient had a low titer antinu-

clear antibody and another one had a positive rheumatoid factor. Two patients underwent liver biopsy showing ring granulomas and granulomatous hepatitis, findings characteristic but not pathognomonic of Q fever.

Fever of unknown origin (FUO) was the most common (75%) reason for consultation while one patient each was referred for evaluation for giant cell arteritis (GCA) and sarcoidosis. In 50% of cases, the rheumatology service thought a rheumatologic disease is less likely and thus recommended additional studies for infectious or oncologic etiology. Rheumatologic differentials included adult-onset Still's disease, Bechet's disease, sarcoidosis, and systemic vasculitis including GCA. An auto-inflammatory gene panel was done in 2 patients and temporal artery biopsy was done in 1 patient with results all negative. On average, Q fever was diagnosed approximately 10.6 days after admission and 5.8 days after rheumatology consultation.

Conclusion: The non-specific presentation of Q fever, accompanied by elevated inflammatory markers, and autoimmune antibodies can mimic various rheumatologic conditions including vasculitis, Still's disease, and sarcoidosis. Our case series demonstrates that Q-fever should be considered as a differential diagnosis especially for patients with FUO and residing in endemic regions.

Disclosure: M. Aggarwal, None; **M. Cabling**, None.

Abstract Number: 1549

Experience from a Diverse Rheumatology Cohort with COVID-19: Are We Doing Better Than We Expected?

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has been particularly concerning for patients with rheumatologic conditions because they are potentially predisposed to more severe outcomes. Studies have suggested that higher steroid dose, rituximab and certain DMARDs were associated with worse COVID-19 outcomes while TNF-inhibitors were associated with better outcomes. However, more studies are needed to confirm these trends particularly in more diverse patient populations. Here, we evaluate a predominantly Black and Hispanic cohort of rheumatology patients with COVID-19 compared to controls on their infection-related outcomes.

Methods: An urban academic medical center has a registry of patients with rheumatological conditions and laboratory confirmed COVID-19 as well as a separate repository of COVID-19 patients without rheumatic disease. Data collected included demographics, comorbidities, medications, hospitalization and hospital course. Chi-squared, independent samples t-test, and logistic regression were used for analyses.

Results: Results are summarized in Tables 1 and 2. 175 rheumatology patients (43 SLE, 52 RA, 26 psoriasis and psoriatic arthritis, 22 other connective tissue diseases, 32 other diagnoses including inflammatory arthritis and myositis) and 481 control patients were evaluated. Both groups had a substantial portion of Black patients while the rheumatology group also included a significant number of Hispanic patients. Prevalence of DM was higher in the control group.

Table 1: Rheumatology patients vs Controls					
		Rheumatology patients (n= 175)	**Control (n= 481)**	**Odds Ratio, 95% CI (adjusted for gender, race, DM)**	**P value**
Age (years±SD)		51±16	52 ± 16		0.305
Gender (n female,%)		138 (79%)	280 (58%)		**0.001**
Ethnicity (n%)	Black	74 (43%)	320 (67%)		**0.001**
	White	30 (17%)	98 (20%)		
	Hispanic	61 (35%)	10 (2%)		
	Asian	2 (1%)	11 (2%)		
	Other	2 (1%)	42 (9%)		
BMI (kg/m2)		33 ± 9	33 ± 8		0.783
DM (n %)		27 (15%)	156 (32%)		**<0.001**
Hospitalization		51 (29%)	160 (33%)	1.3(0.84-2.1)	0.223
	ICU admission	16 (31%)	62 (39%)	0.8(0.4-1.6)	0.545
	Intubation (%)	9 (18%)	40 (25%)	0.7(0.3-1.6)	0.397
	Death	2 (4%)	12 (8%)	0.6(0.1-2.8)	0.503
	Length of stay (mean days)	12 ± 12	8 ± 5		**0.034**

Table 2. Medication related outcomes in rheumatology patients with COVID-19					
		Hospitalization	**OR (95% CI)**	**Death**	**OR (95% CI)**
GS	Yes (n=46)	16 (35%)	1.4 (0.7-2.9)	2 (4%)	5.8 (0.5-66.0)
	No (n=129)	35(28%)		1 (1%)	
DMARDs	Yes (n=62)	17 (27%)	0.9 (0.4-1.7)	2 (3%)	3.7 (0.3-42.0)
	No (n=113)	34 (30%)		1 (1%)	
Anti-TNF	Yes (n=22)	2 (9%)	**0.2 (0.0-.9)**	0 (0%)	1.0 (0.9-1.0)
	No (n=153)	49 (32%)		3 (2%)	
Rituximab	Yes (n=5)	4 (80%)	**10.5 (1.1-96.0)**	1 (20%)	**21.0 (1.6-282.0)**
	No (n=170)	47 (28%)		2 (1%)	

Patients with rheumatic disease had longer length of stay in the hospital (p=0.034), however, overall did not have increased odds of hospitalization, ICU admission, intubation, or death even after adjustment for confounders. GC and DMARD use were not associated with overall outcomes. There was decreased odds of hospitalization with use of TNF-inhibitors. Rituxan use was associated with increased odds of hospitalization and death.

Conclusion: This predominantly Black and Hispanic cohort of rheumatology patients with COVID-19 had very comparable outcomes overall to those without rhematic disease. TNF-inhibitor use was associated with decreased risk of hospitalization while rituximab use was associated with increased risk of hospitalization and death. These results are reassuring for our patients overall but suggest that we need to continue to evaluate subsets of our patients on

specific therapies for potentially better or worse outcomes. Continued sharing of data across the country and world will be invaluable in helping us provide appropriate guidance and management for our patients.

Disclosure: M. Grant, None; **M. Orentas**, None; **S. Hassan**, None; **S. Khandelwal**, None; **D. Moore**, None; **N. Shakoor**, DJO/DR. Comfort, 9, 10.

Abstract Number: 1550

Flares and Side Effects After COVID-19 Vaccination in Patients with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: There is increasing interest in the safety of COVID-19 vaccination in patients with underlying chronic conditions. We investigated the rates of side effects and/or disease flares in the short term after COVID-19 vaccination in patients with rheumatic diseases.

Methods: In this single-center observational study, we analyzed the proportion of self-reported systemic side effects and flares in patients with rheumatic diseases who received one of the approved COVID-19 vaccines in our country (BNT162b2, AZD1222, mRNA-1273 and JNJ-78436735) between Dec. 27, 2020 and May 28, 2021. Demographic data, type of rheumatic disease, activity of the disease determined by clinical scores when applicable, treatment, and previous SARS-CoV-2 infection were also collected.

Results: One-hundred and eighty patients (female=127) were included in the study. Median age was 70 years (range 23-92), due to the fact that our vaccination campaign began with older and fragile patients. Patient characteristics are summarized in Table 1.

Of the 180 patients, 146 received BNT162b2, 25 AZD1222, 8 mRNA-1273, and 1 patient received JNJ-78436735. Six patients reported SARS-CoV-2 infection prior to vaccination. Thirty-four patients (18.9%) reported systemic side effects after the first dose: BNT162b2 23/146 (15.7%); AZD1222 10/25 (40%); mRNA-1273 1/8 (12.5%); JNJ-78436735 0/1. A total of 118 patients had received the second dose of the BNT162b2 or mRNA-1273 vaccine at the time of data collection. Of these, 39 (33.1%) reported systemic side effects after the second dose: BNT162b2 38/112 (33.9%); mRNA-1273 1/6 (16.7%). The most frequent side effects were fever, headache, fatigue and arthromyalgia. All systemic side effects were mild and resolved spontaneously within a few days. Disease flare was reported in 1 out of the 180 patients (0.6%) who received the first dose, and in 4 out of the 118 patients (3.4%) who received the second dose. Two of these five patients had RA and three had PsA. All five had received BNT162b2. These results are illustrated in Table 2.

Conclusion: Preliminary results suggest that disease flares are possible but infrequent after COVID-19 vaccination in patients with rheumatic diseases. Rates of systemic side effects are comparable to the general population. Further

Table 1: Patient characteristics

Disease	Number of patients	Treatment	Disease activity
RA	64	csDMARD (22) bDMARD+csDMARD (11) csDMARD+CS (9) bDMARD (7) bDMARD+csDMARD+CS (4) tsDMARD (1) tsDMARD+csDMARD+CS (1) tsDMARD+csDMARD (1) CS (1) No treatment (7)	Remission (38) Mild disease (9) Moderate (17)
PsA	42	csDMARD (16) bDMARD (9) bDMARD+csDMARD (9) bDMARD+CS (1) CS (1) No treatment (6)	Remission (29) Mild disease (5) Moderate (8)
SpA	11	bDMARD (7) bDMARD+csDMARD (2) csDMARD (1) bDMARD+csDMARD+CS (1)	Remission (7) Mild disease (2) Moderate (2)
LES	4	csDMARD (3) csDMARD+CS (1)	Remission (3) Mild disease (1)
Other connective tissue diseases	20	csDMARD (4) csDMARD+CS (4) bDMARD+csDMARD (1) CS (1) No treatment (10)	NA
Vasculitis	9	CS (6) csDMARD+CS (1) bMDARD+CS (2)	NA
Others	30	CS (7) csDMARD+CS (3) csDMARD (2) bDMARD (1) bDMARD+CS (1) No treatment (16)	NA

Table 2: Disease flares after the first or second vaccine dose

1° DOSE	Treatment	Disease activity before COVID-19 vaccination	Disease activity after COVID-19 vaccination
Patient 1 (RA)	bDMARD+csDMARD+CS*	DAS 28=4.2 (moderate)	DAS 28=5.3 (severe)
2° DOSE	**Treatment**	**Disease activity before COVID-19 vaccination**	**Disease activity after COVID-19 vaccination**
Patient 2 (PsA)	csDMARD	DAPSA=10.1 (mild)	DAPSA=20.13 (moderate)
Patient 3 (PsA)	csDMARD	DAPSA=2.09 (remission)	DAPSA=13.14 (mild)
Patient 4 (PsA)	bDMARD	DAPSA=8.17 (mild)	DAPSA=17.17 (moderate)
Patient 5 (RA)	csDMARD+CS*	DAS28=3.07 (mild)	DAS28=5.5 (severe)

*CS (corticosteroid max 10 mg/day prednisone equivalent)

studies are needed with a larger number of patients with rheumatic diseases to better understand this phenomenon and possibly identify predictive factors for disease flare.

Disclosure: A. Carbone, None; **G. Vukatana**, None; **E. Vandelli**, None; **M. Trevisani**, None; **E. Rossi**, None; **R. Mulè**, None; **M. Fusconi**, None.

Abstract Number: 1551

Generation of Autoantibodies and Their Association with Rheumatic Disease Flares in Adult Patients with Autoimmune Inflammatory Rheumatic Diseases and General Adult Population Following BNT162b2 mRNA Covid-19 Vaccination

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
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Background/Purpose: The rapid spread of the COVID-19 pandemic has created the need for mass vaccination of patients with autoimmune rheumatic disease (AIIRD) despite the lack of information on the effect of BNT162b2 mRNA vaccine on the underlying autoimmune disease and the possible generation of autoantibodies. Our objective was to investigate the generation of autoantibodies following BNT162b2 mRNA vaccine and its association with disease flares in AIIRD patients compared with the general population.

Methods: We investigated the generation of autoantibodies as a part of a prospective study aimed to monitor immunogenicity, efficacy, and safety of the two-dose regimen BNT162b2 mRNAvaccine in adult patients with AIIRD including immune-mediated arthritis, connective tissues diseases (CTD), systemic vasculitis, and idiopathic inflammatory myositis (IIM) compared to control subjects from the general population. Sera were taken prior to vaccination and 2-6 weeks following the second vaccine dose to examine titers of antinuclear antibodies (ANA) measured by immunofluorescence and multiplex, antiphospholipid antibodies (aPL) and rheumatoid factor (RF). Data on generation of autoantibodies was calculated for each type of autoantibody individually based on number of patients with available data. Post-vaccination seroconversion was defined as any first-time ANA, aPL, or RF seropositivity. Pre- and post-vaccination disease activity indices were assessed as appropriate for each disease, and any signs or symptoms of new-onset AIIRD were noted in controls.

Results: A total of 166 AIIRD patients and 59 controls participated in the study, 72.9% (n=121) female. AIIRD patients were significantly older than controls, mean age 58.0±14.6 vs 50.8 ±14.7, respectively (p=0.008). Disease representation in AIIRD group included RA (47.0%), PsA (20.5%), AS (12.0%), SLE (11.4%), vasculitis (5.4%), IIM (2.4%), Sjogren's (0.6%), IGG4-RD (0.6%). A total of 94.6% (n=157) AIIRD patients were treated with immunomodulatory medications. Immunoserologic data before and following vaccination was available for ANA serology in 137 (82.5%) AIIRD patients and 45 (76.3%) controls; aPL serology for 134 (80.7%) AIIRD patients and 51 (86.2%) controls, and RF serology for 138 (83.1%) AIIRD patients and 50 (84.7%) controls. The ANA seroconversion rate was 10.2% (n=14)

in patients with AIIRD compared to 6.7% (n=3) in controls (p=0.570); the aPL seroconversion rate was 1.5% (n=2) in AIIRD compared to 0% in controls (p >0.99). No cases of RF seroconversion were observed in AIIRD patients or controls. There was no statistically significant difference in age or sex among individuals who experienced seroconversion to those who did not, regardless of AIIRD status. Post-vaccination disease activity remained stable in patients who generated autoantibodies and no new signs of disease onset were seen in healthy controls who underwent seroconversion in the followup period.

Conclusion: Vaccination with the BNTb262 vaccine resulted in the generation of autoantibodies in a minority of AIIRD patients and controls. Autoantibody generation was not associated with disease flares or new-onset disease.

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Abstract Number: 1552

Systemic Autoimmune Conditions and Hospital Admissions in Covid-19 Infection

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic continues worldwide and has had a strong impact on public health. From the beginning of the pandemic, efforts were intensified to identify risk factors for development of the severe form of COVID-19.

In patients with rheumatic and musculoskeletal diseases (RMDs) and infected with COVID – 19, we aim to investigate the role of systemic autoimmune conditions compared to other type of RMDs in severity of COVID-19 in terms of hospital admissions.

Methods: An observational longitudinal study was conducted during the epidemic peak in Madrid (1stMar to 20thMay2020). All patients attended at the rheumatology outpatient clinic of a tertiary hospital with a diagnosis of RMDs and Covid-19 infection were included (according to a medical diagnosis or confirmed with a positive SARS-CoV-2 PCR diagnostic test). All patients were included since the time of COVID-19 diagnosis. The main outcome: hospital admissions related to COVID – 19 infection in patients with RMDs. Independent variable: Type of RMD including: autoimmune (systemic autoimmune conditions (SAC) and inflammatory join disease (IJD) and non - autoimmune diseases (mechanical diseases, and inflammatory diseases (mycrocrystaline arthritis and tendonitis)). Covariables: 1) Sociodemographic baseline characteristics. 2) Baseline comorbid conditions. 3) Treatment for the RMDs: a) Glucocorticoids, b) conventional syntethetic DMARDs (csDMARDs) and c) targeted syntethetic/biologic DMARDs

(ts/bDMARDs). Statistical análisis: description of the sociodemographic, clinical and treatment characteristics of the patients. A multivariate logistic regression adjusted by age, sex and comorbidities was used to evaluate the risk of the different types of RMDs in hospital admissions related to COVID – 19. The results were expressed as OR with its corresponding confidence Interval (95% CI).

Results: 405 patients were included with RMDs and COVID – 19 infection. 69, 14% were women with a mean age at diagnosis of 60 ± 15,26 years. The evolution time from the diagnosis of RMD was 8 ± 8,4 years. Of the 405 patients, 243 (60%) had non – autoimmune RMD and 162 (40%) ((106 (65,43%) IJD and 56 (34,56%) SAC) had autoimmune RMD. 36% of all patients were admitted (31% from non - autoimmune RMDs, 36% for autoimmune RMD (IJD) and 57% for autoimmune RMD (SAC) (p =0,001). After adjusting by confounders, the risk of hospital admission in non -autoimmune RMD compared to SAC (OR: 0.28 [0.13-0.59], p = 0.001) and autoimmune RMD IJD compared to SAC (OR IJD: 0.34 [0.15-0.78], p = 0.011) was lower. Advanced age (OR: 1.10 [1.07-1.12], p < 0.001), male (OR female sex (OR: 0.59 [0.34-1.03], p=0.067) and more number of comorbidities (OR: 1.38 [1.01-1.88] increased the risk of hospitalization related to COVID-19.

Conclusion: One third of the RMD patients infected with COVID-19 required hospital admission. This study shows that patients with autoimmune and specifically with systemic autoimmune conditions have a higher risk of hospitalization related to COVID-19. We also show that advanced age, male sex and a higher number of comorbidities can contribute to worsen the prognosis of the COVID-19 disease.

Disclosure: I. Perez - Sancristobal, None; **L. Lopez Pedraza**, None; **M. Álvarez Hernández**, None; **J. Colomer**, None; **A. Madrid - Garcia**, None; **B. Fernandez**, None; **C. Martínez - Prada**, None; **L. Rodriguez Rodriguez**, None; **A. Mucientes**, None; **L. Leon - Mateos**, None; **L. Abasolo**, None.

Abstract Number: 1553

Low-dose Tocilizumab in the Treatment of COVID-19 Pneumonitis: 90-day Mortality Follow-up

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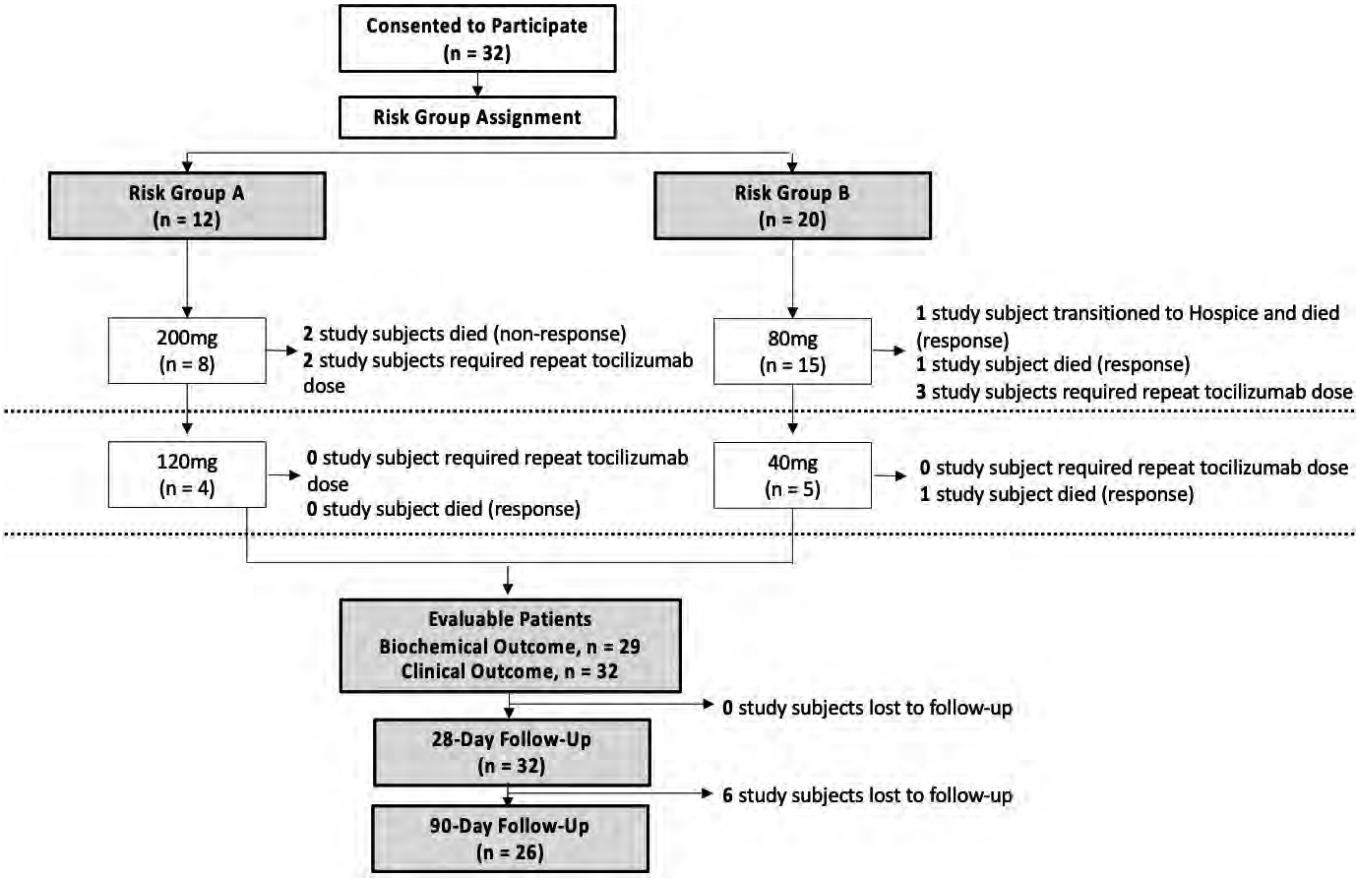
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Tocilizumab (TCZ) for treatment of severe coronavirus disease 2019 (COVID-19) pneumonia decreases the probability of progression to invasive mechanical ventilation (CORIMUNO-TOCI) or death (REMAP-CAP, RECOVERY). Standard doses of 400-800 mg or 8 mg/kg of body weight have been used in previous studies; however, determining the optimal dose is critical given the possibility of increased rates of infection in higher doses and limited global supplies. The COVIDOSE study evaluated the pharmacodynamic and clinical efficacies, safety and dose response of low-dose TCZ in COVID-19.[1] With the emergence of "long COVID" sequelae, we present follow up to COVIDOSE with analysis of 90-day mortality.

Methods: This was an adaptive phase 2 study of low-dose TCZ in hospitalized, non-mechanically ventilated adult patients with COVID-19 pneumonitis, C-reactive protein (CRP) ≥ 40 mcg/mL, and at least 1 epidemiologic risk factor for increased risk of COVID-related death (e.g. underlying medical conditions). Dose cohorts were determined by a



Study design.

trial Operations Committee, with the initial doses of 80 or 200 mg. Doses were decreased to 40 mg and 120 mg after interim assessment. Pre-specified secondary objectives included 28-day mortality; 90-day mortality was a later addendum given the emergence of "long COVID."

Results: Thirty-two patients received low-dose TCZ (Figure 1). Within the 28-day follow up period, 5 (16%) patients died. Within the 90-day follow up period, 6 participants were lost to follow up, and 6 (23%) had died (including 5 who died within the 28-day period). Four out of 6 died during index COVID-19 hospitalization. Mean baseline CRP did not differ between patients who died versus those alive at 90 days (158 ± 96 mcg/mL vs 158 ± 83 mcg/mL). Mean CRP decrease in the 24 hours following first TCZ dose did not differ between patients who died vs those alive at 90 days (38 ± 11% vs 34 ± 15%).

Conclusion: Ninety-day mortality rate in this small phase 2 study was 23%, with 1 out of 26 patients dying between the 28-day and 90-day mark. Previously reported 90-day mortality rate of similar patients with elevated CRP receiving usual care has been reported at 35%.[2] These findings support our actively enrolling randomized controlled trial of low-dose tocilizumab versus standard of care in hospitalized, non-invasively ventilated patients with COVID-19 pneumonia, COVIDOSE2 (ClinicalTrials.gov NCT04479358). (ClinicalTrials.gov COVIDOSE Identifier: NCT04331795)

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Disclosure: L. He, None; **G. Strohbehn**, University of Chicago, 10; **P. Reid**, Co-inventor of a filed patent covering the use of low-dose tocilizumab in viral infections., 10.

Abstract Number: 1554

COVID-19 Vaccine Hesitancy Among Patients with Rheumatic and Other Diseases

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SESSION INFORMATION

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Background/Purpose: Vaccination is fundamental to reduce COVID-19 risk and its complications. Vaccine hesitancy is a threat to COVID-19 vaccination uptake. We assessed the frequency of COVID-19 vaccine hesitancy among RD and other patients.

Methods: Between Nov-Dec 2020 (prior to COVID-19 vaccine roll-out), a cross-sectional survey was completed by patients presenting to a Canadian university-affiliated hospital network for influenza immunization. Sociodemographics, comorbidities, concomitant medications, previous COVID-19 infection, and perceptions related to COVID-19 vaccination (e.g., likelihood of receiving a future COVID-19 vaccine, causes of vaccine hesitancy) were assessed. We defined 3 specific groups: (i) RD, (ii) non-RD immunosuppressed patients (HIV, cancer, transplant, inflammatory bowel disease), and (iii) other. According to self-reported likelihood to receive a future COVID-19 vaccine and the tertile distribution of the responses, patients were classified as significantly hesitant (scores 0-7); somewhat hesitant (scores 7.5-9.5), or non-hesitant (score 10). Logistic regression using backward stepwise variable selection was performed to evaluate determinants of vaccine hesitancy.

Results: Among 2491 people vaccinated, 1793 people completed the survey (72%). Of those, 820 were patients (45.7%), 542 physicians or nurses (30.2%), 228 patients' family members (12.7%), and 203 other (11.3%). Participants had a mean age (±SD) of 52.2±16.9 years, and 58.6% were females. Just over one-tenth (10.7%, n=191) had RD, 9.4% (n=169) were immunosuppressed non-RD patients, and the remaining were other participants. Concerning COVID-19 vaccination, most subjects were non-hesitant (n=1124, 62.7%), 315 were somewhat hesitant (17.6%), and 354 (19.7%) significantly hesitant. RD patients were significantly more hesitant than other groups (hesitant %: RD: 44.5 vs. non-RD immunosuppressed: 30.8 - OR:1.80, 95% CI: 1.17 - 2.78; RD: 44.5 vs. other: 37.1 - OR: 1.36, 95% CI: 1.00 - 1.84). Vaccine hesitancy was associated with the following: perception that COVID-19 vaccines should not be mandatory; having concerns about vaccine safety; and being uncertain if vaccine benefits overweight its risks. Table 1 for predictors of vaccine hesitancy.

Table 1. Factors associated with COVID-19 vaccine hesitancy among people receiving influenza vaccine (no hesitancy as a reference group); (a) HIV, transplant, cancer, and inflammatory bowel disease; (b) Distance to the vaccine provider, time needed to get to the vaccine provider, waiting time at the vaccine provider, cost/parking in getting to the vaccine provider, and efforts of traveling to the vaccine provider; (c) Participants that were not receiving immunosuppressant treatment or did not have a disease that affects the immune system

Predictors of Vaccine Hesitancy	OR (95% CI)
Rheumatic diseases	
COVID-19 vaccine should be compulsory	
No	**8.34 (2.33 - 29.92)**
Unsure	**15.84 (6.42 - 39.10)**
Yes	Ref
Concerned that a future covid vaccine might not be safe	
Very concerned	4.69 (0.74 - 29.89)
A little concerned	**5.55 (1.84 - 16.68)**
Not concerned at all	Ref
Vaccine benefits, in general, overweigh their risks	
No	2.60 (0.42 - 16.22)
Unsure	**2.80 (1.18 - 6.60)**
Yes	Ref
Immunosuppressed (not due to rheumatic diseases)[a]	
Education	
Some High-School or Less	**11.02 (1.26 -96.02)**
High-School Graduate	**6.12 (1.39 - 27.02)**
Technical/Vocational Training	2.08 (0.63 - 6.86)
Bachelor's Degree or Above	Ref
Feeling of receiving enough information about COVID-19 prevention	
No	73.63 (4.51 - >100)
Yes	Ref
COVID-19 vaccine should be compulsory	
No	**31.23 (6.03 - >100)**
Unsure	**26.84 (7.87 - 91.59)**
Yes	Ref
≥1 barrier to access vaccination[b]	
Yes	**0.20 (0.06 - 0.68)**
No	Ref
Concerned that a future covid vaccine might not be safe	
Very concerned	2.73 (0.29 - 25.98)
A little concerned	**8.17 (1.93 - 34.67)**
Not concerned at all	Ref
Vaccine benefits, in general, overweigh their risks	
No	5.61 (0.59 - 53.0)
Unsure	**5.30 (1.67 - 16.82)**
Yes	Ref
Other[c]	
Employment	
No	**1.84 (1.21 - 3.02)**
Yes	**1.73 (1.18 - 2.53)**
Retired	Ref
Education	
Some High-School or Less	**2.21 (1.19 - 4.10)**
High-School Graduate	1.39 (0.92 - 2.10)
Technical/Vocational Training	**1.37 (0.98 - 1.93)**
Bachelor's Degree or Above	Ref
Diabetes	
Yes	**1.91 (1.19 - 3.06)**
No	Ref
Feeling of receiving enough information about COVID-19 prevention	
No	**2.61 (1.45 - 4.69)**
Yes	Ref
COVID-19 vaccine should be compulsory	
No	**7.47 (4.95 - 11.28)**
Unsure	**6.05 (4.46 - 8.23)**
Yes	Ref
Trust pharmaceutical companies to provide safe and effective COVID-19 vaccines	
No	**3.01 (1.58 - 5.73)**
Unsure	**2.20 (1.63 - 3.0)**
Yes	Ref
Concerned that a future covid vaccine might not be safe	
Very concerned	**6.86 (3.38 - 13.91)**
A little concerned	**2.30 (1.57 - 3.39)**
Not concerned at all	Ref
Vaccine benefits, in general, overweigh their risks	
No	1.31 (0.57 - 3.02)
Unsure	**2.68 (1.84 - 3.91)**
Yes	Ref
Perceive social pressure to receive a future COVID-19 vaccine	
Yes	**1.59 (1.13 - 2.23)**
Unsure	**2.24 (1.50 - 3.34)**
No	Ref

Conclusion: COVID-19 vaccine hesitancy was common among RD patients receiving influenza vaccination. Vaccine hesitancy in RD was higher than in other immunosuppressed patients and the general population. Factors associated with vaccine hesitancy are not unique to RD. Education about the benefits and safety of COVID-19 vaccines might enhance vaccine uptake among RD patients.

Disclosure: V. Valerio, None; **E. Rampakakis**, None; **M. Hudson**, None; **S. Bernatsky**, None; **E. Hazel**, None; **I. Colmegna**, None.

Abstract Number: 1555

Clinical Outcomes of Coronavirus Disease-2019 (COVID-19) in Hospitalized Patients with Rheumatic and Musculoskeletal Diseases (RMD)

Ikwinder Kaur[1], Mohsin Mughal[2], Abdul Asbeutah[3], Mili Kakadia[2], Reem Alhashemi[4], Hasan Mirza[5], Harjot Jagdey[6], Rasha Alhashimi[7], vishakha sirpal[2], Punit Jariwala[2] and Eugenio Capitle[8], [1]Monmouth Medical Center, an affiliate of Rutgers health system, Long Branch, NJ, [2]Monmouth Medical Center, Long Branch, NJ, [3]University of Tennessee Health Science Center, Memphis, TN, [4]Monmouth Medical Center, Long Branch, NJ, [5]Berkshire Medical Center, Pittsfield, MA, [6]BronxCare Hospital, Bronx, NY, [7]BIDMC, Havard, Boston, MA, [8]Rutgers New Jersey Medical School, New Brunswick, NJ

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 has been implicated in an exaggerated inflammatory response by activating both innate and adaptive immune responses. Rheumatic disease patients are a vulnerable population because of the underlying dysregulated immune system. The data regarding the impact of COVID-19 on rheumatic disease patients is limited. Data is heterogenous whether the patients on immunomodulatory therapy have lower mortality due to mitigation of immune response. Our study aimed to analyze the clinical characteristics of COVID-19 in hospitalized inflammatory rheumatic disease patients. And, compared the patients on chronic immunosuppression with those who weren't on immunosuppressive therapy.

Methods: This is a single-center study performed in a community hospital in the state of New Jersey. The adult patients with confirmed SARS-CoV-2 infection by nasopharyngeal RT-PCR who were hospitalized from March 2020 to January 2021 were screened for RMD. Data were manually extracted using the hospital's electronic medical record retrospectively after IRB approval. Categorical variables were compared by conducting a chi-square test while continuous ones were compared by conducting a median two-sample t-test. Statistical analysis was done with SAS software.

Results: A total of 600 patients were admitted under medicine service. Out of these, 19 patients (3.1 %) had documented RMD. These included Rheumatoid arthritis (n=4), SLE (n=1), systemic sclerosis (n=2), Sjogren syndrome(n=1), gout (n=8), sarcoidosis (n=1), familial Mediterranean fever (n=1), psoriatic arthritis (n=1), ANCA induced vasculitis (n=1) and polymyalgia rheumatica (n=1). The median age was 73 years, 57.9% were male (Table 1). The most common comorbidity was hypertension (n=13) followed by diabetes mellitus(n=6) and chronic kidney disease (n=5). Shortness of breath was the most common presenting symptom followed by fever. None had a rheumatic disease flare-up. In terms of treatment, 52.6% received steroids, 31.6% hydroxychloroquine, 31.6% remedesivir, 26.1% IL-6 inhibitor, and 10.5 % were treated with convalescent plasma. ICU level of care was required in 26.3% and 10.5%

Table 1. Baseline characteristics

Demography	All patients(n=19)	Cohort-1 (n=12) Patients not on chronic immunosuppression	Cohort-2 (n=7) Patients on chronic immunosuppression	p-value
Age -Median (IQR)	73.0 [63.0-83.0]	73.9 [67.75-91.0]	67.0 [63.0-78.0]	0.227
Male (n,%)	11 (57.9)	8 (66.7)	3 (42.9)	0.377
Caucasian (n,%)	6 (31.5)	2 (16.7)	4 (57.1)	0.129

Table 2. Inflammatory markers

Inflammatory markers (median, IQR)	All patients(n=19)	Cohort-1 (n=12) Patients not on chronic immunosuppression	Cohort-2 (n=7) Patients on chronic immunosuppression	p-value
CRP at admission (median, IQR)	122.0 [47.5-176.5]	122 [9.7-197]	107.7 [29.0-152.1]	0.884
Peak CRP (median, IQR)	146.0 [76.3-196.0]	142.7 [60.1-187.9]	146.0 [68.9-201.5]	1.00
Ferritin at admission (median, IQR)	584.0 [324.5-1096.5]	786.0 [298.8-1193.8]	1294.5 [558.5-1840.8]	0.315
Peak ferritin (median, IQR)	1251.5 [1082.3-1920.5]	1251.5 [1089.8-5161.5]	1501.0 [613.5-1920.5]	0.933
LDH at admission (median, IQR)	383.5 [278.5-583.3]	313.0 [261.0-528.5]	474.0 [434-657.0]	0.073
Peak LDH (median, IQR)	474.5 [307.3-626.5]	423.0 [272.0-624.5]	491.0 [434-695.5]	0.438
D-Dimer at admission (median, IQR)	1.68 [0.57-2.43]	1.82 [0.63-4.28]	0.65 [0.43-2.0]	0.181
Peak D-dimer (median, IQR)	1.82 [0.95-4.35]	2.25 [1.4-4.4]	1.16 [0.54-3.67]	0.368

were intubated. Overall, 84.2% were discharged from the hospital and 15.8% had a poor outcome and died. The patients were further divided into two cohorts. Cohort 2 included patients who were on chronic DMARDs or immunosuppression therapy (methotrexate, cyclosporine, hydroxychloroquine, and oral steroids). None of the patients were on biologic DMARDs. There was no statistically significant difference in inflammatory markers (CRP, LDH, D-dimer, ferritin) on admission and peak values during the hospitalization (Table 2). There was no significant difference in complication rate and final outcomes (ICU admission, intubation, discharged alive) between the two cohorts (Table 3).

Conclusion: Our study revealed that 3.1% of hospitalized COVID-19 patients had the RMD. There was no statistically significant difference in inflammatory markers, complication rate, and final outcomes among patients on chronic immunosuppressive therapy vs those who were not on any immunosuppressant. The limitation of our study is a small sample size and a single-center retrospective data.

Table 3. Complications and final outcomes

Complications (n,%)	**All patients(n=19)**	**Cohort-1 (n=12)** **Patients not on chronic immunosuppression**	**Cohort-2 (n=7)** **Patients on chronic immunosuppression**	**p-value**
Septic shock (n,%)	1 (5.3)	1 (8.3)	0 (0)	1.00
ARDS (n,%)	6 (31.6)	4 (33.3)	2 (28.6)	0.829
AKI (n,%)	1 (5.3)	1 (8.3)	0 (0)	1.00
New dialysis (n,%)	0	0	0	
Superinfection (n,%)	2 (10.5)	1 (8.3)	1 (14.3)	1.00
Thrombosis (n,%)	0	0	0	
Tachyarrhythmias (n,%)	1 (5.3)	1 (8.3)	0 (0)	1.00
None of above (n,%)	5 (26.2)	3 (25)	2 (28.6)	1.00
Final outcome(n,%)				
ICU level of care (n,%)	5(26.3%)	3 (25%)	2(28.6%)	0.509
Intubated (n,%)	2 (10.5)	2 (16.7)	0 (0)	0.509
Discharge alive (n,%)	16 (84.2)	9 (56.3)	7 (43.8)	0.149
Died in the hospital (n,%)	3(15.8)	3 (25)	0 (0)	0.149
Length of stay-days(median, IQR)	7.0 [4-12]	5.5 [4-11]	7 [3-18]	0.312

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Abstract Number: 1556

Mortality Rate Related to COVID-19 in Rheumatic and Musculoskeletal Diseases (RMDs)

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In patients with rheumatic and musculoskeletal diseases (RMDs) and infected with Covid – 19, a) we want to assess the mortality rate (MR) related to COVID-19; and b) to analyze the role of RMDs in mortality risk.

Methods: An observational longitudinal study was conducted during the epidemic peak in Madrid (1stMar to 20thMay2020). All patients attended at the rheumatology outpatient clinic of a tertiary hospital with a diagnosis of RMDs and SARS - CoV 2 infection were included (according to a medical diagnosis or confirmed with a positive SARS-CoV-2 PCR diagnostic test). **Main outcome:** death related to COVID-19 infection. **Independent variable:** type of RMDs including: autoimmune (systemic autoimmune conditions (SAC) and inflammatory joint disease (IJD)) and non–autoimmune (mechanical diseases and inflammatory diseases (microcrystalline arthritis and tendonitis)). **Covariates:** sociodemographic, comorbidities, treatment for the RMDs.

Survival techniques were used to estimate the MR related to COVID-19, given per 1,000 persons-month with a 95% confidence interval [CI]. The time of observation comprised the elapsed time between the date of COVID-19 diagnosis of infection until the date of patient's death, or end of study. Cox multiple regression analysis was run to examine the effect of autoimmune RMDs compared to non-autoimmune RMDs on mortality risk adjusted by sex, age and comorbidities. Results were expressed by Hazard Ratio (HR) and [CI].

Results: 405 patients were included with RMD and COVID – 19 infection with a total follow-up 642.57 patients-month. 69.14 % were women with a mean age at diagnosis of 59.37 ± 15.26 years. The evolution time from the diagnosis of rheumatic disease was 7.62 ± 8.39 years. Of the 405 patients, 243 (60%) had non-autoimmune RMD and 162 (39.9%) (106 (65.43%) IJD, 56 (34.56%) systemic condition) had autoimmune RMD. Of the 405 patients, 44 (11%) died during the follow-up, being 12± 14 days the mean time from infection to death (P50: 6[2-12] and a maximum of 60 days). MR was estimated in 68.48 [50.96-92.01] per 1,000 persons-month. CMR was higher for men (MR 105.45 [68.03-163.45]) than for women (MR 52.99 [35.52-79.06]) and in older people (MR < 60: 4.47, [0.67-31.70]; MR 60-75 years: 32.28 [13.44-77.55]; MR >75Years: 487.18 [354.49-669.53]). The HR of mortality in autoimmune RMDs compared to non-autoimmune RMDs did not achieved statistical significance (HR: 1.39 [0.77-2.5], p=0.27). After adjusting for confounders, we did not find higher risk of mortality among the different types of RMDs (HR autoimmune vs non-autoinmunes: HR: 1.12 [0.6-2.02], p=0.7; HR IJD vs SAC; 1.42 [0.58-3.48], p=0.441; HR non-autoimmune vs SAC: 1.19 [0.52-2.68], P=0.677). Age (HR: 1.13; [1.10-1.15], p< 0.001), and the presence of comorbidities (HR: 2.43; [1.16-4.15], p=0.015) increased the Mortality risk.

Conclusion: In patients with RMD and COVID-19 infection, we found a mortality rate of 68.5 per 1000 persons-month. This study shows that the mortality risk related to COVID-19 is similar between autoimmune and non-autoimmune diseases after adjusting by confounders. We also found that age and comorbidities are risk factors for mortality related to COVID-19 infection.

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Abstract Number: 1557

Immunogenicity and Safety of an Inactivated Virus Vaccine Against SARS-CoV-2 in Patients with Autoimmune Rheumatic Diseases

Ana Medeiros-Ribeiro[1], Nadia Aikawa[1], Carla Gonçalves Schahin Saad[1], Emily Figueiredo Vieira Neves Yuki[1], Tatiana do Nascimento Pedrosa[1], Solange Fusco[1], Priscila Rojo[1], Rosa Pereira[1], Samuel Shinjo[1], Danieli Andrade[1], Percival Sampaio-Barros[1], Carolina Ribeiro[1], Giordano Deveza[1], Victor Adriano de Oliveira Martins[1], Clovis Artur Silva[1], Marta Lopes[1], Alberto Duarte[1], Leila Antonangelo[1], Ester Sabino[1], Esper Kallas[1], Sandra Gofinet Pasoto[2] and Eloisa Bonfá[1], [1]Hospital das Clinicas da Faculdade de Medicina da Universidade de São Paulo, São Paulo, Brazil, [2]Hospital das Clinicas de Medicina da Universidade de São Paulo, São Paulo, Brazil

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Brazil is among the countries with the highest numbers of confirmed cases and deaths by COVID-19. CoronaVac (SARS-CoV-2 inactivated vaccine) has been largely used as the main available immunogen for COVID-19 in several countries and it is reported to have 50.7% efficacy. However, its immunogenicity in immunocompromised individuals has not been established. The objective is to evaluate the immunogenicity and safety of the inactivated virus vaccine against SARS-CoV-2 (CoronaVac) in autoimmune rheumatic diseases (ARD) patients.

Methods: This was a prospective controlled study of 910 adult ARD patients and 182 age- and sex-matched control group (CG) who received two doses of CoronaVac. Both groups had negative serology and neutralizing antibodies for COVID-19 at baseline. **Anti-SARS-CoV-2 IgG and neutralizing antibodies (NAb) were assessed prior to each vaccine shot (D0 and D28) and 6 weeks after the 2nd dose (D69).** Blood samples were collected from all participants for quantitative serological testing for IgG antibodies against SARS-CoV-2 S1/S2 proteins (DiaSorin) and NAb (GenScript). The primary outcome was immunogenicity (seroconversion rate of anti-SARS-CoV-2 IgG, and frequency of patients with NAb) at D69. Geometric mean titers (GMT) and factor increase in GMT (FI-GMT) of anti-SARS-CoV-2 IgG, and median (interquartile) percentage of neutralizing activity of NAb were also calculated. ARD patients and CG were vaccinated with standardized schedule (**28-days interval)** and evaluated using COVID-19 symptoms and adverse events **(AE)** diaries, three face-to-face visits, and 24-hs available phone, Whatsapp and e-mail contact.

Table 1 - Seroconversion (SC) rates and anti-SARS-CoV-2 S1/S2 IgG titers before and after the first and second doses of CoronaVac vaccination in autoimmune rheumatic diseases (ARD) and Control Group (CG)

	Before vaccine 1st dose	After vaccine 1st dose			After vaccine 2nd dose		
	GMT	SC	GMT	FI-GMT	SC	GMT	FI-GMT
CG, n= 179	2.3 (2.1-2.4)	62 (34.6)	10.3 (8.5-12.5)$^{\text{Ŧ}}$	4.6 (3.9-5.4)	171 (95.5)	67.0 (59.8-74.9)$^{\text{Ŧβ}}$	29.7 (26.3-33.5)
ARD, n= 859	2.2 (2.2-2.3)	161 (18.7)*	5.1 (4.7-5.5)*$^{\#}$	2.3 (2.1-2.5)*	605 (70.4)*	27.0 (24.7-29.5)*$^{\#\alpha}$	12.1 (11.0-13.2)*
CIA, n= 430	2.2 (2.1-2.2)	64 (14.9)*	4.4 (4.0-4.9)*	2.1 (1.9-2.3)*	304 (70.7)*	26.3 (23.3-29.8)*	12.2 (10.8-13.8)*
Other ARD, n= 429	2.3 (2.2-2.4)	97 (22.7)*	5.9 (5.3-6.6)*	2.5 (2.3-2.8)*	301 (70.2)*	27.7 (24.3-31.6)*	12.0 (10.5-13.7)*

Results are expressed in geometric mean (95%CI) and n (%). GMT – Geometric mean titers (AU/mL); SC – seroconversion (defined as post vaccination titer > 15 AU/mL - Indirect ELISA, LIAISON® SARS-CoV-2 S1/S2 IgG, DiaSorin, Italy); FI-GMT – factor increase of Geometric mean titers; ARD – autoimmune rheumatic diseases; CG – control group; CIA – chronic inflammatory arthritis (rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis); Other ARD– systemic lupus erythematosus, primary vasculitis, systemic sclerosis, primary Sjögren syndrome, idiopathic inflammatory myopathies and primary antiphospholipid syndrome; * - p<0.001 in comparison among ARD and CG at the same time points; # - p<0.001 for longitudinal comparisons of GMT in ARD at D28 and D69 vs. baseline; α - p<0.001 for longitudinal comparison of GMT in ARD at D69 vs. D28; Ŧ - p<0.001 for longitudinal comparison of GMT in CG at D28 and D69 vs. baseline; β - p<0.001 for longitudinal comparison of GMT in CG at D69 vs. D28.

Table 2 – Frequency of neutralizing antibodies (NAb) and median percentage of neutralizing activity in positive cases, after the first and second doses of CoronaVac vaccination in autoimmune rheumatic diseases (ARD) in comparison to control group (CG).

	After vaccine 1st dose		After vaccine 2nd dose	
	Subjects with positive NAb, N (%)	Neutralizing activity (%) Median (interquartile range)	Subjects with positive NAb, N (%)	Neutralizing activity (%) Median (interquartile range)
CG, n=179	65 (36.3)	45 (34 .5-71.1)	142 (79.3)	64.5 (48.4-81.4)
ARDs, n= 859	177 (20.6)*	42.6 (35.8-60.4)	484 (56.3)*	58.7 (43.1-77.2) ***
CIA, n= 430	75 (17.4)*	41.4 (33.5-57.2)	230 (53.5)*	57.8 (42.5-72.8) **
Other ARDs, n= 429	102 (23.8)**	44.6 (37.3-60.9)	254 (59.2)*	59.4 (44.2-80)

Results are expressed in median (interquartile range) and n (%). Positivity for Nab defined as a neutralizing activity ≥30 % (cPass sVNT Kit, GenScript, Piscataway, USA) ***p<0.05, **p <0.01 and *p <0.001 in comparison to CG ARD – autoimmune rheumatic diseases; CG – control group; CIA – chronic inflammatory arthritis (rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis); Other ARD – systemic lupus erythematosus, primary vasculitis, systemic sclerosis, primary Sjögren syndrome, idiopathic inflammatory myopathies and primary antiphospholipid syndrome.

Table 3 – Baseline characteristics of ARD patients with and without seroconversion (SC) for anti-SARS-CoV-2 S1/S2 IgG antibodies and with and without neutralizing antibodies (NAbs) after two doses of CoronaVac vaccination

	ARD patients without SC (n=254)	ARD patients with SC (n=605)	*p* value	ARD patients without NAbs (n=375)	ARD patients with NAbs (n=484)	*p* value
Demographics						
Current age, years	53 (45-63)	49 (39-59)	**<0.001**	52 (43-62)	49 (39-59)	**<0.001**
Age ≥ 60years	89 (35)	142 (23.5)	**<0.001**	122 (32.5)	109 (22.5)	**0.001**
Female sex	208 (81.9)	452 (74.7)	**0.023**	293 (78.1)	367 (75.8)	0.427
Caucasian race	144 (56.7)	312 (51.6)	0.170	213 (56.8)	243 (50.2)	0.055
ARD						
CIA	126 (49.6)	304 (50.2)	0.864	200 (53.3)	230 (47.5)	0.091
Other ARD	128 (50.4)	301 (49.8)		175 (46.7)	254 (52.5)	
CURRENT THERAPY						
Prednisone	142 (55.9)	188 (31.1)	**<0.001**	185 (49.3)	145 (30.0)	**<0.001**
Prednisone dose, mg	5 (5-10)	5 (5-10)	0.926	5 (5-10)	5 (5-10)	0.731
Prednisone ≥ 20mg/day	14 (5.5)	16 (2.6)	**0.037**	15 (4)	15 (3.1)	0.476
Immunosuppressive drugs	208 (81.9)	330 (54.5)	**<0.001**	272 (72.5)	266 (55)	**<0.001**
Biologic therapy	112 (44.1)	195 (32.2)	**<0.001**	155 (41.3)	152 (31.4)	**0.003**

Results are expressed in median (interquartile range) and n (%). ARD – autoimmune rheumatic disease; CIA – chronic inflammatory arthritis (rheumatoid arthritis, axial spondyloarthritis and psoriatic arthritis); Other ARD – systemic lupus erythematosus, primary vasculitis, systemic sclerosis, primary Sjögren syndrome, idiopathic inflammatory myopathies and primary antiphospholipid syndrome. SC – seroconversion defined as a positive serology (IgG titer > 15 AU/ml) for anti-SARS-CoV-2 S1/S2 IgG antibodies after vaccination (Indirect ELISA, LIAISON® SARS-CoV-2 S1/S2 IgG, DiaSorin, Italy). Positivity for Nabs defined as a neutralizing activity ≥ 30 % (cPass sVNT Kit, GenScript, Piscataway, USA).

Symptomatic cases were tested by RT-PCR for SARS-CoV-2 and a subgroup of positive samples were evaluated for the presence of variants of concern (P.1, B.1.1.7, and B.1.351 lineages).

Results: We observed significant lower anti-SARS-Cov-2 IgG seroconversion (70.4% vs. 95.5%,p< 0.001) and GMT [12.1(95%CI 11.0-13.2) vs. 29.7(95%CI 26.3-33.5),p< 0.001], frequency of NAb (56.3% vs. 79.3%),p< 0.001) and median (interquartile range) neutralization activity [58.7(43.1-77.2)% vs. 64.5(48.4-81.4)%,p=0.013] in ARD patients compared to CG. Vaccine safety analysis revealed similar AE between the groups, with no moderate/severe event. Thirty-nine incident symptomatic cases of COVID-19 confirmed by RT-PCR were observed among ARD patients and CG [36/910 (4%) vs. 3/182 (1.6%), p=0.186] throughout the study. Frequency of cases occurring from D0-D39 (up to 10 days after the second dose) was higher compared to D40-D79 [33/1092 (3.0%) vs. 6/1057 (0.6%), p< 0.0001]. Four ARD patients were hospitalized (up to 10 days after second dose) and none deceased due to COVID-19.

Conclusion: CoronaVac has an excellent safety profile and reasonable rates of seroconversion (70.4%) and adequate neutralization activity (56.3%) in ARD patients. The impact of this reduced immunogenicity in vaccine effectiveness warrants further evaluation.

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Abstract Number: 1558

Therapy Based Outcomes in Patients with Multisystem Inflammatory Syndrome in Children: A Single Center Study

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SESSION INFORMATION
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Management and outcomes of multisystem inflammatory syndrome in children (MIS-C) remain under investigation and vary by institution. This study aimed to describe the outcomes of MIS-C patients treated at our center, and compare these outcomes based on initial management.

Methods: A single center retrospective study was conducted; all patients with MIS-C diagnosis between March 2020 and February 2021 were eligible. Demographic and clinical variables were collected. Patients were divided into 3 groups, based on immunomodulation within the first 24 hours of treatment initiation for patients in the intensive care unit (ICU), or 48 hours for non-ICU patients. The primary outcome was failure of initial therapy defined as need to escalate immunosuppression due to fever, worsening laboratory parameters, and/or lack of improvement/worsening

cardiac or non-cardiac findings. Secondary outcomes included duration of fever and vasoactive support, coronary aneurysms/dilation, length of ICU stay, hospital length of stay, readmission, and number of emergency room (ER) visits up to 6 months after discharge. Groups were compared using Kruskal Wallis test for continuous variables and Fisher/Chi-square test for categorical variables, employing R software. P values of ≤0.05 were considered statistically significant.

Results: Two-hundred and thirty-one MIS-C patients were identified. Patients who did not receive immunomodulation (n=5), required biologics within the first 24 hours (n=3), received intravenous immunoglobulin (IVIG) at another center

Table 1: Demographic features and outcomes of MIS-C patients according to therapy group

Category	Group 1: IVIG+ Steroids (n=116)	Group 2: IVIG alone (n=31)	Group 3: Steroids alone (n=69)	P value
Demographics				
Age in years	8 (5-12)	7 (5-9.5)	10 (6-14)	0.02
Sex				
Female	44 (37.9)	9 (29.0)	27 (39.1)	0.6
Male	72 (62.1)	22 (71.0)	42 (60.9)	
Race/Ethnicity				
Hispanic or Latino	25 (21.6)	4 (12.9)	18 (26.1)	0.38
White	36 (31.0)	7 (22.6)	30 (43.5)	0.08
African American	68 (58.6)	23 (74.2)	30 (43.5)	0.01
Other	13 (11.2)	1 (3.2)	9 (13.0)	0.34
Setting and outcomes				
Critical status at start of therapy	76 (65.5)	22 (71.0)	23 (33.3)	<0.001
Failure of initial therapy	35 (30.2)	17 (54.8)	13 (18.8)	0.001
Duration of fever in days	6 (5-7)	6 (6-7)	5 (4-6)	0.002
Days on vasoactive support	1 (0-3)	0 (0-2.5)	0 (0-0)	<0.001
Coronary artery aneurysms	2 (1.7)	0 (0.0)	1 (1.4)	1
Coronary artery dilation	14 (12.1)	5 (16.1)	4 (5.8)	0.18
ICU stay in days	3 (1-5)	5 (0-5.5)	0 (0-3)	<0.001
Total length of stay in days	6 (4-8)	6 (4.5-8)	4 (3-6)	<0.001
Readmission*	7 (6.0)	1 (3.2)	4 (5.8)	1
Number of ER visits*	0 (0-0)	0 (0-0)	0 (0-0)	0.19

Continuous variables are expressed as median (interquartile range), and categorical variables as n (percentage).
Abbreviations: ER: Emergency room; ICU: Intensive care unit; IVIG: Intravenous immunoglobulin. * Within 6 months after discharge

Table 2: Subsequent therapies used after failure of initial therapy

Medication	Group 1: IVIG+ Steroids (n=116)	Group 2: IVIG alone (n=31)	Group 3: Steroids alone (n=69)
Anakinra	7 (6.0)	1 (3.2)	0 (0.0)
High dose (30 mg/kg) pulse IV steroids	10 (8.6)	2 (6.5)	4 (5.8)
Hydroxychloroquine	1 (0.9)	0 (0.0)	0 (0.0)
Increase steroid dose (not pulse dosing)	14 (12.1)	0 (0.0)	4 (5.8)
Infliximab	2 (1.7)	0 (0.0)	1 (1.4)
IVIG (first dose)	0 (0.0)	0 (0.0)	10 (14.5)
IVIG (second dose)	19 (16.4)	3 (9.7)	1 (1.4)
Steroids (not pulse dosing)	4* (3.4)	12 (38.7)	1* (1.4)
Tocilizumab	2 (1.7)	0 (0.0)	0 (0.0)

Variables are expressed as n (percentage).
Abbreviations: IV: Intravenous; IVIG: Intravenous Immunoglobulin. *Re-initiation of steroid therapy after recurrence of symptoms post-discontinuation.

(n=3), or received therapy escalation without meeting the definition of failure of initial therapy (n=4) were excluded. Of the remaining 216 subjects, 116 received IVIG + steroids (Group 1), 31 received IVIG alone (Group 2), and 69 received steroids alone (Group 3) as initial therapy. Maximum initial steroid dose was methylprednisolone/prednisone 2 mg/kg/day. The groups differed in age and racial distribution; patients in group 3 were older ($p = 0.02$) and less frequently of African American race ($p = 0.01$). ICU status at the start of therapy was less frequent in group 3 (33.3%) vs group 1 (65.5%) and 2 (71%) ($p < 0.001$). Rates of initial therapy failure were lowest in group 3 (18.8% vs 30.2% and 54.8% for groups 1 and 2, respectively; $p = 0.001$). Group 3 had shorter duration of fever (median 5 days vs 6 days in group 1 and 2; $p = 0.002$), ICU length of stay (median 0 days vs 3 and 5 days for group 1 and 2, respectively; $p < 0.001$), and total length of stay (median 4 days vs 6 days in groups 1 and 2; $p < 0.001$). Vasoactive support duration was longer for group 1 (median 1 day vs 0 days for groups 2 and 3; $p < 0.001$). Coronary outcomes, need for readmission and ER visits post-discharge were similar between groups. All patients survived.

Conclusion: A subgroup of MIS-C patients was successfully treated with steroid monotherapy. This group was older, less frequently African American, likely had milder disease (less frequent ICU status), had lower rates of treatment failure and favorable secondary outcomes. For a subset of MIS-C patients, steroid monotherapy could be a suitable alternative to IVIG. Multivariate analysis controlling for severity and prospective studies are needed to further explore these findings.

Disclosure: D. Villacis Nunez, None; **K. Jones**, None; **L. Fan**, None; **W. Moore**, None; **A. Jabbar**, None; **M. Oster**, None; **P. Jaggi**, None; **S. Prahalad**, Novartis, 1.

Abstract Number: 1559

Potential Predictors of Requirement for Mechanical Ventilation in Cases of COVID-19 Related Multisystem Inflammatory Syndrome in Children (MIS-C): Results of a Hospital-based Cohort Study from South India

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	< 5 years (n=18) -no. (%)	5-12 years (n= 19) -no. (%)	>12 years (n= 4) -no. (%)
Dermatological/ mucocutaneous	13 (72)	19 (100)	4 (100)
Gastrointestinal symptoms	16 (89)	17 (90)	4 (100)
Incomplete/ atypical Kawasaki disease	13 (72)	15 (79)	3 (75)
Shock	7 (39)	12 (63)	3 (75)
Macrophage activation syndrome like features	6 (33)	7 (37)	4 (100)
Neurological symptoms	7 (39)	6 (32)	2 (50)
Respiratory Symptoms	4 (22)	1 (5)	2 (50)

1-5%	6-25%	26-50%	51-75%	76-100%

* Percentages may not total 100 because of rounding and overlapping clinical features

Heat map of syndrome clusters based on clinical presentations *

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

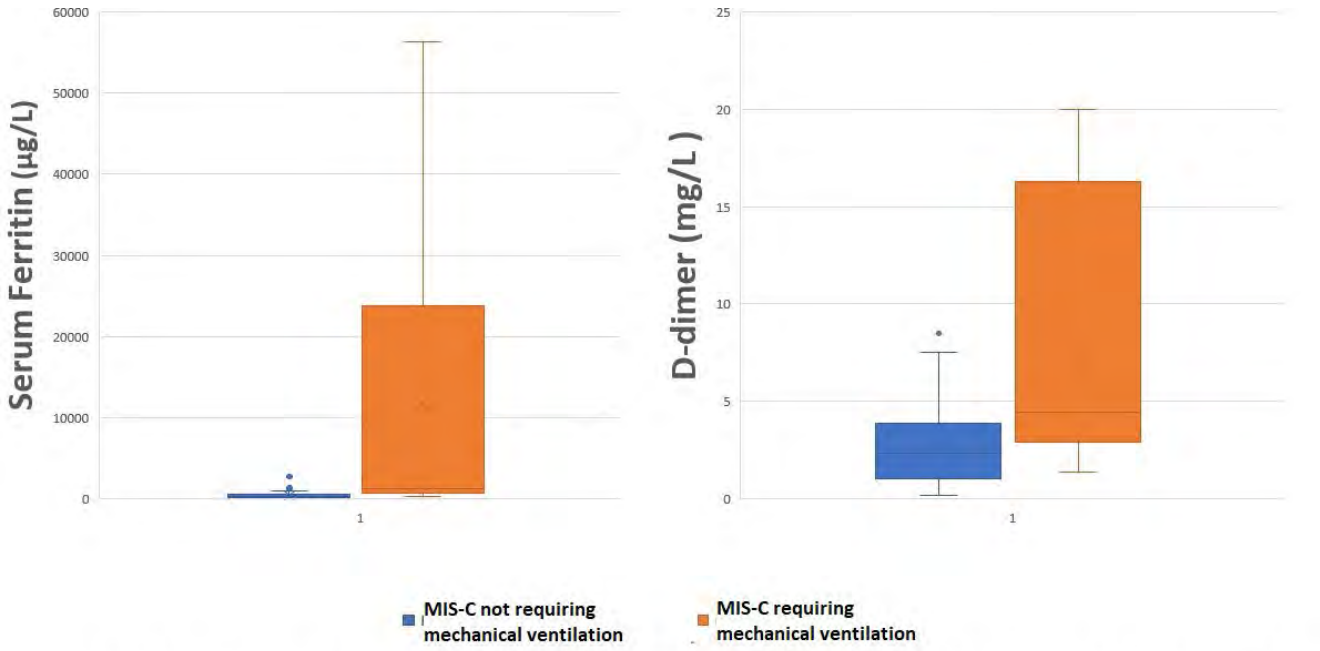
Background/Purpose: COVID-19 related multisystem inflammatory syndrome in children (MIS-C) has varied clinical presentation ranging from fever with mild gastrointestinal and/or mucocutaneous changes to life threatening multi-organ dysfunction. As it is a new disease and factors associated with development of severe MIS-C remain largely unknown. Hence, we planned this study to identify parameters associated with requirement of mechanical ventilation in diagnosed cases of MIS-C.

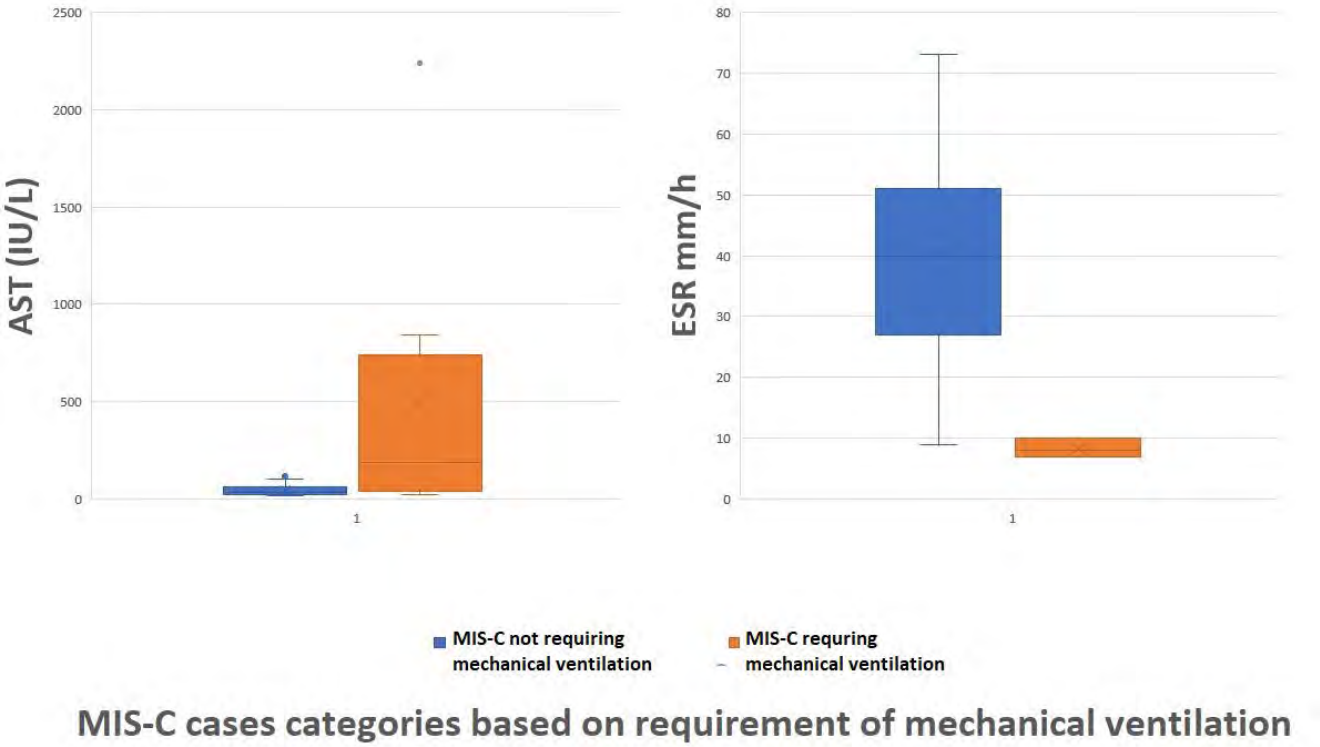
Bivariate Comparison of various clinical and laboratory parameters in MIS-C cases who required mechanical ventilation versus those who did not require mechanical ventilation *

Clinical and laboratory parameters of MIS-C cases	**Mechanical ventilation required (n = 8)**	**Mechanical ventilation not required (n = 33)**	**p-value** ‡
Presence of shock requiring inotropic agents-no.(%)	7 (88)	14 (42)	**0.045**
Median D-dimer mg/L (IQR)	4.5 (2.9-16.3)	2.3 (1.0-3.9)	**0.016**
Median serum ferritin µg/L (IQR)	1178.0 (717.0-23840.0)	266.0 (153.0-555.0)	**0.001**
Median ESR mm/h (IQR)	8.0 (7.0-10.0)	40 (27-51)	**0.016**
- no./total no. (%)	3/8 (38)	11/33 (33)	
Median serum AST IU/L (IQR)	188.0 (37.8-741.2)	33.0 (26.0-60.5)	**0.008**
Median serum procalcitonin µg/L (IQR)	5.4 (2.1-41.5)	11.1(1.6- 51.0)	0.716
- no./total no. (%)	4/8 (50)	12/33 (36)	
Median serum NT-proBNP pg/mL (IQR)	3533.5 (2141.5-46767.5)	1138.0 (349.0-6725.0)	0.096
- no./total no. (%)	6/8 (75)	13/33 (39)	
Median serum troponin ng/L (IQR)	55.2 (14.5-945.3)	15.0 (4.8-29.2)	0.143
- no./total no. (%)	4/8 (50)	26/33 (78)	
Median absolute lymphocyte count (IQR)	825 (521-2218)	1588 (895-3489)	0.061
Lymphopenia at admission -no. (%)§	7 (88)	19 (58)	0.220
Mean CRP mg/L ± SD	101.0 ± 85.3	123 ± 78.9	0.474
Median serum ALT IU/L (IQR)	141.0 (25.0-543.0)	29.0 (21.0-43.5)	0.113
Presence of coronary abnormalities - no. (%)	4 (50)	11 (33)	0.434
Presence of LV dysfunction - no. (%)	3 (38)	7 (21)	0.378

* Percentages may not total 100 because of rounding. IQR denotes interquartile range showing 25th and 75th centiles, ESR erythrocyte sedimentation rate, AST aspartate aminotransferase, NT-ProBNP N-terminal pro–B-type natriuretic peptide, CRP C-reactive protein, SD standard deviation, and ALT alanine aminotransferase.
‡ p-value was calculated by applying appropriate statistical tests according to the distribution of the data. Independent sample t-test or Mann-Whitney tests were applied to compare the potential markers of severity. A p-value of <0.05 was considered statistically significant.
§ Lymphopenia defined as <3000 lymphocytes/µL (<2 years age) , <1500 lymphocytes/µL (2-12 years age), and <1000 lymphocytes/µL (>12 years age).

Bivariate Comparison of various clinical and laboratory parameters in MIS-C cases who required mechanical ventilation versus those who did not require mechanical ventilation





Comparison of selected laboratory parameters in MIS-C cases who required mechanical ventilation versus those who did not

Methods: It was a cohort study conducted at two tertiary care centres in Kerala state of south India from March 2020 to April 2021. Cases diagnosed with MIS-C as per centres for disease control and prevention (CDC) case definitions were enrolled and studied for clinical profile. MIS-C cases were further categorised based on requirement of mechanical ventilation and these groups were compared for baseline clinical characteristics, laboratory parameters and echocardiographic changes in order to identify parameters associated with requirement of mechanical ventilation. Pearson Chi-Square test or Fisher's exact test to compare the categorical variables and the independent sample t-test or Mann-Whitney test were used to compare the continuous variables by age group and severity.

Results: A total of 41 (males-23) cases diagnosed of MIS-C were enrolled in the study. The mean age at onset of MIS-C was 6.16 (SD-4.0) years. Their clinical profile was studied in age categories of less than 5 years, 5-12 years, and more than 12 years. Cases were divided into syndrome clusters of dermatological or mucocutaneous changes, gastrointestinal symptoms, Incomplete or atypical Kawasaki disease. Shock, macrophage activation syndrome (MAS), neurological symptoms, and respiratory symptoms. The heat map of these syndrome clusters in different age groups is shown in figure 1.

MIS-C cases were categorised into two groups based on requirement of mechanical ventilation; 8 (20%) cases required mechanical ventilation whereas 33 (80%) cases did not require ventilatory support. These groups were compared for various clinical, laboratory and echocardiographic parameters shown in figure 2. Out of 8 patients who required mechanical ventilation, 7(88%) had presented in shock treated with ionotropic agents, whereas out of 33 cases who did not require mechanical ventilation 14 (42%) had presented in shock necessitating use of ionotropic agents; the difference was statistically significant ($p=0.045$). Serum D-dimer, serum ferritin, and aspartate aminotransferase (AST) were significantly high and erythrocyte sedimentation rate (ESR) was significantly low in patients of MIS-C requiring ventilatory support as compared to them who did not require it ($p < 0.05$), graphical representation of statistically significant parameters is shown in figure 3.

Conclusion: In our study we found that the presence of shock requiring inotropic agent, high ferritin, high D-dimer, high AST, and low ESR were associated with the requirement of mechanical ventilation in MISC cases ($p< 0.05$). The constellations of these parameters could reflect an ongoing process of Macrophage Activation Syndrome (MAS) in MIS-C cases requiring mechanical ventilation.

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Abstract Number: 1560

A Multidisciplinary Timely Approach to Initiate Immunosuppressive Biologic Therapy and Improve COVID-19 Cytokine Storm Syndrome Outcome

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Coronavirus disease (COVID-19) patients can progress to a state of unregulated inflammation called cytokine storm syndrome (CSS). A multi-disciplinary approach is needed to identify COVID-19 patients

at risk of CSS. Therapy with corticosteroids, anti-interleukin-1 (anti IL-1) and anti-interluekin-6 (anti-IL 6) reduce the systemic inflammatory response, which can prevent rapid progression of cytokine mediated diffuse alveolar damage. There is extremely limited literature on the safety and efficacy of biologic immunosuppressive therapy in COVID-19 patients. Till date there are no formal guidelines, as when to initiate immunosuppressive therapy in COVID-19 patients

Methods: Institutional experts from different sub-specialities formed a COVID-19 CSS task force at Montefiore Medical Center, Bronx, NY. Consensus recommendations regarding biologic therapy were made after daily multi-disciplinary virtual conference. This is a single center retrospective observational study, where we describe the baseline characteristics, clinical and laboratory parameters, and the outcome of our COVID-19 CSS consult cohort patients who received biologic immunosuppressive therapy either anti IL-1 and/or anti IL-6.

Results: Between April 4,2020 and May 7,2020, the CSS consult service evaluated a total of 288 patients for possible COVID-19 CSS, out of these 35 patients received biologic immunosuppressive therapy either anti IL-1 and/or anti IL-6. Among these 35 patients 4 patients received the biologic therapy on admission prior to COVID-19 CSS consult task force consultation and the 31 patients received the biologic therapy after the COVID-19 CSS task force consultation. Fifteen patients (83%) received anti IL-1 therapy, 18 patients (51%) received anti-IL6 therapy and 2 patients (6%) received both. Eleven patients (31%) receiving biologic immunosuppressive therapy survived. The patients who survived were younger with a median age of 42 years versus 55 years in the non-survivor group (p=0.04). A higher proportion of patients who survived, had earlier multidisciplinary CSS task force consultation on day 4 (IQR – 2-12 days) after admission as compared to day 6.5 (IQR- 3-11 days)in the non-survivor group.

Conclusion: We describe a unique approach from our institution where an earlier multi-disciplinary COVID-19 CSS task force consultation on the COVID-19 patients progressing towards CSS, could help alter the disease course by timely intervention with biologic therapy.

Disclosure: A. Kumthekar, None; **B. Ayesha**, None.

Abstract Number: 1561

Prevalence of SARS-CoV2 Infection in Diseases Inflammatory Rheumatology in the Rheumatology Service of the Hospital Docente Padre Billini, Dominican Republic

Jennifer Santana Peralta de Heyaime, Teresandris Polanco Mora, Angelo Cornelio Vasquez, Yamilet Cruz, Edral Rodriguez, Tirso Valdez Lorie, Roberto Munoz and Rafael Alba Feriz, Hospital Docente Padre Billini, Santo Domingo, Dominican Republic

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: SARS-CoV-2 infection is caused by a new coronavirus. The World Health Organization (WHO) had information about the existence of this new virus on December 31, 2019 in Wuhan, China. Common symptoms are fever, cough, dyspnea, and fatigue 1. There is a lack of data to understand the evolution of the disease in patients with inflammatory rheumatological diseases, especially in those undergoing treatment with immunosuppressants or biological therapy 2. It is unknown whether rheumatology patients are a vulnerable population. 3 Overall,

this population appears to have similar or only slightly worse outcomes compared to those without rheumatologic disease. 4,5,6

Methods: Observational, prospective, longitudinal study. Personal and telephone interviews were conducted with patients from the rheumatology service from June 2020 to February 2021. Inclusion criteria: 1) > 18 years of age, 2) History of SARS-CoV2 infection diagnosed by PCR and / or compatible CT, 3) Diagnosis of a rheumatological pathology based on classification criteria. Data were analyzed with SPSS V23.

Results: Of 4,416 consultations, 3,633 met the classification criteria for inflammatory rheumatological disease and 2,040 were in biological treatment. 44 patients met the inclusion criteria. Diagnosis by CoV-2 by PCR 38 and 6 by compatible chest CT. 35 female. The average age 55.3 +17.8 years. Mean time of illness was 7.9 +5.3 years. Rheumatological diagnoses: Rheumatoid arthritis 47.72% (21), Systemic lupus erythematosus 21.95% (9), Axial spondyloarthritis 12.19% (5), Psoriatic arthritis 9.75% (4), Reactive arthritis 5.88% (2), Juvenile idiopathic arthritis 2.94% (1), Adult Still's disease 2.94% (1), Sjögren's syndrome 2.94% (1). Biological treatment in 61.36% (27): Anti-TNF 40.74% (11), Tocilizumab 33.33% (9), anti-IL12 / 23 14.81% (4), Tofacitinib 7.40% (2), anti CD20 3.70% (1). Treatment with csDMARD 38.63% (17), glucocorticoids 9 with a mean dose of 5mg. Comorbidities: 29.54% (13) hypertensive, 15.9% (7) diabetic, 2.27% (1) interstitial lung disease, 2.27% (1) asthma, 6.81% (3) obese. There was one hospitalization and one death during the study period in a patient with systemic lupus erythematosus.

Conclusion: Our study showed that there is no increased risk of Sars-CoV2 infection or increased severity of the disease in patients with rheumatological inflammatory pathology compared to the general population.

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Abstract Number: 1562

B Cell Reconstitution Is Strongly Associated with COVID-19 Vaccine Responsiveness in Rheumatic Disease Patients Treated with Rituximab

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Rituximab (RTX) has previously been shown to impair antibody response to vaccines such as influenza and streptococcus. Recently, diminished COVID-19 vaccine responsiveness in RTX treated patients has been reported. While COVID-19 vaccination guidelines have adopted time since last RTX infusion as a consideration for likelihood of vaccine responsiveness, a retrospective study suggested that B Cell reconstitution may be a more accurate predictor of vaccine response. Our hypothesis was that B Cell reconstitution would be associated with vaccine responsiveness.

Methods: A retrospective chart review was performed to assess patients that visited a rheumatology practice from 2/24-5/20, 2021. Analysis included patients who had received treatment with RTX and had completed COVID-19 vac-

cination. Demographics, diagnoses, concurrent therapies, vaccine type/dates, time from last RTX to first vaccination quantitative serological vaccine response, and % CD19 positive cells in the lymphocyte population were collected. COVID-19 serological response was the primary outcome. Descriptive statistics and bivariate comparisons were

Factor	Value	Negative for antibody response	Positive for antibody response	p-value*
N	58	27	31	
Age, mean (Standard Deviation (SD)	62.6724 (14.7961)	64.6667 (15.0051)	60.9355 (14.6331)	0.34
Age, median (Interquartile range (IQR)	64 (52, 72)	65 (53, 74)	60 (50, 72)	0.29
Sex				0.26
Female	40 (69%)	21 (78%)	19 (61%)	
Male	18 (31%)	6 (22%)	12 (39%)	
Race				0.82
White	52 (90%)	24 (89%)	28 (90%)	
Black of African American	1 (2%)	0 (0%)	1 (3%)	
Asian	5 (9%)	3 (11%)	2 (6%)	
Rheumatoid Arthritis (RA)	6 (10%)	3 (11%)	3 (10%)	1.00
Systemic Lupus Erythematosus (SLE)	3 (5%)	2 (7%)	1 (3%)	0.59
Sjogrens Syndrome	5 (9%)	3 (11%)	2 (6%)	0.66
Systemic Sclerosis (SSc)	4 (7%)	3 (11%)	1 (3%)	0.33
Polymyalgia Rheumatica (PMR)	1 (2%)	1 (4%)	0 (0%)	0.47
IgG4 Disease	1 (2%)	1 (4%)	0 (0%)	0.47
ANCA Associated Vasculitis (AAV)				
Microscopic Polyangitis (MPA)	4 (7%)	2 (7%)	2 (6%)	1.00
Granulomatosis with Polyangiitis (GPA)	27 (47%)	10 (37%)	17 (55%)	0.20
Eosinophilic Granulomatosis with Polyangiitis (EGPA)	1 (2%)	0 (0%)	1 (3%)	
Dermatomyositis	1 (2%)	0 (0%)	1 (3%)	
Mixed Connective Tissue Disease (MCTD)	1 (2%)	0 (0%)	1 (3%)	
Polymyositis	1 (2%)	0 (0%)	1 (3%)	
Relapsing Polychondritis	2 (3%)	2 (7%)	0 (0%)	
Sarcoidosis	1 (2%)	0 (0%)	1 (3%)	
Prior COVID	1 (2%)	0 (0%)	1 (3%)	1.00
Anti-rheumatic therapies other than RTX				
Corticosteroid	12 (21%)	5 (19%)	7 (23%)	0.76
Leflunomide	2 (3%)	1 (4%)	1 (3%)	1.00
Hydroxychloroquine	3 (5%)	1 (4%)	2 (6%)	1.00
Azathioprine	1 (2%)	1 (4%)	0 (0%)	0.47
Upadacitinib	1 (2%)	0 (0%)	1 (3%)	1.00
Methotrexate	2 (3%)	2 (7%)	0 (0%)	0.21
Mycophenolate Mofetil	5 (9%)	4 (15%)	1 (3%)	0.17
Tocilizumab	1 (2%)	1 (4%)	0 (0%)	0.47
Vaccine Type				0.89
Pfizer	31 (53%)	14 (52%)	17 (55%)	
Moderna	26 (45%)	13 (48%)	13 (42%)	
J&J	1 (2%)	0 (0%)	1 (3%)	
B Cell status				**<0.001**
No detectable B Cells	16 (28%)	11 (41%)	5 (16%)	
Detectable B Cells	25 (43%)	2 (7%)	23 (74%)	
missing	17 (29%)	14 (52%)	3 (10%)	

*P-values are from Fisher's exact test, Student's T-test and Wilcoxon rank sum tests

Factor	Value	Negative Antibody Response	Positive Antibody Response	p-value
N (number of patients)	58	27	31	
B Cell % of total lymphocyte population, median (IQR)	.5 (0, 5)	0 (0, 0)	2 (.265, 9.5)	<0.001
B Cell % of total lymphocyte population, mean (SD)	3.6470732 (5.8629132)	.63846154 (2.2134206)	5.0439286 (6.5088341)	0.023
SARS-CoV-2 spike antibody concentration (U/mL), median (IQR)[a]	1.565 (0, 251)	0 (0, 0)	243 (29.3, 1010)	<0.001
SARS-CoV-2 spike antibody concentration (U/mL), mean (SD)[a]	382.84552 (795.30017)	0 (0)	716.29161 (977.2146)	<0.001
Days from last RTX to completion vaccination, median (IQR)	229.5 (124, 662)	138 (68, 197)	594 (248, 1163)	<0.001
Days from last RTX to completion of vaccination, mean (SD)	554.6207 (735.0181)	282.2963 (702.3548)	791.8065 (688.5294)	0.007
Time from last RTX exposure to completion of COVID-19 vaccination (TFLRTX)				<0.001
<6months	21 (36%)	18 (67%)	3 (10%)	
6-12 months	12 (21%)	6 (22%)	6 (19%)	
>12 months	25 (43%)	3 (11%)	22 (71%)	
Days from completion of vaccination to antibody immunoassay, median (IQR)	33 (18, 51)	30 (16, 44)	34 (20, 57)	0.33
Days from completion of vaccination to antibody immunoassay, mean (SD)	35.07018 (23.39098)	32 (25.1289)	37.83333 (21.76534)	0.35

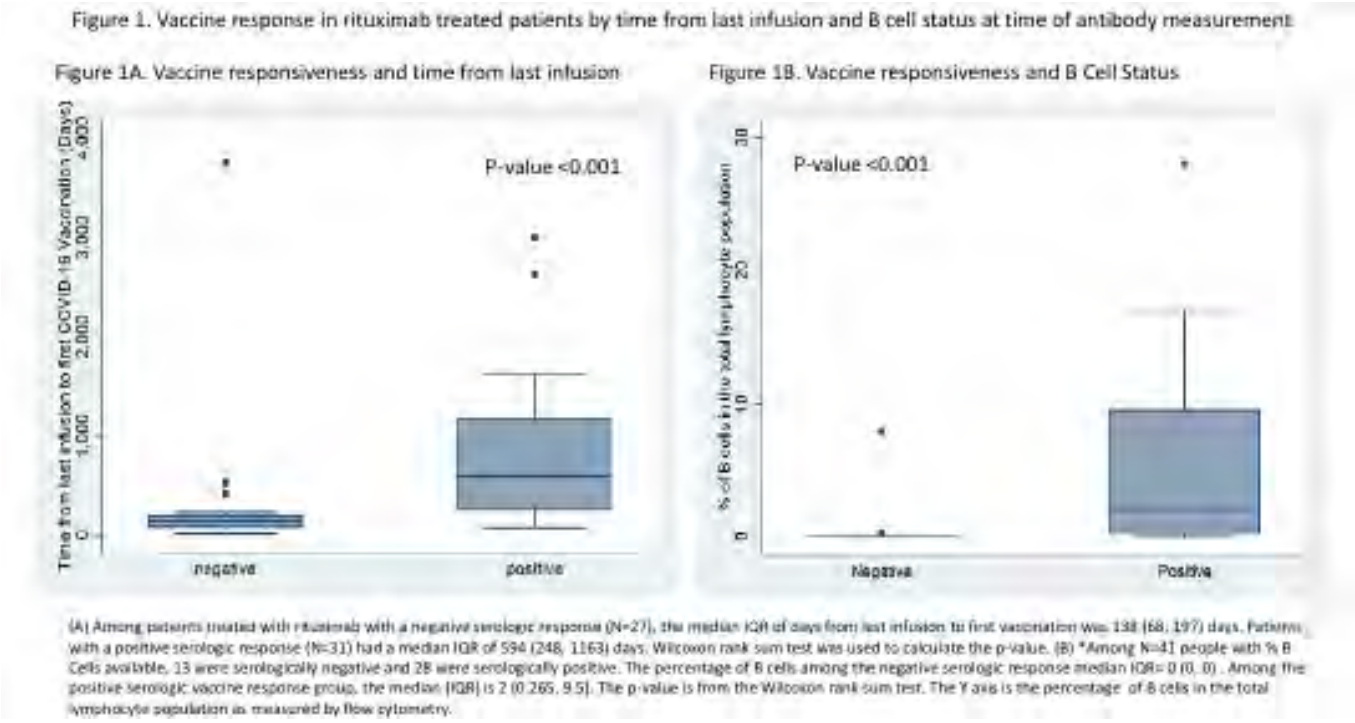
[a] N=54 (93%) had seropositivity measured by Roche Elecsys Anti-SARS-CoV-2, specificity 99.8% sensitivity 99.5%,, N=4 (7%) had seropositivity measured by Siemens Healthineers SARS-CoV-2 total (COV2T) Assay Atellica IM, specificity 99.82% sensitivity 100% or ADVIA Centaur XP/XPT, specificity 99.81% sensitivity 100%

performed. Negative and positive predictive value was calculated between COVID-19 serological response and B Cell reconstitution status.

Results: 58 patients were identified who met criteria for inclusion. The majority were female (40, 69%), white (52, 90%), and the mean age was 62.67 years (Table 1).

41 patients (71%) had B Cell status measured at time of antibody immunoassay. Time from last RTX was significantly longer in seropositive (median #days, IQR 594 (248, 1163) patients compared to seronegative patients

Figure 1. Vaccine response in rituximab treated patients by time from last infusion and B cell status at time of antibody measurement



(A) Among patients treated with rituximab with a negative serologic response (N=27), the median IQR of days from last infusion to first vaccination was 138 (68, 197) days. Patients with a positive serologic response (N=31) had a median IQR of 594 (248, 1163) days. Wilcoxon rank sum test was used to calculate the p-value. (B) *Among N=41 people with % B Cells available, 13 were serologically negative and 28 were serologically positive. The percentage of B cells among the negative serologic response median IQR= 0 (0, 0) . Among the positive serologic vaccine response group, the median (IQR) is 2 (0.265, 9.5). The p-value is from the Wilcoxon rank sum test. The Y axis is the percentage of B cells in the total lymphocyte population as measured by flow cytometry.

(median #days, IQR 138 (68, 197) days) (p-value < 0.001). There was a significant difference in B Cell reconstitution between patients who had positive antibody responses to vaccination (median, IQR 2 (0.265-9.5) % of total lymphocyte population) versus negative responses (median, IQR 0 (0-0) % (p< 0.001) (Table 2). Only 12% (3/25) of patients >12 months since last RTX did not demonstrate a serologic responses, whereas 24% of patients (9/37) > 6 months since last RTX and 50% (6/12) of those 6-12 months from last RTX did not have a serologic response to the vaccine (Figure 1. Table 2).

B Cell reconstitution and time from last RTX were both significant indicators of vaccine response. (Figure 1). Seropositivity was 76% among those >6 months from last RTX exposure, however that increases to 92% in those with detectable B Cells (p=0.006). In patients 6-12 months from RTX exposure, only 50% were seropositive, however that increases to 83.33% in those with detectable B Cells (p=0.190) The positive predictive value of B Cell reconstitution for COVID-19 serologic response was 92% (95%CI: 74%-99%) and the negative predictive value was 68.8% (95%CI: 41.3%-89%).

Conclusion: B Cell reconstitution and longer time from last RTX were associated with a positive serologic response to the COVID-19 vaccine. A substantial number of patients >6 months from last RTX did not have a serologic response, and B cell reconstitution increased the likelihood of a response. Strategies for maximizing vaccine responsiveness in RTX treated patients should incorporate B Cell reconstitution and time from last RTX.

Disclosure: S. Jinich, None; **D. Jannat-Khah**, Cytodyn, 12, own shares of stock, Walgreens, 12, Own stock shares, AstraZeneca, 12, own stock shares, GW Pharmaceuticals, 12, stock ownership; **R. Spiera**, GSK, 2, 5, Boehringer Ingelheim Pharmaceuticals, 5, Chemocentryx, 2, 5, Corbus Pharmaceutical, 5, Formation Biologics, 2, 5, InflaRx, 5, Kadmon, 5, Astra Zeneca, 5, Abbvie, 2, CSL Behring, 2, Sanofi, 2, Janssen Pharmaceuticals, 2, Genentech/Roche, 2, 5.

Abstract Number: 1563

Clinical Characteristics and Management of Olecranon and Prepatellar Septic Bursitis in a Multicenter Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Infection-related Rheumatic Disease Poster (1530–1564)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Septic bursitis (SB) is a common medical problem. However, there are no current guidelines for managing the condition. The study aims to describe the clinical characteristics and management of olecranon and patellar septic bursitis in five French tertiary care centers.

Methods: We performed a retrospective multicenter study. Patients over the age of 18 years requiring hospitalization for olecranon or prepatellar SB from January 1, 2016 to December 31, 2018 were included. SB was diagnosed on the basis of positive cultures of bursal aspirate. In the absence of positive bursal fluid, the diagnosis came from typical clinical presentation, exclusion of other causes of bursitis, and favorable response to antibiotic therapy. The following characteristics were collected: age, gender, occupation, and comorbidities, date of diagnosis, presence of fever > 38.5°C, extensive cellulitis and skin lesion, and NSAIDs intake during the episode. Finally, the results of biological tests (CRP, bursal fluid and blood cultures), management (antibiotic type, route and duration of administration, surgical drainage) and outcomes were obtained from patients' charts. We considered the condition to be healed on the basis of data from follow-up consultations when the patient's symptoms had resolved (pain, fever, skin lesions) or if the patients did not need to be referred again by their general practitioner. For statistics, quantitative data were compared using a Mann-Whitney test, and a Chi square test (or Fisher's exact test for values < 5) was used for qualitative data. Values of $p < 0.05$ were considered significant.

Results: We included 272 patients (median age: 53, 85.3% male, manual occupation for 30.8% and 22.8% with at least one comorbidity). Fifty-one patients were taking NSAIDs to manage symptoms before diagnosis (18.3%). Fever was reported in 91 patients (33.4%) and a history of preceding knee/elbow injury or skin lesion was found in 161 patients (59.3 %). Median CRP level was 98.3 mg/L (range: 0-330). The bursal fluid was aspirated by puncture in 172 patients (63.2%) and collected during surgery in 51 patients (18.8%), while 49 patients (18%) were managed without bursal fluid analysis. A microorganism was identified in 80% of the samples (180/223). Bursal fluid analysis identified staphylococci in 73.4% and streptococci in 19%. Antibiotic treatment was initially administered intravenously (IV) in 41%, and this route was preferred in case of fever (p=0.003) or extensive cellulitis (p=0.002). When treatment was started IV, amoxicillin/clavulanate and oxa-/cloxacillin were most commonly given. When it was started orally, amoxicillin/clavulanate (44.7%) and pristinamycin (34%) were the most prescribed treatments. Twenty-six percent of patients (N=71) were treated surgically. A low failure rate was observed (N=16/272, 5.9%) and failures were more frequent when the antibiotic therapy lasted less than 14 days (p=0.02) in both surgically- and medically-treated patients.

Conclusion: Despite variable treatments, SB resolved in the majority of cases even when the treatment was exclusively medical. Antibiotic therapy shorter than 14 days was associated with more failures.

Disclosure: L. Charret, None; **G. Bart**, None; **E. Hoppé**, None; **E. Dernis**, None; **G. Cormier**, None; **D. Boutoille**, None; **B. Le Goff**, None; **C. Darrieutort-Laffite**, None.

Abstract Number: 1564

Nailfold Capillaroscopy Characterization in COVID-19: A Case Control Study

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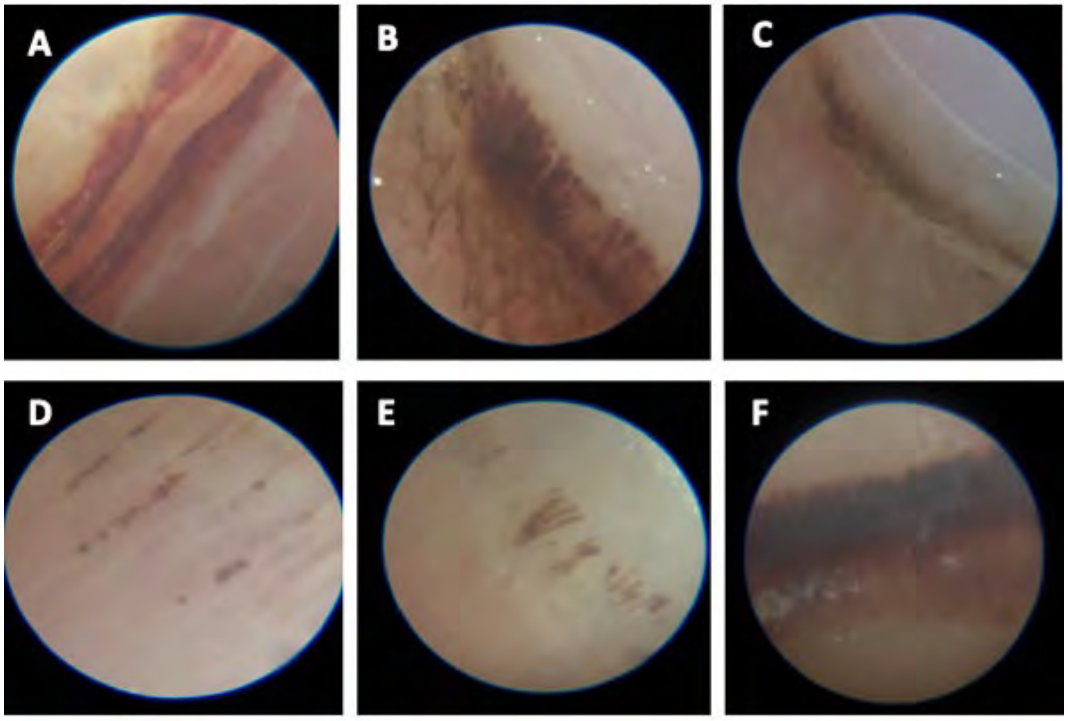
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Infection-related Rheumatic Disease Poster (1530–1564)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Nailfold capillaroscopy is a relatively easy-to-access, low-cost clinical tool that could help identify early coagulopathy in subjects with SARS-CoV-2, but specific findings vs. controls and its possible prognostic role has not been studied.

Methods: We designed a cross-sectional study, carried out in a single care center for critical patients with SARS-CoV-2 pneumonia at the ABC Medical Center, Mexico City, which included patients from an intensive care unit (ICU) and internal medicine ward from March to April 2020. Demographic, biochemical and clinical features were collected. All patients signed the informed consent and the study was approved by the hospital ethics committee. All patients underwent nail capillary imaging of the 3 central fingers of each hand with a portable microscope with 100x magnification coupled to a smartphone with 7 megapixel images in an immersion medium. Capillaroscopy was performed in patients who didn´t have fever or hypothermia, or need vasopressors at the time of evaluation. Control subjects are healthy subjects matched on age and sex from a database of healthy controls without rheumatic diseases. Image evaluation of COVID-19 patients was performed in a blinded way for their characteristics. Prior to the analysis, a pilot test was obtained with 4 rheumatologists in random cases, obtaining an acceptable global agreement in the visualization of capillaries and alterations. (Kappa=0.58, p=0.0019). Obtained data from capillaroscopies were used to be compared between severe and moderate cases of COVID-19. Additionally, we compared the findings against a healthy population in order to establish a reference.

Results: We included data from 27 patients and 32 controls with similar demographic features. Patients with COVID-19 patients had a mean age of 43 +/- 13.8 years, 63% female. Comorbidities were present in 44.4% with: type 2 Diabetes Mellitus 18.5%, systemic hypertension 18.5%, and rheumatoid arthritis 3.7%. The mean length of stay time was 13 +/- 7.1 days, 48.1% were admitted to the ICU, and 40.7% required invasive mechanical ventilation. In the capillaroscopic review remarkable findings of patients vs. controls were hemosiderin deposits (33 vs 12.5%, p=0.05), less frequently observable capillaries (77 vs 100%, p=0.005), any abnormality in capillaries (25.9 vs. 6.3%, p=0.03). Of notice, specific findings in COVID-19 patients were capillary tortuosities in 19%, dilatation 9.5%, serpentine pattern 4.8%, bush pattern 9.5% and decreased density in only 4.8% of the cases. Avascular areas or capillaries of ne-



Description: A. Extensive NB hemorrhage. B. Deposition of hemosiderin in multiple capillaries of the NB. C. Linear deposition of hemosiderin in the NB. D and E. Deposition of hemosiderin in some capillaries in the NB. F. Extensive hemorrhage accompanied by hemosiderin deposition in a large area of the NB.

oformation were not observed. The presence of hemosiderin was associated with worse presentation and risk factors for severe COVID-19: male sex 66.7 vs. 27.8%, (p = 0.024); Admission to ICU 77% vs 33% (p = 0.029); obesity 66.7 vs. 27.8% (p = 0.053). And risk for ICU admission OR = 7.0 (95% CI 1.098 - 44.6).

Conclusion: We present one of the first reports of nailfold capillaroscopic findings in COVID- 19 and the first to compare to healthy controls. Previous data suggests the presence of endothelial dysfunction and microvascular complications such as micro hemorrhage or micro thrombosis. Further studies may confirm these findings and prognostic value for worse outcomes in this illness.

Disclosure: P. Bermudez Bermejo, None; **R. JIMENEZ-SOTO**, None; **A. Sanchez-Rodríguez**, None; **A. Turrent**, None; **D. Mercado- Velasco**, None; **I. Bravo-Lee**, None; **M. Colli-Cortés**, None; **E. Alvarez Hernandez**, None; **M. Amigo**, None.

Abstract Number: 1565

Causal Mediation Analysis of the Relationship of Canakinumab's Protective Effect Against Gout Flares and High-sensitivity C-reactive Protein in the CANTOS Trial

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Previous analyses in the CANTOS trial demonstrated a benefit of canakinumab (CAN; IL-1β inhibitor) on gout flares. We aimed to quantify the mediating role of early inflammatory suppression of high sensitivity C-reactive protein (hsCRP) in explaining the protective role of CAN. If mediation is substantial, hsCRP may be a useful biomarker indicating treatment benefit.

Methods: We conducted a post-hoc analysis for gout flares in CANTOS, an RCT originally undertaken to examine the potential CV benefit of CAN compared to placebo. Our outcome of interest was time to first gout flare after hsCRP and other biomarkers, measured at 3 months. Based on previous analyses with similar gout benefits, we combined 3 different dosages of CAN.

We examined several biomarkers as mediators that may explain some proportion of the protective effect of CAN on future gout flares. hsCRP was the main biomarker of interest. We also analyzed serum urate (SU) as a "negative control mediator" (i.e., not expected to mediate CAN effect but known risk factor for gout flare). In approximately 50% of patients in the biomarker cohort, we also examined IL-6 (hypothesized to be like hsCRP) and IL-18 (not affected by CAN like SU).

We used the regression-based causal mediation analysis. The 3-month change in the log biomarker was the mediator and its relationship with CAN was examined in linear regression. We used Cox regression for the gout flare outcome modeling. We estimated the total effect (TE), natural direct effect (NDE; non-mediated part of TE), natural indirect effect (NIE; mediated part of TE), and proportion mediated (PM). On the hazard ratio (HR) scale, TE=NDE×NIE. We examined the cohort overall as well as stratified by prevalent gout at baseline.

Results: 9,221 patients without known prevalent gout at baseline and 747 with a known prevalent f gout were analyzed. Unadjusted analyses (Table 1) showed similar relative protective effects of CAN on future gout flares regardless of baseline gout. **Figure 1** shows that CAN is associated with early decreases of hsCRP and IL-6, but not SU or IL-18.

Table 2 summarizes the mediation results. As hypothesized, SU and IL-18 analyses consistently gave near-zero PM estimates. For the hsCRP analysis, the overall cohort result was HR 0.51=0.54×0.94, giving a PM of 6%. Mediation was inconsistent in the no prevalent gout cohort (HR 0.44=0.41×1.06). Upon closer examination, this unclear mediation was due to the poor prediction of future gout flare by the first 3-month change in hsCRP with CAN. In the gout

Table 1. Gout flare event rates in the study sample during the follow-up after 3-month biomarker measurement.

Prevalent Gout	Medication	n	Flares	PY	Rate /1000PY	Unadjusted HR
Overall	Overall	9,968	171	34,877.0	4.9 [4.2, 5.7]	–
	Canakinumab	6,659	91	23,405.8	3.9 [3.1, 4.8]	0.56 [0.41, 0.75]
	Placebo	3,309	80	11,471.3	7.0 [5.5, 8.7]	Ref.
No prevalent gout	Overall	9,221	98	32,447.9	3.0 [2.5, 3.7]	–
	Canakinumab	6,151	47	21,731.7	2.2 [1.6, 2.9]	0.45 [0.31, 0.68]
	Placebo	3,070	51	10,716.2	4.8 [3.5, 6.3]	Ref.
Prevalent gout	Overall	747	73	2,429.1	30.1 [23.6,37.8]	–
	Canakinumab	508	44	1,674.0	26.3 [19.1,35.3]	0.69 [0.43, 1.10]
	Placebo	239	29	755.1	38.4 [25.7,55.2]	Ref.

Abbreviations: PY: person-years; HR: hazard ratio.

Table 2. Causal mediation analysis estimates [95% confidence interval] decomposing the total effect (TE) hazard ratio (HR) of canakinumab treatment on gout flare outcome compared to placebo into the natural direct effect (NDE; non-mediated) and natural indirect effect (NIE; mediated) by the biomarker mediators of interest.

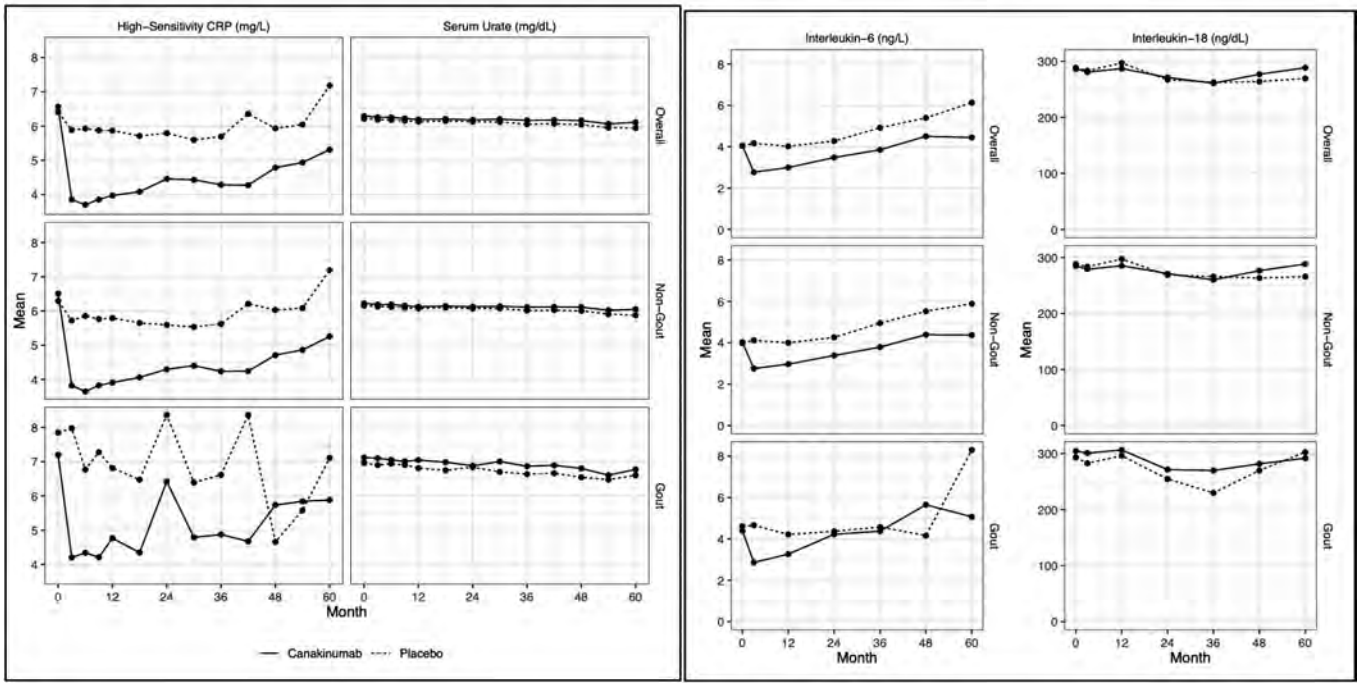
	Mediator: Δ log hsCRP 3mo	Mediator: Δ log SU 3mo	Mediator: Δ log IL-6 3mo	Mediator: Δ log IL-18 3mo
Overall	N = 9,968	N = 9,968	N = 5,013	N = 5,026
Total Effect HR	0.51 [0.38, 0.69]	0.45 [0.33, 0.63]	0.52 [0.35, 0.78]	0.53 [0.36, 0.79]
Natural Direct Effect HR	0.54 [0.39, 0.75]	0.45 [0.32, 0.62]	0.55 [0.36, 0.85]	0.53 [0.36, 0.79]
Natural Indirect Effect HR	0.94 [0.82, 1.09]	1.01 [0.99, 1.03]	0.95 [0.78, 1.15]	1.00 [0.99, 1.01]
%Mediated	6%	-1%*	6%	0%
No Prevalent Gout	N = 9,221	N = 9,221	N = 4,585	N = 4,598
Total Effect HR	0.44 [0.29, 0.65]	0.43 [0.27, 0.68]	0.48 [0.29, 0.78]	0.49 [0.30, 0.81]
Natural Direct Effect HR	0.41 [0.27, 0.65]	0.43 [0.27, 0.67]	0.53 [0.30, 0.91]	0.49 [0.30, 0.81]
Natural Indirect Effect HR	1.06 [0.87, 1.28]	1.01 [0.98, 1.04]	0.91 [0.71, 1.15]	1.00 [0.99, 1.01]
%Mediated	-4%*	-1%*	9%	0%
Prevalent Gout	N = 747	N = 747	N = 428	N = 428
Total Effect HR	0.61 [0.37, 0.98]	0.51 [0.29, 0.88]	0.55 [0.27, 1.13]	0.59 [0.30, 1.18]
Natural Direct Effect HR	0.74 [0.43, 1.28]	0.49 [0.29, 0.85]	0.55 [0.25, 1.18]	0.59 [0.29, 1.18]
Natural Indirect Effect HR	0.82 [0.66, 1.02]	1.03 [0.97, 1.09]	1.01 [0.75, 1.38]	1.00 [0.97, 1.03]
%Mediated	35%	-3%*	-1%*	0%

The TE HR represents the overall benefit of canakinumab compared to placebo on suppressing subsequent gout flare. It "decomposes" multiplicatively as follows: TE=NDE×NIE.

Abbreviations: Δ log hsCRP 3mo: difference of log high sensitivity C-reactive protein at 3 months and baseline; Δ log SU 3mo: difference of log serum urate at 3 months and baseline.

* A negative proportion mediated estimate can arise in cases where NDE and NIE estimates differ in the direction. These are not meaningfully interpretable but were presented for reference.

Figure 1. Mean biomarker values over time by study cohorts and treatment groups.



cohort, HR 0.61=0.74×0.82 (PM35%). This mediation was primarily driven by the interaction between be CAN and hsCRP reduction in the outcome model. That is, the first 3-month hsCRP reduction, when driven by CAN, is protective of gout flares. The overall cohort IL-6 analysis was similar although subgroup results did not concur.

Conclusion: The first 3-month reduction in hsCRP explained 6% of its protective effect on future gout flare suppression with a larger proportion mediated (35%) among prevalent gout patients. There may be a potential role of early hsCRP reduction under canakinumab therapy as a treatment benefit biomarker for future gout flares in addition to its role as a treatment benefit biomarker for future CVD.

Disclosure: K. Yoshida, None; **R. Glynn**, None; **H. Choi**, None; **B. Everett**, None; **Y. Li**, None; **J. MacFadyen**, None; **P. Ridker**, None; **D. Solomon**, Abbvie, 5, Amgen, 5, Genentech, 5.

Abstract Number: 1566

Hyperuricemia Is Associated with Vascular Endothelial Dysfunction – the Impact of Hyperuricemia on Flow Mediated and Nitroglycerin Mediated Dilatation of the Brachial Artery

Rachael Flood, Colm Kirby, David Kane and Ronan Mullan, Tallaght University Hospital, Dublin, Ireland

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Vascular endothelial cells line the entire circulatory system, these cells have very distinct and unique functions that are paramount to vascular biology. Hyperuricemia has been associated with vascular endothelial dysfunction (ED) in cardiovascular disease. Elevated serum urate (sUA) has been shown to directly impair vascular endothelial cell function through inhibition of nitric oxide. While direct measurement of impaired endothelial-dependent dilation during coronary angiography remains the historical "gold-standard", other approaches, including the measurement of brachial artery diameter via non-invasive ultrasound imaging, has been validated both as a sensitive predictor and surrogate endpoint in cardiovascular risk reduction interventional studies. Close concordance between these measurements with coronary artery endothelial-dependent vasodilation have been established. Our objective was to compare vascular endothelial cell function in hyperuricemic patients with normouricemic controls via flow mediated dilatation (FMD) and nitroglycerin mediated dilatation (NMD) of the brachial artery and the subsequent effect of treatment with urate lowering therapy (ULT).

Methods: Following informed consent hyperuricemic individuals (N = 34) underwent FMD and NMD studies of the brachial artery. Results were compared to age and sex matched normouricemic controls (N=16). Changes in brachial artery diameter were expressed as percentage change relative to the baseline vessel diameter. Those who met the criteria for commencement of ULT underwent repeat studies after a period of three months (N=28) treatment with febuxostat or allopurinol.

Results: 34 patients with hyperuricemia (sUA > 380umol/L) and 16 normouricemic controls were recruited and consented for the study. Mean sUA was 472 and 283 umol/L in the case versus control group respectively. There was no significant difference in mean age (Mean± SD) (50.35± 15.56 v 42.44±12.96) estimated glomerular filtration rate ml/min/1.73m^2 (91.82± 16.79 v 94.03±18.75) or total cholesterol (4.86± 1.25 v 4.73±0.72) between cases and controls respectively however there was a significantly greater (P< 0.05) BMI kg/m2 (33.45± 6.9 v 25.94±3.8) in cases. Cases had significantly impaired (P< 0.05) FMD (11.05± 8.71 v 17.26±8.42) and NMD (19.56± 9.15 v 34.16±9.26) when compared with controls. 28 cases underwent treatment with ULT and repeat FMD and NMD studies post 3 months of therapy, there was a trend toward improved of NMD (22.95 ±7.04) but this was not significant.

Parameter (Mean, SD)	Case (N = 34)	Control (N= 16)
Age (years)	50.35 (15.56)	42.44 (12.96)
Male (N, %)	24 (70.6)	8 (50)
uric acid umol/L	471.91 (81.08)*	283.12 (55.19)
eGFR mL/min/1.73 m²	91.82 (16.79)	94.03 (18.75)
CRP (mg/dl)	7.10 (12.33)	4.87 (9.63)
ESR (mm/hr)	15.81 (17.63)	10.2 (9.31)
Cholesterol (mmol/L)	4.9 (1.25)	4.8 (0.72)
Fasting Glucose (mmol/L)	5.6 (0.93)	5.07 (0.61)
Homocysteine (umol/L)	14.98 (10.17)	13.0 (4.44)
Diabetes (N,%)	2 (6.1)	0
Hypertension (N, %)	11 (32.4)	6 (37.5)
CKD (N, %)	0	0
IHD (N, %)	1 (3)	1 (6.3)
Malignancy (N, %)	1 (3)	0
BMI (kg/m2)	33.45 (6.96)*	25.94 (3.8)

Table 1: Case and Control Baseline Data.

SD – Standard Deviation. eGFR- Estimated Glomerular Filtration Rate. CRP- C Reactive Protein. ESR – Erythrocyte Sedimentation Rate. CKD – Chronic Kidney Disease. IHD – Ischaemic Heart Disease. BMI – Body Mass Index.

- * = P < 0.05.

Conclusion: These results suggest that hyperuricemia is associated with impaired vascular endothelial dysfunction which may contribute to the increased risk of cardiovascular disease in this cohort of patients.

Disclosure: R. Flood, None; **C. Kirby**, None; **D. Kane**, None; **R. Mullan**, None.

Abstract Number: 1567

Pharmacokinetics and Pharmacodynamics of Anthocyanins After Oral Administration of Oral Tart Cherry Juice Concentrate to Gout Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Tart cherries (TC) contain high levels of anthocyanins that exert potent antioxidant and anti-inflammatory effects. Approximately 50% of gout patients report using TC to help manage their gout, and preliminary data have demonstrated reduced gout flares in patients consuming TC. Our study aimed to characterize the major anthocyanins in Tart Cherry Juice Concentrate (TCJC) and identify the most prominently available anthocyanins in gout patients consuming TCJC.

Methods: Anthocyanins were determined using liquid chromatography-mass spectroscopy (LCMS). TCJC was diluted with deionized water and anthocyanins analyzed by LCMS using a Dionex UltiMate 3000 LC coupled with a Thermo Q Exactive HF, a Phenomenex Kinetex C18 column, and a gradient of 10% aqueous formic acid: acetonitrile. Cyanidin-3-arabinoside was used as an internal standard. anthocyaninswere identified by their fragmentation patterns and/or authentic standards. All available standards were purchased from Sigma Aldrich (St. Louis, MO), except for cyanidin-3-glucosylrutinoside, purchased from Diagnocine LLC (Hackensack, NJ). Individuals with gout (n=10) were administered either 60 or 120 mL of TCJC in a crossover design. Serial blood samples were drawn and used to characterize the pharmacokinetics and pharmacodynamics of anthocyanins in plasma.

Results: Cyanidin-3-glucosylrutinoside (C3GR) and cyanidin-3-rutinoside (C3R) were the main anthocyanins identified in the TCJC (Table 1). Various anthocyanins were bioavailable with C3GR and C3R achieving the highest plasma concentration in a dose-dependent manner.

Administration of oral TCJC resulted in a significant fold change in antioxidant mRNA gene expression NRF-2, HO-1, and NQO-1 (mean peak fold change 1.3, 1.6, and 1.4 versus baseline, $p< 0.05$; respectively) appreciated as early as 30 minutes after dose administration.

A significant reduction in iNOS and TNF-α mRNA gene expression (mean peak fold change 0.7 and 0.8 versus baseline, $p< 0.05$; respectively) was also observed and peaked at 2 hours post-dose. Only the high dose resulted in significant changes in gene expression. Pharmacokinetic analyses are ongoing.

Table 1. Quantitation of major anthocyanins identified in TCJC

Anthocyanin	Standard curve used	ng/μL
Cyanidin-3-glucosylrutinoside*	Cyanidin-3-glucosylrutinoside	343.3
Cyanidin-3-rutinoside*	Cyanidin-3-rutinoside	143.5
Petunidin deoxyhexose hexose	Cyanidin-3-rutinoside	37.8
Delphinidin deoxyhexose hexose	Cyanidin-3-rutinoside	33.4
Cyanidin-3-sophoroside*	Cyanidin-3-sophoroside	20.6
Delphinidin deoxyhexose hexose hexose	Cyanidin-3-rutinoside	19.2
Cyanidin pentose deoxyhexose hexose	Cyanidin-3-rutinoside	15.7
Peonidin-3-rutinoside*	Peonidin-3-rutinoside	15.5
Cyanidin deoxyhexose hexose	Cyanidin-3-rutinoside	10.0

Conclusion: The present study identifies the main anthocyanins present in the TCJC and patient plasma after oral administration of TCJC, as cyanidin 3-glucosylrutinoside and cyanidin 3-rutinoside. Since these anthocyanins are known to have anti-inflammatory and antioxidant effects, they may explain the benefit of TC in patients with gout.

Disclosure: L. Brunetti, Merck, 5, Astellas Pharma, 5, CSL Behring, 5, Innovative Research, 5, Horizon Blue Cross Blue Shield of NJ, 2, Tabula Rasa, 2; **L. Wang**, None; **A. Wassef**, None; **A. Brinker**, None; **B. Buckley**, None; **P. Lipsky**, Horizon, 2; **A. Kong**, None; **N. Schlesinger**, Horizon, 2, Novartis, 2, Alnylam, 2, Pfizer, 5, AMGEN, 5.

Abstract Number: 1568

AR882, a Potent and Selective Uricosuric Agent, Showed Effectiveness in Patients with Various Degrees of Renal Impairment

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: AR882 is a novel, potent and selective uric acid transporter 1 (URAT1) inhibitor in Phase 2 development for the treatment of hyperuricemia and gout. In Phase 1 and Phase 2a studies AR882 exhibited good dose proportionality, long effective half-life and dose-dependent serum urate (sUA) lowering effect and was well tolerated in healthy subjects or gout patients.

Methods: AR882 had been evaluated in healthy subjects with normal renal function, mild or moderate impairment (estimated creatinine clearance ≥ 90, 60 to < 90, 30 to < 60 mL/min, respectively), or in gout patients with normal renal function or mild renal impairment. Subjects with severe renal impairment (15 to < 30 mL/min) are currently being enrolled for evaluation. AR882 was given as an oral capsule at 50 mg (multiple doses) or 100 mg (single dose). Serial blood and urine samples were collected for measurement of AR882 concentration and sUA levels for PK/PD assessment. Adverse events, laboratory safety tests, vital signs, and electrocardiograms were collected throughout the study.

Results: Following a single oral dose of AR882 at 100 mg, only mild increases in plasma exposure to AR882 was noted in subjects with mild (n=8) or moderate (n=8) impairment when compared to subjects with normal renal function (n=8). The sUA lowering effect of AR882 was not affected in subjects with mild or moderate impairment. Maximal reduction in sUA levels was approximately 50-60% in subjects with renal impairment, similar to those observed in subjects with normal renal function.

In 28 gout patients receiving 50 mg multiple doses for one week in a phase 2a study, similar AR882 plasma exposure was observed between patients with normal renal function (n=18) and those with mild renal impairment (n=10). At steady state, reduction of sUA levels was approximately 53% in both renal function groups. Response rate at target sUA levels were also similar.

Conclusion: AR882 sUA lowering effect is similar in subjects with mild or moderate renal impairment compared to subjects/patients with normal renal function. No clinically relevant serum creatinine elevation was observed in either the phase 2a gout patient study or the phase 1 renal impairment study.

Disclosure: z. shen, None; **E. Polvent**, None; **v. hingorani**, None; **R. Yan**, None; **S. Yan**, None; **L. Yeh**, None.

Abstract Number: 1569

Effect of Elevated Serum Urate on Kidney Function: Analysis of a Randomized Controlled Trial of Inosine Supplementation

Nicola Dalbeth[1], Borislav Mihov[1], Angela Stewart[1], Gregory Gamble[1], Tony Merriman[2], David Mount[3], Lisa Stamp[4], Ian Reid[1] and Anne Horne[1], [1]University of Auckland, Auckland, New Zealand, [2]University of Alabama at Birmingham, Dunedin, New Zealand, [3]Brigham and Women's Hospital, Boston, MA, [4]University of Otago, Christchurch, Christchurch, New Zealand

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Observational studies have reported that serum urate associates with development and progression of kidney disease. However, it is uncertain whether elevated serum urate directly influences kidney function, with recent Mendelian randomization studies and clinical trials of urate-lowering therapy in CKD suggesting that elevated urate does not influence kidney disease. Inosine is a purine nucleoside that increases extra-renal urate production and thus, serum urate concentrations. We analyzed data from a 6-month randomized placebo-controlled trial of inosine supplementation to determine whether moderate hyperuricemia induced by inosine affects kidney function, as assessed by serum creatinine.

Methods: One hundred and twenty post-menopausal women were recruited into a six-month randomized, double-blind, placebo-controlled trial of inosine supplementation for bone health (*Arthritis Rheumatology* 2021, PMID: 33586367). Exclusion criteria included gout, kidney stones, eGFR≤60 ml/min/1.73m^2, and urine pH ≤5.0. Participants were randomized 1:1 to inosine supplements (doses adjusted to maintain serum urate below 8mg/dL), or placebo. Serum creatinine, serum urate, and fractional excretion of uric acid (FEUA) were pre-specified secondary endpoints. Data were analyzed on an intention to treat basis, using a mixed models approach to repeated measures, with false detection rate protected pairwise comparisons at each time point. For analysis of covariance of change from baseline (ANCOVA), baseline values were included in the models.

Results: Administration of inosine supplements led to a significant increase in serum urate and FEUA over the study period (Figure 1. and 1B respectively). The maximum difference between groups in both serum urate and FEUA was observed at week 6; at this time point, the mean (SD) serum urate was 7.3 (1.5) mg/dL in the inosine group, and 4.7 (1.0) mg/dL in the placebo group (P< 0.0001), and the mean (SD) FEUA was 10.1 (3.2)% in the inosine group and 7.7 (2.4)% in the placebo group (P< 0.0001). There was no between-group difference in serum creatinine values at any time point over the 26 week period (P>0.62 Figure 1C). Analysis of the change in serum creatinine from baseline

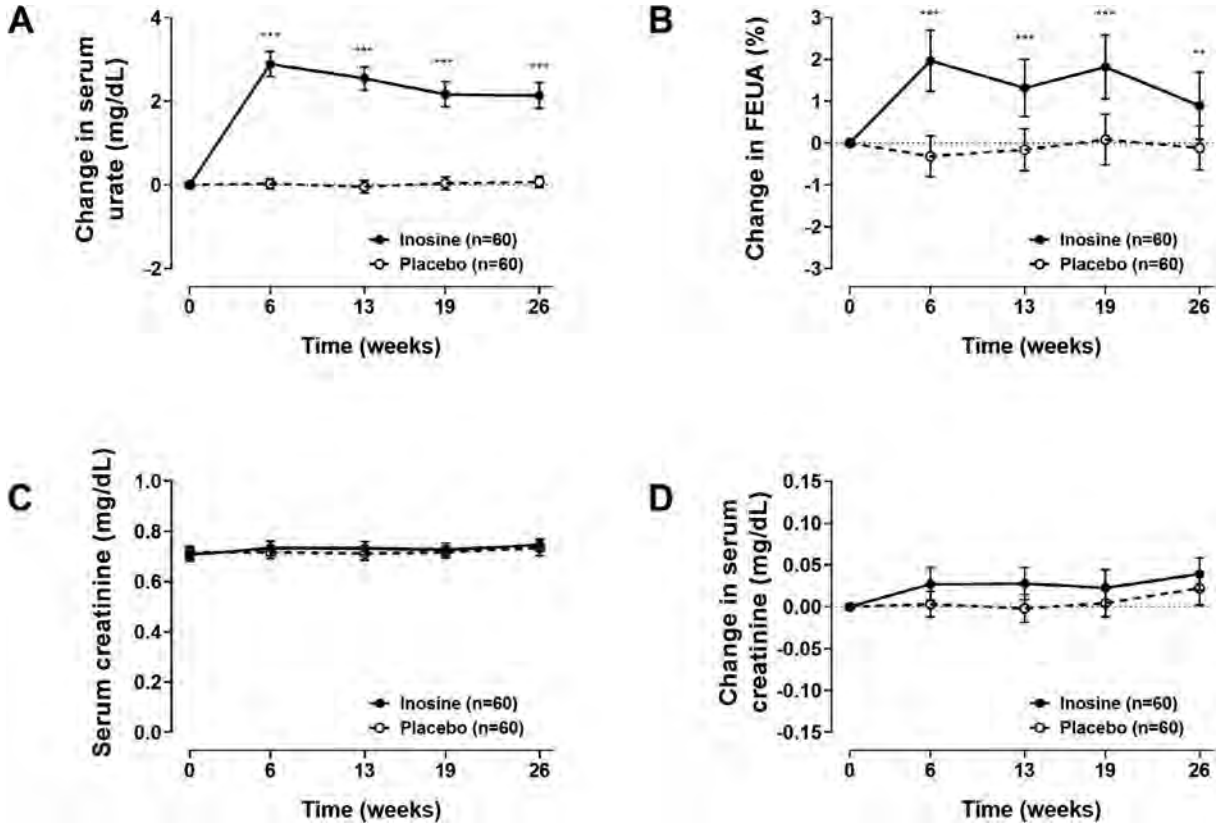


Figure 1. Study endpoints. A. Change in serum urate; B. Change in FEUA; C. Serum creatinine values; D. Change in serum creatinine; Data re presented as mean (95% CI). **false detection rate P<0.01, ***false detection rate P<0.001.

showed a maximal difference between groups at week 13 (with mean (95% CI) difference of +0.029 (-0.005, +0.055) mg/dL, P=0.059, Figure 1D). At all other time points, there was no between-group difference in the change in serum creatinine.

Conclusion: Elevated serum urate due to increased extra-renal urate production does not lead to kidney impairment over a six month period.

Disclosure: N. Dalbeth, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **B. Mihov**, None; **A. Stewart**, None; **G. Gamble**, None; **T. Merriman**, None; **D. Mount**, None; **L. Stamp**, None; **I. Reid**, None; **A. Horne**, None.

Abstract Number: 1570

AR882, a Novel Uricosuric Agent, Exhibited Favorable Pharmacokinetic Profile and Balanced Excretion and Metabolic Pathways in a Human AME Study

Rongzi Yan[1], zancong shen[2], Elizabeth Polvent[3], vijay hingorani[4], Shunqi Yan[5] and **Litain Yeh**[6], [1]Arthrosi Therapeutics, Inc, Irvine, CA, [2]Arthrosi Therapeutics, Inc., San Diego, CA, [3]Arthrosi Therapeutics, Inc., Roseville, CA, [4]Vanguard Healthsciences, Inc., San Diego, CA, [5]Arthrosi Therapeutics, Inc., Laguna Hills, CA, [6]Arthrosi Therapeutics, Inc., Irvine, CA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

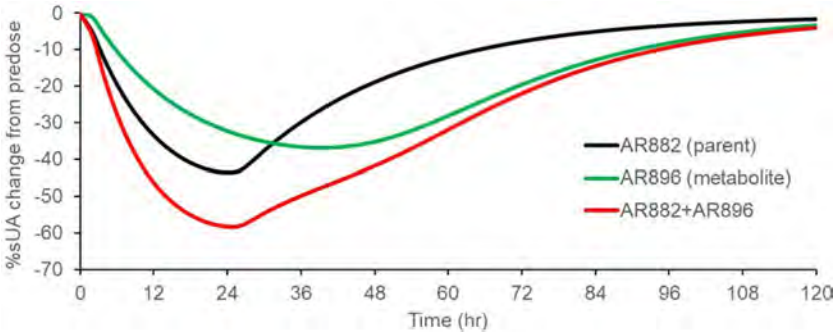
Background/Purpose: AR882, a novel uric acid transporter 1 (URAT1) inhibitor is being developed for the treatment of gout with hyperuricemia. In Phase 1 and Phase 2 studies, AR882 exhibited long lasting serum urate (sUA) lowering effect and good safety in healthy subjects and patients with gout. In a Phase 1 open-label, single-dose study with oral administration of [^{14}C] AR882, the absorption, metabolism, and excretion (AME) profile of AR882 was investigated in healthy subjects.

Methods: Six (6) healthy male subjects received a single oral dose of 100 mg (250 μCi) [^{14}C]AR882 under fasting conditions. Serial blood, urine, and fecal samples were collected up to 144 hours postdose, and then at 24-hour intervals thereafter until the subject was discharged (up to 288 hours). Total radioactivity in plasma, whole blood, urine, and fecal samples was measured using liquid scintillation counting methods. Concentration of AR882 and active metabolite, AR896, in plasma and urine was determined using validated liquid chromatography with tandem mass spectrometry (LC-MS/MS) methods. Metabolite profiling in each matrix and structure identification were performed using high resolution accurate mass LC-RAD-MS/MS with in-line fraction collection and off-line counting to obtain [^{14}C]- radiochromatographic profiles and provide information on the nature of the radioactive components present. In addition, the metabolite profile of AR882 comparison were made cross species.

Results: All 6 subjects completed the full study except one subject withdrew after 7 days due to personal reason. The overall total recovery was 89.2% (34% in urine and 55% in feces) of [^{14}C]AR882 administered and recovery was complete 10 days after dosing. Within 24 hours approximately 20% and 8% of dose was recovered in urine and feces, respectively. Both AR882 and total radioactivity were readily absorbed with terminal half-life of approximate 20 hours. AR882 was accounted for 88% of the circulating radioactivity followed by its active metabolite AR896 (8%).

The renal clearance was approximately 0.02 mL/min and 3.20 mL/min for AR882 and AR896, respectively. AR896 exhibited weak URAT1 inhibition and was identified to contribute to the sustained inhibition of URAT1 and sUA lowering effect of AR882 in a parent-metabolite pharmacokinetics/pharmacodynamic model (**Figure**). Metabolic pathway of AR882 included oxidation, sulfation, glucuronidation, and hydrolysis. There were no disproportional or unique human metabolites identified when compared to AME profiles in rats and monkeys. Based on the metabolic profile in feces and recovery of radioactivity in urine, at least 80% AR882 was absorbed.

Conclusion: The sustainable sUA lowering effect of AR882 observed in clinical studies is attributed to the pharmacological effects of parent drug and its active metabolite as well as its favorable PK properties and balanced metabolic and elimination pathways.



Simulated Serum Urate Lowering Effect of AR882 (Parent) and AR896 (Metabolite) following a Single Oral Dose of 100 mg AR882 based on PK/PD Model

Disclosure: R. Yan, None; **z. shen**, None; **E. Polvent**, None; **v. hingorani**, None; **S. Yan**, None; **L. Yeh**, None.

Abstract Number: 1571

Elevated Lactate, Procalcitonin Levels and SIRS (Systemic Inflammatory Response Syndrome) in a Subset of Patients with Gout

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The intense inflammatory cascade of acute gouty inflammation makes it difficult to differentiate clinically between acute gouty inflammation and sepsis, particularly since they can occur together. A SIRS-like presentation attributed to acute gouty inflammation has been described sporadically [1-6]. In these cases, sepsis is usually considered first, and markers such as lactate and procalcitonin are used to confirm the diagnosis of sepsis. Gout is not even considered as a possibility. However, delayed diagnosis and treatment of gout when it is the cause of the presentation leads to unnecessary antibiotic use and prolonged hospitalization.

We describe a cohort of patients who presented with SIRS, elevated lactate (some markedly high) and/or elevated procalcitonin and even concerning NEWS2 (National Early Warning Scores) scores due to acute gout alone. While sepsis must always be ruled out, we describe those characteristics that may suggest that gout, rather than sepsis, is the presenting cause.

Methods: Retrospective chart review of patients with a gout related hospital encounter between 2014 and 2017 at Regions Hospital. Of 1,041 such episodes, 14 encounters had ≥2 SIRS criteria, elevated lactate/procalcitonin and were admitted for presumed sepsis. Demographics, clinical presentation, laboratory and imaging data are summarized in **Table 1**.

Results: There were 14 patient encounters including 11 patients with one episode and one with three separate similar presentations. All were male, mean age 58.6 years, mean time since gout diagnosis 11.2 years, 8 patients (66.6%) had tophi, and 10 patients (83.3%) had history of ≥5 gout flares. Mean **lactic acid** was elevated in 12/14 ranging from **2-12.2** mmol/L (normal 0.5-2.0 mmol/L), and **procalcitonin** was **0.23-2.79** ng/mL (< 0.24 ng/ml). Use of antibiotics beyond the first 24 hours of admission was seen in 7 presentations (58.3%). No infection was identified. While many patients were concurrently treated with antibiotics for presumed bacterial sepsis, the patient cohort showed rapid clinical improvement within 24-48 hours of starting appropriate gout therapy. Hospital courses are summarized in **Table 1**.

Conclusion: A **SIRS-like** presentation with **elevated lactate** and **procalcitonin** levels occurs in a subset of gout patients. A high index of suspicion for a gout flare is indicated if patients have a) **history of gout of >10 years duration** b) **tophi** c) ≥ **5 gouty flares**. Early recognition of gout as the cause of the marked inflammatory response can limit unnecessary antibiotic use and prolonged hospitalization. Hospitalists, emergency physicians and rheumatologists should be aware of this subset of gouty patients.

Table 1: Background Characteristics, Hospital Course of Gouty SIRS-like Presentation

Patient Case	Age (years)/ Sex	Years Since Gout Diagnosis	Number of Prior Gout Flares	Tophi Present	Peak Uric Acid Prior to Admission (mg/dL)	Presentation	SIRS Criteria Met	NEWS2 Score	Uric Acid (mg/dL)	Procalcitonin (ng/mL)	Lactic Acid (mmol/L)	Infectious Workup	Antibiotics Course (x total doses)	Acute Gout Treatment	Hospital Course
1	56/Male	4	>5	Yes	13.9	Acute polyarticular gout of bilateral knees, MCPs, wrist.	2	2	8.8	0.23	1.0	Negative blood cultures, UA, CXR	None	Oral steroids tapered over 1 week.	Improved within 48 hours of starting steroids
2	66/Male	10	>5	Yes, also urate stones	11.7	Acute polyarticular gout of bilateral hands, shoulder, feet, and ankles	2	3	6.2	-	1.1	Negative blood cultures, UA, CXR.	Aztreonam IV (x1) Vancomycin IV (x1)	Stress-dose IV steroids, then oral steroid taper over 2 weeks. Started on allopurinol, colchicine.	Improved within 48 hours of starting steroids
3	52/Male	15	>5	Yes	11.5	Acute gout of left shoulder	2	5	6.2	-	2.0	Negative blood cultures, UA, CXR, and *Clostridium difficile* stool antigen. CT without intraabdominal abscess	Metronidazole IV (x1) Linezolid IV (x3) Meropenem IV (x8) Zosyn IV (x3) Vancomycin IV (x2)	IV steroids, then oral steroid taper over 2 weeks. Started on allopurinol, colchicine.	Improved within 48 hours of starting steroids
4	37/Male	10	>5	No	-	Acute gout of right knee and hip	2	2	8.3	0.69	2.4	Negative blood cultures, UA, CXR, synovial fluid cultures.	Zosyn IV (x3) Vancomycin IV (x2)	IV then oral steroids	Improved within 24 hours of starting steroids
5a	49/Male	27	>5	Yes	-	ICU admission for shock.	3	11	7.2	-	3.4	Negative blood cultures, UA, *Strep. pneumoniae* and *Legionella* urine antigens.	Zosyn IV (x13) Vancomycin IV (x8) Ceftriaxone IV (x4)	IV stress-dose steroids and intra-articular steroids, then anakinra and oral steroid taper over 1 month. Started on allopurinol.	Gouty symptoms persisted through HD#10 in setting of renal failure
5b						Acute polyarticular gout flare after running out of prednisone and allopurinol after previous admission	3	5	14.8	-	3.5	Negative blood cultures, UA, CXR, HIV. CT without intraabdominal abscess.	None	IV then oral steroids with taper over 1 month. Started on allopurinol, colchicine.	Improved within 48 hours of starting steroids
5c						Acute polyarticular gout after failed medical follow-up from previous admission	3	4	12.1	1.01	2.9	Negative blood cultures, UA	Zosyn IV (x7) Vancomycin IV (x4)	IV then oral steroids. Started on allopurinol.	Improved within 48 hours of starting steroids
6	59/Male	8	>5	Yes	-	Acute polyarticular gout of right knee, right great toe, left elbow, left wrist	3	4	8.8	-	3.7	Negative blood cultures, UA, CXR	Ceftriaxone IV (x1)	Indomethacin	Improved within 72 hours
7	68/Male	1	2	No	12.3	Acute polyarticular gout of bilateral knees	3	3	4.5	0.61	2.9	Negative blood cultures, UA, CXR, synovial fluid cultures.	Zosyn IV 4.5g (x1) Ceftriaxone IV (x3) Vancomycin IV (x4)	Oral steroids. Started on allopurinol, colchicine	Improved within 48 hours of starting steroids
8	53/Male	4	5	Yes	9.7	Acute polyarticular gout or right knee, right elbow, and right wrist.	2	4	5.4	2.24	2.6	Negative blood cultures, UA, synovial fluid culture.	Vancomycin IV (x2)	Intra-articular, IV then oral steroids	Improved within 24 hours of starting steroids
9	53/Male	0	1	No	-	Acute left knee gout	3	4	-	-	3.4	Negative blood cultures, UA, CXR, synovial fluid cultures.	Ceftriaxone IV (x1)	Oral steroids with taper over 1 week.	Rapid improvement with next-day discharge
10	70/Male	15	>5	No	10.3	ICU admission for shock complicated by acute kidney injury	2	6	4.9	-	12.2	Negative blood cultures, UA, CXR, abdominal ultrasound	Zosyn IV (x8) Vancomycin IV (x4)	IV then oral steroids.	Improved within 48 hours of starting steroids
11	69/Male	10	>5	Yes	-	Acute polyarticular gout of bilateral MCPs, elbows, and right knee	3	4	21.4	2.79	2.8	Negative blood culture, UA. Negative synovial fluid cultures.	Zosyn IV 4.5g (x1) Cefepime IV (x2) Vancomycin IV (x1) Metronidazole IV (x3) Nafcillin IV (x1) Cefazolin IV (x3)	Anakinra and intra-articular steroids, then oral steroid taper over 1 month.	Improvement within 24 hours of starting anakinra
12	71/male	30	>5	Yes	-	Acute polyarticular gout of left elbow, left MCPs, bilateral MTPs	3	4	8.5	-	6.8	Negative blood cultures, CXR	Zosyn IV (x11) Vancomycin IV (x1) Augmentin PO (x7)	IV steroids and anakinra, then oral steroids with taper of 2 weeks. Started on colchicine.	Improvement within 24 hours of starting steroids and anakinra

UA: urinalysis; CXR: chest x-ray

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Disclosure: C. Podgorski, None; **P. Skarda**, None; **E. Gertner**, None.

Abstract Number: 1572

Ultrasound Signs of Gout in a Population with Asymptomatic Hyperuricemia

Bilal Bengana[1], Aicha Ladjouze[2], Nabil Baramtane Raaf[3], Chaffa Aimeur[4], Soraya Ayoub[5], Abdenour Boukabous[6] and Salima Lefkir-Tafiani[7], [1]University Hospital of Beni Messous Algiers - Rheumatology Department, Algiers, Algeria, [2]Specialized hospital establishment of Benaknoune, Rheumatology, Algiers, Algeria, [3]Hospital of Bitraria, Biochemistry, El Biar, Algiers, Algeria, [4]University hospital of Mustapha Bacha, Radiology, Sidi Mhamed, Algiers, Algeria, [5]University hospital of Beni Messous, Internal Medicine, BeniMessous, Algiers, Algeria, [6]University Hospital of Beni Messous Algiers- Rheumatology Department, Algiers, Algeria, [7]University Hospital of Beni Messous Algiers - Rheumatology Department, Benimessous, Algeria

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
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Background/Purpose: Hyperuricemia is a common biological abnormality, often clinically asymptomatic. However, it can announce a gout and be linked to many diseases such as metabolic syndrome, high blood pressure or kidney disease. In fact, the majority of learned societies do not recommend any urate lowering therapy (ULT) as long as the hyperuricemia remains asymptomatic. But it turns out that part of the population with asymptomatic hyperuricemia (AH) develops a gout after a few years particularly with genetic predisposition, but also on certain risk factors that need to be confirmed. By this way, musculoskeletal ultrasound (MUS) can detect "asymptomatic gout" by visualizing signs of urate deposits (UD) in subjects with AH.

Our main objective is already to estimate the prevalence of specific signs of gout in Algerian population with AH and assess the factors exposing to UD.

Methods: This is a descriptive cross-sectional study from January 2017 to February 2019, with the recruitment of subjects with AH and serum urate level > 360 µmol/l (6 mg/dl), who do not take any ULT and have not associated any chronic inflammatory rheumatism, where we performed a MUS of the knees, metatarsophalangeal joints MTP1, MTP2 and metacarpophalangeal joint MCP2 and MCP3 with the Achilles, patellar and quadricipital tendons.

Results: We retained 258 subjects with AH, 132 women and 126 men (sex ratio = 0.95), the mean age was 59 years, the mean body mass index (BMI) was 28.4 kg / m2, 42 patients were under diuretics, 37 patients reported being on low-dose of aspirin 100 mg daily. The mean rate of serum urate levels was 460 ± 6 µmol/l , the prevalence of UD found

at the MUS was 22% (n = 58), among them 36 % (21/58) had a sign of the double contour DC on the MTP1 and 29% (17/58) on the knee, 7% (4/58) had tophi on the MTP1 and 3% (2/58) had urate aggregates.

The factors reported to be linked to UD in the sample were: the male gender (p = 0.0016); the high uric acid level (p= 0.0355); BMI (p = 0.0427); taking diuretics for women (p= 0.0002).

Conclusion: Through this work, it is clear that elementary ultrasound lesions related to gout disease are common in a population with AH and concerned one fifth of subjects in our study with a higher risk in men and subjects with obesity and high uric acid level, but also in women taking diuretics. These results need to be enhanced with a randomized controlled study in order to better determine the predisposing factors for gout in any subject with AH.

Disclosure: B. Bengana, None; **A. Ladjouze**, None; **N. Raaf**, None; **C. Aimeur**, None; **S. Ayoub**, None; **A. Boukabous**, None; **S. Lefkir-Tafiani**, None.

Abstract Number: 1573

Vascular Monosodium Urate Crystal Deposition in Gout: A Dual-energy CT and Microscopy Study of Cadaveric Donors

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Background/Purpose: Cardiovascular disease is a common comorbidity in people with gout. A hypothesized link between cardiovascular disease and gout is the deposition of monosodium urate (MSU) crystals in atherosclerotic plaque. Recent dual-energy CT (DECT) studies have reported that color-coded material consistent with MSU crystal deposition is present in calcified vessels of patients with gout. However, it is unclear whether these appearances represent true MSU crystal deposition or artifact during live imaging. The aim of this study was to examine whether MSU crystal deposition is present in the great vessels of cadaveric donors with gout by DECT or microscopic analysis.

Methods: Six cadaveric donors with a documented history of gout (two with visible tophi) were studied. Vascular tissue was dissected from the arch of the aorta through to the descending aorta at the level of the diaphragm, and included the proximal few centimeters of the brachiocephalic, common carotids, and subclavian arteries. Vascular tissue from each donor was scanned by DECT (SOMATOM Definition Flash, Siemens Medical, Erlangen, Germany) and analyzed for urate deposition on a Siemens workstation using proprietary gout software (syngo MMWP VE 36A 2009, Siemens Medical). After scanning, 100µl of phosphate buffered saline was injected into the vessel wall at ten standardized sites across each sample, and aspirated fluid was analyzed by polarizing light microscopy. Positive control tissue included the foot joints of cadaveric donors with tophaceous gout analyzed by DECT and microscopy using the same protocols, as well as synthesized MSU crystals as controls at the time of microscopic analysis.

Results: DECT scanning of the cadaveric vascular tissue showed calcification in all samples, but no evidence of MSU crystal deposition (Figure 1). In contrast, urate deposition was clearly evident in the positive control tophaceous joint tissue by DECT. Microscopic analysis demonstrated plate-like cholesterol crystals from vascular tissue from five of

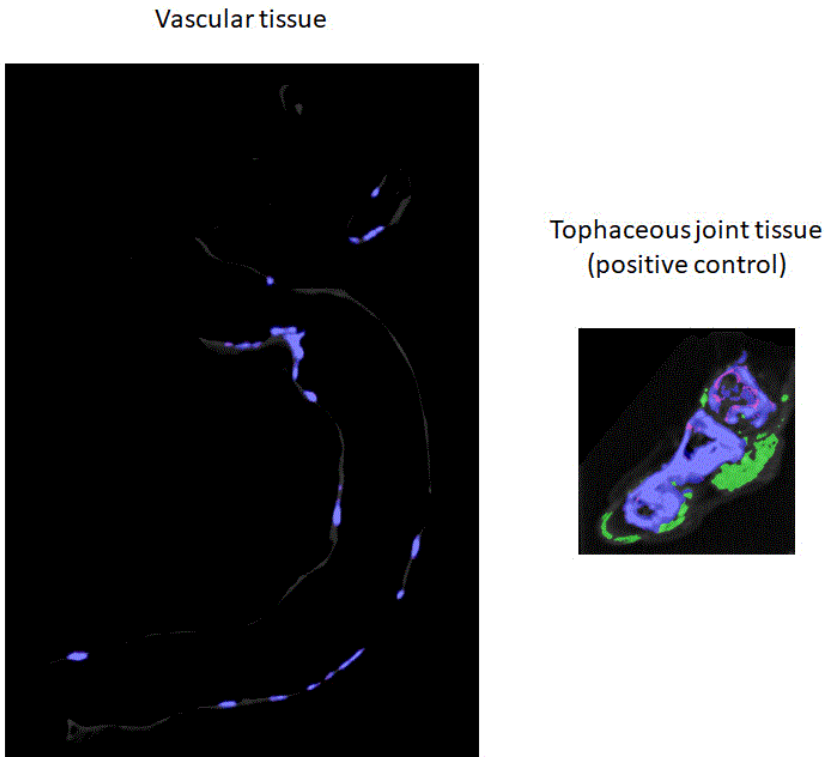

Figure 1. Dual energy CT. Left panel. Representative DECT image of cadaveric vascular tissue demonstrating vascular calcification in blue, but no urate deposition (color-coded green). Right panel. Representative DECT image of positive control cadaveric tophaceous joint tissue demonstrating urate deposition (color-coded green) within tophaceous deposits. Nail artifact is also evident.

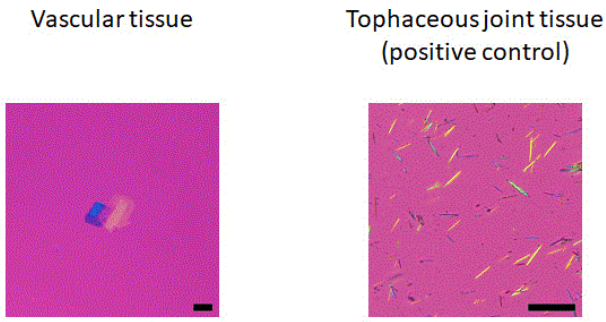

Figure 2. Polarizing light microscopy. Left panel. Representative polarizing microscopy image from cadaveric vascular tissue demonstrating plate-like cholesterol crystals, but no needle-shaped negatively birefringent crystals. Scale bar 10μm. Right panel. Representative polarizing microscopy image from positive control cadaveric tophaceous joint tissue demonstrating numerous needle-shaped negatively birefringent crystals. Scale bar 10μm.

the six donors (mean (SD) 3.2 (1.9) sites/donor, Figure 2). A single negatively birefringent needle shaped crystal was visualized from one of the 60 standardized sites analyzed, with no MSU crystals evident at any other site. In contrast, numerous negatively birefringent needle shaped crystals were present in aspirates from positive control tophaceous joint tissue.

Conclusion: This analysis has not demonstrated extensive MSU crystal deposition in vascular tissue of cadaveric donors with gout by DECT or polarizing light microscopy.

Disclosure: N. Dalbeth, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **M. Alhilali**, None; **P. Riordan**, None; **R. Narang**, None; **A. Chhana**, None; **S. McGlashan**, None; **A. Doyle**, None; **M. ANDRES**, Menarini, 6, Grunenthal, 5, 6.

Abstract Number: 1574

Comparison of Urate Quantification in Gout and Asymptomatic Hyperuricemia by Ultrasound and Dual Energy Computed Tomography

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The diagnostic gold standard for gout remains aspiration and identification of monosodium urate (MSU) crystals under polarised light microscopy. Joint aspiration is invasive and in certain patients may not be possible. The 2015 gout classification criteria include imaging evidence of urate deposition in the diagnostic criteria. The imaging modalities with sufficient published data and investigator experience to support their utility in identifying urate deposition accurately were ultrasound (US) and dual energy computed tomography (DECT). Despite the fact that US and DECT are both candidates to quantify urate deposition and monitor urate depletion, it is still unknown whether these techniques provide similar quantification of the extent of urate deposition in a given patient.

The aim of the study was to compare the quantification of urate deposition by US and DECT in a group of patients with gout and asymptomatic hyperuricaemia (AH).

Methods: Patients with either AH or gout according to 2015 diagnostic criteria were prospectively recruited to undergo quantification of MSU deposition in the knees and feet using US and DECT. A urate quantification score for each imaging modality was calculated, for US images a semiquantitative composite scoring system (1= present, 0 = absent) was used to obtain a sum score for total elementary lesions of urate deposition (double contour, tophi, aggregate or erosion) across all four joints. Exact quantification of urate deposition was calculated using specific

Parameter (Mean, SD)	Gout (N = 25)	Asymptomatic Hyperuricaemia (N=21)	Control (N= 16)
Age (years)	60 (13.11)	58 (12.64)	36 (8.9)
Male (N, %)	22 (88)	9 (43)	3 (19)
uric acid umol/L	398 (157)	472 (120.23)	265 (57.81)
eGFR mL/min/1.73 m²	68.44 (23)	56.0 (25.93)	83.8 (22.53)
CRP (mg/dl)	8.2 (10.1)	4.1 (4.8)	
Diabetes (N,%)	2 (8)	2 (10)	
Hypertension (N, %)	17 (68)	8 (38)	
CKD (N, %)	5 (20)	8 (38)	
IHD (N, %)	6 (24)	6 (29)	
Prednisolone (N, %)	4 (16)	4 (19)	
NSAID (N, %)	6 (24)	3 (14)	
Diuretic (N, %)	7 (28)	3 (14)	
BMI (kg/m2)	31.9 (8.65)	32.6 (12.9)	

Table 1: Baseline Demographics.

SD – Standard Deviation. eGFR – Estimated Glomerular Filtration Rate. CRP – C Reactive Protein. CKD – Chronic Kidney Disease. IHD – Ischaemic Heart Disease. NSAID – Non-Steroidal Anti-Inflammatory Drug. BMI – Body Mass Index

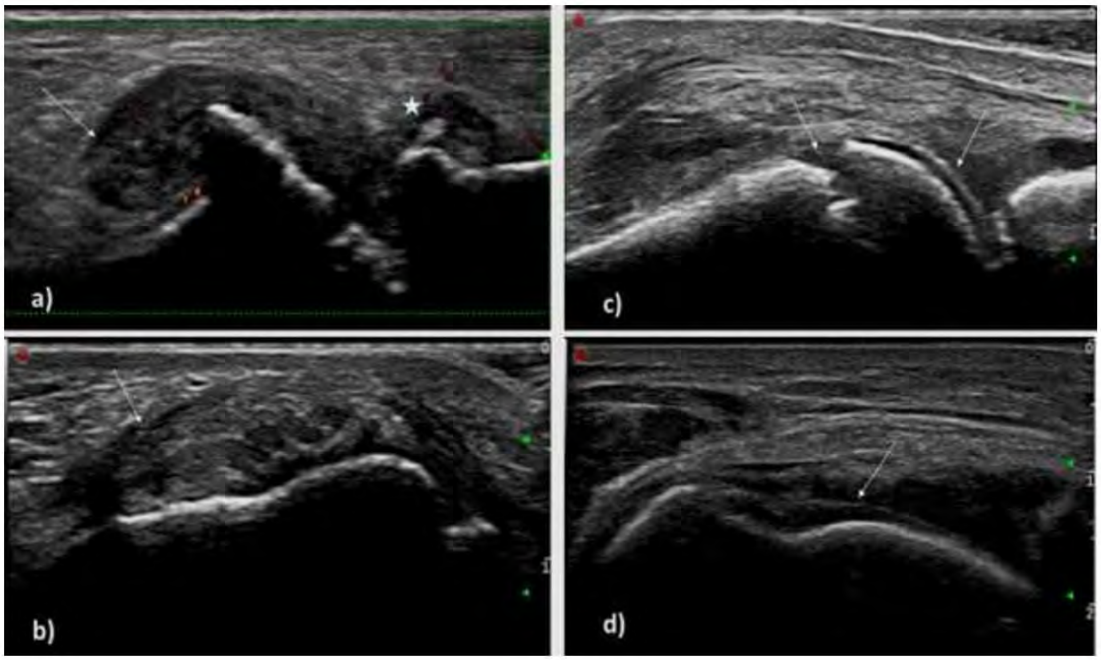

Figure 1: a.) MTP1 tophus (arrow) and aggregates (*) **b).** MTP medial tophus (arrow) **c).** DC and erosion **d).** DC at knee

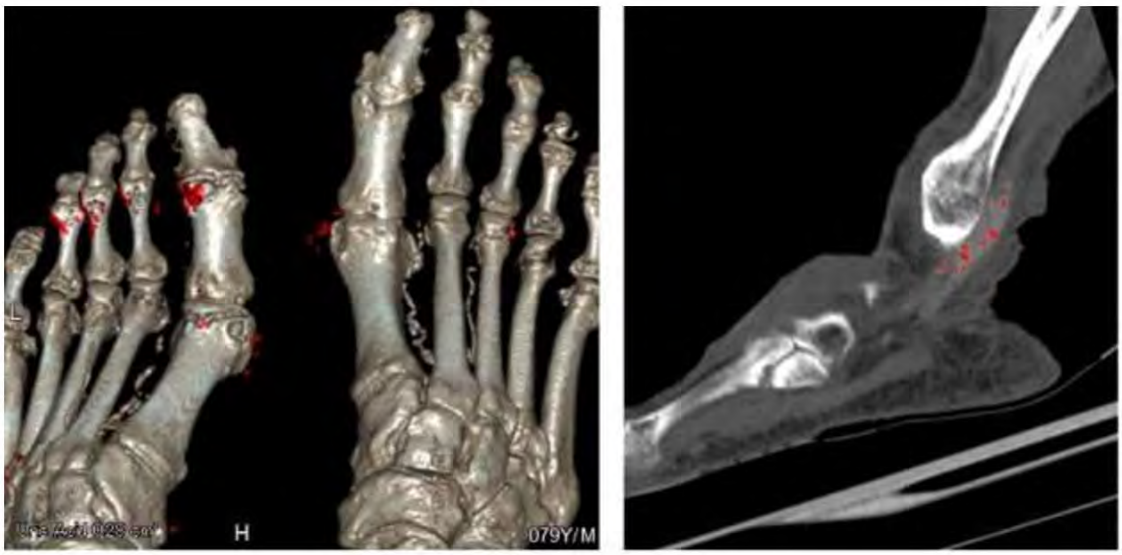

Figure 2: a). Volumetric 3D surface rendered model following post processing of dual energy CT imaging and colour -coding of uric acid deposition as red. Note estimated uric acid volume 0.28cm3. Vascular calcification is correctly not colour coded red. **B.)** Post-processed sagittal oblique dual energy CT image demonstrating uric acid crystal deposition along the peroneal tendons as colour-coded in red.

quantification software and recorded as a deposition urate score during DECT. Gout patients underwent 6 months of treatment with urate lowering therapy (ULT) in a treat to target approach and follow up US and DECT after six months of treatment.

Joint	Elementary lesion (N, %)	Gout Baseline (N= 25)	Gout 6 month (N = 22)	AH Baseline (N = 21)	AH 6 month (N=16)	Control (N = 16)
Right MTP1	Double Contour	13 (52)	11 (50)	4 (19)	3	0
	Tophus	9 (36)	7 (32)	0 (0)	0	0
	Aggregates	13 (52)	8 (36)	1 (5)	1	0
	Erosions	8 (32)	6 (27)	1 (5)	1	0
Left MTP1	Double Contour	12 (48)	6 (27)	4 (19)	1	2
	Tophus	7 (28)	4 (18)	1 (5)	2	0
	Aggregates	9 (36)	3 (14)	2 (10)	2	0
	Erosions	9 (36)	9 (41)	3 (14)	4	1
Right Knee	Double Contour	1 (4)	0 (0)	0 (0)	0	0
	Tophus	1 (4)	1 (5)	1 (5)	0	0
	Aggregates	2 (8)	0 (0)	0 (0)	0	0
	Erosions	0 (0)	0 (0)	0 (0)	0	0
Left Knee	Double Contour	3 (12)	0 (0)	0 (0)	0	0
	Tophus	1 (4)	1 (5)	0 (0)	0	0
	Aggregates	3 (12)	2 (9)	0 (0)	1	0
	Erosions	0 (0)	0 (0)	0 (0)	0	0

Table 2: Ultrasound findings of OMERACT elementary lesions of urate deposition at the knees and feet.

MTP1 – Metatarsophalangeal Joint 1.

Results: A total of 62 patients (gout=25, AH=21, Control=16) were recruited. Mean (SD) age was 60 (13.11) years in gout, 58 (12.64) years in AH and 36 (8.9) years in control groups. Mean sUA umol/L levels at baseline in gout, AH and control were (398, 472 and 265) respectively.

For the gout cohort the mean (SD) US score at baseline was 3.64 (2.52) and on repeat US following 6 months of ULT this reduced to 2.68 (2.01). In the AH group the mean (SD) US score at baseline was 0.81 (0.98). There is a significant difference ($P < 0.01$) between the mean baseline US score in Gout and AH patients.

22 and 18 patients underwent baseline DECT imaging of the feet from the Gout and AH groups respectively. The Mean (SD) deposition urate score in the gout cohort at baseline was 0.104 (0.306.) Following 6 months of ULT the mean (SD) urate deposition score was 0.069 (0.246). The mean (SD) deposition urate score in the AH group was 0.782 (0.155).

In the gout cohort of patients there is a significant correlation between the sum US Score and the DECT deposition urate score (Spearman correlation coefficient .544).

Conclusion: US and DECT imaging modalities demonstrate correlation in urate quantification in patients with gout.

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Abstract Number: 1575

Urate Crystals Regulate a Distinct JNK-Dependent Metabolic and Inflammatory Response

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SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Although metabolic reprograming and its regulation in macrophages after TLR activation is well established, little is known about the regulation and the role of metabolic changes after monosodium urate (MSU) crystal stimulation. Here, we evaluated the transcriptional and epigenetic changes, and its regulation, in macrophages after MSU stimulation.

Methods: RNA-Seq and ATAC-Seq of bone marrow derived macrophages (BMDM) or human monocyte-derived macrophages (mDM) after MSU (0.25 mg/ml) or LPS (100ng/ml) activation. ChIP-Seq for H3K27ac and H3K4me3 was also performed in BMDM. NMR was conducted on sera from patients with acute gout flare and in BMDM after MSU activation. Cytokine production was assessed by ELISA. Experiments with and without pretreatment of SP600125 (5uM), a JNK inhibitor, were also performed. For *in vivo* experiments, murine air pouch and intraarticular MSU injection models of acute gouty inflammation were performed to assess effects of inhibiting JNK (using SP600125, 15mg/kg) and glycolysis inhibition (using BAY-876, a GLUT1 inhibitor, 7.5mg/kg). Infiltrating leukocytes and cytokines from the lavage were quantified.

Results: RNA-seq results highlighted divergence of BMDM or mDM treated with MSU from those treated with LPS (Figure 1). Genes that were up-regulated only in MSU belonged to inflammatory -but not interferon activation- and

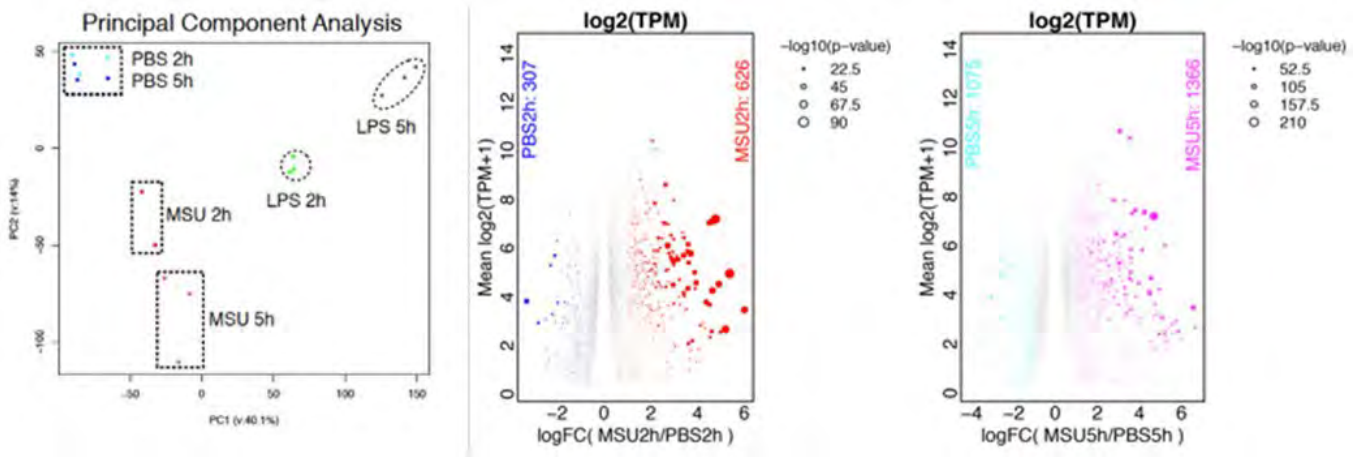


Figure 1. RNA sequencing (RNA-Seq) of bone marrow derived macrophages (BMDM) or human monocyte-derived macrophages (mDM) treated with MSU (0.25 mg/ml) or LPS (100ng/ml) for 2 and 5h. Principal component (PC) and of RNA-seq results highlighted the divergence of BMDM or mDM treated with MSU from those treated with LPS or untreated.

metabolic pathways, including glycolysis. NMR analysis showed low levels of glucose in sera from patients with acute attack, and an increase of glycolytic products in supernatants of BMDM after MSU activation. GSEA showed that whereas up-regulated genes in LPS with increased H3K27ac or H3K4me3 signal belong to inflammatory pathways, up-regulated genes in MSU with increased H3K27ac or H3K4me3 signal belong to inflammation and metabolic pathways, including metabolism of carbohydrates and transport of small molecules (Figure 2). Motif analysis showed that regions of H3K27ac or H3K4me3 up-regulated signal with up-regulated gene transcript in MSU are

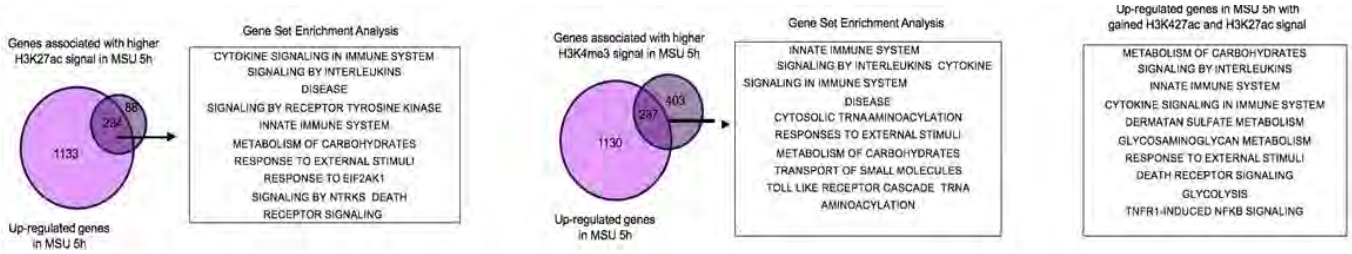
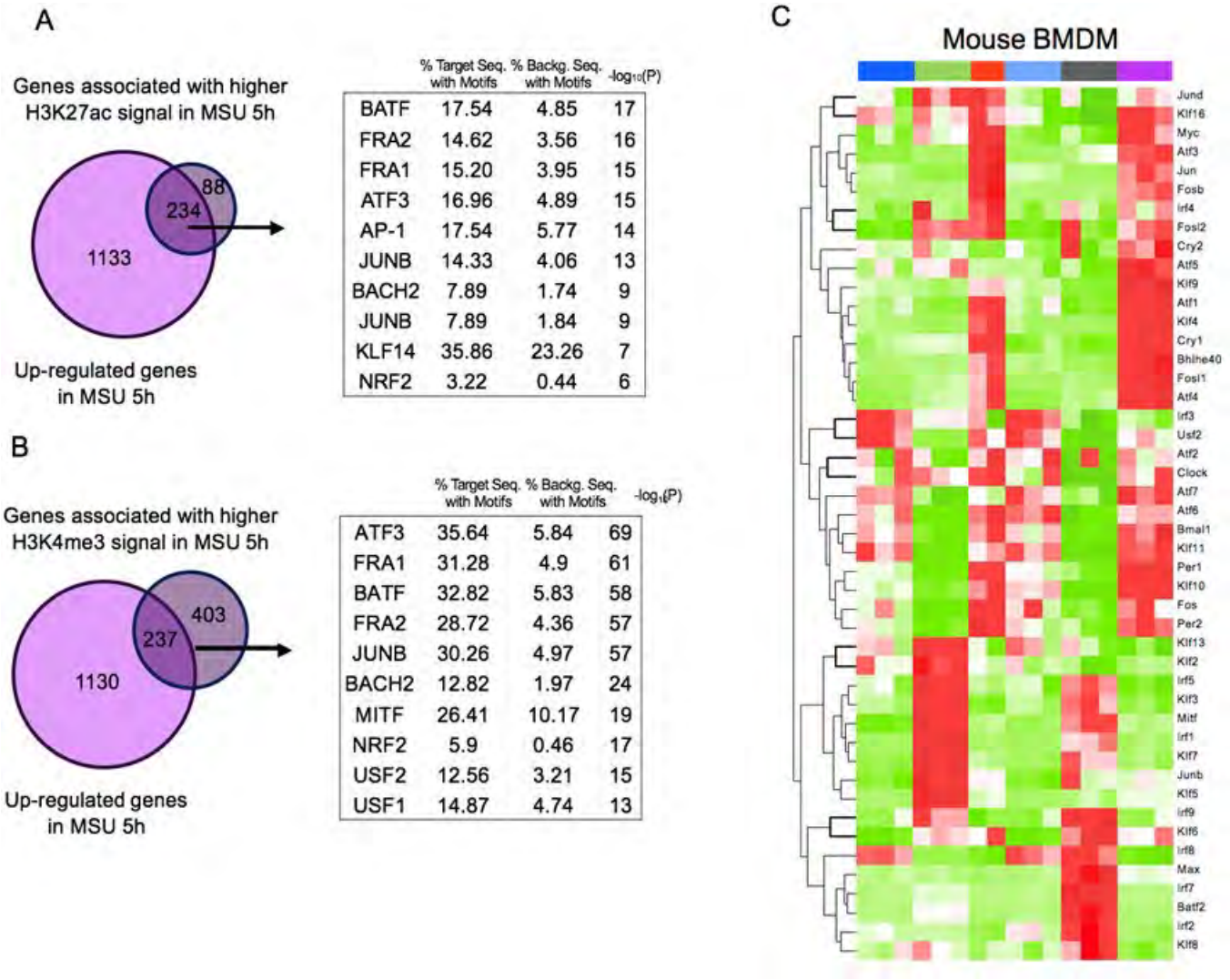


Figure 2. Chromatin immunoprecipitation (ChIP-Seq) for H3K27ac and H3K4me3 was performed to examine alteration in the activity of regions of open chromatin. Up-regulated genes in MSU with increased H3K27ac or H3K4me3 signal belong to inflammation and metabolic pathways, including metabolism of carbohydrates and transport of small molecules.



	% Target Seq. with Motifs	% Backg. Seq. with Motifs	$-\log_{10}(P)$
BATF	17.54	4.85	17
FRA2	14.62	3.56	16
FRA1	15.20	3.95	15
ATF3	16.96	4.89	15
AP-1	17.54	5.77	14
JUNB	14.33	4.06	13
BACH2	7.89	1.74	9
JUNB	7.89	1.84	9
KLF14	35.86	23.26	7
NRF2	3.22	0.44	6

	% Target Seq. with Motifs	% Backg. Seq. with Motifs	$-\log_{10}(P)$
ATF3	35.64	5.84	69
FRA1	31.28	4.9	61
BATF	32.82	5.83	58
FRA2	28.72	4.36	57
JUNB	30.26	4.97	57
BACH2	12.82	1.97	24
MITF	26.41	10.17	19
NRF2	5.9	0.46	17
USF2	12.56	3.21	15
USF1	14.87	4.74	13

Figure 3. Motif analysis showed that regions of H3K27ac or H3K4me3 up-regulated signal with up-regulated gene transcript in MSU are majorly enriched in AP-1 motifs.

majorly enriched in AP-1 motifs (Figure 3). Treatment of BMDM with JNK inhibitor ameliorated the up-regulation of p-JUN^{Ser63} and reduced the of 88.8% of genes up-regulated by MSU, including inflammatory cytokines (*Ccl2*, *Ccl4, Tnf* and *Cxcl1),* metabolic genes (*Slc2a1*, *Eno2, Pfkfb3)* and AP-1 members (*Jun, Junb, Fosl1)*. This reduction in gene expression was accompanied by reduction on H3K27ac and H3K4me3 signal over regions of open chromatin. Finally, SP600125 significantly lowered numbers of infiltrating leukocytes in the air pouch gout flare model (1.34±0.45x10^6 vs 0.49±0.48x10^6, p< 0.01, in the MSU group after PBS or JNK inhibitor respectively) and amounts of CXCL1 and IL-1b. BAY-876 markedly reduced leukocyte infiltration after knee intraarticular injection of MSU (inflammation score: 1.5±0.9 vs 0.8±0.7, p< 0.03, in the MSU group after PBS or BAY-876 respectively).

Conclusion: These results indicated that up-regulation of JUN and p-JUN^{Ser63} via JNK is necessary for up-regulation of the transcriptional program and epigenetic changes induced by MSU in macrophages. Monocyte and macrophage JNK activation are novel targets for blunting metabolic-inflammatory response to MSU crystals in gout.

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Abstract Number: 1576

Development of a Plain Radiographic Scoring System for New Bone Formation in Gout

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Type: Poster Session D

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Background/Purpose: Features of new bone formation (NBF) such as sclerosis and spurs are common on plain radiography in tophaceous gout. While a plain radiographic damage scoring system incorporating bone erosion and joint space narrowing has been developed, there are no published methods for scoring NBF in gout. The aim of this project was to develop a plain radiographic scoring system for NBF in patients with gout.

Methods: Following a systematic review of scoring systems for NBF in other bone and joint diseases, and a structured review of plain radiographs, a range of published scoring systems were tested in 80 individual joints (40 1st MTP joints and 40 5th MTP joints) from 20 patients with gout. Two readers scored the plain radiographs for sclerosis and spur using these scoring systems. Inter-reader reproducibility was assessed using intra-class correlation coefficients (ICC). In addition, construct validity was assessed by comparing plain radiography scores with gold standard computed tomography (CT) measurements of sclerosis and spur of the same joints. The best-performing scoring system was then tested in sets of hand and foot radiographs from an additional 25 patients with gout (n=52 sites/set, scores summed for each individual patient). Inter-reader ICCs were calculated, and NBF scores were correlated with plain radiographic erosion scores (using the gout-modified Sharp-van der Heijde system). All readers were blinded to each other's scores.

Results: A semi-quantitative scoring system for spur and sclerosis (**Table**) was found to have high feasibility and face validity. In the individual joint analysis, the inter-observer ICC (95% CI) using this system was 0.84 (0.76-0.89) for sclerosis and 0.81 (0.72-0.87) for spur. Plain radiographic sclerosis and spur scores correlated with CT measurements (r = 0.65-0.71, P < 0.001 for all analyses). For the hand and foot radiograph sets, the inter-observer ICC (95% CI) was 0.94 (0.90-0.97) for sclerosis score, 0.77 (0.62-0.86) for spur score, and 0.92 (0.86-0.95) for combined sclerosis and spur score. The sclerosis and spur scores correlated highly with plain radiographic erosion scores (r = 0.81-0.94, P < 0.001 for all analyses).

Conclusion: A semi-quantitative plain radiographic scoring method is feasible and reproducible for assessment of NBF in gout. This method may facilitate consistent measurement of NBF in gout.

Sclerosis	
Definition	Increased density of medullary or subcortical bone
Each bone is scored from 0 to 3 (joints with long bones are summed to a maximum score of 6)	0 = normal
	1 = mild (<1/3 bone)
	2 = moderate (1/3-2/3 bone)
	3 = severe (>2/3 bone)
Spur	
Definition	A sharp spicule of dense bone proliferation extending at an acute angle from the cortex
Each bone is scored from 0 to 3 (joints with long bones are summed to a maximum score of 6)	0 = no spur
	1 = mild (1 small spur)
	2 = moderate (≥ 2 small spurs and/or 1 moderate spur)
	3 = severe (≥ 2 moderate spurs and/or ≥ 1 large spur(s))

Definitions and scoring of new bone formation in individual joints.

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Abstract Number: 1577

Interleukin-37: Associations of Plasma Levels and Genetic Variants in Gout

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Session Time: 8:30AM–10:30AM

Background/Purpose: IL-37 is an anti-inflammatory cytokine, member of IL-1 family, related to inflammatory and autoimmune diseases. Here we aimed to investigate the association of genetic variants of IL-37 and IL-37 plasma levels in relation to hyperuricemia/gout.

Methods: The study involved normouricemic controls (n=50), primary hyperuricemia (n=100), primary gout (n=100), tophaceous gout (n=25) and acute gout flare (n=18). All patients met the ACR gout classification criteria (1). Levels of plasma IL-37 were analysed using Enzyme-Linked Immunosorbent Assay. All coding regions and intron-exon boundaries of IL-37, exon 1-5, were amplified and sequenced directly. Differences of measured levels of IL-37 between groups were compared using Wilcoxon test. Variant allele frequencies were compared using binomial test and Fisher exact test.

Results: IL-37 levels were fairly similar across groups except for patients with tophaceous gout that had IL-37 levels significantly increased in contrast to control subjects (p=0.019) and gout patients (p=0.036). We identified 12 IL-37 genetic variants: five intron (rs28947188, rs2466448, rs3811045, rs3811048, rs2708944), and seven non-synonymous allelic variants (rs3811046, rs3811047, rs2708943, rs2723183, rs2723187, rs2708947, rs27231927). Of those, rs28947188 showed a significant under-presentation in hyperuricemic and gout cohorts (no variant found among all 243 patients) compared to normouricemic control group (minor allele frequency: MAF = 0.05) and European population (MAF = 0.083).

Conclusion: Variant rs28947188 showed a significant under-presentation in hyperuricemic/gout cohorts compared to European population MAF/normouricemic cohort. Plasma IL-37 is significantly up-regulated in patients with tophaceous gout compared to other groups. This evidence highlights the role of IL-37 in the pathogenesis of gout.

Acknowledgements: *Supported by MHCR 023728, SVV 260 523 and BBMRI-CZ LM2018125*

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1. *Neogi T, Jansen TL, Dalbeth N, et al. 2015 Gout classification criteria: an American College of Rheumatology/European League Against Rheumatism collaborative initiative. Ann Rheum Dis. 2015;74:1789-98*.

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Abstract Number: 1578

NLRP3 Inflammasome Pathway Expression at Atheroma Plaques from Peripheral Artery Disease According to the Uricemic Status

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SESSION INFORMATION
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Both hyperuricemia and monosodium urate crystals induce persistent inflammation. In vitro, soluble urate can prime innate immune cells and promote NLRP3 inflammasome activation and interleukin-1beta

Table. Pathology findings at atheroma plaques by hematoxylin-eosin and immunostaining, and the comparisons between study groups of uricemia

		Total [n=28]	Normouricemia [n=16]	Hyperuricemia [n=12]	P
Calcification	Absent	9 (32.1)	5 (31.3)	4 (33.3)	1.000
	Present	19 (67.9)	11 (68.8)	8 (66.7)	
Lipid core extension	<10%	18 (64.3)	12 (75.0)	6 (50.0)	0.243
	≥10%	10 (35.7)	4 (25.0)	6 (50.0)	
CD68⁺ macrophages [n=27]	Absent/minor	15 (55.6)	9 (60.0)	6 (50.0)	0.603
	Moderate/heavy	12 (44.4)	6 (40.0)	6 (50.0)	
Neutrophils (elastase)	Absent/minor	27 (96.4)	16 (100)	11 (91.7)	0.240
	Moderate/heavy	1 (3.6)	0 (0)	1 (8.3)	
NLRP3	Absent/minor	20 (71.4)	14 (87.5)	6 (50.0)	**0.044**
	Moderate/heavy	8 (28.6)	2 (12.5)	6 (50.0)	
ASC	Absent/minor	26 (92.9)	16 (100)	10 (83.3)	0.175
	Moderate/heavy	2 (7.1)	0 (0)	2 (16.7)	
Caspase-1	Absent/minor	28 (100)	16 (100)	12 (100)	NC
	Moderate/heavy	0 (0)	0 (0)	0 (0)	
Gasdermin-D	Absent/minor	19 (67.9)	14 (87.5)	5 (41.7)	**0.017**
	Moderate/heavy	9 (32.1)	2 (12.5)	7 (58.3)	

synthesis. These findings need to be confirmed in vivo, as they may help explain the gout-related cardiovascular risk. This study aimed to assess the inflammasome pathway activation at human atheroma plaques regarding the uricemic status.

Methods: Consecutive patients with severe peripheral arterial disease candidates to lower limb amputation were prospectively enrolled. Clinical and laboratory variables were collected; hyperuricemia was established at median serum urate (SU) levels ≥7 mg/dL; other levels, as normouricemia (NU). Patients under colchicine were excluded. A 5cm artery segment of the amputated limb was sampled during the surgical procedure and fixed by 100º absolute alcohol. H-E staining was used to study the degree of calcification, the extension of lipid cores, and the type of plaque according to the AHA grading (I-VI). Macrophages (CD68) and neutrophils (elastase), and the expression of inflammasome components (NLRP3, ASC, caspase-1 and gasdermin-D), were marked using commercial antibodies (Merck) for immunohistochemistry (IHC). Two pathologists reviewed the samples simultaneously, blinded to clinical data. IHC staining was categorized as *absent/minor* (staining with negative or clusters with< 10 cell present) or *moderate/heavy* (cell clusters with >10 cells present or abundance of positive cells) [PMID 30629987]. Comparisons were performed using chi-2 and Fisher's exact tests.

Results: Out of 27 candidates, two were excluded (one for being on colchicine, the other for incomplete IHC process), so 25 participants were finally enrolled, median (IQR) aged 72.0 years (62.0-78.0), being 64.0% males. Ten patients (40%) were HU - two with gout - with a median SU of 7.6mg/dL (7.2-8.7), while 15 (60%) were NU, median SU of 4.4 (3.4-5.0). No patient was on urate-lowering drugs. Twenty-eight artery samples were available (16 from NU, 12 from HU), predominantly from popliteal arteries in both groups (50.0% in NU, 83.3% in HU). Type V (fibroatheroma) were the most common lesions seen in both cases (43.8% in NU, 50.0% in HU). The H-E and immunostaining findings and comparisons between study groups are shown in the **Table**. Similar calcification and lipid extension were seen. No differences were noted on macrophages distribution, while neutrophils were scarce in the samples. Interestingly, in regards to the inflammasome pathway, the plaque content of NLRP3 and gasdermin-D was significantly

larger in those with HU. ASC content was numerically larger in HU as well, while caspase-1 was scantly stained in both groups.

Conclusion: HU was revealed associated with a higher NLRP3 and gasdermin-D expression at human atheroma plaques in patients with peripheral artery disease. This finding needs further replication but may contribute to understanding the relationship between gout and atherosclerosis.

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Abstract Number: 1579

Phenome-Wide Association of Gout Risk Loci

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
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Background/Purpose: Gout is a complex disease involving changes in urate biology and inflammatory responses, and is associated with comorbidities including metabolic syndrome and cardiorenal disease. Phenome-Wide Association Study (PheWAS) is a novel analytical technique where genetic variants are interrogated against a large set of phenotypic traits. PheWAS are a powerful tool to characterize the clinical significance of genetic variants and gain insights into their biological function.

We performed a PheWAS to define phenotypic traits associated with polygenetic risk of gout using 18 known gout risk loci.

Methods: Gout-associated loci were identified through literature review. Variants in linkage disequilibrium were removed, yielding a total of 18 loci which we analyzed in UK Biobank. The 18 loci were classified as urate-related or non-urate related based on association with serum urate ($p< 1 \times 10^{-5}$). Polygenetic risk scores (PRS) were calculated by summing gout risk increasing alleles weighted by published gout association beta estimates (natural log of odds ratios). PRS were then calculated for all loci, urate-associated loci, and non-urate associated loci, and PheWAS was performed using logistic regression on discrete phenotypic traits (e.g. ICD-10 codes) from the UK Biobank study. To limit ethnic/racial confounders, we performed analyses in unrelated European ancestry UK Biobank study participants (n=382,828).

Results: 10 of the 18 SNPs were urate-associated and 8 were not. The all-gout and urate-associated PRSs revealed phenome-wide significant associations with disorders of iron metabolism ($p=7.91 \times 10^{-29}$ PRS_all, $p=9.82 \times 10^{-31}$ PRS urate), celiac disease ($p=1.30 \times 10^{-10}$ PRS_all, $p= 2.42 \times 10^{-12}$ PRS_urate) and non-celiac disease intestinal malabsorption ($p= 1.97 \times 10^{-09}$ PRS_all, $p= 1.86 \times 10^{-10}$ PRS_urate). The non-urate gout PRS did not identify any phenome-wide significance associations. We determined the urate PRS associations were driven largely by rs1165176 on *SLC17A1* ($p= 4.2 \times 10^{-81}$ iron metabolism, $p= 5.0 \times 10^{-17}$ celiac disease). Adjustment for *HFE* SNP rs1800562 (263 kb away on chromosome 6) abrogated the association between rs1165176 and iron metabolism. However, the association of rs1165176 with celiac disease remained significant.

Figure 1. SNPs Utilized in PRS analyses and association With Gout and Urate in UKBB.

Locus	Associated Gene	Effect Allele	Reference Allele	Gout correlation p value	Urate correlation p value
rs1260326	GCKR	C	T	2.07×10^{-13}	4.61×10^{-69}
rs11942223	SLC2A9	C	T	2.00×10^{-47}	9.25×10^{-1296}
rs11733284	NIPAL1	A	G	1.13×10^{-08}	8.25×10^{-08}
rs4148155	ABCG2	G	A	3.64×10^{-08}	1.90×10^{-384}
rs1229984	ADH1B	C	T	5.00×10^{-12}	5.38×10^{-03}
rs1165176	SLC17A1	G	A	1.47×10^{-09}	9.77×10^{-120}
rs2905274	Unknown locus	A	G	1.46×10^{-06}	5.09×10^{-01}
rs12236871	RFX3	G	A	1.48×10^{-10}	5.77×10^{-01}
rs548944057	SLC28A3-NTRK2	T	A	2.91×10^{-08}	3.82×10^{-02}
rs3129500	SHLD2/FAM35A	G	A	4.34×10^{-17}	No effect
rs179785	KCNQ1	A	G	1.28×10^{-08}	3.82×10^{-02}
rs2078267	SLC22A11	T	C	1.72×10^{-12}	1.88×10^{-88}
rs4073582	CNIH-2	A	G	3.56×10^{-08}	9.33×10^{-06}
rs76499759	PIBF1	A	G	2.79×10^{-08}	4.40×10^{-01}
rs11653176	BCAS3	C	T	1.36×10^{-13}	1.94×10^{-12}
rs9952962	MIR302F	C	T	1.67×10^{-08}	2.36×10^{-01}
rs12980365	ZNF724	G	A	9.76×10^{-08}	8.24×10^{-01}
rs150414818	ALDH16A1	G	C	1.50×10^{-16}	2.73×10^{-27}

Conclusion: We performed a PheWAS analysis to interrogate the clinical manifestations of polygenetic risk of gout and identified relationships between gout, celiac disease, and intestinal malabsorption. This relationship was driven by genes associated with both gout and hyperuricemia, and not by genes that were associated with gout but not

with hyperuricemia. Though epidemiological correlation between gout and ferritin levels was previously described by Fatima et al, our results suggests that linkage between *SLC17A1* and *HFE* may underlie this observation.

Disclosure: O. Stens, None; **V. Trang**, None; **S. Cao**, None; **R. Terkeltaub**, Astra-Zeneca, 2, 5, SOBI, 2, Selecta, 2, Allena, 2, Horizon, 2; **R. Salem**, None.

Abstract Number: 1580

Whole Blood Gene Expression and eQTL Analysis Implicate GGT7 and FADS2 in Gout Pathogenesis

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
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Background/Purpose: Gene expression studies of whole blood represent a powerful approach for understanding the pathogenesis of gout because differentially expressed transcripts may reflect the activation and response of immune cells to relevant and gout-specific stimuli. We have previously reported results (ACR 2019 abstract # 1232) of 48 statistically significant differentially expressed genes between gout cases (N=13) and non-gout controls (N =6). If the pathogenic mechanism that generates the differential expression has a genetic basis then we expect, 1) genetic variants near these genes to be associated with gout or its causal factor serum urate, and 2) that these variants co-localize with genetic variants that themselves associate with gene expression; i.e. the variants are *cis*-eQTLs.

Methods: We compared the genes whose expression was at least nominally associated with gout with results from a previously published transancestral meta analysis of serum urate and a separate GWAS of gout (Tin et al. 2019). We then used the Genotype-Tissue Expression (GTEX) database and COLOC (Giambartolomei et al. 2013) to verify whether the identified variants were associated with gene expression and colocalized with the serum urate signal.

Results: Only two out of 48 of the differentially expressed genes (*GGT7* and *FADS2*) were found to harbor variants (*cis*-eQTLs-Figure 1), that co-localized with genome-wide significant loci for serum urate (but not with gout). These genes, *GGT7* = gamma-glutamyltransferase 7, involved in glutathionine metabolism, and *FADS2* = fatty acid desaturase 2, involved in fatty acid metabolism, were both underexpressed in gout cases relative to non-gout controls. These genes are therefore strong candidate genes for a causal pathogenic role in gout.

Conclusion: It may be the case that genetic variation for serum urate and gout that comprise eQTLs manifests as differentially expressed genes between gout cases and controls. However, the most frequent observation from our data is that no genetic signal was found that explained the differences. At least three factors may underly this observation: 1) It is possible that differentially expressed genes could be mediated through eQTLs acting in *trans*. 2) We lack statistical power to detect association of genetic variants and/or gene expression with gout. 3) Epigenetic regulation, and not genetic, may be the preeminent cause of the observed gene expression differences. As additional cell type-specific expression data and highly powered gout GWAS results become available we will continue to identify genetic loci that deserve attention as potentially pathogenetic features of hyperuricemia and gout.

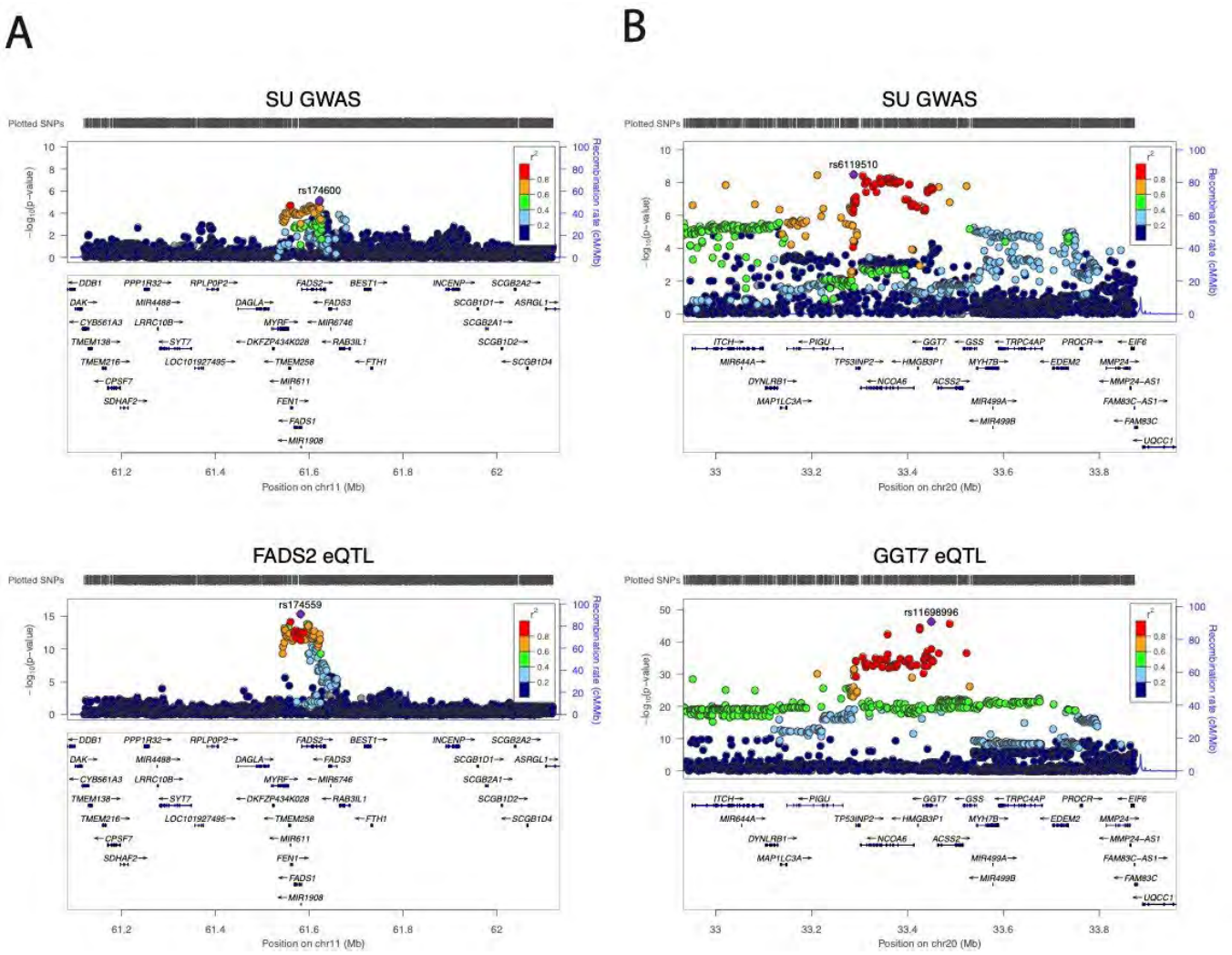

Figure 1. Colocalisation of eQTL and serum urate GWAS for FADS2 and GGT7. Regional association plots for serum urate (Tin et al. 2019) (EUR data) (top) and eQTL for (A) FADS2 (bottom left) and (B) GGT7 (bottom right). Dots indicate individual SNPs while position relative to the left y-axis indicates [-log10 (p-value)] of association. The blue line indicates the recombination rate across the locus. The lead serum urate and eQTL SNPs are indicated by a purple dot. The colouring of the surrounding SNPs indicates the strength of LD of the lead SNP according to the key on the left of each plot, measured as r2 found in the HapMap data for Europeans. The plot was generated using LocusZoom (Prium et al., 2010).

Disclosure: R. Reynolds, None; **R. Takei**, None; **J. Edberg**, None; **N. Sumpter**, None; **T. Merriman**, None; **M. Leask**, None.

Abstract Number: 1581

Genetic Effects on the Transition from Hyperuricemia to Gout

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SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)

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Background/Purpose: There is clear evidence of genetic control of hyperuricemia resulting in increased gout risk, however genetic control of the transition from hyperuricemia to gout is unclear. Recent genome-wide association studies (GWAS) of this transition have used a serum urate threshold of 7 mg/dL to define hyperuricemic (HU) controls and tested for association of variants with gout under these conditions. Our goal was to investigate how modification of the serum urate threshold for HU controls influenced the estimated effects of these genetic variants on gout.

Methods: Using the UK Biobank European cohort (n > 330,000), we first performed a GWAS of HU to gout (using controls with serum urate > 7 mg/dL; gout case n = 7,131, control n = 27,018). We then took the resulting 7 common independent lead variants ($p < 5 \times 10^{-8}$; minor allele frequency > 0.01; independence established using PLINK LD clumping algorithm) and further investigated their association with gout when varying the definition of controls at 5 thresholds (no threshold, > 6, > 7, > 8, and > 9 mg/dL). Cases on urate lowering therapy (ULT) were not excluded as to emulate existing genetic studies of HU to gout. Additionally, we binned cases and controls based on their serum urate levels (after excluding cases on ULT; bins of 1 mg/dL ranging from 4 to > 9 mg/dL) and tested the variants for association with gout in these bins. The 7 variants were also combined into a polygenic risk score and the same models were run on this score. All models were adjusted for sex and age.

Results: We found that the effect size of each variant on gout decreased with increasing mean SU for controls (Figure 1), however, even at high control mean SU, most variants had a residual association with gout. This residual association was even more apparent when cases and controls were binned by SU level and association analysis done using individuals only in the specific bins (Figure 2).

Conclusion: The effect size of genetic variants associated with gout identified using HU controls (SU > 7 mg/dL) decreases as the serum urate threshold for defining controls increases. However, there are still residual effects on gout even at higher HU thresholds for controls. It is possible that these residual effects represent inflammatory genetic components of gout but given that all 7 variants tested have known strong effects on SU, other explanations may be more likely. One such explanation is that the observational study design (single measurements of serum urate) does not adequately capture the lifetime effects of these variants on serum urate and therefore gout, with residual gout associations perhaps indicating an effect of prolonged hyperuricemia due in part to these variants. Therefore, this

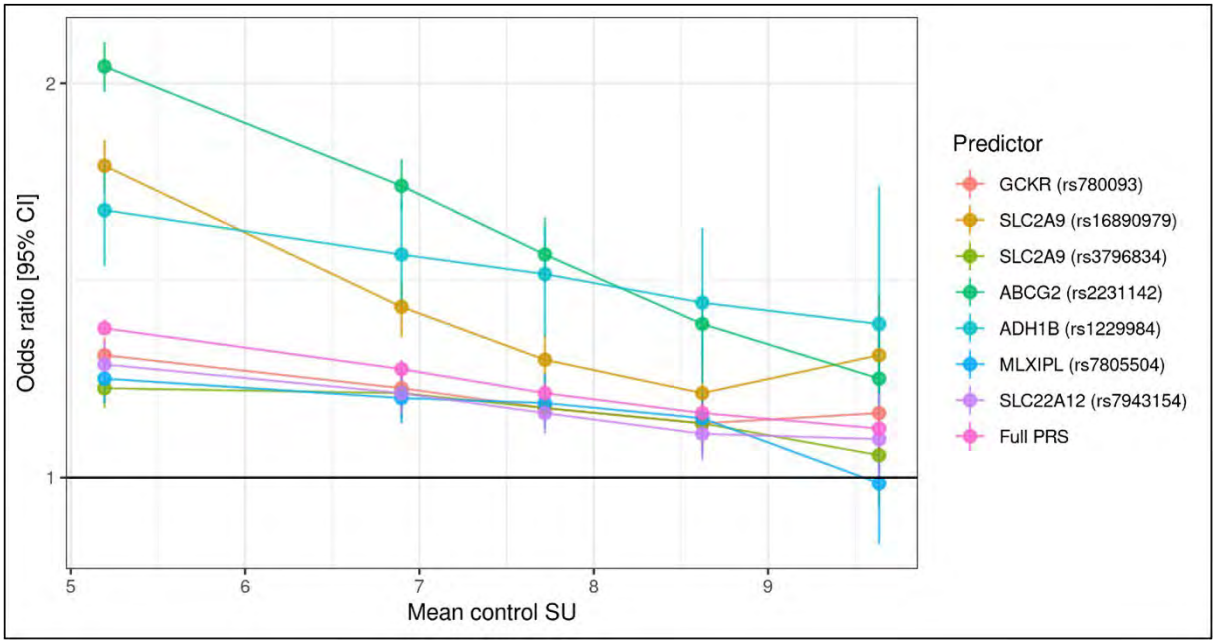

Figure 1. Effect of 7 HU to gout associated variants and their combined polygenic risk score (Full PRS) on gout with varied definitions of HU control. Y-axis shows odds ratio for gout ± 95% CI. X-axis shows mean control SU.

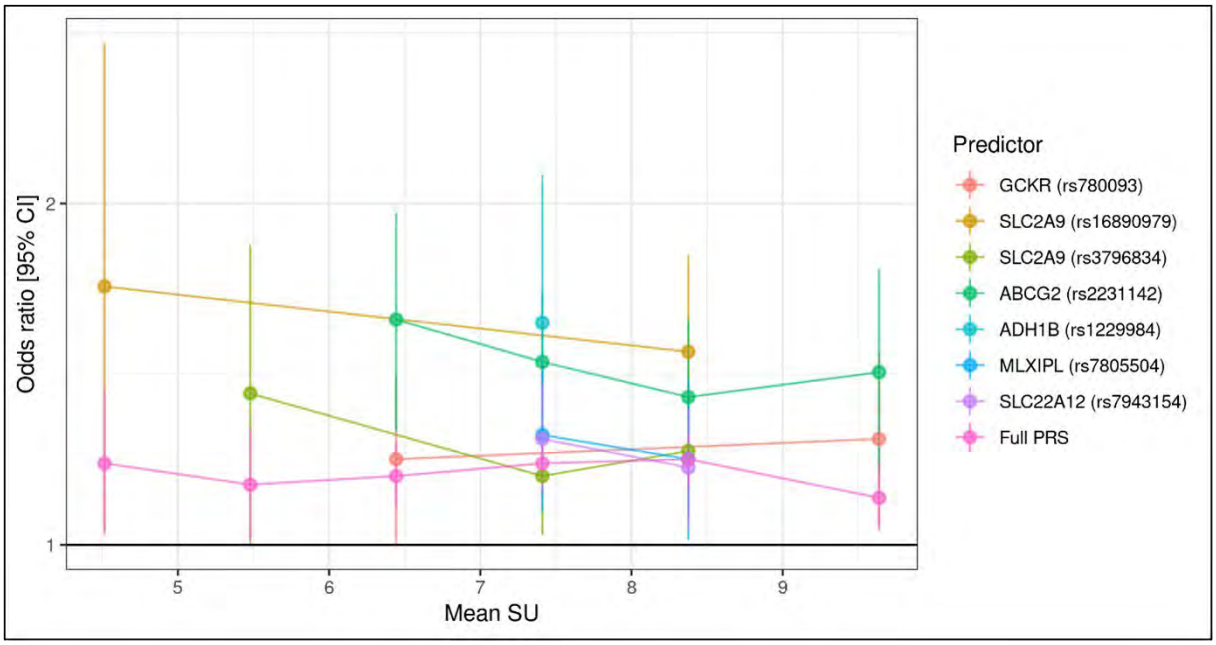

Figure 2. Significant ($p < 0.05$) binned effects of 7 HU to gout associated variants and their combined polygenic risk score (Full PRS) on gout with binned cases and controls (after exclusion of cases on urate lowering therapy). Y-axis shows odds ratio for gout ± 95% CI. X-axis shows mean SU of bin.

study indicates the need for genetic investigations of prolonged elevated serum urate on gout. Such investigations would focus on the lifetime burden of urate exposure, including urate crystal deposits.

Disclosure: N. Sumpter, None; **R. Takei**, None; **R. Reynolds**, None; **T. Merriman**, None.

Abstract Number: 1582

Diagnostic Accuracy and Reliability of Conventional Radiography of the Knee in Calcium Pyrophosphate Deposition Disease by Using New Definitions: An Ancillary Study of the OMERACT Ultrasound – CPPD Group

Silvia Sirotti[1], Fabio Becce[2], Luca Maria Sconfienza[3], Carlos Pineda[4], Marwin Gutierrez[5], Teodora Serban[6], Daryl MacCarter[7], Antonella Adinolfi[8], Anna Scanu[9], Carlo Alberto Scire[10], Ingrid Moller[11], Esperanza Naredo[12], Piercarlo Sarzi-Puttini[13], Abhishek Abhishek[14], Hyon K. Choi[15], Nicola Dalbeth[16], Sara Tedeschi[17], Maria-Antonietta D'Agostino[18], Nemanja Damjanov[19], Helen Keen[20], Lene Terslev[21], Annamaria Iagnocco[22] and Georgios Filippou[23], [1]Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy, [2]Lausanne University Hospital, Lausanne, Switzerland, [3]Department of Biomedical Sciences for Health, Università Degli Studi di Milano, Milan, Italy, [4]Instituto Nacional de Rehabilitacion, Mexico City, Federal District, Mexico, [5]Division of Musculoskeletal and Rheumatic Diseases, Instituto Nacional de Rehabilitacion, Mexico City, Mexico, [6]Ospedale La Colletta, ASL3 Genovese, Genoa, Italy, [7]Rheumatology Department, North Valley Hospital, Whitefish, MT, [8]Rheumatology Unit, Grande Ospedale Metropolitano Niguarda, Milan, Italy, [9]Department of Medicine-DIMED, Rheumatology Unit, University of Padova, Padoa, Italy, [10]SIR Epidemiology, Research Unit, Pavia, Italy, [11]University of Barcelona, Barcelona, Spain, [12]Department of Rheumatology and Joint and Bone Research Unit, Hospital Fundación Jiménez Díaz and Autónoma University, Madrid, Spain, [13]Rheumatology Department, Luigi Sacco University Hospital, Milano, Italy, [14]University of Nottingham, Nottingham, United Kingdom, [15]Massachusetts General Hospital, Lexington, MA, [16]University of Auckland, Auckland, New Zealand, [17]Brigham and Women's Hospital, Boston, MA, [18]Rheumatology Department, Università Cattolica del Sacro Cuore, Policlinico Universitario Agostino Gemelli IRCSS, Rome, Italy, [19]University of Belgrade School of Medicine, Institute of Rheumatology, Belgrade, Serbia, [20]University of Western Australia, Daglish, Australia, [21]Center for Rheumatology and Spine Diseases, Rigshospitalet, Copenhagen University, Glostrup, Denmark, [22]University of Turin, Roma, Italy, [23]Rheumatology Department, Luigi Sacco University Hospital, Siena, Italy

SESSION INFORMATION

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Background/Purpose: Conventional Radiography (CR) has been widely used in Calcium Pyrophosphate Deposition Disease (CPPD) and is considered an important tool for the diagnosis. However, there are very few studies that examine the reliability and the diagnostic accuracy of CR. The aims of this study were to evaluate the diagnostic accuracy of knee CR in CPPD compared to histology and to assess the reliability of CR in CPPD.

Methods: This is an ancillary study of the Criterion Validity of Ultrasound in CPPD study. Consecutive patients with osteoarthritis (OA) awaiting total knee replacement were enrolled in 4 centres. All patients underwent CR of the knees taken maximum 6 months before surgery. DICOM files of the preoperative radiographs were read independently by two radiologists experienced in CPPD for the presence/absence of CPPD at the level of several knee structures. Each reader performed a second evaluation 3 weeks later to calculate the intra-reader agreement. In case of disagreement, for the assessment of accuracy, a consensus decision was taken. The new definitions of the ACR/EULAR taskforce for identification of CPPD in CR were used in this study [paper under submission]: CPPD in CR appears as "linear or punctate opacities in the region of fibro- or hyaline articular cartilage/synovial membrane or joint capsule/within tendons or entheses that are distinct from denser, nummular radio-opaque deposits due to basic calcium phosphate deposition". Menisci and the hyaline cartilage were analysed as described in the main study. Cohen's kappa was used to calculate the agreement between the two readers.

Results: 67 patients with OA were enrolled for the reliability study (65% F, mean age 71yo±8) and 51 for the accuracy study (63% F, mean age 74yo±8). For 16 patients not all specimens were retrieved during surgery, so they were excluded from the accuracy study. CR demonstrated to be a specific exam for identification of CPPD at the knee, but sensitivity remains low in all sites and in the overall evaluation (Table1). According to the results of the predictive

***Table 1**. reliability and accuracy of CR for identification of CPPD by using the new ACR/EULAR taskforce definitions*
Kappa values from 0.01–0.20 are considered as none to slight agreement, 0.21–0.40 as fair, 0.41– 0.60 as moderate, 0.61–0.80 as substantial, and 0.81–1.00 as almost perfect agreement.

	Medial meniscus	Lateral meniscus	Hyaline cartilage	Quadriceps tendon	Patellar tendon	Capsule/ synovia	Menisci + cartilage	Entire joint
RELIABILITY								
Inter-reader	0.62	0.56	0.57	0.38	NA	0.62	0.52	0.45
Intra-reader 1st assessor	0.78	0.85	0.83	0.49	0.66	0.66	0.69	0.68
Intra-reader 2nd assessor	1	0.83	0.96	1	1	0.94	0.97	1
ACCURACY								
Sensitivity	32%	40%	48%				54%	
Specificity	100%	96%	93%				92%	
PPV	100%	91%	87%				87%	
NPV	56%	62%	94%				67%	
AUC	0.66	0.68	0.70				0.73	
Accuracy	66%	68%	70%				73%	

values, the presence of typical deposition on CR allows a definite confirmation of the diagnosis, but a negative radiography does not exclude CPPD. The k values of the inter- and intra-reader agreement in the various structure are indicated in Table1. Inter-reader agreement was substantial at the level of both menisci but only moderate or fair at the other sites of assessment. On the other hand, intra-reader kappa values were substantial or higher in almost all sites.

Conclusion: The presence of typical CPPD calcifications on CR, according to the definitions of the ACR/EULAR task force, are highly specific but have low sensitivity for disease identification. The low sensitivity found in this study could be due to the advanced grade of OA in the cohort of patients. Furthermore, the difference of the intra-reader compared to the inter-reader kappa values, highlight a different application of the definitions for most of the sites, with the exception of the menisci. For that reason the assessment of calcium crystals at the menisci level should be used for identification of CPPD as other sites of the knee seem to present low reliability.

Disclosure: S. Sirotti, None; **F. Becce**, Horizon, 2, Siemens Healthineers, 5; **L. Sconfienza**, None; **C. Pineda**, None; **M. Gutierrez**, None; **T. Serban**, None; **D. MacCarter**, None; **A. Adinolfi**, None; **A. Scanu**, None; **C. Scire**, None; **I. Moller**, None; **E. Naredo**, AbbVie, 6, Roche, 6, BMS, 6, Pfizer, 6, UCB, 6, Lilly, 5, 6, Novartis, 6, Janssen, 6, Celgene GmbH, 6; **P. Sarzi-Puttini**, None; **A. Abhishek**, None; **H. Choi**, None; **N. Dalbeth**, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **S. Tedeschi**, NGM Biopharmaceuticals, 2; **M. D'Agostino**, None; **N. Damjanov**, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Gideon Richter, 2, 6, Merck, 2, 6, Novartis, 2, 6; **H. Keen**, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **L. Terslev**, None; **A. Iagnocco**, None; **G. Filippou**, None.

Abstract Number: 1583

Creation of an Ultrasonographic Scoring System for CPPD Extent: Results from a Delphi Process by the OMERACT US Working Group – CPPD Subgroup

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SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies – Basic & Clinical Science Poster II (1565–1583)
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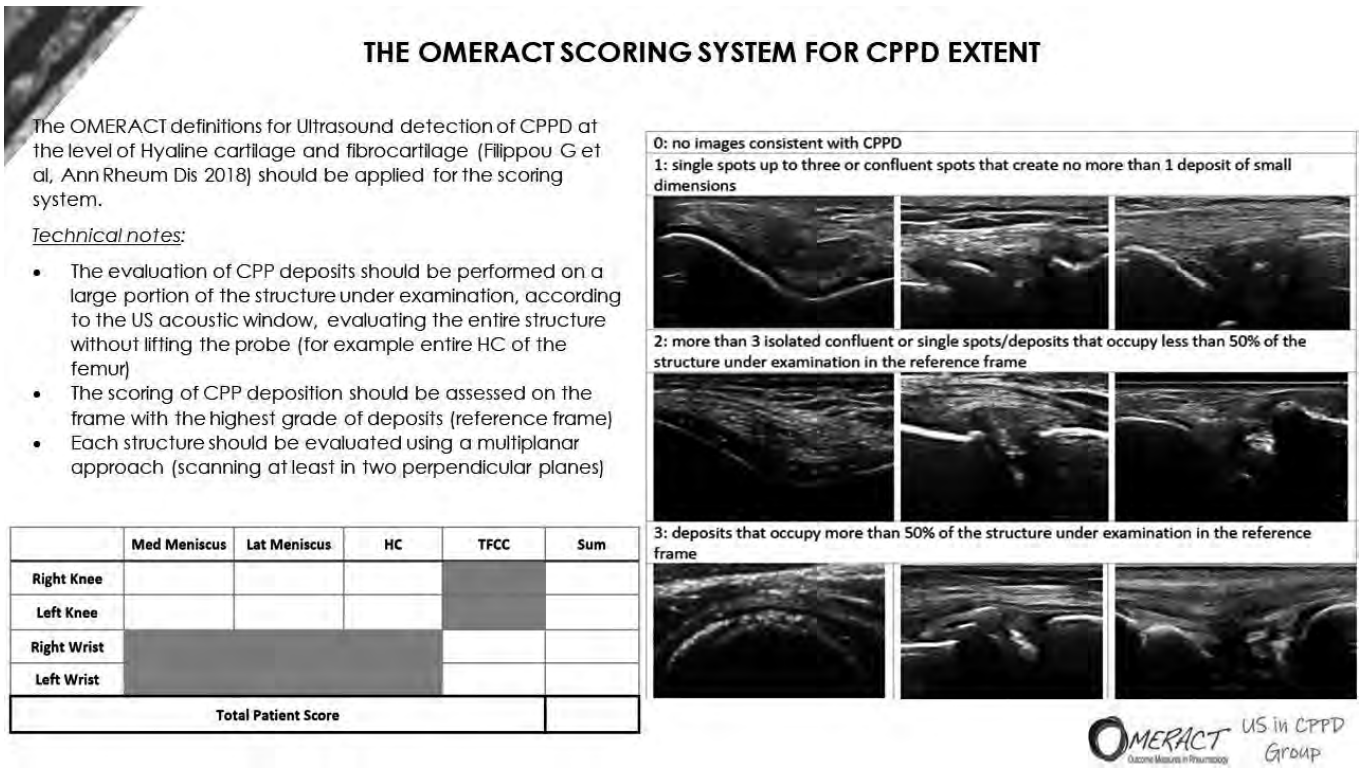
Session Time: 8:30AM–10:30AM

Background/Purpose: Ultrasound (US) has proven to be an excellent technique for detecting Calcium Pyrophosphate (CPP) deposits, however there are no grading systems that allow for a quantification and extent of deposition in patients. The only attempt was made on 2013 by Filippou *et al*. (Filippou G et al. *Ann Rheum Dis* 2013) but that score was never validated. The aim of this study is to create a scoring system for the quantification of CPP deposition at patient level according to the OMERACT framework.

Methods: According to the OMERACT methodology we performed a systematic literature review (SLR) aimed to estimate the prevalence of CPP deposition in peripheral joints by imaging in order to establish relevant joints for Calcium Pyrophosphate Deposition Disease (CPPD) monitoring [abstract submitted separately]. At the same time, a preliminary survey was circulated among the members of the OMERACT US – CPPD subgroup to collect their suggestions on the items to be included in the scoring system according to their personal experience. Subsequently, a Delphi survey was prepared and circulated between members of the OMERACT US – CPPD subgroup, including statements that reflected both the results of the SLR and of the preliminary survey. In total, 32 statements were created regarding the kind of scoring for single structures, the sites to be included, the final scoring at patient level, and the scanning technique. Participants were asked to reply on a Likert Scale and agreement was achieved when 4 and 5 grades reached 75% or more of concordance. In case of disagreement, new statements were proposed according to the members suggestions and proposed for voting in a consequent round.

Results: 3 Delphi rounds were needed in order to reach agreement on all items. 32 participants out of 41 members replied at the first round, 26/32 at the second and 25/26 at the third round. 20 statements were approved in the first round, 3 at the second and 3 at the third. Statements in some cases were grouped together (for example the scale



to use for the scoring) so once agreement was reached for one scoring the others were not proposed anymore. The experts decided to include only the knees (menisci and hyaline cartilage) and the triangular fibrocartilage of the wrists in the final score, using a four-grade scoring system (0-3). The final scoring with the definitions and the relative technical notes is represented in Figure 1.

Conclusion: This is the first attempt to create a scoring system for CPP crystals extent in patients affected by CPPD. In the next future the scoring will be assessed for reliability and hopefully released for use in clinical practice and research.

Disclosure: S. Sirotti, None; **A. Adinolfi**, None; **F. Becce**, Horizon, 2, Siemens Healthineers, 5; **T. Cazenave**, None; **S. Christiansen**, Novartis, 5, BMS, 6, GE, 6; **E. Cipolletta**, None; **A. Delle Sedie**, None; **M. Diaz Cortes**, None; **F. Figus**, None; **E. Filippucci**, None; **P. Mandl**, MSD, 5, 6, Celgene, 5, 6, Lilly, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6; **D. MacCarter**, None; **I. Moller**, None; **M. Mortada**, None; **G. Mouterde**, AbbVie, 2, 5, 6, BMS, 2, 5, 6, Celgene, 2, 5, 6, Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6; **M. Naredo Sanchez**, None; **C. Pineda**, None; **F. Porta**, None; **W. Schmidt**, None; **T. Serban**, None; **L. Terslev**, None; **F. Vreju**, None; **R. Wakefield**, None; **P. Zufferey**, None; **P. Sarzi-Puttini**, None; **M. D'Agostino**, None; **N. Damjanov**, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Gideon Richter, 2, 6, Merck, 2, 6, Novartis, 2, 6; **A. Iagnocco**, None; **H. Keen**, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **G. Filippou**, None.

Abstract Number: 1584

Relation of Depressive Symptoms to Alterations in Conditioned Pain Modulation in Knee Osteoarthritis: The Multicenter Osteoarthritis Study (MOST)

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster (1584–1588)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Inefficiency of descending conditioned pain modulation (CPM) is present in 42-55% of individuals with knee osteoarthritis (OA), which can contribute to more pain and may result in poor response to current treatments. Depressive symptoms can induce increased activity in the forebrain region and limbic system that may influence the descending conditioned pain modulatory pathways. The extent to which depressive symptoms may be a risk factor for alterations in the descending pathways may be clinically important to identify new therapeutic targets for better pain management in people with knee OA. We therefore sought to examine the relation of depressive symptoms to presence and development of inefficient CPM over two years in people with or at risk of knee OA.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of individuals with or at risk of knee OA. We defined depressive symptoms as a score of ≥16 on the Center for Epidemiologic Studies Depression Scale (CES-D). CPM was assessed with pressure pain threshold (PPT) at the wrist as the test stimulus and forearm ischemia as the conditioning stimulus. We calculated the ratio of post-conditioning stimulus PPT to the pre-conditioning stimulus PPT and defined inefficient CPM as a ratio < 1.12 of the post-conditioning

Table: Relation of Depressive Symptoms to Development of Inefficient CPM	
Relation of depressive symptoms at baseline to:	**Adjusted Effect Estimate (95% CI)**
Development of inefficient CPM over 2 years (N=1033)	OR 0.61 (0.40, 0.94)
Baseline inefficient CPM (N=2761)	OR 0.86 (0.68, 1.09)
Change in CPM over 2 years (N=2761)	Beta coefficient 0.03 (-0.02, 0.07)

stimulus PPT to pre-conditioning stimulus PPT based upon published data. For the main analysis, we limited our sample to those with efficient CPM at baseline to assess the relation of depressive symptoms to development of inefficient CPM over two years using logistic regression, adjusting for age, sex, and BMI. Because of concerns regarding potential collider bias given that depressive symptoms are often chronic and likely preceded our study baseline, we additionally performed 2 analyses using the whole study sample: 1) a cross-sectional analysis at baseline; 2) a longitudinal analysis evaluating change in CPM ratio over two years using linear regression; this analysis also aimed to account for potential misclassification of categorization of CPM status.

Results: 1033 participants were included in the main analysis (mean age 65±10.5 years, mean BMI 29.5±5.7 kg/m^2, 41% female). Of those, 13% had depressive symptoms at baseline and 45% developed inefficient CPM over two years. Compared to those without depressive symptoms at baseline, depressive symptoms were associated with 39% reduced odds of developing inefficient CPM (**Table**). When we included whole sample (N=2761) in the cross-sectional analysis, depressive symptoms were non-significantly associated with 14% reduced odds of being inefficient CPM. Depressive symptoms were not associated with change in CPM over two years.

Conclusion: In contrast to our hypothesis, we found that having depressive symptoms was protective of development of inefficient CPM in knee OA. These findings suggest that depressive symptoms may potentially contribute to strengthening or activation of the descending conditioned pain modulatory pathways, such as through enhanced central inhibitory neurotransmitter levels or other central mechanisms.

Disclosure: K. Aoyagi, None; **L. Carlesso**, None; **L. Frey-Law**, None; **G. Rabasa**, None; **C. Lewis**, None; **M. Nevitt**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2.

Abstract Number: 1585

Suprascapular Nerve Block for the Treatment of Adhesive Capsulitis

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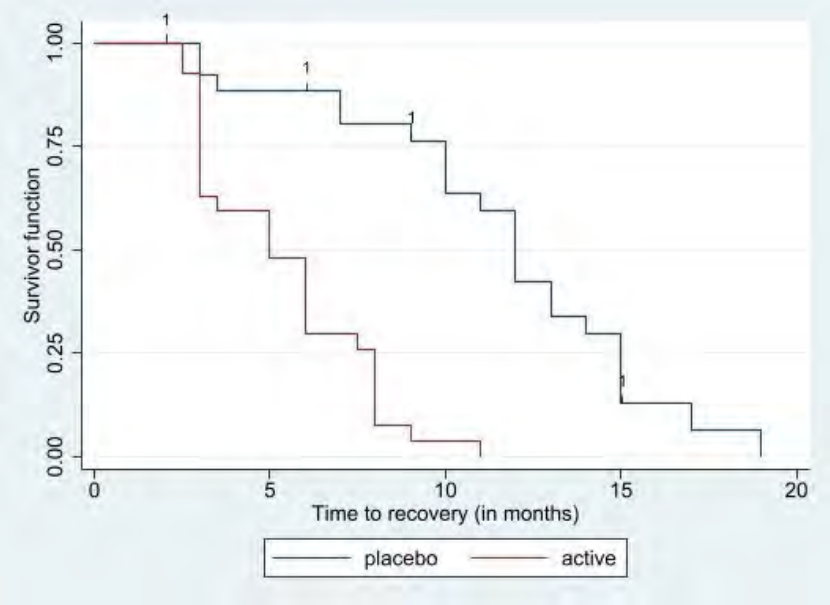
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster (1584–1588)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: To investigate the value of suprascapular nerve block (SSNB) as a treatment option for adhesive capsulitis.

Methods: Patients with adhesive capsulitis confirmed by a rheumatologist were invited to participate in the study. A randomised, double blind placebo controlled trial of standard therapy plus placebo versus standard therapy plus



Survival analysis – Kaplan Meier curve, demonstrates the difference in time to resolution in the two groups.

SSNB was performed. Standard therapy comprised an intra-articular glenohumeral joint injection of 20 mg of triamcenolone at time zero, plus a physiotherapist supervised exercise program. Patients received either a SSNB (10 mls of 0.5% bupivacaine and 40 mg of depomedrol) or placebo (3 mls of subcutaneous normal saline) injection at time zero and then at 3 monthly intervals until resolution. Resolution was defined as a return to full range of movement and a reduction of pain scores to normal, or recovery to the satisfaction of the patient. Pain, disability, range of movement and patient perceived rate of recovery scores were measured at 12 weekly intervals in the two groups.

Results: 54 patients (19 male, 35 female, mean age 54 years (range 32-72) participated. 27 patients received standard therapy plus the SSNB and 27 patients received standard therapy plus a placebo. 4 patients withdrew during the course of the study (all in the placebo group). The mean time to resolution of the symptoms was 5,4 months (CI 4,4-6.3) in the active group versus 11.2 months (CI 9.3-13.0) in the placebo group. Pain, disability, patient perceived rate of recovery and range of movement scores were significantly better in the actively treated group compared with the placebo group at all time intervals. The was one presycopal episode in the actively treated group but no other significant complications.

Conclusion: SSNB is highly effective in reducing the duration of frozen shoulder. It reduces pain significantly and is associated with high levels of patient satisfaction with recovery. It is safe and can be recommended as a useful adjunct therapy.

Disclosure: E. Shanahan, None; **E. Briggs**, None; **T. Gill**, None; **C. Hill**, None; **T. Morris**, None.

Abstract Number: 1586

Individuals with Pre-arthritic Hip Pain Walk with Hip Motion Alteration Common in Individuals with Hip OA

Cara Lewis[1], Anne Halverstadt[2], Kerri Graber[2], Zoe Perkins[2], Emily Keiser[2], Hadwin Belcher[2] and Anne Khuu[2], [1]Boston University, Brookline, MA, [2]Boston University, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster (1584–1588)
Session Type: Poster Session D
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Background/Purpose: Individuals with hip osteoarthritis (OA) commonly walk with less hip extension compared to individuals without hip OA. This alteration is often attributed to walking speed, structural limitation, and/or hip pain. It is unclear if individuals with pre-arthritic hip disease (PAHD), such as dysplasia, femoroacetabular impingement syndrome, and acetabular labral tears, also walk with altered movement patterns. Thus, the objective of this study was to 1) determine if individuals with PAHD walk with less hip extension compared to individuals without pain, and 2) investigate potential reasons for this motion alteration.

Methods: Adolescent and adult individuals with PAHD and healthy controls without pain were recruited. Provocative hip tests (FABER, FADIR, and resisted straight leg raise) were used to confirm presence (PAHD group) or absence (Control group) of hip pain. Kinematic data were collected while walking on a treadmill at three speeds: preferred, fast (25% faster than preferred), and prescribed (1.25 m/s). Peak hip extension, peak hip flexion, and hip excursion were calculated at each walking speed. Linear regression analyses with GEE were used to examine the effects of group, sex, task, side, and their interactions.

Results: Hip angle data from 137 individuals with PAHD and 60 individuals without pain were included in the study (Table 1). The PAHD group was older than the Control group (p=.003). Individuals with PAHD had 2.9° less peak hip extension compared to individuals in the Control group (95% Confidence Interval (CI): 0.6, 5.1; p=.014) when walking at their preferred speed. At the prescribed speed, the PAHD group walked with 2.7° less hip extension than the Control group (95% CI: 0.4, 5.0; p=.022). Given the persistence of the finding despite walking at the same speed, the observed reduction in hip extension was not due to speed alone. When compared to the preferred speed, both groups increased their hip extension, hip flexion, and hip excursion by similar amounts at the fast speed, and no *group-by-task* interaction was noted (p=.206). This finding suggests that the PAHD group had the ability to walk with more hip extension at the preferred speed, and thus, the difference was not due to structural limitation. Within the PAHD group, individuals that reported pain during the walking task did not use different hip angles or excursion compared to individuals reporting no pain (p≥.185); thus, pain during walking was not the primary reason for reduced hip extension.

Conclusion: The results of this study indicate that the kinematic alteration common in individuals with hip OA exists early in the continuum of hip disease and was present in individuals with PAHD. The reduced hip extension during walking was not explained by preferred walking speed, structural limitation, or current pain; therefore, intervening on these factors alone is unlikely to address the habitual motion alteration.

Table 1. Mean (standard deviation or range) demographic data for individuals with pre-arthritic hip disease (PAHD) and individuals without pain (Control)

	PAHD		Control	
	Male (n=37)	Female (n=100)	Male (n=25)	Female (n=35)
Age, years	27.9 (9.5)	27.4 (8.6)	23.6 (5.6)	23.8 (5.4)
Height, meters	1.81 (0.07)	1.66 (0.07)	1.79 (0.07)	1.64 (0.07)
Mass, kg	80.7 (10.7)	66.6 (10.2)	77.5 (12.4)	61.3 (8.4)
BMI, kg/m^2	24.7 (3.1)	24.1 (3.4)	24.1 (2.9)	22.8 (2.5)
UCLA Activity Score (0-10)	8.3 (4-10)	7.8 (2-10)	8.6 (5-10)	8.4 (4-10)
Preferred Walking Speed, m/s	1.23 (0.17)	1.29 (0.18)	1.26 (0.19)	1.29 (0.16)
Modified Harris Hip Score	77.4 (11.1)	73.3 (13.3)	99.9 (0.9)	100 (0.2)

Disclosure: C. Lewis, None; **A. Halverstadt**, None; **K. Graber**, None; **Z. Perkins**, None; **E. Keiser**, None; **H. Belcher**, None; **A. Khuu**, None.

Abstract Number: 1587

Do Physical Therapists Use Recommended Treatments for Chronic Low Back Pain?

Debbie Feldman[1], Jonathan El-Khoury[2], Tatiana Orozco[1], François Desmeules[3], Maude Laliberté[1] and Kadija Perreault[4], [1]Université de Montréal, Montréal, QC, Canada, [2]Université de Sherbrooke, Sherbrooke, QC, Canada, [3]Research Centre of Hôpital Maisonneuve Rosemont, Montréal, QC, Canada, [4]Université Laval, Québec City, QC, Canada

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic low back pain has been the subject of many studies in medicine and physical therapy for over half a century. Clinical practice guidelines based on evidence have not changed much in the past 30 years, recommending patient education and self-management, and generalized exercise programs. Other treatments such as orthotics, acupuncture, electrotherapies are not recommended, whereas manual therapy, psychological therapies are considered helpful in combination with patient education and exercise. Persons with chronic low back pain often consult a physical therapist. The purpose of our study was to determine whether physical therapists provide recommended treatments for a typical case of chronic low back pain. We also sought to identify factors associated with the use of some specific types of treatment, notably, electrotherapy (which is not recommended) and manual therapy (which can be recommended together with exercise).

Methods: We sent an online survey to physical therapists in the province of Quebec, Canada. The survey contained clinical vignettes of four different cases, one of which was chronic low back pain with sciatica. Participants were asked about what kind of treatment they would provide for this patient showing typical signs and symptoms of chronic low back pain with sciatica as well as whether they would refer the patient to another professional. Descriptive statistics were used to illustrate the proportions for each treatment chosen by physical therapists. We explored associations between choice of treatments with physical therapists' demographic and practice related factors, using inferential statistics and regression analyses.

Results: There were 176 physical therapists who responded, 41 who identified as male (23.3%) and the majority (63.6%) worked in private practice. The vast majority of physical therapists would provide education (93.8%) and exercise (81.8% mobility exercises, and 65.9% strengthening exercises). Nearly 73% would use manual therapy while 46% would use electrotherapy. The percentage who selected manual therapy together with any type of exercise was 72.7. Many thought it would be important to refer to another health professional such as a family physician (70.6%), a physical therapist who specializes in backs (62.1%), but not to a rheumatologist (0.4%). Regression analyses revealed certain factors associated with the selection of various treatments. Physical therapists with less experience were more likely to select manual therapy (p=0.01) while those working in rural areas were more likely to choose electrotherapy (p=0.03).

Conclusion: Physical therapists would treat a patient with chronic low back pain with the recommended treatments, i.e. education and exercise. Most would also use manual therapy, and for the majority, this was in conjunction with

both education and exercise. However, there is a need for improved knowledge translation/education since nearly half would still use the non-recommended electrotherapy treatment.

Disclosure: D. Feldman, None; **J. El-Khoury**, None; **T. Orozco**, None; **F. Desmeules**, None; **M. Laliberté**, None; **K. Perreault**, None.

Abstract Number: 1588

Relation of Foot and Ankle Pain to Worsening Knee Pain: The MOST Study

Patrick Corrigan[1], David Felson[2], Tuhina Neogi[3], Cara Lewis[4], James Torner[5], Michael Nevitt[6], Cora Lewis[7] and Joshua Stefanik[1], [1]Northeastern University, Boston, MA, [2]Boston University, Boston, MA, [3]Boston University School of Medicine, Boston, MA, [4]Boston University, Brookline, MA, [5]University of Iowa, Iowa City, IA, [6]University of California San Francisco, Orinda, CA, [7]University of Alabama Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Foot and ankle pain may be a risk factor for worsening knee pain in those with or at risk for knee osteoarthritis (KOA). Foot and ankle pain is associated with biomechanical alterations that shift load from the foot and ankle to the knees. Since increased knee joint loading is a well-established risk factor for KOA, foot and ankle pain may play a key role in the onset and progression of knee pain. Previous work has shown that pain anywhere in the foot or ankle increases the odds of worsening knee pain in those with KOA. However, this work did not account for widespread pain (WSP), which could partially explain the effect of foot and ankle pain on worsening knee pain. We aimed to determine if foot or ankle pain is associated with worsening knee pain while accounting for WSP.

Methods: We used data from the 144- and 168-month visits of the Multicenter Osteoarthritis (MOST) Study, a cohort study of persons with or at risk for KOA. At 144-months, participants were asked "On most days, do you have pain, aching, or stiffness in any joints?" If the participant answered "yes," painful sites were marked on a homunculus. For the current study, our exposure was foot or ankle pain. For our outcome, worsening knee pain, we calculated the change in the Western Ontario and McMaster Universities Osteoarthritis Index – Pain (WOMAC-P) from 144- to 168-months for each knee, then defined "worsening" as an increase of ≥2 points. To determine the relation of foot or ankle pain to worsening pain of the ipsilateral and contralateral knees, we used logistic regression models with generalized estimating equations to account for bilateral data. Models were first adjusted for age, sex, BMI, race, depressive symptoms, and baseline WOMAC-P and Kellgren-Lawrence grade of the outcome knee. To account for WSP, analyses were then repeated adding the number of painful sites above the waist as a covariate. Those with knee replacement or missing data were excluded.

Results: 2201 participants were included (57% female; 81% white; mean (SD) age = 63.6 (10.1) years; mean (SD) BMI = 29.2 (5.6) kg/m^2). Of the 3892 limbs, 1271 (33%) had foot or ankle pain. Knee pain worsened in 758 knees (19.5%). Compared to limbs without foot or ankle pain, limbs with foot or ankle pain had 1.61 (1.30-1.99) and 1.50 (1.22-1.85) times the odds of worsening ipsilateral and contralateral knee pain, respectively (Figure 1). When accounting for the number of painful sites above the waist, limbs with foot or ankle pain had 1.29 (1.03-1.61) and 1.18 (0.95-1.48) times the odds of worsening ipsilateral and contralateral knee pain, respectively (Figure 1). The mean (SD; Min-Max) number of painful sites above the waist was 1.68 (1.77; 0-10), and for each additional painful site the odds of worsening ipsilateral and contralateral knee pain were increased by 1.22 (1.16-1.29) and 1.23 (1.16-1.30) times, respectively.

Conclusion: Foot or ankle pain is associated with increased odds of worsening ipsilateral knee pain, even after accounting for WSP. The odds of worsening contralateral knee pain, on the other hand, seems to be affected by WSP. Clinicians may need to pay attention to foot and ankle pain as well as consider WSP to optimize outcomes for patients with KOA.

Disclosure: P. Corrigan, None; **D. Felson**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **C. Lewis**, None; **J. Torner**, None; **M. Nevitt**, None; **C. Lewis**, None; **J. Stefanik**, None.

Abstract Number: 1589

COVID-19 Vaccine Hesitancy in Rheumatology Patients

Rebecca Sadun[1], Amanda Eudy[1], Jennifer Rogers[1], Kai Sun[2], Lisa Criscione-Schreiber[2], Mithu Maheswaranathan[2], Jayanth Doss[1] and Megan Clowse[3], [1]Duke University, Durham, NC, [2]Duke University School of Medicine, Durham, NC, [3]Duke University, Chapel Hill, NC

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatic diseases on certain immunosuppressant medications are known to be at higher risk for severe COVID-19. The ACR recommends COVID-19 vaccination for nearly all patients with rheumatic diseases. However, some individuals remain hesitant to receive a COVID-19 vaccine. This study assessed the basis for COVID-19 vaccine hesitancy in rheumatology patients. This study assessed the basis for COVID-19 vaccine hesitancy in rheumatology patients seen at a large academic medical center in the Southeastern United States.

Methods: A survey was distributed electronically during the last week of December 2020 and the first week of January 2021 (when in the US, COVID-19 vaccines were available only to health professionals) to rheumatology patients at a large academic center in the Southeastern United States. Patients completed a COVID-19 vaccine belief survey, adapted from the Vaccine Hesitancy Scale (VHS), along with a demographic survey. Patients were asked whether they would get a COVID-19 vaccine and responses were dichotomized as definitely/probably vs probably not/definitely not. Descriptive statistics and logistic regression models evaluated factors associated with vaccine hesitancy.

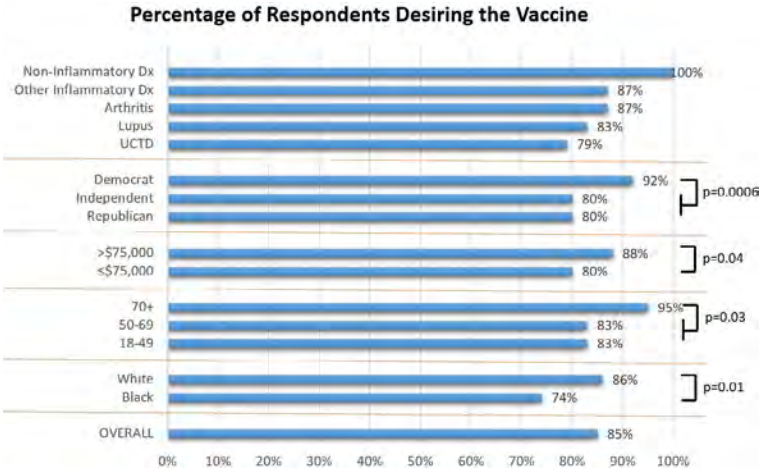

Figure 1. Vaccine hesitancy by rheumatic diagnosis, political affiliation, household income, age, and race.

Results: A total of 433 patients responded to the survey: 48% self-identified as having inflammatory arthritis, 83% as female, 4% as Hispanic, 10% as Black, and 50% as a member of the Democratic Party. Individuals who wanted the COVID-19 vaccine had less hesitancy on 3 survey subscales ($p< 0.001$). Of respondents who identified as White, 86% wanted to receive the vaccine, in comparison to 74% of respondents who identified as Black ($p=0.04$) (Figure 1). Patients over the age of 70, with income >$75,000, or identifying as Democrats were also more likely to desire COVID-19 vaccination. Backward regression models identified White race (OR: 4.43; 95% CI: 1.80, 10.98) and affiliation with the Democratic Party (OR: 4.20; 95% CI: 1.93, 9.20) to be independently associated with wanting the vaccine. The primary reasons cited

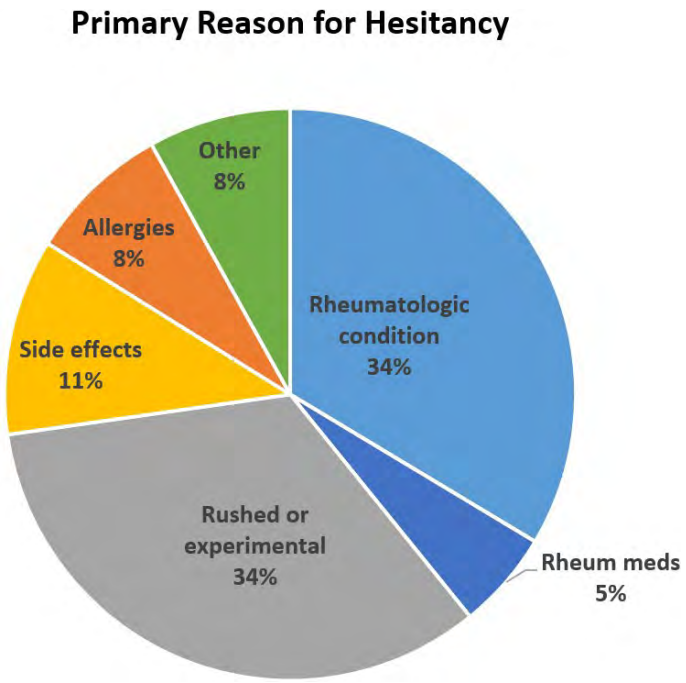

Figure 2. Patients' stated primary reason for COVID-19 vaccine hesitancy (free-response question with qualitative data coded by theme).

Figure 3. Factors rheumatology patients indicate would increase the likelihood of their opting to receive the COVID-19 vaccine in the future (multiple-choice, "select all that apply" question).

for hesitancy were: the vaccine being "rushed" or "experimental" (34%), safety of the vaccine in the context of patients' rheumatologic diagnoses (34%), side effects (11%), and concern for allergic reaction (8%) (Figure 2). Common reasons for vaccine-hesitant patients to consider getting the vaccine were: "evidence the vaccine is safe in patients with my rheumatic condition" (69%) and "the ACR recommends it for people with my condition" (57%) (Figure 3).

Conclusion: Rheumatology patients wanted to be vaccinated against COVID-19 at a rate that was higher than national surveys estimates (85% vs 60-69%) during the same time period. As in national surveys, White race and Democratic Party affiliation were strongly associated with rheumatology patients wanting the vaccine. More than one third of patients revealed factors related to their rheumatologic diagnosis as the primary reason for their hesitancy. Importantly, the majority of patients indicated that they would be more likely to get the COVID-19 vaccine based on recommendations from the ACR or their rheumatologist, or in the setting of evidence of vaccine safety in rheumatic conditions.

Disclosure: R. Sadun, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **J. Rogers**, Exagen, 2, 5, Pfizer, 5, Eli Lilly, 2, Immunovant, 2, Northwestern University, 2; **K. Sun**, None; **L. Criscione-Schreiber**, GlaxoSmithKline, 5; **M. Maheswaranathan**, None; **J. Doss**, Pfizer, 5; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5.

Abstract Number: 1590

Sleep Disturbance Improves with SARS-COV2 Vaccinations in Patients with Rheumatologic and Chronic Inflammatory Diseases

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: As the COVID-19 pandemic unfolded, people across the world experienced a psychological burden with social confinement, concerns about health, potential infection, jobs, financial difficulty, and uncertainty about the future. Immunosuppressed patients with chronic inflammatory diseases (CID) may have experienced an additional burden with their immunocompromised status. The purpose of this study was to examine patient-reported outcomes over time in patients with CID undergoing SARS-CoV2 vaccination.

Methods: This is a prospective cohort of patients at two sites with CID undergoing SARS-CoV2 vaccination. Participants completed 3 study visits (baseline before vaccination (T1), after dose 1 (T2), and after dose 2 (T3)) where blood and clinical data were collected. Patient-reported outcomes were measured with the PROMIS-29, which includes 4-item scales for 7 domains (physical function, fatigue, anxiety, depression, sleep disturbance, social participation, pain interference) and a 1-item pain severity question. PROMIS-29 scales were summed and converted to T scores (population mean [SD] of 50 [10]). Mixed effects models were used to examine how the PROMIS scores compared to baseline after both vaccination doses, adjusting for age, gender and study site.

Results: The cohort was 72% female with a mean (± SD) age of 48.1±15.5 years (Table 1). In the overall cohort, sleep disturbance significantly improved after both doses of SARS-CoV2 vaccinations (T score -2.5, 95%CI -3.4, -1.6) (Ta-

bles 2). Anxiety improved after the second vaccine dose. Improvements in each were within the range of estimated minimally important differences (MID). Physical function worsened, although this did not meet the MID threshold (-1.0, 95% CI -1.6, -0.4). In an analysis stratified by levels of baseline anxiety (High anxiety: PROMIS Anxiety ≥55 vs < 55), improvement in anxiety at T3 was greater for the higher versus lower anxiety group (-5.4, 95% CI -7.2, -3.6 [T3 T1] vs. -3.7, 95%CI -5.6, -1.8). Improvements in fatigue (-2.1, 95% CI -3.6, -0.5) and social participation (2.3, 95% CI 0.5, 4.2) were also noted for the high-anxiety group (Table 2). Similar to the overall cohort, physical function worsened slightly for both groups and sleep disturbance improved significantly.

Conclusion: With the completion of the SARS-CoV2 vaccine series, sleep disturbance decreased in a significant and meaningful way in patients with CID. In patients with higher anxiety at baseline, not only did anxiety decrease, but so did fatigue and sleep disturbance in addition to an increase in social participation. Overall, this suggests vaccines may lead to improvements in mental health and wellbeing of patients with CID, particularly among those with greater anxiety.

Table 1. Demographic and Clinical Characteristics of Participants

Demographic Data	Overall cohort (n=310)	High Anxiety group (n=51)	Low Anxiety group (n=163)	p-value (High vs. Low Anxiety)
Age [years], mean (SD)	48.1±15.5	47.7±2.4	49.2±1.3	0.6
Gender (%female)	71.6	78.43	70.6	0.3
Race (%white)	81.3%	84.3	85.3	0.9
Vaccine				
Pfizer (%)	74.5%	78.4	75.5	0.7
Moderna (%)	25.5%	21.6	24.5	
Immunologic Diagnosis			**N (%)**	
Inflammatory Bowel Disease			32.3	
Rheumatoid Arthritis			25.5	
Spondyloarthritis			19.4	
Systemic Lupus Erythematosus			11.3	
Other Connective Tissue Disease			7.7	
Vasculitis			2.3	
Multiple Sclerosis/ NMO			7.1	
Autoinflammatory Syndrome			1.0	
IgG4-Related Disease			0.7	
Uveitis			4.5	
Other			1.9	
Medications			**N (%)**	
Prednisone			12.3	
Disease Modifying Antirheumatic Drug				
Methotrexate			18.1	
Hydroxychloroquine			18.7	
Mycophenolate Mofetil			5.2	
Azathioprine			6.1	
Leflunomide			3.6	
Sulfasalazine			6.1	
Janus Kinase inhibitors			5.5	
Biological therapies				
Tumor Necrosis Factor inhibitors			30.7	
B cell depleting therapies			9.4	
Belimumab			1.3	
Vedolizumab			8.1	
Interleukin 12/23 or 23 inhibitors			6.5	
Interleukin 17 inhibitors			0.7	
Nonsteroidal Anti-inflammatory Drugs			18.8	

Table 2. **PROMIS Scores with repeated measures**

Overall cohort						
	Time 2 vs. 1			Time 3 vs. 1		
	Coeff	**p-value**	**95%CI**	**Coeff**	**p-value**	**95%CI**
Physical Function	-0.9	0.004	-1.5, -0.3	**-1.000**	**0.0008**	-1.6, -0.4
Fatigue	0.4	0.39	-0.6, 1.4	1.0	0.05	-0.01, 1.9
Anxiety	-0.5	0.24	-1.4, 0.3	**-1.5**	**0.0005**	-2.3, -0.7
Depression	-0.2	0.59	-0.8, 0.5	-0.5	0.2	-1.1, 0.2
Sleep Disturbance	**-1.7**	**0.0003**	-2.5, -0.8	**-2.5**	**2.4E-08**	-3.4, -1.6
Social Participation	-0.3	0.51	-1.2, 0.6	-0.02	0.95	-0.9, 0.8
Pain Interference	-0.1	0.85	-1.0, 0.8	0.5	0.3	-0.4, 1.4
Pain Intensity	-0.1	0.57	-0.3, 0.2	0.3	0.01	0.1, 0.5
Stratified by baseline PROMIS Anxiety score (<55 [reference] vs. ≥55)						
	Time 2 vs. 1			**Time 3 vs. 1**		
	Coeff	**p-value**	**95%CI**	**Coeff**	**p-value**	**95%CI**
Physical Function	**-1.8**	**0.004**	-3.0, -0.6	**-1.3**	**0.04**	-2.4, -0.1
Fatigue	-0.4	0.6	-2.1, 1.2	**-2.1**	**0.01**	-3.6, -0.5
Anxiety	**-3.7**	**0.0001**	-5.6, -1.8	**-5.4**	**4.2E-09**	-7.2, -3.6
Depression	-0.7	0.4	-2.4, 1.0	-1.2	0.2	-2.8, 0.4
Sleep Disturbance	**-1.8**	**0.03**	-3.4, -0.2	**-2.0**	**0.01**	-3.5, -0.4
Social Participation	**1.9**	**0.046**	0.03, 3.9	**2.3**	**0.01**	0.5, 4.2
Pain Interference	-1.3	0.2	-3.1, 0.5	-0.9	0.3	-2.6, 0.8
Pain Intensity	0.02	0.9	-0.4, 0.5	0.03	0.9	-0.4, 0.5

Adjusted for age, gender and study site

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Abstract Number: 1591

Impact of the COVID-19 Pandemic and Lockdown on Wellbeing on Patients with Rheumatic Diseases. Results from the REUMAVID Study (Phase 1)

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has impacted wellbeing of patients with Rheumatic and Musculoskeletal Diseases (RMDs). The aim is to assess wellbeing its associated factors in European RMD patients.

Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at the University of Seville, together with a multidisciplinary team including patient organisations and rheumatologists. The study consists of an online survey gathering data from patients with a diagnosis of 15 RMDs in Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom. 1,800 participants were recruited by patient organisations. Data was collected between April and July 2020. Participants were divided into two groups: 1) Participants with poor wellbeing (World Health Organization-Five Wellbeing Index (WHO-5) ≤ 50), 2) Participants with good wellbeing (WHO-5 >50). The Mann-Whitney and $\chi 2$ tests were used to analyse possible relations between sociodemographic characteristics, lifestyle, and outdoor contact with wellbeing during the beginning of the COVID-19 pandemic. Univariate and multivariate binary logistic regression was used to determine the impact of the independent variables associated with poor wellbeing.

Results: 1,777 patients with 15 different RMDs were included. The mean age was 52.7, 80.2% female, 48.7% had a university degree, and 69.7% were married or in a relationship. The most frequent diagnoses were inflammatory arthritis (75.4%). 49.0% reported poor wellbeing. 57.7% of patients who belonged to a patient organisation reported good wellbeing (vs 46.3% who did not, p< 0.001). Compared to those patients who did not, those who did experienced poor wellbeing had higher disease activity (51.4% vs 41.3%, p< 0.001), a higher risk of anxiety (54.3% vs 41.7%, p< 0.001) and depression (57.0% vs 42.1%, p< 0.001), and poorer self-perceived health (53.0% vs 41.8%, p< 0.001). A higher proportion of those who engaged in physical activity presented good wellbeing (54.0% vs 46.5%, p=0.012). 57.4% of the patients who were unable to attend an appointment with their rheumatologist reported poor wellbeing, compared to 48.2% who did attend (p=0.027). Patients who did not walk outside (56.2%) or who lacked elements in their home to facilitate outside contact (63.3%) experienced poor wellbeing (p< 0.001). The factors associated with poor wellbeing were lack of elements in the home enabling contact with the outside world (OR=2.10), not belonging to a patient organisation (OR=1.51), risk of depression (OR=1.49), and not walking outside (OR=1.36) during the COVID-19 pandemic (Table 1).

Table 1. Logistic regression. Dependent variable: poor wellbeing (N=1,104)

	Univariate logistic analysis		Multivariate logistic analysis	
	OR	95% CI[1]	OR	95% CI[1]
Patient organization. Non-member	1.566	**1.295, 1.894**	1.505	**1.176, 1.925**
Disease activity (VAS ≥ 4)	1.502	**1.212, 1.863**	1.155	0.854, 1.561
Risk of anxiety (HADs, 0-21)	1.667	**1.378, 2.016**	1.203	0.916, 1.581
Risk of depression (HADs, 0-21)	1.828	**1.513, 2.209**	1.492	**1.117, 1.994**
Self-reported health. Fair to very bad	1.575	**1.295, 1.914**	1.256	0.939, 1.679
Change in health status. Worse	1.273	**1.056, 1.534**	1.047	0.797, 1.376
Physical activity. No	1.354	**1.069, 1.714**	1.076	0.829, 1.397
Talked with rheumatologist during COVID-19 pandemic. No	1.452	**1.041, 2.026**	1.044	0.678, 1.610
Walk outside during COVID-19 pandemic. No	1.474	**1.187, 1.830**	1.363	**1.024, 1.814**
Element in home with outdoor contact. No	1.930	**1.423, 2.618**	2.104	**1.408, 3.145**

[1]95% CI for test H_0: OR = 1

Conclusion: Almost half of the patients with RMDs reported poor wellbeing during the beginning of the COVID-19 pandemic. The lack of elements in the home that facilitate outdoor contact, not belonging to a patient organisation, the presence of anxiety, and not walking outside during the pandemic increase the probability of poor well-being. These results highlight the importance of environmental factors and the role of patient organisations in addressing the effects of the pandemic and its containment measures.

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Abstract Number: 1592

ACT for Lupus: Pilot Study of a Novel Acceptance and Commitment Therapy (ACT) Online Program to Support Patients with Lupus During the COVID-19 Pandemic

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic disease associated with significant symptom burden, including fatigue, anxiety, depression, pain, and negative impacts on health-related quality of life (HRQoL). The COVID-19 pandemic has resulted in additional stressors impacting the mental health and well-being of patients with SLE. Acceptance and Commitment Therapy (ACT) is a promising treatment approach that has shown efficacy in addressing many of the symptoms associated with SLE, such as such as depression, anxiety, and chronic pain. The goal of this pilot study was to develop and assess the feasibility and preliminary efficacy of ACT for Lupus, a novel online ACT-based virtual skills training program tailored for patients with lupus.

Methods: Participants with a diagnosis of SLE were primarily recruited through an academic healthcare system in North Carolina, as well as nationally in partnership with a large lupus advocacy organization. A total of 72 participants completed the baseline survey and were invited to attend two weekly one-hour webinar sessions in December 2020, which were delivered through a web-based platform. Educational content was tailored for patients with lupus and delivered by an experienced clinical psychologist who specializes in ACT. Topics and practice exercises encompassed ACT-principles of mindfulness, distress tolerance, self-care and advocacy, goal setting, and action planning. Patient-reported outcomes (PROs) including anxiety (General Anxiety Disorder-7; GAD-7), depression (Patient Health

Table 1. Participant characteristics (n=23)

Characteristics	Values
Age, years, mean ± SD	47.4 ± 13.1
Female, n (%)	20 (87.0)
Race/Ethnicity, n (%)	
White	16 (69.6)
Black/African American	3 (13.0)
Hispanic/Latino	2 (8.7)
Asian	2 (8.7)
Education, n (%)	
Some College, No Degree	3 (13.0)
Bachelor's Degree	12 (52.2)
Graduate Degree or Above	8 (34.8)
Employment Status, n (%)	
Full-Time	8 (34.8)
Part-Time	2 (8.7)
Unemployed	3 (13.0)
Retired	3 (13.0)
Medically Disabled/Unable to Work	6 (26.1)
Recruitment Source, n (%)	
North Carolina	19 (82.6)
Nationally	4 (17.4)
Psychotherapy Use (Past 30 days), n (%)	5 (21.7)
Anxiety Medication Use (Past 30 days), n (%)	13 (56.5)

Questionnaire; PHQ-9), and disease-specific HRQoL (LupusQoL) were assessed at baseline and post-intervention. Additional questions in the follow-up survey assessed participant satisfaction with the program and suggestions/opportunities for refinement. Means and effect sizes (ES) with 95% confidence intervals (CIs) were computed for pre- and post- changes in PROs, adjusted for age, sex and baseline measurements (Table 2).

Results: Data was analyzed for a total of 23 individuals who participated in the program and submitted the end of study assessment survey. Most participants were women (86%), aged ≥ 28 years, and recruited through the North Carolina system (82.6%) (Table 1). In pre- post- analyses of the ACT for Lupus pilot data, we found modest improvements in LupusQoL fatigue scores (ES=0.25) and reduced symptoms of anxiety as indicated by GAD-7 scores (ES= -0.26). Feedback from participants highlighted unmet needs for mindfulness-based programs, tailored to the unique experiences of patients with lupus. Participant feedback included suggestions to inform growth and expansion of the program and added flexibility for participants to access the program at their own pace in a self-directed format.

Table 2. Means (SD) and effect sizes for changes in outcomes from baseline to end of study (n=23)

Outcome Measures	Baseline Mean (SD)	End of Study Mean (SD)	Effect Size
Anxiety GAD-7[a]	9.87 (6.01)	8.43 (4.77)	-0.26
Depression PHQ-9[b]	10.22 (5.55)	10.65 (6.12)	0.07
LupusQoL Domains[c]			
Pain	61.59 (27.38)	65.58 (21.51)	0.16
Physical Health	63.45 (27.61)	66.44 (19.34)	0.13
Planning	68.48 (29.19)	68.48 (23.70)	0.00
Intimate	69.57 (33.67)	73.37 (28.03)	0.12
Burden	56.16 (33.54)	59.06 (24.22)	0.10
Emotional Health	73.55 (18.28)	70.29 (18.00)	-0.18
Body Image	77.28 (20.26)	73.06 (22.54)	-0.20
Fatigue	50.00 (30.68)	56.52 (20.25)	0.25

[a]GAD-7 scores range from 0-21, higher scores represent worse symptoms
[b]PHQ-9 scores range from 0-27, higher scores represent worse symptoms
[c]LupusQoL domain scores range from 0-100, higher scores represent better HRQoL

Conclusion: Preliminary results suggest that an adapted ACT-based virtual skills training program has potential to improve psychological and QoL outcomes among patients with lupus, especially in the face of additional stressors.

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Abstract Number: 1593

Perceived Impact of the COVID-19 Pandemic on Physical Activity Among Adult Patients with Rheumatologic Disease

Teresa Dickson[1], Tessa Englund[1], Emily McCormick[1], Becki Cleveland[1], Kelli Allen[2], Andres Santana[1], Shruti SaxenaBeem[1], Julie Walker[1] and Saira Sheikh[3], [1]Thurston Arthritis Research Center, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, [2]Thurston Arthritis Research Center, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC and Health Services Research & Development, Durham VA Health Care System, Durham, NC, [3]University of North Carolina Thurston Arthritis Research Center, and Department of Medicine, Division of Rheumatology, Allergy and Immunology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC

SESSION INFORMATION
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has triggered nationwide disruptions that limit opportunities for physical activity (PA). Addressing suboptimal levels of PA is important for disease management and reducing risk of comorbidities in patients with rheumatologic conditions. The objective of this cross-sectional study was to

investigate the impact of the COVID-19 pandemic on PA levels of patients with rheumatologic disease and to examine characteristics associated with decreased PA that may inform future PA interventions.

Methods: A convenience sample of adult patients with rheumatologic disease (n=7,776) were identified through electronic medical records from an academic healthcare system in North Carolina. Eligible patients were invited to

Table 1. Respondent sociodemographic characteristics, primary rheumatic diagnosis, and self-reported changes in physical activity since the COVID-19 pandemic began (n = 1,133)

Characteristics	Overall	Same or More Activity	Less Activity
Age, years, mean (SD)	57.6 (15.2)	58.1 (14.3)	57.3 (15.9)
Sex, n (%)			
Female	845 (75.4)	339 (71.8)	485 (77.6)
Race, n (%)			
White	884 (82.3)	389 (84.7)	482 (81.3)
Black or African American	151 (14.1)	52 (11.3)	93 (15.7)
Asian	27 (2.5)	13 (2.8)	13 (2.2)
Native American	12 (1.1)	5 (1.1)	5 (0.8)
Ethnicity, n (%)			
Hispanic or Latino	55 (5.2)	17 (3.8)	36 (6.1)
Rheumatologic Diagnosis, n (%)			
Rheumatoid arthritis	265 (25.6)	129 (29.5)	130 (22.5)
Osteoarthritis	151 (14.6)	57 (13.0)	92 (15.9)
Systemic lupus erythematosus	130 (12.6)	42 (9.6)	84 (14.5)
Psoriatic arthritis	91 (8.8)	41 (9.4)	48 (8.3)
Sjogren's syndrome	47 (4.5)	24 (5.5)	22 (3.8)
Other	414 (37.7)	167 (36.3)	243 (39.3)
Concurrent Diagnosis, n (%)			
Hypertension	310 (27.4)	113 (23.8)	192 (30.5)
Chronic pain	287 (25.3)	104 (21.9)	176 (28.0)
Anxiety	254 (22.4)	95 (20.0)	149 (23.7)
Depression	231 (20.4)	79 (16.7)	145 (23.1)
Thyroid disease	194 (17.1)	76 (16.0)	114 (18.1)
Asthma/Chronic Obstructive Pulmonary Disease	170 (15)	75 (15.8)	93 (14.8)
Fibromyalgia	151 (13.3)	56 (11.8)	88 (14.0)
Osteoporosis	146 (12.9)	61 (12.9)	84 (13.4)
Irritable bowel syndrome	130 (11.5)	50 (10.5)	78 (12.4)
Diabetes	123 (10.9)	43 (9.1)	75 (11.9)
Heart disease	93 (8.2)	34 (7.2)	58 (9.2)
Self-reported current health, n (%)			
Excellent	37 (3.3)	26 (5.5)	11 (1.8)
Very good	289 (25.7)	170 (36.0)	115 (18.3)
Good	422 (37.5)	172 (36.4)	241 (38.4)
Fair	304 (27.0)	84 (17.8)	210 (33.4)
Poor	72 (6.4)	20 (4.2)	51 (8.1)
Highest level of education, n (%)			
Less than high school (grade 1-12)	416 (37.1)	202 (42.8)	209 (33.4)
Graduated high school (grade 12 or GED)	539 (48.1)	214 (45.3)	315 (50.4)
College (1-4 year college, junior college or technical school)	144 (12.8)	50 (10.6)	87 (13.9)
Graduate school (Masters, Doctorate, or professional degree)	22 (2.0)	6 (1.3)	14 (2.2)
Annual gross income, n (%)			
<$25,000	144 (15.5)	51 (12.7)	88 (17.2)
$25,000 - $49,999	177 (19.0)	64 (16.0)	107 (20.9)
$50,000 - $74,999	145 (15.6)	60 (15.0)	84 (16.4)
$75,000 - $99,999	111 (11.9)	49 (12.2)	60 (11.7)
$100,000 - $150,000	173 (18.6)	81 (20.2)	91 (17.7)
>$150,000	181 (19.4)	96 (23.9)	83 (16.2)

Table 2. Age-adjusted odds ratio and 95% confidence intervals of patient characteristics associated with less PA

Characteristics	Category	Less Activity
Sex	Male vs Female	0.75 (0.57-0.99)
Race	Non-White vs White	1.28 (0.92-1.77)
Ethnicity	Hispanic/Latino vs Not Hispanic/Latino	1.49 (0.82-2.73)
Rheumatologic diagnosis	Systemic lupus erythematosus/Lupus	1.59 (1.07-2.37)
	Sjogren's syndrome	0.68 (0.38-1.24)
	Rheumatoid arthritis	0.70 (0.52-0.93)
	Psoriatic arthritis	0.85 (0.55-1.32)
	Osteoarthritis	1.31 (0.91-1.89)
Concurrent diagnosis	Fibromyalgia	1.21 (0.84-1.73)
	Chronic pain	1.38 (1.04-1.82)
	Depression	1.48 (1.09-2.01)
	Anxiety	1.20 (0.89-1.62)
	Heart disease	1.38 (0.88-2.16)
	Hypertension	1.44 (1.10-1.90)
	Diabetes	1.38 (0.93-2.05)
	Osteoporosis	1.09 (0.76-1.56)
	Irritable bowel syndrome	1.17 (0.80-1.71)
	Thyroid disease	1.17 (0.85-1.62)
	Asthma/Chronic Obstructive Pulmonary Disease	0.91 (0.65-1.27)
Self-reported current health	Fair/Poor vs Excellent/Very Good/Good	2.50 (1.91-3.27)
Highest level of education	Less than high school (grade 1-12) vs More	1.39 (0.97-1.98)
Annual gross income	Lower Income after COVID vs the same or more	1.34 (1.01-1.79)

participate in an online survey between July–September 2020. Rheumatologic and concurrent diagnoses as well as patient-reported outcomes during the COVID-19 pandemic were assessed, which included changes in PA, barriers to PA, psychological symptoms, and wellbeing. Descriptive statistics, age-adjusted odds ratios (OR), and 95% confidence intervals (CI) were computed to compare characteristics of those whose activity decreased versus those who did not (stayed the same or increased).

Results: A total of 1,133 participants completed the survey (17.2% response rate, mean age of sample: 57.6 ± 15.2 years, 75.4% female, 82.3% white and 14.1% African American). The most common primary diagnoses reported among participants include RA (25.6%), OA (14.6%), and SLE (12.6%). Over half of participants (55.5%) reported engaging in less PA since the start of the pandemic, followed by unchanged PA (26.6%) and increased PA (15.3%). Factors associated with engaging in less PA were male sex (OR 0.75, CI 0.57-0.99), lower income during the COVID-19 pandemic (OR 1.34, CI 1.01-1.79), and lower self-reported fair/poor health (OR 2.50, CI 1.91-3.27). Among rheumatologic diseases, a diagnosis of SLE was associated with lower self-reported PA (OR 1.59, CI 1.07-2.37). Comorbidities associated with decreased PA include chronic pain (OR 1.38, CI 1.04-1.82), depression (OR 1.48, CI 1.09-2.01), and hypertension (OR 1.44, CI 1.10-1.90). The most common reported barriers to PA include increased overall fear/anxiety (33.5%), lack of motivation (32.4%), and contracting coronavirus infection (32.1%). Most participants reported that they did not meet their exercise goals during the COVID-19 pandemic (67.2%).

Conclusion: The COVID-19 pandemic has further exacerbated barriers to PA in patients with rheumatologic diseases. There is a critical need to provide resources, support and multi-faceted to encourage PA in patients with rheumatologic diseases during the COVID-19 pandemic and beyond.

Disclosure: T. Dickson, None; **T. Englund**, None; **E. McCormick**, None; **B. Cleveland**, None; **K. Allen**, None; **A. Santana**, None; **S. SaxenaBeem**, None; **J. Walker**, None; **S. Sheikh**, Pfizer, 5, GlaxoSmithKline, 2, 5.

Abstract Number: 1594

COVID-19 Pandemic-Related Changes in Health Routines and Self-Reported Physical Functioning Among Systemic Lupus Erythematosus Patients

Laura Plantinga[1], Courtney Hoge[1], C. Barrett Bowling[2], Charmayne Dunlop-Thomas[1], Brad Pearce[1], S Sam Lim[3] and Cristina Drenkard[1], [1]Emory University, Atlanta, GA, [2]Duke University, Durham, NC, [3]Department of Medicine, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic was disruptive to individual health routines. Changes in health routines may worsen disease management and reduce opportunities for physical activity, both of which may affect physical functioning. Leveraging on an ongoing ancillary cohort study [Approaches to Positive, Patient-centered Experiences of Aging in Lupus (APPEAL)], we examined whether pandemic-related changes in health routines were associated with self-reported physical functioning among individuals with systemic lupus erythematosus (SLE).

Methods: APPEAL subjects were recruited from Georgians Organized Against Lupus (GOAL), a population-based cohort of individuals with validated SLE in metropolitan Atlanta. A total of 153 participants (mean age, 48 years; 95% female, 76% Black) were consented (10/6/2020-5/4/2021) for a single visit during the period the COVID-19 survey was administered. Responses to items regarding pandemic-related changes in health habits (changes in activity, difficulty in obtaining food or medications and in obtaining routine medical care) were dichotomized as yes vs. no. Raw physical functioning scores were captured via the PROMIS Physical Functioning-Short Form 12a and converted to *t*-scores (50 = average score for a general adult population; differences of 10 = 1 SD; and higher scores = better physical functioning). Differences in scores were assessed via *t* tests and age-, gender-, and race-adjusted linear regression models.

Results: More than half of participants reported being less physically active, having more interrupted sleep, and more difficulty getting routine medical care as a result of the pandemic; nearly one-third reported having more trouble obtaining food, and nearly one-quarter reported difficulty in obtaining medications (Table). The overall mean physical

Change in health routine:	Yes, n/N (%)	Mean (SD) self-reported physical functioning score		*P*	Age-, gender-, and race-adjusted difference, (95% CI)
		Yes	No		
Less physically active	84/151 (55.6%)	41.1 (8.5)	46.1 (9.5)	*<0.001*	-4.6 (-7.6,-1.7)
More trouble obtaining food	47/153 (30.7%)	39.4 (8.8)	44.9 (8.9)	*<0.001*	-5.4 (-8.5,-2.4)
More interrupted sleep	81/153 (52.9%)	40.5 (9.1)	46.3 (8.4)	*<0.001*	-5.4 (-8.2,-2.6)
More difficulty getting routine medical care	87/153 (56.9%)	40.4 (8.4)	45.4 (9.3)	*0.001*	-5.1 (-7.8,-2.3)
More difficulty obtaining medications	34/153 (22.2%)	39.3 (9.2)	44.4 (9.0)	*0.005*	-4.4 (-7.9,-1.0)
More difficulty obtaining hydroxychloroquine	27/93 (29.0%)	41.6 (10.1)	44.8 (9.8)	*0.16*	-3.6 (-8.0,0.9)

functioning *t*-score (SD) was 43.2 (9.2). Scores were consistently lower (by ~0.5 SD) for those who reported declines in health routines, and the differences were statistically significant for all items except difficulty obtaining hydroxychloroquine; adjustment for age, gender, and race did not substantially change the associations (Table).

Conclusion: While the cross-sectional nature of the study precludes causal inference, our results suggest that experiencing pandemic-related disruptions in health routines was associated with meaningfully lower perceptions of physical functioning. Future studies should explore whether this association persists over time and whether lower perceived functioning is associated with long-term health outcomes.

Disclosure: L. Plantinga, None; **C. Hoge**, None; **C. Bowling**, None; **C. Dunlop-Thomas**, None; **B. Pearce**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **C. Drenkard**, GSK, 1, 5.

Abstract Number: 1595

Concern About the COVID-19 Pandemic and Community Mobility Among Systemic Lupus Erythematosus Patients

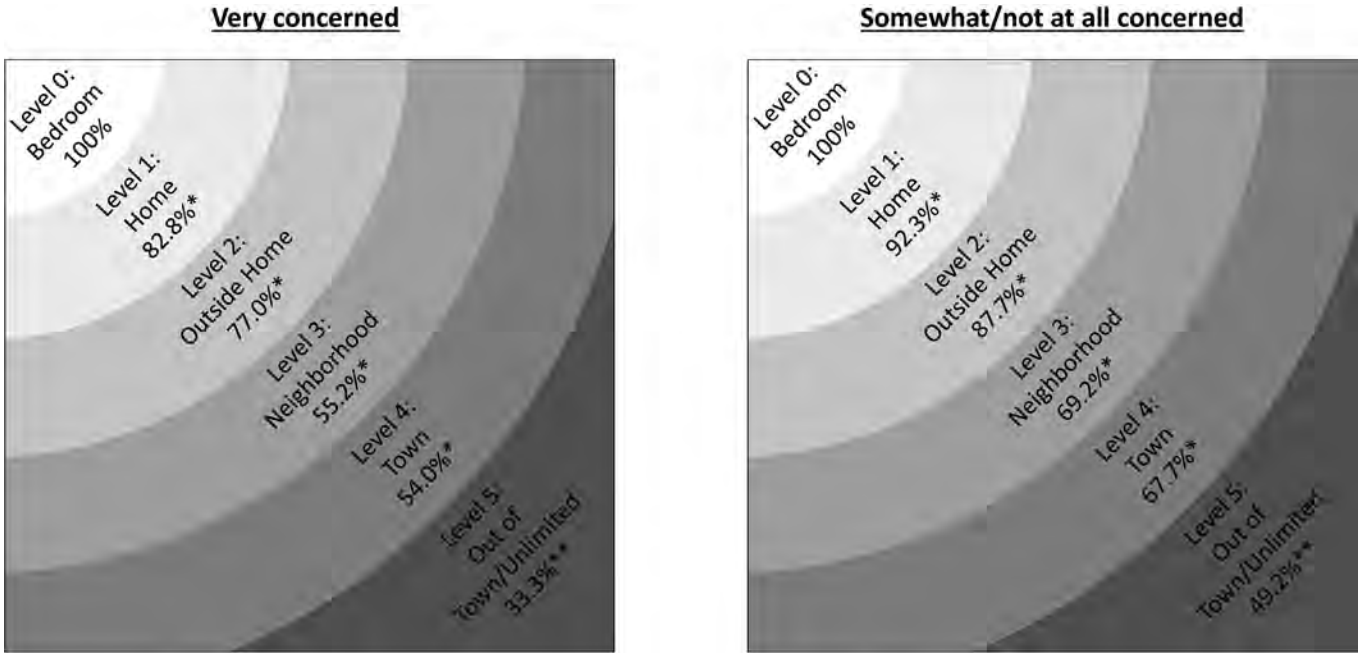
Laura Plantinga[1], Courtney Hoge[1], Cristina Drenkard[1], Charmayne Dunlop-Thomas[1], Brad Pearce[1], S Sam Lim[2] and C. Barrett Bowling[3], [1]Emory University, Atlanta, GA, [2]Department of Medicine, Division of Rheumatology, Emory University School of Medicine, Atlanta, GA, [3]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Opportunities for community mobility, which reflects both physical mobility and social participation, during the COVID-19 pandemic have been limited and may have been related to level of concern about the pandemic. We used data from an ancillary cohort study [Approaches to Positive, Patient-centered Experiences of Aging in Lupus (APPEAL)] to examine the association between level of concern about the pandemic and community mobility among individuals with systemic lupus erythematosus (SLE).

Methods: APPEAL subjects were recruited from the population-based Georgians Organized Against Lupus (GOAL) cohort of individuals with validated SLE. A total of 153 participants (mean age, 48 years; 95% female, 76% Black) were consented (10/6/2020-5/4/2021) for a single visit during the period the COVID-19 survey was administered. Responses to the item "How concerned are you about the COVID-19 pandemic?" (*N*=152) were dichotomized as very concerned vs. somewhat or not at all concerned. Community mobility was measured via the UAB Study of Aging Life-Space Assessment (score range, 0-120), with higher life-space scores representing greater community mobility (movement across greater distances from home, with greater frequency and less help). Scores were described overall and by level of concern [medians (interquartile ranges)], and Wilcoxon rank sum tests were used to obtain *p* values. The percentages of participants reaching each life-space level without personal assistance were calculated and compared by level of concern using chi-square tests. Finally, life-space scores were dichotomized as low (at or below the median, ≤48) vs. high (above the median, >48) in logistic models with concern as the exposure, adjusting for age, gender, and race.

Results: Life-space scores were lower among participants who were very vs. somewhat/not at all concerned about the pandemic [35 (16-72) vs. 58 (24-72); $p = 0.2$]. Overall, without personal assistance, 86.9% of participants reached



Percentages of SLE patients reaching life-space levels without personal assistance, by level of concern about the COVID-19 pandemic (very concerned vs. somewhat/not at all concerned). *p<0.1; **p<0.05.

the life-space level of home (excluding bedroom); 81.7%, outside the home; 61.4%, neighborhood; 60.1%, town; and 40.5% out of town/unlimited. Percentages of patients reaching each life-space level without personal assistance were lower among those who were very concerned about the pandemic, compared to those who were somewhat/not all concerned (Figure). Those who were very vs. somewhat/not at all concerned were 68% more likely to have a low vs. high life-space score [OR=1.68 (95% CI 0.79-3.21)]; adjustment for demographics slightly attenuated this association [OR=1.54 (95% CI 0.79-3.00)]. The associations were similar among older [≥50 years; OR=1.61 (95% CI 0.62-4.17)] and younger [< 50 years; OR=1.73 (95% CI 0.71-4.21); *p*-interaction=0.8] patients. Most of the differences and associations were not statistically significant.

Conclusion: In this cross-sectional study of individuals with SLE, we found that life-space scores were low overall and that these scores were even lower among those who expressed high level of concern about the COVID-19 pandemic. Future studies should explore whether these low levels of community mobility persist beyond the pandemic and whether they are associated with poor physical and/or mental health outcomes in SLE.

Disclosure: L. Plantinga, None; **C. Hoge**, None; **C. Drenkard**, GSK, 1, 5; **C. Dunlop-Thomas**, None; **B. Pearce**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **C. Bowling**, None.

Abstract Number: 1596

Changes in Patient-Reported Outcome (PRO) Scores During the COVID-19 Pandemic: Data from the ArthritisPower Research Registry

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic caused particular concern among patients with autoimmune and rheumatic disease (ARD) due to increased risk of infection, and heightened sense of isolation due to social distancing.[1] We sought to determine whether mean patient-reported outcome scores for mental, social and physical health fluctuated during the COVID-19 pandemic.

Methods: Participants (pts) of ArthritisPower research registry completed PROMIS measures of physical health (Physical Function, Pain Interference, Fatigue, Sleep Disturbance), mental health (Anger, Anxiety, Depression) and social health (Social Isolation, Emotional Support) from January 2020 to April 2021. PROMIS measures are scored 0-100, with US general population mean of 50, and 10 as the standard deviation (SD) of the reference population. We tested the null hypothesis that there was no change in monthly average PROMIS scores across the 15-month pandemic period. Analysis of means (ANOM) compared assessment mean scores for each of the 15 months to overall mean score for each measure during the observed period. Pts with < 2 assessment time points and osteoarthritis with no ARD were excluded from analysis.

Results: A total of 41,547 PRO scores were contributed by 2,266 pts, with 4.5 (6.9) mean (SD) number of observations per pt. Among pts, 87.6% were female, 86.7% white, with mean age of 52.1 (12.7) years (Table 1). Rheumatoid arthritis (n=1,131, 49.9%) was the most common condition. The study sample was younger than the overall ArthritisPower population (55.0 [11.6]; p< 0.001). Most commonly reported measures were the default measures of Pain Interference, Fatigue, Sleep Disturbance and Physical Function; each had more than 9,000 total results. For all measures, PROMIS scores were worse than the US population mean during the observed period (Table 2). Over 15 months, mental health assessment scores varied significantly; mean (SD) overall study period scores were: Anger 61.6 (13.0), Anxiety 63.1 (10.7) and Depression 61.2 (9.5). In January and February 2020, Anger and Anxiety had

Table 1. Demographic characteristics of study sample compared to overall ArthritisPower population

	Study Sample (N=2,266)‡	ArthritisPower (N=26,582)‡	p-value
Age, mean (SD)	52.1 (12.7)	55.0 (11.6)	**<0.001***
Female, n (%)	1,985 (87.6)	23,781 (89.5)	0.006
White, n (%)	1,965 (86.7)	23,245 (87.5)	0.315
Hispanic, n (%)	125 (5.5)	1,498 (5.6)	0.813
Conditions,† n (%)			
Rheumatoid Arthritis	1,131 (49.9)	13,418 (50.5)	0.605
Osteoarthritis	1,025 (45.2)	13,512 (50.8)	**<0.001***
Fibromyalgia	851 (37.6)	11,288 (42.5)	**<0.001***
Axial Spondyloarthritis	438 (19.3)	3,750 (14.1)	**<0.001***
Psoriatic Arthritis	378 (16.7)	4,326 (16.3)	0.615
Osteoporosis	322 (14.2)	4,734 (17.8)	**<0.001***
Psoriasis	319 (14.1)	3,704 (13.9)	0.850
Inflammatory Bowel Disease	260 (11.5)	4,012 (15.1)	**<0.001***
Sjogren's Syndrome	169 (7.5)	1,215 (4.6)	**<0.001***
Lupus	129 (5.7)	1,776 (6.7)	0.069
Gout	106 (4.7)	1,624 (6.1)	0.006

‡Participants with osteoarthritis and no other ARD comorbidities were excluded from the sample

*Statistically significant at p<0.001

†Not mutually exclusive

Table 2. Average assessment scores by month, mean (SD)

	Pain Interf (n= 9,726)	Fatigue (n=9,544)	Sleep Disturb (n=9,477)	Physical Func (n= 9,467)	Depression (n=1,123)	Anxiety (n=773)	Social Iso (n=562)	Emot Support (n=458)	Anger (n=417)
Overall Period	63.6 (7.8)	62.8 (9.4)	58.5 (9.0)	37.6 (7.5)	61.2 (9.5)	63.1 (10.7)	61.7 (9.9)	41.4 (9.7)	61.6 (13.0)
Jan 2020	63.1 (7.9)	62.3 (9.1)	58.5 (8.8)	37.5 (7.1)	**57.6 (8.1)***	**58.7 (9.4)***	62.0 (10.6)	44.3 (8.7)	**55.1 (8.3)***
Feb	63.2 (7.8)	62.4 (9.0)	58.4 (8.8)	37.4 (7.2)	60.4 (7.8)	**59.2 (9.3)***	58.7 (10.1)	**47.3 (10.2)***	**53.6 (8.3)***
Mar	63.6 (7.7)	62.8 (9.3)	58.7 (9.0)	**36.8 (7.2)***	60.9 (8.8)	63.5 (8.8)	59.5 (9.2)	39.5 (9.6)	58.0 (8.8)
Apr	63.2 (9.3)	61.7 (11.3)	58.2 (10.7)	37.2 (8.1)	**64.8 (8.9)***	**67.7 (12.5)***	62.0 (7.6)	39.8 (10.5)	64.3 (16.0)
May	64.6 (8.3)	62.7 (10.3)	58.4 (10.3)	36.8 (7.6)	**66.6 (13.0)***	**72.0 (11.1)***	61.5 (10.5)	43.2 (6.6)	**74.2 (14.1)***
June	64.2 (8.4)	63.1 (10.5)	59.3 (10.5)	37.4 (7.9)	**67.4 (11.1)***	**73.3 (12.3)***	66.0 (7.1)	42.1 (7.2)	**76.4 (12.1)***
July	64.2 (7.5)	63.0 (9.9)	58.3 (9.8)	37.5 (7.7)	62.8 (11.0)	65.0 (11.4)	64.6 (5.8)	40.9 (7.9)	67.9 (12.7)
Aug	64.4 (6.9)	64.2 (8.5)	59.6 (8.7)	37.4 (7.4)	58.7 (9.4)	60.6 (10.8)	59.8 (8.7)	43.3 (10.4)	57.7 (11.0)
Sep	63.2 (7.7)	61.8 (9.1)	58.5 (7.9)	38.8 (8.4)	59.1 (9.5)	60.8 (6.1)	60.6 (9.5)	40.8 (9.1)	58.6 (4.6)
Oct	63.5 (7.7)	64.2 (8.7)	58.2 (8.0)	**39.0 (8.3)***	58.4 (7.5)	63.0 (7.6)	62.1 (5.4)	40.6 (10.7)	56.1 (8.9)
Nov	64.1 (7.9)	63.9 (9.1)	59.0 (8.1)	38.6 (7.9)	59.9 (8.7)	63.9 (11.2)	64.7 (8.2)	37.8 (10.6)	64.6 (5.4)
Dec	64.3 (7.2)	63.5 (9.1)	59.2 (8.6)	38.2 (7.6)	63.3 (8.3)	66.8 (9.9)	62.1 (10.8)	36.7 (9.6)	64.3 (7.5)
Jan 2021	63.0 (7.1)	62.0 (10.1)	58.7 (8.8)	38.4 (7.7)	61.3 (6.2)	61.0 (9.7)	59.5 (11.4)	38.1 (12.1)	61.0 (7.4)
Feb	64.0 (8.2)	63.2 (9.6)	58.2 (8.7)	37.8 (8.5)	60.5 (9.0)	60.5 (10.6)	61.8 (11.6)	40.2 (12.1)	56.4 (13.3)
Mar	63.9 (7.2)	63.7 (9.2)	58.3 (8.8)	37.5 (7.5)	59.5 (8.3)	60.2 (8.9)	64.9 (11.6)	37.0 (9.0)	64.4 (11.8)
Apr	63.1 (7.0)	62.8 (8.6)	57.5 (8.2)	38.4 (7.1)	57.9 (9.2)	62.1 (8.8)	63.0 (11.5)	39.9 (9.2)	61.2 (14.9)

†PROMIS measures are scored 0-100 with mean of 50 for general US population; every 10 points = 1SD
*Statistical significance ($p<0.05$) from ANOM to compare monthly assessment means to the overall assessment mean

significantly lower scores compared to the overall assessment mean. However, during the months of May and June 2020, mean scores were elevated by a standard deviation for Anger (May: 74.2 [14.1], $p< 0.001$; June: 76.4 [12.1], $p< 0.001$) and Anxiety (May: 72.0 [11.1], $p< 0.001$; June: 73.3 [12.3], < 0.001). Depression scores, while lowest in January, increased by half a standard deviation in May (66.6 [13.0], $p< 0.001$) and June 2020 (67.4 [11.1], $p< 0.001$). Among the social health assessments, Social Isolation peaked in June (66.0 [7.1]; overall mean 61.7 [9.9]) and Emotional Support dipped in December 2020 (36.7 [9.6]; overall mean 41.4 [9.7]) (Figure). Scores did not meaningfully vary from the overall mean for any of the physical health assessments across the 15 months.

Conclusion: Despite scores for mental health fluctuating significantly, particularly during the first US wave of the COVID-19 pandemic, scores for physical health remained relatively stable across the pandemic period.

References

1. George M, et al. Rheumatology. 2021;48:603-7

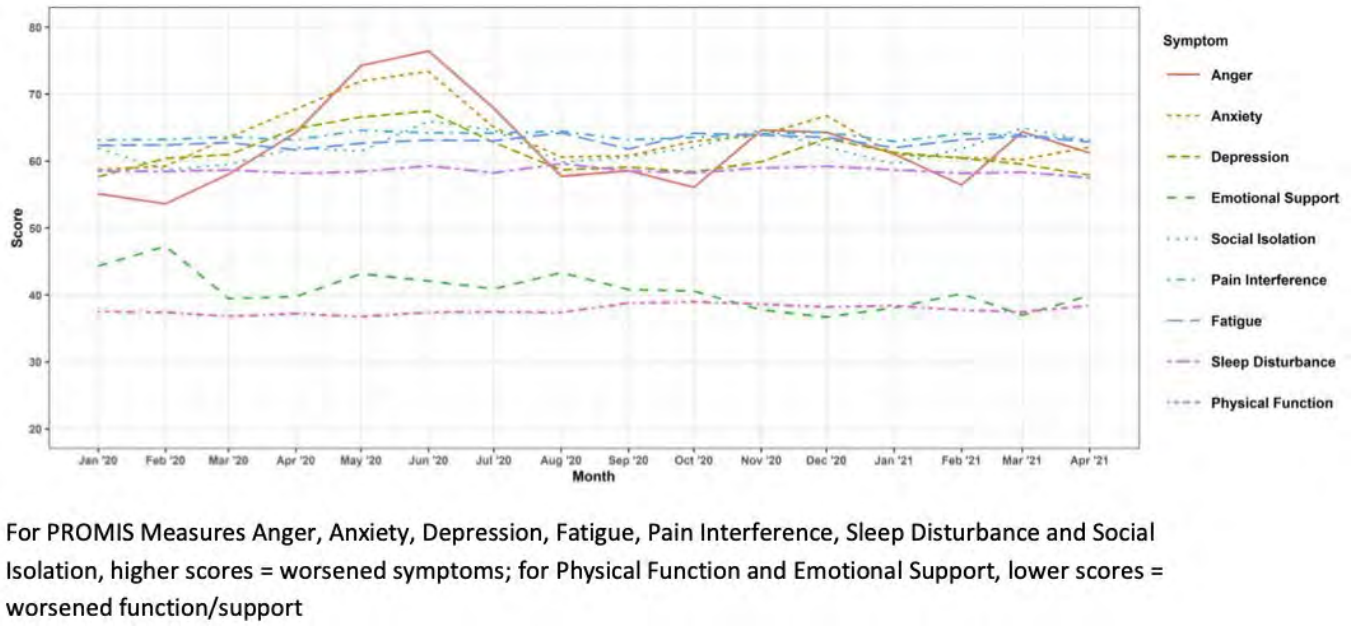

Figure. Patient Reported Outcomes (PROs) Throughout the COVID-19 Pandemic (N=2,266).

Disclosure: K. Gavigan, Global Healthy Living Foundation, 3; **E. Rivera**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **S. Venkatachalam**, None; **L. Stradford**, None; **D. Curtis**, None; **W. Nowell**, Global Healthy Living Foundation, 3, AbbVie, 5, Amgen, 5, Eli Lilly, 5.

Abstract Number: 1597

Arthritis Patient Perspectives on Virtual Care for People Living with Arthritis During the COVID-19 Pandemic and for the Future

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Virtual Care (VC) is the delivery of health care services and information by electronic methods (video, smartphones, email, text) and may support arthritis patients in seeing their health care providers in a timely and convenient way. Arthritis Consumer Experts (ACE) conducted an online survey as little is known about arthritis patients' views and preferences on VC.

Methods: ACE conducted a 23-question online survey (Jan. 20-Feb. 9, 2021) of people with a physician-diagnosed arthritis in English and French. Respondents answered questions on their experiences with in-person and VC services from a health care provider pre-March 2020 and between March 2020-January 2021, their preferences and satisfaction with those services, and the importance of VC availability in the future. Data were analysed in aggregate (including incomplete survey responses). McNemar's test of agreement between time points was performed to com-

pare pre-COVID to during COVID to (anticipated) post-COVID. Chi-square tests (exact tests where possible) were used to test for associations.

Results: 253 responses were analyzed. **Demographics:** 79% were women; 50% had disease less than 10 yrs; 47% rheumatoid arthritis; 19% osteoarthritis; 13% lupus; 8% psoriatic arthritis; 4% ankylosing spondylitis; 66% lived in urban communities; 5.1% identified as Black, Indigenous or a person of colour (BIPOC). **Use of VC:** 59% of respondents reported accessing VC pre-pandemic increasing to 88% during the pandemic. 85% were satisfied with sharing health concerns and getting advice using VC. **Challenges accessing VC:** 32% of respondents reported they were unable to receive arthritis specific VC at a time they felt they needed it during the pandemic. 75% reported it was either very important, important or somewhat important to continue having access to VC when the pandemic ends. 16% faced certain difficulties using VC. **Inequities in VC:** 12% of respondents who identified as non-BIPOC versus

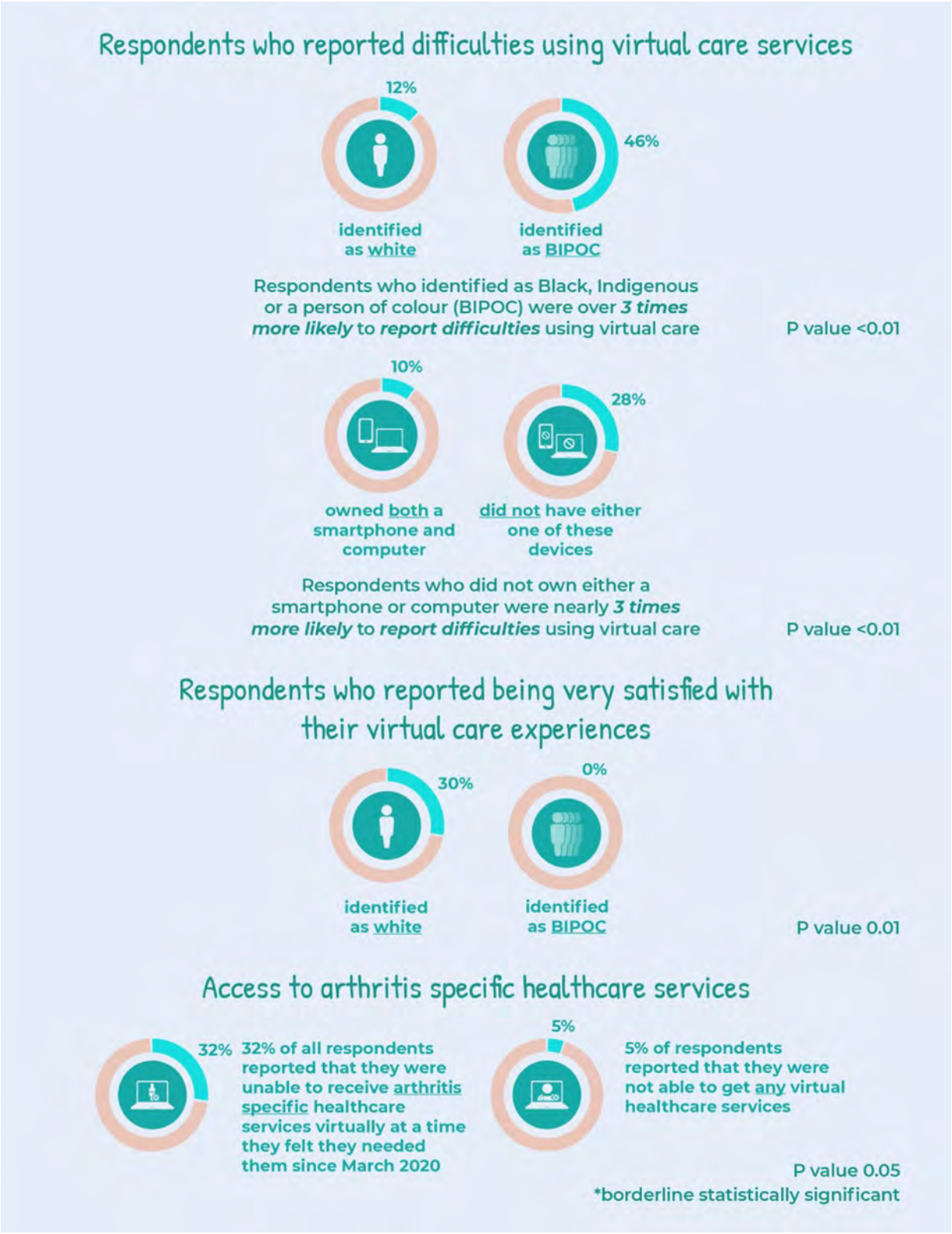
Table 1. Respondent demographics	
	Respondents (N = 253)
Gender identity	
Woman	79%
Man	20%
Gender diverse	<1%
Age group (years)	
<=30	4%%
31-50	17%%
51-70	56%%
71-90	23%%
91+	<1%%
Ethnicity	
white	94.9%
Indigenous	1.6%
People of colour	3.2%
Black	0.8%
Community	
Large urban centre (population of 100,000 or more)	66%
Small-medium sized population centre (population of 16,000 to 99,999)	21%
Rural/ remote community (population of 15,000 or less)	13%

Respondent Demographics

Table 2: Access to VC before, during, and after COVID-19, by type of care

Type of care	Period	Percent	P-value (vs. pre)
General	Pre-COVID	59% already using VC	
General	COVID	88% have accessed VC	<0.001
General	Post-COVID	66% would like continued VC option	<0.066
Rheumatologist	Pre-COVID	36% using some form of VC	
Rheumatologist	COVID	60% have accessed VC	<0.001
Rheumatologist	Post-COVID	49% would like continued VC option	<0.001
Family	Pre-COVID	44% already using VC	
Family	COVID	73% have accessed VC	<0.001
Family	Post-COVID	60% would like continued VC option	<0.001

Access to VC before, during and after COVID-19, by type of care



Difficulties, satisfaction and access inequities to VC

46% of respondents who identified as BIPOC reported difficulties using VC. 7% of white respondents compared to 39% of BIPOC respondents reported feeling uncomfortable or not knowing how to use the VC technology used by their health care provider. **Timeliness of VC:** 15% of respondents reported they were unable to get *any* arthritis

healthcare services in-person since March 2020 while 5% were not able to get *any* arthritis healthcare services virtually.

Conclusion: This community-led survey shows overall patient satisfaction with VC before and during the COVID-19 pandemic. 66% of respondents reported their preference for both in-person and VC services, with a preference of in-person for more complex examinations such as joint counts, and VC to augment care (between in-person visits or to support patient self-care). BIPOC with arthritis were more likely to experience factors that made it difficult to use VC and less likely to be very satisfied with their experiences. BIPOC were more likely to report "I don't feel comfortable" or "know how to use the VC technology being used by my health care provider (38.5% for BIPOC vs 6.7% for white patients; p value < 0.01)". The underrepresentation of BIPOC respondents in this survey suggests their lack of inclusion in arthritis patient organization networks.

Disclosure: M. Joshi, None; **A. Chan**, None; **A. Lima**, None; **K. Lendvoy**, None; **E. Sayre**, None; **C. Koehn**, None.

Abstract Number: 1598

Trends in Medication Interruptions and Associations with Disease Flares During a Public Health Crisis: Longitudinal Data from Patients with Autoimmune Rheumatic Diseases During the COVID-19 Pandemic

Tiffany Dharia[1], Michael George[2], Shilpa Venkatachalam[3], Shubhasree Banerjee[2], Joshua Baker[2], David Curtis[4], Maria I. Danila[5], Kelly Gavigan[4], Peter Merkel[2], Dianne Shaw[6], Jeffrey Curtis[7] and William Nowell[4], [1]Hospital of the University of Pennsylvania, Philadelphia, [2]University of Pennsylvania, Philadelphia, PA, [3]Global Healthy Living Foundation, New York, NY, [4]Global Healthy Living Foundation, Upper Nyack, NY, [5]University of Alabama at Birmingham, Birmingham, AL, [6]Vasculitis Foundation, Kansas City, MO, [7]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has had substantial impact on the care of patients with autoimmune rheumatic diseases (ARDs), resulting in frequent medication interruptions early in the pandemic. This study used longitudinal data to examine trends in medication interruptions and patients' feelings of anxiety throughout the pandemic and to evaluate whether medication interruptions were associated with an increased risk for disease flares.

Methods: Members of the ArthritisPower and Vasculitis Patient Powered Research Network online patient registries and other patient organizations were invited to complete a baseline survey (week 0) and then every 2 weeks until week 8, monthly until week 28, with a final survey at week 38. We analyzed patients with ARDs who completed baseline surveys between March 29 and June 30, 2020 and completed at least one follow-up survey, with follow-up captured through February 2021. Changes over time in PROMIS Anxiety T-scores and medication interruptions due to COVID-19 concerns (among patients receiving DMARDs) were assessed using generalized estimating equation (GEE) models to account for within-person correlations. GEE models were also used to assess associations between medication interruptions and self-reported disease flares at the next survey among patients on DMARDs who were not currently in a flare, adjusting for demographics, medication type, disease type, and calendar time.

Results: A total of 2,396 patients completed a median of 6 surveys (interquartile range 3-9). Mean age was 57 years, 87% were female, and the most common ARDs were rheumatoid arthritis, vasculitis, and psoriatic arthritis (Table 1). Average PROMIS-Anxiety T scores decreased significantly from 59.0 in April 2020 to 55.6 in

Table 1. Baseline Characteristics of Study Participants

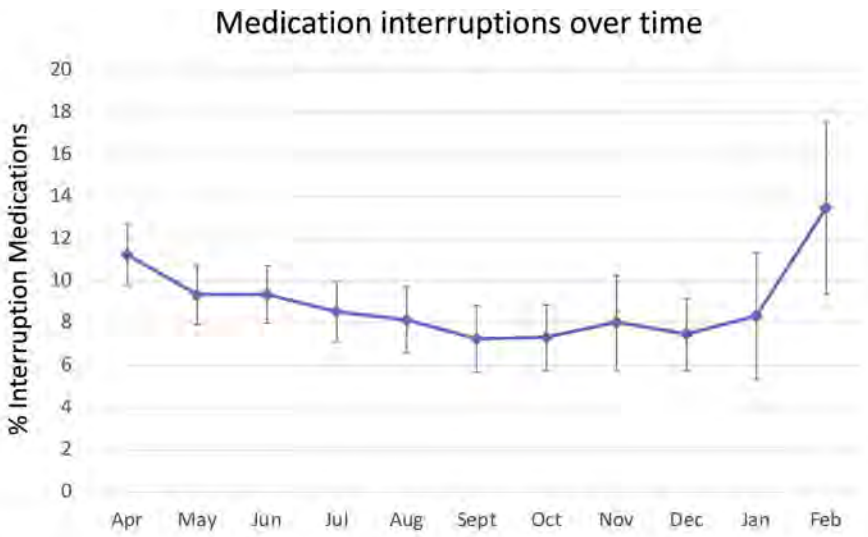
	N = 2396
Age, years	56.8 (12.0)
Female	2074 (86.6%)
White	2175 (90.8%)
Rural residence	273 (12.7%)
Autoimmune disease	
Rheumatoid arthritis	1003 (41.9%)
ANCA-associated vasculitis	353 (14.7%)
Psoriatic arthritis	296 (12.4%)
Ankylosing spondylitis	179 (7.5%)
Other vasculitis	174 (7.3%)
Lupus	121 (5.1%)
Myositis	61 (2.6%)
Other*	209 (8.7%)
Medications	
Biologic/JAK inhibitor	1259 (52.6%)
Methotrexate	717 (29.9%)
Hydroxychloroquine	512 (21.4%)
Glucocorticoids <10 mg/day	571 (23.8%)
Glucocorticoids ≥10 mg/day	111 (4.6%)
PROMIS Anxiety, T-score**	58.9 (8.6)
Stopped a medication because of COVID-19 concerns***	188/1729 (10.9%)

Number (%) or mean (standard deviation) shown

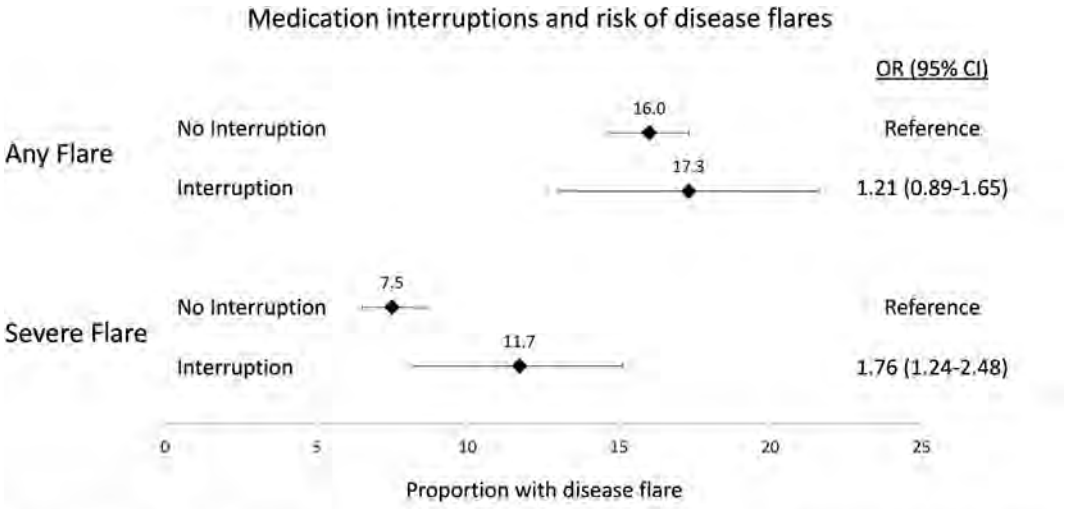
* Other includes patients with other autoimmune conditions (most commonly inflammatory bowel disease, Sjögren's syndrome, or psoriasis) or patients who reported a non-listed autoimmune condition.

** From PROMIS Anxiety short form with range of 1-100, U.S. adult population mean=50 and standard deviation=10.

*** Medication interruptions among patients receiving immune-modulatory medications who did not report a respiratory illness.



Evaluated among patients who were on an immunomodulatory medication and reported that they were not ill. Point estimates and 95% confidence intervals from a GEE model to account for patients contributing multiple observations. $p < 0.001$ for trends in medication interruptions from April to December and $p = 0.001$ for medication interruptions in February vs. December.



Results from GEE models assessing risk of any flare or of severe flares (rated ≥6/10) at the subsequent visit among patients receiving immunomodulatory medications who did not report a respiratory illness or COVID-19 and did not report currently having a flare. Models also included age, sex, race, autoimmune disease type, glucocorticoid use, DMARD type, and month.

February 2021 ($p < 0.001$ for trend) and medication interruptions also decreased significantly from April (11.2%) to December 2020 (7.5%) ($p < 0.001$ for trend) but increased to 13.5% in February 2021 ($p = 0.001$ vs. December) (Figure 1). Medication interruptions were more common in those with higher anxiety ($p < 0.001$), occurring in 10.5% with PROMIS-Anxiety T-score ≥60 vs. 7.8% with score < 60. 1,419 patients had at least one survey response during which they were on DMARDs and did not report a current flare (5,270 total responses). Among this population, 839 (15.9%) reported any flare and 459 (8.7%) a severe flare (≥6/10) at the next survey. Medication interruptions were associated with a significant increase in the risk of severe flare [11.7% vs. 7.5%; OR 1.76 (95% CI 1.24-2.48)] (Figure 2).

Conclusion: Patients with ARDs had high levels of anxiety and frequent medication interruptions at the start of the COVID-19 pandemic. Although anxiety and frequency of medication interruptions improved over time, interruptions increased in February of 2021, possibly related to vaccination efforts or the national surge in COVID-19. Medication interruptions were associated with an increased risk of severe disease flares, highlighting the importance of maintaining continuity of care and avoiding unnecessary medication interruptions during the pandemic and future public health crises.

Disclosure: T. Dharia, None; **M. George**, None; **S. Venkatachalam**, None; **S. Banerjee**, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **D. Curtis**, None; **M. Danila**, Pfizer, 5, Pfizer, 11, AbbVie, 1, Amgen, 5, Amgen, 1, Boehringer Ingelheim, 5, Horizon, 5, WebMD, 12, writer, Novartis, 1; **K. Gavigan**, Global Healthy Living Foundation, 3; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **D. Shaw**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **W. Nowell**, Global Healthy Living Foundation, 3, AbbVie, 5, Amgen, 5, Eli Lilly, 5.

Abstract Number: 1599

Impact of the COVID-19 Pandemic on the Quality of Life of Patients with Rheumatic Conditions: A Qualitative Analysis of Perceived Risk and Decision Making

Courtney Wells[1], Guadalupe Torres[2], William Nowell[3], Shilpa Venkatachalam[3], Laura Stradford[4], Kelly Gavigan[3], Barbara Boyd-Floering[5], Maria I. Danila[6] and Kristine Carandang[7], [1]University of Wisconsin-River Falls, White Bear Lake, MN, [2]Patient Partner, Brooklyn Center, MN, [3]Global Healthy Living Foundation, Upper Nyack, NY, [4]Global Healthy Living Foundation, Nyack, NY, [5]Whelton Virshup CreakyJoints Arthritis Clinic/ Global Healthy Living Foundation, Lake Worth, FL, [6]University of Alabama at Birmingham, Birmingham, AL, [7]Independent, San Diego, CA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The purpose of this qualitative study was to understand the concerns, behaviors, and experiences of adults with autoimmune rheumatic conditions, and to evaluate the impact of the COVID-19 pandemic on their quality of life. Intentional efforts were made to amplify a diverse range of patient voices. Recruitment methods purposefully targeted persons who identify as Black, Indigenous, and People of Color (BIPOC) and/or part of underrepresented and underserved communities.

Methods: Between December 2020 - May 2021, 60-minute interviews were conducted with English- and Spanish-speaking adults, aged ≥ 18 years with self-reported diagnosis of autoimmune rheumatic condition, via phone or videoconference using a semi-structured interview guide. Participants were recruited through social media posts, word-of-mouth, or clinical referral. To ensure rigor while maintaining relevance in response to the changing nature of the COVID-19 pandemic, the research team met regularly to perform preliminary analysis and reflexivity (e.g., acknowledging researchers' pre-conceptions). Ongoing analysis combined methods of phenomenology and content analysis through three steps: 1. Summarizing interviews, 2. Discussing potential units of meaning based on iterative review of transcripts and literature, 3. Axial and selective coding to determine cross-cutting themes.

Results: Participants included 19 adults (40.3 ± 15.1 years old), most reporting a diagnosis of rheumatoid arthritis (52.6%). Demographics included race (52.6% BIPOC), ethnicity (31.6% Hispanic/Latinx), insurance (21.1% Medicare/Medicaid; 15.8% uninsured), employment (26.3% identified as disabled), and representation across U.S. geographic locations. Ongoing analysis produced four preliminary themes (Table 1).

- Theme 1: Based on their learned and experiential knowledge of rheumatic disease and its treatment, most participants perceived themselves to be at higher risk for COVID-19 than the general population.
- Theme 2: Participants vigilantly worked to balance COVID-19 risk, disease management, and mental health. Participants' decisions of whether, how, and when to engage in activities often centered around trust or distrust in their social circles, local geographic communities, and United States politics and public health response.
- Theme 3: Participants felt unsupported by all levels of the healthcare system, from direct interaction with providers to messages received from public health authorities.
- Theme 4: Combined, these factors led to a self-reported increase in autoimmune disease symptoms; relapse or exacerbation of established mental health conditions; and/or new symptoms of trauma, depression, and/or anxiety.

Table 1. Sample Quote(s) per Qualitative Theme

Preliminary Theme Topic	*Sample Quote(s) per Theme*
Theme 1: COVID-19 Risk Perception	*I actually thought I was going to die from it if I had gotten it, because we're told that if you're immuno-compromised, that your chances of getting COVID is higher and it's harder to battle the virus if you do have a pre-existing condition. Being fed all this information, it put me in a state where I felt that unstable feeling and being afraid of going out and making sure that I was doing everything I could to stay healthy. I was washing my hands every 20 minutes and I was like, 'I'm at home. Why am I doing this if I'm at home?'*
Theme 2: Balancing Act	*I can definitely see from the startup of COVID how strict we were [when deciding whether or not to do activities] versus now it's definitely on a scale. Little things started giving way and it was definitely more a mental health thing and less of 'I'm learning more about COVID.'... The type of person I am, I'm like 'Well, if there's any risk, I don't want to take it or you don't need to be doing that. It's unnecessary.' But it got to a point where I can definitely tell you it was necessary for my mental health, for my partner's mental health.*
Theme 3: Interaction with Healthcare System	*I think the misinformation in our community is playing a big role and the historical discrimination against the immigrant communities, in my case, and in the case of the communities [of Color] that I work with. And language barriers, again, the lack of accessibility to information for those families. It has played a major role in these disparities, for example, ... anyone [with or without documentation] can get a vaccine if they're eligible for it, but our community doesn't really know. I think there's this lack of understanding from the authorities that people right now are just focused on surviving the day-to-day basis, like having enough food on their table at the end of the day and paying for rent, not being homeless.*
Theme 4: Physical and Mental Health Symptoms	• *We were on a prayer and a wing, nothing. When the shutdown came, we weren't able to go to the doctor, see the doctor, or talk to the doctor...The shutdown really just took a toll on my body really because I hadn't had any issues with my hands and my fingers in a long time. My fingers were swollen, they were locking up. I mean, when I did have a chance to go to [the doctor], I got two injections in one day, one in each hand.* • *There was the mental toll of quarantine. And then not being able to see my family. Then the chances of getting COVID. Then definitely being Asian, being Chinese, added just a little bit more to that. Because if I wasn't, if I was White, that wouldn't be a thing. I mean I wouldn't be worried that someone would attribute the 'China-virus' to me and that I might get attacked... It added to the stress and anxiety of an already stressful situation.*

Conclusion: Participant interviews during the COVID-19 pandemic revealed critical patient needs for direct and timely communication as well as increased sensitivity to the psychosocial effects of the pandemic on disease symptoms. It is likely these needs will persist post-pandemic.

Disclosure: C. Wells, None; **G. Torres**, None; **W. Nowell**, Global Healthy Living Foundation, 3, AbbVie, 5, Amgen, 5, Eli Lilly, 5; **S. Venkatachalam**, None; **L. Stradford**, None; **K. Gavigan**, Global Healthy Living Foundation, 3; **B. Boyd-Floering**, None; **M. Danila**, Boehringer Ingelheim, 5, Amgen, 1, Amgen, 5, AbbVie, 1, Pfizer, 5, Pfizer, 11, Horizon, 5, Novartis, 1, WebMD, 12, writer; **K. Carandang**, None.

Abstract Number: 1600

Has the COVID 19 Pandemic Impacted the Management of Chronic Musculoskeletal Pain?

Samon Oomen-Lochtefeld[1], Rochelle Tsemekhin[2], Lori Lyn Price[2], Chen Guang[3] and Chenchen Wang[2], [1]Tufts University, Boston, MA, [2]Tufts Medical Center, Boston, MA, [3]Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The management of the patients with chronic conditions such as musculoskeletal pain can be affected by the COVID-19 pandemic. However, the impact of COVID-19 pandemic in the management of pain has not been clearly delineated. We conducted a descriptive review of the impact of the COVID-19 pandemic on chronic musculoskeletal pain management and healthcare system accessibility during 2020-2021 to better inform clinical decision-making.

Methods: We searched MEDLINE and the Cochrane Database from December 2019 to May 2021. We included studies of any design investigating the impact of COVID-19 pandemic on the management of patients with chronic musculoskeletal pain. Screening and data extraction were undertaken by two reviewers. We summarized the disease conditions, demographic information, study design types, duration of observation, treatment accessibility, outcomes measured, and main conclusions.

Results: We identified 114 abstracts and examined 8 published studies from 8 different countries during 2020-2021 on the impact of the COVID-19 pandemic on adults with chronic musculoskeletal pain conditions. **Table 1** summarizes the evidence reviewed according to types of conditions, including osteoarthritis, fibromyalgia, rheumatoid arthritis, chronic lower back pain and miscellaneous chronic musculoskeletal pain. There are 4 cohort and 4 cross-sectional studies with 1,724 participants. The mean age ranged from 36-62 years and data was collected for 1 to 6 months. 59-100% of patients in studies reported reduced treatment accessibility. Of 8 studies, 2 prospective cohort studies on osteoarthritis reported significant increases in pain and loss of function, with an average Visual Analog Score (VAS) increase of 0.7 pre- to post-quarantine. Similarly, higher pain intensity was reported among fibromyalgia and chronic lower back pain patients. Additionally, back pain point prevalence increased from 38.8 to 43.8% within the same sample. In a cross-sectional study, 68 rheumatoid arthritis patients reported increased VAS pain scores and lower quality of life since the onset of the pandemic. 2 other cross-sectional studies with 787 miscellaneous chronic pain patients reported conflicting results; while one study found an 8% average pain severity increase and a 6% average pain interference increase, the other one reported decreases in both average pain severity and pain interference as measured by the Brief *Pain* Inventory scale. Vulnerable patients reported high dependence on others, low ability to self-manage pain, and restricted access to healthcare. Notably, the study with the highest treatment accessibility reported some improvements in pain, depression and sleep quality.

Conclusion: Overall, the COVID-19 pandemic has adversely affected pain severity, physical function and quality of life in patients with chronic musculoskeletal pain. Despite the small number of studies available, our review suggests the pandemic had negative impacts on these patients and lowered treatment accessibility. Further consideration on patient wellbeing and healthcare accessibility for chronic pain management during the pandemic is recommended.

Table 1. summarizes the impacts of the COVID-19 pandemic on patients with chronic musculoskeletal pain

Reference	Condition	N* (F%)	Mean age / range, Race	Study design	Duration (months)	Reduced treatment access	Outcomes measured	Main conclusions
Endstrasser et al., 2020, Austria	94% OA 6% hip dysplasia	68 (44%)	62	Prospective cohort	2	100%	WOMAC, QOL	Significant impact on pain and physical function in patients with end-stage hip and knee OA.
Knebal et al., 2021, Germany	Arthroscopy (35% knee 40% hip) 24% other	77 (44%)	<30 - >80	Cohort	2	79%	Pain, depression	Cancellation of surgery resulted in significant pain levels and in psychosocial distress.
Aloush et al., 2021, Israel	Fibromyalgia	231 (91%)	17 - >61	Cohort	2	98%	Symptom severity, pain, depression, stress, QOL	Patients reported adverse mental and physical outcomes. Reduced treatment accessibility was correlated with higher symptom severity.
Cavalli et al., 2020, Italy	Fibromyalgia	32	ND	Cohort	6	ND	Fibromyalgia impact questionnaire	67% of patients experienced a worsening clinical status, and 33% reported improvement since the pandemic's onset.
Zomalheto et al., 2020, Benin	Rheumatoid arthritis	68 (96%)	50	Cross-sectional	2	87%	Disease activity, QOL	Pandemic had a negative impact on the quality of life of rheumatoid arthritis patients.
Sagat et al., 2020, Saudi Arabia	Chronic back pain (39% pre-quarantine, 44% during)	463 (44%)	36	Cross-sectional	2	ND	Pain, stress	Significant increase in chronic lower back pain intensity from 38.8 to 43.8% since the pandemic's onset.
Hruschak et al., 2021, USA	57% back pain 25% fibromyalgia 11% postsurgical pain	150 (83%)	41 85% white 7% black 8% other	Cross-sectional	1-2	71%	Pain, anxiety, depression, stress, QOL	Patients self-reported an overall significant increase in pain severity and pain interference since the pandemic's onset.
Zambelli et al., 2021, UK	Pain (37% musculoskeletal, 63% other)	637 (87%)	43 94% white 1% black 1% Asian 4% other	Cross-sectional	1-3	59%	Pain, sleep, QOL, anxiety, depression	Small, significant improvements in sleep quality, depression and pain. Vulnerable groups reported increased dependence on others, decreased ability to self-manage pain, and restricted access to healthcare.

Abbreviations: ND: no data; OA: osteoarthritis; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index; QOL: quality of life.

Disclosure: S. Oomen-Lochtefeld, None; **R. Tsemekhin**, None; **L. Price**, None; **C. Guang**, None; **C. Wang**, None.

Abstract Number: 1601

Satisfaction with Telemedicine in Immunosuppressed Children and Young Adults with Autoimmune Disease During the COVID 19 Pandemic: Are Their Needs Really Met? Preliminary Data from a Single Institution

Lakshmi Moorthy[1], **Lauren Freidenrich**[1], Lisa Mikesell[2], Sarah Fadem[2], Vikram Bhise[1], Richard Brodsky[1], Ellen Cahill[1], Joann Carlson[1], Yue Hao[1], Daniel Horton[1], Vivien Hsu[1], Editt Rodriguez[1], Christian Salazar[3], Cynthia Salvant[1] and Lawrence Kleinman[1], [1]Rutgers Robert Wood Johnson Medical School, New Brunswick, NJ, [2]Rutgers Department of Communication, New Brunswick, NJ, [3]NYU Dept. of Epi. and Health Promotion, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

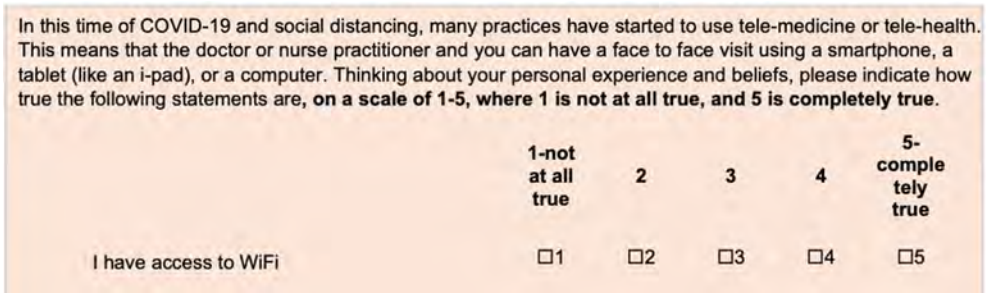
Background/Purpose: COVID-19 can lead to severe and life-threatening complications, which is particularly unnerving for patients with autoimmune disease (AID) on immunosuppressive therapy. Telemedicine has enabled these patients to receive healthcare while socially distant. We describe preliminary data regarding the capacity of telemedicine to meet the healthcare needs of patients with AID who are immunosuppressed.

Methods: This cross-sectional survey included immunosuppressed young adults with AID and parents of immunosuppressed children with AID. The validated Local Inventory of Needs and Knowledge (LINK) survey with a 5-point Likert scale (completely true to completely untrue) was used to assess met and unmet medical and non-medical needs. LINK was modified to address the impact of the pandemic on access to medical care, experience with telemedicine, and health-related behaviors in immunosuppressed AID patients. Consistent with LINK's intention, responses were dichotomized at the extremes, either completely true (5) versus all other responses, or not at all true (1) versus all other responses, depending upon the stem's framing. See figure 1 for a sample of a LINK survey question.

Results: The first 29 respondents were 17 young adults and 12 parents. Patient (7-24 years old) diagnoses included: lupus (n=7), multiple sclerosis (n=6), juvenile arthritis (n=2), uveitis (n=2), vasculitis (n=2), minimal change disease (n=2), neuromyelitis (n=2), nephrotic syndrome (n=1), Henoch-Schonlein purpura (n=1), dermatomyositis (n=1), focal segmental glomerular sclerosis (n=1), post renal transplant (n=1), and systemic sclerosis (n=1).

Within this sample, 24% worried about going to a doctor's office/hospital due to immunosuppressed status. Fear of getting COVID-19 prevented 17% from seeking in-person medical care (Fig 2). Almost all (97%) had access to Wi-Fi, 71% felt comfortable with the idea of seeing a doctor using telemedicine and 59% found it to be a convenient form of healthcare delivery. Many (69%) felt telemedicine was "easy to use" and 59% reported that telemedicine minimized "pandemic-associated stress." Most (72%) believed telemedicine saved time. While 68% of patients were comfortable with in-person appointments, 48% of patients felt "more comfortable with telemedicine appointments during the pandemic." Only 55% thought "all of [their] important healthcare needs were met (Fig 2)." Patients also reported non-medical issues such as difficulties with access to adequate food and housing (data analysis is underway). Responses from young adults and parents were similar.

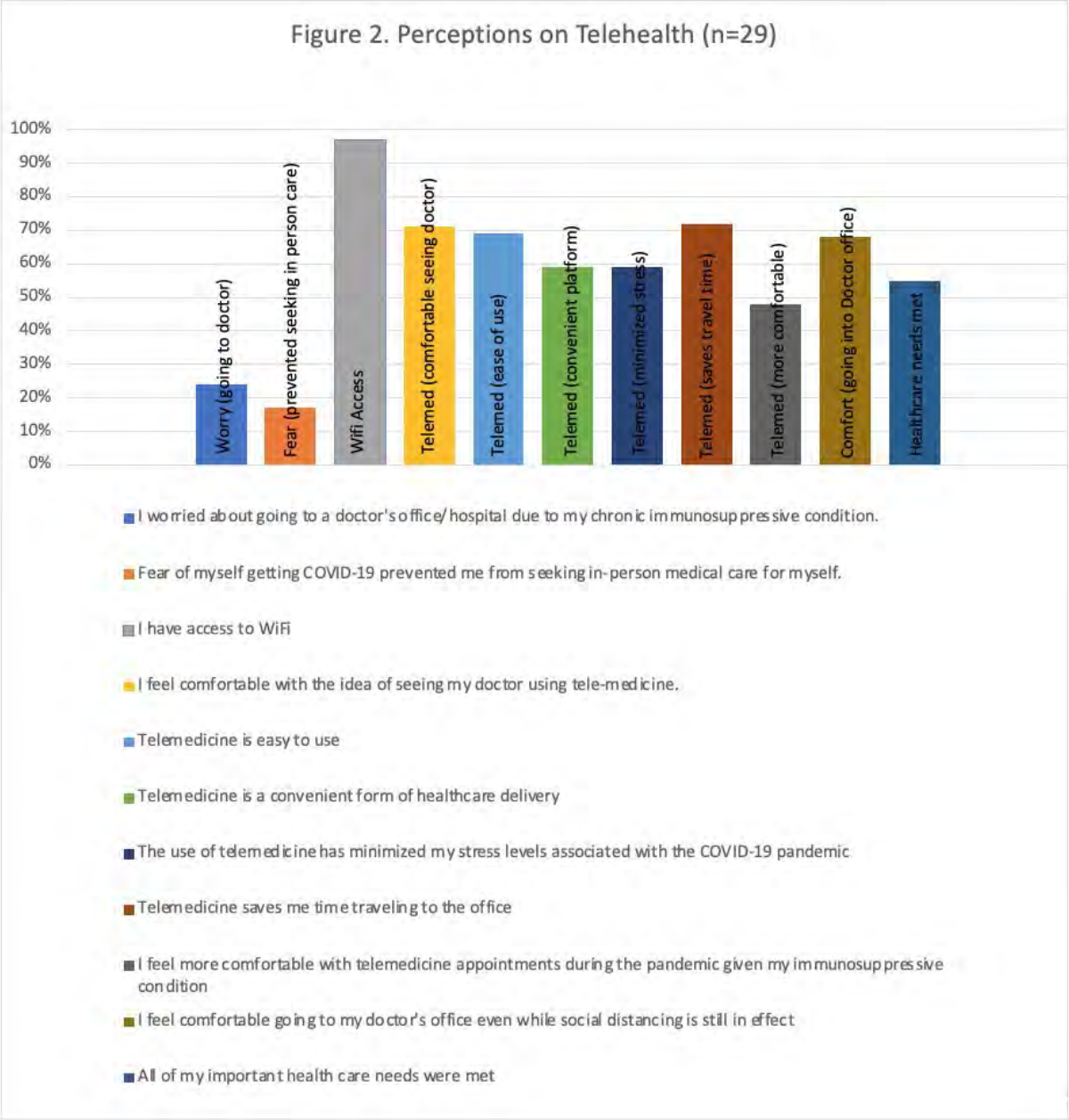
Conclusion: In this sample of immunosuppressed patients with AID and their parents, a majority identified telemedicine as a convenient and effective alternative to in-person appointments during the pandemic. While respondents expressed satisfaction with telemedicine services that were delivered, nearly half (45%) reported that they remained with unmet needs, suggesting that satisfaction alone is insufficient to assess the adequacy of telemedicine in this population. Data collection is ongoing to understand the unmet needs and drawbacks of telemedicine.



In this time of COVID-19 and social distancing, many practices have started to use tele-medicine or tele-health. This means that the doctor or nurse practitioner and you can have a face to face visit using a smartphone, a tablet (like an i-pad), or a computer. Thinking about your personal experience and beliefs, please indicate how true the following statements are, **on a scale of 1-5, where 1 is not at all true, and 5 is completely true.**

	1-not at all true	2	3	4	5-completely true
I have access to WiFi	☐1	☐2	☐3	☐4	☐5

Sample of LINK survey question and response set (only 1 question out of several questions has been included)



Perceptions on Telehealth based on the LINK survey responses (n=29)

Disclosure: L. Moorthy, Bristol Myer Squibb, 5; **L. Freidenrich**, None; **L. Mikesell**, None; **S. Fadem**, None; **V. Bhise**, None; **R. Brodsky**, None; **E. Cahill**, None; **J. Carlson**, None; **Y. Hao**, None; **D. Horton**, Danisco USA Inc., 5; **V. Hsu**, None; **E. Rodriguez**, None; **C. Salazar**, None; **C. Salvant**, None; **L. Kleinman**, None.

Abstract Number: 1602

Factors Associated with COVID-19 Vaccine Hesitancy in Rheumatology Outpatients in New York City

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 vaccination is particularly important for patients with systemic rheumatic diseases (SRDs), who may be at increased risk of infection with SARS-CoV-2 and of worse COVID-19 outcomes. However, despite remarkable vaccine safety and efficacy data, some individuals remain hesitant to be vaccinated. We aimed to measure the degree of vaccine hesitancy in rheumatology outpatients from a U.S. COVID-19 "hotspot" and explore factors associated with hesitancy or refusal in this high-risk patient population.

Methods: We emailed a secure web-based survey on March 5, 2021 to 7,505 patients aged ≥18 years evaluated at least once by a rheumatologist between 2018-2020 at a large Rheumatology center in New York City and who previously agreed to participate in surveys on COVID-19. We included individuals who completed a modified vaccine hesitancy questionnaire (based on *Larson et al. Vaccine. 2015*), with questions specific to COVID-19 vaccination. We also collected data on sociodemographics, medical comorbidities, medication use, other immunizations during adulthood, and COVID-19 history. ICD-10-CM algorithms were used to identify SRD diagnoses. We evaluated patient

Table 1. Baseline Demographic Characteristics of 2,384 Rheumatology Outpatients in New York City by COVID-19 Vaccination Status

	Refusing vaccination N=56	Undecided about vaccination N=88	Willing to be vaccinated or already vaccinated N=2240	P-value
Age, Mean (SD)	52.1 (13.5)	53.4 (12.7)	61.4 (14.4)	**<0.01**
Female Sex	49 (87.5%)	75 (85.2%)	1784 (79.6%)	0.16
Race				**<0.01**
• White	42 (75.0%)	65 (73.9%)	1968 (87.9%)	
• Black	6 (10.7%)	10 (11.4%)	73 (3.3%)	
• Other	2 (3.6%)	7 (8.0%)	82 (3.7%)	
• Missing	6 (10.7%)	6 (6.8%)	117 (5.2%)	
Ethnicity				**<0.01**
• Hispanic/Latinx	8 (14.3%)	12 (13.6%)	113 (5.0%)	
• Not Hispanic/Latinx	45 (80.4%)	69 (78.4%)	2016 (90.0%)	
• Missing	3 (5.4%)	7 (8.0%)	111 (5.0%)	
Body Mass Index, Mean (SD)	26.4 (5.6)	26.8 (7.1)	26.7 (7.5)	0.96
Body Mass Index				0.48
• <25	26 (46.4%)	40 (45.5%)	1051 (46.9%)	
• 25-29	17 (30.4%)	20 (2.7%)	656 (29.3%)	
• 30+	13 (23.2%)	26 (29.6%)	515 (23.0%)	
• Missing	0 (0.0%)	2 (2.3%)	18 (0.8%)	
Employment Status				0.27
• Employed	1 (1.8%)	4 (4.6%)	158 (7.1%)	
• Unemployed/Retired/Other	16 (28.6%)	27 (30.7%)	535 (23.9%)	
• Missing	39 (69.6%)	57 (64.8%)	1547 (69.1%)	
Household Income				**<0.01**
• <$75K	14 (35.0%)	22 (37.3%)	302 (17.9%)	
• $75K-$150K	12 (30.0%)	17 (28.8%)	526 (31.2%)	
• >$150K	14 (35.0%)	20 (33.9%)	856 (50.8%)	
Education				**<0.01**
• High school graduate or Below	3 (5.9%)	7 (9.1%)	68 (3.3%)	
• Any college	34 (66.7%)	45 (58.4%)	999 (48.6%)	
• Masters, Professional, Doctorate	14 (27.5%)	25 (32.5%)	989 (48.1%)	
Marital Status				**0.03**
• Married or partnered	39 (69.6%)	47 (53.4%)	1429 (63.8%)	
• Separated, divorced, single, widowed	15 (26.8%)	37 (42.1%)	777 (34.7%)	
• Missing	2 (3.6%)	4 (4.6%)	34 (1.5%)	

characteristics and vaccine hesitancy questionnaire responses by vaccination status (refusing vaccination, undecided, already received/willing). Categorical variables were calculated using chi-square/Fishers exact test. Continuous variables were tested with one factor ANOVA.

Results: Among 2,384 patients who completed the vaccine hesitancy questionnaire (31.8% response rate), 2,240 (94.0%) patients were willing/already received COVID-19 vaccination. 88 (3.7%) patients were 'undecided', and 56 (2.3%) reported vaccine refusal (Table 1). Compared to patients willing/already received vaccine, those refusing or undecided had lower mean ages (52.1y [SD 13.5] and 53.4 [SD 12.7] versus 61.4 [SD14.4]), higher percentage of Black, Hispanic/Latinx patients, patients with lower household income, and married/partnered patients; they had lower percentage with an advanced education degree (Table 1). Undecided patients were least likely to have received other immunizations during adulthood (Table 2), and those refusing the vaccine were most likely to have had a history of COVID-19 infection (33.9% versus 20.5% versus 9.1%, $p< 0.01$). SRD status differed between the groups, with SLE-like diseases being highest in those refusing the vaccine ($p< 0.01$). No differences in current use of immunosuppressive medications were observed. Vaccine questionnaire responses indicated that those refusing the vaccine were least likely to believe in the importance for health of vaccines in general, and in the safety or efficacy of the COVID-19 vaccine (Table 3). Patients refusing or undecided were most concerned about long-term vaccine side effects, lack of study in rheumatology patients, and the speed of vaccine development (Table 3).

Conclusion: Although vaccine hesitancy/refusal was only reported by 6% of respondents, our study provides useful insights into why rheumatology patients may refuse COVID-19 vaccination, including data that suggest the misperception that previous COVID-19 infection may mitigate the need for immunization.

Table 2. General Medical History and Immunization Status of Rheumatology Outpatients in New York City by COVID-19 Vaccination Status

	Refusing vaccination N= 56	Undecided about vaccination N= 88	Willing to be vaccinated or already vaccinated N = 2240	P-value
General Medical Comorbidities*				0.08
• 0	28 (50.0%)	53 (60.2%)	1056 (47.1%)	
• 1	16 (28.6%)	27 (30.7%)	812 (36.3%)	
• 2+	12 (21.4%)	8 (9.1%)	372 (16.6%)	
Immunization History (During Adulthood)				
• No Immunizations**	5 (8.9%)	13 (14.8%)	57 (2.5%)	**<0.01**
• Influenza vaccine	44 (78.7%)	62 (70.5%)	2091 (93.4%)	**<0.01**
• Pneumonia (Pneumovax/Prevnar)	21 (37.5%)	25 (28.4%)	1331 (59.4%)	**<0.01**
COVID-19 History (Ever)	19 (33.9%)	18 (20.5%)	203 (9.1%)	**<0.01**
Systemic Rheumatic Disease History	37 (75.5%)	59 (79.7%)	1306 (65.7%)	**0.02**
• **Inflammatory Arthritis**	13 (26.5%)	23 (31.1%)	631 (31.7%)	0.74
• **Spondyloarthritis**	9 (18.4%)	11 (14.9%)	256 (12.8%)	0.47
• **Vasculitis/Scleroderma/Myositis**	3 (6.1%)	6 (8.1%)	128 (6.4%)	0.76
• **SLE/Sjogren's/MCTD/UCTD**	16 (32.7%)	21 (28.4%)	373 (18.8%)	**<0.01**
Any active immunomodulatory or immunosuppressive medication use	34 (60.7%)	42 (47.7%)	1080 (48.2%)	0.18
• Hydroxychloroquine	14 (25.0%)	22 (25.0%)	438 (19.6%)	0.28
• Biologics	10 (17.9%)	15 (17.1%)	397 (17.7%)	0.99
• Conventional DMARDS	10 (17.9%)	12 (13.6%)	370 (16.5%)	0.74
• Corticosteroids	9 (16.1%)	5 (5.7%)	187 (8.4%)	0.08
• Small Molecules	4 (7.1%)	2 (2.3%)	78 (3.5%)	0.27
• Other DMARDS (Cyclosporine, Tacrolimus)	0 (0.0%)	0 (0.0%)	17 (0.8%)	1.00

*Comorbidities include any of the following identified by the Centers for Disease Control and Prevention in 2/2021 as being most relevant for COVID-19 risk: Asthma or lung disease, Cancer, Chronic Kidney Disease, Diabetes, Congestive Heart Failure or Myocardial Infarction, Ever smoking, Stroke

**Including influenza, pneumonia, yellow fever, Tetanus (Tdap), Shingrix (first or second dose), Zostavax, Hepatitis B

Table 3. Responses to Vaccine Hesitancy Questionnaire* by Rheumatology Outpatients in New York City, Stratified by COVID-19 Vaccination Status

	Refusing vaccination N= 56	Undecided about vaccination N= 88	Willing to be vaccinated or already vaccinated N = 2240	P-value
Vaccines are important for my health.				**<0.01**
Agree/strongly agree	33 (58.9%)	61 (69.3%)	2148 (95.9%)	
Neither agree nor disagree	16 (28.6%)	21 (23.9%)	59 (2.6%)	
Strongly disagree/disagree	7 (12.5%)	6 (6.8%)	33 (1.5%)	
I am at risk for severe COVID-19 symptoms.				**<0.01**
Agree/strongly agree	21 (37.5%)	45 (51.1%)	1369 (61.1%)	
Neither agree nor disagree	17 (30.4%)	23 (26.1%)	426 (19.0%)	
Strongly disagree/disagree	18 (32.1%)	20 (22.7%)	445 (19.9%)	
I am concerned about the speed at which the COVID-19 vaccine was developed.				**<0.01**
Agree/strongly agree	39 (69.6%)	61 (69.3%)	516 (23.0%)	
Neither agree nor disagree	9 (16.1%)	15 (17.1%)	601 (26.8%)	
Strongly disagree/disagree	8 (14.3%)	12 (13.6%)	1123 (50.1%)	
I am concerned that the COVID-19 vaccine may have long-term side effects.				**<0.01**
Agree/strongly agree	46 (82.1%)	70 (79.6%)	483 (21.6%)	
Neither agree nor disagree	4 (7.1%)	13 (14.8%)	800 (35.7%)	
Strongly disagree/disagree	6 (10.7%)	5 (5.7%)	0957 (42.7%)	
I am concerned that the COVID-19 vaccine has not been studied in patients with rheumatology conditions/arthritis.				**<0.01**
Agree/strongly agree	50 (89.3%)	72 (81.8%)	837 (37.4%)	
Neither agree nor disagree	4 (7.1%)	13 (14.8%)	850 (38.0%)	
Strongly disagree/disagree	2 (3.6%)	3 (3.4%)	553 (24.7%)	
I am concerned that the COVID-19 vaccine may interact with my current medications.				**<0.01**
Agree/strongly agree	31 (55.4%)	45 (51.1%)	442 (19.7%)	
Neither agree nor disagree	21 (37.5%)	29 (33.0%)	771 (34.4%)	
Strongly disagree/disagree	4 (7.1%)	14 (15.9%)	1027 (45.9%)	
I believe the COVID-19 vaccine is safe.				**<0.01**
Agree/strongly agree	10 (17.9%)	14 (15.9%)	1894 (84.6%)	
Neither agree nor disagree	28 (50.0%)	65 (73.9%)	306 (13.7%)	
Strongly disagree/disagree	18 (32.1%)	9 (10.2%)	40 (1.8%)	
I believe the COVID-19 vaccine is effective.				**<0.01**
Agree/strongly agree	16 (28.6%)	30 (34.1%)	1984 (88.6%)	
Neither agree nor disagree	28 (50.0%)	55 (62.5%)	224 (10.0%)	
Strongly disagree/disagree	12 (21.4%)	3 (3.4%)	32 (1.4%)	

* Reference: Larson et al. Vaccine. 2015 Aug 14; 33 (34): 4165-75. Standard questions were modified to be COVID-19 specific. *(Standard question responses not shown due to space constraints.)*

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Abstract Number: 1603

COVID-19 Vaccination Experience in Patients with Rheumatoid Arthritis Treated at the Cleveland VA Medical Center

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Following the introduction of the COVID-19 vaccines, there has been uncertainty as to whether receiving the COVID-19 vaccine would result in overactivation of the immune system and subsequently lead to a

Table 1. Baseline Characteristics

	Number	%
Sex		
Male N	57.00	95.00%
Female N	3.00	5.00%
Age		
Mean	72.23	
Median	73.00	
Range	37-92	
Race		
White	47.00	78.33%
African American	11.00	18.33%
Missing	2.00	3.33%
Seropositivity		
RF	3.00	5.00%
Anti-CCP	13.00	21.67%
Both	23.00	38.33%
Seronegative	21.00	35.00%
Comorbidities		
Diabetes mellitus	22.00	36.67%
Coronary artery disease	15.00	25.00%
Hypertension	47.00	78.33%
Obesity	30.00	50.00%
COVID-19 infection prior to Vaccine		
Yes	2.00	3.33%
No	32.00	53.33%
Missing	26.00	43.33%
On ACE inhibitors		
Yes	17.00	28.33%
No	44.00	73.33%
Rheumatoid arthritis Medications		
Methotrexate or Leflunomide	20.00	33.00%
Hydroxychloroquine or Sulfasalazine	11.00	18.00%
TNF inhibitors	7.00	12.00%
Abatacept	2.00	3.00%
Tocilizumab	1.00	2.00%
RTX	3.00	5.00%
tofacitinib	1.00	2.00%
Methotrexate+TNF-inhibitors	9.00	15.00%
Methotrexate+Abatacept	3.00	5.00%
Metothrexate+Tocilizumab	0.00	0.00%
Metothrexate+rituximab	0.00	0.00%
Methothtrexate+tofacitinib	0.00	0.00%
No medicine	3.00	5.00%
Prednisone		
< or = 5 mg/day	2.00	3.33%
6-10 mg/day	1.00	1.67%
> 10 mg day	0.00	0.00%

rheumatoid arthritis flare. Noteworthy, the mRNA vaccines studies that were conducted excluded patients with rheumatic diseases who are on immunosuppressive therapy, therefore it is still unclear whether the mRNA covid vaccines might provoke flares of underlying rheumatologic diseases.

The purpose of our study is to assess whether rheumatoid arthritis patients who received the mRNA COVID-19 vaccine developed a flare of their disease.

Methods: We conducted a single-center retrospective study at the Louis Stokes Cleveland VA Medical Center. We included all patients with RA who are actively on immunosuppressive therapy and received the Pfizer vaccine. Those patients were contacted by phone and a survey questionnaire was used to collect data about their RA, immunosuppressive therapy, and development of symptoms post vaccinations. We included 60 patients in this abstract. Our primary end point was to calculate the percentage of any flare up of RA after COVID-19 vaccine. Secondary end points were to estimate the side effect profile from the vaccine among this population, to check if patients developed

Table 2. Questionnaire

Compliance to Medications		
Yes	54.00	98.18%
No	1.00	1.82%
Symptom control		
Good	49.00	81.67%
Fair	7.00	11.67%
Poorly Controlled	4.00	6.67%
Symptoms post vaccine		
Yes	17.00	28.33%
No	43.00	71.67%
Stopped Immunosuppressive Medications Before or after Vaccine		
Yes	5.00	9.09%
No	50.00	90.91%
Symptoms		
Fever	0.00	0.00%
Chills	1.00	1.67%
Sweating	1.00	1.67%
Arthralgias	2.00	3.33%
Joint swelling	1.00	1.67%
Joint erythema	0.00	0.00%
Myalgias	0.00	0.00%
Rash	1.00	1.67%
Fatigue	2.00	3.33%
Stiffness	1.00	1.67%
Sore arm	16.00	26.67%
headache	2.00	3.33%
Similarity of symptoms to flare		
Yes	1.00	1.67%
No	16.00	26.67%
ED visit required		
Yes	0.00	
No	17.00	
Rheumatology visit required		
Yes	0.00	
No	17.00	

a COVID infection after they received the vaccine, and to evaluate whether patients stopped their immunosuppressive medications around the time of the vaccine.

Results: Between 3/9/2021 and 5/27/2021, a total of 60 patients were contacted. One out of the sixty patients (1.67%) reported symptoms of RA flare up after taking the vaccine. Most common side effects in our patients were soreness over the injection site (26.27%), fatigue for one day (3.33%), headaches (3.33%) and arthralgias (3.33%), similar to what was reported in the general population. Most of the patients did not stop their immunosuppressive medications before or after the vaccine (90.91%). None of the patients developed COVID-19 infection following the vaccine up till the date of the phone call. Among our RA patients, one patient developed an RA exacerbation after the Pfizer COVID-19 vaccine administration. This patient had poor symptoms control before taking the vaccine however he had worsening of his symptoms following the second dose. Most of the patients had minimal side effects. The question remains as to whether COVID-19 vaccine would confer adequate immune protection in these patients with altered immune response either from underlying rheumatic disease or secondary to disease modifying agents. Some of the Limitations we faced were the small number of patients, and potential recall bias from phone surveys.

Conclusion: Rheumatoid arthritis patients receiving the COVID-19 Pfizer vaccine did not develop major symptoms, flares or side effects following the vaccine. The mRNA COVID vaccine was mostly safe and patients with RA are recommended to receive it. Further research with larger numbers of patients is needed to evaluate the safety and effectiveness of COVID-19 vaccine within patients with autoimmune rheumatic diseases.

Disclosure: S. Abi Doumeth, None; **L. Silversteyn**, None; **D. Anthony**, None; **M. Mattar**, None.

Abstract Number: 1604

Perceptions About COVID-19 Vaccination Among Patients with Rheumatic Diseases Enrolled in a National Patient Registry

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SESSION INFORMATION
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Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 vaccine confidence is key to promoting vaccination efforts to mitigate the spread of COVID-19 among people with rheumatic diseases. The goal of this study was to examine concerns and beliefs about COVID-19 vaccination among patients with rheumatic diseases enrolled in a national patient registry and to determine if education level is associated with COVID-19 vaccine confidence.

Methods: Members of the national ArthritisPower patient research registry were invited to complete an online survey. Vaccination confidence was evaluated using 1-item confidence scale from the validated 5C scale (range 1 = strongly disagree to 7 = strongly agree, higher values are better). Descriptive statistics summarized demographic characteristics, receipt of and concerns and beliefs about COVID-19 vaccination. Multiple regression assessed whether education is associated with vaccine confidence after adjusting for the effect of age, sex, and race and ethnicity (Model 1), age and sex (Model 2), and age (Model 3). Individuals who self-reported being Hispanic, non-Hispanic Black and non-Hispanic other race were grouped together as race and ethnic minority group.

Table 1. Characteristics of Survey Respondents Recruited from ArthritisPower Patient Registry

Variable	N=1,345)
Age, mean (SD), years	58.7 (11.5)
Gender, female	1156 (86.0%)
Education	
≥ 4-year college degree	756 (56.2%)
Some college or 2-year degree	470 (34.9%)
≤ High school	119 (8.85%)
Race and ethnicity	
Non-Hispanic white	1173 (87.2%)
Non-Hispanic Black	41 (3.0%)
Non-Hispanic other race	66 (5.0%)
Hispanic	55 (4.1%)
Occupation	
Healthcare worker, first responder, retail/food service, education worker	260 (19.3%)
Residence	
Rural	203 (15.1%)
Urban	1102 (81.9%)
Region	
Northeast	150 (11.2%)
South	279 (20.8%)
Midwest	299 (22.4%)
Southwest	150 (11.2%)
West	357 (26.5%)
Flu vaccine receipt, 2019-2020	1082 (80.4%)

Frequencies and percentages are shown, unless otherwise noted.

Table 2. Receipt of COVID-19 Vaccine and Vaccine Concerns and Beliefs Among Survey Respondents Recruited from Arthritis Power Patient Registry

Variable	N= 1,345
Offered COVID-19 vaccine	728 (54.1%)
No COVID-19 vaccine receipt	781 (58.1%)
Very unlikely/unlikely to get vaccinated	138 (17.7%)
Reasons for not getting vaccinated among unvaccinated members	
Use of immunosuppressive medications	159 (51.5%)
Concerns of disease flares	157 (50.8%)
Fear of side effects	97 (31.4%)
Prior reactions to other vaccines	66 (21.4%)
Fear of vaccine modifying their DNA	49 (15.9%)
Key information needs during ongoing deliberation about COVID-19	
Long-term efficacy	196 (63.4%)
Side effects of the vaccine in "people like me"	194 (62.8%)
Efficacy among "people like me"	161 (52.1%)
Desire to talk to my doctor	79 (25.6%)
COVID-19 Vaccine beliefs, mean (SD)	
"I am completely confident that the COVID-19 vaccine is safe" (confidence)	5.2 (2.01)
"COVID-19 vaccination is unnecessary because COVID-19 is not common anymore" (complacency)	1.5 (1.1)
"COVID-19 is not so severe that I should get vaccinated" (complacency)	1.7 (1.5)
"Everyday stress prevents me from getting vaccinated with the covid-19 vaccine" (complacency)	1.5 (1.2)
"When I think about getting the COVID-19 vaccine, I weigh benefits and risks to make the best decision possible" (calculation)	6.2 (1.5)
"Getting the COVID-19 vaccine is important because I can help protect other people from getting infected" (collective responsibility)	6.0 (1.7)

Frequencies and percentages are shown, unless otherwise noted. Vaccine beliefs scales range from 1 (strongly disagree to 7 strongly agree); higher scores are better for confidence, calculation, and collective responsibility measures and lower scores are better for complacency and constraints measures.

Results: Between February 9 and March 24, 2021, we received 1345 responses. Mean (standard deviation) age was 59 (11.5) years, 86% were female, 87% were non-Hispanic white (**Table 1**). While 54% stated they had been offered a COVID-19 vaccine, only 42% had received at least one dose of the vaccine (**Table 2**). Among those unvaccinated,

Table 3. Multiple Regression Analysis for Association between Levels of Education and COVID-19 Vaccine Confidence Among Survey Respondents Recruited from ArthritisPower Patient Registry

	Model 1			Model 2			Model 3		
Variable	Estimate	95% CI	p	Estimate	95% CI	p	Estimate	95% CI	p
Age	0.008	-0.002, 0.017	0.10	0.009	0.0001, 0.018	0.05	0.009	0.0003, 0.019	.04
Female (vs. Male)	-1.573	-4.304, 1.157	0.25	-1.496	-4.220, 1.228	0.28	NA	NA	NA
Non-Hispanic white (vs Race and ethnic minority group)	0.238	-0.090, 0.567	0.15	NA	NA	NA	NA	NA	NA
High school or less (vs ≥ 4-year college degree)	-1.261	-1.645, -0.876	<0.01	-1.282	-1.662, -0.903	<0.01	-1.279	-1.659, -0.900	<0.01
Some college or 2-year degree (vs ≥ 4-year college degree)	-0.772	-0.999, -0.544	<0.01	-0.773	-0.999, -0.547	<0.01	-0.784	-1.010, 0.558	<0.01

CI, confidence interval

almost 18% said they were unlikely to get vaccinated. The most common reasons for not getting the vaccine were use of immunosuppressive medications (52%), concerns of disease flare (51%), fear of side effects (31%), prior reactions to other vaccines (21%), fears about the vaccine modifying one's DNA (16%). While deliberating about vaccination, the following information was thought to be important: long-term efficacy of the vaccine (63%), side effects of the vaccine (63%) and its efficacy (52%) among people with the same health condition as the respondent. Compared to vaccinated people, unvaccinated persons had significantly lower scores on the confidence scales [6.3 (1.2) vs 4.5 (2.2), $p< 0.01$]. After controlling for age, sex, and race, lower level of education was associated with lower vaccine confidence (**Table 3**).

Conclusion: During the initial COVID-19 vaccine roll out, a substantial minority of patient members of a large national patient registry had received COVID-19 vaccination. Approximately 1 in 10 said they were unlikely to get vaccinated, even among this highly engaged and research-interested patient population. The main reasons for not getting the vaccine were use of immunosuppressive medications and concerns about a disease flare. Respondents felt they needed more information about the safety and efficacy of the COVID-19 vaccine among people with their conditions. Lower education level was associated with lower vaccine confidence. These findings highlight the need for developing COVID-19 vaccination campaigns that are tailored to different levels of education for people with rheumatic diseases.

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Abstract Number: 1605

Health Related Quality of Life in Rheumatology Outpatients with COVID-19 from New York City over the Course of the Pandemic

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SESSION INFORMATION
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Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The impact of the COVID-19 pandemic on the mental and physical well-being of patients with systemic rheumatic diseases (SRDs) remains to be quantified. We assembled a cohort of Rheumatology outpatients with history of COVID-19 and compared HRQOL in patients with and without SRD over the course of the pandemic.

Methods: Between April 24, 2020 and May 26, 2020 we emailed a secure web-based survey to 26,045 patients ≥age 18 evaluated by a rheumatologist at a specialty hospital in New York City. A follow-up survey was sent in March 2021.SRD and non-SRD patients had relevant ICD-10-CM codes on ≥ 2 visits at least 7 days apart. Patients with an SRD code at only 1 visit were excluded. Non-SRD patients also had no SRD ICD-10-CM code. In this analysis, we included patients diagnosed with COVID-19 by a positive SARS-CoV-2 PCR or antigen test, or who were told by a medical provider they likely had COVID-19. The latter was included because in early 2020 SARS-CoV-2 tests were not readily available. Patients self-reported demographics on the first survey, and select PROMIS-29 domains at both time points. We used paired T-tests to compare within person change, and T-tests and Chi-Square to compare differences between groups.

Table 1. Baseline Characteristics of Rheumatology Outpatients with COVID-19, Stratified by Systemic Rheumatic Disease (SRD) Status

	All Patients with COVID-19 N=354	SRD With COVID-19 N=189	Non-SRD With COVID-19 N=105	p-values
Sociodemographic Factors				
Age (years), Mean (SD)	53.5 (14.8)	53.3 (13.8)	55.1 (16.0)	0.31
BMI kg/m², Mean (SD)	27.5 (13.1)	28.7 (16.9)	25.4 (5.1)	0.052
Female	291 (82.2)	162 (85.7)	84 (80)	0.2
Race, N (%)				0.038
White	282 (79.7)	144 (76.2)	86 (81.9)	
Non-white	58 (16.4)	39 (20.6)	11 (10.5)	
Ethnicity, N (%)				0.52
Hispanic or Latinx	43 (12.1)	23 (12.2)	15 (14.3)	
Not Hispanic or Latinx	304 (85.9)	164 (86.8)	85 (81)	
Patient declined/Unknown	6 (1.7)	2 (1.1)	4 (3.8)	
Marital Status, N (%)				0.21
Married or partnered	229 (64.7)	124 (65.6)	61 (58.1)	
Single	122 (34.5)	64 (33.9)	43 (41)	
Unknown	41 (11.6)	19 (10.1)	18 (17.1)	
Household Income (Jan 1, 2020), N (%)				0.44
≤150,000	236 (43.2)	90 (47.6)	44 (41.9)	
>$150,000	149 (42.1)	75 (39.7)	45 (42.9)	
Unknown	52 (14.7)	24 (12.7)	16 (15.2)	
Education Level, N (%)				0.35
≤ Highschool	60 (16.9)	35 (18.5)	15 (14.3)	
College graduate and/or higher	294 (83.1)	154 (81.5)	90 (85.7)	
Chronic Active Steroids, N (%)	47 (13.3)	34 (18)	3 (2.9)	p<0.0001

Values are reported as n (%) or mean (sd)

Table 2. PROMIS-29 Domains Measured in Rheumatology Outpatients with COVID-19 in April-May 2020, Overall and by SRD Status

PROMIS Score	All Patients with COVID-19 N=354	SRD With COVID-19 N=189	Non-SRD With COVID-19 N=105	p-values
Anxiety T-Score (SD)	58.5 (10.2)	58.8 (9.7)	57.9 (11.2)	0.49
Depression T-Score(SD)	52 (9.2)	52.5 (8.8)	51.8 (9.5)	0.53
Fatigue T-Score(SD)	54.5 (11.4)	55.6 (11)	52.9 (12.1)	0.06
Sleep T-Score(SD)	53.1 (7.2)	53.7 (6.9)	52.8 (7.1)	0.29
Pain T-Score(SD)	54.7 (10.6)	56.1 (10.3)	52.1 (10.4)	0.002
T-score: higher= more of the domain; 50 is the population mean				

Table 3. Mean Within-Person Differences in PROMIS T-Scores Between April/May 2020 and March 2021, Overall and by SRD Status

PROMIS Score	All Patients with COVID-19 N=100	SRD with COVID-19 N=57	Non-SRD with COVID-19 N=32	p-value
Anxiety T-Score(SD)	-2.7 (9.4)	0.7 (9.5)	-1.7 (7.7)	0.19
Depression T-Score(SD)	0.2 (8.9)	0.8 (2)	-0.7 (8.2)	0.32
Fatigue T-Score(SD)	2.5 (10.7)	4.6 (9)	0.4 (7.6)	**0.02**
Sleep T-Score(SD)	-0.7 (9.9)	4 (12.2)	-0.1 (10.5)	0.1
Pain T-Score(SD)	3.3 (8.8)	0.6 (0.9)	2.1 (8.6)	0.33

Results: Of 6584 (25.3%) patients responding to the PROMIS-29 on the first survey, 354 subjects reported having COVID-19; of those 189 met SRD and 105 met non-SRD criteria. SRD and non-SRD patients were of similar age (53.3 vs. 55.1 years), percent female (85.7% vs 80%), and body mass index (28.7 vs. 25.4). Patients with SRD were more likely to be White (76.2% vs. 81.9%; p=0.038) and be on chronic active corticosteroids (18% vs 2.9%; p< 0.0001). Overall, 17.5% went to an emergency room, though few were hospitalized (6.9% SRD vs. 4.8% non-SRD, p=0.47) . At baseline, SRD and non-SRD patients had similar PROMIS-29 T-scores except SRD had worse pain (Table 1). Of 100 subjects reporting PROMIS-29 at both time points, within-person changes for the fatigue domain indicated worsening only in SRD (T-score difference of 4.6; p= 0.02). 44% of SRD subjects compared with only 28% of non-SRD subjects reported clinically meaningful (T-score >=5) worse fatigue at follow up; p< 0.028). There was no significant association between clinically meaningfully worse fatigue at follow up and use of chronic active corticosteroids, going to the ER, or being hospitalized (data not shown).

Conclusion: Although all subjects with a history of COVID-19 had similar PROMIS-29 scores at baseline, subjects with SRD were 1.6 x more likely to report clinically meaningful worsening of fatigue nearly 1 year after COVID-19 diagnosis, compared to non-SRD patients followed at the same Rheumatology practice. Analysis is ongoing to identify predictors of poor HRQOL after COVD-19 in patients with SRD.

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Abstract Number: 1606

Telemedicine for Rheumatology Care During the COVID-19 Pandemic: Patient Perceptions and Preferences

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic disrupted the delivery of medical care and resulted in a substantial uptake in telemedicine care for patients with chronic conditions, including autoimmune rheumatic diseases. The objective of this study was to assess perceptions and preferences about telemedicine among patients with autoimmune rheumatic diseases during the COVID-19 pandemic.

Methods: We conducted an online survey among members of ArthritisPower and Vasculitis Patient Powered Research Network online patient registries and members of the following patient organizations: Myositis Support and

Table 1. Respondents' demographic and clinical characteristics by type of telemedicine visit

Characteristic	All Participants	Video Telemedicine Visit	Phone Telemedicine Visit	No Telemedicine Visit	p-value (Telemedicine yes vs no)
	N=819	N = 303	N = 146	N=370	
Age, years	58.6 (11.6)	56.7 (12.6)	59.8 (10.6)	59.7 (10.8)	**0.01**
Female	702 (85.7)	264 (87.1)	122 (83.6)	316 (85.4)	0.82
Caucasian	759 (92.7)	278 (91.8)	136 (93.2)	345 (93.2)	0.57
Hispanic	37 (4.5)	11 (3.6)	4 (2.7)	22 (6.0)	0.07
Rural residence	99 (13.2)	28 (9.8)	16 (13.8)	55 (15.9)	**0.05**
Autoimmune condition					
Rheumatoid arthritis	353 (43.1)	128 (42.2)	59 (40.4)	166 (44.9)	0.35
ANCA-associated vasculitis	115 (14.0)	47 (15.5)	26 (17.8)	42 (11.4)	**0.04**
Psoriatic arthritis	108 (13.2)	32 (10.6)	21 (14.4)	55 (14.9)	0.20
Ankylosing spondylitis	66 (8.1)	26 (8.6)	9 (6.2)	31 (8.4)	0.76
Other autoimmune rheumatic disease*	54 (6.6)	16 (5.3)	10 (6.9)	28 (7.6)	0.31
Other vasculitis or relapsing polytonicities	54 (6.6)	24 (7.9)	10 (6.9)	20 (5.4)	0.21
Lupus	38 (4.6)	16 (5.3)	6 (4.1)	16 (4.3)	0.70
Myositis	31 (3.8)	14 (4.6)	5 (3.4)	12 (3.2)	0.46
Medications					
Biologic DMARD	385 (47.0)	153 (50.5)	71 (48.6)	161 (43.5)	0.07
Janus kinase inhibitor	70 (8.6)	24 (7.9)	11 (7.5)	35 (9.5)	0.40
Methotrexate	250 (30.5)	101 (33.3)	52 (35.6)	97 (26.2)	**0.02**
Hydroxychloroquine	195 (23.8)	77 (25.4)	36 (24.7)	82 (22.2)	0.32
Glucocorticoids	241 (29.4)	101 (33.3)	47 (32.2)	93 (25.1)	**0.01**
NSAIDS	285 (34.8)	103 (34.0)	52 (35.6)	130 (35.1)	0.85
Comorbidities					
Hypertension	354 (43.2)	136 (44.9)	69 (47.3)	149 (40.3)	0.12
Lung disease**	399 (36.5)	111 (36.6)	52 (35.6)	136 (36.8)	0.90
Diabetes mellitus	101 (12.3)	41 (13.5)	14 (9.6)	46 (12.4)	0.95
Kidney disease	81 (9.9)	28 (9.2)	20 (13.7)	33 (8.9)	0.40
Heart disease	72 (8.8)	21 (6.9)	12 (8.2)	39 (10.5)	0.11
Current smoking	60 (7.3)	21 (6.9)	6 (4.1)	33 (8.9)	0.11
Malignancy	17 (2.1)	5 (1.7)	3 (2.1)	9 (2.4)	0.52
PROMIS Anxiety, T-score***	58.2 (8.8)	58.9 (8.2)	58.1 (9.0)	57.6 (9.1)	0.06

Number (%) and mean +/- standard deviation shown. Urban status shown among participants with available zip code. Statistically significant differences between characteristics of those who had a telemedicine visit vs those who did not are denoted in bold font. *Other rheumatic diseases include anti-phospholipid antibody syndrome, anti-glomerular basement membrane antibody disease, juvenile idiopathic arthritis, mixed connective tissue disease, psoriasis, sarcoidosis, scleroderma, Sjogren's syndrome; **Lung disease includes asthma, emphysema, chronic obstructive pulmonary disease, pulmonary hypertension, other chronic lung disease; *** PROMIS Anxiety short form with range of 1-100, U.S. adult population mean=50 and standard deviation=10. DMARD, disease modifying anti-rheumatic drug; NSAIDs, nonsteroidal anti-inflammatory drugs.

Understanding, Lupus and Allied Disease Association, American Bone Health, and International Foundation for Autoimmune & Autoinflammatory Arthritis. Attitudes about telemedicine (i.e., telemedicine acceptability) were evaluated using the validated telemedicine perception questionnaire (TMPQ). The TMPQ score (range 17 to 85) was calculated; higher scores show higher acceptability. Visit satisfaction was measured using the one question scale from the validated Agency for Healthcare Research and Quality Consumer Assessment of Healthcare Providers and Systems (CAHPS)® survey (0-10 scale, 0 represents worst possible visit, 10 represents best possible visit). T-tests and multivariable linear regression compared the satisfaction and TMPQ scores between respondents who reported participating in video and phone-only visits. Chi-square tests compared preferences for telemedicine visits for specific clinical scenarios between those who had telemedicine visit versus those who had not.

Results: Between June 18 and August 10, 2020, we received 819 responses. Participants had a mean (SD) age of 58.6 (11.6) years and were mostly white (n= 759, 92.7%) and female (n=702, 85.7%). Of 618 participants who said that telemedicine was available to them, 449 (72.7%) reported having a telemedicine visit, with 303 (67.5%) reporting at least one telemedicine video visit; the remainder had a phone-only visit (**Table 1**). On a 0-10 scale, the mean (standard deviation) visit satisfaction score for telemedicine visits was 7.3 (1.8) with 25.8% being very satisfied (score 9 or 10). The mean (SD) telemedicine acceptability as assessed by TMPQ score was 62.8 (10.7). Video visits and higher TMPQ score were associated with higher satisfaction (data not shown). Preference for a telemedicine visit varied

Figure 1. Preference for telemedicine versus in-office visits among all survey respondents by reason for visit (N=819).

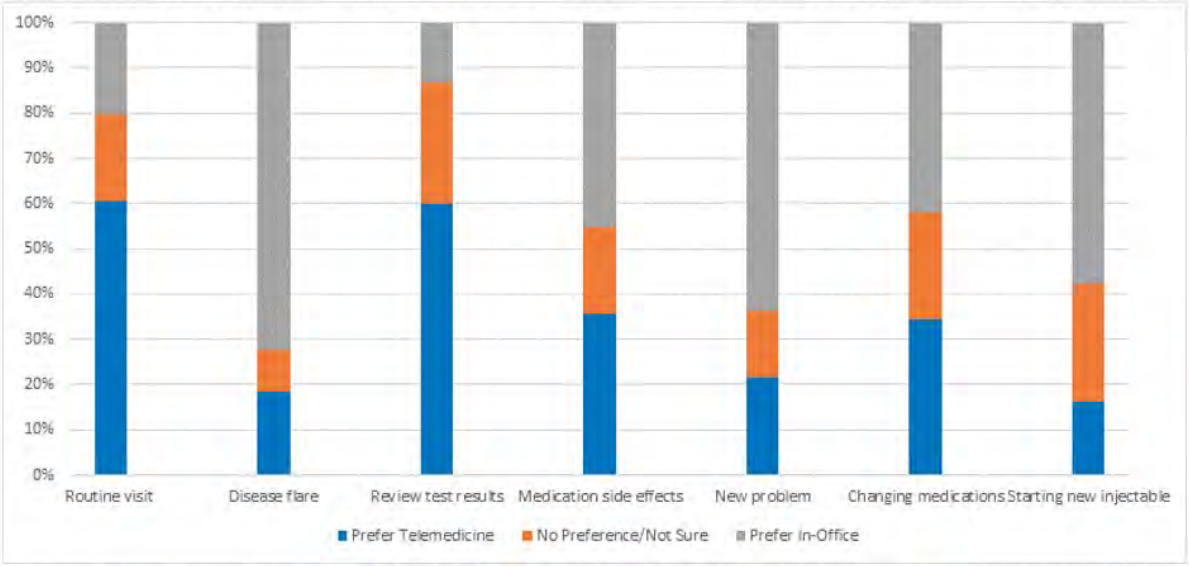

Table 2. Preference for telemedicine visit for different visit reasons by prior experience with telemedicine (N=819)

Reason for clinic visit	All (N=819)	Had a Telemedicine Visit (N=449)	Didn't have a Telemedicine Visit (N=370)	p-value*
Routine care	495 (60.4)	331 (73.7)	164 (44.3)	**<0.001**
Disease flare	150 (18.3)	79 (17.6)	71 (19.2)	0.56
Review of test results	490 (59.8)	291 (64.8)	199 (53.8)	**<0.001**
Medication side effects	293 (35.8)	169 (37.6)	124 (33.5)	0.22
New problem	176 (21.5)	101 (22.5)	75 (20.3)	0.44
Medication change	281 (34.3)	182 (40.5)	99 (26.8)	**<0.001**
Start a new injectable medication	132 (16.1)	85 (18.9)	47 (12.7)	**0.02**

*Statistically significant differences between characteristics of those who had a telemedicine visit vs those who did not are denoted in bold font.

substantially by reasons for the visit (**Figure 1**). Compared to those who had not yet had a telemedicine visit, patients who had experienced telemedicine were more likely to prefer telemedicine for routine visits (73.7% vs 44.3%, p< 0.001), reviewing test results (64.8% vs 53.8%, p< 0.001), when considering changing medications (40.5% vs. 26.8%; p< 0.001), and when starting a new injectable medication (18.9% vs. 12.7%; p=0.02) (**Table 2**).

Conclusion: During the COVID-19 pandemic, patients with autoimmune rheumatic diseases frequently had telemedicine visits, the majority via video, and were often satisfied with these visits. These results suggest that because such patients prefer telemedicine for certain types of visits, maximizing effective use of telemedicine should take into consideration specific clinical scenarios and patient preferences.

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Abstract Number: 1607

The Impact of Health Literacy and Numeracy on COVID-19 Vaccine Hesitancy in SLE

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SESSION INFORMATION
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Background/Purpose: The ACR has issued guidance recommending COVID-19 vaccine for all patients with rheumatic diseases. Vaccine hesitancy research prior to the COVID-19 pandemic has demonstrated associations between health literacy and vaccine hesitancy. In this study, we assessed the relationship between SLE patients' desire to receive a COVID-19 vaccine and their health literacy/numeracy.

Methods: Health literacy was assessed by the Newest Vital Sign (NVS); NVS < 4 denotes limited health literacy. Numeracy was assessed with the Subjective Numeracy Scale (SNS-3); SNS-3 ≤12 was considered to be low numeracy. The Vaccine Hesitancy Scale (VHS) was modified to assess adult vaccine beliefs, with additional questions specific to the COVID-19 vaccine and patients' self-assessed COVID-19 risk. The survey also asked whether patients would choose to get the COVID-19 vaccine if it were made available to them the following week (definitely/probably vs probably not/definitely not). The survey was distributed by email on 02/24/2021 to the 353 patients in the Duke Lupus Registry, all of whom met ACR or SLICC criteria for SLE. Linear regression models adjusted for education estimated the associations of health literacy and numeracy on the desire to receive the COVID-19 vaccine.

Table 1. Study population

	Overall	Adequate health literacy	Limited health literacy		Adequate numeracy	Limited numeracy	
	n=63	n=29	n=9	p	n=43	n=14	p
Wants the vaccine	60 (95%)	28 (97%)	9 (100%)	1.0	41 (95%)	13 (93%)	1.0
Mean age (SD)	52.8 (13.4)	52.6 (14.1)	58.7 (10.2)	0.2	52.6 (14.0)	51.9 (12.0)	0.9
Mean length of disease	17.1 (9.6)	16.5 (9.2)	23.6 (12.5)	0.1	16.2 (9.4)	20.1 (10.0)	0.2
% Female	62 (98%)	28 (97%)	9 (100%)	1.0	42 (98%)	14 (100%)	1.0
Black	28 (44%)	9 (31%)	5 (56%)	0.2	20 (47%)	7 (50%)	1.0
College education	43 (68%)	**24 (83%)**	**4 (44%)**	**0.04**	30 (70%)	8 (57%)	0.5
Medicare, Medicaid, uninsured	33 (52%)	**13 (45%)**	**8 (89%)**	**0.03**	21 (49%)	10 (71%)	0.2
Income <$50,000 (n=60)	26 (43%)	12 (43%)	5 (63%)	0.4	18 (44%)	7 (50%)	0.8
Political Party				0.7			0.5
Democratic	27 (48%)	10 (36%)	4 (57%)	0.4	21 (53%)	5 (45%)	0.7
Republican	7 (13%)	5 (18%)	1 (14%)		3 (8%)	2 (18%)	
Independent	22 (39%)	13 (46%)	2 (29%)		16 (40%)	4 (36%)	
Other party	0 (0%)	0 (0%)	0 (0%)		0 (0%)	0 (0%)	
Missing	7	1	2				

Table 2. Associations between literacy and vaccine beliefs

	Adequate health literacy	Limited health literacy		β (95% CI)	Adj β (95% CI)*
	n=29	n=9	p		
Efficacy	1.7 (0.8)	1.6 (0.4)	0.6	0.11 (-0.44, 0.67)	0.08 (-0.52, 0.68)
Safety	2.6 (0.7)	3.0 (0.5)	0.1	-0.39 (-0.90, 0.13)	-0.36 (-0.92, 0.19)
Vaccines cause autism (G)	**1.8 (0.9)**	**2.4 (0.9)**	**0.05**	**-0.69 (-1.35, -0.03)**	**-0.45 (-1.12, 0.23)**
New vaccines are riskier (VHS)	3.0 (1.2)	3.4 (0.7)	0.4	-0.38 (-1.25, 0.50)	-0.37 (-1.33, 0.59)
Serious adverse effects (VHS)	3.1 (1.3)	3.6 (0.7)	0.3	-0.45 (-1.35, 0.45)	-0.65 (-1.60, 0.30)
Get COVID-19 from vaccine	**1.7 (1.1)**	**2.6 (1.3)**	**0.05**	**-0.87 (-1.69, -0.04)**	**-1.06 (-1.03, -0.19)**
COVID-19 symptoms from vaccine	2.9 (1.3)	2.8 (1.4)	0.8	0.12 (-0.87, 1.11)	0.22 (-0.84, 1.28)
Not tested in lupus	2.2 (1.2)	2.8 (1.3)	0.2	-0.54 (-1.40, 0.33)	-0.54 (-1.47, 0.39)
Could flare lupus	2.7 (1.4)	2.9 (1.5)	0.8	-0.15 (-1.20, 0.90)	-0.26 (-1.36, 0.84)
RNA/DNA risks	2.5 (1.1)	3.0 (0.9)	0.2	-0.50 (-1.25, 0.25)	-0.28 (-1.09, 0.53)
Bad experiences with vaccines	2.8 (1.3)	2.2 (1.2)	0.3	0.54 (-0.41, 1.48)	0.66 (-0.35, 1.68)
COVID-19 vaccine experimental	2.3 (1.3)	3.0 (1.2)	0.1	-0.82 (-1.65, 0.20)	-0.75 (-1.74, 0.25)
COVID-19 vaccine rushed	**2.7 (1.3)**	**3.7 (0.7)**	**0.05**	**-0.95 (-1.84, -0.06)**	**-1.13 (-2.07, -0.18)**
Safe in pregnancy/ breastfeeding	2.9 (0.7)	3.4 (0.9)	0.06	-0.55 (-1.08, -0.02)	-0.35 (-0.89, 0.19)
Safe for children	3.2 (0.8)	3.1 (0.8)	0.7	0.10 (-0.47, 0.66)	0.30 (-0.28, 0.88)
Personal Risk	2.1 (0.4)	2.2 (0.6)	0.8	-0.06 (-0.37, 0.26)	-0.04 (-0.38, 0.29)
Family Risk	1.8 (0.8)	1.7 (0.6)	0.6	0.12 (-0.45, 0.70)	0.25 (-0.36, 0.96)
Trust	1.8 (0.8)	1.9 (0.4)	0.8	-0.06 (-0.60, 0.47)	-0.14 (-0.71, 0.44)
Logistics	1.9 (0.6)	2.0 (0.5)	0.6	-0.10 (-0.53, 0.33)	-0.16 (-0.62, 0.30)
VHS	2.0 (0.7)	2.0 (0.3)	1.0	-0.002 (-0.49, 0.48)	-0.02 (-0.54, 0.50)

Results: A total of 63 patients who completed the COVID-19 vaccine had recently completed an assessment of health literacy or numeracy: 38 patients had completed the NVS, 57 had completed the SNS-3, and 32 had completed both. Overall, 98% of respondents were female, 56% White, and 68% college educated (Table 1). Patients with adequate health literacy were more likely to be college educated (p=0.04), and patients with limited health literacy were more likely to lack private health insurance (p=0.03); these associations were not seen for numeracy.

Importantly, 60 out of 63 SLE patients (95%) wanted to receive the COVID-19 vaccine as soon as possible. Adequate and limited literacy patients had similar VHS scores and were similar on most sub-scales, although there was a trend

Table 3. Associations between numeracy and vaccine beliefs

	High numeracy	Low numeracy		β (95% CI)	Adj β (95% CI)*
	n=43	n=14	p		
Efficacy	1.5 (0.5)	1.8 (0.8)	0.2	-0.31 (-0.66, 0.04)	-0.27 (-0.64, 0.06)
Safety	2.6 (0.7)	2.9 (0.8)	0.3	-0.25 (-0.69, 0.19)	-0.20 (-0.63, 0.22)
Personal Risk	2.1 (0.4)	2.2 (0.6)	0.4	-0.14 (-0.41, 0.13)	-0.12 (-0.39, 0.15)
Family Risk	1.7 (0.6)	2.4 (1.3)	0.07	-0.72 (-1.22, -0.22)	-0.68 (-1.17, -0.18)
Family member is high-risk for COVID-19	**2.0 (1.2)**	**2.9 (1.6)**	**0.04**	**-0.88 (-1.66, -0.09)**	**-0.83 (-1.60, -0.07)**
I want to protect a family member from COVID-19	1.4 (0.6)	2.0 (1.5)	0.2	-0.60 (-1.14, -0.07)	-0.59 (-1.12, -0.05)
Trust	1.7 (0.6)	2.1 (1.0)	0.2	-0.41 (-0.85, 0.04)	-0.40 (-0.85, 0.05)
Logistics	1.8 (0.5)	1.9 (0.6)	0.5	-0.12 (-0.45, 0.21)	-0.14 (-0.47, 0.19)
VHS	1.8 (0.5)	2.1 (0.7)	0.2	-0.29 (-0.62, 0.04)	-0.27 (-0.60, 0.06)

*adjusted for education

toward more hesitancy in the low literacy group for the Safety sub-scale (Table 2). Within this sub-scale, even after adjusting for education, limited literacy patients were more likely to express fear of vaccines causing autism (p=0.05), fear of getting COVID-19 from the vaccine (p=0.05), and fear that the COVID-19 vaccine was rushed (p=0.05). Limited numeracy patients were less likely to agree with having a family member who is high-risk for COVID-19, although their assessment of personal risk for severe COVID-19 was similar to adequate numeracy patients (Table 3).

Conclusion: The vast majority of SLE respondents wanted to receive the vaccine, regardless of health literacy and numeracy status. Patients with limited health literacy were more likely to believe vaccine falsehoods, including concerned that vaccines cause autism, that they could get COVID-19 from the vaccine, and that the COVID-19 vaccine was rushed; such patients may be more susceptible to vaccine conspiracy theories.

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Abstract Number: 1608

Sources of Information About SARS-CoV-2 Used by Patients with Chronic Inflammatory Rheumatic Diseases (CIRD)

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Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with chronic inflammatory rheumatic diseases (CIRD) may be at increased risk of Corona Virus Disease 2019 (COVID-19).1 The quality of information obtained plays a crucial role for patients' decision to be vaccinated. Knowing patients' needs for information and which sources are used is important for the management of CIRD patients by rheumatologists and other physicians.

Table 1. Sociodemographic and disease characteristics

Age (years)	54.7 ± 12.8
Women, No.* (%)	315 (61.3%)
Educational level, No.* (%)	
< 8 years	50 (10.4 %)
8-12 years	275 (57.4 %)
>12 years	154 (32.2 %)
Occupation, No.* (%)	
Full time	198 (38.5 %)
Pensioner	157 (30.5 %)
Part-time	80 (15.6 %)
Housewife/husband	37 (7.2 %)
Occupational incapacity	29 (5.6 %)
In training	7 (1.4 %)
Healthcare	5 (1 %)
CIRD, No.* (%)	
Rheumatoid arthritis	192 (37.3 %)
Axial spondyloarthritis	134 (26.1 %)
Connective tissue disease and vasculitis	106 (22.6 %)
Psoriatic arthritis	72 (14.0 %)
Disease duration, mean (years)	9.8 ± 8.9
Therapy, No.* (%)	
bDMARD	316(61.5 %)
csDMARD	147(28.6 %)
tsDMARD	33 (6.4 %)
no DMARDs	18 (3.5 %)

*number of patients

Table 2. Correlation between age/education level and the information sources regarding SARS-CoV-2

	Kendall's tau-b Correlation Coefficient	Significance	No.*
Age			
Television	0.119	0.005**	511
Radio	-0.103	0.015**	511
Newspaper	0.132	0.002**	511
Search engine	-0.235	0.000**	511
Public health authority	-0.218	0.000**	511
Online news	-0.173	0.000**	509
Social networks	-0.095	0.025***	509
Others	-0.143	0.001**	509
Education level			
Television	-0.129	0.004**	477
Public health authority	0.264	0.000**	475
Online news	0.138	0.002**	475
Health websites	0.089	0.046***	475
Wikipedia	0.089	0.046***	475

*number of patients
** correlation is significant at the 0.01 level (2-tailed)
***correlation is significant at the 0.05 level (1-tailed)

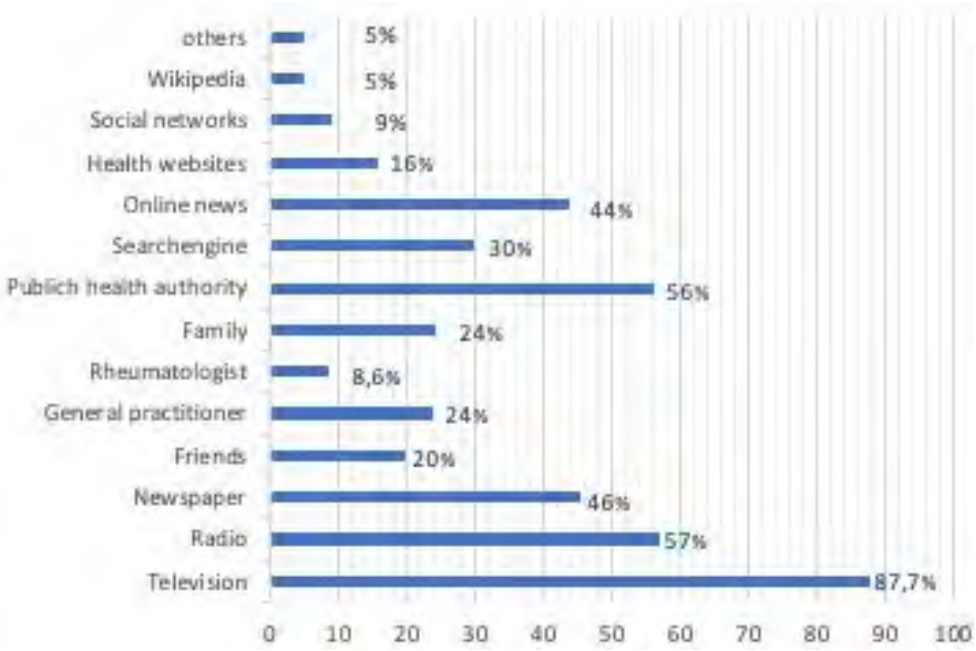

Figure 1. Sources of information of CIRD patients about SARS-CoV-2.

To identify main sources of information on SARS-CoV-2 used by patients with CIRD and to analyze their influence on opinions and willingness to be vaccinated.

Methods: CIRD patients presenting to our tertiary rheumatology hospital were, after informed consent, consecutively included in the study once the vaccination campaign in Germany had started, to fill out a questionnaire. Next to sociodemographic and disease-specific data, vaccination willingness and knowledge regarding SARS-CoV-2 were assessed. Furthermore, patients' sources of information and their concerns about accuracy of information were evaluated. A numerical rating scale (NRS) ranging from 0 (completely disagree) to 10 (completely agree) was used. Values between ³7 were taken as positive answer. Nonparametric tests and multivariate linear regression analyses were performed.

Results: In early 2021, a total of 514 patients were interviewed (table 1). The majority (63.9 %) reported to be well-informed (NRS ³7), whereas 18% had doubts regarding information on SARS-CoV-2. The most often used source of information was television, and only 8.6% reported to have been informed by a rheumatologist (figure 1). About 20% of patients were no longer interested in receiving any information on SARS-CoV-2 through media. Information from rheumatologists, general practitioners, public health authorities or health related web sites did not reach 30.5% of patients. Of interest, 16% of subjectively well-informed patients were hesitant towards vaccination. As many as 43.6% of patients with doubts regarding information about SARS-CoV-2 indicated that they were not willing to be vaccinated. No source of information showed a strong correlation with SARS-CoV-2 vaccination willingness or with knowledge on SARS-CoV-2. Weak positive correlations were found between age and education level on the one hand and information sources about SARS-CoV-2 on the other hand (table 2). A weak negative correlation was found between doubts about information and health authorities, whereas positive correlations were found with social networks, friends and family.

Conclusion: Most CIRD patients think that they are well-informed about SARS-CoV-2. However, their information rarely comes from expert-based sources and rarely from rheumatologists. Thus, there is an unmet need for CIRD patients to receive appropriate and comprehensive information about SARS-CoV-2, its influence on rheumatic diseases, and about vaccination of patients with CIRD.

Reference

1. Strangfeld A et al. Ann Rheum Dis 2021

Disclosure: I. Andreica, None; **I. Roman**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmith-Kline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5.

Abstract Number: 1609

SARS-CoV-2 Vaccination Willingness and Its Predictors in Patients with Chronic Inflammatory Rheumatic Diseases (CIRD)

Iulia Roman, Ioana Andreica, Xenofon Baraliakos, Uta Kiltz and Juergen Braun, Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Whether patients with chronic rheumatic diseases (CIRD) are at increased risk of developing severe COVID 19 infections is not entirely clear. However, some DMARDs seem to be associated with worse outcomes. Out of this perspective vaccination protection should be sought for all CIRD patients. Recent surveys showed in CIRD patients an alarming degree of vaccine hesitancy[1]. Strategies should be developed to increase the vaccination rates in patients with CIRD.

To identify sociodemographic, patient and disease specific predictors of vaccine willingness in CIRD patients and to compare these with a control group.

Methods: Using a cross-sectional study design, a survey was conducted to assess vaccination willingness of consecutive CIRD patients and controls without CIRD presenting to our tertiary rheumatology hospital. In addition to sociodemographic data, patient and disease characteristics including comorbidities and therapy were recorded. A numerical rating scale was used to measure vaccination willingness (0: fully disagree; 10: fully agree). Definite willingness to be vaccinated was assumed if ³7 was selected. Nonparametric tests and multivariate linear regression were performed where appropriate.

Results: A total of 514 CIRD patients and 100 controls were prospectively included (table 1). No significant differences were found regarding the definite vaccination willingness (79.6% vs. 76%) in CIRD vs. control patients. In the CIRD group, the willingness to be vaccinated against SARS-CoV-2 showed a moderate positive correlation with the level of information on influenza and pneumococci as well as a history of travel vaccination (table 2); this was not the case in the control group.

Table 1. Patients and disease characteristics

	CIRD	Control group
Age, mean (years)	54.7 ± 12.8	55.6 ± 9.8
Women, No*. (%)	315 (61.3%)	83 (83.0%)
BMI**, mean	27.9 ± 5.9	30.4 ± 7.8
Disease duration, mean (years)	9.8 ± 8.9	4.05 ± 6.5
Educational level, No.* (%)		
< 8 years	50 (10.4 %)	9 (9.3%)
8-12 years	275 (57.4 %)	67 (69.1%)
>12 years	154 (32.2 %)	21 (21.6%)
CIRD, No.* (%)		
Rheumatoid arthritis	192 (37.3 %)	
Axial spondyloarthritis	134 (26.0 %)	
Psoriatic arthritis	72 (14.0 %)	
Connective tissue disease and vasculitis	106 (22.6 %)	
Therapy, No.* (%)		
bDMARD	316 (61.5 %)	
csDMARD	147 (28.6 %)	
tsDMARD	33 (6.4 %)	
no DMARDs	18 (3.5 %)	

*number of patients
**body mass index

Table 2. Correlation between vaccination willingness and predictor factors

	CIRD			Control group		
	tau-b****	Significance	No.*	tau-b****	Significance	No.*
Travel vaccination	0.131	0.002**	485	0.016	0.865	100
Informed about influenza	0.131	0.002**	499	0.097	0.296	100
Informed about pneumococcal infections	0.193	0.000**	497	0.126	0.172	100
Chronic kidney disease	0.046	0.269	505	0.086	0.354	100
Arterial hypertension	0.141	0.001**	505	0.094	0.309	100
Diabetes (type 1 and 2)	0.059	0.154	505	-0.059	0.523	100
Chronic lung diseases	-0.016	0.704	505	0.139	0.135	100
Cancer diagnosis in the past 5 years	0.015	0.713	505	0.021	0.818	100
Osteoporosis	0.083	0.45***	505	-0.081	0.381	100

*number of patients
** correlation is significant at the 0.01 level (2-tailed)
***correlation is significant at the 0.05 level (1-tailed)
**** Kendall´s tau-b correlation coefficient

Furthermore, a positive correlation was found in CIRD patients with age and an even stronger with educational level, but no correlation was seen with known risk factors for severe outcomes of COVID-19 disease except for hypertension. A status of “no comorbidity” was associated with a lower vaccine acceptancy in CIRD patients. Finally, neither the number nor the type of current immunosuppressive therapy correlated with vaccination willingness. CIRD patients, who did not think that they are at risk for a COVID 19 disease were less likely to accept a SARS-CoV-2 vaccination.

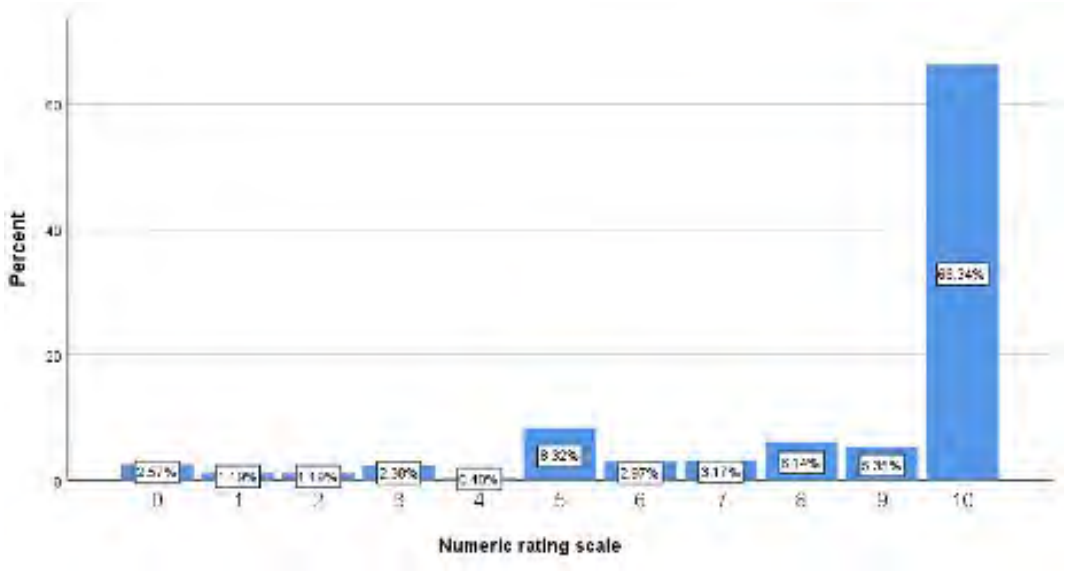

Figure 1. Vaccination willingness of CIRD patients.

Conclusion: The majority of CIRD patients was ready to be vaccinated against SARS-CoV-2. This was especially the case in older patients, those with a higher educational level and those who rated themselves as being at increased risk. Moreover, our survey highlights several factors that are relevant for vaccination willingness, including appropriate information about preventable infections and its relevance in general. The fact that known risk factors for a severe COVID-19 did not show an interference with vaccine acceptancy is alarming and indicates that more patient education is needed.

Reference

1. Felten R et al. Vaccination against COVID-19: Expectations and concerns of patients with autoimmune and rheumatic diseases. Lancet Rheumatol 2021

Disclosure: I. Roman, None; **I. Andreica**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmith-Kline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Braun**, Amgen, BMS, Boehringer, Celgene, Celltrion, Centocor, Chugai, Medac, MSD (Schering-Plough),, 2, 5, 6, Novartis, Pfizer (Wyeth), Roche, Sanofi-Aventis and UCB, 2, 5, 6, Mundipharma, 2, 5.

Abstract Number: 1610

"You Can't Touch, You Can't Bond": COVID-19 and Telehealth Impacts on Communication, Goals, and Experience of Care for Persons with Rheumatoid Arthritis and Their Clinicians

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: A rapid shift to telehealth visits has been a key part of health system response to the ongoing COVID-19 pandemic. This study explores the impacts of the pandemic and care delivery via telehealth on patient goals, patient-clinician goal communication, and management of rheumatoid arthritis (RA).

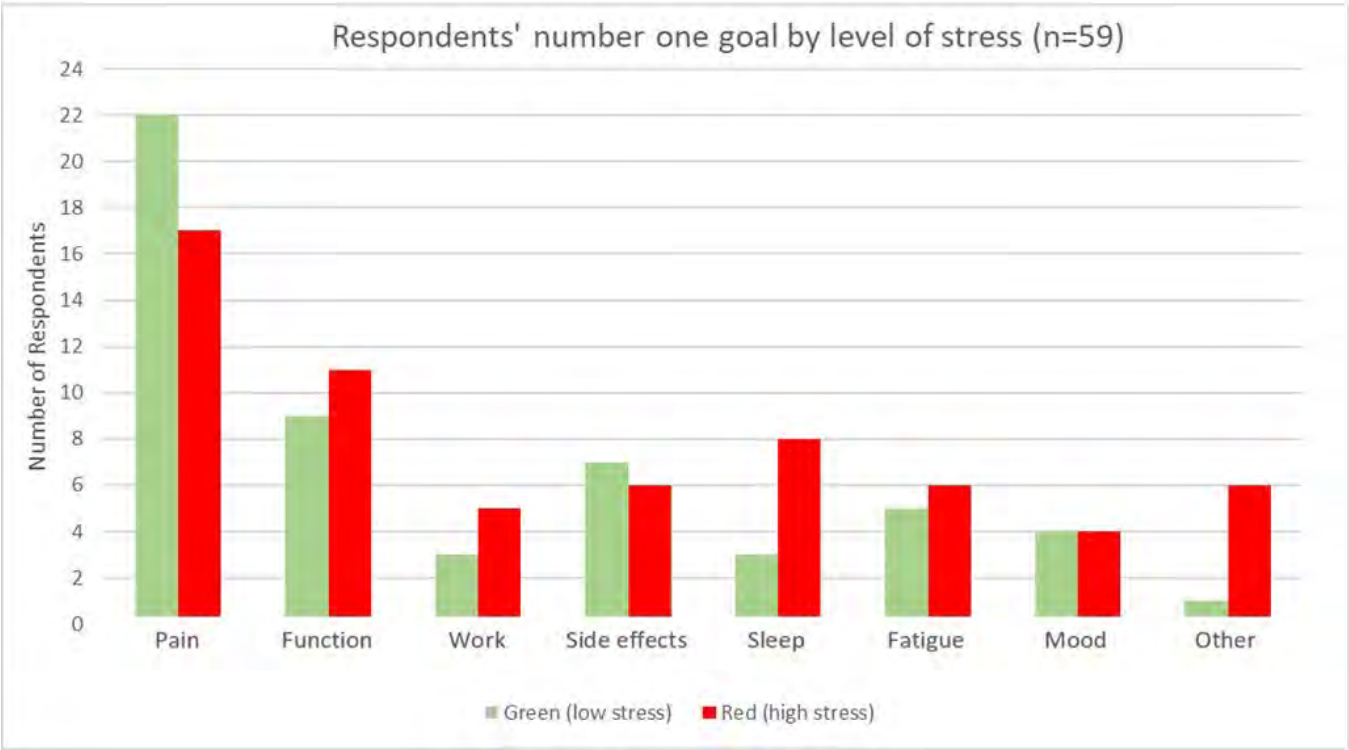
Methods: RA patients who had a telehealth visit between March 1 and July 31, 2020 (university and Veterans Affairs, VA) were invited to participate in a survey study via phone or mail. Survey questions included demographics, health status, COVID-19 impacts, treatment goals, stress, resiliency, and measures of decisional conflict, clinician empathy, communication, and optional-free-text comments. Descriptive and bivariate analyses were conducted on survey items and qualitative content analysis was conducted on free-text comments. Over the same study period, 6 clinicians from university and VA clinics participated in a 60-minute focus group to discuss impacts of telehealth and the COVID-19 pandemic on communication and goal discussions with patients. The focus group was audio-recorded, transcribed verbatim and analyzed using a framework matrix.

Results: Of the 159 eligible patients invited to participate, 59 (37%) completed the survey (28 by phone; 31 by mail). Average age was 69 (± 10.5) years, 71% male, 86% white, 22% with inadequate health literacy and 85% Veterans. Patients overwhelmingly ranked having less pain as their #1 goal (66%) followed by having fewer problems doing daily activities (34%) and avoiding side effects (22%). Over half (58%) reported ≥moderate stress from COVID-19. Compared with patients who reported lower stress, those with ≥ moderate stress reported increased decisional conflict, lower resiliency and clinician empathy (Table). Goals stratified by stress level reflect higher prioritization of function and sleep over less pain among those with ≥moderate stress (Figure). Analysis of free-text responses indicated that patient participants held concerns about medication changes and RA flares, social and relational stress as well as frustrations with government regulations and pandemic response. In the focus group, clinicians perceived that increased use of telehealth presented logistical and safety challenges that undermined development of high-quality relationships with patients due to the absence of physical co-location and change in visit formality.

Table. Measures of emotional support, resiliency, self-efficacy, decisional conflict, empathy and trust in physician by stress level from Covid-19 (moderate to high vs. none or a little) among 59 RA patients

Measure[a]	Total (n=59)	Mean, SD or N (%)	Moderate to high stress (n=34)	Low stress (n=25)	P-value
Emotional support (0-20)	59	17 (4.37)	16.15	18.16	0.075
Resilience scale (0-5)	57	3.76 (0.90)	3.50 (33)	4.10 (24)	0.012
Self-efficacy, mean SD (0-10)	59	6.44 (2.20)	6.00	7.04	0.095
SURE[b] (proportion with a score of 4 out of 4 indicating no decisional conflict)	57	49 (86%)	75% (32)	100%	0.003
CARE (0-50)	59	43.86 (8.33)	42.06	46.31	0.034
Trust in Physician, (0-50)	56	48.38 (6.83)	47.55 (31)	49.40	0.296

[a]Scoring: All scales with higher number indicating higher levels of concept being measured. Ranges: Emotional support (0-20), Resilience scale (0-5), Self-efficacy, (0-10), CARE (0-50), Trust in Physician, (0-50).
[b]SURE is a 4-item measure of decisional conflict (each item solicits dichotomous response, Yes/No). Score of 4 indicates no decisional conflict; score < 4 indicates some decisional conflict.



Conclusion: RA participants with higher pandemic-related stress reported greater decisional conflict, lower resilience and clinician empathy, and prioritized goals of better function and improved sleep over pain reduction, which in a prior study accounted for majority of patient-clinician goal concordance. Clinicians experienced difficulties implementing safe and effective virtual care, leaving little room to focus on fostering high-quality patient relationships. Considering increased patient stress levels and impediments to clinician-patient relationship-building, health systems must implement telehealth-specific supports to both patients and clinicians to ensure effective communication, goal discussion, and access to high-quality care.

Disclosure: E. Hulen, None; **C. Larsen**, None; **R. Matsumoto**, None; **P. Katz**, None; **J. Barton**, None.

Abstract Number: 1611

A Population-Based Evaluation of Telemedicine Use and Satisfaction in SLE Patients During the COVID-19 Pandemic in Atlanta, Georgia

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic resulted in the shift from in-person physician appointments to the development and proliferation of the use of telemedicine in an attempt to give comparable levels of care despite

social distancing and travel restrictions. It is unclear how patients with SLE, particularly from minority communities, used and perceived telemedicine during this time.

Methods: Georgians Organized Against Lupus (GOAL) is a population-based cohort of adult, validated SLE patients in Atlanta. GOAL participants were surveyed by internet, mail, and/or phone from January 19, 2021 through March 25, 2021. Survey questions covered sociodemographics and use and perceptions of telemedicine during the COVID-19 pandemic. Frequency of responses were reported overall and by sex, race, age group, and work status. Differences within groups were evaluated using t-tests and P-values. The 21-item Telemedicine Satisfaction and Usefulness Questionnaire (TSUQ) measures usefulness, effectiveness, ease of use, attitude, intention to use, and compares telemedicine to in-person visits. Each question uses a 5-point Likert scale that ranges from 1 (strongly disagree) to 5 (strongly agree). Being in agreement equated to a score of 4 or 5. Questions that showed significance in univariable analysis by race, age at survey, disease duration, sex, and poverty status were evaluated by multivariable logistic regression.

Results: A total of 732 participants had an average age of 51.4 years with a disease duration of 18.2 years (Table 1). Most were female (93.3%) and self-identified as Black (78.1%) with 26.8% living at or below the Federal poverty level. Although 40.3% were employed, 36.5% were unemployed and 23.3% were off the work force (disabled, retired, student, homemaker). Black participants were more frequently in poverty (32.1 vs. 8.3%) and less likely employed. The youngest age group (18-34) lived in poverty most frequently and the oldest (55+) was the least employed. A total of 74% of respondents had a telemedicine visit during the pandemic with 90% having an adequate internet connection (Table 2). Most connected from home. There were no differences by race, age group, and work status. Smartphones with cameras were used more often by Blacks and younger participants Laptops were also used more frequently by younger and employed individuals. There were no significant

Table 1. Sociodemographics of GOAL Participants

Category		Overall (n=732)	Sex			Race			Age Group				Work Status			
			Male (n=49)	Female (n=682)	P value	Non-Black (n=160)	Black (n=572)	P value	18-34 (n=110)	35-54 (n=318)	55+ (n=304)	P value	Employed (n=287)	Off work force (n=166)	Unemployed (n=260)	P value
Age at Survey (years)	Count (N)	732	49	682		160	572						287	166	260	
	Mean ± SD	51.4 ± 13.7	51.1 ± 12.6	51.4 ± 13.8	0.9	51.4 ± 15.5	51.4 ± 13.3	0.99					47.0 ± 11.7	60.4 ± 14.8	49.7 ± 12.3	<0.0001
	Range	(21.3-86.1)	(26.3-82.2)	(21.3-86.1)		(21.3-86.1)	(21.7-85.0)						(21.9-79.6)	(21.3-85.0)	(21.7-86.1)	
Age Group (years)	Count (N)	732	49	682		160	572						287	166	260	
	18-34	110 (15.0)	7 (14.3)	103 (15.1)	0.97	24 (15.0)	86 (15.0)	0.8					54 (18.8)	18 (10.8)	38 (14.6)	<0.0001
	34-54	318 (43.4)	22 (44.9)	295 (43.3)		73 (45.6)	245 (42.8)						157 (54.7)	28 (16.9)	131 (50.4)	
	55+	304 (41.5)	20 (40.8)	284 (41.6)		63 (39.4)	241 (42.1)						76 (26.5)	120 (72.3)	91 (35.0)	
Disease Duration (years)	Count (N)	727	48	679		157	570						285	164	259	
	Mean ± SD	18.2 ± 10.2	17.1 ± 10.7	18.3 ± 10.2	0.45	18.3 ± 9.9	18.1 ± 10.3	0.83					16.9 ± 9.0	20.7 ± 11.5	17.7 ± 10.3	0.0005
	Range	(1.1-56.8)	(1.7-46.7)	(1.1-56.8)		(3.8-54.6)	(1.1-56.8)						(1.7-51.9)	(1.1-56.8)	(1.1-54.6)	
Age at Diagnosis (years)	Count (N)	727	48	679		157	570						285	164	259	
	Mean ± SD	33.2 ± 12.4	34.0 ± 12.9	33.1 ± 12.4	0.65	32.8 ± 14.0	33.3 ± 11.9	0.69					30.1 ± 10.7	35.8 ± 14.2	32.0 ± 11.2	<0.0001
	Median(IQR)	32.1 (23.4-42.4)	36.0 (24.6-43.5)	31.8 (23.6-41.7)		31.2 (20.8-42.9)	32.2 (24.3-42.1)						28.9 (21.6-37.9)	42.1 (27.4-50.0)	31.0 (23.7-40.5)	
	Range	(7.4-70.4)	(11.3-53.7)	(7.4-70.4)		(10.6-70.4)	(7.4-67.6)						(9.5-67.2)	(7.6-70.4)	(7.4-59.2)	
Sex	Count (N)	731				159	572		110	317	304		287	166	259	
	male	49 (6.7)				14 (8.8)	35 (6.1)	0.23	7 (6.4)	22 (6.9)	20 (6.6)	0.97	21 (7.3)	9 (5.4)	18 (6.9)	0.73
	female	682 (93.3)				145 (91.2)	537 (93.9)		103 (93.6)	295 (93.1)	284 (93.4)		266 (92.7)	157 (94.6)	241 (93.1)	
Race	Count (N)	732	49	682					110	318	304		287	166	280	
	Non-Black	160 (21.9)	14 (28.6)	145 (21.3)	0.23				24 (21.8)	78 (24.5)	63 (20.7)	0.8	87 (30.3)	42 (25.3)	27 (10.4)	<0.0001
	Black	572 (78.1)	35 (71.4)	537 (78.7)					86 (78.2)	245 (77.0)	241 (79.3)		200 (69.7)	124 (74.7)	233 (89.6)	
Below 100% Poverty Level	Count (N)	704	45	658		158	548		109	309	286		281	161	245	
	Yes	189 (26.8)	9 (20.0)	180 (27.4)	0.28	13 (8.3)	176 (32.1)	<0.0001	44 (40.4)	92 (29.8)	53 (18.5)	<0.0001	33 (11.7)	33 (20.5)	118 (48.2)	<0.0001
Current Work Status	Count (N)	713	48	664		156	557		110	316	287		287	166	260	
	Employed	287 (40.3)	21 (43.8)	266 (40.1)	0.73	87 (55.8)	200 (35.9)	<0.0001	54 (49.1)	157 (49.7)	76 (26.5)	<0.0001				
	Off work force	166 (23.3)	9 (18.8)	157 (23.6)		42 (26.9)	124 (22.3)		18 (16.4)	28 (8.9)	120 (41.8)					
	Unemployed	260 (36.5)	18 (37.5)	241 (36.3)		27 (17.3)	233 (41.8)		38 (34.5)	133 (42.1)	91 (31.7)					

Table 2. Ad Hoc Telemedicine Questions

Questions	Category	Overall (n=732)	Sex			Race			Age Group				Work Status			
			Male (n=49)	Female (n=682)	P value	Non-Black (n=160)	Black (n=572)	P value	18-34 (n=110)	35-54 (n=318)	55+ (n=304)	P value	Employed (n=287)	Off work force (n=166)	Unemployed (n=260)	P value
Have you had a telemedicine visit since the start of the pandemic?	Count (N)	732	49	670		158	562		110	314	296		286	161	255	
	Yes	533 (74.0)	37 (75.5)	495 (73.9)	0.8	120 (75.9)	413 (73.5)	0.53	82 (74.5)	231 (73.6)	220 (74.3)	0.97	211 (73.8)	112 (69.6)	198 (77.6)	0.18
When you connect to the internet, is the connection good enough for your needs?	Count (N)	609	38	570		130	479		98	265	247		247	131	227	
	Yes	550 (90.3)	35 (92.1)	514 (90.2)	0.7	121 (93.1)	429 (89.6)	0.23	86 (92.5)	236 (87.7)	228 (92.3)	0.16	214 (90.3)	122 (93.1)	202 (89.0)	0.44
Where do you regularly connect to the internet for telemedicine visits?	Count (N)	628	39	588		152	496		94	277	257		244	138	230	
	none	56 (8.9)	3 (5.1)	54 (9.2)	0.64	7 (5.3)	49 (9.9)	0.094	5 (5.3)	29 (10.5)	22 (8.6)	0.58	24 (9.8)	12 (8.7)	18 (7.8)	0.3
	at home	558 (88.9)	36 (92.3)	521 (88.6)		121 (91.7)	437 (88.1)		88 (95.6)	241 (87.0)	229 (89.1)		210 (86.1)	125 (90.6)	209 (90.9)	
	at work	13 (2.1)	1 (2.6)	12 (2.0)		3 (2.3)	10 (2.0)		1 (1.1)	7 (2.5)	5 (1.9)		9 (3.7)	1 (0.7)	3 (1.3)	
	public access	1 (0.2)		1 (0.2)		1 (0.8)					1 (0.4)		1 (0.4)			
What types of devices do you use to connect for telemedicine visits? (check all that apply)	Count (N)	732	49	682		160	572		110	318	304		287	166	260	
	Desktop	77 (10.5)	5 (10.2)	72 (10.6)	0.94	15 (9.4)	62 (10.8)	0.59	13 (11.8)	32 (10.1)	32 (10.5)	0.87	37 (12.9)	13 (7.8)	24 (9.2)	0.18
	Count (N)	732	49	682		160	572		110	318	304		287	166	260	
	Laptop	281 (38.4)	15 (30.6)	266 (39.0)	0.24	71 (44.4)	210 (36.7)	0.078	51 (46.4)	131 (41.2)	99 (32.6)	0.015	131 (45.6)	61 (36.7)	84 (32.3)	0.005
	Count (N)	732	49	682		160	572		110	318	304		287	166	260	
	Tablet	143 (19.5)	9 (18.4)	131 (19.2)	0.89	27 (16.9)	114 (19.9)	0.39	13 (11.8)	66 (20.8)	62 (20.4)	0.099	57 (19.9)	42 (25.3)	41 (15.8)	0.054
	Count (N)	733	49	682		160	572		110	318	304		287	166	260	
	Smart Phone with Camera	439 (59.8)	28 (57.1)	409 (60.0)	0.7	83 (51.9)	355 (62.1)	0.02	74 (67.3)	202 (63.5)	162 (53.3)	0.0076	168 (58.5)	90 (54.2)	172 (66.2)	0.038

Table 3. Multivariable Logistic Regression for Being In Agreement With Questions from the Telemedicine Satisfaction and Usefulness Questionnaire

Question	Effect	OR (95% CI)	P value
In general, I am satisfied with the telemedicine system.			
	Black Race	0.93 (0.60-1.44)	0.75
	Age at Survey (per 5 years ↑)	0.89 (0.82-0.96)	**0.0021**
	Disease Duration (per 5 years ↑)	1.03 (0.94-1.14)	0.53
	Male Sex	1.14 (0.55-2.36)	0.72
	Not in Poverty	1.98 (1.32-2.97)	**0.0009**
I am more involved in my care using the telemedicine system.			
	Black Race	3.83 (1.85-7.93)	**0.0003**
	Age at Survey (per 5 years ↑)	0.95 (0.86-1.04)	0.28
	Disease Duration (per 5 years ↑)	1.09 (0.97-1.23)	0.14
	Male Sex	1.37 (0.59-3.16)	0.46
	Not in Poverty	0.83 (0.52-1.32)	0.42
I follow my doctor's advice better since working with the telemedicine system.			
	Black Race	3.49 (1.74-7.01)	**0.0004**
	Age at Survey (per 5 years ↑)	0.95 (0.87-1.05)	0.31
	Disease Duration (per 5 years ↑)	1.07 (0.95-1.20)	0.27
	Male Sex	1.30 (0.56-3.02)	0.54
	Not in Poverty	0.55 (0.35-0.85)	**0.0079**
Talking to a nurse during a video visit is as satisfying as talking in person			
	Black Race	2.08 (1.34-3.21)	**0.001**
	Age at Survey (per 5 years ↑)	0.95 (0.89-1.03)	0.21
	Disease Duration (per 5 years ↑)	1.04 (0.95-1.14)	0.39
	Male Sex	1.16 (0.59-2.25)	0.67
	Not in Poverty	0.90 (0.62-1.32)	0.59
Video visits are a convenient form of healthcare delivery for me.			
	Black Race	0.69 (0.45-1.07)	0.1
	Age at Survey (per 5 years ↑)	0.91 (0.85-0.98)	0.012
	Disease Duration (per 5 years ↑)	1.07 (0.97-1.17)	0.17
	Male Sex	1.51 (0.74-3.08)	0.26
	Not in Poverty	2.05 (1.39-3.02)	**0.0003**

Each question is scored: 1: strongly disagree, 2: disagree, 3: neither agree nor disagree, 4: agree, 5: strongly agree. Being in agreement equated to a score of 4 or 5. OR=odds ratio; CI=confidence interval

differences between males and females in any category (Tables 1 and 2). Multivariable logistic regression (Table 3) showed that Blacks were more involved in their care, followed their doctor's advice better, and more satisfied with talking to a nurse. Not being in poverty was associated with being satisfied with telemedicine and finding video visits as convenient. However, those in poverty followed their doctor's advice better. Younger age was associated with higher satisfaction with telemedicine.

Conclusion: In this diverse SLE cohort, telemedicine was widely used during the pandemic. Blacks felt more involved in their care, and Blacks and those in poverty followed their doctor's advice better using telemedicine. Telemedicine may potentially offer an opportunity to mitigate health disparities through the pandemic and beyond.

Disclosure: S. Simmons, None; **C. Drenkard**, GSK, 1, 5; **G. Bao**, None; **C. Dunlop-Thomas**, None; **K. Schofield**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2.

Abstract Number: 1612

Factors Associated with COVID-19 Vaccine Hesitancy Among Individuals with Rheumatic Disease

Kristin Wipfler[1], Adam Cornish[1], Alison Freifeld[2], Patricia Katz[3] and Kaleb Michaud[2], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE, [3]University of California San Francisco, San Francisco, CA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Characteristics of monthly COVID-19 vaccine questionnaire respondents by vaccination status and by intention to be vaccinated (among the unvaccinated population)

	Vaccinated	Not Vaccinated		
	n=1925	All n=654	Will be vaccinated n=456	Won't be vaccinated n=187
Demographics				
Age, years	67.4 (10.5)	60.8 (10.2)	60.7 (10.2)	60.6 (10.2)
Female	79.3	80.5	79.1	83.4
White	94.3	94.1	95.4	90.6
Education, years	15.4 (2.0)	14.9 (2.2)	15.1 (2.3)	14.7 (2.0)
Married	71.0	73.1	73.8	72.0
Rural	17.7	24.4	20.9	32.6
History of smoking	37.3	34.3	34.7	33.2
BMI, kg/m2	27.6 (6.5)	28.5 (7.2)	28.4 (7.3)	28.9 (6.9)
Patient-reported outcomes				
Pain (0-10)	3.1 (2.6)	3.3 (3.0)	3.2 (2.9)	3.7 (3.1)
Global severity (0-10)	3.1 (2.3)	3.3 (2.7)	3.1 (2.6)	3.6 (2.8)
HAQ-II (0-3)	0.7 (0.6)	0.7 (0.7)	0.7 (.6)	0.8 (0.7)
PAS-II (0-10)	2.8 (2.0)	2.9 (2.4)	2.8 (2.3)	3.3 (2.5)
Primary diagnosis				
RA	63.0	63.4	68.3	53.1
OA	16.2	10.1	9.8	10.9
SLE	4.7	6.8	5.2	10.9
FM	3.9	6.4	4.3	10.2
PsA	3.5	3.7	4.0	2.7
AS	1.8	2.1	1.8	2.7
Other	6.1	6.2	5.8	7.5
Medications				
Conventional DMARD	46.5	46.4	46.9	44.2
Biologic DMARD	32.4	30.5	31.3	29.5
JAK inhibitor	5.5	5.7	6.9	2.3
Corticosteroid	15.8	16.9	16.6	17.1
NSAID	31.9	29.7	30.6	28.7
Pandemic response				
COVID-19 stress (0-3)	1.6 (0.8)	1.4 (0.9)	1.6 (0.8)	1.1 (0.9)
Sought COVID-19 testing	46.3	41.1	39.2	46.9
Tested positive for COVID-19	3.3	7.3	5.6	11.7

Values are mean (SD) or %.

Vaccinated = received at least one vaccine dose at the time of the monthly questionnaire response.

Background/Purpose: COVID-19 vaccination efforts are ongoing and there is a need to understand factors associated with vaccine hesitancy. Individuals with rheumatic diseases have been uniquely impacted by the COVID-19 pandemic and little is known about vaccine acceptance rates in this population in the United States. The objective of this study was to identify reasons for vaccine hesitancy as well as associated risk factors in a US-based rheumatic disease population.

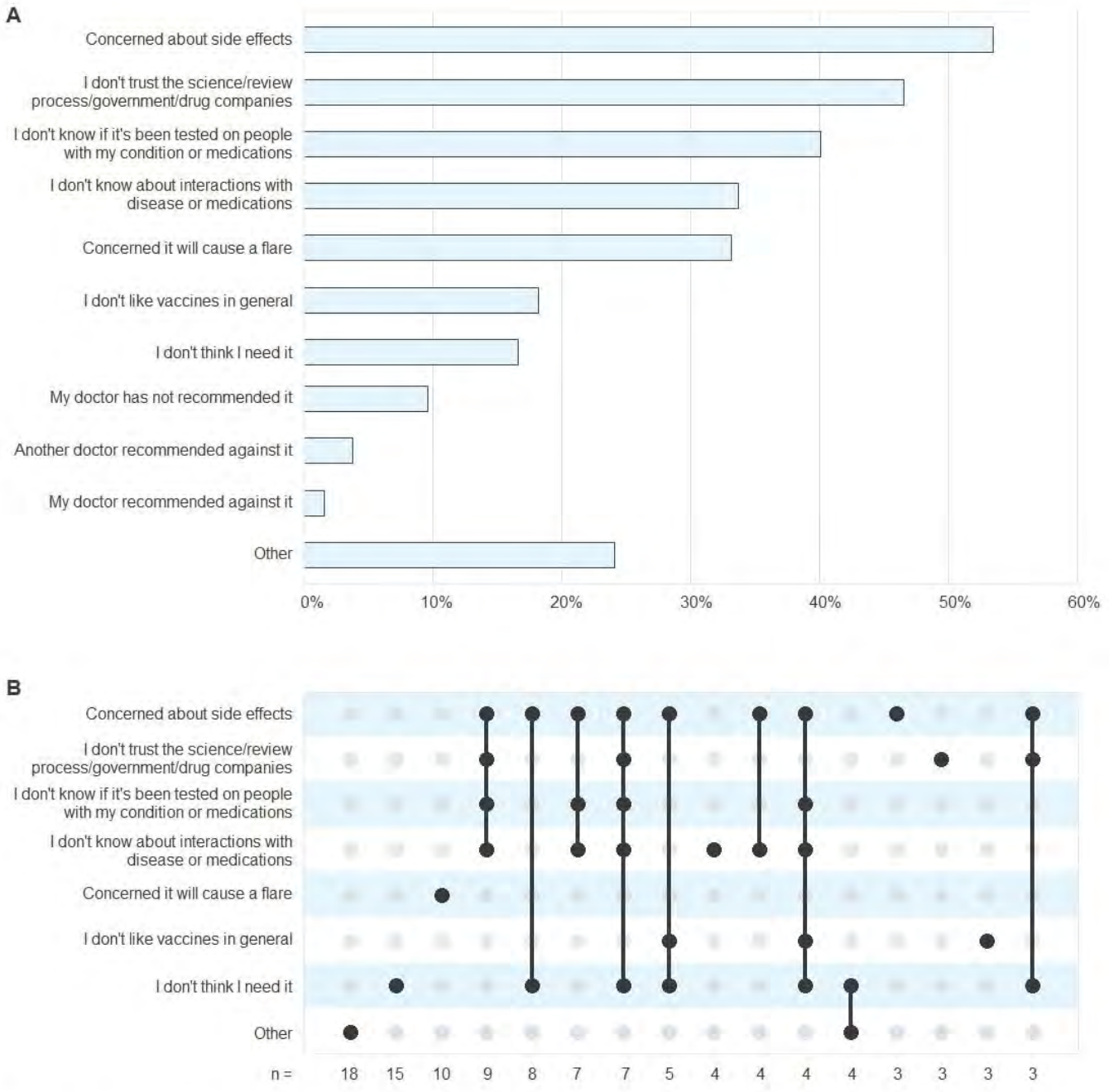

Figure 1. Frequency of reported reasons for vaccine hesitancy among unvaccinated individuals with a rheumatic disease diagnosis (n=187). (A) Percent of respondents reporting each reason for vaccine hesitancy. (B) UpSet plot displaying the most frequently reported individual or grouped reasons for vaccine hesitancy. Filled circles indicate that that reason was reported in conjunction with other filled circles in each column by the number of respondents indicated in the sample size on the x axis. Sets of reasons reported by at least three individuals were included.

Methods: Data were provided by adults enrolled in FORWARD, The National Databank for Rheumatic Diseases. Participants complete comprehensive semiannual questionnaires and were invited to answer supplemental questionnaires focused on COVID-19 vaccination in March and April 2021. Responses to the supplemental questionnaires were linked to each participant's most recently completed semiannual questionnaire for demographics, diagnosis, patient-reported outcome measures, medication use, and pandemic response variables. Respondents were compared by vaccination status, and (among those who were unvaccinated) by intention to be vaccinated. Reported reasons for vaccine hesitancy were described for those respondents who did not intend to be vaccinated, and risk factors associated with vaccine hesitancy were identified with logistic regression adjusted for age, sex, race, education, rural residency, BMI, physical function (HAQ-II), COVID-19-specific stress (Likert scale), and diagnosis (RA reference).

Results: Among the 2,579 unique respondents, 1,925 (75%) reported receiving at least one dose of a COVID-19 vaccine at the time of questionnaire completion. Of those who were not vaccinated, 456 (71%) reported an intention to be vaccinated in the future (Table 1). Of those who did not plan to receive a COVID-19 vaccine (n=187, 7% of respondents), the most frequently reported reason was concern about side effects (54%), followed by distrust (47%), and concern about sufficient testing on individuals with rheumatic diseases (40%; Figure 1A). Many respondents selected multiple reasons for vaccine hesitancy, and the most frequently reported groups of responses are ranked in Figure 1B. Respondents of non-white race were significantly more likely to be vaccine hesitant (OR [95% CI] = 6.7 [2.0, 22]; p=0.002), as were individuals with higher HAQ-II scores (1.8 [1.1, 2.9]; p=0.024; Figure 2). Respondents with a primary diagnosis of SLE were significantly more likely to be vaccine hesitant than were individuals with RA (2.7 [1.1, 7.1]; p=0.038). Individuals who reported higher levels of pandemic-related stress were significantly less likely to be vaccine hesitant (0.4 [0.3, 0.6]; p< 0.001).

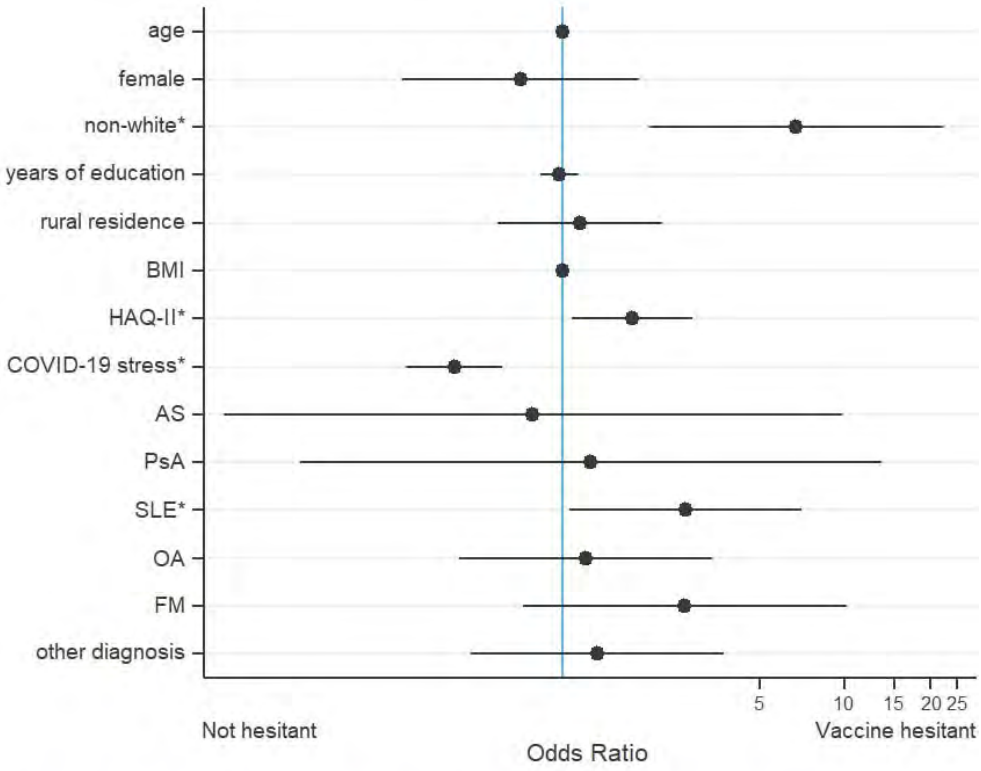

Figure 2. Odds ratios and 95% confidence intervals for factors associated with vaccine hesitancy among individuals with a rheumatic disease diagnosis. All individuals included in the model were unvaccinated at the time of questionnaire response and indicated whether they intended to be vaccinated in the future. RA was the comparator for the diagnosis variable. Statistical significance (p<0.05) is indicated by asterisks (*).

Conclusion: Most individuals in this cohort had already been vaccinated against COVID-19 or intended to be vaccinated. The difference in vaccine hesitancy by race is consistent with reports on vaccine hesitancy in populations not specific to individuals with rheumatic diseases. Most of the frequently reported reasons for vaccine hesitancy were related to concerns about possible physical responses to COVID-19 vaccines or to perceived lack of information/knowledge, both of which could potentially be addressed by education from a health care provider.

Disclosure: K. Wipfler, None; **A. Cornish**, None; **A. Freifeld**, None; **P. Katz**, None; **K. Michaud**, None.

Abstract Number: 1613

Pandemic and Patients: Examining Health-Related Behaviors of Patients with Systemic Sclerosis During the COVID-19 Pandemic

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Patient Outcomes, Preferences, & Attitudes Poster IV: COVID-19 (1589–1613)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Prior to COVID-19, few studies examined how patients with a chronic illness, such as systemic sclerosis (SSc), react to a pandemic. This study examined if fears of COVID are affecting health care for scleroderma patients, their mental and physical functioning, and if patients with SSc engage in COVID-19 risky behavior.

Methods: Participants were 60 people with SSc who had not had COVID-19 and had not yet been vaccinated for COVID. Participants had a mean age of 58 years (*SD* = 11.5) and were primarily female (92%) and white (87%). The ACR-Eular criteria for diagnosis of systemic sclerosis was met for 87% of participants and was unknown for the rest.

Participants completed an online survey after learning about it from a scleroderma organization newsletter or at their visit with a rheumatologist specializing in scleroderma. Data were collected August 2020 through March 2021. Participants completed measures assessing exercise, risk behaviors, vaccination intent, health-related appointments attendance, and PROMIS measures of anxiety, depression, fatigue, sleep disturbance, and physical function.

Results: Eighteen percent of the sample reported exercising less during the pandemic. For COVID-19 risk behaviors, 37% ate indoors at a restaurant, 28% went to an indoor gathering (e.g., wedding), and 58% went to a hair/nail salon. In terms of COVID-19 vaccination intent, 32% would be vaccinated as soon as eligible, 27% intended to wait, 12% might get vaccinated, 16% did not plan to get vaccinated, 8% were letting their physician decide, and 5% were not sure.

As can be seen in Table 1, 29% of respondents had health care appointments in-person, 32% had only telemedicine appointments, 24% had a combination of appointments, and 10% cancelled appointments due to COVID concerns. As can be seen in Table 2, of the respondents for whom pulmonary function tests were relevant, 40% cancelled or postponed these due to COVID concerns. Similarly, among respondents who normally had physical or occupational therapy, 46-50% of them cancelled due to COVID concerns. Patients cancelled 24% of dental appointments due to COVID concerns.

We compared respondents who cancelled one or more appointments due to COVID-19 concerns (N = 28) versus those who did not (N = 32). Participants who cancelled reported higher anxiety, $t(58) = 2.46$, p =.02, sleep disturbance, $t(56) = 3.31$, $p = .002$, and worse physical functioning, $t(56) = 2.00$, $p = .05$.

Many participants reported moderate or severe anxiety (36%), depression (22%), fatigue (32%), sleep disturbance (28%), and physical dysfunction (40%, see Table 3).

Conclusion: The results that a majority of participants were willing to get vaccinated for COVID-19 are encouraging. Less encouraging, almost one in five participants exercised less during the pandemic and half of them did not exercise to begin with. Additionally, almost half of participants cancelled one or more health appointments due to their COVID fears. This subgroup reported significantly higher anxiety, sleep disturbance, and worse physical functioning. Future research should examine the extent to which changes in health-related behavior during the pandemic have implications for disease progression in patients with SSc.

Response option	Percentage (N = 59)
Only attended in-person	29%
Only telemedicine appointments	32%
Combination of in-person and telemedicine appointments	24%
Provider cancelled	3%
Participant cancelled due to COVID concerns	10%
Participant cancelled due to other reasons	2%

Percentage of Respondents who Attended or Cancelled an Appointment with a Health Care Professional Since the Beginning of the COVID-19 Pandemic in the U.S.

Response option	Pulmonary Function Tests		Physical Therapy		Occupational or Hand Therapy		Dentist	
	N	%	N	%	N	%	N	%
Patient kept appointment	16	33%	3	23%	2	20%	31	57%
Provider cancelled	2	4%	2	15%	2	20%	7	13%
Patient cancelled or didn't schedule due to COVID concern	19	40%	6	46%	5	50%	13	24%
Patient cancelled or didn't schedule due to other reasons	5	10%	2	15%	1	10%	3	6%
Not due for appointment	6	13%	0	0%	0	0%	0	0%

Frequency and Percentage of Respondents who Attended or Cancelled a Health-Related Appointment Since the Beginning of the COVID Pandemic in the U.S.

PROMIS Measure	Within Normal Limits	Mild	Moderate	Severe
Anxiety	33%	30%	33%	3%
Depression	48%	30%	20%	2%
Fatigue	50%	17%	29%	3%
Sleep disturbance	57%	16%	28%	0%
Physical dysfunction	43%	17%	35%	5%

Percentage of Scores Within Each Category of Severity on PROMIS Measures

Disclosure: N. Dorr, None; **P. Fennell**, None; **L. Shapiro**, Actelion, 2.

Abstract Number: 1614

Preliminary Results from a Pilot Feasibility and Acceptability Trial of Resilience Coaching for Adolescent Chronic Musculoskeletal Pain

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic musculoskeletal pain (CMP) affects up to 40% of youth and is associated with physical disability and psychological distress. Resilience coaching interventions, such as Promoting Resilience in Stress Management (PRISM), are well-established for reducing stress and building resilience in pediatric chronic illness. Our previous research demonstrated that self-perceived resilience is low among youth with CMP and resilience correlates with symptom severity. It is not known whether youth with CMP would participate in and benefit from resilience coaching. We therefore aimed to 1) assess the feasibility and acceptability of PRISM and 2) explore whether it results in improved clinical outcomes for adolescent CMP.

Methods: We conducted a single center pilot study of PRISM among youth with CMP. Eligible participants were English-speaking youth ages 12-17 years diagnosed with CMP seen for initial evaluation and one of their caregivers. Youth with inflammatory, neurologic or oncologic/hematologic diagnoses or cognitive impairments were ineligible. PRISM is a manualized, skills-based intervention consisting of four (~30 minute) required and one optional one-on-one sessions scheduled every 1-2 weeks. Participants chose mode of delivery: in-person, video chat, or telephone. Youth completed pre- and post- intervention surveys. Both patients and caregivers participated in semi-structured interviews upon study completion. Feasibility of intervention delivery was defined as ≥70% of subjects completing all 4 required sessions. The intervention was defined as acceptable if the mean satisfaction score for patients was ≥ 3 on a 5-point Likert scale (1=very dissatisfied and 5=very satisfied). We also administered the Acceptability of the Intervention Measure (AIM) (1=completely disagree and 5=completely agree) and defined acceptability as a mean AIM ≥ 3. All qualitative interviews were transcribed verbatim and qualitative analyses are ongoing.

Results: We approached 37 eligible patients and enrolled 19 (51%). High feasibility in intervention delivery was demonstrated with 84% (n=16) of youth having completed all study visits. One participant completed session 1 and one participant completed sessions 1 and 2 before early discontinuation; another never started PRISM. Video visit (69%) was the preferred mode of delivery, followed by telephone (25%). High overall satisfaction and acceptability were found. Mean participant satisfaction was 4.19 (SD 1.05) and the average satisfaction score for each session was >4 (Table 1). Similarly, the mean AIM was 4.25 (SD 0.99). Table 1 shows preliminary changes pre-post treatment in clinical outcomes demonstrating increased resilience and clinically relevant outcomes.

Conclusion: Resilience coaching is a feasible and acceptable adjunctive treatment for youth with CMP. Video visit was the preferred delivery format. Exploratory analyses suggest improvements in resilience and clinically relevant

outcomes. Given high feasibility and acceptability, we plan to move forward to conduct a future randomized controlled trial of PRISM using videoconferencing as a delivery platform for this vulnerable patient population.

Table 1. Satisfaction with PRISM among Youth with CMP (n=16)

PRISM Session	Skills	Satisfaction Score, mean (SD)
1: Managing Stress	Mindfulness, relaxation	4.3 (1.14)
2: Setting Goals	Setting specific and realistic goals, planning for roadblocks	4.1 (0.96)
3: Positive reframing	Recognizing and replacing negative self-talk	4.1 (1.12)
4: Making Meaning	Identifying benefits, gratitude, purpose and legacy	4.3 (0.93)
5: Coming Together (optional)	Discussion of what worked; option to include caregivers	4.1 (0.80)
	Average Overall	**4.2 (1.05)**

Legend. One subject did not rate session 5. In-between sessions, subjects had access to worksheets, and the PRISM app to practice and build on skills.

Table 2. Change in Patient-Reported Outcome Measures Pre- and Post- PRISM for Youth with CMP (N=16)

Domain	Measure	Pre-PRISM	Post-PRISM	Direction of Change	Reference Range
Overall HRQOL	PROMIS Pediatric Global Health 7	41.9 (13.1)	42.3 (12.1)	-	MCID= 3.0 T-score with mean as 50, and SD 10
Resilience	Connor-Davidson Resilience Scale 10-item (CD-RISC 10 [0-40])	26.5 [16.0, 32.0]	28.5 [23.5, 34.0]	↑	MCID = 3.0
Self-perceived energy	Self-perceived energy level (0-100)	60.0 [32.0,80.0]	71.5 [55.,80.0]	↑	-----
Functional disability	Functional disability inventory [FDI] (0-60)	21.5 [6.0, 29.5]	14.0 [8.0, 30.0]	↓	MCID = 8.0 0-12: no//minimal 13-20: mild 21-29: moderate ≥30: severe
Psychological Distress	Psychological Distress [K6 Total Score] (0-24)	8.0 [2.5, 13.0]	5.5[3.0, 9.0]	↓	MCID = 2.3 ≥7 = high distress ≥13 = debilitating distress
Pain Catastrophizing	Pain Catastrophizing [PCS-C Total] (0-52)	14.0 [4.5, 34.5]	11.5 [2.0, 24.5]	↓	0-14: low 15-25: moderate ≥26: high
Stress related to COVID-19	COVID PTSD [UCLA Brief COVID-19 Screen for Child/Adolescent PTSD] (0-44)	8.0 [1.5, 16.0)	4.5 [0.5, 10.5]	↓	1-10: minimal 11-20: mild ≥21: potential PTSD
Pain Intensity	PROMIS Pain Intensity (0-10)	6.0 [5.0, 7.0]	6.5 [4.5, 7.0]	-	MCID = 3.0
Pain Widespreadness	Widespreadness of pain [WPI] (0-19)	8.0 [2.5, 15.0]	7 [3.0, 16.5]	-	-----
Symptom severity	Symptom Severity [SSS] (0-12)	7.0 [3.0, 8.5]	5.5 [3.0, 8.0]	-	----

Legend. PRISM = Promoting Resilience in Stress Management. CMP = chronic musculoskeletal pain. MCID = Minimal clinically important difference. PROMIS PGH7=Patient Reported Outcome Measure Information System pediatric global health 7 (T-score with 50 as mean in reference population and 10 is SD). K6=Kessler-6 Psychological Distress Scale, with scores ≥7 consistent with high distress and those ≥ 13 meet criteria for serious or debilitating psychological distress. FDI=Functional disability inventory: No/minimal (0-12), Mild (13-20), Moderate (21-29), and severe (≥30). CD-RISC-10=Connor Davidson Resilience Scale 10 item (40) with higher scores indicating greater resilience. PCS-C=Pain Catastrophizing Scale for Children. PTSD=post-traumatic stress disorder. WPI=Widespread pain index and SSS=symptom severity scale as per the ACR criteria for fibromyalgia syndrome. UCLA=University of California Los Angeles.

Disclosure: S. Gmuca, None; **P. Weiss**, Lilly, 1, 2, Pfizer, 1, 2, Biogen, 2; **M. McGill**, None; **M. Sonagra**, None; **D. Sherry**, None; **P. Cronholm**, None; **J. Gerber**, None; **T. Palermo**, None; **J. Young**, None; **A. Rosenberg**, None.

Abstract Number: 1615

Responsiveness of Quality of Life and Function Assessment to Changes in Topical Eye Medications in Children with Uveitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Children with uveitis often require topical eye medications (eye drops) to control inflammation (glucocorticoids) and complications such as elevated intraocular pressure and synechiae (glaucoma or cycloplegic agents). Eye drops may sting when instilled and be given frequently during the day, which may impact quality of life (QOL) and function. The Effects of Youngsters' Eyesight on QOL (EYE-Q) is a valid pediatric uveitis-focused questionnaire that assesses vision-related QOL (VRQOL) and vision-related function (VRF). The Pediatric Quality of Life Inventory (PedsQL) questionnaire assesses health-related QOL (HRQOL). The purpose of this study was to assess the responsiveness of the EYE-Q and PedsQL to changes in topical medication regimen in children with non-infectious uveitis (NIU).

Methods: Pediatric patients from a tertiary medical care center with a diagnosis of NIU were enrolled. EYE-Q and PedsQL questionnaires were administered to both patients and parent-proxies at baseline and at the 6-month visit. Ophthalmologic examination findings and current treatments were collected. Two comparison groups were created to assess the sensitivity of the EYE-Q based on topical eye medication regimen: Group 1 patients had changes in either type of topical medication or in the frequency of drops between baseline and follow-up. Group 2 patients did not have any changes in topical eye medication regimen. Repeated-measures mixed-models was used to examine changes in scores for both groups. An alpha of $p < 0.05$ was considered statistically significant.

Results: Fifty-nine pediatric patients/parent-proxies participated in the study. Average patient age was 11.1 years (SD=3.4); most were White (85%) and female (70%). 59% had a diagnosis of JIA and uveitis, while 41% had uveitis-only; 18 patients had a change in their topical eye medication regimen (Group 1). Within Group 1, EYE-Q Total scores significantly increased from baseline to 6-month visit (patients, 79 vs. 84; parents 83 vs. 87, p=0.03) (Table 1). Group 1 patients also reported a significant improvement in VRF (81 vs. 87, p=0.02). The PedsQL Total and psychosocial summary scores also increased significantly for patients (81 v. 86, p=0.03; 81 v. 87, p=0.03) and parents (77 v. 84, p= 0.03; 76 v. 83, p=0.02) respectively (Table 1). There were no significant changes in EYE-Q or PedsQL score for Group 2. Despite improved VRQOL scores, Group 1 had significantly lower VRQOL compared to Group 2 (77 vs. 86, $p< 0.05$) at the 6-month visit.

Conclusion: The EYE-Q and PedsQL were sensitive to clinically meaningful differences in QOL in children with NIU who required changes in treatment regimen. A change in topical medications or the frequency of administration of eye drops led to improved QOL and function. Interestingly, children without changes in topical therapy had similar QOL and function at both time points. Improved scores from baseline to 6-month follow-up exam may be attributed

Table 1. Pre and post EYE-Q[a] and PedsQL[b] scores for patients and parent-proxies for children with (Group 1, n=18) and without (Group 2, n=41) a change in topical eye medication regimen including medication type and frequency of instillation

Questionnaire scores per group (0-100)		Parents/Proxies, n = 59			Patients, n = 59		
		Baseline Visit LSM (CI)*	6 mos follow-up Visit	p-value	Baseline Visit LSM (CI)*	6 mos follow-up Visit	p-value
EYE-Q[a]: Total Score	Group 1	**83.2 (77.4-89.0)**	**87.2 (81.4-93.0)**	**0.031****	**78.8 (72.8-84.8)**	**84.0 (78.0-90.0)**	**0.019****
	Group 2	88.7 (84.9-92.6)	89.6 (85.8-93.5)	0.454	88 (84-92)	89.2 (85.3-93.2)	0.402
EYE-Q[a]: Vision-related Functioning Subscore	Group 1	**86.9 (80.2-93.5)**	**90.8 (84.2-97.4)**	**0.069**	**81 (74.4-87.5)**	**87.2 (80.6-93.7)**	**0.016****
	Group 2	90.3 (85.9-94.6)	91.5 (87.1-95.9)	0.369	89.3 (85-93.7)	90.1 (85.8-94.5)	0.635
EYE-Q[a]: Vision-related QOL Subscore	Group 1	**72.8 (65.5-80.0)**	**79.2 (72.0-86.4)**	**0.035****	**68.6 (60.7-76.4)**	**76.8 (69-84.7)**	**0.024****
	Group 2	83.8 (79-88.5)	84.6 (79.8-89.4)	0.654	83.7 (78.5-88.9)	86.2 (81-91.4)	0.300
PedsQL Total Score	Group 1	**77 (70.3-83.7)**	**83.7 (77.1-90.4)**	**0.027****	**81 (74.3-87.7)**	**86.3 (79.6-93)**	**0.025****
	Group 2	85.1 (80.8-89.4)	85.1 (80.7-89.4)	0.979	82.8 (78.7-87)	85.2 (81.1-89.3)	0.102
PedsQL: Physical Summary Score	Group 1	79.6 (71.0-88.1)	86.3 (77.7-94.9)	0.088	81.7 (73.5-89.9)	85.4 (77.2-93.6)	0.171
	Group 2	84.3 (78.8-89.9)	84.5 (79.0-90.1)	0.941	83.2 (78.1-88.2)	84.6 (79.5-89.6)	0.392
PedsQL: Psycho-social Summary Score	Group 1	**75.9 (69.2-82.6)**	**82.5 (75.7-89.2)**	**0.024****	**80.6 (73.5-87.7)**	**86.8 (79.7-94)**	**0.028****
	Group 2	85.5 (81.2-89.9)	85.4 (81.1-89.8)	0.958	82.7 (78.3-87.1)	85.6 (81.2-89.9)	0.095

NOTE: *Least Square Mean (Confidence Interval); [a]EYE-Q: Effects of Youngsters' Eyesight on Quality of Life, scores range from 0-100, lower scores indicate worse vision-related function and vision-related QOL; [b]PedsQL: Pediatric Quality of Life Inventory, scores range from 0-100, higher scores indicate better QOL in total, physical and psychosocial summary scores; **p<0.05

to disease stabilization or adjustment to the implemented changes over time. Further study on the impact of topical eye drops on a child's QOL and function is needed.

Disclosure: V. Miraldi Utz, None; **A. Cassedy**, None; **T. Hennard**, None; **N. Mwase**, None; **S. Angeles-Han**, NIH, 5.

Abstract Number: 1616

Acceptability of COVID-19 Vaccine Among Pediatric Rheumatology Patients in California's Central Valley

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The U.S. FDA has expanded the emergency use authorization of the COVID-19 vaccine to include children >12 years of age. Gaining an understanding of the acceptability of a COVID-19 vaccine among children with autoimmune diseases may help rheumatologists to develop resources and best practices for shared decision making when offering the COVID-19 vaccine to their patients.

The objective of this study is to evaluate the knowledge and perceptions regarding COVID-19 vaccination and determine the self-reported likelihood of receiving a hypothetical COVID-19 vaccine among children with rheumatic diseases.

Methods: We surveyed a convenience sample of 54 children seen in our pediatric rheumatology clinic in May 2021 to estimate the respondents' perceptions regarding the COVID-19 vaccine. Respondents were asked questions to assess their knowledge about COVID-19 and willingness to accept the COVID-19 vaccine.

Results: Of the 54 patients surveyed, the median age of the participants was 12.9 (range 5-18) years and 78% were females. Racial/ethnic minorities contributed about 52% among the respondents. Forty percent of the respondents had juvenile idiopathic arthritis.

Regarding knowledge about COVID-19 disease, 83% agreed with the statement that COVID-19 was caused by a virus but 20% "agreed" or "strongly agreed" with the statement that influenza and COVID-19 were caused by the same virus. Twenty-one percent of respondents perceived that COVID-19 patients were symptomatic, sick, and required hospitalization. Our respondents gathered information about the pandemic from social media (45%) and television (50%). Sixty-eight percent of patients discussed COVID-19 and its implications with their doctor.

Regarding perceptions about the vaccine, 82% of respondents "strongly agreed" or "agreed" with the statement, "There is misinformation regarding COVID-19 vaccine on the internet". Greater than 75% of our respondents practiced social distancing, hand hygiene and wore masks in public spaces. Although 55% of our respondent reported willingness to accept a COVID-19 vaccine, only 39% perceived that the vaccine would provide protection from the disease and 85% stated concerns about side effects. Respondents cited greater concerns about vaccine side effects when compared to disease complications (40%).

We found that the acceptability of the COVID-19 vaccine was higher among whites when compared to racial/ethnic minorities (84% vs. 58%). Similarly, concerns about side effects and was higher among racial/ethnic minorities. Willingness to pay for the vaccine was also lower among racial/ethnic minorities.

Conclusion: Our study identifies the specific knowledge gaps and incorrect perceptions about COVID-19 and the COVID-19 vaccine among children with rheumatic diseases. Concerns about the effectiveness of the vaccine and potential side effects were high. We found that self-reported likelihood of vaccine acceptability was lower among racial/ethnic minorities when compared to whites. The results of this survey study may help inform public health campaigns to address COVID-19 vaccine hesitancy among these special populations.

Disclosure: S. Sukumaran, None; **R. Patel**, None; **D. Singh**, None.

Abstract Number: 1617

Burden of Adverse Childhood Experiences in Pediatric Chronic Pain and Rheumatic Disease

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Adverse childhood experiences (ACEs) serve as stressors that can have negative, lasting effects on health and wellbeing. While there has been increasing evidence to suggest an etiologic role of ACEs in pediatric chronic pain and rheumatic disease, our understanding of how ACEs may shape a child's clinical presentation remains limited. We aimed to determine 1) the association between the presence of ACEs and clinical manifestations of pediatric chronic pain and 2) explore the interaction of ACEs and pediatric rheumatic disease among youth with chronic pain on health-related outcomes.

Methods: This was a retrospective cross-sectional cohort study of patients 3-18 years old with chronic pain seen in a pediatric rheumatology pain clinic between August 2018 and July 2020 and previously enrolled in a patient registry. Abstracted clinical data included demographics, past medical, psychological, and social histories, as well as patient reported outcome (PRO) measures including: functional disability inventory (FDI; 0-60), verbal pain report (0-10), symptom severity score (SSS; 0-12) and widespread pain index (WPI; 0-19). We stratified our sample into three groups: no ACEs, one ACE and ≥2 ACEs. We assessed clinical signs and symptoms associated with the presence of ACEs using Chi-square or Wilcoxon-rank tests. The association between ACEs and functional impairment was tested using simple and multivariable linear regression.

Results: A total of 412 patients were included in the study. More than 75% of patients reported at least one ACE. The most frequently reported ACEs included history of mental illness in a first degree relative (56%) and parental divorce or separation (20%). Those with ≥2 ACEs had more somatic symptoms, worse physical function, and a higher proportion of comorbid mental health conditions than those with no or one ACE (Table 1). Bivariate linear regression indicated positive linear association of patient physical disability (FDI) with WPI, SSS, and verbal pain (all $p < 0.05$; Table 2). Moreover, presence of mental health conditions and autonomic changes were associated with increased FDI scores in patients. Dose dependent interaction between ACEs and co-morbid rheumatologic conditions was found. As compared to the no ACE group, those with one or more than two ACEs were found to have an additional increase in FDI score by 8.5 and 11 points, respectively, for each additional rheumatologic condition. In multivariable regression (Table 3), higher verbal pain score, symptom severity score and presence of autonomic changes were independently associated with estimated average increase in FDI score by 1.05, 1.95 and 4.76 respectively (all $p < 0.01$). The interaction demonstrating worsened functional impairment from rheumatologic disease for those with ACEs was again observed.

Conclusion: Children with chronic pain and/or rheumatologic diseases who are exposed to ACEs are at increased risk of worse disability, greater symptom severity, and a higher burden of co-morbid mental health conditions. Our findings indicate an ongoing need for systemic evaluation of ACEs exposure in children with chronic pain and/or rheumatic disease and incorporation of trauma-based care.

Table 1. Demographics and Clinical Characteristics among Children with Chronic Pain stratified by Adverse Childhood Experiences Exposure (N=412)

	All Patients (N=412)	No ACEs (n=101)	1 ACE (n =194)	≥2 ACEs (n =117)	p-value
Demographics, N (%)					
Sex, female	342 (83%)	82 (81%)	161 (83%)	99 (85%)	0.80
Race					
Caucasian	307 (75%)	68 (67%)	151 (78%)	88 (75%)	0.14
Black	30 (7%)	5 (5%)	11 (6%)	14 (12%)	0.07
Other	73 (18%)	28 (28%)	31 (16%)	14 (12%)	<0.01
Ethnicity, non-Hispanic	372 (90%)	95 (94%)	170 (88%)	107 (92%)	0.41
Age, median (IQR)	14 (12-16)	14 (11-15)	14 (12-16)	15 (13-16)	0.05
Pain and, Patient and Parent Reported Outcomes, N (%)					
Verbal pain score (0-10), median (IQR)	5 (3-7)	5 (3-8	5 (3-7)	5 (3-7)	0.82
Patient FDI (0-60), median (IQR)	23 (14-33)	23 (14-32)	21 (13-32)	27 (17-34)	0.05
Parent FDI (0-60), median (IQR)	24 (13-32)	24 (12-31)	22 (13-31)	26 (18-34)	0.03
WPI (0-19)	5 (2-10)	6 (1-10)	5 (2-9)	6 (2-10)	0.27
SSS (0-12)	6 (4-8)	5 (3-8)	6 (3-8)	7 (4-9)	<0.01
Duration of symptoms (months), median (IQR)	13 (7-36)	12 (7-24)	18 (7-39)	24 (8-48)	0.05
Autonomic Changes°, Yes	107 (26%)	20 (20%)	62 (32%)	25 (22%)	0.03
Self-reported Cognitive and/or Psychological Conditions, N (%)					
Anxiety / Panic attacks	234 (57%)	34 (34%)	115 (59%)	85 (73%)	<0.0001
Depression	134 (33%)	16 (16%)	58 (30%)	60 (51%)	<0.0001
Eating disorder	8 (2%)	0	3 (2%)	5 (4%)	0.06
Hyperactivity / ADHD	54 (13%)	7 (7%)	23 (12%)	24 (21%)	0.01
Obsessive Compulsive Disorder	38 (9%)	3 (3%)	20 (10%)	15 (13%)	0.03
Previous outpatient mental health care±	252 (61%)	53 (53%)	115 (59%)	84 (72%)	0.01
Previous psychiatric hospitalization	23 (6%)	2 (2%)	8 (4%)	13 (11%)	<0.01
Suicide attempt	18 (4%)	3 (3%)	8 (4%)	7 (6%)	0.54
Suicide ideation	78 (19%)	13 (13%)	32 (17%)	33 (28%)	0.01
Co-morbid Rheumatologic condition					
At least one co-morbid Rheumatologic disease	36 (9%)	9 (9%)	16 (8%)	11 (9%)	0.94

Abbreviations:
N= number of subjects, IQR= Interquartile Range, FDI= Functional Disability Index (total scores range from 0-60 where higher scores indicate worse physical function); WPI= Widespread Pain Index (total scores range from 0-19 where higher scores indicate more widespread pain); SSS=Symptom Severity Score (total scores range from 0-12), ADHD= Attention deficit hyperactivity disorder

° Autonomic changes categories: subjects could report or demonstrate an autonomic change (including temperature change, cyanosis, edema) in > 1 category.

± Previous outpatient mental health care defined as seen at least once by a counselor/therapist/psychologist for pain.

Missing Data: Verbal Pain=1, Patient FDI=4, Parent FDI=8, WPI=9, SSS=10, Duration=3

Table 2. Bivariate Linear Regression Model for Functional Disability reported by Patients with Chronic Pain (N=412)

	β Estimates	95% Confidence Interval		p-value
No ACEs	Ref	Ref	Ref	-
1 ACE	-1.02	-3.97	1.92	0.49
≥2 ACEs	2.28	-0.96	5.53	0.17
Verbal pain score(0-10)	1.92	1.55	2.29	<.0001
WPI (0-19)	0.67	0.47	0.87	<.0001
SSS (0-12)	2.26	1.95	2.56	<.0001
Duration of symptoms (months)	-0.03	-0.08	0.01	0.13
Autonomic Changes, Yes	4.97	2.32	7.63	<.001
History of Mental Health conditions¶, Yes	4.62	1.72	7.52	<0.01
Number of Co-morbid Rheumatologic Diseases	-1.54	-4.59	1.51	0.32

Abbreviations:
WPI= Widespread Pain Index (total scores range from 0-19 where higher scores indicate more widespread pain), SSS=Symptom Severity Score (total scores range from 0-12).
¶ History of mental health conditions include presence of one or more cognitive and/or psychological issues including anxiety, depression, OCD, suicidal ideation; or patient who received outpatient or inpatient mental health care.

Table 3. Multiple Linear Regression Model for Functional Disability reported by Patients with Chronic Pain (N=412)

	β Estimates	95% Confidence Interval		p-value
No ACEs	Ref	Ref	Ref	-
1 ACE	-2.96	-5.31	-0.61	0.01
≥2 ACEs	-1.02	-3.69	1.66	0.46
#Rheumatologic Diseases	-6.71	-12.93	-0.49	0.03
1 ACE*#Rheumatologic conditions	6.85	-0.14	13.83	0.05
≥2 ACEs*#Rheumatologic conditions	8.08	0.72	15.44	0.03
Verbal pain score (0-10)	1.05	0.72	1.39	<.0001
Autonomic Change, Yes	4.76	2.67	6.86	<.0001
SSS (0-12)	1.95	1.64	2.27	<.0001
History of Mental Health conditions¶, Yes	-0.33	-2.70	2.03	0.78

Abbreviations:
#Rheumatologic diseases= number of co-morbid rheumatologic conditions, SSS=Symptom Severity Score (total scores range from 0-12).
¶ History of mental health conditions include presence of one or more cognitive and/or psychological issues including anxiety, depression, OCD, suicidal ideation; or patient who received outpatient or inpatient mental health care.

Disclosure: M. Sonagra, None; **J. Jones**, None; **M. McGill**, None; **S. Gmuca**, None.

Abstract Number: 1618

Disease Flares in CANDLE/PRAAS with Dose Reductions of Baricitinib

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures /proteasome-associated autoinflammatory syndrome (CANDLE/PRAAS) respond to treatment with baricitinib but require higher exposure than doses used to treat patients with rheumatoid arthritis (1, 2). After clinical observations of disease flares associated with baricitinib dose reductions due to a possible adverse event, we systematically assessed the effect of baricitinib dose reductions on the CANDLE/PRAAS disease activity and leveraged these observations for developing and validating "disease flare criteria" that can be used to quantify disease activity and in clinical study design.

Methods: Between October 2011 and August 2018, 10 genetically confirmed CANDLE patients were enrolled in an institutional review board approved open label expanded access program (NCT01724580) and treated with baricitinib. Patients or their parents provided written informed consent. We retrospectively identified all instances of dose reductions and assessed clinical symptoms recorded on a daily diary, laboratory markers of inflammation and an interferon (IFN) score. We observed and characterized clinical symptoms and laboratory changes during disease

Table 1.Definition of Clinical and Subclinical CANDLE/PRAAS Disease Flare

Definition	Laboratory Biomarkers*
Clinical Flare A worsening in DDS** by a minimum of 15% or the documentation of flare symptoms in the medical record *AND* changes in 2 or more laboratory biomarkers	• CRP, ESR, IFN score [≥ 20% increase] • WBC, platelets [≥ 20% **decrease**] • ALC and hemoglobin [≥ 15% **decrease**]
Subclinical Flare Less than 15% worsening in DDS** or on physician evaluation compared to the reference visit *AND* changes in 3 or more laboratory biomarkers	• CRP, ESR, IFN score [≥ 20% increase] • WBC, platelets [≥ 20% **decrease**] • ALC and hemoglobin [≥ 15% **decrease**]

*Acute change in laboratory biomarkers with disease flares compared to the reference visit (last visit with documented laboratory biomarkers prior to reduction period). For inclusion as flare criterion, the change of CRP, ESR and/or IFN score must result in a clinically abnormal value and an increase of greater or equal to 20% must occur.

**Mean DDS for 7 days (ranges from 3 days before and after the visit)

CANDLE/PRAAS, Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature/Proteasome-associated Autoinflammatory Syndrome; DDS, daily diary score; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; WBC, white blood cell count; IFN, interferon; ALC, absolute lymphocyte count.

flare periods and developed “flare criteria” that captured clinically meaningful changes (table 1). Time to flare was evaluated using Kaplan-Meier analysis and the Cox proportional hazards model. To validate the flare criteria, we compared the baricitinib dose reduction associated flare rate during the flare period (post dose reduction) with the flare rate during a stable period (on optimal baricitinib dose) for patients who fulfilled flare criteria using a two-sided chi-squared test of homogeneity.

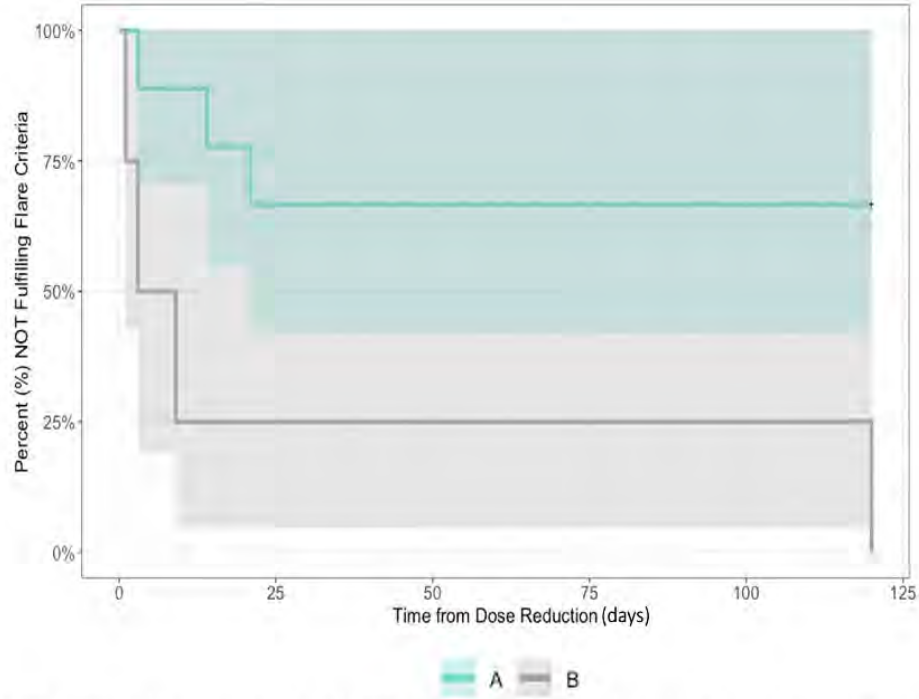

Figure 1. Kaplan-Meier curve depicts the rate of occurrence of baricitinib dose reduction associated disease flares (%) in CANDLE/PRAAS on y axis and time to flare (days) on x axis. Green line represents group A and gray represents group B. Group A is composed of occurrences of 25% or less baricitinib dose reductions (n=9) and group B is composed of occurrences of more than 25% of baricitinib dose reductions (n=4). All four dose reductions (100%) in group B resulted in a disease flare within 120 days whereas 3 out of 9 (33%) baricitinib dose reductions resulted in a disease flare in group A. The difference was significant using the Cox proportional hazards model (p=0.023). One dose reduction was excluded from this analysis and six dose reductions that did not result in a disease flare are censored at 120 days.

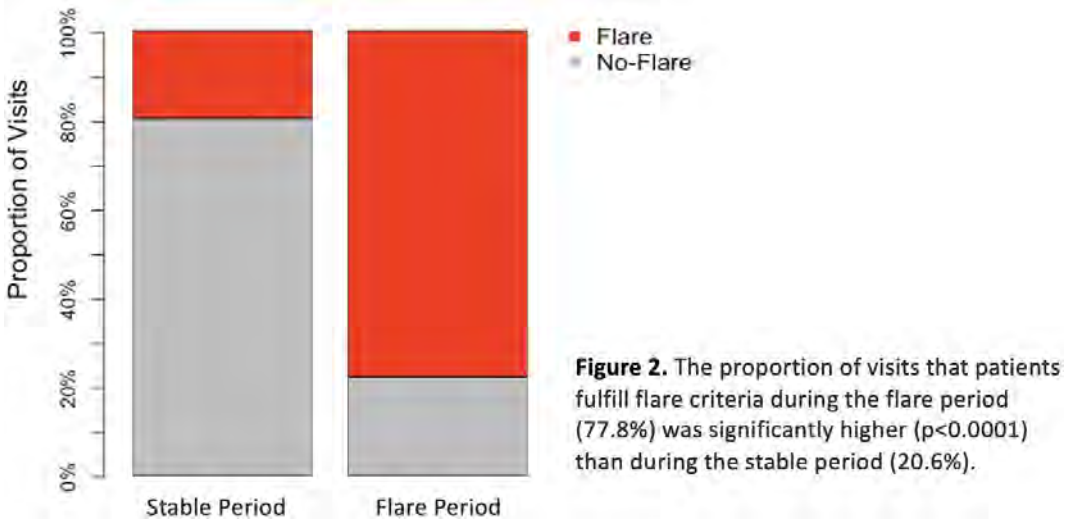

Figure 2. The proportion of visits that patients fulfill flare criteria during the flare period (77.8%) was significantly higher (p<0.0001) than during the stable period (20.6%).

Results: Fourteen baricitinib dose reductions in 9/10 patients occurred and 7/14 (50%) resulted in disease flares in 7/9 patients. A typical flare pattern with acute changes in clinical and/or laboratory biomarkers and cut offs used to define disease flares is outlined in table 1. Time to flare ranged between 1 to 120 days (mean 24 +/- 43 days). A dose reduction of greater than 25% triggered a flare in all patients (figure 1). In patients with baricitinib dose reduction-associated flares, the proportion of visits that patients fulfill flare criteria during the flare period is 77.8% compared to 20.6% during the stable period ($p < 0.0001$) (figure 2).

Conclusion: We observed significant rebound inflammation and disease flares with >25% dose reductions of baricitinib and propose flare criteria that may be used in quantifying diseases flares and in designing clinical studies in CANDLE/PRAAS. It is important to raise awareness of the development of rebound inflammation with baricitinib dose reductions and the need to closely monitor dose reductions.

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2. Montealegre Sanchez GA et al. J Clin Invest 2018; 128(7):3041-3052.

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Abstract Number: 1619

Where Do Multisystem Inflammatory Syndrome in Children (MIS-C) and Pediatric COVID-19 Fit Under the Cytokine Storm Syndrome Umbrella?

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Although COVID-19 has been less severe in the pediatric population, with cases more likely to be mild or asymptomatic, there remains a proportion of pediatric cases with features of cytokine storm syndrome (CSS), leading to hyperinflammation, uncontrolled immune activation, respiratory disease, and end-organ failure. Additionally, multisystem inflammatory syndrome in children (MIS-C) has emerged as a relatively rare post-infectious sequela of COVID-19 with similar hyperinflammation, severe shock, and organ dysfunction. Prior to and during the COVID-19 pandemic, scoring systems have been developed and used to identify patients at risk for CSS. Our study explores the utility of existing CSS, macrophage activation syndrome (MAS), and hemophagocytic lymphohistiocytosis (HLH) scoring systems in identifying pediatric patients at risk for CSS in the setting of MIS-C and COVID-19.

Methods: Pediatric patients with MIS-C and active COVID-19 infection at a single institution were identified. Infectious data, clinical findings, and laboratory values were collected, and patients were stratified by disease severity

into mild MIS-C, severe MIS-C, and severe COVID-19, dependent on symptomology, positive COVID-19 polymerase chain reaction (PCR) or serology, and need for vasopressor and/or ventilatory support. Eight historically utile scoring systems for MAS, HLH, and CSS were used to examine the cohort of MIS-C and pediatric COVID-19 patients for features and diagnosis of cytokine storm.

Table 1. Demographics and Clinical Characteristics

	Mild MIS-C (N=23)	Severe MIS-C (N=18)	MIS-C (N=41)	Severe COVID-19 (n=12)
Age - years (IQR)				
Median	10 (6.5-13.5)	11.5 (10-13)	11 (7-13)	15.5 (2.75-18)
Gender - no. (%)				
Male	11 (48%)	14 (78%)	25 (61%)	8 (67%)
Race/Ethnicity - no. (%)				
White, non-Hispanic	9 (39%)	4 (22%)	13 (32%)	5 (42%)
Black, non-Hispanic	10 (43%)	12 (67%)	22 (54%)	5 (42%)
Hispanic	4 (17%)	2 (11%)	6 (15%)	2 (17%)
Previously Healthy - no. (%)				
Yes	21 (91%)	16 (89%)	37 (90%)	2 (17%)
Underlying Conditions - no. (%)				
Any	2 (9%)	2 (11%)	4 (10%)	10 (83%)
Chronic Lung Disease	0 (0%)	0 (0%)	0 (0%)	2 (17%)
Autoimmune Dx	0 (0%)	0 (0%)	0 (0%)	1 (8%)
Congenital Heart Disease	0 (0%)	0 (0%)	0 (0%)	3 (25%)
Neurodevelopmental Dx	0 (0%)	0 (0%)	0 (0%)	6 (50%)
Symptoms on Presentation - no. (%)				
Fever	23 (100%)	16 (89%)	39 (95%)	8 (67%)
Respiratory Symptoms	3 (13%)	0 (0%)	3 (7%)	11 (92%)
Hypoxia	0 (0%)	0 (0%)	0 (0%)	8 (67%)
Cough	2 (9%)	0 (0%)	2 (5%)	5 (42%)
Shortness of Breath	1 (4%)	0 (0%)	1 (2%)	6 (50%)
Gastrointestinal Symptoms	21 (91%)	17 (94%)	38 (93%)	3 (25%)
Nausea/Vomiting	15 (65%)	11 (61%)	26 (63%)	3 (25%)
Diarrhea	12 (52%)	12 (67%)	24 (59%)	1 (8%)
Abdominal Pain	15 (65%)	12 (67%)	27 (66%)	0 (0%)
Rash	16 (70%)	6 (33%)	22 (54%)	0 (0%)
Conjunctivitis	16 (70%)	10 (56%)	26 (63%)	0 (0%)
Mucosal Changes	4 (17%)	5 (28%)	9 (22%)	0 (0%)
SARS-CoV-2 Positivity - no. (%)				
PCR	9 (39%)	5 (28%)	14 (34%)	12 (100%)
IgG Antibodies - no./total no. (%)	21/22 (95%)	16/16 (100%)	37/38 (97%)	0/2 (0%)
Additional Infectious Agent - no. (%)				
Viral	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Bacterial	2 (9%)	0 (0%)	2 (5%)	2 (17%)
Vasopressor Requirement - no. (%)				
Yes	0 (0%)	18 (100%)	18 (44%)	7 (58%)
No	23 (100%)	0 (0%)	23 (56%)	5 (42%)
Maximum Respiratory Support - no. (%)				
None	17 (74%)	3 (17%)	20 (49%)	0 (0%)
Low Flow Oxygen	4 (17%)	7 (39%)	11 (27%)	1 (8%)
High Flow Oxygen	2 (9%)	2 (11%)	4 (10%)	0 (0%)
Positive pressure ventilation	0 (0%)	6 (33%)	6 (15%)	11 (92%)

Demographics and Clinical Characteristics of Patient Population

Table 2. Cytokine Storm Score On Admission				
	Mild MIS-C	Severe MIS-C	Total MIS-C	Severe COVID-19
HLH-2004	0/23 (0%)	0/18 (0%)	0/41 (0%)	0/12 (0%)
H-score > 169	0/23 (0%)	0/18 (0%)	0/41 (0%)	0/12 (0%)
H-score Median (IQR)	19 (0-46)	19 (19-51.25)	19 (0-49)	50.5 (13.5-72.25)
2016 sJIA/MAS	0/23 (0%)	3/18 (16.7%)	3/41 (7%)	3/12 (25%)
2019 sJIA MS Score > -2.1	11/23 (48%)	11/18 (61.1%)	22/41 (54%)	10/12 (83%)
2019 sJIA MS Score Median (IQR)	-2.10 (-2.3-(-1.42))	-1.42 (-2.94-0.05)	-1.95 (-2.53-(-0.32))	0.163 (-1.59-1.75)
Ferritin/ESR ratio > 11.3	8/23 (35%)	7/18 (38.9%)	15/41 (37%)	9/11 (82%)
Ferritin/ESR ratio > 21.5	2/23 (9%)	5/18 (27.8%)	7/41 (17%)	9/11 (82%)
Ferritin/ESR ratio Median (IQR)	7.56 (6.16-13.94)	11.22 (7.64-25.35)	9.65 (6.23-15.51)	45.47 (32.36-86.9)
Caricchio COVID-CS Criteria	-	-	-	2/11 (18%)
COVID-19 cHIS Criteria Median (IQR)	3 (2-4)	4 (3-4.75)	3 (3-4)	2.5 (1-3.25)
COVID-19 CSS Quick Score	9/23 (39%)	9/17 (52.9%)	18/40 (45%)	1/12 (8%)

Table 3. Maximum Cytokine Storm Score During Hospitalization				
	Mild MIS-C	Severe MIS-C	Total MIS-C	Severe COVID-19
HLH-2004	0/23 (0%)	1/18 (5.6%)	1/41 (2%)	0/12 (0%)
H-score > 169	0/23 (0%)	0/18 (0%)	0/41 (0%)	3/12 (25%)
H-score Median (IQR)	68 (49-68)	68 (52-100.25)	68 (49-79)	101 (55.75-142.5)
2016 sJIA/MAS	4/23 (17%)	6/18 (33.3%)	10/41 (24%)	6/12 (50%)
2019 sJIA MS Score > -2.1	16/23 (70%)	15/18 (83.3%)	31/41 (76%)	12/12 (100%)
2019 sJIA MS Score Median (IQR)	-1.4 (-2.08-(-0.78))	-0.56 (-1.84-0.69)	-0.91 (-1.97-0.47)	1.69 (0.59-2.43)
Ferritin/ESR ratio > 11.3	12/23 (52%)	11/18 (61.1%)	23/41 (56%)	10/11 (91%)
Ferritin/ESR ratio > 21.5	5/23 (22%)	7/18 (38.9%)	12/41 (29%)	9/11 (82%)
Ferritin/ESR ratio Median (IQR)	12.04 (7.42-17.78)	16.69 (12.48-34.48)	13.95 (7.92-30.44)	66.07 (33.57-102.89)
Caricchio COVID-CS Criteria	-	-	-	8/11 (73%)
COVID-19 cHIS Criteria Median (IQR)	4 (2.5-4.5)	4.5 (4-5)	4 (3-5)	4.5 (3-5)
COVID-19 CSS Quick Score	15/23 (65%)	12/17 (70.6%)	27/40 (68%)	10/12 (83%)

Results: 23 patients with mild MIS-C, 18 patients with severe MIS-C, and 12 patients with severe COVID-19 were identified. The HLH-2004 and HScore scoring systems did not identify any MIS-C or COVID-19 patients as having CSS on admission to the hospital, with only one MIS-C patient meeting HLH-2004 criteria and three patients meeting HScore criteria at peak disease severity during hospitalization. The 2016 sJIA/MAS criteria, ferritin/ESR ratio, and COVID-19 CSS Quick Score identified CSS in more patients and was more useful in distinguishing between COVID-19 and MIS-C hyperinflammation and severity. The 2019 MS Score and COVID-19 cHIS criteria were less helpful, as the MS score likely overestimated CSS due to use of headache as a feature of its criteria, and the cHIS resulted in similar scores across the board regardless of severity or disease. The Caricchio COVID-CS did well in identifying CSS in pediatric COVID-19, but was less useful in MIS-C due to its COVID-19 specific criteria.

Conclusion: MIS-C and pediatric COVID-19 result in relatively unique cytokine storm syndromes and patterns of inflammation. Existing scoring systems for cytokine storm syndromes likely do not capture the full breadth of this disease process in MIS-C and pediatric COVID-19.

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Abstract Number: 1620

Pediatric Onset (< 16 Years) Non-infectious Uveitis: Results from Spanish National Registry

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Pediatric noninfectious uveitis is a major clinical challenge for Pediatric ophthalmologists and rheumatologists. The burden of disease is considerable and etiological diagnosis elusive in many cases. Uveitis outcomes have improved dramatically with antirheumatic drugs, especially anti TNFα agents.

Methods: A multicenter cross sectional and retrospective cohort study was conducted from october 2019 to march 2021. Multidisciplinary participation was mandatory for joining the study; to ensure homogeneity data of associated systemic disease and disease modifying antirheumatic drug (DMARD) therapy were provided by rheumatologist and ophthalmology related data were introduced by ophthalmologist, in a web based form. Only patients with uveitis onset before 16th birthday and complete data were included in the analysis. Three distinct groups were made for comparison: Juvenile Idiopathic Arthritis related uveitis (JIAu), Idiopathic childhood uveitis (ICU) and Pars Planitis (PP).

Results: A total of 501 patients from 22 centers were included in the analysis, 310 (61.9 %) with an associated immune disease, 91 (18.2%) with an ophthalmologically distinguishable uveitis and 100 (20%) idiopathic. JIAu accounted for 54.8 % (275), 259 (51.6%) non B27 related; 67 patients (13.3%) had PP. JIAu was significantly associated with female gender, younger age at uveitis onset, ANA positive, anterior location and insidious presentation, with less ocular complications, systemic corticoid use and ocular surgeries. DMARD exposure was more prolonged, started

earlier after uveitis onset and had less unilateral severe visual loss. ICU tended to present as panuveitis and was associated with male gender, older age at onset, ANA negative, acute presentation and acute clinical course. Ocular complications were higher, mainly synechiae at onset and cataracts. Exposure to DMARD was significantly lower for both synthetic and biologic agents. PP showed the highest complication rate within groups (71.6%), especially cataracts during follow up and greater tendency to present vitreoretinal complications (macular edema, epiretinal membrane and retinoschisis), requiring ocular surgery more frequently. PP patients also received more systemic steroids, showing no difference in regards to DMARD use.

Conclusion: We present a large cohort of childhood onset not infectious uveitis. Homogeneity of data was cared for with a multidisciplinary approach, but case selection bias may have occurred as participation and case selection was voluntary. Our data suggest that differences in outcome may correspond partially to differences in treatment

Table 1. Demographic and clinical data

		ALL patients	JIAu patient (B27 excluded)	Idiopathic/nonclassified	Pars Planitis
Number of cases (N)		501	259	100	67
Sex (% female)		64.7	**82.2***	**49***	**40.3***
Age (years +/- SD)		12.35 +/- 4.68	**11.27 +/- 5.01*** **JIA Onset: 3.02 +/-2.68***	**12.13 +/- 4.75 ***	**13.57 +/- 3.93***
Age uveitis onset (years +/- SD)		6.70 +/- 3.99	**4.91 +/- 3.82 ***	**8.60 +/- 3.19 ***	**8.13 +/-2.83 ***
Uveitis followup (months +/- SD)		67.24 +/- 47.32	**75.89 +/- 47.72 ***	**54.94 +/-45.7 ***	64.16 +/- 47.27
Other immune disease; N (%)		48 (9.6)	28 (10.8)	5 (5)	6 (8.9)
Antinucleas antibodies + N (%)		217 (43.3)	**180 (69)***	**21 (21)***	**5 (7.4)***
Laterality	Unilateral N(%)	160 (31.9)	90 (34.7)	28 (28)	14 (20.9)
	Alternate bilateral N(%)	41 (8.3)	24 (9.3)	5 (5)	5 (7.5)
	Bilateral N(%)	300 (59.8)	145 (56)	68 (68)	48 (71.6)
Clinical onset	Acute N(%)	197 (39.3)	**64 (24.8)***	**63 (63)***	23 (34.3)
	Insidious N(%)	304 (60.7)	**195 (75.2)***	**38 (38)***	44 (65.7)
Duration	Self-limmited N(%)	193 (38.5)	107 (41.3)	32 (32)	**10 (14.9)***
	Persistent N(%)	308 (61.5)	152 (58.7)	69 (69)	**57 (85.1)***
Clinical curse	Acute N(%)	83 (16.6)	36 (13.9)	**25 (25)***	**1 (1.5)***
	Acute/recurrent N(%)	77 (15.4)	38 (14.7)	15 (15)	**7 (10.5)***
	Chronic N(%)	341 (68.1)	185 (71.4)	**61 (60.4)***	**59 (88)***

SD: standard deviation ***Statistically significant differences (p<0.05)**

Table 2. Ocular complications, surgery and poor visual outcome

		ALL patients	JIA patient (B27 excluded)	Idiopathic/nonclassified	Pars Planitis
Number of cases (N)		501	259	100	67
Any Complications N(%)		226 (45.1)	**80 (30.9)***	**59 (59)***	**48 (71,6)***
Sinequiae	Anytime N(%)	139 (27.7)	**58 (22.3)***	**38 (38)***	18 (26.8)
	Onset N(%)	106 (21.2)	**39 (15)***	**31 (31)***	13 (19.4)
Ocular hypertension anytime N(%)		53 (10.6)	23 (8.8)	12 (12)	10 (14.9)
Glaucoma anytime N(%)		11 (2.2)	4 (1.5)	3 (3)	2 (2.9)
Cataract	Anytime N(%)	81 (16.2)	**29 (11.1)***	**23 (23)***	**18 (26.9)***
	Onset N(%)	28 (5.6)	**10 (3.8)***	**10 (10)***	**3 (4)***
Mac. Edema	Anytime N(%)	49 (9.8)	**7 (2.7)***	11 (11)	**20 (29.8)***
	Onset N(%)	34 (6.8)	4 (1.5)	11 (11)	13 (19.4)
Epiretineal membrane N(%)		16 (3.2)	**1 (0.3)***	5 (5)	**6 (8.9)***
Band cheratopathy N(%)		66 (13.2)	36 (13.8)	14 (14)	10 (14.9)
Retinosquisis N(%)		12 (2.4)	**1 (0.3)***	**0***	**11 (16.4)***
Ptisis N(%)		4 (0.8)	**2 (0.7)***	0	1 (1.5)
Papilar edema N(%)		32 (6.4)	**6 (2.3)***	8 (8)	10 (14.9)
Surgery N(%)		50 (10)	**13 (5)***	13 (13)	**15 (22.3)***
Poor Visual outcome (AV≤0.3)	Eyes affected N/eyes (%)	26/838 (3.1)	7/338 (2)	6/146 (4)	6/106 (5.6)
	Unilateral patients (N,%)	16 (3.2)	**3 (1.2)***	4 (4)	4 (6)
	Bilateral patients(N,%)	5 (1)	2 (0.8)	1 (1)	1 (1.5)

***Statistically significant differences (p<0.05)**

Table 3. Treatment

		ALL patients	JIAu patient (B27 excluded)	Idiopathic/nonclassified	Pars Planitis
Number of cases (N)		501	259	100	67
Treatment exposure (months +/- SD)		46.6 +/- 39.96	**52.95 +/- 42.81 ***	**35.37 +/- 29.8 ***	**39.12 +/- 32.27 ***
Treatment exposure after uveítis diagnosis (days+/- SD)		1159+/-1111	**1248+/-1208***	**913+/-797***	1190+/-1068
Time from uveítis diagnosis to DMARD start (days +/- SD)		172 +/- 561	**89 +/- 313***	290+/- 805	200+/-313
DMARD synthetic	Last visit N(%)	356 (71)	**206 (79.5)***	61 (61)	**45 (67.1)***
	Anytime N(%)	431 (86)	**252 (97.2)***	**75 (75)***	56 (83.5)
DMARD biologic	Last visit N(%)	294 (58.6)	**78 (69.8)***	44 (44)	35 (52.2)
	Anytime N(%)	329 (65)	**200 (77.2)***	**52 (52)***	39 (58.2)
Systemic steroids for uveitis N(%)		199 (39.7)	**60 (23.1)***	43 (43)	**54 (80.6)***

SD: standard deviation ***Statistically significant differences (p<0.05)**

approach depending on the aetiology or diagnosis associated with the ocular inflammatory disease. Surprisingly, JIAu patients showed the best prognosis despite its chronicity in comparison with the other groups, traditionally considered mild self-limited diseases. Awareness of ophthalmologists and rheumatologists on these observations could ameliorate the burden of disease by inducing rheumatology referral for early treatment.

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Abstract Number: 1621

Self-reported Transition Readiness of Adolescent Patients with Rheumatologic Disease: Do the Parents Agree?

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

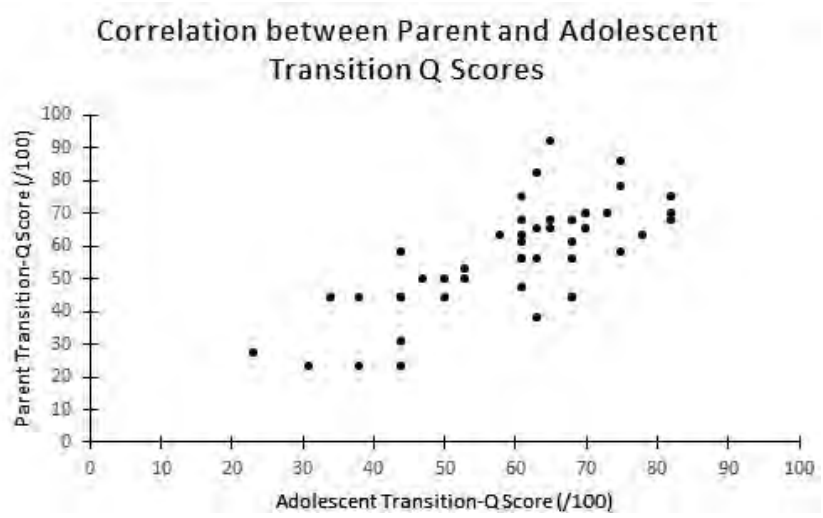

Figure 1. Correlation between parent and adolescent Transition-Q scores.

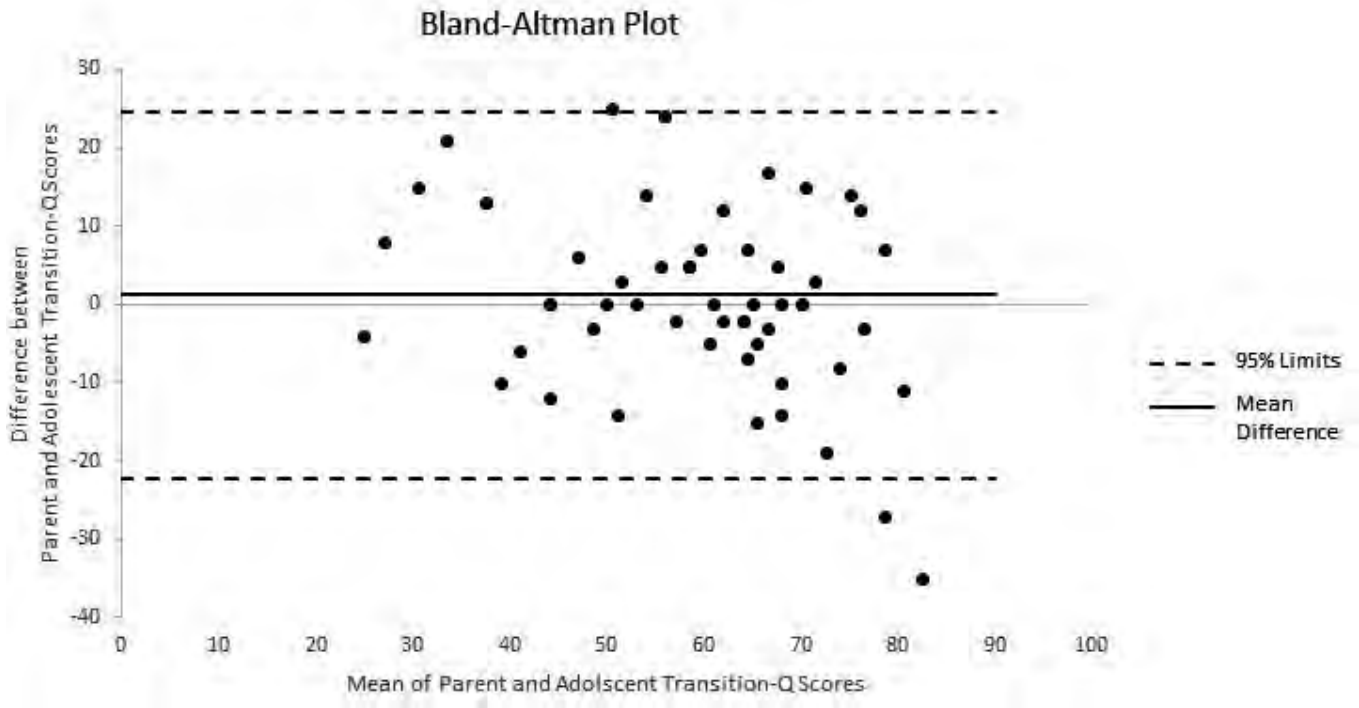

Figure 2. Agreement between parent and adolescent Transition-Q scores illustrated by Bland-Altman plot.

Background/Purpose: The transition from pediatric to adult rheumatology care is associated with increased disease activity and morbidity. The parent-child relationship is a significant relationship in the transition journey and parents play a key role in promoting self-management skills in adolescent patients. Assessing both adolescents' and parents' perception of the adolescent's independence and self-management skills are important to identifying discordant views and developing strategies to improve transition. Thus, we compared transition readiness assessment scales from both perspectives and analyzed their level of agreement.

Methods: Adolescents aged 14-18 years old with JIA or jSLE and their parents were recruited in our multidisciplinary rheumatology transition clinic. The patient and one parent both independently completed the TRANSITION-Q during clinic appointments. The TRANSITION-Q is a 14-item, validated, self-administered questionnaire assessing health-

care self-management skills where higher scores (max. 100) indicate greater transition readiness. Total scores and frequencies of responses to each question ("never", "sometimes" or "always") were recorded and the proportion of agreement between their responses were determined. Pearson correlation analyses determined the correlation between adolescent and parent total transition scores and agreement was analyzed using a Bland-Altman plot.

Results: Among 57 patient/parent dyads, the Pearson correlation coefficient between parents' and adolescents' total scores was 0.71 ($p< 0.001$). Bland-Altman analysis illustrated generally good agreement with a mean difference of 1.2 and no consistent bias between parent and adolescent scores. For each question, dyads agreed an average of 70% of the time. The majority of disagreement was mild (i.e. sometimes/always or sometimes/never). Most frequent disagreements pertained to adolescents' discussion with people about their health condition and asking questions regarding their health. Extreme disagreements (i.e. always/never) were rare and only occurred 7% of the time in relation to whether adolescents contact the doctor when they need to, and 9% of the time in relation to seeing the doctor/nurse on their own.

Conclusion: Adolescents and parents generally agree on the level of the adolescent's transition readiness, however there is occasional disagreement in specific domains. Identifying items more prone to disagreement can help identify areas to target future interventions to improve self-management skills in adolescent patients and successful transition to adult care.

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Abstract Number: 1622

Mind the Gap: The Experience of Adolescents in a Rheumatology Transition Clinic

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The transition from pediatric to adult healthcare is a critical time for the wellbeing of patients with chronic illness including rheumatologic disease. Low patient engagement during transition has been associated with lower treatment adherence, poor clinic attendance, increased hospital admissions and adverse health outcomes. A supportive environment and a multidisciplinary approach to transition, including the presence of both an adult and paediatric rheumatologist, are key components to support youth as they prepare to transition. We aimed to assess the transition clinic experiences of rheumatology patients to identify potential areas for improvement.

Methods: The "Mind the Gap" validated questionnaire was administered to our Rheumatology Transition Clinic patients, with either JIA or jSLE, aged 14-18 years. The questionnaire assesses the transition clinic expectations and experiences and includes 22 questions covering 3 domains: management of environment, provider characteristics and process issues. Patients completed the questionnaire twice on a single occasion; first with respect to their "ide-

Table 1. Mean (min, max) gap scores by domain

Domain	Male (n=20)	Female (n=43)	Total (n=63)
Management of the Environment	0.0 (-1, 2.4)	0.4 (-3.8,5.4)	0.2 (-3.8,5.4)
Provider Characteristics	0.2 (-0.9, 1.5)	0.3 (-1.4,6.9)	0.2 (-1.4,6.9)
Process Issues	0.2 (-1.5, 2)	0.5 (-1.7,5.7)	0.3 (-1.7,5.7)

Table 2. Percentages of patients who recorded a gap score ≥1

	%
Management of Environment	
Provides opportunities for me to meet other young people with arthritis	43
Has a physical environment that caters to my age group	39
Provider Characteristics	
Has staff who understand the realities of being teenagers	34
Has staff I can talk to about sensitive or difficult issues	43
Has staff who know how to talk and listen to teenagers	34
Process Issues	
Let's other people know how arthritis affects me (e.g. school teachers)	45

Only percentages above 33% are reported

al" experience and second regarding their current clinic experience. Responses ranged from strongly disagree (1) to strongly agree (7). For each question, a "gap" score was calculated by subtracting the current from the ideal score. A score of 0 signifies that the current experience is ideal; positive scores suggest current care is less than ideal, and negative scores suggest current care exceeds the ideal experience. The greater the positive gap score, the lower the level of satisfaction. Similarly, the greater the negative gap score, the greater the satisfaction. Descriptive statistics summarized our patients' responses.

Results: Of 63 patients (43 female, 20 male) with a mean (SD) age of 16.4 (1.2), 86% had JIA and 14% had jSLE. For each domain, the mean gap score was between 0 and 1, indicating virtually no gap between current and ideal care (Table 1). Table 2 reveals areas where the gap score ≥1. The largest frequency of patients recording a gap score ≥ 1 was 45%, for the clinic's ability to communicate information to the patient's school teachers. When comparing gap scores for males and females, mean gap scores were similar for the environment and process issues. However, for provider characteristics, mean (SD) gap scores for females (0.41 (1.2)) appeared higher than males (0.0, (0.5)). Females were less satisfied with how well the staff knew them and the staff's "ability to understand the realities of being a teenager".

Conclusion: Although overall Transition Clinic experiences appear to be meeting the expectations of the majority of our rheumatology patients, there is room for improvement within all three domains. Future directions should include developing standardized interventions to address the identified gaps, such as communication with schools and the provider's abilities to discuss sensitive issues.

Disclosure: C. Fine, None; **K. Beattie**, None; **T. Cellucci**, None; **L. Heale**, None; **M. Matsos**, Astra Zeneca, 2, 6, GSK, 6, Abbvie, 6; **S. Garner**, None; **M. Batthish**, Abbvie, 5, Novartis, 6, Mylan, 1, Sobi, 1.

Abstract Number: 1623

Impact of the COVID-19 Pandemic on Presentation of JIA to Pediatric Rheumatology Care in Canada

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The COVID-19 pandemic has disrupted the delivery of routine healthcare and clinical research around the world. Several reports have shown an impact on rheumatology care. The U.K. reported that rheumatologists were averaging a 50% reduction in clinic function during the first six months of the pandemic. Higher rates of JIA disease flares presenting to hospital during the pandemic were reported by our Italian colleagues, perhaps due to delayed follow-up intervals. The aim of this study was to characterize COVID-related disruptions in JIA research and initial presentation of JIA to pediatric rheumatology (PR) care in Canada. We hypothesize that research disruption would be mostly reflected by a drop in study recruitment, while disruption of care would result in prolongation of time from symptom onset to first assessment and a greater severity at presentation.

Methods: Data was collected by the Canadian Alliance of Pediatric Rheumatology Investigators (CAPRI) National JIA Registry, a registry of children newly diagnosed with JIA that collects and shares longitudinal data on disease course, outcomes and adverse events. Data from the year pre-pandemic (March 11, 2019-March 10, 2020) was compared to data from the pandemic year (March 11, 2020-March 10, 2021). The number of patients enrolled in the Registry during the two periods was determined. To assess the pandemic's impact, we compared time from symptom onset to first PR appointment, disease activity at presentation, and parent/patient reported well-being at presentation. Descriptive analysis of the data was performed. Proportions were compared with chi square tests and medians with Mann-Whitney tests.

Results: A total of 225 patients were enrolled in the pre-pandemic year, and 111 in the pandemic year. Registry enrollment was notably decreased during the months of March to June 2020, at the start of the global pandemic (Figure 1). The median time from symptom onset to first assessment was 138 days (IQR 64-365 days) in the pre-pandemic year, and 146 days (IQR 83-359 days) in the pandemic year. The JIA categories of patients enrolled remained stable; predominantly oligoarthritis (44% pre-pandemic, 46.8% pandemic) with the next most common being enthesitis-related arthritis and RF-negative polyarthritis in both cohorts (Table 1). Clinical features and patient reported measures were very similar between the two cohorts. The Physician Global Assessment

Figure 1. Monthly recruitment in the CAPRI JIA Registry pre-pandemic and during pandemic.

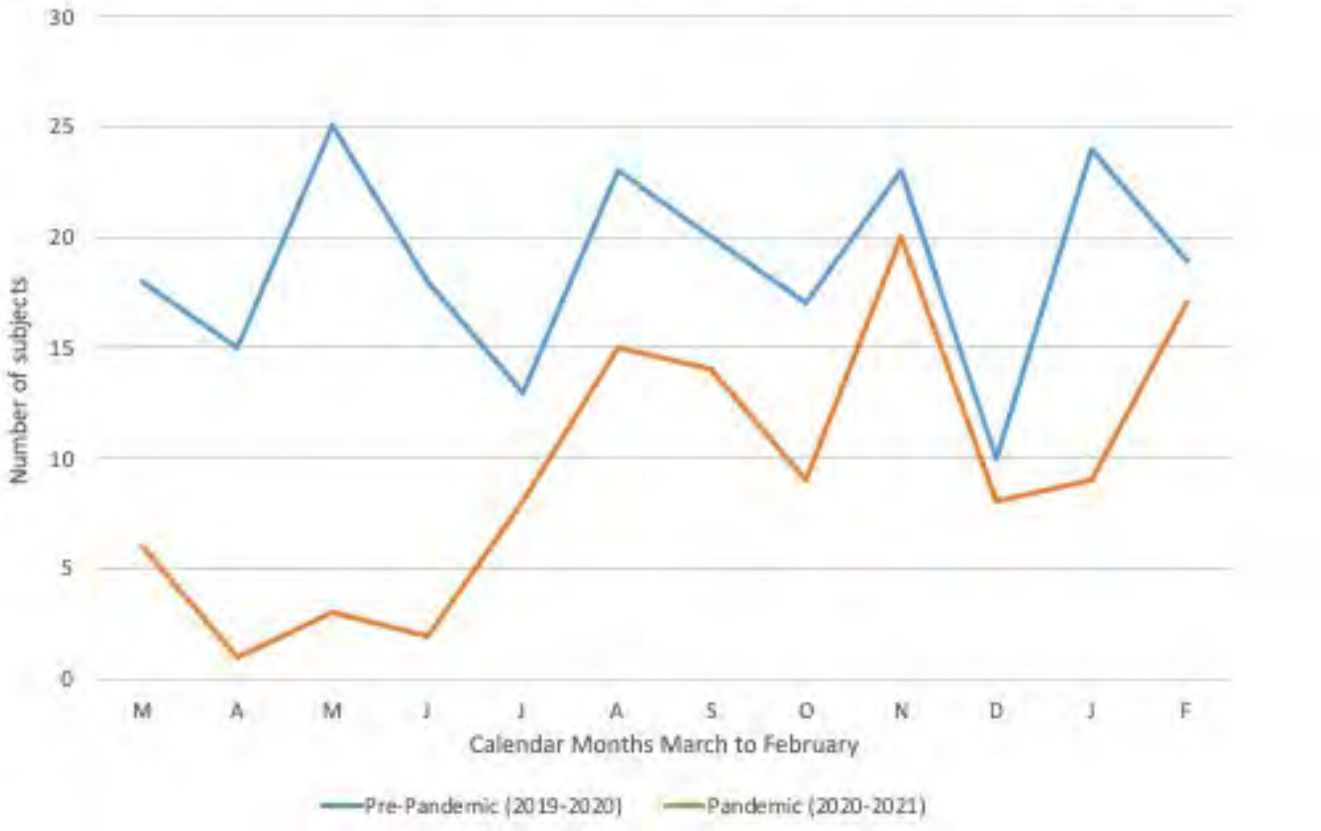

Table 1. JIA category of enrolled patients pre-pandemic and during pandemic.

	Pre-Pandemic Cohort (n=225)	Pandemic Cohort (n = 111)
JIA Category	# (%)	# (%)
Oligoarticular	70 (31.1%)	37 (33.3%)
Oligoarticular – persistent	29 (12.9%)	13 (11.7%)
Oligoarticular – extended	0	2 (1.8%)
Systemic	12 (5.3%)	1 (0.9%)
Polyarticular RF -ve	40 (17.8%)	18 (16.2%)
Polyarticular RF +ve	11 (4.9%)	2 (1.8%)
Psoriatic arthritis	14 (6.2%)	11 (9.9%)
Enthesitis-related arthritis	33 (14.7%)	19 (17.1%)
Undifferentiated	16 (7.1%)	8 (7.2%)

(PGA) of Disease Activity Score and Juvenile Arthritis Quality of Life Questionnaire (JAQQ) were virtually identical (Table 2).

Conclusion: The CAPRI National Registry has allowed us to describe the impact of the global COVID-19 pandemic on JIA presentation to PR care. Research disruption was associated with a 50% enrollment decrease in the pandemic year, most significantly from March to June 2020. It has since improved, consistent with a limit in non-essential research staff presence in hospitals early on. We did not observe the hypothesized delay in presentation and increased severity at presentation. This suggests that within Canada, PR care has adapted well to provide ongoing support and care to new patient consults and avoided significant negative impacts.

Submitted on behalf of the CAPRI Registry Investigators.

Table 2. Characteristics at presentation pre-pandemic and during pandemic.

	Pre-Pandemic Cohort (n=225)	Pandemic Cohort (n = 111)	
Clinical Features at Presentation			*p-value*
Median active joint count (IQR)	2.0 (1.0-5.0)	2.0 (1.0-4.0)	0.835
Median limited joint count (IQR)	1.0 (1.0-4.0)	1.0 (0.0-3.0)	0.257
Percentage of patients with:			
Extraarticular manifestations*	21.8%	20.7%	0.793
Elevated ESR	41.8%	25.4%	<0.0001
Elevated CRP	36.9%	37.8%	0.925
Median PGA (IQR) (0-10)	3.0 (1.9-5.0)	3.0 (1.6-4.9)	0.836
Median JAQQ (IQR) (1-7)	3.0 (1.7-4.0)	2.8 (1.8-3.8)	0.860
Patient Reported Outcomes			
Median Parent Pain Score (IQR) (0-10)	3.0 (1.0-6.0)	3.0 (1.0-6.0)	0.848
Median Patient Pain Score (IQR) (0-10)	4.0 (0.5-7.0)	3.3 (1.0-5.6)	0.680
Median CHAQ Score (IQR) (0-3)	0.4 (0.0-1.0)	0.4 (0.0-0.9)	0.871
Median Quality of My Life Score (IQR) (0-10)	8.0 (5.0-9.0)	7.0 (6.0-9.0)	0.834

* Includes psoriatic rash, nail changes, enthesitis, dactylitis, and systemic JIA manifestations. PGA: Physician Global Assessment of Disease Activity; JAQQ: Juvenile Arthritis Quality of Life Questionnaire; CHAQ: Child Health Assessment Questionnaire.

Disclosure: M. Dushnicky, None; **C. Campbell**, None; **K. Beattie**, None; **R. Berard**, Sandoz, 2, SOBI, 2, Roche, 2; **T. Cellucci**, None; **M. Chan**, Novartis, 2; **T. Gerschman**, None; **K. Houghton**, None; **N. Johnson**, None; **C. LeBlanc**, None; **L. Lim**, None; **N. Luca**, None; **P. Miettunen**, None; **K. Morishita**, None; **J. Proulx-Gauthier**, None; **D. Rumsey**, None; **H. Schmeling**, Pfizer, 12, Sponsor of clinical trial, Roche, 12, Sponsor of clinical trial, Bristol-Myers Squibb, 5, UCB Biosciences GmbH, 12, Sponsor of clinical trial, Janssen, 12, Sponsor of clinical trial, Sanofi-Aventis, 12, Sponsor of clinical trial; **R. Scuccimarri**, Novartis, 1, Bristol Myers Squibb, 5; **H. Tam**, None; **J. Guzman**, None; **M. Batthish**, Abbvie, 5, Novartis, 6, Mylan, 1, Sobi, 1.

Abstract Number: 1624

Patient-Reported Care Utilization, Socioeconomic Status, and Health Status Among Young Adults with JIA

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Young adulthood is a vulnerable period for individuals with childhood-onset rheumatic diseases, especially the transition from pediatric to adult care. Our objective was to determine patterns in patient-reported care utilization, socioeconomic status, and health status among young adults with juvenile idiopathic arthritis (JIA), including factors associated with completed transfer to adult rheumatology.

Methods: We analyzed prospectively collected observational data from the Childhood Arthritis and Rheumatology Research Alliance (CARRA) JIA Registry. Enrollment began in 2015, collecting clinical information from pediatric

Table 1. Patient-reported care utilization, socioeconomic status, and health status in patients with JIA ≥ 18 years at first CARRA Long-Term Follow-Up Call Registry visit

	Total (n=187)	Adult Rheumatology Transfer Complete (n=101)	Transfer Not Complete (n=86)	p-value
Female gender, n (%)	144 (77)	82 (81)	62 (72)	0.130
Race/ethnicity, n (%)				0.104*
White	147 (79)	78 (77)	69 (80)	
Hispanic	23 (12)	15 (15)	8 (9)	
Black	9 (5)	2 (2)	7 (8)	
Other	8 (4)	6 (6)	2 (2)	
"Transition", reason for inactive status, n (%)	111 (59)	75 (74)	36 (42)	**<0.001**
Transition Preparedness (0-10), median (IQR)	9 (7-10)	9 (7-10)	9 (7-10)	0.639**
Care Utilization, n (%)				
Hospitalizations	17 (9)	7 (7)	10 (12)	0.135
ER Visits	10 (5)	2 (2)	8 (9)	0.999
Socioeconomic Status, n (%)				
Current Private Insurance Status	148 (79)	88 (87)	63 (70)	**0.006**
Receiving Disability	11 (6)	6 (6)	5 (6)	0.992
Highest Year of School Completed				**0.003***
Some college	115 (62)	72 (71)	43 (51)	
Grade 12 or GED	60 (32)	22 (22)	38 (45)	
Current Employment Status				**0.049***
Full-time student	123 (66)	74 (73)	49 (58)	
Full-time or part-time employment	36 (19)	12 (12)	24 (28)	
Not employed	11 (6)	6 (6)	5 (6)	
JIA Status at Last CARRA Registry Visit				
Physician global assessment (0-10), median (IQR)	0.5 (0-2)	1 (0-2)	0.5 (0-2)	0.331**
Patient global assessment (0-10), median (IQR)	1 (0-5)	2 (0-5)	1 (0-3)	0.150**
Total number of active joints, median (IQR)	0 (0-2)	0 (0-2)	0 (0-2)	0.847**
Total number of limited joints, median (IQR)	0 (0-1)	0 (0-2)	0 (0-1)	0.948**
Morning stiffness, n (%)	100 (53)	58 (57)	42 (49)	0.361
JIA Status at First Call Registry Visit				
Average age at first Call Registry visit, mean (SD)	20.0 (1.4)	20.4 (1.4)	19.7 (1.2)	**<0.001****
Time between last CARRA Registry visit and first Call Registry visit, mean (SD) months	7.8 (4.0)	7.7 (4.2)	7.8 (3.9)	0.621**
Time between diagnosis and first Call Registry visit, mean (SD) years	7.5 (4.9)	7.8 (5.0)	7.0 (4.8)	0.229**
Global assessment of well-being (0-10), median (IQR)	2 (0-5)	3 (1-5)	1 (0-5)	0.389**
Pain over the past week (0-10), median (IQR)	3 (1-6)	4 (1-6)	2 (0-5)	**0.028****
Disease activity over the past week (0-10), median (IQR)	2 (0-5)	3 (1-5)	1.5 (0-3.5)	**0.011****
Any joint pain or swelling last 6 months, n (%)	111 (63)	62 (65)	49 (61)	0.583
Morning stiffness over past week, n (%)	69 (42)	44 (44)	25 (33)	**0.044**

Note: Transfer not complete category includes patients under the care of pediatric rheumatologist, both adult and pediatric rheumatologist, or not any rheumatologist. *Bold indicates significance, p<0.05; *Fisher Exact Test, **Wilcoxon Two-Sample Test

Table 2. Active medication entries at last CARRA Registry visit and first Call Registry visit for young adults with JIA in the CARRA Long-Term Follow-Up Call Registry visit

	Last CARRA Registry Visit, n (%)	First Call Registry Visit, n (%)
Biologic monotherapy	61 (33)	63 (34)
Combination Biologic + conventional DMARD	50 (27)	42 (22)
Conventional DMARD	20 (11)	15 (8)
NSAID only	10 (5)	13 (7)
Non-JIA medication	2 (1)	2 (1)
No active medication entries	44 (24)	52 (28)
Total	187	187

rheumatology centers every 6 months. After a 6-month period of Registry inactive status, patients are automatically enrolled in the Long-Term Follow-Up Call Registry which collects patient-reported information via phone surveys every 6 months. We included patients in the Call Registry with JIA who were ≥18 years old at their first Call visit. We

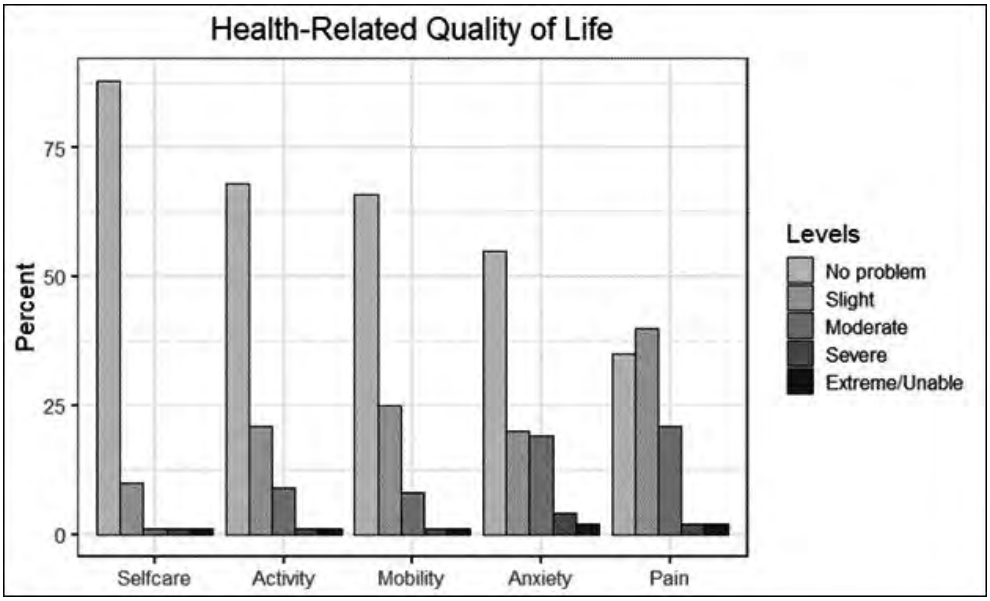

Figure 1. Reported problems in health-related quality of life (EQ-5D domains) among young adults with JIA in the CARRA Long-Term Follow-Up Call Registry.

extracted available demographic, care utilization, and socioeconomic and health status data from each patient's last CARRA Registry visit and first Call Registry visit. We compared characteristics of patients who completed transfer to adult rheumatology care to those who did not.

Results: Of 187 young adults in the Call Registry, 101 (54%) had completed transfer to an adult rheumatologist, 30 (16%) reported still being under the care of a pediatric rheumatologist, 9 (5%) were under the care of both an adult and pediatric rheumatologist, and 56 (30%) were not under the care of any rheumatologist. "Transition" was the most common reason for inactive CARRA Registry status and was more likely for those who completed transfer compared to those who did not, though there was no difference in reported transition preparedness between groups (Table 1). Transferred patients were more likely to have private insurance, have completed some college, be full-time students, and were older at first Call visit compared to those who had not completed transfer. JIA disease activity at the last CARRA Registry visit was not associated with transfer to adult care. Biologic medication use was high at both visits (Table 2) and did not differ by transfer status. However, 63% reported problems with pain/discomfort and 44% with anxiety/depression using the EQ-5D generic health status scale (Figure 1). Patients who completed transfer to adult rheumatology reported higher pain scores, higher self-assessed disease activity, and more morning stiffness compared to those who did complete transfer.

Conclusion: Young adult respondents with JIA commonly report problems in the pain and anxiety/depression domains of health-related quality of life. There was persistent high use of biologic medications, and those who completed transfer to adult rheumatology had higher pain and self-reported disease activity than those who did not, despite high levels of perceived transition preparedness. Additional work is needed to understand how best to address comorbid pain and anxiety/depression during the peri-transition period. Care of young adults with childhood-onset rheumatic disease entering adult care should include efforts to minimize the impact of these comorbidities.

Disclosure: E. Smitherman, None; **R. Chahine**, None; **N. Bitencourt**, None; **A. Rahman**, None; **E. Lawson**, None; **J. Chang**, GlaxoSmithKline, 5.

Abstract Number: 1625

Clinical Characteristics of Multisystem Inflammatory Syndrome in Children: A Provincial Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Multisystem Inflammatory Syndrome in Children (MIS-C) is a post-infectious complication of COVID-19 infection with overlapping features of Kawasaki Disease (KD) and Toxic Shock Syndrome (TSS). In April 2020, a provincial multidisciplinary working group was developed expeditiously in anticipation of emerging MIS-C cases following the first wave of COVID-19 infections. The clinical characteristics of children evaluated for MIS-C in British Columbia are presented.

Methods: We included all children evaluated for MIS-C at British Columbia Children's Hospital, a provincial quaternary care centre, from May 2020 to April 2021. We developed an evidence based guideline adopting the World Health Organization MIS-C case definition. We prospectively collected patient demographics, clinical and laboratory characteristics, treatment, and outcomes.

Results: Fifty-two children were included. Median age was 6.0 years (interquartile range [IQR] 2.0-12.5 years) and 53% were female. 11 were diagnosed as confirmed MIS-C cases and 41 were ruled out cases without evidence of an epidemiologic link.

10/11 (91%) MIS-C cases presented with shock and prominent gastrointestinal, conjunctivitis, and mucocutaneous involvement. Common laboratory features included elevated C-reactive protein (CRP), D-Dimer, Troponin, and Brain Natriuretic Peptide (BNP). On echocardiography, 4/11 (36%) had myocardial dysfunction and 3/11 (27%) had coronary artery abnormalities. All patients tested positive for SARS-CoV-2 serology, 7/11 (64%) tested positive for Polymerase Chase Reaction (PCR), and 3/11 (27%) had a PCR-confirmed infection 4-6 weeks prior to admission for MIS-C. 10/11 (91%) received IVIG and intravenous corticosteroids, 5/11 (45%) required inotropic support, and 3/11 (27%) were intubated and ventilated. Median hospital stay was 6 days (IQR 4-9 days) and 7/11 (64%) required ICU admission. There were no deaths.

Of the 41 ruled out cases, diagnoses included KD, TSS, viral infections, bacterial infections, and other new systemic inflammatory syndromes. When compared to ruled out cases, MIS-C patients were more likely to have shock (91% vs 37%, p = 0.002); require ICU admission (64% vs 15%, p = 0.003); have myocardial dysfunction (36% vs 6%, p=0.02); and have higher D-Dimer (3339 vs 2050 mcg FEU/L, p = 0.03), Troponin (0.05 vs 0.0004 mcg/L, p = 0.02), and BNP (384 vs 109 ng/L, p = 0.02). MIS-C cases were also more likely to be treated with IVIG (91% vs 56%; p = 0.02), and corticosteroids (91% vs 37%; p = 0.002).

Conclusion: Our provincial cohort of MIS-C patients were more likely to present with shock and cardiac dysfunction, require ICU admission, and be treated with corticosteroids compared to ruled out cases. Our working group's

evolving process ensured children with features of MIS-C were rapidly identified, had standardized evaluation, and received appropriate treatment in our province.

Disclosure: H. Tam, None; **A. Lopez**, None; **M. Patel**, None; **J. Rayment**, None; **L. Tucker**, None; **C. Biggs**, None.

Abstract Number: 1626

Use of Total Hip Arthroplasty in Patients Under 21 Years Old: A U.S. Population Analysis

J. Alex Gibbons[1], Cynthia Kahlenberg[1], Deanna Jannat-Khah[1], Susan Goodman[1], Lisa Mandl[1], Peter Sculco[1], Stuart Goodman[2], Mark Figgie[1] and **Bella Mehta**[3], [1]Hospital for Special Surgery, New York, NY, [2]Stanford University, Stanford, CA, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Total hip arthroplasty (THA) is a treatment option for young patients with severe hip pathology due to congenital, developmental, rheumatologic, traumatic, and other acquired conditions. However, the frequency with which THA is used to treat patients in this population in the United States is unknown. Knowledge of the epidemiology of use of THA in this population may help to guide health policy and future research into the indications, outcomes, and failure modes of THA in very young patients. Therefore, the purpose of this study was to evaluate the use of THA in patients under 21 years of age in the United States.

Methods: We retrospectively reviewed the Kids' Inpatient Database (KID), an inpatient US national database of hospital admissions in patients under 21 years of age from approximately 4,200 hospitals in 46 states. We queried the database using current procedural terminology (CPT) codes for elective and non-elective primary THA from 2000-2016. Descriptive statistics such as means and percentages, along with their 95% confidence intervals were calculated using the appropriate sample weights as recommend by the Agency for Healthcare Research and Quality (AHRQ) for use with the KID dataset. Discharge weights were used for nationwide estimates.

Results: The weighted total number of THAs performed in patients under 21 in the KID increased from 347 in 2000 to 551 in 2016, while the total pediatric population in the US remained stable (**Figure 1**). The mean age of patients under 21 undergoing THA was 17.1 years (95% confidence interval: [16.9, 17.4]) (**Table 1)**. The mean age remained consistent (between 17.0 and 17.4) throughout the course of the study. Most patients were white (55.3%) and had private insurance (56.5%). During the study period, 80% of THAs were performed in urban teaching hospitals, 17% were performed in urban non-teaching hospitals, and 2% were performed in rural hospitals. The most common diagnoses were osteonecrosis, osteoarthritis, and juvenile idiopathic arthritis (JIA)/inflammatory arthritis. During the study period (2000-2016), the frequency of THA for osteonecrosis increased from 24% to 38%, while the frequency of THA for JIA/inflammatory arthritis decreased from 27% to 4% (**Figure 2**).

Conclusion: The number of THAs in patients under 21 has increased over the past two decades and these procedures are increasingly performed in urban teaching hospitals. The decrease in THA for inflammatory arthritis in this

Table 1. Demographic characteristics of patients <21 who underwent THA

	2000	2003	2006	2009	2012	2016	Overall
Variable	N = 347	N = 397	N = 365	N = 469	N = 539	N = 551	N = 2,665
Age, mean (95% CI)	17.4 (16.9, 17.9)	17.0 (16.6, 17.4)	17.4 (17.0, 17.8)	17.0 (16.7, 17.3)	17.4 (17.2, 17.7)	17.2 (17.1, 17.4)	17.1 (16.9, 17.4)
Sex: Female	64.4 (55.8, 72.1)	56.0 (49.2, 62.7)	56.0 (48.9, 62.9)	55.6 (49.6, 61.4)	48.9 (43.7, 54.1)	54.5 (52.0, 56.9)	50.6 (45.5, 55.6)
Race							
White	61.4 (48.4, 72.9)	61.1 (51.4, 70.0)	59.4 (49.9, 68.3)	65.9 (59.6, 71.7)	56.8 (50.8, 62.5)	59.5 (56.2, 62.8)	55.3 (49.3, 61.2)
Black	19.3 (11.7, 30.1)	19.4 (14.0, 26.2)	23.2 (16.6, 31.3)	20.2 (14.9, 26.7)	19.0 (14.2, 24.8)	20.5 (18.0, 23.2)	22.0 (17.6, 27.1)
Hispanic	13.2 (8.0, 21.1)	11.3 (5.7, 21.0)	10.7 (6.6, 17.0)	8.3 (5.5, 12.3)	12.7 (9.0, 17.6)	11.9 (9.9, 14.3)	14.2 (10.2, 19.5)
Asian/Pacific Islander	**	**	**	**	**	2.2 (1.5, 3.1)	2.8 (1.4, 5.3)
Native American	—	—	**	**	**	**	—
Other	3.9 (1.6, 9.6)	5.4 (2.6, 10.8)	4.6 (2.1, 9.7)	3.6 (1.5, 8.3)	9.0 (6.0, 13.2)	5.7 (4.4, 7.3)	5.7 (3.3, 9.7)
Payor							
Medicare	**	**	3.9 (1.8, 8.1)	3.1 (1.6, 5.8)	**	2.0 (1.4, 3.0)	1.7 (0.7, 4.3)
Medicaid	27.3 (18.0, 39.0)	25.9 (19.2, 33.9)	35.9 (29.7, 42.7)	30.1 (24.9, 36.0)	29.1 (23.9, 35.0)	31.0 (28.2, 34.0)	36.4 (30.6, 42.7)
Private Insurance	66.1 (55.0, 75.8)	65.2 (57.0, 72.5)	52.4 (45.2, 59.6)	60.0 (54.2, 65.4)	58.9 (52.5, 65.0)	59.6 (56.5, 62.6)	56.5 (50.4, 62.5)
Self-pay	**	**	4.1 (1.7, 9.5)	**	**	**	1.3 (0.5, 3.0)
No charge	—	—	—	—	**	**	**
Other	4.3 (1.4, 12.4)	6.3 (3.6, 10.8)	3.7 (1.9, 7.2)	5.6 (3.5, 8.9)	7.7 (5.1, 11.4)	5.3 (4.2, 6.8)	3.7 (2.2, 6.2)
Median household income (by patient's zip code)							
0^{th}-25^{th} %tile	4.8 (2.4, 9.3)	23.0 (17.2, 30.0)	25.4 (19.9, 31.9)	31.0 (25.6, 36.9)	27.7 (23.0, 33.0)	24.5 (22.3, 27.0)	29.0 (23.9, 34.6)
26^{th}-50^{th} %tile	30.7 (22.3, 40.6)	30.7 (24.1, 38.2)	24.9 (19.3, 31.4)	19.4 (15.2, 24.4)	22.5 (18.7, 26.8)	24.9 (22.6, 27.3)	24.1 (20.0, 28.7)
51^{st}-75^{th} %tile	28.2 (20.5, 37.5)	21.3 (16.3, 27.3)	25.3 (19.3, 32.4)	25.5 (20.9, 30.8)	20.6 (16.7, 25.1)	24.0 (21.8, 26.3)	24.3 (20.4, 28.8)
76^{th}-100^{th} %tile	36.2 (27.8, 45.7)	25.0 (19.3, 31.8)	24.4 (18.3, 31.7)	24.1 (19.1, 29.8)	29.3 (24.5, 34.6)	26.6 (23.9, 29.4)	22.6 (18.2, 27.6)
Admission type							
Non-elective	n.d.	10.2 (5.6, 17.9)	9.3 (6.0, 14.1)	7.8 (4.8, 12.7)	5.2 (3.2, 8.3)	7.9 (6.0, 10.2)	7.8 (4.2, 14.1)
Elective	n.d.	89.8 (82.1, 94.4)	90.7 (85.9, 94.0)	92.2 (87.3, 95.2)	94.8 (91.6, 96.8)	92.1 (89.8, 93.9)	92.1 (85.9, 95.8)

Note: all data presented as Percentage (95% Confidence Interval) unless stated otherwise. N represents weighted estimate. All values were estimated using sampling weights. n.d. = no data.
** Per HCUP guidelines, cell sizes ≤10 have been omitted to protect patient confidentiality.

population likely reflects improvements in medical management during the study period. Knowledge of the epidemiology of use of THA in this population may help to guide health policy and future research into the indications, outcomes, and failure modes of THA in very young patients.

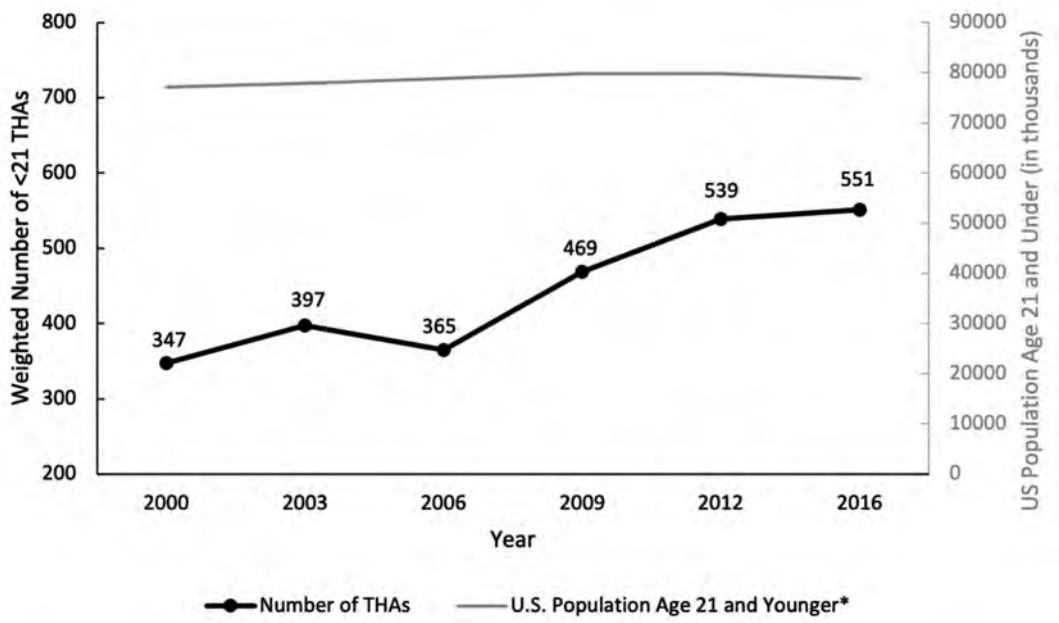

Figure 1. Weighted Total Number of THAs in Patients <21 per year *U.S. population estimates from National Center for Education Statistics. Table 100.10. Estimates of resident population, by age group: 1970 through 2019. https://nces.ed.gov/programs/digest/d19/tables/dt19_101.10.asp (Accessed 12 May 2021).

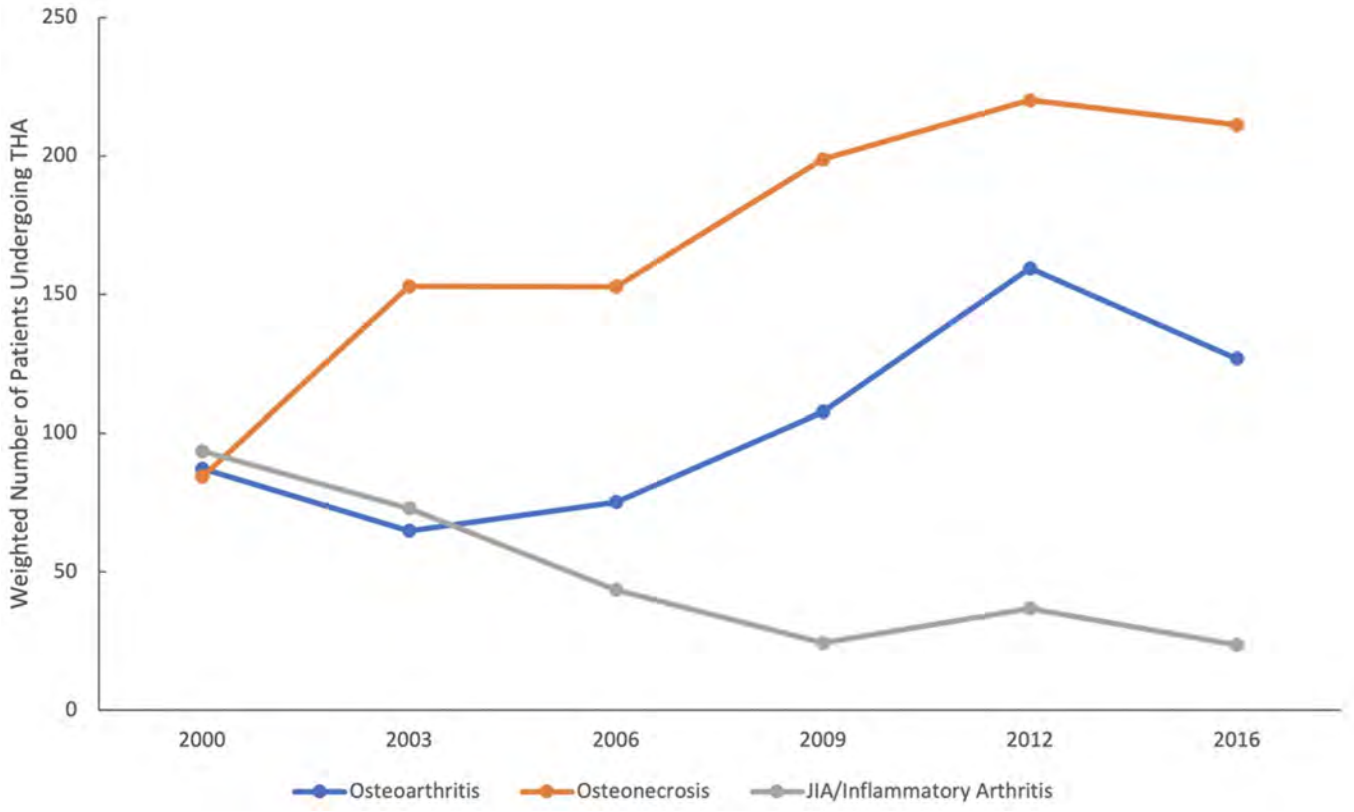

Figure 2. Changes in Frequencies of Most Common Diagnoses.

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Surgical, 2, 5, 6, 11, Lima Corporate, 2, Parvizi Surgical, 11, Zimmer, 2; **S. Goodman**, WishBone Medical, 2, Pluristem, 2, Hyalex, 11, Accelalox, 11, Merck, 9, Journal of Orthopedic Research, 4, 9, Biomatierals, 4, 9, Journal of Arthroplasty, 4, Clinical Orthopedics, 4, Journal of Orthopedic Research, 4, Journal of Biomedical Materials Research, 4, Biomaterials, 4, Open Orthopaedic Journal, 4, Journal of Orthopaedic Translation, 4, Journal of Orthopaedic Surgery and Research, 4, Bone & Joint Research, 4, PLOS ONE, 4; **M. Figgie**, HS2, 11, Lima, 2, 10, mekanika, 11, Wishbone, 2, 10, 11; **B. Mehta**, Novartis, 1, 6.

Abstract Number: 1627

Long Term Follow-Up of Patients with Childhood-Onset Lupus Nephritis After Transition to Adult Care

Dahima Cintrón[1], Suheiry Márquez[1] and Luis Vilá[2], [1]University of Puerto Rico Medical Sciences Campus, San Juan, PR, [2]University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Approximately 20% of patients with systemic lupus erythematosus (SLE) are diagnosed before 18 years of age. Pediatric patients have a worse disease course when compared to adults, and nearly 50% present with renal involvement. Most studies on childhood-onset lupus nephritis (cLN) are limited to the pediatric period. Therefore, we sought to determine the long term clinical outcomes in patients with cLN after reaching adulthood.

Methods: A cohort of Hispanics from Puerto Rico with SLE (per 1997 American College of Rheumatology classification criteria) was studied. Lupus nephritis (LN) was defined as the presence of proteinuria >0.5 g per day, urinary cellular casts, and/or a renal biopsy consistent with LN. Demographic parameters, clinical manifestations, comorbidities, disease activity (per Systemic Lupus Erythematosus Disease Activity Index ([SLEDAI]), disease damage (per Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index [SDI]), pharmacologic therapy, renal response, and chronic kidney disease staging (per National Kidney Foundation) were gathered at LN onset (baseline) and at last visit. Data from patients with cLN were compared to those with adult-onset LN (aLN) using Chi-square test, Fisher's exact test, or Mann-Whitney test, as appropriate.

Results: In total, 142 SLE patients with LN were studied; 27 (19%) had cLN and 115 (81%) had aLN. Among cLN patients, 88% were female. The mean (standard deviation [SD]) age at SLE diagnosis and LN onset for cLN patients were 14.6 (3.2) and 16.1 (3.9) years, respectively. The mean (SD) LN duration and follow-up after reaching adulthood were 14.7 (7.8) and 13.4 (7.7) years, respectively. No significant differences were found at baseline and last visit for lupus manifestations, comorbidities, SLEDAI and SDI scores, and pharmacologic treatment (induction and maintenance therapeutic modalities) between patients with cLN and aLN. Renal outcomes are depicted in table1. No significant differences were found for renal outcomes between these groups.

Conclusion: In this cohort of Puerto Ricans with SLE, patients with cLN followed through adulthood for more than a decade had a favorable outcome. Most patients remained in chronic kidney disease stage 1 or 2 and few evolved into end-stage-renal disease. Furthermore, long term renal outcomes were similar to those with aLN. The results of this study differ from those from other ethnic populations that show poor clinical outcomes in patients with cLN.

Table 1. Renal outcomes of childhood-onset lupus nephritis (cLN) and adult-onset lupus nephritis (aLN) at last visit

	cLN n= 27 %	aLN n= 115 %	p value
Renal response			
Complete renal response	50.0	37.7	0.774
Partial renal response	0.0	13.2	
Chronic kidney disease stage			
1	58.3	44.6	0.223
2	16.7	22.3	0.539
3A	8.3	10.7	1.000
3B	8.3	6.3	0.659
4	0.0	6.3	0.353
5	0.0	1.8	---
End-stage renal disease	8.3	8.0	0.504
Mortality	11.1	9.0	0.728

Disclosure: D. Cintrón, None; **S. Márquez**, None; **L. Vilá**, None.

Abstract Number: 1628

Reproductive Health Knowledge Gaps, Needs, and Barriers Identified by Pediatric Rheumatology Providers

Kimberly Hays[1], Catherine Lavallee[2], **Brittany Huynh**[3], Tova Ronis[4], Barbara Edelheit[5], Kathryn Cook[6], Veronica Mruk[7] and Cuoghi Edens[8], [1]Penn State Health, Hershey, PA, [2]Virginia Tech Carilion School of Medicine, Roanoke, VA, [3]Riley Hospital for Children at Indiana University, Indianapolis, IN, [4]Children's National Hospital, Washington, MD, [5]CT Children's Medical Center, Hartford, CT, [6]Akron Childrens Hospital, Copley, OH, [7]Ohio State University / Nationwide Children's Hospital, Columbus, OH, [8]University of Chicago, Chicago, IL

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatic diseases and their treatments present unique challenges to sexual and reproductive health (SRH) issues facing patients and clinicians. Despite this, literature in the adult population suggests SRH is often unaddressed by health care providers, and providers report gaps in knowledge in this area. We sought to understand pediatric rheumatology providers' knowledge, needs, and practices regarding the SRH care of their patients.

Methods: An electronic survey was distributed to the Childhood Arthritis and Rheumatology Research Alliance (CARRA) providers in the fall of 2020. 248 CARRA members completed the 37-item online survey about SRH issues facing pediatric rheumatology providers.

Results: Survey response rate was 82%. Participants were mostly pediatric rheumatologists, female, practicing in the United States and affiliated with an academic hospital (Table 1). Fifty percent of respondents were in fellowship

or less than 10 years out of training. Sixty-six percent reported more than 50% of their time devoted to clinical care. Over 90% surveyed felt it was within their scope to address SRH topics with their patients. Top three SRH concerns reported by clinicians: teratogenic medications, contraception, and long-term medication safety. Fertility and pregnancy were also of high importance, with 70% of respondents having at least one pregnant patient in their career, 4% having >15 pregnancies. Lack of time and knowledge were the most common reasons cited for not discussing SRH with patients. Only a minority of providers speak to patients alone or routinely address sexual activity.

The majority of those surveyed were able to identify key teratogens used in pediatric rheumatology, however some pregnancy-compatible medications were incorrectly identified as teratogenic (Figure 1). Estrogen-containing contraceptives were erroneously identified as inappropriate in those without antiphospholipid antibodies (APLs) (Table 2). Progestin-only methods were underrecognized as appropriate in those with positive APLs or thrombus history, with hormonal IUDs and implants the most improperly identified. Immunosuppression and nulliparity were appropriately not seen as barrier to long-acting reversible contraceptives. The effectiveness of various contraceptives was overestimated. Emergency contraception, an intervention with no disease restrictions, was not well-recognized as safe for those with SLE with negative or positive APLs (Table 2) Potential fertility sequelae plays a role in medication

Table 1. Survey Respondent Characteristics

Total CARRA members participating	248 (82%)
Country	
United States	232 (94%)
Canada	16 (6%)
Position	
Pediatric Rheumatologist	170 (68%)
Adult/Pediatric Rheumatologist	12 (5%)
Fellow in a pediatric rheumatology program	47 (19%)
Fellow in a combined adult and pediatric rheumatology program	10 (4%)
Rheumatology nurse practioners or physician assistant	9 (4%)
Current practice/training environment	
Academic setting	235 (95%)
Nonacademic setting	13 (5%)
Gender of participants	
Female	184 (74%)
Male	63 (25%)
Chose not to answer	1 (1%)
Percent clinical time	
0-10%	6 (2%)
11-20%	22 (9%)
21-30%	29 (12%)
31-40%	5 (2%)
41-50%	22 (9%)
51-60%	20 (8%)
61-70%	27 (11%)
71-80%	45 (18%)
81-90%	31 (12%)
91-100%	41 (17%)
Percentage of patients between 14-26 years old	
0-24%	14 (5%)
25-49%	121 (49%)
50-74%	104 (42%)
>75%	9 (4%)

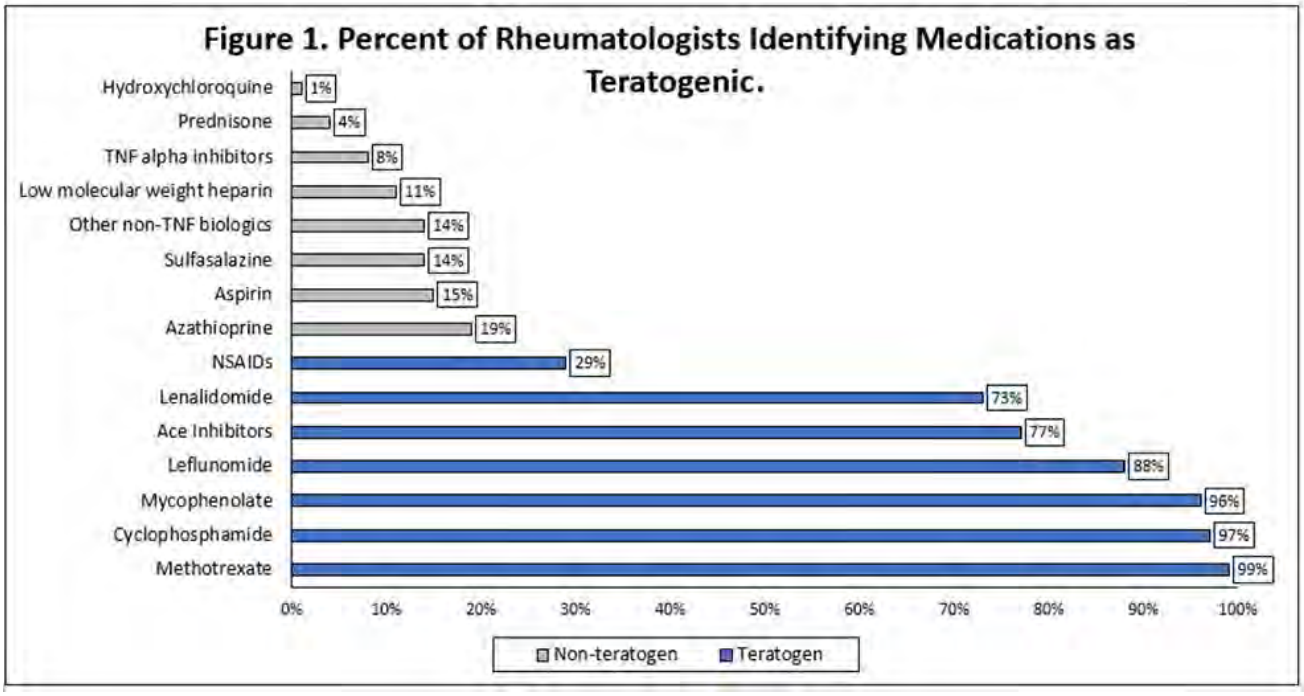

Table 2. Pediatric Rheumatologists Reporting Contraception Compatibility* in SLE patients with or without history of VTE/APLs

Contraception Type	-VTE/APLs	+VTE/APLs
Condoms	98%	95%
Combined Hormone OCP	64%	3%
Contraceptive Ring/Patch	66%	12%
Progesterone Only Pill	95%	85%
DMPA Injection	92%	71%
Hormonal Implant	87%	54%
Hormonal IUD	87%	54%
Copper IUD	94%	90%
Emergency Contraceptive Pill	82%	47%

Systemic lupus erythematosus = SLE; Venous thromboembolism = VTE; Anti-phospholipid antibodies = APLs; Oral Contraceptive Pill=OCP; Depot medroxyprogesterone acetate = DMPA; Intrauterine device = IUD

* Compatibility was adapted from the 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases (Arthritis & Rheumatology; Vol 72. No 4, April 2020, p531-532)

Dark green = Highly compatible; Light green = Likely compatible; Pink=Unlikely compatible; Red = Not compatible

decisions, however methotrexate and mycophenolate were incorrectly identified as affecting fertility. Fertility preservation was rarely pursued for males or females.

Conclusion: Sexual and reproductive health is an area pediatric rheumatology providers feel is within their clinical purview, barred by time and knowledge. Knowledge gaps recognizing pregnancy compatible medications, appropriate contraception based on disease characteristics, contraception effectiveness, and medications effecting fertility were identified. Emergency contraception safety awareness was lacking. This survey highlights future opportunities for provider education in pediatric rheumatology SRH.

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Abstract Number: 1629

Effect of Drug Withdrawal on Interleukin-1 or Interleukin-6 Inhibitor Associated Diffuse Lung Disease

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Severe delayed hypersensitivity reactions (DHR) are under-recognized in inflammatory conditions, particularly drug reaction with eosinophilia and systemic symptoms (DRESS). Previous work has shown this reaction to occur implicating inhibitors of IL-1 and IL-6 during treatment of Stills disease.[1] The purpose of the present analysis of newly identified cases is to assess outcomes based on timeliness of recognizing drug reaction and withdrawal of the implicated medications.

Methods: This is a retrospective observational study of subjects with Stills disease who experienced a DRESS reaction implicating one or more of anakinra, canakinumab, tocilizumab or rilonacept. Classification as DHR required scoring as probable or definite using the validated scoring system RegiSCAR for DRESS.[2] Cases with and without diffuse parenchymal lung disease during treatment (DLD) were included. Variables included duration of drug exposure, development

Table. Drug duration and outcomes in Stills subjects with DRESS to inhibitors of IL-1 or IL-6

All DHR subjects (n= 59)				
	IL-1 and/or IL-6 inhibitor treatment < 6 months	IL-1 and/or IL-6 inhibitor treatment 6 months to 4.3 years[1]	*P* value	OR(95%CI)
DLD	8/59 (14%)	33/59 (56%)	2.1×10^{-6}	8.3 (3.3-20.0)
Deceased[2]	1/59 (2%)	11/59 (19%)	4.1×10^{-3}	13.3 (1.7-106.7)
DLD survivors with > 3 months of follow up (n= 25)				
	Permanently discontinued IL-1 and IL-6 inhibitors <3 months after DLD recognized		*P* value	OR(95%CI)
	Yes	No		
DLD improved	7/25 (28%)	0/25 (0%)	0.01	infinite

DHR, delayed hypersensitivity reaction; DLD, diffuse lung disease developing during treatment with IL-1 or IL-6 inhibitors; DLD improved, asymptomatic without supplemental oxygen plus improved CT and/or decreased or resolved clubbing

[1]Longest latency from inhibitor start to DLD was 4.3 years.

[2]Fatalities occurred only in subjects with DLD (41/59 DHR cases). Fatality rate is 29%(12/41) with median follow up from DLD to data close of 10 months (med(IQR),10 months (7,26)).

of diffuse lung disease, lung disease status at data close and death. Lung disease resolution was defined as absence of respiratory symptoms without supplemental oxygen, normal chest CT and resolution or absence of digital clubbing. DLD improvement differed from resolution by allowing improved chest CT or digital clubbing with neither worsening. Comparisons were made using Fishers exact test and odds ratios with 95% confidence intervals. 59 subjects met inclusion criteria for DHR implicating inhibitors of IL-1 and/or IL-6. Class II HLA associations were considered as available.

Results: Median age at Stills onset was 4 years (range 0.5-17.7 years), 69% (41/59) had DLD and 61% (36/59) were female. Fatalities occurred solely in subjects developing DLD (12/41,29%). Median latency from drug initiation to detection of DLD was 1.3 yrs (range 2 weeks-4.3 years). When biopsied, pathology in DLD was pulmonary alveolar proteinosis, as described.[1] Three cases resolved lung disease; all 3 had permanently discontinued IL-1 and IL-6 inhibitors within 6 weeks of DLD detection. DHR subjects without DLD who stopped IL-1 or IL-6 inhibitors did not develop DLD, during median follow-up of 1 year after drug stop (range 0.2-6.5 years). Drug withdrawal improved outcomes (table). HLA-DRB1*15 was present in 31/37(84%), strikingly exceeding population frequencies.[3]

Conclusion: Timely recognition of DRESS reactions and withdrawal of all IL-1 and IL-6 inhibitors improve outcomes in Stills disease, lessens risk of the often fatal drug-associated lung disease and may allow resolution of DLD. Mechanisms underlying cross reactions between these structurally different drugs are not known. Determination of HLA may limit the incidence of DHR.

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Abstract Number: 1630

Multisystem Inflammatory Syndrome in Children: Clinical Characteristics and Predictors for Length of Hospitalization

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Multisystem Inflammatory Syndrome in Children (MIS-C) is a recently defined post-infectious phenomena associated with coronavirus disease 2019 (COVID-19). We assessed the demographics, clinical characteristics, hospital course, and short-term outcomes of patients admitted with MIS-C.

Methods: We performed a retrospective analysis of patients who met the World Health Organization definition of MIS-C and were admitted to Duke Children's Hospital from August 3, 2020 to March 25, 2021. Demographic and clinical data were collected from the electronic medical record. Associations between admission lab values and hospital length of stay (LOS) were examined using univariate and multivariate linear regression after log transformation for variables with skewed distribution.

Results: Twenty patients were included. The mean (±SD) age was 9.5 (5.4) years; 10 patients (50%) were male; 16 (80%) were Black. Twelve patients (60%) were previously healthy; the most common comorbidity was obesity in 8 (40%) children. All patients presented with fever, cardiovascular dysfunction, and coagulopathy. Other common manifestations were gastrointestinal distress (80%), acute kidney injury (60%), respiratory compromise (50%), and mucocutaneous symptoms (45%). Echocardiographic abnormalities were noted in 18 (90%) patients, with coronary artery changes in 14 (70%) and reduced systolic ejection fraction in 12 (60%) (Figure 1). Intensive care unit admission, ionotropic support, and mechanical ventilation were indicated in 80%, 70%, and 20% of patients, respectively. All patients were treated with intravenous immunoglobulin (IVIG), with 19 (95%) requiring additional treatment: 17 (85%) with 1-4 mg/kg/day intravenous glucocorticoids, 6 (30%) with pulse dose glucocorticoids, and 7 (35%) with anakinra (Figure 2). Treatment complications included IVIG-associated hemolytic anemia (10%) and steroid-related adverse effects such as hypertension, bradycardia, hyperglycemia, and delirium (35% collectively). All patients survived and were discharged home. Median (IQR) LOS was 8 (7, 11) days. All echocardiograms normalized in a median (IQR) of 16.5 (3, 41) days. Univariate analyses of admission lab values and LOS revealed a positive association between ferritin (p=.004) and a negative association between Hgb (p=.036) and albumin (p=.001). Controlling for all significant variables in a multivariate linear regression model, ferritin (adjusted p=.043) and albumin (adjusted p=.017) remained significantly associated with LOS (adjusted R^2=.59).

Clinical Presentation	Prevalence (n=20)
Fever	20 (100%)
Cardiovascular dysfunction	20 (100%)
Coagulopathy	20 (100%)
Gastrointestinal symptoms	16 (80%)
Acute kidney injury	12 (60%)
Respiratory symptoms	10 (50%)
Mucocutaneous symptoms	9 (45%)
Neurologic symptoms	6 (30%)

Cardiac Manifestations	Values (n=20)
Any coronary involvement	14 (70%)
Dilation only (z-score 2-2.5)	6/14 (43%)
Small aneurysm (z-score >2.5-5)	7/14 (50%)
Medium aneurysm (z-score >5-10)	1/14 (7%)
Large aneurysm (z-score >10)	0/14 (0%)
Reduced systolic ejection fraction	12 (60%)
Mild	4/12 (33%)
Moderate	6/12 (50%)
Severe	2/12 (17%)
Days to Normal Echocardiogram	
Average	27.4
Median	16.5

Figure 1. Clinical presentations and cardiac manifestations of MIS-C patients admitted to Duke Children's Hospital.

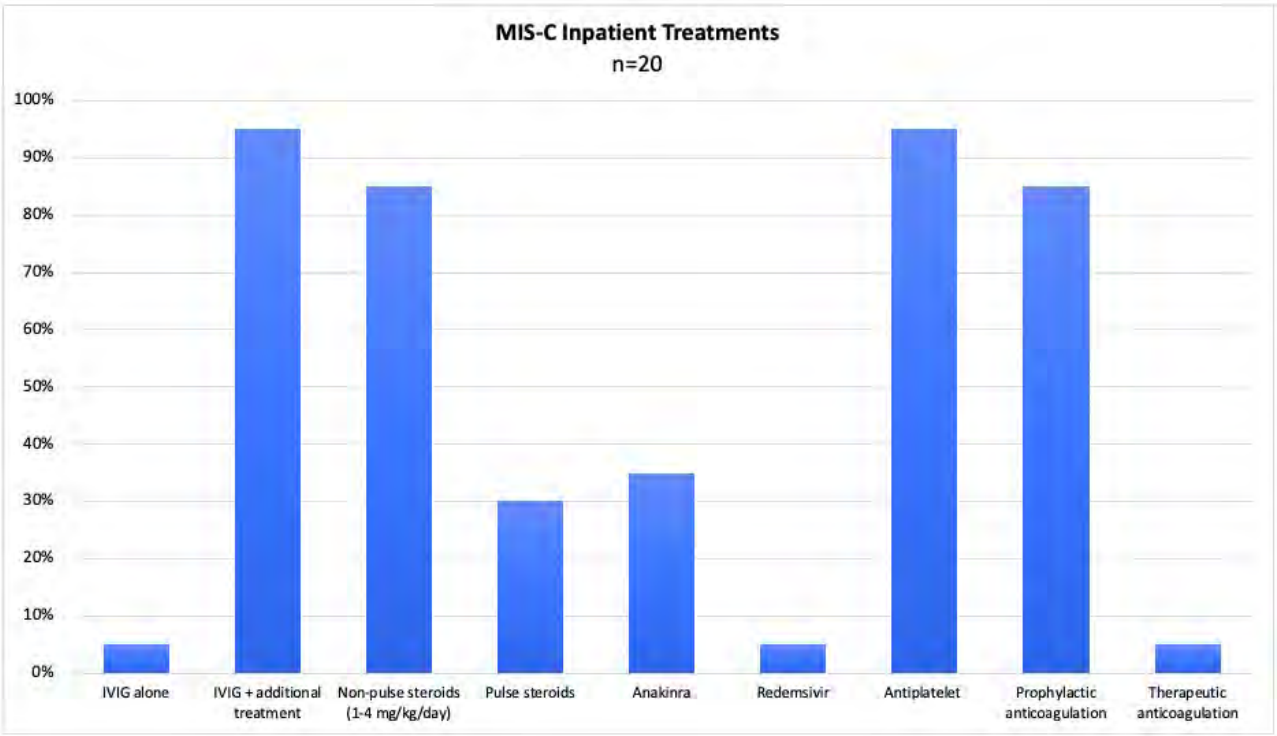

Figure 2. Therapies received by admitted MIS-C patients at Duke Children's Hospital.

Conclusion: MIS-C is a novel entity of high morbidity and low mortality in children previously infected with COVID-19. In this case series, children with MIS-C presented with fever and multiorgan failure, with cardiovascular compromise being most common. Higher baseline ferritin level and lower serum albumin were associated with longer LOS. Treatment with IVIG, glucocorticoids, and anakinra resulted in favorable short-term outcomes.

Disclosure: L. Covert, None; **M. Becker**, None; **R. Sadun**, None; **H. Van Mater**, None.

Abstract Number: 1631

Predictive Factors for Lack of Response to Treatment in a Long-term Cohort of Patients with Juvenile Idiopathic Arthritis-associated Uveitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Uveitis is the main extraarticular complication of juvenile idiopathic arthritis (JIA) with still a significant impact on JIA morbidity, despite continuous improvement in systemic treatment. Although antinuclear antibody positivity and early onset of JIA have been associated with a high risk of uveitis onset, no clinical features have been widely recognized as predictive factors for JIA-associated uveitis (JIA-U) lack of response to treatment, so far. The aim of our study is to investigate clinical features associated with lack of response to systemic treatment in a long-term cohort of patients with JIA-U.

Methods: Clinical records of patients with JIA-U were retrospectively reviewed with regard to clinical features, therapeutic choices and outcome. The role of potential predictors for lack of response to treatment has been assessed at bivariate and multivariate levels. Furthermore, a multivariable logistic model has been applied in order to estimate the strength of association between predictors and outcome, adjusting for potential confounders.

Results: Data from 152 JIA-U patients were analysed (82.2% female), with a median follow up of 12.0 years (IQR 9.9) and a median age at uveitis onset of 4.8 (4.1) years. In 72 patients (43.4%) at least one biologic DMARD (bDMARDs) to control uveitis was required. Compared to patients responsive to a monotherapy with a DMARD (n=38), children requiring a bDMARDs for uveitis had a lower median age at uveitis onset, a longer disease duration and a greater frequency of bilateral uveitis at onset (**Table 1**). No difference was observed in uveitis activity grade at onset. Despite similar frequency of ocular damage at onset, patients not responsive to DMARDs showed a higher percentage of ocular damage at last visit (66.7% vs 39.5% p=0.011). Multivariable analysis confirmed younger age at disease onset as an independent factor for lack of response to DMARDs (p 0.018). Male gender is associated with higher frequency of ocular surgery (33.3% vs 12.4%, p=0.043), and, despite the inaccuracy of the estimate due to limited sample size, acts as an independent factor in multivariable analysis with an almost 9 times higher risk to lack of response to DMARDs (p=0.049).

	Monotherapy with DMARDs (n=38)	bDMARDs for uveitis (n=72)	p-value
Gender, %M (n)	7.9 (3)	25.0 (18)	0.055
Age at uveitis onset (yr), median (IQR)	6.0 (3.3)	4.1 (4.3)	0.008
Duration of disease (yr), median (IQR)	10.4 (8.0)	13.4 (10.7)	0.047
Oligoarthritis persistent course, % (n)	84.2 (32)	72.2 (52)	0.053
ANA positive, % (n)	89.5 (34)	94.4 (68)	0.444
Positive acute phase reactants at onset, % (n)	68.2 (15)	78.4 (29)	0.575
Active arthritis at uveitis onset, % (n)	57.6 (19)	72.7 (48)	0.197
Ocular damage at onset, % (n)	18.2 (6)	26.9 (18)	0.480
Bilateral uveitis at onset % (n)	50.0 (19)	77.8 (56)	0.006

Conclusion: Younger age at uveitis onset and male gender are predictors of a worse response to DMARDs, while the length of follow-up exerts a confounding effect on bilateral uveitis. Children resistant to conventional treatment need prompt recognition and additional strategies to improve long-term outcome.

Disclosure: F. Minoia, None; **L. Marelli**, None; **F. Pregnolato**, None; **G. Beretta**, None; **C. Mapelli**, None; **G. Leone**, None; **G. Cincinelli**, None; **P. Nucci**, None; **T. Giani**, None; **E. Miserocchi**, None; **R. Cimaz**, None.

Abstract Number: 1632

Clinical Features and Colchicine Response in Patients with Undifferentiated Systemic Autoinflammatory Disease Carrying E148Q vs. Other *MEFV* Mutations

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Undifferentiated systemic autoinflammatory diseases (uSAID) are diverse syndromes characterized by acute flares of fever and inflammation, which do not meet clinical criteria for known disorders like Familial Mediterranean Fever (FMF). As part of the uSAID workup, many patients undergo genetic testing, sometimes revealing variants of uncertain significance in genes associated with autoinflammation. E148Q is a common polymorphism in exon 2 of the *MEFV* gene, which is not thought to be a disease-causing variant for FMF. The contribution of E148Q mutations in patients with uSAID is poorly understood, and it is unknown how it may respond to empiric treatment with colchicine, which is first line for FMF. To compare the clinical characteristics and colchicine response of children with uSAID identified to have E148Q vs non-E148Q mutations in the *MEFV* gene.

Methods: Children with uSAID ≤18 years old at initial evaluation seen at a single-center during 2000-2019 were included if they received ≥3 months of colchicine therapy and carried at least one *MEFV* mutation but did not meet clinical criteria for FMF (n = 25). Data on demographics, clinical features, laboratory/genetic studies, and treatment responses were collected.

Table 1. Characteristics of uSAID patients with heterozygous MEFV mutations

	E148Q group (n=8)	Non-E148Q group (n=17)	p value
Complete response, (%)	2 (25)	12 (70.6)	0.03
Mean episode duration (days), (SD)	8.3 (6.5)	3.7 (1.4)	0.009
Asian ancestry, (%)	3 (37.5)	0 (0)	0.04
GI symptom, (%)	5 (62.5)	8 (47.1)	0.47
MSK symptom, (%)	3 (37.5)	9 (52.9)	0.47
Pharyngitis, (%)	3 (37.5)	5 (29.4)	0.69
Rash, (%)	3 (37.5)	11 (64.7)	0.20

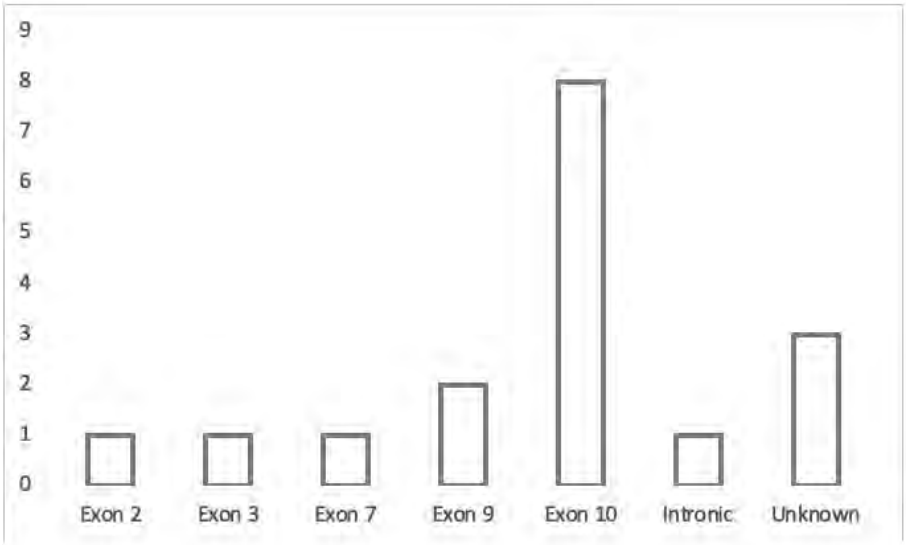

Figure 1. Location of non-E148Q MEFV mutations in uSAID patients (n=17).

Results: In our cohort of 25 children with uSAID and *MEFV* mutations, 8 (32%) were heterozygous for E148Q mutations. Half of these patients also carried another non- exon 10 *MEFV* mutation (2x 369S, 1x L110P, 1x I591T). Distribution of the remaining variants on *MEFV* gene is shown in Figure 1. Clinical features of children with E148Q vs. other *MEFV* mutations are shown in Table 1. Asian ancestry was seen in 3/8 (37%) children with E148Q mutations and in no child with other *MEFV* mutations. Children with E148Q mutations had longer length of febrile episodes (8.3±6.5 vs. 3.4±1.4 days; p=0.009) and were less likely to have a full response to colchicine (25% vs 70%; p = 0.03).

Conclusion: In our cohort of children with uSAID and *MEFV* mutations, E148Q was associated with longer duration of fever flares and a reduced colchicine response. Larger studies will be helpful in elucidating the unique role of these mutations in autoinflammation.

Disclosure: B. Egeli, None; **H. Wobma**, Immplacate Inc, 4, 8; **M. Correia Marques**, None; **J. Hausmann**, Novartis, 2, Biogen, 2, Pfizer, 2; **F. Dedeoglu**, Novartis, 2, UptoDate, 9.

Abstract Number: 1633

Epidemiology of Musculoskeletal Manifestations in Paediatric Inflammatory Bowel Disease: A Systematic Review

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

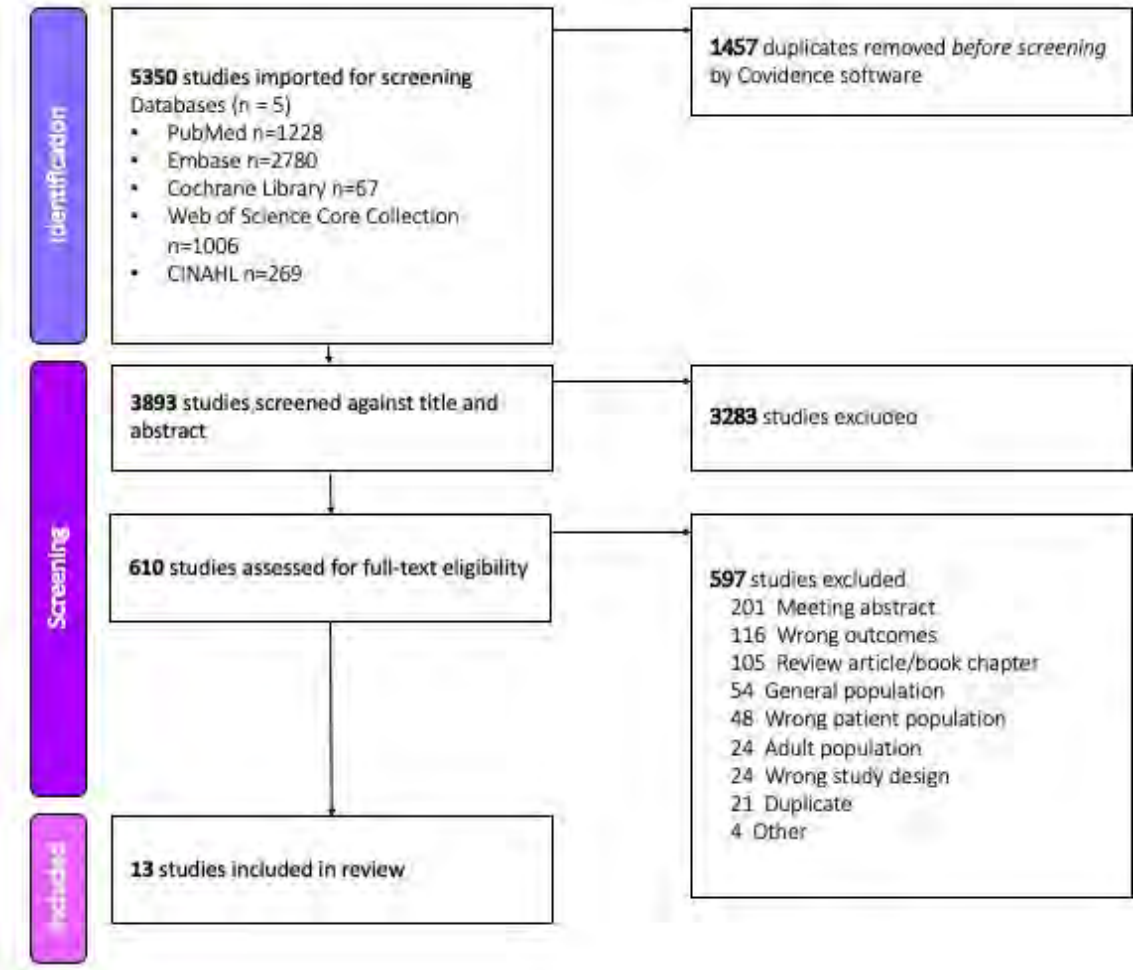
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Paediatric inflammatory bowel disease (p-IBD) is a chronic and relapsing gastrointestinal disorder of childhood with associated long-term morbidity. Several extraintestinal manifestations (EIMs) are de-

Figure 1. PRISMA flowchart of the study search and selection for inclusion in the systematic review.



PRISMA flowchart for study inclusion.

scribed, the most common being joint pain and/or inflammation. In 1986, Passo et al. were the first to describe the association of arthritis in p-IBD patients. In this retrospective study, arthritis was described in 9% of children with ulcerative colitis (UC) and in 15.5% of children with Crohn's disease (CD). Arthralgia was more common than arthritis, occurring in 32% of patients with UC and 22% with CD. Data on the epidemiology, patient and disease factors associated with the development of, treatments required for, and outcomes of p-IBD associated musculoskeletal (MSK) disease is lacking. Our study aims to summarize the literature on the epidemiology of MSK EIMs in p-IBD in the era of biologics.

Methods: A systematic review of the literature was performed. PubMed, Embase, Cochrane Library, Web of Science Core Collection, and CINAHL databases were searched with relevant keywords. English studies published from January 1, 2000 to December 21, 2020 were included. In total, 3,893 papers were identified, and screening was

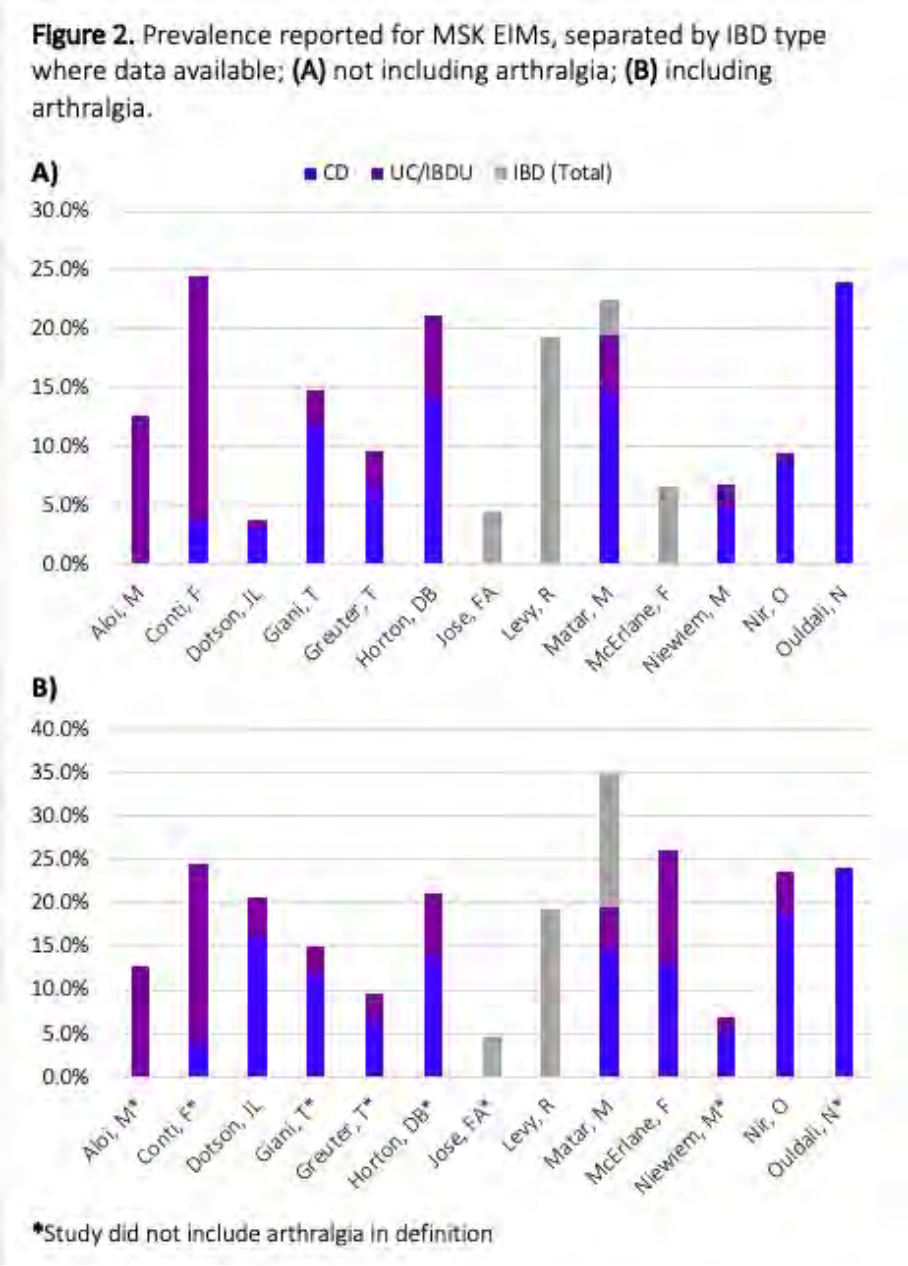


Figure 2. Prevalence reported for MSK EIMs, separated by IBD type where data available; **(A)** not including arthralgia; **(B)** including arthralgia.

MSK EIM reported prevalence rates.

performed by two independent reviewers (AA, MS; Figure 1). Conflicts were resolved by a third reviewer (EC or RB). Characteristics of the study such as research design, setting, and sample size, as well as phenotypic characteristics of the population were recorded. The primary outcomes of interest were MSK symptoms at presentation and course, method of diagnosis and definitions used for MSK EIMs. Risk of bias assessment was performed using the JBI Prevalence Study Critical Appraisal Tool.

Results: Thirteen studies were included for full review, which were primarily single-centre observational studies with retrospective or cross-sectional design. The method of diagnosis for MSK EIMs varied greatly across the studies, with only 4 studies stating the involvement of a rheumatologist in the diagnosis. The definitions used also varied, with MSK-related features such as peripheral arthritis, axial arthritis, enthesopathy, myalgia, and arthralgia included. Only 6 studies focused on MSK EIMs as their primary outcome, while the remainder reported on all p-IBD associated EIMs. There was a wide range in the prevalence of MSK EIMs from 3.7-34.8% (Figure 2a, 2b). Four studies reported on the therapeutic response of MSK EIMs to pharmacotherapy, and only 3 of those reported on biologic use. Risk of bias demonstrated heterogeneity in the quality of included studies.

Conclusion: This is the first systematic review of the literature for MSK EIMs in p-IBD. Analysis was limited due to variability in study design and data-reporting methods. Included studies reported prevalence of MSK EIMs, but the ascertainment of MSK EIMs, both method and definition varied with a clear lack in standardization. Our study demonstrates the need for research to capture the presentation, diagnosis, management, and morbidity associated with MSK EIMs in p-IBD.

Disclosure: A. Ali, None; **M. Schmidt**, None; **D. Piskin**, None; **E. Crowley**, AbbVie, 5, 6, Alimentiv, 2; **R. Berard**, Sandoz, 2, SOBI, 2, Roche, 2.

Abstract Number: 1634

Patient Activation and Health Literacy in the Pediatric to Adult Transition in Juvenile Systemic Lupus Erythematosus: Patient and Health Care Team Perspectives

Ashley Ciosek[1], Una Makris[2], Justin Kramer[3], Tracey Wright[4] and Nicole Bitencourt[5], [1]UT Southwestern Medical Center, Dallas, TX, [2]UT Southwestern Medical Center, Dallas Veterans Administration, Dallas, TX, [3]Texas A&M University, College Station, [4]UT Southwestern Medical Center, Children's Health, Texas Scottish Rite Hospital for Children, Plano, TX, [5]Loma Linda University Medical Center, Redlands, CA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Advances in treatment of juvenile-onset systemic lupus erythematosus have ensured increased survival such that long-term quality of life and disease management must be considered. Interventions to improve jSLE transition outcomes require an understanding of the challenges faced by patients and their health care teams during this time.

In this qualitative study, we had a unique opportunity to interview uninsured or publicly insured young adults with jSLE who recently transitioned to adult rheumatology care, along with health care professionals caring for pediatric and adult jSLE patients. Interviews identified influential factors affecting pediatric-to-adult rheumatology transition suc-

cess. A subset of influential factors are described herein, organized under the conceptual frameworks of patient activation and health literacy (HL). Recommendations to improve transition success were also elicited from each cohort.

Methods: Semi-structured in-depth interviews with patients and health care professionals were conducted from November 2019 - May 2020, until thematic saturation. Thirteen post-transfer adult participants diagnosed with jSLE (in concordance with 2019 EULAR/ACR classification) were recruited from a public safety-net hospital system or from private practice. Thirteen health care team members were recruited from two pediatric and four adult rheumatology clinical sites in the same metropolitan area. Interviews were recorded, transcribed, coded, and analyzed using thematic analysis.

Results: Our interviews suggest that patient activation is driven by internalization of the implications of jSLE diagnosis, capacity and willingness to engage in self-education, autonomy, introspection, and trustworthy doctor-patient relationships (Table 1). Patients and health professionals acknowledged numerous HL components as determinants of transition success, including: language fluency and baseline education, extent of SLE-specific knowledge, self-efficacy (ability to make appointments, fill prescriptions, and obtain and utilize insurance), and accurate knowledge of personal medical history (Table 2). When asked how to improve the transition process, patients valued access to their secure online electronic medical record and recommended multimodal SLE-specific educational materials and increased access to social work services (Table 3). Health care professionals stressed the importance of early preparation for transition, utilization of mobile medical applications, and endorsed interventions such as lupus camp and increased partnership with psychologists and social workers (Table 3).

Table 1. Patient & Health Care Professionals' Perspectives on Patient Activation

Understanding disease severity: P: You guys [the clinical team] can only do so much that you can. It's really up to us because we're the ones that are going through it…if we want to be able to get better, get well, be here with our families, we're gonna have to put everything else to the side and realize that this is very, very serious.

- HP: Pediatric lupus can present terribly, so the disease could be extremely severe…these patients [with jSLE] are pretty well informed, but as kids get older, they do tend to be a little bit more complacent about their disease.

Range of activation: HP: Some [patients] are very responsible, and they want to be well so they take charge, and they know about their symptoms, they're good about telling you how they feel, but others are just not that interested.

Engagement in self-education: P: Listen and read up about your condition…Just find out different stuff that you probably don't even know that your condition deals with or affect…and be able to sit there and ask the doctor questions and tell them what you're going through….

- P: Now [in adult care] I actually ask when I don't understand something. I'm more into the conversation than when I was at [the pediatric center].

Realized autonomy: P: When you take your medicine, you feel complete. You feel like I've done everything that I'm supposed to do. So if there was something that was to happen to me, I could say that- well, I done everything I'm supposed to do.

- HP: Around the age of…16 I try to have a private conversation with the patients and talk to them about taking control of their management, their medications…on being an advocate for themselves.

Physician-Patient Alliance: P: They wouldn't prescribe it to me if it wouldn't help me. Now if I have an issue when I'm taking a medication and it makes me feel some type of way, I let it be known... because I know I gotta stay healthy, and if they give me something to make me stay healthy, I'm gonna take it. I had to learn it though. I was one of those teenagers that wasn't taking it at first, so [when] I transitioned up to an adult and I changed up and got better with myself.

- HP: I usually empower [patients]. I want them to know about their health history without relying on the parents. So I tell them they're in control.

P = Patient, HP = Health care professional

Table 2. Patient & Health Care Professionals' Perspectives on Health Literacy

Functional Health Literacy

Language fluency: HP: If they're not Spanish or English [speaking]- I don't know how these families navigate…it is amazing to me that they are doing as well as they are.

Baseline level of education: P: I think people who are in college or people who have higher education I think that helps a lot…I have family members who are like immigrants and…I see how hard it is for them to go to doctors and understand what's being done and understand …I definitely think education plays a big part in being able to properly transition

Interactive Health Literacy

SLE-specific knowledge

Jargon: I: Did you understand- when the doctor, the nurse or whoever told you it looked like you had lupus, did you understand what lupus was? P: No…. I still have a hard time knowing what [is going on] I: …did you ask your doctor about what it is that lupus is or anything like that or have anyone explain to you what it is? P: They have, but since it's doctor's talk, I still don't get it that much.

- P: … my doctors never told me what my medications do and so- and I think that could be [helpful too]. I think if you understand [it] in layman's terms… [in a way] that makes sense.

Time constraints: HP: It's a little bit sad because our office visits we can only achieve so much. I do feel confident they know their medications and their dose and how they're gonna get the meds, but I feel less confident that they are able to fully explain their disease manifestations.

- HP: If you get a 17-year-old that you tell all of a sudden you have lupus, there's a lot of education that has to happen in a short period of time…They just haven't had a chance to absorb all that information and then take ownership of it [prior to transitioning].

Self-efficacy

Delayed self-efficacy: I: Do [patients] typically have a pretty good understanding of where they're at health wise? HP: Not necessarily, and I think it comes from the part that some of these kids have been sick since they were very young, and it's the parents who have been making all the decisions.

Transition of family involvement: P: It [the transition period] was just really confusing because, everything was completely different and my mom- she's also the one that handles most of my medical care stuff so I didn't know much of what that process was like.

Obtaining/utilizing insurance: P: [The pediatric hospital] never really- they never touched base on like- Hey, you're gonna have to have insurance once you transition. We never really talked about it. We just talked about like- You're not gonna see us no more. You're gonna get new doctors. You know, that's basically what it was…

- HP: Many patients come to me and think they're going to be able to keep Medicaid forever and so sometimes I've had to kind of break down that- Actually, no, it's gonna cutoff when you're 19.

Insurance literacy: P: As far as navigating insurance I feel like that's something that's really still confusing to me…I've tried to fill out applications for myself, and it's like a really confusing process.

Personal Medical History Knowledge

Information preparedness: P: [During my first adult rheumatology appointment] my nurse talked to me about what medications I was taking and I personally- I don't know literally every medication I'm taking name from name, and I remember that was like- you're an adult, you should know this, your mom can't answer for you no more…and to me it was like- this is my first appointment…you have to give me time.

- HP: I want to know that [patients] can independently identify their disease that they have, like an appropriate understanding of their disease, they know what the treatment for that is, they can accurately report on these are the medicines I'm taking, this is how much I'm taking, this is when I take them, these are the side effects to look out for.

P = Patient, HP = Health care professional, I = Interviewer

Patient & Health Care Professionals' Perspectives on Health Literacy.

Conclusion: Patient activation and HL are acknowledged by patients and health care teams as substantially influencing pediatric-to-adult transition success among an uninsured/publicly insured urban jSLE cohort. Further research is needed to evaluate whether improved patient activation and HL positively influence jSLE transition outcomes.

Table 3. Patient and Health Care Team Members' suggestions to improve jSLE transition

Multimodal education: P: I like people to talk to me, explain the paper to me, and maybe just like a few drawings like on the consequences like flareups or your muscles being icky or stuff like that.

- P: [On education about medications] I think another way either probably be a pamphlet and the doctors just kind of summarize it a little bit, but the pamphlet will be for the teenager to have and, you know, to read it on their own time, and I think a video's also helpful too

***Early preparation*:** HP: If you start coming up with your [transition] plan early then that is huge…for example, are you thinking about going to college in the middle of nowhere? Are you sure that they're going to have a rheumatologist somewhere in the middle of nowhere?...Can you give yourself your own injections?

Effect of lupus camp: HP: I've never been to Lupus Camp, but the patients that I've had that have come back from camp seem to have a better understanding, they feel, you know, a little more accepted, they have met some people that have lupus too. They don't feel like they're the only ones out there having to take medicines and dealing with stuff.

Engagement with Social Workers: P: There's places where they assign caseworkers to people who kinda check in with them and making sure that they're like taking their med, making sure that they're going to their appointments, and if they need anything, helping provide them with those resources… figure out how to navigate that issue.

- HP: The adult rheumatology team is more limited in terms of resources. We don't have a social worker. We don't have physical therapies. We don't have a psychologist or other things that I know that they have available [in pediatrics].

Mobile medical applications: P: [The patient-facing EMR] helps a lot, I mean you can have full communication with your nurses…so to me MyChart is like- it was a- it's a pretty big help…

- HP: [Patients] can actually access all of their labs and all their medications and things like that. So it is inherently all accessible to them. However, that clearly benefits a certain subsegment who will be able to understand and utilize that system and then it doesn't benefit people that are not as capable of navigating that type of system.

P = Patient, HP = Health care professional

Patient & Health Care Team Members' Suggestions to Improve jSLE Transition.

Disclosure: A. Ciosek, None; **U. Makris**, None; **J. Kramer**, None; **T. Wright**, None; **N. Bitencourt**, None.

Abstract Number: 1635

Nailfold Capillary Microscopy in Children with Raynaud's Phenomenon. Potential Predictive Value of Capillary Loss for Future Connective Tissue Disease?

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Nailfold capillary microscopy (NCM) is a cornerstone in the diagnosis of Systemic Sclerosis (SSc) in adulthood. Although Raynaud's phenomenon (RP) is common in childhood, studies on diagnostic methods to differentiate between primary RP (PRP) and secondary RP (SRP) at a young age are scarce. The aim of this study was to determine the value of NCM in differentiating between PRP and SRP in children and adolescents with RP.

Methods: In this nested case-control study, 83 patients diagnosed with RP and having undergone NCM in childhood were retrospectively included. Based on whether they were diagnosed with a connective tissue disease (CTD) during follow-up, patients were classified as PRP or SRP. Patients were considered to have SRP if they had received a CTD diagnosis based on current ACR/ EULAR classification criteria: SSc, Mixed CTD (MCTD) systemic lupus erythematosus (SLE), adult and juvenile idiopathic inflammatory myopathies (IIM), rheumatoid arthritis (RA) primary Sjögren's syndrome (SS). NCM was judged visually by a vascular technician. PRP and SRP patients were compared on demographics, NCM, and serology. Variables associated with SRP were included in a multivariate logistic regression model. Predictive values were calculated for NCM, ANA positivity, and the combination of NCM and ANA positivity.

Results: At the time of the NCM, the mean age of the RP patients was 15.4±2.3 years (Table 1). Of these patients, 78% were classified as PRP and 22% as SRP at mean follow-up of 6.4±3.20 years. Of the SRP patients, 22% had an

Table 1. Baseline characteristics for the whole study population, and the PRP group and SRP group separately

Characteristics	All patients n=83	PRP-patients n=65	SRP-patients n=18	p-value
Demographics				
Age at NCM, mean ±sd	15.4 ±2.26	15.7 ±1.81	14.3 ±3.26	**0.10**
Female gender, n (%)	64 (77)	49 (75)	15 (83)	0.48
NCM				
Capillary loss (<18/3mm), n (%)*	18 (22)	10 (16)	8 (44)	**0.01**
Dilated capillaries (>3/3mm), n (%)	40 (48)	32 (49)	8 (44)	0.72
Giant capillaries (>0/3mm), n (%)	21 (25)	15 (23)	6 (33)	0.38
Haemorrhages (>0/3mm), n (%)	14 (17)	10 (15)	4 (22)	0.49
Number of capillaries/3mm, mean ±sd*	20.6±2.87	21.0±2.47	19.2±3.76	**0.06**
Number of dilated capillaries/3mm, mean ±sd	4.1±4.36	4.3±4.27	3.8±4.8	0.43
Number of giant capillaries/3mm, mean ±sd	0.3±0.93	0.2±0.70	0.5±1.42	0.39
Number of haemorrhages/3mm, mean±sd	0.2±0.67	0.2±0.65	0.3±0.73	0.42
Serology				
Positive ANA screening, n (%)*	21 (26)	9 (14)	12 (67)	**<0.001**
Positive ENA screening, n (%)**	12 (22)	3 (8)	9 (50)	**<0.001**

Notes: *The last column shows p-value (in bold: p < 0.10) for comparison between PRP and SRP.*

**1 missing value (1.5%). **2 missing values (2.4%).*

Abbreviations: *ANA = Antinuclear antibodies; NCM = nailfold capillary microscopy; PRP = Primary Raynaud's phenomenon; SRP = Secondary Raynaud's phenomenon; SSc = Systemic sclerosis.*

undifferentiated CTD, 22% had a MCTD, 17% had SLE, 11% had IIM, 6% had SSc, 6% had SS, 6% had incomplete SLE, 6% had incomplete SSc and 6% had incomplete SS. In total, half of patients had dilated capillaries, 25% had giant capillaries, 22% had capillary los, 17% had hemorrhages. Giant capillaries were confined to patients with SSc (1 out of 1), MCTD (3 out of 4), and IIM (2 out of 2). An SSc-like NCM pattern was observed in only 25%, which did not differentiate between those who developed CTD and those who did not. Of the NCM parameters, only capillary loss was associated with SRP (p=0.01). In a multivariate logistic regression model, capillary loss was an independent predictor (OR=3.98, CI 95% 1.22-12.99) (Table 2). After including ANA in the model, capillary loss was not an independent predictor of SRP. Capillary loss had a sensitivity of 44% and a specificity of 84% for SRP. PRP was correctly predicted in 99%, while SRP was correctly predicted in 27% of the cases by using capillary loss. ANA combined with capillary loss had a sensitivity of 67% and a specificity of 86% (Table 3).

Conclusion: Of all NCM findings, only capillary loss was predictive of SRP in children presenting with RP. Using NCM in childhood should be done with caution since the majority of children developing future CTDs present without specific NCM abnormalities. However, if present, capillary loss on NCM has a high specificity for future CTD. Because of this, we believe NCM could be useful as a screening method to exclude SRP when combined with serology. Our study underlines that future research should determine the predictive value of NCM and its specific abnormalities for individual CTDs in children presenting with RP.

Table 2. Multivariate logistic regression model showing predictive value of baseline variables for SRP excluding ANA positivity

Independent variables	B(SE)	OR (95% CI)	p-value
Age at NCM	-0.23 (0.12)	0.79 (0.63-1.00)	**0.05**
Capillary loss (<18/3mm)	1.38 (0.60)	3.98 (1.22-12.99)	**0.02**

***Notes**: Variables associated with SRP in the univariate analysis (p<0.10) were considered for inclusion in the multivariate logistic regression model. Variables included in the model were: age at NCM and capillary loss. The number of capillaries was not included because of its correspondence to capillary loss.*
***Abbreviations:** CI = confidence interval; NCM = nailfold capillary microscopy; OR = odds ratio; SE = standard error.*

Table 3. Predictive value of logistic regression models comprising different independent variables for prediction of SRP

	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	% correctly classified
ANA screening	67	86	57	90	82
Capillary loss (<18/3mm)	44	84	44	84	76
ANA screening + Capillary loss (<18/3mm)	67	86	57	90	82

***Notes:** A classification cut-off of 0.44 was used for all models.*
***Abbreviations:** ANA = Antinuclear antibodies; NPV = Negative predictive value; PPV = Positive Predictive value.*

Disclosure: C. Farenhorst, None; **A. Van Roon**, None; **A. van Gessel**, None; **A. Stel**, None; **H. Bootsma**, Bristol Myers Squibb, 2, 5, 6, Roche, 2, 5, Novartis, 2, 6, Medimmune, 2, Union Chimique Belge, 2; **W. Armbrust**, None; **D. Mulder**, None.

Abstract Number: 1636

Pediatric Rheumatologists' Perspectives on Diagnosis, Treatment and Outcomes of Sjögren Syndrome in Children and Adolescents

Rachel Randell[1], Sara Stern[2], Heather Van Mater[1], Scott Lieberman[3] and Matthew Basiaga[4], [1]Duke University, Durham, NC, [2]University of Utah, Salt Lake City, UT, [3]University of Iowa, Iowa City, IA, [4]Mayo Clinic, Inver Grove Heights, MN

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Sjögren syndrome in children and adolescents often presents differently from adult disease, with many pediatric patients failing to meet adult criteria. Additionally, treatment and outcomes in children and adolescents are not well defined. The objective of this study is to describe the current perspectives of pediatric rheumatologists on diagnosis, treatment and outcomes of pediatric Sjögren syndrome (pedSS).

Methods: A voluntary survey containing 17 questions was distributed via email to providers (pediatric rheumatologists, fellows, and advanced care providers) participating in the Childhood Arthritis and Rheumatology Research Alliance and/or the American College of Rheumatology Childhood Sjögren's Study Group at the 2020 Annual Meeting. Descriptive statistics were used to report the findings.

Results: Between September 21 and November 16, 2020, 152 providers participated in the survey. The majority were pediatric rheumatology attendings from the United States. Most (85%) saw five or fewer, half (51%) saw one to two, and 15% had not seen any patients with pedSS in the past year. About three quarters (73%) felt pedSS is a spectrum of adult disease, while one quarter (24%) felt that pedSS is a distinct entity from adult disease. To make the diagnosis of pedSS, most (77%) use clinical judgment and/or experience guided by adult criteria. Parotitis, dry eye and/or dry mouth, and constitutional symptoms were among the most specific and most commonly observed symptoms. Arthralgias were more common but less specific, and dental caries were less common but more specific. Serologic tests were routinely used by >70% of providers for diagnosis. Amongst diagnostic tests, minor salivary gland biopsy was "always" used by 8% and "often" used by 43% of providers for diagnosis; other diagnostic tests were utilized less frequently. The most commonly prescribed systemic medications were hydroxychloroquine (85%), corticosteroids (67%), methotrexate (60%), rituximab (37%), and mycophenolate mofetil (34%). Providers perceived fatigue to be the most frequent symptom affecting quality of life, although only 15% would initiate systemic medication for fatigue. Providers also reported dryness and parotitis frequently affected quality of life for patients. Seven providers had observed malignancy in a patient with pedSS, including one death.

Conclusion: Pediatric rheumatologists are diagnosing and treating pedSS, although most providers see only a few patients per year. Most providers rely on clinical judgment and serologic testing for diagnosis, and some recognize pedSS as a distinct entity from adult disease. The most frequently prescribed systemic medications are hydroxychloroquine and corticosteroids, but substantial experience is reported with disease-modifying antirheumatic agents including methotrexate, mycophenolate mofetil, and biologics. Malignancy is observed in pediatric patients. More studies are critically needed to understand the natural history of pedSS, prognostic factors, and the impact of systemic medications on disease course and outcomes over time.

Disclosure: R. Randell, biogen, 12, my husband is a former employee of biogen and owns stock in the company, merck, 12, my husband is a current employee of merck; **S. Stern**, None; **H. Van Mater**, None; **S. Lieberman**, None; **M. Basiaga**, None.

Abstract Number: 1637

Covid-19 Infection Among Pediatric Rheumatology Patients: A Single Center Experience

Eric Kok, Martha Curry, Andrea Ramirez, Eyal Muscal and Marietta DeGuzman, Baylor College of Medicine, Houston, TX

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Infection with novel coronavirus (COVID-19) in children, unlike adults, is generally asymptomatic or causes mild disease although some may develop severe illness. In particular, pediatric rheumatology patients may be at higher risk due to their immunosuppression. There are few publications describing COVID-19 infection among children with rheumatologic diseases. The Southwest region has had multiple COVID-19 surges and less prominent mitigation than other parts of the country with perhaps greater risks to children with chronic illness. This study reports on COVID-19 infections, risk factors for morbidities, and outcomes in pediatric rheumatology patients cared for in a large urban tertiary pediatric health system.

Methods: With approval from the Institutional Review Board of Baylor College of Medicine, a retrospective review was conducted of pediatric rheumatology patients followed at Texas Children's Hospital (TCH) from March 10, 2020 to April 10, 2021. We abstracted charts for demographic data, rheumatologic diagnoses, immunomodulatory therapies, COVID-19 infection and hospital course if admitted. The SlicerDicer Epic tool (Madison, WI) was used to assess number of active patients seen during the study period. Analyses were performed with Stata v16.1. Categorical variables were compared using Fisher's Exact test.

Results: There were approximately 1593 pediatric rheumatology patients actively followed during the study, including 800 JIA patients and 204 lupus patients. During the study period, 43 had COVID-19 infection (43/1593, 2.7%), with an incidence of 2.1% in JIA patients and 5.9% in lupus patients. Table 1 summarizes demographic and clinical characteristics. Twenty-one held their rheumatologic therapy; of these, 5 patients (24%) had a flare of their condition. No patient developed MIS-C.

Eight patients were hospitalized, 3 (37.5%) whom required intensive care. The median length of stay was 6.5 days (1-81), and 8 days (2-42) for ICU patients. Majority were Hispanic (75%), and 6 (75%) were female. There was a statistically significant association between obesity with hospitalization as well as Steroid dose of ≥10 mg; all 3 ICU patients were taking ≥10 mg. No association was found between specific DMARD or biologic and hospitalization.

The characteristics and course of 3 ICU patients, 2 with SLE and 1 with a rare autoinflammatory syndrome, are presented in Table 2. All presented with fever ≥101°F (≥38.3°C), and 2 required supplemental O_2. One lupus patient required mechanical ventilation and passed away from respiratory failure.

Conclusion: In a county with a high COVID-19 prevalence, only a small percentage of pediatric rheumatology patients presented to medical care with confirmed infections. Most had mild courses that did not affect their underlying

Table 1. Demographic and clinical characteristics of COVID + pediatric rheumatology patients

Demographic and clinical characteristics	COVID + n = 43 (%)	Hospitalized n = 8 (%)	ICU admission n = 3 (%)
Age, in years (mean, SD)	13.1 (4.1)	14.4 (2.4)	12.2 (2.1)
Gender (# female, %)	37 (86)	7 (87.5)	3 (100)
Ethnicity			
White	13 (30)	1 (12.5)	0
Hispanic	27 (63)	6 (75)	3 (100)
Black	3 (7)	1 (12.5)	0
BMI percentile (median, range)	78 (2-99)	94 (75-99)	94 (92-94)
Selected Comorbidities			
Obesity	14 (33)	3 (37.5)	0
Hypertension	3 (7)	2 (25)	1 (33)
Diabetes	1 (2)	0	0
Rheumatologic diagnoses			
JIA	17 (40)	3 (37.5)	0
SLE	12 (28)	4 (50)	2
CRMO	3 (7)	0	0
GPA	1 (2)	0	0
Periodic Fever	2 (2)	0	0
SCTD	3 (7)	0	0
Overlap	2 (5)	0	0
Uveitis	3 (5)	0	0
DAH	1 (2)	0	0
Other	2 (2)	1 (12.5)	1
Immunosuppressive therapies			
DMARDS			
Methotrexate	14 (32)	1 (12.5)	1 (33)
Mycophenolate	5 (12)	1 (12.5)	1 (33)
Azathioprine	4 (9)	0	0
Leflunomide	1 (2)	0	0
Myfortic Acid	1 (2)	0	0
Mycophenolate + Methotrexate	1 (2)	0	0
Plaquenil	16 (37)	0	0
Colchicine	1 (2)	0	0
Biologics			
TNF-alpha	11 (26)	2 (25)	1 (33)
Tocilizumab	5 (12)	0	
Anakinra	2 (5)	1 (12.5)	1 (33)
Abatacept	2(5)	0	
Rituximab	1 (2)	1 (12.5)	1 (33)
Corticosteroids (mg prednisone)	n = 14	n = 8	n = 3
≥10 mg or equivalent	8 (70)	6 (75)	3 (100)

Table 2. Characteristics and clinical course of 3 patients admitted to the ICU for COVID-19

Patient	Patient 1	Patient 2	Patient 3
Age at time of infection (years)	9.9	12.8	13.9
Gender	Female	Female	Female
Diagnosis	NEMO* , a rare autoinflammatory syndrome	SLE	SLE
Associated complications	Severe immunodeficiency, Long-term steroid use	Antiphospholipid antibody (+), hemolytic anemia	Hypogammaglobulinemia, Lupus Anticoagulant Hypo-prothrombinemia Syndrome, Hypertension
Current steroid dose (mg)	10	10	50 - additionally received recent steroid pulse
Immunomodulatory drugs	Anakinra, IVIG	Adalimumab, methotrexate, hydroxychloroquine	Rituximab (2 months prior to infection), Mycophenolate mofetil, Hydroxychlorquine
Presenting symptoms	Fever Tmax 101°F (38.3°C), loss of taste and smell, myalgias	Fever Tmax 101°F (38.3°C) , chest pain, shortness of breath	Fever Tmax 102.9°F (39.4°C), shortness of breath, septic shock
Maximum respiratory support	High flow nasal cannula 12 L	Room air	Intubation, mechanical ventilation, oscillator
Clinical course	Severe pneumonia, pancytopenia	Uneventful course, stable on RA. Nomal cardiopulmonary workup. Diagnosed with lupus flare.	Severe pneumonia, respiratory failure, complications including recurrent pulmonary hemorrhage, and decompensation
COVID-19 therapies	Dexamethasone, Remdisivir, Anakinra, convalescent plasma	Dexamethasone	Dexamethasone, Remdesivir, Convalescent Plasma, IVIG, Anakinra,Lovenox
Outcome	Recovered	Recovered	Passed away

*NEMO - Nuclear factor-kappa B Essential Modulator (NEMO) deficiency syndrome, a rare autinflammatory immunodeficiency

disease. As per adult experiences, obesity and higher steroid doses were observed in admitted patients. Children with SLE and from underrepresented minorities represented a large proportion of those affected, suggesting a significant role of socioeconomic factors with increased risk of exposures. The effect of vaccine protection on pediatric rheumatology patients will be studied during the upcoming year.

Disclosure: E. Kok, None; **M. Curry**, None; **A. Ramirez**, None; **E. Muscal**, None; **M. DeGuzman**, None.

Abstract Number: 1638

Clinical Manifestations of COVID-19 and Its Impact on Pediatric Patients with Rheumatic Disease

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Spread of SARS-COV-2 during the COVID-19 pandemic has raised concerns for patients with rheumatic disease. Rheumatology patients have an increased risk of developing infectious complications due to their underlying disease and chronic use of immunomodulating medications. Reports suggest children with rheumatic disease are not at an increased risk of developing severe symptoms from acute COVID-19; however, there are growing concerns that SARS-COV-2 may trigger their underlying disease, causing exacerbation or new diagnosis of diseases. We report clinical manifestations of SARS-COV-2 and its impact on underlying rheumatic disease activity on pediatric rheumatology patients at our tertiary care center.

Methods: Retrospective chart review of the Children's Hospital Los Angeles rheumatology clinic population from March 2020 to May 2021 identified pediatric rheumatology patients with reported positive SARS-COV-2 qualitative PCR test and/or positive SARS-COV-2 antibody test. Data including demographics, rheumatic disease diagnosis, medications, co-morbidities, acute symptoms of COVID-19, and rheumatic disease complications were collected. Acute COVID-19 manifestations and rheumatic disease complications (and/or exacerbations) were categorized into numeric scale of 0-3 (COVID-19 manifestations: 0 = No symptoms, 1 = Mild symptoms not requiring hospitalization, 2 = Respiratory distress requiring floor admission, 3 = Respiratory failure requiring intensive care unit (ICU) admission; Rheumatic disease complications: 0 = No flare, 1 = Flare with no escalation of treatment, 2 = Flare requiring escalation of treatment, 3 = Flare requiring hospitalization).

Results: A population of 82 patients of ages 0 to 21 were identified via chart review. Their demographics, diagnosis, medications are included in Table 1. The majority of patients were female (76%) and between ages of 16 to 21 (51%). Most had diagnosis of juvenile idiopathic arthritis (38%) and were taking methotrexate (22%). There were 14 patients with identified co-morbidities, and the most common co-morbidity was obesity (78%). Acute COVID-19 severity scores are demonstrated in Table 2. Most patients scored 1 (55%), followed by 0 (28%). Rheumatic disease complications scores are demonstrated in Table 3. Most patients scored 0 (77%), followed by 3 (13%).

Conclusion: Our findings were consistent with previous reports that many pediatric patients with rheumatic disease experience mild or no symptoms of acute COVID-19. Most patients did not have complications or exacerbations of their underlying disease after contracting SARS-COV-2, although there were cases that required

Table 1. Demographics and Medical History of Patients with Positive SARS-COV-2 Test (N = 82)

Gender	N = 82	%
Female	62	76%
Male	20	24%

Age	N = 82	%
From 0 to 5	4	5%
From 6 to 10	11	13%
From 11 to 15	25	30%
From 16 to 21	42	51%

Diagnosis	N = 82	%
ANCA vasculitis	5	6%
CNS Vasculitis	1	1%
Juvenile Dermatomyositis (JDM)	2	2%
Juvenile Idiopathic Arthritis (JIA)	31	38%
Localized Scleroderma	1	1%
Mixed Connective Tissue Disease	2	2%
Overlap Syndrome	4	5%
Periodic Fever Syndrome	4	5%
Systemic JIA	1	1%
Systemic Lupus Erythematosus (SLE)	18	22%
Takayasu Arteritis	3	4%
Undifferentiated Connective Tissue Disease (UCTD)	4	5%
Uveitis	6	7%

Medications	N = 116	%
Abatacept	3	3%
Adalimumab	9	8%
Azathioprine	2	2%
Baricitinib	1	1%
Canakinumab	2	2%
Colchicine	3	3%
Cyclophosphamide	1	1%
Etanercept	9	8%
Hydroxychloroquine	16	14%
infliximab	5	4%
Leflunomide	1	1%
Methotrexate	25	22%
Mycophenolate Mofetil	7	6%
Naproxen	1	1%
Prednisone	15	13%
Rituximab	2	2%
Secukinumab	1	1%
Tocilizumab	9	8%
Tofacitinib	4	3%

Comorbidities	N = 14	%
Obesity	11	79%
Diabetes Mellitus	2	14%
Hemodialysis	1	7%

Table 2. Severity Score of Acute COVID-19 Manifestations (N= 82)

Severity Score: Acute COVID-19	N = 82	%
0 (No symptoms)	23	28%
1 (Mild symptoms*)	45	55%
2 (Respiratory distress requiring floor admission)	5	6%
3 (Respiratory failure requiring ICU admission)	0	0%
Unknown	9	11%

*Mild cough, rhinorrhea, sore throat, loss of taste and/or smell, fever, nausea/vomiting, abdominal pain, diarrhea, headaches, and fatigue

Table 3. Severity Score of Rheumatic Disease Complications/Flare (N = 82)

Severity Score: Disease Complications/Flare	N = 82	%
0 (No Complication)	63	77%
1 (Flare with no escalation of treatment)	5	6%
2 (Flare requiring escalation of treatment)	3	4%
3 (Flare requiring hospitalization)	11*	13%

*5 out of 11 patients presented with a new diagnosis of SLE, ANCA vasculitis, JDM, and UCTD

hospitalized care, including those who presented with new-onset rheumatic disease. Autoimmune diseases are often triggered by viral infections, and it may be important for pediatric rheumatologists to pay closer attention to disease activity of patients who contracted SARS-COV-2.

Disclosure: B. Yi, None; **S. Mohandas**, None; **M. Cidon**, None.

Abstract Number: 1639

A Comparison of Cardiovascular Health Indicators in Children with Juvenile Idiopathic Arthritis Who Meet and Do Not Meet the Physical Activity Guidelines

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Children with juvenile idiopathic arthritis (JIA) engage in less physical activity than their healthy peers. The Canadian 24-h Movement Guidelines recommend children take part in at least 60 minutes of moderate-to-vigorous physical activity (MVPA) per day to help maintain optimal health. Meeting these physical activity guidelines may be even more important for children with JIA, as research suggests they may be at increased risk for accelerated cardiovascular disease. The aim of this study was to compare cardiovascular health indicators in children with JIA who meet and do not meet the MVPA guidelines.

Methods: Children with single diagnosis of JIA between 7 to 17 years of age were recruited from McMaster Children's Hospital and completed 2 study visits. During Visit #1, height, weight, and body fat were measured. Participants then wore an accelerometer for 7 consecutive days to estimate habitual levels of MVPA. During Visit #2, cardiovascular health indicators were assessed in a fasted state. Carotid artery b-stiffness and intima-media thickness (cIMT) were measured by ultrasound. Whole body arterial stiffness was assessed as carotid – foot pulse wave velocity (PWV). Endothelial function was measured using flow-mediated dilation (FMD) of the brachial artery. Participants were divided into two groups based on meeting (MET) or not meeting (NOT) guidelines of an average of ≥60-min MVPA per day. Participant characteristics, carotid artery b-stiffness and cIMT for MET and NOT were compared using independent sample t-tests, while PWV and FMD were assessed using analysis of covariance, with height or baseline artery diameter as a covariate, respectively.

Results: Twenty-one participants (12 girls) completed this study. Nine children (43%) were in the MET group and had a mean MVPA of 72.9±16.2 min/day, while 12 children (57%) were in the NOT group and engaged in 38.6±13.2 min/day. There were no between group differences in age, height, weight, or body fat (Table 1). There were no between group differences in cardiovascular health indicators including carotid b-stiffness, cIMT and relative FMD (Table 2). There was a trend towards MET having better PWV than NOT (4.8±0.42 m/s vs. 5.2±0.35 m/s, $F(1,18)=2.7$, $p=0.083$, partial $h^2 = 0.129$; Figure 1).

Conclusion: Over half of children with JIA in our sample did not meet physical activity guidelines. While we did not find any significant differences in cardiovascular health indicators between children who meet and did not meet the MVPA guidelines, these results, and particularly PWV, may be underpowered to detect differences. These findings highlight the need for further investigation of physical activity and cardiovascular health in JIA.

This study was funded by a Grant-in-Aid from the Heart and Stroke Foundation of Canada.

Table 1: Participant Characteristics

	MET	NOT	T (df)	p
N	9	12	-	-
Age (years)	11.9 ± 2.6	13.2 ± 3.1	1.32 (19)	0.873
Height (m)	1.50 ± 0.13	1.58 ± 0.14	1.038 (19)	0.572
Weight (kg)	48.9 ± 18.7	55.4 ± 18.2	0.806 (19)	0.883
Body fat (%)	25.2 ± 10.5	29.2 ± 8.6	0.954 (18)	0.505
MVPA (min/day)	72.9 ± 16.2	38.6 ± 13.2	-5.36 (19)	<0.001

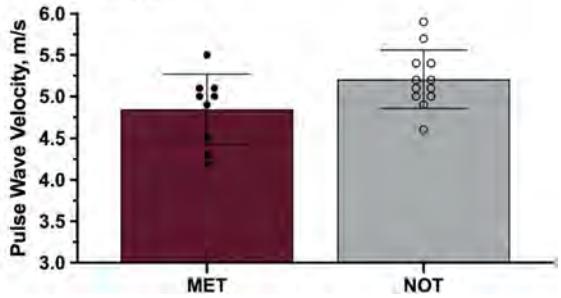
df = degrees of freedom; MVPA = moderate-to-vigorous physical activity. Data are presented as mean ± standard deviation.

Table 2: Cardiovascular Health Indicators

	MET	NOT	T or F (df)	p
N	9	12	-	-
Carotid artery β-stiffness (AU)	3.9±0.9	4.3±1.2	0.804 (19)^{T}	0.598
cIMT (mm)	0.38±0.03	0.39±0.04	0.416 (19)^{T}	0.349
Relative FMD (%)	8.3±2.2	7.3±1.7	0.194 (12)^{F}	0.732

cIMT = carotid intima media thickness; FMD = flow-mediated dilation. Data are presented as mean ± standard deviation. T = T statistic (degrees of freedom); F = F statistic (degrees of freedom).

Figure 1: PWV in MET vs. NOT



Data are presented as mean ± SD, with individual data displayed in closed circles for MET and open circles for NOT.

Disclosure: M. Byra, None; **N. Proudfoot**, None; **S. Chen**, None; **M. MacDonald**, None; **T. Cellucci**, None; **M. Batthish**, Abbvie, 5, Novartis, 6, Mylan, 1, Sobi, 1; **B. Timmons**, None; **J. Obeid**, None.

Abstract Number: 1640

Multisystem Inflammatory Syndrome in Children at Two Tertiary Hospitals in Cape Town, South Africa: Clinical Phenotype and Distinguishing Features from Similar Acute Inflammatory Conditions

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Distinguishing Multisystem Inflammatory Syndrome in Children (MIS-C) associated with Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV2) from acute, pyrexial childhood illness can be challenging. We present a case series from two tertiary hospitals and compare the clinical phenotype of MIS-C with mimicking systemic inflammatory disorders.

Methods: Children with MIS-C admitted to two tertiary hospitals in a province between 22 June 2020 and 5 March 2021 were recruited. At one of the two hospitals, children with suspected MIS-C with an ultimate alternate diagnosis (inflammatory controls) were also recruited. Clinical data were collected. Statistics were performed using SPSS V. 27.

Results: During the time period, 70 children had confirmed MIS-C and 27 suspected MIS-C cases had an alternate diagnosis including typhoid, tuberculosis, sepsis and appendicitis among others. Sixty five percent of children with MIS-C had no SARS-CoV2 contact but all had evidence of SARS-CoV2 exposure by antibody (90%) or PCR tests (14%). There was no difference in age, sex or ethnic distribution between children with MIS-C and inflammatory controls (Table 1). The most common presenting features of MIS-C were fever (100%), tachycardia (99%), rash (86%), conjunctivitis (79%), and abdominal pain (60%). Compared to inflammatory controls, the presence of tachycardia, abdominal pain and conjunctivitis resulted in 96%; 93% and 91% respectively increased odds of a diagnosis of MIS-C after controlling for all other presenting features. Compared to inflammatory controls, children with MIS-C had lower platelets, sodium and albumin and higher troponin-T and pro-brain natriuretic peptide (pro-BNP)(Table 1).

The median minimum ejection fraction in MIS-C was lower than inflammatory controls (52% vs 63%, p=0.048). Ninety four percent of MIS-C patients received at least one dose of intravenous immunoglobulin (IVIG), 63% required methylprednisolone and 6% received IL-6 inhibition. Children with MIS-C were more commonly admitted to the intensive care unit (ICU) compared to inflammatory controls (38% vs 12.5%, p=0.013) although there was no difference in mean hospital stay which was 8.2 days in MIS-C. There was no difference in requirement for inotropes (p=0.142) or ventilation (p=0.493). No children died.

Conclusion: Distinguishing MIS-C from acute infectious or inflammatory causes of childhood fever may be challenging. The presence of conjunctivitis, tachycardia or abdominal pain associates with higher odds of MIS-C in this pop-

Table 1

	MIS-C N=70	Inflammatory Controls N=27	p-value
Median age in years (IQR)	7.0 (2.4, 9.7)	5.3 (2.0, 9.5)	0.53
Sex: male (%)	36 (51.4)	16 (59.2)	0.506
Ethnicity: black African (%)	43 (61.4)	14 (51.8)	0.216
Minimum platelets ($x10^9$/L)	219.2	300.4 N=25	0.021*
Minimum sodium (mmol/L)	128.9	133.8 N=26	<0.001*
Minimum albumin (g/L)	27.6 N=65	32.1 N=16	0.015*
Maximum troponin-T (ng/L)	79.5 N=46	11.7 N=14	0.001*
Maximum pro-BNP (ng/L)	11981.4 N=63	2712.4 N=19	0.002*

ulation. Differences in widely available blood tests like sodium, albumin and platelets may be useful to differentiate MIS-C in the acute setting.

Disclosure: C. Butters, None; **D. Abraham**, None; **H. Facey-Thomas**, None; **D. Abrahams**, None; **A. Faleye**, None; **H. Rabie**, None; **C. Scott**, None; **L. Zühlke**, None; **K. Webb**, None.

Abstract Number: 1641

Long-term Cardiovascular Disease and Mortality Following Kawasaki Disease in Childhood: A Systematic Review

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Kawasaki Disease (KD) is a common vasculitis of childhood, with an annual North American incidence of 20-26 per 100,000 children (< 5 years of age). Coronary artery aneurysms (CAAs) develop in 25% of

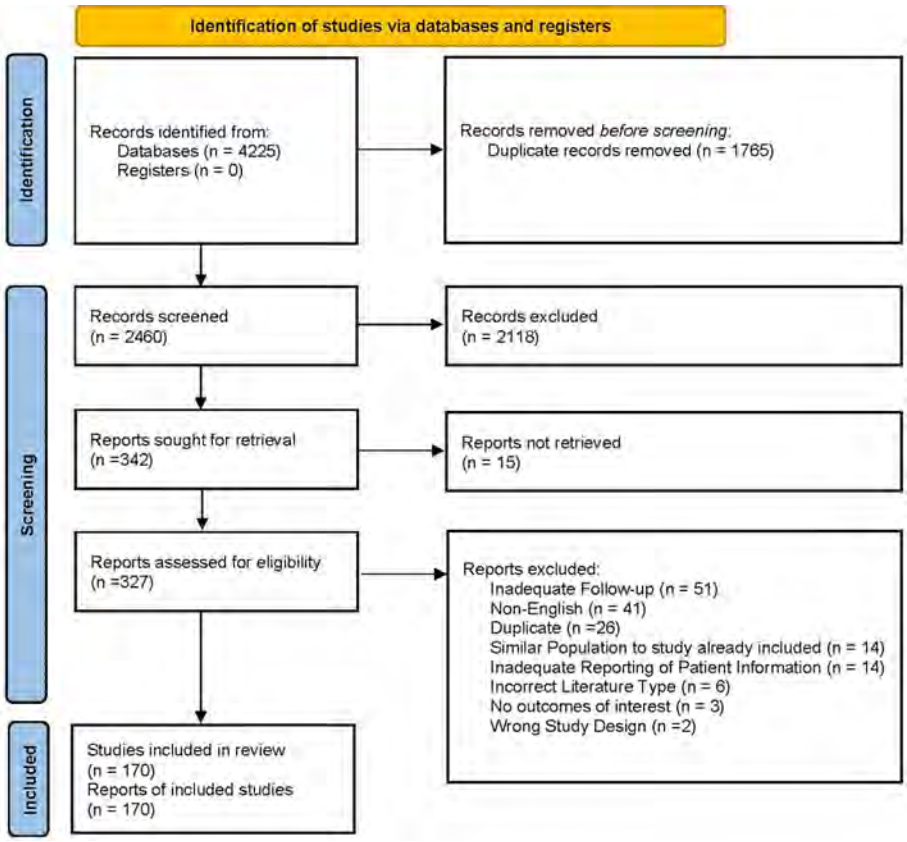

Figure 1. PRISMA flow diagram of study selection.

untreated KD patients. There are no precise estimates of the long-term cardiovascular (CV) events following childhood KD diagnosis. We aimed to determine the incidence of long-term CV events and mortality following KD diagnosis.

Methods: A systematic search of MEDLINE, EMBASE, CINAHL, Cochrane, and Web of Science databases was performed through 2019. Initial screening was performed by 2 independent reviewers. Inclusion criteria included English-only publications, patients 0-18 years at KD diagnosis, minimum follow-up >1 year, and ≥10 patients included in original clinical data. CV events (myocardial infarction (MI), heart failure (HF), cardiac arrest) and mortality were extracted and pooled for analysis. The Newcastle-Ottawa Scale assessed study quality focusing on participant selection, comparability, and measurement of outcome or ascertainment of exposure. This review was submitted to PROSPERO on November 23, 2019 and registered on April 28, 2020.

Results: Of 4225 articles identified, 170 were included in the review (Figure 1). The distribution of study designs was: 123 retrospective cohort studies, 54 prospective cohort studies, 2 case series, 13 cross-sectional studies, 1 case control study, and 4 interventional studies. A total of 167 articles had quality assessment scores ≥6 out of a maximum score of 9. The number of studies reporting coronary artery stenosis, coronary artery thrombosis, coronary artery occlusion, CV events and death are displayed in Table 1.

Among 86,812 KD patients across 110 studies, there were 1519 events of MI, HF, or cardiac arrest (1.8%). A subgroup analysis was performed, stratifying studies by CAA status of participants: no/few CAAs (≤ 10% of study participants), some CAAs (11-99% of study participants), all CAAs (100% of study participants). This was performed to determine the effect of CAAs on incidence of CV events and mortality. Composite CV events occurred in 457 of 29,393 (1.55%)

Table 1. Number of studies reporting at least one case of coronary artery stenosis/thrombosis/occlusion, CV events and death

	# studies reporting ≥1 case
Coronary artery stenosis	72
Coronary artery thrombosis	40
Coronary artery occlusion	58
Myocardial Infarction	99
Heart Failure	25
Cardiac Arrest	25
Death	70

Table 2. Incidence of cardiovascular events (myocardial infarction, heart failure, and cardiac arrest) and all-cause mortality

	Cardiovascular Events (MI, HF, Cardiac Arrest)				All-Cause Mortality			
Characteristic of Studies	# of studies	# of events	# of patients	Incidence	# of studies	# of deaths	# of patients	Incidence
All Studies	110	1519	86812	1.75%	99	1137	106497	1.07%
# of CAAs reported	99	1405	48412	2.90%	87	346	52092	0.66%
# of CAAs Not Reported	11	116	38495	0.30%	12	791	54405	1.45%
No/Few patients have CAA (≤ 10% of study participants))	9	457	29393	1.55%	10	75	33845	0.22%
Some patients have CAAs (11-99% of study participants)	49	502	15049	3.34%	41	157	14299	1.10%
All patients have CAAs (100% of study participants)	41	446	3970	11.23%	36	114	3948	2.89%

in no/few CAAs study participants, 502 of 15,049 (3.34%) some CAAs study participants, and 446 of 3970 (11.23%) all CAAs study participants (Table 2).

Across 99 studies, 1137 of 106,497 KD (1.07%) patients died. When stratified based on the proportion of patients in the study with CAAs: death occurred in 75 of 33,845 (0.22%) in no/few CAAs study participants, 157 of 14299 (1.10%) in some CAAs participants, and 114 of 3948 (2.89%) in all CAAs study participants (Table 2).

Conclusion: This study comprises the largest review of long-term cardiovascular outcomes of KD. Children with KD are at risk of developing long-term CV events, including MI, heart failure and cardiac arrest. Those with coronary artery aneurysms are especially at higher risk. Further studies are needed to better define these risks.

Disclosure: F. Lao, None; **C. Robinson**, None; **M. Schlorff**, None; **J. Ewusie**, None; **K. Beattie**, None; **M. Batthish**, Abbvie, 5, Novartis, 6, Mylan, 1, Sobi, 1.

Abstract Number: 1642

Baseline Body-mass-index and Risk for Obesity in Children with Rheumatic Disease on Moderate to High-dose Prednisone Therapy

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Prednisone is a glucocorticoid (GC) medication commonly used in moderate (>7.5 mg per day) to high doses (≥ 1 mg/kg/day) for children with moderate to severe presentations of rheumatic disease. Adverse effects (AE) to GCs impose a significant burden on health and quality of life. We sought to evaluate a possible relationship between baseline patient body-mass-index (BMI) measure and development of select GC-mediated toxicity within the first 12 months of prednisone therapy. Secondary outcomes were to examine rates of GC-mediated hypertension, osteopenia, and osteoporosis.

Methods: We performed a retrospective chart review on children with rheumatic disease age 17 years and younger treated with moderate and high-dose prednisone therapy at a single Canadian academic hospital between January 1, 2010 and December 31, 2019. Demographic variables collected included diagnosis, age, sex, ethnicity. Clinical variables collected include weight, height, and body-mass-index (BMI), hepatitis (transaminases greater than two-fold upper normal limit), proteinuria (>0.1 g/L), and presence of hypoalbuminemia (< 38g/L) at baseline. We collected weight, height, and body-mass-index (BMI), at 6 and 12 months, the maximum BMI, and transformed them to z-scores according to the World Health Organization's Child Growth standards. Cumulative prednisone dose (mg/kg/12 months), total days on prednisone in the first 12 months of therapy were also obtained, in addition to bone-mineral-density scores after 12 months of prednisone therapy where available.

Baseline characteristics which were significant for the subsequent development of obesity during the first 12 months at the bivariate level ($p < 0.05$) were included as predictors of obesity in separate logistic regression analyses. In each regression analysis, we also adjusted for baseline BMI, and for confounding variables of hepatitis, hypoalbuminemia

(albumin less than 38 grams per litre), proteinuria and prednisone dose. All analyses were performed using SPSS v.26 (IBM Corp., Armonk, NY, USA), and p-values < 0.05 were considered statistically significant.

Results: Seventy-six charts were reviewed, and 73 patients met criteria for analysis. The diagnoses included 20 (26.3%) systemic JIA, 12 (15.8%) JIA, 24 (31.6%) SLE, and 8 (10.5%) JDM patients. Rates of adverse effects were as follows: obesity 27.6%, hypertension 34.2%, symptomatic vertebral fractures 2.2%, long-bone fractures 6.8%. Of 25 patients who had bone mineral density studies, 3 (12%) met criteria for pediatric osteoporosis. Greater BMI at baseline was associated with greater total weight gain (OR 3.358, 95% CI = [1.847-6.103, p< 0.001). Normal albumin (> 38 g/L was negatively associated with GC-related obesity (OR 0.349, 95% CI [0.132-0.921], p=0.035).

Conclusion: Greater baseline patient BMI was a predictor of GC-related obesity initiated with moderate to high-dose prednisone therapy in children with rheumatic disease. Further work is required to determine methods for individualized prednisone dosing and counseling and behavioral interventions to mitigate risk for weight gain.

Disclosure: R. Berard, Sandoz, 2, SOBI, 2, Roche, 2; **M. Rieder**, None; **E. Demirkaya**, SOBI, 5; **M. Miller**, None; **R. Pang**, None.

Abstract Number: 1643

Increased Incidence of Pediatric SLE and Other Interferon Activated Diseases During COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19, as a member of the Coronavirus family, has been described to trigger host immune response via type I interferon (IFN) signaling pathways with variable degrees. Some patients have mild IFN activation, while some develop hyperinflammation. In pediatric patient population COVID-19 has been a mild infection partially explained by the robust acute innate system activation early in the clinical phase of the infection. Etiopathogenesis of rheumatologic diseases like systemic lupus erythematosus (SLE) also involves IFN dysregulation and hyperinflammation as well, so do juvenile and adult dermatomyositis (JDM, DM), polymyositis (PM), systemic sclerosis (SSc) and scleroderma (SD). We hypothesized that COVID-19 infection may increase the incidence of autoimmune rheumatologic diseases that are known to have etiopathogenetic link with type I IFN-dysregulation.

Methods: Data were obtained from the COVID-19 Research Network of TriNetX, a real-world database collected from electronic health records in 61 health-care organizations globally. We created queries of patients who had been diagnosed with rheumatologic diseases (SLE, JDM, DM, PM, and SSc) one year before the pandemic (defined as March 1st, 2019 to February 29th, 2020) and during the pandemic (defined as March 1st, 2020 to February 28th, 2021). For patients diagnosed with SLE, two separate queries were created to divide patients into pediatric and adult population. We compared the incidence of these rheumatologic diseases during and before COVID-19 pandemic and their incidence in COVID-19 affected and unaffected population. We compared COVID-19 incidence in these rheumatologic diseases to those in regular population. We used chi square statistics for establishing significance.

Results: Incidence of pediatric SLE and JDM increased by 22% and 44% respectively during the pandemic as compared to before the pandemic. Incidence of adult SLE, PM, DM, SSc decreased by 8%, 20%, 10% and 15% accordingly (Table 1).

COVID-19 incidence in pediatric SLE patients (3.2%) is greater than COVID-19 incidence in regular pediatric population (1.2%). COVID-19 incidence in adult SLE (4.4%), PM (5.4%), DM (3.6%) and SSc (3.7%) patients is greater than COVID-19 incidence in general adult population (2.8%) (Table 2).

Incidence of pediatric and adult SLE in COVID-19 affected population were significantly higher when compared to COVID-19 unaffected population (pediatric SLE 0.027% vs 0.009%, p=0.00033; adult SLE 0.13% vs 0.077%, $p < 0.00001$) (Table 3).

Conclusion: Those pediatric rheumatologic diseases known to have dysregulation in type I interferon signaling showed increased incidence rate during COVID-19 pandemic. Our results indicate that COVID-19 infection may induce type I interferon activation in children and may result in particular autoimmune disease activity regulated with abnormal interferon pathway signaling. Further studies of pediatric patients affected by COVID-19 infection who

Table 1. Incidence of rheumatologic diseases with type I IFN dysregulation before and during pandemic.

	2019-2020 Before pandemic	2020-2021 During pandemic	% change
SLE⩽17	0.009%	0.011%	**22%**
SLE⩾18	0.106%	0.098%	-8%
JDM	0.00063%	0.00091%	**44%**
PM	0.005%	0.004%	-20%
DM	0.011%	0.01%	-10%
SSc	0.019%	0.016%	-15%

Table 2. Incidence of COVID-19 infection in rheumatologic population with type I IFN dysregulation comparing to those in regular population.

	COVID-19 affected Patient Incidence
SLE⩽17	3.2%
SLE⩾18	4.4%
JDM	0 (NA)
PM	5.4%
DM	3.6%
SSc	3.7%
Regular population⩽17	1.2%
Regular population ⩾18	2.8%
Regular population all age groups	2.6%

Table 3. Incidence of rheumatologic diseases with type I IFN dysregulation in COVID-19 affected population comparing to those in COVID-19 unaffected population.

	SLE⩽17	SLE⩾18	JDM	PM	DM	SSc
Incidence of COVID-19 unaffected patients (%)	0.009	0.077	0.002	0.007	0.014	0.014
Incidence of COVID-19 affected patients (%)	0.027	0.134	0	0.008	0.013	0.02
% Change	200%	74%	-100%	14%	-7%	43%
P-value	0.00033	<0.00001	NA	0.41	0.56	0.48

proceed to develop new onset autoimmune disease activity are required to help understanding the disease pathogenesis of type I interferon induced pediatric rheumatologic diseases.

Disclosure: X. Dou, None; **D. Kaelber**, None; **H. Bukulmez**, None.

Abstract Number: 1644

Storytelling of Young Adults with Chronic Rheumatologic Illnesses: A Pilot Study

Aviya Lanis[1], Emilee Tu[2], Malki Peskin[3], Maryann Melendez[1], Gabriel Tarshish[4], Alisha Akinsete[5], Alicia Hoffman[1], Kathleen Kenney-Riley[6], Tamar Rubinstein[7] and Dawn Wahezi[1], [1]Children's Hospital at Montefiore, Bronx, NY, [2]Albert Einstein School of Medicine, Bronx, NY, [3]Montefiore, Bronx, NY, [4]Children's Hospital at Montefiore, New York, NY, [5]Montefiore, Wayne, NJ, [6]Mercy College, Dobbs Ferry, NY, [7]Albert Einstein College of Medicine, White Plains, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Pediatric Rheumatology – Clinical Poster III: Miscellaneous Rheumatic Disease (1614–1644)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Storytelling is a universal form of communication that allows expression of experiences. Narrative medicine can be described as a subset of storytelling in which patients reconstruct their medical experiences through written or oral portrayals of emotions and perspectives. By sharing these experiences, research has shown participants build experiential knowledge and a mutual depiction of illness while creating a sense of belonging. Currently, there are limited available group-sharing opportunities for pediatric patients with chronic rheumatologic illnesses, a population with a high prevalence of mental health symptoms and worse health-related quality of life. The current study aims to assess the feasibility of a storytelling intervention in this patient population. The primary hypothesis was that the study would be feasible, where 80% of all recruited participants were expected to complete all surveys as well as post-participation interviews.

Methods: This is a mixed methods study of English-speaking patients with chronic rheumatologic diseases, 13-21 years old, followed in the pediatric rheumatology clinic at the Children's Hospital of Montefiore in the Bronx, NY. Participants completed an hour-long interactive virtual creative writing session focused on patient experience with chronic disease. Pre- and post- questionnaires were completed to assess potential risks and benefits of storytelling, and post-participation video interviews were completed to assess personal experiences of participating in the storytelling session. Questionnaires included Peds Quality of Life Inventory (PedsQL), Pediatric Symptom Checklist-17 (PSC-17), Patient Health Questionnaire-9 (PHQ-9), and the Child Attitude Toward Illness Scale (CATIS). Post-participation interviews were reviewed by three independent researches using qualitative software (Dedoose) for coding and thematic analysis.

Results: Thirteen female patients, ages 14-21 years, were divided amongst four creative writing sessions, with groups ranging from two to six participants per session. Diseases included lupus, juvenile dermatomyositis, systemic sclerosis, juvenile idiopathic arthritis, polyarteritis nodosa, and amplified musculoskeletal pain syndrome. Twelve of the 13 patients completed pre-study questionnaires and 10 completed post-study questionnaires, with 100% completion of the post-participation interviews. PedsQL surveys showed a trend toward improvement in physical health, with pre-participation median 64.95 [IQR 56.25-79.95] and post-participation median 78.15 [IQR 62.5-93.8]. Preliminary analysis revealed no significant difference between pre- and post-scores for any of the questionnaires. Preliminary

post-participation interview analysis showed thematic domains of writing motivation, prior writing experience, illness experience, relating to others, relationship with providers, and support.

Conclusion: Creative writing is an intervention that is feasible and acceptable for youth with rheumatologic illnesses. Further evaluation is needed to understand if such interventions improve mental and physical symptoms, and children's attitude towards their illnesses.

Disclosure: A. Lanis, None; **E. Tu**, None; **M. Peskin**, None; **M. Melendez**, None; **G. Tarshish**, None; **A. Akinsete**, None; **A. Hoffman**, None; **K. Kenney-Riley**, National Institute on Disability, Independent Living, and Rehabilitation Research (NIDILRR), 5; **T. Rubinstein**, None; **D. Wahezi**, None.

Abstract Number: 1645

Elevations in Adipocytokines and Mortality in Rheumatoid Arthritis

Joshua Baker[1], Bryant England[2], Michael George[1], Katherine Wysham[3], Gail Kerr[4], Andreas Reimold[5], Paul Monach[6], Gary Kunkel[7], Brian Sauer[7], Bartlett Hamilton[8], Carlos Hunter[2], Michael Duryee[2], Geoffrey Thiele[2] and Ted Mikuls[2], [1]University of Pennsylvania, Philadelphia, PA, [2]University of Nebraska Medical Center, Omaha, NE, [3]VA Puget Sound/University of Washington, Seattle, WA, [4]Washington D.C., Veterans Affairs Medical Center (VAMC)/Georgetown and Howard Universities, Washington, DC, [5]University of Texas – Southwestern Medical Center/Dallas Veterans Affairs Medical Center (VAMC), Dallas, TX, [6]Brigham and Women's Hospital, Boston, MA, [7]University of Utah, Salt Lake City, UT, [8]University of Nebraska, Omaha, NE

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Adipokines are metabolic regulators and are associated with adverse outcomes in chronic conditions and among older adults. Elevations in one adipokine, adiponectin, have been associated with radiographic progression in rheumatoid arthritis (RA), suggesting an association with disease severity. We hypothesized that chronic inflammation leads to metabolic dysregulation and elevations in adipokines, which might serve as important

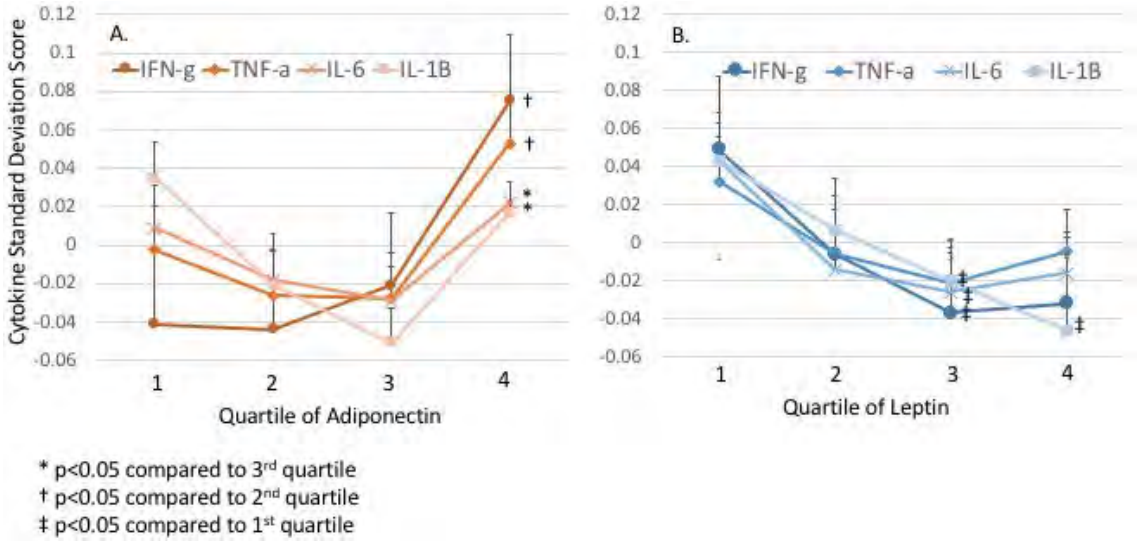

Figure 1. Line plots showing inflammatory cytokine levels by A) adiponectin quartile, and B) leptin quartile.

biomarkers and predict adverse outcomes. We assessed whether adiponectin and leptin were associated with higher overall and cause-specific mortality in RA independent of other known risk factors.

Methods: Participants were adults with physician-confirmed RA, enrolled in a Veteran's Affairs study, enrolled between 2003 and 2018. Adipokines and inflammatory cytokines (IFN-g, TNF, IL-6, IL-1b) were measured as part of a multi-analyte panel on banked serum from enrollment and were log-adjusted and standardized (per 1 SD). Dates of death and causes of death were derived from the Corporate Data Warehouse and the National Death Index. Covariates were derived from medical record databases, biorepository data, and registry databases. Levels of inflammatory cytokines were assessed over adipokine quartiles. Multivariable Cox proportional hazard models evaluated associations between clinical factors and all-cause and cause-specific mortality adjusting for demographics, comoribidity, and RA disease characteristics, including RA disease activity, at enrollment.

Results: A total of 2583 participants were included in this analysis with mean (SD) age of 71.9 (10.3). There were 960 deaths among 19,178 person-years of follow-up. The most common causes of death were cardiovascular (N=215), cancer (N=154), and respiratory (N=118). Higher adiponectin levels at enrollment were associated with older age, male sex, white race, lower BMI, higher rates of seropositivity, higher rates of radiographic damage, longer

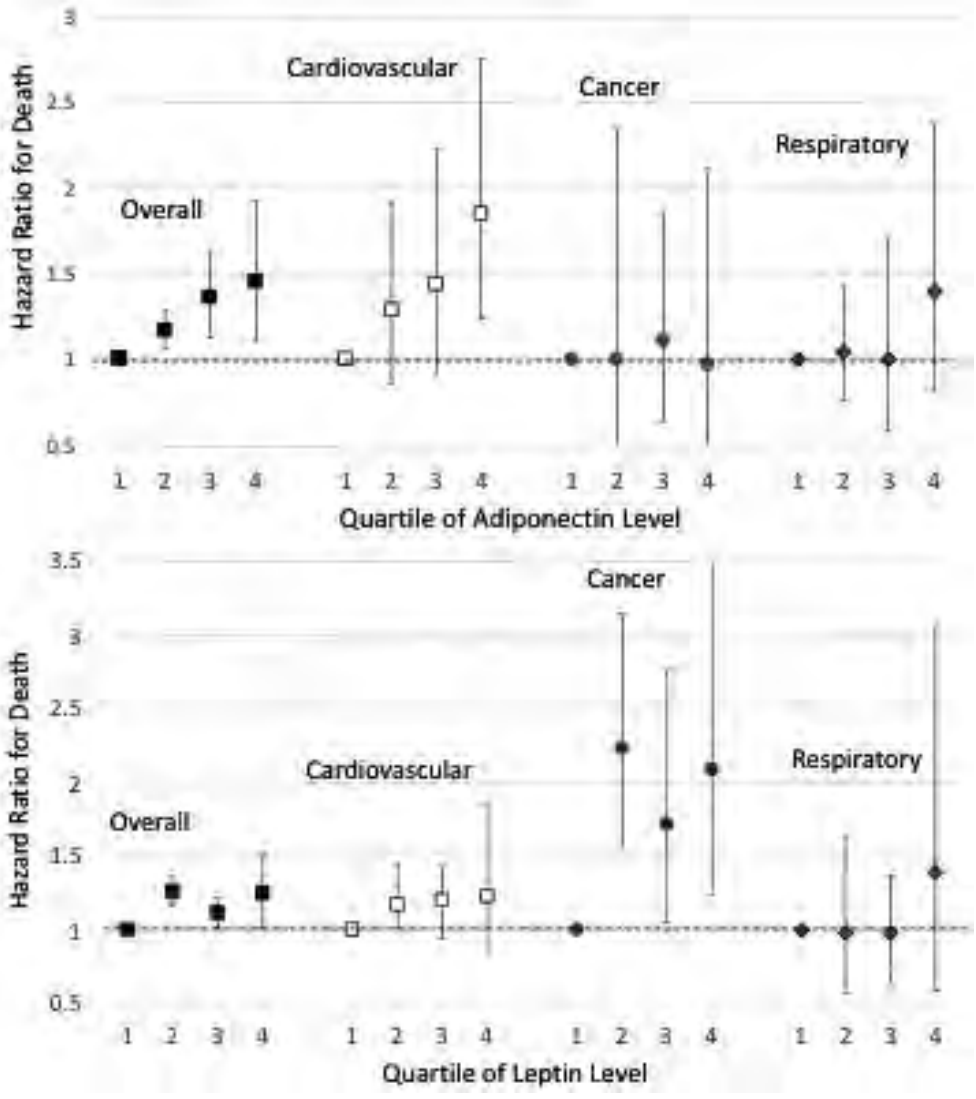

Figure 2. All-cause and cause-specific mortality in adjusted models by A) adiponectin quartile, and B) leptin quartile.

disease duration, use of prednisone, and higher rates of osteoporosis. High levels of adiponectin were also associated with higher levels of circulating inflammatory cytokines (**Figure 1.** but not with higher clinical disease activity (not shown). Leptin was primarily associated with greater BMI and obesity-related comorbidity as well as lower levels of inflammatory cytokines (particularly IL-1b). The highest quartile of adiponectin was independently associated with higher all-cause mortality [HR: 1.46 1.11, 1.93) p=0.009] which was largely driven by cardiovascular mortality [HR: 1.85 (1.24, 2.75) p=0.003] (**Figure 2**). Higher leptin levels were also independently associated with greater overall and cancer mortality.

Conclusion: Elevations in adipokine levels are associated with age, BMI, comorbidity, and seropositive and erosive RA and are independently predictive of early mortality. These observations suggest that adipokines may serve to identify patients with adverse metabolic profiles and may serve as important predictors of long-term risks. Associations noted between adiponectin and inflammatory cytokines support the hypothesis that chronic subclinical inflammation and metabolic changes, including elevations in adipokines, are interrelated.

Disclosure: J. Baker, Bristol-Myers Squib, 2, Pfizer, 2; **B. England**, Boehringer-Ingelheim, 2; **M. George**, None; **K. Wysham**, None; **G. Kerr**, Aurinia, 6, Novartis, 5, Bristol Myers Squibb, 1, 5, Pfizer, 1, Horizon, 1; **A. Reimold**, None; **P. Monach**, Kiniksa, 1, Celgene, 2, Chemocentryx, 1; **G. Kunkel**, None; **B. Sauer**, None; **B. Hamilton**, None; **C. Hunter**, None; **M. Duryee**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1646

Abnormal Cerebrovascular Biomarkers in Patients with Rheumatoid Arthritis: Results from a Prospective Study of Cognitive Aging

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of cognitive impairment compared to the general population. This association might be due to chronic systemic inflammation and the associated cardiovascular risk factors (Sood A and Raji MA, 2021). Studies on RA and neuroimaging biomarkers associated with cognitive impairment are limited. The purpose of the study was to examine the associations between RA and dementia/vascular neuroimaging biomarkers in older adults.

Methods: The study included 34 RA cases and 101 participants without RA (≥50 years old) of a prospective study of cognitive aging in community-dwelling older adults, matched 1:3 for age, sex, education, cognitive status at baseline, and the availability of at least one MRI. All RA cases satisfied the 1987 ACR classification criteria. The outcomes of interest were the following neuroimaging biomarkers: global beta-amyloid (Aβ) using PiB-PET; neurodegeneration [glucose brain hypometabolism via FDG-PET, hippocampal volume and cortical thickness via structural MRI], and cerebrovascular pathology via FLAIR-MRI [white matter hyperintensity burden (WMH), subcortical, and cortical infarctions]. All participants had MRI; 47 (12 RA /35 non-RA) had Aβ PET, 45 (10 RA / 35 non-RA) had FDG PET, 55 (17 RA / 38 non-RA) were assessed for infarctions and 49 (14 RA / 35 non-RA) for WMH%TIV. We used Kruskal-Wallis rank-sum and Fisher's exact tests to compare the neuroimaging measures between the groups.

Table 1. Participants' baseline characteristics

Variables	With RA	Without RA	p-value*
Age (years) , mean (SD)	76.2 (7.9)	75.7 (7.9)	0.79
Male	13 (38)	37 (37)	1.00
Education (years) , mean (SD)	14.5 (2.5)	14.4 (2.4)	0.74
Apolipoprotein E ε4 carrier	6 (18)	26 (26)	0.49
Cognitively unimpaired	26 (76)	80 (79)	0.91
Mild cognitive impairment	7 (21)	18 (18)	
Dementia	1 (3)	3 (3)	
White matter hyperintensity volume % TIV, mean (SD)	1.12 (0.57)	0.76 (0.69)	0.01
Cortical infarctions, mean (SD)	0.24 (0.44)	0.05 (0.32)	0.02
Cortical thickness, mean (SD)	2.62 (0.16)	2.64 (0.15)	0.73
FDG SUVR, mean (SD)	1.51 (0.16)	1.59 (0.18)	0.46
Amyloid PET SUVR, mean (SD)	1.54 (0.40)	1.52 (0.33)	0.75
N (%) unless otherwise stated; SD=standard deviation; RA= Rheumatoid Arthritis; SUVR= standardized uptake value ratio; TIV= Total intracranial volume. *Kruskal-Wallis rank sum or Fisher's exact test.			

Results: Participants with vs. without RA did not differ in age, sex, years of education, Apolipoprotein E ε4 carrier status, or major comorbidities. No significant difference was observed between RA cases and non-cases in Aβ burden, and neurodegeneration measures. Although the sample size was small, we observed that RA participants (vs. without RA) had greater mean WMH volume relative to the total intracranial volume (TIV) (mean (SD) % : 1.12 (0.57) % vs 0.76 (0.69) % of TIV, p=0.01), were more likely to have cortical infarctions (4 vs. 1, p = 0.03), and had a higher mean (SD) number of cortical infarctions (0.24 (0.44) vs. 0.05 (0.32) (p=0.02) (Table 1). These associations persisted when the comparisons were limited to cognitively unimpaired individuals.

Conclusion: Patients with RA had more abnormalities in cerebrovascular imaging biomarker measures compared to individuals without RA, despite similar sociodemographics, Apolipoprotein E ε4 carrier status, markers of neurodegeneration, and similar proportion of cognitively impaired patients between the groups. Studies are ongoing to examine these associations further and understand their potential value for prognostication and prevention of cognitive decline and dementia in RA patients.

Reference

1. Sood A, Raji MA. Cognitive impairment in elderly patients with rheumatic disease and the effect of disease-modifying anti-rheumatic drugs. Clin Rheumatol. 2021 Apr;40(4):1221-1231

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Abstract Number: 1647

Interaction Effect of Systemic Inflammation and Dietary Protein Intake on Resting Energy Expenditure in Individuals with RA

Beatriz Hanaoka[1], Jing Zhao[1], Kristen Heitman[1], Fahad Khan[1], Guy Brock[1], Jeff Volek[1], Wael Jarjour[1] and Barbara Gower[2], [1]Ohio State University, Columbus, OH, [2]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In rheumatoid cachexia (RC), high resting energy expenditure (REE) has been associated with loss of muscle mass driven by proinflammatory cytokines. The objectives of this study were to evaluate alterations of REE, body composition, metabolic parameters and physical function in individuals with RA, and to investigate the interaction between systemic inflammation and modifiable risk factors for RC on REE.

Methods: A prospective, cross-sectional study was performed in RA individuals (n=35) and age/sex/race/BMI-matched healthy controls (n=11). Participants underwent measures for REE by indirect calorimetry, body composition by dual energy x-ray absorptiometry, in addition to anthropometric, biochemical and DAS-28 CRP measures.

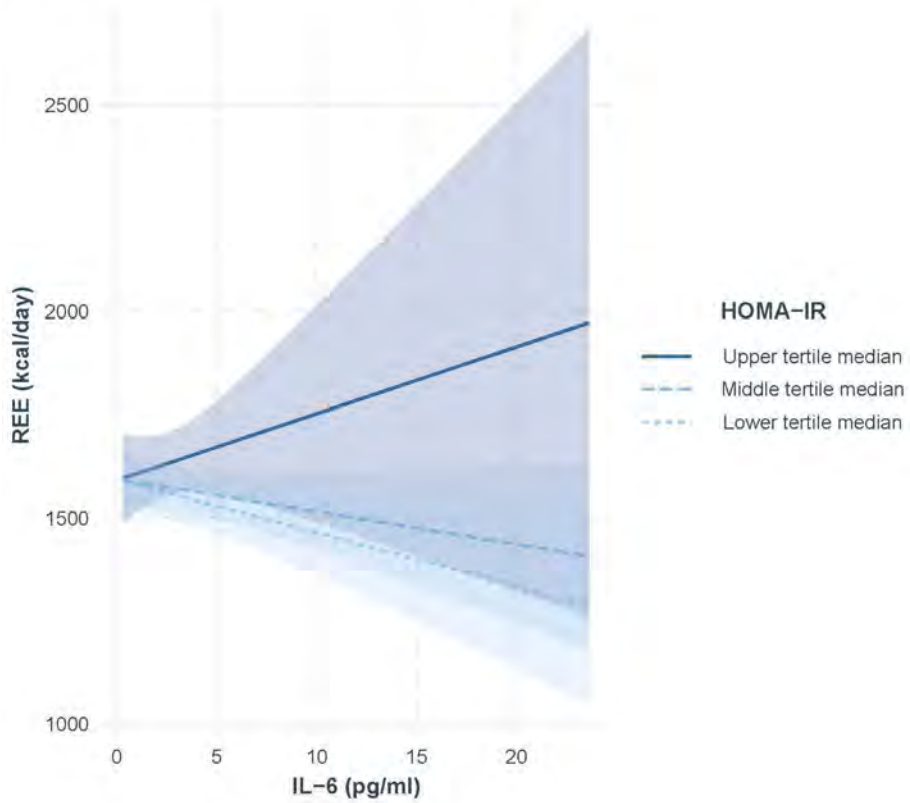
Table 1. RA and non-RA controls general characteristics, anthropometric measures, body composition by DXA, physical activity, physical performance tests, dietary intake and biochemical parameters

	RA (N=35)	Non-RA (N=19)	*p*-value
Demographic and clinical characteristics			
Age, years (median [IQR])	54.00 [50.50, 60.00]	52.00 [43.50, 59.50]	0.43
Sex= Female (%)	33 (94.3)	17 (89.5)	0.92
Race (%)			0.37
White	31 (88.6)	14 (73.7)	
Black or African American	3 (8.6)	4 (21.1)	
More than one race	1 (2.9)	1 (5.3)	
Co-morbidities (%)			
Hypercholesterolemia	10 (28.6)	0 (0)	0.03
Hypertension	10 (28.6)	0 (0)	0.03
T2DM	0 (0)	0 (0)	-
COPD	0 (0)	0 (0)	-
Thyroid disease	10 (28.6)	2 (10.5)	0.24
Smoking status (%)			0.20
Never smoked	19 (54.3)	15 (78.9)	
Past smoker	9 (25.7)	2 (10.5)	
Current smoker	7 (20.0)	2 (10.5)	
Anthropometric measures			
BMI (kg/m^2) (median [IQR])	30.50 [26.10, 36.90]	28.40 [24.40, 32.40]	0.32
Waist-to-hip ratio (mean (SD))	0.88 (0.08)	0.84 (0.07)	0.10
Body composition measures by DXA			
FFMI, kg/ m^2 (median [IQR])	16.72 [15.75, 17.89]	16.20 [15.09, 17.91]	0.33
FMI, kg/ m^2 (mean (SD))	14.91 (6.43)	11.71 (4.49)	0.06
Physical performance tests			
5-repetition sit-to-stand, s (median [IQR])	9.55 [8.72, 11.36]	6.48 [5.96, 8.91]	0.002
Knee extensor MVIC, Nm/g*10^2 (mean (SD))	23.16 (8.17)	27.82 (5.29)	0.03
5-repetition average power, Watts/g *10^2 (mean (SD))	15.38 (8.48)	20.03 (6.86)	0.05
Resting energy expenditure			
REE kcal/day (median [IQR])	1479.00 [1353.00, 1738.00]	1442.00 [1336.00, 1552.00]	0.68
Biochemical parameters			
HOMA-IR (median [IQR])	1.90 [1.31, 3.96]	*1.20 [0.78, 2.01]*	0.006
IR status, HOMA-IR>2.5 (%)	13 (37.1)	*2 (10.5)*	0.08
IL-6, pg/ml (median [IQR])	1.04 [0.66, 2.16]	0.82 [0.59, 1.20]	0.13
CRP, mg/dL (median [IQR])	3.21 [0.57, 6.34]	1.38 [0.93, 2.34]	0.43
Dietary intake			
Total energy intake, kcal/d (mean (SD))	1544.57 (468.28)	1607.90 (540.40)	0.68
Energy per kg (median [IQR])	17.61 [15.35, 21.86]	18.29 [14.79, 27.10]	0.60
% Energy intake from protein (mean (SD))	17.94 (4.83)	16.75 (5.21)	0.45
Protein per weight, g/kg/day (mean (SD))	0.79 (0.26)	0.81 (0.32)	0.83
Tertile 1	0.50 (0.10)	0.52 (0.11)	
Tertile 2	0.77 (0.08)	0.77 (0.08)	
Tertile 3	1.09 (0.16)	1.18 (0.17)	
Physical activity			
METs	1.05 [1.02, 1.07]	1.08 [1.06, 1.16]	0.004
Total Activity Count (TAC/d)	900080.43 [678314.18, 1050311.02]	1068815.31 [882578.74, 1496606.76]	0.03
Step Counts	27096.50 [19861.50, 37523.75]	44354.00 [33033.50, 57268.50]	0.001

Physical activity (METs, total activity count/ day and step counts) and physical performance (5-repetition sit-to-stand, knee extensor MVIC and 5-repetition average power) data were also collected. Dietary intakes were estimated using consecutive four-day food records. Homeostasis model assessment for insulin resistance (HOMA-IR) and serum interleukin-6 (IL-6) were used as parameters of insulin resistance (IR) and systemic inflammation, respectively. Regression models tested association between REE and dependent variables, including pre-specified interaction tests involving HOMA-IR and IL-6 and dietary protein intake and IL-6.

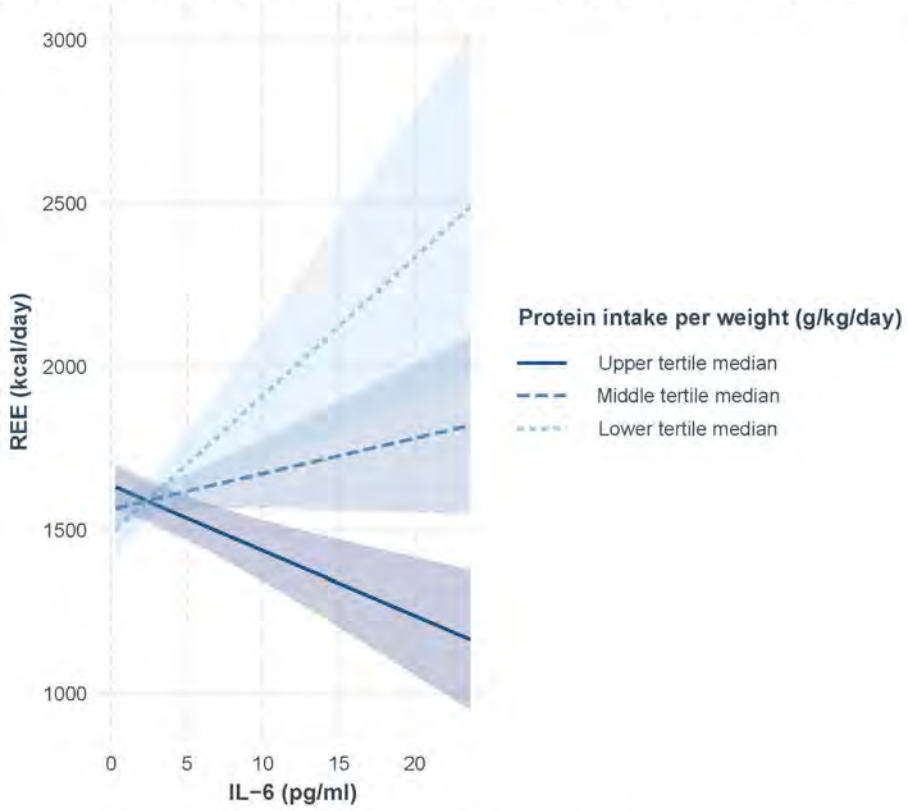
Results: RA subjects were mostly women (94%), with a median age of 54 years (50.5, 70), BMI of 30.5 kg/m^2 (26.1, 36.9), disease duration of 7.8 years (4.9, 18.1) and DAS-28 CRP of 1.77 (1.2; 2.8). Approximately two-thirds of RA subjects were either positive for rheumatoid factor on anti-CCP. Only 17% of RA subjects were on prednisone, at a median dose of 5.0 mg/ day (4.0, 5.0), and all RA subjects were on DMARD therapy. RA subjects demonstrated significantly lower levels of physical activity [METs (p= 0.004), total activity count/ day (p=0.03), step counts (p=0.001)], poorer physical performance [5-repetition sit-to-stand (p=0.002), knee extensor maximum voluntary isometric contraction (MVIC, p=0.03) and higher levels HOMA-IR (p=0.006)] compared to non-RA controls. Fat mass index [FMI] (p=0.06) and fat free mass index [FFMI] (p= 0.33) were not significantly different between RA and non-RA controls. Among RA subjects, HOMA-IR (β= 4.66; p=0.80), IL-6 (β=-9.45; p=0.24) and the interaction between HOMA-IR and IL-6 (β= 6.00; p=0.29) were not significantly associated with REE, after adjustment for age and FFMI. However, we observed a significant interaction effect between protein intake per weight (PPW) and serum IL-6 on REE among RA

Figure 1: Association between IL-6 and REE, stratified by HOMA-IR tertiles in RA subjects



Value of HOMA-IR	Estimate	S.E.	2.5%	97.5%	t value	*p*-value
1.09	-13.05	8.43	-30.28	4.19	-1.55	0.13
1.95	-7.89	8.11	-24.48	8.70	-0.97	0.34
5.96	16.17	25.60	-36.19	68.52	0.63	0.53

Figure 2: Association between IL-6 and REE, stratified by PPW tertiles in RA subjects



Value of PPW	Estimate	S.E.	2.5%	97.5%	t-value	*p*-value
0.53	42.24	18.48	4.25	80.23	2.29	0.03
0.79	10.89	9.65	-8.94	30.73	1.13	0.27
1.04	-19.97	7.51	-35.41	-4.54	-2.66	0.01

subjects in the multivariate model. The upper tertile of PPW demonstrated a significant negative correlation between REE and IL-6 (β=-19.97, 95% CI [-35.41, -4.54], p=0.01). The lower tertile of PPW demonstrated a significant positive correlation between REE and IL-6 (β=42.24, 95% CI [4.25, 80.23], p=0.03).

Conclusion: Inflammation is likely a common antecedent leading to both elevated REE and IR in patients with RA. While IR can lead to muscle catabolism, IR does not seem to be a major driver of REE in patients with RA. Higher dietary protein intake could attenuate the effect of systemic inflammation on REE in RA patients.

Disclosure: B. Hanaoka, None; **J. Zhao**, None; **K. Heitman**, None; **F. Khan**, None; **G. Brock**, None; **J. Volek**, Virta Health, 11, Simply Good Foods, 1; **W. Jarjour**, None; **B. Gower**, None.

Abstract Number: 1648

Increasing Rates of Positivity of Autoantibodies Indicates a Shorter Time-to-Diagnosis of Future Rheumatoid Arthritis

Dylan Bergstedt[1], Ryan Peterson[2], Marie Feser[1], LauraKay Moss[1], Geoffrey Thiele[3], Ted Mikuls[3], Jess Edison[4], V. Michael Holers[1] and Kevin Deane[5], [1]University of Colorado Denver, Aurora, CO, [2]Colorado School of Public Health, Aurora, CO, [3]University of Nebraska Medical Center, Omaha, NE, [4]Walter Reed National Military Medical Center, Bethesda, MD, [5]University of Colorado Denver, Denver, CO

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) has a 'pre-RA' period that can be defined by elevations in autoantibodies to citrullinated protein antigens (ACPA) and rheumatoid factor (RF) prior to clinically-apparent inflammatory arthritis. ACPA and RF elevations can be used to predict future RA; however, most models of prediction have only used autoantibody data from a single time point. To address this gap, we evaluated changing autoantibody positivity and timing of future RA in a sample set of pre- and post-RA samples from the Department of Defense Serum Repository.

Methods: We evaluated serial pre- and post-RA diagnosis serum samples from a cohort of 215 individuals with RA (213 with RA classified by 1987 criteria; 2 cases by diagnosis by a board-certified rheumatologist). All samples were tested for ACPA using the CCP3 assay (Inova, positivity based on manufacturer's recommendation) and RF-IgM, IgA and IgG (Inova, positivity based on level present in < 2% of healthy controls) We stratified cases by sex and utilized a Cox regression model that assumed a Markov renewal process to estimate the hazard of developing RA based on concurrent positivity of autoantibodies within individuals over time.

Results: Descriptive characteristics of the cases are presented in the **Table**. Overall, women were more likely than men to be positive for any RF pre- and post-RA diagnosis. Within cases stratified by gender, an increasing number of positive autoantibodies was associated with a shorter time to diagnosis of RA (**Figure**). In particular, positivity for CCP3 and any RF indicated a median time-to-diagnosis of RA of 1.52 years in men, and 1.08 years in women. Notably, if an individual's autoantibody positivity increased, their hazard of developing RA would increase (i.e. their time to diagnosis would update to a new estimate) (**Figure**).

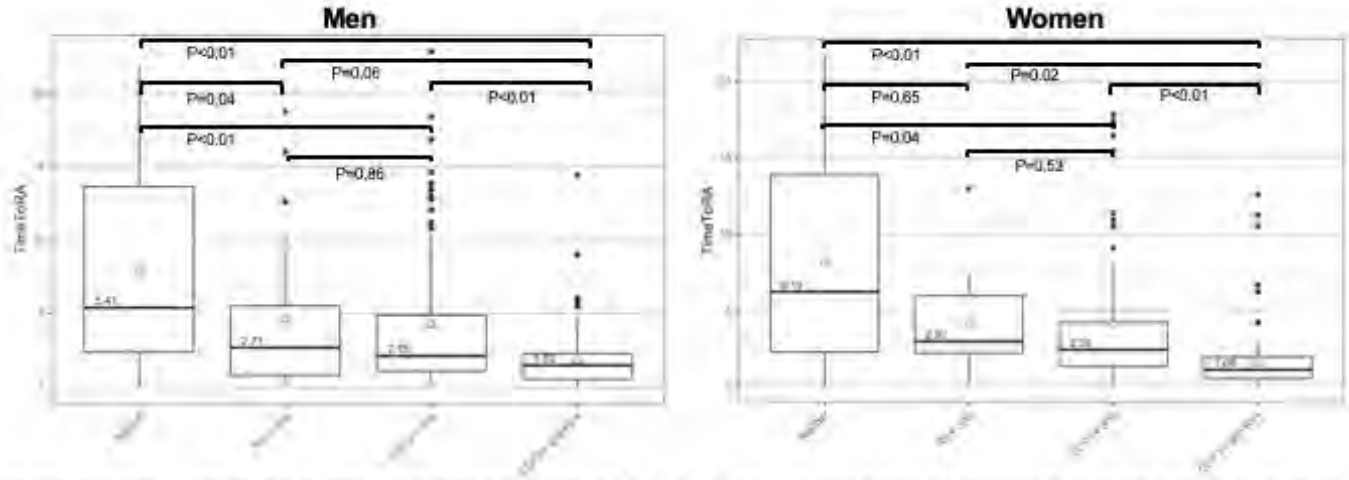
Conclusion: In this pre-RA cohort, prevalence of positivity of a combination of CCP3 and RF occur closer to diagnosis. This suggests an expansion of autoimmunity across the development of RA where biologic processes influencing both ACPA and RF production culminate in the transition to clinically-apparent RA. Furthermore, while predictive ability herein is limited given the retrospective design of this project, prior work has established that autoantibody positivity, especially ACPA positivity, is predictive for future RA (reviewed in Deane Arthritis Rheum 2021). As such, if these findings are further validated, they could be applied in a 2-step fashion to identify an individual's overall risk for future RA, then evaluate the changing positivity of autoantibodies over time to estimate their evolving risk and

Descriptive characteristics of the 215 cases with rheumatoid arthritis from the Department of Defense Serum Repository, by gender

	Males				Females			
	Earliest Pre-RA Diagnosis Sample	Interim Pre-RA Diagnosis Sample	Immediate Pre-RA Diagnosis Sample	Post-RA Diagnosis Sample	Earliest Pre-RA Diagnosis Sample	Interim Pre-RA Diagnosis Sample	Immediate Pre-RA Diagnosis Sample	Post-RA Diagnosis Sample
Years from a diagnosis of RA, mean (SD)	-12(5)	-3(2)	-1(1)	1(1)	-11(5)	-2(1)	-1(1)	1(1)
Age at time of Sample, mean (SD)	25(6)	34(8)	36.2(8.0)	39(8)	25(6)	34(8)	35(8)	37(9)
Any RF positivity, n subjects, %	7(6%)	**32(28%)[1]**	**48(43%)[1]**	**47(42%)[1]**	12(12%)	**43(43%)[1]**	**64(63%)[1]**	**65(64%)[1]**
CCP3 positivity, n subjects (%)	24(21%)	61(54%)	77(69%)	79(71%)	24(24%)	66(65%)	80(79%)	82(81%)

1. At these times points, women had significantly higher prevalence of RF positivity than men p<0.05).

Abbreviations: RA=rheumatoid arthritis, SD=standard deviation; RF=rheumatoid factor; CCP3=anti-cyclic citrullinated peptide-3 antibody



Median times from positivity of autoantibodies to time of diagnosis of RA, by gender. Overall, there is trend for increasing CCP3 and RF positivity as individuals move closer to a time of RA diagnosis. The shortest time between sample positivity and diagnosis seen in CCP3 and RF positive samples. Notably, using this approach (Cox regression with Markov renewal process) and with these case samples if an individual's autoantibody positivity increased, they would move to a different estimate of their time to diagnosis; for example, a women who had no positive antibodies would be in the group with a median time to diagnosis of ~6 years; however, if she developed positivity for CCP3 and any RF, she would move to the group with a median time of ~1 years to diagnosis. *Abbreviations: RA=rheumatoid arthritis; CCP3=cyclic citrullinated peptide-3; RF=rheumatoid factor.*

timing of future RA. Notably, the literature regarding the rate of autoantibody positivity in RA in men and women is conflicting, and issues such as diagnostic bias can influence these findings; however, the gender differences seen herein in the prevalence of autoantibody positivity and prediction of timing of future RA needs further investigation. Finally, while additional study is needed, these findings also suggest that in clinical trials for RA prevention altering the development of new autoantibodies may be a measure to understand success of an intervention.

Disclosure: D. Bergstedt, None; **R. Peterson**, None; **M. Feser**, None; **L. Moss**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **J. Edison**, None; **V. Holers**, None; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6.

Abstract Number: 1649

Parameters by FDG-PET/CT Are Useful for Predicting Spontaneous Regression in MTX Associated Lymphoproliferative Disorder

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Methotrexate associated lymphoproliferative disorder (MTX-LPD) has various histological types from benign and malignant. Some MTX-LPDs spontaneously regress after discontinuation of MTX, even though

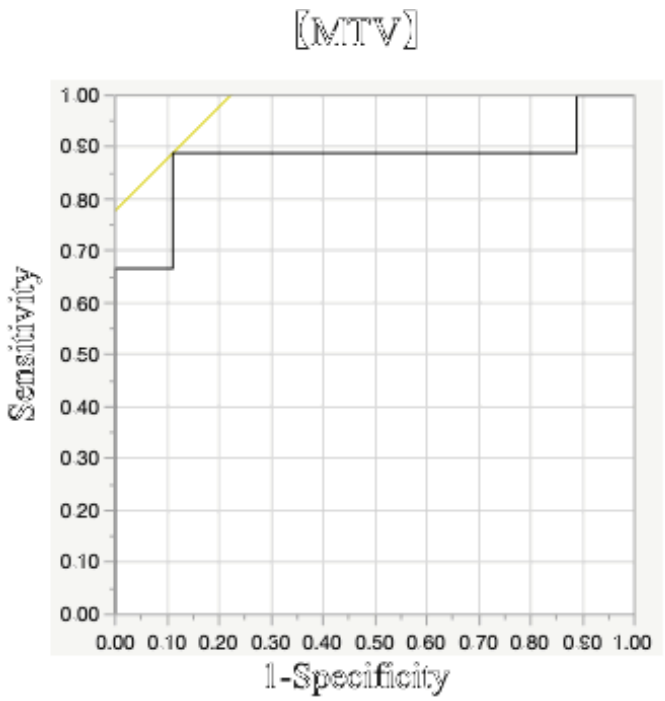
they have been diagnosed with malignant lymphoma. However it is difficult to predict spontaneous regression (SR) of MTX-LPD. On the other hand, FDG-PET/CT is used for diagnosis of malignant lymphoma.

We investigate the usefulness of FDG-PET/CT for predictive factor of SR in MTX-LPD.

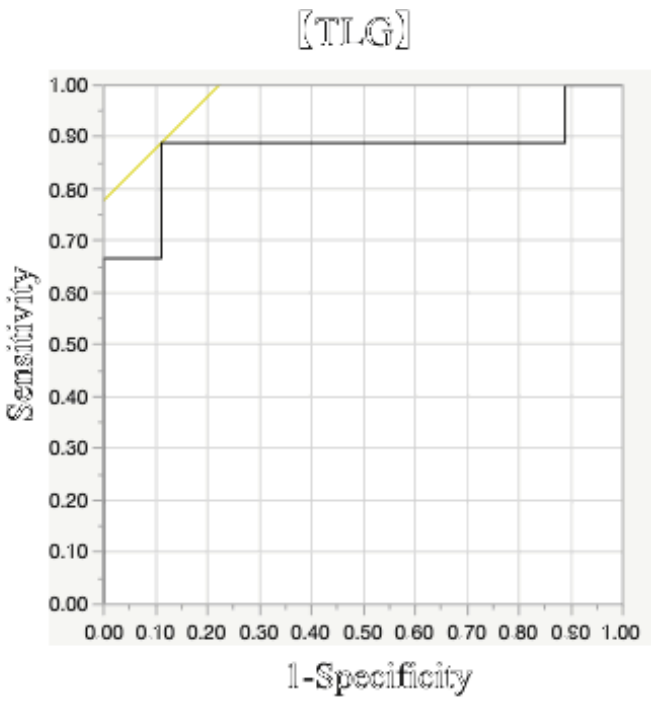
Methods: We enrolled 18 MTX-RA-LPD patients, which was histopathologically determined to be malignant and performed FDG-PET/CT from 2005 to 2019. We divided these cases into spontaneous regression cases (SR group; 9 cases) and cases that treated with chemotherapy after MTX discontinuation (CTx group; 9 cases), and compared the difference as follow subjects between two groups; biomarker (serum LDH and sIL-2R) at LPD onset, SUVmax to evaluate malignant tumor activity by FDG-PET/CT, metabolic tumor volume (MTV) and total lesion glycolysis (TLG) which refer to metabolically active volume of the tumor segmented FDG-PET/CT. In addition, we analyzed cut off levels, sensitivity and specificity using statistical software JMP.

Results: The level of sIL-2R was significantly lower in SR group. In addition, MTV and TLG by FDG-PET/CT was significantly lower in SR group, although SUVmax is no difference between two groups. Cut off levels of sIL-2R, MTV and TLG were1728 U/ml (sensitivity; 77.8%, specificity; 88.9%) 103.42 ml (sensitivity; 88.9%, specificity; 88.9%) and 361.75 ml (sensitivity; 88.9%, specificity; 88.9%), respectively.

Conclusion: We suggested that serum sIL-2R, MTV and TLG were useful for predict of SR in MTX-LPD.



Cut-off value	103.42ml.
Sensitivity	88.9%
Specificity	88.9%



Cut-off value	361.75ml.
Sensitivity	88.9%
Specificity	88.9%

Disclosure: T. Kameda, None; **S. Nakashima**, None; **H. Shimada**, None; **R. Wakiya**, None; **M. Fahmy Mansour**, None; **M. Kato**, None; **K. Sugihara**, None; **R. Semba**, None; **M. Mizusaki**, None; **N. Kadowaki**, None; **H. Dobashi**, None.

Abstract Number: 1650

Identifying Trajectories and Endotypes in the Evolution of Pre-Rheumatoid Arthritis with Autoantibody Testing and Artificial Adaptive System Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) has a 'pre-RA' period that can be defined by elevations of antibodies to citrullinated protein antibodies (ACPA), rheumatoid factor (RF), and other measures of inflammation prior to clinically-apparent inflammatory arthritis. Evaluating the evolution of these biomarkers in pre-RA may provide novel understanding of mechanisms of disease development. In addition, advanced analytic techniques may provide unique insights into biomarker evolution. As such, as a proof-of-concept, we evaluated ACPA and RF changes over time in pre-RA using artificial adaptive systems (AAS) in a sample set of pre- and post-RA samples from the Department of Defense Serum Repository.

Descriptive characteristics of RA cases and controls

	RA Cases(n=214)				Controls(n=210)*
	Time 1 Earliest Pre-RA diagnosis sample	Time 2 Intermediate Pre-RA diagnosis sample	Time 3 Immediate Pre-RA diagnosis sample	Time 4 Post-RA diagnosis sample	Time 4 Matched to RA case post-diagnosis sample
Time of sample from diagnosis of RA, mean (in years)	-11	-4	-1	+1	-
Age at diagnosis of RA, mean*	-	-	-	37	37
% Female	-	-	-	48%	48%
% Non-Hispanic white	-	-	-	58%	55%
% anti-CCP3.1 positive	17%	51%	74%	76%	4%
% any RF isotype positive	6%	28%	43%	60%	6%*

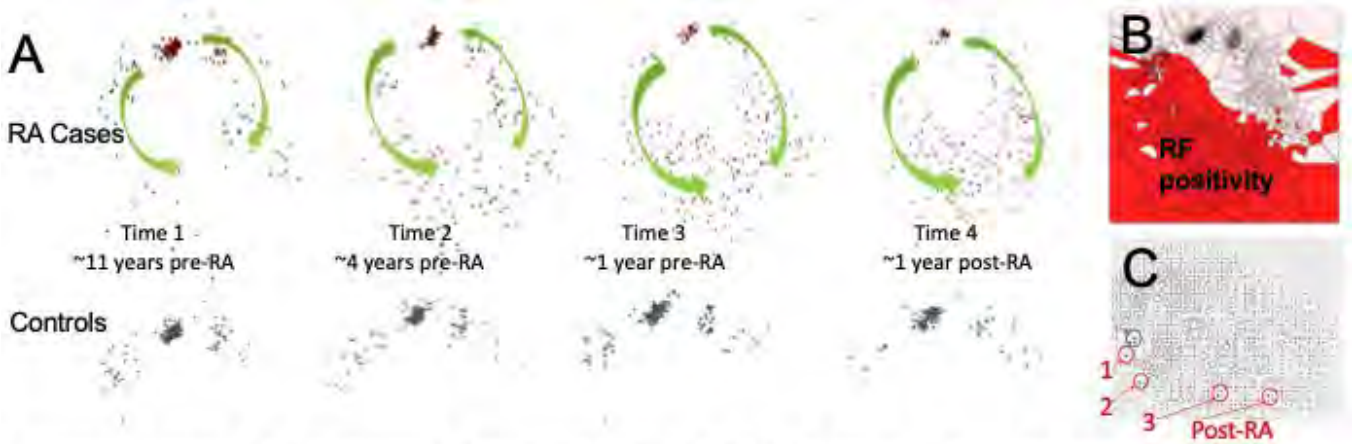
*For controls, only data from the last serum sample is presented; the age of controls is the mean age at time of index sample to their case.
**The positive levels for RF isotypes was determined in a subset of 156 Controls; as such, the % positive for any RF isotype was determined in the remainder of 54 controls.

Abbreviations: RA=rheumatoid arthritis; anti-CCP3.1=anti-cyclic citrullinated peptide antibody 3.1; RF=rheumatoid factor

Methods: We evaluated serial pre- and post-RA diagnosis serum samples obtained from a cohort of 215 individuals with RA (213 with RA classified by 1987 criteria; 2 cases by diagnosis by a board-certified rheumatologist) as well as serial samples from age, gender and race-matched controls. All samples were tested for ACPA using commercial assays for CCP2 (Axis-Shield), CCP3.1 (Inova) and RF-IgA, -IgM and -IgG (Inova). In addition, all samples were tested on a bead-based array containing citrullinated and non-citrullinated antigens. In total, there were 54 biomarkers. We analyzed these biomarkers using AAS and deep artificial neural networks (ANN's) that characterized biomarker abnormalities within individuals to a single point in time; then, the movement of that point was evaluated over time. Specifically, an Auto Contractive Map (Buscema 2018) was used to project weighted functional links among the biomarkers, an Auto Self Organizing Map (Massini 2021) was then applied to examine how the autoantibodies were clustered at the different temporal steps of the disease evolution, and a multi-dimensional scaling algorithm Population (Massini 2013) was used to understand how each individual summated biomarker profile 'moves' over time.

Results: The characteristics of the cases and controls are presented in the **Table**. At the earliest time point (mean 11 years pre-diagnosis), many RA cases were indistinguishable from controls; however, over time, most RA cases evolved over time to a distinct profile that was present prior to and post-RA diagnosis (Figure, Panel A). In addition, within RA cases, there were two distinct endotypes within cases, with one endotype characterized by RF positivity (Figure, Panel B). Furthermore, within the overall patterns of disease development, an individual RA case's trajectory could be identified with a clear separation from a control pattern (Figure, Panel C).

Conclusion: Testing for a panel of 54 autoantibodies and application of AAS identified the temporal evolution of RA cases from a state that was initially similar to controls, to a distinct state. Furthermore, within the evolution of RA, there were distinct endotypes of development that included RF-positivity. In addition, an individual's course could be plotted to estimate their specific time point in the course of disease evolution. Future studies utilizing these analytic approaches with additional biomarkers can be used to identify specific pathways of disease development as well as improve prediction models for future RA.



Evolution across the development rheumatoid arthritis (RA). In Panel A, each dot represents an artificial adaptive system-derived summation of 54 autoantibody biomarkers for each case and matched control at the specified time period. The cases (upper panels/red dots) demonstrate general movement from the upper left to lower right over time and in two 'pathways' (green arrows). This is distinct from controls who remain stable over time (lower panels/blue dots). Panel B demonstrates that within the lower pathway is weighted by an endotype of subjects with rheumatoid factor (RF) positivity (red regions). In additional analyses (Panel C), an individual RA case's (red circles and arrows) biomarker movement over the pre- and post-RA time periods was distinct from their matched control (blue arrow and circle).

Disclosure: P. Buscema, None; **G. Massini**, None; **F. Della Torre**, None; **M. Asadi-Zeydabadi**, None; **C. O'Donnell**, None; **F. Newman**, None; **R. Tagg**, None; **W. Lodwick**, None; **C. Collora**, None; **M. Feser**, None; **L. Moss**, None; **W. Robinson**, None; **G. Thiele**, Regeneron, 6; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **J. Edison**, None; **V. Holers**, None; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6.

Abstract Number: 1651

Symptom Trajectories in the Transition from Pre-Rheumatoid Arthritis to Clinically-Apparent Inflammatory Arthritis

Salina Haville[1], Jennifer Seifert[1], Saman Barzideh[1], LauraKay Moss[1], Navin Rao[2], Alyssa Johnsen[3], Jane Buckner[4], Eddie James[5], Sylvia Posso[4], Gary Firestein[6], David Boyle[7], William Robinson[8], V. Michael Holers[9] and Kevin Deane[10], [1]University of Colorado Denver, Aurora, CO, [2]Janssen R&D, Spring House, PA, [3]Janssen R&D, Princeton Junction, NJ, [4]Benaroya Research Institute at Virginia Mason, Seattle, WA, [5]Benaroya Research Institute at Virginia Mason, Monroe, WA, [6]University of California San Diego, San Diego, CA, [7]University of California San Diego, La Jolla, CA, [8]Stanford University, Palo Alto, CA, [9]University of Colorado, Denver, CO, [10]University of Colorado Denver, Denver, CO

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) has a 'pre-RA' period definable as elevations of antibodies to citrullinated protein antibodies (ACPA) before clinically-apparent inflammatory arthritis (IA). ACPA elevations can predict future IA; however, most prospective studies have studied symptomatic ACPA+ individuals. As such, it is unclear how ACPA may relate to future IA in asymptomatic individuals. Furthermore, there is limited understanding of the trajectory of symptoms prior to a transition to IA, or how individuals who are prospectively followed to IA may compare with individuals with new RA found through standard rheumatology referrals.

Table 1. Baseline characteristics of CCP- and CCP+ subjects

	CCP-	CCP+ Non-Converter to IA	CCP+ Converter to IA	p-values*
n	175	84	19	-
Age, mean (SD)	58 (13)	58 (16)	57 (9)	0.91
% Female	67%	64%	74%	0.83
% NHW	79%	85%	68%	0.26
Any swollen joint (self-report)	13%	7%	26%	0.06
Any painful joint (self-report)	47%	58%	63%	0.44
Any stiff joint (self-report)	25%	29%	37%	0.51
Any joint symptoms (self-report)	55%	61%	74%	0.12
# of painful joints, mean (SD) [self-report]	2 (5)	2 (5)	4 (5)	0.43
# of stiff joints, mean (SD) [self-report]	2 (5)	1 (5)	4 (9)	0.12
# of swollen joints, mean (SD) [self-report]	1 (4)	1 (1)	1 (1)	0.39
# of minutes of morning stiffness, mean (SD)	**7 (19)**	**9 (23)**	**28 (58)**	**<0.01**
Pain level on VAS, mean (SD)	1 (2)	2 (2)	2 (2)	0.18
Fatigue level on VAS, mean (SD)	2 (2)	2 (2)	3 (3.0)	0.21
Overall well-being on VAS, mean (SD)	1 (2.0)	1 (2)	2 (2)	0.34
DAS28CRP	1.6 (0.5)	1.6 (0.5)	1.6 (0.5)	0.89
CCP3 level	**4 (1)**	**72 (73)**	**129 (106)**	**<0.01**
RF level	**3 (10)**	**10 (23)**	**33 (46)**	**<0.01**

**p-values represent comparisons between CCP+ converters and non-converters*

Abbreviations: CCP=cyclic citrullinated peptide antibody; SD=standard deviation; VAS=visual analog scale; DAS28CRP=Disease Activity Score 28 Joints C-Reactive Protein; RF=rheumatoid factor

Table 2. Comparison of disease activity in individuals 'converting' to IA during prospective follow-up with individuals presenting with EarlyRA through standard referrals to rheumatology clinics

	Converters at time of identification of IA	EarlyRA within 30 days of initial identification of IA by a rheumatologist	p-value
n	19	57	-
Age, mean (SD)	58 (8)	53 (12)	0.09
% Female	71%	66%	0.76
% NHW	79%	67%	0.53
# of painful joints, mean (SD)	**8 (8)**	**24 (14)**	**<0.01**
# of stiff joints, mean (SD)	**5 (6)**	**23 (17)**	**<0.01**
# of swollen joints, mean (SD)	**3 (4)**	**16 (12)**	**<0.01**
# of minutes of morning stiffness, mean (SD)	**22 (48)**	**59 (57)**	**0.03**
DAS28CRP	**2.8 (0.9)**	**3.9 (1.2)**	**<0.01**
CCP3 level	**145 (99)**	**213 (82)**	**0.01**
RF level	49 (52)	67 (46)	0.20

Abbreviations: CCP=cyclic citrullinated peptide antibody; SD=standard deviation; VAS=visual analog scale; DAS28CRP=Disease Activity Score 28 Joints C-Reactive Protein; RF=rheumatoid factor

Methods: Through clinics and screening of relatives of patients with RA and health fairs we identified 86 ACPA(+) individuals (CCP3, Inova) who had no history or examination evidence of IA. They were followed prospectively for IA development. We also evaluated 57 CCP3+ patients with EarlyRA from clinics with a baseline study visit < 30 days since confirmation of IA by a rheumatologist. Joint symptoms were captured by questionnaires capturing pain, stiffness and swelling in 68 joints. We evaluated trajectories of joint symptoms, physical examination and disease activity (DAS28CRP) through incident IA, and between individuals who transitioned to IA compared to patients with established EarlyRA.

Results: Nineteen of 86 (22%) of anti-CCP3+ developed IA ('converters') at a median of 509 days of follow-up and 79% met 2010 ACR/EULAR criteria at time IA identification. At baseline, CCP3+ converters reported longer duration of morning stiffness, and a trend towards an increased prevalence of swollen joints compared to CCP3+ subjects who did not develop IA; in addition converters had higher levels of CCP3 and RFIgM (**Table 1**). In the converters there were 2 trajectories of symptoms prior to IA: 1) waxing and waning of joint symptoms and 2) period of minimal symptoms followed by steady worsening of symptoms over < 200 days prior to IA identification (these trajectories were not different than those who did not develop IA). In the 'converters', those without any joint symptoms at baseline (n=5) trended towards a longer duration to appearance of IA compared to those with baseline symptoms (median of 686 days vs 363 days, p~0.09). At the time of diagnosis of IA 'converters' had lower levels of symptoms, DAS28CRP and CCP3 than patients with EarlyRA (**Table 2**).

Conclusion: In this study, in CCP3+ individuals, self-reported morning stiffness and higher levels of CCP3 and RFIgM were associated with incident IA; in addition, there are 2 types of trajectories of joint symptoms in transition to IA, and a subset of CCP3+ individuals without symptoms developed IA. These findings can be considered in understanding the natural history of RA and building prediction models for future disease as well as to correlate biomarker changes with symptoms. Furthermore, the lower disease activity in 'converters' to IA compared to EarlyRA could indicate that prospective follow-up of ACPA+ individuals can identify IA at a time point where disease activity and CCP3 levels are less than in standard referral patterns, perhaps indicating a stage of disease more responsive to therapy.

Disclosure: S. Haville, None; **J. Seifert**, Janssen R&D, 5; **S. Barzideh**, Janssen R&D, 5; **L. Moss**, None; **N. Rao**, Janssen R&D, 3; **A. Johnsen**, Janssen R&D, 3; **J. Buckner**, Janssen R&D, 5; **E. James**, Janssen R&D, 5, Pfizer, 5, Novartis, 5, Provention Bio, 1, BMS, 5; **S. Posso**, Janssen R&D, 5; **G. Firestein**, Eli Lilly, 5; **D. Boyle**, Janssen R&D, 5; **W. Robinson**, None; **V. Holers**, Jansson, 5; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6.

Abstract Number: 1652

Symptom Burden in Anti-citrullinated Protein Antibody Positive Individuals At-risk for Rheumatoid Arthritis Is Changing over Time and Comparable to Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Symptom burden in individuals at risk for developing rheumatoid arthritis (RA) - positive for anti-citrullinated peptide antibodies (ACPA) and musculoskeletal complaints - has not been explored. We aim to evaluate patient-reported symptoms in individuals in the risk phase for RA in comparison to patients with early seropositive RA (eRA).

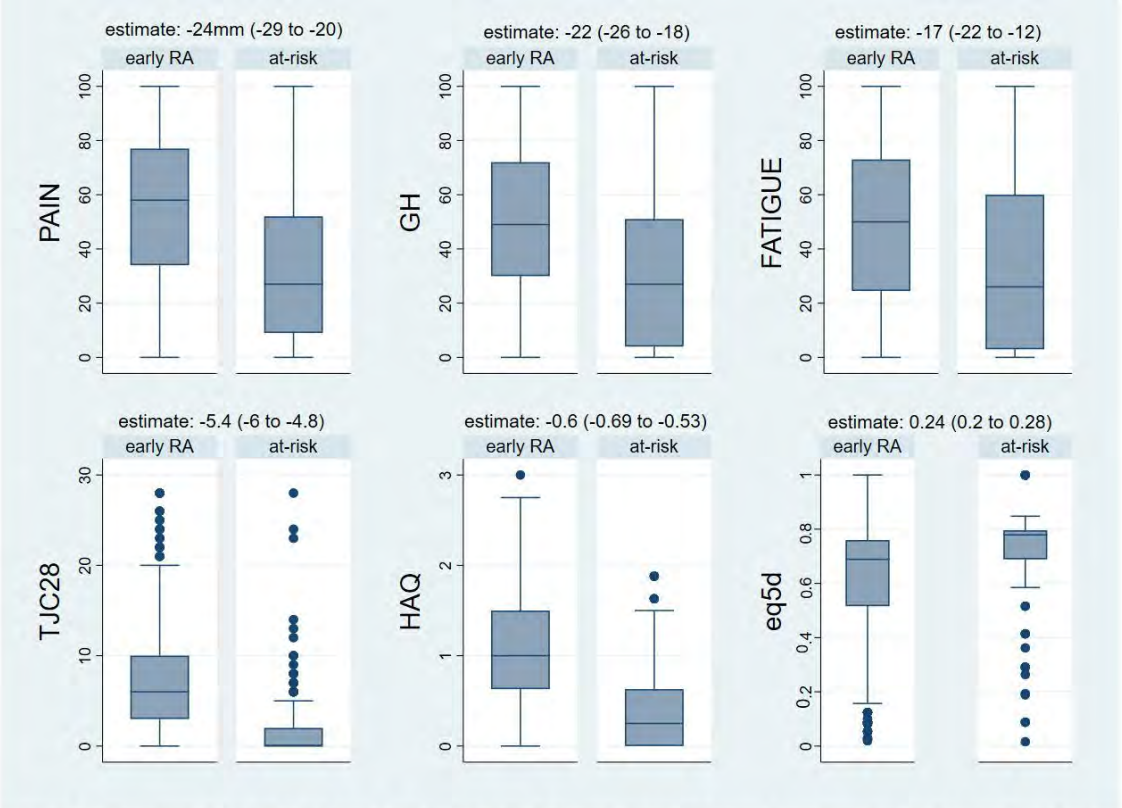
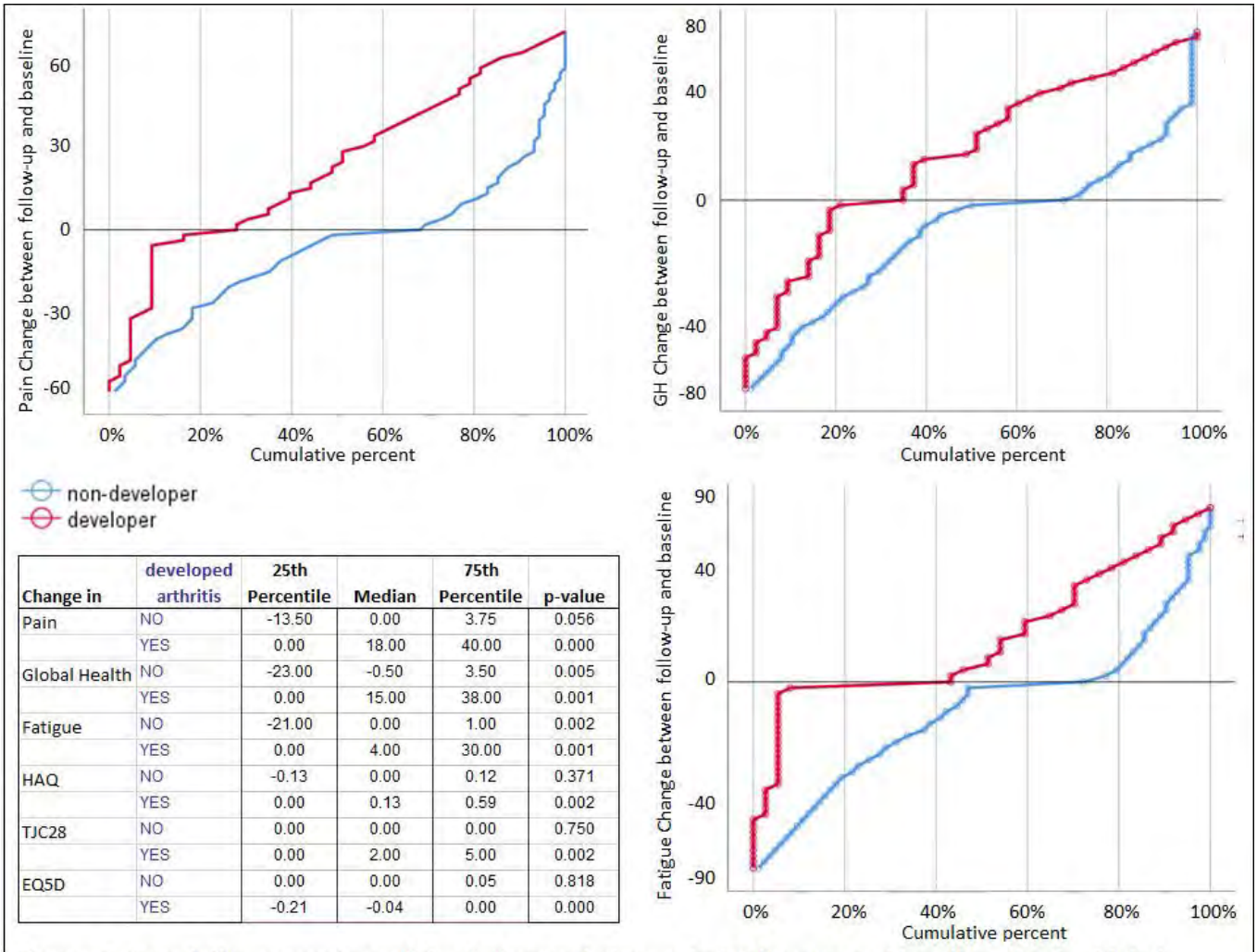


Figure 1: Boxplots of pain, global health, fatigue, TJC28, EQ5D and HAQ, separately displayed for people with early seropositive RA and individuals at-risk. Population effect estimates (all p<0.001) comparing at-risk at baseline to early RA are provided for every pair, with 95% confidence interval in brackets.



Change in	developed arthritis	25th Percentile	Median	75th Percentile	p-value
Pain	NO	-13.50	0.00	3.75	0.056
	YES	0.00	18.00	40.00	0.000
Global Health	NO	-23.00	-0.50	3.50	0.005
	YES	0.00	15.00	38.00	0.001
Fatigue	NO	-21.00	0.00	1.00	0.002
	YES	0.00	4.00	30.00	0.001
HAQ	NO	-0.13	0.00	0.12	0.371
	YES	0.00	0.13	0.59	0.002
TJC28	NO	0.00	0.00	0.00	0.750
	YES	0.00	2.00	5.00	0.002
EQ5D	NO	0.00	0.00	0.05	0.818
	YES	-0.21	-0.04	0.00	0.000

Figure 2: Cumulative percentage plots of changes between last follow-up and baseline of pain, Global Health (GH) and fatigue. Changes of HAQ TJC28 and EQ5D also outlined in integrated table (p-values provided concerning change in time in the respective outcome and group). Blue lines represent non-arthritis developers and red those that develop arthritis.

Methods: ACPA positive individuals with musculoskeletal complaints, but without clinical or ultrasound signs of joint inflammation were identified from the RISK RA Karolinska cohort. Data from baseline visit (BL) and the last follow-up visit (LF) in arthritis developers (A-D) and non-arthritis developers (n-A-D) were extracted. Additionally patients with early seropositive (ACPA and/or rheumatoid factor positive) RA (eRA) were identified as controls in the Swedish Rheumatology Quality Register. Data from the date of diagnosis were used. eRA and Risk-RA individuals were matched 1:3 by sex and age using the nearest neighbour method utilizing Mahalanobis distance, corrected for sample bias and exact matches on sex. Effect estimates for pain, patient global (GH), fatigue, health assessment questionnaire (HAQ), TJC28 and the EuroQol-5D (EQ5D; range: 0-1) were compared. Propensity score matching was used as sensitivity analyses. Via pairwise-comparisons changes between BL and LF were tested.

Results: In total 223 Risk-RA individuals were compared to 820 matched eRA patients. The distribution of symptoms and differences between Risk-RA at BL and eRA individuals are shown in Figure 1. Risk-RA individuals show 24mm of lower pain scores at BL than eRA ($p < 0.001$). This difference is less (-17mm, 95%CI: -24 to -11) when the estimate is additionally matched for the TJC. The TJC28 was on average 5.4 joints lower than in eRA. GH scores were 22mm lower (rate themselves better), fatigue scores 17mm lower and HAQ by 0.6 points lower in Risk-RA than eRA. Mean

EQ5D in Risk-RA was only 0.74 (95%CI: 0.71 to 0.77), which is 0.24 higher than in eRA. Sensitivity analyses revealed similar results.

Symptom burden in Risk-RA individuals developing and not developing arthritis: At BL no differences between future arthritis developers (A-D, n: 66) and non-developers (n-A-D, n: 157) were found. At LF differences between A-D and n-A-D were seen in all scores when comparing the visit at/or close to arthritis onset with the visit in individuals not progressing. When looking at changes between BL and FL in A-D and n-A-D separately, A-D showed increases in all variables, whereas n-A-D decreased in pain, fatigue and GH during follow-up (Figure 2).

Conclusion: The symptom burden in the Risk-RA phase is substantial, although less than in eRA. Initially the symptom burden in Risk-RA individuals developing arthritis is not different from those not developing arthritis in the future. By time the non-developers, take another path in the Risk-phase with decreasing of symptoms, potentially due to normalized immune and inflammatory processes, and as expected the arthritis developers worsen. This stresses the need for management strategies of Risk-RA individuals.

Disclosure: P. Studenic, None; **A. Circiumaru**, None; **D. Aletaha**, AbbVie, 2, 5, Janssen, 2, 5, Medac, 2, 5, Merck, 2, 5, 6, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Novartis, 2, 5, 6, Bristol-Myers Squibb, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6; **K. Chatzidionysiou**, None; **A. Catrina**, None; **A. Haj Hensvold**, None.

Abstract Number: 1653

Positron Emission Tomography-Detected Uptake of ^{18}F-Fluorodeoxyglucose in Visceral and Subcutaneous Adipose Tissue Is Associated with Articular Disease Activity and Arterial Inflammation in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

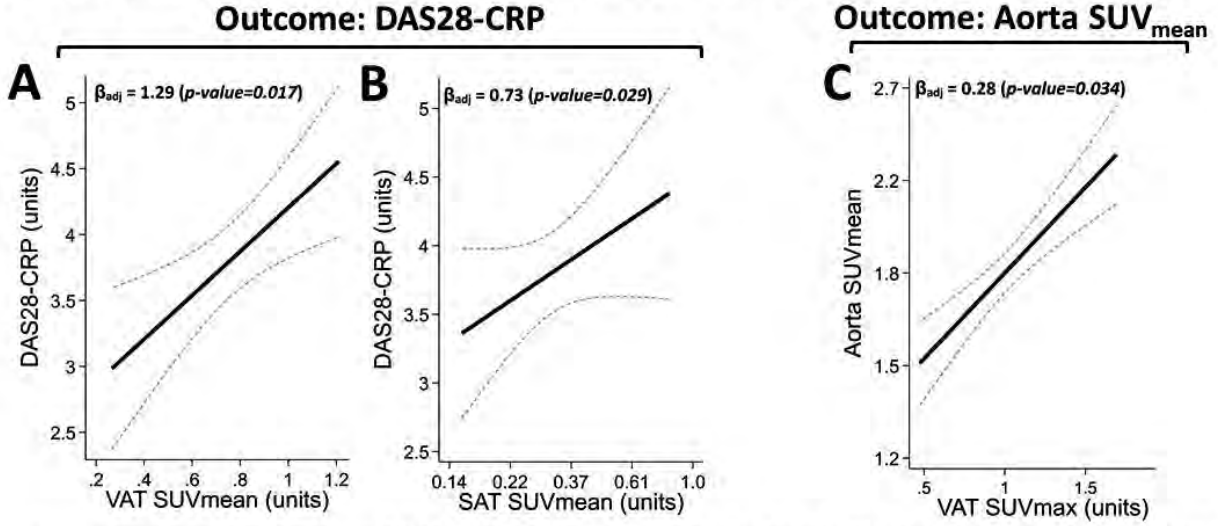
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Subcutaneous adipose tissue (SAT) from people with RA contains more macrophages and expresses higher levels of cytokines, chemokines, and other inflammatory mediators compared with otherwise similar people without RA. Visceral adipose tissue (VAT), located within the thorax and surrounding mesenteric organs, tends to be more inflammatory than SAT and is more strongly associated with cardiometabolic outcomes, such as insulin resistance and atherosclerotic cardiovascular disease (CVD). However, due to its inaccessibility, little is known about the immunophenotype of VAT in RA and whether adipose inflammation is associated with other RA-specific features.

Methods: RA patients participating in a cohort study of CVD in RA underwent total body ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT). VAT and SAT regions were manually traced and the mean and maximal standardized uptake values (SUV_{mean} and SUV_{max}) for FDG uptake were calculated for each adipose depot. Abdominal VAT and SAT volumes were measured at the L2/3 interspace. Mean and maximal uptake

Figure. Adjusted Associations of Visceral and Subcutaneous Adipose Uptake of ^{18}F-Fluorodeoxyglucose with Articular Disease Activity and Vascular Inflammation in RA



Least-squares estimates and 95% confidence intervals depicted. DAS28-CRP models adjusted for race, RA duration, anti-CCP seropositivity, current prednisone use. Aorta SUV model adjusted for age, diabetes, hypertension, and anti-CCP seropositivity. VAT and SAT covariates were modeled simultaneously.
SUV=standardized uptake value; VAT=visceral adipose tissue; SAT=subcutaneous adipose tissue

of FDG in the arterial wall of the ascending aorta was measured and reported for the entire vessel (SUV_{mean}) and for the most diseased segment (SUV_{MDS}). Generalized linear models were used to explore the associations of VAT and SAT volumes and SUV measures with RA features and aortic SUV.

Results: VAT and SAT FDG uptake was analyzed in 47 RA patients (81% women; mean age 55 years; median BMI=27.6 kg/m^2; median RA duration=6.7 years; mean DAS28-CRP=3.80; current methotrexate, biologics, and prednisone in 49%, 36%, and 32%, respectively). Average SUV_{mean} and SUV_{max} were higher in VAT than SAT [(SUV_{mean}: 0.76 vs. 0.34 SUV units, respectively; p< 0.001) (SUV_{max}: 1.02 vs. 0.52 units, respectively; p< 0.001). Both VAT and SAT SUV_{mean} were significantly and independently associated with DAS28-CRP, even after adjusting for pertinent confounders (Fig A & B). This association was driven by associations with swollen and tender joint counts, but not with CRP. VAT and SAT SUV_{mean} accounted for 20% of the explainable variability in DAS28-CRP (Model total R^2=0.58). Body mass index, VAT volume, and SAT volume were not associated with DAS28-CRP when comodeled with VAT and SAT SUV_{mean}. VAT SUV_{max} was significantly associated with all measures of aorta SUV (shown for Aorta SUV_{mean} in Fig C), even after confounder adjustment. SAT SUV was not associated with Aorta SUV.

Conclusion: Both visceral and subcutaneous adipose uptake of ^{18}F-FDG, representing increased metabolic activity and/or adipose inflammation, was highly associated with articular disease activity and aortic FDG uptake, representing atherosclerotic plaque inflammation. These findings suggest that adipose inflammation could be a contributor to articular and vascular inflammation in RA, and potentially a target for intervention.

Disclosure: J. Giles, AbbVie, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 2, 5, UCB, 2; **J. Bathon**, None; **H. Zureigat**, None; **A. Tawakol**, None.

Abstract Number: 1654

Comparative Characteristics of the Natural Course of Early Rheumatoid Arthritis with Onset at a Young Age (18-49 Years) and Older (50 Years and Older) Patients Who Did Not Take DMARDs, Biologics, Other Targeted Drugs, Corticoids According to the Russian Register of Arthritis OREL

Azamat Satybaldyev, Galina Gridneva, Anna Misiyuk, Natalia Demidova, Kamalia Kasumova and Evgeny Nasonov, V.A. Nasonova Reseach Institute of Rheumatology, Moscow, Russia

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Comparison of frequency of different clinical features of the natural course at the stage of early rheumatoid arthritis (RA) in patients with young and older age are not sufficiently covered in the literature.

Comparative study of early RA with onset at young (18-49 years) and older age (50 years and older) before start of DMARDs, biologics and other targeted therapy and glucocorticoids.

Methods: 292 patients with RA were included into the All-Russian register of patients with arthritis "OREL" in the period from January 01, 2012 to December 31, 2018 with research data at the time of the first visit. All patients did not receive DMARDs (synthetic, biological or other targeted drugs) and glucocorticoid systemic therapy before being entered into the registry and were investigated before prescribing DMARDs. 141/292 patients (25 men, 116 women, mean age 39.27 ± 7.97 years, mean duration of disease 5,7±2,75 months) had RA onset at a younger (18-49 years old) age – group 1, 151/292 (men - 41, women - 110, mean age 66.05 ± 7.34 years, mean duration of disease 4,3±3,6 months) had RA onset at senior age (50 years and older) – group 2. RA was diagnosed in accordance with 1987 ACR and 2010 ACR/EULAR criteria. Disease activity was assessed according to DAS-28 index, X-ray stage – according to Steinbrocker, modified stages, functional disorders – in accordance with functional class (FC).

Results: In the group 2, the male / female ratio was higher (1: 2.8) than in the group 1 (1: 4.6) (p=0,055), which indicates a tendency to equalization of the sex ratio with age. Following disorders developed more often in group 2 than group 1: restriction of mobility and morning stiffness (82% vs 59%) (p< 0.05), the frequency of damage to small joints of the hands (76% vs 65%) (p >0.05), wrists (65% vs 52%) (p< 0.05), elbow (33% vs 17%) (p< 0.05), knee (53% vs 36%) (p< 0.05), shoulder (44% vs 19%) (p< 0.05), the total number of affected joints also significantly prevailed in the group 2 (in total cases p< 0,05). Group 2 patients showed stronger and more frequently inflammatory process patients of group 2 comparatively with the Group 1 was (high inflammatory activity - 66% versus 35%, respectively) (p< 0.05), as well as destructive changes (erosive arthritis - 52% versus 29%; p< 0.05) in the joints and functional disorders (FC 3 - 68% versus 15%, respectively) (p< 0.05). Extra-articular manifestations in the form of rheumatoid nodules were more often recorded in the group 2 (10% versus 2%) (p< 0.05). At the same time, ACPAs was not significantly more often detected in group 1 (89% versus 78%) (p > 0.05) with the common frequency of RF detection (72% and 72%).

Conclusion: Comparative study of the clinical characteristics of the natural course of early RA with onset in young adult (18-49 years) and with onset in older (50 years and older) age according to the data of the All-Russian register of

patients with arthritis OREL showed that RA with onset in older age is characterized by stronger and more frequently inflammatory process, destructive and functional disorders in the joints than RA with onset at a younger age.

Disclosure: A. Satybaldyev, None; **G. Gridneva**, None; **A. Misiyuk**, None; **N. Demidova**, None; **K. Kasumova**, None; **E. Nasonov**, None.

Abstract Number: 1655

Severe Respiratory Infections in Rheumatoid Arthritis Patients with Biologic Therapy: Comparative Study Between Vaccinated and Non Vaccinated Patients

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

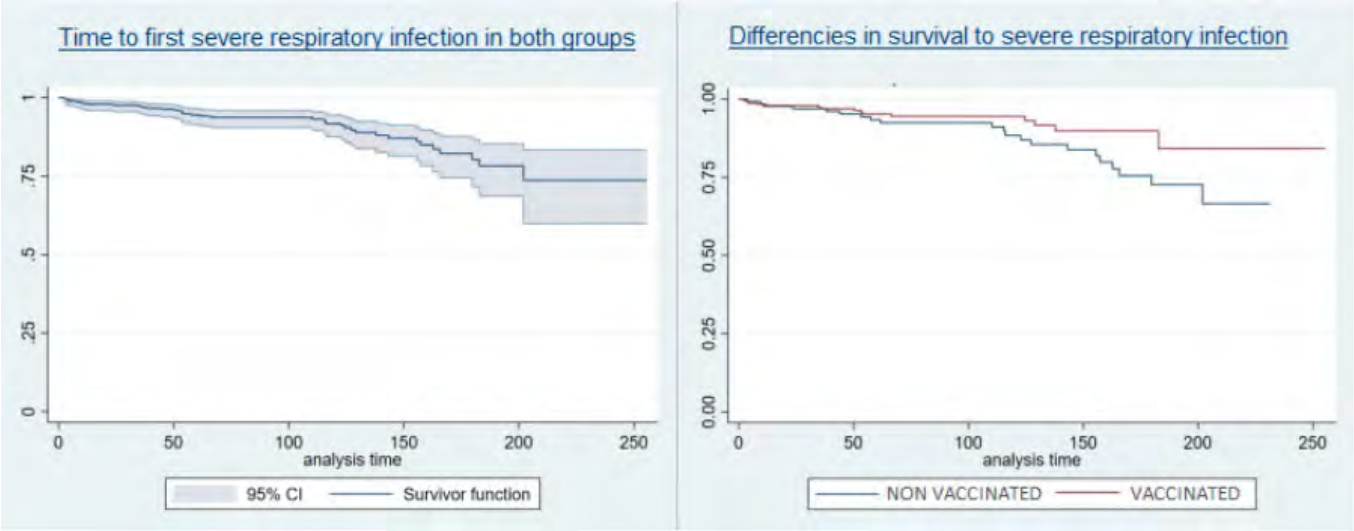
Background/Purpose: Rheumatoid arthritis (RA) patients are at increased risk of severe infections due to the disease itself, and the immunosuppressive treatment. Vaccination programs are designed to decrease the risk of infections.

Our aim was to assess **a)** the incidence of severe respiratory infections and **b)** to compare the risk between vaccinated and non vaccinated patients in patients with RA treated with biologic therapy (BT)

Methods: Observational study of 431 patients diagnosed with RA that iniciated BT. One group of patients participated in the vaccination program of the Preventive Medicina and Rheumatologúa departments of our hospital from

Table. Main general features at BT onset

	Group 1 Vaccination program N=299	Group 2 Non vaccination program N=132	p
Age (years) mean±SD	61.3±13	67.9±14.2	0.32
Women, n (%)	231 (77.3%)	105 (79.5%)	0.59
Duration of RA (months) mean±SD	73.2±10.4	112.6±60.2	
Positive RF/ Positive ACPA, n (%)	177(59.2)/172 (57.5%)	93(70.5%)98 (74.2%)	0.02
Erosive disease, n (%)	116 (38.8%)	70 (53%)	0.06
Vasculitis, n (%)	15 (5%)	2 (1.5%)	0.08
Interstitial lung disease n (%)	12 (4%)	7 (5.3%)	0.54
Subcutaneous nodules n (%)	16 (5.4%)	6 (4.5%)	0.72
Corticosteroids	299 (100%)	132 (100%)	1
Number of conventional DMARDs, mean±SD	1.6±0.9	2±1	0.3



October 2011 to October 2016 (*Group 1*). The other group was not included in the vaccination program (*Group 2*). The follow-up was made until June 2017 with a minimum follow-up period of 8 months and a maximum of 5.5 years.

Information on severe respiratory infections, defined as those that required hospitalization or at least one dose of intravenous antibiotic treatment at the emergency room, was retrieved from the hospital medical records.

Results: We studied 431 patients (335 women/96 men); mean age 63.4±13.7 years. In the vaccination program *(group 1)* were included 299 (69.4%) patients and in the *group 2;* 132 patients (30.6%). The main features of both groups are summarized in the **TABLE**.

During the follow-up, we registered 299 hospital admissions due to severe respiratory infections in both groups (incidence density 9,9 (95% CI: 6,9-13,6).

In group 1, vaccinated patients, this incidence density was reduced to 7,1 (95% CI: 4,1-11,6). **Figure**.

The vaccination program reduced the general incidence of severe respiratory infection in 44%.

Conclusion: RA patients with BT included in the vaccination program present a lower incidence of severe respiratory infections compared with non vaccinated patients.

Disclosure: L. Dominguez Casas, None; **P. Rodriguez-Cundin**, None; **T. Dierssen**, None; **M. gonzalez-Gay**, None; **R. Blanco**, None.

Abstract Number: 1656

Women with Rheumatoid Arthritis Have More Multimorbidity Than Men in a Large Nationwide US Study

Hayley Dykhoff[1], Elena Myasoedova[1], Madeline Peterson[1], John Davis[1], Vanessa Kronzer[1], Caitrin Coffey[1], Tina Gunderson[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Eyota, MN

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with RA have an increased burden of multimorbidity. Although many comorbidities vary by sex, sex differences in multimorbidity among individuals with RA have not been examined. We aimed to compare multimorbidity between women and men with RA and comparators without RA.

Methods: We used a longitudinal, real-world database with de-identified administrative claims for commercial and Medicare Advantage enrollees to identify cases of RA and matched controls. Cases were defined as patients aged ≥18 years with ≥2 diagnoses of RA in January 1, 2010 - June 30, 2019 and ≥1 prescription fill for a DMARD any time after the first RA diagnosis. Controls were persons without RA matched 1:1 to RA cases on age, sex, census region, calendar year of index date (corresponding to the date of second diagnosis code for RA), and length of prior medical/pharmacy coverage. Race was classified as non-Hispanic White (White), non-Hispanic Black (Black), Asian, Hispanic, or other/unknown, based on self-report or derived rule sets. Multimorbidity (2 or more comorbidities, MM2+) and substantial multimorbidity (5 or more comorbidities, MM5+) were defined using 44 preidentified chronic comorbidities (England et al. ARD 2020) assessed during the year prior to index date. Logistic regression models were used to estimate odds ratios (OR) with 95% confidence intervals (CI).

Results: The study included 155,631 cases with RA and 155,631 matched non-RA comparators (mean age 59.6 years, 76.0% female for both cohorts). In both cohorts, women were slightly younger (mean age 60.0 vs. 62.0 years). Among RA patients, women were more racially/ethnically diverse than men, with 70% of women (76% men) being White, 11% (9%) Hispanic, 11% (7%) Black, 3% (2%) Asian, and 6% (6%) other/unknown. Racial/ethnic diversity was more similar among non-RA women and men with 72% women (74% men) being White, 9% (9%) Hispanic, 10% (8%) Black, 3% (4%) Asian, and 6% (6%) other/unknown. Overall, patients with RA had more MM2+ than non-RA subjects (69.9% vs 53.5%), and more MM5+ than non-RA subjects (30.5% vs 18.2%).

Observed rates of MM5+ were similar in women and men without RA (18.1% vs 18.5%, p=0.09), but among RA patients, women had higher observed rates of MM5+ than men (30.9% vs 29.0%, p< 0.0001). This pattern persisted following adjustment for age, race/ethnicity, and geographic region, showing increased rates of MM5+ among RA women versus men (OR: 1.18; 95% CI: 1.16-1.22) and similar rates among non-RA women and men (OR: 1.04; 95% CI: 1.00-1.08). Examination of individual comorbidities showed that women with RA had more depression, hypothyroidism, fibromyalgia, chronic back pain, asthma, gastroesophageal reflux disease, osteoarthritis, and osteoporosis compared to men with RA and women without RA.

Conclusion: This large nationwide study showed increased occurrence of multimorbidity in women with RA compared to men with RA, while women and men without RA had similar levels of multimorbidity, even after adjustment for age, race/ethnicity, and geographic region. The underlying mechanisms for these sex differences require further investigation.

Disclosure: H. Dykhoff, None; **E. Myasoedova**, None; **M. Peterson**, None; **J. Davis**, Pfizer, 5; **V. Kronzer**, None; **C. Coffey**, None; **T. Gunderson**, None; **C. Crowson**, None.

Abstract Number: 1657

Comprehensive Assessment of Multimorbidity Burden in a Population-based Cohort of Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Multimorbidity is common in patients with rheumatoid arthritis (RA), and it is associated with poor outcomes. The literature on multimorbidity suffers from numerous definitions that make comparisons difficult. We aimed to use our population-based cohort to validate a list of morbidities proposed by England et al. (ARD 2020).

Methods: In this retrospective, population-based study, residents of a geographically well-defined area with prevalent RA on 1-1-2015 were identified from a comprehensive medical record linkage system. Age and sex-matched non-RA comparators were selected from the same underlying population. Diagnostic codes were retrieved for a 5-year period prior to the prevalence date. Using 2 codes at least 30 days apart, the 44 morbidities described by England were defined, as well as 78 Clinical Classification Software (CCS) categories with chronic disease flags that did not overlap with the 44 morbidities. Rheumatoid arthritis and categories likely representing diagnostic uncertainty with RA (e.g., lupus, polymyalgia rheumatica) were excluded from the morbidities for comparability between cohorts. False discovery rate methods were used to compare the prevalence of each morbidity in the RA vs non-RA cohorts adjusting for multiple comparisons.

Results: A total of 1409 patients with prevalent RA (72% female; 92% Caucasian; mean age 63.5 years) and 1409 non-RA (72% female; 90% Caucasian; mean age 63.4 years) were studied with 96% of RA and 90% of non-RA having at least 5 years of prior medical history. Multimorbidity (defined as 2+ morbidities) was present in 1187 (84%) of RA and 953 (68%) of non-RA subjects using the 44 morbidities with 5+ morbidities present in 749 (53%) of RA and 492 (35%) of non-RA ($p < .001$ for both). RA patients had significantly higher prevalence compared to non-RA of 20 of the 44 morbidities with 33 of 44 morbidities yielding OR >1.20 (Table). The modest sample size of this cohort may have reduced the number of significant findings compared to the original report on the 44 morbidities. Among the additional 78 CCS categories, 9 were significantly higher in RA than non-RA. The majority of these morbidities (i.e., embolism/thrombosis, organic sleep disorders, hyperparathyroidism, vitamin D deficiency, chronic skin ulcers, and foot deformities) are known to be more common in patients with RA. Some morbidities (i.e., thrombocytopenia, leukopenia, other upper respiratory infections) could reflect complications of RA therapy.

Conclusion: Patients with RA have a higher prevalence of multimorbidity compared to non-RA subjects. These results validate the previously published list of 44 morbidities, and only identify a small number of other morbidities to consider in patients with RA. Further research is needed to unify the list of morbidities used to study multimorbidity in patients with RA.

Table. Comparison of morbidity prevalence in patients with and without RA.

Morbidity	RA (%)	Non-RA (%)	Odds Ratio [95%CI] RA vs. Non-RA	Q-value
Multimorbidity (2+)	1187 (84.2)	953 (67.6)	2.92 [2.41-3.56]	<0.001
Multimorbidity (5+)	749 (53.2)	492 (34.9)	2.53 [2.13-3.01]	<0.001
Morbidities (England Categories)				
Fibromyalgia	131 (9.3)	43 (3.1)	3.28 [2.32-4.72]	<0.001
Osteoporosis	237 (16.8)	97 (6.9)	3.13 [2.41-4.10]	<0.001
Post-Traumatic Stress Disorder	17 (1.2)	6 (0.4)	2.89 [1.19-8.04]	0.097
Osteoarthritis	586 (41.6)	301 (21.4)	2.88 [2.42-3.43]	<0.001
Interstitial Lung Disease	76 (5.4)	29 (2.1)	2.78 [1.81-4.38]	<0.001
Pulmonary Circulation Disorders	55 (3.9)	21 (1.5)	2.72 [1.66-4.63]	<0.001
Chronic Back Pain	580 (41.2)	324 (23)	2.39 [2.03-2.83]	<0.001
Drugs	28 (2)	13 (0.9)	2.20 [1.15-4.41]	0.081
Gout	50 (3.5)	24 (1.7)	2.15 [1.32-3.58]	0.012
Neuropathy	205 (14.5)	106 (7.5)	2.10 [1.64-2.70]	<0.001
Peptic Ulcer Disease	15 (1.1)	8 (0.6)	1.89 [0.82-4.70]	0.44
Severe Vision Reduction	489 (34.7)	345 (24.5)	1.89 [1.57-2.27]	<0.001
Anemia	288 (20.4)	181 (12.8)	1.79 [1.46-2.21]	<0.001
Dementia	7 (0.5)	4 (0.3)	1.78 [0.53-6.86]	0.86
Chronic Obstructive Pulmonary Disease	100 (7.1)	61 (4.3)	1.71 [1.23-2.40]	0.008
Hypothyroid	310 (22)	205 (14.5)	1.70 [1.39-2.07]	<0.001
Sleep Disorder	150 (10.6)	93 (6.6)	1.69 [1.29-2.22]	<0.001
Liver Disease	47 (3.3)	29 (2.1)	1.64 [1.03-2.65]	0.13
Bipolar	13 (0.9)	8 (0.6)	1.64 [0.69-4.17]	0.69
Peripheral Vascular Disease/Aneurysm	180 (12.8)	123 (8.7)	1.62 [1.25-2.09]	0.003
Depression	331 (23.5)	228 (16.2)	1.60 [1.33-1.94]	<0.001
Chronic Headache	148 (10.5)	98 (7)	1.58 [1.21-2.08]	0.004
Gastroesophageal Reflux Disease	254 (18)	175 (12.4)	1.56 [1.27-1.93]	<0.001
Hypertension	700 (49.7)	578 (41)	1.56 [1.32-1.85]	<0.001
Coronary Artery Disease	198 (14.1)	142 (10.1)	1.55 [1.21-1.98]	0.006
Congestive Heart Failure	90 (6.4)	64 (4.5)	1.47 [1.05-2.08]	0.10
Urinary Incontinence	66 (4.7)	47 (3.3)	1.44 [0.98-2.13]	0.21
Cardiac Arrhythmias	221 (15.7)	168 (11.9)	1.42 [1.14-1.79]	0.016
Inflammatory Skin Diseases	113 (8)	82 (5.8)	1.41 [1.05-1.90]	0.081
Asthma	131 (9.3)	99 (7)	1.36 [1.03-1.79]	0.097
Diverticulitis/Diverticulosis	69 (4.9)	52 (3.7)	1.35 [0.93-1.97]	0.32
Obesity	231 (16.4)	190 (13.5)	1.26 [1.02-1.55]	0.097
Hyperlipidemia	645 (45.8)	588 (41.7)	1.21 [1.03-1.42]	0.097
Renal Disease	74 (5.3)	63 (4.5)	1.19 [0.84-1.70]	0.69
Cerebrovascular Disease	75 (5.3)	64 (4.5)	1.19 [0.84-1.70]	0.69
Valvular Heart Disease	90 (6.4)	77 (5.5)	1.19 [0.86-1.64]	0.68
Parkinson's Disease	13 (0.9)	11 (0.8)	1.19 [0.53-2.74]	1.00
Anxiety	182 (12.9)	158 (11.2)	1.18 [0.94-1.48]	0.40
Alcohol Abuse	21 (1.5)	18 (1.3)	1.17 [0.62-2.23]	1.00
Prostatic Hyperplasia	50 (12.7)	46 (11.7)	1.11 [0.71-1.75]	1.00
Diabetes	227 (16.1)	214 (15.2)	1.07 [0.87-1.32]	0.86
Hearing Loss	113 (8)	108 (7.7)	1.05 [0.79-1.40]	1.00
Non-Inflammatory Gynecologic Disorders	164 (16.1)	169 (16.6)	0.96 [0.76-1.23]	1.00
Cancer	106 (7.5)	122 (8.7)	0.85 [0.65-1.12]	0.61
Morbidities (CCS Categories)				
CCS116 - Aortic and Peripheral Arterial Embolism/Thrombosis	9 (0.6)	0 (0)	19.18 [2.43-2474.01]	0.015
CCS199 - Chronic Ulcer of Skin (e.g., pressure ulcers)	61 (4.3)	15 (1.1)	4.32 [2.50-7.95]	<0.001
CCS208 - Acquired Foot Deformities (e.g., bunions)	105 (7.5)	27 (1.9)	4.16 [2.74-6.52]	<0.001
CCS63 - Diseases of White Blood Cells (e.g., leukocytopenia)	60 (4.3)	21 (1.5)	2.94 [1.81-4.97]	<0.001
CCS62 - Coagulation and Hemorrhagic Disorders (e.g., thrombobytopenia)	33 (2.3)	15 (1.1)	2.23 [1.23-4.25]	0.042
CCS52 - Nutritional Deficiencies (e.g., vitamin D deficiency)	92 (6.5)	44 (3.1)	2.18 [1.52-3.17]	<0.001
CCS126 - Other Upper Respiratory Infections (e.g., sinusitis)	82 (5.8)	40 (2.8)	2.12 [1.45-3.15]	<0.001
CCS51 - Other Endocrine Disorders (e.g., hyperparathyroid)	58 (4.1)	31 (2.2)	1.91 [1.24-3.00]	0.017
CCS259 (Modified) - Sleep Apnea, Organic	183 (13)	136 (9.7)	1.40 [1.11-1.78]	0.021

Q-values are p-values adjusted for multiple comparisons using false discovery rate methods.

Disclosure: C. Crowson, None; **T. Gunderson**, None; **E. Myasoedova**, None; **E. Atkinson**, None; **V. Kronzer**, None; **C. Coffey**, None; **J. Davis**, Pfizer, 5.

Abstract Number: 1658

Risk of Other Autoimmune Conditions Among Relatives of Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Autoimmune conditions appear to cluster in families, as may be expected by shared genetic risk factors in conditions such as rheumatoid arthritis (RA), autoimmune thyroiditis (AITD), celiac disease, and systemic lupus erythematosus (SLE). However, these conditions are polygenic, individual risk alleles have small effect sizes, and only a handful of alleles are shared across diseases. There are limited data on how to consider risk for autoimmune diseases among family members with RA. The objective of this study was to determine the risk of developing AITD, celiac, and SLE among first-, second-, and third- degree relatives (FDR, SDR, TDR) of RA patients.

Methods: This study was performed in the Utah Population Database (UPDB) containing genealogical data from the 1850s to modern day descendants. We analyzed UPDB genealogy data linked to in- and outpatient diagnosis code data from the University of Utah Health Sciences Center (UUHSC) electronic health record data from 1994-2020. International classification of diseases (ICD) 9th and 10th revision data were extracted on RA, AITD, celiac, inflammatory bowel disease (IBD), and SLE for RA patients and FDR, SDR and TDRs. Cases were defined using ≥1 diagnosis code. Odds ratios (OR) were estimated by comparing the number of autoimmune cases among relatives of RA patients to the expected cohort-matched population rates estimated using linked UUHSC EHR data. We calculated OR for RA among relatives of RA patients as a positive control; IBD served as a negative control.

Results: We studied 5,603 subjects with RA and 18,844 first-, 37,413 second-, and 78,169 third-degree relatives with linked UUHSC data. Among FDRs of RA subjects, we observed a significantly higher risk of AITD (OR 1.28, 95% CI 1.08. 1.50), celiac (OR 1.51, 95% CI 1.18, 1.92) and SLE (OR 1.34, 95% CI 1.11, 1.59) compared to population rates (**Figure**). Among the autoimmune conditions, only SLE had an increased risk among SDRs of RA patients. No

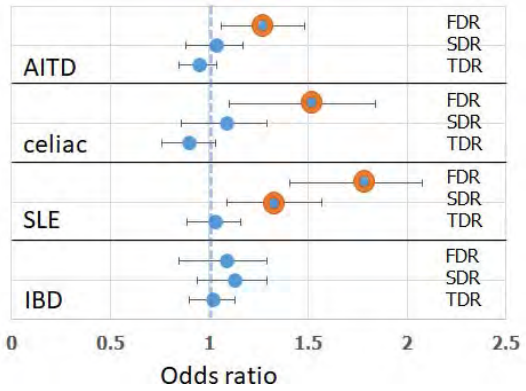

Figure. Risk of autoimmune thyroiditis (AITD), celiac, systemic lupus erythematosus (SLE), and inflammatory bowel disease (IBD) among first-, second-, and third-degree (FDR, SDR, TDR) among relatives of patients with rheumatoid arthritis (RA) compared to the population. [Orange circle, p<0.01].

significant increased risk for AITD, celiac or SLE was observed among TDRs compared to the overall population. The OR for FDRs of RA patients was 2.23 (95% CI 2.1-2.4), OR 1.37 (95% CI 1.3, 1.5) for SDRs, in line with prior studies. Rates of IBD among relatives of RA patients were similar to population rates.

Conclusion: Results from this unique dataset linking genealogy with phenotypic data in a large population suggest that a lower threshold for screening FDRs, i.e. the siblings, offspring, and parents of RA subjects, is warranted among relatives who exhibit signs or symptoms for AITD, celiac or SLE. Our data do not support a higher need to screen for these autoimmune conditions among TDRs, e.g. first cousins, of RA patients.

Disclosure: K. Liao, None; **T. Seyok**, None; **L. Cannon-Albright**, None.

Abstract Number: 1659

Increased All-Cause Mortality Risk in Patients with Incident Rheumatoid Arthritis After First Antidepressant Dispensing: Results from the Nationwide DANBIO Database

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Depression occurs with a prevalence of about 17% (95% confidence interval (CI): 10-24) in patients with RA (1) and both disorders may share common proinflammatory pathways affecting neural and extra-neural tissues (2). Recently, in an incident RA single center cohort, we have shown that the main indication for dispensing antidepressants is depression and the frequency of dispensing coincides with the occurrence of depression reported in the medical literature (3). In the present study, we used the first dispensing of antidepressants as proxy for clinical depression with the aim to describe the mortality risk associated with depression in patients with incident RA.

Methods: In DANBIO (4), we identified 18,085 patients diagnosed with RA (index date) from January 1, 2008 to September 30, 2018 by their unique personal registration numbers. We excluded patients with a recorded dispensing of MTX (Anatomic Therapeutic Chemical code L01BA01) and/or antidepressants (N06A) in the Danish National Prescription Register or recorded hospital contacts with RA (International Classification of Diseases (version 10) codes M05 or M06) in the Danish National Patient Register, 3 years prior to the index date. From the index date, we defined depression as first dispensing of antidepressants and collected death dates from the Danish Civil Registration System. The patients were followed until December 31, 2018 and all-cause mortality was estimated in two dynamic risk periods: the period from the index date until first dispensing of antidepressants (if it occurred) and the period after dispensing of antidepressants. We calculated hazard rate ratios (HRR) by modelling dispensing of antidepressants as time-varying exposure and adjusted for potential confounders: age, gender, comorbidity, cohabitation, employment status, highest attained education, and income.

Table 1. Baseline characteristics of RA patients by depression status defined as first dispensing of antidepressants (no missing observations unless otherwise stated)

	No antidepressants (n=10,076)	Antidepressants (n=1,111)
Age (years), %		
≤55	37	38
>55 to ≤70	38	33
>70	25	29
Female, %	65	72
Charlson comorbidity index, %		
0	76	69
1	13	17
≥2	10	14
Cohabitation, %		
Living alone	24	29
Together	74	69
Missing	1	2
Employment, %		
Employed	48	35
Unemployed	2	2
Not in labor market	43	46
Missing	7	17
Highest attained education, %		
Low	36	43
Medium	56	52
High	6	2
Missing	3	3
Yearly household income (5-year average before RA index date, USD), %		
Low (<33,000)	8	13
Medium low (33-49,999)	17	23
Medium high (50-66,000)	16	17
High (>66,000)	57	46
Missing	1	2

Table 2. Crude and adjusted HRR (95% CI) for death, comparing mortality in the risk period until and after dispensing of antidepressants

	No. deaths/person-years at risk		HRR	
Follow-up	Risk period until dispensing of antidepressants	Risk period after dispensing of antidepressants	Crude	Adjusted
0-2 years	93/20,125	15/437	3.67 (2.12-6.33)	3.53 (2.03-6.14)
0-11 years	511/54,084	162/3,862	3.36 (2.80-4.03)	3.23 (2.63-3.97)

Results: We included 11,187 incident RA patients of which 1,111 (10%) were initiators of antidepressants (Table 1). Initiation of antidepressants was a strong predictor of both 2-year mortality (adjusted HRR 3.53) and mortality during the total follow-up period (adjusted HRR 3.23) (Table 2).

Conclusion: Depression, defined as first dispensing of antidepressants, was associated with more than 3-fold increased mortality risk in patients with incident RA.

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Disclosure: j. Pedersen, None; **L. Wang**, None; **A. Pedersen**, None; **K. Andersen**, None; **C. Sørensen**, None; **T. Ellingsen**, None.

Abstract Number: 1660

Relationship Between Risk of New Onset Diabetes Mellitus and Exposure to Individual Antirheumatic Drugs in Patients with Rheumatoid Arthritis: A Nationwide Population Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

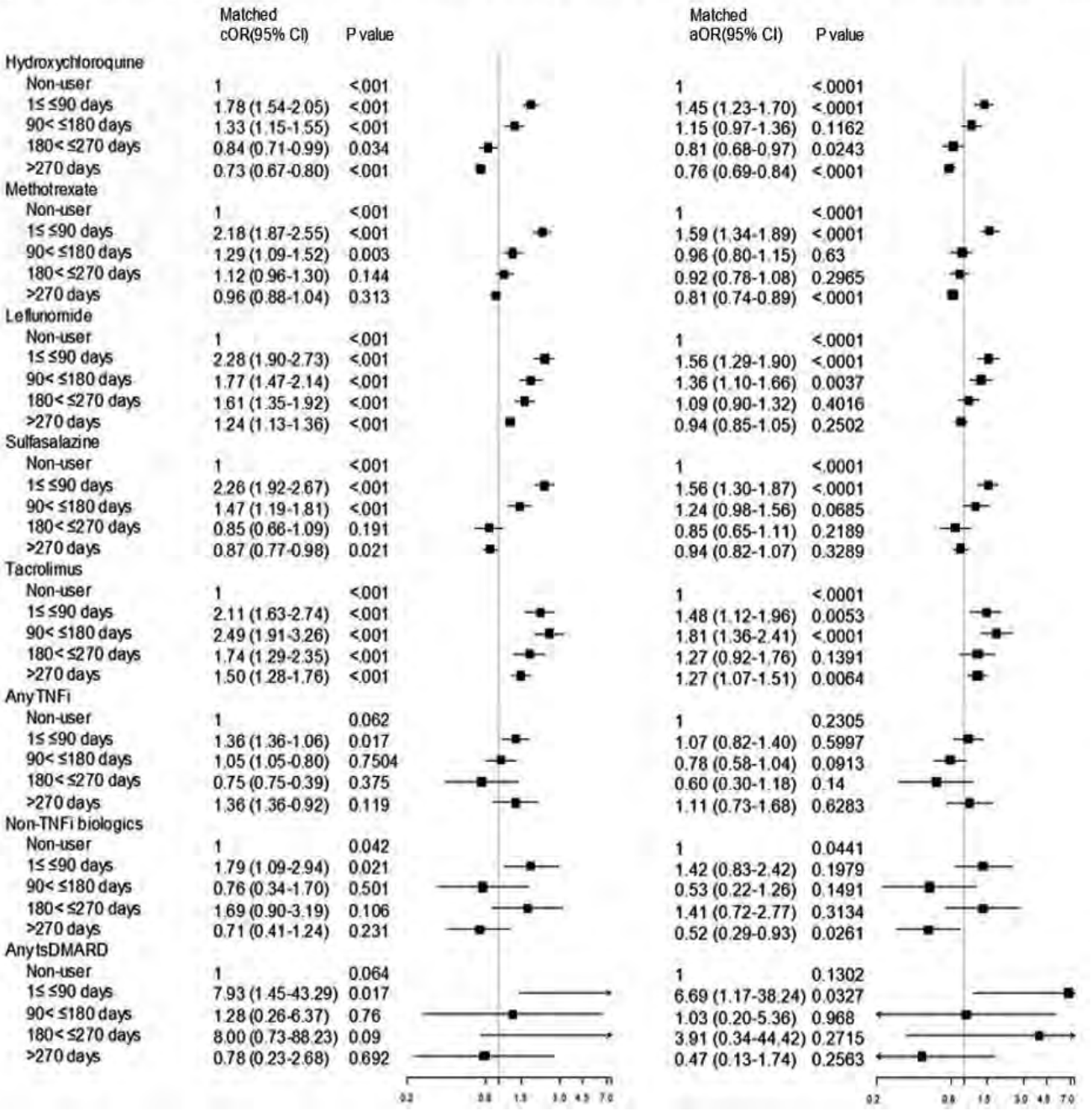
Background/Purpose: Rheumatoid arthritis (RA) is a systemic inflammatory disease that affects glucose metabolism, mainly insulin resistance, which can lead to diabetes mellitus (DM). Although there have been reports that anti-inflammatory therapy can reduce the risk of diabetes in RA, the relationship between individual antirheumatic drugs and DM has not been sufficiently investigated. Therefore, we aimed to investigate the effect of disease-modifying antirheumatic drugs (DMARDs) on the incidence of DM in the RA population.

Methods: We conducted a nested case-control study in a cohort of 69 779 DM-naïve adult (≥ 18 years old) patients with RA from the Korean Health Insurance Review and Assessment Service claims data from 2011 to 2019. Cases with incident DM were identified and individually matched to randomly selected controls (RA cases without DM) by the age of RA diagnosis, sex, and disease duration (1:4 matched). Comorbidities including hypertension, chronic kidney disease, Charlson Comorbidity Index (CCI), and concomitant drug use were measured for one year prior to the event or index date. DMARDs use was stratified by duration of exposure. The association of each DMARD use with DM risk was estimated using conditional logistic regression adjusted for CCI and concomitant drug use.

Results: 3772 (5.4%) patients were diagnosed with DM (mean age, 62.3 ± 10.9 years; 77,6% women), and the mean duration between RA diagnosis and incident DM was 2.6 ± 2.1 years. A total of 146139 controls were matched, and DM risk was associated with corticosteroids use and cumulative dosage. 3515 of 3772 (93.2%) patients with DM have been treated with conventional DMARDs. The risk of incident DM was dependent on the type and the duration of exposure of DMARDs (Figure). In a multivariable-adjusted analysis, exposure of less than 90 days per year to hydroxychloroquine (HCQ), methotrexate (MTX), sulfasalazine, leflunomide, tacrolimus (TAC), or any targeted synthetic DMARDs (tsDMARDs) was associated with an increased risk of DM compared with no use. However, at exposure exceeding 270 days per year, HCQ (adjusted OR, 0.76; 95% CI, 0.69-0.84; $p < 0.001$) and MTX (adjusted OR, 0.81; 95% CI, 0.74-0.89; $p < 0.001$) were associated with a significant decrease in DM risk, and TAC (adjusted OR, 1.27; 95% CI, 1.07-1.51; $p = 0.006$) was associated with an increased risk. Among biologic DMARDs, use of TNF inhibitors or non-TNF inhibitors was not related to DM risk at exposure less than 90 days per year, but non-TNF inhibitors was associated with a significant decrease in DM risk at exposure more than 270 days per year (adjusted OR, 0.52; 95% CI, 0.29-0.93, $p = 0.026$).

Conclusion: This study suggested that long-term use of HCQ, MTX, or non-TNF inhibitors for periods more than 270 days per year was associated with a reduction in the incidence of DM. Thus, these regimens could be considered to control disease activity especially in patients with high risk of DM.

Figure. Forest plot of diabetes mellitus associated with DMARDs in patients with RA



Abbreviations: DMARDs, disease-modifying anti-rheumatic drugs; RA, rheumatoid arthritis; OR, odds ratio; CI, confidence interval; TNFi, tumor necrosis factor inhibitor; tsDMARDs, targeted synthetic disease-modifying anti-rheumatic drugs; CCI, Charlson Comorbidity Index. Adjusted for CCI (ordinal), use of steroid (cumulative prescribed dose quintiles), use of statin (yes/no), use of other DMARDs, or use of TNFi

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Abstract Number: 1661

Sex-Stratified Patterns of Multimorbidity at RA Onset and Associated Longitudinal Impacts on Disability Over the First Year Follow Up: Results from the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

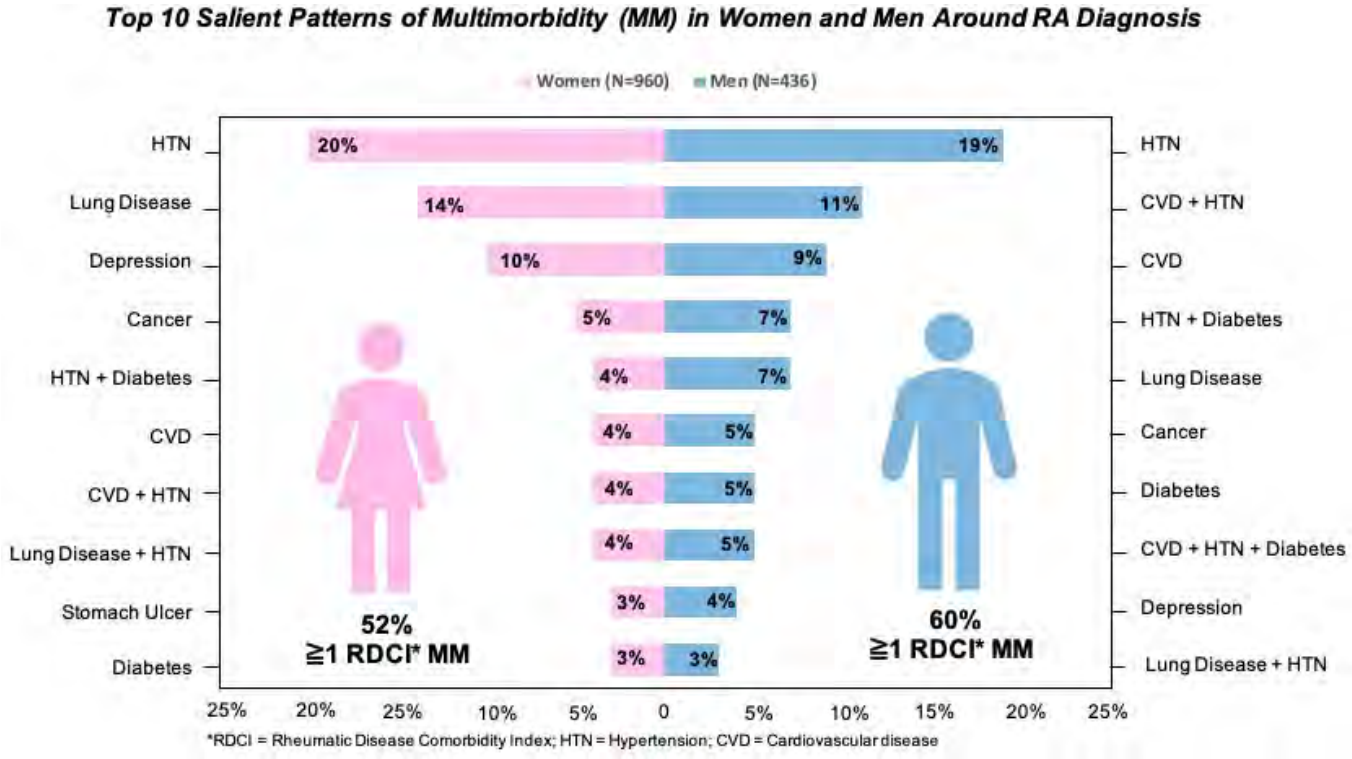
Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic disease multimorbidity (MM) is prevalent in RA. As MM can vary in complexity and different combinations of chronic conditions may have different physical and psychological impacts on patients, there is an increasing need to identify which specific conditions may cluster around the time of RA onset. The objective of the present study was to identify the top 10 most prevalent MC patterns in women and men around RA diagnosis and estimate their associations with disability over the first year of follow up, in a large real-world incident RA cohort.

Methods: Data were from early RA patients (< 1-year of symptoms; 88% meeting RA classification criteria) diagnosed and treated in rheumatology clinics across Canada enrolled in CATCH (Canadian Early Arthritis Cohort) from Jan 2007 through March 2020. Participants were included in the present study if they completed the Rheumatic Disease Comorbidity Index (RDCI) at baseline and repeat assessments of disease activity (DAS28) and disability (MHAQ) every 3- months over 1 year follow up. The RDCI is a validated weighted comorbidity index (range 0-9) assessing the presence of 11 conditions selected based on associations with RD health outcomes (lung disease, CVD (MI, stroke, and other CV), HTN, fracture, depression, diabetes, cancer, ulcer or stomach problem). We identified the top 10 most prevalent MM patterns in women and men by first coding the presence/ absence of each condition for each participant and then ranking the prevalence of all possible reported combinations by sex. We estimated sex-stratified longitudinal associations between prevalent MM patterns and repeated measures of disability in the first year follow up with generalized estimating equations (GEE), adjusted for age, education, symptom duration, smoking, obesity and time-varying measures of DAS28 disease activity.

Results: The sample included 2,576 ERA patients, 1843 (72%) were female, with a mean(sd) age of 56 (15) years and 6 (3) months of symptoms. At baseline 2,449 (95%) were treated with csDMARDs (mostly methotrexate (74%)) and 40 (2%) with a biologic. More than half of patients (54%) reported >=1 MM. Prevalence, patterns and complexity of MM differed by sex. HTN, lung disease and depression were the most prevalent MM patterns reported in women and HTN, CVD, and CVD+HTN were the most prevalent patterns reported in men (Figure). More complex MM patterns involving multiple conditions were more prevalent in men (26%) than in women (12%) (Figure). In multivariable GEE models, depression (beta: 0.14, 95% CI: 0.04, 0.24) in women, and lung disease + HTN (beta: 0.22, 95% CI: 0.03, 0.42) in men, were significantly associated with higher disability over time.

Conclusion: Results from this large real-world incident cohort study suggest that multimorbidity is common around RA diagnosis and differs between men and women. MM patterns significantly associated with increased disability



over time included depression in women, and lung disease + HTN in men. Results suggest potential shared risk factors and pathways between identified MM patterns and highlight the need to screen for and treat MM conditions, particularly those which increase disability.

Disclosure: O. Schieir, None; **S. Bartlett**, Merck Canada, 2, 6, Pfizer Canada, 2, 6, Janssen Canada, 2, 6, PROMIS Health Organization, 4, American Thoracic Society, 4, Arthritis Health Professionals Association, 4, UCB, 1, RAND Corporation, 1; **M. Valois**, None; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **G. Boire**, Abbvie, 1, 6, 7, BMS, 6, 7, Janssen, 1, 5, 6, Eli Lilly, 1, 7, Amgen, 7, Novartis, 6, 7, Pfizer, 7, Sandoz, 6, 7, Viatris, 1, 6, Samsung Bioepis, 1; **G. Hazlewood**, None; **E. Keystone**, AbbVie, 2, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb Company, 2, Celltrion, 2, Gilead Sciences, 2, F. Hoffmann-La Roche, 2, 6, Janssen, 2, 6, Eli Lilly, 2, Merck, 2, 5, 6, Myriad Autoimmune, 2, Novartis, 6, Pfizer Inc, 2, 5, 6, PuraPharm, 5, Sandoz, 2, Sanofi-Genzyme, 2, 6, Samsung Bioepis, 2; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **D. Tin**, None; **V. Bykerk**, National Institutes of Health, 1, 5, Canadian Institutes of Health Research, 5, Amgen, 2, 5, BMS, Celgene, 2, 6, Gilead, 2, Sanofi, 2, 6, Regeneron, 2, Eli Lilly and Company, 6, Pfizer, 6, UCB, 6.

Abstract Number: 1662

Unrecognised, Subclinical, Structural or Functional Lung Changes in Rheumatoid Arthritis Is Associated with a Higher Risk of Developing Serious Respiratory Tract Infection

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The incidence of lung disease within the rheumatoid arthritis is well described and likely underestimated. Additionally, RA patients are at higher risk for developing significant infections (SI).

In our own cohort the most common infections recorded were respiratory tract infections (RTI) and this was most likely to lead to increased mortality. This accords with studies showing that hospitalisations from pneumonia are higher in RA cohort compared to matched cohorts.

To determine if pre-existing subclinical functional or structural lung disease had an association with an increased risk of respiratory tract infections, including viral pneumonias, as opposed to other infections.

Methods: All patients in our tertiary hospital RA cohort, in the last 3 years, who had any SI were included. The patient's medical history was examined to determine if they had evidence of functional or structural lung damage prior to the infection using imaging records and previous pulmonary function tests. Patients presenting to hospital, or their general practitioner, and their diagnosis on discharge was either community acquired pneumonia, viral respiratory tract infection or other lower respiratory tract infection were included. Patients with RTI were compared to a sample of patients with RA and any non-respiratory SI (Table 1).

A Chi-Square analysis was used to compare the groups. The two groups were matched for daily steroid use, smoking history and vaccination status, there was no statistical difference between these two groups.

Results: 142 patients were identified as having an SI in the past 3 years in our cohort. 48 patients developed RTI and 94 patients who developed other infections including Urinary traction infections, skin and soft tissue infections. Of the 48 who developed RTI, 32 had evidence of subclinical lung disease compared to 16 with no evidence of lung disease. Of the 94 who developed other SI, only 21 had evidence of subclinical lung disease compared to 73 with no evidence of subclinical lung disease (Table 2).

Table 1. Patient demographics and selected investigations (n =142)

	Patients with evidence of sub-clinical lung changes (n=55)	Patients with no evidence of sub-clinical lung changes (n=87)
Patient Age, mean ± SD, years	58.58 ± 14.1	57.24 ± 13.3
Gender, No. (% female)	42 (76.4)	65 (74.7)
Duration symptoms, mean ± SD, years	21.4 ± 5.6	22.7 ± 5.1
Known pre-existing lung disease	11 (7.7%)	N/A
No known pre-existing lung disease	50 (90.1%)	81 (93.1%)
Functional lung abnormality	21 (14.8%)	N/A
Radiological lung abnormality	34 (23.9%)	N/A
Average daily steroid dose, mean ± SD, mg/day	2.2 ± 0.6	2.1 ± 0.5
Smoking history, mean ± SD, pack years	12.3 ± 17.7	11.7 ± 15.4
Vaccinated against pneumococcal disease	34 (61.8 %)	54 (62.1%)

Table 2. Type of infections suffered and evidence of subclinical lung disease (n = 142)

	Respiratory Tract infections (RTI)	Other significant infections (SI)
No evidence of lung abnormality	16	71
Evidence of subclinical lung disease	32	23

A Chi-Square analysis of the data was performed

$X^2 = (1, N = 142) = 23.84, p < 0.001$

allowing us to consider that pre-existing lung disease may be involved in this subset of RA patients being more susceptible to LRTIs. Patients with known pre-existing lung disease where excluded from this analysis.

Conclusion: A greater number of patients within the RTI group had previous lung abnormality compared to patients in the non-pulmonary infection group. This supports evolving literature that even subclinical lung abnormality should be considered within the suite of risk factors for RTI risk in RA.

Given the current climate and fear surround viral pneumonias, screening this cohort will allow for better risk stratification and management of these patients. This may include early admission and intervention or, in the outpatient setting, highlight the need for discussion around vaccinations to reduce this risk.

Disclosure: B. Worcester, None; **D. Wang**, None; **S. Morton**, None; **M. Leech**, None.

Abstract Number: 1663

The Influence of Comorbidity on Mortality in Patients with Rheumatoid Arthritis 1980-2015: A Longitudinal Population-based Study in Western Australia

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) contributes to excess morbidity and mortality in RA patients compared with the general population. In Australia, there is a paucity of published literature on the mortality and morbidity rates in RA patients, despite the significant morbidity and mortality burden on health care costs due to RA. Linked data is the preferred method to estimate morbidity and mortality outcomes as they provide the best case ascertainment. The aim of this study was to describe temporal changes in mortality rates for patients with Rheumatoid arthritis (RA) in relation to comorbidity accrual from 1980-2015 in Western Australia (WA).

Methods: Using population-level linked data from WA health administrative datasets (hospital morbidity, emergency department and death data), we followed 17,125 RA patients (ICD-10-AM M05.00–M06.99, ICD-9-CM 714) from 1980- 2015. Comorbidity was ascertained using the Charlson Comorbidity Index (CCI). Mortality rate ratios (MRR) were calculated per decade between the RA cohort and the WA general population by direct age standardisation

Table 1. Mortality rates observed among patients with rheumatoid arthritis, based on Charlson Comorbidity Index, per 1000 hospital separations, Western Australia hospitals (1980-2015)

Time period	1980-1990	1991-2000	2001-2010	2011-2015
Total number of hospital separations	82099	107731	185398	80410
Number of deaths	1620	2875	3183	1277
CCI score				
0	481 (29.7%)	1024 (35.6%)	1197 (37.6%)	565 (44.2%)
1	838 (51.7%)	1271 (44.2%)	1358 (42.6%)	467 (36.6%)
2	273 (16.8%)	518 (18%)	581 (18.3%)	232 (18.2%)
3	1 (0.1%)	4 (0.2%)	2 (0.1%)	0 (0%)
6	27 (1.7%)	58 (2%)	45 (1.4%)	13 (1%)
In-hospital RA mortality per 1000 hospital separation	19.7	26.7	17.2	15.9
Parentage of average annual change per annum in the period	0	3.8	-4.8	-2.6
Parentage of average annual change since 1980	0	1.5	-1.4	-0.2

CCI= Charlson Comorbidity Index.

method, while temporal trends of comorbidities and in-hospital mortality were estimated per 1000 hospital separations in three consecutive decades.

Results: During 356,069 patient-years, a total of 8955 (52%) deaths occurred in the RA cohort. The leading causes of deaths were cardiovascular diseases 2386 (26.6%), cancer 1511 (16.8%), rheumatic diseases 519 (5.8%), chronic pulmonary disease 491 (5.5%), dementia 269 (3.0%) and diabetes 235 (2.6%). The highest prevalence of comorbidity (688.6 per 1000 separations) was in the period 1991-2000 following a 1.3% average annual increase since 1980. In-hospital mortality rate was also highest (26.7 deaths per 1000 separations) in the same period. After 2001, both RA comorbidity and mortality rates decreased annually by -0.5% and -4.8%, respectively, with annual changes of -4.4% to -2% and from 2011- 2015, respectively. The overall mortality rate in RA patients after age adjustment was 2.5-times (95%CI: 2.52-2.65) higher than the general population between 1980- 2015 and 1.5-times (95%CI: 1.39-1.81) for the period 2011-2015.

Conclusion: The annual comorbidity prevalence and mortality rates in WA have decreased significantly since 2001, reflecting improvements in the management of RA and comorbidity. Nonetheless, the mortality rate in RA patients in WA remains 1.5-times higher than their community counterparts suggesting that there is room to achieve further improvements.

Disclosure: K. Almutairi, None; **J. Nossent**, None; **D. Preen**, None; **H. Keen**, Roche, 6, Abbvie, 6, Roche, 12, education/travel; **C. Inderjeeth**, None.

Abstract Number: 1664

Changes in Physical Function Were Not Associated with Clinically Important Changes in Muscle Strength or Physical Performance over Time - A Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The Health Assessment Questionnaire Disability Index (HAQ) is negatively associated with muscle strength by handgrip test and positively associated with physical performance by timed up and go test (TUG test) in patients with rheumatoid arthritis (RA). Although the HAQ score may improve during treatment of inflammatory arthritis, the association between the self-reported HAQ scores and objective assessments of muscle strength or physical performance over time has not been clearly defined. We therefore aimed to evaluate the association between HAQ and clinical features, muscle strength and directly-assessed physical performance at baseline among patients with RA. Second, we aimed to determine the association between changes over time in self-reported physical function and disease activity, muscle strength, and physical performance.

Methods: In a prospective cohort design, two independent RA cohorts were retrospectively analyzed. Physical function was assessed by HAQ. Disease activity was assessed by the Disease Activity Score in 28 joint (DAS-28-CRP). Pain was assessed by The Visual Analog Scale for Pain (VAS Pain). Muscle strength was assessed by handgrip test and chair test. Physical performance was assessed by TUG test and The Short Physical Performance Battery (SPPB). T test for independent samples, Mann-Whitney U test of independent samples, Pearson's chi-squared test, Spearman correlation coefficients was performed.

Descriptive data of physical function, muscle strength and physical performance on the two cohorts at baseline.

	Combined cohorts	North American Cohort	Brazilian Cohort	P
HAQ-DI scores	0.8 (0.2 -1.5)	0.7 (0.2-1.3)	1.1 (0.3-1.9)	
Women	-	0.8 (0.1-1.4)	1,0 (0.2-1.8)	0.153[2]
Men	-	0.6 (0.2-1.1)	1.8(0.7-2.1)	0.00[2]
Handgrip test				
Women (kg), mean ± SD	16.9 ± 9.0	19.8 ± 9.2	14.7 ± 8.3	0.013[1]
Men (kg), mean ± SD	27.0 ± 11.4	26.6 ± 10.7	28.5±14.3	0.678[1]
Chair stand test				
Women (s), median (IQR)	15.1 (12.9 – 18.3)	10.3 (7.3 – 12.3)	15.5 (13.8 -18.9)	<0.001[2]
Men (s), median (IQR)	11.4 (8.6-15.6)	11.5 (8.3 – 15.2)	14.6 (13.4 -18.1)	0.007[2]
TUG	-	-	10.7 (9.4-13.0)	
Women (s), median (IQR)	-	-	10.9 (9.4-13.1)	
Men (s), median (IQR)	-	-	8.3 (7.3-11.1)	
SPPB	-	11.0 (9.0-12.0)	-	
Women (points), median (IQR)	-	12.0 (9.0 – 12.0)		
Men (points), median (IQR)	-	11.0 (9.0 – 12.0)		

p, values of the difference the American group and Brazilian group. 1 t test for independent samples; 2 Mann-Whitney U test of independent samples. HAQ-DI,by the Health Assessment Questionnaire Disability Index; TUG test, Timed up and go test; SPPB, The Short Physical Performance Battery.

Association among physical function (by HAQ-DI) and clinical features, muscle strength and physical performance.

	Combined cohorts	American cohorts	Brazilian Cohorts
DAS28-CRP	0.6 (0.000)	0.6 (0.000)	0.5 (0.000)
VAS pain scale	0.6 (0.000)	0.6 (0.000)	0.6 (0.000)
Muscle strength by Handgrip test	- 0.4 (0.000)	-0.5 (0.000)	-0.3 (0.001)
Muscle strength by Chair Test	0.5 (0.000)	0.5 (0.000)	0.5 (0.000)
Physical performance by TUG test	0.6 (0.000)	-	0.6 (0.000)
Physical performance by SPPB	-0.6 (0.000)	-0.6 (0.000)	-

*Spearman correlations; DAS-28–CRP, the Disease Activity Score-28 with C reactive protein; VAS pain, The Visual Analog Scale for Pain; HAQ-DI,by the Health Assessment Questionnaire Disability Index; TUG test, Timed up and go test; SPPB, The Short Physical Performance Battery.

Results: A total of 205 RA patients were studied [North American Cohort (N=115); Brazilian Cohort (N=90)]. At baseline, the mean age was 56.2 ± 10.5 years old in the combined cohort and not statistically different between the two cohorts (p=0.75). The majority of patients were in low disease activity and this was not statistically different between the two cohorts (p=0.92). Brazilian men had greater HAQ than North American men (p< 0.001), while HAQ was not statistically different among women (p=0.15). Brazilian women had lower muscle strength by handgrip test and chair test than North American women (p< 0.05), while Brazilian men showed less muscle strength by chair test than North American men (p< 0.05). In both cohorts the RA patients showed good physical performance. At baseline, HAQ was strongly associated with DAS28-CRP, VAS pain, muscle strength and physical performance (p< 0.05). Patients that experienced a change in HAQ as much as the minimal clinically important difference (0.22) (either improvement or worsening) were not more likely to experience a clinically important change in muscle strength or physical performance over time (p >0.05) in both cohorts. American patients that had a worsening of HAQ over time did show worsening on SPPB (p=0.022).

Conclusion: Poor physical function as measured by HAQ is closely associated with disease activity, pain, muscle strength, and physical performance among patients with RA. However, in this sample, the clinically important changes physical function were not associated with clinically important changes in muscle strength or physical performance over time. These observations highlight a disconnect between changes in self-report of disability over time in patients with RA compared to direct assessments of physical function.

Disclosure: R. Espírito Santo, None; **J. Baker**, None; **J. Silva**, None; **L. Filippin**, None; **J. Portes**, None; **C. Brenol**, None; **R. Chakr**, None; **R. Xavier**, Abbvie, 2, Janssen, 2, UCB, 2, Pfizer, 2, Novartis, 2, Amgen, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2.

Abstract Number: 1665

Physical Activity Moderates Inflammatory Gene Expression in Rheumatoid Arthritis

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Prior studies show an independent association between greater physical activity and lower inflammatory markers among adults in the general population, but the impact of physical activity on systemic inflammation in people with rheumatoid arthritis (RA) is unknown. We aimed to determine whether physical activity associates with differential expression of inflammatory genes in RA.

Methods: Data derived from baseline assessments of a prospective observational cohort of RA patients. At each study visit, we obtained clinical data, collected peripheral whole blood for RNA sequencing, and provided

Table. Characteristics of Patients with Rheumatoid Arthritis by Physical Activity Category

Characteristics	Overall	Physical Activity** Status			P
		Active	Intermediate	Inactive	
	(N = 35)	(N = 13)	(N=14)	(N = 8)	
Sociodemographic Factors:					
Age, mean ± SD	55.6 ± 12.1	49.7 ± 10.6	55.9 ± 10.7	62.9 ± 12.0	**0.04**
Female	89.5%	100.0%	92.9%	75.0%	0.13
Race					0.21
Asian	8%	0%	14%	13%	
African American	11%	0%	7%	25%	
White	32%	23%	29%	50%	
Unknown	40%	62%	36%	13%	
Multiple	11%	15%	14%	0%	
Hispanic ethnicity	40%	62%	36%	13%	0.08
Education < college degree	50%	62%	43%	50%	0.62
RA Specific Characteristics:					
RA disease duration, years, mean ± SD	13.1 ± 11.3	11.9 ± 11.1	14.3 ± 12.7	14.9 ± 11.6	0.82
Disease activity by RADAI, mean ± SD	3.9 + 1.9	3.9 + 1.3	4.5 + 2.1	3.1 + 1.8	0.21
Treated with methotrexate	55%	62%	36%	75%	0.17
Treated with TNFi	37%	23%	50%	25%	0.28
Treated with any conventional DMARD	68%	68%	57%	88%	0.34
Treated with any biologic DMARD	53%	46%	71%	25%	0.10
Current systemic glucocorticoid use	29%	23%	29%	25%	0.95
Comorbidities and Health Status:					
Cardiovascular Disease	10.5%	0.0%	7.1%	12.5%	0.47
Diabetes Mellitus	13.2%	7.7%	21.4%	12.5%	0.59
Asthma	15.8%	15.4%	7.1%	25.0%	0.51
History of malignancy	10.5%	0.0%	7.1%	25.0%	0.14
Body Mass Index (kg/m2), mean ± SD	28.8 ± 5.5	29.0 ± 6.8	28.9 ± 5.2	28.6 ± 4.1	0.33
Current nicotine use	5.3%	7.7%	0.0%	12.5%	0.44

*Values are percent unless otherwise indicated. P-values calculated using chi-squared tests for categorical measures and ANOVA for continuous measures.

**Physical activity was categorized by lower (inactive), middle (intermediate), and upper (active) tertiles for percentage of time spent in moderate or vigorous physical activity among all study participants.

RADAI - Rheumatoid Arthritis Disease Activity Index

TNFi - tumor necrosis factor inhibitor

DMARD - disease modifying antirheumatic drug

CVD - history of stroke, coronary artery disease, and/or myocardial infarction

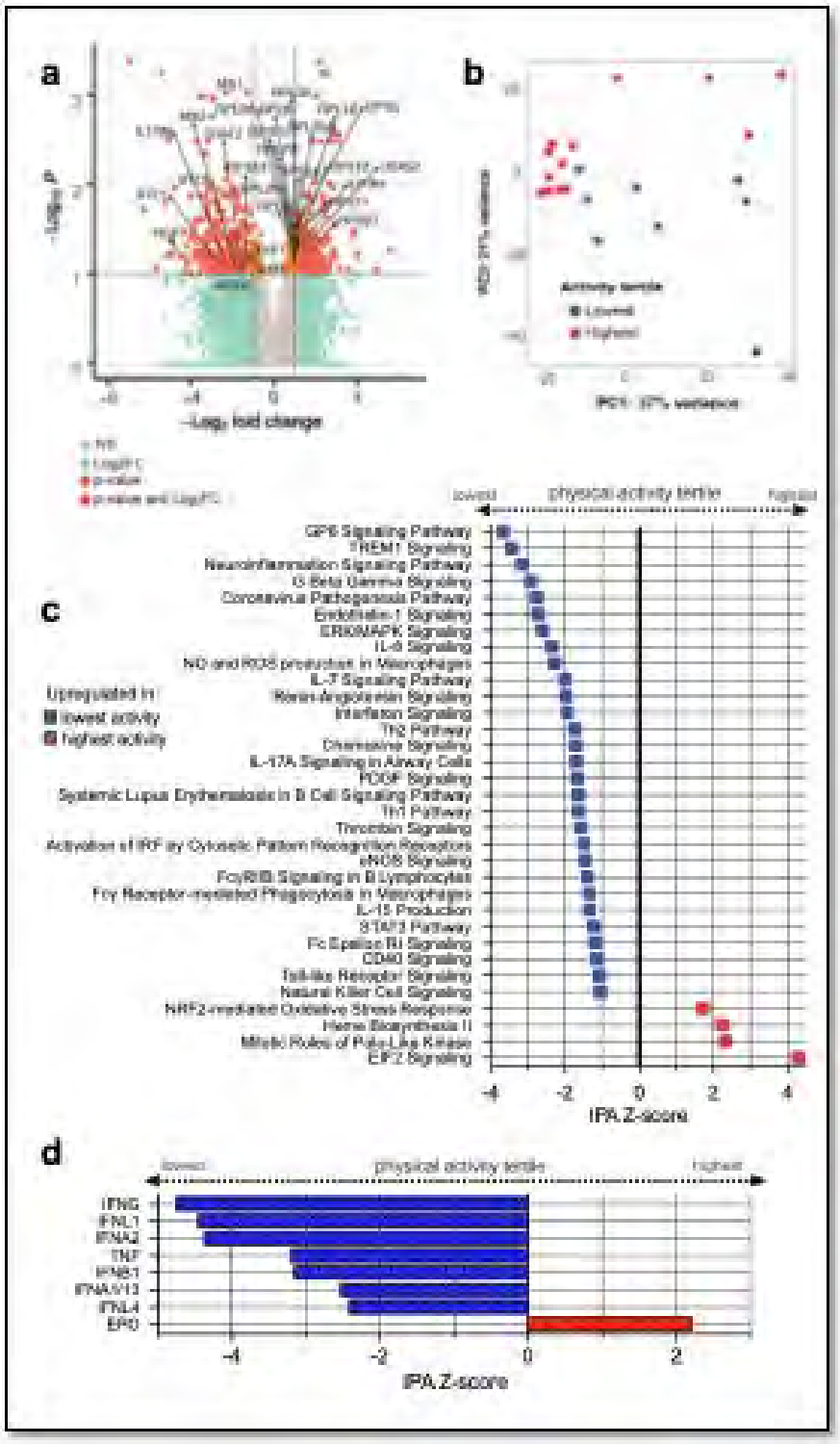

Figure 1. Differentially expressed (DE) genes and related signaling pathways identified from peripheral blood transcriptional profiling of RA patients with the highest versus lowest tertiles of physical activity. a) Volcano plot of DE genes depicting 365 genes up-regulated in the highest activity tertile and 402 down-regulated genes at an adjusted P-value < 0.1 with respect to the highest physical activity tertile. Genes related to immune signaling and translation are highlighted. b) Principal Component Analysis based on the DE genes demonstrates separation of patients based on tertile of physical activity. c) Ingenuity Pathway Analysis (IPA) based on differential gene expression analyses demonstrating expression of canonical signaling pathways. Significant IPA results were defined as those with a Z-score absolute value greater than 2 or an overlap P value < 0.05. Depicted are the top three up- and down-regulated canonical pathways based on Z-score, as well as all pathways related to immunity and inflammation with an |Z| > 1 and overlap P value < 0.05. d) Predicted activation state of upstream cytokines in the highest versus lowest physical activity tertiles. Cytokines with a |Z| > 2 and overlap P value < 0.05 plotted.

participants with actigraphs (GT9X ActiGraph Link device) to objectively measure physical activity for 7 consecutive 24-hour periods. Physical activity groups were defined by the highest and lowest tertiles for percentage of time spent in moderate/vigorous physical activity (metabolic equivalent level ≥2.00) across the sample. RNA extraction, library preparation, Illumina sequencing, and gene expression data processing were performed using established methods. Genes differentially expressed in the most versus least physically active groups were identified using DESeq2 with the Independent Hypothesis Weighting (IHW) multiple testing procedure. Sex, age, race and ethnicity were included as covariates in the linear model. Ingenuity Pathway Analysis (IPA) Canonical Pathway and Upstream Regulator Analyses were employed on differentially expressed genes with a $P < 0.1$ ranked by log2 fold change to identify biological pathways most affected by physical activity.

Results: 35 patients had complete clinical, actigraphy, and transcriptomic data available for analysis. Mean age was 56 years (SD 12.1), and 90% were female. Race/ethnicity was 32% white, 11% African American, 8% Asian, and 40% Hispanic (Table). Participants spent 48%, 41%, and 12% of time awake in sedentary, light, and moderate physical activity, respectively. None of the participants achieved vigorous activity. We identified 767 differentially expressed genes between the highest versus lowest physical activity tertiles at an adjusted P value < 0.1 (Figure 1a). IPA canonical pathway analysis revealed that the most physically active patients exhibited down regulation of diverse innate and adaptive immune signaling pathways (Figure 1c). Assessment of upstream cytokine activation states demonstrated inhibition of type I, II and III interferons and activation of EPO in the highest physical activity tertile patients (Figure 1d).

Conclusion: Among a racially and ethnically diverse RA cohort, participants who spent more time in moderately intense physical activity had down-regulation of genes involved in both innate and adaptive immune signaling compared to those who were more sedentary. These findings provide mechanistic evidence to support a disease-modifying effect of physical activity in RA.

Disclosure: S. Patterson, None; **S. Sun**, None; **D. Rychkov**, None; **A. Tsitsiklis**, None; **P. Hayakawa Serpa**, None; **P. Katz**, None; **C. Langelier**, None; **M. Sirota**, None.

Abstract Number: 1666

Association of Objectively Measured Sleep Characteristics with Rheumatoid Arthritis Disease Activity

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: A large proportion of individuals with rheumatoid arthritis (RA), between 45%-70%, report sleep problems. Despite frequent reports of sleep problems, however, studies using objective measures of sleep in RA are rare, but are needed to provide greater accuracy than classifications based on self-report. Sleep disturbances may have unique causes and consequences in RA related to disruptions in the circadian rhythms of inflammatory and neuroendocrine biomarkers. We report objectively measured sleep characteristics among a cohort of individuals with RA and the associations with self-reported and physician-assessed disease activity.

Methods: Data are from the baseline assessment of an ongoing longitudinal study of sleep disturbances in RA, in which 111 participants completed at least 4 nights of sleep monitoring using an Actigraph GT9X. The following sleep parameters were examined and compared to age and sex reference values from polysomnography: total sleep time, sleep efficiency (minutes sleeping/minutes in bed), number of awakenings/night (measure of fragmented sleep), and duration of awakenings/night (WASO [wake after sleep onset], also a measure of fragmented sleep). Total time in bed was also examined. The RA Disease Activity Index (RADAI) was used as a patient-reported measure of disease activity. RADAI includes self-reports of pain, painful joint counts, morning stiffness time, and patient global assessments. Physician-assessed disease activity using the Clinical Disease Activity Index (CDAI) and the Disease Activity Score-28 joints (DAS28-CRP) was available for a subset of participants who had in-person research visits prior to the

Table 1. Sample characteristics (n = 111)	
Age, years	57.8 ± 13.3
Female	89.2% (99)
Race	
White	54.1% (60)
Black	8.1% (9)
Asian	6.3% (7)
Other/mixed	31.5% (35)
Latinx	31.5% (35)
RA duration, years	16.6 ± 12.8
Using glucocorticoids	30.6% (34)
Mean dose (mg)	77.0 ± 32.4
Methotrexate use	42.3% (47)
Biologic	58.6% (65)
Patient-reported disease	
RADAI	3.4 ± 1.9
Pain	3.3 ± 2.5
Physician-assessed disease	
CDAI (n=42)	14.6 ± 11.6
DAS28-CRP (n = 38)	6.8 ± 3.7

RADAI = RA Disease Activity Index
CDAI = Clinical Disease Activity Index
DAS28-CRP = Disease Activity Score, 28 joints, with C-reactive protein.
Pain rated 0 – 10

Table 2. Sleep characteristics	
Sleep time (hours)	
Mean	6.8 ± 1.0
Short*	57.9% (77)
Sleep efficiency (% time sleeping while in bed)	
Mean	83.7 ± 5.8
Low*	74.4% (99)
Wake after sleep onset (WASO) (minutes)	
Mean	77.0 ± 32.4
High*	87.4% (97)
Number of awakenings	
Mean	21.4 ± 7.7
High*	19.8 (22)
Time in bed (hours)	
Mean	8.2 ± 1.1
High†	26.1% (29)

* Short sleep time, low sleep efficiency, high WASO, and high number of awakenings based on age and sex estimates from polysomnography (Herstenstein E et al. *J Clin Sleep Med* 2018;14:523).

Cutpoints for each:
Short sleep: ranged from <6.5 hrs (men, 51-60 y) to <7.2 hrs (women, 19-30 y)
Low sleep efficiency: ranged from <8.5% (men, 51-60 y) to <90.6% (women, 19-30 y)
High WASO: ranged from >22.5 (women, 19-30 y) to >60.4 (men, 51-60 y)
High number of awakenings: ranged from >17.1 (women, 19-30 y) to >30.9 (men,41-50 y)

† High time in bed based on upper quartile of study sample (≥ 9 hrs)

Table 3. Associations between sleep characteristics and RA disease activity

		Patient-reported	Physician-assessed	
		RADAI	CDAI	DAS28 CRP
Poor sleep efficiency	no	**2.7 ± 1.6**	(n=11) 11.8 ± 9.4	(n=10) 6.0 ± 3.3
	yes	**3.5 ± 2.1**	(n=37) 15.4 ± 11.8	(n=28) 7.1 ± 3.9
	p	**.02**	.36	.44
High WASO	no	2.5 ± 1.7	(n=4) 10.4 ± 8.1	(n=3) 6.4 ± 3.2
	yes	3.5 ± 1.9	(n=38) 15.1 ± 11.9	(n=35) 6.8 ± 3.8
	p	.08	.45	.83
Short sleep	no	3.3 ± 1.9	**(n=19) 20.0 ± 13.5**	**(n=17) 8.0 ± 4.3**
	yes	3.4 ± 2.1	**(n=29) 11.0 ± 7.9**	**(n=21) 5.8 ± 2.9**
	p	.79	**.01**	**.06**
High number of awakenings	no	3.4 ± 1.9	**(n=32) 12.3 ± 9.5**	**(n=31) 6.0 ± 3.2**
	yes	3.3 ± 2.0	**(n=10) 22.1 ± 14.8**	**(n=7) 10.3 ± 4.3**
	p	.88	**.02**	**.03**
High time in bed	no	3.3 ± 1.9	**(n=32) 10.9 ± 7.8**	**(n=29) 5.6 ± 2.9**
	yes	3.6 ± 2.0	**(n=10) 26.5 ± 13.9**	**(n=9) 10.5 ± 3.8**
	p	.48	**.006**	**.0002**

onset of the pandemic. Analyses tabulated the frequency of poor sleep based on reference values and used t-tests to examine differences in RADAI, CDAI, and DAS28-CRP between those with poor vs. normal sleep.

Results: Participant characteristics are shown in Table 1. Sleep characteristics are shown in Table 2. Compared to age and sex references, 57.9% had short sleep time, 74.4% had poor sleep efficiency, 87.4% had high WASO, and 19.8% had a high number of awakenings. Poor sleep efficiency was associated with significantly worse patient-reported disease activity (Table 3). There were no significant associations between other sleep parameters and patient-reported disease activity. Short sleep time, a high number of nighttime awakenings, and long time in bed were each associated with significantly worse physician-assessed disease activity (Table 3). There were no significant associations between sleep efficiency or WASO and physician-assess disease activity.

Conclusion: In this sample of individuals with RA, a high proportion exhibited sleep disturbances compared to age and sex reference groups, and sleep disturbances were associated with both patient-reported and physician-assessed disease activity. It will be important in future studies to examine the causal directions of the relationships between poor sleep and disease activity.

Disclosure: P. Katz, None; **S. Patterson**, None; **M. Nakamura**, None; **A. Prather**, None; **L. Trupin**, None; **S. Rush**, None; **K. Stone**, None.

Abstract Number: 1667

Efficacy of Plasma Phosphoethanolamine as a Biomarker for Rheumatoid Arthritis-associated Depression

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The odds of patients with rheumatoid arthritis (RA) experiencing depression is 1.42 (95% CI: 1.3–1.5; approximately 15% of patients) compared with healthy individuals. Diagnosis of depression is based on an interview, which is subjective to both psychiatrist and patient, and auxiliary diagnoses such as a self-rating scale for depression are uncertainty. Phosphoethanolamine (PEA), a plasma biomarker, has been reported to be a useful diagnostic biomarker for depression. We examined the efficacy of PEA as a biomarker for RA-associated depression.

Methods: This study included 52 registered RA patients who were recruited between 2019 and 2020. Patients provided written informed consent to participate and the study was approved by the Institutional Ethics Committee of the Showa University. The following background factors were investigated: age, sex, and disease duration. RA disease activity was evaluated using the Simplified Disease Activity Index. The depression status was evaluated using the Patient Health Questionnaire (PHQ)-9 as a standard scale. Questionnaires for depression, anxiety, and ego were also performed. Items of these questionnaire were converted into Scale A (depression/anxiety scale) and Scale B (adaptation scale). Plasma PEA was measured in Human Metabolome Technologies Inc. Statistical analysis was performed using the chi-square test and one-way analysis of variance.

Results: Forty-nine RA patients with no missing data were included in the analysis. The PHQ-9 score, the gold standard, was used to stratify patients by disease severity—normal, 33; mild depression, 12; moderate depression, 3; and severe depression, 1. Each group was compared between groups.

①The patient visual analog scale (VAS) score was significantly high among patients with depression ($p = 0.00157$). The difference in VAS scores of patients and doctors was significantly high considering patients with depression ($p = 0.00409$).

②The Scale A score was significantly high among patients with depression ($p = 1.19 \times 10^{-10}$), and the ratio of Scale A score to PEA was significantly high ($p = 1.64 \times 10^{-7}$) among patients.

③A significant difference was noted between the groups for the plasma PEA concentration ($p = 0.0272$). The plasma PEA concentration was low in patients with mild and moderate depression and high in a patient with severe depression.

④The Scale B score tended to be higher among patients with depression compared with others, without significant difference.

Conclusion: Plasma PEA alone presents a weak performance as a diagnostic biomarker for depression in patients with RA. However, a composite measure for diagnosing depression, including questionnaires for depression, anxiety, and ego may be used as an auxiliary diagnosis.

Disclosure: Y. Miwa, Pfizer Japan Inc., 5; **Y. Ohashi**, None; **H. Tomatsu**, None; **Y. Mitamura**, None.

Abstract Number: 1668

Unmet Need in Early Rheumatoid Arthritis - Why Do Some Patients Do Badly Despite Modern Treat-to-target Strategies of Care? Results from the Scottish Early RA (SERA) Inception Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: 'Treat to target' strategies of care have significantly improved outcomes in people with early rheumatoid arthritis; nonetheless, a significant proportion of patients have impaired health related quality of life (HR-QOL). Identifying baseline predictors of poor HR-QOL could enable us to direct appropriate resources towards people at high risk for adverse outcomes.

Methods: The Scottish Early Rheumatoid Arthritis study (Dale et al, PMID:27829394) is an inception cohort of patients with newly diagnosed RA and undifferentiated arthritis recruited in Scotland between 2011 and 2015 and followed up prospectively. Data were collected on demographics (age, gender, body mass index [BMI], employment

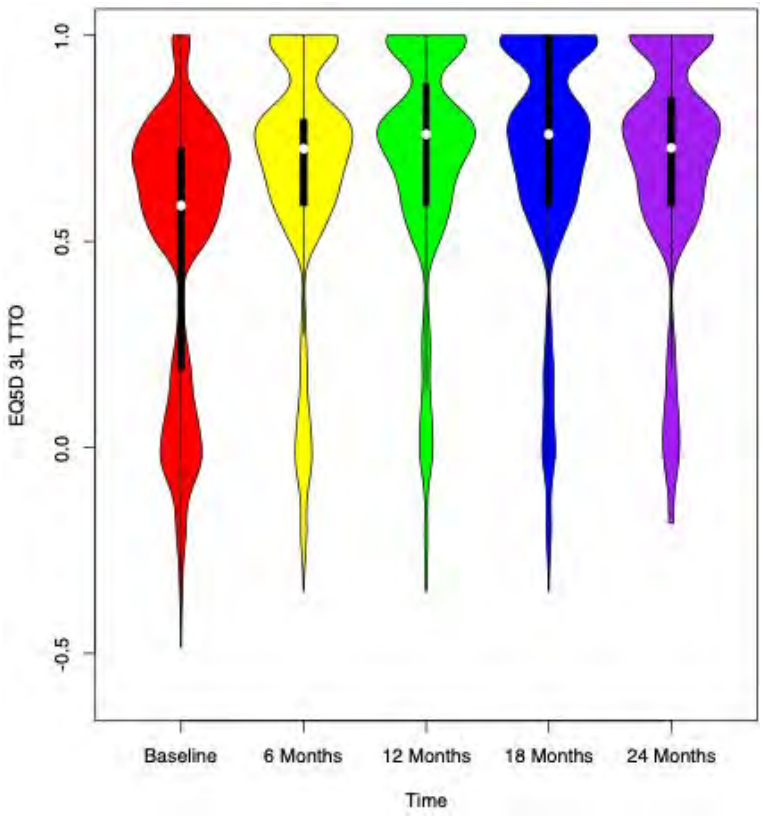

Figure 1. Violin Plot of EQ5D Time Trade Off (TTO) changes over 24 months.

status), serology, mood (Hospital Anxiety and Depression Score [HAD]), disease activity (SDAI), disability (Health Assessment Questionnaire [HAQ]) and socioeconomic status (Scottish Index of Multiple Deprivation [SIMD]). HR-QOL was measured using EQ5D; index scores calculated using the UK EQ5D-3L time trade off value set (Dolan et al, PMID:9366889). Univariate and multivariate models were developed to identify baseline predictors of HR-QOL at 12 months.

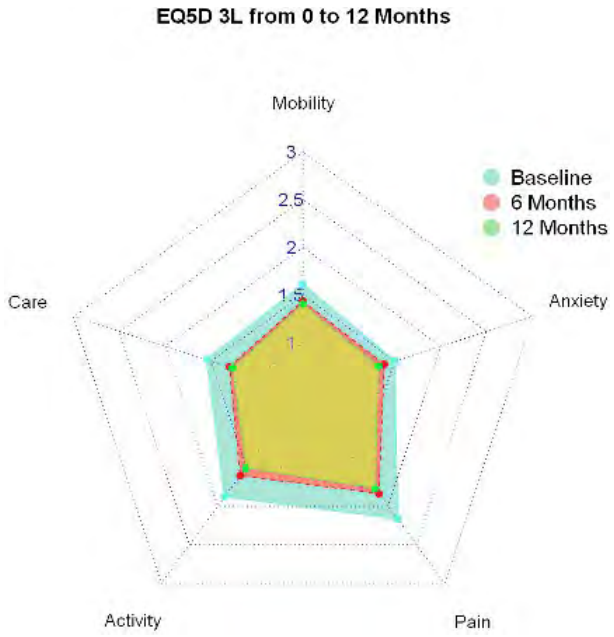

Figure 2. EQ5D 3L at baseline, 6 months, and 12 months.

Table 1. Model of EQ5D Time Trade Off (TTO) at 12 Months with Scottish Index of Multiple Deprivation

Variable	(95% CI)P-value
Model without interactions	
Intercept	56.818 (51.786 , 61.849) ; p<0.001
EQ5D at Baseline	0.204 (0.145 , 0.263) ; p<0.001
Gender Female (c.w. Male)	-0.804 (-3.981 , 2.373) ; p=0.620
Age (Decades)	0.405 (-0.746 , 1.556) ; p=0.491
SIMD 2nd quintile (c.w. most deprived)	3.711 (-1.058 , 8.479) ; p=0.128
SIMD 3rd quintile (c.w. most deprived)	5.511 (0.863 , 10.359) ; p=0.026
SIMD 4th quintile (c.w. most deprived)	6.565 (1.970 , 11.160) ; p=0.005
SIMD 5th quintile (c.w. most deprived)	8.708 (3.744 , 13.671) ; p<0.001
	AIC=4497.399 R^2=0.085

Results: HR-QOL over time shows a non-parametric distribution (fig 1). Improvement was seen in all EQ5D dimensions (Mobility, Self-Care, Usual Activities, Pain/Discomfort, Anxiety/Depression) at 6 and 12 months compared to baseline (fig 2), with most improvement within 6 months. Those in the lowest quartile of HR-QOL at 12 months (EQ5D TTO 0.32 v 0.82, p< 0.001) had substantial unmet need compared to those in the other quartiles: persistent disease activity (SDAI 20.1 v 7.6, p< 0.001), disability (HAQ 1.6 v 0.5, p< 0.001), anxiety (49% v 11%, p< 0.001) and depression (41% v 4%, p< 0.001). Univariate prediction models showed that baseline social deprivation, unemployment, disability (HAQ >1), and presence of anxiety or depression were significantly associated with lower HR-QOL at 12 months; age, gender, BMI and baseline disease activity were not predictive. Patients in the lowest quartile of HR-QOL at 12 months were more likely to live in the most socially deprived areas (SIMD lowest quintile: 36% v 14%, p< 0.001; see table 1), had higher baseline disability (HAQ 1.53 v 1.02, p< 0.001), were more likely to have anxiety (HAD-anxiety >8: 49% v 21%, p< 0.001) and depression (HAD-depression >8: 42% v 12%, p< 0.001) compared to those in other quartiles. Multivariate prediction models identified social deprivation, employment status, anxiety and depression as statistically significant independent predictors of HR-QOL at 12 months.

Conclusion: Social deprivation, employment status, depression, and anxiety are independent predictors of poor HR-QOL outcomes in patients with newly diagnosed RA/inflammatory arthritis. Psychological ill-health and the impact of social deprivation are potentially modifiable. Research is needed into the efficacy of strategies (such as psychological support) that aim to mitigate the negative impact of these factors on HR-QOL. "*Health inequalities and the social determinants of health are not a footnote to the determinants of health. They are the main issue.*" (Prof M Marmot) - our data support this assertion in patients with RA.

Disclosure: E. Clarke, None; **C. Wood**, None; **A. Tindell**, None; **K. Graham**, None; **A. McIntosh**, None; **F. Morton**, None; **D. Porter**, Galvani, 5, Abbvie, 12, Sponsorship to attend scientific meetings.

Abstract Number: 1669

Minimal Erosive Volume Needed for Radiographic Identification of Erosions in the Metacarpophalangeal Joints in Rheumatoid Arthritis. a Comparative Analysis of High Resolution Peripheral Quantitative Computed Tomography and Conventional Radiography

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The purpose of this study was to estimate the minimal erosive volume identified by High-Resolution peripheral Quantitative Computed Tomography (HR-pQCT) needed in order to identify erosive damage by conventional radiography (CR) assessed by the Sharp/van der Heijde method in patients with rheumatoid arthritis (RA).

Methods: In this single-centre cross-sectional study with paired measurements, 353 patients with established RA (disease duration ≥ five years) had their second and third MCP joints of the dominant hand investigated by HR-pQCT and CR. Empirical estimation was used to find the optimal cutoff value for the number, and the total volume of erosions needed to be identified by CR assessed according to the Sharp/van der Heijde method.

Results: The second and third MCP joints from 353 patients were investigated. Erosive damage was identified in 157 of the 706 MCP joints by CR, whereas 464 of the 706 MCP joints had erosive damage by HR-pQCT. Patients with a total erosive volume in the second and third MCP joints by HR-pQCT below 48.9 mm3 (Sensitivity 79%, Specificity 0.85, area under the receiver operating characteristic curve (AUC) 0.82) were not consistently identified by CR. The empirical estimation of the optimal cutoff value for the number of erosions in the second and third MCP joints by HR-pQCT was 8.5 erosions (Sensitivity 73%, Specificity 0.90, AUC 0.81).

Conclusion: Conventional radiography could not consistently identify erosive damage in the second and third MCP joints in patients with a total erosive volume below approximately 48.9 mm3 and missed two-thirds of erosions identified by HR-pQCT; this suggests that HR-pQCT may be a valuable tool for earlier detection of erosion progression in RA allowing for earlier intervention.

Disclosure: R. Klose-Jensen, Novo Nordic Foundation, 5, Aarhus University, 5, The Danish Rheumatism Association, 5, A.P. Møller Fonden, 5; **J. Therkildsen**, None; **A. Garm Blavnsfeldt**, None; **B. L. Langdahl**, Eli Lilly, 6, Amgen, 6, UCB, 6, Gilead, 6, Gideon-Richter, 6, Novo Nordisk, 5, Amgen, 5; **A. Zejden**, None; **J. Thygensen**, None; **K. Keller**, None; **E. Hauge**, AbbVie, 6, Sanofi, 6, Sobi, 6, SynACT Pharma, 6, Novo Nordic Foundation, 5, Roche, 5, Novartis, 5.

Abstract Number: 1670

Increased Prevalence of Gastroesophageal Disease Among Patients with Rheumatoid Arthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

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Background/Purpose: Recent experimental studies have suggested that systemic inflammatory response could lead to impairment of lower esophageal function, resulting in gastroesophageal reflux disease (GERD). Epidemiologic studies also support this association as increased prevalence of GERD has been observed in several systemic inflammatory disorders, including rheumatoid arthritis (RA), although the evidence is still quite limited. The current systematic review and meta-analysis is conducted with the aim to summarize data from all available studies.

Methods: Potentially eligible studies were identified from Medline and EMBASE databases from inception to April 2021 using search strategy that comprised terms for "gastroesophageal reflux disease " and " rheumatoid arthritis ". Eligible study must be cohort study that consists of one cohort of individuals with RA and another cohort of individuals without RA. Then, the study must report prevalence of GERD in each group or report odds ratio (OR) and 95% confidence interval (CI) comparing prevalence of GERD between the groups. OR of all included studies were combined together to calculate pooled OR using the generic inverse variance method of DerSimonian and Laird, which assigned weight of each study in reverse to its standard error. Funnel plot was used for assessment of publication bias.

Results: After two rounds of independent review by two investigators, a total of five eligible studies were identified. The meta-analysis found a significantly increased prevalence of GERD among patients with RA with the pooled OR

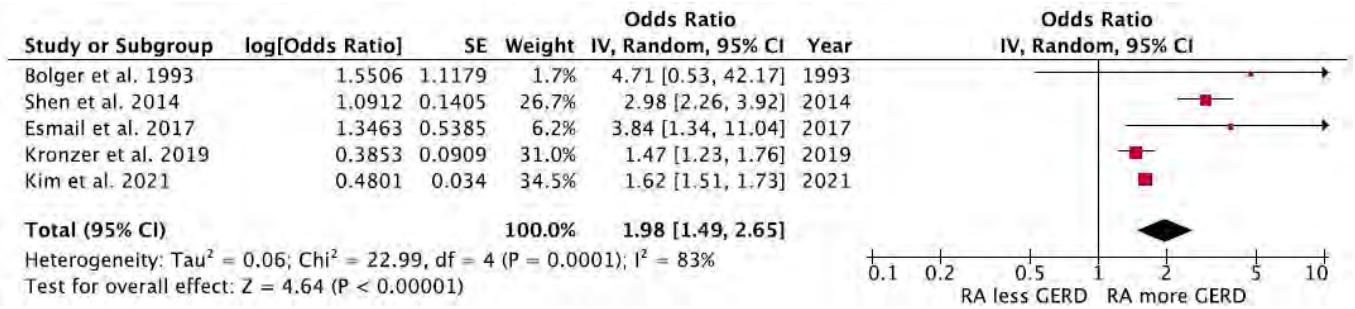

Figure 1. Forest plot of this meta-analysis.

of 1.98 (95% CI, 1.49 – 2.65; I^2 83%) compared with individual without RA (Figure 1). Funnel plot of this study was symmetric and was not suggestive of publication bias.

Conclusion: A significantly increased prevalence of GERD among patients with RA was observed in this study.

Disclosure: P. Ungprasert, None; **N. Charoenngam**, None; **B. Ponvilawan**, None; **P. Yingchoncharoen**, None; **J. Thongpiya**, None.

Abstract Number: 1671

COVID-19 in Patients with Rheumatoid Arthritis Compared to Patients with Osteoarthritis During the Pandemic in New York City

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SESSION INFORMATION

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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: COVID-19 in patients with rheumatoid arthritis (RA) is poorly understood. A recent study of mostly men with RA demonstrated increased COVID-19 risk in RA patients and more severe outcomes compared to matched non-RA patients; however, generalizability may be limited and findings need to be confirmed. We analyzed COVID-19 risk factors within RA patients overall and compared to those with osteoarthritis (OA) from our large musculoskeletal hospital during the initial wave of the pandemic in New York City.

Methods: We emailed a secure web-based survey to 26,045 patients ≥18 years old evaluated at least once by a rheumatologist between 2018-2020. Patients completed the survey between April 24, 2020-July 1, 2020. We collected data on demographics, COVID-19, medical history, and medication use. COVID-19 was suspected if the diagnosis was provided by a healthcare worker, and confirmed by a positive nasopharyngeal PCR antigen test. The former was included due to the lack of available testing early in the pandemic. ICD-10-CM algorithms were used to identify RA and OA. We used descriptive statistics as appropriate to compare patients with and without COVID-19 among RA and OA patients. We also compared RA versus OA subgroup of patients with COVID-19.

Results: Of the 6,583/26,045 (27.1%) patients who responded to our survey, 1,320 (20.1%) had RA and 675 (10.3%) had OA. Mean age of RA patients was 60.2 [14.4] years and 84.0% were female; mean age of OA patients was

69.7[12.1] years, and 75.2% were female. 5.7% of RA patients and 3.3% of OA patients self-reported COVID-19 (p=0.02). Compared to RA patients without COVID-19, RA patients with COVID-19 had higher BMI, were more likely to be Hispanic/Latinx and employed, and to have underlying asthma (Table 1). No difference in baseline steroid use or immunomodulatory medications were noted (Table 2). OA patients with COVID-19 were younger, more likely to

Table 1. Characteristics of Adult Patients Evaluated in the Division of Rheumatology from an Academic Hospital in New York City, Stratified by COVID-19 Status and Disease

	RA with COVID-19 N=75	RA without COVID-19 N=1245	p-value[1]	OA with COVID-19 N=22	OA without COVID-19 N=653	p-value[2]	(RA vs OA, COVID subgroup) p-value[3]
Mean Age, SD (years)	58.5 (11.1)	60.2 (14.5)	0.32	66.0 (11.2)	69.9 (12.1)	0.14	**<0.01**
Mean BMI kg/m2	28.7 (6.4)	26.6 (6.2)	**<0.01**	26.9 (5.1)	27.5 (6.1)	0.65	0.06
Female Sex* N (%)	61 (81.3)	996 (80)	0.50	14 (63.6)	450 (71.3)	0.02	**0.048**
Race N(%)			0.23			1.00	0.10
• White	52 (69.3)	988 (79.4)		21 (95.5)	535 (84.8)		
• Non-White	14 (18.7)	184 (14.8)		1 (4.5)	50 (7.9)		
• Missing	9 (12)	73 (5.9)		0 (0)	46 (7.3)		
Ethnicity N(%)			**0.01**			**0.03**	0.73
• Hispanic/Latinx	11 (14.7)	85 (6.8)		4 (18.2)	35 (5.5)		
• Not Hispanic/Latinx	56 (74.7)	1035 (83.1)		14 (63.6)	524 (83)		
• Missing	8 (10.7)	125 (10)		4 (18.2)	72 (11.4)		
Income N(%)			0.42			0.10	0.07
• <150,000	37 (49.3)	529 (42.5)		7 (31.8)	259 (41)		
• $150,000+	23 (30.7)	410 (32.9)		12 (54.5)	194 (30.7)		
• Missing	15 (20)	306 (24.6)		3 (13.6)	178 (28.2)		
Education N(%)			0.58			**0.047**	0.45
• Masters, Professional, or Doctorate Degree	27 (36)	498 (40)		6 (27.3)	305 (48.3)		
• College graduate or below	43 (57.3)	689 (55.3)		15 (68.2)	291 (46)		
• Missing	5 (6.7)	58 (4.7)		1 (4.5)	35 (5.5)		
Employment* N(%)			**0.04**			>0.99	**0.02**
• Employed	46 (61.3)	594 (47.7)		8 (36.4)	218 (34.5)		
• Unemployed/Retired, Disabled/ Student	29 (38.7)	615 (49.4)		16 (72.7)	392 (62.1)		
• Missing	0 (0)	36 (2.9)		0 (0)	21 (3.3)		
General Medical History N(%)							
• Asthma	22 (29.3)	177 (14.2)	**<0.01**	4 (18.2)	101 (16)	0.77	0.41
• Blood clotting problem	5 (6.7)	52 (4.2)	0.37	2 (9.1)	26 (4.1)	0.24	0.66
• Cancer	9 (12)	144 (11.6)	0.85	2 (9.1)	145 (23)	0.19	1.00
• Chronic Kidney Disease	1 (1.3)	17 (1.4)	1.00	0 (0)	13 (2.1)	1.00	1.00
• Diabetes	4 (5.3)	63 (5.1)	0.79	1 (4.5)	34 (5.4)	1.00	1.00
• Myocardial infarction	1 (1.3)	14 (1.1)	0.59	1 (4.5)	13 (2.1)	0.38	0.40
• Congestive heart failure	1 (1.3)	10 (0.8)	0.48	0 (0)	12 (1.9)	1.00	1.00
• Hypertension	14 (18.7)	349 (28)	0.08	7 (31.8)	248 (39.3)	0.52	0.24
• Lung disease	2 (2.7)	50 (4)	0.77	1 (4.5)	16 (2.5)	0.45	0.54
• Obesity	8 (10.7)	113 (9.1)	0.68	3 (13.6)	81 (12.8)	0.76	0.71
• Stroke or Transient Ischemic Attack (TIA)	2 (2.7)	32 (2.6)	1.00	1 (4.5)	21 (3.3)	0.54	0.54

[1]RA with COVID-19 versus RA without COVID-19; [2]OA with COVID-19 versus OA without COVID-19; [3]RA with COVID-19 versus OA with COVID-19
*66 missing sex from RA group, 37 from OA group
**Employment columns will not add up as patients were allowed to select multiple options

Table 2. Baseline Medication Use* by Patients with Rheumatoid Arthritis from a Division of Rheumatology in New York City, Stratified by COVID-19 Status

	RA with COVID-19 N=75	RA without COVID-19 N=1245	P-value
Medications N(%)			
Any Immunomodulatory Medications	60 (80)	1049 (84.3)	0.33
• Hydroxychloroquine	25 (33.3)	357 (28.7)	0.39
• JAK inhibitors (Tofacitinib, Baricitinib, Upadicitinib)	8 (10.7)	82 (6.6)	0.17
• Biologics**	24 (32)	479 (38.5)	0.26
• Conventional DMARDS***	30 (40)	588 (47.2)	0.22
• Other DMARDS	0 (0)	7 (0.6)	0.52
Any corticosteroid use N(%)	16 (21.3)	311 (25)	0.58

*Any medication use in the previous 6 months
**Abatacept, TNF-inhibitors (Infliximab, Etanercept, Adalimumab, Golimumab, Certolizumab, Tocilizumab, IL-12/23 inhibitors (Ustekinumab, Guselkumab), IL-17 inhibitors (Secukinumab, Ixekizumab), Rituximab
***Leflunomide, Methotrexate, Mycophenolate Mofetil, Azathioprine/6-MP, Sulfasalazine

Table 3. Baseline Characteristics and Presenting Symptoms of Patients with RA versus OA at Time of COVID-19 Diagnosis			
	RA with COVID-19 N=75	OA with COVID-19 N=22	p-value
COVID-19 Symptoms N (%)			
• Abdominal/Belly Pain	22 (29.3)	3 (13.6)	0.17
• Chest Pain	23 (30.7)	8 (36.4)	0.61
• Chills	43 (57.3)	12 (54.5)	0.81
• Confusion/Irritability	10 (13.3)	3 (13.6)	1.00
• Cough	52 (69.3)	19 (86.4)	0.17
• Diarrhea	30 (40)	10 (45.5)	0.81
• Dizziness/lightheadedness	37 (49.3)	10 (45.5)	0.81
• Fatigue or Malaise	54 (72)	14 (63.6)	0.44
• Fever	53 (70.7)	15 (68.2)	0.80
• Headache or migraine	48 (64)	10 (45.5)	0.14
• Joint Pain	42 (56)	10 (45.5)	0.47
• Loss of smell or taste	39 (52)	11 (50)	1.00
• Muscle Aches	40 (53.3)	10 (45.5)	0.63
• Runny nose	21 (28)	12 (54.5)	**0.04**
• Shortness of Breath	32 (42.7)	9 (40.9)	1.00
• Sore throat or scratchy throat	34 (45.3)	12 (54.5)	0.48
• Vomiting or Nausea	18 (24)	6 (27.3)	0.78
• Other	5 (6.7)	4 (18.2)	0.20
Disease Severity, N(%)			
• ER	15 (20.6)	3 (13.6)	0.55
• Hospitalized	6 (8.2)	1 (4.6)	>0.99

be male and Hispanic/Latinx, and had higher education compared to OA without COVID-19; no differences in race, income, employment or general medical history were noted (Table 1). RA patients with COVID-19 were younger (58.5[11.1] vs. 66.0[11.2] years), more likely to be female (81.3% vs. 63.6%) and employed (61.3% vs. 36.4%) than OA with COVID-19; no differences in general medical problems were noted. Although RA patients with COVID-19 had a non-significantly higher prevalence of abdominal pain, headaches, joint pain, vomiting, and fatigue, OA patients had significantly higher rhinorrhea (Table 3). ER visits and hospitalization were similar in RA versus OA patients with COVID-19 (Table 3).

Conclusion: In a cohort of rheumatology outpatients in New York City during the early pandemic surge, COVID-19 incidence was higher in RA versus OA patients, but there was no difference in ER or hospitalization. In RA patients COVID-19 was associated with higher BMI, Hispanic/Latinx ethnicity, being employed, and a history of asthma. In OA patients, COVID-19 was associated with younger age, Hispanic race/ethnicity, and lower education. These findings are hypothesis generating and will be evaluated prospectively using multivariable analyses to help identify predictors of COVID-19 in potentially high risk patients.

Disclosure: J. Levine, None; **V. Bykerk**, National Institutes of Health, 1, 5, Canadian Institutes of Health Research, 5, Amgen, 2, 5, BMS, Celgene, 2, 6, Gilead, 2, Sanofi, 2, 6, Regeneron, 2, Eli Lilly and Company, 6, Pfizer, 6, UCB, 6; **L. Lally**, None; **L. Mandl**, Regeneron Pharmaceuticals, 5; **M. Barbhaiya**, None.

Abstract Number: 1672

Many Better, Many Worse: Mean PROMIS-29 Scores Mask Significant Shifts During COVID-19 in RA

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatic diseases (RD) are chronic conditions that require potent immunosuppressants to control systemic inflammation. Fears associated with increased vulnerability from being on immunosuppressants plus medications shortages (e.g., hydroxychloroquine) resulted in considerable stress for patients in the early months of the COVID-19 pandemic. We evaluated changes in HRQL in the initial months of the COVID-19 in adults with RD and hypothesized that multiple PROMIS-29 domains scores would be negatively impacted.

Methods: The sample included patients followed (virtually or in-person) in Rheumatic Disease clinics at Johns Hopkins 3/15/2020 to 6/30/2020. Patients complete the PROMIS-29 as part of routine care, and scores were compared with the most recent visit prior to 3/15. Anxiety was classified as worse (≥ 4.0 points), same (-3.9 to 3.9) or better (≤-4.0) at the second visit.

Results: Data were available for 151 patients with a mean (SD) age of 55 who were mostly white (81%) women (73%) with RA (50%), PSA (27%), AS/SPA (15%) or other RD (9%). Mean (SD) changes in PROMIS-29 scores ranged from -0.9 for Fatigue [7.6] and Depression [7.9] to 1.4 (9.7) for Anxiety. 45 (30%) patients were classified with worse anxiety, 40 (27%) with improved anxiety, and 66 (44%) the same. Change in anxiety was not associated with age, sex, race, or disease.

Table 1. PROMIS-29 scores in patients with rheumatic diseases before and during initial months of COVID-19 pandemic

PROMIS-29 Domain	Pre Pandemic	Pandemic	Mean Change	95% Lower CI	95% Upper CI	Sig
Anxiety	53.3 (10.7)	54.7 (9.4)	1.4	-0.1	3.0	0.072
Depression	50.9 (10.2)	49.9 (9.3)	-0.9	-2.2	0.4	0.156
Pain Interference	57.1 (9.6)	57.4 (8.4)	0.3	-0.8	1.4	0.59
Physical Function	42.2 (9.5)	42.8 (9.6)	0.6	-0.4	1.6	0.254
Fatigue	56.6 (11.2)	55.7 (10.5)	-0.9	-2.1	0.4	0.169
Sleep Disturbance	52.7 (8.6)	52.8 (9.5)	0.2	-1.2	1.6	0.807
Participation	47.9 (10.5)	48.2 (9.5)	0.3	-0.8	1.5	0.548

Table 2. Change in PROMIS in patients with improved, same or worsening anxiety during the initial months of COVID-19 pandemic

PROMIS Domain	Change in Anxiety During Pandemic					
	Improved (≤-4.0)		Same		Worse (≥4.0)	
	Mean	SD	Mean	SD	Mean	SD
Anxiety	-8.9_a	5.8	$.3_b$	2.3	12.3_c	8.0
Depression	-5.0_a	7.0	-1.2_b	6.9	3.2_c	8.0
Pain Interference	-2.5_a	7.9	$.4_b$	6.0	2.7_b	6.5
Physical Function	2.1_a	8.4	$.1_a$	4.7	$-.1_a$	5.4
Fatigue	-4.4_a	7.9	$-.3_b$	5.8	1.5_b	8.7
Sleep Disturvance	-3.4_a	8.5	$.1_b$	8.8	3.5_c	7.9
Participation	3.1_a	7.8	$.0_b$	6.6	-1.6_b	6.0

Note: Values in the same row not sharing the same subscript are significantly different at p< .05.

Table 3. Change in perceived rheumatic disease activity in patients with improved, same or worsening anxiety during the initial months of COVID-19 pandemic

Change in RD	Change in Anxiety During Pandemic					
	Improved (≤-4.0)		Same		Worse (≥4.0)	
	N	%	N	%	N	%
Lot worse	0	0%	6_a	50%	6_a	50%
Little worse	8_a	25%	12_a	38%	12_a	38%
Same	9_a	20%	20_a	43%	17_a	37%
Little Better	$7_{a,b}$	29%	14_a	58%	3_b	13%
Lot Better	6_a	43%	6_a	43%	2_a	14%

Note: Values in the same row not sharing the same subscript are significantly different at p< .05.

Among patients reporting worse anxiety (mean [SD] change +12.3 [9.0]), Depression was significantly worse (3.2 [8.0]) compared to patients with same (-1.2 [6.9] or improved anxiety (-5.0 [7.0]) (p's< .05). Among patients whose anxiety improved, Fatigue (-4.4 [7.9]) and Participation (3.1 [7.8] improved. Changes in anxiety were not associated with changes in physical function.

Patient Global Impression of Disease Change scores (N=128) indicated 34% of patient reported their disease was worse, 30% had improved, and 36% were the same. Most (88%) patients with worse anxiety reported worse (45%) or the same (43%) disease activity; 43% with improved anxiety had improved disease, 30% the same, and 27% were worse.

Conclusion: While the average within-person change in PROMIS-29 scores were trivial, a substantial proportion of patients experienced worsening or improved anxiety which also tracked with meaningful changes in several other PROMIS-29 domains.

Disclosure: S. Bartlett, Merck Canada, 2, 6, Pfizer Canada, 2, 6, Janssen Canada, 2, 6, PROMIS Health Organization, 4, American Thoracic Society, 4, Arthritis Health Professionals Association, 4, UCB, 1, RAND Corporation, 1; **D. DiRenzo**, None; **M. Jones**, None; **C. Bingham**, Bristol Myers Squibb, 5, Abbvie, 2, Gilead, 2, Eli Lilly, 2, Janssen, 2, Regeneron, 2, Pfizer, 2, Sanofi, 2.

Abstract Number: 1673

Riding Multiple Waves of Uncertainty: Real World Canadian RA Patient Outcomes over 1 Year of COVID-19 Restrictions

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Outcomes, Trajectory of Disease, & Epidemiology (1645–1673)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: During the COVID-19 pandemic, Canadians adults with RA faced considerable uncertainty due to greater risk of infection, hospitalization, changing access to RA medications, and very limited access to in-person RA care due to stringent pandemic-related restrictions. We examined trends in perceived stress, physical, emotional, and social health, perceived disease activity and flares prior to and during the first two waves of COVID-19 in adults with RA.

Methods: Participants were enrolled in the Canadian Early Arthritis Cohort with available data. Descriptive statistics examined trends in Perceived Stress and PROMIS-29 from 6 months pre-pandemic (9/19-2/20) through Waves 1 (3/20-6/20) and Wave 2 (10/20-1/21). Disease activity was assessed using the RA-FQ, a validated PRO; scores ≥20 are consistent with inflammatory flares.

Results: A total of 858 visits were collected from 3/16/20 through 1/31/21 and compared with 956 pre-pandemic visits. Participants were mostly white (86%) women (72%) with a mean age of 55 years. Pre-pandemic mean PROMIS-29 scores were in the normal range. Monthly trends showed that pandemic impacts were greatest in April 2020 (Fig 1) where mean PROMIS-29 scores worsened for all domains except Participation (mean Δ -0.4); the largest changes were in Depression (Δ+4.8) and Anxiety (Δ+4.2)(p's< .01). Compared with pre-pandemic visits, by April higher proportions had moderate-severe Anxiety (12% vs 23%), Depression (11% vs 23%), Fatigue (18% vs 25%), Sleep Disturbance (10% vs 19%), Pain (23% vs 40%), Participation (15% vs 21%) and Disability (25% vs 34%) (all p's< 0.05). By July 2020, mean PROMIS-29 scores had improved for Depression (Δ -4.5), Anxiety (Δ -3.2), Fatigue (Δ -2.0) and Perceived Stress (Δ -0.7). The proportions of patients with moderate-severe symptoms (≥60) were similar to pre-pandemic for all domains except Pain, Function, Participation, and Sleep where 29%, 34%, 21% and 17%, respectively, continued to have moderate-severe impairments. Wave 2 scores were higher than pre-pandemic, but lower than Wave 1, with the largest changes in depression (p=.02) and anxiety (p=.06).

Mean RA-FQ increased from the pre-pandemic period, peaking in April 2020 and Dec 2020-Jan 2021 (Fig 2). More patients had RA-FQ scores consistent with disease flares in April (45%) and December (35%) than in the pre-pandemic period.

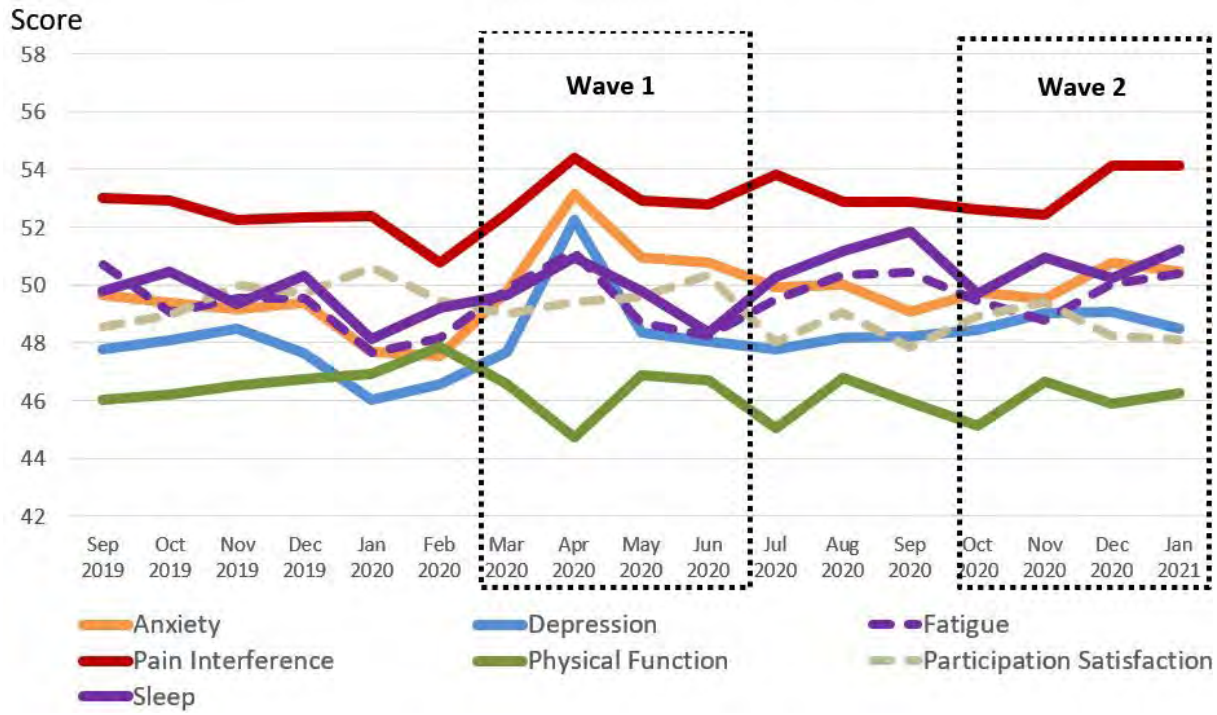
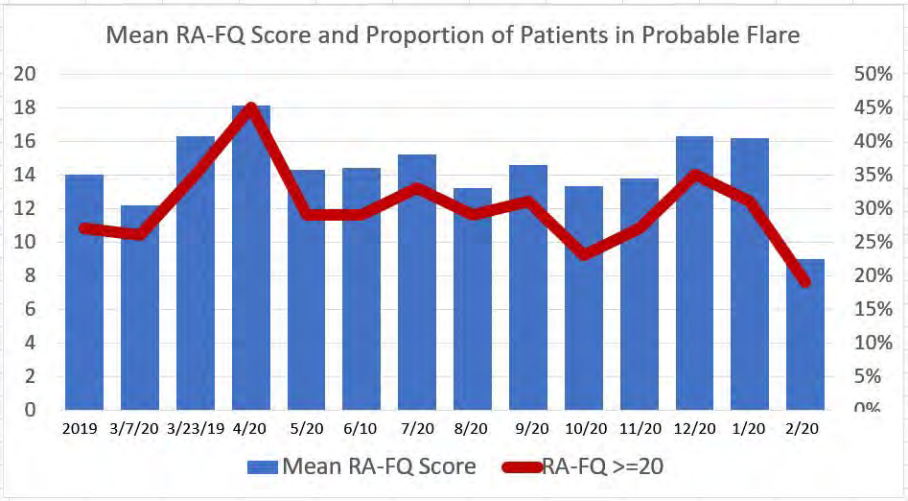


Figure 1. PROMIS-29 scores prior to and during the COVID-19 pandemic in Canadian RA patients.



Conclusion: Stringent COVID-19 pandemic restrictions impacted care across Canada in Waves 1 and 2 resulting in considerable stress, higher perceived disease activity and flares, and meaningfully worse physical and emotional health. More than 1/3 experienced moderate-severe anxiety, depression, fatigue, sleep disturbance, pain, and disability.

Disclosure: O. Schieir, None; **S. Bartlett**, Merck Canada, 2, 6, Pfizer Canada, 2, 6, Janssen Canada, 2, 6, PROMIS Health Organization, 4, American Thoracic Society, 4, Arthritis Health Professionals Association, 4, UCB, 1, RAND Corporation, 1; **M. Valois**, None; **L. Bessette**, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Janssen, 2, 5, 6, Roche, 2, 5, 6, UCB, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Merck & Co, 2, 5, Celgene, 2, 5, 6, Sanofi, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Gilead, 2, 5, 6, Sandoz, 2, 5, 6, Teva, 2, 6; **G. Boire**, Abbvie, 1, 6, 7, BMS, 6, 7, Janssen, 1, 5, 6, Eli Lilly, 1, 7, Amgen, 7, Novartis, 6, 7, Pfizer, 7, Sandoz, 6, 7, Viatris, 1, 6, Samsung Bioepis, 1; **G. Hazlewood**, None; **C. Hitchon**, Pfizer, 5, UCB Canada, 5; **E. Keystone**, AbbVie, 2, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb Company, 2, Celltrion, 2, Gilead Sciences, 2, F. Hoffmann-La Roche, 2, 6, Janssen, 2, 6, Eli Lilly, 2, Merck, 2, 5, 6, Myriad Autoimmune, 2, Novartis, 6, Pfizer Inc, 2, 5, 6, PuraPharm, 5, Sandoz, 2, Sanofi-Genzyme, 2, 6, Samsung Bioepis, 2; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **D. Tin**, None; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **V. Bykerk**, Amgen Inc., 2, 6, Bristol Myers Squibb, 2, 6, Gilead, 2, 6, Pfizer, 2, 6, Regeneron, 2, 6, Sanofi-Genzyme, 2, 6, UCB, 2, 6; **C. Investigators**, None.

Abstract Number: 1674

Effectiveness and Safety of Tofacitinib in Canadian Patients with RA: Primary Results from a Multicenter, Observational Study

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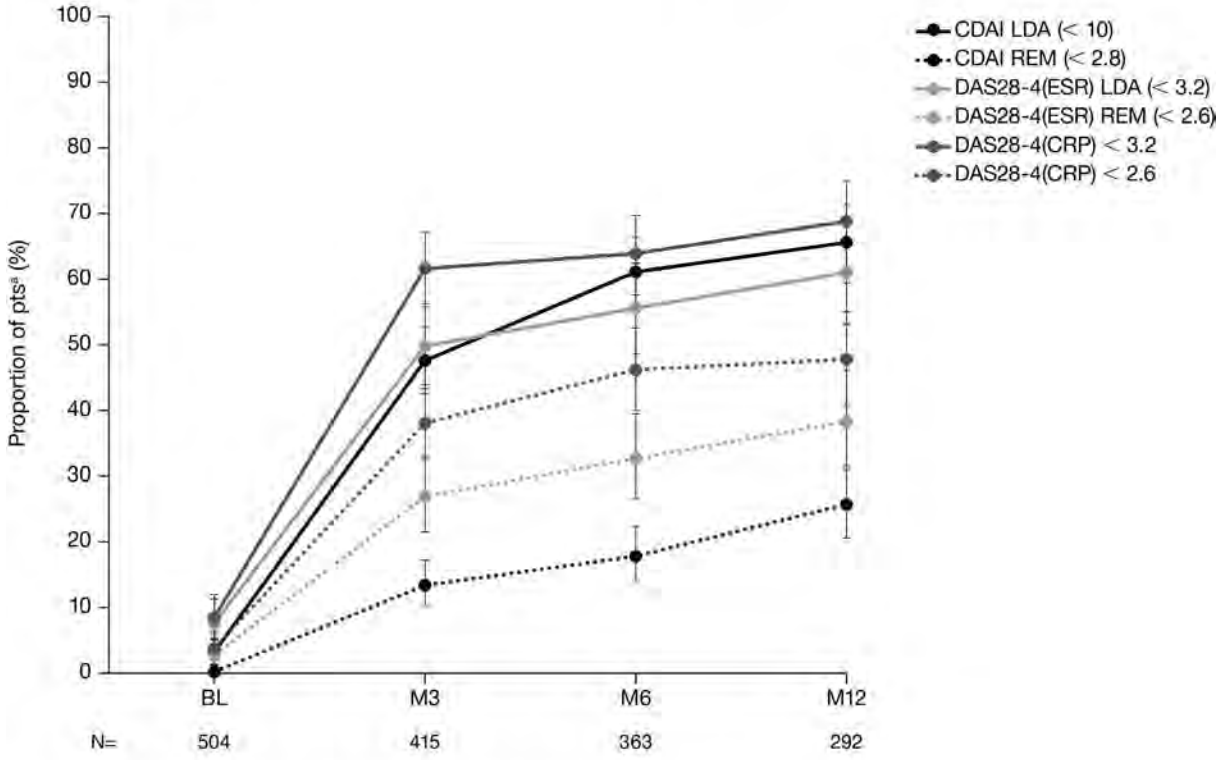
SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor (JAKi) for the treatment of RA. CANTORAL is the first large-scale, national, observational study assessing effectiveness and safety of a JAKi (tofacitinib) in Canadian patients (pts) with RA. Here we describe primary and key secondary effectiveness and safety endpoints from the CANTORAL study. Exploratory safety analyses were also conducted in pts with baseline (BL) cardiovascular (CV) risk factors.

Methods: Pts with moderate to severe active RA who initiated tofacitinib between Nov 2017–Jul 2020 were enrolled across 45 Canadian sites and managed per clinical standard of care. Effectiveness (up to Month [M]12) was assessed in enrolled pts (full analysis set), and safety (up to M36) was evaluated in pts with ≥ 1 post-BL visit (safety analysis set) as of Feb 26, 2021. An exploratory safety analysis was also conducted in pts aged ≥ 50 yrs with ≥ 1 CV risk factor (CV+ cohort), similar to ORAL Surveillance (NCT02092467) entry criteria. Co-primary endpoints included proportions of pts achieving CDAI low disease activity (LDA; < 10) and remission (REM; < 2.8) at M6. Secondary endpoints included proportions of pts achieving CDAI LDA and REM, DAS28-4(ESR) LDA (< 3.2) and REM (< 2.6), and DAS28-4(CRP) < 3.2 and < 2.6, over time; proportions of pts achieving improvements in HAQ-Disability Index (HAQ-DI) ≥ minimum

Figure. Proportions of pts who achieved CDAI and DAS28-4(ESR) LDA or REM, or DAS28-4(CRP) < 3.2 or < 2.6, over time (full analysis set)



[a]Proportions of pts were based on the total number of pts at each visit

BL, baseline; CDAI, Clinical Disease Activity Index; DAS28-4(CRP), Disease Activity Score in 28 joints, CRP; DAS28-4(ESR), Disease Activity Score in 28 joints, ESR; LDA, low disease activity; M, Month; N, number of pts in each group; pts, patients; REM, remission

Table. Safety analysis in all enrolled pts and CV+ cohort over 36 months

n (%) [IR; number of events per 100 PY]	SAS (N=495; PY=710.64)[a,b]	CV+ (N=272; PY=392.94)[a,b]
TEAEs	321 (64.8) [126.6]	187 (68.8) [136.9]
SAEs	52 (10.5) [11.1]	38 (14.0) [16.0]
Deaths[c]	3 (0.6) [0.7]	3 (1.1) [1.3]
Most frequent TEAEs (≥ 3% in any group)		
Upper respiratory tract infection	27 (5.5) [5.1]	17 (6.3) [5.8]
Urinary tract infection	20 (4.0) [4.4]	13 (4.8) [5.8]
Headache	20 (4.0) [3.7]	12 (4.4) [3.8]
Hypertension	16 (3.2) [2.8]	11 (4.0) [3.5]
Pneumonia	13 (2.6) [2.8]	10 (3.7) [4.2]
Diarrhea	17 (3.4) [3.0]	9 (3.3) [2.9]
Nausea	15 (3.0) [2.8]	6 (2.2) [1.9]
AEs of special interest		
Serious infection	19 (3.8) [4.6]	15 (5.5) [6.7]
MACE	3 (0.6) [0.4]	3 (1.1) [0.8]
Gastrointestinal perforation	0 (0.0) [0]	0 (0.0) [0]
HZ (non-serious/serious)[d]	8 (1.6) [1.4]	6 (2.2) [1.9]
Malignancies (excluding NMSC)	8 (1.6) [1.4]	7 (2.6) [2.3]
NMSC	4 (0.8) [0.8]	2 (0.7) [0.8]
Thrombosis[e]	1 (0.2)[f] [0.2]	1 (0.4)[f] [0.32]

[a]Pts with ≥ 1 post-BL visit

[b]Mean (SD) duration of follow-up: 14.3 (9.2) months (SAS); 14.8 (9.4) months (CV+)

[c]Renal failure and sepsis, n=1; salmonella bacteremia and sepsis, n=1; myocardial infarction, n=1

[d]One case of serious HZ

[e]Venous and arterial thrombotic events

[f]Non-occlusive thrombus in right posterior tibial vein

AE, adverse event; BL, baseline; CV+, cohort of pts aged ≥ 50 yrs with ≥ 1 cardiovascular risk factor; HZ, herpes zoster; IR, incidence rate; MACE, major adverse cardiovascular events; n, number of unique pts with an event; N, number of pts in each group; NMSC, non-melanoma skin cancer; pt, patient; PY, pt-yrs; SAE, serious adverse event; SAS, safety analysis set; SD, standard deviation; TEAE, treatment-emergent adverse event

clinically important difference (MCID; ≥ 0.22), HAQ-DI normative values (≤ 0.25), and ≥ 50% improvement in Pain (VAS) at M3; and least squares (LS) mean change from BL (ΔBL) in tender joint count (TJC), swollen joint count (SJC), HAQ-DI, and Pain, over time. Safety outcomes included treatment-emergent adverse events (TEAEs), serious AEs (SAEs), deaths, and AEs of special interest.

Results: 504 pts were eligible for analysis; most were female (77.8%), white (82.9%), with a mean age of 59.3 yrs and disease duration of 10.2 yrs. Most pts were biologic DMARD-naïve (66.5%), taking BL background conventional synthetic DMARDs (62.5%). At M6, 61.1% and 17.8% of pts achieved CDAI LDA and REM, respectively, with most also achieving outcomes at M3 (Figure); similar findings were seen for DAS28-4(ESR) and DAS28-4(CRP) (Figure). LS mean ΔBL at M3 ($p < 0.001$) in TJC, SJC, HAQ-DI, and Pain were -5.7, -5.1, -0.3, and -20.5, respectively, wherein improvements were continued/maintained to M12. At M3, HAQ-DI MCID and normative values were achieved by 53.7% and 19.9% of pts, respectively; ≥ 50% Pain improvement was achieved by 42.9% of pts. 54.0% (n=272) of pts met inclusion criteria for the CV+ cohort, of whom 25.4% were smokers and 8.1% had a history of coronary artery disease; hypertension, diabetes mellitus, and RA-associated extra-articular features were reported in 58.8%, 17.6%, and 26.8% of CV+ pts, respectively. Most TEAEs, SAEs, deaths, and AEs of special interest were reported in CV+ pts (Table).

Conclusion: Results of CANTORAL are consistent with tofacitinib efficacy and safety in the RA clinical program, including ORAL Surveillance, and Canadian observational studies of advanced therapies. AEs were more likely to occur in pts aged ≥ 50 yrs with CV risk factors.

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Abstract Number: 1675

Risk of Malignancy in Patients Treated with Tofacitinib: Results from the Safety of TofAcitinib in Routine Care Patients with Rheumatoid Arthritis (STAR-RA) Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Initial reports from "ORAL Surveillance" post-marketing safety trial have suggested that tofacitinib, in comparison with tumor necrosis factor inhibitors (TNFI), may be associated with increased risk of malignancies in RA patients. We conducted a multi-database population-based study to further examine this safety concern in real-world settings.

Methods: The 'Optum' Clinformatics (2012-2020), IBM 'MarketScan' (2012-2018), and Medicare (parts A, B, and D, 2012-2017) claims databases were used to construct two cohorts of RA patients initiating treatment with tofacitinib and TNFI. The first cohort, "real-world evidence" (RWE), included a representative cohort of RA patients treated in routine practice. As a calibration exercise, we mimicked the inclusion and exclusion criteria of the ORAL Surveillance trial which consisted of patients minimum 50 years of age and with at least one cardiovascular risk factor, in the second cohort ("RCT-duplicate"). The primary endpoint, a composite cancer outcome, was defined using previously validated claims-based algorithms for any malignancy excluding non-melanoma skin cancer. In the primary as-treated analysis, patients were followed from treatment initiation until study outcomes, treatment discontinuation or switch, insurance disenrollment, death, or end of the study period, whichever occurred first. Cox proportional hazards models were used to generate hazard ratios (HR) and 95% confidence intervals (CI). Propensity score (PS)

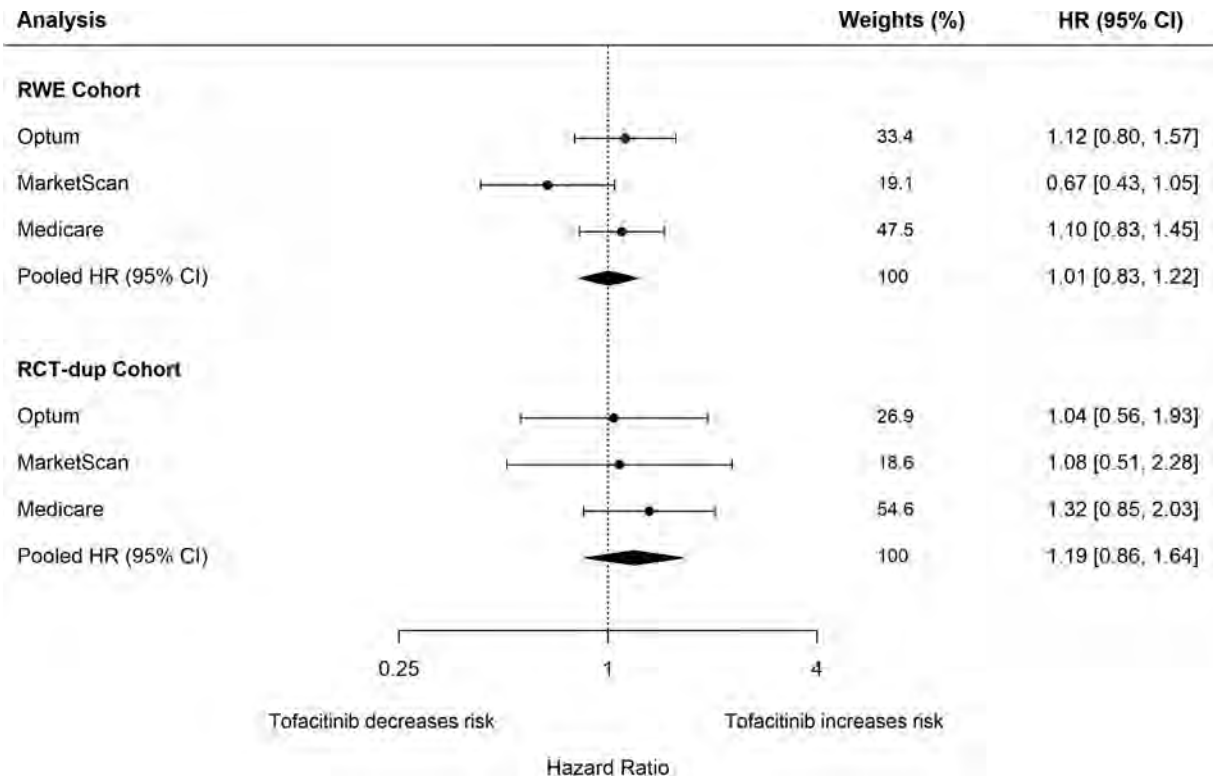

Figure. Risk of composite cancer outcomes when comparing tofacitinib with TNF inhibitors (reference) in patients with RA.

fine-stratification weighting accounted for over 60 potential confounders. Database-specific estimates were pooled using fixed effects models with inverse variance.

Results: The RWE cohort included 25,389 patients in Optum, 29,511 in MarketScan, and 28,374 in Medicare of whom 13.0%, 15.3%, and 9.5% initiated treatment on tofacitinib, respectively. The majority of RA patients were female across the three databases (77%-80%). The mean age was 54 and 52 in Optum and MarketScan and 71 in Medicare. The median follow-up time on treatment was 199-218 days. The crude incidence rates (95%CI) per 100 person-years of composite cancer endpoint comparing tofacitinib and TNFI users were 1.65 (1.21-2.19) and 1.36 (1.20-1.52) in Optum, 0.60 (0.39-0.90) and 0.84 (0.73-0.96) in MarketScan, and 2.70 (2.07-3.46) and 2.48 (2.28-2.70) in Medicare. The pooled PS-weighted HR (95%CI) for composite cancer outcome comparing tofacitinib with TNFI was 1.01 (0.83-1.22). The pooled PS-weighted HR (95%CI) was 1.19 (0.86-1.64) in RCT-duplicate cohort (versus Oral Surveillance trial, HR: 1.48, 95%CI: 1.04-2.09). Consistent results were observed in sensitivity analyses implementing a 90- day exposure lag for latency of treatment effect and a180-day grace period for persistence of effect after treatment cessation.

Conclusion: In this large population-based study, tofacitinib, in comparison with TNFI, was not associated with risk of malignancies in RA patients in the real-world setting. However, our results cannot rule out an elevated risk of cancer associated with tofacitinib among patients who were at least 50 years of age with one cardiovascular risk factor. Additional studies with long-term follow-up are required to corroborate these findings.

Disclosure: F. Khosrow-Khavar, None; **R. Desai**, Bayer, 5, Vertex Pharmaceuticals, 5, Novartis, 5; **H. Lee**, None; **S. Lee**, None; **S. Kim**, AbbVie, 5, Roche, 5, Pfizer, 5, Bristol-Myers Squibb, 5.

Abstract Number: 1676

Safety of Baricitinib in Japanese Patients with Rheumatoid Arthritis (RA): The 2020 Interim Report from All-case Post Marketing Surveillance in Clinical Practice

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: An all-case post marketing surveillance (PMS) of baricitinib, that started in Sep 2017, collects safety and effectiveness for the first 24 weeks of treatment and continues to collect serious adverse events (SAEs) for 3 years. The objective of this analysis was to evaluate safety of baricitinib in RA patients in clinical practice.

Methods: We report patient baseline demographics and adverse events (AEs) up to 24 weeks for patients whose case report files for 24-week data were completed as of Jun 2020.

Results: Data from 3445 patients were analyzed (females=80%, mean age=64 years, mean RA duration=12 years). Baricitinib dose regimen was as follows: 4mg, 60%, 2mg, 27%, 4mgà2mg, 5%, 2mgà4mg, 5%, and others, 2%. Concomitant use of MTX and glucocorticoid was 65% and 48%, respectively. Overall, 74% continued treatment for 24 weeks. AE and SAE were recognized in 887 (26%) and 122 patients (4%), respectively. Six patients died of pneumonia, aspiration pneumonia, bacterial pneumonia, cerebral infarction/interstitial lung disease (ILD)/aspiration pneumonia, adenocarcinoma, and colorectal cancer. Major AEs were as follows: herpes zoster=3%, liver dysfunction=3%, serious infection=1%, anemia=1%, hyperlipidemia=1%, malignancy=0.3%, interstitial pneumonia=0.2%, major adverse cardiovascular event (MACE)=0.1%, and venous thromboembolism (VTE)=0.1%.

Conclusion: Data do not show new safety concerns and encourage guideline-compliant use of Baricitinib.

Disclosure: T. Fujii, Chugai Pharmaceutical Co. Ltd, 5, 6, Eisai Co. Ltd, 6, Eli Lilly Japan K.K., 5, 6, Janssen Pharmaceutical K.K., 6, Ono Pharmaceutical Co. Ltd., 5, 6, Asahikasei Pharma Corp, 2, 5, AbbVie Japan GK, 5, Mitsubishi-Tanabe Pharma Co., 5; **T. Atsumi**, AbbVie Japan GK, 2, 6, Astellas Pharma Inc., 5, 6, Bristol-Myers Squibb Co. Ltd, 6, Chugai Pharmaceutical Co. Ltd, 5, 6, Daiichi Sankyo Co. Ltd, 5, 6, Eisai Co. Ltd., 6, Eli Lilly Japan K.K, 6, Mitsubishi Tanabe Pharma Co.;, 5, 6, Pfizer Japan Inc, 2, 5, 6, Takeda Pharmaceutical Co. Ltd, 5, 6, UCB Japan Co. Ltd, 6, AstraZeneca plc, 2, Boehringer Ingelheim Co. Ltd, 2, Medical & Biological Laboratories Co. Ltd, 2, Novartis Pharma K.K, 2, Ono Pharmaceutical Co. Ltd, 2, Alexion Inc, 5, Otsuka Pharmaceutical Co., Ltd, 5, Gilead Sciences, Inc., 5, 6; **N. Okamoto**, AbbVie Japan GK, 6, Asahikasei Pharma Co., 6, AYUMI Pharmaceutical Co, 6, Eisai Co. Ltd, 6, Bristol-Myers Squibb Co. Ltd, 6, Eli Lilly Japan K.K, 6, Mitsubishi Tanabe Pharma Co.;, 6, Pfizer Japan Inc, 6, Chugai

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Abstract Number: 1677

Effects of Biological-DMARDs on the Serum Low-density Lipoprotein (LDL) / High-density Lipoprotein (HDL) - Cholesterol Ratio in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) and dyslipidemia are associated with inflammation. Although the low-density lipoprotein cholesterol (LDL-C) is normal range, the high-density lipoprotein cholesterol (HDL-C) is reduced in RA patients. We aimed to investigate the influence of biological disease-modifying antirheumatic drugs (bDMARDs) on the LDL-C / HDL-C ratio in patients with RA.

Methods: Patients with RA treated with bDMARDs from 2008 to 2018 were studied based on the All Showa University of RA (ASHURA) database. The association between LDL-C and HDL-C level reduction and treatment was evaluated. Of 629 patients treated with the bDMARDs, 346 patients with available LDL-C and HDL-C levels medical records were included. The following background factors were investigated: age; sex; type of bDMARDs; dosage of methotrexate (MTX) and prednisolone (PSL); usage of conventional synthetic DMARDs, dyslipidemia drugs and nonsteroidal anti-inflammatory drugs; body mass index (BMI); smoking history; HbA1c; presence or absence of hypertension and dyslipidemia; and serum creatinine, C-reactive protein, and matrix metalloproteinase-3 levels. We also used the simplified disease activity index (SDAI) to evaluate RA disease activity. The primary endpoint was LDL-C and HDL-C

levels before, and after 6 months and 1 year, which was determined using the repeated-measures analysis of variance (ANOVA).

Results: The LDL-C / HDL-C ratio were from 1.94 ± 0.76 to 1.88 ± 0.73 and 1.86 ± 0.74 before treatment and after 6 months and 1 year, respectively (p=0.328). Variation was within normal range (less than 2.0). The HDL-C levels increased from 61.8 ± 19.2 (mg/dL) to 64.8 ± 19.0 and 66.0 ± 19.2 before treatment and after 6 months and 1 year, respectively (p=0.013). Variation was within normal range (40-119). On the other hand, the LDL-C levels were not significant change from 110.2 ± 28.8 (mg/dL) to 112.3 ± 27.8 and 113.1 ± 28.1 before treatment and after 6 months and 1 year, respectively (p=0.372). Variation was within normal range (70-139).

Conclusion: Our study suggests that bDMARDs may affect increased HDL-C levels, not affect changes LDL-C levels and not affect LDL-C / HDL-C ratio in patients with RA.

Disclosure: Y. Miwa, Pfizer Japan Inc., 5; **Y. Mitamura**, None.

Abstract Number: 1678

Favorable Balance of Benefit and Harm of Long-Term, Low Dose Prednisolone Added to Standard Treatment in Rheumatoid Arthritis Patients Aged 65+: The Pragmatic, Multicenter, Placebo-Controlled GLORIA Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Low-dose glucocorticoid (GC) therapy is widely used in rheumatoid arthritis (RA) but the balance of benefit and harm is still unclear. We studied the effects of prednisolone (5 mg/day, 2 years) added to standard of care in patients aged≥65 with active RA (1988 or 2010 criteria).

Methods: Pragmatic double-blind placebo-controlled randomized trial; all co-treatments and changes therein were allowed during the trial except long-term open label GC; Ca/D supplementation was advised in all patients. Minimal exclusion criteria were tailored to seniors.

Benefit outcomes: disease activity (DAS28) and joint damage (Sharp/van der Heijde).

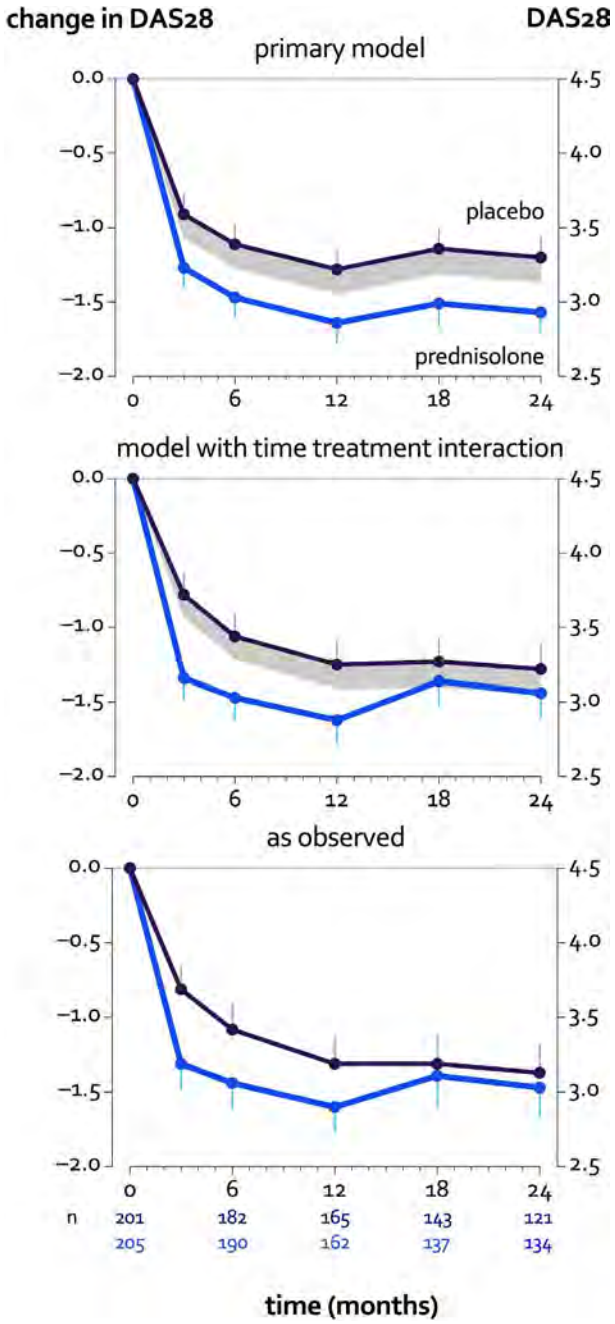

Figure 1. Change in DAS28 estimated in primary model, model with time-treatment interactions, and as observed, with numbers of patients. The grey area depicts the one-sided 95%confidence bound for the difference at each time point. Error bars depict one half of the two-sided 95%CI for the group means.

Harm outcome: proportion of patients with ≥1 adverse event (AE) of special interest: includes serious events, GC-specific events and those causing study discontinuation.

Analysis: longitudinal models, one-sided testing and 95% confidence limits (95%CL).

Results: We randomized 451 patients with established, impactful RA and mean 2.1 comorbidities: mean age 72 (max 88) years, 70% female, RA duration 11 years; 67% were RF+, 56% ACPA+, 96% had joint damage on radiographs; mean DAS28 4.5. 79% were on disease-modifying treatment, including 14% on biologics. 63% prednisolone vs 61%

Table 1. Important adverse events, per 100 patient-years.*

	SAE		other AESI	
	pred	placebo	pred	placebo
infection	7	4	35	26
ischemic cardiovascular	2.3	1.7	0.0	0.6
symptomatic fracture	0.6	1.1	3.1	1.7
new onset				
hypertension	0.3	0	1.1	2.0
diabetes mellitus	0	0	0.6	0.3
cataract	0	0.6	2.0	1.7
glaucoma	0	0	0.3	0.8
other	12	10	13	7
total	**23**	**18**	**55**	**39**

* SAE: Serious Adverse Events, mostly for hospitalization;
other AESI: other Adverse Events of Special Interest: mostly for treatment or study discontinuation

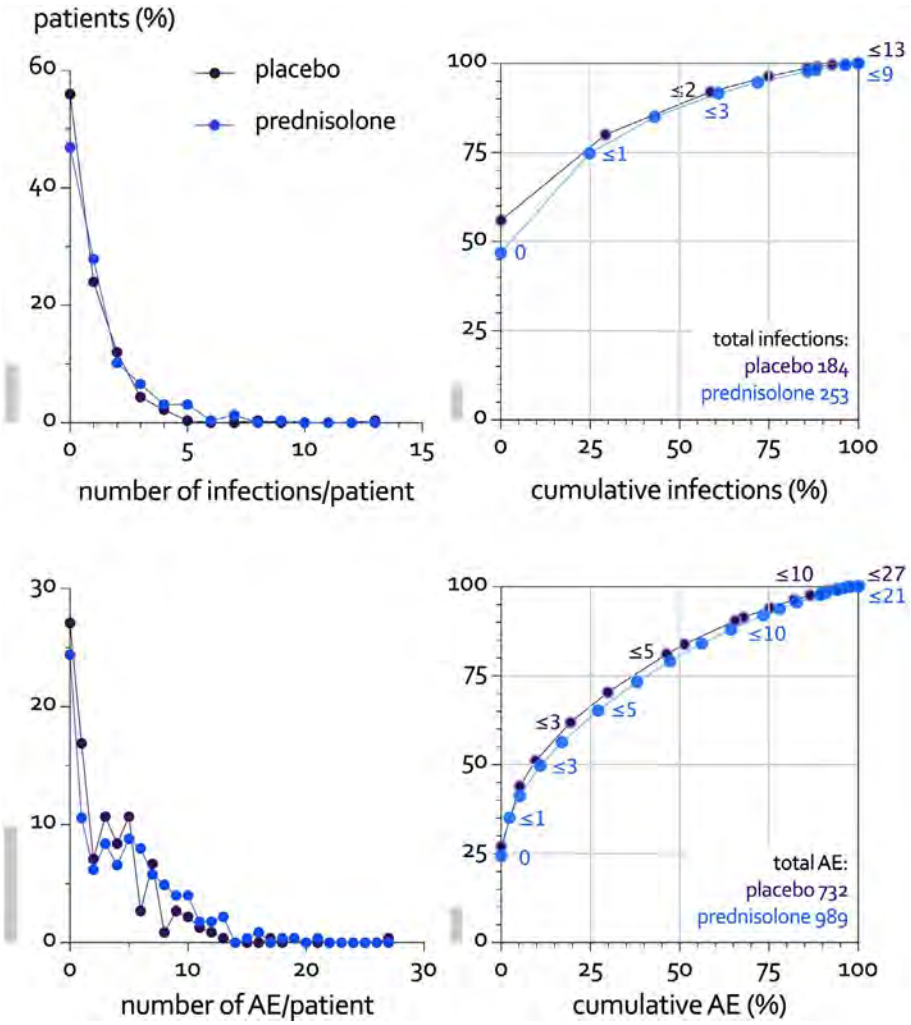

Figure 2. Patients with multiple adverse events (AE) have a major impact on the total number of events in both treatment groups: infection events in top panels, all AE in bottom panels. Left panels show the distribution of patients by number of events/patient. This shows most patients experience no or only a few events. Right panels plot bivariate cumulative distributions of patients by AE. The numbers next to the series indicate the maximum number of events of the population at that point. The right panels show the impact of multiple events: for example, 75% of patients (with 0 or 1 infection) contribute only 25% of all infections (top right panel); read in reverse, 50% of patients (with 2 resp. 3 or more events) contribute almost 90% of all AE (bottom right panel). To facilitate interpretation, grey vertical bars indicate 10% on the vertical scale.

placebo patients completed the trial. Discontinuations were for AE (14%), active disease (4%), and for other (incl. covid-related) reasons (20%) in both groups; mean time in study 19 months.

Prednisolone resulted in more benefit and harm than placebo. Disease activity rapidly declined in the first 3 months and stabilized after 1 year (Figure 1), and was lower in prednisolone patients (adjusted mean difference in DAS28 over 2 years: 0.37, 95%CL 0.23, p< 0.0001). In 331 patients adherent to protocol on stable treatment ('pure treatment comparison') the mean difference in DAS28 after 3 months was 0.62 (95%CL 0.44). Significant time-treatment interaction in secondary analyses suggested a decrease in contrast after the first year; this was most likely caused by significantly more changes in DMARD treatment favoring the placebo group. Joint damage progression over 2 years was 1.7 point lower in the prednisolone group (95%CL 0.7, p=0.003).

60% prednisolone vs 49% placebo patients experienced the harm outcome: 60 vs 49%, adjusted RR 1.24, 95%CL 1.04, p=0.02; largest contrast in (mostly non-severe) infections (Table 1). Other GC-specific events were rare. In both groups, AE clustered in a subgroup of patients (Figure 2).

Conclusion: Add-on low dose prednisolone has powerful long-term effects in established RA, with a tradeoff of 24% relative (11% absolute) increase in the number of patients with adverse events, mostly non-severe; this suggests a favorable balance of benefit and harm.

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Abstract Number: 1679

Effectiveness and Safety of Tocilizumab SC Every 10 Days in Patients with Rheumatoid Arthritis Who Previously Used Tocilizumab EV During the COVID 19 Pandemic at the Hospital Docente Padre Billini, Dominican Republic

Teresandris Polanco Mora, Jennifer Santana Peralta de Heyaime, Angelo Cornelio Vasquez, Yamilet Cruz, Edral Rodriguez, Tirso Valdez Lorie, Roberto Munoz and Rafael Alba Feriz, Hospital Docente Padre Billini, Santo Domingo, Dominican Republic

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Rheumatoid arthritis (RA) is an autoimmune disease systemic, with a prevalence 0.5 - 1% of the population, with predilection for the female sex. (1) Tocilizumab (TCZ) is a humanized monoclonal antibody directed against the receptor Soluble and Membrane Interleukin-6, (2) Different Studies have demonstrated the non-inferiority of subcutaneous (sc) TCZ compared to intravenous (iv) TCZ. (3,4,5) Evidence of its efficacy in patients with sustained remission of 24 weeks or plus. 6 Following the COVID 19 pandemic and with initial results promising use of IV TCZ in these patients, the authorities of Our country considered it appropriate to change the administration of this drug in patients with RA who used it to TCZ sc every 10 days, from May 2020, with the aim of rationalizing and avoiding shortages and use IV TCZ in patients with COVID 19.

Methods: Observational, prospective, and longitudinal study, between May and October 2020, consultation patients with RA at weeks 0, 12 and 24 of rheumatology service of the Hospital Docente Padre Billini. CDAI, DAS 28, ESR, hemogram, TGO, TGP, Cholesterol, Triglycerides were measured. Inclusion criteria: > 18 years, diagnosis of RA according to the ACR / EULAR 2010 classification criteria, previous treatment with Tocilizumab EV in mono or therapy combined for more than 6 months of continuous use. The data is analyzed with SPSS V23.

Results: 119 met inclusion criteria. 93.2% (111) female, 78.15% (93) concomitant scDMARD, 21.8% (26) monotherapy, 12.6% (15) glucocorticoids. Baseline DAS28: 65.54% (78) low activity, 23.5% (28) remission, 9.2% (11) moderate activity, 1.6% (2) high activity. Baseline DAS28 mean: 2.75. CDAI baseline: 52.94% (63) remission, 44.53% (53) low activity, 2.52% (3) moderate activity, mean baseline CDAI: 2. 76.4% (91) ESR elevated. Week 12: DAS28: 62.1% (74) low activity, 26.8% (32) remission, 10.9% (13) moderate activity. CDAI week 12: 55.46% (66) remission, 31% (40) low activity, 10.92% (13) moderate activity. 73.1% (87) elevated ESR. Week 24: DAS 8: 58.8% (70) low activity, 16.8% (20) remission, 14.2% (17) moderate activity and 3.3% (4) high activity. CDAI week 24: 83.19% (99) remission, 10.92% (13) low activity, 2.52% (3) moderate activity, 2.52% (3) high activity. 76.4% (91) ESR elevated. Average DAS28: 2.9 and Average CDAI: 1 at week 24. Worsening at week 24 (DAS 28) 6.7% (8) from remission to low activity, 5.04% (7) low to moderate activity and 2.52% from moderate to high activity, CDAI showed improvement from low activity to remission of 22.6% and worsening from moderate to high activity 2.5%. ΔDAS 28: 0.15, CDAI: -1. Adverse events 1.6% (2) site reaction of injection, 2.52% (3) TGO and elevated TGP, were not reported hematologic events, dyslipidemia, or serious infections.

Conclusion: In our study, the change in the administration route and time of application of Tocilizumab did not demonstrate exacerbation, this option assessed circumstantially could be a possibility of dose optimization in patients with low clinical activity or remission for at least 6 months and good safety profile, which would reduce costs in the long term. We recommend a study with a longer period.

Disclosure: T. Polanco Mora, None; **J. Santana Peralta de Heyaime**, None; **A. Cornelio Vasquez**, None; **Y. Cruz**, None; **E. Rodriguez**, None; **T. Valdez Lorie**, None; **R. Munoz**, None; **R. Alba Feriz**, None.

Abstract Number: 1680

Impact of Race on the Efficacy and Safety of Tofacitinib in Patients with RA: A Post Hoc Analysis of Phase 2, 3, and 3b/4 Clinical Trials

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SESSION INFORMATION

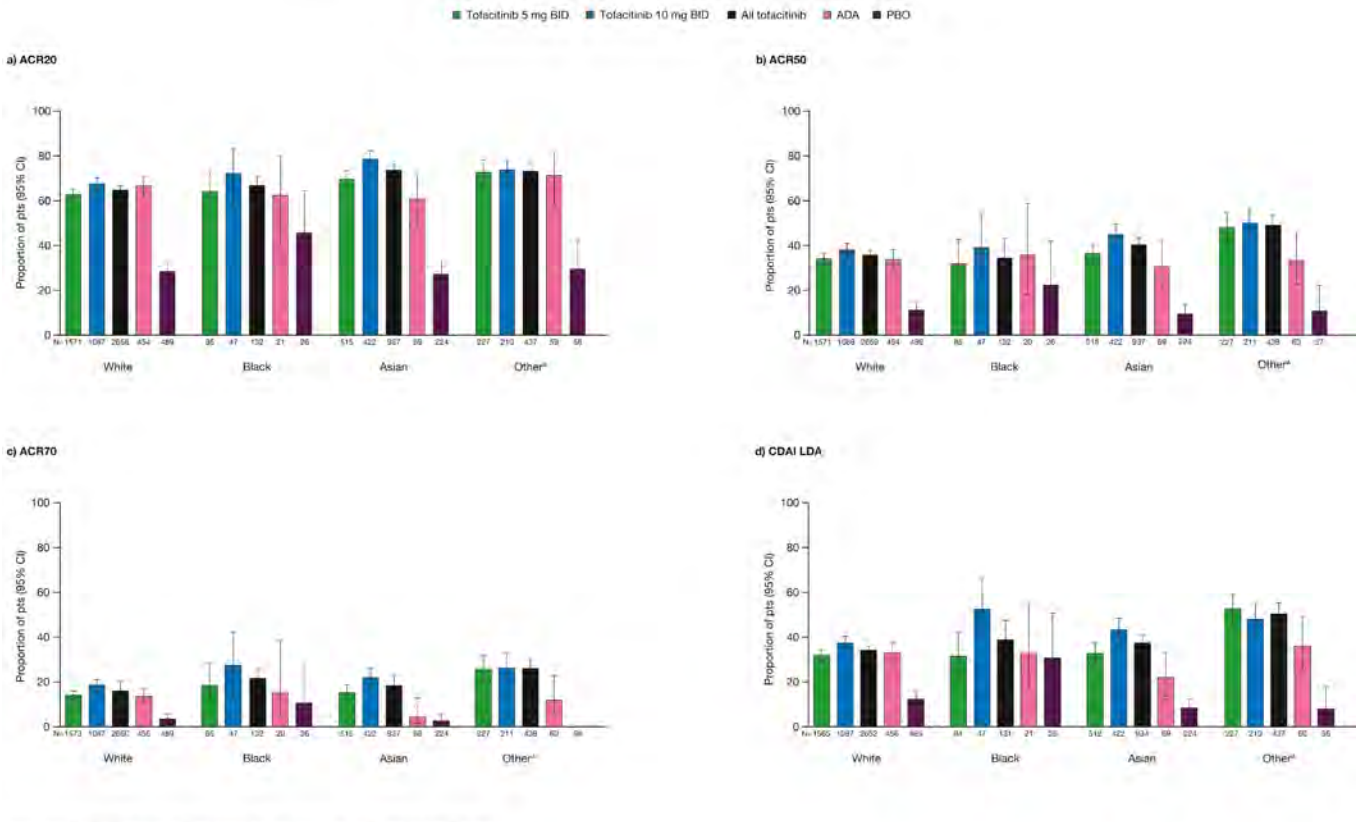
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: While racial disparities in clinical outcomes for RA patients (pts) receiving bDMARDs or csDMARDs have been described,[1] there remains a paucity of data on racial differences in response to advanced therapies. Here, we evaluate impact of race on tofacitinib efficacy and safety in RA pts.

Methods: This post hoc analysis used pooled data from 8 Phase (P)2, 6 P3, and 1 P3b/4 RCTs of pts treated with tofacitinib 5 or 10 mg BID, adalimumab (ADA; 40 mg Q2W), or placebo (PBO), stratified by self-reported pt race (White, Black, Asian, Other) at baseline (BL) visit. Efficacy outcomes at Month (M)3 were: ACR20/50/70 and CDAI/DAS28-4(ESR) LDA (scores ≤ 10 and ≤ 3.2, respectively) rates, and least squares (LS) mean change from BL (Δ) in DAS28(ESR) and HAQ-DI. Incidence rates (IRs; unique pts with events/100 pt-yrs) were estimated for adverse events (AEs), serious AEs, discontinuations due to AEs, and all-cause mortality.

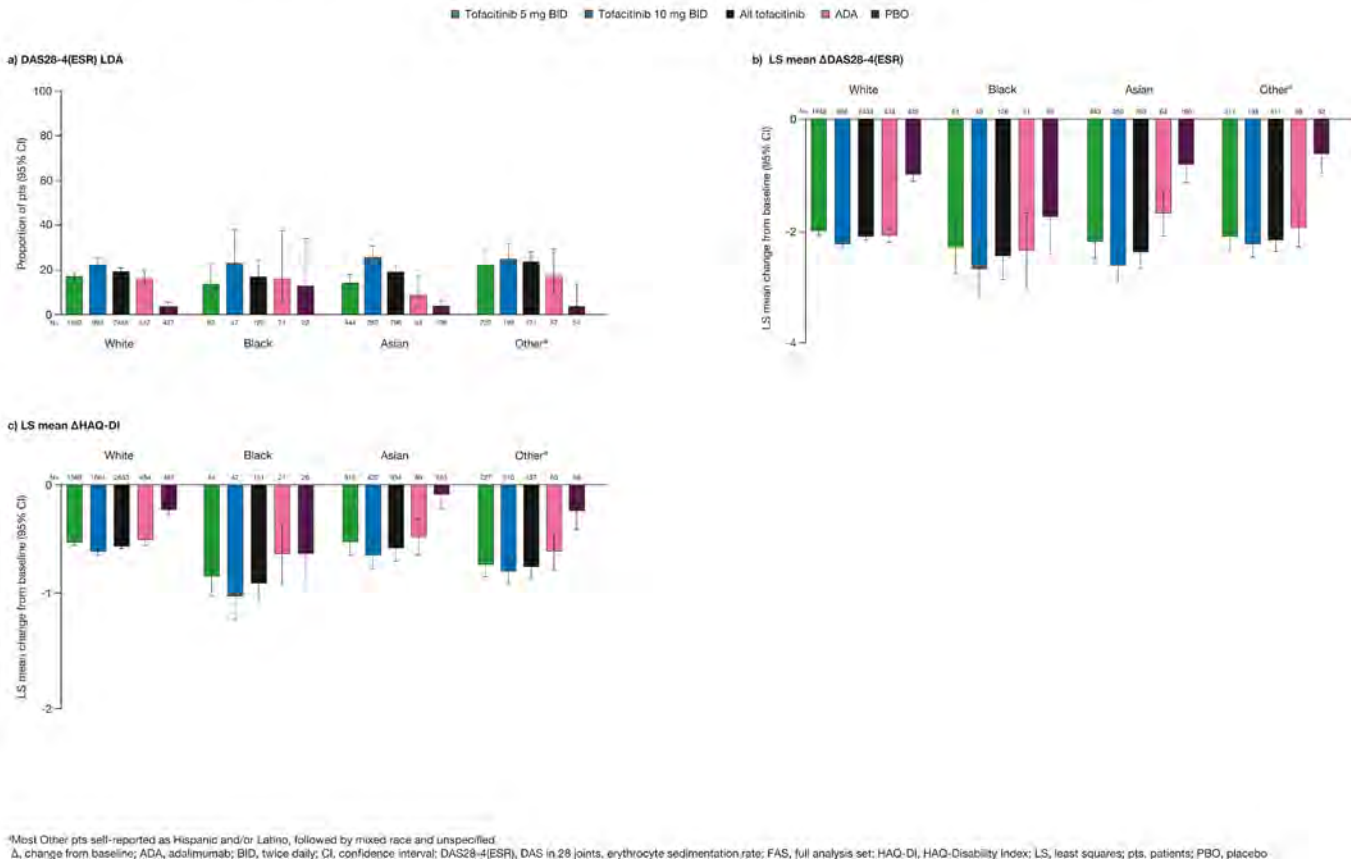
Results: 6,355 pts were included (White, n=4,145; Black, n=213; Asian, n=1,348; Other, n=649). BL characteristics were generally similar across treatment/racial groups, excepting higher rates of prior bDMARD exposure in White/Black vs Asian/Other pts. Across treatment arms, White, Black, Asian, and Other pts most commonly enrolled from Europe (40.9%), North America (68.1%), East/South Asia (97.9%), and Latin America (80.6%), respectively; most Other pts self-reported as Hispanic and/or Latino, followed by mixed race and unspecified. At M3, ACR20/50/70 and CDAI LDA rates were mostly higher in Other vs White pts with tofacitinib, similar across racial groups with ADA, and

Figure 1. Proportions of pts achieving a) ACR20, b) ACR50, and c) ACR70 responses, and d) CDAI LDA across treatment groups at Month 3, stratified by race (FAS)



[a]Most Other pts self-reported as Hispanic and/or Latino, followed by mixed race and unspecified
ACR20/50/70, ACR ≥20%, ≥50%, or ≥70% response criteria; ADA, adalimumab; BID, twice daily; CDAI, Clinical Disease Activity Index; CI, confidence interval; FAS, full analysis set; LDA, low disease activity; PBO, placebo; pts, patients

Figure 2. a) Proportions of pts achieving DAS28-4(ESR) LDA, and LS mean change from baseline in b) DAS28-4(ESR), and c) HAQ-DI across treatment groups at Month 3, stratified by race (FAS)



[a]Most Other pts self-reported as Hispanic and/or Latino, followed by mixed race and unspecified.
Δ, change from baseline; ADA, adalimumab; BID, twice daily; CI, confidence interval; DAS28-4(ESR), DAS in 28 joints, erythrocyte sedimentation rate; FAS, full analysis set; HAQ-DI, HAQ-Disability Index; LS, least squares; pts, patients; PBO, placebo

numerically higher in Black vs White/Asian/Other pts with PBO (Figure 1a–d). DAS28-4(ESR) LDA rates and LS mean ΔDAS28-4(ESR) were broadly similar across racial groups with active treatment, and numerically higher in Black vs White/Asian/Other pts with PBO (Figure 2a–b). Across active treatment arms, LS mean ΔHAQ-DI was generally comparable across racial groups with some numerical differences, and higher in Black vs White/Asian pts with PBO (Figure 2c). Safety outcomes were broadly similar across treatment arms, with some higher IRs for AEs seen with Black/Other vs White/Asian pts (Table).

Conclusion: Across racial groups, tofacitinib efficacy/safety was consistent with previous findings from the tofacitinib RA clinical program, although results should be interpreted with caution due to low pt numbers in some groups. Noting this limitation, some trends in efficacy outcomes were seen between racial groups; higher ACR20/50/70 and CDAI LDA rates in Other vs White pts with tofacitinib may be attributable to prior treatment history/regional practice norms. Numerically higher PBO responses in Black vs White/Asian/Other pts may reflect demographic differences, notably country of enrollment, across racial groups participating in RCTs. Safety findings were generally consistent across racial/treatment groups. Future analyses should focus on the impact of socio-economic, cultural, genetic, or practice-based differences that may underpin these results.

References

1. Greenberg JD et al. Am J Med 2013; 126: 1089-98.

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by K Woollcott, CMC Connect, funded by Pfizer Inc.

Table. Summary of safety outcomes across treatment groups, stratified by race (SAS)

White pts	Tofacitinib 5 mg BID (N=1,699; PY=1,588.3)		Tofacitinib 10 mg BID (N=1,264; PY=1,175.4)		All tofacitinib (N=2,963; PY=2,763.7)		ADA (N=484; PY=390.4)		PBO (N=698; PY=177.3)	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
AEs	1,150 (67.7)	141.9 (133.8, 150.3)	919 (72.7)	188.5 (176.5, 201.1)	2,069 (69.8)	159.4 (152.6, 166.4)	318 (65.7)	140.4 (125.4, 156.7)	369 (52.9)	311.6 (280.6, 345.1)
SAEs	146 (8.6)	9.1 (7.7, 10.7)	103 (8.1)	8.9 (7.3, 10.8)	249 (8.4)	9.0 (7.9, 10.2)	31 (6.4)	7.6 (5.2, 10.8)	23 (3.3)	12.5 (7.9, 18.7)
Discontinuations due to AEs	113 (6.7)	6.9 (5.7, 8.3)	98 (7.8)	8.3 (6.7, 10.1)	211 (7.1)	7.4 (6.5, 8.5)	46 (9.5)	11.2 (8.2, 14.9)	23 (3.3)	12.4 (7.9, 18.7)
All-cause mortality	5 (0.3)	0.3 (0.1, 0.7)	3 (0.2)	0.3 (0.1, 0.7)	8 (0.3)	0.3 (0.1, 0.6)	1 (0.2)	0.2 (0.0, 1.3)	0	0.0 (0.0, 2.0)
Black pts	**Tofacitinib 5 mg BID (N=93; PY=81.8)**		**Tofacitinib 10 mg BID (N=60; PY=49.8)**		**All tofacitinib (N=153; PY=131.6)**		**ADA (N=22; PY=18.6)**		**PBO (N=38; PY=10.0)**	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
AEs	76 (81.7)	244.14 (192.4, 305.6)	48 (80.0)	434.3 (320.2, 575.8)	124 (81.0)	294.0 (244.5, 350.5)	16 (72.7)	162.2 (92.7, 263.4)	23 (60.5)	424.9 (269.4, 637.6)
SAEs	15 (16.1)	19.1 (10.7, 31.4)	2 (3.3)	3.9 (0.5, 14.3)	17 (11.1)	13.1 (7.7, 21.0)	2 (9.1)	10.3 (1.3, 37.4)	1 (2.6)	9.4 (0.2, 52.2)
Discontinuations due to AEs	8 (8.6)	9.5 (4.1, 18.7)	4 (6.7)	7.9 (2.2, 20.3)	12 (7.8)	8.9 (4.6, 15.5)	2 (9.1)	10.5 (1.3, 37.9)	1 (2.6)	9.4 (0.2, 52.2)
All-cause mortality	0	0.0 (0.0, 4.3)	0	0.0 (0.0, 7.3)	0	0.0 (0.0, 2.7)	0	0.0 (0.0, 18.4)	0	0.0 (0.0, 34.3)
Asian pts	**Tofacitinib 5 mg BID (N=560; PY=548.8)**		**Tofacitinib 10 mg BID (N=462; PY=487.2)**		**All tofacitinib (N=1,022; PY=1,036.0)**		**ADA (N=73; PY=60.1)**		**PBO (N=253; PY=72.3)**	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
AEs	382 (68.2)	150.0 (135.4, 165.9)	338 (73.2)	178.4 (159.9, 198.5)	720 (70.5)	162.2 (150.5, 174.5)	51 (69.9)	157.0 (116.9, 206.5)	122 (48.2)	251.5 (208.9, 300.3)
SAEs	61 (10.9)	11.3 (8.6, 14.5)	47 (10.2)	9.7 (7.1, 12.9)	108 (10.6)	10.5 (8.6, 12.7)	9 (12.3)	14.5 (6.6, 27.5)	8 (3.2)	10.9 (4.7, 21.4)
Discontinuations due to AEs	69 (12.3)	12.4 (9.7, 15.7)	58 (12.6)	11.8 (9.0, 15.3)	127 (12.4)	12.1 (10.1, 14.4)	10 (13.7)	15.9 (7.6, 29.2)	11 (4.3)	14.9 (7.4, 26.6)
All-cause mortality	2 (0.4)	0.4 (0.0, 1.3)	1 (0.2)	0.2 (0.0, 1.1)	3 (0.3)	0.3 (0.1, 0.8)	0	0.0 (0.0, 5.8)	1 (0.4)	1.3 (0.0, 7.4)
Other pts[a]	**Tofacitinib 5 mg BID (N=257; PY=245.9)**		**Tofacitinib 10 mg BID (N=238; PY=239.8)**		**All tofacitinib (N=495; PY=485.7)**		**ADA (N=64; PY=49.5)**		**PBO (N=90; PY=24.5)**	
	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)	n (%)	IR (95% CI)
AEs	205 (79.8)	227.1 (197.1, 260.4)	190 (79.8)	234.3 (202.2, 270.1)	395 (79.8)	230.5 (208.4, 254.4)	44 (68.8)	161.6 (117.4, 216.9)	48 (53.3)	271.4 (200.1, 359.8)
SAEs	17 (6.6)	6.7 (3.9, 10.8)	15 (6.3)	6.2 (3.5, 10.2)	32 (6.5)	6.5 (4.4, 9.1)	1 (1.6)	1.9 (0.1, 10.4)	3 (3.3)	11.5 (2.4, 33.6)
Discontinuations due to AEs	15 (5.8)	5.9 (3.3, 9.7)	20 (8.4)	8.2 (5.0, 12.6)	35 (7.1)	7.0 (4.9, 9.7)	4 (6.3)	7.5 (2.0, 19.2)	3 (3.3)	11.5 (2.4, 33.6)
All-cause mortality	1 (0.4)	0.4 (0.0, 2.2)	0	0.0 (0.0, 1.49)	1 (0.2)	0.2 (0.0, 1.1)	0	0.0 (0.0, 6.9)	0	0.0 (0.0, 13.9)

[a]Most Other pts self-reported as Hispanic and/or Latino, followed by mixed race and unspecified

IRs were calculated as the number of unique pts with events per 100 PY, naïve estimate; censored at the day of first event or up to last dose +28 days

PY shown in the table are total pt-yrs of exposure to treatment

ADA, adalimumab; AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate; PBO, placebo; pt, patient; PY, pt-yrs; SAE, serious adverse event; SAS, safety analysis set

Disclosure: G. Wright, Amgen, 2, 6, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Pfizer Inc, 2, UCB, 2, 6, Myriad Autoimmune, 2, 6, Janssen, 2, Association of Women in Rheumatology, 4, United Rheumatology, 4; **E. Mysler**, Eli Lilly, 5, 6, Pfizer Inc, 5, 6, Roche, 5, 6, AbbVie, 6, Bristol-Myers Squibb, 6, Janssen, 6, Sanofi, 6; **Y. Chen**, Bristol-Myers Squibb, 5, GSK, 5, Pfizer Inc, 5; **C. Kinch**, Pfizer Canada ULC, 3, 11; **A. Yndestad**, Pfizer Inc, 3, 11; **K. Kwok**, Pfizer Inc, 3, 11; **M. Cadatal**, Pfizer Inc, 3, 11; **R. Germino**, Pfizer Inc, 3, 11; **A. Ogdie**, Novartis, 2, 5, 11, Pfizer Inc, 2, 11, AbbVie, 2, 6, Amgen, 2, 6, 11, Bristol-Myers Squibb, 2, Celgene, 2, 6, Eli Lilly, 2, CorEvitas, 2.

Abstract Number: 1681

ATI-450, an Investigational MK2 Inhibitor, Is Well Tolerated and Demonstrated Clinical Activity in Patients with Mod/severe RA: A 12-week Phase 2a, Randomized, Investigator/patient-blind Study Investigating the Safety, Tolerability, PK and PD of ATI-450 + MTX vs PBO + MTX in MTX IR Patients

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: p38 inhibition has been a focus of research in RA but efficacy in clinical studies was underwhelming, possibly because a large number of pro and anti-inflammatory pathways as well as negative feedback loops were modulated by this target. ATI-450 specifically blocks the downstream MK2-mediated inflammatory drive on the p38 pathway and may therefore avoid the tachyphylaxis associated with p38 inhibitors. Inhibition of ex vivo-stimulated IL1, IL6, TNFa and IL8 was seen in phase 1. This study explored whether MK2 inhibition was well tolerated and could deliver sustained anti-inflammatory effect leading to durable clinical activity in patients with RA.

Methods: A phase 2a, randomized, investigator/patient-blind, sponsor-unblinded, placebo (PBO) controlled study was conducted to investigate safety, tolerability, PK, and PD of ATI-450 versus PBO (both + MTX) in MTX inadequate responders with moderate to severe RA. Patients were randomized in a 3:1 ratio to receive oral ATI-450 (50 mg) or PBO, both BID. A 12-week treatment period was followed by a 4-week follow-up period. The primary endpoint was safety and tolerability. Secondary and exploratory endpoints included DAS28-CRP, ACR20/50/70, change from baseline in hsCRP and relevant endogenous cytokine levels in blood. MRI imaging will be reported elsewhere. The study was not powered to detect statistical significance on efficacy endpoints.

Results: Nineteen subjects were randomized (16:ATI-450, 3:PBO). Mean DAS28-CRP at baseline was 5.71 in the treatment arm and 5.77 in the PBO arm. Seventeen subjects (15 ATI-450, and 2 PBO) completed 12 weeks of treatment. One subject from each arm withdrew during the treatment period: the ATI-450 subject withdrew for an AE of elevated CPK.

ATI-450 was generally well tolerated. No serious adverse events were reported during the treatment period (1 unrelated SAE of COVID-19 pneumonia was reported off-treatment in the follow-up period in the ATI-450 arm). The most common adverse events (each reported in 2 subjects) were urinary tract infection and ventricular extrasystoles. All adverse events were mild to moderate.

In the per-protocol analysis (includes 15 ATI-450, 2 PBO who completed 12 weeks), the mean change from baseline in DAS28-CRP score at week 12 was -2.0 in the ATI-450 arm versus +0.35 in the PBO arm. 40% and 20% of ATI-450 subjects had a DAS28-CRP score ≤ 3.2 and < 2.6 at week 12, respectively, versus 0 PBO patients. ACR20/50/70 was observed at week 12 in 60%, 33% and 20% of 15 ATI-450 subjects versus 0% of 2 PBO subjects. The median reduction from baseline in hsCRP was >40% throughout the 12-week treatment period in the treatment arm; a sustained median reduction was not observed in the placebo arm. A marked and sustained inhibition of median endogenous plasma concentrations of TNFα, IL6, IL8, and MIP1β was observed in the treatment arm over the 12-week period.

Conclusion: ATI-450 was generally well tolerated and demonstrated durable clinical activity over 12 weeks in RA. This study is the first to demonstrate that MK2 inhibition can overcome key deficiencies associated with p38 inhibition. ATI-450 has potential to be an important new drug in RA and progression to phase 2b is supported.

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Abstract Number: 1682

Impact of Type, Dose and Duration of Oral Polyunsaturated Fatty Acid Supplementation on Disease Activity in Inflammatory Rheumatic Diseases: A Systematic Literature Review and Meta-analysis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: This systematic literature review and meta-analysis aimed to better estimate the effect of oral supplementation with polyunsaturated fatty acid (PUFA; omega (n)-3 and n-6) on inflammatory rheumatic disease (IRD) activity in terms of duration, dose, type and source.

Methods: The literature was searched in PubMed, EMBASE and Cochrane Library databases up to October 2020. Studies were reviewed in accordance with PRISMA guidelines. The effect of PUFA supplementation on disease ac-

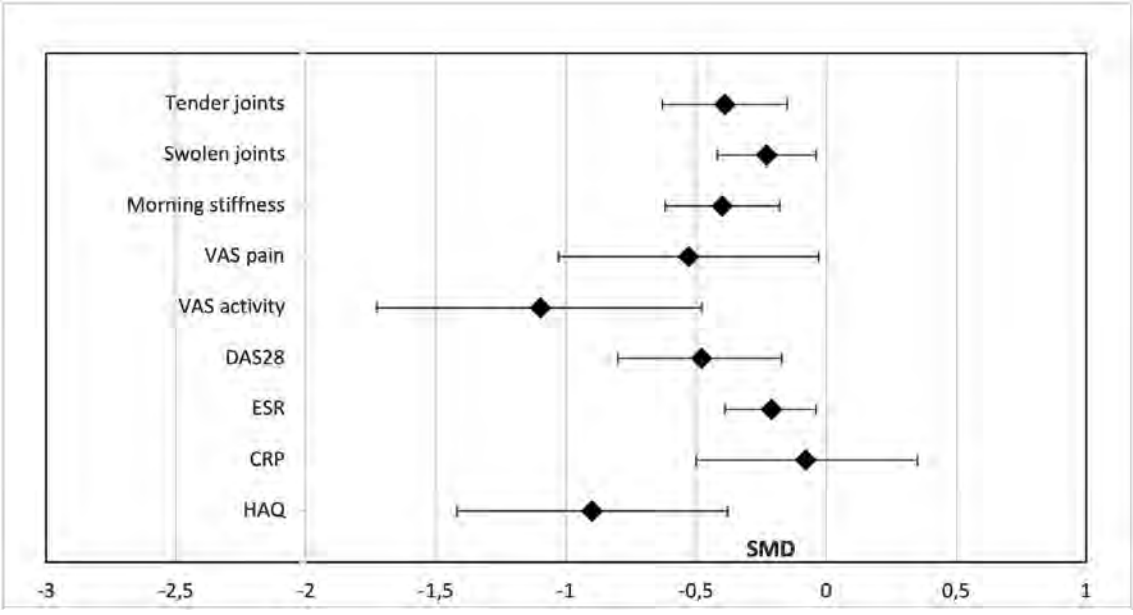

Figure 1. Overall effect of oral PUFA supplementation as compared with controls on parameters of rheumatoid arthritis (RA) Data are standardized mean difference (SMD) (95% confidence interval [CI]). VAS= visual analog scale; DAS28= Disease Activity Score in 28 joints; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; HAQ= Health Assessment Questionnaire.

tivity was expressed as the standardized mean difference. Metaregression and subgroup analyses involved type of IRD, Jadad score, PUFA source (animal or vegetable) and doses.

Results: We obtained 43 references; 31 randomized controlled studies compared the effects of PUFA and placebo on disease activity (732 IRD patients receiving PUFA supplementation and 732 receiving placebo, most with rheumatoid arthritis). We found a significant improvement in pain, swollen and tender joint count, Disease Activity Score in 28 joints, and Health Assessment Questionnaire score in IRD patients receiving PUFA supplementation as compared with controls, with a significant decrease in erythrocyte sedimentation rate but not C-reactive protein level. Although meta-regression revealed no difference by IRD type or source or dose of PUFA supplementation, subgroup analysis revealed more parameters significantly improved with animal- than vegetable-derived PUFAs and 3-to 6-month supplementation. Most studies examined high-dose supplementation (>2 g/day).

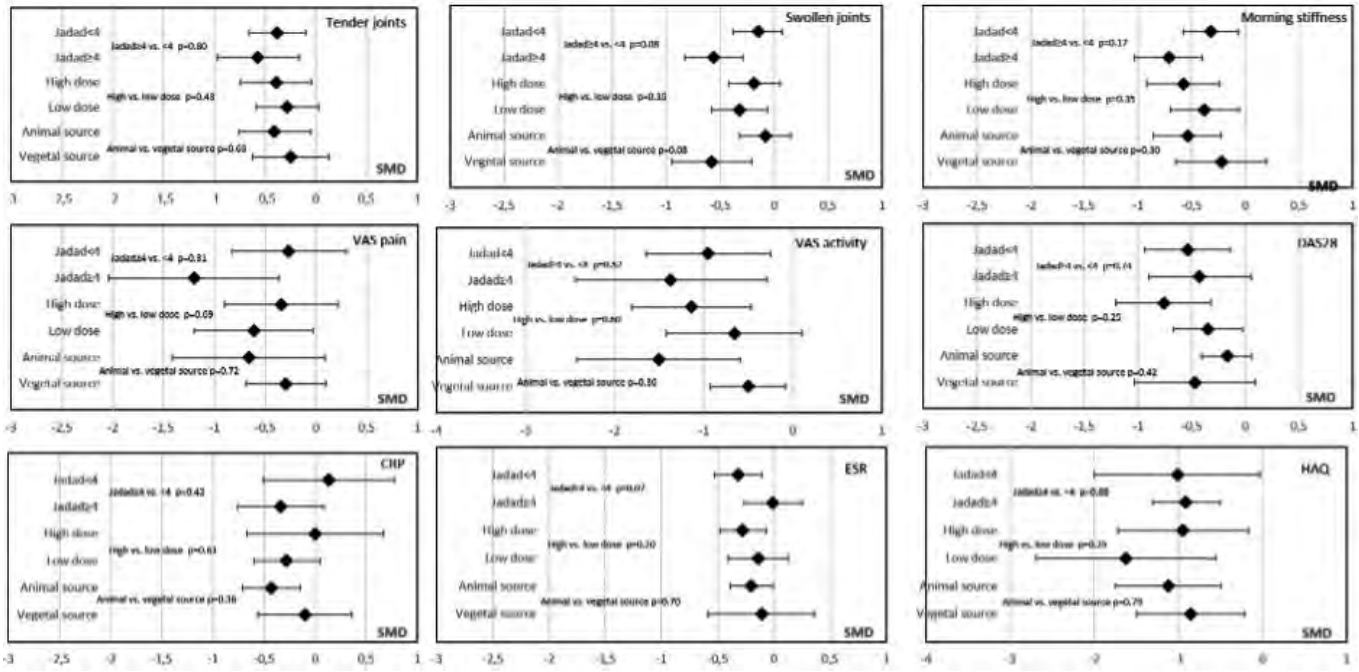

Figure 2. Meta-regression analysis of effect of oral PUFA supplementation as compared with controls on parameters of RA Data are standardized mean difference (SMD) (95% CI). VAS= visual analog scale; DAS28= Disease Activity Score in 28 joints; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; HAQ= Health Assessment Questionnaire.

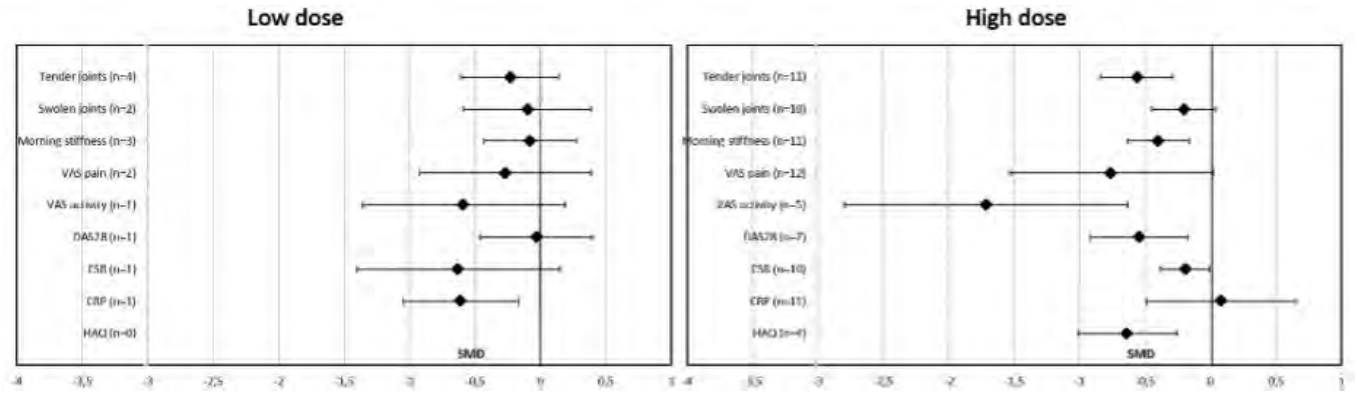

Figure 3. Effect of oral PUFA supplementation on RA disease activity by PUFA dosage (> or < 2 g/day). Data are standardized mean difference (SMD) (95% CI). VAS= visual analog scale; DAS28= Disease Activity Score in 28 joints; ESR= erythrocyte sedimentation rate; CRP= C-reactive protein; HAQ= Health Assessment Questionnaire.

Conclusion: PUFA consumption, especially omega-3 from animal source >2 g/day, may improve IRD activity and might be an adjuvant therapy in rheumatoid arthritis.

Disclosure: J. Sigaux, None; **S. Mathieu**, None; **Y. N guyen**, None; **P. Sanchez**, None; **J. LETAROUILLY**, Pfizer, 5; **M. Soubrier**, None; **s. czernichow**, None; **R. FLIPO**, Novartis, 2, 6, Lilly, 2, 6, Abbvie, 2, 6, Pfizer, 2, 6, MSD, 2, 6; **J. Sellam**, MSD, 2, Pfizer, 2, Roche, 6, BMS, 6, Fresenius Kabi, 2, 6, Biogen, 2, Abbvie, 2, Janssen, 2, 6, Novartis, 2; **C. Daïen**, None.

Abstract Number: 1683

Abatacept in Usual and in Non-Specific Interstitial Pneumonia Associated to Rheumatoid Arthritis. National Multicenter Study of 190 Patients

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Interstitial lung disease (ILD) is a severe complication of Rheumatoid Arthritis (RA). Usual interstitial pneumonia (UIP) is considered to be more frequent and severe in RA than non-specific interstitial pneumonia (NSIP). Abatacept (ABA) and Rituximab have demonstrated efficacy in RA-ILD [Fernández-Díaz C, et al. Semin Arthritis Rheum. 2018 Aug;48(1):22-27; Fernández-Díaz C, et al. Rheumatology (Oxford). 2020 Dec 1;59(12):3906-16; Atienza-Mateo B, et al. J Clin Med. 2020 Sep 23;9(10):3070]. Our aim was to compare the efficacy of ABA in RA-ILD patients according to radiological patterns of UIP or NSIP.

Methods: From an observational multicenter study of 263 RA-ILD patients treated with ABA, we selected those with UIP or NSIP. We analyzed in the 2 groups from baseline up to 24 months the following outcomes: **a)** Forced Vital Capacity (FVC), **b)** Carbon monoxide diffusing capacity (DLCO), **c)** Chest High Resolution Computed Tomography (HRCT), and **d)** dyspnea. Differences between final follow-up and basal visit were calculated as the average difference and 95% Confidence Interval (95% CI). Multivariable linear regression was used to assess the differences between the 2 groups.

Results: We studied 190 patients with UIP (n=106) and NSIP (n=84). Patients with UIP were older, had more positivity for rheumatoid factor and had received more sulfasalazine **(Table 1)**. ILD duration up to ABA initiation was relatively short in both groups, with a median [IQR] of 16 [4-50] and 11 [2-36] months in UIP and NSIP patterns, respectively. Mean baseline values of FVC and DLCO were > 80% and > 60%, respectively, in the 2 groups, with a lower FVC in

Table 1. Main general features at baseline. ABA, abatacept; ACPA, anti-citrullinated protein antibodies; DMARD, disease-modifying antirheumatic drug, ILD, Interstitial lung disease; MTX, methotrexate; NSIP, non-specific interstitial pneumonia; RA, rheumatoid arthritis; TNF, tumor necrosis factor; UIP, usual interstitial pneumonia

	UIP (n=106)	NSIP (n=84)	p value
Age, years, mean±SD	66±10	63±10	**0.049**
Women, n (%)	59 (56)	49 (58)	0.71
Smoker ever, n (%)	51 (48)	45 (54)	0.46
ILD duration up to ABA, months, median [IQR]	16 [4-50]	11 [2-36]	0.57
RF, n (%)	100 (94)	71 (85)	**0.041**
ACPA, n (%)	96 (91)	75 (89)	0.83
FVC (% of the predicted), mean±SD	82±21	89 ±19	**0.025**
DLCO (% of the predicted), mean±SD	63 ±19	65 ±16	0.46
ABA monotherapy, n (%)	45 (42)	41 (49)	0.38
ABA combined+ MTX // + other cDMARD, n (%)	15 (14) // 46 (43)	16 (19) // 27 (32)	0.17
Prednisone at baseline, mg/day, median [IQR]	7.5 [5-10]	10 [5-10]	0.20
Previous immunosuppressive therapy, n (%)			
MTX	81 (76)	68 (81)	0.45
Leflunomide	48 (45)	31 (37)	0.25
Sulfasalazine	16 (15)	5 (6)	**0.046**
Hydroxychloroquine	24 (23)	16 (19)	0.55
Anti-TNF drugs	37 (35)	30 (36)	0.80
Rituximab	19 (18)	15 (18)	0.99
Tocilizumab	12 (11)	12 (14)	0.54

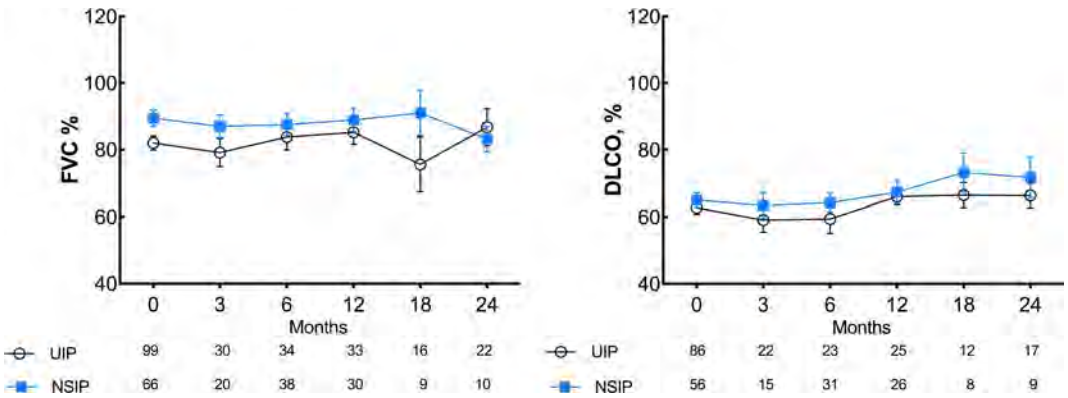

Figure 1. Evolution of pulmonary function tests in RA-ILD patients with UIP and NSIP patterns. FVC and DLCO are expressed as mean (95%CI) and compared between the 2 groups.

UIP (82% vs 89% in NSIP, p< 0.05). The evolution of FVC and DLCO is shown in **Figure 1.** Both parameters remained stable during 24 months of ABA therapy. Available chest HRCT images improved/ stabilized in 73.1% and 72.9% of UIP and NSIP patterns, respectively. With multivariable linear regression analysis, no differences were found in the changes of FVC, DLCO, or HRCT images. Stabilization or improvement of dyspnea was found in 91% and 95% of UIP and NSIP patterns, respectively.

Conclusion: ABA seems to be equally effective in stabilizing of DLCO, FVC and HRCT in UIP and NSIP in RA-ILD. Our results suggest that an early administration of ABA in ILD, before significant structural lung damage development, may be preferable to prevent interstitial progression, regardless of the radiological pattern.

Disclosure: B. Atienza-Mateo, None; **C. Fernández-Díaz**, Brystol Myers Squibb, 6; **S. Castañeda**, None; **R. Melero**, None; **F. Ortiz-Sanjuán**, None; **I. Casafont**, None; **S. Rodríguez-García**, None; **I. Ferraz-Amaro**, None; **M. gonzalez-Gay**, None; **R. Blanco**, Brystol Myers Squibb, 6.

Abstract Number: 1684

Incidence of Infections in Patients Aged ≥ 50 Years with RA and ≥ 1 Additional Cardiovascular Risk Factor: Results from a Phase 3b/4 Randomized Safety Study of Tofacitinib vs TNF Inhibitors

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous clinical trial and real-world data suggest that risk of serious infection events (SIEs) and opportunistic infections (OIs) is similar with tofacitinib 5 mg twice daily (BID; recommended dosage for RA) vs

Table. Summary of infections and infestations in ORAL Surveillance

Pts with events, n (%)	Tofacitinib 5 mg BID (N=1,455)	Tofacitinib 10 mg BID[a] (N=1,456)	TNFi[b] (N=1,451)
Infections and infestations (System Organ Class)	1,036 (71.2)	1,055 (72.5)	930 (64.1)
Most frequently reported,[c] by Preferred Term			
Upper respiratory tract infection	308 (21.2)	312 (21.4)	255 (17.6)
Bronchitis	222 (15.3)	237 (16.3)	163 (11.2)
Urinary tract infection	186 (12.8)	221 (15.2)	184 (12.7)
HZ (non-serious/serious)[d]	180 (12.4)	178 (12.2)	58 (4.0)
Nasopharyngitis	164 (11.3)	165 (11.3)	158 (10.9)
Pneumonia	95 (6.5)	101 (6.9)	78 (5.4)
Sinusitis	92 (6.3)	79 (5.4)	91 (6.3)
Pharyngitis	86 (5.9)	79 (5.4)	75 (5.2)
Influenza	90 (6.2)	91 (6.3)	71 (4.9)
Latent tuberculosis	87 (6.0)	67 (4.6)	91 (6.3)
Gastroenteritis	64 (4.4)	79 (5.4)	53 (3.7)
Respiratory tract infection	43 (3.0)	43 (3.0)	31 (2.1)
Cellulitis	36 (2.5)	32 (2.2)	50 (3.4)

[a]The tofacitinib 10 mg BID group included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019

[b]In the TNFi group, pts in North America (US, Canada, and Puerto Rico) received adalimumab 40 mg every other week, and pts in the rest of the world received etanercept 50 mg every week

[c]≥ 3% of pts with events in any treatment group

[d]Includes all HZ events from the clinical database and adjudicated events

The censoring time for the analyses was the 28-Day On-Treatment period, defined as the minimum of last contact date and last study treatment dose date +28 days. The last contact date was the maximum of event start date, event stop date, last study visit date, withdrawal date, and telephone contact date. If a pt died, the last contact date was the death date

BID, twice daily; HZ, herpes zoster; N, number of pts in treatment group; n, number of pts with events; pts, patients; TNFi, TNF inhibitors

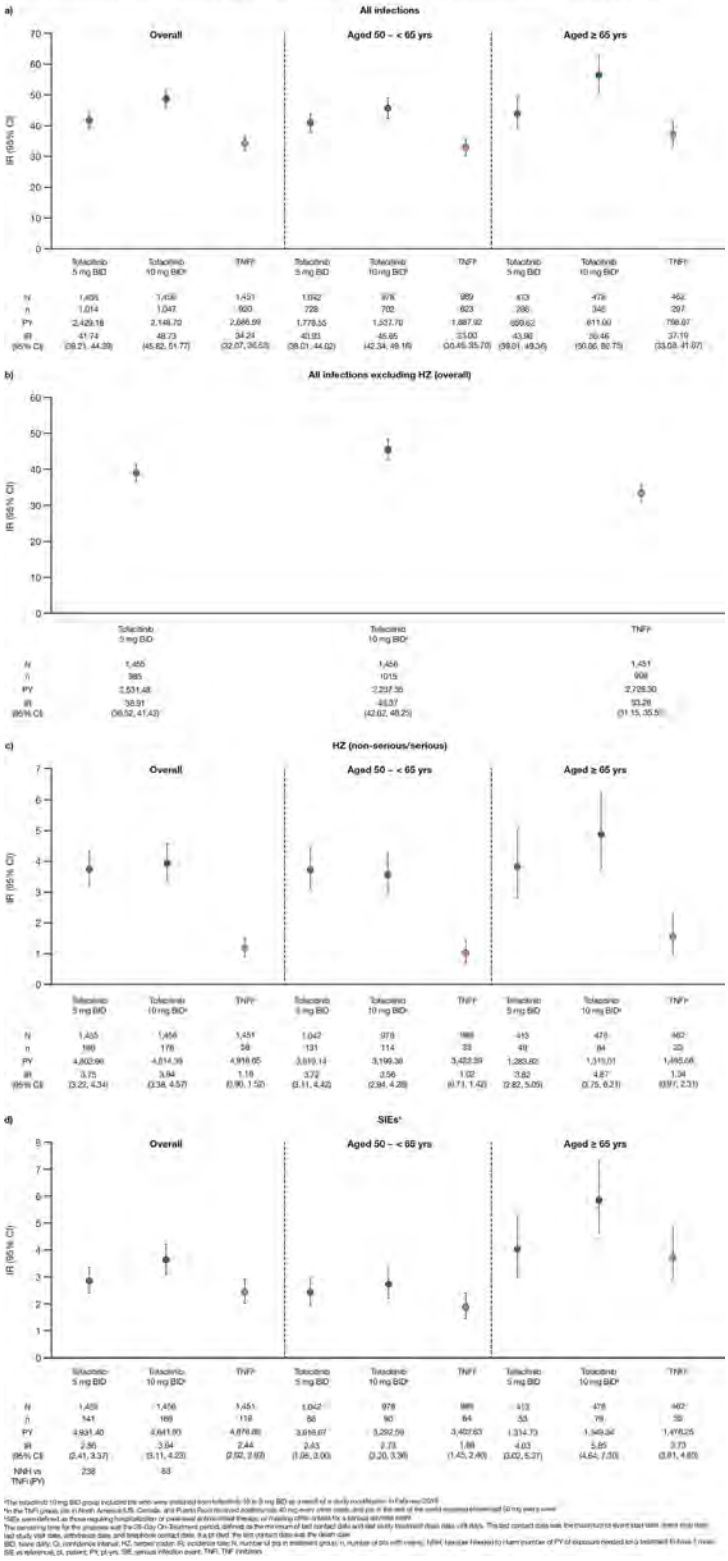

Figure 1. IRs (95% CI) in ORAL Surveillance for a) all infections (overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs]), b) all infections excluding HZ (overall), c) HZ (non-serious/serious; overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs]), and d) SIEs (overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs])

TNFi,[1,2] while herpes zoster (HZ) rates are higher with tofacitinib.[2] Here, we characterized infections in ORAL Surveillance (NCT02092467).

Methods: ORAL Surveillance was a long-term, randomized, open-label, non-inferiority, Phase 3b/4 safety endpoint study of tofacitinib vs TNFi in patients (pts) aged ≥ 50 yrs with active RA despite MTX treatment and ≥ 1 additional

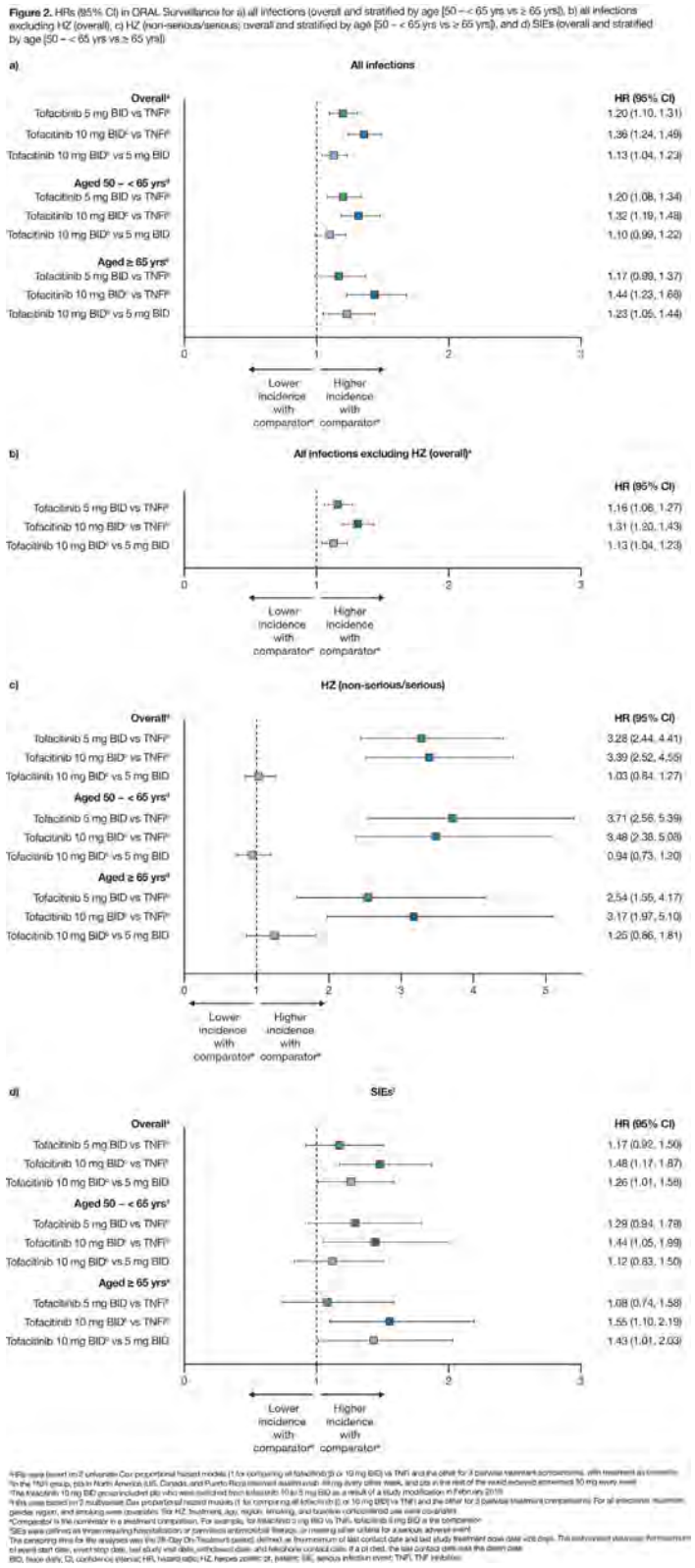

Figure 2. HRs (95% CI) in ORAL Surveillance for a) all infections (overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs]), b) all infections excluding HZ (overall), c) HZ (non-serious/serious; overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs]), and d) SIEs (overall and stratified by age [50 – < 65 yrs vs ≥ 65 yrs])

cardiovascular (CV) risk factor. Pts were randomized 1:1:1 to receive open-label tofacitinib 5 or 10 mg BID or a TNFi (adalimumab 40 mg every other week [North America]; etanercept 50 mg every week [rest of the world]) with stable background MTX. Incidence of all infections regardless of severity (any adverse event in the infections and infesta-

tions System Organ Class), HZ (non-serious/serious), and SIEs were analyzed overall and by age (50 – < 65 yrs; ≥ 65 yrs). Overall OI and tuberculosis (TB) incidence were also analyzed. Incidence rates (IRs; pts with events per 100 pt-yrs [PY]), hazard ratios (HRs), and Number Needed to Harm (NNH; number of PY of exposure needed for a treatment to have 1 more SIE vs reference) were calculated. First infection events occurring ≤ 28 days after the last dose or up to the last contact date were considered.

Results: Of 4,362 treated pts, 3,009 (69%) were aged 50 – < 65 yrs and 1,353 (31%) were aged ≥ 65 yrs. At baseline, mean age was 61.2 yrs, mean RA duration was 10.4 yrs, and pts had active disease (mean Clinical Disease Activity Index 39.8). Across treatment groups, 5.3–5.9% of pts were reported to have been vaccinated for HZ prior to or during the study. Respiratory infections, urinary tract infections, and HZ were the most common infections with tofacitinib (Table). Incidence of all infections was higher for tofacitinib vs TNFi, with notably higher HZ incidence for tofacitinib (Figure 1a–c, Figure 2a–c). Across treatments, > 90% of HZ cases were non-serious, and > 92% were mild/moderate in severity. IRs of all infections, HZ, and SIEs were generally higher in pts aged ≥ 65 vs 50 – < 65 yrs (Figure 1). For SIEs, IRs were numerically higher for tofacitinib vs TNFi (Figure 1d). HRs for SIEs were > 1 for tofacitinib 5 or 10 mg BID vs TNFi and tofacitinib 10 vs 5 mg BID; for tofacitinib 10 mg BID vs TNFi, 95% CIs were > 1 (Figure 2d). NNH for SIEs were 238 PY and 83 PY for tofacitinib 5 and 10 mg BID vs TNFi, respectively (Figure 1d). OI IRs were numerically higher for tofacitinib vs TNFi, due to HZ OI (adjudicated; data not shown). TB IRs were: tofacitinib 5 mg BID, 0.02; tofacitinib 10 mg BID, 0.10; TNFi, 0.10.

Conclusion: In pts aged ≥ 50 yrs with RA and ≥ 1 additional CV risk factor, overall incidence of infections was higher for tofacitinib vs TNFi, with notably higher HZ IRs. Incidence of SIEs was numerically higher for both tofacitinib doses vs TNFi and for tofacitinib 10 vs 5 mg BID; for tofacitinib 10 mg BID vs TNFi, 95% CIs for SIE HRs were > 1.

References

1. Fleischmann R et al. Lancet 2017; 390: 457-68.

2. Kremer JM et al. ACR Open Rheumatol 2021; 3: 173-84.

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Disclosure: A. Bălănescu, AbbVie, 2, 6, Pfizer Inc, 1, 2, 6, Amgen, 2, 6, AstraZeneca, 6, Angelini, 6, Bristol-Myers Squibb, 1, 6, Berlin-Chemie, 6, MSD, 1, 2, 6, Novartis, 1, 2, 6, Roche, 1, 2, 6, Sandoz, 6, Teva, 6, UCB, 1, 3, 6, Zentiva, 6, Akros, 1, 2, Alfasigma, 6, Biogen, 2, Eli Lilly, 2, GSK, 1, Mylan, 2; **G. Citera**, AbbVie, 2, 5, Eli Lilly, 2, Genzyme, 2, Pfizer Inc, 2, Sanofi-Genzyme, 2, 5, Amgen, 2, 5, Gema, 2, 5, Novartis, 2, 5; **V. Pascual-Ramos**, Instituto Nacional de Ciencias Médicas y Nutrición, 3, Bristol-Myers Squibb, 12, Principal Investigator in sponsored studies, Pfizer Inc, 12, Principal Investigator in sponsored studies; **C. Connell**, Pfizer Inc, 3, 11; **D. Gold**, Pfizer Inc, 3, 11; **A. Chen**, Pfizer Inc, 3, 11; **H. Shi**, Pfizer Inc, 3, 11; **A. Shapiro**, Pfizer Inc, 3, 11; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **H. Schulze-Koops**, Roche/Chugai, 2, 5, 6, Sobi, 6, Novartis, 2, 5, 6, AbbVie, 2, 5, 6, Amgen, 2, 6, Bristol-Myers Squibb, 2, 6, Celgene, 2, 6, Celltrion, 2, 6, Chugai, 2, 6, Gilead Sciences, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, Pfizer Inc, 2, 6, Sanofi, 2, 6, Galapagos, 1, 2, UCB, 1, 2.

Abstract Number: 1685

Efficacy and Safety of Olokizumab in a Phase III Trial of Patients with Moderately to Severely Active Rheumatoid Arthritis Inadequately Controlled by Methotrexate – Placebo and Active Controlled Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Olokizumab (OKZ) is a humanized monoclonal antibody targeting IL-6 [1]. Here we present the results of a global phase III, head-to-head, randomized placebo (PBO) controlled clinical trial (RCT) in patients with active Rheumatoid Arthritis (RA) despite methotrexate (MTX) with a comparator arm of adalimumab (ADA).

Methods: This double-blind RCT (ClinicalTrials.gov Identifier NCT02760407, CREDO2) was conducted in the United States, European Union, Latin America, United Kingdom and Russia. Patients were randomized 2:2:2:1 to receive subcutaneous (SC) injections of OKZ 64 mg every 2 weeks (q2w), OKZ 64 mg once every 4 weeks (q4w), ADA 40mg q2w or PBO for 24 weeks, on background of MTX.

After week (Wk) 24, eligible patients could continue into an open-label study or enter a Safety Follow-Up Period of 20 weeks.

The primary endpoint was the percent of patients achieving an American College of Rheumatology 20 response (ACR20) at Wk 12.

Secondary endpoints at Wk 12 included the percentage of subjects achieving Disease Activity Score 28-joint count - C-reactive protein (DAS28-CRP) < 3.2 and improvement of physical ability from baseline to Wk 12 measured by the Health Assessment Questionnaire-Disability Index (HAQ-DI); at Wk 24, ACR50 response rate and percentage of sub-

Table 1. Demographic and Other Baseline Characteristics (intent-to-treat population). 1 - 100% patients were on MT; 2 - upper limit of normal 6 mg/L; TJC, tender joint count; SJC, swollen joint count

	OKZ q2w	OKZ q4w	ADA q2w	PBO
Number of Subjects	**464**	**479**	**462**	**243**
Age, mean (SD) years	53.3(11.9)	53.7(12.1)	54.3(12.3)	54.7(11.9)
Female, n (%)	352(75.9)	378(78.9)	363(78.6)	190(78.2)
Duration of RA, mean (range) years	7.5(0.3-38.9)	7.4(0.3-40.5)	7.4(0.3-40.2)	6.9(0.3-42.5)
MTX dose mg/week, mean (SD)[1]	17.0(4.1)	17.2(4.0)	17.3(4.0)	17.1(4.0)
Glucocorticoid use, n (%)	285(61.4)	283(59.1)	257(55.6)	149(61.3)
CRP, mean (SD) mg/L[2]	19.0(21.1)	18.4(18.6)	18.6(18.5)	17.1(17.2)
TJC, mean (SD)	23.9(12.5)	23.6(12.9)	23.9(12.7)	22.4(12.3)
SJC, mean (SD)	14.6(7.3)	15.4(8.8)	15.5(8.0)	14.9(8.5)
DAS28-CRP, mean (SD)	5.9(0.8)	5.8(0.8)	5.9(0.9)	5.8(0.8)
CDAI, mean (SD)	39.4(11.0)	39.4(11.3)	39.3(11.7)	38.7(11.4)
HAQ-DI score, mean (SD)	1.7(0.58)	1.7(0.60)	1.7(0.57)	1.7(0.62)

jects achieving Clinical Disease Activity Index (CDAI) ≤2.8. Safety outcomes included adverse events (AEs), serious adverse events (SAEs) and laboratory abnormalities.

Results: A total of 1648 subjects were randomized. Baseline characteristics were comparable across treatment arms (Table 1).

Most patients completed 24 weeks of treatment: 421 (90.7%) in q2w arm, 437 (91.2%) in q4w arm, 413 (89.4%) in ADA arm and 208 (85.6%) in PBO arm and most enrolled into the open-label extension study: 410 (88.4%), 127 (89.4%), 422 (88.1%), 397 (85.9%) and 199 (81.9%) patients, respectively.

Table 2. Key efficacy results (intent-to-treat population) NRI. NRI, non-responder imputation; LSM, least squares mean; 1, non-Inferiority for each OKZ arm vs ADA is achieved if the lower limit of the 97.5% CI is greater than the protocol defined non-inferiority margin of -12%; 2, non-inferiority for each OKZ arms vs ADA is achieved if the lower limit of the 97.5% CI is greater than the protocol defined non-inferiority margin of -7.5%; **p-value difference from PBO<0.001; ***p-value difference from PBO<0.0001; SE, Standard Error

	OKZ q2w	OKZ q4w	ADA q2w	PBO
Number of Subjects	**464**	**479**	**462**	**243**
ACR20 Response, n (%), Wk 12 (primary endpoint)	326(70.3)***	342(71.4)***	309(66.9)***	108(44.4)
Comparison vs. ADA[1]				
Risk Difference	0.034	0.045		
97.5% Confidence Interval	-0.035, 0.102	-0.022, 0.112		
DAS28-CRP<3.2, n (%), Wk 12	210(45.3)***	219(45.7)***	177(38.3)***	31(12.8)
Comparison vs. ADA[2]				
Risk Difference	0.069	0.074		
97.5% Confidence Interval	-0.003, 0.141	0.002, 0.145		
HAQ-DI, Wk 12				
LSM (SE)	-0.64(0.027)	-0.61(0.026)	-0.61(0.027)	-0.42(0.038)
Treatment Comparison vs PBO				
LSM Difference (SE)	-0.22*** (0.046)	-0.19*** (0.046)	-0.19 (0.046)	
ACR50 Response, n (%), Wk 24	234(50.4)***	240(50.1)***	214(46.3)	55(22.6)
CDAI ≤2.8, n (%), Wk 24	52(11.2)**	58(12.1)**	60(13.0)	10(4.1)

Table 3. Number and percentage of TESAE (Safety Population)

	OKZ q2w	OKZ q4w	ADA q2w	PBO
Number of Subjects	**463**	**477**	**462**	**243**
Subjects with at Least One TESAE	22(4.8%)	20(4.2%)	26(5.6%)	12(4.9%)
Infections and infestations	6(1.3%)	7(1.5%)	16(3.5%)	4(1.6%)
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	3(0.6%)	2(0.4%)	2(0.4%)	3(1.2%)
Investigations (Liver function tests increased)	3(0.6%)	2(0.4%)	1(0.2%)	2(0.8%)
General disorders and administration site conditions	2(0.4%)	1(0.2%)	1(0.2%)	1(0.4%)
Hepatobiliary disorders	2(0.4%)	2(0.4%)	0	1(0.4%)
Nervous system disorders	3(0.6%)	0	2(0.4%)	0
Vascular disorders	2(0.4%)	2(0.4%)	1(0.2%)	0
Cardiac disorders	0	2(0.4%)	2(0.4%)	0
Respiratory, thoracic and mediastinal disorders	1(0.2%)	0	3(0.6%)	0
Gastrointestinal disorders	1(0.2%)	0	2(0.4%)	0
Musculoskeletal and connective tissue disorders	1(0.2%)	0	2(0.4%)	0
Blood and lymphatic system disorders	0	1(0.2%)	1(0.2%)	0
Injury, poisoning and procedural complications	1 (0.2%)	0	0	1 (0.4%)
Eye disorders	0	1 (0.2%)	0	0
Metabolism and nutrition disorders	0	0	1(0.2%)	0
Psychiatric disorders	0	0	1(0.2%)	0
Reproductive system and breast disorders	0	1 (0.2%)	0	0
Surgical and medical procedures	0	1 (0.2%)	0	0

Both regimens of OKZ were statistically superior to PBO in all primary and secondary endpoints. Furthermore, non-inferiority to ADA was demonstrated for the pre-defined endpoints of ACR20 and DAS28-CRP< 3.2 for both OKZ treatment groups (Table 2).

The efficacy outcomes were maintained throughout the 24-week period of the study.

Overall incidence of treatment-emergent adverse events (TEAEs) was 70.0% in OKZ q2w arm; 70.9% in OKZ q4w arm, 65.4% in ADA arm and 63.4% in PBO, TEAEs leading to study treatment discontinuation were reported in 4.5%, 6.3%, 5.6% and 3.7% patients, respectively. The number of deaths were comparable among arms: 3 (0.6%; 2 infections, 1 cerebrovascular accident) in the OKZ q2w arm, 2 (0.4%; 1 infection, 1 myocardial ischemia) in OKZ q4w arm, 1 (0.2%; infection) in ADA arm and 1 (0.4%; sudden death) in PBO.

The most common treatment-emergent serious adverse events (TESAEs) were infections (Table 3).

Conclusion: Treatment with OKZ 64 mg q2w and OKZ 64 mg q4w plus MTX was associated with significant improvements in the signs, symptoms and physical function of RA compared to PBO plus MTX and non-inferior to ADA plus MTX over a 24-week period.

OKZ was generally well tolerated and no new safety signals have been observed.

References

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Disclosure: E. Feist, R-Pharm, 2, 6, Abbvie, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, AB2Bio, 6, BMS, 6, Celgene, 6, Janssen, 6, Eli Lilly, 2, 5, 6, Medac, 6, MSD, 6, Roche/Chugai, 2, 5, 6, Sanofi, 6, Sobi, 6, UCB, 6; **S. Fatenejad**, R-Pharm, 2, 4, Pfizer, 9; **S. Grishin**, R-Pharm, 3; **E. Korneva**, R-Pharm, 3; **E. Nasonov**, Eli Lilly, 2, Abbvie, 2, Pfizer, 2, Hoffmann-La Roche, 2, Biocad, 2, R-Pharm, 2; **A. Rowińska-Osuch**, R-Pharm, 5; **M. Samsonov**, R-Pharm, 3; **R. Fleischmann**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Celltrion, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sanofi-Aventis, 2, 5, UCB, 2, 5, GSK, 2, 5, AstraZeneca, 2, 5, Bayer, 2, 5, Biogen, 5, Flexion, 2, 5, Galapagos, 5, Galvani, 2, 5, Gilead Sciences, 2, 5, Horizon, 5, Noven, 5, Samumed, 5, Scipher, 5, Selecta, 5, Teva Pharmaceuticals, 5, Viela, 5, Vorso, 5.

Abstract Number: 1686

Efficacy and Safety of Olokizumab in a Phase III Trial of Patients with Moderately to Severely Active Rheumatoid Arthritis Inadequately Controlled by TNF-α Inhibitor Therapy

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Olokizumab (OKZ), a humanized monoclonal antibody targeting IL-6, was studied in patients with active Rheumatoid Arthritis (RA) despite methotrexate (MTX) (NCT02760368, NCT02760407) [1]. Here we present the results of a global phase III; randomized placebo (PBO) controlled clinical trial (RCT) in patients with RA with an incomplete response to tumor necrosis factor inhibitors (TNFi).

Methods: Patients with active RA who had failed TNFi (NCT02760433) were enrolled in this double-blind RCT conducted in 11 countries including the USA. Patients were randomized in a 2:2:1 ratio to receive subcutaneous (SC) injections of OKZ 64 mg every 2 weeks (q2w), OKZ 64 mg once every 4 weeks (q4w) or PBO, plus MTX. At week (Wk) 16, all subjects in the PBO group were randomized in a 1:1 ratio to receive either OKZ regimens. After Wk 24, subjects could continue in an open-label study or entered a Safety Follow-Up Period for another 20 weeks.

The primary endpoint was the percent of patients achieving an American College of Rheumatology 20 response rate (ACR20) at Wk 12. Secondary endpoints at WK 12 included the percentage of subjects achieving a Disease Activity Score 28-joint count - C-reactive protein (DAS28-CRP) < 3.2, improvement of physical ability from baseline to Wk 12 measured by the Health Assessment Questionnaire-Disability Index (HAQ - DI), ACR50 response and percentage of subjects achieving a Clinical Disease Activity Index (CDAI) ≤2.8. Safety outcomes were assessed. A hierarchical statistical scheme was pre-defined to control for multiple comparisons.

Results: 368 subjects were randomized and 320 patients (87%) completed the 24-week treatment period. Baseline characteristics were comparable across arms (Table 1).

Both regimens of OKZ were statistically significantly better than PBO in achieving the primary endpoint (Table 2). The efficacy of OKZ was maintained to Wk 24.

Overall incidences of treatment-emergent adverse events (TEAEs) were 65.5% in OKZ q2w, 65.0% in OKZ q4w and 50.7% in PBO. Subsequent randomization of PBO arm to OKZ at Wk 16 did not substantially change the TEAE incidence rate per treatment group: 64.3% in any OKZ q2w and 59.7% in any OKZ q4w. The majority of TEAEs in all groups were of mild or moderate severity.

Incidence of treatment-emergent serious adverse events (TESAEs) were: 12 (7.0%) in subjects treated with OKZ q2w; 6 (3.2%) in subjects treated with OKZ q4w (Table 3).

The most frequently reported TESAEs across all treatment groups were infections and infestations: 2 (1.1%) in OKZ q4w group, 2 (1.2%) in OKZ q2w group.

Table 1. Demographic and Other Baseline Characteristics (intent-to-treat population). 1, 100% patients were on MTX; 2, upper limit of normal 6 mg/L; SD, standard deviation; BMI, body mass index; TJC, tender joint count; SJC, swollen joint count

	OKZ q2w	OKZ q4w	PBO
Number of Subjects	**138**	**161**	**69**
Age, mean (SD) years	53.4(12.7)	53.9(11.7)	53.0(13.7)
BMI, mean (SD)	28.8(7.0)	29.2 (6.0)	28.4 (5.6)
Female, n (%)	122 (88.4%)	130 (80.7%)	55 (79.7%)
Duration of RA, mean (SD) years	11.8(9.2)	12.7 (8.8)	9.8(7.0)
MTX dose mg/week, mean (SD)[1]	16.3(3.7)	16.7(3.8)	16.5(3.8)
Glucocorticoid use, n (%)	78(56.5)	94(58.4)	46(66.7)
CRP, mean (SD) mg/L[2]	20.7(21.7)	21.4(24.3)	19.4(20.2)
TJC, mean (SD)	26.0(13.7)	25.6(12.8)	28.2(13.7)
SJC, mean (SD)	16.8(8.2)	17.0(7.8)	19.3(9.5)
DAS28-CRP, mean (SD)	5.9(0.9)	6.0(0.8)	6.2(0.9)
CDAI, mean (SD)	40.7(12.5)	41.7(10.6)	44.4(11.7)
HAQ-DI score, mean (SD)	1.79(0.533)	1.78(0.558)	1.78(0.639)

Table 2. Key efficacy results (intent-to-treat population) NRI. NRI, non-responder imputation; LSM, least squares mean; respectively; 1, following the gate-keeping strategy, testing for both OKZ regimens was stopped after the HAQ-DI endpoint testing for formal comparison; SE, Standard Error

	OKZ q2w	OKZ q4w	PBO
Number of Subjects	**138**	**161**	**69**
ACR20 Response, n (%) Wk 12 (primary endpoint)	84(60.9)	96(59.6)	28(40.6)
Comparison vs. **PBO** p-value	0.0029	0.0040	-
DAS28-CRP<3.2 Response, n (%) Wk 12	55(39.9)	45(28.0)	8(11.6)
Comparison vs. **PBO** p-value	<0.0001	0.0035	-
HAQ-DI Wk 12			
LSM (SE)	-0.49 (0.048)	-0.39 (0.044)	-0.32 (0.068)
Comparison vs. **PBO** p-value[1]	0.0227	0.1814	
ACR50 Response, n (%) Wk 12	46(33.3)	52(32.3)	11(15.9)
CDAI ≤2.8 Response, n (%) Wk 12	9(6.5)	5(3.1)	0

Table 3. Number and percentage of TESAE (Safety Population). Adverse effects that occurred after the first administration of PBO and prior to any administration of OKZ at or after Week 16 are summarized as a TEAE under PBO

	OKZ q2w	OKZ q4w	PBO
Number of Subjects	**139**	**160**	**69**
Subjects with at Least One TESAE	12(8.6%)	6(3.8%)	0
Infections and infestations	2(1.4%)	2(1.3%)	0
Pneumonia	0	1(0.6%)	0
Sepsis	1(0.7%)	0	0
Cellulitis	1(0.7%)	1(0.6%)	0
Pilonidal cyst	1(0.7%)	0	0
Neoplasms benign, malignant and unspecified (incl. cysts and polyps)	1(0.7%)	0	0
Invasive ductal breast carcinoma	1(0.7%)	0	0
Investigations	2(1.4%)	1(0.6%)	0
Alanine aminotransferase increased	0	1(0.6%)	0
Aspartate aminotransferase increased	1(0.7%)	0	0
Transaminases increased	1(0.7%)	0	0
Immune system disorders	0	1(0.6%)	0
Anaphylactic reaction	0	1(0.6%)	0
Hepatobiliary disorders	1(0.7%)	0	0
Cholecystitis	1(0.7%)	0	0
Renal and urinary disorders	0	1(0.6%)	0
Renal failure	0	1(0.6%)	0
Vascular disorders	1(0.7%)	0	0
Hypertensive crisis	1(0.7%)	0	0
Cardiac disorders	0	1(0.6%)	0
Sinus bradycardia	0	1(0.6%)	0
Gastrointestinal disorders	0	1(0.6%)	0
Gastrointestinal disorder	0	1(0.6%)	0
Musculoskeletal and connective tissue disorders	3(2.2%)	0	0
Intervertebral disc protrusion	1(0.7%)	0	0
Musculoskeletal chest pain	1(0.7%)	0	0
Osteoarthritis	1(0.7%)	0	0
Injury, poisoning and procedural complications	1 (0.7%)	0	0
Hip fracture	1 (0.7%)	0	0
Ulna fracture	1 (0.7%)	0	0
Psychiatric disorders	1(0.7%)	0	0
Anxiety	1(0.7%)	0	0
Death	0	0	0

No serious opportunistic infections including active tuberculosis, major adverse cardiovascular events, gastrointestinal perforations or deaths were reported.

Conclusion: In this global Phase III trial in patients with active RA inadequately controlled by TNFi, treatment with OKZ 64 mg q2w and OKZ 64 mg q4w plus MTX was associated with significant improvements in the signs and symptoms of RA compared to PBO plus MTX over a 24-week period.

Treatment with OKZ q2w and q4w in this difficult to treat population was generally well tolerated and was similar with the established safety profile of IL-6 inhibitors.

References

1. https://clinicaltrials.gov/ct2/home

Disclosure: E. Feist, R-Pharm, 2, 6, Abbvie, 2, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, AB2Bio, 6, BMS, 6, Celgene, 6, Janssen, 6, Eli Lilly, 2, 5, 6, Medac, 6, MSD, 6, Roche/Chugai, 2, 5, 6, Sanofi, 6, Sobi, 6, UCB, 6; **S. Fatenejad**, R-Pharm, 2, 4, Pfizer, 9; **S. Grishin**, R-Pharm, 3; **E. Korneva**, R-Pharm, 3; **M. Luggen**, R-Pharm, 5, Abbvie, 5, Sun Pharmaceuticals, 5, Pfizer, 5, Novartis, 5, Eli Lilly, 5, GSK, 5, Genentech, 2, 5, 6, Nichi-Iko, 2, 5, 6, Amgen, 2, 5, 6; **E. Nasonov**, Eli Lilly, 2, Abbvie, 2, Pfizer, 2, Hoffmann-La Roche, 2, Biocad, 2, R-Pharm, 2; **M. Samsonov**, R-Pharm, 3; **R. Fleischmann**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Celltrion, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sanofi-Aventis, 2, 5, UCB, 2, 5, GSK, 2, 5, AstraZeneca, 2, 5, Bayer, 2, 5, Biogen, 5, Flexion, 2, 5, Galapagos, 5, Galvani, 2, 5, Gilead Sciences, 2, 5, Horizon, 5, Noven, 5, Samumed, 5, Scipher, 5, Selecta, 5, Teva Pharmaceuticals, 5, Viela, 5, Vorso, 5.

Abstract Number: 1687

Integrated Laboratory Abnormality Profiles of Upadacitinib with up to 4.5 Years of Exposure in Patients with Rheumatoid Arthritis Treated in a Phase 3 Clinical Trial

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Upadacitinib (UPA) is an oral Janus kinase inhibitor approved for the treatment of rheumatoid arthritis (RA). The safety and efficacy of UPA has been evaluated across a spectrum of patients (pts) with RA in the Phase 3 SELECT clinical program.[1,2]

We describe long-term laboratory profiles (cut-off date: Jun 30, 2020) associated with exposure to UPA, adalimumab (ADA), and methotrexate (MTX) in pts with RA treated in the SELECT trials.

Methods: Data were analyzed from 6 randomized controlled UPA RA trials.[1,2] The proportions of pts experiencing potentially clinically significant laboratory changes at a single time point were summarized for the following groups: pooled UPA 15 mg once daily (QD; UPA15; 6 trials), pooled UPA 30 mg QD (UPA30; 4 trials), ADA 40 mg every other week (EOW; 1 trial), and MTX monotherapy (1 trial). Pts received UPA with/without background conventional synthetic disease-modifying antirheumatic drugs. Treatment-emergent adverse events are reported as exposure-adjusted

event rates (events/100 patient years [E/100 PY]). Toxicity was graded per OMERACT criteria, or NCI CTCAE for creatine phosphokinase (CPK) and creatinine.

Results: 4413 pts received ≥1 dose of UPA (UPA15 [n=3209]; UPA30 [n=1204]). Exposures were comparable between treatment groups (**Table**). Proportions of pts with Grade (Gr) 3 and 4 decreases in hemoglobin were highest with UPA30 and MTX (**Table**). Rates of anemia, as reported by the investigator, were comparable between UPA15, ADA, and MTX groups (**Figure**); the frequency of UPA-treated pts who discontinued due to anemia was uncommon in all arms. Gr 3 and 4 decreases in neutrophil and lymphocyte counts with UPA were dose-dependent and higher vs ADA or MTX. Discontinuations due to neutropenia and lymphopenia were rare (< 0.1%). Transaminase elevations were more frequent with UPA and MTX vs ADA; however, the proportion of pts who discontinued due to increases in alanine (ALT) or aspartate aminotransferase (AST) were comparable between UPA15 and ADA, and numerically higher with UPA30 and MTX. CPK elevations were more frequent with UPA (**Figure**). Most events were asymptomatic, and the 1 case of rhabdomyolysis in the UPA30 group was unrelated to study drug (which was attributed to influenza).

Conclusion: This long-term analysis of UPA-treated pts with RA showed dose-dependent relationships for several laboratory abnormalities. Incidences of these with UPA15 were similar to MTX but typically higher than with ADA. Treatment discontinuations due to laboratory abnormalities were infrequent and similar across all treatment groups.

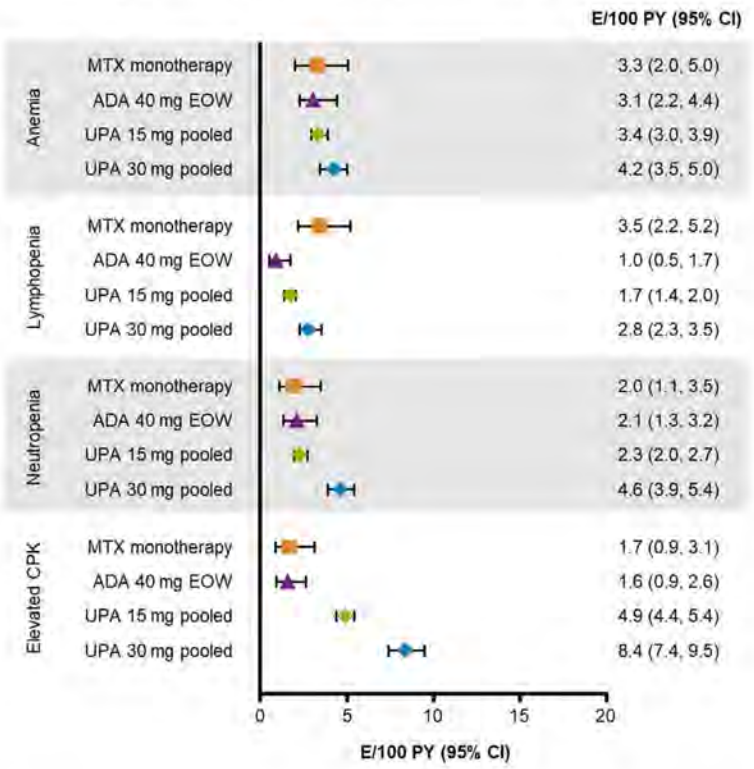
Table. Pts with potentially clinically significant laboratory changes

Variable, n (%)	MTX monotherapy (N=314; 637.4 PY)	ADA 40 mg EOW (N=579; 1051.8 PY)	UPA 15 mg QD (N=3209; 7023.8 PY)	UPA 30 mg QD (N=1204; 3091.6 PY)
Mean (SD) exposure, weeks	106 (67)	95 (70)	114 (64)	134 (66)
Median (range) exposure, weeks	144 (1–221)	118 (2–231)	136 (0–232)	160 (0–231)
Hemoglobin (g/L)				
Gr 3 (70–<80 or decreased 21–<30)	28[a] (9.0)	24[b] (4.2)	254[d] (7.9)	169[f] (14.2)
Gr 4 (<70 or decreased ≥30)	16[a] (5.1)	16[b] (2.8)	101[d] (3.2)	78[f] (6.5)
Neutrophils (10^9/L)				
Gr 3 (0.5–<1.0)	3[a] (1.0)	3[b] (0.5)	40[d] (1.2)	37[g] (3.1)
Gr 4 (<0.5)	1[a] (0.3)	1[b] (0.2)	10[d] (0.3)	5[g] (0.4)
Lymphocytes (10^9/L)				
Gr 3 (0.5–<1.0)	74[a] (23.7)	53[b] (9.2)	802[d] (25.1)	423[g] (35.5)
Gr 4 (<0.5)	5[a] (1.6)	3[b] (0.5)	75[d] (2.3)	47[g] (3.9)
ALT (U/L)				
Gr 3 (3.0–8.0 x ULN)	26[a] (8.3)	13[c] (2.3)	152[e] (4.8)	71[h] (5.9)
Gr 4 (>8.0 x ULN)	5[a] (1.6)	4[c] (0.7)	26[e] (0.8)	10[h] (0.8)
AST (U/L)				
Gr 3 (3.0–8.0 x ULN)	15[a] (4.8)	9[c] (1.6)	101[e] (3.2)	36[h] (3.0)
Gr 4 (>8.0 x ULN)	1[a] (0.3)	5[c] (0.9)	18[e] (0.6)	8[h] (0.7)
CPK (U/L)				
Gr 3 (>5.0–10.0 x ULN)	2[a] (0.6)	3[c] (0.5)	65[e] (2.0)	36[i] (3.0)
Gr 4 (>10.0 x ULN)	0[a] (0)	3[c] (0.5)	27[e] (0.8)	15[i] (1.3)
Creatinine (µmol/L)				
Gr 3 (>3.0–6.0 x ULN)	0[a] (0)	1[c] (0.2)	3[e] (<0.1)	2[i] (0.2)
Gr 4 (>6.0 x ULN)	0[a] (0)	4[c] (0.7)	8[e] (0.3)	1[i] (<0.1)

[a]n=312. [b]n=576. [c]n=577. [d]n=3201. [e]n=3199. [f]n=1193. [g]n=1192. [h]n=1195. [i]n=1196. [j]n=1197

ULN, upper limit of normal

Figure. TEAEs of special interest in pts treated with UPA, MTX, and ADA[a]



MTX: n=314, PY=637.4; ADA 40 mg EOW: n=579, PY=1051.8; UPA 15 mg pooled: n=3209, PY=7023.8; UPA 30 mg pooled: n=1204, PY=3091.6

[a]Pts who switched from placebo, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from UPA to ADA were included in the ADA analysis set from the start of ADA, and were censored at the time of switch. MTX monotherapy was censored at time of rescue to combination therapy (addition of UPA)

ADA, adalimumab; CI, confidence interval; CPK, creatine phosphokinase; E/100 PY, events per 100 patient-years; EOW, every other week; MTX, methotrexate; pts, patients; PY, patient-years; TEAEs, treatment-emergent adverse events; UPA, upadacitinib

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Disclosure: C. Charles-Schoeman, AbbVie, 2, 5, Bristol-Myers Squibb, 5, Pfizer Inc, 2, 5, Gilead Sciences, 2, Sanofi-Regeneron, 2; **J. Giles**, AbbVie, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Gilead, 2, Pfizer, 2, 5, UCB, 2; **N. Lane**, Amgen, 2, Pfizer, 2, BriOri Biotech, 4, Makikroft, 2, 6, GSK, 2, UCB, 1; **E. Choy**, Bio-Cancer, 2, 5, Biogen, 2, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 1, 2, 5, 6, Sanofi, 1, 2, 5, 6, UCB, 1, 2, 5, 6, Amgen, 2, 5, 6, Biocon, 2, Chugai Pharma, 2, 5, 6, Eli Lilly, 1, 2, 5, 6, 12, Support for attending meetings and/or travel, Gilead, 1, 2, 5, 6, 12, Support for attending meetings and/or travel, Janssen, 2, 5, Regeneron Pharmaceuticals, Inc., 2, 5, 6, Abbvie, 2, 12, Support for attending meetings and/or travel, Bristol Myers Squibb, 2, 5, 6, Galapagos, 1, 2, 6, Merck Serono, 2, Boehringer Ingelheim, 2, 5, 6, AstraZeneca, 2, 5, Celgene, 2, 5, Chelsea Therapeutics, 2, 5, Daiichi Sankyo, 2, 5, Ferring Pharmaceuticals, 2, 5, GlaxoSmithKline, 2, 5, Hospira Pharmaceuticals, 2, 5, Ionis Pharmaceuticals, 2, 5, Jazz Pharmaceuticals, 2, 5, MedImmune, 2, 5, Merck Sharp & Dohme, 2, 5, 6, Merrimack Pharmaceuticals, 2, 5, Napp, 2, 5, Novimmune, 2, 5, ObsEva, 2, 5, R-Pharm, 2, 5, SynAct Pharma, 2, 5, Tonix, 2, 5; **D. Furst**, Actelion, 2, 5, Amgen, 2, 5, BMS, 2, 5, Corbus, 2, 6, Galapagos, 2, 5, GSK, 6, Sanofi, 2, 5, 6, Roche/Genentech, 5, National Institutes of Health, 5, Novartis, 2, 5, Pfizer, 2, 5; **J. Vencovsky**, AbbVie, 1, 6, Boehringer Ingelheim, 2, Eli Lilly, 1, 6, Gilead, 1, Octapharma, 1, Biogen, 6, MSD, 6, Pfizer, 6, Roche, 6, Sanofi, 6, UCB, 6, Novartis, 6, Werfen, 6; **A. Wilson**, None; **G. Burmester**, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6; **T. Shaw**, AbbVie, 3, 11;

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Abstract Number: 1688

Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis up to 9.3 Years: An Updated Integrated Safety Analysis

Peter C Taylor[1], Tsutomu Takeuchi[2], Gerd Burmester[3], Patrick DUREZ[4], Josef Smolen[5], Walter Deberdt[6], Jinglin Zhong[7], Jorge Ross Terres[6], Natalia Bello[6] and Kevin Winthrop[8], [1]University of Oxford, Oxford, United Kingdom, [2]Div. Rheumatology, Keio University, Tokyo, Japan, [3]Charité University Medicine Berlin, Berlin, Germany, [4]Pôle de Recherche en Rhumatologie, Institut de Recherche Expérimentale et Clinique, Brussels, Belgium, [5]Medical University of Vienna, Vienna, Austria, [6]Eli Lilly and Company, Indianapolis, IN, [7]IQVIA, Morrisville, NC, [8]Oregon Health & Science University, Portland, OR

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib (bari) is an oral selective Janus kinase (JAK)1/JAK 2 inhibitor approved for the treatment of adult patients with moderately to severely active rheumatoid arthritis (RA). The objective of this analysis was to report bari's safety profile with data up to 9.3 years of treatment.

Methods: Pooled data from 9 randomized (5 Phase 3, 3 Phase 2, 1 Phase 1b) and 1 long-term extension (LTE) study were assessed. Incidence rates (IR) per 100 patient-years at risk (PYR) were calculated for all patients treated with ≥1 dose of bari (All-bari-RA). Adverse events (AEs) of interest were assessed over time in 48-month intervals. Major adverse cardiovascular events (MACE) were adjudicated in 5 Phase 3 studies and the LTE. Incidence rates for MACE were also evaluated in subgroups of patients age ≥50 years and presenting with ≥1 cardiovascular risk factor (current smoker, hypertension, high-density lipoprotein cholesterol < 40 mg/dL, diabetes, or arteriosclerotic cardiovascular disease). To account for aging of the cohort, a standardized incidence ratio (SIR) for malignancy (excluding non-melanoma skin cancer [NMSC]) was estimated using the Surveillance, Epidemiology, and End Results 17 (SEER17), 2013-2017 US population cancer rates, and a standardized mortality ratio (SMR) was estimated using 2019 US population mortality calculated as compared to the general US population with the same age distribution. Exposure adjusted IRs (EAIRs) for deep vein thrombosis (DVT), pulmonary embolism (PE), and DVT and/or PE (DVT/PE) were also calculated for groups of patients while receiving bari 2-mg or bari 4-mg within All-bari-RA.

Results: A total of 3770 patients received bari for 14,744.4 PYE with a median exposure of 4.6 years and a maximum exposure of 9.3 years; 80.5% of PYE were bari 4-mg and 18.1% of PYE were bari 2-mg. Overall, EAIRs per 100 PYE for any treatment-emergent AE and serious AE (including death) were 22.6 and 7.4, respectively (Table). Overall IRs per 100 PYR were 2.58 for serious infections; 0.35 for DVT, 0.26 for PE, 0.49 for DVT/PE, 0.51 for MACE, and 0.92 for malignancy; IRs remained stable over time (Figure). The IR (95% CI) of MACE for patients age ≥50 years was 0.68 (0.52, 0.88). In patients age ≥50 with ≥1 of the cardiovascular risk factors, IR (95% CI) of MACE was 0.77 (0.56, 1.04). The SIR (95% CI) for malignancies excluding NMSC based on the SEER17 standard was 1.07 (0.90, 1.26); the SMR (95% CI) was 0.74 (0.59, 0.92) showing that the incidence of malignancy and death in patients treated with bari appear similar to the general US population. EAIRs (95% CI) for patients while receiving bari 2-mg (PYE=2678) and bari 4-g (PYE=11,872) were DVT 2-mg 0.41 (0.21, 0.73) and 4-mg 0.35 (0.25, 0.48); PE 2-mg 0.26 (0.11, 0.54) and 4-mg 0.27 (0.18, 0.38); and DVT/PE 2-mg 0.49 (0.26, 0.83) and 4-mg 0.51 (0.39, 0.66).

Safety summary among patients with RA treated with at least one dose of baricitinib (All-bari-RA analysis set)	
	n (EAIR per 100 patient years exposure)
Treatment emergent AE	3421 (22.63)
Serious AE (including death)	1117 (7.39)
Temporary d/c due to AE	1282 (8.48)
Permanent d/c due to AE	704 (4.66)
	N (IR per 100 patient years at risk)
Death	85 (0.56)
Serious infection	372 (2.58)
Opportunistic infection (excluding tuberculosis, including multidermatomal herpes zoster)	69 (0.46)
Herpes zoster	422 (2.98)
Tuberculosis	19 (0.13)
Major adverse cardiovascular events*	73 (0.51)
DVT	52 (0.35)
PE	39 (0.26)
DVT and/or PE	73 (0.49)
Malignancies excluding NMSC	139 (0.92)
NMSC	50 (0.33)
Lymphoma	9 (0.06)
Lung cancer	24 (0.16)
Gastrointestinal perforation	9 (0.06)

Note: Data are IR unless otherwise indicated.
IR is 100 times the number of patients experiencing the adverse event divided by the event-specific exposure to treatment (exposure time up to the event for patients with the event and exposure time up to the end of the period including follow up for patients without the event), in years.
EAIR is expressed as the number of patients experiencing an adverse event per 100 patient years of exposure and is 100 times the number of patients experiencing the adverse event divided by the sum of all patient exposure time (in years).
AE=adverse event; D/C= discontinuation; DVT=deep vein thrombosis; EAIR=exposure adjusted incidence rate; IR=incidence rate per 100 patient-years at risk; NMSC=non-melanoma skin cancer; PE=pulmonary embolism.

Table.

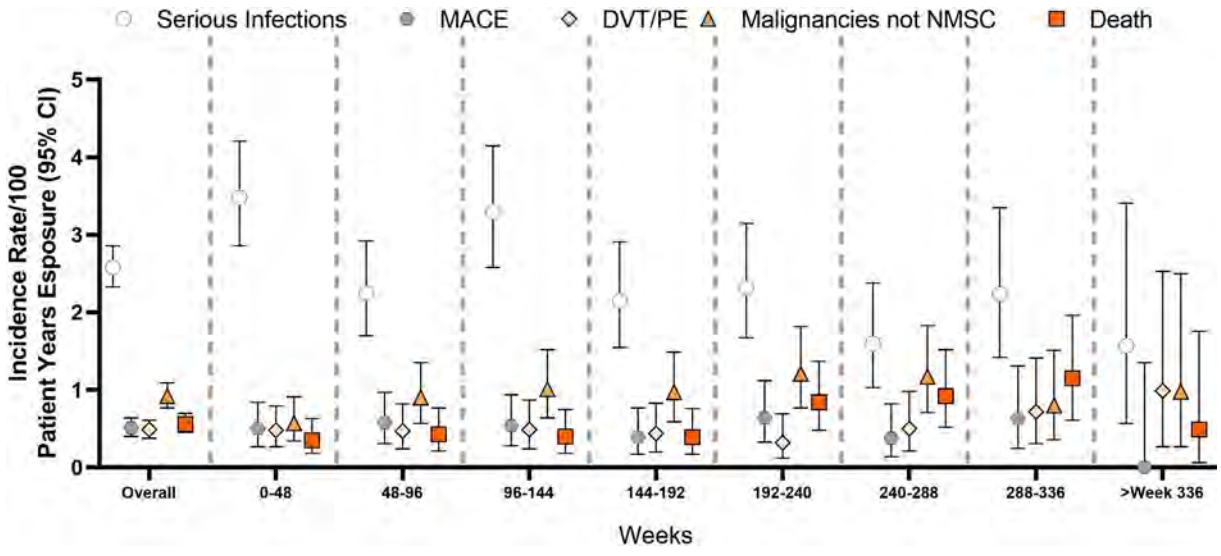

Figure. Incidence rates by 48-week exposure intervals.

Conclusion: In this report with 14,774 PYE, bari maintained a safety profile similar to that previously reported[1-3] with no increase of IRs across safety events through exposures up to 9.3 years.

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2. Genovese MC et al. Ann Rheum Dis. 2019;78(supp. 2):A308
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Abstract Number: 1689

Safety, Tolerability, Pharmacokinetics, Receptor Occupancy, and Suppression of T-cell-Dependent Antibody Response in a Phase 1 Study with KPL-404, an anti-CD40 Monoclonal Antibody

Manoj Samant[1], Alistair Wheeler[2], Guang-Liang Jiang[1], Moses Njenga[1], Madeline Spiers[1], Arian Pano[1] and John F Paolini[1], [1]Kiniksa Pharmaceuticals Corp., Lexington, MA, [2]Kiniksa Pharmaceuticals, Ltd., Hamilton, Bermuda

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: T-cell priming and T-cell-dependent B-cell responses require an intact cluster of differentiation (CD)40/CD40L pathway. CD40 is expressed on the surface of B-cells, dendritic cells, antigen-presenting cells, and non-immune cell types; its ligand, CD40L (CD154), is expressed on the surface of activated T-cells, platelets, and other cell types. Blockade of CD40/CD40L interaction has been shown to ablate primary and secondary T-cell dependent antibody response (TDAR). We hypothesized that KPL-404, an anti-CD40 monoclonal antibody which inhibits interaction between CD40 and CD40L, would block T-cell dependent, B-cell-mediated autoimmunity in this Phase 1 study in healthy participants.

Methods: This randomized, double-blind, placebo-controlled, first-in-human study of KPL-404 in healthy participants was designed with two single-ascending-dose arms: single intravenous (IV) doses of 0.03 mg/kg, 0.3 mg/kg, 1 mg/kg, 3 mg/kg, or 10 mg/kg and single subcutaneous (SC) doses of 1 mg/kg or 5 mg/kg. The primary objective was safety and tolerability of KPL-404; secondary and exploratory objectives included pharmacokinetic (PK) parameters, TDAR

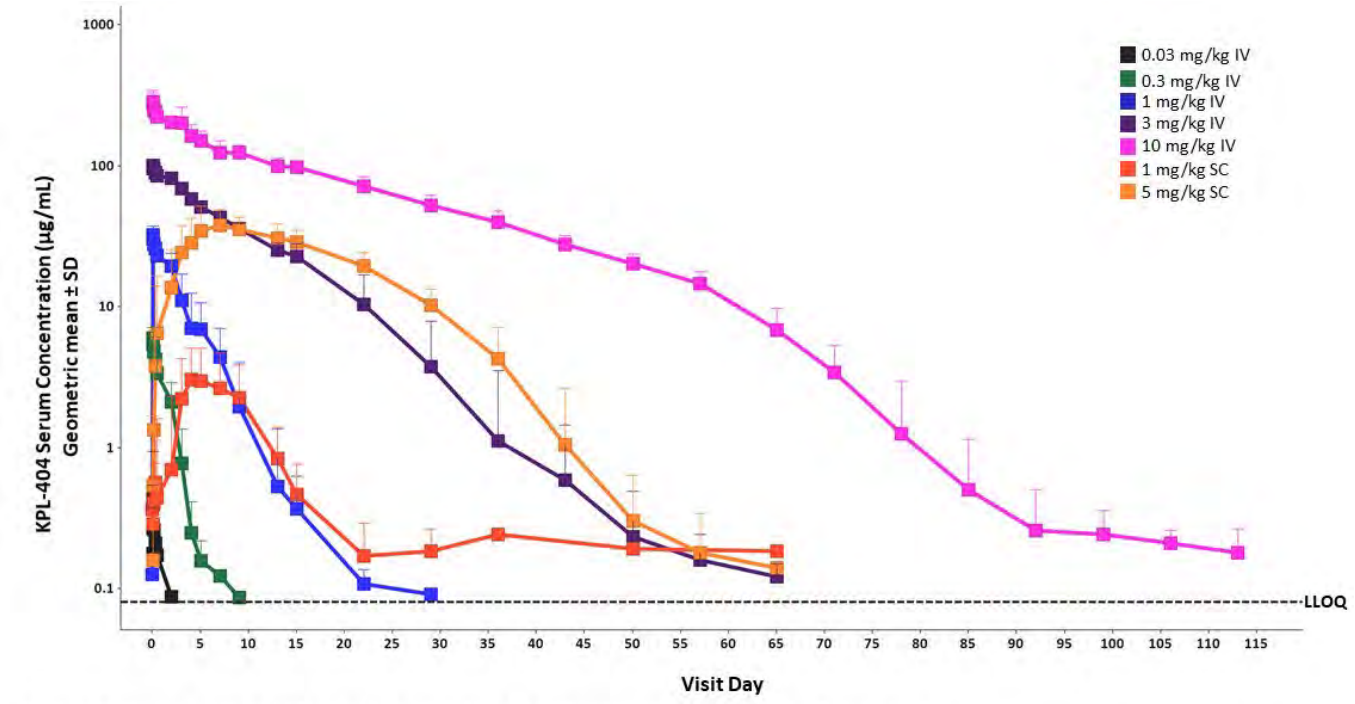

Figure 1. Pharmacokinetic profiles for KPL-404.

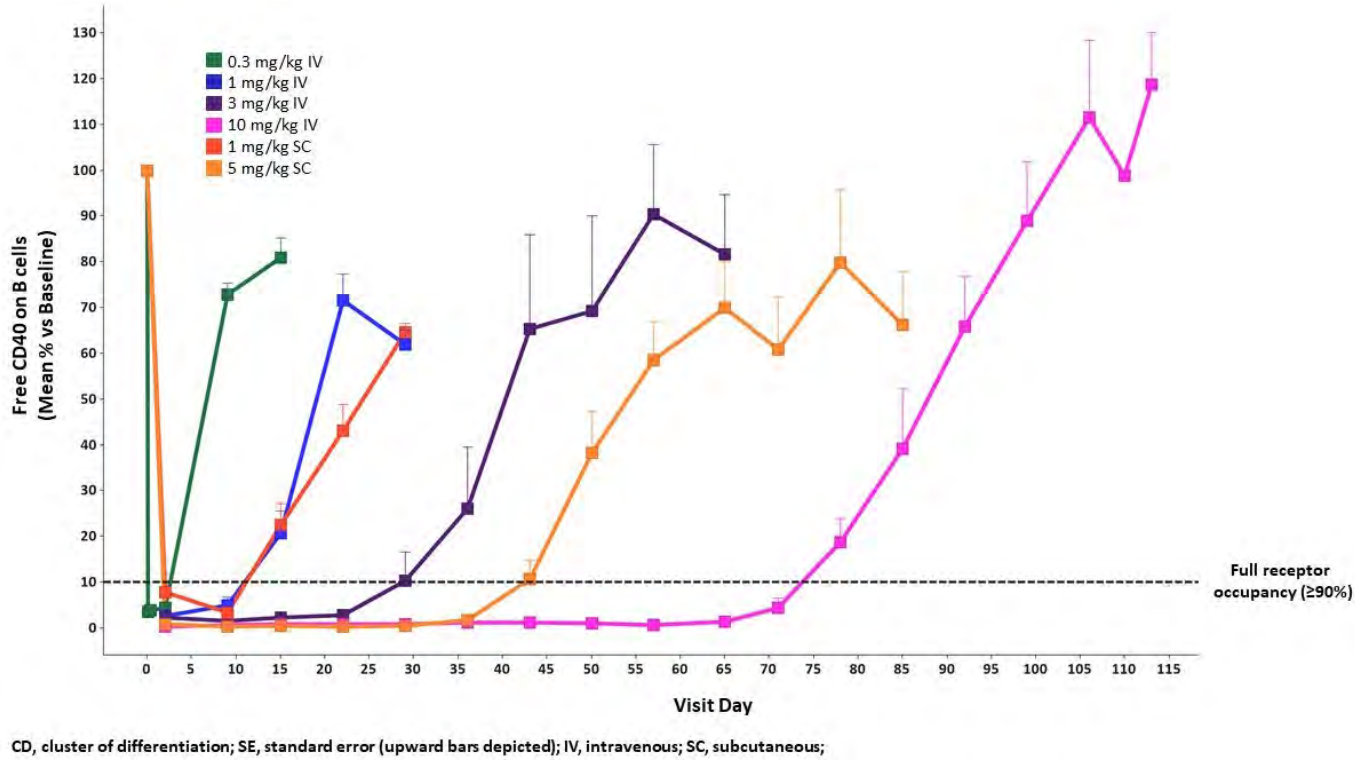

Figure 2. CD40 Receptor Occupancy (RO) on B cells (whole blood) as compared to baseline.

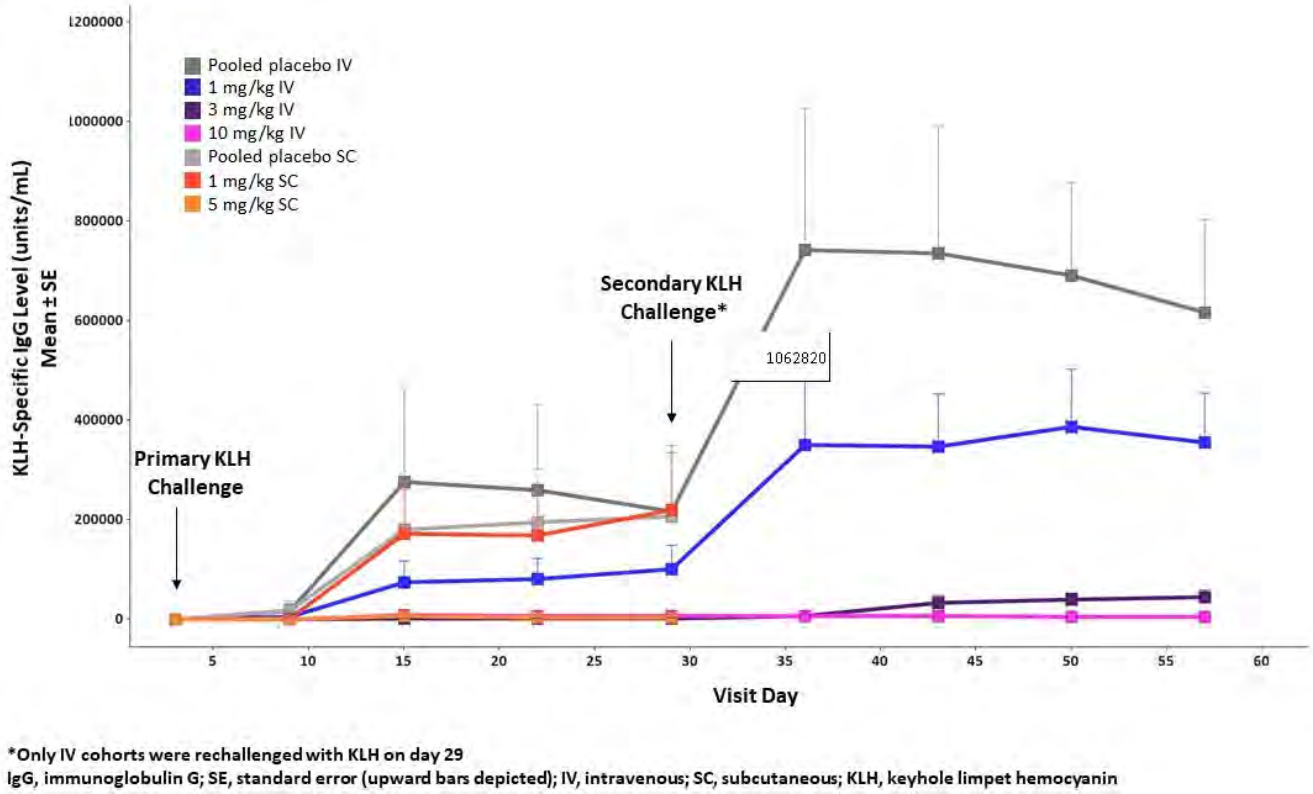

Figure 3. T-Cell Dependent Antibody Response (TDAR) to KLH antigen challenge.

inhibition, and receptor occupancy (RO). To evaluate TDAR inhibition, participants post-KPL-404 administration were immunized with 1 mg intramuscular injection of the test antigen Keyhole Limpet Hemocyanin (KLH) on day 4 and day 29 to elicit a primary and secondary Immunoglobulin (Ig) response, respectively. To evaluate RO, free and total CD40 receptor levels (percent change from baseline) on B-cells (whole blood) were measured using flow cytometry.

Results: There were no dose-limiting or dose-related safety findings in healthy participants after KPL-404 administration. One unrelated serious adverse event (patella fracture following a fall) occurred in the 10 mg/kg IV arm. The PK profile of KPL-404 in serum after IV or SC administration had low to moderate variability between individuals; elimination was dose-dependent and consistent with target-mediated drug disposition (TMDD) (Figure 1). For participants receiving 10 mg/kg IV, full receptor occupancy was observed through day 71 (Figure 2), complete TDAR suppression was observed through Day 57 (Figure 3), and anti-drug antibodies to KPL-404 were suppressed for at least 57 days; the suppression of antibody responses to the drug itself is an independent indicator of target engagement and pharmacodynamic effect. For participants receiving 5 mg/kg SC, full receptor occupancy was observed through day 43 (Figure 2), and complete TDAR suppression was observed through Day 29 (Figure 3). The TDAR response to KLH antigen correlated with the observed full RO.

Conclusion: The safety and tolerability data and the PK/PD profile of KPL-404 support further investigation of KPL-404 in a broad range of autoimmune diseases, including rheumatoid arthritis. These data support the optionality for studying chronic KPL-404 dosing in patients with subcutaneous and/or intravenous administration.

Disclosure: M. Samant, Kiniksa Pharmaceuticals Corp., 3, 11; **A. Wheeler**, Kiniksa Pharmaceuticals, Ltd., 2; **G. Jiang**, Kiniksa Pharmaceuticals Corp., 3, 11; **M. Njenga**, Kiniksa Pharmaceuticals Corp., 3, 11; **M. Spiers**, Kiniksa

Pharmaceuticals Corp., 3, 11; **A. Pano**, Kiniksa Pharmaceuticals Corp., 3, 11; **J. Paolini**, Kiniksa Pharmaceuticals Corp., 2, 10, 11.

Abstract Number: 1690

Safety and Efficacy of Long-term Sarilumab Treatment in Patients with Active Rheumatoid Arthritis: EXTEND and MONARCH Open Label Extension Studies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In patients who experience intolerance or fail to respond to methotrexate, IL-6 receptor inhibitors (e.g. sarilumab) are one of the recommended options. The aim of this analysis was to assess the long-term safety and efficacy of sarilumab in patients with RA using data from two open-label studies: EXTEND (NCT01146652) and MONARCH (NCT02332590) open label extension (OLE).

Methods: EXTEND included patients from five trials which evaluated patients who were either inadequate responders to conventional synthetic DMARDs or biologic DMARDs. Patients enrolled in EXTEND received sarilumab 150 mg or 200 mg q2w (once every two weeks) based on their initial treatment for ≥264 weeks. MONARCH OLE included patients who completed the 24-week double blind (DB) period of the MONARCH study and opted to receive open label sarilumab 200 mg q2w for 276 weeks. Safety endpoints included treatment emergent adverse events (TEAEs), serious adverse events (SAEs), adverse events of special interest (AESI), and anti-drug antibody (ADA) positivity. Key efficacy endpoints were ACR 20/50/70 responses, mean change from baseline in DAS28-CRP, and clinical disease activity index for RA (CDAI). Safety and efficacy analyses in both open-label studies were descriptive.

Results: Total duration of sarilumab (N=111) and sarilumab+DMARD (N=1910) exposure was 453.8 patient years (PY) and 8552.7 PY in EXTEND and the cumulative duration of exposure to sarilumab (N=320) in MONARCH OLE was 1131.9 PY. Both studies had more females with a mean age of approximately 50 years. At least one TEAE was reported in 92.1% and 88.3% of patients in EXTEND and 86.9% of patients in MONARCH OLE; infections and infestations were the most common TEAEs in both studies. At least one SAE was reported in 32.3% and 24.3% of patients in EXTEND and 17.5% of patients in MONARCH OLE. In both studies, approximately 2.0% of patients died due to TEAEs. The number of patients who discontinued the treatment due to TEAEs were 26.0% and 13.5% in EXTEND and 13.1% in MONARCH OLE. Herpes Zoster was the most frequently reported opportunistic AESI in EXTEND (44/74 opportunistic infections) and MONARCH OLE (7/10 opportunistic infections). A detailed summary of adverse events reported in both studies is presented in **Table**. ADA positivity was low in both EXTEND and MONARCH OLE and was not associated with hypersensitivity reactions or discontinuations due to lack of efficacy. Clinical efficacy, measured as ACR 20/50/70 responses, mean changes from baseline in DAS28-CRP, and CDAI was maintained throughout the duration of both studies (**Figure 1 and Figure 2**).

Table. Summary of AESI and most common TEAEs, SAEs, and TEAEs leading to discontinuation in EXTEND and MONARCH OLE

	EXTEND (Safety population)			
	Sarilumab, (N=111)	Sarilumab, n_E (n_E/100 PY) (PY=464.3)	Sarilumab+DMARD, (N=1910)	Sarilumab+DMARD, n_E (n_E/100 PY) (PY=8758.5)
Any TEAE	98 (88.3%)	584 (125.8)	1760 (92.1%)	14839 (169.4)
Most Common TEAEs[a]				
Accidental overdose[b]	20 (18.0%)	22 (4.7)	331 (17.3%)	497 (5.7)
Neutropenia	18 (16.2%)	64 (13.8)	351 (18.4%)	796 (9.1)
Rheumatoid arthritis	17 (15.3%)	32 (6.9)	254 (13.3%)	389 (4.4)
Upper respiratory tract infection	16 (14.4%)	21 (4.5)	305 (16.0%)	576 (6.6)
Urinary tract infection	14 (12.6%)	22 (4.7)	267 (14.0%)	432 (4.9)
Nasopharyngitis	14 (12.6%)	26 (5.6)	249 (13.0%)	390 (4.5)
Bronchitis	12 (10.8%)	19 (4.1)	218 (11.4%)	305 (3.5)
Hypertension	4 (3.6%)	5 (1.1)	237 (12.4%)	273 (3.1)
Alanine aminotransferase increased	4 (3.6%)	4 (0.9)	209 (10.9%)	296 (3.4)
Any SAEs	27 (24.3%)	41 (8.8)	617 (32.3%)	1081 (12.3)
Most Common SAEs[c]				
Osteoarthritis	2 (1.8%)	2 (0.4)	45 (2.4%)	52 (0.6)
Pneumonia	1 (0.9%)	1 (0.2)	52 (2.7%)	55 (0.6)
Rheumatoid arthritis	1 (0.9%)	1 (0.2)	32 (1.7%)	33 (0.4)
Cholelithiasis	0	0	24 (1.3%)	24 (0.3)
Cellulitis	0	0	21 (1.1%)	24 (0.3)
TEAEs leading to discontinuation	15 (13.5%)	16 (3.4)	496 (26.0%)	553 (6.3)
Most common TEAEs leading to discontinuation[c]				
Herpes Zoster	1 (0.9%)	1 (0.2)	32 (1.7%)	32 (0.4)
Pneumonia	1 (0.9%)	1 (0.2)	20 (1.0%)	20 (0.2)
Neutropenia	0	0	39 (2.0%)	39 (0.4)
Rheumatoid arthritis	0	0	19 (1.0%)	19 (0.2)
AESI				
Infections	61 (55.0%)	168 (36.2)	1246 (65.2%)	3974 (45.4)
Serious Infections	6 (5.4%)	8 (1.7)	225 (11.8%)	288 (3.3)
Opportunistic Infections	0	0	74 (3.9%)	80 (0.9)
Tuberculosis	0	0	7 (0.4%)	7 (0.1)
Diverticulitis/potential GI perforations[d]	2 (1.8%)	2 (0.4)	28 (1.5%)	36 (0.4)
Malignancy	2 (1.8%)	3 (0.6)	45 (2.4%)	49 (0.6)
Malignancy excluding NMSC	2 (1.8%)	3 (0.6)	35 (1.8%)	35 (0.4)
Adjudicated treatment-emergent MACE	3 (2.7%)	3 (0.6)	45 (2.4%)	50 (0.6)

	MONACRCH OLE (Safety population)	
	Sarilumab, (N=320)	Sarilumab, n_E (n_E/100 PY) (PY=1165.4)
Any TEAE	278 (86.9%)	1854 (159.1)
Most Common TEAEs[a]		
Nasopharyngitis	60 (18.8%)	107 (9.2)
Bronchitis	41 (12.8%)	63 (5.4)
Upper respiratory tract infection	36 (11.3%)	52 (4.5)
Accidental overdose[b]	39 (12.2%)	54 (4.6)
Neutropenia	59 (18.4%)	150 (12.9)
Any SAEs	56 (17.5%)	94 (8.1)
Most Common SAEs[c]		
Pneumonia	5 (1.6%)	6 (0.5)
Osteoarthritis	5 (1.6%)	6 (0.5)
Cholelithiasis	4 (1.3%)	4 (0.3)
TEAEs leading to discontinuation	42 (13.1%)	50 (4.3)
Most common TEAEs leading to discontinuation[c]		
Herpes Zoster	5 (1.6%)	5 (0.4)
AESI		
Infections	177 (55.3%)	498 (42.7)
Serious Infections	13 (4.1%)	16 (1.4)
Opportunistic Infections	10 (3.1%)	11 (0.9)
Tuberculosis	1 (0.3%)	1 (0.1)
Diverticulitis/potential GI perforations[d]	1 (0.3%)	1 (0.1)
Malignancy	9 (2.8%)	10 (0.9)
Malignancy excluding NMSC	9 (2.8%)	10 (0.9)
Adjudicated treatment-emergent MACE	3 (0.9%)	3 (0.3)

[a]defined as ≥10% in either group; [b]overdose was defined as the administration of ≥2 sarilumab doses <11 calendar days if sarilumab was administered q2w; [c]defined as ≥1% in either group; [d]cases were medically reviewed to identify cases of GI perforation.
AESI, adverse event of special interest; GI, gastrointestinal; MACE, major adverse cardiac event; n_E, number of events; NMSC, non-melanoma skin cancer; PY, patient years, q2w, once every two weeks; SAE, serious adverse event; TEAE, treatment emergent adverse event.

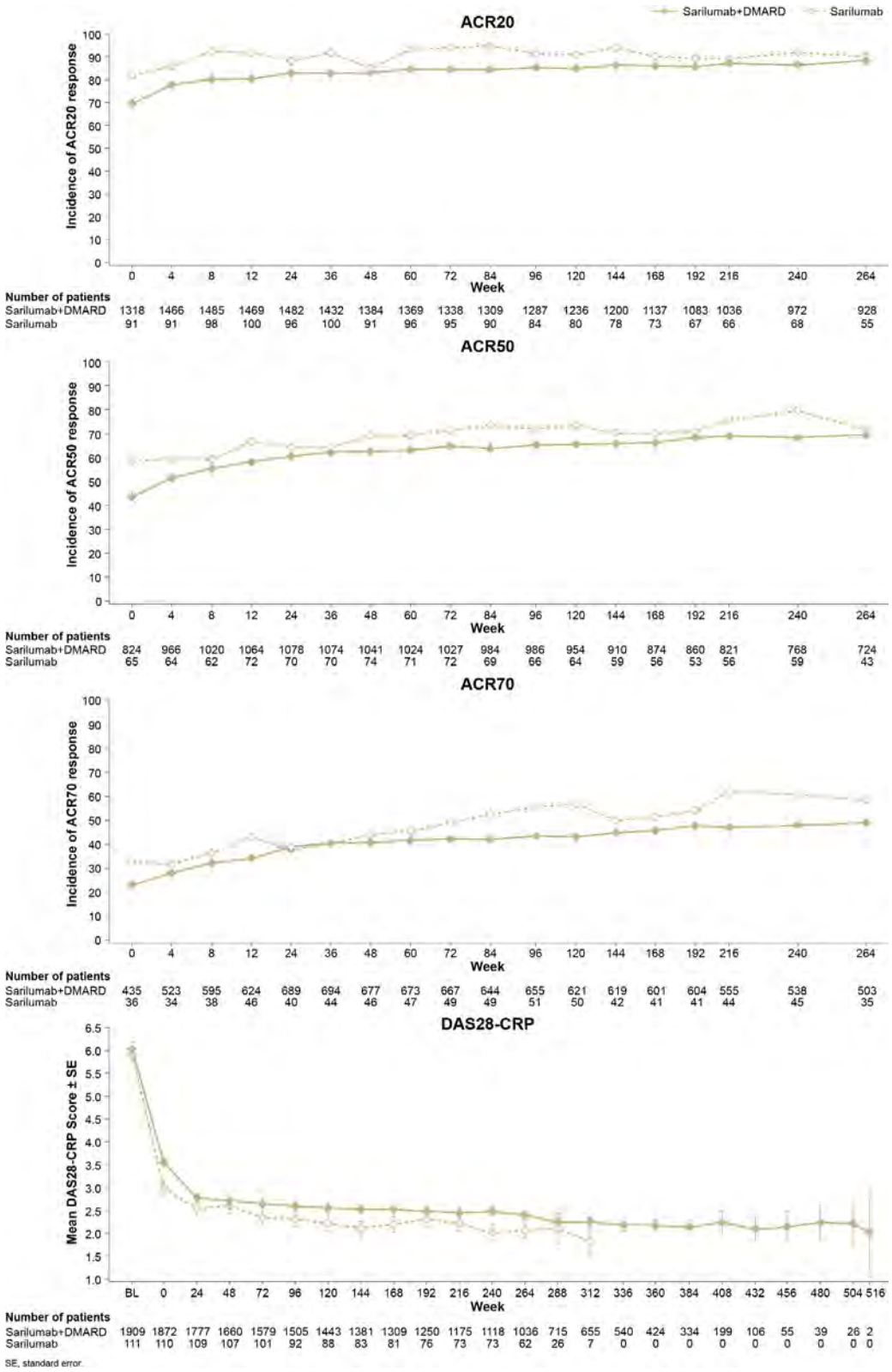
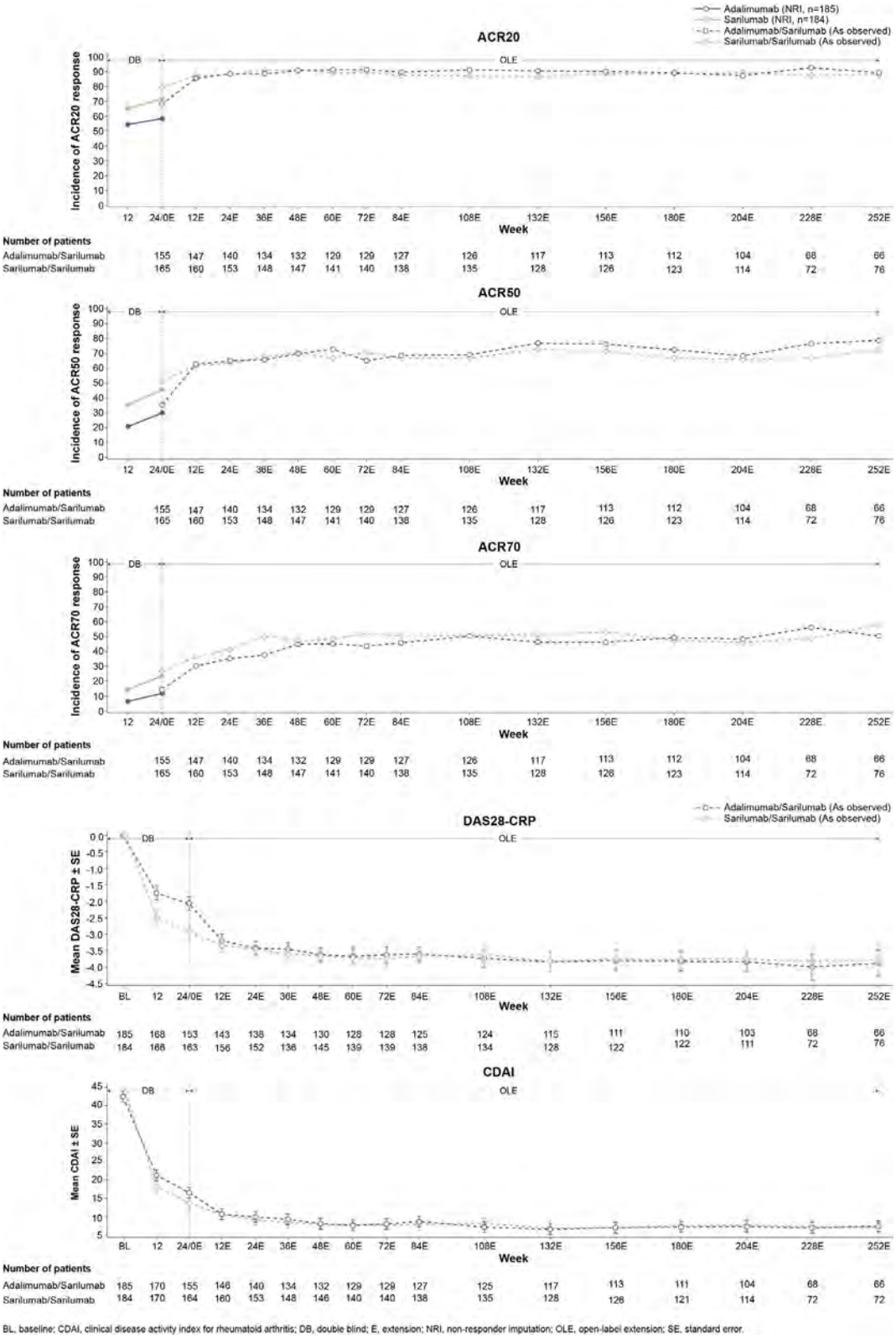


Figure 1. Summary of Efficacy Outcomes in EXTEND (Safety Population).



BL, baseline; CDAI, clinical disease activity index for rheumatoid arthritis; DB, double blind; E, extension; NRI, non-responder imputation; OLE, open-label extension; SE, standard error.

Figure 2. Summary of Efficacy Outcomes in MONARCH OLE (Full Intention to Treat Population).

Conclusion: Treatment of RA patients with sarilumab in EXTEND and MONARCH OLE revealed no new safety findings. Treatment with sarilumab demonstrated maintenance of efficacy, achieved during the DB period, over the entire open label treatment.

Disclosure: G. Burmester, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6; **V. Strand**, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2; **A. Kivitz**, Pfizer, 2, 6, 11, 12, Sanofi, 2, 6, 11, 12, GlaxoSmithKline, 11, Gilead Sciences, Inc.,, 2, 11, Novartis, 2, 6, 12, AbbVie, 2, 6, 11, Boehringer Ingelheim, 2, Janssen, 2, Regeneron, 2, 6, 12, SUN Pharma Advanced Research, 2, Amgen, 11, Lilly, 6, Celgene, 6, 12, Flexion, 2, 6, Genzyme, 2, 6, 12, Merck, 6, 12, UCB, 6, Horizon, 6, 12; **C. Hu**, Sanofi, 3; **S. Wang**, Sanofi, 3; **H. van Hoogstraten**, Sanofi, 3, 11; **R. Tao**, Sanofi, 3; **R. Fleischmann**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Celltrion, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, Sanofi-Aventis, 2, 5, UCB, 2, 5, GSK, 2, 5, AstraZeneca, 2, 5, Bayer, 2, 5, Biogen, 5, Flexion, 2, 5, Galapagos, 5, Galvani, 2, 5, Gilead Sciences, 2, 5, Horizon, 5, Noven, 5, Samumed, 5, Scipher, 5, Selecta, 5, Teva Pharmaceuticals, 5, Viela, 5, Vorso, 5.

Abstract Number: 1691

Long-Term Safety Profile of Upadacitinib in Patients with Rheumatoid Arthritis, Psoriatic Arthritis, or Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The efficacy and safety of the oral Janus kinase inhibitor, upadacitinib (UPA), has been evaluated for several rheumatic diseases. The objective of this analysis is to describe the long-term safety profile of UPA across rheumatoid arthritis (RA), psoriatic arthritis (PsA), and ankylosing spondylitis (AS) from the SELECT clinical program.

Methods: Safety data (cut-off: 30 June 2020) from the UPA SELECT clinical program were compiled for RA (6 trials[1]), PsA (2 trials[2]), and AS (1 trial[3]) for this analysis. Treatment-emergent adverse events (TEAEs; onset on or after first dose and ≤30 days after last dose for UPA and methotrexate [MTX] or ≤70 days for adalimumab [ADA]) were summarized for RA (pooled UPA 15 mg once daily [QD], ADA 40 mg every other week [EOW], and MTX), PsA (pooled UPA 15 mg QD and ADA 40 mg EOW), and AS (UPA 15 mg QD). TEAEs are reported as exposure-adjusted adverse event rates (EAERs; events/100 patient-years [E/100 PY]).

Table: TEAEs in Patients Treated with UPA, ADA, or MTX Across RA, PsA, and AS[†]

	RA			PsA		AS
	UPA 15 mg QD N=3209	ADA 40 mg EOW N=579	MTX N=314	UPA 15 mg QD N=907	ADA 40 mg EOW N=429	UPA 15 mg QD N=182
Exposure						
Total, PY	7023.8	1051.8	637.4	1247.2	549.7	291.1
Median (min, max), weeks	136 (0, 232)	118 (2, 231)	144 (1, 221)	69 (0, 155)	68 (2, 152)	90 (1, 118)
Overall TEAEs, E/100 PY (95% CI)						
Any AE	230.7 (227.2, 234.3)	216.6 (207.8, 225.7)	227.8 (216.2, 239.8)	263.9 (254.9, 272.9)	286.5 (272.4, 300.7)	237.7 (220.3, 256.1)
Any serious AE	13.0 (12.2, 13.9)	13.3 (11.2, 15.7)	10.4 (8.0, 13.2)	10.3 (8.6, 12.1)	9.6 (7.0, 12.2)	6.2 (3.7, 9.8)
Any AE leading to discontinuation	5.6 (5.0, 6.1)	6.8 (5.3, 8.5)	6.3 (4.5, 8.5)	6.7 (5.2, 8.1)	7.8 (5.5, 10.2)	5.5 (3.1, 8.9)
Deaths[‡]	0.4 (0.3, 0.6)	0.9 (0.4, 1.6)	0.5 (0.1, 1.4)	0.2 (-0.1, 0.4)	0.2 (-0.2, 0.5)	0
TEAEs of special interest, E/100 PY (95% CI)						
Serious infection	3.3 (2.9, 3.7)	3.1 (2.2, 4.4)	2.4 (1.3, 3.9)	2.3 (1.5, 3.2)	1.3 (0.3, 2.2)	0
Opportunistic infection[§]	0.3 (0.2, 0.4)	0.2 (0.0, 0.7)	0.2 (0.0, 0.9)	0.4 (0.0, 0.8)	0	0.7 (0.1, 2.5)
Herpes zoster	3.3 (2.9, 3.8)	1.1 (0.6, 2.0)	0.8 (0.3, 1.8)	3.8 (2.8, 4.9)	0.5 (-0.1, 1.2)	1.7 (0.6, 4.0)
Active TB	<0.1 (0.0, 0.2)	0.2 (0.0, 0.7)	0	0	0	0
Malignancy (excl. NMSC)	0.8 (0.6, 1.1)	0.8 (0.3, 1.5)	0.9 (0.3, 2.0)	0.7 (0.3, 1.2)	0.7 (0.0, 1.4)	0.3 (0.0, 1.9)
NMSC	0.3 (0.2, 0.4)	<0.1 (0.0, 0.5)	0	0.8 (0.3, 1.3)	0.4 (-0.1, 0.9)	0
MACE (adjudicated)[‖]	0.4 (0.3, 0.6)	0.3 (0.1, 0.8)	0.3 (0.0, 1.1)	0.3 (0.0, 0.6)	0.5 (-0.1, 1.2)	0
VTE (adjudicated)[¶]	0.5 (0.3, 0.6)	0.5 (0.2, 1.1)	0.3 (0.0, 1.1)	0.3 (0.0, 0.6)	0.4 (-0.1, 0.9)	0
GI perforation (adjudicated)	<0.1 (0.0, 0.2)	0	0	<0.1 (-0.1, 0.2)	0	0
Anemia	3.4 (3.0, 3.9)	3.1 (2.2, 4.4)	3.3 (2.0, 5.0)	2.2 (1.4, 3.1)	1.6 (0.6, 2.7)	1.7 (0.6, 4.0)
Neutropenia	2.3 (2.0, 2.7)	2.1 (1.3, 3.2)	2.0 (1.1, 3.5)	1.8 (1.0, 2.5)	4.7 (2.9, 6.5)	2.7 (1.2, 5.4)
Lymphopenia	1.7 (1.4, 2.0)	1.0 (0.5, 1.7)	3.5 (2.2, 5.2)	2.2 (1.3, 3.0)	0.2 (-0.2, 0.5)	0.7 (0.1, 2.5)
Hepatic disorder	11.7 (10.9, 12.5)	8.6 (6.9, 10.5)	13.3 (10.7, 16.5)	13.6 (11.5, 15.6)	26.6 (22.3, 30.9)	8.2 (5.3, 12.3)
Elevated CPK	4.9 (4.4, 5.4)	1.6 (0.9, 2.6)	1.7 (0.9, 3.1)	9.1 (7.4, 10.7)	7.5 (5.2, 9.7)	10.3 (7.0, 14.7)

ADA, adalimumab; AE, adverse event; AS, ankylosing spondylitis; CI, confidence interval; CPK, creatine phosphokinase; E, event; EOW, every other week; GI, gastrointestinal; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, non-melanoma skin cancer; PsA, psoriatic arthritis; PY, patient years; QD, once daily; RA, rheumatoid arthritis; TB, tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolic event

[†]AEs defined using standardized MedDRA query or company MedDRA query search criteria

[‡]Includes non-treatment-emergent deaths

[§]Excluding TB and herpes zoster

[‖]MACE defined as cardiovascular death, non-fatal myocardial infarction, and non-fatal stroke

[¶]VTE includes deep vein thrombosis and pulmonary embolism

Results: In total, 4298 patients (RA, N=3209; PsA, N=907; AS, N=182) received ≥1 dose of UPA 15 mg, totaling 8562 PY of exposure, with the majority of exposure from RA studies (**Table**). AEs leading to discontinuation were generally similar across all treatment groups (UPA, ADA, and MTX) and patient populations (RA, PsA, and AS). The most common adverse events leading to discontinuation with UPA were pneumonia (RA), psoriatic arthropathy flare or worsening (PsA), and headache (AS). Rates of serious infection and opportunistic infection were generally similar across all treatment groups within each population and across RA, PsA, and AS. Pneumonia was both the most common serious infection and serious AE in RA and PsA. No serious infections were reported in patients with AS. Herpes zoster and increased CPK were reported more often with UPA compared to ADA or MTX, with UPA showing similar rates of herpes zoster across RA, PsA, and AS. Malignancies excluding NMSC were reported at similar rates across all treatment groups and populations. NMSC was not common, with numerically higher rates observed with UPA versus MTX and/or ADA in RA and PsA. Similar rates of adjudicated major adverse cardiovascular events (MACE) and adjudicated venous thromboembolic events (VTE) were observed across all treatment groups, with no events reported in patients with AS. Rates of death reported in these clinical studies were not higher than expected in the general populations. As anticipated for the patient populations, the most common cause of death observed was cardiovascular in nature.

Conclusion: With the exception of herpes zoster, exposure-adjusted adverse event rates were generally similar across UPA, ADA, and MTX in RA, as well as UPA and ADA in PsA. No new safety risks were identified with long-term

treatment in RA, PsA, or AS. UPA 15 mg demonstrated a consistent safety profile across RA, PsA, and AS populations in the SELECT clinical program.

References

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2. Burmester GR, et al. *Ann Rheum Dis*. 2021;80(Suppl 1):1287-8
3. van der Heijde D, et al. *Lancet.* 2019;394:2108-17

Disclosure: G. Burmester, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6; **S. Cohen**, AbbVie, 2, 5, Amgen, 2, 5, Boehringer Ingelheim, 2, 5, Gilead, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 2, 5; **K. Winthrop**, Pfizer, 2, 5, Bristol-Myers Squibb, 2, 5, UCB Pharma, 2, 5, AbbVie, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Glaxo-SmithKline, 2, Regeneron, 2, Sanofi, 2; **P. Nash**, Janssen, 2, 5, 6, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Novartis, 2, 5, 6, Eli Lilly, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Sanofi, 2, 5, 6, Merck, 2, 5, 6, UCB, 2, 5, 6, Gilead/Galapagos, 2, 5, 6, Celgene, 2, 5, 6, Samsung, 2, 5, 6; **A. Rubbert-Roth**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Chugai, 2, 6, Roche, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Eli Lilly, 2, 6, Sanofi, 2, 6, Amgen, 2, 6, Novartis, 2, 6; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **O. Elkayam**, AbbVie, 2, 5, 6; **E. Mysler**, AbbVie, 2, 5, AstraZeneca, 2, 5, Eli Lilly, 2, 5, Pfizer, 2, 5, Roche, 2, 5, BMS, 2, 5, Sandoz, 2, 5, GSK, 2, 5, Janssen, 2, 5; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 6, Novartis, 6, YL Biologics, 6, Bristol-Myers Squibb, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi-kasei, 5, 6, GSK, 2, 6, Mitsubishi-Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Ayumi, 2, Taisho, 2; **J. Liu**, AbbVie, 3, 11; **A. Lacerda**, AbbVie, 3, 11; **B. Pierre-Louis**, AbbVie, 3, 11; **T. Shaw**, AbbVie, 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1692

Long-Term Efficacy and Safety of Upadacitinib in Patients with Rheumatoid Arthritis: 3-year Results from the SELECT-EARLY Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Upadacitinib (UPA), an oral Janus kinase inhibitor, demonstrated significant improvements in signs, symptoms, and structural inhibition as monotherapy (mono) vs methotrexate (MTX) in MTX-naïve patients (pts)

with rheumatoid arthritis (RA) through 48 weeks (wks).[1] The objective of this analysis was to report the efficacy and safety of UPA vs MTX mono up to 156 wks in pts with RA from the ongoing long-term extension (LTE) of the SELECT-EARLY trial.

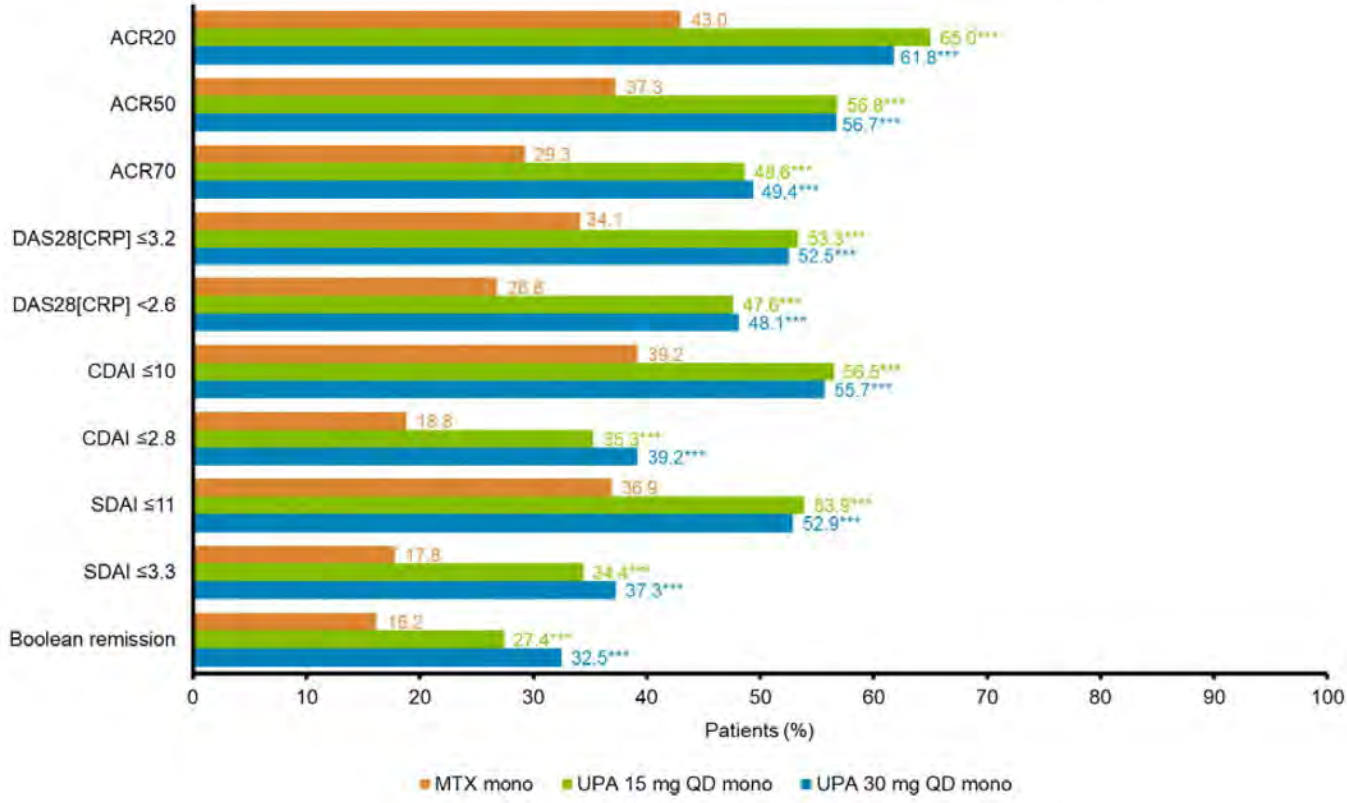
Methods: During the 48-wk double-blind study period, pts were randomized to UPA 15 or 30 mg once daily (QD) or MTX (titrated to 20 mg/wk by Wk 8). At Wk 26, pts who did not achieve Clinical Disease Activity Index (CDAI) remission (≤2.8) and had < 20% improvement from baseline in tender or swollen joint count received blinded rescue therapy (addition of MTX for UPA groups and UPA 15 or 30 mg for the MTX group). In the LTE, pts received open-label treatment once the last pt reached Wk 48. Efficacy assessments up to Wk 156 were summarized by randomized

Table. Safety overview

E/100PY (95% CI)	MTX mono (N=314; PY=601.9)	UPA 15 mg QD mono (N=317; PY=703.4)	UPA 30 mg QD mono (N=314; PY=687.6)
Any AE	240.2 (228.0, 252.9)	268.0 (256.0, 280.4)	292.5 (279.8, 305.5)
Any serious AE	10.8 (8.3, 13.8)	12.2 (9.8, 15.1)	16.3 (13.4, 19.6)
Any AE leading to discontinuation of study drug	6.5 (4.6, 8.9)	7.3 (5.4, 9.5)	7.7 (5.8, 10.1)
Any death[a]	0.7 (0.2, 1.7)	0.9 (0.3, 1.9)	1.0 (0.4, 2.1)
Serious infection	2.5 (1.4, 4.1)	3.3 (2.1, 4.9)	4.4 (2.9, 6.2)
Opportunistic infection excluding TB and HZ	0.2 (0.0, 0.9)	0.1 (0.0, 0.8)	0.3 (0.0, 1.1)
HZ	0.8 (0.3, 1.9)	4.5 (3.1, 6.4)	4.7 (3.2, 6.6)
Active TB	0	0.3 (0.0, 1.0)	0.3 (0.0, 1.1)
NMSC	0	0.4 (0.1, 1.2)	1.0 (0.4, 2.1)
Malignancy other than NMSC	1.0 (0.4, 2.2)	0.6 (0.2, 1.5)	1.2 (0.5, 2.3)
Hepatic disorder	14.1 (11.3, 17.5)	12.5 (10.0, 15.4)	15.0 (12.2, 18.2)
GI perforation (adjudicated)	0	0	0.4 (0.1, 1.3)
Neutropenia	2.2 (1.2, 3.7)	4.5 (3.1, 6.4)	5.7 (4.0, 7.8)
CPK elevation	1.8 (0.9, 3.3)	7.7 (5.8, 10.0)	15.4 (12.6, 18.6)
MACE (adjudicated)	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)
VTE (adjudicated)	0.3 (0.0, 1.2)	0.4 (0.1, 1.2)	0.6 (0.2, 1.5)

Data were censored at the time of MTX or UPA addition for rescued pts. [a]Includes treatment-emergent (≤30 days of the last dose of study drug) and non-treatment-emergent deaths

Figure. Efficacy endpoints up to Week 156 (non-responder imputation)



***Nominal p<0.001 vs MTX mono. CRP, C-reactive protein; DAS28, disease activity score for 28 joints; ESR, erythrocyte sedimentation rate; mono, monotherapy

group and included American College of Rheumatology (ACR) responses, remission and low disease activity (LDA) measures, and change in modified Total Sharp Score (mTSS; up to 96 wks). Treatment-emergent adverse events (AEs) per 100 pt-years (PY) for pts on continuous mono were summarized through 156 wks. Non-responder imputation was used for binary endpoints for missing data and when pts received rescue therapy or prematurely discontinued the study drug.

Results: Of 945 pts randomized and treated, 775 entered the LTE on study drug (including 57 rescued pts; MTX, 33; UPA 15 mg, 17; UPA 30 mg, 7). Overall, 161 (21%) pts discontinued during the LTE. At Wk 156, higher proportions of pts randomized to UPA achieved a 20/50/70% improvement in ACR response (ACR20/50/70), LDA, and remission vs MTX (Figure). Change from baseline in mTSS at Wk 96 favored UPA vs MTX (data not shown). Most AEs were numerically more frequent with UPA 30 mg. The overall rate of serious infection was numerically higher with UPA vs MTX (Table). Herpes zoster (HZ), neutropenia, non-melanoma skin cancer (NMSC), and creatine phosphokinase (CPK) elevation were more frequent with UPA vs MTX. Two active tuberculosis (TB) events were reported in each UPA arm; 3 adjudicated gastrointestinal (GI) perforation events were observed in the UPA 30 mg arm. Adjudicated major adverse cardiovascular event (MACE) or venous thromboembolism (VTE) were comparable across treatment arms.

Conclusion: UPA monotherapy showed sustained superior clinical responses including remission vs MTX through Wk 156 but higher rates of several AEs, including HZ, neutropenia, and CPK elevations; no new safety risks were observed compared with previous results.[1,2]

References

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Disclosure: R. van Vollenhoven, Bristol-Myers Squibb, 2, 5, 6, GlaxoSmithKline, 2, 5, 6, Eli Lilly, 5, Pfizer, 2, 5, 6, Roche, 5, UCB, 2, 5, 6, AbbVie, 2, 6, AstraZeneca, 2, 6, Biogen, 2, 6, Biotest,, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Sanofi, 2, 6, Servier, 2, 6, Velabio, 2, 6, BMS, 5, GSK, 5, Celgene, 2, 6; **T. Takeuchi**, Astellas Pharma, 2, 5, 6, Chugai Pharmaceutical, 2, 5, 6, Asahi Kasei Pharma, 5, Mitsubishi Tanabe, 2, 5, 6, AbbVie, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Shionogi, 5, Takeda, 5, UCB Japan, 5, Eli Lilly Japan, 2, 6, AYUMI, 6, Bristol-Myers Squibb, 6, Gilead Sciences, Inc., 6, Novartis, 6, Pfizer Japan, 6, Sanofi, 6, Dainippon Sumitomo, 6; **J. Aelion**, AbbVie, 5, Amgen, 5, AstraZeneca, 5, Bristol-Myers Squibb, 5, Celgene, 5, Eli Lilly, 5, Galapagos/Gilead, 5, Genentech, 5, GlaxoSmithKline,, 5, Horizon, 5, Janssen, 5, Mallinckrodt, 5, Nektar, 5, Nichi-Iko, 5, Novartis, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Sanofi-Aventis, 5, Selecta, 5, UCB, 5; **N. Chavez**, AbbVie, 2, 5, 6, Galapagos, 5, Gilead, 5, Pfizer, 2, 5, 6, Sanofi, 5, Janssen, 2, 6; **P. Mannucci**, AbbVie, 2, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Genentech/Roche, 5, GlaxoSmithKline, 5, Janssen, 5, UCB, 5; **A. Singhal**, AbbVie, 2, 5, Aclaris, 2, 5, Amgen, 2, 5, AstraZeneca, 2, 5, Bristol-Myers Squibb, 2, 5, Gilead, 2, 5, Eli Lilly, 2, 5, Idorsia, 2, 5, Novartis, Oscotec, 2, 5, Pfizer, 2, 5, Regeneron-Sanofi, 2, 5, Roche/Genentech, 2, 5, Selecta, 2, 5, Takeda, 2, 5, UCB, 2, 5, Vielabio, 2, 5; **J. Swierkot**, AbbVie, 2, 5, 6, Sandoz, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, UCB, 2, 5, 6, MSD, 2, 5, 6, Accord, 2, 5, 6, Janssen, 2, 5, 6; **A. Friedman**, AbbVie, 3, 11; **N. Khan**, AbbVie, 3, 11; **Y. Li**, AbbVie, 3, 11; **X. Bu**, AbbVie, 3, 11; **J. Klaff**, AbbVie, 3, 11; **V. Strand**, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2.

Abstract Number: 1693

Lower Adverse Event and Infection Rates During Tocilizumab Therapy Without Concomitant GC: An Analysis of the ICHIBAN Study

Christof Specker[1], Martin Aringer[2], Gerd Burmester[3], Marvin A. Peters[4], Michael W. Hofmann[5], Herbert Kellner[6], Frank Moosig[7], Hans-Peter Tony[8] and Gerhard Fliedner[9], [1]Evangelisches Krankenhaus, Kliniken Essen-Mitte, Essen, Germany, [2]Rheumatology, Medicine III, University Medical Center & Faculty of Medicine, TU Dresden, Dresden, Germany, [3]Charité University Medicine Berlin, Berlin, Germany, [4]Roche Pharma AG, Grenzach-Wyhlen, Germany, [5]Chugai Pharma Germany GmbH, Frankfurt am Main, Germany, [6]Hospital Neuwittelsbach, Center for Rheumatology and Gastroenterology, Munich, Germany, Munich, Germany, [7]Rheumatology Center Schleswig-Holstein Middle, Neumünster, Germany, [8]Universitätsklinikum Würzburg, Wuerzburg, Germany, [9]Rheumatology Practice, Osnabrueck, Germany

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: To limit the risk of serious infections, guidelines recommend short term (< 3 months) or low-dose (≤10 mg/day) adjunct glucocorticoids (GCs) to control rheumatoid arthritis (RA) flares or high disease activity[1]. In the ICHIBAN study, which analysed the safety and effectiveness of tocilizumab (TCZ), similar proportions of patients with (61.2%) and without (62.5%) concomitant baseline (BL) GCs achieved DAS28-ESR remission[2]. Here, we examine the efficacy and safety of TCZ in subgroups according to BL concomitant GCs in detail.

Table 1. Adverse events (AEs) and serious adverse events (SAEs) in patients treated with tocilizumab in subgroups according the concomitant baseline glucocorticoids (GCs)

E (%) [rate/100 PY]	With concomitant GCs (n = 2550)	Without concomitant GCs (n = 607)
AEs	3546 (46.9) [112.9]	731 (45.8) [91.0]
Considered related	1203 (22.3) [38.3]	231 (21.3) [28.8]
SAEs	790 (15.2) [25.2]	153 (13.8) [19.1]
Considered related	200 (5.0) [6.4]	24 (3.1) [3.0]
AEs leading to withdrawal	301 (8.3) [9.6]	63 (9.1) [7.8]
Infections	965 (21.8) [30.7]	194 (19.8) [24.2]
SAEs	134 (3.8) [4.3]	19 (2.5) [2.4]

All patients with at least one dose of tocilizumab included in the analysis. AE; adverse event; PY, patient year; SAE, serious AE; SAF, safety analysis set. E, total number of events; % is the percent of patients with at least one event.

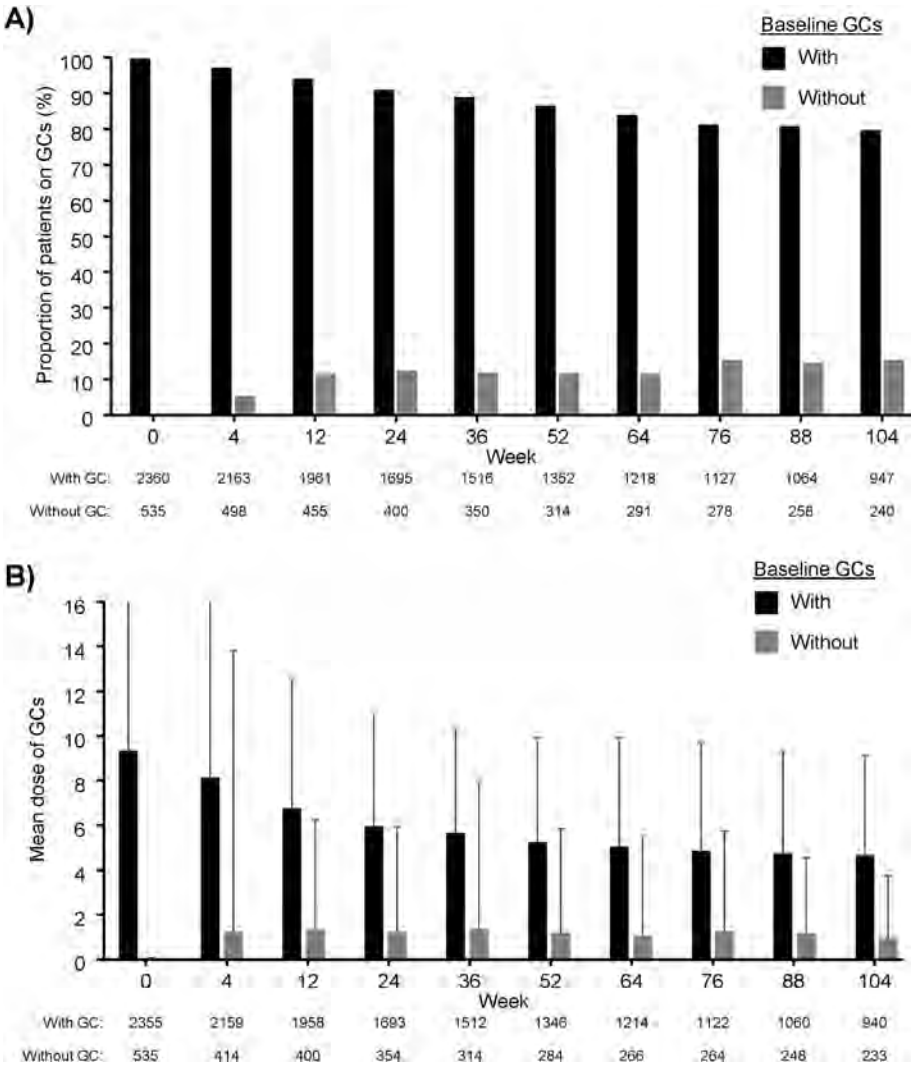

Figure 1. A) The proportion of patients treated with concomintant glucocorticoids (GCs) and B) mean GC dose throughout ICHIBAN by subgroup according to concomitant GCs at baseline. Analysis includes all patients treated with tocilizumab with no prior tocilizumab treatment. Means include patients with no GCs. Error bars represent standard deviation.

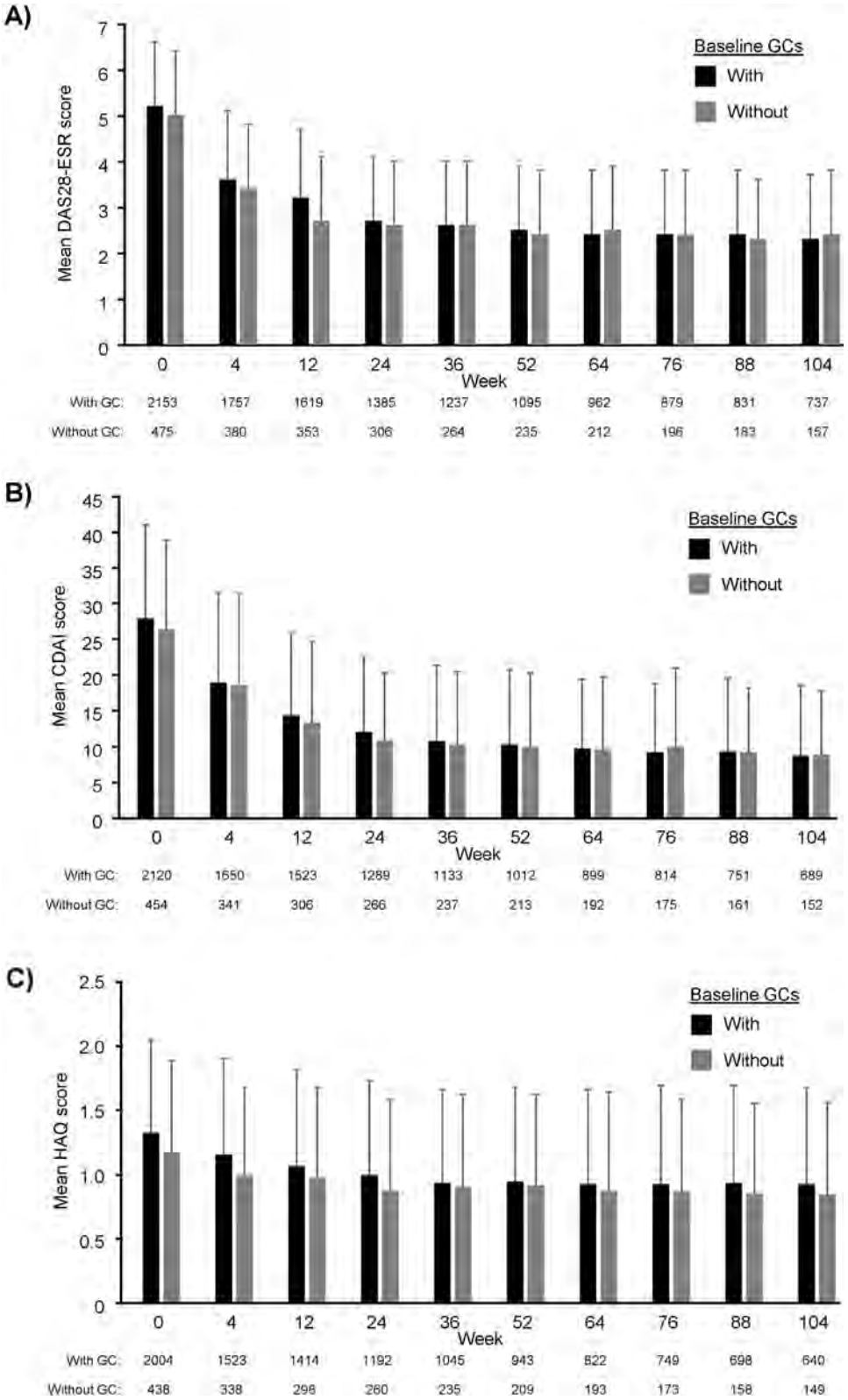

Figure 2. Mean disease activity of patients treated with tocilizumab with or without concomitant baseline glucocorticoids (GCs). A) Mean DAS28-ESR, B) CDAI and C) HAQ-DI scores throughout the ICHIBAN study. Analysis includes all patients treated with tocilizumab with no prior tocilizumab treatment. Error bars represent standard deviation. Missing data was not substituted; CDAI, Clinical Disease Activity Index; DAS28-ESR, Disease Activity Score (DAS) 28 -erythrocyte sedimentation rate, HAQ-DI, Health Assessment Questionnaire – Disability Index.

Methods: ICHIBAN was a prospective, multi-center, non-interventional study (NCT01194401; ML22928) that included adults with active, moderate-to-severe RA who received TCZ according to the local label in Germany. All patients who received ≥1 TCZ infusion were included in the safety population (SAF, n=3164). Effectiveness (DAS28-ESR and CDAI) and concomitant medication were analysed in all SAF patients with no prior TCZ (n=2902).

Results: In ICHIBAN, 2,550 (80.6%) patients received concomitant GCs, while 607 (19.2%) received no GCs (7 missing) at BL. Patients with or without GCs were of similar mean [SD] age (55.9 [13.0] vs 53.8 [13.6] years old). The proportion of female patients was numerically lower in the group with BL GCs (73.4%) than in those without GCs (80.9%). A numerically greater proportion of patients with BL GCs (73.1%) had comorbidities than those without (67.9%). Common comorbidities in patients with and without GCs were hypertension (37.4% vs 35.1%), degenerative joint disorder/spinal disease (20.4% vs 14.2%), and osteoporosis (19.1% vs 9.1%).

Throughout the study, patients with and without BL GCs had a similar mean exposure (SD) to TCZ (1.2 [0.85] vs 1.3 [0.87] years). Still, patients without BL GCs experienced lower rates (events/100 patient years) of adverse events (AEs) and serious AEs (SAEs) considered related to treatment, infections and serious infections (**Table 1**).

At week 104, 79.9% of the patients with baseline GCs and 15.4% of patients without BL GCs were receiving concomitant GC therapy (**Figure 1A**). The median GC dose changed by –2.5 mg/d in patient with and by 0.0 mg/d in patients without BL GCs (**Figure 1B**). Furthermore, the proportion of patients on csDMARDs decreased in both subgroups from BL to week 104 (with GC, 51.2–46.8%; without, GCs 48.4–37.5%).

Similar reductions in mean DAS28-ESR score were observed in patients with and without BL GCs (**Figure 2A**). CDAI also decreased in both subgroups (**Figure 2B**), with a mean (SD) reduction of 18.3 (13.3) in patients with and 16.6 (12.6) in those without BL GCs over 104 weeks. Similar reductions in HAQ-DI were also seen in both subgroups during ICHIBAN (**Figure 2C**).

Conclusion: Even though the majority had low dose GCs only, patients without BL GCs had numerically lower rates of AEs considered related to treatment and infections throughout the ICHIBAN study. Effectiveness endpoints were similar in both subgroups. In patients with BL GCs, the proportion of patients on and dose of GCs decreased throughout the study.

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Abstract Number: 1694

Sustainability of Response to Upadacitinib Among Patients with Active Rheumatoid Arthritis Refractory to Biological Disease-Modifying Anti-Rheumatic Drugs

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

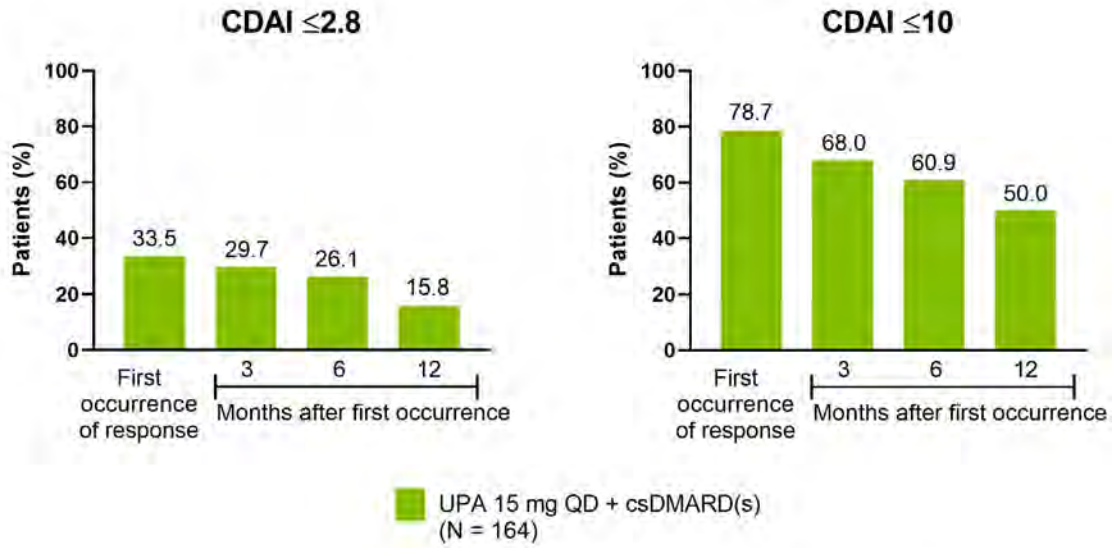
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Sustained clinical remission (REM) is the primary treatment goal for patients with rheumatoid arthritis (RA), with low disease activity (LDA) being an appropriate target for treatment-refractory patients.[1,2] This analysis evaluated the sustainability of response to the JAK inhibitor, upadacitinib (UPA) 15 mg once daily (QD), among patients with prior inadequate response or intolerance to biologic DMARDs.

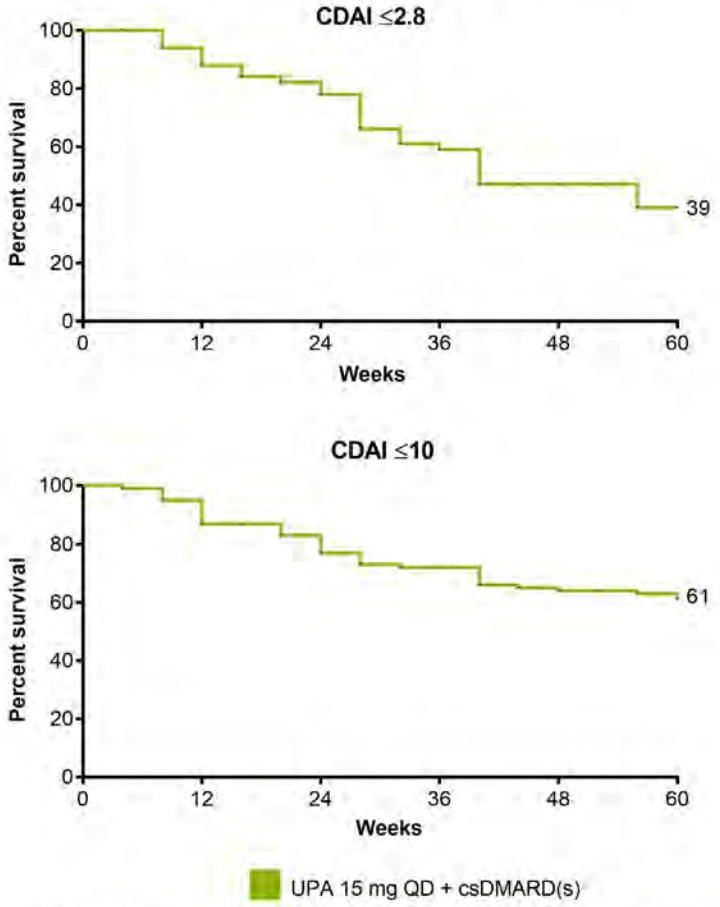
Figure 1. Proportion of Patients Sustaining CDAI Remission or Low Disease Activity at 3, 6, and 12 Months After Initial Occurrence of Response Among the Total Randomized Population



Treatment group is by initial randomization; non-responder imputation was used for missing data.

CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic disease-modifying antirheumatic drugs; QD, once daily; UPA, upadacitinib.

Figure 2. Kaplan-Meier Analysis of Time to Loss of CDAI Remission or Low Disease Activity After the First Occurrence of Response



Treatment groups are by initial randomization. Results are for patients who had achieved CDAI remission or low disease activity. UPA 15 mg QD + csDMARD(s): CDAI ≤10: n = 129; CDAI ≤2.8: n = 55.

Data were censored at the cut-off (16 April 2018, when all patients had reached the Week 60 visit; censored = stopped collecting data). Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.
CDAI, Clinical Disease Activity Index; QD, once daily; UPA, upadacitinib.

Methods: Data come from the 12-week, phase 3 randomized, placebo (PBO)-controlled SELECT-BEYOND trial of UPA 15 mg or 30 mg QD in patients with moderate to severe RA on stable background conventional synthetic (cs) DMARDs. Initiation, change, or discontinuation of background RA medications, including ≤2 csDMARDs, was allowed starting at Week 24. Patients completing the 12-week trial were able to enter a long-term extension of up to 5 yrs with all PBO patients switching to UPA.[3] This post hoc analysis evaluated REM (CDAI ≤2.8; SDAI ≤3.3), LDA (CDAI≤10; SDAI≤11), and DAS28(CRP) < 2.6/≤3.2 at first occurrence of response before Week 60, as well as at 3, 6, and 12 months following initial response in patients randomized to UPA 15 mg. For those patients who achieved REM/LDA, Kaplan-Meier was used to define the time from when the response was first achieved to the earliest date at which the response was lost at two consecutive visits or discontinuation of study drug. The predictive ability of time to REM/LDA was evaluated using Harrell's concordance (c)-index (range: 0 to 1, where 0.5 indicates a model that is no better at predicting an outcome than random chance). The date of the last follow up was 16 April 2018, when all patients had reached the Week 60 visit. Non-responder imputation was used for missing data. Only data from the approved 15 mg dosage are reported here.

Results: In patients with active RA despite prior treatment with at least one bDMARD, 34% and 79% of those receiving UPA 15 mg + background csDMARD(s) achieved CDAI REM or LDA through Week 60, respectively. Sustained CDAI REM was attained by 30%, 26%, and 16% of patients randomized to UPA at 3, 6, and 12 months post initial

response, while CDAI LDA was achieved by 68%, 61%, and 50% of patients during the same time points (**Figure 1**). Time to initial clinical response weakly predicted sustained REM but did not predict sustained LDA, with a c-index (95% CI) of 0.62 (0.49, 0.74) and 0.52 (0.44, 0.61), respectively. Through the last follow-up visit at Week 60, 39/61% of patients on UPA remained in CDAI REM/LDA (**Figure 2**). Of those who lost CDAI REM, 58% remained in CDAI LDA, and 22% recaptured REM by the cut-off date; 18% of patients who lost CDAI LDA recaptured response. Similar results were observed for REM and LDA based on SDAI and for DAS28(CRP) < 2.6/≤3.2.

Conclusion: Among patients with inadequate response or intolerance to bDMARDs, over three-quarters on UPA 15 mg achieved CDAI LDA, a relevant therapeutic target for these treatment-refractory patients, and nearly two-thirds of those maintained this response through 60 weeks. Additionally, about one-third of UPA-treated patients attained CDAI REM and maintained that response over 60 weeks.

References

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3. Genovese, et al. Lancet 2018;391:2513–24.

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Abstract Number: 1695

Erythrocyte Methotrexate Polyglutamates Are Substantially Higher After Subcutaneous Methotrexate Treatment in Rheumatoid Arthritis Patients in the First Months of Treatment

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Optimal dosing of methotrexate (MTX) for individual rheumatoid arthritis (RA) patients to achieve adequate disease control remains challenging. Assessment of erythrocyte MTX-polyglutamates (PGs) levels

Table 1. Linear regression of MTX-PG levels and administration route, corrected for age, baseline DAS28, smoking, BMI, eGFR and MTX dose

	ß at month 1 [95% CI] (P-value)	*ß at month 2 [95% CI] (P-value)*	*ß at month 3 [95% CI] (P-value)*	*ß at month 6 [95% CI] (P-value)*
MTX-PG1-6	*1.74 [1.15-2.62] (0.009)*	*1.60 [1.03-2.47] (0.037)*	0.84 [0.53-1.34] (0.464)	1.52 [0.94-2.35] (0.072)
MTX-PG1,2	1.14 [0.73-1.79] (0.553)	1.28 [0.79-2.06] (0.306)	1.24 [0.78-1.99] (0.357)	0.78 [0.48-1.27] (0.315)
MTX-PG3	*1.81 [1.22-2.69] (0.004)*	*1.64 [1.09-2.50] (0.019)*	1.34 [0.88-2.02] (0.166)	0.94 [0.62-1.43] (0.765)
MTX-PG4-6	*2.25 [1.14-4.43] (0.020)*	*2.48 [1.25-4.88] (0.010)*	*1.90 [1.01-3.55] (0.046)*	1.27 [0.67-2.42] (0.462)

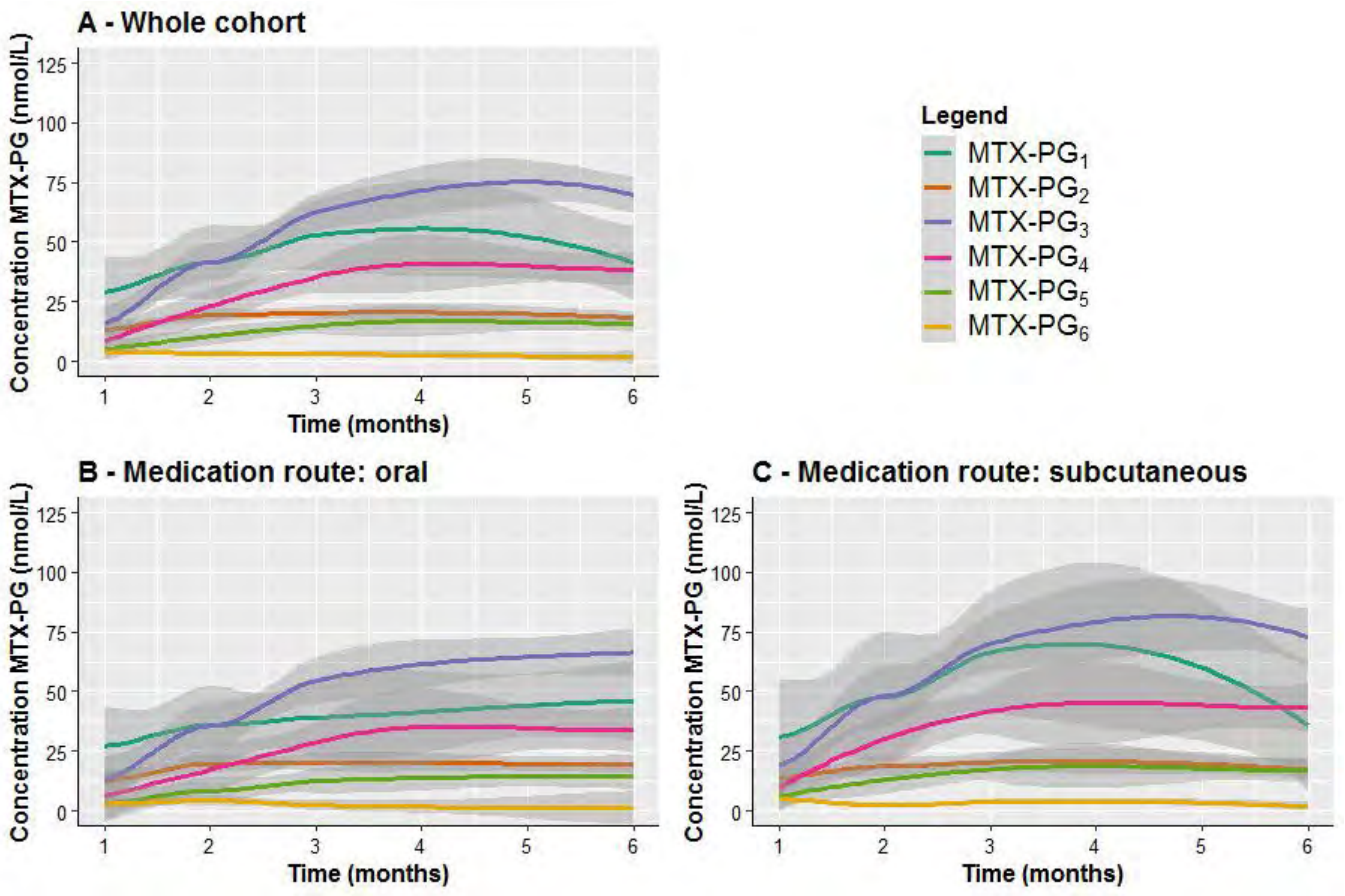

Figure 1. Erythrocyte individual MTX-PG accumulation in RA patients (A) during the first 6 months of oral (B) or subcutaneous (C) MTX administration. At 6 months, 18 patients using oral and 18 patients using subcutaneous MTX were still continuing MTX treatment. Means (colored lines) and standard errors (shaded areas) are depicted (Loess regression).

has been used as a tool to monitor clinical response of RA patients in the first 3-12 months of treatment and MTX-PG_{2-4} as well as total MTX-PGs were associated with lower DAS28 over 9 months. However, data per route of administration and from earlier time points, including MTX-PG_6 levels are lacking.

We investigated the pharmacokinetics and -dynamics of erythrocyte MTX-PG accumulation in RA patients receiving oral or subcutaneous MTX in the early phase (1, 2, 3 months) and later stage (6 months) of MTX treatment.

Methods: In a clinical prospective cohort study (MeMo study: NTR7149), newly diagnosed RA patients were treated with oral (n=24) or subcutaneous (n=22) MTX mostly according to the COBRA-light schedule (start 10 mg MTX, increased to 25 mg MTX in 8 weeks, with prednisolone). At 1, 2, 3 and 6 months after start of therapy, blood was collected and individual MTX-PGs (MTX-PG_1 – MTX-PG_6) were analyzed in erythrocytes using a validated UHPLC-MS/MS method with labeled internal standards. (De Rotte 2015) Dosing, concomitant treatments and DAS28-ESR assessments were in conformity with clinical practice. Adverse events were recorded. We used a linear mixed model analysis to assess the association between MTX-PG levels and DAS28-ESR (per group and total), with corrections for age, baseline DAS28, eGFR, MTX dose (1 month before sampling), smoking and BMI.

Results: 46 consecutive patients were included in this study of which 76% female, mean age was 57.8 years, BMI was 25.8, 20% were smokers, mean baseline DAS28-ESR was 3.5. MTX dose at baseline was 10.5 mg (SD: 1.5) for both groups, 15.4 (4.4) and 16.8 (1.8) at 1 month and 22.8 (3.9), 22.4 (5.2) at 2 months, 20.1 (6.3) and 20.8 (5.6) at 3 months and 19.0 (6.5) and 18.6 (8.6) at 5 months for oral and subcutaneous use, respectively. On average, patients starting subcutaneous MTX had significantly higher levels of long chain MTX-PGs (MTX-PG_{3-6}) in erythrocytes when compared to patients in the oral MTX group at 1 and 2 months (Figure 1. and 1C, Table 1). Similarly, erythrocyte MTX-PG_{1-6} and MTX-PG_3 concentrations were significantly higher in subcutaneous MTX-users at month 1 compared to the oral group (median 68.6 nmol/L (IQR:40.5) vs 51.9 (55.6) and 17.4 (11.1) vs 11.2 (15.6), respectively (Figure 1. and 1C, Table 1). This difference remained present at month 2. Erythrocyte MTX-PG accumulation reached a plateau after 3 months.

Apart from small positive and negative correlations, no (clinically) significant relation between MTX-PG concentrations and DAS28 was observed during the first 6 months of treatment; DAS28 decreased with 1.2 in the oral group and 1.6 in the subcutaneous group.

Side effects, mostly headache and dizziness were similar in both groups and not correlated with MTX-PG levels.

Conclusion: This study demonstrated significantly higher accumulation of long-chain and total MTX-PGs following subcutaneous versus oral MTX administration in the first 3 months. Early phase erythrocyte MTX-PG analyses may hold promise for optimization of individual patient MTX dose scheduling.

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Abstract Number: 1696

Clinical Outcomes up to Week 48 of Ongoing Filgotinib RA Long-term Extension Trial of Biologic DMARD Inadequate Responders Initially on Filgotinib or Placebo in a Phase 3 Trial

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SESSION INFORMATION

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Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The preferential Janus kinase-1 inhibitor filgotinib (FIL) is approved to treat RA in Europe and Japan. We assessed FIL efficacy and safety in patients (pts) with inadequate response (IR) to biologic DMARDs (bDMARDs) in a long-term extension trial (LTE; NCT03025308) enrolled from a Phase 3 parent study (PS; NCT02873936).[1]

Methods: bDMARD-IR pts received FIL 200 mg (FIL200), FIL 100 mg (FIL100), or placebo (PBO) all with stable conventional synthetic (cs)DMARDs up to 24 weeks (W). At W14 of the PS, pts with IR to FIL or PBO (< 20% improvement in swollen [66] and tender [68] joint counts) switched to standard of care (SOC; investigator's choice of appropriate treatment). Pts completing the PS on FIL, PBO, or SOC could enter the LTE. PS FIL pts were maintained, blinded, on their FIL dose; PS PBO and PS SOC pts were rerandomized, blinded, to FIL200 or FIL100. We report efficacy up to LTE W48 for ACR 20%, 50%, and 70% improvement (ACR20/50/70), DAS in 28 joints with CRP (DAS28[CRP]) ≤3.2 and < 2.6, and Clinical Disease Activity Index (CDAI) ≤10 and ≤2.8. Exposure-adjusted incidence rates (EAIR)/100 pt-years of exposure of treatment-emergent adverse events (TEAEs) and AEs of special interest (AESIs) are summarized up to data cutoff of June 1, 2020.

Results: The PS included 147, 153, and 148 pts on FIL200, FIL100, and PBO. Of the 121 pts who entered LTE from PS on FIL200, 80 (66%) continued study drug at June 1, 2020, as did 76/110 (69%) FIL100 pts. Pts still on LTE FIL from PBO were 35/47 (75%) FIL200 and 32/46 (70%) FIL100 pts; from SOC: 13/23 (57%) FIL200 and 13/22 (59%) FIL100 pts. LTE baseline (BL) characteristics were similar in FIL200 and FIL100 pts (mean RA duration: 13.2 and 12.8 years, DAS28[CRP]: 3.5 and 3.7). During LTE, PS FIL ACR20/50/70 response rates decreased modestly by W48 (**Table 1**). Among PS PBO pts, response rates were lower at LTE BL but reached similar levels as PS FIL pts by W48; rates increased up to W48 in PS SOC pts on either FIL dose but not to levels of other groups. Percentages of pts attaining DAS28(CRP) ≤3.2, DAS28(CRP) < 2.6, CDAI ≤10, and CDAI ≤2.8 were maintained up to W48 for FIL/FIL pts, while PBO/FIL and SOC/FIL pts showed similar patterns as for ACR responses (**Table 2**). At W48, DAS28 ≤3.2

Table 1. Proportions of patients achieving ACR20/50/70, NRI, FAS, up to LTE w48. ACR20/50/70 is calculated based on PS BL. Analysis used the logistic regression model, including treatment group and stratification factors. NRI: patients with missing values were considered nonresponders. BL, baseline; csD, conventional synthetic DMARDs; FAS, full analysis set; FIL, filgotinib; LTE, long-term extension; NRI, nonresponder imputation; PBO, placebo; PS, parent study; w, week

	FIL200+csD→ FIL200+csD n = 121	PBO+csD→ FIL200+csD n = 47	SOC+csD→ FIL200+csD n = 23	FIL100+csD→ FIL100+csD n = 110	PBO+csD→ FIL100+csD n = 46	SOC+csD→ FIL100+csD n = 22
ACR20, proportion of responders, n (%)						
LTE BL	98 (81.0%)	23 (48.9%)	3 (13.0%)	81 (73.6%)	27 (58.7%)	2 (9.1%)
LTE w12	95 (78.5%)	34 (72.3%)	13 (56.5%)	80 (72.7%)	32 (69.6%)	10 (45.5%)
LTE w48	77 (63.6%)	30 (63.8%)	10 (43.5%)	72 (65.5%)	30 (65.2%)	6 (27.3%)
ACR50, proportion of responders, n (%)						
LTE BL	63 (52.1%)	13 (27.7%)	1 (4.3%)	55 (50.0%)	15 (32.6%)	0
LTE w12	65 (53.7%)	17 (36.2%)	4 (17.4%)	56 (50.9%)	18 (39.1%)	3 (13.6%)
LTE w48	53 (43.8%)	22 (46.8%)	4 (17.4%)	41 (37.3%)	15 (32.6%)	2 (9.1%)
ACR70, proportion of responders, n (%)						
LTE BL	45 (37.2%)	5 (10.6%)	1 (4.3%)	31 (28.2%)	7 (15.2%)	0
LTE w12	37 (30.6%)	10 (21.3%)	3 (13.0%)	26 (23.6%)	13 (28.3%)	2 (9.1%)
LTE w48	30 (24.8%)	14 (29.8%)	3 (13.0%)	28 (25.5%)	11 (23.9%)	2 (9.1%)

Table 2. Proportions of patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, CDAI ≤10, CDAI ≤2.8, NRI up to LTE w48. Analysis used the logistic regression model, including treatment group and stratification factors. NRI: patients with missing values were considered nonresponders. BL, baseline; CDAI, clinical disease activity index; csD, conventional synthetic DMARDs; DAS28(CRP), disease activity score for 28 joint count using CRP; FIL, filgotinib; LTE, long-term extension; NRI, nonresponder imputation; PS, parent study; w, week

	FIL200+csD→ FIL200+csD n = 121	PBO+csD→ FIL200+csD n = 47	SOC+csD→ FIL200+csD n = 23	FIL100+csD→ FIL100+csD n = 110	PBO+csD→ FIL100+csD n = 46	SOC+csD→ FIL100+csD n = 22
DAS28(CRP) ≤3.2, proportion of responders, n (%)						
LTE BL	69 (57.0%)	15 (31.9%)	1 (4.3%)	55 (50.0%)	16 (34.8%)	0
LTE w12	68 (56.2%)	27 (57.4%)	8 (34.8%)	53 (48.2%)	25 (54.3%)	4 (18.2%)
LTE w48	62 (51.2%)	26 (55.3%)	6 (26.1%)	53 (48.2%)	22 (47.8%)	6 (27.3%)
DAS28(CRP) <2.6, proportion of responders, n (%)						
LTE BL	45 (37.2%)	8 (17.0%)	1 (4.3%)	37 (33.6%)	10 (21.7%)	0
LTE w12	49 (40.5%)	18 (38.3%)	5 (21.7%)	41 (37.3%)	16 (34.8%)	2 (9.1%)
LTE w48	45 (37.2%)	23 (48.9%)	3 (13.0%)	36 (32.7%)	12 (26.1%)	3 (13.6%)
CDAI ≤10, proportion of responders, n (%)						
LTE BL	69 (57.0%)	18 (38.3%)	1 (4.3%)	58 (52.7%)	21 (45.7%)	0
LTE w 12	70 (57.9%)	27 (57.4%)	7 (30.4%)	58 (52.7%)	26 (56.5%)	3 (13.6%)
LTE w48	63 (52.1%)	25 (53.2%)	7 (30.4%)	59 (53.6%)	21 (45.7%)	4 (18.2%)
CDAI ≤2.8, proportion of responders, n (%)						
LTE BL	28 (23.1%)	3 (6.4%)	1 (4.3%)	23 (20.9%)	6 (13.0%)	0
LTE w12	27 (22.3%)	10 (21.3%)	2 (8.7%)	23 (20.9%)	6 (13.0%)	0
LTE w48	27 (22.3%)	10 (21.3%)	2 (8.7%)	21 (19.1%)	6 (13.0%)	2 (9.1%)

Table 3. EAIRs of TEAEs in LTE, as of June 1, 2020. Data presented as EAIR (95% CI)/100 PYE. EAIR and 95% CI were estimated using Poisson regression model including treatment group with an offset of natural log of exposure time. If any treatment had 0 event, exact Poisson method was applied. csD, conventional synthetic DMARD; DVT, deep-vein thrombosis; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MACE, major adverse cardiovascular event; PBO, placebo; PE, pulmonary embolism; PYE, patient-years of exposure; SOC, standard of care; TE, treatment-emergent; TEAE, TE adverse event

	FIL200+csD→ FIL200+csD n = 121 PYE = 228.4 n (%) EAIR (95% CI)	PBO+csD→ FIL200+csD n = 47 PYE = 98.1 n (%) EAIR (95% CI)	SOC+csD→ FIL200+csD n = 23 PYE = 42.1 n (%) EAIR (95% CI)	FIL100+csD→ FIL100+csD n = 110 PYE = 223.3 n (%) EAIR (95% CI)	PBO+csD→ FIL100+csD n = 46 PYE = 91.1 n (%) EAIR (95% CI)	SOC+csD→ FIL100+csD n = 22 PYE = 38.2 n (%) EAIR (95% CI)
TEAE	107 (88.4%) 46.9 (38.8, 56.6)	38 (80.9%) 38.7 (28.2, 53.2)	22 (95.7%) 52.2 (34.4, 79.3)	90 (81.8%) 40.3 (32.8, 49.5)	37 (80.4%) 40.6 (29.4, 56.1)	19 (86.4%) 49.8 (31.8, 78.0)
TEAE Grade ≥3	24 (19.8%) 10.5 (7.0, 15.7)	10 (21.3%) 10.2 (5.5, 18.9)	8 (34.8%) 19.0 (9.5, 38.0)	23 (20.9%) 10.3 (6.8, 15.5)	12 (26.1%) 13.2 (7.5, 23.2)	7 (31.8%) 18.3 (8.7, 38.5)
TE serious AE	28 (23.1%) 12.3 (8.5, 17.8)	12 (25.5%) 12.2 (6.9, 21.5)	9 (39.1%) 21.4 (11.1, 41.1)	18 (16.4%) 8.1 (5.1, 12.8)	12 (26.1%) 13.2 (7.5, 23.2)	8 (36.4%) 21.0 (10.5, 41.9)
Death	3 (2.5%) 1.3 (0.4, 4.1)	1 (2.1%) 1.0 (0.0, 5.7)	0 0.0 (0.0, 8.8)	1 (0.9%) 0.4 (0.1, 3.2)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 9.7)
TE infections	78 (64.5%) 34.2 (27.4, 42.6)	22 (46.8%) 22.4 (14.8, 34.1)	15 (65.2%) 35.6 (21.5, 59.1)	50 (45.5%) 22.4 (17.0, 29.5)	24 (52.2%) 26.3 (17.7, 39.3)	15 (68.2%) 39.3 (23.7, 65.2)
TE serious infections	8 (6.6%) 3.5 (1.8, 7.0)	2 (4.3%) 2.0 (0.5, 8.2)	3 (13.0%) 7.1 (2.3, 22.1)	2 (1.8%) 0.9 (0.2, 3.6)	2 (4.3%) 2.2 (0.5, 8.8)	3 (13.6%) 7.9 (2.5, 24.4)
Opportunistic infections	0 0.0 (0.0, 1.6)	0 0.0 (0.0, 3.8)	0 0.0 (0.0, 8.8)	0 0.0 (0.0, 1.7)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 9.7)
TE herpes zoster	5 (4.1%) 2.2 (0.7, 5.1)	1 (2.1%) 1.0 (0.1, 7.2)	0 0.0 (0.0, 8.8)	0 0.0 (0.0, 1.7)	2 (4.3%) 2.2 (0.5, 8.8)	1 (4.5%) 2.6 (0.1, 14.6)
TE MACE (adjudicated)	3 (2.5%) 1.3 (0.4, 4.1)	1 (2.1%) 1.0 (0.1, 7.2)	0 0.0 (0.0, 8.8)	2 (1.8%) 0.9 (0.2, 3.6)	1 (2.2%) 1.1 (0.2, 7.8)	0 0.0 (0.0, 9.7)
TE DVT/PE (adjudicated)	2 (1.7%) 0.9 (0.2, 3.5)	0 0.0 (0.0, 3.8)	1 (4.3%) 2.4 (0.1, 13.2)	1 (0.9%) 0.4 (0.1, 3.2)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 9.7)
Malignancies (excl NMSC)	3 (2.5%) 1.3 (0.4, 4.1)	3 (6.4%) 3.1 (1.0, 9.5)	2 (8.7%) 4.7 (0.6, 17.2)	4 (3.6%) 1.8 (0.7, 4.8)	3 (6.5%) 3.3 (1.1, 10.2)	0 0.0 (0.0, 9.7)
NMSC	0 0.0 (0.0, 1.6)	0 0.0 (0.0, 3.8)	2 (8.7%) 4.7 (0.6, 17.2)	0 0.0 (0.0, 1.7)	0 0.0 (0.0, 4.0)	0 0.0 (0.0, 9.7)

and < 2.6 response rates were highest among PBO/FIL200 pts. By W12, more SOC/FIL200 pts attained DAS28 and CDAI activity scores versus SOC/FIL100, but rates were similar by W48 (except for CDAI ≤10). TEAE, serious AE, and serious infection EAIRs were higher in SOC/FIL pts vs FIL/FIL or PBO/FIL pts, with 2 nonmelanoma skin cancers on SOC/FIL200, but samples were small, and confidence intervals overlapped (**Table 3**). 5 pts died: FIL200/FIL200, n=3; PBO/FIL200, n=1; FIL100/FIL100, n=1. There were no opportunistic infections. EAIRs of major cardiovascular events were low, absent in PS SOC pts. Deep vein thrombosis and pulmonary embolism occurred in 2 FIL200/FIL200, 1 FIL100/FIL100, and 1 SOC/FIL200 pts.

Conclusion: Efficacy was mostly maintained in PS FIL pts up to W48. Response among PS PBO and SOC pts increased from BL to W48, but response in PS SOC pts continued to be lower than in other groups; these pts may represent a refractory population. FIL safety was largely consistent between PS and LTE.

Reference

1. Genovese MC et al. *JAMA*. 2019;322:315–25.

Disclosure: M. Buch, AbbVie, 2, 5, 6, Gilead Sciences, 2, 5, 6, Pfizer Inc, 2, 5, 6, UCB, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Roche, 2, 5, Sanofi, 2, 5, 6; **T. Takeuchi**, Astellas Pharma, 2, 5, 6, Chugai Pharmaceutical, 2, 5, 6, Asahi Kasei Pharma, 5, Mitsubishi Tanabe, 2, 5, 6, AbbVie, 5, 6, Daiichi Sankyo, 5, 6, Eisai, 5, 6, Shionogi, 5, Takeda, 5, UCB Japan, 5, Eli Lilly Japan, 2, 6, AYUMI, 6, Bristol-Myers Squibb, 6, Gilead Sciences, Inc., 6, Novartis, 6, Pfizer Japan, 6, Sanofi, 6, Dainippon Sumitomo, 6; **V. Rajendran**, Galapagos NV, 3, 11; **J. Gottenberg**, BMS, 2, 5, Pfizer, 2, 5, Gilead, 2, 6, Galapagos, 2, 6, Sanofi Genzyme, 2, 6, Lilly, 2, 6, Abbvie, 6, Roche, 6, UCB, 2, 6; **A. Pechonkina**, Gilead Sciences, Inc., 3, 11; **Y. Tan**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 11; **Q. Gong**, Gilead Sciences, Inc., 3, 11; **K. Van Beneden**, Galapagos, 3, 11; **R. Caporali**, Abbvie, 2, 6, BMS, 2, 6, Celltrion, 2, 6, Fresenius Kabi, 2, 6, Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Sanofi, 2, 6, Sandoz, 2, 6, Novartis, 6, MSD, 2, 6, Gilead Sciences, Inc., 2, 6, Galapagos NV, 2, 6, Roche, 2, 6, SamSung-Bioepis, 2, 6.

Abstract Number: 1697

Clinical Outcomes up to Week 48 of Filgotinib Treatment in an Ongoing Long-term Extension Trial of RA Patients with Inadequate Response to MTX Initially Treated with Filgotinib or Adalimumab During the Phase 3 Parent Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The preferential Janus kinase (JAK)-1 inhibitor filgotinib (FIL) is approved for treatment of moderately to severely active RA in Europe and Japan. We assessed efficacy and safety of FIL in patients (pts) with

Table 1. Proportions of patients achieving ACR20/50/70, NRI, FAS, up to LTE w48. FIL200+MTX and FIL100+MTX groups include patients who were initially on PBO but later were rerandomized at W24 to FIL200+MTX or FIL100+MTX to W52. ACR20 is calculated based on parent study baseline. Analyzed using the logistic regression model including treatment group and stratification factors; no formal comparison of efficacy outcomes was performed. ADA, adalimumab; BL, baseline; FAS, full analysis set; FIL, filgotinib; LTE, long-term extension; MTX, methotrexate; NRI, nonresponder imputation; PBO, placebo; W, week

	FIL200+MTX→ FIL200+MTX n = 571	ADA+MTX→ FIL200+MTX n = 128	FIL100+MTX→ FIL100+MTX n = 570	ADA+MTX→ FIL100+MTX n = 130
ACR20, proportion of responders, n (%)				
LTE BL	525 (91.9%)	117 (91.4%)	515 (90.4%)	115 (88.5%)
LTE w12	502 (87.9%)	115 (89.8%)	452 (79.3%)	110 (84.6%)
LTE w48	503 (88.1%)	108 (84.4%)	454 (79.6%)	107 (82.3%)
ACR50, proportion of responders, n (%)				
LTE BL	412 (72.2%)	96 (75.0%)	399 (70.0%)	91 (70.0%)
LTE w12	385 (67.4%)	98 (76.6%)	346 (60.7%)	85 (65.4%)
LTE w48	391 (68.5%)	94 (73.4%)	356 (62.5%)	84 (64.6%)
ACR70, proportion of responders, n (%)				
LTE BL	294 (51.5%)	62 (48.4%)	246 (43.2%)	62 (47.7%)
LTE w12	264 (46.2%)	69 (53.9%)	221 (38.8%)	61 (46.9%)
LTE w48	279 (48.9%)	69 (53.9%)	230 (40.4%)	57 (43.8%)

Table 2. Proportions of patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, CDAI ≤10, CDAI ≤2.8, NRI up to LTE w48. FIL200+MTX and FIL100+MTX groups include patients who were initially on PBO but later were rerandomized at W24 to FIL200+MTX or FIL100+MTX to W52. Analyzed using the logistic regression model including treatment group and stratification factors; no formal comparison of efficacy outcomes was performed. ADA, adalimumab; BL, baseline; CDAI, Clinical Disease Activity Index; FAS, full analysis set; FIL, filgotinib; LTE, long-term extension; MTX, methotrexate; NRI, nonresponder imputation; PBO, placebo; W, week

	FIL200+MTX→ FIL200+MTX n = 571	ADA+MTX→ FIL200+MTX n = 128	FIL100+MTX→ FIL100+MTX n = 570	ADA+MTX→ FIL100+MTX n = 130
DAS28(CRP) ≤3.2, proportion of responders, n (%)				
LTE BL	439 (76.9%)	98 (76.6%)	413 (72.5%)	92 (70.8%)
LTE w12	417 (73.0%)	98 (76.6%)	351 (61.6%)	93 (71.5%)
LTE w48	422 (73.9%)	94 (73.4%)	370 (64.9%)	93 (71.5%)
DAS28(CRP) <2.6, proportion of responders, n (%)				
LTE BL	344 (60.2%)	77 (60.2%)	301 (52.8%)	70 (53.8%)
LTE w12	345 (60.4%)	84 (65.6%)	257 (45.1%)	75 (57.7%)
LTE w48	347 (60.8%)	76 (59.4%)	275 (48.2%)	68 (52.3%)
CDAI ≤10, proportion of responders, n (%)				
LTE BL	443 (77.6%)	100 (78.1%)	409 (71.8%)	94 (72.3%)
LTE w 12	406 (71.1%)	93 (72.7%)	362 (63.5%)	91 (70.0%)
LTE w48	420 (73.6%)	96 (75.0%)	376 (66.0%)	86 (66.2%)
CDAI ≤2.8, proportion of responders, n (%)				
LTE BL	190 (33.3%)	32 (25.0%)	159 (27.9%)	39 (30.0%)
LTE w12	184 (32.2%)	43 (33.6%)	133 (23.3%)	37 (28.5%)
LTE w48	193 (33.8%)	41 (32.0%)	159 (27.9%)	37 (28.5%)

Table 3. EAIRs of TEAEs in LTE, as of June 1, 2020. Data presented as EAIR (95% CI)/100 patient-years. FIL200+MTX and FIL100+MTX groups include patients who were initially on placebo but were later rerandomized to FIL200+MTX or FIL100+MTX in FINCH 1. EAIR and 95% CI were estimated using Poisson regression model including treatment group with an offset of natural log of exposure time. If any treatment had 0 event, exact Poisson method was applied. ADA, adalimumab; AE, adverse event; DVT, deep vein thrombosis; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; LTE, long-term extension; MACE, major cardiovascular event; MTX, methotrexate; NMSC, nonmelanoma skin cancer; PE, pulmonary embolism; PYE, patient years of exposure; TE, treatment emergent

	FIL200+MTX→ FIL200+MTX N = 571 PYE = 859.4 n (%) EAIR (95%)	ADA+MTX→ FIL200+MTX N = 128 PYE = 197.8 n (%) EAIR (95%)	FIL100+MTX→ FIL100+MTX N = 570 PYE = 852.3 n (%) EAIR (95%)	ADA+MTX→ FIL100+MTX N = 130 PYE = 192.6 n (%) EAIR (95%)
TEAE	429 (75.1%) 49.9 (45.4, 54.9)	91 (71.1%) 46.0 (37.5, 56.5)	443 (77.7%) 52.0 (47.4, 57.0)	88 (67.7%) 45.7 (37.1, 56.3)
TEAE Grade ≥3	64 (11.2%) 7.4 (5.8, 9.5)	15 (11.7%) 7.6 (4.6, 12.6)	72 (12.6%) 8.4 (6.7, 10.6)	7 (5.4%) 3.6 (1.7, 7.6)
TE serious AE	52 (9.1%) 6.1 (4.6, 7.9)	13 (10.2%) 6.6 (3.8, 11.3)	60 (10.5%) 7.0 (5.5, 9.1)	9 (6.9%) 4.7 (2.4, 9.0)
Death	3 (0.5%) 0.3 (0.1, 1.1)	2 (1.6%) 1.0 (0.3, 4.0)	3 (0.5%) 0.4 (0.1, 1.1)	2 (1.5%) 1.0 (0.3, 4.2)
TE infections	243 (42.6%) 28.3 (24.9, 32.1)	52 (40.6%) 26.3 (20.0, 34.5)	249 (43.7) 29.2 (25.8, 33.1)	43 (33.1%) 22.3 (16.6, 30.1)
TE serious infections	7 (1.2%) 0.8 (0.4, 1.7)	2 (1.6%) 1.0 (0.3, 4.0)	13 (2.3%) 1.5 (0.9, 2.6)	1 (0.8%) 0.5 (0.1, 3.7)
Opportunistic infections	2 (0.4%) 0.2 (0.0, 0.8)	0 0 (0.0, 1.9)	2 (0.4%) 0.2 (0.0, 0.8)	0 0 (0.0, 1.9)
TE herpes zoster	16 (2.8%) 1.9 (1.1, 3.0)	5 (3.9%) 2.5 (1.1,6.1)	13 (2.3%) 1.5 (0.9, 2.6)	1 (0.8%) 0.5 (0.1, 3.7)
TE MACE (adjudicated)	1 (0.2%) 0.1 (0.0, 0.6)	0 0.0 (0.0, 1.9)	3 (0.5%) 0.4 (0.1, 1.1)	3 (2.3%) 1.6 (0.5, 4.8)
TE DVT/PE (adjudicated)	3 (0.5%) 0.3 (0.1, 1.0)	0 0.0 (0.0, 1.9)	3 (0.5%) 0.4 (0.1, 1.0)	0 0.0 (0.0, 1.9)
Malignancies (excluding NMSC)	5 (0.9%) 0.6 (0.2, 1.4)	3 (2.3%) 1.5 (0.5, 4.7)	4 (0.7%) 0.5 (0.1, 1.2)	0 0.0 (0.0, 1.9)
NMSC	3 (0.5%) 0.3 (0.1, 1.0)	0 0.0 (0.0, 1.9)	2 (0.4%) 0.2 (0.0, 0.8)	0 0.0 (0.0, 1.9)

inadequate response to MTX (MTX-IR) who completed a Phase 3 trial (NCT02889796)[1] and went on to enroll in a long-term extension (LTE; NCT03025308).

Methods: Pts who completed the parent study[1] (PS) on study drug were eligible to enter the LTE. LTE data cutoff was June 1, 2020, and safety data are reported to that date, with median exposure 2.2 years. Efficacy data to W48 are reported for 4 treatment groups (all with background MTX): pts who received FIL 200 mg (FIL200) or FIL 100 mg (FIL100) in the PS and continued their dose in LTE (FIL200/FIL200, FIL100/FIL100) and ADA pts who were rerandomized, double blind, to FIL200 or FIL100 for LTE (ADA/FIL200, ADA/FIL100). ACR 20%, 50%, and 70% response rates (ACR20/50/70), DAS in 28 joints with CRP (DAS28[CRP]) ≤3.2 and < 2.6, and Clinical Disease Activity Index (CDAI) ≤10 and ≤2.8 are reported. Exposure-adjusted incidence rates (EAIR)/100 pt-years of exposure of treatment-emergent adverse events (TEAEs) and AEs of special interest (AESIs) are summarized.

Results: As of June 1, 2020, 522/571 (91%) FIL200/FIL200, 502/570 (88%) FIL100/FIL100, 118/128 (92%) ADA/FIL200, and 115/130 (89%) ADA/FIL100 pts were still on study drug. LTE baseline (BL) disease characteristics were similar between groups: mean duration of RA was approximately 8.7 years; DAS28(CRP) was 2.55, and mean

concurrent MTX dosage was 15.0 mg/week. In general, proportions of pts achieving ACR20/50/70, DAS28(CRP) ≤3.2, < 2.6, and CDAI ≤10, ≤2.8 were maintained in all 4 LTE groups through W48 (**Tables 1, 2**). Numerically greater proportions of pts met response criteria at W48 in the FIL200 groups vs FIL100, regardless of PS treatment. TEAEs, serious AEs, and AEs Grade ≥3 were largely comparable between groups and lowest in ADA/FIL100 pts (**Table 3**). There were 3 deaths in each PS FIL group and 2 in each PS ADA group; EAIRs for deaths were lower for FIL/FIL groups compared with ADA/FIL groups. Opportunistic infections occurred only in FIL/FIL pts (2 in each group). Non-melanoma skin cancer (NMSC; n=5) occurred only in FIL/FIL groups, and malignancies excluding NMSC occurred in all groups except ADA/FIL100.

Conclusion: During the LTE through W48, response rates generally were maintained for FIL/FIL and ADA/FIL pts. Though there were differences between LTE groups, safety was largely comparable and consistent with that observed in the PS[1] and in previously reported results of safety data from 7 trials[2]: rates of AESIs were low, and all confidence intervals were overlapping. Limitation: the LTE was not formally randomized for comparison between FIL/FIL and ADA/FIL treatment groups, the groups were of unequal size, and the switch from ADA to FIL for LTE was by design, rather than based on disease activity.

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Abstract Number: 1698

Integrated Safety Analysis Update for Filgotinib in Patients with Moderately to Severely Active Rheumatoid Arthritis Receiving Treatment over a Median of 2.2 Years

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The preferential Janus kinase (JAK)-1 inhibitor filgotinib (FIL) significantly improved signs and symptoms of RA in Phase 2 and 3 trials,[1–5] and FIL is approved for treatment of moderately to severely active RA in Europe and Japan. Integrated safety analysis of FIL with patient data through 2019 was presented at the 2020 ACR virtual meeting.[6] This abstract reports updated, as-treated data with increased study-drug exposure (median, 2.2 years [y]; maximum, 6.8 y).

Methods: Data were integrated from 2 Phase 2 (NCT01668641, NCT01894516), 3 Phase 3 (NCT02889796, NCT02873936, NCT02886728), and 2 long-term extension (LTE) (NCT02065700, NCT03025308) trials. Phase 2 and 3 LTE data were through Nov 2020 and Jun 2020, respectively. The as-treated analysis set included all available data for patients receiving ≥1 dose FIL 200 (FIL200) or 100 mg (FIL100), including those rerandomized to filgotinib for LTE. Exposure-adjusted incidence rates (EAIR)/100 patient-years exposure (PYE) of treatment-emergent adverse events (TEAEs; onset after first dose and no later than 30 days after last dose or new drug first dose date –1 day) and TEAEs of special interest (AESIs)—including serious infections, opportunistic infections, herpes zoster, adjudicated major adverse cardiovascular events, adjudicated venous thromboembolism, atrial systemic thrombotic events, nonmelanoma skin cancer (NMSC), non-NMSC malignancies, and gastrointestinal perforations—are presented. EAIR and 95% CIs were estimated with Poisson models with treatment and study as covariates and natural log of exposure as offset, unless otherwise specified.

Results: 3691 patients received FIL200 or FIL100 for 8085.1 PYE (median 2.2, maximum 6.8 y). In the as-treated set, 61% of FIL200 and 45% of FIL100 patients received filgotinib for ≥2 years (**Table 1**). EAIR for TEAEs was higher with FIL100 than with FIL200; EAIRs for deaths were 0.5 and 0.3 for FIL200 and FIL100 (**Table 2**). Incidences of infections and serious infections were numerically greater for FIL100 vs FIL200, while EAIRs for other AESIs were comparable between doses (**Table 3**). EAIRs for AESIs tended to decrease since the previous update, except for VTE (total FIL 0.1 to 0.2) and non-NMSC malignancies (total FIL 0.5 to 0.6).

Table 1. Summary of exposure

	Long-term, as-treated		
	FIL 200 mg	**FIL 100 mg**	**Total FIL**
N	2267	1647	3691
Total PYE	5302.5	2782.6	8085.1
Treatment duration, median y (Q1, Q3)	2.3 (1.4, 2.8)	1.9 (0.5, 2.5)	2.2 (1.3, 2.7)
Exposed to study drug ≥ 1 y, n (%)	1909 (84.2)	1176 (71.4)	3093 (83.8)
Exposed to study drug ≥ 2 y, n (%)	1385 (61.1)	746 (45.3)	2145 (58.1)
Exposed to study drug ≥ 3 y, n (%)	419 (18.5)	79 (4.8)	505 (13.7)
Exposed to study drug ≥ 4.5 y, n (%)	256 (11.3)	8 (0.5)	272 (7.4)

PYE was defined as (last dose date – first dose date + 1)/365.25. Duration of exposure to study drug (years) = (last dosing date – first dosing date + 1)/365.25. A 7-day window was applied to the on-treatment Week 52 to match with the protocol-specified visit window. FIL, filgotinib; PYE, patient-years of exposure; Q, quartile; y, years.

Table 2. Overall summary of EAIRs of TEAEs, as-treated set

	FIL 200 mg N = 2267 PYE = 5302.5	FIL 100 mg N = 1647 PYE = 2782.6	Total FIL N = 3691 PYE = 8085.1
TEAE, n (%)	1881 (83.0)	1230 (74.7)	3048 (82.6)
EAIR (95% CI)	32.9 (31.2, 34.7)	54.4 (50.0, 59.1)	33.5 (32.0, 35.0)
TEAE Grade ≥3, n (%)	364 (16.1)	250 (15.2)	613 (16.6)
EAIR (95% CI)	5.8 (5.1, 6.6)	7.2 (5.1, 10.0)	6.0 (5.3, 6.7)
TE serious AE, n (%)	318 (14.0)	205 (12.4)	521 (14.1)
EAIR (95% CI)	5.9 (5.2, 6.7)	6.9 (5.2, 9.3)	6.0 (5.3, 6.6)
TEAE leading to premature discontinuation, n (%)	275 (12.1)	119 (7.2)	394 (10.7)
EAIR (95% CI)	5.4 (4.8, 6.1)	6.6 (5.3, 8.2)	5.5 (5.0, 6.1)
All deaths, n (%)	26 (1.1)	9 (0.5)	35 (0.9)
EAIR (95% CI)	0.5 (0.3, 0.7)	0.3 (0.2, 0.6)*	0.4 (0.3, 0.6)*

*Except when any study had 0 event within the treatment, the Poisson model was not adjusted by study. PYE was defined as (last dose date – first dose date + 1)/365.25. AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate per 100 PYE; FIL, filgotinib; PYE, patient-years of exposure; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

Table 3. Treatment-emergent adverse events of special interest, as-treated set

	FIL 200 mg N = 2267 PYE = 5302.5	FIL 100 mg N = 1647 PYE = 2782.6	Total FIL N = 3691 PYE = 8085.1
Infectious AEs, n (%)	1206 (53.2)	747 (45.4)	1927 (52.2)
EAIR (95% CI)	21.1 (19.7, 22.5)	30.2 (26.8, 34.0)	21.0 (19.9, 22.3)
Serious infectious AEs, n (%)	80 (3.5)	57 (3.5)	137 (3.7)
EAIR (95% CI)	1.5 (1.1, 1.9)	2.7 (1.9, 3.9)	1.6 (1.3, 2.0)
Opportunistic infections, n (%)	5 (0.2)	4 (0.2)	9 (0.2)
EAIR (95% CI)	0.1 (0.0, 0.2)*	0.1 (0.1, 0.4)*	0.1 (0.1, 0.2)*
Active TB, n (%)	0	3 (0.2)	3 (<0.1)
EAIR (95% CI)	0	0.1 (0.0, 0.3)*	0.0 (0.0, 0.1)*
Herpes zoster, n (%)	84 (3.7)	30 (1.8)	114 (3.1)
EAIR (95% CI)	1.6 (1.2, 2.0)	1.1 (0.8, 1.5)*	1.4 (1.1, 1.7)
MACE[a], n (%)	19 (0.8)	14 (0.9)	33 (0.9)
EAIR (95% CI)	0.3 (0.2, 0.5)	0.5 (0.3, 0.8)*	0.4 (0.2, 0.6)
VTE[b], n (%)	11 (0.5)	4 (0.2)	15 (0.4)
EAIR (95% CI)	0.2 (0.1, 0.4)*	0.1 (0.1, 0.4)*	0.2 (0.1, 0.3)*
ASTE[a], n (%)	1 (<0.1)	1 (<0.1)	2 (<0.1)
EAIR (95% CI)	0.0 (0.0, 0.1)	0.0 (0.0, 0.3)	0.0 (0.0, 0.1)
Malignancy excluding NMSC, n (%)	32 (1.4)	17 (1.0)	49 (1.3)
EAIR (95% CI)	0.6 (0.4, 0.9)	0.6 (0.4, 1.0)*	0.6 (0.4, 0.8)
NMSC, n (%)	15 (0.7)	5 (0.3)	20 (0.5)
EAIR (95% CI)	0.3 (0.2, 0.5)*	0.2 (0.1, 0.4)*	0.2 (0.2, 0.4)*
Gastrointestinal perforations, n (%)	3 (0.1)	1 (<0.1)	4 (0.1)
EAIR (95% CI)	0.1 (0.0, 0.2)*	0.0 (0.0, 0.3)*	0.0 (0.0, 0.1)*

*Except when any study had 0 event within the treatment, the Poisson model was not adjusted by study. PYE was defined as (last dose date – first dose date + 1)/365.25. aPositively adjudicated. bAdjudicated as DVT or PE AE, adverse event; AESI, AE of special interest; ASTE, arterial systemic thrombotic event; CI, confidence interval; DVT, deep vein thrombosis; EAIR, exposure adjusted incidence rate per 100 PYE; FIL, filgotinib; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; PYE, patient years of exposure; TB, tuberculosis; TE, treatment emergent; VTE, venous thromboembolism.

Conclusion: With 1 additional year of exposure since the 2020 report, FIL continues to be well tolerated with no new safety concerns emerging. EAIRs of TEAEs, including deaths, and AESIs remained stable or decreased since the 2020 report, except for slight increases in rates of NMSC and non-NMSC malignancies. In the context of demonstrated efficacy, both FIL doses had an acceptable risk/benefit profile.

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Abstract Number: 1699

The "ITIS" Diet Improves Fatigue in Patients with Rheumatoid Arthritis and Is Associated with Changes in Metabolome and Fecal Microbiome

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Fatigue is common symptom in rheumatoid arthritis (RA), associated with decreased quality of life and productivity. Fatigue mechanisms have not been well studied, hence, a poorly understanding of this symptom leads to a poor clinical management. Moreover, despite the high number of drugs available for RA, it can be a persistent symptom despite reaching a low/minimum disease activity.

Methods: We evaluated the effect of diet on fatigue in an open-label pilot trial which had as a main objective the evaluation of feasibility and efficacy of a 2-week anti-inflammatory diet (ITIS) in RA patients. 20 patients with active RA (at least 3 tender and 3 swollen joints) participated. Physical examination and collection of fecal and plasma samples for microbiome and metabolomics were performed, along with collection of data on fatigue on a visual analogue scale from 0 to 10 among other clinical outcomes. 16S rRNA gene amplicon profiling of the stools and untargeted mass spectrometry-based metabolomics in stool and plasma were performed.

Results: Patients had moderate disease activity (DAS28CRP 3.86 ± 0.73) and an average fatigue of 4.78 ± 2.71 (Table 1). Fatigue was more intense in patients with higher disease activity, suggested by the positive correlation between fatigue and DAS28CRP (r=0.5, p=0.02). Post-intervention, fatigue significantly improved from 4.78 ± 2.71 before vs 2.49 ± 2.37 after diet, $p < 0.01$. Of note, fatigue did not correlate with DAS28CRP after diet (r=0.04, p=0.85). Using a 50% improvement in fatigue, patients were categorized as responders (R, N=9) or non-responders (NR, N=11). At baseline, R microbiome was enriched in *Dialister* and *Anaerofilum*, with decreased fecal deoxycholic and chenodeoxycholic acid and increased plasma L-kynurenine, octadecadienoic and elaidic acid (Figure 1). No differences in alpha diversity (within subject) of fecal microbiome and metabolome, nor plasma metabolome, were observed between R and NR before or after the diet. Only plasma metabolome beta-diversity (between subjects) was different between R and NR after the diet (Figure 2A). Post intervention, R microbiome was enriched in *Tissierellaceae* family and *Gemmiger* and *Anaerofilum* genus, while *Bacteroides* genus was decreased (Figure 2B). R fecal metabolome was enriched in dypeptides (Val-Arg, Leu-Val), Guanine and Hirsutanone (plant derived), which has potential anti-inflammatory properties (Figure 2C). Fecal cis 8,5,11 eicosatrienoic acid and 8-oxo-OTrE, potentially pro-inflammatory, were decreased in R. R also had higher levels of glychochenodeoxycholate and omega-hydroxydecanoate, derivative of 10-hydroxydecanoc acid, a medium-chained fatty acid with potential anti-inflammatory properties (Figure 2D).

Conclusion: Fatigue significantly improved after the "ITIS" diet, however it didn't parallel the improvement in disease activity. This was associated with changes in fecal microbiome and anti-inflammatory compounds. Our results sug-

Table 1. Baseline Characteristics of patients

Characteristic	Baseline - Mean (SD)
Age	57.5 (12.2)
Sex (F%)	90
BMI (Body Mass Index)	28.1 (5.2)
Pain (1-10 on Visual Analogue Scale)	3.93 (1.67)
Visual Analogue Scale General Health Status Patient	3.97 (2.32)
Visual Analogue Scale General Health Status Physician	4.38 (1.75)
Health Assessment Questionnaire	0.8 (0.66)
Morning Stiffness (minutes)	40.75 (39.94)
Tender Joint Count	11.5 (6)
Swollen Joint Count	7.8 (4)
Fatigue (1-10 on Visual Analogue Scale)	4.78 (2.71)
Clinical Disease Activity Index (CDAI)	27.66 (11.74)
Simplified Disease Activity Index (SDAI)	28.95 (11.84)
Disease Activity Index 28 (DAS28CRP)	3.86 (0.73)
C reactive protein (mg/L)	1.29 (0.98)

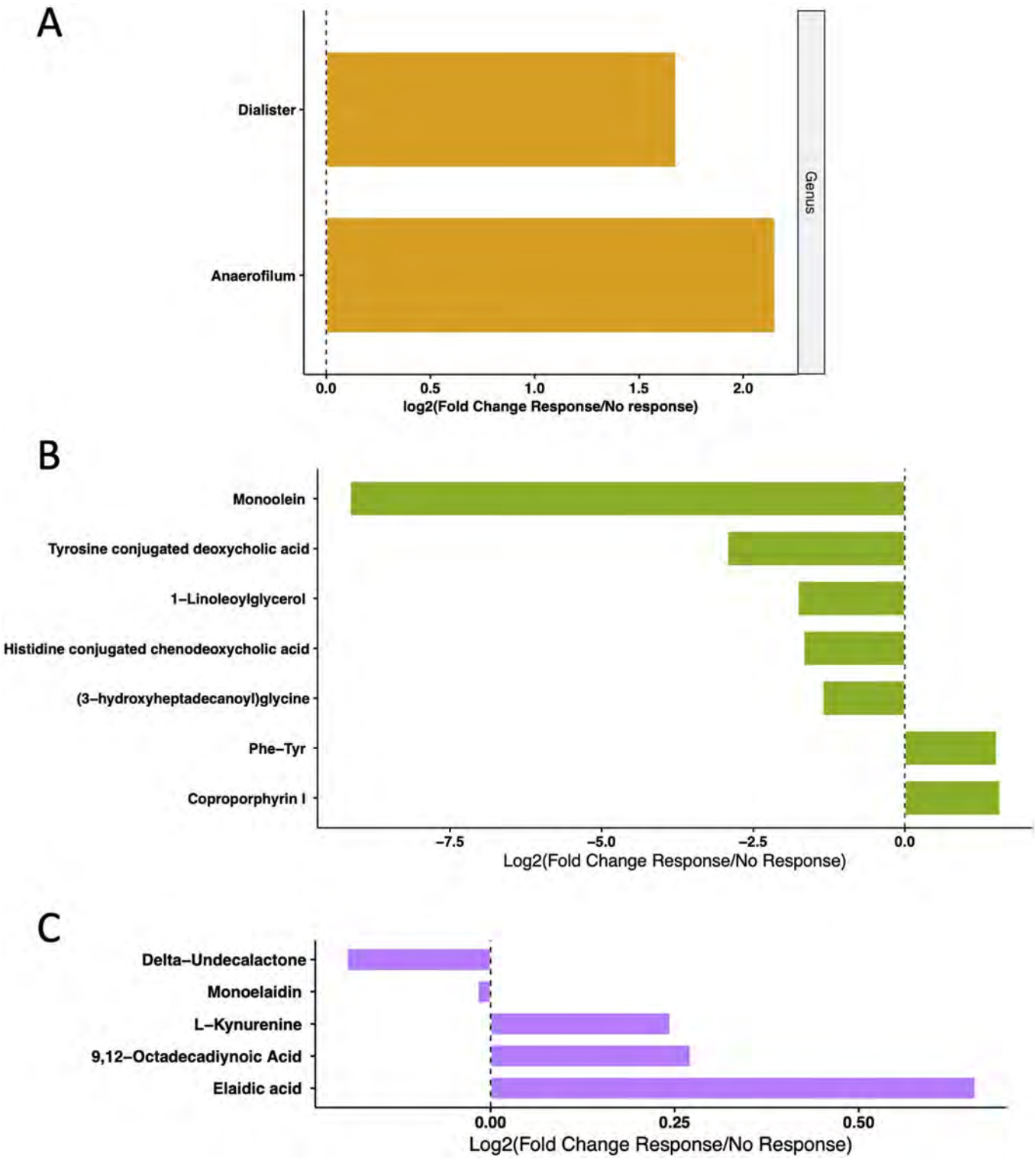

Figure 1. Characteristics of Fecal Microbiome and Plasma and Fecal Metabolome at Baseline A. Log Fold Change of the differentially abundant microbes in R compared to NR at baseline. B. Log Fold Change of the differentially abundant fecal metabolites in R compared to NR at baseline. C. Log Fold Change of the differentially abundant plasma metabolites in R compared to NR at baseline. R – 50% improvement in fatigue; NR – less than 50% improvement in fatigue.

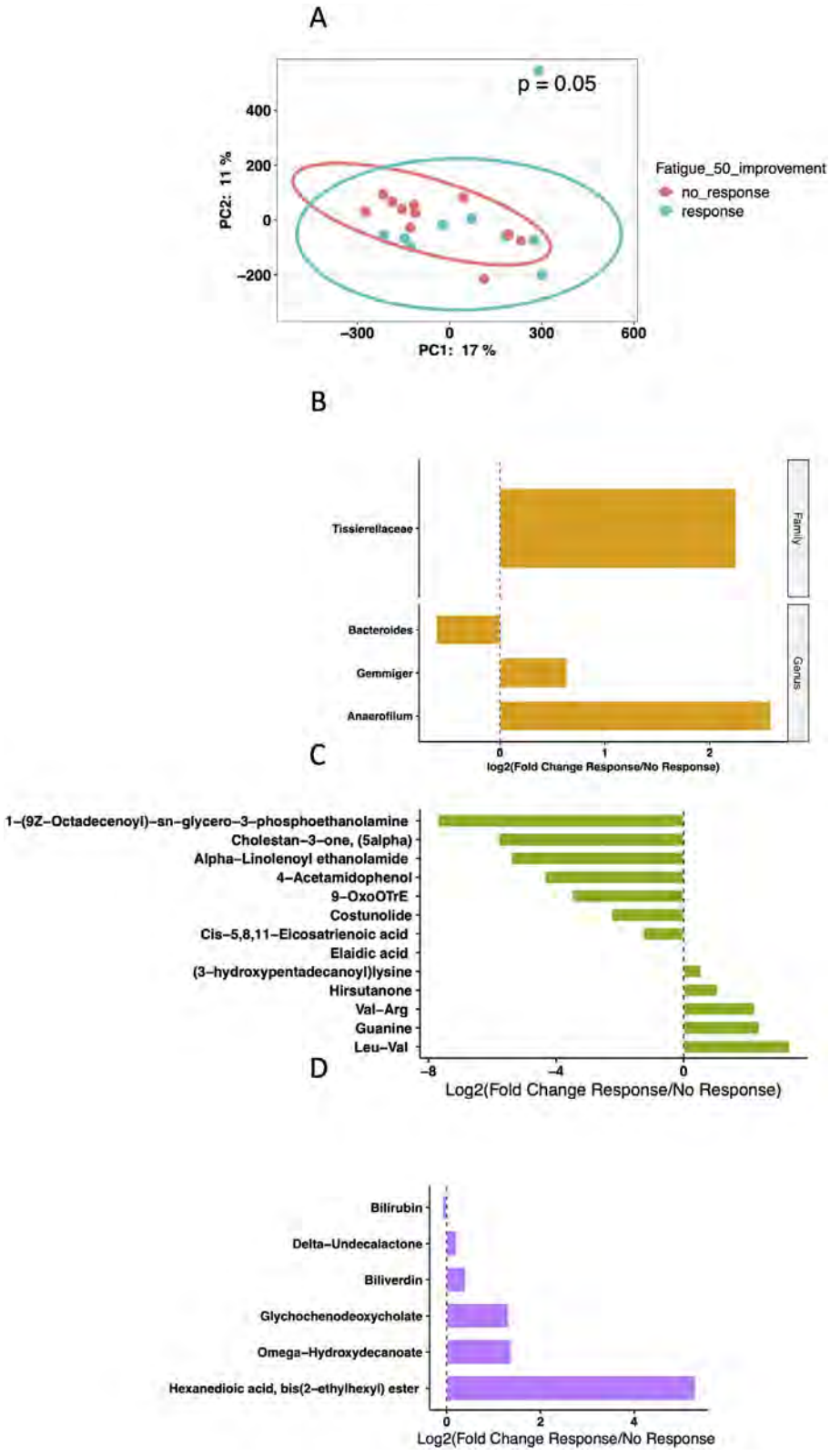

Figure 2. Characteristics of Fecal Microbiome and Plasma and Fecal Metabolome after Diet A. Principal Coordinate Analysis of the Unweighted UniFrac for the plasma metabolome after diet, in R and NR. B. Log Fold Change of differentially abundant microbes in R compared to NR on day +14. C. Log Fold Change of differentially abundant fecal metabolites in R compared to NR on day +14. D. Log Fold Change of differentially abundant plasma metabolites in R compared to NR on day +15. R – 50% improvement in fatigue; NR – less than 50% improvement in fatigue.

gest a potential role of diet in the management of fatigue in RA patients. Further studies are needed to establish the scientific basis for using diet to adjust the gut microbiome to improve fatigue management not only in RA patients, but perhaps in all rheumatic disease.

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Abstract Number: 1700

Pharmacokinetic Boosting to Enable Once-Daily Reduced Dose Tofacitinib

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Tofacitinib is an effective, yet costly, drug for treatment of RA and PsA. Tofacitinib is metabolized mainly by the cytochrome P450-enzyme CYP3A4, and the manufacturer recommends to halve the dose of tofacitinib when patients use concomitant medication that strongly inhibits CYP3A4. Therefore, we hypothesized that coadministration of cobicistat, an CYP3A4-inhibitor approved for boosting of antiretroviral drugs, next to half dose tofacitinib would lead to pharmacokinetics equivalent to standard doses tofacitinib. The aim of this study was thus

Table 1. Baseline characteristics. Either displayed as number (percentage), mean ± standard deviation or median (interquartile range). Percentages were calculated over the total number of participants unless indicated

	Participants (n=27)
Age (years)	59 (49-67)
Female gender	15 (56%)
Disease	
• RA	17 (63%)
• RF and/or ACPA positive (RA only)	14 (82%)
• PsA	10 (37%)
Disease duration (years)	11 (4-18)
Duration of tofacitinib use at inclusion (months)	1 (1-1)
DAS28CRP at first sampling day	3.27 ± 1.41
Concomitant csDMARD use	
• methotrexate	4 (15%)
• leflunomide	4 (15%)
Previous biological or targeted synthetic DMARDs (n)	3 (2-4)
Adaptations made to comedication interacting with CYP3A4 prior to inclusion (multiple adaptations possible)	
• simvastatin/atorvastatin replaced by pravastatin	5 (19%)
• amlodipine replaced by hydrochlorothiazide	1 (4%)
• amlodipine replaced by enalapril	1 (4%)
• metoprolol replaced by bisoprolol	1 (4%)

to investigate the bioequivalence of tofacitinib 5 mg and cobicistat 150 mg once daily (QD) compared to tofacitinib 5 mg twice daily (BID) alone.

Methods: This open label, non-randomized, cross-over, bioequivalence study was performed between September 2019 and March 2021 in the Netherlands. Patients with RA or PsA, using tofacitinib and no other concomitant medication which could be significantly affected by cobicistat use, were included. After using tofacitinib 5 mg BID for at least 14 days, plasma samples of tofacitinib were collected pre-dose and 0.5, 1, 2, 3, 4, 6, 9 and 12 hours post-dose. After this first sampling day, patients switched treatment to tofacitinib 5 mg and cobicistat 150 mg QD. Two to six weeks after, plasma samples of both tofacitinib and cobicistat were collected at the same timepoints, with the addition of a sample at 24 hours post-dose. Bioequivalence of the average tofacitinib concentration (C_{avg}) was assessed of tofacitinib 5 mg with cobicistat 150 mg QD compared to tofacitinib 5 mg BID: the 90% confidence intervals of the geometric mean ratio of C_{avg} should be between 80% and 125% for bioequivalence. Secondary endpoints included efficacy (change in mean DAS28CRP measured at both sampling days), safety, and patient preference (7-point Likert Scale at study end).

Results: Twenty seven patients were included, of which five underwent adaptations to comedication prior to inclusion due to CYP3A4 interactions (Table 1). The geometric mean ratio for the C_{avg} was 84.8% (90% CI 75.1% - 95.6%), thus full bioequivalence could not be concluded. The change in mean DAS28CRP was 0.05, 95% CI -0.49 to 0.59. No serious adverse events occurred during the study. The majority of patients preferred the combination regime: 56% preferred combination therapy (score on Likert scale 5-7), 18% monotherapy (score 1-3) and 26% neutral (score 4), leading to a net promotor score of 38%.

Conclusion: Tofacitinib 5 mg with cobicistat 150 mg QD combination therapy was not bioequivalent to standard tofacitinib 5 mg BID. However, we think this combination treatment shows promise as a slightly reduced exposure is not expected to result in reduced efficacy, based on prior dose finding studies[1], combined with the fact that both drugs are registered and readily available. In addition, there was no difference in disease activity and a clear preference by patients. Further research should focus on safety and efficacy at longer use.

[1]Lamba M, et al. Clin Pharmacol Ther. 2017 Jun;101(6):745-753.

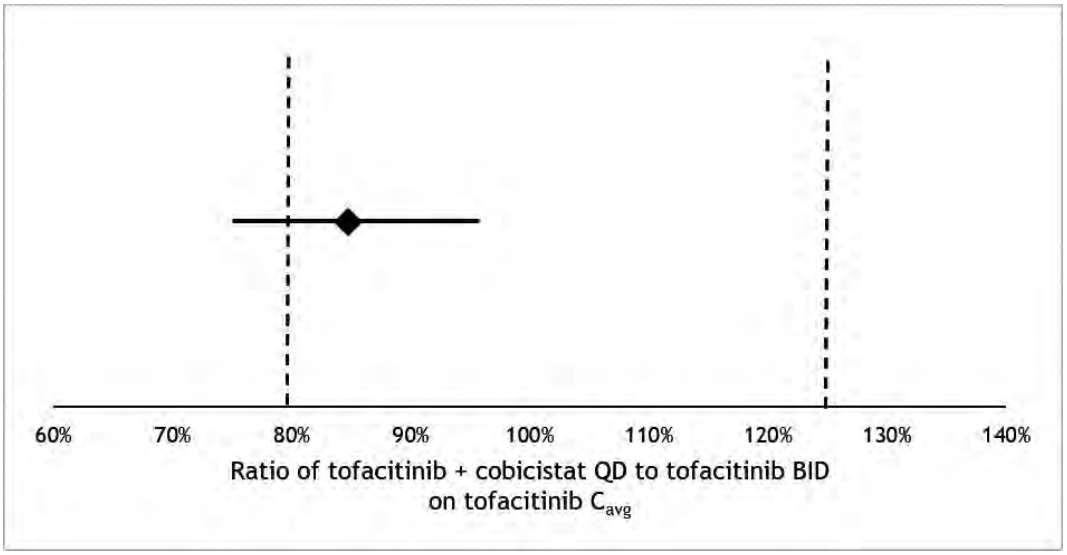

Figure 1. Visual representation of primary study result on bioequivalence. Geometric mean ratio with 90% confidence interval of the tofacitinib Cavg (tofacitinib 5 mg BID compared to tofacitinib 5 mg and cobicistat 150 mg QD) represented as horizontal line. Equivalence margins are represented as vertical dotted lines at 80% and 125%.

Disclosure: C. van der Togt, None; **L. Verhoef**, None; **N. den Broeder**, None; **R. ter Heine**, None; **B. van den Bemt**, None; **A. den Broeder**, Amgen, 12, Expert witness fee adalimumab biosimilar litigation, Galapagos, 12, Congress invitation, Sanofi, 12, Congress invitation, Abbvie, 12, Editorial work education, Novartis, 12, Editorial work education, Abbvie, 5, Pfizer, 5, Lilly, 5, Novartis, 5, Sanofi, 5.

Abstract Number: 1701

Evaluation of Cardiovascular Risk Factors and Atherosclerosis in Rheumatoid Arthritis Patients, Treated with Biological Agents: 6-month Follow-up

Georgios Papamichail[1], Theodora Markatseli[2], Athanasios Georgiadis[3], Vasileios Xydis[4], Haralampos Milionis[1], Alexandros Drosos[2] and Paraskevi Voulgari[2], [1]Internal Medicine, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, [2]Rheumatology Clinic, Department of Internal Medicine, Medical School, University of Ioannina, Ioannina, Greece, [3]Private Practice, Ioannina, Greece, Athens, Greece, [4]Radiology, Department of Radiology, Medical School, University of Ioannina, Ioannina, Greece, Ioannina, Greece

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Despite new therapeutic approaches in RA, the mortality gap between RA patients and the general population persists, and may even be increasing. Cardiovascular (CV) complications consist the leading cause of this increase in mortality. In this study, we tried to investigate the impact of biological agents (BA) on cardiovascular risk factors in RA patients.

Methods: Forty-nine, biologic-naïve RA patients, fulfilling the 2010 ACR/EULAR classification criteria with no previous history of CV disease were recruited in the study. We compared total cholesterol (TC), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c), triglycerides (TGs), Apolipoprotein A1 (ApoA1), Apolipoprotein B (ApoB), Lipoprotein A (LpA), systolic blood pressure, inflammatory markers such as CRP and ESR between baseline and after 6 months of BA initiation. An ultrasonographic measurement of intima-media thickness (IMT) of carotids was performed by an experienced sonographer at baseline and after 6-month follow-up in order to determine the presence of subclinical atherosclerosis. The titer of autoantibodies against oxidised LDL (anti-oxLDL) was also estimated in a subgroup of 35 patients.

Table 1. Characteristics of patients included in the study

Total Number of Patients	49
Female N (%)	36 (73.5%)
Male N (%)	13 (26.5%)
Age (mean±SD) (years)	53.4±14.8
Smokers N (%)	11 (22.4%)
Disease Duration (mean±SD) (years)	4.5±1.3
Anti-TNF use N (%)	37 (75.5%)
RF (+) N (%)	32 (65.3%)
ACPA (+) N (%)	29 (59.18%)

Table 2. Results of CV risk parameters comparison between baseline and 6-month follow-up

CV RISK PARAMETERS	Baseline	6 months	P value
Systolic Blood Pressure[median (IQR)]	135 (125-147.5)	125 (120-132.5)	<0.001
Diastolic Blood Pressure [median (IQR)]	80 (75-85)	80 (75-85)	0.218
Heart Rates (mean ± SD)	78 ± 7	76 ± 9	0.060
DAS28 Score[median (IQR)]	3.39 (2.75-3.675)	2.89 (2.255-3.215)	<0.001
CRP [median (IQR)]	4 (2-7)	3 (2-4)	0.001
ESR [median (IQR)]	22 (12-38)	11 (6-22)	<0.001
TCHOL (mean ± SD)	209 ± 63	227 ± 48	0.030
TRG [median (IQR)]	107 (89.5-142.5)	101 (85-125)	0.622
HDL (mean ± SD)	58 ± 15	69 ± 17	<0.001
LDL (mean ± SD)	139 ± 39	135 ± 37	0.272
LpA [median (IQR)]	14.8 (5.6-27.05)	10.7 (4.8-27)	0.323
ApoA1 (mean ± SD)	162.4 ± 31.8	174.6 ± 32.9	<0.001
ApoB (mean ± SD)	95.6 ± 23.8	94.7 ± 26.2	0.696
IMT [median (IQR)]	0.9 (0.8-1)	0.7 (0.6-0.8)	<0.001
oxLDL (mean ± SD)	0.190 ± 0.056	0.132 ± 0.042	<0.001

Results: As regards the characteristics of patients, the mean (SD) age was 53.4 (14.8) years, 73.5% were women and 22.4% were smokers (Table 1). BA were administered in all patients and anti-TNF use was the most common (75.5% of patients). Six months after treatment initiation, patients presented with a significant increase in mean (SD) HDL [69 (17) vs 58 (15)] and ApoA1 [174 (33) vs 162 (32)] levels ($p< 0.001$) with a simultaneous significant reduction of mean (SD) systolic blood pressure [125 (12.5) vs 135 (22.5)] and the titer of anti-oxLDL [0.132 (0.042) vs 0.190 (0.056)]. IMT was also reduced after 6-month reassessment [0.7 (0.2)mm vs 0,9 (0.2)mm, ($p< 0.001$ for all comparisons)] (Table 2).

Conclusion: An improved lipid profile (increased HDL-c in combination with reduction of the anti-oxLDL titer) and a significant reduction of IMT were observed in a six-month period of BA administration. This study confirms that RA patients are prone to early atherosclerosis and BA initiation correlates strongly with more favorable values of CV risk parameters.

Disclosure: G. Papamichail, None; **T. Markatseli**, None; **A. Georgiadis**, None; **V. Xydis**, None; **H. Milionis**, None; **A. Drosos**, None; **P. Voulgari**, Genesis Pharma SA, 3.

Abstract Number: 1702

Efficacy and Safety of Baricitinib in B/tsDMARDs Naive and B/tsDMARDs-IR Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib, an oral selective inhibitor of Janus kinase (JAK) 1 and 2, improved signs and symptoms of rheumatoid arthritis(RA).We analyze efficacy and safety of baricitinib in real-world data.

Methods: Cases were recruited to SHin-yokohama Arthritis REgister (SHARE) between 2015 and 2020 (n=3,961). 154 Patients were diagnosed according to ACR/EULAR 2010 classification criteria and treated with baricitinib over 15 months. 32 cases fulfilled EULAR definition for difficult-to-treat RA (D2T-RA). In 154 (Male25, Female129 cases, RA duration 11.4+/-7.8years) cases, Clinical Disease Activity Index (CDAI), Health Assessment Questionnaire-Disability Index (HAQ-DI), anti-CCP2 and other clinical parameters were analyzed. They were arrayed based on previous treatments as b/tsDMARD-naïve and b/tsDMARD-insufficient responders (IR) after the failure or intolerance to bDMARDs. Tapering MTX dose was also analyzed in these two groups.

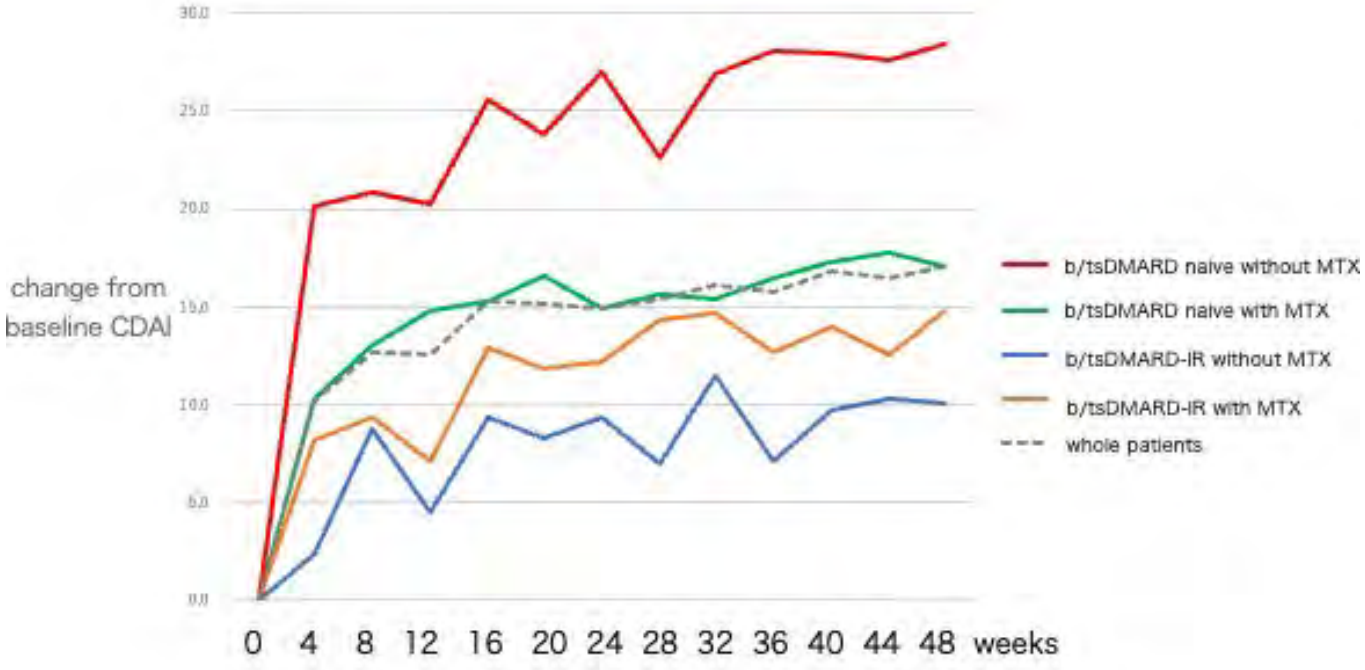

Fig. 1. Change from baseline CDAI

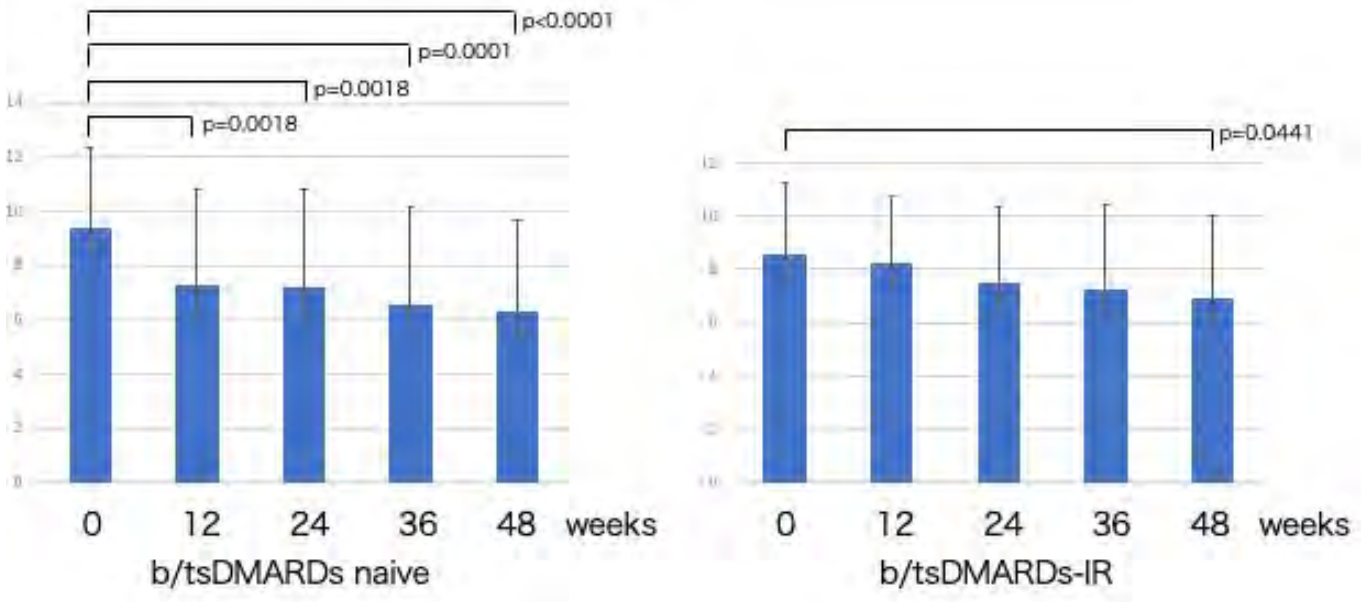

Fig. 2. MTX dose inn patients at 0, 12, 24, 36 and 48 weeks of treatment in baricitinib.

Table1. Predictors to detect patients who achieved LDA and/or REM in b/tsDMARDs group

	b/tsDMARD naive					
	CDAI≤10	10<CDAI		multivariate logistic regression		
n	n=65, 84.4%	n=12, 15.6%	p value	pvalue	OR	95%CI
M/F	13/52	1/11	0.336			
age	59.1+/-12.4	62.0+/-12.3	0.461			
RA duration	7.2+/-5.3	10.3+/-7.2	0.209			
ACPA	54.3+/-78.1	181.1+/-310.3	0.453			
PSL, cases, %	14, 21.5%	1, 9.1%	0.337			
PSL, dose	0.2+/-0.8	0.7+/-1.6	0.291			
MTX, cases, %	57, 87.7%	8, 66.7%	0.090			
MTX, dose	7.0+/-5.4	8.2+/-4.2	0.841			
CDAI at baricitinib 0W	20.6+/-11.1	33.4+/-11.1	0.023	0.0258	1.1	1.0075-1.1240
BARI 2/4mg, cases	55/10	3/9	<0.0001	0.0008	14.3	0.0145-0.3322

Results: 79 (51.3%) b/tsDMARDs naïve and 75(48.7%)b/tsDMARDs-IR patients were enrolled. There were no differences in RA duration time (11.4+/-7.8 vs. 12.9+/-8.3), anti-CCP2 positive(ave.242.6+/-158.9), and CDAI(20.2+/-12.4 vs. 17.8+/-11.3) at the beginning of baricitinib. Baricitinib withdrawal for inefficacy showed no difference between b/tsDMARDs naive and b/tsDMARDs-IR patients in RA with/without MTX (logrank p=0.8589). In b/tsDMARDs naïve group, 45(59.5%) patients were achieved LDA and 18 (22.8%) were acheived remission at 12 weeks. In b/tsDMARDs-IR group, 35(46.7%) patients were achieved LDA and 11(14.7%) patients were achieved remission. b/tsDMARDs naïve group showed more changes from baseline CDAI. In b/tsDMARDs group, predictors to detect patients who achieved LDA and/or remission were lower CDAI(20.6+/-11.1 vs. 33.4+/-11.1) and baricitinib 2mg/day in multivariate logistic regression(OR 1.1 and 14.3, 95%CI 1.0075-1.1240 and 0.0145-0.3322, p=0.023 and p< 0.0001, respectively). In A significant reduction in the dose of MTX was seen at 48 weeks in both b/tsDMARDs naïve group and b/tsDMARDs-IR group (p< 0.0001 vs. p=0.0441). 11(13.9%) parients were discontinued baricitinib due to herpes zoster (8.1/100PY). There were no thrombotic event in our cohort.

Conclusion: Our data confirm the efficacy and safety profiles of baricitinib in RA. It also showed baricitinib 2mg/day was effective in b/tsDMARD naïve patients.

Disclosure: M. YAMASAKI, None.

Abstract Number: 1703

AP1189: A Novel Oral Biased Melanocortin Agonist with Anti-inflammatory and Pro-resolving Effect for the Treatment of Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Melanocortin (MC) type 1 and type 3 receptor stimulation is associated with anti-inflammation and promotion of inflammatory resolution. AP1189 is a biased MC type 1 and 3 receptor agonist aimed for oral administration currently in clinical development for treatment of active Rheumatoid Arthritis.

Methods: The pharmacokinetic profile of the compound has been evaluated in healthy male volunteers at three dose levels (N=27). Following once daily dosing with oral suspension for 14 days, PK analyses showed rapid absorption with tmax observed 1.5-2.5 hours post dosing. Elimination half-time between 19 (lowest dose) and 23 (highest dose) hrs (CV%: 13 and 21%). Approximately 10% of the compound was excreted unchanged in the urine. No drug accumulation was observed after steady state had been reached at day 7. Expose (based on AUC) was supra-proportional with a moderate increase of 2.25 when the dose was doubled. The most common side effects observed were nausea and headache with low to moderate intensity and observed in the time matched placebo controls too. Specifically, no sign of immunosuppression was observed. No, treatment related effect on vital signs were observed and telemetric CV safety evaluation did not reveal any QTcF prolongation nor other cardiac safety concerns.

The compound is currently tested in a double-blind placebo-controlled Phase 2a clinical trial in Europe with once daily dosing for four weeks as add on to Methotrexate (MTX) in previous MTX naïve patients with clinical disease activity (CDAI) above 22. The primary aim of the study is to evaluate safety and tolerability and potential treatment effects of the compound relative to placebo. The primary efficacy readout is defined as fraction of patients where disease activity goes for high (ie CDAI >22) to mediate or lower disease activity. The aim is to include a minimum of 105 subjects treated with either 50 mg AP1189, 100 mg AP1189 or placebo.

Results: An interim analysis of the first 26 patients showed the following:

16 women, 10 men, median age 57 (high/low: 79/27), median CDAI: 34 (high/low: 49/24) were treated with MTX according to the investigator's discretion (10-15 mg po once weekly increasing to 15-25 mg during the 4 weeks study period). 9 were treated with placebo, 9 with 50 mg AP1189 and 8 with 100 mg AP1189 as add on to the MTX treatment. There were no dropouts, and no serious adverse events were observed. The most common reported adverse events were nausea (9 cases disturbed equally between the three treatment groups) and 3 cases of headache. No signs of immunosuppression were observed. Median CDAI at end of treatment between groups were 18.5 (high/low: 46/4). 7 patients had low disease activity (CDAI 2.9-10); 9 had moderate disease activity (CDAI 10,1-22), 10 pts had high disease activity (CDAI >22). CDAI at end of treatment distributed between the three treatment groups: Placebo: 4 out of 9 (44%); 50 mg AP1189: 6 out of 9 (67%), 100 mg: 6 out of 8 (75%). To secure blinding of investigators and sponsor no further evaluation of group specific effects was made. Completion of the study is planned for third quarter 2021.

Conclusion: AP1189 is novel oral available compound with anti-inflammatory and pro-resolving effect with the potential to treat active RA

Disclosure: T. Jonassen, SynAct Pharma AB, 4, 8; **T. Duvauchelle**, SynAct Pharma AB, 2; **B. Telmer**, SynAct Pharma, 2, 7; **I. Sandholdt**, SynAct Pharma, 2, 7; **T. Boesen**, SynAct Pharma AB, 4, 8; **E. Hauge**, AbbVie, 6, Sanofi, 6, Sobi, 6, SynACT Pharma, 6, Novo Nordic Foundation, 5, Roche, 5, Novartis, 5.

Abstract Number: 1704

Tofacitinib in Rheumatoid Arthritis: Is There a Correlation Between a Rapid Analgesic Effect and a Decrease in Activity After 3 and 6 Months?

Elena Pogozheva[1], Andrey Karateev[1], Evgeniy Nasonov[1], Alexander Lila[1], Vadim Mazurov[2], Rusanna Samigullina[3], Diana Chakieva[4], Anna Dadalova[4], Anna Dyo[4], Andrey Baranov[5], Natalia Lapkina[5], Ekaterina Kol'tsova[6], Ivan Shchendrigin[7], Tatyana Rasevich[8], Antonina Davydova[9], Irina Shafieva[10], Inna Bashkova[11], Daria Bobrikova[12], Irina Kushnir[13], Elena Kalinina[14], Tatiana Sal'nikova[15], Valentina Sorotskaya[16], Irina Marusenko[17], Olga Semagina[18], Irina Vinogradova[19], Diana Krechikova[20], Natalia Kiryukhina[21], Irina Semizarova[22], Dzhamilya Murtazalieva[23] and Marina Semchenkova[24], [1]V.A. Nasonova Reseach Institute of Rheumatology, Moscow, Russia, [2]Mechnikov North-Western State Medical University, Saint Petersburg, Russia, [3]Mechnikov North-Western State Medical University, St.Petersburg, Russia, [4]Mechnikov North-Western State Medical University, St. Petersburg, Russia, [5]Yaroslavl State Medical University, Yaroslavl, Russia, [6]Scientific and Research Institute of Health Care Organization, Moscow, Russia, [7]Stavropol Regional Clinical Hospital, Stavropol, Russia, [8]Astrakhan Region Alexandro-Mariinsky Regional Clinical Hospital, Astrakhan, Russia, [9]Regional Clinical Hospital №1 named. prof. S. V. Ochapovskogo, Krasnodar, Russia, [10]Samara State Medical University of the Ministry of Health of the Russian Federation, Samara, Russia, [11]Advisory Polyclinic Chuvash State University named after I. N. Ulyanov, Cheboksary, Russia, [12]Regional Clinical Hospital No. 1, Tyumen', Russia, [13]Kemerovo regional clinical hospital, Kemerovo, Russia, [14]Volgograd State Medical University, Volgograd, Russia, [15]Regional Clinical Hospital, Tula, Russia, [16]Tula State Medical University, Tula, Russia, [17]Petrozavodsk State University, Petrozavodsk, Russia, [18]Regional Clinical Hospital, Samara, Russia, [19]Regional Clinical Hospital, Ulyanovsk, Russia, [20]Smolensk State Medical University, Smolensk, Russia, [21]National Medical and Surgical Center named after N.I. Pirogov" of the Ministry of Healthcare of the Russian Federation, Moscow, Russia, [22]Regional Clinical Hospital, Krasnodar, Russia, [23]Moscow Clinical Scientific and Practical Centre named after Loginov A.S., Moscow, Russia, [24]Medical Clinical Centre, Smolensk, Russia

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: to investigate the correlation between the rapid analgesic effect of tofacitinib and a decrease in RA activity after 3 and 6 months.

Methods: The study group consisted of 88 RA patients, age 53±11.5, 79.3% women, 89.8% RF "+", DAS28 5.2±1.2, who received DMARDs (59.5% methotrexate and 19.8% leflunomide), who had ineffectiveness or intolerance to biological therapy. All patients were prescribed tofacitinib 10 mg / day. The severity of pain was assessed using the Brief pain inventory (BPI) questionnaire, the presence of a neuropathic pain component (NPC) using the painDETECT questionnaire, and signs of central sensitization (CS) using the Central Sensitivity Inventory (CSI) questionnaire in the early stages after tofacitinib administration, and RA activity by DAS28 at 3 and 6 months.

Results: Pain intensity at baseline was 5.3±2.0 on the visual analog scale (VAS 0-10), 51.1% of patients had signs of central sensitization (CSI ≥ 40), 15.9% had NPC (painDETECT ≥18). 7 days after starting tofacitinib, there was a statistically significant decrease in pain intensity - to 4.1±1.8 ($p< 0.05$) and CS-CSI from 40.4±13.5 to 36.5±12.5 ($p=0.01$). After 28 days, the pain intensity (VAS) was 2.8±1.6 ($p=0.000$), painDETECT decreased from 11.8±5.6 to 6.8±3.1 ($p=0.000$), CSI to 31.6±13.9 ($p=0.000$). DAS28 after 3 and 6 months was 3.7±1.3 and 3.6±1.2. The number of patients with pain reduction ≥ 50% after 28 days of therapy was 59.9%. Low RA activity after 3 months (DAS28 ≤3.2) was achieved in 64.4% of patients. This was a clear correlation between the number of patients with significant pain reduction after 28 days and the number of patients who achieved low RA activity after 3 and 6 months ($rS=0.548$, $p=0.000$; $rS=0.790$, $p=0.000$). 6 patients dropped out of the study due to inefficiency or social reasons. No serious adverse reactions were observed.

Conclusion: Tofacitinib rapidly reduces the intensity of pain and signs of CS in RA. A quick response to this drug (pain reduction) makes it possible to predict a decrease in RA activity after 3 and 6 months of therapy.

Disclosure: E. Pogozheva, None; **A. Karateev**, None; **E. Nasonov**, Eli Lilly, 2, Abbvie, 2, Pfizer, 2, Hoffmann-La Roche, 2, Biocad, 2, R-Pharm, 2; **A. Lila**, None; **V. Mazurov**, None; **R. Samigullina**, None; **D. Chakieva**, None; **A. Dadalova**, None; **A. Dyo**, None; **A. Baranov**, None; **N. Lapkina**, None; **E. Kol'tsova**, None; **I. Shchendrigin**, None; **T. Rasevich**, None; **A. Davydova**, None; **I. Shafieva**, None; **I. Bashkova**, None; **D. Bobrikova**, None; **I. Kushnir**, None; **E. Kalinina**, None; **T. Sal'nikova**, None; **V. Sorotskaya**, None; **I. Marusenko**, None; **O. Semagina**, None; **I. Vinogradova**, None; **D. Krechikova**, None; **N. Kiryukhina**, None; **I. Semizarova**, None; **D. Murtazalieva**, None; **M. Semchenkova**, None.

Abstract Number: 1705

The Impact of Age and Drug-Drug Interactions on QT Interval in Chronic Hydroxychloroquine Users

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) has been used safely for over 60 years in rheumatic patients. However, following its recent use in covid-19 disease, its safety has been questioned, following controversial reports of cardiac toxicity, possibly related to a prolongation of the QT interval. Furthermore, it was recently shown that concomitant administration of different drugs can affect QT interval in hydroxychloroquine chronic users.

Methods: 12-lead electrocardiograms were recorded in 355 ambulatory patients (SLE = 85, RA = 80, SSc = 71, UCTD = 68, other CTDs = 51). The analysis was performed on corrected QT intervals (QTc) calculated according to Framingham formula (QTc = QT+0.154 (1–RR)), with ULN = 449 ms in males, and 467 ms in females. Glomerular filtrate rate (eGFR) was calculated with the CKD-EPI equation. The influence on QTc values of demographic variables, chronic (≥3 months) HCQ treatment, and of the use of 23 comedications -including corticosteroids, immunosuppressants, biologics, statins, aspirin, angiotensin converting enzyme inhibitors, angiotensin receptor blockers, diuretics, betablockers, endothelin antagonists, duloxetine, selective serotonin reuptake inhibitors, gabapentinoids, proton-pump inhibitors (PPI), calcium channel blockers (CCBs) – were evaluated by parametric or non parametric statistical methods, as appropriate. All statistic analyses were performed with the IBM SPSS statistical package version 25.

Results: Demographic variables, and the use of comedications were not different in HCQ+ and HCQ- patients (Table 1). In the whole population, the QTc mean duration was 416.44 ± 19.53 ms, and was correlated with age (Fig. 1; $r = 0.211$, $p < 0.001$), but not with gender (F: 417.79±19.02 ms, M: 413.21±23.73 ms, $p = 0.303$), eGFR ($r = -0.83$, $p = 0.120$), BMI (-0.001, $p = 0.984$) or disease ($p = 0.139$). In only 4 patients (HCQ+: 3 (1.5%) – HCQ-: 1 (0.6%), $p = 0.629$) QTc duration was above ULN.

Table 1. Demographic and clinical variables in patients treated with HCQ (HCQ+) and in controls (HCQ-)

Tab. 1. Demographic and clinical variables in patients treated with HCQ (HCQ+) and in controls (HCQ-).									
	N	Age Yrs ±SD	Female N %	eGFR mL/min /1.73m² ±SD	BMI Mean ±SD	Hypo-thyroidism N %	VitD N %	PPI N %	CCB N %
All	355	57.74 ±14.25	320 90.1	87.00 19.44	24.65 4.70	52 14.6	237 66.8	202 57.1	53 14.9
HCQ+	194	57.56 ±14.40	177 91.2	86.35 20.10	24.24 4.49	26 13.4	138 71.1	112 58.0	30 15.5
HCQ-	161	57.96 ±14.10	143 88.8	87.79 18.63	25.17 4.91	26 16.1	99 61.5	90 55.9	23 14.3
p		0.069	0.280	0.476	0.074	0.548	0.070	0.384	0.438

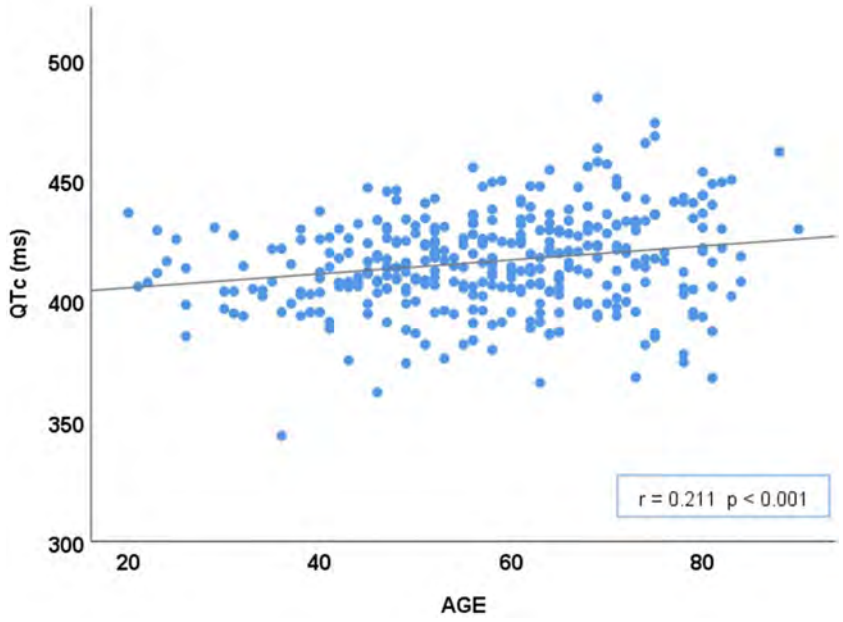

Figure 1. Correlstion between age and Qtc interval.

The patients were heavily cotreated, with 5.64 ± 3.47 concomitant medications on average (HCQ+ 5.58±3.47; HCQ- 5.59±3.33, p=0.804). Among the 23 cotreatments evaluated in univariate analyses, QTc duration was associated only with the assumption of vitamin D (418.95±19.56 ms vs 411.38±18.53 ms, p = 0.001), PPIs (419.14±20.00 ms vs 412.89±16.86 ms, p = 0.003), and CCBs (421.61±24.41 ms vs 415.53±18.44 ms, p = 0.036). In the analysis of covariance on age-adjusted data, only HCQ (p < 0.001) and Vitamin D (p =0.046) but not PPIs (p = 0.121) nor CCBs (p = 0.200) were still significantly correlated to QTc interval. Furthermore, as reported in Fig. 2, our data show a trend - albeit not statistically significant - towards an additive effect on QT prolongation of the association of Vitamin D, PPIs and CCBs with HCQ, even more evident in the case of association of the 3 drug classes.

Conclusion: In this study, the QTc interval duration was correlated to age and was significantly prolonged in patients treated with hydroxychloroquine as compared to controls, although significant prolongation was extremely infrequent. Furthermore, our data revealed signs of drug-drug interference, suggesting that regular monitoring of the electrocardiogram is advisable in these patients, often undergoing cotreatment with multiple drugs.

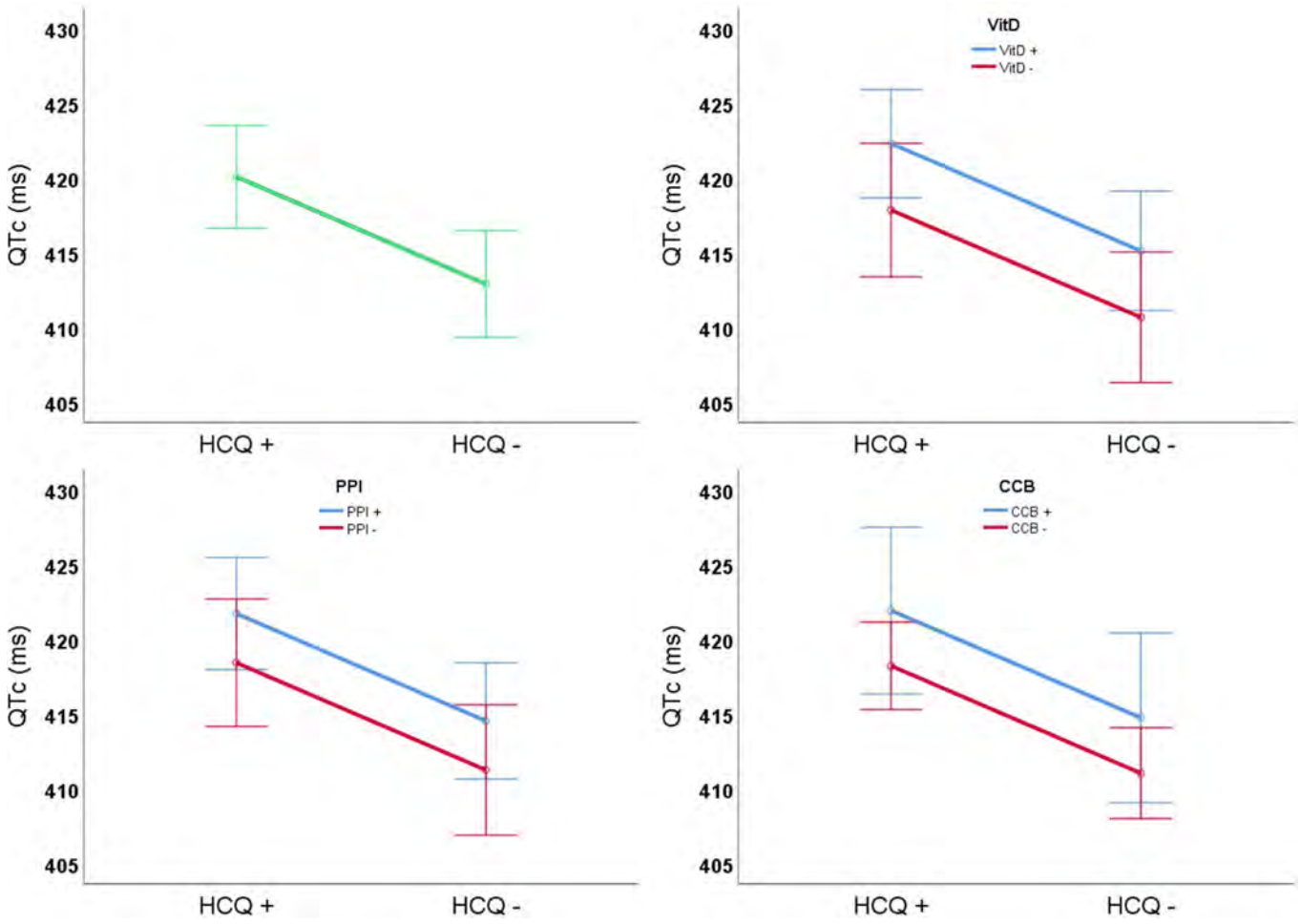

Figure 2. Influence of selected cotreatments in patients treated with HCQ and in controls.

Disclosure: M. Antivalle, None; **M. Agosti**, None; **G. La Paglia**, None; **A. Batticciotto**, None; **M. Ditto**, None; **S. PARISI**, None; **P. Sarzi-Puttini**, None.

Abstract Number: 1706

Twenty-four-week Follow-up of a Randomized Controlled First-in-Human Trial of the Safety and Efficacy of Neurostimulation with a Miniaturized Vagus Nerve Stimulation Device in Patients with Multidrug-Refractory Rheumatoid Arthritis

Norman Gaylis[1], Mark Genovese[2], David Sikes[3], Alan Kivitz[4], Diane Horowitz[5], Charles Peterfy[6], Yaakov Levine[7] and David Chernoff[8], [1]Arthritis and Rheumatic Disease Specialties, Aventura, FL, [2]Stanford University, Sunnyvale, CA, [3]Florida Medical Clinic, Wesley Chapel, FL, [4]Altoona Center for Clinical Research, Duncansville, PA, [5]Northwell Health, Jericho, NY, [6]Spire Sciences, Inc., Boca Raton, FL, [7]SetPoint Medical, Manhassest, NY, [8]SetPoint Medical, Sausalito, CA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Vagus nerve stimulation (VNS) activates innate neuroimmune reflexes that have been shown to reduce pro-inflammatory cytokines and clinical disease activity in subjects with rheumatoid arthritis (RA) (Koopman PNAS 2016). We previously reported primary clinical outcomes from a first-in-human, double-blind study of a novel, implanted VNS device called a MicroRegulator (MR). That study showed 5/10 subjects with drug-refractory RA met or exceeded the minimal clinically important difference (MCID) in DAS28-CRP; 2 subjects achieved DAS28 remission (DAS28-CRP < 2.6); and pro-inflammatory cytokines were decreased by >30% following 12 weeks of VNS (Genovese et al. Lancet Rheum 2020). We now report 24-week efficacy and safety findings from this study.

Methods: The primary study was enrolled in 2 stages: Stage 1 (n=3) was open-label, and Stage 2 (n=11) was randomized and sham-controlled (Figure 1). Three weeks after MR implantation, the first 3 subjects were stimulated 1 min QD in Stage 1. Following safety review board approval, the remaining 11 patients were implanted with the MR and randomized to 1 min of sham, QD, or QID VNS in Stage 2. At Week 12, the blind was lifted, sham subjects were re-randomized to either QD or QID active VNS dosing, and all actively treated subjects remained on their dosing through Week 24. Safety and tolerability were assessed, and several secondary efficacy endpoints were evaluated measuring the change in disease activity from the start of VNS to Week 24.

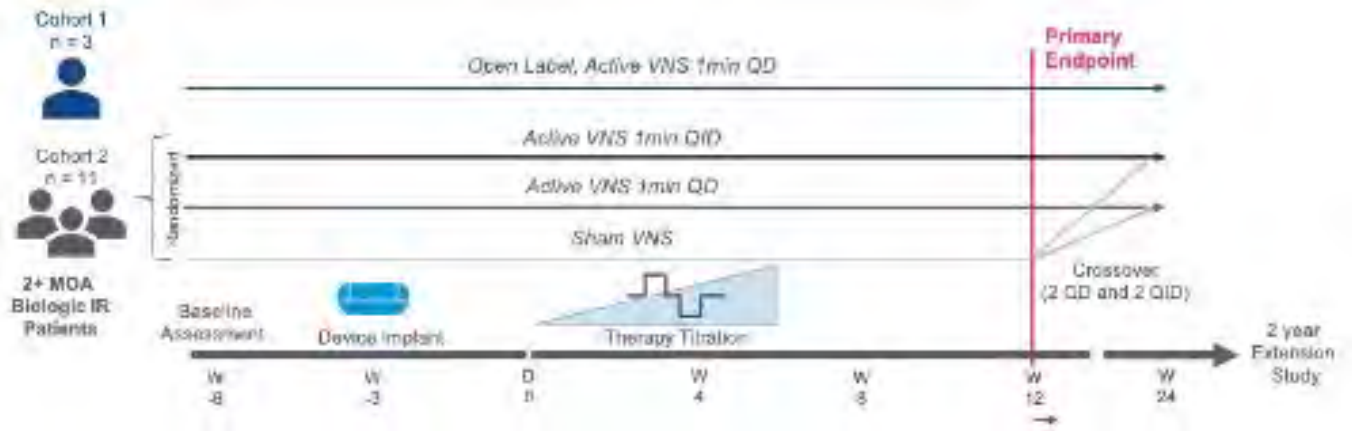

Figure 1. Study Schematic.

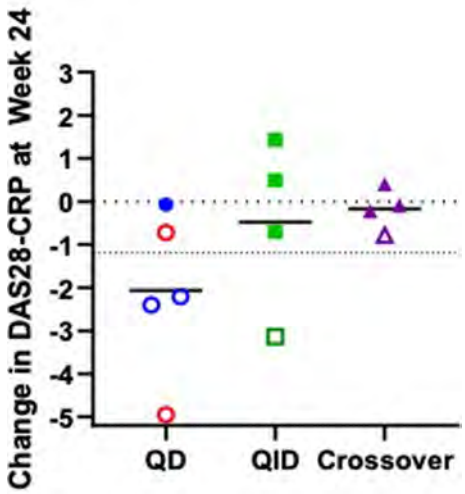

Figure 2. Change in DAS28-CRP at Week 24. Open shapes represent EULAR good and moderate responders. Red shapes represent subjects with a biologic added back as co-therapy with VNS.

Results: There were no device-related adverse events from Week 12 through Week 24. Improvement in clinical disease activity was sustained through Week 24: 5/9 patients within the original treatment groups met or exceeded EULAR response criteria for DAS28-CRP at Week 24 vs. 5/10 at Week 12 (one Week 12 responder was lost to follow-up). Similarly, 6/9 patients in the original treatment groups met or exceeded the MCID in CDAI at Week 24 vs. 5/10 at Week 12. In the long-term extension, 1/4 sham crossover patients had both EULAR and CDAI response after 12 weeks of VNS (1/2 QD, 0/2 QID). VECTRA composite scores and component analysis revealed an 18-point drop in median multi-analyte disease activity index in the QD group over 24 weeks of VNS with a decrease in serum levels of several analytes in key component categories (IL-6, serum amyloid A, and VCAM-1). Erosion progression by hand MRI was stabilized or decreased in all but 1 of the stimulated patients at Week 24.

Conclusion: Improvements in clinical disease activity, pro-inflammatory cytokine suppression, and joint preservation were maintained through 24 weeks of VNS treatment. Safety outcomes continue to support the risk/benefit profile of VNS as a treatment option for patients with RA with inadequate responses or intolerance to conventional DMARDS and biologic and targeted synthetic drugs.

Disclosure: N. Gaylis, None; **M. Genovese**, Setpoint, 2, Gilead, 3; **D. Sikes**, Myriad, 2, Abbvie, 6; **A. Kivitz**, Pfizer, 2, 6, 11, 12, Sanofi, 2, 6, 11, 12, GlaxoSmithKline, 11, Gilead Sciences, Inc.,, 2, 11, Novartis, 2, 6, 12, AbbVie, 2, 6, 11, Boehringer Ingelheim, 2, Janssen, 2, Regeneron, 2, 6, 12, SUN Pharma Advanced Research, 2, Amgen, 11, Lilly, 6, Celgene, 6, 12, Flexion, 2, 6, Genzyme, 2, 6, 12, Merck, 6, 12, UCB, 6, Horizon, 6, 12; **D. Horowitz**, None; **C. Peterfy**, Spire Sciences, 3, 8, Amgen, 6, Bristol-Myers Squibb, 6, Aclaris, 2, Centrexion, 2, Daiichi Sankyo, 2, EMD Serono, 2, Five Prime Therapeutics, 2, Flexion Therapeutics, 2, Genentech, 2, Gilead, 2, GlaxoSmithKline, 2, Istresso, 2, Eli Lilly, 2, Myriad, 2, Novartis, 2, Roche, 2, Setpoint, 2, Sorrento, 2, UCB, 2; **Y. Levine**, Setpoint Medical, 3; **D. Chernoff**, Setpoint Medical, 3.

Abstract Number: 1707

A Bioengineered Probiotic for the Oral Delivery of an Immunomodulator in Rheumatoid Arthritis

Yuqing Wang[1], Duolong Zhu[1], Laura Ortiz-Velez[2], Jacob Perry[1], Michael Pennington[3], Joseph Hyser[1], Robert Britton[1] and Christine Beeton[1], [1]Baylor College of Medicine, Houston, TX, [2]TMC Innovation, Houton, [3]AmbioPharm Inc., North Augusta, SC

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: CCR7– effector memory T (T_{EM}) lymphocytes are targets for immunomodulation for the treatment of rheumatoid arthritis (RA). Following activation, T_{EM} cells upregulate the expression of the potassium channel Kv1.3, and blocking this channel inhibits T_{EM} cell proliferation and secretion of pro-inflammatory cytokines with minimal effects of CCR7+ naïve and central memory T cells. Analogs of the small peptide ShK, engineered to enhance their selectivity for Kv1.3, are effective in reducing disease severity in animal models of RA and other autoimmune diseases and in patients with active plaque psoriasis. However, like most biologics, these peptides must be injected repeatedly. Here, we propose a novel approach for the delivery of the ShK analog ShK-235 by inducing its production and secretion by a probiotic bacterium, *Lactobacillus reuteri*, for oral delivery into the gastrointestinal tract.

Methods: We designed LrS235, a bioengineered *L. reuteri* that secretes the ShK-235 peptide and used a single-cell patch-clamp to quantify ShK-235 in the culture supernatant of LrS235 and in the circulation of healthy rats gavaged with LrS235. We used functional assays to define the effects of ShK-235 secreted by LrS235 on the proliferation of T_{EM} cells *in vitro*. We next tested the efficacy of LrS235 in two animal models, delayed-type hypersensitivity (DTH) and collagen-induced arthritis (CIA).

Results: Supernatants from LrS235 block Kv1.3 currents and inhibit human T_{EM} cells proliferation and IL-2 and IFN-g production *in vitro*. A single oral gavage of LrS235 in healthy rats results in sufficient levels of ShK-235 in the circulation to block Kv1.3 channels and reduces inflammation in the DTH model. The daily oral gavage of LrS235 is efficacious in reducing clinical signs of disease and joint inflammation in rats with CIA.

Conclusion: Our results demonstrate the potential of using the probiotic *L. reuteri* as a novel oral delivery system for ShK-235, and possibly other biologics, to treat RA.

Disclosure: Y. Wang, None; **D. Zhu**, None; **L. Ortiz-Velez**, None; **J. Perry**, None; **M. Pennington**, AmbioPharm Inc., 10; **J. Hyser**, AmbioPharm Inc., 10; **R. Britton**, AmbioPharm Inc., 10, Mikrovia, 12, Co-founder, PanaBio, 12, Co-founder; **C. Beeton**, AmbioPharm Inc., 10.

Abstract Number: 1708

The Efficacy and Safety of Piclidenoson vs Methotrexate in Early Rheumatoid Arthritis: Phase 3 Randomized, Double-blind, Placebo-controlled Study

Tatiana Reitblat[1], Alexandra Gurman- Balbir[2], Zivit Harpaz[3], Motti Farbstein[3], Michael Silverman[3], William Kerns[3] and **Pnina Fishman**[3], [1]Barzilai Medical Center, Ashkelon, Israel, [2]Rambam Medical Center, Haifa, Israel, [3]Can-Fite BioPharma, Petah Tikva, Israel

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Piclidenoson, a highly selective A3 adenosine receptor (A3AR) agonist, demonstrated safety and efficacy in phase 2 clinical studies in rheumatoid arthritis (RA) and psoriasis. Piclidenoson induces selective apoptosis of inflammatory cells via a molecular mechanism which entails de-regulation of the Wnt signaling pathway.

Methods: This randomized, double-blind, active- and placebo-controlled, parallel-group study enrolled patients with clinically active RA who were methotrexate (MTX)-naïve. Eligible patients were randomized to 4 groups in a 2:2:2:1 ratio: piclidenoson 1 mg; piclidenoson 2 mg; MTX; or matching placebo tablets/capsules. Piclidenoson or matching placebo tablets were administered every 12 h for up to 24 weeks of treatment. MTX or matching placebo capsules were administered once a week according to the dosing schedule. The primary endpoint was efficacy (noninferiority) of piclidenoson administered for 12 weeks relative to oral MTX, as assessed by the proportion of patients achieving a disease activity score (DAS) of low disease activity (LDA). Additional analyses of the primary efficacy parameter included comparison of each dose of piclidenoson to placebo at Week 12. Secondary endpoints included comparing response rates (ACR20, ACR50, and ACR70) between piclidenoson (each dose) and MTX or placebo. The study was designed to enroll 525 patients.

Results: Due to the SARS-CoV-2 pandemic, enrollment was paused and an interim analysis was performed after 50% of participants reached the Week 12 visit evaluation. The interim analysis included a total of 252 patients (72, 73, 73, and 34, in the piclidenoson 1 mg, piclidenoson 2 mg, MTX, and placebo groups, respectively). Patient demographics and baseline characteristics were overall similar between the groups. For the entire population included in the interim analysis, the median (range) age was 56 (18-75) years, and 197 (78%) were females. Piclidenoson was

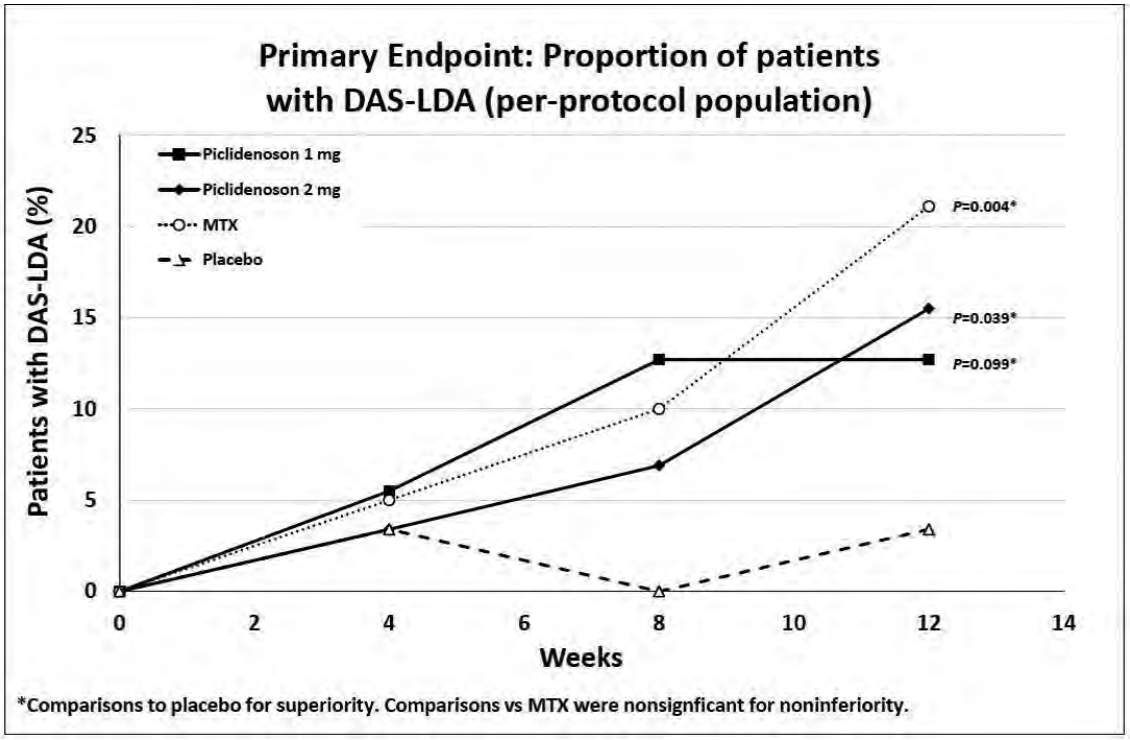

Figure.

Table.

ACR20/50/70 Response Rates at Week 12 and Week 24 (intent-to-treat population)

	Piclidenoson 1 mg (N=69)	Piclidenoson 2 mg (N=71)	MTX (N=71)	Placebo (N=33)	*P*-value (piclidenoson vs placebo)[a]	*P*-value (piclidenoson vs MTX)[b]
Week 12						
ACR20	37 (54%)	36 (51%)	47 (66%)	17 (52%)	1 mg: 0.842 2 mg: 1.000	1 mg: 0.384 2 mg: 1.000
ACR50	18 (26%)	12 (17%)	21 (30%)	5 (15%)	1 mg: 0.181 2 mg: 0.819	1 mg: 0.064 2 mg: 0.370
ACR70	9 (13%)	7 (10%)	9 (13%)	1 (3%)	1 mg: 0.047 2 mg: 0.140	1 mg: 0.003 2 mg: 0.011
Week 24						
ACR20	31 (45%)	26 (37%)	34 (48%)	14 (42%)	1 mg: 0.811 2 mg: 1.000	1 mg: 0.077 2 mg: 0.325
ACR50	22 (32%)	15 (21%)	26 (37%)	10 (30%)	1 mg: 0.871 2 mg: 1.000	1 mg: 0.100 2 mg: 1.000
ACR70	11 (16%)	6 (9%)	15 (21%)	5 (15%)	1 mg: 0.918 2 mg: 1.000	1 mg: 0.067 2 mg: 0.346

[a] *P*-value for comparison to placebo for superiority.
[b] *P*-value for comparison of each dose of piclidenoson to MTX for non-inferiority with margin of 15%.

safe and very well tolerated. The proportion of patients experiencing any treatment emergent adverse events (TEAEs) were similar for all groups (17%, 25%, 26%, and 29%, respectively) and the majority of TEAEs were mild. Although piclidenoson efficacy was significantly superior to placebo, the study did not meet the primary endpoint which was noninferiority vs MTX (Figure). At 12 and 24 Weeks, ACR20, ACR50 and ACR70 response rates were overall similar between the piclidenoson 1 mg (which was more effective than the 2 mg dose) and the MTX groups. The clinical benefits of piclidenoson 1 mg (as reflected in the ACR50 and ACR70 response rates) seemed more pronounced after 24 weeks (Table).

Conclusion: Piclidenoson was safe, but did not meet the primary endpoint in the current study; although it was superior to placebo in the DAS-LDA analysis. Since the primary endpoint was not met, the trial was discontinued by the sponsoring company.

Disclosure: T. Reitblat, None; **A. Gurman- Balbir**, None; **Z. Harpaz**, Can-Fite BioPharma, 3, 8; **M. Farbstein**, Can-Fite BioPharma, 3, 8; **M. Silverman**, Can-Fite BioPharma, 2; **W. Kerns**, Can-Fite BioPharma, 2, 11; **P. Fishman**, Can-Fite BioPharma, 3, 8.

Abstract Number: 1709

Long-term Safety of a Single Infusion of Human Umbilical Cord Blood-derived Mesenchymal Stem Cell Therapy in Rheumatoid Arthritis: The 5-year Follow-up of the Phase I Clinical Trial

Min Jung Kim[1], Eun Hye Park[2] and Kichul Shin[3], [1]Seoul Metropolitan Government–Seoul National University Boramae Medical Center, Seoul, Republic of Korea, [2]Chung-Ang University Hospital, Seoul, Republic of Korea, [3]Seoul Metropolitan Government- Seoul National University Boramae Medical Center, Seoul, Republic of Korea

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Mesenchymal stem cell (MSC) therapy represents a promise for the treatment of autoimmune diseases due to its potent immunomodulatory effect. We investigated the long-term safety of a single treatment of human umbilical cord blood-derived (hUCB)-MSCs in patients with rheumatoid arthritis (RA).

Methods: Patients with RA who met the 2010 ACR/EULAR classification criteria and received a single intravenous infusion of hUCB-MSCs (3 groups; 2.5 x 10^7, 5.0 x 10^7, 1.0 x 10^8 cells) in a phase I trial (NCT02221258) entered this 5-year observational study. Safety assessments were carried out at 3, 6, and 12 months for the first year after the hUCB-MSC administration and annually thereafter for the remaining period. Key safety endpoints included overall adverse events (AEs), serious adverse events (SAEs) and AEs of special interest including infection, thromboembolism, and benign/malignant tumor. Physical examination, laboratory tests and electrocardiograms were also performed.

Results: A total of nine patients were treated after the phase I trial at a single center. The most frequent AEs (Table) over 5 years were osteoarthritis (66.7%), nasopharyngitis (44.4%), abdominal pain (33.3%), osteopenia or osteoporosis (33.3%), lumbar spinal stenosis (22.2%), and hypertension (22.2%). SAEs occurred in 5 patients (55.6%); a serious infection (cellulitis) happened in one patient in the 1.0 x 10^8 group that resolved after treatment. Three years after administration of MSCs, a benign ovarian tumor and a breast adenoma were reported in the 2.5 x 10^7 and 5.0 x

Table. Summary of AEs up to 5 years

	Total (N = 9)	2.5 x 10^7 (N = 3)	5.0 x 10^7 (N = 3)	1.0 x 10^8 (N = 3)
Events of any AE, N	97	37	30	30
Severe AE (CTCAE v4.0 grade 3 or 4)				
Number of patients, N (%)	3 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
Number of events, N	7	5	1	1
Any SAE				
Number of patients, N (%)	5 (55.6)	3 (100)	1 (33.3)	1 (33.3)
Number of events, N	9	6	1	2
AEs reported in ≥3 of patients in any group, N (%)				
Musculoskeletal and connective tissue disorders	9 (100)	3 (100)	3 (100)	3 (100)
Infections and infestations	6 (66.7)	2 (66.7)	2 (66.7)	2 (66.7)
Gastrointestinal disorders	5 (55.6)	1 (33.3)	2 (66.7)	2 (66.7)
General disorders and administration site conditions	3 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
Injury, poisoning and procedural complications	3 (33.3)	1 (33.3)	1 (33.3)	1 (33.3)
Neoplasms benign, malignant and unspecified	3 (33.3)	1 (33.3)	2 (66.7)	0 (0)
AEs of special interest, N (%)				
Serious infections	1 (11.1)	0	0	1 (33.3)
Opportunistic infections	0	0	0	0
Thromboembolism	0	0	0	0
Malignancies	0	0	0	0
Benign tumor				
Benign ovarian tumor	1 (11.1)	1 (33.3)	0	0
Breast adenoma	1 (11.1)	0	1 (33.3)	0

10^7 groups, respectively. However, no death, thromboembolism or malignancy occurred during the follow up period. The incidence of AEs increased over time after administration of MSCs, but similar across the dose groups. There were no clinically significant laboratory finding, except for a case of hypertriglyceridemia and a case of anemia.

Conclusion: The long-term safety profile of a single dose of intravenous hUCB-MSC in patients with RA was reasonable and acceptable.

Disclosure: M. Kim, None; **E. Park**, None; **K. Shin**, None.

Abstract Number: 1710

Clinical Outcomes of MTX-Naïve RA Patients on Filgotinib Long-term Extension Trial Initially on FIL or MTX During Phase 3 Parent Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: RA – Treatments Poster III: RA Treatments & Their Safety (1674–1710)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The preferential Janus kinase (JAK)-1 inhibitor filgotinib (FIL) is approved for treatment of moderately to severely active RA in Europe and Japan. In this post hoc, exploratory analysis, we assessed efficacy and safety of long-term treatment with FIL (with or without MTX) in MTX-naïve patients (pts) treated with FIL or MTX in the Phase 3 parent study (PS; NCT02886728).[1]

Methods: Pts received FIL 200 mg (FIL200)+MTX, FIL 100 mg (FIL100)+MTX, FIL200 alone, or MTX alone up to 52 weeks (w) in the PS.[1] Those who completed the PS on study drug could enter the long-term extension (LTE; NCT03025308). MTX completers were rerandomized, blinded, to FIL200 or FIL100; pts who took FIL in the PS remained on the same dose in LTE. MTX was washed out for 4 w at LTE baseline (BL); pts could (re)start MTX and/or other csDMARDs ≥4 w after LTE first dosing.[1] We report proportions of pts who achieved ACR 20%, 50%, and 70% response (ACR20/50/70), DAS in 28 joints with CRP (DAS28[CRP]) ≤3.2 and < 2.6, and Clinical Disease Activity Index (CDAI) ≤10 and ≤2.8. Exposure-adjusted incidence rates (EAIR)/100 pt-years of exposure of treatment-emergent adverse events (TEAEs) and AEs of special interest (AESIs) are summarized, with data cutoff of June 1, 2020.

Results: As of June 1, 2020, 439 of 492 (89%) pts who entered LTE from the PS FIL200 groups and 144/169 (85%) from the PS FIL100 group were still on LTE study treatment; of those rerandomized from MTX, 131/148 (89%) FIL200 and 133/151 (88%) FIL100 pts were still on study treatment. LTE BL characteristics were similar between FIL200 and FIL100 groups: mean RA duration was 3.1 and 3.3 years; mean DAS28(CRP) was 2.5 and 2.7. After MTX washout, only 17% of FIL200 and 23% of FIL100 pts (re)started MTX (at clinical judgment). ACR20/50/70 response rates among pts from PS FIL arms decreased modestly from LTE BL to W12 then stabilized. Among pts who switched from PS MTX to LTE FIL, response rates remained stable or improved to approach those of PS FIL pts by W48 **(Table 1)**. Similar trends were seen in proportions of pts attaining DAS28(CRP) ≤3.2, DAS28(CRP) < 2.6, CDAI ≤10, and CDAI

Table 1. Proportions of patients achieving ACR20/50/70, NRI, FAS, up to LTE w48

	FIL200+MTX→ FIL200 LTE n = 325	FIL200 Mono→ FIL200 LTE n = 167	FIL100+MTX→ FIL100 LTE n = 169	MTX→ FIL200 LTE n = 148	MTX→ FIL100 LTE n = 151
ACR20, proportion of responders, n (%)					
LTE BL	306 (94.2%)	153 (91.6%)	147 (87.0%)	123 (83.1%)	127 (84.1%)
LTE w12	279 (85.8%)	140 (83.8%)	139 (82.2%)	124 (83.8%)	127 (84.1%)
LTE w48	275 (84.6%)	137 (82.0%)	132 (78.1%)	119 (80.4%)	130 (86.1%)
ACR50, proportion of responders, n (%)					
LTE BL	253 (77.8%)	122 (73.1%)	122 (72.2%)	93 (62.8%)	106 (70.2%)
LTE w12	230 (70.8%)	114 (68.3%)	108 (63.9%)	99 (66.9%)	101 (66.9%)
LTE w48	228 (70.2%)	113 (67.7%)	103 (60.9%)	104 (70.3%)	100 (66.2%)
ACR 70, proportion of responders, n (%)					
LTE BL	197 (60.6%)	88 (52.7%)	81 (47.9%)	52 (35.1%)	70 (46.4%)
LTE w12	174 (53.5%)	84 (50.3%)	82 (48.5%)	69 (46.6%)	71 (47.0%)
LTE w48	166 (51.1%)	83 (49.7%)	79 (46.7%)	77 (52.0%)	72 (47.7%)

LTE FIL represents FIL dose with and without MTX. ACR20/50/70 is calculated based on PS BL. Data are presented as n (%). Analysis by logistic regression model, including treatment group and stratification factors. NRI: patients with missing values were considered nonresponders. BL, baseline; FAS, full analysis set; FIL, filgotinib; LTE, long-term extension; NRI, nonresponder imputation; w, week.

Table 2. Proportions of patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) <2.6, CDAI ≤10, CDAI ≤2.8, NRI up to LTE W48

	FIL200+MTX→ FIL200 LTE n = 325	FIL200 Mono→ FIL200 LTE n = 167	FIL100+MTX→ FIL100 LTE n = 169	MTX→ FIL200 LTE n = 148	MTX→ FIL100 LTE n = 151
DAS28(CRP) ≤3.2, proportion of responders, n (%)					
LTE BL	279 (85.8%)	131 (78.4%)	124 (73.4%)	95 (64.2%)	102 (67.5%)
LTE w12	239 (73.5%)	123 (73.7%)	114 (67.5%)	108 (73.0%)	110 (72.8%)
LTE w48	252 (77.5%)	121 (72.5%)	115 (68.0%)	106 (71.6%)	107 (70.9%)
DAS28(CRP) <2.6, proportion of responders, n (%)					
LTE BL	211 (64.9%)	93 (55.7%)	85 (50.3%)	66 (44.6%)	63 (41.7%)
LTE w12	203 (62.5%)	97 (58.1%)	82 (48.5%)	85 (57.4%)	84 (55.6%)
LTE w48	205 (63.1%)	100 (59.9%)	85 (50.3%)	90 (60.8%)	82 (54.3%)
CDAI ≤10, proportion of responders, n (%)					
LTE BL	270 (83.1%)	129 (77.2%)	127 (75.1%)	101 (68.2%)	103 (68.2%)
LTE w12	240 (73.8%)	121 (72.5%)	117 (69.2%)	106 (71.6%)	115 (76.2%)
LTE w48	243 (74.8%)	124 (74.3%)	116 (68.6%)	105 (70.9%)	110 (72.8%)
CDAI ≤2.8, proportion of responders, n (%)					
LTE BL	137 (42.2%)	51 (30.5%)	58 (34.3%)	34 (23.0%)	35 (23.2%)
LTE w12	134 (41.2%)	50 (29.9%)	53 (31.4%)	56 (37.8%)	48 (31.8%)
LTE w48	128 (39.4%)	56 (33.5%)	54 (32.0%)	52 (35.1%)	41 (27.2%)

LTE FIL represents FIL dose with and without MTX. Data are presented as n (%). Analysis by logistic regression model, including treatment group and stratification factors. NRI: patients with missing values were considered nonresponders. BL, baseline; CDAI, clinical disease activity index; DAS28(CRP), disease activity score for 28 joint count using CRP; FIL, filgotinib; LTE, long-term extension; NRI, nonresponder imputation; w, week.

Table 3. EAIRs of TEAEs through June 2020

	FIL200+MTX→ FIL200 LTE N = 325 PYE = 474.4 n (%) EAIR (95%)	FIL200→ FIL200 LTE N = 167 PYE = 232.5 n (%) EAIR (95%)	FIL100+MTX→ FIL100 LTE N = 169 PYE = 236.4 n (%) EAIR (95%)	MTX→ FIL200 LTE N = 148 PYE = 213.4 n (%) EAIR (95%)	MTX→ FIL100 LTE N = 151 PYE = 215.4 n (%) EAIR (95%)
TEAE	236 (72.6) 49.7 (43.8, 56.5)	109 (65.3) 46.9 (38.9, 56.6)	118 (69.8) 49.9 (41.7, 59.8)	108 (73.0) 50.6 (41.9, 61.1)	100 (66.2) 46.4 (38.2, 56.5)
TEAE Grade ≥3	34 (10.5) 7.2 (5.1, 10.0)	15 (9.0) 6.5 (3.9, 10.7)	24 (14.2) 10.2 (6.8, 15.1)	15 (10.1) 7.0 (4.2, 11.7)	15 (9.9) 7.0 (4.2, 11.6)
TE serious AE	28 (8.6) 5.9 (4.1, 8.5)	14 (8.4) 6.0 (3.6, 10.2)	21 (12.4) 8.9 (5.8, 13.6)	14 (9.5) 6.6 (3.9, 11.1)	14 (9.3) 6.5 (3.9, 11.0)
Death	5 (1.5) 1.1 (0.3, 2.5)	1 (0.6) 0.4 (0.1, 3.1)	0 0.0 (0.0, 1.6)	0 0.0 (0.0, 1.7)	0 0 (0.0, 1.7)
Infections	135 (41.5) 28.5 (24.0, 33.7)	69 (41.3) 29.7 (23.4, 37.6)	65 (38.5) 27.5 (21.6, 35.1)	61 (41.2) 28.6 (22.2, 36.7)	59 (39.1) 27.4 (21.2, 35.4)
Serious infections	5 (1.5) 1.1 (0.4, 2.5)	7 (4.2) 3.0 (1.4, 6.3)	6 (3.6) 2.5 (1.1, 5.7)	4 (2.7) 1.9 (0.7, 5.0)	4 (2.6) 1.9 (0.7, 4.9)
Opportunistic infections	1 (0.3) 0.2 (0.0, 1.5)	0 0.0 (0.0, 1.6)	2 (1.2) 0.8 (0.2, 3.4)	0 (0.0, 1.7)	0 0.0 (0.0, 1.7)
Herpes Zoster	4 (1.2) 0.8 (0.3, 2.2)	4 (2.4) 1.7 (0.6, 4.6)	2 (1.2) 0.8 (0.2, 3.4)	4 (2.7) 1.9 (0.7, 5.0)	2 (1.3) 0.9 (0.2, 3.7)
MACE[a]	3 (0.9) 0.6 (0.1, 1.8)	2 (1.2) 0.9 (0.2, 3.4)	0 0.0 (0.0, 1.6)	0 0.0 (0.0, 1.7)	0 0.0 (0.0, 1.7)
VTE[b]	1 (0.3) 0.2 (0.0, 1.2)	1 (0.6) 0.4 (0.1, 3.1)	0 0.0 (0.0, 1.6)	0 0.0 (0.0, 1.7)	0 0.0 (0.0, 1.7)
Malignancies (excluding NMSC)	3 (0.9) 0.6 (0.2, 2.0)	0 0.0 (0.0, 1.6)	4 (2.4) 1.7 (0.6, 4.5)	1 (0.7) 0.5 (0.0, 2.6)	0 0.0 (0.0, 1.7)
NMSC	3 (0.9) 0.6 (0.2, 2.0)	1 (0.6) 0.4 (0.1, 3.1)	2 (1.2) 0.8 (0.2, 3.4)	1 (0.7) 0.5 (0.0, 2.6)	0 0.0 (0.0, 1.7)

[a]Positively adjudicated. bVTE adjudicated for DVT and PE. LTE FIL represents FIL dose with and without MTX. EAIR and 95% CIs were estimated using Poisson regression model including treatment group with an offset of natural log of exposure time. AE, adverse event; CI, confidence interval; DVT, deep vein thrombosis; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; LTE, long-term extension; MACE, major adverse cardiovascular event; NMSC, nonmelanoma skin cancer; PBO, placebo; PE, pulmonary embolism; PYE, patient-years of exposure; TE, treatment-emergent; VTE, venous thromboembolism.

≤2.8 **(Table 2)**. TEAEs, Grade ≥3 AEs, serious AEs, and infections were largely comparable across groups and did not appear to increase after MTX to FIL switch **(Table 3)**. There were 6 deaths, all among PS FIL200 pts. There were 5 major cardiovascular events, 3 in PS FIL200+MTX and 2 in PS FIL200 monotherapy pts and 2 venous thromboembolisms, 1 each in PS FIL200+MTX and PS FIL200 monotherapy pts. EAIRs of herpes zoster were comparable across groups regardless of PS treatment. EAIRs for other AESIs were low.

Conclusion: Overall, response rates improved from LTE BL to W48 for pts switched from PS MTX to FIL and decreased modestly for PS FIL pts. In general, rates of AESIs were low and tended to be higher in pts maintained on FIL from PS. Safety findings in this subpopulation were comparable with the PS through W52[1] and with a 7-trial integrated safety analysis.[2] Limitations: the LTE was not formally randomized at BL, the groups were of unequal size, and the switch from MTX to FIL for LTE was by design, rather than based on disease activity.

References

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Disclosure: D. Aletaha, AbbVie, 2, 5, Janssen, 2, 5, Medac, 2, 5, Merck, 2, 5, 6, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Novartis, 2, 5, 6, Bristol-Myers Squibb, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6; **R. Westhovens**, galapagos, 12, advisory board and principal investigator, gilead, 1, celltrion, 1; **T. Atsumi**, AbbVie Japan GK, 2, 6, Astellas Pharma Inc., 5, 6, Bristol-Myers Squibb Co. Ltd, 6, Chugai Pharmaceutical Co. Ltd, 5, 6, Daiichi Sankyo Co. Ltd, 5, 6, Eisai Co. Ltd., 6, Eli Lilly Japan K.K, 6, Mitsubishi Tanabe Pharma Co.;, 5, 6, Pfizer Japan Inc, 2, 5, 6, Takeda Pharmaceutical Co. Ltd, 5, 6, UCB Japan Co. Ltd, 6, AstraZeneca plc, 2, Boehringer Ingelheim Co. Ltd, 2, Medical & Biological Laboratories Co. Ltd, 2, Novartis Pharma K.K, 2, Ono Pharmaceutical Co. Ltd, 2, Alexion Inc, 5, Otsuka Pharmaceutical Co., Ltd, 5, Gilead Sciences, Inc., 5, 6; **Y. Tan**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 11; **A. Pechonkina**, Gilead Sciences, Inc., 3, 11; **Q. Gong**, Gilead Sciences, Inc., 3, 11; **V. Rajendran**, Galapagos NV, 3, 11; **S. Strengholt**, Galapagos, BV, 3, 11; **G. Burmester**, AbbVie, 2, 5, 6, Eli Lilly, 2, 5, 6, MSD, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Galapagos, BV, 2, 6, Gilead Sciences, Inc., 2, 6.

Abstract Number: 1711

Increasing Preeclampsia Knowledge in SLE with a Specific Educational Tool: Preliminary Results

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Pregnant women with systemic lupus erythematosus (SLE) are at high risk of preeclampsia, leading to substantial maternal and fetal morbidity. Aspirin reduces preeclampsia risk but recent studies suggest aspirin is used only in a minority of SLE pregnancies. There is an urgent need to improve preeclampsia counselling and management in this vulnerable population. Therefore, we are conducting the PREPARE (PREeclamPsia knowledge & Aspirin adheRence in lupus prEgnancies) trial, a randomized controlled trial (RCT) evaluating an educational tool on preeclampsia knowledge and aspirin adherence among pregnant women with SLE. We present preliminary analyses of the effect of this tool on preeclampsia knowledge.

Methods: We are recruiting consecutive pregnant SLE women (diagnosed according to the SLICC criteria) until the 16th gestational week at 5 Canadian SLICC centers (i.e. Montreal, Halifax, Quebec, Winnipeg, and Calgary) since May 2018. Participants are randomly assigned to receive either the specifically-designed educational tool (intervention group) or standard of care (control group). At baseline (i.e. first trimester) and second trimester visits, the participants complete self-administered preeclampsia knowledge questionnaires (scored out of 30 by the research team blinded to the intervention). We restricted the current analysis to participants enrolled at the coordinating center (accounting for nearly half of the total planned sample size). We performed a univariate linear regression analysis to assess the effect of the educational tool on preeclampsia knowledge (i.e. mean score difference between the two groups from baseline to second trimester visit).

Table 1. Baseline characteristics in the study population

	Intervention (n=16)	**Control (n=17)**
Age, mean years (SD)	32 (± 4.6)	34 (± 4.2)
Disease duration, mean years (SD)	10 (± 7.7)	10 (± 6.9)
Post-secondary education, n (%)		
No	3 (20%)	3 (20%)
Yes	12 (80%)	12 (80%)
Ethnicity, n (%)		
Caucasian	5 (31%)	12 (71%)
Native North American	1 (6%)	0
Hispanic	3 (19%)	0
Black	4 (25%)	3 (18%)
Asian	3 (19%)	1 (6%)
Other	0 (0%)	1 (6%)
Body mass index, mean kg/m^2 (SD)	24 (4.7)	24 (3.8)
Antiphospholipid syndrome, n (%)		
Any pregnancy morbidity & antiphospholipid antibodies (APA)	0	0
Vascular thrombosis & APA	1 (6%)	0
Any pregnancy morbidity & vascular thrombosis & APA	0	0
Prior eclampsia or preeclampsia, n (%)	1 (6%)	0
Prior or current lupus nephritis, n (%)	6 (38%)	3 (18%)
Heparin use, n (%)		
Prophylactic	1 (6%)	1 (6%)
Therapeutic	1 (6%)	1 (6%)

Results: Thirty-three pregnant SLE women were included in the study, among which 16 were exposed to the intervention and 17 were unexposed. Baseline characteristics were well-balanced between the two groups with similar mean maternal age between intervention group (32.2 years, standard deviation, SD, 4.6) and control group (34.1 years, SD 4.2) and identical proportion of participants with post-secondary education (i.e. 80%) (**Table 1**). The difference in mean preeclampsia knowledge scores between second trimester and baseline visits in the intervention group was 4.4 points (95% CI -0.1, 9.0) and in the control group was 1.5 points (95% CI -2.7, 5.7). The mean difference in knowledge scores (from baseline to second trimester) for those receiving the educational tool was 2.7 points higher (95% CI -1.5, 6.9) than those receiving standard of care.

Conclusion: Approximately midway into the trial, we observed a trend for improvement in preeclampsia knowledge from the baseline to the second trimester visit in pregnant women with SLE who received a specifically-designed educational tool compared to the control group, although the CIs included the null. Our RCT is well-poised to provide a new evidence-based approach to improve preeclampsia knowledge in pregnant women with SLE, which could help to optimize aspirin use and outcomes in this vulnerable population.

Disclosure: J. Lee, None; **A. Mendel**, None; **I. Malhamé**, None; **S. Bernatsky**, None; **E. Vinet**, None.

Abstract Number: 1712

Adverse Outcomes and Rehospitalization After Delivery Among Women with Systemic Lupus Erythematosus or Rheumatoid Arthritis and Their Infants

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Women with rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE) have greater risk of adverse obstetric and birth outcomes than women without these conditions. Infant outcomes are less well-studied. It is unknown whether re-hospitalization after delivery occurs more often for affected mothers and their infants.

Methods: This population-based cohort study used linked birth-hospital discharge data from Washington State for 1987-2014. International Classification of Disease 9th revision (ICD9) codes identified all women with RA (ICD9 714.X, 725.X) and SLE (ICD9 710, 710.0, 710.1) in the hospital discharge record at delivery, and a 10:1 comparison group of women without these codes. Analyses were restricted to singleton live births (1,223 RA; 1,354 SLE). Poisson regression with robust standard errors estimated relative risks (RR) and 95% confidence intervals (CI) for selected outcomes, accounting for delivery year, maternal age, and parity.

Results: Many adverse outcomes were more common among RA and SLE cases than among comparison women. Preeclampsia occurred more often during pregnancies of women with RA (RR 1.42, 95% CI 1.17-1.71) or SLE (RR 2.33, 95% CI 2.01-2.70), as did preterm rupture of membranes (PROM, RR 2.85, 95% CI 2.20-3.72 for RA; RR 3.28, 95% CI 2.54-4.23 for SLE). Cesarean deliveries were more common among nulliparous women in both groups (RR

1.32, 95% CI 1.18-1.48 for both conditions). Infants of women with RA or SLE were more likely to weigh < 2500 g (RR 2.08, 95% CI 1.72-2.52 for RA; RR 4.88, 95% CI 4.27-5.58 for SLE), be small for gestational age (RR 1.25, 95% CI 1.07-2.50; RR 2.30; 2.04-2.59, respectively), delivered at < 32 weeks gestation (RR 1.83, 95% CI 1.13-2.97; RR 5.13, 95% CI 3.75-7.01, respectively), and require neonatal intensive care unit admission (NICU, RR 1.89, 95% CI 1.56-2.30; RR 2.71, 95% CI 2.25-3.28, respectively). Infants of women with SLE were more likely to have a malformation (RR 1.46, 95% CI 1.21-1.75) or die within 2 years (RR 2.11, 95% CI 1.21-3.67). Rehospitalization levels among both women with RA (RR 2.22; 1.62-3.04) and SLE (RR 2.78, 95% CI 2.15-3.59) were greatest < 6 months of delivery and declined over time. Infants of women with SLE had increased rehospitalization < 6 months (RR 1.64, 95% CI 1.36-1.98).

Conclusion: Consistent with prior literature, we found women with RA or SLE experienced many adverse outcomes. In our data, these included preeclampsia, PROM, and cesarean deliveries, with increased risks more notable among women with SLE. Infants of women with either condition were more likely to weigh < 2500g, be < 32 weeks gestation, small for gestational age, and require NICU admission than infants of comparison women. Only infants of women with SLE had increased malformations. Maternal rehospitalization after delivery was more common in both groups; most marked at < 6 months. Infant rehospitalizations were increased in both cohorts to a lesser extent. Close follow-up during this time period is crucial to minimize adverse outcomes.

Disclosure: J. Sabo, None; **N. Singh**, None; **D. Crane**, None; **D. Doody**, None; **M. Schiff**, None; **B. Mueller**, None.

Abstract Number: 1713

Risk of Serious Infections in Offspring Exposed in Utero to Ustekinumab or Vedolizumab

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Ustekinumab, an IL-12/23 inhibitor, is indicated in adult patients with inflammatory bowel disease (IBD), psoriasis (PsO), and psoriatic arthritis (PsA) and vedolizumab, an $\alpha_4\beta_7$ receptor antagonist is indicated in IBD only. Both are monoclonal antibodies harbouring an Fc portion, which are actively transported across the placenta, often reaching higher fetal than maternal levels. As fetuses could be exposed to therapeutic or supra-therapeutic levels of these drugs, there are concerns that these agents could cause immunosuppression after birth. However, evidence is lacking.

We compared the risk of serious infections in offspring exposed to ustekinumab, vedolizumab, tumour necrosis factor inhibitors (TNFi), and non-biologic immunosupressives versus offspring unexposed during pregnancy among women with IBD, PsO and/or PsA.

Methods: We conducted a retrospective cohort study using the US MarketScan database, an employment insurance database. We included live births (01/2011-12/2018) among women with PsO, PsA, and/or IBD. Drug exposure was defined as ≥1 filled prescription or infusion procedure code during pregnancy. In offspring, we evaluated serious

infections within the first year of life as any single inpatient infection code. We performed multivariate analyses using logistic regression, adjusting for maternal age, co-morbidities, corticosteroid use, concomitant drug use, preterm birth and disease state.

Results: We included 16,115 offspring born to 7,612 women with PsO/PsA, 8,315 with IBD, and 188 with PsO/PsA and IBD. A total of 52 offspring were exposed to ustekinumab, 43 to vedolizumab (including 7 to both TNFi and vedolizumab),1,585 to TNFi, 1,857 to non-biologic immunosuppressives alone, and 12,585 unexposed to any drug. The percentage of serious infections in offspring exposed to ustekinumab was 3.8% (95% CI 0.4-13.9), versus 2.7% (95% CI 1.9-3.6) for TNFi, 2.3% (95% CI 0.4-12.0) for vedolizumab and 2.6 (95% CI 2.3-2.8) for those unexposed to any drug, though all estimates had wide, overlapping confidence intervals. Compared to children unexposed to any drug, there was a potential trend for increased risk with ustekinumab (OR 1.6, 0.4-6.8), but CIs were wide and included the null. For those exposed to vedolizumab (OR 0.9, 0.1-6.2) or TNFi (OR 1.0, 0.6-1.4) there was no clear excess risk.

Conclusion: In a large cohort, we did not detect a clear excess risk for offspring exposed in-utero to, vedolizumab or anti-TNF's, compared to unexposed patients; there was a signal for more events with ustekinumab, but confidence intervals were wide. Ongoing caution, as well as more research on short and long-term effects, is warranted for biologics actively transported across the placenta.

Disclosure: J. Gorodensky, None; **S. Bernatsky**, None; **W. Afif**, Janssen, 2, Dynacare, 2, Arena Pharmaceuticals, 2, Amgen, 2, Abbvie, 2, Merck, 2, Novartis, 2, Pfizer, 2, Sandoz, 2, Takeda, 2; **Y. St-Pierre**, None; **K. Filion**, None; **E. Vinet**, None.

Abstract Number: 1714

Exploring the Sexual and Reproductive Health (SRH) Needs of Men with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Few studies have comprehensively evaluated the information needs and priorities that men with rheumatic diseases have about their sexual and reproductive health (SRH). This qualitative study sought to explore their SRH needs within the rheumatology context.

Methods: Men aged 18-45 years who were diagnosed with at least one rheumatic disease and used at least one disease-modifying anti-rheumatic drug or immunosuppressive medication were recruited from academic outpatient rheumatology clinics in western Pennsylvania. Research coordinators engaged participants in phone-based semi-structured qualitative interviews about their reproductive histories, parenting experience, perceptions of how their diseases and medications affected their SRH, and experiences of SRH-related clinical care. Interviews were audio-recorded and transcribed verbatim. Thematic saturation was reached after the twelfth interview, and additional interviews were conducted to verify that no new information emerged. Research coordinators developed a preliminary codebook based on the interview content. Using an inductive approach, two coders applied the codebook to the transcripts and adjudicated coding differences to full agreement. The finalized codebook was used to conduct a thematic analysis.

Results: The 18 participants ranged in age from 22 to 44 years old, and identified as Black (n=2), White (n=14), and Asian (n=2). The most common disease diagnoses were spondyloarthritis, systemic lupus erythematosus, and rheumatoid arthritis. Most men were married or in a heterosexual relationship; no men were in a same-sex relationship. Twelve men had at least one child, and six men had no children. Six participants were vasectomized— five of whom had the procedure prior to their disease diagnosis.

Four major themes were elicited from the interviews: 1) Men had family planning concerns, particularly related to the heritability of their diseases, their fertility, and potential effects of their medications on their offspring's health; 2) Men felt that fatigue, disability, and/or pain from their diseases either impaired or would impair their abilities to parent; 3) Men rarely discussed SRH with their rheumatologists, who they assumed would initiate the discussion if relevant to their health; 4) Men rarely discussed sexual dysfunction with their rheumatologists, even when they believed that it arose from their diseases or anti-rheumatic drugs.

Conclusion: In this study, men expressed a number of concerns related to their diseases, particularly the health and well-being of their children and physical challenges with parenting. Men rarely articulated these concerns to their rheumatologists, who, in turn, rarely initiated family planning conversations with them. Men who experienced sexual dysfunction generally implicated their diseases or medications as the cause but did not discuss this health issue with their rheumatologists. Our study found that some men's information needs are incompletely addressed in the current rheumatology clinical setting and suggests that rheumatologists may need to include SRH in their routine counseling and care of male patients.

Disclosure: O. Stransky, None; **N. Hunt**, None; **J. Richards**, None; **M. Birru Talabi**, None.

Abstract Number: 1715

Providing High Quality Family Care Planning for Women with Rheumatic Disease in Rheumatology Clinics: Perspectives of Rheumatology Clinicians

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: While rheumatologists in several descriptive studies have acknowledged the importance of family planning in their care of women with rheumatic diseases, they have also identified key barriers to this care, including time constraints, competing priorities, and inadequate communication with women's health providers. We conducted a series of focus groups composed of rheumatologists and rheumatology advanced practice providers (APPs) to synthesize their ideas for potential tools and solutions to overcome these barriers within the rheumatology clinical setting.

Methods: Semi-structured qualitative focus groups were conducted with rheumatologists (N=3 groups) and APPs (N=2 groups). Trained independent qualitative analysts conducted the focus groups via Zoom video conferencing. Discussions were transcribed and two trained research coordinators developed a content-based codebook. They

applied the codebook to transcripts, and discrepancies adjudicated to full agreement with the principal investigator. Differences in codes between the groups by provider type were also identified. The codes were synthesized and used to conduct a thematic analysis.

Results: A total of 22 clinicians participated in the study, most of whom were women (75%) working within academic practice settings (60%). Clinicians had practiced rheumatology for an average of six years (range 1-17 years). Four themes emerged from the focus groups: 1) Clinicians desired patient-directed tools and resources to educate and prepare patients to discuss reproductive health issues at the rheumatology visit; 2) Most clinicians were aware of existing reproductive health resources, but desired additional training or resources around contraception and medication safety; 3) Clinicians desired tools to facilitate contact with women's health providers to ensure early and uncomplicated access to reproductive health care (e.g., electronic consults); 4) Clinicians were less interested in using electronic health record (EHR) pop-up reminders or alerts to support family planning care, but more interested in using prepopulated text within the EHR to include in patient notes or educational information to add to patient visit summaries. Although similar ideas were generated between the APP and rheumatologist groups, the rheumatologists were generally more interested in additional training and education, whereas APPs were more interested in EHR prompts and tools.

Conclusion: In this study, rheumatologists and rheumatology APPs from primarily academic practice settings described tools and resources that could help them to provide more consistent and higher-quality family planning care to patients with childbearing potential. Future work should focus on the development of patient-facing tools and resources to prepare patients for family planning conversations with rheumatology clinicians. Additional educational resources are needed to address providers' knowledge gaps around contraception and medication safety in the context of pregnancy. Finally, individual health systems and practices need to prioritize the development of accessible pathways to reproductive health care for women with rheumatic disease.

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Abstract Number: 1716

Teratogenic Medication Use Associated with Favorable Odds of Contraception Counseling in a Cohort of Women with Systemic Lupus Erythematosus at a Large Tertiary Academic Medical Center

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) primarily affects women of childbearing age, who have an increased risk of pregnancy complications such as preterm labor and preeclampsia, especially in the setting of active disease.[1] Contraception counseling is important in this population given the teratogenic nature of some med-

Table 1. Summary of characteristics of patients in the SLE cohort (N=478 women). Characteristics are divided into categories: demographics, counseling, immunosuppression, contraception, and pregnancy. Both number of women and percentages are reported. Unless otherwise specified, SD=standard deviation

Characteristics	n*	%*
Demographics		
Age (range=15-46), mean ± SD years	33.6	± 8.0
Race		
(missing)	26	5.4
African American	248	51.9
Caucasian	118	24.7
Other	66	13.8
Asian	15	3.1
American Indian / Native Alaskan (AI / NA)	5	1.0
Counseling		
Specialty of contraception counseling (not mutually exclusive)		
Rheum/Immunology	272	56.9
OB/GYN	155	32.4
Nephrology	97	20.3
Family Medicine	48	10.0
Internal Medicine	45	9.4
Other	40	8.4
Hematology	22	4.6
Pharmacy	15	3.1
Number of counseling specialties used		
0	103	21.5
1 (most common groups (n=): Rheum/Immunology (92), OB/GYN (36), Family (12), Nephrology (11))	165	34.5
2 (Rheum/Immunology+OB/GYN (45), Rheum/Immunology+Nephrology (24))	127	26.6
3 (Rheum/Immunology+OB/GYN+Nephrology (12), Rheum/Immunology+Nephrology+Internal (9))	60	12.6
4 (Rheum/Immunology+OB/GYN+Nephrology+Other (6))	21	4.4
5 (Rheum/Immunology+OB/GYN+Nephrology+Internal+Other)	1	0.2
6 (Rheum/Immunology+OB/GYN+Nephrology+Other+Hematology+Pharmacy)	1	0.2
at least 1 counseling specialty used	375	78.5
at least 2 counseling specialties used	210	43.9
at least 3 counseling specialties used	83	17.4
Immunosuppression		
Immunosuppression use (not mutually exclusive)		
Hydroxychloroquine (HCQ)	412	86.2
Mycophenolate mofetil (MMF)	143	29.9
Monoclonal Antibody (mAb) (missing=1)	73	15.3
Methotrexate (MTX)	33	6.9
Cyclophosphamide (CYC) (missing=1)	10	2.1
Teratogenic (MMF, MTX, CYC)	183	38.3
Number of immunosuppression types used		
(missing)	2	0.4
0	23	4.8
1 (most common groups (n=): HCQ (230), MMF (18), mAb (11))	266	55.6
2 (HCQ+MMF (102), HCQ+mAb (30), HCQ+MTX (18))	159	33.3
3 (HCQ+MMF+mAb (15), HCQ+mAb+MTX (9))	28	5.9
at least 1 type of immunosuppression used (missing=2)	453	94.8
at least 2 types of immunosuppression used (missing=2)	187	39.1
Positivity of antiphospholipid antibodies (missing=91)	152	31.8
Contraception		
Type of contraception (n=)		
none documented (106) or documented as not using (38)	144	30.1
Levonorgestrel IUD (65), Nexplanon (27), Copper IUD (10), patch (1) or ring (1)	104	21.8
Tubal ligation/salpingectomy (58) or partner vasectomy (6)/orchiectomy (1)	65	13.6
Depo-Provera injections (32) or Progestin-only OCPs (16)	48	10.0
Condoms	35	7.3
Abstinence	32	6.7
Combination OCPs	30	6.3
Currently pregnant (8), menopausal (7), or same sex partner (5)	20	4.2
Pregnancy		
Pregnancy outcome 2016-2018 (missing=9)	71	14.8
SAB (GA<20 weeks)	15	21.1
TAB	8	11.3
PTD	9	12.7
FTD	38	53.5
IUFD (GA>20 weeks)	1	1.4
Adverse pregnancy outcome (SAB, PTD, or IUFD)	25	35.2

*unless otherwise specified; SD=standard deviation

ications used for treatment.[2] Our study describes the frequency of contraception counseling provided by multiple subspecialties to women with SLE, and investigates the associations between teratogenic medication use and receiving contraception counseling.

Methods: This was a retrospective cohort study following 478 women (aged 15-44) with an ICD diagnosis code of SLE over a 2-year period (6/2016-6/2018). Women were seen in outpatient subspecialty clinics in a large tertiary academic medical center. Those with a history of hysterectomy/bilateral oophorectomy were excluded. Demographic data was retrieved via the university-affiliated central data repository, and additional data, including documentation of contraception counseling, was obtained via manual chart abstraction. Univariable associations between categorical demographics or other clinical information and contraception counseling were assessed to produce unadjusted odds ratios and 95% confidence intervals (OR, 95% CI). T-tests were used to assess difference in age by contraception counseling.

Results: Data from 478 women (52% African American (AA), 25% Caucasian) with SLE were included **(Table 1)**. Rheumatology/immunology was the subspecialty to most frequently provide contraception counseling (57%). Nearly 80% of women received counseling from at least one subspecialty, 44% from at least two. Factors associated with receiving contraception counseling were younger age, AA race, and use of more than one immunosuppressive medication **(Table 2)**. Women on teratogenic medications (methotrexate (MTX), mycophenolate mofetil (MMF), or cyclophosphamide (CYC)) had higher odds of receiving contraception counseling from at least 1 subspecialty (OR, 2.01; 95% CI 1.23-3.26), from two or more subspecialties (OR, 2.18; 95% CI, 1.50-3.17), and from rheumatology/immunology (OR, 1.86; 95% CI, 1.27-2.73) **(Table 3)**.

Table 2. Description of odds ratios (OR) and 95% confidence intervals (95% CI) for the univariable associations of various factors (demographics, immunosuppression types and number of medications, APL antibody positivity, and contraception methods) and receiving contraception counseling. Overall counts and percentages provided. Unadjusted odds ratio with asymptotic confidence intervals are provided and shown in bold when the null effect is excluded at alpha= 0.05. For continuous age, mean +/- standard deviation (SD) are shown and t-test used to test the difference between the counseling groups using the pooled method assuming equal variances

Exposures	n missing	Categories	Count	No contraception counseling (n=103, 22%)	Any contraception counseling (n=375, 78%)	OR (asymptotic 95% CI)
Age		*continuous years (range=15-46)*	33.6±8.0	35.7±8.3	33.0±7.8	Difference, mean (95% CI) **2.7 (1.0, 4.4)** years
Race	*26*	*African American*	248	41 (17%)	207 (83%)	1.00 (ref)
		Caucasian	118	33 (28%)	85 (72%)	**0.51 (0.30, 0.86)**
		Other / Asian / AI/NA	86	21 (24%)	65 (76%)	0.61 (0.34, 1.11)
Immunosuppression		*no Hydroxychloroquine*	66	16 (24%)	50 (76%)	1.00 (ref)
		Hydroxychloroquine	412	87 (21%)	325 (79%)	1.20 (0.65, 2.20)
		no Mycophenolate mofetil	335	81 (24%)	254 (76%)	1.00 (ref)
		Mycophenolate mofetil	143	22 (15%)	121 (85%)	**1.75 (1.04, 2.95)**
	1	*no Monoclonal Ab*	404	88 (22%)	316 (78%)	1.00 (ref)
		Monoclonal Ab	73	15 (21%)	58 (79%)	1.08 (0.58, 1.99)
		no Methotrexate	445	100 (22%)	345 (78%)	1.00 (ref)
		Methotrexate	33	3 (9%)	30 (91%)	2.90 (0.87, 9.69)
	1	*no Cyclophosphamide*	467	100 (21%)	367 (79%)	1.00 (ref)
		Cyclophosphamide	10	2 (20%)	8 (80%)	1.09 (0.23, 5.21)
		no teratogenic	295	76 (26%)	219 (74%)	1.00 (ref)
		Any teratogenic	183	27 (15%)	156 (85%)	**2.01 (1.23, 3.26)**
Number of types of immunosuppression used		*0*	23	8 (35%)	15 (65%)	1.00 (ref)
		1-3	453	94 (21%)	359 (79%)	2.04 (0.84, 4.95)
		0-1	289	73 (25%)	216 (75%)	1.00 (ref)
		2-3	187	29 (16%)	158 (84%)	**1.84 (1.14, 2.97)**
Positivity of antiphospholipid (aPL) antibodies	*91*	*Not aPL positive*	235	43 (18%)	192 (82%)	1.00 (ref)
		aPL positive	152	25 (16%)	127 (84%)	1.14 (0.66, 1.96)
Type of contraception		*none documented or documented as not using*	144	60 (42%)	84 (58%)	1.00 (ref)
		Levonorgestrel IUD, Nexplanon, Copper IUD, patch, or ring	104	10 (10%)	94 (90%)	**6.71 (3.23, 14.0)**
		Tubal ligation/salpingectomy or partner vasectomy/orchiectomy	65	16 (25%)	49 (75%)	**2.19 (1.14, 4.21)**
		Depo-Provera injections or Progestin-only OCPs	48	4 (8%)	44 (92%)	**7.86 (2.68, 23.0)**
		Condoms	35	1 (3%)	34 (97%)	**24.3 (3.23, 182)**
		Abstinence	32	1 (3%)	31 (97%)	**22.1 (2.94, 167)**
		Combination OCPs	30	6 (20%)	24 (80%)	**2.86 (1.10, 7.42)**
		Currently pregnant, menopausal, or same sex partner	20	5 (25%)	15 (75%)	2.14 (0.74, 6.22)

OR>1 higher odds of contraception counseling defined; OR<1 lower odds of contraception counseling defined, compared to the reference (ref) group

Table 3. Description of odds ratios (OR) and 95% confidence intervals (95% CI) for the univariable associations of various factors (demographics, immunosuppression types and number of medications, APL antibody positivity, and contraception methods) and receiving contraception counseling from rheumatology/immunology. Overall counts and percentages provided. Unadjusted odds ratio with asymptotic confidence intervals are provided and shown in bold when the null effect is excluded at alpha= 0.05. For continuous age, mean +/- standard deviation (SD) are shown and t-test used to test the difference between the counseling groups using the pooled method assuming equal variances

Exposures	n missing	Categories	Count	No Rheumatology / Immunology contraception counseling (n=206, 43%)	Rheumatology / Immunology contraception counseling (n=272, 57%)	OR (asymptotic 95% CI)
Age		*continuous years (range=15-46)*	33.6±8.0	34.8±7.9	32.6±7.9	Difference, mean (95% CI) **2.1 (0.7, 3.6)** years
Race	*26*	*African American*	248	99 (40%)	149 (60%)	1.00 (ref)
		Caucasian	118	56 (47%)	62 (53%)	0.74 (0.47, 1.14)
		Other / Asian / AI/NA	86	39 (45%)	47 (55%)	0.80 (0.49, 1.31)
Immunosuppression		*no Hydroxychloroquine*	66	29 (44%)	37 (56%)	1.00 (ref)
		Hydroxychloroquine	412	177 (43%)	235 (57%)	1.04 (0.62, 1.76)
		no Mycophenolate mofetil	335	157 (47%)	178 (53%)	1.00 (ref)
		Mycophenolate mofetil	143	49 (34%)	94 (66%)	**1.69 (1.13, 2.54)**
	1	*no Monoclonal Ab*	404	179 (44%)	225 (56%)	1.00 (ref)
		Monoclonal Ab	73	26 (36%)	47 (64%)	1.44 (0.86, 2.41)
		no Methotrexate	445	196 (44%)	249 (56%)	1.00 (ref)
		Methotrexate	33	10 (30%)	23 (70%)	1.81 (0.84, 3.89)
	1	*no Cyclophosphamide*	467	202 (43%)	265 (57%)	1.00 (ref)
		Cyclophosphamide	10	3 (30%)	7 (70%)	1.78 (0.45, 6.96)
		no teratogenic	295	144 (49%)	151 (51%)	1.00 (ref)
		Any teratogenic	183	62 (34%)	121 (66%)	**1.86 (1.27, 2.73)**
Number of types of immunosuppression used		*0*	23	14 (61%)	9 (39%)	1.00 (ref)
		1-3	453	190 (42%)	263 (58%)	2.15 (0.91, 5.08)
		0-1	289	140 (48%)	149 (52%)	1.00 (ref)
		2-3	187	64 (34%)	123 (66%)	**1.81 (1.23, 2.64)**
Positivity of antiphospholipid (aPL) antibodies	*91*	*Not aPL positive*	235	97 (41%)	138 (59%)	1.00 (ref)
		aPL positive	152	54 (36%)	98 (64%)	1.28 (0.84, 1.94)
Type of contraception		*none documented or documented as not using*	144	85 (59%)	59 (41%)	1.00 (ref)
		Levonorgestrel IUD, Nexplanon, Copper IUD, patch, or ring	104	38 (37%)	66 (63%)	**2.50 (1.49, 4.21)**
		Tubal ligation/salpingectomy or partner vasectomy/orchiectomy	65	26 (40%)	39 (60%)	**2.16 (1.19, 3.93)**
		Depo-Provera injections or Progestin-only OCPs	48	18 (38%)	30 (63%)	**2.40 (1.23, 4.70)**
		Condoms	35	6 (17%)	29 (83%)	**6.96 (2.72, 17.8)**
		Abstinence	32	11 (34%)	21 (66%)	**2.75 (1.23, 6.13)**
		Combination OCPs	30	15 (50%)	15 (50%)	1.44 (0.65, 3.17)
		Currently pregnant, menopausal, or same sex partner	20	7 (35%)	13 (65%)	**2.68 (1.01, 7.11)**

OR>1 higher odds of contraception counseling defined; OR<1 lower odds of contraception counseling defined, compared to the reference (ref) group

Seventy-one women (15%) had a documented pregnancy outcome during the study period; of those, 25 (35%) had an adverse pregnancy outcome (spontaneous abortion, preterm delivery, or intra-uterine fetal demise).

Conclusion: In this study, women with SLE on teratogenic medications (MTX, MMF, CYC) had higher odds of receiving contraception counseling from their rheumatologist and from at least two subspecialties. Multidisciplinary approaches to enhance contraception counseling should be encouraged. Further investigation is needed to understand factors associated with adverse pregnancy outcomes in this high-risk patient population.

Clowse ME, Jamison M, Myers E, James AH. A national study of the complications of lupus in pregnancy. Am J Obstet Gynecol. 2008;199(2):127.e1-127.e1276.

Sammaritano LR, Bermas BL, et al. 2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Care Res (Hoboken). 2020 Apr;72(4):461-488.

Disclosure: S. Chandramouli, None; **C. Alvarez**, None; **R. Silverstein**, None; **S. Sheikh**, Pfizer, 5, GlaxoSmithKline, 2, 5.

Abstract Number: 1717

One Year After the Publication of the American College of Rheumatology (ACR) Guidelines for Management of Reproductive Health in Rheumatic Diseases, Has Anything Changed? An Analysis of Rheumatology Practice at a Tertiary Care Medical Center

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Successful pregnancies in patients with rheumatic disease are possible when they are well-monitored, adequately treated, and planned during periods of disease quiescence. Previously, a lack of standardized guidelines and physician-patient discussions around reproductive health created risks for poorer outcomes. The ACR's reproductive guidelines include recommendations on contraception use, medication, and pregnancy with an emphasis on patients' inputs on pregnancy desires.[1] This study evaluates changes in rheumatologists' practice at an academic medical center following the publication of the ACR's reproductive guidelines.

Methods: Retrospective chart review was performed on reproductive age females (18 – 45 years) with ≥2 rheumatology office visits during the period of April 1st2019 to March 31st2021 and with the diagnoses of RA, SLE, and inflammatory arthritis (IA). The following data were collected: demographics, pre-pregnancy counseling, pregnancy wish, contraception usage via review of medication list or documentation, gynecology visit, and teratogenicity of medication. Generalized linear mixed models were used to evaluate for improvements in documentation regarding pre-pregnancy counseling/wish and contraception use, the year after the publication of the ACR guidelines (Period 2) compared to

Table 1. Demographics of Reproductive Age Females: Pregnant and Non-Pregnant Patients

Characteristics	Value
Total Number of Non-Pregnant Patients	319
Race (%)	
Black	97 (30.41)
White	122 (38.24)
Asian	23 (7.21)
Other	77 (24.14)
Age (± SD)	33.48 ± 6.89
Primary Rheumatological Diagnosis (%)	
Rheumatoid Arthritis	95 (29.78)
Systemic Lupus Erythematosus	139 (43.57)
Inflammatory Arthritis	85 (26.65)
Obstetrician-Gynecologist (%)	
Follows	161 (50.47)
Given Referral	29 (9.09)
Total Number of Pregnant Patients	46
Race (%)	
Black	12 (26.10)
White	17 (37.00)
Asian	4 (8.70)
Other	13 (28.30)
Age (± SD)	32.07 ± 5.23

Table 2. Differences in pregnancy counseling/wish documentation and contraception use when comparing office visits the year before (Period 1) with the year after (Period 2) the publication of the ACR's Reproductive Guidelines: N=319 non-pregnant, reproductive age females

Outcomes Based on Primary Rheumatological Diagnosis	Period 1: Office Visit(s) in Year Prior to 4/2020 (%)	Period 2: Office Visit(s) in Year After 4/2020 (%)	Odds Ratio (95% CI)	P-Value
Rheumatoid Arthritis	**N=85**	**N=75**		
Pregnancy Counseling Documentation	36 (42.35)	51 (68.00)	3.3252 (1.6388-6.747)	0.001
Discussion of Pregnancy Wish Documentation	34 (40.00)	49 (65.33)	3.2697 (1.6167-6.6126)	0.001
Any Contraception Documentation	44 (51.76)	40 (53.33)	1.0529 (0.4962-2.2344)	0.8925
Highly Effective Contraception Documentation *	12 (14.11)	13 (17.33)	1.2783 (0.4721-3.4615)	0.6271
Patients on Highly Teratogenic Medications#:	54 (63.53)	41 (54.67)		
Any Contraception Documentation	44 (81.48)	23 (56.10)	1.4014 (0.5144-3.8178)	0.5054
Highly Effective Contraception Documentation*	12 (22.22)	8 (20.00)	2.1694 (0.5491-8.5709)	0.2659
Systemic Lupus Erythematosus	**N=115**	**N=108**		
Pregnancy Counseling Documentation	50 (43.48)	71 (65.74)	3.003 (1.6455-5.4804)	0.0004
Discussion of Pregnancy Wish Documentation	46 (40.00)	63 (58.33)	2.341 (1.2867-4.2592)	0.0055
Any Contraception Documentation	52 (45.22)	55 (50.93)	1.4114 (0.7549-2.639)	0.279
Highly Effective Contraception Documentation*	19(16.52)	20 (18.52)	1.4008 (0.6112-3.2104)	0.4241
aPL Labs Checked	91 (79.13)	91 (84.26)	1.6533 (0.7587-3.6027)	0.2047
Patients on Highly Teratogenic Medications#:	49 (42.61)	35 (32.41)		
Any Contraception Documentation	28 (57.14)	24 (68.57)	1.904 (0.6232-5.8171)	0.2547
Highly Effective Contraception Documentation*	13 (26.53)	11 (31.43)	1.6484 (0.5071-5.3578)	0.4014
Inflammatory Arthritis	**N=60**	**N=56**		
Pregnancy Counseling Documentation	9 (15.00)	25 (44.64)	3.5256 (1.3887-8.9503)	0.0085
Discussion of Pregnancy Wish Documentation	7 (11.37)	22 (39.29)	4.1067 (1.4859-11.3501)	0.0069
Any Contraception Documentation	37 (61.67)	37 (66.07)	1.4285 (0.573-3.5616)	0.4409
Highly Effective Contraception Documentation*	10 (16.67)	12 (21.43)	1.526 (0.506-4.6018)	0.4497
Patients on Highly Teratogenic Medications#:	15 (25.00)	10 (17.86)		
Any Contraception Documentation	9 (60.00)	9 (90.00)	7.4165 (0.5096-107.93)	0.1353
Highly Effective Contraception Documentation*	1 (6.67)	0 (0.00)	N/A	N/A

* highly effective contraception per ACR guidelines, such as intrauterine device.

highly teratogenic medication, which are strongly recommended against per ACR guidelines, such as methotrexate, leflunomide, cyclophosphamide, mycophenolate mofetil.

Table 3. Outcomes of 46 Pregnant Patients from April 1st, 2019 to March 31st, 2021

Characteristics	Value (%)
Primary Rheumatological Diagnosis (%)	
Rheumatoid Arthritis	4 (8.70)
Systemic Lupus Erythematosus	14 (30.40)
Sjogren's Syndrome	3 (6.50)
Other	24 (52.20)
Rheumatoid Arthritis and Sjogren's Syndrome	1 (2.20)
Presented to the Rheumatology Office Visit Already Pregnant	15 (32.61)
High Disease Activity (RAPID 3>12) at First Office Visit **	11 (23.91)
Moderate Disease Activity (RAPID 3 (6.01-12)) at First Office Visit **	5 (10.87)
aPL Panel:	
Negative	22 (47.83)
Positive:	5 (10.90)
Anticoagulation	1 (20.00)
Aspirin	4 (80.00)
Not Checked	19 (41.30)
SSA/SSB:	
Negative	21 (45.65)
Positive:	14 (30.43)
Hydroxychloroquine use	7 (50.00)
Fetal Monitoring	14 (100.00)
Not Checked	11 (23.91)
Compliance with Rheumatology Visits (1 visit per Trimester)	14 (30.43)

** Routine assessment of patient index data 3 (RAPID3) is a patient reported outcome routinely used to assess disease activity and validated for use in multiple rheumatic conditions.

the year before (Period 1). For pregnant patients, additional data on aPL status, SSA/SSB, and pregnancy monitoring were collected and expressed as percentages depicting degree of compliance with the guidelines.

Results: Out of a total of 425 patients, 60 had undergone permanent birth control. Demographics for the remaining 319 non-pregnant women are shown in Table 1. There was a significant improvement in documentation related to pre-pregnancy counseling and discussion of pregnancy wish in Period 2 as compared to Period 1 as illustrated by the following odds ratios (OR): RA 3.33 [95% confidence interval (95% CI) 1.64-6.75], 3.27 [95% CI 1.62-6.61]; SLE 3.00 [95% CI 1.65-5.48], 2.34 [95% CI 1.29-4.26]; IA 3.53 [95% CI 1.39-8.95], 4.11 [95% CI 1.49-11.35], respectively. There were no improvements in areas of contraception use/documentation in all disease categories: patients on any contraceptive: 133 (51%) in Period 1 and 132 (55 %) in Period 2 (Table 2).

Of the 46 pregnant patients, all were followed by an obstetrician but only 14 (30 %) followed with their rheumatologist once per trimester. 15 patients (33%) presented to their rheumatology visit already pregnant and 16 (35%) conceived with high/moderate disease activity. Of the pregnant patients with positive SSA/SSB, all had adequate fetal monitoring but only half were on hydroxychloroquine (Table 3).

Conclusion: In the year following the publication of the ACR reproductive guidelines, there was improvement in documentation related to pre-pregnancy counseling and pregnancy wish. However, we identify ongoing practice gaps with regards to encouraging contraception use and aspects of pregnancy management.

1. Sammaritano LR et al. 2020 American College of Rheumatology Guidelines for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases. Arthritis Rheumatol 2020 Apr;72(4): 529-556.

Disclosure: Y. Zhou, None; **S. Hassan**, None.

Abstract Number: 1718

Use of Gonadotropin Releasing Hormone Agonist for Ovarian Preservation in SLE Patients on Cyclophosphamide

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: SLE is an autoimmune disease which predominantly affects women of childbearing age (age 20-40). Most of the medications used for treating SLE can adversely affect fertility, pregnancy, and fetal outcomes. Cyclophosphamide (CYC) is an immunosuppressive agent indicated for the treatment of severe SLE. The use of CYC cause ovarian insufficiency and lead to dormant primordial follicle activation and loss. Gonadotropin releasing hormone agonist (GnRHa) may preserve ovarian function by preventing early stage development of ovarian follicles from maturation. This may decrease the number of follicles that are vulnerable to chemotherapy.

There is conflicting data on whether GnRHa preserve ovarian function when given before cyclophosphamide. Furthermore, there are inconsistent guidelines from various professional societies regarding the administration of GnRHa for ovarian protection. We attempted to develop evidence-based practice guidelines for the use of GnRHa in SLE patients undergoing treatment with CYC.

Methods: We reviewed published literature on the use of GnRHa for ovarian protection by searching PubMed. The available evidence was discussed in multidisciplinary conferences for consensus building. The current guidelines

Table 1.

	2020 American College of Rheumatology Guideline for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases	Fertility Preservation in Patients With Cancer: ASCO Clinical Practice Guideline Update
Year Released	2020	2018
Articles Reviewed	2 randomized double-blind trial, 1 case control study, 1 cross sectional study, 4 Retrospective review, 1 guideline	7 randomized controlled trials, 4 systematic review, 7 guidelines
Recommendation	To prevent inducing primary ovarian insufficiency in premenopausal women with RMD receiving monthly intravenous CYC, we conditionally recommend monthly gonadotropin-releasing hormone agonist co-therapy. This was based on evidence supporting benefits in early breast cancer, evidence more specific to rheumatic disease patients is less robust but positive.	It may be offered to patients in hope of reducing the likelihood of chemo induced ovarian insufficiency, but not be used in place of proven fertility preservation methods.

and alternate option for ovarian preservation were also reviewed. The final document for evidence-based practice guidelines will be developed in future.

Results: ACR guideline and American Society of Clinical Oncology (ASCO) conditionally recommends GnRHa to prevent ovarian insufficiency while on IV CYC (Table 1). Five research studies showed a protective effect of GnRHa on ovarian preservation (Table 2). An in vitro study using CYC showed no ovarian protection with GnRHa. The studies from use of GnRHa in patients with breast cancer showed conflicting results on its efficacy for ovarian preservation.

Conclusion: Most of the studies done in autoimmune diseases had a smaller cohort with no uniform criteria for defining ovarian insufficiency and preservation. Three studies were retrospective chart reviews which poses selection bias. The data from in-vitro study done with the removal of ovarian tissue was not replicated in clinical trials. In the breast cancer studies, patients were on several types of chemotherapy and the dose of CYC was much higher as compared to studies done in autoimmune diseases. Side effects of GnRHa mimic a hypo estrogen state. The alternate options for ovarian preservation involve surgical options with ovarian stimulation which could pose a risk of disease flare or thrombosis in SLE.

The evidence for the use of GnRHa for ovarian preservation while on CYC is not robust, but it is the least invasive procedure. A review of the evidence should be presented to the patient in a shared decision-making process and be evaluated by a multi-disciplinary team. The effectiveness and safety of GnRHa in SLE needs to be studied prospectively in a much larger population with well-defined outcome measures.

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Abstract Number: 1719

Pandemic-Associated Complications in Pregnant Women with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Pregnant women with rheumatic diseases may have been particularly vulnerable to the various consequences of the current pandemic, whether or not they were infected with SARS-CoV-2. Some of these consequences include increased stress, anxiety and depression, substance use, and reduced compliance with prenatal care, all of which could negatively impact pregnancy outcome. In addition, comorbidities may present increased risk of infection in women with underlying rheumatic diseases.

Methods: As part of the ongoing OTIS/MotherToBaby Autoimmune Diseases in Pregnancy Project, between February, 2017, and February, 2021, 382 pregnant women with rheumatic diseases were enrolled. The study assessed comorbidities, administered standardized measures of stress (PSS-10), anxiety (STAI state and trait) and depression (EPDS) mid-gestation or at enrollment if later than mid-gestation, captured maternal report of recreational substances used anytime in pregnancy, as well as compliance with routine prenatal care procedures such as ultrasound scans for

Table. Characteristics of pregnant women with rheumatic diseases before and during the SARS-CoV-2 pandemic

Measure	Rheumatic Diseases Pandemic Year COVID-19 Positive N = 25	Rheumatic Diseases Pandemic Year Not COVID-19 Positive N = 96	Rheumatic Diseases Pre-pandemic Period N = 261	p-value[a]
PSS-10 Stress Screen Positive Moderate to Severe (≥14)	75.0%	56.9%	50.0%	0.218
STAI Anxiety – State Screen Positive (>45)	33.3%	31.6%	14.8%	0.019
STAI Anxiety – Trait Screen Positive (>45)	25.0%	29.8%	14.8%	0.056
EPDS Depression Screen Positive (≥10)	41.7%	33.3%	21.8%	0.122
Ultrasound for Structure – Mid-Gestation	75.0%	75.6%	90.3%	0.001
Screening for Gestational Diabetes	77.7%	69.0%	88.5%	0.001
Any Alcohol Use in Pregnancy	60.0%	42.7%	44.1%	0.278
Comorbidities				
Asthma	28.0%	15.6%	13.0%	0.130
Pre-Pregnancy Body Mass Index ≥30	52.0%	27.1%	23.4%	0.005
Psychiatric Diagnosis	56.0%	36.5%	33.0%	0.068

[a]Chi-squared test for categorical variables or Fisher's Exact Test where expected cell number <5.

structure and screening for gestational diabetes. From the onset of the pandemic, COVID-19 test positive status at any time in pregnancy was assessed. Those enrolled in the pre-pandemic period (N = 261) were compared to those enrolled in the pandemic year (N = 121), stratified by COVID-19 test positivity in pregnancy.

Results: As shown in the Table, compared to the pre-pandemic period, pregnant women with rheumatic diseases were more likely to screen positive on state or trait anxiety. Screening positive on stress or depression was more common in those women who were infected compared to other groups, but not significantly so. Similarly, alcohol use was increased only among those with rheumatic diseases in the pandemic year who tested positive for COVID-19 in pregnancy. Pregnant women with rheumatic diseases who had a pre-pregnancy body mass index in the obese range (≥30) were significantly more likely to test positive for the virus in the pandemic year.

Conclusion: These data suggest that pregnant women with rheumatic diseases were particularly vulnerable during the pandemic year to complications that could influence pregnancy outcome.

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Abstract Number: 1720

Cervical Dysplasia and HPV Infection in Women with Vasculitis

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SESSION INFORMATION
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Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
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Background/Purpose: The most common cause of cervical cancer is persistent human papillomavirus (HPV) infection in the cervical epithelium, causing precancerous cervical dysplasia and ultimately cervical cancer in a complex oncogenic pathway. HPV is commonly cleared by the immune system; however, an impaired immune system can facilitate the persistence of HPV infection in the cervix leading to increased risk of progression to cervical dysplasia and cancer. Women with autoimmune diseases have impaired immune systems through the presence of both rheumatic disease and immunosuppressive medications, and increased rates of cervical dysplasia have been reported in women with systemic lupus erythematous and rheumatoid arthritis. However, women with systemic vasculitis have not been included in these analyses. This study aims to fill this gap and evaluate the risk of cervical dysplasia in the female vasculitis population.

Methods: We performed a retrospective chart review of the women with vasculitis at The Ohio State University Wexner Medical Center. Criteria for inclusion included: female, diagnosis of vasculitis, documented Papanicolau (Pap) smear after date of vasculitis diagnosis and in years 2010-2019.

Results: We identified 119 patients for inclusion in this study. Of the 254 total Pap smears, 44 pap smears (17% of 254) in the 119 patients had abnormal results. Of the 254 Pap smears analyzed, 26 pap smears (10%) in 16 patients showed Atypical Squamous Cells of Undetermined Significance (ASC-US), 15 (6%) in 10 patients had Low-Grade Squamous Intraepithelial Lesion (LSIL), and 1 each resulted with Atypical Squamous Cells-Cannot Rule Out High Grade Squamous Intraepithelial Lesion, High-Grade Squamous Intraepithelial Lesion, and Squamous Cell Carcinoma. Additionally, 112 of the Pap smears were also tested for high-risk HPV, and nearly 20% (21 Pap smears in 85 patients) tested positive for this.

Conclusion: Out study show insights into the prevalence of cervical dysplasia and HPV infection in the female vasculitis population. The United States incidence of abnormal Pap smears is 4% with 2.8% resulting as ASC-US and 0.97% as LSIL; we found more than quadruple the rate of ASCUS and six-fold the rate of LSIL in our study population. We found a higher rate of high-risk HPV-positive pap smears in our vasculitis patient population compared to the 11% reports for SLE patients in prior studies. These elevated rates of cervical abnormalities should be considered for cervical cancer screening recommendations in this population.

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Abstract Number: 1721

A Womb with Rheum: Women's Health Providers' Confidence and Educational Needs in the Care of Those with Rheumatic Diseases

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
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Background/Purpose: Reproductive age women with rheumatic diseases are commonly cared for by non-rheumatologists who provide contraceptive counseling, preconception, pregnancy, and post-partum management. When women's health and rheumatology providers disagree, patients voice frustration and provider distrust. The education received by women's health providers pertaining to the recognition and management of rheumatic diseases in child-bearing age patients is not well-defined. This study aims to assess knowledge gaps, specify aspects of care with greatest uncertainty, and assess current resources used by women's health providers regarding their clinical management in those with rheumatic diseases.

Methods: An electronic survey was distributed nationally to physicians and allied health professionals who care for reproductive age women and are trained in Obstetrics and Gynecology (OBGYN), Internal Medicine, or Family Med-

Table 1: Demographics of Survey Respondents

Profession	
Resident	39 (37%)
PGY-1	9
PGY-2	15
PGY-3	10
PGY-4	5
Fellow	5 (5%)
Attending Physician	53 (51%)
<5 years since training	15
6-10 years since training	14
11-15 years since training	7
>16 years since training	17
Midwife	3 (3%)
Physician Assistant or Registered Nurse Practitioner	4 (4%)
Specialty	
Family Medicine	4 (4%)
Internal Medicine (including Med-Peds)	18 (17%)
OBGYN (General, including Midwives)	64 (62%)
OBGYN (Subspecialty)	18 (17%)
Practice setting	
University hospital, academic medical center or affiliated clinic	71 (70%)
Teaching hospital not a part of a University hospital	13 (13%)
Community hospital or affiliated clinic	12 (12%)
Office based or private clinic	5 (5%)

Figure 1: Categorical Knowledge Percentages and Confidence Ratings

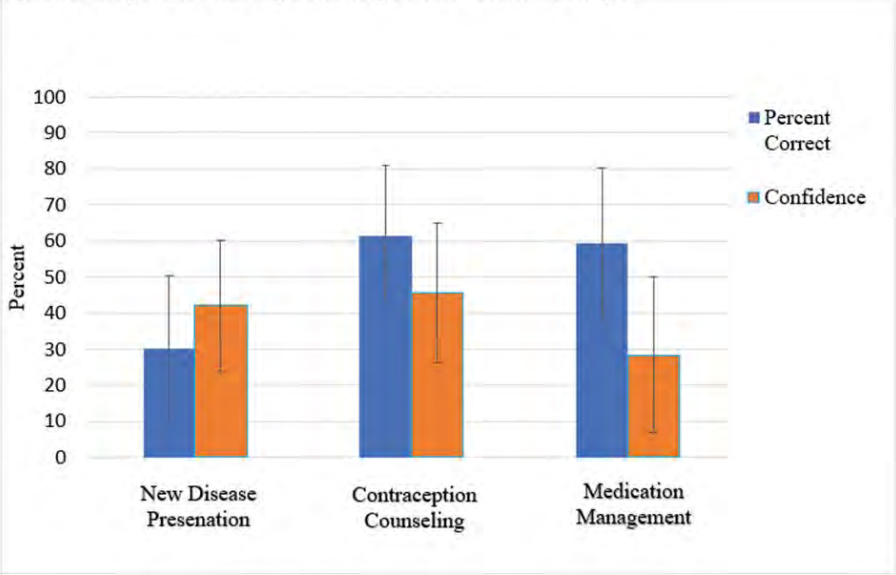

Table 2: Prior Exposure to Rheumatology and Reproductive Health Topics and Resources

Prior exposure to educational experiences involving reproductive health of patients with rheumatologic diseases	
None	68 (65%)
Attended or presented a lecture on the topic	28 (27%)
I or someone in my family has a rheumatic disease	5 (5%)
I helped create guidelines or committee statements on the topic	1 (1%)
I am involved in research about this topic	2 (2%)
Top resources used in clinical practice to find information on rheumatic diseases in pre-conception/pregnant/postpartum patients	
Consult to MFM/high risk OB	63 (61%)
ACOG resources	50 (48%)
Consult Rheumatologist or other subspecialist	36 (35%)
Preferred method for future educational resources	
Website	71 (68%)
Published formal guidelines	67 (64%)
Smartphone App	64 (61%)

icine. The survey consisted of three sections: 1) patients presenting with new rheumatic diseases, 2) contraception, and 3) preconception/antepartum medication management. Participants were also asked about resource utilization. Survey questions and scenarios were based on the ACR Guidelines for the Management of Reproductive Health in Rheumatic and Musculoskeletal Diseases and relevant American College of Obstetrics and Gynecology (ACOG) Committee Opinions. Responses and confidence ratings were captured using RedCap and analyzed using descriptive statistics.

Results: The survey was completed by 104 participants, majority being academic OBGYN generalists. (Table 1). Respondents performed the poorest in recognizing new rheumatic disease presentations including RA and SLE in patients presenting with post-partum joint pain or proteinuria and thrombocytopenia in pregnancy, respectively (Figure 1). The least confidence was reported when answering medication management questions. Contraception was the area of highest performance and confidence, although areas for contraceptive knowledge expansion exist. Most participants chose to discontinue medications in a pregnant patient with RA, despite these being deemed pregnancy-compatible by ACR guidelines and ACOG Committee Opinion. However, when counseling the same patient post-partum, 72% of respondents successfully chose the breastfeeding-compatible therapies.

Most respondents had no prior exposure to the reproductive health issues facing female patients with rheumatic diseases (Table 2), identified consultants as their main resource used in clinical practice, and would prefer more information to be provided as a website, published guidelines, or Smartphone App.

Conclusion: Women's health providers lack confidence, educational opportunities, and therefore knowledge across the spectrum of common clinical scenarios and management questions facing reproductive-aged women with rheumatic diseases. Recognizing new disease presentations and antepartum medication management have the largest educational needs. Collaborative resources created by women's health and rheumatology societies, including websites and smart phone apps, are most desired to fill educational needs and hopefully will improve patient care.

Disclosure: L. He, None; **R. Karani**, None; **G. Arenas**, None; **C. Edens**, None.

Abstract Number: 1722

Risk of Pre-eclampsia and Impact of Disease Activity and Anti-rheumatic Treatment in Women with Rheumatoid Arthritis, Axial Spondylarthritis, and Psoriatic Arthritis - A Collaborative Matched Cohort Study from Sweden and Denmark

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SESSION INFORMATION

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Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Pre-eclampsia is a pregnancy-related syndrome with potentially fatal outcomes. In RA, high disease activity has been associated to adverse pregnancy outcomes such as preterm birth and low birth weight. The risk of pre-eclampsia in relation to disease activity and anti-rheumatic treatment in women with chronic inflammatory arthritis has not been assessed. The objective of this study was to evaluate the overall risk of pre-eclampsia in pregnant women with RA, Axial (Ax)SpA, and PsA and to assess the impact of disease activity and anti-rheumatic treatment.

Table 1

Risk of preeclampsia in pregnant women with RA, AxSpA, and PsA overall and in relation to anti-rheumatic treatment strategy **pre-pregnancy**

	Pregnancies, n	Pre-eclampsia, n (%)	Crude OR (95% CI)	Adjusted OR 1[4] (95% CI)
All RA pregnancies	1739	67 (3.9)	1.27 (0.98, 1.64)	1.27 (0.96, 1.67)
No treatment	410	14 (3.4)	1.13 (0.66, 1.93)	1.19 (0.70, 2.03)
Monotherapy[1]	661	23 (3.5)	1.14 (0.75, 1.74)	1.02 (0.67, 1.56)
Combination therapy[2]	668	30 (4.5)	**1.48 (1.02, 2.15)**	**1.59 (1.09, 2.31)**
Controls[3]	17390	535 (3.1)	REF	REF
All AxSpA pregnancies	819	34 (4.2)	1.29 (0.87, 1.91)	1.17 (0.76, 1.78)
No treatment	402	15 (3.7)	1.18 (0.69, 2.01)	1.12 (0.65, 1.91)
Monotherapy[1]	289	11 (3.8)	1.20 (0.66, 2.16)	1.03 (0.57, 1.86)
Combination therapy[2]	128	8 (6.2)	1.87 (0.95, 3.69)	1.62 (0.82, 3.20)
Controls[3]	8190	267 (3.3)	REF	REF
All PsA pregnancies	489	26 (5.3)	**2.07 (1.32, 3.24)**	**1.85 (1.10, 3.12)**
No treatment	189	9 (4.8)	1.66 (0.77, 3.58)	1.71 (0.75, 3.91)[5]
Monotherapy[1]	194	13 (6.7)	**2.88 (1.63, 5.09)**	**2.71 (1.43, 5.12)**[5]
Combination therapy[2]	**106**	4 (3.8)	1.36 (0.42, 4.48)	1.06 (0.23, 4.88)[5]
Controls[3]	4890	129 (2.6)	REF	REF

Only singleton pregnancies. One woman may contribute with one or more pregnancies. ORs were estimated using logistic regression and generalized estimation-equation method. 1) csDMARD, bDMARD, or CS, 2) csDMARD, bDMARD, and CS in any combination of at least two, 3) Matched 1:10 on maternal age group, parity, and year, 4) Adjusted for maternal age, parity, year, country, BMI group, smoking, and educational level, 5) Not adjusted for BMI due to low numbers. Abbreviations: AxSpA, Axial SpA; BMI, Body Mass Index; CI, Confidence Interval; OR, Odds Ratio.

Table 2

Risk of preeclampsia in pregnant women with RA, AxSpA, and PsA overall and in relation to disease activity **during** pregnancy

	Pregnancies, n	Pre-eclampsia, n (%)	Crude OR (95% CI)	Adjusted OR[5] (95% CI)
All RA pregnancies	1739	67 (3.9)	1.27 (0.98, 1.64)	1.27 (0.96, 1.67)
DAS28-CRP[2]				
<3.2	447	19 (4.3)	1.41 (0.88, 2.23)	1.39 (0.85, 2.29)
≥3.2	239	13 (5.4)	**1.82 (1.03, 3.20)**	**1.95 (1.10, 3.49)**
Missing	1053	35 (3.3)	1.09 (0.77, 1.54)	1.05 (0.72, 1.53)
HAQ				
<1	506	21 (4.2)	1.37 (0.88, 2.12)	1.41 (0.88, 2.26)
≥1	196	14 (7.1)	**2.42 (1.40, 4.20)**	**2.02 (1.12, 3.66)**
Missing	1039	32 (3.1)	1.01 (0.70, 1.45)	1.02 (0.69, 1.50)
CRP (mg/L)				
<10	457	21 (4.6)	1.53 (0.98, 2.38)	1.55 (0.96, 2.49)
≥10	248	13 (5.2)	1.74 (0.99, 3.05)	**1.78 (1.01, 3.13)**
Missing	1034	33 (3.2)	1.04 (0.73, 1.40)	1.01 (0.68, 1.49)
Any DAS28-CRP[2] ≥3.2, HAQ ≥1, or CRP ≥10 mg/L				
No	368	12 (3.3)	1.07 (0.60, 1.90)	1.06 (0.56, 2.01)
Yes	388	24 (6.2)	**2.08 (1.37, 3.17)**	**1.96 (1.26, 3.04)**
Missing[3]	983	31 (3.2)	1.03 (0.71, 1.49)	1.03 (0.70, 1.53)
Controls[1]	17390	535 (3.1)	REF	REF
All AxSpA pregnancies	819	34 (4.2)	1.29 (0.87, 1.91)	1.17 (0.76, 1.78)
Any HAQ ≥1 or CRP ≥10 mg/L				
No	174	8 (4.6)	1.53 (0.79, 2.98)	1.20 (0.55, 2.64)
Yes	113	3 (2.7)	0.76 (0.25, 2.22)	0.57 (0.18, 1.75)
Missing[4]	532	23 (4.3)	1.33 (0.84, 2.11)	1.33 (0.81, 2.18)
Controls[1]	8190	267 (3.3)	REF	REF
All PsA pregnancies	489	26 (5.3)	**2.07 (1.32, 3.24)**	**1.85 (1.10, 3.12)**
Any DAS28-CRP[2] ≥3.2, HAQ ≥1, or CRP ≥10 mg/L				
No	94	4 (4.3)	1.72 (0.62, 4.78)	2.07 (0.71, 6.00)
Yes	85	5 (5.9)	2.37 (0.95, 5.91)	1.89 (0.59, 6.05)
Missing[3]	310	17 (5.5)	**2.09 (1.20, 3.63)**	1.75 (0.91, 3.38)
Controls[1]	4890	129 (2.6)	REF	REF

Only singleton pregnancies. One woman may contribute with one or more pregnancies. ORs were estimated using logistic regression and generalized estimation-equation method. 1) Matched 1:10 on maternal age group, parity, and year, 2) DAS28-CRP was calculated including CRP and without Global Health-Visual Analog Scale (VAS) 3) No measurements of either DAS28-CRP, HAQ, or CRP 4)No measurements of neither HAQ, nor CRP, 5) Adjusted for maternal age, parity, year, country, BMI group, smoking, and educational level. Abbreviations: AxSpA, Axial SpA; BMI, Body Mass Index; CI, Confidence Interval; DAS28-CRP, 28-joint DAS, CRP adjusted; NA, Not Applicable; OR, Odds Ratio.

Methods: We conducted a register-based matched cohort study using data from Swedish and Danish nationwide clinical and health registers. We identified RA, AxSpA, and PsA singleton pregnancies (2006-2018) by linking medical birth registers (MBR) to rheumatology registers in Sweden (SRQ) and Denmark (DANBIO). Control pregnancies from the MBRs were matched 1:10 on age, birth year, and parity.

We obtained information on anti-rheumatic treatment nine months before (pre-pregnancy) and during pregnancy, and disease activity (DAS28-CRP/HAQ/CRP) during pregnancy. Information on pre-eclampsia was obtained from the National Patient Registers. The risk of pre-eclampsia was estimated using logistic regression and presented by odds ratios (aOR) with 95% confidence intervals (CI). Adjustments were made for maternal age, parity, year, country, BMI, smoking, and educational level.

Results: We identified 1739 RA, 819 AxSpA, and 489 PsA pregnancies. For RA and AxSpA pregnancies, there were no major differences in maternal characteristics compared to their control pregnancies. Pregnant women with PsA were more likely to be obese, smokers, and less educated compared to their controls.

We found an overall increased risk of pre-eclampsia in PsA pregnancies as compared to control pregnancies (aOR 1.85; 95% CI 1.10, 3.12), whereas the risk was not increased in RA or AxSpA (**Table 1**). Women with RA receiving pre-pregnancy combination therapy (conventional synthetic (cs)DMARD, biologic (b)DMARD, and CS in any combination of at least two) had a moderately increased risk compared to controls, whereas no treatment or monotherapy (csDMARD, bDMARD, or CS) did not increase the risk (**Table 1**). For PsA, pre-pregnancy monotherapy was associated with pre-eclampsia (**Table 1**). We observed no significantly increased risk of pre-eclampsia for any of the disease groups when stratifying on treatment during pregnancy.

Among RA exposed pregnancies with available information on disease activity during pregnancy (n=756, 43%), we observed a doubled risk of pre-eclampsia associated with high disease activity compared to control pregnancies (**Table 2**). In AxSpA and PsA, we found no such association, but numbers of events were low (**Table 2**).

Conclusion: Pregnant women with PsA, but not AxSpA, are at increased risk of pre-eclampsia overall. For RA pregnancies, our results indicate that severe disease, i.e. combination treatment before pregnancy and high disease activity during pregnancy, is a risk factor for pre-eclampsia.

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Abstract Number: 1723

Factors Associated with Postpartum Flare in Women with Lupus

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SESSION INFORMATION

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Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
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Background/Purpose: Several prior studies have assessed disease activity in the setting of pregnancy and have shown that certain factors such as thrombocytopenia, systemic lupus erythematosus (SLE) disease activity at pregnancy onset, lupus nephritis, hypertension, antiphospholipid syndrome, and history of preeclampsia are associated with higher rates of SLE flare in pregnancy (1). However, few have focused on the postpartum period and have shown varying results. While some studies showed an increase in flares in the postpartum period (2-4), others showed no flares in the postpartum period (5). The objective of this study was to identify factors associated with the occurrence

of SLE flares in the 6-month postpartum period. Identifying these factors is important for stratifying and monitoring lupus patients in the postpartum period.

Methods: Lupus pregnancies were retrospectively identified via chart review at a tertiary care center in New York from 2005 – 2020. Flares in the 6-month postpartum period were physician reported, as documented in the patient chart by the treating rheumatologist, or identified by an escalation in medication regimen.

Results: Of the 103 lupus pregnancies reviewed, 73 pregnancies had documented follow up in the 6-month postpartum period, of which 20 (27%) were identified to have had SLE flares. This sample was representative of the overall population of pregnant women at our center. The median (IQR) age of the patient population was 29 (24, 34) years old. Thirty-eight (52%) patients self-identified as Hispanic or Latina, 25 (34%) as Black or African American, 5 (7%) as Asian and 5 (7%) as Caucasian (Table). Patients with postpartum flare were more likely to have history of thrombosis (40% vs 14%, p=0.02), lupus nephritis (60%, vs 20%, p=0.001), and SLE flare in the 6 months prior to conception (40% vs 12%, p=0.007) when compared to those without flare. Women who experience postpartum flares were younger (median IQR) [25 (22, 30) years old vs 31 (25, 35) years old, p=0.003] and more likely to have fewer than 3 total pregnancies (80% vs 57%, p=0.07). The median (IQR) SLEPDAI score amongst those with postpartum flare was higher in comparison to those without [2 (0, 4) vs 0 (0, 2), respectively, (p=0.06)]. Pre-pregnancy flares were associated with postpartum flares

	Total pregnancies (n=73)	**Postpartum flare – (n=53)**	**Postpartum flare + (n=20)**	**p-value**
Age, years, median (IQR)	29 (24, 34)	31 (25, 35)	25 (22, 29.5)	0.003
Race, n (%) White Black/African American Asian Unknown	 5 (7) 25 (34) 5 (7) 38 (52)	 3 (6) 17 (32) 5 (9) 28 (53)	 2 (10) 8 (40) 0 10 (50)	0.51
Ethnicity, n (%) Hispanic/Latino Not Hispanic/Latino Unknown	 38 (52) 30 (41) 5 (7)	 26 (49) 22 (41) 5 (9)	 12 (60) 8 (40) 0	0.33
Planned pregnancy, n (%)*	28 (52)	22 (55)	6 (43)	0.43
Adverse pregnancy outcome, n (%)†	12 (17)	8 (16)	4 (20)	0.66
Number of pregnancies >3, n (%)	26 (37)	22 (43)	4 (20)	0.07
History of pregnancy morbidity, n (%)‡	15 (21)	11 (22)	4 (20)	0.88
History of thrombosis, n (%)	15 (21)	7 (14)	8 (40)	0.02
History of lupus nephritis, n (%)	22 (31)	10 (20)	12 (60)	0.001
Pre-pregnancy disease flare, n (%)	14 (20)	6 (12)	8 (40)	0.007
SLE activity score, median (IQR)	0 (0, 2)	0 (0, 2)	0 (0, 4)	0.06
Lupus anticoagulant (LAC)+ §	9 (19)	8 (24.24)	1 (7.14)	0.17

*Data on planned vs. unplanned pregnancy was available for 54 (76.06%) of patients.
†Adverse outcomes included fetal death >12 weeks gestation, neonatal death, and delivery at <36 weeks for preeclampsia, gestational hypertension, placental insufficiency, and/or small for gestational age (<5%)
‡Pregnancy morbidity was defined as fetal death >10 weeks gestation, premature birth <34 weeks gestation due to severe preeclampsia or placental insufficiency, and/or ≥3 unexplained spontaneous abortions <10 weeks gestation
§LAC data was available for 47 (67.14%) of patients.

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even after adjusting for SLEPDAI during pregnancy (OR 4.4, CI 1.15-16.81, p=0.03). Ethnicity, adverse pregnancy outcomes, pregnancy morbidity, and planned vs unplanned pregnancy were not associated with postpartum flare.

Conclusion: This study shows that younger women with fewer total pregnancies, history of thrombosis, lupus nephritis, and active disease prior to conception should be closely monitored for postpartum flare. Patients with these characteristics can be risk stratified and should be counseled appropriately to monitor for signs of flare in the postpartum period.

Disclosure: A. Ramu, None; **M. Veyseh**, None; **B. Lally**, None; **S. Wang**, None; **A. Broder**, None.

Abstract Number: 1724

More Than 50% of Women with Chronic Rheumatic Inflammatory Diseases Present an Unfavorable Pregnancy Outcome: A Descriptive Analysis of the National French Healthcare Database

Anna Molto[1], Barbara Roux[2], Diep Tran[2], Aya Ajrouche[2], nathalie costedoat-Chalumeau[3], Elisabeth Elefant[4], Vassilis Tsatsaris[5], Jeanne Fresson[6], Brigitte Bader-Meunier[7], Bruno Fautrel[8] and Florence Tubach[2], [1]Rheumatology department, Cochin hospital, APHP, Paris, France, [2]CEPHEPI, APHP, Paris, France, [3]Inserm DR Paris 5, Paris, France, [4]Teratogenic agents refernce center (CRAT) , Hôpital Trousseau, APHP, Paris, France, [5]Obstetrics Department, Port Royal Maternity, Cochin Hospital, APHP, Paris, France, [6]CHU Nancy, Nancy, France, [7]Pediatric Immuno-hematology, Necker Hospital, APHP, Paris, France, [8]Pitié Salpêtrière Hospital, APHP, Sorbonne Université, Paris, France

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Women with chronic rheumatic inflammatory diseases (CRID, i.e. rheumatoid arthritis (RA) or spondyloarthritis (SpA)) have been reported to have poorer pregnancy outcomes than the general population. The objective of this analysis was to describe the singleton pregnancy outcomes of women with CRID in France over the past decade.

Methods: This is a retrospective cohort study within the French Healthcare database (SNDS), which covers 97% of the French population. Adult women were included if they had RA or SpA according to CIM-10 codes, had started a singleton pregnancy between 2008 and 2017 (index date), and were continuously covered by this health insurance from 1-year before pregnancy onset to 1-year after end of the pregnancy or death (whichever came first). Both maternal and pregnancy outcomes were considered. Outcomes were identified either by ICM-10 codes or hospital discharge summaries between 2008 and 2018.

Results: Among the 35,737 adult women with a CRID (40.7% with RA and 59.3% with SpA) and a past history of DMARD reimbursement, 11,274 (41.7%) started a singleton pregnancy during the study period. Among them, 6,501 (57.7%) were exposed to at least one DMARD preconceptionally (6 months before last menstrual period) and during pregnancy.

Mean (SD) age of women at the start of pregnancy was 32 (5) years, and disease duration was 4 (4) years. Live-birth represented by far the most frequent pregnancy outcome (76.9%), but 56.6% patients presented at least one unfavorable outcome among those listed in the table.

Conclusion: More than 75% pregnancies in patients with CRID resulted in a live-birth, but half of patients presented at least an unfavorable pregnancy outcome. Prevalence of miscarriage was lower than reported in the literature, probably reflecting the fact that very early miscarriages often do not need hospitalization/ specific intervention, and thus are difficult to identify in claims databases. Maternal and infant outcomes seemed comparable to general population. Whether medications had an impact on such outcomes needs further evaluation.

	Unfavourable outcome	N(%)
Pregnancy outcomes	Miscarriage	590 (5.2%)
	Medical termination	97 (0.9%)
	Extra-uterine pregnancy	165 (1.5%)
	Other abortions*	48 (0.4%)
	Stillbirth	48 (0.4%)
	Intrauterine growth restriction	348 (3.1%)
	Low birth weight (<3th percentile)	135 (1.2%)
	Pre-term birth (<37 WG)	3366 (29.9%)
	Eclampsia/Pre-eclampsia	214 (1.9%)
	Perinatal death	2 (0.0%)
	Cesarean section	2304 (20.4%)
Maternal outcomes	Severe maternal infection	225 (2.0%)
	Maternal mortality	2 (0.0%)
	Gestational diabetes	853 (7.6%)
Infant outcomes	NCIU admission for more than 48h in infants born after 37 WG	95 (0.8%)
	Major congenital malformation	287 (2.5%)
	Severe infections during the first year of life	603 (5.3%)

*Hydatidiform mole or other abnormal products of conception.

Unfavourable pregnancy outcomes in patients with chronic rheumatic inflammatory diseases

Disclosure: A. Molto, None; **B. Roux**, None; **D. Tran**, None; **A. Ajrouche**, None; **n. costedoat-Chalumeau**, None; **E. Elefant**, None; **V. Tsatsaris**, None; **J. Fresson**, None; **B. Bader-Meunier**, None; **B. Fautrel**, AbbVie, 5, Pfizer, 5, Janssen, 2, Medac, 2, Novartis, 2, Sanofi-Genzyme, 2, Roche, 2, UCB, 2, Abbvie, 2, Amgen, 2, Biogen, 2, BMS, 2, Celltrion, 2, Fresenius Kabi, 2, Galapagos, 2, Gilead, 2, Lilly, 2, 5, MSD, 2, MSD, 5, Mylan, 2, Nordic Pharma, 2, Pfizer, 2, Sandoz, 2, SOBI, 2; **F. Tubach**, None.

Abstract Number: 1725

Higher Prevalence of Aspirin Use with a Specific Educational Tool in SLE Pregnancies: Preliminary Results

Joo Young (Esther) Lee[1], Arielle Mendel[2], Isabelle Malhamé[2], Sasha Bernatsky[1] and Evelyne Vinet[3], [1]McGill University, Montréal, QC, Canada, [2]McGill University Health Centre, Montréal, QC, Canada, [3]McGill University Health Centre, Mont Royal, QC, Canada

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Pregnant women with SLE are at substantial risk of preeclampsia. Best international practice guidelines recommend aspirin (ASA) in this population, as it reduces preeclampsia risk by more than 50% in high-risk women. However, recent evidence suggests that only 25% of pregnant SLE women use ASA. It is therefore imperative to understand ASA use patterns in SLE pregnancies to promote ASA adherence. With this objective, we are conducting the PREPARE (PREeclamPsia knowledge & Aspirin adheRence in lupus prEgnancies) trial, a randomized controlled trial, evaluating a specifically-designed educational tool. In this analysis, we aimed to assess ASA use, adherence, and dosage at baseline and 2nd study visits according to the intervention status.

Methods: Since 2018, we are recruiting consecutive pregnant SLE women (diagnosed according to the SLICC criteria) until the 16th gestational week at 5 Canadian centers. Participants are randomly assigned to receive the educational tool (intervention) or standard of care (control). At baseline (i.e. 1st trimester) and 2nd visits (i.e. 2nd trimester, 20-24 weeks, for ongoing pregnancies or 4-8 weeks after end of pregnancy for women who miscarried), the participants complete self-reported ASA adherence questionnaires and the modified Adherence to Refills and Medications Scale (ARMS), scored out of 44 (lower score meaning better adherence). We defined the participants 'ASA users' if they were using ASA in ongoing pregnancies or if they had used ASA but had a miscarriage. Current analysis includes participants enrolled at the coordinating center (accounting for nearly half of the total planned sample size). We measured the proportion of ASA users, mean ARMS scores, and dosage at both visits. We estimated a 95% CI for difference in proportion of ASA users between the groups using the Wilson procedure and mean ARMS score difference between the groups using the Student's t test.

Results: Thirty-three participants were included, 16 exposed to the intervention and 17 controls. Baseline characteristics were well-balanced with mean age of 32.2 years (standard deviation, SD, 4.6) in the intervention and 34.1 years (SD, 4.2) in the control group, and an identical proportion of participants who had post-secondary education (i.e. 80%) (**Table 1**). Baseline mean gestational age was 61.6 days (SD, 19.4) and 61.2 days (SD, 21.4) and baseline ASA use prevalence was 56% and 41% in the intervention and control group, respectively. Proportion of ASA users at the 2nd visit was 100% in the intervention and 82% in the control group, with a difference of 18% (95% CI -5, 41). At the 2nd visit, mean ARMS score was not different in the intervention (12.4 points) and control (12.2 points) groups [difference of 0.3 points (95% CI -0.8, 1.3)]. Among ASA users at the 2nd visit, 6% and 14% used 80-81mg, and 75% and 71% used 160-162mg in the intervention and control group, respectively.

Conclusion: Halfway into the trial, we observed a trend for higher ASA use in pregnant SLE women who received a specifically-designed educational tool compared to those receiving standard of care. The PREPARE trial is on track to provide a new evidence-based approach to optimize aspirin use and potentially improve outcomes in this population.

Table 1. Baseline characteristics in the study population

	Intervention (n=16)	Control (n=17)
Age, mean years (SD)	32 (± 4.6)	34 (± 4.2)
Disease duration, mean years (SD)	10 (± 7.7)	10 (± 6.9)
Post-secondary education, n (%)		
No	3 (20%)	3 (20%)
Yes	12 (80%)	12 (80%)
Ethnicity, n (%)		
Caucasian	5 (31%)	12 (71%)
Native North American	1 (6%)	0
Hispanic	3 (19%)	0
Black	4 (25%)	3 (18%)
Asian	3 (19%)	1 (6%)
Other	0 (0%)	1 (6%)
Body mass index, mean kg/m^2 (SD)	24 (4.7)	24 (3.8)
Antiphospholipid syndrome, n (%)		
Any pregnancy morbidity & antiphospholipid antibodies (APA)	0	0
Vascular thrombosis & APA	1 (6%)	0
Any pregnancy morbidity & vascular thrombosis & APA	0	0
Prior eclampsia or preeclampsia, n (%)	1 (6%)	0
Prior or current lupus nephritis, n (%)	6 (38%)	3 (18%)
Heparin use, n (%)		
Prophylactic	1 (6%)	1 (6%)
Therapeutic	1 (6%)	1 (6%)

Disclosure: J. Lee, None; **A. Mendel**, None; **I. Malhamé**, None; **S. Bernatsky**, None; **E. Vinet**, None.

Abstract Number: 1726

A Pregnancy Planning Quality Score to Assess a Systematic Intervention to Improve Pregnancy Planning for Women with SLE

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The safest pregnancies for women with SLE coincide with periods of disease quiescence maintained by pregnancy-compatible medications. In the US, Black women are more likely to experience unplanned pregnancy and experience higher rates of maternal and infant morbidity, possibly due to inequitable provider-patient planning discussions. The HOP-STEP Pregnancy Planning handout, which is aligned with the ACR Reproductive Health Guidelines, was created to facilitate pregnancy planning discussions between rheumatologists and their SLE patients. We have assessed the systematic ascertainment of pregnancy interest and pregnancy planning discussions in a lupus clinic to identify its impact on pregnancy planning quality and equitable care.

Methods: All women age 18-44 in a prospective registry who met ACR or SLICC criteria for SLE completed an intake form for each visit which included 1) whether she wanted to get pregnant in the next year and 2) contraceptive use. A woman was identified as 'not medically ready for pregnancy' if she was on a teratogen, had proteinuria ≥ 500 mg or a physician's global assessment (PGA) ≥ 1.5. Race was self-reported. We identified 10 Pregnancy-Planning Quality (PPQ) Measures, awarding one-point for each measure. If a woman interested in pregnancy was seen multiple times between 2/2018-12/2019, her score accounted for the accrual of points over subsequent visits.

Results: Pregnancy interest was reported by 26 of 152 (17%) women. Of those interested in pregnancy, the average age was 32.7 years (SD 5.5); 65% identified as Black and 15% as Hispanic. Fifteen patients (58%; 10 Black, 5 non-

Table 1. Cumulative Data Summarizing Factors Contributing to Lack of Medical Readiness for Pregnancy and Assessment of Pregnancy Planning Amongst Women with SLE

Pregnancy Incompatible Factor	Overall N=26	Non-Black N=9	Black N=17	p-value
Not Ready for Pregnancy at Any Study Visits	15 (58%)	5 (56%)	10 (59%)	1.0
On a Teratogen	10 (38%)	3 (33%)	7 (41%)	
Mycophenolate	8	2	6	
Methotrexate	2	1	1	
Cyclophosphamide	0	0	0	
Leflunomide	0	0	0	
Proteinuria ≥500mg	4 (15%)	1 (11%)	3 (18%)	
PGA ≥1.5	7 (27%)	3 (33%)	4 (24%)	
Pregnancy Planning Quality Measure	**Overall**	**Non-Black**	**Black**	**p-value**
Pregnancy Planning Discussion:				
1. MD knew patient intended pregnancy	25 (96%)	9 (100%)	16 (94%)	1.0
2. Documented use of HOP-STEP handout[1]	8 (31%)	1 (11%)	7 (41%)	0.2
Medication Preparation for Pregnancy:				
3. Hydroxychloroquine prescribed	25 (96%)	9 (100%)	16 (94%)	1.0
4. Plan to continue pregnancy-compatible medications in pregnancy	24 (92%)	9 (100%)	15 (88%)	0.5
5. Azathioprine prescribed	14 (54%)	6 (67%)	8 (47%)	0.4
6. Of those ever on a teratogen: teratogen switch plan	8/10 (80%)	2/3 (67%)	6/7 (86%)	1.0
7. Multivitamin	13 (50%)	6 (67%)	7 (41%)	0.4
Testing and Referral:				
8. Referred to Maternal-Fetal Medicine	7 (27%)	3 (33%)	4 (24%)	0.7
9. Known anti-phospholipid antibodies	25 (96%)	8 (89%)	17 (100%)	0.3
Positive anti-phospholipid antibodies	*3/25 (12%)*	*1/8 (13%)*	*2/17 (12%)*	*1.0*
10. Known Ro/SSA and La/SSB antibodies	25 (96%)	8 (89%)	17 (100%)	0.3
Positive Ro/SSA, La/SSB antibodies	*13/25 (52%)*	*2/8 (25%)*	*11/17 (65%)*	*0.1*
Pregnancy Planning Quality Score (0-10) Mean (SD)	7.3 (1.6)	7.4 (1.4)	7.2 (1.8)	0.7

Footnote: Fifteen patients were not medically ready for pregnancy at any visit with 10 taking a teratogen. Two women on a teratogen were able to switch to pregnancy-compatible medications during this period making them ready for pregnancy.

[1] The HOP-STEP Pregnancy Planning handout is free to use and available at LupusPregnancy.org, created in an Independent Medical Education grant from GSK.

Black) were not medically ready for pregnancy across visits, with 10 taking a teratogen, 4 with proteinuria, and 7 with a PGA ≥ 1.5. Two women on teratogens were able to switch to pregnancy-compatible medications during this period.

There were no differences in PPQ Scores between Black (7.2) and non-Black (7.4) patients (Table 1). All but one visit included a discussion of pregnancy planning, and the majority of women were given instructions to continue their appropriate medications in pregnancy.

As of 4/2021, 10 women had 12 pregnancies in the follow-up period; 9 (75%) of these were planned and occurred when the patient was medically ready to conceive. One was unplanned and conceived in the midst of a severe cutaneous flare; two were conceived by the same woman when she was taking MMF. Five women had not conceived due to ongoing teratogen use or disease activity. Seven women no longer desired pregnancy due to personal, non-medical reasons.

Conclusion: This study demonstrates that systematic, patient-reported measures of pregnancy interest and proactive pregnancy planning are feasible in an academic specialty clinic. More than half of all women were not medically ready for a safe pregnancy. The risks of poor pregnancy outcomes can be mitigated by addressing plans for pregnancy. Within our study population the majority of pregnancies were planned. The non-pregnant patients cite social issues, medications, and ongoing disease as reasons to not pursue pregnancy. This method shows promise for improving current clinic protocols regarding pregnancy planning.

Disclosure: C. Sims, UCB Pharma, 5; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **J. Doss**, Pfizer, 5; **L. Criscione-Schreiber**, None; **K. Sun**, None; **R. Sadun**, None; **J. Rogers**, Exagen, Inc, 5; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5.

Abstract Number: 1727

Behcet's Disease: A Meta-analysis of Pregnancy Outcomes

Leah Rooney[1], Aine Gorman[2], Matthew Turk[3], Louise Moore[4], Celine O'Brien[5], Jared Bierbrier[6], Anne Clohessy[5], Eamonn Molloy[7], Lorraine O Neill[8], Fionnuala M. Mc Auliffe[5] and Douglas Veale[9], [1]St Vincent's University Hospital, Dublin, Ireland, [2]St Vincents Hospital, Dublin, Ireland, [3]St. Vincents University Hospital, Dublin, Ireland, [4]Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W, Kinnegad, Ireland, [5]Perinatal Research Centre, Obstetrics and Gynaecology, School of Medicine, University College Dublin and National Maternity Hospital, Dublin, Dublin, Ireland, [6]McMaster University, Hamilton, ON, Canada, [7]St Vincent's Healthcare Group, Dublin, Ireland, [8]St. Vincent's Hospital, Dublin, Ireland, [9]University College Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Behcet's disease is a systemic inflammatory disease which commonly presents with episodes of acute inflammation, oral and genital ulcers, uveitis and skin lesions. It presents most commonly during the second and third decades of life, therefore frequently involves women during their reproductive years. The objective of our work was to determine the effect of Behcet's disease on pregnancy by evaluating the prevalence of fetal and maternal complications through systematic review and meta-analysis.

Methods: We performed a systematic review of the literature using Medline, Web of Science, and the Cochrane library from their inceptions until March 26, 2021. Studies were included if they presented the frequency of complications in

cohorts of pregnant patients with a diagnosis of Behcet's disease. Studies were selected by two independent reviewers and statistics were performed using REVMAN5.4.

Results: 6638 studies were identified of which 16 were included. Among patients' with Behcet's disease during pregnancy the prevalence of caesarean section was 23% (CI 10-36% , Figure 1), pre-term birth 11% (CI 8-15%, Figure 2), miscarriage 11% (CI 8-14%), pre-eclampsia 4% (CI 3-6%), intrauterine death 4% (CI 2-7%), new hypertension

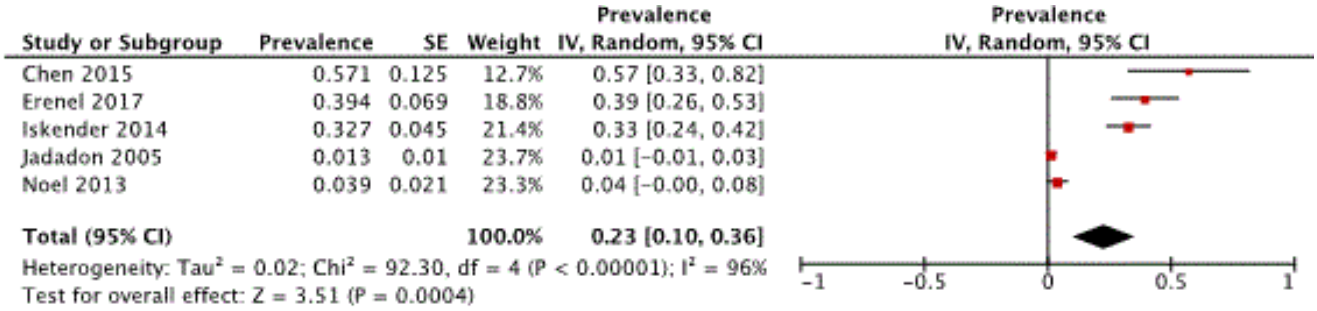

Figure 1. forest plot analysis of cesarian sections in patients with Behcet's disease

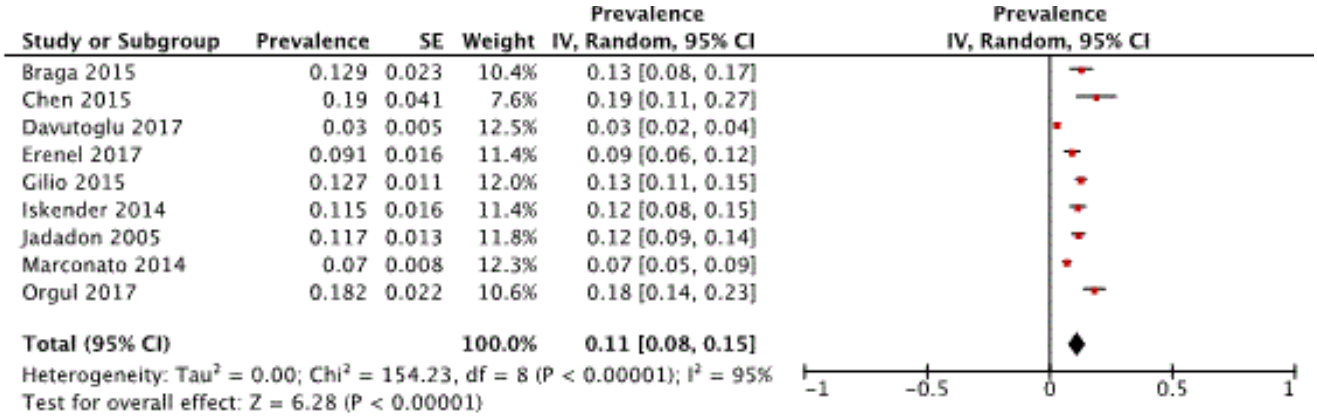

Figure 2. forest plot analysis of pre-term birth in patients with Behcet's disease

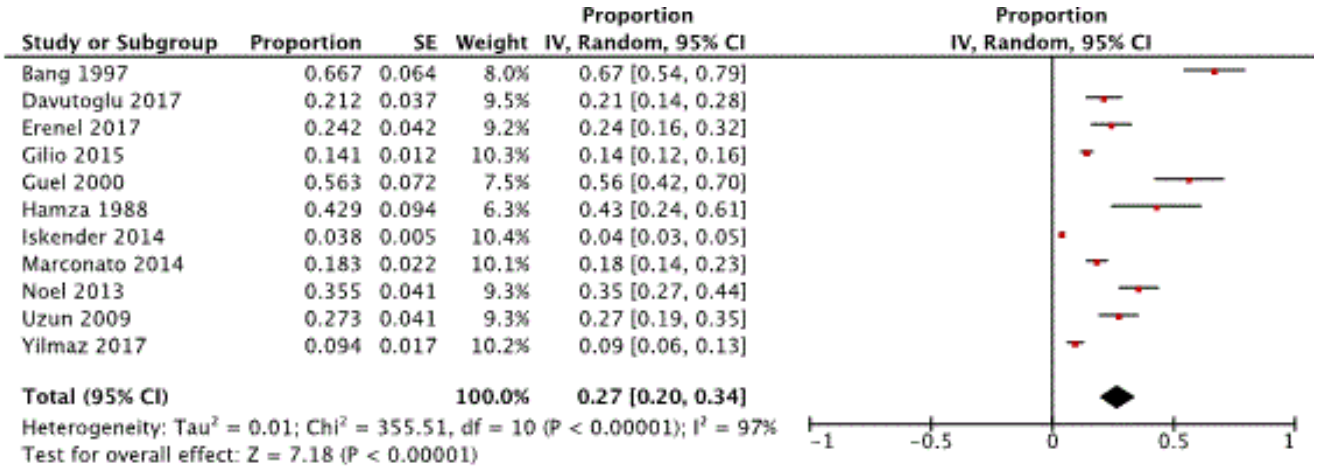

Figure 3. forest plot analysis of pre-term birth in patients with Behcet's disease

6% (2-10%) and 27% of women reported worsening of symptoms related to Behcet's disease during pregnancy (CI 20-34 , Figure 3).

Conclusion: Approximately one quarter of patients experienced worsening of symptoms related to Behcet's disease during pregnancy, 1 in 10 had a pre-term delivery and almost 1 in 4 delivered their baby by caesarean section. These results show the importance of close monitoring of patients with Behcet's disease during pregnancy – both for pregnancy complications and for worsening Behcet's symptoms.

Disclosure: L. Rooney, None; **A. Gorman**, None; **M. Turk**, None; **L. Moore**, None; **C. O'Brien**, None; **J. Bierbrier**, None; **A. Clohessy**, None; **E. Molloy**, None; **L. O Neill**, None; **F. Mc Auliffe**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6.

Abstract Number: 1728

Takayasu's Arteritis and Pregnancy: A Meta-analysis

Aine Gorman[1], Leah Rooney[2], Matthew Turk[1], Louise Moore[3], Jared Bierbrier[4], Celine O'Brien[5], Anne Clohessy[6], Eamonn Molloy[7], Lorraine O Neill[8], Fionnuala McAuliffe[9] and Douglas Veale[10], [1]St Vincents Hospital, Dublin, Ireland, [2]St Vincent's University Hospital, Dublin, Ireland, [3]Our Lady's Hospice and Care Services, Harold's Cross, Dublin 6W, Kinnegad, Ireland, [4]McMaster University, Hamilton, ON, Canada, [5]Perinatal Research Centre, Obstetrics and Gynaecology, School of Medicine, University College Dublin and National Maternity Hospital, Dublin, Dublin, Ireland, [6]National Maternity Hopistal, Dublin, Ireland, [7]St Vincent's Healthcare Group, Dublin, Ireland, [8]St. Vincent's Hospital, Dublin, Ireland, [9]National Maternity Hopsital Dublin, Dublin, Ireland, [10]University College Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Takayasu's arteritis is a systemic autoimmune disease characterised by large vessel vasculitis. It usually affects women of childbearing age, with 90% of patients diagnosed < 30 years of age, and previous

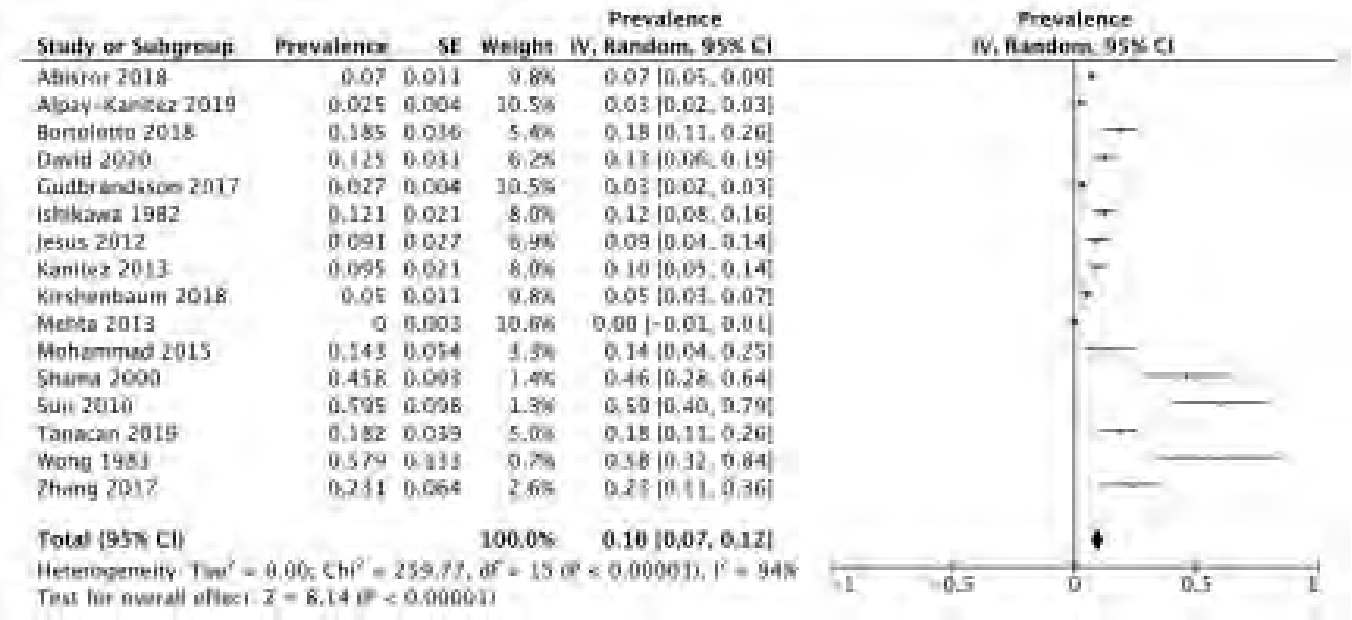

Figure 1. Prevalence of preeclampsia in Takayasu's arteritis patients.

studies suggest it is associated with adverse pregnancy outcomes. There is a vast discrepancy within the literature; some studies suggest preeclampsia occurring in 4.5% of patients, while others suggest a rate of 61%. The purpose of our work was to determine the prevalence of both maternal and fetal outcomes in patients with Takayasu's arteritis through a systematic review and meta-analysis.

Methods: We performed a systematic review of the literature using Medline, Web of Science, and the Cochrane library from their inceptions until March 26, 2021, to identify studies that reported pregnancy outcomes in patients with Takayasu's arteritis. Demographic information, maternal outcomes, foetal outcomes, prednisolone use, and information on disease activity were extracted from studies. Two authors independently selected the studies, extracted the data and assessed for risk of bias.

Results: Our systematic review identified 6638 abstracts, of which 23 articles were included. The miscarriage rate was 11 [7-16] % and an intrauterine death rate of 1[0-3] %. Preeclampsia was reported in 10[7-12] % of patients (Figure 1). Preterm delivery occurred in 15[12-19] %. New hypertension in pregnancy was reported in 12[8-16] %.

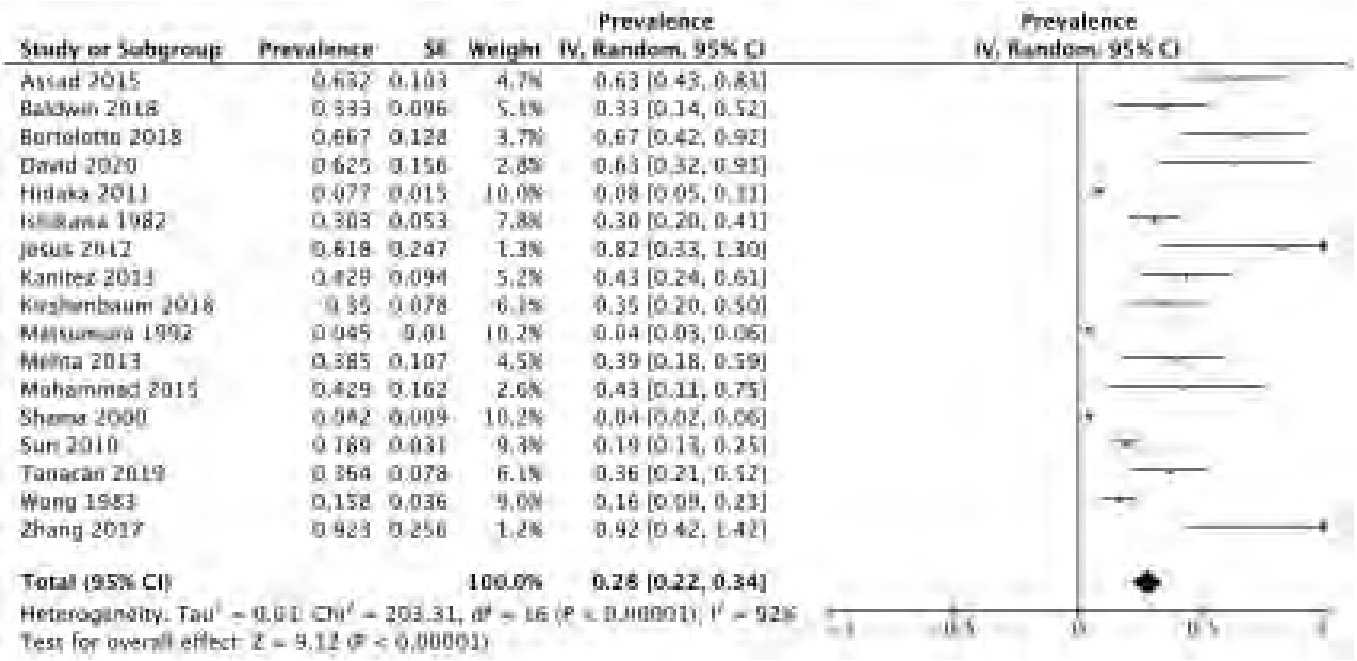

Figure 2. Prevalence of caesarean section in Takayasu patients.

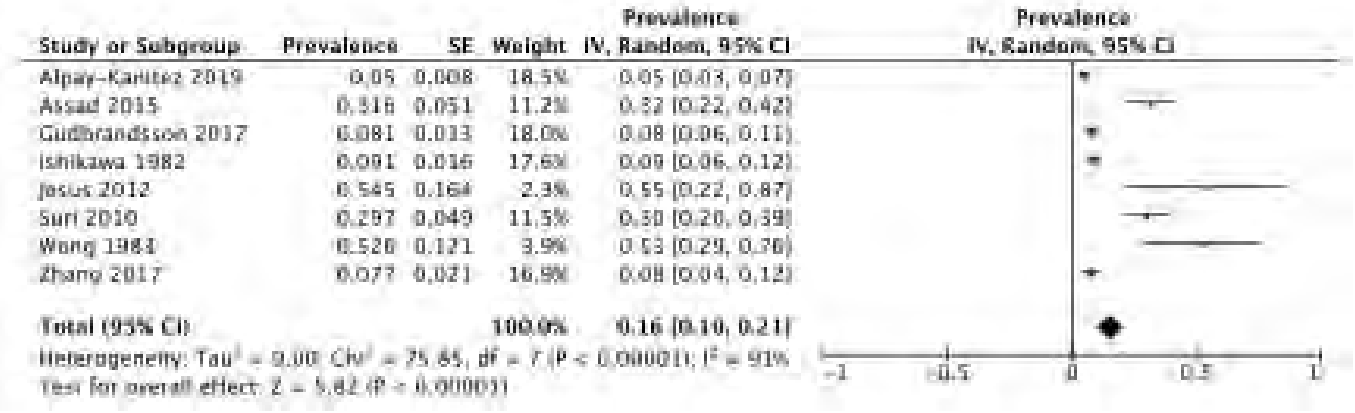

Figure 3. Prevalence of low birth weight among Takayasu patients.

Intrauterine growth restriction occurred in 16[10-21] % of pregnancies. The prevalence of caesarean sections among Takayasu patients was 28 [22-28] % (Figure 2). In terms of fetal outcomes, low birth weight was associated with 16[10-21] % of live births (Figure 3). Flares of vasculitis occurred in 11[8-15] % of patients.

Conclusion: There is a high prevalence of both maternal and fetal adverse outcomes in pregnant patients with Takayasu's arteritis, who require careful management by a multidisciplinary team during pregnancy.

Disclosure: A. Gorman, None; **L. Rooney**, None; **M. Turk**, None; **L. Moore**, None; **J. Bierbrier**, None; **C. O'Brien**, None; **A. Clohessy**, None; **E. Molloy**, None; **L. O Neill**, None; **F. McAuliffe**, None; **D. Veale**, Abbvie, 1, 5, 6, BMS, 1, 5, Pfizer, 1, 5, 6, Janssen, 1, 5, 6, Eli Lilly, 1, 5, 6, UCB, 1, 5, 6, Novartis, 1, 5, 6, Galapagos/Gilead, 1, 6.

Abstract Number: 1729

Predicting Adverse Pregnancy Outcomes in Women with Systemic Lupus Erythematosus (SLE) Using 2nd Trimester Estimated Glomerular Filtration Rate (eGFR)

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Women with SLE are at increased risk for adverse maternal and fetal outcomes with increased odds of preeclampsia, hypertension, Cesarean and preterm deliveries, low birth weight, and congenital defects. Many markers of SLE disease activity fail to identify all women at risk for adverse pregnancy outcomes. Previous studies found a U-shaped relationship between 2nd trimester eGFR and adverse pregnancy outcomes. Both very low and high eGFR had a high risk for adverse pregnancy outcomes. The purpose of this study was to determine the relationship of 2nd trimester eGFR and adverse pregnancy outcomes in women with SLE.

Methods: This was an individual patient-level meta-analysis including 684 pregnant women with SLE who received rheumatology care at academic centers in North America and Europe from 1995 to 2017. Preeclampsia, preterm birth, fetal loss, and poor pregnancy outcome (composite outcome) were outcomes of interest. Polynomial and logistic regression models were used to evaluate the relationship between eGFR and adverse outcomes. Women with an eGFR 120-135 ml/min/1.73m^2 were in the reference group, based on previous studies demonstrating low adverse pregnancy outcome in this range. eGFR was stratified into groups based on established cut-offs from previous studies. Multivariable regression models adjusted for race, age, and SLE disease activity.

Results: Among 684 women, 52 women had very low eGFR (< 90ml/min/1.73m^2), 232 had low eGFR (90-120ml/min/1.73m^2), 336 had normal eGFR (121-135ml/1.73m^2), and 64 women had very high eGFR (>135ml/min/1.73m^2). Greater than a third of women had lupus nephritis and 22% of women were of Black race. A U-shaped relationship between 2nd trimester eGFR and adverse outcomes was observed. Women with very low eGFR had higher odds

of fetal loss, preterm birth, preeclampsia, and poor pregnancy outcome. Very high eGFR was associated with poor pregnancy outcome and preterm birth.

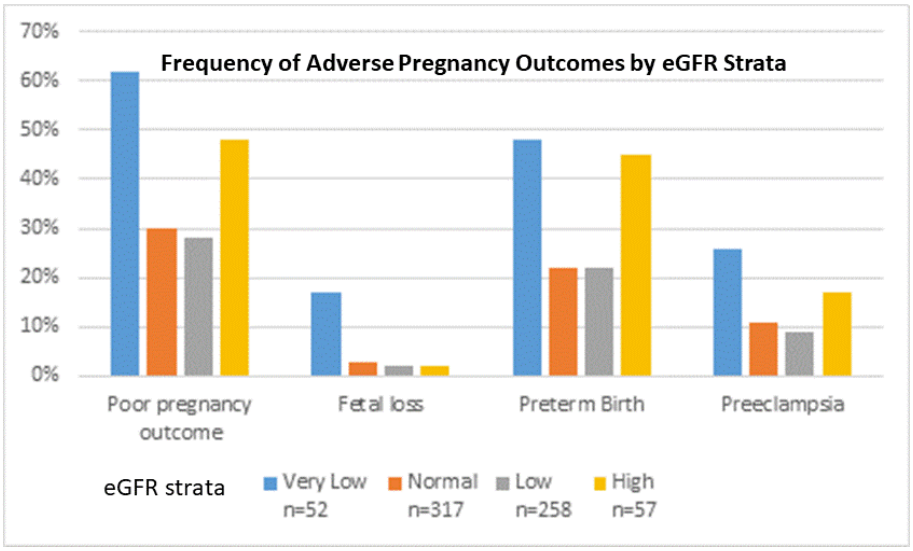
Conclusion: We demonstrate a U-shaped relationship between 2nd trimester eGFR and adverse pregnancy outcomes in women with SLE. Both women with very low eGFR defined as < 90ml/min/1.73m^2 and high eGFR, defined as >135ml/min/1.73m^2 had higher odds of adverse pregnancy outcomes. Measurement of kidney function with 2nd trimester GFR estimates may be an additional tool that can be utilized to predict adverse outcomes in pregnant women with SLE.

Table 1. Association of 2nd Trimester eGFR and Adverse Pregnancy Outcome

eGFR strata	Preterm Birth Unadjusted OR (95%CI)	Preeclampsia Unadjusted OR (95%CI)	Fetal Loss Unadjusted OR (95%CI)	Poor Pregnancy Outcome Unadjusted OR (95%CI)
Very Low eGFR<90	3.16 (1.63, 6.12)	2.91 (1.32, 6.37)	5.82 (2.28, 14.86)	3.79 (2.00, 7.19)
Low eGFR90-120	1.01 (0.67, 1.51)	0.83 (0.46, 1.52)	0.55 (0.19, 1.60)	0.92 (0.62, 1.35)
Normal eGFR 121-135	1.0	1.0	1.0	1.0
Very High eGFR>135	2.80 (1.55, 5.06)	1.69 (0.75, 3.81)	0.50 (0.06, 3.92)	2.19 (1.22, 3.92)

Table 2. Association of 2nd Trimester eGFR strata and Adverse Pregnancy Outcomes. Adjusted for race, SLEDAI score, and age

eGFR strata	Preterm Birth Adjusted OR (95%CI)	Preeclampsia Adjusted OR (95%CI)	Fetal Loss Adjusted OR (95%CI)	Poor Pregnancy Outcome Adjusted OR (95%CI)
Very Low eGFR<90	3.10 (1.55, 6.21)	2.53 (1.12, 5.72)	3.68 (1.13,12.01)	3.43 (1.76, 6.68)
Low eGFR90-120	1.28 (0.82, 1.98)	0.92 (0.49, 1.74)	0.82 (0.28,2.43)	1.07 (0.70, 1.63)
Normal eGFR 121-135	1.0	1.0	1.0	1.0
Very High eGFR>135	2.42 (1.30, 4.47)	1.12 (0.48, 2.63)	0.21(0.04,1.02)	1.94 (1.05, 3.57)



Frequency of Adverse Pregnancy Outcomes by eGFR Strata Depicting U-shaped relationship

Disclosure: A. Lucas, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 5, Pfizer, 5, Exagen, 5; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **R. Fischer-Betz**, UCB Pharma, 2, Janssen, 2, Pfizer, 2, AbbVie, 2, BMS, 2, Celgene, 2, Chugai, 2, Eli Lilly, 2, Novartis, 2, Sanofi, 2; **A. Nabil**, None; **C. Nalli**, None; **L. Andreoli**, None; **A. Tincani**, Novartis, 2, UCB, 2, Janssen, 2, Gsk, 6; **Y. Molad**, None; **S. Balevic**, None; **M. Clowse**, UCB Pharma, 2, Pfizer, 5, GSK, 2, 5.

Abstract Number: 1730

Disease Activity and Outcome in Pregnancies of Patients with SpA - Data from the German Pregnancy Register RHEKISS

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: SpA is a severe chronic inflammatory disease, which affects quality of life and functional status. It frequently occurs in women of childbearing age. Active disease and TNFi discontinuation at early pregnancy were found to be risk factors for flares during pregnancy (1). The aim of this study was to compare disease activity during pregnancy in patients with or without biological DMARD (bDMARD) exposure at conception and during pregnancy and to assess pregnancy outcomes.

Methods: RHEKISS is a prospective longitudinal cohort study including patients with confirmed diagnose of inflammatory rheumatic disease. Pregnant patients are eligible to be enrolled until the 20th week of gestation regardless of drug treatment. During observation, information on treatment, disease and pregnancy course, and outcome are collected from rheumatologists and patients. For this analysis, pregnancies of patients with SpA and a reported outcome since the beginning of the registry until June 8th 2020 were selected and stratified into three groups according to their exposure to bDMARDs.

Results: Of 140 SpA pregnancies included, 74 (53%) were not exposed to bDMARDs at conception (group 1), 38 (27%) were exposed to bDMARDs at conception, but not during pregnancy (group 2) and 28 (20%) were continuously exposed to bDMARDs at conception and during pregnancy (group 3). The bDMARDs prescribed were Certolizumab in 50%, Adalimumab in 21%, Etanercept in 12%, Infliximab in 9%, Golimumab in 2 patients, Sekukinumab and Ustekinumab in one patient each. Baseline characteristics according to treatment exposure are shown in table 1. Frequency of flares was highest in group 2: 21%, 38%, and 39% of patients flared during the 1st, 2nd, and 3rd trimester. These rates were 20%, 25%, and 21% in group 1 and 8%, 20%, and zero in group 3. The difference in flare rates was also mirrored in the course of mean physicians' assessed global disease activity (fig. 1). Whereas patients in group 1 seemed to have a quite stable disease activity during pregnancy, those who were in group 2 had an increasing activity

Table 1. Baseline characteristics; numbers are n (%) if not otherwise specified; * value at beginning of pregnancy: first 22 weeks after conception

Parameter	no bDMARD at conception (group 1) n=74	bDMARD at conception and discontinued during pregnancy (group 2) n=38	bDMARD at conception and continued during pregnancy (group 3) n=28	Total n=140
Singleton	72 (97)	37 (97.4)	28 (100)	137 (97.9)
Twin	1 (1.4)	1 (2.6)	0	2 (1.4)
Triple	1 (1.4)	0	0	1 (0.7)
New-York criteria fulfilled	21 (33)	17 (49)	10 (48)	48 (40)
disease duration in years, mean (SD)	6.4 (5.9)	7 (4.1)	5.8 (4)	6.4 (5.1)
age*, mean (SD)	33.4 (4.9)	32.3 (4)	31.6 (3.4)	32.7 (4.4)
severity of illness*: asymptomatic	4 (6)	0 (0)	3 (14)	7 (6)
mild	31 (48)	6 (17)	4 (19)	41 (34)
moderate	24 (38)	21 (60)	14 (67)	59 (49)
severe	5 (8)	8 (23)	0	13 (11)
HLA-B27 positive	41 (62)	24 (80)	15 (75)	80 (69)
CRP in mg/l *, mean (SD)	6.6 (8.2)	5.4 (8.2)	5.2 (4.9)	6 (7.6)
CRP >5mg/l *	25 (41)	9 (30)	8 (35)	42 (37)
physician global* (NRS 0-10), mean (SD)	2.6 (2)	2.3 (2.5)	1.7 (1.4)	2.4 (2.1)
BASDAI* (0-10), mean (SD)	3.2 (2)	2.9 (2.3)	2.8 (1.5)	3.1 (2)
patient global* (NRS 0-10), mean (SD)	3.3 (2.7)	3 (2.8)	3 (2.3)	3.1 (2.6)

of disease during pregnancy with an even higher increase of disease activity after giving birth. Patients in group 3 had the lowest disease activity during the total observation period.

Of 137 singleton pregnancies, 130 (95%) ended in live birth. Two spontaneous abortions in group 1 occurred in the same patient in gestational week 10 and 7. The spontaneous abortions in group 2 and 3 occurred in different patients in gestational week 10 and 16 (group 2) and in week 9 and 11 (group 3). One pregnancy in group 1 was terminated in gestational week 22 due to suspected malformation. In one triple pregnancy, one baby was born alive and two aborted in week 13. All babies of the two twin pregnancies were born healthy.

Conclusion: SpA patients treated with bDMARDs at conception are not at higher risk for adverse pregnancy outcomes compared to those without bDMARD exposure. Furthermore, our results confirmed the findings of smaller studies that discontinuation of bDMARDs after conception is associated with increased disease activity during pregnancy and after birth and a higher risk of flares.

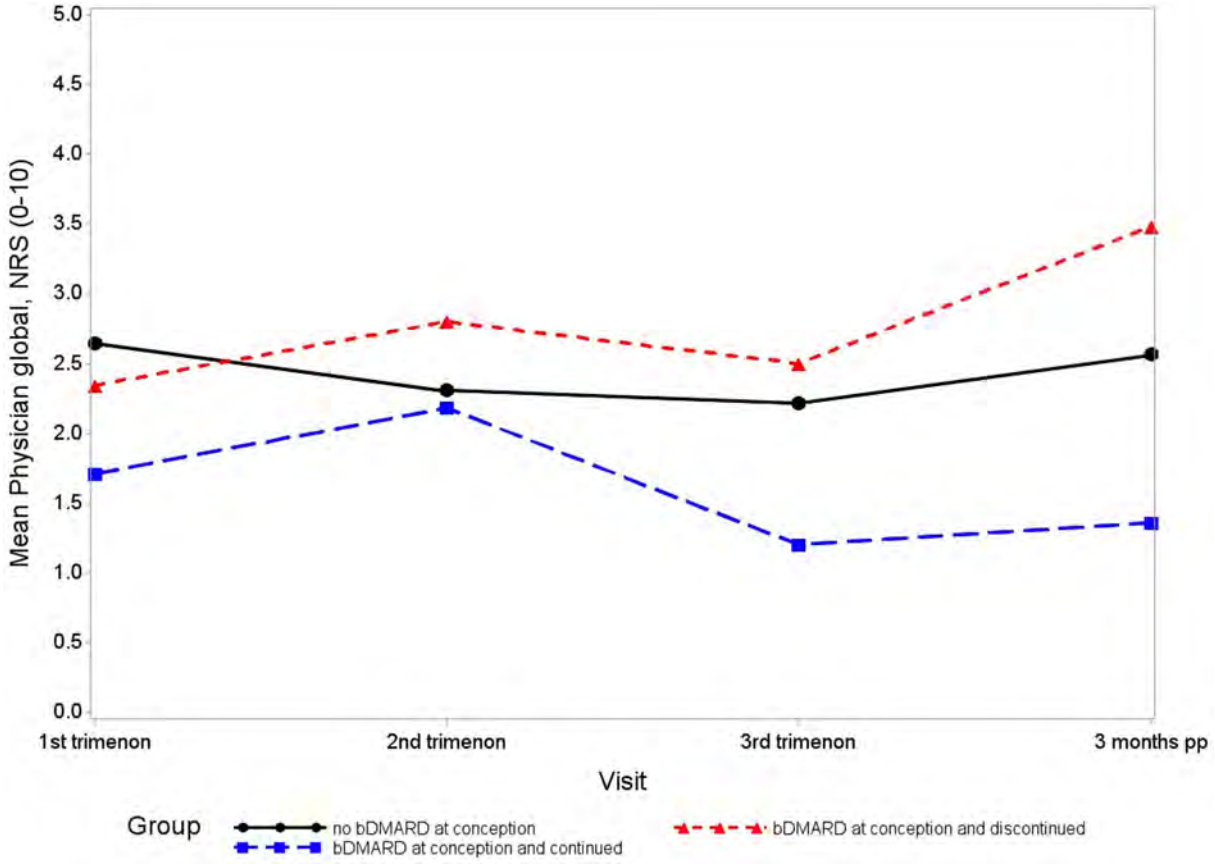

Figure 1. Mean course of physicians' assessed global disease activity.

Disclosure: A. Weiß, None; **C. Bungartz**, None; **J. Richter**, Abbvie, 2, Lilly, 2, 6, Pfizer, 6, Sanofi, 2, 6; **S. Späthling-Mestekemper**, None; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **P. Aries**, None; **R. Fischer-Betz**, UCB Pharma, 2, Janssen, 2, Pfizer, 2, AbbVie, 2, BMS, 2, Celgene, 2, Chugai, 2, Eli Lilly, 2, Novartis, 2, Sanofi, 2; **A. Strangfeld**, Pfizer, 6, Roche, 6, MSD, 6, BMS, 6, Abbvie, 6, Celltrion, 6.

Abstract Number: 1731

Construction and Validation of a Reproductive Health Questionnaire for Women with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Reproductive Issues in Rheumatic Disorders Poster (1711–1731)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Autoimmune rheumatic diseases (ARDs) commonly affect women of childbearing age. Active maternal disease in the months prior to conception increases the risk of flares during pregnancy and adverse pregnancy outcomes. Therefore, maternal and fetal health can be optimized by planning conception when the disease is controlled so that a treatment regimen can be kept throughout the pregnancy.

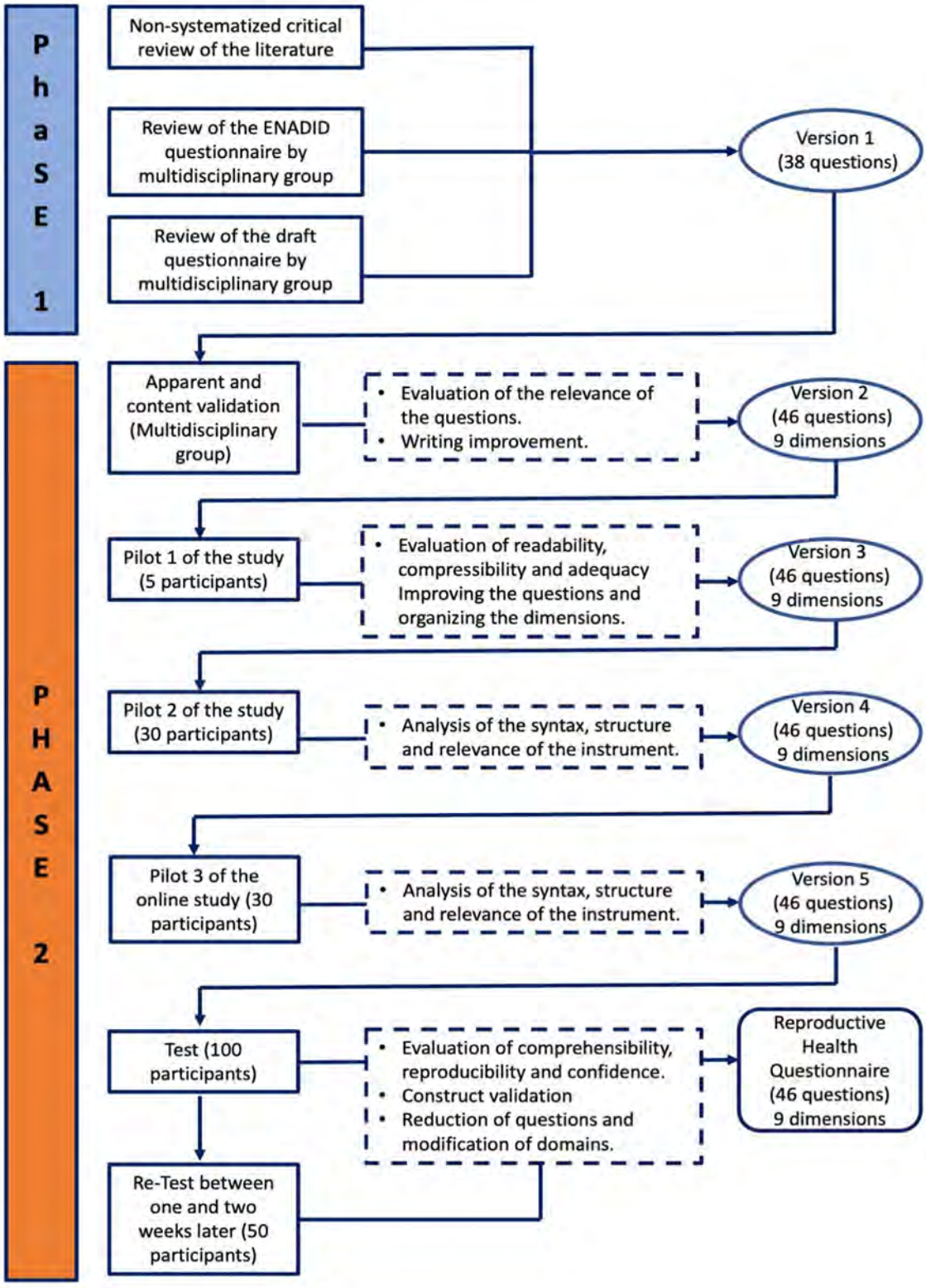

Figure 1. Phases.

This study aims to carry out the construction and validation of a Reproductive Health Questionnaire (RHQ) for patients with ARDs.

Methods: A validation and construction of a RHQ was carried out in women of reproductive age (18 to 50 years) with ARDs. The validation was realized in two phases. First phase: The National Demographic Dynamics Survey (2018) was used as the basis for obtaining the questions to form the draft questionnaire, as well as a previous non-validated questionnaire then a review of the literature and construction of the questionnaire was performed by a multidisciplinary team of experts, then the first version of the questionnaire was made. Second phase: During face and content validity, the multidisciplinary group met to assess the relevance of the written questions to create the second version of the questionnaire, following we carried out pilot tests to create versions 3, 4, and 5. Figure 1. A Cross-sectional study was conducted to complete the validation and estimate Cronbach's alpha based on tetrachoric correlation coefficients, correlation matrix, and Cohen's kappa coefficient test. The stability of the instrument was measured by comparing two measurements on the same study subject (re-test) with a time-lapse between them.

Results: A convenience sampling was carried out with a sample of 165 women, 65 women participated in the cross-cultural adaptation phase and 100 in the validation phase.

First phase: we developed an instrument of 38 questions; some drafting questions were modified because of the confusion or disconcerting they caused to some patients, furthermore more response options were added (Figure 1). In the second phase, version 5 of the RHQ was applied to 100 women with ARDs, the average age of the patients was 35 years. The most frequent disease was rheumatoid arthritis (54%). We founded a difference of 6 months between the onset of the symptoms of the disease and the diagnosis. The correlation matrices showed good to moderate correlations in dimensions 3, 5, 6, 7, 8, and 10 (0.53, 0.82, 0.84, 0.54, 0.35, and 0.45 respectively), we founded difficulties in two dimensions, therefore they were restructured. The test-retest analysis showed perfect correlations in 34 of the 41 items, moderate correlations in 6 items, and a negative correlation on one of the items due to a change in the reproductive status of one patient.

Conclusion: The RHQ is a useful and practice tool to assess reproductive health (fertility, reproductive preferences, contraception, preconception counseling, sexuality, and breastfeeding) in women with ARD, and could help with timely intervention on reproductive health issues, decreasing both fetal and maternal adverse outcomes.

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Abstract Number: 1732

Effects of B Cell Activating Factors/B Lymphocyte Stimulator Inhibitors Added to Standard of Care on Infection in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-Analysis of Randomized Controlled Trials

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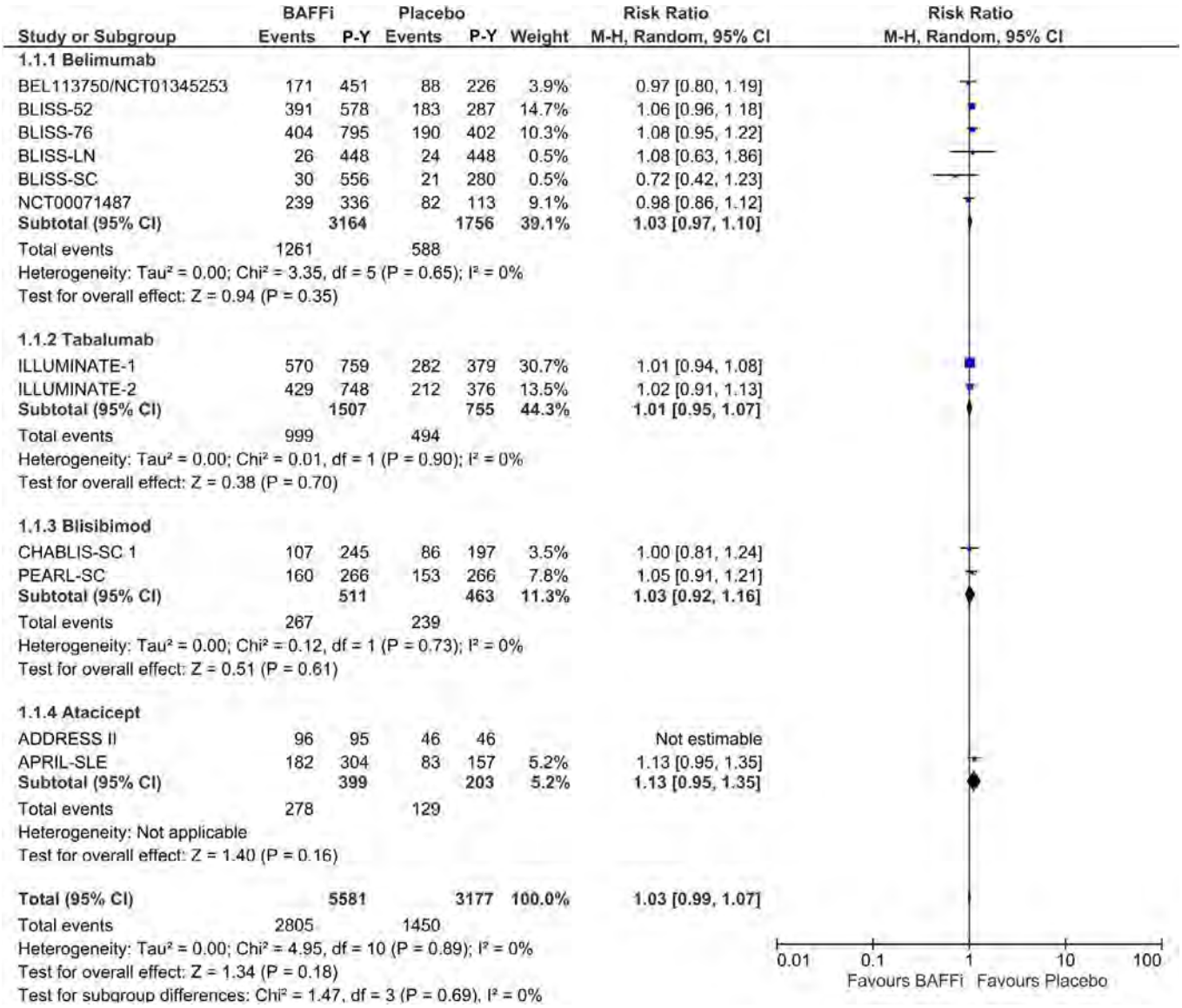
SESSION INFORMATION

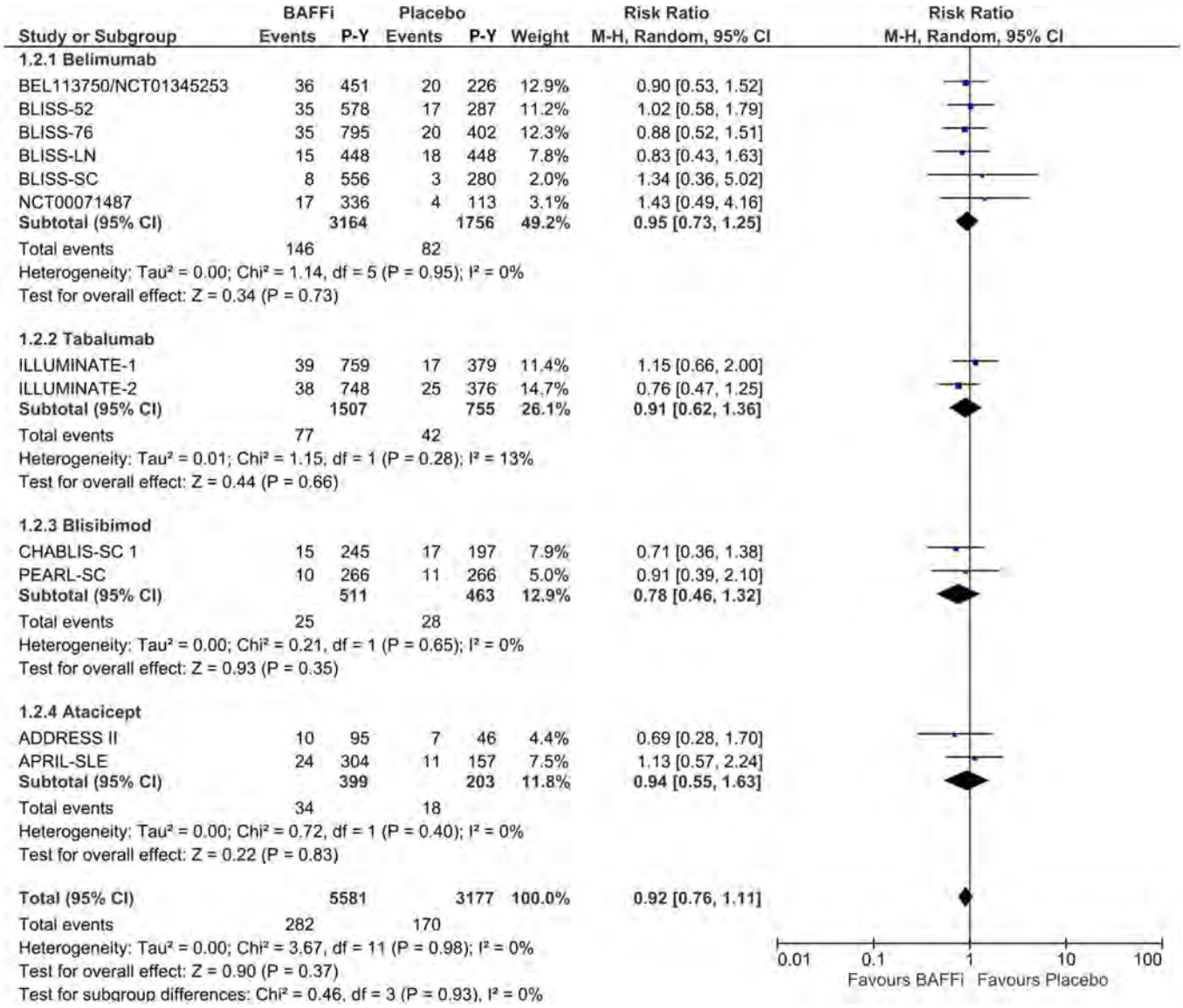
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The efficacy of B cell activator factor/B lymphocyte stimulator inhibitors (BAFFi/BLySi) for systemic lupus erythematosus (SLE) has been proven in clinical trials. However, it remains unclear whether the addition of BAFFi/BLySi to the Standard of Care (SoC) impacts infection risk in SLE. Therefore, the objective of this study was to determine the effects of BAFFi/BLySi on infection in patients with SLE via meta-analysis.

Methods: A systematic literature review was performed in PubMed, Embase, Cochrane Library databases from inception to Feb 2021 to identify randomized controlled trials (RCTs) of BAFFi/BLySi, including belimumab, tabalumab, blisibimod and atacicept. Relative risks (RR) and 95% confidence intervals (CIs) were calculated to compare infection



Relative Risks (RRs) of all infections in patients with systemic lupus erythematosus (SLE) treated with B cell activator factor/B lymphocyte stimulator inhibitors (BAFFi/BLySi) compared with placebo in addition to standard of care. P-Y, patient-year

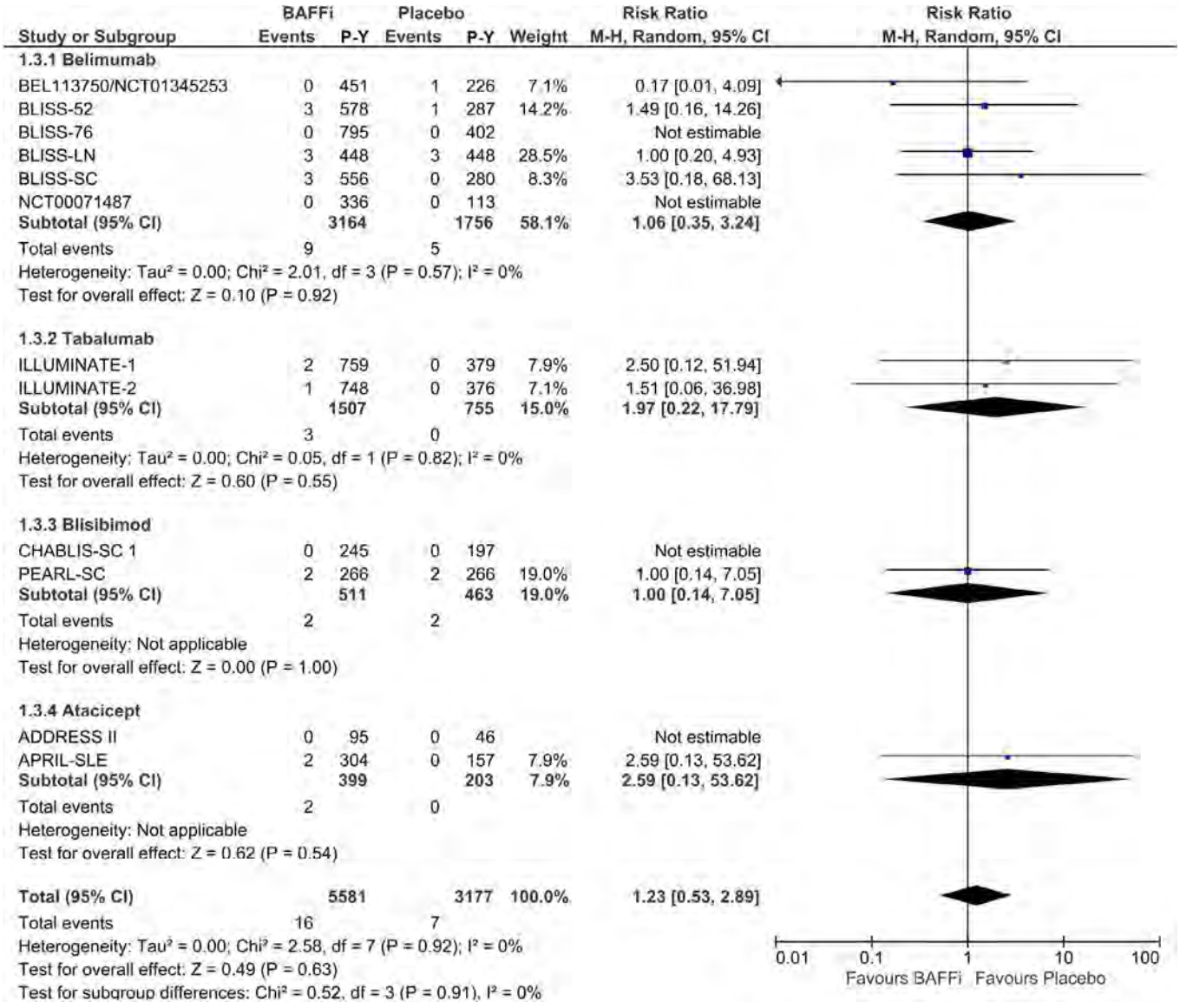


RRs of serious infections in patients with SLE treated with BAFFi/BLySi compared with placebo in addition to standard of care. P-Y, patient-year

events, serious infection events and mortality secondary to infection between BAFFi/BLySi and placebo in addition to SoC by using the Mantel-Haenszel random-effect method.

Results: A total of 443 articles were identified and 12 RCTs were included in the final analysis that comprised 8104 patients and 8387 patient-years. Forest plots of RR between BAFFi/BLySi and placebo for infections, serious infections and fatal infections are presented in *Figure 1.* *Figure 2* and *Figure 3.* respectively. There was no statistically significant difference between belimumab, tabalumab, blisibimod or atacicept and placebo in infection (RR=1.03; 95% CI (0.99,1.07)), neither serious infections (RR=0.92; 95% CI (0.76,1.11)) nor fatal infections (RR=1.23; 95% CI (0.53,2.89)). Dose-dependent effect of BAFFi/BLySi on the risk of infections was undetectable (RR=1.03; 95% CI (0.97,1.10)).

Conclusion: Adding BAFFi/BLySi to SoC in patients with SLE was not associated with increased risk of infection, serious infection, nor fatal infection.



RRs of fatal infections in patients with SLE treated with BAFFi/BLySi compared with placebo in addition to standard of care. P-Y, patient-year

Disclosure: R. Ni, None; **J. Zheng**, None; **R. Guo**, None.

Abstract Number: 1733

Classification of Patients with Systemic Lupus Erythematosus Enrolled in 2 Phase 3 Trials by EULAR/ACR 2019 Criteria

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The TULIP-1 and TULIP-2 trials of anifrolumab, an anti–type I IFN receptor mAb, enrolled autoantibody-positive (ANA, anti-dsDNA, and/or anti-Smith [anti-Sm]) patients, who fulfilled the ACR 1997 classification criteria for SLE.[1–3] The aim of this analysis was to assess how many patients who participated in the TULIP trials also met the updated EULAR/ACR 2019 criteria.[4]

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenously administered anifrolumab in patients with moderate to severe SLE despite standard therapy. Inclusion criteria included fulfilling at least 4 of the ACR 1997 criteria for SLE, positivity for ANA, anti-dsDNA, and/or anti-Sm antibodies, and moderate to severe SLE. Data for investigating classification using EULAR/ACR 2019 criteria were combined from the ACR criteria, BILAG-specific SLE history, and documented medical history.

Results: The TULIP-1 and TULIP-2 data pool included 726 patients with SLE. Of these, all but 2 (99.7%) met the ACR 1997 SLE criteria (**Table**). The EULAR/ACR 2019 classification criteria for SLE were met by 712/726 patients (98.1%). Thus, most patients (97.9% [711/726]) were concordant in meeting both the ACR 1997 and EULAR/ACR 2019 SLE classification criteria. Of the patients classified as having SLE using ACR 1997 criteria, 1.8% (13/726) did not meet the EULAR/ACR 2019 criteria. Of these 13 discordant patients, 8 were ANA negative but either anti-dsDNA or anti-Sm antibody positive, 5 were ANA positive and were discordant mainly due to photosensitivity not being included in the EULAR/ACR 2019 criteria. Two patients did not meet ACR 1997 criteria at baseline; one patient was not classified as having SLE using either ACR 1997 or EULAR/ACR 2019 criteria, and the other patient was classified as having SLE using EULAR/ACR 2019 criteria. This latter discordant patient did not meet ACR 1997 criteria, having just nonerosive arthritis and positive ANA, but met EULAR/ACR 2019 criteria with positive ANA, fever, nonscarring alopecia, and joint

Table. Classification According to ACR 1997 or EULAR/ACR 2019 in Patients Enrolled in the TULIP-1 and TULIP-2 Trials (Pooled Data)

Patients, n (%)	Placebo (n=366)	Anifrolumab 300 mg (n=360)	Total (n=726)
ACR 1997 classification			
Patients classified SLE	364 (99.5)	360 (100)	724 (99.7)
Patients not classified SLE	2 (0.5)	0	2 (0.3)
EULAR/ACR 2019 classification			
Patients classified SLE	361 (98.6)	351 (97.5)	712 (98.1)
Patients not classified SLE	5 (1.4)	9 (2.5)	14 (1.9)
Concordance	361 (98.6)	351 (97.5)	712 (98.1)
Patients classified SLE according to both classifications	360 (98.4)	351 (97.5)	711 (97.9)
Patients not classified SLE according to both classifications	1 (0.3)	0	1 (0.1)
Discordance	5 (1.4)	9 (2.5)	14 (1.9)
Not SLE using ACR 1997 but SLE using EULAR/ACR 2019	1 (0.3)	0	1 (0.1)
SLE using ACR 1997 but not SLE using EULAR/ACR 2019	4 (1.1)	9 (2.5)	13 (1.8)

involvement. At study baseline, positive ANA (97.2%) and nonerosive arthritis (97.5%) were the 2 most frequent ACR 1997 criteria among all patients.

Conclusion: Nearly all patients enrolled in the TULIP-1 and TULIP-2 trials were classifiable as having SLE using both the ACR 1997 criteria and the EULAR/ACR 2019 criteria. Of the patients not meeting the new criteria, most were ANA negative but had detectable autoantibodies against dsDNA and/or Sm.

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Disclosure: M. Aringer, AstraZeneca, 1, 6; **I. Bruce**, AstraZeneca, 2, 6, GlaxoSmithKline, 2, 5, 6, UCB, 2, 6, Eli Lilly, 2, Aurinia, 2; **R. Furie**, AstraZeneca, 2; **E. Morand**, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, GlaxoSmithKline, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **E. Maho**, Idorsia Pharmaceuticals Ltd, 3, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1734

Efavaleukin Alfa, a Novel IL-2 Mutein, Selectively Expands Regulatory T Cells in Patients with SLE: Interim Results of a Phase 1b Multiple Ascending Dose Study

Nadia Tchao[1], Hamid Amouzadeh[2], Nandita Sarkar[1], Vincent Chow[2], Xuguang Hu[1], Mark Kroenke[2], Hui Wang[2], Rong Zhang[2], Kevin Gorski[1], Richard Furie[3], Alan Kivitz[4] and Stanley Cohen[5], [1]Amgen Inc., South San Francisco, CA, [2]Amgen Inc., Thousand Oaks, CA, [3]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [4]Altoona Center for Clinical Research, Duncansville, PA, [5]Metroplex Clinical Research Center, Dallas, TX

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Diminished IL-2 as well as both quantitative and qualitative abnormalities in regulatory T cells (Treg) are associated with autoimmune diseases including SLE. Efavaleukin alfa is a novel IL-2 mutein Fc fusion protein designed to selectively expand Treg. In healthy subjects, a single dose of efavaleukin alfa was well tolerated and demonstrated Treg selectivity with minimal changes in CD4+ conventional T cells (Tcon), CD8+ T cells, or NK cells (Tchao N *Blood* 2017). This interim analysis of an ongoing phase 1b study (NCT03451422) reports the safety, tolerability, pharmacokinetics (PK), and pharmacodynamic effects of multiple doses of efavaleukin alfa in patients with SLE.

Methods: Four of five ascending dosing cohorts are reported in this analysis. A total of 29 patients with SLE (age 18-70 years; 82.8% female; SLE diagnosed using SLICC or ACR criteria with ANA ≥1:80 and/or elevated anti-dsDNA antibodies) were randomized to receive efavaleukin alfa or placebo (5:2 ratio for cohorts 1–3; 3:1 ratio for cohort 4) subcutaneously every 2 weeks (Q2W; cohorts 1, 2, and 4) or every week (QW; cohort 3) in addition to standard of care

therapy for a total of 12 weeks, with 6 weeks of follow-up. Endpoints assessed in this analysis included treatment-emergent adverse events (TEAEs), serum PK profiles of efavaleukin alfa, changes in numbers of Treg, CD4+ Tcon, CD8+ T cells, and NK cells, and levels of cytokines in peripheral blood.

Figure 1: Fold change from baseline in number of Foxp3+ regulatory T cells following biweekly administration of efavaleukin alfa.

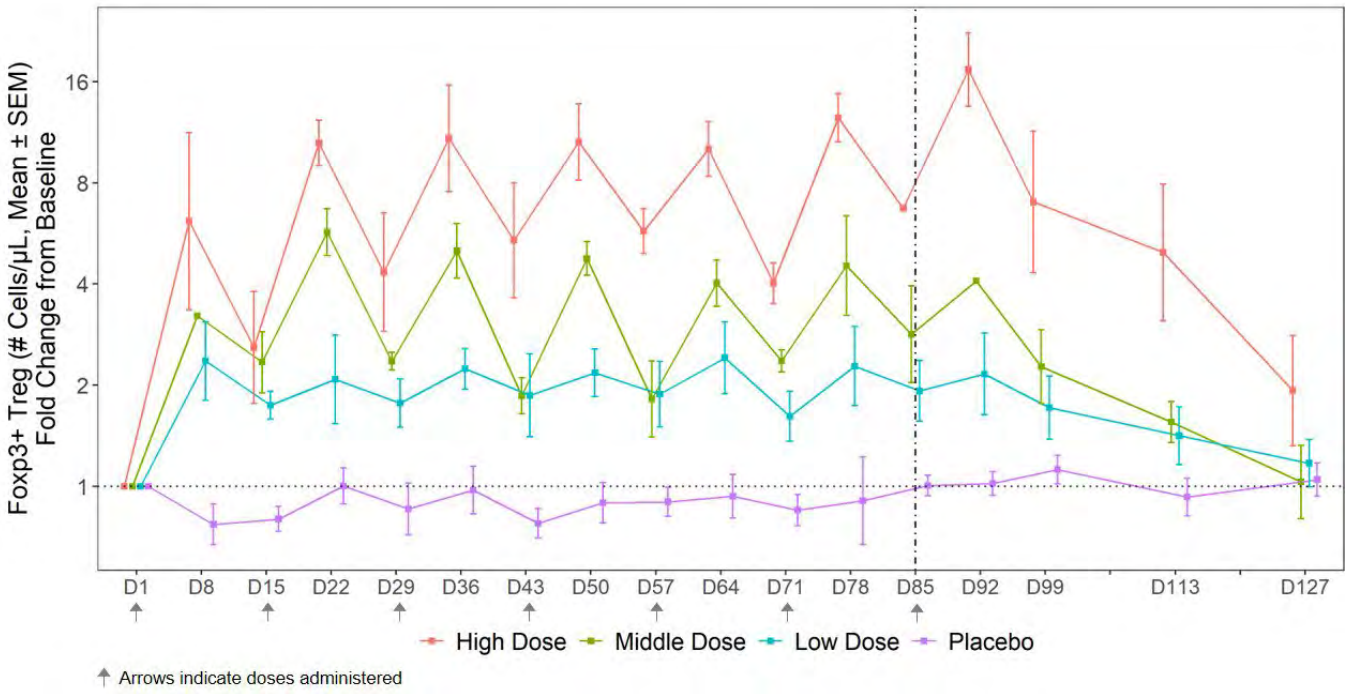
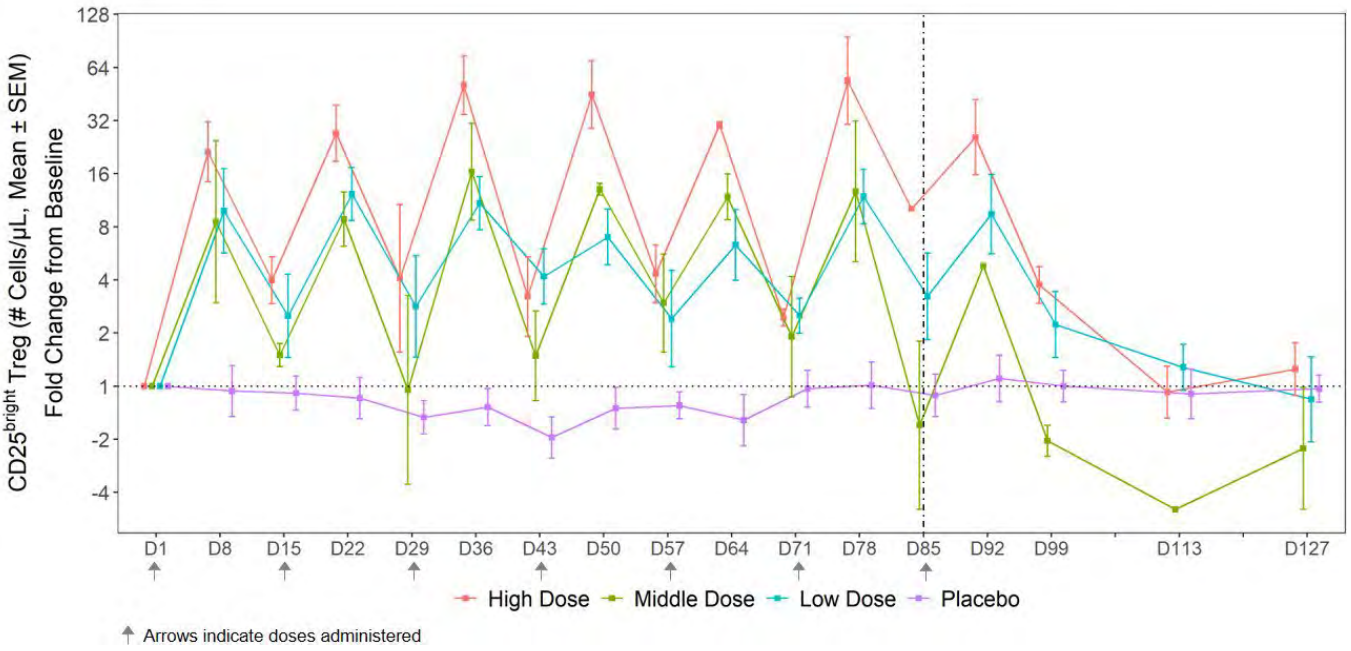


Figure 2: Fold change from baseline in number of $CD25^{bright}$ regulatory T cells following biweekly administration of efavaleukin alfa.



Results: The most commonly reported TEAEs (≥25% of all subjects) included non-serious, mild or moderate (grade 1–2) injection site reactions. No dose-limiting toxicities, treatment-related serious AEs, or deaths were reported. Efavaleukin alfa PK was generally linear and dose-proportional, with a terminal half-life ranging from 18 to 30 hours. Peak Foxp3+ Treg expansion was observed at 8 days post-dose, and the magnitude of the peaks was generally sustained after multiple QW or Q2W doses. Treg numbers remained above baseline for an average of 42 days after the last dose (**Figure 1**). The mean peak increases in Foxp3+ Treg were 17.4-, 5.7-, 2.4-, and 1.1-fold above baseline for the high, middle, and low Q2W efavaleukin alfa and placebo cohorts, respectively. At the highest dose, the mean peak increase in $CD25^{bright}$ Treg was 53.8-fold above baseline (**Figure 2**). Treatment with efavaleukin alfa expanded CD31+ recent thymic emigrant and naïve Treg populations; increases in these Treg subsets persisted longer than increases in memory Treg subsets. The majority of expanded Treg expressed markers associated with suppressive activity, including Helios, PD-1, ICOS, CD39, and GITR. There were no meaningful changes in numbers of CD4+ Tcon, CD8+ T cells, or NK cells or serum levels of pro-inflammatory cytokines with treatment.

Conclusion: Multiple doses of efavaleukin alfa were well tolerated in SLE patients. Treatment with efavaleukin alfa resulted in robust and prolonged dose-dependent Treg expansion, with minimal changes in other IL-2-responsive cells highlighting pharmacodynamic selectivity. These findings confirm and extend previous results in healthy subjects and support the ongoing phase 2b adaptive randomized controlled trial in patients with SLE.

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Abstract Number: 1735

Glucocorticoid Discontinuation in Patients with Systemic Lupus Erythematosus with Prior Severe Organ Manifestation

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SESSION INFORMATION
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Session Type: Poster Session D
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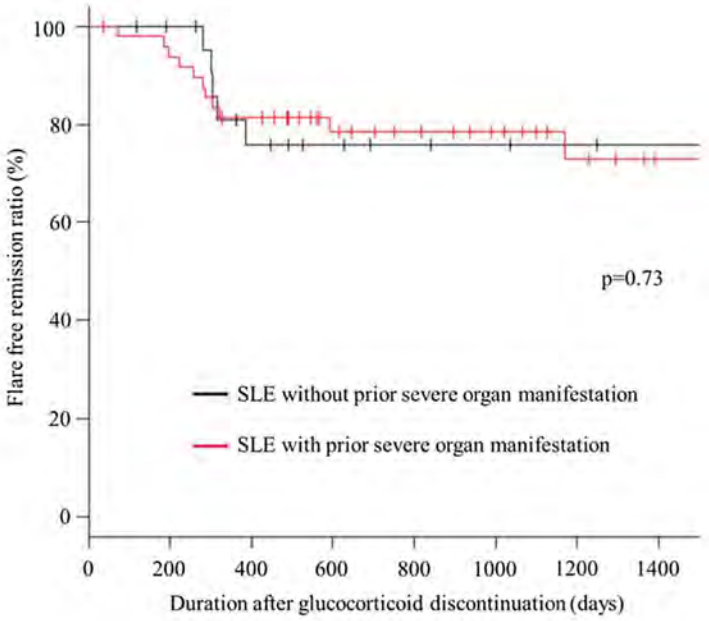
Background/Purpose: Most long-term damage in systemic lupus erythematosus (SLE) has been attributed to continuous glucocorticoid use; however, glucocorticoid discontinuation is occasionally associated with disease flare-ups. Therefore, we evaluated the risk factors for disease flares and flare rates with gradual glucocorticoid tapering, especially in patients with prior severe organ manifestation.

Methods: Patients with SLE who had their glucocorticoid doses tapered off at our institute were retrospectively analyzed. We divided the patients according to the presence of prior severe organ manifestations and compared the 52-week flare rates after glucocorticoid discontinuation. Furthermore, risks/protective factors against flares after glucocorticoid cessation were investigated.



Number at risk								
SLE without prior severe organ manifestation	24	22	15	12	10	9	8	7
SLE with prior severe organ manifestation	49	45	38	29	24	20	13	9

Kaplan-Meier curve for flare free remission rate after glucocorticoid discontinuation

	Fisher's exact test			Cox proportional hazard model	
Factor	Flare (-) (n=54)	Flare (+) (n=19)	p value	Hazard ratio	p value (95% CI)
Prior severe organ manifestation	36 (66.7)	13 (68.4)	1	1.19	0.73 (0.44–3.17)
Renal manifestation	26 (48.1)	8 (42.1)	0.79	0.99	1.0 (0.39–2.53)
Neurological manifestation	6 (11.1)	0 (0.0)	0.33	N/A	N/A
history of treatment with PSL 1 mg/kg/day	21 (38.9)	8 (42.1)	1	1.16	0.76 (0.46–2.91)
history of treatment with mPSL pulse therapy	12 (22.2)	4 (21.1)	1	0.97	0.95 (0.32–2.95)
history of treatment with B cell targeting/cytotoxic medication	4 (7.4)	0 (0.0)	0.57	N/A	N/A
Hypocomplementemia on the day of glucocorticoid discontinuation	12 (23.1)	9 (50.0)	0.04	3.77	<0.01 (1.43–9.90)
Elevated anti-dsDNA antibody on the day of glucocorticoid discontinuation	3 (11.5)	3 (30.0)	0.32	2.45	0.21 (0.61–9.93)
Duration of SLE >5000 days	21 (38.9)	3 (15.8)	0.09	0.43	0.18 (0.12–1.48)
Anti-dsDNA antibody	33 (61.1)	15 (78.9)	0.26	2.15	0.18 (0.71–6.49)
Anti-Smith antibody	4 (7.5)	6 (31.6)	0.02	3.5	0.01 (1.31–9.35)
Anti-Ro/SSA antibody	22 (42.3)	11 (57.9)	0.29	2.19	0.10 (0.87–5.55)
Anti-RNP antibody	7 (15.2)	11 (64.7)	<0.01	6.8	<0.01 (2.36–19.63)
HCQ use on the day of glucocorticoid discontinuation	29 (53.7)	7 (36.8)	0.29	0.75	0.56 (0.29–1.97)
Achievement of LLDAS on the day of glucocorticoid discontinuation	52 (96.3)	17 (89.5)	0.28	0.25	0.07 (0.06–1.1)

Risk factors for flares after glucocorticoid discontinuation

Results: In total, 309 patients with SLE were followed up; 298 had prednisolone tapered to less than 7.5 mg/day and 75 had glucocorticoids discontinued. Seventy-three patients met the inclusion criteria; 49 were classified as SLE with prior severe organ manifestation. No statistical differences were noted in the 52-week flare rate and time to first flare after glucocorticoid discontinuation between patients with and without prior severe organ manifestation (52-week flare rate: 16.7% vs. 18.2%, p=1.0; time to first flare: 322 [280, 1169] vs. 385 [304, 2345] days, p=0.33). A positive anti-Smith/anti-ribonucleoprotein antibody negatively influenced flare-free remission. Although this result was not statistically significant, the achievement of lupus low disease activity state (LLDAS) on the day of glucocorticoid discontinuation positively influenced flare-free remissions after glucocorticoid discontinuation.

Conclusion: Glucocorticoid discontinuation can be achieved in patients with SLE with prior severe organ manifestations. Achievement of LLADS is key for reaching flare-free remission after glucocorticoid discontinuation.

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Abstract Number: 1736

Treatment of Lupus Nephritis with Belimumab Is Associated with Reduction in Urinary CD23

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Urine proteomic approaches have shown promise in identifying dynamic biological pathways in lupus nephritis (LN) which are not captured on renal histopathology or by measurement of proteinuria alone. We sought to investigate how the urine proteome changes with belimumab therapy and whether these changes might indicate any pathophysiologic explanations for the renal benefit of this drug.

Methods: Urine samples from 54 participants with biopsy-proven LN from the BLISS-LN trial (Furie *et al*., NEJM 2020) were collected at Week 0 (time of randomization), Week 24, and Week 52. A total of 1,000 urinary proteins were quantified using antibody microarrays (Raybiotech Kiloplex) at each time point and normalized using urine creatinine. The abundance of each urinary protein was compared in participants treated with belimumab (n = 28) versus standard of care (n = 26) at each time point using the Wilcoxon rank-sum test with Benjamini-Hochberg correction. Longitudinal fold change (e.g. fold change from Week 0 to 24) was also assessed for each protein in each treatment group.

Results: When comparing participants in the belimumab treatment group versus those in the standard of care group, there was no significant difference in the urine proteome at Week 0 per FDR threshold, as expected. At Week 24, five urinary proteins were found to be present at a significantly lower (CD23, Siglec-5) or higher (AIF, CRELD2, ROR2) level in those treated with belimumab (**Figure 1**). Numerically, lower CD23 and Siglec-5 (but not higher AIF, CRELD2,

or ROR2) in the belimumab group persisted into Week 52, though this was no longer significant per FDR threshold (CD23 p = 0.002, q = 0.69; Siglec-5 p = 0.004, q = 0.69). Belimumab therapy was particularly associated with a negative fold change in CD23 between Week 0 and 24 (**Figure 2**). Specifically, the median fold change was -6.02 (IQR

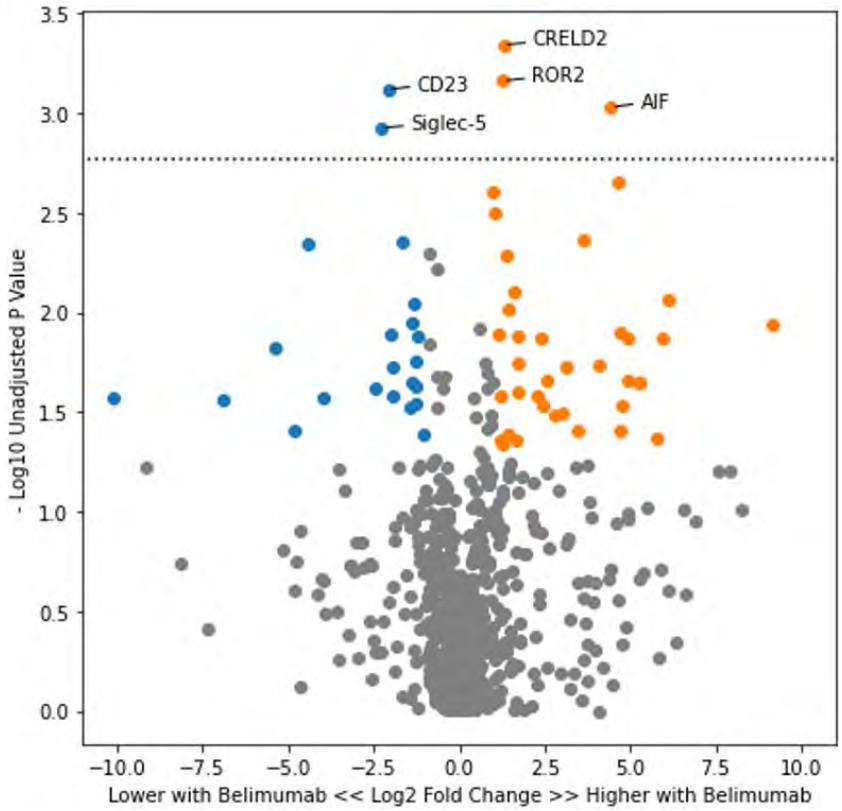

Figure 1. Volcano plot of urinary proteins at Week 24 in the belimumab versus standard of care treatment arms. Points in orange represent proteins which were higher in those treated with belimumab and had an unadjusted p value of < 0.05. Points in blue represent proteins which were lower in those treated with belimumab with an unadjusted p value of < 0.05. The dashed line is the p value threshold for a false discovery rate of 25% – this threshold was chosen given the relatively small sample size and exploratory nature of this work.

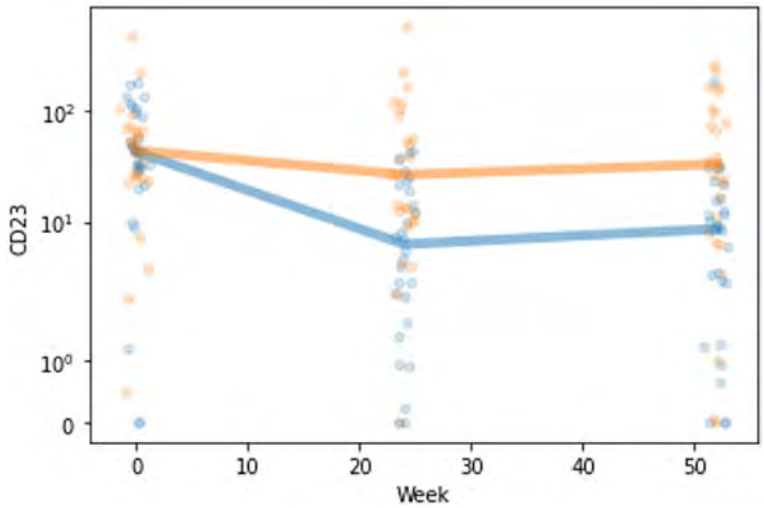

Figure 2. Abundance of CD23 over time in the belimumab (blue) and standard of care (orange) treatment groups. Each small circle represents one participant's CD23 value at the given time, and the thick lines represent the median CD23 value per group at each time point.

-14.42 to -3.82) in belimumab recipients versus -1.25 (IQR -2.60 to +1.56) in the standard of care arm (p = 0.0001, q = 0.12). With respect to longitudinal fold change, no other protein exhibited this behavior.

Conclusion: Significant reduction in urinary CD23 by Week 24 was most characteristic of belimumab therapy versus standard of care. CD23 is the low affinity receptor for IgE on B cells and also regulates IgE synthesis. CD23+ B cell-mediated antigen presentation of IgE-antigen complexes has been implicated in the enhancement of antibody and CD4+ T cell responses to said antigens. Anti-dsDNA IgE is common in SLE and is associated with active LN and worsened disease activity overall. Modulation of this CD23-mediated immune enhancement pathway might contribute to the added renal benefit of belimumab therapy versus standard of care alone. More generally, this work also provides evidence that treatment with specific medications can be detected in the urine proteome and could potentially be used for drug monitoring. We note that the full breadth of belimumab's effect on the urine proteome may not be captured here, given that participants in BLISS-LN were treated with mycophenolate mofetil or cyclophosphamide-azathioprine for up to two months prior to randomization, thereby potentially blunting pro-inflammatory urinary signals that can only be seen before immunosuppression is started.

Disclosure: E. Weeding, None; **A. Fava**, None; **C. Mohan**, None; **D. Goldman**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2.

Abstract Number: 1737

Reduction in Urinary CD163 Is Associated with Treatment Response in the Belimumab Lupus Nephritis Trial

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
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Background/Purpose: Urinary CD163 is a macrophage marker which correlates with histological activity index and response to treatment in lupus nephritis (LN), as evidenced by urine proteomic analyses in at least two independent cohorts. We investigated whether this finding could be confirmed in the BLISS-LN trial.

Methods: A total of 54 BLISS-LN (Furie *et al*., NEJM 2020) participants with biopsy-proven LN were included in this study. LN response status was determined at Week 52 based on proteinuria < 500 mg/mg, serum creatinine no greater than 1.25 times the Week 0 value, and prednisone dosage of no greater than 10 mg per day. Note that this response definition was specific to this series and differed from the BLISS-LN endpoints, which were not available. Urine samples were collected at Week 0 (time of randomization), Week 24, and Week 52, and 1,000 urinary proteins including CD163 were quantified using antibody microarrays (Raybiotech Kiloplex) at each time point and normalized using urine creatinine. The abundance of each urinary protein was compared in complete responders (n = 31) versus non-responders (n = 22) at each time point using the Wilcoxon rank-sum test with Benjamini-Hochberg correction for multiple comparisons with a false discovery rate (FDR) of 5%. One participant was excluded from analysis due to missing the clinical information required to determine response status.

Results: By Week 52, CD163 was the urine protein with the most significant difference in abundance between complete responders (median 1.8 pg/mg, IQR 0.8-2.6 pg/mg) versus non-responders (median 8.3 pg/mg, IQR 4.0-48.4 pg/mg) with a p value of 0.0004 after adjustment for multiple comparisons (**Figure 1**). This divergence in CD163 abundance was also observed at Week 24 though at a lower degree of significance between complete (median 3.5 pg/mg,

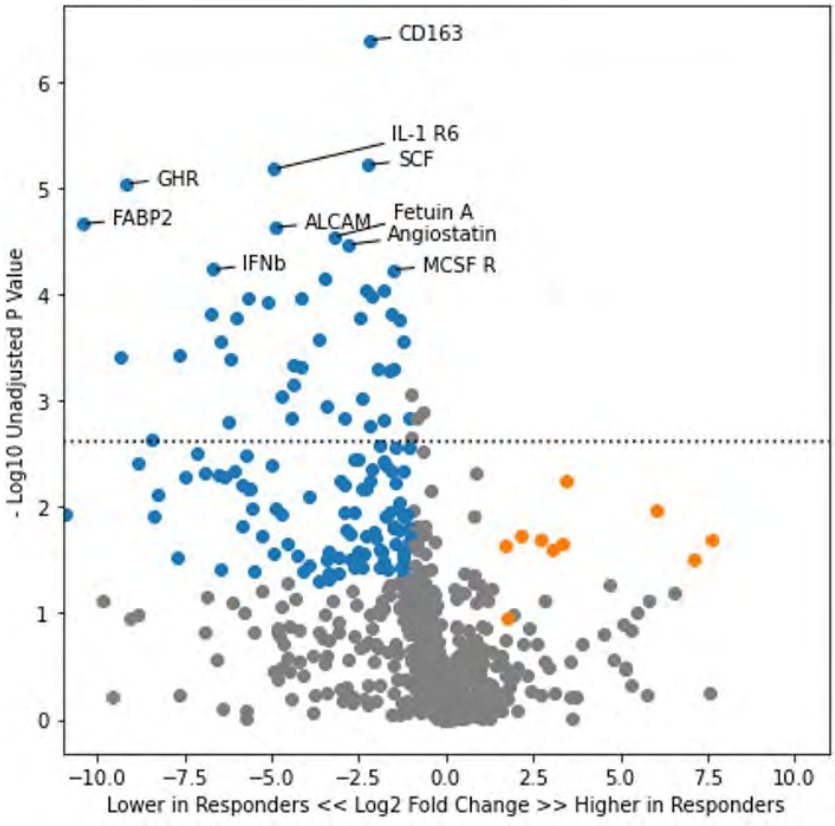

Figure 1. Volcano plot of urinary proteins at Week 52 in the complete responders versus non-responders. Points in blue represent proteins which were lower in the complete response group with an unadjusted p value of < 0.05. Points in orange represent proteins which were higher in the complete response group with an unadjusted p value of < 0.05. The dashed line is the p value threshold for a false discovery rate of 5%.

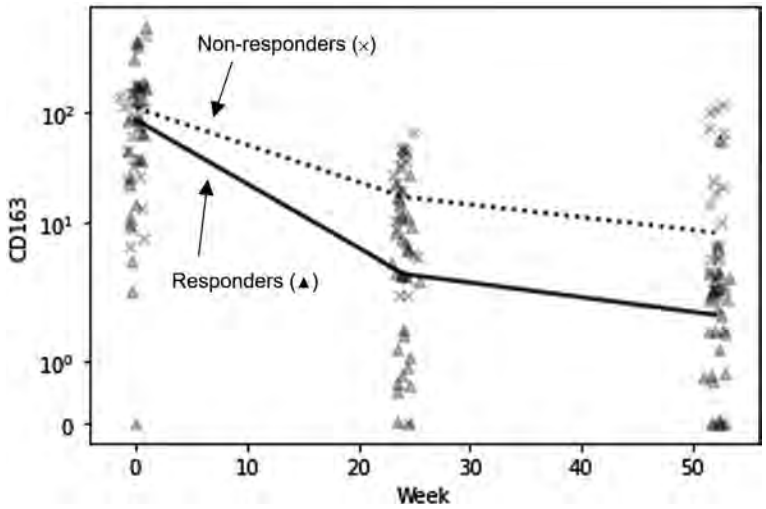

Figure 2. Abundance of CD163 over time in complete responders and non-responders. Each symbol represents one participant's CD163 value at the given time, and the lines represent the median CD163 value per response group at each time point.

IQR 1.1-10.4 pg/mg) and non-responders (median 17.4 pg/mg, IQR 6.2-36.1 pg/mg; adjusted p value = 0.07). CD163 versus time is shown in **Figure 2.** demonstrating a longitudinal reduction in both groups, but with a more robust reduction in CD163 in complete responders. All of the above findings were similarly found within both the belimumab and standard of care treatment subgroups (not shown).

Conclusion: Longitudinal reduction in urinary CD163 abundance was strongly associated with complete response (per the definition used in Methods) in the BLISS-LN trial. These results are consistent with our previous findings in the Accelerating Medicines Partnership SLE project and also those of Mejia-Vilet *et al*. (J Am Soc Nephrol, 2020), and support the potential use of specific urinary biomarkers such as CD163 as noninvasive measures of lupus nephritis response.

Disclosure: E. Weeding, None; **A. Fava**, None; **C. Mohan**, None; **D. Goldman**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2.

Abstract Number: 1738

Uveitis Status in Patients with Ankylosing Spondylitis or Psoriatic Arthritis Under Secukinumab Treatment - Real World Data from a German Observational Study

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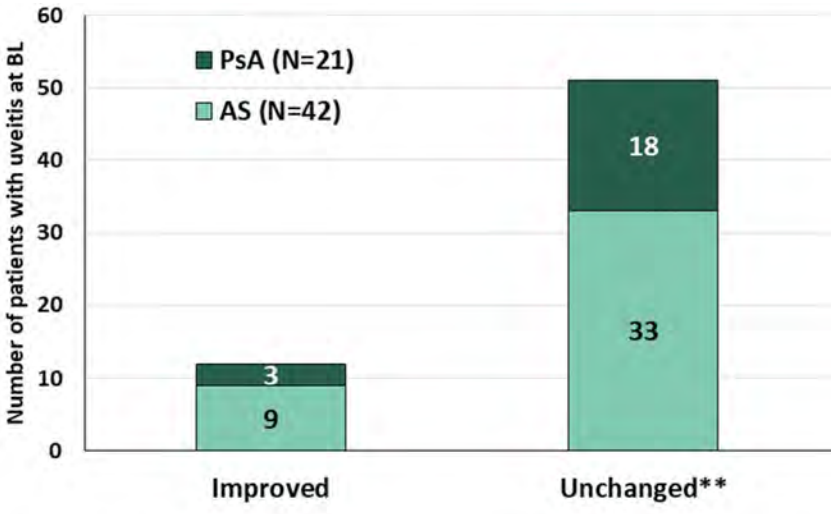
Background/Purpose: Uveitis is a well-known non-musculoskeletal manifestation of spondyloarthropathies. Patients typically suffer from blurred vision, pain, and photophobia and have an increased risk of ocular complications. Prevalence varies greatly, as uveitis occurs in up to 50% of patients with ankylosing spondylitis (AS) and in approximately 7% of patients with psoriatic arthritis (PsA).[1] The German non-interventional study AQUILA provides real-world data on the development of uveitis in patients with AS or PsA under treatment with secukinumab, a fully human monoclonal antibody that selectively inhibits interleukin-17A. The aim of this interim analysis is to compare baseline (BL) characteristics depending on the presence of uveitis, as well as frequencies and course of uveitis during the study.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 3000 secukinumab treated patients with active AS or PsA. Patients were observed from BL up to week 52 according to clinical routine. Real-world data was assessed prospectively and analyzed as observed. Uveitis and its severity (mild, moderate, severe) was determined by the treating rheumatologist at BL and subsequent study visits. This interim analysis focuses on the subgroups of patients with or without uveitis at BL.

Results: At BL, 668 AS and 1216 PsA patients were included with information on uveitis status available: Prevalence of uveitis at BL was 6.3% (n=42) in AS and 1.7% (n=21) in PsA patients. Demographic data (Table 1) showed that the percentage of males was higher in AS patients with uveitis (78.6%) compared to those without (58.5%). PsA patients did not show this distribution as the percentage of males was lower in patients with uveitis (38.1% versus 41.7%). For both AS and PsA patients, the proportion of obesity (i.e. BMI >30 kg/m^2) was higher in patients with uveitis. One AS patient was included with a moderate uveitis which resolved and came back later with the same severity (uveitis status of this patient was considered as unchanged compared to BL; Figure 1). In all other cases, uveitis status improved or remained unchanged (Figure 1). Furthermore, most of the patients with uveitis remained on secukinumab treatment up to 52 weeks (AS: 61.9%, n=26; PsA: 81.0%, n=17). Both AS and PsA patients with uveitis, had a numerically higher percentage of pretreatment with bDMARDs (biological disease-modifying antirheumatic drugs). In addition, more patients with uveitis received concomitant corticosteroids compared to patients without uveitis throughout 52 weeks observational period (Table 1). Regarding patients without uveitis at BL, 3 patients (1 out of 626 with AS and 2 out of 1195 with PsA) developed new onset uveitis during the study.

Table 1. Overview of BL characteristics depending on the presence of uveitis

	AS		PsA	
Demographics*	**With uveitis at BL (N=42)**	**Without uveitis at BL (N=626)**	**With uveitis at BL (N=21)**	**Without uveitis at BL (N=1195)**
Male	33 (78.6)	366 (58.5)	8 (38.1)	498 (41.7)
Female	9 (21.4)	260 (41.5)	13 (61.9)	697 (58.3)
Age, years	48.4 (11.4)	46.3 (12.2)	52.3 (12.2)	52.4 (11.3)
BMI, kg/m^2	27.8 (4.4)	27.4 (5.0)	30.8 (6.9)	29.1 (5.8)
BMI ≤25 kg/m², n (%)	11 (26.8)	209 (34.2)	5 (23.8)	298 (26.0)
BMI >25 to ≤30 kg/m², n (%)	17 (41.5)	245 (40.1)	6 (28.6)	409 (35.7)
BMI >30 kg/m², n (%)	13 (31.7)	157 (25.7)	10 (47.6)	439 (38.3)
Medication prior to secukinumab initiation, n (%):				
bDMARDs	29 (69.0)	399 (63.7)	14 (66.6)	720 (60.3)
Concomitant medication, n (%):				
Corticosteroids	19 (45.2)	155 (24.8)	11 (52.4)	503 (42.1)
*variables given as mean (SD)				



*Change is defined as alteration of the severity grade (mild, moderate, severe) of uveitis.

**One AS patient started with a moderate uveitis which resolved and then came back later with moderate severity (uveitis status of this patient was considered as unchanged compared to BL)

Figure 1. Change of uveitis status* within 52 weeks of observational period.

Conclusion: In a real-world setting, the number of new onset uveitis under treatment with secukinumab was low. In most patients with uveitis at BL, uveitis status remained unchanged or even improved throughout 52 weeks observational period. Altogether, real-world data of this interim analysis are in line with those of Phase 3 studies and show that secukinumab did not increase the risk of uveitis.

Disclosure: U. Kiltz, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5; **J. Brandt-Jrgens**, Abbvie, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Sanofi-Aventis, 2, 6, Novartis, 2, 6, Eli Lilly, 2, 6, MSD, 2, 6, UCB, 2, 6, BMS, 2, 6, Janssen, 2, 6, Medac, 2, 6; **P. Kästner**, Chugai, 2, Novartis, 2; **E. Riechers**, AbbVie, 2, 5, Chugai, 2, 5, Eli Lilly, 5, Janssen, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 5, UCB, 2, 5; **D. Peterlik**, Novartis, 3; **A. Boas**, Novartis, 3; **H. Tony**, AbbVie, 2, Astra-Zeneca, 2, BMS, 2, Chugai, 2, Janssen, 2, Lilly, 2, MSD, 2, Novartis, 2, Pfizer, 2, Roche, 2, Sanofi, 2.

Abstract Number: 1739

SLE Treatment History and Anifrolumab Efficacy by Baseline Standard Therapies in Patients with SLE from 2 Phase 3 Trials

Susan Manzi[1], Richard Furie[2], Eric Morand[3], Yoshiya Tanaka[4], Gabriel Abreu[5], Catharina Lindholm[5] and Raj Tummala[6], [1]Allegheny Health Network, Pittsburgh, PA, [2]Zucker School of Medicine at Hofstra/Northwell Health, Great Neck, NY, [3]Monash University, Melbourne, Australia, [4]University of Occupational and Environmental Health, Kitakyushu, Japan, [5]BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden, [6]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: In the phase 3 TULIP-1 and TULIP-2 trials, anifrolumab, a type I IFN receptor mAb, improved disease activity versus placebo in patients with moderate to severe SLE despite standard therapy with oral glucocorticoids (GCs), antimalarials, and/or immunosuppressants.[1,2] We investigated prior standard therapy use, and whether baseline standard therapy impacted anifrolumab efficacy in pooled data from TULIP-1 and TULIP-2.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were 52-week trials of intravenous anifrolumab 300 mg or placebo every 4 weeks for 48 weeks, in which eligible patients fulfilled the ACR 1997 criteria for SLE. At screening, patients had moderate to severe SLE (SLEDAI-2K ≥6, ≥1 A or ≥2 B BILAG-2004 organ domain scores, Physician's Global Assessment ≥1) and were required to be receiving ≥1 of the following standard therapies: oral GCs, antimalarials, immunosuppressants (azathioprine, mizoribine, mycophenolate mofetil, mycophenolic acid, and/or methotrexate). Patients were divided into subgroups depending on which standard therapies they were receiving at baseline; BILAG–based Combined Lupus Assessment (BICLA) response at Week 52 was compared across subgroups using a stratified Cochran–Mantel–Haenszel approach.

Results: Overall, 726 patients received anifrolumab 300 mg (n=360) or placebo (n=366) in TULIP-1 and TULIP-2. Demographics and baseline disease characteristics were generally balanced between treatment groups. The median time from SLE diagnosis to randomization was 84.5 months, during which most patients had received GCs (89.5%), antimalarials (84.3%), and immunosuppressants (68.0%), and 100%, 34.3%, or 57.3% of patients had received ≥1, 2, or ≥3 SLE-related immunomodulatory therapies, respectively. At baseline, patients were re-

Table. Background Standard Therapy Regimens Prior to and at Baseline in TULIP-1 and TULIP-2

SLE standard therapies		Prior to baseline[a]		At baseline[b]	
		Anifrolumab 300 mg (n=360)	Placebo (n=366)	Anifrolumab 300 mg (n=360)	Placebo (n=366)
Any oral GC[c]		325 (90.3)	325 (88.8)	291 (80.8)	304 (83.1)
	Oral GC only	28 (7.8)	21 (5.7)	56 (15.6)	38 (10.4)
	Oral GC + antimalarial and/or immunosuppressant	297 (82.5)	304 (83.1)	235 (65.3)	266 (72.7)
Any antimalarials		299 (83.1)	313 (85.5)	243 (67.5)	267 (73.0)
	Antimalarial only	28 (7.8)	27 (7.4)	32 (8.9)	38 (10.4)
	Antimalarial + oral GC and/or immunosuppressant	271 (75.3)	286 (78.1)	211 (58.6)	229 (62.6)
Any immunosuppressants		248 (68.9)	246 (67.2)	173 (48.1)	177 (48.4)
	Azathioprine	121 (33.6)	113 (30.9)	62 (17.2)	61 (16.7)
	Cyclophosphamide	50 (13.9)	39 (10.7)	-	-
	Leflunomide	9 (2.5)	9 (2.5)	-	-
	Methotrexate	104 (28.9)	135 (36.9)	56 (15.6)	73 (19.9)
	Mizoribine	9 (2.5)	11 (3.0)	4 (1.1)	3 (0.8)
	Mycophenolate[d]	82 (22.8)	79 (21.6)	54 (15.0)	45 (12.3)
	Tacrolimus	18 (5.0)	23 (6.3)	-	-
	≥2 different immunosuppressants	103 (28.6)	102 (27.9)	3 (0.8)	5 (1.4)

GC, glucocorticoid

[a]Includes any standard therapy with SLE indication used since SLE diagnosis with start date prior to randomization; [b]Baseline is defined as the last measurement prior to randomization and investigational product dose administration on Day 1; [c]Prednisone or equivalent; [d]Mycophenolate or mycophenolic acid.

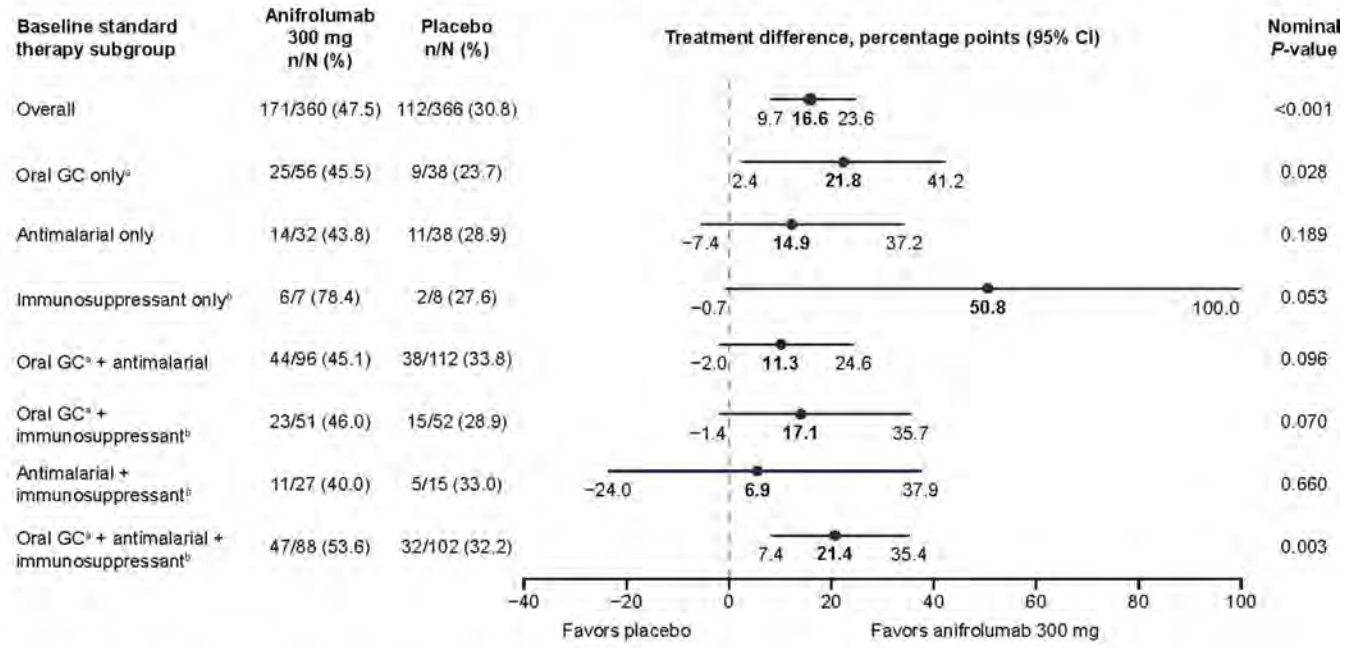
ceiving GCs (82.0%), antimalarials (70.2%), and/or immunosuppressants (48.2%), with most patients receiving combinations of the three (**Table**). Anifrolumab 300 mg was associated with higher BICLA response rates versus placebo across all evaluated baseline standard therapy subgroups (**Figure**); however, the impact of differing dosages of standard therapy on efficacy was not investigated. The positive treatment differences ranged from 6.9% (antimalarial + immunosuppressant) to 50.8% (immunosuppressant only), but these groups had small sample sizes (n=42 and n=15, respectively), which may limit interpretation of these treatment differences. Clear positive treatment differences favoring anifrolumab 300 mg vs placebo were observed in the 190 patients who were likely to have refractory or severe disease, as they were receiving GCs + antimalarials + immunosuppressants at baseline (53.6% vs 32.2%; Δ=21.4%; 95% CI: 7.4–35.4).

Conclusion: In 2 phase 3 trials, anifrolumab 300 mg was associated with consistently higher BICLA response rates than placebo, regardless of baseline standard therapy usage, including in patients with potentially more treatment-refractory SLE, requiring treatment with GCs, immunosuppressants, and antimalarials.

1. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.

2. Morand EF. *N Engl J Med*. 2020;382:211–21.

Figure. Forest Plot of BICLA Response According to Baseline Standard Therapy in Patients With SLE in TULIP-1 and TULIP-2



BICLA, BILAG-based Composite Lupus Assessment; CI, confidence interval; GC, glucocorticoid; IFNGS, interferon gene signature; n, number of responders; N, number of patients in the group; PGA, Physician's Global Assessment.
A BICLA response required: Reduction of all baseline BILAG-2004 A and B domain scores to B/C/D and C/D, respectively, and no worsening in other BILAG-2004 organ systems (worsening defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items); no increase in SLEDAI-2K score from baseline; no increase ≥0.3 points in PGA score from baseline; no use of restricted medications beyond protocol-allowed thresholds; and no discontinuation of investigational product. The response rates, the differences in response rates, and associated 95% CIs were calculated using a stratified Cochran–Mantel–Haenszel method with stratification factors of SLEDAI-2K score at screening (<10 vs ≥10), baseline oral GC dosage (<10 vs ≥10 mg/day prednisone or equivalent), IFNGS status (high vs low), and study.

[a]Prednisone or equivalent. [b]Immunosuppressants were ≥1 of: azathioprine, methotrexate, mycophenolate, or mycophenolic acid.

Disclosure: S. Manzi, AstraZeneca, 1, 5, Exagen Diagnostics, Inc, 2, 9, 10, Lupus Foundation of America, 4, UCB, 2, Merck-Serono, 5, AbbVie, 5, University of Pittsburgh, 10, Allegheny Singer Research Institute, 10, Cugene, 2, GlaxoSmithKline, 2, 5, Eli Lilly, 2; **R. Furie**, AstraZeneca, 2; **E. Morand**, GlaxoSmithKline, 2, 5, 6, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 2, 6, Novartis, 6, YL Biologics, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi Kasei, 5, 6, Mitsubishi Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Taisho, 2, Ayumi, 2, Bristol Myers Squibb, 6, GlaxoSmithKline, 2, 6; **G. Abreu**, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 2, 11.

Abstract Number: 1740

Efficacy of Anifrolumab in Patients with SLE Previously Treated with Biologics: Post Hoc Analysis of Data from 2 Phase 3 Trials

Richard Furie[1], Eric Morand[2], Kenneth Kalunian[3], Konstantina Psachoulia[4], Emmanuelle Maho[5], Catharina Lindholm[6] and Raj Tummala[4], [1]Zucker School of Medicine at Hofstra/Northwell Health, Great Neck, NY, [2]Monash University, Melbourne, Australia, [3]University of California, La Jolla, CA, [4]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, [5]BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [6]BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In the phase 3 TULIP-1 and TULIP-2 trials, anifrolumab, a type I IFN receptor mAb, improved disease activity in patients with SLE.[1,2] We investigated whether prior biologic exposure impacted anifrolumab efficacy and safety in TULIP-1 and TULIP-2 pooled data.

Table 1. Baseline Demographics, Disease Characteristics, and SLE Treatments in Biologic-Experienced and Biologic-Naïve Patients With SLE Pooled From the TULIP-1 and TULIP-2 Trials

Patients, n (%)		Biologic experienced (n=145)	Biologic naïve (n=581)
Demographics			
Median age (range), years		45 (18–69)	41 (18–69)
Female		134 (92.4)	540 (92.9)
Race	White	95 (65.5)	384 (66.1)
	Black	22 (15.2)	72 (12.4)
	Asian	13 (9.0)	63 (10.8)
	Other[a]	15 (10.3)	62 (10.7)
Geographic region	Asia Pacific	10 (6.9)	60 (10.3)
	Europe	35 (24.1)	202 (34.8)
	Latin America	15 (10.3)	101 (17.4)
	USA/Canada	78 (53.8)	201 (34.6)
	Rest of world	7 (4.8)	17 (2.9)
Baseline disease characteristics			
SLEDAI-2K score ≥10		101 (69.7)	419 (72.1)
BILAG-2004 organ scores	≥1 A	73 (50.3)	280 (48.2)
	0 A and ≥2 B	61 (42.1)	271 (46.6)
	0 A and <2 B	11 (7.6)	30 (5.2)
CLASI activity score ≥10		36 (24.8)	165 (28.4)
≥6 swollen and ≥6 tender joints		63 (43.4)	291 (50.1)
SDI global score ≥1[b]		64 (44.1)	181 (31.2)
Median time from SLE diagnosis to randomization (range), months		128 (16–503)	74 (0–555)
IFNGS high[c]		128 (88.3)	472 (81.2)
Serologies	Anti-dsDNA positive	72 (49.7)	250 (43.0)
	Low C3	54 (37.2)	213 (36.7)
	Low C4	33 (22.8)	136 (23.4)
Baseline SLE treatments			
Oral GC[d]	Any	121 (83.4)	474 (81.6)
	≥10 mg/day	71 (49.0)	304 (52.3)
Antimalarials		103 (71.0)	407 (70.1)
Immunosuppressants	Any[e]	70 (48.3)	280 (48.2)
	Azathioprine	20 (13.8)	103 (17.7)
	Methotrexate	28 (19.3)	101 (17.4)
	Mycophenolate[f]	24 (16.6)	75 (12.9)
NSAIDs		28 (19.3)	124 (21.3)

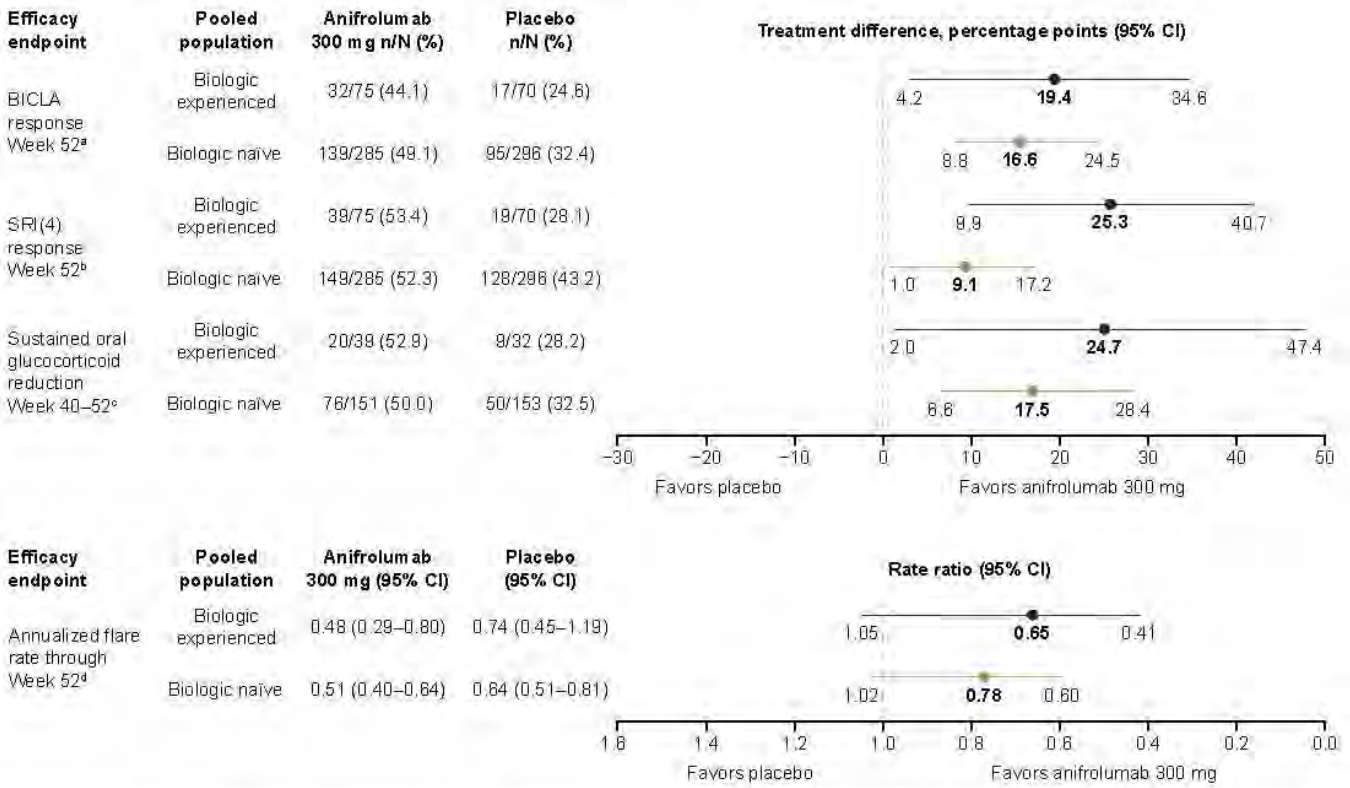
C3, complement 3; C4, complement 4; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; GC, glucocorticoid; IFNGS, interferon gene signature; SDI, SLICC/ACR Damage Index.
Values are n (%) of patients unless otherwise specified.

[a]The other category includes patients with missing race data; [b]A score ≥1 is indicative of organ damage; [c]At screening rather than baseline; [d]Prednisone or equivalent; [e]Immunosuppressants include azathioprine, methotrexate, mycophenolate mofetil, mycophenolic acid, and mizoribine; [f]Mycophenolate or mycophenolic acid.

Methods: This analysis included patients who received intravenous anifrolumab 300 mg or placebo every 4 weeks for 48 weeks in the 52-week TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) trials, for which eligible patients met the ACR 1997 SLE criteria, had moderate to severe SLE, and were permitted prior biologic use with a 3–6 month washout period, regardless of the reason for cessation. Patients were split into biologic-experienced or biologic-naïve subgroups (≥1 or 0 previous biologic immunomodulators, respectively). Baseline SLE disease characteristics, efficacy, and safety were compared across subgroups. Efficacy measures included BILAG–based Combined Lupus Assessment (BICLA) response at Week (W) 52; SLE Responder Index of ≥4 (SRI[4]) response at W52; sustained oral glucocorticoid (GC) taper (≤7.5 mg/day prednisone equivalent, W40–52, if ≥10 mg/day at baseline); and annualized flare rate through W52. Binary endpoints and safety were analyzed with a Cochran–Mantel–Haenszel approach controlling for randomization stratification factors and study. Annualized flare rate was analyzed with a negative binomial regression model with treatment, randomization stratification factors, and study as covariates.

Results: There were 145 biologic-experienced patients (anifrolumab [n=75]; placebo [n=70]), and 581 biologic-naïve patients (anifrolumab [n=285]; placebo [n=296]). Most previous biologic use was with belimumab (n=70), epratuzumab (n=49), tabalumab (n=18), or rituximab (n=14). Baseline demographics, disease characteristics, and non-biologic SLE treatments were generally similar between groups. However, compared with biologic-naïve patients, biologic-

Figure. Forest Plot of Efficacy Endpoints in the Biologic-Experienced and Biologic-Naïve Patients With SLE in Data Pooled From the TULIP-1 and TULIP-2 Trials



BICLA, BILAG-based Composite Lupus Assessment; CI, confidence interval; IFNGS, interferon gene signature; n, number of responders; N, number of patients in the group; PGA, Physician's Global Assessment; SRI(4), SLE Responder Index ≥4.
The response rates, the differences in response rates, and associated 95% CIs were calculated using a stratified Cochran–Mantel–Haenszel method with stratification factors of SLEDAI-2K score at screening, baseline oral glucocorticoid dosage, IFNGS status, and study; therefore, percentages do not equal n/N*100. Annualized flare rate was analyzed with a negative binomial regression model.
[a]A BICLA response required: Reduction of all baseline BILAG-2004 A and B domain scores to B/C/D and C/D, respectively, and no worsening in other BILAG-2004 organ systems (worsening defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items), no increase in SLEDAI-2K score from baseline, no increase ≥0.3 points in PGA score from baseline, no use of restricted medications beyond protocol-allowed thresholds, and no discontinuation of investigational product; [b]An SRI(4) response required: ≥4-point reduction in SLEDAI-2K, <1 new BILAG-2004 A or <2 new BILAG-2004 B organ domain scores, <0.3-point increase in PGA from baseline; no use of restricted medications beyond protocol-allowed thresholds; and no discontinuation of investigational product; [c]Defined as oral glucocorticoid dosage reduction to ≤7.5 mg/day from Week 40 to 52 in patients with baseline dosage ≥10 mg/day prednisone or equivalent; [d]A flare is defined as either ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items compared with the previous visit.

Table 2. Safety in Biologic-Experienced and Biologic-Naïve Patients With SLE in Data Pooled From the TULIP-1 and TULIP-2 Trials

AE category, n (%)	Biologic experienced		Biologic naïve	
	Anifrolumab 300 mg (n=75)	Placebo (n=69)	Anifrolumab 300 mg (n=285)	Placebo (n=296)
Any AE	68 (90.7)	61 (88.9)	250 (87.8)	234 (79.2)
Any SAE[a]	12 (15.7)	16 (23.3)	28 (9.9)	44 (14.9)
Any AE leading to discontinuation of investigational product	4 (5.4)	5 (7.4)	13 (4.6)	13 (4.5)
Any AESI	9 (12.8)	9 (13.3)	37 (13.0)	27 (9.2)
Non-opportunistic serious infections	3 (4.2)	7 (10.3)	13 (4.6)	15 (5.1)
Opportunistic infections	0	0	1 (0.4)	0
Anaphylaxis	0	0	0	0
Malignancy	0	1 (1.3)	3 (1.1)	2 (0.7)
Herpes zoster	4 (5.7)	1 (1.6)	19 (6.7)	4 (1.4)
Tuberculosis (including latent)	0	0	2 (0.7)	1 (0.3)
Influenza	1 (1.5)	1 (1.6)	5 (1.7)	7 (2.4)
Vasculitis (non-SLE)	0	0	0	0
Major adverse cardiovascular events	1 (1.5)	0	0	0

AE, adverse event; AESI, adverse event of special interest; SAE, serious adverse event.
Safety was analyzed in the safety population, which excluded 1 biologic-experienced patient who received placebo. The percentages were adjusted with a stratified Cochran–Mantel–Haenszel method with stratification factors of SLEDAI-2K score at screening, baseline oral glucocorticoid dosage, IFNGS status, and study; therefore, percentages do not equal n/N*100.
[a]Including events with outcome of death.

experienced patients had longer times from SLE diagnosis, were more likely to be from USA/Canada, have SLICC/ACR Damage Index score ≥1, anti-dsDNA antibodies, and IFN gene signatures, and less likely to have swollen/tender joints (**Table 1**). There were lower placebo responses (potentially more refractory disease) in biologic-experienced vs biologic-naïve patients (**Figure**). Anifrolumab was associated with comparable/greater treatment differences over placebo (Δ) in biologic-experienced vs biologic-naïve patients across endpoints, including BICLA (Δ=19.4 vs Δ=16.6), SRI(4) (Δ=25.3 vs Δ=9.1), and GC tapers (Δ=24.7 vs Δ=17.5). Incidence of serious adverse events was higher in biologic-experienced vs biologic-naïve patients with anifrolumab and placebo (**Table 2**). Herpes zoster incidence was higher with anifrolumab vs placebo in both biologic-experienced and biologic-naïve patients.

Conclusion: Regardless of whether patients with SLE had previously received biologics, anifrolumab 300 mg provided clinically meaningful benefit over placebo across efficacy endpoints and was generally well tolerated.

1. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.

2. Morand EF. *N Engl J Med*. 2020;382:211–21.

Disclosure: R. Furie, AstraZeneca, 2; **E. Morand**, GlaxoSmithKline, 2, 5, 6, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **K. Kalunian**, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Pfizer, 2, Genentech/Roche, 2, Equillium, 2, Kezar, 2, Kirin, 2, Amgen, 2, Biogen, 2, Janssen, 2, VielaBio, 2, Chemocentrix, 2, Gilead, 2, GlaxoSmith-Kline, 2; **K. Psachoulia**, AstraZeneca, 3; **E. Maho**, Idorsia Pharmaceuticals Ltd, 3, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1741

Anifrolumab Results in Favorable Responses Regardless of SLE Disease Duration: Post Hoc Analysis of Data from 2 Phase 3 Trials

Kenneth Kalunian[1], Maria Dall'Era[2], Richard Furie[3], Eric Morand[4], Konstantina Psachoulia[5], Emmanuelle Maho[6], Catharina Lindholm[7] and Raj Tummala[5], [1]University of California, La Jolla, CA, [2]University of California San Francisco, San Francisco, CA, [3]Zucker School of Medicine at Hofstra/Northwell Health, Great Neck, NY, [4]Monash University, Melbourne, Australia, [5]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg, MD, [6]BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [7]BioPharmaceuticals R&D, AstraZeneca, Gothenburg, Sweden

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: In 2 phase 3 trials, TULIP-1 and TULIP-2, anifrolumab, a type I IFN receptor mAb, improved disease activity in patients with SLE.[1,2] Here, we compared the efficacy of anifrolumab in patients with recent onset vs established SLE disease (defined by time since diagnosis), using pooled data from the TULIP trials.

Methods: TULIP-1 (NCT02446912) and TULIP-2 (NCT02446899) were randomized, placebo-controlled, 52-week trials of intravenous anifrolumab 300 mg every 4 weeks for 48 weeks in eligible patients who fulfilled the ACR 1997 criteria for SLE and had moderate to severe SLE despite standard therapy.[1,2] Baseline characteristics and BILAG–based Composite Lupus Assessment (BICLA)[3] response rates at Week 52 for anifrolumab 300 mg vs placebo were compared between patients who at the time of their baseline study visits were within 2 years of their SLE diagnosis (recent onset) and patients who were diagnosed beyond 2 years (established). Efficacy was analyzed with a stratified Cochran–Mantel–Haenszel approach controlling for randomization stratifications factors and study.

Results: Of the 726 patients included from TULIP-1 and TULIP-2 (anifrolumab, n=360; placebo, n=366), 594 had established disease (anifrolumab, n=301; placebo, n=293), and 132 had recent onset disease (anifrolumab, n=59; placebo, n=73) at baseline. In contrast to patients with recent onset disease, patients with established disease had a higher median age (43 vs 37 years), were more likely to be female (94.1% vs 87.1%), and less likely to be black (12.1% vs 16.7%). At baseline, patients with established disease were more likely to be IFN gene signature high (83.5% vs 78.8%), anti-dsDNA antibody-positive (45.6% vs 38.6%), have ≥1 BILAG-2004 A item (49.7% vs 43.9%), have a higher mean global SDI score (0.7 vs 0.1), and be receiving oral glucocorticoids (83.2% vs 76.5%), and immunosuppressants (49.8% vs 40.9%), but not anti-malarials (69.5% vs 78.0%) (**Table**). The numbers of BILAG-2004 A or B items across organ domains at baseline were comparable in patients with established or recent onset disease, excluding the renal domain, where a higher proportion of patients with established disease had more severe scores (A or B items; 8.9% vs 3.0%) (**Figure**). Treatment benefit of anifrolumab vs placebo, assessed by BICLA response at Week 52, was observed in patients with established (difference [95% CI] 17.1% [9.3–24.8], nominal $P<0.001$) and recent onset disease (difference [95% confidence intervals (CI)] 14.4% [–2.2–31.1], nominal $P=0.090$).

Table. Baseline Demographics, SLE Disease Characteristics, and Treatments in Data Pooled from TULIP-1 and TULIP-2 Trials

		Duration of disease					
		Recent onset (≤2 years)			Established (>2 years)		
		Anifrolumab 300 mg (n=59)	Placebo (n=73)	Total (n=132)	Anifrolumab 300 mg (n=301)	Placebo (n=293)	Total (n=594)
Demographic characteristic							
Age (years)	Median (min–max)	38 (18–68)	35 (18–65)	37 (18–65)	43 (18–69)	42 (19–69)	43 (18–69)
Sex, n (%)	Female	53 (89.8)	62 (84.9)	115 (87.1)	280 (93.0)	279 (95.2)	559 (94.1)
Race, n (%)	White	35 (59.3)	47 (64.4)	82 (62.1)	200 (66.4)	197 (67.2)	397 (66.8)
	Black	10 (16.9)	12 (16.4)	22 (16.7)	36 (12.0)	36 (12.3)	72 (12.1)
	Asian	8 (13.6)	5 (6.8)	13 (9.8)	33 (11.0)	30 (10.2)	63 (10.6)
	Other	5 (8.5)	8 (11.0)	13 (9.8)	25 (8.3)	23 (7.8)	48 (8.1)
	Missing	1 (1.7)	1 (1.4)	2 (1.5)	7 (2.3)	7 (2.4)	14 (2.4)
SLE disease characteristic							
IFNGS at screening, n (%)	High	47 (79.7)	57 (78.1)	104 (78.8)	251 (83.4)	245 (83.6)	496 (83.5)
SLEDAI-2K score	Mean (SD)	11.7 (3.2)	10.8 (3.2)	11.2 (3.2)	11.3 (4.0)	11.7 (3.8)	11.5 (3.9)
	≥10 points, n (%)	47 (79.7)	52 (71.2)	99 (75.0)	207 (68.8)	214 (73.0)	421 (70.9)
BILAG-2004, n (%)	≥ 1 A item	22 (37.3)	36 (49.3)	58 (43.9)	152 (50.5)	143 (48.8)	295 (49.7)
	No A and ≥2 B items	33 (55.9)	34 (46.6)	67 (50.8)	137 (45.5)	128 (43.7)	265 (44.6)
PGA score	Mean (SD)	1.8 (0.5)	1.8 (0.3)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)	1.8 (0.4)
CLASI activity score	Mean (SD)	9.4 (9.3)	9.0 (9.6)	9.2 (9.4)	8.2 (7.2)	7.5 (6.5)	7.9 (6.9)
Swollen joints[a]	Mean (SD)	6.5 (5.8)	7.5 (5.9)	7.1 (5.8)	6.8 (5.8)	7.1 (5.7)	7.0 (5.7)
Tender joints[a]	Mean (SD)	9.7 (7.6)	11.7 (7.8)	10.8 (7.7)	10.4 (7.4)	10.6 (7.5)	10.5 (7.4)
SDI global score	Mean (SD)	0.1 (0.3)	0.2 (0.5)	0.1 (0.4)	0.7 (1.1)	0.7 (0.9)	0.7 (1.0)
Anti-dsDNA, n (%)	Positive	25 (42.4)	26 (35.6)	51 (38.6)	142 (47.2)	129 (44.0)	271 (45.6)
SLE related treatment							
Oral glucocorticoids[b], n (%)	Any	45 (76.3)	56 (76.7)	101 (76.5)	246 (81.7)	248 (84.6)	494 (83.2)
	≥10	31 (52.5)	38 (52.1)	69 (52.3)	159 (52.8)	147 (50.2)	306 (51.5)
Antimalarials, n (%)		44 (74.6)	59 (80.8)	103 (78.0)	199 (66.1)	208 (71.0)	407 (69.5)
Immunosuppressants[c], n (%)		23 (39.0)	31 (42.5)	54 (40.9)	150 (49.8)	146 (49.8)	296 (49.8)

CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; IFNGS, interferon gene signature; n, number of patients; PGA, Physician's Global Assessment; SD, standard deviation; SDI, SLICC/ACR Damage Index; WHO-DD SDG, World Health Organization-Drug Dictionary Standardised Drug Groupings.
Percentages are based upon all patients in the full analysis set within the respective treatment group.
Phase 3 pool includes TULIP-1 and TULIP-2 (excluding the anifrolumab 150 mg group from TULIP-1).
[a]Joint count is based on 28 joints.
[b]Oral glucocorticoids contain prednisone or equivalent. It is defined as oral medications listed in the WHO-DD SDG "Corticosteroids."
[c]Immunosuppressants: azathioprine, methotrexate, mycophenolate mofetil, mycophenolic acid, and mizoribine.

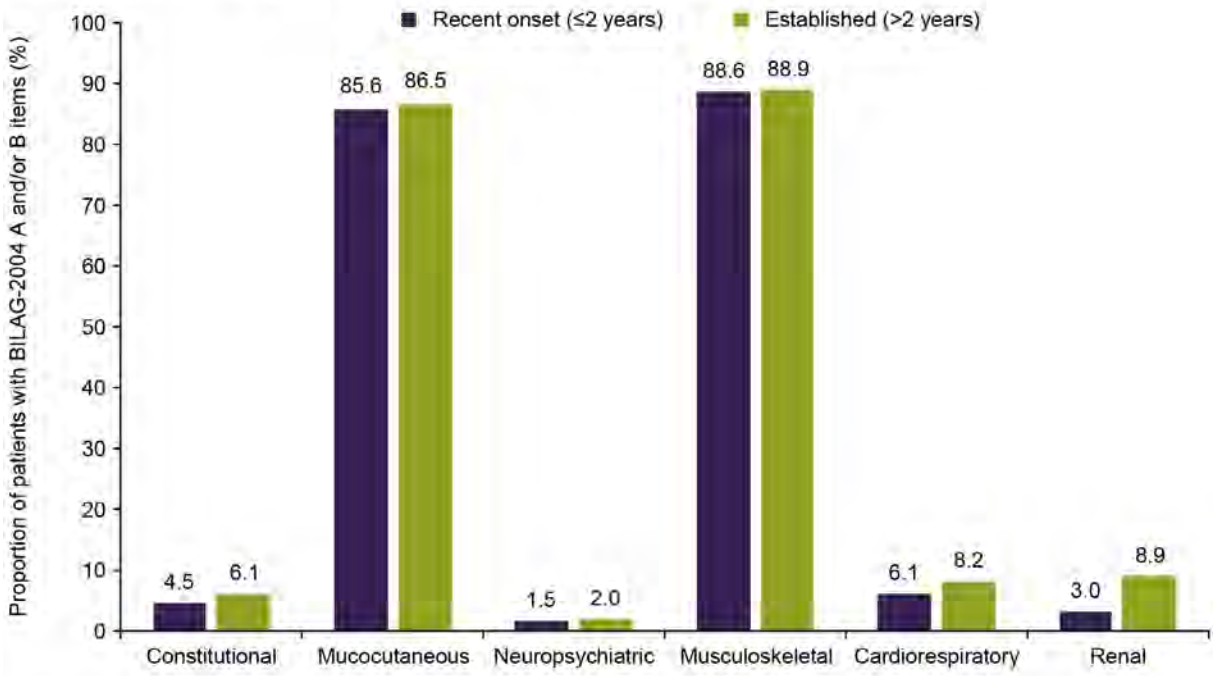
Conclusion: Data from the TULIP trials support the efficacy of anifrolumab in patients with SLE who have either established or recent onset disease.

1. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.

2. Morand EF. *N Engl J Med*. 2020;382:211–21.

3. Wallace DJ. *Ann Rheum Dis.* 2014;73:183–90.

Figure. BILAG-2004 Organ Involvement Scores at Baseline by Disease Duration



Percentages are based upon all patients within the respective disease duration group, who were either treated with anifrolumab 300 mg or placebo. Organ domains (gastrointestinal, ophthalmic, hematologic) were not included on the graph, as <1% of patients in either disease duration group had a BILAG-2004 A or B score. Phase 3 pool includes TULIP-1 and TULIP-2 (excluding the anifrolumab 150 mg group from TULIP-1).

Disclosure: K. Kalunian, AstraZeneca, 2, BMS, 2, Eli Lilly, 2, Pfizer, 2, Genentech/Roche, 2, Equillium, 2, Kezar, 2, Kirin, 2, Amgen, 2, Biogen, 2, Janssen, 2, VielaBio, 2, Chemocentrix, 2, Gilead, 2, GlaxoSmithKline, 2; **M. Dall'Era**, Aurinia, 1, GSK, 1, AstraZeneca, 1, Biogen, 1; **R. Furie**, AstraZeneca, 2; **E. Morand**, GlaxoSmithKline, 2, 5, 6, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **K. Psachoulia**, AstraZeneca, 3; **E. Maho**, Idorsia Pharmaceuticals Ltd, 3, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1742

Efficacy of Anifrolumab in Serological Subgroups of Patients with SLE Participating in 2 Phase 3 Trials

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

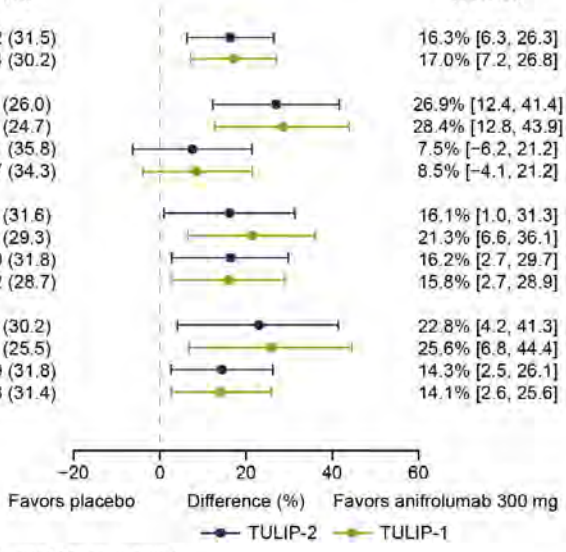
Background/Purpose: In the TULIP-2 and TULIP-1 trials of patients with SLE, the type I IFN receptor mAb anifrolumab resulted in higher BILAG–based Composite Lupus Assessment (BICLA) response rates vs placebo at Week 52.[1,2] Subgroup analyses revealed concordant BICLA response rates across clinically distinct SLE subgroups, including disease severity and SLE therapies.[3] Here, we compare BICLA response rates in serological subgroups (low complement, anti-dsDNA positivity, or both).

Methods: TULIP-2 (NCT02446899) and TULIP-1 (NCT02446912) were phase 3, randomized, placebo-controlled, 52-week trials of intravenous anifrolumab every 4 weeks for 48 weeks in eligible patients who fulfilled the ACR 1997 criteria for SLE and had moderate to severe SLE despite standard therapy.[1,2] BICLA response rates at Week 52 for anifrolumab vs placebo groups were compared across patient subgroups of baseline complement C3/C4 levels (low/normal) and anti-dsDNA antibody status (positive/negative).

Results: In TULIP-2 and TULIP-1, 180 patients in each trial received anifrolumab 300 mg, and 182 and 184 patients received placebo, respectively. BICLA response rates in the overall anifrolumab groups were similar in TULIP-2 (47.8%) and TULIP-1 (47.1%), with treatment differences (Δ) favoring anifrolumab over placebo (Δ=16.3% and 17.0%, respectively) (**Figure**). Anifrolumab response rates were generally higher in serologically abnormal vs normal subgroups in TULIP-2 (47.7%–52.9% vs 43.3%–47.9%) and TULIP-1 (50.6%–53.0% vs 42.8%–45.5%); the greatest anifrolumab response rate was seen in the low C3/C4 subgroup (TULIP-2: 52.9%; TULIP-1: 53.0%), while anifrolumab response rates were similar regardless of anti-dsDNA positivity. In contrast, placebo response rates were generally lower in serologically abnormal vs normal subgroups in TULIP-2 (26.0%–31.6% vs 31.8%–35.8%) and TULIP-1 (24.7%–29.3% vs 28.7%–34.3%), although placebo responses were similar regardless of anti-dsDNA positivity. Anifrolumab and placebo subgroup response rates did not vary by more than ±6% from the overall population. These variations in response rates led to greater treatment differences favoring anifrolumab in patients with low C3/C4, alone or in combination with anti-dsDNA positivity, vs the overall population; the largest difference was seen for patients with low C3/C4 (TULIP-2: Δ=26.9%; TULIP-1: Δ=28.4%). In the subgroups with normal serology, treatment

Figure. BICLA Response at Week 52 by Subgroup in the TULIP-2 and TULIP-1 Trials

	Anifrolumab 300 mg n/N (%)	Placebo n/N (%)	Treatment difference, percentage points (95% CI)
All patients	86/180 (47.8)	57/182 (31.5)	16.3% [6.3, 26.3]
	85/180 (47.1)	55/184 (30.2)	17.0% [7.2, 26.8]
Low complement (C3 or C4)	46/87 (52.9)	21/81 (26.0)	26.9% [12.4, 41.4]
	35/66 (53.0)	19/77 (24.7)	28.4% [12.8, 43.9]
No low complement (neither C3 nor C4)	40/93 (43.3)	36/101 (35.8)	7.5% [−6.2, 21.2]
	50/114 (42.8)	36/107 (34.3)	8.5% [−4.1, 21.2]
Anti-dsDNA positive	41/86 (47.7)	23/73 (31.6)	16.1% [1.0, 31.3]
	41/81 (50.6)	24/82 (29.3)	21.3% [6.6, 36.1]
Anti-dsDNA not positive	45/94 (47.9)	34/109 (31.8)	16.2% [2.7, 29.7]
	44/99 (44.5)	31/102 (28.7)	15.8% [2.7, 28.9]
Low complement (C3 or C4) and anti-dsDNA positive	27/51 (52.9)	16/53 (30.2)	22.8% [4.2, 41.3]
	24/47 (51.1)	13/51 (25.5)	25.6% [6.8, 44.4]
No (Low complement [C3 or C4] and anti-dsDNA positive)	59/129 (46.1)	41/129 (31.8)	14.3% [2.5, 26.1]
	61/133 (45.5)	42/133 (31.4)	14.1% [2.6, 25.6]



BICLA, BILAG–based Composite Lupus Assessment; C3, complement 3; C4, complement 4; CI, confidence interval; CMH, Cochran–Mantel–Haenszel; n, number of responders; N, number of patients in treatment subgroup.
The responder rates (percentages) and associated 95% CIs are weighted and are calculated using a stratified CMH approach, with stratification factors (SLEDAI-2K score at screening [<10 points vs ≥10 points], Week 0 oral glucocorticoid dose [<10 mg/day vs ≥10 mg/day prednisone or equivalent], and type I IFN gene signature test result at screening [high vs low]). Percentages are based upon all subjects in the full analysis set within subgroups. Baseline is defined as the last measurement prior to randomization and dose administration on Day 1.

differences ranged from 7.5%–16.2% in TULIP-2 and 8.5%–15.8% in TULIP-1; thus, treatment differences favored anifrolumab vs placebo in all evaluated serology subgroups.

Conclusion: BICLA response rates in clinically distinct subgroups of SLE were generally consistent with the overall TULIP-2 and TULIP-1 results.[3] Patients with low complement at baseline appeared to have a greater treatment effect than those with normal complement, while anti-dsDNA antibody status did not associate with response. The subgroup analyses indicate efficacy of anifrolumab 300 mg across all evaluated serological subgroups of SLE.

1. Furie, *Lancet Rheumatol* 2019;1:e208-10.

2. Morand. *N Engl J Med* 2020;382:211–21.

3. Morand. *Ann Rheum Dis* 2020(S1);79:32.

Disclosure: I. Bruce, AstraZeneca, 2, 6, GlaxoSmithKline, 2, 5, 6, UCB, 2, 6, Eli Lilly, 2, Aurinia, 2; **R. Van Vollenhoven**, BMS, 5, GlaxoSmithKline, 5, 6, Lilly, 5, UCB, 2, 5, 6, AbbVie, 2, 6, AstraZeneca, 2, Biogen, 2, Biotest, 2, Celgene, 2, Galapagos, 2, 6, Gilead, 2, Janssen, 2, 6, Pfizer, 2, 12, Support for educational programs, Sanofi, 2, Servier, 2, VielaBio, 2, Roche, 12, Support for educational programs; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 2, 6, Novartis, 6, YL Biologics, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi Kasei, 5, 6, Mitsubishi Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Taisho, 2, Ayumi, 2, Bristol Myers Squibb, 6, GlaxoSmithKline, 2, 6; **E. Morand**, GlaxoSmithKline, 2, 5, 6, Amgen, 2, AstraZeneca, 2, 5, 6, Biogen, 2, Bristol Myers Squibb, 2, 5, Genetech, 2, Eli Lilly, 2, 5, 6, Janssen, 5, Neovacs, 2, Servier, 2, Wolf, 2, EMD Serono, 2, 5, Novartis, 6, Sandoz, 2, Sanofi, 6; **R. Furie**, AstraZeneca, 2; **K. Psachoulia**, AstraZeneca, 3; **E. Maho**, Idorsia Pharmaceuticals Ltd, 3, AstraZeneca, 3; **C. Lindholm**, AstraZeneca, 3; **C. Kleoudis**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1743

Whole Blood Hydroxychloroquine Levels Do Not Correlate with QTc Intervals in a Cohort of 84 SLE Patients: Evidence That Antimalarials Are Not Associated with Cardiac Conduction System Toxicity

Mayce Haj-Ali[1] and **H. Michael Belmont**[2], [1]NYU Grossman School of Medicine, New York, NY, [2]NYU School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is an antimalarial drug used in the treatment of systemic lupus erythematous (SLE). There is limited data assessing cardiac toxicity as arrhythmias in association with HCQ exposure based on dose prescribed or pharmacy records and none relying on measured drug levels. Some of the risk factors associated with conduction abnormalities in the setting of hydroxychloroquine use include presence of chronic kidney disease, older age, underlying cardiomyopathy, and the use of concomitant prolonging QTc agents. In a retrospective study of 194 SLE patients on HCQ, the authors found that there was no significant difference in mean QTc based on HCQ use. Additionally, patients with CKD were more likely to have prolonged QTc when compared to those without CKD, but there was no significant difference in mean QTc based on HCQ use as well in this subset. Severe prolongation of QTc was rare in all groups and no episodes of serious tachyarrhythmia or Torsade de Pointes

were observed. The purpose of this study is to determine the relationship between whole blood HCQ levels and QTc intervals on simultaneous EKG performed during a routine visit.

Methods: This prospective study was IRB approved and all patients provided consent. At the time of data lock, 84 patients fulfilled ACR/SLICC criteria for SLE. These patients were on HCQ for at least 3 months at doses used for standard of care treatment. Whole blood levels were drawn and EKGs were obtained during a routine outpatient faculty practice visit for patients consecutively seen between February 5 and May 10, 2021 with senior author. Statistical analyses was performed using one way ANOVA, Pearson's correlation coefficient and t-test.

Results: 84 patients, 93% female, 47% European, 35% African, 15% Asian, and 25% Hispanic were included (Table 1). HCQ levels were higher in patients on 400 mg, lower after 10 years of exposure, and unrelated to eGFR (Table 2). There was no correlation between blood HCQ levels and QTc intervals in the 84 patients (r=-0.017; p=0.87) (Fig 1a).

Table 1. Demographics

Total (N=84)	Number of patients (%)
GENDER	
Female	78 (93%)
Male	6 (7%)
RACE	
African ancestry	29 (35%)
Asian ancestry	15 (18%)
European ancestry	40 (47%)
ETHNICITY	
Non-Hispanic	63 (75%)
Hispanic	21 (25%)

Table 2A: HCQ blood levels and different HCQ dosing

	HCQ 400 mg daily (n= 51)	HCQ 300 mg daily (n= 8)	HCQ 200 mg daily (n = 22)	HCQ 200 mg TIW (n = 5)
HCQ mean level (ng/mL)	1250 ± 678	776 ± 542	662 ± 392	378 ± 299

*p= 0.0001; f-ratio=7.637

Table 2B: HCQ blood levels by duration of exposure

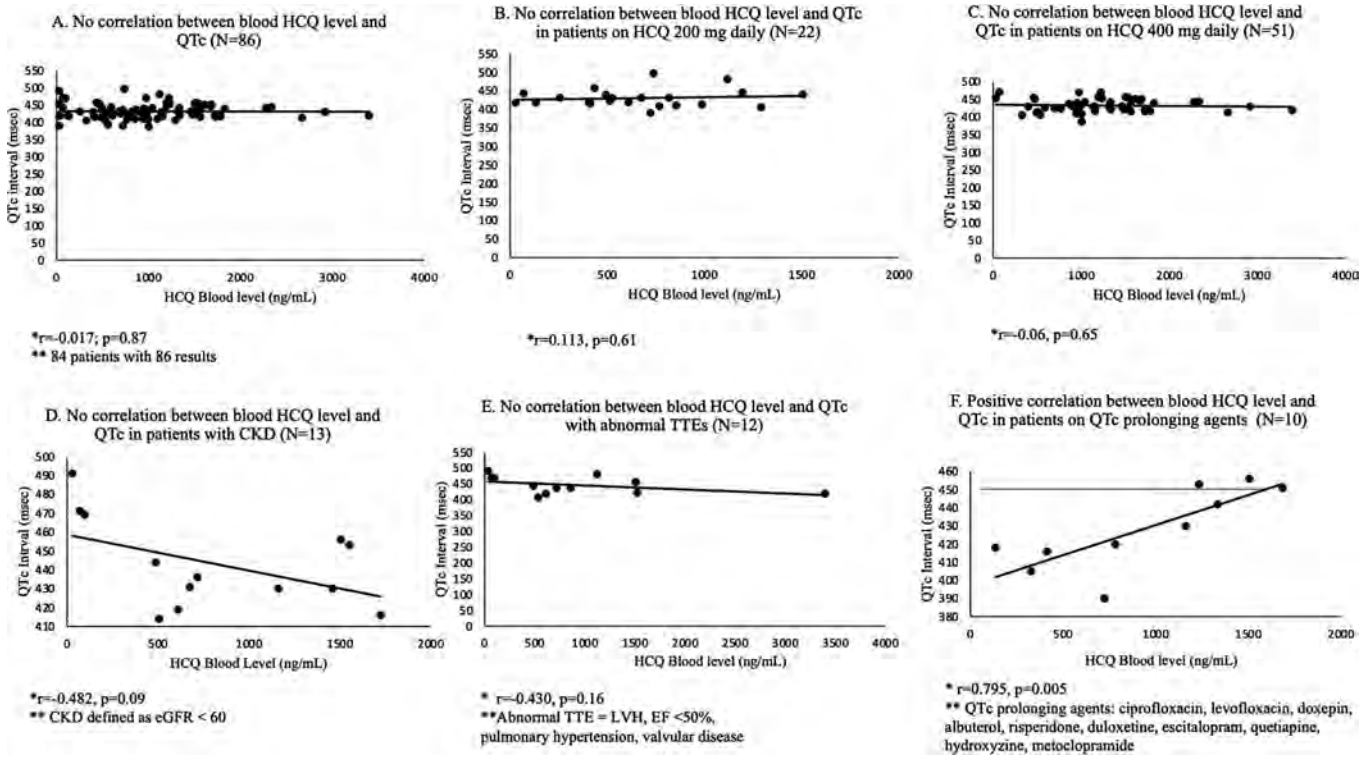
Duration of Exposure (years)	HCQ mean level, ng/mL (mean, +/- SD)
0-5	1385 ± 692
5-10	1099 ± 733
>10	769 ± 493

*p= 0.001; f-ratio=7.489

Table 2C: HCQ blood levels by eGFR

	eGFR <60 (n= 13)	eGFR >60 (n= 73)
HCQ mean level, ng/mL (mean, +/-SD)	815 ± 601	1038 ± 664

*p= 0.262



Additionally, there was no correlation between blood HCQ levels and QTc intervals in patients on 200 mg or 400 mg of HCQ (r=0.113, p=0.61; r=-0.06, p=0.65) (Fig 1b-c). There was no correlation between blood HCQ levels and QTc intervals in patients who had chronic kidney disease (defined as eGFR < 60), (r=-0.482, p=0.09) or those with underlying cardiac abnormalities noted on transthoracic echocardiogram (r=-0.430, p=0.16) (Fig 1d-e). However, there was a positive correlation between blood HCQ levels and QTc intervals in patients who were on concomitant QTc prolonging agents, (r=0.795, p=0.005). but none in excess of 456 msec (Fig 1f).

Conclusion: Our study provides reassurance that hydroxychloroquine is not associated with QTc prolongation in patients with SLE and across different subsets of patients irrespective of blood level, dose prescribed, CKD or underlying cardiac abnormalities. There was a positive correlation between blood HCQ levels and QTc intervals in patients on concomitant QTc prolonging agents, but none were severely prolonged (eg > 500 msec). This is the first study relying on measured blood levels demonstrating the absence of consequential increase in QTc levels in HCQ treated SLE patients.

Disclosure: M. Haj-Ali, None; **H. Belmont**, Alexion, 6.

Abstract Number: 1744

Improvement of Renal and Non-Renal SLE Outcome Measures on Sirolimus Therapy – a 21-year Follow-up Study of 73 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The clinical heterogeneity of the SLE makes it often challenging for the treating clinician and also remains one of the many reasons behind failed treatment trials in the past (1). Sirolimus inhibits the mechanistic target of rapamycin (mTOR), a serine-threonine kinase, which is one of the key drivers behind the

Table 1. Demographic and clinical characteristics of the SLE patients at baseline.
*Mean±SD

Patient characteristics	Nephritis cohort (N=12)	Non-nephritis cohort (N = 61)
Age in Years	40.3 ±15.9*	52.9 ±12.4*
Sex (%)		
Female	9/12 (75%)	57/61 (93.5%)
Male	3/12 (25%)	04/61 (6.5%)
Race (%)		
White	11/12 (91.7%)	52/61 (85.2%)
African American	0/12 (0%)	09/61 (14.8%)
Asian	1/12 (8.3%)	0/61 (0 %)
Other	0/12 (0%)	0/61 (0%)
Duration of sirolimus use in months	35.5 ±28.1*	39.5 ±36.3*
Number of SLICC Criteria Positive	7.08 ±1.24*	5.02 ±1.14*
Serum Creatinine in mg/dL	1.13 ±0.63*	0.85 ±0.24*
Urine protein/creatinine ratio in mg/mg	4.37 ±4.48*	0.12 ±0.08*
Persistent hematuria/Cast (%)	6/12 (50%)	3/61 (4.9%)
Persistent Sterile Pyuria (%)	3/12 (25%)	2/61 (3.3%)
Positive Ds DNA antibody (%)	9/12 (75%)	24/61(39.3%)
Positive Smith antibodies (%)	8/12 (66%)	18/61 (29.5%)
Frequency of hypocomplementemia (%)	11/12 (91.6%)	16/61(26.2%)
Renal biopsy results (%)		
Class III or Class IV	6/12 (50%)	
Class V	4/12 (33.3%)	N/A
Class II	1/12 (8.33%)	
No biopsy available	1/12 (8.33%)	
Dialysis required (%)	1/12 (8.33%)	0/61 (0%)
Renal Transplant required (%)	0/12 (0%)	0/61 (0%)
Number of other medical comorbidities		
Diabetes		
Hyperlipidemia	2/12 (16.6%)	11/61 (18.0%)
Hypertension	1/12 (8.3%)	13/61 (21.3%)
CKD (All causes)	7/12 (58.3%)	23/61 (37.7%)
Vascular disease	12/12 (100%)	9/61 (14.7%%)
	3/12 (25%)	12/61 (19.6%)
Prior use of immunosuppressants for more than 3 months		
Hydroxychloroquine	12/12 (100%)	59/61 (96.7%)
Mycophenolate	12/12 (100%)	44/61 (72.1%)
Azathioprine	4/12 (33.3%)	31/61 (50.8%)
Cyclophosphamide	2/12 (16.66%)	2/61 (3.2%)
Belimumab	5/12 (41.66%)	33/61 (54.1%)
Rituximab	0/12 (0%)	5/61 (8.2%)
Calcineurin inhibitors	1/12 (8.33%)	9/61 (14.75%)
Methotrexate	2/12 (16.6%)	26/61 (42.6%)
Leflunomide	2/12 (16.6%)	19/61 (31.1%)
Prior Chronic Steroid Use (%)	12/12 (100%)	9/61 (14.75%)
SLE related thrombocytopenia, anemia or leukopenia	7/12(58.3%)	9/61 (14.75%)

pro-inflammatory immune cell lineage specification in SLE (2). We herein, aim to define the safety, tolerance and selected renal and non-renal outcome measures in SLE patients who received sirolimus therapy in our institution over the past 21 years.

Table 2. Analysis of Selected Lupus outcome measures on nephritis and non-nephritis lupus cohort with sirolimus treatment. Data are presented as mean and SD for each patient subset. Effect of sirolimus was analyzed with two-tailed paired t-tests and chi-squared test, p values < 0.05 were considered significant (S*): Y, yes; N, no.

Outcome Measures	Nephritis Cohort				Non-Nephritis Cohort			
	Before sirolimus	After sirolimus	p value	S*	Before sirolimus	After Sirolimus	p value	S*
Urine Protein Creatinine ratio mg/mg	4.37 ± 4.48	1.59 ± 2.35	0.0287	Y	0.12 ± 0.07	0.11 ± 0.06	0.6251	N
Serum creatinine (mg/dL)	1.13 ± 0.63	0.93 ± 0.33	0.3330	N	0.85 ± 0.24	0.87 ± 0.34	0.1763	N
Hematuria or red cell cast (N/HPF)	12.6 ± 16.1	1.5 ± 3.1	0.0232	Y	2.1 ± 13.8	2.8 ± 20.0	0.4604	N
Change in sterile pyuria (N/HPF)	9.25 ± 25.5	1.0 ± 0.85	0.2808	N	0.8 ± 3.8	1.0 ± 6.7	0.5882	N
Anti-DNA antibody titers (IU)	244.4 ± 217	63.1 ± 74	0.0028	Y	158.4 ± 56	33.3 ± 45.9	0.0332	Y
C3 levels (mg/dL)	73.4 ± 17.2	104.1 ± 32.6	0.0070	Y	70.6 ± 16.8	94.9 ± 19.5	0.0021	Y
C4 levels (mg/dL)	11.2 ± 6.8	18.3 ± 9.5	0.0063	Y	10.7 ± 6.3	16.7 ± 9.1	0.0042	Y
CH 50 levels (U/ml)	61.2 ± 39	68.7 ± 34	0.4721	N	37 ± 5.5	41 ± 27.8	0.1112	N
Mean steroid dose (mg)	19.4 ± 12.4	2.8 ± 1.9	0.0200	Y	10.25 ± 7.3	2.43 ± 5.1	0.0163	Y
Change in Mycophenolate use	12/12 (100%)	7/12 (58.3%)	0.0593	N	N/A	N/A	N/A	N/A
Change in thrombocytopenia	3/12 (25%)	1/12 (8.3%)	0.2733	N	7/61	6/61 (9.83%)	0.7691	N
Change in leukopenia	2/12 (16.7%)	1/12 (8.3%)	0.5370	N	3/61	4/61 (6.56%)	0.6970	N
Change in SLE related anemia	6/12 (50%)	4/12 (8.3%)	0.4076	N	4/61	3/61 (4.92%)	0.6970	N

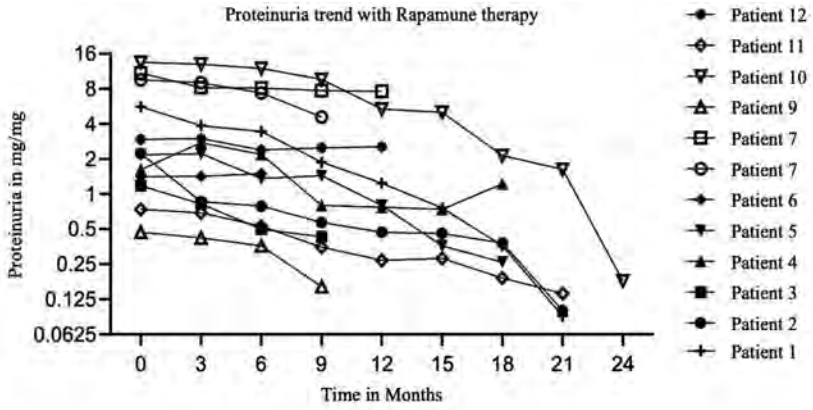

Figure 1. Longitudinal changes in proteinuria (urine protein/creatinine ratio - mg/mg) in twelve patients who received sirolimus therapy. The overall trend depicts the reduction of proteinuria over time.

Methods: We identified a total of 87 SLE patients in our institution who were on sirolimus therapy from March 2000 to March 2021 with the use of Epic EMR slicer-dicer. We included 73 patients, who met the SLE International Collaborating Clinics 2012 criteria and could tolerate sirolimus for at least 3 months (mean duration 38.8±34.9 months), and the rest were excluded. All patients received oral sirolimus with a starting dose of 2 mg daily, and further titrated based on their tolerance to maintain a therapeutic range of 6–15 ng/mL. We evaluated the influence of sirolimus on selected outcome measures. Continuous and categorical variables were analyzed by paired t-test and chi-squared test, respectively. Two-tailed p-value < 0.05 was considered significant.

Results: The details of the baseline demographic and clinical characteristics are summarized in Table 1. The mean age of the total population is 50.6 ± 14.1, consisting of 66/73 (90.4%) females and 7/73 (9.6%) males. The ethnic diversity of the total population consists of 63/73 86.3% whites, 9 (12.3%) African Americans, and (1/73)1.4% Asians. Treatment of active lupus nephritis with sirolimus resulted in a statistically significant reduction in proteinuria (Figure 1), and microscopic hematuria. (Table 2) In the lupus nephritis cohort 12 patients, the reduction was observed in urine protein creatinine ratio (p=0.0287), hematuria (p=0.0232), anti-DNA antibody levels (p=0.0028) and mean steroid dose (p=0.0200). In the non-renal cohort of 61 patients, anti-DNA antibody levels (p=0.0332) and mean steroid dosages were reduced (p=0.0163). Both in the renal and non-renal cohorts, increases of in complement levels C3 (renal p=0.0070; non-renal p=0.0021) and C4 were observed (renal p=0.0063; non-renal p=0.0042). Adverse effects of mouth sores (2/73), headaches (1/73), and gastrointestinal discomfort were noted in a minority of patients (6/73). Sirolimus was only discontinued in two of 73 patients due to headache and recurrent infections, respectively.

Conclusion: This study suggests that sirolimus is well tolerated and exerts long-term therapeutic efficacy in controlling renal and non-renal manifestations of SLE. Double-blind placebo-controlled trials are needed to further substantiate the significance of these findings.

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2. Perl A. Activation of mTOR (mechanistic target of rapamycin) in rheumatic diseases. Vol. 12, Nature Reviews Rheumatology. Nature Publishing Group; 2016. p. 169–82.

Disclosure: P. Piranavan, None; **A. Perl**, None.

Abstract Number: 1745

Pre-pregnancy Switching from Mycophenolate to Azathioprine in Patients with Lupus Nephritis: A Retrospective Outcome Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Mycophenolate Mofetil is not recommended in pregnancy due to teratogenic effects. A previous small prospective study found that switching from MMF to AZA rarely led to renal flares. Our aim was to assess the impact of switching from MMF to AZA on renal flares and pregnancy outcomes in a lupus nephritis cohort.

Methods: A retrospective analysis of the records of patients attending the renal and antenatal clinics at St Thomas's Hospital in London who underwent pre-pregnancy counselling and switched from MMF to AZA was undertaken between January 2019 and December 2020. Inclusion criteria included a diagnosis of SLE based on the 2019 EULAR/ACR classification criteria for SLE and lupus nephritis assessed by a biopsy and classified according to the International Society of Nephrology/Renal Pathology Society 2003 classification. A flare was defined as rising urine PCR, decreasing serum albumin, decreasing serum complement and rising dsDNA antibodies and/or an increase in serum creatinine. Analyses included descriptive statistics [mean (standard deviation) and median (interquartile ranges) for continuous variables and frequency (percent) for categorical values].

Results: Twenty-seven patients were included in this study. 55% were of Afro-Caribbean or Asian background and remaining were Caucasian. The median age at SLE diagnosis was 22 (18-26) years. The average disease duration prior to treatment switch was 8 years. The median time between biopsy and switching was 32 months (17-69). 25.9% of patients had a diagnosis of APS. 48% were Ro positive, while 85.2% were positive for dsDNA antibodies. The median serum creatinine was 69 umol/L (58-84), median serum albumin was 42g/L (38-47) and median PCR was 26.5mg/mol (12-61) prior to switching. Our study showed that 9 patients (33.3%) flared after switching (Table 1). 5 patients (18.5%) flared during pregnancy. 10 (37%) patients went onto have successful pregnancies, 2 (7.4%) had miscarriages, 3 (11.1%) patients developed preeclampsia. 46% of patients with class III/IV Nephritis on biopsy developed complications in pregnancy. 36% of patients with dsDNA had poor pregnancy outcomes compared to 25% who were dsDNA negative. 42.2% of patients of Afro-Caribbean/Asian background flared during pregnancy compared to 25% of their Caucasian counterparts.

Table 1. Characteristics of SLE patients who flared

	No. of women	Flare*	No Flares
Total Number of women	27	9 (33.3%)	18 (66.6%)
Age			
<40	13	6 (46.1%)	7 (53.8%)
>40	14	7 (50%)	7 (50.0%)
Ethnicity			
Afro-Caribbean/Asian	14	4 (28.5%)	9 (64.2%)
Caucasian	12	5 (41.6%)	7 (58.3%)
Serum Albumin (g/L)			
<40	5	4 (80.0%)	1 (20.0%)
>40	19	5 (26.3%)	14 (73.6%)
Serum Creatinine (umol/L)			
<65	10	3 (30.0%)	7 (70.0%)
>65	16	7 (43.7%)	9 (56.2%)
Urine PCR (mg/mol)			
<50	17	5 (29.4%)	12 (70.5%)
>50	5	3 (60%)	2 (40%)
Hypocomplementemia	19	7 (36.8%)	12 (63.1%)
DsDNA positive	23	9 (39.1%)	14 (60.8%)
DsDNA negative	4	1 (25.0%)	3 (75.0%)

***refers to flare after switching and during pregnancy**

Conclusion: Although Azathioprine is an option in patients with lupus nephritis who are planning pregnancy, there is a need to identify patients at risk of a disease flare on switching from MMF. This study showed that patients with low serum albumin, creatinine >65, urine PCR >50 and positive dsDNA antibodies at the time of the switch were more likely to flare after switching and in pregnancy.

Disclosure: S. Ali, None; **S. Sangle**, None; **M. Al Falah**, None; **D. D'Cruz**, None.

Abstract Number: 1746

Baricitinib Decreases Anti-dsDNA and IgG Antibodies in Adults with Systemic Lupus Erythematosus from a Phase 2 Double-Blind, Randomized, Placebo-Controlled Trial

Thomas Dörner[1], Ronald Van Vollenhaven[2], Andrea Doria[3], Bochao Jia[4], Damiano Fantini[4], Jorge Ross Terres[4], Maria Silk[5], Stephanie de Bono[4], Peter Fischer[6] and Daniel Wallace[7], [1]Charite Universitätsmedizin Berlin and Deutsches Rheumaforschungszentrum (DRFZ), Berlin, Germany, [2]University Medical Center, Amsterdam, Netherlands, [3]University of Padova, Padova, Italy, [4]Eli Lilly and Company, Indianapolis, IN, [5]Eli Lilly and Company, Carmel, IN, [6]Eli Lilly and Company, North Easton, MA, [7]Cedars-Sinai, Los Angeles, CA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib (BARI), an oral, selective Janus kinase (JAK)1 and JAK2 inhibitor, improved disease activity in adults with systemic lupus erythematosus (SLE) receiving standard background therapy in a phase 2 trial[1].

There were no meaningful reductions in least squares mean change from baseline (BL) in levels of serologic biomarkers for SLE with BARI treatment, including anti-double-stranded deoxyribonucleic acid (anti-dsDNA) antibodies and complement component (C)3 and C4[1]. The objective was to evaluate the median change from BL in serologic biomarkers in subgroups and the overall population of BARI-treated patients (pts) with SLE, in addition to the SLE Responder Index-4 (SRI-4) response by normalization of anti-dsDNA.

Methods: Data were assessed from the phase 2 trial JAHH (NCT02708095). All pts met ACR or SLICC classification criteria for SLE [2,3]. The median change from BL in anti-dsDNA, IgG, C3, C4, anti-Smith, Anti-cardiolipin IgM (aCL IgM), Anti-cardiolipin IgG (aCL IgG), Anti-cardiolipin IgA (aCL IgA), Anti-nuclear ribonucleoprotein (anti-RNP), Anti- Sjogren's-syndrome-related (SS) antigen-A (Ro/SSA) and Anti-SS antigen-B (Ro/SSB) were evaluated over time among the following populations at BL: anti-dsDNA positive (≥30 IU/mL), low C3 (< 90 mg/dL), low C4 (< 10 mg/dL), anti-Smith (≥30 IU/mL), aCL IgM (>12MPL), aCL IgG (>14 GPL), aCL IgA (>11 APL), anti-RNP (≥30 IU/mL), Ro/SSA and Ro/SSB (>20 IU/mL). Statistical tests were conducted for BARI 2-mg and 4-mg compared with placebo (PBO). Among pts who were anti-dsDNA positive at BL, SRI-4 responder rate was compared for those who stayed positive or achieved normal levels by Week (Wk) 24.

Results: Among pts who were anti-dsDNA positive at BL, significant decreases of anti-dsDNA antibodies were observed for BARI 2-mg and 4-mg compared to PBO beginning at Wks 2 and 4, respectively, and continuing through

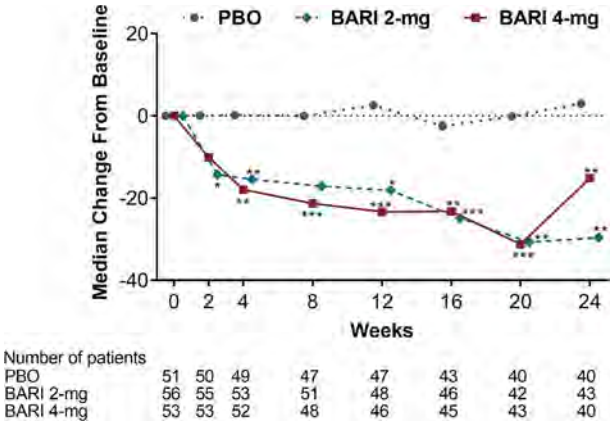

Figure 1. Median change from baseline in anti-dsDNA (IU/mL) (*p≤0.05, **p≤0.01 for BARI vs. PBO, BARI=baricitinib; Ig=immunoglobulin; PBO=placebo).

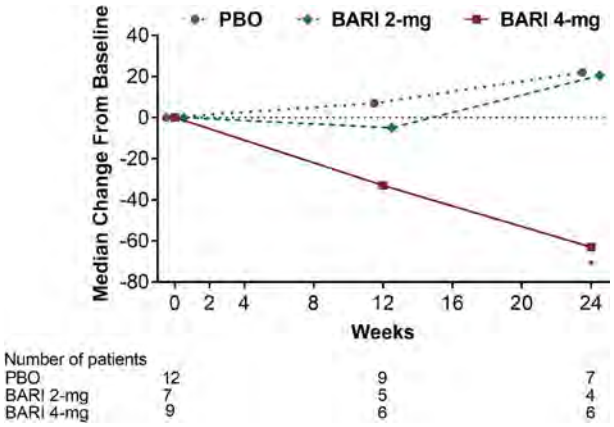

Figure 2. Median change from baseline in Anti-Smith (IU/mL) (*p≤0.05, **p≤0.01 for BARI vs. PBO, BARI=baricitinib; Ig=immunoglobulin; PBO=placebo).

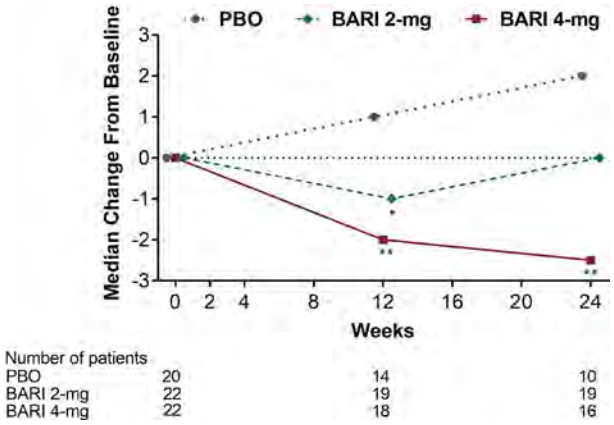

Figure 3. Median change from baseline in Anti-Cardiolipin IgM (IU/mL) (*p≤0.05, **p≤0.01 for BARI vs. PBO, BARI=baricitinib; Ig=immunoglobulin; PBO=placebo).

Wk 24 (Fig 1). Moreover, reductions of IgG levels were found for BARI-treated pts including significant decreases for BARI 4-mg compared to PBO at Wks 12 and 24. Among pts who had low levels of C3 and C4 at BL, no significant differences in median change from BL were observed over time with BARI compared to PBO. Among pts who had high levels of anti-Smith and aCL IgM at baseline, significant decreases in median levels were observed over time for BARI 4-mg compared with PBO (Fig 2 and 3). However, no significant changes in median values from BL were observed for aCL IgG, aCL IgA, anti-RNP, Ro/SSA and Ro/SSB autoantibodies. For pts who were anti-dsDNA positive at BL, no relationship in SRI-4 responder rate was observed for those who stayed positive or achieved normal levels by Wk 24, possibly due to the limited sample size.

Conclusion: BARI treatment resulted in a rapid and sustained significant decrease in anti-dsDNA antibodies compared to PBO among anti-dsDNA positive pts with SLE at BL. Treatment with BARI 4-mg also resulted in a statistically significant decrease in IgG and anti-cardiolipin IgM levels at Wks 12 and 24, and anti-Smith at Wk 24, compared to PBO. These data suggest that BARI may have an effect on B cell activity in SLE.

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[2] Hochberg et al. *Arthritis Rheum* 1997; 1725-1734.

[3] Petri et al. *Arthritis Rheum* 2012; 2677-2686.

Disclosure: T. Dörner, Eli Lilly, 2, Novartis, 2, Janssen, 2, GSK, 2, Sanofi, 2, Deutsche Forschungsgemeinschaft, 5, AbbVie, 2, Roche, 2, Boston Pharmaceuticals, 2; **R. Van Vollenhaven**, Abbvie, 2, 4, 6, Biotest, 2, 4, 6, Eli Lilly and Company, 5, GSK, 5, Janssen, 2, 4, 6, Pfizer, 2, 4, 6, UCB, 2, 4, 5, 6, BMS, Celgene, 2, 4, 5, 6, AstraZeneca, 2, 4, 6, Biogen, 2, 4, 6, Galapagos, 2, 4, 6, Gilead, 2, 4, 6, Servier, 2, 4, 6; **A. Doria**, GSK, 2, 6, Eli Lilly and Company, 6, Janssen, 6, Roche, 6; **B. Jia**, Eli Lilly and Company, 3; **D. Fantini**, Eli Lilly and Company, 3, 11; **J. Terres**, Eli Lilly and Company, 3, 11; **M. Silk**, Eli Lilly and Company, 3, 11; **S. de Bono**, Eli Lilly and Company, 3, 11; **P. Fischer**, Eli Lilly and Company, 3, 11; **D. Wallace**, GlaxoSmithKline, 2, 6, Eli Lilly and Company, 2, 6, AstraZeneca, 2, 6, Aurunia, 2, 6, EMD Serono, 2.

Abstract Number: 1747

BIIB059 Demonstrates Improvement in Joint Manifestations in Participants with Systemic Lupus Erythematosus in Part a of a Phase 2, Randomized, Double-Blind, Placebo-Controlled Study

Ronald van Vollenhoven[1], Richard Furie[2], Kenneth Kalunian[3], Maria Dall'Era[4], Victoria Werth[5], Xiaobi Huang[6], Hua Carroll[6], Cristina Musselli[6], Catherine Barbey[7] and Nathalie Franchimont[6], [1]Department of Rheumatology and Clinical Immunology, Amsterdam University Medical Center, Amsterdam Rheumatology Center, Amsterdam, Netherlands, [2]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [3]UC San Diego, La Jolla, CA, [4]University of California San Francisco, Corte Madera, CA, [5]Philadelphia VAMC, Philadelphia, PA, USA and Department of Dermatology, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [6]Biogen, Cambridge, MA, [7]Biogen, Baar, Switzerland

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

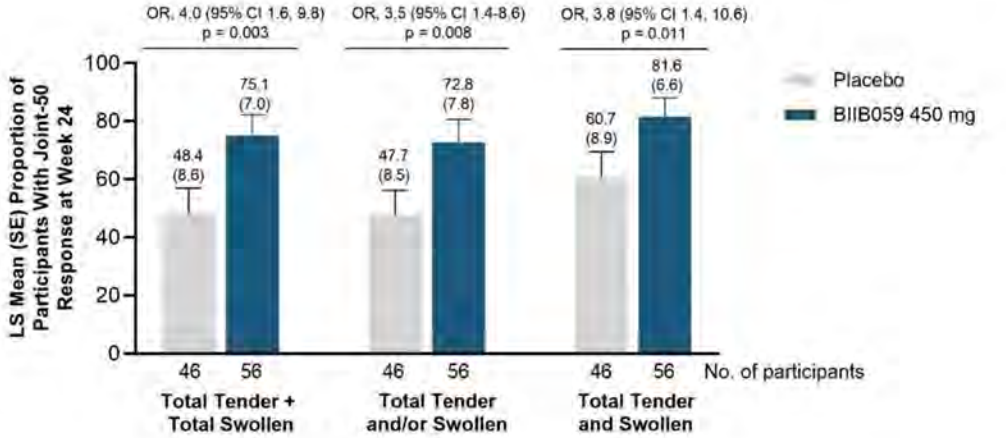
Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Joint involvement, a frequent manifestation of SLE, can be assessed using global lupus disease activity indices (SLEDAI-2K, BILAG-2004) and/or by assessing joint tenderness and swelling (28-joint count).[1] This post-hoc analysis evaluated changes in joint manifestations in the LILAC Part A trial of BIIB059 versus placebo (NCT02847598)[2] using various definitions.

Figure 1. Joint-50 Response at Week 24 With BIIB059 Versus Placebo in LILAC Part A Participants[a,b]



[a]Joint 50 response was defined as a ⩾50% decrease from baseline in joint count based on the following definitions: 1) sum of the tender joints plus the sum of the swollen joints (joints could be counted twice; primary endpoint definition); 2) sum of the joints that are either tender OR swollen (if a joint is both tender and swollen, it is only counted once); 3) sum of the joints that are both tender AND swollen. [b]Participants included in this analysis must have had ≥ 4 tender joints based on assessment of 28 joints. Participants must have had ≥ 4 swollen joints based on assessment of 28 joints, with ≥ 4 of the swollen joints occurring in the proximal interphalangeal, metacarpophalangeal, or wrist joints. Participants who were considered as treatment failures or discontinued treatment are considered as nonresponders at visits post treatment failure or treatment discontinuation. Participants who completed treatment but had a missing score at primary timepoint were classified as nonresponder for that timepoint. Based on generalized linear regression adjusted for treatment, baseline corticosteroid usage level (⩽10 mg, > 10 mg), and region (USA, Asia, Latin America, and Europe), Systemic Lupus Erythematosus Disease Activity Index 2000 at baseline, Physician Global Assessment Visual Analogue Scale at baseline, using a logit link function (logistic regression) for the odds ratios and p-values, and using an identity link function (linear probability model) for the LS means and LS mean differences.

Methods: The randomized, double-blind, placebo-controlled LILAC Part A study enrolled participants who fulfilled 4 of 11 revised ACR 1997 SLE classification criteria[3,4] and who had ≥4 tender and ≥4 swollen joints, active skin disease, and positive lupus antibodies (ANA and/or anti-dsDNA). "Joint-50" response was defined as a 50% reduction from baseline in active joint count at Week 24. Three definitions of total active joint count were used: (1) sum of total tender plus total swollen joints; (2) sum of joints that were tender and/or swollen; (3) sum of joints that were both tender and swollen. Arthritis scored on SLEDAI-2K and BILAG-2004 was also analyzed.

Results: The analysis included 56 and 46 participants treated with BIIB059 450mg and placebo, respectively. At Week 24, a greater proportion of BIIB059-treated participants achieved a Joint-50 response compared to placebo; findings were consistent across the 3 different definitions (Figure 1). The percentage of participants with resolution of arthritis by SLEDAI-2K was greater in BIIB059-treated participants (48.2%) versus placebo (21.7%); similar findings were seen with the BILAG-2004 arthritis (musculoskeletal domain) evaluation. Incidence and severity of adverse events were similar with BIIB059 versus placebo in LILAC Part A.

Conclusion: BIIB059 treatment was associated with improvement in SLE arthritis. More participants achieved a Joint-50 response with BIIB059 versus placebo, regardless of how active joint count was defined.

1. Mahmoud. *Curr Opin Rheumatol*. 2017;29(5):486-492. 2. Furie. *Arthritis Rheum*. 2020;72(S10):0935. 3. Hochberg. *Arthritis Rheum*.1997;40(9):1725. 4.Tan. *Arthritis Rheum*. 1982;25(11):1271-7.

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Abstract Number: 1748

The Peroxisome Proliferator-Activated Receptor-γ (PPAR) Agonist Pioglitazone Improves Vascular and Metabolic Dysfunction in Patients with Systemic Lupus Erythematosus (SLE)

Sarfaraz Hasni[1], Yenealem Temesgen-Oyelakin[2], Michael Davis[3], Sarthak Gupta[4], Elaine Poncio[5], Mohammad Naqi[1], Xinghao Wang[6], Christopher Oliveira[7], Dillon Claybaugh[1], Amit Dey[1], Shajia Lu[1], Philip Carlucci[8], Zerai Manna[1], Yinghui Shi[1], Isabel Ochoa[5], Donald Thomas[9], Theo Heller[10], Massimo Gadina[11], Jun Chu[4], Monica Purmalek[1], Xiaobai Li[12], Martin Playford[13], Nehal Mehta[13] and Mariana Kaplan[1], [1]National Institutes of Health, Bethesda, MD, [2]National Institutes of Health (NIH), Bethesda, MD, [3]NIAMS, Bethesda, MD, [4]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [5]NIH/NIAMS, Bethesda, MD, [6]NIAMS/NIH, Bethesda, MD, [7]National Institutes of Health (NIH), Vienna, VA, [8]New York University School of Medicine, New York, NY, [9]Arthritis and Pain Associates of Prince George's County, Silver Spring, MD, [10]NIDDK/National Institutes of Health, Bethesda, MD, [11]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [12]Clinical Center, National Institutes of Health, Bethesda, MD, [13]NHLBI/National Institutes of Health, Bethesda, MD

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Premature cardiovascular events in SLE are associated with significant mortality and morbidity with no effective treatments described to date. Both immune dysregulation characteristics of SLE and metabolic disturbances appear to play a prominent role in the induction of vascular disease. In previous studies, the peroxisome proliferator-activated receptor (PPAR) agonist pioglitazone (PGZ) suppressed lupus phenotype, immune dysregulation, organ damage and vasculopathy in murine lupus. In human lupus peripheral blood mononuclear cells (PBMCs), in vitro PGZ modified T cell-specific responses and suppressed effector function. We hypothesized that PGZ could improve markers of vascular dysfunction and improve cardiometabolic parameters in SLE.

Methods: Eighty SLE subjects with mild to severe disease activity (SLEDAI 2K score between 4-20) were randomized to a sequence of PGZ (titrated up to 45 mg/day)followed by placebo for 3 months, or vice versa, in a 1:1 allocation ratio in a double-blind cross-over design with a 2 month wash out period. The primary endpoints were parameters of vascular endothelial function as measured by non-invasive multimodal vascular function studies. In a subset of patients, arterial inflammation was assessed by fluorodeoxyglucose positron emission tomography CT (FDG PET/CT). Additional outcome measures of disease activity, metabolic disturbances, adverse events (AEs), and gene expression studies were performed.

Results: A total of 72 subjects completed the study. The use of PGZ was associated with a decrease of 0.322±0.75 (mean±SD) in cardio ankle vascular index (CAVI) values compared to the placebo (0.02±0.65, p=0.005). Metabolic parameters also improved with PGZ, including the homeostasis model assessment of insulin resistance (HOMA2 IR) (p=0.0003), HDL-C (p=0.008), HDL particle size and number (p=< 0.0001; p=0.0009, respectively), and triglycerides (p=0.005). There were 249 predominantly mild adverse events (AE), 52.61% on PGZ and 47.39% on placebo. Most of the AEs experienced while on PGZ were related to fluid retention and mild transaminitis, which resolved with reduction in PGZ dose.

Conclusion: PGZ was well tolerated in SLE subjects with mild to severe disease activity. There was a significant improvement in vascular stiffness as well as improved cardiometabolic parameters. The results suggest that PGZ should be further explored as a modulator of cardiovascular disease risk in non-diabetic SLE patients.

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Abstract Number: 1749

Treatment Patterns in Latin American Patients with Lupus Nephritis over a 20-year Period

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SESSION INFORMATION

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Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex and heterogeneous autoimmune disease. Over the last decade, changes have occurred in the treatment of these patients, related to the inclusion of new agents, the strong recommendation to use lower doses of glucocorticoids and data favoring the use of antimalarials. The aim of this study is to describe lupus nephritis (LN) treatments in two Latin American cohorts over a 20-year period.

Methods: Two cohorts from the Latin American Lupus Study Group (GLADEL, *Grupo Latino Americano De Estudio del Lupus*) have been evaluated. The first, GLADEL 1.0, is an inception cohort started in 1997 that up to 2002 enrolled 1,480 patients; the second, GLADEL 2.0, is an observational prevalent and incident cohort initiated in 2019 that so far has enrolled 880 patients. In both cohorts, LN has been defined by kidney biopsy according to the International Society of Nephrology and Renal Pathology Society, and includes two groups: non-proliferative (class II/V) and proliferative (III/IV). The different therapeutic regimens used in both cohorts are described. In addition, the sociodemographic and serological variables and the histological characteristics are compared. Numeric variables are reported as medians (interquartile ranges) and compared using Mann-Whitney test; categorical variables are reported as frequencies (percentages) and compared using Chi-square or Fisher test, as appropriate.

Results: A total of 546 patients with LN diagnosis have been included; 362 from GLADEL 1.0 and 184 from GLADEL 2.0. One hundred and two and 35 patients form the respective cohorts were classified into LN-Class II/V; 260 and 149 patients were classified into LN-Class III/IV (Table1). LN patients from GLADEL 2.0 had longer disease duration, [months, median (Q1-Q3)] [73 (33-141) vs. 54 (32-75), p< 0.0001] compared to GLADEL 1.0. The comparison of the sociodemo-

Table 1. Comparison of the different treatments used in both GLADEL cohorts

Treatment	Class II/V		p value	Class III/IV		p-value
	GLADEL 1.0 (n=102)	GLADEL 2.0 (n=35)		GLADEL 1.0 (n=260)	GLADEL 2.0 (n=149)	
Oral Glucocorticoids; n(%)	91 (89.2)	31 (88.5)	0.999	230 (88.5)	135 (90.6)	0.501
Intravenous (IV) glucocorticoids; n(%)	26 (25.5)	8 (22.9)	0.756	103 (39.6)	46 (30.9)	0.077
Antimalarials; n(%)	55 (53.9)	31 (88.6)	0.003	87 (33.5)	123 (82.5)	<0.0001
Azathioprine; n(%)	19 (18.6)	0 (0.00)	0.004	35 (13.5)	11 (7.4)	0.061
Intravenous (IV) cyclophosphamide; n(%)	43 (42.2)	4 (11.4)	0.001	208 (80.0)	43 (28.9)	<0.0001
Intravenous (IV) immunoglobulin; n(%)	2 (1.9)	1 (2.9)	0.999	2 (0.8)	2 (1.3)	0.625
Cyclosporin; n(%)	0 (0.0)	1 (2.9)	0.256	2 (0.8)	0 (0.0)	0.536
Mycophenolate mofetil; n(%)	—	25 (71.4)	—	—	75 (50.3)	—
Tacrolimus; n(%)	—	4 (11.4)	—	—	13 (8.7)	—
Rituximab; n(%)	—	4 (11.4)	—	—	11 (7.4)	—
Belimumab; n(%)	—	0 (0.0)	—	—	0 (0.0)	—
Plasma exchange; n(%)	—	0 (0.0)	—	—	1 (0.7)	—

graphic variables showed that patients from GLADEL 2.0 have a higher proportion of Mestizos (71.2% vs. 44.4%), had a higher proportion of higher and middle socioeconomic status (19.6% vs. 5.5%, and 42.9% vs. 32.0%, respectively, p< 0.0001), and a higher level of formal education [years, median (Q1-Q3)] (13 (11-16) vs. 11 (7-139), p< 0.0001)]. In GLADEL 1.0, a higher number of patients with LN-Class III/IV had Hypocomplementemia (65.4% vs. 43.6%, p< 0.0001), and anti-dsDNA antibodies (58.1% vs 36.2), p< 0.0001) when compared with patients from GLADEL 2.0.

In GLADEL 2.0 a statistically significant increase in the use of antimalarials and decrease in the use of IV cyclophosphamide were observed. Azathioprine showed the same tendency as IV cyclophosphamide but no statistical significance was reached. As expected, new drugs were incorporated into the treatment scheme, mainly mycophenolate mofetil and less frequently tacrolimus and rituximab.

Conclusion: The management of LN in Latin America has changed over the last 20 years. New treatments have been included, there has been a trend towards a high use of mycophenolate mofetil and a decrease of cyclophosphamide. A higher use of antimalarials over time has also been observed.

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Abstract Number: 1750

Itolizumab, a Novel anti-CD6 Therapy, in Systemic Lupus Erythematosus Patients: Interim Safety Results from the Phase 1b EQUALISE Dose-escalation Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: CD6, a co-stimulatory receptor predominantly expressed on T cells, promotes CD4+ T cell proliferation and differentiation into Th1/Th17 cells. The CD6 ligand, activated leukocyte cell adhesion molecule

Table 1. Baseline demographics of study participants

Baseline Characteristic	Cohort 1 (0.4 mg/kg) N=6	Cohort 2 (0.8 mg/kg) N=7	Cohort 3 (1.6 mg/kg) N=7	Cohort 4 (2.4 mg/kg) N=6	Cohort 5 (3.2 mg/kg) N=8	Total N=34
Age (years) Mean (SD)	59.5 (12.9)	44.6 (16.2)	47.1 (6.8)	48.2 (11.6)	57.3 (9.4)	51.4 (12.5)
Sex (F/M)	6/0	7/0	6/1	6/0	7/1	32/2
Race (White/Black or African American)	3/3	5/2	6/1	5/1	6/2	25/9
Ethnicity: Hispanic or Latino (Y/N)	4/2	5/2	3/4	4/2	0/8	16/18
SLEDAI-2K Mean (SD)	7.0 (2.5)	7.1 (4.3)	7.1 (1.6)	5.7 (2.9)	6.0 (3.1)	6.6 (2.9)
Current use of low dose corticosteroids n (%)	4 (66.7%)	1 (14.3%)	1 (14.3%)	2 (33.3%)	1 (12.5%)	9 (26.5%)
eGFR (ml/min/1.73m^2) Mean (SD)	97.2 (17.6)	110.1 (25.3)	92 (23.0)	104.7(17.1)	90.6 (15.8)	98.6 (20.4)
C3 (mg/dL) Mean (SD)	138 (22) Ref range 81-157	133 (31) Ref range 81-157	123 (37) Ref range 81-157	141 (28) Ref range 83-193	132 (24) Ref range 83-193	-
C4 mg/dL Mean (SD)	26 (11) Ref range 13-39	33 (12) Ref range 13-39	29 (10) Ref range 13-39	37 (17) Ref range 15-57	27 (6) Ref range 15-57	-
Anti-dsDNA (IU/ml) Mean (SD)	24 (32) Positive >36	33 (44) Positive >36	8 (6) Positive >36	37 (44) Positive > 50	19 (10) Positive > 50	-

Table 2. Summary of types of adverse events by cohort

Subjects with:	Cohort 1 (0.4 mg/kg) N=6	Cohort 2 (0.8 mg/kg) N=7	Cohort 3 (1.6 mg/kg) N=7	Cohort 4 (2.4 mg/kg) N=6	Cohort 5 (3.2 mg/kg) N=8	Total (N=34)
Any Adverse Event	0	2 (28.6%)	4 (57.1%)	3 (50.0%)	7 (87.5%)	16 (47.1%)
Any Serious Adverse Event	0	0	0	0	1 (12.5%)	1 (2.9%)
Treatment-Related TEAEs	0	2 (28.6%)	4 (57.1%)	3 (50.0%)	5 (62.5%)	14 (41.2%)
TEAEs by Maximum CTCAE Severity Grade						
Grade 1 - Mild	0	2 (28.6%)	2 (28.6%)	2 (33.3%)	0	6 (17.6%)
Grade 2 - Moderate	0	0	2 (28.6%)	0	6 (75.0%)	8 (23.5%)
Grade 3 - Severe	0	0	0	1 (16.7%)	1 (12.5%)	2 (5.9%)
Grade 4/5 - Life-threatening/death	0	0	0	0	0	0
TEAEs Leading to Withdrawal of Treatment	0	0	1 (14.3%)	1 (16.7%)	0	2 (5.9%)
TEAEs Leading to Death	0	0	0	0	0	0

(ALCAM), is expressed on antigen presenting cells, as well as epithelial and endothelial cells. Itolizumab (ITO) is a humanized IgG1 monoclonal antibody that binds CD6 and blocks ALCAM interaction to inhibit T cell activation and trafficking. ITO is being evaluated as a treatment for systemic lupus erythematosus (SLE) and lupus nephritis (LN).

Methods: EQUALISE is an open-label Phase 1b 2-part study that is evaluating the safety, pharmacokinetics (PK), pharmacodynamics (PD), and clinical activity of subcutaneous doses (SC) of ITO (0.4 to 3.2 mg/kg). Part A enrolled

adult patients with active or inactive SLE who had received ≥1 SLE treatment. Treated subjects received ITO SC Q2 weeks x 2. Part B of the study, which is evaluating ITO treatment of subjects with active proliferative Class III/IV LN for 24 weeks, is currently enrolling (NCT04128579).

Results: Part A enrolled 34 subjects in 5 cohorts: 0.4 mg/kg (n=6), 0.8 mg/kg (n=7), 1.6 mg/kg (n=7), 2.4 mg/kg (n=6), and 3.2 mg/kg (n=8). Similar baseline characteristics were noted across cohorts. The mean age was 51, with 94% female, 74% white (47% Hispanic) and ~11 years since SLE diagnosis (Table 1). The mean baseline SLEDAI-2K was 6.6.

SC dosing of cohorts 1-4 (0.4 mg/kg through 2.4 mg/kg (N=26)) was well tolerated (Table 2), with 3 subjects not receiving both doses, 1 due to a protocol eligibility deviation and 2 due to adverse events (AEs) (lymphopenia and urticaria). The most frequent AEs reported in these cohorts were mild to moderate injection site reactions. No serious adverse events (SAEs) were reported. For Cohort 5 (3.2 mg/kg), 8 subjects received at least 1 SC dose of ITO in at least 2 separate injection sites. In this cohort >85% of subjects reported an AE, the most common being injection site reactions, mainly moderate grade 2 reactions with erythema or pruritis. One subject (3.2 mg/kg) experienced 1 SAE (hypotension and syncope) that occurred in the follow-up period > 40 days after ITO. 4 subjects (50%) in Cohort 5 (3.2mg/kg) discontinued treatment after 1 dose. Across all cohorts, there were no notable changes in vital signs, ECGs, or safety lab parameters, with the exception of transient declines in absolute lymphocyte counts without clinical sequelae.

Preliminary PK results indicate dose-proportional increases in ITO exposure and rapid and dose-dependent decreases in CD4 cell surface expression of CD6, a PD marker of target engagement.

Conclusion: 2 SC doses of ITO up to 2.4 mg/kg in SLE subjects were well tolerated. There was reduced tolerability to the 3.2 mg/kg dose with 50% of patients discontinuing after the first dose. The PK, PD and safety data to date support continued evaluation of ITO in SLE/LN and other chronic autoimmune diseases. The ongoing EQUALISE Part B will assess ITO safety and efficacy in Class III/IV LN patients.

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Voclosporin Is Effective in Achieving Complete Renal Response Across Lupus Nephritis Biopsy Classes: Pooled Data from the AURA-LV and AURORA 1 Trials

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Voclosporin is a novel calcineurin inhibitor recently approved for the treatment of adult patients with active lupus nephritis in combination with background immunosuppressive therapy. Voclosporin has a favorable metabolic profile and a consistent dose-concentration relationship, eliminating the need for therapeutic drug monitoring. Pooled data from the similarly designed Phase 2 AURA-LV and the Phase 3 AURORA 1 trials demonstrated that compared with standard of care agents (mycophenolate mofetil [MMF] and low-dose steroids) alone, the addition of voclosporin resulted in higher complete renal response rates (CRR) at 24 weeks (31.7% vs 20.3%; odds ratio [OR] 2.01; p=0.0008) and one year (43.7% vs 23.3%; OR 2.76; p< 0.0001) of treatment in patients with lupus nephritis. This abstract reports CRR by biopsy class in the same pooled data.

Methods: AURA-LV and AURORA 1 enrolled patients with a diagnosis of systemic lupus erythematosus according to ACR criteria, biopsy-proven active lupus nephritis (Class III, IV, or V ± III/IV) and proteinuria of ≥1.5 mg/mg (≥2 mg/mg for Class V). Treatment randomization was stratified by biopsy class (Class V only vs Others) and by MMF use at screening. Pooled data included 268 patients in the voclosporin (23.7 mg BID) arm (89 from AURA-LV and 179 from AURORA 1) and 266 patients in the control arm (88 from AURA-LV and 178 from AURORA 1). All patients received MMF (1 g BID) and low-dose steroids (rapidly tapered to 2.5 mg/day at week 16). Though the trials were not powered to detect a significant difference between treatments groups by biopsy class, a post-hoc analysis of CRR by biopsy class subgroups was conducted.

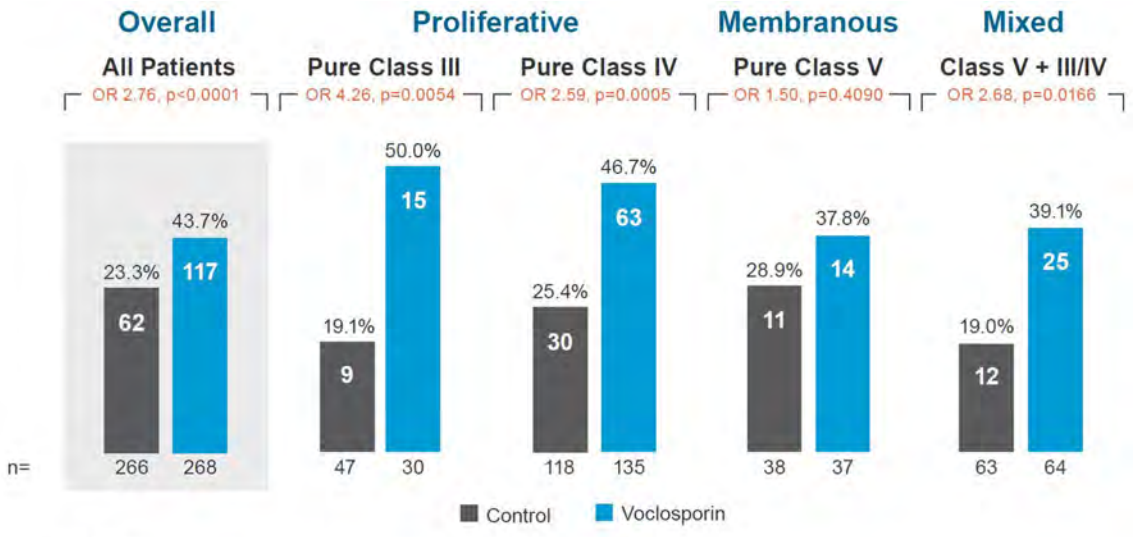
Results: Demographic and clinical characteristics of the pooled population are shown in Table 1. The pooled analysis includes 79 (14.8%) patients with pure Class III, 253 (47.4%) with pure Class IV, 75 (14.0%) with pure Class V, and 127 (23.8%) with mixed Class V + III/IV lupus nephritis. The OR for CRR at one year in the voclosporin arm compared to control arm was 4.26 for pure Class III, 2.59 for pure Class IV, 1.50 for pure Class V, and 2.68 for mixed Class V + III/IV (Figure 1). Overall, 93.7% of patients in the voclosporin arm and 75.2% of patients in the control arm achieved ≥50% reduction from baseline in UPCR; the median time to ≥50% reduction in UPCR was 29 days for voclosporin arm and 58 days for the control arm (HR 1.96; log rank p< 0.0001; Figure 2). At 6 months, 83.2% of patients in the voclosporin arm and 85.0% of patients in the control arm were on ≤2.5 mg/day prednisone. At 12 months, 75.8% and 73.9% of patients in each arm, respectively, were on prednisone ≤2.5 mg/day.

Table 1. Baseline and Demographic Characteristics

	Control (n=266)	Voclosporin (n=268)
Age, years		
Median (Min, Max)	32.0 (18, 72)	30.0 (18, 66)
Race, n (%)		
White	103 (38.7)	98 (36.6)
Asian	92 (34.6)	105 (39.2)
Black	24 (9.0)	29 (10.8)
Other	47 (17.7)	36 (13.4)
Ethnicity, n (%)		
Hispanic or Latino	72 (27.1)	66 (24.6)
Not Hispanic or Latino	193 (72.6)	202 (75.4)
Unknown	1 (0.4)	0
Region, n (%)		
North and Latin America	93 (35.0)	87 (32.5)
USA	32 (12.0)	31 (11.6)
Asia	87 (32.7)	104 (38.8)
Europe and South Africa	86 (32.3)	77 (28.7)
eGFR, mL/min/1.73 m^2		
Median (Min, Max)	98.0 (25.0, 153.0)	92.0 (39.0, 168.0)
UPCR, mg/mg		
Median (Min, Max)	3.1 (0.8, 19.3)	3.5 (0.2, 29.7)
Biopsy Class, n (%)		
Pure Class III	47 (17.6)	32 (11.9)*
Pure Class IV	118 (44.4)	135 (50.4)
Pure Class V	38 (14.3)	37 (13.8)
Mixed Class V + III/IV	63 (23.7)	64 (23.9)

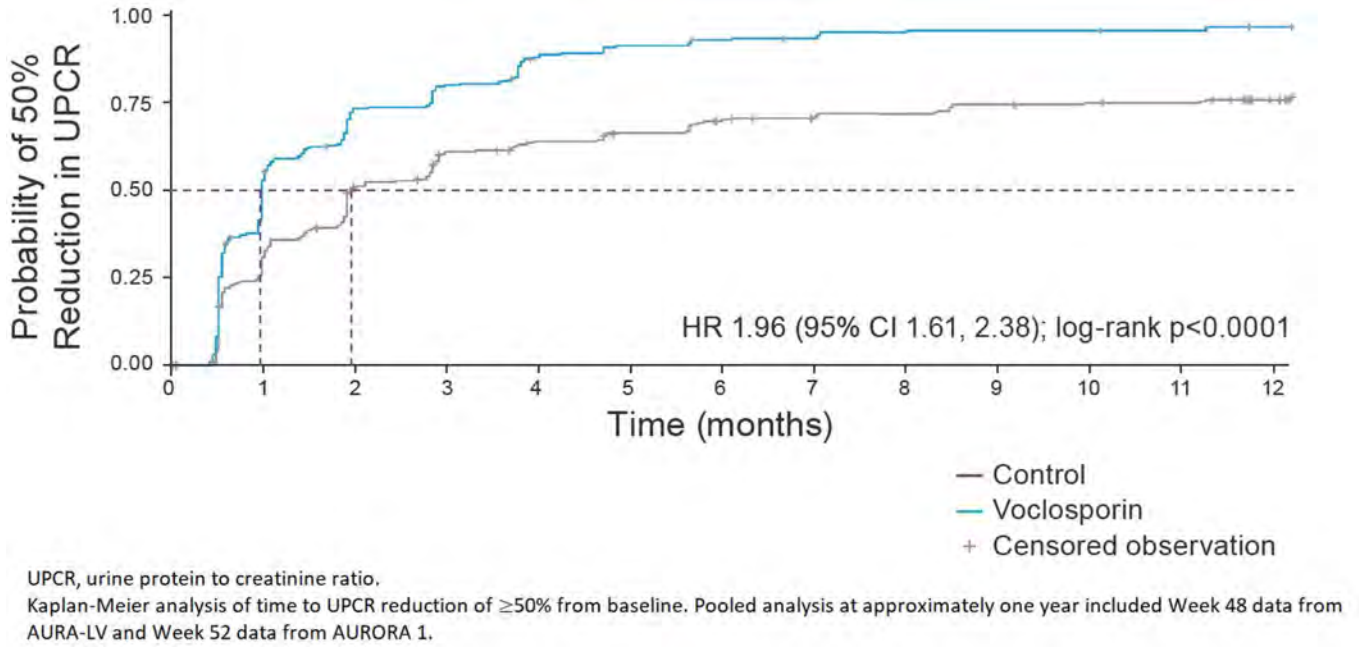
eGFR, estimated glomerular filtration rate; Max, maximum; Min, minimum; UPCR, urine protein to creatinine ratio.
*After the biopsy subgroup analysis was conducted, an additional two patients were identified to have pure Class III lupus nephritis that are not included in the subgroup analysis.

Conclusion: Patients with lupus nephritis treated with voclosporin in addition to MMF and low-dose steroids had improved CRR rates (OR >1) across all biopsy class subgroups compared to the control arm, with the highest OR seen in pure Class III. This analysis further supports the efficacy of voclosporin and the critical need to consider lower doses of steroids in the treatment of lupus nephritis.



OR, odds ratio.
Complete renal response defined as UPCR ≤0.5 mg/mg, stable renal function (eGFR ≥60 mL/min/1.73 m^2 or no decrease >20% from baseline), presence of sustained, low-dose steroids (in the 8 weeks prior to assessment) and no rescue medication. Pooled analysis at approximately one year included Week 48 data from AURA-LV and Week 52 data from AURORA 1.

Figure 1. Complete Renal Response by Biopsy Class at One Year.



UPCR, urine protein to creatinine ratio.
Kaplan-Meier analysis of time to UPCR reduction of ≥50% from baseline. Pooled analysis at approximately one year included Week 48 data from AURA-LV and Week 52 data from AURORA 1.

Figure 2. Time to UPCR Reduction of ≥50%.

Disclosure: A. Askanase, GSK, 2, 5, AstraZeneca, 1, 5, Amgen, 1, Aurinia, 2, Abbvie, 1, Pfizer, 5, Eli Lilly, 5, Idorsia, 5; **S. Randhawa**, Aurinia Pharmaceuticals Inc., 3, 11; **L. Lisk**, Aurinia Pharmaceuticals Inc., 3, 11; **P. Mina-Osorio**, Aurinia Pharmaceuticals Inc., 3, 11.

Abstract Number: 1752

Efficacy of Voclosporin in Recent Onset Lupus Nephritis

Meggan Mackay[1], Matt Truman[2], Nicole England[2], Vanessa Birardi[3] and Paola Mina-Osorio[4], [1]Feinstein Institutes for Medical Research, Manhasset, NY, [2]Aurinia Pharmaceuticals Inc., Victoria, BC, Canada, [3]Aurinia Pharmaceuticals Inc, Rockville, MD, [4]Aurinia Pharmaceuticals Inc., New York, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Voclosporin is a novel calcineurin inhibitor recently approved for the treatment of adults with active lupus nephritis (LN) in combination with background immunosuppressive therapy. Voclosporin has a favorable metabolic profile and a consistent dose-concentration relationship eliminating the need for therapeutic drug monitoring.

Previously reported results from the Phase 3 AURORA 1 study and the Phase 2 AURA-LV study showed that compared with mycophenolate mofetil (MMF) and low-dose steroids, the addition of voclosporin significantly increased the complete renal response (CRR) rate and reduced proteinuria, as measured by urine protein-creatinine ratio (UPCR), in patients with LN at approximately one year of treatment (48 weeks in AURA-LV and 52 weeks in AURORA 1).

Table 1. Demographic and Baseline Characteristics

Parameter	Recent LN Onset <6 months (N=91)	LN Onset >6 Months (N=216)
Sex, n (%)		
Male	9 (9.9)	28 (13.0)
Female	82 (90.1)	188 (87.0)
Race, n (%)		
White	27 (29.7)	82 (38.0)
Asian	24 (26.4)	74 (34.3)
Black	14 (15.4)	19 (8.8)
Other	26 (28.6)	41 (19.0)
Ethnicity, n (%)		
Hispanic or Latino	38 (41.8)	57 (26.4)
Not Hispanic or Latino	52 (57.1)	159 (73.6)
Unknown	1 (1.1)	
Time since LN diagnosis, years		
Mean (SD)	0.2 (0.1)	5.4 (5.3)
Time since SLE diagnosis, years		
Mean (SD)	2.6 (4.3)	7.2 (6.0)
eGFR, mL/min/1.73 m^2		
Mean (SD)	90.6 (28.6)	88.6 (30.2)
UPCR, mg/mg		
Mean (SD)	4.3 (2.7)	4.0 (2.5)
Complement 3		
Mean (SD), mg/dL	71.6 (29.4)	87.0 (36.8)
Low (<90 mg/dL), n (%)	64 (70.3)	116 (53.7)
Anti-dsDNA		
Mean (SD), IU/mL	111.4 (129.6)	107.7 (129.4)
High (≥10), n (%)	72 (79.1)	157 (72.7)

anti-dsDNA, anti-double stranded DNA; eGFR, estimated glomerular filtration rate; LN, lupus nephritis; SD, standard deviation; UPCR, urinary protein-creatinine ratio.

We describe here the results of a post-hoc analysis of AURORA 1 to assess whether patients with recent onset LN treated with voclosporin respond similarly to the overall population.

Methods: Patients with a diagnosis of systemic lupus erythematosus according to ACR criteria, biopsy-proven (Class III, IV, or V ± III/IV) LN and proteinuria of ≥1.5 mg/mg (≥2 mg/mg for pure Class V) were eligible to enroll in AURORA 1. Overall, 179 patients were randomized to the voclosporin (23.7 mg BID) arm and 178 patients were randomized to receive placebo treatment in the control arm. All patients received MMF (1 g BID) and low-dose oral steroids (tapered over 16 weeks to 2.5 mg/day).

In this post-hoc analysis, 45 patients in the voclosporin arm and 46 patients in the control arm were identified as having recent onset LN, defined as LN diagnosis within an estimated 6 months of study start based on reported year of diagnosis, study start date and date of biopsy. Disease duration and baseline clinical characteristics were evaluated and compared with the rest of the trial population to ensure the population was relevant to patients with recent onset disease seen in clinical practice (Table 1). Patients with biopsy pure class V LN (n=50) were excluded. Achievement of CRR (defined as UPCR ≤0.5 mg/mg with stable renal function in the presence of sustained, low-dose steroids and no rescue medication) was assessed at approximately one year of treatment.

Results: Patients with recent onset LN (n=91) had a mean (SD) LN disease duration of 0.2 (0.1) years compared to 5.4 (5.3) years for the rest of the population (n=216); baseline demographic and clinical characteristics were similar

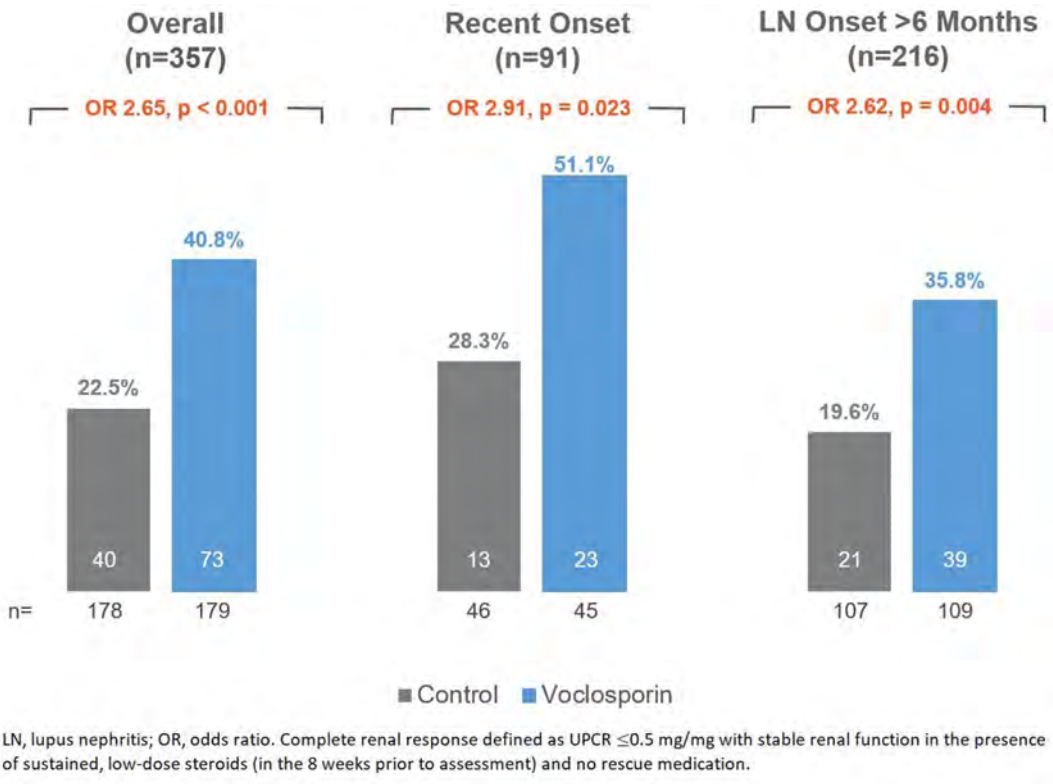


Figure 1. Complete Renal Response Rates at One Year in the Overall Patient Population, Recent Onset Disease, and Disease Onset >6 Months.

between the treatment arms (Table 1). Among recent onset patients, CRR was significantly increased in the voclosporin arm compared to the control arm (CRR of 51.1% vs 28.3%, respectively; OR 2.91; p=0.023) at one year of treatment (Figure 1).

Conclusion: Patients with recent onset LN treated with voclosporin in combination with MMF and low-dose steroids had clinically meaningful reductions in proteinuria and achieved significantly higher rates of CRR compared to patients treated with MMF and low-dose steroids alone. The efficacy benefit of voclosporin in recent onset LN patients is comparable with the efficacy in the overall population of patients participating in the Phase 3 AURORA 1 study. This post-hoc analysis also suggests significant efficacy benefit in the population with much longer duration of LN.

Disclosure: M. Mackay, None; **M. Truman**, Aurinia Pharmaceuticals Inc., 2; **N. England**, Aurinia Pharmaceuticals Inc., 3, 11; **V. Birardi**, Aurinia Pharmaceuticals Inc., 3, 11; **P. Mina-Osorio**, Aurinia Pharmaceuticals Inc., 3, 11.

Abstract Number: 1753

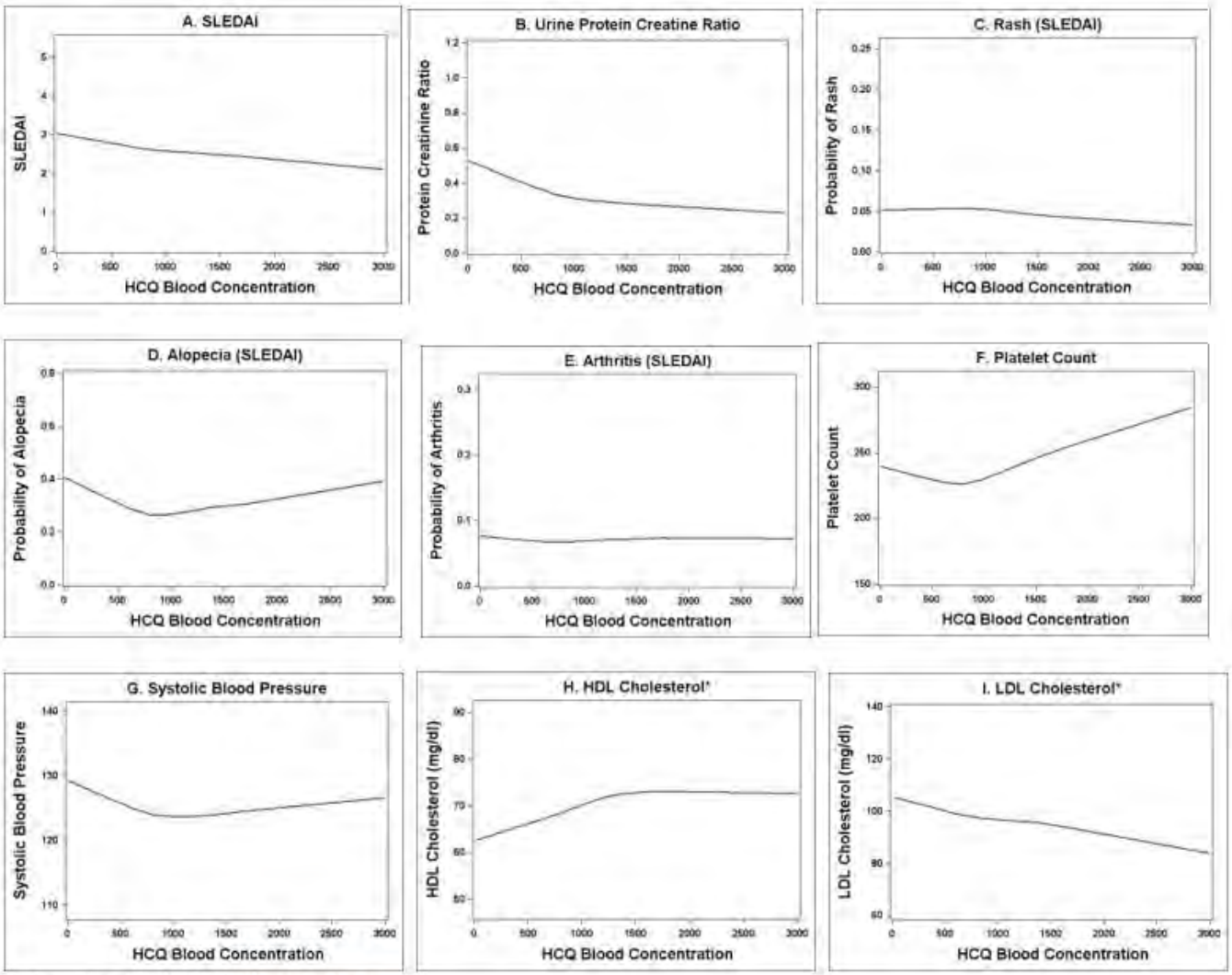
Hydroxychloroquine Blood Levels Are Associated with Reduced SLE Disease Activity and Improvements in Cardiovascular Risk Factors

Laurence Magder[1], Michelle Petri[2] and Daniel Goldman[2], [1]University of Maryland, Baltimore, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: In SLE, treatment with hydroxychloroquine (HCQ) has been shown to be associated with reduced SLE flares and reduced risk of damage in several different organ systems. However, high HCQ blood levels

Figure 1. Estimated mean levels of various physiologic measures by blood concentration of HCQ (ng/ml)



* Based on only 323 observations

Table 1. Association between changes in HCQ blood levels and changes in various physiologic measures in consecutive visits.

Physiologic Measure	Changes in physiologic measures per 500 ng/ml change in HCQ levels			
	In the range of 0 to 1000	P-value	In the range of 1000-3000	P-value
SLEDAI	-0.11	0.059	-0.08	0.051
Urine Protein Creatinine Ratio	-0.038	0.0055	0.010	0.33
Probability of Rash	-0.005	0.27	0.000	0.97
Probability of Alopecia	0.014	0.079	0.008	0.15
Probability of Arthritis	-0.008	0.20	0.002	0.71
Platelet count (10^3 / mm^3)	2.63	0.0025	7.11	<0.0001
Systolic Blood Pressure (mmHg)	-1.24	<0.0001	-1.14	<0.0001
High Density Lipoprotein (mg/dl)	0.51	0.69	0.02	0.98
Low Density Lipoprotein (mg/dl)	-5.29	0.084	-0.99	0.67

over time are associated with retinopathy. To provide insight into the optimal treatment strategy, we determined the level of blood HCQ concentration needed for protection against several different manifestations of SLE disease.

Methods: The analysis was based on data from a large single-center clinical cohort of patients with SLE. Since 2013, whole blood levels of HCQ were measured at quarterly clinic visits among patients prescribed HCQ using liquid chromatography–tandem mass spectrometry. At each visit, numerous disease activity measures were performed (a visual analog scale for each organ and SLEDAI). Initially, we used loess to examine the shape of the cross-sectional relationship between blood levels of HCQ and average values of disease activity or cardiovascular risk factors. We then examined the association between changes in HCQ and concurrent changes in disease activity in consecutive visits from the same patient using a mixed effects model.

Results: The analysis was based on 10,370 clinic visits from 1095 different patients who were predominately Caucasian (46%) or African American (43%). Figure 1 shows the cross-sectional relationship between HCQ blood levels and various measures of SLE disease activity and other physiologic measures. Higher HCQ blood levels were associated with lower mean SLEDAI (Fig 1A), lower urine protein-creatine ratio (Fig 1B), lower systolic blood pressure (Fig 1G) and higher platelet counts (Fig 1F). For some measures, the relationship was strongest over HCQ concentrations in the range of 0 to 1000 ng/ml. Table 1 shows the association between changes in HCQ concentration between two consecutive visits and concurrent changes in physiologic measures. Within a patient, increases in HCQ concentration in the range of 0 to 1000 ng/ml were associated with decreases in urine protein-creatinine ratio, decreases in systolic blood pressure, and increases in platelets. Increases in the range of 1000 to 3000 ng/ml were associated with decreases in systolic blood pressure and increases in platelet counts. Surprisingly, changes in blood concentration were not significantly associated with changes in skin or joint manifestations of SLE.

Conclusion: We found that small but statistically significant improvements in physiologic measures are associated with increases in blood HCQ concentration. Interestingly, for most measures, the impact of increases in HCQ were seen primarily in the range of 0 to 1000 ng/ml, suggesting that 1000 ng/ml may be a good target to achieve protection without accruing a high risk of retinopathy.

Disclosure: L. Magder, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **D. Goldman**, None.

Abstract Number: 1754

Effect of Belimumab on Autoantibodies, Complement, and B-Cell Subsets in Patients with Lupus Nephritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Lupus nephritis (LN) is a complication affecting ~40% of patients with systemic lupus erythematosus (SLE). Belimumab (BEL), an anti–B-lymphocyte stimulator therapy, was approved in the USA and in the EU for active LN in adult patients. When given to patients without LN for 52 weeks, BEL reduced anti-double stranded DNA (anti-dsDNA) by 41% in patients with anti-dsDNA at baseline (BL; BLISS-52 & -76). The aim of this study was to evaluate changes in autoantibodies, complement, and B-cell subsets in response to BEL plus standard therapy versus placebo (PBO) plus standard therapy in patients with LN enrolled in BLISS-LN.

Methods: BLISS-LN was a Phase 3, 104-week study (GSK Study BEL114054; NCT01639339) in adult patients with active LN. Patients were randomized (1:1) to receive monthly BEL 10 mg/kg intravenous (IV) or PBO, plus standard therapy (high-dose corticosteroids plus either cyclophosphamide followed by azathioprine [CYC/AZA] or mycophenolate mofetil [MMF]). Changes from BL at Week 104 were determined for anti-dsDNA and anti-C1q antibodies (in patients with positive BL anti-dsDNA [≥30 IU/mL] or anti-C1q [≥22.2 IU/mL]), C3/C4, and B-cell subpopulations.

Results: Among patients with autoantibodies at BL, greater reductions in anti-dsDNA and anti-C1q levels were observed with BEL versus PBO in both standard therapy groups. There were notable increases in C3/C4 levels in favor of BEL in both standard therapy groups. BEL significantly reduced the total CD19+ and naïve B cells versus PBO, driven mainly by the MMF subgroup. However, the reduction in circulating memory B cells was numerically smaller with BEL versus PBO. BEL reduced plasmablasts versus PBO in both standard therapy groups (data in **Table**).

Conclusion: Treatment with BEL improved complement (numerically for C3) and anti-dsDNA and anti-C1q antibody levels in patients with LN to greater degrees than standard therapy alone, consistent with the mechanism of action of BEL. There were greater reductions in CD19+ B cells, naïve B cells and plasmablasts with BEL compared with PBO; however, there was a numerically smaller reduction in circulating memory B cells with BEL versus PBO.

Funding: GSK

Table. Biomarker percent change from BL at Week 104 (mITT population)

	CYC/AZA		MMF		Total		
	PBO N=59	BEL N=59	PBO N=164	BEL N=164	PBO N=223	BEL N=223	p-value*
Anti-dsDNA Antibody (IU/mL),† n (%)	25 (42.4)	24 (40.7)	72 (43.9)	83 (50.6)	97 (43.5)	107 (48.0)	
Median (IQR) % change from BL	-32.4 (-64.1, 32.4)	-74.5 (-86.4, -50.4)	-38.5 (-73.0, 27.5)	-74.2 (-84.5, -49.5)	-36.6 (-69.7, 28.6)	-74.2 (-85.1, -49.5)	<0.0001
Anti-C1q Antibody (IU/mL),† n (%)	25 (42.4)	26 (44.1)	75 (45.7)	90 (54.9)	100 (44.8)	116 (52.0)	
Median (IQR) % change from BL	-58.1 (-65.7, -43.0)	-69.4 (-84.1, -30.4)	-57.6 (-78.3, -24.7)	-73.6 (-84.0, -63.1)	-57.9 (-76.1, -33.2)	-73.2 (-84.1, -59.0)	0.0004
C3 (mg/dL), n (%)	31 (52.5)	31 (52.5)	98 (59.8)	111 (67.7)	129 (57.8)	142 (63.7)	
Median (IQR) % change from BL	9.9 (-13.3, 43.9)	21.4 (-8.1, 68.7)	14.7 (-10.8, 43.6)	24.8 (0.8, 52.2)	14.3 (-11.0, 43.6)	23.2 (0.0, 53.3)	0.0954
C4 (mg/dL), n (%)	31 (52.5)	31 (52.5)	98 (59.8)	111 (67.7)	129 (57.8)	142 (63.7)	
Median (IQR) % change from BL	-3.9 (-25.0, 50.0)	36.4 (0.0, 81.8)	21.2 (-8.3, 63.6)	31.3 (0.0, 114.3)	16.7 (-11.8, 63.2)	32.6 (0.0, 106.7)	0.0243
CD19+ (cells/µL), n (%)	29 (49.2)	30 (50.8)	92 (56.1)	102 (62.2)	121 (54.3)	132 (59.2)	
Median (IQR) % change from BL	-72.4 (-86.4, -54.4)	-81.8 (-90.6, -71.3)	-42.3 (-76.7, 15.9)	-82.4 (-90.3, -68.6)	-55.8 (-79.0, -12.5)	-82.2 (-90.5, -69.0)	<0.0001
Naïve CD19+ CD20+ CD27- (cells/µL), n (%)	27 (45.8)	22 (37.3)	91 (55.5)	97 (59.1)	118 (52.9)	119 (53.4)	
Median (IQR) % change from BL	-82.1 (-90.6, -60.3)	-87.3 (-96.4, -77.9)	-42.7 (-79.1, 37.0)	-89.5 (-94.1, -80.6)	-60.2 (-82.2, 0.0)	-89.5 (-94.4, -80.0)	<0.0001
Plasmablasts CD19+ $CD27^{BRIGHT}$ $CD38^{BRIGHT}$ (cells/mL), n (%)	27 (45.8)	28 (47.5)	92 (56.1)	98 (59.8)	119 (53.4)	126 (56.5)	
Median (IQR) % change from BL	-10.8 (-68.8, 69.1)	-72.0 (-86.5, -23.0)	-24.4 (-80.4, 253.7)	-64.6 (-85.7, 51.1)	-21.1 (-79.8, 247.4)	-66.9 (-85.9, 36.4)	0.0004
Memory CD19+ CD20+ CD27+ (cells/µL), n (%)	27 (45.8)	22 (37.3)	91 (55.5)	97 (59.1)	118 (52.9)	119 (53.4)	
Median (IQR) % change from BL	-76.2 (-89.2, 0.0)	-51.3 (-82.8, 3.7)	-66.7 (-79.0, -24.0)	-53.9 (-75.0, -20.8)	-67.8 (-83.3, -24.0)	-53.9 (-76.7, -5.9)	0.0548

*ANCOVA or Rank ANCOVA model comparing BEL and PBO, covariates: treatment group, BL autoantibody value or complement value or B-cell value, induction regimen (CYC vs MMF), and race (Black African ancestry vs other); †In patients with positive BL anti-dsDNA (≥30 IU/mL) or anti-C1q (≥22.2 IU/mL)

n reflects the number of patients with observed on-treatment values at Week 104

ANCOVA, analysis of covariance; IQR, interquartile range; mITT, modified intention-to-treat

Disclosure: B. Rovin, GlaxoSmithKline, 2, 5; **R. Furie**, GlaxoSmithKline, 2, 5; **A. Malvar**, GlaxoSmithKline, 1, 6, Roche, 1; **C. Aranow**, GlaxoSmithKline, 2, 5; **J. Pego-Reigosa**, GlaxoSmithKline, 2, 6, Boehringer-Ingelheim, 2, Pfizer, 5, Lilly, 2; **E. Zakharova**, None; **A. Schwarting**, AbbVie, 5, Pfizer, 5, 6, Novartis, 5, 6, GlaxoSmithKline, 5, 6, Actelion, 5, Roche, 6, Amgen, 6; **A. Jones-Leone**, GlaxoSmithKline, 3, 8, 11; **A. Madan**, GlaxoSmithKline, 3, 8, 11; **J. Gilbride**, GlaxoSmithKline, 3, 8, 11; **D. Roth**, GlaxoSmithKline, 3, 8, 11; **Y. Green**, GlaxoSmithKline, 3, 8, 11; **A. van Maurik**, GlaxoSmithKline, 3, 8, 11.

Abstract Number: 1755

Increasing Participation of Underrepresented Groups in Lupus Clinical Trials: Insights from Qualitative Interviews with Patients and Physicians

Saira Sheikh[1], Maria Naylor[2], Becky Lane[2], Jennifer Sacks[2], Janine Gaiha-Rohrbach[2] and Cherie Butts[2], [1]University of North Carolina Thurston Arthritis Research Center, and Department of Medicine, Division of Rheumatology, Allergy and Immunology, University of North Carolina at Chapel Hill School of Medicine, Chapel Hill, NC, [2]Biogen, Cambridge, MA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Demographics of Patient Participants

Characteristic, n (%)	Participating Patients[a] (n = 33)
Patient age	
18–35 years	4 (12)
36–45 years	9 (27)
46–65 years	17 (52)
66+ years	3 (9)
Female	29 (88)
Race/Ethnicity	
Black/African American	16 (48)
Latino/a	10 (30)
Asian/Pacific Islander	5 (15)
Native American	2 (6)
Region	
Northeast	11 (33)
Midwest	5 (15)
South	12 (36)
West	5 (15)
Education level	
Currently in school	1 (3)
Some high school or less	1 (3)
Some college	8 (24)
Graduated college/technical school	17 (52)
Postgraduate degree	6 (18)
Employment status	
Full time	11 (33)
Part time	4 (12)
Retired	4 (12)
On disability	8 (24)
Other[b]	6 (18)
Type of lupus	
SLE	23 (70)
CLE	4 (12)
Both SLE and CLE	3 (9)
Unknown/not sure	3 (9)
Severity of lupus	
Mild	4 (12)
Moderate	23 (70)
Severe	6 (18)
Current treatment	
Antimalarials	17 (52)
Corticosteroids	15 (45)
Monoclonal antibody	5 (15)
Other immunosuppressant	15 (45)
Untreated	4 (12)

CLE = cutaneous lupus erythematosus; SLE = systemic lupus erythematosus

[a]Patient participants were recruited from a database of individuals who agreed to be contacted for research purposes. Interviews were conducted between November 2020 and January 2021.

[b]Includes homemaker (n = 4), unemployed, looking for work (n = 1), and student (n = 1)

Background/Purpose: Systemic lupus erythematosus disproportionately affects Black/African American (AA) and Latino/a populations.[1] Challenges to engage and include these populations in clinical trials (CTs) can be grouped into patient-side barriers to participation and provider-side barriers to referring patients.[1] Our aim was to address barriers in engaging with racial/ethnic populations and potential ways to ensure representation in lupus CTs.

Table 2. Demographics of Physician Participants

Characteristic, n (%)	Participating Physicians[a] (n = 20)
Specialty	
Rheumatology	11 (55)
Dermatology	9 (45)
Investigator vs referring physician	
Referring physician	14 (70)
Investigator	6 (30)
Years experience post-residency	
5–19 years	13 (65)
20+ years	7 (35)
Physician race	
White/Caucasian	12 (60)
Asian/Pacific Islander	4 (20)
Black/African American	2 (10)
American Indian/Alaskan Native	1 (5)
Prefer not to disclose	1 (5)
Region	
Northeast	8 (40)
Midwest	1 (5)
South	8 (40)
West	3 (15)
Lupus patients managed	
5–49 patients per month	12 (60)
50+ patients per month	8 (40)
Patient race	
Majority Black or African American (> 50% of patients)	7 (35)
Majority White/Caucasian (> 50% of patients)	4 (20)
Mix (all races < 50% of patients)	9 (45)
Patient living setting	
Physicians with ≥ 50% urban patients	9 (45)
Physicians with ≥ 50% suburban patients	6 (30)
Physicians with ≥ 10% rural patients	10 (50)
Patient insurance coverage	
Physicians with commercially/privately insured (> 50% of patients)	11 (55)
Physicians with Medicare insured (> 50% of patients)	1 (5)
Physicians with mix (private and Govt insured, all < 50% of patients)	8 (40)

[a]Physician participants were recruited from a database of individuals who agreed to be contacted for research purposes. Interviews were conducted between December 2020 and February 2021.

Methods: In-depth qualitative interviews were conducted with lupus patients from underrepresented populations (Black/AA, Latino/a, Native American, Asian/Pacific Islander) and physicians (investigators or referring physicians in dermatology or rheumatology). Participants were screened to fulfill demographic quotas and assess conflicts of interest; those who qualified provided consent to be interviewed and were compensated for their participation. Interviews followed a semi-structured format in which participants were asked open-ended questions about CT awareness and motivating factors/barriers for CT participation.

Results: A total of 33 patients and 20 physicians participated in the study. Patient characteristics varied by age, region, education, employment status and type/severity of lupus (Table 1); physicians had varied practice settings and work experience (Table 2). The primary barrier to CT participation reported by patients was concern for investigational drug safety/efficacy (Figure 1). This included potential side effects, unknown efficacy and risk of missed benefit with placebo. Patients also reported impact of CT burden, such as time, transportation and financial impact of visits. Fewer patients reported mistrust of the healthcare system as a barrier; historical factors such as mistreatment of

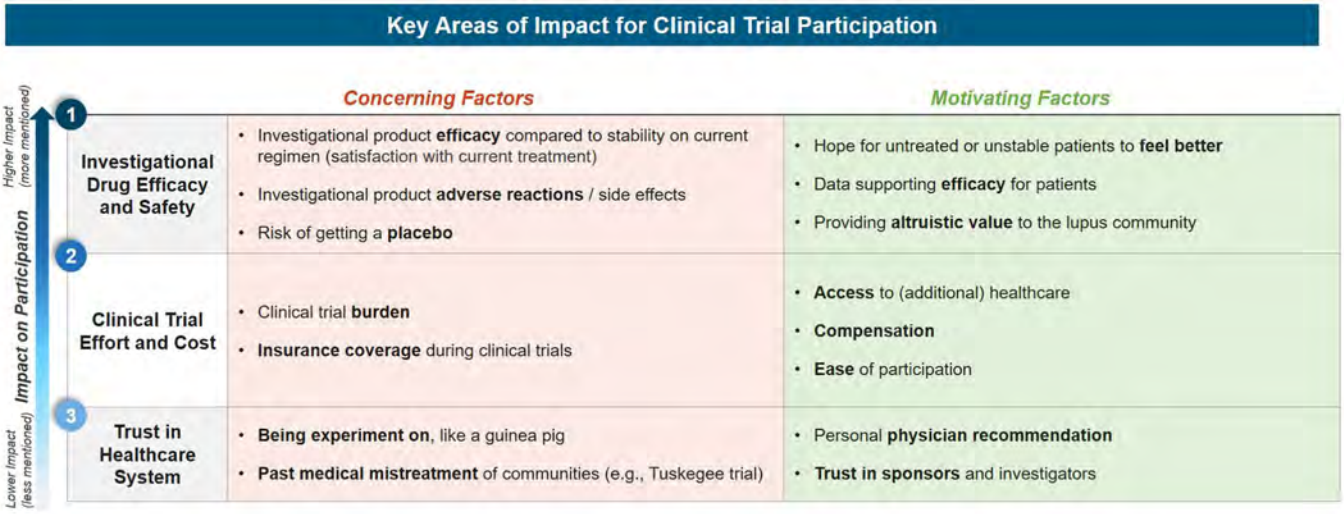

Figure 1. Patient-Reported Drivers and Barriers to Lupus Clinical Trial Participation Among Underrepresented Racial and Ethnic Groups.

underrepresented groups were less impactful than day-to-day challenges. Patients noted that participation could be improved by highlighting the value of CTs to individuals and their communities in a culturally competent way, minimizing trial burden and increasing trust through personal recommendation from treating physicians. From the physician perspective, < 50% were aware of ongoing CTs locally and some reported insufficient information for referring patients appropriately. Unconscious/implicit bias, such as assuming patients will not want to participate or be adherent, was also reported to influence physicians. Providing physicians with a centralized CT information source (website) and networking support, building patient awareness through trusted sources (churches, community centers) and including a broader mix of investigators from underrepresented communities may remove these perceived barriers.

Conclusion: Increasing participation of underrepresented racial/ethnic groups in lupus CTs is essential for assessing drug safety and efficacy, especially when these populations are most affected by the disease. Patient education, reduced CT burden, physician awareness of available CTs and strategies and educational efforts to address potential implicit bias should be critical components of health equity efforts.

References

1. Sheikh. *J Clin Med*. 2019;8:1245.

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Disclosure: S. Sheikh, Pfizer, 5, GlaxoSmithKline, 2, 5; **M. Naylor**, Biogen, 3, 12, Shareholder; **B. Lane**, Biogen, 3, 12, Shareholder; **J. Sacks**, Biogen, 3, 12, Shareholder; **J. Gaiha-Rohrbach**, Biogen, 3, 12, Shareholder; **C. Butts**, Biogen, 3, 12, Shareholder.

Abstract Number: 1756

Class V Systemic Lupus Erythematosus Nephritis Patients Are Undertreated and Face Similar Adverse Renal Outcomes as Class III/IV Patients

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Few studies have investigated treatment patterns and renal outcomes in class V systemic lupus erythematosus (SLE) nephritis patients compared to class III/IV patients. Prior findings are mainly from older clinical trial data. Using real-world, electronic health record (EHR) data, we compared prescribing patterns, laboratory data, and renal outcomes in class V compared to class III/IV SLE nephritis patients.

Methods: Using a large, de-identified EHR database called the Synthetic Derivative with over 3.2 million subjects, we identified incident SLE nephritis patients. We used previously published and validated SLE EHR algorithms with positive predictive values ranging from 86 to 95% and then searched for patients with keywords of "nephritis." We conducted chart review to ensure patients were incident SLE nephritis cases and had a diagnosis based on a renal biopsy. We also collected demographic and medication data prescribed at diagnosis (baseline), 6 months, and 12 months. We also assessed serum creatinine (mg/dL) and spot urine protein to creatinine ratios at baseline, 6-months, and 12-months. We examined for renal replacement therapy, defined as ever received dialysis or renal transplant. For

Table 1. Demographics and baseline data in Class III/IV vs. Class V SLE nephritis.

Patient Characteristics	Class III/IV SLE nephritis (n = 86)	Class V SLE nephritis (n = 43)	p value
Sex (%)			
Female	71 (83%)	36 (84%)	p = 0.87
Race (%)			
White	41 (48%)	13 (30%)	p = 0.06
Black	38 (44%)	26 (60%)	p = 0.08
Asian/Pacific	4 (5%)	4 (10%)	p = 0.30
Missing/Other	3 (3%)	0 (0%)	p = 0.72
Ethnicity (%)			
Hispanic	3 (3%)	0 (0%)	p = 0.72
Baseline medications (%)			
Antimalarials	60/80 (75%)	22/42 (52%)	**p = 0.01**
Immunosuppressants	74/85 (87%)	23/42 (55%)	**p < 0.001**
Corticosteroids	80/85 (94%)	32/42 (76%)	**p = 0.003**
Baseline laboratory values			
Serum creatinine mg/dL (± standard deviation)	1.90 ± 2.38	1.04 ± 0.88	**p = 0.002**
Spot urine protein/creatinine ratio (± standard deviation)	3.72 ± 3.18	3.44 ± 3.60	p = 0.50
Renal replacement therapy* (%)	24/86 (28%)	8/44 (18%)	p = 0.22
Deceased (%)	13 (15%)	5 (12%)	p = 0.59

*Renal replacement therapy defined as ever received dialysis or renal transplant.

Table 2. Six month and twelve-month data in Class III/IV vs. Class V SLE nephritis.

Patient Characteristics	Class III/IV SLE nephritis	Class V SLE nephritis	p value
6-month medications (%)			
Antimalarials	60/79 (76%)	25/39 (64%)	p = 0.18
Immunosuppressants	73/79 (92%)	27/37 (73%)	**p = 0.01**
Corticosteroids	69/79 (87%)	32/37 (86%)	p = 0.90
6-month laboratory values			
Serum creatinine mg/dL (± standard deviation)	2.09 ± 2.75	0.94 ± 0.49	**p = 0.01**
Spot urine protein to creatinine ratio (± standard deviation)	1.66 ± 2.92	2.26 ± 3.81	p = 0.17
12-month medications (%)			
Antimalarials	56/69 (81%)	28/40 (70%)	p = 0.18
Immunosuppressants	57/68 (84%)	24/36 (67%)	**p = 0.04**
Corticosteroids	58/70 (83%)	26/39 (67%)	**p = 0.05**
12-month laboratory values			
Serum creatinine mg/dL (± standard deviation)	1.83 ± 2.47	0.94 ± 0.47	p = 0.22
Spot urine protein to creatinine ratio (± standard deviation)	1.13 ± 1.59	0.98 ± 0.40	p = 0.58

SLE nephritis patients with multiple classes, we included patients with pure class V nephritis and patients with either class III, IV, or III + IV nephritis.

Results: We identified 43 incident class V and 86 incident class III/IV SLE nephritis patients. Sex, race, and ethnicity were all similar in class V vs. III/IV patients (Table 1). At baseline, class V SLE nephritis patients were less likely to be on antimalarials (52% vs. 75%, p = 0.01), immunosuppressants (55% vs. 87%, p < 0.001), and corticosteroids (76% vs. 94%, p = 0.003) compared to class III/IV patients. Class V SLE nephritis patients were also less likely to be prescribed immunosuppressants at 6 months (73% vs. 92%, p = 0.01) and 12 months (67% vs. 84%, p = 0.04) compared to class III/IV patients (Table 2). At 12 months, there were lower corticosteroid rates in class V vs. class III/IV (67% vs. 83%, p = 0.05). For baseline laboratory values, class V patients had similar spot urine protein to creatinine ratios but lower serum creatinine levels compared to class III/IV patients (1.04 mg/dL ± 0.87 vs. 1.90 mg/dL ± 2.38, p = 0.002). This lower serum creatinine trend for class V vs. class III/IV nephritis patients continued at 6 months (0.94 ± 0.49 vs. 2.09 ± 2.75, p = 0.01) with similar values at 12 months (Table 2). Class V patients had similar rates of renal replacement therapy (18% vs. 28%, p = 0.22) and death (12% vs. 15%, p = 0.59) compared to class III/IV SLE nephritis patients.

Conclusion: Our study demonstrated that class V patients were undertreated for their renal disease compared to class III/IV patients, particularly at time of diagnosis but also at 6 and 12 months after diagnosis. Class V patients may get undertreated for their renal disease, as it is generally thought that these patients will have a better prognosis compared to class III/IV patients. Our real-world, EHR data suggest that class V SLE nephritis patients are still at risk for adverse renal outcomes at similar rates to class III/IV patients and need appropriate treatment.

Disclosure: A. Barnado, None; **A. Camai**, None.

Abstract Number: 1757

Clinical Use of Belimumab for Systemic Lupus Erythematosus in the Setting of Advanced Chronic Kidney Disease and End-Stage Renal Disease on Dialysis: A Case Series

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SESSION INFORMATION
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Background/Purpose: Belimumab is FDA approved for treatment of SLE and Lupus Nephritis. Patients with an eGFR < 30 ml/min/1.73m^2 were excluded from clinical trials, thus limiting data on its use in SLE patients with advanced chronic kidney disease (CKD) and end-stage renal disease (ESRD). We describe a case series on the safety and utility of belimumab in these patients.

Methods: We conducted a retrospective chart review of patients >18 years old, at Northwell Health, with SLE and CKD stage 4 or worse (sustained eGFR < 30) or ESRD on hemodialysis/peritoneal dialysis. Patients treated with both intravenous and subcutaneous belimumab from 2010 to 2020 were included. We excluded patients with a transient eGFR < 30. Clinical and laboratory data and concomitant immunosuppressive medications were collected in 3-month intervals from 12 months before belimumab initiation to the last time point of belimumab use. The primary

Table 1: Baseline Characteristics and Belimumab Information

	Age – year	Sex	Race/ Ethnicity	Type of dialysis	SLE duration (years)	LN duration (years)	Average prednisone dose before belimumab (mg/day)	Concomitant immunosuppressive medications	Belimumab dose (Route)	Duration of belimumab therapy (months)
Patient 1	30	Female	African American	Hemodialysis	14	14	8.39	None	200mg/week (SQ)	12
Patient 2	62	Female	African American	Hemodialysis	21	21	10.94	None	760mg/month (IV)	22
Patient 3	29	Female	African American	Hemodialysis	10	7	12.01	None	200mg/week (SQ)	10
Patient 4	25	Female	African American	Peritoneal	9	5	18.35	Thalidomide	760mg/month (IV)	10
Patient 5	33	Female	African American	Hemodialysis	4	2	16.96	Azathioprine	670mg/month (IV)	14*
Patient 6	36	Female	American Indian/Native Alaskan	None	20	11	0	Mycophenolate Mofetil	663mg/month (IV)	42*

*Denotes patient was still on Belimumab at time that chart review ended
SLE = Systemic Lupus Erythematous
LN =Lupus Nephritis
SQ = Subcutaneous
IV = Intravenous
IVIG = Intravenous Immunoglobulin

Table 2: Number and Type of Adverse Events Recorded while on Belimumab

	Infections		Allergic Reactions	
	Mild/Moderate	*Severe**	*Mild/Moderate*	*Severe**
Patient 1	0	0	0	0
Patient 2	2 URI	1 MSSA Bacteremia	0	0
Patient 3	0	0	0	0
Patient 4	0	1 Herpes zoster ophthalmicus / Varicella zoster meningitis	2 Rash	0
Patient 5	1 URI 1 Oral Herpes (Herpes Simplex)	0	0	0
Patient 6	0	0	0	0

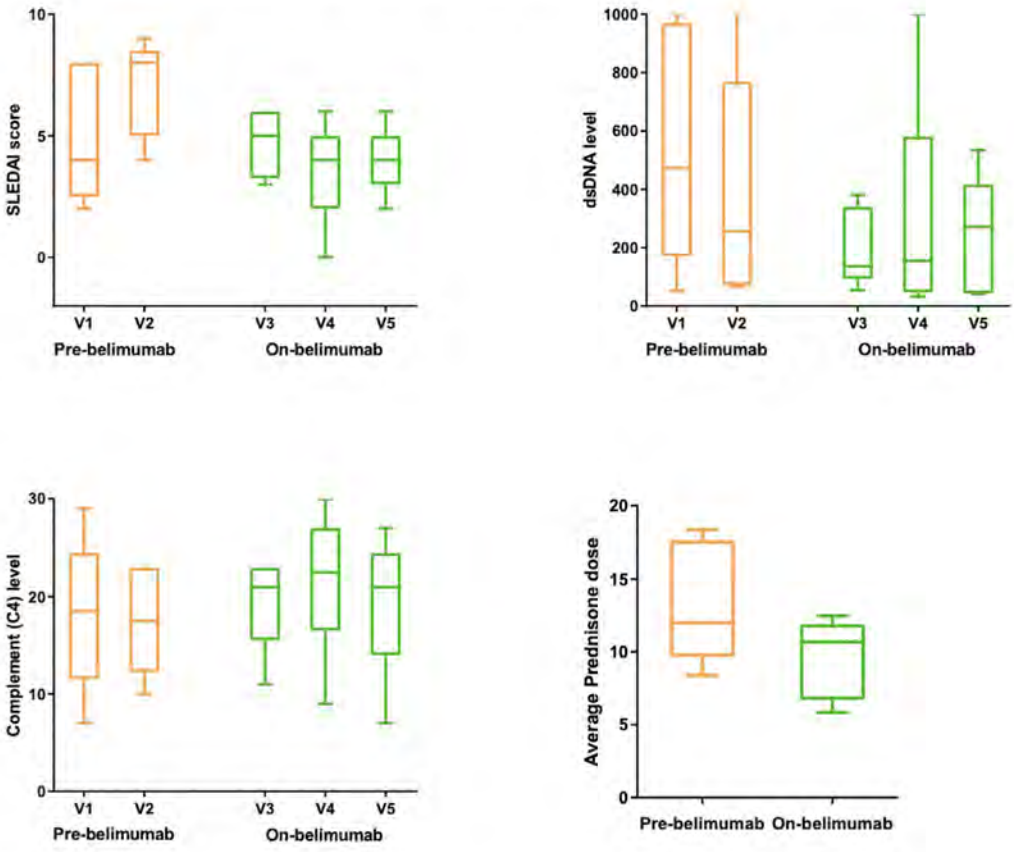
*Severe adverse events defined as those requiring ED visit, hospitalization, change in dose/frequency of Belimumab, or discontinuation of Belimumab
MSSA= Methicillin-sensitive Staphylococcus aureus
URI= Upper Respiratory Infection

endpoint was safety defined by absence of events of interest, including allergic reactions, infections (viral, bacterial, and opportunistic), depression, suicide, and death. As secondary endpoints, we compared median SLEDAI change, serologic parameters, prednisone dose equivalent, and number of flares as determined by SLEDAI SELENA flare index for 12 months before belimumab use and while on belimumab. The only time points that had all data available were analyzed for efficacy.

Results: Of 353 patients, we identified six patients with sustained eGFR < 30 or requiring dialysis on belimumab therapy. Baseline demographic and clinical characteristics are recorded in **Table 1**. The average time of belimumab use in this group was 1.5 years (10-42 months). All patients were alive at the time of analysis. Belimumab was discontinued in 4 patients: 2 for renal transplant, 1 for infectious complications, and 1 for worsening of chronic heart failure. A total of 6 infections were recorded over 9 patient years with multiple events seen in 3 patients. Two infectious events were severe and 4 were mild/moderate. Belimumab was resumed after resolution in all but one patient with systemic H. zoster infection. All patients with infections were on concomitant prednisone (4-10mg/day), 1 patient was on thalidomide (100mg/day), and 1 patient was on azathioprine (150mg/day). No depression, suicide, leukopenia, hypogammaglobulinemia were identified **(Table 2)**. Median SLEDAI score decreased by 50% (from 8 to 4) after 6 months of belimumab use. During the same time frame, median dsDNA titers reduced by more than half (from 390 IU/mL to 167 IU/mL), but there was no change in median complement 4 level (from 18.5mg/dL to 21mg/dL). The cumulative prednisone dose decreased by a mean of 3.75 mg/day (from 13.33 mg/day to 9.58 mg/day) comparing time periods before and while on belimumab **(Figure 1)**. Arthralgia was recorded as improved in two-thirds of patients. There was no change in the median number of flares.

Conclusion: Belimumab is relatively safe in SLE patients with advanced CKD and ESRD on dialysis and may be helpful in reducing SLE activity and steroid use in these patients. However, it is important to be cognizant of the risk of infection, especially with concomitant use of other immunosuppressants.

Figure 1: Clinical Characteristics for each Visit Pre-Belimumab and On-Belimumab



= Visits pre-belimumab

= Visits on-belimumab

V1 = Visit 1 (Time range: 6-11months pre-belimumab initiation)
V2 = Visit 2 (Time range: 1-8 months pre-belimumab initiation)
V3 = Visit 3 (Time range: 0-3 months on-belimumab)
V4 = Visit 4 (Time range: 3-6 months on-belimumab)
V5 = Visit 5 (Time range: 6-8 months on-belimumab)

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Influenza A(H3N2)/Singapore Component Vaccine in Systemic Lupus Erythematosus: A Distinct Pattern of Immunogenicity

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
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Background/Purpose: Influenza A(H3N2) virus is the most important cause of seasonal influenza morbidity and mortality in the last 50 years surpassing the impact of H1N1. Data assessing immunogenicity and safety of this virus component is lacking in systemic lupus erythematosus (SLE) and restricted to small reports with other H3N2 strains.

Methods: 81 consecutive SLE patients and 81 age- and sex-matched healthy controls(HC) were vaccinated with influenza A/Singapore/INFIMH-16-0019/2016(H3N2)-like virus. Percentage of seroprotection(SP), seroconversion(SC), geometric mean titer(GMT), factor increase in geometric mean titer(FI-GMT) and adverse events were assessed before and 4 weeks post-vaccination. Disease activity and therapies were also evaluated.

Results: Before immunization, both groups had a high SP rate (89% vs. 77%,p=0.060) and elevated GMT titer with higher levels in SLE [129.1(104.1-154.1) vs. 54.8(45.0–64.6),p< 0.001]. Frequency of two previous years influenza vaccination was high and comparable in patients and HC(89% vs. 90%,p=1.000). Four weeks post-vaccination, median GMT increased for both groups and remained higher in SLE compared to HC [239.9(189.5-290.4) vs. 94.5(72.6-116.4),p< 0.0001] with a comparable FI-GMT [2.3(1.8-2.9) vs. 1.9(1.5-2.3),p=0.061]. Frequency of SC rates was low and comparable for both groups(16% vs. 11%,p=0.974,respectively). Disease activity scores remained stable throughout the study(p=1.000) and severe side effects were not identified.

Conclusion: Influenza A(H3N2)/Singapore vaccine has an adequate safety profile. The distinct immunogenicity pattern from other influenza A components characterized by a remarkably high pre- and post-vaccination SP rate and high GMT levels may be associated with previous influenza A vaccination. (www.clinicaltrials.gov, NCT03540823). (FAPESP #2018/16162-3)

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An Analysis of Medication Responsiveness Based on Subtype and Race Within a Cohort of Cutaneous Lupus Erythematosus Patients

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SESSION INFORMATION

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Session Title: SLE – Treatment Poster (1732–1772)

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Background/Purpose: Cutaneous lupus erythematosus (CLE) can present in association with or without concomitant SLE, and with skin manifestations varying by subtype – acute CLE, subacute CLE (SCLE), and chronic CLE, of which the most common type is discoid (DLE). There is evidence of heterogeneity of response to therapy between subtypes, and surveys have shown that providers have preference for prescribing different medications based on subtype. Additionally, studies have shown that black patients are disproportionately affected by lupus, have a higher risk of damage, and have a higher incidence of CLE (specifically DLE) than white patients. However, there is a lack of evidence-based studies comparing medication response by subtype or race.

Methods: In this retrospective study of our longitudinal prospective database, we examined response rates to methotrexate (MTX), mycophenolate mofetil (MMF), and azathioprine (AZA), the most commonly used immunosuppressive medications in our cohort, by subtype and by race. Response or non-response was determined by 50% improvement or lack thereof in skin activity measured by the Cutaneous Lupus Erythematosus Disease Area and Severity

Table 1. Comparison of response rates for each medication between SCLE and DLE patients*

Medication	Response Type	SCLE	DLE	p-value from Fisher's exact test
MTX		n=18	n=13	0.262
	Responders	13 (72%)	6 (46%)	
	Non-responders	5 (27%)	7 (54%)	
MMF		n=7	n=27	>0.999
	Responders	5 (71%)	19 (70%)	
	Non-responders	2 (29%)	8 (30%)	
AZA		n=4	n=9	0.105
	Responders	0 (0%)	5 (56%)	
	Non-responders	4 (100%)	4 (44%)	

n=instances of medication use analyzed

*analysis excludes patients with ACLE, tumid LE, bullous LE, and patients with multiple subtypes

Table 2. Comparison of response rates for each medication between black and white patients*

Medication	Response Type	Black	White	p-value from Fisher's exact test
MTX		n=12	n=28	0.311
	Responders	6 (50%)	19 (68%)	
	Non-responders	6 (50%)	9 (32%)	
MMF		n=22	n=22	>0.999
	Responders	14 (64%)	14 (64%)	
	Non-responders	8 (36%)	8 (36%)	
AZA		n=7	n=8	0.0406*
	Responders	6 (86%)	2 (25%)	
	Non-responders	1 (14%)	6 (75%)	

n=instances of medication use analyzed
*analysis includes all subtypes, including patients excluded from Table 1 analysis

Index (CLASI) and/or chart abstraction, and analyzed using Fisher's exact test.[1] Discontinuations due to side effects were analyzed separately.

Results: Of the 191 patients with SCLE and DLE identified with sufficient longitudinal follow-up, 73 took at least one of these medications, including 34 with concomitant SLE by ACR 1997 criteria; the other subtypes were not powered for analysis and were excluded. Mean response rate was 52.6% (95% CI 30.3-74.9%). No statistically significant difference was found in rate of response to each medication when comparing SCLE vs DLE ($p > 0.05$). Results suggest that MMF may be more effective in DLE than MTX, but our sample was not powered to show this difference ($p=0.175$). Additionally, response rates were analyzed between black CLE patients and white CLE patients taking these medications. Of the 97 black CLE patients identified, 38 took at least one of these medications, including 19 with concomitant SLE by ACR 1997 criteria; of the 159 white, 53 did, including 21 with concomitant SLE by ACR 1997 criteria. Mean response rate was 59.3 (95% CI 43-75.6%). No statistically significant difference was found in rate of response to MTX or MMF in black vs white CLE patients ($p > 0.05$). Rate of response to AZA was higher in black patients than white patients ($p = 0.0406$).

Conclusion: These findings suggest that MTX and MMF appear equally efficacious between SCLE and DLE patients and between black and white patients, and AZA may work better in black patients than in white CLE patients. Further studies are needed to assess whether MMF may work better than MTX in DLE. Clinicians may then use other factors to guide medication choice, such as side effect profile and comorbid conditions.

References

1. Chakka S, Krain RL, Ahmed S, et al. Evaluating change in disease activity needed to reflect meaningful improvement in quality of life for clinical trials in cutaneous lupus erythematosus. *J Am Acad Dermatol*. 2021 Jun;84(6):1562-1567.

Table 3. Rates of discontinuation of medications due to side effects

Medication	SCLE	DLE	Black	White
MTX	7 (28%)	3 (19%)	2 (14%)	8 (22%)
MMF	6 (46%)	5 (16%)	4 (15%)	11 (33%)
AZA	4 (50%)	5 (36%)	3 (43%)	9 (53%)

note: percentages are for rate of discontinuation due side effects from all instances of that medication use within the population subset

Disclosure: E. Keyes, None; **A. Jobanputra**, None; **M. Grinnell**, None; **R. Feng**, None; **T. Vazquez**, None; **D. Diaz**, None; **V. Werth**, Celgene, 5, Resolve, 2, Janssen, 2, 5, Eli Lilly, 2, Biogen, 2, 5, Bristol Myers Squibb, 2, Gilead, 2, 5, Amgen, 2, EMD Serono, 2, Viela Bio, 2, 5, Kyowa Kirin, 2, AstraZeneca, 2, AbbVie, 2, GlaxoSmithKline, 2.

Abstract Number: 1760

Long-term Opioid Use Among Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic condition that can be associated with both acute and chronic musculoskeletal pain as well as fibromyalgia. Opioids are rarely indicated for long-term management of chronic pain due to lack of efficacy and risk for dependency and developing medical comorbidities, such as osteoporosis and cardiovascular disease. By using a population-based cohort, we assessed the prevalence of opioid use among patients with and without SLE and examined potential risk factors for long-term opioid use among SLE patients.

Methods: By using an established population-based research infrastructure that links the medical records of all individuals in a geographically well-defined 27-county US population, we identified SLE cases meeting the 2019 ACR/EULAR classification criteria and living in the region on 1-1-2015. SLE patients were matched on age, sex, race/ethnicity and county to non-SLE comparators. Ambulatory opioid prescription data were used to define an episode of opioid use for patients using opioids on 1-1-2015. An episode was defined as contiguous prescriptions prior to 1-1-2015 with gaps < 30 days between prescriptions. Long-term users were defined following the Consortium to Study Opioid Risks and Trends (CONSORT) definition (opioid use episode that spans ≥ 90 days or ≥ 10 prescriptions). Data on SLE duration, presence of mood disorder (depression, dysthymia, bipolar disorder) and fibromyalgia diagnoses were abstracted, and area deprivation index (ADI) was obtained. Chi-square and rank sum tests were used to compare characteristics between the groups. Logistic regression was used to examine factors associated with long-term opioid use among patients with SLE.

Results: We identified 479 SLE patients and 479 non-SLE comparators. Mean age of SLE patients and the matched non-SLE comparators was 53.2 (SD 16.2) years, 82% were female and 85% were white. Mean SLE duration was 13.5 years (SD 11.6). On 1-1-2015, 13% of SLE patients used opioids compared to 3% of non-SLE comparators ($p< 0.001$), and 10% of SLE patients were long-term opioid users compared to 1% of comparators. 38% had a concurrent mood disorder diagnosis compared to 23% among comparators ($p< 0.001$), whereas, 14% had a concurrent fibromyalgia diagnosis compared to 5% among comparators ($p< 0.001$) (Table 1). Factors associated with long-term use among patients with SLE included age (odds ratio [OR]: 1.20 per 10 year increase; 95% CI: 1.00-1.46), SLE duration (OR: 1.34 per 10 years; 95% CI: 10.00-1.63), mood disorder (OR: 3.06; 95% CI: 1.64-5.71), and fibromyalgia (OR: 6.78; 95% CI: 3.44-13.39).

Table 1. SLE and Non-SLE Characteristics			
Characteristic	**SLE patients N=479**	**Non SLE Comparators N= 479**	**P-Value**
Age, years, Mean (SD)	53.2 (16.2)	53.2 (16.2)	0.99
Female sex, N (%)	394 (82)	394 (82)	1.00
Race/Ethnicity, N (%)			0.93
White	404 (85)	412 (86)	
Asian	15 (3)	17 (4)	
other/mixed	8 (2)	5 (1)	
Black	18 (4)	19 (4)	
American Indian	2 (0)	2 (0) 24 (5)	
Hispanic	29 (6)		
Opioid use, N (%)	63 (13)	13 (3)	<0.001
Long-term opioid use, N (%)	48 (10)	6 (1)	<0.001
SLE duration, years, Mean (SD)	13.5 (11.6)	--	--
Mood disorder, N (%)	182 (38)	112 (23)	<0.001
Fibromyalgia, N (%)	66 (14)	25 (5)	<0.001
Area Deprivation Index, Mean (SD)	94.4 (12.7)	94.5 (12.4)	0.99

Conclusion: In this study, 13% of SLE patients were opioids users compared to 3% among non-SLE comparators. Among SLE patients, 10% met the CONSORT definition for long-term opioid use. SLE duration and having a co-morbid mood disorder or fibromyalgia diagnosis were identified as significant risk factors for long-term opioid use.

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Abstract Number: 1761

Comparison of Belimumab and Standard of Care by Inverse Probability of Treatment Weighting Analyses Based on Propensity Score in Patients with Systemic Lupus Erythematosus in the Maintenance Phase

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Development of molecular-targeted agents is essential in treat-to-target treatment strategies for systemic lupus erythematosus (SLE). We analyzed the efficacy and safety of belimumab (BEL) in the clinical practice, focusing on SLE patients in the maintenance phase.

Methods: This study included the patients with SLE in the maintenance phase (SELENA-SLEDAI< 10, glucocorticoid (GC) dose ≤12.5 mg/day). The efficacy of BEL combined with standard-of-care (BEL+SoC group, n=100) was

compared with standard-of-care (SoC group including patients using either mycophenolate mofetil or hydroxychloroquine, n=103). Selection bias was reduced to a minimum using propensity score-based inverse probability of treatment weighting (IPTW). We analyzed the trajectories of changes in GC dosage in all patients in this study using growth mixture modeling (GMM). The observation period of the study was 52 weeks.

Results: No significant difference was observed in patient characteristics between the BEL+SoC and SoC groups after adjustment by propensity score-based IPTW. Only one case of BEL discontinuation (involving drug-induced eruption) was observed, and the 52-weeks retention rate was 99% (99/100). The BEL+SoC group had significantly lower GC doses at 52 weeks compared to the SoC group (BEL+SoC group, 2.2±2.7 vs. SoC group, 4.4±3.9 mg/day, respectively, p< 0.001), but no differences in SELENA-SLEDAI, 50% hemolytic complement, and anti-double stranded DNA antibodies was observed. The BEL+SoC group had a lower rate of relapse (defined as new appearance of BILAG A1 or B2 items) compared to the SoC group (BEL+SoC group, 0.9% vs. SoC group, 6.3%, respectively, p=0.031). The incidence of ≥ Grade 2 adverse events infections, as specified by the Common Terminology Criteria for Adverse Events, was significantly lower in the BEL+SoC group compared to the SoC group before adjustment by propensity score-based IPTW (BEL+SoC group, 4.0% vs. SoC group, 17.5%, respectively, p=0.003).

The trajectory of GC dose was divided into four groups by GMM; in a group (GC-free group), GC dosage could be reduced to 0 within 6 months, without any relapse. The majority of the GC-free group (87.5%) consisted of cases with concomitant BEL administration. When multivariable logistic regression analysis was performed for all patients, the factors contributing to belonging to GC-free group was onlyBEL use (odds ratio (OR) 8.86, 95% confidence interval (CI) 2.55-30.78, p< 0.001). Next, multivariable logistic regression analysis was performed for BEL+SoC group. The patients had lower the SELELNA-SLEDAI score (OR 0. 82, 95% CI 0. 68-0.98, p=0.03) and GC doses (OR 0. 75, 95% CI 0. 59-0.98, p=0.02) were more likely to belong to GC-free group.

Conclusion: In maintenance-phase SLE, administration of BEL was able to achieve reduction of GC dose while ensuring strict control of disease activity and suppression of flare-ups.

The present study suggests that among the patients who received BEL, those with low baseline SLEDAI and GC doses could discontinue GC without relapse.

Disclosure: y. Miyazaki, None; **S. Nakayamada**, None; **S. Iwata**, None; **K. Hanami**, None; **S. Fukuyo**, None; **K. Sonomoto**, None; **A. Kawabe**, None; **Y. Inoue**, None; **N. Okubo**, None; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 6, Novartis, 6, YL Biologics, 6, Bristol-Myers Squibb, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahi-kasei, 5, 6, GSK, 2, 6, Mitsubishi-Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Ayumi, 2, Taisho, 2.

Abstract Number: 1762

Hydroxychloroquine Alone Does Not Increase QTc in the Absence of Other QT-prolonging Medications

Haihui Wang, Upstate Medica University, Fayetteville, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is one of the widely used immunomodulator in rheumatology. Its temporary trendy use during the early phase of COVID pandemic stresses its short-term QT prolonging effect on COVID 19 patients. Many patients with autoimmune diseases have concurrent fibromyalgia or depression or psychiatric disorder that will require them to be on other chronic medication with potential QT prolongation effect. To clarify if HCQ or other medications is the culprit for prolonging QTc, we looked at the QTc prolongation effect in patients specifically not on other QT prolonging medications.

Methods: All adult patients, age >18 years, from Jan 2015 to Dec 2020 followed at SUNY Upstate Medical University who were prescribed HCQ were included in the study.

Results: 9484 patients were treated with HCQ, of which only 3917 were on HCQ without other QT prolonging medications (anti depression, antipsychotics, antiarrhythmics), among which 1036 patients had 1 EKG done, and 635 had 2 EKG done. Among the patients only on HCQ as potential QT prolong medications with 2 EKGs, only 68 patients had 1 EKG done before HCQ and 1 EKG done after HCQ initiation. Among these patients, 13 patients had prolonged QTc (>460ms) on their first EKG, and 7 remained to have prolonged QTc on repeat, 6 patients with initial long QTc had normal QTc on repeat; 16 patients had prolonged QTc on their 2nd EKG, 9 were new from normal QTc on initial EKG, shown as table below.

Number of patients on HCQ	9484
Number of patients on HCQ as only QT prolonging medication	3917
Number of patients on HCQ as only QT prolonging medication with 1 EKG	1036
Number of patients on HCQ as only QT prolonging medication with 2 EKG	635
Number of patients on HCQ as only QT prolonging medication with EKG done before and after initiation of HCQ	68

long QTc on 1st EKG	QTc remain long on 2ndEKG	QT normal on 2ndEKG
13	7	6
long QTc on 2nd EKG	QTc long on 1st EKG	QTc normal on 1stEKG
16	7	9

Conclusion: HCQ causing prolongation is a well-known drug effect, however routine EKG screening before starting HCQ is not done. This project showed that it is very common for patients on HCQ to be simultaneously on other QT prolonging medication chronically which may potentially have add-on effect. For those patients on HCQ only with EKG to compare before and after, this project was unable to show the QTc prolongation effect on HCQ, but this may be due to limited available samples.

Disclosure: H. Wang, None.

Abstract Number: 1763

Baricitinib Reduces Proinflammatory Serum Cytokines in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Baricitinib, a Janus kinase (JAK)1/JAK2 inhibitor, improved disease activity in systemic lupus erythematosus (SLE) adults receiving standard background therapy in a phase 2 trial (NCT02708095).[1] The aim of this study was to elucidate the mechanism of action of baricitinib in SLE.

Methods: Patients with SLE were treated with baricitinib-2mg or -4mg in a phase 2, randomized, placebo-controlled study. Sera from 68 patients (baricitinib-2mg: n=29; baricitinib-4mg: n=25; placebo: n=14) were collected at baseline and Week 12 and analyzed for cytokines using a Proximity Extension Assay (PEA) with 87 detectable analytes (Target 96 Inflammation Panel (Olink)). Interferon (IFN) scores were determined using a Modaplex assay. Spearman correlations were computed. Analyte changes from baseline at Week 12 were compared between baricitinib-4mg and placebo groups by Wilcoxon rank-sum or t-tests. Adjusted $p< 0.05$ was considered significant.

Results: At baseline, CXCL10 (r=0.50), CXCL11 (r=0.38), and CCL19 (r=0.45) correlated with the IFN signature. Confirming previous findings using Quanterix assays[2], PEA analysis indicated that baricitinib-4mg, but not placebo, reduced IL-6 and IL-12p40 in SLE. Additionally, baricitinib-4mg significantly downregulated 1) serum cytokines that mediate lymphocyte and monocyte/macrophage recruitment (CCL19, TNFRSF9, TNF-β/Lymphotoxin-α), and 2) cytokines that induce bone turnover and augment joint pain (TRANCE/RANKL and Artemin).

Conclusion: These results suggest that downregulation of key cytokines that have proinflammatory and/or regulatory functions may play a role in the mechanism by which baricitinib acts to improve SLE disease activity.

References

1. Wallace DJ, et al. *Lancet*. 2018;392(10143):222-31.
2. Dörner T, et al. *Lupus Sci Med*. 2020;7(1).

Disclosure: T. Dörner, Eli Lilly, 2, Novartis, 2, Janssen, 2, GSK, 2, Sanofi, 2, Deutsche Forschungsgemeinschaft, 5, AbbVie, 2, Roche, 2, Boston Pharmaceuticals, 2; **Y. Tanaka**, Daiichi-Sankyo, 2, 5, 6, Eli Lilly, 6, Novartis, 6, YL Biologics, 6, Bristol-Myers Squibb, 6, Eisai, 5, 6, Chugai, 5, 6, AbbVie, 2, 5, 6, Astellas, 6, Pfizer, 6, Sanofi, 2, 6, Asahikasei, 5, 6, GSK, 2, 6, Mitsubishi-Tanabe, 5, 6, Gilead, 6, Janssen, 6, Takeda, 5, Ayumi, 2, Taisho, 2; **D. Wallace**, GlaxoSmithKline, 2, 6, Eli Lilly and Company, 2, 6, AstraZeneca, 2, 6, Aurunia, 2, 6, EMD Serono, 2; **D. Fantini**, Eli Lilly and Company, 3, 11; **A. Koch**, Eli Lilly and Company, 3; **M. Silk**, Eli Lilly and Company, 3, 11; **J. Terres**, Eli Lilly and Company, 3, 11; **J. Sims**, Eli Lilly and Company, 3; **P. Fischer**, Eli Lilly and Company, 3, 11; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2.

Abstract Number: 1764

Estimation of the Prevalence of Hydroxychloroquine-Induced Retinopathy in a Cohort of Hydroxychloroquine-Compliant Patients

Kelley Brady, Roberta Alexander, Rory Bloch, Mark Rudolph, Karina Baggiani, Deborah Stimson and Anja Kammensheidt, Exagen Inc., Vista, CA

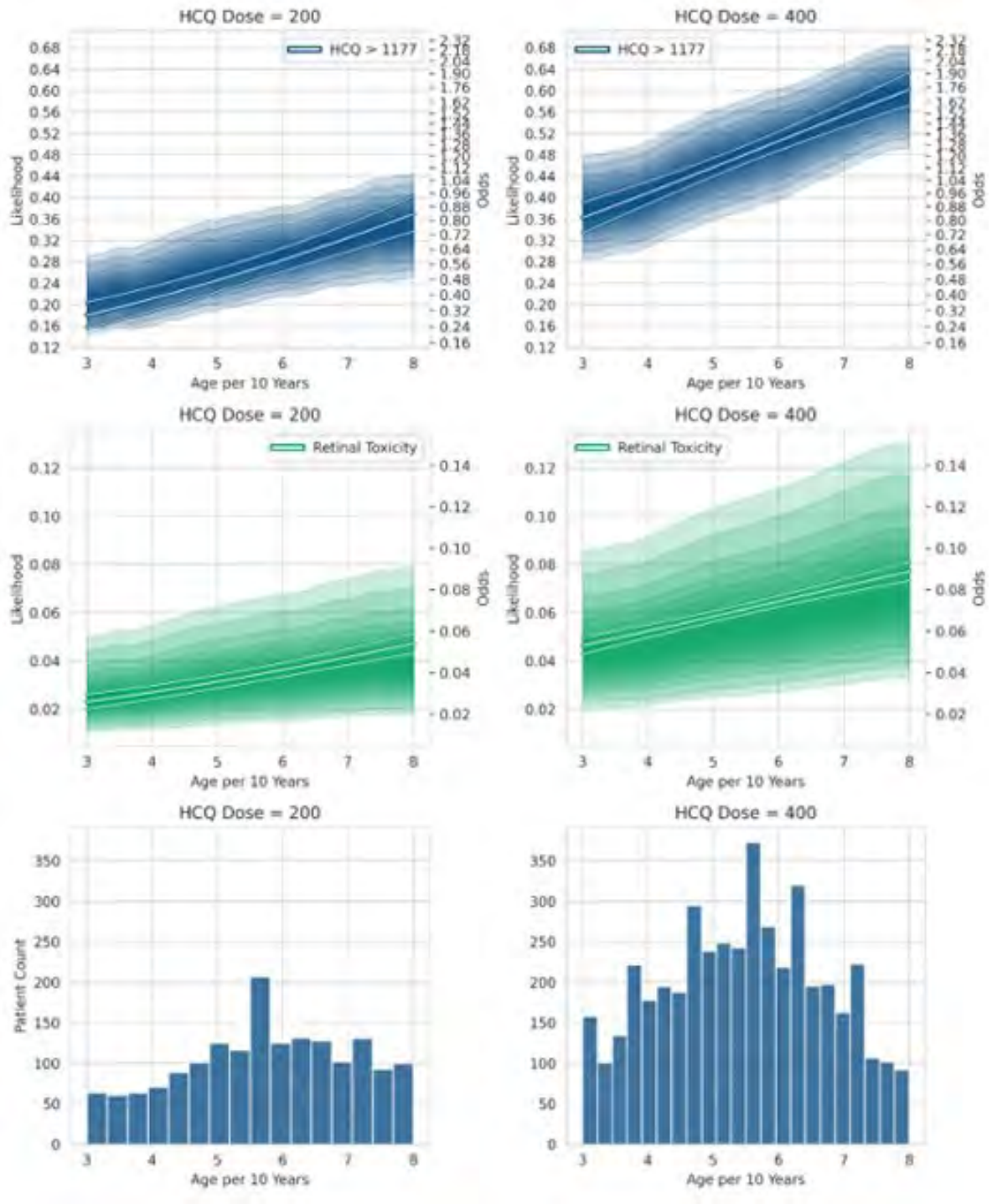
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: HCQ is an antimalarial drug effective in the treatment of rheumatologic conditions. High blood levels, advanced age, and extended treatment duration are associated with HCQ-induced retinopathy (R_{HCQ})(Petri et al. [Arthritis Rheum] 2020). We combined these insights with large amounts clinical therapeutic drug monitoring (TDM) data and deidentified patient information to develop interpretable linear models for the estimation of the overall prevalence of R_{HCQ} in a cohort of HCQ-therapy-compliant patients, and the odds of an individual patient presenting R_{HCQ} given HCQ dose and age.

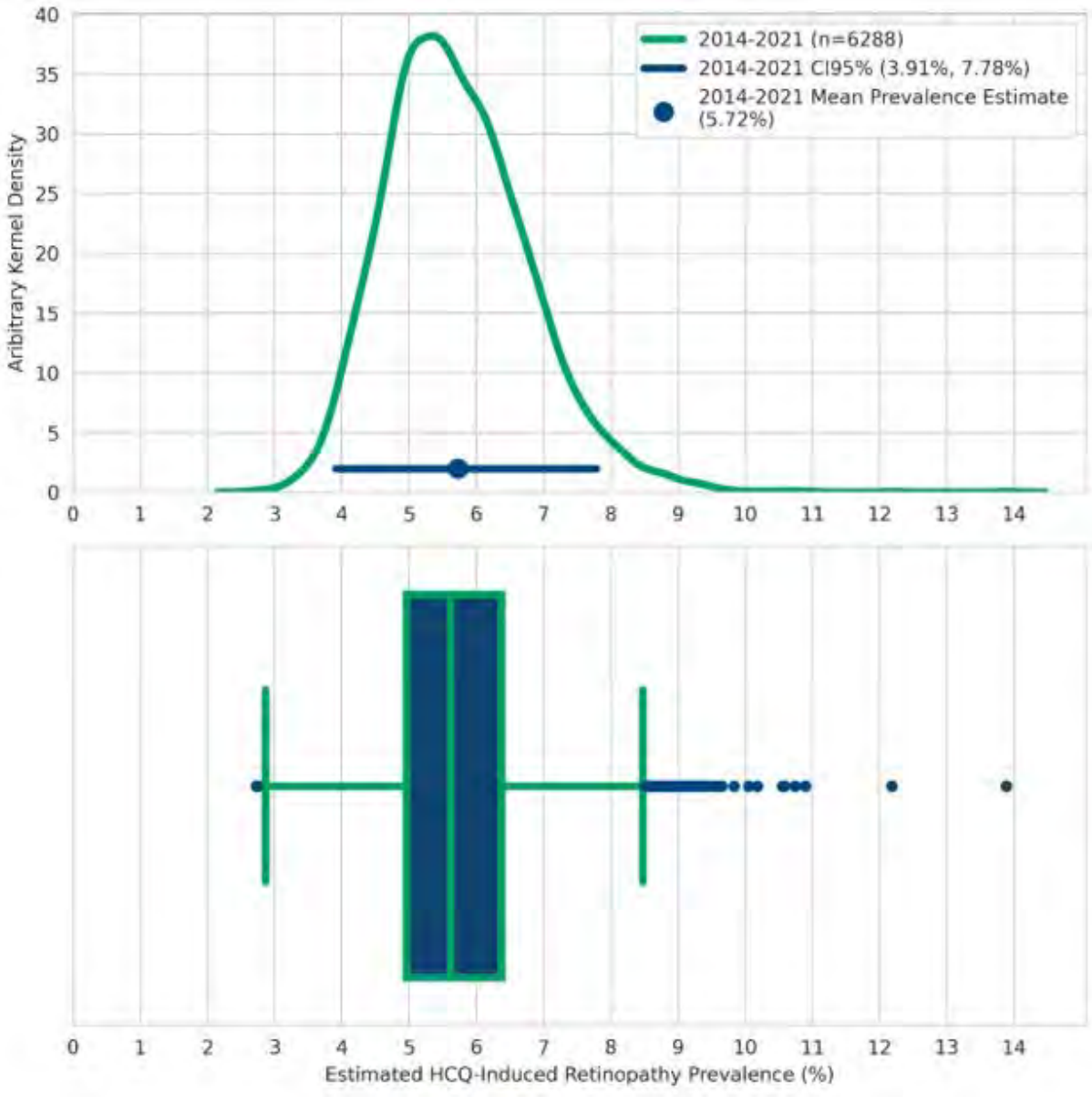
Methods: US ordering providers (n=986) submitted specimens collected from patients receiving therapy HCQ to Exagen Inc's CAP accredited clinical laboratory between December 2014 and April 2021 (Table 1). HCQ levels were measured in EDTA blood or capillary blood collected on micro-samplers using LC-MS/MS and reported to clinicians within 5 days of specimen receipt. Recommendation was made to collect specimens after 6 months therapy (steady state). The relationship between age per 10 years and HCQ dose per 200 mg qd with the likelihood of having HCQ levels greater than 1177 ng/mL was modeled using random intercept logistic regression. That estimated likelihood was combined with estimates of the sensitivity and positive predictive value of the cutoff HCQ ≥ 1177 ng/mL for the

Table 1. Patient Characteristics. 'Patients with HCQ Dose' refers to the subset of patients for whom HCQ monitoring was ordered, and the ordering provider opted to indicate dosing information at the time of test requisition submission. The subset 'Patients with HCQ Dose' was further filtered to include only patients with venous blood HCQ ≥ 500. 'All Patients with HCQ Order' refers to any patient for whom HCQ monitoring was ordered, including non-compliant patients and patients for whom HCQ dose was not indicated. Only the most recent visit per patient are included

	Patients with HCQ Dose (HCQ ≥ 500, Most Recent Visit)	All Patients with HCQ Order (Most Recent Visit)
Age (years)	55.3 ± 12.6	54.0 ± 12.8
% Female	90.40%	90.40%
n Unique Patients	6288	12979
n Unique NPI's	676	986
HCQ Dose (Mean mg/day)	349.0 ± 96.0	N/A
HCQ Dose (Median mg/day)	400	N/A
Mean Venous Blood HCQ (ng/mL)	1192.8 ± 504.2	945.3 ± 625.0
% Patients Having HCQ < 50 ng/mL	N/A	10.40%
% Patients Having HCQ < 200 ng/mL	N/A	14.50%
% Patients Having HCQ > 500 ng/mL	100%	75.20%
% Patients Having HCQ > 1177 ng/mL	43%	32.70%



Y-Axes are shared across each row; x-axes are conserved across all subplots. Top: Theoretical population mean estimates for the likelihood of achieving HCQ≥1177 ng/mL in a cohort of HCQ-therapy-compliant patients with prediction intervals describing the estimated likelihood of HCQ≥1177 ng/mL for individuals drawn from a population described by our cohort in increments of 10%, for 10%-90%, and 95%. Middle: Theoretical population mean estimates for the likelihood of R_HCQ in a cohort of HCQ-therapy-compliant patients with prediction intervals describing the estimated likelihood of R_HCQ for individuals drawn from a population described by our cohort in increments of 10%, for 10%-90%, and 95%. Bottom: Histograms describing the distribution patients by age allow an examination of the weight assigned to each vertical slice of likelihood in the middle plot when constructing the estimate of R_HCQ in Figure 3.



Top: Kernel density plot of estimated R_HCQ shows the uncertainty in the estimate of R_HCQ in a cohort of HCQ-therapy-compliant patients with CI95% and mean R_HCQ. Bottom: Box plot of the same distribution with outliers, minimum, 25th percentile, median, 75th percentile, and maximum.

prediction of the incidence of R_{HCQ}; thus allowing the estimation of the likelihood of R_{HCQ} given age and HCQ dose and the estimation of the overall rate of R_{HCQ}. Probabilistic modeling was performed with PyMC3 and compared to generalized estimating equations (GEE) implemented with StatsModels. Random intercept and GEE grouping was performed per ordering provider using only the most recent visit per patient. To ensure the analysis was performed using patients likely to be at least partially adherent to HCQ therapy, patients having HCQ < 500 ng/mL were excluded.

Results: Odds of having HCQ ≥ 1177 increased by 22% (CI95%Proba: [17%, 27%] | CI95%GEE: [15%, 26%]) per 10 years of age and 158% (CI95%Proba: [129%, 189%] | CI95%GEE: [102%, 206%]) per 200 mg HCQ prescribed qd. Figure 2 presents the theoretical population mean estimates (regression estimates with CI95%) and prediction intervals for individuals drawn from the cohort in increments of 10% from 10%-90%, and 95%. The estimated incidence of R_{HCQ} in the cohort of patients having HCQ ≥ 500 was 5.72% (CI95% = [3.91%, 7.78%], Figure 3).

Conclusion: The estimated CI95% ([3.91%,7.78%]) for the prevalence of R_{HCQ} in patients compliant to HCQ-therapy overlapped with estimates produced by previous studies. Model estimates for the population mean likelihoods agreed with individual prediction intervals, but the relatively wider prediction intervals emphasize the importance of appropriate utilization of HCQ TDM in patients chronically prescribed HCQ.

Disclosure: K. Brady, Exagen, Inc, 3, 11; **R. Alexander**, Exagen Inc., 3, 11; **R. Bloch**, Exagen, Inc, 3, 11; **M. Rudolph**, Exagen, Inc, 3, 11; **K. Baggiani**, Exagen Inc, 3, 11; **D. Stimson**, Exagen Inc, 3, 11; **A. Kammensheidt**, Exagen Inc., 3, 4, 11.

Abstract Number: 1765

Should SLE Patients Entering Clinical Trials Be Required to Have at Least One BILAG A and/or Two BILAG B Domain Scores?

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: High placebo response rates have challenged interpretation of clinical trial results in SLE and may have contributed to failure of some effective treatments. One hypothesis to explain inflated placebo responses is that patients may not have sufficient disease activity at baseline. Most SLE study designs require a score of ≥6 on the SLE Responder Index (SLEDAI) at entry. Some have attempted to enrich for more active disease by adding an additional inclusion criterion for score A (severe) in ≥1 organ system and/or B (moderate) in ≥2 organ systems on the

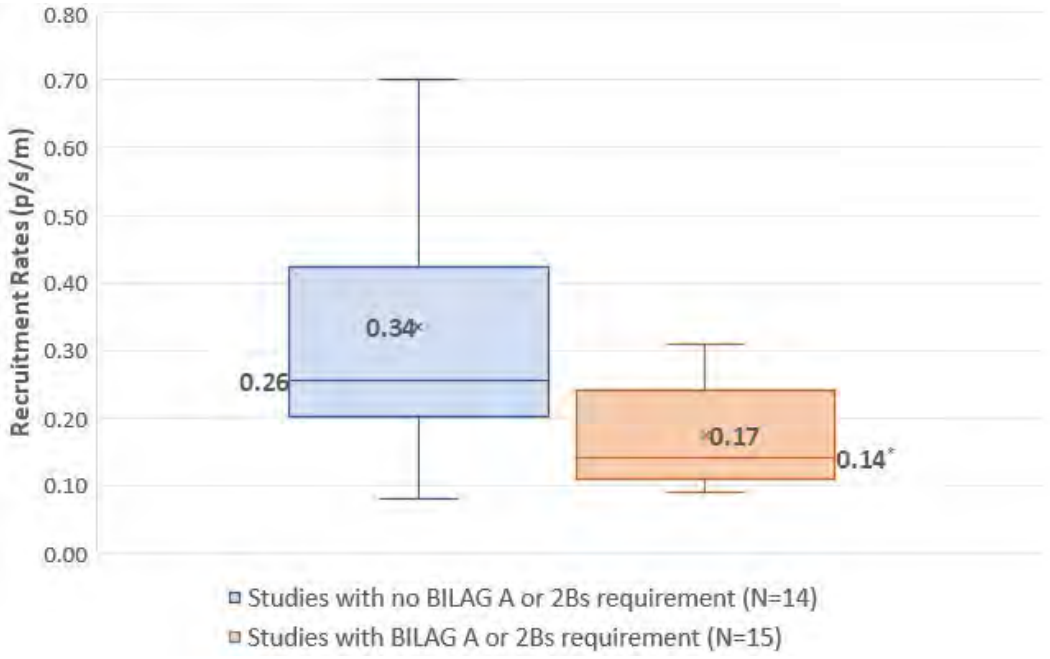

Figure 1. Impact of at least 1 BILAG A or 2 B scores requirement on recruitment rates: comparison of recruitment rates (patients/site/month) of trials that had this requirement with the ones that di not (*p<0.05, Mann-Whitney Rank Sum).

British Isles Lupus Assessment Group (BILAG) index (at least 1 BILAG A or 2 B). However, the impact of this requirement on enrollment and study outcomes, including placebo response has not been previously examined.

Methods: Data from completed Phase II and III SLE trials that enrolled ≥100 subjects and reported endpoints using SLEDAI and/or BILAG (SRI-4 and/or BICLA responses) were included in the analysis. In trials that did not require minimal BILAG scores, the proportions of patients who had at least 1 BILAG A or 2 B scores at baseline were examined. Trials that included the BILAG requirement were compared to those that did not for recruitment rates, meeting primary endpoint, and placebo SRI-4 and BICLA response rates.

Results: Thirty (16 Phase II and 14 Phase III) trials met the initial search criteria; one was excluded from the analysis because patients with BILAG A at screening were not allowed. Most of the studies (70%) required SLEDAI score ≥6 at entry; 15 (51.7%) trials required at least 1 BILAG A or 2 B scores and 14 (48.9%) did not. In studies with no BILAG requirement, the mean percent of patients with at least 1 BILAG A or 2 B scores was 61.1%.

Mean/median recruitment rates for all 29 studies combined were 0.25/0.21 patients/site/month (p/s/m). Trials with no BILAG requirement enrolled twice as fast as the ones that required at least 1 BILAG A or 2 B scores: mean/median recruitment rates 0.34/0.26 p/s/m versus 0.17/0.14 p/s/m ($p < 0.05$, Figure 1).

Eleven out of the 29 (39.7%) trials met the primary endpoint; average SRI-4 and BICLA placebo response rates were 44.4% and 34.8% respectively. More studies with no BILAG requirement met their primary endpoint and had lower means of placebo response for both SRI-4 and BICLA than the trials with at least 1 BILAG A or 2 B scores required (Figure 2).

Conclusion: It has been hypothesized that adding minimal BILAG requirement to the traditional SLEDAI criterion at entry will increase the probability of positive outcomes and decrease the inflated placebo response seen in trials of SLE. However, results from the completed studies suggest the opposite: at least 1 BILAG A or 2 B scores requirement at entry was associated with higher placebo response rates and lower likelihood of meeting the primary endpoint, and at the same time, significantly lower enrollment rates. This unexpected finding merits further investigation.

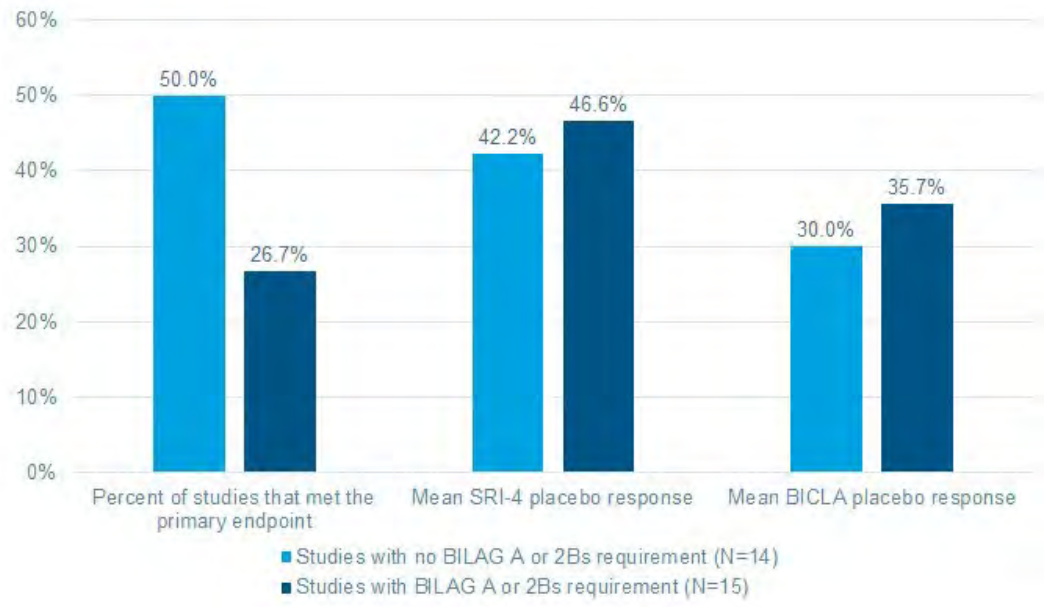

Figure 2. Impact of adding 1 BILAG A or 2 B scores requirement as inclusion on study outcomes: Percent of studies that met their primary endpoint and mean proportions of placebo patients achieving SRI-4 and BICLA responses.

Disclosure: E. Olech, IQVIA, 3; **F. Hussain**, IQVIA, 3; **J. Merrill**, GlaxoSmithKline, 2, 5, UCB, 2, AbbVie, 2, EMD Serono, 2, Remegen, 2, Celgene/Bristol Myers Squibb, 2, AstraZeneca, 2, 5, Daiichi Sankyo, 2, Servier, 2, Immupharma, 2, Amgen, 2, Janssen, 2, Lilly, 2, Genentech, 2, Resolve, 2, Alpine, 2, Aurinia, 2, Astellas, 2, Alexion, 2, Provention, 2.

Abstract Number: 1766

Itolizumab-induced Modulation of Cell Surface CD6 Is a Pharmacodynamic Marker of Drug Activity in SLE Patients

Dalena Chu[1], Leslie Chinn[2], Jeanette Ampudia[1], Krishna Polu[1], Joel Rothman[1], Maple Fung[3], Dolca Thomas[4], Chaim Putterman[5], Cherie Ng[1] and Stephen Connelly[1], [1]Equillium, Inc., La Jolla, CA, [2]Equillium, Inc., South San Francisco, CA, [3]Equillium, Inc., San Diego, CA, [4]Equillium, Inc., Brooklyn, NY, [5]Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Itolizumab (ITO) is a novel first-in-class monoclonal antibody (IgG1-k) specific for CD6, a co-stimulatory receptor that is highly expressed on T cells that plays an important role in their activity and trafficking.

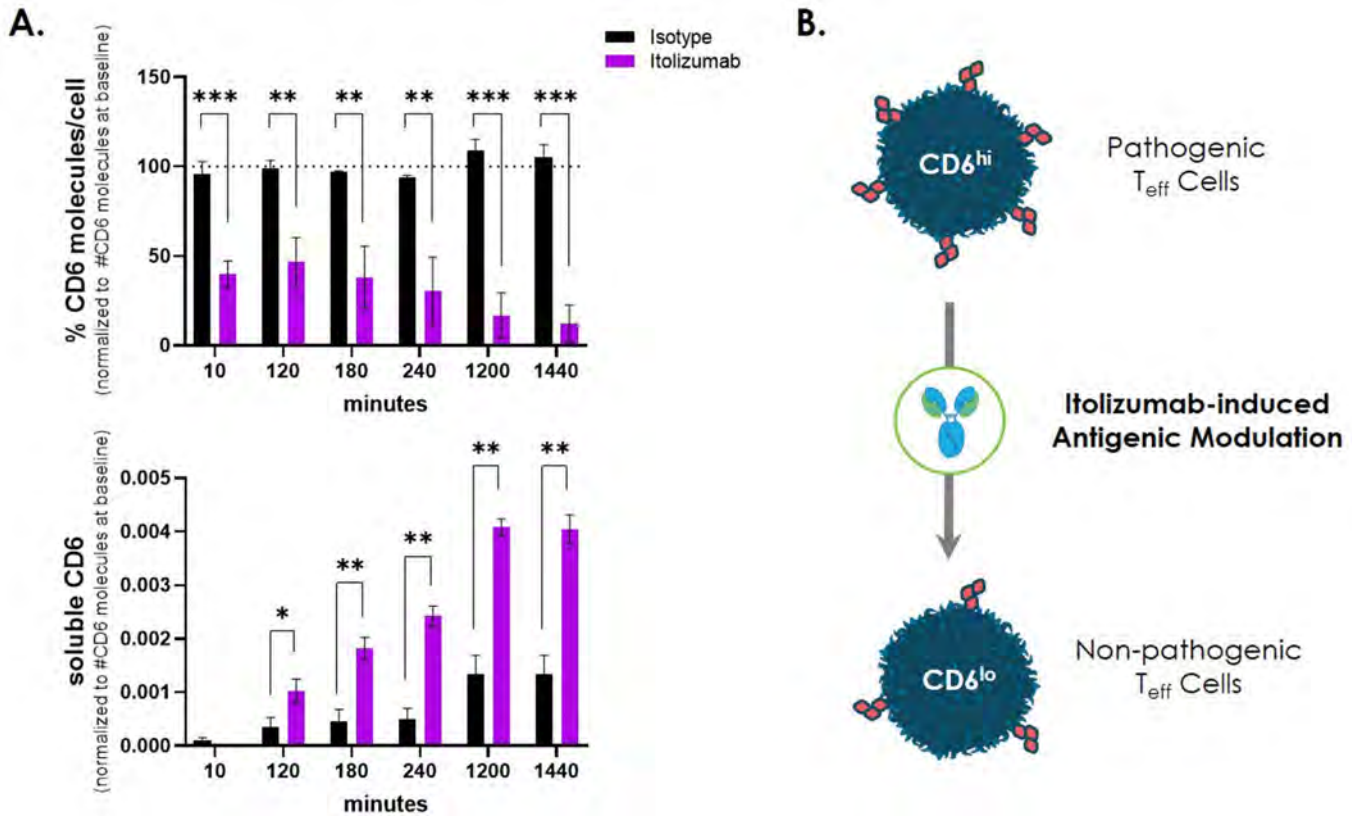

Figure 1. Itolizumab induces loss of CD6 from the T cell surface. (A) PBMCs from 3 different donors were incubated with 10ug/ml of itolizumab and cell surface expression of CD6 was assessed on CD4 T cells and soluble CD6 quantitated in the PBMC supernatant at the indicated timepoints. The calculated number of CD6 receptors on CD4 T cells at baseline as assessed by flow cytometry was used to normalize values across the 3 donors. (B) Schematic of how itolizumab-induced loss of CD6 (antigenic modulation) might affect T cell activity, transforming the cell to possess a less inflammatory phenotype. ***p<0.001, ** p<0.01, * p<0.05.

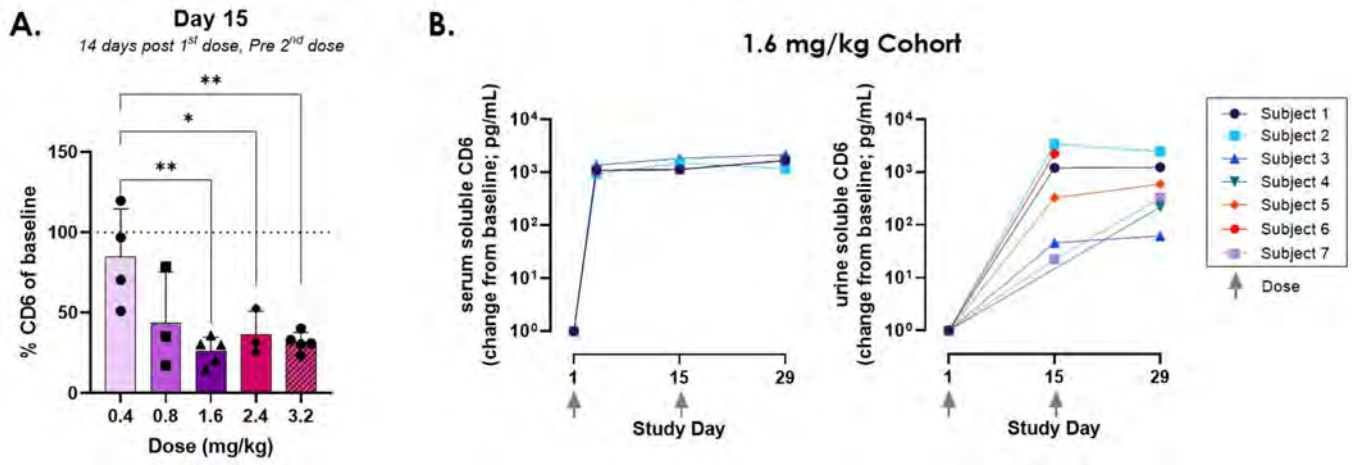

Figure 2. Changes in CD6 in EQUALISE subjects. (A) Cell surface CD6 expression on CD4 T cells decreases following first dose of itolizumab. Expression calculated as % of baseline (pre-drug) expression. (B) Levels of soluble CD6 in serum and urine increase after first dose of itolizumab. Data shown as change from baseline (pre-drug). ***p<0.001, ** p<0.01, * p<0.05.

Excessive activation through CD6 has been implicated in the pathogenesis of multiple autoimmune and inflammatory diseases, including systemic lupus erythematosus (SLE) and lupus nephritis (LN). Consequently, ITO is being evaluated as treatment for SLE and LN. Here, we demonstrate that ITO induces cleavage of cell surface CD6, leading to decreased T cell activity, and that the levels of cell and soluble CD6 in SLE patients dosed with ITO is a pharmacodynamic marker of drug activity.

Methods: Mechanistic experiments were carried out *ex vivo* using PBMCs from normal donors. Samples from patients dosed with ITO, including blood, serum and urine, were collected as part of the EQUALISE trial, an open label Phase 1b 2-part study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), and clinical activity of subcutaneous doses of ITO (0.4 to 3.2 mg/kg on Day 1 and Day 15) in patients with SLE (NCT04128579). Cell surface CD6 was assessed by flow cytometry using an anti-CD6 antibody that does not compete with the binding of ITO, while soluble CD6 in cell supernatants, serum and urine was quantified by an electrochemiluminescent assay.

Results: When PBMCs were incubated with ITO (0.01-10ug/ml), CD4 and CD8 T cell populations exhibited loss of surface CD6 in a dose- and time-dependent manner. Cell surface loss was accompanied by a concomitant increase in soluble CD6 in the supernatant (Figure 1). The resulting $CD6^{low}$ T cells showed reduced T-cell activity (as indicated by activation markers and cytokine production), compared to isotype-treated $CD6^{high}$ cells, despite removal of ITO from the system. In samples from SLE patients dosed with ITO, significant loss of cell surface CD6 on T cells was observed after the first dose. Decreases in cell surface CD6 from baseline were most pronounced at doses ≥1.6 mg/kg and were accompanied by increases in soluble CD6 in the serum and urine (Figure 2). PK/PD analysis of the relationship between ITO concentrations and cell surface CD6 levels indicated that the data were described by an E_{max} model, which predicted a maximal decrease in CD6 expression of approximately 78%.

Conclusion: Cell surface CD6 regulates T cell activity and ITO-induced loss of CD6 leads to inhibition of T cell activity and can be used to monitor PD activity. SLE patients in the EQUALISE trial demonstrate dose-dependent loss of CD6 with maximal loss occurring at 1.6mg/kg, suggesting that higher doses are not necessary to achieve the greatest inhibition of T cell activity.

Disclosure: D. Chu, Equillium, Inc., 3, 10, 11; **L. Chinn**, Equillium, Inc., 3, 11, Genentech/Roche, Inc., 3, 10, 11, Principia, a Sanofi company, 3, 11; **J. Ampudia**, None; **K. Polu**, Equillium, Inc., 2, 3, 11; **J. Rothman**, Equillium, Inc, 3, 4, 11; **M. Fung**, Equillium Inc, 3, Arena Pharmaceuticals, 3; **D. Thomas**, Chinook, 4, Equillium, 4, Principia, 4; **C. Putterman**, equllium, 2, 5, Progentec, 2, Kidneycure, 2; **C. Ng**, Equillium, Inc, 3, 11; **S. Connelly**, None.

Abstract Number: 1767

CXCL5 Dampens Inflammation in Murine Lupus by Orchestral Suppression of Effector Cell Proliferation and Leukocyte Extravasation

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a potentially fatal autoimmune disease characterized by dysregulation of both innate and adaptive immunity. Current therapeutic options are limited, and 20-40% of patients are unresponsive to treatment. C-X-C motif chemokine ligand 5 (CXCL5) is known as a chemoattractant and activator of neutrophils. Our prior work identified CXCL5 as a key active factor secreted by mesenchymal stromal cells (MSCs) that was able to improve survival and reduce disease activity in a pre-clinical mouse model of graft versus host disease. However, whether CXCL5 could dampen inflammation and abrogate the pathological processes of SLE is unknown.

Methods: 16-week-old MLR/lpr (Fas^{lpr}) lupus-prone mice were treated with ten weekly intravenous doses of CXCL5 (3 μg/kg) and monitored for ten weeks. Immune and cytokine profiles were determined by flow cytometry and Luminex assays. Anti-DS DNA autoantibody levels were measured by ELISA. Proteinuria was evaluated by albumin creatinine ratio. Renal immune cell infiltration and complement 3 deposition were determined by Haematoxylin & Eosin and immunofluorescence staining. Potential molecular changes were identified by bulk RNA sequencing.

Results: Indeed, in MLR/lpr (Fas^{lpr}) lupus-prone mice, we found that intravenous treatment with CXCL5 significantly improved mouse survival with a concomitant reduction in anti-dsDNA levels, proteinuria, renal complement C3 deposition, leukocyte infiltration and neutrophil extracellular trap (NET) formation. Immune and molecular profiling and pharmacokinetic studies showed that CXCL5 treatment reduced inflammation via the orchestral suppression of effector cell (T_H17 cells, neutrophils and macrophages) proliferation mediated through T_H1 and T_H2 cells and leukocyte extravasation through restoration of the dysregulated CXCL5 blood-tissue chemokine gradient.

Conclusion: CXCL5 may represent a novel therapeutic option for SLE by restoring dysregulated innate and adaptive immune responses.

Disclosure: X. Fan, None; **C. Ng**, None; **D. Guo**, None; **F. Lim**, None; **A. Law**, None; **J. Thumboo**, None; **W. Hwang**, None; **A. Low**, None.

Abstract Number: 1768

Additional Hydroxychloroquine Therapy Regulates Adipokines in Systemic Lupus Erythematosus with Stable Disease Activity

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: SLE – Treatment Poster (1732–1772)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In systemic lupus erythematosus (SLE), atherosclerosis is strongly associated with vital prognosis. On the other hand, arteriosclerosis is strongly influenced by serum adipokines. The effect on serum adipokine by hydroxychloroquine (HCQ) therapy, which has a vital prognostic benefit in systemic lupus erythematosus, has not been fully investigated. The purpose of this study is to determine the effect of HCQ treatment on serum adipokines in SLE.

Table 1. Characteristics of SLE patients enrolled in this study Anti-dsDNA positive means anti ds-DNA titer increases over 12 IU/ml Low complement means any of C3, C4 and CH50 decreases to less 68mg/dl, less 12mg/dl, 30U/ml. APS: Anti-phospholipid antibody syndrome, NPSLE: neuropsychiatric SLE, LLDAS: lupus low disease activity state

Characteristics	n=41, no.(%)
Female, no(%)	37(90)
Age, years, mean±SD	41.3±13.2
Disease duration, years, mean±SD	14.9±11.3
Past involvement	
Renal involvement	18 (44)
NPSLE	3 (7)
Complication	
APS	8 (20)
Dyslipidemia	1 (2)
Diabetes	1(2)
Hypertension	8 (20)
Concomitant immunosuppressive treatments	
Prednisone No.(%) Median Dosage, mg/day (range)	 34 (83) 4.5 (1-10)
Disease activity	
SLENA-SLEDAI score, Median(range)	4.0 (0-8)
Current skin involvement	23 (56)
anti-dsDNA positive, no(%)	15 (37)
low complement, no(%)	20 (49)
LLDAS	25 (61)
Clinical remission on treatment	4 (10)

Methods: To determine the effect of HCQ treatment alone on serum adipokines, SLE patients with stable disease activity who had not previously received HCQ treatment were included in the study. Additional HCQ therapy was started in these patients from 2016 to 2020. Disease activity was assessed by SLEDAI, CLASI and LLDAS and serum complement titers, anti-ds-DNA antibodies. Serum adipokines (adiponectin, resistin and leptin) were analyzed using ELISA kit (Adiponectin/Acrp30 Quantikine ELISA Kit, R&D and Simple Plex, ProteinSimple) before and 3 months after starting additional HCQ treatment.

In addition, we measured serum cytokines (TNF-α, IL-6, IL-8, MCP-1, MIP-1a, IL-1ra, IL-2) reported to be associated with the pathogenesis of SLE using multiplex immunoassay (Luminex Assay, R&D) and analyzed the relationship with changes of serum adipokines.

Results: Forty-one patients (4 males, 37 females, mean age 41.3±13.2 years) without changing treatment regimens, including glucocorticoids and immunosuppressive drugs other than HCQ were included (Table 1).

Serum adiponectin levels were significantly increased and serum resistin levels were significantly decreased 3 months after additional HCQ administration compared to baseline. No significant changes were observed in serum leptin levels (Fig. 1).

Regarding the association between these adipokines and disease activity parameters, changes of these adipokines by HCQ treatment were not associated with those of hypocomplement. However, change of leptin alone were positively correlated with decreasing anti-dsDNA antibodies.

On the other hand, additional HCQ administration decreased serum TNF-α, IL-6, IL-1ra and IL-2 levels significantly 3 months after compared to baseline.

Regarding the association between these cytokines change and disease activity, the change of TNF-α levels were related to improvement of hypocomplementemia (C3 and C4). Furthermore, the reduction of IL-1ra by additional HCQ treatment was associated with the achievement of LLDAS .

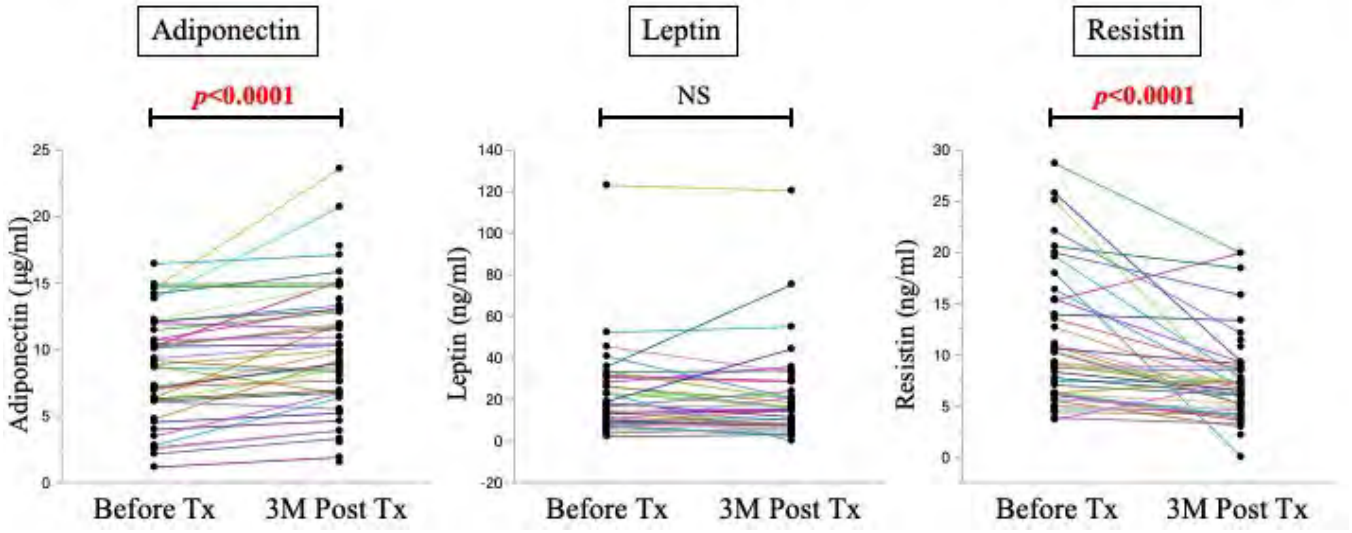

Figure 1. Serum adipockine levels before and after HCQ treatment. Serum levels of the indicated cytokines and factors were measured before or after 3 months (3M Post) treatment (Tx) with HCQ. Colored lines represent individual patients. NS: not significant. P values were determined by the Wilcoxon signed-rank test.

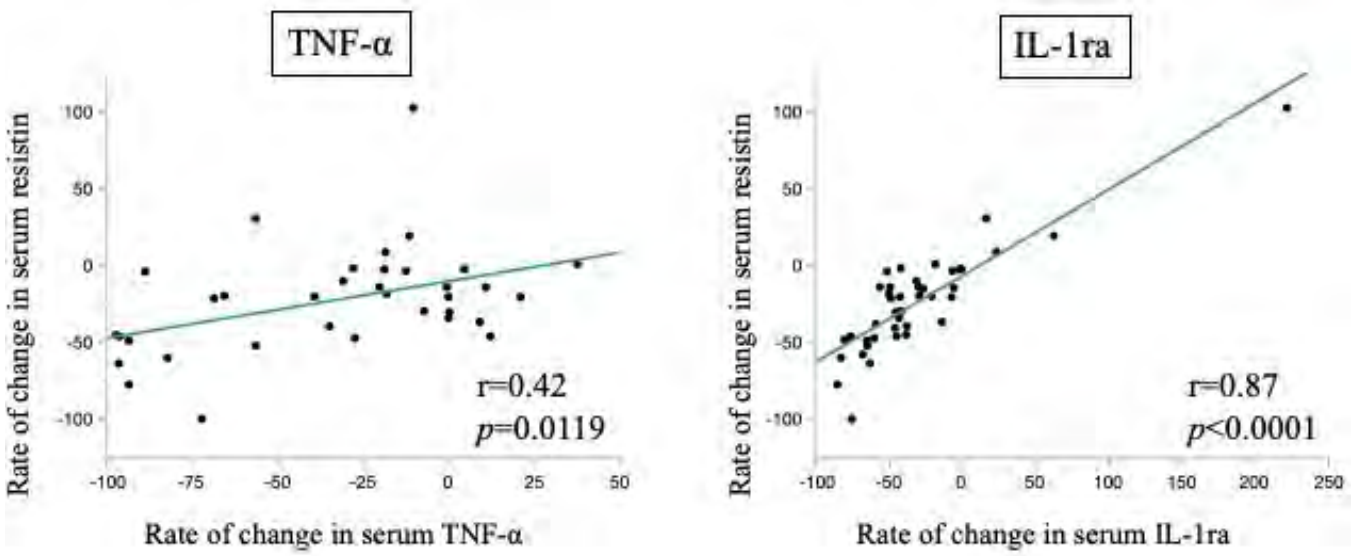

Figure 2. Association between changes in serum cytokines and resistin after HCQ treatment. Reduction of resistin was correlated with reduction of TNF-α or IL-1ra by HCQ therapy significantly. P values were determined by univariate analysis. r: correlation coefficient.

Among of these adipokines, change of resistin was correlated with reduction of TNF-α or IL-1ra by HCQ therapy significantly (Fig. 2). However, the increasing adiponectin was not correlated with change of these cytokines.

Conclusion: HCQ treatment could regulate serum adipocytokine in SLE patients. Resistin was modulated through the effect of HCQ on disease activity. However, the effect of HCQ on serum adiponectin was suggested to be independent on change of disease activity parameters or several cytokines associated with SLE disease activity.

Disclosure: R. Wakiya, None; **K. Ueeda**, None; **H. Shimada**, None; **S. Nakashima**, None; **M. Kato**, None; **T. Miyagi**, None; **M. mai**, None; **K. Sugihara**, None; **R. Semba**, None; **M. Mizusaki**, None; **T. Kameda**, None; **H. Dobashi**, None.

Abstract Number: 1769

BMS-986256, an Oral Novel Toll-like Receptor 7 and 8 (TLR7/8) Inhibitor, Does Not Affect the Pharmacokinetics of Mycophenolate Mofetil in Healthy Subjects

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Toll like receptor (TLR) 7 and TLR8 are activated as part of the disease pathophysiology of systemic lupus erythematosus (SLE), including lupus nephritis (LN), and related autoimmune diseases, such as

Sjögren's Syndrome. BMS-986256, an orally administered, potent and selective inhibitor of TLR7/8, has demonstrated efficacy in animal models of lupus as well as favorable PK and acceptable safety profiles in healthy subjects. It is now in clinical development for the treatment of SLE. Mycophenolate mofetil (MMF) is an immunosuppressive agent that is widely used in immune-mediated diseases and is often used in the treatment of patients with more serious presentations of active SLE. MMF gets converted to its active metabolite mycophenolic acid (MPA) following oral administration. Therapeutic drug monitoring for MMF and MPA is recommended in certain cases, especially when used as a first-line therapy. Given that MMF is often used in the treatment of SLE, it is likely that BMS-986256 will be administered concomitantly with MMF in Phase 2 studies, and more importantly, in clinical practice. Thus, the effect of BMS-986256 on the exposures of the MMF active metabolite MPA and the phenolic glucuronide of MPA (MPAG) were evaluated.

Methods: This was an open label, single sequence crossover study in which 24 healthy participants received a single oral dose of MMF 1000 mg on Day 1. Starting on Day 5 through Day 28, participants received 30 mg BMS-986256 QD oral dose. On Day 26, subjects received a second oral dose of MMF 1000 mg (in addition to QD dose of BMS-986256). Blood samples were collected after each treatment for PK evaluation. Safety evaluations (adverse events (AEs)), physical and skin examinations, vital signs, electrocardiograms, laboratory tests) were performed during the course of the study.

Results: Co-administration of BMS-986256 with MMF resulted in no clinically meaningful increase in exposures of MPA with geometric mean maximum concentration (Cmax) and total exposure (area under the curve extrapolated to infinity AUC(INF)) increased by 27 % and 17.8%, respectively, compared with MMF alone. Exposures of the MPA metabolite, MPAG, were comparable in both treatment groups, indicating no impact on metabolism of MPA by BMS-986256. In addition, single oral dose MMF did not alter steady state BMS-986256 and BMT-271199 (metabolite) exposures. BMS-986256 was generally safe and well-tolerated with and without MMF. There were no concerning abnormal laboratory test results, including tests of hepatic function and no serious AEs, deaths, or AEs leading to discontinuation. All treatment-emergent AEs were mild and resolved spontaneously.

Table. Statistical Analysis of the Effect of Steady-State BMS-986256 on Single Dose of MMF for MPA and MPAG PK Parameters

	Geometric LS Mean					
	BMS-986256 with MMF Day 26 (Test)		MMF (1000 mg, single dose) Day 1 (Ref)		Geometric LS Mean Ratio (Test/Ref)	
Parameter	n	Result	n	Result	Estimate	90% CI
MPA						
Cmax (µg/mL)	22	23.4	24	18.5	1.270	(1.078, 1.495)
AUC(0-T) (h•µg/mL)	22	59.0	24	51.3	1.150	(1.073, 1.233)
AUC(INF) (h•µg/mL)	19	62.1	23	52.7	1.178	(1.092, 1.271)
MPAG						
Cmax (µg/mL)	22	37.9	24	34.6	1.095	(0.999, 1.200)
AUC(0-T) (h•µg/mL)	22	437.9	24	412.9	1.061	(1.010, 1.113)
AUC(INF) (h•µg/mL)	22	444.6	24	417.6	1.065	(1.015, 1.116)

AUC(INF) = area under the concentration-time curve from time of dosing extrapolated to infinity; AUC(0-T) = area under the concentration-time curve from time of dosing to the time of the last quantifiable concentration observed; CI = confidence interval; Cmax = maximum plasma concentration; LS = least squares; MMF = Mycophenolate mofetil; MPA = mycophenolic acid; MPAG = phenolic glucuronide of mycophenolic acid; N = number of participants; n = number of observations; PK = pharmacokinetics; Ref = reference

Conclusion: BMS-986256 at steady state had no clinically meaningful effect on the PK of a single dose of MMF. MMF alone or in combination with BMS986256 was safe and well tolerated in this study. Given the lack of clinically meaningful DDI, MMF can be co-administered with BMS-986256 without any dose adjustment.

Disclosure: M. Chiney, Bristol Myers Squibb, 3; **I. Girgis**, Bristol Myers Squibb, 3, 11; **M. Harrison**, Bristol-Myers Squibb, 3, Pfizer, 12, Stock holder, Pfizer, 3; **X. Zhang**, Bristol Myers Squibb, 3; **Y. Shen**, Bristol Myers Squibb, 3; **M. Dawes**, None; **L. Dong**, Bristol-Myers Squibb, 3; **D. Shevell**, Bristol Myers Squibb, 3; **U. Aras**, Bristol Myers Squibb, 3; **B. Murthy**, Bristol Myers Squibb, 3.

Abstract Number: 1770

Interim Analysis of Cohort 1 in the Mesenchymal Stromal Cell Trial in Systemic Lupus Erythematosis: Safety and Data Management During the Pandemic

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: There is heightened interest in the use of mesenchymal stromal cells (MSCs) for the treatment of autoimmune diseases. There are a number of reports of efficacy of MSCs with minimal safety concerns in lupus and rheumatoid arthritis. There are, however, only a very limited number of controlled trials to assess true efficacy and safety of MSCs in rheumatic diseases. There are no controlled trials of MSCs in lupus, while there are a number of uncontrolled trials, primarily from one center in China, reporting over 60% efficacy of MSCs in refractory lupus patients. The MSC in systemic lupus erythematosus trial (MiSLE) is the first double blind placebo controlled multi-center trial of MSCs as a treatment for refractory lupus.

Methods: The MiSLE trial is a two-cohort dose escalation trial at 9 centers in the United States. A total of 81 patients will be randomized. Cohort one is complete, consisting of 41 patients receiving either $1x10^6$ MSCs/kg or placebo in a 2/1 ratio. The MSCs are allogenic MSCs derived from umbilical cords of women undergoing elective C sections. They were prepared using standard ISCT protocols at our Clean Cell Facility. The blind is being maintained for cohort 1 through the completion of cohort 2. The second cohort of 40 patients, enrolling now, will receive $5x10^6$ MSCs/kg. Patients had a SLEDAI of 6 or greater at screening, had failed at least one immunosuppressant, and were on 0.5mg/kg prednisone or less. Clinical response was measured as a primary outcome using the SRI4 at 24 weeks post the single MSC infusion. Due to COVID, some of the followup visits were performed by Telehealth, using investigator judgement as to what parts of the SLEDAI and BILAG could be reliably scored.

Results: Forty-one patients were enrolled into cohort one of the MiSLE trial. Due to COVID, no new patients were enrolled from March 2020 through August 2020. The cohort consists of 90% women, 49% Caucasian, 39% African American and 12% other. Average age was 38. All 7 sites active in Cohort 1 enrolled patients. The organ systems

Table 1. Cumulative Adverse Events Summary

	Subjects N (%)[1][2]	Events N (events per subject)
Total subjects	41(100)	189(4.6)
Events Requiring 24 Hour Reporting		
BILAG A	8(19.5)	10(0.2)
Pregnancy	0(0)	0(0)
Serious Adverse Events	10(24.4)	15(0.4)
SAEs Related to:		
SLE	5(12.2)	5(0.1)
Study Intervention	0(0)	0(0)
Infection	3(7.3)	5(0.1)
Adverse Events	36(87.8)	189(4.6)
AEs Related to:		
SLE	25(61)	74(1.8)
Study Intervention	6(14.6)	7(0.2)
Infection	19(46.3)	41(1)
AEs By Severity		
Grade 1*	2(4.9)	3(0.1)
Grade 2	35(85.4)	154(3.8)
Grade 3	16(39)	30(0.7)
Grade 4**	2(4.9)	2(0)
Grade 5	0(0)	0(0)
Infusion Reaction	2(4.9)	2(0)
Deaths	0(0)	0(0)

Adverse events in Cohort 1 of the MiSLE trial

involved were 41.5% mucocutaneous, and 78.1% musculoskeletal. 14.6% had renal involvement. Mean SLEDAI score was 10.3 and 71% of patients were anti-dsDNA positive. 66% of patients were on prednisone. There were no deaths, no significant infusion reactions nor any SAEs attributed to the Investigational Product. Fifteen SAEs were reported in 10/41 participants. 10 BILAG A flares occurred in 5 patients. As expected, a number of the AEs and SAEs were infections, though MSCs are not believed to enhance infection risks. Notably a few patients contributed to most of the SAEs and lupus flares. The major issue arising due to the pandemic was delayed data entry and data inconsistency due to remote work and video visits.

Conclusion: The first cohort of patients in the MiSLE trial are infused and nearing completion of 52 weeks. There were a number of SAEs reported, but there was not a safety signal by DSMB review. Changes in data management and reporting are being instituted to improve prompt and accurate data entry. Overall, the safety data confirm that there are almost no infusion reactions with MSCs and the safety profile is sufficient to proceed to the higher dose cohort.

Disclosure: G. Gilkeson, None; **D. Kamen**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **R. Ramsey-Goldman**, None; **K. Kalunian**, Amgen, 2, AbbVie, 2, AstraZeneca, 2, Biogen, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Equillium, 2, Genentech/Roche, 2, Gilead, 2, Janssen, 2, Lupus Research, 5, Pfizer, 5, Sanford Consortium, 5, Vielabio, 2, Aurinia, 2, Alliance, 2, Nektar, 2; **S. Sheikh**, Pfizer, 5, GlaxoSmithKline, 2, 5; **M. Ishimori**, None; **D. Wallace**, None.

Abstract Number: 1771

First-in-Human Safety, Pharmacokinetic and Pharmacodynamic Study of Escalating Single- and Multiple-Doses of BMS-986256, a Novel, Potent, Oral Inhibitor of TLR7 and TLR8

Melanie Harrison[1], Manoj Chiney[1], Diane Shevell[2], Lixian Dong[3], Michelle Dawes[1] and Ihab Girgis[3], [1]Bristol Myers Squibb, Lawrenceville, NJ, [2]Bristol Myers Squibb, Lawrenceville, [3]Bristol Myers Squibb, Princeton, NJ

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Toll-like receptor (TLR)7 and TLR8 are endosomal receptors that are normally activated by pathogen-associated RNA. They are also activated by self-RNA as part of the pathophysiology of systemic lupus erythematosus (SLE) and related autoimmune diseases. Inhibition of TLR7 and TLR8 may be effective in the treatment of these diseases. BMS-986256 is an oral, potent and selective TLR7 and TLR8 inhibitor. It demonstrates robust pharmacodynamic (PD) activity and efficacy in multiple mouse models of lupus. The objective of this first-in-human, single ascending dose (SAD) and multiple ascending dose (MAD) study was to evaluate the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of BMS-986256 in healthy volunteers (HV)

Methods: Each of the SAD and MAD parts of the study were randomized, double-blind, placebo-controlled trials in which HV were randomized 3:1 (BMS-986256:placebo) within each dose cohort. In the SAD part of the study, a total of 48 HV were enrolled across 6 dose cohorts (1mg through 120mg) of 8 participants each and followed for up to 28 days. In the first of two MAD parts of the study, 24 non-Japanese HV were enrolled across 4 dose cohorts (once daily 3mg through 60mg) for up to 21 days and followed for up to 42 days. A second MAD part (J-MAD) enrolled 24 Japanese HV across 3 dose cohorts, (once daily 10mg through 60mg) for up to 21 days and followed for up to 42 days. Safety, tolerability, PK and PD were assessed throughout the study and reviewed following each dose level prior to initiation of successive dose escalation cohorts.

Results: Across all cohorts, the frequency of treatment emergent adverse events (TEAEs) was low and the majority were unrelated to BMS-986256. There were no serious adverse events and all TEAEs were classified as mild except for 2 moderate TEAEs (viral upper respiratory infection and tooth fracture), both unrelated to BMS-986256. One participant in the J-MAD part of the study discontinued BMs-986256 for asymptomatic, elevated ALT, which then resolved. BMS-986256 has linear PK over the dose range evaluated in SAD and MAD parts. It has a long half-life of approximately 80 hours to support once daily dosing. BMS-986256 has low inter-individual variability in exposures and low level of single circulating metabolite (< 2 % of parent). An ex vivo assay that measured BMS-986256 inhibition of TLR7-agonist or TLR8-agonist induced IL-6 production showed rapid target engagement at all doses tested in the SAD and MAD parts. The effect was dose-dependent and durable, reaching >90% target engagement. BMS-986256 also exhibited dose dependent, robust effects in 2 other ex vivo assays that measured TLR7-agonist stimulation of CD69 expression on B cells and TLR8-agonist stimulated CD319 expression on monocytes, using flow cytometry.

Conclusion: BMS-986256 was generally safe and well-tolerated following single and multiple doses administered across the dose range studied. It has favorable PK properties. These findings along with its robust biomarker response support its further development as a treatment for SLE and related autoimmune diseases.

Disclosure: M. Harrison, Bristol-Myers Squibb, 3, Pfizer, 12, Stock holder, Pfizer, 3; **M. Chiney**, Bristol Myers Squibb, 3; **D. Shevell**, Bristol Myers Squibb, 3; **L. Dong**, Bristol-Myers Squibb, 3; **M. Dawes**, None; **I. Girgis**, Bristol Myers Squibb, 3, 11.

Abstract Number: 1772

Autologous EBV-specific Cytotoxic T Cells in Systemic Lupus Erythematosus: An Innovative Phase I/IIa Clinical Trial

Antoine Enfrein[1], Beatrice Clemenceau[2], Soraya Saiagh[3], Céline Bressollette[4], Zahir Amoura[5], Henri Vie[2] and Mohamed Hamidou[1], [1]Médecine interne, CHU de Nantes, Nantes, France, [2]Inserm U1232, Université de Nantes, Nantes, France, [3]Unité de Thérapie Cellulaire et Génique, CHU de Nantes, Nantes, France, [4]Laboratoire de Virologie, CHU de Nantes, Nantes, France, [5]Médecine interne, Hôpital Pitié Salpêtrière, AP-HP, Paris, France

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: SLE – Treatment Poster (1732–1772)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Epstein-Barr Virus (EBV) has been suggested as a potential environmental factor in systemic lupus erythematosus (SLE) onset and disease activity. Here, we report the results of a phase I/IIa clinical trial assessing the safety and the effects of anti-EBV CTL infusion in patients with non severe disease.

Methods: Nine patients meeting the American College of Rheumatology (ACR) criteria for SLE were included, and received a unique dose of 5.10^6/kg autologous CTL. They were then prospectively followed for one year. Clinical activity scores and main biologic parameters such as anti-DNA, C3 and C4 levels, lymphocytes, IFN-α plasmatic levels count were recorded. Humoral anti EBV responses were monitored with ELISA assays for anti VCA, EBNA, EA/D antibodies. We also assessed frequency of EBV-specific T-cell with IFN-γ ELISPOT assays and plasmatic EBV viral loads. Adverse events were collected according to Common Terminology Criteria for Adverse Events (CTCAE) guidelines.

Results: Average SLEDAI score at inclusion was 6,9, and three patients presented active EBV replication with positive PCR on blood (mean 3,17log ±0,65). Six patients were clinically stable during follow-up, one patient improved but with co-administration of other medications, two presented a flare requiring treatment intensification, but not immediately after injection.No critical adverse events related to the treatment were observed. We observed no significant changes in humoral and cellular anti-EBV responses after CTL infusion. Patients follow-up seems to show a relationship between IFN-α level and some serological parameters of the anti-EBV response, which needs to be confirmed in a larger group.

Conclusion: Although no serious adverse events were observed, and this treatment appears to be safe to use, none of the patients showed significant clinical improvement or changes in anti-EBV humoral or cellular responses. A larger demonstration of the relationship between IFN signature and EBV serological responses could justify pursuing this approach with adjustments in treatment.

Disclosure: A. Enfrein, None; **B. Clemenceau**, None; **S. Saiagh**, None; **C. Bressollette**, None; **Z. Amoura**, Amgen, 1, 5, Astra Zeneca, 1, 5, GSK, 1, 5, Roche, 5, Kezar, 1, Boehringer, 5, Novartis, 5; **H. Vie**, None; **M. Hamidou**, GSK, 4, Novartis, 4.

Abstract Number: 1773

Comparing Efficacy of Guselkumab versus Ustekinumab in Patients with Psoriatic Arthritis: An Adjusted Comparison Using Individual Patient Data from DISCOVER 1&2 and PSUMMIT Trials

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab is an anti-interleukin (IL)-23 monoclonal antibody recently approved for the treatment of psoriatic arthritis (PsA). In two large Phase III trials of patients with PsA (DISCOVER 1&2), guselkumab has shown to be superior versus placebo. In this indication no direct comparison is available between guselkumab and ustekinumab, a monoclonal antibody targeting IL-12 and IL-23. Indirect comparisons based on relative treatment

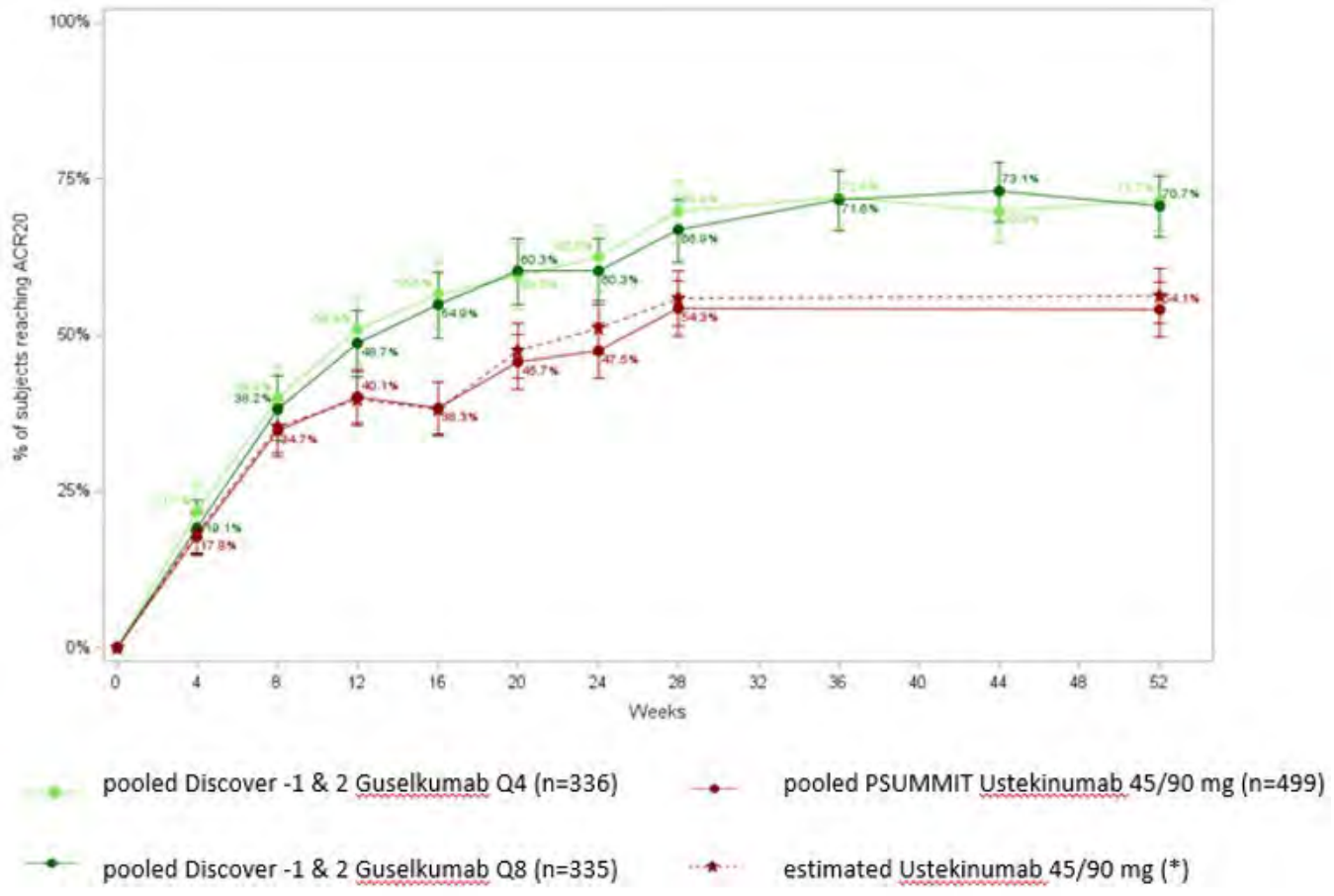


Figure 1. ACR 20 response for guselkumab vs ustekinumab in bio-naïve patients.

effects versus a common comparator (placebo) only allow for analyses up to week 24 due to cross-over to active arms in available PsA trials. The objective of this study was to indirectly compare joint and skin efficacy of guselkumab versus ustekinumab up to week 52, using pooled patient-level trial data from DISCOVER 1&2 and PSUMMIT 1&2, adjusting for cross-trial population differences.

Methods: Patient level data, including baseline characteristics and outcome data on ACR response and Psoriasis Area Severity Index (PASI) response from the guselkumab arms of DISCOVER 1&2 were pooled with the data from the ustekinumab trials PSUMMIT 1&2. Analyses were performed for bio-naïve and bio-experienced populations separately. Differences in patient characteristics across trial populations were adjusted for using multivariate logistic regression, including gender, age, body mass index, previous TNF use, disease duration, PASI level, number of swollen and tender joints. This method of indirect comparisons allows for analysis of comparative efficacy beyond controlled induction period. Odds ratios resulting from this model were translated into predicted response rates for ustekinumab, assuming same patient population, as enrolled in the guselkumab trial arms.

Results: Majority of baseline characteristics for patients on guselkumab (100mg q8w; 100mg q4w) were comparable to patients on ustekinumab 45/90mg, in both the bio-naïve and bio-experienced group of patients. The probability of reaching a ACR 20 in both the bio-naïve & bio-experienced population was significantly higher for guselkumab vs ustekinumab at weeks 52 for both dosing regimens of guselkumab (bio-naïve ACR 20: q8w OR= 1.88 [1.28;2.76]), q4w (OR= 1.92 [1.29;2.86]; bio experienced ACR20 q8w OR= 2.72[1.17;6.31], q4w OR=4.77 [1.95;11.63]). Similarly, guselkumab was superior to ustekinumab on PASI 90 outcome at week 52 in both bio-naïve & bio-experienced patients with BSA ≥3% at baseline (bio-naïve: q8w OR= 2.59 [1.68;3.99]), q4w OR= 3.19 [2.03;5.00], and bio-experienced q8w OR= 3.96[1.39,11.27], q4w OR=13.10[4.18,41.04]). Figure 1 represents unadjusted pooled DISCOVER 1&2 trial results and estimated proportions of ustekinumab treated patient group achieving ACR 20 in bio-naïve patient group up to week 52 using the method described above.

Conclusion: An adjusted comparison using patient level data from pivotal Phase III studies demonstrates both dosages of guselkumab to be significantly more effective versus ustekinumab in both skin and joint outcomes in both bio-naïve & bio experienced patients up to week 52.

Disclosure: J. Diels, Janssen, 3, 11; **P. Thilakarathne**, Janssen, 3; **A. Schubert**, Janssen, 3, 11; **F. Hassan**, Janssen, 3, 11; **S. Peterson**, Janssen, 3, 11; **W. Noël**, Janssen, 3, 11.

Abstract Number: 1774

Blood-based Immune Profiling Combined with Machine Learning Discriminates Psoriatic Arthritis from Psoriasis Patients

Michelle Mulder[1], Xuehui He[2], Juul van den Reek[2], Paulo Urbano[2], Charlotte Kaffa[2], Xinhui Wang[3], Bram van Cranenbroek[2], Esther van Rijssen[2], Frank van den Hoogen[4], Irma Joosten[2], Wynand Alkema[5], Elke de Jong[2], Ruben Smeets[2], Mark Wenink[6] and Hans Koenen[2], [1]Sint Maartenskliniek, Nijmegen, Netherlands, [2]Radboud University Medical Center, Nijmegen, Netherlands, [3]University of Luxembourg, Belvaux, Luxembourg, [4]Sint Maartenskliniek, Ubbergen, Netherlands, [5]Hanze University of Applied Sciences, Groningen, Netherlands, [6]Sint Maartenskliniek, Malden, Netherlands

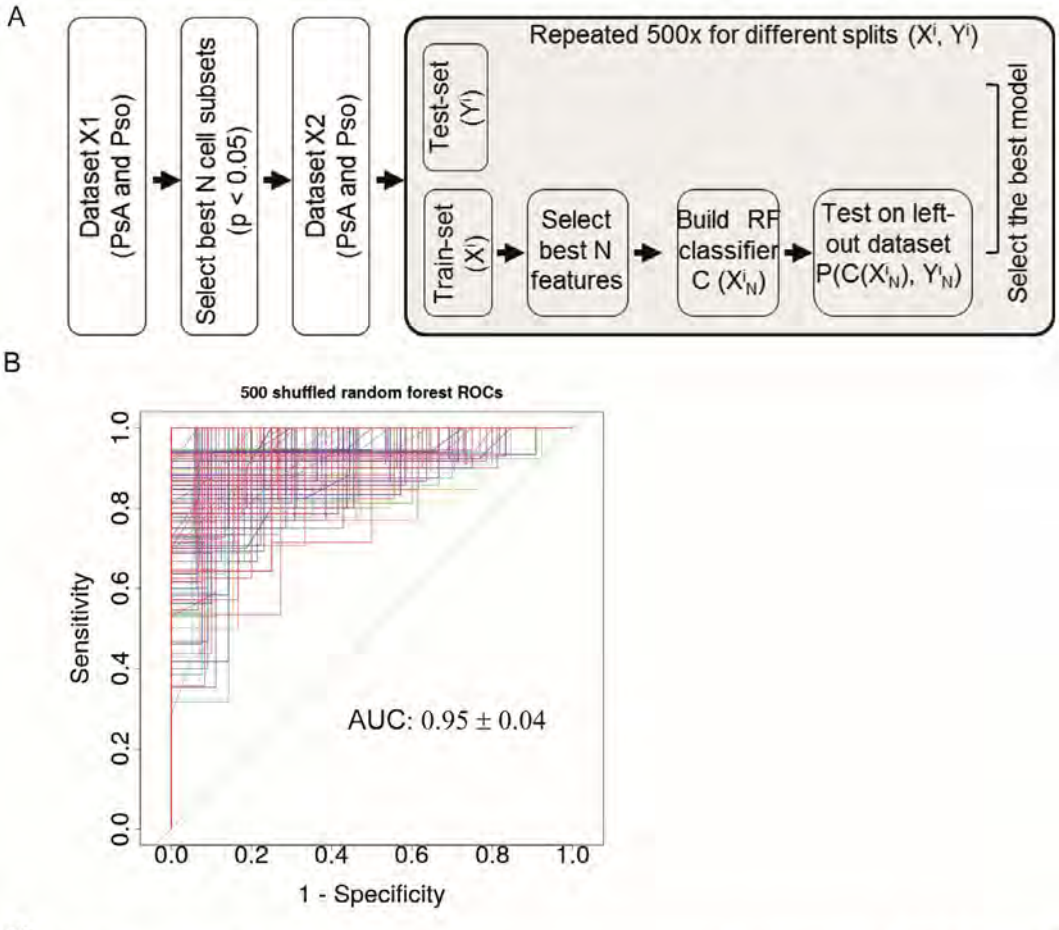
SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM



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Immune cell lineages	Cell subsets	Gini score	Fold changes (Pso/PsA)
T lymphocytes	CD4+CD197+CD45RA-	1091.129	1.398
T lymphocytes	CD4+CD196+CD183-CD194+	988.993	0.594
Monocytes	CD196+Monocytes	978.392	2.565
T lymphocytes	CD45RO+CD45RA-	939.038	1.549
T lymphocytes	CD8+CD45RA-CD27-	883.292	2.524
Monocytes	CD197+Monocytes	816.475	2.331
T lymphocytes	CD4+CD45RA-CD27-	719.209	1.821
T lymphocytes	CD4+CD25+CD127lo(Treg)	622.067	1.254
T lymphocytes	CD4+CD196-CD183-CD194+	557.678	0.614
Lymphocytes	Lymphocytes	444.391	0.969

Figure 1. Discrimination of PsA from Pso patients using a random forest classification model. (A) Schematic overview of the data analysis procedure. The significantly different cell subsets in PsA vs Pso were selected based on the univariate analysis as shown in Fig 1A and the highly correlated cell subsets were excluded. Randomly splitting for training X' (70%) and test Y' (30%) dataset was repeated 500 times. The RF classification model (containing 1000 forests) was built using the training dataset and the test dataset was shuffled to cross-validate the model. (B) Overview of the ROC curves derived from 500 RF classification models. The AUC value was shown as mean ± SD. (C) Top 10 most relevant-cell subsets contributing to the classifications of PsA and Pso. Cell subsets were ranked based on gini-score. Fold change is computed as the ratio of mean values of each cell subset's percentage in Pso vs PsA. Names of ICS in red indicate these cells are higher in PsA than in Pso.

Background/Purpose: Early detection of psoriatic arthritis (PsA) in psoriasis (Pso) patients is crucial for timely treatment and prevention of structural joint damage. We aimed to identify disease-specific immune profiles discriminating Pso from PsA patients, potentially facilitating adequate referral.

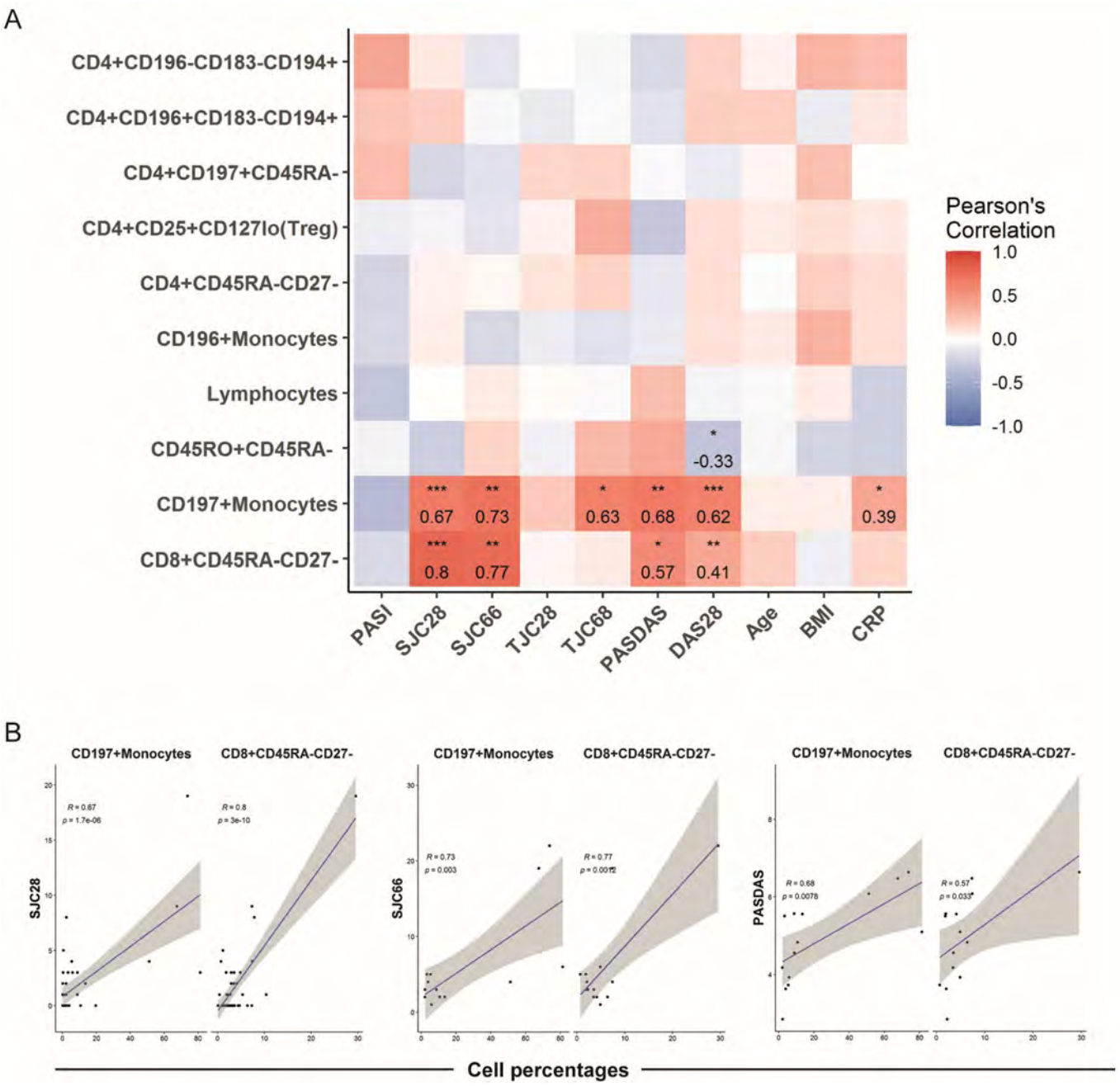

Figure 2. Correlation of clinical parameters with PsA-classifying immune cells. (A) Heatmap showing the pearson's correlation between percentages of cell subsets with clinical parameters in PsA. Numbers indicate the Pearson's correlation coefficient, * p<0.05; ** p<0.01; *** p<0.001. (B) Scatter plots showing the pearson's correlation of the percentages of CD197+ monocytes and CD8+CD45RA-CD27- memory T-cells with swollen joint count 28/66 and Psoriatic Arthritis Disease Activity Score (PASDAS).

Methods: The phenotype of PBMCs of consecutive Pso (N=45) and PsA (N=41) patients was determined using multi-color flowcytometry and univariate analysis to compare percentages of cell subsets between Pso and PsA. Disease-specific immune profiles were defined by machine learning using a random forest (RF) classification model. 1) The dataset was randomly split into a training (70%) and test-set (30%). 2) An RF model consisting of 1000 forests was built and optimized with internal cross-validation. 3) Step 1 and 2 were repeated 500 times. This procedure resulted in 500 RF-based models, each of which was evaluated by an Area under the Curve (AUC) analysis (Figure 1A/1B).

Results: In-depth immune phenotyping resulted in over one hundred different cell subsets for each blood sample being evaluated. A number of cell subsets was significantly different in Pso vs PsA. Key PsA identifying immune cell subsets selected by the RF classification model (AUC value of 0.95) included increased proportions of differentiated $CD4^+CD196^+CD183^-CD194^+$ and $CD4^+CD196^-CD183^-CD194^+$ T-cells and reduced proportions of $CD196^+$ and $CD197^+$ monocytes, memory CD4+ and CD8+ T-cells and CD4+ regulatory T-cells (Figure 1C shows top 10 PsA/Pso-classifying immune cell populations). Within PsA, joint scores showed a strong association with memory CD8+CD45RA-CCR7- effector T-cells and $CD197^+$ monocytes (Figure 2A/2B).

Conclusion: Through the integration of an extensive phenotyping of blood immune cell subsets and a machine learning approach, we identified an immune profile which discriminates PsA from Pso. This immune profile may facilitate timely diagnosis of PsA in Pso and it highlights the possibility of using a combination of selected immune cell subsets as a method for detecting PsA in Pso patients.

Disclosure: M. Mulder, None; **X. He**, None; **J. van den Reek**, Abbvie, 6, Janssen, 1, 6, BMS, 1, 6, Almirall, 1, Leo Pharma, 1; **P. Urbano**, None; **C. Kaffa**, None; **X. Wang**, None; **B. van Cranenbroek**, None; **E. van Rijssen**, None; **F. van den Hoogen**, None; **I. Joosten**, None; **W. Alkema**, None; **E. de Jong**, Abbvie, 2, 5, 6, Novartis, 2, 5, 6, Janssen, 2, 5, 6, Pharmaceutica, 2, 5, 6, Leo Pharma, 2, 5, 6, UCB, 2, 5, 6, Lily, 2, 6, Sanofi, 2, 6; **R. Smeets**, None; **M. Wenink**, None; **H. Koenen**, None.

Abstract Number: 1775

Isolated Axial versus Concomitant Peripheral Disease in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: Isolated axial involvement exists in 2 to 5% of all psoriatic arthritis (PsA) patients. However, it is currently unknown whether patients with isolated axial disease are clinically different than those with concomitant peripheral disease. The primary objective of this study was to determine clinical features associated with isolated axial disease among PsA patients with axial disease irrespective of peripheral involvement. Furthermore, we evaluated predictors for the development of peripheral disease from isolated axial disease over time.

Methods: A longitudinal single center cohort was analyzed to identify PsA patients (all patients fulfilled CASPAR criteria) who had axial disease from January 1978 to October 2020 inclusive, as defined by ≥ grade 2 sacroiliitis bilaterally or ≥ grade 3 sacroiliitis unilaterally on sacroiliac joint radiographs, according to the modified New York criteria. Isolated axial disease was defined by the absence of active/damaged joints or dactylitis. Descriptive statistics determined the percentage of patients with isolated axial and axial with peripheral disease. A logistic regression model

Table 1. Clinical Parameters between PsA Patients with Isolated Axial Disease versus those with Concomitant Peripheral Disease at First Presentation of Axial Disease

Variable	Isolated axial group (N=32)	Axial and peripheral group (N=463)	*p*-value
Demographics			
Age	43.09 (14.06)	45.54 (13.22)	0.346
Male (%)	71.88	63.28	0.431
Caucasian (%)	87.50	85.53	0.963
Age at diagnosis of PsA in years	37.44 (12.36)	35.06 (13.36)	0.302
Age at diagnosis of psoriasis in years	25.78 (17.31)	27.32 (14.31)	0.627
Smoker (%)	59.38	46.65	0.226
Clinical features			
Sacroiliitis grade[a]	2.75 (0.67)	2.59 (0.69)	0.189
Enthesitis[*] (%)	3.13	14.90	0.068
Elevated ESR (%)	39.29	46.71	0.560
PASI	6.06 (8.00)	7.29 (9.61)	0.517
BSA	10.13 (18.30)	9.79 (18.01)	0.946
Nail lesion (%)	53.13	74.95	0.013
Uveitis (%)	18.75	9.72	0.185
Inflammatory bowel disease[*] (%)	6.25	7.78	1.000
Inflammatory back pain[b] (%)	50.00	33.96	0.172
Back metrology[c]			
Neck rotation (degrees)	67.81 (22.80)	71.84 (20.81)	0.506
Lateral Flexion, Domjan method (degrees)	15.03 (5.78)	15.58 (4.54)	0.709
Schober test (cm)	4.07 (1.65)	4.52 (1.31)	0.263
Chest expansion (cm)	5.67 (2.76)	5.35 (2.65)	0.551
Comorbidities			
BMI	26.61 (6.08)	29.26 (6.61)	0.101
Cardiovascular disease[*] (%)	12.50	18.36	0.485
Diabetes[*] (%)	7.41	7.19	1.000
Patient reported outcomes			
BASDAI	1.97 (1.73)	4.65 (2.58)	0.0003
HAQ	0.16 (0.29)	0.68 (0.61)	<0.0001
SF-36 physical	46.75 (10.36)	36.61 (12.07)	0.009
SF-36 mental	52.68 (8.66)	46.50 (12.11)	0.042
Human leukocyte antigen (HLA) types			
HLA-B27 (%)	34.62	21.46	0.188
HLA-B38[*] (%)	15.38	15.66	1
HLA-B39[*] (%)	0	8.84	0.152
HLA-B8[*] (%)	11.54	19.95	0.442
HLA-B13 (%)	11.54	7.32	0.435
HLA-B40[*] (%)	0	1.52	1
HLA-C6 (%)	23.08	25.38	0.977
Medications			
NSAIDs (%)	50.00	69.98	0.031
DMARDs (%)	28.13	47.30	0.055
Biologics (%)	18.75	13.39	0.558

Where applicable, figures reported as mean (standard deviation); % denotes percentage of patients in the respective groups; [a]The sacroiliac joint with the highest grade was used preferentially for analysis; [b]Low back pain or neck pain and stiffness for more than 3 months that improves with exercise but is not relieved by rest; [c]The side with the lowest numeric value was used preferentially for analysis, where applicable; [*]Fisher's exact test used due to low sample size in each sub-group; PsA, psoriatic arthritis; ESR, erythrocyte sedimentation rate; PASI, psoriasis area and severity index; BSA, body surface area of psoriasis; BMI, body mass index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ, health assessment questionnaire; SF-36, short form health survey; NSAID, nonsteroidal anti-inflammatory drug; DMARD, disease-modifying antirheumatic drug.

determined factors associated with isolated axial disease at initial presentation of axial disease. A cox proportional-hazards model using time-dependent covariates evaluated predictors for the development of peripheral disease from the first presentation of isolated axial disease.

Table 2. Multivariate Logistic Regression Analysis for Predictors of Isolated Axial Disease at First Presentation of Axial Disease (N=237)

Variable	Odds ratio	95% CI	*p*-value
Sex (male)	0.588	(0.097, 3.570)	0.564
Age at diagnosis of PsA in years	1.061	(0.990, 1.138)	0.095
Sacroiliitis grade[a]	2.021	(0.698, 5.852)	0.195
Enthesitis	0.000	(0.000, ∞)	0.995
Elevated ESR	3.298	(0.599, 18.173)	0.170
Nail lesion	0.445	(0.075, 2.633)	0.372
HLA-B27	25.000	(3.033, 206.114)	0.003
Uveitis	0.859	(0.040, 18.311)	0.922
HAQ	0.004	(0.000, 0.284)	0.010
SF-36 PCS	0.919	(0.817, 1.034)	0.161

[a]The sacroiliac joint with the highest grade was used preferentially for analysis
CI, confidence interval; PsA, psoriatic arthritis; ESR, erythrocyte sedimentation rate; HAQ, health assessment questionnaire; SF-36 PCS, short form health survey physical health

Results: Of the 1576 PsA patients evaluated, 495 (31.4%) had axial disease, of which 32 (2.0%) had isolated axial disease and 463 (29.4%) had concurrent peripheral disease (Table 1). Full protocol information was available for 237 patients for multivariate logistic analysis (Table 2). At initial presentation of axial disease, HLA-B*27 positivity (Odds ratio 25.00, p< 0.003) and lower Health Assessment Questionnaire (HAQ) scores (Odds ratio 0.004, p< 0.010) were associated with isolated axial disease. For the 32 patients with isolated axial disease, univariate cox proportional-hazards model adjusted for sex and age of PsA diagnosis did not reveal any significant predictors for the development of peripheral disease over clinic follow-up (Table 3).

Conclusion: In our PsA cohort, 2.0% patients had isolated axial disease at presentation. At presentation, PsA patients with isolated axial disease had a significantly higher chance of HLA-B*27 positivity. Moreover, those with isolated axial disease compared with concomitant peripheral disease also had lower HAQ scores at presentation,

Table 3. Time-dependent Univariate Cox Proportional Regression for the Development of Peripheral Disease amongst PsA patients who Presented with Isolated Axial disease, adjusted by Sex and Age at Diagnosis of PsA (N=32)

Variable	Hazard ratio	95% CI	*p*-value
Sex (male)			
Age at diagnosis of PsA in years			
Sacroiliitis grade[a]	1.302	(0.497, 3.406)	0.591
Enthesitis	0.000	(0.000, ∞)	0.998
Elevated ESR	1.292	(0.454, 3.672)	0.631
Nail lesion	0.984	(0.388, 2.500)	0.974
PASI	1.039	(0.984, 1.098)	0.167
Uveitis	2.752	(0.883, 8.572)	0.081
HAQ	0.035	(0.001, 1.603)	0.086
NSAIDS	0.924	(0.322, 2.655)	0.884
DMARDS	1.454	(0.570, 3.710)	0.434
Biologics	1.086	(0.335, 3.515)	0.891

[a]The sacroiliac joint with the highest grade was used preferentially for analysis; CI, confidence interval; PsA, psoriatic arthritis; ESR, erythrocyte sedimentation rate; PASI, psoriasis area and severity index; HAQ, health assessment questionnaire; NSAID, nonsteroidal anti-inflammatory drug; DMARD, disease-modifying antirheumatic drug

suggesting better functional status. Lastly, there does not appear to be any predictors over time for the development of peripheral disease amongst patients who present with isolated axial disease, though analysis was limited by small sample size.

Disclosure: T. Kwok, None; **M. Sutton**, None; **R. Cook**, None; **D. Pereira**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5.

Abstract Number: 1776

Stakeholder Outcome Prioritization in the Biologic Abatement and Capturing Kids' Outcomes and Flare Frequency in Juvenile Spondyloarthritis Trial

Pamela Weiss[1], Cora Sears[1], Timothy Brandon[1], Rui Xiao[2], Tory Aquino[3], Kweli Archie[1], Aamena Hameed[4], English Holland[5], Miles Holland[5], Asad Khan[1], Melanie Kohlheim[6], Jennifer Leal[7], Lynn Murphy[8], Sean Murphy[8], Antoinette Neu[9], Emily Neu[9], Jerome Neu[9], Justin Neu[9], Rachel Richmond[10], Theresa Suplee[11], Dylan Suplee[11] and Christopher Forrest[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, [3]Children's Hospital of Philadelphia, Aliquippa, PA, [4]Children's Hospital of Philadelphia, Franklin Park, NJ, [5]Children's Hospital of Philadelphia, Williamsburg, VA, [6]Children's Hospital of Philadelphia, Granville, OH, [7]Children's Hospital of Philadelphia, Columbus, OH, [8]Children's Hospital of Philadelphia, Haddon Heights, NJ, [9]Children's Hospital of Philadelphia, Sidney, OH, [10]Children's Hospital of Philadelphia, Albuquerque, NM, [11]Children's Hospital of Philadelphia, Maple Shade, NJ

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

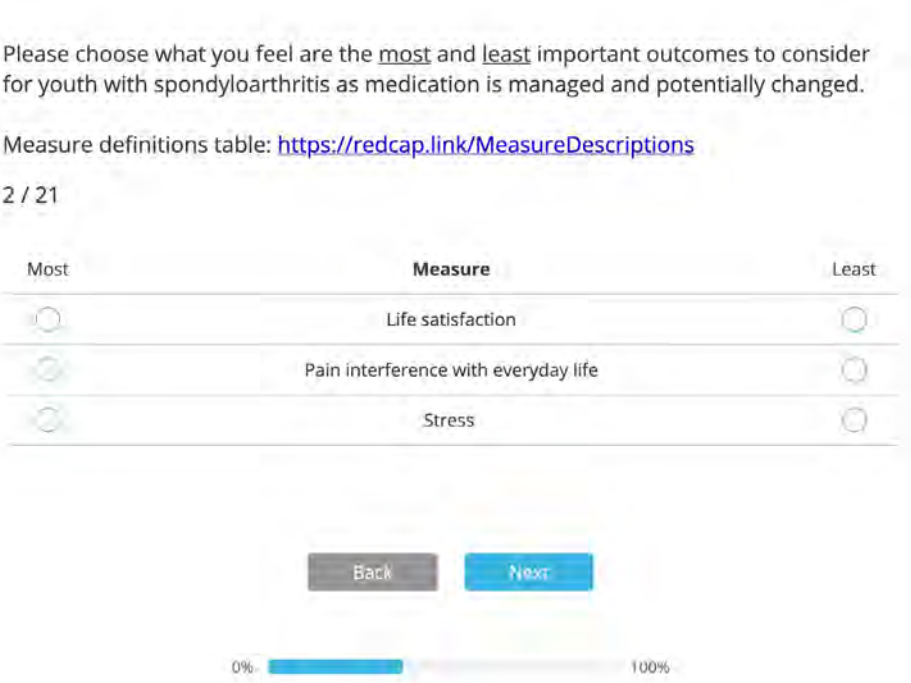
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The BACK-OFF JSpA Study is a randomized pragmatic trial that will investigate different TNFi de-escalation strategies for children who have sustained asymptomatic disease. As part of the study design we aimed to identify the most important patient-reported outcomes (PRO) of interest to stakeholders that should be examined as part of the trial.

Methods: To identify the most important outcomes of interest to stakeholders we conducted a discrete choice experiment – a user-friendly, quantitative, choice-based approach to evaluate individuals' preferences regarding potential PROs (Sawtooth Software). With this software, stakeholders assessed a discrete list of 21 NIH Patient-Reported Outcome Measurement Information System (PROMIS) pediatric domains across four general categories of outcomes: physical health, mental health, social health and global health. PROMIS measures are self-reported instruments designed for use in the general population and chronic medical conditions. Rather than asking stakeholders to "rate" all items at once, only 3 domains were shown at a time. Within each set, stakeholders chose the outcomes they felt were "most" and "least" important to consider during TNFi therapy de-escalation. This process was repeated for 21 sets of unique outcome combinations, with each outcome being shown an equal number of times. Stakeholders were required to make choices instead of expressing the strength of a preference (as would be done with a Likert scale or Delphi rating process). Using this process left no opportunity for scale use bias, where respondents often rate the different attributes similarly.

Results: Fourteen caregivers, 12 patients (ages 9-22 years old), 16 rheumatologists and 3 payors completed the exercise, which took approximately 10 minutes. The discrete choice experiment resulted in an estimate of the relative



Sample question from the discrete choice experiment.

importance of each outcome and rank (Table). All stakeholder groups agreed that the primary PRO should be "Pain Interference", a measure that evaluates the effect of pain on a child's everyday activities, including impact upon social, emotional, mental, and physical health. Patients and caregivers were mostly aligned in their top priorities, with patients valuing physical health domains (50% of top 10) whereas caregivers were more interested in mental health domains (60% of top 10). Rheumatologists and payors were most interested in physical health domains, which were ranked as 80% and 60% of their top 10 PROs, respectively. Overall, the patients had the most diverse set of domains,

Table. Outcomes prioritization exercise

Pediatric Domains	Category	Rank order of importance				Relative importance				
		Patients	Caregivers	Rheumatologists	Payers	Patients	Caregivers	Rheumatologists	Payors	All
Pain interference	physical	1	1	1	1	9.779	11.216	11.393	10.919	10.893
Mobility	physical	2	2	2	9	8.932	8.404	10.606	5.769	9.174
Pain behaviors	physical	4	5	5	5	7.076	6.368	7.975	7.14	7.201
Life satisfaction	mental	3	4	7	6	8.306	6.514	6.109	7.1	6.863
Physical activity	physical	10	12	3	2	4.807	4.274	8.707	10.511	6.495
Global health	global	8	13	4	3	5.761	4.099	8.632	7.719	6.464
Upper extremity function	physical	5	9	8	10	6.061	4.909	6.014	5.344	5.645
Cognitive function	mental	7	8	11	4	5.763	5.173	3.384	7.393	4.813
Sense of life's meaning	mental	6	6	13	8	5.928	6.367	2.539	5.925	4.799
Fatigue	physical	12	14	6	21	3.893	4.091	6.705	0.345	4.752
Depressive symptoms	mental	11	3	12	13	4.054	6.704	3.337	3.772	4.568
Impact on strength activities	physical	14	21	9	12	3.236	1.838	4.667	3.889	3.391
Stress	mental	13	10	16	18	3.435	4.855	2.456	1.59	3.371
Family relationships	social	9	17	14	17	5.492	2.569	2.534	1.785	3.249

including at least one of each category in their top 10 rank order of importance. Patients were also the only stakeholders to prioritize an outcome from the "social" category.

Conclusion: The discrete choice experiment resulted in an estimate of the relative importance of each PRO and rank. Patients and caregivers were mostly aligned in their top priorities. The rank-order list directly informed the primary and secondary PROs for our upcoming trial.

Disclosure: P. Weiss, Lilly, 1, 2, Pfizer, 1, 2, Biogen, 2; **C. Sears**, None; **T. Brandon**, None; **R. Xiao**, None; **T. Aquino**, None; **K. Archie**, None; **A. Hameed**, None; **E. Holland**, None; **M. Holland**, None; **A. Khan**, None; **M. Kohlheim**, None; **J. Leal**, None; **L. Murphy**, None; **S. Murphy**, None; **A. Neu**, None; **E. Neu**, None; **J. Neu**, None; **J. Neu**, None; **R. Richmond**, None; **T. Suplee**, None; **D. Suplee**, None; **C. Forrest**, None.

Abstract Number: 1777

Association of Opioid Use and Opioid-Related Costs with Patient-Reported Outcomes in Patients with Psoriatic Arthritis or Ankylosing Spondylitis

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SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with psoriatic arthritis (PsA) or ankylosing spondylitis (AS) experience chronic pain due to inflammatory attributes of their disease. Nonsteroidal anti-inflammatory drugs and biologics are recommended to improve symptoms, and biologics are recommended to inhibit disease progression. Many patients with chronic pain syndromes may receive opioid therapies; however, opioids do not treat underlying inflammation and are associated with adverse events. Limited data exist on the relationship between disease burden and opioid use in patients with PsA or AS. This study evaluated the association of patient-reported outcome measures with opioid use and related costs in patients with PsA or AS from a national US registry.

Methods: This retrospective cohort study included adult participants enrolled in the FORWARD databank between July 2009 and June 2019. FORWARD is a longitudinal observational registry for rheumatic diseases that prospectively collects patient-reported data by questionnaires administered bi-annually. This sample included patients who completed ≥ 1 questionnaire from January 2010 to December 2019; patients had a physician-reported diagnosis of PsA or AS and responded to the Health Assessment Questionnaire Disability Index (HAQ-DI) or HAQ-DI and/or Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; added in 2018), respectively. The primary outcomes were current opioid use and related costs at the time of the most recent questionnaire. The relationships between HAQ-DI or BASDAI and opioid use and related costs were assessed using logistic regression models for opioid use outcomes and generalized linear models with gamma distribution and log-link function for cost outcomes.

Results: This study included 828 patients with PsA and 334 patients with AS (**Table 1**). Overall, 177 patients with PsA (21.4%) and 91 with AS (27.3%) received opioids, with mean (SD) annualized related costs of $861 ($3669) and $1070 ($4617), respectively. There was a significant positive association (OR [95% CI]) between opioid use and HAQ-DI (1.99 [1.50-2.64] and 4.14 [2.59-6.63] in patients with PsA and AS, respectively; both $P < 0.01$) and BASDAI (1.22 [1.02-1.47] in patients with PsA; $P < 0.05$ and 1.94 [1.27-2.97] in patients with AS; $P < 0.01$). A 1-unit increase in HAQ-DI or BASDAI score was significantly associated (RR [95% CI]) with a 2.31 (1.40-3.81; $P < 0.01$) or 2.05 (1.09-3.86; $P < 0.05$) times increase, respectively, in opioid-related costs for patients with PsA, and a 17.82 (5.82-54.51; $P < 0.01$) or 8.20 (1.15-58.59; $P < 0.05$) times increase, respectively, in opioid-related costs for patients with AS (Figure 1).

Table 1. Demographics, Clinical Characteristics, and Disease Activity Measures in Patients With PsA or AS[a]

Characteristic	Patients with PsA (n = 828)	Patients with AS (n = 334)
Age, mean (SD), years	58.5 (13.5)	54.4 (14.3)
Female, n (%)	599 (72.3)	206 (61.7)
White, n (%)	697 (92.3)	282 (94.6)
Insurance status, n (%)		
Private	263 (31.8)	114 (34.1)
Medicare	362 (43.7)	135 (40.4)
Medicaid	68 (8.2)	30 (9.0)
Other	120 (14.5)	43 (12.9)
None	15 (1.8)	12 (3.6)
Disease duration, mean (SD), years [n]	17.5 (12.4) [759]	17.5 (12.4) [303]
Current treatment use, n (%)		
csDMARDs	360 (43.5)	78 (23.4)
b/tsDMARDs	407 (49.2)	153 (45.8)
General arthritis[b]	530 (64.0)	220 (65.9)
NSAIDs	298 (36.0)	160 (47.9)
Prednisone	93 (11.2)	33 (9.9)
Opioids[c]	177 (21.4)	91 (27.3)
Other drugs[d]	628 (75.9)	245 (73.4)
Any drug	751 (90.7)	298 (88.6)
Disease activity, mean (SD) [n]		
HAQ-DI	0.9 (0.7) [828]	0.9 (0.7) [333]
BASDAI	3.7 (2.4) [204]	3.7 (2.3) [81]
Current working status, n (%)	n = 801	n = 325
Unemployed	27 (3.4)	15 (4.6)
Employed	342 (42.7)	140 (43.1)
Retired	241 (30.1)	76 (23.4)
Disabled	126 (15.7)	69 (21.2)
Other	65 (8.1)	25 (7.7)

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; b/tsDMARD, biologic/targeted-synthetic disease-modifying antirheumatic drug; COX-2, cyclooxygenase-2; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire Disability Index; NSAIDs, nonsteroidal anti-inflammatory drugs.

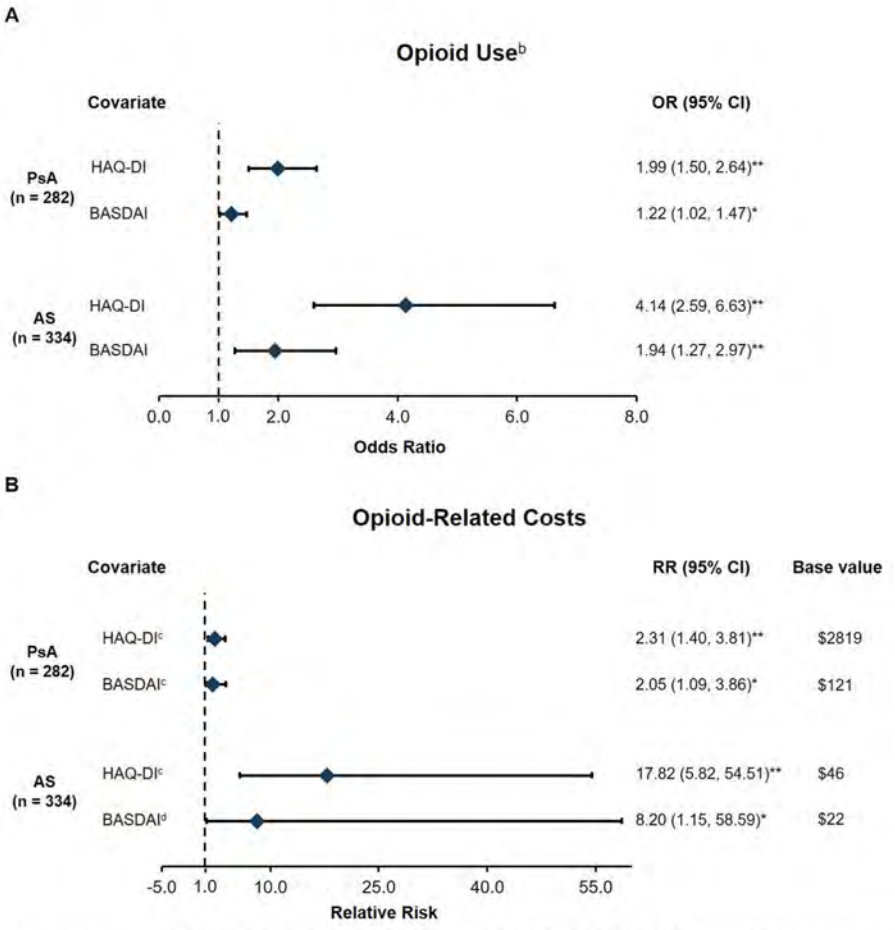
[a] Includes data for patients with PsA who responded to HAQ-DI and patients with AS who responded HAQ-DI and/or BASDAI.

[b] General arthritis: general arthritis drugs (glucosamine, hyaluronate, intra-articular injections, ketorolac, prednisone, topicals, and vitamins), NSAIDs, COX-2 inhibitors (celecoxib), analgesics, and acetaminophen.

[c] Opioids: mild opioids (codeine, hydrocodone, acetaminophen with codeine, acetaminophen with propoxyphene, acetaminophen with hydrocodone, acetaminophen with tramadol, and tramadol alone) and strong opioids (fentanyl, hydromorphone, methadone, morphine, narcotics, oxycodone, oxymorphone, and acetaminophen with oxycodone).

[d] Other drugs: Any medication for conditions other than PsA or AS.

Figure 1. Association of **(A)** Opioid Use and **(B)** Drug-Related Costs With HAQ-DI and BASDAI Among Patients With PsA or AS[a]

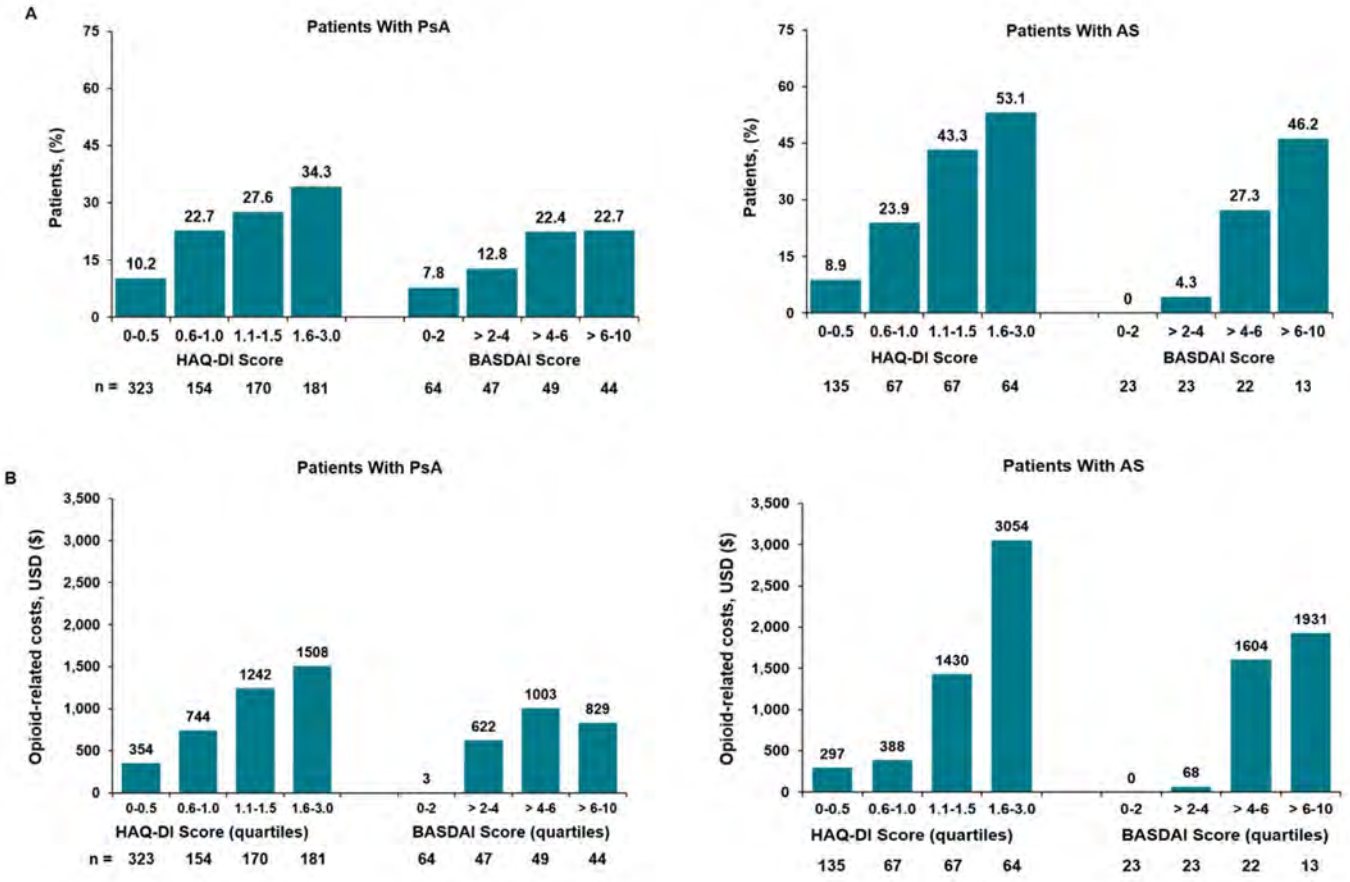


AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ-DI, Health Assessment Questionnaire Disability Index; OR, odds ratio; PsA, psoriatic arthritis; RR, relative risk.
[a] HAQ-DI and BADSAI were modeled as continuous variables; includes data for patients with PsA who responded to HAQ-DI and patients with AS who responded HAQ-DI and/or BASDAI.
[b] Models adjusted for education level (PsA), smoking habits (PsA and AS), sex (PsA), rheumatic disease comorbidity index (PsA and AS), total income (AS), and physician-diagnosed disease (PsA and AS).
[c] Models adjusted for age (PsA and AS), education level (AS), and smoking habits (AS).
[d] Univariate model; covariates not significant.
* $P < 0.05$.
** $P < 0.01$.

Annualized average opioid use and costs increased with increasing HAQ-DI and BASDAI scores for patients in both cohorts (Figure 2).

Conclusion: Increased opioid use was associated with higher HAQ-DI and BASDAI scores among patients with PsA or AS. These findings suggest that, among patients with more severe disease, opioid use and related costs were numerically greater for patients with AS than patients with PsA.

Figure 2. Average Annualized Patient **(A)** Opioid Use and **(B)** Opioid-Related Costs Across HAQ-DI and BASDAI Scores for Patients With PsA or AS[a]



AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ-DI, Health Assessment Questionnaire Disability Index; PsA, psoriatic arthritis.

[a] Includes data for patients with PsA who responded to HAQ-DI and patients with AS who responded HAQ-DI and/or BASDAI.

Disclosure: A. Ogdie-Beatty, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2; **M. Hwang**, Novartis, 2, UCB, 2, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 5; **P. Veeranki**, PRECISIONheor, 3; **A. Portelli**, PRECISIONheor, 3; **J. Shafrin**, PRECISIONheor, 3; **S. Pedro**, FORWARD, the National Data Bank for Rheumatic Diseases, 3; **E. Yi**, Novartis, 3; **S. Hass**, H. E. Outcomes, 3, Novartis, 2; **K. Michaud**, None.

Abstract Number: 1778

The Role of Cathepsin G in Joint Destruction in Patients with Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Cathepsin G (CTSG) is a member of the serine protease family. It is stored in primary granules of myeloid cells, dendritic cells, plasma cells, and others, and when cells are stimulated by immune complexes, pharmacological agents, or phagocytosis, CTSG is released into the extracellular space or binds to the surface of those cells that have receptors for it. Cathepsin G plays an important role in the development of inflammation, as it promotes the migration of neutrophils, monocytes, and antigen-presenting cells by changing chemokines and converting prochemerin to chemerin, and by activating cell surface receptors.

The aim of the study was to examine the level of Cathepsin G in the synovial fluid of patients with psoriatic arthritis.

Methods: The level of CTSG in the synovial fluid of 156 patients with psoriatic arthritis was studied (56 of them with DAPSA≤14, 50 with DAPSA≥14.1≤28, and 50 with DAPSA≥ < 28.1). Control groups included 50 patients with activated gonarthrosis and 10 healthy volunteers. . The synovial fluid was taken by arthrocentesis by an experienced rheumatologist, after signing the informed consent of all persons examined and observing the principles of good clinical practice. The study was conducted in the Immunology Laboratory of the Bulgarian Academy of Sciences, Sofia through ELISA. Statistical processing includes descriptive and correlation analyzes, with statistical significance $p< 0.05$.

Results: The level of CTSG in the synovial fluid of patients with psoriatic arthritis and DAPSA≤14 is 0.113 ± 0.02 ng/ml, of those with DAPSA≥14.1≤28 - 0.152 ± 0.02 ng/ml, of those with DAPSA≥ < 28.1 - 0.179 ± 0.02 ng/ml). The level of CTSG in the synovial fluid of patients with gonarthrosis and effusion is 0.07 ± 0.01 ng/ml and in healthy controls 0.064 ± 0.01 ng/ml. The level of CTSG in the synovial fluid of patients with psoriatic arthritis was higher than that of patients with gonarthrosis and healthy controls ($p < 0.05$). The level of CTSG in the synovial fluid of patients with psoriatic arthritis correlated positively with the disease activity assessed by DAPSA ($R_{x,y}$= 0.89).

Conclusion: The level of CTSG in the synovial fluid of patients with psoriatic arthritis is significantly higher in patients with high disease activity, which is associated with more severe joint destruction.

Disclosure: M. Geneva-Popova, None; **S. Popova**, None; **A. Batalov**, None.

Abstract Number: 1779

A Comparison of Quality of Life Outcomes Between Psoriatic Arthritis and Psoriasis Patients: Data from the Brigham Cohort for Psoriasis and Psoriatic Arthritis Registry (COPPAR)

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. PsO and PsA Patient Characteristics

	PsO (N=28)	PsA (N=126)	*p*-value
Age, mean (SD), years	**50.8 (16.7)**	**55.6 (13.2)**	0.23
Female, n (%)	**13 (46.4)**	**72 (57.1)**	0.40
Race, n (%)			**0.03**
Caucasian	23 (82.2)	114 (90.5)	
Non-Caucasian	5 (18.8)	12 (9.5)	
Ethnicity, n (%)			-
Non-Hispanic	28 (100)	126 (100)	
Education, n (%)			0.91
Advanced degree (post-graduate)	8 (38.1)	44 (43.1)	
College (Bachelor's degree)	9 (42.8)	41 (40.2)	
Some college, high school/GED or lower	4 (19.1)	17 (16.7)	
Currently employed, n (%)	15 (68.2)	55 (59.1)	0.44
BMI, kg/m^2 mean (SD)	29.5 (6.2)	29.9 (6.7)	0.97
BMI classifications, n (%)			
Normal/underweight (<25.0)	5 (26.3)	28 (26.2)	
Overweight (2.0 to<30.0)	5 (26.3)	34 (31.7)	
Obese (>=30)	9 (47.4)	45 (42.1)	
Smoking status (current), n (%)	0	4 (3.2)	0.34
Alcohol intake, n (%)	22 (78.6)	102 (81.0)	0.77
Comorbidities, n (%)			
Hypertension	8 (28.6)	34 (27.0)	0.87
Hyperlipidemia	7 (25.0)	18 (14.3)	0.16
Hematology/oncology disease[a]	2 (8.7) *	17 (16.7) **	0.52
Cardiovascular disease	2 (7.1)	14 (11.1)	0.74
Psychiatric illness	2 (13.3) ‡	14 (24.6) ¶	0.50
Inflammatory bowel disease	2 (7.1)	3 (2.4)	0.22
Diabetes	1 (3.6)	3 (2.4)	0.56

GED: Graduate Equivalency Degree, BMI: Body mass index *Not reported: n=5, **Not reported: n=24, ‡Not reported: n=13, ¶Not reported n=69,
[a]Including following conditions; lymphoma, cancer (e.g., breast, lung, prostate, renal, other), leukemia (acute/chronic), thrombocytopenia, any tumor with metastases.

Background/Purpose: To report the demographics, clinical characteristics, and differential impacts on quality of life measures among participants in the Psoriasis (PsO) and Psoriatic Arthritis (PsA) Registry (COPPAR).

Methods: The COPPAR registry is a prospective, longitudinal registry for patients ≥ 18 years of age who have a diagnosis of PsO or PsA and were enrolled from a dermatology-rheumatology combined clinic and an arthritis center at a large academic medical center. Descriptive characteristics and biospecimens were collected every six months. Patient data included demographics, clinical and patient-reported outcomes, comorbidities, and treatment history. Baseline demographics and disease characteristics at enrollment were summarized for each group and compared using univariate statistics. Quality of life outcomes were compared between PsO and PsA subjects in regression analyses adjusting for age and sex.

Results: As of April 30, 2021, 154 subjects were enrolled, including 28 PsO subjects and 126 PsA subjects. Demographic characteristics were mean age of 53.2 years, 55.2% female, 89% white, and 25.3% were overweight and 35.1% were obese (Table 1). The mean disease duration was 19.7 years [SD 11.1] for PsO and 13.3 years [SD 14.4] for PsA (p< .001) (Table 2). PsO subjects had a higher mean BSA compared with PsA subjects (4.4 % [SD 5.4] vs. 3.2% [SD 8.7], p< .001). Both PsO and PsA groups had a high percentage of biologic therapy (60.7 % for PsO and 78.5 % for PsA). The mean static physician's global assessment (sPGA) score was higher among PsO subjects (2.1

Table 2. PsO and PsA Disease Characteristics and Treatment

Disease characteristics	PsO (N=28)	PsA (N=126)	p-value
Duration of disease, years (SD)	19.7 (14.4)	13.3 (11.1)*	**<.001**
Psoriasis severity			
sPGA, mean (SD)	2.1 (1.0)	1.2 (1.1)	**<.001**
PASI, mean (SD)	4.5 (5.6)	2.3 (4.7)	**<.001**
BSA %, mean (%)	4.4 (5.4)	3.2 (8.7)	**<.001**
Mild: BSA<=3	19 (67.9)	102 (81.0)	
Moderate: BSA>3 - <10,	5 (17.9)	13 (10.3)	
Severe: BSA >=10	4 (14.3)	11 (8.7)	
PsA clinical assessment			
LEI, mean (SD)	-	0.9 (1.5)	
Dactylitis, mean (SD)	-	0.2 (0.7)	
Total tender joints, mean (SD)	-	4.4 (5.9)	
Total swollen joints, mean (SD)	-	3.4 (4.9)	
Treatment			
Current medication use			
Biologic monotherapy, n (%)	14 (50.0)	73 (57.9)	0.44
Methotrexate combination with biologics, n (%)	3 (10.7)	26 (20.6)	0.29
Synthetic DMARD use, n (%)	1 (3.6)	10 (7.9)	0.69
Biologic			
Anti-TNF	4 (14.3)	55 (43.7)	
Anti IL17	3 (10.7)	35 (27.8)	
Anti IL12/23	2 (7.1)	3 (2.4)	
Anti-IL23	5 (17.9)	3 (2.4)	
PDE4 inhibitors	2 (7.1)	3 (2.4)	
Synthetic DMARD			
Methotrexate	4 (14.3)	34 (27.0)	
Sulfasalazine	0	2 (1.6)	
Hydroxychloroquine	0	2 (1.6)	
Leflunomide	0	1 (0.8)	
Other			
Topical medication, n (%)	16 (57.1)	71 (56.8)	
Anti-inflammatory medication (P.O.), n (%)	1 (3.6)	36 (28.6)	
Pain medication (P.O.), n (%)	1 (3.6)	15 (11.9)	
Corticosteroids (P.O.), n (%)	0	12 (9.5)	
Anti-itch medication (P.O.), n (%)	0	7 (5.6)	

sPGA: Static Physician's Global Assessment, PASI: Psoriasis Area and Severity Index, BSA: body surface area, LEI: LEEDS Enthesis Index, DMARD: Disease-modifying antirheumatic drug, P.O.: Per os (by mouth), *Exclude duration of PsO.

Table 3. Multivariate Comparisons of Quality of Life Outcome Measures between PsO and PsA subjects+

	PsO (N=28)	PsA (N=126)	*p*-value
EQ-5D, mean (SD)	0.9 (0.1)	0.8 (0.1)	**<.001**
SF-12, mean (SD)			
Physical Component Summary (PCS)	49.2 (11.3)	43.7 (11.6)	**0.04**
Mental Component Summary (MCS)	51.6 (7.7)	53.0 (8.6)	0.75
PHQ-8, mean (SD)	2.1 (2.4)	2.5 (3.6)	0.49
PROMIS anxiety short form, mean (SD)	44.9 (8.6)	45.9 (8.8)	0.50
FACIT-F, mean (SD)	43.8 (7.9)	41.0 (10.2)	0.15
DLQI, mean (SD)	3.3 (4.9)	2.4 (3.4)	0.45
WPAI, mean (SD)			
% Work hours missed	4.1 (13)	1.1 (5.1)	0.17
% Impairment while working	10.0 (19.6)	11.5 (19.6)	0.79
% Overall work hours affected	14.1 (21.6)	12.0 (20.7)	0.73
% Daily activities impaired	6.0 (14.5)	16.7 (22.8)	0.08
PtGA-Skin, mean (SD)	7.4 (2.1)	5.9 (5.7)	0.40
PtGA-PsA, mean (SD)	-	5.9 (5.7)	-
PtGA-Joint, mean (SD)	-	6.9 (2.6)	-
Pain VAS, mean (SD)		5.8(5.0)	
MHAQ, mean (SD)	-	1.3 (1.4)	-

EQ-5D: European Quality of Life- 5 dimensions, SF-12: The 12-Item Short Form Health Survey, PHQ-8: The eight-item Patient Health Questionnaire depression scale, PROMIS: Patient-Reported Outcomes Measurement Information System, FACIT-F: Functional Assessment of Chronic IllnessTherapy – Fatigue, DLQI: Dermatology Life Quality Index, WPAI: Work Productivity and Activity Impairment, PtGA: Patient GlobalAssessment, VAS: Visual Analogue Scale, MHAQ: Modified Health Assessment Questionnaire

*Outcome comparisons adjusted for age and sex.

[SD 1.0] compared to PsA subjects (1.2 [SD 1.1], p< 0.001). The mean Psoriasis Area and Severity Index (PASI) was higher for PsO subjects (4.5 [SD 5.6] for PsO vs. 2.3 [SD 4.7] for PsA subjects(p< .001)). Multivariate comparisons of quality of life measures between PsO and PsA subjects indicated lower EuroQol- 5 Dimension (EQ-5D) scores in PsA subjects (PsA: mean 0.8 [SD 0.1] vs. PsO: mean 0.9 [SD 0.1], p< .001) and lower physical health status (SF-12 PCS) among PsA subjects (mean 43.7 [SD 11.6]) compared with PsO subjects (mean 49.2 [SD 11.3], p=0.04) (Table 3). There were no significant differences between the groups in PHQ-8, PROMIS anxiety, FACIT-fatigue, or Dermatology Life Quality Index (DLQI) scores. PsA subjects had slightly more daily work activity impairment (WPAI PsA: mean 16.7% [SD 22.8] vs. PsO: mean 6.0% [SD 14.5], p=0.08). There were no significant differences in patient global skin scores between PsO subjects (mean 7.4 [SD 2.1]) and PsA subjects (mean 5.9 [SD 5.7], p=0.4).

Conclusion: Subjects enrolled in a combined dermatology-rheumatology and arthritis center clinic at a tertiary academic medical center had mild to moderate disease activity with a high prevalence of biologic therapy. PsA subjects reported worse general physical health and lower quality of life than PsO subjects despite PsO subjects having worse overall psoriasis severity.

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Novartis, 2, EqRx, 2; **J. Merola**, AbbVie, 2, Biogen, 2, Bristol Myers Squibb, 2, Dermavant, 2, Eli Lilly, 2, 5, Janssen, 2, Novartis, 2, Pfizer, 2, UCB Pharma, 2, Amgen, 2, 5, Sanofi, 2, Regeneron, 2, Leo Pharma, 2.

Abstract Number: 1780

Racial Disparities in Comorbidities of Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Racial heterogeneity of the US population makes it imperative to study the racial differences in clinical characteristics, medication use and co-morbidities of PsA patients to reduce the disparities in health care. We hypothesize that African-Americans (AA) with PsA have higher burden of co-morbidities then Caucasians in the US. We aimed to examine the racial differences in clinical characteristics, medication usage and co-morbidities in PsA patients.

Methods: We conducted a retrospective study using the IBM Explorys platform, a clinical research informatics tool that utilizes a health data gateway (HDG) server behind the firewall of 26 major integrated healthcare systems in the US from 1999, comprising of over 60 million patients in the participating healthcare organizations. The Explorys collects aggregated, standardized and normalized clinical data from different electronic health records, automatically updated in near real time (at least every 24 h), presented in a HIPAA and HITECH-compliant de-identified way from each participating healthcare organization and are passed into the Explorys data grid. Diagnosis, findings, and procedures are mapped into the systematized nomenclature of medicine (SONOMED-CT) hierarchy. Search criteria for PsA included the ICD diagnosis code of PsA and at least two visits with a rheumatologist, between 1999-2019. Cohorts were further stratified by adding the following variables to the search tool: race, gender, elevated ESR or CRP, smoker, peripheral arthritis, enthesopathy, dactylitis, uveitis, psoriasis, inflammatory bowel disease,TNF inhibitor or DMARD use) and co-morbidity (hypertension, diabetes, osteoporosis, fibromyalgia, heart disease and depression). Data sets were recorded as proportions and compared using chi-squared test ($p < 0.05$).

Results: A total of 26010 patients with PsA were identified. 95% of these patients were Caucasians whereas 5% were AA and 63% were females. 17% of PsA patients were smokers (n=4350) of which 4150 were Caucasians and 200 were AA, ($p < 0.05$). Comparisons of clinical features of PsA between racial groups can be found in Table 1. Treatment differences were also noted amongst racial groups. NSAIDs were used in 80% of Caucasians and 78% of AAs ($p < 0.0097$). TNFs were used in 51% of Caucasians and 41% of AAs ($p < 0.0001$). DMARDs were used in 72% of

Table 1.

	N	AA	Caucasian	P-value
Enthesopathy	6930	27%	25%	<0.0073
Dactylitis	30	0%	0.12%	<0.1971
Peripheral Arthritis	470	1%	18%	<0.0001
Axial Arthritis	470	2%	7%	<0.0001
Onycholysis	180	1%	2%	<0.0001
Elevated CRP	9870	37%	38%	<0.0195
Elevated ESR	8610	33%	34%	<0.0146

Table 2.

	N	AA	Caucasian	P-value
HTN	13730	59%	52%	<0.0001
DM	6080	31%	23%	<0.0001
Obesity	7940	37%	30%	<0.0001
Gout	2190	12%	8%	<0.0001
Uveitis	180	2%	0.6%	<0.0001
Malignancy	5200	16%	20%	<0.0002
Anxiety	7190	23%	28%	<0.0001
Osteoporosis	3600	12%	14%	<0.05

Caucasians and 98% of AAs (p< 0.0001). Significant difference in comorbidities between the 2 groups are shown in Table 2. Prevalence of other comorbidities including hyperlipidemia, coronary artery disease, depression and fibromyalgia were not significantly different among Caucasians and AA with PsA.

Conclusion: Our findings from a large US real world database revealed hypertension, diabetes, obesity, and gout were more prevalent in AA with PsA as compared to Caucasians. However, malignancy, osteoporosis and anxiety were more prevalent in Caucasians. The co-morbidities were significantly higher in AA patients with PsA and this warrants increased risk stratification. There was increased biologic use in Caucasians with PsA compared to AA who had a much higher use of DMARDs.

Disclosure: S. Jaleel, None; **Y. Ross**, None; **M. Magrey**, Novartis, 2, Eli Lilly, 2, Abbvie, 2, Pfizer, 2, UCB Pharma, 2.

Abstract Number: 1781

A Direct-to-Patient PsA Screening Survey for Earlier Identification of At-Risk Psoriasis Patients and Reduction of Physician Burden

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Diagnostic delays are common with psoriatic arthritis (PsA) and contribute to unnecessary impairments in quality of life and function. Screening surveys for identifying at-risk patients are infrequently used in busy clinical practices. The goal was to develop a direct-to-patient screening approach that does not burden providers with PsA screening tasks. Objective 1 was to characterize patterns of rheumatology referrals and PsA diagnoses in psoriasis patients randomized to receive a screening survey (intervention group) vs. not receive a survey (control group). Objective 2 was to characterize referral and diagnostic patterns in subgroups of intervention group patients instructed to either contact study staff for a rheumatology appointment (direct access [DA] group) or discuss a rheumatology referral with their doctor (standard of care [SOC] group), if they screened positively for elevated PsA risk.

Methods: Patients with an International Classification of Diseases (ICD) code for psoriasis but not PsA in the electronic health record (EHR) were randomized to the control group vs. intervention groups (DA or SOC) (Figure 1). The Psoriasis Epidemiology Screening Tool Survey[1] was disseminated electronically and via postal mail beginning

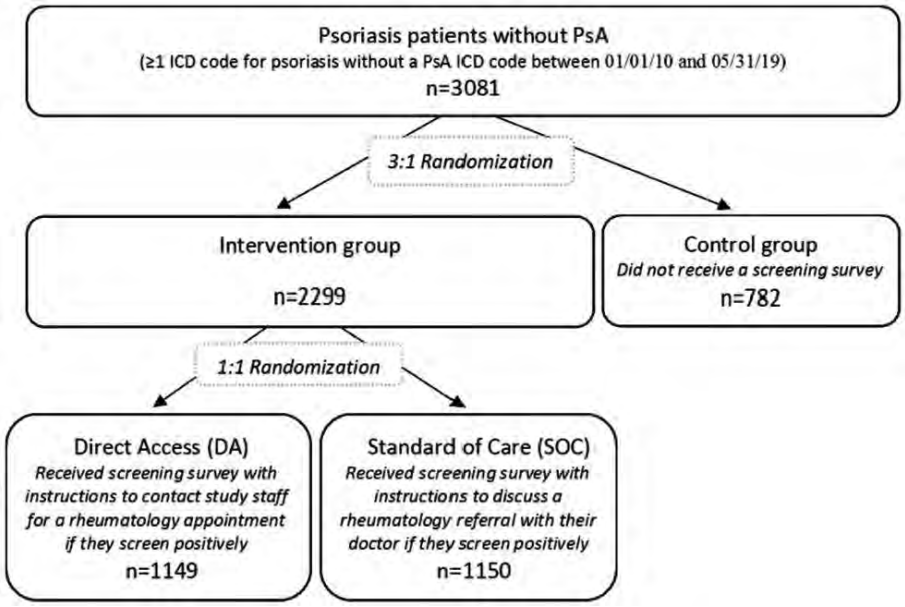

Figure 1. Attrition.

09/18/20 (index date). Referral and diagnostic outcomes were extracted from the EHR for preliminary analysis on 2/2/2021 and compared between DA, SOC, and control groups.

Results: The population included 3081 patients (Figure 1) with 51.5% females and a mean age of 50.1 years. 15.4% completed the online survey, of whom 29.3% screened positively. Among DA patients, 8.6% contacted study staff, of whom 32.5% screened positively, and 29.3% requested a rheumatology appointment. In EHR data, rheumatology appointments occurred with 1.4% DA, 0.7% SOC, and 0.1% control patients, and the mean times to a rheumatology appointment were 77.4, 60.6, and 133.0 days in DA, SOC, and control groups, respectively (Figure 2). PsA diagnosis occurred in 0.4% DA, 0.3% SOC, and 0 control patients, and mean times to PsA diagnosis were 66.0 days in DA and 77.0 days in SOC groups.

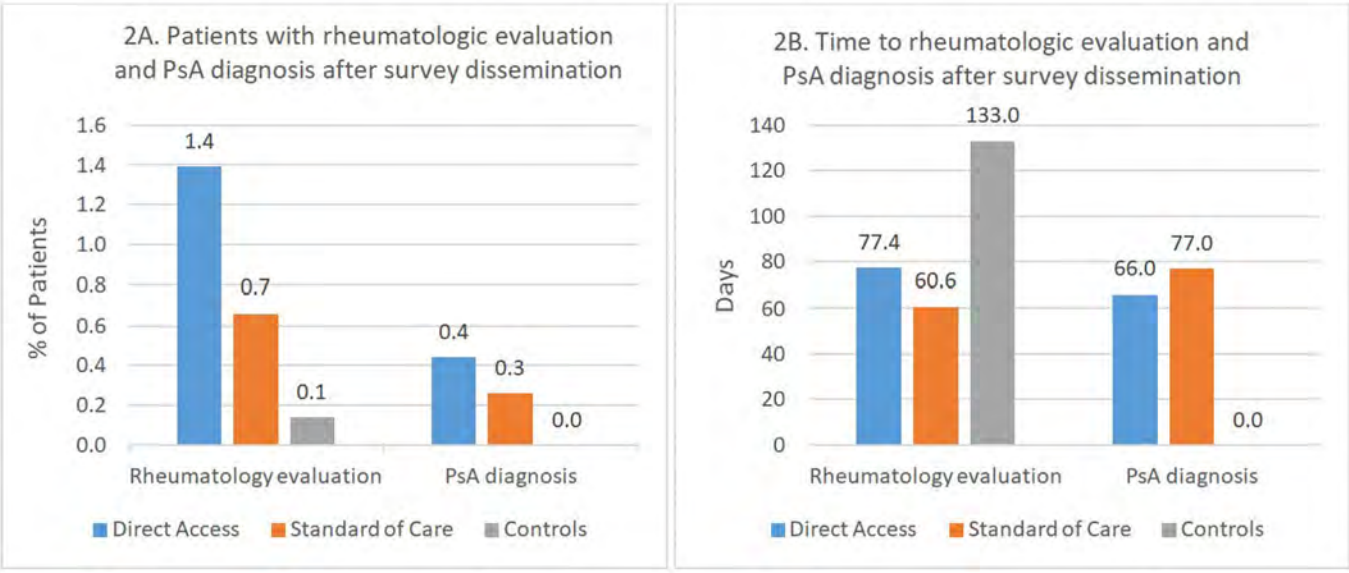

Figure 2. Referral and diagnostic patterns for PsA in patients with psoriasis.

Conclusion: Rheumatologic evaluations and PsA diagnoses were more frequent and earlier in patients exposed to a screening survey than unexposed patients. Rates of rheumatologic evaluations and PsA diagnosis were low, but patient engagement may improve with future study cohorts (n≈24,000 patients), as the impacts of the COVID-19 pandemic decline.

Reference

1. Ibrahim GH, et al. Clin Exp Rheumatol. 2009; 27:469-74.

Disclosure: M. Meier, None; **J. Walsh**, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5; **S. Pei**, None.

Abstract Number: 1782

Disease Activity in Psoriatic Arthritis Patients with Enthesitis Across Different Therapies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Evidence on the treatment of enthesitis, a common feature of psoriatic arthritis (PsA), is limited. This post-hoc, cross-sectional study examined if prevalent treatment choices were related to enthesitis, or other prevalent characteristics of PsA patients.

Methods: Patients enrolled in the Corrona PsA database were included in this study if they had prevalent use of therapeutic drugs and indication of clinical enthesitis. Prevalent use was defined as drug initiation at least two months prior to visit. Enthesitis was defined as having at least one tender point of the 18 sites described by the validated enthesitis scoring index, spondyloarthritis research consortium of Canada (SPARCC) enthesitis index. Treatments groups included cDMARDs, TNF inhibitors (TNFi), and IL-17 inhibitors (IL-17i). The primary outcome was the association of enthesitis activity across different therapies. Secondary outcomes included differences between drug groups in the following disease domain measurements: CDAI, psoriasis body surface area (BSA) %, 68 tender joint count, 66 swollen joint count, health assessment questionnaire (HAQ) score, patient reported pain, patient reported fatigue score, patient global assessment, physician global assessment, and work productivity and activity impairment (WPAI) questionnaire. One-way analysis of variance was used to determine the association between SPARCC scores and prevalent drug use after adjusting for covariates at baseline. Logistic regression (unadjusted analysis) was used to find an association between disease activity and prevalent drug use. Principal component analysis (PCA) derived the primary dimensions of disease activity scores and examined for patterns of clustering among the different prevalent drug groups based on such scores.

Results: 394 PsA patients with enthesitis were identified with 151 patients taking a cDMARD, 167 patients taking a TNFi and 76 patients taking a IL-17i. Complete patient demographics are presented in Table 1. There was a trend of lower SPARCC scores in the IL-17i (3.09+2.54) and TNFi groups (3.28+2.62) as compared to the cDMARD group (3.87+3.28) but the global p-score was not statistically significant. Complete analysis of other disease domain scores

Table 1. Patient Characteristics

	cDMARD	TNFi	IL-17i
N*	151 (38.3)	167 (42.4)	76 (19.3)
Age (years): Mean (SD)	58.5 (12.7)	55.4 (12.6)	54.0 (11.0)
Gender: n (%)			
Male	51 (34.0)	57 (31.1)	20 (26.3)
Female	99 (66.0)	110 (65.9)	56 (73.7)
Race: n (%)			
White	144 (95.4)	156 (93.4)	71 (93.4)
Black	1 (0.7)	3 (1.8)	0 (0.0)
Asian	2 (1.3)	1 (0.6)	1 (1.3)
Other	4 (2.7)	6 (3.6)	3 (4.0)
Unknown	0 (0.0)	1 (0.6)	1 (1.3)
Employment: n (%)			
Currently Employed	67 (46.2)	89 (54.6)	42 (55.3)
Smoking Status: n (%)			
Never	74 (50.0)	98 (59.8)	44 (58.7)
Previous	54 (36.5)	47 (28.7)	25 (33.3)
Current	20 (13.5)	19 (11.6)	6 (8.0)
Alcohol use: n (%)			
Drinker	77 (51.3)	98 (59.8)	43 (58.1)
Non-drinker	73 (48.7)	66 (40.2)	31 (41.9)
Weight (in lbs): Mean (SD)	198.5 (51.0)	204.0 (52.7)	213.6 (60.8)
BMI: Mean (SD)	32.0 (7.4)	32.3 (8.1)	35.0 (9.3)
Insurance: n (%)			
Private	120 (79.5)	156 (93.4)	72 (94.7)
Medicare	51 (33.8)	55 (32.9)	15 (19.7)
Medicaid	15 (9.9)	12 (7.2)	5 (6.6)
Duration of Disease: Mean (SD)	5.7 (7.0)	10.7 (7.9)	9.3 (8.3)
Chronic Disease History:			
CV disease	6 (4.0)	6 (3.6)	0 (0.0)
Diabetes	18 (11.9)	31 (18.6)	18 (23.7)
Cancer (not incl. non-melanoma skin CA)	21 (13.9)	11 (6.6)	4 (5.3)

is presented in Table 2. With age and disease duration excluded, lower physician global assessment and lower mHAQ scores were associated with prevalent TNFi use when compared to cDMARD use (Table 2). Lower physician global assessment was associated with prevalent IL-17i use compared to cDMARD use. Age, duration of disease course,

Table 2. Comparison of disease activity measures by drug and Logistic Regression Model Across Different Drugs

	cDMARD	TNFi	IL-17i	p-value
SPARCC: Mean (SD)	3.87 (3.28)	3.28 (2.62)	3.09 (2.54)	0.085
Swollen joint count 66: Mean (SD)	3.05 (4.94)	2.02 (3.87)	2.07 (4.64)	0.097
Tender joint count 68: Mean (SD)	12.60 (13.39)	9.17 (10.62)	8.54 (12.33)	0.016
Patient Global Assessment: Mean (SD)	49.99 (27.66)	42.43 (27.86)	47.59 (24.01)	0.045
MD Global Assessment: Mean (SD)	32.83 (25.11)	23.05 (19.42)	24.39 (19.36)	<0.001
CDAI: Mean (SD)	17.83 (11.81)	12.86 (9.65)	14.42 (11.55)	<0.001
mHAQ: Mean (SD)	0.65 (0.52)	0.46 (0.42)	0.51 (0.44)	0.002
BSA: Mean (SD)	0.77 (0.42)	0.83 (0.37)	0.83 (0.38)	0.420
Patient Pain: Mean (SD)	56.71 (27.84)	48.45 (28.25)	53.03 (23.83)	0.030
Patient Fatigue: Mean (SD)	59.04 (26.69)	48.34 (29.68)	53.32 (25.11)	0.003
WPAI: Mean (SD)	46.16 (30.11)	40.83 (27.89)	44.37 (27.80)	0.266
cDMARD v. TNFi				
		OR	**95% CI**	**p-value**
MD Global Assessment		0.984	(0.973, 0.996)	0.008
MHAQ		0.557	(0.324, 0.959)	0.035
cDMARD v. IL-17i				
		OR	**95% CI**	**p-value**
MD Global Assessment		0.985	(0.971, 0.998)	0.022
TNFi v. IL-17i*				
**No significant factors*				

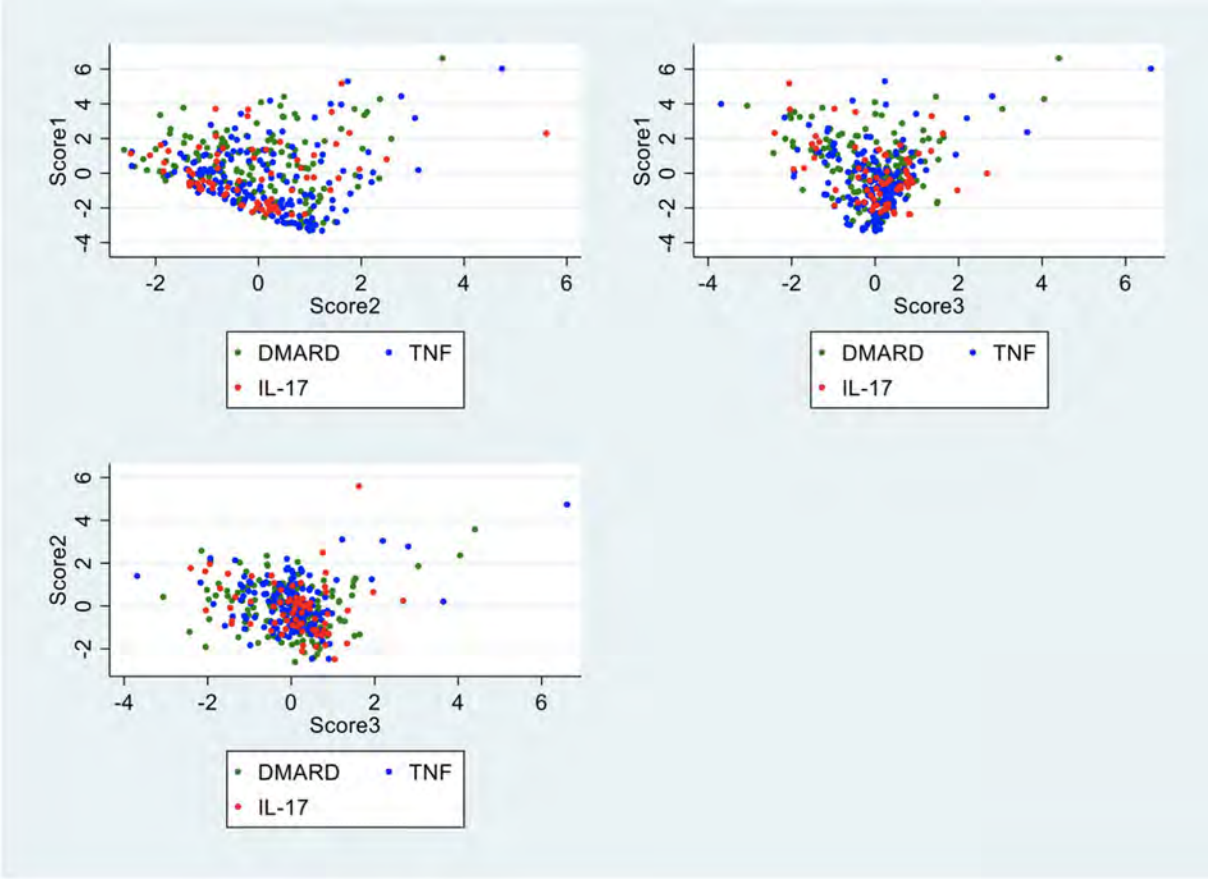

Figure 1. Principle component analysis of PsA disease activity measures across different therapies.

nor any disease activity measures were associated with prevalent use of TNFi compared to IL-17i. PCA resulted in three major dimensions representing 72% of the variation. Plots of the scores illustrated similar distributions of scores among the drug groups that mainly overlapped with no particular clustering (Figure 1).

Conclusion: Prevalent drug utilization was not related to enthesitis activity. Patients with prevalent use of cDMARDs were noted to have higher physician global assessment scores compared to TNFi and IL-17i use. In aggregate, there was no pattern of correlation in disease activity scores amongst the use of different prevalent PsA drug therapies.

Disclosure: R. Chao, None; **G. Reed**, CorEvitas, LLC, 2, Corrona Research Foundation, 2; **J. Kremer**, Abbvie, 2, 5, Pfizer, 2, 5, Bristol Myers Squibb, 2, CorEvitas, 2, Eli Lilly, 2, 5, Novartis, 2, 5, Genentech, 2, Regeneron, 2, Sanofi, 2; **A. Kavanaugh**, AbbVie, 5, 12, Expert advice, Amgen, 5, 12, Expert advice, Bristol Myers Squibb, 5, 12, Expert advice, Janssen, 5, 12, Expert advice, Pfizer, 5, 12, Expert advice, UCB, 5, 12, Expert advice, AstraZeneca, 5, 12, Expert advice, Celgene, 5, 12, Expert advice, Roche, 5, 12, Expert advice, Novartis, 5.

Abstract Number: 1783

National Trends in Hospitalizations for Serious Infections in People with Psoriatic Arthritis Using the National Inpatient Sample 2012 – 2017

Vagishwari Murugesan[1], Eleni Pilitsi[2], Gabriela Rabasa[3] and Maureen Dubreuil[4], [1]Boston University Medical Center, Boston, MA, [2]Boston Medical Center, Boston, MA, [3]Boston University, Boston, MA, [4]Boston University School of Medicine/ VA Boston, Boston, MA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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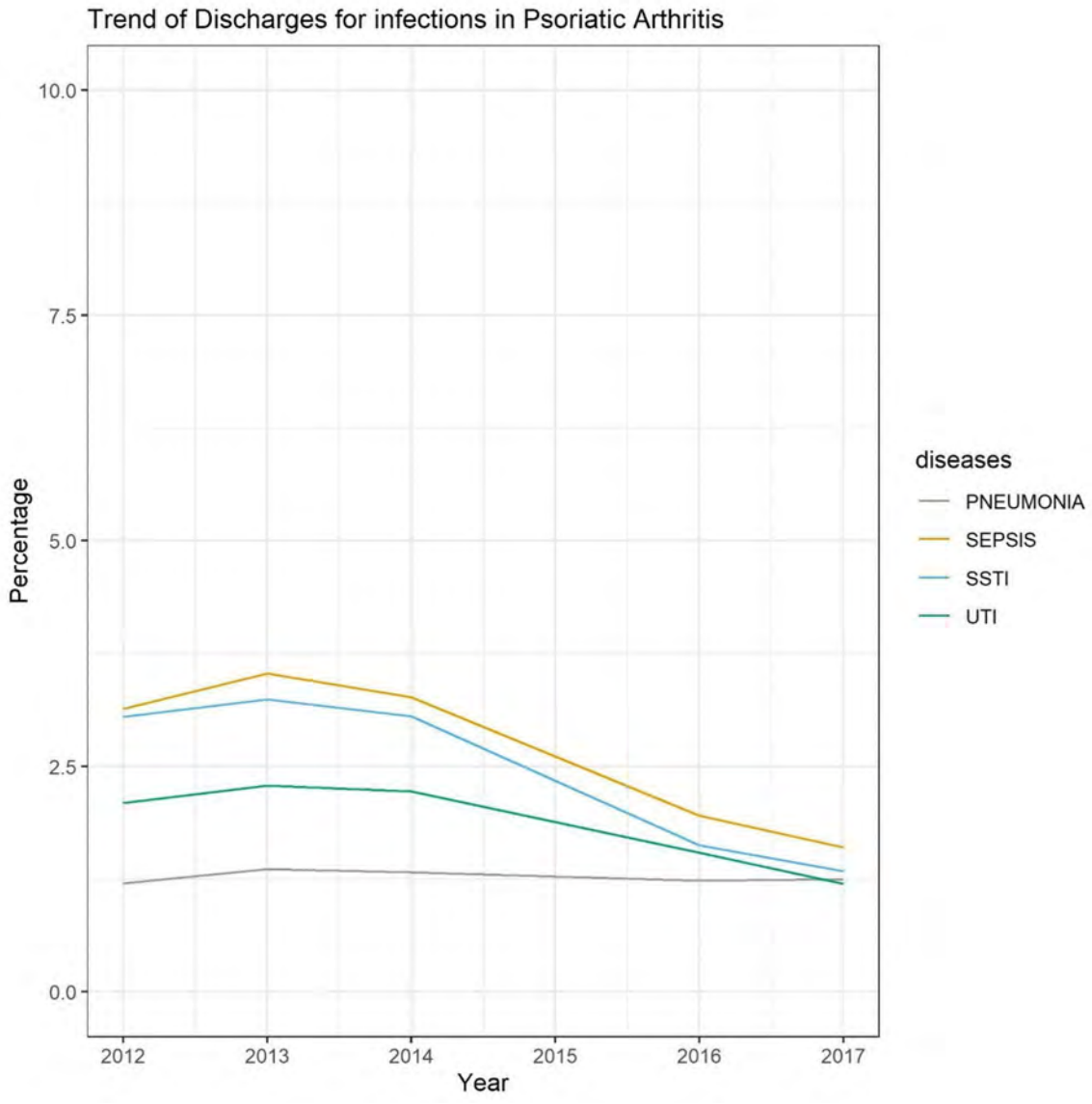
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Given that uptake of biologic therapies has increased over recent years, we sought to investigate the national trends in serious infections in patients with psoriatic arthritis from the years 2012 – 2017 in the United States.

Methods: The NIS approximates a 20% stratified sample of all discharges from U.S. community hospitals, excluding rehabilitation and long-term acute care hospitals, with approximately 7 million discharge records. We examined data from 2012–2017 and identified any discharge diagnosis for PsA with a principal or secondary diagnosis of pneumonia, sepsis, urinary tract infection (UTI) and/or skin and soft tissue infections (SSTIs) using ICD-9 & ICD 10 codes. We standardized results for years 2012-2017 to match age distributions in the US population in the year 2012. We then



tested for a trend over years 2012-2017 using chi squared tests, evaluating for an increase in serious infections over the years.

Results: For the year 2012, the mean age of discharged patients overall was 59.5 ± 14.3 years. Females comprised 56% of discharged patients and Caucasians for 88.5%. The mean (SD) length of stay was 4.7 ± 4.7 days. For the year 2017, the mean age for discharged patients overall was 60.8 ± 14.1. Females accounted for 57.7% and Caucasians for 88.4 %. The mean (SD) length of stay was 4.9 ± 5.8 days.

In the year 2012, there were a total of 50,700 discharge diagnoses of PsA, of which 125 patients had a diagnosis of pneumonia, 230 patients with sepsis, 312 patients with a skin and soft tissue infection and 174 patients with a urinary tract infection (UTI). For comparison in 2017, there were a total of 179,400 discharge diagnoses of PsA, of which 344 patients had pneumonia, 374 patients had sepsis, 681 patients had SSTI and 348 patients had UTI.

From 2012 – 2017 there was a statistically significant decrease in discharges for sepsis, skin and soft tissue infections and UTI ($p < 0.001$ for all) over the years after standardizing for age. There was no statistical difference in the trend of pneumonia between the years ($p = 0.89$).

Conclusion: Our data shows statistically significant decrease in sepsis, skin and soft tissue infections and UTI in patients with PsA despite the increased use of biologics over the years. There was no statistical difference in pneumonia discharges after standardizing for age.

Disclosure: V. Murugesan, None; **E. Pilitsi**, None; **G. Rabasa**, None; **M. Dubreuil**, UCB, 2.

Abstract Number: 1784

Characterizing Musculoskeletal Disease Burden in Mild to Moderate Psoriasis Patients Suggestive of Comorbid PsA: Analysis of CorEvitas' Psoriasis Registry

Alexis Ogdie-Beatty[1], Bruce Strober[2], Mark Lebwohl[3], Angel Cronin[4], Tin-chi Lin[4], Hyung-Joo Kang[4], Nicole Middaugh[4], Jacqueline O'Brien[4], Shauna Jardon[5], Sven Richter[6], Yuri Klyachkin[7] and Philip Mease[8], [1]University of Pennsylvania, Philadelphia, PA, [2]Yale University, New Haven, CT, [3]Icahn School of Medicine at Mount Sinai, New York, NY, [4]CorEvitas, LLC, Waltham, MA, [5]Amgen Inc., Gilbert, AZ, [6]Amgen Inc., Thousand Oaks, CA, [7]Amgen Inc., Lexington, KY, [8]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Patients (pts) with mild to moderate psoriasis (PsO) and musculoskeletal disease burden may be diagnosed with PsA upon referral to a rheumatologist. Early intervention in pts with PsA may result in improved joint, skin, and quality-of-life (QoL) outcomes. This analysis of CorEvitas' Psoriasis Registry sought to identify characteristics and musculoskeletal disease burden among pts naive to systemic treatment with mild to moderate psoriasis based on evidence of potential comorbid PsA.

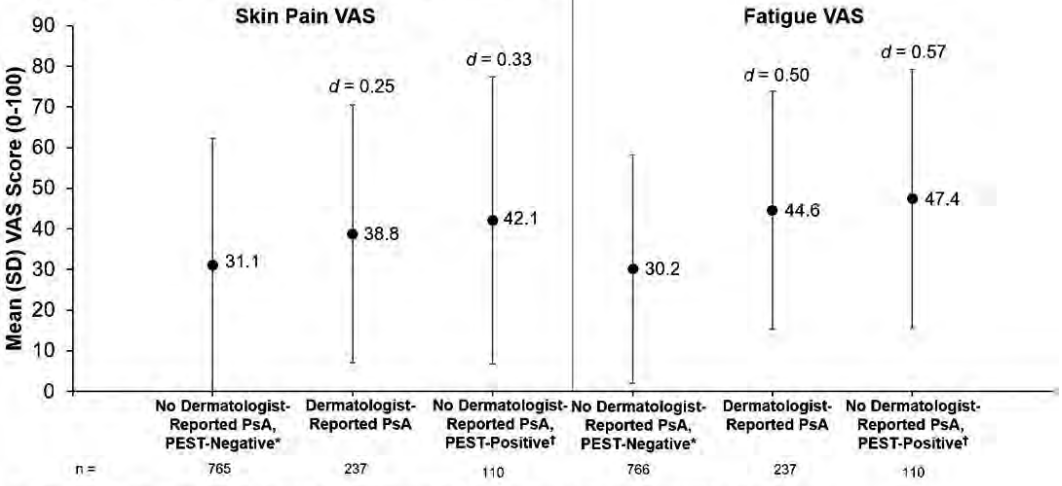
Demographics and Pt Characteristics

Characteristic	No Dermatologist-Reported PsA, PEST-Negative* N = 766	Dermatologist-Reported PsA N = 237		No Dermatologist-Reported PsA, PEST-Positive† N = 110	
	Parameter	Parameter	*d*‡	Parameter	*d*‡
Age, mean (SD), years	47.1 (16.8)	48.9 (13.6)	0.12	55.4 (14.8)	0.52
Female, n (%)	353 (46)	131 (55)	0.18	62 (56)	0.21
White, n (%)	543 (71)	181 (76)	0.12	88 (80)	0.21
Hispanic, n (%)	106 (14)	23 (9.8)	0.13	6 (5.5)	0.29
Body weight, mean (SD), kg	85.6 (23.0)	91.2 (23.4)	0.24	91.2 (25.8)	0.23
BMI, mean (SD), kg/m^2	29.2 (6.8)	31.6 (7.9)	0.32	31.7 (8.7)	0.33
BMI (kg/m^2) categories, n (%)			0.22§		0.29§
<25 (underweight/normal)	216 (29)	48 (20)		19 (17)	
25-30 (overweight)	234 (31)	71 (30)		35 (32)	
>30 (obese)	306 (40)	118 (50)		56 (51)	
History of comorbidities, n (%)					
Cardiovascular disease	41 (5.4)	28 (12)	0.23	9 (8.2)	0.11
Hypertension	212 (28)	95 (40)	0.26	45 (41)	0.28
Hyperlipidemia	139 (18)	68 (29)	0.25	28 (25)	0.18
Diabetes	73 (9.5)	36 (15)	0.17	14 (13)	0.10
Metabolic syndrome	1 (0.13)	1 (0.42)	0.06	1 (0.91)	0.11
Hepatic events	2 (0.26)	2 (0.84)	0.08	2 (1.8)	0.15
GI perforation	3 (0.39)	0 (0)	0.09	2 (1.8)	0.14
Peptic ulcer	10 (1.3)	4 (1.7)	0.03	1 (0.91)	0.04
Crohn's disease	2 (0.26)	6 (2.5)	0.19	0 (0)	0.07
Ulcerative colitis	2 (0.26)	2 (0.84)	0.08	0 (0)	0.07
Indeterminate IBD and other GI disorders	31 (4.0)	27 (11)	0.28	5 (4.5)	0.02
Depression	103 (13)	52 (22)	0.22	25 (23)	0.24
Anxiety	114 (15)	74 (31)	0.40	27 (25)	0.24
Duration of psoriatic disease, mean (SD) years	9.3 (11.6)	11.4 (11.7)	0.18	10.5 (13.9)	0.10
Duration of PsA disease, mean (SD) years	NA	4.2 (6.9)	NA	NA	NA
PEST positive screen (≥3), n (%)	NA	125 (53)	1.49	NA	NA
WPAI currently employed, n (%)	541 (71)	156 (66)	0.10	58 (53)	0.37

*No dermatologist-reported PsA and negative PEST screen (<3). †PEST screen ≥3 without dermatologist-reported PsA. ‡The *d* values (absolute value) vs group with No PsA, PEST-Negative group, respectively. §Tested for any difference across the 3 BMI levels. BMI = body mass index; GI = gastrointestinal; IBD = inflammatory bowel disease; NA = not applicable; WPAI = Work Productivity and Activity Impairment (questionnaire).

Methods: The prospective, observational CorEvitas' Psoriasis Registry enrolls adults with dermatologist-diagnosed PsO who initiated or switched to an eligible systemic treatment at enrollment or within 12 months before enrollment. Pts with mild to moderate PsO (Investigator Global Assessment: 2 or 3) initiating first systemic treatment at enrollment

Figure 1. Mean Skin Pain and Fatigue VAS Scores

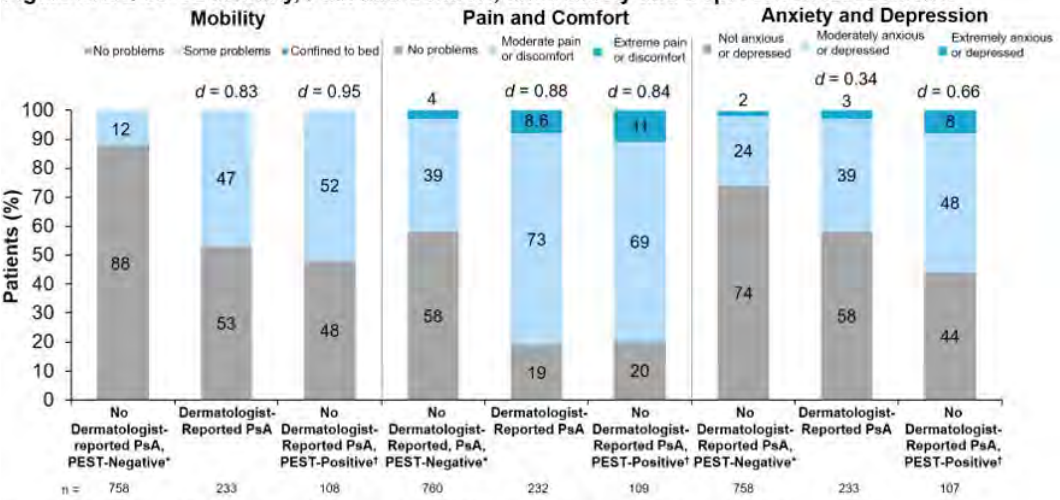


*No dermatologist-reported PsA and negative PEST screen (<3). †PEST screen ≥3 without dermatologist-reported PsA.
d values vs the No PsA, PEST-Negative group.

(April 2015−June 2020) were grouped by musculoskeletal disease burden. This descriptive analysis compares pts with no evidence of PsA (no dermatologist-reported PsA and negative Psoriasis Epidemiology Screening Tool [PEST] screen [< 3]) to pts with dermatologist-reported PsA and to pts without dermatologist-reported PsA but positive PEST (≥3). Standardized differences were calculated (potentially meaningful difference: $d > 0.1$; moderate difference: $d > 0.5$).

Results: Of the 1,113 pts enrolled, 766 (68.8%) had no evidence of PsA, 237 (21.3%) had dermatologist-reported PsA, and 110 (9.9%) had a positive PEST screen (PEST ≥3) without dermatologist-reported PsA. Concordance between dermatologist-reported PsA and positive PEST screen was 80%: 112 pts (10%) had dermatologist-reported PsA and negative PEST screen and 110 pts (10%) had positive PEST screen without dermatologist-reported PsA. For all groups, mean PsO duration was >9 years. For pts with dermatologist-reported PsA, mean PsA duration was 4 years (Table). Comorbidity histories were often higher in pts with dermatologist-reported PsA or positive PEST screen without dermatologist-reported PsA vs pts with no evidence of PsA (Table). Current employment was less prevalent among pts with dermatologist-reported PsA or positive PEST screen without dermatologist-reported PsA vs pts with

Figure 2. EQ-5D-3L Mobility, Pain and Comfort, and Anxiety and Depression Assessments



*No dermatologist-reported PsA and negative PEST screen (<3). †PEST screen ≥3 without dermatologist-reported PsA.
d values vs No PsA, PEST-Negative group.

no evidence of PsA (Table). Mean skin pain visual analog scale (VAS) and fatigue VAS scores were higher for pts with dermatologist-reported PsA or positive PEST screen without dermatologist-reported PsA vs no evidence of PsA (Figure 1). Also, EuroQol-5 Dimension 3 Level assessments indicated that pts with dermatologist-reported PsA or positive PEST screen without dermatologist-reported PsA had greater problems with mobility, pain and comfort, and anxiety and depression compared with pts with no evidence of PsA (Figure 2).

Conclusion: Pts naive to systemic treatment who have mild to moderate PsO and either PsA or musculoskeletal disease suggestive of comorbid PsA had greater comorbidity burden, symptom burden, and QoL impairment compared with pts with no evidence of PsA in this analysis from CorEvitas' Psoriasis Registry.

Disclosure: A. Ogdie-Beatty, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2; **B. Strober**, AbbVie, Amgen, Eli Lilly, Janssen, Sanofi-Genzyme, 6, AbbVie, Cara, CorEvitas' Psoriasis Registry, Dermavant, Dermira, and Novartis, 12, Investigator, Journal of Psoriasis and Psoriatic Arthritis, 6, 12, Editor-in-Chief (honorarium), CorEvitas' Psoriasis Registry, 2, 12, co-scientific director (consulting fee), AbbVie, Almirall, Amgen Inc., Arcutis, Arena, Aristea, Boehringer Ingelheim, Bristol Myers Squibb, 2, 6, Connect Biopharma, Dermavant, Dermira, Eli Lilly, Equillium, GlaxoSmithKline, Immunic Therapeutics, 2, 6, Janssen, LEO Pharma, Maruho, Meiji Seika Pharma, Mindera, Novartis, Ortho Dermatologics, 2, 6, Pfizer, Regeneron, Sanofi-Genzyme, Sun Pharma, and UCB, 2, 6; **M. Lebwohl**, Aditum Bio, 2, Abbvie, 5, Allergan, 2, Almirall, 2, Amgen, 5, Arcutis, Inc., 2, 5, Avotres Therapeutics, 2, BirchBioMed Inc., 2, BMD skincare, 2, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Cara Therapeutics, 2, Castle Biosciences, 2, CorEvitas, LLC, 2, Dermavant Sciences, 2, 5, Evelo, 2, Eli Lilly, 5, Evommune, 2, 5, Facilitate International Dermatologic Education, 2, Foundation for Research and Education in Dermatology, 2, Inozyme Pharma, 2, Kyowa Kirin, 2, Leo Pharmaceutucals, 2, 5, Meiji Seika Pharma, 2, Incyte, 5, Janssen, 5, Menlo, 2, Mitsubishi, 2, Neuroderm, 2, Ortho Dermatologics, 5, Pfizer, 2, 5, Promius/Dr. Reddy's Laboratories, 2, Serono, 2, Theravance, 2, Verrica, 2, UCB, 5; **A. Cronin**, CorEvitas, LLC, 3; **T. Lin**, CorEvitas, LLC, 3; **H. Kang**, CorEvitas, LLC, 3; **N. Middaugh**, CorEvitas, LLC, 3; **J. O'Brien**, CorEvitas, LLC, 3; **S. Jardon**, Amgen Inc., 3, 11; **S. Richter**, Amgen Inc., 3, 11; **Y. Klyachkin**, Amgen Inc., 3, 11; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1785

Prevalence and Incidence of PsA in Germany – a Cohort Study with 65 Million Participants

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

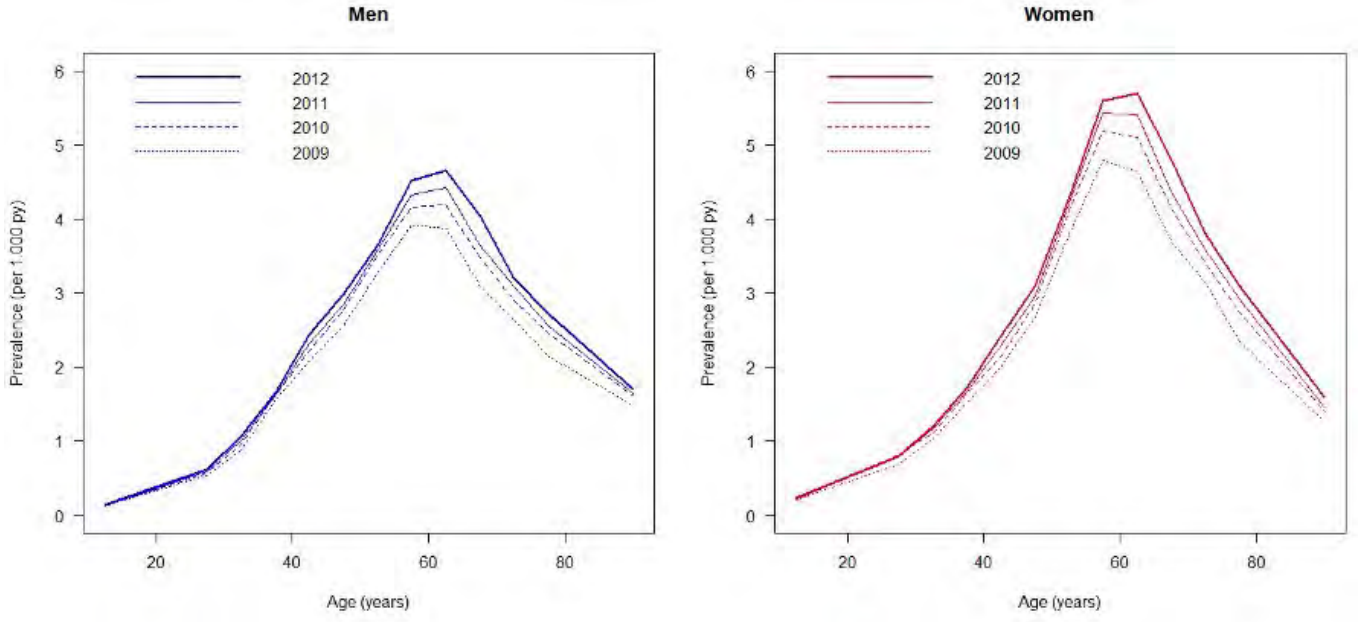

Figure 1. Age- and sex-specific prevalence of PsA in Germany (2009-2012).

Background/Purpose: Patients suffering from Psoriatic-Arthritis (PsA) can experience a substantial burden of disease, which may result in a significant reduction of their quality of life. Due to the relatively small sample size, the validity of previous cohort studies is partly reduced. Therefore, larger and more representative samples are urgently necessary to investigate prevalence and especially incidence in the real world. The present datasets enable a comprehensive examination of the epidemiology of the PsA in Germany.

Methods: The data was provided by the statutory health insurance as part of the morbidity-based risk adjustment. There, a cohort study collected the data of 65 million Germans with a statutory insurance from 2009 to 2012.

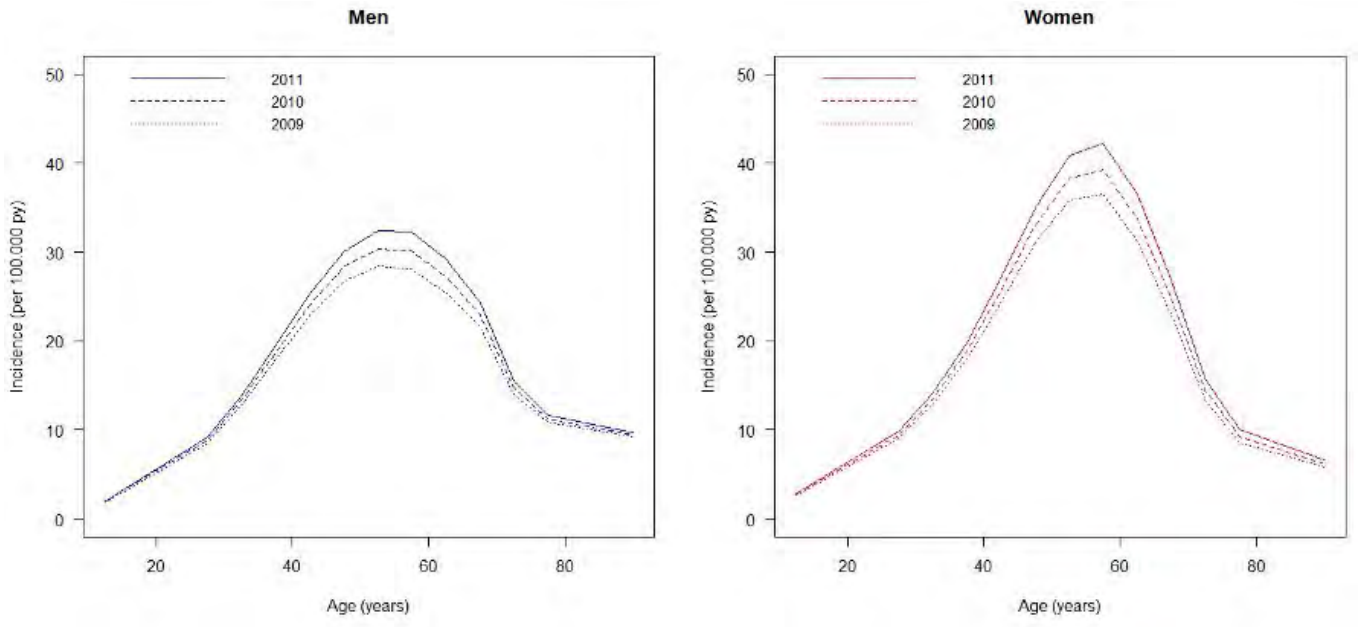

Figure 2. Age- and sex-specific incidence of PsA in Germany (2009-2011).

The main focus of this paper is to interpret the varying prevalence within the different age groups. Further, it aims to identify potential influences on this distribution. Especially the drastic decrease in the prevalence after the age of 60 remains in need of explanation.

A second step calculates the incidence values for PsA in Germany. For this purpose, we used a formula introduced by Brinks et. al., which requires the prevalence as well as the general mortality and the relative mortality associated with the disease (1, 2).

Results: The total number of persons suffering from PsA rose to approximately 127.000 in 2009 and 156.000 in 2012. A steady increase was observed for the age- and sex-specific prevalence over the lifetime of men and women, until it reached a plateau and declined thereafter. The prevalence plateaued at maximum of 5 per 1,000 py for men and 6 per 1,000 py for women. As previously mentioned, there is a sharp decrease in the prevalence in both sexes after the age of 60 (Fig. 1).

In contrast to the prevalence, the age- and sex-specific incidence peaks slightly earlier. The latter assumes a maximum value of 30 per 100,000 in men and 40 per 100,000 py in women. The subsequent decline of the incidence is less pronounced than for the prevalence (Fig. 2).

In general, an overall rise in the prevalence as well as the incidence can be observed during the study period.

Conclusion: In conclusion we demonstrated that there are considerable fluctuations in both the prevalence and incidence within the different age groups. A possible explanation for the change in the prevalence is the correlation between PsA and additional comorbidities, which coincide with an increased morbidity and mortality. Likewise, further influences such as an increased awareness for the diagnosis of PsA should be considered. Not only changed coding behavior of ICD codes but also the development of new therapeutic approaches has a significant impact on PsA prevalence and incidence.

References

Brinks, R., Landwehr, S., Icks, A., Koch, M. & Giani, G. (2013) Deriving age-specific incidence from prevalence with an ordinary differential equation. Statist. Med., 32, 2070–2078.
Brinks, R. & Landwehr, S. (2015) A new relation between prevalence and incidence of a chronic disease. Math. Med. Biol., 32, 425-35.

Disclosure: M. Denke, None; **M. Schneider**, GlaxoSmithKline, 2, 5, 6, UCB, 5, 6, AbbVie, 2, 5, Alexion, 2, AstraZeneca, 2, 6, Boehringer-Ingelheim, 2, Janssen-Cilag, 2, 6, Lilly, 2, 6, Novartis, 2, Pfizer, 2, 6, Roche, 2, Sanofi-Aventis, 2, Biogen, 6, BMS, 6, Celgene, 6, Chugai, 6; **R. Brinks**, None; **P. Sewerin**, AbbVie, 2, 5, Amgen, 2, 5, Axiom Health, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, Chugai Pharmaceutical Co. Ltd, 2, Deutscher Psoriasis Bund, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Johnson & Johnson, 2, Medi-login, 2, Mediri, 2, Novartis, 2, 5, Onkowissen, 2, Pfizer, 2, 5, Roche, 2, 5, Rheumazentrum Rhein-Ruhr, 2, 5, Sanofi, 2, 5, Swedish Orphan Biovitrum, 2, UCB, 2, 5, Bundesministerium fuer Bildung und Forschung, 5, Deutsche Forschungsgesellschaft, 5, Hexal, 5.

Abstract Number: 1786

Association of the Improvement of Synovitis and Enthesitis with Quality of Life/Patient Reported Outcomes in Patients with PsA Treated with Ixekizumab

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: PsA is an inflammatory rheumatic disease with manifestations including synovitis and enthesitis. During extensive study programs, IXE has shown a treatment effect across domains affected by PsA. Ixekizumab (IXE) is an IL17A inhibitor approved for the treatment of active PsA and axial SpA.

We sought to determine whether there is any association between the improvement of synovitis with that of enthesitis from baseline (BL) through week (wk) 52 in patients (pts) with PsA treated with IXE. Additionally, the association between the improvement of synovitis and enthesitis on health-related quality of life and patient-reported outcomes was investigated.

Methods: Data from SPIRIT-P1 (NCT01695239), SPIRIT-P2 (NCT02349295) and SPIRIT-H2H (NCT03151551) were analyzed. These were randomized, phase 3 trials involving pts with active PsA either biologic DMARD-naïve (P1, H2H); or who were TNF-inhibitor-experienced (P2).

We examined the patient population randomized to IXE-treatment (80 mg of ixekizumab every 4 weeks [IXEQ4W]), that had both synovitis and enthesitis at BL. For each study, a standardization procedure was applied to each study data in order to overcome the differences in score range between LEI and SJC. The Pearson correlation coefficient between improvement from BL in enthesitis and synovitis was calculated at each time point.

The mean improvement in the SF-36 Physical Component Summary score [PCS], the Patient's Global Assessment of Disease Activity [Pt GA], and the EuroQOL five dimensions [EQ5D]-visual analogue [VAS] score) was calculated over time for pts who reached or did not reach resolution of both enthesitis and synovitis at wk 52.

Missing data were imputed with modified Baseline Carried Out Forward (mBOCF) for continuous outcomes. Non-responder imputation was used for pts with missing resolution of enthesitis or synovitis.

Results: At BL, 68 (63% of patients treated with IXEQ4W in the ITT population), 68 (56%) and 159 (56%) pts from P1, P2 and H2H respectively, had both synovitis and enthesitis. In all 3 trials, the standardized mean change from baseline in synovitis and enthesitis showed a similar pattern over time (Figure 1). When statistically significant, Pearson correlation coefficient values ranged from 0.16 to 0.40 (Table), indicating a positive association between mean improvement in synovitis and enthesitis.

Pts were grouped according to whether they achieved resolution of both synovitis and enthesitis at wk 52, either or neither. We observed an improvement of SF-36 over the 52 wks regardless of the resolution of synovitis or enthesitis. The most pronounced improvement was shown by pts achieving resolution of both synovitis and enthesitis followed by the pts achieving one or the other (Figure 2). There was no difference in the trajectories for EQ5D and PtGAD in pts regardless of resolution of synovitis and/or enthesitis (data not shown).

Conclusion: Across the SPIRIT trials, treatment with IXE led to the significant improvement in synovitis and enthesitis with a positive association between the improvement of both. Furthermore, those pts that resolve both measures at wk 52, experienced an earlier and greater improvement in the SF-36 Physical Component Scale.

Figure 1: Standardised Change from Baseline in enthesitis and synovitis through wk 52

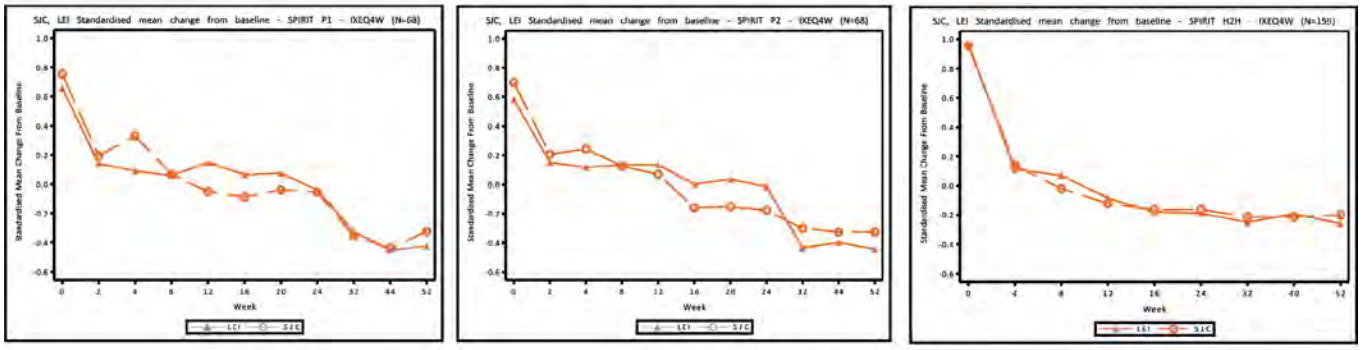

Figure footnote: LEI = Leeds Enthesitis Index; SJC = Swollen Joint Count; N= number of patients

Figure footnote: LEI= Leeds Enthesitis Index; SJC = Swollen Joint Count; N = number of patients.

Correlation coefficient	W4	W8	W12	W16	W24	W32	W52
SPIRIT P1 - IXE Q4	0.17	-0.05	0.30	0.35	0.35	0.16	0.37
SPIRIT P2 - IXE Q4	0.10	0.29	0.40	0.26	0.21	0.32	0.35
SPIRIT H2H - IXE Q4	0.23	0.18	0.17	0.19	0.11	0.16	0.25

Table footnote: Correlation coefficients range from -0.05 to 0.40. A more intense color represents a higher correlation.

Figure 2 :SF-36 PCS in patients who reached resolution of both enthesitis and synovitis, either enthesitis or synovitis or neither, at week 52

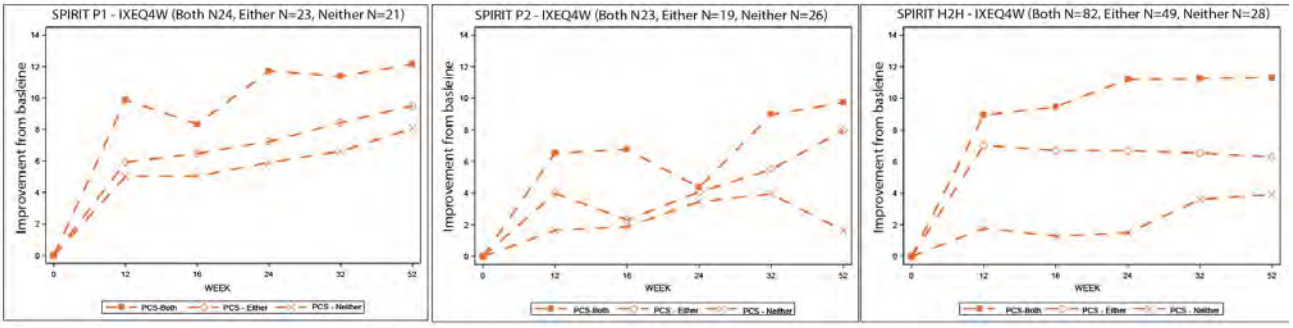

Figure footnote: Both = patients who achieved resolution of both enthesitis & synovitis at wk 52; Either = patients who achieved either resolution of enthesitis or synovitis at wk 52; N= number of patients; Neither = patients who did not achieve resolution of enthesitis nor synovitis at wk 52; PCS – Physical Component Score.

Disclosure: L. Kristensen, UCB, 2, 5, 6, Abbvie, 2, 6, Eli Lilly, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 6, Gilead, 6, Janssen, 2, 6, Novartis, 2, 5, 6; **D. McGonagle**, Novartis, 5, 6, Roche, 6, Sobi, 6; **M. Rudwaleit**, Abbvie, 1, 6, BMS, 1, 6, Janssen, 1, 6, Chugai, 6, Lilly, 1, 6, Novartis, 1, 6, UCB, 1, 2, 6, Galapagos, 12, reimbursement of congress attandance; **H. Kameda**, Asahi-Kasei, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 5, 6, Chugai, 5, 6, Mitsubishi-Tanabe, 5, 6, Astellas, 2, Eli Lilly, 2, 6, Pfizer, 6, Eisai, 5, 6, Gilead Sciences, 2, Janssen, 2, 6, Sanofi, 2, UCB, 2; **T. Holzkaemper**, Eli Lilly, 3, 12, Shareholder; **C. El Baou**, Eli Lilly Ltd, 7; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5.

Abstract Number: 1787

What Is Peripheral SpondyloArthritis? Identifying Disease Phenotype and Burden: A Post Hoc Analysis of the ASAS-PerSpA International Study

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Peripheral spondyloarthritis (pSpA) shows features that overlap with psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) and other forms of SpA and is unsatisfactorily defined despite the introduction of the

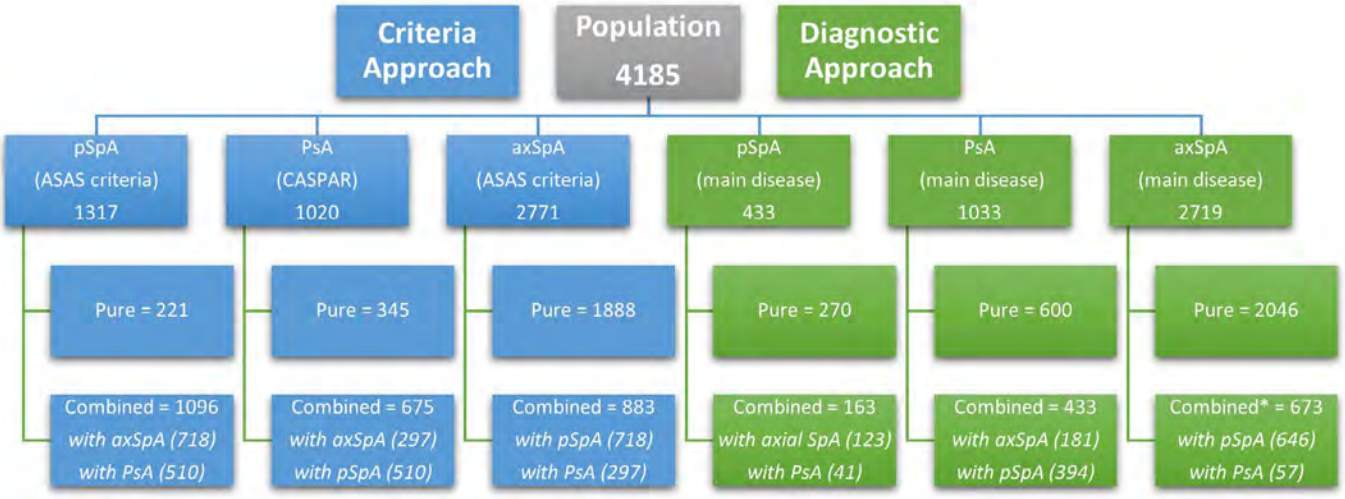

Figure 1. Prevalence of the pure and combined forms of spondyloarthritis (peripheral SpA (pSpA), psoriatic arthritis (PsA) and axial SpA (axSpA), using the criteria (ASAS and CASPAR) and to the diagnostic approach.

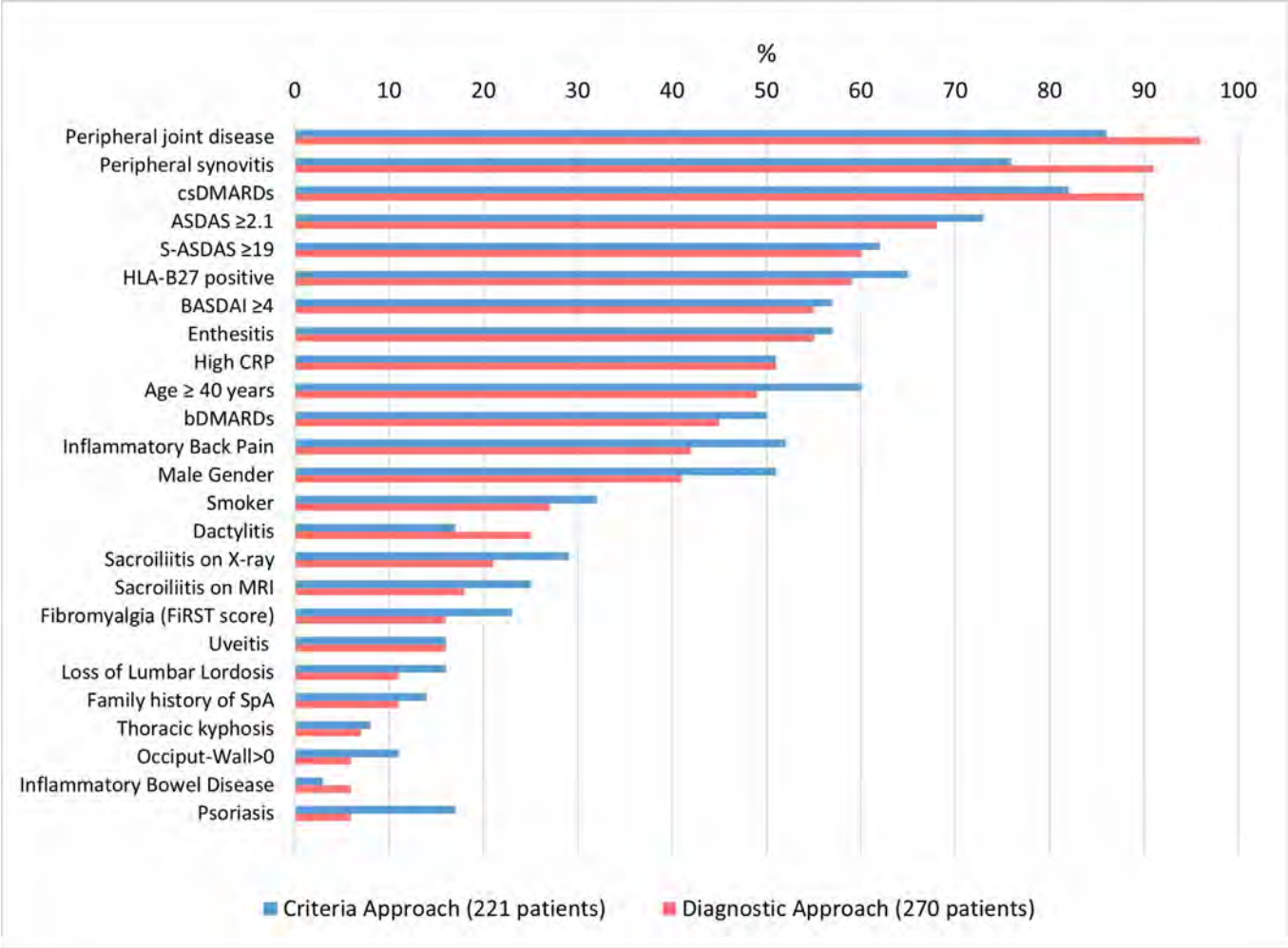

Figure 2. Phenotypic profile of patients with peripheral spondyloarthritis.

ASAS classification criteria in 2011. The objective of this study was to estimate the prevalence of pSpA among patients with SpA, to identify the phenotype and burden of patients with pure pSpA and to compare these findings with that of pure PsA, pure axSpA and combined forms of SpA.

Methods: This is a post hoc analysis of the ASAS-Peripheral involvement in SpA (PerSpA) study, based on 4,185 patients diagnosed by their rheumatologists with pSpA, PsA and axSpA. Two parallel approaches were used to define the disease subtypes (Fig.1). First, the criteria approach categorized the patients in 6 groups: pure disease (fulfilling either pSpA, or axSpA ASAS classification criteria, or CASPAR criteria) and combined disease (patients who fulfill more than one of the above-mentioned criteria). Second, the diagnostic approach categorized the patients in 6 groups as well: pure disease (diagnosed with pSpA, axSpA or PsA as the main SpA disease, exclusively) and combined disease (patients with overlapping features according to rheumatologists' judgement). Socio-demographic characteristics, clinical, biological, imaging phenotype, and disease burden were compared among patients with pure pSpA, PsA, axSpA and the combined forms of SpA (grouped together), using Chi-square, ANOVA and Kruskal-Wallis as appropriate.

Results: The prevalence of all pSpA was 31.5% using the criteria approach and 10% using the diagnostic approach (Fig.1). pSpA was pure in only 17% of pSpA using the criteria approach (compared to 34% pure PsA and 68% pure axSpA), and in 62% of pSpA using the diagnostic approach (compared to 58% pure PsA and 75% pure axSpA). Patients with pure pSpA had a socio-demographic profile and disease phenotype with "intermediate" features between PsA and axSpA

Table 1. Patient profile, disease phenotype and burden in patients with pure SpA compared to pure PsA, pure axSpA, and combined forms using the criteria approach

	Pure peripheral SpA	Pure Psoriatic Arthritis	Pure axial SpA	Combined forms of SpA	p-value
Number of patients	221	345	1888	1731	
Socio-Demographic Data					
World region, N (% in rows)					
- Latin America = 487	35 (7.2)	54 (11.1)	135 (27.7)	263 (54.0)	<0.001
- Europe & NA = 1603	60 (3.7)	165 (10.3)	778 (48.5)	600 (37.4)	
- Asia = 913	53 (5.8)	58 (6.4)	433 (47.4)	369 (40.4)	
- MENA = 1182	73 (6.2)	68 (5.8)	542 (45.9)	499 (42.2)	
Age (continuous), years, mean (SD)	46.8 (14.8)	54.0 (13.8)	41.2 (12.6)	46.0 (13.8)	<0.001
Gender, male, N (%)	113 (51.1)	183 (53.0)	1357 (71.9)	914 (52.8)	<0.001
BMI Kg/m^2, mean (SD)	26.2 (5.0)	28.2 (6.1)	25.8 (5.0)	26.9 (5.6)	<0.001
Educational level, N (%)					
- Primary school	53 (24.1)	80 (23.3)	253 (13.4)	308 (17.8)	<0.001
- Sec. School	90 (40.9)	158 (45.9)	783 (41.5)	761 (44.0)	
- University	77 (35.0)	106 (30.8)	850 (45.1)	662 (38.2)	
Employed, N (%)	101 (45.7)	180 (52.3)	1235 (65.5)	928 (53.7)	<0.001
Smoker, N (%)	71 (32.1)	169 (49.1)	845 (44.8)	722 (41.7)	<0.001
Age at SpA onset, mean (SD)	37.4 (14.8)	37.1 (15.7)	26.7 (9.6)	31.9 (13.6)	<0.001
HLA-B27 positive, N (%)	85 (64.9)	12 (8.2)	1266 (82.2)	629 (55.2)	<0.001
Family history of SpA, N (%)	29 (14.1)	6 (2.0)	391 (21.3)	216 (13.4)	<0.001
Disease duration, Median [IQR]	6.6 [12.0]	14.5 [17.8]	11.8 [14.6]	11.6 [15.0]	<0.001
Diagnostic delay, Median [IQR]	1.2 [5.8]	4.7 [13.7]	3.0 [7.0]	3.3 [9.61]	<0.001
Disease Phenotype					
Peripheral Joint Disease, N (%)	190 (86.0)	331 (95.9)	596 (31.6)	1209 (69.8)	<0.001
Synovitis, N (%)	167 (75.6)	321 (93.0)	504 (26.7)	1099 (63.5)	<0.001
Enthesitis, N (%)	125 (56.6)	134 (38.8)	671 (35.5)	904 (52.2)	<0.001
TJC, mean (SD)	4.1 (6.1)	2.1 (5.7)	0.7 (2.5)	4.4 (8.0)	<0.001
SJC, mean (SD)	2.1 (3.3)	0.01 (0.2)	0.0 (0.0)	1.7 (4.5)	<0.001
Inflammatory Back Pain, N (%)	116 (52.5)	79 (22.9)	1800 (95.3)	1155 (66.7)	<0.001
Dactylitis, N (%)	37 (16.7)	154 (44.6)	92 (4.9)	363 (21)	<0.001
Psoriasis, N (%)	38 (17.2)	334 (96.8)	92 (4.9)	733 (42.2)	<0.001
Uveitis, N (%)	35 (15.8)	9 (2.6)	416 (22.0)	230 (13.3)	<0.001
Inflammatory Bowel Disease, N (%)	6 (2.7)	2 (0.6)	93 (4.9)	62 (3.6)	0.001
CRP mg/l, mean (SD)	16.3 (31.2)	10.0 (30.0)	9.2 (21.0)	14.5 (30.1)	<0.001
Sacroiliitis on X-ray, N (%)	65 (29.4)	33 (9.6)	1456 (78.2)	826 (47.7)	<0.001
Sacroiliitis on MRI, N (%)	55 (24.9)	16 (4.6)	1053 (55.8)	621 (35.9)	<0.001
Disease Burden					
PGA mean (SD)	5.1 (2.5)	3.7 (2.5)	3.8 (2.6)	5.0 (2.7)	<0.001
BASDAI, mean (SD)	4.5 (2.3)	3.3 (2.3)	3.2 (2.2)	4.6 (2.5)	<0.001
ASDAS, mean (SD)	2.8 (1.1)	2.2 (1.0)	2.3 (1.0)	2.8 (1.7)	<0.001
S-ASDAS, mean (SD)	23.7 (12.2)	17.5 (11.4)	17.7 (11.3)	16.2 (11.3)	<0.001
BASFI, mean (SD)	3.4 (2.8)	2.3 (2.3)	2.6 (2.5)	3.5 (2.7)	<0.001
ASAS-HI, mean (SD)	7.5 (4.5)	5.6 (4.4)	5.7 (4.4)	7.6 (4.6)	<0.001
Bamboo spine, N (%)	13 (5.9)	3 (0.9)	273 (14.5)	190 (11)	<0.001
Loss of lumbar lordosis, N (%)	36 (16.3)	20 (5.8)	673 (35.6)	482 (27.8)	<0.001
Thoracic kyphosis, N (%)	17 (7.7)	7 (2.0)	426 (22.6)	325 (18.8)	<0.001
Occiput-Wall Distance >0, N (%)	24 (10.9)	8 (2.3)	519 (27.5)	356 (20.6)	<0.001
FiRST score, N (%)	51 (23.1)	58 (16.8)	231 (12.2)	401 (23.2)	<0.001
WPAI, mean (SD)	28.7 (17.4)	23.2 (16.5)	24.4 (18.8)	28.7 (19.1)	<0.001
EQ-5D, mean (SD)	0.59 (0.23)	0.71 (0.22)	0.70 (0.22)	0.60 (0.25)	<0.001
Treatment Modalities					
csDMARDs, N (%)	182 (82.4)	317 (91.9)	909 (48.1)	1337 (77.2)	<0.001
bDMARDs, N (%)	110 (49.8)	218 (63.2)	1146 (60.7)	1030 (59.5)	0.009

All percentages are presented in columns, except for world region, where they are presented in rows.

ASAS-HI: ASAS Health Index, ASDAS: Ankylosing Spondylitis Disease Activity Score, b-DMARDS: biological disease-modifying anti-rheumatic drugs, BASDAI: Bath Ankylosing Spondylitis Disease Activity Index, BASFI: Bath Ankylosing Spondylitis Functional Index, CRP: C-Reactive Protein, cs-DMARDs: conventional synthetic disease-modifying anti-rheumatic drugs, FiRST: Fibromyalgia Rapid Screening Tool, PGA: Patient Global Assessment of well-being S-ASDAS: Simplified ASDAS, SJC: Swollen Joint Count, SpA: Spondyloarthritis, TJC: Tender Joint Count, WPAI: Work Productivity Loss.

(Fig.2). Using criteria and diagnostic approach, respectively, pure pSpA patients had a high prevalence of peripheral joint disease (86 and 96%), synovitis (76 and 91%), and enthesitis (57 and 55%), a positive HLA-B27 in 65 and 59%, a high C-Reactive Protein level in 51% and inflammatory back pain in 52 and 42%. However, compared to pure PsA and pure axSpA, they had a significantly higher disease burden (BASDAI, ASDAS, ASAS-HI, BASFI, FiRST, WPAI and EQ-5D), with scores being in a similar range to that of the combined forms of SpA (Table 1), when using the criteria approach. This higher disease burden was confirmed in the diagnostic approach in comparison with axSpA only. Still, patients with pure pSpA had lower use of biological Disease-Modifying Drugs (b-DMARDs) using both approaches.

Conclusion: The prevalence of pSpA varies when using the classification criteria or the rheumatologist's diagnosis. It occurs in a pure form (i.e., associated with neither PsA nor axSpA) less frequently than PsA and axSpA. Pure pSpA has a distinct clinical phenotype with intermediate features between pure PsA and pure axSpA but with a higher disease burden compared to both diseases, and a lower use of b-DMRADs.

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Abstract Number: 1788

Improving Care and Capacity Through Capturing and Recording Patient Reported Outcomes with Digital Solutions in Spondyloarthritis

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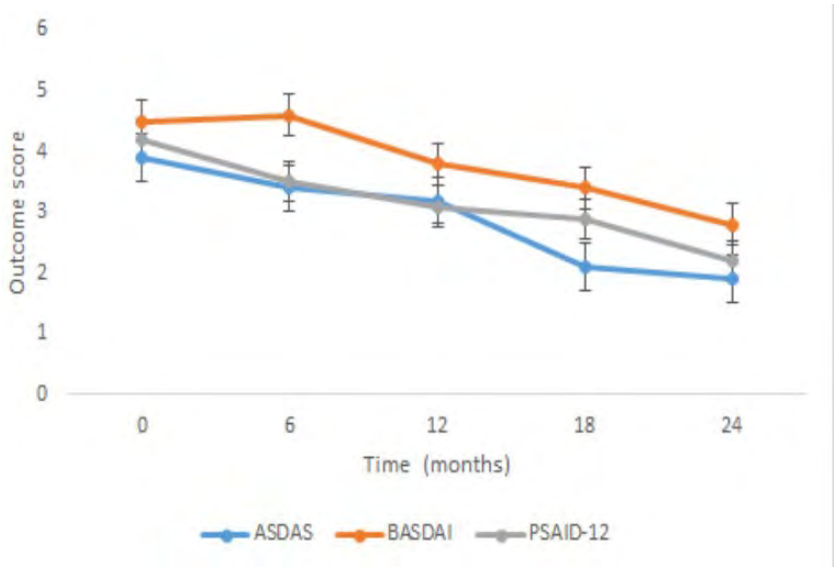
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Patient-reported outcomes (PROs) have always been at the forefront for the assessment of spondyloarthritis (SpA) which includes axial Spa (axSpA) and psoriatic arthritis (PsA). With the increasing adoption of electronic health records (EHRs), collecting PROs electronically (ePRO) presents a great opportunity for advancing patient care in SpA. Electronic PROs are useful for guiding treatment decisions, with the aim of improving health outcomes through patient empowerment.

Methods: Electronic PROs were incorporated the in to routine clinical practice and the EHR at Royal Berkshire Hospital in Reading, UK since 2018. AxSpA patients meeting the ASAS criteria routinely completed the outcome measures BASDAI, BASFI, Spinal NPRS, and BASG. PsA patients meeting the CASPAR criteria completed patient assessed tender joint, swollen joint, global assessment, PSAID-12. Patients were sent reminders to complete the questionnaires through email or text messaging before each appointment and every 6 months routinely. The development of a clinician dashboard captures a range of multidimensional ePROs that was used proactively to support patient-centric appointment scheduling. Appointments were expedited or deferred depending on the clinical outcome scores. This enabled the clinical team to arrange non face to face / virtual follow-up appointments with some patients.



Outcome measure (ASDAS, BASDAI and PSAID-12) scores at baseline and 6 month interval for 24 months.

Results: There are 998 patients with AxSpA and PsA of which approximately 70% (n=692) completed the ePRO questionnaires. Over a 2.5 year period (2018-2021), a total of n=692 patients (n=470 axSpA and n=222 PsA patients) were recruited into the ePRO system. The mean (SD) age for axSpA patients were 44.7(13.3) and PsA 54 (9.9) years. n=308 (44%) patients were on biologics. At group level, there was a trend to the reduction in mean (SD) ASDAS at months 0, 6, 12, 18 and 24 (3.9±1.2, 3.4±1.1, 3.2±1.5, 2.1±0.9, 1.9±1.0) and BASDAI (4.5±2.7, 4.6±1.9, 3.8±2.4, 3.4±2.3, 2.8±1.2). In the PsA group, there was also a trend to the reduction in the mean (SD) PSAID-12 level (4.2±1.8, 3.5±0.8, 3.1±1.2, 2.9±1.1, 2.2±1.3). The reduction in ASDAS, BASDAI and PSAID-12 was most evident in patients on biologic treatments. In patients with an ASDAS of < 1.3 and PSAID-12 < 2, appointments were moved from routine 6 monthly to 12 monthly. In this group of patients, the appointments were also switched from face to face to video consultation. This resulted in a saving of 250 hours of clinical time. Over 90% of clinician and patient user rated the ePRO application as good or very good.

Conclusion: For this cohort of SpA patients, a trend based on questionnaire scores collated over a period was more informative, particularly when considered alongside interventions that were introduced into the clinics such as physiotherapy, psychological therapy and biologic treatment. In addition, by facilitating timely and effective use of ePROs, clinic workload has reduced allowing time for 'flare' slots and virtual clinics as well as the opportunity to stratify patients according to their disease activity e.g. mild/ moderate/severe. The system allows clinical encounters where needed, and more individualised treatment by identifying the patient perceptions of disease impact.

Disclosure: A. Chan, None; **K. Rigler**, None; **L. van Rossen**, None.

Abstract Number: 1789

Prediction of Psoriatic Arthritis in Patients with Psoriasis Using DNA Methylation Profiles

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) poses an immense clinical burden with significantly increased morbidity and mortality risk compared to psoriasis alone. PsA may develop in 30% of psoriasis patients, however, a large proportion of individuals with PsA remain undiagnosed due to several factors, including a lack of patient and clinical awareness, and a lack of means of predicting which psoriasis patients will develop PsA.

Regulation of gene expression through DNA methylation can be altered by stochastic events or environmental factors and can potentially trigger and maintain PsA pathophysiological processes. With this research, we hope to identify DNA methylation changes that can predict which psoriasis patients will develop PsA at an early stage of the disease, helping prevent permanent joint damage and disability.

Methods: We obtained blood samples from 60 psoriasis patients that developed arthritis (converters) and 60 psoriasis patients that did not (biologic naive, matched for age, sex, psoriasis duration, and duration of follow up). Genome-wide DNA methylation was assessed using Infinium Methylation EPIC BeadChips (Illumina, San Diego, CA, USA). Array data preprocessing, normalization, and correction for technical sources of variation were performed in the R programming environment as recommended in the ChAMP package pipeline. Methylation differences between converters and non-converters were identified by a multivariate linear regression model including clinical covariates (age, sex, BMI, smoking) and conversion status using the Limma package.

The predictive performance of methylation markers was assessed by developing machine learning classification models. Support vector machine models were trained using 75% of samples, keeping the other 25% as an independent set for evaluating the prediction of conversion or non-conversion. Prediction performance of differentially methylated markers was compared to that achieved by an unbiased model trained on the complete set of methylation markers.

Results: We identified 36 significantly differentially methylated positions (with FDR-adjusted p-values lower than 0.05 and a minimum change in methylation of 0.05). This set of 36 highly relevant methylation markers were found across 15 genes and several intergenic regions. Enrichment analysis of the 15 genes with highly relevant methylation markers showed no significantly enriched functional pathways.

The support vector machine classification model for the set of 36 significantly methylated markers achieved an accuracy of 93%, outperforming an unbiased classification model based on the complete set of methylation markers that showed 90% accuracy.

Conclusion: We identified a set of 36 highly significant methylation markers associated with the development of PsA in psoriasis patients. This work shows that DNA methylation patterns at an early stage of psoriatic disease can distinguish between psoriasis patients that will develop PsA from those that will not.

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Abstract Number: 1790

Regional Differences in Clinical Characteristics and Treatment of Psoriatic Arthritis with Axial Involvement: Results from the Cross Sectional International ASAS PerSpA Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) shares genetic and clinical features with other forms of spondyloarthritis (SpA). However, no studies have evaluated regional differences regarding characteristics of PsA with axial involvement (axPsA). The aim of this study is to evaluate regional differences regarding clinical characteristics of axPsA patients.

Table 1. Prevalence of axial involvement among psoriatic arthritis across regions all over the world.

	Europe and North America	Latin America	Japan	Asia except for Japan	Middle East and North Africa
Total SpA patients (n)	1677	538	197	778	1275
PsA among total SpA patients (n, %)	489 (29.2)	176 (32.7)	90 (45.7)	75 (9.6)	203 (15.9)
Axial involvement among PsA (n, %)	164 (33.5)	56 (31.8)	37 (41.1)	32 (42.7)	78 (38.4)

Methods: Data from the ASAS-PerSpA study, a cross-sectional database recruiting SpA patients between July 2018 and February 2020 from 68 centers worldwide, was analyzed. For this analysis, PsA patients presenting at any time with axial involvement per physician judgement were defined as axPsA. AxPsA was further categorized by 5 regions (Europe and North America, Latin America, Japan, Asia (except for Japan) and Middle East and North Africa). Patient and disease characteristics, activities, and treatments were compared.

Table 2. Characteristics of patients who have psoriatic arthritis with axial involvement across regions.

	Europe and North America n=164	Latin America n=56	Japan n=37	Asia except for Japan n=32	Middle East and North Africa n=78	p-value
Sex (male)	83 (50.6)	32 (57.1)	24 (64.9)	24 (75.0)	33 (42.3)	0.013
Age	51.5 (12.7)	51.5 (12.0)	52.1 (13.6)	42.8 (12.6)	47.2 (11.6)	0.488
High level of education	43 (26.2)	18 (32.1)	14 (41.2)	17 (53.1)	21 (26.9)	0.034
Smoking habit (ever)	89 (54.3)	28 (50.0)	23 (62.2)	14 (43.8)	27 (34.6)	0.024
Alcohol (ever)	87 (53.0)	26 (46.4)	26 (70.3)	14 (43.8)	10 (12.8)	<0.001
HLA B27 positive	23/77 (29.9)	9/41 (22.0)	1/14 (7.1)	9/17 (52.9)	12/33 (36.4)	0.046
Family history of SpA (first or second degree relatives of SpA)	61 (37.2)	20 (35.7)	13 (35.1)	15 (15.5)	26 (33.3)	0.757
Disease duration	16.8 (12.1)	22.1 (12.5)	16.1 (13.0)	12.8 (10.7)	17.1 (12.3)	0.010
Diagnosis delay, years	7.8 (11.1)	11.9 (11.6)	12.4 (13.0)	7.90 (9.1)	10.3 (11.2)	0.046
Inflammatory back pain, n/N (%)	145 (88.4)	46 (82.1)	34 (91.9)	24 (75.0)	68 (87.2)	0.135
Peripheral arthritis	140 (85.4)	51 (91.9)	30 (81.1)	32 (100)	65 (83.3)	0.097
Radiographic sacroiliitis, mNY criteria, n/N (%)	71/142 (50.0)	31/53 (58.5)	23/37 (62.2)	13/24 (54.2)	47/72 (65.3)	0.256
Positive MRI-SIJ according to ASAS definition, n/N (%)	51/100 (51.0)	23/39 (58.0)	21/30 (70.0)	6/11 (54.6)	40/45 (88.9)	<0.001
ASAS criteria	62 (37.8)	28 (50.0)	25 (67.6)	16 (50.0)	54 (69.2)	<0.001
ASAS clinical arm only	19 (11.6)	8 (14.3)	1 (2.7)	8 (25.0)	12 (15.4)	0.082
ASAS imaging arm only	56 (34.1)	25 (44.6)	25 (67.6)	13 (40.6)	53 (67.9)	<0.001
CASPAR criteria	106 (64.6)	48 (85.7)	35 (94.6)	25 (78.1)	60 (76.9)	<0.001
PGA (0-10)	4.7 (3.0)	5.4 (3.0)	3.7 (2.4)	5.1 (3.0)	5.7 (2.6)	0.007
BASDAI (0-100)	4.6 (2.4)	5.4 (2.8)	3.5 (2.4)	4.8 (3.0)	4.8 (2.3)	0.009
BASFI (0-100)	3.1 (2.6)	3.8 (3.0)	1.6 (2.3)	2.2 (2.4)	3.2 (2.6)	<0.001
ASDAS-CRP	2.5 (1.0)	3.2 (1.2)	2.2 (1.0)	3.2 (1.5)	2.9 (1.0)	<0.001
ASAS HI (0-17)	7.9 (4.5)	8.8 (4.9)	7.1 (4.9)	9.5 (5.3)	8.2 (4.9)	0.206
Current steroid intake	0.9 (2.1)	2.1 (3.9)	0.3 (1.6)	3.2 (5.3)	1.1 (2.5)	<0.001
csDMARD (ever)	153 (93.3)	55 (98.2)	29 (78.4)	32 (100)	70 (89.7)	0.002
bDMARD (ever)	134 (81.7)	34 (60.7)	21 (27.4)	20 (62.5)	54 (69.2)	0.002
Specific drug for axial involvement						
NSAIDs	149 (90.9)	51 (91.1)	35 (94.6)	29 (90.6)	53 (67.9)	0.142
csDMARD	100 (61.0)	23 (41.1)	23 (62.2)	10 (31.3)	31 (39.7)	0.011
bDMARD	98 (59.8)	24 (42.9)	19 (51.4)	6 (18.8)	33 (42.3)	0.001

Values are expressed as n (%) or the mean ± standard deviation unless otherwise indicated.

Results: Of 4465 SpA patients from the study, 1033 (23.1%) had psoriatic arthritis (PsA). 367 AxPsA patients (35.5% of those with PsA) were compared by region. Percentage of axPsA patients among PsA by region were as follows: 164/489 (34%) from Europe and North America; 56/176 (32%) from Latin American; 37/90 (41%) from Japan; 32/75 (43%) from other Asian countries; and 78/203 (38%) from Middle East and North Africa (Table 1). At 12.4 years (SD 13.0), diagnostic delay in Japan was longer than those in other parts of the world (Table 2). Patients in Europe and North America had less AxSpA, with only 38% fulfilling ASAS AxSpA criteria. Disease activity was lower in Japan with mean ASDAS-CRP score of 2.2 (SD 1.0), despite less frequency of csDMARD (78%) and bDMARD (27%) use. In patients treated specifically for axial involvement, however, AxPsA patients in Japan demonstrated more frequent csDMARD (62%) and bDMARD (51%) use. Both Latin America and Asia showed higher disease activity with mean ASDAS-CRP of 3.2 (SDv1.2) and 3.2 (SD 1.5), respectively; both regions demonstrated less bDMARD use (43% and 19%, respectively) as a specific treatment for axial involvement.

Conclusion: This study suggests axPsA patients demonstrate differing disease manifestations, activities, and treatments by region.

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Abstract Number: 1791

Psoriasis Onset Before Rheumatic Symptoms in Patients with Spondyloarthritis: Does It Relate to Clinical Characteristics and the Rheumatologist's Diagnosis? Data from REGISPONSER Registry

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: To describe if the time of the onset of psoriasis (Pso) relative to the appearance of rheumatic symptoms in patients with spondyloarhtritis (SpA) is associated with a clinical phenotype, the rheumatologist's diagnosis and the evolution of the disease.

Methods: This was a cross-sectional study with data extracted from the REGISPONSER (Spondyloarhritis Registry of the Spanish Rheumatology Society) registry. Patients were classified in two groups to compare the clinical characteristics, disease activity, radiographic damage, functional ability and received treatment: "Pso as first symptom" and "Pso after rheumatic symptoms". Moreover, the rheumatologist's diagnosis was compared between the two groups. We use chi-square test and Student t-test to compare qualitative and quantitative variables in both groups, respectively. Multivariate analysis was performed in variables with significant differences.

Results: A total of 433/2367 (18.3%) patients included in the REGISPONSER database had Pso onset data available. Patients with Pso as first symptom had less body mass index [0.90 (95% CI 0.83 - 0.96)], shorter disease duration [0.94 (95% CI 0.91 – 0.97)], less prevalence of HLA-B27 antigen [0.22 (95% CI 0.11 – 0.44)] and higher prevalence of dactylitis [2.12 (95% CI 1.01 – 4.46)] with regard to patients with Pso after rheumatic symptoms. Furthermore, a higher prevalence of Psoriatic Arthritis (PsA) diagnosis [257/329 (78.1%) vs 57/101 (56.4%); p< 0.001)] and a lower prevalence of ankylosing spondylitis (AS) diagnosis [68/329 (20.7%) vs 38/101 (37.6%); p< 0.001] were found in patients with Pso as first symptom vs. Pso after rheumatic symptoms. Indeed, axial involvement was less frequent in patients with Pso as first symptom [29/330 (8.8%) vs 20/103 (19.4%); p=0.003], while peripheral involvement was more frequent [192/330 (58.2%) vs 39/103 (37.9%; p< 0.001]. The use of DMARDs was not statistically different between the two groups.

Conclusion: The moment of appearance of psoriasis influences significantly the clinical phenotypic of spondyloarthritis. Thus, the presence of psoriasis before the rheumatic symptoms could determine a more frequent diagnosis of PsA by Rheumatologist.

Disclosure: I. Gomez-Garcia, None; **T. García-Puga**, None; **N. Barbarroja**, None; **M. Puche Larrubia**, None; **P. Font**, None; **C. López Medina**, None.

Abstract Number: 1792

Participation in Psoriatic Arthritis (PART2) – a Cross-sectional Study of Work Impairment in Psoriatic Arthritis Patients in the Netherlands

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) can lead to pain, disability and a loss of quality of life [Rosen, Rheumatology 2012]. PsA can also lead to impairments in work and social activities, increasing societal costs. The magnitude and determinants of these impairments in Dutch PsA patients is insufficiently researched.

Methods: This cross-sectional study used sociodemographic and clinical data collected from the electronic patient files of PsA patients treated at the department of rheumatology of the Sint Maartenskliniek, Netherlands. All patients were treated according to Psoriatic Arthritis Disease Activity Score (PASDAS) driven treat-to-target, as described previously [Mulder, Rheumatology 2020]. Data about work and activity impairment were collected via the Work Productivity and Activity Impairment (WPAI) questionnaire. To compare our PsA-cohort with the Dutch general population (GP), we used age- and sex-matched data derived from the Central Bureau of Statistics. Regression analyses were performed to examine determinants of impairment.

Results: 246 patients were included in this study, of which 125 (48.8%) were male. Mean age was 55.7 years (SD=13.2). Over half of the patients had a paid job (work-for-pay, WFP, 53%). Compared to the age-and sex-matched Dutch GP, less patients with PsA had a paid job (Dutch GP 63% vs. PsA cohort 53%, $p < 0.001$). A lower age and a better physical function (Health Assessment Questionnaire-Disability Index (HAQ-DI)) were associated with WFP-status. Overall work impairment of those with a paid job was 10% (interquartile range, 10-40%). In this subgroup, higher disease activity score (PASDAS), worse physical function (HAQ-DI) and worse mental health-related quality of life (Mental Component Summary score – MCS-12) were associated with more work impairment ($p< =0.05$). Notably, age, sex and treatment modality were not associated with work impairment.

Conclusion: Our study indicates that Dutch patients with PsA were less likely to have a paid job compared to the Dutch general population. When working, they suffered an average productivity loss of 10%. Physical function seems to be a shared factor in the risk for work impairment as well as the risk for not having a paid job. Lower disease activity as measured by PASDAS seems to protect against work impairment, regardless of treatment modality. We suggest that by maintaining adequate disease control, patients can be protected from work impairment and future inability to work or loss of job.

Disclosure: T. van Hal, Novartis, 6, UCB, 6, 12, paid congress visit, Eli Lily, 6; **M. Mulder**, None; **M. Wenink**, None; **J. Vriezekolk**, None.

Abstract Number: 1793

Impact of Gender and Age on Psoriatic Arthritis Patient Profiles at Golimumab Initiation and 12-Month Outcomes

Arthur Karasik[1], Isabelle Fortin[2], Proton Rahman[3], Regan Arendse[4], Emmanouil Rampakakis[5], Odalis Asin-Milan[6], Allen Lehman[6], Francois Nantel[7] and Meagan Rachich[6], [1]Arthur Karasik Medicine Professional Corporation, Toronto, ON, Canada, [2]CREQ, Rimouski, QC, Canada, [3]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [4]University of Saskatchewan, Saskatoon, SK, Canada, [5]JSS Medical Research, Montréal, QC, Canada, [6]Janssen Inc., Toronto, ON, Canada, [7]., Montréal, QC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Gender and age have been previously identified as independent predictors of response to anti-TNFs. The aim of this analysis was to compare, between genders and age groups, the profile and outcomes of psoriatic arthritis (PsA) patients treated with golimumab during routine Canadian care.

Methods: This is a post-hoc analysis of data from the Biologic Treatment Registry Across Canada (BioTRAC). Patients with PsA who initiated treatment with subcutaneous golimumab were included. Patients were grouped into age tertiles: Young: 19.7–47.0 years; Middle: 47.1–59.3; Old: 59.4–85.4) and further stratified by gender. The impact of age and gender on outcomes and retention were assessed with multivariate logistic and cox regressions, respectively, adjusting for age tertile, gender, and respective outcome at baseline.

Results: 281 patients were included with a mean (SD) age of 52.8 (13.2) years and disease duration of 6.1 (7.7) years. Across age tertiles, significant differences ($p< 0.05$) were observed at baseline in disease duration, weight, employment status, insurance coverage, previous smoking status, previous/concomitant use of oral steroids, HAQ-DI, TJC28, and SJC28. Gender, RF status, anti-CPP status, family history, current smoking status, previous/concomitant use of DMARDs, NSAIDs, or MTX, number of previous DMARDs, experience with biologics, enthesitis, and dactylitis, and PASI were statistically comparable. Between genders, significant differences were observed in weight, employment status, number of previous DMARDs, concomitant NSAIDs, and baseline HAQ-DI, TJC28, and SJC28.

Based on multivariate regression, patients in Young age tertiles (OR [95% CI]: 9.44 [3.88–23.0]) and Middle (2.5 [1.05–5.95]), along with male patients (2.07 [1.03-4.18]), were more likely to achieve MDA-LDA at 6 months. Compared to Old age tertile, achievement of MDA-LDA at 12 months (3.40 [1.36–8.48]), VLDA at 6 (6.69 [2.09–21.4]) and 12 (6.59 [1.92–22.7]) months, and HAQ< 0.5 at 6 (7.68 [3.23–18.3]) and 12 (4.84 [1.98–11.82]) months were more likely among patients in Young age tertile. Male patients were less likely have enthesitis (0.37 [0.15–0.87]) at 6 months and dactylitis at both 6 (0.27 [0.08–0.97]) and 12 (0.17 [0.03–0.88]) months. There was no association between age tertile or gender and PASI75 achievement.

In terms of safety, notable differences were observed across genders and age tertiles in both adverse event incidence and profile. Furthermore, male gender (HR [95%]: 1.66 [1.14-2.44]), but not age tertile, was associated with higher odds of retention.

Conclusion: Significant variations in baseline characteristics, treatment outcomes, and safety profile exist across age groups and gender.

Disclosure: A. Karasik, Janssen Inc., 6, Janssen Inc., 2, 6; **I. Fortin**, Janssen Inc., 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **R. Arendse**, None; **E. Rampakakis**, None; **O. Asin-Milan**, Janssen, 3; **A. Lehman**, Janssen Inc., 3; **F. Nantel**, None; **M. Rachich**, Janssen, 3, 11.

Abstract Number: 1794

Application of Treat to Target and Impact of Sustained Low Disease Activity or Remission on Function in Psoriatic Arthritis Patients

Proton Rahman[1], Regan Arendse[2], Philip Baer[3], Michel Zummer[4], Emmanouil Rampakakis[5], Allen Lehman[6], Meagan Rachich[6], Francois Nantel[7] and Odalis Asin-Milan[6], [1]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [2]University of Saskatchewan, Saskatoon, SK, Canada, [3]Baer Weinberg MPC, Scarborough, ON, Canada, [4]CH Maisonneuve-Rosemont, Montréal, QC, Canada, [5]JSS Medical Research, Montréal, QC, Canada, [6]Janssen Inc., Toronto, ON, Canada, [7]Montréal, QC, Canada

SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous analyses have identified enrolment year as an independent predictor of real-world retention on anti-TNF treatment whereby patients enrolled in later periods were more likely to be switched. The aim of this analysis was to compare between enrolment periods for psoriatic arthritis (PsA) treatment outcomes and frequency of treating to target, and to assess the impact of target type on long-term function.

Methods: This is a post-hoc analysis of data from the Biologic Treatment Registry Across Canada (BioTRAC). Patients were grouped into enrolment periods: 2005-2008, 2009-2012, 2013-2015, 2016-2017. Achievement of MDA (5/7 of: TJC28≤1, SJC28≤1, PASI≤1, pain≤15mm, PtGA≤20mm, HAQ≤0.5, tender entheseal points≤1), VLDA (7/7 criteria), and sustained MDA or VLDA (at 6 and 12 months) were compared between enrolment periods with the Chi-square test. The impact of achieving MDA or VLDA at 6 months, 12 months, or both (sustained) on HAQ-DI at 18 months was assessed with one-way ANOVA and generalized linear models.

Results: 392 PsA patients treated with anti-TNFs (IFX: n=111; GLM: n=281) were included. Across enrolment periods, a significant increase in baseline age (48.5 vs. 50.3 vs. 51.9 vs. 54.8 years; p=0.021) was observed. At 6 and 12 months, 44.2% and 45.6% achieved MDA, 18.4% and 19.9% achieved VLDA, while 36.8% and 13.2% achieved sustained MDA and VLDA, respectively, without significant differences across enrolment periods.

Among patients not achieving LDA at 6 and 12 months, an intervention was applied in 40-45% of patients, without significant differences between enrolment periods. Between 6 and 12 months, the most common intervention was anti-TNF discontinuation (71.2% of non-LDA achievers), followed by DMARD addition (12.1%), DMARD dose increase (7.6%) or NSAID addition (7.6%). Similar results were obtained post 12 months.

Patients achieving sustained MDA, followed by those achieving MDA either at 6 or 12 months had significantly lower HAQ at 18 months compared to patients not achieving MDA at either timepoint (0.2 vs. 0.6 vs. 1.2; p< 0.001). Similar results were observed when evaluating achievement of remission albeit with greater impact on HAQ at 18 months (0.1 vs. 0.2 vs. 0.9; p< 0.001). Adjustment for baseline HAQ did not impact the results.

Conclusion: Target achievement among PsA patients has remained stable over time with relatively infrequent regimen optimization prior to anti-TNF discontinuation. Achieving stricter targets was associated with greater benefits in terms of long-term patient function.

Disclosure: P. Rahman, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **R. Arendse**, None; **P. Baer**, Janssen, 2, 5, 6, Abbvie, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, Amgen, 2, 6, Teva, 2, Innomar, 2, McKesson, 2, Novartis, 2, 6, Fresenius Kabi, 2, 6, Gilead, 2, Merck, 2, Mylan, 2, Celltrion, 2; **M. Zummer**, Janssen Inc., 6; **E. Rampakakis**, None; **A. Lehman**, Janssen Inc., 3; **M. Rachich**, Janssen, 3, 11; **F. Nantel**, None; **O. Asin-Milan**, Janssen, 3.

Abstract Number: 1795

Validation of the Disease Activity Index for Psoriatic Arthritis (DAPSA) with a Quick QuantitativeC-reactive Protein Assay (Q-DAPSA) in Patients with Psoriatic Arthritis (PsA): A Prospective,national, Multicenter Study

Fabian Proft[1], Julia Schally[2], Henning Christian Brandt[3], Jan Brandt-Jrgens[4], Gerd Burmester[1], Hildrun Haibel[5], Henriette Käding[2], Kirsten Karberg[6], Susanne Lüders[7], Burkhard Muche[2], Mikhail Protopopov[1], Judith Rademacher[1], Valeria Rios Rodriguez[1], Murat Torgutalp[1], Maryna Verba[8] and Silke Zinke[9], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Berlin, Germany, [3]Praxis für Rheumatologie und Innere Medizin, Berlin, Germany, [4]Rheumatologische Schwerpunktpraxis, Berlin, Germany, [5]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, [6]Praxis für Rheumatologie und Innere Medizin, Berlin, Germany, Berlin, Germany, [7]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, Berlin, Germany, [8]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Berlin, Germany, [9]Rheumapraxis Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Disease activity categories by Q-DAPSA vs. DAPSA

		Q-DAPSA (n = 104)			
		Remission (≤ 4)	Low Disease Activity (> 4 and ≤ 14)	High Disease Activity (> 14 and ≤ 28)	Very high Disease Activity (> 28)
DAPSA	Remission (≤ 4)	36 (34.6%)	1 (1.0%)		
	Low Disease Activity (> 4 and ≤ 14)		39 (37.5%)		
	High Disease Activity (> 14 and ≤ 28)			22 (21.2%)	
	Very high Disease Activity (> 28)				6 (5.8%)

The fields highlighted in red indicate that disease activity categories do not match.
DAPSA = Disease activity index for Psoriatic Arthritis, Q-DAPSA = DAPSA calculated based on a quick quantitative CRP

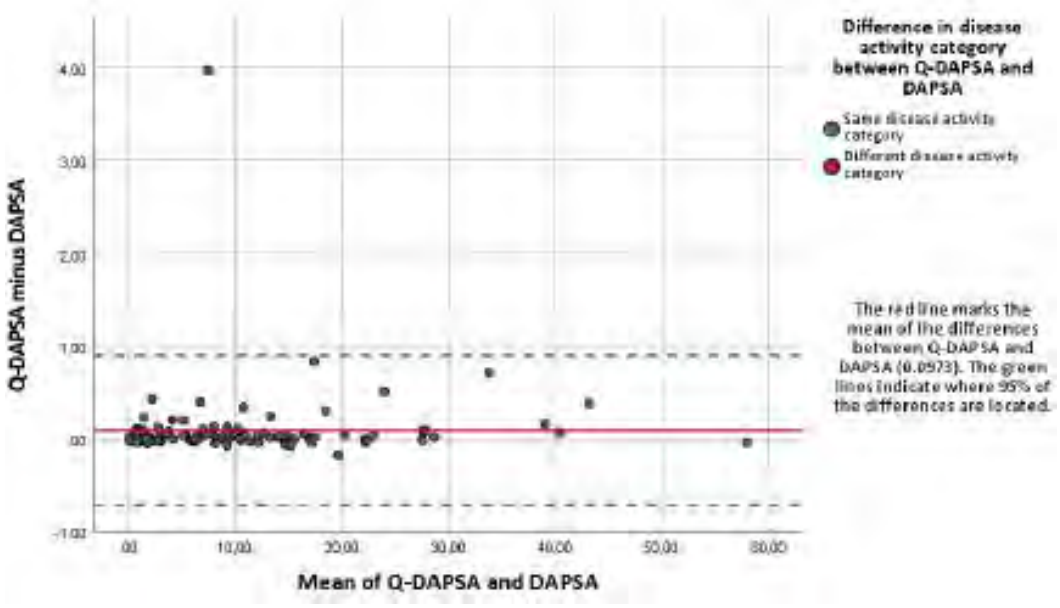

Figure 1. Bland-Altman plot for Q-DAPSA and DAPSA.

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease with multiple musculoskeletal and dermatological manifestations. Due to this multifaceted clinical appearance, international guidelines do not provide a clear recommendation for one specific score to assess disease activity in PsA [1]. The Disease Activity Index for Psoriatic Arthritis (DAPSA), a validated, unidimensional score focusing on joint involvement, is one of the recommended options [1]. However, routine determination of C-reactive protein (CRP) to calculate DAPSA values takes hours to days. In contrast, quick quantitative CRP (qCRP) tests require only a few minutes and might facilitate regular assessment of the DAPSA (as Q-DAPSA) in clinical routine.

The objective of our study was to validate the Q-DAPSA in a prospective, multicenter study of PsA patients. Since the Disease Activity Score 28 (DAS28) is not only used in rheumatoid arthritis, but also in PsA patients, the study also investigated the performance of a qCRP based DAS28 (DAS28-qCRP) in a PsA cohort.

Methods: The study was conducted in five centers in Berlin, Germany. Consecutive adult (≥ 18 years) PsA patients were included. In addition to a rheumatological assessment, including patient reported outcomes (PROs), routine CRP and erythrocyte sedimentation rate (ESR) were measured in the local labs. Additionally, a qCRP testing with the „QuikRead go instrument“ (Aidian Oy, Finland) was performed locally at the study center (measurement range 0.5 - 200 mg/l for hematocrit concentrations of 40 – 45%). Statistical analysis included descriptive statistics, cross tabulation and weighted Cohen´s kappa comparing disease activity categories, Bland-Altman plots and intraclass correlation coefficient (ICC) for DAPSA, Q-DAPSA, DAS28- CRP and DAS28-qCRP.

Results: In this study 104 patients were included between January and October 2020 (mean age: 51.2 years, mean disease duration: 7.1 years, 49 patients (47.1%) were male). 53 patients (51.0%) were treated with a bDMARD and 37 patients (35.6%) with csDMARDs. CRP and qCRP showed mean values of 5.20 and 6.17 mg/l, respectively. With the Q-DAPSA, 103 patients (99.0%) were assigned to the same disease activity category when compared to DAPSA (Table 1). Weighted Cohen´s kappa was 0.990 (95%CI 0.970; 1.000). ICC for numerical values of DAPSA and Q-DAPSA was 1.000 (95%CI 0.999; 1.000). The agreement of Q-DAPSA and DAPSA is shown in a Bland-Altman plot (Figure 1). DAS28-CRP and - qCRP were available for 103 patients; 101 patients (98.1%) showed the same disease activity category in the DAS28-qCRP and weighted Cohen´s kappa was 0.951 (95%CI 0.886; 1.000).

Conclusion: The Q-DAPSA and DAPSA showed an almost perfect agreement on the assignment to disease activity categories (99%) with the important advantage of time. With Q-DAPSA, rheumatologists could base their clinical decision-making on a disease activity measurement by using a composite score immediately. Consequently, Q-DAPSA can be integrated in clinical routine and clinical trials and could be implemented into the treat-to-target concept in PsA patients. For rheumatologists who prefer DAS28-CRP for assessing disease activity in PsA patients, DAS28-qCRP may serve as a suitable alternative.

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Abstract Number: 1796

Early Identification of Psoriatic Arthritis with Axial Involvement Among Patients with Psoriasis: A Prospective Multicenter Study

Fabian Proft[1], Susanne Lüders[2], Theresa Hunter[3], Gustavo Luna[4], Valeria Rios Rodriguez[1], Mikhail Protopopov[1], Katharina Meier[5], Georgios Kokolakis[5], Kamran Ghoreschi[5] and Denis Poddubnyy[6], [1]Charité University Medicine Berlin, Berlin, Germany, [2]Department of Gastroenterology, Infectiology and Rheumatology (including Nutrition Medicine), Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, Berlin, Germany, [3]Eli Lilly and Company, Indianapolis, IN, USA, Indianapolis, IN, [4]ICON plc, Stockholm, Sweden, [5]Department of Dermatology, Venereology and Allergology – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin and Humboldt-Universität zu Berlin, Berlin, Germany, Berlin, Germany, [6]Department of Rheumatology, Charité – Universitätsmedizin, Berlin, Germany

SESSION INFORMATION

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Session Time: 8:30AM–10:30AM

Background/Purpose: In the absence of reliable serological and/or imaging biomarkers for early psoriatic arthritis (PsA) and an existing diagnostic delay there is a need for screening tools for detection of early PsA. While different validated screening/referral tools focusing on peripheral manifestations of PsA exist[1], validated referral algorithms for PsA with axial involvement (axPsA) are missing. In this prospective, multicenter study we applied a dermatologist-centered screening tool to identify signs of axial involvement among patients with psoriasis (PsO) attending dermatology clinics.

Methods: Consecutive patients with PsO were screened by their dermatologist for eligibility for referral to a specialized rheumatology clinic. Eligible patients were ≥ 18 years with a confirmed diagnosis of PsO who reported having chronic back pain (≥ 3 months) with onset prior to 45 years of age and who had not been treated with any biologic or targeted synthetic DMARD in the 12 weeks prior to screening. For those patients who qualified for referral and attended the rheumatology clinic, a rheumatologic investigation including clinical, laboratory and genetic assessments as well as imaging with conventional radiography and MRI of sacroiliac joints and spine was performed. The primary outcome of the study was the proportion of patients diagnosed with axPsA among all referred PsO patients.

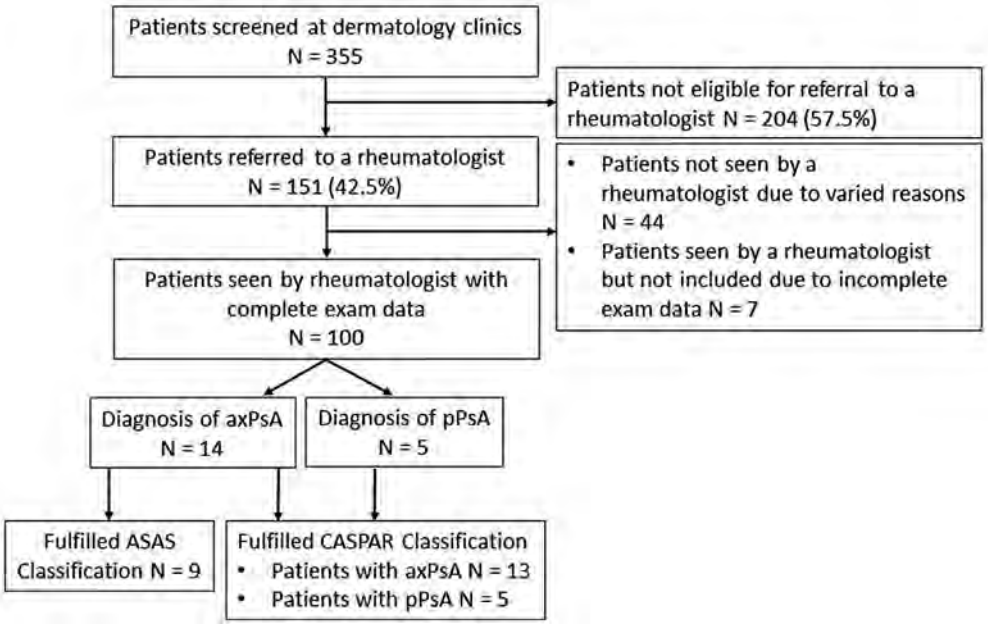
Table 1: Demographic and clinical characteristics of PsO patients with pPsA, axPsA and patients not diagnosed with PsA

Patient characteristics	Patients seen at rheumatology (N=100)	pPsA (N=5)	axPsA (N=14)	No PsA (N=81)	p-value[1]
Age (years) – Mean (SD)	45.6 (13.0)	42.6 (9.0)	46.2 (13.6)	45.7 (13.3)	0.883
Female – n (%)	56 (56.0)	2 (40.0)	9 (64.3)	45 (55.6)	0.543
BMI (kg/m2) – Mean (SD)	27.4 (5.5)	23.6 (1.2)	27.8 (6.6)	27.5 (5.4)	0.933
Positive family history of SpA – n (%)	48 (48.0)	3 (60.0)	7 (50.0)	39 (48.1)	0.511
Psoriasis, current – n (%)	100 (100.0)	5 (100.0)	14 (100.0)	81 (100.0)	
Psoriasis, duration (years) – Mean (SD)	19.2 (16.0)	16.6 (19.4)	13.6 (9.2)	20.3 (16.7)	0.291
PASI – Mean (SD)	4.0 (4.4)	3.3 (2.1)	4.3 (4.9)	4.0 (4.5)	0.971
Inflammatory back pain – n (%)	49 (49.0)	5 (100.0)	8 (57.1)	36 (44.4)	0.379
Duration of back pain (years) – Mean (SD)	17.3 (14.6)	10.8 (11.7)	12.2 (15.2)	18.8 (14.6)	0.058
HLA-B27 positive – n (%)	16 (16.0)	0	4 (28.6)	12 (14.8)	0.204
CRP (mg/L) – Mean (SD)	3.5 (6.1)	8.0 (15.4)	8.0 (10.8)	2.5 (3.1)	0.039
Elevated CRP (>5 mg/L) – n (%)	17 (17.0)	1 (20.0)	5 (35.7)	11 (13.6)	0.041
Peripheral arthritis, current – n (%)	11 (11.0)	5 (100.0)	3 (21.4)	3 (3.7)	0.012
Enthesitis, current – n (%)	8 (8.0)	0	0	8 (9.9)	0.219
Dactylitis, current – n (%)	1 (1.0)	0	1 (7.1)	0	0.016
Uveitis, ever – n (%)	1 (1.0)	1 (20.0)	0	0	
Sacroiliitis as per mNY criteria – n (%)	5 (5.0)	0	4 (28.6)	1 (1.2)	<0.001
Sacroiliitis >=grade 2 unilaterally – n (%)	9 (9.0)	0	5 (35.7)	4 (4.9)	<0.001
Active inflammation, sacroiliac joint (MRI) – n (%)	8 (8.0)	0	8 (57.1)	0	<0.001
Structural (post)inflammatory changes, sacroiliac joint (MRI) – n (%)	8 (8.0)	0	8 (57.1)	0	<0.001
Active inflammation, spine (MRI) – n (%)	13 (13.0)	0	13 (92.9)	0	<0.001
Structural (post)inflammatory changes, spine (MRI) – n (%)	8 (8.0)	0	8 (57.1)	0	<0.001
ASDAS (0-10) – Mean (SD)	2.4 (0.8)	3.1 (1.2)	2.9 (0.8)	2.3 (0.7)	0.017
BASDAI (0-10) – Mean (SD)	4.4 (1.7)	5.6 (2.1)	4.8 (1.5)	4.2 (1.7)	0.239
DAPSA – Mean (SD)	12.7 (9.5)	23.2 (14.2)	17.5 (14.3)	11.2 (7.4)	0.112
NSAIDs use, current – n (%)	42 (42.0)	3 (60.0)	8 (57.1)	31 (38.3)	0.185
Analgesics (non-opioid)	10 (10.0)	0	2 (14.3)	8 (9.9)	0.620
Analgesics (opioid)	5 (5.0)	0	2 (14.3)	3 (3.7)	0.102
Systemic psoriasis therapy – n (%)					
Methotrexate	11 (11.0)	0	2 (14.3)	9 (11.1)	0.732
Systemic retinoids	2 (2.0)	0	1 (7.1)	1 (1.2)	0.155
Phosphodiesterase inhibitor	1 (1.0)	0	1 (7.1)	0	0.016
Systemic glucocorticoids	1 (1.0)	0	1 (7.1)	0	0.016
Other therapies	3 (3.0)	1 (20.0)	0	2 (2.5)	0.552
Topical psoriasis therapy – n (%)					
Topical steroids	78 (78.0)	5 (100.0)	12 (85.7)	61 (75.3)	0.394
Vitamin D analogues	52 (52.0)	1 (20.0)	4 (28.6)	47 (58.0)	0.041
Topical retinoids	1 (1.0)	0	0	1 (1.2)	0.676
Calcineurin inhibitors	1 (1.0)	0	0	1 (1.2)	0.676
UVB therapy	1 (1.0)	0	0	1 (1.2)	0.676

Abbreviation: ASDAS=ankylosing spondylitis disease activity, axPsA=axial psoriatic arthritis, BASDAI=Bath ankylosing spondylitis disease activity index, BMI=body mass index, CRP=C-reactive protein, DAPSA=disease activity in psoriatic arthritis, HLA-B27=human leucocyte antigen B27, MRI= magnetic resonance imaging, N=number, NSAIDs=non-steroidal anti-inflammatory drugs, PASI=psoriasis area and severity index, pPsA=peripheral psoriatic arthritis, SD=standard deviation, SpA=spondyloarthritis, UVB=ultraviolet B.
[1]Statistically significant differences between the axPsA and no PsA groups of patients were determined by using Mann–Whitney U test for continuous data and Chi-square test for categorical data.

Results: In total 355 patients were screened at 14 dermatology sites, of whom 151 (42.5%) qualified for referral to rheumatology clinic. Rheumatologists ultimately examined 100 (28.2%) patients (Figure 1). The diagnosis of axPsA was confirmed in 14 patients (14%) (3/14 with both, axial and peripheral involvement) and the diagnosis of peripheral PsA (pPsA) without axial involvement was made in five patients (5%). 81 (81%) patients were diagnosed with neither pPsA nor axPsA. Clinical, lab and imaging characteristics of the study population, as well as subgroups with and without axial involvement, are presented in Table 1. All patients diagnosed with axPsA had active inflammatory and/or structural (post) inflammatory changes in the sacroiliac joints and/or spine on imaging. In five (35.7%) patients, MRI changes indicative of axial involvement were found only in the spine. The Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA were fulfilled in nine (64.3%) of the patients diagnosed

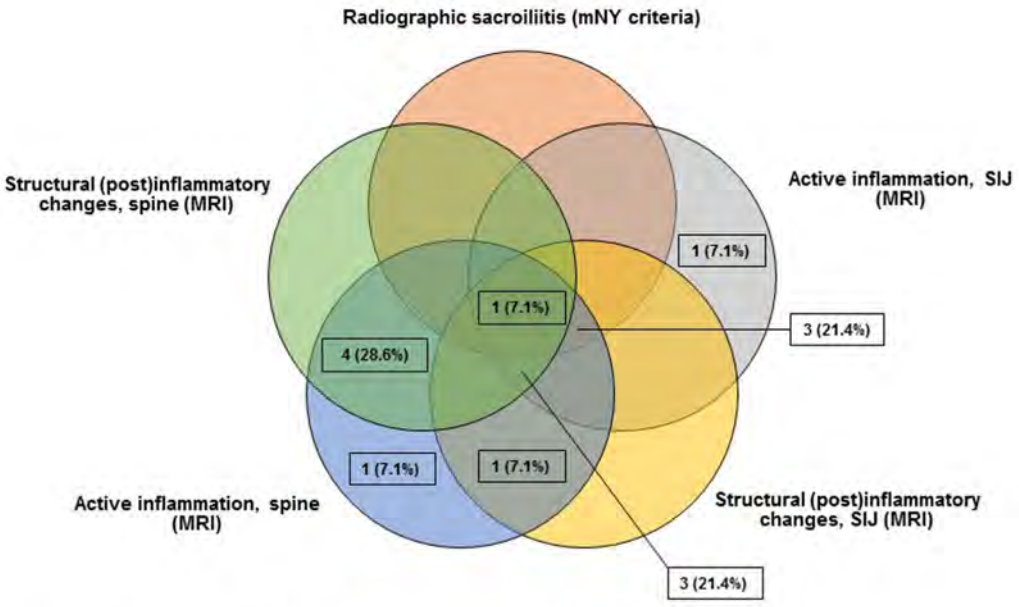
Figure 1: Patient disposition, total number of patients screened, referred and seen by a rheumatologist



with axPsA. All but one patient diagnosed with PsA (13/14 with axPsA and 5/5 with pPsA) fulfilled the Classification Criteria for Psoriatic Arthritis (CASPAR) for PsA as illustrated in Figure 1.

Conclusion: Our study revealed that applying a dermatologist-centered screening tool is useful for the detection of axPsA and pPsA in PsO patients at-risk. These results provide valuable real-world insights into the possibility of

Figure 2: Imaging features of axial involvement in PsO patients diagnosed with axPsA



Abbreviation: MRI=magnetic resonance imaging, SIJ=sacroiliac joint, mNY=modified New York

diagnosing axPsA and pPsA early with the ultimate goal of improving the care and quality of life of patients living with the disease.

Mishra S et al. BR J Dermatol. 2017;176(3):765-770.

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Abstract Number: 1797

Are Smoking and Alcohol Associated with Peripheral Musculoskeletal Involvement in Patients with Spondyloarthritis? Results from the ASAS-PerSpA Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

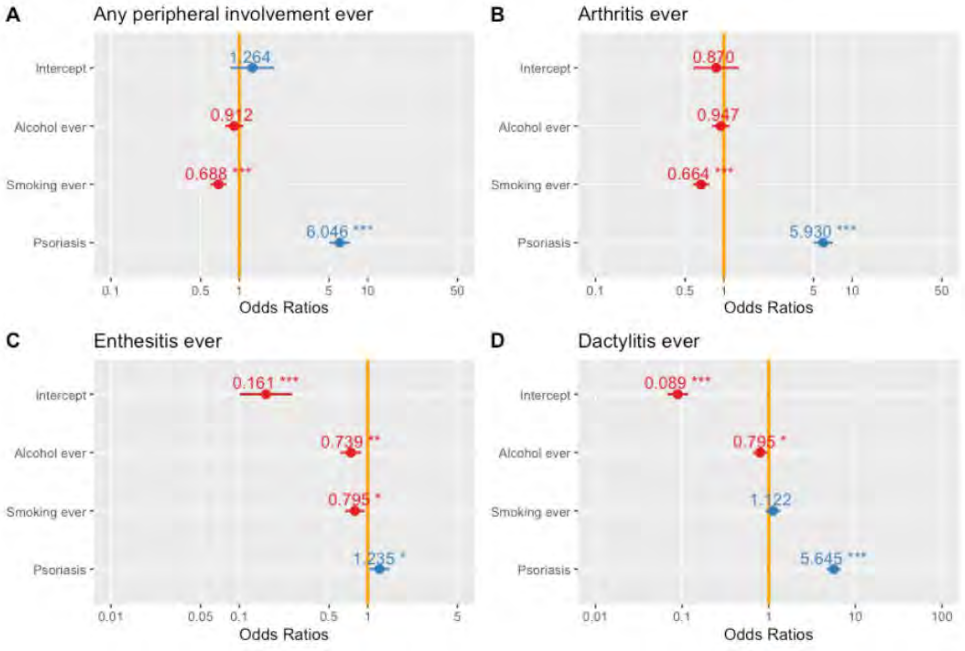
Session Time: 8:30AM–10:30AM

Background/Purpose: There are controversies around the role of smoking in manifestations of axial spondyloarthritis (axSpA) such as peripheral involvement. It has been observed an inverse association between alcohol consumption and disease activity and functional impairment, although it is still unclear its association with peripheral manifestations of SpA. Objectives: 1) To evaluate the association between smoking/alcohol intake and the prevalence of peripheral articular manifestations (i.e., arthritis, enthesitis or dactylitis); 2) to assess the association between smoking/alcohol intake and the specific location of such manifestations.

Table 1. Association between peripheral musculoskeletal manifestations and smoking and alcohol

Any peripheral manifestation ever				
	Yes = 2601	No = 1860	OR (95%CI) univariate	p-value
Alcohol ever	1057 (40.6%)	754 (40.5%)	1.00 (0.89 – 1.13)	0.945
Smoking ever	1034 (39.8%)	866 (46.6%)	0.76 (0.67 – 0.85)	<0.001
Psoriasis	1023 (39.4%)	187 (10.1%)	5.80 (4.91 – 6.90)	<0.001
Arthritis ever				
	Yes = 2292	No = 2169	OR (95%CI) univariate	p-value
Alcohol ever	929 (40.4%)	882 (40.7%)	0.99 (0.98 – 1.14)	0.929
Smoking ever	887 (38.7%)	1013 (46.7%)	0.72 (0.64 – 0.81)	<0.001
Psoriasis	949 (41.4%)	261 (12.0%)	5.17 (4.44 – 6.03)	<0.001
Enthesitis ever				
	Yes = 765	No = 3696	OR (95%CI) univariate	p-value
Alcohol ever	276 (36.1%)	1535 (41.5%)	0.79 (0.68 – 0.93)	0.005
Smoking ever	312 (40.8%)	1588 (43.0%)	0.91 (0.78 – 1.07)	0.267
Psoriasis	279 (36.5%)	931/3695 (25.2%)	1.70 (1.44 – 2.01)	<0.001
Dactylitis ever				
	Yes = 685	No = 3776	OR (95%CI) univariate	p-value
Alcohol ever	299 (43.6%)	1512 (40.0%)	1.16 (0.98 – 1.37)	0.077
Smoking ever	277 (40.4%)	1623 (43.0%)	0.90 (0.76 – 1.06)	0.216
Psoriasis	414 (60.4%)	796 (21.1%)	5.72 (4.82 – 6.80)	<0.001

Figure 1. Association between peripheral musculoskeletal manifestations and both alcohol and smoking, adjusting for the presence of psoriasis (multivariate analysis).



Methods: Patients from the cross-sectional ASAS-PerSpA study with available data for both the smoking status and alcohol intake were included. Mixed logistic regressions using the peripheral manifestation (or the location) as a dependent variable, the smoking status or alcohol intake and the presence of psoriasis as fixed effect and the country as random effect were used. The interaction between smoking and alcohol was tested.

Results: A total of 4451 patients with either axSpA, peripheral SpA or Psoriatic Arthritis were included in the analysis. 59.5% had smoked at any moment and 42.7% had been alcohol drinkers. Patients who have ever suffered arthritis showed a lower frequency of smoking habit (OR 0.72, 95%CI 0.63-0.82) and a lower alcohol consumption(OR 0.82, 95%CI 0.71-0.94) (table 1). In addition, among patients with arthritis, smoking was associated with a predominantly upper limbs involvement (OR 0.78, 95%CI 0.65-0.94), while alcohol was associated with a predominant mono/oligoarticular involvement (OR 1.13, 95%CI 0.94-1.36).

Patients who have ever suffered enthesitis also showed a lower frequency of smoking habit and alcohol intake (OR 0.75, 95%CI 0.63-0.89 and OR 0.69, 95%CI 0.57-0.83, respectively). No association was found with regard to the prevalence of dactylitis.

At the moment of the study visit, 20.4% patients were current smokers and 32.2% consumed alcohol. Current alcohol intake was associated with a lower prevalence of both current arthritis (26.9% vs. 33.6% (OR 0.76, 95%CI 0.64-0.91)) and current enthesitis (21.1% vs. 34.6% (OR 0.78, 95%CI 0.62-0.96)), while current smoking did not show significant differences.

No interaction was found in the association between alcohol and tobacco with regard to the prevalence of peripheral symptoms in the past. However, when assessing current arthritis, current smokers and no drinkers were found to be associated with arthritis in the lower limbs.

Conclusion: Taking into account the country and the presence of psoriasis, smoking and alcohol are associated with a lower prevalence of peripheral manifestations. Smoking seems to be associated with predominantly upper limbs arthritis while alcohol intake seems to be associated with a predominantly oligo/mono articular involvement. Future studies are required including the influence of psoriatic arthritis in the relationship between alcohol and smoking and its association with peripheral manifestations.

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Abstract Number: 1798

The Transition to Psoriatic Arthritis: What Factors Predict a Shorter Transition from Psoriasis to Psoriatic Arthritis?

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Linear Regression Analysis for Time between PsO and PsA Diagnoses

Factor	Level	Estimate (95%CI)	Pvalue	Omnibus test of the variable
Sex	F (v M)	0.85 (-1.44, 3.13)	0.468	0.468
Age	IQR Increase	-11.88 (-13.64, -10.12)	***<0.001***	***<0.001***
Family History of PsO	Yes (v No)	-1.77 (-7.62, 4.08)	0.554	0.554
BMI	IQR Increase	-1.19 (-2.49, 0.11)	0.074	0.074
Treatment	oral DMARD (v NSAID only)	-3.36 (-7, 0.27)	0.07	0.065
	bDMARD (v NSAID only)	-4.52 (-8.3, -0.74)	0.02	
Nail Involvement	Yes (v No)	0.16 (-4.06, 4.38)	0.942	0.942
DLQI	IQR Increase	0.03 (-0.08, 0.15)	0.578	0.578
CVD	Yes (v No)	1.27 (-2.97, 5.51)	0.558	0.558
Hypertension	Yes (v No)	1.14 (-1.53, 3.82)	0.402	0.402
Diabetes	Yes (v No)	1.05 (-2.16, 4.27)	0.522	0.522
Hyperlipidemia	Yes (v No)	2.51 (-0.14, 5.15)	0.064	0.064
Elevated ESR/CRP	Yes (v No)	1.57 (-0.89, 4.03)	0.21	0.211
Alcohol	often (v never)	1.21 (-2.44, 4.87)	0.516	0.689
	occasional (v never)	-0.61 (-3.5, 2.28)	0.678	
	quit (v never)	-0.1 (-4.61, 4.41)	0.966	
Smoking	Ever (v Never)	0.97 (-1.27, 3.22)	0.396	0.396

Background/Purpose: Psoriatic arthritis (PsA) occurs in up to 30% of patients with psoriasis (PsO), and usually follows the development of PsO by an average of 7-10 years. However, there is significant variability in the timing of transition from PsO to PsA which contributes to delays in diagnosis and high rates of undiagnosed PsA. In this study, we aim to identify clinical and demographic features associated with the time to transition from PsO to PsA.

Methods: In our longitudinal psoriatic disease cohort, we identified patients with PsO and PsA diagnoses. Time between PsO and PsA diagnoses was calculated as number of years between the 2 diagnoses dates, and were modeled as a continuous outcome variable using multivariable linear regression. Candidate predictors included: gender,

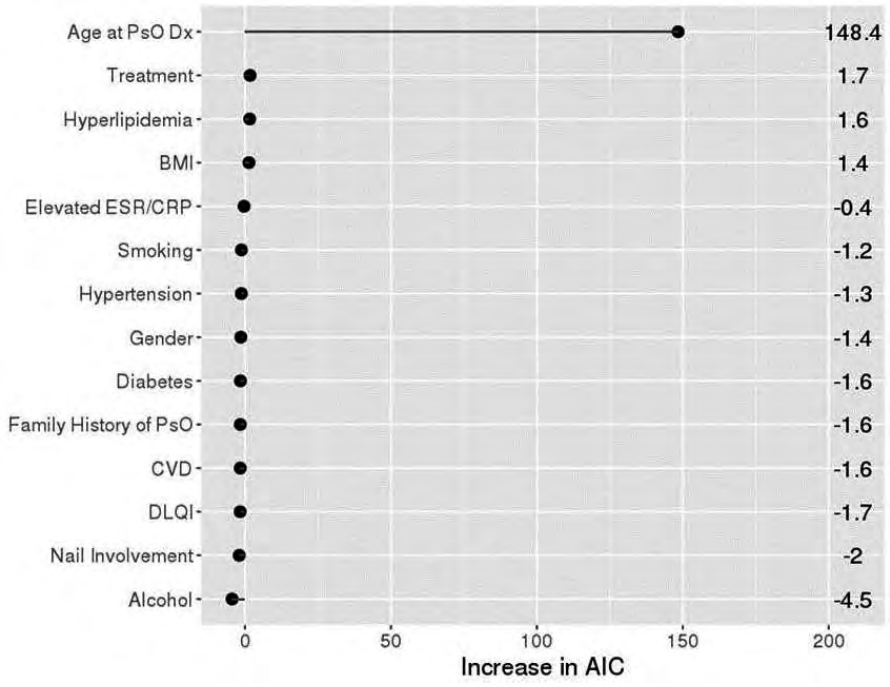

Figure 1. Ranking of Predictors for Time between PsO and PsA Diagnoses.

age at PsO diagnosis, family history of PsO, BMI, treatment, cardiovascular disease, hypertension, diabetes, dyslipidemia, nail involvement, DLQI, elevated ESR/CRP, alcohol and smoking. A subgroup model was built using patients with BSA data, and using a subset of predictors including age at PsO diagnosis, smoking, elevated ESR/CRP, BMI, family history of PsO and % body surface area (BSA). Model results were presented using coefficient estimates and respective 95% confidence intervals. Variables were ranked based on their relative contribution to the models, as assessed by AIC increase upon removal of the variable from the full model. All tests were two-sided, assuming an alpha level of 0.05.

Results: Our analysis cohort included 384 patients. The median age at PsO diagnosis was 30.4 years, and 52.2% of patients were female. Age at Diagnosis of PsO is statistically significantly associated with transition time from PsO to PsA. Patients aged 42.6 years (Q3) have on average around 12 years less between PsO to PsA compared to patients aged 18.9 years (Q1), after controlling for relevant variables in the model (-11.88 (-13.64, -10.12); $p < 0.001$). Patients on bDMARD have on average 4.5 years less between PsO to PsA compared to patients on NSAID only, after controlling for other variables in the model (-4.52 (-8.3, -0.74), $p = 0.02$). Although the use of bDMARDs appears to show a trend towards less years (4.5 yrs) compared to non bDMARDs, the overall effect of treatment was not statistically significant. Patients with BSA of 5% (Q3) have on average 1.1 years more (more number of years) from PsO to PsA compared to patients with BSA of 0.5% (Q1), after controlling for other variables in the model (1.11 (-0.44, 2.65), $p = 0.16$), though the overall effect of BSA is not significant. Age at PsO diagnosis contributed the most to the model according to the Akaike Information Criterion (AIC). AIC >= 2 justifies statistically improved model, which means it is beneficial to include age in the model.

Conclusion: Our study demonstrated that age of psoriasis onset is important predictor of time to transition from psoriasis to psoriatic arthritis. Patients diagnosed with PsO at an older age have a shorter interval before they develop PsA. The time difference is clinically significant; compared to younger patients (18.9 years, Q1), older patients (42.6 years, Q3) develop PsA on average 12 years sooner. These results suggest that older patients diagnosed with PsO may benefit from earlier screening for PsA.

Disclosure: S. Cheemalavagu, None; **Y. Jin**, None; **E. Husni**, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2.

Abstract Number: 1799

Gender Based Differences in Clinical and Sonographic Assessment Among Patients with Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) can affect differently women and men. Ultrasound (US) is an important tool in the evaluation of disease activity of PsA. To the best of our knowledge, there is no study that compared sonographic features of PsA between female and male patients.

The aim of this study is to investigate gender-based differences among PsA patients concomitantly evaluated by clinical examination and US.

Methods: The study population included prospectively recruited consecutive adult patients with PsA (CASPAR criteria). Patients' assessment included physical examination of joints (66/68 tender and swollen joint count, TJC/SJC), enthesitis (LEEDS and SPARCC), dactylitis, skin (PASI) and several patients reported outcome. All the patients underwent a detailed US evaluation (gray scale and Doppler), including 52 joints, 40 tendons and 14 points of entheses

Table 1. Demographics and clinical characteristics according to gender

Characteristics	Female PsA n = 89 (56 %)	Male PsA n = 70 (44 %)	p-Value
Age, mean (± s.d)	53.48 (13.42)	50.99 (12.45)	0.23
BMI, mean (± s.d)	27.43 (5.14)	27.90 (5.10)	0.57
Smoking history, n (%)	36 (41.90)	26 (37.10)	0.83
Employed, n (%)	52 (58.40)	57 (81.40)	0.01
Education, academic, n (%)	70 (78.70)	55 (78.60)	0.27
PSO duration, mean (± s.d)	19.74 (13.21)	18.06 (15.25)	0.47
PsA duration, mean (± s.d)	10.63 (11.11)	11.86 (11.89)	0.50
TJC, mean (± s.d)	8.19 (9.97)	8.89 (10.10)	0.66
SJC, mean (± s.d)	0.83 (1.76)	1.73 (3.66)	0.04
Leeds enthesitis, mean (± s.d)	1.29 (1.70)	0.87 (1.38)	0.095
SPARCC enthesitis, mean (± s.d)	3.14 (3.70)	2.11 (3.20)	0.07
Dactylitis (≥1) (%)	0.11 (0.49)	0.43 (1.73)	0.10
PASI, mean (± s.d)	1.05 (1.84)	2.49 (6.34)	0.04
GPhA, mean (± s.d)	1.86 (1.83)	2.25 (2.33)	0.24
PGA, mean (± s.d)	5.33 (2.98)	5.34 (3.21)	0.98
Pain, mean (± s.d)	5.06 (3.05)	4.98 (3.24)	0.86
CRP mg/l, mean (± s.d)	7.79 (9.94)	8.77 (18.16)	0.66
ESR, mm/h, mean (± s.d)	26.62 (17.83)	16.74 (12.25)	<0.001
HAQ, mean (± s.d)	0.92 (0.82)	0.82 (0.81)	0.39
SF36 (PCI), mean (± s.d)	53.55 (27.71)	57.44 (33.44)	0.43
SF36 (MCI), mean (± s.d)	61.36 (22.38)	64.15 (22.88)	0.45
Facit, mean (± s.d)	29.39 (13.36)	30.67 (12.89)	0.55
Depression, mean (± s.d)	13.60 (12.10)	12.22 (11.23)	0.48
MDA, n (%)	28 (32.5)	27 (39.6)	0.44
VLDA, n (%)	18 (20.2)	23 (32.9)	0.10
CPDAI, mean (± s.d)	8.38 (3.54)	7.52 (4.09)	0.17
DAPSA, mean (± s.d)	20.29 (14.52)	21.75 (16.83)	0.56
PASDAS	3.54 (1.91)	3.54 (2.55)	0.99
Fibromyalgia	28 (31.50)	14 (20.0)	0.15
Tender points, mean (± s.d)	4.48 (5.60)	2.27 (4.18)	0.007
Treatment			
csDMARDs, n (%)	39 (43.80)	29 (41.40)	0.88
Otezla, n (%)	1 (1.1)	3 (4.3)	0.45
Biologics, n (%)	48 (53.90)	38 (54.30)	1

Table 2. Sonographic scores according to gender

Score	Female PsA n = 88	Male PsA n = 70	p-Value
Total US score*, mean (± s.d)	35.14 (20.43)	38.62 (22.79)	0.2
Total Gray scale score, mean (± s.d)	30.46 (18.27)	34.76 (18.97)	0.16
Total power Doppler score, mean (± s.d)	5.06 (5.78)	5.16 (6.97)	0.92
Synovitis* score, EULAR-OMERACT score, mean (± s.d)	12.72 (10.73)	11.49 (9.04)	0.3
Synovitis Gray scale score, mean (± s.d)	12.69 (10.43)	11.44 (9.00)	0.43
Synovitis power Doppler score, mean (± s.d)	1.42 (2.14)	1.34 (2.71)	0.84
Tenosynovitis score, mean (± s.d)	3.62 (5.00)	4.01 (4.64)	0.62
Tenosynovitis Gray scale score, mean (± s.d)	2.51 (3.80)	2.91 (3.65)	0.50
Tenosynovitis power Doppler score, mean (± s.d)	1.11 (1.96)	1.10 (1.75)	0.96
Enthesitis score, mean (± s.d)	17.55 (9.96)	23.33 (16.22)	0.008
Enthesitis Inflammatory score, mean (± s.d)	8.74 (5.95)	12.07 (9.01)	0.007
Enthesitis structural score, mean (± s.d)	9.05 (6.59)	11.53 (9.22)	0.055

*Synovitis was based upon the EULAR-OMERACT score

Table 3. Comparison of US enthesitis feature by enthesitis site between female and male

	Female	Male	p-Value
Lateral epicondyle			
Total score	3.69 (3.49)	3.13 (2.95)	0.30
Inflammatory score	2.14 (2.52)	2.19 (2.15)	0.88
Structural score	1.55 (1.89)	0.94 (1.52)	0.03
Triceps to olecranon			
Total score	1.72 (2.41)	3.12 (3.84)	0.007
Inflammatory score	0.88 (1.82)	1.40 (2.32)	0.12
Structural score	0.84 (1.40)	1.72 (2.52)	0.007
Quadriceps			
Total score	3.20 (2.88)	4.15 (3.56)	0.07
Inflammatory score	0.92 (1.53)	1.58 (2.16)	0.03
Structural score	2.28 (2.06)	2.56 (2.08)	0.41
Dist patellar insertion			
Total score	1.19 (2.09)	2.33 (3.47)	0.01
Inflammatory score	0.67 (1.56)	1.22 (2.33)	0.08
Structural score	0.51 (1.15)	1.10 (1.70)	0.01
Tibial Tuberosity insertion	2.65 (2.82)	3.94 (3.33)	0.01
Total score	2.25 (2.46)	3.03 (2.44)	0.052
Inflammatory score	0.40 (0.97)	0.91 (1.55)	0.01
Structural score			
Achilles tendon	3.41 (3.52)	4.75 (3.87)	0.03
Total score	0.81 (1.73)	1.66 (2.11)	0.007
Inflammatory score	2.59 (2.58)	3.09 (2.35)	0.22
Structural score			
Plantar fascia	1.87 (2.35)	2.07 (2.35)	0.61
Total score	0.99 (1.43)	0.99 (1.45)	0.99
Inflammatory score	0.88 (1.32)	1.09 (1.40)	0.35
Structural score			

(according to MASES index plus lateral epicondyles). The score of the US was based on the summation of a semi-quantitative score (0-3) for synovitis (EULAR-OMERACT definition), tenosynovitis, and enthesitis score. The US enthesitis score was categorized to inflammatory (hypoechogenicity, thickening, bursitis and Doppler) and to structural score (erosions and enthesophytes). All the evaluations occurred on the same day, and the sonographer was blinded to the clinical data. Patients were asked to stop NSAIDS 3 days before the evaluation.

The association between gender and US scores was assessed by multivariate ordinal logistic regression models adjusted for potential confounders (age, BMI, PsA duration, CRP, csDMARDS, and biologics).

Results: The study population included 159 PsA patients, 70 males and 89 females (table 1). The rate of employment was significantly higher in males compared to females (p=0.007). PASI and SJC were significantly higher in males compared to females (p=0.04). Disease duration, other indices of PsA activity, and treatment profile were similar in both genders.

The total US score and its subcategories, synovitis and tenosynovitis scores, were similar between the genders, whereas the total enthesitis score and its subcategory, inflammatory enthesitis score, were significantly higher in males vs females (23.33 ± 16.22 vs 17.55 ± 9.96 and 12.07±9.01 vs 8.74± 5.95, p=0.007, respectively) (table 2). In addition, male had significantly more prevalent hypoechogenicity, thickening, bursitis and enthesophytes compared to females (p< 0.001). Furthermore, there was a gender-based significant difference of US enthesitis total scores by anatomical sites: triceps to olecranon, quadriceps to patella, patellar tendon insertion to distal patella and to tibial tuberosity and Achilles tendon insertion which had a significantly higher US enthesitis score in males compared to females (table 3).

Finally, multivariate ordinal logistic regression models showed that male were prone to higher US inflammatory enthesitis score (OR 1.88, p=0.04).

Conclusion: The main gender-based sonographic difference in PsA patients was higher enthesitis score in males, in particular, higher inflammatory US enthesitis score, whereas these differences were not reflected by the standardized clinical enthesitis and disease activity scores.

Disclosure: V. Furer, None; **J. Wollman**, None; **D. Ievartovsky**, None; **V. Aloush**, None; **S. Borok Lev-Ran**, None; **D. Paran**, None; **O. Elkayam**, NOVARTIS, 1, 2, 6, Pfizer, 1, 2, 5, 6, Lilly, 1, 2, 6, Abbvie, 1, 6, BI, 1, 6; **A. Polachek**, None.

Abstract Number: 1800

Altered Metabolic Profiles in the Transition from Psoriasis to Psoriatic Arthritis: A Longitudinal Analysis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes Poster IV: Clinical Aspects of PsA & Peripheral SpA (1773–1800)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

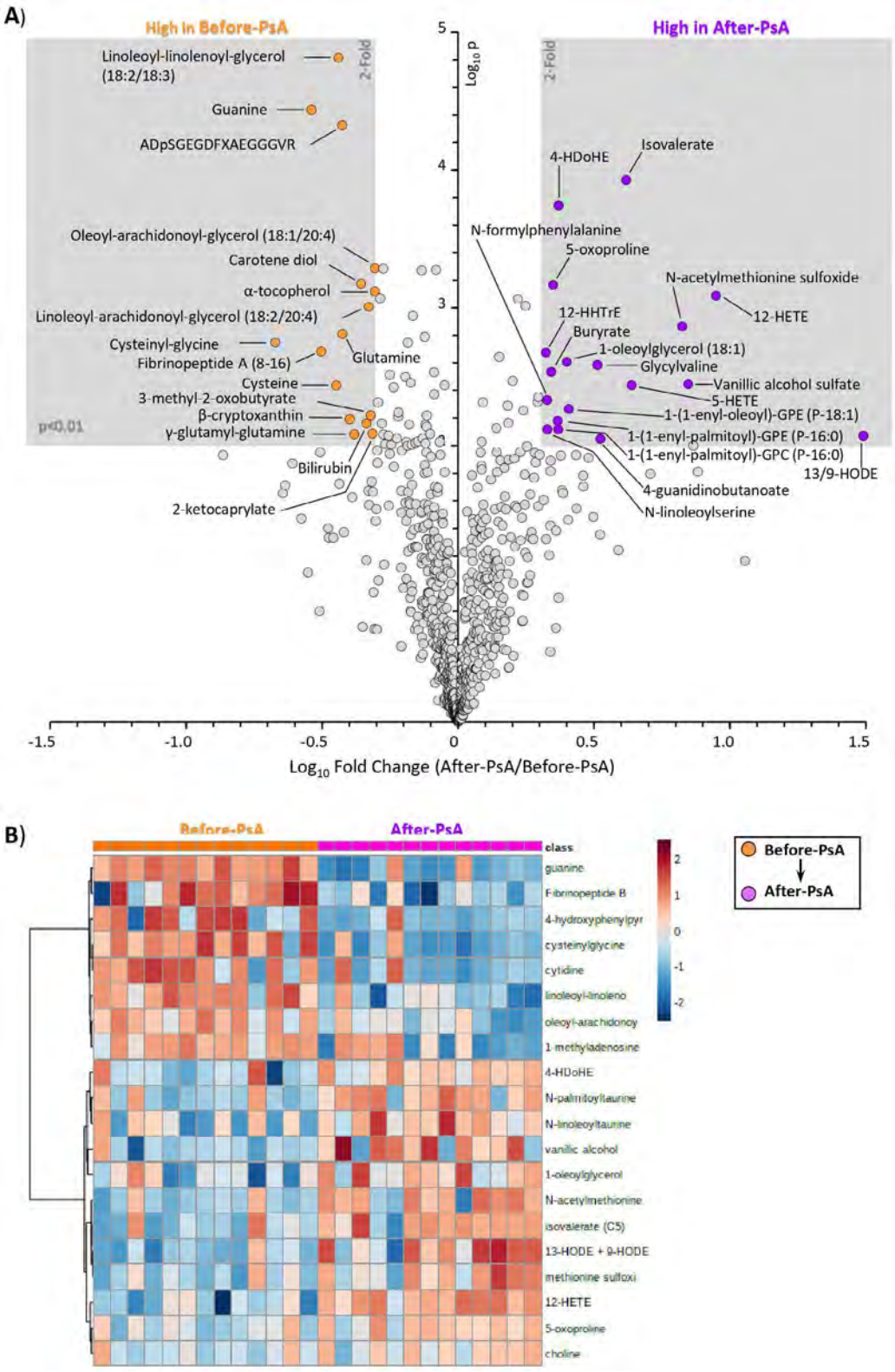


Figure 1. Metabolites different between before- and after the onset of PsA. (A) Volcano plot shows comparison between samples collected before (Before-PsA, orange) and after (After-PsA, purple) the onset of PsA (matched samples). X-axis shows Log10 of fold change. Y-axis shows –Log10 of p-value (pair-wise t-test). Metabolites achieving both statistical significance ($p<0.01$) and greater than 2-fold difference between groups, are shown inside the shaded gray areas, and identified with labels. Data are means from n = 13 individuals. (B) Heat Map showing metabolite abundance (top 25) in individual patients (n = 13).

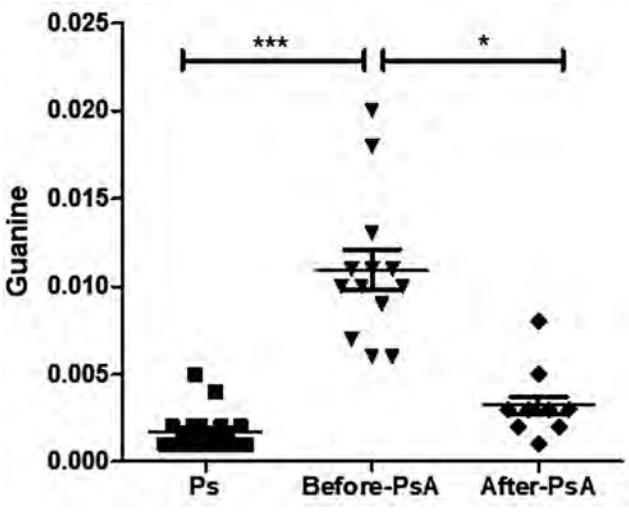


Figure 2. Guanine levels in converters (PsP) and non-converters (PsNP). Serum guanine levels were compared between samples from patients who did (PsP, n = 13) or did not covert (PsNP, n = 20) to PsA and normalized data presented as a dot plot. For the PsA-converters samples were collected before (Before-PsA), and after (After-PsA) the onset of PsA (matched samples). '***' indicates p-value less than 0.0001 and '*' indicates p-value less than 0.01.

Background/Purpose: The transition to psoriatic arthritis (PsA) occurs in 20-30% of psoriasis (Ps) patients, but the mechanisms underlying the emergence of musculoskeletal disease are not well understood. We compared serum metabolites of Ps and PsA patients to identify potential biomarkers of arthritis risk in Ps patients.

Methods: To identify differentially abundant metabolites in the sera of Ps patients, we analyzed serum samples for metabolites in cohorts of psoriasis patients who progressed (PsP) and did not progress (PsNP) to PsA. We performed unbiased metabolomic profiling using reverse-phase, and Hydrophilic Interaction Liquid Chromatography coupled to Q-Exactive Mass Spectrometry of the serum samples collected from PsNP (n=20), and PsP (n=13), and healthy controls (HC, n=18).

Results: We identified several key metabolites linked to diverse metabolic pathways that differed between patients who did or did not progress to PsA and healthy controls. Among the differentially abundant metabolites were those related to purine, pyrimidine, glutathione, and lipid metabolism (Figure 1). We also noted that guanine and linoleoyl-linolenoyl-glycerol were significantly decreased (more than 50%, $p < 0.001$), after the onset of arthritis. In contrast, multiple metabolites related to lipid metabolism (4-HDoHE, 12-HETE, 12-HHTrE, and 1-oleoylglycerol), were elevated (more than 2-fold, $p< 0.01$) and 5-oxoproline, a metabolite related to glutathione metabolism, was also elevated in the samples (more than 2-fold, $p< 0.001$) collected after the onset of arthritis (Figure 1). These changes were not noted in HCs. We also found that guanine levels were elevated in PsP compared to PsNP patients (Figure 2). Most intriguingly, we also noted that serum guanine levels significantly decreased after the onset of arthritis (Figure 2).

Conclusion: We identified a set of metabolites that were differentially abundant before and after the onset of arthritis in Ps patients. During the transition from psoriasis to PsA, we observed a changing pattern of purine, lipid and amino acid metabolites over time. The elevated guanine levels in Ps patients at risk for arthritis was particularly striking and may reflect altered proliferation of immune cells and enhanced cytokine expression. These metabolites represent potential biomarkers for PsA risk in Ps patients.

Disclosure: A. Paine, None; **P. Brookes**, None; **D. Li**, None; **S. Bhattacharya**, None; **M. Garcia-Hernandez**, None; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2.

Abstract Number: 1801

The Effect of Ixekizumab versus Adalimumab on Individual Components of the ACR Composite Score, with and Without Concomitant Methotrexate or Other Conventional Synthetic DMARDs at 52 Weeks in Patients with Psoriatic Arthritis

Elaine Husni[1], Sona Kamat[2], Keri Stenger[3], Rebecca Bolce[3], Thorsten Holzkaemper[4], Cameron Helt[3], So Young Park[3], Jeffrey Lisse[5] and Luca Idolazzi[6], [1]Cleveland Clinic, Cleveland, OH, [2]St Louis University, Saint Louis, MO, [3]Eli Lilly and Company, Indianapolis, IN, [4]Eli Lilly and Company, Bad Homburg, Germany, [5]Eli Lilly and Company, Tucson, AZ, [6]University of Verona, Verona, Italy

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

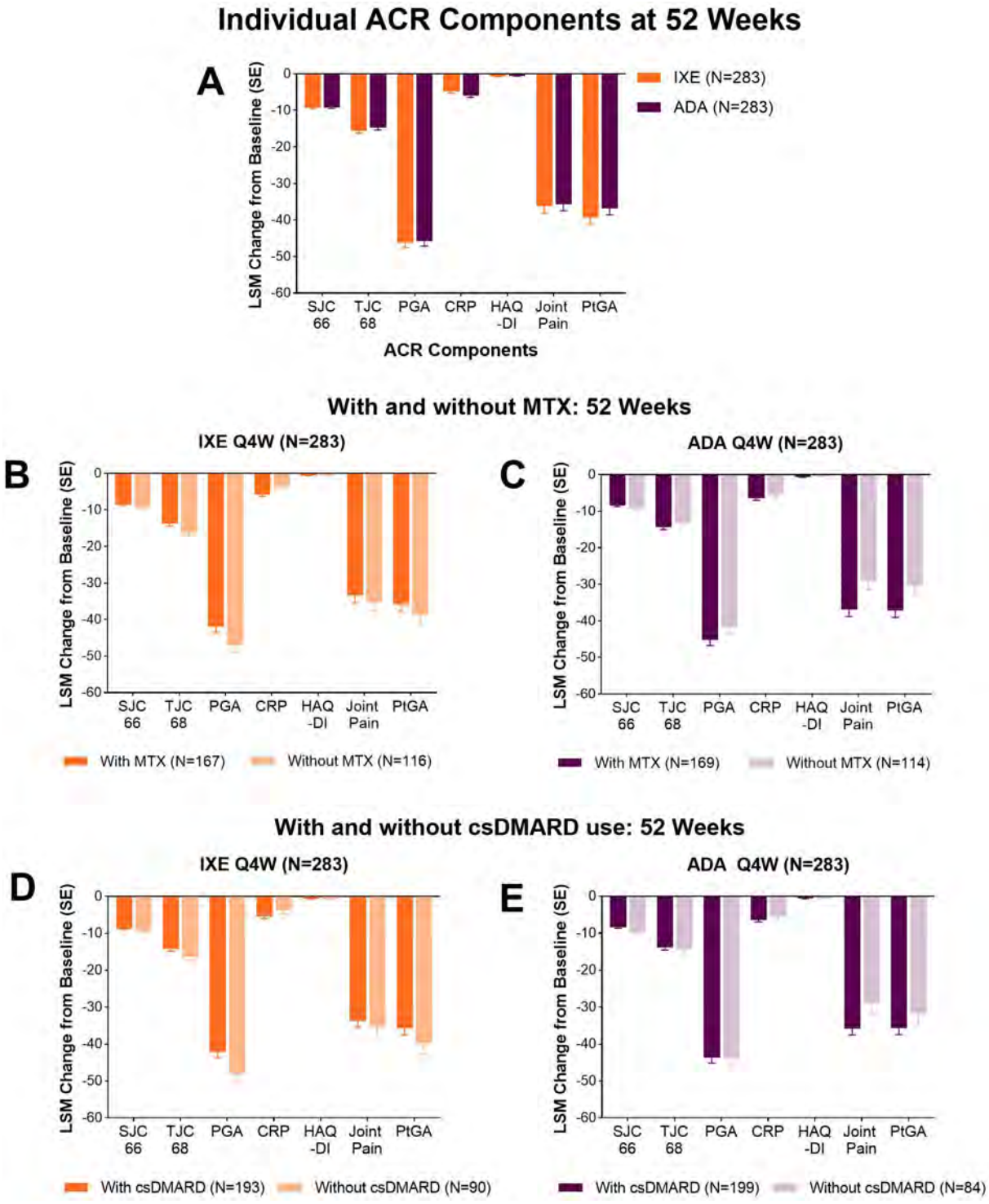
Background/Purpose: It is important to understand how to select among the multiple treatment options for active psoriatic arthritis (PsA). Since individual patient domains may influence treatment choice, it is useful to evaluate individual American College of Rheumatology (ACR) components in large trials. SPIRIT-H2H showed superiority of ixekizumab (IXE) over adalimumab (ADA) in patients with PsA and inadequate response (IR) to conventional synthetic disease modifying antirheumatic drugs (csDMARDs) [1]. This analysis describes the effect of IXE and ADA on individual ACR components at week (Wk) 52, with and without concomitant methotrexate (MTX) and csDMARDs.

Methods: Patients from SPIRIT-H2H (NCT03151551, 52 Wk randomized multicenter study) who met Classification Criteria for Psoriatic Arthritis (CASPAR) (N=566), were randomized (1:1, stratified by baseline concomitant csDMARDs

Table. Baseline demographics and disease characteristics for patients treated with IXE or ADA in the ITT population.

	ITT Population	
	IXE Q4W (N=283)	ADA Q2W (N=283)
Age (years)	47.5 (12.0)	48.3 (12.3)
Female, n (%)	121 (42.8)	133 (47.0)
Disease Duration (years)	5.9 (6.4)	6.6 (7.4)
SJC66	10.1 (7.5)	10.7 (8.1)
TJC68	19.1 (12.7)	21.3 (15.4)
PGA	58.9 (17.5)	59.4 (18.2)
CRP	9.8 (13.7)	10.5 (19.3)
HAQ-DI	1.2 (0.6)	1.3 (0.7)
Joint Pain	59.7 (21.9)	62.4 (21.1)
PtGA	62.4 (20.3)	65.2 (20.7)

Data presented as mean (SD) unless otherwise specified. Abbreviations: ADA, adalimumab; CRP, C-reactive protein; HAQ-DI, health assessment questionnaire disability index; ITT, intent-to-treat; IXE, ixekizumab; PGA, physicians' global assessment, PtGA, patients global assessment; Q2W, every two weeks; Q4W, every four weeks; SJC, swollen joint count; TJC, tender joint count.



Change from baseline in the individual components of the ACR composite score at week 52 in patients treated with IXE or ADA (A) in the ITT population, (B and C) with and without MTX use at baseline and (D and E) with and without csDMARD use at baseline. Data presented as least square mean (LSM) change from baseline (mBOCF) + SE. Abbreviations: ACR, American College of Rheumatology; ADA, adalimumab; CRP, C-reactive protein; csDMARD, conventional synthetic disease modifying antirheumatic drug; HAQ-DI, health assessment questionnaire disability index; ITT, intent-to-treat; IXE, ixekizumab; mBOCF, modified baseline observation carried forward; MTX, methotrexate; PGA, physicians global assessment, PtGA, patients global assessment; Q2W, every two weeks; Q4W, every four weeks; SJC, swollen joint count; TJC, tender joint count.

and moderate-to-severe PsO) to IXE or ADA on-label PsA or PsO dosing. Patients were bDMARD-naïve with IR to csDMARDs, active PsA (≥3 tender joints [TJC] and ≥3 swollen joints [SJC]) and had psoriasis (PsO) ≥3% BSA (body surface area). Patient's Global Assessment (PtGA) and Physicians Global Assessment (PGA), Health Assessment Questionnaire-Disability Index (HAQ-DI), and joint pain were assessed by visual analog scale, and TJC and SJC as well as C-reactive protein (CRP) were analyzed. All post-hoc analyses were performed on the intent-to-treat (ITT) population. Change from baseline (CFB) in individual ACR components was analyzed using an Analysis of Covariance (ANCOVA) model, for overall as well as with and without concomitant therapies (e.g., MTX or csDMARD). Least square mean (LSM) and standard error (SE) are presented. Missing data were imputed using modified baseline observation carried forward (mBOCF). Nine patients with active PsO and BSA ≥3% were assessed as Psoriasis Area and Severity Index (PASI)=0 at baseline, a medical inconsistency that was resolved using medical judgment. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

Results: A total of 566 patients received either IXE (N=283) or ADA (N=283). Baseline values for individual ACR components were balanced between IXE and ADA (Table). At Wk 52, IXE demonstrated efficacy across all individual ACR components in the ITT population, specifically in PGA, PtGA and Joint Pain; ADA also demonstrated numerical efficacy (Fig. A). Improvements from baseline for IXE were observed across ACR components, with or without MTX or csDMARD (Fig. B-E). The effect of MTX (with or without) was notably different between IXE and ADA in TJC68, PGA, Joint Pain, and PtGA.

Conclusion: In this analysis, there was improvement with IXE in all components of the ACR composite score at Wk 52, irrespective of MTX or csDMARD use (with or without). In the ITT population, IXE showed comparable efficacy to ADA at Wk 52 in all components of ACR, demonstrating improvement across musculoskeletal domains. These results may provide further confidence of the clinical benefits of ixekizumab across musculoskeletal domains in patients with PsA, regardless of MTX or csDMARD use.

References

1. Mease PJ. et al. *Ann Rheum Dis* 2020;79(1)

Disclosure: E. Husni, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2; **S. Kamat**, Abbvie, 2, 6, Eli Lilly and Company, 6, Amgen, 6; **K. Stenger**, Eli Lilly and Company, 3, 11; **R. Bolce**, Eli Lilly and Company, 3, 11; **T. Holzkaemper**, Eli Lilly, 3, 12, Shareholder; **C. Helt**, Eli Lilly and Company, 3, 11; **S. Park**, Eli Lilly and Company, 3, 11; **J. Lisse**, Eli Lilly and Company, 3, 11; **L. Idolazzi**, Eli Lilly and Company, 6, UCB, 6, Celgene, 6, MSD, 6, Abbvie, 6, Novartis, 6.

Abstract Number: 1802

Comparison of Axial and Peripheral Manifestations in Patients with Psoriatic Arthritis and Ankylosing Spondylitis in Upadacitinib Clinical Trials

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Table Baseline demographics, medical history, and disease characteristics

Mean (SD), unless otherwise specified	PsA with axial involvement n=626	PsA without axial involvement n=1289	AS with peripheral involvement n=135	AS without peripheral involvement n=52	p-value (PsA with axial involvement versus AS with peripheral involvement)
Male, n (%)	300 (47.9)	583 (45.2)	88 (65.2)	44 (84.6)	**0.0003**
Age, years	50.7 (12.6)	52.0 (12.0)	46.6 (12.7)	42.2 (11.4)	**0.0008**
Body mass index, kg/m^2	30.3 (7.1)	30.7 (6.8)[a]	26.7 (4.9)	26.8 (5.2)	*
Duration of disease symptoms, years	11.2 (9.3)[b]	10.4 (9.5)[a]	14.6 (10.9)	14.0 (10.6)	**0.0009**
Duration of disease since diagnosis, years	7.7 (8.0)	7.3 (8.0)	7.0 (9.2)	6.8 (8.4)	0.3738
TJC68	23.6 (16.4)	20.6 (14.6)	5.3 (8.2)	0	*
SJC66	11.9 (9.0)	11.2 (8.2)	1.5 (3.2)	0	*
Psoriasis, n (%)	616 (98.4)	1269 (98.4)	7 (5.2)	0	*
Uveitis, n (%)	1 (0.2)	5 (0.4)	3 (2.2)	1 (1.9)	**0.0191**
Inflammatory bowel disease, n (%)	10 (1.6)	13 (1.0)	2 (1.5)	2 (3.8)	1.0000
PhGA	6.7 (1.7)	6.5 (1.7)	6.7 (1.5)[c]	6.9 (1.7)[b]	0.6960
Pain, VAS 0–10	6.3 (2.0)[a]	6.1 (2.2)[a]	6.9 (1.6)[a]	6.8 (1.7)[a]	**0.0002**
ASDAS(CRP)	3.4 (1.0)[c]	3.1 (1.0)[i]	3.5 (0.7)[a]	3.7 (0.8)[a]	**0.0351**
BASDAI (Total score)	6.0 (2.1)[a]	5.5 (2.2)[i]	6.4 (1.6)	6.3 (1.8)[a]	**0.0076**
BASDAI Q2 (Back pain)	6.1 (2.7)[a]	4.8 (3.2)[i]	7.2 (1.7)	7.2 (1.6)[a]	*
BASDAI Q3 (Peripheral pain/ swelling)	6.3 (2.4)[a]	6.0 (2.6)[i]	5.9 (2.4)	5.5 (2.4)[a]	0.0747
BASDAI Q4 (Tenderness)	5.8 (2.6)[c]	5.6 (2.7)[i]	6.1 (2.5)	5.7 (2.4)[a]	0.3196

*p<0.0001
Data missing for [a]n=1, [b]n=3, [c]n=6, [d]n=11, [e]n=4, [i]n=14

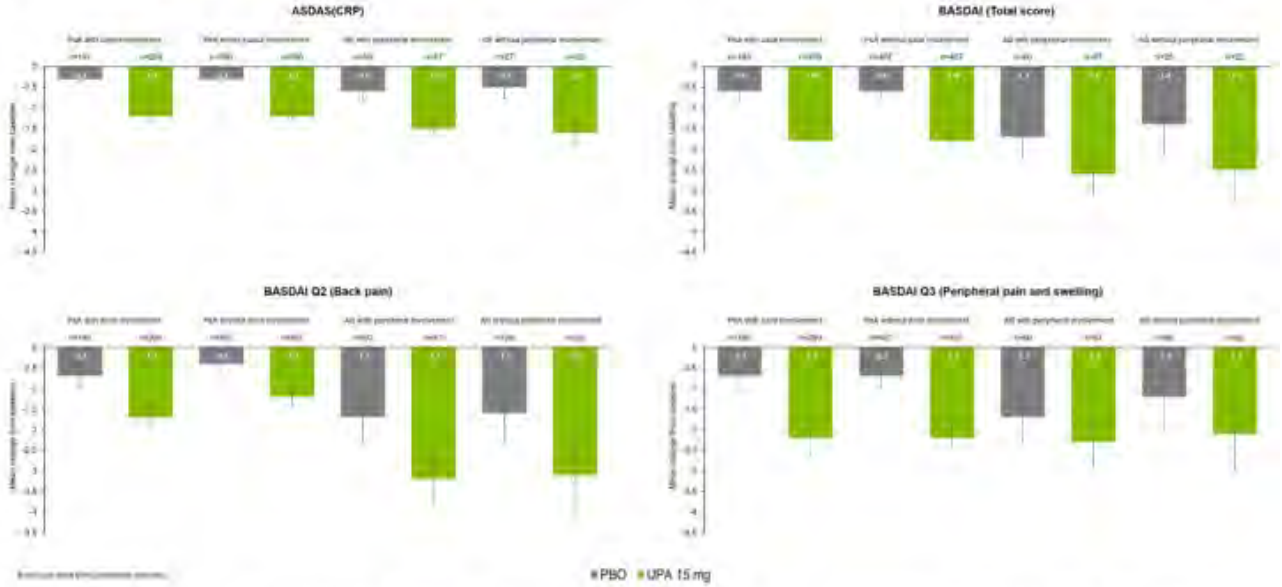
SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Axial, peripheral, and other disease manifestations often overlap between psoriatic arthritis (PsA) and ankylosing spondylitis (AS). Upadacitinib (UPA) is an oral Janus kinase inhibitor under evaluation for the treatment of PsA and AS. The objective of this analysis was to describe and compare baseline characteristics and UPA efficacy across 4 subgroups of patients (pts) from clinical trials: active PsA (with/without axial involvement) and active AS (with/without peripheral involvement).

Methods: Baseline characteristics and efficacy of UPA in reducing axial and peripheral signs and symptoms were assessed via an integrated analysis across the 4 pt subgroups from the SELECT-PsA 1,[1] SELECT-PsA 2,[2] and SELECT-AXIS[3] studies. Analyses of baseline characteristics included pts in the UPA 15 mg once daily (QD), UPA 30 mg QD, and placebo (PBO) groups; efficacy analyses included pts in the UPA 15 mg QD group only. Axial involvement in PsA (axial PsA) was determined by investigator assessment. Peripheral involvement in AS was defined based on presence of tender or swollen joints (TJC68 >0 or SJC66 >0), or presence of enthesitis at baseline (Maastricht Ankylosing Spondylitis Enthesitis Score >0).

Figure Mean change from baseline (95% confidence interval) in ASDAS(CRP), BASDAI, back pain, and peripheral pain and swelling at Week 12, by patient subgroup (UPA 15 mg group)



AS, ankylosing spondylitis; ASDAS(CRP), Ankylosing Spondylitis Disease Activity Score with C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; PBO, placebo; PsA, psoriatic arthritis; Q, question; UPA, upadacitinib

Results: 2102 pts (UPA 15 mg; UPA 30 mg; PBO) were evaluated across the 4 subgroups (PsA [with/without axial involvement]: 626/1289; AS [with/without peripheral involvement]: 135/52). 33% of pts with PsA had axial PsA; 72% of pts with AS had peripheral symptoms. Pts with axial PsA had higher peripheral joint (TJC68 and SJC66) and skin (psoriasis) burden than pts with AS with peripheral involvement ($p< 0.0001$). Pts with AS with peripheral involvement had significantly greater overall pain (pt's assessment of pain; $p=0.0002$) and back pain (BASDAI Q2; $p< 0.0001$) scores, and higher total BASDAI ($p=0.0076$) and ASDAS ($p=0.0351$) scores than pts with axial PsA; physician's global assessment of disease activity, and peripheral pain and tenderness (BASDAI Q3 and Q4) were numerically similar for these 2 subgroups (**Table**). The efficacy of UPA 15 mg (measured using ASDAS and BASDAI) was generally consistent across the 4 pt subgroups regardless of peripheral or axial involvement (**Figure**).

Conclusion: Pts with PsA with axial involvement and pts with active AS showed some differences in baseline characteristics but similar improvements versus placebo with UPA 15 mg QD.

References

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Disclosure: X. Baraliakos, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **R. Ranza**, AbbVie, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **S. Rednic**, AbbVie, 2, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 5; **F. Ciccia**, Eli Lilly and Company, 1, 2, 6, AbbVie, 1, 2, 6, Celgene, 1, 2, 6, Amgen, 1, 2, 6, Novartis, 1, 2, 6, Janssen, 1, 2, 6, UCB, 1, 2, 6, Roche, 1, 2, 6, Pfizer, 1, 2, 6, Galapagos, 1, 2, 6, Glaxo, 1, 2, 6; **F. Ganz**, AbbVie, 3, 11; **T. Gao**, AbbVie, 3, 11; **A. Lertratanakul**, AbbVie, 3, 11; **I. Song**, AbbVie, 3, 11; **A. Ostor**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli

Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Janssen, 1, 2, UCB, 1, 2, Paradigm, 1, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2.

Abstract Number: 1803

Long-term Safety of Guselkumab (TREMFYA®) in Patients with Active Psoriatic Arthritis: Pooled Results from 3 Randomized Clinical Trials Through up to 2 Years

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Number of adverse events per 100 PY (95% CI)

		PBO→GUS 100 mg		GUS 100 mg Q4W		GUS 100 mg Q8W		GUS 100 mg
	PBO W0 to W24[c]	PBO→GUS Q4W W24 to 2Y[a,d]	PBO→GUS Q8W W24 to 1Y[a,d]	W0 to W24	W24 to 1-2Y[a]	W0 to W24	W24 to 1-2Y[a]	Combined[a,b]
Pts, N	421	352	29	373	373	475	475	1229
Total PY	192	461	17	172	645	218	748	1871
Mean PY	0.5	1.3	1.6	0.5	1.7	0.5	1.6	1.5
AEs/100 PY[e]	212.0 (191.9, 233.6)	124.1 (114.1, 134.7)	51.8 (23.7, 98.3)	222.7 (201.0, 246.2)	138.7 (129.74, 148.1)	236.3 (216.3, 257.6)	167.5 (158.3, 177.0)	145.8 (140.4, 151.4)
NNH[f]		-	-	29	-	-	-	-
SAEs/100 PY[e]	8.8 (5.2, 14.1)	5.9 (3.9, 8.5)	0.0 (0.0, 17.2)	5.2 (2.4, 9.9)	4.7 (3.1, 6.6)	3.7 (1.6, 7.2)	6.4 (4.7, 8.5)	5.6 (4.6, 6.8)
NNH[f]		-	-	-	-	-	-	-
AEs leading to study agent d/c/100 PY[e]	3.6 (1.5, 7.5)	3.3 (1.8, 5.4)	0.0 (0.0, 17.2)	7.0 (3.6, 12.2)	2.9 (1.8, 4.6)	3.2 (1.3, 6.6)	2.3 (1.3, 3.6)	2.7 (2.0, 3.6)
NNH[f]		-	-	101	-	-	-	-
Infections/100 PY[e]	60.8 (50.3, 72.9)	39.7 (34.2, 45.9)	5.8 (0.2, 32.1)	62.6 (51.4, 75.6)	41.2 (36.4, 46.5)	56.9 (47.3, 67.8)	46.4 (41.7, 51.6)	42.6 (39.7, 45.7)
NNH[f]		-	-	114	-	-	-	-
Serious infections/100 PY[e]	3.6 (1.5, 7.5)	2.6 (1.4, 4.6)	0.0 (0.0, 17.2)	1.7 (0.4, 5.1)	0.8 (0.3, 1.8)	0.5 (0.0, 2.6)	2.0 (1.1, 3.3)	1.7 (1.2, 2.4)
NNH[f]		159	-	549	-	-	-	-
Malignancies/100 PY[e]	0.5 (0.0, 2.9)	0.4 (0.1, 1.6)	0.0 (0.0, 17.2)	0.0 (0.0, 1.7)	0.0 (0.0, 0.5)	0.9 (0.1, 3.3)	0.4 (0.1, 1.2)	0.3 (0.1, 0.6)
NNH[f]		-	-	-	-	250	-	-
MACE/100 PY[e]	0.5 (0.0, 2.9)	0.0 (0.0, 0.7)	0.0 (0.0, 17.2)	0.6 (0.0, 3.2)	0.5 (0.1, 1.4)	0.5 (0.0, 2.6)	0.1 (0.0, 0.8)	0.2 (0.1, 0.6)
NNH[f]		-	-	1642	-	-	-	-

[a]Through W56 for Ph2, W60 for D-1, W112 for D-2; [b]Combined pts treated with GUS Q4W and Q8W (including pts who crossed over from PBO); [c]For pts in the PBO group who crossed over to GUS Q4W, only data prior to the first administration of GUS are included; [d]For pts in the PBO group who crossed over to GUS, only data on and after first administration of GUS were included; [e]Results reported are number of events/100-PY (95%, CI); [f]Only positive NNH values are reported

d/c, discontinuation; MACE, major adverse cardiovascular events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke)

Table 2. Proportions of pts (%) with clinical laboratory abnormalities according to maximum NCI-CTCAE toxicity grade and by baseline MTX use

		PBO→GUS 100 mg		GUS 100 mg Q4W		GUS 100 mg Q8W		GUS 100 mg
	PBO W0 to W24[a,b]	PBO→GUS Q4W W24 to 2Y[a,c]	PBO→GUS Q8W W24 to 1Y[a,c]	W0 to W24	W24 to 1-2Y[c]	W0 to W24	W24 to 1-2Y[c]	Combined[a,d]
ALT increased, N	**419**	**351**	**28**	**371**	**371**	**473**	**473**	**1223**
Grade 1 (>ULN to ≤3.0X ULN)	29.6	34.8	42.9	35.0	44.2	28.8	38.5	39.2
Grade 2 (>3.0 to ≤5X ULN)	1.2	3.1	0	2.7	5.4	1.3	3.0	3.7
Grade 3 (>5 to <20X ULN)	0.7	0.3	0	1.1	1.3	0.6	1.1	0.9
Grade 4 (≥20X ULN)	0.2	0	0	0	0	0	0	0
Baseline MTX use, N	244	213	11	216	216	254	254	694
Grade 1	34.4	37.6	36.4	38.0	44.9	32.3	42.5	41.6
Grade 2	2.0	3.8	0	3.2	5.6	2.0	3.5	4.2
Grade 3	0.4	0.5	0	0.9	1.4	0.8	1.6	1.2
Grade 4	0	0	0	0	0	0	0	0
No baseline MTX use, N	175	138	17	155	155	219	219	529
Grade 1	22.9	30.4	47.1	31.0	43.2	24.7	33.8	36.1
Grade 2	0	2.2	0	1.9	5.2	0.5	2.3	3.0
Grade 3	1.1	0	0	1.3	1.3	0.5	0.5	0.6
Grade 4	0.6	0	0	0	0	0	0	0
AST increased	**419**	**351**	**28**	**371**	**371**	**473**	**473**	**1223**
Grade 1 (>ULN to 3.0X ULN)	20.0	25.1	35.7	21.6	31.3	17.5	26.6	27.8
Grade 2 (>3.0 to 5X ULN)	0.5	2.0	3.6	1.6	3.8	1.9	3.6	3.2
Grade 3 (>5 to <20X ULN)	1.0	0.9	0	1.6	2.4	0.4	0.8	1.3
Grade 4 (≥20X ULN)	0	0	0	0	0	0	0	0
Baseline MTX use, N	244	213	11	216	216	254	254	694
Grade 1	24.6	25.4	36.4	25.9	32.9	18.9	29.5	29.4
Grade 2	0.4	2.3	9.1	1.9	4.2	2.4	3.9	3.6
Grade 3	0.4	0.9	0	0.9	1.4	0.4	0.4	0.9
Grade 4	0	0	0	0	0	0	0	0
No baseline MTX use, N	175	138	17	155	155	219	219	529
Grade 1	13.7	24.6	35.3	15.5	29.0	16.0	23.3	25.7
Grade 2	0.6	1.4	0	1.3	3.2	1.4	3.2	2.6
Grade 3	1.7	0.7	0	2.6	3.9	0.5	1.4	1.9
Grade 4	0	0	0	0	0	0	0	0
Blood Bilirubin increased, N	**419**	**351**	**28**	**371**	**371**	**473**	**473**	**1223**
Grade 1 (>ULN to ≤1.5X ULN)	1.2	5.1	3.6	5.7	8.4	4.0	4.4	5.8
Grade 2 (>1.5 to ≤3X ULN	1.2	1.1	3.6	0.5	1.1	1.3	3.2	2.0
Grade 3 (>3 to ≤10X ULN)	0	0	0	0	0	0	0	0
Grade 4 (>10X ULN)	0	0	0	0	0	0	0	0
Baseline MTX use, N	244	213	11	216	216	254	254	694
Grade 1	0.4	5.6	0	6.5	9.7	3.1	4.3	6.3
Grade 2	0.8	1.4	0	0.5	1.4	0.8	2.4	1.7
Grade 3	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0
No baseline MTX use, N	175	138	17	155	155	219	219	529
Grade 1	2.3	4.3	5.9	4.5	6.5	5.0	4.6	5.1
Grade 2	1.7	0.7	5.9	0.6	0.6	1.8	4.1	2.3
Grade 3	0	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0	0

Data presented as percentage (%) of pts. [a]Through W56 for Ph2, W60 for D-1, W112 for D-2; [b]For pts in the PBO group who crossed over to GUS, only data prior to the first administration of GUS are included. [c]For pts in PBO group who crossed over from PBO to GUS, only data on and after first administration of GUS were included; [d]Combined pts treated with GUS Q4W and Q8W (including pts who crossed over from PBO)

ALT, alanine aminotransferase; AST, aspartate aminotransferase; ULN, upper limit of normal

Background/Purpose: Guselkumab (GUS), a targeted IL-23 inhibitor, demonstrated significant improvements in signs and symptoms of psoriatic arthritis (PsA) and a favorable safety profile through week (W) 24 in one Phase (Ph)2[1] and two Ph3 (DISCOVER [D]-1&2)[2-4] randomized controlled trials (RCTs). In this study, we assessed GUS safety by pooling data across the 1-year (Y) Ph2, 1-Y D-1, and 2-Y D-2 RCTs.

Methods: Patients (Pts) with active PsA (≥3% BSA affected by psoriasis in Ph2; ≥3 tender/swollen joints and CRP ≥0.3 mg/dL in Ph2 and D-1; ≥5 tender/swollen joints and CRP ≥0.6 mg/dL in D-2), biologic naïve except 13/149 Ph2 and 118/381 D-1 pts who received prior 1-2 TNF inhibitors (TNFi), were randomized to subcutaneous GUS 100 mg at W0, W4, and every 8 weeks (Q8W) or placebo (PBO) in Ph2 or to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, Q8W; or PBO in D-1 & D-2. At W24, PBO pts switched to GUS 100 mg Q8W (Ph2) or Q4W (D-1 & D-2). In these pooled post-hoc analyses, adverse events (AEs; number standardized for 100 patient-years of follow-up [PY]),

laboratory investigations (abnormalities classified by National Cancer Institute Common Terminology Criteria for AEs [NCI-CTCAE] grade), and injection site reactions (ISRs) were reported through W56 for the Ph2 trial, W60 for D-1, and W112 for D-2.

Results: Across the 3 RCTs, 1,229 pts with active PsA received GUS 100 mg (725 Q4W, 504 Q8W) and were followed for an average of 1.5 Y, representing 1871 PY. Incidences of AEs, serious AEs, infections, serious infections, discontinuations due to an AE, malignancies, and major adverse cardiovascular events were similar between PBO and GUS through W24. No increased rates were seen with up to 2 Y of GUS, except for a somewhat higher rate of SAEs and serious infections in the GUS 100 mg Q8W group during long-term follow-up, although confidence intervals overlapped with those seen during the PBO-controlled period (Table 1). The majority of GUS-treated pts with elevated aminotransferases and blood bilirubin had NCI-CTCAE Grade 1/2, with very few Grade 3 and no Grade 4, elevations. The proportions of pts with elevated aminotransferases at W24 were somewhat higher in the GUS Q4W vs Q8W/PBO groups; no unexpected increase was observed with longer duration of treatment. Elevations were more common in pts with vs without methotrexate (MTX) use at baseline. The proportions of pts with Grade 1 elevated bilirubin were higher in GUS vs PBO groups; few Grade 2 and no Grade 3/4 elevations were seen (Table 2). ISRs occurred in similar proportions of GUS (1%) and PBO (0.5%) pts at W24, with no disproportional increase with up to 2 Y of GUS.

Conclusion: In pts with active PsA pooled across 3 RCTs, GUS demonstrated a favorable safety profile through up to 2 Y of treatment; the GUS safety profile in PsA was comparable to that observed through up to 5 Y of GUS in pts with moderate-to-severe psoriasis.[5]

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Abstract Number: 1804

Targeted Safety Analyses of Guselkumab (TREMFYA®): Long-term Results from Randomized Clinical Trials in Patients with Active Psoriatic Arthritis and Moderate to Severe Psoriasis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Baseline Disease Characteristics and Medications

	PsA Trials					PsO Trials			
Mean (SD) or %	GUS 100 mg Q4W (N=373)	GUS 100 mg Q8W (N=475)	GUS Combined (N=848)	PBO (N=421)	Total (N=1269)	GUS 100 mg Q8W (N=823)	ADA (N=581)	PBO (N=422)	Total (N=1826)
Age (yrs)	46.5 (11.52)	46.5 (12.10)	46.5 (11.84)	46.8 (11.67)	46.6 (11.78)	43.8 (12.42)	43.0 (12.30)	43.9 (12.61)	43.6 (12.43)
Male, %	55.8	52.4	53.9	48.0	51.9	71.4	71.9	69.2	71.1
Weight (kg)	86.1 (18.90)	84.2 (19.94)	85.0 (19.50)	84.6 (19.47)	84.9 (19.49)	89.3 (20.55)	89.2 (21.53)	88.4 (21.94)	89.1 (21.18)
Body mass index (kg/m^2)	29.4 (5.76)	29.1 (6.50)	29.2 (6.18)	29.3 (6.17)	29.3 (6.18)	29.7 (6.36)	29.7 (6.51)	29.3 (6.70)	29.6 (6.49)
Disease duration (yrs)	5.9 (6.06)	5.9 (6.06)	5.9 (6.06)	6.3 (6.50)	6.0 (6.21)	17.9 (12.09)	17.3 (11.44)	17.8 (12.10)	17.7 (11.89)
Psoriatic BSA (%)	17.1 (19.74)	16.0 (19.13)	16.5 (19.40)	15.2 (18.23)	16.0 (19.02)	28.4 (16.71)	28.8 (16.67)	27.1 (16.31)	28.2 (16.61)
PASI score (0-72)	10.4 (11.16)	9.8 (11.04)	10.1 (11.09)	8.9 (9.34)	9.7 (10.55)	22.0 (9.09)	22.1 (8.97)	21.1 (8.30)	21.8 (8.88)
PsA medications, %									
Prior TNFi	10.2	10.5	10.4	10.2	10.3	—	—	—	—
Non-biologic DMARD	67.6	63.2	65.1	64.8	65.0	—	—	—	—
Methotrexate	58.4	53.9	55.9	58.4	56.7	—	—	—	—
Oral corticosteroids	16.6	16.8	16.7	18.3	17.3	—	—	—	—
NSAIDs	64.3	64.8	64.6	66.7	65.3	—	—	—	—
PsO medications, %									
Prior systemic non-biologic	—	—		—	—	65.7	64.2	57.1	63.3
Prior biologic	—	—		—	—	20.9	20.5	20.9	20.8

ADA=Adalimumab; BSA=Body surface area; DMARD=Disease-modifying anti-rheumatic drug; NSAID=Non-steroidal anti-inflammatory drug; PASI=Psoriasis area and severity index; TNFi=Tumor necrosis factor inhibitor.

Background/Purpose: Guselkumab (GUS), a human monoclonal antibody that specifically binds to the p19 subunit of IL-23, demonstrated efficacy and a favorable safety profile in active PsA in the Phase (Ph) 2[1] and Ph3 DISCOVER-1&2 trials[2,3] and in moderate-to-severe plaque psoriasis (PsO) in the Ph3 VOYAGE-1&2 trials.[4,5]

Methods: Using pooled safety data through 2 years (yrs) from the PsA trials (N=1229; GUS 100 mg every 4 or 8 weeks [Q4W/Q8W])[1-3] and through 5 yrs from the PsO trials (N=1721; GUS 100 mg Q8W),[4,5] the incidences of serious adverse events (SAEs); gastrointestinal (GI)-related SAEs and other targeted AEs; including candidiasis, uveitis, and opportunistic infections (OIs; e.g., active tuberculosis [TB]) were evaluated. GI-related SAEs were identified using the Medical Dictionary for Regulatory Activities (MedDRA) system-organ class "GI disorders;" OIs, uveitis/iridocyclitis, and candidiasis were classified through medical review of preferred terms and/or a specified MedDRA search strategy. Patients (pts) with a history of IBD were not excluded in the PsA/PsO trials. Rates of overall SAEs, GI-related SAEs, and other targeted AEs were calculated as the number of events per 100 pt-yrs of follow-up (PY), along with 95% confidence intervals (CI). Pooled safety data are presented for the placebo (PBO)-controlled periods (W0-16: PsO trials; W0-24: PsA trials) and active treatment periods through 2 yrs in PsA trials (W56: Ph2; W60: DISCOVER-1; W112: DISCOVER-2) and through 5 yrs in PsO trials (W264: VOYAGE-1&2). Maximum duration of exposure was W100 for the PsA trials and W252 for the PsO trials.

Table 2. Targeted AEs of Interest Through PBO-controlled Periods

	Pooled PsA				Pooled PsO	
	Through W24				Through W16	
	GUS 100 mg Q4W (N=373)	GUS 100 mg Q8W (N=475)	GUS Combined (N=848)	PBO (N=421)[a]	GUS 100 mg Q8W (N=823)	PBO (N=422)[a]
Total PY	172	218	390	192	255	128
Mean PY	0.5	0.5	0.5	0.5	0.3	0.3
Events/100 PY (95% CI)[b,c]						
Overall SAEs	5.22 (2.39, 9.91)	3.67 (1.58, 7.23)	4.35 (2.54, 6.97)	8.83 (5.15, 14.14)	6.27 (3.58, 10.17)	5.45 (2.19, 11.23)
GI-related SAEs[d]	0.00 (0.00, 1.74)	0.46 (0.01, 2.56)	0.26 (0.01, 1.43)	0.52 (0.01, 2.90)	0.00 (0.00, 1.17)	0.78 (0.02, 4.34)
OIs[e]	0.00 (0.00, 1.74)	0.00 (0.00, 1.37)	0.00 (0.00, 0.77)	0.00 (0.00, 1.56)	0.00 (0.00, 1.17)	0.00 (0.00, 2.33)
Candida infections[f]	0.00 (0.00, 1.74)	0.00 (0.00, 1.37)	0.00 (0.00, 0.77)	0.00 (0.00, 1.56)	0.78 (0.09, 2.83)	1.56 (0.19, 5.62)
Non-pathogen specific fungal infections, suspicious for candida[g]	0.00 (0.00, 1.74)	0.46 (0.01, 2.56)	0.26 (0.01, 1.43)	0.00 (0.00, 1.56)	0.78 (0.09, 2.83)	0.00 (0.00, 2.33)
Uveitis/ Iridocyclitis	0.00 (0.00, 1.74)	0.00 (0.00, 1.37)	0.00 (0.00, 0.77)	0.52 (0.01, 2.90)	0.00 (0.00, 1.17)	0.00 (0.00, 2.33)

Note: In PsA Ph2, data after early escape at W16 were excluded from analyses. Pts treated with ADA in PsO VOYAGE-1 & VOYAGE-2 were excluded from the analyses. AEs are coded using MedDRA Version 23.1.

[a]For pts in PBO group who changed treatment from PBO to GUS inadvertently prior to W16 in PsO VOYAGE-1 & VOYAGE-2 or W24 in PsA Ph2, PsA DISCOVER-1 & DISCOVER-2, only data prior to first administration of GUS were included in the analyses. Data on and after the first administration of GUS were not included.

[b]CIs based on exact method assuming that the observed number of events follows a Poisson distribution.

[c]For number of the said events, events are counted only once if events were started from same date with same MedDRA Preferred Terms.

[d]Search criteria: MedDRA SOC "GI Disorders."

[e]Search criteria: medical review for PsO VOYAGE-1 & VOYAGE-2, MedDRA SMQ for PsA DISCOVER-1 & DISCOVER-2.

[f]Candida Infections search criteria: MedDRA high level term "Candida infections."

[g]Non-pathogen specific fungal infections, suspicious for candida as defined by diagnosis and location; search criteria included MedDRA Preferred Terms of "fungal balanitis," "genital infection fungal," "vulvovaginal mycotic infection," "oral fungal infection," "tongue fungal infection," "oropharyngitis fungal," "fungal oesophagitis."

ADA=Adalimumab; SMQ=Standard MedDRA query; SOC=System organ class.

Table 3. Targeted AEs of Interest Through End of Study

	Pooled PsA					Pooled PsO		
	Through 2 Yrs					Through 5 Yrs		
	GUS 100 mg Q4W (N=373)	GUS 100 mg Q8W (N=475)	PBO→GUS 100 mg Q4W (N=352)[a]	PBO→GUS 100 mg Q8W (N=29)[a]	GUS Combined (N=1229)	GUS 100 mg Q8W (N=1221)[b]	ADA→GUS 100 mg Q8W (N=500)[c]	GUS Combined (N=1721)
Total PY	645	748	461	17	1871	5254	1912	7166
Mean PY	1.7	1.6	1.3	0.6	1.5	4.3	3.8	4.2
Events/100 PY (95% CI)[d,e]								
Overall SAEs	4.65 (3.14, 6.64)	6.42 (4.73, 8.51)	5.86 (3.86, 8.52)	0.00 (0.00, 17.24)	5.61 (4.59, 6.79)	5.18 (4.58, 5.83)	4.55 (3.64, 5.61)	5.01 (4.50, 5.56)
GI-related SAEs[f]	0.46 (0.10, 1.36)	0.27 (0.03, 0.97)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.27 (0.09, 0.62)	0.44 (0.28, 0.66)	0.42 (0.18, 0.82)	0.43 (0.29, 0.61)
OIs[g]	0.00 (0.00, 0.46)	0.27 (0.03, 0.97)	0.22 (0.01, 1.21)	0.00 (0.00, 17.24)	0.16 (0.03, 0.47)	0.00 (0.00, 0.06)	0.00 (0.00, 0.16)	0.00 (0.00, 0.04)
Candida infections[h]	0.31 (0.04, 1.12)	0.00 (0.00, 0.40)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.11 (0.01, 0.39)	0.49 (0.32, 0.73)	0.52 (0.25, 0.96)	0.50 (0.35, 0.70)
Non-pathogen specific fungal infections, suspicious for candida[i]	0.00 (0.00, 0.46)	0.27 (0.03, 0.97)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.11 (0.01, 0.39)	0.11 (0.04, 0.25)	0.16 (0.03, 0.46)	0.13 (0.06, 0.24)
Uveitis/ Iridocyclitis	0.00 (0.00, 0.46)	0.13 (0.00, 0.75)	0.00 (0.00, 0.65)	0.00 (0.00, 17.24)	0.05 (0.00, 0.30)	0.00 (0.00, 0.06)	0.00 (0.00, 0.16)	0.00 (0.00, 0.04)

Note: In PsA Ph2, data after early escape at W16 were excluded from analyses. AEs are coded using MedDRA Version 23.1.

[a]For pts in PBO group who changed treatment from PBO to GUS due to cross-over or inadvertently, only data on and after first administration of GUS were included in this group. Data prior to the first administration of GUS were not included in this group.

[b]PBO crossover pts were included in the GUS column after crossover to GUS.

[c]Events which occurred prior to GUS administration (ADA events) were excluded from the analyses. Only includes pts who were randomized to ADA at W0 and crossed over to receive GUS at or after W52 for PsO VOYAGE-1 & W28 for PsO VOYAGE-2.

[d]CIs based on exact method assuming that the observed number of events follows a Poisson distribution.

[e]For number of the said events, events are counted only once if events were started from same date with same MedDRA Preferred Terms.

[f]Search criteria: MedDRA SOC "GI Disorders."

[g]Herpes zoster disseminated, fungal oesophagitis, and meningitis listeria (1 report of each); search criteria: medical review for PsO VOYAGE-1 & VOYAGE-2, MedDRA SMQ for PsA DISCOVER-1 & DISCOVER-2.

[h]Candida Infections search criteria: MedDRA high level term "Candida infections."

[i]Non-pathogen specific fungal infections, suspicious for candida as defined by diagnosis and location; search criteria included MedDRA Preferred Terms of "fungal balanitis," "genital infection fungal," "vulvovaginal mycotic infection," "oral fungal infection," "tongue fungal infection," "oropharyngitis fungal," "fungal oesophagitis."

ADA=Adalimumab; SMQ=Standard MedDRA query; SOC=System organ class

Results: The PsA and PsO populations had comparable mean age and BMI. Prior or concomitant medication use reflected standard of care and study entry criteria (**Table 1**). Incidence rates of SAEs and GI-related SAEs were generally similar between GUS- and PBO-treated pts during the PBO-controlled periods, and between PsA pts receiving GUS Q4W or Q8W for up to 2 yrs and PsO pts receiving GUS Q8W for up to 5 yrs (**Tables 2,3**). Rates of other targeted AEs of interest were low in GUS-treated PsA/PsO pts. OIs did not occur in PsO pts and were infrequent in PsA pts (1 case each of herpes zoster disseminated, fungal oesophagitis, meningitis listeria). Candidal infections were reported infrequently and were non-serious (**Tables 2,3**). Iridocyclitis was reported in 1 PBO-treated PsA pt and 1 GUS Q8W-treated PsA pt. No cases of exacerbations or new onset of IBD were reported in GUS-treated PsA/PsO pts. No cases of active TB occurred in GUS-treated PsA/PsO pts.

Conclusion: Incidence rates of SAEs; GI-related SAEs; and AEs of interest including candidiasis, uveitis, and OIs were low, or no cases were reported. No new safety concerns were identified with GUS treatment through 2 yrs and 5 yrs of follow-up in the pooled PsA and PsO trials, respectively, supporting a durable and favorable GUS safety profile consistent between pts with active PsA and moderate-to-severe PsO.

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Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Foley**, AbbVie, 1, 5, 6, 12, Travel grants, Amgen, 1, 5, Celgene, 1, 5, 6, Aslan, 1, 5, Janssen, 1, 2, 5, 6, 12, Travel grants, Leo Pharma, 1, 2, 5, 6, 12, Travel grants, Eli Lilly, 1, 2, 5, 6, 12, Travel grants, Merck, 1, 2, 5, 6, 12, Travel grants, Novartis, 1, 2, 5, 6, 12, Travel grants, Pfizer, 1, 2, 5, 6, 12, Travel grants, Sanofi, 2, 5, 12, Travel grants, Sun Pharma, 1, 2, 5, 12, Travel grants, AstraZeneca, 5, Arcutis, 5, Boehringer Ingelheim, 2, Hexima, 5, UCB Pharma, 2, 5, Valeant, 5, 6, Bristol Myers Squibb, 1, 2, 5, Celtaxsys, 5, CSL, 5, Cutanea, 5, Dermira, 5, Galderma, 1, 5, 6, Genentech, 5, GlaxoSmithKline, 1, 5, 6, Regeneron, 5, Reistone, 5, Roche, 2, 5, 6, 12, Travel grants; **K. Reich**, AbbVie, 1, 5, 6, Amgen, 1, Janssen, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, UCB Pharma, 1, 5, Affibody, 1, 5, Almirall, 1, 5, 6, Boehringer Ingelheim, 1, 5, Bristol Myers Squibb, 1, 5, 6, Celgene, 1, 5, 6, Forward Pharma, 1, 5, Galderma, 1, 5, Kyowa Kirin, 1, 5, Leo Pharma, 1, 5, 6, Eli Lilly, 1, 5, 6, Medac, 1, 5, 6, Ocean Pharma, 1, 5, Sanofi, 1, 5, 6, MoonLake Immunotherapeutics, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Yang**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Miller**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **J. Yu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Wang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Sheng**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. You**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6.

Abstract Number: 1805

Low Rates of Radiographic Progression with 2 Years of Guselkumab (TREMFYA®), a Selective Inhibitor of the Interleukin-23p19 Subunit: Results from a Phase 3, Randomized, Double-blind, Placebo-controlled Study of Biologic-naïve Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table. Observed erosion, joint space narrowing, and total PsA-modified vdH-S scores through W100 of DISCOVER-2

	GUS Q4W			GUS Q8W			PBO→GUS Q4W		
Baseline PsA-modified vdH-S score, n	221			228			215		
Erosion	14.2 (23.3)			12.0 (21.9)			12.1 (21.9)		
Joint space narrowing	13.8 (21.8)			11.9 (19.5)			13.5 (21.6)		
Total	28.0 (43.6)			23.9 (40.4)			25.6 (42.4)		
Mean (SD) change in PsA-modified vdH-S score	**W0-24 N=221**	**W24-52 N=221**	**W52-100 N=211**	**W0-24 N=228**	**W24-52 N=228**	**W52-100 N=216**	**W0-24 N=215**	**W24-52 N=213**	**W52-100 N=202**
Erosion	0.27 (1.91)	0.36 (1.77)	0.45 (2.90)	0.51 (1.96)	0.20 (1.24)	0.26 (1.75)	0.73 (2.20)	0.25 (1.85)	0.09 (1.98)
Joint space narrowing	0.21 (1.17)	0.21 (1.11)	0.30 (1.32)	0.17 (0.69)	0.12 (0.66)	0.20 (0.92)	0.39 (1.72)	0.09 (1.11)	0.04 (1.90)
Total	0.48 (2.70)	0.57 (2.66)	0.75 (4.02)	0.68 (2.36)	0.31 (1.57)	0.46 (2.42)	1.12 (3.80)	0.34 (2.79)	0.13 (3.74)

Data presented as mean (standard deviation).

Background/Purpose: Guselkumab (GUS), an IL-23p19-subunit inhibitor, is efficacious in treating patients (pts) with psoriasis and psoriatic arthritis (PsA). In the Phase 3, double-blind, placebo (PBO)-controlled DISCOVER-2 study, GUS 100mg given every 4 or 8 weeks (Q4W or Q8W) significantly improved joint and skin symptoms; GUS-treated pts had smaller mean changes in radiographic progression vs. placebo (PBO) at W24.[1] Clinical response rates and a favorable safety profile were durable through W100.[2, 3] We now report details of radiographic assessments comprising the third reading session through W100 of DISCOVER-2, including relationships between radiographic changes and measures of clinical outcomes.

Methods: Biologic-naïve adults with active PsA (≥5 swollen joint count + ≥5 tender joint count; CRP ≥0.6 mg/dL) were randomized (1:1:1) to GUS 100mg Q4W; GUS 100 mg at W0, W4, then Q8W; or PBO with crossover to GUS 100 mg Q4W (PBO→Q4W) at W24, all through W100. Radiographic Reading Session 3 included assessments at W0, W24, W52, and W100 (or at discontinuation after W52) from pts continuing study treatment at W52; readers were blinded to treatment group and timepoint. Observed mean changes in total PsA-modified van der Heijde-Sharp (vdH-S), joint space narrowing (JSN), and erosion scores are reported. Changes in total vdH-S scores from W0-100 were deter-

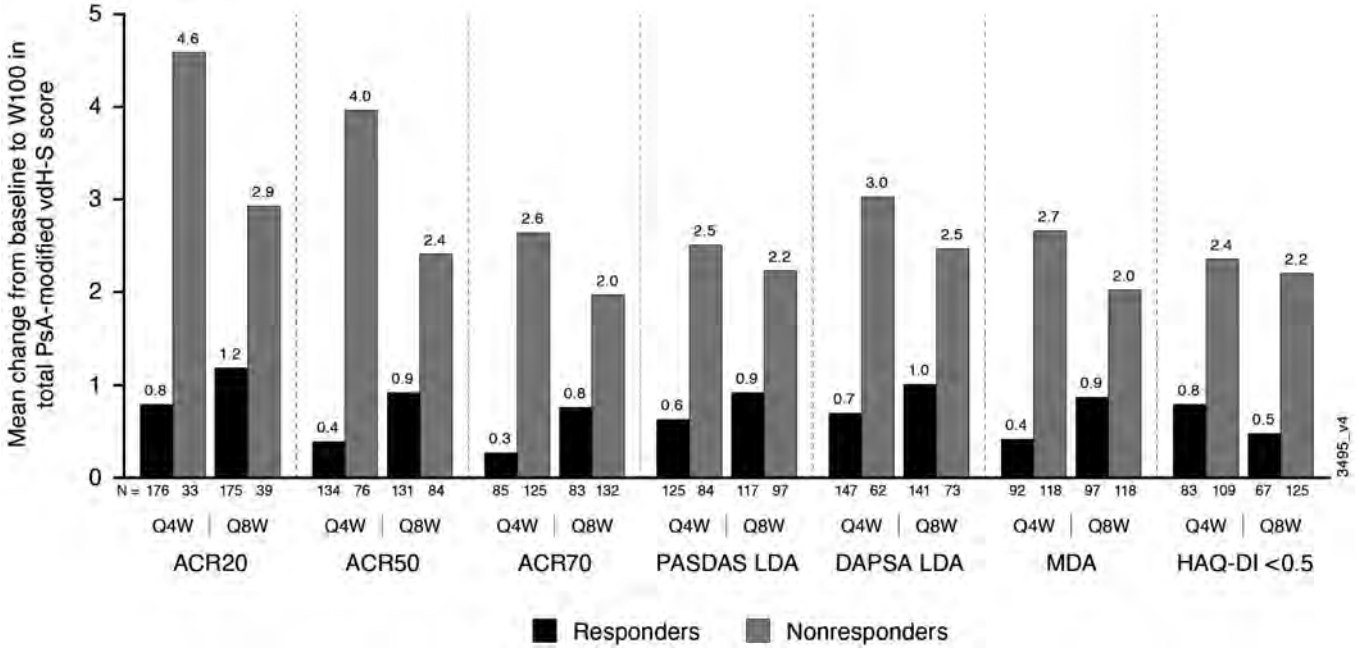

Figure. Mean changes in PsA-modified total vdH-S score from W0-100 for patients who did and did not achieve select clinical responses at W100.

mined in pts who did and did not achieve clinical response at W100, assessed by ACR20/50/70, low disease activity (LDA) based on Disease Activity in Psoriatic Arthritis score (DAPSA; ≤14) or Psoriatic Arthritis Disease Activity Score (PASDAS; ≤3.2), minimal disease activity (MDA), and normalized HAQ-DI score (< 0.5).

Results: Of 739 enrolled and treated pts, 664 had evaluable data from Reading Session 3; 629 pts had evaluable data from W52-100. Mean total baseline vdH-S scores were 28.0 (Q4W), 23.9 (Q8W), and 25.6 (PBOàQ4W). Mean progression of joint damage from W0-24 was numerically lower in GUS- than PBO-treated pts for erosion, JSN, and total vdH-S scores (Table), consistent with the results from Reading Session 1.[1] Mean changes in radiographic scores from W52-100 indicated low rates of radiographic progression across GUS groups. Among GUS-randomized pts, mean changes in vdH-S score from W0-100 were numerically lower for pts achieving clinical response assessed using a variety of outcome measures (ACR20/50/70, DAPSA LDA, PASDAS LDA, MDA, and HAQ-DI < 0.5) when compared with pts not achieving response at W100 (Figure).

Conclusion: In a population of biologic-naïve pts with active PsA enriched for greater risk of radiographic progression, GUS 100 mg (Q4W or Q8W) was associated with low rates of radiographic progression through 2 years. Pts achieving clinical response across several global measures of disease activity or normalized physical function at W100 had lower mean changes in total PsA-modified vdH-S scores compared with nonresponders.

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Abstract Number: 1806

Designing a Phase 3b, Multicenter, Randomized, Double-blind, Placebo-controlled Study to Investigate the Effect of Guselkumab (TREMFYA®/ sup>) Dosing Interval in Psoriatic Arthritis Patients with Inadequate Response to Tumor Necrosis Factor Inhibition

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) are frequently chosen as the first biologic therapy for patients (pts) with PsA, though a sizeable proportion of pts have an inadequate response (IR), and some may also have intolerance. Guselkumab (GUS), a human mAb that targets the IL-23 p19 subunit, provides an alternative mechanism of action by which to treat PsA. In the Phase 3 (Ph3) DISCOVER-1 study of GUS in active PsA, GUS Q4W and Q8W clinical response rates were generally consistent between TNFi-naïve (263 pts) and TNFi-experienced (118 pts) cohorts. In the TNFi-experienced cohort and the limited number of DISCOVER-1 pts with IR to their prior TNFi (N=44), ACR 50% improvement (ACR50) and ACR70 response rates at W24 were numerically higher in GUS Q4W- than Q8W-treated pts.[1] Seeking to further investigate whether GUS Q4W could provide incremental benefit to some TNFi-IR PsA pts, we analyzed the existing DISCOVER-1 dataset to facilitate the design of a new clinical trial.

Table 1. Clinical efficacy at W24 among DISCOVER-1 TNFi-experienced pts

	Placebo	GUS Q8W	GUS Q4W
ACR20	17.9% (7/39)	56.1% (23/41)	57.9% (22/38)
ACR50	5.1% (2/39)	26.8% (11/41)	34.2% (13/38)
ACR70	2.6% (1/39)	2.4% (1/41)	21.1% (8/38)
MDA	2.6% (1/39)	17.1% (7/41)	26.3% (10/38)
IGA 0/1[a]	7.7% (2/26)	48.3% (14/29)	67.9% (19/28)

[a]IGA score of 0 (clear) or 1 (almost clear) among pts with ≥3% BSA of psoriatic involvement and an IGA score ≥2 (mild-to-severe psoriasis) at baseline.

Table 2. Power calculations for SOLSTICE primary endpoint (ACR20 response rate at W24)

Historical Trial Data	ACR20 response rate		Effect size	Power (α=0.05)[b]
	Placebo	GUS Q8W/Q4W		
DISCOVER-1[a]	22%	52% Q8W	30%	>99%
		59% Q4W	37%	>99%

[a]Based on the entirety of the DISCOVER-1 study population (N=381). [b]Based on N=150 per study group (1:1:1 randomization) and 2-sided significance of 0.05 utilizing a Chi-square test to compare treatments.

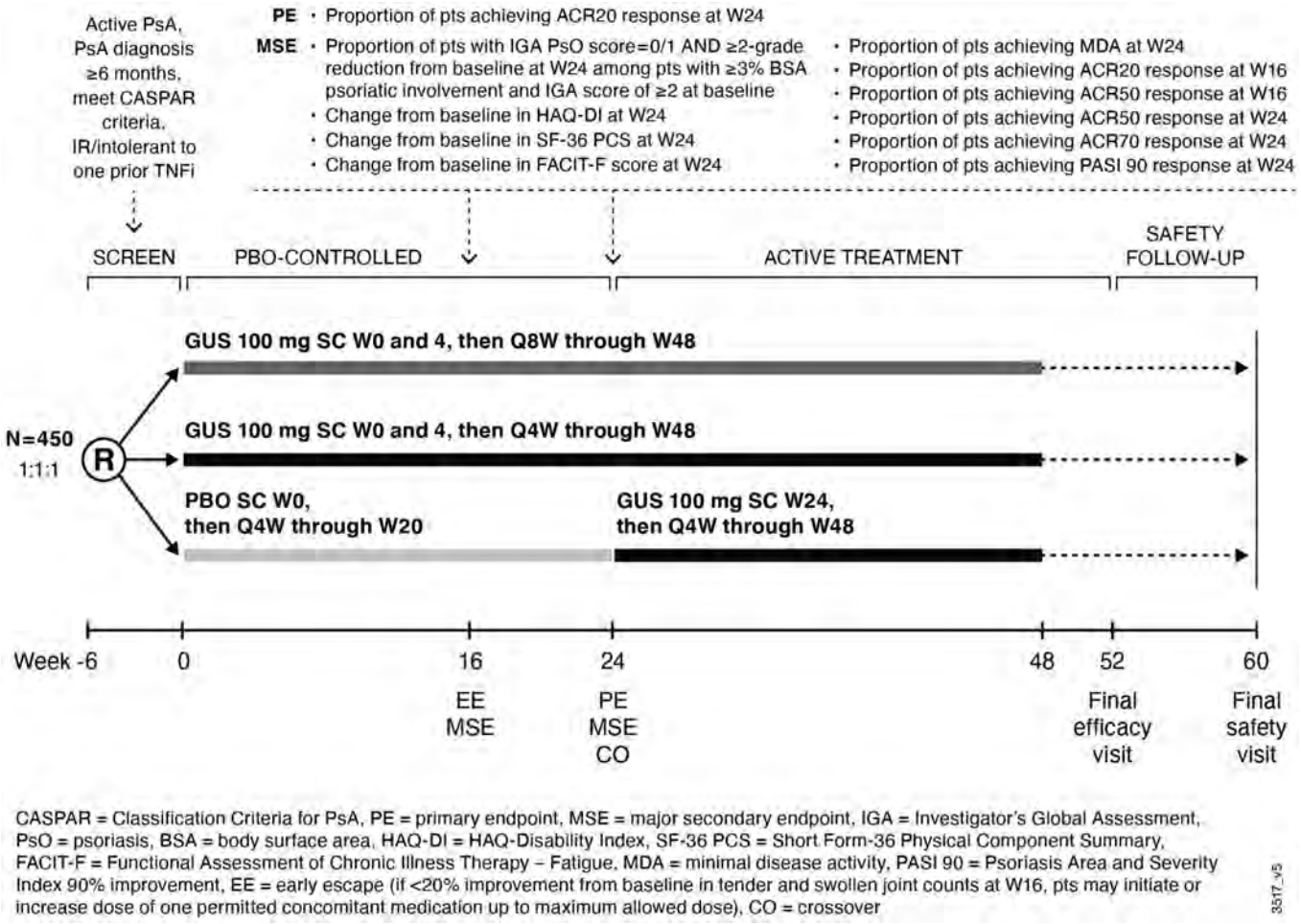

Figure. SOLSTICE study design.

Methods: Study feasibility assessments included comparison of key efficacy endpoints by treatment group at W24 among TNFi-experienced pts receiving GUS Q8W and Q4W in DISCOVER-1. Results from the DISCOVER-1 study also informed sample size power calculations for a primary endpoint of ACR20 response at W24 in a future trial in a TNFi-IR PsA pt population.

Results: Comparison of several efficacy endpoints (ACR70 response, minimal disease activity [MDA], Investigator's Global Assessment [IGA] of psoriasis 0/1 response) across treatment group in the TNFi-experienced DISCOVER-1 cohort supports a potential dose response, with more frequent GUS administration eliciting numerically higher response rates (Table 1). A similar trend was observed for ACR20/50/70 responses in the smaller TNFi-IR population[1], though these findings should be interpreted with caution due to limited sample size. ACR20 response rates at W24 of DISCOVER-1 were employed to estimate sample size requirements for a new study. Assuming comparable rates of GUS treatment effect seen in DISCOVER-1, a sample size of 150 randomized pts per group for PBO, GUS Q8W, and GUS Q4W would provide >90% power to detect a significant difference between each GUS group and PBO for ACR20 response at W24 (Table 2). Based on these findings, a new Ph3b, multicenter, randomized, double-blind, PBO-controlled study, SOLSTICE, was designed to further evaluate the efficacy and safety of GUS in approximately 450 pts with active PsA who had IR to one prior TNFi, and to investigate the effect of GUS dosing interval in this important cohort of pts with PsA (Fig).

Conclusion: PsA pts with TNFi-IR are typically difficult to treat. Overall data from the pivotal DISCOVER-1 trial of GUS in pts with active PsA showed consistent clinical response between doses and between TNFi-naïve and TNFi-

experienced pts. Analyses based on limited numbers of TNFi-experienced pts from DISCOVER-1 demonstrated potential incremental benefit for achievement of higher response criteria with more frequent dosing in some TNFi-IR pts. SOLSTICE, a Ph3b, randomized, placebo-controlled trial, will test this hypothesis.

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Abstract Number: 1807

Relationships Between Fatigue and Hemoglobin/C-Reactive Protein Levels and Associations Between Fatigue and Clinical Response in Patients with Active Psoriatic Arthritis: Results from Two Randomized Controlled Trials of Guselkumab (TREMFYA®)

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table. Mean (SD) of FACIT-F Scores and CRP/Hgb Levels by Visit: Pooled DISCOVER-1 and -2 Studies

Visit	N	FACIT-F	N	CRP (mg/dL)*	Pearson: CRP vs Fatigue*,†	N	Hgb (g/dL)	Pearson: Hgb vs Fatigue†,¥
W0	1119	29.9 (9.96)	1120	1.8 (2.29)	-0.11	1120	13.6 (1.53)	0.16
W8	1111	33.8 (10.04)	1092	1.2 (1.70)	-0.21	1086	13.7 (1.50)	0.20
W16	1102	35.1 (10.11)	1085	1.1 (1.65)	-0.19	1079	13.8 (1.51)	0.21
W24	1094	35.7 (10.33)	1091	1.0 (1.73)	-0.17	1071	13.9 (1.51)	0.20

SD=standard deviation
*Normal range: <0.3 mg/dL
†Determined by Pearson correlation coefficient; p-values derived from hypothesis tests of correlation ρ=0 (ie, no correlation)
¥p<0.0001 at each time point

Background/Purpose: Fatigue is a key patient (pt)-reported symptom of psoriatic arthritis (PsA).[1,2] Utilizing data from the Phase 3 DISCOVER-1 (D1) and -2 (D2) studies, these post hoc analyses explored: 1) correlation of fatigue with systemic inflammation (CRP) and hemoglobin (Hgb); 2) relationship between improvements in fatigue and clinical outcomes with guselkumab (GUS), a selective IL-23p19 inhibitor.

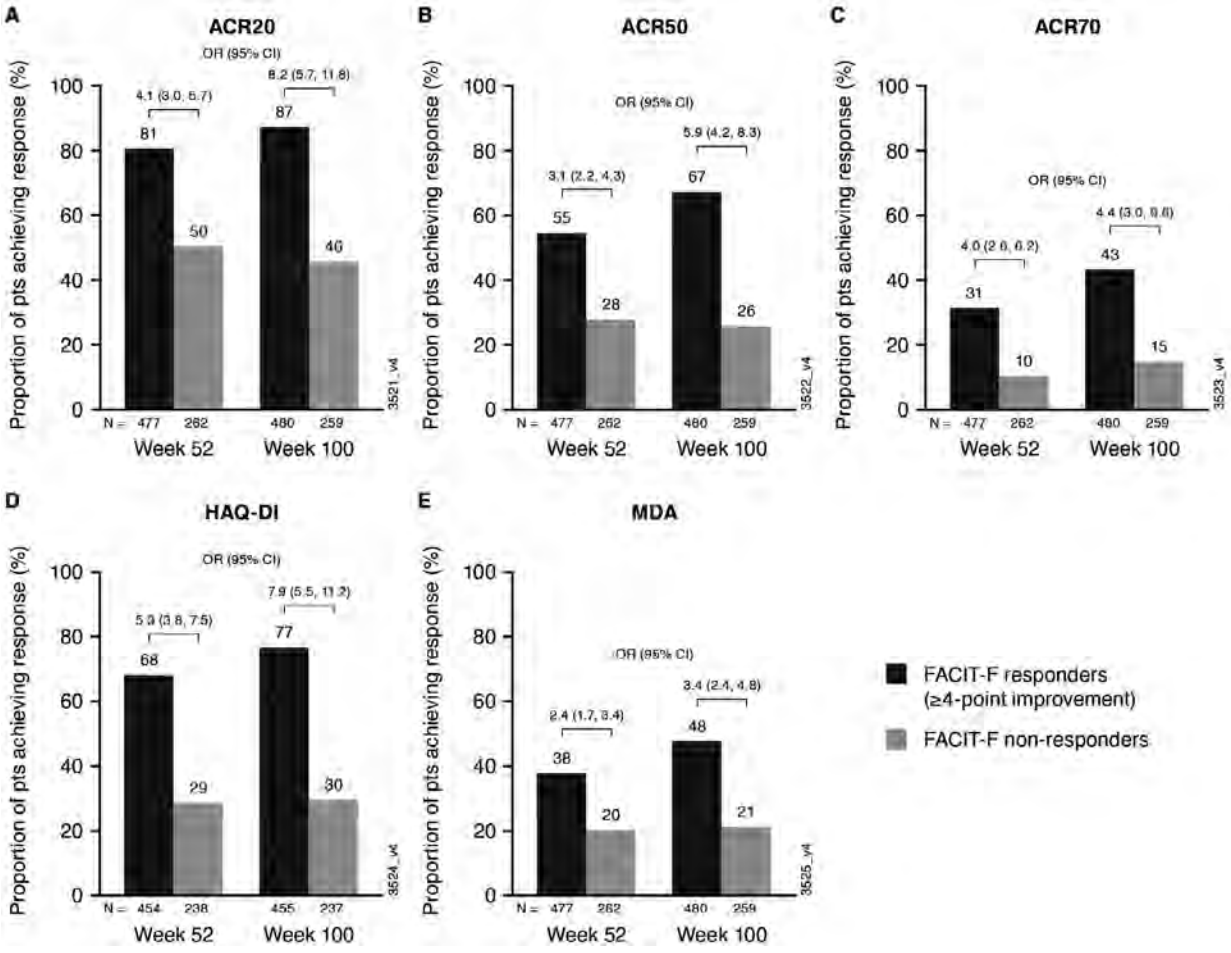

Figure. Achievement of ACR20/50/70, HAQ-DI, and MDA Responses by FACIT-F Response Status Among GUS-treated Patients at W52 and W100 of DISCOVER-2.

Methods: Pts with active PsA despite standard therapies in D1 (swollen joint count [SJC] ≥3, tender joint count [TJC] ≥3, CRP ≥0.3 mg/dL) and D2 (SJC ≥5, TJC ≥5, CRP ≥0.6 mg/dL) were randomized 1:1:1 to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W; or placebo (PBO) with crossover to GUS 100 mg Q4W at W24 (PBOàQ4W). Fatigue was evaluated using the Functional Assessment of Chronic Illness Therapy Fatigue (FACIT-F) scale (0–52 [higher score=less fatigue]; clinically meaningful improvement ≥4 points). FACIT-F scores, as well as their correlation (Pearson) with CRP and Hgb were determined in pts with anemia (Hgb < 13.5 [males] or < 12 [females] g/dL) and without anemia through W24. Relationships between FACIT-F score (outcome) and CRP/Hgb (predictors, along with visit) were assessed via a mixed model for repeated measures (MMRM). Associations between FACIT-F response in GUS-treated pts (Q4W+Q8W+PBOàQ4W) and achievement of American College of Rheumatology (ACR) 20/50/70, Health Assessment Questionnaire Disability Index (HAQ-DI), and Minimal Disease Activity (MDA) responses were evaluated at W52 for D1/D2 and at W100 for D2 (nonresponder imputation).

Results: In pooled analyses (N=1120), mean baseline (BL) FACIT-F scores for 583 males (31.3) and 537 females (28.5) were [3]). Utilizing all pts pooled across treatment groups, significant correlations between FACIT-F scores and mean CRP/Hgb levels were seen at each visit (Table). Through W24, anemic pts had numerically lower FACIT-F scores (28.7-33.3) vs non-anemic pts (30.3-36.3). Among 112 pts with anemia at BL but not at W24, mean FACITF scores improved from 31 (W0) to 37 (W24). MMRM results showed that CRP and Hgb levels were statistically significant predictors of FACIT-F (each p< 0.0001; data not shown). GUS-treated pts achieving ≥4-point improvement in FACIT-F score at W52 (52-62% of 381 pts in D1 and 64-66% of 739 bio-naïve pts in D2) were more likely to also achieve ACR20/50/70, HAQ-DI, and MDA responses than FACIT-F nonresponders (D1 data not shown; D2 Figure). With continued GUS through W100, 65% of D2 pts with FACIT-F response showed an even stronger propensity than FACIT-F nonresponders for achieving ACR20 (odds ratio [OR]=8.2 [5.7, 11.8]), ACR50 (OR=5.9 [4.2, 8.3), ACR70 (OR=4.4 [3.0, 6.6]), HAQ-DI (OR=7.9 [5.5, 11.2]), and MDA (OR=3.4 [2.4, 4.8]) responses vs FACIT-F nonresponders (Figure).

Conclusion: In pts with active PsA, systemic inflammation and Hgb levels were key predictors of FACIT-F scores. FACIT-F responders were more likely to achieve favorable clinical outcomes through up to 2 years of GUS.

References

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Disclosure: P. Rahman, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **L. Gossec**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **A. Kavanaugh**, AbbVie, 5, 12, Expert advice, Amgen, 5, 12, Expert advice, Bristol Myers Squibb, 5, 12, Expert advice, Janssen, 5, 12, Expert advice, Pfizer, 5, 12, Expert advice, UCB, 5, 12, Expert advice, AstraZeneca, 5, 12, Expert advice, Celgene, 5, 12, Expert advice, Roche, 5, 12, Expert advice, Novartis, 5; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Liu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Lin**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11.

Abstract Number: 1808

Guselkumab-Treated Patients with Psoriatic Arthritis Achieved Clinically Meaningful Improvements in General Health Outcomes Measured with PROMIS-29 Through 52 Weeks: Results from the Phase 3 DISCOVER-1 Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

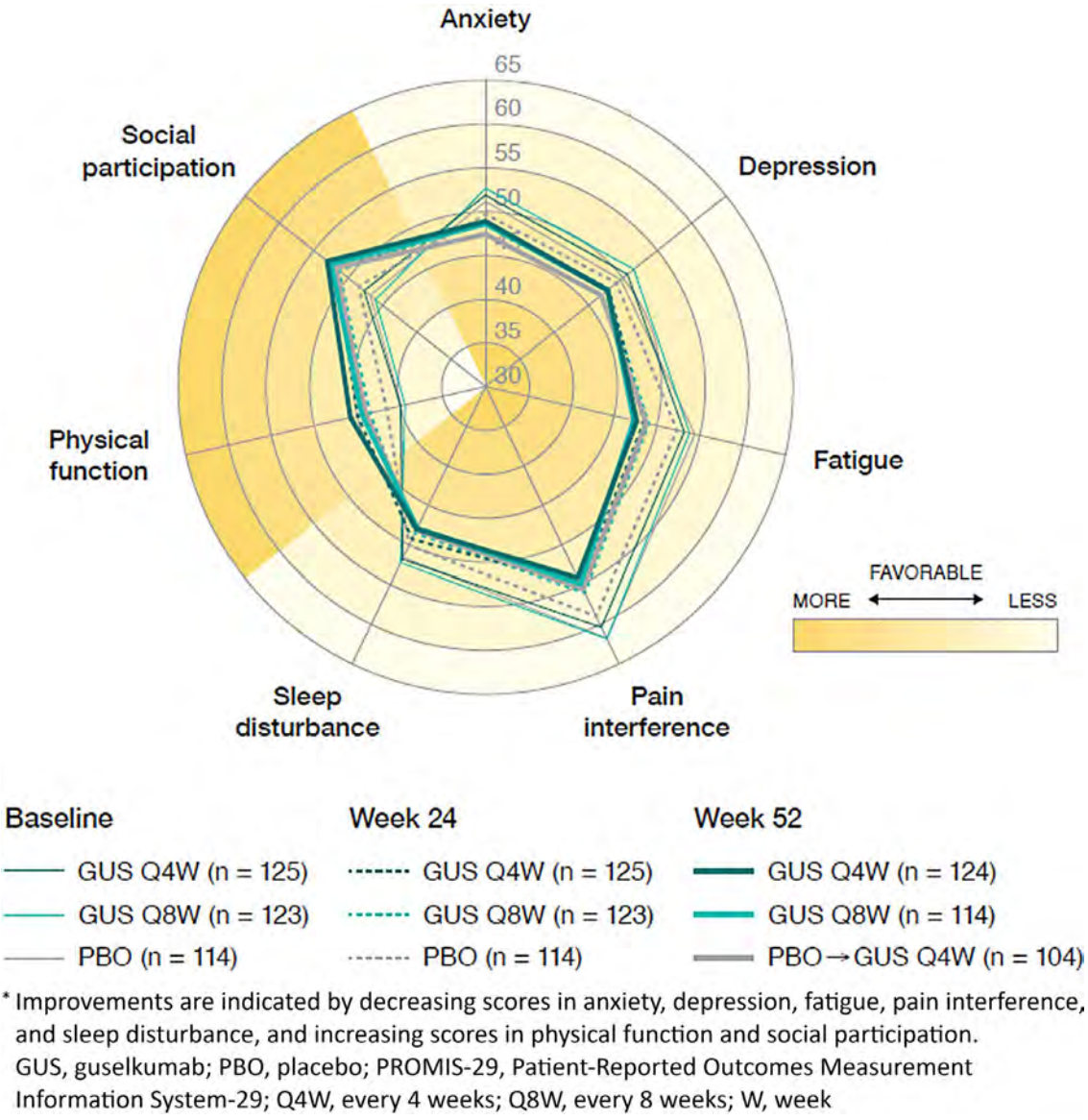
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In the DISCOVER-1 study, the anti-interleukin-23p19-subunit monoclonal antibody guselkumab (GUS) demonstrated robust efficacy across joint and skin clinical manifestations of psoriatic arthritis (PsA).[1] Patients with PsA also experience a broad range of symptoms that negatively impact health-related quality of life (eg, pain, fatigue, anxiety, depression, sleep disturbance, poor physical function).[2] This study assessed the treatment effect of GUS on general health outcomes in patients with PsA in the DISCOVER-1 trial through Week (W) 52 using the Patient-Reported Outcomes Measurement Information System-29 (PROMIS-29) instrument.

Methods: Patients with active PsA (≥3 swollen + ≥3 tender joints; C-reactive protein ≥0.3 mg/dL) and inadequate response to standard conventional therapies were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then Q8W; or placebo (PBO). PBO patients switched to GUS 100 mg Q4W at W24. PROMIS-29 contains 4 items for each of 7 domains (anxiety, depression, fatigue, pain interference, physical function, sleep disturbance, social participation) and 1 pain intensity item; 28 items are scored on a 5-point Likert-type scale, and pain intensity is rated from 0 to 10. The raw score of each domain is converted to a standardized T-score, with norms based on a general population mean score=50 and a standard deviation (SD)=10. Higher scores in anxiety, depression, fatigue, pain interference, and sleep disturbance indicate more severe symptoms; higher physical function and social participation scores indicate better health outcomes. Changes ≥5 points (1/2 SD of T-score) are considered clinically meaningful. Analyses were performed using both observed (mean scores/changes, effect sizes) and imputed (clinically meaningful response, whereby change from baseline was set to 0 at W24/52 for patients who had missing data or at W24 for patients who met treatment failure criteria prior to W24).

Results: At baseline, mean PROMIS-29 T-scores for physical function, social participation, sleep disturbance, pain, and fatigue were worse in the 381 PsA patients enrolled in DISCOVER-1 than in the general US population. Across all 7 domains, observed mean PROMIS-29 T-scores showed improvements in GUS-treated patients from baseline to W24 and W52 (Figure). Observed mean changes from baseline to W24 and W52, with calculated effect size, are shown (Table). In all patients, including those with imputed data, significantly higher percentages of patients in both GUS treatment groups vs PBO had ≥5-point improvements in fatigue, pain interference, physical function, sleep



* Improvements are indicated by decreasing scores in anxiety, depression, fatigue, pain interference, and sleep disturbance, and increasing scores in physical function and social participation.
GUS, guselkumab; PBO, placebo; PROMIS-29, Patient-Reported Outcomes Measurement Information System-29; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week

Figure. Mean PROMIS-29 T-scores at Baseline, W24, and W52 (Observed data)*.

disturbance, social participation, and pain intensity domains at W24 (all nominal $p< 0.05$). Mean improvements in PROMIS-29 domains were maintained through W52.

Conclusion: In patients with active PsA, PROMIS-29 results indicate that GUS treatment was associated with clinically meaningful reductions in fatigue and pain and improvement in physical function and social participation, which were maintained through 1 year.

References

1. Deodhar A, et al. *Lancet*. 2020;395:1115-25
2. Orbai A, et al. *Ann Rheum Dis*. 2017;76:673-80

Table. Mean Change and Effect Size of Change from Baseline in PROMIS-29 Domain Scores at W24 and W52 (Observed Data)

	Mean Change From Baseline [Effect Size]					
	GUS Q4W		GUS Q8W		PBO W0-24	GUS Q4W W24-52
	W24	W52	W24	W52	W24	W52
Anxiety	−3.1 [−0.3]	−3.1 [−0.3]	−3.7 [−0.4]	−4.3 [−0.5]	−1.5 [−0.2]	−3.6 [−0.4]
Depression	−2.7 [−0.3]	−3.0 [−0.4]	−4.0 [−0.4]	−4.0 [−0.4]	−0.6 [−0.1]	−2.5 [−0.3]
Fatigue	−4.8 [−0.5]	−5.6 [−0.6]	−4.8 [−0.5]	−6.8 [−0.7]	−2.1 [−0.2]	−5.7 [−0.6]
Pain interference	−5.4 [−0.8]	−6.2 [−1.0]	−5.8 [−1.0]	−7.0 [−1.1]	−2.8 [−0.4]	−6.3 [−1.0]
Physical function	5.0 [0.8]	5.9 [0.9]	4.1 [0.6]	5.0 [0.7]	1.7 [0.2]	4.2 [0.6]
Sleep disturbance	−2.5 [−0.4]	−3.9 [−0.6]	−3.8 [−0.6]	−4.4 [−0.6]	−1.5 [−0.2]	−3.3 [−0.5]
Social participation	4.2 [0.5]	5.3 [0.7]	5.3 [0.6]	6.6 [0.8]	1.7 [0.2]	4.9 [0.6]
Pain intensity*	−2.3 [−1.2]	−2.8 [−1.5]	−2.1 [−1.1]	−2.7 [−1.4]	−0.7 [−0.4]	−2.5 [−1.3]

*Raw score; all other domains reported as T-score.
GUS, guselkumab; PBO, placebo; PROMIS-29, Patient-Reported Outcomes Measurement Information System-29; Q4W, every 4 weeks; Q8W, every 8 weeks; W, week

Disclosure: A. Orbai, AbbVie, 5, Eli Lilly, 2, 5, Celgene, 5, Novartis, 2, 5, Janssen, 2, 5, Horizon, 5, Pfizer, 2, UCB, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Sheng**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Jiang**, Cytel, Inc., providing statistical support (funded by Janssen), 3; **Y. Liu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11.

Abstract Number: 1809

Efficacy of Tofacitinib on Enthesitis in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Enthesitis (inflammation where the tendon, ligament, or joint capsule insert into the bone) has been associated with higher disease activity and reduced quality of life in patients (pts) with PsA,[1] and is therefore recognized as an important domain to consider during treatment.[2] Tofacitinib, an oral Janus kinase inhibitor for the

Table. Baseline demographics and disease characteristics of patients with LEI > 0, treated with tofacitinib 5 mg BID (green), tofacitinib 10 mg BID (blue), and placebo (purple), stratified by enthesitis location[a] and severity (pooled data from OPAL Broaden and OPAL Beyond)

	Lateral epicondyle humerus	Medial femoral condyle	Achilles' tendon insertion	1 site	2 sites	3–6 sites
Tofacitinib 5 mg BID	(N=102)	(N=94)	(N=87)	(N=37)	(N=47)	(N=73)
Tofacitinib 10 mg BID	(N=119)	(N=100)	(N=92)	(N=31)	(N=37)	(N=95)
Placebo	(N=110)	(N=91)	(N=81)	(N=37)	(N=43)	(N=78)
Female, n (%)	58 (56.9)	49 (52.1)	47 (54.0)	19 (51.4)	26 (55.3)	39 (53.4)
	80 (67.2)	66 (66.0)	55 (59.8)	14 (45.2)	20 (54.1)	66 (69.5)
	68 (61.8)	60 (65.9)	50 (61.7)	15 (40.5)	26 (60.5)	53 (67.9)
Age, yrs, mean (SD)	50.8 (11.8)	49.2 (11.6)	48.7 (12.2)	50.0 (11.6)	49.4 (11.5)	49.7 (12.1)
	50.6 (11.6)	50.2 (11.5)	50.5 (11.6)	48.2 (13.5)	48.4 (11.5)	51.4 (11.3)
	49.2 (13.0)	49.3 (12.3)	49.6 (12.4)	48.1 (13.2)	50.0 (13.0)	49.6 (12.7)
Race, White, n (%)	96 (94.1)	89 (94.7)	83 (95.4)	35 (94.6)	46 (97.9)	69 (94.5)
	112 (94.1)	94 (94.0)	88 (95.7)	28 (90.3)	34 (91.9)	92 (96.8)
	104 (94.5)	85 (93.4)	77 (95.1)	34 (91.9)	41 (95.3)	73 (93.6)
BMI, kg/m^2, mean (SD)	30.2 (6.4)	31.0 (6.9)	30.8 (6.3)	29.1 (7.3)	30.7 (7.1)	30.4 (6.0)
	30.7 (6.3)	31.0 (6.5)	30.6 (6.8)	29.3 (5.6)	29.3 (6.9)	31.1 (6.5)
	29.7 (5.8)	29.5 (5.8)	30.4 (6.1)	29.9 (4.7)	29.3 (5.9)	30.0 (6.2)
PsA duration, yrs, mean (SD)	7.6 (6.6)	9.6 (8.5)	8.7 (7.7)	10.4 (9.4)	7.5 (7.1)	8.5 (7.2)
	6.9 (5.9)	7.5 (5.8)	7.6 (6.3)	7.1 (5.2)	6.8 (6.9)	7.5 (5.9)
	7.5 (6.0)	8.5 (7.8)	8.0 (6.8)	10.0 (8.9)	9.5 (7.1)	6.8 (5.9)
CRP, mg/L, mean (SD)	9.8 (16.1)	11.3 (18.0)	13.8 (22.5)	17.4 (26.9)	17.1 (29.4)	8.3 (8.3)
	11.0 (20.9)	16.3 (29.9)	13.6 (27.8)	14.7 (21.1)	8.9 (15.1)	14.5 (28.7)
	10.6 (21.0)	11.2 (18.9)	10.5 (17.7)	17.7 (33.4)	9.7 (11.3)	9.4 (16.5)
LEI,[b] mean (SD) [N1][c]	3.3 (1.6) [101]	3.4 (1.6)	3.3 (1.7) [86]	1.0 (0.0)	2.0 (0.0)	4.2 (1.1)
	3.7 (1.7)	4.0 (1.6)	3.9 (1.8)	1.0 (0.0)	2.0 (0.0)	4.4 (1.1)
	3.2 (1.6) [109]	3.5 (1.5) [90]	3.3 (1.7) [80]	1.0 (0.0)	2.0 (0.0)	4.1 (1.1)

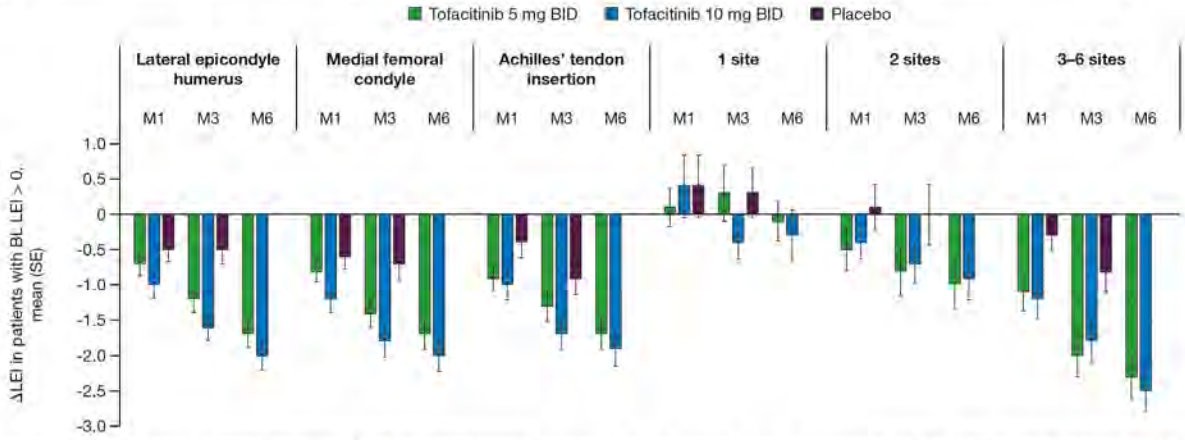
[a]For each site, both left and right sides were assessed and results were combined

[b]Pain was assessed in right and left lateral epicondyle humerus, medial femoral condyle, and Achilles' tendon insertion, and a score was assigned for each location dichotomously, where 0=no pain and 1=pain. LEI is calculated as the sum of those scores, ranging from 0–6, with a score of 6 being the highest enthesitis severity[5]

[c]N1, number of patients with non-missing data and BL LEI > 0

BID, twice daily; BL, baseline; LEI, Leeds Enthesitis Index; N, total number of patients with BL LEI > 0 in that particular location or number of affected sites; n, number of patients applicable for each category; SD, standard deviation

Figure 1. Change from baseline in LEI in patients with baseline LEI > 0, stratified by enthesitis location[a] and severity (pooled data from OPAL Broaden and OPAL Beyond)

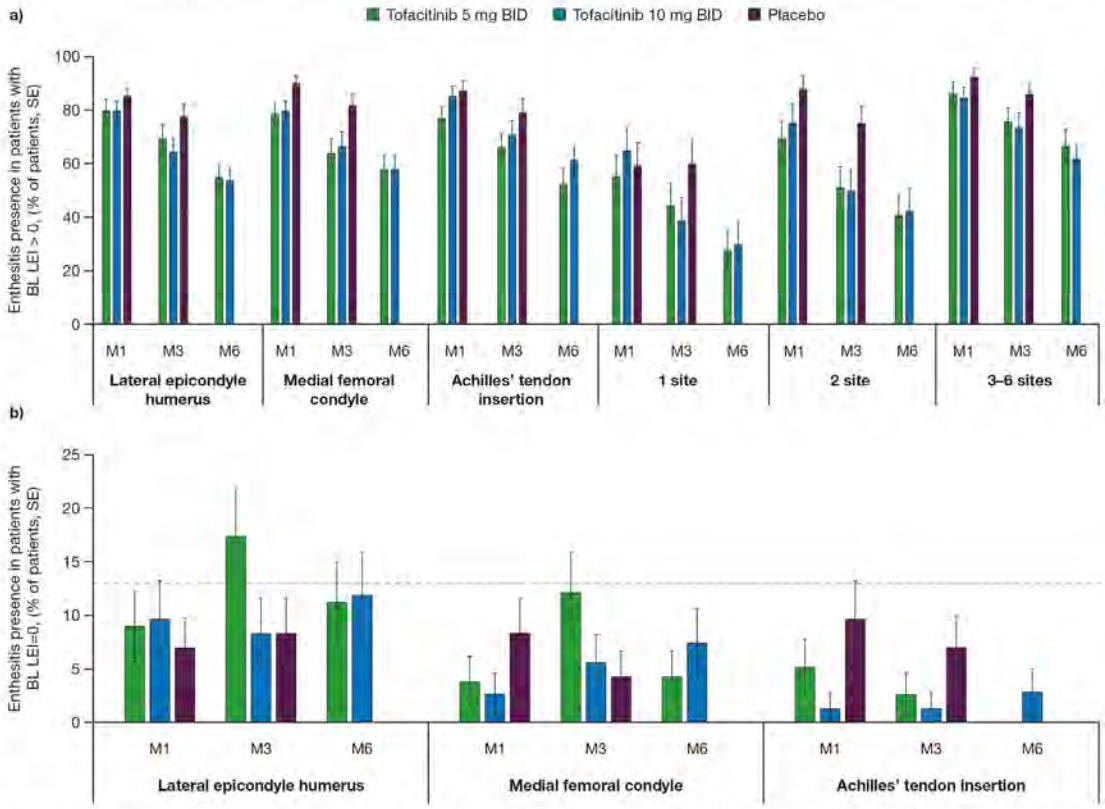


At M1, N ranged from: 99–114 for lateral epicondyle humerus; 88–98 for medial femoral condyle; 80–88 for Achilles' tendon insertion; 15–19 for 1 site; 21–24 for 2 sites; and 44–51 for 3–6 sites. At M3, N ranged from: 96–107 for lateral epicondyle humerus; 83–90 for medial femoral condyle; 71–82 for Achilles' tendon insertion; 15–19 for 1 site; 18–22 for 2 sites; and 41–46 for 3–6 sites. At M6, N ranged from: 95–106 for lateral epicondyle humerus; 88 for both groups for medial femoral condyle; 80 for both groups for Achilles' tendon insertion; 15–19 for 1 site; 19–23 for 2 sites; and 44–46 for 3–6 sites

[a]For each site, both left and right sides were assessed and results were combined

Δ, change from BL; BID, twice daily; BL, baseline; LEI, Leeds Enthesitis Index; M, Month; N, total number of patients with BL LEI > 0 in that particular location or number of affected sites at each visit; SE, standard error

Figure 2. Presence of enthesitis in patients with a) baseline LEI > 0, stratified by location[a] and severity, and b) baseline LEI = 0, by location[a] (pooled data from OPAL Broaden and OPAL Beyond)



Panel a: N is total number of patients with BL LEI > 0 in that particular location or number of affected sites at each visit. At M1, N ranged from: 100–114 for lateral epicondyle humerus; 89–98 for medial femoral condyle; 81–88 for Achilles' tendon insertion; 31–38 for 1 site; 36–46 for 2 sites; and 72–91 for 3–6 sites. At M3, N ranged from: 96–107 for lateral epicondyle humerus; 84–90 for medial femoral condyle; 72–82 for Achilles' tendon insertion; 31–36 for 1 site; 34–43 for 2 sites; and 70–84 for 3–6 sites. At M6, N ranged from: 96–106 for lateral epicondyle humerus; 88 for both groups for medial femoral condyle; 80–82 for Achilles' tendon insertion; 30–36 for 1 site; 31–44 for 2 sites; and 69–84 for 3–6 sites.

Panel b: N is total number of patients with BL LEI=0 at each visit. N ranged from: 72–77 at M1; 71–74 at M3; and 67–71 at M6 for all locations. The dashed line indicates < 13% of patients with BL LEI=0 who had developed enthesitis by M6

[a]For each site, both left and right sides were assessed and results were combined

BID, twice daily; BL, baseline; LEI, Leeds Enthesitis Index; M, Month; SE, standard error

treatment of PsA, has been associated with improvements in enthesitis.[3, 4] Here, we assessed the effects of tofacitinib on enthesitis by location and severity in pts with active PsA.

Methods: This post hoc analysis pooled data from 2 Phase 3 studies: OPAL Broaden (12 months; NCT01877668)[4] and OPAL Beyond (6 months; NCT01882439)[3], in pts with active PsA receiving tofacitinib 5 or 10 mg twice daily (BID) or placebo (up to Month [M]3); pts received a stable background dose of a single conventional synthetic DMARD. Enthesitis at baseline (BL) was defined as Leeds Enthesitis Index (LEI)[5] > 0 (no enthesitis: BL LEI=0); pts were stratified by BL enthesitis location (for each site, both left and right sides were assessed and results were combined) and severity (LEI site counts: 1/2/3–6 sites). Endpoints (assessed at M1/3/6) included change from BL in LEI score and presence of enthesitis. The proportion of pts without BL enthesitis (LEI=0) developing enthesitis at each location was also assessed.

Results: Data were pooled from 479 pts with LEI > 0 and 227 pts with LEI=0 at BL. For pts with BL LEI > 0, demographics and disease characteristics were generally similar across treatment groups (Table). BL LEI scores across all locations were higher in pts treated with tofacitinib 10 mg BID; BL CRP was higher in pts with 2 affected sites treated with tofacitinib 5 mg BID and in pts with 3–6 affected sites treated with tofacitinib 10 mg BID compared with other treatment groups (Table). Improvements in LEI with tofacitinib were observed as early as M1 and maintained up to M6 across all locations and in pts with greater BL enthesitis severity (≥ 2 sites affected; Figure 1). By M3, fewer pts treated with tofacitinib vs placebo had enthesitis, regardless of BL location or severity (Figure 2a). At M6, the proportion of pts with enthesitis at the specified locations was generally reduced by ~ 50%; similar results were reported for pts with lower BL severity (1 or 2 affected sites; Figure 2a). For pts with high BL disease severity (3–6 affected sites), while the proportion of pts with enthesitis decreased over time from BL, enthesitis was present at M6 in about 2/3 of pts (Figure 2a). By M6, < 13% of pts with BL LEI=0 in each treatment group had developed enthesitis (Figure 2b).

Conclusion: In pts with PsA, tofacitinib treatment resulted in improvements in enthesitis, regardless of location or severity. Therefore, tofacitinib is a treatment option for pts with PsA who have enthesitis.

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Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **A. Orbai**, AbbVie, 5, Eli Lilly, 2, 5, Celgene, 5, Novartis, 2, 5, Janssen, 2, 5, Horizon, 5, Pfizer, 2, UCB, 2; **O. FitzGerald**, Novartis, 5, 6, UCB, 5, 6, Pfizer, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Lilly, 5, 6, Biogen, 6, Eli Lilly, 5, 6; **M. Bedaiwi**, AbbVie, 6, Pfizer Inc, 6; **D. Fleishaker**, Pfizer Inc, 3, 11; **R. Mundayat**, Pfizer Inc, 3, 11; **P. Young**, Pfizer Inc, 3, 11; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1.

Abstract Number: 1810

Current Medication Practices and Preferences Among Patients with Psoriatic Arthritis (PsA)

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The advent of targeted synthetics and biologics has greatly broadened the options for effective treatment in PsA. Guidelines published in 2018 by the American College of Rheumatology/National Psoriasis Foundation (ACR/NPF) support the use of biologic agents, including as initial therapy. Despite clear directives, there is a paucity of data regarding medication use in real world clinical practice and patient medication preferences.

Methods: This is a cross-sectional survey of Classification Criteria for Psoriatic Arthritis (CASPAR) criteria defined PsA patients recruited from a single academic center PsA registry from June-September 2020. Preferences were ranked on a 5-point Likert scale ranging from 'not at all important' to 'extremely important.'

Results: One hundred thirty-seven(29%) PsA patients responded. Median age was 60 years (IQR 51-70). Median duration of PsA skin symptoms, joint symptoms and PsA diagnosis by a physician was 19 (IQR 10-34), 12 (IQR 8-21) and 8 (IQR 4-17) years, respectively.
Non-steroidal anti-inflammatory drugs were the first medication used for PsA in 62%. The most common initial immunomodulatory medications were anti-TNF-α (35%), followed by methotrexate (19%), anti-phosphodiesterase-4 (anti-PDE4) (12.4%), other conventional synthetic disease modifying anti-rheumatic medications (csDMARDs) (11.7%), anti-IL17 (5.1%), and anti-IL23 (2.9%). At survey administration, the most common immunomodulatory therapies were anti-TNF-α (30%), followed by anti-IL17 (20.4%), methotrexate (10.2%), anti-PDE4 (8.8%), other csDMARDs (8.0%), Janus kinase inhibitors (2.2%), and anti-cytotoxic T-lymphocyte-associated protein 4 (CTLA 4) (1.5%), while 28% of patients were not on any immunomodulatory therapy. After 2018, when updated guidelines from the ACR/NPF were published, a significantly higher percentage of patients' first medication was an anti-IL17 compared to 2018 or earlier (30% vs 3.5% $p< 0.001$); a pattern also seen with anti-PDE4 (40% vs 11.5% $p< 0.012$).
Medication preferences most ranked as "extremely" important were prevention of joint damage, (80%), ability to perform daily activities (71%), prevention of pain (70%), rheumatologist recommendation (63%) and medication side effects (62%).

Conclusion: The significant increase of anti-IL17 and anti-PDE4 medications as initial treatment after 2018 may reflect their inclusion as potential initial therapy in updated guidelines, along with the importance placed by patients on medication side effects. Surprisingly, over a quarter of patients were not on any immunomodulatory therapy. Given the expanding armamentarium of PsA medications, it is increasingly important to align patient preferences and therapeutic options to ensure durable use of effective therapy.

Disclosure: M. Schwartzman, None; **Z. Abutalib**, None; **L. Mandl**, Regeneron Pharmaceuticals, 5.

Abstract Number: 1811

Efficacy of Guselkumab Across BASDAI Components in Treating Axial-Related Symptoms of Psoriatic Arthritis: Results from Two Phase 3, Randomized, Placebo-controlled Studies

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), an anti-interleukin-23p19 subunit monoclonal antibody, is approved to treat psoriatic arthritis (PsA). Post hoc analyses of DISCOVER-1&2 suggested that GUS may be effective in improving symptoms of axial manifestation of PsA. This study evaluated the efficacy of GUS across components of the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in improving symptoms of axial manifestations of active PsA patients using data from phase-3, randomized, placebo (PBO)-controlled studies.

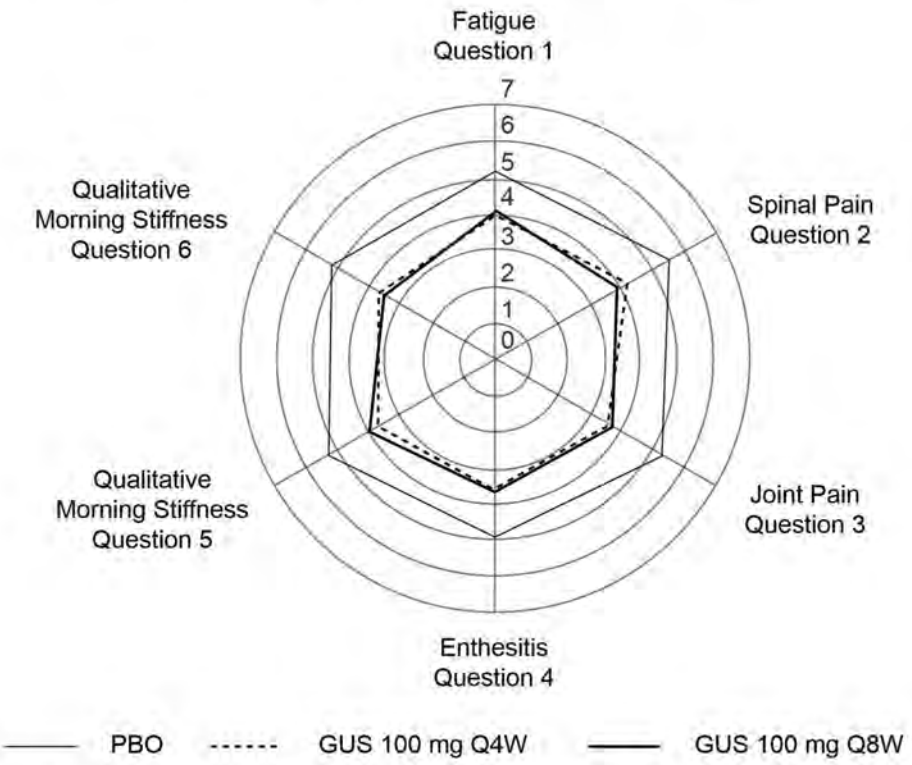
Methods: In DISCOVER-1&2, patients with active PsA were randomized to subcutaneous injections of GUS 100 mg every 4 weeks (Q4W) or at Week 0, 4, and Q8W, or PBO. These post hoc analyses included patients who were identified by the investigator as having axial symptoms and sacroiliitis (prior X-ray or MRI or screening X-ray). BASDAI scores were assessed at Weeks 0, 8, 16, 24, and 52. Mean BASDAI component scores through Week 52 are reported

Table: Baseline demographic and disease characteristics for patients who were identified by physicians as having symptoms consistent with spondylitis and had sacroiliitis confirmed via prior radiograph/MRI or screening radiograph

	GUS Q4W	GUS Q8W	Placebo
Patients, n	103	91	118
Male, n (%)	68 (66)	54 (59)	69 (59)
Age, years	44.9 ± 11.8	45.0 ± 10.7	45.3 ± 11.0
BASDAI			
Patients, n	95	84	110
Score	6.4 ± 1.7	6.5 ± 1.8	6.6 ± 1.5
BASDAI Components			
Fatigue	6.4 ± 2.0	6.7 ± 1.9	6.5 ± 1.9
Spinal pain	6.6 ± 2.1	6.5 ± 2.3	6.7 ± 2.0
Joint pain	6.3 ± 1.9	6.5 ± 2.2	6.8 ± 1.7
Enthesitis	6.3 ± 2.1	6.4 ± 2.2	6.3 ± 2.2
Qualitative morning stiffness	6.8 ± 2.1	6.7 ± 2.5	7.0 ± 2.0
Quantitative morning stiffness	6.2 ± 2.9	5.7 ± 2.9	6.1 ± 2.8

Data are mean ± standard deviation unless otherwise noted.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; GUS, guselkumab; MRI, magnetic resonance imaging; Q4W, every 4 weeks; Q8W, every 8 weeks

Figure. Mean scores of BASDAI components at week 24, DISCOVER-1 and DISCOVER-2



BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; GUS, guselkumab; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks

by treatment group. Pooled data from the two studies are reported. Mean BASDAI component scores are reported using observed data; total BASDAI scores with missing components were set to missing. The proportion of patients achieving ≥50% improvement in BASDAI (BASDAI 50) was also determined; patients with missing data or who met the treatment failure criteria (discontinued study agent or used prohibited medications) were considered nonresponders at all subsequent timepoints.

Results: These analyses included 312 patients from DISCOVER-1&2 (103 GUS Q4W, 91 GUS Q8W, 118 PBO); mean total BASDAI scores at Week 0 were 6.4, 6.5, and 6.6, respectively. Demographics and mean baseline BASDAI component scores (ie, fatigue, spinal pain, joint pain, enthesitis, qualitative morning stiffness, and quantitative morning stiffness) were similar across treatment groups (Table). In comparison with the total study population, this subgroup of patients had a higher mean C-reactive protein level at baseline and a higher proportion of patients with enthesitis and included a slightly higher proportion of males. Mean scores for all six BASDAI components, including spinal pain, decreased through Week 24 in GUS-treated patients, with separation from PBO observed as early as Week 8; improvements were maintained at Week 52. At Week 24, BASDAI 50 response rates were higher in the Q4W and Q8W groups versus PBO (38% and 40% versus 19%).[1] At Week 52, mean BASDAI component scores for PBO patients who crossed over to GUS Q4W at Week 24 were similar to those for patients who were randomized to GUS.[2] A similar trend was observed for BASDAI 50 response.

Conclusion: Among PsA patients with axial symptoms and sacroiliitis (via investigator-confirmed imaging) in the DISCOVER-1&2 trials, GUS treatment resulted in lower mean scores for all six BASDAI components compared with PBO as early as Week 8 and through Week 24, with mean scores maintained at Week 52.

References

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Disclosure: F. Behrens, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, AbbVie, 2, 6, Boehringer Ingelheim, 2, 6, Eli Lilly, 2, 6, Galapagos, 6, Genzyme, 2, 6, Gilead, 2, 6, Janssen, 2, 5, 6, MSD, 2, 6, Novartis, 2, 6, Sanofi-Aventis, 2, 6, UCB, 2, 6, Amgen, 2, 6, Bionorica, 5, Sandoz, 2, 6, Bristol Myers Squibb, 2, 6; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Noel**, Janssen Global Services, LLC, 3, 12, Owns stock in Johnson & Johnson; **S. Chakravarty**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Xu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **Y. Wang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **X. Baraliakos**, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2.

Abstract Number: 1812

Correlations Between Reductions in Fatigue Severity and Improvements in Physical Function and Clinical Response in Patients with Psoriatic Arthritis: Results from the Phase 3 DISCOVER Program

Arthur Kavanaugh[1], Yan Liu[2], Atul Deodhar[3], Proton Rahman[4], Philip Mease[5], Philip S Helliwell[6], Laure Gossec[7], Alexa Kollmeier[8], Elizabeth Hsia[2], May Shawi[9] and Chenglong Han[2], [1]Division of Rheumatology, Allergy and Immunology, Department of Medicine, University of California San Diego, La Jolla, CA, [2]Janssen Research & Development, LLC, Spring House, PA, [3]Oregon Health & Science University, Portland, OR, [4]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [5]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [6]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [7]Sorbonne Université and Hôpital Pitié-Salpêtrière, Paris, France, [8]Janssen Research & Development, LLC, La Jolla, CA, [9]Janssen Immunology Global Commercial Strategy Organization, Toronto, ON, Canada

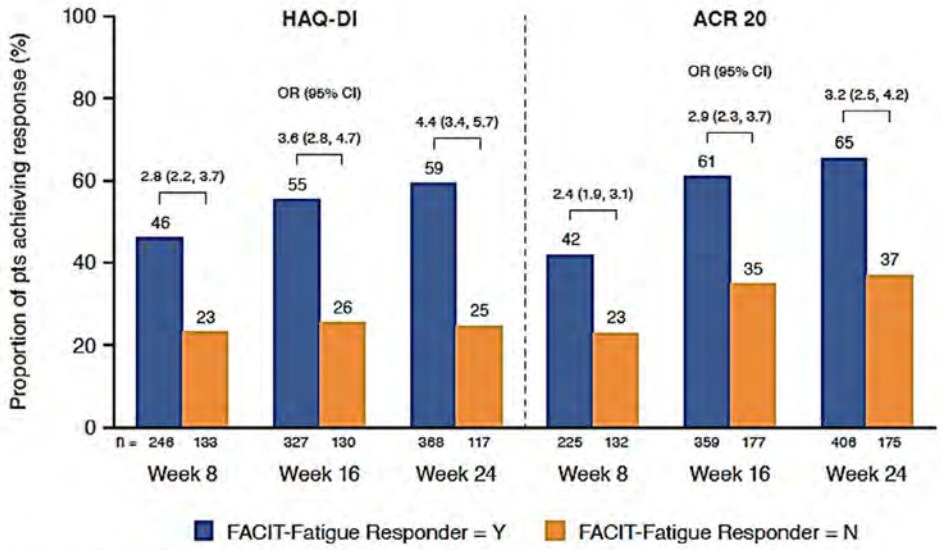
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Table. Correlation* of FACIT-Fatigue and HAQ-DI

Visit	HAQ-DI and FACIT Fatigue Scores	Changes From Baseline in HAQ-DI and FACIT-Fatigue Scores
W8	−0.61 (p<0.0001)	−0.42 (p<0.0001)
W16	−0.60 (p<0.0001)	−0.47 (p<0.0001)
W24	−0.62 (p<0.0001)	−0.50 (p<0.0001)

*Determined by Pearson correlation coefficient; p-values derived from hypothesis tests of correlation ρ=0 (ie, no correlation).
FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire-Disability Index; W, week.

Figure. HAQ-DI and ACR 20 Responders by FACIT-Fatigue Responder Status (Y/N)



ACR 20, American College of Rheumatology 20% improvement; CI, confidence interval; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire-Disability Index; OR, odds ratio; pts, patients.

Background/Purpose: In patients (pts) with PsA, fatigue is a major driver of perceived impact of disease and has been identified as an important domain to be assessed in clinical trials.[1,2] The association between fatigue and other PsA domains (eg, physical function) or clinical response is not well understood. Fatigue was measured with the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue questionnaire in the pivotal DISCOVER-1 & -2 phase 3 studies of guselkumab (GUS) vs placebo (PBO). This post hoc analysis explores the correlation between FACIT-Fatigue and physical function and clinical response in the DISCOVER program.

Methods: This analysis used pooled data from pts (N=1120) treated with GUS or PBO. In DISCOVER-1 & -2, 381 pts with active PsA (swollen joint count [SJC] ≥3, tender joint count [TJC] ≥3, CRP ≥0.3 mg/dL) and 739 pts with active PsA (SJC ≥5, TJC ≥5, CRP ≥0.6 mg/dL) and inadequate response to standard therapies, respectively, were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week (W) 0, W4, then Q8W; or PBO. PBO pts switched to GUS 100 mg Q4W at W24. The FACIT-Fatigue questionnaire has 13 items that assess self-reported fatigue/tiredness over the last 7 days. Items are scored from 0 (very much fatigued) to 4 (not at all fatigued). FACIT-Fatigue response was defined as an increase of ≥4 points from baseline. Physical function was evaluated with the Health Assessment Questionnaire-Disability Index (HAQ-DI). HAQ-DI response was defined as a decrease of ≥0.35 points from baseline. Clinical response was defined as achievement of ACR 20 criteria. Relationships between FACIT-Fatigue and HAQ-DI at W8/16/24 were assessed by Pearson correlation coefficients. Mean changes in HAQ-DI scores at W8/16/24 were summarized in FACIT-Fatigue responders and nonresponders. A logistic regression model was applied to estimate odds ratios (ORs) for achievement of HAQ-DI and ACR 20 response by FACIT-Fatigue response status at each visit. A multiple linear regression model was used to evaluate the association between FACIT-Fatigue and HAQ-DI at W24 after adjusting for SJC, TJC, CRP, and pt assessment of pain.

Results: FACIT-Fatigue and HAQ-DI scores and changes from baseline were negatively correlated at W8, W16, and W24 (Table). Mean changes in HAQ-DI were –0.31, –0.43, and –0.48 at W8, W16, and W24, respectively, in FACIT-Fatigue responders and –0.06, –0.07, and –0.09, respectively, in FACIT-Fatigue nonresponders. FACIT-Fatigue responders were significantly more likely than nonresponders to achieve HAQ-DI and ACR 20 response (OR [95% CI] at W8, 2.8 [2.2-3.7] and 2.4 [1.9-3.1]; at W16, 3.6 [2.8-4.7] and 2.9 [2.3-3.7]; and at W24, 4.4 [3.4-5.7] and 3.2 [2.5-

4.2], respectively; Figure). Correlations between FACIT-Fatigue and HAQ-DI remained significant after adjusting for SJC, TJC, CRP, and pt assessment of pain.

Conclusion: In pts with PsA, fatigue response is a clinically meaningful predictor of improvements in physical function and achievement of ACR 20 response, reinforcing the importance of assessing fatigue in PsA disease management.

References

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Disclosure: A. Kavanaugh, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **Y. Liu**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **P. Helliwell**, Pfizer Inc, 1, Novartis, 6, Janssen, 1, 6, AbbVie, 6, Galapagos, 1, Eli Lilly, 1; **L. Gossec**, Galapagos, 5, Sandoz, 5, Sanofi, 5, AbbVie, 2, Amgen, 2, 5, Bristol Myers Squibb, 2, Biogen, 2, Celgene, 2, Eli Lilly, 2, 5, Gilead, 2, Janssen, 2, 5, Novartis, 2, Pfizer, 2, 5, Samsung Bioepis, 2, Sanofi-Aventis, 2, UCB, 2; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11.

Abstract Number: 1813

Clinical Characteristics & Outcomes Associate with Work Productivity in Bio-naïve Patients with Active Psoriatic Arthritis Through Week 24 of the DISCOVER-2 Study

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SESSION INFORMATION

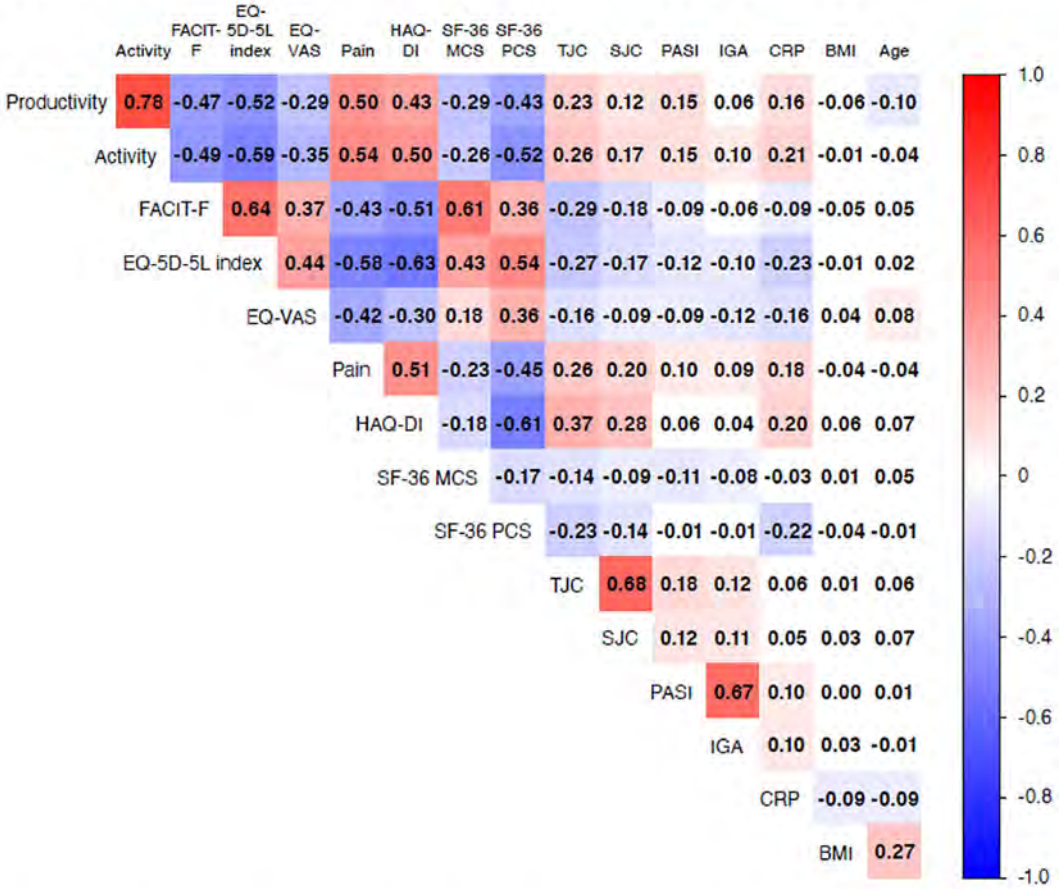
Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Figure. Spearman correlations between pt/disease characteristics & WPAI domains at W0



BMI, body mass index; CRP, C-reactive protein; EQ-5D-5L index, EuroQoL-5 dimension questionnaire index; EQ-VAS, EQ5D visual analog scale; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; IGA, Investigator's Global Assessment; PASI, Psoriasis Area Severity Index; pt, patient; SF-36 MCS, Short Form-36 Mental Component Summary; SF-36 PCS, Short Form-36 Physical Component Summary; SJC, swollen joint count; TJC, tender joint count; W, week; WPAI, Work Productivity & Activity Impairment

Table. Multivariate analysis of clinical characteristics/outcomes & WPAI domains at W0 & W24

Parameter	Absenteeism[a]		Presenteeism[a]		Productivity Loss[a]		Activity Impairment[b]	
	Estimate	p-value	Estimate	p-value	Estimate	p-value	Estimate	p-value
Age	-0.05	0.42	-0.27	**<0.001**	-0.28	**<0.001**	-0.06	0.17
Female	0.91	0.46	-1.54	0.22	-1.74	0.20	2.38	**0.02**
CRP	0.73	**0.04**	0.97	**0.01**	1.01	**0.01**	0.89	**<0.001**
FACIT-F	-0.31	**<0.001**	-0.67	**<0.001**	-0.73	**<0.001**	-0.75	**<0.001**
Pain	1.03	**<0.001**	4.15	**<0.001**	4.25	**<0.001**	4.02	**<0.001**
PASI	0.06	0.36	0.16	**0.02**	0.14	**0.05**	0.15	**0.003**
SJC	0.08	0.48	-0.05	0.61	-0.05	0.66	0.03	0.75
TJC	-0.10	0.13	0.11	0.09	0.09	0.19	0.10	**0.04**
Dactylitis (Y/N)	-1.10	0.39	2.47	**0.05**	2.58	**0.05**	0.54	0.57
Enthesitis (Y/N)	1.52	0.20	2.38	**0.04**	2.99	**0.01**	2.40	**0.01**

[a]Pts working at baseline

[b]All pts in study

CRP, C-reactive protein; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; N, no; PASI, Psoriasis Area Severity Index; Pts, patients; SJC, swollen joint count; TJC, tender joint count; W, week; WPAI, Work Productivity & Activity Impairment; Y, yes

Background/Purpose: PsA, a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis and skin/nail psoriasis, causes impaired physical function, disability, and loss of work productivity. We evaluated associations between PsA clinical characteristics and outcomes including fatigue and work productivity using Work Productivity & Activity Impairment Questionnaire: PsA (WPAI-PsA).

Methods: Phase 3 DISCOVER-2 trial assessed guselkumab (GUS), an anti-IL-23p19-subunit human mAb, in bio-naïve adults with active PsA (swollen joint count [SJC] ≥5, tender joint count [TJC] ≥5, CRP ≥0.6 mg/dL) despite standard therapies.[1] Patients (Pts) were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week (W)0, W4, then Q8W; or placebo (PBO). WPAI-PsA assesses PsA-related work time missed (absenteeism), impairment while working (presenteeism), productivity loss (absenteeism+presenteeism), and daily activity during previous week. Spearman correlation testing evaluated relationships between pt demographics & PsA disease characteristics and WPAI domain scores based on observed values at baseline. Univariate linear regression assessed associations between WPAI, and these variables based on observed data at W0 and W24. Variables with $p< 0.10$ were included in a multivariate analysis employing a mixed-effects model for repeated measures, controlling for all other variables; resulting p-values < 0.05 were considered statistically significant.

Results: As reported,[2] least-squares mean % changes from baseline at W24 were -3.8/-19.5/-20.0/-20.5 for GUS Q4W, -3.1/-19.4/-19.7/-21.5 for GUS Q8W, and -3.5/-10.2/-10.9/-10.3 for PBO for absenteeism, presenteeism, absenteeism+presenteeism, and daily activity impairment, respectively. Among 738 pts, WPAI domain scores were moderately to strongly correlated (ie, ≥0.4) with pt-reported pain (0-10 visual analog scale), physical function (Health Assessment Questionnaire-Disability Index [HAQ-DI]), fatigue (Functional Assessment of Chronic Illness Therapy-Fatigue [FACIT-F] scale) and 36-Item Short Form Health Survey (SF-36) Physical Component Summary (PCS) score, but weakly correlated with other variables (Figure). Based on univariate analyses and evaluation of collinearity between variables, attributes included in multivariate models were age, BMI, gender, CRP, FACIT-F, pain, Psoriasis Area Severity Index (PASI), TJC, SJC, enthesitis and dactylitis. In final model, CRP, FACIT-F, and pain were statistically significantly associated with all WPAI domains (Table). Presence of enthesitis and higher PASI score were significantly associated with higher loss of work productivity and activity outside work.

Conclusion: In PsA pts, extra-articular symptoms, fatigue, pain, and elevated CRP were significantly associated with WPAI-assessed work and activity impairment. Treating all major clinical manifestations of PsA is needed to improve work and activity impairment. GUS effectively treats all major clinical manifestations[1] and improves work and activity impairment in PsA.[2]

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1. Mease P. *Lancet* 2020;395:1126-36
2. Curtis J. *ACR* 2020; Poster 0332

Disclosure: J. Curtis, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **F. Yang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Peterson**, Janssen, 3, 11; **P. Agarwal**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson

& Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1814

Patient Characteristics and Clinical Features Associate with Health-Related Quality of Life in Bio-naïve Patients with Active Psoriatic Arthritis Through Week 24 of the DISCOVER-2 Study

Jeffrey Curtis[1], Iain McInnes[2], Proton Rahman[3], Dafna Gladman[4], Feifei Yang[5], Steven Peterson[6], Prasheen Agarwal[7], Alexa Kollmeier[8], Elizabeth Hsia[9], Chenglong Han[9], May Shawi[10], William Tillett[11] and Philip Mease[12], [1]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, [2]University of Glasgow, School of Medicine, Glasgow, Scotland, United Kingdom, [3]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [4]Schroeder Arthritis Institute, Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [5]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [6]Janssen Immunology Global Commercial Strategy Organization, Raritan, NJ, [7]Department of Biostatics, Janssen Research & Development, LLC, Spring House, Spring House, PA, [8]Janssen Research & Development, LLC, La Jolla, CA, [9]Janssen Research & Development, LLC, Spring House, PA, [10]Janssen Immunology Global Commercial Strategy Organization, Toronto, ON, Canada, [11]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [12]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA

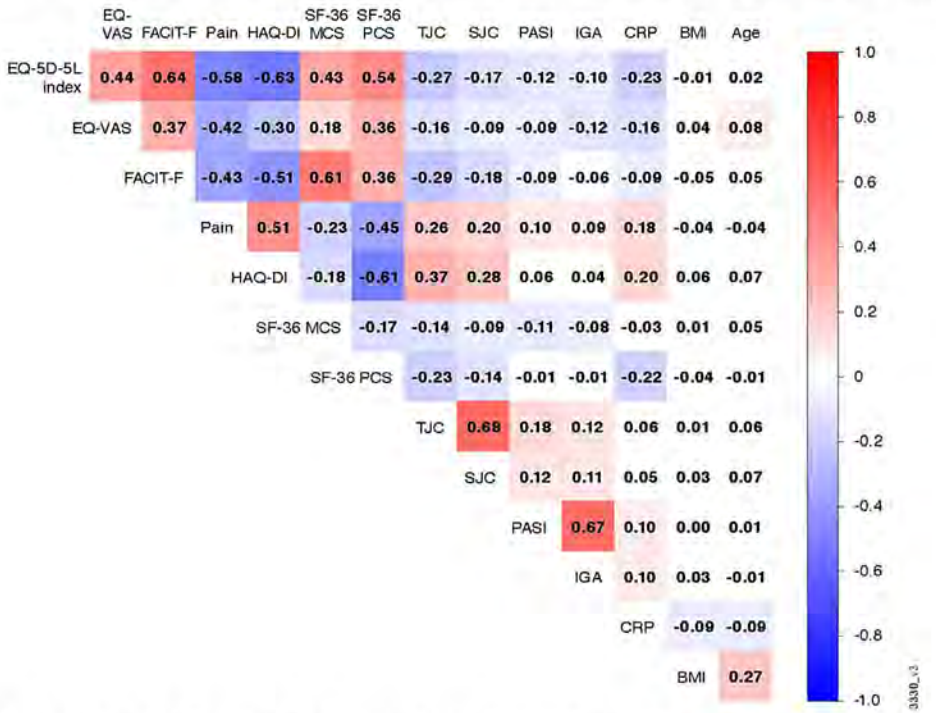
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: PsA is a chronic inflammatory disease characterized by peripheral arthritis, axial inflammation, dactylitis, enthesitis, & skin/nail psoriasis. Patients (pts) with PsA often experience reduced health-related quality of life (HRQoL) due to these features. Using EuroQoL-5 dimension-5 level (EQ-5D-5L) questionnaire index & visual analog scale (EQ-VAS) scores, we assessed HRQoL in PsA pts & its association with pt characteristics & clinical features of PsA, including fatigue.

Methods: The phase 3 DISCOVER-2 trial evaluated guselkumab (GUS), an anti-IL-23p19-subunit mAb, in bio-naïve adults with active PsA (swollen joint count [SJC] ≥5, tender joint count [TJC] ≥5, CRP ≥0.6 mg/dL) despite standard therapies.[1] Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week (W) 0, W4, then Q8W; or placebo (PBO). EQ-5D-5L index assesses mobility, self-care, usual activities, pain/discomfort, & anxiety/depression. EQ-VAS assesses pt health state. Spearman correlation testing was used to evaluate relationships between baseline (BL) pt characteristics & PsA clinical features & BL EQ-5D-5L index & EQ-VAS scores (Fig). Employing absolute observed scores at W0 & W24, univariate linear regression was used to assess the association between EQ-5D-5L index & EQ-VAS scores & pt characteristics/PsA clinical features. Variables with $p < 0.20$ in the univariate analysis were included in a multivariate analysis employing mixed-effect model for repeated measures (MMRM), controlling for all other variables; $p < 0.05$ was considered statistically significant. Least-squares (LS) mean changes in EQ-5D-5L index & EQ-VAS were assessed at W24 using MMRM.

Results: Among 738 pts, BL EQ-5D-5L index & EQ-VAS scores were moderately to strongly correlated (≥0.4) with BL pt-reported pain (0-10 VAS), physical function (HAQ-Disability Index [DI]), fatigue (Functional Assessment of Chronic

Figure. Spearman correlations between BL pt characteristics/clinical features & BL EQ-5D-5L index & EQ-VAS scores at W0



BL, baseline; BMI, body mass index; CRP, C-reactive protein; EQ-5D-5L, EuroQoL-5 dimension-5 level questionnaire; EQ-VAS, EuroQoL-visual analog scale; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; IGA, Investigator's Global Assessment; MCS, mental component summary; PCS, physical component summary; PASI, Psoriasis Area & Severity Index; SF, Short Form Health Survey; W, week; SJC, swollen joint count; TJC, tender joint count

Illness Therapy-Fatigue [FACIT-F] scale), & 36-item Short Form Health Survey (SF-36) physical & mental component summary (PCS & MCS) scores; & weakly correlated with other variables (Fig). Based on univariate analyses ($p < 0.20$) & evaluation of collinearity between variables, attributes at W0 & W24 included in the multivariate models were age, sex, CRP, FACIT-F, pain, Psoriasis Area & Severity Index (PASI) score, TJC, SJC, enthesitis, & dactylitis. In the final model, CRP, FACIT-F, pain, PASI score, & the presence of dactylitis were significantly associated with EQ-5D-5L index & EQ-VAS scores. A higher TJC was significantly associated with a worse EQ-5D-5L index score. A higher SJC was significantly associated with a worse EQ-VAS score (Table). For reference, in the GUS Q4W (N=244), GUS Q8W

Table. Multivariate analysis of patient characteristics/clinical features & EQ-5D-5L index & EQ-VAS scores at Week 0 & Week 24

Parameter	EQ-5D-5L Index		EQ-VAS	
	Estimate	p value	Estimate	p value
Age (y)	-0.0001	0.69	0.06	0.12
Female	-0.003	0.53	1.11	0.20
CRP (mg/dL)	-0.005	**<0.001**	-0.51	**0.007**
FACIT-F (0-52)	0.007	**<0.001**	0.57	**<0.001**
Pain (0-10)	-0.02	**<0.001**	-3.47	**<0.001**
PASI (0-72)	-0.001	**0.03**	-0.17	**<0.001**
SJC (0-66)	-0.001	0.21	-0.17	**0.02**
TJC (0-68)	-0.001	**0.04**	-0.04	0.41
Dactylitis (Y/N)	0.01	**0.02**	1.74	0.49
Enthesitis (Y/N)	-0.004	0.33	-0.98	0.22

CRP, C-reactive protein; EQ-5D-5L, EuroQoL-5 dimension-5 level questionnaire; EQ-VAS, EuroQoL-visual analog scale; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; PASI, Psoriasis Area & Severity Index; W, week; SJC, swollen joint count; TJC, tender joint count

(N=246), & PBO (N=244) groups, LS mean changes from BL at W24 were 0.12, 0.12, & 0.05, respectively, for EQ-5D-5L index & 18.1, 18.4, & 6.8, respectively, for EQ-VAS.

Conclusion: Joint & skin symptoms, dactylitis, fatigue, pain, & elevated CRP levels were significantly associated with reduced HRQoL (measured by EQ-5D-5L index & EQ-VAS) in bio-naïve pts with active PsA. Treatment of multiple PsA domains may help optimize HRQoL. Improvement across clinical domains[1] & in HRQoL was observed in GUS-treated PsA pts.

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1. Mease P, et al. *Lancet* 2020;395:1126-36.

Disclosure: J. Curtis, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **F. Yang**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **S. Peterson**, Janssen, 3, 11; **P. Agarwal**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Hsia**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **C. Han**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1815

Randomised, Double-blind, Placebo-controlled Study of Iguratimod in the Treatment of Active Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Iguratimod, also known as T-614, is a new type of small molecule compound with anti-inflammatory and immunomodulatory effects; It was listed in China(2011) and Japan(2012) for the treatment of rheumatoid arthritis;its safety and effectiveness have been verified in patients with rheumatoid arthritis. As Iguratimod could inhibit the production of inflammatory cytokines, such as IL-1 and TNF; block the IL-17 signalling pathway and inhibit cyclooxygenase, Iguratimod may be effective in the treatment of SPA/AS. However, no rigorous clinical research exists to confirm this speculation. Therefore, this study aimed to evaluate the efficacy and safety of Iguratimod in patients with active SpA.

Methods: Subjects with active SpA were enrolled and randomly divided into two groups at a ratio of 1:2 (placebo vs. Iguratimod). On the basis of non-steroidal anti-inflammatory drugs, combined treatment with Iguratimod or placebo, followed by follow-up every 4 weeks for 24 weeks. The primary efficacy endpoint was to evaluate the alleviation rate of ASAS20; the important improvement of ASDAS and the efficacy of spinal mobility, physical function and quality of life at the 24th week.

Results: A total of 48 cases in the Iguratimod group and 25 cases in the placebo group were included in the final analysis. On the 24th week, the percentage of responders to ASAS20 (80% vs. 44%) and ASAS40 (56% vs. 20%) treated with Iguratimod were significantly higher than that in the placebo group ($P < 0.05$). Twelve cases had gastrointestinal discomfort, of which eight were in the Iguratimod group (16.7%, one case withdrew from the study due to diarrhoea) and four were in the placebo group (16.0%). No significant difference was found between the two groups ($P < 0.05$). Three cases of elevated transaminase were observed in the Iguratimod group and none in the placebo group, with no significant difference ($P < 0.05$).

Conclusion: Iguratimod could significantly reduce the symptoms and signs of patients with active SpA. It could improve the physical function and quality of life of these patients and the overall safety and tolerance are good.

Disclosure: y. li, None; **K. Li**, None; **Z. Zhao**, None; **y. wang**, None; **J. Jin**, None; **j. zhang**, None; **J. Zhu**, None; **f. huang**, None.

Abstract Number: 1816

Treatment of Non-biologic-DMARD-IR PsA Patients with Upadacitinib or Adalimumab Results in the Modulation of Distinct Functional Pathways: Proteomics Analysis of a Phase 3 Study

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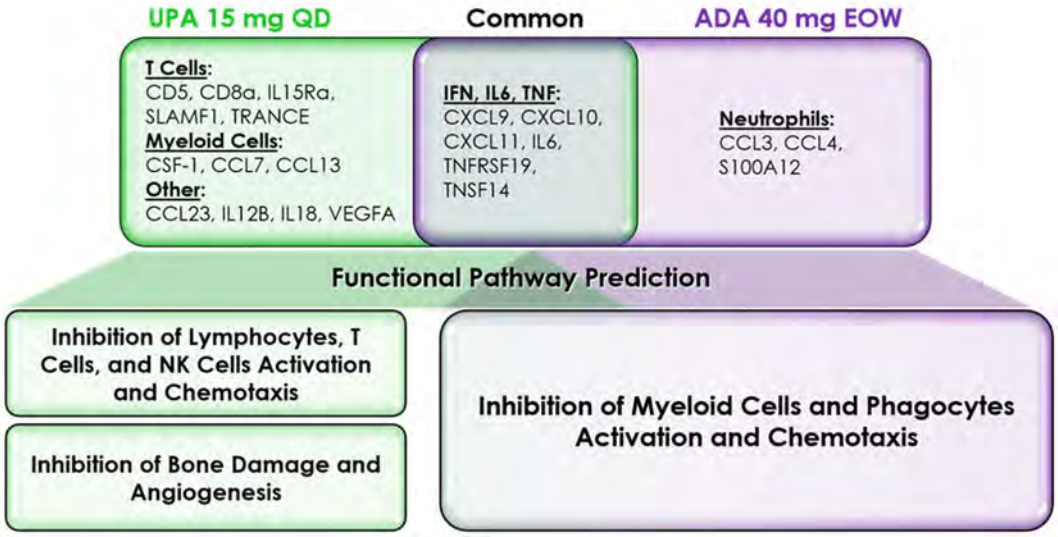
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Treatment of non-biologic-DMARD-IR (DMARD-IR) PsA patients with upadacitinib (UPA) at 15 mg QD, an oral JAK1 selective inhibitor, resulted in improvement in musculoskeletal symptoms, psoriasis, physical function, fatigue, quality of life, and inhibited radiographic progression; improvements were observed as early as Week 2 (ACR20 and ACR50). UPA 15 mg QD was non-inferior to ADA 40 mg EOW for ACR20.[1] The objective of this analysis was to determine the relative biological pathway modulation of UPA compared with ADA in patients with PsA via the evaluation of a pre-defined set of plasma proteins associated with inflammation.

Methods: Patients from the SELECT-PsA 1 study (DMARD-IR PsA patients) were randomly selected (PBO, n=100; UPA 15 mg QD, n=100; ADA 40 mg EOW, N = 100). The levels of 92 inflammation related protein biomarkers (pBM) were analyzed using the Olink® platform in plasma samples collected at baseline, week 2, and 12; change from baseline in protein levels were expressed as Log_2 Fold Change; a Repeated Measure Mixed Linear Model identified proteins modulated by UPA and ADA compared to Baseline. Functional pathway prediction was performed with Inge-



nuity® Pathway Analysis (Qiagen Inc.) where 52 significantly modulated pBM (mean $|Log_2 FC| \geq 0.1$ AND FDR ≤ 0.05) were selected; results were summarized based on 3 core biological groups: 1) adaptive immune system, 2) innate immune system, and 3) non-immune connective and vascular systems.

Results: At the single pBM-level, at the week 2 and 12 time points, treatment with UPA 15 mg QD resulted in distinct down modulation of T cell-associated (CD5, CD8a, IL15Ra, SLAMF1, TRANCE) and myeloid cell-associated pBM (CSF-1, CCL7, CCL13) that was not observed in the ADA treated group. Reciprocally, treatment with ADA 40 mg EOW resulted in a specific down modulation of a subset of neutrophil associated pBM (CCL3, CCL4, and S100A12). Both treatments resulted in the down modulation of IFN-, IL6-, and TNF-related pBM (CXCL9, CXCL10, CXCL11, IL6, TNFRSF19, and TNSF14) suggesting a common node of activity related to these pivotal cytokine-signaling pathways.

Functional pathway prediction based on the pBM data revealed that treatment with UPA is preferentially associated with the inhibition of T cells, but also NK cells and lymphocytes, compared to the predicted effects of treatment with ADA. Treatment with UPA also preferentially inhibited pathways related to bone damage and angiogenesis, as compared to the predicted effect of treatment with ADA. Finally, both treatments were predicted to inhibit multiple pathways associated with the activity of myeloid cells and phagocytes.

Conclusion: Consistent with previous observations in RA[2], UPA is predicted to inhibit multiple functional pathways associated the pathobiology of PsA belonging to the general categories of adaptive and innate immunity but also non-immune vascular and connective tissue biology. In contrast, treatment with ADA appears to affect more specifically functional pathways associated with the innate immune system.

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Disclosure: T. Sornasse, AbbVie, 3, 11; **J. Anderson**, AbbVie, 3, 11; **K. Kato**, AbbVie, 3, 11; **A. Lertratanakul**, AbbVie, 3, 11; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **I. McInnes**, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, UCB, 2, 5, Gilead, 2, AbbVie, 2, AstraZeneca, 5, Boehringer Ingelheim, 2, Amgen, 2, 5, 6, Pfizer, 2, 5, 6.

Abstract Number: 1817

Comparison of Composite Indices for Disease Activity in Patients with Psoriatic Arthritis Treated with Upadacitinib: A Post-Hoc Analysis from SELECT-PsA 1

Josef Smolen[1], Ennio Lubrano[2], Mitsumasa Kishimoto[3], Andra R Bălănescu[4], Vibeke Strand[5], Tianming Gao[6], Nancy Vranich[6], Ralph Lippe[7] and William Tillett[8], [1]Medical University of Vienna, Vienna, Austria, [2]Department of Medicine and Health Sciences Vincenzo Tiberio, University of Molise, Campobasso, Italy, [3]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan, [4]"Carol Davila" University of Medicine and Pharmacy, Department of Internal Medicine and Rheumatology "Sf. Maria" Hospital, Bucharest, Romania, [5]Stanford University School of Medicine, Portola Valley, CA, [6]AbbVie Inc., North Chicago, IL, [7]AbbVie Deutschland GmbH & Co. KG, Berlin, Germany, [8]Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom

SESSION INFORMATION

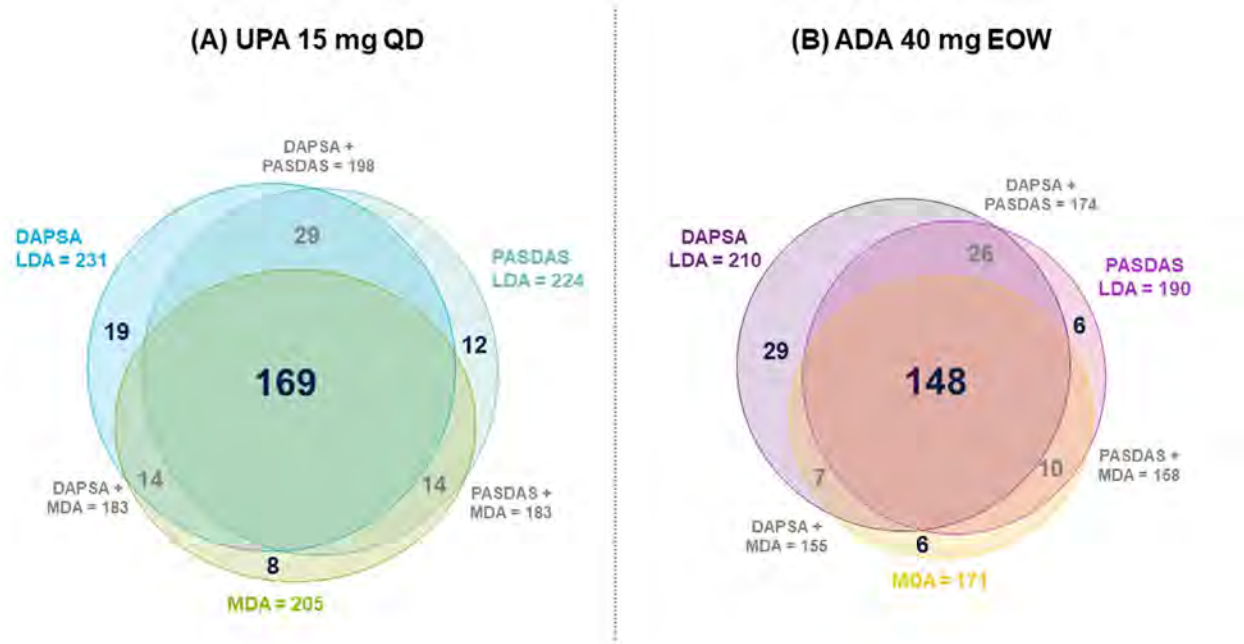
Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Figure 1: Number of PsA Patients Treated with UPA or ADA in LDA by MDA,† DAPSA,‡ and/or PASDAS§



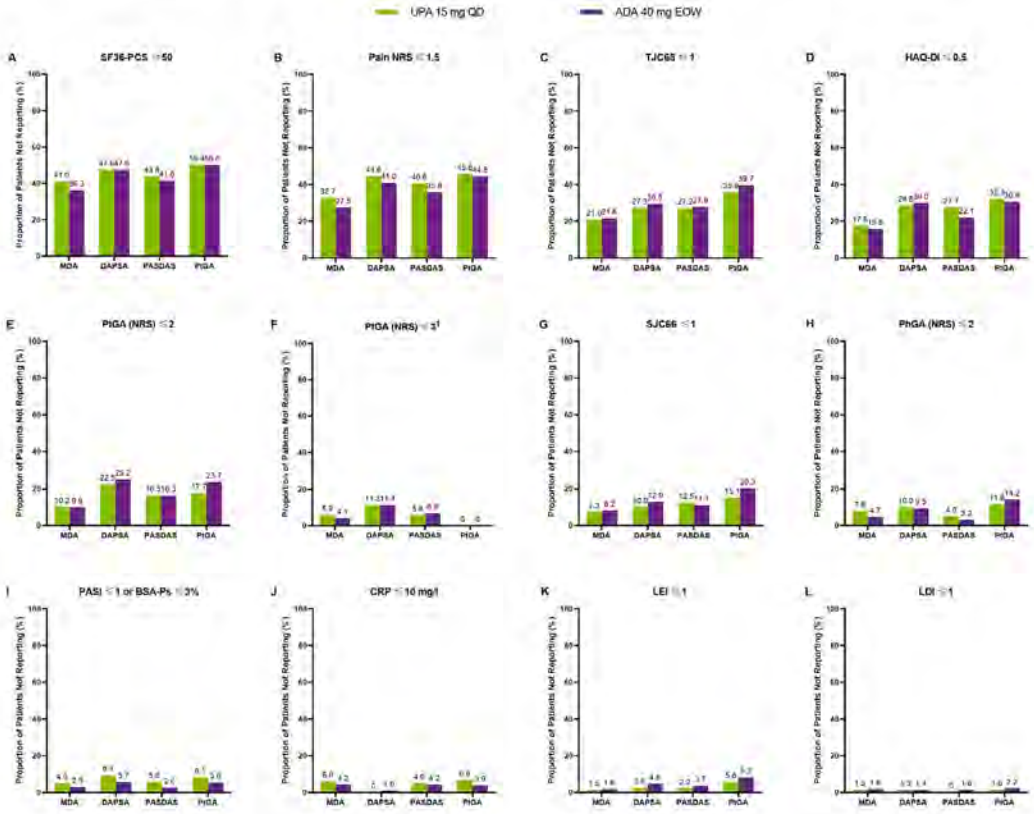
ADA, adalimumab; BSA-Ps, Body Surface Area with Psoriasis; DAPSA, Disease Activity in PsA; EOW, every other week; HAQ-DI, Health Assessment Questionnaire - Disability Index; LDA, Low Disease Activity; LEI, Leeds Enthesitis Index; MDA, Minimal Disease Activity; NRS, Numeric Rating Scale; PASDAS, PsA Disease Activity Score; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; PtGA, Patient Global Assessment of Disease Activity; Pain NRS, Patient Assessment of Pain; QD, once daily; SJC66, Swollen Joint Count 66; TJC68, Tender Joint Count 68; UPA, upadacitinib

†MDA defined as achieving 5/7 of the following criteria: TJC68 ≤1, SJC66 ≤1, PASI ≤1 or BSA-Ps ≤3%, Pain NRS ≤1.5 (0-10 scale), PtGA NRS ≤2.0 (0-10 scale), HAQ-DI ≤0.5, and LEI ≤1

‡LDA threshold for DAPSA: ≤14

§LDA threshold for PASDAS: ≤3.2

Figure 2: Proportion of PsA Patients Treated with UPA or ADA in LDA by MDA, DAPSA, PASDAS, or PtGA ≤3, but Not Reporting Meaningful Improvements in Individual Index Components



ADA, adalimumab; BSA-Ps, Body Surface Area with Psoriasis; DAPSA, Disease Activity in PsA; HAQ-DI, Health Assessment Questionnaire - Disability Index; CRP, C reactive protein; EOW, every other week; LDA, Low Disease Activity; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MDA, Minimal Disease Activity; NRS, Numeric Rating Scale; PASDAS, PsA Disease Activity Score; PASI, Psoriasis Area Severity Index; PhGA, Physician's Global Assessment of disease activity; PsA, psoriatic arthritis; PtGA, Patient Global Assessment of disease activity; Pain NRS, Patient Assessment of Pain; QD, once daily; SF36-PCS, SF-36 Physical Component Summary; SJC66, Swollen Joint Count 66; TJC68, Tender Joint Count 68; UPA, upadacitinib

†LDA threshold for PtGA was defined as ≤ 3; therefore, due to the definition applied for this post-hoc analysis, all patients met this threshold (ie, 0% not achieving)

Background/Purpose: Achieving low disease activity (LDA) or remission is a main treatment target in PsA. Composite indices used to assess disease activity include Disease Activity index for PsA (DAPSA) and PsA Disease Activity Score (PASDAS), which both have cut points for the states of remission and LDA. In addition, LDA and remission can be assessed by the pure state instrument Minimal Disease Activity (MDA)/Very Low Disease Activity (VLDA). These analyses aim to identify overlap and differences between these composite indices in PsA patients treated with upadacitinib (UPA), a Janus kinase inhibitor, or adalimumab (ADA) in the phase 3 SELECT-PsA 1 trial.

Methods: In SELECT-PsA 1 (phase 3, randomized controlled trial, with long-term extension up to 5 years), patients with moderate to severely active PsA with prior inadequate response or intolerance to ≥1 non-biologic DMARD were randomized to oral UPA at doses of 15 mg or 30 mg (once daily), subcutaneous ADA 40 mg (every other week), or placebo.[1] LDA was assessed using MDA (threshold: 5/7 criteria), DAPSA (≤14), PASDAS (≤3.2), and Patient Global Assessment of Disease Activity (PtGA; ≤3).[2,3] These post-hoc descriptive analyses include 1-year (cut off: week 56) *as observed* data from UPA 15 mg and ADA.

Results: In total, 858 patients (UPA 15 mg: n=429; ADA: n=429) were included in these analyses. Patients receiving UPA and ADA were on average 52 years of age, 54% were female, with an average disease duration of approximately 6 years.[1] With both UPA and ADA, there was a high degree of overlap in the proportion of patients achieving LDA thresholds in MDA, DAPSA, and PASDAS (**Figure 1**), with reported PtGA improvements showing a similar trend. Defining LDA according to MDA or respective cut points for DAPSA, PASDAS, or PtGA, the proportion of "non-

responders" (ie, patients who did not reach such states) is shown in **Figure 2**. Of the individual components included in these indices, fewer patients reported low levels of SF-36 Physical Component Summary (SF36-PCS), Patient Assessment of Pain Numeric Rating Scale (Pain NRS), and Health Assessment Questionnaire - Disability Index (HAQ-DI) scores, as well as Tender Joint Count 68 (TJC68), with similar responses observed across all indices.

Conclusion: In this post-hoc analysis from the SELECT-PsA 1 trial, there was a high degree of overlap between patients in LDA across the composite indices, including MDA, DAPSA, and PASDAS, irrespective of treatment with UPA 15 mg or ADA and despite variability in inclusion of certain components in some indices but not others. Across all indices, fewer patients reported low levels of SF36-PCS, Pain NRS, and HAQ-DI scores, and TJC68. These data show that improvements in (subjective) "patient-driven" components were the most challenging to achieve. These data indicate a similar pattern of residual disease activity, or influence by residual damage or external factors, regardless of composite endpoint utilized.

References

1. McInnes IB et al. *N Engl J Med*. 2021; 384(13):1227-39
2. Kerschbaumer et al. *Baillieres Best Pract Res Clin Rheumatol*. 2018; 32:401-14
3. Gorlier et al. *Ann Rheum Dis*. 2019; 78:201-208

Disclosure: J. Smolen, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **E. Lubrano**, AbbVie, 2, 5, 6, Celegene, 2, 5, 6, Janssen, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Galapagos, 2, 5, 6, Pfizer, 2, 5, 6; **M. Kishimoto**, AbbVie, 2, 6, Amgen-Astellas BioPharma, 2, 6, Asahi-Kasei Pharma, 2, 6, Astellas, 2, 6, Ayumi Pharma, 2, 6, BMS, 2, 6, Celegene, 2, 6, Chugai, 2, 6, Daiichi-Sankyo, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, Janssen, 2, 6, Kyowa Kirin, 2, 6, Novartis, 2, 6, Ono Pharma, 2, 6, Pfizer, 2, 6, Tanabe-Mitsubishi, 2, 6, UCB, 2, 6; **A. Bălănescu**, AbbVie, 2, 6, Pfizer Inc, 1, 2, 6, Amgen, 2, 6, AstraZeneca, 6, Angelini, 6, Bristol-Myers Squibb, 1, 6, Berlin-Chemie, 6, MSD, 1, 2, 6, Novartis, 1, 2, 6, Roche, 1, 2, 6, Sandoz, 6, Teva, 6, UCB, 1, 3, 6, Zentiva, 6, Akros, 1, 2, Alfasigma, 6, Biogen, 2, Eli Lilly, 2, GSK, 1, Mylan, 2; **V. Strand**, Abbvie, 2, Amgen, 2, Genentech / Roche, 2, Janssen, 2, Novartis, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Bristol-Myers Squibb, 2, Boehringer Ingelheim, 2, Celltrion, 2, Arena, 2, Gilead, 2, GlaxoSmithKline, 2, Ichnos, 2, Inmedix, 2, Kiniksa, 2, Merck, 2, Myriad Genetics, 2, Regeneron Pharmaceuticals, Inc., 2, Samsung, 2, Sandoz, 2, Setpoint, 2, Galapagos, 2, Horizon, 2, Lilly, 2, Rheos, 2, R-Pharma, 2, Scipher, 2, Sun Pharma, 2; **T. Gao**, AbbVie, 3, 11; **N. Vranich**, AbbVie, 3, 11; **R. Lippe**, AbbVie, 3, 11; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2.

Abstract Number: 1818

Real-World Efficacy of TNF Inhibitors for Treatment of Psoriatic Arthritis by Disease Domains: 6-Month Findings from the CorEvitas Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Baseline Clinical Characteristics for TNFi Initiators

Characteristic	TNFi
PsA domains[a], n (%)	N = 631
Peripheral arthritis	536 (85)
Any skin disease	508 (81)
Nail psoriasis	351 (56)
Moderate/high skin disease	317 (50)
Enthesitis	216 (34)
Oligoarthritis[b]	209 (33)
Dactylitis	148 (23)
Axial PsA disease	115 (18)
Age, mean (SD), years	53.0 (12.8) (N = 629)
Female, n (%)	359 (57) (N = 627)
White, n (%)	568 (90) (N = 631)
Body mass index, mean (SD), kg/m^2	32.3 (7.8) (N = 611)
Years since PsA diagnosis, mean (SD)	6.4 (8.2) (N = 626)
Years since PsA symptom onset, mean (SD)	9.5 (9.8) (N = 618)
BSA >0%, mean (SD), %	7.5 (12.8) (N = 451)
BSA category, n (%)	N = 615
0%	164 (27)
>0% to <3%	196 (32)
≥3% to <10%	157 (26)
≥10%	98 (16)
Tender joint count (0-68), mean (SD)	6.7 (9.8) (N = 617)
Swollen joint count (0-66), mean (SD)	3.6 (5.4) (N = 616)
Patient Global Assessment of PsA,[c] mean (SD)	45.2 (26.3) (N = 620)
Physician Global Assessment of PsA,[c] mean (SD)	30.5 (22.6) (N = 625)
cDAPSA, mean (SD)	20.0 (15.4) (N = 593)
Patients in MDA, n (%)	117 (20) (N = 582)
Patient-reported pain,[c] mean (SD)	50.5 (27.8) (N = 617)
Patient-reported fatigue,[c] mean (SD)	50.4 (29.0) (N = 626)
Patient-reported spine pain,[c] mean (SD)	33.6 (30.4) (N = 621)
ASDAS-CRP, mean (SD)	2.7 (1.1) (N = 163)
BASDAI, mean (SD)	4.8 (2.5) (N = 616)
HAQ-DI, mean (SD)	0.9 (0.7) (N = 619)
HAQ-S, mean (SD)	0.9 (0.7) (N = 619)
Nail psoriasis VAS, mean (SD)	10.9 (21.2) (N = 604)
SPARCC enthesitis count, mean (SD)	1.0 (2.2) (N = 631)
Dactylitis count, mean (SD)	0.5 (1.5) (N = 631)
b/tsDMARD line of treatment, n (%)	N = 631
First	251 (40)
Second	208 (33)
Third	94 (15)
Fourth or higher	78 (12)
Prior cDMARD, n (%)	N = 631
0	177 (28)
1	349 (55)
2+	105 (17)
Prior bDMARD, n (%)	N = 631
0	297 (47)
1	187 (30)
2+	147 (23)
Concomitant treatment, n (%)	N = 631
Monotherapy	364 (58)
Combination with methotrexate	224 (35)
Combination with non-methotrexate nbDMARD	43 (7)
Therapy added after initiation,[d] n (%)	N = 631
None	274 (43)
Methotrexate	270 (43)
Non-methotrexate cDMARD	60 (10)
TNFi	<5
Non-TNFi	68 (11)

[a]A patient may have involvement in more than 1 PsA domain. [b]Tender joint count (68) and swollen joint count (66) >0 and ≤4, as reported by the physician at the initiation visit or at any point prior to the initiation visit. [c]Measured using a 100-point VAS. [d]Up to and including the 6-month visit. ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score-C-reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; bDMARD = biologic disease-modifying antirheumatic drug; BSA = body surface area; cDAPSA = Clinical Disease Activity Index for Psoriatic Arthritis; cDMARD = conventional disease-modifying antirheumatic drug; HAQ-DI = Health Assessment Questionnaire-Disability Index; HAQ-S = Health Assessment Questionnaire for Spondyloarthropathies; nbDMARD = non-biologic disease-modifying antirheumatic drug; PsA = psoriatic arthritis; tsDMARD = targeted synthetic DMARD; VAS = visual analog scale.

Table 2. Outcomes at 6 Months Among TNFi Initiators and by PsA Domain

Outcome, n, Mean Change From Baseline (95% CI)	Overall TNFi	Peripheral Arthritis	Any Skin Disease	Nail Psoriasis	Moderate/High Skin Disease	Enthesitis	Oligoarthritis	Dactylitis	Axial PsA
BSA	587 -1.7 (-2.5, -0.8)	500 -2.0 (-2.9, -1.1)	479 -2.3 (-3.3, -1.3)	329 -2.7 (-4.0, -1.3)	300 -4.0 (-5.5, -2.4)	203 -1.2 (-2.0, -0.4)	199 -0.9 (-2.2, 0.4)	139 -1.9 (-3.1, -0.7)	107 -1.6 (-3.9, 0.2)
BSA category									
0%	155 1.2 (0.4, 1.9)	130 0.8 (0.5, 1.2)	47 1.2 (0.4, 2.0)	73 1.5 (0.1, 2.9)	19 1.7 (-0.2, 3.6)	52 0.8 (0.3, 1.3)	54 0.6 (0.3, 0.9)	36 0.5 (0.1, 0.9)	30 0.7 (0.1, 1.3)
0% to <3%	191 0.5 (0.0, 0.9)	160 0.4 (-0.1, 0.9)	191 0.5 (0.0, 0.9)	101 0.0 (-0.3, 0.4)	40 0.8 (-0.7, 2.2)	82 0.5 (-0.2, 1.2)	62 0.7 (-0.4, 1.8)	50 0.5 (-0.7, 1.7)	33 0.2 (-1.0, 1.3)
3% to <10%	147 -0.7 (-2.0, 0.5)	127 -0.5 (-1.9, 0.9)	147 -0.7 (-2.0, 0.5)	88 -0.8 (-1.8, 0.2)	147 -0.7 (-2.0, 0.5)	40 -2.0 (-2.7, -1.3)	55 0.9 (-2.2, 3.9)	33 -2.8 (-3.7, -2.0)	28 -0.1 (-2.6, 2.4)
≥10%	94 -12.2 (-16.3, -8.1)	83 -13.4 (-17.7, -9.1)	94 -12.2 (-16.3, -8.1)	67 -13.6 (-19.0, -8.3)	94 -12.2 (-16.3, -8.1)	29 -8.4 (-12.8, -4.1)	28 -10.8 (-16.5, -5.0)	20 -10.8 (-17.7, -3.8)	16 -13.8 (-25.9, -1.6)
Tender joint count (0-68)	599 -2.5 (-3.1, -1.8)	513 -3.1 (-3.8, -2.3)	487 -2.2 (-2.9, -1.5)	332 -2.8 (-3.7, -1.9)	302 -2.0 (-2.8, -1.2)	210 -4.5 (-5.9, -3.2)	202 -0.2 (-1.1, 0.7)	139 -4.5 (-6.0, -2.9)	105 -0.8 (-2.5, 1.0)
Swollen joint count (0-66)	598 -1.8 (-2.2, -1.4)	512 -2.2 (-2.6, -1.8)	486 -1.9 (-2.3, -1.4)	332 -1.9 (-2.4, -1.3)	301 -1.5 (-2.0, -1.1)	209 -2.4 (-3.2, -1.7)	202 -0.7 (-1.1, -0.4)	139 -4.2 (-5.4, -3.1)	105 -1.0 (-1.5, -0.4)
Patient Global Assessment of PsA VAS (0-100)	605 -5.4 (-7.8, -3.1)	512 -6.5 (-9.0, -3.9)	487 -5.3 (-7.8, -2.7)	333 -4.2 (-7.2, -1.3)	306 -5.4 (-8.8, -2.1)	206 -6.9 (-11.0, -2.9)	202 -5.3 (-9.5, -1.1)	144 -8.6 (-13.3, -3.9)	108 -0.3 (-5.9, 5.4)
Physician Global Assessment of PsA VAS (0-100)	612 -12.5 (-14.4, -10.6)	523 -14.1 (-16.2, -12.0)	494 -12.2 (-14.2, -10.1)	338 -11.4 (-14.0, -8.8)	305 -13.2 (-16.0, -10.5)	211 -14.0 (-17.1, -10.8)	206 -11.2 (-14.6, -7.8)	145 -18.8 (-23.3, -14.3)	107 -12.4 (-17.2, -7.7)
Physician Global Assessment of PsA and PsO	582 -13.8 (-15.9, -11.7)	497 -15.0 (-17.3, -12.7)	472 -14.1 (-16.5, -11.8)	315 -13.7 (-16.8, -10.7)	289 -16.4 (-19.6, -13.2)	200 -13.5 (-16.9, -10.2)	194 -13.3 (-17.3, -9.4)	138 -20.5 (-25.1, -15.8)	99 -11.7 (-17.1, -6.2)
cDAPSA	588 -5.7 (-6.9, -4.5)	478 -7.0 (-8.2, -5.7)	453 -5.5 (-6.7, -4.3)	305 -5.8 (-7.4, -4.2)	282 -4.9 (-6.3, -3.5)	197 -8.4 (-10.5, -6.3)	187 -2.3 (-3.8, -0.8)	133 -10.6 (-13.5, -7.6)	96 -2.6 (-5.1, -0.1)
Patient-reported pain VAS (0-100)	607 -8.1 (-10.4, -5.8)	519 -9.0 (-11.5, -6.5)	490 -8.1 (-10.7, -5.6)	337 -7.2 (-10.2, -4.1)	306 -8.4 (-11.5, -5.2)	211 -8.6 (-12.5, -4.7)	203 -7.0 (-11.1, -3.0)	141 -11.2 (-16.7, -5.7)	110 -6.0 (-11.6, -0.4)
Patient-reported fatigue VAS (0-100)	618 -7.2 (-9.4, -5.1)	525 -7.7 (-10.0, -5.4)	499 -8.0 (-10.3, -5.7)	345 -7.6 (-10.3, -5.0)	311 -8.8 (-11.8, -5.9)	214 -8.3 (-11.9, -4.8)	207 -5.1 (-8.8, -1.5)	145 -11.5 (-16.1, -6.9)	113 -7.0 (-11.4, -2.7)
Patient-reported spine pain VAS (0-100)	605 -4.2 (-6.5, -1.9)	512 -4.2 (-6.8, -1.7)	486 -3.4 (-6.0, -0.9)	335 -3.7 (-6.8, -0.5)	303 -3.1 (-6.4, 0.2)	208 -3.8 (-7.9, 0.2)	203 -5.2 (-9.1, -1.3)	143 -5.2 (-10.0, -0.5)	111 -4.5 (-9.2, 0.2)
ASDAS-CRP	82 -0.3 (-0.5, 0.0)	67 -0.3 (-0.6, -0.1)	67 -0.3 (-0.6, -0.1)	57 -0.3 (-0.6, -0.1)	42 -0.4 (-0.8, -0.1)	32 -0.3 (-0.7, 0.0)	29 -0.3 (-0.8, 0.2)	18 -0.9 (-1.5, -0.2)	16 -0.3 (-1.1, 0.4)
BASDAI	591 -0.8 (-1.0, -0.6)	503 -0.9 (-1.1, -0.7)	480 -0.8 (-1.0, -0.6)	329 -0.7 (-1.0, -0.5)	297 -0.9 (-1.2, -0.6)	209 -0.8 (-1.1, -0.6)	200 -0.7 (-1.0, -0.3)	138 -1.3 (-1.7, -0.9)	110 -0.5 (-0.9, 0.0)
HAQ-DI	610 -0.10 (-0.14, -0.06)	520 -0.11 (-0.16, -0.07)	491 -0.11 (-0.15, -0.06)	338 -0.11 (-0.16, -0.06)	306 -0.12 (-0.18, -0.06)	210 -0.11 (-0.18, -0.04)	204 -0.06 (-0.14, 0.01)	143 -0.18 (-0.27, -0.08)	110 -0.01 (-0.10, 0.07)
HAQ-S	610 -0.10 (-0.14, -0.06)	520 -0.12 (-0.16, -0.07)	491 -0.11 (-0.15, -0.06)	338 -0.11 (-0.17, -0.06)	306 -0.12 (-0.18, -0.06)	210 -0.11 (-0.18, -0.04)	204 -0.07 (-0.14, 0.00)	143 -0.17 (-0.27, -0.08)	110 -0.02 (-0.10, 0.07)
Nail psoriasis VAS (0-100)	578 -5.0 (-6.5, -3.5)	490 -5.4 (-7.1, -3.8)	471 -5.1 (-6.7, -3.5)	328 -10.0 (-12.4, -7.7)	294 -6.4 (-8.6, -4.2)	197 -6.0 (-8.4, -3.7)	193 -2.7 (-5.1, -0.4)	137 -7.8 (-11.7, -4.0)	103 -6.6 (-10.3, -2.8)
SPARCC enthesitis index count (0-16)	631 -0.4 (-0.5, -0.3)	536 -0.5 (-0.6, -0.3)	508 -0.4 (-0.5, -0.2)	351 -0.4 (-0.5, -0.2)	317 -0.2 (-0.4, -0.1)	216 -1.4 (-1.8, -1.1)	209 -0.1 (-0.3, 0.0)	148 -0.4 (-0.7, -0.1)	115 -0.6 (-1.0, -0.2)
Dactylitis count (0-20)	631 -0.2 (-0.4, -0.1)	536 -0.3 (-0.4, -0.2)	508 -0.2 (-0.4, -0.1)	351 -0.2 (-0.4, -0.1)	317 -0.2 (-0.4, 0.0)	216 -0.4 (-0.6, -0.2)	209 -0.1 (-0.3, 0.0)	148 -1.2 (-1.6, -0.8)	115 -0.3 (-0.6, -0.1)
MDA, n/N (%)	120/465 (25.8)	110/433 (25.4)	95/383 (24.8)	58/267 (21.7)	61/252 (24.2)	38/181 (21.0)	44/156 (28.2)	42/123 (34.1)	16/82 (19.5)

ASDAS-CRP = Ankylosing Spondylitis Disease Activity Score-C-reactive protein; BASDAI = Bath Ankylosing Spondylitis Disease Activity Index; BSA = body surface area; cDAPSA = Clinical Disease Activity Index for Psoriatic Arthritis; HAQ-DI = Health Assessment Questionnaire-Disability Index; HAQ-S = Health Assessment Questionnaire for Spondyloarthropathies; MDA = minimal disease activity; PsA = psoriatic arthritis; PsO = psoriasis; SPARCC = Spondyloarthritis Research Consortium of Canada; TNFi = tumor necrosis factor inhibitor; VAS = visual analog scale.

Background/Purpose: The burden of PsA and its chronic symptoms may have considerable impact on patient function and quality of life. Real-world research is limited on treatment response in PsA patients with different manifestations of PsA who are treated with a biologic DMARD. The objective of this study was to describe patient characteristics and disease outcomes within different PsA domains for patients initiating treatment with a TNF inhibitor (TNFi).

Table 3. Time to Discontinuation and Proportion Persistent Over Time

Treatment Group	Median (95% CI) Time to Discontinuation (Months)	Proportion (95% CI) Persistent [$N_{at\ risk}$] at:		
		6 months	12 months	24 months
Overall TNFi	16 (14, 19)	0.75 (0.72, 0.79) [492]	0.57 (0.53, 0.61) [281]	0.39 (0.34, 0.43) [124]
Peripheral arthritis	16 (13, 19)	0.75 (0.71, 0.79) [413]	0.56 (0.51, 0.60) [235]	0.38 (0.33, 0.43) [103]
Any skin disease	18 (15, 21)	0.75 (0.71, 0.79) [398]	0.58 (0.53, 0.62) [234]	0.40 (0.35, 0.45) [104]
Nail psoriasis	16 (12, 19)	0.74 (0.69, 0.78) [270]	0.56 (0.50, 0.61) [160]	0.35 (0.30, 0.41) [73]
Moderate/high skin disease	19 (15, 24)	0.77 (0.72, 0.81) [254]	0.59 (0.53, 0.65) [146]	0.41 (0.34, 0.48) [68]
Enthesitis	12 (9, 16)	0.75 (0.68, 0.80) [162]	0.49 (0.42, 0.56) [89]	0.33 (0.26, 0.41) [37]
Oligoarthritis	20 (16, 36)	0.79 (0.73, 0.84) [165]	0.64 (0.56, 0.70) [94]	0.44 (0.35, 0.52) [43]
Dactylitis	16 (13, 21)	0.74 (0.67, 0.81) [114]	0.60 (0.51, 0.68) [72]	0.35 (0.26, 0.44) [28]
Axial PsA	13 (8, 19)	0.75 (0.65, 0.82) [96]	0.52 (0.42, 0.61) [48]	0.32 (0.22, 0.42) [24]

$N_{at\ risk}$ = number of patients at risk; PsA = psoriatic arthritis; TNFi = tumor necrosis factor inhibitor.

Methods: The CorEvitas PsA/Spondyloarthritis (SpA) Registry is a prospective, observational registry for patients with PsA or SpA under care of a rheumatologist. This study included adults with PsA who initiated treatment with a TNFi (adalimumab, etanercept, certolizumab pegol, infliximab, golimumab) from January 2013–January 2020. We present unadjusted change in disease activity and patient-reported measures from baseline to 6 months for each PsA domain (enthesitis, dactylitis, peripheral arthritis, oligoarthritis, axial PsA disease, nail psoriasis, any skin disease, and moderate/high skin disease). We examined median time to therapy discontinuation and proportions of patients persistent on TNFi at 6, 12, and 24 months.

Results: A total of 631 patients with PsA initiated TNFi treatment. Peripheral arthritis (85%), skin disease (81%), and nail psoriasis (56%) were the most common PsA manifestations (Table 1). Most patients were receiving first- or second-line therapy (73%) (Table 1). At 6 months, improvements were observed for the overall population of TNFi initiators and within the subgroups defined by PsA domains (Table 2). Mean change from baseline in scores for Physician Global Assessment of Disease Activity (100-point VAS) ranged from –11.2 in patients with oligoarthritis to –18.8 in patients with dactylitis (Table 2). Similar patterns of improvement were seen in a subanalysis of patients treated with etanercept.

Among the overall population of patients who were not in minimal disease activity (MDA) at baseline, 25.8% achieved MDA at 6 months. Among the subtypes, the proportion of patients achieving MDA ranged from 19.5% in patients with axial PsA to 34.1% in patients with dactylitis (Table 2). Persistency at 6, 12, and 24 months for patients treated with a TNFi was 0.75, 0.57, and 0.39, respectively, and was similar across subgroups of patients with PsA manifestations (Table 3). Time to discontinuation was shortest in patients with enthesitis and axial PsA (12 and 13 months, respectively) and longest in those with oligoarthritis (20 months) (Table 3).

Conclusion: This analysis highlights the heterogeneity in presentation of PsA domains. In this real-world population, improvement was seen across all PsA domains after initiation of TNFi treatment.

Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **T. Blachley**, CorEvitas, 3; **J. O'Brien**, CorEvitas, LLC, 3; **N. Middaugh**, CorEvitas, LLC, 3; **G. Kricorian**, Amgen Inc., 3, 11; **S. Stryker**, Amgen Inc, 3; **D. Collier**, Amgen Inc., 3, 11; **A. Ogdie-Beatty**, AbbVie, 2, Amgen, 2, 5, BMS, 2, Celgene, 2, CorEvitas (formerly Corrona), 2, Janssen, 2, Eli Lilly, 2, Novartis, 2, Pfizer, 2, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5, Pfizer (to University of Pennsylvania), 5, AbbVie (to University of Pennsylvania), 5, Novartis (to University of Pennsylvania), 5, Gilead, 2.

Abstract Number: 1819

Tildrakizumab Efficacy and Safety in Patients with Psoriatic Arthritis by Metabolic Syndrome Status

Arthur Kavanaugh[1], Siba Raychaudhuri[2], Christopher Ritchlin[3], Akihiko Asahina[4], Proton Rahman[5], Fred Murphy[6], Stephen Rozzo[7], Siu-Long Yao[7], Richard C Chou[8] and Elaine Husni[9], [1]Division of Rheumatology, Allergy and Immunology, Department of Medicine, University of California San Diego, La Jolla, CA, [2]Division of Rheumatology, Allergy & Clinical Immunology, University of California School of Medicine, Davis, Sacramento, CA, [3]Division of Allergy, Immunology, and Rheumatology, School of Medicine and Dentistry, University of Rochester Medical Center, Rochester, NY, [4]Department of Dermatology, The Jikei University School of Medicine, Tokyo, Japan, [5]Department of Medicine, Eastern Health and Memorial University of Newfoundland, St John's, NL, Canada, [6]Altoona Center for Clinical Research, Duncansville, PA, [7]Sun Pharmaceutical Industries, Inc., Princeton, NJ, [8]University at Buffalo School of Medicine and Biomedical Sciences, Buffalo, Buffalo, NY, [9]Cleveland Clinic, Cleveland, OH

SESSION INFORMATION

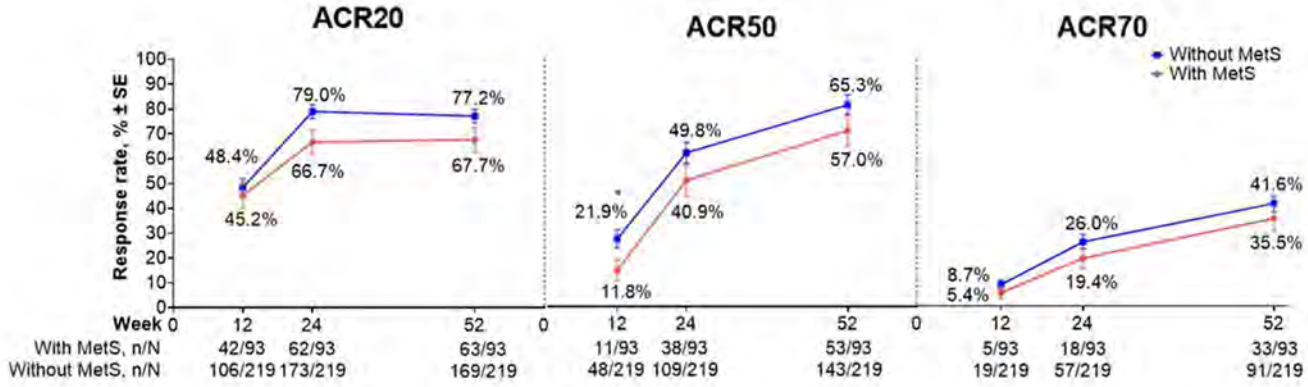
Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Figure. ACR response rate by MetS status through Week 52.



ACR20/50/70 response, 20%/50%/70% improvement from baseline by American College of Rheumatology criteria; MetS, metabolic syndrome.

*P <0.05.

Table. Change from baseline in ACR core components at Week 24/52

	Week 24		Week 52	
	With MetS n = 93 [a]	Without MetS n = 219 [a]	With MetS n = 93 [a]	Without MetS n = 219 [a]
SJC	−6.8 ± 6.4	−7.4 ± 6.2	−6.8 ± 7.9	−7.1 ± 6.5
TJC	−11.4 ± 12.9	−11.5 ± 10.6	−11.2 ± 13.2	−12.2 ± 11.3
HAQ-DI	−0.2 ± 0.5	−0.3 ± 0.5	−0.4 ± 0.6	−0.4 ± 0.5
CRP	−1.4 ± 7.3	−3.6 ± 12.6	−1.8 ± 8.0	−4.6 ± 13.5
PtGA	−26.5 ± 25.3	−32.4 ± 23.2	−31.7 ± 28.3	−36.1 ± 26.3
PGA	−31.7 ± 21.6	−36.4 ± 19.1	−31.9 ± 24.7	−38.9 ± 22.3

Data presented as mean change from baseline ± SD.

[a]Number of tildrakizumab-treated patients in the full analysis set.

ACR, American College of Rheumatology; CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; MetS, metabolic syndrome; PGA, Physician Global Assessment; PtGA, Patient Global Assessment; SD, standard deviation; SJC, swollen joint count; TJC, tender joint count.

Background/Purpose: Metabolic syndrome (MetS) is a combination of specific risk factors for cardiovascular disease.[1] The prevalence of MetS in patients (pts) with PsA has been reported to range from 40%–60%; it has been associated with reduced efficacy of PsA treatment.[2,3] This study assessed whether MetS status affected efficacy and safety of tildrakizumab—a monoclonal IgG1-κ antibody targeting interleukin-23p19—in pts with PsA.[4]

Methods: This post-hoc subgroup analysis of a recently completed Phase 2b study (NCT02980692)[4] includes data from all pts who received any dose of tildrakizumab (200 mg every 4 weeks [Q4W], 200 mg Q12W, 100 mg Q12W, 20→200 mg Q12W) from baseline through W52, stratified by baseline MetS status.[4] Per modified National Cholesterol Education Program Adult Treatment Panel III criteria, MetS was defined by the presence of at least 3 of the following criteria: BMI >30 kg/m^2, blood pressure ≥130 mmHg (systolic) and/or 85 mmHg (diastolic), fasting triglycerides ≥150 mg/dL, fasting high-density lipoprotein cholesterol < 40 mg/dL (men) or < 50 mg/dL (women), and fasting glucose >110 mg/dL.[1] Efficacy endpoints included proportions of pts achieving 20%/50%/70% improvement from baseline by ACR criteria (ACR20/50/70 response) and change from baseline in swollen joint count, tender joint count, CRP, Patient Global Assessment (PtGA; 0–100 mm visual analog scale [VAS]), patient-reported pain VAS, and Physician Global Assessment (PGA; 0–100 mm VAS) at W24 and W52. Missing data were imputed as nonresponse. Incidence of adverse events (AEs), serious AEs (SAEs), and AEs of interest were evaluated at W24 and W52. Data are presented descriptively.

Results: Median baseline weight and BMI were substantially greater in pts with MetS (n = 93) vs those without MetS (n = 219). Tildrakizumab efficacy was generally lower for pts with vs without MetS but was well maintained through W52 in both subgroups (W52 ACR20 response rate [standard error], 67.7% [4.9%] vs 77.2% [2.8%] in pts with vs without MetS; **Figure**). The ACR50 and ACR70 response rates increased from W24 to W52 regardless of MetS status. Improvements from baseline in ACR response components were observed in both subgroups and maintained through W52. Improvements from baseline in CRP, PtGA, and PGA were numerically greater in pts without vs those with MetS (CRP, −4.6 ± 13.5 vs −1.8 ± 8.0; PtGA, −36.1 ± 26.3 vs −31.7 ± 28.3; PGA, −38.9 ± 22.3 vs −31.9 ± 24.7; **Table**). The incidence rate of SAEs in pts with vs without MetS was generally low (W0–W24, 4/93 [4.3%] vs 3/219 [1.4%]; W24–W52, 0/93 [0%] vs 3/219 [1.4%]).

Conclusion: In this Phase 2 trial, the efficacy of tildrakizumab in pts with active PsA tended to be lower among pts with comorbid MetS, with improvements from baseline across efficacy measures generally larger in pts without MetS vs those with MetS. Larger studies are necessary to investigate the long-term effects of MetS on tildrakizumab efficacy, safety, and drug survival in PsA.

References

1. National Institutes of Health. 2001; https://www.nhlbi.nih.gov/files/docs/guidelines/atp3xsum.pdf 2. Haroon M et al. *J Rheumatol*. 2014;41:1357–65. 3. Costa L et al. *Immunol Res*. 2015;61:147–53. 4. Mease PJ et al. *Ann Rheum Dis*. 2021. In press.

Disclosure: A. Kavanaugh, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5; **S. Raychaudhuri**, AbbVie, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharmaceutical Industries, Inc., 5, Amgen, 2, Eli Lilly, 2, Janssen, 2, 5; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **A. Asahina**, Sun Pharmaceutical Industries, Inc., 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Celgene, 5, 6, Eisai, 5, 6, Kyowa Kirin, 5, 6, LEO Pharma, 5, 6, Maruho, 5, 6, Mitsubishi Tanabe Pharma, 5, 6, Taiho Pharma, 5, 6, Torii Pharmaceutical, 5, 6, UCB, 5, 6, Eli Lilly Japan, 5, 6; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **F. Murphy**, Novartis, 2, 6, Sanofi, 2, 6, Horizon, 2, 6, AbbVie, 2, 6; **S. Rozzo**, Sun Pharmaceutical Industries, Inc., 3; **S. Yao**, Sun Pharmaceutical Industries, Inc., 3; **R. Chou**, Sun Pharmaceutical Industries, Inc., 2; **E. Husni**, AbbVie, 2, Amgen, 2, Janssen, 2, Novartis, 2, Eli Lilly, 2, UCB, 2, Regeneron, 2.

Abstract Number: 1820

Efficacy of Deucravacitinib, an Oral, Selective Tyrosine Kinase 2 Inhibitor, in Musculoskeletal Manifestations of Active PsA in a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial

Philip Mease[1], Atul Deodhar[2], Désirée van der Heijde[3], Frank Behrens[4], Alan Kivitz[5], Tom Lehman[6], Lan Wei[6], Marleen Nys[7], Subhashis Banerjee[6] and Miroslawa Nowak[6], [1]Swedish Medical Center/Providence St. Joseph Health and University of Washington, Seattle, WA, [2]Oregon Health & Science University, Portland, OR, [3]Department of Rheumatology, Leiden University Medical Center, Meerssen, Netherlands, [4]CIRI/Rheumatology and Fraunhofer Institute, Translational Medicine and Pharmacology ITMP, Goethe University, Frankfurt, Germany, [5]Altoona Center for Clinical Research, Duncansville, PA, [6]Bristol Myers Squibb, Princeton, NJ, [7]Bristol Myers Squibb, Braine-l'Alleud, Belgium

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

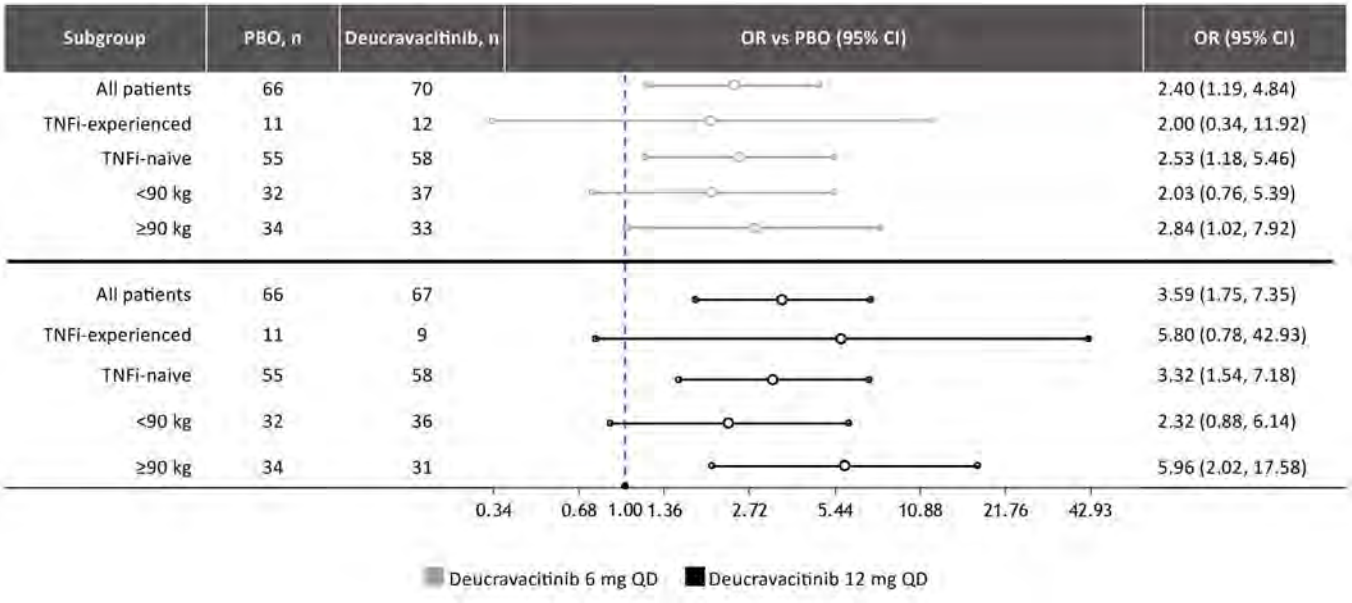
Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates IL-23, IL-12, and IFNα/β signaling. Deucravacitinib is a novel, oral selective inhibitor of TYK2 acting via the TYK2 regulatory domain. In a Phase 2 trial in patients with active PsA, the primary endpoint, ACR 20 response at Week (Wk) 16, was met and deucravacitinib was well tolerated versus placebo (PBO).[1] This analysis further evaluated improvements in musculoskeletal disease manifestations in patients in the Phase 2 PsA trial.

Methods: This Phase 2 trial (NCT03881059) enrolled patients who had a PsA diagnosis for ≥6 months, fulfilled Classification Criteria for Psoriatic Arthritis, had active disease (≥3 tender joints, ≥3 swollen joints, CRP ≥3 mg/L), and

Figure. ACR 20 subgroup analysis at Week 16



Comparative data for the TNFi-experienced groups should be interpreted with caution due to small sample sizes. OR and corresponding 95% CIs were obtained using the CMH test. Analyses were performed using NRI for patients with missing data.
ACR, American College of Rheumatology; CI, confidence interval; CMH, Cochran-Mantel-Haenszel; NRI, nonresponder imputation; OR, odds ratio; PBO, placebo; QD, once daily; TNFi, tumor necrosis factor inhibitor.

Table. Mean (SD) change from baseline for ACR components

	TJC	SJC	PtGA	Pain	PGA	HAQ-DI	hCRP
Baseline[a]							
PBO	16.9 (9.8)	10.5 (7.7)	66.2 (15.8)	64.9 (18.2)	63.8 (14.8)	1.3 (0.6)	20.4 (39.1)
DEUC 6	18.1 (10.3)	11.9 (7.0)	68.2 (16.8)	63.6 (21.7)	68.2 (14.7)	1.3 (0.6)	17.6 (23.6)
DEUC12	19.4 (11.8)	11.3 (9.0)	63.6 (15.6)	63.8 (15.9)	63.3 (16.1)	1.3 (0.6)	16.5 (21.7)
Week 16[b]							
PBO	-4.6 (9.7)	-4.3 (8.0)	-13.4 (23.5)	-13.8 (21.5)	-19.9 (21.8)	-0.1 (0.4)	-3.3 (22.6)
DEUC 6	-9.3 (9.7)	-7.7 (5.8)	-28.7 (23.1)	-25.3 (26.1)	-33.6 (23.0)	-0.4 (0.5)	-14.2 (24.5)
DEUC 12	-12.2 (10.2)	-8.5 (9.1)	-27.6 (25.8)	-27.5 (25.0)	-32.2 (25.0)	-0.4 (0.6)	-10.9 (22.8)

PBO, n/N=58/66; DEUC 6, n/N=63/70; DEUC 12, n/N=59/67; n/N=number of patients who completed treatment/number of patients randomized; the number of patients with data available for individual components at each time point may vary.

[a]Mean (SD). [b]Mean (SD) change from baseline.

ACR, American College of Rheumatology; DEUC 6, deucravacitinib 6 mg QD; DEUC 12, deucravacitinib 12 mg QD; HAQ-DI, Health Assessment Questionnaire-Disability Index total score; hCRP, high-sensitivity C-reactive protein; PBO, placebo; PGA, Physician's Global Assessment of psoriatic arthritis; PtGA, Patients' Global Assessment of disease activity; QD, once daily; SJC, swollen joint count; TJC, tender joint count.

had at least 1 active skin lesion. Patients either failed or were intolerant to ≥1 NSAID, corticosteroid, conventional synthetic DMARD, and/or 1 TNF inhibitor (TNFi; ≤30%). Patients were randomized 1:1:1 to deucravacitinib 6 mg QD or 12 mg QD or PBO, and stratified by TNFi status (experienced vs naive) and body weight (< 90 vs ≥90 kg). The current prespecified subgroup analysis assessed the likelihood of achieving ACR 20 response at Wk 16 based on study stratification factors. A post hoc analysis evaluated mean change from baseline (BL) to Wk 16 in ACR components (tender joint count, swollen joint count, Physician's Global Assessment of PsA, Patients' Global Assessment of disease activity, Patients' Global Assessment of pain, high-sensitivity CRP [hCRP], and HAQ-DI score). Analyses were descriptive using data as observed.

Results: Of 203 patients randomized, 180 (89%) completed 16 wks of treatment (deucravacitinib 6 mg QD, 63/70 [90%]; deucravacitinib 12 mg QD, 59/67 [88%]; PBO, 58/66 [88%]). Demographic and BL disease characteristics were similar across groups. Mean age was 49.8 years and median PsA duration since diagnosis was 4.5 years. Patients treated with deucravacitinib were numerically more likely to achieve ACR 20 response at Wk 16 compared with PBO-treated patients regardless of TNFi experience or body weight, although some of these groups were small (**Figure**). Improvements for deucravacitinib 6 mg and 12 mg QD versus PBO were observed in all ACR components (**Table**), with apparent separation occurring as early as Wk 4 on, for example, HAQ-DI (mean change from BL, -0.2 vs -0.2 vs -0.1, respectively) and hCRP (mean change from BL, -7.4 vs -5.2 vs 0.3, respectively), and maintained through Wk 16. No serious adverse events, including serious infections, herpes zoster infection, opportunistic infections, malignancies, or thromboembolic events, were reported in any deucravacitinib treatment group.

Conclusion: Analyses confirmed the efficacy of deucravacitinib versus PBO across TNFi and body weight subgroups. With deucravacitinib treatment, improvements were displayed in all ACR components.

Reference

1. Mease PJ et al. Presented at the 2020 ACR Convergence, American College of Rheumatology; Nov 5-9, 2020.

Disclosure: P. Mease, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **D. van der Heijde**, AbbVie, 2, Amgen, 2, Astellas,

2, AstraZeneca, 2, Bayer, 2, BMS, 2, Boehringer Ingelheim, 2, Celgene, 2, Cyxone, 2, Daiichi, 2, Eisai, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, GlaxoSmithKline, 2, Janssen, 2, Merck, 2, Novartis, 2, Pfizer, 2, Regeneron, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB Pharma, 2, Imaging and Rheumatology BV, 4; **F. Behrens**, Pfizer, 2, 5, 6, Janssen, 5, Chugai, 2, 5, 6, Celgene, 2, 5, 6, Roche, 2, 5, AbbVie, 2, 6, Sanofi, 2, 6, Lilly, 2, 6, Novartis, 2, 6, Genzyme, 2, 6, Boehringer, 2, 6, Janssen, 2, 6, MSD, 2, 6, Bristol Myers Squibb, 2, 6, UCB Pharma, 2, 6; **A. Kivitz**, Pfizer, 2, 6, 11, 12, Sanofi, 2, 6, 11, 12, GlaxoSmithKline, 11, Gilead Sciences, Inc.,, 2, 11, Novartis, 2, 6, 12, AbbVie, 2, 6, 11, Boehringer Ingelheim, 2, Janssen, 2, Regeneron, 2, 6, 12, SUN Pharma Advanced Research, 2, Amgen, 11, Lilly, 6, Celgene, 6, 12, Flexion, 2, 6, Genzyme, 2, 6, 12, Merck, 6, 12, UCB, 6, Horizon, 6, 12; **T. Lehman**, Bristol Myers Squibb, 3, 11; **L. Wei**, Bristol Myers Squibb, 3, 11; **M. Nys**, Bristol Myers Squibb, 3, 11; **S. Banerjee**, Bristol Myers Squibb, 3, 11; **M. Nowak**, Bristol Myers Squibb, 3, 11.

Abstract Number: 1821

Role of Patient Organizations in Implementation of Recommended Non-pharmacological Treatment Modalities in Spondyloarthritis: Evidence for the Effectiveness of Self-management Strategies

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: This study aimed to characterize the impact of pt advocacy group membership and its association with NPTM frequency and clinical parameters in axSpA pts. EULAR recently recommended the implementation of self-management strategies, such as participation in patient (pt) organizations to improve pt self-management and participation[1]. Non-pharmacological treatment modalities (NPTM)[2] are recommended in axial spondyloarthritis (axSpA) treatment guidelines[3], and are part of ASAS quality standards[4]. Evidence regarding improvements in pt participation in NPTM associated with membership in pt advocacy groups is limited.

Methods: Pts with a physician-judged axSpA diagnosis were enrolled in the multicenter, observational ATTENTUS-axSpA survey, conducted across Germany (11-2019 to 07-2020). Prescribed NPTM measures were assessed to study the effect of membership in pt advocacy groups. Demographics, clinical parameters and pt-related data were collected electronically.

Results: In total, 787 axSpA pts were enrolled in ATTENTUS; this analysis was conducted on the overall population (n=770) and working population (n=695), which was based on pre-defined criteria of working staus[5]. Overall, 12.2% (n=85) pts were members of a pt advocacy group and 87.8% (n=610) were not. Pt advocacy group members were older, had higher Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores, increased functional impairment (BASFI, Bath Ankylosing Spondylitis Functional Index) and higher impact of axSpA on health (ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index) (**Table 1**). Despite worse prognostic factors, there was no significant difference in Work Productivity and Activity Impairment (WPAI) score [40.6 (27.0) for pt advocacy group

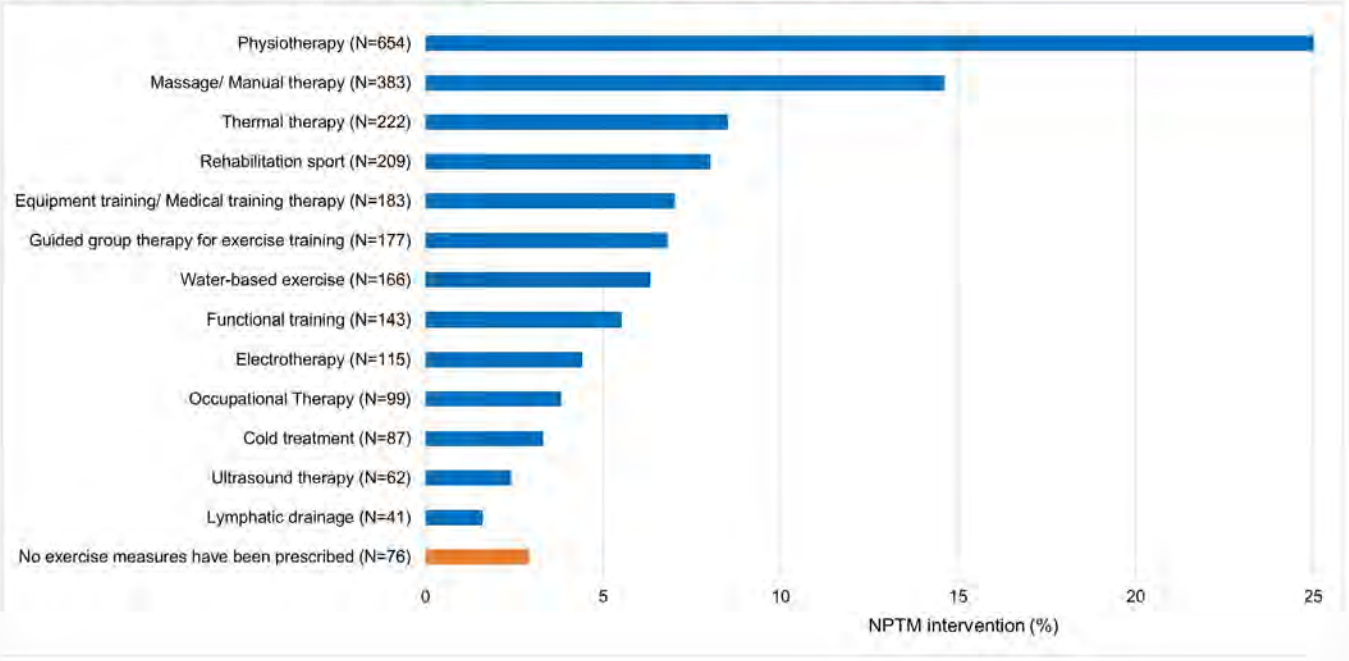
	Table 1. Descriptive characteristics of the study population and impact of membership in pt advocacy group in working patient population			
Descriptive characteristics	**Pts member of patient advocacy group (n=85)**	**Pts not member of patient advocacy group (n=610)**	**Total (n=695)**	**p-value**
Age, years, mean (SD)	50.2 (7.7)	44.6 (11.1)	45.3 (10.9)	**< 0.001**
BMI (kg/m2) mean (SD)	27.5 (5.0)	28.0 (12.7)	28.0 (12.0)	0.713
Male, n (%)	45 (52.9)	378 (62.0)	423 (60.9)	0.128
Disease duration (yrs) mean (SD)	13.7 (10.3)	12.5 (11.1)	12.6 (11.0)	0.303
Level of education attained, n (%), university degree	29 (34.1)	157 (25.7)	186 (26.8)	0.076
In a relationship, n (%)	61 (71.8)	408 (66.9)	469 (67.5)	0.330
ASAS-HI, 0-17	7.3 (3.4)	6.4 (3.9)	6.5 (3.8)	**0.045**
BASDAI, 0-10	4.3 (1.9)	3.8 (2.2)	3.9 (2.2)	**0.044**
BASDAI ≥4, n (%)	49 (57.6)	275 (45.1)	324 (46.6)	**0.025**
BASFI, 0-10	3.9 (2.3)	3.2 (2.5)	3.3 (2.4)	**0.015**
Biologic treatment, n (%)	52 (61.2)	312 (51.1)	364 (52.4)	0.072
Full time employment, n (%)	48 (56.5)	410 (67.2)	458 (65.9)	0.06
Absenteeism*	8.4 (21.2)	10.9 (26.8)	10.6 (26.2)	-
Presenteeism*	38.4 (24.6)	31.8 (25.7)	32.6 (25.6)	-
Overall work impairment score*	40.6 (27.0)	36.8 (29.9)	37.2 (29.6)	0.380
Activity impairment	46.7 (21.7)	40.5 (26.8)	41.3 (26.4)	0.058
Pts having ever received medicinal rehabilitation measurements, mean (SD)	67 (78.8)	328 (53.8)	395 (56.8)	**< 0.001**
Prescribed supervised group NPTM#, mean (SD)	49 (57.6)	210 (34.4)	259 (37.3)	**< 0.001**
Regular physical training†, mean (SD)	76 (89.4)	515 (84.4)	591 (85.0)	0.231

*Work-related questions of WPAI-score have been calculated for pts stated being employed (N=340); †Regular physical training in the context of their axSpA; #rehabilitation sport/functional training or both. ASAS-HI, Assessment of SpondyloArthritis International Society-Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BMI, Body Mass Index; n, number of pts; pts, patients; SD, Standard Deviation; WPAI, Work Productivity and Activity Impairment; yrs, years.

members vs 36.8 (29.9) for non-members; p=0.380]. Importantly, membership in a pt advocacy group was associated with increased prescribed, supervised NPTM (57.6% [n=49] vs 34.4% [n=210]) and increased likelihood of having ever received medicinal rehabilitation (78.8% [n=67] vs 53.8% [n=328]) vs non-members. Pts reported to have ever received 2.6 rehabilitation measures in total, and ≥3.0 different rehabilitation NPTM measures. Cumulatively, 25.0% (N=654) of rehabilitation measures were physiotherapy, 8.0% (N=209) were rehabilitation sport and 5.5% (N=143) functional training (**Figure 1**). Importantly, there was no difference between self-applied regular physical training between groups (89.4% [n=76] vs 84.4% [n=515]).

Conclusion: Pt advocacy group membership was associated with increased prescribed NPTM in axSpA. Our data provide evidence for a significant role of patient organizations in the implementation of guideline-supported treat-

Figure 1. NPTM measures ever received in patients with axSpA (2617 answers from 770 pts)



Multiple answers were permitted. A total of 2617 answers were submitted from 770 patients. N, total number of pts. NPTM, non-pharmacological treatment modalities.

ments, as well as improvement of self-management strategies in pts with axSpA, which may have an influence on important health domains such as work participation.

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Disclosure: D. Meyer-Olson, Abbvie, 2, 6, Amgen, 2, 6, Berlin Chemie, 2, 6, Bristol Myers Squibb, 2, 6, Cellgene, 2, 6, Chugai, 2, 6, Fresenius Kabi, 2, 6, GSK, 2, 6, Jansen Cilag, 2, 6, Eli Lilly, 2, 6, Medac, 2, 6, Merck Sharp & Dome, 2, 6, Mylan, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Sandoz Hexal, 2, 6, Sanofi, 2, 6, UCB, 2, 6; **K. Hoeper**, Abbvie, 2, 6, Chugai, 2, 6, Gilead, 2, 6, Eli Lilly, 2, 6, Novartis, 2, 6, Sandoz Hexal, 2, 6, Sanofi, 2, 6; **L. Hammel**, None; **S. Lieb**, Novartis, 3; **A. Haehle**, Novartis, 3; **U. Kiltz**, AbbVie, 2, 5, 6, Biocad, 2, 6, Eli Lilly, 2, 6, Grünenthal, 2, 6, Janssen, 2, 6, MSD, 2, 6, Amgen, 5, Biogen, 5, Fresenius, 5, GlaxoSmithKline, 5, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 6, UCB, 2, 6, Hexal, 2, 5, Chugai, 2, 5.

Abstract Number: 1822

Relationships Between Dermatologic Symptoms and Health-related Quality of Life in Patients with Psoriatic Arthritis: Post Hoc Analysis of Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

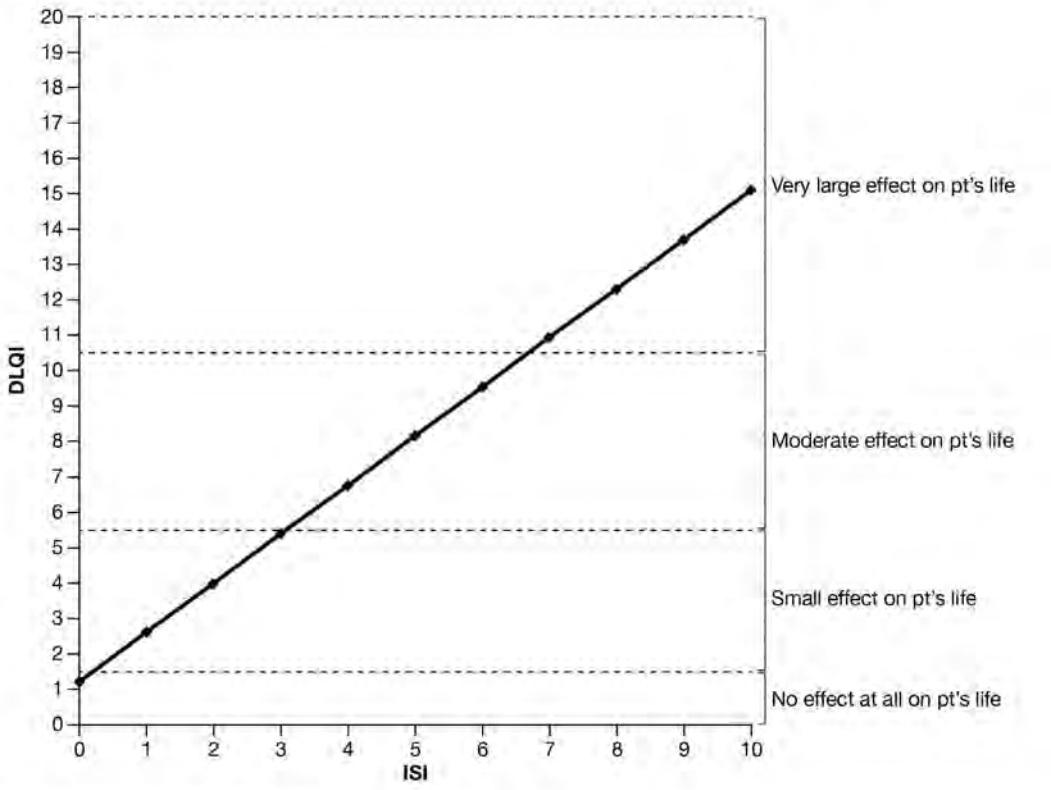
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Dermatologic symptoms of PsA can substantially impact patient (pt) health-related quality of life (HRQoL);[1] itch is the most commonly reported, and among the most bothersome of, symptoms.[2] In pts treated with tofacitinib, an oral Janus kinase inhibitor for the treatment of PsA,[3,4] improvements were observed in itch, Physician Global Assessment of Psoriasis (PGA-PsO), and HRQoL measures;[5] however, the relationships between these

Figure. Relationship between ISI and DLQI (pooled data from OPAL Broaden and OPAL Beyond)



ISI: 0 (no itching) to 10 (worst possible itching)

DLQI: score 0–1, no effect at all on pt's life; 2–5, small effect on pt's life; 6–10, moderate effect on pt's life; 11–20, very large effect on pt's life[6]

All available data from baseline to the end of the study were used. The mid points between adjacent severity categories were used as cut-offs for interpretation of the relationships of ISI and DLQI

DLQI, Dermatology Life Quality Index; ISI, Itch Severity Item; pt, patient

Table. Relationship between ISI, PGA-PsO, and PSA with DLQI and SF-36v2 domains (pooled data from OPAL Broaden and OPAL Beyond)

	SF-36v2 domains										DLQI
	PF	RP	BP	GH	VT	SF	RE	MH	PCS	MCS	
Responder-level CIC[a,b]	3.5	3.2	4.5	5.7	5.5	5.0	3.8	5.5	3.1	3.8	4.0
Dermatologic (anchor) assessment	**Improvements in SF-36v2 domains corresponding to 4-point/3-point/40-mm VAS improvements in ISI/PGA-PsO/PSA**										**DLQI improvements corresponding to 3-point/2-point/40-mm VAS improvements in ISI/PGA-PsO/PSA**
ISI	**3.8**	**3.9**	**4.7**	3.2	3.9	4.8	**4.4**	4.5	**3.5**	**4.3**	**4.2**
PGA-PsO	**4.8**	**4.6**	**6.2**	3.9	5.1	**5.9**	**5.1**	5.3	**4.5**	**4.9**	**4.1**
PSA	**4.0**	**4.1**	**5.5**	3.3	4.2	**5.0**	**4.7**	4.2	**3.9**	**4.2**	**4.4**

[a]Based on Optum's 1998 United States general population sample normative dataset[7]

[b]For general inflammatory skin conditions, a change in DLQI total score of at least 4 points is considered clinically important[8]

Bold numbers represent improvements larger than CIC

All available data from baseline to the end of the study were used

BP, bodily pain; CIC, clinically important change; DLQI, Dermatology Life Quality Index; GH, general health; HRQoL, health-related quality of life; ISI, Itch Severity Item; MCS, Mental Component Summary; MH, mental health; PCS, Physical Component Summary; PF, physical functioning; PGA-PsO, Physician Global Assessment of Psoriasis; PSA, Patient's Global Skin Assessment (assessed by 100 mm VAS); RE, role-emotional; RP, role-physical; SF, social functioning; SF-36v2, Short Form-36 Health Survey version 2; VAS, Visual Analog Scale; VT, vitality

outcomes have not been quantified. This post hoc analysis aimed to evaluate and quantify relationships between dermatologic symptoms and HRQoL in pts with PsA.

Methods: Data were pooled from 2 Phase 3 trials of pts with active PsA receiving tofacitinib 5 or 10 mg twice daily, or placebo (12-month OPAL Broaden [NCT01877668]; and 6-month OPAL Beyond [NCT01882439]).[3,4] A repeated measures longitudinal model assessed relationships between Itch Severity Item (ISI; numeric scale 0 [no itching]–10 [worst possible itching]), PGA-PsO (5-point severity scale defined by descriptors of erythema, induration, and scaling), and Patient's Global Skin Assessment (PSA; 100-mm Visual Analog Scale [VAS]) as predictors, and Dermatology Life Quality Index (DLQI; general dermatology questionnaire) and Short Form-36 Health Survey version 2 (SF-36v2) domains (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, mental health, Physical Component Summary, Mental Component Summary) as outcomes. Each longitudinal model included one predictor and one outcome.

Results: An approximately linear relationship was observed between ISI, PGA-PsO, and PSA with total DLQI score, and each SF-36v2 domain. There was a direct relationship between itch severity (measured by ISI), severity of illness (measured by PGA-PsO), and pts' perception of disease (measured by PSA) and general dermatology QoL (measured by DLQI; Figure), as well as between ISI, PGA-PsO, and PSA and SF-36v2 domains. 3-point/2-point/40-mm VAS improvements from baseline (BL) in ISI/PGA-PsO/PSA, respectively, were associated with clinically meaningful improvements in DLQI (> 4 points; Table). 4-point/3-point/40-mm VAS improvements from BL in ISI/PGA-PsO/PSA were generally associated with clinically important improvements across SF-36v2 domains (Table). A 4-point ISI improvement was associated with a 4.7-point improvement in SF-36v2 bodily pain domain.

Conclusion: Substantial and quantifiable links exist between dermatologic symptoms and HRQoL in pts with PsA; physical and mental domains are ameliorated by tofacitinib. These findings help to inform pt care and pt-centered research.

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Abstract Number: 1823

Efficacy of Upadacitinib in Patients with Active Psoriatic Arthritis and a Low or High Swollen Joint Count: A Subgroup Analysis of 2 Phase 3 Studies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Although most patients with psoriatic arthritis (PsA) enrolled in clinical trials have polyarticular arthritis, patients in clinical practice may present with oligoarthritis. Data on the efficacy of Janus kinase inhibitors in patients with PsA with low joint counts are limited. The objective of this analysis was to evaluate the efficacy of upadacitinib (UPA) in subgroups of patients with PsA with a low (baseline swollen joint count [SJC] < 5) or high (SJC ≥5) SJC (LSJ or HSJ).

Methods: Data were pooled across the SELECT-PsA 1[1] (non-biologic disease-modifying antirheumatic drug [non-bDMARD] inadequate response [IR] or intolerance) and SELECT-PsA 2[2] (bDMARD IR or intolerance) trials, which both enrolled patients with ≥3 involved joints (SJC ≥3 and tender joint count [TJC] ≥3). Subgroup analysis was performed for patients with LSJ or HSJ treated with UPA 15 mg once daily (QD) or placebo (PBO). Efficacy endpoints included

Table Baseline characteristics

	PBO		UPA 15 mg QD		Total	
	LSJ n=120	HSJ n=515	LSJ n=95	HSJ n=545	LSJ n=215	HSJ n=1060
Female, n (%)	65 (54.2)	266 (51.7)	49 (51.6)	302 (55.4)	114 (53.0)	568 (53.6)
Age (years), mean (SD)	52.2 (12.7)	51.5 (12.0)	52.0 (10.6)	52.0 (12.4)	52.1 (11.8)	51.8 (12.2)
Duration since PsA symptoms (years), mean (SD)	10.5 (9.2)	11.1 (10.2)	9.8 (8.2)	10.3 (8.9)	10.2 (8.7)	10.7 (9.6)
BMI, mean (SD)	29.7 (6.3)	31.1 (7.2)	29.8 (6.2)	30.7 (6.9)	29.7 (6.2)	30.9 (7.0)
Prior failed bDMARDs, n (%) 0 1 2 ≥3	 3 (2.5) 22 (18.3) 4 (3.3) 4 (3.3)	 15 (2.9) 113 (21.9) 31 (6.0) 20 (3.9)	 1 (1.1) 22 (23.2) 7 (7.4) 7 (7.4)	 15 (2.8) 104 (19.1) 28 (5.1) 27 (5.0)	 4 (1.9) 44 (20.5) 11 (5.1) 11 (5.1)	 30 (2.8) 217 (20.5) 59 (5.6) 47 (4.4)
Use of ≥1 non-bDMARD at baseline, n (%)	87 (72.5)	360 (69.9)	63 (66.3)	388 (71.2)	150 (69.8)	748 (70.6)
Dactylitis (LDI >0), n (%)	21 (17.5)	169 (32.8)	15 (15.8)	176 (32.3)	36 (16.7)	345 (32.5)
Enthesitis (LEI >0), n (%)	60 (50.0)	325 (63.1)	60 (63.2)	343 (62.9)	120 (55.8)	668 (63.0)
TJC68, mean (SD)	12.5 (11.3)	23.9 (15.8)	14.6 (13.5)	23.1 (15.8)	13.4 (12.3)	23.5 (15.8)
SJC66, mean (SD)	3.5 (0.5)	13.2 (8.3)	3.6 (0.5)	12.9 (9.0)	3.6 (0.5)	13.0 (8.7)
HAQ-DI, mean (SD)	1.0 (0.6)	1.2 (0.7)	0.9 (0.6)	1.2 (0.6)	0.9 (0.6)	1.2 (0.7)
hs-CRP > ULN (mg/L), n (%)	82 (68.3)	363 (70.5)	62 (65.3)	388 (71.2)	144 (67.0)	751 (70.8)
BSA-Ps, median (range)	3.0 (0.1–70.0)	4.0 (0.1–95.0)	2.0 (0.1–80.0)	3.0 (0.1–97.0)	3.0 (0.1–80.0)	3.0 (0.1–97.0)
BSA-Ps ≥ 3%, n (%)	57 (47.5)	285 (55.3)	44 (46.3)	300 (55.0)	101 (47.0)	585 (55.2)
PASI (baseline BSA-Ps ≥ 3%), mean (SD)	7.7 (7.5)	12.1 (11.9)	8.2 (7.0)	10.2 (10.0)	7.9 (7.2)	11.1 (11.0)
PASI (baseline BSA-Ps ≥ 3%), median (range)	5.3 (0.1–39.4)	7.9 (0.3–64.8)	6.5 (0.2–35.4)	6.8 (0.1–70.8)	6.0 (0.1–39.4)	7.3 (0.1–70.8)

minimal disease activity (MDA), very low disease activity (VLDA), Psoriatic Arthritis Disease Activity Score (PASDAS) low disease activity (LDA; ≤3.2), PASDAS remission (≤1.9), and 20/50/70% improvement in American College of Rheumatology (ACR) criteria (ACR20/50/70), all at Week 24, and Psoriasis Area Severity Index (PASI) 75 and static Investigator Global Assessment of Psoriasis (sIGA) 0/1 at Week 16.

Results: At baseline, patients with HSJ (n=1060) had similar demographic characteristics but tended to have higher overall disease activity than patients with LSJ across multiple disease domains (n=215; **Table**). UPA efficacy appeared comparable in patients with LSJ and HSJ, with similar proportions of patients achieving composite (MDA, VLDA, PASDAS LDA, and PASDAS remission) measures at Week 24, and skin endpoints (PASI 75 and sIGA 0/1) at Week 16 (**Figure**). At Week 24, 60.0/36.8/22.1% of patients with LSJ receiving UPA 15 mg achieved ACR20/50/70 vs 40.0/17.5/5.8% in the PBO group; rates were 70.3/49.7/26.2% (UPA 15 mg) and 36.1/15.3/3.3% (PBO) in those with HSJ.

Conclusion: UPA efficacy was generally similar in patients with PsA with LSJ or HSJ, with both patient groups showing improvements in composite clinical endpoints and skin responses vs PBO.

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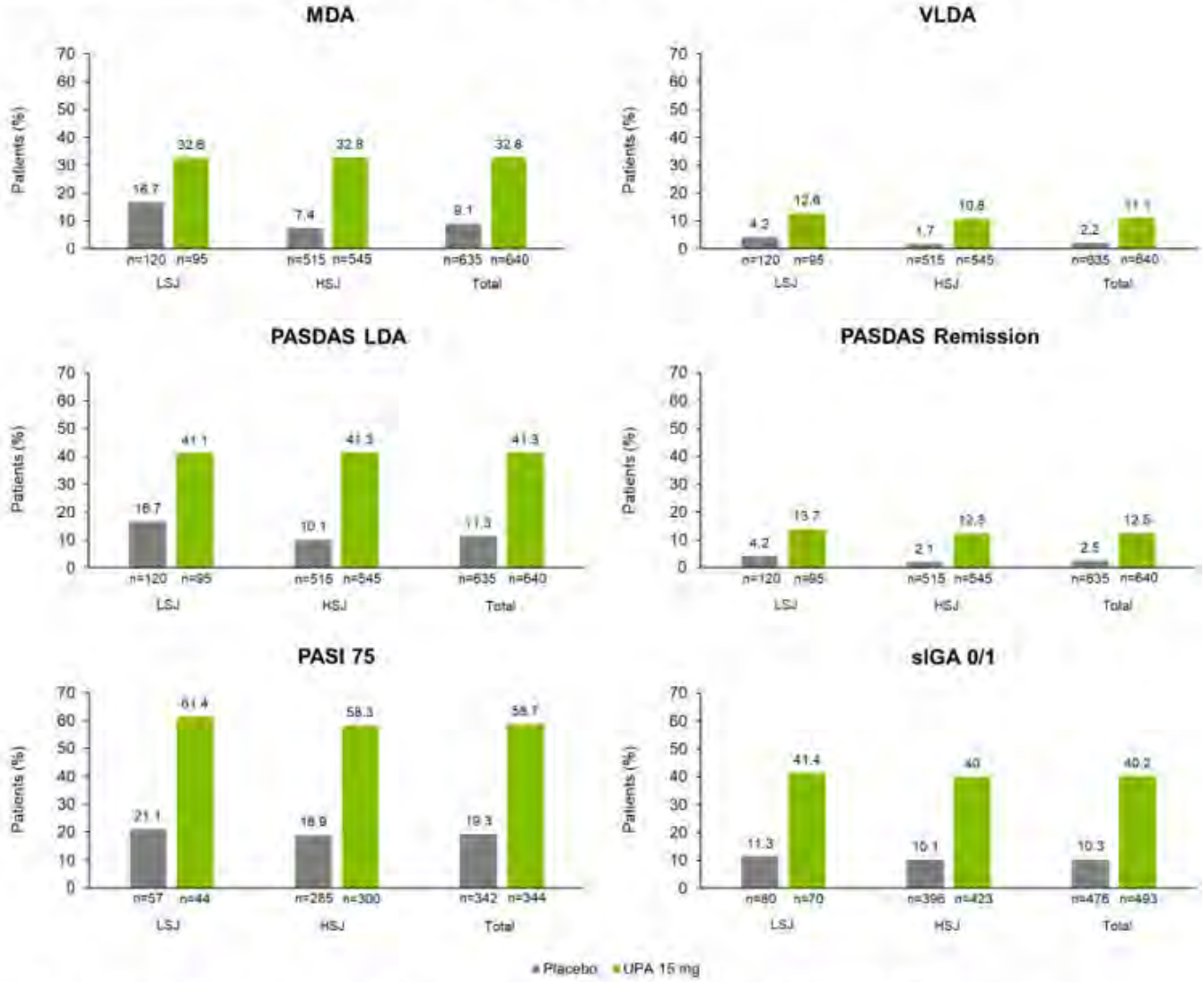
Figure Proportion of patients (%) achieving MDA, VLDA, PASDAS LDA, and PASDAS remission at Week 24, and PASI 75 and sIGA 0/1 at Week 16 for UPA vs PBO, by arthritis subtype



HSJ, high swollen joint count; LDA, low disease activity; LSJ, low swollen joint count; MDA, minimaldisease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area Severity Index; PBO, placebo; sIGA, static Investigator Global Assessment of Psoriasis; UPA, upadacitinib; VLDA, very low disease activity

Disclosure: L. Gossec, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **E. McDearmon-Blondell**, AbbVie, 3, 11; **P. Sewerin**, AbbVie, 2, 5, Amgen, 2, 5, Axiom Health, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, Chugai Pharmaceutical Co. Ltd, 2, Deutscher Psoriasis Bund, 2, 5, Eli Lilly, 2, 5, Fresenius Kabi, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Johnson & Johnson, 2, Medi-login, 2, Mediri, 2, Novartis, 2, 5, Onkowissen, 2, Pfizer, 2, 5, Roche, 2, 5, Rheumazentrum Rhein-Ruhr, 2, 5, Sanofi, 2, 5, Swedish Orphan Biovitrum, 2, UCB, 2, 5, Bundesministerium fuer Bildung und Forschung, 5, Deutsche Forschungsgesellschaft, 5, Hexal, 5; **C. Ritchlin**, UCB, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, Pfizer, 2, Novartis, 2, Gilead, 2, Janssen, 2; **D. Feng**, AbbVie, 3, 11; **A. Lertratanakul**, AbbVie, 3, 11; **R. Ranza**, AbbVie, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6;

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Abstract Number: 1824

Secukinumab Treatment Provides Sustained Resolution of Enthesitis at Individual Joints Through 52 Weeks in a Phase 3b, Double-Blind, Randomized, Active-Controlled Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Enthesitis is a key musculoskeletal manifestation of psoriatic arthritis (PsA). In the double-blind, head-to-head EXCEED study (NCT02745080), although the primary endpoint of superiority of ACR20 response for secukinumab (SEC) vs adalimumab (ADA) was not met, similar efficacy was observed across a range of musculoskeletal endpoints, including resolution of enthesitis at Week 52.[1] However, a detailed, site-level analysis of enthesitis was not conducted. Here, we report the baseline anatomical distribution of enthesitis, site-level entheseal response to SEC and ADA treatment through 52 weeks, and the dynamics of response based on the number of entheseal sites at baseline.

Methods: In this post hoc, descriptive analysis of patients in the EXCEED study who received SEC 300 mg or ADA 40 mg, enthesitis was assessed using the Spondyloarthritis Research Consortium of Canada Enthesitis Index (SPARCC). We reported the anatomical distribution of enthesitis at baseline based on the 16 sites targeted by SPARCC. Through descriptive efficacy analysis, we explored resolution of enthesitis at site level through Week 52 across the 2 treatment groups. Patients were further classified into subgroups of baseline enthesis severity as follows: mild (SPARCC < 3), moderate (SPARCC ≥ 3 to ≤ 6), or severe (SPARCC > 6 to ≤ 16). Resolution of enthesitis at Week 52 was assessed in patients stratified by baseline enthesitis severity. For enthesitis severity subgroups, resolution of enthesitis was assessed at Week 52, and time to resolution was estimated using Kaplan-Meier analysis with nonresponder imputation for missing data. Descriptive statistics are provided for each endpoint using an observed-case approach.

Results: Overall, 301 of 426 patients (70.7%) randomized to receive SEC and 331 of 427 patients (77.5%) randomized to ADA had enthesitis at baseline as determined by SPARCC. Baseline distribution of enthesitis sites was well balanced among patients across the 2 treatment groups (Figure 1). By Week 12, a high proportion of patients

Table. Proportion of Patients With Site-Level Resolution of SPARCC Enthesitis at Weeks 12, 24, and 52

Patients with enthesitis at site, n/M (%)	Secukinumab 300 mg (N = 426)	Adalimumab 40 mg (N = 427)
Achilles tendon insertion into calcaneum		
Week 12	229/286 (80.1)	246/311 (79.1)
Week 24	232/274 (84.7)	235/293 (80.2)
Week 52	234/267 (87.6)	232/263 (88.2)
Greater trochanter		
Week 12	212/286 (74.1)	230/311 (74.0)
Week 24	225/274 (82.1)	234/293 (79.9)
Week 52	225/267 (84.3)	229/263 (87.1)
Lateral epicondyle		
Week 12	215/286 (75.2)	222/311 (71.4)
Week 24	216/274 (78.8)	227/293 (77.5)
Week 52	226/267 (84.6)	229/263 (87.1)
Medial epicondyle		
Week 12	226/286 (79.0)	232/311 (74.6)
Week 24	235/274 (85.8)	227/293 (77.5)
Week 52	232/267 (86.9)	229/263 (87.1)
Patellar ligament insertion into inferior pole of patella or tibial tubercle		
Week 12	234/286 (81.8)	242/311 (77.8)
Week 24	238/274 (86.9)	249/293 (85.0)
Week 52	242/267 (90.6)	237/263 (90.1)
Plantar fascia insertion into calcaneum		
Week 12	247/286 (86.4)	276/311 (88.7)
Week 24	243/274 (88.7)	255/293 (87.0)
Week 52	239/267 (89.5)	244/263 (92.8)
Quadriceps insertion into superior border of patella		
Week 12	236/286 (82.5)	263/311 (84.6)
Week 24	243/274 (88.7)	255/293 (87.0)
Week 52	242/267 (90.6)	238/263 (90.5)
Supraspinatus insertion into greater tuberosity of humerus		
Week 12	212/286 (74.1)	256/311 (82.3)
Week 24	227/274 (82.8)	244/293 (83.3)
Week 52	229/267 (85.8)	230/263 (87.5)

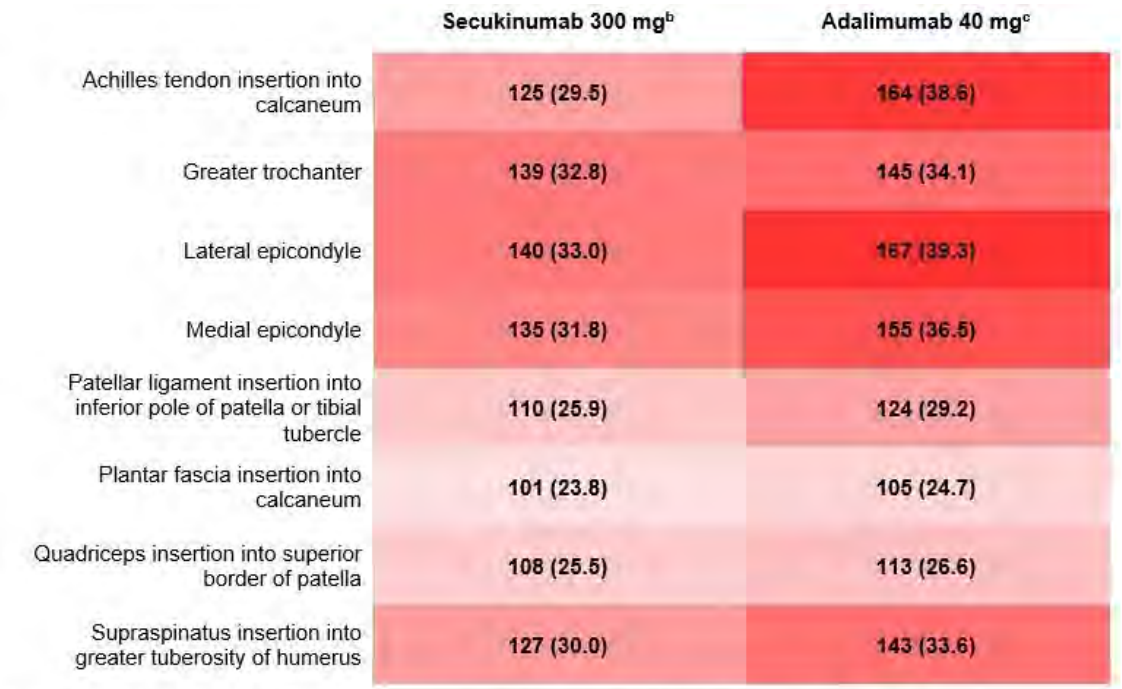
n, number of patients with enthesitis resolution at site; M, number of patients evaluated; SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index.

in both treatment groups achieved similar resolution of enthesitis at the level of individual entheses with sustained improvement through Week 52 (Table). Achievement of enthesitis resolution at Week 52 was similar between treatment groups irrespective of disease severity (Figure 2). Median (95% CI) number of days to resolution of enthesitis increased with increasing baseline enthesitis severity and was similar for SEC and ADA groups with mild (SEC: 29, 29-57; ADA: 31, 29-57), moderate (SEC: 100.5, 58-169; ADA: 113, 85-120), and severe (SEC: 372, 282-not estimable [NE]; ADA: 386, 281-NE) enthesitis.

Conclusion: The anatomical distribution of enthesitis at baseline was mostly balanced between the upper and lower extremities in both SEC and ADA groups in a pattern consistent with previous reports.[2] These analyses also highlight the early and sustained resolution of enthesitis through 52 weeks at site level with both drugs. SEC and ADA displayed similar dynamics of response on enthesitis irrespective of enthesitis severity at baseline.

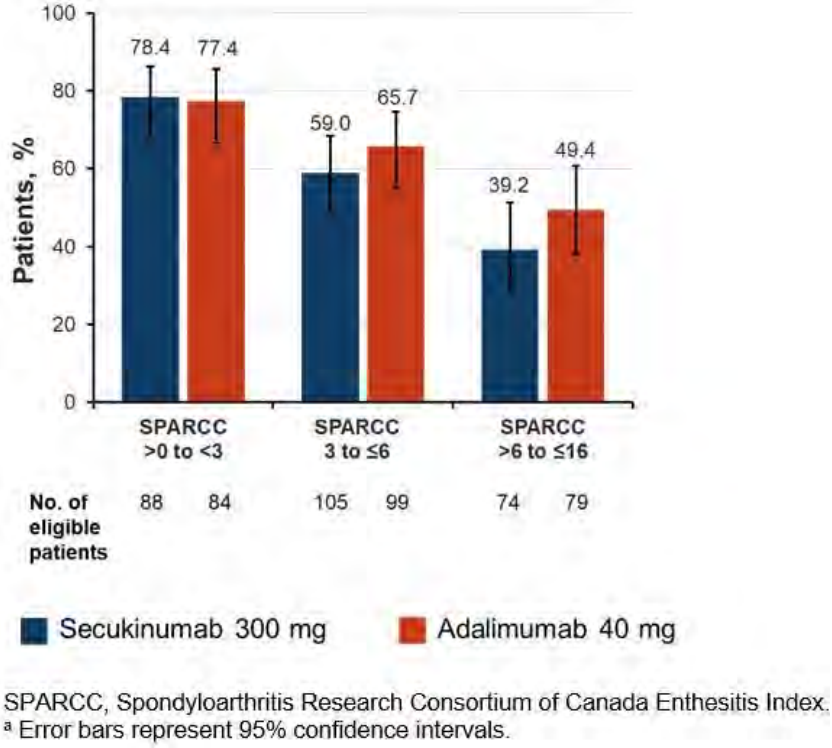
References

1. McInnes IB, et al. *Lancet*. 2020;395:1496-1505.
2. Mease PJ, et al. *J Rheumatol*. 2021;48:367-375.



n, number of patients with enthesitis present at site at baseline; SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index.
[a] Extent of red shading indicates the relative proportion of patients with enthesitis at the indicated site.
[b] n = 424 patients evaluated for enthesitis.
[c] n = 425 patients evaluated for enthesitis.

Figure 1. Baseline Enthesitis Prevalence at Individual SPARCC Enthesitis Sites Among Patients in EXCEED as Determined by the Number (%) of Patients With Enthesitis at Site.



SPARCC, Spondyloarthritis Research Consortium of Canada Enthesitis Index.
[a] Error bars represent 95% confidence intervals.

Figure 2. Proportion of Patients Achieving Resolution of Enthesitis at Week 52 by SPARCC Enthesitis Severity.

Disclosure: G. Kaeley, Novartis, 2; **G. Schett**, Janssen, 6, Novartis, 6, AbbVie, 6, Bristol Myers Squibb, 6, Celgene, 6, Eli Lilly, 6, UCB, 6, Roche, 6; **P. Conaghan**, AbbVie, 2, 6, BMS, 2, 6, Eli Lilly, 2, 6, Galapagos, 2, 6, Gilead, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, AstraZeneca, 2, 6; **D. McGonagle**, Novartis, 5, 6, Roche, 6, Sobi, 6; **F. Behrens**, AbbVie, 5, 6, Chugai, 5, 6, Biotest, 6, Boehringer Ingelheim, 6, Celgene, 5, Eli Lilly, 6, 12, Investigator, Genzyme, 6, Janssen, 5, 6, Roche, 5, 6, Pfizer, 5, 6, Novartis, 6, UCB, 6, Merck Sharp & Dohme, 2, Sanofi, 2; **P. Goupille**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Biogen, 2, 5, 6, Bristol Myers Squibb, 2, 5, 6, Celgene, 2, 5, 6, Chugai, 2, 5, 6, Janssen, 2, 5, 6, Lilly, 2, 5, 6, Merck Sharpe & Dohme, 2, 5, 6, Nordic Pharma, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sanofi, 2, 5, 6, UCB, 2, 5, 6, Medac, 2, 5, 6; **C. Gaillez**, Novartis Pharma AG, 3, 11, BMS, 11; **B. Parikh**, Novartis Pharmaceuticals Corporation, 3; **X. Meng**, Novartis Pharmaceuticals Corporation, 3; **C. Bakewell**, AbbVie, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Janssen, 2, 6, UCB, 2, 6, Sanofi Genzyme/Regeneron, 2, 6.

Abstract Number: 1825

Secukinumab Provides Clinical Improvements in Patients with Active Oligoarticular Psoriatic Arthritis: Results from a Pooled Analysis of 5 Phase 3 Studies

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

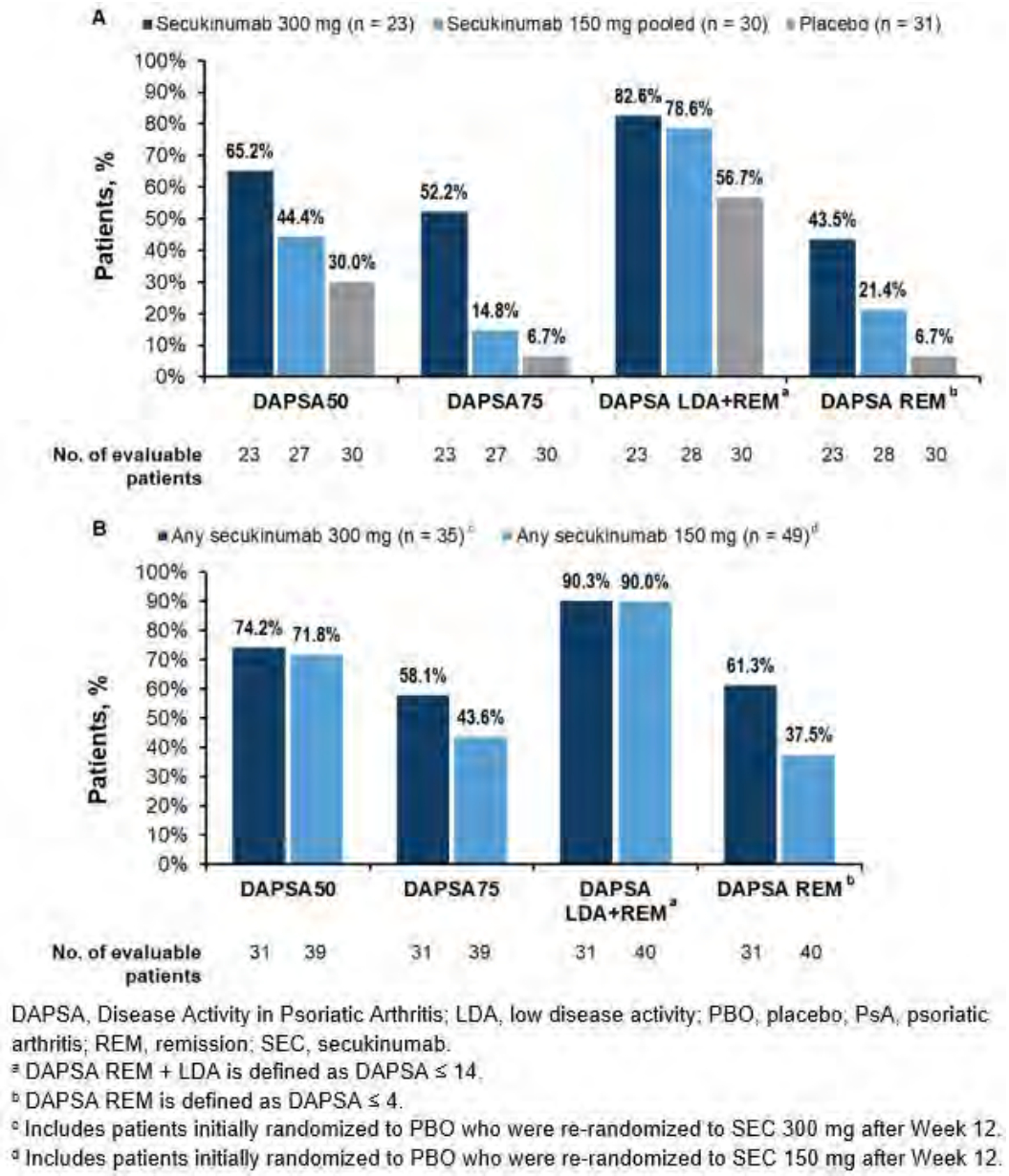
Background/Purpose: Oligoarticular psoriatic arthritis (PsA), defined as involvement of ≤ 4 joints, affects approximately 50% of the PsA population.[1,2] Disease burden is comparable for patients with oligoarticular or polyarticular disease, and most patients progress from oligoarticular to polyarticular PsA.[1,2] Evidence for the efficacy of biologics in patients with oligoarticular PsA is limited, as inclusion criteria for randomized controlled trials in PsA typically require ≥ 3 swollen and tender joints. We evaluated the efficacy of the interleukin 17 inhibitor secukinumab (SEC) in patients with oligoarticular PsA pooled from 5 phase 3 studies.

Methods: This post hoc analysis included patients with oligoarticular PsA from the FUTURE 2-5 and MAXIMISE trials (NCT01649375, NCT01989468, NCT02294227, NCT02404350, and NCT02721966). Oligoarticular PsA was defined as the presence of 1-4 tender joints and 1-4 swollen joints at baseline as measured by the tender joint count of 78 joints (TJC78) and the swollen joint count of 76 joints (SJC76), respectively. For this analysis, patients were pooled by treatment received at Week 12 and Week 52 according to the following groups: Week 12 (SEC 300 mg, SEC 150 mg

Table. Demographics and Baseline Disease Characteristics

Characteristic	SEC 300 mg (n = 23)	SEC 150 mg, pooled (n = 30)	PBO (n = 31)
Age, mean (SD), years	38.8 (13.3)	43.2 (12.1)	46.8 (14.3)
Male, n (%)	16 (69.6)	19 (63.3)	19 (61.3)
White, n (%)	22 (95.7)	29 (96.7)	31 (100)
BMI, mean (SD), kg/m^2	27.0 (5.8)	29.4 (6.0)	28.1 (4.3)
TJC78, mean (SD)	3.3 (0.9)	3.3 (1.0)	3.4 (0.7)
SJC76, mean (SD)	3.0 (1.1)	2.7 (1.1)	2.7 (1.0)
DAPSA, mean (SD)	18.0 (4.7)	16.7 (4.8)	17.6 (4.5)
HAQ-DI, mean (SD)	0.9 (0.5)	1.1 (0.7)	1.0 (0.7)
Time since PsA diagnosis, mean (SD), years	3.0 (3.5)	4.1 (6.4)	5.1 (5.8)

BMI, body mass index; DAPSA, Disease Activity in Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; PBO, placebo; SEC, secukinumab; SJC76, swollen joint count of 76 joints; TJC78, tender joint count of 78 joints.

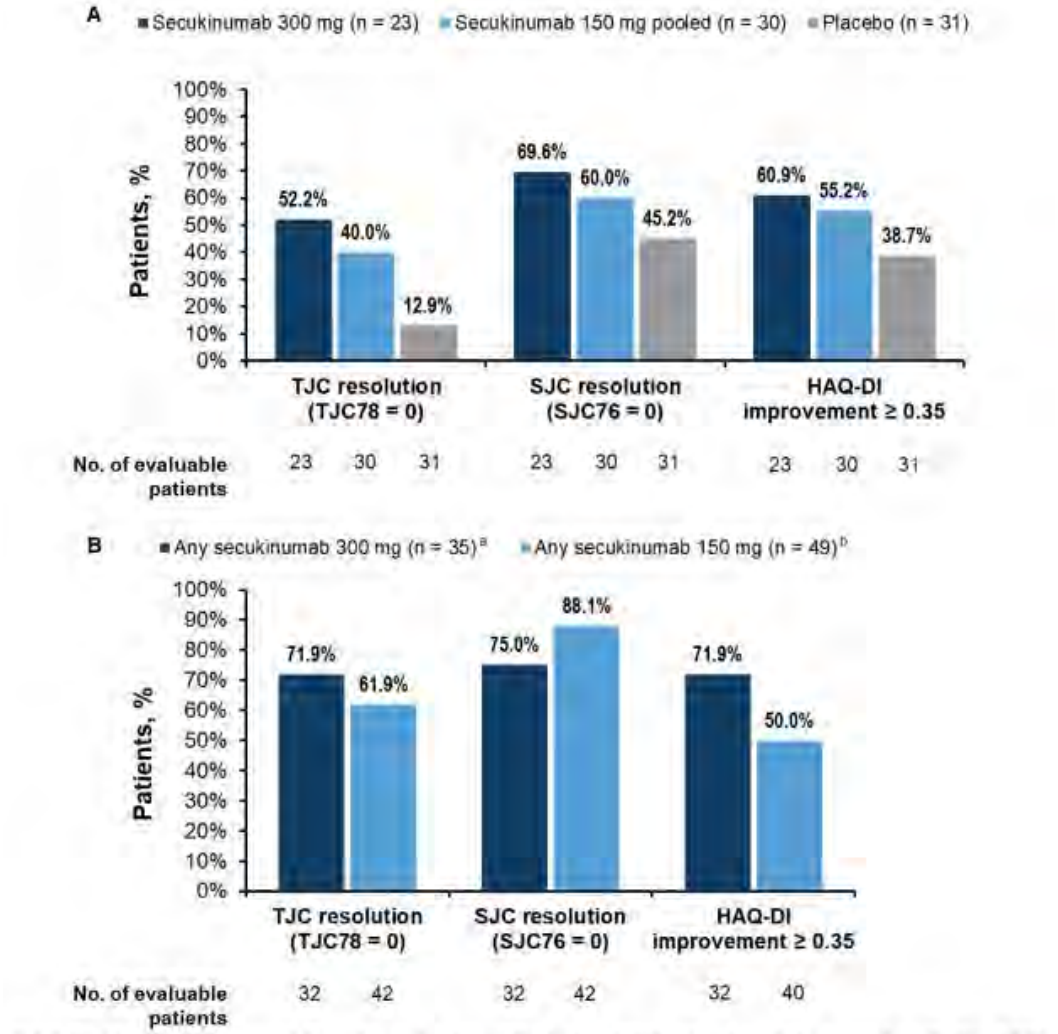


DAPSA, Disease Activity in Psoriatic Arthritis; LDA, low disease activity; PBO, placebo; PsA, psoriatic arthritis; REM, remission; SEC, secukinumab.
[a] DAPSA REM + LDA is defined as DAPSA ≤ 14.
[b] DAPSA REM is defined as DAPSA ≤ 4.
[c] Includes patients initially randomized to PBO who were re-randomized to SEC 300 mg after Week 12.
[d] Includes patients initially randomized to PBO who were re-randomized to SEC 150 mg after Week 12.

Figure 1. Proportion of Patients With Oligoarticular PsA Achieving DAPSA Responses at (A) Week 12 and (B) Week 52 (observed).

with or without loading dose [LD], or placebo [PBO]) and Week 52 (any SEC 300 mg or any SEC 150 mg). Efficacy was assessed by the proportion of patients achieving 50% improvement in Disease Activity in Psoriatic Arthritis (DAPSA50), DAPSA75, DAPSA-based low disease activity (LDA) and remission (REM), resolution of TJC78, resolution of SJC76, and a ≥ 0.35-point improvement in the Health Assessment Questionnaire-Disability Index score. Descriptive statistics are provided for each endpoint using an observed-case approach. Logistic regression analysis was used to identify potential predictors of DAPSA response at Weeks 12 and 52; multivariate logistic regression analyses were performed thereafter.

Results: In total, 84 patients were included in this analysis: 48 with active PsA from the FUTURE 2-5 trials and 36 with active PsA and axial manifestations from the MAXIMISE trial. Demographics and baseline disease characteristics



HAQ-DI, Health Assessment Questionnaire-Disability Index; PBO, placebo; PsA, psoriatic arthritis; SEC, secukinumab; SJC76, swollen joint count of 76 joints; TJC78, tender joint count of 78 joints.
[a] Includes patients initially randomized to PBO who were re-randomized to SEC 300 mg after Week 12.
[b] Includes patients initially randomized to PBO who were re-randomized to SEC 150 mg after Week 12.

Figure 2. Proportion of Patients With Oligoarticular PsA Achieving Resolution of TJC, Resolution of SJC, and a ≥ 0.35-Point HAQ-DI Score Improvement at (A) Week 12 and (B) Week 52 (observed).

are presented in the Table. At Week 12, notable improvements were observed for the SEC vs PBO groups across all the assessed outcome measures (Figures 1A, 2A). These improvements were sustained or increased further through Week 52 (Figures 1B, 2B). More than 90% of patients who received any SEC 300 mg or SEC 150 mg achieved LDA or REM at Week 52 (Figure 1B). At Week 52, a higher proportion of patients who received any SEC 300 mg vs any SEC 150 mg achieved higher hurdle endpoints of DAPSA 75 and DAPSA REM (Figure 1B). At Week 12, younger age was a predictor for the achievement of DAPSA LDA or REM and the achievement of DAPSA50, while lower baseline SJC was a predictor of the achievement of DAPSA REM ($P < .05$). No predictors were identified at Week 52.

Conclusion: SEC provides greater improvements vs PBO across a number of disease activity and physical function outcome measures in patients with oligoarticular PsA at Week 12, with sustained responses through Week 52.

References

1. Huscher D, et al. *Arthritis Rheumatol*. 2015;67(suppl 10). Abstract 679.
2. Gladman D, et al. *Arthritis Rheumatol*. 2019;71(suppl 10). Abstract 2495.

Disclosure: A. Ogdie, Amgen, 2, 5, AbbVie, 2, BMS, 2, Celgene, 2, Gilead, 2, Lilly, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Eli Lilly, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **E. Pournara**, Novartis, 3, 11; **X. Meng**, Novartis Pharmaceuticals Corporation, 3; **B. Parikh**, Novartis Pharmaceuticals Corporation, 3; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1826

Reduced Burden on Paid and Household Work Productivity with Stringent Thresholds of Disease Control: Further Results from Long-Term Certolizumab Pegol Treatment in Patients with Psoriatic Arthritis

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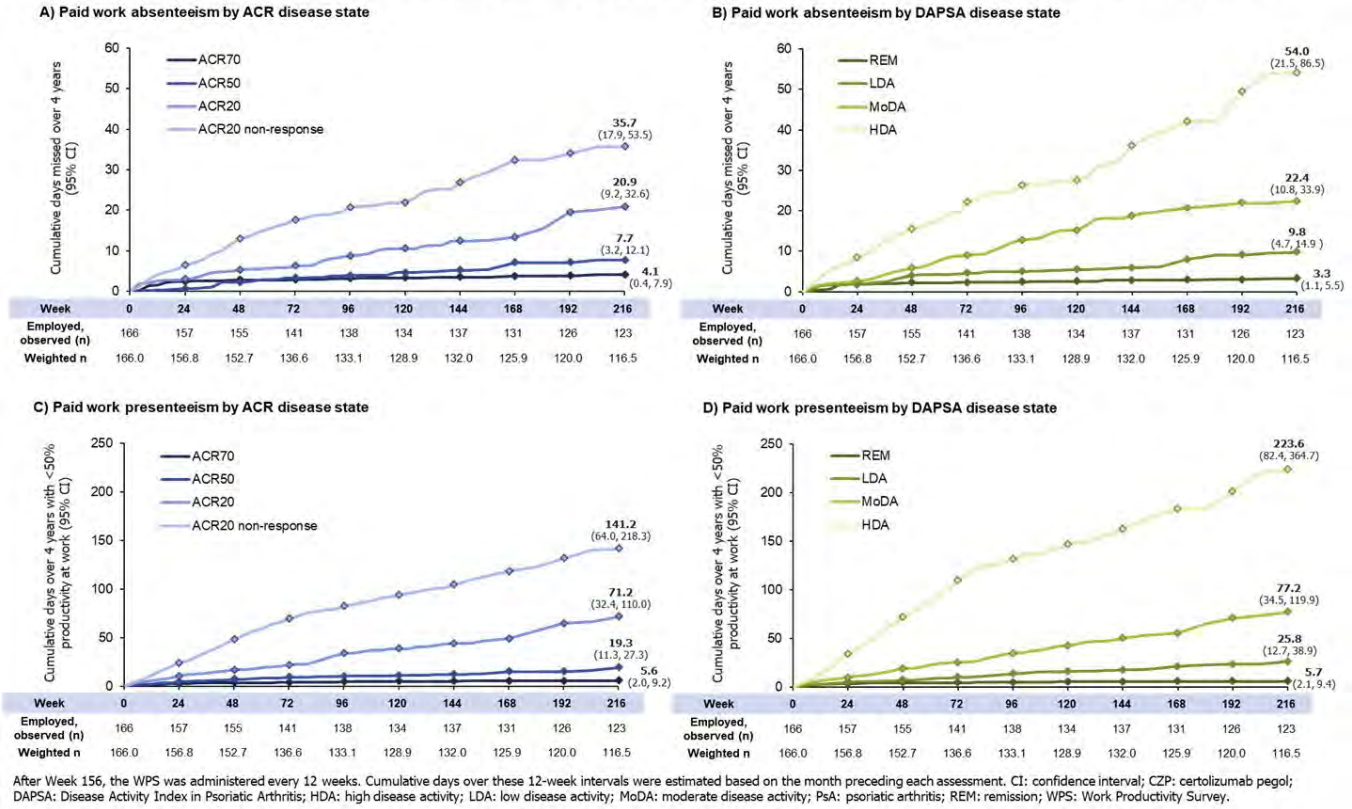
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is associated with a reduction in workplace productivity,[1] which may extend into household productivity.[2] Certolizumab pegol (CZP) is a tumor necrosis factor inhibitor, clinically effective at improving disease activity outcomes for patients (pts) with PsA.[3] We have previously reported an association between stringent thresholds of disease control in pts with PsA, measured by ACR response criteria, and paid/household work productivity.[4] However, it is also important to assess the relationship between disease activity and paid/household work productivity using a measure more relevant to real-world practice, such as Disease Activity Index in PsA (DAPSA).

Our purpose was to evaluate the association between DAPSA disease states and burden on paid/household work productivity in pts with PsA during long-term treatment with CZP.

Methods: These analyses used data from pts originally randomized to CZP in RAPID-PsA (NCT01087788), a 216-week phase 3 study.[3] Pts were classified according to the ACR20/50/70 criteria and DAPSA disease states (high disease activity [HDA], moderate disease activity [MoDA], low disease activity [LDA] and remission [REM]). Paid/household work productivity, assessed with the arthritis-specific Work Productivity Survey, was compared for each threshold of disease control. An inverse probability weight model was used to account for predictors of dropout over

Figure 1. Paid work absenteeism and presenteeism by disease activity, assessed by (A, C) ACR 20/50/70 response criteria and (B, D) DAPSA disease states for CZP-randomized population



After Week 156, the WPS was administered every 12 weeks. Cumulative days over these 12-week intervals were estimated based on the month preceding each assessment. CI: confidence interval; CZP: certolizumab pegol; DAPSA: Disease Activity Index in Psoriatic Arthritis; HDA: high disease activity; LDA: low disease activity; MoDA: moderate disease activity; PsA: psoriatic arthritis; REM: remission; WPS: Work Productivity Survey.

216 weeks. Cumulative days affected since study baseline were estimated using a weighted generalized estimating equations model.

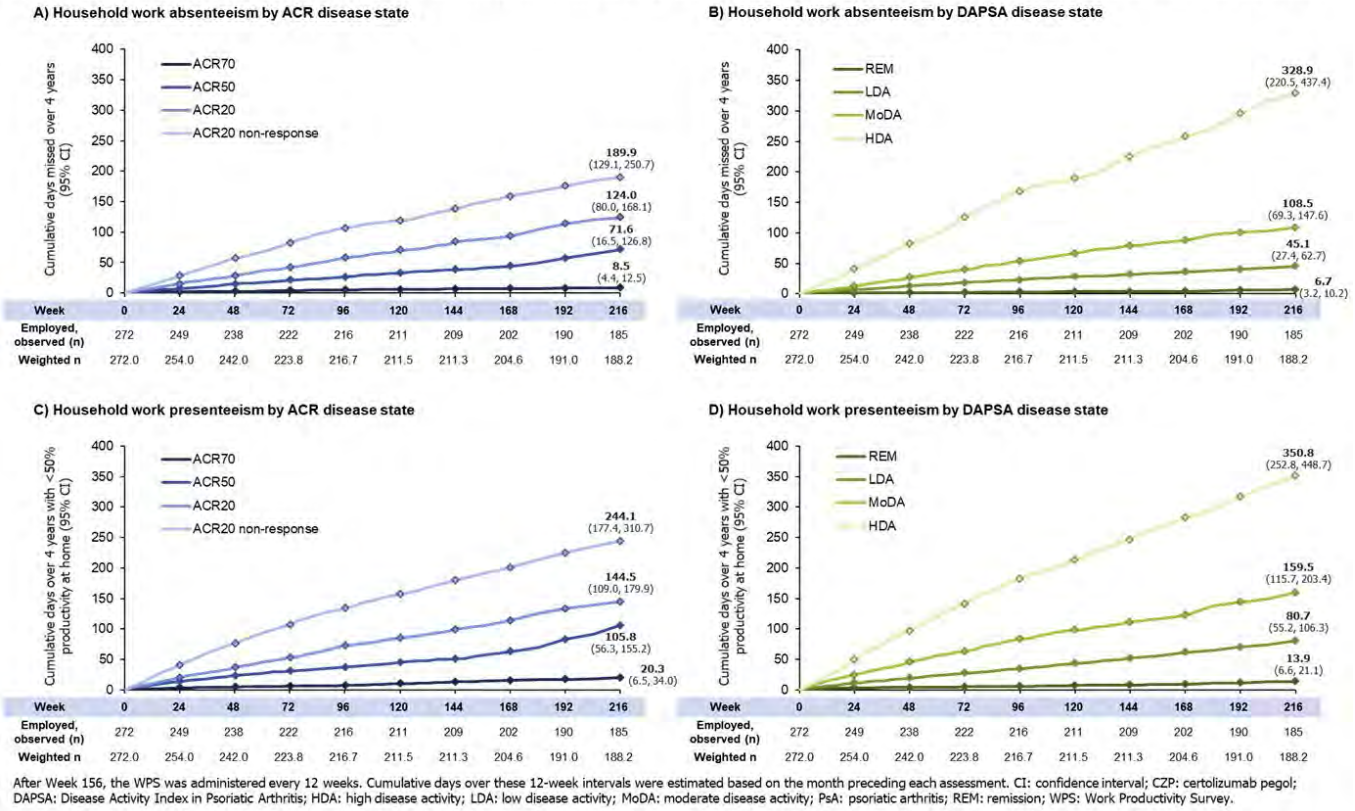
Results: 273 pts were randomized to CZP, 183 (67.0%) of these pts completed Week 216. At baseline, 60.8% of pts were employed outside the home. Through Week 216, fewer days of paid work absence (absenteeism) were reported by pts achieving ACR70 (4.1 [95% confidence interval: 0.4, 7.9]), DAPSA REM (3.3 [1.1, 5.5]) and the intermediate measures, than ACR20 non-responders (35.7 [17.9, 53.5]) and those with DAPSA HDA (54.0 [21.5, 86.5]; **Figure 1A**, **B**). These findings extended to household work absenteeism; again pts achieving ACR70 (8.5 [4.4, 12.5]) and DAPSA REM (6.7 [3.2, 10.2]) reported fewer absences than ACR20 non-responders (189.9 [129.1, 250.7] and those with DAPSA HDA (328.9 [220.5, 437.4]; **Figure 2A**, **B**).

Improved ACR and DAPSA outcomes also correlated with larger reductions in the number of days with < 50% productivity at work/home (presenteeism; **Figure 1C**, **D** & **Figure 2C**, **D**), compared with absenteeism.

Conclusion: Cumulative estimates of the number of work days affected by PsA, as correlated with DAPSA status, support earlier findings[4] that achievement of more stringent thresholds of disease control are associated with reduced burden on paid/household work productivity.

References: 1. Kennedy M. Clin Exp Rheumatol 2014;32:342–8; **2**. Osterhaus JT. Arthritis Res Ther 2014;16:R164; **3**. van der Heijde D. RMD Open 2018;4:e000582; **4**. Tillett W. Value Health 2020;23:S411.

Figure 2. Household work absenteeism and presenteeism by disease activity, assessed by (A, C) ACR 20/50/70 response criteria and (B, D) DAPSA disease states for CZP-randomized population



After Week 156, the WPS was administered every 12 weeks. Cumulative days over these 12-week intervals were estimated based on the month preceding each assessment. CI: confidence interval; CZP: certolizumab pegol; DAPSA: Disease Activity Index in Psoriatic Arthritis; HDA: high disease activity; LDA: low disease activity; MoDA: moderate disease activity; PsA: psoriatic arthritis; REM: remission; WPS: Work Productivity Survey.

Disclosure: W. Tillett, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **S. Kiri**, UCB Pharma, 3, 11; **V. Taieb**, UCB Pharma, 2; **P. Mease**, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, 6, Galapagos, 2, 5, Celgene, 2, Boehringer Ingelheim, 2, Genentech, 2, 5, 6, Janssen, 2, 5, 6, Gilead Sciences, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Sun Pharma, 2, 5, UCB Pharma, 2, 6, GSK, 2.

Abstract Number: 1827

Psoriatic Arthritis, Female Sex and Increased Baseline Skin Severity Are Associated with Drug Persistence in Ustekinumab-Treated Patients with Psoriasis in the BADBIR Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Baseline characteristics of patients with PsO treated with UST in the BADBIR (N=6302). BADBIR, British Association of Dermatologists Biologic and Immunomodulators Register; BMI, body mass index; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab

Baseline characteristic		Patients, n (%)
Comorbid PsA	No PsA	5353 (84.9)
	PsA	949 (15.1)
Biologic experience	No prior biologic	5206 (82.6)
	Prior biologic	1096 (17.4)
PASI (n=6281)	PASI ≤3	1125 (17.9)
	PASI >3–≤10	1723 (27.4)
	PASI >10–≤20	2643 (42.1)
	PASI >20	790 (12.6)
Sex	Female	2698 (42.8)
	Male	3604 (57.2)
Depression	No depression	4901 (77.8)
	Depression	1401 (22.2)
Obesity (BMI, kg/m^2) (n=5758)	<30	2979 (51.7)
	≥30	2779 (48.3)

Background/Purpose: Skin and joint symptoms both contribute to the burden of disease in psoriatic arthritis (PsA).[1] More severe skin symptoms in patients with both skin and joint involvement have been reported to be associated with poorer quality of life, higher disability and lower work productivity.[2] The objective of this study was hence to evaluate to what extent baseline (BL) factors, such as comorbid PsA and psoriasis (PsO) severity, are associated with ustekinumab (UST) persistence in patients with PsO enrolled in the British Association of Dermatologists Biologic and Immunomodulators Register (BADBIR).

Methods: This retrospective observational study used data from patients with PsO receiving UST in the BADBIR (first enrolled, 07/2009; data cut-off, 10/2020). Time to discontinuation (TTD) was defined as the time from treatment start date until treatment stop date, censoring for loss to follow-up where patients were lost to follow-up or active in the registry without a recorded treatment stop date. Hazard ratios (HRs), confidence intervals and p-values (Wald test) for the association between obesity, sex, PsA status, prior biologic exposure, depression, Psoriasis Area and Severity

Table 2. Cox regression model for time to discontinuation of UST in patients with PsO. *Indicates interaction between covariates. BMI, body mass index; HR, hazard ratio; PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab

Covariate	Status	HR	p-value
Comorbid PsA	No PsA	Reference	–
	PsA	1.98	<0.0001
Biologic experience	No prior biologic	Reference	–
	Prior biologic	1.08	0.3
PASI	PASI ≤3	Reference	–
	PASI >3–≤10	1.35	0.002
	PASI >10–≤20	1.23	0.019
	PASI >20	1.77	<0.0001
Sex	Female	Reference	–
	Male	0.72	<0.0001
Depression	No depression	Reference	–
	Depression	1.21	0.0007
Obesity (BMI, kg/m^2)	<30	Reference	–
	≥30	1.08	0.15
PsA*prior biologic experience	PsA, no prior biologic	Reference	–
	PsA, prior biologic	2.35	0.005
PsA*PASI	PsA, PASI ≤3	Reference	–
	PsA, PASI >3–≤10	1.72	0.2
	PsA, PASI >10–≤20	1.35	0.0008
	PsA, PASI >20	1.37	0.004

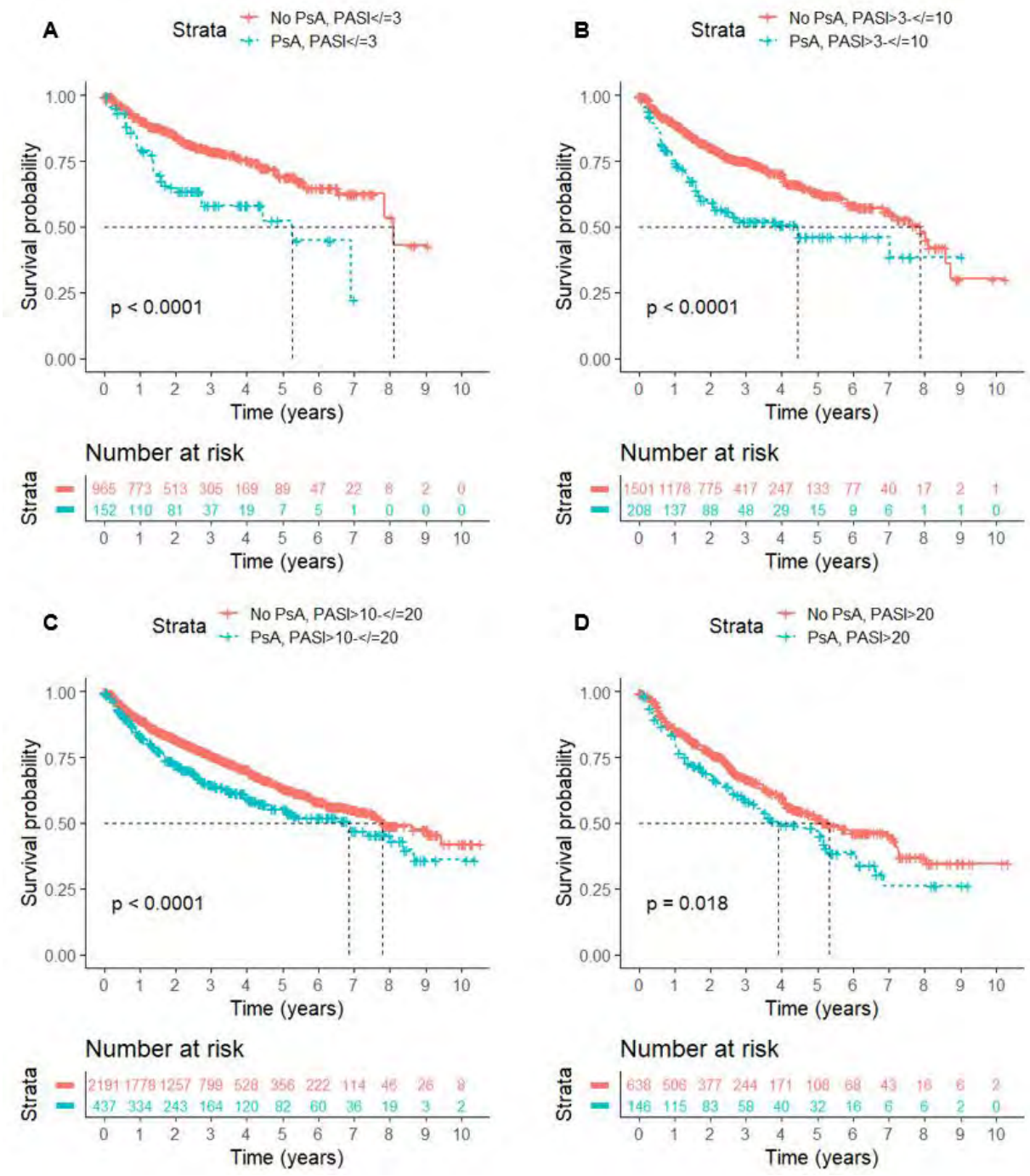

Figure 1. Drug survival in patients with PsO treated with UST, stratified by presence of comorbid PsA and according to PASI strata of (A) ≤3, (B) >3–≤10, (C) >10–≤20 and (D) >20. PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; UST, ustekinumab.

Index (PASI) strata, and interactions between covariates and TTD were generated using Cox proportional hazards regression. Kaplan–Meier analysis was used to estimate probability of TTD. Patients were stratified by PsA diagnosis at BL and PASI. The log-rank test was used to compare persistence among groups.

Results: Patient BL characteristics are listed in Table 1. Multivariable analysis (Table 2) found that median TTD was shorter for patients with comorbid PsA vs. PsO alone (HR 1.98; p< 0.0001). Median TTD was shorter in patients with depression vs. no depression (HR 1.21; p=0.0007). Men were at lower risk of discontinuation vs. women (HR 0.72; p<

0.0001). Prior biologic experience reduced TTD in patients with comorbid PsA vs. biologic-naïve patients with PsA (HR 2.35; p=0.005). PASI >3 at BL was associated with increased probability of discontinuation vs. PASI ≤3 (PASI >3–≤10, HR 1.35, p=0.002; PASI >10–≤20, HR 1.23, p=0.019; PASI >20, HR 1.77, p< 0.0001). In patients with comorbid PsA, higher skin severity at BL also led to a shorter TTD, with PsA seeming to have a greater impact on UST persistence in patients with lower skin severity at BL. Median TTD in patients with PsO alone and PASI ≤3 was 8.11 years vs. 5.27 years for patients with comorbid PsA (p< 0.0001). In patients with PASI >20, median TTD for patients with PsO alone was 5.33 years vs. 3.89 years for patients with comorbid PsA (p=0.018; Figure 1).

Conclusion: PsA, female sex and depression were associated with a shorter TTD of UST. More severe skin disease at BL had a higher association with discontinuation, irrespective of comorbid PsA, and comorbid PsA had a greater association with shorter TTD in patients with lower PASI scores. This suggests that patient-centric, multidisciplinary care needs to be considered to achieve the best possible outcomes in psoriatic disease.

References:

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Disclosure: A. Ogdie, Amgen, 2, 5, AbbVie, 2, BMS, 2, Celgene, 2, Gilead, 2, Lilly, 2, Janssen, 2, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 5, Rheumatology Research Foundation, 5, National Psoriasis Foundation, 5; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2; **A. Passey**, Janssen, 3; **P. Gorecki**, Janssen, 3.

Abstract Number: 1828

Safety Profile of Ixekizumab for the Treatment of Psoriatic Arthritis and Axial Spondyloarthritis up to 3 Years: An Updated Integrated Safety Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets IL-17A approved for the treatment of psoriasis, psoriatic arthritis (PsA), active ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) with objective signs of inflammation. We report a summary of the safety outcomes with over 2000 patient-years (PY) of exposure up to 3 years in patients with PsA and axSpA.

Methods: Long-term safety of IXE was assessed from 8 randomized trials. Treatment-emergent adverse events (TEAEs) adjusted incidence rates (IRs) per 100 PY within 1-year time periods through 19 March 2021 were calculated for all patients treated with ≥1 dose of IXE. Safety outcomes included TEAEs, serious AEs (SAEs), discontinuations

Table. Safety Outcomes		
	Pooled PsA IXE (N=1401)	**Pooled axSpA IXE (N=932)**
Total patient-years	2247.7	2096.2
	n (IR) 95% CI	**n (IR)** 95% CI
TEAEs	**1131 (50.3)** 47.5 – 53.3	**798 (38.1)** 35.5 – 40.8
Nasopharyngitis	**202 (9.0)** 7.8 – 10.3	**176 (8.4)** 7.2 – 9.7
Upper respiratory tract infection	**186 (8.3)** 7.2 – 9.6	**122 (5.8)** 4.9 – 6.9
SAEs	**134 (6.0)** 5.0 – 7.1	**101 (4.8)** 4.0 – 5.9
Deaths[a]	**6 (0.3)** 0.1 – 0.6	**3 (0.1)** 0.0 – 0.4
Discontinuations due to adverse events	**115 (5.1)** 4.3 – 6.1	**66 (3.1)** 2.5 – 4.0
Adverse events of special interest		
Infections	**759 (33.8)** 31.4 – 36.3	**540 (25.8)** 23.7 – 28.0
Serious infections	**28 (1.2)** 0.9 – 1.8	**23 (1.1)** 0.7 – 1.7
Opportunistic infections[b]	**40 (1.8)** 1.3 – 2.4	**17 (0.8)** 0.5 – 1.3
Candida infections[c]	**45 (2.0)** 1.5 – 2.7	**26 (1.2)** 0.8 – 1.8
Injection-site reactions	**260 (11.6)** 10.2 – 13.1	**156 (7.4)** 6.4 – 8.7
Allergic/hypersensitivity reactions[d]	**102 (4.5)** 3.7 – 5.5	**89 (4.2)** 3.4 – 5.2
Cytopenias[e]	**56 (2.5)** 1.9 – 3.2	**28 (1.3)** 0.9 – 1.9
Neutropenia grade ≥1[f]	**219 (9.7)** 8.5 – 11.1	**170 (8.1)** 7.9 – 9.4
Malignancies	**15 (0.7)** 0.4 – 1.1	**9 (0.4)** 0.2 – 0.8
MACE[g]	**12 (0.5)** 0.3 – 0.9	**6 (0.3)** 0.1 – 0.6
Depression[h]	**37 (1.6)** 1.2 – 2.3	**19 (0.9)** 0.6 – 1.4
Iridocyclitis (anterior uveitis)	**0 (0.0)** 0.0 – 0.0	**58 (2.8)** 2.1 – 3.6
Inflammatory bowel disease[i]	**3 (0.1)** 0.0 – 0.4	**17 (0.8)** 0.5 – 1.3
Ulcerative colitis	**1 (0.0)** 0.0 – 0.3	**10 (0.5)** 0.3 – 0.9
Crohn's disease	**2 (0.1)** 0.0 – 0.4	**7 (0.3)** 0.2 – 0.7

axSpA, axial spondyloarthritis; IR, incidence rate; IXE, ixekizumab; MACE, major adverse cerebro-cardiovascular events; n, number of patients in each category; PsA, psoriatic arthritis; SAEs, serious adverse events; SMQ, Standardised MedDRA Queries; TEAEs, Treatment-emergent adverse events. Adverse event (AE) terms were derived from MedDRA v23.1. aThe 6 reported deaths in the PsA population were due to cardiovascular event (n=2), metastatic renal cell carcinoma (n=1), cerebrovascular accident (n=1), pneumonia (n=1), and drowning (n=1). In the axSpA population, the causes of deaths were suicide (n=1), sepsis (n=1), and murder (n=1). bOpportunistic infections included esophagus candidiasis, oral candidiasis, hepatitis B reactivation, and herpes zoster. cSome Candida infections cases were also considered as opportunistic infections. All cases of Candida infection were localized. In PsA program, most cases were mild (34/45, IR=1.5 per 100 patient-years) to moderate (10/45, IR=0.4 per 100 patient-years) in severity, except 1 case of esophagus candidiasis considered severe. The patient who reported severe esophagus candidiasis did not discontinue the study drug due to this AE. In axSpA program, all cases were mild (16/26, IR=0.8 per 100 patient-years) or moderate (10/26, IR=0.5 per 100 patient-years) in severity. Across indications, no cases of systemic candidiasis were reported. dNo cases of anaphylaxis were confirmed after medical reviews. eBroad, according to SMQ classification. fBased on neutrophils count lab results. Neutropenia grade ≥3, n (IR) [95%CI] PsA= 8 (0.4) [0.2, 0.7], axSpA= 4 (0.2) [0.1, 0.5]. gThe data represents events confirmed by adjudication. hBroad, according to SMQ or sub-SMQ classification. iThe data represents confirmed cases per external adjudication. In the PsA population, none of the patients with confirmed IBD per external adjudication had medical history of IBD. Three patients had events of IBD confirmed by adjudication. One patient had more than 1 event. In the axSpA population, of the 17 patients with adjudicated IBD, 5 patients had a history of IBD.

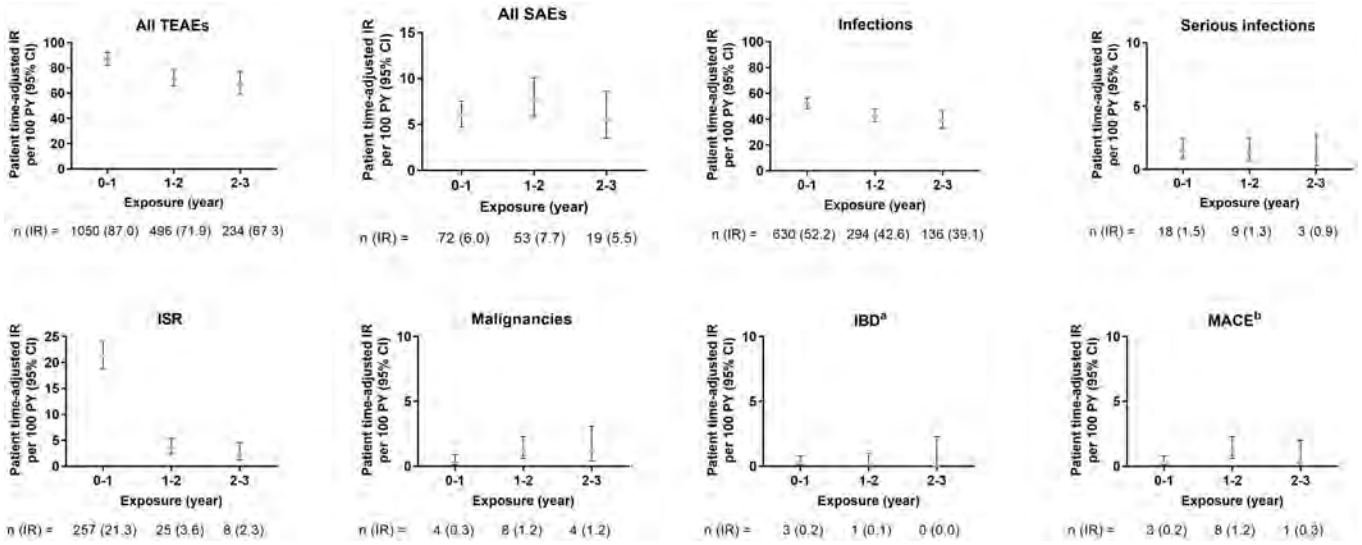

Figure 1. Exposure-adjusted incidence rate of TEAEs, SAEs, and selected AEs in PsA pooled population. The data points on the graph are the IR (95% CI)/100 patient-years at successive year intervals from year 0 to year 3. The CIs for the IRs are from likelihood ratio test of treatment effect from the Poisson regression model. aThe data represents confirmed cases per external adjudication. Three patients had events of IBD confirmed by adjudication. One patient had more than 1 event. bThe data represents events confirmed by adjudication. AEs, adverse events; CI, confidence interval; IBD, inflammatory bowel disease; IR, incidence rates; ISR, injection-site reactions; MACE, major adverse cerebro-cardiovascular events; PsA, psoriatic arthritis; SAE, serious adverse events; TEAEs, treatment-emergent adverse events.

due to AEs, deaths, and selected safety topics of interest. Major adverse cerebro-cardiovascular event (MACE) and inflammatory bowel disease (IBD) reported cases were adjudicated.

Results: A total of 1401 patients with PsA and 932 patients with axSpA with a cumulative IXE exposure of 2247.7 PY for PsA and 2096.2 PY for axSpA were included in this analysis (Table). The IRs per 100 PY for any TEAE were 50.3 for PsA and 38.1 for axSpA. Serious AEs were reported by 134 patients with PsA (IR=6.0), and 101 patients with axSpA (IR=4.8). A total of 9 deaths was reported, including 6 in PsA (IR= 0.3) and 3 in axSpA (IR=0.1). The IRs per 100 PY

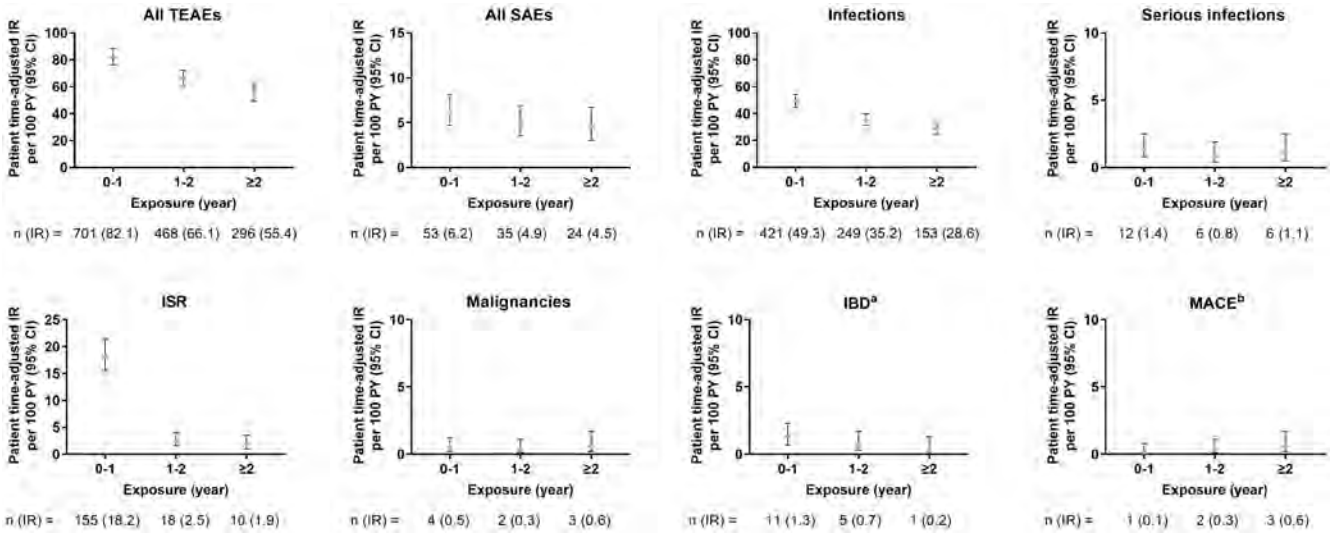

Figure 2. Exposure-adjusted incidence rate of TEAEs, SAEs, and selected AEs in axSpA pooled population. The data points on the graph are the IR (95% CI)/100 patient-years at successive year intervals from year 0 to ≥2 year. The CIs for the IRs are from likelihood ratio test of treatment effect from the Poisson regression model. aThe data represents confirmed cases per external adjudication. bThe data represents events confirmed by adjudication. AEs, adverse events; axSpA, axial spondyloarthritis; CI, confidence interval; IBD, inflammatory bowel disease; IR, incidence rates; ISR, injection-site reactions; MACE, major adverse cerebro-cardiovascular events; SAE, serious adverse events; TEAEs, treatment-emergent adverse events.

of discontinuation from the study drug due to AE were 5.1 (PsA) and 3.1 (axSpA). IRs of serious infections were low (PsA: IR= 1.2, axSpA: IR=1.1). IRs of opportunistic infections (PsA: IR= 1.8, axSpA: IR=0.8) and *Candida* infections (PsA: IR= 2.0, axSpA: IR=1.2) were low. There were no confirmed cases of reactivation of tuberculosis. Injection site reactions occurred with IRs of 11.6 (PsA) and 7.4 (axSpA). The IRs for allergic/hypersensitivity reactions were 4.5 (PsA) and 4.2 (axSpA). No confirmed events of anaphylaxis were reported. Across indications, IRs were low for cytopenia (≤2.5), malignancies (≤0.7), MACE (≤0.5), depression (≤1.6), and iridocyclitis (≤2.8). Per external adjudication, 20 patients had confirmed IBD (including 3 patients with PsA and 17 with axSpA) of which 1 was confirmed as ulcerative colitis for PsA (IR=0.0) and 10 for axSpA (IR=0.5); 2 events were confirmed as Crohn's disease for PsA (IR=0.1) and 7 for axSpA (IR=0.3). Across safety topics, IRs were decreased or remained constant over time (Figures 1 and 2).

Conclusion: In this updated analysis with 2247.7 PY for PsA and 2096.2 PY for axSpA, IXE maintained a safety profile consistent to that previously reported,[1-3] with no new or unexpected safety events through exposure up to 3 years.

References

[1]Mease P et al. Arthritis Care Res (Hoboken) 2019;71(3):367-78
[2]Combe B et al. Arthritis Res Ther 2020;22(1):14
[3]Genovese MC et al. Rheumatology (Oxford) 2020;59(12):3834-44

Disclosure: S. Schwartzman, Abbvie, 2, 6, Janssen, 2, 6, Eli Lilly and Company, 2, 6, Novartis, 2, 6, Pfizer, 2, 8, Regeneron, 2, 6, Sanofi, 2, 6, UCB, 2, 6, National Psoriasis Foundation, 4, Aurinia, 6, Myriad, 2, 4; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2; **B. Combe**, AbbVie, 2, 4, 5, 6, Bristol-Myers Squibb, 6, Celltrion, 4, 6, Eli Lilly, 2, 4, 5, 6, Gilead/Galapagos, 2, 4, 6, Janssen, 4, Merck, 6, Pfizer, 5, 6, Roche/Chugai, 4, 6, Novartis, 4, 5, 6, Sanofi, 2, Novartis, 5, UCB, 6; **A. Accioly**, Eli Lilly and Company, 3, Sanofi, 3; **A. Kronbergs**, Eli Lilly and Company, 3; **B. Janos**, Eli Lilly and Company, 3, 11; **D. Zhu**, Eli Lilly and Company, 3; **D. Sandoval Calderon**, Eli Lilly and Company, 3; **P. Rahman**, Janssen, 2, 5, 6, Novartis, 2, 5, 6, AbbVie, 2, 6, Amgen, 2, 6, Bristol Myers Squibb, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6, Pfizer, 2, 6, UCB, 2, 6, Merck, 2, 6; **D. Poddubnyy**, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6.

Abstract Number: 1829

Pharmacological Treatment of Enthesitis - A Systematic Review on the Efficacy of the Available Options

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Enthesitis is a recognized as a hallmark of spondyloarthrtis (SpA), including psoriatic arthritis (PsA). However, it is an underestimated disease domain in both in clinical trials and clinical practice (1).

This systematic literature review (SLR) assessed the efficacy of the available pharmacological options for enthesitis.

Table.

Disease	Tested drug vs Reference	Superiority of the treatment arm against reference arm (p<0.05)	Reference
PsA	TNFi vs PBO	YES	NCT00051623 (IFX) NCT00265096 (GOL) NCT01087788 (CZP)
	TNFi+MTX vs PBO+MTX (PBO+ETN one study) vs PBO+MTX	NO	NCT00367237 (IFX) NCT02065713 (GOL) NCT02376790 (ETN)
	UST vs PBO	YES	NCT01009086 NCT01077362
	UST vs TNFi	YES	EudraCT 2017-003799-29 β
	GUS q4w vs PBO GUS q8w vs PBO	YES NO	NCT03162796 NCT03158285
	SEC (pooled dose) vs PBO	YES	NCT01392326 NCT01752634
	SEC 300mg vs PBO SEC 150mg vs PBO	YES NO	NCT01989468
	SEC 300mg with loading vs PBO SEC 150mg with loading vs PBO SEC 150mg no loading vs PBO	YES YES NO	NCT02404350
	IXE vs PBO ADA vs PBO	YES NO PsA Bionaive	NCT01695239
	IXE vs PBO	NO PsA Bioexperienced	NCT02349295
	IL17i (SEC/ ADA) vs TNFi	NO	NCT02745080 (SEC) NCT03151551 (ADA) β
	APR 20mg vs PBO APR 30mg vs PBO	NO YES	NCT01172938
	TOF 5mg vs PBO TOF 10mg vs PBO ADA 40mg vs PBO	NO YES NO	NCT01877668 (TNFi-naive)
	TOF vs PBO	NO	NCT01882439 (TNFi-failure)
SpA	ETN vs SSZ	YES (imaging)/ NO (clinical) axSpA	NCT00844142
	ETN vs PBO	YES for nr-axSpA	NCT01258738
	ADA vs PBO	YES for r-axSpA NO for nr-axSpA YES for perSpA	NCT00195819 NCT00939003 NCT01064856
	GOL IV vs PBO	YES for r-axSpA	NCT02186873
	GOL 100mg vs PBO GOL 50mg vs PBO	YES NO For r-axSpA	NCT00265083
	GOL vs PBO	YES nr-axSpA	NCT01453725

β-Open-label; PsA: Psoriatic arthritis; r-axSpA: Radiologic axial spondylarthritis; nr-axialSpA: non radiological axial spondylarthritis; PBO: Placebo; TNFi: Tumor necrosis factor inhibitors; ETN: Etanercept; IFX: Infliximab; ADA: Adalimumab; GOL: Golimumab; UST: Ustekinumab; CZP: Certolizmab; GUS: Guselkumab; SEC: Secukinumab; IXE: Ixekizumab; APR: Apremilast; TOF: Tofacitinib; MTX - Methotrexate

Methods: A SLR was conducted following the PRISMA reporting guidelines. Studies were sourced from PubMed and Embase databases, using the MeSH terms: enthesitis, entheses, treatment, spondylarthritis, ankylosing spondylitis and psoriatic arthritis. The search was limited to articles in English published between January 2000 and July 2020. Two independent reviewers screened the titles and abstracts.

Results: A total of 65 articles matched the research criteria. The included populations, the time to assessment of the primary endpoint and the chosen outcome for assessment of enthesitis was heterogeneous across studies. There were no studies assessing the effect of non-steroidal anti-inflammatory drugs, glucocorticoids, or csDMARDs. In PsA, all TNFis showed superiority in monotherapy against placebo (PBO). However, when combined with methotrexate (MTX), only some TNFi showed superiority against MTX monotherapy. In SpA, there was conflicting evidence

regarding the efficacy of TNFi in enthesitis. Regarding IL23i in PsA, Ustekinumab was superior to PBO, and to TNFis. Guselkumab was superior to PBO when given every 4 weeks. Regarding IL7i, Secukinumab (SEC) was superior to PBO, only for some dosing schemes. Ixekizumab (IXE) was superior to PBO for the treatment of enthesitis only in TNF-naïve patients. Studies comparing SEC and IXE to ADA, showed no difference. There was no reported data on IL17i for enthesitis in SpA. In PsA, Tofacitinib was superior to PBO in naïve patients, and Tofacitinib 10mg was superior to PBO in bioexperienced patients. Apresmilast 30mg showed superiority to PBO for enthesitis. All findings are summarized on Table.

Conclusion: This SLR emphasizes the current heterogeneity in the assessment and report of enthesitis. There is still an unmet need for further studies to improve our understanding about enthesopathy.

1 - Schett G. et al. Enthesitis: from pathophysiology to treatment. Nat Rev Rheumatol. 2017;13(12):731-41.

Disclosure: R. Torres, None; **S. Manica**, Novartis, 6, MSD, 5, 6, Janssen, 6, Abbvie, 6; **F. Santos**, None.

Abstract Number: 1830

Discontinuation of Tumor Necrosis Factor Inhibitors in Psoriatic Arthritis and Psoriasis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory disease of the joints and skin that affects 1/1000 people in the US. Tumor necrosis factor-alpha (TNF-α) inhibitors are used when symptoms are severe. However, current research describing TNF-α inhibitors persistence rates, defined as time from initiation to discontinuation of the drug, is inconsistent and incomplete. This study examined characteristics associated with persistence of and response to TNF-α inhibitors, as well as reasons for discontinuation.

Methods: US veterans enrolled in the Program to Understand the Longterm Outcomes in Spondyloarthritis (PULSAR) database across 11 medical centers in the United States from 2007 – 2017 who 1) were diagnosed with PsA or psoriasis by a rheumatologist or dermatologist and 2) had been treated with a TNF-α inhibitor were included in the study. Length of treatment with a biologic was determined using VA prescription data. Drug discontinuation was defined as the length between the usual dose of the TNF-α inhibitor plus 90 days without treatment. Course was defined as the difference between the date the prescription was first filled and date of discontinuation without >90-day gap in treatment. Reasons for agent discontinuation were documented into PULSAR by a provider at rheumatology appointments. The following reasons for discontinuation were included: primary failure (no efficacy within 6 months

Table 1. Characteristics of TNF-α Inhibitor Discontinuation

	Univariate Regression				Initial Multivariate Regression				Final Multivariate Regression			
Variable	Haz Ratio	p value	[95% Con	Interval]	Haz Ratio	p value	[95% Con	Interval]	Haz Ratio	p value	[95% Con	Interval]
Age (years)	0.949	0.066	0.897	1.003	0.927	0.172	0.832	1.033				
Gender, % male	0.898	0.369	0.710	1.136	1.016	0.930	0.707	1.461				
Caucasian, %	1.040	0.645	0.880	1.229	0.791	0.638	0.298	2.099				
African American, %	0.924	0.520	0.725	1.176	0.600	0.372	0.196	1.841				
Hispanic, %	1.108	0.501	0.822	1.492	0.885	0.822	0.305	2.566				
Asian, %	1.614	0.243	0.722	3.605	1.103	0.841	0.423	2.874				
American Indian, %	1.551	0.059	0.983	2.447	0.728	0.538	0.264	2.003				
Other Race, %	1.249	0.220	0.876	1.780	1.000							
Never smoker	1.055	0.508	0.900	1.236	0.841	0.317	0.600	1.180				
Former smoker	0.862	0.039	0.748	0.993	0.790	0.086	0.603	1.034	0.827	0.037	0.692	0.989
Current smoker	1.150	0.085	0.981	1.347	1.000							
Education, years	0.997	0.871	0.966	1.030	1.040	0.200	0.979	1.105				
Duration Ps (years)	0.998	0.507	0.992	1.004	0.998	0.742	0.988	1.009				
Duration PsA (years)	0.991	0.008	0.984	0.998	0.997	0.578	0.987	1.007	0.991	0.009	0.984	0.998
HLA-B27 Positive, %	0.886	0.169	0.746	1.053	0.965	0.811	0.723	1.288				
Mean CRP (mg/L)	0.999	0.716	0.991	1.006	1.003	0.789	0.983	1.023				
Mean ESR (mm/hr)	0.998	0.387	0.993	1.003	0.997	0.541	0.986	1.007				
Course	1.100	0.000	1.063	1.138	1.085	0.004	1.026	1.147	1.096	<0.001	1.058	1.135
Charlson Comorbidity Index	0.986	0.371	0.957	1.016	0.976	0.431	0.920	1.036				

Ps = Psoriasis; PsA = Psoriatic Arthritis; CRP = C-reactive Protein; ESR = Erythrocyte Sedimentation Rate; p-value < 0.05 is considered significant

of treatment), secondary failure (loss of efficacy after 6 months of treatment), adverse event, concern for an adverse event, financial/access barrier, non-adherence, and other. Stata was used to conduct time-to-event and multivariate analyses.

Results: 321 individuals with 931 TNF-α inhibitor courses, including adalimumab (N = 381), certolizumab (N = 24), etanercept (N = 397), golimumab (N = 42), and infliximab (N = 87), were included in the study. The mean age was 55.4 years, and 252 of the 321 patients had a diagnosis of both PsA and psoriasis. 83.8% of the cohort continued at least one TNF-α inhibitor course at one year, and 64.8% continued at two years. On average, the probability of discontinuing a TNF-α inhibitor increased by 9.6% for each additional biologic trial (HR 1.096, p< 0.001). Former smoker (HR 0.827, p=0.037) and PsA duration in years (HR 0.991, p< 0.001) were also significantly correlated with discontinuation of a TNF-α inhibitor. On univariate and multivariate analyses, infliximab had a lower discontinuation rate than adalimumab (HR 2.114, p< 0.001), etanercept (HR 2.360, p< 0.001), and certolizumab (HR 3.048, p=0.001); however, the discontinuation rate of golimumab was lower than that of infliximab on univariate analysis only (HR 3.035, p< 0.001). The most commonly cited reason for discontinuing TNF-α inhibitor treatment was secondary failure (33%).

Conclusion: The majority of patients in this study continued at least one TNF-α inhibitor course at both 12 and 24 months. Secondary failure was the most prevalent reason for discontinuation, suggesting that further research should be conducted to examine reasons for loss of efficacy and immunogenicity of TNF-α inhibitors.

Table 2. Discontinuation of TNF-α Inhibitor Compared to Infliximab

	Univariate Regression				Initial Multivariate Regression				Final Multivariate Regression			
	Haz. Ratio	p value	[95% Conf	Interval]	Haz. Ratio	p value	[95% Conf	Interval]	Haz. Ratio	p value	[95% Conf	Interval]
Adalimumab	2.737	<0.001	2.038	3.675	1.409	0.339	0.697	2.849	2.114	<0.001	1.422	3.143
Etanercept	2.623	<0.001	1.969	3.495	2.123	0.052	0.993	4.540	2.360	<0.001	1.578	3.529
Golimumab	3.035	<0.001	1.933	4.766	0.606	0.474	0.153	2.393	2.217	0.006	1.254	3.919
Certolizumab	3.959	<0.001	2.268	6.911	8.936	0.077	0.787	101.428	3.048	0.001	1.539	6.037

p-value < 0.05 is considered significant

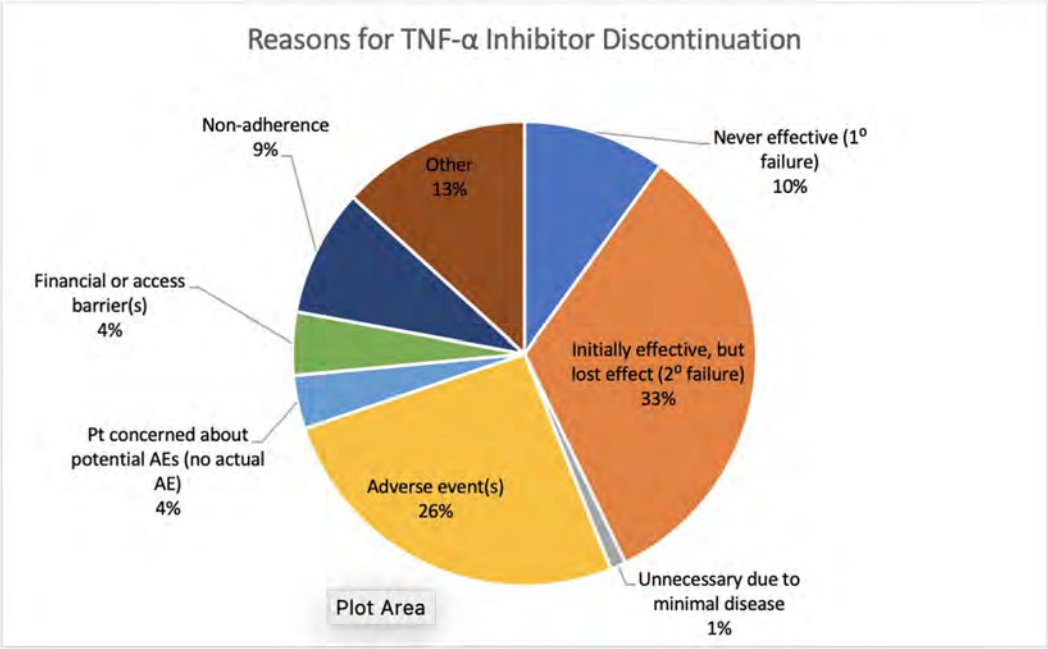

Figure 1. Reasons for TNF-α Inhibitor Discontinuation.

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Abstract Number: 1831

Predictors of Response, Adverse Events and Treatment Retention in Psoriatic Arthritis Patients Treated with Golimumab in a Prospective, Observational Registry

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: The Biologic Treatment Registry Across Canada (BioTRAC) was a prospective, observational registry that enrolled psoriatic arthritis (PsA) patients treated with subcutaneous golimumab (GLM) between 2010 and 2017.

Methods: Patient visits occurred at baseline and every 6 months thereafter. Multivariate logistic regression was used to identify independent predictors of achieving specific efficacy and safety endpoints and included the following covariates: age, gender, disease duration, enrolment period, concomitant medication, smoking and employment.

Results: A total of 281 patients were enrolled and followed for a mean duration of 1.9 years. The proportion of male gender was 46.3% and the mean disease duration at baseline was 6.1 years.

MDA was more likely to be achieved with lower baseline DAS28-CRP [OR (95% CI): 0.62 (0.45–0.84); p=0.002] and in patients who were employed [2.64 (1.22–5.71); p=0.014]. VLDA was more likely to be achieved with lower age [OR (95% CI): 0.96 (0.94–0.99); p=0.005], lower baseline DAS28-CRP [0.63 (0.44–0.89); p=0.009] and in patients who were employed [6.45 (2.30–18.27); p< 0.001], whereas VLDA was less likely to be achieved in patients who smoked [0.30 (0.10–0.92); p=0.035].

DAPSA LDA was more likely to be achieved with lower baseline DAPSA [OR (95% CI): 0.96 (0.94–0.98); p< 0.001]. DAPSA remission was more likely to be achieved with lower age [OR (95% CI): 0.98 (0.95–1.00); p=0.048] and lower baseline DAPSA [0.98 (0.96–1.00); p=0.043], while less likely to be achieved with later enrolment [2016-2017 vs. 2010–2012: 0.30 (0.11–0.78); p=0.014] and in patients who smoked [0.37 (0.15–0.93); p=0.035]. HAQ < 0.5 was more likely to be achieved in male vs. female gender [OR (95%): 2.03 (1.08–3.83); p=0.028] and in patients with lower baseline HAQ scores [0.19 (0.11–0.34); p< 0.001].

AEs were more likely to occur with baseline concomitant DMARD [1.97 (1.07–3.63); p=0.030] or NSAID use [1.88 (1.05–3.37); p=0.033], yet less likely in male vs. female [0.54 (0.30–0.98); p=0.043]. SAEs were more likely to occur with older age [1.04 (1.00–1.07); p=0.041], and less likely in patients enrolled later [2013–2015 vs. 2010–2012: 0.05 (0.01–0.18); p< 0.001 and 2016–2017 vs. 2010–2012: 0.03 (0.01–0.14); p< 0.001]. Being employed at baseline was a significant positive predictor of GLM retention [0.61 (0.38–0.97); p=0.035].

Conclusion: In PsA patients treated with golimumab, young age, employment and lower disease activity at baseline were associated with better treatment outcomes.

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Abstract Number: 1832

Secukinumab Therapy in Biologic-naïve vs. Biologic-experienced Patients: Real-world Effectiveness, Persistence and Safety Results from the Rheumatic Diseases Portuguese Registry

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	Naïve N=107	Biologic-experienced N=227	p-value
Age (years), mean (SD)	45.8 (12.5)	49.0 (11.3)	NS
Gender (male), N (%)	62 (57.9%)	101 (44.5%)	0.026
Ethnicity, Caucasian, N (%)	61 (98.4%)	147 (94.8%)	NS
BMI, kg/m^2, mean (SD)	27.2 (4.7)	26.4 (4.3)	NS
Current smokers, N (%)	10 (17.5%)	47 (30.7%)	NS
Scholarity, years, median (IQR)	12 (3)	10 (9)	NS
Employment Status, Full Time, N (%)	30 (62.5%)	79 (56.4%)	NS
HLA-B27 positive, N (%)	25 (51.0%)	79 (56.4%)	NS
Presence of comorbidities, N (%)	70 (65.4%)	181 (79.7%)	0.006
Age at disease beginning, years, mean (SD)	37.9 (13.5)	33.4 (12.3)	0.017
Age at disease diagnosis, years, mean (SD)	41.8 (12.7)	37.9 (12.3)	0.029
Diagnostic delay, years, median (IQR)	1.0 (2.6)	2.0 (5.5)	NS
Age at first biologic, years, mean (SD)	45.8 (12.5)	43.7 (11.3)	NS
Disease duration at first biologic, years, median (IQR)	6.7 (11.4)	7.1 (13.3)	NS
Age at beginning of secukinumab, years, mean (SD)	45.8 (12.5)	49.0 (11.3)	0.020
Disease duration until secukinumab, years, median (IQR)	6.7 (11.4)	14.0 (14.1)	<0.001
Extra-articular manifestations, N (%)	31 (29.0%)	98 (43.2%)	0.016
Psoriasis, N (%)	45 (42.1%)	100 (44.1%)	NS
Uveitis, N (%)	3 (2.8%)	21 (9.3%)	0.040
Inflammatory bowel disease, N (%)	0 (0.0%)	3 (1.3%)	NS
Co-medications at beginning of secukinumab			
Non-steroidal anti-inflammatory drugs	16 (15.0%)	84 (37.0%)	<0.001
Classic disease modifying antirheumatic drugs	49 (45.8%)	88 (38.8%)	NS
Oral Steroids	25 (23.4%)	65 (28.6%)	NS

SD: standard deviation; IQR: interquartile range; NS: non-significant;

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Secukinumab has demonstrated to be efficacious for both psoriatic arthritis (PsA) and ankylosing spondylitis (AS): PASI, ACR and ASAS magnitudes of response have generally been higher in the anti-TNF-naïve population. However, real world data on effectiveness in quality of life (QoL) and function are missing.

To analyze the differences of secukinumab therapy (effectiveness in disease activity and QoL, persistence and safety profile) in biologic-naïve versus biologic-experienced patients.

Methods: Multicenter, observational study of PsA and AS patients using real world anonymous patient-level data from the Portuguese national register database - Reuma.pt. We analyzed data at baseline and after 3, 6 and 12

	Baseline			*3 months*			*6 months*			*12 months*		
	Naïve	Biologic-experienced	p-value	Naïve	Biologic-experienced	p-value	Naïve	Biologic-experienced	p-value	Naïve	-biologic-experienced	p-value
PtGA, mean (SD)	63.1 (25)	66.2 (23)	NS	40.0 (30)	44.6 (25)	NS	37.6 (28)	50.5 (27)	0.009	30.0 (27)	42.0 (27)	0.016
PhGA, mean (SD)	46.5 (19)	50.6 (23)	NS	18.5 (18)	27.8 (19)	0.004	15.8 (16)	24.1 (2.5)	0.008	13.6 (14)	23.0 (17)	0.004
CRP mg/L, median (IQR)	8.0 (14.3)	8.1 (16.6)	NS	3.4 (6.5)	5.2 (11.0)	NS	3.9 (6.5)	2.2 (8.9)	NS	3.5 (5.0)	5.0 (7.6)	0.041
ESR, median (IQR)	18.5 (28)	23 (31)	NS	9 (12)	17 (20)	0.002	11 (18)	19 (30)	0.008	10 (19)	15 (23)	NS
BASDAI, mean (SD)	5.7 (2.1)	5.8 (2.1)	NS	3.8 (2.9)	4.2 (2.4)	NS	3.5 (2.5)	4.9 (2.2)	0.006	3.2 (2.8)	4.3 (2.2)	NS
Δ BASDAI, mean (SD)				2.0 (1.9)	1.7 (2.0)	NS	2.1 (2.1)	1.2 (1.9)	NS	2.7 (1.6)	1.8 (2.1)	NS
BASDAI 50, n (%)	-	-	-	13 (54%)	38 (45%)	NS	13 (56%)	31 (35%)	NS	13 (65%)	45 (49%)	NS
ASDAS-PCR, mean (SD)	3.4 (1.1)	3.5 (0.9)	NS	2.3 (1.1)	2.7 (1.1)	NS	2.3 (1.0)	2.9 (1.0)	0.008	2.1 (1.1)	2.6 (1.0)	0.038
Δ ASDAS-PCR, mean (SD)				1.1 (1.1)	0.9 (0.9)	NS	1.3 (1.1)	0.6 (0.8)	0.003	1.5 (1.3)	1.0 (1.0)	0.046
ASDAS-PCR CII (Δ > 1.1), n (%)	-	-	-	11 (50%)	30 (41%)	NS	8 (47%)	19 (25%)	NS	12 (63%)	26 (43%)	NS
ASDAS-PCR MI (Δ > 2.0), n (%)				3 (14%)	9 (12%)	NS	4 (24%)	5 (6.5%)	NS	6 (32%)	12 (20%)	NS
DAPSA, mean (SD)	119.8 (56)	146.0 (45)	0.018	66.9 (55)	93.4 (53)	NS	86.3 (64)	88.9 (54)	NS	69.9 (62)	86.9 (56)	NS
Δ DAPSA, mean (SD)	-	-	-	62.4 (66)	51.8 (62)	NS	56.0 (54)	64.7 (62)	NS	77.7 (56)	46.4 (45)	NS
DAS28 4V, mean (SD)	4.0 (1.6)	4.7 (1.4)	NS	2.8 (1.9)	3.4 (1.3)	NS	2.7 (1.3)	3.2 (1.5)	NS	2.5 (1.2)	3.2 (1.4)	0.048
Δ DAS28 4V, mean (SD)	-	-	-	1.4 (1.7)	1.5 (1.2)	NS	1.1 (0.8)	1.5 (1.5)	NS	2.1 (1.5)	1.3 (1.4)	NS
Tender joint count, median (IQR)	3.0 (5)	4.0 (9)	NS	0.0 (1.0)	1.0 (1.0)	NS	0.0 (2)	1.0 (4)	NS	0.0 (1)	0.0 (3)	NS
Swollen joint count, median(IQR)	2.0 (4)	1.0 (5)	NS	0.0 (1.0)	0.0 (1.0)	NS	0.0 (0)	0.0 (1)	NS	0.0 (0)	0.0 (1)	0.030
ASAS 20, n (%)	-	-	-	9 (38%)	31 (47%)	NS	11 (50%)	19 (26%)	0.041	11 (69%)	22 (40%)	0.049
ASAS 40, n (%)	-	-	-	7 (28%)	16 (23%)	NS	8 (36%)	13 (18%)	NS	8 (47%)	11 (19%)	0.030
ASAS 70, n (%)	-	-	-	5 (19%)	5 (6.8%)	NS	7 (32%)	1 (1.3%)	<0.001	5 (28%)	6 (10%)	NS
ACR 20, n (%)	-	-	-	7 (47%)	18 (42%)	NS	3 (38%)	10 (39%)	NS	9 (82%)	9 (41%)	NS
ACR 50, n (%)	-	-	-	5 (31%)	5 (9.4%)	0.045	1 (11%)	5 (11%)	NS	4 (36%)	4 (15%)	NS
ACR 70, n (%)	-	-	-	2 (9.1%)	4 (6.7%)	NS	0 (0.0%)	3 (4.8%)	NS	1 (9.1%)	0 (0.0%)	NS
MASES, median (IQR)	0 (3)	1 (5)	NS	0.0 (2.0)	0.0 (1.0)	NS	0.0 (2.0)	0.0 (4.0)	NS	0.0 (1.0)	0.0 (3.0)	NS

ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score; ASDAS CII: ASDAS Clinically important improvement; ASDAS MI: ASDAS Major Improvement; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CRP: C-reactive protein; DAPSA: Disease Activity in PSoriatic Arthritis; DAS 28: Disease Activity Score; ESR: erythrocyte sedimentation rate; IQR: interquartile range; MASES: Maastricht Ankylosing Spondylitis Enthesis Score; NS: non-significant; PtGA: patient global assessement; PhGA: physician global assessment; SD: standard deviation; Δ: variation between evaluation and baseline

	Baseline			*3 months*			*6 months*			*12 months*		
	Naïve	Biologic-experienced	p-value	Naïve	Biologic-experienced	p-value	Naïve	Biologic-experienced	p-value	Naïve	biologic-experienced	p-value
BASFI, mean (SD)	5.1 (2.6)	6.2 (2.1)	0.011	3.9 (3.1)	4.6 (2.6)	NS	3.0 (2.8)	5.5 (2.4)	< 0.001	3.5 (3.0)	4.7 (2.7)	NS
HAQ, mean (SD)	0.98 (0.8)	1.61 (0.9)	0.001	0.65 (0.6)	1.01 (0.8)	NS	0.86 (0.8)	1.2 (1.1)	NS	0.60 (0.8)	1.3 (0.7)	0.006
EQ-5D index score, mean (SD)	0.42 (0.2)	0.41 (1.0)	NS	0.45 (0.3)	0.42 (0.2)	NS	0.57 (0.4)	0.51 (0.8)	NS	0.53 (0.4)	0.43 (0.3)	NS
EQ-5D VAS, mean (SD)	44.9 (19)	49.0 (25)	NS	55.6 (29)	48.2 (26)	NS	67.8 (18)	50.0 (23)	0.034	61.6 (26)	53.2 (18)	NS
SF-36												
PCS, mean (SD)	40.1 (20)	29.7 (16)	0.011	49.6 (24)	38.9 (19)	NS	61.6 (27)	37.9 (20)	0.013	55.7 (24)	43.2 (21)	NS
MCS, mean (SD)	56.1 (21)	47.2 (19)	NS	66.4 (19)	56 (20)	NS	71.3 (19)	54.8 (22)	0.023	63.7 (21)	58 (26)	NS
ASQoL, mean (SD)	13.7 (17)	13.3 (11)	NS	8.1 (5.7)	10.0 (6.1)	NS	4.1 (4.4)	9.9 (5.6)	0.008	3.0 (2.3)	8.3 (5.9)	0.003
FACIT-F, mean (SD)	31.2 (26)	25.5 (12)	NS	32.3 (10)	30.4 (11)	NS	33.9 (13)	29.0 (11)	NS	35.8 (10)	32.7 (10)	NS
HADS												
Anxiety, mean (SD)	7.0 (3.4)	8.8 (4.0)	NS	5.6 (3.9)	7.2 (4.3)	NS	5.4 (3.7)	8.4 (4.9)	NS	4.2 (2.9)	7.7 (4.8)	0.029
Depression, mean (SD)	6.2 (3.7)	7.6 (4.2)	NS	5.5 (4.1)	6.4 (4.2)	NS	5.6 (4.1)	7.3 (4.7)	NS	5.2 (4.1)	6.7 (5.0)	NS

BASFI: Bath Ankylosing Spondylitis Functional Activity Index; EQ-5D: Euro Quality-of-Life 5 dimensions; FACIT-F: Functional Assessment of Chronic Illness Therapy Fatigue Scale; HADS: Hospital Anxiety and Depression Scale; HAQ: Health Assessment Questionnaire; IQR: interquartile range; NS: non-significant; SF-36: Short-Form Health Survey 36; SD: standard deviation;

months after secukinumab initiation, between January 2017 and January 2021. We collected data on sociodemographic characteristics and safety (discontinuation and adverse events); effectiveness [ACR and ASAS response, patient global assessment (PtGA), physician global assessment (PhGA), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), BASDAI, ASDAS-CRP, DAPSA and DAS28 4 V]; function and QoL [ASQoL (Ankylosing Spondylitis QoL questionnaire), EQ-5D (Euro-QoL-5 dimensions), FACIT-F (Functional Assessment of Chronic Illness Therapy-Fatigue); HADS (Hospital Anxiety and Depression Scale); HAQ (Health Assessment Questionnaire); BASFI and SF-36 (Health Questionnaire Short-Form 36)].

Results: We included 334 patients (166 with PsA and 168 with AS), 68% were biologic-experienced. Differences between biologic naïve and biologic-experienced patients' clinical characteristics are shown in Table 1. When we analyzed disease activity, we found that PhGA (p=0.004) and ESR (p=0.002) were significantly lower in naïve patients and more naïve patients reached ACR50 response (p=0.045) at 3 months. At 6 months evaluation, in addition to PhGA (p=0.008) and ESR (p=0.008) that remained significantly lower in naïve patients, PtGA (p=0.009), ASDAS-PCR (p=0.008) and BASDAI (p=0.006) were also lower in naïve patients. In the last evaluation, at 12 months, besides the variables described, also DAS 28 4V was lower in naïve patients (p=0.048) (Table 2).

Regarding QoL and function, at 6 months, BASFI (p< 0.001), EQ5D-VAS (p=0.034), SF-36 scores, physical (p=0.013) and mental (p=0.023) domains and ASQoL (p=0.008) were significantly better in naïve patients. After a year of follow-up (12 months evaluation) naïve patients had a better health status (HAQ and ASQoL) (p=0.006 and p=0.003 respectively) and biologic-experienced patients had more anxiety (HADS, p=0.029) (Table 3).

Regarding, drug persistence, although not statistically significant, biologic-experienced patients were more prone to discontinue the drug (18.5% and 11.2%, respectively, p=0.091)

Regarding safety, there were no differences in the number or type of severe (naïve patients: 3/107 vs biologic-experienced: 9/227) or mild (naïve patients: 4/107 vs biologic-experienced: 7/227) adverse effects.

Conclusion: Secukinumab treatment showed a larger magnitude of response (disease activity, function and QoL) in the biologic-naïve population, both in PsA and AS patients. No differences on safety profile were found.

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Abstract Number: 1833

Risk of Major Adverse Cardiovascular Events (MACE) with Biologic and Targeted Synthetic Antirheumatic Agents in Psoriatic Arthritis: A Systematic Review and Network Meta-analysis

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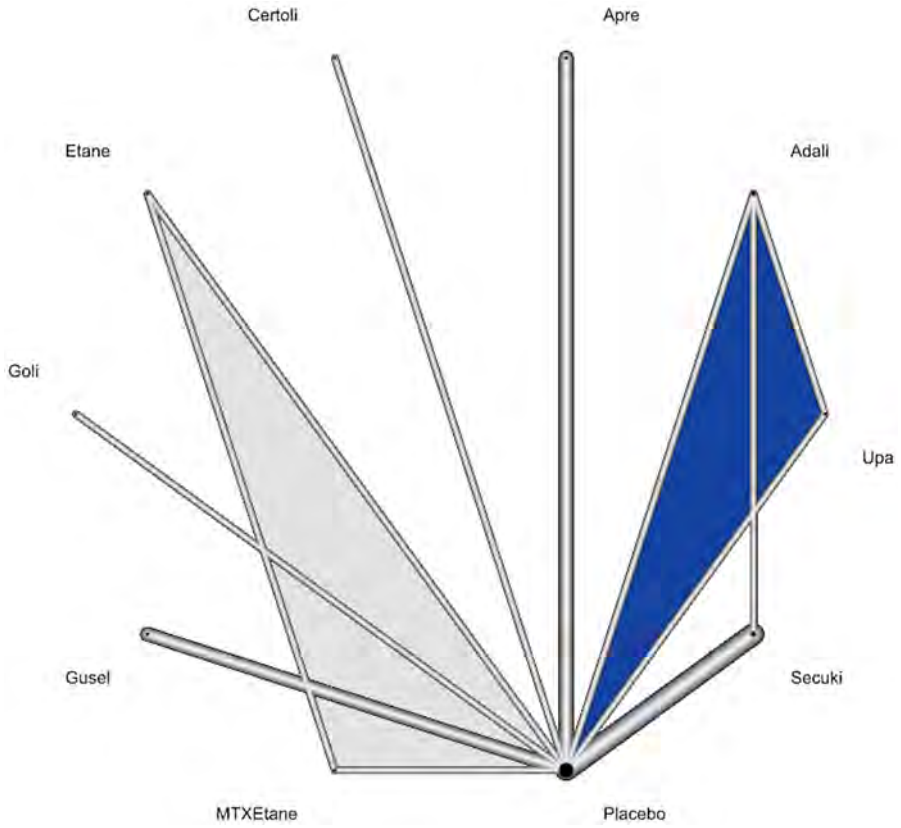
SESSION INFORMATION

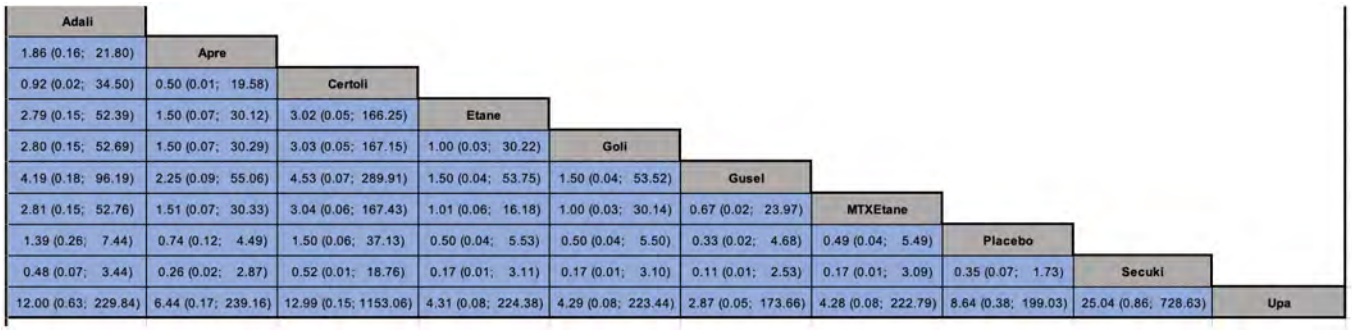
Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The efficacy of biologics and targeted synthetic disease modifying antirheumatic agents approved for treatment of psoriatic arthritis (PsA) is well documented, but cardiovascular safety profile of these agents is still a matter of debate. We examined risk of major adverse cardiovascular events (MACE) associated with use of biologics and targeted synthetic disease modifying antirheumatic agents in PsA.

Methods: Medline, PubMed, Embase, Scopus, Cochrane Central, and clinicaltrials.gov were searched to identify phase 3 and 4 randomized clinical trials (RCTs) reporting safety data of biologics and targeted synthetic disease modifying antirheumatic agents used in PsA. Outcome of interest was MACE within on-treatment or placebo-controlled duration. Mantel–Haenszel approach was used to pool data after continuity correction of zero events. Mixed treatment comparisons were computed using a fixed-effect NMA within frequentist framework. Effect estimates were expressed as odds ratio (OR) with 95% confidence intervals (CIs). P-scores were calculated to establish relative rankings of different treatment options. A sensitivity analysis was conducted using non-central hypergeometric (NCH) approach with Breslow approximation. All statistical analyses were conducted in R (v4.0.2).

Results: 33 trials met inclusion criteria; 12 RCTs [n=8501] with10 unique treatments and event(s) in at least one arm were included in network meta-analysis (Figure 1). Ten trials were excluded based on lack of reported data on MACE and 11 trials were excluded based on zero reported events in both or all arms (in case of multi-arm trials). A total of 27 (0.3%) MACE outcomes were observed among different treatments. Mixed treatment comparisons showed no statistically significant differences with upadacitinib (OR 0.12; 95% CI 0.01-2.66), guselkumab (OR 0.33; 95% CI





0.02-4.68,) methotrexate-etanercept (OR 0.49; 95% CI 0.04-5.49), golimumab (OR 0.50; 95% CI 0.04-5.50), etanercept (OR 0.50; 95% CI 0.04-5.53), apremilast (OR 0.74; 95% CI 0.12-4.49), adalimumab (OR 1.39, 95% CI 0.26-7.44), certolizumab (OR 1.50; 95% CI 0.06-37.13), and secukinumab (OR 2.85 95% CI 0.58-14.48) when compared to placebo. Similarly, no significant differences were observed among different biologics and targeted synthetic agents (Figure 2). Certainty of evidence was low due to very serious imprecision. The results were consistent with sensitivity analysis with NCH approach.

Limitations included study-level data with a relatively small number of studies and events of interest, sparse direct evidence, and open network.

Conclusion: During limited follow-up period in controlled clinical trials, composite MACE outcomes were not different among PsA patients treated with biologics and targeted synthetic disease modifying antirheumatic agents.

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Abstract Number: 1834

To What Extent Do Clinical Features of PsA Predict Achievement of Minimal Disease Activity at Week 24: A *Post Hoc* Analysis of the Phase III Clinical Trial Program of Guselkumab in a Bio-naïve Patient Population

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Guselkumab (GUS), a human monoclonal antibody targeting the interleukin-23p19-subunit, has demonstrated efficacy across joint and skin endpoints at Week 24 (W24) in the Phase 3 DISCOVER-1 and -2 clinical trials of patients with active psoriatic arthritis (PsA).[1,2] The aim of this *post hoc* analysis was to identify clinical phenotypic predictors of minimal disease activity (MDA) response to GUS treatment at W24 in patients with active PsA.

Methods: Data from bio-naïve patients with active PsA who were treated with GUS 100 mg every 4 or 8 weeks (Q4W; Q8W) were pooled across DISCOVER-1 and -2. Patients in DISCOVER-1 were required to have ≥3 swollen and ≥3 tender joints and C-reactive protein (CRP) ≥0.3 mg/dL; patients in DISCOVER-2 were required to have ≥5 swollen and ≥5 tender joints and CRP ≥0.6 mg/dL. Logistic regression analysis was performed to identify potential predictors of MDA response to GUS at W24; odds ratios, 95% confidence intervals and p-values were calculated. Missing data for MDA at W24 were imputed as non-response; a few missing baseline (BL) values in 4 patients were imputed. Potential predictors of response were characterized by patients' baseline clinical features, including swollen and tender joint counts, affected joint location (including temporomandibular joint, hands, feet, wrist, elbow, shoulder, hip, and knee), BL dactylitis and enthesitis, Psoriasis Area Severity Index (PASI) score, and psoriasis (PsO) localization (including hands and feet, scalp, or nail involvement). Other selected BL characteristics are also described (Table 1).

Results: Clinical characteristics of 669 bionaïve, GUS-treated patients, which were generally consistent across DISCOVER-1 (n=176) and DISCOVER-2 (n=493), indicated substantial disease burden at BL. Patients had a mean tender and swollen joint count of 20.3 and 11.5, respectively, and a mean PASI score of 9.7; 63.5% had enthesitis, and 43.2% had dactylitis at BL (Table 1). At W24, MDA was achieved by 24.4% (163/669) of pooled GUS Q4W- and Q8W-treated patients. Lower body mass index (BMI) and tender joint count, CRP < 1 mg/dL, and higher PASI at BL (all $p < 0.05$) were significant predictors of MDA response at W24. Patients with presence of dactylitis at BL were significantly less likely than those without this manifestation to achieve MDA at W24 (Table 2; $p < 0.01$). The localization of PsO, affected joint location, or current tobacco use were not predictive of MDA response at W24 (Figure 1).

Table 1. Baseline characteristics of bio-naïve patients with psoriatic arthritis treated with guselkumab 100 mg Q4W or Q8W.

Baseline characteristics	Guselkumab 100 mg (Q4W and Q8W pooled)	IQR
Number of randomized and treated patients	699	–
Age, years	46.1 (11.8)	37.0–55.0
Female, n (%)	309 (46.2)	–
BMI, kg/m²	29.1 (6.1)	24.7–32.7
PsA duration, years	5.4 (5.8)	1.3–7.2
BSA with PsO, %	16.3 (19.7)	3.0–21.0
PASI score	9.7 (11.1)	2.4–12.6
CRP, mg/dL	1.7 (2.2)	0.5–2.1
Swollen joint count, 0–66	11.5 (7.4)	7.0–14.0
Tender joint count, 0–68	20.3 (13.1)	11.0–25.4
HAQ-DI	1.2 (0.6)	0.8–1.6
Patients with dactylitis at BL, n (%)	289 (43.2)	–
Dactylitis Severity Score (0–60)	3.6 (7.7)	0.0–4.0
Patients with enthesitis at BL, n (%)	425 (63.5)	–
LEI score	1.8 (1.8)	0.0–3.0

Data are mean (SD) or %. BL, baseline; BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire Disability Index; IQR, interquartile range; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; Q4W, every 4 weeks; Q8W, every 8 weeks; SD, standard deviation.

Table 2. Odds ratios and 95% confidence intervals for potential predictors of minimal disease activity response to guselkumab 100 mg Q4W or Q8W at Week 24 in patients with psoriatic arthritis.

Characteristic/clinical feature	Odds Ratio (95% CI)	p-value
Clinical features		
Swollen joint count, 0–66	0.99 (0.94–1.03)	0.51
Tender joint count, 0–68	0.97 (0.94–1.00)	0.04
Shoulder involvement	0.83 (0.60–1.16)	0.29
Elbow involvement	0.80 (0.60–1.07)	0.13
Knee involvement	0.99 (0.79–1.26)	0.90
Hip involvement	0.89 (0.71–1.11)	0.31
Foot joint involvement	0.85 (0.65–1.13)	0.24
Hand joint involvement	0.82 (0.60–1.11)	0.18
Wrist involvement	0.90 (0.72–1.13)	0.32
Temporomandibular joint involvement	1.44 (0.81–2.53)	0.20
Baseline dactylitis, Yes vs. No	0.54 (0.34–0.85)	<0.01
Baseline enthesitis, Yes vs. No	0.65 (0.43–1.00)	0.06
Baseline PASI	1.03 (1.01–1.05)	<0.01
Hand/foot PsO, Yes vs. No	1.45 (0.97–2.16)	0.07
Nail PsO, Yes vs. No	1.23 (0.80–1.88)	0.34
Scalp PsO, Yes vs. No	0.82 (0.49–1.37)	0.46
Baseline characteristics		
Age	0.98 (0.97–1.00)	0.05
Sex, Female vs. Male	0.75 (0.49–1.15)	0.18
BMI	0.96 (0.93–1.00)	0.03
PsA duration	1.00 (0.96–1.03)	0.91
CRP, <1 vs. ≥1 mg/dL	1.60 (1.06–2.41)	0.02
Current alcohol use, Yes vs. No	1.25 (0.83–1.87)	0.26
Current tobacco use, Yes vs. No	0.99 (0.60–1.64)	1.00

BMI, body mass index; BsA, body surface area; CI, confidence interval; CRP, C-reactive protein; PASI, Psoriasis Area Severity Index; PsO, psoriasis; Q4W, every 4 weeks; Q8W, every 8 weeks.

Conclusion: PsA phenotypes at BL are significant positive (lower tender joint count, higher PASI) or negative (presence of dactylitis) predictors of achieving the multidomain composite endpoint MDA at W24. BL BMI and CRP may also affect the prospect of reaching MDA. These data emphasize that all domains of PsA should be taken into account, and that more complex disease requires particular attention.

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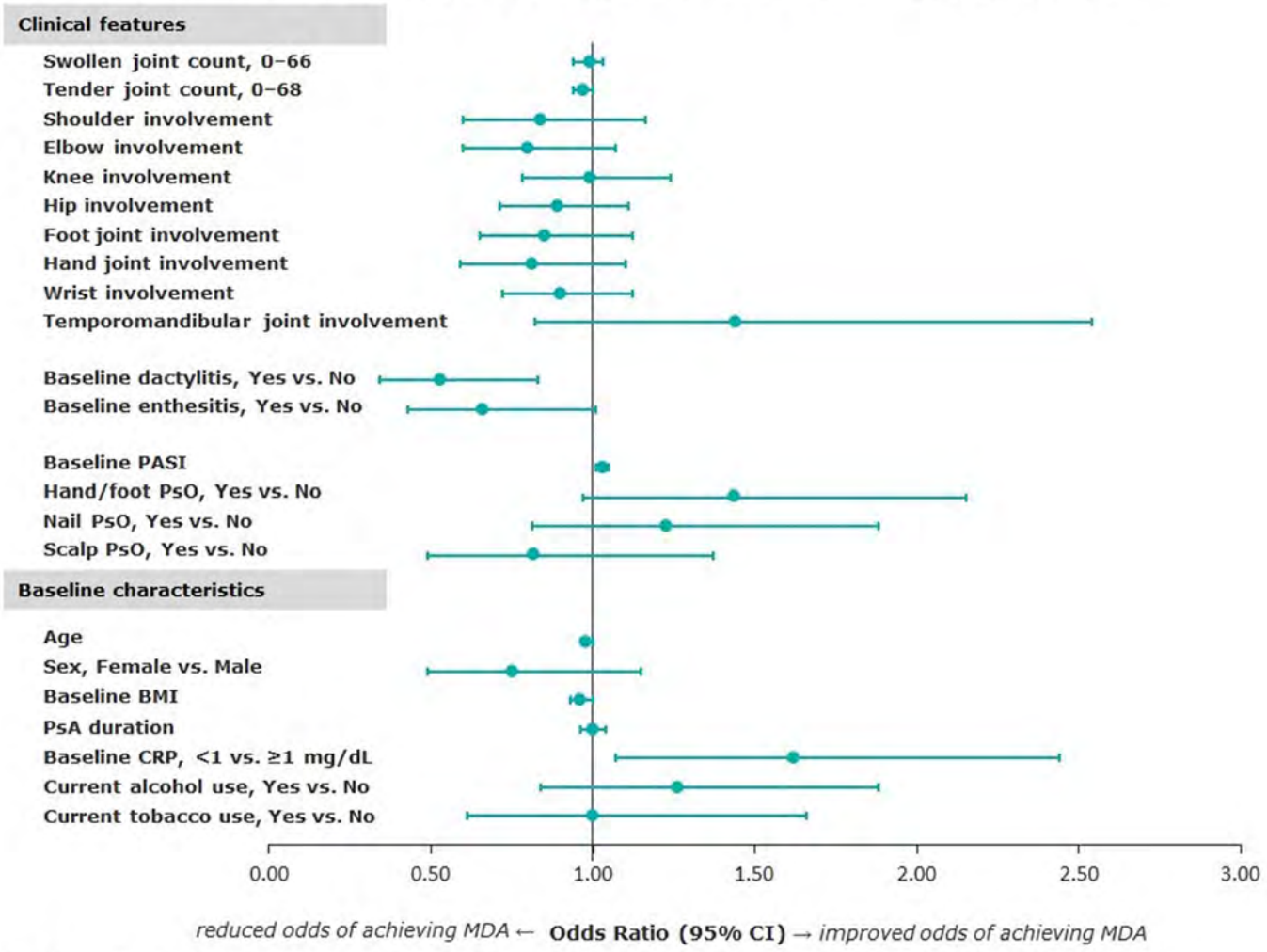
2. Mease PJ *et al. Lancet* 2020; 395: 1126–1136.

Figure 1. Odds ratios and 95% confidence intervals for potential predictors of MDA response to guselkumab 100 mg Q4W or Q8W at Week 24 in bio-naïve patients with active psoriatic arthritis.



BMI, body mass index; CI, confidence interval; CRP, C-reactive Protein; MDA, minimal disease activity; PASI, Psoriasis Area Severity Index; PsO, psoriasis; Q4W, every 4 weeks; Q8W, every 8 weeks.

Disclosure: M. Vis, AbbVie, 2, 5, 6, Amgen, 2, 5, 6, Celgene, 2, 5, 6, Janssen, 2, 5, 6, Eli Lilly, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6; **P. Richette**, AbbVie, 1, 6, Amgen, 1, 6, Celgene, 1, 6, Janssen, 1, 6, Eli Lilly, 1, 6, MSD, 1, 6, Novartis, 1, 6, Pfizer, 1, 6, UCB, 1, 6; **R. Julio**, AbbVie, 2, 6, Amgen, 2, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB, 2, 6; **M. Neuhold**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **R. Wapenaar**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **E. Theander**, Janssen Scientific Affairs, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Noel**, Janssen Global Services, LLC, 3, 12, Owns stock in Johnson & Johnson; **M. Shawi**, Janssen Global Services, LLC (a subsidiary of Johnson & Johnson), 3, 11; **A. Kollmeier**, Janssen Research & Development, LLC (a subsidiary of Johnson & Johnson), 3, 11; **W. Tillett**, AbbVie, 1, 2, 6, Amgen, 1, 2, 6, Celgene, 1, 2, 6, Eli Lilly, 1, 2, 6, Janssen, 1, 2, 6, Novartis, 1, 2, 6, MSD, 1, 2, 6, Pfizer, 1, 2, 6, UCB, 1, 2, 6, Merck Sharp & Dohme, 2.

Abstract Number: 1835

Secukinumab Effects on Cardiometabolic Risk and Systemic Inflammation in Patients with Psoriasis, Psoriatic Arthritis and Axial Spondyloarthritis: Results from Post Hoc Analyses of Pooled Data from 19 Phase 3/4 Clinical Studies

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Table 1. Inflammatory Risk Parameters: Weeks 12/16 and 52

Median	PsO			PsA			AxSpA		
	Secukinumab		PBO	Secukinumab		PBO	Secukinumab		PBO
	300 mg N=3,285	150 mg N=765	N=692	300 mg N=887	150 mg N=907	N=681	300 mg N=76	150 mg N=1,177	N=727
Overall population									
hsCRP (mg/L)									
Baseline	2.3	2.6	2.5	4.6	4.2	4.4	6.8	6.2	6.0
Week 12/16^	1.8*	1.7*	2.2	2.4*	2.6*	4.3	2.2*	2.9*	5.4
Week 52	1.9	1.9	-	2.4	2.5	-	3.6	2.7	-
NLR									
Baseline	3.2	2.5	2.6	2.6	2.6	2.5	2.2	2.5	2.5
Week 12/16^	2.1*	2.1*	2.4	2.2*	2.2*	2.5	2.0§	2.1*	2.5
Week 52	2.0	2.1	-	2.1	2.2	-	2.1	2.1	-
High-risk patients subgroup (baseline hsCRP >10 mg/L in PsA/AxSpA and >4 mg/L in PsO)									
hsCRP (mg/L)									
	N=757	N=272	N=229	N=244	N=219	N=167	N=28	N=420	N=262
Baseline	7.3	8.0	8.7	17.5	19.9	17.9	16.6	19.6	23.3
Week 12/16^	4.5†	4.0†	6.6	5.2*	5.8*	14.3	5.2*	6.3*	16.2
Week 52	4.2	4.2	-	4.8	6.2	-	5.8	5.5	-
NLR									
Baseline	2.8	2.9	3.0	3.0	3.3	3.1	2.7	3.0	2.9
Week 12/16^	2.2*	2.3*	2.8	2.4*	2.5	2.9	2.1§	2.3*	2.7
Week 52	2.2	2.3	-	2.2	2.4	-	2.1	2.2	-

*P-value <0.0001, †<0.001 and §<0.01 versus PBO. P-values are 2-sided derived from Wilcoxon 2-sample test of equality of distributions unadjusted for multiplicity. Baseline is defined as the last observation, on the day of or before the first dose of study drug. Data are reported 'as observed' in patients with baseline value and at least one post-baseline value.

^Assessing difference in change from baseline was performed at Week 16 in PsA and AxSpA studies and at Week 12 in PsO studies.

hsCRP, high sensitivity C-reactive Protein; NLR, Neutrophils/Lymphocytes ratio; PBO, placebo; SEC, secukinumab

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Spondyloarthritis Including PsA – Treatment Poster III: Psoriatic Arthritis II (1801–1835)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Psoriasis (PsO), Psoriatic Arthritis (PsA) and Axial Spondyloarthritis (AxSpA) are chronic immune-mediated inflammatory diseases (IMIDs) requiring long-term treatment. Systemic inflammation in these IMIDs is associated with cardiovascular (CV) disease[1,2]. High sensitivity C-reactive protein (hsCRP) is an independent surrogate CV risk marker. Recently, high neutrophil-lymphocyte ratio (NLR) has emerged as a novel inflammatory biomarker predictive of CV disease and overall mortality[3]. Here, we report the effect of IL-17A inhibition with secukinumab on CV risk parameters in PsO, PsA and AxSpA patients over 1 year of treatment.

Methods: This is a post-hoc analysis of pooled Phase 3/4 secukinumab studies in PsO, PsA and AxSpA. CV-related exclusion criteria included uncontrolled hypertension and congestive heart failure. Traditional (body mass index [BMI], fasting glucose, blood pressure, cholesterol and lipids) and inflammatory CV risk parameters (hsCRP, absolute neutrophil count and NLR) were assessed. Exploratory statistical comparison of median change from baseline to Week 12 (PsO) or Week 16 (PsA/AxSpA) for secukinumab *vs* placebo was performed by Wilcoxon 2-sample test. Subgroup analyses were performed in high-risk patients (baseline hsCRP >10 mg/L in PsA/AxSPA and >4 mg/L in PsO).

Results: In total, 9,197 patients from 19 clinical trials (8 in PsO, n=4,742; 5 in PsA, n=2,475; 6 in AxSpA, n=1,980) were included. All traditional CV risk parameters remained stable in secukinumab-treated patients through 1 year (**Table 1**). Secukinumab administration rapidly reduced both hsCRP and the NLR, compared with placebo at Week 12 (PsO) or Week 16 (PsA/AxSPA) in the overall population and in high-risk patients defined by having high baseline hsCRP (all p< 0.01). This reduction was maintained for at least 1 year of secukinumab therapy in all indications (**Table**

Table 2. Traditional CV Risk Factors: Week 52

Median		PsO		PsA		AxSpA	
		Secukinumab		Secukinumab		Secukinumab	
		300 mg N=3,285	150 mg N=765	300 mg N=887	150 mg N=907	300 mg N=76	150 mg N=1,177
Serum Fasting Glucose (mmol/L)	Baseline	5.2	5.2	5.2	5.2	4.8	5.0
	Week 52	5.2	5.2	5.3	5.2	5.1	5.1
Systolic blood pressure (mmHg)	Baseline	128.0	127.0	126.0	128.0	127.5	124.0
	Week 52	127.0	126.0	126.0	126.5	124.0	122.0
Diastolic blood pressure (mmHg)	Baseline	80.0	80.0	80.0	80.0	80.0	78.0
	Week 52	80.0	80.0	78.0	80.0	79.0	77.0
Body Mass Index (Kg/m^2)	Baseline	27.9	28.4	28.1	29.1	25.6	27.2
	Week 52	28.0	28.6	28.3	29.3	27.9	25.7
Ratio of Total Cholesterol / HDL	Baseline	3.9	4.0	3.4	3.6	3.4	3.4
	Week 52	4.0	4.1	3.5	3.6	3.4	3.3
Triglycerides (mmol/L)	Baseline	1.3	1.4	1.3	1.3	1.0	1.1
	Week 52	1.4	1.6	1.4	1.4	1.1	1.2

Baseline is defined as the last observation, on the day of or before the first dose of study drug. Data are reported 'as observed' in patients with baseline value and at least one post-baseline value.

2). In some patients where available follow-up data allowed exploratory analysis through five years, secukinumab induced sustained reductions in hsCRP and NLR; traditional CV risk factors did not change.

Conclusion: Secukinumab rapidly reduced hsCRP and the NLR in patients with IMIDs with a high systemic inflammatory burden. Traditional CV risk factors remained stable for at least 1 year in patients with PsO, PsA and AxSpA.

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3. Kim, et al. *JAMA Cardiol*. 2018;3:455-62.

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Abstract Number: 1836

Outcomes Linked to Eligibility for Stem Cell Transplantation Trials in Diffuse Cutaneous Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Autologous haematopoietic stem cell transplantation (SCT) has emerged as an effective treatment for patients with severe diffuse systemic sclerosis (dcSSc) based upon the results of two large clinical trials demonstrating long term benefit for survival, skin and lung involvement and quality of life. Over the past two decades routine management of dcSSc has improved and immunosuppressive drugs are increasingly administered in the early course of the disease. These developments may have improved survival of cases that would have been eligible for SCT trials compared with historically predicted outcomes. The aim of this study was to explore outcomes in a cohort of dcSSc patients fulfilling eligibility criteria for SCT studies but receiving contemporary standard treatment.

Methods: From a single-centre cohort dcSSc patients (n=636) were selected using the SCT trials' inclusion criteria (Table 1). Patients meeting the trials' exclusion criteria were excluded. Overall survival and event free survival (EFS)

Table 1. Inclusion criteria from SCT trials

ASTIS (2014)	SCOT (2018)	UPSIDE (2020)
Inclusion criteria		
Age 16-65 years	**Age 18-65 years**	**Age 18-65 years.**
- DcSSc*	**- DcSSc***	**- DcSSc****
- Disease duration < 4yr from non-RP	**- Disease duration ≤4 yr from non-RP**	**- Disease duration ≤ 2yr from non-RP**
- mRSS > 20 + ESR > 25mm + Hb 11 or **- mRSS > 15 +** **DLco and/or FVC ≤ 80%** + HRCT abnormalities And/or **Renal or cardiac involvement**	**- mRSS ≥ 16** And at least one: **- FVC < 70% or DLco < 70%** + HRCT abnormalities - **Renal involvement**	**- mRSS ≥ 15** and/or **- DLco and/or FVC ≤ 85%** and HRCT abnormalities or **FVC decline of >10% or DLco decline of >15% within 12 months. and/or - Renal or cardiac involvement**
Exclusion criteria		
- PAH - LVEF < 45% **- DLco < 40%** **- Creatinine clearance <40 ml/min**	**- PAH** - LVEF < 50%. Pacemaker/ICD **- DLCO < 40%** **- FVC < 45%** **- Creatinine clearance <40 ml/min, active SRC** - Previous iv CYC > 6 months (>4 months oral CYC) - Active GAVE - Active hepatitis	**- PAH** - LVEF < 45% **- DLco < 40%** **- Creatinine clearance <40 ml/min, active SRC** - Previous treatments with MMF, MTX, AZA, RTX, steroids > 6 months - Previous CYC - ZUBROD-ECOG-WHO performance Status Scale > 2

ASTIS, Autologous Stem Cell Transplantation International Scleroderma; AZA, azathioprine; CYC, cyclophosphamide; dcSSc, diffuse cutaneous systemic sclerosis; DLco, diffusing capacity of the lungs for carbon monoxide; ESR, estimated sedimentation rate; FVC, forced vital capacity; GAVE, gastric antral vascular ectasia; Hb, haemoglobin; HRCT, High-resolution computed tomography; ICD, implantable cardioverter-defibrillator; LVEF, left ventricular ejection fraction; MMF, mycophenolate mofetil; mRSS, modified Rodnan skin score; MTX, methotrexate; PAH, pulmonary arterial hypertension; RP, Raynaud's phenomenon; RTX, rituximab; SCOT, Scleroderma: Cyclophosphamide Or Transplantation; SCT, stem cell transplantation; UPSIDE, UPfront autologous hematopoietic Stem cell transplantation versus Immunosuppressive medication in early DiffusE cutaneous systemic sclerosis.

* According to ARA-Classification Criteria Systemic Sclerosis
**According to 2013 ACR-EULAR classification criteria for diffuse cutaneous systemic sclerosis

In bold: criteria used to select patients for this study.

of patients eligible for one or more of the studies (ASTIS, SCOT or the ongoing UPSIDE trial) were assessed using Kaplan-Meier survival estimates. Hazard ratios (HR) were calculated using Cox proportional hazards regression analysis. EFS was defined as the time in years from eligibility until the occurrence of death due to any cause or development of major organ damage, defined as severe cardiac involvement or pulmonary fibrosis, scleroderma renal crisis (SRC) or pulmonary hypertension (PH).

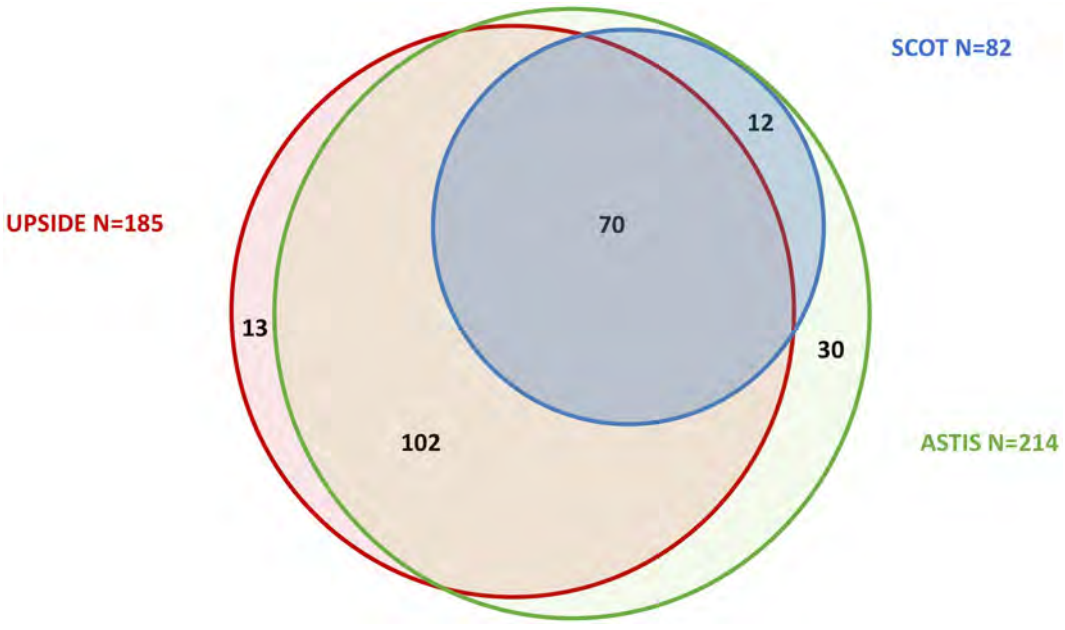
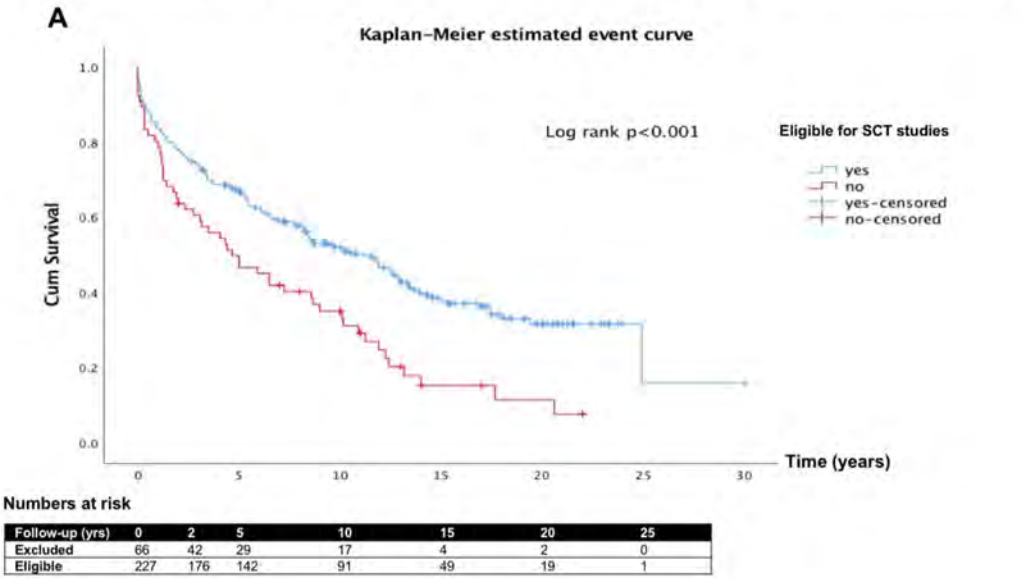


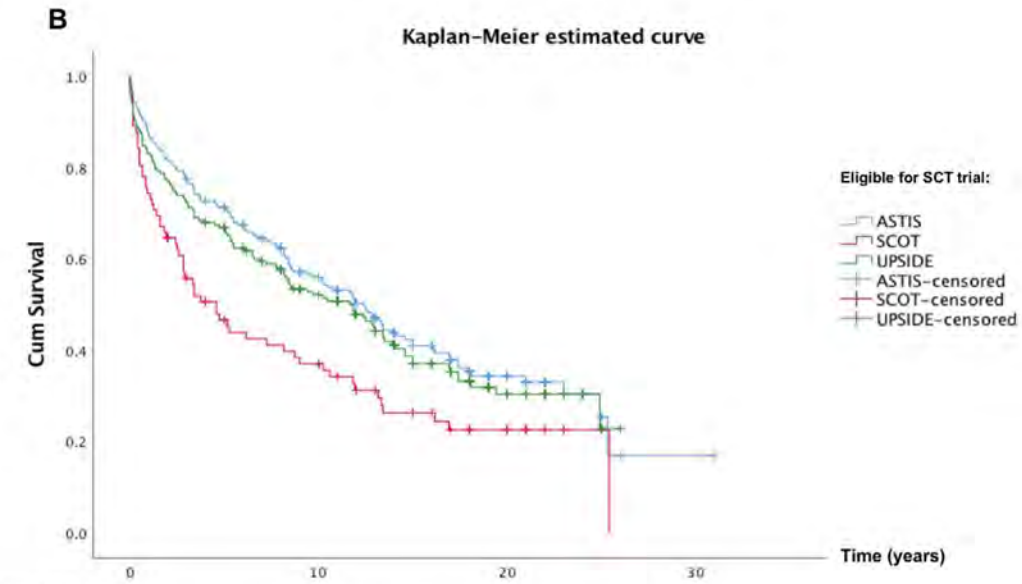
Figure 1. Venn diagram showing overlap of patients eligible for stem cell transplantation trials.

Figure 2. Event free survival
Comparison between patients eligible for SCT studies and patients excluded (A) and between SCT trials (B)



Numbers at risk

Follow-up (yrs)	0	2	5	10	15	20	25
Excluded	66	42	29	17	4	2	0
Eligible	227	176	142	91	49	19	1



Numbers at risk

Follow-up (yrs)	0	2	5	10	15	20	25
ASTIS	212	173	145	98	55	25	2
SCOT	82	50	33	25	14	5	0
UPSIDE	183	141	117	77	42	16	1

Results: Of the 227 eligible patients, 214 met the inclusion criteria for ASTIS, 82 for SCOT and 185 for the UPSIDE trial. 66 patients were excluded based on age > 65 years, low DLco, pulmonary hypertension or creatinine clearance < 40ml/min. There was overlap between eligible patient groups (Figure 1). The median follow-up time was 12 years (IQR 9). Among eligible patients, 103 (45.4%) died. Survival was 96% at 2-, 88% at 5-, 73% at 10- and 43% at 20 years. Compared to this 'SCT-eligible' cohort, those patients who would have been excluded from SCT trials had a worse long-term overall survival (97% at 2-, 77% at 5-, 52% at 10- and 15% at 20 years, log rank p< 0.001). Excluded

patients also had a significantly worse EFS (Figure 2A). Differences between the three different trials were observed as well (Figure 2B). Hazard of death was higher in patients with higher age at onset (HR 1.05, p< 0.001), higher ESR at onset (HR 1.01, p=0.025) and males (HR 2.12, p=0.008). Male sex was also an independent risk factors for a serious event (HR 1.97, 95% CI 1.34-2.88, p=0.001). Higher DLco at onset was associated with a lower hazard for an event (HR 0.98, 95% CI 0.97-0.99, p=0.001) in the multivariable Cox regression analysis.

Conclusion: This study demonstrates that SCT inclusion criteria identify patients with poor outcome despite current best practice treatment as long-term outcomes were unfavorable in our cohort compared to SCT in the trials. It shows that SCT trials have overlapping eligibility criteria but may recruit different populations which requires caution when comparing results. Our findings emphasize the need for better treatment strategies for the very poor outcome patients who are excluded from SCT.

Disclosure: J. Spierings, Boehringer Ingelheim, 5, Miltenyi, 5; **S. Nihtyanova**, GSK, 3, Roche, 2; **E. Derrett-Smith**, None; **K. Clark**, None; **J. van Laar**, Abbvie, 6, Arxx Tx, 6, Galapagos, 6, Gesyntha, 6, Leadiant, 6, Roche, 6, Boehringer Ingelheim, 5, Astra Zeneca, 5, MSD, 5, Roche, 5; **V. Ong**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 1837

KL-6, CXCL11 and CTGF Are Potential Biomarkers in Response to Treatment in CTD-ILD

Yu-Hsiang Chiu[1], Mareye Voortman[1], Eveline Delemarre[1], Stefan Nierkens[1], Pim de Jong[1], Firdaus Mohamed Hoesein[1], Jan Grutters[2], Jacob van Laar[1] and Julia Spierings[3], [1]University Medical Centre Utrecht, Utrecht, Netherlands, [2]St. Antonius Hospital, Nieuwegein, Netherlands, [3]University Medical Center Utrecht, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Connective tissue disease related interstitial lung disease (CTD-ILD) is common and an important cause of morbidity and mortality. We aimed to identify biomarkers in CTD-ILD correlating with radiographic characteristics and response to immunosuppressive therapy at one-year follow-up.

Methods: An exploratory set of 38 biomarkers were measured in serum of patients with CTD-ILD at baseline and one year of follow-up. The high resolution computed tomography (HRCT) patterns were classified according to the classification for idiopathic interstitial pneumonia and categorised into fibrotic or inflammatory. The predictivity of baseline biomarker, responsiveness of biomarkers to treatment, and correlations between the variation of biomarkers and pulmonary function test after one year of treatment were examined.

Results: Sixteen patients were included (12 females (75.0%), median age 51 years (IQR 45-62). The established CTD diagnoses, comorbidities, immunosuppressive therapies, and HRCT patterns were summarized in Table 1. Patients with inflammatory HRCT patterns showed less decline in forced vital capacity (FVC), 7.7% versus 33.3% in patients with fibrotic HRCT patterns. In patients with inflammatory HRCT patterns, CXCL11 reduced from a median 307.8 pg/ml to 253.8 pg/ml (p = 0.011), CTGF from 48.5 pg/ml to 9.5 pg/ml (p = 0.033) and KL-6 from 1221 U/ml to 543 U/ml (p = 0.040). (Figure 1) Additionally, an increase in levels of galectin-3 at one-year follow-up was associated with

Table 1. Baseline demography. Abbreviations: IQR, interquartile range; CTD, connective tissue disease; HRCT, high resolution computed tomography; HSCT, hematopoietic stem-cell transplantation; LIP, lymphocytic interstitial pneumonia; MCTD, mixed connective tissue disease; NSIP, non-specific interstitial pneumonia; OP, organising pneumonia; PPFE, pleuroparenchymal fibro-elastosis; SLE, systemic lupus erythematosus; SSc, systemic sclerosis; UCTD, undifferentiated connective tissue disease; UIP, usual interstitial pneumonia

Characteristic	Patients (N=16) n (%)
Female	12 (75)
Age (years), median (IQR)	51 (45–62)
Disease duration of CTD (months), median (IQR)	6 (2–22)
CTD	
SSc	5 (31.3)
Sjogren's syndrome	1 (6.3)
Myositis	6 (37.5)
Rheumatoid arthritis	1 (6.3)
SLE	1 (6.3)
MCTD	1 (6.3)
UCTD	1 (6.3)
Comorbidities	
Coronary artery disease	2 (12.5)
Congestive heart failure	0
Pulmonary hypertension	0
Diabetes mellitus	0
Cerebrovascular event	1 (6.3)
Smoking status	
Current	0
Former	8 (50)
Never	8 (50)
Immunosuppressive treatment	
Azathioprine	2 (12.5)
Mycophenolate mofetil	7 (43.8)
Methotrexate	3 (18.8)
Hydroxychloroquine	6 (37.5)
Cyclosporin	1 (6.3)
Rituximab	1 (6.3)
HSCT	1 (6.3)
Steroid	11 (68.8)
Fibrotic HRCT patterns	
UIP	0
Fibrotic NSIP	2 (12.5)
PPFE	1 (6.3)
Inflammatory HRCT patterns	

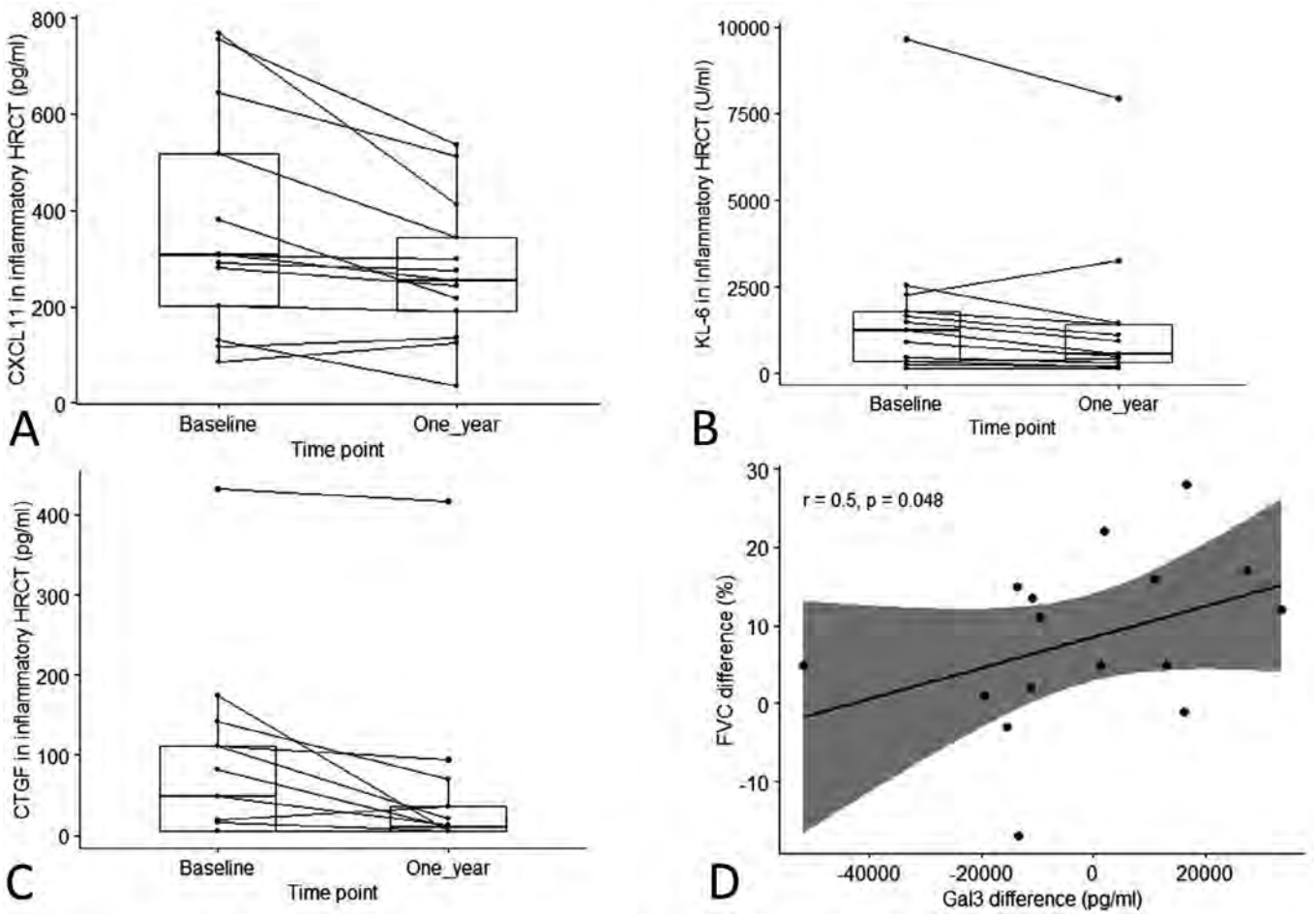


Figure 1. Decline in CXCL11 (A), Krebs von den Lungen 6 (KL-6) (B), and connective tissue growth factor (CTGF) (C) over one year of treatment was associated with inflammatory high resolution computed tomography (HRCT) pattern. (D) Correlation between changes of Galectin-3 (Gal3) and forced vital capacity (FVC) after one year of treatment. An increase of Galectin-3 reflected the improvement of lung function.

improved FVC (Rho 0.5, p = 0.048). (Figure 1D) A visualized baseline biomarkers heatmap showed that the biomarker concentrations are determined less by ILD but more by underlying CTD manifestations. (Figure 2)

Conclusion: In this study, CXCL11, CTGF, and KL-6 reduction were associated with inflammatory HRCT patterns and better pulmonary outcome. In contrast to previous research in severe ILD, there was a positive correlation between

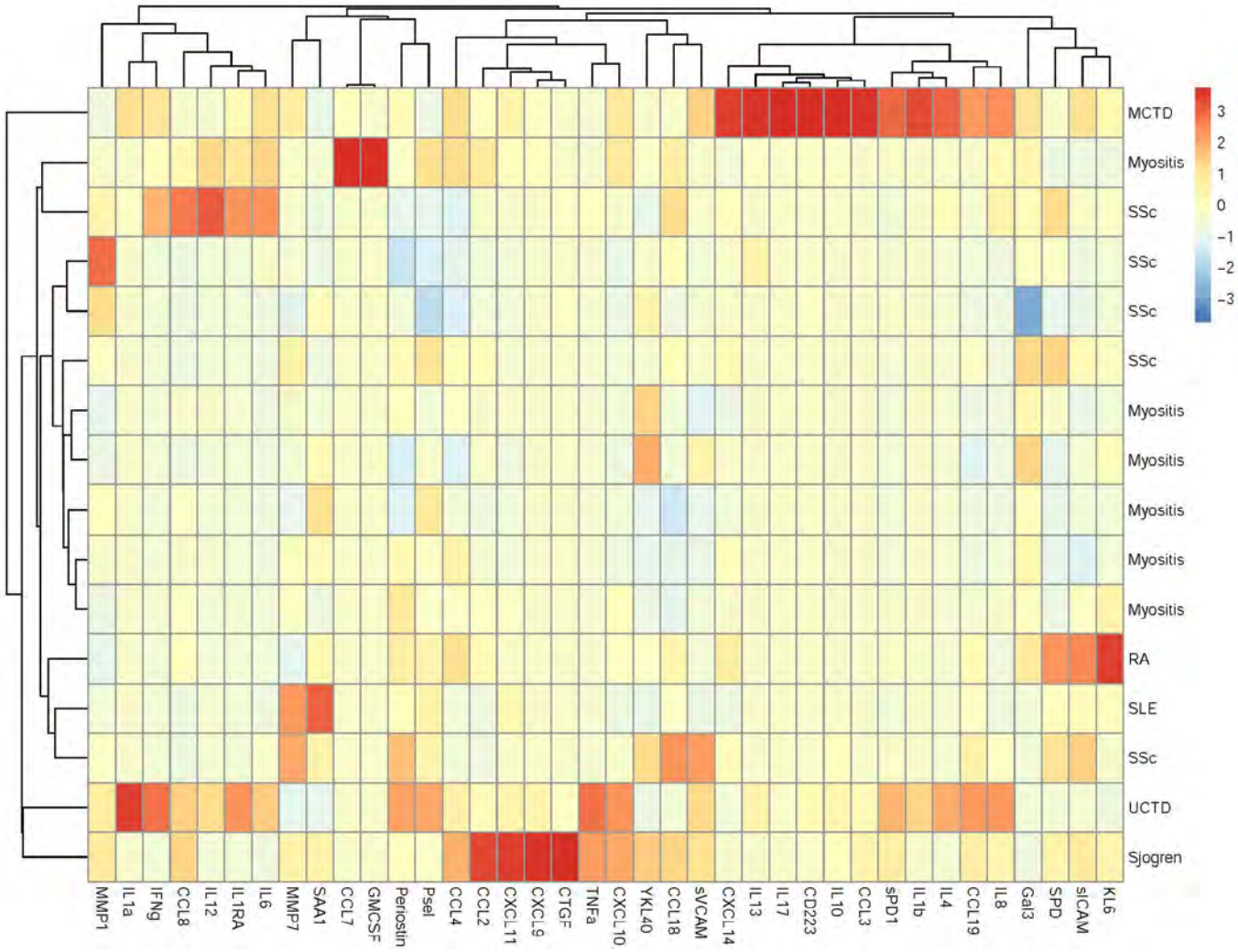


Figure 2. Baseline biomarkers heatmap. Hierarchical clustering of biomarkers measured at baseline was visualized in the heatmap. The concentration of each biomarker was normalized and presented in colour, the closer to red the higher. MCTD, mixed connective tissue disease; SSc, systemic sclerosis; SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; UCTD, undifferentiated connective tissue disease. KL6, Krebs von den Lungen 6; sICAM, soluble intercellular adhesion molecule-1; SPD, surfactant protein D; Gal3, Galectin-3; sPD1, soluble programmed death-1; sVCAM, soluble vascular cell adhesion molecule-1; YKL40, also known as chitinase 3-like 1; TNFa, tumor necrosis factor alpha; CTGF, connective tissue growth factor; Psel, P-selectin; GMCSF, granulocyte-macrophage colony-stimulating factor; MMP, matrix metalloproteinase; SAA1, serum amyloid A1; IL1RA, interleukin (IL)-1 receptor antagonist; IFNg, interferon gamma.

changes of galectin-3 and FVC in our study. Further research in a larger group and focusing on combining biomarkers to predict outcome and prognosis is needed.

Disclosure: Y. Chiu, None; **M. Voortman**, None; **E. Delemarre**, None; **S. Nierkens**, None; **P. de Jong**, Sanifit, 2, Inozyme, 2; **F. Mohamed Hoesein**, None; **J. Grutters**, None; **J. van Laar**, Abbvie, 6, Arxx Tx, 6, Galapagos, 6, Gesyntha, 6, Leadiant, 6, Roche, 6, Boehringer Ingelheim, 5, Astra Zeneca, 5, MSD, 5, Roche, 5; **J. Spierings**, Boehringer Ingelheim, 5, Miltenyi, 5.

Abstract Number: 1838

Further Construct Validation of the

Julia Spierings[1], Voon Ong[2] and Christopher Denton[3], [1]University Medical Center Utrecht, Utrecht, Netherlands, [2]University College London Medical School Royal Free Campus, London, United Kingdom, [3]University College London Division of Medicine, Centre for Rheumatology and Connective Tissue Diseases, London, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Evaluation of skin is central in clinical management of systemic sclerosis (SSc). Due to the COVID-19 pandemic remote consultations were widely implemented, which inevitably limited skin assessment using the modified Rodnan Skin Score (mRSS). In order to monitor skin during the pandemic, we developed and validated the PASTUL (Patient self-Assessment of Skin Thickness in Upper Limb) questionnaire. (Spierings J et al Ann Rheum Dis. 2021: https://doi.org/10.1136/annrheumdis-2020-219775. PMID: 33514506) We now explored utility of the PASTUL questionnaire in trials to translate the benefit of its use in clinical practice back into research in different subgroups of patients.

Methods: Patients included in the validation study were divided into subgroups: disease duration < 4 and > 4 years, males and females, diffuse cutaneous SSc (dcSSc) and limited cutaneous SSc (lcSSc), antibody profiles and age categories. The PASTUL questionnaire specifies a grading of skin (normal (0), mild (1), moderate (2), severely (3) thickening) at 8 sites corresponding to mRSS. To simplify the assessment, maximum score of an anatomical area was asked. Correlation between PASTUL, mRSS, Scleroderma Skin Patient reported Outcome (SSPRO) and Scleroderma Health Assessment (SHAQ) was assessed using Pearson's correlation coefficient (0-0.19 = negligible, 0.2-0.39 = weak, 0.4-0.59 = moderate, 0.6-0.79 = strong, 0.8-1.0 = very strong).

Results: Of the 104 patients included, 86% was female, 55 (53%) had lcSSc and 49 (47%) dcSSc, 75 (72%) had a disease duration > 4 years, 70 (67%) were older than 50 years. Mean age was 57 years (SD 12), mean disease du-

Table 2. Correlations (Pearson's correlation coefficient) of PASTUL with other outcome measures in different subgroups

Characteristics	Subset			Sex			Age categories			Disease duration			Antibody profiles			
	LcSSc (N=55)	DcSSc (N=49)	P-value*	Male N=14	Female N=90	P-value*	≤50 yrs N=34	>50 yrs N=70	P-value*	≤4 yrs N=29	>4 yrs N=75	P-value*	ACA N=30	ATA N=30	ARA N=17	Other N=27
Age, mean yrs (SD)	60 (12)	53 (10)	0.003	56 (12)	57 (11)	0.893	43 (6)	63 (8)	<0.001	53 (10)	58 (13)	0.060	62 (10)	49 (10)	60 (9)	56 (14)
Female (%)	49 (89)	41 (84)	0.419				28 (82)	62 (89)	0.378	24 (83)	66 (88)	0.527	28 (93)	24 (80)	15 (88)	23 (85)
SSc subtype (%)						0.567			0.059			0.008				
- lcSSc				6 (43)	49 (54)		13 (38)	42 (60)		9 (45)	46 (61)		28	9	2	16
- dcSSc				8 (57)	41 (46)		21 (62)	28 (40)		20 (69)	29 (39)		2	21	15	11
Disease duration, mean yrs (SD)	12 (8)	10 (10)	0.163	12 (9)	9 (8)	0.258	8 (6)	13 (10)	0.001	3 (1)	14 (8)		13 (8)	9 (7)	11 (10)	12 (11)
mRSS total, mean (SD)	9 (7)	20 (10)	<0.001	13 (11)	14(10)	0.607	18 (10)	13 (9)	0.027	16 (10)	14 (9)	0.265	10 (9)	19 (10)	18 (10)	10 (8)
mRSS upper limbs, mean (SD)	5 (4)	11 (6)	<0.001	8 (7)	8 (6)	0.517	11 (5)	7 (6)	0.003	9 (5)	8 (6)	0.307	6 (5)	11 (6)	10 (6)	6 (4)
PASTUL, mean (SD)	9 (7)	20 (10)	<0.001	9 (7)	12 (6)	0.133	12 (6)	11 (7)	0.261	15 (5)	9 (6)	<0.001	9 (7)	12 (6)	14 (5)	11 (7)
SHAQ, mean (SD)	1.3(0.9)	1.6(0.6)	0.051	1.2(0.8)	1.4 (0.8)	0.299	1.4(0.7)	1.4(0.8)	0.893	1.5(0.7)	1.4(0.8)	0.657	1.3(0.7)	1.3(0.7)	1.7(0.6)	1.4(1.0)
SSPRO total, mean (SD)	41 (28)	56 (24)	0.004	46 (32)	49 (26)	0.760	56 (28)	45 (26)	0.054	61 (23)	44 (27)	0.003	40 (23)	53 (28)	54 (25)	49 (30)
SSPRO subdomains, median (IQR)																
- Physical effects	16 (12)	17(10)	0.264	17 (14)	16 (10)	0.739	19 (9)	15 (10)	0.045	19 (6)	15 (11)	0.038	16 (10)	19 (10)	15 (10)	16 (12)
- Physical limitations	9 (11)	16 (9)	<0.001	14 (15)	12 (12)	0.797	15 (9)	10 (12)	0.034	16 (8)	10 (12)	0.004	10 (11)	15 (10)	16 (9)	12 (16)
- Emotional effects	13 (16)	19 (24)	0.038	11 (16)	16 (18)	0.577	19 (25)	13 (18)	0.122	21 (19)	12 (18)	0.008	12 (14)	19 (20)	16 (24)	15 (17)
- Social effects	1 (8)	5 (8)	0.003	5 (13)	4 (9)	0.706	6 (9)	3 (8)	0.111	6 (8)	3 (8)	0.007	1 (7)	5 (10)	5 (8)	5 (12)

* Independent Samples T Test, Fisher's exact test and Mann-Whitney U.

ACA, anti-centromere antibodies; ARA, anti-polymerase III antibodies; ATA, anti-topoisomerase antibodies; DcSSc, diffuse cutaneous systemic sclerosis; IQR, interquartial range; lcSSc, limited cutaneous systemic sclerosis; mRSS, modified Rodnan Skin Score; SD, standard deviation; SHAQ, Scleroderma Health Assessment Questionnaire; SSPRO, Scleroderma Skin Patient-Reported Outcome; yrs, years.

Outcome measures	Subset		Sex		Age categories		Disease duration		Antibody profiles			
	LcSSc	DcSSc	Male	Female	<50 yrs	>50 yrs	<4 yrs	>4 yrs	ACA	ATA	ARA	Other
mRSS	0.53 (p<0.001)	0.43 (p=0.005)	0.28 (p=0.428)	0.61 (p<0.001)	0.56 (p=0.005)	0.54 (p<0.001)	0.45 (p=0.053)	0.59 (p<0.001)	0.82 (p<0.001)	0.46 (p=0.033)	0.13 (p=0.670)	0.45 (p=0.069)
mRSS upper limbs	0.59 (p<0.001)	0.44 (p=0.007)	0.46 (p=0.178)	0.61 (p<0.001)	0.68 (p<0.001)	0.53 (p<0.001)	0.58 (p=0.009)	0.58 (p<0.001)	0.78 (p<0.001)	0.50 (p=0.017)	0.27 (p=0.355)	0.45 (p=0.067)
SHAQ	0.38 (p=0.005)	0.30 (p=0.039)	0.31 (p=0.274)	0.37 (p<0.001)	0.31 (p=0.070)	0.41 (p=0.001)	0.29 (p=0.130)	0.42 (p<0.001)	0.55 (p=0.002)	0.27 (p=0.154)	0.07 (p=0.785)	0.35 (p=0.078)
SSPRO	0.51 (p<0.001)	0.62 (p<0.001)	0.62 (p=0.018)	0.60 (p<0.001)	0.69 (p<0.001)	0.54 (p<0.001)	0.44 (p=0.016)	0.57 (p<0.001)	0.37 (p=0.042)	0.69 (p<0.001)	0.73 (p=0.001)	0.59 (p<0.001)
SSPRO subdomains												
Physical effects	0.52 (p<0.001)	0.69 (p<0.001)	0.60 (p=0.024)	0.60 (p<0.001)	0.63 (p<0.001)	0.57 (p<0.001)	0.50 (p=0.006)	0.58 (p<0.001)	0.44 (p=0.015)	0.65 (p<0.001)	0.76 (p<0.001)	0.65 (p<0.001)
Physical limitations	0.49 (p<0.001)	0.64 (p<0.001)	0.56 (p=0.037)	0.64 (p<0.001)	0.63 (p<0.001)	0.61 (p<0.001)	0.38 (p=0.044)	0.63 (p<0.001)	0.49 (p=0.006)	0.59 (p=0.001)	0.73 (p=0.001)	0.64 (p<0.001)
Emotional effects	0.46 (p<0.001)	0.43 (p=0.002)	0.58 (p=0.029)	0.46 (p<0.001)	0.63 (p<0.001)	0.39 (p=0.001)	0.37 (p=0.047)	0.44 (p<0.001)	0.18 (p=0.332)	0.64 (p<0.001)	0.59 (p=0.012)	0.48 (p=0.012)
Social effects	0.33 (p=0.015)	0.40 (p=0.005)	0.47 (p=0.091)	0.43 (p<0.001)	0.59 (p<0.001)	0.32 (p=0.008)	0.24 (p=0.205)	0.39 (p=0.001)	0.18 (p=0.336)	0.55 (p=0.002)	0.57 (p=0.017)	0.32 (p=0.100)

ACA, anti-centromere antibodies; ARA, anti-polymerase III antibodies; ATA, anti-topoisomerase antibodies; DcSSc, diffuse cutaneous systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis; mRSS, modified Rodnan Skin Score; SHAQ, Scleroderma Health Assessment Questionnaire; SSPRO, Scleroderma Skin Patient-Reported Outcome; yrs, years.

ration 11 years (SD 9), mean SHAQ 1.4 (SD 0.8) and mean SSPRO 48 (SD 27). MRSS was measured in 78 patients (75%), mean mRSS was 14 (SD 10). Table 1 shows characteristics of the different groups.

An overview of correlations between PASTUL and mRSS, SSPRO and SHAQ scores in the subgroups is provided in Table 2. Correlation between PASTUL and mRSS was very strong in ACA positive patients (r=0.82) and strong in females (r=0.61). Correlations between PASTUL and mRSS were stronger in lcSSc compared to dcSSc (r=0.53 vs 0.43), in females compared to males (r=0.61 vs 0.28), in patients with disease duration > 4 years (r=0.45 vs 0.59) and ACA positives compared to patients with ATA, ARA or other antibodies (r=0.82, 0.46, 0.13 and 0.45, respectively). PASTUL was moderately correlated with SHAQ in ACA positives (r=0.55) only. SSPRO and subdomains correlated weakly to moderately in this group, in contrast to other subgroups in which a stronger correlation between SSPRO and PASTUL was found.

Conclusion: Almost all subgroups showed moderate to strong correlations between PASTUL and mRSS and SSPRO. Correlations between PASTUL scores and mRSS were strongest in ACA positives and females, while ARA positive patients showed strongest PASTUL correlation with SSPRO. These correlations support potential utility of PASTUL as outcome measure and further validation in larger cohorts will define the role of PASTUL in future clinical trials.

Disclosure: J. Spierings, Boehringer Ingelheim, 5, Miltenyi, 5; **V. Ong**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 1839

Hispanic Patients with Systemic Sclerosis Have More Severe Disease and Higher Mortality: A Longitudinal Cohort Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) shows disparities in incidence, disease manifestations, and prognosis in different ethnic groups. The data regarding disease characteristics and outcomes in Hispanic Americans are

Table 1. Baseline demographics and clinical variables

Variable	Overall, N= 427[1]	Hispanic, N= 124[1]	White, N=220[1]	AA, N=83[1]	Hispanic/ White P-value[2]	Hispanic/ AA P-value[2]
Female	351 (82%)	106 (85%)	178 (81%)	67(81%)	0.355	0.475
Annual income > $29,999	248 (61%)	51 (44%)	159 (74%)	38 (49%)	**<0.001**	0.652
Associate's degree or above	139 (34%)	23 (21%)	91 (43%)	25 (31%)	**<0.001**	0.147
Age	49 (39,57)	46 (36,55)	51 (43,59)	48 (37, 56)	**0.001**	0.424
Limited disease	175 (41%)	53 (43%)	101 (46%)	21 (25%)	0.652	**0.012**
ACA Positive	60 (14%)	20 (17%)	36 (17%)	4 (5.0%)	1.00	**0.014**
Topo Positive	73 (17%)	23 (19%)	34 (16%)	16 (20%)	0.451	0.858
RNA Pol III Positive	91 (22%)	30 (25%)	46 (21%)	15 (19%)	0.600	0.474
RNP Positive	34 (8.1%)	17 (14%)	10 (4.6%)	7 (8.8%)	**0.003**	0.278
Pulmonary Fibrosis Ever on CXR/HRCT	205 (54%)	58 (56%)	103 (51%)	44 (59%)	0.47	0.76
SLE	10 (2.8%)	5 (5.4%)	1 (0.5%)	4 (5.6%)	**0.014**	1.00
Rheumatoid Arthritis	26 (7.2%)	7 (7.6%)	15 (7.5%)	4 (5.8%)	1.00	0.759
Myositis	52 (14%)	14 (15%)	24 (12%)	14 (20%)	0.58	0.408
Disease Duration	2.3 (1.2, 3.6)	2.7 (1.3, 3.8)	2.10 (1.1, 3.4)	2.35 (1.4, 3.6)	**0.049**	0.646
mRSS	13 (6, 26)	14 (6, 25)	12 (5, 25)	16 (10, 27)	0.682	0.114
FVC (% predicted)	81 (67, 93)	75 (62, 86)	85 (71, 96)	77 (62, 89)	**<0.001**	0.26
mHAQ	0.7 (0.2, 1.3)	0.77 (0.3, 1.5)	0.55 (0.1, 1.2)	1.14 (0.4, 1.5)	**0.013**	0.277

[1] Statistics presented: n (%); Median (Interquartile range) [2] Based on Fischer Exact and Wilcoxon Tests

Table 2. Cox survival regressions:

Predictor	Survival Model with Socioeconomic Factors		
	HR[1]	95% CI[1]	P-value
Ethnicity			
AA[2]	1.84	1.17, 2.89	**0.008**
Hispanic[2]	1.59	1.03, 2.45	**0.036**
Age	1.03	1.01, 1.04	**<0.001**
Female	0.59	0.38, 0.92	**0.020**
Associate's Degree or Above	0.85	0.55, 1.33	0.5
Annual income > $29,999	0.66	0.45, 0.97	**0.037**

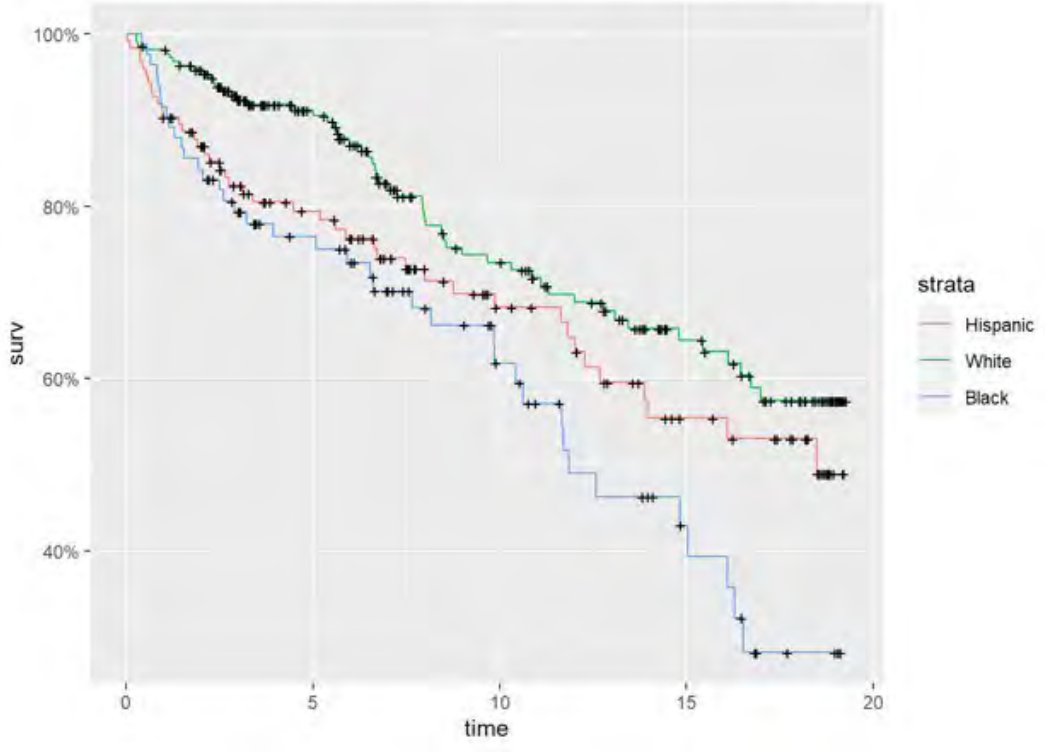
[1] HR = Hazard Ratio, CI = Confidence Interval; [2] Non-Hispanic White race is the reference group

scarce. Herein, we characterize SSc clinical features, antibody profile, and prognosis in Hispanic as compared to non-Hispanic White and African American (AA) patients.

Methods: Longitudinal clinical characteristics were collected prospectively in the Genetics versus Environment in Scleroderma Outcome Study (GENISOS) cohort. All patients fulfilled the ACR/EULAR Classification Criteria for SSc and had a disease duration less than five years at enrollment. Only patients with self-reported White, AA and Hispanic ethnicity were included in the present study. Mixed effect linear regression models were used to compare the longitudinal levels of modified Rodnan skin score (mRSS), Forced vital capacity % predicted (FVC%) and Health Assessment Questionnaire (HAQ) during the study period among three ethnic groups. Cox regression models were used for mortality analysis.

Results: A total of 427 patients, consisting of 124 Hispanic, 220 non-Hispanic White, and 83 non-Hispanic AA participants, were analyzed. The median follow-up time was 3.7 years. Table 1 shows the cross-sectional comparison

Figure. Kaplan-Meier survival estimates in systemic sclerosis based on ethnicity



of demographic and clinical characteristics of Hispanic patients to White and AA patients at the baseline visit. In comparison to Whites, Hispanic patients were significantly younger but had longer disease duration, had higher frequency of RNP positivity and an overlap disease with systemic lupus erythematosus (SLE), lower FVC%, and higher perceived functional disability (ie higher HAQ scores). Compared to AAs, Hispanic patients had more frequently limited cutaneous involvement and anti-centromere antibodies.

In the longitudinal analysis (FVC%: 1457, mRSS: 2239, and mHAQ: 1917 data points), Hispanic patients had significantly lower FVC% (point estimate=-9.3%, p< 0.001) than Whites but not AAs (p=0.6). Hispanic patients had similar serially obtained mRSS like Whites (p=0.9) but had lower longitudinal mRSS measurements than AA patients (point estimate = -3.2, p=0.029). Hispanic patients had significantly higher serially obtained perceived functional disability than White (point estimate=0.2, p < 0.001) but did not differ significantly from AA patients (p=0.6).

Hispanic patients had higher mortality than Whites (HR= 1.7, p= 0.011) after adjustment for age and gender but not in comparison to AAs (p=0.2) (also see Figure). As shown in Table 2, the higher mortality in Hispanic patients in comparison to Whites persisted even after adjustment for income and education levels.

Conclusion: SSc disease manifestations and prognosis differ in Hispanic American patients from other ethnic groups. Hispanic patients have higher likelihood of having RNP positivity and SLE overlap, lower lung volumes, as well as higher rate of mortality than White patients while they less frequently have diffuse cutaneous involvement and experience milder skin involvement than AA patients.

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Abstract Number: 1840

Can Dual-energy CT Lung Perfusion Detect Abnormalities at the Level of Lung Circulation in Systemic Sclerosis (SSc) ? Preliminary Experience in 101 Patients

Vincent Koether[1], Antoine Dupont[2], Julien Labreuche[3], Paul Felloni[4], Thierry Perez[5], Pascal Degroote[5], Jacques Remy[4], Martine Remy-Jardin[5] and David Launay[6], [1]CHU Lille, Service de Médecine Interne et Immunologie Clinique, Centre de référence des maladies autoimmunes systémiques rares du Nord et Nord-Ouest de France (CeRAINO), Lille, France, [2]CHRU de Lille, Hopital Calmette, Lille, France, [3]CHU Lille, Lille, [4]CHU Lille; Hopital Calmette, Lille, France, [5]CHU Lille, Lille, France, [6]Univ. Lille, Inserm, CHU Lille, Service de Médecine Interne, U1286 - INFINITE - Institute for Translational Research in Inflammation, F-59000 Lille, France, Lille Cedex, France

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disorder that is characterized by a interplay of vascular abnormalities, immune system activation and an uncontrolled fibrotic response associated with interstitial lung disease affecting about 40% of patients. Identification of ILD relies on high-resolution CT that identify features suggestive of the histologic patterns of SSc(1). CT is used to determine pattern and extent of ILD and participates in

the prediction of ILD progression(2). All group of pulmonary hypertension (PH) may occur with an overall prevalence reported in up to one fifth of patient. Whereas extensive SSc-ILD can be responsible for PH, PH can also be seen as a consequence of myocardial abnormalities or as primarily affecting small pulmonary arteries and classified as pulmonary arterial hypertension. Dual-energy CT introduction offers perspectives in the evaluation of SSc-related pulmonary manifestations. While these are not strictly perfusion images, they have been reported as adequate surrogate markers of lung perfusion (3). In the field of PH, detection of perfusion defects highly concordant with V/Q scintigraphic findings has been reported in the diagnostic approach of CTEPH but also in the differential diagnosis between PAH and peripheral forms of CTEPH (4). Our objective is to investigate lung perfusion abnormalities in patients with SSc

Methods: The study population included 101 patients who underwent dual-energy CT (DECT) angiography in the follow-up of SSc. CT examinations were obtained on a 3rd-generation dual-source CT system with reconstruction of morphologic and perfusion images. All patients underwent pulmonary function tests within two months of the follow-up CT scan. Fifteen patients had right heart catheterization-proven PH.

Results: Our population included patients without SSc lung involvement (Group 1; n=37), patients with SSc-related ILD (Group 2; n=56) of variable extent (Group 2a: ≤10%: n=17; Group 2b: between 11-50%: n=31; Group 2c: >50%: n=8) and patients with PVOD/PCH (Group 3; n=8). Lung perfusion was abnormal in 8 patients in G 1 (21.6%), 14 patients in G 2 (25%) and 7 patients in G 3 (87.5%). Perfusion changes were mainly composed of bilateral perfusion defects, including patchy, PE-type perfusion defects and areas of hypoperfusion of variable size. In G 1 and G 2a (n=54): (a) patients with abnormal lung perfusion (n=14) had a significantly higher proportion of NYHA III/IV scores of dyspnea (p=0.031), a shorter mean walking distance at the 6MWT (p=0.042) and a trend towards lower mean DLCO% (p=0.055) when compared to patients with normal lung perfusion (n=40); (b) a negative albeit weak correlation was found between the iodine concentration in both lungs and the DLCO% (r=- 0.27; p=0.059) whereas no correlation was found with PAPs (r=0.16; p=0.29) and walking distance during the 6MWT (r=-0.029; p=0.84).

Conclusion: DECT lung perfusion provides complementary information to HRCT scans, depicting perfusion changes in SSc patients with normal or minimally infiltrated lung parenchyma.

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Abstract Number: 1841

Presence of Autoantibodies to Dense-Fine-Speckled 70 (DFS70) Do Not Necessarily Rule out Connective Tissue Diseases

Louisa-Marie Mockenhaupt[1], Ramona Dolscheid-Pommerich[1], Charlotte Behning[1], Birgit Stoffel-Wagner[2], Peter Brossart[1] and **Valentin Schäfer**[1], [1]University Hospital Bonn, Bonn, Germany, [2]University Hospital Bonn, Bonn

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Antinuclear antibodies (ANA) are serological markers for the presence of connective tissue diseases [1]. In some patients, a pattern can be detected in ANA immunofluorescence that resembles an anti-dense-

a) ANA-Titer ≥ 1:80		
N=362	*No present CTD*	*Present CTD*
DSF70 positive	52	21
DFS70 negative	145	144
	Sensitivity: 26.4%	Specificity: 87.3%
Positive predictive value= 71.2%		
b) ANA-Titer ≥ 1:160		
N=326	*No present CTD*	*Present CTD*
DSF70 positive	45	21
DSF70 negative	122	138
	Sensitivity: 26.9%	Specificity: 86.8%
Positive predictive value= 68.2%		
c) ANA-Titer ≥ 1:640		
N=167	*No present CTD*	*Present CTD*
DSF70 positive	17	14
DSF70 negative	48	88
	Sensitivity: 26.2%	Specificity: 86.3%
Positive predictive value= 54.8%		

Sensitivity, specificity and positive predictive value of anti-DSF70 autoantibody in different ANA titers (borderline patients excluded)

fine-speckled-70 antibody (anti-DSF70)[2]. This is detected less frequently in patients with connective tissue diseases (CTD) and is therefore often used as an exclusion criteria for CTD [2]. To date, however, it remains unclear how the presence of an anti-DSF70 reliably rules out CTD. We aimed to investigate the extent to which CTD can be excluded by the presence of anti-DFS70 and whether there are discrepancies between patients with CTD and negative anti-DSF70 and those with CTD and positive anti-DSF70.

Methods: We analyzed data of 460 patients who were tested for the presence of anti-DSF70 at the University Hospital Bonn, Germany. Patients were examined with regard to clinical symptoms and signs, type of rheumatic disease, type of CTD, fulfillment of the classification criteria for the particular CTD, presence of anti-DSF70, other systemic autoantibodies and ANA titers by indirect immunofluorescence (IIF) assays and immunoblots. Gold standard for presence of a CTD was the diagnosis of the treating rheumatologist.

Differences between anti-DSF70 positive patients with CTD and anti-DSF70 negative patients with CTD were examined.

In addition, specificity, sensitivity, and positive predictive value for different ANA titers were calculated.

Results: 182 out of 460 patients (79.8% female) had a CTD. 354 patients (77.0%) were anti-DSF70 negative, 81 (17.6%) anti-DSF70 positive and 25 (5.4%) had a borderline anti-DSF70 result.

21 patients with a positive anti-DSF70 were diagnosed with a CTD, which accounts for 25.9% of all anti-DSF70 positive patients. Concerning age, gender, symptoms, clinical signs and other disease-specific antibodies, no significant differences were found between anti-DSF70-positive patients with CTD and anti-DSF70 negative patients with CTD.

Of the 21 DSF70-positive patients with CTD, 12 (57.1%) were tested for the presence of disease-specific autoantibodies. Specific autoantibodies were detected in all of the tested patients with systemic lupus erythematosus, systemic sclerosis, Sjögren's syndrome and mixed connective tissue disease.

	All patients	Anti-DSF70 positive patients n=81	Anti-DSF70 negative patients n=354	Borderline anti-DSF70 patients n=25
Rheumatic disease	270 (100%)	36 (13.3%)	219 (81.1%)	15 (5.6%)
Connective tissue disease	182 (100%)	21 (11.5%)	151 (83.0%)	10 (5.5%)
Systemic lupus erythematosus	71 (100%)	5 (7.0%)	62 (87.3%)	4 (5.6%)
Systemic sclerosis	22 (100%)	3 (13.6%)	16 (72.7%)	3 (13.6%)
Sjögren's syndrome	32 (100%)	3 (9.4%)	28 (87.5%)	1 (3.1%)
Mixed CTD	21 (100%)	5 (23.8%)	16 (76.2%)	0
Myositis	11 (100%)	2 (18.2%)	8 (72.7%)	1 (9.1%)
Undifferentiated CTD	36 (100%)	3 (8.3%)	31 (86.1%)	2 (5.6%)
Other rheumatic diseases				
Rheumatoid arthritis	58 (100%)	9 (15.5%)	45 (77.6%)	4 (6.9%)
Spondylarthritis	8 (100%)	2 (25.0%)	6 (75.0%)	0
Psoriatic arthritis	14 (100%)	2 (14.3%)	11 (78.6%)	1 (7.1%)
Polymyalgia rheumatica	4 (100%)	0	4 (100%)	0
Reactive arthritis	2 (100%)	2 (100%)	0	0
Enteropathic arthritis	3 (100%)	0	3 (100%)	0
Undifferentiated arthritis	4 (100%)	0	4 (100%)	0
Small vessel vasculitis	2 (100%)	0	2 (100%)	0
Large vessel vasculitis	5 (100%)	0	5 (100%)	0

Occurrence of anti-DSF70 in different systemic autoimmune and rheumatic diseases

Anti-DSF70 had a specificity of 86.8%, a sensitivity of 26.9% and a positive predictive value of 68.2% at an ANA titer of ≥1:160, with respect to the absence of a connective tissue disease.

Conclusion: Autoantibodies to DSF70 often occur in CTD patients and are therefore not a valid exclusion criteria for a CTD. We observed no CTD in 68.2% of patients who were tested positive. Thus, the DSF70 test can be helpful in ambiguous situations. The additional exclusion of other autoantibodies may make CTD even less probable.

1. Mahler M, Fritzler MJ. Epitope specificity and significance in systemic autoimmune diseases: Epitope specificity. *Ann N Y Acad Sci*. 2010
2. Mahler M, Hanly JG, Fritzler MJ. Importance of the dense fine speckled pattern on HEp-2 cells and anti-DFS70 antibodies for the diagnosis of systemic autoimmune diseases. *Autoimmun Rev*. 2012

Disclosure: L. Mockenhaupt, None; **R. Dolscheid-Pommerich**, None; **C. Behning**, None; **B. Stoffel-Wagner**, None; **P. Brossart**, BMS, 1, 2, 5; **V. Schäfer**, None.

Abstract Number: 1842

Peripheral Blood Cell Gene Expression Profiling Predicts Response to Mycophenolate in Systemic Sclerosis Related Interstitial Lung Disease

Shervin Assassi[1], Wenjin Zheng[2], Elizabeth Volkmann[3], Xuan Wang[4], Holly Wilhalme[5], Marka Lyons[6], Michael Roth[5] and Donald Tashkin[5], [1]University of Texas McGovern Medical School at Houston, Houston, TX, [2]School of Biomedical Informatics at the University of Texas Health Science Center at Houston, Houston, TX, [3]Department of Medicine, Division of Rheumatology, University of California, David Geffen School of Medicine, Los Angeles, CA, [4]Baylor Scott & White Health, Dallas, TX, [5]University of California Los Angeles, Los Angeles, CA, [6]Division of Rheumatology, University of Texas McGovern Medical School at Houston, Houston, TX

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Significantly changed transcript modules in pairwise comparison of 12-month to baseline samples in the CYC arm

Module	Annotation	Log Fold Change*	P_{FDR}
M2.3	Erythropoiesis	1.21	<0.0001
M6.18	Erythropoiesis	0.93	<0.0001
M3.1	Erythropoiesis	0.91	<0.0001
M4.4	Erythropoiesis	0.57	<0.0001
M5.15	Neutrophils / Granulocytes	0.53	<0.0001
M4.2	Inflammation	0.47	<0.0001
M5.3	Erythropoiesis	0.39	<0.0001
M1.1	Coagulation / Platelets	0.35	0.002
M3.3	Cell Cycle / Proliferation	0.34	<0.0001
M3.2	Myeloid Lineage	0.31	<0.0001
M6.11	Cell Cycle / Proliferation	0.28	0.0042
M4.14	Monocytes	0.27	<0.0001
M6.14	Coagulation / Platelets	0.26	0.0001
M6.6	Myeloid Lineage	0.26	<0.0001
M3.4	IFN Response	0.24	0.0103
M4.6	Myeloid Lineage	0.23	0.0001
M4.13	Inflammation	0.21	0.0055
M6.13	Inflammation	0.2	<0.0001
M3.6	Cytotoxic / NK Cell	-0.23	0.0095
M4.3	Protein Synthesis	-0.25	0.0021
M6.12	Lymphoid Lineage	-0.26	<0.0001
M4.7	Lymphoid Lineage	-0.3	<0.0001
M6.9	Lymphoid Lineage	-0.36	<0.0001
M4.15	Cytotoxic / NK Cell	-0.46	<0.0001
M6.15	T cells	-0.51	<0.0001
M6.19	T cells	-0.62	<0.0001
M4.1	T cells	-0.82	<0.0001
M4.11	Plasmablasts	-0.98	<0.0001
M4.10	B cells	-1.29	<0.0001

Table 2. Significantly changed transcript modules in pairwise comparison of 12-month to baseline samples in the MMF arm

Module	Annotation	Log Fold Change*	P_{FDR}
M3.3	Cell cycle	-0.43	<0.0001
M6.11	Cell cycle/DNA repair	-0.39	0.0009
M4.11	Plasma Cells	-0.77	<0.0001

Background/Purpose: Response to immunosuppression is variable in systemic sclerosis (SSc) related interstitial lung disease (ILD). Contrary to pulmonary tissue, peripheral blood cell (PBC) RNA can be obtained during routine clinical care and can be used as easily accessible source for biomarker development. This study aims to examine the PBC gene expression changes ensuing from mycophenolate mofetil (MMF) or cyclophosphamide (CYC) treatment and to determine the predictive significance of baseline PBC transcript scores for response to immunosuppressive treatment in SSc-ILD.

Methods: All patients with an available baseline PBC RNA sample (stored in PAXgene tubes) enrolled in the Scleroderma Lung Study II (SLS II) were included. Baseline and 12-month samples corresponding to the active treatment period in both MMF and CYC arms were investigated by global RNA sequencing. A paired-end 150 bp sequencing strategy was used to generate an average of 99 million reads per sample. A modular analysis using 62 curated whole blood modules was pursued as previously described (Chaussabel et al. Nat Rev Immunol 2014). Each treatment arm was analyzed separately. First, a paired analysis comparing the 12-month to baseline samples was performed. Next, the predictive significance of baseline composite modular scores for the course of forced vital capacity (FVC) % predicted measurements from 3 to 12 months was investigated using a joint model (combines a mixed effects model

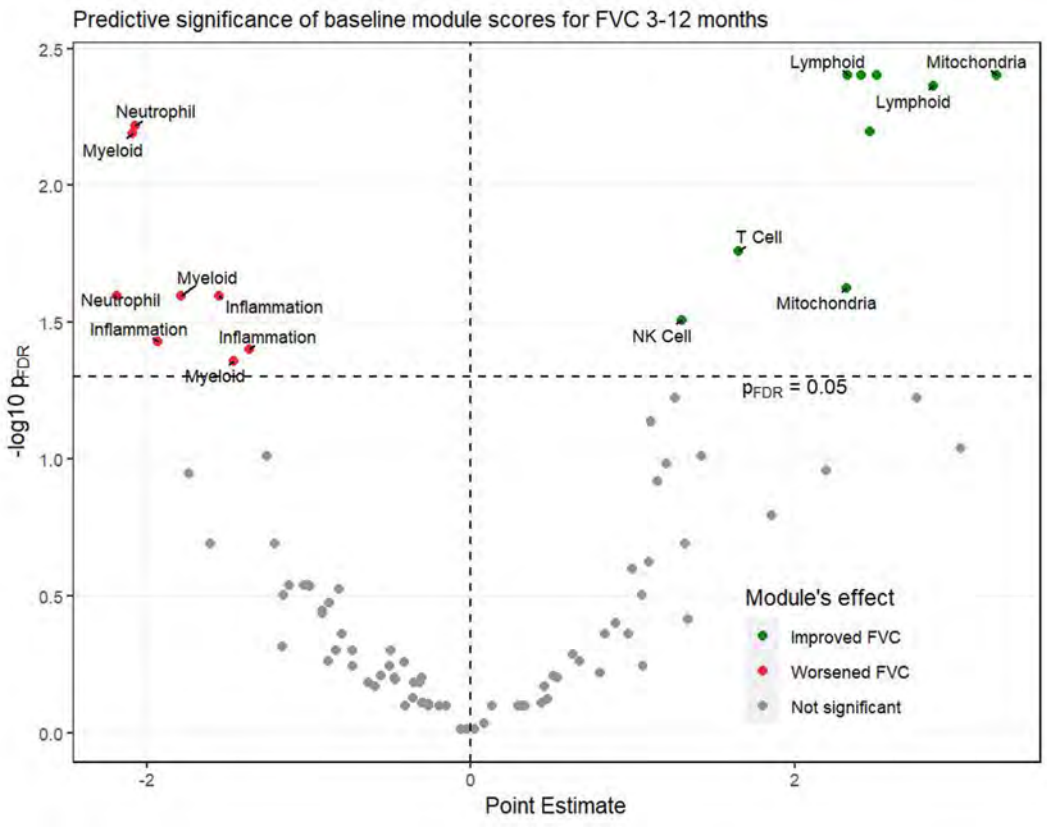

Figure 1. Predictive significance of baseline modular scores for FVC% during 3-12 month visits in the MMF arm. Higher T- and B-lymphocyte module scores predicted better ILD course while higher neutrophil/myeloid lineage module scores predicted worse ILD course. Of note, the modular analysis method can assign the same biological function to multiple modules.

for the longitudinally obtained FVC%s with a survival model to handle non-ignorable missing data). All analyses were corrected for multiple comparison by FDR method.

Results: A total of 134 patients with SSc-ILD (CYC=69 and MMF=65) enrolled in SLS II were investigated. The pairwise comparison of 12 month to baseline samples showed an upregulation of erythropoiesis, inflammation, and myeloid lineage related modules and a down-regulation of lymphoid lineage related modules in the CYC arm (Table 1). The modular changes resulting from MMF treatment were more modest. Plasma cell and cell cycle modules were downregulated after MMF treatment (Table 2).

In the longitudinal joint model, none of the baseline composite transcript module scores significantly predicted the course of FVC% in the CYC arm. In contrast, composite scores of certain transcript modules showed differential predictive significance in the MMF arm (Figure 1). Specifically, higher baseline Lymphoid Lineage (including T-cells and Cytotoxic/NK cells), and Mitochondrial Modules predicted better subsequent FVC% course, while higher baseline Myeloid Lineage (including Neutrophils / Granulocytes) and Inflammation modules predicted worse subsequent FVC% course in the MMF arm.

Conclusion: Oral CYC has a profound impact on the PBC gene expression profile in patients with SSc-ILD. MMF treatment leads to more modest gene expression changes including a decline in plasma cell modules. The predictive significance of immune related modules for response to MMF treatment varies as follows: Consistent with the primary mechanism of action of MMF on lymphocytes, patients with higher baseline lymphoid modules have a better response to MMF, while those with a higher myeloid cell lineage activation score have a poorer response.

Disclosure: S. Assassi, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2; **W. Zheng**, None; **E. Volkmann**, Boehringer Ingelheim, 2, 6, Corbus, 5, Forbius, 5, Kadmon, 5; **X. Wang**, None; **H. Wilhalme**, None; **M. Lyons**, None; **M. Roth**, Genentech/Roche, 5; **D. Tashkin**, None.

Abstract Number: 1843

Perceptions and Concerns Regarding COVID-19 Vaccination in Patients with Systemic Sclerosis in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Hesitancy about COVID-19 vaccination exists among patients with rheumatic and musculoskeletal diseases, but previous studies have not assessed this specifically in patients with systemic sclerosis (SSc, or scleroderma). We surveyed patients enrolled in the Scleroderma Patient-centered Intervention Network (SPIN) Cohort regarding their willingness to be vaccinated as well as their perceptions and concerns about the vaccines.

Methods: Participants were adults with physician-verified SSc enrolled in the SPIN Cohort. SPIN includes 47 international centers and has approximately 1600 active participants. From April 9 to May 15, 2021, participants from the SPIN Cohort were invited by email and popups during regular SPIN Cohort assessments to participate in a COVID-19 vaccine survey, which was conducted in English and French. Participants were asked if they had received the vac-

Table 1. Demographic and clinical description of survey responders

Clinical Variable	Total (N=932)
Age, years, mean (SD)[a]	59.9 (12.0)
Female, n (%)	830 (89.1)
Race/ethnicity, n (%)[b]	
White	794 (86.5)
Black	45 (4.9)
Other	79 (8.6)
Location, n (%)[a]	
Canada	261 (28.4)
United Kingdom	85 (9.3)
Australia	22 (2.4)
United States of America	260 (28.3)
France	275 (30.0)
Scleroderma subtype, n (%)	
Limited	553 (59.3)
Diffuse	334 (35.8
Sine	36 (3.9)
Time since onset of first non-Raynaud's symptom, years, mean (SD) [c]	15.3 (9.3)
Use of immunosuppressive or immunomodulator, n(%)	
Steroid	191 (20.5)
Hydroxychloroquine	136 (14.6)
Methotrexate	89 (9.5)
Azathioprine	20 (2.1)
Mycophenolate	205 (22.0)
Tocilizumab	21 (2.3)
Abatacept	7 (0.8)
Tofacitinib	7 (0.8)
Cyclophosphamide	12 (1.3)
Rituximab	30 (3.2)
Stem cell transplant	24 (2.6)
Other Medication for SSc	501 (53.8)
History of ILD, n (%)	251 (26.9)
History of PH, n (%)	143 (15.3)
Tobacco use, current, n (%)	44 (4.7)
History of COVID-19 infection, n (%)	77 (8.3)
Legend: ILD=interstitial lung disease; PH=pulmonary hypertension. [a] N = 931 [b] N = 918 [c] N = 859	

Table 2. Perceptions of patients based on degree of hesitancy

	Received vaccine or plan to do so 842 (90.3%)		Unsure/Unlikely/Certainly will not get vaccine 90 (9.7%)		
	n (%) imp/very important	Likert rating Mean (SD)	n (%) imp/very important)	Likert rating Mean (SD)	mean difference (95% CI)
A. How important are each of the following considerations to you for getting the vaccine already or for considering getting it in the future?					
It reduces the chance of getting sick with COVID-19	809 (96%)	4.79 (0.54)	44 (49%)	3.14 (1.55)	1.64 (1.31, 1.97)
It protects others from getting COVID-19	788 (94%)	4.67 (.71)	48 (53%)	3.24 (1.49)	1.42 (1.10, 1.74)
It increases one's ability to socialize with friends and family	734 (87%)	4.50 (.88)	48 (53%)	3.21 (1.57)	1.28 (.95, 1.62)
It allows people to get back to or closer to normal life and routines.	762 (91%)	4.58 (.77)	47 (52%)	3.29 (1.51)	1.29 (.97, 1.61)
Proof of vaccination may be required in the future to travel or socialize	640 (76%)	4.09 (1.14)	37 (41%)	2.84 (1.63)	1.25 (.90, 1.59)
It is our duty to receive the COVID19 vaccine to set a good example to others	625 (74%)	4.07 (1.19)	12 (13%)	1.93 (1.26)	2.14 (1.86, 2.41)
We all need to work together to end this pandemic.	783 (93%)	4.66 (.74)	45 (50%)	3.33 (1.42)	1.33 (1.02, 1.63)
Someone close to me has been very sick with COVID-19	441 52%)	3.20 (1.68)	34 (38%)	2.79 (1.57)	.42 (.07, .76)
B. How important are the following to you in making a decision about getting a COVID-19 vaccine?					
The recommendation of the doctor who cares for my scleroderma	672 (80%)	4.23 (1.15)	45 (50%)	3.26 (1.45)	0.97 (0.66, 1.28)
The ability to obtain information and discuss any concerns with my doctor	626 (74%)	4.07 (1.17)	56 (62%)	3.64 (1.49)	.42 (.10, .75)
The opportunity to review publicly available data on vaccine effectiveness and safety	644 (77%)	4.09 (1.07)	58 (64%)	3.81 (1.45)	.28 (-.03, .59)
Information on whether or not my doctor received the vaccine	307 (37%)	2.77 (1.55)	37 (41%)	2.82 (1.64)	-.06 (-.41, .30)
The experiences of friends or family members who received the vaccine.	405 (48%)	3.24 (1.40)	40 (44%)	3.10 (1.47)	.14 (-.18, .46)
The experiences of other people with scleroderma who have received the vaccine	429 (51%)	3.33 (1.41)	58 (64%)	3.72 (1.52)	-.39 (-.72, -.06)
Guidelines for people with scleroderma and COVID-19 vaccination from trustworthy sources	597 (71%)	3.98 (1.24)	56 (62%)	3.74 (1.49)	.234 (-.09, .56)
Evidence that people with scleroderma have received the vaccine without major adverse reactions	553 (66%)	3.78 (1.31)	60 (67%)	3.8 (1.49)	-.06 (-.38, .27)
That enough time has passed for me to be comfortable that there are no long-term negative effects of the vaccines	500 (59.4%)	3.62 (1.36)	72 (80%)	4.36 (1.01)	-.74 (-.97, -.51)
The ability to have a vaccine appointment that is convenient for me	468 (55.6%)	3.46 (1.46)	25 (28%)	2.56 (1.55)	.91 (.57, 1.25)
Results are presented as the number (%) of patients who responded that a point was important or very important as well as the mean (SD) of the group's response on the Likert scale. The mean difference of these scores is presented with the 95% confidence interval. Results that cross zero are not significant.					

cine and if not, whether they planned to and their degree of certainty. All were asked to rate factors of importance in the decision to get vaccinated using a 5-point Likert scale (1 – not important, 2 – slightly important, 3 – somewhat important, 4 – important, 5 – very important). These questions were developed based on previous surveys by SPIN investigators in conjunction with patient partners. Responses of those who had or who planned to receive the vaccine were compared to those who were unsure, unlikely or certainly would not get the vaccine. Descriptive statistics and t-tests for mean item differences are presented.

Results: The demographic and clinical characteristics of the 932 responders are shown in Table 1. Of these, 699 (75%) had received at least one dose of COVID-19 vaccine, and 842 (90.3%) had either been vaccinated or planned

to do so. 90 participants (9.7%) reported feeling unsure [35 (3.8%)], unlikely [31 (3.4%)], or that they would certainly not [24 (2.6%)] get vaccinated.

Responses were compared based on hesitancy (table 2). Patients who received the vaccine or who planned to do so rated multiple considerations of higher importance than those who were hesitant. (2A) The highest mean differences were noted for the following factors: civic duty/setting an example, reducing risk of illness, protecting others. When asked about decision making about getting the vaccine, hesitant patients were more likely to rank as important or very important that enough time had passed to assess risk of long-term side effects and the experiences of other SSc patients. Compared to those who were hesitant, patients who had received the vaccine or who planned to were more likely to rank as important or highly important: their rheumatologist's recommendation, the ability to discuss concerns with their doctor, and convenience. (2B)

Conclusion: Approximately 1 in 10 participants reported vaccine hesitancy. These results identify factors associated with hesitancy in this group of SSc patients and highlight topics that may be emphasized in providing education which may be helpful for hesitant SSc patients.

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Abstract Number: 1844

Efficacy and Safety of Nintedanib in Patients with Systemic Sclerosis-Associated ILD (SSc-ILD) and Differing Comorbidity Burden: Subgroup Analyses of the SENSCIS Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) vs placebo. Patients with SSc-ILD frequently have comorbidities that add to their functional impairment and complicate their care. We investigated the efficacy and safety of nintedanib in subgroups based on comorbidity burden.

Table 1. Baseline characteristics of subgroups of patients in the SENSCIS trial by number of comorbidities and CCI score.

	Number of comorbidities		CCI score	
	≤2 (n=371)	>2 (n=205)	≤1 (n=338)	>1 (n=238)
Female	273 (73.6)	160 (78.0)	258 (76.3)	175 (73.5)
Age, years	51.5 (12.5)	58.4 (10.3)	46.2 (9.2)	65.0 (5.8)
BMI, kg/m^2	25.4 (4.7)	26.7 (5.4)	25.7 (5.0)	26.2 (5.0)
Years since onset of first non-Raynaud symptom	3.5 (1.7)	3.5 (1.7)	3.6 (1.7)	3.3 (1.7)
Diffuse cutaneous SSc	199 (53.6)	100 (48.8)	198 (58.6)	101 (42.4)
ATA positive	243 (65.5)	107 (52.2)	225 (66.6)	125 (52.5)
Modified Rodnan skin score*	11.4 (8.8)	10.6 (9.3)	12.4 (9.4)	9.3 (8.1)
FVC % predicted	71.7 (16.5)	74.0 (16.9)	69.8 (16.2)	76.5 (16.5)
SGRQ total score†	38.4 (20.3)	43.1 (20.6)	40.4 (20.8)	39.7 (20.3)

Data are n (%) of patients or mean (SD). *2 patients had missing data. †11 patients had missing data. ATA, anti-topoisomerase I antibody; FVC, forced vital capacity; SGRQ, St George's Respiratory Questionnaire.

Methods: The SENSCIS trial enrolled patients with SSc-ILD with first non-Raynaud symptom in the last ≤7 years and an extent of fibrotic ILD on HRCT ≥10%. Patients with clinically significant pulmonary hypertension were excluded. Comorbidities at baseline were counted in categories based on organ group. In the Charlson Comorbidity Index (CCI), ages of 50–59 years, 60–69 years, 70–79 years and ≥80 years are assigned 1, 2, 3 and 4 points, respectively. The presence and severity of specific comorbidities are scored 1, 2, 3 or 6 points each. Patients with certain comorbidities used to calculate the CCI (e.g. metastatic solid tumor, AIDS) were not eligible for inclusion in the trial. SSc

Figure. Rate of decline in FVC (mL/year) over 52 weeks in the SENSCIS trial in subgroups by number of comorbidities and CCI score at baseline.

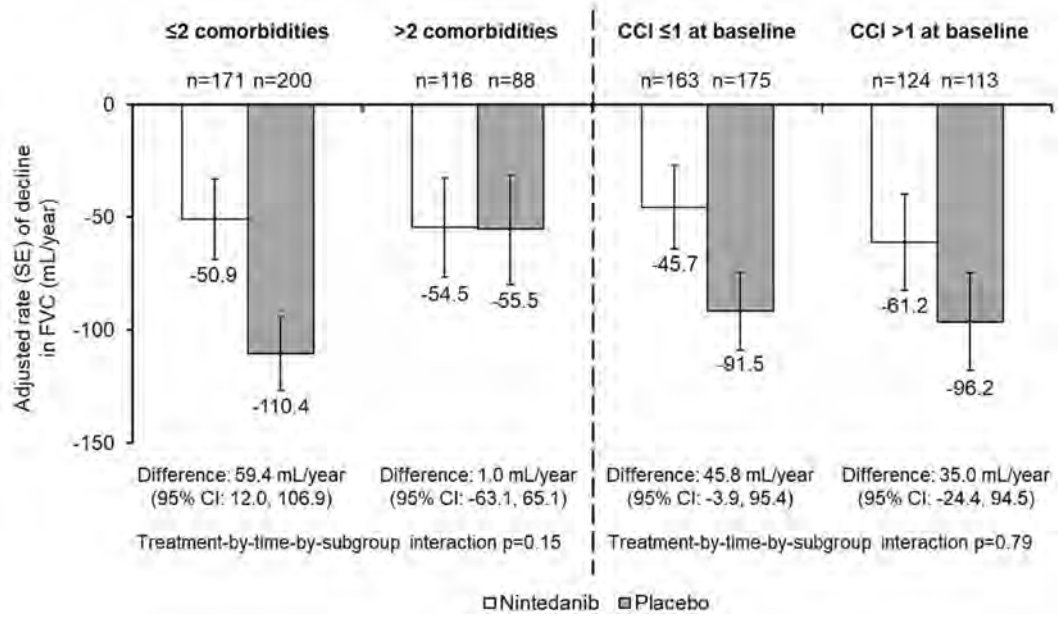

Table 2. Adverse events in subgroups of patients in the SENSCIS trial by number of comorbidities and CCI score at baseline.

	≤2 comorbidities		>2 comorbidities		CCI score ≤1		CCI score >1	
	Nintedanib (n=171)	Placebo (n=200)	Nintedanib (n=117)	Placebo (n=88)	Nintedanib (n=163)	Placebo (n=175)	Nintedanib (n=125)	Placebo (n=113)
Most frequent adverse events*								
Diarrhea	128 (74.9)	58 (29.0)	90 (76.9)	33 (37.5)	129 (79.1)	57 (32.6)	89 (71.2)	34 (30.1)
Nausea	47 (27.5)	21 (10.5)	44 (37.6)	18 (20.5)	49 (30.1)	28 (16.0)	42 (33.6)	11 (9.7)
Skin ulcer	37 (21.6)	33 (16.5)	16 (13.7)	17 (19.3)	35 (21.5)	35 (20.0)	18 (14.4)	15 (13.3)
Vomiting	40 (23.4)	18 (9.0)	31 (26.5)	12 (13.6)	38 (23.3)	21 (12.0)	33 (26.4)	9 (8.0)
Cough	19 (11.1)	36 (18.0)	15 (12.8)	16 (18.2)	21 (12.9)	38 (21.7)	13 (10.4)	14 (12.4)
Nasopharyngitis	20 (11.7)	32 (16.0)	16 (13.7)	17 (19.3)	18 (11.0)	30 (17.1)	18 (14.4)	19 (16.8)
Upper respiratory tract infection	17 (9.9)	23 (11.5)	16 (13.7)	12 (13.6)	23 (14.1)	26 (14.9)	10 (8.0)	9 (8.0)
Abdominal pain	24 (14.0)	16 (8.0)	9 (7.7)	5 (5.7)	16 (9.8)	14 (8.0)	17 (13.6)	7 (6.2)
Fatigue	15 (8.8)	12 (6.0)	16 (13.7)	8 (9.1)	17 (10.4)	17 (9.7)	14 (11.2)	3 (2.7)
Weight decrease	17 (9.9)	8 (4.0)	17 (14.5)	4 (4.5)	16 (9.8)	6 (3.4)	18 (14.4)	6 (5.3)
Serious adverse events	41 (24.0)	45 (22.5)	28 (23.9)	17 (19.3)	36 (22.1)	39 (22.3)	33 (26.4)	23 (20.4)
Adverse events leading to treatment discontinuation	23 (13.5)	16 (8.0)	23 (19.7)	9 (10.2)	21 (12.9)	10 (5.7)	25 (20.0)	15 (13.3)

Data are n (%) of patients with ≥1 such event reported on-treatment over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). *Adverse events, coded using the Medical Dictionary for Regulatory Activities (MedDRA), reported in >10% of patients in either treatment group in the overall trial population are shown.

was not counted as a comorbidity. We investigated the rate of decline in FVC (mL/year) and adverse events over 52 weeks in subgroups with ≤2 vs >2 comorbidities and CCI score ≤1 vs >1 at baseline.

Results: Among 576 patients treated in the SENSCIS trial, 205 (35.6%) had >2 comorbidities and 238 (41.3%) had a CCI score >1 at baseline. At baseline, compared with patients with ≤2 comorbidities, those with >2 comorbidities had a higher mean age, FVC % predicted, and St George's Respiratory Questionnaire total score, a greater proportion were female, and a smaller proportion had diffuse cutaneous SSc (dcSSc) (Table 1). Compared with patients with a CCI score ≤1, those with a CCI score >1 had a higher mean age and FVC % predicted and a smaller proportion had dcSSc (Table 1). In the placebo group, the rate of decline in FVC over 52 weeks was numerically greater in patients with ≤2 than >2 comorbidities, but similar between patients with CCI score ≤1 and >1. The effect of nintedanib versus placebo on reducing the rate of FVC decline was numerically greater in patients with ≤2 than >2 comorbidities and similar between patients with CCI score ≤1 and >1, but no heterogeneity in the treatment effect was detected (interaction p-values 0.15 and 0.79, respectively) (Figure). The adverse event profile of nintedanib was generally similar across the subgroups (Table 2). Adverse events leading to discontinuation were more frequent in patients treated with nintedanib than placebo and, in both treatment groups, were more frequent in patients with higher comorbidity burden.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, patients with greater comorbidity burden had higher FVC at baseline. The rate of decline in FVC over 52 weeks in the placebo group, and the effect of nintedanib on the rate of FVC decline, were numerically greater in patients with ≤2 than >2 comorbidities, but no statistically significant heterogeneity was detected in the effect of nintedanib between the subgroups. Treatment discontinuation due to adverse events was more common in patients with greater comorbidity burden. Proactive management of adverse events is important to help patients stay on antifibrotic therapy.

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Abstract Number: 1845

Six-minute Walk Test as a Prognostic Marker in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Pulmonary arterial hypertension (PAH) and interstitial lung disease (ILD) are the leading causes of mortality in systemic sclerosis (SSc). Although the six-minute walk test (6MWT) is generally used for evaluating physical functioning in PAH and ILD, its relevance in clinical practice is still uncertain. The purpose of this study was to evaluate which variables of 6MWT are correlated with demographic, clinical and serological data.

Methods: In this cross-sectional study, 75 SSc patients (all patients met the 2013 ACR-EULAR systemic sclerosis classification criteria) were evaluated regarding the following characteristics: demographic, clinical including diagnosis of SSc, disease duration, calcinosis, NYHA functional class, modified Rodnan skin score (MRSS), pulmonary function, ILD, c-reactive protein (CRP - mg/L) and immunological data (anti-topoisomerase-I, anticentromere and RNP antibodies) – table 1. Patients were submitted to 6MWT. A Kruskal-Wallis test followed by Dunn's multiple non-parametric pairwise tests was used to compare the categorical items with 6MWT variables (table 2). The numerical items were compared applying Spearman correlation coefficient (table 3). All the data were analyzed using 5% level of significance ($p < 0.05$).

Results: Total distance was negatively associated with age and advanced age at diagnosis. Predicted distance was positively related to age, disease duration, greater forced vital capacity (FVC) and lesser NYHA functional class (I >II; II >III/IV) class. Borg scale was positively related to higher NYHA functional class (I< II, II< III/IV). Drop of saturation was positively associated with worse FVC and anti-topoisomerase-I positivity. There were no associations between 6MWT variables and race, clinical classification of SSc (limited, diffuse or sine scleroderma), presence of calcinosis, MRSS, anti-centromere, anti-RNP, presence of ILD and CRP values.

Conclusion: The performance on 6MWT was well correlated with pulmonary function, anti-topoisomerase-I positivity, NYHA functional class, disease duration and age. 6MWT is a straightforward and inexpensive test, useful in identifying SSc patients with adverse outcomes in clinical practice. Prospective studies are necessary to confirm our findings.

Table 1. Characteristics of subjects

Variables	N	Values
Demographic data		
Age, mean ± SD years (range)	75	49 ± 11,9 (20-81)
Age at diagnosis, mean ± SD years (range)	75	41,5 ± 11,8 (17-67)
Gender, nº (%)	75	Women 57 (76%) / Men 18 (24%)
Skin tone, nº (%)	75	White 53 (70,6%) / Non-white 22 (29,3%)
Clinical data		
Hipertension, nº (%)	75	23 (30,6%)
Diabetes, nº (%)	75	3 (4%)
Hypercholesterolemia, nº (%)	75	14 (18,6%)
Disease data		
Clinical diagnosis of SSc	75	
- limited cutaneous SSc, nº (%)		29 (38,6%)
- diffuse cutaneous SSc, nº (%)		39 (52%)
- sine scleroderma SSc, nº (%)		7 (9,3%)
Calcinosis, nº (%)	75	2 (2,6%)
Disease duration, mean ± SD years (range)	75	
- 0-5 years, nº (%)		18 (24%)
- 6-10 years, nº (%)		38 (50,6%)
- >10 years, nº (%)		19 (25,3%)
NYHA functional class	75	
- Class I, nº (%)		39 (52%)
- Class II, nº (%)		26 (34,6%)
- Class III/IV, nº (%)		10 (13,3%)
Modified Rodnan skin score, mean ± SD years (range)	65	11,87 ± 9,54 (0-44)
Exams		
Immunological profile	75	
- Anti-topoisomerase I antibodies, nº (%)		27 (36%)
- Anti-centromere antibodies, nº (%)		2 (2,6%)
- Anti-RNP antibodies, nº (%)		14 (18,6%)
Intersticial lung disease (CT), nº (%)	75	69 (92%)
FVC (% predicted)	68	
- <60%, nº (%)		29 (42,6%)
-60-80%, nº (%)		27 (39,7%)
- >80%, nº (%)		12 (17,6%)
CRP (mg/L)	75	11,9 ± 25 (0,25-192)
Total distance (m), mean ± SD years (range)	75	429,7 ± 84,9 (90-559)
Predicted distance (%), mean ± SD years(range)	75	73,5 ± 15,5 (15-101)
Drop saturationO2 (%),mean ± SD years(range)	64	-7,8 ± 7,1 (-26-+3)
Final Borg Score, mean ± SD years(range)	75	3,8 ± 2,8 (0-10)

Table 2. Comparison of categorical demographic, clinical and disease data and 6MWT parameters

Variables	6-minute walk test parameters			
	Total distance (m)	Predicted distance (%)	Drop saturation O2 (%)	Final Borg Score
Gender:				
Women	420,6±89,7 (90-552)	73,7±15,9 (15-99)	-8,2±7,1 (-26-+1)	4±2,8 (0-10)
Men	458,3±60,8 (330-559)	72,7±14,7 (53-101)	-6,6±7,5 (-22-+3)	3,1±2,9 (0-10)
p value*	0.1103	0.1903	0.4284	0.1670
Disease duration:				
0-5 (1)	416,9±112,2 (90-551)	66±18,1 (15-95)	-7,5±7,5 (-18-+3)	3,2±2,6 (0-10)
6-10 (2)	434,4±70,6 (259-559)	74,9±12,6 (46-101)	-8,4±6,9 (-22-+1)	3,6±2,8 (0-10)
>10 (3)	432,3±84,9 (120-523)	77,7±16,3 (24-97)	-7,1±7,7 (-26-+1)	4,6±2,8 (0-10)
p value*	0.9067	0.0196 (1#2, 1#3)	0.7221	0.2349
Skin tone:				
White	437,1±83,8 (120-559)	74,2±15,1 (24-101)	-7,9±7,4 (-26-+3)	3,6±2,7 (0-10)
Non-white	411,8±86,9 (90-512)	71,7±16,8 (15-99)	-7,8±6,7 (-19-0)	4,2±3,1 (0-10)
p value*	0.1711	0.3805	0.8851	0.3431
Clinical diagnosis				
diffuse cutaneous SSc	434,7±89 (90-559)	73,1±15,9 (15-100)	-9,6±7,2 (-26-+3)	3,5±2,7 (0-10)
limited cutaneous SSc	424,8±87,3 (120-552)	73,6±16,4 (24-101)	-5,6±6,8 (-22-+2)	4,1±3 (0-10)
sine scleroderma SSc	422,1±53,2 (349-498)	75,1±10,3 (60-91)	-8,1±6,2 (-19-3)	4±3,1 (0-9)
p value*	0.5116	0.9370	0.0767	0.6236
Calcinosis				
Yes	429,4±86 (90-559)	73,3±15,7 (15-101)	-7,7±6,8 (-22-+3)	3,7±2,8 (0-10)
No	439,5±19 (426-453)	78,5±2,1 (77-80)	-13±18,2 (-26-0)	5±2,8 (3-7)
p value*	0.8821	0.5427	0.7425	0.4658
NYHA functional class				
I (1)	455±59,9 (307-559)	76±9,8 (57-101)	-7,9±7,8 (-26-+2)	2,9±2 (0-8)
II (2)	433,1±56 (259-512)	77,3±12,2 (45-97)	-6,5±6,7 (-19-+3)	4,1±3,1 (0-10)
III/IV (3)	322,1±140,4 (90-471)	53,8±25,6 (15-99)	-11±5,1 (-19-+4)	6,4±3,2 (1-10)
p value*	0.0045 (1#2, 2#3)	0.0068 (1#2, 2#3)	0.2500	0.0063 (1#2, 2#3)
Interstitial lung disease				
Yes	427,4±87 (90-559)	72,8±15,8 (15-101)	-8,3±7 (-26-+3)	3,8±2,8 (0-10)
No	455,8±54 (420-551)	81,5±10,3 (69-97)	-3,5±7,8 (-19-+1)	3,6±2,6 (0-7)
p value*	0.7468	0.1509	0.0585	0.8594
FVC				
30-59% (1)	411,1±95,4 (90-540)	67,9±16,2 (15-100)	-9,5±7,9 (-26-+1)	4,4±2,9 (0-10)
60-80% (2)	454,8±65,7 (307-559)	79,1±12,2 (46-101)	-9,2±6,7 (-20-+2)	3,6±2,4 (0-9)
>80% (3)	423,5±44,2 (360-498)	79,2±10,6 (60-97)	-3,7±5,4 (-16-+1)	3,6±3,1 (0-9)
p value*	0.0646	0.0033 (1#2, 1#3)	0.0282 (1#2, 1#3)	0.5410
Anti-centromere antibodies				
Yes	364,5±21,9 (349-380)	74,5±3,5 (72-77)	-5,5±2,1 (-7-4)	2±2,8 (0-4)
No	431,5±85,3 (90-559)	73,4±15,7 (15-101)	-7,9±7,2 (-26-+3)	3,8±2,8 (0-10)
p value*	0.0752	0.9475	0.8468	0.4072
Anti-topoisomerase I antibodies				
Yes	420,9±96,7 (90-552)	69,7±17 (15-99)	-11,7±6,6 (-26-0)	3,8±2,7 (0-10)
No	434,6±76,8 (120-559)	75,6±14,3 (24-101)	-5,8±6,6 (-20-+3)	3,7±2,9 (0-10)
p value*	0.9251	0.1316	0.0013	0.7259
Anti-RNP antibodies				
Yes	430±80 (90-559)	73,3±15,8 (15-101)	-8±7 (-26-+3)	3,9±2,8 (0-10)
No	429,7±84,9 (90-559)	73,5±15,5 (15-101)	-7,8±7,1 (-26-+3)	3,6±2,8 (0-10)
p value*	0.4098	0.1611	0.1336	0.3992

* Kruskal-Wallis test

Table 3. Comparison of numerical variables and 6MWT parameters

Variables	6-minute walk test parameters			
	Total distance (m) p-value**	Predicted distance (%) *p*-value**	Drop saturation O2 (%) *p*-value**	Final Borg Score *p*-value**
Age	-0.3902 0.0005	0.4190 0.0002	0.1183 0.3517	-0.1179 0.3138
Age at diagnosis	-0.4190 0.0002	0.2245 0.0528	0.0521 0.6824	-0.1951 0.0935
Modified Rodnan skin score	0.1777 0.1566	0.0561 0.6574	-0.0984 0.4622	-0.1618 0.1978
CRP (mg/L)	-0.0553 0.6375	-0.1808 0.1207	-0.1921 0.1253	0.0673 0.5664

** Spearman correlation coefficient

Disclosure: V. Soubihe, None; **J. Gaino**, None; **A. Pugliesi**, None; **A. Del Rio**, None; **Z. Sachetto**, None; **M. Dos Santos**, None; **L. Palhares**, None.

Abstract Number: 1846

Effect of Nintedanib in Patients with Systemic Sclerosis-associated Interstitial Lung Disease and Risk Factors for Rapid Decline in Forced Vital Capacity: Further Analyses of the SENSCIS Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Figure 1. Rate of decline in FVC (mL/year) over 52 weeks in all patients and in patients with risk factors for rapid decline in FVC at baseline in the SENSCIS trial.

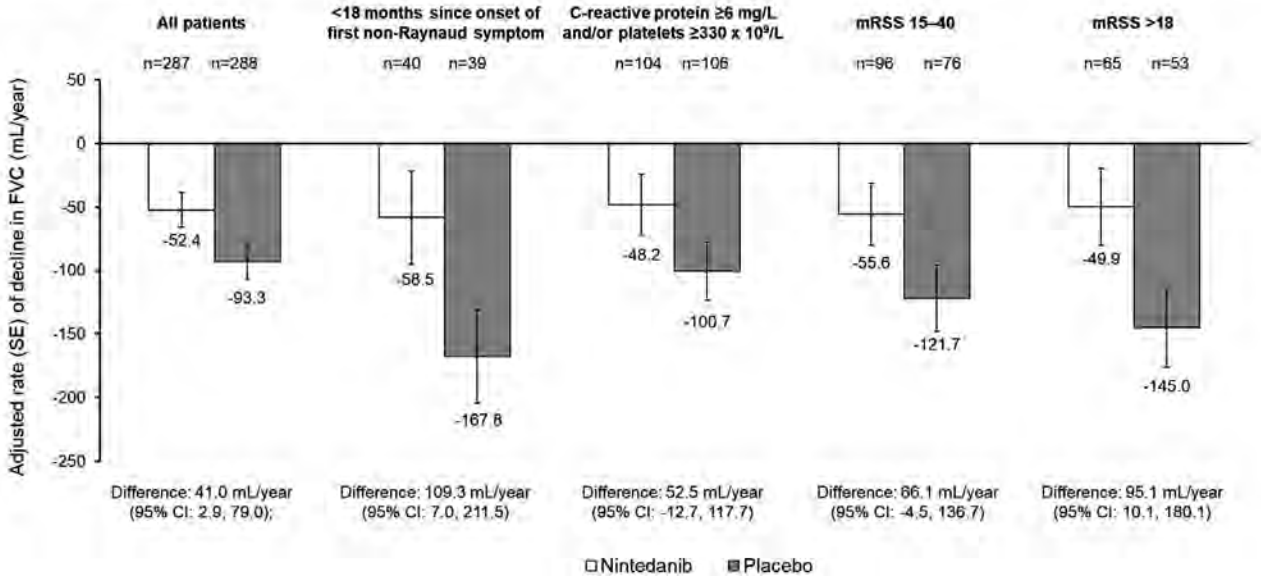
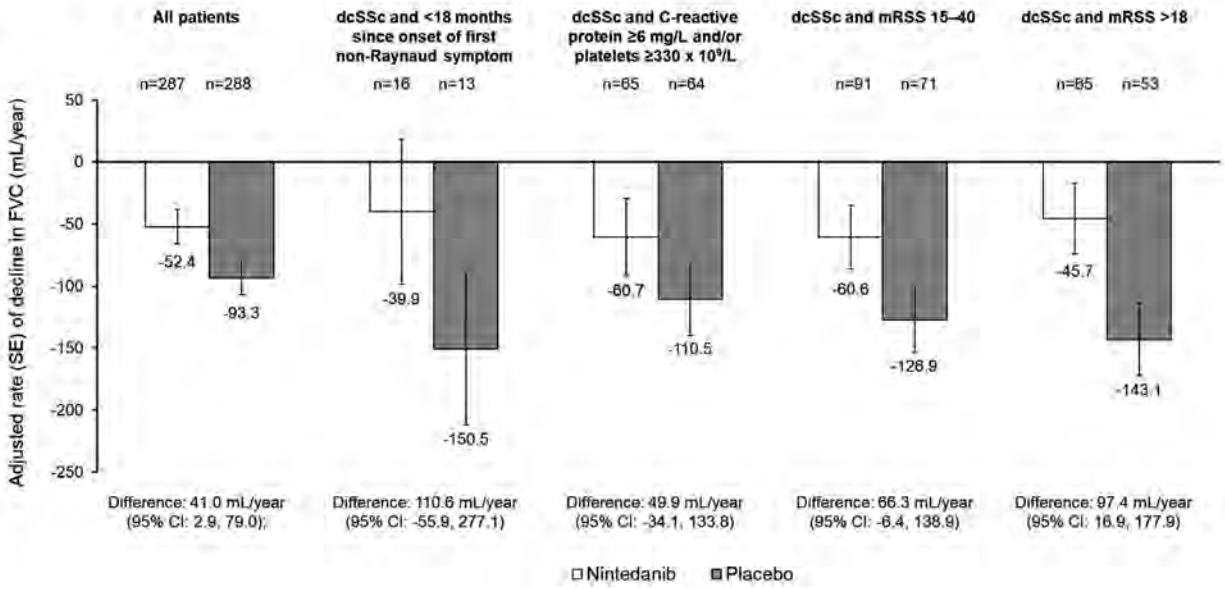


Figure 2. Rate of decline in FVC (mL/year) over 52 weeks in all patients and in patients with dcSSc and risk factors for rapid decline in FVC at baseline in the SENSCIS trial.



Background/Purpose: In the SENSCIS trial conducted in a population of subjects with systemic sclerosis-associated interstitial lung disease (SSc-ILD), with a mean time since onset of first non-Raynaud symptom of 3.5 years and 52% with diffuse cutaneous SSc (dcSSc), nintedanib reduced the rate of decline in FVC (mL/year) over 52 weeks by 44% versus placebo. Risk factors for a rapid decline in FVC in patients with SSc include early SSc, elevated inflammatory markers, significant skin involvement, and dcSSc. Patients with SSc with these risk factors for rapid progression of ILD are typically given immunosuppressants but not nintedanib. We analyzed the rate of decline in FVC and the effect of nintedanib on FVC decline in subjects with these risk factors in the SENSCIS trial.

Methods: In post-hoc analyses of data from the SENSCIS trial, we analyzed the rate of decline in FVC (mL/year) over 52 weeks in all subjects and in those with early SSc (< 18 months since onset of first non-Raynaud symptom), elevated inflammatory markers (C-reactive protein ≥6 mg/L and/or platelets ≥330 x 10^9/L), or significant skin fibrosis using two approaches (modified Rodnan skin score [mRSS] 15-40 or mRSS >18) at baseline. We also analyzed the rate of decline in FVC over 52 weeks in subjects with one of these risk factors and dcSSc.

Results: Of 575 subjects analyzed, 79 (13.7%) had < 18 months since onset of first non-Raynaud symptom, 210 (36.5%) had elevated inflammatory markers, 172 (29.9%) had mRSS 15-40 and 118 (20.5%) had mRSS >18. Of 299 subjects with dcSSc, 29 (9.7%) had < 18 months since onset of first non-Raynaud symptom, 129 (43.1%) had elevated inflammatory markers, 162 (54.2%) had mRSS 15-40 and 118 (39.5%) had mRSS >18. In the placebo group, the rate of decline in FVC over 52 weeks was numerically greater in subjects with these risk factors for rapid decline in FVC compared with all subjects. Across the subgroups, the rate of decline in FVC was numerically lower in subjects treated with nintedanib than placebo (Figures).

Conclusion: The SENSCIS trial included a broad range of subjects with a fibrotic ILD complicating SSc, including those with risk factors for a rapid decline in FVC. In the placebo group, subjects with these risk factors had a more rapid decline in FVC over 52 weeks compared with the overall trial population. By targeting fibrosis with nintedanib, the rate of decline in FVC in patients with risk factors for FVC decline was reduced in patients treated with nintedanib than placebo.

Disclosure: D. Khanna, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **T. Maher**, Apellis, 2, Bayer, 2, Biogen, 2, Blade Therapeutics, 2, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 2, Galapagos NV, 2, Galecto, 2, GlaxoSmithKline, 2, Indalo, 2, Novartis, 2, Respivent, 2, Roche, 2, Trevi, 2, UCB, 2; **E. Volkmann**, Boehringer Ingelheim, 2, 6, Corbus, 5, Forbius, 5, Kadmon, 5; **Y. Allanore**, Bayer, 2, Boehringer Ingelheim, 2, 12, Clinical trial investigator, Roche, 2, Chemomab, 2, Curzion, 2, Sanofi, 2, 12, Clinical trial investigator; **V. Smith**, Boehringer Ingelheim, 2, 6, Janssens, 2, 6; **S. Assassi**, Novartis, 2, Boehringer Ingelheim, 2, 5, 6, 12, Travel, Corbus, 2, Integrity Continuing Education, 6, Medscape, 6, Momenta, 5, CSL Behring, 2, Janssen, 5, Abbvie, 2; **M. Kreuter**, Boehringer Ingelheim, 2, 5, Galapagos NV, 2, Roche, 2, 5; **A. Hoffmann-Vold**, Actelion, 1, 2, 6, Arxx Therapeutics, 1, 2, Bayer, 5, Boehringer Ingelheim, 1, 2, 5, 6, Lilly, 6, Medscape, 2, 6, Merck Sharp & Dohme, 6, Roche, 6; **M. Kuwana**, Boehringer Ingelheim, 5, 6, One Pharmaceuticals, 5, 6, Chugai, 6, Janssen, 6, Astellas, 6, Tanabe Mitsubishi, 6, Pfizer, 6, Nippon Shinyaku, 6, Corbus, 2, Mochida, 2, Kissei, 2, MBL, 9; **C. Stock**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **S. Sambevski**, Boehringer Ingelheim, 3; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 1847

Severity of Gastroesophageal Reflux, but Not the Use of Proton Pump Inhibitors, Is Associated with Radiographic Progression of Interstitial Lung Disease in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Table 1. Severity of gastroesophageal reflux, but not PPI use, is associated with radiographic progression of fibrosis (QLF) in the whole lung in patients receiving treatment for SSc-ILD.

Covariate	Estimate	95% CI	P-value
Baseline QLF	-0.18	-0.30, -0.07	0.002
Treatment arm	-0.05	-1.67, 1.57	0.951
Baseline reflux score	2.19	0.69, 3.69	0.005
PPI use	-0.26	-2.33, 1.81	0.807

Table 2. Severity of gastroesophageal reflux, but not PPI use, is associated with radiographic progression of ILD (QILD) in the whole lung in patients receiving treatment for SSc-ILD.

Covariate	Estimate	95% CI	P-value
Baseline QILD	-0.23	-0.36, -0.09	0.001
Treatment arm	1.09	-2.45, 4.63	0.541
Baseline reflux score	3.45	0.18, 6.72	0.039
PPI use	0.53	-5.00, 3.95	0.815

Background/Purpose: Esophageal dysmotility is a common feature of systemic sclerosis (SSc) and aspiration of gastric contents may serve as an inciting and/or exacerbating factor in the pathogenesis of interstitial lung disease (ILD). The present study aimed to: (1) determine whether the severity of gastroesophageal reflux predicts progression of SSc-ILD and (2) evaluate whether proton pump inhibitors (PPI) moderate the relationship between reflux severity and ILD progression as defined both radiographically and physiologically.

Methods: The UCLA SCTC GIT 2.0 was used to assess the severity of reflux in participants of Scleroderma Lung Study (SLS) II (Tashkin et al. Lancet Resp Med 2016). SLS II compared 24 months of mycophenolate versus 12 months cyclophosphamide followed by 12 months of placebo in patients with active SSc-ILD. A multivariable linear regression analysis was used to evaluate the relationship between baseline reflux scores and change in quantitative extent of radiographic ILD (QILD) and fibrosis (QLF) in the whole lung at 24 months. A joint model was created to evaluate the relationship between baseline reflux scores and the course of the forced vital capacity (FVC)%-predicted

Table 3. Severity of gastroesophageal reflux is not associated with the course of the FVC%-predicted over 24 months in patients receiving treatment for SSc-ILD based on a joint model analysis.

Covariate	Estimate	95% CI	P-value
Baseline FVC	0.92	0.83, 1.02	<0.001
Time trend A (3-12 months)	0.28	0.17, 0.40	<0.001
Time trend B (12-21 months)	-0.13	-0.36, 0.11	0.295
Time trend C (21-24 months)	-0.41	-1.05, 0.16	0.168
Treatment arm	1.00	-1.09, 3.12	0.352
Baseline reflux score	-0.34	-2.08, 1.40	0.720
PPI use	0.56	-1.79, 2.91	0.625
Time trend A x Treatment arm	-0.10	-0.26, 0.06	0.231
Time trend B x Treatment arm	-0.01	-0.36, 0.32	0.991
Time trend C x Treatment arm	0.22	-0.63, 1.07	0.595

measured every 3 months over 24 months. All models controlled for treatment arm and baseline ILD severity, and tested whether PPI use was associated with ILD progression.

Results: 141 of the 142 SLS II participants had reflux scores at baseline and the mean score was 0.57, indicating moderate severity. There were no significant correlations between baseline reflux score and FVC%-predicted, QLF, QILD, disease duration, skin score, gender or the presence of diffuse cutaneous disease. Among participants with follow up HRCT scans (N=96), increased severity of reflux was significantly associated with increased QLF (Table 1) and QILD (Table 2) scores at 24 months. However, increased severity of reflux was not significantly associated with the course of the FVC%-predicted (N=130; Table 3). 112 (78.9%) of SLS II participants were taking a PPI at baseline; PPI users had higher reflux scores than non-users (P= < 0.0001). PPI use was not significantly associated with progression of ILD in any of the models.

Conclusion: Among patients receiving treatment for SSc-ILD, increased severity of gastroesophageal reflux symptoms was associated with ILD progression, based on worsening extent of radiographic fibrosis and total ILD, but not with the course of the FVC. PPI use was not associated with progression of ILD, suggesting that aspiration of non-acid gastric contents may play a role in perpetuating inflammation and fibrosis in SSc-ILD. Future studies are needed to assess whether other reflux treatments (e.g., pro-motility agents) moderate the relationship between reflux severity and ILD progression in SSc.

Disclosure: E. Volkmann, Boehringer Ingelheim, 2, 6, Corbus, 5, Forbius, 5, Kadmon, 5; **D. Tashkin**, None; **M. Leng**, None; **G. Kim**, None; **J. Goldin**, None; **M. Roth**, Genentech/Roche, 5.

Abstract Number: 1848

Untangling the Gut: A Phenome-Wide Association Study of Drugs and Diseases with Gastrointestinal Dysfunction in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Gastrointestinal dysfunction (SSc-GI) is a significant burden to patients with systemic sclerosis (SSc), particularly in those with longstanding disease. The management of SSc-GI is often challenging. Whilst hallmark mechanisms including vasculopathy, fibrosis, and inflammation underlie gut pathogenesis, reflected in autoantibody (ANA) associations, off-target effects of drugs used in SSc may contribute to GI dysfunction. We sought to discover and confirm associations with SSc-GI dysfunction in a Phenome-Wide Association Study (PheWAS).

Methods: Archived clinic letters (12,535 letters) of 2,058 consented patients at the Royal Free Hospital (UK) between 2002-2021 were parsed into a database. Patients with at least three letters were included. Two 'dictionaries', one of diagnoses (Disease Ontology project *CC0*, modified to included ANA) and another of drugs (DrugBank Open Data *CC0*) were used to label each patient. Using the PheWAS approach for six SSc-GI outcomes (constipation, diarrhoea,

Table 1. Study Cohort

PheWAS cohort	n	1546
Female	%	84
Limited	%	67
Disease onset (year)	range	1959 - 2019
ACA	%	26
ATA	%	24
ARA	%	11
PM-Scl	%	4.6
U1RNP	%	5.8
U3RNP	%	3.9
ThT0	%	0.5
Validation cohort (UCLA GIT 2.0)	n	516

dysmotility, incontinence, reflux, small intestinal bacterial overgrowth [SIBO]), we assessed every diagnosis and drug in univariate logistic regressions. P values were adjusted for false discovery rate (Benjamini-Hochberg). Significant PheWAS predictors ($p < 0.05$) were validated against the UCLA GIT 2.0 questionnaire score (UCLA GIT) in a second dataset of 516 patients including total GI, reflux, bloating, diarrhoea, soilage, constipation, social, and emotional scores.

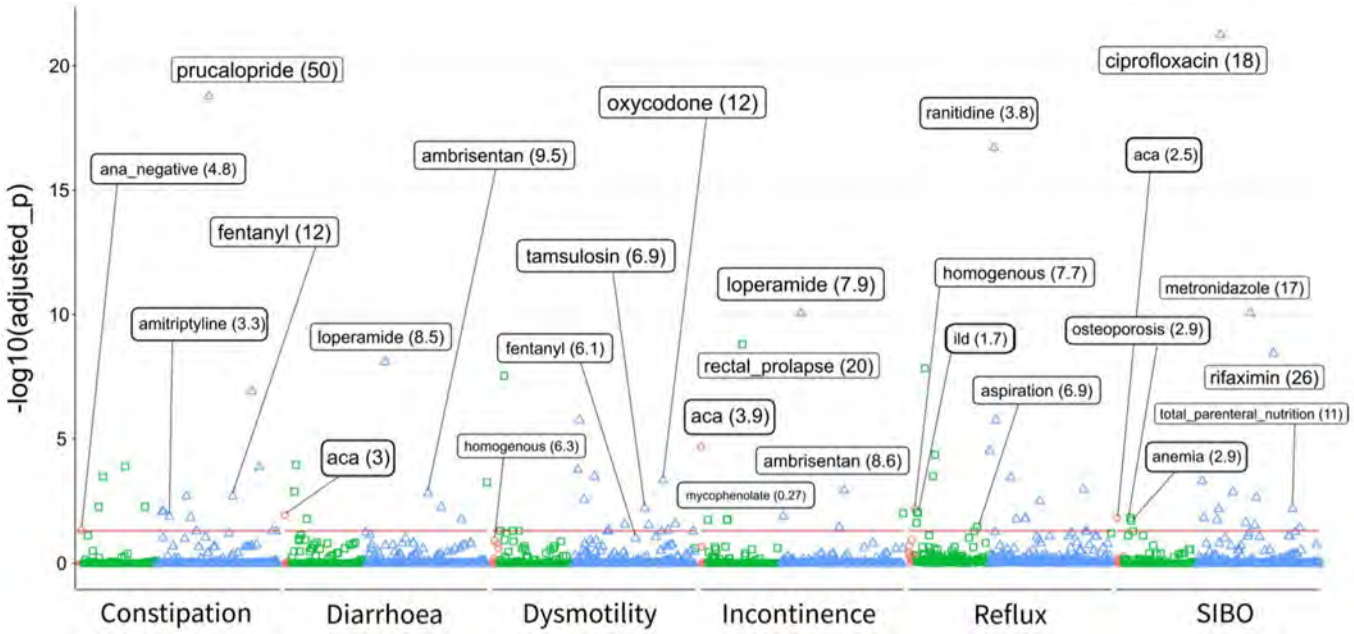

Figure 1. PheWAS analysis demonstrated significant associations between ANAs (red circles), diagnoses (green squares), and drugs (blue triangles) in six key SSc-GI areas. The red horizontal line indicates adjusted p values < 0.05. Key associations with named variables are presented; odds ratios in brackets.

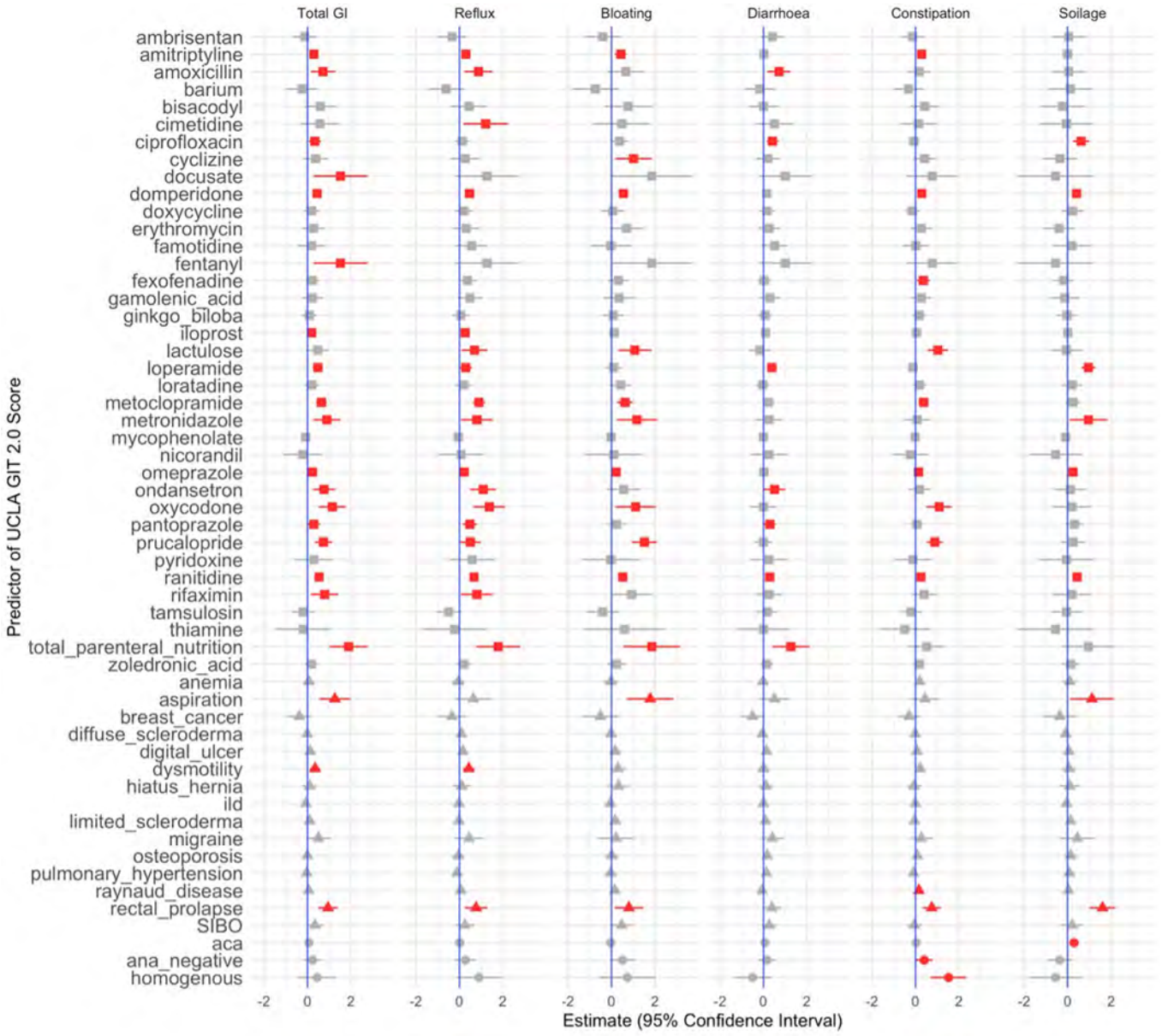

Figure 2. PheWAS hits were validated in a linear model against UCLA GIT 2.0 domain scores: total GI, reflux, bloating, diarrhoea, constipation, and soilage domains are shown. Estimates with 95% CIs are presented; red highlights $p < 0.05$. Square – drugs; triangle – diagnoses; circle – ANA.

Results: Table 1 presents cohort demographics. Using the diagnosis and drug dictionaries, we identified 673 diagnoses (including ANAs) and 634 drugs. Top drugs (prevalence): omeprazole 56%, losartan 49%, lansoprazole 42%, and mycophenolate mofetil (MMF) 40%; top diagnoses: limited SSc 65%, Raynaud's 50%, interstitial lung disease (ILD) 36%, and overlap 27%.

PheWAS analysis demonstrated significant associations across the six key SSc-GI outcomes (Fig. 1). Constipation was linked to fentanyl (OR = 12), amitriptyline (OR = 3.3), migraine (OR = 14), ANA negative (OR = 4.8), aspiration (OR = 15), and incontinence (OR = 5.3). Diarrhoea was linked to ambrisentan (OR = 9.5) and ACA (OR = 3). Dysmotility was linked to ANA homogenous (OR = 6.3), tamsulosin (OR = 6.9), fentanyl (OR = 6.1), and oxycodone (OR = 12). Incontinence was linked to ACA (OR = 3.9), ambrisentan (OR = 8.6), and inversely linked to MMF (OR = 0.27). Reflux was linked to ILD (OR = 1.7) and ANA homogenous (OR = 7.7). SIBO was linked to ACA (OR = 2.5), total parenteral nutrition (OR = 11), osteoporosis (OR = 2.9), and anemia (OR = 2.9).

Significant PheWAS associations were validated against UCLA GIT domain scores (Fig. 2). For the total GI score – 18 drugs and 3 diagnoses were validated; soilage – 6 drugs, 1 ANA, and 2 diagnoses; reflux – 17 drugs and 2 diagnoses; bloating – 11 drugs and 2 diagnoses; diarrhoea – 7 drugs; social – 19 drugs and 3 diagnoses; emotional – 17 drugs and 5 diagnoses; constipation – 2 ANA, 9 drugs, and 2 diagnoses.

Conclusion: Using a hypothesis-free PheWAS approach, we revealed potential contributors to SSc-GI dysfunction, including drugs such as opioids, anti-muscarinics, and endothelin receptor antagonists; and ANAs including ACA, ANA-homogenous and ANA-negative subtypes.

Disclosure: R. Maclean, None; **F. Ahmed**, None; **V. Ong**, None; **C. Murray**, Janssen, 6, Abbvie, 6, Biogen, 6, Takeda, 6, Tillotts, 6; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2.

Abstract Number: 1849

False Positive Anti-Topoisomerase I (Scl-70) Antibody Results: A Case Series from a Scleroderma Referral Center

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Background/Purpose: Systemic sclerosis (SSc) is a progressive autoimmune disease with high morbidity and mortality, making early diagnosis and management critical. Anti-Topoisomerase I antibody (anti-Topo I, also known as Scl-70) has important diagnostic and prognostic roles in SSc. Although positivity for anti-Topo I antibody is considered highly specific for SSc, the testing methods typically utilized in commercial laboratories have lower specificity than the immunodiffusion method. To highlight potential harms of a false-positive anti-Topo I antibody result, we describe a series of cases in which patients who tested positive for anti-Topo I antibody in a commercial laboratory were found to be negative for anti-Topo I antibody by the immunodiffusion method.

Methods: Patients seen in our clinic who had previously tested positive for anti-Topo I antibody performed by a commercial laboratory, but who lacked sufficient clinical criteria to be classified as SSc, were invited to undergo testing for anti-Topo I antibody by immunodiffusion in our research laboratory. Each patient's clinical features, commercial anti-Topo I antibody results, additional diagnostic testing, and clinical diagnosis at initial and follow up visits were recorded.

Results: Over a six-year period, 19 patients who fulfilled the above criteria underwent testing for anti-Topo I antibody by immunodiffusion (Table 1). 16 (84.2%) were found to be negative. 11 of the 19 patients (57.9%) had at least one follow up visit, typically 6-12 months after initial visit. Of those 11 patients with at least one follow up visit, all three patients who tested positive for anti-Topo I antibody by immunodiffusion, but none of the eight patients who tested

Table 1. Demographics, clinical features, and diagnostic testing

	Negative for anti-Topo I antibody by immunodiffusion (n = 16)	Positive for anti-Topo I antibody by immunodiffusion (n = 3)
Age in years, mean (SD)	44 (11.2)	40 (2)
Female, n (%)	16 (100)	2 (66.7)
History of Raynaud's prior to baseline visit, n (%)	5 (31.3)	2 (66.7)
Points in 2013 ACR/EULAR systemic sclerosis classification criteria at initial visit, median (min, max) *	2.5 (0, 7)	5 (4, 8)
Positive ANA by indirect immunofluorescence, n (%)^	10/14 (71.4)	3 (100)
Underwent chest CT, n (%)	7 (43.8)	2 (66.7)
Classifiable SSc at follow up visit, n (%)#	0/8 (0)	3 (100)

*Not including anti-Topo I antibody result from commercial laboratory

^of those tested by indirect immunofluorescence in a commercial laboratory

#of those who had at least one follow up visit

negative, developed sufficient criteria to be classified as SSc on follow up. One of the patients with a false-positive anti-Topo I antibody result was diagnosed with morphea, one with Sjogren's syndrome, one with antiphospholipid antibody syndrome, and two with undifferentiated connective tissue disease. The other 11 patients with false-positive anti-Topo I antibody results (68.8%) did not have a rheumatologic condition in the judgement of the treating physician. 7 of the 16 patients with false-positive anti-Topo I antibody (43.8%) had undergone chest CTs to screen for interstitial lung disease, one had been started on treatment with Mycophenolate Mofetil, and one had undergone pre-evaluation for autologous hematopoietic stem cell transplantation.

Conclusion: Our findings highlight the propensity of commercial laboratories to produce false-positive anti-Topo I antibody results. In the cases reported here, unnecessary referrals to a scleroderma specialty clinic, and in some cases unnecessary chest CTs, occurred after patients tested falsely positive for anti-Topo I antibody, demonstrating some of the potential negative impacts on patients and the healthcare system. While a thorough history and physical exam remain the mainstays of SSc evaluation, testing for anti-Topo I antibody using a more specific method such as immunodiffusion would likely help physicians and patients to avoid misdiagnoses, unnecessary referrals and diagnostic testing, and potentially risky treatments.

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Abstract Number: 1850

Continued Treatment with Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Two-Year Data from SENSCIS-ON

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SESSION INFORMATION

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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

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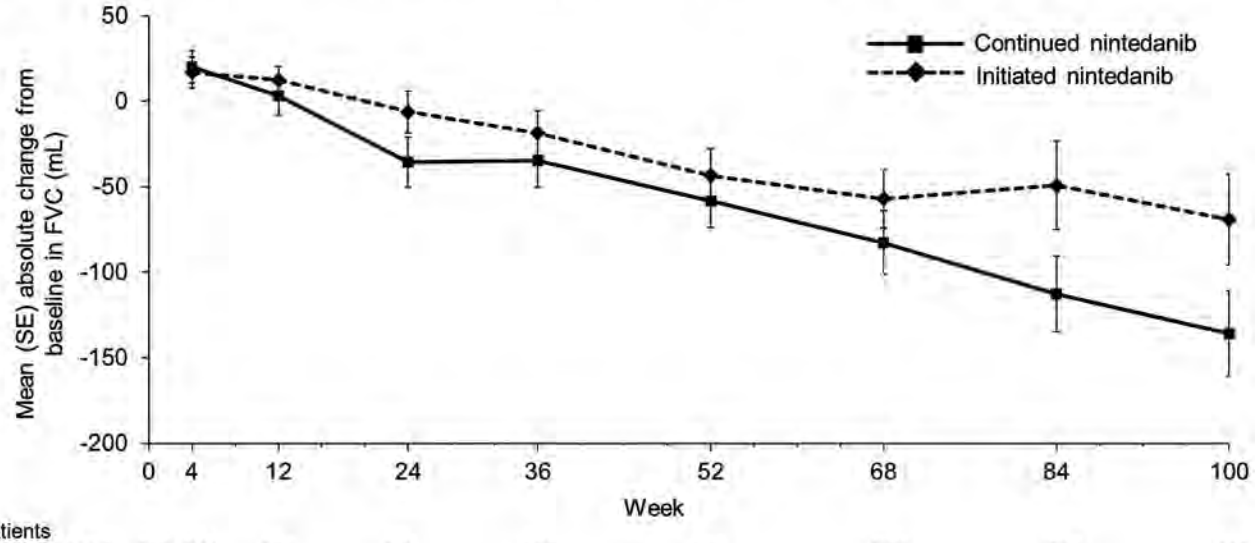
Session Time: 8:30AM–10:30AM

Background/Purpose: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo, with adverse events that were manageable for most patients. The safety and efficacy of nintedanib over the longer term are being assessed in the open-label extension trial, SENSCIS-ON.

Figure. Change from baseline in FVC (mL) over 100 weeks in SENSCIS-ON



No. of patients									
Continued nintedanib	191	189	187	185	181	176	139	107	111
Initiated nintedanib	243	238	230	215	197	180	143	81	99

At week 84, 12.7% and 12.6% of patients in the continued and initiated nintedanib groups, respectively, completed a phone visit rather than a clinic visit, and so did not provide an FVC measurement; at week 100, 4.6% and 3.6% of patients in these groups, respectively, completed a phone visit.

Table. Adverse events reported over 100 weeks in SENSCIS-ON

	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Any adverse event(s)	193 (98.0)	245 (99.2)
Most frequent adverse events*		
Diarrhea	147 (74.6)	179 (72.5)
Nausea	37 (18.8)	68 (27.5)
Skin ulcer	45 (22.8)	48 (19.4)
Vomiting	35 (17.8)	56 (22.7)
Nasopharyngitis	29 (14.7)	38 (15.4)
Upper respiratory tract infection	36 (18.3)	29 (11.7)
Cough	34 (17.3)	27 (10.9)
Arthralgia	24 (12.2)	28 (11.3)
Weight decreased	19 (9.6)	30 (12.1)
Abdominal pain	9 (4.6)	36 (14.6)
Alanine aminotransferase increased	10 (5.1)	34 (13.8)
Aspartate aminotransferase increased	9 (4.6)	32 (13.0)
Liver test abnormalities†	26 (13.2)	56 (22.7)
Serious adverse event(s)‡	62 (31.5)	77 (31.2)
Adverse event(s) leading to treatment discontinuation	19 (9.6)	65 (26.3)

Data are n (%) of patients with ≥1 such event reported over 100 weeks (or until 7 days after last trial drug intake for patients who discontinued trial drug before week 100). *Events reported in >12% of patients in either group, coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). †Based on the standardized MedDRA query "liver related investigations, signs and symptoms" (broad definition). ‡Adverse events that resulted in death, were life-threatening, resulted in hospitalization or prolongation of hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

Methods: In the SENSCIS trial, patients were randomized to receive nintedanib or placebo until the last patient reached week 52 but for ≤100 weeks. Patients with SSc-ILD who completed the SENSCIS trial or a drug–drug interaction (DDI) study of nintedanib and oral contraceptive (NCT03675581) were eligible to enter SENSCIS-ON. In descriptive analyses, we analyzed changes from baseline in FVC (mL) and adverse events over 100 weeks in patients who received nintedanib in SENSCIS and continued nintedanib in SENSCIS-ON (the "continued nintedanib" group) and in patients who received placebo in SENSCIS and initiated nintedanib in SENSCIS-ON or who received nintedanib for ≤28 days in the DDI study (the "initiated nintedanib" group). Analyses were based on observed FVC data available at the respective time-point.

Results: The continued nintedanib group comprised 197 patients and the initiated nintedanib group comprised 247 patients (231 from SENSCIS; 16 from the DDI study). In these groups, respectively, mean (SD) FVC at inclusion in SENSCIS-ON was 2379 (754) mL and 70.4 (18.1) % predicted and 2443 (814) mL and 70.8 (17.9) % predicted. In total, 148 (75.1%) and 145 (58.7%) patients in the continued nintedanib and initiated nintedanib groups, respectively, were receiving nintedanib at week 100 of SENSCIS-ON. Mean (SE) changes in FVC from baseline to week 100

of SENSCIS-ON were –135.7 (24.7) mL in patients who continued nintedanib in SENSCIS-ON, –69.2 (26.5) mL in patients who initiated nintedanib in SENSCIS-ON, and –104.3 (18.2) mL in all patients in SENSCIS-ON (Figure), similar to the change from baseline to week 100 in nintedanib-treated patients in the SENSCIS trial (–100.0 [36.7] mL) and lower than the change from baseline to week 100 in the placebo group of the SENSCIS trial (–164.4 [38.4] mL). Diarrhea was the most frequent adverse event (Table). Over 100 weeks, liver test abnormalities were reported in 26 patients (13.2%) in the continued nintedanib group and 56 patients (22.7%) in the initiated nintedanib group. Adverse events led to discontinuation of nintedanib in 19 (9.6%) patients in the continued nintedanib group and 65 (26.3%) patients in the initiated nintedanib group.

Conclusion: The safety profile of nintedanib over 100 weeks in SENSCIS-ON was consistent with that reported in the SENSCIS trial. The decline in FVC over 100 weeks in patients treated with nintedanib in SENSCIS-ON was consistent with the decline in FVC in patients treated with nintedanib over 100 weeks in the SENSCIS trial. These findings support a clinically meaningful benefit of nintedanib in slowing the progression of SSc-ILD.

Disclosure: Y. Allanore, Bayer, 2, Boehringer Ingelheim, 2, 12, Clinical trial investigator, Roche, 2, Chemomab, 2, Curzion, 2, Sanofi, 2, 12, Clinical trial investigator; **M. Vonk**, None; **O. Distler**, AbbVie, 12, Project scoring fee for Rheumatology Grant, Amgen, 2, Eli Lilly, 2, Pfizer Inc, 2; **A. Azuma**, Boehringer Ingelheim, 1, Pfizer, 12, Data Safety Monitoring Board, Sanofi, 1, Shino-Test, 1, Taiho Pharmaceutical Co, Ltd, 1, Toray, 1; **M. Mayes**, Actelion Pharma, 1, Mitsubishi-Tanabe, 1, Corbus Pharma, 5, Boehringer-Ingelheim, 1, 5, Eicos, 1, 5, Galapagos Pharma, 1, 5; **M. Gahlemann**, Boehringer Ingelheim, 3; **A. James**, Boehringer Ingelheim, 3; **V. Kohlbrenner**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **D. Khanna**, AbbVie, 2, Acceleron, 2, Actelion, 2, Amgen, 2, Bayer, 2, 5, Boehringer Ingelheim, 2, Bristol-Myers Squibb, 5, CiviBioPharma/Eicos Sciences, Inc, 12, Leadership/Equity position (Chief Medical Officer), Corbus, 2, CSL Behring, 2, Eicos Sciences, Inc, 11, Galapagos NV, 2, Genentech/Roche, 2, Gilead, 2, GlaxoSmithKline, 2, Horizon Therapeutics, 2, 5, Immune Tolerance Network, 5, Merck Sharp & Dohme, 2, Mitsubishi Tanabe Pharma, 2, National Institutes of Health, 5, Pfizer, 5, Sanofi-Aventis, 2, United Therapeutics, 2, Prometheus, 2, Theraly, 2, AstraZeneca, 2; **K. Highland**, Boehringer Ingelheim, 2, 5, 6.

Abstract Number: 1851

Early Intervention with Immunomodulators Leads to Better Outcomes in Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a complex disease characterized by microvascular abnormalities, immune dysregulation and chronic inflammation, and subsequent excessive fibrosis of the skin and internal organs. This leads to irreversible tissue remodeling and organ damage, resulting in increased morbidity and mortality. Recent accumulating evidence has shown that therapeutic disease modification is possible in SSc patients using immunomodulators. In rheumatoid arthritis, it has been shown that early disease is more susceptible to treatment, but we still don't know whether therapeutic "window of opportunity" exists in SSc patients.

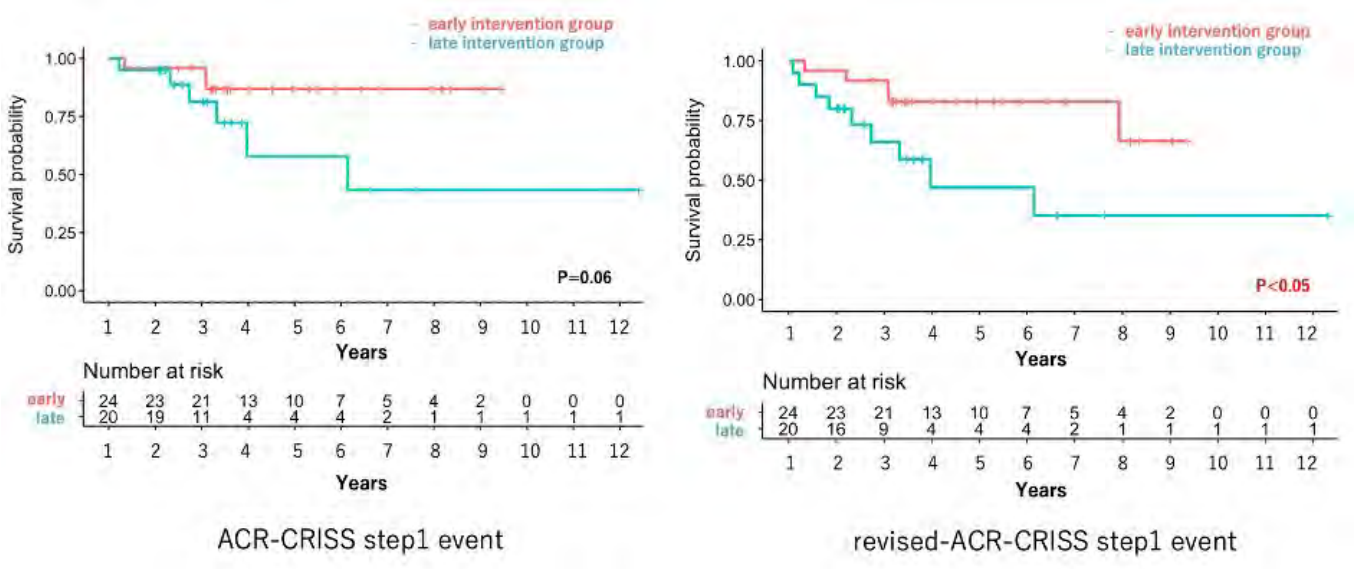


Figure 1. Time to clinical worsening defined by original and revised ACR-CRISS step 1 event.

Methods: This was a single-center, retrospective study enrolling SSc patients who received disease-modifying therapy for diffuse cutaneous SSc (dcSSc) or interstitial lung disease (ILD). Eligible patients were selected from our SSc database, and included those who i) fulfilled the 2013 ACR/EULAR classification criteria for SSc; ii) received treatment with cyclophosphamide, mycophenolate mofetil or tocilizumab for dcSSc or ILD within 6 years after onset of non-Raynaud's symptoms; and iii) had been on treatment for least one year. The patients were divided into early and late intervention groups based on the disease duration of ≤18 months or >18 months at treatment introduction. We evaluated changes of modified Rodnan total skin score (mRSS) and percent predicted forced vital capacity (ppFVC) from baseline to one year. Patients experiencing decrease of mRSS by ≥ 5 or relative increase of ppFVC by ≥10% were regarded as improvers. Clinical worsening was defined as development of at least one original or revised ACR-

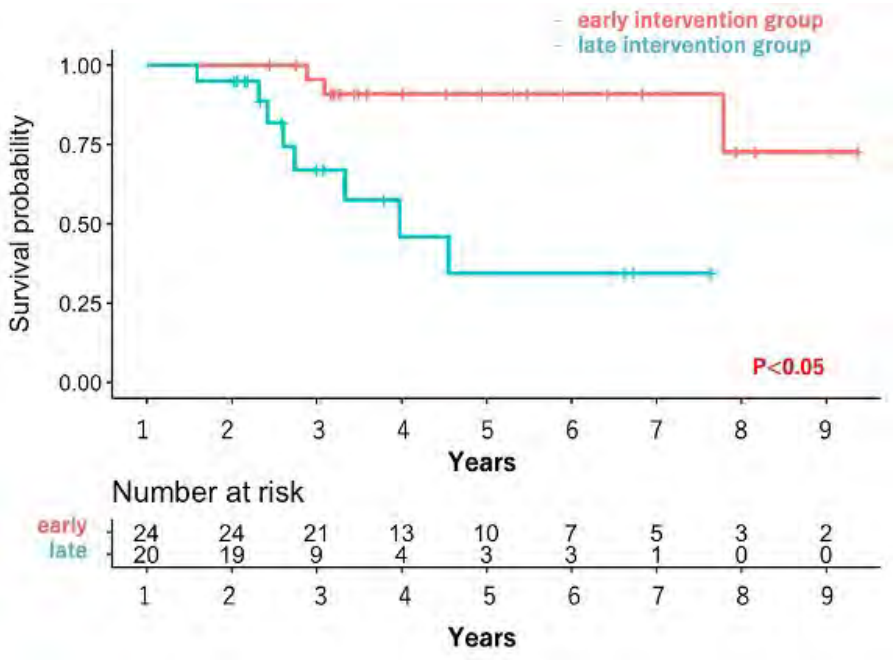


Figure 2. Time to clinical worsening defined by PF-ILD.

CRISS step 1 event or progressive fibrosing ILD (PF-ILD). Cumulative rates for clinical worsening were assessed using Kaplan-Meier analysis, and were compared between the groups with log-rank test.

Results: We enrolled 44 patients, including 24 in the early intervention group and 20 in the late intervention group. Disease duration at treatment introduction was 8.6 ± 4.2 and 34.3 ± 20.3 months in early and late intervention groups, respectively. Baseline characteristics were principally similar between the groups except ppFVC, which was significantly better in the early than late intervention group (93.2 ± 13.8 versus 80.4 ± 18.2; $P < 0.05$). There was no significant difference in changes of mRSS or ppFVC over one year between the two groups, but improvers tended to be more common in the early versus late intervention groups (37.5% versus 22.2% for mRSS, and 47.6% versus 16.7% for ppFVC). The Kaplan-Meier analysis revealed that the original and revised ACR-CRISS step 1 event tended to occur less frequently in the early than the late intervention group ($P = 0.06$ and $P < 0.05$, respectively; Figure 1). In addition, patients received early intervention developed PF-ILD less frequently, compared with those received late intervention ($P < 0.05$; Figure 2).

Conclusion: Our findings suggest that early intervention with immunomodulators in patients with dcSSc and/or SSc-ILD prevents clinical worsening, although further prospective study involving a larger number of patients is necessary to confirm the "window of opportunity" theory in the treatment of SSc.

Disclosure: K. Yomono, None; **M. Kuwana**, Boehringer Ingelheim, 5, 6, One Pharmaceuticals, 5, 6, Chugai, 6, Janssen, 6, Astellas, 6, Tanabe Mitsubishi, 6, Pfizer, 6, Nippon Shinyaku, 6, Corbus, 2, Mochida, 2, Kissei, 2, MBL, 9.

Abstract Number: 1852

Healthcare Utilization and Economic Burden in Systemic Sclerosis

Leonardo Martin Calderon[1], Mitali Chaudhary[1] and Janet Pope[2], [1]Western University, London, ON, Canada, [2]University of Western Ontario, London, ON, Canada

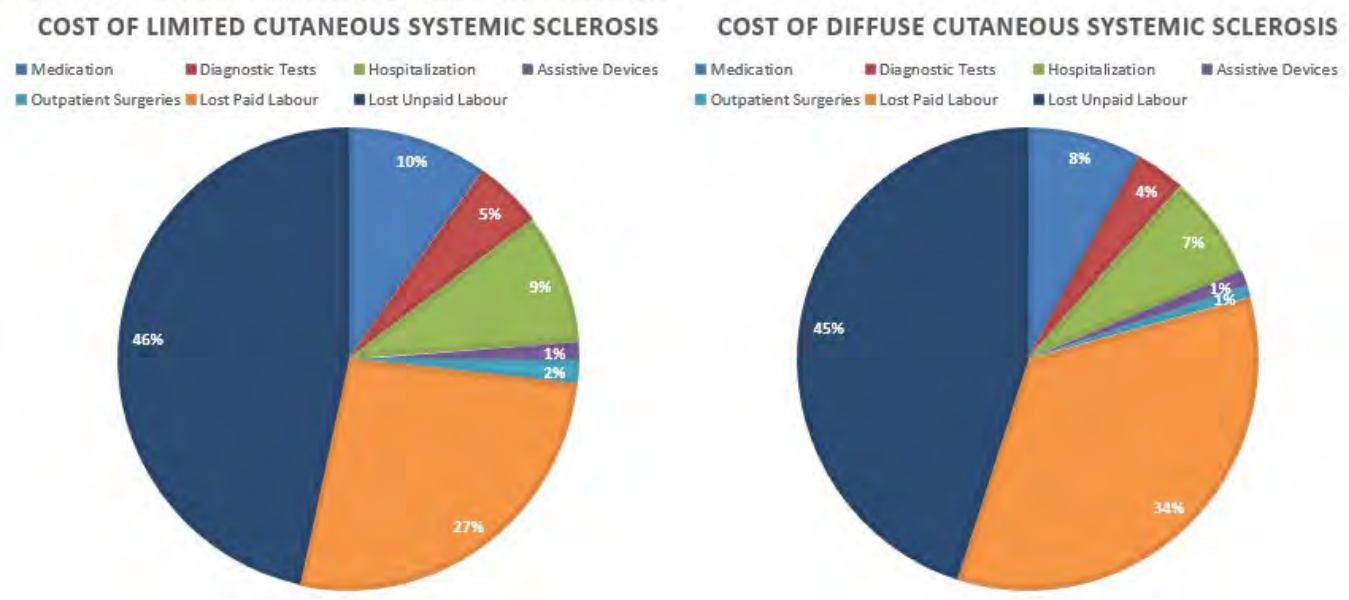
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic Sclerosis (SSc) is a multi-system autoimmune disease, characterized by vasculopathy, fibrosis of the skin and internal organs, and autoimmunity with distinct antibodies. SSc associated complications include interstitial lung disease, pulmonary hypertension, and digital ulcers which lead to substantial morbidity and

Table 1. Overall Systemic Sclerosis Cost by Region

Region	Total cost	Direct cost	Indirect cost	Medication cost	Hospitalization cost
Canada (2)	$10,673-$18,453	$5,038	$13,415	$1,575	$1,448
USA (8)	$14,959-$23,268	$4,694-$16,269	$5,170-$10,228	$1,017-$5,746	$2,092-$6,502
Europe (5)	€4,607-€30,797	€1,215-€17,301	€10,526	€145-€4,258	€788-€7,951
Oceania (5)	$7,060-$11,607	-	-	$1,126-$3,617	$3,228-$4,730
Asia (1)	$1,005-1,440	-	-	$1,046-$1,143	-
South America (1)	-	-	-	-	R$14,180 (CAD $3,191)

Figure 1. Distribution of Annual Cost of Systemic Sclerosis Sub-types



disability for patients. Secondary to medical and functional limitations, patients with SSc may require considerable healthcare resources resulting in significant economic impact. The purpose of this systematic review is to provide a narrative summary of the economic impact and healthcare resource utilization associated with SSc.

Methods: MEDLINE and EMBASE were searched without language restriction from inception to January 20th, 2021. Studies were included if they provided information regarding overall SSc total, direct, and indirect medical costs including medication, diagnostic test, and assistive devices costs. The cost of SSc subtypes and associated complications was additionally collected. Included observational studies had risk of bias assessments through the Joanna Briggs Institute cross-sectional and case series checklists, and the Newcastle-Ottawa Cohort and Case-Control study scales.

Results: The search retrieved 1777 studies, of which 35 were included representing 20 cross-sectional, 11 cohort, and 4 case-control studies. Studies used various methods of calculating cost including prevalence-based cost-of-illness approach, bottom-up cost analysis, humanistic approach, and health resource units cost analysis. Overall SSc total annual medical cost ranged from USD $14,959-$23,268 in USA, CAD$10,673-$18,453 in Canada, €4,607-€30,797 in Europe, and AUD $7,060 to $11,607 in Oceania. Annual cost for SSc associated with interstitial lung disease and pulmonary arterial hypertension was USD $31,285-$55,446 and $44,454-$63,320, respectively.

Conclusion: Globally, SSc represents significant patient and systemic economic burden. SSc complications are associated with higher economic burden and are highly variable depending on geographical location and medical access. Governmental policies should emphasize prevention of SSc complications as a strategy to mitigate overall cost.

Disclosure: L. Martin Calderon, None; **M. Chaudhary**, None; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2.

Abstract Number: 1853

Scleroderma Presentation in the Canadian Scleroderma Research Group Indigenous Population

Curtis Sobchak, Karen Beattie and Maggie Larche, McMaster University, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Given the well-known burden of rheumatic disease in Canadian Indigenous populations, the Canadian Rheumatology Association (CRA) has highlighted Aboriginal Rheumatology as an area needing greater understanding, specifically on issues such as delays in care and access to specialists. Indigenous patients with rheumatoid arthritis (RA) often have worse disease than the general population yet are less likely to see specialized care. Indigenous populations appear to have earlier onset systemic sclerosis (SSc) than the general population. However, it is unclear if they experience delayed diagnosis (symptom onset to disease diagnosis), or more/less healthcare utilization during this time. We analyzed data from the Canadian Scleroderma Research Group (CSRG) registry to compare the length of time from symptom onset to disease diagnosis and healthcare utilization between North American Indigenous (NAI) and non-NAI populations. We also determined if these data were impacted by a person's rural or urban location.

Methods: Data was obtained from the CSRG, a national longitudinal registry of patients >18 years old with SSc. All patients were included irrespective of underlying comorbidities. Patients who self-identified as Métis, Inuit and First Nations were included as NAI. We characterized the study population at entry into the registry (sex, tobacco use, income, education, location comorbidities). Location was deemed urban or rural by Canada Post guidelines. Time from first symptom to SSc diagnosis was compared between those who were and were non-NAI. Healthcare utilization related to SSc presentation (visits to health practitioners including family doctors and rheumatologists, tests done, and hospitalizations) was compared between groups.

Results: Of 1561 patients, 79 self-identified as NAI. Age, gender and comorbidities were similar between the two groups, with NAI having a higher proportion of tobacco use and lower level of education and income (Table 1). Only

Table 1. Baseline demographics

Variable	NAI (n = 79)	Non-NAI (n=1482)
Age – mean (SD)	51.2 (11.9)	55.6 (12.2)
Female sex – no. (%)	68 (86.1)	1245 (86.4)
Education high school or greater – no. (%)	47 (59.4)	1108 (74.7)
Income $80,000 or greater – no. (%)	6 (7.5)	366 (24.7)
Current tobacco Use – no. (%)	21 (26.6)	187 (12.7)
Rural location – no. (%)	41 (51.9)	291 (19.6)
Diabetes Mellitus – no. (%)	8 (10.3)	86 (5.8)
Chronic Obstructive Pulmonary Disease – no. (%)	7 (8.9)	136 (9.2)
Rheumatoid Arthritis – no. (%)	22 (27.8)	255 (17.2)

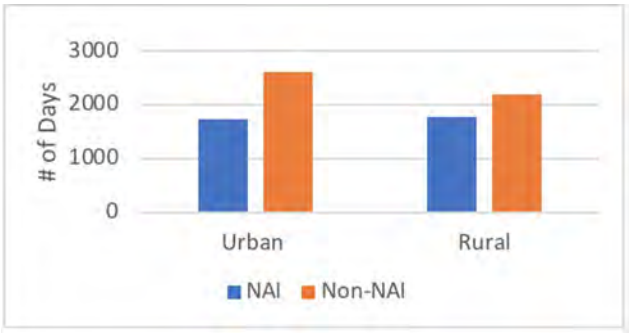


Figure 2. Number of Days from Raynaud's to systemic scleroderma diagnosis.

19.6% of non-NAI populations lived rurally compared to 51.9% of NAI patients. There was no significant difference in time from Raynaud's to diagnosis or 1st other symptom to diagnosis between NAI and non-NAI populations, regardless of location (Figure 2 and 3). There was also no difference in health care utilization, including visits to healthcare professionals, tests performed and hospitalizations.

Conclusion: This study suggests that, unlike other rheumatological conditions, SSc appears to be appropriately diagnosed without a time delay in those who are NAI compared to non-NAI patients. NAI SSc patients also access care at the same rate as non-NAI populations prior to SSc diagnosis.

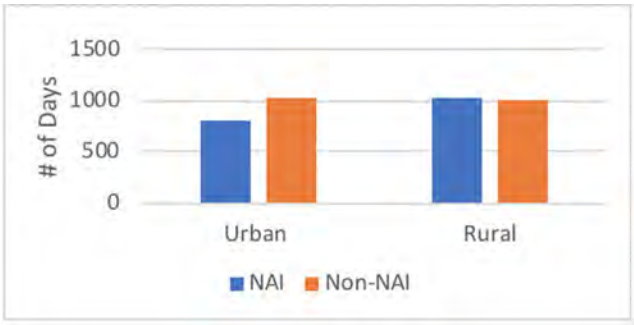


Figure 3. Number of Days from 1st other symptom to systemic scleroderma diagnosis.

Disclosure: C. Sobchak, None; **K. Beattie**, None; **M. Larche**, Adiga Life Science Inc, 10.

Abstract Number: 1854

Disease Characteristics and Social Determinants in African Americans with Systemic Sclerosis: A Single Center Experience

Sarah Compton, DeAnna Baker Frost, Richard Silver and Diane Kamen, Medical University of South Carolina, Charleston, SC

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disease categorized on the basis of skin involvement as either limited or diffuse cutaneous SSc, the latter of which manifests in more severe skin and internal organ involvement. SSc disproportionately affects women and, similar to other chronic diseases, health disparities have been noted in SSc with African American (AA) patients experiencing poor outcomes more frequently than patients from other ethnic/racial groups. We utilized a longitudinal cohort of well-characterized SSc patients to compare disease characteristics between AAs and non-AAs and look at gender and social determinants of health.

Methods: Data were collected as part of an ongoing IRB-approved longitudinal registry of SSc patients, including demographics, clinical disease manifestations and medical history. Patients were seen over a 16-year period at a single academic center. Retrospective chart review was performed to confirm age of onset, SSc disease type, and selected criteria for SSc to assess severity of disease. Pearson's chi-squared and Fisher's Exact testing for categorical measures, two-sample t-tests for continuous measures, and univariate logistic regression modeling was used.

Results: A total of 372 patients with SSc (79.6% female, 37.9% AA) were identified. AA patients developed SSc at a significantly younger age compared to the non-AA patient subset (41.8±14.3 yrs., 48.9±13.5yrs., respectively, p< 0.0001). Females developed SSc at a younger age than males (45.4±13.9 yrs., 50.2±11.3 yrs, p< 0.01) as shown in Figure 1. Comparing outcomes for diffuse cutaneous SSc, renal crisis, interstitial lung disease and restrictive lung disease were statistically significant in Figure 2A. Comparing AA to non-AA, there was statistically significant risk of all outcomes except renal crisis as shown in Figure 2B. Outcomes in AA versus non-AA and controlling for disease duration, mortality (p< 0.05), diffuse disease (p< 0.0001), pulmonary hypertension (p=0.01), and interstitial lung dis-

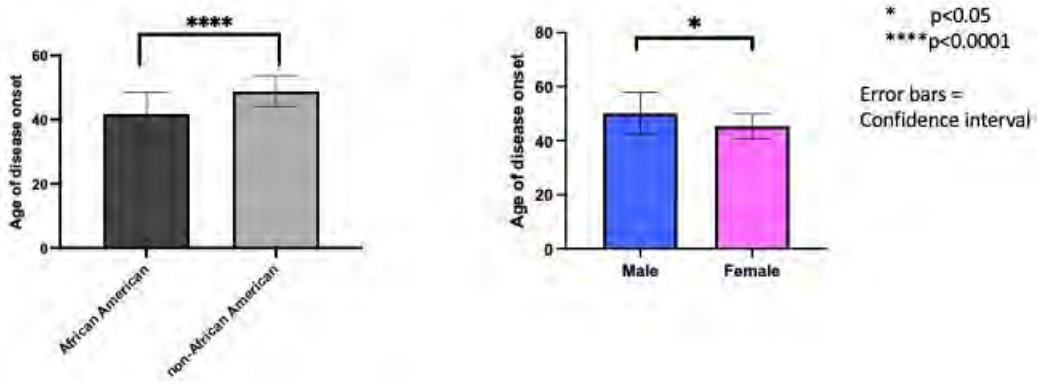


Figure 1. Age of SSc Disease Onset.

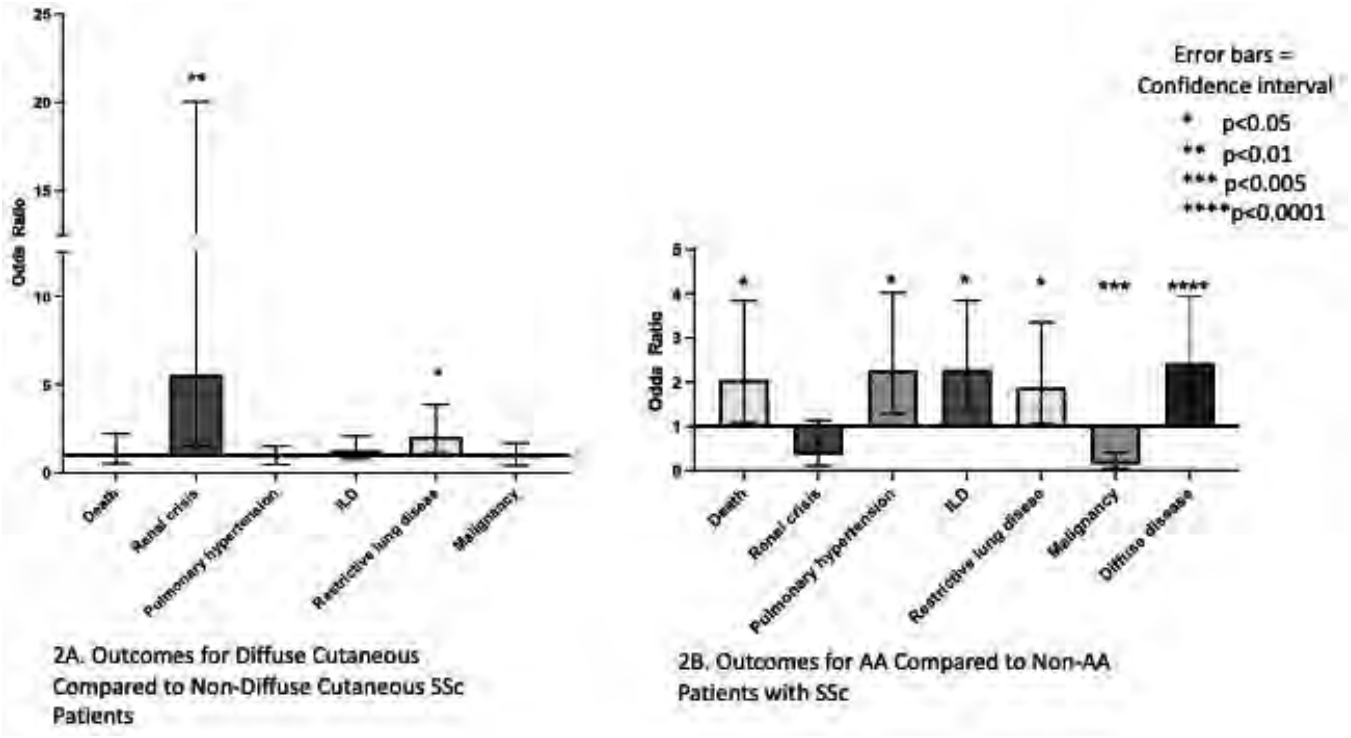


Figure 2. Outcomes.

ease (p=0.01) still remained statistically significant. We looked at two social determinants private insurance and high school graduate with no statistical difference in gender but a statistical significance in race (Table 1). 43.75% of AA had private insurance compared to 66.83% of non-AA (p< 0.0001). 96.39% of non-AA graduated high school compared to 89.72% of AA (p< 0.05). We found males had statistically significant higher percentages of diffuse disease (73.21%), dysphagia (24.59%), and restrictive lung disease (55.81%) compared to females.

Conclusion: We found that AA SSc patients were younger at disease onset and more likely to have diffuse cutaneous disease, compared to non-AA SSc patients. AAs compared to non-AAs with SSc had higher mortality and multiple poor prognostic features, with the exception of renal crisis which was more frequent among non-AAs. Two determinants, private insurance and high school graduate, may be associated with these outcomes. These data support the conclusion that AA have more severe disease with a more unfavorable SSc prognosis. Further investigation into the multifactorial causes for this disparity is needed in order to identify strategies to reduce them.

Table 1. Social Determinants

	Race/Sex	*Percentage*	*p-value*
Private insurance	African American	43.75	p<0.0001
	Non-African American	66.83	
	Female	58.08	ns
	Male	61.11	
High school graduate	African American	89.72	p<0.05
	Non-African American	96.39	
	Female	94.35	ns
	Male	92.45	

Disclosure: S. Compton, None; **D. Baker Frost**, boehringer ingelheim, 1, Atheneum Partners, 2; **R. Silver**, None; **D. Kamen**, None.

Abstract Number: 1855

Up-regulation of TNFα Gene in Peripheral Blood Is Useful for Predicting the Development of Exercise-induced Pulmonary Hypertension, Which Is Early Stage of Pulmonary Vascular Disease Associated with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Pulmonary hypertension (PH) is prominent as a vascular involvement of systemic sclerosis (SSc), which remains a leading cause of death in spite of current best treatments. The definition of PH was updated from mPAP≥25mmHg to mPAP >20mmHg and PVR≥3WU (G. Simonneau et al. Eur Respir J 2019, 53). Although it may enable to improve the prognosis of PH associated with SSc, it seems be still insufficient because more than 2/3 of the pulmonary circulation is already impaired before meeting the definition. Therefore, the ideal therapeutic intervention should be started at the subclinical stage of PH in SSc patients, but little is known about underlying pathological mechanisms. Recently, it was reported that TNFα drives PH by suppressing the BMP type-II receptor and altering NOTCH signalling (LA. Hurst et al., Nat Commun 2017. 13;8:14079). In this study, we try to detect the gene expressions in peripheral blood involved in the progression to exercise-induced PH (exPH), considered as subclinical PH, in the prospective registry of high-risk population for developing PH associated with SSc.

Methods: Total of 180 patients who had not met PH criteria with Raynaud phenomenon, skin sclerosis or SSc-related autoantibody was registered. To detect the early pulmonary vessel disease (PVD), exercise Doppler echocardiography (exDE) was carried out every 6 or 12 months for up to 6 years. The definition of exPH was maximum sPAP >40mmHg or increase in sPAP >20mmHg estimated by exDE during exercise (*R. Naeije et al., Am J resp and critical care med 2013, 187, 576-583*). For gene expression analysis, total RNAs from whole peripheral blood cells were extracted and then multiplex sequencing was done. To identify candidate genes involved in the progression to exPH, random forest machine learning method was employed. Volcano plots, a scatter plots to visualize fold-changes and p-values of differentially expressed genes (DEGs) between exPH and others (exN), were also used for seeking the important genes for disease progression.

Results: At the time of registration, 34.4% of patients met exPH criteria, and 15.6% of patients developed exPH during follow-up period (35.0±18.1 months). Expression of TNF gene was selected as the most useful genes to predict progression to exPH by random forest, and the accuracy of the model was about 87%. Volcano plots indicated that expressions of TMEM176A and TMEM176B were prominent (fold-change >2.4 and -log10 p-value >3.5) in exPH patients. The accuracy was improved to 90% if the expression of TNF and TMEMA/B were used for the prediction of progression to exPH. We found that the statistically significant increase in expression of TNF was eliminated at the time of fulfilling the exPH criteria, while the increase in expressions of TMEM A/B were still kept.

Conclusion: Our findings suggest that TNFα plays important role only in the period of pre-exPH. On the other hand, increase in expressions of TMEM A/B were observed through the period of pre-exPH to post-exPH. It suggests that there are multiple phases before developing PH associated with SSc. It is very important to understand the phases for the precise treatment to arrest the progression of PVD.

Disclosure: Y. Koyama, Asahikasei, 6, Ayumi, 6, BMS, 6, Tanabe-Mitsubishi, 6, Shin-nihon, 6, Asteras, 6, Eli-Lilly, 5; **Y. Sato**, None; **T. Shoji**, None; **S. Fuke**, None; **T. Umayahara**, None; **M. Sakamoto**, None.

Abstract Number: 1856

Serum IFN Score Predicts Long Term Outcome in Limited Cutaneous SSc

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Limited cutaneous systemic sclerosis (lcSSc) carries a highly variable prognosis and to date there are no stratification tools to predict clinical outcomes. Evidence suggests that type-I Interferon (IFN) pathway is involved in progression of clinical manifestations of diffuse cutaneous SSc (dcSSc). However, the role of type-I IFNs in lcSSc has not yet been explored. Here we set out to determine in the context of an observational study the value of serum Type I IFN activation in stratifying for clinical outcome in lcSSc using a novel composite score developed for the MINIMISE clinical trial of mycophenolate mofetil in lcSSc (EudraCT: 2019-004139-21)

Methods: Consecutive patients with lcSSc (according to LeRoy) were selected within our observational cohort. Serum IFN score was measured as the average of the logged concentration of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11, assessed by Luminex assay. 38 healthy volunteers were assayed as controls (HC). The composite morbi-mortality endpoint capturing "meaningful disease progression" included (i) New lung fibrosis on HRCT (FVC< 70%), (ii) Deterioration of established lung fibrosis, (iii) Significant progression of skin score, (iv) New major cardiac complication, (v) Scleroderma renal crisis, (vi) new RHC diagnosis of pulmonary hypertension, (vii) Severe SSc related GI disease, (viii) Severe digital vasculopathy and (ix) Mortality. Baseline observation serum from patients was assessed for IFN score. The statistical methodology employed included Pearson/Spearman correlation analysis and Fisher exact test as appropriate. Kaplan Meier curves compared event-free survival.

Results: HC had a mean IFN Score of 4.7 +/- 0.3 STDV. 66 lcSSC patients (64 F, mean age 65.5 years) were included in the analysis. Median(IQR) disease duration was 12 years (5 to 16), with 68 months median Follow up (33 to 88). 33 (50%) patients met the morbi-mortality endpoint within the follow-up period with a mean (STDV) time to event of 43 (26) months. Forty-two (63.63%) patients had anticentromere antibodies of which 35 had no other autoantibody detected. IFN score in lcSSC was not normally distributed. Median (IQR) IFN score of lcSSc patients was significantly higher than HC (5.2 (5,5.4), p< 0.0001). Within the patient cohort, median (IQR) IFN score of patients carrying only ACA was significantly lower than others (5.1 (4.9,5.3) vs 5.4 (5,5.7), p=0.003)). 49 (74%) patients had IFN score higher than Mean+ STDV of HC (IFN HI). 17 (35%) of the IFN HI patients met the morbi-mortality endpoint within 36 months

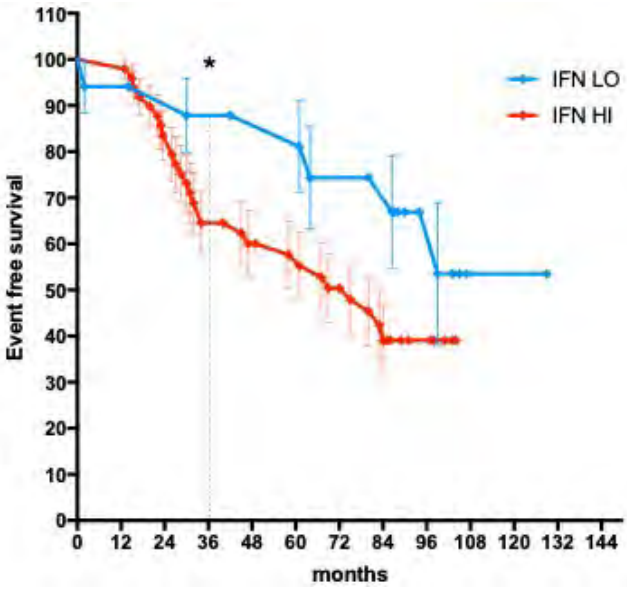

Figure 1. Kaplan Meier curves for event-free survival and difference at 36 months.

with a mean (STDV) time to endpoint of 40 (23) months, vs only 2 (12%) IFN LO patients (mean time to event 57 months (23))(One-Sided Chi-Square =0.036).

Conclusion: Within the limitations of retrospective analysis of observational cohort, our data suggest that patients with lcSSc do show evidence of Type I IFN dysregulation. Patients with HI Serum IFN scores tend to have worse outcomes than patients with normal or low IFN scores. Once confirmed in additional cohorts, IFN score could be a valuable tool for stratification of lcSSc and may help to better integrate clinical management of limited and diffuse subsets of SSc and facilitate timely implementation of organ-specific therapy across both subsets.

Disclosure: R. Karanth, None; **G. Abignano**, None; **V. Kakkar**, None; **R. Ross**, None; **C. Denton**, Acceleron, 2, 6, Actelion, 2, 6, Arxx Therapeutics, 2, 6, Boehringer Ingelheim, 2, 6, Bristol-Myers Squibb, 2, 6, Corbus, 2, 6, CSL Behring, 2, 6, Galapagos NV, 2, 6, GlaxoSmithKline, 2, 6, Horizon, 2, 6, Inventiva, 2, 6, Roche, 2, 6, Sanofi, 2, 6, Servier, 2; **F. Del Galdo**, Boehringer-Ingelheim, 1, 2, 5, 6, Astra-Zeneca, 1, 2, 5, 6, Jannsenn, 6, Chemomab, 2, 5, Capella Biosciences, 2, 5, Mitsubishi-Tanabe, 2, 5.

Abstract Number: 1857

Ultra-High Frequency Ultrasound Compared to Durometry and Skin Score for Cutaneous Assessment in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III (1836–1861)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: To assess skin involvement in a cohort of patients with systemic sclerosis (SSc) comparing results obtained from modified Rodnan skin score (mRSS), durometry and ultra-high frequency ultrasound (UHFUS). Additionally, correlations with clinical characteristics of the disease were analyzed.

Methods: SSc patients were enrolled along with healthy controls (HC), assessing disease-specific characteristics. Five regions of interest were investigated in the non-dominant upper limb: the central dorsal side of the distal, intermediate and proximal phalanx of the second finger, the dorsum of the hand and the volar side of the forearm. Each patient underwent rheumatological evaluation of the mRSS, measurement of skin thickness with durometer, and UHFUS assessment with a 70 MHz probe. Moreover, the mean grayscale value (MGV) of the dermal and epidermal layers in US images was collected.

Results: Forty-seven SSc patients (87% female, mean age 56.4 years, mean disease duration 10.8 years) and 15 HC were enrolled. Durometry showed a good correlation with mRSS (p=0.025, rho=0.34). When performing UHFUS, SSc patients had a significantly thicker epidermal layer (p< 0.001) and lower epidermal MGV (p=0.01) than HC in almost all the different regions of interest. Among the various SSc-characteristics, patients with interstitial lung disease and those with pulmonary arterial hypertension presented a significant lower MGV of both epidermal and dermal layers in several regions of interest. No correlations were found between UHFUS results either with mRSS or durometry.

Conclusion: UHFUS in SSc showed that skin thickness and echogenicity can be related to lung involvement. The lack of correlations between UHFUS and both mRSS and durometry suggests that these are not equivalent techniques, but indeed may represent complementary methods for a full skin evaluation in SSc.

Disclosure: M. Di Battista, None; **S. Vitali**, None; **S. Barsotti**, None; **A. Della Rossa**, None; **V. Dini**, None; **M. Romanelli**, None; **M. Mosca**, None.

Abstract Number: 1858

Serum Interferon Score Is a Biomarker of Active Disease in Patients with Early Diffuse Cutaneous Systemic Sclerosis Enrolled in the Prospective Registry of Early Systemic Sclerosis (PRESS) Cohort

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

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Session Time: 8:30AM–10:30AM

Background/Purpose: Several published studies have demonstrated activation of the interferon type 1 (IFN) pathway in sera from patients with systemic sclerosis (SSc). Specifically, levels of IFN activation correlate with severity of skin and lung fibrosis, cardiac involvement, quality of life, and measures of collagen turnover. Microarray and proteomic

studies have indicated that the serum concentrations of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11 significantly correlate with the IFN-induced activation of peripheral blood mononuclear cells (PBMCs). The study goal was to determine the association between the serum IFN score at baseline and longitudinal outcomes at follow-up in the Prospective Registry of Early Systemic Sclerosis (PRESS) Cohort.

Methods: We performed a retrospective cohort study of patients enrolled in the PRESS Registry at eleven sites in the US between April 2012 and January 2019. Patients had early diffuse cutaneous (dc)SSc (disease duration < 2 years from the onset of the first non-Raynaud Phenomenon SSc symptom) and fulfilled the ACR/EULAR 2013 Classification Criteria for SSc. Serum from age- and sex- matched healthy controls obtained at one academic center as well as serum from SSc patients collected at the baseline visit was subjected to Luminex xMAP technology (Myriad-Ruled Based Medicine, Austin, TX). A serum IFN score was generated for each patient by averaging the natural logarithm of the concentrations of CCL2, CCL8, CCL19, CXCL9, CXCL10, and CXCL11. Dichotomization of scores were based on Mean + 2 standard deviations (SD) of healthy control, used as cut off for normal (or IFN Low vs IFN High). We compared baseline and follow-up clinical features of patients classified as IFN High or Low according to a score greater than (IFN High) or within two SD from mean of healthy controls (IFN Low).

Results: Sera from the baseline visit were available for 110 PRESS patients who were 69% female. Patients with IFN High Scores were older and had longer SSc disease duration compared to the IFN Low Score patients (Table 1). At baseline, IFN High versus Low patients had higher mRSS (mean [SD] 23.4 [9.6] vs. 20.7 [11.3], p-value 0.2037), and lower forced vital capacity (FVC) % predicted (76.0 [20.1] vs. 84.4 [18.1], p-value 0.0750) and lung diffusion for carbon monoxide (DLCO) % predicted (59.8 [21.1] vs. 80.6 [27.3], p-value 0.0023). The Health Assessment Questionnaire-

Table 1. PRESS Patient Clinical Characteristics

Variable Mean (SD) or as indicated	All Patients N=110	Interferon High N=68	Interferon Low N=42	P-Value
Age, years	50.2 (15.0)	52.5 (13.3)	46.3 (16.8)	0.0342
Female Sex, N (%)	76 (69%)	47/68 (69%)	29/42 (69%)	0.9938
Time from NRP to serum collection	1.3 (0.7)	1.2 (0.7)	1.4 (0.8)	0.2844
mRSS				
Baseline	22 (10)	23 (10)	21 (11)	0.2037
12-months	17 (9)	18 (9)	15 (8)	0.1327
Last Follow-up	12 (9)	13 (9)	8 (9)	0.0112
Anti-Topoisomerase I Positive, n/N (%)	28/97 (29)	16/61 (26)	12/36 (33)	0.4557
Anti-RNA Polymerase III, Positive, n/N (%)	43/86 (50)	26/54 (48)	17/32 (53)	0.6555
Baseline (% Predicted)				
FVC	79 (20)	76 (20)	84 (18)	0.0750
DLCO	67 (26)	60 (21)	81 (27)	0.0023
12-months (% Predicted)				
FVC	78 (22)	75 (20)	83 (25)	0.3274
DLCO	64 (21)	60 (19)	74 (21)	0.0732
Last Follow-up (% Predicted)				
FVC (Median, range) Follow-up, months: 34.0 (19.8-54.0)	78 (21)	73 (19)	87 (22)	0.0262
DLCO (Median, range) follow-up months: 34.0 (22.5, 54.0)	64 (23)	56 (15)	82 (28)	0.0049
HAQ-DI				
Baseline	1.1 (0.7)	1.2 (0.7)	0.9 (0.7)	0.0204
12-months	1.0 (0.7)	1.1 (0.7)	0.8 (0.6)	0.1589
Last Follow-up	1.0 (0.8)	1.1 (0.8)	0.7 (0.6)	0.0789

NRP= Non-Raynaud Phenomenon, mRSS= modified Rodnan skin score, FVC= Forced Vital Capacity, DLCO = Lung Diffusion for Carbon Monoxide, HAQ-DI= Health Assessment Questionnaire-Disability Index

Disability Index (HAQ-DI) was also higher in the IFN High versus IFN Low patients. At last follow-up, IFN High patients maintained significantly higher mRSS and lower lung function parameters (Table 1).

Conclusion: Patients with early dcSSc enrolled in the PRESS Cohort with a IFN High Score at baseline had worse FVC and DLCO % predicted, worse mRSS and worse HAQ-DI, which they kept at last available follow up. While we could not measure treatment effects given the observational nature of this cohort, the data support the notion that serum interferon score may be a biomarker for active disease in patients with early dcSSc.

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Abstract Number: 1859

Bone Mineral Density in Patients Diagnosed with Giant Cell Arteritis Taking Glucocorticoids: A Case-control Study

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SESSION INFORMATION
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Session Time: 8:30AM–10:30AM

Background/Purpose: The standard treatment for Giant Cell Arteritis (GCA) is high dose glucocorticoid (GC). It is unknown whether steroids are more detrimental to the spine or the hip. The aim of this study was to examine bone mineral density (BMD) of the lumbar spine, left neck of femur, right neck of femur, left total hip and right total hip in patients diagnosed with GCA being treated with GC.

Methods: We collected data from patients with GCA who were referred to the rheumatology department at two hospitals in the North West of England between 2010 and 2019. Patient's details recorded at time of scan included age, gender, Body Mass Index (BMI), and drug treatment, specifically GC use. Dual X-Ray absorptiometry (DEXA) assessed BMD in the spine (mean of L1-L4 vertebrae), left femoral neck, right femoral neck, left total hip and right total hip. Two patient groups were identified, patients with GCA on current GC (cases) and matched 1:4 to those referred for a DEXA scan with no reason for scanning (controls). The prevalence of BMD in each group was compared by a two sample t-test. A comparison was made between the two groups using logistic regression adjusting for age and gender.

Results: A total of 309 patients were included. 61 of these patients were diagnosed with GCA and had a DEXA scan performed (48 females, 13 males). In comparison the control group had 248 patients (196 females, 52 males). Patients diagnosed with GCA had higher values of BMD than patients not diagnosed with GCA that were of the same age and gender. This gave an odds ratio (OR) of 0.68(95%CI 0.18; 2.64) at the lumbar spine, OR of 2.05(95%CI 0.22; 19.45) at the left femoral neck, OR of 3.27(95%CI 0.33; 32.73) at the right femoral neck, OR of 4.26(95%CI 0.27; 66.52) at the left total hip and OR of 8.01(95%CI 0.43; 147.91) at the right total hip. The numeric values of BMD at all sites were higher in the patients with GCA than in the controls.

Conclusion: The study has shown a surprising protective effect GCA has on BMD. Patients diagnosed with GCA receiving GC treatment have shown to have a higher BMD compared to patients without GCA of the same age and gender. Possible confounders include length of time on steroid when scanned or unmeasured confounders in the controls.

Disclosure: A. Geressu, None; **M. Bukhari**, None.

Abstract Number: 1860

Three Distinct Transcriptional Profiles of Monocytes Correlate with Disease Activity in SSc Patients

Hadijat Makinde[1], Gaurav Gadhvi[1], Salina Dominguez[1], Miranda Gurra[1], Kathleen Aren[2], Mary Carns[2], Tracy Frech[3], Dinesh Khanna[4], Shervin Assassi[5], Lutfiyya Muhammad[6], Carla Cuda[1], Monique Hinchcliff[7], Deborah Winter[2] and Harris Perlman[1], [1]Northwestern University, Chicago, IL, [2]Northwestern University Division of Rheumatology, Chicago, IL, [3]University of Utah, Salt Lake City, UT, [4]University of Michigan, Ann Arbor, MI, [5]University of Texas McGovern Medical School at Houston, Houston, TX, [6]Northwestern University Feinberg School of Medicine, Chicago, IL, [7]Yale School of Medicine, Westport, CT

SESSION INFORMATION
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Background/Purpose: Patients with SSc display a complex clinical phenotype.Our group has made important contributions to an emerging understanding of monocytes and macrophages as central to SSc pathogenesis. There are numerous studies that relate transcriptional signatures from PBMC or whole skin of SSc patients to disease activity. Like all whole tissue RNA-sequencing studies, these studies are subject to changes in cellular composition that can drive gene expression signatures and a loss of the ability to detect biologically important transcriptional changes within minority cell populations. Here, we focused circulating monocytes, which have been shown to exist as two central populations classical (CM) and non-classical (NCM).

Methods: SSc patients were recruited from four different sites that form PRESS: Northwestern University (Drs. Monique Hinchcliff and Chase Correia), University of Texas, University of Michigan and University of Utah. Comprehensive clinical data was collected for all patients. We isolated CM and NCM monocytes from these patients and age, sex, and race-matched healthy volunteers were used as controls. RNA-seq was performed on CM and NCM populations as well as on isolated bulk macrophages from skin.

Results: We first performed RNA-seq on CM, which are the predominant population in circulation. In order to capture the variability across the SSc cohort, we defined 1790 differentially expressed genes in each patient. We then used

these genes to cluster patients into 3 subgroups: Groups A-C. Group A exhibited the strongest interferon signature and innate immune pathways. Group B patients expressed genes in the same pathways but was also enriched for response to cAMP and corticosteroids. Both Group B and Group C exhibited upregulation of genes associated with vasculature development and blood vessel formation. Group C uniquely upregulated TGFB pathways. Next, we performed RNA-seq on NCM isolated from the same patients. When NCM were clustered based on the same 1790 genes as CM, we found that Groups A and C were recapitulated, while Group B was less cohesive. Our analysis stratified SSc patients based on their transcriptional profiles in monocytes but was agnostic to their clinical presentation. We found that Group B and C patients exhibited significantly worsened lung function at the time monocyte isolation than Group A patients. However, there were no significant differences in skin disease. We then isolated macrophages from skin biopsies of SSc patients and showed that the transcriptional profile of Group A and C in SSc patients was conserved. We also used gene expression data from another study on monocytes which stratified patients based on disease presentation. We found that Group A accurately distinguished dcSSc and ncSSc patients from controls, but not lcSSc.

Conclusion: We are the first to show that transcriptomic analysis of classical and non-classical circulating monocytes can unbiasly stratify SSc patients and correlate with disease activity outcome measures.

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Abstract Number: 1861

Epidermal Growth Factor Receptor Pathway and Fibrosis in Systemic Sclerosis Skin

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SESSION INFORMATION
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Background/Purpose: Systemic sclerosis (SSc) is a rare autoimmune disorder with chronic morbidity and high mortality. Disease pathogenesis involves microvascular damage, immune dysregulation, and fibrosis affecting skin and internal organs. There are no FDA approved antifibrotic treatments for skin disease. Tyrosine kinase inhibitors have demonstrated antifibrotic effects on SSc skin in clinical trials with variable efficacy and poor patient tolerance. Epidermal growth factor receptor (EGFR) is a receptor tyrosine kinase whose circulating ligands correlate with modified Rodnan skin score (mRSS) as part of a recently identified gene expression signature specific for SSc skin. EGFR

Characteristic Mean (Standard deviation), or as indicated	SSc N=7	HC N=14
Age, years	50.7 (±9.9)	43 (±13.1)
Women (n, %)	5 (71)	10 (71)
Race, Caucasian (n,%)	7 (100)	-
SSc disease duration in months* (mean, SD)	14.7 (±10.2)	-
dcSSc (n,%)	6 (86)	-
mRSS total (median, IQR)	11 (8)	-
• Right Arm	1 (1.5)	-
• Left Arm	1 (1.5)	-
Serum autoantibodies (n,%)		
ANA pattern		
homogenous	4 (57)	-
speckled	5 (71)	-
nucleolar	5 (71)	-
Anticentromere	0 (0)	-
Anti-RNA polymerase III	3 (43)	-
Anti-topoisomerase I (Scl-70)	3 (43)	-

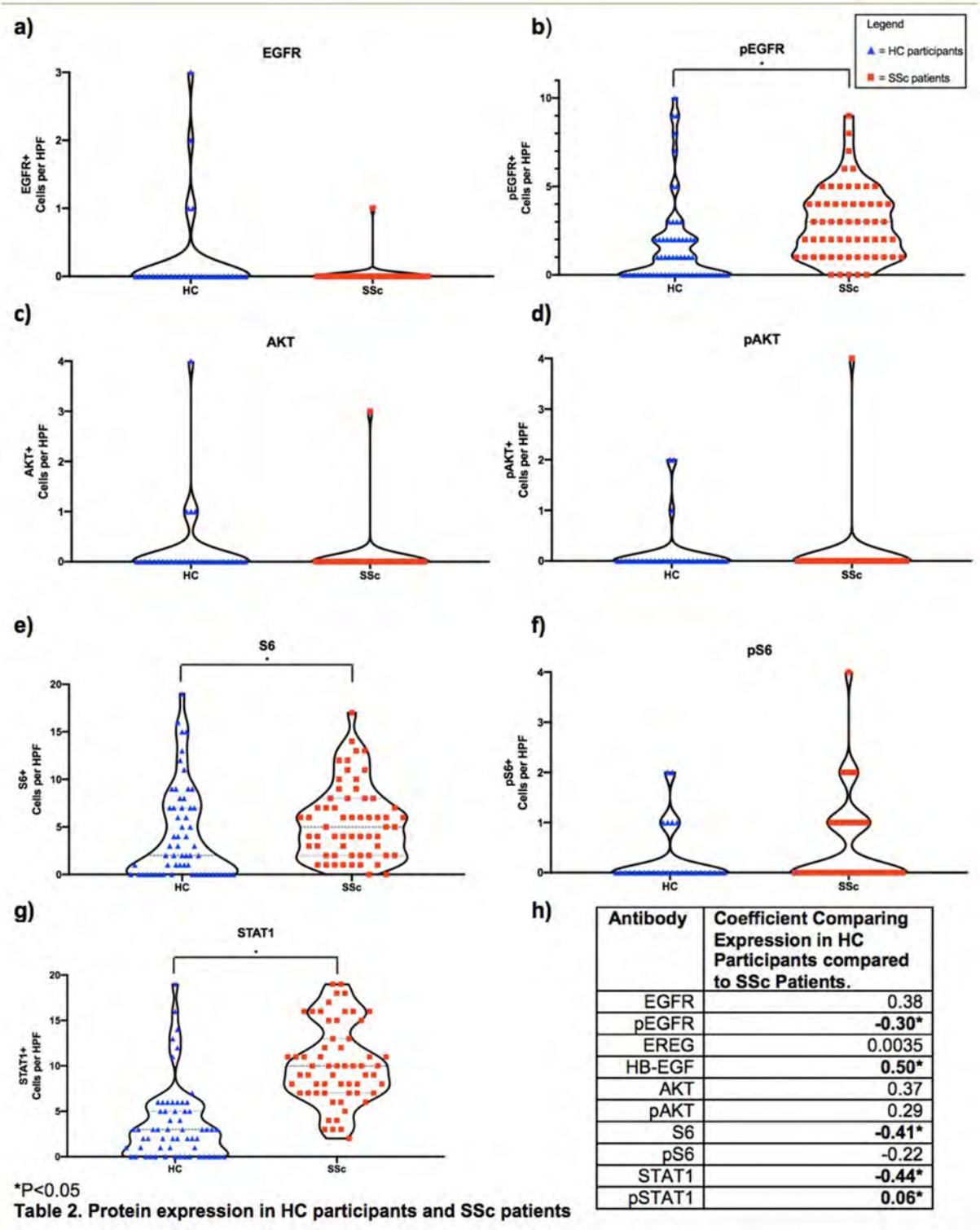
Table 1. Baseline demographics and clinical characteristics of SSc patients and HC participants.
*Months between date of onset of first non-Raynaud systemic sclerosis (SSc) symptom and date of skin biopsy. SSc = systemic sclerosis patients, HC = healthy control participants, dcSSc = diffuse cutaneous SSc, mRSS = modified Rodnan Skin score, SD = standard deviation, ANA = antinuclear antibody, anti-RNA polymerase III = anti-ribonucleic acid polymerase III

activates multiple downstream signaling pathways, including PI3K/AKT (phosphatidylinositol 3-kinase, protein kinase B), MAPK (mitogen-activated protein kinase), and JAK/STAT (janus kinase/signal transducer and activator of transcription) pathways. The purpose of this project was to identify activation of EGFR and which of its downstream pathways occur in SSc patient skin.

Methods: Archived forearm skin biopsies from seven SSc patients who met the 2013 ACR/EULAR classification criteria and 14 matched healthy control participants (HC) were subjected to immunohistochemical (IHC) staining using antibodies to EGFR, phospho-EGFR (p-EGFR), and downstream transcription factors AKT, phospho-AKT (pAKT), ribosomal protein S6 (S6), phospho-S6 (pS6), signal transducer and activator of transcription 1 (STAT1), and phospho-STAT1 (pSTAT1). To focus on fibroblasts, non-vascular positively stained cells were enumerated by counting the number per high powered field (hpf) in the dermis. Outcomes measures also included correlation with mRSS for each SSc patient. Statistical analysis was done using based comparison around the two groups (SSc and HC), clustered at the patient level. Clustered spearman correlation was performed for IHC and mRSS.

Results: Baseline demographics and clinical characteristics of SSc patients and HCs are shown in Table 1. Among the skin biopsies, there was 1.3-fold higher staining for pEGFR ($p=0.008$), 1.41-fold higher S6 ($p< 0.00$), and 1.44-fold higher STAT1 ($p< 0.00$) in SSc dermis compared to HC biopsies. There were no statistically significant differences in staining for EGFR, AKT, pAKT, and pS6 (Table 2). We did not detect phosphorylation of STAT1 by IHC in the SSc samples. pEGFR staining showed an inverse correlation with mRSS.

Conclusion: The EGFR pathway appears activated in SSc patients compared to HCs as evidenced by increased staining of its phosphorylated protein. EGFR activation may reflect extent or stage of disease based on its inverse correlation with mRSS. More fibroblasts expressed STAT1 and S6 protein in SSc skin, which suggests a higher



Antibody	Coefficient Comparing Expression in HC Participants compared to SSc Patients.
EGFR	0.38
pEGFR	**-0.30***
EREG	0.0035
HB-EGF	**0.50***
AKT	0.37
pAKT	0.29
S6	**-0.41***
pS6	-0.22
STAT1	**-0.44***
pSTAT1	**0.06***

*P<0.05

Table 2. Protein expression in HC participants and SSc patients

Protein expression in HC participants and SSc patients (a-g) with coefficients comparing expression in HC to SSc (h). EGFR = epidermal growth factor receptor, pEGFR = phospho-epidermal growth factor receptor, AKT = protein kinase B, pAKT = phospho-protein kinase B, S6 = ribosomal protein S6, pS6 = phospho-ribosomal protein S6, STAT1 = signal transducer and activator of transcription 1, HC = healthy control participants, SSc = systemic sclerosis patients.

number of a certain fibroblast subtype. However, we did not observe differences in phosphorylation of STAT1 or S6, so if EGFR signals through these pathways, it may occur with phosphorylation of a different amino acid or through unphosphorylated protein complexes.

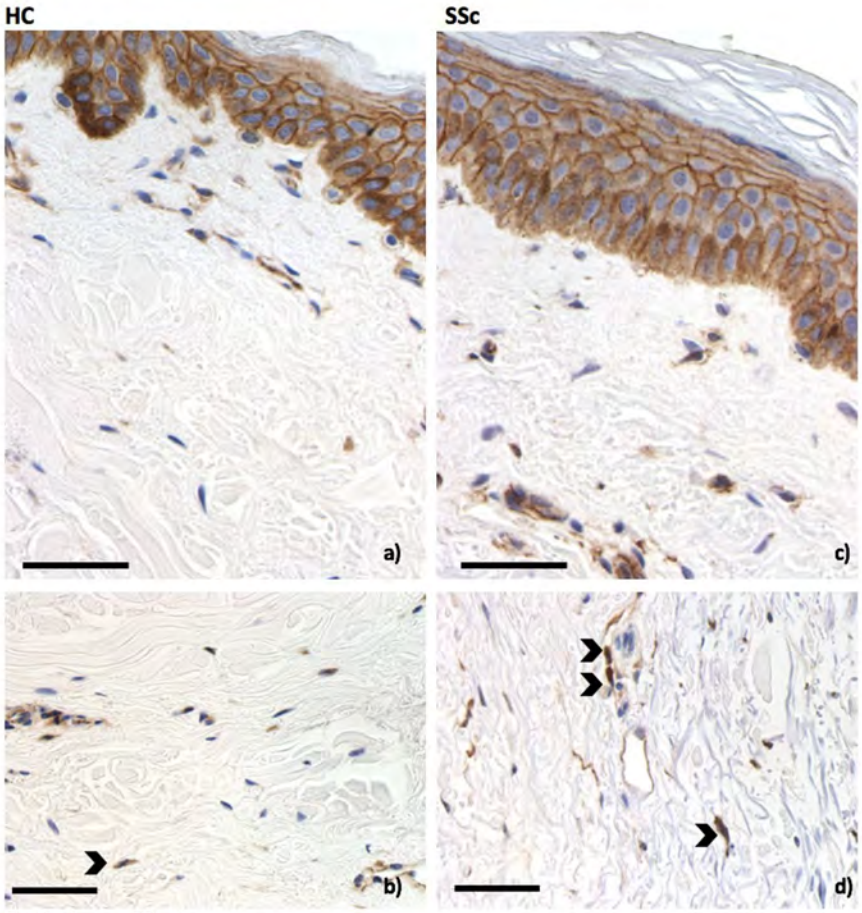


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Figure 1. pEGFR in SSc patient skin.

a) pEGFR HC epidermis and dermis, 0 cells per high-power field b) pEGFR HC dermis, 1 cells per high-power field c) pEGFR SSc epidermis and dermis, 0 cells per high-power field d) pEGFR SSc dermis, 3 cell per high-power field. HC = healthy control participant, SSc = systemic sclerosis patient, pEGFR = phospho-epidermal growth factor receptor.

Disclosure: M. Carnaru, None; **M. Hinchcliff**, None; **I. Odell**, None; **F. Wilson**, None.

Abstract Number: 1862

Clonal Hematopoiesis Across the Age Spectrum in Patients with Systemic Vasculitis

Kristina Wells[1], Fernanda Gutierrez-Rodrigues[2], Bhavisha Patel[2], Kaitlin Quinn[3], Keith Sikora[1], Neal Young[4] and Peter Grayson[5], [1]National Institute of Arthritis, Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD, [2]National Heart, Lung, and Blood Institute (NHLBI), National Institutes of Health (NIH), Bethesda, MD, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Washington, DC, [4]National Heart, Lung, and Blood Institute (NHLBI), National Institues of Health, Bethesda, MD, [5]National Institutes of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), National Institutes of Health (NIH), Bethesda, MD

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Clonal hematopoiesis (CH) is a pre-malignant state characterized by somatic mutations in hematologic precursor cells in genes associated with myeloid malignancies. Incidence of CH increases exponentially with age in healthy people and is associated with an increased risk for all-cause mortality and cardiovascular disease. Small studies report increased prevalence of CH in various inflammatory diseases. To what extent age versus inflammation underlies these associations is unclear. In this study, vasculitis patients with giant cell arteritis (GCA), ANCA-associated vasculitis (AAV), or Takayasu's arteritis (TAK) were screened for CH to determine the relationship between CH and vasculitis in a cohort of patients with inflammatory disease across a wide age spectrum.

Methods: An error-correcting targeted sequencing panel was used to screen 137 vasculitis patients (GCA, AAV, TAK) and 30 healthy controls (HC) for somatic variants in peripheral blood in 40 genes related to CH. Variants were called if the variant allele fraction (VAF) > 0.5% and if the variants were predicted to impair protein function. Prevalence of CH in vasculitis was compared to controls using chi square test. Logistic regression was used to assess associations of age and vasculitis with CH. Relative contribution of predictor variables was assessed using standardized beta coefficients. Clinical features were compared using Fisher's exact test, Wilcoxon rank sum test, or logistic regression as appropriate. Correlation between clone size and clinical features was assessed by linear regression.

Results: The prevalence of CH in GCA, AAV and TAK was 54.1% (26/48), 36.1% (13/36), and 11.3% (6/53) respectively, compared to 6.7% (2/30) in HC (p= 0.0007). Median age for GCA, AAV, TAK, and HC was 71.5 (range: 50-88), 60 (range: 19-77), 32 (range: 3-57), and 47 (range: 14-71) years, respectively. In a logistic regression model, age and vasculitis were independently associated with CH (Age: *B*=0.05, standardized *b*=0.99, p< 0.0001; Vasculitis: *B*=0.77, standardized *b*=0.53, p=0.04). Median VAF was 1.3% (0.51-51.3%) and did not differ by diagnosis. Clones at VAF >10% were found in 7.3% (10/137) of patients. Of the somatic mutations identified, *DNMT3A* (48/71=67.6%) and *TET2*(12/71=16.9%) were the most frequently mutated genes. Patients with CHIP had lower percent lymphocytes (17.4% vs 25.5%, p=0.02) and higher absolute neutrophil count (6.1 vs 5.2 K/uL, p=0.04) than those without CH. Adjusting for daily prednisone dose, neutrophil to lymphocyte ratio was significantly associated with presence of CH (*B*=0.06, p=0.04). The VAF of somatic mutations was positively associated with age (*B*=0.01, p=0.01) and monocyte count (*B*=0.83, p=0.01).

Conclusion: There is a complex relationship between age, inflammation and CH. Age is 1.9x more strongly associated with CH than vasculitis, but each are independent contributors. CH is associated with skewing of peripheral blood counts towards myeloid lineages in patients with vasculitis. Still unanswered is to what extent CH directly contributes to inflammation in vasculitis, or conversely what role systemic inflammation plays in generation of mutations and clonal selection.

Disclosure: K. Wells, None; **F. Gutierrez-Rodrigues**, None; **B. Patel**, None; **K. Quinn**, None; **K. Sikora**, None; **N. Young**, None; **P. Grayson**, None.

Abstract Number: 1863

Consistent Efficacy with Apremilast in Men and Women to Treat Oral Ulcers Associated with Behçet's Syndrome: Results from Phase 3 Researching Oral Apremilast Safety and Efficacy in Behçet's Disease (RELIEF) Study

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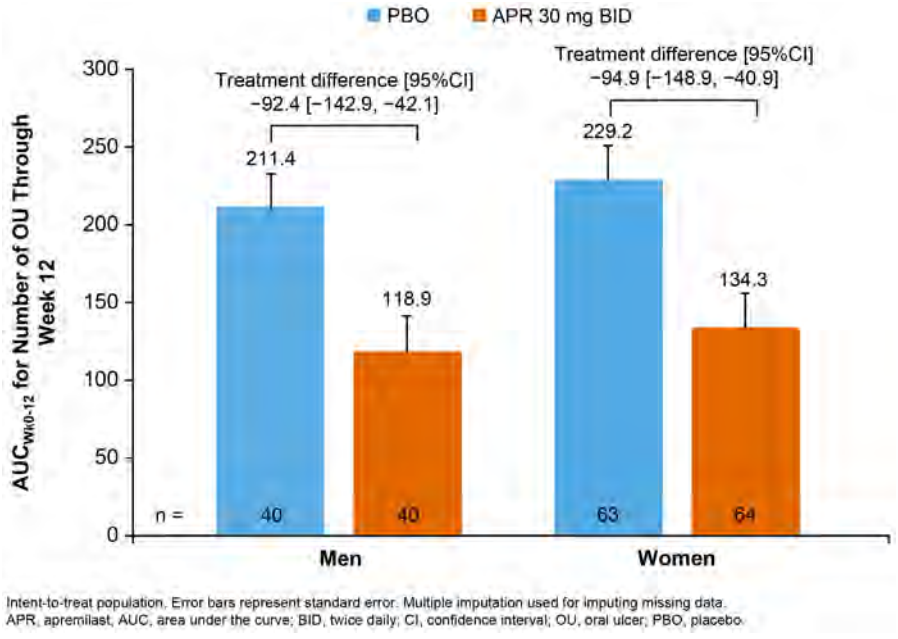
SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Painful, recurring oral ulcers (OU) associated with Behçet's syndrome negatively affect quality of life (QoL). Differences across sexes were reported in the frequency of disease manifestations, disease course, and response to colchicine. The phase 3, randomized, double-blind, placebo (PBO)-controlled RELIEF study showed overall efficacy of apremilast (APR) for OU associated with Behçet's syndrome, including improvements in OU pain, disease activity, and QoL. The objective of this subgroup analysis is to evaluate the consistency of efficacy with APR in men and women with Behçet's syndrome.

Methods: Adults with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement, were randomized to APR 30 mg BID or PBO during the 12-week PBO-controlled treatment phase. Randomization was stratified by sex. The primary endpoint was area under the curve for the number of OU through Week 12 (AUC_{Wk0-12}) to assess continued efficacy over the time period in a symptom that waxed and waned. Key secondary endpoints included OU pain, complete response (OU-free), maintenance of complete response, and QoL at Week 12. Disease activity was also assessed using Behçet's Syndrome Activity Score (BSAS) and Behçet's Disease Current Activity Index Form (BDCAF). QoL was assessed using Behçet's Disease QoL (BDQoL). Prespecified subgroup analyses in men and women were performed to assess treatment effect in primary and secondary endpoints.

Results: Eighty men and 127 women were randomized and received ≥1 dose of study medication. Mean age was 38.7 years (men) and 40.8 years (women). Mean (SD) OU count at baseline was 3.4 (1.4) (PBO) and 3.7 (1.5) (APR) for men and 4.3 (3.2) (PBO) and 4.5 (4.5) (APR) for women. Greater improvements in favor of APR vs PBO were observed in AUC_{Wk0-12} in men and women (Figure). Consistency in efficacy with APR was observed between men and women, with greater reduction in pain and achievement of OU complete response (OU-free) and maintenance of response at Week 12 vs PBO (Table). In men and women, consistent treatment effects in favor of APR vs PBO were observed for



Intent-to-treat population. Error bars represent standard error. Multiple imputation used for imputing missing data.
APR, apremilast; AUC, area under the curve; BID, twice daily; CI, confidence interval; OU, oral ulcer; PBO, placebo

Area Under the Curve for the Number of OU From Baseline Through Week 12 (Primary Endpoint)

The Effect of Apremilast and Placebo on Secondary Efficacy Outcomes by Gender in Patients With Behçet's Syndrome

	Key Secondary Efficacy Outcomes at Week 12					
	Men			Women		
	PBO (n = 40)	APR (n = 40)	Tx Difference [95% CI]	PBO (n = 63)	APR (n = 64)	Tx Difference [95% CI]
OU CR, n/N (%)	8/40 (20.0)	21/40 (52.5)	32.6 [12.8, 52.4]	15/63 (23.8)	34/64 (53.1)	29.3 [13.2, 45.4]
OU CR 6+6*, n/N (%)	1/40 (2.5)	10/40 (25.0)	22.8 [8.8, 36.8]	4/63 (6.3)	21/64 (32.8)	26.5 [13.6, 39.3]
Pain (VAS)†	−12.0 (4.8)	−37.6 (4.9)	−25.6 [−37.2, −14.1]	−17.4 (4.4)	−41.5 (4.3)	−24.1 [−34.9, −13.3]
BSAS†	−1.3 (2.4)	−14.4 (2.4)	−13.1 [−18.8, −7.3]	−7.7 (2.4)	−19.7 (2.4)	−12.0 [−18.0, −6.0]
BDCAF†						
BDCAI	−0.1 (0.3)	−0.5 (0.3)	−0.4 [−1.1, 0.4]	−0.7 (0.3)	−1.3 (0.3)	−0.6 [−1.2, 0.0]
Patient's Perception of Disease Activity	−0.2 (0.3)	−1.4 (0.3)	−1.2 [−1.9, −0.5]	−1.0 (0.2)	−1.8 (0.2)	−0.9 [−1.4, −0.3]
Clinician's Overall Perception of Disease Activity	−0.2 (0.3)	−1.5 (0.3)	−1.3 [−1.9, −0.7]	−1.0 (0.2)	−1.7 (0.2)	−0.7 [−1.3, −0.2]
BDQoL†	−0.7 (1.0)	−2.2 (1.0)	−1.5 [−3.8, 0.8]	−0.3 (0.9)	−4.4 (0.9)	−4.1 [−6.3, −2.0]

LOCF analyses. *Proportion of patients achieving an OU CR by Week 6, and remaining OU-free for ≥6 additional weeks during the 12-week PBO-controlled treatment phase. †LS mean (SE) change from baseline. n represents number of patients randomized to treatment.
APR, apremilast; BDCAF, Behçet's Disease Current Activity Form; BDCAI, Behçet's Disease Current Activity Index; BDQoL, Behçet's Disease Quality of Life; BSAS, Behçet's Syndrome Activity Scores; CI, confidence interval; CR, complete response; LOCF, last observation carried forward; OU, oral ulcer; PBO, placebo; Tx, treatment; VAS, visual analog scale.

disease activity and QoL measures, although moderate treatment differences were observed in BDCAI (men/women) and BDQoL (men) (Table).

Conclusion: Consistent treatment effects in favor of APR vs PBO in clinically relevant outcomes, including OU number and pain, OU complete response, and disease activity measures, were observed in men and women with OU associated with Behçet's syndrome.

Disclosure: G. Hatemi, Celgene, 5, AbbVie, 6, Novartis, 6, UCB, 6; **A. Mahr**, Celgene, 2, Chugai, 2, 6, Roche, 6, Amgen, 1, 6; **M. Takeno**, Celgene, 2, Novartis, 5, AbbVie, 6, Eisai, 6, Mitsubishi Tanabe, 6; **D. Kim**, None; **M. Melikoğlu**, None; **S. Cheng**, Amgen Inc., 3; **S. Richter**, Amgen Inc., 3, 11; **S. Jardon**, Amgen Inc., 3, 11; **M. Paris**, Amgen Inc., 3; **M. Chen**, Amgen Inc., 3; **Y. Yazici**, Bristol Myers Squibb, 2, Celgene, 2, Genentech, 2, Sanofi, 2.

Abstract Number: 1864

^{18}F-Fluorodeoxyglucose PET/MRI as an Alternative Hybrid Imaging Modality: Comparative Study in a Prospective, Longitudinal Cohort of Patients with Large-Vessel Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Imaging modalities play an important role in the diagnosis and management of patients with large-vessel vasculitis (LVV). Use of 18F-fluorodeoxyglucose (FDG) positron emission tomography - computed tomography (PET/CT) to assess patients with LVV is well established; however, concerns about ionizing radiation exposure may limit its use, particularly in younger populations. PET coupled with magnetic resonance imaging (PET/MRI) offers potential for simultaneous acquisition of PET and angiography at substantially less radiation exposure than PET/CT. We aimed to investigate whether PET/MRI is a useful surrogate to PET/CT in LVV.

Methods: Participants who fulfilled the 1990 ACR Classification Criteria for Takayasu's arteritis (TAK) or modified 1990 ACR Criteria for giant cell arteritis (GCA), were prospectively recruited into an observational cohort. Following injection of one radiotracer dose, patients underwent a whole body PET/MR at 1-hour acquisition time and, when-

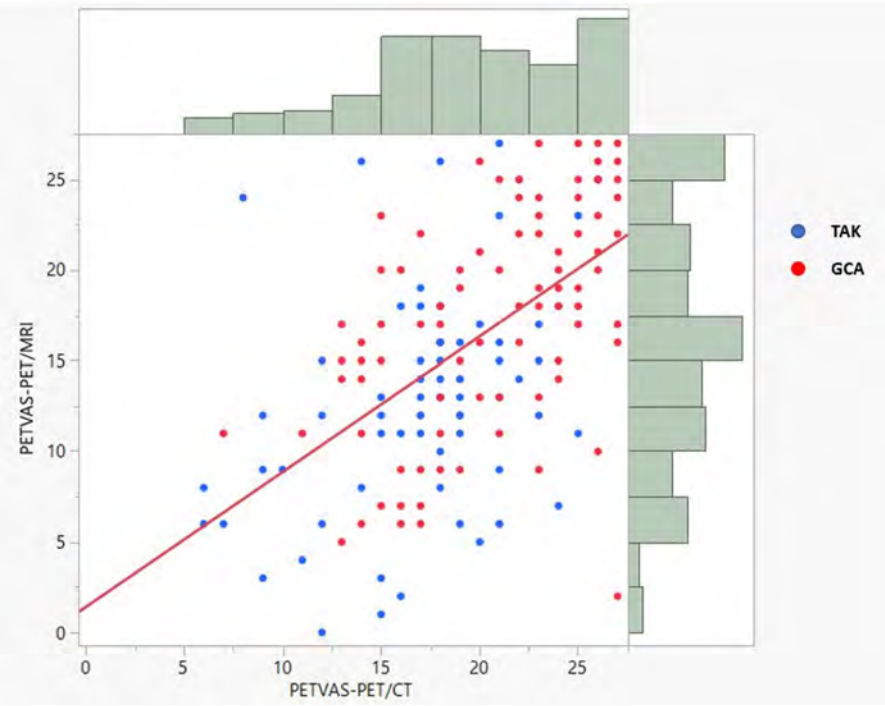

Figure 1. Distribution of PET/MRI-based and PET/CT-based PETVAS in patients with Takayasu's arteritis and giant cell arteritis.

ever possible, a PET/CT at 2-hour acquisition time. A single reader with vascular imaging expertise interpreted FDG uptake relative to liver uptake by visual assessment (scale 0-3) in 9 arterial territories. The PET Vascular Activity Score (PETVAS) was calculated for each study (scale 0-27)). MR angiography was obtained concurrently with the PET/MR study. Angiographic damage, defined as stenosis, occlusion, or aneurysm, was evaluated in 4 segments of the aorta and 13 branch arteries and compared to PET findings in the same territories. Patients could be studied repeatedly at ≥ 6-month intervals.

Results: PET/MR was obtained in 203 scans from 76 LVV patients (TAK: 93 scans in 36 patients and GCA: 110 scans in 40 patients). Eighteen scans were performed in 9 pediatric patients (< 18 years old). For 178 visits (87.8%), simultaneous PET/CT scans were obtained on the same day. PET/MRI-based PETVAS scores correlated with PET/CT based scores for both TAK and GCA (Spearman's correlation coefficient (r)= 0.59, CI95%: 0.48-0.67, p< 0.001; Figure-1). PET/CT scores were consistently higher than PET/MR scores (Median:19 and IQR: 8 vs Median:16 and IQR: 10.25) likely due to effects of delayed imaging acquisition (1 versus 2-hour uptake time). Out of 2041 arterial territories from 154 scans with both MRI angiography (MRA) and PET/MRI data; PET and MRA showed concordant abnormalities in 1446 territories (71%) and discordant finding in 595 territories (29%). No PET activity or damage was seen in 1254 territories (61%). PET activity with damage was seen in 192 territories (9%). PET activity without damage was seen in 238 territories (12%). Damage without PET activity was seen in 357 territories (17%). (Table-1 and Figure-2).

Conclusion: PET/MRI findings correlate with PET/CT findings in LVV. PET provides complimentary data to MRA that may better inform a clinician about vascular inflammation and damage. Given the need to minimize ionizing radiation

Table 1. Vascular damage by MRA and metabolic activity by PET/MRI according to different vascular territories

Territories	PETMRI Activity – MRA Damage – n (row %)	**PETMRI Activity + MRA Damage +** n (row %)	**PETMRI Activity +** MRA Damage – n (row %)	PETMRI Activity – **MRA Damage +** n (row %)	**Total**
Ascending Aorta	113 (74.8)	4 (2.6)	25 (16.9)	9 (6)	**151**
Aortic Arcus	85 (55.2)	15 (9.7)	33 (21.4)	21 (13.6)	**154**
Descending Aorta	81 (52.6)	20 (13.0)	39 (25.3)	14 (9.1)	**154**
Abdominal Aorta	79 (52.7)	18 (12.0)	22 (14.7)	31 (20.7)	**150**
Innominate Artery	108 (71.5)	9 (6.0)	22 (14.7)	12 (7.9)	**151**
Right Carotid Artery	73 (48.3)	25 (16.6)	20 (13.2)	33 (21.9)	**151**
Left Carotid Artery	54 (35.5)	27 (17.8)	21 (13.8)	50 (32.9)	**152**
Right Vertebral Artery	38 (88.4)	0 (0)	1 (2.3)	4 (9.3)	**43**
Left Vertebral Artery	38 (90.5)	0 (0)	1 (2.4)	3 (7.1)	**42**
Right Subclavian Artery	63 (41.7)	30 (19.9)	11 (7.3)	47 (31.1)	**151**
Light Subclavian Artery	53 (34.9)	35 (23.0)	14 (9.2)	50 (32.9)	**152**
Right Axillary Artery	136 (93.2)	0 (0)	10 (6.8)	0 (0)	**146**
Left Axillary Artery	93 (63.3)	5 (3.4)	3 (2.0)	46 (31.3)	**147**
Right Iliac Artery	109 (77.3)	2 (1.4)	9 (6.4)	21 (14.9)	**141**
Left Iliac Artery	115 (82.1)	2 (1.4)	7 (5.0)	16 (11.4)	**140**
Right Femoral Artery	8 (100)	0 (0)	0 (0)	0 (0)	**8**
Left Femoral Artery	8 (100)	0 (0)	0 (0)	0 (0)	**8**
Total	**1254 (61)**	**192 (9)**	**238 (12)**	**357 (17)**	2041

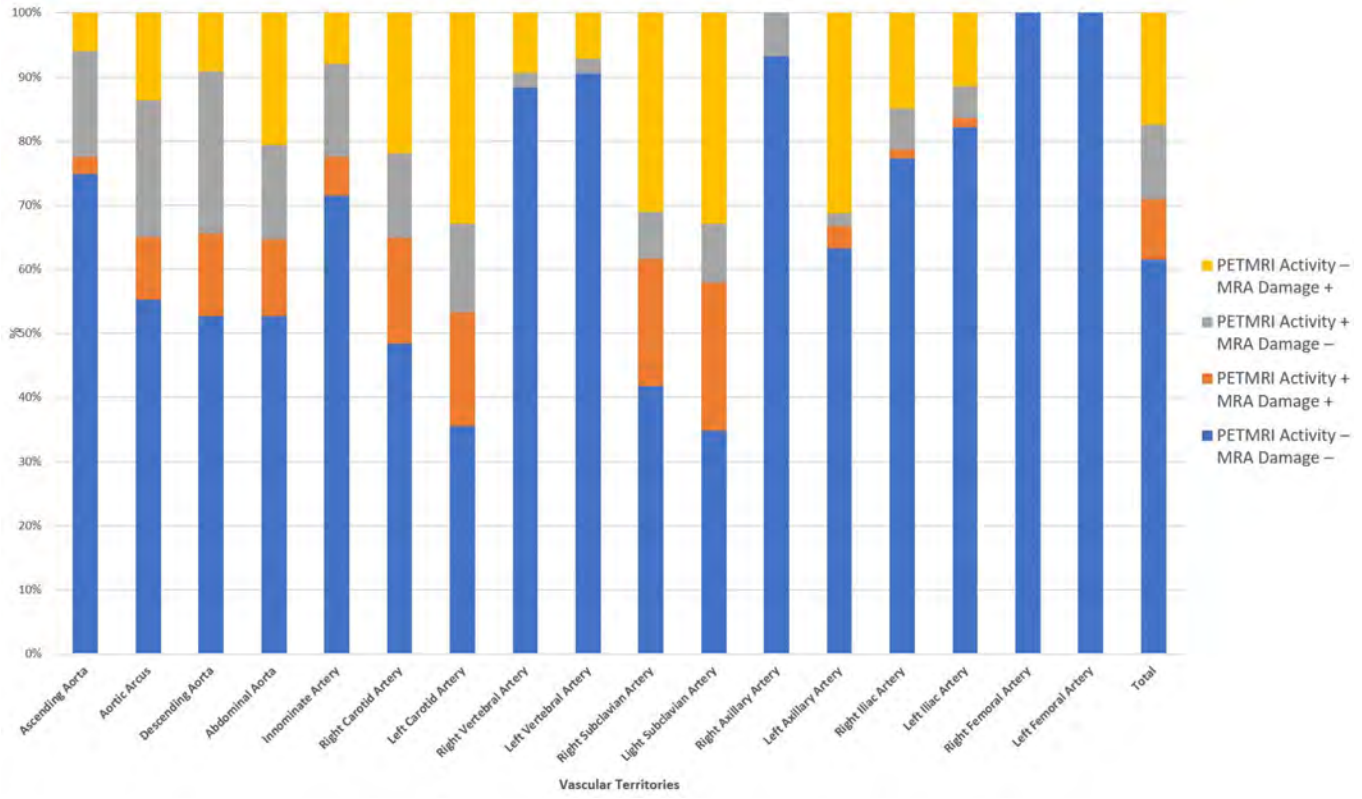

Figure 2. Percentage distribution of vascular damage by MRA and metabolic activity by PET/MRI according to different vascular territories.

exposure in younger patients who will potentially undergo serial imaging studies, PET/MRI is a safe and reliable alternative to PET/CT in patients with LVV.

Disclosure: E. bolek, None; **K. Quinn**, None; **H. Alessi**, None; **E. Novakovich**, None; **M. Ahlman**, None; **P. Grayson**, None.

Abstract Number: 1865

Incidence, Prevalence, and Mortality of Chronic Periaortitis: A Population-based Study

Umar Ghaffar[1], Kenneth Warrington[2], Stephanie Duong[1], Cynthia Crowson[3], Michelle Burke[1], Boyd Viers[1], Aaron Potretzke[1], Haraldur Bjarnason[1] and **Matthew Koster**[1], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, Minnesota, [3]Mayo Clinic, Eyota, MN

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Chronic periaortitis is an inflammatory condition that typically involves the infrarenal portion of the abdominal aorta. To date, no epidemiologic studies have been performed in North America. The purpose of this

study was to evaluate the epidemiology, presentation and outcomes of patients with chronic periaortitis from 1998 through 2018.

Methods: An inception cohort of patients with incident chronic periaortitis from January 1, 1998 through December 31, 2018, in Olmsted County, MN, USA, was identified based on comprehensive individual medical record review utilizing the Rochester Epidemiology Project medical record linkage system. Inclusion required radiographic and/or histologic confirmation of periarterial soft tissue thickening around at least part of the infra-renal abdominal aorta or the common iliac arteries. Data were collected on demographic characteristics, clinical presentation, renal and radiographic outcomes, and mortality. Incidence rates were age and sex adjusted to the 2010 United States white population.

Results: Eleven incident cases of chronic periaortitis were identified during the study period. Average age at diagnosis was 61.8±13.4 years. The cohort included 9 men (82%) and 2 women (18%). The most common presenting symptom was pain with 55% (6/11) reporting abdominopelvic-pelvic pain, 36% (4/11) back pain, and 18% (2/11) flank pain. Obstructive uropathy was present in 73% (8/11) subjects: 3 (27%) unilateral left, 1 (9%) unilateral right, and 4 (36%) bilateral. Mean±SD creatinine at presentation was 2.7±3.4 mg/dL. Ureteral stenting was required at diagnosis in seven patients, unilateral left in 2, unilateral right in 1 and bilateral in 4. All 11 patients received glucocorticoids with a median (IQR) dose of 40 (30, 60) mg/day. Additional non-glucocorticoid therapeutics were used in 10 patients.

Renal function stage at last follow up declined in 2 patients, remained the same in 3 patients and improved in 6 patients. Mean (±SD) creatinine at last follow-up was 1.2±0.2 mg/dL. Among the 7 patients requiring baseline indwelling ureteral stent placement only two required ongoing ureteral stenting at last follow up. None of the four patients without ureteral stenting at diagnosis progressed to require stenting during the follow-up period. No patient underwent ureterolysis surgery in this cohort. Periarterial soft tissue thickening at last follow up had increased in thickness in 1 (9%), was unchanged in 2 (18%), decreased in size but did not resolve in 6 (55%), and fully resolved in 18%.

Age- and sex-adjusted incidence rates per 100,000 population were 0.26 for females, 1.56 for males and 0.87 overall. Overall prevalence on January 1 , 2015 was 8.98 per 100,000 population. Median (IQR) length of follow-up was 10.1 (2.5, 13.8) years. Overall mortality was similar to the expected age, sex, and calendar estimates of the Minnesota population with standardized mortality ratio (95% CI) for the entire cohort 2.07 (0.67, 4.84).

Conclusion: This study reports the first epidemiologic data on chronic periaortitis in the United States. In this cohort of patients with chronic periaortitis, men were 4 times more commonly affected than women. Mortality was not increased compared to the general population.

Disclosure: U. Ghaffar, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **S. Duong**, None; **C. Crowson**, None; **M. Burke**, None; **B. Viers**, None; **A. Potretzke**, None; **H. Bjarnason**, None; **M. Koster**, None.

Abstract Number: 1866

Vasculitis in Patients with Sarcoidosis: A Single-Institution Case Series of 17 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Vasculitis in patients with sarcoidosis is rare and can affect blood vessels of any size. Limited information describing this association is available. The purpose of this study is to describe a large, single-institution case-series of patients with sarcoidosis and vasculitis.

Methods: A single-institution retrospective study was performed reviewing all patients with a diagnosis code for sarcoidosis and vasculitis between January 1, 1998 and December 31, 2019. Medical records were individually reviewed, and data regarding diagnosis, treatment, and outcomes were abstracted. Sarcoidosis was diagnosed based on histologic, radiographic, and clinical data with exclusion of alternative diagnoses. Diagnosis for small vessel vasculitis (SVV) required biopsy confirmation. Patients with large or medium-vessel vasculitis (L/MVV) required biopsy and/or arterial imaging. Comparison between patients presenting with L/MVV versus patients with only SVV was performed.

Table 1. Characteristics of vasculitis in patients with sarcoidosis

Case	Sex	Age Sarcoid / Vasculitis Dx, yr	WASOG Organ Involvement*	Vessel size	Arterial involvement on imaging†¥ or biopsy**
1	M	44/44	B-J, ET-LN, Sk	LVV, MVV	AA (e), Ant Tib (s), Ax (s), Br (o), V (s), Ca (s), CF (b), I (b), Innom (b), Mes (b, o, s), Per (b), Pop (a), Re (b), SF (b), Sub (o, pa, wt), TA (a)
2	F	66/68	BM, ET-LN, Li, Lu, NS, S	LVV	TA (hm)
3	F	55/55	Lu, Sp	MVV	IMA (a, s, o, wt), Sp (a)
4	M	81/80	Lu	LVV	AA (hm), Car (hm), Innom (hm), Sub (hm), TA (hm)
5	F	72/72	Eye, NS, Lu	LVV, MVV	ACA (b), ICA (b, en, s), MCA (b), SMA (wt)
6	M	43/45	Lu	LVV, MVV	Br (o, s), Ce (s), SMA (s), Sp (s), TA (wt)
7	F	53/54	B-J, Eye, Lu, Sk	MVV	Skin – medium vessel
8	M	24/20	Eye, Li, Lu, Sp	MVV	Hep (a), Sp (a)
9	F	40/79	Lu	LVV	Temporal artery
10	M	55/57	Li, Lu, NS	SVV	Sural nerve
11	F	53/50	ET-LN, Lu, Sk	SVV	Skin
12	M	60/62	Lu	SVV	Skin
13	F	67/82	ET-LN, Lu	SVV	Skin
14	F	52/56	Eye, Lu, NS, Sk	SVV	Skin
15	M	39/37	Eye, Lu, NS, Sk	SVV	Skin
16	F	57/56	Lu, Sk	SVV	Skin
17	M	32/71	Lu	SVV	Skin

*WASOG Organ Involvement: B-J, bone-joint; BM, bone marrow; ET-LN, extra-thoracic lymph node; Li, liver; Lu, lung; NS, nervous system; Sk, skin; Sp, spleen. **Granulomatous vasculitis was observed in cases 7, 9, 10, 11, 14, 15, 16; leukocytoclastic vasculitis in cases 12, 13, 17)
† a, aneurysm; b, beaded irregularities; e, ectasia; en, enhancement; hm, hypermetabolism (on positive emission tomography); o, occlusion; pa, pseudoaneurysm; s, stenosis; wt, wall thickening
¥ AA, abdominal aorta; ACA, anterior cerebral artery; Ant Tib, anterior tibial; Ax, axial; Br, brachial; Ca, carotid; Ce, celiac; CF, common femoral; Hep, hepatic; I, iliac; ICA, internal carotid artery; IMA, inferior mesenteric artery; Innom, innominate; MCA, middle cerebral artery; Mes, mesenteric branch; PCA, posterior cerebral artery; Per, peroneal; Pop, popliteal; Re, renal; SF, superficial femoral; Sp, splenic; Sub, subclavian; TA, thoracic aorta; V, vertebral

Results: Seventeen patients were identified during the study period. Nine patients (56% female) had L/MVV and 8 (50% female) had SVV. Mean±SD age at sarcoidosis diagnosis was 53.2±17.8 and 51.9±11.4 years and mean±SD age at vasculitis diagnosis was 57.4±19.6 and 59.0±13.4 years in L/MVV and SVV groups, respectively. Number of organ systems involved by sarcoidosis was similar [median (IQR) 3 (1,4) L/MVV vs. 2.5 (1.75, 3.25) SVV]. Sarcoid organ involvement and vasculitis vessel distributions are noted in Table 1. Mean length of follow-up was 11.5±12.8 years in L/MVV and 13.1±14.3 years in SVV. All patients were treated with glucocorticoids for vasculitis. More patients with L/MVV were treated with at least one DMARD/biologic (8/9, 89%) compared to SVV (3/8, 38%, p=0.05). Complete response to therapy for vasculitis was observed in 8/9 L/MVV and 7/8 in SVV. Four patients in SVV group were able to stop all immunosuppression but only one patient with L/MVV was off all therapy at last follow-up.

Conclusion: Vasculitis in patients with sarcoidosis is uncommon. Variability exists in the vessels involved and the treatments utilized. Overall this series observed favorable outcomes with a high percentage achieving complete response, regardless of vessel size affected.

Disclosure: B. Kimbrough, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **H. Langenfeld**, None; **C. Crowson**, None; **E. Carmona**, None; **A. Virata**, None; **M. Koster**, None.

Abstract Number: 1867

Investigating Adenosine Deaminase 2 Activity in Large Vessel Vasculitis

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Table 1. Demographic data. LV-GCA - large vessel giant cell arteritis. ITAS - Indian Takayasu clinical Activity Score. ESR - Erythrocyte sedimentation rate. CRP - C-reactive protein

	Takayasu Arteritis			LV-GCA	Intracranial vasculitis	Healthy Control
	Active Disease	Grumbling Disease	Stable Disease			
N	41	23	71	44	7	52
Female	39 (95.1)	18 (78.3)	66 (93)	36 (81.2)	4 (57.1)	42 (81)
Age	38.7 [17.1 - 65.5]	48.3 [24.9 - 70.8]	45.9 [17.7 - 73.7]	67.3 [56.8 - 84.1]	50.0 [33.4 - 77.9]	42.6 [22.7 - 70.0}
Ethnicity						
Caucasian	24 (58.5)	12 (52.2)	35 (49.3)	35 (79.5)	5 (71.4)	40 (77)
Asian	13 (31.7)	6 (26.1)	29 (40.8)	5 (11.4)	2 (28.6)	7 (13.4)
Mixed	2 (4.8)	0	1 (1.4)	1 (2.3)	0	0
Afro-Caribean	1 (2.4)	0	2 (2.8)	1 (2.3)	0	3 (5.8)
Middle East	1 (2.4)	3 (13)	1 (1.4)	0	0	2 (3.8)
African	0	2 (8.7)	1 (1.4)	0	0	0
Other	0	0	2 (2.8)	2 (4.5)	0	0
ESR	42.1 [1 - 120]	38.5 [1 - 85]	25 [0 - 90]	30.5 [4 - 124]	16 [2 - 47]	n/a
CRP	15.8 [0.2 - 60.1]	13.6 [0.2 - 44.9	3.4 [0.2 - 13.3]	18.7 [0.2 - 188.9]	6.3 [0.3 - 22.6]	n/a
ITAS 2010	6.0 [2 - 22]	0.4 [0 - 1]	0 [0]	n/a	n/a	n/a
ITAS 2010 ESR	7.5 [2 - 22]	1.9 [0 - 4]	0.7 [0-3]	n/a	n/a	n/a
ITAS 2010 CRP	7.4 [2 - 22]	1.65 [0 - 4]	0.3 [0 - 2]	n/a	n/a	n/a

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Deficiency of adenosine deaminase 2 (DADA2) leads to a broad phenotype that in some resembles polyarteritis nodosa with fever and rash, but in others is characterised by stroke or immunodeficiency. Small, medium and large vessel vasculitis has been reported. In contrast, plasma ADA2 activity is elevated in inflammatory conditions including systemic lupus erythematosus and systemic juvenile idiopathic arthritis with macrophage activation syndrome. The role of ADA2 and how its deficiency associates with the vasculitides is not yet understood. Using a well-characterised large vessel vasculitis cohort we sought to establish the potential role of ADA2 activity.

Methods: ADA2 activity was measured in adults with Takayasu arteritis (TA), large vessel giant cell arteritis (LV-GCA), intracranial vasculitis (IV) and healthy control (HC) subjects (Table 1), using a coupled spectrophotometric assay as previously described. Plasma from 11 patients with genotyped DADA2 and 10 patients heterozygous for pathogenic variants in ADA2 were used to define thresholds for deficiency and carrier status respectively (DADA2 activity 0 - 0.90 U/L, ADA2 carrier activity 2.02 - 10.62 U/L). Activity levels above the upper limit of normal (ULN) were defined as >99th

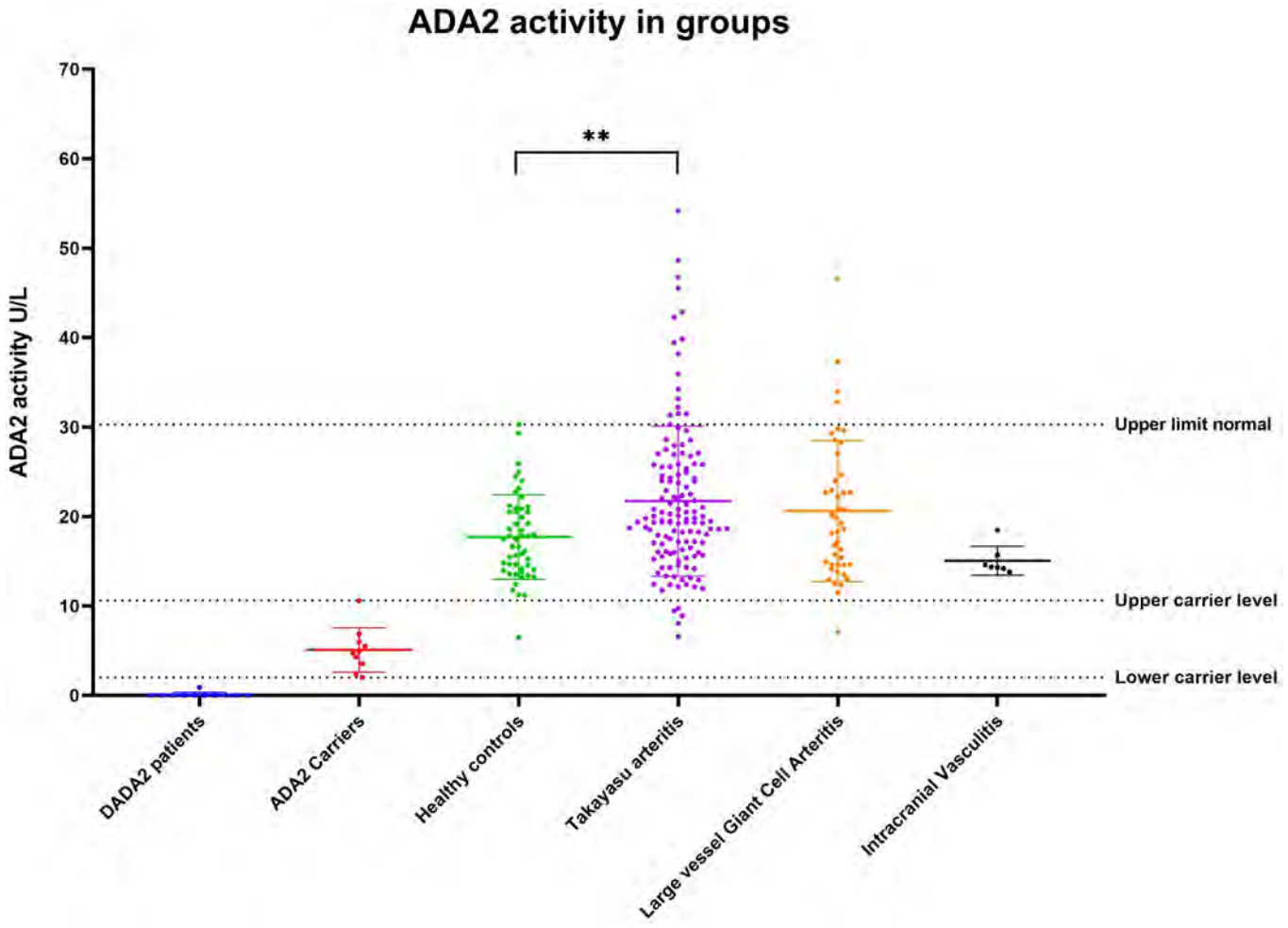

Figure 2. ADA2 activity in groups. Upper limit normal - defined as >99% percentile of HC activity (30.3U/L). Upper and lower carrier level (2.02-10.62U/L) - determined from 10 patients heterozygous for pathogenic variants in ADA2. ** p<0.01.

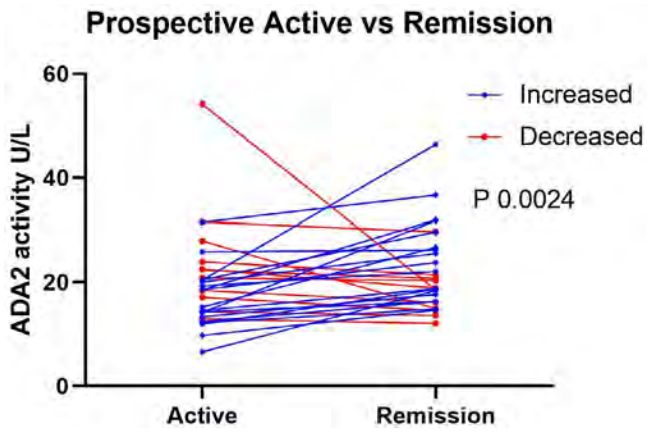

Figure 3. ADA2 activity in prospective active and remission samples. Increased - ADA2 activity higher in remission vs active. Decreased - ADA2 activity lower in remission vs active.

percentile of the HC activity (30.3 U/L). To assess potential associations with TA disease status, ADA2 was measured prospectively in matched active and remission samples.

TA disease activity was determined as active, grumbling or stable using clinical and radiological features, physician impression, CRP, ESR and Indian Takayasu clinical Activity Score (ITAS).

Median values are presented with differences between groups analysed using non-parametric tests, $P< 0.05$ was considered significant.

Results: No patients were found to have ADA2 deficiency while 7 subjects had activity within the carrier range (1 HC (1.9%), 5 TA (3.7%), 1 LV-GCA (2.3%)). Compared to HC levels (17.43 [14.11 – 20.78] U/L), activity in the TA group was significantly increased (TA 19.68U/L, p= 0.0061), while LV-GCA and IV were not significantly different (Figure 2). In 20 cases activity exceeded the upper limit of normal; 16 TA (11.9%, p=0.044; 4 active, 2 grumbling, 10 stable) and 4 LV-GCA (9.1%, ns). In TA, there was a positive correlation between ADA2 activity and ESR (Spearman R = 0.2863, p=0.0009) but not with CRP or ITAS score.

Subgroup analysis revealed that ADA2 activity was most prominently elevated in the stable group relative to HCs (TA stable 20.54 U/L [8.08 - 48.66], median +17.8%, p= 0.0006), but not with active or grumbling disease. Consistent with this, prospective analysis demonstrated a significant increase in ADA2 activity in remission vs active disease (p=0.024), with activity increasing in 18 (62%) patients achieving remission (Figure 3).

Conclusion: There were no cases of ADA2 deficiency in this cohort. Consistent with other inflammatory conditions, ADA2 activity was elevated in TA compared to HC subjects. Surprisingly, increased ADA2 activity was linked to stable TA in both cross-sectional and prospective analyses. This may suggest a potential role of ADA2 enzyme activity in vascular repair and regrowth – possibly tying in with known elevated levels of ADA2 activity in growing children

Disclosure: A. Porter, None; **R. Maughan**, None; **C. Pericleous**, None; **A. Kiprianos**, None; **H. Jee**, None; **P. Lee**, None; **T. Youngstein**, None; **J. Mason**, None.

Abstract Number: 1868

Neutrophil Extracellular Trap Formation in Patients with Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Neutrophil extracellular trap (NET) formation, the extrusion of chromatin and granular components from activated neutrophils, is essential in host defense. However, NET formation has also been linked to inflammation and autoimmunity, including in anti-neutrophil cytoplasmic autoantibody (ANCA)-associated vasculitis (AAV), a disease of small blood vessels. Neutrophil infiltration is seen in aortic specimens of patients with Takayasu's arteritis (TAK) and affected arteries of giant cell arteritis (GCA), two types of large-vessel vasculitis (LVV). Whether NET formation and autoimmunity against NET antigens such as extracellular histones, a common NET-related autoantigen in other autoimmune diseases including systemic lupus erythematosus and rheumatoid arthritis, occurs in LVV is not known. The purpose of this study was to compare levels of NET formation and anti-histone antibodies across different types of vasculitis.

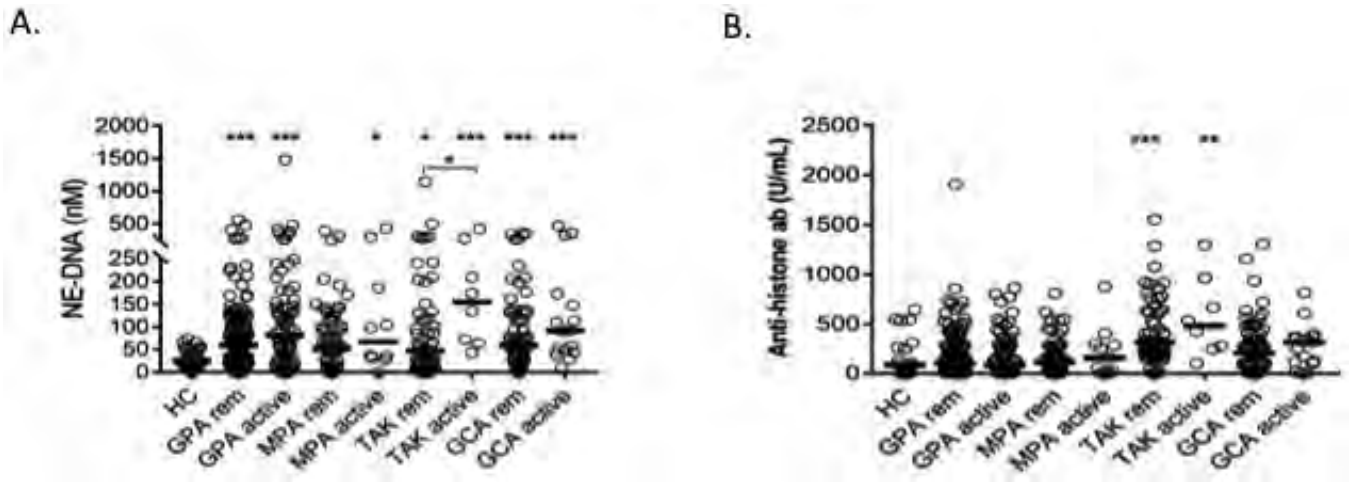

Figure 1. Levels of NE-DNA complexes and anti-histone antibodies in patients with vasculitis. Levels of A) NE-DNA complexes and B) anti-histone antibodies were analyzed in healthy controls (HC), and patients with vasculitis at times of remission (rem) and active disease. Statistical analyses were done by Mann-Whitney U test with *p<0.05, **p<0.01 and ***p<0.001. Unless otherwise indicated, all analyses are compared to healthy controls. Each circle represents an individual sample, with the bar representing the median of the group. GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; TAK: Takayasu's arteritis; GCA: giant cell arteritis.

Methods: Plasma levels of NETs (neutrophil elastase (NE)-DNA complexes) and anti-histone antibodies were analyzed in healthy controls (n=30), and patients with AAV (granulomatosis with polyangiitis (GPA, n=196), microscopic polyangiitis (MPA, n=74)), TAK (n=66), and GCA (n=82), at times of remission or flare. Disease activity was assessed using physician global assessments (PGA).

Results: Compared to healthy controls (HC) NE-DNA complexes were significantly elevated in all patients with vasculitis, both at flare and remission, except at remission for patients with MPA (Figure 1A). In patients with TAK, but none of the other conditions, elevated levels of NE-DNA complexes were seen at time of flare as compared to remission ($p< 0.05$), with NE-DNA levels correlating with PGA ($r=0.28$, $p< 0.05$). Levels of NETs did not correlate with C-reactive protein, a marker of general inflammation. Only patients with TAK had significantly higher levels of anti-histone antibodies in their circulation regardless of disease activity ($p< 0.01$) (Figure 1B). In patients with TAK, levels of anti-histone antibodies correlated with presence of NETs ($r=0.35$, $p< 0.01$).

Conclusion: NET formation, as assessed by NE-DNA complexes, is elevated in both small- and large-vessel vasculitis, suggesting a potential common disease link across vasculitides. The association of anti-histone antibodies with NETs in TAK suggests NETs may be a source of autoantigens in this disease. Further studies are needed to explore the role of NETs and anti-histone antibodies in the pathogenesis of vasculitis.

Disclosure: D. Michailidou, None; **R. Kuley**, None; **T. Mustelin**, None; **D. Cuthbertson**, None; **P. Grayson**, None; **N. Khalidi**, Roche, 12, Advisory Board for GCA CME November 2020, BMS, 12, Clinical Trial (Investigator Initiated- BMS supplied drug only, no fees received from BMS), Sanofi, 12, Clinical Trial 2020 GCA and PMR, Abbvie, 12, Clinical Trial 2020-2021 GCA; **C. KOENING**, None; **C. Langford**, None; **C. McAlear**, None; **L. Moreland**, None; **C. Pagnoux**, Gsk, 2, 5, 6, Roche, 2, 5, 6, Otuska, 2, Pfizer, 5, 6, Chemocentryx, 2, Astrazeneca, 1; **P. Seo**, Amgen, 1, Janssen, 1; **U. Specks**, ChemoCentryx, 2, 5, Genentech, 5, Bristo-Myer Squibb, 5, InflxRX, 5, Astra Zeneca, 1, 5, GSK, 5; **A. Sreih**, None; **K. Warrington**, Eli Lilly, 5, Kiniksa, 5; **P. Monach**, Kiniksa, 1, Celgene, 2, Chemocentryx, 1; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **C. Lood**, Exagen Diagnostic, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 5, Horizon Diagnostic, 5.

Abstract Number: 1869

The Role of Faecal Calprotectin in IgA Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Gastrointestinal involvement (GI) is associated with significant morbidity in acute IgA vasculitis (IgAV). Besides the abdominal pain, bowel ischemia could lead to bleeding, perforation, or ileus among others. Our aim was to investigate the role of faecal calprotectin measurement in patients with adult IgAV.

Table 1. Characteristics of IgA vasculitis patients with elevated vs. normal fecal calprotectin

Clinical characteristics	Elevated calprotectin (28)	Normal calprotectin (42)	P value
Male gender (%)	64.3	64.3	1.0
Age (years)*	67.9 (59.9; 75.9)	56.8 (39.1; 65.3)	0.003
Symptom duration (days)*	7 (5-21)	8 (5-14)	0.195
Constitutional symptoms (%)	17.9	7.1	0.252
Purpura above waistline (%)	60.7	40.5	0.143
Skin necroses (%)	57.1	35.7	0.091
Arthritis (%)	17.9	19.0	1.0
Renal involvement (%)	60.7	42.9	0.222
GI involvement (%)	28.6	21.4	0.574
ESR (mm/h) *	40 (28; 66)	27 (11; 52)	0.036
CRP (g/l) *	48 (12; 70)	19 (2; 44)	0.043
Elevated serum IgA (%)	46.4	54.8	0.626

Legend: * median and IQR; GI gastrointestinal;

Methods: Faecal calprotectin was determined at presentation in 70 patients with histologically proven adult IgAV diagnosed at our secondary/tertiary rheumatology center. Based on the calprotectin level, patients were stratified into two groups - those with elevated vs. normal level (the cut off >50 μg/g). Clinical features of patients with elevated vs. normal faecal calprotectin were compared. Logistic regression was used to determine factors associated with elevated faecal calprotectin in IgAV.

Results: Our cohort consisted of 45 males (64.3%) and 25 females (35.7%), median (IQR) age 63.9 (45.9; 69.2) years, with median (IQR) IgAV symptom duration time 7 (4; 21) days. Seventeen patients (24.3%) had GI involvement (abdominal pain, overt GI bleeding, occult GI bleeding, diarrhoea, ileus developed in 15, 4, 12, 6 and 1 patient, respectively). Twenty-eight out of 70 patients (40.0%) had elevated faecal calprotectin, with median (IQR) level of 86.3 (64.0; 192.8) μg/g, of them 8 had clinically GI involvement. We found no significant association between clinical GI involvement and elevated faecal calprotectin (p=0.574). Characteristics of IgAV patients with elevated vs. normal faecal calprotectin are presented in Table 1. Multivariate analysis showed that elevated calprotectin was associated with increasing patient age (OR 1.04 (95%CI 1.01-1.08); p=0.018), purpura above waistline (OR 3.37 (95%CI 1.07-10.58); p=0.037) and C-reactive protein (OR 1.02 (95%CI 1.00-1.03); p=0.017

Conclusion: Our result show that the role of faecal calprotectin measurements in evaluating GI involvement adult IgAV is rather limited.

Disclosure: A. Hocevar, None; **M. Bajzelj**, None; **M. Tomšič**, None; **K. Lakota**, None.

Abstract Number: 1870

Comparative Study on Anti-TNF vs Tocilizumab for Treatment of Refractory Uveitic Cystoid Macular Edema Due to Behcet's Disease: Multicenter Study of 49 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Posterior segment involvement is the most serious affection of uveitis in Behçet's disease (BD), with cystoid macular edema (CME) being the leading cause of blindness. Anti-TNF, especially adalimumab (ADA) and infliximab (IFX), have demonstrated efficacy as first-line biologic agents in BD-related uveitis [Arthritis Rheumatol. 2019;71(12):2081-2089; Ophthalmology. 2018;125(9):1444-1451]. Moreover, the anti-IL6R tocilizumab (TCZ) has shown excellent results in highly refractory BD-uveitis and noninfectious uveitic CME [Rheumatology (Oxford). 2018;57(5):856-864; Am J Ophthalmol.2019;200:85-94; Clin Exp Rheumatol. 2014;32(4 Suppl 84): S54-7; Clin Exp Rheumatol. 2016;34(6 Suppl 102): S34-S40. Our aim was to compare the efficacy of ADA vs IFX vs TCZ in patients with refractory CME due to BD.

Methods: Observational multicenter study of patients with BD-associated CME refractory to conventional and/or biological immunosuppressive drugs. From a cohort of 177 patients treated with anti-TNF and 14 patients treated with TCZ, we selected those with CME at baseline. CME was defined as macular thickness > 300μm (measured by optic coherence tomography). We analyzed in the 3 groups of treatment (ADA, IFX, TCZ) from baseline up to 4 years the evolution of macular thickness (main outcome), best-corrected visual acuity (BCVA) and intraocular inflammation (Tyndall and vitritis). Differences between basal and final follow-up were evaluated. Multivariable linear regression was used to assess the differences between the 3 groups.

Table 1. Demographic and clinical characteristics of 49 patients with cystoid macular edema due to Behçet's disease receiving ADA, IFX or TCZ. Data are presented as mean ± SD or median (IQR) when data were not normally distributed. ADA, adalimumab; BCVA, best corrected visual acuity; CME, cystic macular edema; IFX, infliximab; TCZ, tocilizumab

	ADA (n=25)	IFX (n=15)	TCZ (n=9)	p
Number of eyes with CME, n	40	21	11	-
Age, years	41 ± 11	38 ± 9	43 ± 16	0.55
Sex, men/women	12/13	7/8	5/4	0.91
HLA–B51 positive, n (%)	19 (76)	10 (67)	6 (67)	0.75
Duration of uveitis before anti-TNF/ anti-IL6R, median [IQR] months	30 [12-82]	15 [8-60]	32 [24-144]	0.35
Ocular features at start of anti-TNF/anti-IL6R				
Macular thickness, mean ± SD µm	445 ± 130	484 ± 131	415 ± 104	0.30
BCVA, mean ± SD	0.40 ± 0.25	0.30 ± 0.25	0.20 ± 0.25	**0.015**
Anterior chamber inflammation grade (Tyndall), median [IQR]	2 [1-3]	1 [0-1]	1 [0.5-2]	**0.039**
Vitritis grade, median [IQR]	3 [1-3]	1 [0-2]	2 [1-2]	**0.033**
Treatment before start of anti-TNF/anti-IL6R, n (%)				
Oral glucocorticoids	18 (72)	4 (27)	7 (78)	0.27
Intravenous pulse methylprednisolone	13 (52)	9 (60)	8 (88)	0.15
Methotrexate	13 (52)	8 (53)	8 (88)	0.13
Cyclosporine A	22 (88)	13 (87)	6 (67)	0.31
Azathioprine	14 (56)	8 (54)	2 (22)	0.20
Adalimumab	0 (0)	0 (0)	7 (78)	-
Infliximab	0 (0)	0 (0)	3 (33)	-
Prednisone dosage at start of anti-TNF/anti-IL6R, median [IQR] mg/day	45 [30-60]	30 [20-60]	30 [30-30]	0.44
Combined treatment, n (%)				
Cyclosporine A	10 (40)	5 (33)	1 (11)	0.24
Azathioprine	10 (40)	5 (33)	1 (11)	0.25
Methotrexate	4 (16)	2 (13)	3 (33)	0.55
Duration of follow-up, median [IQR] months	24 [24-42]	24 [3-36]	13 [3-38]	0.26

Results: A total of 49 patients were included. ADA was used in 25 patients (40 eyes with CME), IFX in 15 (21 eyes with CME) and TCZ in 9 (11 eyes with CME). Thus, a sum of 72 affected eyes was analyzed. No statistically significant baseline differences were observed between the 3 groups **(Table 1)** except for a lower basal BCVA in patients treated with TCZ and a higher basal degree of intraocular inflammation in patients treated with ADA. Most patients from all groups had received several conventional immunosuppressive drugs. In addition, most patients in the group of TCZ had also received anti-TNF (5 patients received ADA, 1 received IFX and 2 received both ADA and IFX, in different times). Biological therapy was used in monotherapy or combined with azathioprine (n=10, 5 and 1 in ADA, IFX and TCZ group, respectively), cyclosporine A (n=10, 5 and 1) or methotrexate (n=4, 2 and 3). Macular thickness progressively decreased in the 3 groups, with no signs of CME after 1 year of treatment **(Figure 1)**. Similarly, BCVA improvement and inflammatory ocular remission was reached in all groups.

Conclusion: Refractory CME associated to BD's uveitis can be effectively treated with ADA, IFX or TCZ. Moreover, TCZ is effective in patients resistant to anti-TNF therapy.

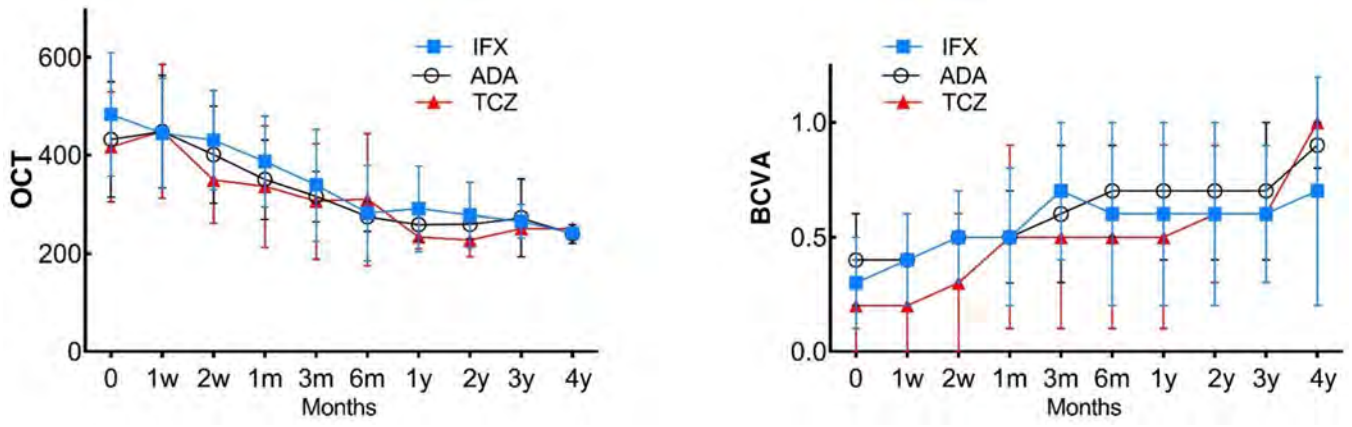

Figure 1. Evolution of ocular parameters in 49 patients with cystoid macular edema due to Behçet's disease receiving ADA, IFX or TCZ.

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Abstract Number: 1871

Characterization of Symptoms of Nasal Disease in Relapsing Polychondritis Using Patient-Reported Data

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Nasal chondritis is a well-recognized manifestation of relapsing polychondritis (RP), occasionally leading to saddle nose deformity. Early symptoms of nasal chondritis such as nose pain are often overlooked. The objective of this study was to characterize nose pain and identify associated symptoms reported by patients with RP.

Methods: Patients with self-reported RP were invited to participate in an online survey. Participants were asked questions about nose pain such as location, onset, duration, frequency, quality, diurnal variation, aggravating and alleviat-

Table 1: Comparison of Clinical Manifestations among Patients with Relapsing Polychondritis Presenting with and without Nose Pain

	RP with nose pain n=430	RP without nose pain n= 215	P value
Eye inflammation n (%)	246 (57)	108 (50)	0.08
Saddle nose deformity n (%)	69 (16)	20 (9)	0.02
Ear pain, redness, swelling n (%)	397 (92)	189 (88)	0.05
Cauliflower ear n (%)	72 (17)	30 (14)	0.1
Hearing loss n (%)	134 (31)	54 (25)	0.2
Audio vestibular symptoms*n (%)	275 (64)	115 (53)	0.004
Airway damage** n (%)	108 (25)	62 (28)	0.5
Joint pain / swelling n (%)	369 (86)	165 (77)	0.01

*Audio vestibular symptoms: tinnitus, vertigo; **Airway damage: damage to trachea and/or bronchi

ing factors, associated symptoms, and saddle nose deformity. Participants with physician-diagnosed RP, aged ≥ 18 years, who meet McAdams diagnostic criteria were included in the study. Fisher's exact test was used to compare clinical characteristics between patients with and without nose pain.

Results: A total of 659 subjects were included, of which 484 (73%) were from the United States. The majority (n=548, 83%) identified themselves as Caucasians, and 574 (87%) were female. Mean age was 50 years (interquartile range = 41-58). Many patients (n=430, 65%) reported nose pain. RP diagnosis was commonly made by rheumatologists (n=313,73%) and otolaryngologists (101, 23%) in patients with nose pain. Compared to patients without nose pain, those with nose pain were more likely to report saddle nose deformity, audio vestibular symptoms, joint pain and swelling (Table 1). Treatment with prednisone was reported by 429 (99%) patients, of which 423 (99%) reported symptom relief with prednisone.

In patients with nose pain (n=430), pain was described as stabbing (n=147, 34%), sharp (n=73, 17%), dull (n=73, 17%), or burning (n=46, 10%); majority (n=313, 73%) reported at least two types of pain and (n=137, 32%) did not report a pain descriptor. Associated nasal pressure (n=150, 34%), tingling (n=119, 27%), or throbbing (n=61, 14%) was reported. Factors felt to aggravate nose pain were minimal trauma (n=240, 55%), stress (n=210, 48%), and cold exposure (n= 104, 24%); 50% reported more than one aggravating factor. Majority (n=322, 75%) reported the pain lasted for ≥1day. Frequency of reported nasal symptoms were daily (n=65, 15%), weekly (n=73, 17%), monthly (n=83, 19%), and few times/year (n=109, 25%). Onset of pain was mostly reported as variable (n=127, 30%) or gradual (n=138, 32%). The location of pain included bridge of the nose (n=252, 58%), sides (n=171, 39%), the base (n=146, 34%), or the tip (n=134, 31%) with 275 (64%) reporting pain in at least two locations. Many patients reported nose pain during the day (n=262, 60%), some reported nighttime pain (n=169, 39%) and pain during sleep (n=108, 25%). Most common associated symptoms were redness, swelling, and congestion, each reported by 50% of patients with nose pain.

Conclusion: Most patients with RP reported a wide range of symptoms of nasal disease. Commonest nasal complaints were stabbing pain with associated redness, swelling and congestion that lasts longer than a day, involves the bridge of the nose, and is aggravated by minor trauma. Detailed assessment of nasal manifestations could be helpful for clinicians for establishing a diagnosis and monitoring disease activity.

Disclosure: S. Banerjee, None; **N. Linn**, None; **n. costedoat-Chalumeau**, None; **G. Moulis**, Amgen, 5, Novartis, 1; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **P. Grayson**, None; **M. Ferrada**, None.

Abstract Number: 1872

Differentiating Primary Central Nervous System Vasculitis from Non-inflammatory Intracranial Vasculopathy

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Establishing the diagnosis of Primary central nervous system vasculitis CNSV is challenging. In this study we aimed to investigate distinguishing primary CNSV compared to non-inflammatory intracranial vasculopathy using features in clinical presentation and blood and cerebrospinal fluid (CSF) markers.

Methods: We evaluated all cases enrolled in CNS vasculopathy registry (2012- present) which include patients with CNSV and other vasculopathies that mimics CNSV. Final diagnoses was verified with the last follow up. Final diagnosis of primary CNSV was based on criteria proposed by Calabrese and Mallek namely (1) the presence of an unexplained neurologic deficit after thorough clinical and laboratory evaluation, (2) documentation by cerebral angiography and/or tissue examination of an arteritic process within the central nervous system, and (3) no evidence of a systemic vasculitis or any other condition to which the angiographic or pathologic features could be secondary. In cases without evidence of histological confirmation, the diagnosis of CNSV was made according to the clinical pictures, MRI abnormalities, cerebral vascular imaging, and the presence of inflammatory CSF profiles and absolute certainty of the diagnosis that lead to therapeutic trial. Infectious vasculopathy, reversible cerebral vasoconstriction syndrome, systemic inflammatory disease, and cardio-embolic disease were excluded (Table 1). Clinical features on first presentation such as gender, ethnicity, clinical presentation, past medical history, and medications in addition to serum and CSF findings were investigated for their ability to predict the final diagnosis. CSF pleocytosis was defined as CSF white blood cell count ≥ 5 cells/μL and elevated CSF protein > 45 mg/dL.

Results: A total of 206 patients were identified with definite final diagnosis. 36 patients with CNSV and 26 with non-inflammatory vasculopathies (large vessel atherosclerotic disease, small vessel disease, intracranial dissection, and amyloid vasculopathy) were included. Demographics, clinical presentation, and comorbidities in two groups were not

Table 1. Flowchart of Inclusion and ExclusionDiagnoses within the Cohort

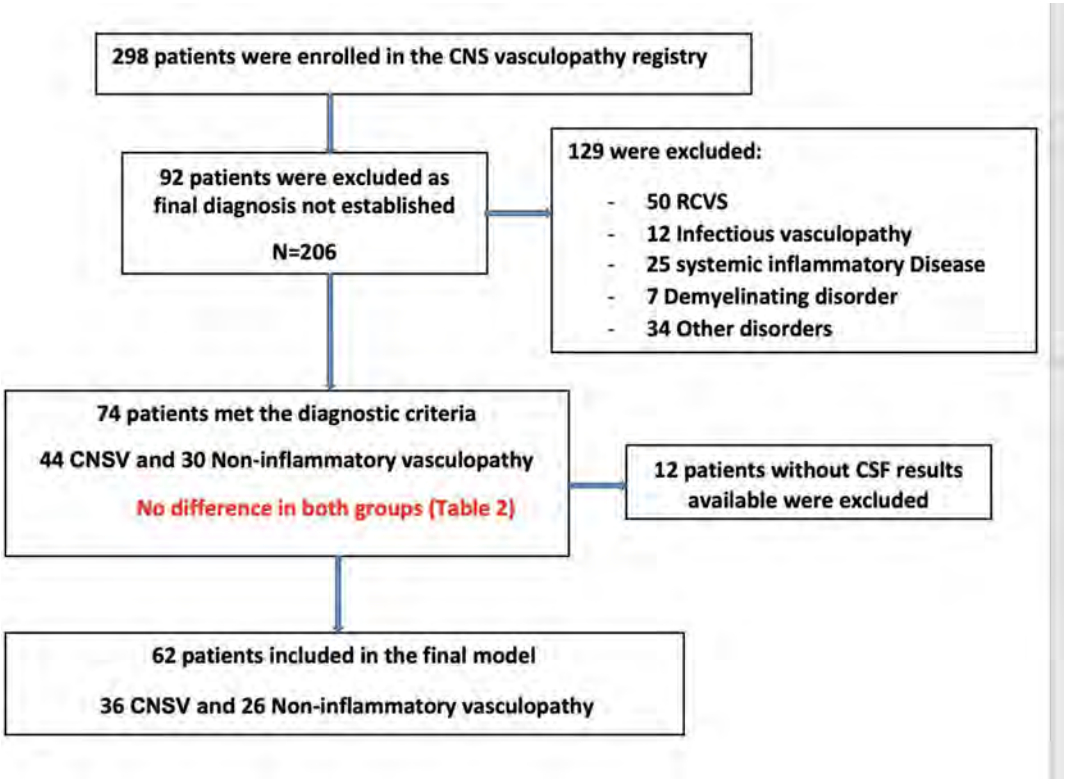

Table 2. Comparison of CNSV vs Non -inflammatory vasculopathies

	CNSV (N = 44)	Noninflammatory (N = 30)	P value
Gender			
Male, N (%)	26 (59.1)	10 (33.3)	0.030*
Race			
White, N (%)	39 (88.6)	24 (80)	0.305
African American, N (%)	1 (2.3)	4 (13.3)	0.063
Clinical presentation			
Headache, N (%)	23 (52.3)	14 (46.7)	0.636
Seizure, N (%)	9 (20.5)	10 (33.3)	0.213
Visual symptoms, N (%)	16 (36.4)	8 (26.7)	0.382
Language deficits, N (%)	22 (50.0)	7 (23.3)	0.021*
Focal neurological deficit, N (%)	19 (43.2)	11 (36.7)	0.575
Altered mental status, N (%)	14 (31.8)	6 (20.0)	0.261
Memory impairment, N (%)	22 (50.0)	10 (33.3)	0.155
Behavioral disturbance, N (%)	15 (34.1)	7 (23.3)	0.320
Past medical history			
Hyperlipidemia, N (%)	11 (25.0)	16 (53.3)	0.013*
Hypertension, N (%)	15 (34.1)	14 (46.7)	0.277
Diabetes mellitus, N (%)	8 (18.2)	6 (20.0)	0.845
Meningitis, N (%)	2 (4.5)	2 (6.7)	0.692
Head trauma, N (%)	3 (6.8)	2 (6.7)	0.980
Serum			
Elevated CRP, N (%)	6 (14.0)	1 (3.3)	0.129
Abnormal ANA, N (%)	2 (4.7)	4 (13.3)	0.184
CSF			
Pleocytosis, N (%)	24 (66.7)	3 (11.5)	< 0.001*
Mean ± SD (cells/μL)	46.8 ± 132.9	5.3 ± 13.7	0.119
Elevated protein, N (%)	24 (66.7)	11 (42.3)	0.056
Mean ± SD (mg/dL)	67.0 ± 31.4	47.3 ± 23.2	0.009*

Statistically significant results are highlighted with *. N=number. SD = standard deviation. CRP= C-reactive protein. ANA = antinuclear antibody.

significantly different with the exception higher prevalence of male gender and language deficits in CNSV group and higher prevalence of transient ischemic attack and hyperlipidemia in the past medical history of non-inflammatory vasculopathy group (Table 2). A logistic regression model was evaluated with the top 3 features identified in descending order included CSF pleocytosis (coefficient: 1.682), past medical history of hyperlipidemia (coefficient: -0.638), and seizure at presentation (coefficient: 0.478). The model predicted CNSV in validation cohort with sensitivity of 69% and specificity of 76%. This model was then cross-validated and was able to predict CNSV with AUC 0.81, sensitivity 69.44% and specificity 75.86%. The calibration plot for this model is demonstrated in Figure 1.

Conclusion: In this study, we demonstrated that differentiating inflammatory form non-inflammatory CNS vasculopathy can be enhanced using a simple logistic regression model based on patient's past medical history, clinical presentation, and CSF profile using a logistic regression model.

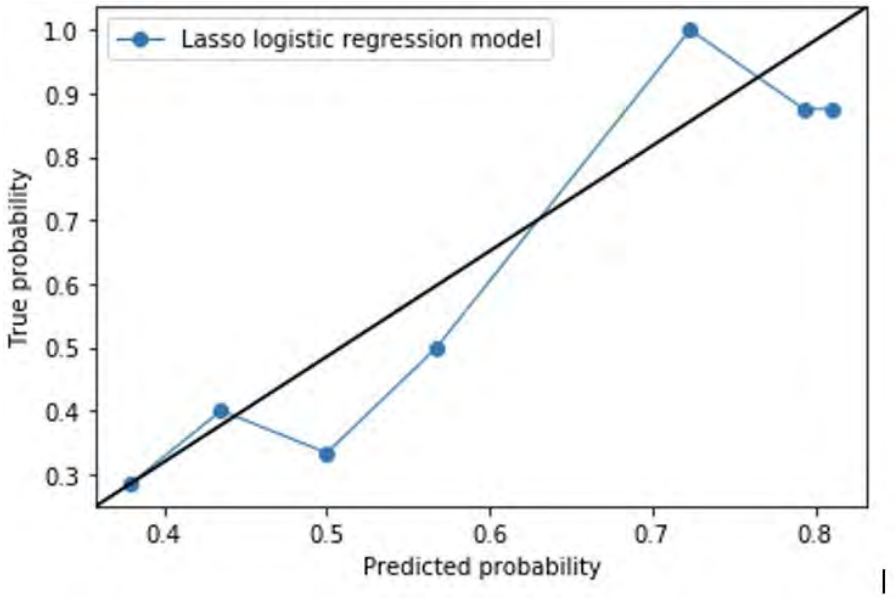

Figure 1. Logistic regression model.

Disclosure: M. Amin, None; **T. Shimoyama**, None; **K. Uchino**, Abbott Laboratories, 1; **L. Calabrese**, Lilly, 2, BMS, 2, Genentech, 2; **R. Hajj-Ali**, Novartis, 6, Rockpointe, INC., 6, Projects In Knowledge, 6, UpToDate, 9.

Abstract Number: 1873

The Importance of Lower Extremity Vein Wall Thickness in Patients with Behcet's Syndrome

Hasan Emre Kocabay[1], M. Enes Yayla[2], Evren Ustuner[1], **Emine Uslu yurteri**[3], Emine Aydemir Guloksuz[4], Serdar Sezer[2], Kinikli Gulay[4], Murat Turgay[4] and Askin Ates[4], [1]Ankara University, Ankara, Turkey, [2]Ankara Training and Research Hospital, Ankara, Turkey, [3]Hatay Training and Research Hospital, Hatay, Turkey, [4]Ankara University Faculty of Medicine, Department of Internal Medicine, Division of Rheumatology, Ankara, Turkey

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Behçet's syndrome (BS) is a multisystemic chronic vasculitic disease that has mucocutaneous and joint involvement in addition to vascular, neurological and gastrointestinal involvement (1).

Earlier studies. showed that Behcet's Syndorme patients have increased vein wall thickness (2-3) .

We aimed to show that vein wall thickness may be an indicator of vascular involvement in Behcet's syndrome patients.

Methods: We enrolled 30 mucocutaneous BS, 30 vascular BS, 30 ankylosing spondylitis (AS) and 30 healthy controls (HC). Bilateral lower extremity vein wall thickness evaluated by B-mode ultrasonography by a blinded radiologist. The thickest part of vein wall was measured in milimeters.

Table 1-Demographic characteristics

	Helathy control	Ankylosing spndylitis	MC BS	Vasc BS	P
Age	49±9.4	44.4±9.7	43.7±9.5	43.7±12.1	0.033
Gender Male Female	 8 (26.7) 22(73.3)	 13((43.3) 17(56.7)	 10(33.3) 20(66.7)	 16(53.3) 20(66.7)	0.162
Ever smoked	13(43.3)	12(40)	9 (30)	15 (50)	0.460
BMI	25.1±3.7	26.5±2.9	25.2±4	24.9±4.5	0.363
ESR (mm/h)	8 (8.3)	11.5 (19)	10 (13.3)	7 (12)	0.387
CRP (mg/L)	3.71.95(3.8)	3.3 (5.9)	2(4.8)	2.4(6.7)	0.137

(Abbreviation: BMI: Body mass index, MC BS: mucocutaneous Behcet's syndrome Vas BS:vascular Behcet's syndrome ESR:erythrocyte sedimentation rate, CRP: C-reactive protein)

Patients were compared between groups by measuring vein wall thickness with lower extremity vein doppler ultrasound.

Results: The demographic characteristics of the patient groups and the healthy group included in the study are given in Table 1.

While there was no differences between the four groups in terms of vascular wall thickness in the common femoral vein (CFV) and popliteal vein. Venous wall thickness in the vena saphena parva and magna, which are the superficial vein, was found to be significantly higher in patients with vascular BS patients compared to the other groups (table 2).

Table 2-Evaluation of venous venous wall thickness of healthy control and patient groups

	Healthy control (30)	Ankylosing spondylitis(n=30)	MC BS (30)	Vasc BS (30)	P
Right Common femoral vein	0.13±0.02	0.13±0.02	0.14±0.02	0.14±0.04	0.246
Left Common femoral vein	0.12±0.02	0.12±0.03	0.13±0.02	0.13±0.04	0.399
Right femoral vein	0.13±0.02	0.12±0.03	0.12±0.02	0.15±0.08	0.357
Left femoral vein	0.12±0.02	0.11±0.02	0.12±0.02	0.16±0.07	**0.001**
Rignt Vena Saphena magna distalis	0.14±0.08	0.18±0.12	0.20±0.14	0.40±0.22	**<0.001**
Left Vena Saphena magna distalis	0.14±0.10	0.16±0.09	0.18±0.10	0.39±0.18	**<0.001**
Riht Vena Saphena Parva	0.19±0.16	0.18±0.12	0.27±0.19	0.47±0.27	**<0.001**
Left Vena Saphena Parva	0.20±0.19	0.17±0.12	0.26±0.18	0.44±0.24	**<0.001**
Right popliteal vein	0.12±0.02	0.13±0.03	0.13±0.02	0.19±0.18	0.05
Left popliteal vein	0.12±0.02	0.13±0.03	0.13±0.02	0.21±0.31	0.095

(Abbreviation:, MC BS: mucocutaneous Behcet's syndrome Vas BS:vascular Behcet's syndrome)

Table 3-Vessel wall thickness on the affected and unaffected side

	Limb on the effected side (n:12)	Limb on the non effected side n(12)	p
Common femoral vein	0.13±0.02	0.13±0.02	1
Femoral vein	0.18±0.11	0.18±0.10	0.772
Vena Saphena magna distalis	0.44±0.27	0.38±0.19	0.527
Vena saphena parva	0.43±0.26	0.36±0.17	0.470
Popliteal Verin	0.21±0.0.28	0.26±0.46	0.450

In 12 BS patients with unilateral deep vein thrombosis (DVT), ipsilateral affected vein and non-affected controlateral vein wall thicknesses were compared. No significant difference was found between the affected vein and the non-affected vein wall thickness (table 3).

Conclusion: In a study by Alibaz-Öner et al., CFV wall thickness was found to be significantly higher in BS patients (2). In a study conducted by Seyahi et al. in 2019, the wall thickness of the superficial and deep veins in vascular BS patients was found to be higher than those of BS patients without vascular involvement and healthy controls.(3). In our study, significant difference was found in all superficial veins,but not all deep veins.

In a study conducted with non-inflammatory DVT patients, it was shown that the venous wall vessel thickness with DVT was higher than the healthy side (4). However, when we look vascular BS patients an increase in affected and nonaffected vessels wall thickness was observed in our study.

In this context, measurement of vessel wall thickness in healthy veins in patients with unkown origin DVT may perhaps guide us in the diagnosis of Behçet's syndrome. The fact that our number of patients is only 12 limits our interpretation in this case.

The slower blood flow in superficial veins than in deep veins may prolong the exposure time of these vessels to inflammatory cytokines. This may cause a more pronounced increase in the superficial vein wall thickness.

In this study, we wanted to investigate a method to predict vascular involvement in BS patientes. We found a marked increase in the superficial venous wall thickness in patients with vascular BS. Measurement of superficial vein wall vessel thickness may be an effective way to predict vascular involvement in BS patients.

The fact that there is no other patient group with thrombosis and that the ultrasonography is performed by a single radiologist are important limitations of our study.

Disclosure: H. Kocabay, None; **M. Yayla**, None; **E. Ustuner**, None; **E. Uslu yurteri**, None; **E. Aydemir Guloksuz**, None; **S. Sezer**, None; **K. Gulay**, None; **M. Turgay**, None; **A. Ates**, None.

Abstract Number: 1874

Using 18F-fluorodeoxyglucose Positron Emission Tomography to Standardize Clinical Trial Recruitment in Takayasu's Arteritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Disease activity assessment can be challenging in Takayasu's arteritis (TAK), which can lead to difficulty in determining eligibility for enrollment into randomized clinical trials (RCTs). FDG-PET can complement clinical assessment of disease activity. The study objective was to determine whether incorporation of PET data, in addition to clinical assessment, influences decisions about trial enrollment in TAK.

Methods: An online survey was completed by physicians with expertise in TAK. Participants were asked background questions, including personal experience with use of PET. Clinical vignettes of commonly-encountered clinical scenarios were presented, based on actual cases derived from a prospective, observational cohort. In part A of each vignette, clinical symptoms, examination findings, acute phase reactant (APR) levels, and angiographic data were presented. Participants were asked if there was sufficient evidence of active vasculitis to enroll into a RCT studying a new treatment agent and to rate level of confidence about their assessment (scale of 0-100). In part B, detailed information from the same patient's PET scan was presented and participants were again asked whether they would enroll

Table 1: Disease activity assessments from part A and part B of the clinical vignettes in the context of potential enrollment of the patient into a clinical trial for Takayasu's arteritis

	Clinical symptoms	Acute phase reactants	Part A: Enrolled (n, %)	Part A: Not Enrolled (n, %)	FDG-PET	Part B: Enrolled (n, %)	Part B: Not Enrolled (n, %)	Level of Confidence (Part A→Part B)
Case 1	Active symptoms (carotidynia, headache)	Elevated	54 (84%)	10 (16%)	Active	63 (98%)	1 (2%)	79%→93%
Case 2	Symptoms of damage (stable arm claudication)	Normal	1 (2%)	61 (98%)	Active	20 (33%)	41 (67%)	74%→69%
Case 3	Symptoms of damage (stable arm claudication)	Normal	0 (0%)	61 (100%)	Inactive	1 (2%)	60 (98%)	82%→91%
Case 4	Fatigue	Elevated	19 (31%)	42 (69%)	Active	54 (89%)	7 (11%)	62%→80%
Case 5	Fatigue	Elevated	16 (26%)	45 (74%)	Inactive	9 (15%)	52 (85%)	64%→75%
Case 6	Fatigue	Elevated	24 (39%)	37 (61%)	Active	55 (90%)	6 (10%)	65%→80%
Case 7	No symptoms	Normal	1 (2%)	60 (98%)	Active	21 (34%)	40 (66%)	83%→69%
Case 8	No symptoms	Normal	2 (3%)	59 (97%)	Inactive	3 (5%)	58 (95%)	83%→93%

FDG-PET: 18F-fluorodeoxyglucose Positron Emission Tomography

Table 2: Generalized linear mixed model to evaluate associations between PET activity, acute phase reactant levels, and enrollment decisions in part A and part B

	Predictor Variable*	Effects Estimate (95% confidence interval)	p-value
Part A	Elevated acute phase reactants (yes/no)	4.61 (2.68 - 6.55)	p<0.001
Part B	Elevated acute phase reactants (yes/no)	3.58 (2.77 - 4.39)	p<0.001
	PET activity (yes/no)	4.63 (3.62 - 5.65)	p<0.001

* All models adjusted for participant and case as random effects.

the patient into a RCT and level of confidence about their assessment. Generalized linear mixed models, adjusting for correlated data, were used to evaluate associations between PET activity, APR levels, and enrollment decisions.

Results: Sixty-eight vasculitis experts completed the survey. The majority of physicians were from Europe [n=45 (66%)] or North America [n=16 (24%)] and most were rheumatologists [n=54 (79%)]. Physicians had varying experience with managing patients with TAK: < 10 patients [n=15 (22%)], 10-40 patients [n=32 (47%)], and >40 patients [n=21 (31%)]. Most physicians reported using PET to diagnose TAK [n=56 (82%)] and to monitor disease activity [n=45 (66%)].

In part A of the vignettes, greater variability in trial enrollment decision was observed in cases of constitutional symptoms alone (e.g. fatigue) and elevated APR levels (Cases 4-6) **(TABLE 1)**.

In Part B, level of confidence improved when PET findings aligned with clinical assessment from Part A (Case 1,3,8). In cases where PET findings did not align with clinical assessment in part A (e.g. absent clinical symptoms with active PET scan, “subclinical inflammation”), the degree of variability about whether to enroll/not enroll increased in Part B and level of confidence worsened (Case 2, 7). In cases with the highest variability about enrollment in part A (Cases 4-6), PET activity drove the decision of whether to enroll in Part B and level of confidence improved. PET activity and APR levels independently contributed to trial enrollment decisions **(TABLE 2)**.

Conclusion: Physicians vary about which patients with TAK should be enrolled into RCTs. Incorporation of PET findings with clinical assessment influences trial enrollment decisions and improves physician confidence about disease activity assessment. Cases of subclinical inflammation pose unique challenges for trial enrollment. Future RCTs in TAK should consider incorporating PET findings into eligibility criteria.

Disclosure: K. Quinn, None; **H. Alessi**, None; **E. Rose**, None; **M. Ahlman**, None; **C. Redmond**, None; **Y. Luo**, None; **E. bolek**, None; **C. Langford**, None; **C. Ponte**, None; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **P. Grayson**, None.

Abstract Number: 1875

Hyoscine Butylbromide Inhibits Neutrophil Cell Death Induction by Cocaine-levamisole. a Proof of Concept for the Management of Vasculopathy Induced by Cocaine-Levamisole

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The Vasculopathy induced by Cocaine-Levamisole (VICOL) is a recently described vasculopathy characterized by the presence of tissue necrosis. One of the possible mechanisms associated with this disease is the presence of NETosis a type of cell neutrophil cell death. The content of Nets is involved in endothelial activation and could explain the clinical manifestations. The muscarinic receptors M3 could be activated by levamisole and induce Netosis, an event that triggers the inflammation associated with the disease.

Methods: Neutrophils from healthy controls were isolated on a density gradient Ficoll-Dextran 3%, and cell viability and purity were assessed by stain with PI, DIOC6, and CD45-PCy7 and CD33-PE, respectively. After that, the induction of NETosis was evaluated through treatment with 40μM of Cocaine and 20nM of Levamisole and a mix of two components (40μM and 20nM). Then, neutrophils were cultured in polystyrene test tubes for 6 hours. As a positive

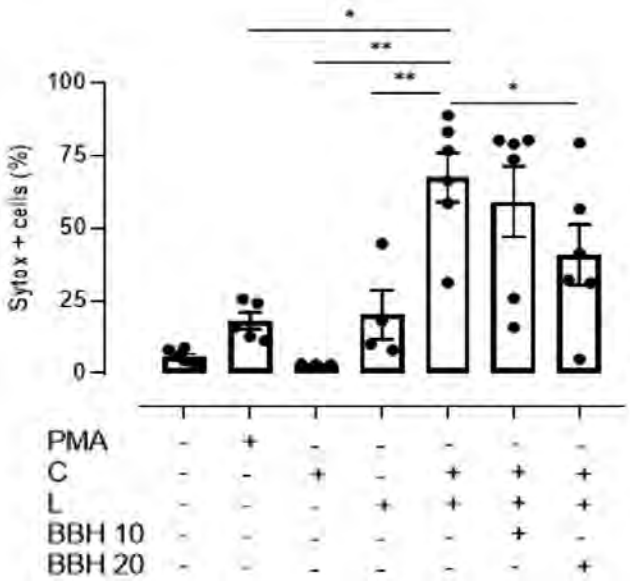

Figure 1. Hyoscine Butylbromide inhibits neutrophil cell death induction by cocaine-levamisole. Percentage of neutrophils cell death stimulated by PMA [10 nM], cocaine (C) [40 μM], levamisole (L) [20 nM] cocaine-levamisole (C-L) and non-stimulated cells (n=5). Inhibition of cell death by Hyoscine Butyl bromide (BBH) at 10nM and 20 nM induced by cocaine-levamisole (C-L+I) (n=5). ANOVA I and Bonferroni comparison of means was used to calculate the p-value. Error bars represent mean ± SEM. *p < 0.05, **p< 0.01, ***p<0.001.

control, 10 nM PMA was used. The presence of cell death was established by stains with 2μM Sytox and 1μg/μl Hoechst using cytometry. The double-positive cells indicate the presence of cell death. For the evaluation of inhibition, 10 nM and 20 nM of Hyoscine Butylbromide were added to the cultures before the stimulus, and the presence of cell death was also evaluated by cytometry. Flow cytometer data was analyzed using FlowJo, and statistical analysis was performed using GraphPad Prism V.8.

Results: The induction of neutrophil cell death was observed in the presence of cocaine and levamisole. A mean of 2.52% (range 0.443-3.35) and 20.28% (8.02-44.7) of neutrophils suffer cell death in the presence of cocaine and levamisole, respectively. The mix of Cocaine-Levamisole increases the median of cell death by 67.43% (31.3-88.8). The PMA was used as a control and induce cell death of 17.96% (11.3- 25.6). The cell death inhibition was assessed in neutrophils treated with Cocaine-Levamisole in the presence of 10nM and 20nM Hyoscine Butylbromide. The percentage of inhibition observed was 59.15% (15.9-80.3) with 10 nM of inhibitor and 40.95% (4.9-79.4) with 20 nM of inhibitor. As negative control not treated- neutrophils were evaluated and showed a cell death induction of 5,86% (3.5-8.9).

Conclusion: These results show that Levamisole induces a higher proportion of cell death than Cocaine, the mix of Cocaine-Levamisole enhanced the percentage of cell death. Hyoscine Butylbromide can inhibit the cell death induced by Cocaine-Levamisole. This is the first evidence of the capacity of Hyoscine Butylbromide to inhibit this phenomenon. In this study, we used flow cytometry as a tool for the evaluation of cell death that suggests NETosis. However, this strategy of flow cytometry should be assessed with antibodies against molecules involved in NETosis. The evidence of this study could suggest the potential use of this medicament to reduce the clinical manifestations of VICOL.

Carmona-Rivera C, et al. A role for muscarinic receptors in neutrophil extracellular trap formation and levamisole-induced autoimmunity. JCI Insight. 2017 Feb 9;2(3):e89780.

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Abstract Number: 1876

A Prospective Observational Cohort Study and Systematic Review of 40 Patients with Mouth and Genital Ulcers with Inflamed Cartilage (MAGIC) Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Background/Purpose: Mouth and genital ulcers with inflamed cartilage (MAGIC) syndrome is a rare and poorly understood entity with clinical features of both relapsing polychondritis (RP) and Behcet's disease (BD). This study characterized the clinical features of MAGIC syndrome and derived a disease definition for use in future studies.

Methods: Adult patients within an ongoing prospective, observational cohort study in RP were clinically assessed for MAGIC syndrome. A systematic review was conducted to identify additional cases of MAGIC syndrome. Clinical characteristics were compared between the pooled cases of MAGIC syndrome and cases of non-MAGIC RP. The performance characteristics of three different criteria to classify MAGIC syndrome were evaluated.

Results: Of the 96 patients with RP in the cohort study, 13 (14%) had MAGIC syndrome. The systematic review identified 27 additional MAGIC syndrome cases in literature. Patients reported in the literature were more likely to have ear chondritis (96% vs 54%, $p < 0.01$) and less likely to have nasal chondritis (63% vs 100%, $p = 0.02$), airway chondritis (19% vs 69%, $p < 0.01$), and costochondritis (7% vs 85%, $p < 0.01$) when compared with patients in the cohort study. When comparing clinical manifestations seen in BD, patients with MAGIC reported in the literature had a greater prevalence of BD-related cutaneous involvement (erythema nodosum, pseudofolliculitis or pathergy) than patients in the cohort study (48% vs 8 %, $p = 0.01$). Raynaud's phenomenon was reported in 54% patients in the cohort study but was not described in any cases of MAGIC syndrome reported in literature. Anti-collagen II antibodies were not reported in any MAGIC syndrome cases in literature.

Pooling the 40 cases together and comparing them with non-MAGIC RP, there was significantly higher prevalence of almost all BD-related features in patients with MAGIC syndrome, including BD-related ocular involvement (uveitis or retinal vasculitis (, 28% vs 4%, $p < 0.01$), BD-related cutaneous involvement (erythema nodosum, pseudofolliculitis or pathergy (, 35% vs 1%, $p < 0.01$), GI involvement (23% vs 4%, $p < 0.01$) and CNS involvement (8% vs 0, $p=0.04$). There was also a higher prevalence of aortitis (23% vs 1%, $p < 0.01$) and Raynaud's phenomenon (54% vs 11%, $p < 0.01$) and anti-collagen II antibodies (50% vs 9%, $p=0.04$) in MAGIC syndrome. Fulfillment of either McAdam's or Damiani's Criteria for RP plus the International Criteria for Behçet's Disease (ICBD) had excellent sensitivity (98%) to classify cases of MAGIC syndrome. Use of presence of oral and genital ulcers to define MAGIC syndrome had lower sensitivity (88%). In contrast, the International Study Group (ISG) criteria performed poorly for defining MAGIC syndrome with low sensitivity (43%).

Conclusion: MAGIC syndrome can be diagnosed in a substantial proportion of patients with RP. These patients have features of RP, BD, and other unique features such as aortitis, Raynaud's phenomenon and anti-collagen II antibodies. Fulfillment of McAdam's or Damiani's criteria for RP and the ICBD criteria for BD can be used to define MAGIC syndrome in future research studies.

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Abstract Number: 1877

Takayasu Arteritis Patients with Tuberculosis Have Unique Clinical Characteristics

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Takayasu's arteritis (TAK) is an idiopathic inflammatory disease primarily affecting the aorta and its major branches. *Mycobacterium tuberculosis* is prevalent in developing countries and can cause latent or active tuberculosis (TB) of the lung or other organs. Increased prevalence of TB has been reported in TAK but a causal relationship has not been established. The study objective was to determine if clinical characteristics differ among patients with TAK with known TB exposure.

Methods: Patients with TAK were recruited to a prospective observational cohort. All patients fulfilled the 1990 ACR Classification Criteria for TAK. TB was identified by medical history and/or Quantiferon-Gold screening. Categorical and continuous variables were compared using the Fisher's exact test and Mann-Whitney test, respectively. Vascular calcification was based on radiology report of high-density lesions consistent with calcium deposition in large- or medium-size arterial territories on CT scans. Relapse was defined as clinical assessment showing recurrence of active vasculitis requiring escalation of immunosuppressive therapy after a period of stable remission. Incidentally found was defined as receiving diagnostic work up for non-TAK non-TB related indications which leads to unexpected discovery of vascular pathology. Asymptomatic was defined as complete absence of any vascular or systemic symptoms.

Results: Among 80 patients with TAK, 10 patients had a history of TB. 8 patients had latent TB, 1 patient had TB endometritis, and 1 patient had TB lymphadenitis and erythema induratum. All patients with active TB completed anti-active TB treatment. 7 of out 8 patients with latent TB completed anti-latent treatment and 1 patent with latent TB was recommended to start treatment. The majority of the patients were female (9 (90%) in TB-TAK and 61 (87%) in non-TB TAK). Compared to those without TB, TAK patients with TB were older at diagnosis (35 vs 26 years, p=0.03) and less likely to be Caucasian (9 (10%) vs 51 (73%), p=0.002). TAK patients with TB had longer disease duration (17 vs 9 years, p=0.03), were more likely to be asymptomatic at diagnosis (2 (20%) vs 1 (1%), p=0.001) or diagnosed based on incidentally found vascular pathology (50% vs 6%, p=0.005). Patients with TB-TAK had distinct patterns of vascular disease, including increased thoracic aorta involvement (80% vs 40%, p=0.037), aortic aneurysms (5 (50%) vs 4 (16%), p=0.01), and vascular calcification (4 (40%) vs 9 (13%), p=0.05). In terms of treatment, patients with TAK-TB were less likely to have ever received treatment with glucocorticoids (5 (50%) vs 64 (91%), p=0.003), DMARDs (6 (60%) vs 65 (93%), p=0.012), or biologics (2 (20%) vs 43 (61%), p=0.018). Despite receiving less treatment, relapse was less frequent in patients with TB-TAK (3 (30%) vs 45 (66%), p=0.039).

Conclusion: Patient with TAK and TB have unique clinical characteristics. Compared to other patients, patients with TAK and TB are more likely to have clinically indolent disease, have more structural damage to the aorta, receive less

	TAK with TB n = 10	TAK without TB n = 70	P value
Demographic Information			
Age (mean years, SD)	49 (38-61)	36 (23-50)	0.006
Sex, Female n (%)	9 (90)	61 (87)	1.000
Race, White n (%)	1 (10)	51 (73)	0.002
Clinical characteristics			
Age at symptom onset (mean year, SD)	31 (17-45)	24 (12-36)	0.103
Age at diagnosis (mean years, SD)	35 (24-46)	26 (14-38)	0.031
Diagnostic delay (mean years, SD)	4.5 (2.1-8.2)	3.9 (-0.4-6.7)	0.148
Disease duration (mean years, SD)	17 (5-28)	9 (1-18)	0.033
Incidentally found n (%)	5 (50)	4 (6)	0.005
Asymptomatic n (%)	2 (20)	1 (1)	0.001
Constitutional symptoms n (%)	2 (20)	14 (20)	1.000
Elevated ARP at diagnosis n (%)	5 (50)	39 (57)	0.740
Rash n (%)	2 (20)	18 (26)	1.000
Inflammatory eye disease n (%)	0 (0)	4 (6)	1.000
Arthritis n (%)	1 (10)	7 (10)	1.000
Preceding recurrent pharyngitis n (%)	1 (10)	9 (13)	1.000
Venous thromboembolism n (%)	1 (10)	3 (4)	0.420
Vascular involvement			
R carotid artery n (%)	3 (30)	37 (53)	0.311
L carotid artery n (%)	4 (40)	50 (71)	0.070
R subclavian artery n (%)	3 (30)	28 (40)	0.733
L subclavian artery n (%)	4 (40)	43 (61)	1.000
R axillary artery n (%)	1 (10)	15 (21)	0.677
Pulmonary arteries n (%)	2 (20)	10 (14)	0.641
Thoracic aorta n (%)	8 (80)	28 (40)	0.037
Abdominal aorta n (%)	5 (50)	22 (31)	0.293
Mesenteric arteries n (%)	4 (40)	18 (26)	0.450
R renal artery n (%)	3 (30)	15 (21)	0.686
L renal artery n (%)	4 (40)	16 (23)	0.258
R iliac artery n (%)	3 (30)	9 (13)	0.168
L iliac artery n (%)	2 (20)	5 (7)	0.210
Vascular calcification n (%)	4 (40)	9 (13)	0.052
Active vasculitis on PET n (%)	4 (57)	34 (78)	0.352
Treatment			
Steroid n (%)	5 (50)	64 (91)	0.003
csDMARD n (%)	6 (60)	65 (93)	0.012
Biological or ts- DMARD n (%)	2 (20)	43 (61)	0.018
Outcomes			
Relapse n (%)	3 (30)	45 (66)	0.039
Interventional procedures n (%)	5 (50)	24 (34)	0.483
Aortic aneurysm n (%)	5 (50)	11 (16)	0.014
Cerebrovascular accident n (%)	2 (20)	9 (13)	0.621

a. 51 TAK patients have PET-CT data available, 7 TB TAK and 44 non-TB TAK.

treatment, and are less likely to experience relapse. These data provide preliminary evidence in support of a potential causal relationship between TAK and TB.

Disclosure: Y. Luo, None; **K. Quinn**, None; **M. Ferrada**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 1878

Tocilizumab in Caucasian Patients with Takayasu Arteritis: Multicenter Study of 54 Patients

Diana Prieto-Peña[1], Pilar Bernabeu[2], Paloma Vela[3], Javier Narvaez[4], Jesús Carlos Fernández-López[5], Mercedes Freire[6], Beatriz González-Alvarez[7], Roser Solans-Laqué[8], José Luis Callejas[9], Norberto Ortego[10], Carlos Fernández-Díaz[11], Esteban Rubio Romero[12], Salvador Garcia-Morillo[13], Mauricio Minguez[14], Cristina Carballido[14], Eugenio De Miguel[15], Sheila Melchor[16], Eva Salgado[17], Beatriz Bravo[18], Susana Romero-Yuste[19], Juan Salvatierra[20], Cristina Hidalgo[21], Sara Manrique Arija[22], Carlos Romero Gomez[23], Patricia Moya[24], Noelia Álvarez-Rivas[25], Javier Mendizábal-Mateos[26], Francisco Ortiz-Sanjuán[27], Ivan Perez De Pedro[28], Jose L Alonso-Valdivielso[29], Laura Perez-Sanchez[30], Rosa Roldan[31], Nagore Fernandez-Llanio[32], Ricardo Gómez de la Torre[33], Silvia Suarez[33], Mara Jess Montesa Cabrera[34], MONICA DELGADO SANCHEZ[35], Javier Loricera[1], Belén Atienza-Mateo[36], Miguel Ángel gonzalez-Gay[37] and Ricardo Blanco[38], [1]Hospital Universitario Marqués de Valdecilla, santander, Spain, [2]Hospital General Universitario de Alicante-ISABIAL, Alicante, Spain, [3]Hospital General Universitario de Alicante, Alicante, Spain, [4]Division of Rheumatology, Hospital Universitario de Bellvitge, Barcelona, Spain, [5]Hospital Universitario Juan Canalejo, A Coruña, Spain, [6]Rheumatology Service. CHU Coruña, La Coruña, Spain, [7]H. NªSª de la Candelaria, Tenerife, Spain, [8]Hospital Vall d'Hebron, Barcelona, Spain, [9]Hospital San Cecilio, Granada, Spain, [10]Medicine Department, Universidad de Granada, Granada, Spain, [11]Hospital Universitario Reina Sofía, Murcia, Spain, [12]HOSPITAL UNIVERSITARIO VIRGEN DEL ROCIO, Seville, Spain, [13]H Virgen del Rocio, Sevilla, Spain, [14]H. San Juan, Alicante, Spain, [15]Hospital Universitario La Paz, Madrid, Spain, [16]H. 12 de Octubre, Madrid, Spain, [17]Complejo Hospitalario Universitario de Ourense, Ourense, Spain, [18]Hospital Universitario Virgen de las Nieves, Granada, Spain, [19]Complejo Hospitalario Universitario de Pontevedra, Pontevedra, Spain, [20]H San Juan, Alicante, Spain, [21]Hospital Universitario Salamanca, Salamanca, Spain, [22]Hospital Regional de Málaga, Málaga. Spain., Malaga, Spain, [23]H. Regional de Malaga, Malaga, Spain, [24]Hospital Sant Pau, Barcelona, Spain, [25]Hospital San Agustín, Aviles, Spain, [26]H. Navarra, Navarra, Spain, [27]H. La Fe, Valencia, Spain, [28]H. Carlos Haya, Malaga, Spain, [29]H. Burgos, Burgos, Spain, [30]IMIBIC/Reina Sofia Hospital/University of Córdoba, Córdoba, Spain, [31]H. Reina Sofia, Cordoba, Spain, [32]H. Arnau de Vilanova, Valencia, Spain, [33]H. Asturias, Oviedo, Spain, [34]Hospital Universitario Nuestra Seora de la Candelaria, Santa Cruz de Tenerife, Spain, [35]H NªSª Candelaria, Tenerife, Spain, [36]Group "Research in genetic epidemiology and atherosclerosis of systemic diseases and in bone metabolic diseases of the locomotor system", IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [37]Research group on Genetic Epidemiology and Atherosclerosis in Systemic Diseases and in Metabolic Bone Diseases of the Musculoskeletal System, IDIVAL, Division of Rheumatology, Hospital Universitario Marqués de Valdecilla; School of Medicine, Universidad de Cantabria, Santander, Spain. Cardiovascular Pathophysiology and Genomics Research Unit, School of Physiology, Faculty of Health Sciences, University of the Witwatersrand, Johannesburg, South Africa, [38]Hospital Universitario Marqués de Valdecilla, IDIVAL, Santander, Spain

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

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Session Time: 8:30AM–10:30AM

Background/Purpose: Tocilizumab (TCZ) has shown to be effective for large vessel vasculitis including Takayasu arteritis (TAK) **(1-3)**. Most evidence in TAK comes from Asian patients. However, white patients seem to have different clinical and prognostic features.

Our aims were to: **a)** assess the efficacy and safety of TCZ in white patients with refractory TAK, **b)** determine if clinical improvement correlates with imaging outcomes, **c)** compare TCZ in monotherapy (TCZ_{MONO}) vs combined with conventional immunosuppressive drugs (TCZ_{COMBO}).

Methods: Multicenter study of white patients with refractory TAK who received TCZ.Outcomes variables were remission, glucocorticoid-sparing effect, improvement in imaging techniques, and adverse events. A comparative study between patients who received TCZ_{MONO} and TCZ_{COMBO} was performed.

Table.

	Baseline n=54	**Month 1** N=54	**Month 3** N=49	**Month 6** N=44	**Month 12** N=36
Clinical remission, n (%)		12 (22.2)	19 (38.8)	23 (52.3)	27 (75.0)
Laboratory improvement					
CRP (*mg/dL*), median [IQR]	1.5 [0.5-3.5]	0.2 [0.1-0.7]*	0.2 [0.5-0.5]*	0.2 [0.1-0.5]*	0.1 [0.0-0.4]*
ESR (*mm/1st hour*), median [IQR]	30.5 [8.7-52.7]	7.0 [3.0-14.0]*	4.5 [2.0-8.0]*	5.0[2.0-6.0]*	4.0 [2.0-9.5]*
Hemoglobin (*g/dL*), mean ± SD	12.4 ±1.5	13.0 ±1.2*	13.0 ±1.4*	13.2 ±1.5*	12.9 ±1.6*
Prednisone dose, median [IQR]	30.0 [12.5-50.0]	20.0 [10.0-30.0]*	10.0 [5.0-20.0]*	5.0 [5.0-10.5]*	5.0 [0.0-5.6]*

CRP: C-Reactive Protein; **ESR**: Erythrocyte Sedimentation Rate; **IQR:** interquartile range; n: number. *p<0.01 vs baseline (Wilcoxon test).

Results: 54 patients (46 women/8 men; median age 42.0 [32.5-50.5] years). TCZ was started after 12.0 [3.0-31.5] months since TAK diagnosis. Remission was achieved in 12/54 (22.2%), 19/49 (38.8%), 23/44 (52.3%) and 27/36 (75%) at 1, 3, 6 and 12 months, respectively. Prednisone dose was reduced from 30.0 [12.5-50.0] to 5.0 [0.0-5.6] mg/day at 12 months (**Table**). 10 (26.3%) of the 38 patients in whom an imaging follow-up test was performed showed no radiographic improvement after a median of 9.0 [6.0-14.0] months. 4 of them were in clinical remission.23 (42.6%) patients were on TCZ_{MONO} and 31 (57.4%) on TCZ_{COMBO}: MTX (n=28), cyclosporine A (n=2), azathioprine (n=1). Patients on TCZ_{COMBO} were younger (38.0 [27.0-46.0] vs 45 [38.0-57.0] years; p= 0.048), with a trend to longer TAK duration (21.0 [6.0-38.0] vs 6.0 [1.0-23.0] months; p= 0.08) and higher C-reactive protein (2.4 [0.7-5.6] vs 1.3 [0.3-3.3] mg/dL; p=0.16). Despite these differences, similar outcomes were observed in both groups (log rank p=0.862) (**Figure**).

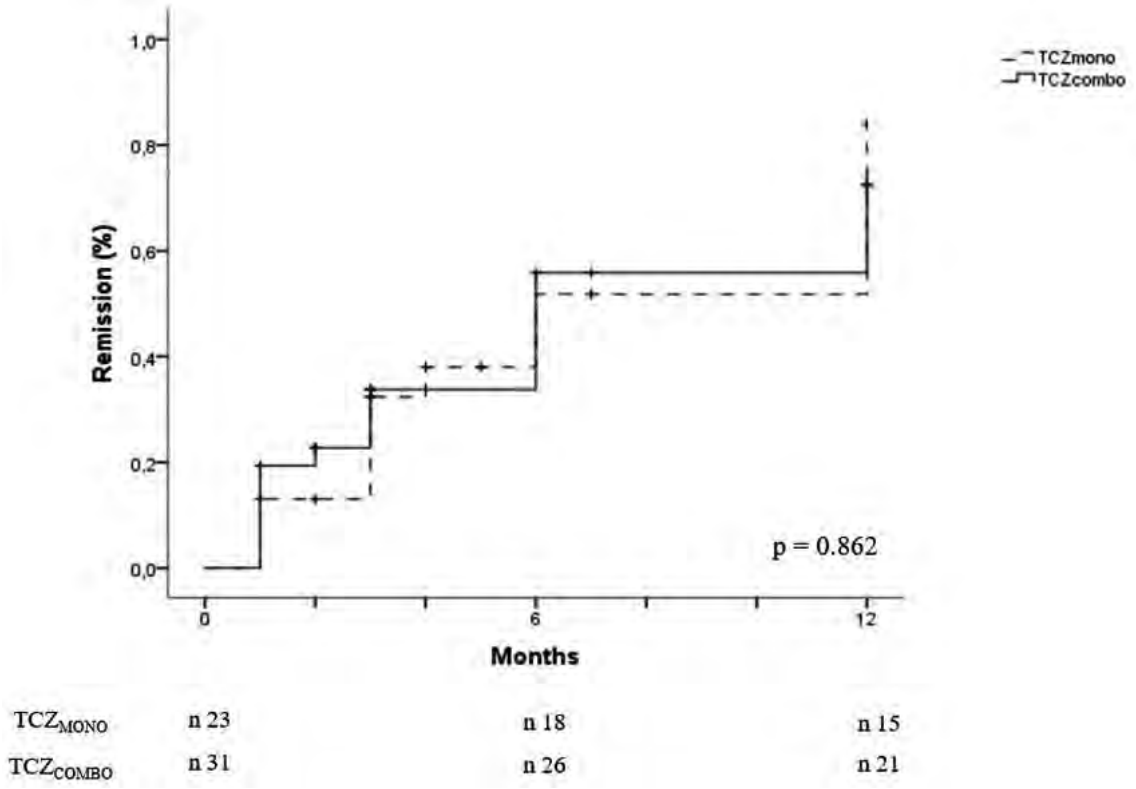

Figure.

Relevant adverse events were reported in 6 (11.1%) patients, but only 3 developed severe events that required TCZ withdrawal.

Conclusion: TCZ is effective and safe in white patients with refractory TAK. A discordance between clinical and imaging activity assessment may exist.

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Abstract Number: 1879

Delayed Diagnosis of IgG4 Related Disease Is Associated with Worse Outcome: A Retrospective, Real-life Observational Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: The purpose of this study was to characterize clinical and pathological features as well as disease outcome of an Israeli incident cohort of patients with IgG4-related disease (IgG4-RD).

Methods: Retrospective, single-center study of incident patients with IgG4-RD diagnosed between 2010 and 2020. IgG4-RD was classified as 'definite', 'probable' or 'possible' according to international consensus guidelines and comprehensive diagnostic criteria for IgG4-RD or if patients fulfilled organ-specific criteria, as well as the 2019 ACR/EULAR classification criteria. Disease activity was determined by means of the IgG4-RD Responder Index (IgG4-RD RI). Disease features, as well as treatment and disease outcome were retrieved from the patients' electronic charts. Disease remission was defined as no clinical and imaging evidence of active disease.

Results: Thirty-six incident patients (30.6% female) with median age of 54.9 years were included in the study: 11 patients (30.56 %) - "definite", 10 patients (27.77%) - "possible", and 15 (41.67%)- "probable" IgG4RD, and 22 patients (61.1%) fulfilled the 2019 ACR/EULAR classification criteria. Nineteen patients (52.8%) had a single-organ disease, 8 patients (22.2%) had involvement of two organs, and 9 patients (25%) had 3 or more organs involved. The most involved organs were lymph nodes (36%), retroperitoneal fibrosis (25%), and pancreas (16.7%). Median follow-up was 28 months (IQR 13.2-40.7). Thirty-three patients (91.67%) had biopsies available for analysis. Lymphoplasmacytic infiltrate, fibrosis and obliterative phlebitis were found in 88.9%, 61.1%, and 11.1%, respectively. Thirty-four patients (94.4%) were treated with prednisone, 38.9% were treated with methotrexate, 27.8% with azathioprine, 5.6% with mycophenolate mofetil and 47.2% with rituximab. Median IgG4-RD RI at diagnosis and at last encounter was 6.0 (IQR 6.0-9.0) and 1.0 (IQR 0.0-2.0), respectively. Six patients died (16.7%) and malignancy was diagnosed in 8 patients (22.2%). At the time of charts review, 16 patients (44.4%) were in remission after a median time of 16 months (IQR 6.0-30.0). Only two patients (5.6%) relapsed. Disease remission was significantly associated with a shorter time from the first symptom to the time of diagnosis (median 3.5 months vs. 18.5 months, p=0.04), lower ACR/EULAR criteria index at diagnosis (p=0.01), and a trend toward lower number of organs involved and higher initial daily prednisone dose (p=0.06 for each parameter). Neither serum IgG4 level at diagnosis, nor type of organ involvement or type of immunosuppressive/biologic drugs used were associated with disease remission. Significantly higher rates of malignancy (p=0.01) and mortality (p=0.03) were demonstrated amongst patients who did not achieve remission

Conclusion: Our data suggest that remission is an achievable target in the management of IgG4-RD and that delayed diagnosis of IgG4-RD is negatively associated with remission.

Disclosure: E. Pokroy-Shapira, None; **I. Sagy**, None; **K. Meridor**, None; **Y. Molad**, None.

Abstract Number: 1880

Description of an Internet-Based Cohort with a Self-Reported Diagnosis of Polyarteritis Nodosa

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Polyarteritis nodosa (PAN) is form of medium-vessel vasculitis with an estimated annual incidence of 1 per million. The rarity of the disease makes traditional center-based approaches to research in PAN challenging. The purpose of this study was to describe an internet-based cohort of participants with a self-reported diagnosis of PAN, and, to determine how many patients met established criteria for this disease.

Table 1. Means of diagnostic confirmation and manifestations of polyarteritis nodosa

Confirmation of diagnosis based on	Number (%)
Biopsy	60 (75)
Symptoms	41 (51)
Labs	37 (46)
General imaging	23 (29)
Angiogram	20 (25)
I don't know	1 (1)
Vasculitis-related manifestations	**Number/responses (%)**
Nerve damage	65/75 (87)
Muscle pain	62/72 (86)
Rash	59/78 (76)
Weight loss	47/78 (60)
Testicular pain (males)	18/34 (53)
Hypertension	27/74 (36)
Kidney problems	25/75 (33)

Methods: Participants with a self-reported diagnosis of PAN were included in a prospective, internet-based, longitudinal registry from November 2014 to May 2020. All patients completed standardized forms collecting data on disease manifestations, diagnostic testing, and treatment. Patients reporting a history of a positive test for ANCA (n=19) were excluded.

Results: 80 participants (58% female) self-reported a diagnosis of PAN without a history of ANCA. Two participants reported a history of hepatitis B viral infection. Race/ethnicity distribution: 87% Caucasian/White, 9% Asian, 8% His-

Table 2. Treating physicians and reported medications at enrollment

Specialty of physician treating the vasculitis	Number (%)
Rheumatology	66 (83)
Primary care	24 (30)
Nephrologist	9 (11)
Dermatologist	5 (6)
Neurologist	3 (4)
Pulmonologist	3 (4)
ENT	1 (1)
Cumulative use of medications	**Number (%)**
Glucocorticoids	69 (86)
Azathioprine	36 (45)
Cyclophosphamide	39 (49)
oral	*20 (25)*
intravenous	*19 (24)*
Methotrexate	28 (35)
Mycophenolate mofetile	16 (20)
Aspirin	12 (15)
Sulfamethoxazole/Trimethoprim	9 (11)
Colchicine	7 (9)
Dapsone	7 (9)

panic/Latino, 5% African American/Black, and 1% Native American. Enrollment included participants from across the world including North America (57), Europe (8), Australia (3), Asia (2), and South America (1). The mean age of onset of symptoms and diagnosis was 42.7 (SD 0.28) and 44.1 (SD 0.30) years. Only 13 participants (16%) were > 65 years old at the time of registration. Four participants were < 18 years old at the onset of symptoms.

Patients reported that the diagnosis was made based on biopsy (75%), symptoms (51%), laboratory studies (46%), or angiogram (25%) (**Table 1**). The most common manifestations of vasculitis included: nerve damage (87%), muscle pain (86%), skin involvement (76%), weight loss (60%), and testicular pain (53% of males) (**Table 1**). Blood clots were reported in 18%. 6 participants reported only skin involvement. The majority (83%) of patients reported that a rheumatologist was their treating physician (**Table 2**). The most common drug exposures included glucocorticoids (86%), cyclophosphamide (49%), and azathioprine (45%) (**Table 2**). 95% of participants met the 1990 American College of Rheumatology Classification Criteria for PAN. 95% of participants met the 2012 Chapel Hill Consensus Conference Definition of PAN.

Conclusion: In an internet platform based on self-reported patient information, the majority of patients met well-established criteria for PAN and reported disease manifestations in similar frequencies to published data from physician-reported cohorts. These results support the use of online patient cohorts to conduct research in PAN.

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Abstract Number: 1881

Surgical Outcomes After Operative Procedures in Patients with Behcet's Disease

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Behcet's disease (BD) is characterized by hyper-inflammatory response to trauma, which is called the pathergy phenomenon. Therefore, there are concerns about post-operative complications when the affected patients undergo surgical procedures. Here, we comprehensively investigated the incidences of postoperative complications after surgical procedures.

Methods: We retrospectively reviewed all the patients with BD who underwent surgeries at Seoul National University Hospital between January 2003 to December 2019. Diagnosis of BD was based on the International Study Group criteria or revised diagnostic criteria for the Behcet's Disease Research Committee of Japan (Japanese criteria). The incidence of surgical complications and the associated factors of surgical wound complications were analyzed.

Results: The patients were composed of 270 patients (49.1 ± 13.6 years at operation, 107 men) and they underwent 356 surgeries. A total of 38 cases (10.7 %) of postoperative complications were found, of which 32 (9 %) were sur-

Table. The incidence of surgical wound complications, reoperations due to surgical wound problems, and death

Type of surgery (N=356)	Surgical wound complications (%)	Reoperations (%)*	Death (%)†
Cardiac (30)	**10 (33.3)**	**6 (20)**	**3 (10)**
Valvular (26)	10 (38.5)	6 (23.1)	3 (11.6)
CABG (3)	0 (0)	0 (0)	0 (0)
Congenital (1)	0 (0)	0 (0)	0 (0)
Vascular (27)	**7 (26)**	**4 (14.8)**	**0 (0)**
Aortic (19)	5 (26.3)	3 (15.8)	0 (0)
Carotid(2)	1 (50)	0 (0)	0 (0)
Peripheral (6)	1 (16.7)	1 (16.7)	0 (0)
Abdominal (64)	**8 (12.5)**	**5 (7.8)**	**0 (0)**
Gastric (3)	1 (33.3)	0 (0)	0 (0)
Intestinal (35)	5 (14.3)	3 (8.6)	0 (0)
Hernia (3)	1 (33.3)	1 (33.3)	0 (0)
Hemorrhoid and anal fistula (6)	0 (0)	0 (0)	0 (0)
HBP (4)	1 (25)	1 (25)	0 (0)
Laparoscopic appendectomy (4)	0 (0)	0 (0)	0 (0)
Laparoscopic cholecystectomy (7)	0 (0)	0 (0)	0 (0)
Other intraabdominal (2)	0 (0)	0 (0)	0 (0)
ENT (25)	**2 (8)**	**0 (0)**	**0 (0)**
Others including skin and soft tissue (26)	**2 (7.7)**	**1 (3.8)**	**0 (0)**
Neurologic (23)	**1 (4.3)**	**0 (0)**	**0 (0)**
Brain (3)	0 (0)	0 (0)	0 (0)
Spine (11)	0 (0)	0 (0)	0 (0)
Vascular (9)	1 (11.1)	0 (0)	0 (0)
Urologic (25)	**1 (4)**	**0 (0)**	**0 (0)**
Gynecologic (42)	**1 (1.6)**	**0 (0)**	**0 (0)**
Opthopedic (55)	**0 (0)**	**0 (0)**	**0 (0)**
Hip (12)	0 (0)	0 (0)	0 (0)
Knee (16)	0 (0)	0 (0)	0 (0)
Others (27)	0 (0)	0 (0)	0 (0)
Thoracic (21)	**0 (0)**	**0 (0)**	**1 (20)**
Endocrinologic (15)	**0 (0)**	**0 (0)**	**0 (0)**
Breast (11)	**0 (0)**	**0 (0)**	**0 (0)**
total	32	16	4

CABG: coronary artery bypass surgery, ENT: ear, nose and throat, HBP: hepatobiliary and pancreatic

* Reoperations due to surgical wound problems

† Death due to current operations

gical wound complications including 16 wound dehiscences (50 %), 11 bleedings (34.4 %), 6 anastomotic dehiscences (18.8 %), 3 wound infections (9.4 %), 2 graft occlusions (6.3 %), and 1 fistula formation (3.1 %) with median time interval 10 days from the operation date (interquartile range (IQR) 5 to 19 days). Sixteen cases (4.5 %) required reoperations due to wound problems, and there were four operation-related deaths (1.1 %). Seventeen cases of long-term surgical recurrences were identified within the median follow-up of 21.5 months (IQR 16.8 to 52.5 months). Most postoperative wound complications occurred after cardiac (33.3 %), vascular (26 %), and gastrointestinal (12.5 %) surgeries, while those rarely occurred after orthopedic, thoracic, endocrinologic, and breast surgeries.

Conclusion: Incidences of postoperative complications vary among different surgeries in BD. The incidences of surgical wound complications are higher in cardiac, vascular, and gastrointestinal surgeries in patients with BD. Special perioperative care is recommended for these surgeries in BD patients.

Disclosure: Y. Jung, None; **E. Lee**, None.

Abstract Number: 1882

Clinical Characteristics and Reliability of a Self-Reported Diagnosis of Large-Vessel Vasculitis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: To compare the clinical characteristics and determine the reliability of a self-reported diagnosis of giant cell arteritis (GCA) or Takayasu's arteritis (TAK) from an international, internet-based cohort.

Methods: Patients with GCA and TAK enrolled in an internet-based registry were included. Data provided by patients were collected through standardized forms, including type of vasculitis, symptoms, results of diagnostic testing, and medication use. The percentage of patients who met the 1990 American College of Rheumatology (ACR) classification criteria were calculated. For the 2012 Chapel Hill Consensus Conference (CHCC) definitions, age >50 years and report of a positive biopsy or imaging were used as surrogates for a diagnosis of GCA, and age < 50 years with diagnosis on imaging were used as surrogates for a diagnosis of TAK.

Results: The study included 250 patients with self-reported diagnoses (126 GCA and 124 TAK).

GCA cohort: The cohort was 80% female, mean (±SD) age 65 (±11.9) years. Mean (±SD) age at diagnosis of GCA was 62 (± 13.5) years. One patient aged 16 years was excluded. 9 patients (7%) reported age < 50 years old at the time of diagnosis (range 31 to 48 years). Of these, 2 patients had a temporal artery biopsy with 1 reported as positive in a 48 year-old. 93 patients (74%) reported having a temporal artery biopsy which was positive in 59 patients (63%). Abnormal imaging was reported in 39 patients (31%), 27 of whom also reported symptoms of limb claudication. The self-reported clinical symptoms of GCA are in Table 1. 87% met ACR classification criteria and 60% met the CHCC definition for GCA (93% met either, 87% met both).

TAK cohort: The cohort was 94% female, mean (±SD) age 42 (±15) years. Mean (±SD) age at diagnosis of TAK was 35 (±14.3) years. Twenty-six (21%) patients with TAK were ≥50 years at diagnosis, 15 patients (12%) with symptom onset at age ≥50 years. 97/112 patients (87%) reported blood pressure discrepancy in the upper extremities. Abnormal imaging was reported in 115 patients (93%). The self-reported clinical symptoms of TAK are outlined in Table 1.The subset of 26 patients ≥50 years old reported similar manifestations as the other patients with TAK, including abnormal angiogram (92%), limb claudication (77%), upper extremity blood pressure discrepancy (77%), bruits (77%). 95% of patients met ACR classification criteria. 75% met the CHCC definition for TAK; the majority who failed to meet the definition criteria did so on account of age. 96% patients met either ACR classification criteria or CHCC definition with 74% meeting both.

Conclusion: Patients with a self-reported diagnosis of GCA or TAK were able to reliably provide information about their symptoms and diagnosis. Clinical symptoms and treatments reported were consistent with what would be expected. The majority in both cohorts met ACR classification criteria or CHCC definitions. The high proportion of patients ≥50 years diagnosed as TAK likely reflects the uncertainty in clinical practice in this age group and classifi-

Table 1: Clinical manifestations in patients with a self-reported diagnosis of giant cell arteritis and Takayasu's arteritis

Clinical Manifestation	GCA* N=126	TAK* N=124
Weight loss >10 pounds	48/74 (65%)	65/118 (55%)
Fever >100.4°F	38/98 (39%)	41/89 (46%)
Myalgia	79/113 (70%)	96/116 (83%)
Headache	102/117 (87%)	70/104 (67%)
Scalp tenderness	93/121 (77%)	29/104 (28%)
Tenderness of temples	98/122 (80%)	36/107 (34%)
Vision loss	33/121 (27%)	28/115 (24%)
Pain/morning stiffness >30 minutes	89/115 (77%)	81/114 (71%)
Dizziness, syncope	60/106 (57%)	74/118 (63%)
Stroke	3/119 (3%)	17/115 (15%)
Chest pain or heart attack	21/119 (18%)	39/109 (36%)
Rash (including livedo, nodules)	34/109 (34%)	34/114 (30%)
Renal problems	15/119 (13%)	21/120 (18%)
Absent/weak pulse	25/91 (28%)	103/118 (87%)
Limb claudication	70/111 (63%)	82/116 (71%)
Bruit, neck/upper chest	9/111 (8%)	81/114 (71%)
Bruit, abdomen	5/111 (5%)	41/108 (38%)
Elevated blood pressure	41/103 (40%)	69/109 (63%)
Abnormal angiogram	31/117 (26%)	104/119 (87%)
Temporal artery biopsy	93/126 (73%)	9/117 (8%)
Abnormal ESR or CRP	106/119 (89%)	100/114 (88%)
Medication use for vasculitis		
Prednisone	121/124 (98%)	115/121 (95%)
Methotrexate	41/124 (33%)	81/121 (67%)
Azathioprine	0	35/121 (29%)
Mycophenolate mofetil	3/124 (3%)	31/121 (26%)
Anti-TNF therapy	2/124 (2%)	43/121 (36%)
Tocilizumab	18/124 (15%)	7/121 (6%)

* Numerator is the number of patients with this manifestation or treatment use; denominator is number of patients who responded Yes/No (response of "I don't know" excluded), data presented as number.

GCA=giant cell arteritis, TAK=Takayasu's arteritis, N=number, ESR=erythrocyte sedimentation rate, CRP=c-reactive protein

cation by phenotype. These results provide support for the feasibility of conducting some types of research in these rare diseases through online registries.

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Abstract Number: 1883

Neuro-Behcet's Disease: 20 Years Single Center Experience of Cyclophosphamide for Induction of Remission

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
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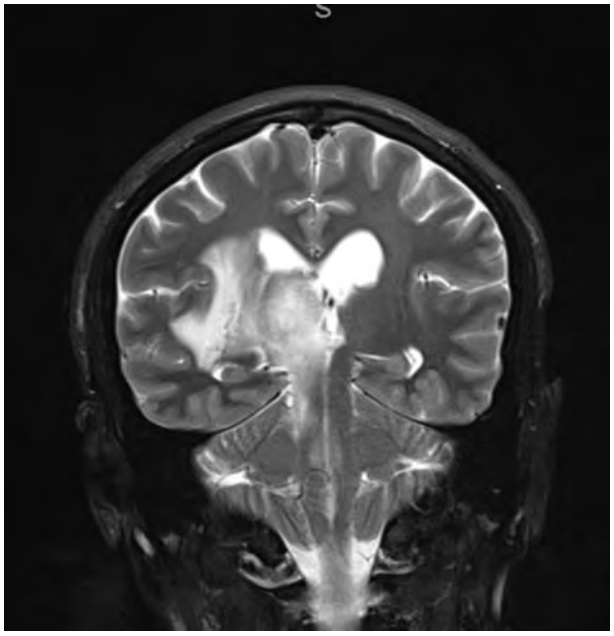
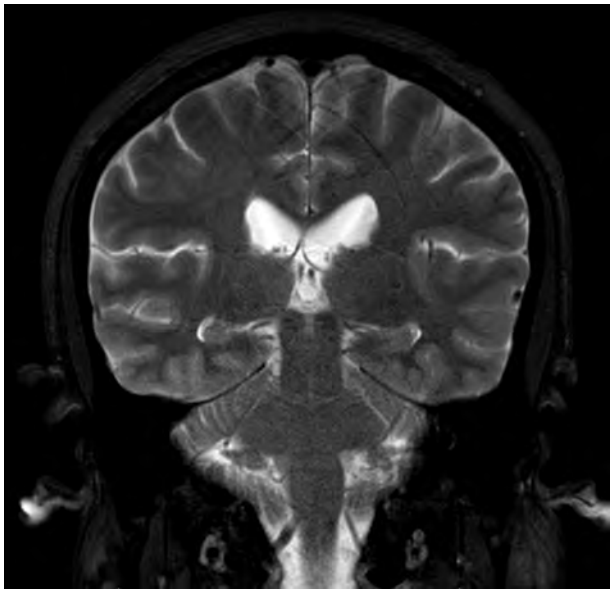
Session Time: 8:30AM–10:30AM

Background/Purpose: Behçet's disease (BD) is a systemic vasculitis. Neurological involvement, also known as Neuro-Behçet's disease (NBD), leads to great morbimortality. Diagnosis is challenging, since clinical presentation fluctuate greatly and systemic findings may be scarce, even after 2014 Classification Criteria included neurological manifestations. Treatment is based on corticosteroids and immunosuppressants, with azathioprine being widely used and tumor necrosis factor inhibitors (TNFi) as an option in refractory cases. Since access to TNFi is difficult, cyclophosphamide (CYC) may be used in severe NBD cases. However, strong evidence to corroborate its indications and treatment regimens are lacking. Our objective isto describe NBD patients' features, as well as safety and efficacy data of twenty years' experience of CYC use at a tertiary rheumatology center.

Methods: Retrospective cohort with data collected from electronic medical record, from January 2000 to December 2020, using keywords determinants. Treatment regimens allowed were methylprednisolone 1g for 3 to 5 days, followed by CYC 0.5 - 1g/m2 monthly for at least three months and compared to other immunosuppressant regimens (azathioprine, mycophenolate, TNFi). Subjects were divided in CYC and non-CYC groups and chi-square was used for statistical analysis.



Acute stage rhomboencephalitis.



After three months of treatment.

Results: Fifty-nine patients were included, 27 in the non-CYC group (55,55% women) and 32 in the CYC group (56,25% women). Mean age at BD diagnosis was 32.48 years in the non-CYC group and 29.75 years in the CYC group (p >0.05). Mean time from BD diagnosis to NBD was 26.85±9 months in the non-CYC group and 22.96±9,8 months in the CYC group (p >0.05). Mean follow-up months were 139.14 ±88 months in the non-cycle group and 78.78 ±43 months in the CFF group. Relapse rate was 14.8% in non-CYC versus 37.5% in CYC group (p >0.05), however relapse rate at 12-months follow-up was 50% at non-CYC group versus 12,5% at CYC group (p >0.05). Mean time for relapse was 30.5 versus 57.9 months at non-CYC and CYC groups, respectively (p >0.05). Mean cumulative CYC dose was 12.09g with an average of 10 infusions. There were 3 serious adverse events in each group (p >0.05).

Conclusion: Lower relapse rate at 12-months follow-up was a tendency in CYC patients in addition to sustained remission for a longer time, compared to other immunosuppressants. CYC use for NBD induction of remission presented a good safety profile, with few adverse effects and acceptable mean cumulative dose. Our study could not reach statistical significance due to small sample analysis and prospective studies are necessary to confirm relapse rates and establish the best CYC therapeutic schemes.

Disclosure: P. Fonseca, None; **H. Giardini,**, None; **C. Gonçalves**, None; **L. Prado**, None.

Abstract Number: 1884

Real-life Data for the Use of Anti-TNF Treatment in DADA2

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
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Background/Purpose: Deficiency of adenosine deaminase 2 enzyme (DADA2) is an autosomal recessive autoinflammatory disorder associated with ADA2 mutations. ADA2 works as a growth factor and its deficiency causes derangements in vascular integrity, increases in the proinflammatory type of macrophages, and results in tumor necrosis

Table 1. Demographic and clinical characteristics of patients

Patient ID	Current age, years/ Gender	Age at symptom onset, years	Age at diagnosis, years	Diagnosis date	All the treatments used	Initial organ involvement	Exitus
ID-1 (Index case)	*-M	20	22	2013	CS, Colchicine, Tocilizumab, CYC, AZA, IVIG, FFP	Livedo reticularis, erythema nodosum, skin nodule strabismus, myelofibrosis, proteinuria , HSM, AA amyloidosis	Yes
ID-2	53-m	40	40	PAN; 2008 DADA2 2015	CS, CYC, AZA,	Ischemia in mesencephalon , livedo reticularis, hypogamaglobulinemia, proteinuria	No
ID-3	28/f	19	19	2013	CS, CYC, AZA	Polyneuropathy and left pontin hypo-hyperdense signal associated with vasculitic involvement, livedo reticularis, renal microaneurysms	No
ID-4	22/M	22	22	2021	CS	Mononeuritis multiplex, livedo reticularis, recurrent abdominal pain	No
ID-5	31/M	7	29	2019	IVIG, CS,	Livedo reticularis, digital necrosis, hypogamaglobulinemia, proteinuria, HT recurrent abdominal pain,	No
ID-6	28/F	14	23	2016	CS, CYC, MMF, AZA, Colchicine	Putamen hemorrhage, livedo reticularis, erythema nodosum, RP, proteinuria, HT, aneurysm, recurrent abdominal pain,	No
ID-7	27/F	11	21	2015	Colchicine	Livedo reticularis, vasculitic skin lesions biopsy suggesting PAN, proteinuria	No
ID-8	*/M	4	22	2014	CS, Colchicine, CYC, AZA, FFP	Optic neuritis, lacunar infarcts on MRI, deafness, livedo reticularis, digital ulcers, optic neuritis, proteinuria, FSGS (collapsing variant), aneurysm recurrent abdominal pain	Yes
ID-9	23/M	2	17	2015	Colchicine	Hemorrhagic and ischemic stroke, lesion in pons and bilateral thalamus, peripheral neuropathy, diplopia livedo reticularis, horizontal nystagmus hypogamaglobulinemia , proteinuria, recurrent abdominal pain, HSM	No
ID-10	31/F	9	31	2021	Colchicine, CS, AZA, EPO,	Ischemic lacunar infarcts, livedo reticularis, strabismus, pancytopenia, proteinuria, FSGS, HM	No
ID-11	22/M	3.5	18	2018	Colchicine, CS	Sensorimotor axonal polyneuropathy, livedo reticularis, proteinuria (mesangial proliferative glomerulonephritis), HT, recurrent abdominal pain, HM, testicular involvement	No
ID-12	21/M	12	17	2017	CYC, CS	Digital ischemia, ulcer and RP, lymphopenia, proteinuria, HT, aneurysm recurrent abdominal pain, HSM, superior mesenteric artery stenosis on angiography	No
ID-13	21/M	8	15	2015	CYC, AZA,MMF, MTX, CS, Colchicine	Peripheral neuropathy, pontin ischemic lacunar infarct, livedo reticularis, MAS, recurrent abdominal pain, intestinal perforation	No
ID-14	21/F	7	14	2014	NSAID, Colchicine, MTX, CS, MMF	Livedo reticularis, recurrent abdominal pain, arthritis	No
ID-15	19/M	14	14	2016	Colchicine, CS	Sensorimotor axonal polyneuropathy on EMG, livedo reticularis, recurrent abdominal pain, HM	No
ID-16	9/M	1	5	2017	CS	Fever episodes	No
ID-17	18/F	4	10	2013	AZA, MTX, CS, FFP	Fever, arthritis, livedo reticularis, neuropathy, pontin ischemia on MRI	No
ID-18	8/F	1.5	2	2015	AZA	Fever, arthritis, livedo reticularis, neuropathy	No
ID-19	19/F	4 months	17	2019	-	Diamond Blackfan anemia and arthritis	No
ID-20	5.5/F	3 months	3	2019	-	Diamond Blackfan anemia and livedo reticularis	No
ID-21	15/M	4	10	2016	CS	Cerebral infarct, arthritis, livedo reticularis	No
ID-22	11/F	1 months	8	2018	-	Livedo reticularis, arthritis	No
ID-23	10/F	6	6	2017	CS, IVIG, Bone marrow trans.	Abdominal pain, lymphopenia, myalgia, fever, hypogamaglobulinemia,	Yes
ID-24	9.5	10 months	8	2019	IVIG, CS	Fever, arthritis, livedo reticularis, abdominal pain, myalgia, lymphopenia, Noonan syndrome	No
ID-25	8	3	5	2018	Colchicine	Livedo reticularis, vasculitis on skin biopsy	No
ID-26	9.5	11 months	9	2020	CS, AZA, colchicine	Fever, livedo reticularis, abdominal pain, myalgia, hypertension, optic neuritis, renal microaneurysms	No

PAN: Polyarteritis nodosa; ADA2: Adenosine deaminase 2; DADA2: Deficiency of ADA2; AZA: Azathioprine; CS: Corticosteroid; CYC: Cyclophosphamide; FFP: Fresh Frozen Plasma; FSGS: Focal Segmental Glomerulosclerosis; HM: Hepatomegaly; HSM: Hepatosplenomegaly; IVIG: Intravenous Immunoobulin; MTX: Methotrexate; MMF: Mycophenolate mofetil; RP: Raynaud phenomenon; AA Amyloidosis: Reactive amyloidosis, HT: Hypertension, MRI: Magnetic Resonance imaging, EMG: Electromyography

factor (TNF) mediated vascular inflammation. Given the importance of TNF in the pathophysiology, our aim was to understand the real-life outcomes of Anti-TNF treatment in patients with DADA2.

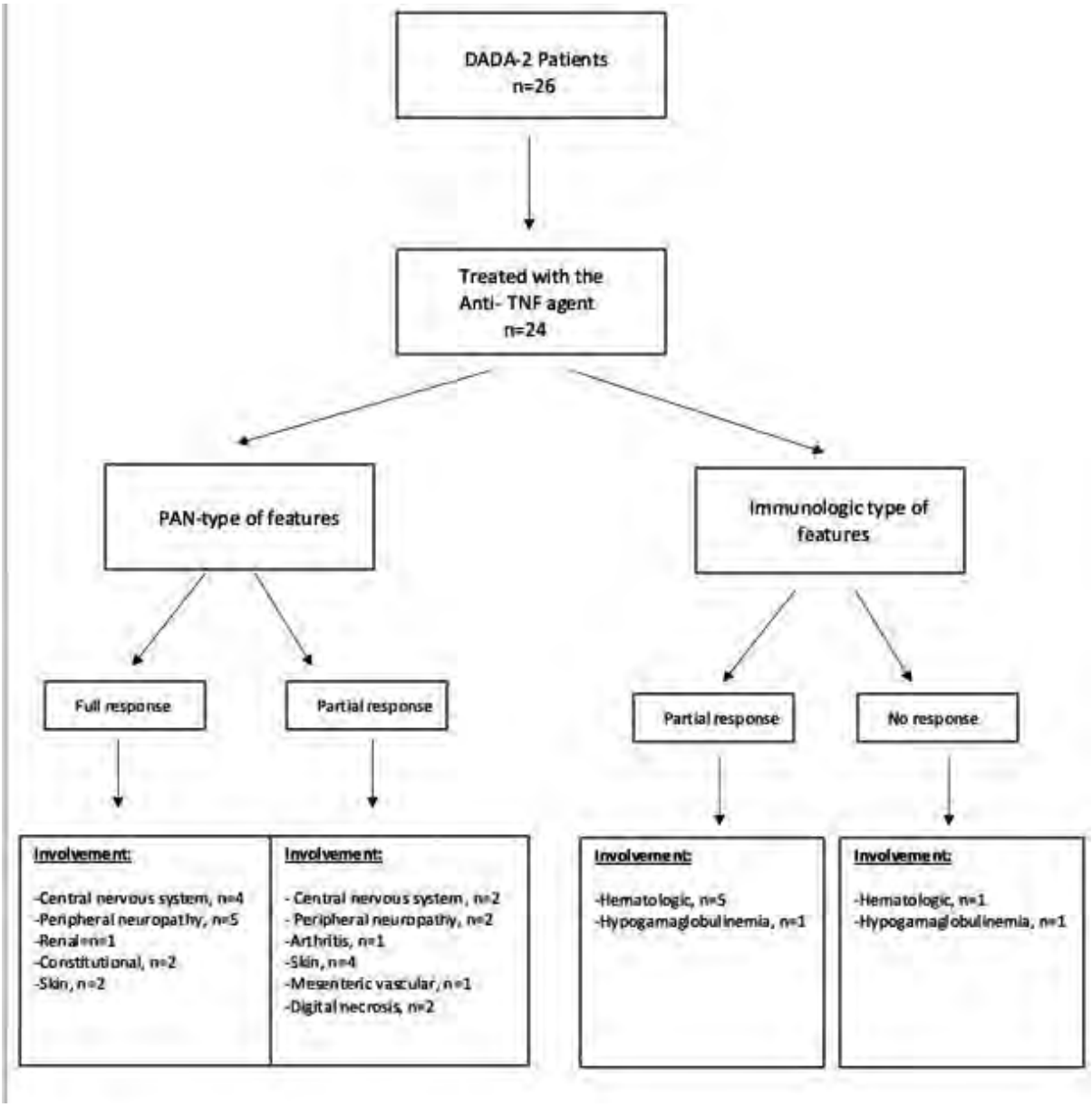
Methods: All DADA2 Adult or Pediatric patients among our Vasculitis Research Centre prospective database were included in this descriptive assessment. Demographics, clinical characteristics, and treatment details were recorded. From the overall cohort, patients who were initiated an anti-TNF agent were further assessed for the duration, dosage, indication of the treatment, and the outcome of the patients. Treatment response was evaluated according to physicians' reports (full-response, partial response-no response). A full response was defined as the symptom-free status of patients with normal acute phase reactants (AFRs)

Results: Totally 26 patients (Adult/Childhood age: 16/10) were analyzed. Mean (SD) current age was 25.6 (8.7) years in adults and 9.5 (2.5) years in children. The mean diagnosis age was 15.65 (9.2) years. The G47R mutation was homozygote in 19/21(90.5%) and heterozygote in 2/21 (9.5 %) of the patients. During a median (IQR) 48.5 (24-72)

Table 2. The details of the Anti-TNF treatment and the outcomes of the patients

Patient ID	Anti-TNF start date	Dosage	Still on Anti-TNF	Anti-TNF duration, months	Anti-TNF indication	Anti-TNF response
ID-2	September 2015	50 mg/ week ETN	Yes	69	Neurologic (central) involvement	Full
ID-3	N/A	40 mg/biweekly ADA	No	N/A	Constitutional symptoms	N/A
ID-4	March 2021	50 mg/ week, ETN	Yes	3	Neurologic involvement (peripheral)	Partial
ID-5	June 2020	50 mg/ week, ETN	Yes	12	Digital necrosis	Partial
ID-6	August 2016	50 mg/ week, ETN	Yes	58	Neurologic involvement (central)	Full
ID-8	December 2014	50 mg/ week, ETN	No	3	Digital necrosis	Partial
ID-9	February 2016	50 mg/week, ETN	Yes	64	Neurologic involvement (central and peripheral)	N/A
ID-10	April 2021	50 mg/ week, ETN	Yes	2	Neurologic involvement (central) and hematologic involvement	Partial
ID-11	March 2016	25 mg/ week, ETN	Yes	62	Neurologic (peripheral), skin and renal involvement	Full
ID-12	February 2017	25mg/ week, ETN	No	24	Mesenteric vascular involvement and hematologic involvement*	Partial
ID-13	N/A	35mg/ week ETN	Yes	N/A	Neurologic involvement (central +peripheral)	Full
ID-14	February 2015	25 mg/10 days, ETN	Yes	76	Skin involvement	Full
ID-15	February 2016	25 mg/ week, ETN	Yes	64	Neurologic involvement (peripheral)	Full
ID-16	October 2017	25mg/biweekly, ETN	Yes	56	Fever attacks	Full
ID-17	August 2013	35mg/ week, ETN	Yes	94	Neurologic involvement (central and peripheral)	Full
ID-18	March 2016	12.5mg/ week, ETN	Yes	63	Neurologic involvement (peripheral)	Full
ID-19	January 2019	40mg/ week, ETN	Yes	29	Hematological involvement	Partial
ID-20	January 2019	10mg/ week ETN	Yes	29	Hematologic and skin involvement	Partial
ID-21	January 2016	25mg/biweekly, ETN	Yes	65	Neurologic involvement (central)	Partial
ID-22	November 2018	25mg/ week, ETN	Yes	33	Skin involvement and arthritis	Partial
ID-23	January 2018	25mg/ week, ETN	No	6	Hematologic involvement, hypogamaglobulinemia, fever episodes	No
ID-24	October 2019	25 mg/ week, ETN	Yes	20	Hematological involvement, hypogamaglobulinemia	Partial
ID-25	March 2018	15mg/ week, ETN	Yes	39	Skin vasculitis	Partial
ID-26	July 2020	20 mg/ week, ADA	Yes	10	Neurologic (peripheral), skin involvement	Partial

Anti-TNF: Anti-Tumor necrosis factor; ETN: Etanercept: ADA: Adalimumab
*Anti-TNF agent was stopped because of dilated cardiomyopathy



Flowchart of the patient outcomes.

months of follow-up, anti-TNF agents (Etanercept, n=22; Adalimumab, n= 2) were prescribed to 24 of the patients. Throughout median (IQR) 36 (11.5-64) months of follow-up on anti-TNF treatment, none of the patients with hematologic involvement (n=6) showed a full response. Overall, 9 (37.5%) of the patients showed a full response. Patients with full response had received anti-TNF agents for predominant nervous system involvement (central, n=4; peripheral, n=5), renal involvement (n=1), constitutional symptoms (n=2), or skin involvement (n=2).

Regarding the patients with partial responses (50%), the predominant manifestations were: nervous system involvement (central, n=2; peripheral, n=2), renal involvement (n=1), skin involvement (n=4), digital necrosis (n=2), mesenteric vascular involvement (n=1), arthritis (n=1), hematologic involvement (n=5) and hypogammaglobulinemia (n=1) (Figure).

Two of three deceased patients were on TNFi: One patient with hematologic involvement had no response to anti-TNF and the patient died after bone marrow transplantation. The other patient died after 3 months of treatment in 2015. In one patient Anti-TNF agent was discontinued because of cardiomyopathy (Table-2).

Conclusion: Anti-TNF treatment enables full recovery for the vasculitic and inflammatory lesions (including neurologic involvement) in 40% of the patients and partial response in the others. However, we once again confirm that hematologic involvement does not have a satisfactory response to anti-TNF; bone marrow transplantation or new modalities of treatment are indicated for this group of patients

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Abstract Number: 1885

Biological Therapy in Refractory Neurobehçet's Disease. Multicenter Study of 42 Patients

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Neurobehçet's disease (NBD) is a severe complication of Behcet's disease (BD). Despite well-established therapies, with glucocorticoids and conventional immunosuppressants (cIS) a significant proportion of patients are refractory. The aim of this study is to assess efficacy and safety of biologic therapy (BT) in NBD refractory to glucocorticoids and at least one cIS.

Methods: Open-label multicenter study of refractory NBD from 22 different referral Spanish Hospitals. The main outcome variables were safety and clinical response measured at baseline, 6, 12 and 24 months. Other outcome variables were improvement in analytical parameters and corticosteroid-sparing effect of biological therapy.

Table. Underlying neurologic manifestation of 41 patients with refractory neurobehçet's disease treated with biologic therapy

Parenchymal subtype, n (%)	**34 (81.0)**
- Hemiparesis	8 (19.0)
- Polineuropathy	8 (19.0)
- Encephalopathy	6 (14.3)
- Cognitive impairments	4 (9.5)
- Optic neuropathy	4 (9.5)
- Ophtalmoparesis	4 (9.5)
- Other cranial nerve involvement	3 (7.1)
- Hemihypoesthesia	3 (7.1)
- Cerebellar dysarthria	1 (2.4)
- Cerebellar involvement	1 (2.4)
- Non-esteroidal psicosis	1 (2.4)
Non-parenchymal subtype, n (%)	**17 (40.5)**
- Aseptic meningitis	12(28.6)
- Thrombosis	4 (9.5)
- Intracranial hypertension	1 (2.4)

Results: We studied 42 patients (21 women/21 men; mean age 40.4±10.8 years). HLA B51 was positive in 15 (40.5%) out of 37 patients tested. Non-neurological manifestations were oral ulcers (n=41, 97.6%), genital ulcers (n=31, 73.8%), skin lesions (n=28, 66.7%), arthralgia (n=27, 64.3%), uveitis (n=21, 50.0%), arthritis (n=9, 21.4%), venous thrombosis (n=9, 21.4%) and arterial thrombosis (n=4, 9.5%). The underlying neurologic manifestation were parenchymal (n=34, 81 %) and non-parenchymal (n=17, 40.5%) involvement **(TABLE)**. The first BT used was infliximab (n=20), adalimumab (n=13), golimumab (n=3), tocilizumab (n=3) and etanercept (n=2).

After 58.2±51.4 months since initiation of BT, neurological response was complete (n=27; 64.3%), or partial (11, 26.1%). Only 4 (9.5%) patients did not respond **(FIGURE)**. After 6 months of BT, ESR improved from.31.5±25.6 to 15.3±11.9 mg/L (p=0.005) and CRP from 1.4 [0.2-12.8] to 0.3 [0.1-3] mg/L (p= 0.002). Likewise, a decrease in oral prednisone dose was also achieved from 45.6±17.3 mg/day at baseline to 5.17±2.85 mg/day after 24 months (p< 0.0001).

Primary failure was observed in 16 (38.1%) patients due to inefficacy (n=11, 68.8%) or adverse effects (n=5, 31.3%). Similarly, secondary failure was detected in 6 (14.3%) patients due to inefficacy (n=5, 83.3%) or adverse effects (n=1, 16.7%). No serious adverse effects were observed.

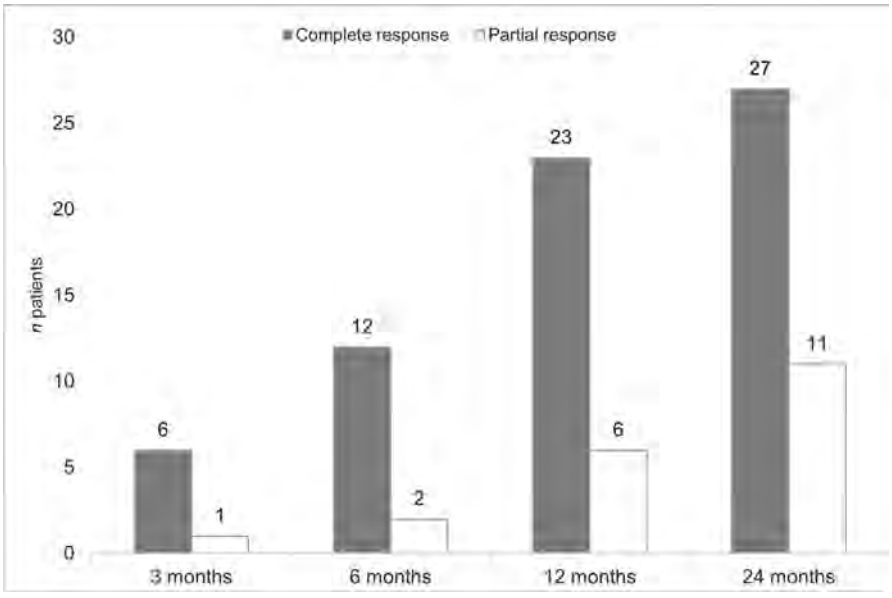

Figure. Neurological response after initiation of biological therapy.

Conclusion: BT, especially monoclonal anti-TNF drugs, seems effective and safe in patients with refractory NBD.

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Abstract Number: 1886

Validation of Angiographic Patterns of Disease in a Turkish Cohort of Patients with Takayasu's Arteritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)

Session Type: Poster Session D

Session Time: 8:30AM–10:30AM

Background/Purpose: Previous studies using computer-driven methods have identified subsets of patients with Takayasu's arteritis based on angiographic patterns of disease. These subsets were consistent between independent cohorts in North America and India, however, the prevalence of each subset differed between continent. The objective of this current study was to validate in an independent cohort from Turkey angiographic patterns of disease in Takayasu's arteritis and determine if the prevalence of these patterns is more similar to cohorts from India, North America, or neither.

Methods: Angiograph data were derived from records of patients with Takayasu's arteritis from 12 tertiary rheumatology centers in Turkey. All patients underwent whole-body angiography of the aorta and branch vessels, with cat-

Table 1. Arterial distribution in clusters for a Turkish cohort of patients with Takayasu's arteritis. A heatmap of arterial distribution, where the darker the red indicates that more patients within that cluster had involvement of the territory. Displayed in each cell is the number and percent of patients in the cluster that had involvement of the territory

	Cluster One n = 90	Cluster Two n = 148	Cluster Three n = 183
Ascending aorta	18 (20%)	39 (26%)	32 (17%)
Aortic arch	14 (16%)	18 (12%)	24 (13%)
Thoracic aorta	29 (32%)	40 (27%)	35 (19%)
Abdominal aorta	44 (49%)	30 (20%)	51 (28%)
Left subclavian	63 (70%)	107 (72%)	112 (61%)
Right subclavian	34 (38%)	104 (70%)	45 (25%)
Innominate	5 (6%)	38 (26%)	14 (8%)
Left axillary	8 (9%)	18 (12%)	19 (10%)
Right axillary	6 (7%)	19 (13%)	12 (7%)
Left carotid	43 (48%)	129 (87%)	50 (27%)
Right carotid	33 (37%)	125 (84%)	9 (5%)
Left vertebral	17 (19%)	14 (09%)	19 (10%)
Right vertebral	10 (11%)	16 (11%)	6 (3%)
Left renal	77 (86%)	7 (5%)	9 (5%)
Right renal	67 (74%)	8 (5%)	10 (5%)
Mesenteric	65 (72%)	26 (18%)	31 (17%)
Left iliac	9 (10%)	4 (3%)	11 (6%)
Right iliac	10 (11%)	3 (2%)	13 (7%)
Left femoral	3 (3%)	2 (1%)	0 (0%)
Right femoral	0 (0%)	3 (2%)	2 (1%)

egorization of involvement (stenosis, occlusion, or aneurysm) in 13 arterial territories. K-means cluster analysis was performed to identify subgroups of patients based on pattern of angiographic involvement.

Results: Data from 421 patients in the cohort in Turkey were available for analysis. Using K-means clustering, three distinct clusters were identified for the Turkish cohort; these three clusters were identical to those previously identified in the Indian and North American cohorts (**Table 1**). Patients in Cluster 1 have significantly more disease in the abdominal aorta, renal, and mesenteric arteries ($p < 0.01$). Patients in Cluster 2 have significantly more bilateral disease in the carotid and subclavian arteries ($p < 0.01$). Compared to patients in Clusters 1 and 2, patients in Cluster 3 have asymmetric disease with fewer involved territories ($p < 0.01$).

The prevalence in each of the three clusters for patients from Turkey (current analysis) compared to the prevalences for patients from India and North America (previously published data) is outlined in **Table 2**. The distribution of pa-

Table 2. Distribution of patients with Takayasu's arteritis in angiographically-defined clusters among patients in India, North America, and Turkey

	India (n = 581)	North America (n = 225)	Turkey[1,2] (n = 421)
Cluster One	236 (40.6%)	53 (23.6%)	90 (21.4%)
Cluster Two	159 (27.4%)	79 (35.1%)	148 (35.2%)
Cluster Three	186 (32.0%)	93 (41.3%)	183 (43.5%)

[1]$p < 0.01$ vs. India; [2]$p = 0.79$ vs. North America; displayed in each cell is the number and percent of patients in each cohort that are assigned to each cluster

tients among the three clusters was quite similar among patients from Turkey and North America (p = 0.79), but these two cohorts differed in this respect from patients from India.

Conclusion: This study provides strong, independent confirmation that there are distinct subsets of Takayasu's arteritis based on angiographic disease. These patterns are consistent between continents; however, the prevalence of each pattern differs. Genetic and/or environmental factors may contribute to patterns of angiographic disease in patients with Takayasu's arteritis.

Disclosure: **K. Gribbons**, None; **S. KAYMAZ-TAHRA**, None; **F. Alibaz**, None; **E. bolek**, None; **O. Karadag**, Omer Karadag has received research grants from Roche, Pfzer as study investigator and received consulting fees from Celltrion., 6; **B. Ince**, None; **M. Inanc**, None; **S. Kocaer**, None; **F. Onen**, Pfizer, 1, 6, Abbvie, 1, 6, MSD, 6, Amgen, 1, 6, Novartis, 1, 6, Lily, 1, 6, UCB, 1, 6, Roche, 1, 6, Jansenn, 6, Celltrion, 6, Menarini, 1, 6; **K. AKSU**, None; **G. Keser**, None; **A. Ates**, None; **A. Yazici**, None; **A. Cefle**, None; **N. Alpay Kanitez**, None; **A. Omma**, None; **O. Gercik**, None; **S. Akar**, AbbVie, 2, 5, 6, Lilly, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Janssen, 2, 5, 6, UCB, 2, 5, 6, Amgen, 2, 5, 6, Gilead, 2, 5, 6, Abdi Ibrahim, 2, 5, 6, Ilko, 2, 5, 6; **V. Cobankara**, None; **N. Yasar Bilge**, None; **T. Kasifoglu**, None; **M. Kara**, None; **K. Quinn**, None; **P. Grayson**, None; **P. Merkel**, AbbVie, 2, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 2, Dynacure, 2, Eicos, 2, EMDSerono, 2, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Jannsen, 2, Kiniksa, 2, Magenta, 2, Neutrolis, 2, Novartis, 2, Pfizer, 2, Sanofi, 5, Star Therapeutics, 2, Takeda, 2, Talaris, 2, UpToDate, 9; **H. Direskeneli**, None.

Abstract Number: 1887

Evidence-Based Behçet's Disease Activity Scale (EBDA) – A New Instrument with Improved Acuity for Major Organ Disease Activity and Remission Depth Assessment

Maria Caterina Lagdameo[1], Hyungrok Do[2] and **Johannes Nowatzky**[1], [1]Division of Rheumatology, New York University School of Medicine, New York, NY, [2]Department of Population Health, NYU School of Medicine, New York

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: Most current Behçet's disease (BD) activity assessment tools are strongly based on patient-reported symptoms and findings allowing a wide range of observer-dependent interpretations and do not always differentially weigh organ-threatening vs non-organ-threatening disease activity or degrees of remission depth. Here we aimed to develop and test a BD-specific disease activity instrument that is focused to a high extent on objective findings, dissects the impact of organ-threatening from non-organ-threatening disease, and classifies remission depth.

Methods: We generated an instrument that requires the verification of reported symptoms through findings on physical exam and diagnostic studies and incorporates results of screening and follow-up studies in four minor system categories, including "mucosal", "cutaneous", "cutaneous pathergy", "articular", and four major system categories, including "ocular", "vascular", "CNS", "GI". Evidence of one or more phenotypically eligible findings in any category triggered scoring with major categories receiving a 3-fold weighed score over minor ones. EBDA and Behçet's Disease Current Activity Form (BDCAF, the current standard) scoring was applied to 59 BD patient encounters compris-

ing a wide range of degrees of BD severity and prototypical manifestations. Scores were analyzed using Pearson's, Spearman's, Kendall's correlation coefficients, and Lin's concordance correction.

Results: There was moderate positive correlation between EBDA and BDCAF across all scores (Pearson's 0.5817, $p< 0.0001$; Kendall's 0.5568, Spearman's 0.6328, $p< 0.000001$) without a linear relationship (Lin's 0.1019, 99.9% confidence). On analysis of categorized scores for lower (EBDA < 12, which excludes major organ involvement) vs higher activity (EBDA ≥ 12, which includes major organ involvement) there was evidence for moderate positive correlation with BDCAF for lower (Kendall's 0.4123, $p< 0.001$; Spearman's 0.4031, $p< 0.01$), but not for higher activity scores (Kendall's 0.2965, p=0.2546; Spearman's 0.3045, p=0.2698). BDCAF appeared to underestimate organ-threatening (mostly ocular and major vascular) disease in >70% and missed it completely in 13% of cases.

Conclusion: EBDA is a new instrument for the finding-based assessment of BD activity which may exhibit improved performance in moderate-severe and severe, potentially organ-threatening BD. In addition, the instrument allows estimates of disease remission depth. Given its strong focus on objectively verifiable findings directly relevant to the time point of assessment, EBDA may be especially suitable in research-intense settings such as for the classification of study subjects for analysis of presumably disease activity-dependent molecular or cellular responses and immune phenotypes.

Disclosure: M. Lagdameo, None; **H. Do**, None; **J. Nowatzky**, None.

Abstract Number: 1888

Usefulness of 2019 ACR/EULAR Classification Criteria (AECC) for IgG4-Related Disease Differs Between Clinical Phenotypes of IgG4-RD

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II (1862–1888)
Session Type: Poster Session D
Session Time: 8:30AM–10:30AM

Background/Purpose: ACR/EULAR Classification criteria for IgG4-related disease (IgG4-RD) newly published [1]. On the other hand, four distinctive phenotypes of IgG4-RD have been described [2]. We aimed to identify clinical phenotypes of IgG4-RD and the evaluate usefulness of 2019 ACR/EULAR classification criteria (AECC) for clinical phenotypes in our cohort.

Methods: In the prospective database of the Hacettepe University Vasculitis Research Centre (HUVAC) 92 IgG4-RD patients meeting the 2011 comprehensive diagnostic criteria for IgG4-RD were registered by the end of the May 2021. We reviewed the medical records and determined the following clinical factors: Age, gender, serum levels of IgG4, presence of ANCA or other specific autoantibodies, histopathologies with immunostaining (if available) and distributions of organ involvement. An AECC score was calculated for all cohort.

Table. Clinical Phenotypes of IgG4-related disease

	Retroperitoneal and aorta (n=37)	Head and neck (n=22)	Mikulicz and systemic (n=15)	Pancreato-hepato-biliary (n=10)	Undefined phenotype (n=8)	P value
Sex, male, n (%)	67.6	31.8	46.7	50.0	37.5	0.091
Age, median (IQR) (years)	60 (50-67)	56 (33-66)	61 (31-69)	48 (41-70)	45 (32-55)	0.129
IgG4 level, median (IQR) (mg/dl)	202 (132-370)	119 (61-299)	335 (66-660)	210 (86-625)	144 (77-264)	0.628
AECC points, median (IQR)	23 (12-31)	18 (15-25)	23 (19-36)	24 (8-29)	15 (4-20)	0.037*
2019 AECC, n (%)	57	45	73	60	25	0.474

Results: We included 92 patients (M/F:47/45) with IgG4-RD. 61% of the patients had multiorgan involvement, median (IQR) organ involvement was 2 (1-3) and median (IQR) IgG4 level was 179 mg/dL (89-368). Majority of the patients had retroperitoneal fibrosis/periaortitis (Table). Retroperitoneal and aorta (RPF-Aortitis) accounted for 40% of the phenotypes, followed by head and neck (24%), Mikulicz and systemic (16%), and pancreato-hepato-biliary (PHB) (11%). Nine per cent had an undefined phenotype. Head and neck group had female predominance whereas RPF/aortitis group had male predominance. Mikulicz and systemic group had the highest IgG4 levels.

All of the patients fulfilled the entry criteria for AECC for IgG4-RD. Of the 42 false-negative cases, 7 met one exclusion criteria whereas 35 did not achieve sufficient inclusion criteria scores. 49 (53%) patients got a score ≥20 points, with a mean score of 29.3 points (SD.7.3). MS, PHB and RPF/Aortitis phenotypes met 2019 AECC at a higher rate, although the differences were not statistically significant.

Conclusion: Phenotype results of our cohort are concordant with Asian and American cohorts. RPF-Aortitis phenotype was more prevalent, while PHB and MS were less frequent. The 2019 AECC was met over half of the patients.

Disclosure: G. Yardımcı, None; **B. Farisogulları**, None; **G. Ayan**, None; **L. Kilic**, None; **S. Apraş Bilgen**, None; **O. Karadag**, Omer Karadag has received research grants from Roche, Pfzer as study investigator and received consulting fees from Celltrion., 6.

Abstract Number: 1889

Arthritogenic T Cells Harbor a Transcriptional Program of T Cell Activation and a Repertoire Pruned by Endogenous Superantigen

JUDITH F ASHOURI, Elizabeth McCarthy, Steven Yu, Noah Perlmutter, Charles Lin, Chun Jimmie Yu and Arthur Weiss, University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Animal Models (1889–1892)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: It is widely accepted that activation of specific CD4 T cells through their TCRs by self-antigen (Ag) is necessary for rheumatoid arthritis (RA) onset. Yet, the transcriptional profiles and TCR identities of the disease-causing pathogenic CD4 T cells remain unknown. SKG is an ideal platform to study questions relevant to RA since this model not only captures many of the important features of human RA, but also recapitulates the paradoxical ability of CD4 T cells to differentiate into pathogenic effector cells despite their impaired response to TCR engage-

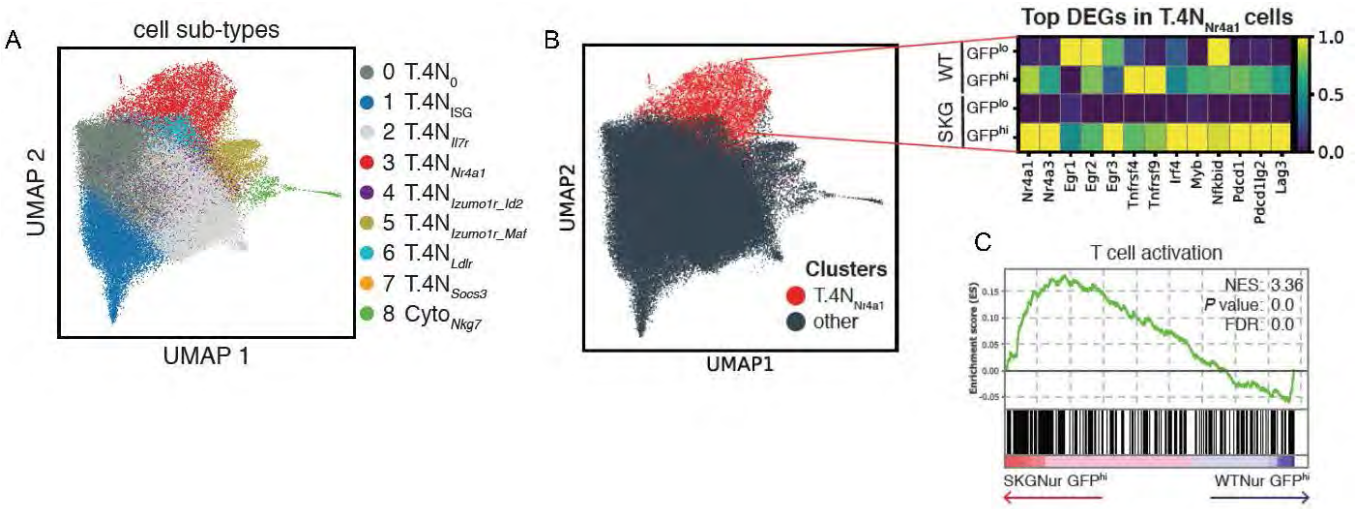

Figure 1. Arthritogenic SKG T cells upregulate a transcriptional TCR signaling program. (A) UMAP of 99,074 naïve T cells derived from 8 samples (2 replicates from each WT and SKG GFPlo and GFPhi subset); cells colored according to annotated leiden clusters. (B) Heatmap shows average expression of top DEGs (abs value(log2(FC)) > 2.8, adj P value < 0.05) of cells in T.4N_Nr4a1 (Nr4a1 high) cluster vs other cells by subgroup normalized by standard scale by column. (C) Enrichment plot of T cell activation pathway from GSEA analysis for ranked genes in T.4N_Nr4a1 cells from SKG GFPhi v. WT GFPhi differential expression analysis. FDR, false discovery rate. NES, normalized enrichment score.

ment. We combined SKG mice with a fluorescent reporter tethered to the regulatory region of *Nr4a1* (Nur77—which is rapidly and selectively upregulated in response to Ag, but not inflammatory stimuli) to read out the relative strength of TCR signaling (termed by us SKGNur mice). Using these mice we previously identified a CD4 T cell subpopulation that is greatly enriched for their arthritogenic potential (in the GFP^{hi} fraction). In this study, we examine the T cell repertoire and signaling networks invoked by endogenous Ag encounter in pre-arthritogenic T cells to study the evolution of autoimmune arthritis.

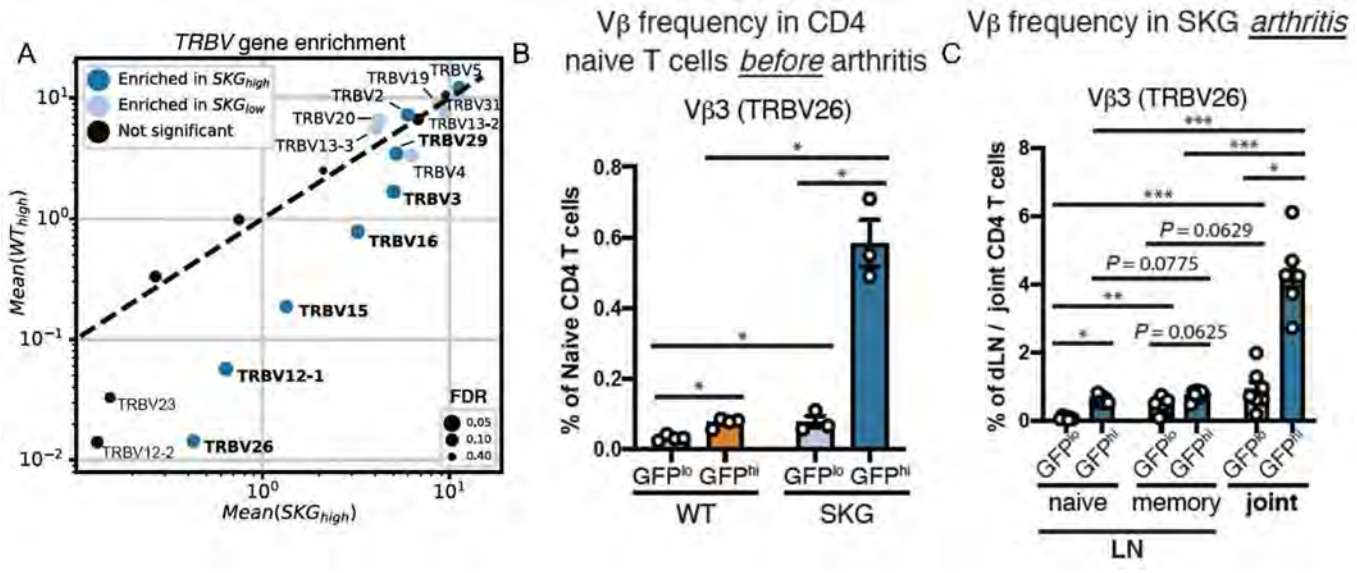

Figure 2. SKG T cells harbor a biased TCR Vb repertoire likely pruned by endogenous superantigen(s). (A) Scatterplot of mean frequency of cells expressing each TCR variable beta gene (TRBV) gene for SKGNur vs WTNur GFPhi. Dots for each TRBV gene are sized according to FDR from one-sided paired t-test comparing frequency in SKG GFPhi vs SKG GFPlo. Dots colored as either significantly enriched (FDR < 0.1) in SKG GFPhi (dark blue), SKG GFPlo (light blue), or not significantly enriched in either subgroup (black). Labels for TRBV genes significantly enriched in SKG GFPhi and more highly expressed in SKG GFPhi vs WT GFPhi samples are bolded. (B-C) Mean frequency (± SEM) of indicated CD4 T cell subset with TCR Vb3 protein usage determined by flow cytometry in GFPlo and GFPhi T cells from lymph nodes (LN) prior to arthritis induction (B) or LN and joints 2.5 weeks after arthritis (C), repeated > 2 times.

Methods: We used bulk and paired single-cell RNA and TCR-sequencing (scRNAseq and TCRseq) to simultaneously profile the transcriptome and TCR repertoire of self-reactive pathogenic T cells before arthritis onset in SKGNur mice. Analysis was performed on sorted naïve SKG and BALB/c (WT) CD4 T cells based on their Nur77-eGFP levels (GFP^{hi} and GFP^{lo}) using Q^2 Solutions and the 5' 10X platform respectively. After filtering of the latter, there were 99,074 cells with a mean of 12,384 cells per condition. We examined our datasets for differentially expressed genes (DEG) and TCR variable genes enriched in the arthritogenic SKGNur GFP^{hi} T cells. Flow cytometry was used to validate genes that were found to be up or down-regulated in arthritogenic T cells.

Results: In our bulk RNAseq dataset >990 DEGs were identified and clustered into 6 gene modules that capture the transcriptional differences between the SKGNur and WTNur GFP^{hi} and GFP^{lo} subgroups. Gene set enrichment analysis revealed a T cell activation signature in the naïve SKGNur GFP^{hi} CD4 T cells. Our scRNAseq dataset revealed significant heterogeneity within the unperturbed naïve CD4 T cell compartment with 8 distinct clusters further refining our bulk RNAseq results. We found that T cells expressing the highest levels of *Nr4a1 (red cluster in* **Fig 1***)* upregulate TCR signaling gene modules, which are enhanced in SKG mice despite their hypomorphic mutation in ZAP70, a tyrosine kinase critical for proximal TCR signaling. In simultaneous investigation of their TCR sequences, we uncovered a previously unknown biased TCR Vb usage in the SKG repertoire (**Fig 2**, DNS). The Vb genes whose expression is uniquely enriched in the SKGNur GFP^{hi} subset are well known to recognize endogenous mouse mammary tumor virus superantigen. We detect still further enrichment of these Vb's in the SKG arthritic joint (**Fig 2,** DNS).

Conclusion: Our results suggest both transcriptional activation and repertoire selection driven by endogenous viral superantigen(s) act as inter-related mechanisms that prime arthritogenic SKG T cells prior to disease onset.

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Abstract Number: 1890

Cellular Origin and Functions of Osteoclasts in Inflammatory Arthritis

Hannah Nelson[1], Ellen Gravallese[2], Julia Charles[1] and **Christian Jacome-Galarza**[1], [1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Harvard Medical School, Chestnut Hill, MA

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Animal Models (1889–1892)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Inflammatory arthritis (IA) is an autoimmune disease targeting multiple joints and characterized by joint destruction caused by osteoclasts (OC), leading to physical disability. However, the precise cellular origins of OC are poorly understood. Myeloid lineage cells including OC and macrophages can derive from either hematopoietic stem cells (HSC) or erythro-myeloid progenitors (EMP). Previous studies *in vitro* suggest that in IA, HSC-derived monocytes differentiate into OC and others showed that macrophages can fuse to form OC under the influence of inflammatory cytokines. We hypothesized that in IA, embryonically derived Erythro-Myeloid Progenitor macrophages and Hematopoietic Stem Cell-derived progenitors can independently contribute to the formation of OC in vivo. These cell lineage tracing systems will allow to discriminate among distinct OC populations by their cell surface phenotype and selectively target them for therapeutic purpose.

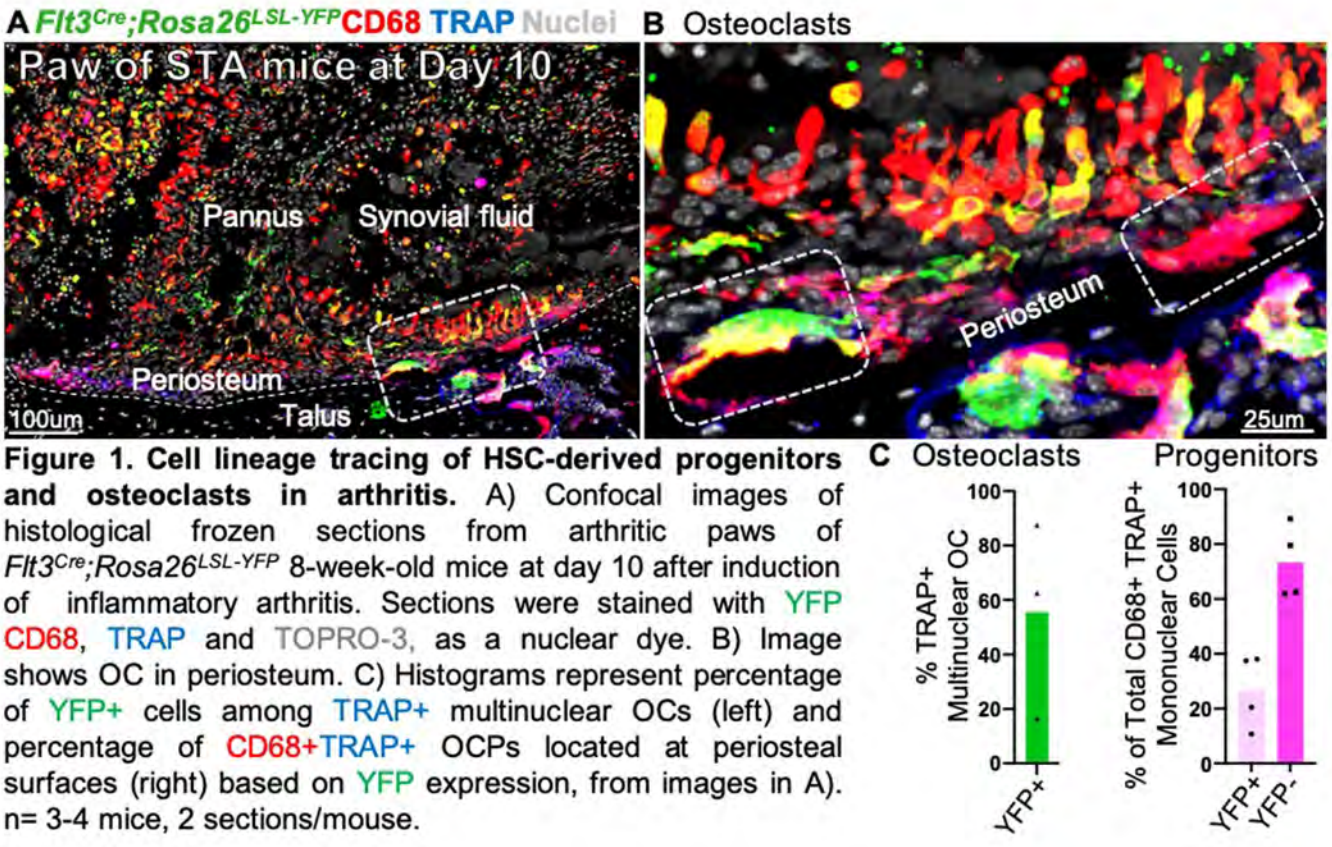

Figure 1. Cell lineage tracing of HSC-derived progenitors and osteoclasts in arthritis. A) Confocal images of histological frozen sections from arthritic paws of *Flt3*^{Cre}*;Rosa26*$^{LSL\text{-}YFP}$ 8-week-old mice at day 10 after induction of inflammatory arthritis. Sections were stained with YFP CD68, TRAP and TOPRO-3, as a nuclear dye. B) Image shows OC in periosteum. C) Histograms represent percentage of YFP+ cells among TRAP+ multinuclear OCs (left) and percentage of CD68+TRAP+ OCPs located at periosteal surfaces (right) based on YFP expression, from images in A). n= 3-4 mice, 2 sections/mouse.

Methods: To test this hypothesis, we used bone frozen sections and immunofluorescence, as well as flow cytometry (FACS) from cell lineage tracing systems, to discriminate among these progenitors. We used *Flt3*^{Cre}*;Rosa26*$^{LSL\text{-}YFP}$ mice to label HSC and their progeny and both *Csf1r*$^{Mer\text{-}iCre\text{-}Mer}$*;Rosa26*$^{LSL\text{-}tdTomato}$ and *Cx*$_3$*cr*$_1^{CreERT2}$*;Rosa26*$^{LSL\text{-}tdTomato}$ mice, pulsed with 4-hydroxytamoxifen at E8.5 and E9.75 respectively, to label EMP-derived progenitors.

Results: Histology of ankle joints from healthy *Flt3*^{Cre}*;Rosa26*$^{LSL\text{-}YFP}$ embryos at E16.5, newborn at P0 and 8 week-old mice showed that ~7 % of synovial F4/80+ or CD68+ cells were of HSC origin, suggesting that EMPs are the major source of synovial macrophages. We confirmed, using both *Csf1r*$^{Mer\text{-}iCre\text{-}Mer}$*;Rosa26*$^{LSL\text{-}tdTomato}$ and *Cx*$_3$*cr*$_1^{CreERT2}$*;Rosa26*$^{LSL\text{-}tdTomato}$ mice, that ~40% of all F4/80+ synovial macrophages were TdTomato+, showing for the first time an EMP-origin. To test the HSC origin of OC in IA, adult *Flt3*^{Cre}*;Rosa26*$^{LSL\text{-}YFP}$ mice were treated with K/BxN arthritogenic serum and ankle joints were harvested at day 10 (peak inflammation). Unexpectedly, we found that only 56% of OC were YFP-positive, indicating that a large proportion of synovial OC are not HSC-derived. Further, we identified CD68+TRAP+ cells localized to periosteal surfaces as candidate progenitors of synovial OC. Consistent with the dual origin of synovial OC, CD68+TRAP+ progenitors derive from both HSC (27%) and non-HSC (73%) lineages.

Conclusion: These data suggest that both HSC-derived and EMOP-derived osteoclast precursor cells independently contribute to OC formation in IA. These cell lineage tracing systems will help us to identify unique differences among OC of distinct origins. These differences will allow for differential targeting of OC via unique cell surface markers and for the development of new targets to inhibit OC formation and prevent bone and cartilage erosions in IA.

Disclosure: H. Nelson, None; **E. Gravallese**, None; **J. Charles**, Ultragenyx, 1; **C. Jacome-Galarza**, None.

Abstract Number: 1891

Variable Effects of Testosterone on Male versus Female Derived Macrophages in Inflammatory Arthritis

Kiana Chen[1], Xi Lin[1], Lianping Xing[2], H. Mark Kenney[3], Richard Bell[4], Edward Schwarz[5] and Homaira Rahimi[5], [1]University of Rochester School of Medicine and Dentistry, Rochester, NY, [2]University of Rochester Medical Center, Webster, NY, [3]University of Rochester Medical Center, Rochester, NY, [4]Hospital for Special Surgery, New York, NY, [5]University of Rochester, Rochester, NY

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Animal Models (1889–1892)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory joint disease that is female predominant. The TNF-transgenic (TNF-Tg) mouse model of RA also develops a sexually dimorphic inflammatory arthritis with earlier disease appearing in female mice (1). While the mechanism of the sexual dimorphism is unknown, studies suggest androgens can provide a protective effect against inflammatory disease progression (2,3). We hypothesize that androgens' anti-inflammatory effects on myeloid cells in the joint may mediate inflammatory arthritis progression.

Methods: Orchiectomy and sham control procedures were performed on 4-week old male TNF-Tg mice (n=3 mice/group). Mice were sacrificed at 3-months old for serum and tissue collection. Testosterone and TNFα levels were compared between groups, and knee joints sections were H&E and TRAP stained for histological scoring. Bone marrow-derived macrophages (BMDMs), plated from 3-month old male and female TNF-Tg mice (n=3 mice/group), were treated with 0.1μM, 0.5μM, and 1μM of testosterone propionate (T), followed by murine IFNɣ and LPS stimulation. After 48 hours, supernatant was assayed in an ELISA for murine TNFα. Groups were analyzed using unpaired t-tests for orchiectomy studies and two-way ANOVA for in vitro studies. Values are reported as the mean ± standard deviation.

Results: Orchiectomized (Orch) mice joints had significantly higher (i.e. worse) histology scores than sham controls for synovial inflammatory infiltrate, pannus invasion, and TRAP+ area (2 Orch vs 1 Sham, 1.6 Orch vs 0.7 Sham, 1.4 Orch vs 0.3 Sham, $p< 0.05$). Orchiectomized TNF-Tg mice were confirmed to have low testosterone levels (0.078 ng/mL (0.054-0.12) ng/mL, normal=1.3 ± 0.4 ng/mL). Serum human (h) and mouse (m)TNFα levels remained unchanged between orchiectomized and sham TNF-Tg mice (827 pg/mL, range 271-1400 pg/mL Orch vs 841 pg/mL, range 613-1011 pg/mL Sham hTNF and 8.5 pg/mL, range 7-10 pg/mL Orch vs 8.8 pg/mL, range 8-9.8 pg/mL Sham mTNF). Male derived BMDMs did not have a significant change in TNFα expression when treated with T at any concentration compared to untreated cells (74.84 ± 101.9 pg/mL T 0.1μM, 107.1 ± 97.05 pg/mL T 0.5μM, 71.92 ± 64.55 pg/mL T 1μM vs 73.56 ± 72.48 pg/mL Untreated, $p >0.05$). Remarkably, female derived BMDMs had increased TNFα expression at a concentration of 0.1μM compared to untreated cells (544.06 ± 363.6 pg/mL T 0.1μM vs. 21.50 ± 22.48 pg/mL Untreated, $p< 0.01$) (Fig 1).

Conclusion: Here we show that reduced levels of testosterone from orchiectomies is associated with increased synovial inflammation in TNF-Tg males, yet does not affect systemic TNFα levels. In vitro studies of BMDMs indicate that macrophages from TNF-Tg mice have sex and testosterone concentration specific release of TNFα, suggesting a sexual dimorphism at the cellular level. Further trials of in vivo and in vitro T administration to both sexes is necessary to clarify local versus systemic immune responses in TNF-Tg mice.

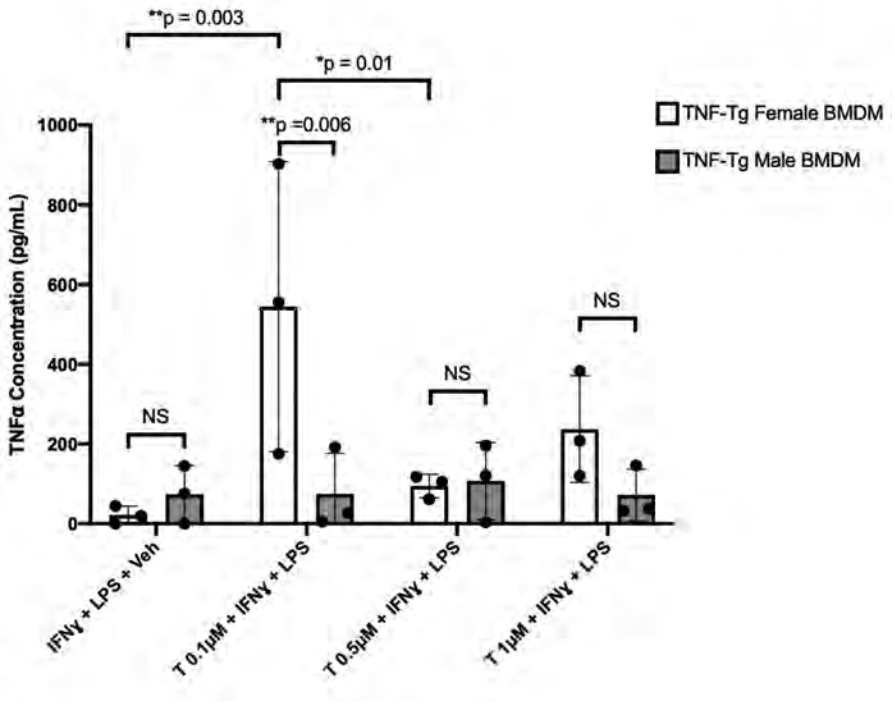

Figure 1. Female versus male TNF-Tg murine TNFα concentrations of stimulated bone marrow derived (BMDM) treated with testosterone propionate (T). TNF-Tg BMDMs from 3-month-old females (n = 3) and males (n = 3) were plated and treated with a T concentration of 0.1μM, 0.5μM, or 1μM or vehicle as control. BMDMs were then stimulated with 50ng/mL of murine IFNɣ and 50ng/mL of LPS. Murine TNFα ELISA of supernatant revealed a significant increase in TNFα concentration in the female derived T 0.1μM-treated cells compared to female vehicle control cells and compared to male derived treated cells. Male derived treated cells did not have a significant change in TNFα concentration compared to the vehicle control cells. NS = not significant (p>0.05).

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2. Traish A et al. *J Clin Med* 7(12):549. 2018.
3. Lashkari M et al. *Electron Physician* 10(3):6500-6505. 2018.

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Abstract Number: 1892

Promotion of Autoimmune Arthritis via Tryptophan Metabolism and Production of the Bacterial-Derived Tryptophan Metabolite Indole

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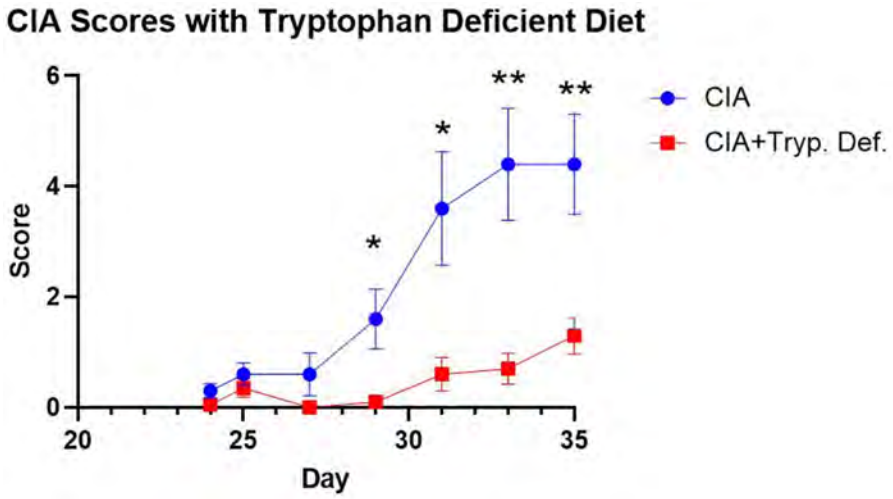
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Animal Models (1889–1892)
Session Type: Abstract Session
Session Time: 9:00AM–10:00AM

Background/Purpose: Significant changes in gut bacterial richness and diversity occur during the development of inflammatory arthritis, in both murine models and human patients; however, the mechanisms by which dysbiosis

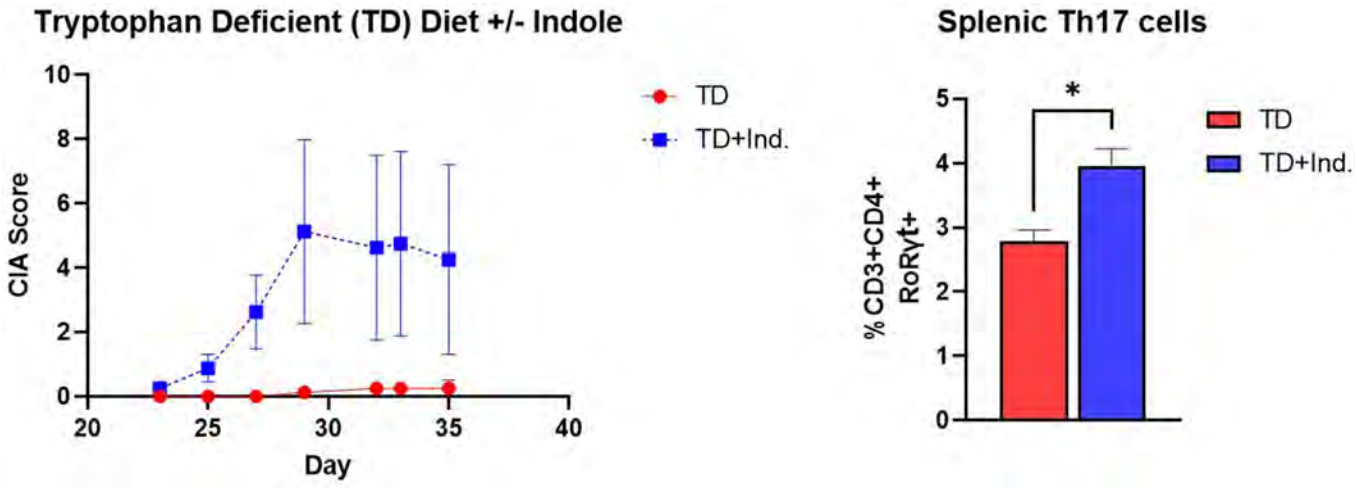


Amelioration of CIA in mice given a tryptophan deficient diet.

promotes disease pathogenesis remain unclear. Because microbiota can shape host physiology through catabolism and production of metabolites, we hypothesized that an altered microbiome during inflammatory arthritis leads to an altered metabalome, which impacts the development of autoimmune B and T cells.

Methods: Cecal metabolites were screened by LC-MS during CIA with antibiotic vs control treatment. CIA was induced by immunization of male 6–8-week-old DBA/1 mice with bovine type II collagen emulsified in complete Freund's adjuvant at days 0 and 21. To assess how the altered metabolites affected CIA, mice were provided a tryptophan deficient or control amino acid diet starting at day -1 and throughout CIA (with amino acid diet provided on the weekend to compensate weight loss). To supplement indole, 10mM of indole was provided in the drinking water or by oral gavage every other day. To perform the 4-Hydroxy-3-nitrophenylacetyl – chicken gamma globulin (NP-CGG) immunization, NP-CGG was given intraperitoneally (50µg) with 50µg alum adjuvant at days 0 and 10. Finally, to assess direct effects of indole on adaptive immune cells, splenic B cells were evaluated ex vivo after stimulation with LPS and/or anti-IgM for naïve B cells or type II collagen for memory B cell responses.

Results: Products of bacterial catabolism of dietary tryptophan were found to be significantly altered in the cecum of mice. Therefore, mice were given a tryptophan-free diet and found to have significantly decreased CIA associat-



Restoration of a CIA disease phenotype in mice administered the tryptophan bacterial metabolite, indole, during a tryptophan deficient diet.

ed with an increase in splenic regulatory T cells (Treg). One specific bacterial-derived tryptophan metabolite indole strongly correlated with CIA severity, and direct administration of indole during CIA with antibiotic treatment promoted disease and led to increases in T follicular cell (Tfh) and B cell populations in the Peyer's patches and mesenteric lymph nodes. Additionally, administration of indole to CIA mice fed a tryptophan deficient diet resulted in greater CIA incidence and splenic Th17 cell frequency. Indole administration was also found to increase splenic activated T cell (CD69+), Tfh, and plama cell numbers in an NP-CGG immunization model. Finally, *ex vivo* stimulation of B cells was conducted to understand the direct effect of indole, which resulted in significantly increased IgG production and a ≈10% increase in the frequency of CD23+ B cells.

Conclusion: Our results suggest that gut dysbiosis due to CIA results in altered tryptophan metabolism and indole production, promoting CIA pathogenesis via activation of T and B cell populations and antibody production. We hypothesize that the ability of indole to promote Th17 and plasma cell differentiation drives increased CIA development. Precise understanding of which indole metabolites are involved and how they engage cellular receptors will help elucidate the role of intestinal dysbiosis in autoimmunity.

Disclosure: B. Trent, None; **M. Chriswell**, None; **W. Jubair**, None; **K. Kuhn**, None.

Abstract Number: 1893

"From Where I Stand": Using Multiple Anchors Yields Different Benchmarks for Meaningful Improvement and Worsening in the Rheumatoid Arthritis Flare Questionnaire (RA-FQ)

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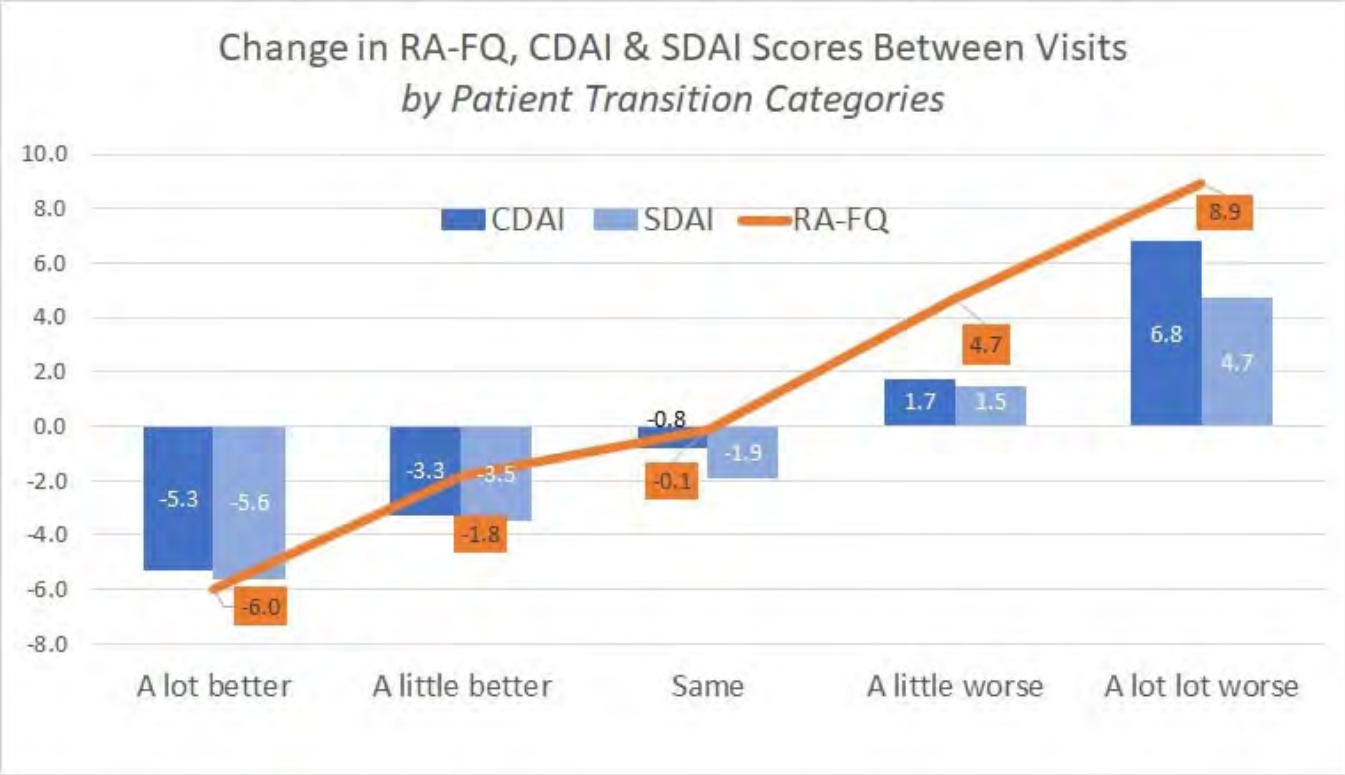
Background/Purpose: The RA-FQ is a patient-reported measure of current disease activity in RA that can be used to identify disease flares. The RA-FQ queries pain, physical function, fatigue, stiffness, and participation and yields a score from 0-50. We previously reported on reliability, validity, and responsiveness. Our goal was to compare changes in the RA-FQ that represent minimal and meaningful improvement or worsening from the perspective of people living with RA, treating rheumatologists, and in relation to disease activity indices.

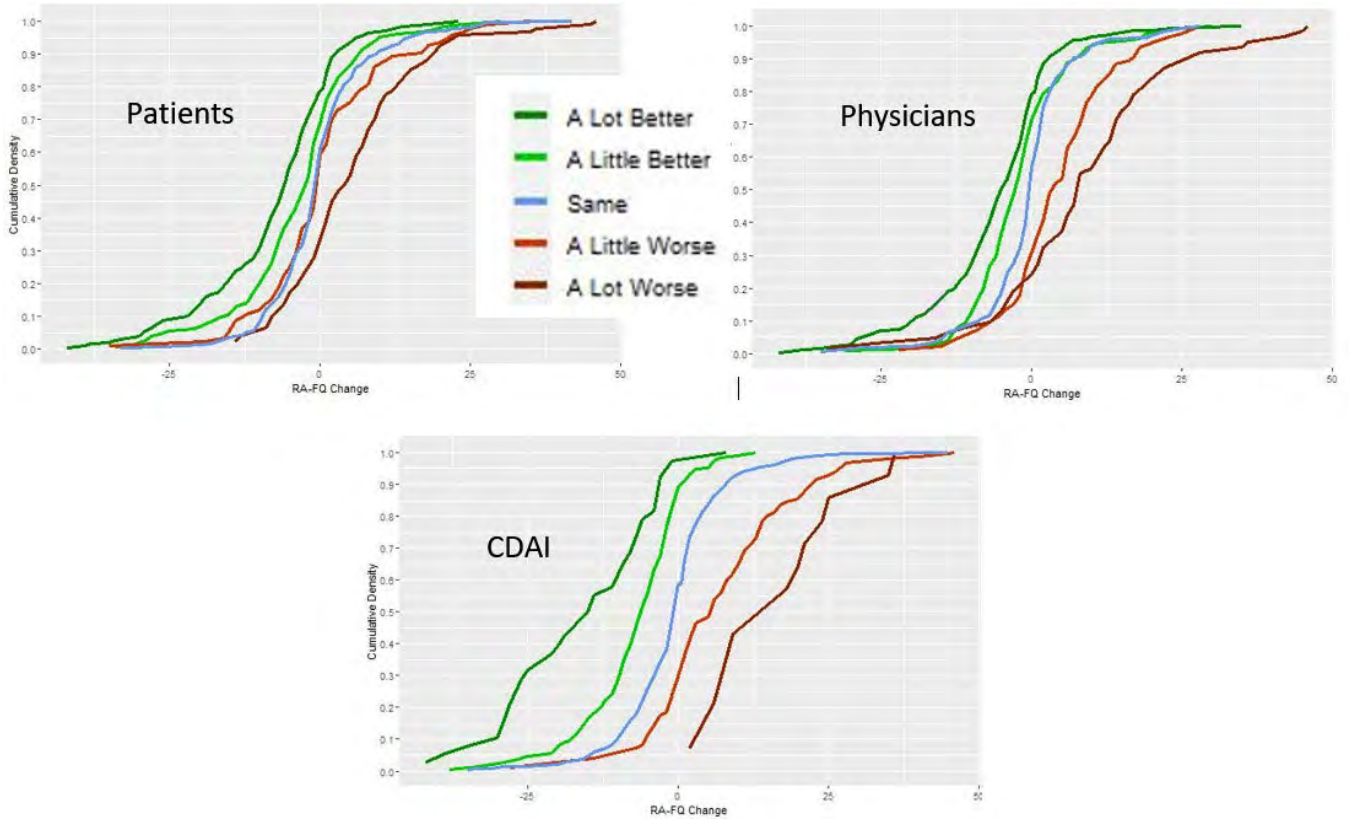
Methods: We used data from adults with early RA (symptoms < 1 year) enrolled in the CATCH (Canadian Early Arthritis Cohort), a prospective study of real-world patients treated across Canada. Participants completed the RA-FQ, Patient Global, and RA Global Change Impression item (a little vs. a lot better or worse or same) at 3- and 6-month

Domain	A Lot Better (N=346; 43%)			A Little Better (N=132; 16%)			The Same (N=174; 21%)			A Little Worse (N=94; 12%)			A Lot Worse (N=62; 8%)		
	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD	Δ	95% CI	SD
RA-FQ Total (0-50)	-6.0	(-7.1, -4.9)	10.3	-1.8	(-3.2, -0.3)	8.4	-0.1	(-1.3, 1.1)	8.1	4.7	(2.9, 6.6)	9.1	8.9	(5.1, 12.7)	15.0
Pain	-1.2	(-1.4, -0.9)	2.4	-0.4	(-0.8, 0.0)	2.3	0.0	(-0.2, 0.3)	1.8	1.3	(0.8, 1.7)	2.2	2.0	(1.2, 2.9)	3.3
Physical Function	-1.3	(-1.6, -1.1)	2.4	-0.3	(-0.6, 0.1)	2.1	0.0	(-0.3, 0.3)	2.1	0.9	(0.4, 1.4)	2.4	1.8	(0.8, 2.7)	3.7
Fatigue	-1.1	(-1.4, -0.8)	2.6	-0.4	(-0.7, 0.0)	1.9	0.0	(-0.3, 0.3)	2.1	0.7	(0.3, 1.1)	2.1	1.3	(0.5, 2.1)	3.2
Stiffness	-1.1	(-1.4, -0.9)	2.4	-0.4	(-0.7, 0.0)	2.0	-0.1	(-0.4, 0.2)	2.0	1.1	(0.6, 1.5)	2.2	1.8	(1.0, 2.7)	3.3
Participation	-1.2	(-1.5, -1.0)	2.5	-0.1	(-0.5, 0.3)	2.1	-0.1	(-0.4, 0.2)	2.2	0.8	(0.4, 1.3)	2.2	2.0	(1.1, 2.8)	3.4
Disease Activity															
CDAI*	-5.3	(-6.3, -4.3)	9.1	-3.3	(-5.4, -1.3)	11.5	-0.8	(-2.0, 0.5)	8.1	1.7	(-0.1, 3.5)	8.8	6.8	(3.7, 9.8)	12.0
SDAI	-5.6	(-6.8, -4.4)	9.2	-3.5	(-6.1, -0.9)	12.2	-1.9	(-3.6, -0.2)	8.9	1.5	(-0.7, 3.7)	9.2	4.7	(1.0, 8.4)	12.2
DAS28-CRP	-0.7	(-0.8, -0.6)	1.01	-0.5	(-0.7, -0.2)	1.2	-0.2	(-0.4, 0.0)	1.0	0.3	(0.1, 0.5)	1.0	0.5	(0.2, 0.9)	1.2
Patient Global (0-10)	-1.3	(-1.5, -1.0)	2.7	-0.5	(-0.9, -0.1)	2.1	-0.1	(-0.4, 0.2)	2.1	1.3	(0.8, 1.8)	2.4	2.9	(2.1, 3.6)	3.1
MD Global (0-10)	-1.2	(-1.4, -1.0)	1.9	-0.7	(-1.1, -0.3)	-0.1	-0.1	(-0.4, 0.2)	1.9	0.1	(-0.3, 0.5)	2.8	0.7	(0.0, 1.5)	2.8
Swollen Joints (28)	-1.4	(-1.7, 1.0)	3.2	-1.0	(-1.8, -0.2)	4.6	-0.4	(-0.9, 0.0)	3.0	0.0	(-0.7, 0.7)	3.4	1.3	(0.2, 2.5)	4.6
Tender Joints (28)	-1.5	(-1.9, -1.1)	3.9	-1.3	(-2.2, -0.3)	5.5	0.0	(-0.7, 0.6)	4.3	0.3	(-0.7, 1.2)	4.5	2.2	(0.8, 3.5)	5.4

Change in RA-FQ scores between visits by patient ratings of RA status.

visits. Rheumatologists recorded joint counts and MD Global. We compared mean change across categories of improvement and worsening disease activity using patient, physician and CDAI anchors and created cumulative distribution function curves to visually examine separation among categories.





Cumulative distribution function curves for patient, physician and CDAI anchors.

Results: The 808 adults were mostly white (84%) women (71%) with a mean (SD) age of 55 (15) and moderate-high disease activity (85%) at enrollment. At the second visit, 79% of patients reported that their RA had changed; 59% were better and 20% worse. Patients who were *a lot worse* had a mean increase of 8.9 points whereas those who rated themselves as *a lot better* had a -6.0 decrease on the RA-FQ (Figure). Minimal worsening and improvement were associated with 4.7 and -1.8 change on the RA-FQ, respectively, while patients who rated their RA unchanged had stable RA-FQ scores (Table). Physicians and CDAI classified more patients as worse than patients, and minimal and meaningful RA-FQ thresholds differed by group. Similar changes were evident in CDAI, SDAI, and DAS indices (Table). Larger differences were observed with patient vs. physician global scores and tender vs. swollen joints. Across measures, the change associated with worsening was greater than for improvement. Results supported all prespecified hypotheses.

Conclusion: In this large cohort of adults with ERA, the RA-FQ was responsive to change and generally distinguished between minimal and meaningful improvement and worsening. These data add to growing evidence demonstrating robust psychometric properties of the RA-FQ and offer initial guidance about the amount of change associated with improvement or worsening, supporting its use in RA care, research and decision-making.

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Squibb Company, 2, Celltrion, 2, Gilead Sciences, 2, F. Hoffmann-La Roche, 2, 6, Janssen, 2, 6, Eli Lilly, 2, Merck, 2, 5, 6, Myriad Autoimmune, 2, Novartis, 6, Pfizer Inc, 2, 5, 6, PuraPharm, 5, Sandoz, 2, Sanofi-Genzyme, 2, 6, Samsung Bioepis, 2; **J. Pope**, AbbVie, 2, Amgen, 2, Bayer, 2, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, Merck, 2, Novartis, 2, Pfizer Inc, 2, Roche, 2, 5, Sanofi, 2, Seattle Genetics, 5, UCB, 2, 5, Actelion, 2, Sandoz, 2; **D. Tin**, None; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **C. Bingham**, Bristol Myers Squibb, 5, Abbvie, 2, Gilead, 2, Eli Lilly, 2, Janssen, 2, Regeneron, 2, Pfizer, 2, Sanofi, 2; **C. Investigators**, None.

Abstract Number: 1894

Natural Language Processing Tool for Extraction of Patient-Reported Outcomes from a National Multi-Electronic Health Records Registry

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SESSION INFORMATION
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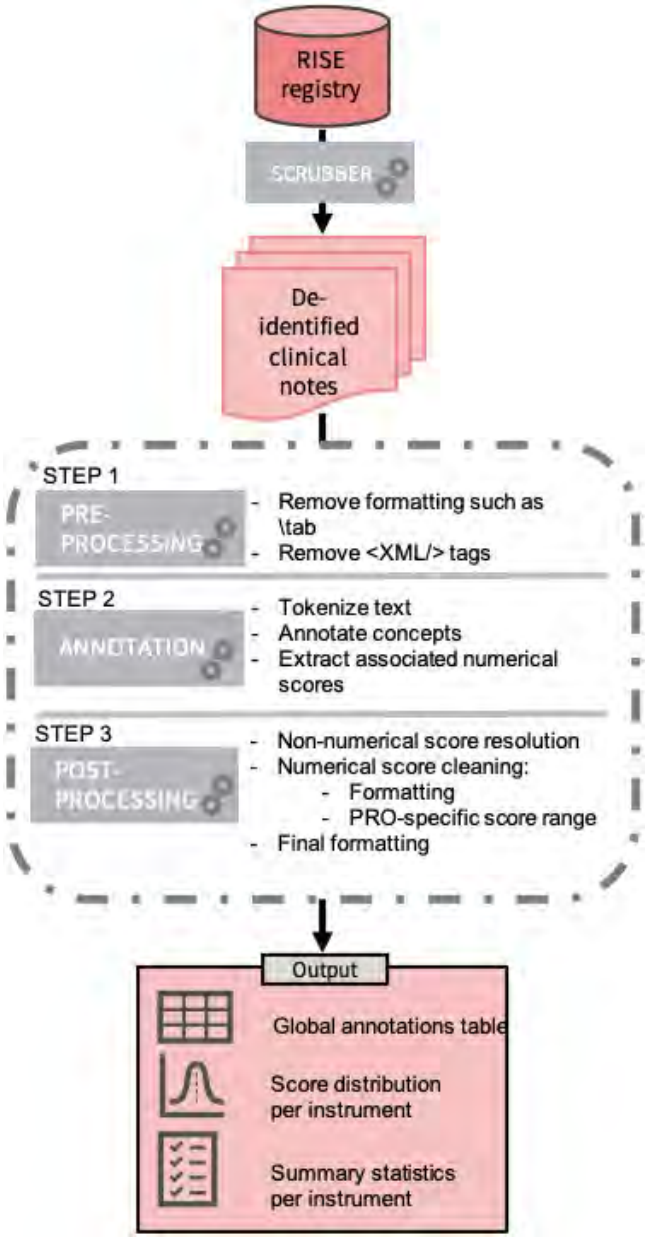
Background/Purpose: Patient reported outcomes (PROs) are increasingly used to track disease activity and facilitate shared decision making in patients with RA. Assessments of disease activity (DA) and functional status (FS) PROs during routine clinical care are recommended in national RA guidelines. However, many rheumatologists do not have support from health IT to reconfigure their EHR systems to collect PROs as structured data. We developed and evaluated a natural language processing (NLP) pipeline for extracting DA and FS scores from clinical notes within the ACR's Rheumatology Informatics System for Effectiveness (RISE) registry.

Methods: We examined de-identified notes and structured electronic health record (EHR) data from all patients with a confirmed diagnosis of RA (2 ICD codes at least 30 days apart), from January 1, 2015, to December 30, 2018 in the RISE registry. The NLP tool was developed in a stepwise approach to extract scores corresponding to Clinical Disease Activity Index (CDAI), Routine Assessment of Patient Index Data 3 (RAPID3), Multidimensional Health Assessment Questionnaire (MDHAQ), and HAQ (Figure 1). First, in a text pre-processing step, we harmonized the notes' format. Next, the concepts of interest (PRO instruments and scores) were annotated. A post-processing step involved formatting and score resolution. The performance of the NLP pipeline was evaluated against a gold standard of human chart review of 100 PRO mentions within 48 randomly-selected notes. We calculated an inter-rater agreement between the NLP-extracted scores and structured scores where available. Agreement was calculated according to (1) "exact" matching based on the numerical scores and (2) for DA scores, "fuzzy" matching, based on score categories (remission, low, etc).

Results: Over 34 million notes from 854,628 patients, from 158 practices, and 24 EHR systems were processed through the NLP pipeline. The majority of practices (n=134) had structured data available for comparison. Overall, our system achieved good fidelity for PRO instrument and score extraction, resulting in a sensitivity of 93.2%, specificity of 80.5% and positive predictive value of 87.3%. DA measures (CDAI and RAPID3) showed substantial agreement between notes and structured data; FS measures (MDHAQ and HAQ) showed almost perfect agreement (Table 1).



NLP pipeline.

Conclusion: The developed NLP pipeline demonstrated good performance, was able to extract PROs from clinical notes of practices in the absence of structured data and can potentially facilitate reporting of quality and performance measures for outpatient rheumatology practices. Further studies are needed to evaluate the potential generalizability of the NLP pipeline to other types of PRO instruments, and to determine whether NLP performance varies by EHR, practice or note type.

		Number of scores compared	Exact matching based on numerical scores	"Fuzzy" matching based on score categories
CDAI		234,400	0.43	0.87
RAPID3		140,680	0.68	0.69
	RAPID3(0-10)	6,218	0.91	0.94
	RAPID3(0-30)	134,462	0.66	0.68
MDHAQ		37,874	0.98	n/a
HAQ		1,313	0.86	n/a

Inter-rater agreement scores between the NLP extractions and the structured data obtained from RISE.

Disclosure: M. Humbert-Droz, None; **Z. Izadi**, None; **G. Schmajuk**, None; **M. Gianfrancesco**, None; **J. Yazdany**, Astra Zeneca, 2, 5, Pfizer, 2, 6, Gilead, 5, BMS Foundation, 5; **S. Tamang**, None.

Abstract Number: 1895

Achievement of Target Serum Uric Acid Among Gout Patients Treated with Long-term Urate Lowering Therapy in the ACR's Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION

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Background/Purpose: The American College of Rheumatology's (ACR) 2012 guidelines for the management of gout recommend using a treat-to-target (T2T) approach to lower serum uric acid (SUA). However, few studies report the frequency of achieving a target of SUA < 6 mg/dL for treated gout patients at a population level. Using the ACR's RISE registry, we examined the proportion of patients with gout receiving long-term urate-lowering therapy (ULT) who achieved an SUA level < 6.0 mg/dL.

Methods: Included patients were required to have at least 1 ICD9/10 diagnosis for gout (ICD9: 274.*; ICD10: M10.*, M1A.*), at least 2 visits with a rheumatology provider prior to December 31, 2019, and continuous use of a ULT (Allopurinol, Febuxostat, Lesinurad, Probenecid, Pegloticase) for a minimum of 12 months. Continuous use was defined as having a prescription or reported use of any ULT medication with an allowable gap of < 90 days for oral medications or < 60 days IV infusions. The primary outcome was the proportion of patients who achieved SUA < 6.0 mg/dL (0.36 mmol/l) while still receiving ULT, during the measurement year (2019), consistent with the ACR's quality measure assessing T2T for patients with gout. Patient characteristics including sociodemographic, comorbidities, and treatment information were extracted from the RISE database. Bivariate analyses were performed across patient characteristics using independent t-tests or chi-square tests, as appropriate. We examined practice-level performance on this measure among practices with > 20 patients in the denominator.

Table 1. Basic characteristics of all patients.

Characteristics		Total patients (N=8,981)	Patients who achieved SUA target (N=3,308)	Patients who did not achieve SUA target (N=5,673)	P value
Age (years); mean (SD)		67.2 (12.7)	67.3 (12.3)	67.1 (13.0)	0.4761
Sex (male); N (%)		6,703 (74.6)	2,467 (74.6)	4,236 (74.7)	0.922
Race; N (%)	White	6,042 (67.3)	2,258 (68.3)	3,784 (66.7)	<0.001
	Black or African American	890 (9.9)	277 (8.4)	613 (10.8)	
	Asian	234 (2.6)	58 (1.7)	176 (3.1)	
	Other*	140 (1.6)	44 (1.3)	96 (17.0)	
	Missing	1,675 (18.6)	671 (20.3)	1,004 (17.7)	
Insurance; N (%)	Medicare	3,121 (34.7)	1,064 (32.2)	2,057 (36.3)	0.001
	Private	2,353 (26.2)	789 (23.8)	1,564 (27.6)	
	Medicaid	153 (1.7)	40 (1.2)	113 (2.0)	
	Other	265 (2.9)	71 (2.1)	194 (3.4)	
	Missing	3,089 (34.4)	1,344 (40.6)	1,745 (30.8)	
U.S. geographic division; N (%)	East North Central	83 (0.92)	39 (1.2)	44 (0.78)	<0.001
	West North Central	1,304 (14.5)	499 (15.1)	805 (14.2)	
	Mid-Atlantic	875 (9.7)	358 (10.8)	517 (9.1)	
	Mountain	481 (5.4)	261 (7.9)	220 (3.9)	
	New England	3,300 (36.7)	1,221 (36.9)	2,079 (36.6)	
	Pacific	1,281 (14.3)	318 (9.6)	963 (16.9)	
	South Atlantic	665 (7.4)	206 (6.2)	459 (8.1)	
	East South Central	193 (2.1)	97 (2.9)	96 (1.7)	
	West South Central	668 (7.4)	264 (8.0)	404 (7.1)	
	Missing	131 (1.5)	45 (1.4)	86 (1.5)	
Comorbidities; N (%)	CCI score; mean (SD)	1.5 (1.1)	1.5 (1.0)	1.6 (1.1)	<0.001
	Hypertension	2,854 (31.8)	950 (28.7)	1,904 (33.6)	<0.001
	Hyperlipidemia	1,436 (16.0)	408 (12.3)	1,028 (18.1)	0.285
	Diabetes mellitus	929 (103)	244 (7.4)	685 (12.1)	<0.001
	Coronary heart disease	169 (1.9)	54 (1.6)	115 (2.0)	0.184
	Chronic kidney disease	1,687 (18.8)	535 (16.2)	1,152 (20.3)	<0.001
	Patients with BMI results in RISE	7,841 (87.3)	2,986 (90.3)	4,855 (85.6)	
	BMI ≥ 30 kg/m² among those with results; N (%)	4,592 (58.5)	1,729 (57.8)	2,863 (58.9)	0.338
Laboratory markers	Patients with SUA results in 2019	4,687 (52.2)	3,308 (100)	1,319 (23.2)	
	Serum uric acid in mg/dL among those tested; median (IQR)	5.2 (4.3, 6.1)	4. (4.0, 5.3)	7.0 (6.3, 8.0)	<0.001
Healthcare utilization	Number of visits in RISE during 2019; mean (SD)				0.088
	Median (IQR)	1.9 (1.3)	1.8 (1.4)	1.9 (1.3)	
		1.5 (1, 2)	1.5 (1, 2)	1.5 (1, 2)	
	Patients with ≥2 visits during 2019; N (%)	5,918 (65.9)	2,231 (67.4)	3,687 (65.0)	0.018
Medications; N (%)	Allopurinol	7,158 (79.7)	2,652 (80.1)	4,506 (79.4)	0.087
	Febuxostat	1,486 (16.6)	557 (16.8)	929 (16.4)	
	Probenecid	193 (2.2)	58 (1.7)	135 (2.4)	
	Lesinurad§	11 (0.12)	<10	<10	
	Pegloticase	133 (1.5)	38 (1.2)	95 (1.7)	
Practice type	Single Specialty Group Practice	7,045 (78.4)	2,638 (79.7)	4,407 (77.9)	<0.001
	Multi- Specialty Group Practice	758 (8.4)	306 (9.2)	452 (8.0)	
	Solo Practitioner	826 (9.2)	294 (8.9)	532 (9.4)	
	Group practice	95 (1.1)	36 (1.1)	59 (1.0)	
	Health System	257 (2.9)	34 (1.0)	223 (3.9)	

SUA: serum uric acid, CCI: Charlson comorbidity index, and IQR: interquartile range. Other race= AMERICAN INDIAN OR ALASKA, NATIVE HAWAIIAN, Hispanic or Latino, and Multi-racial. †SUA results were for 1,319 patients. §For privacy protections, we reported no cell sizes < 10.

Results: Overall, 8,981 patients were included. The mean (SD) age was 67.2 (12.7) years, 74.6% were males, and 67.3% were White (Table 1). Most patients were using allopurinol (79.7%) or febuxostat (16.6%). Among patients tested (N=4,627), the median (IQR) SUA level in 2019 was 5.2 (4.3, 6.1) mg/dL. 36.8% of patients reached an SUA < 6.0 mg/dL, while 14.6% had an SUA ≥ 6.0 mg/dL, and 48.4% did not have an SUA recorded during the measurement

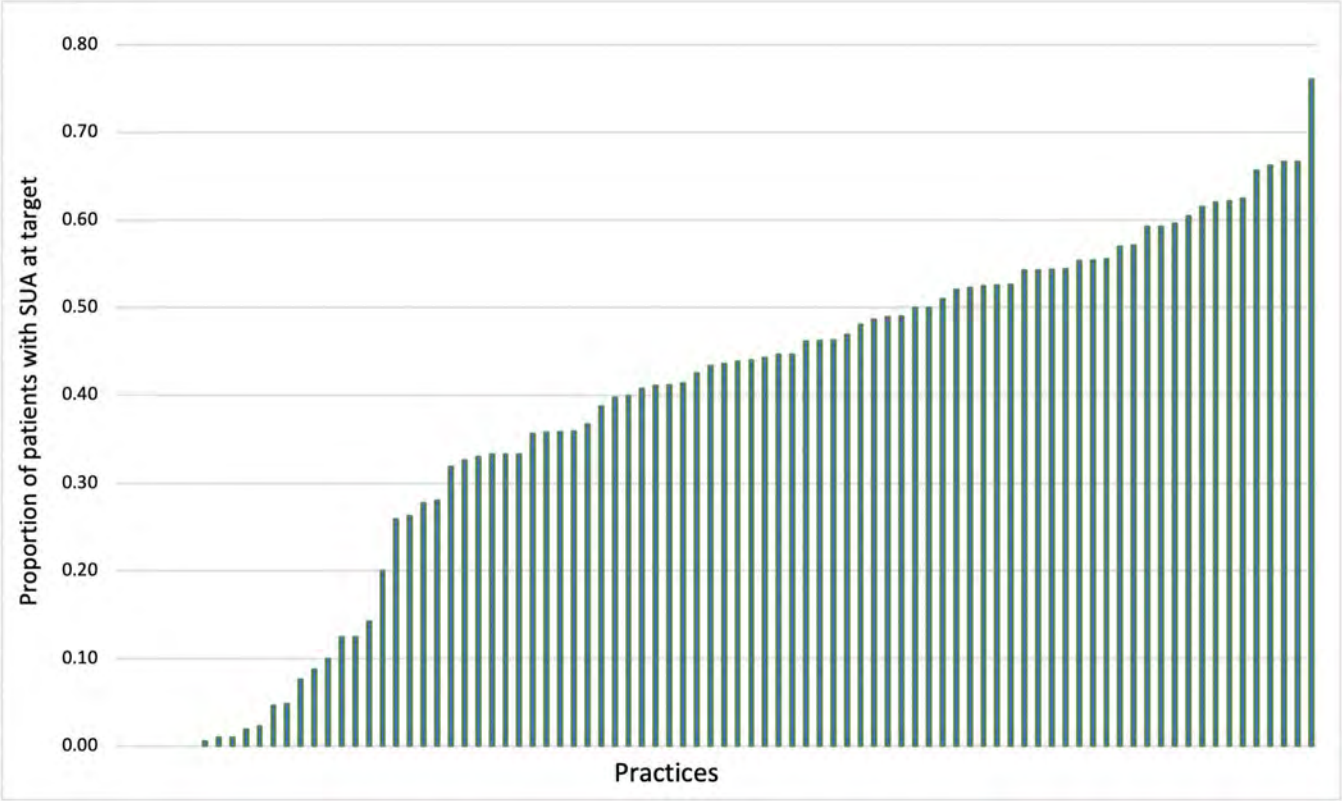

Figure 1. Practice-level performance on quality measure assessing serum uric acid for patients with gout among practices with at least 20 patients eligible (N practices = 88).

year. In bivariate analyses, patients who did not achieve the target SUA were more likely to be Black and have more comorbidities (see Table 1).

Among practices with at least 20 patients in the denominator, median practice-level performance on this quality measure was 43.5 (27.0, 53.5) (see Figure 1). In the 19 practices with the lowest performance (< 20.0% proportion of patients at target), more than 90% of patients did not have SUA assessed during the measurement year.

Conclusion: Among gout patients followed longitudinally by rheumatologists who were receiving long-term ULT, only one third had a documented SUA at the target level, suggesting that there is significant room for improvement in the management of gout. Quality improvement initiatives should focus on improving the documentation of SUA and optimizing ULT among patient groups less likely to be at target. Routine measurement of serum uric acid to monitor the achievement of a T2T strategy is a first step toward improving quality of care for patients with gout.

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

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Abstract Number: 1896

Initial Results from the Implementation of a National Hydroxychloroquine Safe Prescribing Dashboard Within the Veterans Health Administration

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SESSION INFORMATION

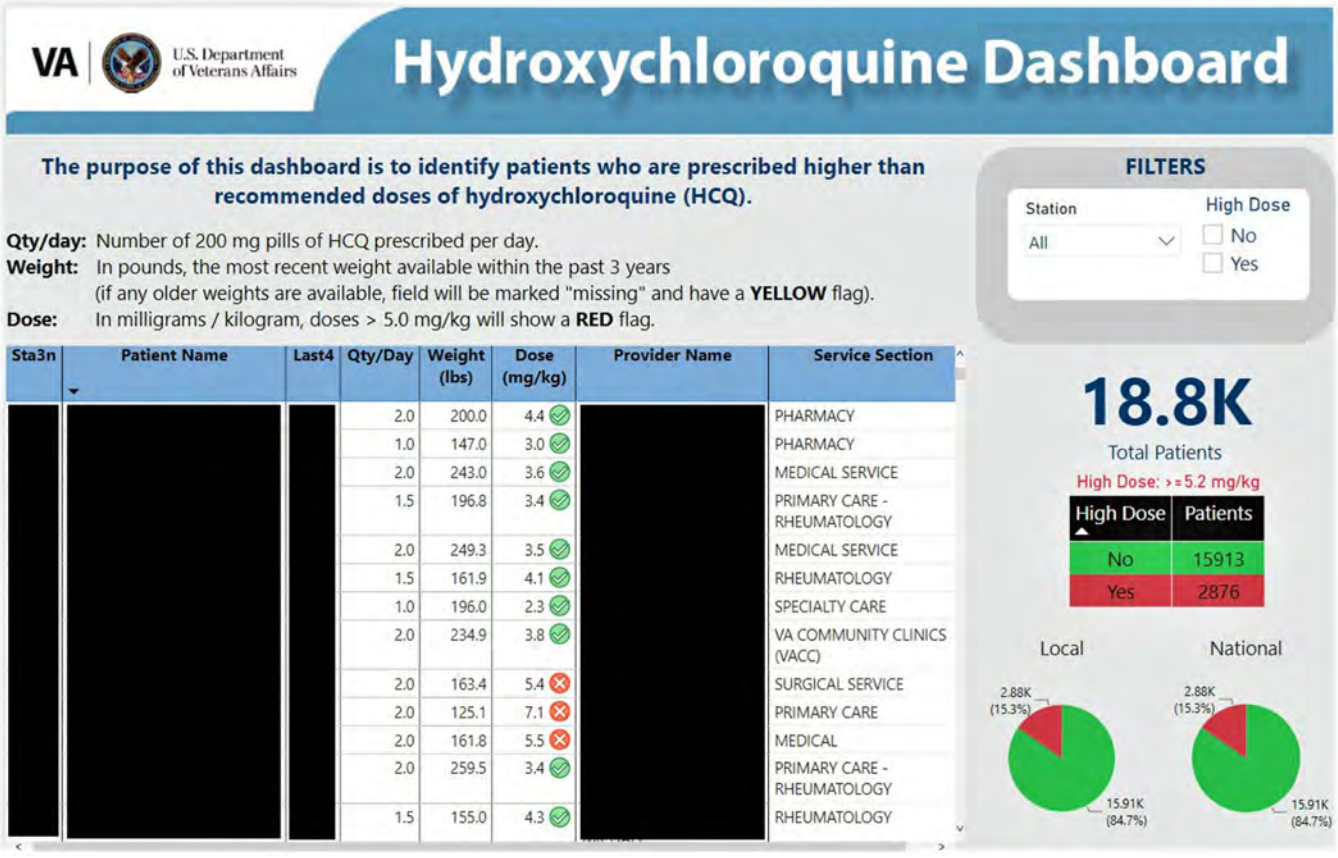
Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Measures & Measurement of Healthcare Quality (1893–1896)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Background/Purpose: Hydroxychloroquine (HCQ) is a commonly used medication for patients with lupus erythematosus, rheumatoid arthritis, and other autoimmune conditions. However, HCQ daily doses of ≥ 5 mg/kg/day can cause retinal toxicity with long-term use. We developed and piloted a medication safety dashboard to improve safe prescribing of HCQ.



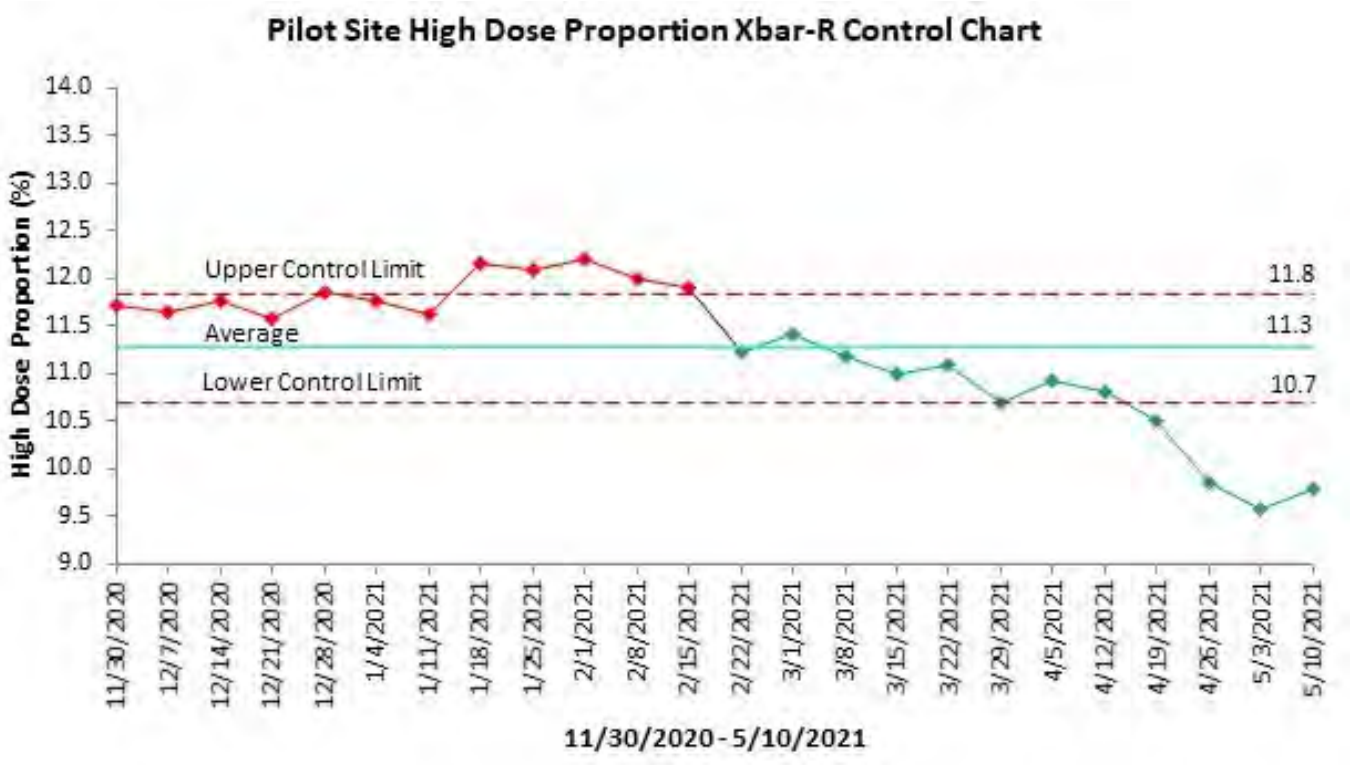
Hydroxychloroquine Dashboard (PHI removed).

Methods: The dashboard was created using Power BI (Microsoft), a data management software package available within the Veterans Health Administration (VHA) for approved users with secure access to EHR data. We extracted values for patients' most recently prescribed HCQ dose and body weight to calculate HCQ dose in mg/kg/day. The dashboard displayed patient identifiers, HCQ dose with a flag if ≥ 5.2 mg/kg/day, and prescriber name and service. It also displayed national-, facility-, and prescriber-level performance (proportion of patients with inappropriate HCQ doses/total number of patients receiving HCQ) for benchmarking (Figure 1).

We enlisted providers from 6 VHA pilot sites to test the dashboard based on their willingness to participate and sub-optimal facility-level performance on HCQ dosing (< 75th percentile nationally). We used Xbar-R control charts to assess the proportion of patients with inappropriate HCQ doses over 7 months. Pilot site leaders (N=7) were asked to provide qualitative feedback on the dashboard's usability, features, and the likelihood of recommending it to others via an online survey (Survey Monkey).

Results: There were 18,635 users of HCQ nationwide across the VHA. 80% of HCQ users had a rheumatology visit within the past 5 years. 1,365 were included at the 6 pilot sites. Pilot site performance improved from 11.7% to 9.8% by May 2021. The Xbar-R control chart showed a significant improvement in the proportion of patients with inappropriate HCQ doses over this 6-month period (Figure 2). Non-participating sites' performance was stable within the chart's control limits from November 2020 to May 2021 (16.0-15.8%).

6 leaders from 5 pilot sites completed the user feedback survey. 5 out of 6 reported the dashboard to be easy to use and would recommend the dashboard to a trainee or colleague. Respondents reported using the dashboard for quality improvement projects and as part of local pay-for-performance programs.



Bar-R Control Chart showing mean proportion of patients receiving inappropriate HCQ doses (≥ 5.2 mg/kg/day) across six pilot sites. X-axis shows 2-week time segments during the study period; y-axis shows proportion of patients with an active prescription for HCQ who were receiving inappropriate doses. Turquoise and red-dotted lines show the average and upper and lower control limits. Red and green dots represent performance at baseline and after a change in a stability trend, respectively.

Conclusion: Use of a medication safety dashboard to improve safe prescribing of HCQ resulted in significant improvement across 6 pilot sites over a 6-month period. With continued feedback from pilot sites, we plan to disseminate the dashboard to VHA clinics nationwide and evaluate performance on safe HCQ dosing over time. Rapid deployment of EHR-based dashboards can facilitate quality improvement by providing key measures and actionable reports directly to clinicians.

Disclosure: A. Montgomery, None; **G. Tarasovsky**, None; **I. Ehiorobo**, None; **M. Whooley**, None; **J. Barton**, None; **K. Sheth**, None; **K. Reiter**, None; **M. Keller**, None; **L. Chung**, Boerhinger Ingelheim, 1, 5, 6, Eicos, 1, 2, Genentech, 2, Reata, 1; **L. Bennett**, None; **J. Dana**, None; **E. Wahl**, None; **G. Schmajuk**, None.

Abstract Number: 1897

A Randomized Double-Blind Controlled Trial of Intensive Serum Urate Lowering with Oral Urate-Lowering Therapy for Erosive Gout

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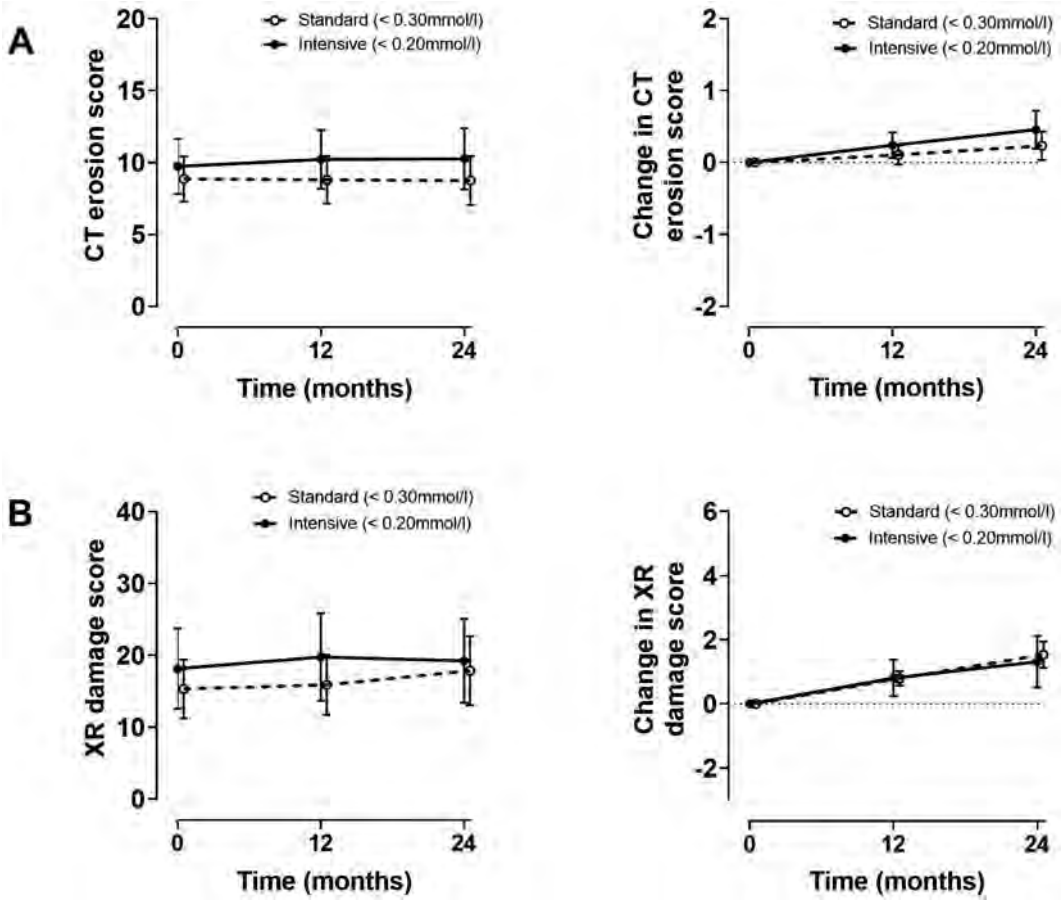

Figure. Primary and key secondary endpoint. A. CT erosion scores. B. Plain radiographic damage scores. Data are presented as mean (95% confidence intervals).

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (1897–1900)
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Session Time: 10:30AM–11:30AM

Background/Purpose: Bone erosion is a common consequence of tophaceous gout, and leads to joint deformity and disability. In small case series, intensive urate-lowering with intravenous pegylated uricase improved erosion scores in gout. However, the optimal strategy for management of erosive gout with oral urate-lowering therapy (ULT) is currently unknown. The aim of this randomized controlled trial was to determine whether intensive lowering of serum urate to a target to below 0.20mmol/L (3.3mg/dL) results in improved bone erosion scores, compared to the standard serum urate target to below 0.30mmol/L (5mg/L) in patients with erosive gout on oral ULT.

Methods: Two-year, randomized controlled trial of 104 participants with erosive gout on oral ULT and serum urate ≥ 0.30mmol/L. Participants were randomly assigned to serum urate target 0.10-0.19 mmol/L (intensive group) or 0.20-0.29 mmol/L (standard group). Both participants and study staff who had contact with participants were blinded to the serum urate target and serum urate results throughout the trial, and oral ULT was titrated using a standardized protocol until the target was reached (with allopurinol to 900mg daily, probenecid to 2g daily, febuxostat to 120mg daily, and benzbromarone to 100mg daily). The primary endpoint was total CT erosion score, and key secondary endpoint was the gout-modified Sharp-van der Heijde plain radiographic damage score. The OMERACT gout core outcome domains were also secondary endpoints.

Results: Over the study period, the serum urate was significantly lower in the intensive group compared to the standard group (P=0.002). However, fewer participants in the intensive group achieved the randomized serum urate target (at week 52, 53% vs 83%, P< 0.01, and at week 104, 62% vs 83%, P< 0.05). In the intensive group, allopurinol doses were higher (mean (SD) 746 (210) mg/day vs 496 (185) mg/day, P< 0.001), and more combination therapy was used (P=0.0004). Small increases in CT erosion scores were observed in both groups over two years, with no between-group difference (P=0.29), Figure. Similar findings were observed for the plain radiographic damage score (P=0.58), Figure. Other OMERACT gout core outcome domains (gout flares, tophus, pain, patient global assessment, health related quality of life, and activity limitation) improved in both groups over the two-year study period, with no between-group differences. Adverse event and serious adverse event rates were similar between groups.

Conclusion: Intensive serum urate lowering below 0.20mmol/L is difficult to achieve with oral ULT, leads to high medication burden, and does not improve bone erosion scores in patients with erosive gout. When using oral ULT, a serum urate target below 0.30mmol/L is sufficient to achieve clinical benefit in this patient group.

Disclosure: N. Dalbeth, AstraZeneca, 2, JW Pharmaceutical Corporation, 2, PK Med, 2, Horizon, 2, Selecta, 2, Dyve Biosciences, 2, Arthrosi, 2, Amgen, 5; **A. Doyle**, None; **K. Billington**, None; **G. Gamble**, None; **P. Tan**, None; **K. Latto**, None; **T. Parshu Ram**, None; **R. Narang**, None; **R. Murdoch**, None; **D. Bursill**, None; **B. Mihov**, None; **L. Stamp**, None; **A. Horne**, None.

Abstract Number: 1898

Risk of Major Adverse Cardiovascular Events in a Large Cohort of Patients with Acute Calcium Pyrophosphate Crystal Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (1897–1900)

Session Type: Abstract Session

Session Time: 10:30AM–11:30AM

Table. Baseline characteristics of acute CPP crystal arthritis and general patient cohorts

	Acute CPP crystal arthritis cohort n=1275	General patient cohort n=4148
Age at index date	73.6 (10.7)	73.7 (12.0)
Male	47.5	42.2
Race		
White	82.8	80.5
Black	7.8	10.8
Other	9.5	8.7
Body mass index, kg/m^{2+}	28.6 (5.8)	27.7 (5.7)
Ever smoker	12.9	8.2
Number of encounters from EHR entry to index date	134.2 (143.0)	58.5 (67.9)
Multimorbidity score++	16.9 (16.6)	9.8 (12.0)
Comorbidities*		
Hypertension	66.6	45.7
Hyperlipidemia	51.1	33.4
Cancer	32.0	24.8
Diabetes	21.7	13.4
Atrial fibrillation	17.6	9.1
Chronic kidney disease	10.6	3.8
Peripheral artery disease	10.5	4.3
Osteoarthritis	59.8	25.9
Gout	17.3	3.2
Rheumatoid arthritis	12.5	3.2
Medications**		
Aspirin	23.6	9.5
Platelet aggregation inhibitor	2.1	0.8
Oral anticoagulant	9.7	4.2
Heparins	17.6	3.7
Anti-anginal	1.7	0.6
ACE inhibitor or ARB	23.8	12.8
Anti-arrhythmic	4.8	1.7
Beta-blocker	27.1	12.8
Calcium channel blocker	22.7	10.9
Diuretic	21.6	10.4
Anti-lipemic	28.7	14.7
Insulin	6.1	1.2
Non-insulin diabetes medication	8.0	3.7
Glucocorticoid	30.7	8.3
NSAID	21.0	6.0
Colchicine	11.8	0.5
Urate-lowering therapy	6.8	1.1

Presented as mean (SD) or percentage

+Body mass index missing for 325 acute CPP crystal arthritis subjects and 1969 general subjects

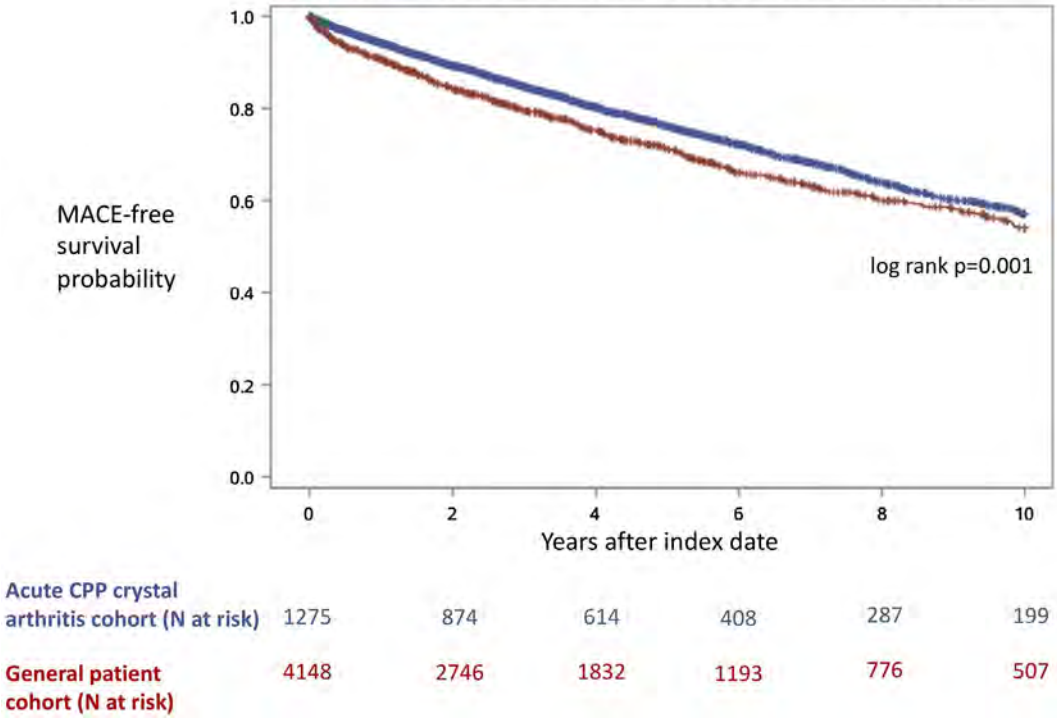
++Weighted multimorbidity score based on billing codes for 40 chronic conditions

*Defined by ≥2 ICD-9/10 codes from 1st EHR encounter through index date

**Prescribed at any time from 90d before index date through index date (oral, IV or SC)

EHR: electronic health record

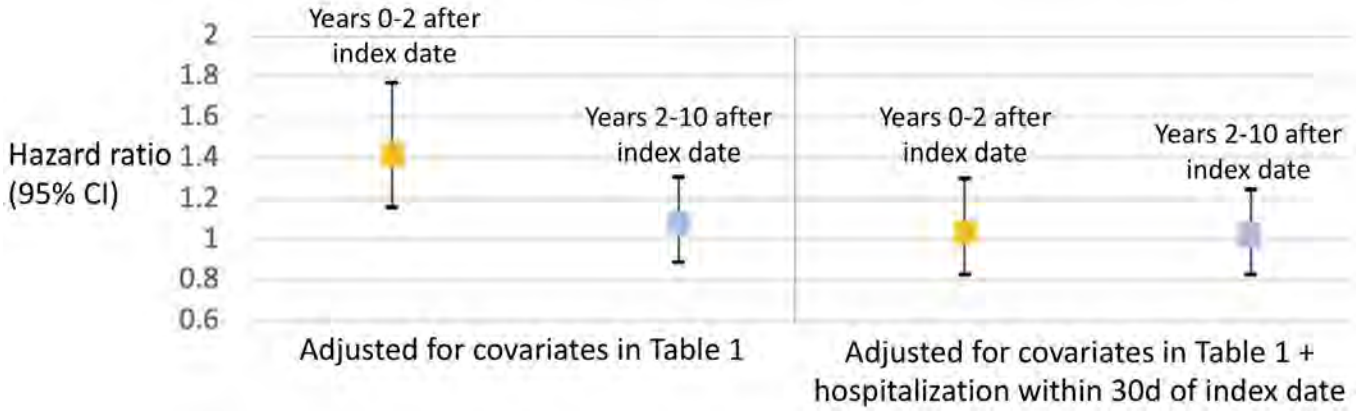
Figure 1. Unadjusted Kaplan-Meier curves for MACE-free survival



Background/Purpose: Acute calcium pyrophosphate (CPP) crystal arthritis, also known as pseudogout, causes an acute inflammatory arthritis that shares clinical similarities with gout. We investigated the risk of incident cardiovascular events in patients with acute CPP crystal arthritis.

Methods: We performed a matched cohort study using electronic health record (EHR) data at an academic medical center, 1990-2017. Major adverse cardiovascular event (MACE), defined as myocardial infarction, re-vascularization, stroke or death, was identified using inpatient diagnosis codes, inpatient/outpatient procedure codes, and vital status. We applied an EHR-based algorithm with a positive predictive value of 81% for acute CPP crystal arthritis to identify the exposed cohort, which we matched to an unexposed general patient cohort on year of EHR entry and index date. Follow-up began at index date (1st mention of "pseudogout" in notes or 1st positive synovial fluid CPP crystal result, or a matched encounter date for the general patient cohort) and ended at MACE or the last encounter before/at 10 years of follow-up. We required age ≥50, ≥180d enrollment before index date and ≥2 encounters dur-

Figure 2. Hazard ratios for MACE stratified by time after index date, comparing the acute CPP crystal arthritis cohort to the general patient cohort (reference)



ing that window for both cohorts. Subjects with MACE occurring from 1st EHR encounter through index date were excluded. Incidence rates (IR) and IR ratios (IRR) were estimated. A Kaplan-Meier curve and log-rank test compared MACE-free survival between the cohorts. Cox proportional hazards models estimated risk of MACE, adjusting for baseline traditional cardiovascular risk factors and healthcare utilization, and allowed for differential effects of acute CPP crystal arthritis over time.

Results: The acute CPP crystal arthritis cohort included 1,275 patients (mean age 72.9 years, 54.4% female) that were matched to 4,148 general patients (mean age 72.9 years, 59.0% female) with 23,144 total person-years follow-up. Cardiovascular comorbidities including hypertension, hyperlipidemia, and diabetes were more common in the acute CPP crystal arthritis cohort, as were prescriptions for NSAIDs and glucocorticoids (Table). MACE IR was highest in the first year after index date in each cohort: 10.1 per 100 person-years in the acute CPP crystal arthritis cohort and 6.2 per 100 person-years in the general cohort (IRR 1.64, 95% CI 1.31, 2.05). Acute CPP crystal arthritis was associated with significantly greater risk for MACE compared to the general cohort in the first two years after index date (HR 1.43, 95% CI 1.16, 1.77), but not in later years (Figures). Additional adjustment for hospitalization within 30 days of index date attenuated the HR during the first two years after index date (HR 1.04, 95% CI 0.83, 1.30).

Conclusion: Patients with acute CPP crystal arthritis were at increased risk for MACE in the first two years after index date, but not in subsequent years. Diagnosis of this acute, episodic crystalline arthritis in the inpatient setting confounds this association and partially explains the observed increased risk.

Disclosure: S. Tedeschi, NGM Biopharmaceuticals, 2; **W. Huang**, None; **K. Yoshida**, None; **D. Solomon**, Abbvie, 5, Amgen, 5, Genentech, 5.

Abstract Number: 1899

Mortality in Patients with Sub-Optimally Treated Gout in the Veteran's Health Administration: A National Retrospective Cohort Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (1897–1900)
Session Type: Abstract Session
Session Time: 10:30AM–11:30AM

Background/Purpose: Patients with gout have an increased risk of mortality. Current ACR guidelines for the treatment of gout recommend a treat-to-target approach with titration of urate lowering therapy (ULT) based on serum urate (SU) concentrations. However, it remains to be determined whether this treat-to-target approach improves long-term outcomes in gout. Therefore, the goal of this study was to examine whether ULT administration and SU values concordant with a treat-to-target approach are associated with all-cause mortality.

Methods: We performed a retrospective cohort study, identifying patients with gout using national Veteran's Health Administrative (VHA) data from 1/1999-9/2015 based on the presence of ≥2 ICD-9 codes for gout (274.X) (Helget LN et al. Arthritis Care Res 2020). Patients' gout treatment status was categorized in a time-varying manner as either "well-treated" or "sub-optimally treated" during each 365 days of follow-up. Gout patients were considered "well-treated" if during the preceding 365-day period had: 1) ≥2 fills of ≥90 days duration for ULT and 2) a mean SU < 6 mg/

Table 1. Study patients, follow-up, mortality rate and risk of death associated with treatment status

Number of Gout Patients	506,981	
Number of Deaths	176,591	
Patient Years of Follow Up	3,004,816	
Overall Mortality Rate	58.8 deaths / 1,000 PY	
Characteristic	**Unadjusted HR (95% CI)**	**Adjusted HR (95% CI)**
Gout Treatment Status		
Well Treated	Referent	Referent
Sub-Optimally Treated	1.24 (1.23-1.26)	1.22 (1.21-1.24)

dL, using VHA pharmacy and laboratory data. Gout patients who did not meet these criteria were classified as "sub-optimally treated". Patients were followed from the index date (date fulfilling gout algorithm) until death (identified through linkage with the National Death Index) or censoring due to end of study period (12/2015). We assessed the association of time-varying gout treatment status with all-cause mortality using multivariable Cox regression models adjusting for demographics and comorbidities obtained from VHA administrative data.

Results: We identified 506,981 gout patients in the VHA during our study period. Patients were predominantly male (99%) and had a mean (SD) age of 66.6 (11.6) years. During follow-up, 61.3% received at least one ULT prescription and >78% had at least one SU measurement. Over 3,004,816 patient-years of follow-up, there were 176,591 deaths. Kaplan-Meier survival curves demonstrated reduced survival in gout patients who were "sub-optimally treated" (log-rank p-value < 0.0001) (**Figure 1**). In unadjusted models, patients with gout who were "sub-optimally treated" had

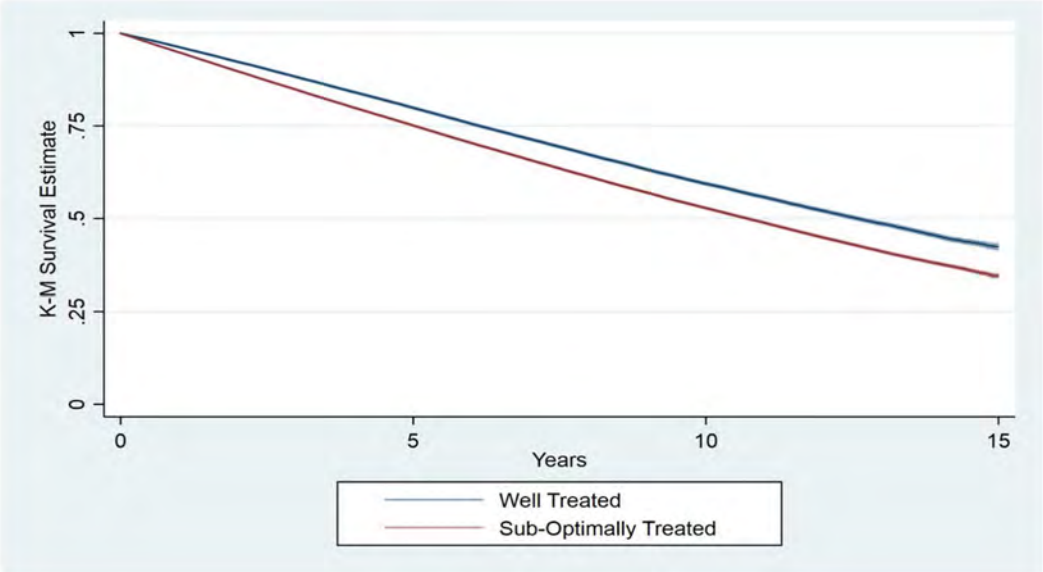

Figure 1. Kaplan-Meier survival estimates demonstrating increased all-cause mortality among sub-optimally treated gout patients (red line) compared to well-treated patients with gout (blue line); log-rank test p-value <0.0001.

a 24% higher risk of all-cause mortality (aHR 1.24 [95% CI 1.23-1.26]). These results were not changed following multivariable adjustment (**Table 1**).

Conclusion: Using data from the largest integrated health system in the U.S., we found that patients with gout receiving suboptimal gout management based on ULT administration and SU measurements demonstrated an approximately 22% higher rate of all-cause mortality. These findings illustrate the long-term consequences of suboptimal treatment and support current ACR guidelines recommending a treat-to-target approach in the management of chronic gout. Additional research is needed to better understand factors mediating the relationship between optimal management and survival, as this information will be essential in informing future strategies aimed at improving long-term outcomes in gout.

Disclosure: L. Helget, None; **B. England**, Boehringer-Ingelheim, 2; **P. Roul**, None; **H. Sayles**, None; **A. Petro**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1900

Urate Lowering Therapy in the Treatment of Gout: A Multicenter, Randomized, Double-blind Comparison of Allopurinol and Febuxostat Using a Treat-to-Target Strategy

James O'Dell[1], Tuhina Neogi[2], Michael Pillinger[3], Paul Palevsky[4], Jeff Newcomb[1], Mary Brophy[5], Hongsheng Wu[5], Annie Davis-Karim[6], Ryan Ferguson[5], David Pittman[6], Robert Terkeltaub[7], Amy Cannella[1], Bryant England[1], Lindsay Helget[1], Ted Mikuls[1] and Tomas Taylor[8], [1]University of Nebraska Medical Center, Omaha, NE, [2]Boston University School of Medicine, Boston, MA, [3]New York University Grossman School of Medicine, New York,, NY, [4]Pittsburgh University, Pittsburgh, PA, [5]Boston VA, Boston, MA, [6]Albuquerque VA, Albuquerque, NM, [7]VA/UCSD, San Diego, CA, [8]White River Junction VA, White River Junction, VT

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Metabolic & Crystal Arthropathies – Basic & Clinical Science (1897–1900)
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Background/Purpose: Urate lowering therapy (ULT) is a cornerstone treatment in the management of gout. A paucity of data exists about the relative efficacy and safety of the two major oral ULTs, allopurinol and febuxostat, when administered as part of a treat-to-target approach as recommended by ACR and EULAR. Evidence regarding the comparative efficacy and safety of these agents is particularly needed in the context of chronic kidney disease (CKD), a common comorbid condition among gout patients. This multicenter, randomized, double-blind, non-inferiority trial was designed to examine the comparative efficacy and safety of these ULTs in gout management.

Methods: Patients with gout and a serum urate (SU) concentration ≥ 6.8 mg/dl were randomized 1:1 between 2017-2019 to receive appropriately titrated allopurinol or febuxostat in this non-inferiority 72-week trial. Patients with persistent hyperuricemia, despite treatment with allopurinol (≤ 300 mg/dl), were eligible and the protocol specified that ≥ 1/3 would have CKD stage 3. The trial had 3 phases: 1) ULT titration (weeks 0-24), 2) Maintenance (weeks 25-48), and 3) Observation, with continued stable ULT (weeks 49-72). Allopurinol and febuxostat were initiated in daily doses of 100 mg and 40 mg with maximum titration to 800 mg and 120 mg (reduced to 80 mg in 2019 per FDA's request), respectively. Patients received anti-inflammatory prophylaxis chosen by site investigator according to 2012 ACR guidelines until the beginning of phase 3. The primary endpoint was the proportion of patients experiencing ≥ 1

Table 1. Baseline Characteristics of Patients with Gout

Demographics	Allopurinol (N=468)	Febuxostat (N=472)	Total (N=940)
Demographics			
Age, years; mean (SD)	62.9 (11.8)	61.3 (12.9)	62.1 (12.4)
Male, %	98.5	98.3	98.4
Race/ethnicity, %			
White	66.7	68.2	67.5
Black/African American	22.0	21.6	21.8
Comorbidity			
Chronic kidney disease (stage 3), %	38.7	36.0	37.3
Serum creatinine, mg/dl; mean (SD)	1.2 (0.3)	1.2 (0.3)	1.2 (0.3)
Hypertension, %	78.0	74.8	76.4
Diabetes, %	35.0	31.6	33.3
Cardiovascular disease, %	30.1	23.5	26.8
Body mass index, (SD)	33.6 (6.6)	33.7 (6.6)	33.7 (6.6)
Gout Related Factors			
Serum urate, mg/dl; mean (SD)	8.6 (1.4)	8.5 (1.3)	8.5 (1.4)
Serum urate ≥ 9 mg/dl, %	34.2	31.4	32.8
Allopurinol use (300 mg/d or less), %	38.0	35.4	36.7
Gout duration, years; mean (SD)	9.7 (10.6)	10.2 (11.4)	10.0 (11.0)
Presence of Tophi, %	17.3	15.0	16.2
C-reactive protein, mg/L; mean (SD)	9.6 (18.7)	8.2 (15.4)	8.9 (17.1)

Values shown as mean (standard deviation) or %; Cardiovascular disease = history of coronary artery disease, myocardial infarction, or heart failure, Stage 3 chronic kidney disease defined by estimated glomerular filtration rate (eGFR) of 30-60 ml/min at enrollment; patients excluded if prior febuxostat use or eGFR <30 ml/min

flare during phase 3 with a pre-specified margin of < 8% difference indicative of non-inferiority. Secondary endpoints included: efficacy/tolerability in CKD stage 3, proportion achieving SU < 6 mg/dl at the end of phase 2, and serious adverse events (SAE).

Results: : Characteristics of the 940 patients with gout (n=21 sites) receiving at least 1 dose of study medication are shown in **Table 1**. Overall, 20% withdrew prior to completion with similar proportions by treatment arm. During phase 3, 35% of patients treated with allopurinol had ≥ 1 flare compared to 42% of participants treated with febuxostat ($p < 0.001$ for non-inferiority) (**Table 2**). Overall, 80% of patients achieved SU < 6.0 mg/dl (92% achieved SU < 6.8 mg/dl) during phase 2 with no difference according to ULT treatment. Likewise, there were no treatment differences in SAEs (including percent of patients with cardiovascular events) in those with or without CKD. Additional secondary outcomes are shown in **Table 2**.

Conclusion: This large, randomized double-blind trial demonstrates that allopurinol, when dosed appropriately as part of a treat-to-target strategy, is non-inferior to febuxostat in the treatment of gout. Both ULTs were highly efficacious in this context with 80% of patients achieving and maintaining SU goals after 1 year and more than 90% achieving SU < 6.8 mg/dl. There was no evidence of increased cardiovascular toxicity with febuxostat compared to

Table 2. Results

	Allopurinol	Febuxostat	Total	P Value
Primary Endpoint[1]				
≥ 1 Gout flare in Phase 3, %	34.7	42.2	38.5	< 0.001
Secondary Endpoints[1]				
All study Participants				
Serum Urate < 6.0 mg/dl in phase 2[2], %	81.1	78.4	79.8	0.34
Serious Adverse Event, %	26.7	26.1	26.4	0.60
Cardiovascular event[3], %	8.1	6.8	7.5	0.82
Early study termination, %	20.5	19.7	20.1	0.82
C Reactive Protein, mg/L; mean (SD)	7.1 (11.0)	7.2 (20.8)	7.1 (16.7)	0.97
Serum Creatinine, mg/dl; mean (SD)	1.3 (0.4)	1.3 (0.6)	1.3 (0.5)	0.42
Participants with CKD 3				
≥ 1 Gout flare in Phase 3, %	29.9	43.8	36.8	< 0.001
Serious Adverse Events, %	38.1	35.9	37.0	0.66

[1] Primary endpoint assessed on 780 patients entering phase 3 (p-value represents test of non-inferiority); phase 2 serum urate measures assessed in 785 patients completing phase 2; serious adverse events assessed on all patients taking at least one dose of study drug (n=940); proportion with CKD3 and flare in phase 3 assessed in 291 patients (351 CKD patients assessed for serious adverse events)

[2] Definition of serum urate in Phase 2 = mean concentration at weeks 36, 42, and 48; 46 (5.9%) at week 36, 144 (18.5%) at week 42, and 33 (4.2%) serum urate measurements are missing

[3] Adjudicated cardiovascular events

allopurinol. Moreover, the comparative efficacy and safety of these two agents extended to patients with CKD stage 3, highly relevant as nearly one in every two gout patients suffers from renal insufficiency.

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Abstract Number: 1901

Severe Foot Symptoms Are Associated with Mortality: The Johnston County Osteoarthritis Project

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Orthopedics, Low Back Pain, & Rehabilitation (1901–1904)

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Session Time: 10:30AM–11:30AM

Background/Purpose: Foot symptoms (i.e., pain, aching, and stiffness [PAS]) are common in middle-aged to older adults and are linked to restricted physical activity, poorer physical function and balance, disability, and falls. Their contribution to mortality is not known. This longitudinal analysis examined whether presence and severity of foot symptoms were associated with mortality in a large prospective community-based cohort of Black and White men and women 45+ years old.

Methods: Data were from three study visits (baseline [1999-2004], 1st follow-up [2006-2010], and 2nd follow-up [2013-2015]) of the Johnston County Osteoarthritis Project (JoCoOA). Presence of foot PAS (yes/no) was assessed by the question: "On most days, do you have pain, aching or stiffness in your left/right foot?" Foot PAS severity was recorded as none (referent=0), mild=1, moderate=2, or severe=3. Foot PAS Severity Count summed severity across both feet (0 [none] to 6 [severe in both feet]). All-cause mortality was determined for participants at each follow-up study visit using data from the National Death Index to determine date and cause of death through December 31, 2015. Static covariates (did not change or changed at same rate for all participants over time) were enrollment cohort (original [1991-1997] or enrichment [2003-2004]), birth cohort, age, sex, race, and education level. Time-varying

Table 1. Participants Characteristics, by Study Visit.

	Study Visit		
Characteristic	**Baseline** n=2613	**1st Follow-Up** n=1604 6.4±0.7 years	**2nd Follow-Up** n=850 11.8±1.2 years
Foot Symptoms Measures			
Any Foot Pain, Aching, Stiffness (PAS), n (%)	969 (37)	401 (25)	175 (21)
Foot PAS worst severity from either foot, n (%)			
None	1644 (63)	1207 (75)	675 (79)
Mild	332 (13)	142 (9)	54 (6)
Moderate	409 (16)	181 (11)	45 (5)
Severe	228 (9)	74 (6)	76 (9)
Foot PAS Severity Count for both feet, n (%)			
0	1644 (63)	1207 (75)	675 (79)
1	68 (3)	53 (3)	18 (2)
2	360 (14)	128 (8)	42 (5)
3	61 (2)	35 (2)	35 (4)
4	296 (11)	132 (8)	28 (3)
5	21 (1)	9 (1)	8 (1)
6	163 (6)	40 (3)	44 (5)
Demographic/Clinical Characteristics			
Age, mean±SD years	63±11	68.4±9	71±8
Women, n (%)	1704 (65)	1069 (67)	574 (68)
Black, n (%)	856 (33)	492 (31)	280 (33)
<12 years formal education, n (%)	716 (27)	341(21)	119 (14)
Body Mass Index, mean±SD kg/m^2	31±7	31±7	31±7
Self-Reported Health Measures			
Ever smoked, n (%)	1058 (41)	865 (54)	462 (54)
Any alcohol use, n (%)	957 (37)	658 (41)	348 (41)
<150 MVPA minutes/week, n (%)	791 (30)	341 (21)	145 (17)
NSAID use, n (%)	1259 (48)	1082 (68)	584 (69)
Hypertension, n (%)	1265 (48)	1087 (68)	690 (81)
Cardiovascular Disease, n (%)	575 (22)	566 (35)	364 (43)
Diabetes, n (%)	425 (16)	383 (24)	253 (30)
Depressive Symptoms, n (%)	344 (13)	187 (12)	101 (12)
Liver disease, n (%)	36 (1)	32 (2)	22 (3)
Cancer, n (%)	28 (1)	41 (3)	81 (10)
Any knee PAS, n (%)	1321 (51)	608 (38)	325 (38)
Any hip PAS, n (%)	1005 (39)	474 (30)	288 (34)

Table 2. Adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for association between foot symptoms and all-cause mortality (1999-2015), total sample and by race, obesity, and diabetes.

Foot Symptom Definition		By Race		By Obesity		By Diabetes	
	Overall	White	Black	BMI<30	BMI≥30	No Diabetes	Diabetes
	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)	aHR (95% CI)
No foot PAS	ref	ref	ref	ref	ref	ref	ref
Any foot PAS	1.16 (0.99, 1.35)	1.14 (0.95, 1.37)	1.19 (0.91, 1.54)	1.14 (0.93, 1.40)	1.18 (0.95, 1.48)	1.11 (0.93, 1.33)	1.27 (0.96, 1.68)
No foot PAS	ref	ref	ref	ref	ref	ref	ref
Mild foot PAS severity	0.90 (0.71, 1.15)	0.85 (0.63, 1.13)	1.05 (0.69, 1.60)	0.94 (0.69, 1.28)	0.86 (0.59, 1.26)	0.82 (0.61, 1.10)	1.16 (0.75, 1.78)
Moderate foot PAS severity	1.20 (0.98, 1.47)	1.25 (0.98, 1.58)	1.08 (0.75, 1.56)	1.25 (0.95, 1.65)	1.16 (0.87, 1.55)	1.26 (1.00, 1.59)	1.06 (0.72, 1.56)
Severe foot PAS severity	**1.59 (1.23, 2.04)**	**1.54 (1.14, 2.10)**	**1.66 (1.12, 2.47)**	1.41 (0.97, 2.05)	**1.72 (1.24, 2.38)**	**1.46 (1.07, 1.99)**	**1.85 (1.25, 2.74)**
PAS severity count for both feet (1 unit increase)	**1.07 (1.03, 1.12)**	**1.07 (1.03, 1.13)**	1.07 (1.00, 1.14)	**1.06 (1.01, 1.12)**	**1.08 (1.02, 1.14)**	**1.06 (1.01, 1.11)**	**1.09 (1.02, 1.16)**

Adjusted enrollment cohort (original 1991-1997 or enrichment 2003-2004), age, sex, race, education level, body mass index, smoking, alcohol use, minutes/week of moderate/vigorous physical activity, non-steroidal anti-inflammatory drug use, diabetes, count of 5 comorbidities (hypertension, cardiovascular disease, diabetes, depressive symptoms, liver disease), knee PAS, hip PAS
All models stratified by decade birth cohort (before 1920, 1920-<1930, 1930-<1940, 1940-<1950, 1950-<1960) to account for calendar effects, as recommended for longitudinal analyses of healthy people and when the calendar effect is likely to affect the outcome (e.g., mortality) and other risk factors.
Cox proportional hazard modeling time to death to provide adjusted HR and 95% confidence intervals that are **bold** when significant at alpha=0.05
An interaction term is used to provide adjusted HR by race, obesity, and diabetes respectively; *=interaction is significant at p-value<0.1
Multiple imputation model including all baseline variables was used to impute missing covariate values (5.8%); 10 multiple imputed datasets were analyzed.

covariates were body mass index (BMI), smoking, alcohol use, minutes/week of moderate/vigorous physical activity, non-steroidal anti-inflammatory drug use, hypertension, cardiovascular disease, diabetes, depressive symptoms, liver disease, knee PAS, and hip PAS. For each foot symptom measure (PAS, PAS severity, PAS Severity Count), separate Cox proportional hazards regression models with covariates were used to estimate adjusted hazard ratios (aHR) and 95% confidence intervals (CI) for the total sample and stratified by sex, race, obesity (BMI< 30 vs. ≥30 kg/m^2), and diabetes (test for interaction significant at p< 0.1).

Results: At baseline, mean age was 63 years, 2/3 were women, 1/3 were Black, mean BMI was 31 kg/m^2, and 37% had foot PAS (Table 1). Mean follow-up time was 11.8 years, and there were 818 deaths. In adjusted models (Table 2), foot PAS was related to a 16% greater hazard of all-cause mortality (aHR 1.16, 95%CI 0.99, 1.35). Compared to no foot PAS, severe foot PAS was associated with a 59% greater hazard of excess mortality (aHR 1.59, 95% CI 1.23, 2.04). Every 1-unit increase in PAS Severity Count was associated with a 7% greater hazard of all-cause mortality (aHR 1.07, 95% CI 1.03, 1.12). There were no statistically significant differences by sex, race, obesity, or diabetes.

Conclusion: In the JoCoOA, individuals who had greater severity of foot symptoms had increased mortality, independent of confounders. Although mechanisms for this relationship are not yet understood, foot symptoms may contribute to less physical activity and loss of physical function, which over time leads to factors that impact mortality, such as comorbid conditions from increasing BMI or falls from muscle weakness/impaired balance. Strategies to prevent and treat more severe foot pain may be needed to reduce mortality.

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Gait Alterations Associated with Worsening Knee Pain over 2 Years: A Machine-learning Approach in the MultiCenter Osteoarthritis Study

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Background/Purpose: Altered gait is related to structural worsening of knee osteoarthritis (OA). However, it is not known if altered gait is associated with increased risk of pain worsening over time. We applied machine learning approaches to gait data collected in a large epidemiological cohort to identify markers of gait alterations in people with worsening knee pain over 2 years.

Methods: The MultiCenter Osteoarthritis (**MOST**) study includes participants age 45-90 with, or at risk for, knee OA. Participants were categorized by presence of worsening knee pain over 2-years, defined as MCID increase in WOMAC pain (2+ points on 0-20 point scale). Gait was assessed at the 144 month visit using inertial sensors (OPAL, APDM, Portland, OR) worn on the trunk and both ankles during a 20-meter walk test in which participants walked at a self-selected pace.

We used an ensemble machine learning technique ("super learning") that uses multiple algorithms (Table 1 footnote) to improve outcome classification. All gait variables (both legs, Table 1 footnote), presence of pain during walking and K-L grade of each knee, age, BMI, depressive symptoms (CES-D), and sex were included as predictors. Data

Table 1. Variables contributing to prediction of worsening knee pain over 2 years (Frequency % across 100 test iterations from an ensemble prediction model[a])

The top ten variables selected during 100 iterations (n= frequency %)

- CES-D[b] (100)
- Gait speed (90)
- BMI[b] (82)
- Phase Coordination Index (72) : a measure of the bilateral coordination of gait
- Stride Time coefficient of variation (61) : quantifies magnitude of stride-to-stride variability in stride time
- Gait Asymmetry (51) : a measure of temporal left-right asymmetry of swing time
- Phase Difference (51) : % of the absolute difference from 180 degrees; a higher value indicates increased asymmetry
- Walking pain at 144 months, for designated knee (47)
- Stride Time (47): time measure of the average gait cycle
- Step Length (40)

Notes a.Algorithms included: Bayesian adaptive regression trees (BART), extreme gradient boosting, generalized linear models with convex penalties (that consisted least absolute shrinkage and selection operator [LASSO], ridge regression, and elastic net), logistic regression, random forest, and support vector machine.
b. BMI: Body Mass Index; CES-D: Center for Epidemiologic Studies Depression Scale; KL: Kellgren and Lawrence Grading System.
c. Gait parameters extracted include those describing spatiotemporal features (e.g., step length, velocity, cadence, stride time, double stance time, swing time), gait symmetry (e.g., step acceleration symmetry, phase coordination index, swing time symmetry), and gait variability (e.g., step regularity, entropy).

Table 2. GEE regression model: association of worsening knee pain over 24 months with predictors chosen by ensemble ML methods. Adjusted odds ratio (95% confidence intervals) are presented.

Parameters[c]	All knees, Total=4375, Cases=851	No walking pain at baseline Total=2699, Cases=471	Walking pain at baseline Total=1296, Cases=380
Phase Coordination Index (PCI)[a]	1.06(0.93-1.21)	1.03(0.84-1.25)	1.06(0.88-1.26)
Gait Asymmetry[a]	1.11(0.99-1.26)	1.13(0.92-1.39)	1.11(0.95-1.29)
Stride Time[a]	0.99(0.81-1.20)	0.91(0.66-1.25)	1.03(0.79-1.35)
Step Length[a]	**1.34(1.05-1.72)**	**1.60(1.09-2.34)**	1.17(0.83-1.64)
Stride Time coefficient of variation[a]	0.99(0.91-1.07)	1.00(0.90-1.12)	1.04(0.89-1.21)
Walking pain, ipsilateral limb (baseline)	**0.32(0.21-0.48)**	-	**0.33(0.22-0.49)**
Walking pain, contralateral limb (baseline)	1.32(0.97-1.80)	-	1.34(0.97-1.84)
Gait Speed[a]	0.76(0.54-1.06)	0.60(0.36-1.01)	0.91(0.57-1.45)
K-L[b] Grade >1, ipsilateral limb (baseline)	**1.36(1.08-1.71)**	**1.60(1.19-2.16)**	1.13(0.79-1.61)
K-L[b] Grade >1, contralateral limb (baseline)	**1.28(1.02-1.60)**	**1.52(1.13-2.05)**	1.03(0.73-1.46)
CES-D[a]	**1.23(1.13-1.35)**	**1.34(1.17-1.52)**	1.11(0.98-1.26)
BMI[a]	**1.16(1.06-1.28)**	**1.21(1.05-1.40)**	1.12(0.98-1.28)
Age[a]	0.98(0.87-1.09)	0.90(0.78-1.05)	1.07(0.89-1.29)
Male Sex	**0.72(0.58-0.90)**	0.74(0.55-1.01)	**0.70(0.51-0.97)**
Race	**1.31(1.03-1.67)**	1.09(0.76-1.55)	**1.54(1.10-2.16)**

Notes
a. Continuous variables are standardized: PCI, Gait Asymmetry, Stride Mean Time, Average Step Length, Stride Time CV, age, BMI, CES_D, Gait Speed
b. K-L: Kellgren and Lawrence Grading System
c. Phase Difference variable was dropped from the GEE model due to collinearity concerns.

were randomly split into 70% training and 30% test sets; the data split and model training and testing were repeated 100 times. We used a variable importance measure (VIM) statistic to identify the top 10 variables that most frequently contributed to the prediction of worsening knee pain. A Generalized Estimating Equation (GEE) model accounting for correlated outcomes (2 knees/person) was used to evaluate the association of "important" variables with worsening knee pain over 2 years. Potential confounders age, BMI, sex, baseline walking pain and K-L status were included. Analyses stratified by baseline walking pain are also presented.

Results: Our sample included 4464 knees for 2232 participants (mean age 63.6 [SD: 10.5] years, 57% female). 19.5% of knees had worsening pain over 2 years. Top contributing variables from ensemble machine learning process (AUC=0.69) are shown in **Table 1**.

In a GEE model (**Table 2**), longer step length was associated with increased likelihood of worsening pain over 2 years. However, when stratified by baseline pain, the association of step length and pain worsening was only significant in people without pain at baseline.

Conclusion: Our results suggest higher step length was associated with worsening knee pain over 2 years in individuals with or at risk of knee OA who do not have pain during walking at baseline. Walking with longer step length is associated with greater knee joint loading and shortening step length has been recommended as a gait intervention to reduce knee joint loading in people with knee OA. Our findings, using gait data from a large cohort and using machine learning to agnostically identify important gait variables, provide further support for this recommendation.

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Abstract Number: 1903

Does Limited Stair Climbing Lead to Poor Future Health? The Relationship Between Short-term Trajectories of Stair Climbing Frequency and Incident Slow Gait Speed over 1 and 2 Years in Adults with Knee Osteoarthritis

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SESSION INFORMATION
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Background/Purpose: Knee osteoarthritis (OA) is a common cause of functional limitation in older adults, and difficulty with climbing stairs is one of the first limitations to be reported. As such, reducing the frequency of stair climbing may serve as an early warning sign of future poor health outcomes. Little is known, however, about how stair use may fluctuate over time and if such fluctuations are related to future health – particularly slow gait speed given its strong relationship with poor health outcomes (e.g., hospitalization, early mortality). Therefore, the purpose of this study was to identify and describe trajectories of stair climbing frequency over 2 years in adults with or at high risk for knee OA and to determine the association between said trajectories and incident slow gait speed at 1- and 2-years.

Methods: Using data from the Osteoarthritis Initiative (OAI), stair climbing frequency was assessed by asking "How often do you climb up a total of 10 or more flights of stairs during a typical week, in the past 30 days?". Choices included None, 1-2 days per week, 2-3 days per week, 4-5 days per week, & nearly every day or every day. Responses were collected at baseline and at the 1- and 2-year clinic visits. Our study outcome was slow gait speed, defined as walking < 1.22 m/s over 20 meters, which is the pace needed for a timed crosswalk. We measured incident slow gait

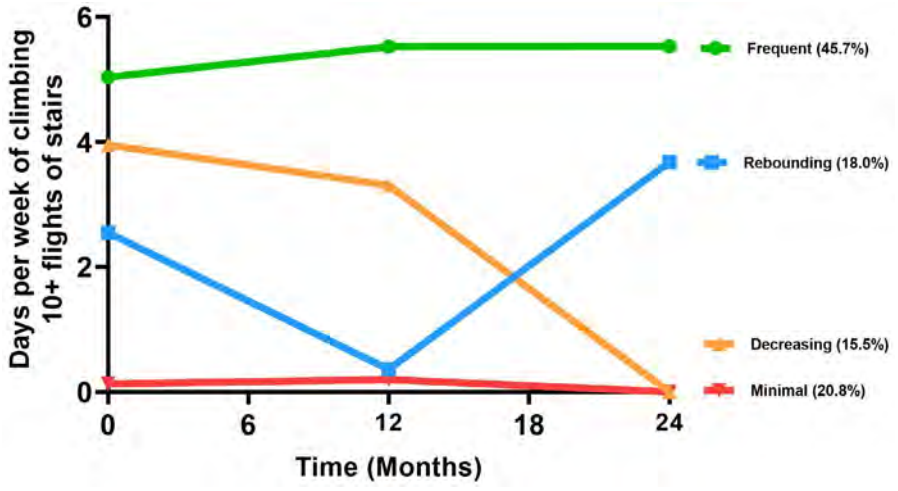

Figure 1. Short-term trajectories of stair climbing frequency over 2 years.

Table 1. Descriptive characteristics of the overall sample and each stair climbing frequency trajectory group at analytic baseline

	Overall Sample (n=2748)	Frequent (n=1232, 45.7%)	Rebounding (n=446, 18.0%)	Decreasing (n=480, 15.5%)	Minimal (n=590, 20.8%)
Age, years	61.8 ± 8.7	61.6 ± 8.5	62.0 ± 8.8	61.2 ± 9.0	62.7 ± 9.0
Sex, % female	53.7%	51.1%	52.2%	57.3%	57.5%
BMI, kg/m²	27.9 ± 4.6	27.3 ± 4.5	28.1 ± 4.6	28.3 ± 4.6	28.7 ± 4.7
Race, % non-white	12.9%	14.4%	12.1%	14.6%	9.2%
Education, % college degree	69.3%	73.5%	65.8%	67.6%	64.3%
Comorbidities, % ≥1	21.5%	18.5%	23.9%	22.7%	24.9%
Knee pain, % >3/10 VAS	51.9%	49.4%	54.0%	52.5%	55.1%
Radiographic knee OA, %	54.9%	53.7%	59.3%	51.5%	56.9%
Gait speed, m/s	1.42 ± 0.15	1.43 ± 0.15	1.42 ± 0.15	1.42 ± 0.14	1.40 ± 0.14
Posterior probabilities, %	---	96.9%	90.3%	83.4%	93.2%

Note: knee pain severity of 3/10 is the Patient Acceptable Symptom State; radiographic knee OA was determined using the Kellgren-Lawrence (KL) grading criteria (KL grade ≥ 2 = ROA present); posterior probabilities are the average probability of each individual trajectory fitting in their respective trajectory group

speed at the 3-year and 4-year clinic visits (i.e., 1- and 2-years of follow-up) in separate analyses. Our analytic dataset included those without slow gait speed at the 2-year clinic visit. Trajectories of stair climbing frequency over 2 years were identified using group-based modeling. Posterior probabilities of individual trajectories into the larger groups were used to describe model fit. Subject characteristics for trajectory groups were described using descriptive statistics. To determine the association of trajectory group membership with incident slow gait speed, we used binomial regression models to calculate relative risks (RR) and 95% confidence intervals (95% CI), adjusted for potential confounders at the 2-year clinic visit, i.e., our analytic baseline.

Results: Four distinct trajectory groups were generated (Fig 1): Frequent (45.7%), Rebounding (18.0%), Decreasing (15.5%), Minimal (20.8%), and descriptive characteristics are listed in Table 1. Compared to the Frequent stair climbing group, risk for incident slow gait speed was 45%, 68%, and 59% greater for the Rebounding, Decreasing, and Minimal Frequency groups, respectively, after 1 year (Table 2). We found similar findings for incident slow gait speed after 2 years (Table 2).

Conclusion: Compared to those who engaged in frequent stair climbing (at least 5 days per week), adults with knee OA who either seldom used the stairs, decreased their stair climbing over 2 years, or had a fluctuating pattern of stair climbing all were at greater risk for developing a slow gait speed by both subsequent years of follow-up. Given that stair climbing is a high-demand functional task, the stark increased risk in worsening function (via slow gait speed) over a short period of time is of concern. Adults with knee OA who report decreased stair climbing are prime targets for early intervention to prevent future loss of general function.

Table 2. RRs & 95% CIs for the association between stair climbing frequency trajectories and incident slow gait speed at 1 and 2 years

	% w/ GS <1.22 m/s at 1yr	Incident Slow GS at 1yr Adjusted RR [95% CI]	% w/ GS <1.22 m/s at 2yrs	Incident Slow GS at 2yrs Adjusted RR [95% CI]
Frequent Stair Climbing Frequency	134/1183 (11.3%)	1.0 [REF]	193/1182 (16.3%)	1.0 [REF]
Rebounding Stair Climbing Frequency	71/432 (16.4%)	1.45 [1.11, 1.89]*	96/431 (22.3%)	1.36 [1.10, 1.70]*
Decreasing Stair Climbing Frequency	89/468 (19.0%)	1.68 [1.31, 2.15]*	114/467 (24.4%)	1.50 [1.22, 1.84]*
Minimal Stair Climbing Frequency	71/432 (18.0%)	1.59 [1.26, 2.01]*	140/569 (24.6%)	1.51 [1.24, 1.83]*

Note: asterisk (*) indicates statistical significance; each model was adjusted for age, sex (female vs male), BMI, race (non-white vs white), education (college degree vs no college degree), knee pain severity, presence of radiographic knee OA (KL grade ≥2 vs KL grade <2), presence of comorbidities (1+ vs none), presence of depressive symptoms (≥16 on CESD vs <16 on CESD), physical activity level (PASE)

Disclosure: **J. Jakiela**, None; **Y. Zhang**, None; **D. Voinier**, None; **T. Bye**, None; **J. Copson**, None; **D. White**, None.

Abstract Number: 1904

"Why Does My Knee Hurt After I Got My Knee Replaced?": Evaluation of Neuropathic-like Symptoms and Objective Signs of Neuropathy Post-Knee Replacement in Patients with Knee Osteoarthritis

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Background/Purpose: Some people with knee osteoarthritis (OA) have persistent pain post-knee replacement, but why this occurs is not fully understood. One possibility is post-surgical neuropathy. We aimed to examine presence of neuropathy with objective clinical assessments and neuropathic-like pain evaluated with the self-reported PainDETECT questionnaire (PDQ) as potential contributors to persistent pain post-knee replacement. We also evaluated the association between objective neuropathy assessments and PDQ.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of individuals with or at risk of knee OA. Participants in the study who had a knee replacement were invited for a study visit ~1 year post-surgery. We obtained clinical assessments for neuropathy (von Frey 2g and 26g monofilaments (allodynia and hypoesthesia) and pin prick (hyperalgesia and hypoesthesia)) at the replaced knee. Each test was assessed 4 times, and considered abnormal if there was no response on ≥3 of the 4 trials (hypoesthesia) or if there was pain on ≥3 of the 4 trials (allodynia for the monofilaments, hyperalgesia for the pin prick). We also obtained the PDQ (0-38) and WOMAC pain (0-20). We defined the patient acceptable symptom state (PASS) based upon published thresholds for WOMAC as ≤5/20 for knee replacement samples. A PDQ score of ≥12 was considered neuropathic-like pain. We evaluated the relation of the clinical neuropathy assessments and the PDQ to achievement of the PASS post-knee replacement, using logistic regression, adjusting for potential confounders (age, sex, BMI, diabetes, depressive symptoms).

Table: Relation of clinical assessments of neuropathy and of PainDETECT to likelihood of not achieving the Patient Acceptable Symptom State post-knee replacement

Assessment of 'neuropathy':	Adjusted† OR (95% CI) for not achieving the WOMAC PASS post-knee replacement
PainDetect score per SD unit increase	2.09 (1.38-3.14)
PainDetect score ≥12 ("neuropathic-like pain")	3.95 (1.15-13.5)
Any abnormality on clinical assessments of neuropathy*	1.43 (0.50-4.12)

*defined as either: pain response in ≥3/4 trials OR no response in ≥3/4 trials to any one of the clinical assessments (von Frey monofilaments (2g, 26g) or pinprick)
†adjusted for age, sex, BMI, depressive symptoms, diabetes

Results: We evaluated 171 participants ~1 year post-knee replacement (mean age 69, 62% female, mean BMI 32.6). Overall, 57% had an abnormality on the clinical neuropathy assessment at the replaced knee, with 51% exhibiting hypoesthesia, and 10% exhibiting allodynia or hyperalgesia. The mean post-knee replacement PDQ score was 4.4 (SD 4.7) and 9% had PDQ ≥12, reflecting neuropathic-like pain. The presence of any abnormality on any of the clinical assessments was not associated with achieving the PASS (Table). Similar results were obtained when we analyzed each individual clinical assessment. In contrast, higher PDQ scores and PDQ score ≥12 were significantly associated with higher likelihood of not achieving the PASS (Table). There was no association between having any abnormality on the clinical assessments of neuropathy and PDQ score (OR 1.13, 95% CI 0.75-1.72) or PDQ score ≥12 (OR 0.68 (95% CI 0.17-2.72).

Conclusion: Objective clinical assessments of neuropathy were not associated with worse pain status post-knee replacement, defined as not achieving the PASS for WOMAC. However, higher PDQ scores and having a PDQ score in the 'neuropathic-like pain' range were associated with worse pain post-knee replacement. Thus, clinically evident neuropathy does not appear to explain persistent pain post-knee replacement. The PDQ, including in the 'neuropathic-like pain' range, does not appear to correlate with clinical assessments of neuropathy. It is possible that the PDQ is reflective of pain severity in general, and potentially nociplastic, rather than neuropathic-like, pain.

Disclosure: D. Driscoll, None; **P. Ballal**, None; **N. Wang**, None; **L. Frey-Law**, None; **C. Lewis**, None; **M. Nevitt**, None; **T. Neogi**, Pfizer/Lilly, 2, Regeneron, 2, Novartis, 2.

Abstract Number: 1905

CD11c+ Expression Associates with IFN-λ Responsiveness in Human B Cells with Clinical Implications for SLE

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1905–1908)
Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Type I interferon (IFN), namely IFN- α, and B cell aberrations are long recognized in systemic lupus erythematosus (SLE) pathogenesis. Type I IFN receptor blockade has undergone clinical trials in SLE with varying degrees of success. Type III IFN (IFN-λ) produce a gene signature currently indistinguishable from that of type I in responsive cell types. IFN-λ are not blocked by type I IFN receptor blockade as they utilize a unique receptor (IFNLR1). Type III IFN are appreciated to have an important role in viral infection at epithelial barriers where IFNLR1 is strongly expressed. The effects of IFN-λ on immune cells remain understudied and are different between human and murine models. We have previously shown that human B cells can transcribe type I IFN genes after IFN-λ treatment including those associated with SLE. We have found that IFN-λ is detected in the serum of human SLE patients and correlates with IgD- CD27- CD21- CD24- (DN2) B cells, a compartment which contains CD11c+ age/autoimmunity B cells (ABC). ABC are a target of interest as recent studies suggest they are poised for plasma cell differentiation and enriched in autoreactivity and thus have the potential to contribute to SLE pathogenesis.

Methods: Patients meeting 1997 ACR systemic lupus erythematosus classification criteria (n = 8) and healthy donors (HD, n = 5) had blood drawn under IRB-approved protocol. The transcriptome of sorted IgD+ CD27- naïve and

IgD- CD27- (DN) B cells was measured by bulk RNA sequencing for differential expression and gene set enrichment analysis. Cell phenotype and STAT1 phosphorylation (pSTAT1) in IFN-α2 and IFN-λ1 treated PBMC was measured by flow cytometry (n =10).

Results: Naïve and DN cells display a prominent type I IFN gene expression profile in SLE. Transcript for type I, type II, and type III IFN receptors (IFNAR1, IFNAR2, IFNGR1, IFNGR2, IFNLR1, and IL10RB) are detected in HD and SLE B cells. CD11c+ CD21- frequency increased in DN compared to naïve B cells for SLE and HD (both $p< 0.001$). The mean and range of CD11c+ CD21- frequency was higher in SLE DN (30.7± 9.5%, mean±SEM; range 4.8-74.7%) compared to HD DN (7.6%±1.0%,3.6-9.4%). Increased IFNLR1 transcript correlated with CD11c+ CD21- B cell expansion (r^2=0.922, $p< 0.0001$). Increased pSTAT1 after IFN-α2 treatment is found in monocytes, T cells, and B cells but only in the B cells after IFN-λ1 treatment. Naïve, DN, switched, and unswitched memory HD B cells are responsive to type I and type III IFN, but demonstrated a higher pSTAT1 fold change with type I IFN treatment compared to type III IFN. In all B cell subsets, CD11c+ cells had a higher pSTAT1 fold change after IFN-λ1 stimulation than did CD11c- B cells. In HD with well-defined populations of CD11c+ CD21- DN cells, pSTAT1 fold change for IFN-λ approached that of IFN-α2.

Conclusion: All human B cell subsets defined by CD27 and IgD respond to IFN-α and IFN-λ, but those expressing CD11c+ have increased responsiveness to IFN-λ. CD11c+ cells expand in SLE and associate with autoreactive plasma cell development. Thus, the role of IFN-λ may take on increased clinical significance in the setting type I IFN receptor blockade. These results suggest IFN-λ is an underappreciated driver of the IFN signature and B cell aberrations in SLE.

Disclosure: J. Barnas, None; **J. Barnard**, None; **C. Baker**, None; **N. Meednu**, None; **A. McDavid**, None; **R. Looney**, None; **J. Anolik**, None.

Abstract Number: 1906

IL-13Ra1-Mediated Signaling Regulates Age-Associated/Autoimmune B-Cell Expansion and Lupus Pathogenesis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1905–1908)

Session Type: Abstract Session

Session Time: 2:00PM–3:00PM

Background/Purpose: Age-associated B cells (ABCs) are an emerging B cell subset that aberrantly expand in SLE. ABC generation and differentiation exhibit marked sexual dimorphism and TLR7 engagement is a key contributor to these sex differences. ABC generation is also controlled by IL-21 and its interplay with IFNg and IL-4. Here we

investigated whether IL-13Ra1, an X-linked receptor that transmits IL-4/IL-13 signals, can regulate ABCs and lupus pathogenesis.

Methods: Mice lacking DEF6 and SWAP-70 (Double-Knock-out=DKO) that develop lupus preferentially in females were crossed with IL-13Ra1ko mice. IL-13Ra1 kos were also crossed to Yaa-DKO males, which develop severe disease due to TLR7 overexpression. ABCs were assessed by FACS and RNA-seq and lupus pathogenesis was evaluated by serologic and histological analyses.

Results: ABCs express higher levels of IL-13Ra1 than follicular B cells. Absence of IL-13Ra1 in either DKO females or Yaa-DKO males decreased the accumulation of ABCs, their differentiation into plasmablasts, and autoantibody production. Lack of IL-13Ra1 also prolonged survival and delayed the development of tissue inflammation. IL-13Ra1 deficiency diminished the *in vitro* generation of ABCs, an effect that, surprisingly, could be observed in response to IL-21 alone. RNAseq revealed that ABCs lacking IL-13Ra1 downregulated BCR signaling pathways but upregulated myeloid markers and proinflammatory mediators.

Conclusion: These studies uncover a novel role for IL-13Ra1 in the control of ABC generation and differentiation and suggest that IL-13Ra1 contributes to these effects by regulating a subset of IL-21-mediated signaling events. These studies also suggest that X-linked genes in addition to TLR7 participate in the regulation of the ABC compartment in lupus.

Disclosure: D. Flores Castro, None; **Z. Chen**, None; **S. Gupta**, None; **M. Manni**, None; **J. Rivera Correa**, None; **M. Chao**, None; **Y. Chinenov**, None; **T. Pannellini**, None; **H. Zaghouni**, None; **R. Jessberger**, None; **A. Pernis**, None.

Abstract Number: 1907

Increased Otoferlin Expression in B Cells Is Associated with Muscle Weakness in Untreated Juvenile Dermatomyositis: A Pilot Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: B Cell Biology & Targets in Autoimmune & Inflammatory Disease (1905–1908)
Session Type: Abstract Session
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Background/Purpose: Juvenile Dermatomyositis (JDM) is a rare pediatric inflammatory myopathy with a complex pathophysiology. Previously our group showed a significant increase in Otoferlin mRNA expression in JDM patients' PBMCs and muscle compared to healthy controls. Otoferlin is a member of the dysferlin family, which plays an essential role in regulating calcium-sensitive exocytosis in inner ears sensory hair cells. To understand the role of this novel aspect of JDM disease pathophysiology, we next identified the cell expressing of Otoferlin and its association with disease activity in untreated children with JDM.

Methods: This IRB approved study was conducted at the Ann & Robert H. Lurie Children's Hospital of Chicago. Otoferlin expression was determined by qRT-PCR in peripheral blood mononuclear cells from untreated children with JDM and age, race, sex matched controls. The arm to freezer time was held at 2 hours or less. Clinical and laboratory variables, including age, gender, duration of untreated disease (DUD) and Disease Activity Scores (DAS skin, muscle, total), MSA, neopterin, and the status of the TNFα 308 allele were obtained from the Lurie Children's Juvenile Myositis Registry REDCap database. To identify cells expressing otoferlin, the cells were first stained with live dead stain to exclude dead cell. The following surface markers were determined (CD45, CD3, CD19, CD16, CD56, CD14 and CD11b) to characterize the otoferlin positive cells. We fixed and permeabilized the cells and then stained for cytoplasmic otoferlin expression. The otoferlin positive cells were primarily B cells; more detailed flow cytometry was performed with the following markers (CD19, IgM, IgD, IgG, CD27, CD21, CD24 and CD38) to characterize these B cells further.

Results: 30 untreated JDM (87% female, 90 % white, 43% P155/140+ve, 13% MJ+ve. 13% Mi-2+ve ,7% MDA+ve) and 15 healthy controls were included in this study. With the live dead stain (trypan blue) the cells were >90% viable. There was a significant increase in otoferlin expression in JDM children compared to controls (Median 47.6 vs. 2.1; p=0.002). There was a positive correlation between mRNA otoferlin expression and disease activity markers: neopterin (R^2=0.33, p=0.003), DAS-total (R^2=0.23 p=0.008), DAS-Muscle (R^2=0.18, p=0.024). Of note, otoferlin expression was not associated with DAS-Skin. Otoferlin expression was assessed by flowcytometry in 8 JDM patients and 3 controls which showed an increased percentage of otoferlin positive lymphocyte (Median 1.9% vs. 0.2% p= 0.03). The majority of the otoferlin positive cells were B cells (63% - 99.4%). Detailed B cell phenotyping in two samples showed that these B cells were IgD+, IgM+ CD27- naive B cell with 65-75% of them expressing plasmablast markers (CD19+, IgM+, CD38 hi, CD24-).

Conclusion: In this pilot study, we found that otoferlin expression by qRT-PCR was associated with muscle weakness, suggesting its possible utility as a biomarker of disease activity. Furthermore, we identified B cells and plasmablasts as the primary cells expressing otoferlin. Further investigation is required to identify the role of otoferlin in both B cell activation and its contribution to JDM pathophysiology.

Disclosure: A. Bukhari, None; **A. Khojah**, None; **W. Marin**, None; **G. Morgan**, None; **L. Pachman**, None.

Abstract Number: 1908

Interferon (IFN)-Stimulated Gene 15: A Novel Biomarker for Lymphoma Development in Sjögren's Syndrome

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
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Session Type: Abstract Session
Session Time: 2:00PM–3:00PM

Background/Purpose: Primary Sjögren's syndrome (SS), an autoimmune exocrinopathy, is expressed either as a local disease or as a systemic illness with an enhanced risk for the development of lymphoma. Several clinical, laboratory, histopathological and molecular markers have been identified, but the pathogenetic pathway of lymphoma

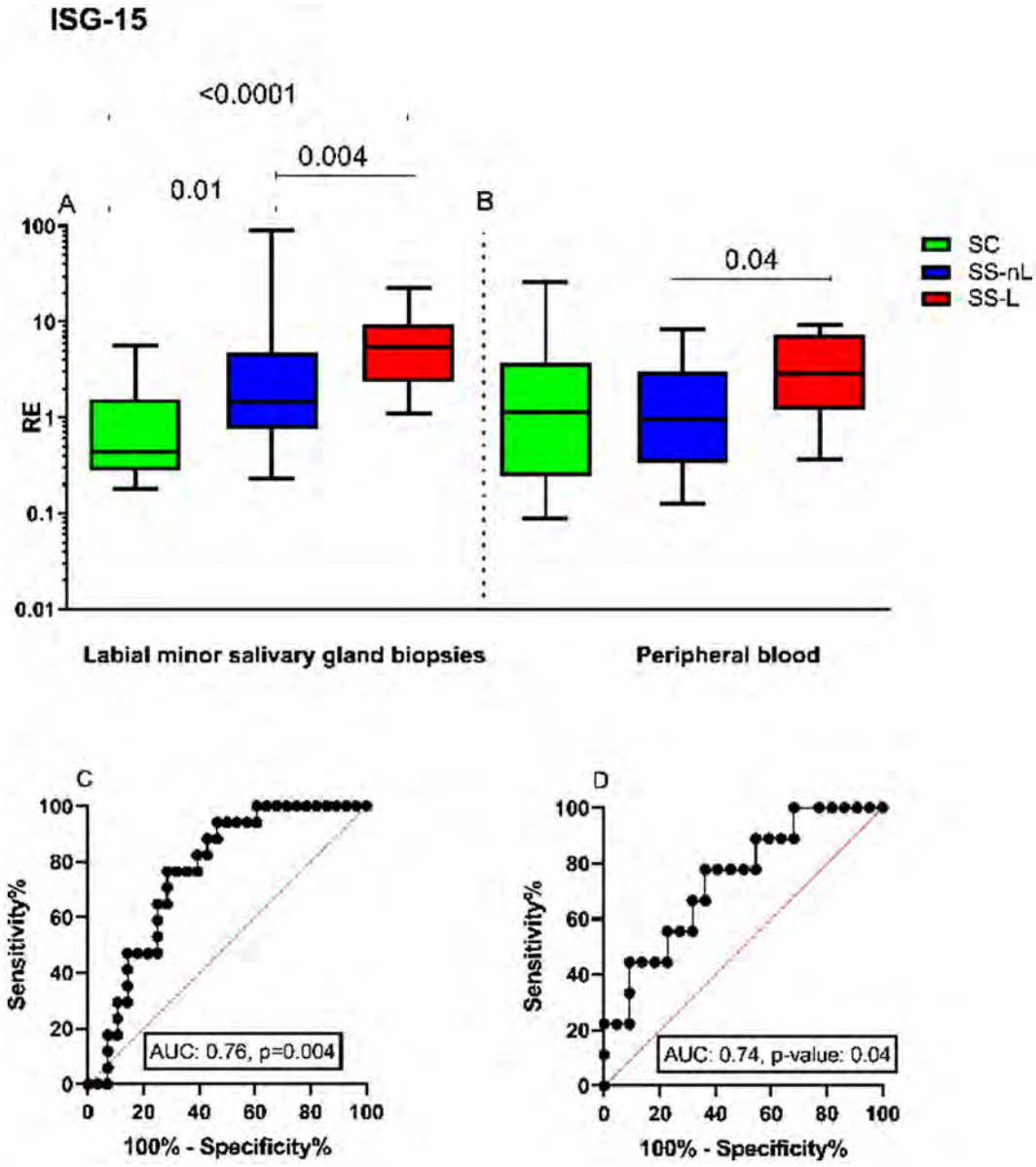

Figure 1. Relative expression of ISG-15 in 45 labial LMSG samples and 31 PB samples of SS patients and in 15 SC both in LMSG biopsies and PB samples.

development remains to a large extent unknown. We investigated whether interferon (IFN) induced genes could serve as biomarkers for the detection of lymphoma development among patients with SS.

Methods: Total RNA was extracted from 98 labial minor salivary glands (LMSG) biopsies of SS patients [61 not complicated by lymphoma (SS-nL) and 37 complicated by NHL (SS-L)] and from 67 matched to LMSG biopsies peripheral blood (PB) samples. Additionally, 30 LMSG biopsies and 17 matched PB of patients presenting with subjective dry eyes and/or dry mouth symptoms without fulfilling SS classification criteria (sicca controls, SC) were implemented. RNA sequencing was performed in total RNA extracted from 6 LMSG biopsies of 5 SS patients (2 at high risk and 3 at low risk for lymphoma development) and one SC. Expression analysis of type I (MX-1, IFIT-1, IFI44 and ISG-15) and type II IFN induced (CXCL9/MIG-1, GBP-1) genes was performed by real time PCR.

Results: Genes preferentially induced by type I IFNs including MX-1, IFIT-1 and IFI44 as well as ISG-15 and the type II IFN induced CXCL9/MIG-1 gene were up-regulated in “high risk” SS patients by next-generation sequencing (NGS).

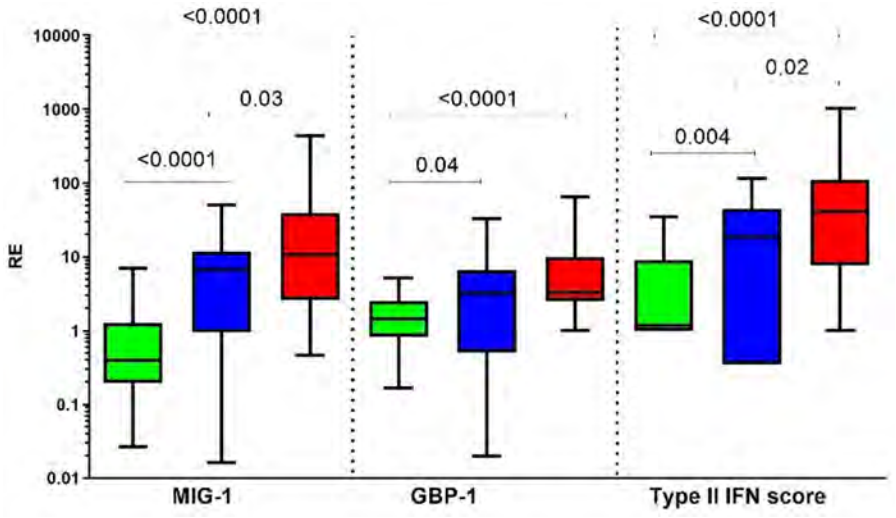

Figure 2. Relative expression of type II IFN inducible genes in LMSG tissues samples of SS patients and SC.

ISG-15 transcript levels measured by quantitative real time PCR were also higher in SS patients complicated by lymphoma (SS-L), compared to SS patients without lymphoma (SS-nL) in both LMSG tissues and PB specimens (mean ± SD: 6.6 ± 5.4 vs 6.3 ± 17.1, p = 0.004 and 4.2 ± 3.4 vs 1.9 ± 2.2, p = 0.04 respectively). ROC analysis revealed that both LMSG and PB ISG-15 gene expression has the potential to distinguish between SS-L and SS-nL patients (MSGB: AUC= 0.76, CI (95%): 0.62–0.90, p-value: 0.004 and PB: AUC= 0.74, CI (95%): 0.56–0.93, p-value: 0.04).

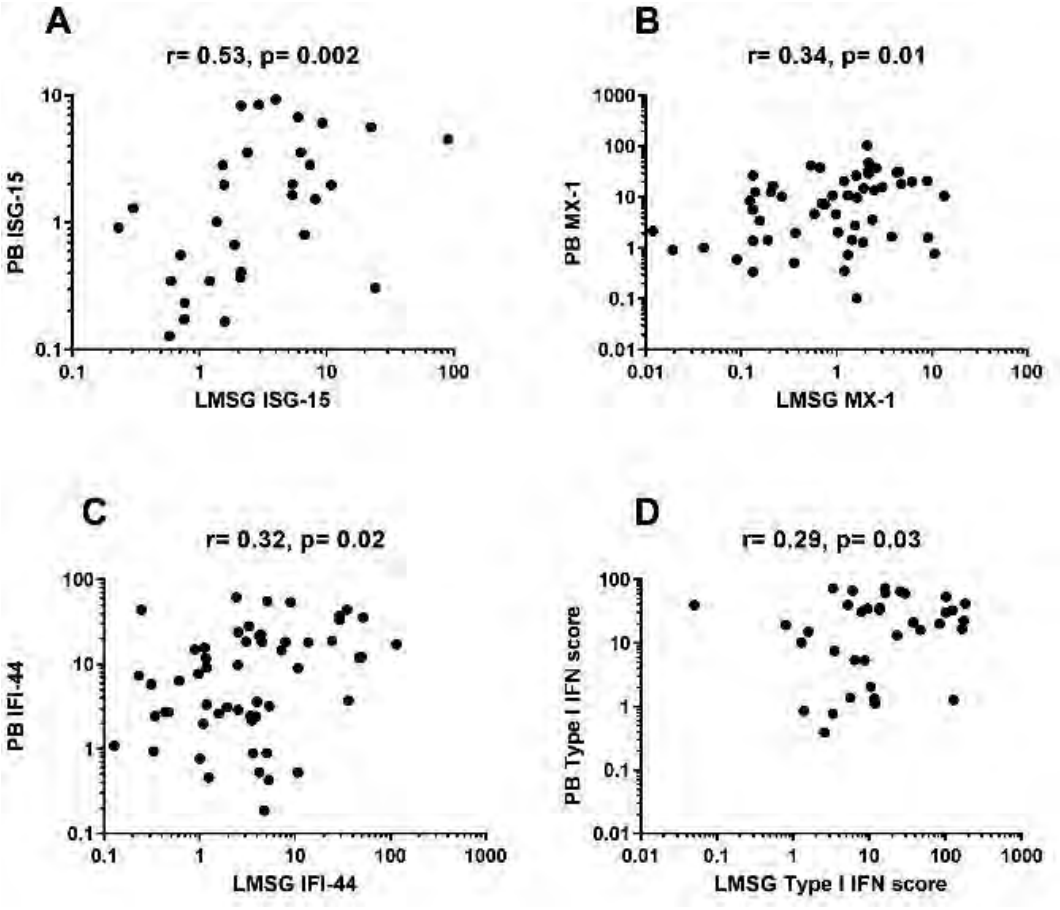

Figure 3. Correlation of relative gene expression in LMSG tissues and PB samples of type I and type II IFN induced genes.

(Figure 1) Only relative expression of MIG-1 and type II IFN score in LMSG tissues but not in peripheral blood were higher in SS-L patients compared to SS-nL patients (42.74 ± 93.18 vs 8.51 ± 9.95, p = 0.03 and 102.8 ± 205.2 vs 26.69 ± 30.27, p = 0.02, respectively) (Figure 2). Three of the genes preferentially induced by type I IFNs in LMSGs, ISG-15, MX-1 and IFI44, as well as type I IFN score in LMSG tissues were correlated with the corresponding values in PB (Spearman r = 0.53, p = 0.002, Spearman r = 0.34, p = 0.01, Spearman r = 0.33, p = 0.02 and Spearman r = 0.29, p = 0.03) (Figure 3). No other type I or II IFN inducible genes tested either at PB or LMSG level was predictive for lymphoma development in SS patients.

Conclusion: ISG-15 gene expression was able to distinguish SS-nL and SS-L at both periphery and tissue level and therefore could represent a novel biomarker for lymphoma development among SS patients. PB and LSMG seem to share a common transcriptional profile of type I IFN pathway.

Disclosure: I. Cinoku, None; **K. Verrou**, None; **E. Piperi**, None; **M. Voulgarelis**, None; **H. Moutsopoulos**, None; **C. Mavragani**, None.

Abstract Number: 1909

Impact of Antimalarial Adherence on Cardiovascular Mortality Among Patients with Newly Diagnosed Rheumatoid Arthritis and Systemic Lupus Erythematosus: A Population-based Study

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Literature has shown poor adherence to antimalarial (AM) medications in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients, with the percentage of adherers ranging from 25% to 57%. However, the impact of AM adherence on cardiovascular (CVD) mortality has not been extensively studied. Our objective is to examine the association between AM adherence and CVD mortality among newly diagnosed incident RA and SLE patients.

Methods: We used administrative databases from British Columbia (BC), Canada, to conduct a retrospective study of population-based incident RA and SLE cohorts with incident AM use. The incident RA and SLE cases first met previously published RA, and SLE, criteria using administrative data between January 1997 and March 2015. Follow-up started on the first day of receiving AM and meeting either RA or SLE criteria. Subjects were followed until they died, left BC, or March 2015, whichever occurred first. The outcomes were mortality for the following CVD causes: myocardial infarction (MI), stroke, or venous thromboembolism (VTE). We used marginal structural models (MSM) to estimate the effect of AM adherence on CVD mortality, accounting for potential confounders and competing events due to death unrelated to CVD. In the analysis, follow-up time was divided into 90-days windows. For each window, the proportion of days covered (PDC), representing the proportion of time when medications were taken as prescribed, was calculated and categorized as adherent (PDC≥0.90), non-adherent (0< PDC< 0.90), and discontinued (PDC=0). The analyses were controlled for baseline demographics and the indicator of having RA or SLE, as well as

Table 1. Overall risk of CVD mortality in incident RA and SLE patients during follow-up

Adherence Levels	Number of Deaths	Total Person-years	IR per 1000 person-years	IR Ratios (95% CI)	MSM aHRs (95% CI)
Discontinuation [Reference]	602	106,476	5.65	1.00	1.00
Non-adherence	165	35,272	4.68	0.82 (0.70-0.98)	1.08 (0.91-1.31)
Adherence	133	42,910	3.10	0.55 (0.45-0.66)	**0.51 (0.42-0.62)**
Contrast: Adherence vs. Non-adherence				0.66 (0.53-0.83)	**0.47 (0.37-0.60)**

Discontinuation: PDC=0, Non-adherence: 0<PDC<0.90, Adherence: PDC≥0.90. Abbreviations: **IR**, incidence rate; **aHR**, adjusted hazard ratio; **MSM**, marginal structural model; **CI**, confidence interval; **PDC**, proportion of days covered.

The multivariable models were adjusted for baseline covariates including demographic variables (age, sex, location of residence, neighborhood income quintile), indicator of having RA or SLE, health resource utilization (hospital visits, physician and specialist visits including rheumatologist, nephrologist, and psychiatrist visits), medication usage (statins, other cardiovascular drugs, hormone replacement therapy, glucocorticoids, anticoagulant therapy, Cox-2 inhibitors, immunosuppressive drugs), comorbidities (hypertension, chronic obstructive pulmonary disease, angina), and the Romano adaptation of the Charlson comorbidity index for administrative data. Also, the time-varying variables of health resource utilization, medication usage, Charlson comorbidity index, and comorbidities were used to calculate weights in marginal structural model.

the following sets of baseline and time-varying covariates: medication usage, health resource utilization, comorbidities, and Romano adaptation of Charlson comorbidity index (see footnote of Table 1). The MSM analysis produces valid estimates in the presence of time-varying confounding and competing events by balancing the distributions of time-varying confounders among the three adherence groups through inverse probability weighting.

Results: We identified 21,114 individuals with incident RA or SLE (mean age 55.8 years, 75.9% were women) who had filled at least one AM prescription. Over the mean follow-up of 8.6 years, 900 (4.3%) patients died due to a CVD cause: MI, stroke, or VTE. The incidence rate (IR) of CVD mortality when patients were adherent, non-adherent, and discontinued AM were 3.10, 4.68, and 5.65 per 1000 person-years. Using MSM, the adjusted CVD mortality hazard ratios (HRs) obtained for AM non-adherence and adherence in RA or SLE patients were 1.08 (95% CI: 0.91-1.31) and 0.51 (95% CI: 0.42-0.62), respectively, relative to discontinuation (**Table 1**). Also, the adjusted HR for adherence compared to non-adherence was 0.47 (95% CI: 0.37-0.60). Similar findings were obtained for each cause of CVD mortality individually except VTE (**Table 2**).

Conclusion: When RA and SLE patients adhere to AM therapy, they have a 49% lower risk of CVD mortality than when patients discontinue AM. Also, the protective effect of AM was not observed when patients were taking less than 90% of the prescribed AM dose.

Table 2. Overall risk of death caused by MI, stroke, and VTE in incident RA and SLE patients during follow-up

	MI Mortality			Stroke Mortality			VTE Mortality		
Adherence Levels	Number of Deaths	IR Ratios (95% CI)	MSM aHRs (95% CI)	Number of Deaths	IR Ratios (95% CI)	MSM aHRs (95% CI)	Number of Deaths	IR Ratios (95% CI)	MSM aHRs (95% CI)
Discontinuation [Reference]	293	1	1	276	1	1	78	1	1
Non-adherence	94	0.97 (0.77-1.23)	1.27 (0.98-1.63)	63	0.69 (0.53-0.91)	0.91 (0.68-1.22)	15	0.57 (0.33-0.99)	0.75 (0.42-1.33)
Adherence	85	0.72 (0.57-0.92)	**0.65 (0.51-0.84)**	36	0.32 (0.23-0.46)	**0.30 (0.21-0.43)**	21	0.66 (0.41-1.07)	**0.69 (0.42-1.15)**
Contrast: Adherence vs. Non-adherence		0.74 (0.55-0.99)	0.51 (0.38-0.69)		0.47 (0.31-0.71)	0.33 (0.22-0.51)		1.15 (0.59 –2.23)	0.93 (0.48-1.81)

Discontinuer: PDC=0, Non-adherent: 0<PDC<0.90, Adherent: PDC≥0.90. Abbreviations: **MI**, myocardial infarction; **VTE**, venous thromboembolism; **IR**, incidence rate; **aHR**, adjusted hazard ratio; **MSM**, marginal structural model; **CI**, confidence interval; **PDC**, proportion of days covered.

The multivariable models were adjusted for baseline covariates including demographic variables (age, sex, location of residence, neighborhood income quintile), indicator of having RA or SLE, health resource utilization (hospital visits, physician and specialist visits including rheumatologist, nephrologist, and psychiatrist visits), medication usage (statins, other cardiovascular drugs, hormone replacement therapy, glucocorticoids, anticoagulant therapy, Cox-2 inhibitors, immunosuppressive drugs), comorbidities (hypertension, chronic obstructive pulmonary disease, angina), and the Romano adaptation of the Charlson comorbidity index for administrative data. Also, the time-varying variables of health resource utilization, medication usage, Charlson comorbidity index, and comorbidities were used to calculate weights in marginal structural model.

Disclosure: M. Hoque, None; **J. Avina-Zubieta**, None; **D. Lacaille**, None; **M. De Vera**, None; **Y. Qian**, None; **J. Esdaile**, None; **H. Xie**, None.

Abstract Number: 1910

Association Between Clinically Meaningful Improvements in Patient-Reported Outcomes and Stringent Measures of Disease Activity in Patients with Psoriatic Arthritis Treated with Upadacitinib versus Placebo or Adalimumab: Results from a Phase 3 Trial

Laure Gossec[1], Nemanja Damjanov[2], Shigeyoshi Tsuji[3], Apinya Lertratanakul[4], Ralph Lippe[5], Jayeshkumar Patel[4], Patrick Zueger[6] and Kurt de Vlam[7], [1]Sorbonne Université; APHP, Rheumatology Department, Pitié-Salpêtrière Hospital, Paris, France, [2]University of Belgrade School of Medicine, Institute of Rheumatology, Belgrade, Serbia, [3]Department of Orthopaedics/Rheumatology, National Hospital Organization, Osaka Minami Medical Center, Osaka, Japan, [4]AbbVie Inc., North Chicago, IL, [5]AbbVie Deutschland GmbH & Co. KG, Berlin, Germany, [6]AbbVie Inc., Mettawa, IL, [7]Department of Rheumatology, Universitaire Ziekenhuizen Leuven, Leuven, Belgium

SESSION INFORMATION

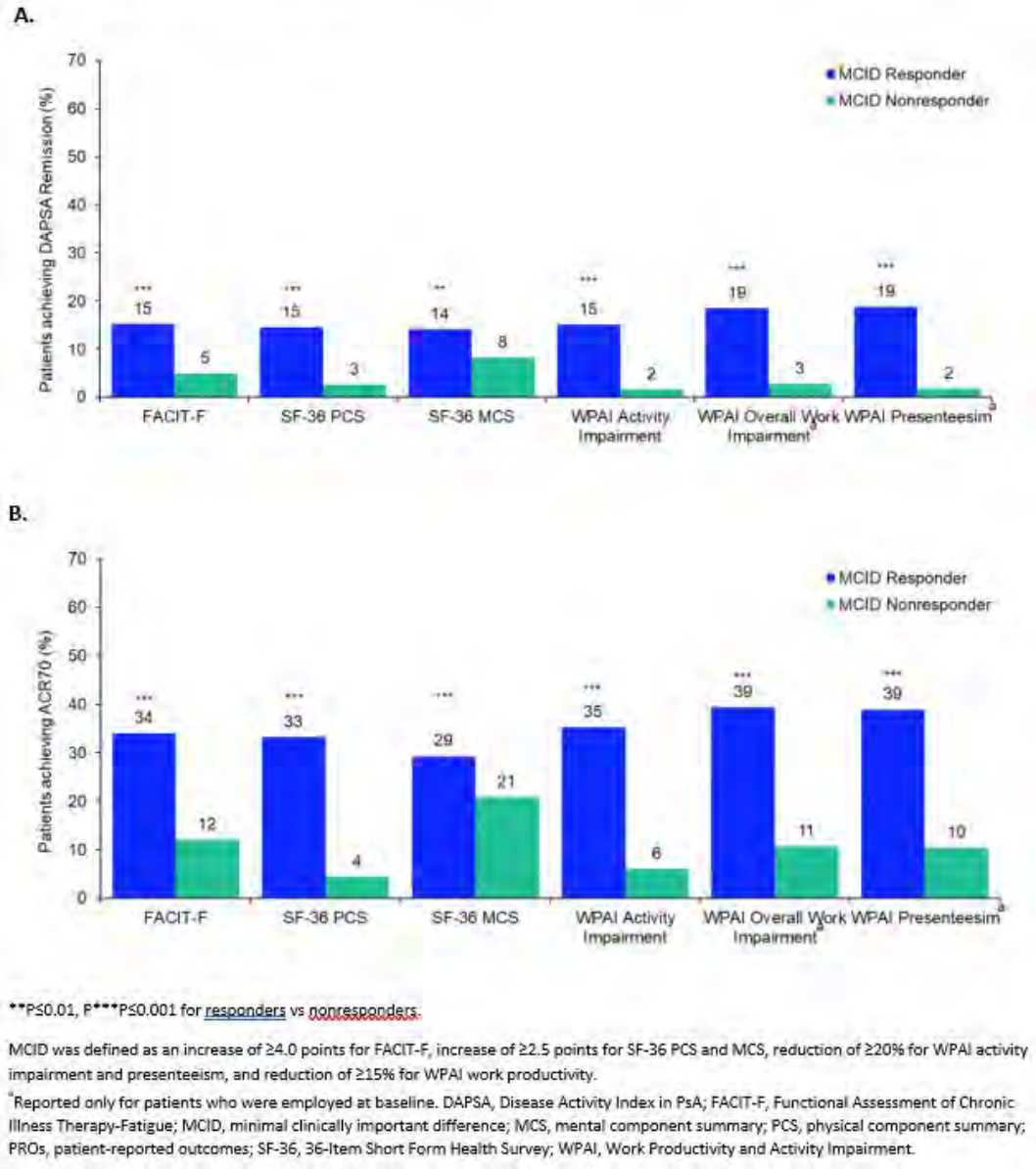
Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Figure 1. Proportions of Patients Achieving (A) DAPSA Remission or (B) ACR70 as a Function of PRO Improvements ≥MCID at Week 24



P≤0.01, P*P≤0.001 for responders vs nonresponders.

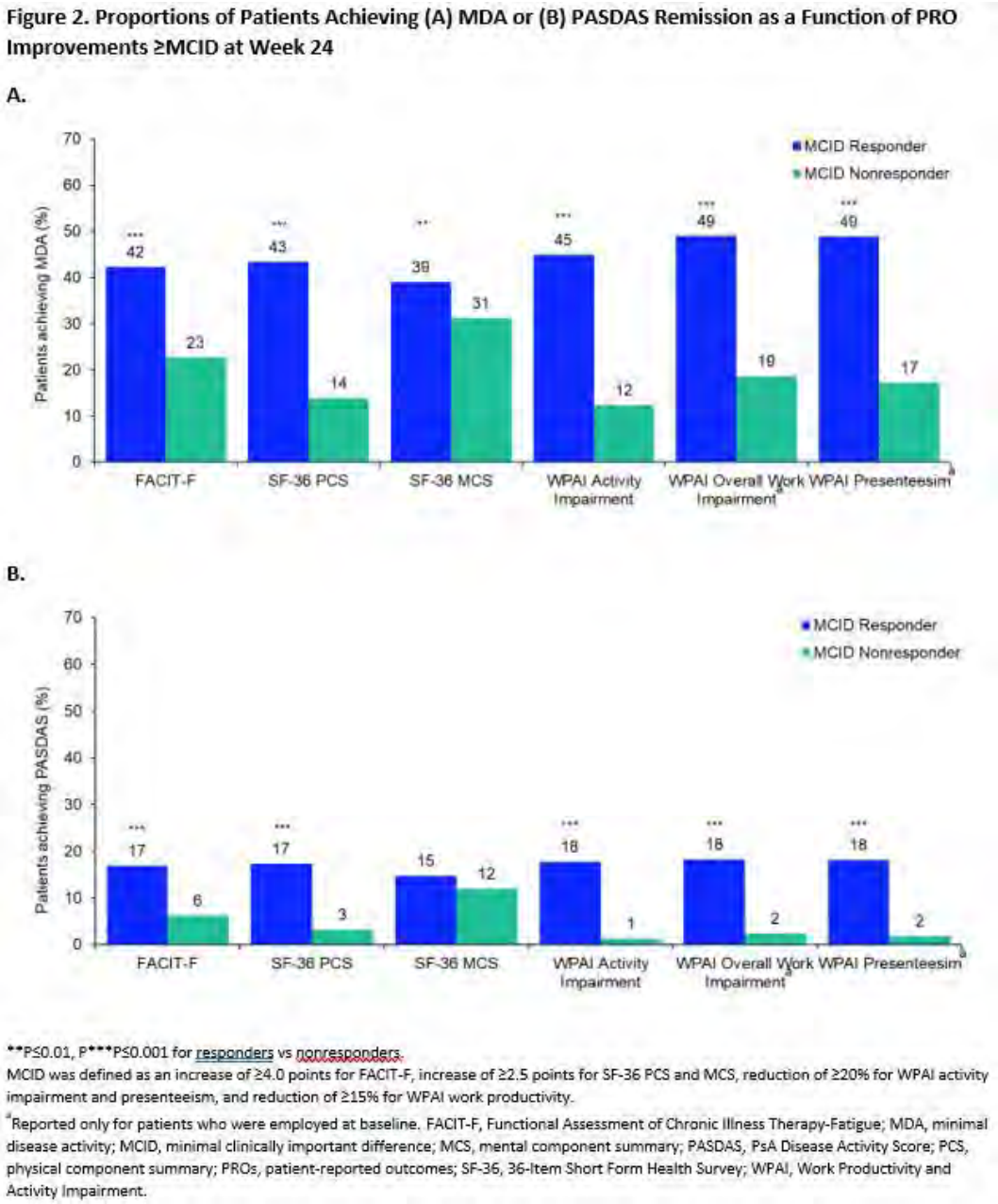
MCID was defined as an increase of ≥4.0 points for FACIT-F, increase of ≥2.5 points for SF-36 PCS and MCS, reduction of ≥20% for WPAI activity impairment and presenteeism, and reduction of ≥15% for WPAI work productivity.

[a]Reported only for patients who were employed at baseline. DAPSA, Disease Activity Index in PsA; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; MCID, minimal clinically important difference; MCS, mental component summary; PCS, physical component summary; PROs, patient-reported outcomes; SF-36, 36-Item Short Form Health Survey; WPAI, Work Productivity and Activity Impairment.

Background/Purpose: The achievement of disease control has been shown to be associated with improved prognosis in PsA, though no single measure of low disease activity or remission is currently universally accepted. Patient-reported outcomes (PROs) have been well-established in PsA and are important indicators of patient improvement while on treatment. To date, the association between PROs and disease control in PsA has not been fully characterized. We examined the association between clinically meaningful improvement in PROs and stringent measures of disease control among patients with PsA enrolled in the Phase 3 SELECT-PsA 1 trial.

Methods: Patients with active PsA and an inadequate response to ≥1 non-biologic DMARDs were randomized to receive upadacitinib (UPA) 15 mg once daily (QD), UPA 30 mg QD, adalimumab (ADA) 40 mg every other week, or PBO for 24 weeks. PROs included: Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F), 36-Item Short-Form Health Survey (SF-36), and Work Productivity and Activity Impairment (WPAI). Measures of stringent disease control included achievement of minimal disease activity (MDA), ACR70 response, and remission based on Disease Activity Index in PsA (DAPSA ≤4.0) or PsA Disease Activity Score (PASDAS ≤1.9). The percentage of patients

Figure 2. Proportions of Patients Achieving (A) MDA or (B) PASDAS Remission as a Function of PRO Improvements ≥MCID at Week 24



P≤0.01, P*P≤0.001 for responders vs nonresponders.
MCID was defined as an increase of ≥4.0 points for FACIT-F, increase of ≥2.5 points for SF-36 PCS and MCS, reduction of ≥20% for WPAI activity impairment and presenteeism, and reduction of ≥15% for WPAI work productivity.
[a]Reported only for patients who were employed at baseline. FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; MDA, minimal disease activity; MCID, minimal clinically important difference; MCS, mental component summary; PASDAS, PsA Disease Activity Score; PCS, physical component summary; PROs, patient-reported outcomes; SF-36, 36-Item Short Form Health Survey; WPAI, Work Productivity and Activity Impairment.

achieving stringent disease control was determined among patients reporting vs not reporting PRO improvements ≥ minimal clinically important differences (MCID) in the combined active treatment and PBO group at Week 24.

Results: A total of 1704 patients were included in the SELECT PsA 1 trial, of whom 59.2%, 72.4%, 51.3%, 62.3%, 64.6%, and 63.9% reported improvements ≥ MCID (MCID responders) in FACIT-F, SF-36 physical component summary score, SF-36 mental component summary (MCS) score, WPAI activity impairment, WPAI overall work impairment, and WPAI presenteeism, respectively, at week 24. The percentage of patients achieving MDA, ACR70 or DAPSA remission at week 24 was significantly higher (nominal $P \leq 0.01$) among patients who reported improvements ≥ MCID for all PROs vs those who did not (Figures 1,2). Similar results were seen in patients achieving PASDAS remission except for SF-36 MCS score (Figure 2). Among patients reporting improvements ≥ MCID across all PROs, more patients achieved ACR70 and MDA responses (29%-49%) with fewer patients achieving DAPSA or PASDAS remission (14%-19%).

Conclusion: PsA patients who reported clinically meaningful improvements in key PROs: fatigue, quality of life, and work productivity were more likely to achieve stringent measures of disease control. These results suggest a close association between meaningful improvements in patient-centric outcomes and achievement of stringent disease control.

Disclosure: L. Gossec, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 6, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **N. Damjanov**, AbbVie, 2, 5, 6, Pfizer, 2, 5, 6, Roche, 2, 5, 6, Gideon Richter, 2, 6, Merck, 2, 6, Novartis, 2, 6; **S. Tsuji**, AbbVie, 5, 6, Eli Lilly, 2, 6, Janssen, 2, 6, Novartis, 2, 6, UCB, 2, 6; **A. Lertratanakul**, AbbVie, 3, 11; **R. Lippe**, AbbVie, 3, 11; **J. Patel**, AbbVie, 3; **P. Zueger**, AbbVie, 3, 11; **K. de Vlam**, Celgene, 2, 5, 6, Galapagos, 2, 5, 6, Eli Lilly, 2, 6, Novartis, 2, 6, UCB, 2, 6.

Abstract Number: 1911

Patient's and Rheumatologist's Perspectives on the Burden of Adverse Drug Reactions Attributed to Biologics: A Qualitative Study

Henrike Westerink[1], Leanne Kosse[2], Naomi Jessurun[2], Astrid van Tubergen[3], Harald Vonkeman[4], Mike Nurmohamed[5], Bart van den Bemt[6] and Marieke de Vries[7], [1]Netherlands Pharmacovigilance Centre Lareb, Nijmegen, Netherlands, [2]Netherlands Pharmacovigilance Centre Lareb, 's-Hertogenbosch, Netherlands, [3]Maastricht UMC+, Maastricht, Netherlands, [4]Medisch Spectrum Twente; University of Twente, Enschede, Netherlands, [5]Reade; Amsterdam Rheumatology & Immunology Center, Amsterdam, Netherlands, [6]Sint Maartenskliniek; Radboud University Medical Center, Ubbergen, Netherlands, [7]Radboud University Medical Centre, Nijmegen, Netherlands

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

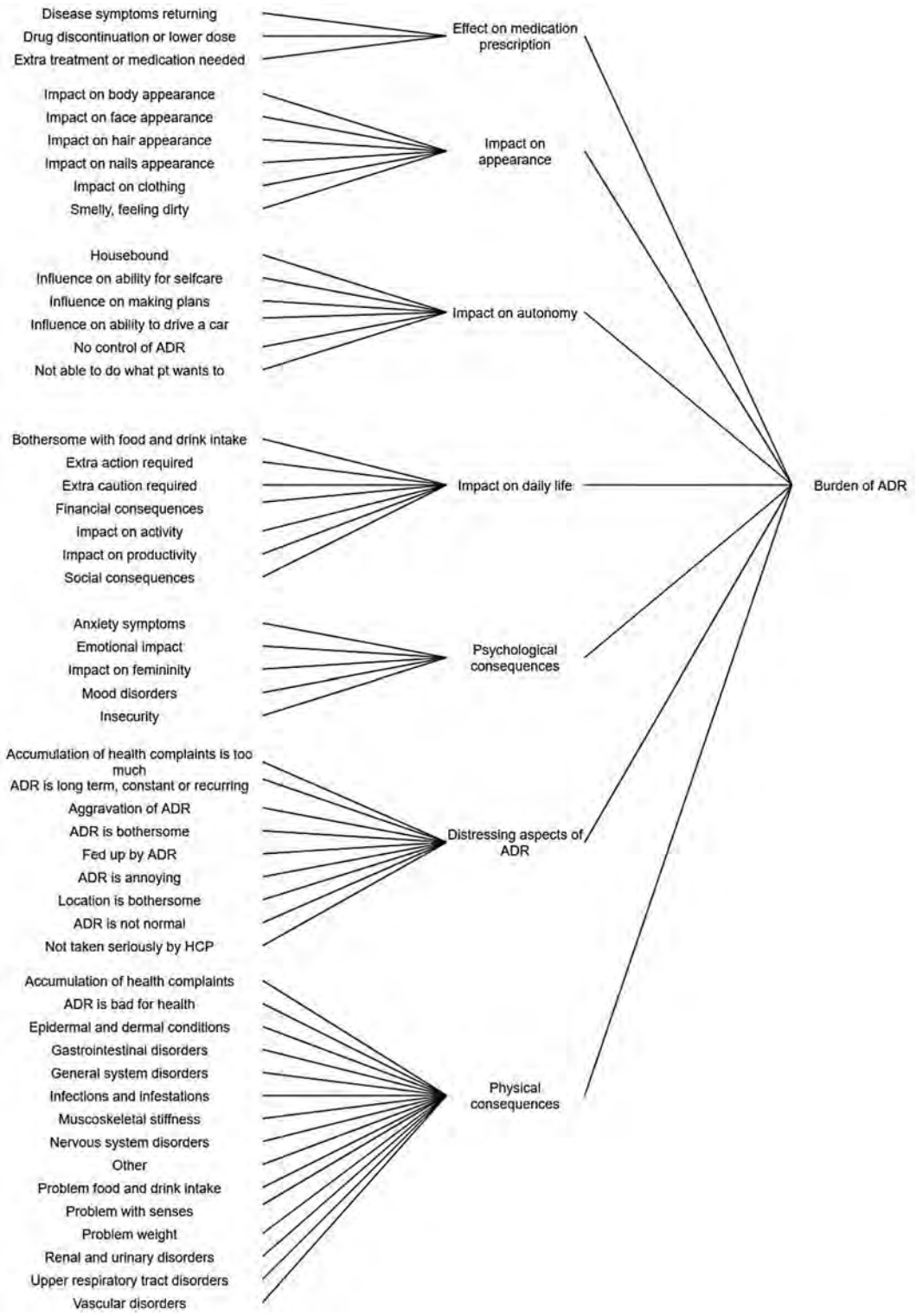
Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

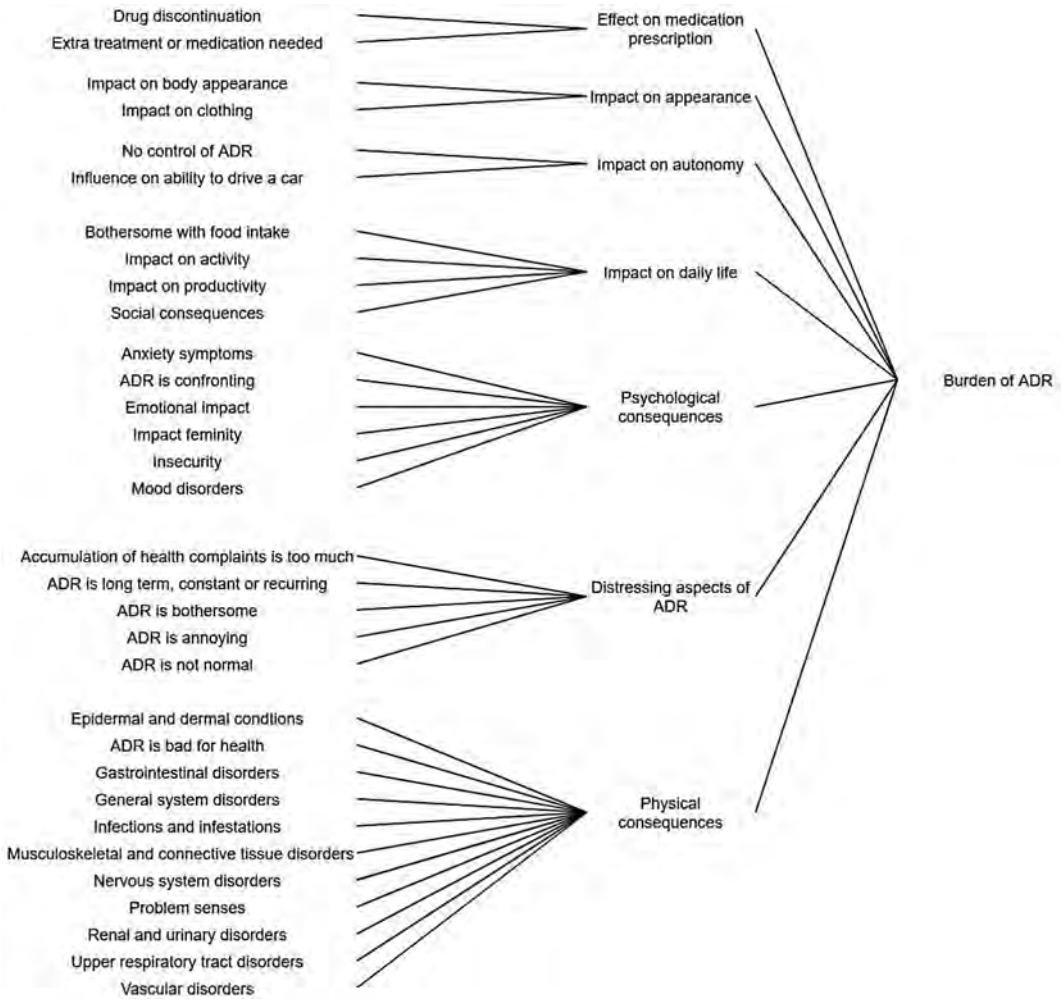
Background/Purpose: Previous studies showed a discrepancy between patient's and HealthCare Professional (HCP) perspective on the burden of Adverse Drug Reactions (ADRs), where HCPs often underestimate the burden. However, it is unknown which factors determine whether a patient perceives an ADR as burdensome. This study aimed to provide more insight into the burden of ADRs reported by patients with inflammatory rheumatic diseases that are attributed to the use of biologics, by identifying the factors that determine patient-perceived burden. Furthermore, this study aimed to compare both patient's and rheumatologist's perspective on these factors, to give more insight in the discrepancy between their perspectives.

Methods: Qualitative data from the Dutch Biologic Monitor (DBM) was used to assess the patient's perspective on the burden of ADRs. In the DBM, immune-mediated inflammatory disease patients were asked to fill out a bimonthly questionnaire on experienced ADRs attributed to the biologic, start and stop date, course, and the burden of the ADR using a five-point Likert-type scale ranging from 1 (no burden) to 5 (very high burden). Inclusion criteria for this substudy were: patients with inflammatory rheumatic diseases (i.e. rheumatoid arthritis, psoriatic arthritis and spondyloarthritis), reporting an ADR, and elaboration on the burden in an open text-field. Answers of the patients in open-text fields on the burden of the experienced ADR was analysed with a thematic analysis to develop a conceptual framework. Semi-structured interviews with 13 rheumatologists were performed and used to develop a conceptual framework on their perspective on the burden of ADRs. The two frameworks were compared to each other to highlight differences in perspectives.



Conceptual framework of ADR burden attributed to biologics from the patient's perspective. Participants were inflammatory rheumatic disease patients (n=440). ADR = Adverse Drug Reaction. HCP = HealthCare Professional. Medical Dictionary for Regulatory Activities (MedDRA®) terminology (version 21.0) was used for various subthemes in psychical consequences.

Results: A total of 440 unique patients were included in this study. Seven themes were identified that lead to the burden of ADRs according to patients. These were: effect on medication prescription, impact on appearance, impact on autonomy, impact on daily life, psychological consequences, distressing aspects of ADRs, and physical conse-



Conceptual framework of ADR burden attributed to biologics from the rheumatologist's perspective. Themes emerged from interviews with rheumatologists (n=11) and rheumatologists in training (n=2). ADR = Adverse Drug Reaction. HCP = HealthCare Professional. Medical Dictionary for Regulatory Activities (MedDRA®) terminology (version 21.0) was used for various subthemes in psychical consequences.

quences. Each theme consisted of several subthemes, shown in Figure 1. Most of these themes were also mentioned by the rheumatologists, but some subthemes were missing, e.g. influence on making plans (Fig. 2). Conversely, one subtheme was only mentioned by the rheumatologists, i.e. 'ADR is confronting', where the ADR would confront them with being ill or dependent on medication. In comparison to the patient's perspective, the rheumatologists paid less attention to the impact on the patient's autonomy and daily life, and more attention to the psychological aspects.

Conclusion: Overall, the patient perspective and the rheumatologist perspective on burden of ADRs were broadly comparable, but rheumatologists likely underestimated practical aspects that lead to burden of ADRs, and overestimated the psychological burden. The insights of this study facilitate the development of a Patient-Reported Outcome Measure on the burden of ADRs and create more awareness among rheumatologists.

Disclosure: H. Westerink, None; **L. Kosse**, None; **N. Jessurun**, None; **A. van Tubergen**, Novartis, 2, 5, UCB, 5; **H. Vonkeman**, Novartis, 1, 6, Sanofi, 1, 6, Janssen-Cilag, 1, Roche, 6, Pfizer, 1, 6, Galapagos, 1; **M. Nurmohamed**, Abbvie, 4, Eli Lilly, 2, Celltrion, 2, GSK, 2, Novartis, 5, Janssen, 6, Pfizer, 5, Galapagos, 5; **B. van den Bemt**, None; **M. de Vries**, None.

Abstract Number: 1912

Meteorological Variables Have Different Effect on Core Measures of Disease Activity in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)

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Session Time: 2:00PM–3:30PM

Background/Purpose: The notion that weather conditions may influence the symptoms and course of rheumatic and musculoskeletal diseases goes back to ancient times. We aimed to evaluate whether meteorological variables influence disease activity in patients with rheumatoid arthritis (RA).

Methods: We assessed the correlation between individual meteorological variables: temperature, effective temperature, saturation vapor pressure, absolute humidity, relative humidity, dew point, precipitation and clinical measures of disease activity: simplified disease activity index (SDAI), self-reported pain, patient's global assessment (PGA), 28 tender joint count (TJC) and 28 swollen joint count (SJC). Assessments documented in the Care for RA database were matched with weather variables on a daily basis for a period of 12 years between 2005 and 2017, and analyzed using generalized estimating equations (longitudinal data analysis). Patients with < 5 visits in the study period, those with < 1 visit/quarter or with pain=0 in ≥3 consecutive visits and those living outside of the catchment area were excluded.

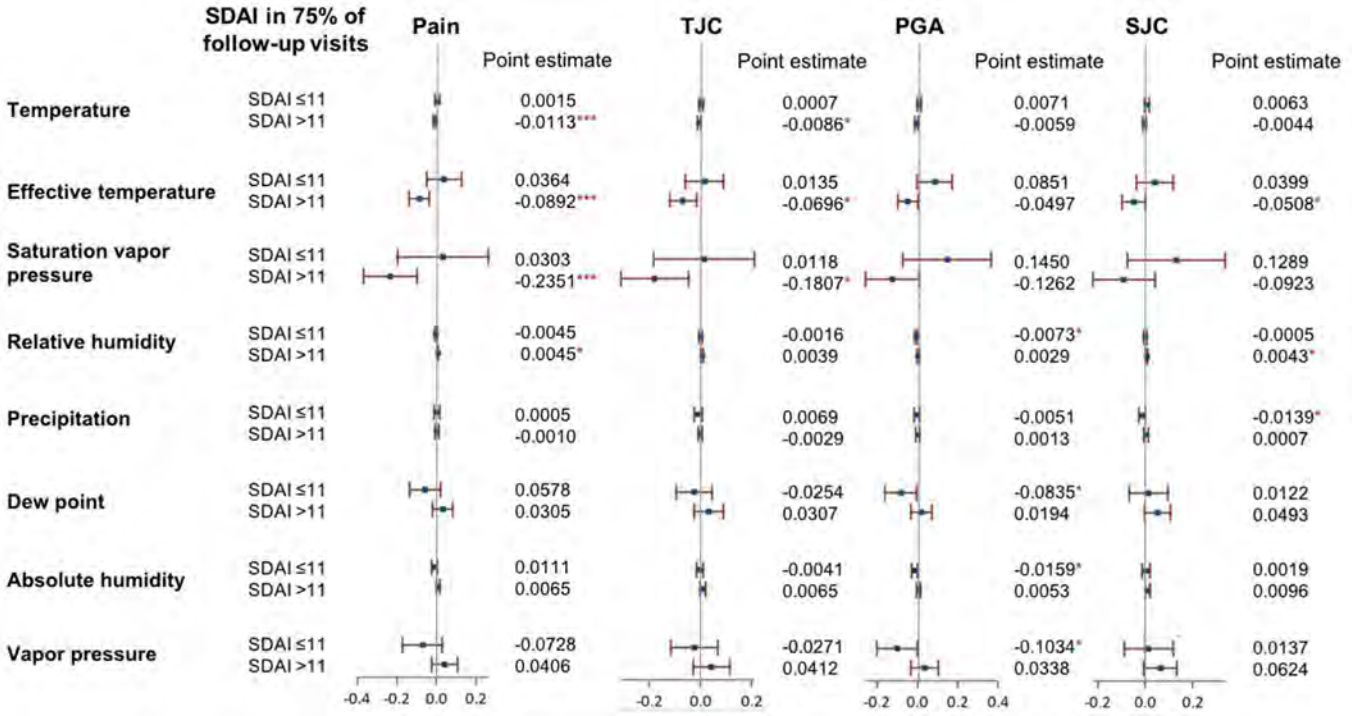

Figure 1. Association of meteorological variables and clinical measures of disease activity. PGA: patient's global assessment; SDAI: simplified disease activity index; SJC: swollen joint count; TJC: tender joint count; * p≤ 0.05, ** p≤ 0.01, *** p≤ 0.001.

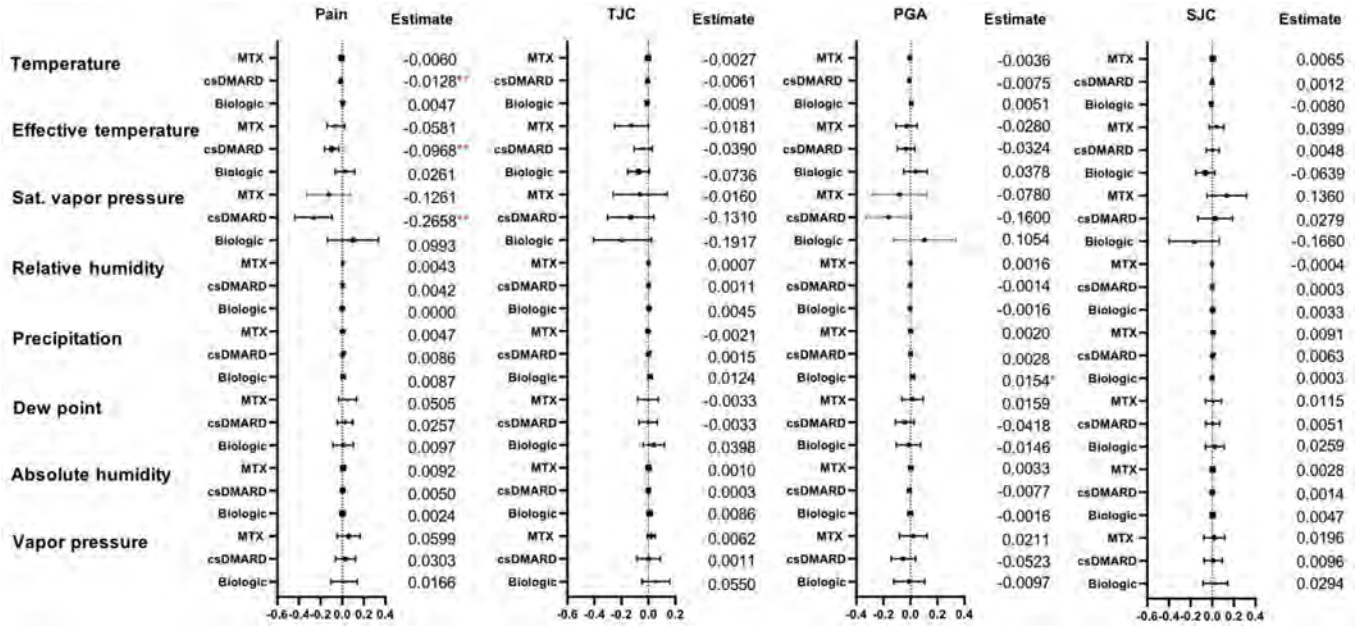

Figure 2. Association of meteorological variables and clinical measures of disease activity in stable therapy periods. csDMARD: conventional synthetic disease modifying anti-rheumatic drug; MTX: methotrexate; PGA: patient's global assessment; SDAI: simplified disease activity index; SJC: swollen joint count; TJC: tender joint count; * p≤ 0.05, ** p≤ 0.01, *** p≤ 0.001.

Patients were grouped into low (≤11) vs. moderate/high (>11) disease activity based on SDAI, and additionally considering only subsequent outpatient visits (>3 visits) where the therapy was stable (>6 months). On this basis three treatment groups were established: patients taking (1) methotrexate, (2) csDMARD or (3) bDMARD in mono- or combination therapy respectively.

Results: A total of 461 patients with an average disease duration at first visit of 5.7±7.4 years, age of 55.3±14.5 years, mean SDAI: 22.1±12.7 were analyzed. Among patients with moderate/high disease activity, higher temperature/effective temperature and saturation vapor pressure were associated with lower pain and TJC. On the contrary, higher relative humidity was associated with higher pain and higher SJC. Among patients with low disease activity higher relative humidity, absolute humidity, vapor pressure or dew point were associated with lower PGA. Higher precipitation was associated with lower SJC in the low disease activity group (Figure 1). When analysed according to stable treatment period, patients treated with csDMARD in mono- or combination therapy showed the same association between higher average daily temperature/effective temperature or saturation vapor pressure and lower pain as seen in patients with moderate/high disease activity (Figure 2).

Conclusion: In this largest association study of meteorological parameters with RA, both temperature and humidity were shown to have significant effects on pain, TJC and SJC, while PGA was mostly influenced by humidity. Weather had different effects depending on RA disease activity.

Disclosure: P. Mandl, MSD, 5, 6, Celgene, 5, 6, Lilly, 5, 6, BMS, 5, 6, AbbVie, 5, 6, Janssen, 5, 6, Novartis, 5, 6, Roche, 5, 6, UCB, 5, 6; **P. Studenic**, None; **F. Alasti**, None; **R. Kaltenberger**, None; **A. Kerschbaumer**, ABBVIE, 2, bristol-meyers squibb, 2, celgene, 2, Eli Lilly, 2, gilead, 2, Merck Sharp and Dohme, 2, Novartis, 2, Pfizer, 2; **T. Krennert**, None; **J. Smolen**, AbbVie, 2, 5, BMS, 2, 5, Celegene, 2, 5, Chugai, 2, 5, Gilead, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis-Sandoz, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Samsung, 2, 5, Sanofi, 2, 5, UCB, 2, 5; **D. Aletaha**, AbbVie, 2, 5, Janssen, 2, 5, Medac, 2, 5, Merck, 2, 5, 6, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5, Novartis, 2, 5, 6, Bristol-Myers Squibb, 6, Amgen, 2, 6, Celgene, 2, 6, Eli Lilly, 2, 6.

Abstract Number: 1913

Patient Perceptions of Telemedicine Use in Rheumatology Clinics During the COVID-19 Pandemic: An Analysis from the COVID-19 Global Rheumatology Alliance

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)

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Session Time: 2:00PM–3:30PM

Background/Purpose: During the COVID-19 pandemic, healthcare systems rapidly expanded telemedicine to ensure continued access to care. Few studies have explored patient perceptions of the telemedicine experience during the COVID-19 pandemic. The aim of this study was to better understand patient perspectives related to telemedicine use, including effectiveness and barriers of telemedicine use.

Methods: The COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Telemedicine Survey was an anonymous, cross-sectional online survey of participants with rheumatic and musculoskeletal diseases (RMD) from December 2020 to May 2021. Information on diagnoses, demographics, socioeconomic status, and respondents' perspectives on benefits and limitations of telemedicine use were collected. Data were summarized with descriptive statistics. Multivariable regression models adjusted for age, sex, country, disease type, and education level to perform relative risk estimates for dichotomous outcomes.

Results: The cohort included 596 respondents, of which 87% (514) were female, 47% (281) were 41-60 years of age. Race and ethnicity data were only collected for U.S respondents in which 81% (211) were white (Table 1). Common diagnoses were SLE (33%, 196) and RA (21%, 125). Most respondents were from the USA (44%, 262) or the United Kingdom (32%, 190). 79% (468) had completed a college or university degree or higher.

Of the 78% (467) respondents who used telemedicine during the pandemic, 65% (305) used audio (telephone) and 52% (242) used video (Table 2); about 70% (323) reported no problems when using video for telemedicine visits. 61% (283) found telemedicine effective compared to in-person visit and 40% (186) reported it would be important after the COVID-19 pandemic.

After adjusting for age, sex, country, disease type, and education level, UK respondents were more likely to report lower satisfaction with telemedicine care by their rheumatologists during the COVID-19 pandemic compared to US respondents. Those in high school were more likely to report lower satisfaction with telemedicine care compared to college graduates. Groups that rated telemedicine as less effective in their rheumatologic care included people over 60, respondents from the UK, Canada and Australia/New Zealand, as well as participants with graduate level education. Groups that reported post-pandemic telemedicine use as less important in their care included people over age 60 and respondents from the UK and Norway (Table 3).

Table 1: Demographics of Respondents.

Demographic Variable	Summary Values (%) N=596
Age	
Under 20	61 (10.2)
21- 40	131 (22.0)
41-60	281 (47.1)
61 and above	123 (20.6)
Gender	
Male	70 (11.9)
Female	514 (87.4)
Non-Binary	4 (0.7)
Declined	8 (1.3)
Ethnicity (US only)	
Hispanic	16 (6.1)
Not Hispanic	246 (93.9)
Race/Ethnicity (US only)	
American Indian or Alaska Native	1 (.4)
Asian	11 (4.2)
Black or African American	11 (4.2)
Native Hawaiian or Other Pacific Islander	1 (0.4)
White	211 (80.5)
Multiracial/Other	27 (10.3)
Country of Residence	
USA	262 (44.0)
United Kingdom	190 (31.9)
Canada	35 (5.9)
Norway	34 (5.7)
Australia/New Zealand	10 (1.7)
Other*	65 (10.9)
Education	
Currently in school or Less than high school	53 (8.9)
High School Graduate / GED	75 (12.6)
College or University Graduate	250 (41.9)
Graduate Education / Post-Graduate	218 (36.6)
RMD Diagnoses⁺:	
Systemic Lupus Erythematosus	196 (32.9)
Rheumatoid Arthritis	125 (21.0)
Ankylosing Spondylitis	47 (7.9)
Psoriatic Arthritis	34 (5.7)
Systemic JIA (Still's Disease)	28 (4.7)
Autoinflammatory Diseases	24 (4.0)
Sjogren's Disease	20 (3.4)
Others not listed above	122 (20.5)

*Other: Asian, African and European countries

⁺RMD: Rheumatic and Musculoskeletal Diseases

Conclusion: The majority of patients with rheumatic disease found telemedicine as effective or more effective than in-person visits, with about half of the respondents reporting telemedicine as helpful when disease is stable or alternating with in-person visits. However, over a quarter of respondents said telemedicine would not play a

Table 2: Characteristics and Attitudes towards Telemedicine

	N (%)
Telemedicine Visits During COVID-19	
Yes, had telemedicine	467 (78.4)
No, have not had telemedicine	129 (21.6)
Telemedicine Types Used During COVID-19*	
Phone	305 (51.2)
Video	242 (40.6)
None	129 (21.6)
Reason for Telemedicine Visit*	
concern about disease flare	186 (39.8)
concerns about coronavirus	118 (25.3)
check-in/regularly scheduled follow-up visit	391 (83.7)
Lab Monitoring with Telemedicine	
No, I did not get labs done or missed labs	64 (13.7)
Yes, I got labs done but less frequently	143 (30.6)
Yes, I got labs done on time	260 (55.7)
Telemedicine Importance after the COVID-19 Pandemic is Over	
Very important to me	86 (18.4)
Important to me	100 (21.4)
Somewhat important to me	97 (20.8)
I do not have a preference	54 (11.6)
Unimportant to me	130 (27.8)
Preferred Future Frequency of Telemedicine Visits	
Appointments when I am doing fine	182 (39.0)
Every third appointment	22 (4.7)
Every other appointment	101 (21.6)
Every appointment	41 (8.8)
None; prefer only in-person visits	121 (25.9)
Telehealth Effectiveness Compared to In-Person Visits (Overall)	
Less Effective	184 (39.4)
As Effective	248 (53.1)
More Effective	35 (7.5)

role in their care after the pandemic and preferred only in-person visits post-pandemic. These patient preferences can help inform policy decisions related to ongoing telemedicine use and insurance coverage of telemedicine visits.

Table 3: Multivariable Logistic Regression Analysis

	Effectiveness of Telemedicine		Provider Satisfaction		Importance of Telemedicine Post-Pandemic	
	"Telemedicine is less effective" vs "Telemedicine is more effective or as effective" as in-person visits		"Satisfied", "somewhat satisfied", or "Not satisfied" vs. "Yes very satisfied"		"Somewhat important," "I don't have a preference," or "Unimportant" vs. "Very important" or "Important"	
	OR	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age						
41-60	(ref)		(ref)		(ref)	
≤20	1.10	[0.46 - 2.67]	1.13	[0.51 - 2.54]	2.01	[0.90 - 4.52]
21-40	1.22	[0.73 - 2.03]	1.29	[0.78 - 2.15]	1.35	[0.80 - 2.26]
61+	1.90	[1.10 - 3.27]	1.68	[0.97 - 2.89]	2.01	[1.14 - 3.56]
Gender						
Female	(ref)		(ref)		(ref)	
Male	0.48	[0.23 - 1.01]	0.56	[0.28 - 1.13]	1.17	[0.58 - 2.34]
Non-Binary	1.52	[0.20 - 11.8]	3.52	[0.33 - 37.2]	0.24	[0.02 - 2.50]
Country of Residence						
USA	(ref)					
UK	2.51	[1.54 - 4.11]	2.96	[1.81 - 4.86]	3.30	[1.97 - 5.52]
Norway	1.61	[0.56 - 4.61]	1.62	[0.62 - 4.26]	3.96	[1.33 - 11.8]
Canada	2.58	[1.11 - 5.98]	0.74	[0.31 - 1.74]	1.69	[0.73 - 3.94]
Aus/NZ	7.90	[1.81 - 34.5]	1.67	[0.45 - 6.17]	3.00	[0.73 - 12.3]
Education						
College Grad	(ref)		(ref)		(ref)	
In School	1.62	[0.38 - 6.84]	0.85	[0.21 - 3.36]	1.17	[0.26 - 5.13]
Left <18yo	0.95	[0.38 - 2.40]	1.29	[0.46 - 3.61]	1.40	[0.43 - 4.58]
High School	0.97	[0.50 - 1.89]	2.03	[1.06 - 3.89]	0.71	[0.37 - 1.35]
Graduate Ed	1.70	[1.08 - 2.68]	1.00	[0.65 - 1.56]	0.87	[0.55 - 1.36]
Disease Type						
RA	(ref)					
SLE	1.73	[0.94 - 3.17]	1.35	[0.75 - 2.43]	1.62	[0.89 - 2.98]
Other IA	1.05	[0.53 - 2.12]	0.94	[0.49 - 1.82]	1.05	[0.54 - 2.03]
Vas/GCA/APS	1.26	[0.30 - 5.30]	0.42	[0.09 - 1.88]	2.31	[0.43 - 12.2]
Other	1.32	[0.69 - 2.53]	1.10	[0.60 - 2.05]	0.96	[0.51 - 1.79]

p<0.05 in highlighted cells

Key:
IA = inflammatory arthritis
Vas = vasculitis
GCA = giant cell arteritis
APS = antiphospholipid antibody syndrome
Graduate Ed = Graduate Education, Post-Graduate Education or Advanced Degree
AUS = Australia
NZ = New Zealand

Disclosure: M. Maheswaranathan, None; **B. Miller**, None; **C. Harrison**, Aurinia Pharmaceuticals Inc, 1, 11, Astra Zeneca Pharmaceuticals, 1, 2, GlaxoSmithKline, 2, 7; **R. Sinha**, None; **B. Egeli**, None; **B. Degirmenci**, None; **E. Sirotich**, None; **R. Grainger**, Pfizer New Zealand, 6, 12, support to travel to conference, Jansenn Autralia, 6, 12, travel to symposia, AbbVie New Zealand, 6, Cornerstones, 6, novartis, 1; **J. Hausmann**, Novartis, 2, Biogen, 2, Pfizer, 2; **J. Liew**, None; **Y. Chock**, None.

Abstract Number: 1914

Immunomodulatory and Immunosuppressive Medication Modification Among Rheumatology Patients at the Time of COVID-19 Vaccination

Jonah Levine[1], Deanna Jannat-Khah[1], Vivian Bykerk[2], Lisa Mandl[1] and Medha Barbhaiya[1], [1]Hospital for Special Surgery, New York, NY, [2]Division of Rheumatology, Hospital for Special Surgery, New York City, NY

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Patient Outcomes, Preferences, & Attitudes (1909–1914)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Table 1. Immunomodulatory and Immunosuppressive Medication Modifications Among 1852 Rheumatology Patients at Each COVID-19 Vaccination Dose

	1st Vaccine Dose N=1852				2nd Vaccine Dose N=1173				
N (%)	Overall Use N=1373	Any Modification Before Vaccine N=215	Medication Taken Early Before Vaccine N=41	Medication Delayed or Skipped Before Vaccine N=174	Overall Use N=899	Any Modification Before or After Vaccine N=251	Medication Delayed or Skipped Between 1st and 2nd Dose N= 105	Medication Taken Early Before Vaccine N=41	Medication Delayed or Skipped After Vaccine N=105
Any Immunomodulatory Use	**1203 (87.6)**	**204 (94.9)**	**37 (90.2)**	**167 (96)**	**796 (88.5)**	**241 (96)**	**102 (97.1)**	**36 (87.8)**	**103 (98.1)**
Hydroxychloroquine	**381 (27.7)**	**24 (11.2)**	**11 (26.8)**	**13 (7.5)**	**219 (24.4)**	**20 (8)**	**5 (4.8)**	**13 (31.7)**	**2 (1.9)**
Biologics	**364 (26.5)**	**94 (43.7)**	**13 (31.7)**	**81 (46.6)**	**245 (27.3)**	**104 (41.4)**	**46 (43.8)**	**10 (24.4)**	**48 (45.7)**
• **Abatacept**	31 (8.5)	16 (17)	3 (23.1)	13 (16)	19 (7.8)	13 (12.5)	5 (10.9)	2 (20)	6 (12.5)
• **Adalimumab**	89 (24.5)	18 (19.1)	5 (38.5)	13 (16)	59 (24.1)	13 (12.5)	6 (13)	3 (30)	4 (8.3)
• **Anakinra**	2 (0.5)	1 (1.1)	0 (0)	1 (1.2)	2 (0.8)	1 (1)	0 (0)	1 (10)	0 (0)
• **Belimumab**	19 (5.2)	6 (6.4)	1 (7.7)	5 (6.2)	14 (5.7)	10 (9.6)	5 (10.9)	0 (0)	5 (10.4)
• **Canakinumab**	2 (0.5)	0 (0)	0 (0)	0 (0)	1 (0.4)	0 (0)	0 (0)	0 (0)	0 (0)
• **Certolizumab**	14 (3.8)	4 (4.3)	1 (7.7)	3 (3.7)	10 (4.1)	6 (5.8)	3 (6.5)	0 (0)	3 (6.3)
• **Etanercept**	64 (17.6)	23 (24.5)	1 (7.7)	22 (27.2)	34 (13.9)	17 (16.3)	7 (15.2)	2 (20)	8 (16.7)
• **Golimumab**	10 (2.7)	0 (0)	0 (0)	0 (0)	4 (1.6)	0 (0)	0 (0)	0 (0)	0 (0)
• **Guselkumab**	4 (1.1)	0 (0)	0 (0)	0 (0)	2 (0.8)	1 (1)	0 (0)	0 (0)	1 (2.1)
• **Infliximab**	28 (7.7)	4 (4.3)	0 (0)	4 (4.9)	18 (7.3)	5 (4.8)	3 (6.5)	0 (0)	2 (4.2)
• **Ixekizumab**	8 (2.2)	2 (2.1)	0 (0)	2 (2.5)	9 (3.7)	7 (6.7)	4 (8.7)	0 (0)	3 (6.3)
• **Rituximab**	21 (5.8)	8 (8.5)	1 (7.7)	7 (8.6)	17 (6.9)	9 (8.7)	4 (8.7)	0 (0)	5 (10.4)
• **Sarilumab**	5 (1.4)	0 (0)	0 (0)	0 (0)	5 (2)	3 (2.9)	1 (2.2)	1 (10)	1 (2.1)
• **Secukinumab**	27 (7.4)	5 (5.3)	0 (0)	5 (6.2)	21 (8.6)	11 (10.6)	4 (8.7)	1 (10)	6 (12.5)
• **Tocilizumab**	28 (7.7)	6 (6.4)	1 (7.7)	5 (6.2)	22 (9)	8 (7.7)	4 (8.7)	0 (0)	4 (8.3)
• **Ustekinumab**	12 (3.3)	1 (1.1)	0 (0)	1 (1.2)	8 (3.3)	0 (0)	0 (0)	0 (0)	0 (0)
Conventional DMARDS	**381 (27.7)**	**76 (35.3)**	**12 (29.3)**	**64 (36.8)**	**275 (30.6)**	**106 (42.2)**	**48 (45.7)**	**11 (26.8)**	**47 (44.8)**
• **Azathioprine/6-MP**	18 (4.7)	3 (3.9)	2 (16.7)	1 (1.6)	14 (5.1)	3 (2.8)	1 (2.1)	1 (9.1)	1 (2.1)
• **Leflunomide**	31 (8.1)	7 (9.2)	1 (8.3)	6 (9.4)	20 (7.3)	9 (8.5)	4 (8.3)	1 (9.1)	4 (8.5)
• **Methotrexate**	234 (61.4)	57 (75)	5 (41.7)	52 (81.3)	180 (65.5)	84 (79.2)	38 (79.2)	7 (63.6)	39 (83)
• **Mycophenolate Mofetil/Mycophenolic Acid**	45 (11.8)	3 (3.9)	1 (8.3)	2 (3.1)	30 (10.9)	4 (3.8)	2 (4.2)	1 (9.1)	1 (2.1)
• **Sulfasalazine**	53 (13.9)	6 (7.9)	3 (25)	3 (4.7)	31 (11.3)	6 (5.7)	3 (6.3)	1 (9.1)	2 (4.3)
Small Molecules	**64 (4.7)**	**10 (4.7)**	**1 (2.4)**	**9 (5.2)**	**49 (5.5)**	**11 (4.4)**	**3 (2.9)**	**2 (4.9)**	**6 (5.7)**
• **Apremilast**	16 (25)	2 (20)	1 (100)	1 (11.1)	14 (28.6)	2 (18.2)	0 (0)	2 (100)	0 (0)
• **Baricitinib**	2 (3.1)	0 (0)	0 (0)	0 (0)	1 (2)	0 (0)	0 (0)	0 (0)	0 (0)
• **Tofacitinib**	38 (59.4)	4 (40)	0 (0)	4 (44.4)	29 (59.2)	7 (63.6)	2 (66.7)	0 (0)	5 (83.3)
• **Upadicitinib**	8 (12.5)	4 (40)	0 (0)	4 (44.4)	5 (10.2)	2 (18.2)	1 (33.3)	0 (0)	1 (16.7)
Corticosteroids	**170 (12.4)**	**11 (5.1)**	**4 (9.8)**	**7 (4)**	**103 (11.5)**	**10 (4)**	**3 (2.9)**	**5 (12.2)**	**2 (1.9)**
• **Prednisone**	128 (75.3)	8 (72.7)	2 (50)	6 (85.7)	80 (77.7)	7 (70)	2 (66.7)	4 (80)	1 (50)
• **Methylprednisolone**	34 (20)	3 (27.3)	2 (50)	1 (14.3)	21 (20.4)	3 (30)	1 (33.3)	1 (20)	1 (50)
• **Steroid Injection ("Cortisone Shot")**	8 (4.7)	0 (0)	0 (0)	0 (0)	2 (1.9)	0 (0)	0 (0)	0 (0)	0 (0)

Medications without any reported usage at the time of vaccination: Chloroquine, Cyclosporine, Tacrolimus, Rilonacept, Cyclophosphamide.
Percentages are reported as column percentages.

Background/Purpose: Due to concerns about underlying immune dysregulation and immunosuppression, patients with systemic rheumatic diseases (SRD) may have modified their medications at the time of COVID-19 vaccination to optimize their immune response. Although the American College of Rheumatology COVID-19 Vaccine Clinical Guidance Task Force issued management guidelines on February 8, 2021, it is unclear how rapidly these guidelines were disseminated. Our study evaluated real-world medication modification at the time of COVID-19 vaccination by Rheumatology patients at a single center in New York City.

Methods: We emailed a secure web-based survey to 7,505 patients aged ≥18 years evaluated at least once by a rheumatologist between April 1, 2018-April 21, 2020 at a large Rheumatology center in New York City. A follow-up survey was sent between March 5, 2021 and March 25, 2021. In the current analysis, we included individuals who indicated receiving at least the 1st vaccine dose. We collected data on immunomodulatory and immunosuppressive medication usage and modifications at the time of COVID-19 vaccination. We also collected the source responsible for the medication modifications (i.e. rheumatologist, other physician, patient).

Results: 1852/7505 (24.7%) patients responded to vaccination and medication modification questions (mean age: 63±13.2 years, 79.6% female, 87.4% white, 4.8% Hispanic/Latinx). 1852 patients received at least 1COVID-19 vaccine dose (53.9% Pfizer, 44.3% Moderna, 1.4%% Janssen, 0.38% Other) and 1173 reported having two doses. At 1st dose, there were 1373 individual reports of immunomodulatory or corticosteroid use (27.7% hydroxychloroquine, 26.5% biologics, 27.7% conventional DMARDs, 12.7% corticosteroids, 4.7% small molecules, 0.9% other DMARDs). Before the 1st vaccine dose, 204 medications (15.7%) were modified; of these, 19% were taken earlier than scheduled, and 81% were delayed/skipped. At 2nd dose, out of 899 individual medication reports, 251 medica-

Table 2. Source of Immunomodulatory and Immunosuppressive Medication Modifications Among Rheumatology Patients At the time of COVID-19 Vaccination

	1st Dose N=1852		2nd Dose N=1173		
N (%)	Medication Taken Early Before Vaccine	Medication Delayed or Skipped Before Vaccine	Medication Delayed or Skipped Between 1st and 2nd Vaccine Dose	Medication Taken Early Before Vaccine	Medication Delayed or Skipped After Vaccine
Any Immunomodulatory Medication or Corticosteroids	41(100)	174(100)	105(100)	41(100)	105(100)
• By rheumatologist	17(41.5)	77(44.3)	51(48.6)	10(24.4)	55(52.4)
• By another physician	3(7.3)	6(3.4)	4(3.8)	1(2.4)	6(5.7)
• By patient	21(51.2)	91(52.3)	50(47.6)	30(73.2)	44(41.9)
Any Immunomodulatory Medication	37(90.2)	167(96)	102(97.1)	36(87.8)	103(98.1)
• By rheumatologist	15(40.5)	75(44.9)	50(49)	9(25)	54(52.4)
• By another physician	3(8.1)	5(3)	4(3.9)	1(2.8)	6(5.8)
• By patient	19(51.4)	87(52.1)	48(47.1)	26(72.2)	43(41.7)
Hydroxychloroquine	11(26.8)	13(7.5)	5(4.8)	13(31.7)	2(1.9)
• By rheumatologist	1(9.1)	1(7.7)	0(0)	3(23.1)	0(0)
• By another physician	1(9.1)	1(7.7)	1(20)	1(7.7)	0(0)
• By patient	9(81.8)	11(84.6)	4(80)	9(69.2)	2(100)
Biologics	13(31.7)	81(46.6)	46(43.8)	10(24.4)	48(45.7)
• By rheumatologist	8(61.5)	32(39.5)	20(43.5)	3(30)	21(43.8)
• By another physician	2(15.4)	2(2.5)	2(4.3)	0(0)	4(8.3)
• By patient	3(23.1)	47(58)	24(52.2)	7(70)	23(47.9)
Conventional DMARDs	12(29.3)	64(36.8)	48(45.7)	11(26.8)	47(44.8)
• By rheumatologist	6(50)	36(56.3)	28(58.3)	3(27.3)	31(66)
• By another physician	0(0)	2(3.1)	1(2.1)	0(0)	2(4.3)
• By patient	6(50)	26(40.6)	19(39.6)	8(72.7)	14(29.8)
Small Molecules	1(2.4)	9(5.2)	3(2.9)	2(4.9)	6(5.7)
• By rheumatologist	0(0)	6(66.7)	2(66.7)	0(0)	2(33.3)
• By another physician	0(0)	0(0)	0(0)	0(0)	0(0)
• By patient	1(100)	3(33.3)	1(33.3)	2(100)	4(66.7)
Corticosteroids	4(9.8)	7(4)	3(2.9)	5(12.2)	2(1.9)
• By rheumatologist	2(50)	2(28.6)	1(33.3)	1(20)	1(50)
• By another physician	0(0)	1(14.3)	0(0)	0(0)	0(0)
• By patient	2(50)	4(57.1)	2(66.7)	4(80)	1(50)

tions (27.9%) were modified. Of these, 105 medications (41.8%) were delayed/skipped between the 1st and 2nd dose, 41 (16.3%) were taken earlier than scheduled and 105 (41.8%) were delayed/skipped after the 2nd vaccine dose. Biologics, typically anti-TNF inhibitors, and conventional DMARDs, typically methotrexate, accounted for most of the medications modified before or after the vaccine doses **(Table 1)**. Patients modified their own medications >50% of the time before the 1st vaccine dose, and opted to take medication early >70% of the time before the 2nd vaccine dose **(Table 2)**. Over half of the medications that were delayed/skipped after the 2nd vaccine were recommended by a rheumatologist **(Table 2)**.

Conclusion: Up to 28% of immunomodulatory or immunosuppressive medications were modified around the time of COVID-19 vaccination, and patients were responsible for up to 73% of modifications. The wide variety of medication modification provides insight into patient behavior and underscores the need for increased usage of evidence-based guidelines to inform patient and physician guidelines. Future studies will assess the implications of these medication modifications on SRD activity and flares post-vaccination.

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Abstract Number: 1915

Risk of Cardiovascular Outcomes with Low-Dose Glucocorticoids in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Heart & Lung (1915–1918)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Many guidelines recommend limiting glucocorticoids to short-term use in patients with rheumatoid arthritis (RA), but up to 40% of patients remain on glucocorticoids long-term. In this study we evaluated the cardiovascular risk of long-term, low-dose glucocorticoid use by studying patients on stable DMARD treatments.

Methods: Using Medicare claims and Optum's deidentified Clinformatics Data Mart from 2006 to 2015, we identified patients with RA (2 diagnosis codes ≥7 days apart) who remained on stable DMARD therapy for >180 days (no gaps >90 days and no new DMARDs), excluding patients with previous myocardial infarction (MI), stroke, coronary artery bypass grafting, or percutaneous coronary intervention using all available data during or prior to the baseline period. The 180 days before DMARD initiation and the first 180 days of stable DMARD course comprised the baseline period. Average glucocorticoid dose was assessed during the final 90 days of the baseline period and categorized as none, ≤5mg, 5-10mg, or >10mg/day. Inverse probability weights for the likelihood of being prescribed each glucocorticoid dose category were constructed using multinomial logistic regression. Cause-specific proportional hazards models with inverse probability weights and clustering to account for patients with multiple treatment periods were used

Table 1. Select Medicare and Optum Cohort Characteristics Before Inverse Probability Weighting

	Average glucocorticoid dose over past 3 months				
	None	≤5 mg/day	>5-10 mg/day	>10 mg/day	Total
Medicare Cohort					
Treatment periods, n	101,624	57,800	23,413	6,103	188,940
Age, years	67.7 (11.9)	68.4 (11.8)	66.9 (12.1)	63.8 (13.0)	67.7 (12.0)
Female	84,222 (83%)	47,623 (82%)	18,216 (78%)	4,492 (74%)	154,553 (82%)
White	71,724 (71%)	41,397 (72%)	16,818 (72%)	4,448 (73%)	134,387 (71%)
Smoking	9,985 (10%)	6,747 (12%)	3,332 (14%)	1,183 (19%)	21,247 (11%)
Prior biologics	30,733 (30%)	19,422 (34%)	8,750 (37%)	2,508 (41%)	61,413 (33%)
Stable DMARD course					
Methotrexate	54,877 (54%)	31,510 (55%)	12,322 (53%)	2,905 (48%)	101,614 (54%)
TNF inhibitor	32,411 (32%)	16,800 (29%)	6,785 (29%)	1,926 (32%)	57,922 (31%)
Non-TNF biologic/JAKi	14,336 (14%)	9,490 (16%)	4,306 (18%)	1,272 (21%)	29,404 (16%)
Medication use in past 3 months					
Statin	28,617 (28%)	15,661 (27%)	6,016 (26%)	1,445 (24%)	51,729 (27%)
Opioids	41,645 (41%)	27,945 (48%)	13,367 (57%)	4,109 (67%)	87,066 (46%)
Comorbidities					
Charlson Comorbidity Score	1 [0-3]	1 [0-3]	2 [0-3]	2 [0-4]	1 [0-3]
Angina	1,548 (2%)	921 (2%)	349 (2%)	89 (2%)	2,907 (2%)
Chronic Ischemic Heart Disease	10,107 (10%)	6,337 (11%)	2,571 (11%)	688 (11%)	19,703 (10%)
Peripheral vascular disease	11,249 (11%)	7,253 (13%)	3,022 (13%)	856 (14%)	22,380 (12%)
Diabetes mellitus	20,309 (20%)	10,719 (19%)	4,675 (20%)	1,396 (23%)	37,099 (20%)
Hyperlipidemia	32,954 (32%)	18,436 (32%)	7,245 (31%)	1,812 (30%)	60,447 (32%)
Hypertension	52,920 (52%)	31,613 (55%)	12,739 (54%)	3,418 (56%)	100,690 (53%)
Chronic kidney disease	5,692 (6%)	3,838 (7%)	1,646 (7%)	546 (9%)	11,722 (6%)
Congestive heart failure	5,246 (5%)	3,732 (7%)	1,761 (8%)	585 (10%)	11,324 (6%)
Extra-articular RA	2,247 (2%)	1,611 (3%)	831 (4%)	343 (6%)	5,032 (3%)
ED visit in past year	30,910 (30%)	21,589 (37%)	10,067 (43%)	3,204 (53%)	65,770 (35%)
Hospitalization in past year	16,836 (17%)	12,166 (21%)	6,024 (26%)	2,157 (35%)	37,183 (20%)
Optum Cohort					
Treatment periods, n	31,457	13,438	5,039	1,361	51,295
Age, years	55.5 (13.7)	57.7 (13.4)	57.9 (13.0)	56.6 (13.0)	56.4 (13.6)
Female	24,825 (79%)	10,535 (78%)	3,660 (73%)	897 (66%)	39,917 (78%)
White	22,745 (72%)	9,611 (72%)	3,608 (72%)	994 (73%)	36,958 (72%)
Smoking	2,313 (7%)	1,291 (10%)	585 (12%)	219 (16%)	4,408 (9%)
Prior biologics	8,711 (28%)	4,006 (30%)	1,663 (33%)	469 (34%)	14,849 (29%)
Stable DMARD course					
Methotrexate	14,518 (46%)	7,241 (54%)	2,752 (55%)	725 (53%)	25,236 (49%)
TNF inhibitor	13,800 (44%)	4,716 (35%)	1,638 (33%)	424 (31%)	20,578 (40%)
Non-TNF biologic/JAKi	3,139 (10%)	1,481 (11%)	649 (13%)	212 (16%)	5,481 (11%)
Medication use in past 3 months					
Statin	5,450 (17%)	2,502 (19%)	854 (17%)	235 (17%)	9,041 (18%)
Opioids	8,788 (28%)	5,128 (38%)	2,276 (45%)	717 (53%)	16,909 (33%)
Comorbidities					
Charlson Comorbidity Score	0 [0-1]	0 [0-2]	0 [0-2]	0 [0-2]	0 [0-1]
Angina	319 (1%)	141 (1%)	48 (1%)	17 (1%)	525 (1%)
Chronic Ischemic Heart Disease	1,418 (5%)	726 (5%)	287 (6%)	104 (8%)	2,535 (5%)
Peripheral vascular disease	1,207 (4%)	646 (5%)	280 (6%)	85 (6%)	2,218 (4%)
Diabetes mellitus	3,915 (12%)	1,677 (12%)	678 (13%)	239 (18%)	6,509 (13%)
Hyperlipidemia	7,189 (22%)	3,273 (24%)	1,233 (24%)	346 (25%)	12,041 (23%)
Hypertension	10,091 (32%)	4,835 (36%)	1,943 (39%)	573 (42%)	17,442 (34%)
Chronic kidney disease	1,030 (3%)	598 (4%)	225 (4%)	68 (5%)	1,921 (4%)
Congestive heart failure	646 (2%)	363 (3%)	199 (4%)	64 (5%)	1,272 (2%)
Extra-articular RA	713 (2%)	328 (2%)	168 (3%)	65 (5%)	1,274 (2%)
ED visit in past year	7,799 (25%)	3,971 (30%)	1,503 (30%)	461 (34%)	13,734 (27%)
Hospitalization in past year	3,663 (12%)	2,040 (15%)	997 (20%)	349 (26%)	7,049 (14%)

Values are in the format: mean (standard deviation), n (%), or median [interquartile-range]

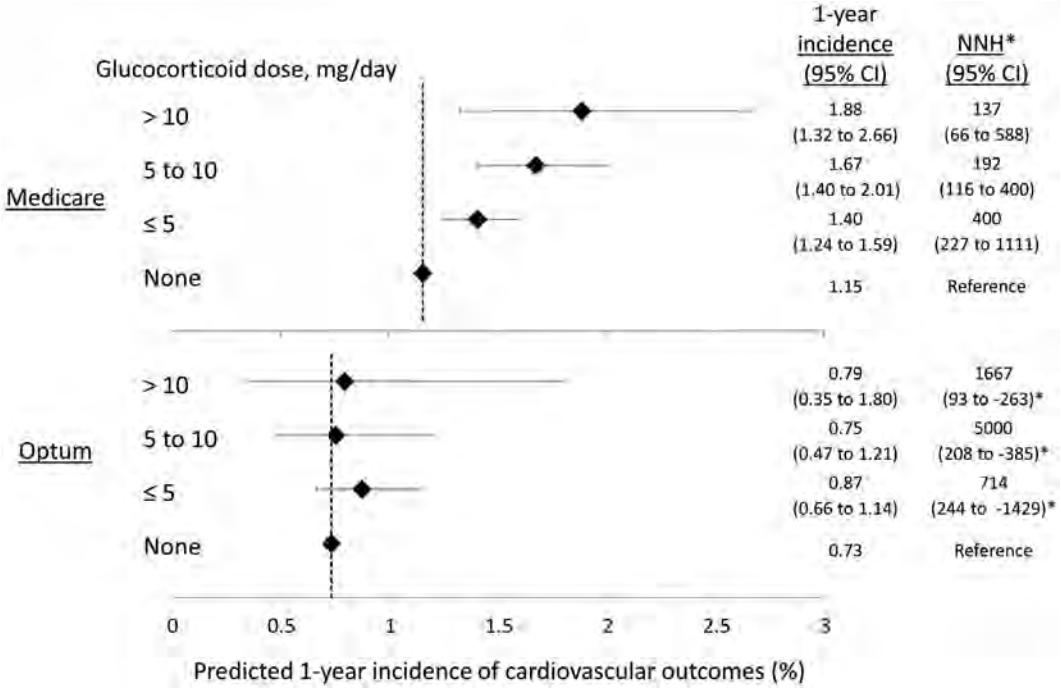
to estimate the effect of glucocorticoid use on composite cardiovascular outcomes (stroke or MI). Patients were censored at the end of the stable DMARD course, end of enrollment, 9/30/2015, death in Medicare data, or 90 days after a change in glucocorticoid dose category (the completion of a treatment period). Predicted 1-year incidence of events was calculated from the weighted models to estimate risk by glucocorticoid dose while controlling for confounding factors.

Table 2. Association of Average Daily Glucocorticoid Dose with Composite Cardiovascular Outcomes

Glucocorticoid dose, mg/day	Observations, n	Person-years	Outcome (incidence*)	Unadjusted HR (95% CI)	IPWS HR (95% CI)
Medicare					
None	101,624	106,945	1242 (1.2)	Reference	Reference
≤ 5	57,800	39,267	601 (1.5)	1.35 (1.23-1.49)	1.22 (1.10-1.35)
5 to 10	23,413	10,309	180 (1.7)	1.60 (1.36-1.87)	1.46 (1.23-1.74)
≥ 10	6,103	2,318	44 (1.9)	1.75 (1.29-2.37)	1.64 (1.16-2.32)
Optum					
None	31,457	27,610	207 (0.7)	Reference	Reference
≤ 5	13,438	6,970	75 (1.1)	1.48 (1.13-1.94)	1.19 (0.90-1.58)
5 to 10	5,039	1,868	23 (1.2)	1.73 (1.11-2.69)	1.06 (0.66-1.69)
≥ 10	1,361	428	8 (1.9)	2.65 (1.29-5.46)	1.24 (0.58-2.65)

Hazard ratios (HR) and confidence intervals (CI) are from unadjusted cause-specific proportional hazard models and from propensity adjusted models using stabilized inverse probability weights (IPWS). * Incidence per 100 person-years

Results: There were 188,940 treatment periods among 135,583 patients in Medicare and 51,295 treatment periods among 39,272 patients in Optum (Table 1). Medicare patients had 158,839 years at risk with 2,067 composite cardiovascular outcomes and Optum patients had 36,876 years at risk with 313 outcomes corresponding to an incidence of 1.3 and 0.8 per 100 person-years, respectively. In Medicare, glucocorticoids were associated with a dose-dependent increase in cardiovascular risk in weighted models (Table 2) with predicted 1-year incidence of 1.4% (95% CI 1.2-1.6) for ≤5mg, 1.7% (1.4-2.0) for 5-10mg, and 1.9% (1.3-2.7) for >10mg versus 1.1% for no glucocorticoids (Figure 1). Unadjusted results were similar in the younger Optum population, but adjusted results were not significant with predicted 1-year incidence of 0.9% (95% CI 0.7-1.1), 0.8% (0.5-1.2), and 0.8% (0.4-1.8), respectively, versus 0.7% with no glucocorticoids.



Predicted 1-year incidence of myocardial infarction or stroke calculated from inverse probability weighted cause-specific hazards models. Hazard ratios for these models are shown in Table 2. * NNH = number needed to harm. The NNH 95% confidence intervals (CI) for each glucocorticoid dose category in the Optum dataset overlaps with the reference estimate for no glucocorticoids. Negative estimates can be interpreted as the number needed to treat to avoid a composite cardiovascular outcome.

Conclusion: Among older RA patients on stable DMARD therapy, long-term use of low-dose glucocorticoid was associated with increased risk for stroke or MI. Higher doses of glucocorticoids were associated with even greater risk. The absolute risk in the younger Optum cohort was lower and research with larger patient populations will be needed to determine if risks exist among younger patients with lower baseline cardiovascular risk.

Disclosure: B. Coburn, None; **M. George**, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **J. Hsu**, None; **Q. Wu**, None; **L. Chen**, None; **F. Xie**, None; **H. Yun**, Pfizer, 5; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5.

Abstract Number: 1916

Antibodies to Malondialdehyde-Acetaldehyde (MAA) Modified Proteins Predict Incident Rheumatoid Arthritis-Associated Interstitial Lung Disease

Bryant England[1], Geoffrey Thiele[1], Dana Ascherman[2], Michael Duryee[1], Carlos Hunter[1], Yangyuna Yang[1], Punyasha Roul[1], Harlan Sayles[1], Andreas Reimold[3], Gail Kerr[4], Joshua Baker[5], Jill Poole[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pittsburgh, Pittsburgh, PA, [3]University of Texas – Southwestern Medical Center/Dallas Veterans Affairs Medical Center (VAMC), Dallas, TX, [4]Washington D.C., Veterans Affairs Medical Center (VAMC)/Georgetown and Howard Universities, Washington, DC, [5]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Heart & Lung (1915–1918)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Table 1. Associations of anti-MAA antibodies with incident RA-ILD

	Primary analysis (n=2317)		Excluding ILD in first year (n=2296)	
	HR (95% CI)	P value	HR (95% CI)	P value
Anti-MAA-albumin				
IgA	1.26 (1.05, 1.52)	0.01	1.32 (1.08, 1.62)	0.007
IgM	1.26 (1.05, 1.51)	0.01	1.28 (1.06, 1.56)	0.01
IgG	1.17 (0.98, 1.40)	0.08	1.19 (0.98, 1.44)	0.08
Anti-MAA-collagen				
IgA	1.04 (0.89, 1.21)	0.63	0.97 (0.83, 1.14)	0.73
IgM	1.13 (0.97, 1.32)	0.12	1.07 (0.91, 1.25)	0.40
IgG	1.02 (0.88, 1.19)	0.79	0.95 (0.82, 1.12)	0.56

Values are hazard ratios (95% confidence intervals) per 1 standard deviation change in antibody concentration

Each antibody tested in separate Cox models adjusting for age, sex, race, smoking status, anti-CCP antibody positivity, and DAS28.

Abbreviations: CI, confidence interval; HR, hazard ratio; MAA, malondialdehyde-acetaldehyde

Background/Purpose: Because interstitial lung disease (ILD) causes substantial morbidity and mortality in rheumatoid arthritis (RA), there is a need for methods to facilitate early identification and diagnosis. Peripheral biomarkers including RA-autoantibodies, inflammatory cytokines/chemokines, and tissue remodeling proteins identify patients with established RA-ILD. Less is known, however, whether peripheral biomarkers predict incident RA-ILD. This is particularly relevant as the RA-related autoantibodies, anti-CCP and RF, are not highly predictive of future ILD risk (Natalini JG. *Ann Am Thorac Soc* 2021). Previously, antibodies to malondialdehyde-acetaldehyde adducts (anti-MAA), a

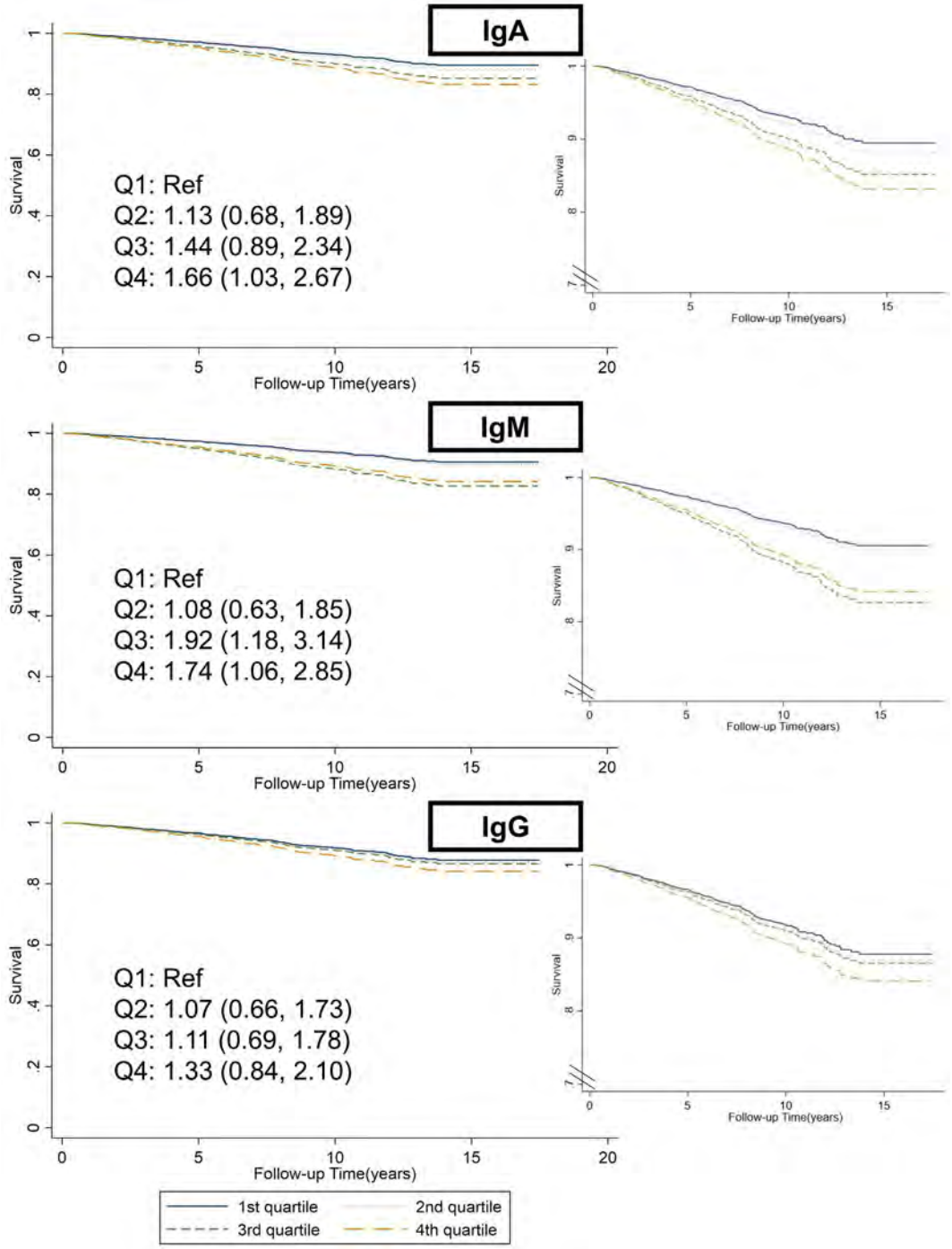


Figure 1. RA-ILD free survival by quartiles of anti-MAA-albumin antibodies. Values hazards ratios (95% confidence intervals) from Cox regression models adjusted for age, sex, race, smoking status, anti-CCP antibody positivity, and DAS28.

RA-related autoantibody, were found to be closely associated with prevalent RA-ILD (England BR. *Arthritis Rheumatol* 2019). In this study, we aimed to determine if anti-MAA antibodies were associated with risk of incident RA-ILD.

Methods: We studied participants in the Veterans Affairs Rheumatoid Arthritis registry, a prospective cohort of U.S. Veterans with RA. Patients with RA-ILD at the time of enrollment were excluded. Demographics, smoking status, and RA measures were collected from the registry. We measured anti-MAA antibody concentrations (IgA, IgM, and IgG) by ELISA on banked serum from registry enrollment for both MAA-modified albumin and MAA-modified collagen. Anti-MAA antibody values were log-transformed, standardized, and categorized into quartiles. Incident ILD consisted of ILD diagnoses occurring after registry enrollment, determined through a previously validated approach that included systematic review of medical records for clinical diagnoses, imaging findings, and biopsy reports. In sensitivity analyses, we excluded ILD cases developing ILD within 1 year of enrollment. Multivariable Cox regression models assessed associations of anti-MAA antibody with incident ILD adjusting for age, sex, race, smoking status, anti-CCP antibody positivity, and enrollment DAS28.

Results: Among 2,317 RA patients, 190 developed ILD over 18,044 patient-years of follow-up. Patients were male predominant (90%), with a mean age of 64 years, and had frequent smoking history (79%) and anti-CCP antibody positivity (77%). Higher IgA and IgM anti-MAA-albumin antibody concentrations were associated with an increased risk of incident RA-ILD (Table 1). Effect sizes were smaller for IgG and were not statistically significant. Those with the highest quartiles of IgA and IgM anti-MAA-albumin antibodies had a higher risk of incident ILD (Q4 vs Q1 HR: IgA 1.66 [1.03, 2.67], IgM 1.74 [1.06, 2.85]; Figure 1). In contrast, anti-MAA-collagen antibodies were not significantly associated with incident RA-ILD risk (Table 1). Results were consistent in sensitivity analysis excluding ILD cases occurring in the first year after registry enrollment (Table 1).

Conclusion: Serum anti-MAA-albumin antibodies are associated with a higher risk of developing ILD among RA patients. These findings highlight the role novel autoantibodies may serve in the pathogenesis of RA-ILD as well as support the development of risk models to predict ILD onset.

Disclosure: B. England, Boehringer-Ingelheim, 2; **G. Thiele**, Regeneron, 6; **D. Ascherman**, None; **M. Duryee**, None; **C. Hunter**, None; **Y. Yang**, None; **P. Roul**, None; **H. Sayles**, None; **A. Reimold**, None; **G. Kerr**, Aurinia, 6, Novartis, 5, Bristol Myers Squibb, 1, 5, Pfizer, 1, Horizon, 1; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **J. Poole**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1917

Sputum TGF-β1 Is Elevated in Subclinical and Clinically Significant Rheumatoid Arthritis-Associated Interstitial Lung Disease and Correlates with Soluble IL-6R Levels

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Heart & Lung (1915–1918)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Table 1. Clinical characteristics and pulmonary function in RA-no-ILD, RA-sub-ILD and RA-ILD

				p-value**		
	RA-no-ILD* (n=24)	RA-sub-ILD* (n=22)	RA-ILD* (n=16)	RA-no-ILD vs RA-sub-ILD	RA-no-ILD vs RA-ILD	RA-sub-ILD vs RA-ILD
Age	53 ± 13	57 ± 14	69 ± 8	NS	<0.001	NS
Female	79%	73%	44%	NS	NS	NS
Ever smoker	33%	41%	56%	NS	NS	NS
Smoking pack-years	5 ± 10	9 ± 13	23 ± 36	NS	0.03	NS
% predicted FVC	103 ± 13	93 ± 16	80 ± 17	NS	0.001	0.05

*Values displayed as mean ± SD or %.
**Based on Chi-square or t-test where appropriate, NS = not significant, P>0.05.
Clinical data was missing for: % predicted FVC in 10 RA-no-ILD, 2 RA-ILD.

Background/Purpose: Increased levels of transforming growth factor β1 (TGF-β1) in the lung have been implicated in the pathogenesis of several fibrotic lung diseases, but their role in the lung in rheumatoid arthritis-associated interstitial lung disease (RA-ILD) has not been well studied. Evidence suggests that increased TGF-β1 production in the

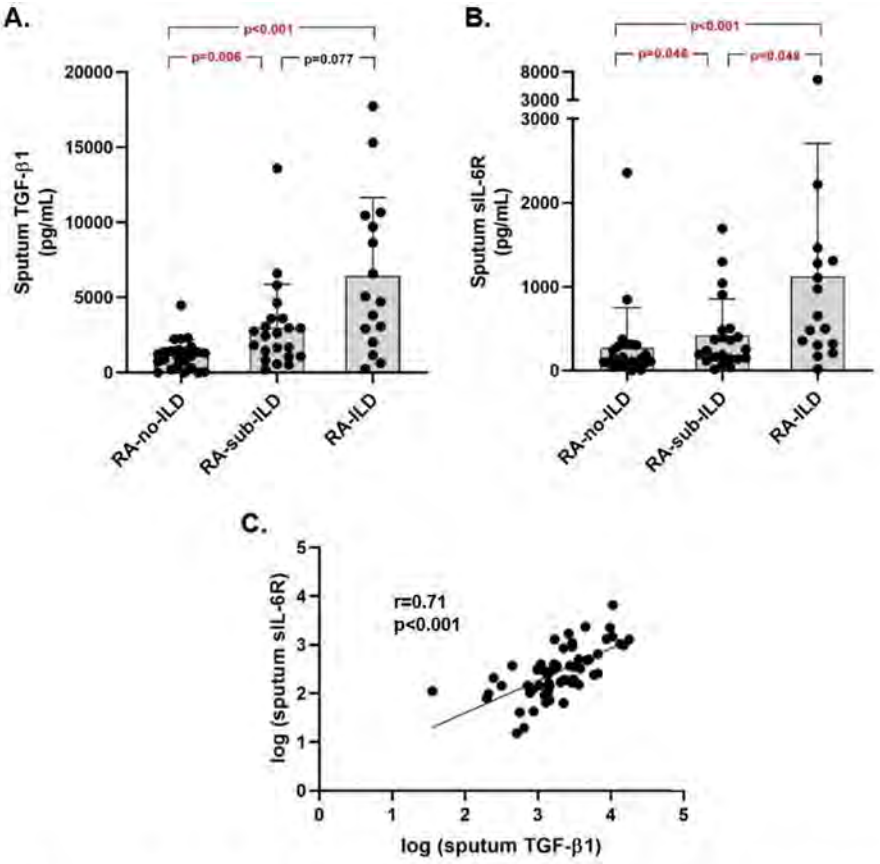

Figure 1. Sputum TGF-β1 and sIL-6R levels. (Panel A-B) Mean sputum supernatant levels + SD for TGF-β1 and sIL-6R in RA-no-ILD (n=24), RA-sub-ILD (n=22), and RA-ILD (n=16). P-values based on Wilcoxon rank-sum test. (Panel C) Log transformed sIL-6R levels correlated with log transformed TGF-β1 and IL-6 levels. Correlations calculated using Spearman's correlation coefficient (r-value).

lung can be driven by IL-6 trans-signaling, which requires soluble IL-6 receptor (sIL-6R) complexed with IL-6 binding to membrane-bound gp130; this is in contrast to IL-6 classical-signaling that requires IL-6 binding to membrane-bound IL-6R (mIL-6R). Importantly, gp130, and not mIL-6R, is present on lung fibroblasts which play a key role in lung fibrosis. Also, mIL-6R is present on neutrophils and can be released to form sIL-6R during neutrophil extracellular trap (NET) formation. In this study, we sought to evaluate the relationships between TGF-β1, sIL-6R, NETs and the presence of ILD across a spectrum of patients with RA.

Methods: We included 16 RA patients with clinically significant ILD (RA-ILD), 22 RA patients with subclinical ILD defined as having parenchymal changes on lung high resolution computed tomography (HRCT) (i.e. fibrosis, traction bronchiectasis, reticulation and/or ground glass opacities) but no clinical diagnosis of ILD and normal pulmonary physiology (RA-sub-ILD), and 24 RA patients without ILD on HRCT (RA-no-ILD). All subjects underwent pulmonary function testing (PFT) and induced sputum was collected using hypertonic saline. Sputum was tested for TGF-β1 (Meso Scale Diagnostics) and sIL-6R (R&D Systems). Sputum IL-6 was measured in a subset of 8 RA-ILD, 4 RA-sub-ILD and 3 RA-no-ILD (Luminex) and sputum NET remnants in a subset of 11 RA-ILD and 3 RA-sub-ILD patients (sandwich ELISA for DNA-neutrophil elastase (NE) and DNA-citrullinated histone H3 (DNA-citH3)).

Results: Patient demographics are summarized in Table 1. Sputum TGF-β1 and sIL-6R levels were significantly higher in RA-sub-ILD and RA-ILD compared to RA-no-ILD (Figure 1A and 1B). In regression analyses adjusting for age and smoking, TGF-β1 and sIL-6R levels remained significantly associated with RA-sub-ILD and RA-ILD. Sputum TGF-β1 correlated with sIL-6R levels (Figure 1C) while there was no correlation between TGF-β1 and IL-6. In a subset of RA-sub-ILD and RA-ILD subjects, sputum NET remnants positively correlated with sputum sIL-6R levels (Figure 2A and 2B) but not TGF-β1 levels ($p > 0.20$).

Conclusion: We found for the first time that sputum TGF-β1 and sIL-6R levels are increased in subclinical and clinically significant RA-ILD. The strong correlation between sputum TGF-β1 and sIL-6R along with the correlation between sputum sIL-6R and NET remnants suggest that increased TGF-β1 in the lung may be due to NET-associated increases in sIL-6R and subsequent IL-6 trans-signaling of lung fibroblasts. Future studies are needed to better understand the use of sputum TGF-β1 and sIL-6R as prognostic biomarkers in RA-ILD as well as mechanisms by which TGF-β1 production and IL-6 trans-signaling in the lung may contribute to RA-ILD.

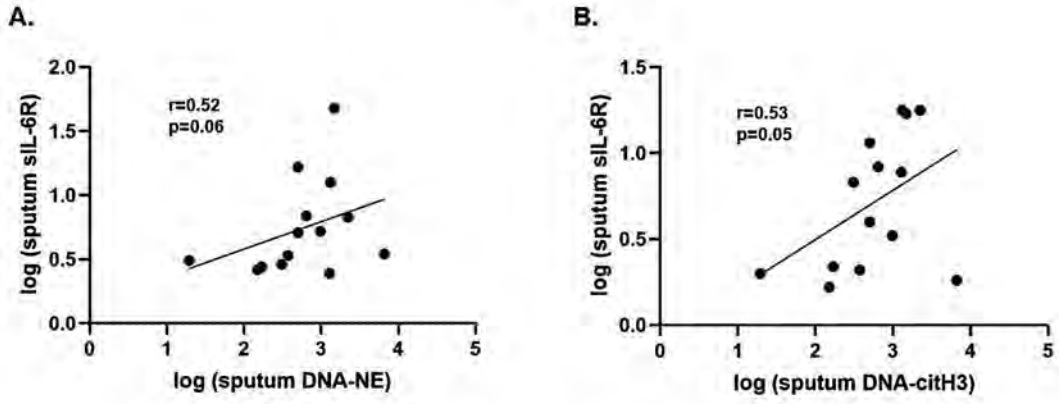

Figure 2. Correlation of sputum sIL-6R and NET remnant levels. Log transformed sIL-6R levels correlated with log transformed DNA-NE (Panel A) and DNA-citH3 (Panel B) levels in RA-ILD (n=11) and RA-sub-ILD (n=3). Correlations calculated using Spearman's correlation coefficient (r-value).

Disclosure: T. Wilson, None; **K. Deane**, Inova Diagnostics, Inc, 5, Bristol Meyers Squibb, 1, 5, Janssen Research and Development, LLC, 5, imaware, 2, ThermoFisher, 2, 5, Medscape, 6; **J. Lee**, None; **C. Collora**, None; **M. Feser**, None; **M. Kaplan**, None; **J. Solomon**, None; **K. Demoruelle**, Pfizer, 5.

Abstract Number: 1918

Don't Forget About the Arthritis in RA-ILD! Impact of Pulmonary and RA Disease Severity on Survival

Rebecca Brooks[1], Joshua Baker[2], Yangyuna Yang[1], Punyasha Roul[1], Gail Kerr[3], Andreas Reimold[4], Gary Kunkel[5], Katherine Wysham[6], Namrata Singh[7], Deana Lazaro[8], Paul Monach[9], Jill Poole[1], Dana Ascherman[10], Ted Mikuls[1] and Bryant England[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Pennsylvania, Philadelphia, PA, [3]Washington D.C., Veterans Affairs Medical Center (VAMC)/Georgetown and Howard Universities, Washington, DC, [4]University of Texas – Southwestern Medical Center/Dallas Veterans Affairs Medical Center (VAMC), Dallas, TX, [5]University of Utah, Salt Lake City, UT, [6]VA Puget Sound/University of Washington, Seattle, WA, [7]University of Washington, Bellevue, WA, [8]VA New York Harbor Healthcare system, Brooklyn, NY, [9]Brigham and Women's Hospital, Boston, MA, [10]University of Pittsburgh, Pittsburgh, PA

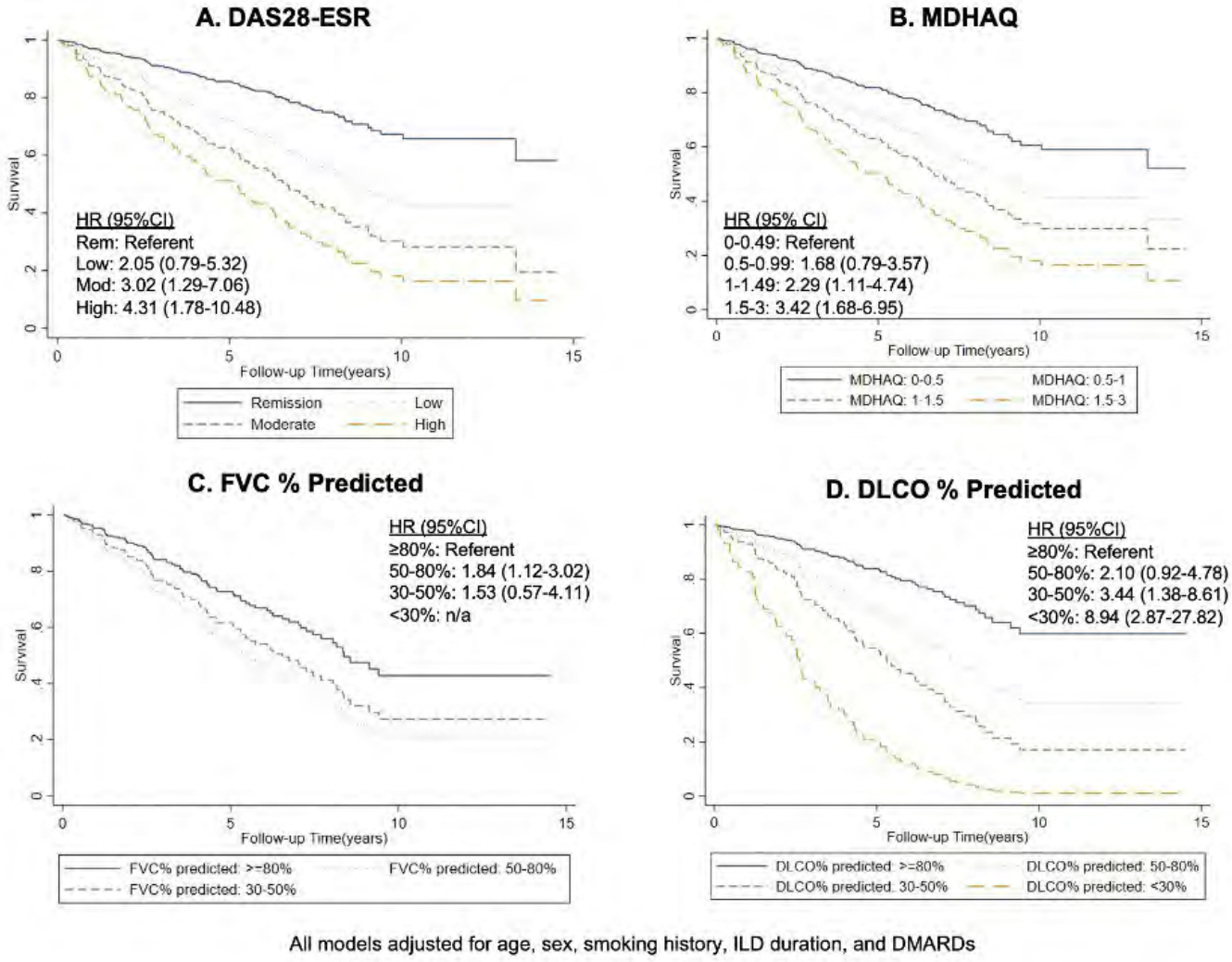

Figure 1. Adjusted Survival Curves in RA-ILD by Disease Activity, Functional Status, and Pulmonary Function Test Categories.

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Diagnosis, Manifestations, & Outcomes II: Heart & Lung (1915–1918)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Long-term outcomes following a diagnosis of rheumatoid arthritis associated interstitial lung disease (RA-ILD) are poor, with a median survival estimated between 3 to 8 years. Despite the profound impact on survival, relatively few prognostic factors are known in RA-ILD. More severe pulmonary disease is associated with reduced survival, but little is understood regarding the contribution of RA disease activity to long-term outcomes in RA-ILD. We aimed to determine whether RA disease activity and functional status, as measured by DAS28-ESR and MDHAQ, were independently associated with survival in RA-ILD.

Methods: We performed a cohort study of patients with RA-ILD nested within a multicenter, prospective RA cohort (Veteran Affairs Rheumatoid Arthritis Registry) that contained patient data from 2003-2019. RA was diagnosed by a rheumatologist and fulfilled ACR criteria while ILD diagnoses were validated through detailed medical record confirmation (clinical diagnoses and corresponding dates, imaging findings, lung biopsy and pulmonary function [FVC and DLCO %-predicted] results). Demographics, seropositivity, RA disease duration, and RA medications were collected from the registry and linked administrative data. RA disease activity (DAS28-ESR) and functional status (MDHAQ) were collected longitudinally through routine care. Death was ascertained through linkage with administrative records and the National Death Index. Multivariable Cox regression models assessed the independent associations of RA disease activity and ILD severity with survival adjusting for age, sex, smoking status, and DMARDs.

Results: Patients with RA-ILD (n=227) had mean (SD) age of 69 (9) years, were 93% male, 75% white, frequently had a smoking history (85%), and a mean DAS28-ESR of 4.0 (1.3), MDHAQ of 1.0 (0.6), FVC % predicted of 77.2 (17.9), and DLCO % predicted of 60.2 (21.9). After RA-ILD diagnosis, the median survival was 8.5 years. Over 1,073 person-years of follow-up, 108 deaths occurred with respiratory disease being the leading cause of death (28% of deaths). When examined in separate models, DAS28-ESR, MDHAQ, and pulmonary (FVC and DLCO % predicted) measures of severity were independently associated with survival (Figure 1A-D). The association between DAS28-ESR (per 1-

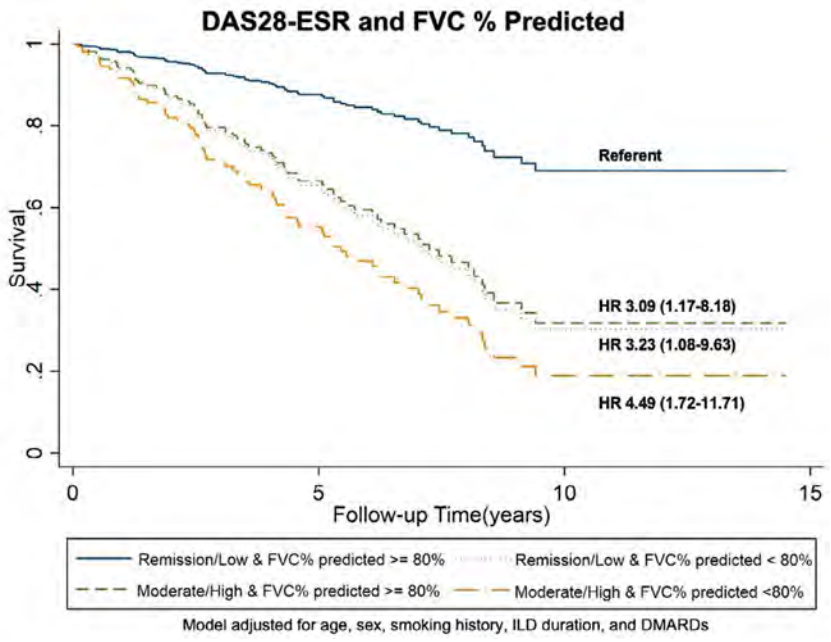

Figure 2. Survival in RA-ILD by Combined Disease Activity and Forced Vital Capacity Classification.

unit HR 1.22 [95% CI 1.04-1.43]) and MDHAQ (per 1-unit HR 1.89 [95% CI 1.33-2.69]) with mortality persisted after adjusting for FVC % predicted. When assessing RA disease activity and pulmonary severity together, moderate/high RA disease activity or impaired FVC (< 80% predicted) alone were associated with >3-fold higher risk of death compared to those with remission/low disease activity and normal FVC (Figure 2). The combination of moderate/high disease activity and impaired FVC carried the highest risk of death (HR 4.49 [95% CI 1.72-11.71];Figure 2).

Conclusion: Among patients with RA-ILD, more severe RA disease activity and impaired functional status were associated with poorer survival independent of ILD severity. To optimize long-term outcomes in RA-ILD, treatment should be targeted at both controlling the disease activity in RA and pulmonary disease manifestations.

Disclosure: R. Brooks, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **Y. Yang**, None; **P. Roul**, None; **G. Kerr**, Aurinia, 6, Novartis, 5, Bristol Myers Squibb, 1, 5, Pfizer, 1, Horizon, 1; **A. Reimold**, None; **G. Kunkel**, None; **K. Wysham**, None; **N. Singh**, None; **D. Lazaro**, None; **P. Monach**, Kiniksa, 1, Celgene, 2, Chemocentryx, 1; **J. Poole**, None; **D. Ascherman**, None; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2; **B. England**, Boehringer-Ingelheim, 2.

Abstract Number: 1919

Detection of Radiographic Sacroiliitis with an Artificial Neural Network in Patients with Suspicion of Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes II (1919–1922)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Conventional radiography of the sacroiliac joints is still recommended as the first imaging method for the diagnosis of axial spondyloarthritis (axial SpA). In many clinical settings around the world, this is the only widely available imaging method to diagnose axial SpA. A high specificity of radiographic detection in the diagnostic setting is required to avoid improper diagnosis of axial SpA. We have recently developed a deep convolutional neural network (CNN) that was able to detect radiographic sacroiliitis with expert-like accuracy in two cohorts of patients with axial SpA, i.e., performing classification as radiographic or non-radiographic (Bressem KK, et al. Arthritis Res Ther 2021;23:106). The aim of the present study was to evaluate the performance of this CNN in detecting definite radiographic sacroiliitis in a diagnostic setting.

Methods: We evaluated sacroiliac radiographs of patients with chronic back pain who presented to a rheumatologist with a suspicion of axial SpA within the OptiRef study (Proft F, et al. Semin Arthritis Rheum 2020;50:1015-21). A total of 361 patients received a structured rheumatologic diagnostic work-up that resulted in the final diagnosis of axial SpA/no axial SpA. Radiographs of sacroiliac joints were evaluated according to the modified New York criteria; the consensus judgement of rheumatologist and radiologist on the presence of definite radiographic sacroiliitis (>=grade 2 bilaterally or >=grade 3 unilaterally) was used as a reference. The predictions of the deep CNN's inference on all available pelvic radiographs was compared to this reference judgement.

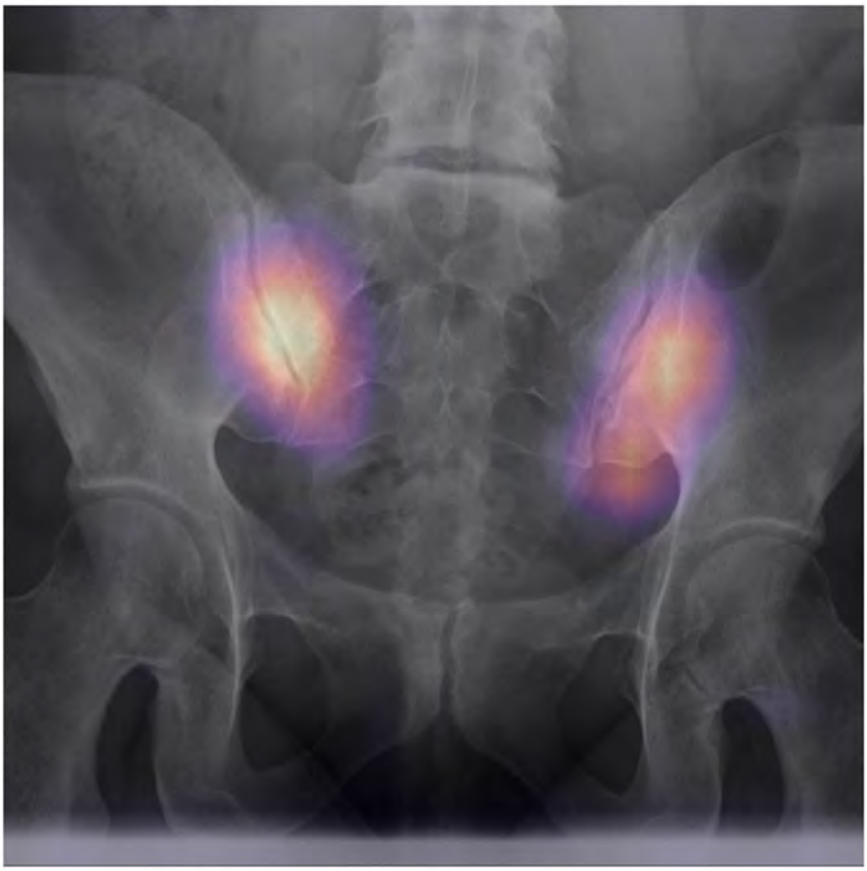
Table 1. Convolutional neural network predictions of the presence of definite radiographic sacroiliitis in patients with suspected axial SpA according to the final diagnosis by rheumatologist in OptiRef (N=340).

	CNN's prediction	
Clinical diagnosis	**Radiographic sacroiliitis present**	**Radiographic sacroiliitis absent**
Radiographic axial SpA	48/61 (78.7%)	13/61 (21.3%)
Non-radiographic axial SpA	4/49 (8.2%)	45/49 (91.8%)
No axial SpA	14/230 (6.1%)	216/230 (93.9%)

CNN=convolutional neural network, SpA=spondyloarthritis.

Results: Pelvic radiographs of 340 out of 361 patients (110 diagnosed with axial SpA including 61 patient with radiographic and 49 with non-radiographic axial SpA, and 230 without SpA) were available for the CNN evaluation. We used a balanced cutoff of 0.724 for the predictions of the model that was derived from the training and validation step previously. The deep CNN achieved a sensitivity of 79% for the diagnosis of radiographic axial SpA. The specificity of

Figure 1. Inference of the proposed CNN on a pelvic radiograph from the OptiRef study.



This exemplary class activation map shows that our CNN almost exclusively and correctly focusses on the sacroiliac joints to predict whether definite radiographic sacroiliitis is present or not. In this case, no definite radiographic sacroiliitis was detected.

radiographic sacroiliitis detection was 94% (table 1). The area under the receiver operating characteristics curve for the prediction of the presence of definite radiographic sacroiliitis was 88%. The absolute agreement on the classification as radiographic or non-radiographic axial SpA between the CNN and the reference was 85%. Figure 1 shows an exemplary class activation map of our CNN.

Conclusion: The artificial neural network showed good generalizability and a high specificity with acceptable sensitivity in the detection of radiographic sacroiliitis when applied in the diagnostic setting of patients with chronic back pain and suspicion of axial SpA. Thus, the trained CNN can therefore be used by non-specialized centers as an assistant tool for interpretation of sacroiliac radiographs as a part of the diagnostic approach.

Disclosure: D. Poddubnyy, AbbVie, 2, 5, 6, Eli Lilly and Company, 2, 5, 6, MSD, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 6, BMS, 2, 6, Roche, 2, 6; **F. Proft,** Novartis, 1, 5, 6, Eli Lilly and Company, 1, 5, UCB, 1, 5, 6, AbbVie, 1, 6, Amgen, 1, 6, Bristol-Myers Squibb, 1, 6, Hexal, 1, 6, MSD, 1, 6, Pfizer, 1, 6, Roche, 1, 6; **K. Hermann,** None; **L. Spiller,** None; **S. Niehues,** None; **L. Adams, None; M. Protopopov,** Novartis, 1, 5, 6; **V. Rios Rodriguez,** None; **B. Muche,** None; **J. Rademacher,** None; **M. Torgutalp,** None; **K. Bressem,** None; **J. Vahldiek,** None.

Abstract Number: 1920

Association of C-reactive Protein and Non-Steroidal Anti-inflammatory Drugs with Cardiovascular Events in Patients with Psoriatic Arthritis: A Time-dependent Cox Regression Analysis

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes II (1919–1922)
Session Type: Abstract Session
Session Time: 2:00PM–3:30PM

Background/Purpose: Psoriatic arthritis (PsA) is associated with accelerated atherosclerosis due to underlying inflammation. Whether inflammatory burden and drugs used to suppress inflammation over time are associated with cardiovascular (CV) events remained unclear. This study aims to examine the time-varying effect of C-reactive protein (CRP) levels and the use of drugs including non-steroidal anti-inflammatory drugs (NSAIDs) on the risk of CV events independent of traditional CV risk factors in PsA patients.

Methods: A retrospective cohort analysis was performed in patients with PsA who were recruited from 2008 to 2015 and followed till the end of 2019. The outcome was occurrence of a first CV event. Framingham risk score (FRS) was used to quantify the traditional CV risk. Cox proportional hazard models with time-varying CRP levels and drugs used were analyzed to identify the risk factors for CV events in PsA patients. Kaplan-Meier survival curve and log-rank test was used to illustrate CV event free survival distribution.

Results: 200 patients with PsA (median age: 47.5[40.0 – 56.0]; male: 119 [59.5%]) were recruited (Table 1). After a mean follow-up of 8.8±3.8 years, 30 (15%) patients developed a first CV event. The Kaplan-Meier survival curve and the log-rank test indicated a significant difference in the CV event-free survival between patients with and without CRP level >3 mg/L (Figure 1A) and an inverse relationship between time-varying NSAIDs exposure and CV event-free

Table 1. Comparison of the baseline demographic and clinical characteristics, cardiovascular risk factors and treatments according to cardiovascular outcomes and baseline NSAID use.

Variables	CVD -ve, n=170	CVD +ve, n=30	*p*-value	NSAID -ve, n=61	NSAID +ve, n=139	*p*-value
Male, n (%)	100 (58.6%)	19 (63.3%)	0.228	39 (63.9%)	80 (57.6%)	0.397
Age, yrs	46.5 (37.7 – 54.0)	57.0 (45.3 – 65.8)	<0.001*	49.0 (44.0 – 56.5)	46.0 (38.0 – 54.8)	0.176
BMI, kg/m^2	25.3 (22.8 – 29.1)	25.2 (23.7 – 27.2)	0.718	25.4 (23.7 – 28.2)	25.1 (22.2 – 29.1)	0.732
Disease duration, yr	4.1 (1.7 – 7.0)	6.0 (2.1 – 8.6)	0.066	4.6 (1.5 – 8.7)	4.3 (1.9 – 7.3)	0.393
Diabetes, n (%)	30 (17.6%)	15 (50.0%)	<0.001*	10 (16.4%)	35 (25.2%)	0.171
Hypertension, n (%)	46 (27.1%)	22 (73.3%)	<0.001*	21 (34.4%)	47 (33.9%)	0.933
CRP, mg/L	4.2 (1.5 – 12.0)	11.3 (2.4 – 19.6)	0.035*	5.5 (1.7 – 15.1)	7.2 (1.4 – 15.8)	0.770
ESR, mm/hr	20 (9 – 35)	31 (14 – 60)	0.038*	21 (7 – 33)	21 (11 – 43)	0.291
Total cholesterol, mmol/L	4.9 (4.2 – 5.6)	5.1 (4.3 – 5.6)	0.476	4.9 (4.4 – 5.6)	4.9 (4.2 – 5.6)	0.909
HDL, mmol/L	1.3 (1.1 – 1.5)	1.4 (1.0 – 1.6)	0.809	1.4 (1.2 – 1.6)	1.2 (1.0 – 1.5)	0.056
LDL, mmol/L	2.9 (2.4 – 3.3)	2.8 (2.2 – 3.4)	0.912	2.9 (2.4 – 3.3)	2.9 (2.3 – 3.4)	0.949
Triglycerides, mmol/L	1.2 (0.9 – 1.8)	1.4 (1.1 – 2.0)	0.156	1.2 (0.8 – 1.7)	1.2 (1.0 – 1.5)	0.746
Glucose, mmol/L	5.1 (4.8 – 5.5)	5.2 (4.8 – 6.0)	0.167	5.0 (4.6 – 5.4)	5.1 (4.8 – 5.6)	0.137
Systolic blood pressure, mmHg	124 (115 – 137)	144 (129 – 160)	<0.001*	123 (118 – 137)	125 (115 – 141)	0.889
Diastolic blood pressure, mmHg	78 (70 – 84)	82 (72 – 90)	0.199	78 (72 – 86)	78 (70 – 85)	0.697
Ever smoker, n (%)	50 (35.0%)	8 (30.8%)	0.678	20 (37.7%)	38 (32.8%)	0.527
Ever drinker, n (%)	42 (33.9%)	8 (32.0%)	0.857	13 (28.9%)	37 (35.6%)	0.427
FRS	7.5 (3.3 – 14.0)	19.6 (13.4 – 43.0)	<0.001*	7.9 (3.5 – 15.5)	8.7 (4.2 – 17.1)	0.885
Current treatment						
Lipid-lowering drug, n (%)	25 (14.7%)	5 (16.7%)	0.782	9 (14.8%)	21 (15.1%)	0.949
MTX, n (%)	81 (47.6%)	18 (60.0%)	0.212	25 (41.0%)	74 (53.2%)	0.111
bDMARDs, n (%)	13 (7.6%)	4 (13.3%)	0.303	6 (9.8%)	11 (7.9%)	0.654
NSAIDs, n (%)	119 (70.0%)	20 (66.7%)	0.715	N/A	N/A	N/A
Steroid, n (%)	2 (1.2%)	0 (0%)	1.000	1 (1.6%)	1 (0.7%)	0.518

**statistically significant at p= 0.05*

CVD+ve, patients who developed cardiovascular events during subsequent follow-up; CVD-ve, patients who did not developed cardiovascular events during subsequent follow-up; BMI, body mass index; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; HDL, high-density lipoprotein cholesterol; LDL, low-density lipoprotein cholesterol; FRS, Framingham Risk Score; MTX, methotrexate; bDMARDs, biological disease-modifying antirheumatic drugs; NSAIDs, nonsteroidal anti-inflammatory drugs; N/A, not available.

survival (Figure 1B). The multivariable Cox regression model showed that time-varying CRP level (HR 1.02, 95% CI 1.00 to 1.04) and NSAIDs exposure (HR 0.30, 95% CI 0.15 to 0.95) were significantly associated with CV events after adjusting for baseline FRS (HR 5.04, 95% CI 1.83 to 13.85).

Conclusion: Increased inflammatory burden as reflected by elevated CRP level was associated with increased risk of CV events, while the risk was significantly reduced with NSAIDs use in PsA patients.

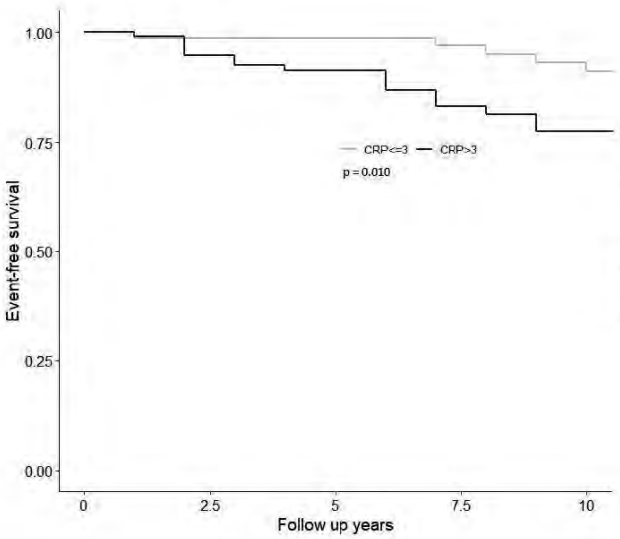


Figure 1A

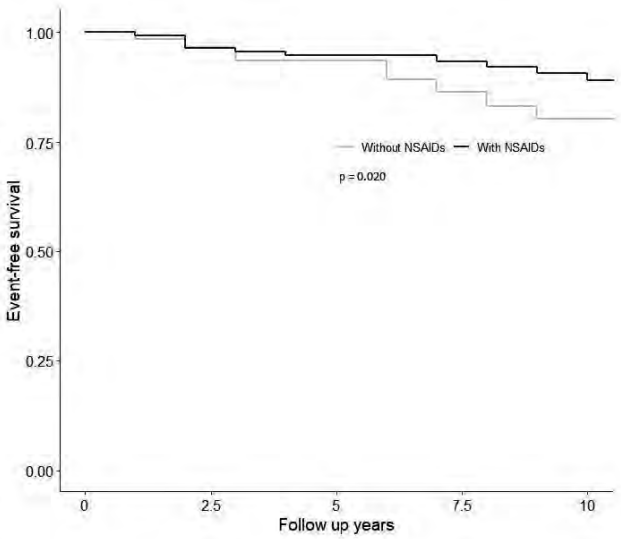


Figure 1B

Figure 1. Kaplan-Meier curves showing the cardiovascular event-free survival between patients with A) CRP≤3 mg/L and CRP>3 mg/L; B) treated with NSAIDs and without NSAIDs use during their follow-up intervals.

Disclosure: H. Lam, None; **H. So**, None; **I. Cheng**, None; **E. Li**, None; **P. Wong**, None; **T. Li**, None; **A. Lee**, None; **L. Tam**, Janssen, 2, 5, Pfizer, 2, 5, GlaxoSmithKline, 5, AbbVie, 2, Novartis, 5, Amgen, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, Sanofi, 2.

Abstract Number: 1921

Axial Psoriatic Arthritis: Correlation Between Whole Spine MRI Abnormalities and Clinical Findings

Pamela Diaz[1], Iris Eshed[2], Joy Feld[3] and Lihi Eder[1], [1]University of Toronto, Toronto, ON, Canada, [2]Sheba Medical Center, Ramat Gan, Israel, [3]Carmel and Zvulun Medical Centre, Haifa, Israel

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes II (1919–1922)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: Psoriatic Arthritis (PsA) typically affects peripheral joints, but in some patients the disease can involve the spine. While magnetic resonance imaging (MRI) is an important diagnostic tool for spondyloarthritis, especially in early phases, there is minimal information about MRI features of axial PsA.

The purpose of the study was to describe the prevalence of inflammatory and structural lesions by whole-spine MRI in patients with psoriatic disease, and assess the correlation of MRI-defined spondyloarthritis (MRI-SpA) with clinical and laboratory features and with classification criteria for axial spondyloarthritis (axSpA).

Methods: In this retrospective analysis we included 93 patients selected from 2 populations: 1) 41 patients with active PsA, who were referred for a whole-spine MRI irrespective of whether they had axial symptoms, and 2) 52 pa-

Table 1- Study population characteristics and imaging findings. Mean (SD), median (IQR)

Variable	All population N = 93	Population 1* N = 41	Population 2† N = 52
Age	43.3 (13)	47.9 (12.2)	39.7 (12.7)
Sex, Female	49 (52.7%)	20 (48.8%)	29 (55.8%)
Diagnosis of PsA Psoriasis and axial symptoms	65 (69.9%) 28 (30.1%)	41 (100%)	24 (46.2%) 28 (53.9%)
Duration of PsA, years	1.6 (0.9)	1.7 (2.1)	1.4 (1.1)
Axial symptoms	76 (81.7%)	28 (68.3%)	48 (92.3%)
Inflammatory back pain: ○ By rheumatologist ○ Berlin criteria ○ ASAS criteria	 53 (57%) 34 (36.6%) 34 (36.6%)	 21 (51.2%) 12 (29.3%) 10 (24.4%)	 32 (61.5%) 22 (42.3%) 24 (46.2%)
Peripheral joint pain	83 (89.3%)	40 (97.6%)	43 (82.7%)
Dactylitis (y/n)	15 (16.1%)	12 (29.3%)	3 (5.8%)
Enthesitis (y/n)	44 (47.3%)	27 (65.9%)	17 (32.7%)
BASDAI	5.2 (2.2)	5.6 (2.3)	4.8 (2.2)
ASDAS	2.5 (1.2)	2.8 (1.2)	2.2 (1.1)
HLA-B27	10 (10.9%)	5 (12.2%)	5 (9.8%)
Erosions in peripheral joints	14 (15.4%)	12 (30.8%)	2 (3.9%)
Radiographic sacroiliitis and/or spondylitis‡	18 (19.4%)	11 (26.8%)	7 (13.5%)
MRI definitions ○ MRI-Spondylitis – ASAS§ ○ MRI-Spondylitis – radiologist¶ ○ Spondylitis without sacroiliitis	 9 (9.7%) 12 (12.9%) 3 (3.2%)	 8 (19.5%) 9 (22%) 2 (4.9%)	 1 (1.9%) 3 (5.8%) 1 (1.9%)

* Patients with active PsA who were referred for a whole-spine MRI regardless of axial symptoms. † Patients with psoriasis and confirmed or suspected PsA, referred for a whole-spine MRI due to suspected axial PsA. ‡ At least 1 syndesmophyte. § Spondylitis and/or sacroiliitis according to ASAS. (Spondylitis: anterior/posterior BME in ≥3 sites / fatty lesions at several sites. Active sacroiliitis: ≥2 BME lesions on a single SIJ slice and/or ≥ 1 BME lesion on 2 consecutive slices.) ¶ Spondylitis and/or sacroiliitis according to radiologist impression (considering inflammatory and structural lesions).

tients with psoriasis and suspected or confirmed PsA who were referred to a whole-spine MRI for suspected axPsA. Patients on biologic advanced therapies were excluded.

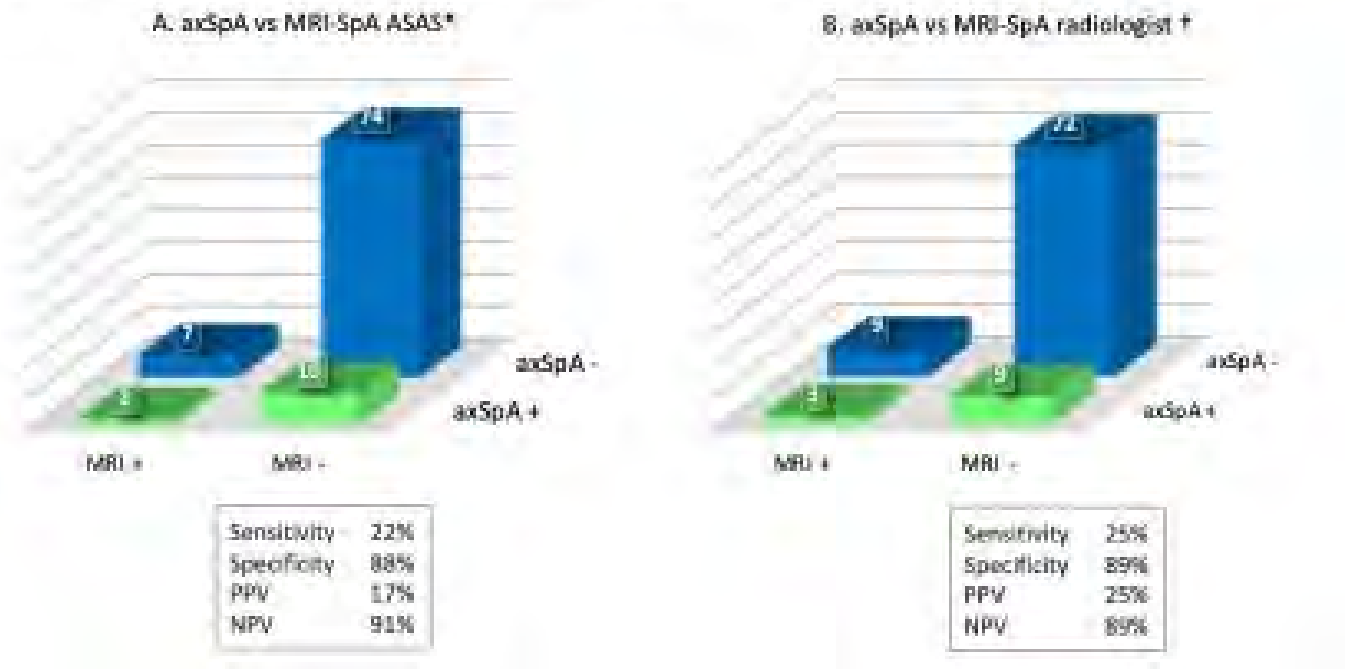
Clinical, radiographic and laboratory data were analyzed. Inflammatory back pain (IBP) was defined according to 3 criteria: Berlin, Assessment of Spondyloarthritis International Society (ASAS) and rheumatologist impression.

Table 2- Correlation between inflammatory back pain (IBP) according 3 definitions and MRI-SpA by ASAS and by radiologist impression

	MRI-SpA ASAS			MRI-SpA radiologist		
	IBP Rheumatologist*	IBP Berlin[1]	IBP ASAS[2]	IBP Rheumatologist*	IBP Berlin[1]	IBP ASAS[2]
Sensitivity	56%	22%	22%	50%	33%	33%
Specificity	43%	62%	62%	42%	63%	63%
PPV	9%	6%	6%	11%	12%	12%
NPV	90%	88%	88%	85%	86%	86%

* Inflammatory back pain according to rheumatologist impression at the clinical visit (considering symptoms but no images) 1. Rudwaleit M, et al. Arthritis Rheum. 2006;54(2):569-78. 2. Sieper J, et al. Ann Rheum Dis. 2009;68(6):784-8.

Fig. 1- Correlation between the ASAS classification criteria for axSpA and MRI-defined Spondyloarthritis (MRI-SpA) according to ASAS consensus* (A) and according to radiologist impression (B)†



*Spondylitis and/or sacroiliitis according to ASAS/OMERACT definitions (Spondylitis: anterior/posterior BME in ≥ 3 sites / fatty lesions at several sites. Sacroiliitis: ≥ 2 BME lesions on a single SIJ slice and/or ≥ 1 BME lesion on 2 consecutive slice). † Spondylitis and/or sacroiliitis according to radiologist impression (considering inflammatory and structural lesions).

MRI scans of the sacroiliac joints and whole-spine (T1W and STIR) were assessed by a musculoskeletal radiologist blinded to the clinical and radiographic data. MRI-SpA was defined as: 1) ASAS consensus for active spondylitis/sacroiliitis, and 2) the radiologist impression (considering inflammatory and structural lesions).

The agreement between MRI-SpA as a gold standard, and the ASAS classification criteria for axSpA and different definitions of IBP was assessed. Logistic regression evaluated the association between MRI-SpA and clinical, demographic and laboratory factors.

Results: 93 patients were analyzed (mean age 43.3 ±13, 52.7% women, Table 1). The prevalence of HLA-B*27 was 10.9%. Axial symptoms were present in 81.7%, being defined as IBP in 36.6%/36.6%/57% according to Berlin, ASAS and rheumatologist criteria, respectively. MRI-SpA was found in only 9 (9.7%) patients by ASAS definition and 12 (12.9%) by radiologist impression.

Overall, low agreement was found between the three IBP definitions and MRI-SpA (Table 2). IBP by rheumatologist impression was the most sensitive (50-56%) and ASAS and Berlin criteria for IBP were most specific (62-63%). Poor sensitivity was found for the ASAS criteria for axSpA and MRI-Spondylitis (ASAS definition 22.2%; radiologist impression 25%, Fig. 1). Onset of axial pain after the age of 40 and absence of axial pain accounted for most patients with MRI-SpA not meeting the ASAS axSpA criteria or IBP criteria. Male sex was associated with MRI-Spondylitis (OR 6.9; 95% CI 1.4, 33.6) in multivariable regression analysis.

Conclusion: The overall prevalence of axial inflammatory and structural spondylitis by whole-spine MRI was low despite the high prevalence of axial symptoms. Poor correlation was found between imaging and clinical findings highlighting the need for further research of the underlying mechanisms of axial involvement in PsA.

Disclosure: P. Diaz, None; **I. Eshed**, Novartis, 6, Abbvie, 6; **J. Feld**, None; **L. Eder**, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5.

Abstract Number: 1922

Early and Accurate Diagnosis of Patient with Axial Spondyloarthritis Using Machine Learning: A Predictive Analysis from Electronic Health Records in United Kingdom

Raj Sengupta[1], Shruti Narasimham[2], Borja Mato[3], Matic Meglic[3], Chiara Perella[3], Paula Pamies[4] and Paul Emery[5], [1]The Royal National Hospital for Rheumatic Diseases, Bath, United Kingdom, [2]Novartis Ireland Ltd, Dublin, Ireland, Dublin, Ireland, [3]Novartis Pharma AG, Basel, Switzerland, [4]Novartis Pharmaceuticals UK Ltd, London, UK, London, United Kingdom, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and Leeds NIHR Biomedical Research Centre, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Diagnosis, Manifestations, & Outcomes II (1919–1922)

Session Type: Abstract Session

Session Time: 2:00PM–3:30PM

Background/Purpose: On an average, there is a delay of 6.7 years between symptom onset and diagnosis of axial spondyloarthritis (axSpA)[1]. Since traditional approaches to improving early axSpA identification have had limited success, predictive automated analyses on patient records may help alleviate the burden on healthcare providers[2-5].

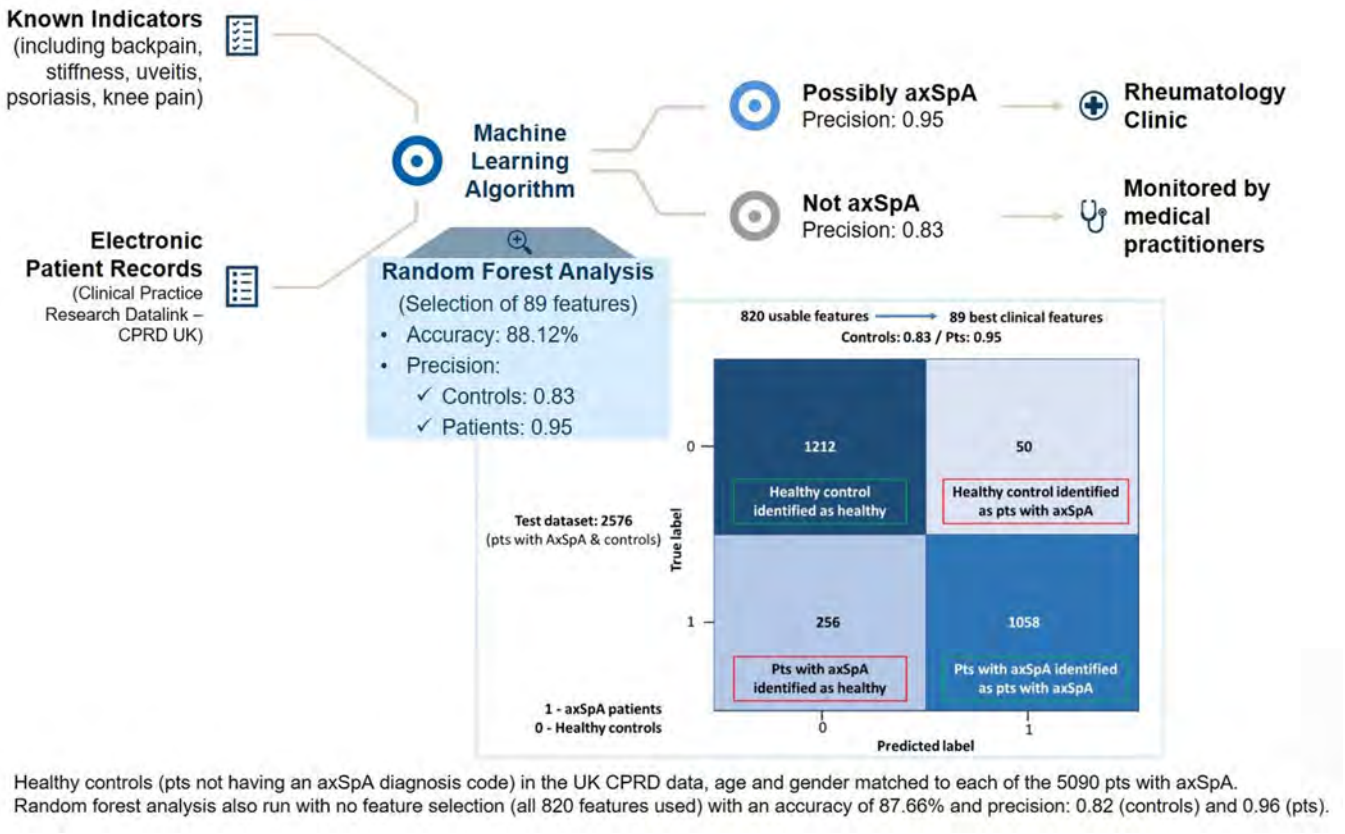


Figure. Automated axSpA diagnosis/rheumatology referral via pattern recognition in electronic patient data using ML.

Here, we report the results from a machine learning (ML) algorithm developed with UK electronic health records (EHRs) Clinical Practice Research Datalink (CPRD) data, to estimate the probability or likelihood of a pt being diagnosed with axSpA based on prior clinical indicators and pt history.

Methods: Primary care UK EHR data - CPRD GOLD was used to identify pts with axSpA and healthy controls (HC) (**Figure**). Pts aged ≥18 years, with first diagnosis date of axSpA within the identification period (01-Jan-2005 to 31-Dec-2018) and fulfilling CPRD research acceptability criteria were included in the study. Data pertaining to clinical presentation, consultation, referral, test, and therapy history were extracted for individual pt prior to diagnosis of axSpA. A total of 5090 pts with axSpA satisfied the acceptability criteria. HC were randomly sampled to create a subset of one unique HC matched to each pt with axSpA, resulting in 5089 HC. ML usable features derived from the total population (pts with axSpA and HC) numbered 820. After using a further exclusion criterion for the pts with axSpA and HC who had ≥1 out of 820 usable features, the final dataset included 7813 pts (3902 pts with axSpA and 3911 HC). This combined dataset was randomly split (67:33) into a train (N=5237) and a test (N=2576) dataset. A Random Forest (RF) model was trained on the train dataset. Cross-validation was performed for hyper-parameter tuning of the RF classifier. Once the model was trained, accuracy, precision, and F-1 scores were obtained with the test dataset.

Results: The RF based algorithm resulted in a high level of accuracy (88.12%), with precision of 0.95 for pts with axSpA and 0.83 for HC (**Figure**). RF algorithm identified 89 best clinical predictors (out of 820 used as inputs) that differentiated between pt and HC such as: total number of tests, total number of referrals, first age of consultation, first symptom age, number of low back pain symptoms. The sensitivity of the model was 75.04% and positive predictive value was 80.88%. The specificity of the model was 0.96 and negative predictive value was 82.56%.

Conclusion: The ML algorithm demonstrated a high level of accuracy and precision in the identification of possible cases of axSpA, which may be useful in reducing the delay in diagnosis. Previous studies have successfully demonstrated automated cohort identification of axSpA in large datasets, with only a few using ML based approaches for diagnosis from patient medical history. While the model supports previous work in axSpA[2-5], it needs further validation in routine clinical practice and this exploration is ongoing.

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Disclosure: R. Sengupta, Merck Sharp & Dohme, 1, 5, 6, AbbVie, 1, 5, 6, Biogen, 1, 5, 6, Celgene, 1, 5, 6, Novartis, 1, 5, 6, Pfizer, 1, 5, 6, Roche, 1, 5, 6, UCB, 1, 5, 6; **S. Narasimham**, Novartis, 3, 11; **B. Mato**, Novartis, 3, 11; **M. Meglic**, Novartis, 3; **C. Perella**, Novartis, 3; **P. Pamies**, Novartis, 3; **P. Emery**, Abbvie, 2, 5, 6, Sanofi, 2, 6, BMS, 2, 5, 6, Novartis, 2, 6, Gilead, 2, 6, Samsung, 2, 5, 6, Celltrion, 2, 6, Eli Lilly, 2, 5, 6, MSD, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Amgen Inc., 2, 6, Sandoz, 2, UCB, 1, 5, 6, Boehringer Ingelheim, 1, 5, 6, Merck, 1, 5, 6.

Abstract Number: 1923

Has the Incidence of Total Joint Arthroplasty in Rheumatoid Arthritis Decreased in the Era of Biologics Use? A Population-based Incident Cohort Study 1995–2015

Vivienne Zhou[1], Diane Lacaille[1], Na Lu[2], Jacek Kopec[3], Don Garbuz[1], Yi Qian[4], J. Antonio Avina-Zubieta[1], John Esdaile[2] and Hui Xie[1], [1]Arthritis Research Canada, Richmond, BC, Canada, [2]Arthritis Research Canada, Vancouver, BC, Canada, [3]University of British Columbia, Richmond, BC, Canada, [4]University of British Columbia, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

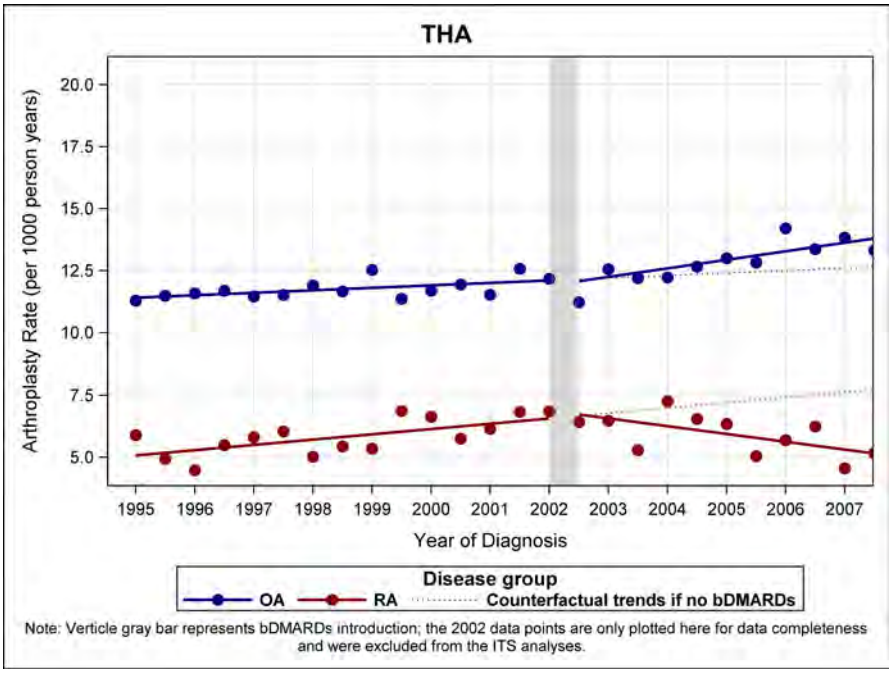
Session Title: Abstracts: Epidemiology & Public Health II: Inflammatory Arthritis (1923–1926)

Session Type: Abstract Session

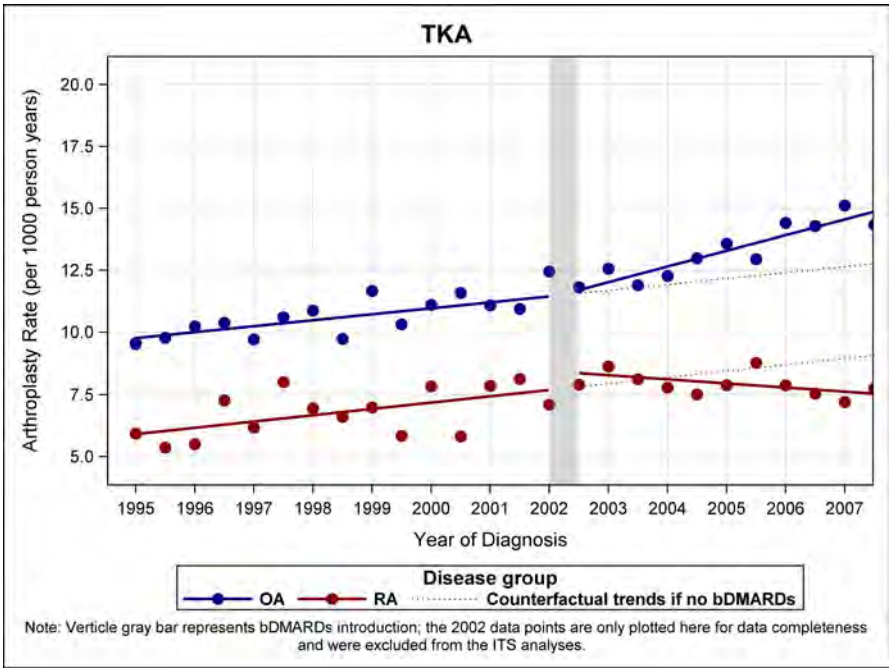
Session Time: 3:30PM–4:30PM

Background/Purpose: Total joint arthroplasty (TJA) is an undesirable long-term outcome of rheumatoid arthritis (RA) due to joint damage from uncontrolled inflammation. Although biological disease-modifying anti-rheumatic drugs (bDMARDs) would be expected to reduce the need for TJA due to better control of inflammation, evidence is conflicting. We aim to investigate whether the introduction of bDMARDs was associated with reduced incidences of total hip and knee arthroplasty (THA/TKA) among patients with RA compared with osteoarthritis (OA).

Methods: Using a population-based cohort in British Columbia, Canada, RA and OA patients diagnosed between 1995–2007 were divided into semi-annual cohorts according to diagnosis date. For each cohort, we calculated 8-year incidence rates of THA and TKA. We compared levels and trends of THA and TKA incidence in people with RA/OA diagnosis during pre-bDMARDs (1995–2001) and post-bDMARDs (2003–2007) periods using interrupted time-series analysis, adjusting for baseline characteristics



8-year incidence rate (per 1000 person years) of total hip arthroplasty (THA) among RA patients compared with OA patients. Abbreviations – bDMARDs: biological disease-modifying anti-rheumatic drugs; ITS: interrupted time-series.



8-year incidence rate (per 1000 person years) of total knee arthroplasty (TKA) among RA patients compared with OA patients. Abbreviations – bDMARDs: biological disease-modifying anti-rheumatic drugs; ITS: interrupted time-series.

Results: We identified 60,227 RA and 288,260 OA incident cases. For cohorts diagnosed pre-bDMARDs, 8-year incidence rates of THA and TKA increased over time in both RA and OA. For cohorts diagnosed post-bDMARDs, these rates decreased over time in RA but continued to increase for OA. For RA, differences between the post- and pre-bDMARDs secular trends in incidence rates were -0.49 (p=0.002) for THA and -0.36 (p=0.003) for TKA, compared to +0.40 (p=0.006) and +0.54 (p< 0.001), respectively, for OA. For cohorts with RA diagnosis five years after bDMARDs became available, 8-year incidence rates were 26.9% and 12.6% lower for THA and TKA, respectively, than expected rates based on extrapolation of pre-bDMARDs trends. In contrast, corresponding rates in OA were higher by 11.7%, and 16.6%, respectively.

Table Results of ITS analysis of eight-year incidence rates of surgery outcomes, adjusting for gender, age, comorbidities, and medication use

Type	Parameter	RA					OA				
		Est. with Pre-Period Regression (95% CI) p-value	Est. with Post-Period Regression (95% CI) p-value	Unadj. Diff (95% CI) p-value	Adj. Diff (95% CI)[a] p-value	Robustness Checking Adj. Diff (95% CI)[b] p-value	Est. with Pre-Period Regression (95% CI) p-value	Est. with Post-Period Regression (95% CI) p-value	Unadj. Diff (95% CI) p-value	Adj. Diff (95% CI)[a] p-value	Robustness Checking Adj. Diff (95% CI)[b] p-value
THA	Trend	0.21 (0.08, 0.35) 0.0053	-0.31 (-0.54, -0.09) 0.0116	-0.53 (-0.79, -0.27) 0.0007	-0.49 (-0.74, -0.23) 0.0015	-0.50 (-0.77, -0.24) 0.002	0.10 (0.04, 0.16) 0.0062	0.34 (0.21, 0.48) 0.0001	0.25 (0.08, 0.41) 0.0077	0.40 (0.15, 0.65) 0.0061	0.42 (0.14, 0.69) 0.0091
	level (1 year post-intervention)	6.78 (6.14, 7.42) <.0001	6.57 (5.85, 7.29) <.0001	-0.21 (-1.18, 0.76) 0.678	-0.10 (-1.02, 0.81) 0.8306	-0.17 (-1.11, 0.78) 0.7358	12.20 (11.79, 12.60) <.0001	12.24 (11.91, 12.56) <.0001	0.04 (-0.40, 0.48) 0.8575	-0.11 (-0.58, 0.35) 0.6394	-0.08 (-0.55, 0.40) 0.7602
	5 years post-intervention	7.63 (6.48, 8.78) <.0001	5.31 (4.91, 5.71) <.0001	-2.32 (-3.53, -1.11) 0.0013	-2.05 (-3.08, -1.02) 0.001	-2.18 (-3.15, -1.22) 0.0005	12.60 (11.94, 13.25) <.0001	13.62 (13.27, 13.96) <.0001	1.02 (0.26, 1.79) 0.0163	1.48 (0.56, 2.40) 0.0054	1.60 (0.52, 2.68) 0.0108
TKA	Trend	0.25 (0.10, 0.41) 0.0053	-0.17 (-0.29, -0.04) 0.018	-0.42 (-0.64, -0.21) 0.001	-0.36 (-0.57, -0.16) 0.0028	-0.26 (-0.50, -0.02) 0.0486	0.24 (0.16, 0.32) <.0001	0.63 (0.46, 0.80) <.0001	0.39 (0.22, 0.56) 0.0002	0.54 (0.30, 0.78) 0.0004	0.55 (0.27, 0.83) 0.0017
	level (1 year post-intervention)	7.95 (7.11, 8.78) <.0001	8.29 (7.88, 8.70) <.0001	0.34 (-0.54, 1.23) 0.4541	0.32 (-0.55, 1.19) 0.48	0.50 (-0.69, 1.70) 0.423	11.67 (11.24, 12.11) <.0001	12.01 (11.55, 12.46) <.0001	0.33 (-0.37, 1.04) 0.3641	-0.06 (-0.59, 0.47) 0.8286	-0.02 (-0.54, 0.51) 0.9485
	5 years post-intervention	8.96 (7.52, 10.41) <.0001	7.62 (7.30, 7.95) <.0001	-1.34 (-2.83, 0.15) 0.0939	-1.13 (-2.49, 0.22) 0.119	-0.55 (-2.52, 1.42) 0.5934	12.64 (11.91, 13.37) <.0001	14.54 (14.20, 14.89) <.0001	1.91 (1.12, 2.69) 0.0001	2.10 (1.27, 2.92) 0.0001	2.20 (1.13, 3.26) 0.0012

[a]Interrupted-time series (ITS) model estimation results, adjusting for age, gender, and selected comorbidity and glucocorticoids use at the disease diagnosis year, using stepwise model selection.
[b]Estimation results by adding % with use of ≥ two tDMARDs within one year of diagnosis as a covariate into the ITS models in [a] above.
[c]Estimates and p-values were derived from GMM. 95% Confidence interval (CI) were obtained using critical value = 1.96.
[d]ITS: interrupted-time series; RA: rheumatoid arthritis; OA: osteoarthritis; THA: total hip arthroplasty; TKA: total knee arthroplasty; est: estimates; unadj: unadjusted; adj: adjusted; diff: difference.

Conclusion: Arthritis onset after the introduction of bDMARDs is associated with a significant decrease in THA and TKA incidence in RA, but not in OA.

Disclosure: V. Zhou, None; **D. Lacaille**, None; **N. Lu**, None; **J. Kopec**, None; **D. Garbuz**, None; **Y. Qian**, None; **J. Avina-Zubieta**, None; **J. Esdaile**, None; **H. Xie**, None.

Abstract Number: 1924

Patient Clustering Based on Multimorbidity Patterns Predicts Healthcare Utilization and Mortality in Rheumatoid Arthritis Within Independent Real-World Datasets

Bryant England[1], Yangyuna Yang[1], Punyasha Roul[1], Christian Haas[2], Harlan Sayles[1], Fang Yu[1], Brian Sauer[3], Joshua Baker[4], Kaleb Michaud[1], Jeffrey Curtis[5] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]University of Nebraska Omaha, Omaha, NE, [3]University of Utah, Salt Lake City, UT, [4]University of Pennsylvania, Philadelphia, PA, [5]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Epidemiology & Public Health II: Inflammatory Arthritis (1923–1926)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Rheumatoid arthritis (RA) leads to substantial healthcare utilization and premature mortality. Prior work has demonstrated that the overlapping presence of comorbid chronic conditions, termed multimorbidity, is a primary driver of these long-term outcomes. However, optimal methods to assess multimorbidity in RA in the clinical setting are not established. For example, traditional comorbidity indices (e.g. Charlson Comorbidity Index, Rheumatic Disease Comorbidity Index [RDCI]) have little clinical utility. Therefore, we aimed to derive informative multimorbidity clusters that could be readily applied in the day-to-day care of patients with RA.

Methods: We constructed RA cohorts within a large commercial insurance database (MarketScan) and the Veterans Health Administration (VA) between 2006 and 2015 using validated administrative algorithms for RA. Pre-selected chronic conditions (n=42) were identified using diagnosis codes from outpatient and inpatient encounters. We performed k-means clustering of factor analysis scores (reflecting morbidity patterns) that were generated from the aforementioned chronic conditions independently in both datasets. Associations of unique cluster assignment with healthcare utilization (number of inpatient, emergency room [ER], and outpatient encounters) over up to 5 years was evaluated separately in both datasets using generalized estimating equations models adjusting for age and sex. In the VA, we also used multivariable Cox regression models to compare survival between clusters adjusting for age, sex, race, smoking status, and calendar year.

Results: From the multimorbidity patterns, we identified 4 distinct patient clusters in MarketScan (n=113,425) and 3 clusters in the VA (n=32,640) based on cubic clustering criterion (**Figure 1**). Based on the frequency of chronic conditions present, we identified “low”, “moderate”, and “severe” multimorbidity clusters. Patients in the “moderate/severe” multimorbidity clusters were older, more frequently male, and had higher RDCI and Charlson scores (**Table 1**). A cluster characterized by mental health and chronic pain diseases was also identified in both datasets. Referent to the “low” multimorbidity cluster, patients in the other clusters had significantly higher rates of inpatient, ER, and outpatient encounters (**Table 2**). In VA survival analyses, 9,415 deaths occurred over 228,534 patient-years

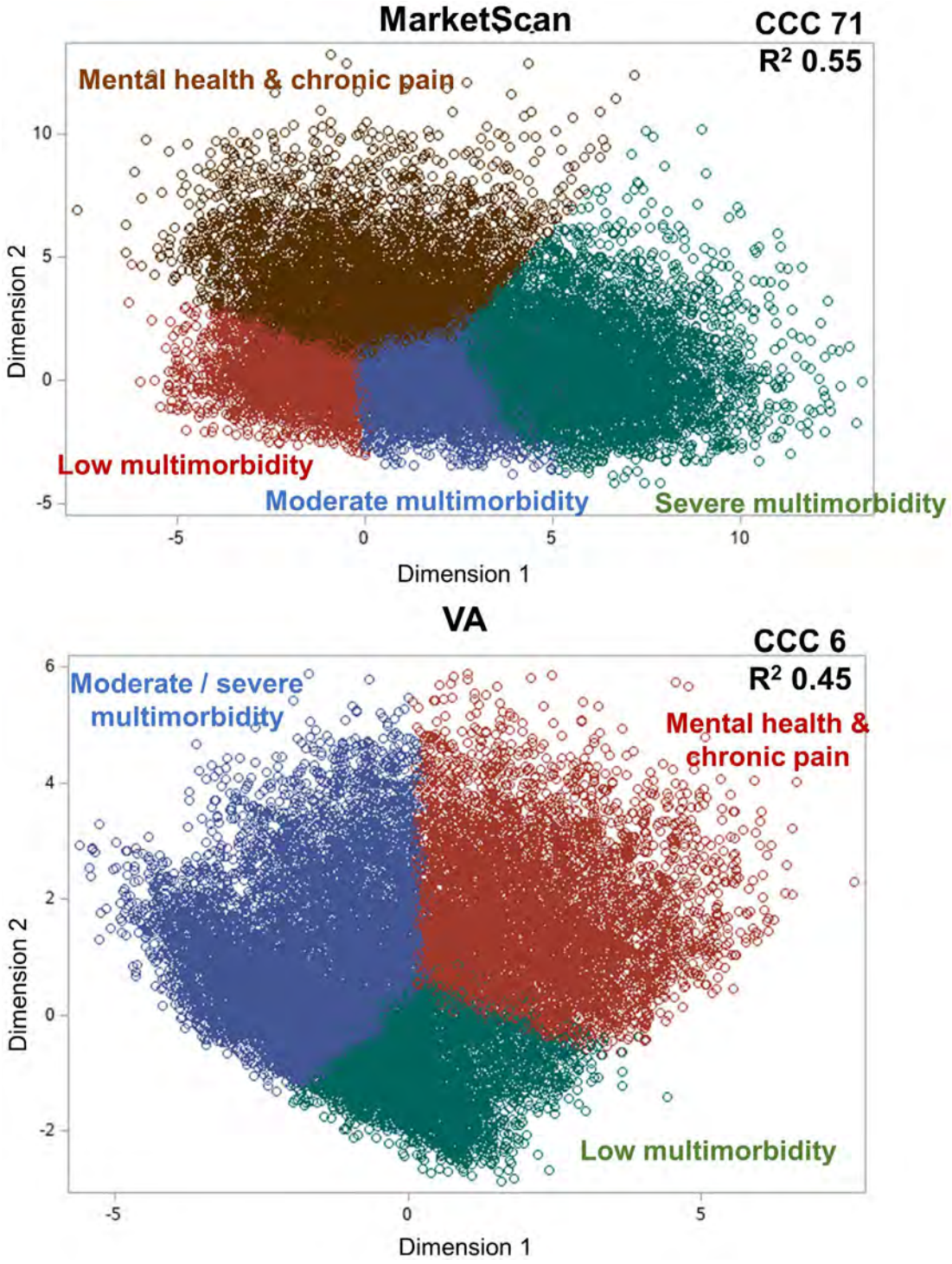


Figure 1. Clusters of RA patients based on multimorbidity patterns in MarketScan and the VA. Clustering of RA patients in both datasets performed using k-means clustering of factor analysis scores derived from the presence of 42 chronic conditions. Abbreviations: CCC, cubic clustering criterion.

of follow-up. Crude mortality rates were higher in both multimorbid clusters, but after multivariable adjustment, only the mental health and chronic pain cluster was significantly associated with higher mortality (HR 1.11 [95% CI 1.04, 1.18]).

Table 1. Characteristics of patients within each multimorbidity cluster

Cluster description *	N	Age	Female (%)	RDCI score	Charlson score
MarketScan					
Low multimorbidity	60,626	53 (14)	78	0.3 (0.9)	0.2 (0.5)
Moderate multimorbidity	28,486	60 (12)	72	1.3 (1.0)	0.5 (0.8)
Severe multimorbidity	14,153	62 (11)	71	2.0 (1.1)	1.0 (1.1)
Mental health & chronic pain	10,160	53 (12)	88	1.1 (1.2)	0.4 (0.7)
VA					
Low multimorbidity	14,203	62 (13)	14	0.4 (0.9)	1.4 (0.8)
Moderate / severe multimorbidity	11,630	67 (10)	7	1.0 (1.4)	2.3 (1.4)
Mental health & chronic pain	6,807	58 (11)	22	0.7 (1.2)	1.8 (1.1)

Values mean (SD) unless otherwise indicated.

*Cluster description based on RDCI score, Charlson score, and frequency of 42 chronic conditions (not shown)

Abbreviations: RDCI, Rheumatic Disease Comorbidity Index

Conclusion: Machine-learning approaches identified meaningful multimorbidity clusters among RA patients in two independent real-world datasets. Our approach highlights mental health and chronic pain multimorbidity, a pattern not accounted for in some widely used comorbidity indices, as a key determinant of long-term outcomes in RA. By retaining the ability to predict health outcomes with the simplicity of a cluster group assignment, this approach represents a crucial step forward in assessing multimorbidity at the point of care in clinical settings.

Table 2. Healthcare utilization over up to 5 years of follow-up by multimorbidity clusters

	Hospitalizations per year	Emergency room visits per year	Outpatient visits per year
MarketScan			
Low multimorbidity	Ref	Ref	Ref
Moderate multimorbidity	0.38 (0.34, 0.42)	0.32 (0.29, 0.36)	0.23 (0.22, 0.24)
Severe multimorbidity	0.57 (0.53, 0.62)	0.55 (0.51, 0.59)	0.41 (0.40, 0.42)
Mental health & chronic pain	0.80 (0.74, 0.86)	0.95 (0.89, 1.00)	0.49 (0.48, 0.50)
VA			
Low multimorbidity	Ref	Ref	Ref
Moderate / severe multimorbidity	0.36 (0.31, 0.42)	0.32 (0.27, 0.37)	0.39 (0.37, 0.41)
Mental health & chronic pain	0.59 (0.52, 0.65)	0.48 (0.43, 0.53)	0.52 (0.49, 0.54)

Values beta coefficients (95% confidence interval) from generalized estimating equations (GEE) models adjusted for age and sex.

Disclosure: B. England, Boehringer-Ingelheim, 2; **Y. Yang**, None; **P. Roul**, None; **C. Haas**, None; **H. Sayles**, None; **F. Yu**, None; **B. Sauer**, None; **J. Baker**, Bristol-Myers Squib, 2, Pfizer, 2; **K. Michaud**, None; **J. Curtis**, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **T. Mikuls**, Gilead Sciences, 2, Horizon, 2, 5, Pfizer Inc, 2, Sanofi, 2, Bristol-Myers Squibb, 2.

Abstract Number: 1925

Risk of Heart Failure in Patients with Inflammatory Disease: A Population-Based Study

Sahil Koppikar[1], Bindee Kuriya[2], Jacob Udell[3], Bing Yu[4], Anna Chu[4], Laura Ferreira-Legere[5], Douglas Lee[3], Jessica Widdifield[6] and Lihi Eder[3], [1]Women's College Hospital, Toronto, ON, Canada, [2]University of Toronto - Toronto, Toronto, ON, Canada, [3]University of Toronto, Toronto, ON, Canada, [4]ICES, Toronto, ON, Canada, [5]ICES, Toronto, Canada, [6]Sunnybrook Research Institute; ICES; Institute of Health Policy, Management & Evaluation, University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Epidemiology & Public Health II: Inflammatory Arthritis (1923–1926)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Individuals with inflammatory diseases (ID) have an increased risk of cardiovascular disease, frequently compared to that of diabetes mellitus (DM). However, the magnitude of risk for heart failure (HF) and potential etiologies of HF in ID have not been well described. We aimed to evaluate the risk of incident HF as well as its etiology in patients with ID compared to the general population with and without DM.

Methods: We linked multiple population-based health to construct a cohort of adults living in Ontario, Canada on January 1, 2011 and followed to December 2019. Patients diagnosed with rheumatoid arthritis (RA), ankylosing spondylitis (AS), psoriatic arthritis (PsA) and psoriasis (PsO) were identified using validated case definitions and matched by age, sex and geographic region with individuals without ID. We excluded all patients with a prior history of HF. The primary study outcome was incident HF defined as a first hospitalization for HF after January 1, 2011. Incidence rates of HF, per 1000 person-years (PY) for each exposure group were calculated. Hazard ratios (HRs, 95% confidence interval) for HF were calculated using Cox proportional hazard models, adjusting for demographics, cardiac risk factors and other comorbidities. The etiology of HF was descriptively classified in hierarchical order to mutually exclusive groups based on comorbidities prior to and at the time of HF hospitalization: 1) ischemic heart disease; 2) valvular disease; 3) atrial fibrillation; 4) hypertension/DM; 5) other.

Results: A total of 243,061 subjects had ID (35% RA, 8% AS, 3% PsA, 54% PsO) and 13% had co-morbid DM associated with their ID. There were 9,270,512 non-ID comparators, of which 8.3% had DM. The crude incidence rate for HF in ID was 2.70 per 1000/PY, with the highest rate in RA (3.93 per 1000/PY) and lowest in AS (1.80 per 1000/PY). All individual ID groups had significantly higher rates compared to the general population (0.84 per 1000/PY), but significantly lower HF incidence compared to subjects with DM alone (5.01 per 1000/PY, $p< 0.001$) (Figure 1).

In multivariable analyses, ID remained independently associated with an elevated risk of HF compared to non-ID subjects (HR 1.34, 95% CI 1.30, 1.38; Table 1); this relative risk was highest among subjects with RA and lowest in PsO. When stratified by DM, the risk of HF in ID was attenuated but remained increased (HR 1.11, 95% CI 1.06, 1.16). The leading cause of HF in all ID groups was ischemic heart disease (33%), followed by atrial fibrillation (27%), hypertension (23%), and valvular heart disease (12%) (Figure 2). The distribution of HF etiology was similar among non-ID comparators.

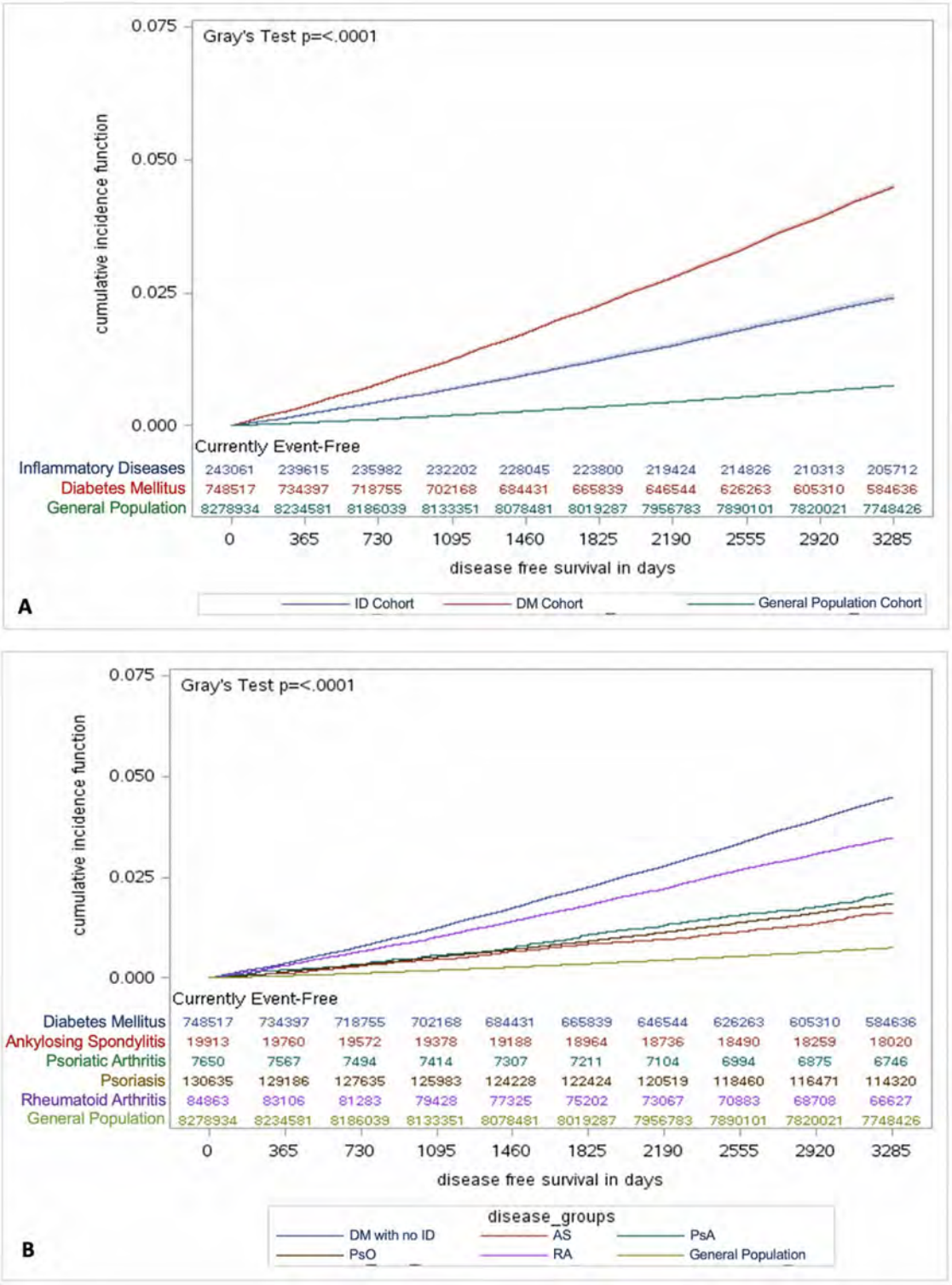


Figure 1. (A) Cumulative incidence of HF hospitalization in combined inflammatory diseases, diabetes, and general population comparators. (B) Cumulative incidence HF hospitalization in the individual inflammatory diseases, diabetes, and general population comparators.

Table 1. Multivariable Cox Proportion Hazards Models for HF hospitalization risk among all patients with inflammatory disease vs. non-inflammatory disease comparators, stratified by the presence of diabetes mellitus

	All ID (N=243,061) HR (95% CI)	RA (N=84,863) HR (95% CI)	AS (N=19,913) HR (95% CI)	PsA (N=7,650) HR (95% CI)	PsO (N=130,635) HR (95% CI)
Total number of HF events	**5836**	**2951**	**321**	**160**	**2404**
All patients with inflammatory disease					
With DM	1.11 (1.06, 1.16)	1.13 (1.06, 1.21)	1.24 (1.04, 1.47)	1.13 (0.88, 1.45)	1.08 (1.01, 1.15)
Without DM	1.34 (1.30, 1.38)	1.61 (1.54, 1.68)	1.19 (1.03, 1.37)	1.34 (1.10, 1.63)	1.09 (1.03, 1.15)
Males with inflammatory disease					
With DM	1.07 (1.00, 1.15)	1.05 (0.94, 1.18)	1.29 (1.04, 1.61)	0.88 (0.62, 1.26)	1.07 (0.98, 1.17)
Without DM	1.24 (1.18, 1.31)	1.55 (1.43, 1.68)	1.38 (1.16, 1.64)	1.19 (0.89, 1.59)	1.04 (0.97, 1.12)
Females with inflammatory disease					
With DM	1.14 (1.07, 1.22)	1.16 (1.06, 1.26)	1.20 (0.91, 1.58)	1.66 (1.18, 2.35)	1.09 (0.99, 1.20)
Without DM	1.42 (1.36, 1.48)	1.64 (1.56, 1.73)	0.92 (0.72, 1.19)	1.52 (1.15, 1.99)	1.14 (1.06, 1.23)

All models adjusted for age, sex, rural residence, ethnicity, hypertension, history of MI, PCI, CABG, COPD, Asthma, atrial fibrillation, CKD, and type of inflammatory disease

CI, confidence interval; CABG, coronary artery bypass graft surgery; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease; DM, diabetes mellitus; HF, heart failure; HR, hazard ratio; MI, myocardial infarction; PCI, percutaneous coronary intervention

Conclusion: The risk of HF hospitalization is increased in patients with ID compared to the general population, but lower than in DM. Ischemic heart disease and atrial fibrillation are leading causes of HF hospitalization in ID. The effect of inflammation underlying ID on HF risk may be independent of traditional risk factors, such as DM.

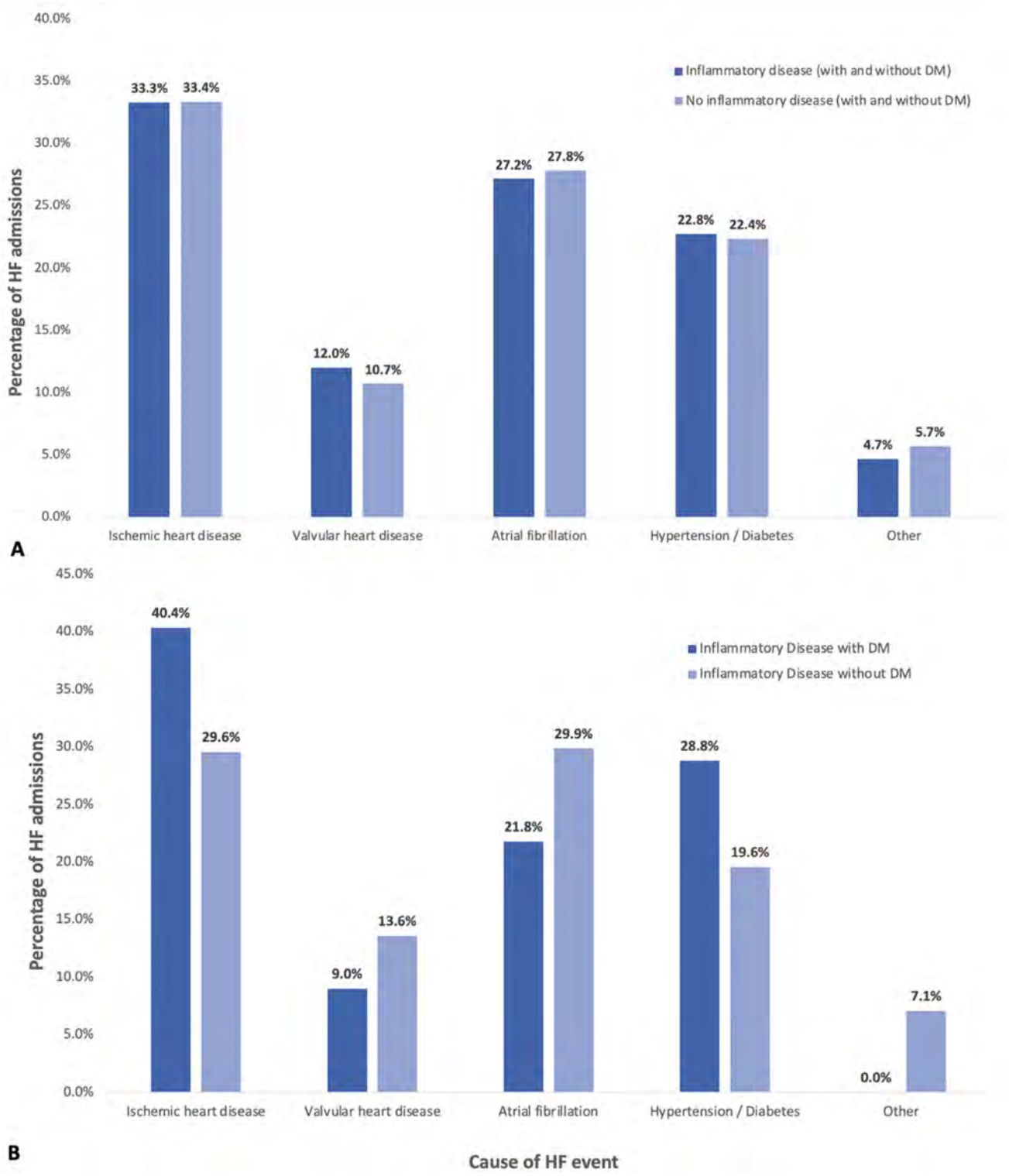


Figure 2. (A) Incident HF hospitalization by underlying etiology in patients with and without inflammatory disease. (B) Incident HF hospitalization by underlying etiology in all patients with inflammatory diseases.

Disclosure: S. Koppikar, Abbvie, 2, 6, Fresenius Kabi, 2, Janssen, 2, 6; **B. Kuriya**, None; **J. Udell**, Boehringer-Ingelheim, 1, 5, 6, Sanofi, 1, 5, 6, Bayer, 5, Novartis, 1, 5; **B. Yu**, None; **A. Chu**, None; **L. Ferreira-Legere**, None; **D. Lee**, None; **J. Widdifield**, None; **L. Eder**, Pfizer, 1, 5, UCB, 5, Abbvie, 1, 5, Novartis, 2, Eli Lily, 1, 5, Fluidigm, 5, 12, Family member - employee, Janssen, 5.

Abstract Number: 1926

Effectiveness of the Making It Work™ Program at Improving Absenteeism in Workers with Inflammatory Arthritis – Results of a Randomized Controlled Trial

Andre Luquini[1], Yufei Zheng[2], Hui Xie[2], Catherine L. Backman[3], Pamela Rogers[4], Alex Kwok[4], Astrid Knight[4], Monique Gignac[5], Dianne Mosher[6], Linda Li[3], John Esdaile[7], Carter Thorne[8] and Diane Lacaille[2], [1]University of British Columbia / Arthritis Research Canada, Fort Saint John, BC, Canada, [2]Arthritis Research Canada, Richmond, BC, Canada, [3]University of British Columbia, Vancouver, BC, Canada, [4]Arthritis Research Canada / UBC, Vancouver, BC, Canada, [5]Institute for Work & Health, Toronto, ON, Canada, [6]University of Calgary, Calgary, AB, Canada, [7]Arthritis Research Canada, Vancouver, BC, Canada, [8]Southlake Regional Health Centre, Newmarket, ON, Canada

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Epidemiology & Public Health II: Inflammatory Arthritis (1923–1926)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Despite advances in treatment, absenteeism remains a major problem for workers living with inflammatory arthritis (IA), leading to reduced income and quality of life. Yet, health services addressing employment needs of people with arthritis are lacking. We evaluated the effectiveness of the Making-it-Work™ (MIW), an online program developed to help people with IA deal with employment issues, at preventing days missed from work and work interruptions.

Methods: A multi-center RCT evaluated the effectiveness of MIW at improving absenteeism over two years. Participants were recruited from rheumatologist practices, consumer organizations and arthritis programs, in three provinces. Eligibility criteria included: diagnosis of IA, being employed, age 18-59, and concerned about ability to work.

Table 1. Baseline Characteristics

Variable	Control	Intervention
n	282	282
Age, median (IQR)	49.19 (13.65)	47.79 (15.19)
Sex, Female, n (%)	217 (77.0)	222 (78.7)
Ethnicity, Caucasian, n (%)	224 (80.6)	231 (83.1)
Completed Post Secondary Education, n (%)	209 (74.1)	220 (78.3)
Job Type, n (%)		
management, science, health and education	210 (74.7)	222 (78.7)
sales, services, arts and sports	54 (19.2)	42 (14.9)
transportation, trades	17 (6.0)	18 (6.4)
Arthritis Duration, Years, mean (SD)	10.62 (9.73)	9.31 (9.15)
Self Employed, n (%)	52 (18.5)	47 (16.7)
Joint Pain, NRS, mean (SD)	3.89 (2.38)	4.06 (2.71)
Disease Activity, RADAI, mean (SD)	3.66 (1.85)	3.70 (2.03)
Physical Function, HAQII, mean (SD)	0.72 (0.50)	0.74 (0.48)
Fatigue, NRS, mean (SD)	5.11 (2.53)	5.27 (2.70)

Table 2. Beta binomial logistic regression model estimating the effect of the intervention on absenteeism

	Univariate Model (N=532)		Multivariable Model (N=525)	
Outcomes	**Odds Ratio (95%CI)**	**P values**	**Odds Ratio (95%CI)**	**P values**
Sick Days per 100 workable days	0.79 (0.63, 0.97)	0.028	0.76 (0.61, 0.95)	0.014
Work Interruptions > 2 months per 100 days of follow-up	0.70 (0.47, 1.02)	0.064	0.7 (0.46, 1.06)	0.09
Combined per 100 days of follow-up	0.74 (0.6, 0.91)	0.004	0.73 (0.59, 0.91)	0.005

Participants were randomized 1:1 to MIW or usual care plus printed material on workplace tips. MIW consists of five online self-learning modules and group meetings, and individual vocational counselling and ergonomic assessments. Questionnaires were administered every 6 months. Outcomes were 1) number of sick days (occasional days missed from work and sick leaves shorter than 2 months duration), calculated as a rate per 100 workable days; 2) work interruptions greater than 2 months duration, calculated per 100 days of follow-up, and 3) the combined outcome (sum of sick days taken and work interruptions of any duration, calculated per 100 days of follow-up. Intention-to-treat analysis using Beta-binomial logistic regression models were used to evaluate the intervention effects on the three absenteeism outcomes, in separate analyses, accounting for the potential overdispersion in binomial outcomes. Odds ratios (OR) representing the intervention's effect on the daily risk of each absenteeism outcome, adjusting for baseline characteristics [age, sex, education, ethnicity, job type, RA duration, pain, disease activity (RADAI), fatigue, and physical function (HAQII)], 95% confidence intervals and Wald-tests were computed using robust standard errors accounting for potential model mis-specifications. Analyses were conducted using STATA 16.

Results: A total of 564 participants were recruited, with 85% completing 2-year follow-up. Baseline characteristics were similar between groups (Table 1). Mean (SD) number of sick days were 2.7 (4.6) and 2.3 (4.3) per 100 workable days, for controls and MIW, respectively; and mean (SD) number of days of work interruptions were 10.5 (22) and 8.8 (21.2) per 100 days of follow-up, respectively. The intervention group had a 21% lower odds of taking sick days from work (p=0.028), a 30% lower odds of work interruptions (p=0.064), and a 26% lower odds of the combined outcome (sick days and work interruptions) (p=0.004) (Table 2).

Conclusion: Results of the RCT reveal that the program was effective at improving absenteeism by decreasing the odds of sick days, and work interruptions, although the latter was of borderline statistical significance. Effectiveness at preventing long-term work disability will be assessed at 5 years. This program fills one of the most important unmet needs for people with inflammatory arthritis.

Disclosure: A. Luquini, None; **Y. Zheng**, None; **H. Xie**, None; **C. Backman**, None; **P. Rogers**, None; **A. Kwok**, None; **A. Knight**, None; **M. Gignac**, None; **D. Mosher**, None; **L. Li**, None; **J. Esdaile**, None; **C. Thorne**, AbbVie, 1, Amgen Inc, 1, Celgene, 1, Eli Lilly, 1, Medexus/Medac, 1, 2, 6, Merck, 1, 2, Novartis, 1, 5, Pfizer, 1, 5, Sandoz, 1, Sanofi, 1, Centocor, 2; **D. Lacaille**, None.

Abstract Number: 1927

Heterogeneity of Juvenile Idiopathic Arthritis Synovial Fibroblasts Correlates to Disease Progression and Provides Compelling Diagnostic Data

Megan Simonds[1], Kathleen Sullivan[2], Carlos Rose[3] and **AnneMarie Brescia**[4], [1]Nemours, Wilmington, DE, [2]The Children's Hospital of Philadelphia, Philadelphia, PA, [3]Thomas Jefferson University/duPont Hospital for Children, Wilmington, DE, [4]Nemours/A.I.duPont Hospital for Children, Wilmington, DE

SESSION INFORMATION

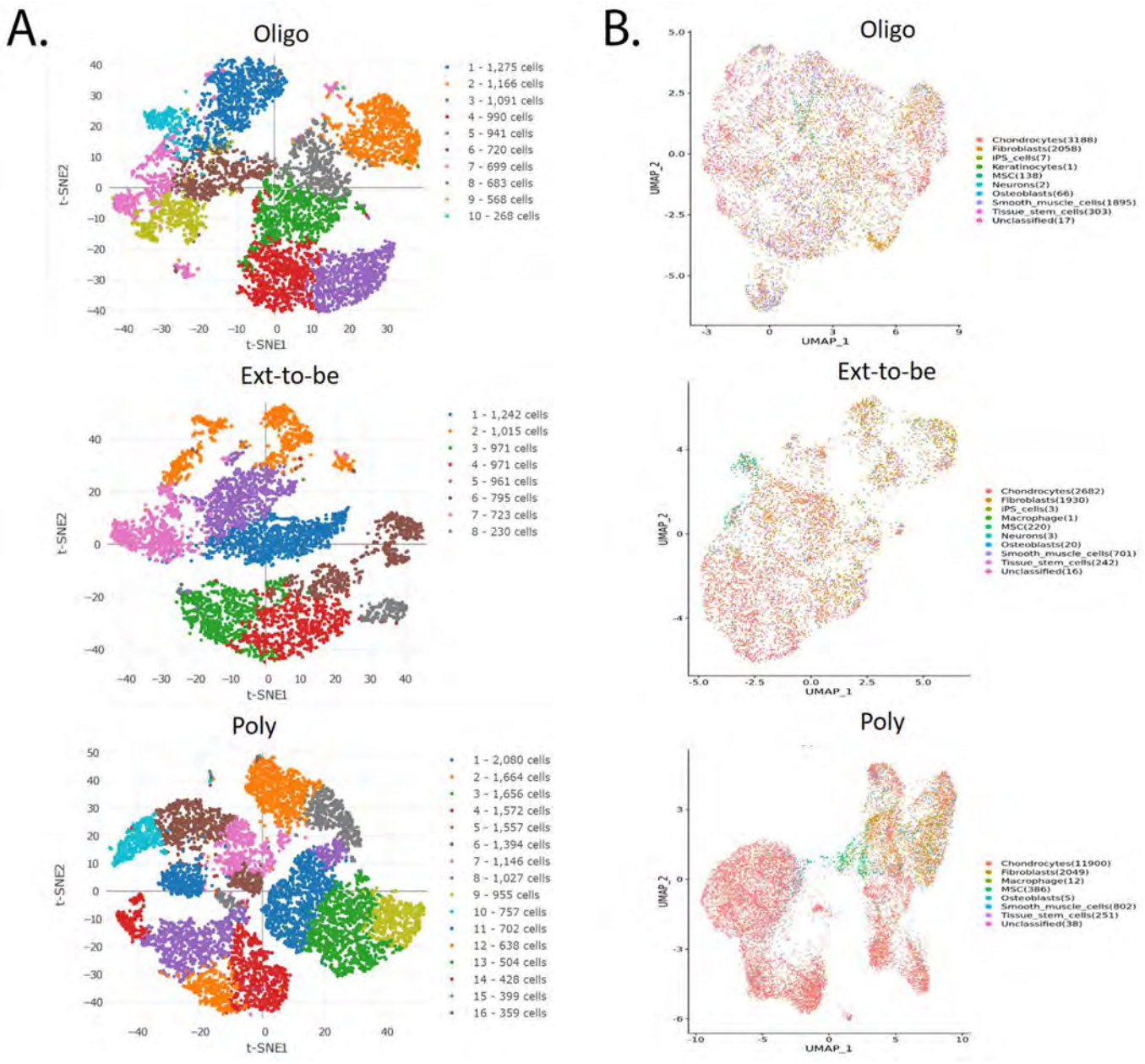
Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Pediatric Rheumatology – Basic Science (1927–1930)

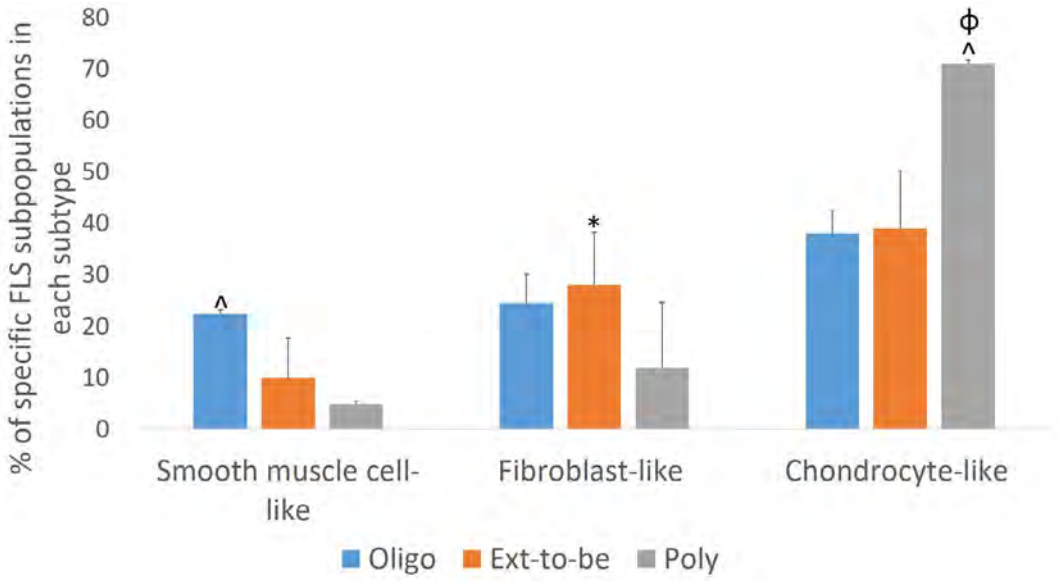
Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Juvenile Idiopathic Arthritis (JIA) induces growth disturbances in affected joints. Fibroblast-like synoviocytes (FLS) play a crucial role in JIA pathogenesis; however, the mechanisms by which they contribute to disease progression is not well described. Previous studies demonstrated that rheumatoid arthritis (RA) FLS are heterogeneous, and subpopulations with transformed, aggressive phenotypes cause invasive and destructive dis-



t-SNE (A) and UMAP (B) of FLS from patients with oligoarticular JIA who stayed persistent course (top row) or went on to an extended course (ETB, middle row) or with polyarticular JIA.

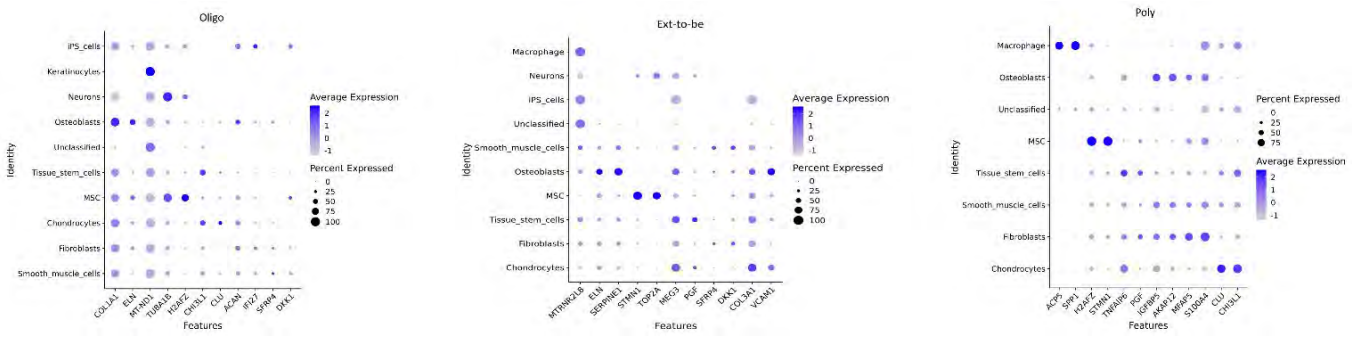


Percentage of FLS subpopulations in cultured FLS from patients with oligoarticular (Oligo), ETB, and polyarticular (Poly) JIA. Smooth muscle-like cells decrease in more severe subtypes of JIA. Percentage of fibroblast-like cells significantly increases in ETB compared to Oligo.

ease activity (1). Here, we employ single-cell RNA sequencing (scRNA-seq) to investigate JIA FLS heterogeneity and its' influence on disease extension.

Methods: JIA FLS cell lines from oligoarticular (oligo), extended-to-be (ETB), and polyarticular (poly) types were cultured. scRNA-seq was performed by Genewiz according to 10x Genomics Chromium protocols. Cell ranger software aggregated data from each patient to compare single-cell gene expressions within each JIA type. SeuratR package was used for QC, analysis, and exploration of data.

Results: Using t-Distributed Stochastic Neighbor Embedding (t-SNE), distinct clusters within each JIA FLS type illustrated heterogeneity (Figure 1A). Cells with similar expression patterns cluster together as indicated by a single color. Clusters in close proximity have similar gene expression profiles. Seurat performed Uniform Manifold Approximation and Projection (UMAP) dimensionality reduction, and the clusters co-localized. Majority of clusters within each type co-localize with greater distance between clusters within ETB and poly (Figure 1B). Cells were annotated based on similarity to a reference dataset of cells with known labels (Human Primary Cell Atlas Data) using SingleR data package. Subpopulation percentages were calculated from cell counts (Figure 2). Smooth muscle cell-like cells decreased in more severe JIA types ($p < 0.05$ in oligo v poly). Fibroblast-like cell percentage was higher in ETB than oligo ($p < 0.05$). Chondrocyte-like cells percentage increased in poly compared to oligo and ETB ($p < 0.05$). Differen-



Seurat single analysis identified the top features or genes of each projected cell type for each subtype. The dot plot shows the average expression of each feature in each cell type and the percent of cells that express that feature.

tially expressed genes were revealed within cell-type subpopulations between subtypes of JIA (Table 1). Specifically, ETB downregulate COL1A1 and ACAN and upregulate IFI27 and SERPINE1 in FLS-like cells when compared to oligo ($p< 0.00$). COL3A1 and VCAM were upregulated in chondrocyte-like cells in ETB when compared to oligo ($p< 0.00$).

Conclusion: Heterogeneity of FLS from JIA patients could present a novel JIA diagnostic tool. While single cells still co-localize by UMAP, known cell types were identified including: smooth muscle cell-like, fibroblast-like, and chondrocyte-like subpopulations. Differences in subpopulations composition in conjunction with differentially expressed genes within a subpopulation can contribute to distinguishing between subtypes of JIA. Specifically, predicting whether a patient will extend will allow clinicians to better determine therapeutic intervention.

1. Mizoguchi F, Slowikowski K, Wei K, Marshall JL, Rao DA, Chang SK, et al. Functionally distinct disease-associated fibroblast subsets in rheumatoid arthritis. Nature Communications. 2018;9(1):789.

Disclosure: M. Simonds, None; **K. Sullivan**, None; **C. Rose**, None; **A. Brescia**, None.

Abstract Number: 1928

In Vitro and *In Vivo* Evidence for DOCK8 as a Risk Allele for Cytokine Storm Syndrome, Including COVID-19 and MIS-C

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Pediatric Rheumatology – Basic Science (1927–1930)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Table. DOCK8 mutations identified in children and adults with various cytokine storm syndromes, including COVID-19 and MIS-C

#	Age (yrs)	Sex	Disease	Trigger	Mutation	Frequency
1	16	M	?	*Bartonella*	c.782C>T, p.Ala261Val	novel
2	19	M	T cell leukemia	?	c.54-1G>T (splice acceptor)	0.03%
3	24	M	Still disease	?	c.187G>A, p.Asp63Asn	12%
4	36	F	Polyarteritis nod.	*Streptococcus*	c.187G>A, p.Asp63Asn	12%
5	4	M	MIS-C	SARS-CoV-2	c.2695C>T, p.Arg899Trp	0.03%
6	16	F	MIS-C	SARS-CoV-2	c.4G>A, p.Ala2Thr	novel
7	10	M	MIS-C	SARS-CoV-2	c.2060C>T, p.Pro687Leu	0.04%
8	2	M	MIS-C	SARS-CoV-2	c.1193G>A, p.Arg398Gln	0.08%
9	13	M	HLA-B27+ IBD/JIA	Disease flare	c.4850A>G, p.Gln1617Arg	0.1%
10	47	M	COVID-19	SARS-CoV-2	c.1567G>A, p.Gly523Arg	novel
11	anakinra	trial	COVID-19	SARS-CoV-2	c.53+199C>G	0.2%
12	anakinra	trial	COVID-19	SARS-CoV-2	c.1249T>C, p.Phe417Leu	0.001%
13	anakinra	trial	COVID-19	SARS-CoV-2	c.3784C>G, p.Leu1262Val	0.09%
14	anakinra	trial	COVID-19	SARS-CoV-2	c.3815A>G, p.Try1272Cys	0.27%
15	19	F	MIS-C	SARS-CoV-2	c.3104A>T, p.Asp1005Val	0.01%
16	7	M	MIS-C	SARS-CoV-2	c.686C>A, p.Ala 229Asp	0.006%

Background/Purpose: Cytokine storm syndromes (CSS) are frequently fatal complications of a variety of oncologic, rheumatic, and infectious diseases. Many patients with CSS possess heterozygous missense mutations in genes related to the familial CSS, hemophagocytic lymphohistiocytosis (HLH). We recently identified missense mutations in a potentially novel CSS gene, *DOCK8*, among CSS patients. During the pandemic, we screened SARS-CoV-2 CSS patients (COVID-19 & MIS-C) for *DOCK8* mutations, and studied the role of *DOCK8* as a CSS gene using a murine model of HLH.

Methods: To date, 20 adult patients enrolled in a COVID-19 CSS clinical trial at UAB had whole genome sequencing. Four (20%) had rare heterozygous *DOCK8* mutations (3 missense, 1 intronic) (Table). *DOCK8* missense mutations were also identified in 6 children (UAB & Northwell) hospitalized with MIS-C (Table). *DOCK8* mutations, or wild-type (WT) sequence controls, were introduced into human NK-92 cells by FOAMY virus transduction. WT and mutant *DOCK8*-expressing NK-92 cells were incubated with K562 target cells and compared for cytolysis and degranulation (CD107a) by flow cytometry. *DOCK8* knock-out (KO) mice were compared to WT mice using an LCMV viral model of familial HLH (Jordan MB et al. *Blood* 2004;104:735). Following infection, mice were tracked for weight and changes in peripheral blood cell counts and cytokines as previously described (Rood JE et al. *Blood* 2016;127:426). After 8 days of infection, mice were euthanized and quantified for splenomegaly (weight) and liver pathology (scored by microscopy). Appropriate statistical approaches were employed for comparing nominal and ordinal data sets, respectively.

Results: Introduction of all *DOCK8* missense mutations (from COVID-19 adults and children with MIS-C) into NK-92 cells resulted in diminished NK cell cytolysis and degranulation (Figure 1). In comparison to WT mice, *DOCK8* KO mice displayed increased splenomegaly and prolonged weight loss (Figure 2). In addition, thrombocytopenia was statistically significantly pronounced in the *DOCK8* KO mice, as was increased serum interferon-gamma (Figure 2). Histopathology revealed statistically significant liver endothelial cell activation in the *DOCK8* KO mice (Figure 2).

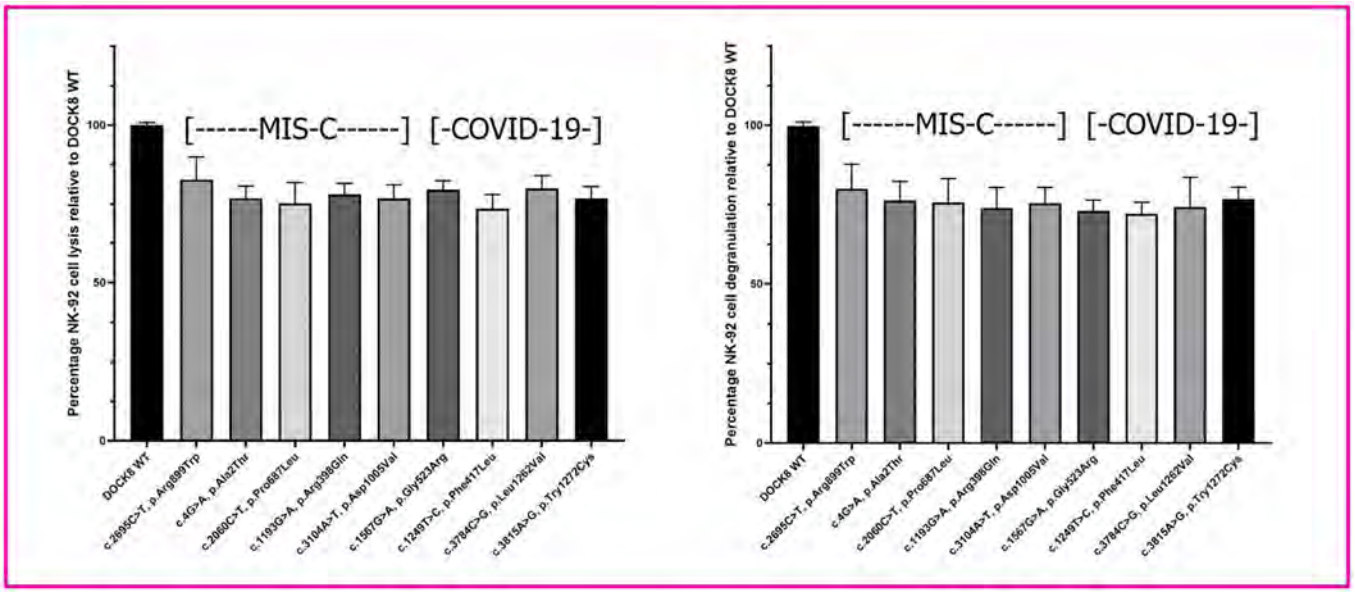

Figure 1. Functional analyses of DOCK8 patient mutations. Human NK-92 natural killer cells were infected with FOAMY viruses expressing DOCK8 wild-type (WT) or patient missense mutations. NK-92 cells were sorted by flow cytometry based on co-expression of green fluorescent protein. LEFT: NK-92 cell lytic activity versus K562 target cells was assessed for each patient DOCK8 missense mutation and compared to control (WT). Mean percentages +/- SEM are presented relative to WT (n=3). RIGHT: Degranulation of NK-92 cells stimulated by incubation with K562 target cells was assessed for each patient DOCK8 missense mutation by detection of cell surface CD107a by flow cytometry in comparison to WT control. Mean percentages +/- SEM are presented relative to WT (n=3). Studies were conducted as previously detailed (Zhang M et al. J. Immunol. 2016;196:2492).

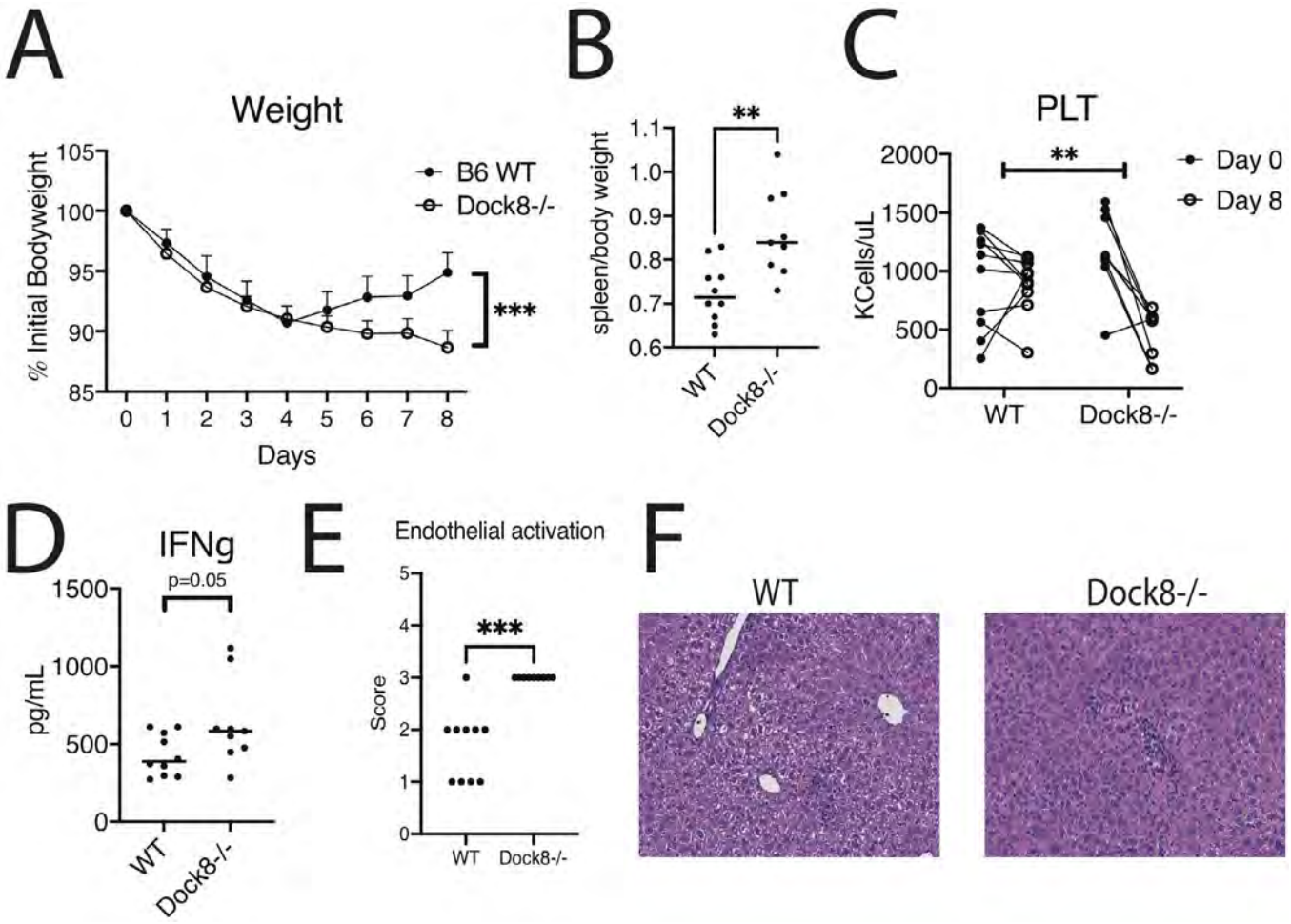

Figure 2. LCMV infection model of cytokine storm syndrome in DOCK8 deficient mice. Wild-type (WT) or DOCK8-/- mice were infected with LCMV as described (Rood JE et al. Blood 2016;127:426). A. Daily body weight as a percentage of initial body weight is graphed for B6 WT (closed circles) and DOCK8-/- (open circles) with means + SEM (n=9 per group). B. Splenomegaly was assessed by spleen weight after euthanization 8 days post-infection (n=9 per group). C. Platelet counts were assessed prior to (closed circles) and 8 days post-infection (open circles) for WT (left) and DOCK8-/- mice (right) (n=8 per group). D. Serum interferon-gamma levels were assessed at day 8 post-infection for WT and DOCK8-/- animals (n=10 per group). E. Endothelial cell activation was assessed by a pathology based scoring system for WT and DOCK8-/- mice (n=10 per group). F. Representative H&E stains of liver pathologic specimens for WT (left) and DOCK8-/- (right) mice 8 days after infection.

Conclusion: *DOCK8* partial dominant-negative missense mutations are present in CSS patients with COVID-19 and MIS-C and likely are risk factors for CSS development. A murine familial HLH model demonstrates a requirement for the presence of *DOCK8* to prevent a hyper-inflammatory CSS-like disease state.

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Abstract Number: 1929

Metabolomics Identifies Early Mechanisms of Atherogenic Dyslipidaemia in Juvenile-SLE Patients Associated with Inflammation

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Pediatric Rheumatology – Basic Science (1927–1930)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Cardiovascular disease (CVD) is a leading cause of mortality in patients with juvenile-onset systemic lupus erythematosus (JSLE) through atherosclerosis, the build-up of lipids and inflammation in the sub-endothelial intimal layer of medium-sized to large arteries. Our findings in adult-onset SLE link immune cell dysregulation with dyslipidaemia, however, little is known about the immune profile or whether dyslipidaemia contributes to inflammation and atherosclerosis in JSLE.

Methods: Serum NMR metabolomics (130 lipid measures), proteomics (Proximity Extension Assay) and anti-high density lipoprotein(HDL) antibody (ELISA) analysis was performed on a cohort of JSLE patients (n=65, median age 19, 22 active, 43 inactive by SLE Disease Activity Index, SLEDAI) and healthy controls (HCs, n=32, median age=19). Data was analysed using balanced random forest (BRF) machine learning with 10-fold cross-validation and logistic regression (adjusted for demographic characteristics) and linear regression analysis correlating features with measures of disease activity. Flow cytometry evaluated the activation (CD69 and HLA-DR) and inflammatory lipid profile (lipid raft signalling platforms enriched in glycosphingolipids and cholesterol) of immune subsets.

Results: The BRF machine learning model could predict JSLE patients from HCs with a 76% accuracy based on all 130 serum lipid measures with the most important variables being a lower expression of atheroprotective small and medium HDL subsets in JSLE compared to HCs. In support, linear and logistic regression analysis of serum lipids identified atherogenic dyslipidaemia in JSLE patients compared to HCs exacerbated by active disease and altered liver function. Specifically, patients with active disease had significantly increased atherogenic very-low, intermediate and low density lipoproteins (VLDL, IDL and LDL) and decreased atheroprotective HDL compared to patients with low disease activity and HC's. Strikingly, HDL levels correlated negatively with anti-HDL antibodies ($r=-0.49$, $p=0.012$) and atherogenic lipoproteins correlated positively with T-cell and B-cell lipid rafts and activation markers. In addition, lymphocyte culture with serum isolated from JSLE patients with active disease induced a significant increase in cellular cholesterol and activation markers compared to serum isolated from patients with low disease activity and HC's. Finally, JSLE patients had increased serum levels of ICAM1 ($p=0.013$), VCAM1 ($p=0.007$) and lipoprotein lipase ($p=0.028$) compared to HCs, suggesting increased vascular inflammatory cell recruitment and atherogenic lipoprotein conversion in JSLE respectively.

Conclusion: Multi-omic analysis identified potential early mechanisms of dyslipidaemia in JSLE patients associated with inflammation and atherosclerosis. This could help to inform early lipid targeted therapies in JSLE to improve cardiovascular outcomes and quality of life for patients.

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Abstract Number: 1930

Single-Cell Genomics Reveals a Shared Monocyte Interferon Program in a Subset of Patients with Systemic Juvenile Idiopathic Arthritis, Macrophage Activation Syndrome and Lung Disease

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Session Type: Abstract Session
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Background/Purpose: Systemic juvenile idiopathic arthritis (SJIA) is a clinically heterogenous disease and can be complicated by macrophage activation syndrome (MAS) and lung disease (LD) thought to be driven by interferon signaling, though the contributing cell populations and distinctions between IFNγ and IFNα/β are undefined. To identify novel prognostic transcripts and potential patient subtypes, we aimed to characterize single-cell heterogeneity and patient-specific transcriptomics responses from the peripheral blood of children with SJIA, MAS and LD.

Methods: 10x Genomics single-cell RNA Sequencing (scRNA-Seq) was performed on PBMCs from 7 active SJIA and 5 inactive SJIA patients, 2 SJIA-MAS and 6 SJIA-LD patients and 5 healthy controls. Integration analyses were performed with the software Seurat 3 to identify discrete cell populations while correcting for donor and disease-level differences. To identify subsets of patients with cell-type specific signatures, we developed a new hybrid supervised/unsupervised computational pipeline in the software AltAnalyze, called cellHarmony 2.0, designed specifically for large cohort single-cell genomic studies.

Results: scRNA-Seq analysis was performed on a total of 234,128 individual cells (ranging from 6,662-12,647 cells/patient), with a mean number of 21,637 genes detected per sample. To assess cell-population level differences, we identified and annotated based on marker genes 34 discrete cell populations across all submitted samples. This indicated a consistent increase in Natural Killer (NK) cells and decrease in naïve and regulatory T cells in SJIA-LD, with the distribution of cells from inactive SJIA patients similar to that of controls. To exploit anticipated heterogeneity within this cohort, we applied our new cell-type aware patient subtype discovery algorithm cellHarmony 2.0. We computed an aggregate cell signature for all cell populations or pseudo-bulks (n=34) for each patient and their associated fold differences relative to matched control cell clusters, and performed unsupervised clustering of the pseudo-bulks to identify patient subtypes associated within one or more cell types. This analysis uncovered 11 pseudo-clusters of cell type gene expression differences, both shared and unique across the patients. Specifically, pseudo-cluster 4 was defined by IL-2 mediated signaling genes, composed of mostly NK cells from all SJIA subtypes except MAS. SJIA-MAS PBMCs were almost exclusively represented in three separate pseudo-clusters that contained genes mediating T-cell receptor activation, immune response and interferon signaling. Finally, pseudo-cluster 8 was composed of mainly monocytes/macrophages with specific upregulation of IFNα/β induced genes IFITM3, IFI6 and ISG15, only in active SJIA, SJIA-MAS and SJIA-LD.

Conclusion: Unsupervised single-cell cohort analysis provides new opportunities to uncover novel disease molecular programs and pathways in clinically heterogenous patient groups. Here, we found active SJIA, SJIA-MAS and SJIA-

LD PBMCs have distinct monocytic responses characterized by upregulation of interferon-induced genes, highlighting the role for both IFNγ and IFNα/β in driving disease pathogenesis.

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Abstract Number: 1931

The Burden of Thirty-day Readmission and Independent Predictors of Readmission in Patients with Systemic Lupus Erythematosus: A Nationwide Analysis

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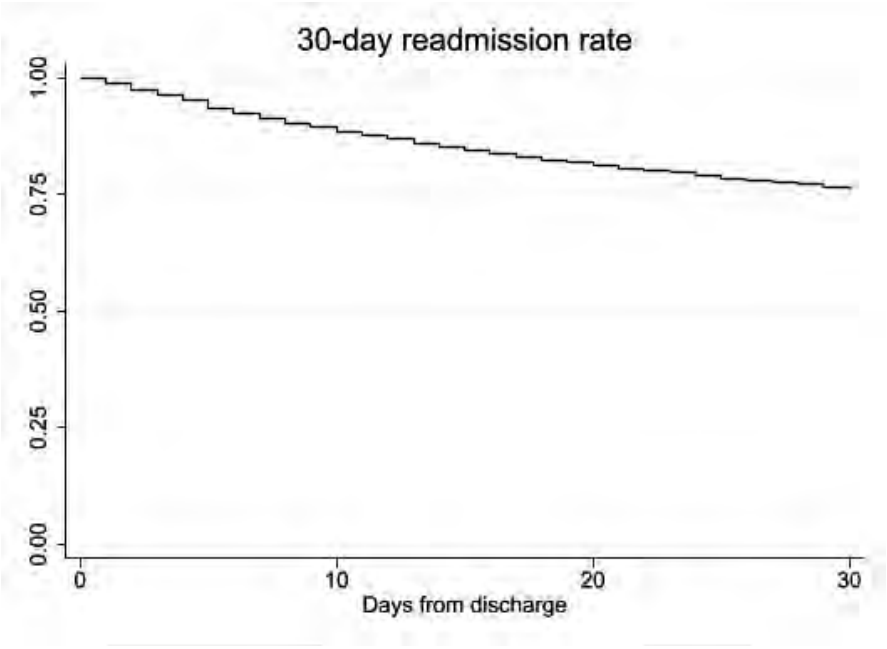
SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Predictors & Longitudinal Outcomes (1931–1934)
Session Type: Abstract Session
Session Time: 3:30PM–4:30PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic immune-mediated disease with 20-25% patients needing hospital admission annually. Early readmissions add to the clinical and economic burden on the healthcare system. Strategies to reduce readmission are now a crucial aspect of management. Therefore, we conducted this study to investigate the outcomes and predictors of 30-day readmission in patients with SLE.

Methods: We queried the 2017 Nationwide Readmission Database (NRD) using ICD-10-CM diagnosis codes to identify all patients admitted with a primary diagnosis of SLE. Outcomes assessed were 30-day readmission rates, mortality, length of stay (LOS) and hospitalization costs. A multivariate cox regression was done to obtain Hazard Ratio (HR) and identify independent predictors of readmission. Statistical analysis was performed using STATA software.

Results: A total of 8,664 adult patients were admitted with a primary diagnosis of SLE in 2017, with in-hospital mortality rate of 0.87%. Of the patients discharged, 23.72% patients were readmitted within 30-days. The most common primary diagnosis at readmission was “Systemic lupus erythematosus, unspecified” (12.99%). When compared to index admission, readmitted patients had higher in-hospital mortality (3.16% vs 0.87%, $p< 0.01$), longer mean LOS (7.05 days vs 6.4 days, $p< 0.05$) and higher mean hospitalization charges ($76,055 vs $68,087, $p< 0.01$). Readmissions added 14,427 inpatient days and $36 million in hospitalization cost to the healthcare burden. Higher Charlson comorbidity score (HR 1.08, $p< 0.01$), CHF (HR 1.36, $p< 0.01$), AKI (HR 1.24, $p< 0.01$), CKD (HR 1.32, $p< 0.01$), ESRD (HR 1.29, $p< 0.01$), and discharge other than home discharge (HR 1.36, $p< 0.01$) were independently associated with increased likelihood of 30-day readmission.

Conclusion: We performed a comprehensive assessment of patients admitted with SLE with the national inpatient data using the newer specific ICD-10 codes. In the US, about 1 in 4 patients with SLE are readmitted within 30-days of discharge. Readmission is associated with significantly increased in-hospital mortality, LOS, and hospitalization costs. 30-day readmissions resulted in an increased burden to healthcare resource utilization, adding considerable in-patient stay days and hospitalization costs. Patients with AKI, CHF, CKD, ESRD, discharge other than home discharge and higher comorbidity burden were significantly more likely to be readmitted within 30-days. Further



KM graph of 30-day readmission.

prospective studies are needed to assess the high-risk populations to reduce early readmission and improve value-based care.

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Abstract Number: 1932

Identifying Clusters of Longitudinal Autoantibody Profiles Associated with Systemic Lupus Erythematosus Disease Outcomes

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Predictors & Longitudinal Outcomes (1931–1934)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Prior studies of SLE clusters based on autoantibodies have utilized cross-sectional data from single centers. We applied clustering techniques to longitudinal and comprehensive autoantibody data from a large multinational, multi-ethnic inception cohort of well characterized SLE patients to identify clusters associated with disease outcomes.

Table 1. Demographic and clinical characteristics that were statistically significant[1] at baseline and five-year follow-up between the four SLE longitudinal autoantibody clusters

	Group 1 (n=137)	Group 2 (n=171)	Group 3 (n=71)	Group 4 (n=212)	P-value	FDR
Enrolment Demographics						
Mean Age of Diagnosis (SD), yrs	32.0 (10.8)	36.9 (13.9)	32.9 (14.0)	34.9 (14.0)	0.003	0.003
% Ethnicity						
White	32	62	68	43	<0.001	<0.001
Asian	31	20	14	31	0.001	0.004
African	27	10	6	15	<0.001	<0.001
Mean BMI (SD), kg/m^2	25.5 (6.1)	26.4 (6.6)	26.9 (6.9)	24.9 (5.4)	0.015	0.041
% Former smoker	17	23	28	12	0.002	0.005
Clinical Characteristics at Year 5 Follow-Up						
% Nephritis[2]	42	30	46	42	0.028	0.009
Mean SLEDAI-2K Score (SD)						
Total Score[3]	4.3 (4.5)	2.3 (3.3)	3.0 (3.1)	3.6 (3.2)	<0.001	<0.001
Adjusted Mean Score[4]	4.3 (3.1)	2.9 (2.5)	3.7 (2.2)	4.1 (2.6)	<0.001	<0.001
Hematological Subscale	0.16 (0.39)	0.06 (0.23)	0.06 (0.25)	0.11 (0.31)	0.003	0.008
Immunological Subscale	1.7 (1.69)	0.82 (1.30)	1.82 (1.54)	2.12 (1.62)	<0.001	<0.001
Low Complement	0.82 (0.99)	0.43 (0.82)	1.01 (1.01)	1.03 (1.00)	<0.001	<0.001
Mucocutaneous Subscale	0.83 (1.98)	0.33 (0.87)	0.20 (0.69)	0.37 (0.97)	<0.001	<0.001
Mean SLICC Damage Index (SD)						
Neuropsychiatric Domain	0.11 (0.40)	0.16 (0.52)	0.32 (0.82)	0.08 (0.32)	0.003	0.009
Cerebrovascular accident	0.02 (0.15)	0.04 (0.22)	0.14 (0.45)	0.04 (0.19)	0.002	0.007
Seizures	0.01 (0.12)	0.03 (0.16)	0.08 (0.27)	<0.01(0.07)	0.004	0.012
Skin Domain	0.15 (0.42)	0.07 (0.29)	0.03 (0.16)	0.07 (0.28)	0.011	0.030
Alopecia	0.11 (0.31)	0.04 (0.20)	0.01 (0.11)	0.04 (0.19)	0.002	0.007
Medications Ever						
% Immunosuppressives/ Biologics	79	60	61	72	<0.001	<0.001
% Imuran	51	31	41	41	<0.001	<0.001
% Mycophenolic Acid	34	21	18	25	0.014	0.039
Medications Current						
% Immunosuppressives/ Biologics	62	45	48	55	0.004	0.012

1.Comparison between cluster groups using one-way ANOVA test and a Benjamini-Hochberg correction with false discovery rate (FDR) alpha = 0.05
2.Lupus nephritis was diagnosed by renal biopsy or fulfillment of the renal item on the ACR classification criteria.
3.The total score of SLEDAI-2K is the sum of all 24 descriptor scores. The total SLEDAI-2K score falls between 0 and 105, with higher scores representing higher disease activity.
4.A measurement of lupus disease activity over time determined by the calculation of the area under the curve of SLEDAI-2K over time by adding the area of each of the blocks of visit interval and then dividing by the length of time for the whole period.
Abbreviations: BMI, body mass index; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC, Systemic Lupus International Collaborating Clinics; yrs, years.

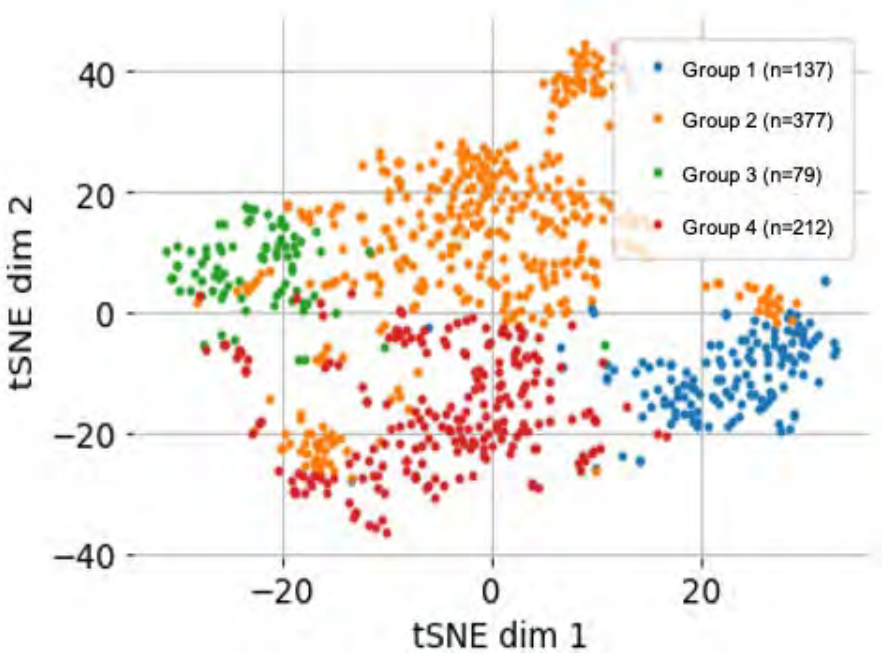

Figure 1. Four autoantibody cluster groups identified among 805 SLE patients followed from enrolment through years 3 and 5. Latent space visualized using a t-distributed stochastic neighbor embedding (t-SNE) with colors based on cluster labels.

Methods: We used demographic, clinical, and serological data at enrolment and follow-up visits years 3 and 5 from 805 patients who fulfilled the 1997 Updated ACR SLE Classification Criteria and were enrolled within 15 months of diagnosis. For each visit, ANA (HEp-2 indirect immunofluorescence assay), dsDNA, Sm, U1-RNP, SSA/Ro60, SSB/La, Ro52/TRIM21, histones, ribosomal P, Jo-1, centromere B, PCNA, antiphospholipid antibodies (IgG and IgM for anticardiolipin, anti–β2GP1, and aPS/PT, lupus anticoagulant (LAC), and IgG anti-β2GP1 D1), and anti-dense-fine speckled 70 were performed at a single lab (except LAC). K-means clustering algorithm on principal component analysis (10 dimensions) transformed longitudinal ANA and autoantibody profiles was used. We compared cluster demographic and clinical outcomes, including longitudinal disease activity (total and adjusted mean SLEDAI-2K [AMS]), SLICC/ACR damage index and organ-specific domains, SLE therapies and survival, using one-way ANOVA test and a Benjamini-Hochberg correction with false discovery rate alpha = 0.05. Results were visualized using t-distributed stochastic neighbor embedding (t-SNE).

Results: Four unique patient clusters were identified (**Table 1, Figure 1**). Cluster 1 (n=137), characterized by high frequency of anti-Sm and anti-RNP antibodies over time, was the youngest group at disease onset with a high proportion of subjects of Asian and African ancestry. At year 5, they had the highest disease activity (total SLEDAI-2K 4.3 [4.5] and AMS 4.3 [3.1]), were more likely to have active hematologic and mucocutaneous involvement, and to be on/exposed to immunosuppressants/biologics. Cluster 2 (n=377), the largest cluster, had low frequency of anti-dsDNA, were oldest at disease onset, and at year 5, had the lowest disease activity (total SLEDAI-2K 2.3 [3.3] and AMS 2.9 [2.5]), and were less likely to have nephritis and be on/exposed to immunosuppressants/biologics. Cluster 3 (n=79) had the highest frequency of antiphospholipid antibodies over time (**Figure 2**), were more likely to be of European ancestry, have an elevated body mass index, be former smokers, and by year 5, to have nephritis, neuropsychiatric involvement, including strokes and seizures (SLICC/ACR damage index). Cluster 4 (n=212) was characterized by anti-SSA/Ro60, SSB/La, Ro52/TRIM21, and histone antibodies, and active immunologic involvement (low complements) at year 5. Overall, survival of the 805 subjects was 94% at 5 years, and none of the clusters predicted survival.

Conclusion: Four SLE patient clusters associated with disease activity, organ involvement, and treatment were identified in this analysis of longitudinal ANA and autoantibody profiles in relation to SLE outcomes, suggesting these

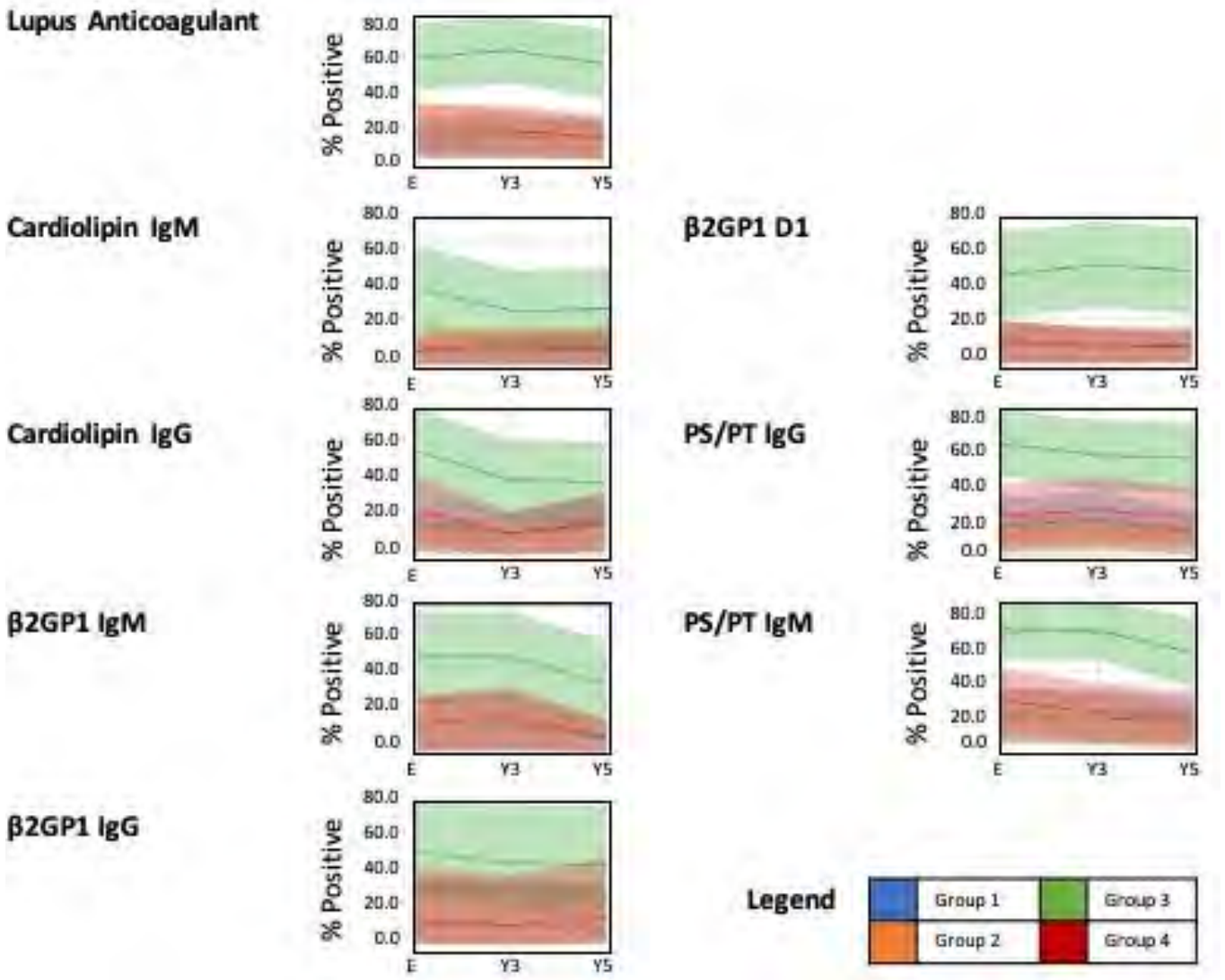

Figure 2. Antiphospholipid antibodies of the four cluster groups over time (E=enrolment, Y3=year 3, Y5=year 5). Group 3 had the highest frequency of antiphospholipid antibodies, including lupus anticoagulant, IgG and IgM anticardiolipin, IgG and IgM anti–β2-glycoprotein-1 (β2GP1), IgG anti-β2GP1 Domain 1 (D1), IgG and IgM antiphosphatidylserine/prothrombin (aPS/PT), over time compared to the other three clusters. Other connective tissue disease autoantibodies not shown. Line indicates the mean, shading indicates the standard deviation.

SLE subsets might be identifiable based on extended autoantibody profiles early in the disease and carry prognostic information.

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Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Celgene, 2, 5, Bristol Myers Squibb, 2, 5; **I. Bruce**, None; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **E. Ginzler**, None; **M. Dooley**, None; **R. Ramsey-Goldman**, None; **S. Manzi**, Astra Zenecs, 2, 5, Cugene, 2, Eli Lilly, 2, Exagen, 2, 5, 10, UCB, 2, GSK, 2; **A. Jnsen**, None; **G. Alarcn**, None; **R. van Vollenhoven**, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, UCB, 2, 5, 6, Pfizer, 2, 6, 12, Support for educational programs; institutional grants, Roche, 12, Support for educational programs; institutional grants, Janssen, 2, 6, AbbVie, 2, 6, AstraZeneca, 2, Biotest, 2, GlaxoSmithKline, 2, 6, Biogen, 2, Galapagos, 2, 6, Gilead, 2, Sanofi, 2, Servier, 2, Vielabio, 2; **C. Aranow**, GlaxoSmithKline, 2, 5; **M. Mackay**, None; **G. Ruiz-Irastorza**, None; **S. Lim**, Bristol Myers Squibb, 5, GlaxoSmithKline, 2, ACR, 4, AstraZeneca, 5, Pfizer, 2, UCB, 2; **M. Inanc**, None; **K. Kalunian**, Amgen, 2, AbbVie, 2, AstraZeneca, 2, Biogen, 2, Bristol Myers Squibb, 2, Eli Lilly, 2, Equillium, 2, Genentech/Roche, 2, Gilead, 2, Janssen, 2, Lupus Research, 5, Pfizer, 5, Sanford Consortium, 5, Vielabio, 2, Aurinia, 2, Alliance, 2, Nektar, 2; **S. Jacobsen**, None; **C. Peschken**, AstraZeneca, 2, GlaxoSmithKline, 2, Eli Lilly, 2; **D. Kamen**, None; **A. Askanase**, GSK, 2, 5, AstraZeneca, 1, 5, Amgen, 1, Aurinia, 2, Abbvie, 1, Pfizer, 5, Eli Lilly, 5, Idorsia, 5; **D. Sontag**, CurAI, 2, GNS Healthcare, 2, ASAPP, 3; **K. Costenbader**, Neutrolis, 11, Merck, Exagen, Gilead, 5, Astra Zeneca, Neutrolis, 2.

Abstract Number: 1933

Association Between Race/Ethnicity and COVID-19 Outcomes in Systemic Lupus Erythematosus (SLE) in United States Patients: Data from the COVID-19 Global Rheumatology Alliance

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Predictors & Longitudinal Outcomes (1931–1934)

Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Table: Characteristics associated with poor COVID-19 outcomes among individuals with SLE.*

	OR (95% CI)
Age (continuous)	1.02 (1.00, 1.04)
Gender	
Female	Ref
Male	1.57 (0.76, 3.24)
Race/Ethnicity	
White	Ref
African American	2.18 (1.07, 4.31)
Hispanic	2.14 (1.07, 4.31)
Other	0.76 (0.21, 2.79)
Time Period	
<=June 15, 2020	Ref
June 16-Sept 30, 2020	0.80 (0.36, 1.77)
Oct 1, 2020- April 12,2021	0.39 (0.21, 0.72)
Glucocorticoid Dose	
0 mg/day	
0-5 mg/day	1.14 (0.61, 2.12)
5-10 mg/day	7.33 (1.96, 27.40)
=>10 mg/day	2.61 (1.33, 5.13)
Medication Category	
Antimalarial only	Ref
No SLE treatment	2.33 (0.99, 5.49)
Other IS drugs as monotherapy (MMF, tacrolimus, cyclophosphamide, cyclosporine, azathioprine, methotrexate, leflunomide, sulfasalazine only)	1.77 (0.92, 3.43)
b/ts IS only	1.76 (0.51, 6.04)
b/ts IS + csIS combo	2.25 (1.02, 4.99)
Number of Comorbidities (Not Including Renal, Cardiovascular, or Hypertension)	1.44 (0.92, 2.25)
Chronic renal insufficiency or end stage renal disease	2.61 (1.35, 5.04)
Cardiovascular/Hypertension	1.24 (0.73, 2.11)
Disease Activity	
Remission	Ref
Minimal or low	1.07 (0.56, 2.05)
Moderate	1.74 (0.77, 3.92)
Severe or high	0.47 (0.09, 2.35)

IS: immunosuppressive; b/ts: biologics/target synthetic; OR: Odd ratio; CI: confidence interval

*The ordinal outcomes was: 1 not hospitalized, 2 hospitalized without supplementary oxygen or with non-invasive ventilation, 3 hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 4 death. This assumed that the relationship between each pair of outcome groups is of the same direction and magnitude.

Background/Purpose: Hispanic and African American race/ethnicities have been associated with poor COVID-19 outcomes in the general population and in rheumatic disease patients within the COVID-19 Global Rheumatology Alliance (GRA); however, such associations within SLE patients have not been evaluated. The aim of this study is to determine the association between race/ethnicity and COVID-19 outcomes in SLE patients from the US.

Methods: US SLE patients from the COVID-19 GRA enrolled between March 24th 2020 and April 12th 2021 were studied. Variables included were age, gender, race/ethnicity (White, African American, Hispanic and others), comorbidities (chronic renal disease, cardiovascular disease, and the number of other comorbidities), disease activity (remission, low, moderate, high), time period, glucocorticoid dose, antimalarials and immunosuppressive (IS) drug use. Drugs were categorized into five groups: antimalarials only (reference), no SLE therapy, classic IS drugs monotherapy, biologics/target synthetic IS drugs, and combination therapy. The ordinal outcome categories were: 1. hospitalized without supplementary oxygen and/or not hospitalized, 2. hospitalized with non-invasive ventilation, 3. hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 4. death. We constructed ordinal logistic regression models evaluating the relationship between COVID-19 severity and race/ethnicity, adjusting for possible confounders.

Results: Five-hundred and four patients were included; 458 (90.9%) were women and the median age was 46.8 (SD: 13.9) years. Four hundred and three (80.0%) patients were not hospitalized; 36 (7.1%) patients were hospitalized without oxygen or with non-invasive ventilation, 49 (9.7%) patients were hospitalized with mechanical ventilation/extracorporeal membrane oxygenation and 16 (3.2%) died. In a multivariable model, African American [OR=2.18 (1.07-4.31)] and Hispanic [OR=2.14 (1.07-4.31)] race/ethnicities were associated with poorer outcomes. Additionally, prednisone-equivalent doses between 5-10 mg/d [OR=7.33 (1.96-27.40)] and >10 mg/d [OR=2.61 (1.33-5.13)], IS drugs (combinations) [OR =2.25 (1.02, 4.99)] and chronic renal disease [OR =2.61 (1.35, 5.04)] were associated with more severe COVID-19 outcomes. COVID-19 diagnosis between October and April 2021 vs. earlier time periods [OR=0.39 (0.21-0.72)] was associated with less severe COVID-19 outcomes (Table 1).

Conclusion: African American and Hispanic individuals with SLE experienced more severe COVID-19 outcomes, which is consistent with findings in the US general population. These results likely reflect socioeconomic and health disparities and suggest that more aggressive efforts are needed to prevent infection in this population.

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Abstract Number: 1934

Intra-Individual Change in Cognitive Function Among Adults with Systemic Lupus Erythematosus: A Markov Analysis over 7 Years

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: SLE – Diagnosis, Manifestations, & Outcomes II: Predictors & Longitudinal Outcomes (1931–1934)

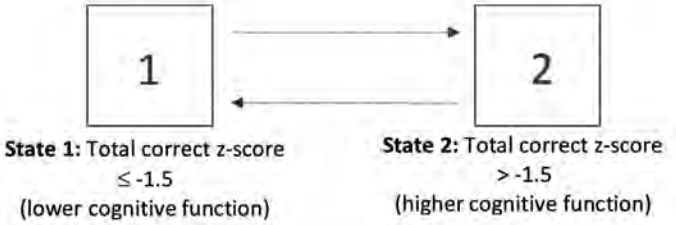
Session Type: Abstract Session

Session Time: 3:30PM–4:30PM

Background/Purpose: Cognitive impairment is a prevalent neuropsychiatric manifestation of SLE. Studies have primarily focused on the prevalence of cognitive impairment cross-sectionally; however, there remain gaps in understanding how SLE affects patients' cognition longitudinally and more importantly at the intra-individual level. We studied if and how cognitive function changes in SLE on repeated assessments (intra-individual change) and examined what factors influence cognitive change.

Methods: Data was drawn from a single centre longitudinal study that followed 1281 patients with SLE using annual telephone interviews. The Hopkins Verbal Learning Test-Revised (HVTL-R-verbal learning and memory) and the Controlled Oral Word Association Test (COWAT-verbal fluency) were the measures of cognition. The Systemic Lupus Activity Questionnaire (SLAQ) and Center of Epidemiologic Studies Depression Scale (CES-D) were used to assess disease severity and depressive symptoms respectively. A two-state Markov Analysis was used to model probabilities of transition between cognitive states: lower cognitive function [Z score ≤ -1.5] and higher cognitive function [Z score > -1.5] (**Figure 1**). Logistic regression analyses were used to examine what factors were associated with cognitive change.

Results: Most SLE patients demonstrated stability in cognition overtime. However, among those with change as assessed by the COWAT, individuals with SLE were 18 times more likely to improve in cognition than to experience cognitive decline over time (Improvement Intensity of 0.91 vs. Decline Intensity of 0.05). Higher levels of depressive



Transition To		State 1	State 2
Transition From	State 1	No Change	Cognitive Improvement
	State 2	Cognitive Decline	No Change

Figure 1. Two-state reversible Markov model for HVLT-R & COWAT to model the probabilities of transition between cognitive states.

Table 1. Multi-state regression model with COWAT

	Multivariate Regression Analysis Using COWAT Z-scores			
Cognitive Transition States	Covariate	RR	95% CI	*p*
1→2 (improvement in cognition)	Age: Per 1 Year	0.99	(0.98, 1.01)	0.52
	Education: Level 3-6 vs. Level 1-2	1.55	(0.94, 2.57)	0.09
	Steroids IV: Yes vs. No	0.95	(0.53, 1.68)	0.85
	SLAQ Score: Per 1 unit	1.01	(0.98, 1.04)	0.52
	CESD Score: Per 1 Unit	0.98	(0.96, 0.99)	0.02*
2→1 (decrease in cognition	Age: Per 1 Year	0.99	(0.97, 1.01)	0.54
	Education: Level 3-6 vs. Level 1-2	0.65	(0.36, 1.87)	0.15
	Steroids IV: Yes vs. No	1.24	(0.60, 2.55)	0.56
	SLAQ Score: Per 1 unit	1.05	(1.02, 1.09)	0.01*
	CESD Score: Per 1 Unit	1.00	(0.97, 1.02)	0.81

All models were adjusted for age; included assessments had complete covariates (number of patients = 911; total number of patient assessments = 3,097)

symptoms by CES-D were associated with less likelihood of experiencing improvement in cognition (RR 0.98; 95% CI 0.96-0.99); and greater disease severity by SLAQ was associated with an increased risk of cognitive decline (RR 1.05; 95% CI 1.02-1.09) (**Table 1**). As assessed by the HVLT-R, individuals were 3 times as likely to improve in cognition than to experience cognitive decline over time (Improvement Intensity of 0.20 vs. Decline Intensity of 0.07). Increasing age (RR 1.02; 95% CI 1.01-1.03) and higher education level (RR 1.82; 95% CI 1.29-2.58) were associated with a greater likelihood of improving cognition assessed by HVLT-R. Higher disease severity by SLAQ (RR 1.05; 95% CI 1.03-1.07) and depressive symptoms by CES-D (RR 1.02; 95% CI 1.01-1.03) were also associated with an increased risk of worsening cognition (**Table 2**).

Table 2. Multi-state regression model with HVLT-R

	Multivariate Regression Analysis Using HVLT-R Z-scores			
Cognitive Transition States	Covariate	RR	95% CI	*p*
1→2 (improvement in cognition)	Age: Per 1 Year	1.02	(1.01, 1.03)	0.00*
	Education: Level 3-6 vs. Level 1-2	1.82	(1.29, 2.58)	0.00*
	Steroids IV: Yes vs. No	1.18	(0.74, 1.88)	0.50
	SLAQ Score: Per 1 unit	1.02	(1.00, 1.04)	0.13
	CESD Score: Per 1 Unit	0.99	(0.98, 1.00)	0.14
2→1 (decrease in cognition	Age: Per 1 Year	1.00	(0.99, 1.01)	0.80
	Education: Level 3-6 vs. Level 1-2	0.71	(0.50, 1.00)	0.05
	Steroids IV: Yes vs. No	1.32	(0.81, 2.17)	0.27
	SLAQ Score: Per 1 unit	1.05	(1.03, 1.07)	0.00*
	CESD Score: Per 1 Unit	1.02	(1.01, 1.03)	0.00*

All models were adjusted for age; included assessments had complete covariates (number of patients = 1,023; total number of patient assessments = 5,283)

Conclusion: This study demonstrates that the majority of individuals with SLE experience stability in cognitive function over time. However, among those SLE patients that do experience change in cognition, improvement in cognition was more common than decline. Cognitive improvement over time was more noticeable in the verbal fluency domain (COWAT) than in the learning and memory domain (HVLT-R). Increasing age and higher education levels were associated with a greater chance of cognitive improvement. Self-reported higher levels of SLE disease severity and depressive symptoms were barriers to experiencing cognitive improvement and were risk factors for experiencing cognitive decline in both assessments.

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Abstract Number: 1935

Skewed Escape from X-inactivation: Insights into the Female Bias of Sjögren's Syndrome

Teressa Shaw[1], Wei Zhang[2], Sara McCoy[3], Xueer Qiu[1], Adam Pagenkopf[1], Robert Hal Scofield[4], Jacques Galipeau[3] and **Yun Liang**[1], [1]University of Wisconsin-Madison, Madison, WI, [2]University of California San Diego, La Jolla, CA, [3]University of Wisconsin, Madison, WI, [4]Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Genetics, Genomics & Proteomics (1935–1938)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

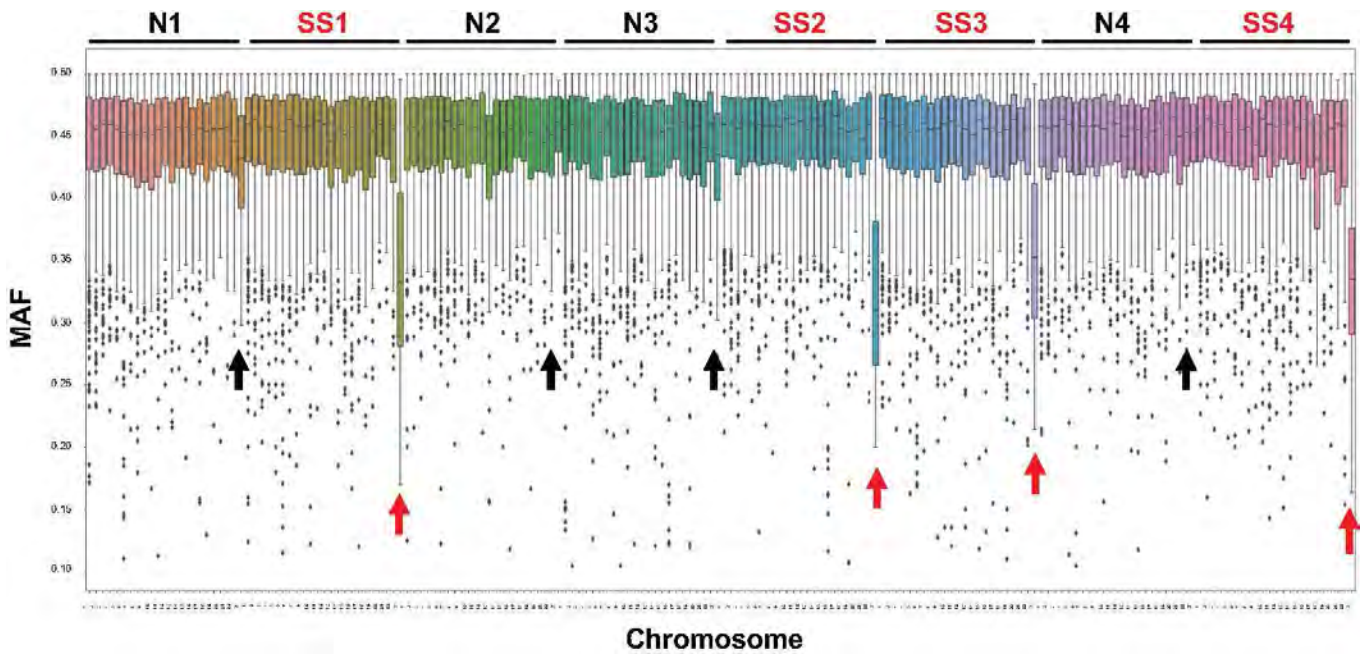

Figure 1. pSS MSCs demonstrate marked X skewing. Allele-specific transcriptomic profiling of control (N1 - N4) and pSS (SS1 – SS4) female MSCs, showing MAF (minor allele frequency) of heterozygous common SNPs on each chromosome. MAF of ~0.5 suggests equal contribution from maternal and paternal alleles, while MAF < 0.4 suggests skewing. For each sample, MAFs are shown for each chromosome (chromosomes 1-22, X; from left to right), with arrows pointing to MAFs on chromosome X (black for control, red for pSS).

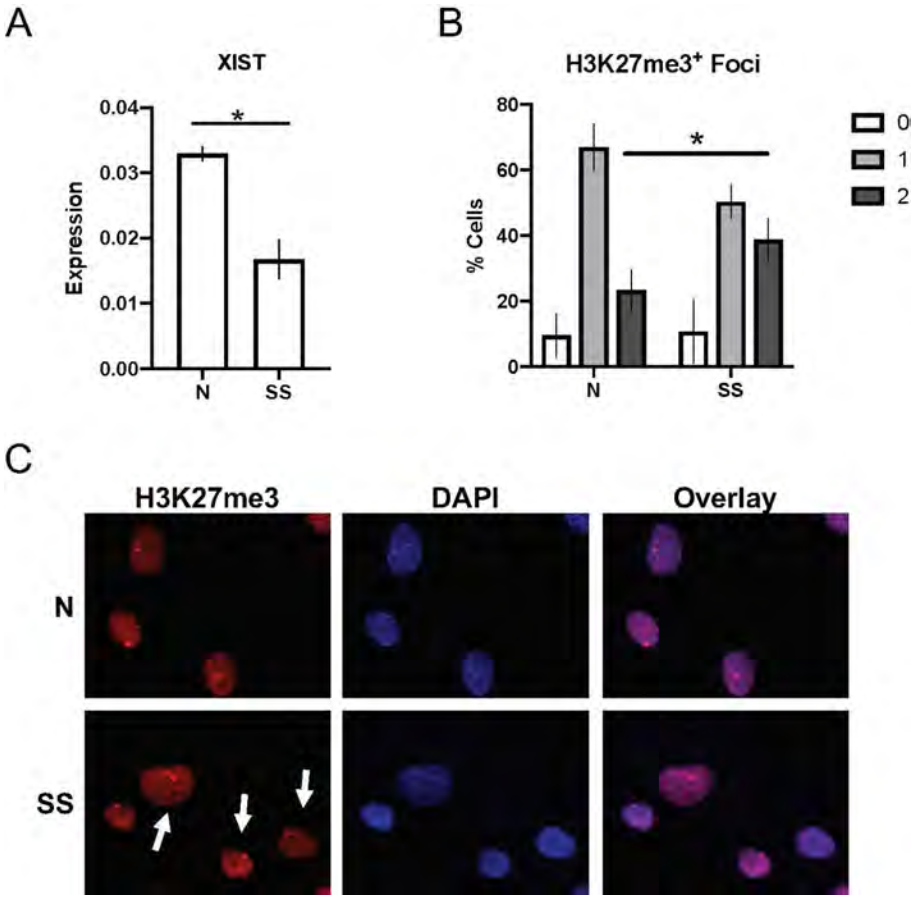

Figure 2. pSS MSCs exhibit XCI defects. A, qRT-PCR of XIST expression levels in control (N) and pSS (SS) MSCs. B, quantification of cells with 0, 1, and 2 H3K27me3+ nuclear foci in control (N) and pSS (SS) MSCs. C, immunofluorescence images of H3K27me3 and DAPI staining of control (N) and pSS (SS) MSCs, with arrows pointing to pSS cells with ectopic H3K27me3+ foci. Mean ± sem, * $P < 0.05$, two-tailed Student's t-test.

Background/Purpose: Many autoimmune diseases feature increased prevalence in females, with primary Sjögren's syndrome (pSS) being the most female-predominant autoimmune disease with a female-to-male ratio of 14:1. Recent evidence suggests that the presence of two X chromosomes may underlie the female bias in pSS. However, the exact X chromosomal alterations on a single-gene level in pSS and their contribution to the female bias in pSS remain elusive. The objective of this study is to define the contribution of X-linked gene expression to pSS pathogenesis, focusing on minor salivary gland-derived mesenchymal stromal cells (MSCs) which are critical players maintaining salivary gland homeostasis.

Methods: Genome-wide, allele-specific expression profiling was performed using MSCs derived from female pSS subjects meeting 2016 ACR/EULAR criteria (n=4) and female control subjects with sicca symptoms but without clinical or laboratory features of autoimmunity (n=4). qRT-PCR of *XIST* (X-inactive-specific transcript) and quantitative immunostaining of H3K27me3 were performed to assess status of X-chromosome inactivation (XCI) in pSS and control MSCs. Protein localization was analyzed by quantitative immunofluorescence in pSS and control MSCs. Expression levels of IL4 were measured by qRT-PCR before and after MSC adipogenesis to assess the immunomodulatory properties of MSCs. Student's t-test (two-sample, unequal variances) was used to compare experiment versus control groups for statistical significance.

Results: All pSS MSCs analyzed demonstrated marked skewing of X-linked genes that escape XCI (i.e. escapees), while all control MSCs exhibited balanced escapee expression (Fig. 1). Concomitantly, pSS MSCs showed decrease

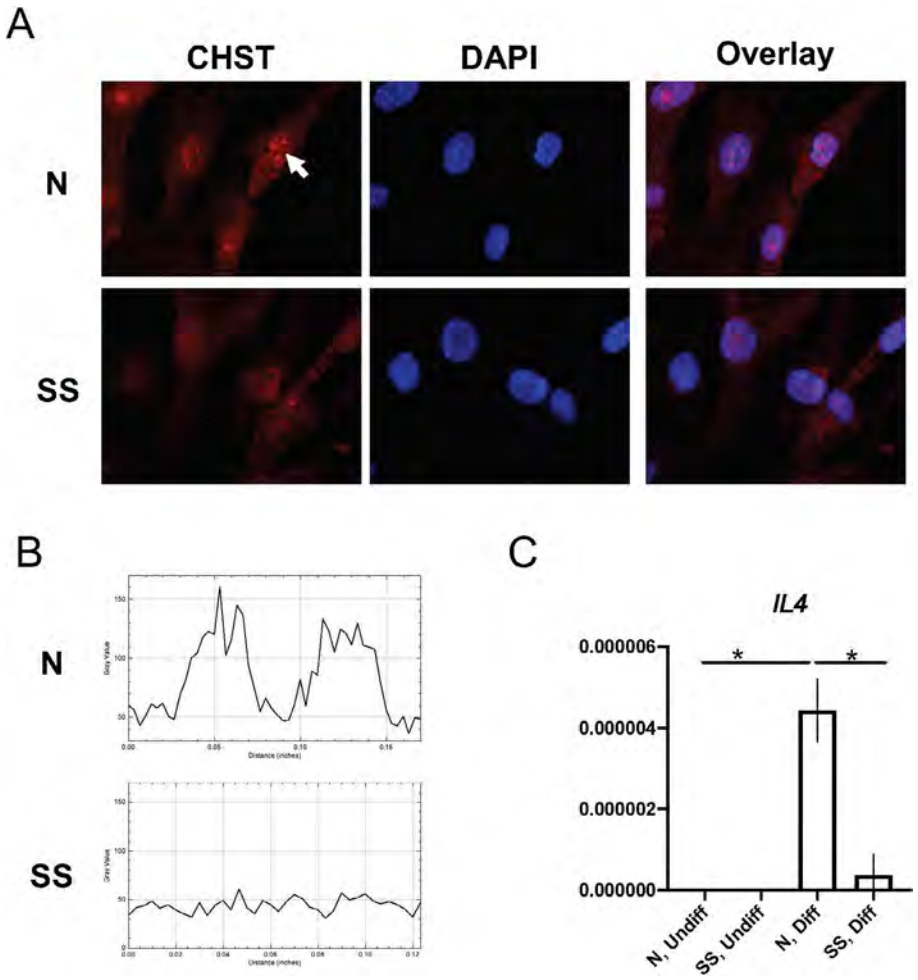

Figure 3. Escapee skewing in pSS MSCs is accompanied by escapee protein mislocalization and MSC inflammatory differentiation. A, immunostaining of a representative escapee, CHST, in control (N) and pSS (SS) MSCs. Arrow points to CHST+ nuclear foci that are absent in pSS MSCs. B, quantitative nuclear foci analysis in control (N) and pSS (SS) MSCs. C, qRT-PCR of IL4 in undifferentiated (Undiff) and differentiated (Diff) control (N) and pSS (SS) MSCs. Mean ± sem, * $P < 0.05$, two-tailed Student's t-test.

in *XIST* expression levels ($P < 0.05$) and reorganization of heterochromatic, silencing foci in the nucleus ($P < 0.05$), suggesting a global disruption in XCI maintenance (Fig. 2). The skewing in X-inactivation escape in pSS MSCs was accompanied by mislocalization of protein products encoded by the escapees as well as inflammatory differentiation of MSCs ($P < 0.05$), consistent with the hallmark features of inflammation and fibrosis in pSS salivary glands (Fig. 3).

Conclusion: We discovered global skewing of X-linked genes in pSS but not control MSCs, and identified escapee skewing as a new mechanism underlying pSS pathogenesis. Given that XCI is a female-specific process, our data suggests that dysregulation of XCI escape contributes to the female bias in pSS.

Disclosure: T. Shaw, None; **W. Zhang**, Bristol Myers Squibb, 3, Goldfinch Bio, Inc., 3; **S. McCoy**, BMS, 2, Novartis, 1, Boehringer Ingelheim, 6; **X. Qiu**, None; **A. Pagenkopf**, None; **R. Scofield**, None; **J. Galipeau**, CAMBIUM MEDICAL TECHNOLOGIES, 8; **Y. Liang**, None.

Abstract Number: 1936

A Neutrophil Degranulation Signature Identifies Proliferative Lupus Nephritis

Andrea Fava[1], Jessica Li[1], Daniel Goldman[2], Brendan Antiochos[1], Jose Monroy-Trujillo[1], Derek Fine[1], Mohamed G. Atta[1], Jill Buyon[3], Joel Guthridge[4], Judith James[4], Michelle Petri[2] and Accelerating Medicines Partership (AMP) RA/SLE Network[5], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Baltimore, MD, [3]NYU School of Medicine, New York, NY, [4]Oklahoma Medical Research Foundation, Oklahoma City, OK, [5]Brigham and Women's Hospital, Everett, MA

SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Genetics, Genomics & Proteomics (1935–1938)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: The identification of intrarenal pathological processes is key to develop better diagnostic and treatment strategies in lupus nephritis (LN). But the direct comprehensive study of renal tissue can be limited by tissue degradation, availability, and cell survival. We employed urine proteomics to define the molecular pathways involved in proliferative LN

Methods: We quantified 1200 biomarkers (Kiloplex, RayBiotech) in urine samples collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy in SLE patients with urine protein to creatinine ratio on random or 24 hr collection of > .5. Urine proteomic profiles were analyzed with respect to lupus nephritis histological features.

Results: A total of 195 patients were included: 138 (71%) had a proliferative histological class (III or IV +/- V), 57 (29%) pure membranous (V). There were 21 (FDR 1%) differentially abundant urinary proteins in proliferative compared to pure membranous LN (Figure 1A). These included several neutrophil granule proteins (Figure 1B) in addition to previously reported biomarkers such as IL-16 and CD163. Unsupervised clustering based on the proliferative LN signature identified 3 groups characterized by low, medium or high protein abundance (Figure 2). Higher proliferative signature

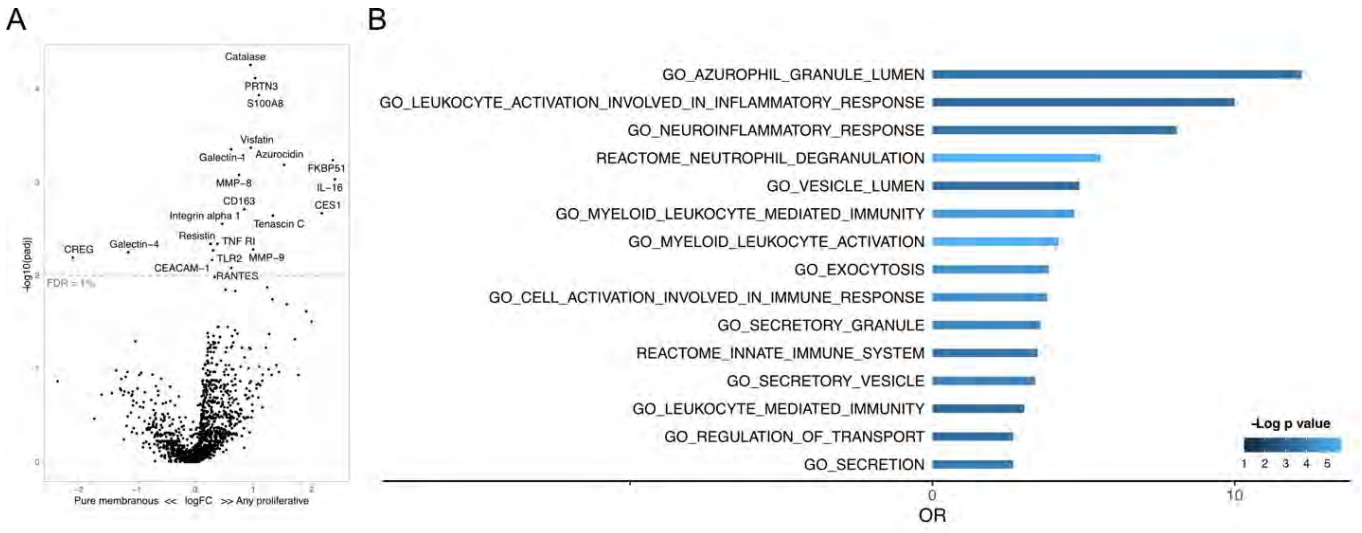

Figure 1. Urine proteomic profile of proliferative LN. (A) Volcano plot displaying the log fold change (FC) and adjusted p values of the differential abundance of 1200 urinary proteins. (B) Pathway enrichment analysis (Gene Ontology and Reactome) of the proteins enriched (FDR <1%) in proliferative LN. Odds ratios based on the hypergeometric test are displayed.

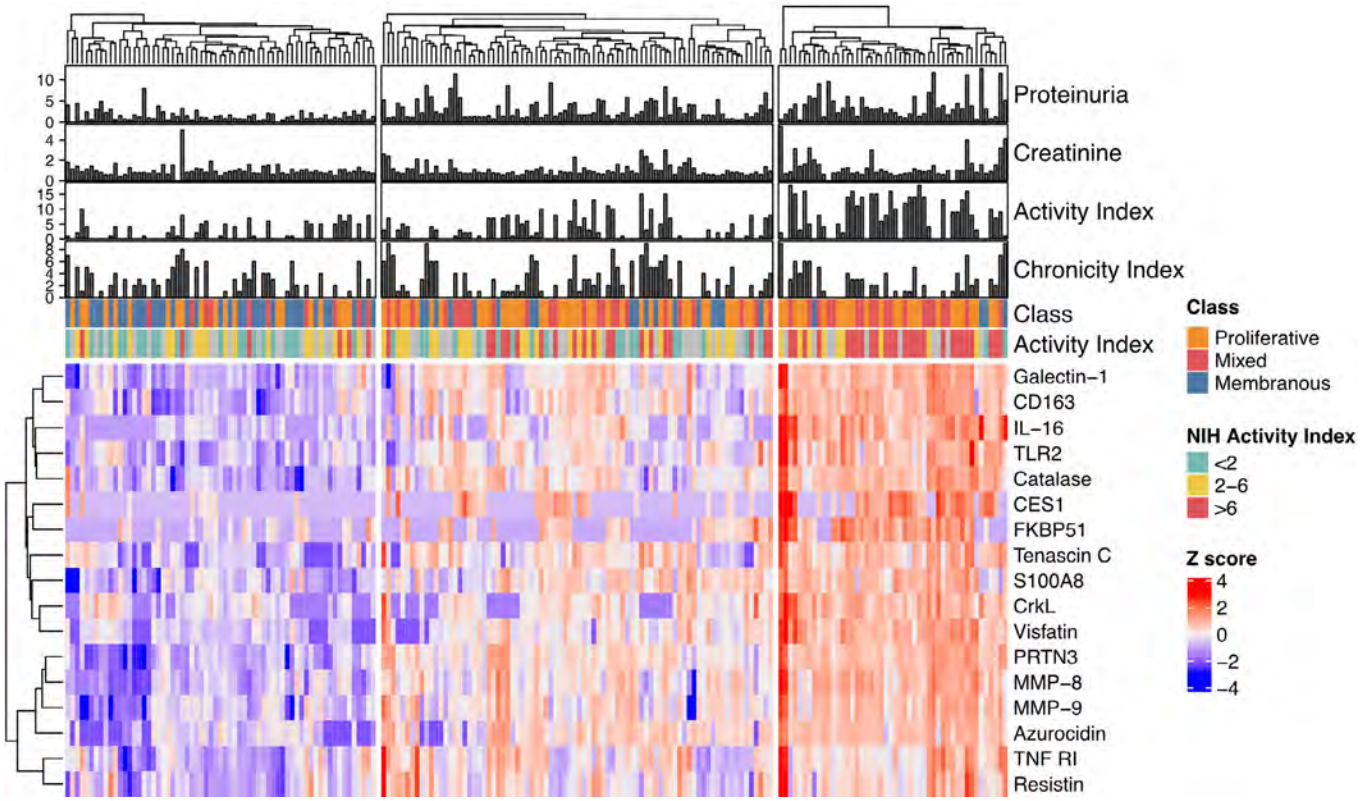

Figure 2. Higher urinary neutrophil signature is associated with higher lupus nephritis activity. Heatmap of the urinary protein differentially abundant in proliferative LN. Hierarchical clustering based on protein abundance identified 3 groups. Proteinuria in mg protein/mg creatinine.

abundance (right cluster) was associated with higher histological activity (NIH Activity Index). Immunofluorescence revealed an abundant MPO+ neutrophil infiltrate in proliferative LN (Figure 3).

Conclusion: Proliferative LN was associated with a urinary neutrophil degranulation signature, especially in patients with higher histological activity. Neutrophil activity could be non-invasively monitored to assist with the diagnosis of proliferative LN. These findings implicate neutrophils in LN activity and pathogenesis, nominate urinary neutrophil signatures as noninvasive biomarkers, and support the study of treatment targeted to neutrophils.

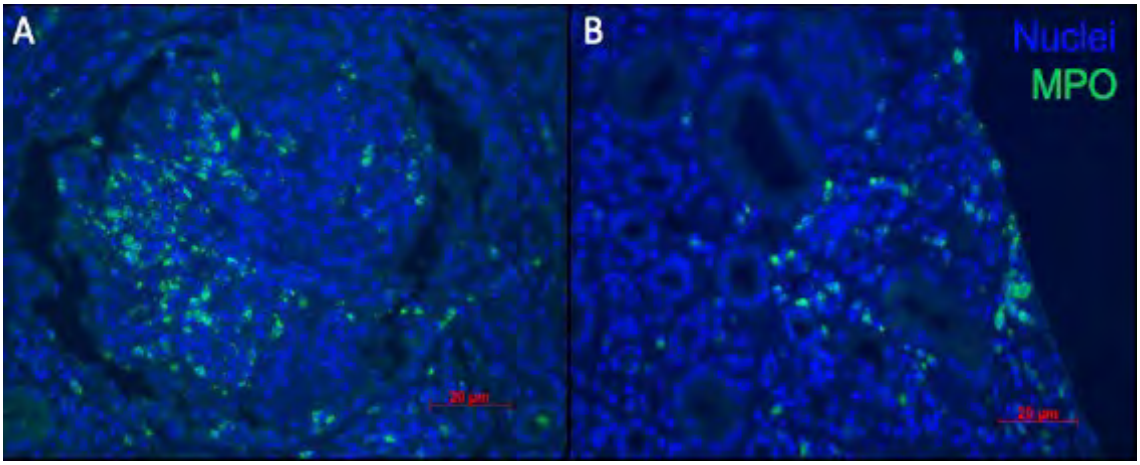

Figure 3. Neutrophil infiltrate in proliferative lupus nephritis. Immunofluorescence imaging of glomerular (A) and tubulointerstitial (B) neutrophil infiltration in a patient with class IV lupus nephritis. Myeloperoxydase (MPO) in green and DAPI in blue.

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Abstract Number: 1937

IL-16 Is Linked to Lupus Nephritis Activity

Andrea Fava[1], Deepak Rao[2], Chandra Mohan[3], Ting Zhang[3], Avi Rosenberg[1], Paride Fenaroli[4], H. Michael Belmont[5], Peter Izmirly[6], Robert Clancy[7], Jose Monroy-Trujillo[1], Derek Fine[1], Arnon Arazi[8], Celine Berthier[9], Anne Davidson[10], Judith James[11], Betty Diamond[12], Nir Hacohen[13], David Wofsy[14], Soumya Raychaudhuri[2], Accelerating Medicines Partership (AMP) RA/SLE Network[15], Jill Buyon[5], Michelle Petri[16] and The Accelerating Medicines Partnership in RA/SLE[17], [1]Johns Hopkins University, Baltimore, MD, [2]Brigham and Women's Hospital, Boston, MA, [3]University of Houston, Houston, TX, [4]Universita` degli Studi di Parma, Parma, Italy, [5]NYU School of Medicine, New York, NY, [6]New York University School of Medicine, New York, NY, [7]NYU Grossman School of Medicine, New York, NY, [8]Feinstein Institutes for Medical Research, Melrose, MA, [9]University of Michigan, Ann Arbor, MI, [10]Institute of Molecular Medicine, Feinstein Institutes for Medical Research, Manhasset, NY, [11]Oklahoma Medical Research Foundation, Oklahoma City, OK, [12]Northwell Health, Manhasset, NY, [13]Broad Institute, Cambridge, MA, [14]University of California San Francisco, San Francisco, CA, [15]Brigham and Women's Hospital, Everett, MA, [16]Johns Hopkins University School of Medicine, Baltimore, MD, [17]Multiple Institutions, Multiple

SESSION INFORMATION

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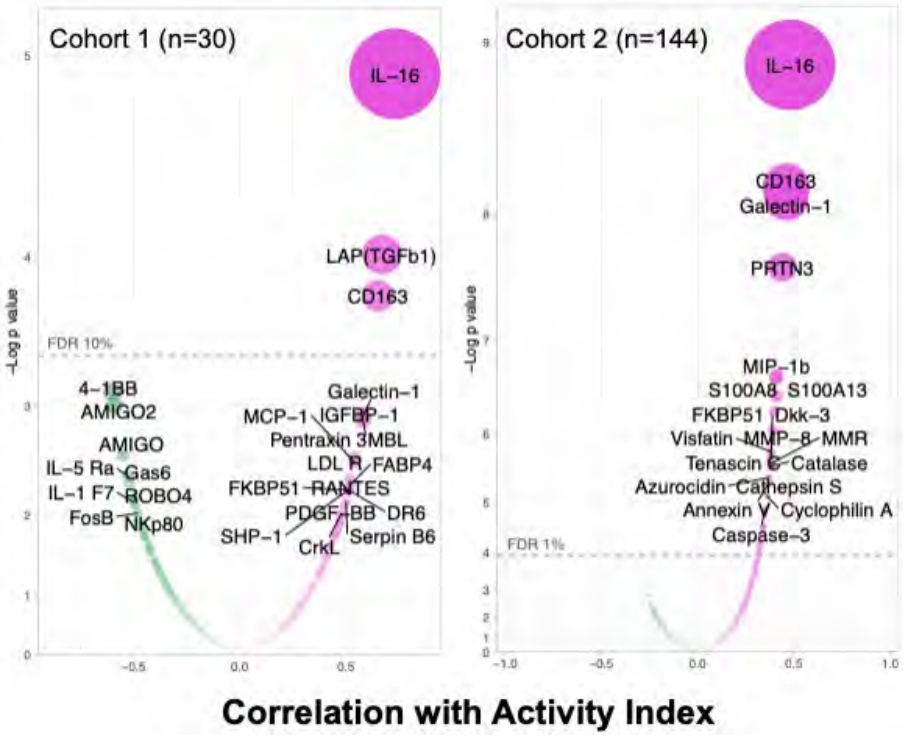

Figure 1. Urinary biomarkers associated with the LN NIH Activity Index. Volcano plots displaying Spearman correlation coefficient for 1000 (left) and 1200 (right) urinary biomarkers with LN histological activity. FDR = false discovery rate.

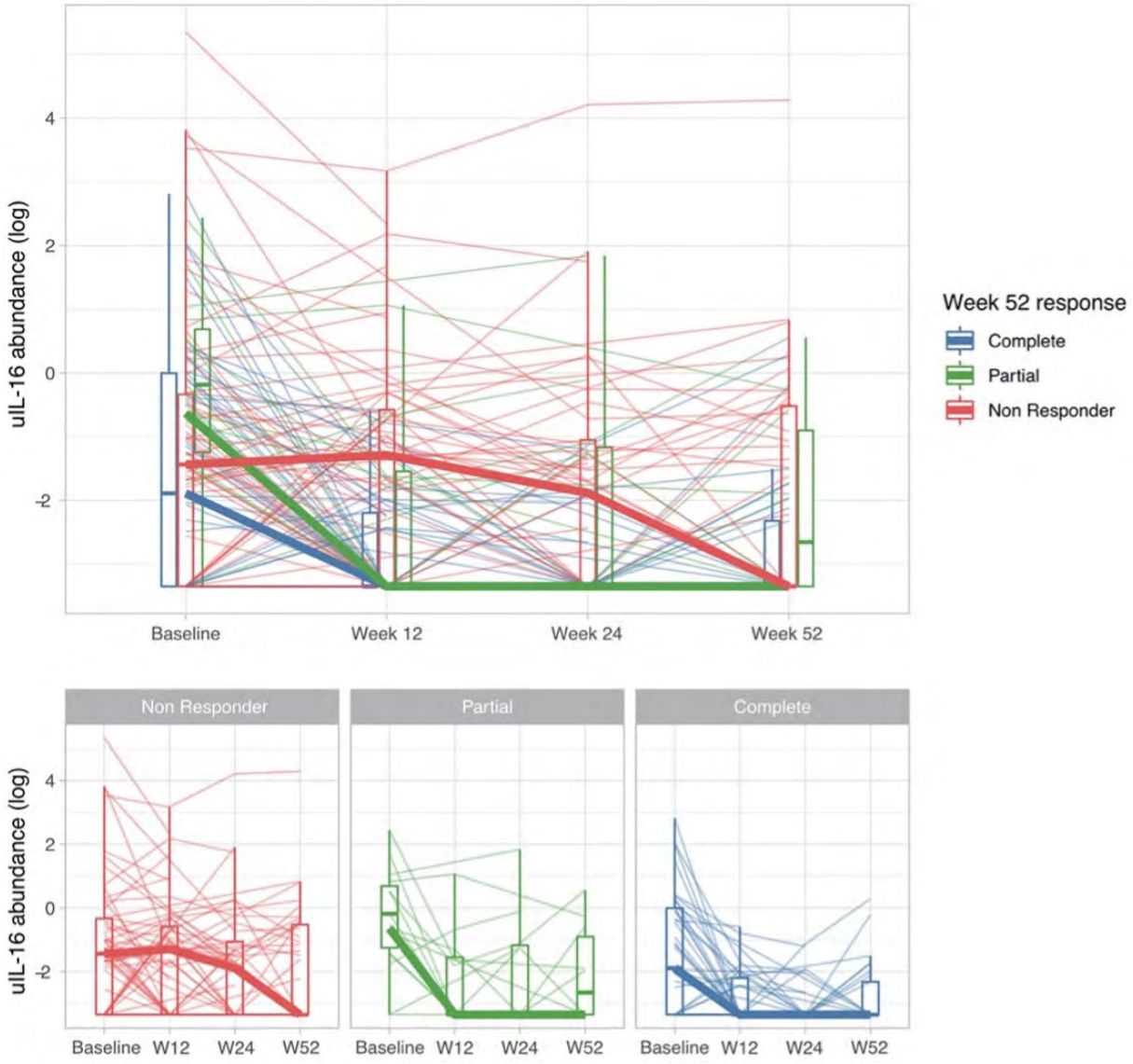

Figure 2. Urinary IL-16 declined early in treatment responders. Longitudinal trajectories of urinary IL-16 in patients with class III, IV, or V LN (n=351) according to their response status. Thick lines connect the medians at each time point. Response was defined at 52 weeks from renal biopsy (Complete, urine pr/cr (UPCR) <0.5, serum creatinine <125% of baseline, prednisone <10mg/day; Partial, UPCR < 50% from baseline but >0.5, same creatinine and prednisone requirements; Non responder, not meeting previous definitions).

Background/Purpose: There is a pressing need to identify novel therapeutic targets in lupus nephritis. Multiomic approaches hold great potential for discovery. We integrated urine proteomics and kidney single cell transcriptomics to discover biological processes and biomarkers associated with histologically active LN.

Methods: Urinary proteins (up to 1200) were quantified (RayBiotech Kiloplex) in urine samples from two independent cohorts of SLE patients with lupus nephritis (n=30 and n=144). Samples were collected on the day of (73%) or within 3 weeks (27%) of kidney biopsy in SLE patients with proteinuria > 500mg/d. The NIH Activity Index was determined by a renal pathologist at each site. Intrarenal expression of candidate biomarkers was evaluated using single cell transcriptomics of renal biopsies from patients with active lupus nephritis (n=24).

Results: A total of 174 patients were included: 127 (73%) had a proliferative histological class (III or IV +/- V), 47 (27%) pure membranous (V). Urinary IL-16 showed the strongest positive correlation with histological activity (NIH

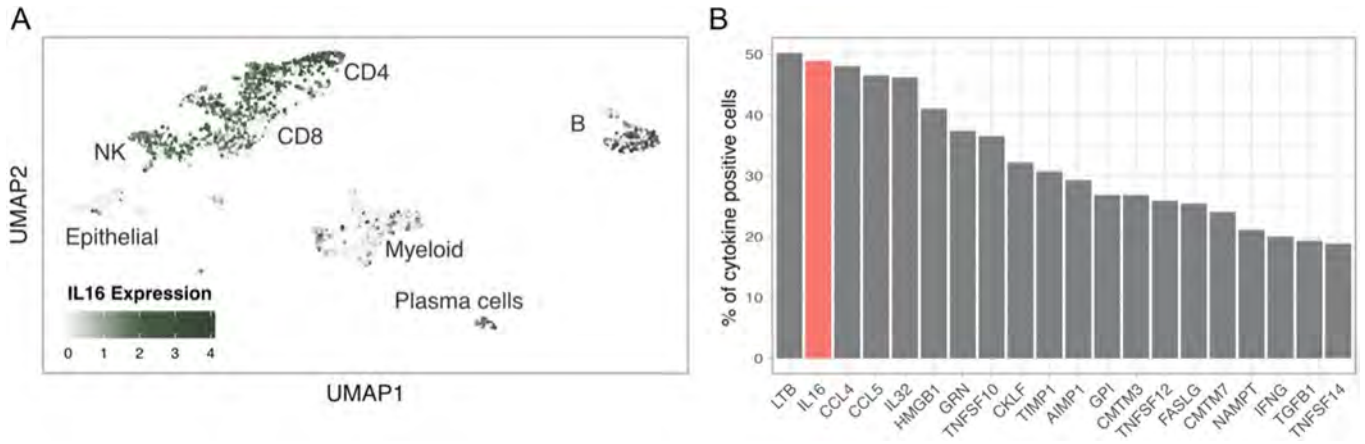

Figure 3. Intrarenal expression of IL16 based on single cell RNA sequencing of lupus nephritis kidney biopsies. (A) UMAP plot showing IL16 expression by all kidney infiltrating immune cells. (B) Percentage of cytokine positive cells across all kidney infiltrating immune cells. The bar plot shows the top 25 cytokines out of a comprehensive list of 236 obtained from the "Cytokine Registry" (Immport) and the Gene Ontology database.

Activity Index) in two independent cohorts (r=0.69, p=9·10^{-5}; r=0.49, p=3·10^{-10}; **Figure 1)**. Response to treatment was paralleled by an early reduction of urinary IL-16 (**Figure 2**). Single cell RNA sequencing independently demonstrated that IL16 is the second most widely expressed cytokine by most infiltrating immune cells in lupus nephritis kidneys (**Figure 3**).

Conclusion: Urine proteomics can profoundly change the diagnosis and management of lupus nephritis by noninvasively monitor active intrarenal biological pathways. These findings implicate IL-16, a proinflammatory chemokine, in lupus nephritis pathogenesis designating it as a potentially treatable target and biomarker.

Disclosure: A. Fava, None; **D. Rao**, Janssen, 5, 6, Bristol-Myers Squibb, 1, 5, Scipher Medicine, 2, Pfizer, 6, Merck, 6; **C. Mohan**, None; **T. Zhang**, None; **A. Rosenberg**, None; **P. Fenaroli**, None; **H. Belmont**, Alexion, 6; **P. Izmirly**, Momenta/Janssen, 1; **R. Clancy**, None; **J. Monroy-Trujillo**, None; **D. Fine**, None; **A. Arazi**, None; **C. Berthier**, None; **A. Davidson**, None; **J. James**, Progentec Diagnostics, Inc., 2; **B. Diamond**, ISD, 2, nextcure, 2, J5J, 2, astlia, 2, dbv, 2, cyxone, 2; **N. Hacohen**, None; **D. Wofsy**, None; **S. Raychaudhuri**, Mestag Therapeutics, 2, 12, Founder, Johnson & Johnson, 1, 2, Pfizer, 1, 2, Biogen, 5, Gilead Sciences, 2; **A. (AMP) RA/SLE Network**, None; **J. Buyon**, Bristol Myers Squibb, 1, GlaxoSmithKline, 2, Janssen, 2, Ventus, 2, Equillium, 2; **M. Petri**, Alexion, 1, Amgen, 1, Astrazeneca, 1, 5, Aurinia, 5, 6, Eli Lilly, 5, Emergent Biosolutions, 1, Exagen, 5, Gilead Biosciences, 2, GSK, 1, 5, IQVIA, 1, Idorsia Pharmaceuticals, 2, Janssen, 1, 5, Merck EMD Serono, 1, Momenta Pharmaceuticals, 2, PPD Development, 1, Sanofi, 2, Thermofisher, 5, UCB Pharmaceuticals, 2; **T. Accelerating Medicines Partnership in RA/SLE**, None.

Abstract Number: 1938

A Phenome-Wide Association Study of Genes Associated with COVID-19 Severity Reveals Shared Genetics with Rheumatic Conditions

Anurag Verma[1], Noah Tsao[1], Lauren Thomann[2], Yuk-Lam Ho[2], Rotonya Carr[1], Dana crawford[3], Jimmy efird[4], Jennifer Huffman[2], Adriana Hung[5], Kerry Ivey[2], Sudha Iyengar[3], Michael Levin[6], Shiuh-Wen luoh[7], Julie Lynch[8], Pradeep Natarajan[9], Saiju Pyarajan[10], alexander Bick[11], Lauren Costa[2], Giulio Genovese[12], Richard Hauger[13], Ravi madduri[14], Gita Pathak[15], Renato polimanti[15], Benjamin Voight[1], Marijana Vujkovic[1], Maryam Zekavat[15], Hongyu Zhao[15], Marylyn Ritchie[1], Kyong-Mi Chang[16], Kelly Cho[2], Juan casas[2], Phil Tsao[17], J. Michael Gaziano[2], Christopher ODonnell[2], Scott Damrauer[1] and Katherine Liao[18], [1]University of Pennsylvania, Philadelphia, PA, [2]VA Boston Healthcare System, Boston, MA, [3]Case Western Reserve University, Cleveland, OH, [4]DVAHCS, Durham, [5]Vanderbilt University Medical Center, Nashville, TN, [6]University of Pennsylvania, Philadelphia, [7]Oregon Health & Science University, Portland, [8]VA Informatics and Computing Infrastructure, VA Salt Lake City Health Care System, Salt Lake City, UT, [9]Massachusetts General Hospital, Boston, MA, [10]Partners, Boston, [11]Vanderbilt University, Nashville, TN, [12]Harvard Medical School, Boston, MA, [13]University of California San Diego, San Diego, CA, [14]Argon National Lab, Chicago, IL, [15]Yale University, New Haven, CT, [16]VA Philadelphia, Philadelphia, PA, [17]VA Palo Alto, Palo Alto, CA, [18]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

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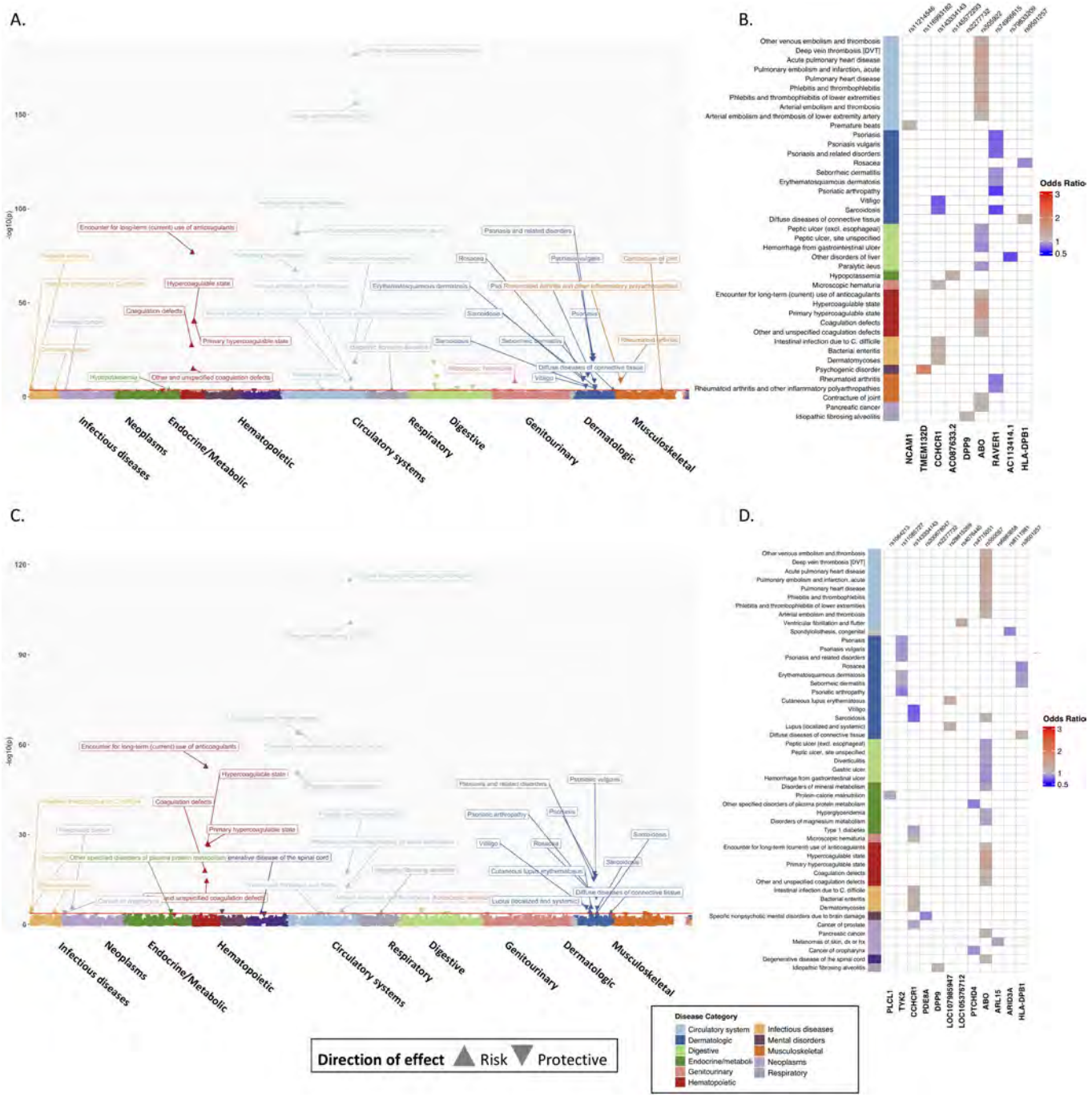
Background/Purpose: Severe coronavirus disease 2019 (COVID-19) is associated with a broad range of clinical conditions. International efforts have led to the identification of risk alleles associated with severe COVID-19. The objective of this study was to apply the Phenome-Wide Association Study (PheWAS) approach to study conditions sharing risk alleles with severe COVID-19 to inform potential shared pathways across conditions.

Methods: We performed the PheWAS in two mega-biobanks with linked clinical and genomic data: 1) Veteran Affairs (VA) Million Veteran Program (MVP), discovery cohort, 2) United Kingdom Biobank (UKBB), replication cohort. Genetic variants associated with a critical illness (n=48) or hospitalization (n=39) due to COVID-19 were selected from COVID-19 Host Genetics Initiative genome-wide association studies. Phenotypes were defined using a published PheWAS approach using International Classification of Diseases (ICD) codes mapped to clinically relevant groups. Data were extracted on subjects before 2019/pre-COVID-19 to avoid potential confounding. Logistic regression was applied to examine each SNP and phenotypes association and adjusted for sex, age, and the 1st 20 principal components. Ancestry-specific PheWAS was first performed across European (EUR), African (AFR), Hispanic, Asian ancestries and then meta-analyzed using an inverse-variance weighted fixed-effects model.

Results: We studied 455,683 US Veterans from MVP, mean age 68 years, 89% male; 68% EUR, and 19% AFR ancestry. Variants associated with severe COVID-19 were tested for association across 1,559 phenotypes. Genetic variants at the *ABO* locus (rs550057, rs505922) were associated with the largest number of phenotypes ($n_{rs55057}$= 53 and $n_{rs505922}$=61); strongest association with venous embolism (odds ratio $(OR)_{rs550057}$ 1.27, p=5.28 x 10^{-116}), and thrombosis ($OR_{rs505922}$=1.31, p=3.5 x10^{-183}). Among 67 respiratory conditions tested, only idiopathic pulmonary fibrosis, ($OR_{rs2277732}$ 1.17, p=1.3410^{-05}), and asthma ($OR_{rs143334143}$ 0.94, p=2.31 x10^{-04}), shared variants with severe COVID-19 (Figure). The *RAVER1* locus (rs74956615) associated with reduced risk for autoimmune conditions, e.g. psoriasis (OR 0.71, p= 1.53 x10^{-22}), rheumatoid arthritis (OR 0.78, p=1.04 x 10^{-09}) with findings replicating in UKBB (Table). A known functional missense variant (rs34536443, TYK2) in the region had the highest linkage disequilibrium with rs74956615, suggesting the signal stemmed from *TYK2*. MVP PheWAS results stratified by genetic ancestry did not demonstrate a significant difference in associations across ancestry.

Conclusion: We observed a shared genetic architecture between severe COVID-19 with thrombosis and asthma; this same genetic architecture was also associated with reduced risk of rheumatic conditions, e.g., RA. This divergent association may in part be explained by a *TYK2* variant known to impair type 1 interferon signaling, reducing risk for autoimmunity and simultaneously impairing viral host defense. Consideration is needed when targeting pathways that may balance immune tolerance and immunodeficiency to treat COVID-19.



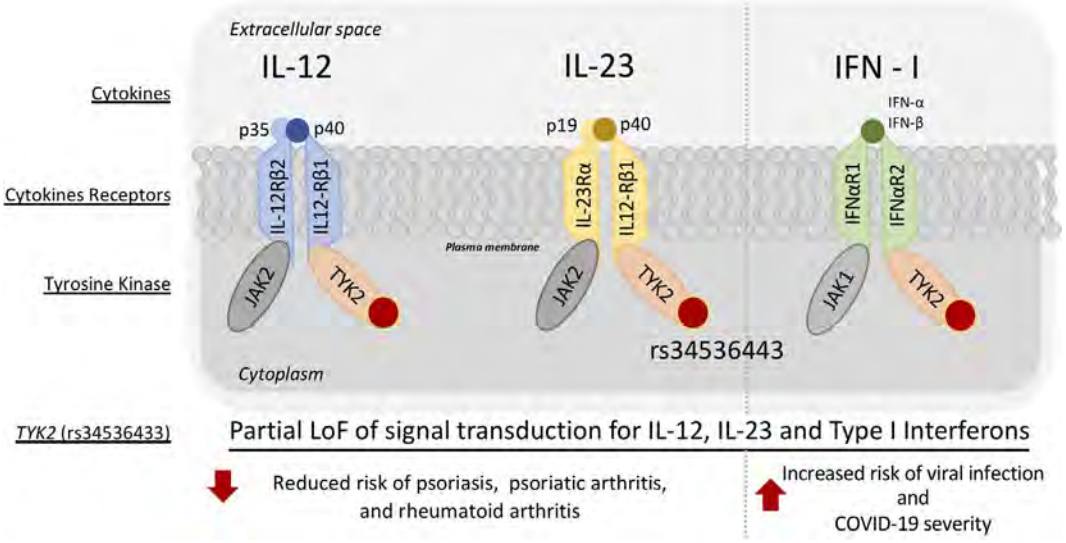
PheWAS results of candidate SNPs from GWAS of critically ill and hospitalized COVID-19. Significant associations between 48 SNPs from critical ill COVID GWAS (A) and 39 SNPs from hospitalized COVID (C) and EHR-derived phenotypes in the Million Veteran Program. The phenotypes are represented on the x-axis and ordered by broader disease categories. The red line denotes the significance threshold using a false discovery rate of 10% using the Benjamini-Hochberg procedure. The description of phenotypes is highlighted for the associations with FDR < 0.1 and

odds ratio < 0.90 or odds ratio > 1.10. B) and D) A heatmap plot of SNPs with at least one significant association (FDR < 0.1). The odds ratio represents the direction of effect disease risk. A red color indicates increased risk, and blue color indicated reduced risk. The results with odds ratio < 0.90 or odds ratio > 1.10 are shown.

Phenotype	OR (95% CI)	p-value	Gene (SNP)	SNP (MAF)	COVID-severity
Psoriasis	0.72 [0.67 - 0.77]	1.5×10^{-22}	RAVER1	rs74956615-A (0.02)	Both
	0.88 [0.86 – 0.91]	1.35×10^{-17}	TYK2	rs11085727-T (0.3)	Critical
Rosacea	0.84 [0.81 - 0.89]	2.5×10^{-11}	HLA-DPB1	rs9501257-G (0.2)	Critical
Seborrheic dermatitis	0.86 [0.83 - 0.9]	1.8×10^{-10}	RAVER1	rs74956615-A (0.02)	Hospitalized
Psoriatic arthropathy	0.81 [0.76 - 0.87]	3.5×10^{-09}	TYK2	rs11085727-T (0.3)	Critical
	0.60 [0.51 – 0.71]	9.5×10^{-10}	RAVER1	rs74956615-A (0.02)	Hospitalized
Rheumatoid arthritis	0.79 [0.73 - 0.85]	1.0×10^{-09}	RAVER1	rs74956615-A (0.02)	Hospitalized
Vitiligo	0.69 [0.6 - 0.81]	2.4×10^{-06}	CCHCR1	rs143334143-A (0.09)	Critical
Sarcoidosis	0.73 [0.64 - 0.83]	4.3×10^{-06}	CCHCR1	rs143334143-A (0.09)	Hospitalized
	0.63 [0.51 – 0.78]	3.1×10^{-05}	RAVER1	rs74956615-A (0.02)	Hospitalized
Other disorders of the liver	0.64 [0.53 - 0.78]	8.2×10^{-06}	AC113414.1	rs79833209-T (0.01)	Hospitalized
Hemorrhage from GI ulcer	0.85 [0.79 - 0.92]	4.0×10^{-05}	ABO	rs550057-T (0.2)	Critical
Other specified disorders of plasma protein metabolism	0.80 [0.72 - 0.89]	5.61×10^{-05}	PTCHD4	rs4715051-G (0.5)	Critical
Specific nonpsychotic mental disorders attributable to brain damage	0.82 [0.75 - 0.9]	6.0×10^{-05}	PDE8A	rs200678047-A (0.1)	Critical

*OR<0.9 and P<10-5 shown in the table, full results in supplementary; if multiple related conditions, e.g., psoriasis, psoriasis vulgaris, psoriasis, and related disorders, description with the lowest p-value selected shown in the table.

Phenotypes sharing association with variants also associated with severe COVID-19 infection, with reduced odds of disease listed in order of p-value*.



Conceptual model of the relationship between TYK2 (rs34536133) with reduced risk for psoriasis, psoriatic arthritis, rheumatoid arthritis, and simultaneously increased risk of COVID-19 severity.

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Abstract Number: 1939

Risk of Cardiovascular Outcomes in Patients Treated with Tofacitinib: First Results from the Safety of TofAcitinib in Routine Care Patients with Rheumatoid Arthritis (STAR-RA) Study

Farzin Khosrow-Khavar, Seoyoung Kim, Hemin Lee, Su Been Lee and Rishi Desai, Brigham and Women's Hospital, Boston, MA

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Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

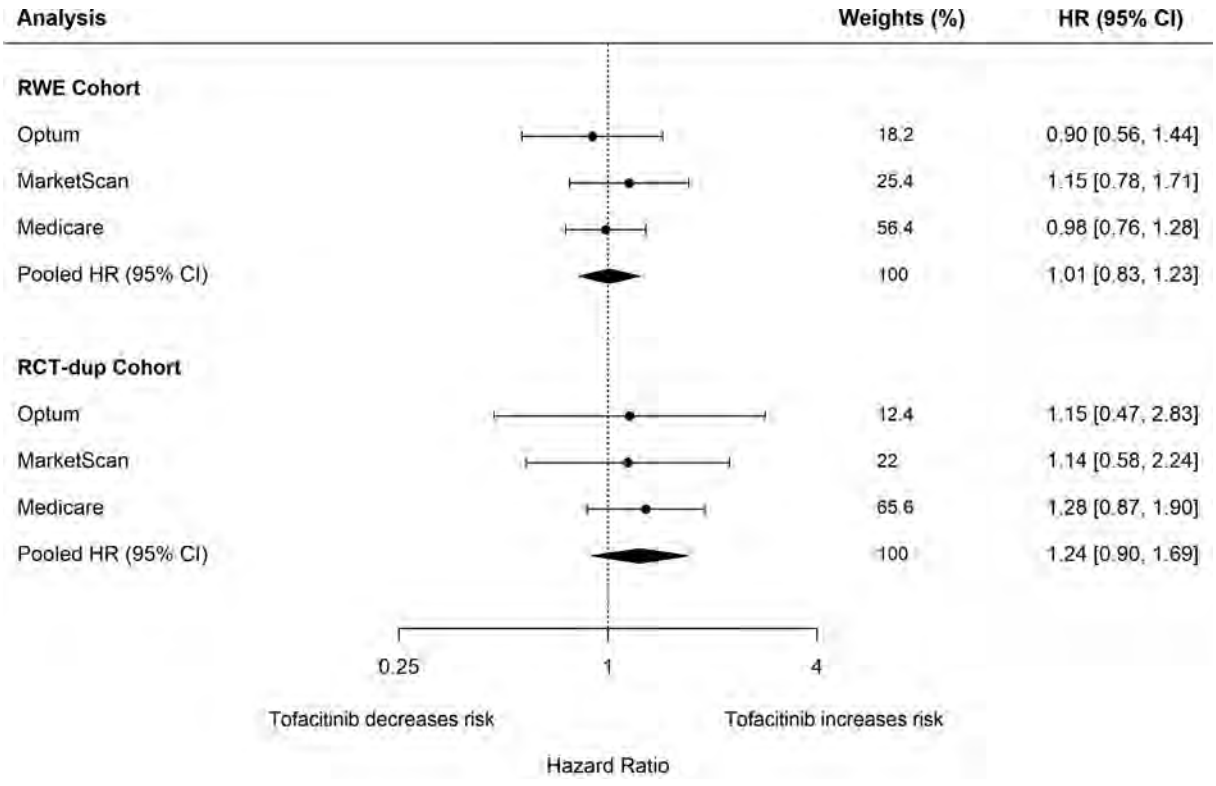


Figure. Risk of composite CV outcomes when comparing tofacitinib with TNF inhibitors (reference) in patients with RA.

Background/Purpose: Recent reports from a post-marketing safety trial, "ORAL Surveillance", indicated an increased risk of cardiovascular (CV) outcomes in RA patients treated with tofacitinib. Thus, the aim of this study was to examine the risk of CV outcomes associated with tofacitinib, compared with tumor necrosis factor inhibitors (TNFI), in patients with RA.

Methods: Using U.S. claims data from 'Optum' Clinformatics (2012-2020), IBM 'MarketScan' (2012-2018), and Medicare (parts A, B, and D, 2012-2017) databases, we created two study cohorts of RA patients initiating treatment with tofacitinib or TNFI: 1) A restrictive "RCT-duplicate cohort" mimicking inclusion/exclusion criteria of the ORAL Surveillance trial to calibrate our findings against trial results, 2) a broader "real-world evidence (RWE) cohort" including representative population from routine care. Patients were followed from treatment initiation for study outcomes until treatment discontinuation or switch, insurance disenrollment, death, or end of the study period. The primary composite CV outcome, was defined using inpatient claims for myocardial infarction or stroke. Cox proportional hazards models with propensity score fine-stratification weighting were used to generate hazard ratios (HR) and 95% confidence intervals (CI) and accounted for over 60 potential confounders in each of the datasets. Fixed effects models with inverse variance were used to pool database-specific effect estimates. Secondary analysis was conducted by baseline cardiovascular disease (RWE cohorts only).

Results: In RWE study population, 28,568, 34,083, and 39,612 patients were identified from Optum, MarketScan, and Medicare, respectively, of whom 13.2%, 15.6%, and 9.5% initiated treatment on tofacitinib. The mean age was 55, 53, and 72 years in Optum, MarketScan, and Medicare, respectively. In RWE cohort, 13% of patients in Optum, 10% in MarketScan, and 31% in Medicare had a history of cardiovascular disease. The crude incidence rates of the primary CV endpoint per 100 person-years (95% CI) for tofacitinib and TNFI users were 0.73 (0.47-1.09) and 0.61 (0.51-0.72) in Optum; 0.75 (0.52-1.05) and 0.52 (0.44-0.61) in MarketScan; and 2.14 (1.66-2.70) and 1.86 (1.71-2.02) in Medicare. Overall, in the RWE cohort, the pooled HR (95% CI) for CV outcomes comparing tofacitinib with TNFI was 1.01 (0.83-1.23). Results from the RCT-duplicate cohort were in alignment with reports from the ORAL Surveillance trial (pooled HR: 1.24, 95% CI: 0.90-1.69 vs trial: 1.33, 95% CI: 0.91-1.94). Among RWE patients with baseline cardiovascular disease, the pooled HR (95% CI) was 1.27 (0.95-1.70). Consistent results were observed across other secondary and sensitivity analyses.

Conclusion: This multi-database large population-based study did not find evidence for an increased risk of CV outcomes with tofacitinib, in comparison with TNFI, in the overall RA patient population treated in the real-world setting. However, similar to the reported results from ORAL Surveillance trial, tofacitinib, in comparison with TNFI, was associated with an increased, but statistically non-significant, risk of CV outcomes in RA patients with CV risk factors or a history of cardiovascular disease.

Disclosure: F. Khosrow-Khavar, None; **S. Kim**, AbbVie, 5, Roche, 5, Pfizer, 5, Bristol-Myers Squibb, 5; **H. Lee**, None; **S. Lee**, None; **R. Desai**, Bayer, 5, Vertex Pharmaceuticals, 5, Novartis, 5.

Abstract Number: 1940

Malignancies in Patients Aged ≥ 50 Years with RA and ≥ 1 Additional Cardiovascular Risk Factor: Results from a Phase 3b/4 Randomized Safety Study of Tofacitinib vs TNF Inhibitors

Jeffrey Curtis[1], Kunihiro Yamaoka[2], Yi-Hsing Chen[3], Levent M Gunay[4], Naonobu Sugiyama[5], Carol A Connell[6], Cunshan Wang[6], Joseph Wu[6], Sujatha Menon[6], Ivana Vranic[7] and Juan J Gomez-Reino[8], [1]Division of Clinical Immunology and Rheumatology, Department of Medicine, Department of Epidemiology, University of Alabama at Birmingham, Birmingham, AL, [2]School of Medicine, Department of Rheumatology and Infectious Diseases, Kitasato University, Sagamihara, Japan, [3]Taichung Veterans General Hospital, Taichung, Taiwan (Republic of China), [4]Pfizer Inc, Istanbul, Turkey, [5]Pfizer Japan Inc, Tokyo, Japan, [6]Pfizer Inc, Groton, CT, [7]Pfizer Inc, Tadworth, Surrey, United Kingdom, [8]Hospital Clínico Universitario, Santiago de Compostela, Spain

Table. IRs (95% CI, pts with events per 100 PY) of all malignancies excluding NMSC, NMSC, and cancer subtypes of interest in ORAL Surveillance

	Tofacitinib 5 mg BID (N=1,455)		Tofacitinib 10 mg BID[a] (N=1,456)		All tofacitinib (N=2,911)		TNFi (N=1,451)	
	n (%)	IR (95% CI, per 100 PY) [PY]	n (%)	IR (95% CI, per 100 PY) [PY]	n (%)	IR (95% CI, per 100 PY) [PY]	n (%)	IR (95% CI, per 100 PY) [PY]
All malignancies excluding NMSC	62 (4.26)	1.13 (0.87, 1.45) [5,491]	60 (4.12)	1.13 (0.86, 1.45) [5,312]	122 (4.19)	1.13 (0.94, 1.35) [10,803]	42 (2.89)	0.77 (0.55, 1.04) [5,482]
Breast cancer[b]	10 (0.86)	0.22 (0.11, 0.41) [4,473]	7 (0.62)	0.17 (0.07, 0.35) [4,173]	17 (0.74)	0.20 (0.11, 0.31) [8,645]	10 (0.90)	0.24 (0.11, 0.43) [4,249]
Colorectal cancer	4 (0.27)	0.07 (0.02, 0.18) [5,550]	4 (0.27)	0.07 (0.02, 0.19) [5,368]	8 (0.27)	0.07 (0.03, 0.14) [10,918]	4 (0.28)	0.07 (0.02, 0.19) [5,525]
Lymphoma	4 (0.27)	0.07 (0.02, 0.18) [5,548]	6 (0.41)	0.11 (0.04, 0.24) [5,364]	10 (0.34)	0.09 (0.04, 0.17) [10,913]	1 (0.07)	0.02 (0.00, 0.10) [5,526]
Lung cancer	13 (0.89)	0.23 (0.12, 0.40) [5,542]	17 (1.17)	0.32 (0.18, 0.51) [5,359]	30 (1.03)	0.28 (0.19, 0.39) [10,901]	7 (0.48)	0.13 (0.05, 0.26) [5,517]
Melanoma	1 (0.07)	0.02 (0.00, 0.10) [5,548]	1 (0.07)	0.02 (0.00, 0.10) [5,371]	2 (0.07)	0.02 (0.00, 0.07) [10,919]	5 (0.34)	0.09 (0.03, 0.21) [5,517]
Pancreatic cancer	3 (0.21)	0.05 (0.01, 0.16) [5,549]	1 (0.07)	0.02 (0.00, 0.10) [5,371]	4 (0.14)	0.04 (0.01, 0.09) [10,920]	1 (0.07)	0.02 (0.00, 0.10) [5,526]
Prostate cancer[c]	1 (0.35)	0.09 (0.00, 0.52) [1,070]	8 (2.41)	0.68 (0.29, 1.34) [1,175]	9 (1.46)	0.40 (0.18, 0.76) [2,245]	3 (0.90)	0.24 (0.05, 0.69) [1,262]
NMSC	31 (2.13)	0.61 (0.41, 0.86) [5,116]	33 (2.27)	0.69 (0.47, 0.96) [4,812]	64 (2.20)	0.64 (0.50, 0.82) [9,927]	16 (1.10)	0.32 (0.18, 0.52) [5,020]
Basal cell carcinoma	19 (1.31)	0.37 (0.22, 0.58) [5,133]	16 (1.10)	0.33 (0.19, 0.54) [4,834]	35 (1.20)	0.35 (0.24, 0.49) [9,967]	13 (0.90)	0.26 (0.14, 0.44) [5,027]
Cutaneous squamous cell carcinoma	15 (1.03)	0.29 (0.16, 0.48) [5,150]	22 (1.51)	0.45 (0.29, 0.69) [4,837]	37 (1.27)	0.37 (0.26, 0.51) [9,987]	8 (0.55)	0.16 (0.07, 0.31) [5,030]

For all malignancies excluding NMSC and cancer subtypes of interest, total time was the censoring time, and was defined as the time from the first study dose to the last contact date. For NMSC and skin cancer subtypes of interest, the 28-day on-treatment period was the censoring time (time from the first study dose until the last study dose + 28 days or to the last contact date, whichever was earlier). The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date

PY includes time to first event for pts with events; pts with no events were censored at the end of the risk period

[a]The tofacitinib 10 mg BID arm included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019

[b]Female only: tofacitinib 5 mg BID, N=1,169; tofacitinib 10 mg BID, N=1,124; all tofacitinib, N=2,293; TNFi, N=1,117

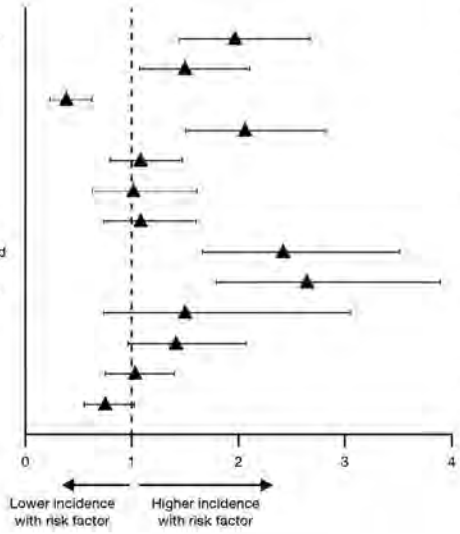
[c]Male only: tofacitinib 5 mg BID, N=286; tofacitinib 10 mg BID, N=332; all tofacitinib, N=618; TNFi, N=334

AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (pts with events per 100 PY); N, pts in safety analysis set; n, pts with events; NMSC, non-melanoma skin cancer; pt, patient; PY, pt-yrs; TNFi, TNF inhibitors

Figure 1. Risk factors at baseline for all malignancies excluding NMSC in ORAL Surveillance: a) univariate analysis of potential risk factors and their interaction with treatment[a]; b) multivariate analysis of potential independent overall risk[b]

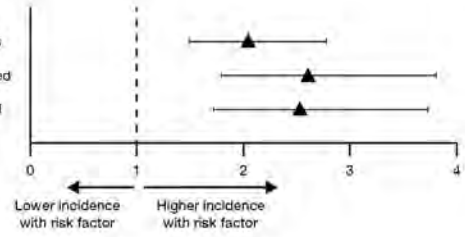
a)

Risk factor (at baseline)	Comparison	HR of risk factor HR (95% CI)	p value	Treatment-by-risk-factor interaction p value
Age ≥ 65 yrs	Age ≥ 65 yrs vs 50 – < 65 yrs	1.97 (1.44, 2.67)	< 0.0001	0.7649
Male	Male vs female	1.50 (1.07, 2.10)	0.0194	0.7394
Non-white	Non-white vs white	0.38 (0.23, 0.62)	0.0001	0.0572
Geographic region (by TNF use), North America[c]	North America vs RoW	2.06 (1.51, 2.81)	< 0.0001	0.4833
BMI ≥ 30 kg/m² (yes)	Yes vs No	1.08 (0.79, 1.47)	0.6219	0.3402
CRP > 2.87 mg/L (yes)	Yes vs No	1.01 (0.63, 1.61)	0.9772	0.3689
History of diabetes (yes)	Yes vs No	1.08 (0.73, 1.60)	0.7071	0.9694
Current smoker	Current smoker vs never smoked	2.42 (1.66, 3.51)	< 0.0001	0.2524
Past smoker	Past smoker vs never smoked	2.64 (1.79, 3.89)	< 0.0001	
Oral contraceptive or HRT use (yes)	Yes vs No	1.50 (0.73, 3.05)	0.2668	0.6619
Aspirin use (yes)	Yes vs No	1.41 (0.96, 2.07)	0.0776	0.8108
Corticosteroid use (yes)	Yes vs No	1.03 (0.75, 1.40)	0.8609	0.3399
Cox-1 or Cox-2 inhibitor use (without aspirin use) (yes)	Yes vs No	0.75 (0.55, 1.02)	0.0639	0.1713



b)

Risk factor (at baseline)	Comparison	HR (95% CI)	p value
Age ≥ 65 yrs	Age ≥ 65 yrs vs 50 – < 65 yrs	2.04 (1.49, 2.78)	< 0.0001
Current smoker	Current smoker vs never smoked	2.61 (1.79, 3.81)	< 0.0001
Past smoker	Past smoker vs never smoked	2.53 (1.72, 3.73)	< 0.0001



Total time was the censoring time and was defined as the time from the first study dose to the last contact date. The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date

[a]HR of risk factor based on a Cox model (separate model for each risk factor) with treatment and risk factor as covariates. Treatment-by-risk-factor interaction based on a Cox model (separate model for each risk factor) with treatment, risk factor, and treatment-by-risk-factor as covariates

[b]A backward model selection algorithm was used on a multivariate Cox model with effects of treatment and a pre-selected set of overall risk factors, where $p < 0.1$ for each risk factor and $p \neq 0.2$ for treatment-by-risk-factor interaction in the univariate Cox analyses. This set of overall risk factors were subject to model selection ($p < 0.1$ to stay in model), except for treatment, which was mandatorily included. Geographic region was not considered in the multivariate Cox analyses

[c]United States, Puerto Rico, and Canada. At baseline, there were higher percentages of pts with alcohol use, oral contraceptives or HRT use, aspirin use, anticoagulant use, antidepressant use, prior depression, history of DVT or PE, prior coronary heart disease, diabetes, hypertension, MI, history of CA procedures, and a family history of coronary heart disease in first-degree relatives in those from North America vs those from the RoW. Pts from North America were older and had a higher BMI, and a higher proportion were male vs pts from the RoW. Geographic differences at baseline were generally consistent across treatment arms

AE, adverse event; BMI, body mass index; CA, coronary artery; CI, confidence interval; CRP, C-reactive protein; DVT, deep vein thrombosis; HR, hazard ratio; HRT, hormone replacement therapy; MI, myocardial infarction; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; pt, patient; RoW, rest of world; TNFi, TNF inhibitors

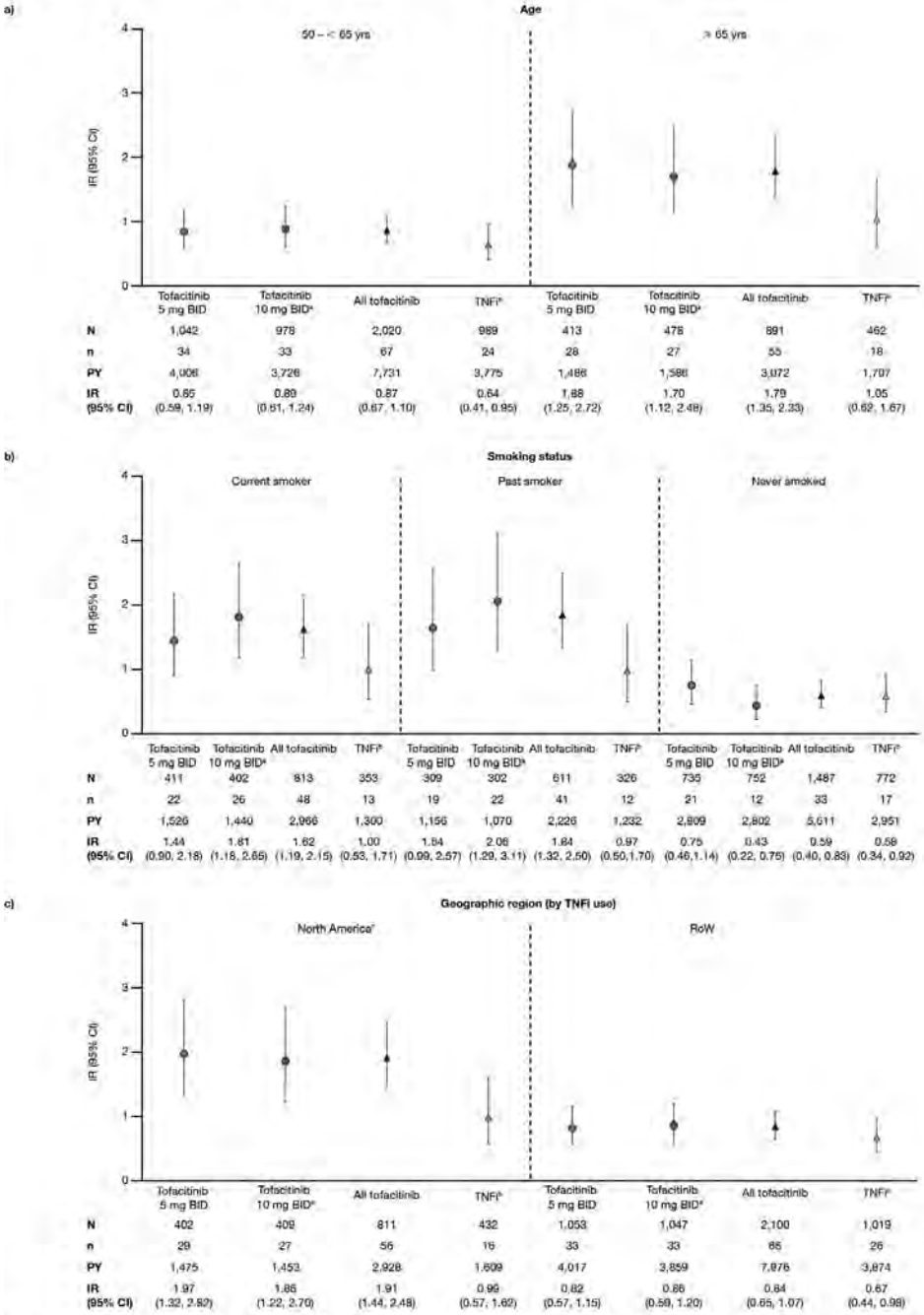
SESSION INFORMATION

Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Treatments I: Safety & Harms (1939–1942)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: ORAL Surveillance (NCT02092467) was a post-authorization safety study to assess the relative risk of tofacitinib vs TNF inhibitors (TNFi), based on observed increases in lipids and malignancies in patients (pts) with RA following tofacitinib treatment in the Phase 3 development program. Here, we characterized malignancies in ORAL Surveillance.

Methods: ORAL Surveillance was a long-term, randomized, open-label, non-inferiority, Phase 3b/4 safety study of tofacitinib vs TNFi in pts with RA aged ≥ 50 yrs, with ≥ 1 additional cardiovascular risk factor and an inadequate

Figure 2. IRs (95% CI, pts with events per 100 PY) for all malignancies excluding NMSC in ORAL Surveillance, stratified by a) age (50 – < 65 or ≥ 65 yrs), b) smoking status (current smoker, past smoker, or never smoked), and c) geographic region (proxy for TNFi use)



Total time was the censoring time and was defined as the time from the first study dose to the last contact date. The last contact date was the maximum of: AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date. If a pt died, the last contact date was the death date.

[a]The tofacitinib 10 mg BID arm included pts who were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019.

[b]In the TNFi group, pts in North America received adalimumab 40 mg every other week, and pts in the RoW received etanercept 50 mg every week.

[c]United States, Puerto Rico, and Canada. At baseline, there were higher percentages of pts with alcohol use, oral contraceptives or HRT use, aspirin use, anticoagulant use, antidepressant use, prior depression, history of DVT or PE, prior coronary heart disease, diabetes, hypertension, MI, history of CA procedures, and a family history of coronary heart disease in first-degree relatives in those from North America vs those from the RoW. Pts from North America were older and had a higher BMI, and a higher proportion were male vs pts from the RoW. Geographic differences at baseline were generally consistent across treatment arms.

AE, adverse event; BID, twice daily; CA, coronary artery; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate (pts with events per 100 PY); MI, myocardial infarction; N, number of evaluable pts; n, number of pts with events; NMSC, non-melanoma skin cancer; PE, pulmonary embolism; pt, patient; PY, pt-yrs; RoW, rest of world; TNFi, TNF inhibitors.

response to MTX. Pts were randomized 1:1:1 to receive open-label tofacitinib 5 or 10 mg twice daily (BID) or a TNFi (adalimumab 40 mg every two weeks [North America; NA] or etanercept 50 mg once weekly [rest of world; RoW]) while on stable background MTX doses. Incidence rates (IRs; pts with events/100 pt-yrs [PY]) of all malignancies excluding non-melanoma skin cancer (NMSC), NMSC, and cancer subtypes of interest were determined for each

treatment arm. Number Needed to Harm (NNH; PY of treatment exposure needed for 1 more pt to report an event vs reference) was evaluated post hoc for all malignancies excluding NMSC. Potential risk factors for all malignancies excluding NMSC were analyzed via univariate/multivariate Cox models (post hoc). IRs of all malignancies excluding NMSC were analyzed post hoc by baseline (BL) characteristics (eg age, smoking status, and geographic region [proxy for TNFi use]).

Results: In 4,362 treated pts (tofacitinib 5 mg BID, N=1,455; tofacitinib 10 mg BID, N=1,456; TNFi, N=1,451), mean age was 61.0 yrs, 78% were female, and 49% were current/past smokers. Differences in BL demographics were seen in pts from NA vs RoW (described in Figure 1 and 2 footnotes). IRs for all malignancies excluding NMSC, and for NMSC, were numerically higher with both tofacitinib doses vs TNFi (Table); hazard ratio (tofacitinib vs TNFi) for all malignancies excluding NMSC: 1.48 (95% CI 1.04, 2.09). Excluding NMSC, the most frequently reported cancer subtypes of interest (greatest number of pts with events) were lung cancer (tofacitinib) and breast cancer (TNFi) (Table). There were 10 pts with lymphoma in the tofacitinib arm (both doses) and 1 in the TNFi arm (Table). The NNH for all malignancies excluding NMSC was 276 PY for tofacitinib 5 mg BID vs TNFi, and 275 PY for tofacitinib 10 mg BID vs TNFi. Univariate and multivariate Cox analyses identified age (≥ 65 vs 50 – < 65 yrs) and smoking status (current/past smoker vs never smoked) as independent overall risk factors across treatment arms for all malignancies excluding NMSC (Figure 1a, b). Across treatment arms, IRs for all malignancies excluding NMSC were numerically higher in pts aged ≥ 65 vs 50 – < 65 yrs (Figure 2a), current/past smokers vs pts who had never smoked (Figure 2b), and pts in NA vs RoW (Figure 2c).

Conclusion: In pts with RA in ORAL Surveillance, IRs for malignancies were numerically higher with tofacitinib vs TNFi. Older age (≥ 65 vs 50 – < 65 yrs) and current/past smoking (vs never smoking) were independent risk factors for increasing malignancy rate across treatments.

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Disclosure: J. Curtis, AbbVie, 2, Amgen, 2, 5, Bristol-Myers Squibb, 2, Janssen, 2, Eli Lilly, 2, Myriad, 2, Pfizer Inc, 2, 5, Roche/Genentech, 2, UCB, 2, CorEvitas, 2, 5, Crescendo Bio, 5; **K. Yamaoka**, Actelion, 2, 6, Astellas, 2, 6, Chugai, 2, 6, Eisai, 2, 6, Eli Lilly, 2, 6, GSK, 2, 6, Janssen, 2, 6, Mitsubishi Tanabe, 2, 6, Nippon Shinyaku, 2, 6, Pfizer Inc, 2, 6, Takeda, 2, 6; **Y. Chen**, Bristol-Myers Squibb, 5, GSK, 5, Pfizer Inc, 5; **L. Gunay**, Pfizer Inc, 3, 11; **N. Sugiyama**, Pfizer Inc, 3, 11; **C. Connell**, Pfizer Inc, 3, 11; **C. Wang**, Pfizer Inc, 3, 11; **J. Wu**, Pfizer Inc, 3, 11; **S. Menon**, Pfizer Inc, 3, 11; **I. Vranic**, Pfizer Inc, 3, 11; **J. Gomez-Reino**, Pfizer Inc, 2, 5, Biogen, 2, 5, Gilead Sciences, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Roche, 2, 5.

Abstract Number: 1941

The Risk of Venous Thromboembolic Events in Patients with RA Aged ≥ 50 Years with ≥ 1 Cardiovascular Risk Factor: Results from a Phase 3b/4 Randomized Safety Study of Tofacitinib vs TNF Inhibitors

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SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: RA – Treatments I: Safety & Harms (1939–1942)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

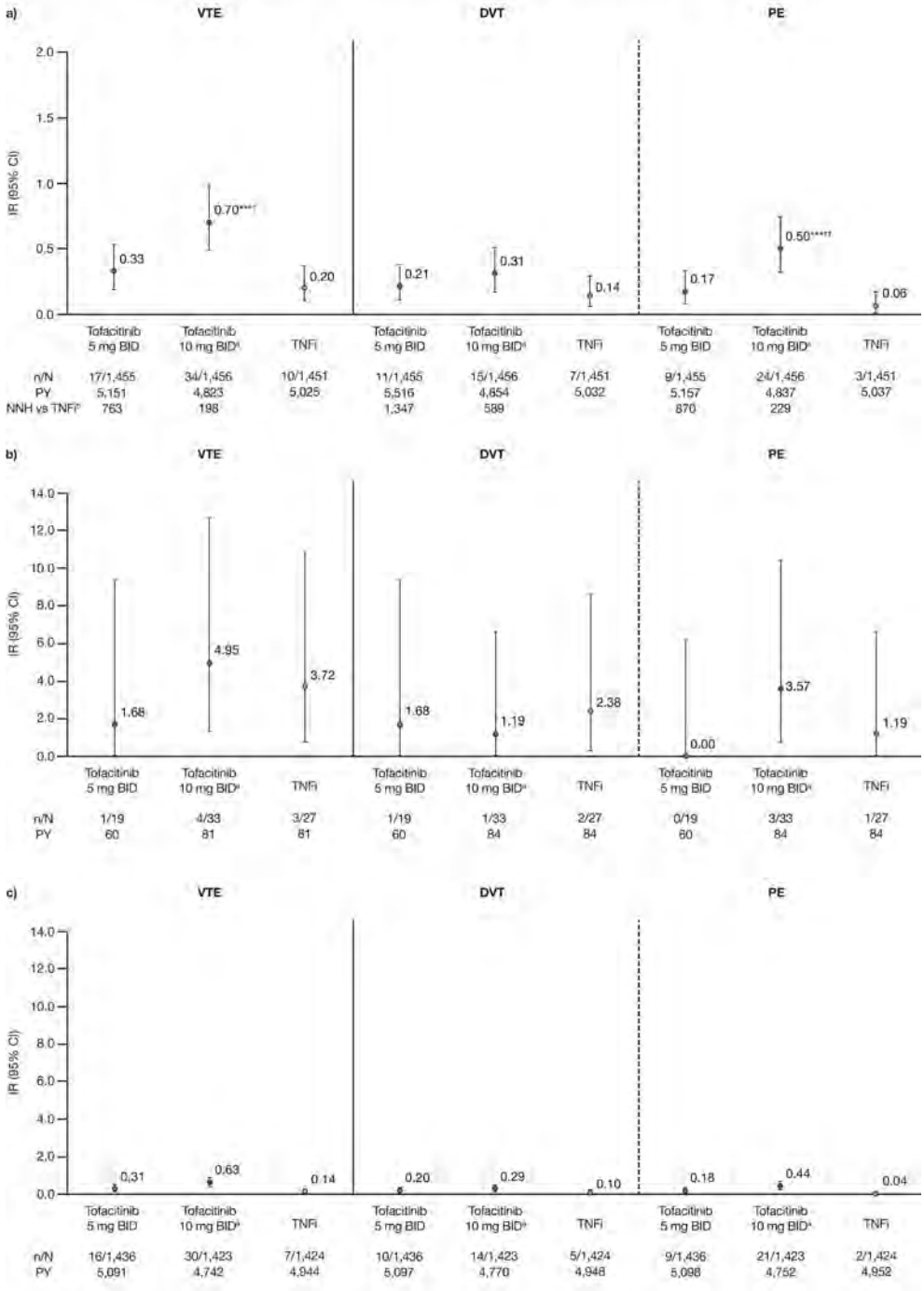
Background/Purpose: ORAL Surveillance (NCT02092467) was a randomized, open-label, non-inferiority, Phase 3b/4 study that assessed the relative risk of major adverse cardiovascular (CV) events (MACE) and malignancies with tofacitinib 5 and 10 mg twice daily (BID) vs TNF inhibitors (TNFi) in patients (pts) with active, moderate to severe RA, who had an inadequate response to MTX and a high risk of MACE (age ≥ 50 yrs; ≥ 1 additional CV risk factor). This analysis assessed the risk of venous thromboembolic events (VTE; including deep vein thrombosis [DVT] and pulmonary embolism [PE]) in ORAL Surveillance.

Methods: Pts were randomized 1:1:1 to receive tofacitinib 5 or 10 mg BID or a TNFi (etanercept 50 mg every week or adalimumab 40 mg every 2 weeks) with background MTX. A 2019 review by the Tofacitinib Rheumatology Data Safety Monitoring Board observed a statistically and clinically important difference in the occurrence of PE within the tofacitinib 10 mg BID treatment arm, compared with the TNFi control arm, resulting in a dose switch from tofacitinib 10 to 5 mg BID for the rest of the trial. All data are reported per randomized treatment. Incidence rates (IRs; pts with events/100 pt-yrs [PY]) were reported for adjudicated VTEs, DVT, and PE, and nominal p values comparing treatment arms were generated post hoc. The probability of not having an adjudicated event was assessed by Kaplan-Meier plots. Numbers Needed to Harm (NNH) were calculated post hoc. Multivariate Cox regression models were used post hoc to identify overall independent baseline (BL) risk factors for PE using backward model selection.

Results: This analysis included 1,455, 1,456, and 1,451 pts receiving tofacitinib 5 mg BID, 10 mg BID, and TNFi, respectively; BL pt characteristics were similar across treatment groups, with high mean disease activity (Clinical Disease Activity Index score, 39.7–39.9) and mean/median age of 61.2/60.0 yrs. In pts with VTE (n=66), mean age was 62.9–66.5 yrs across treatment groups. IRs for VTE, DVT, and PE were < 1.0 across treatment groups (Figure 1a); VTE, DVT, and PE IRs and probability of event were higher with tofacitinib 10 vs 5 mg BID, and higher for both tofacitinib doses vs TNFi (Figure 1a, Figure 2). NNH for tofacitinib 5 and 10 mg BID, respectively, vs TNFi were 763 and 198 PY for VTE, 1,347 and 589 PY for DVT, and 870 and 229 PY for PE. Across treatment groups, VTE, DVT, and PE IRs were higher in pts with vs without a history of VTEs (Figure 1b–c). Identified overall independent risk factors for PE across treatment groups included history of VTE; BL use of oral contraceptives or HRT; BL BMI ≥ 30 kg/m^2; age ≥ 65 yrs; and history of hypertension (Figure 3).

Conclusion: VTE, DVT, and PE IRs were higher for tofacitinib (10 > 5 mg BID) vs TNFi, and were < 1.0 across treatment groups. IRs were generally consistent with ranges reported for tofacitinib and biologic DMARDs among pts at

Figure 1. IRs (95% CI) for adjudicated VTE, DVT, and PE in a) all pts, b) pts with a history of VTE, and c) pts without a history of VTE



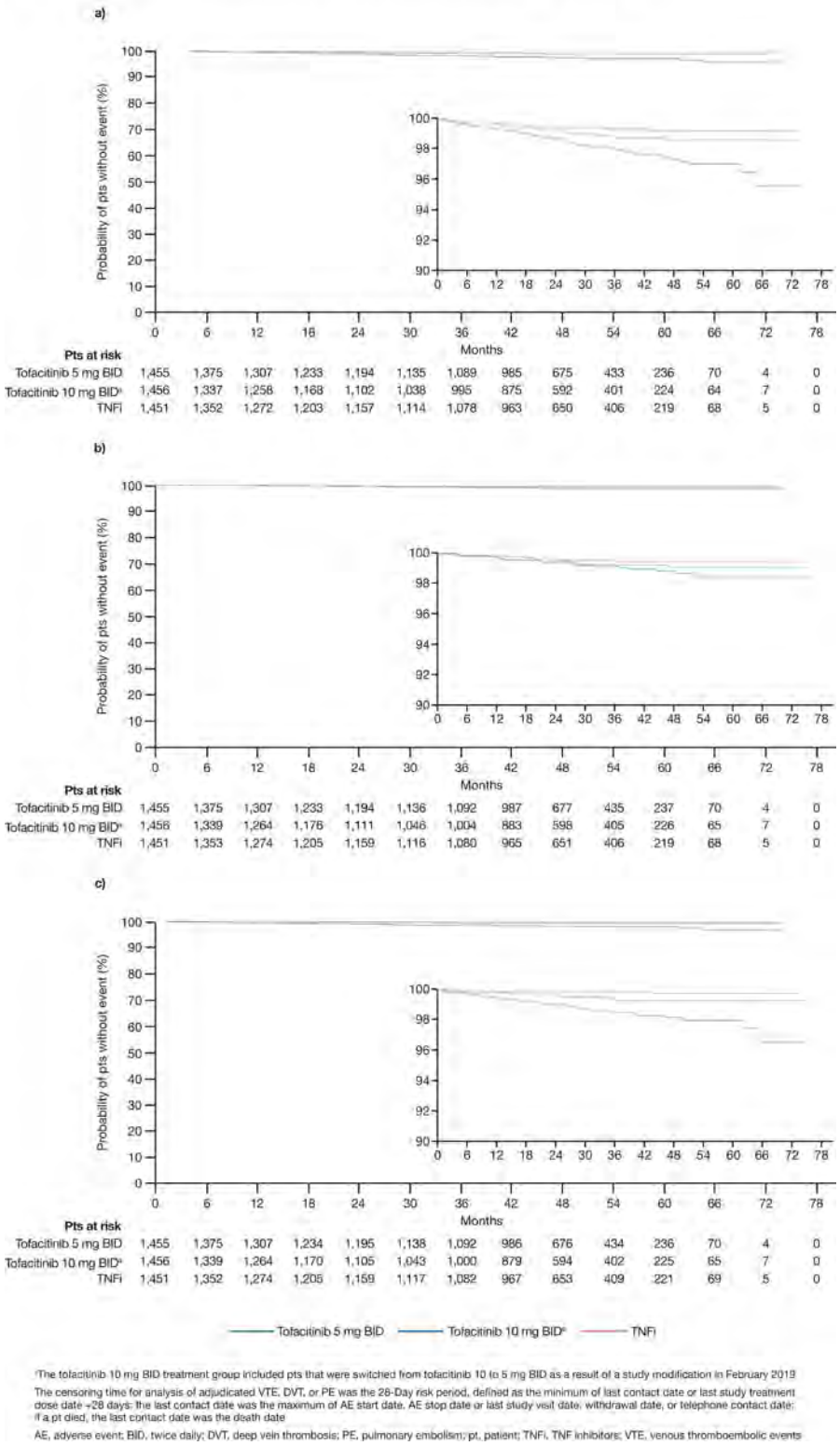
‡The tofacitinib 10 mg BID treatment group included pts that were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019; §NNH was defined as the number of PY of exposure needed for 1 more pt to report an event with tofacitinib vs TNFi

***Nominal p < 0.001, for tofacitinib vs TNFi; †nominal p ≤ 0.05; ††nominal p < 0.01, for tofacitinib 10 vs 5 mg BID

Nominal p values (for descriptive purpose and hypothesis generating only) were based on a univariate Cox proportional hazard model, with treatment as a covariate; the censoring time for analysis of adjudicated VTE, DVT, or PE was the 28-Day risk period, defined as the minimum of last contact date or last study treatment dose date +28 days; the last contact date was the maximum of AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date; if a pt died, the last contact date was the death date

AE, adverse event; BID, twice daily; CI, confidence interval; DVT, deep vein thrombosis; IR, incidence rate (pts with events per 100 PY); N, number of pts in a treatment group; n, number of pts with an event; PE, pulmonary embolism; pt, patient; PY, pt-yrs; TNFi, TNF inhibitors; VTE, venous thromboembolic events

Figure 2. Kaplan-Meier plots of probability of not having an adjudicated event of a) VTE, b) DVT, and c) PE



[a]The tofacitinib 10 mg BID treatment group included pts that were switched from tofacitinib 10 to 5 mg BID as a result of a study modification in February 2019

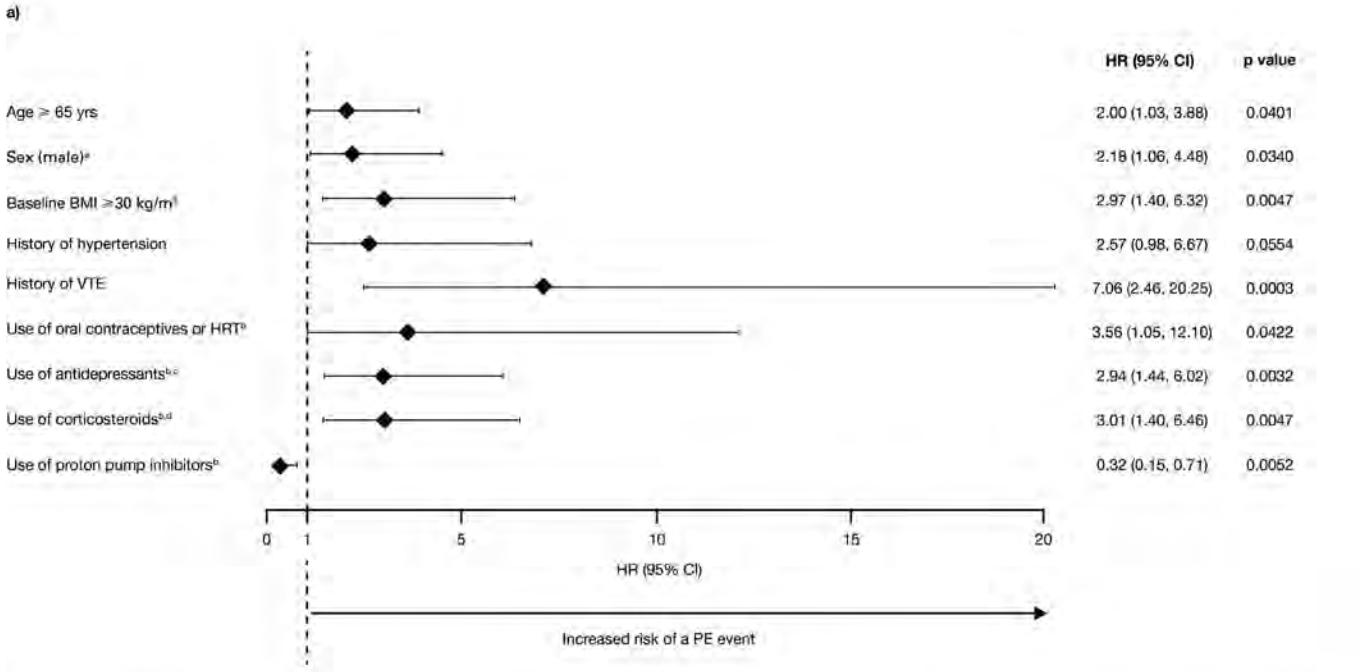
The censoring time for analysis of adjudicated VTE, DVT, or PE was the 28-Day risk period, defined as the minimum of last contact date or last study treatment dose date +28 days; the last contact date was the maximum of AE start date, AE stop date or last study visit date, withdrawal date, or telephone contact date; if a pt died, the last contact date was the death date

AE, adverse event; BID, twice daily; DVT, deep vein thrombosis; PE, pulmonary embolism; pt, patient; TNFi, TNF inhibitors; VTE, venous thromboembolic events

a high risk of a CV event;[1] PE IR with tofacitinib 10 mg BID in ORAL Surveillance was higher than those reported in tofacitinib or biologic DMARD clinical trial or registry data.[1]

1. Mease P et al. Ann Rheum Dis 2020; 79: 1400-13

Figure 3. Multivariate Cox regression analyses for identifying overall independent risk factors across treatment groups for PE



[a]HR for sex (male) demonstrated a statistically significant HR in previous univariate analyses (HR 1.80 [95% CI 0.90, 3.61]), but HRs in this analysis were inconsistent between the tofacitinib 5 and 10 mg BID groups (HRs 0.52 and 2.43, respectively), and the overall HR for combined tofacitinib doses was similar to TNFi, therefore the impact of sex on PE risk was considered inconclusive; [b]Use at baseline; [c]Baseline antidepressant use was an indicator of an underlying condition of depression, and subgroup analysis did not identify any difference in HRs for depression across treatment groups; [d]Baseline corticosteroid use was a proxy for elevated baseline disease activity; HRs for baseline corticosteroid use were similar between all tofacitinib doses combined and TNFi

Multivariate Cox regression model using backward selection included effects of treatment (ie tofacitinib 5 and 10 mg BID, and TNFi; not subject to model selection) and overall potential independent risk factors (ie those affecting PE IRs equally across all 3 treatment groups; subject to model selection) identified from a prior set of Cox regression analyses (which included treatment and a single candidate risk factor in each model fitting, cycling through a predetermined set of risk factors); the cut-off for a risk factor to stay in the model was $p < 0.10$

The censoring time for analysis of adjudicated PE was the 28-Day risk period, defined as the minimum of last contact date or last study treatment dose date +28 days; the last contact date was the maximum of AE start date, AE stop date, last study visit date, withdrawal date, or telephone contact date; if a pt died, the last contact date was the death date

AE, adverse event; BID, twice daily; CI, confidence interval; HR, hazard ratio; IR, incidence rate (pts with events per 100 PY); PE, pulmonary embolism; pt, patient; PY, pt-yrs; TNFi, TNF inhibitors; VTE, venous thromboembolic events

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Abstract Number: 1942

Occurrence of Basal Cell and Squamous Cell Carcinomas of the Skin Under Different DMARD Therapies

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: RA – Treatments I: Safety & Harms (1939–1942)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: Squamous and basal cell carcinomas are the most common malignancies of the skin; they are subsumed under non-melanoma skin cancer (NMSC). The risk of NMSC is increased with sun exposure. Whether treatment with certain DMARDs influences their occurrence is not clear. A study of Swedish registry data reported an increased risk of NMSC in patients with rheumatoid arthritis (RA) treated with abatacept, calling for replication (1). Using data from the German RABBIT registry, we studied the risk of NMSC under different DMARD therapies.

Methods: Data from patients with RA who were enrolled in RABBIT with the start of a biologic (b), conventional synthetic (cs) or targeted synthetic (ts) DMARD treatment were analyzed. Patients enrolled between January 2007 and October 2020 with at least one follow-up visit were included. Crude incidence rates of NMSC under different treatments using an induction period of 3 months were determined. Adjusted hazard ratios (HRs) of NMSC were calculated using Cox regression. Further adjustment for factors influencing treatment decision ("confounding by indication") was performed using inverse probability weighting (IPW).

Results: A total of 13,870 patients were included in the analysis. There were 17 squamous cell carcinomas (0.12%) and 120 basal cell carcinomas (0.85% of patients) reported. Clear differences in patient characteristics at the start of each treatment (table 1) were seen between the classic first-line bDMARDs (tumour necrosis factor (TNF) inhibitors) and the second-line bDMARDs, with longer disease duration, significantly more severe functional limitations, higher number of prior treatment failures and more comorbidities. A comparison of crude incidence rates of NMSC under different DMARD treatments showed that the occurrence of NMSC was significantly more frequent under abatacept than under TNF inhibitors (figure).

In the adjusted Cox regression, a significantly increased risk of NMSC was observed with abatacept treatment (HR: 2.00 [95% confidence interval, CI: 1.28-3.11]) compared to csDMARD treatment. Furthermore, increasing age and number of comorbidities were significantly associated with a higher risk of NMSC occurrence (table 2). In the analysis performed with IPW, the effect for abatacept was amplified (HR: 2.18 [95% CI: 1.30-3.65]), with age and number of comorbidities also remaining significantly associated with a higher risk of NMSC (table 2).

Conclusion: This analysis of a prospective cohort study investigated the incidence rates and risk of NMSC in RA patients treated with different modes of action. Basal cell and squamous cell carcinomas were most commonly reported with abatacept treatment. Even after adjusting for differences in patient characteristics, there was a significantly increased risk of NMSC in patients treated with abatacept. It should be noted that patients initiated abatacept therapy

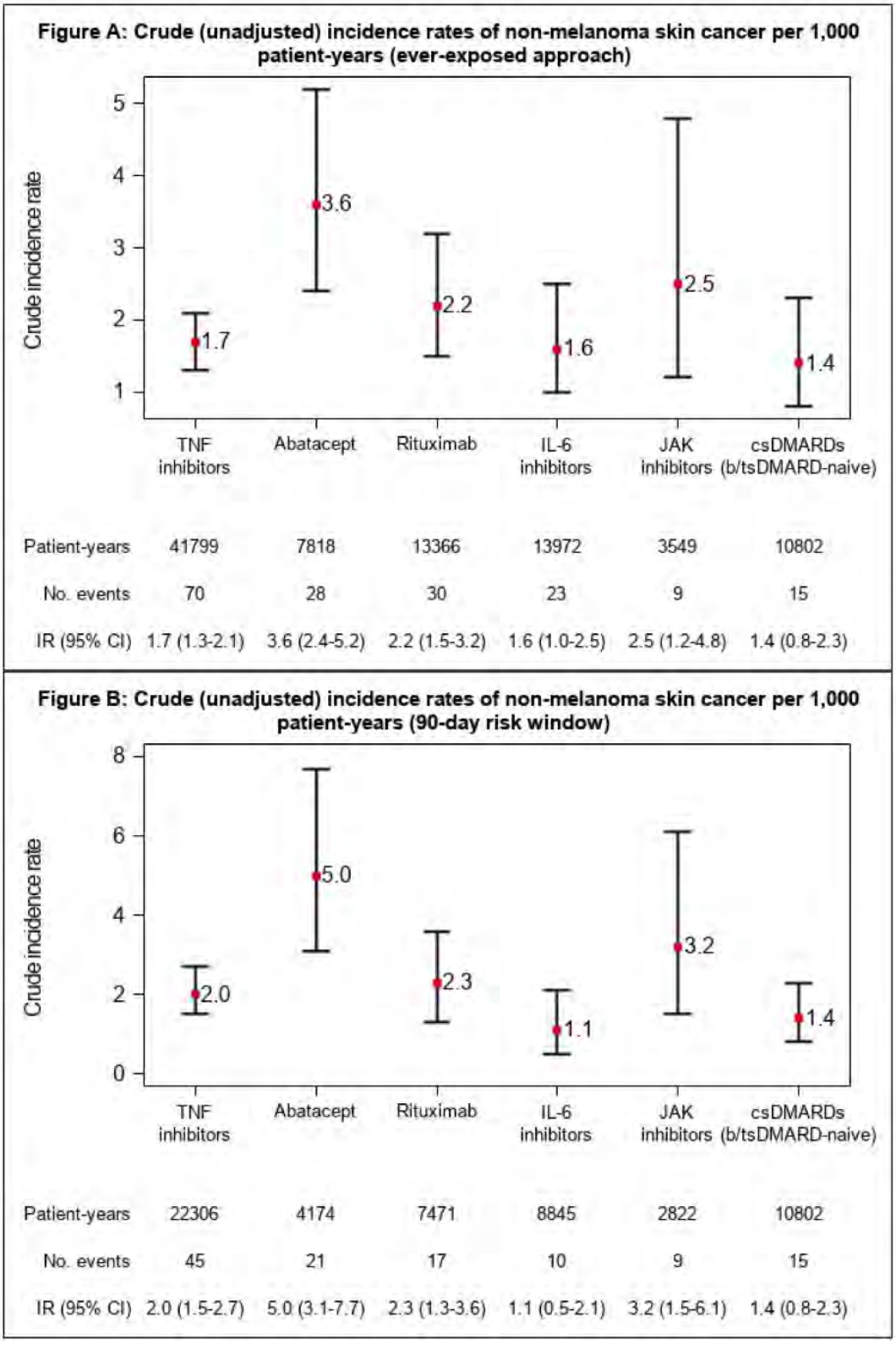

Figure 1. Crude incidence rates of non-melanoma skin cancer under different DMARD treatments.

had higher burden of comorbidity and considerable differences compared to all other treatment options. The higher risk of NMSC may be attributed to residual and unmeasured confounding due to higher burden of comorbidity or cumulative effect of therapies when used as a second or third line bDMARD.

Table 1. Characteristics of patients (N=13,870) at the beginning of a therapy episode

	TNF inhibitors	Abatacept	Rituximab	IL-6 inhibitors	Janus kinase inhibitor	csDMARDS (b/tsDMARD-naive)
No. of therapy episodes	7647	1934	2351	3243	2173	3782
Women	73.7%	76.5%	75.2%	76.2%	77.3%	73.8%
Age, y (MV)	56.9	58.4	58.4	57.2	59.8	59.0
Duration of illness, y (MV)	7.1	10.1	11.1	8.9	10.1	3.1
FFbH, 0-100% (MV)	67.0	59.3	57.9	65.5	65.7	72.0
DAS28, 0-10 (MV)	4.6	4.8	5.1	4.5	4.4	4.4
CRP, mg/l (median)	5.1	8.0	6.1	4.9	6.2	4.0
No. comorbidities (MV)	2.0	4.0	2.0	1.2	1.8	1.8
No. csDMARD failure (MV)	2.4	2.8	3.0	2.6	2.4	2.3
No. b/tsDMARD failure (MV)	1.5	2.9	2.8	2.5	3.0	0.0

No.: number; b/cs/tsDMARD: Biological/conventional synthetic/targeted synthetic DMARD; CRP: C-reactive protein; DAS28: Disease Activity Score with 28 joints; FFbH: Function Questionnaire Hanover (0-100); MV: mean value; TNF: Tumornecrosisfactor; y: year

Table 2. Risk of non-melanoma skin cancer: results of multivariable Cox regression analysis with and without inverse probability weighting (IPW). Therapies were analysed with an ever-exposed approach using an induction period of 3 months

	Model without IPW		Model with IPW	
	Adjusted HR (95% CI)	P-value	Adjusted HR (95% CI)	P-value
Gender, female vs. male	0.87 (0.71-1.07)	0.1856	0.87 (0.68-1.10)	0.2447
Age per 10 years	1.65 (1.37-2.00)	**<.0001**	1.79 (1.47-2.18)	**<.0001**
DAS28 per unit	0.92 (0.78-1.07)	0.2709	0.86 (0.72-1.02)	0.0909
Smoking, ever vs. never	0.90 (0.61-1.34)	0.6037	0.79 (0.49-1.26)	0.3228
Psoriasis, yes vs. no	1.24 (0.45-3.42)	0.6735	1.13 (0.37-3.43)	0.8306
Comorbidities per unit	1.11 (1.03-1.19)	**0.0060**	1.11 (1.03-1.19)	**0.0045**
csDMARDs treatment (b/tsDMARD-naive)	*Reference*		*Reference*	
TNF inhibitors	1.07 (0.73-1.56)	0.7206	1.01 (0.66-1.55)	0.9501
Abatacept	2.00 (1.28-3.11)	**0.0023**	2.18 (1.30-3.65)	**0.0030**
Rituximab	0.93 (0.57-1.50)	0.7604	0.89 (0.52-1.53)	0.6717
IL-6 inhibitors	0.75 (0.47-1.19)	0.2211	0.80 (0.46-1.38)	0.4215
Janus kinase inhibitors	1.29 (0.65-2.58)	0.4643	0.90 (0.42-1.93)	0.7940

b/cs/tsDMARD: biological/conventional synthetic/targeted synthetic DMARD; DAS28: Disease Activity Score with 28 joints; HR: hazard ratio; IPW: inverse probability weighting; CI: confidence interval; TNF: tumour necrosis factor.

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Abstract Number: 1943

Post-inflammatory and Degenerative Changes in Patients with Psoriatic Arthritis and Axial Manifestations: Post-hoc Analysis from a Double-blind, Randomized, Phase 3b Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment II: Biologic Therapies (1943–1946)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

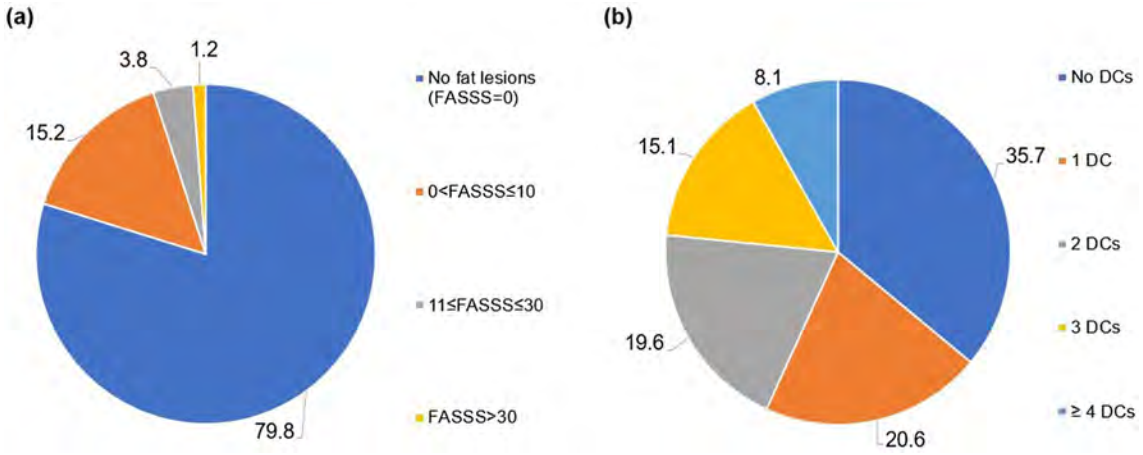

Figure 1. (a) Prevalence of FASSS categories (b) Prevalence of degenerative changes DC, degenerative change; FASSS, FAt Spondyloarthritis Spine Score.

Background/Purpose: Axial psoriatic arthritis (PsA) is the only one of the PsA manifestations, still not clearly defined, with no currently available universally acceptable clinical and imaging criteria.[1] MAXIMISE, the first RCT which has proven efficacy of a bDMARD in the management of axial manifestations of PsA, provides a dataset of MRIs in a population of PsA patients (pts) with a clinical diagnosis of axial disease and may address the gap in determining the role of MRI in diagnosis and classification of axial PsA.[2] So far, structural lesions such as fat lesions, which were shown to follow resolution of inflammation in the spine of pts with axial spondyloarthritis (axSpA) [3] or the presence of degenerative changes (DCs) which may delay or confound the diagnosis of axial PsA have not been assessed in any PsA cohort with axial involvement. This post-hoc exploratory analysis of baseline MRIs from the MAXIMISE trial[2] investigated: (1) the post-inflammatory changes by FAt Spondyloarthritis Spine Score (FASSS) [4], (2) the inflammatory changes in the posterior spinal elements (spinal process) and (3) the prevalence of DCs. [5]

Table 1: Specific degenerative changes (combined locations) by whole spine and spinal sub-locations (overall population)

Variable, n (%)	Whole spine	Cervical	Thoraic	Lumbar
Modic	107 (22.1)	26 (5.4)	10 (2.1)	88 (18.1)
Schmorl's Node with or without BME	57 (11.8)	2 (0.4)	44 (9.1)	22 (4.5)
Disc herniation/high intensity zone	178 (36.7)	102 (21.0)	29 (6.0)	116 (23.9)
Erosion	33 (6.8)	2 (0.4)	10 (2.1)	26 (5.4)
Sclerosis	1 (0.2)	0	1 (0.2)	0
Pfirrmann grade ≥3	248 (51.1)	80 (16.5)	39 (8.0)	203 (41.9)

The following changes such that a score of 1 on either denotes an overall score of 1, were combined as follows: Modic 1 and Modic 2; Schmorl's node with BME and Schmorl's node without BME; disc herniation and high intensity zone. Pfirrmann grade was dichotimized at each DVU: a score of 1 or 2 = 0; a score of 3 or greater = 1. BME, Bone marrow edema; DVU, disco-vertebral unit; n, number of patients with at least one DVU showing as 'present' for the associated spinal degenerative change variable in the whole spine

Methods: The baseline spinal-MRIs (T1 and STIR) for pts from the MAXIMISE trial fulfilling the pre-defined clinical criteria for active axial disease (BASDAI ≥4, spinal pain (VAS) ≥40 and inadequate response to ≤ 2 NSAIDs, N=485) were re-read. FASSS is a scoring method which addresses the spectrum of fat lesions according to anatomical localization and phenotypic diversity with a sum score ranging from 0 to 456 for the 23 disco-vertebral units (DVUs) [4]. Spinal process inflammation (SPi) was documented. The degenerative changes i.e., Modic 1, Modic 2, Schmorl's node with or without bone marrow oedema (BME), disc degeneration (herniation or marginally located high intensity zone), erosion, sclerosis, Pfirrmann changes, were also included in the reading protocol.[3, 5]

Results: For approximately 80% of the pts, no fat lesions were identified **(Figure 1a)**. The mean (SD) FASSS at baseline for the overall population was 1.8 (5.7), 0.2 (1.2), 1.0 (3.6) and 0.6 (1.9) for the whole spine, cervical, thoracic, and lumbar regions, respectively. SPi were documented for 11.1% of the patients. Approximately 63% of the pts had at least one type of DC **(Figure 1b)**. The most prevalent DCs for the overall population were: Pfirrmann changes (grade ≥3), 51.1%; disc degeneration, 36.7%; Modic 1 or Modic 2, 22.1%; Schmorl's node with or without BME, 11.8 %. The proportion of pts with specific changes in the spinal sub-locations are presented in **Table 1**.

Conclusion: Re-reading the baseline MRIs from the MAXIMISE trial, the largest cohort of PsA pts with active axial disease diagnosed by clinical criteria, revealed fat lesions and DCs for approximately 20% and 63% of the pts, respectively, while SPi occurred much less frequently. These data shed light into the imaging characteristics of patients with PsA and axial manifestations.

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Abstract Number: 1944

Sustained Remission/Low Disease Activity Is Feasible in the Long Term in Patients with Psoriatic Arthritis Treated with IL-23/12 Inhibition with Ustekinumab (STELARA®) and Tumor Necrosis Factor Inhibitors in a Real-World, Multicenter Study

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment II: Biologic Therapies (1943–1946)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

Background/Purpose: Among treatment options for PsA, IL-23/12 inhibition with ustekinumab (UST) was the first new biologic after TNF inhibitors (TNFi). Few data compare long-term effectiveness between UST and TNFi. Here we present the final 3-year analysis from the real-world PsABio study, focusing on the achievement of minimal disease

Table 1. Observed baseline characteristics of overall patients (n=895) and remainers (n=374)

Mean (95% CI)	UST (overall)	TNFi (overall)	UST (remainers)	TNFi (remainers)
N	439	456	186	188
Age, years	**51.1 (49.9 ; 52.2)**	**48.5 (47.3 ; 49.6)**	**51.5 (49.6 ; 53.4)**	**46.4 (44.6 ; 48.3)**
Male, %	43.7 (39.0 ; 48.5)	45.6 (41.0 ; 50.3)	46.2 (38.9 ; 53.7)	58.0 (50.6 ; 65.1)
BMI, kg/m^2	28.6 (28.0 ; 29.2)	27.8 (27.2 ; 28.3)	29.0 (28.0 ; 30.0)	27.3 (26.6 ; 28.1)
Time since initial diagnosis, years	7.5 (6.7 ; 8.3)	6.2 (5.6 ; 6.9)	7.7 (6.5 ; 8.9)	6.74 (5.8 ; 7.7)
Cardiometabolic disease, %	41.9 (37.3 ; 46.7)	35.5 (31.1 ; 40.1)	44.6 (37.3 ; 52.1)	33.0 (26.3 ; 40.2)
Dactylitis at baseline, %	18.1 (14.5 ; 22.2)	22.6 (18.6 ; 27.0)	20.2 (14.7 ; 26.8)	28.4 (22.0 ; 35.5)
Enthesitis at baseline, %	47.8 (42.8 ; 52.8)	50.9 (45.9 ; 55.9)	48.9 (41.5 ; 56.4)	50.3 (42.9 ; 57.6)
Line of bDMARD treatment, %				
First line	**45.1 (40.4 ; 49.9)**	**55.0 (50.3 ; 59.7)**	47.8 (40.5 ; 55.3)	58.0 (50.6 ; 65.1)
Second line	34.4 (30.0 ; 39.0)	32.9 (28.6 ; 37.4)	33.3 (26.6 ; 40.6)	32.4 (25.8 ; 39.6)
Third line	**20.5 (16.8 ; 24.6)**	**12.1 (9.2 ; 15.4)**	18.8 (13.5 ; 25.2)	9.6 (5.8 ; 14.7)
PsA characteristics, %				
Axial involvement*	2.7 (1.4 ; 4.7)	2.4 (1.2 ; 4.3)	3.2 (1.2 ; 6.9)	3.2 (1.2 ; 6.8)
Oligoarticular	22.4 (18.6 ; 26.7)	29.0 (24.8 ; 33.4)	28.8 (22.4 ; 35.9)	30.1 (23.5 ; 37.3)
Polyarticular	66.8 (62.1 ; 71.3)	63.8 (59.2 ; 68.3)	61.4 (54.0 ; 68.5)	63.9 (56.5 ; 70.9)
BSA, %				
Clear/almost clear	29.4 (24.7 ; 34.4)	32.8 (27.9 ;37.9)	18.8 (13.2 ; 25.5)	30.4 (23.5 ;37.9)
<3% but not clear/almost clear	10.0 (7.1 ; 13.5)	15.1 (11.6 ;19.3)	8.2 (4.6 ; 13.4)	17.9 (12.4 ; 24.5)
3–10%	34.3 (29.5 ; 39.5)	37.3 (32.2 ; 42.5)	35.9 (28.7 ; 43.6)	35.1 (27.9 ; 42.8)
>10%	**26.3 (21.8 ; 31.2)**	**14.8 (11.3 ; 19.0)**	**37.1 (29.8 ; 44.8)**	**16.7 (11.4 ; 23.2)**
cDAPSA	30.4 (28.4 ; 32.5)	29.1 (27.2 ; 31.0)	29.7 (26.7 ; 32.7)	29.5 (26.7 ; 32.3)
Swollen joint count (66 joints)	5.8 (5.0 ; 6.6)	5.9 (5.2 ; 6.7)	5.7 (4.5 ; 6.9)	6.5 (5.4 ; 7.6)
Tender joint count (68 joints)	12.3 (11.1 ; 13.6)	11.2 (10.1 ; 12.3)	12.5 (10.5 ; 14.4)	11.4 (9.8 ; 13.0)
CRP (mg/dL)	1.3 (1.0 ; 1.7)	1.4 (1.1 ; 1.7)	1.8 (1.1 ; 2.4)	1.4 (1.1 ; 1.8)
Total PsAID score (over past week)	5.7 (5.5 ; 5.9)	5.5 (5.3 ; 5.7)	5.4 (5.0 ; 5.7)	5.3 (5.0 ; 5.6)

Bold text indicates significant differences (non-overlapping 95% CI).

*Denotes physician-confirmed isolated axial PsA.

bDMARD, biologic DMARD; BMI, body mass index; BSA, body surface area; cDAPSA, clinical Disease Activity in Psoriatic Arthritis; CI, confidence interval; CRP, C-reactive protein; N/A, not available; PsAID, Psoriatic Arthritis Impact of Disease; TNFi, TNF inhibitor; UST, ustekinumab.

activity (MDA)/very low disease activity (VLDA) and low disease activity (LDA) or remission, as measured by clinical disease activity in psoriatic arthritis (cDAPSA).

Methods: The PsABio study (NCT02627768) evaluated effectiveness, tolerability and persistence of 1st, 2nd, or 3rd-line UST or TNFi in patients (pts) with PsA. Here we present proportion of pts reaching MDA/VLDA and cDAPSA LDA or remission up to 3 years (assessments for pts under the initial treatment at 3 years). Descriptive statistics included the last observation carried forward (LOCF) endpoint created in case of missing 3-year effectiveness data; for example, due to COVID-19. Cohort comparison was done among pts who stayed on their initial UST or TNFi treatment for the full 3 years (remainer analysis), and among those who switched/stopped their original treatment, imputed as non-responders (overall analysis). Logistic regression analysis presenting odds ratios (ORs) and 95% confidence intervals (CIs), including propensity score (PS), stratified on quintiles (inverse probability of treatment weighting as sensitivity analysis) to adjust for imbalanced baseline (BL) covariates.

Results: The overall analysis (n=895) included 439 UST and 456 TNFi-treated pts who had evaluable BL and follow-up data up to 3 years. The remainer analysis included 186 (42.4%) UST and 188 (41.2%) TNFi-treated pts staying on their initial treatment up to 36 ± 3 months. In both the overall and remainer analyses, UST and TNFi groups had significant BL differences in age and psoriasis skin involvement (body surface area >10%); in the overall analysis, significant difference was seen for 1st and 3rd bDMARD line of treatment (**Table 1**).

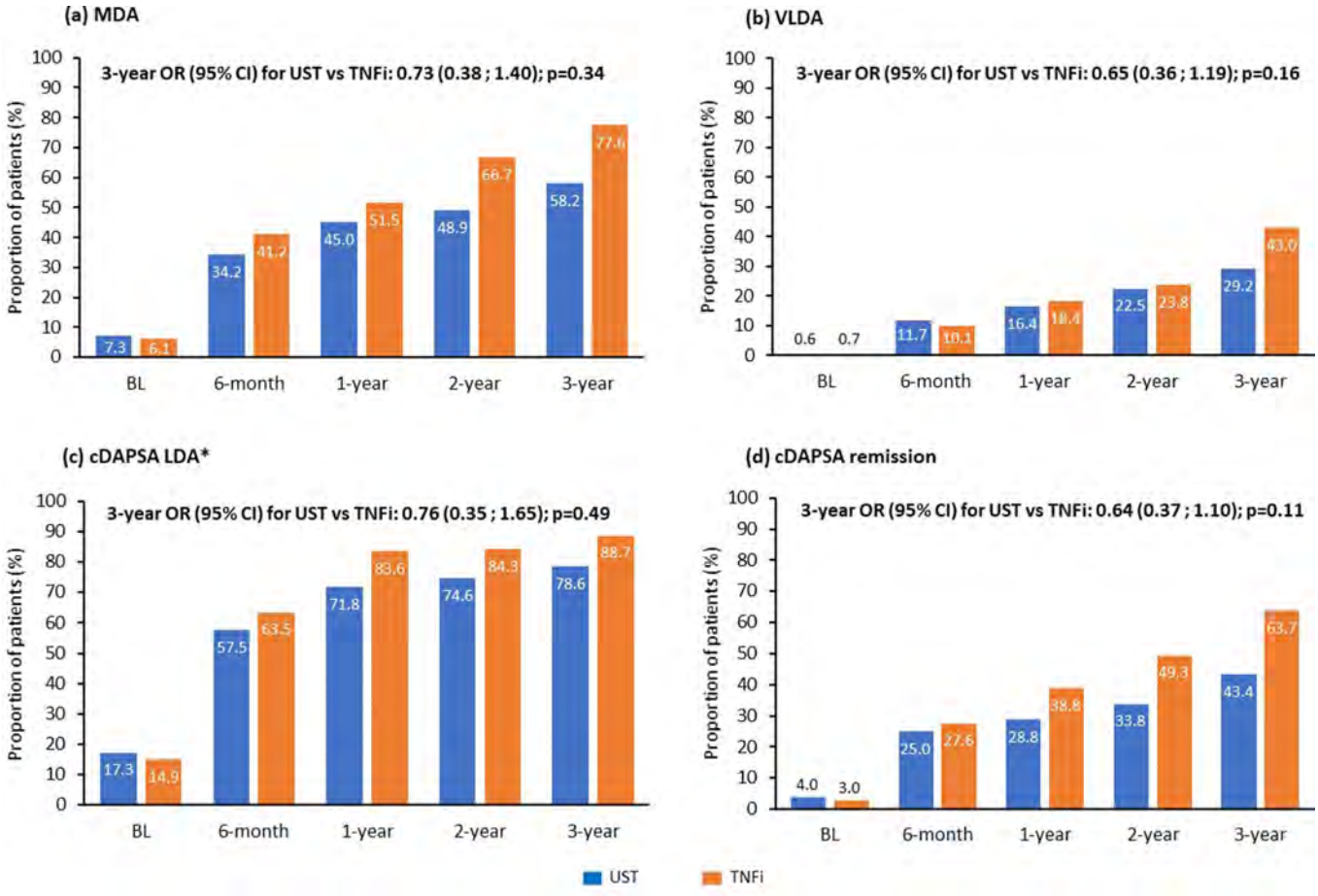

Figure 1. Observed proportions of patients and PS-adjusted ORs (95% CI) achieving: (a) MDA; (b) VLDA; (c) cDAPSA LDA; and (d) cDAPSA remission with UST or TNFi up to 3 years (remainer analysis). Results reflect 3-year LOCF data from assessments for patients still under initial treatment at 3 years. *Includes remission. BL, baseline; CI, confidence interval; LOCF, last observation carried forward; LDA, low disease activity; MDA; minimal disease activity; OR, odds ratio; PS, propensity score; TNFi, TNF inhibitor; UST, ustekinumab; VLDA, very low disease activity.

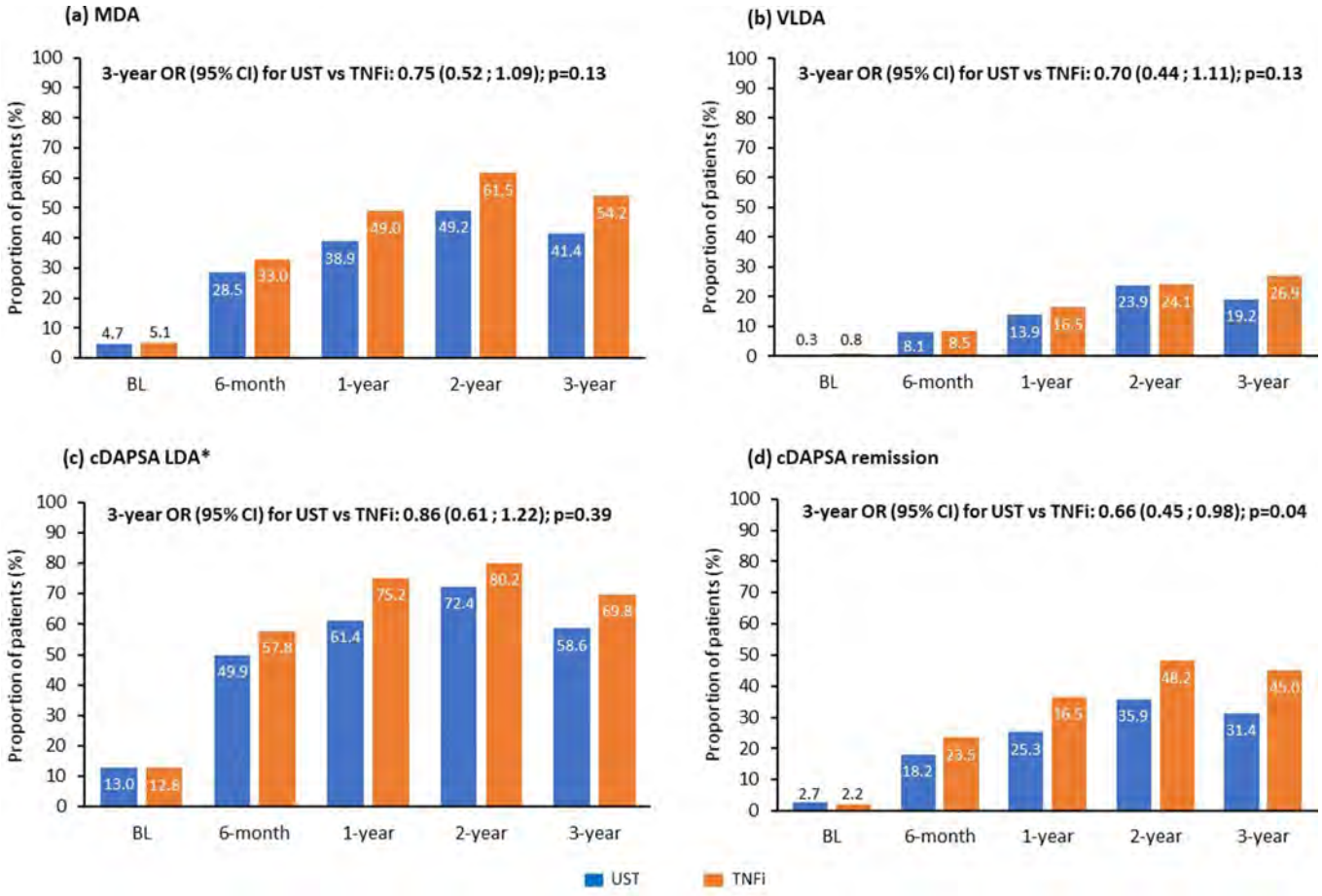

Figure 2. Observed proportions of patients and PS-adjusted ORs (95% CI) achieving: (a) MDA; (b) VLDA; (c) cDAPSA LDA; and (d) cDAPSA remission with UST or TNFi up to 3 years (overall analysis). The overall analysis included patients switching/stopping their original treatment during the 3-year observation period. The PS-adjusted ORs resulting from the overall analysis included non-response imputation in case of stop/switch initial treatment. *Includes remission. BL, baseline; CI, confidence interval; LOCF, last observation carried forward; LDA, low disease activity; MDA; minimal disease activity; OR, odds ratio; PS, propensity score; TNFi, TNF inhibitors; UST, ustekinumab; VLDA, very low disease activity.

In the remainer analysis, both UST and TNFi treatments led to a significant proportion of pts achieving MDA (up to 78%; **Figure 1a**), VLDA (up to 43%; **Figure 1b**), cDAPSA LDA (up to 89%; **Figure 1c**), and cDAPSA remission (up to 64%; **Figure 1d**). The PS-adjusted ORs (95% CI) indicated a similar response in both cohorts (**Figure 1a–d**). The overall analysis, which included pts switching/stopping initial treatment during the 3-year period, showed similar results (**Figure 2a–d**).

Conclusion: In the prospectively followed PsABio study across Europe, slightly more than 40% of pts with PsA stayed on UST or TNFi for 3 years or more. This long-term treatment, when used as 1st-, 2nd-, or 3rd-line bDMARD in a routine care setting, provided sustained improvement of disease signs and symptoms, enabling achievement of MDA, VLDA, cDAPSA LDA, or cDAPSA remission. While numerically more TNFi-treated pts achieved LDA or remission states, UST was used in more treatment-resistant patients and there was no statistical difference between the treatment groups; the improvements were maintained over the 3-year period. The findings demonstrate that remission/LDA are feasible when using targeted drugs in PsA.

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Abstract Number: 1945

Efficacy of Upadacitinib on Psoriatic Arthritis with Axial Involvement Defined by Investigator Assessment and PRO-Based Criteria: Results from Two Phase 3 Studies

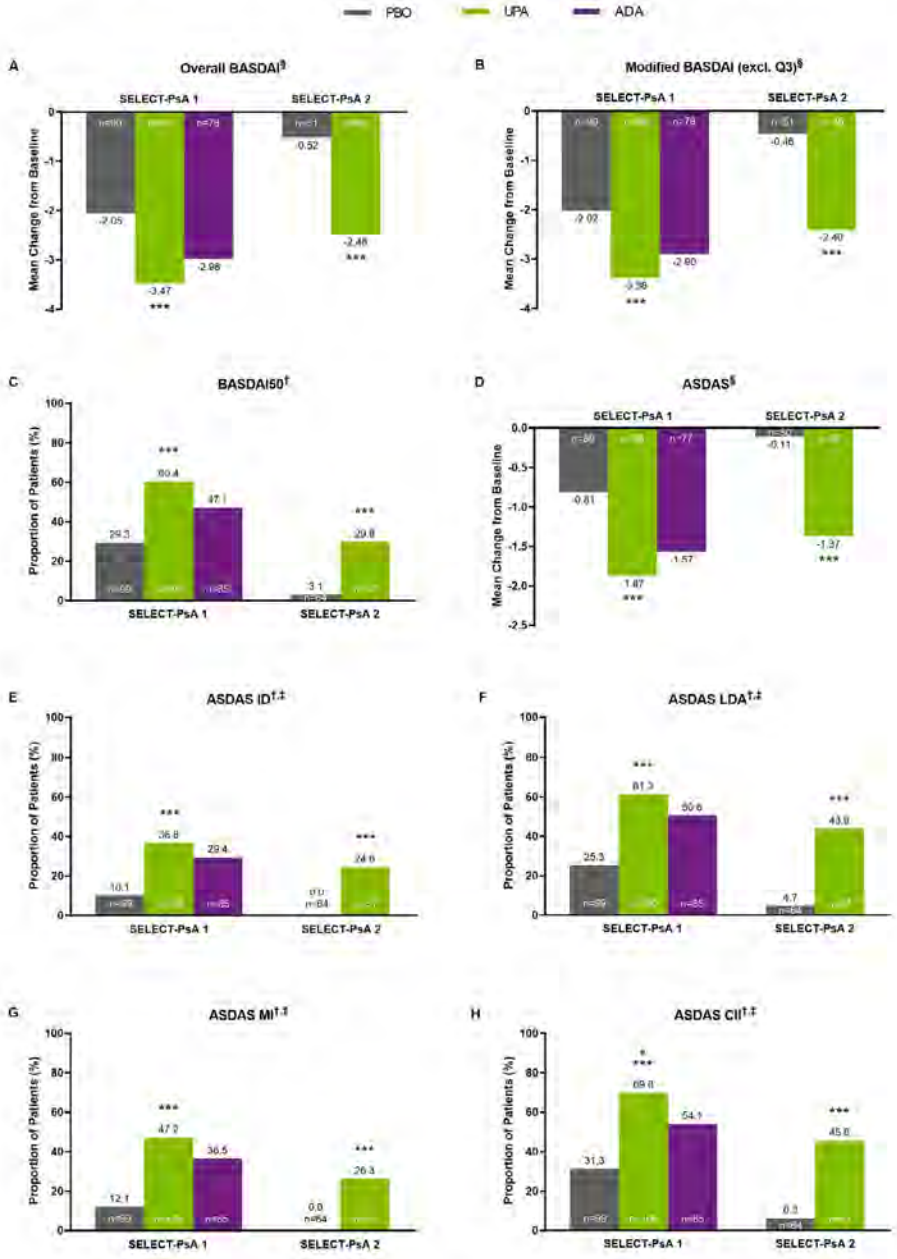
Xenofon Baraliakos[1], Roberto Ranza[2], Andrew Ostor[3], Francesco Ciccia[4], Laura Coates[5], Simona Rednic[6], Jessica Walsh[7], Tianming Gao[8], Apinya Lertratanakul[8], In-Ho Song[8], Fabiana Ganz[8], Kevin Douglas[8] and Atul Deodhar[9], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-Universität Bochum, Herne, Germany, [2]Hospital de Clinicas, Universidade Federal de Uberlândia, Uberlandia, MG, Brazil, [3]Monash University, Cabrini Hospital, and Emertius Research, Malvern, Australia, [4]University of Campania Luigi Vanvitelli, Napoli, Italy, [5]Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences, University of Oxford, Oxford, United Kingdom, [6]Emergency Clinical County Hospital, Rheumatology and Iuliu Hatieganu University of Medicine and Pharmacy, Cluj Napoca, Romania, [7]Salt Lake City Veteran Affairs Medical Center (VAMC)/University of Utah Hospital, Salt Lake City, UT, [8]AbbVie Inc., North Chicago, IL, [9]Oregon Health & Science University, Portland, OR

SESSION INFORMATION
Session Date: Tuesday, November 9, 2021
Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment II: Biologic Therapies (1943–1946)
Session Type: Abstract Session
Session Time: 4:00PM–5:00PM

Background/Purpose: Patients with PsA and axial involvement have higher disease activity and greater reductions in quality of life;[1] however, there are no accepted criteria for identifying axial involvement in PsA. The objective of this post-hoc analysis is to assess the efficacy of upadacitinib (UPA), a Janus kinase inhibitor, on axial symptoms in patients with active PsA and axial involvement defined by investigator assessment and PRO-based criteria from two phase 3 SELECT trials.[2,3]

Methods: Patients with active PsA (≥3 swollen joints and ≥3 tender joints) and prior inadequate response or intolerance to ≥1 non-biologic (SELECT-PsA 1) or ≥1 biologic (SELECT-PsA 2) DMARD were randomly assigned to once daily oral UPA 15 mg or 30 mg, placebo (PBO), or every other week subcutaneous adalimumab (ADA) 40 mg (SELECT-PsA 1 only).[2,3] At baseline, axial involvement in PsA was determined by investigator assessment based on the totality of clinical information, such as duration and character of back pain, age of onset, and previous imaging. In addition to investigator assessment, PRO-based criteria for axial involvement (BASDAI ≥4 and BASDAI Question 2 ≥4 at baseline) were applied for this analysis to identify patients with active disease. Efficacy in the sub-group of pa-

Figure: Clinical Responses in Patients with Axial Involvement Defined by Investigator Assessment and PRO-Based Criteria at Week 24 from SELECT-PsA 1 and SELECT-PsA 2



ADA, adalimumab; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CII, clinically important improvement; EOW, every other week; ID, inactive disease; LDA, low disease activity; MI, major improvement; MMRM, mixed-effect model repeated measures; NRI, non-responder imputation; PBO, placebo; QD, once daily; UPA, upadacitinib

***P<0.001, UPA 15 mg vs. PBO; *P<0.05, UPA 15mg vs. ADA; nominal P-values are presented and were not adjusted for multiple comparisons
†NRI analysis constructed using Cochran-Mantel-Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no) was used for binary endpoints
‡ASDAS thresholds: ID <1.3; LDA <2.1; MI change from baseline ≥2; CII change from baseline ≥1.1
§MMRM analysis with unstructured variance-covariance matrix, including treatment, visit, treatment-by-visit interaction, the stratification factor current DMARD use (yes/no) as fixed factors and the continuous fixed covariate of baseline measurement was used for continuous endpoints

tients defined using both investigator assessment and PRO-based criteria was evaluated at week 24 for UPA 15 mg vs PBO and ADA (SELECT-PsA 1 only). Data were analyzed using mixed-effect model repeated measures (MMRM) or non-responder imputation (NRI), with nominal *P*-values shown.

Results: Based on investigator assessment alone, 31.3% (n=534/1704) of patients in SELECT-PsA 1 and 34.2% (n=219/641) in SELECT-PsA 2 were defined as having axial involvement. When both investigator assessment and PRO-based criteria were applied, 23.1% (n=393/1704) of patients in SELECT-PsA 1, or 73.6% (n=393/534) of those defined using investigator assessment alone, and 27.5% (n=176/641) in SELECT-PsA 2, or 80.4% (n=176/219) using investigator assessment alone, met the combined criteria for axial involvement. In both studies, UPA 15 mg showed significantly greater clinical responses vs PBO at week 24 across all endpoints assessed (**Figure**). In SELECT-PsA 1, UPA showed numerically greater responses than ADA at week 24 across all BASDAI and Ankylosing Spondylitis Disease Activity Score (ASDAS) endpoints. The proportion of patients achieving ASDAS clinically important improvement (CII) at week 24 was significantly greater with UPA vs ADA based on nominal *P*-value.

Conclusion: Patients with active PsA and axial involvement defined by both investigator assessment and PRO-based criteria demonstrated statistically greater clinical responses related to their axial involvement with UPA 15 mg compared to PBO, and consistently numerically higher responses compared to ADA, at week 24 in the SELECT-PsA trials. Findings from this post-hoc analysis are consistent with previous data based on investigator assessment alone.[4]

References

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2. McInnes IB et al. *N Engl J Med*. 2021; 384(13):1227-39
3. Mease PJ et al. *Ann Rheum Dis*. 2020; 80(3):312-20
4. Deodhar A et al. *Arthritis Rheumatol*. 2020; 72(Suppl 10)

Disclosure: X. Baraliakos, AbbVie, 2, 5, 6, Chugai, 2, 5, 6, Novartis, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Bristol-Myers Squibb, 2, 5, 6, Celegene, 2, 5, 6, Merck, 2, 6, Werfen, 2; **R. Ranza**, AbbVie, 2, 6, Janssen, 2, 6, Novartis, 2, 6, Pfizer, 2, 6; **A. Ostor**, AbbVie, 2, 6, Bristol-Myers Squibb, 2, 6, Eli Lilly, 2, 6, Gilead, 2, 6, MSD, 2, 6, Novartis, 2, 6, Pfizer, 2, 6, Roche, 2, 6, Janssen, 1, 2, UCB, 1, 2, Paradigm, 1, 2; **F. Ciccia**, AbbVie, 2, 5, 6, Celgene, 2, 5, 6, Pfizer, 2, 5, 6, UCB, 2, 5, 6, Roche, 5, Bristol-Myers Squibb, 2, 6, MSD, 2, Novartis, 2, 6, Janssen, 2, Sanofi, 2, Sandoz, 2, Galapagos, 2, Sobi, 2; **L. Coates**, Abbvie, 5, 6, Amgen, 5, 6, Biogen, 6, Celgene, 5, 6, Gilead, 6, Janssen, 6, Eli Lilly, 5, 6, Medac, 6, Novartis, 5, 6, Pfizer, 5, 6, UCB Pharma, 6, Galapagos, 6, GSK, 6, Boehringer Ingelheim, 6, Domain, 2; **S. Rednic**, AbbVie, 2, 5, Boehringer Ingelheim, 2, 5, Eli Lilly, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 5; **J. Walsh**, AbbVie, 2, 5, Merck, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Eli Lilly, 1, 2, Novartis, 2, 5, Amgen, 2, 5; **T. Gao**, AbbVie, 3, 11; **A. Lertratanakul**, AbbVie, 3, 11; **I. Song**, AbbVie, 3, 11; **F. Ganz**, AbbVie, 3, 11; **K. Douglas**, AbbVie, 3, 11; **A. Deodhar**, Amgen, 2, Celgene, 2, Boehringer Ingelheim, 2, 12, Paid Instructor, AbbVie, 2, 5, Eli Lilly, 2, 5, Glaxo Smith & Kline, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, 6, 12, Paid Instructor, UCB, 2, 5, Janssen, 2, 6, Bristol-Myers Squibb, 2.

Abstract Number: 1946

Therapeutic Drug Monitoring Compared to Standard Infliximab Therapy in Patients with Immune-mediated Inflammatory Diseases: A Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Tuesday, November 9, 2021

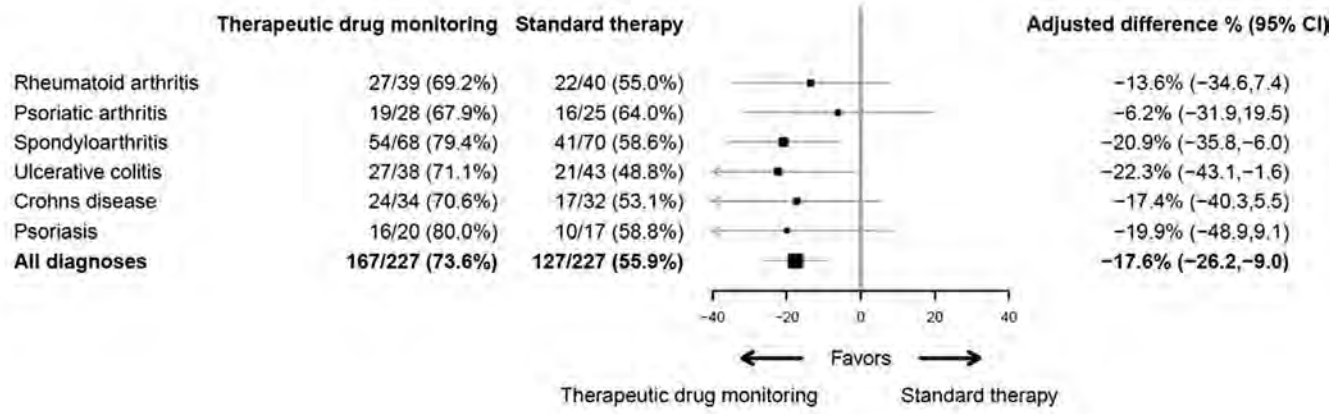
Session Title: Abstracts: Spondyloarthritis Including PsA – Treatment II: Biologic Therapies (1943–1946)

Session Type: Abstract Session

Session Time: 4:00PM–5:00PM

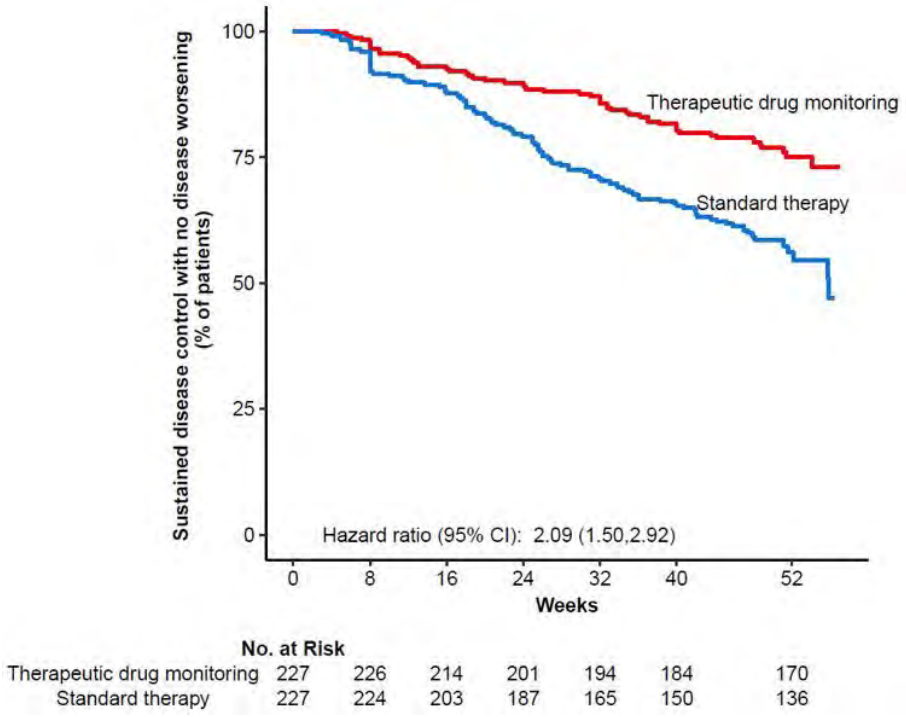
Background/Purpose: Proactive therapeutic drug monitoring (TDM), a treatment strategy based on scheduled assessments of serum drug levels, has been proposed to optimize efficacy and safety of infliximab and other TNF inhibitors. It is still unclear whether proactive TDM improves clinical outcomes. The NOR-DRUM trials (A and B) are the first randomized trials to assess the impact of proactive TDM of infliximab in a range of immune-mediated inflammatory diseases. The NOR-DRUM A trial focused on the induction phase of infliximab.[1] The aim of the present trial, NOR-DRUM B, was to assess effectiveness of TDM during maintenance infliximab therapy.

Figure 1. Sustained Disease Control with no Disease Worsening (Primary Endpoint)



Forest plot depicting the adjusted difference in the rate of sustained disease control without disease worsening during 52-weeks follow-up (95% confidence interval) overall (the primary endpoint) and by disease subgroup.

Figure 2 Kaplan-Meier Curve of Time to Disease Worsening



Methods: In this 52-week randomized, open-label, multicentre trial, adult patients with rheumatoid arthritis (n=79), spondyloarthritis (n=138), psoriatic arthritis (n=53), ulcerative colitis (n=81), Crohns disease (n=66) or psoriasis (n=37) on infliximab therapy for a minimum of 30 weeks were randomly assigned 1:1 to infliximab based on TDM or standard therapy. In the TDM group, infliximab doses- and intervals were adjusted according to an algorithm to maintain serum infliximab levels within the prespecified therapeutic range 3-8 mg/L. In the standard therapy group, administration of infliximab was based on clinical judgement. The primary endpoint was sustained disease control without disease worsening. Disease worsening was defined by disease specific composite scores or a consensus on disease worsening between investigator and patient leading to major change in treatment. The primary analysis was performed by mixed effect logistic regression.

Results: Between June 7, 2017, and December 12, 2019, 458 patients were randomized and 454 received the allocated strategy and were included in the primary analyses. During the 52-week follow-up, the primary endpoint of sustained disease control without disease worsening was achieved in 167 (73.6 %) patients in the TDM group compared to 127 (55.9%) patients in the standard therapy group. The estimated adjusted difference was -17.6% (95% confidence interval -26.2 to -9.0, p=< 0.001). (Figure 1) Results were consistent in sensitivity analyses. The two groups were balanced regarding baseline characteristics (Table 1). Time to disease worsening was different in the two groups, hazard ratio (95% CI) 2.1 (1.5-2.9) (Figure 2). Secondary endpoints comparing disease activity and patient reported outcomes at week 52 did not show significant differences between the groups. Mean infliximab dose received during the trial was 4.8 mg/kg in both groups. Twenty-one (9.2%) in the TDM group and 27 (15.0 %) in the control group developed clinically significant levels of anti-drug antibodies. Adverse events were reported in 137 (60%) and 142 (63%) patients in the TDM and standard therapy groups, respectively.

Conclusion: Proactive TDM proved more effective than standard therapy in sustaining disease control without disease worsening. These results support implementation of proactive TDM as a general strategy during maintenance therapy with infliximab and have the potential to change clinical practice across specialities.

Table 1 Characteristics of the Patients at Baseline

	Therapeutic Drug Monitoring (n=227)	Standard Therapy (n=227)
Demographics		
Age – yr	45.1±14.2	44.6±14.3
Female sex – no. (%)	117 (51.5)	99 (43.6)
Disease duration (range) – yr	6.2 (2.0-15.1)	5.3 (2.1-12.8)
Diagnoses		
Rheumatoid arthritis – no. (%)	39 (17)	40 (18)
Spondyloarthritis – no. (%)	68 (30)	70 (31)
Psoriatic arthritis – no. (%)	28 (12)	25 (11)
Ulcerative colitis – no. (%)	38 (17)	43 (19)
Crohn's disease – no. (%)	34 (15)	32 (14)
Psoriasis – no. (%)	20 (9)	17 (8)
Therapy		
Infliximab treatment duration (range) – weeks	40.0 (37.9-61.0)	39.9 (37.9-61.0)
Concomitant immunosuppressive therapy* – no. (%)	123 (54.2)	130 (57.3)
Concomitant use of glucocorticoids – no. (%)	15 (6.6)	13 (5.7)
Use of biologic therapy# prior to infliximab – no. (%)	62 (27.3)	63 (27.8)
Disease activity at baseline		
Erythrocyte sedimentation rate (range) – mm/h	7.0 (3.0-12.0)	5.0 (2.0-11.0)
C-reactive protein (range) – mg/L	1.0 (1.0-3.0)	1.0 (1.0-3.0)
Patient's global assessment of disease activity	25.8±21.6	22.5±19.1
Physician's global assessment of disease activity	13.8±15.8	11.2±12.6
Disease specific baseline characteristics		
Rheumatoid arthritis		
Disease activity score in 28 joints$^{\Delta}$	2.4±1.0	2.3±1.2
Spondyloarthritis		
Ankylosing spondylitis disease activity score¶	1.6±0.8	1.5±0.8
Psoriatic arthritis		
Disease activity score in 28 joints$^{\Delta}$	2.1±1.1	1.6±1.0

*Plus–minus values are means ±SD, range denotes interquartile range, TDM therapeutic drug monitoring, TNF tumor necrosis factor

*Concomitant immunosuppressive medication includes: Methotrexate, leflunomide, sulfasalazine, and azathioprine.

#Biologic therapy includes: Etanercept, adalimumab, certolizumab pegol, golimumab, abatacept, efalizumab, rituximab, secukinumab, tocilizumab, ustekinumab and vedolizumab.

[1]Syversen SW et al. JAMA. 2021

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Patient Perspectives

Abstract Number: PP01

Unicycling for a Cure: My UNIque Physical Activity Intervention for Rheumatoid Arthritis During the COVID19 Pandemic

Dana Guglielmo, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: I was diagnosed with rheumatoid arthritis at age 17. In my 20s, I joined Racing For A Cure of the Arthritis National Research Foundation, a community platform for athletes thriving with rheumatic disease. Being an athlete and physical activity researcher have taught me that physical activity can reduce anxiety and fatigue, which are my most prominent symptoms. However, the COVID19 pandemic amplified both symptoms, and I felt exhausted and unmotivated to exercise. With each trip outside increasing my risk of COVID19, I became disheartened that most days it felt easier to stay inside.

Intervention: I troubleshooted my multifaceted problem and identified my barriers to physical activity: 1) Routine, repetitive exercise left me disengaged with my external surroundings and led to my mind getting consumed by internal anxiety; and 2) I felt unmotivated to exercise given my low energy levels and the risk of COVID19. Next, I identified my exercise needs: 1) low-impact and arthritis-friendly; 2) challenging enough to distract me from my anxiety; and 3) the most important: FUN! I thought back to my favorite childhood sport (Figure 1), and realized this same sport would meet these criteria with flying colors: unicycling!

Maintenance: I have improved my fitness, flexibility, strength, balance, and coordination, all of which allow me to safely ride my unicycle with rheumatoid arthritis. To maintain fitness, I engage in activities like plyometric drills, juggling, lifting weights, balance training, and stretching (Figure 2). I ride my unicycle 1-2x per week, and incorporate my love of adventure by finding cool new places to ride (Figure 3). To stay motivated and accountable, I communicate with other athletes with arthritis, many of whom are on social media (e.g., Athletes Beating Rheumatoid Arthritis Facebook group). The camaraderie of those who have successfully overcome their own exercise challenges helps keep me motivated, and I love sharing my own experiences to encourage others.

Quality of Life: A fun childhood sport took on new meaning in adulthood, as it became an activity I could look forward to during a traumatic year. My UNIque physical activity intervention led to subjectively improved fitness, physical functioning, mindfulness, self-efficacy, and quality-of-life, and reduced anxiety and fatigue. People with rheumatic conditions can utilize the same process I did to identify their own personal needs. Having social support is critical to sustaining physical activity. Joining a community of athletes with arthritis including Racing For A Cure can provide an avenue for social connection, peer support, and the ability to troubleshoot and overcome exercise barriers. When I ride my unicycle, I feel strong and capable. It makes all of the challenges, hardships, dedication, and perseverance feel worth it. My advice to others living with chronic disease is to choose fun over fear, and always be UNIque!

Figure 1. Where it all began: Dana unicycling as a child in New Jersey.

Figure 2. Behind the scenes: strength and balance training.

Figure 3. Dana unicycling at Ballona Creek Bike Path in Marina Del Rey, California.

Disclosure: D. Guglielmo, None.

Abstract Number: PP02

Leveraging Digital Health Tracking to Improve Arthritis Management

Katie Roberts, Annapolis, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: I was diagnosed with psoriasis when I was age 10 in 1986. At that time, my treatment plan consisted of regular application of Eucerin lotion, tar-based ointments, tanning beds, & frequent baths. Later I added

corticosteroids into my treatment plan. By the early 90's, novel treatments became available like steroid injections, PUVA, and methotrexate. When I turned 17, my diagnosis was amended to psoriatic arthritis. I cycled through many treatments for my condition, including up to 150 mg of methotrexate three times a week, steroid & gold injections, and eventually Remicade when it became available in the late nineties.

In 2003 I started taking Enbrel and have been taking it ever since. In addition to my biologic, I manage my arthritis with topical corticosteroids, steroid injections, and ibuprofen along with alternative medicine like massage therapy, acupuncture, a strict nutritional plan, herbal supplements, and heat therapy. All of these interventions allow me to live an active lifestyle, I frequently exercise and enjoy weight training, cardio, walking, pilates, yoga, and standup paddleboarding.

Intervention: Digital health tools like my Garmin Fenix 6 smartwatch, the TrainingPeaks training program, and the Arthritis Foundation's pain management app, Vim, inform my exercise regimen and care plan with patient reported data. With the support of my watch, I am able to track my pain & log my activity to identify the best exercise regimen for my care through an app called TrainingPeaks. A personal exercise coach reviews my data and builds exercise rec-

ommendations to meet my unique needs, and as I progress through my workout plans, I log notes about the impact of the activity on my joints. This log is even imported into my pain management app, Vim. When I meet with my rheumatologist, I am able to export the notes about my experience and discuss the data with them at my appointment. This in turn, informs my care plan.

Maintenance: I have been actively using my smart watch and exercise tracking tools for more than 3 years. Every day, my watch provides haptic feedback that reminds me to continue to track my progress and health. Weekly, my training coach at TrainingPeaks reviews the data and provides a recommended exercise plan for the upcoming week. After each workout, I diligently track how I'm feeling, what worked well during my exercise and what I feel I need more support on. Trends from the data are used to inform future workout plans, and I download the reports to use in talking with my rheumatologist. Bringing data into my doctor's office helps my doctor and I engage in shared decision making about my care, and it is much easier to report back to them how I've been doing with the support of consistently reported health data.

Quality of Life: Since incorporating digital health tracking tools into my routine, I have been able to stay active and keep my joints moving. The more I move the less I flare. This approach has helped me manage my disease activity. With tracking, I am more perceptive to my pain signals and have been able to detect early signs of a flare more easily – helping me be more proactive about my energy and effort conservation and self-care treatments. I am thankful that since adding digital health tracking into my care, I have had less disease activity.

Disclosure: K. **Roberts**, None.

Abstract Number: PP03

Navigating Maintenance of a Rare Autoimmune Rheumatic Disease in the Context of the COVID-19 Pandemic

Ida Hakkarinen, Greenbelt, MD

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: On March 13th, 2020, the President of the United States issued a proclamation declaring that the outbreak of coronavirus disease 2019 (COVID-19) was a risk to the public health and safety of the Nation. Three days later, my workplace instituted mandatory telework. In a prescient tweet at the end of the month, Tseng (2020) shared a conceptual framework (Fig. 1) of four waves of the COVID-19 pandemic and potential impacts upon health care. Since my initial diagnosis of Granulomatosis with Polyangiitis (GPA) in January 2012 and two relapses, closely monitoring my health became an ongoing part of life. Navigating maintenance care for GPA brought challenges in the era of COVID-19.

Intervention: My medical team pivoted to telehealth in lieu of in-person appointments and established a secure collaboration tool for visits. Dao (2020) offered appointment tips for rheumatologists much like what I experienced with other doctors. Being able to see and speak with my physicians virtually lessened the isolation I felt in my single person household with no pets. Laboratory results showed my GPA remained quiescent. My pharmacy provided free medication delivery during the initial lockdown period.

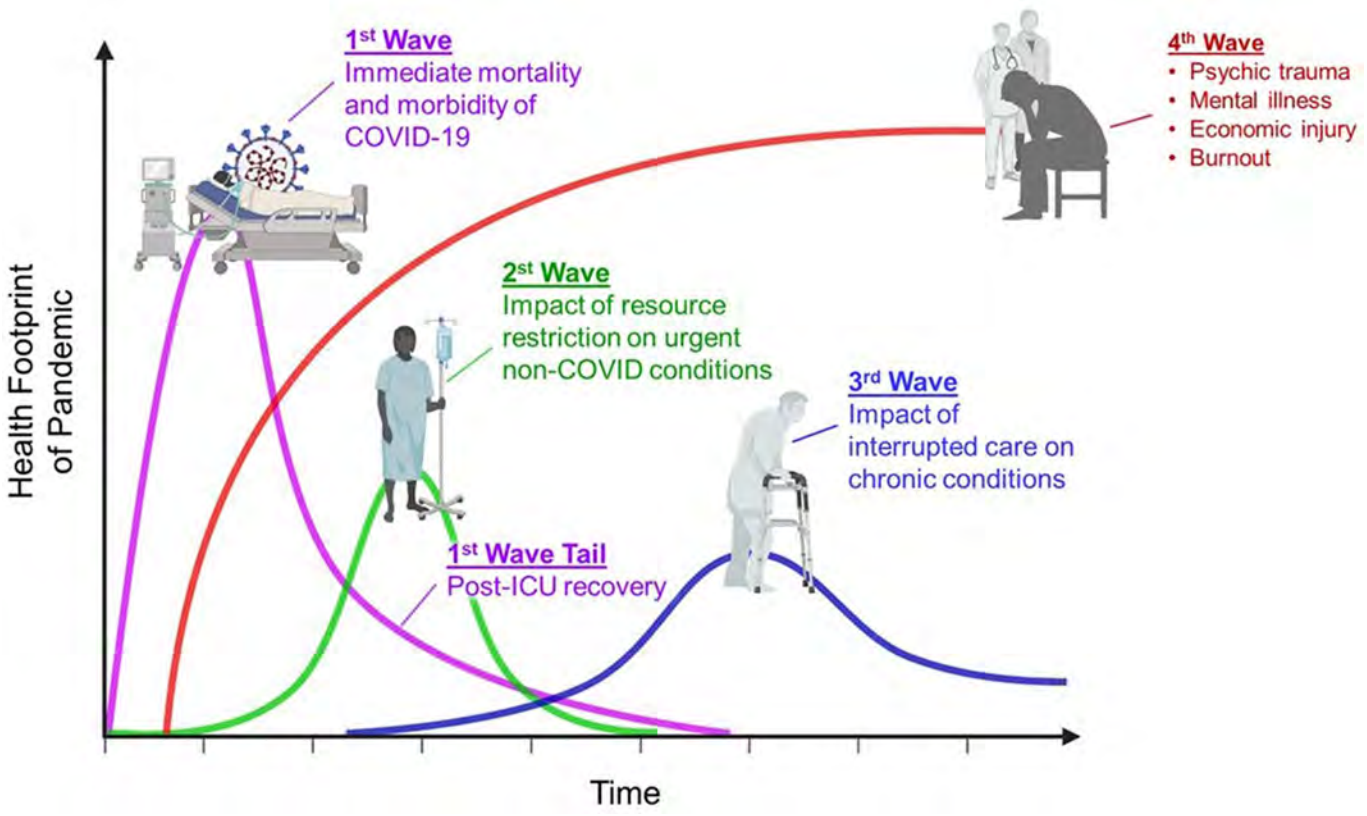


Figure 1. Conceptual model of the four waves of the COVID-19 pandemic (Tseng, 2020).

Maintenance: Gathering information from reputable sources enabled me to gain perspectives on the risks of COVID-19 infection and the benefits of early treatments and vaccines. Thoughtful comments from physician-scientists and clinicians helped me filter out "noise" found on social media. The Vasculitis Foundation hosted webinars where rheumatologists shared the latest data and information about COVID-19 and its potential impacts upon patients. The American College of Rheumatology also hosted webinars about patients with rheumatic diseases.

The global rheumatology community came together in a grass-roots collaborative effort to form the COVID-19 Global Rheumatology Alliance to collect, analyze and disseminate information about COVID-19 and rheumatology to patients, physicians and others. The group developed a patient experience survey that received over 14,000 responses in a year. With the advent of COVID-19 vaccines, it launched a patient experience vaccine survey (Fig. 2) to learn how people with rheumatic disease make decisions regarding the vaccines.

Quality of Life: Shortly before receiving my first dose of the Moderna vaccine (Fig. 3), I was able to enroll in an observational prospective study at the National Institutes of Health about the effects of COVID-19 infection and/or vaccination on patients with autoimmune diseases. Being able to contribute to scientific research has been very meaningful in the midst of these chaotic times.

References

Dao, K. (2020, March 18). A Rheumatologist's Tips: Telemedicine in 6 Easy Steps. RheumNow.com. Retrieved from rheumnow.com/content/rheumatologist%E2%80%99s-tips-telemedicine-6-easy-steps

Figure 2. Global Rheumatology Alliance announcement about COVID-19 vaccination survey.

Tseng, V. [@VectorSting]. (2020, March 30). As our friends and colleagues brave the front lines, we must also get ready for a series of aftershocks. It's very hard to plan this far ahead while we're in survival mode. We must prepare early

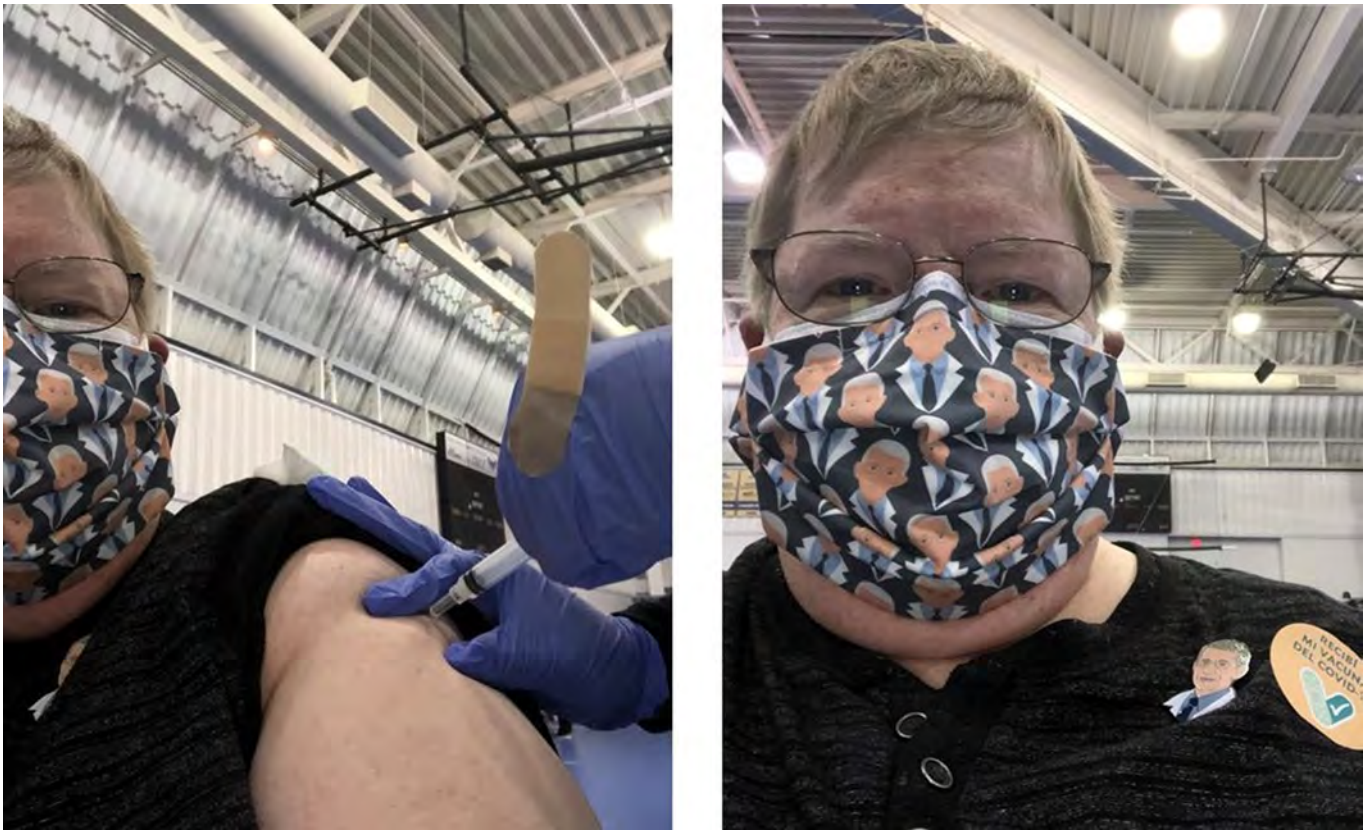


Figure 3. The author receiving first dose of the Moderna COVID-19 vaccine.

and strategize our response to the collateral damage of #COVID19 [Tweet]. Retrieved from twitter.com/VectorSting/status/1244671755781898241

Disclosure: I. Hakkarinen, None.

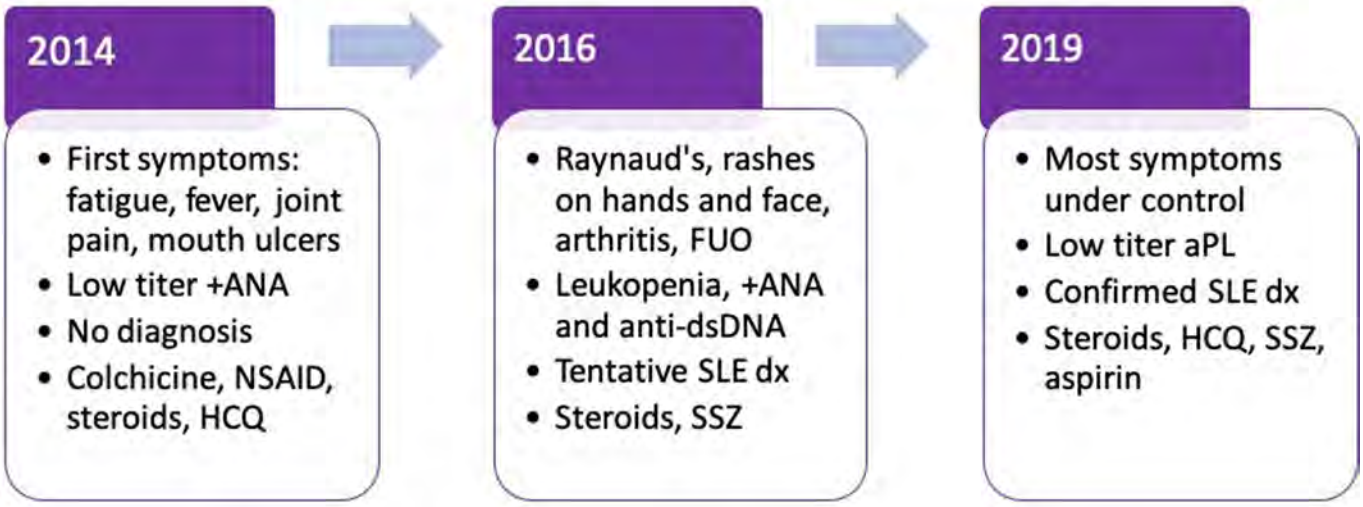
Abstract Number: PP04

Dual Roles: Thriving with SLE as a Medical Student

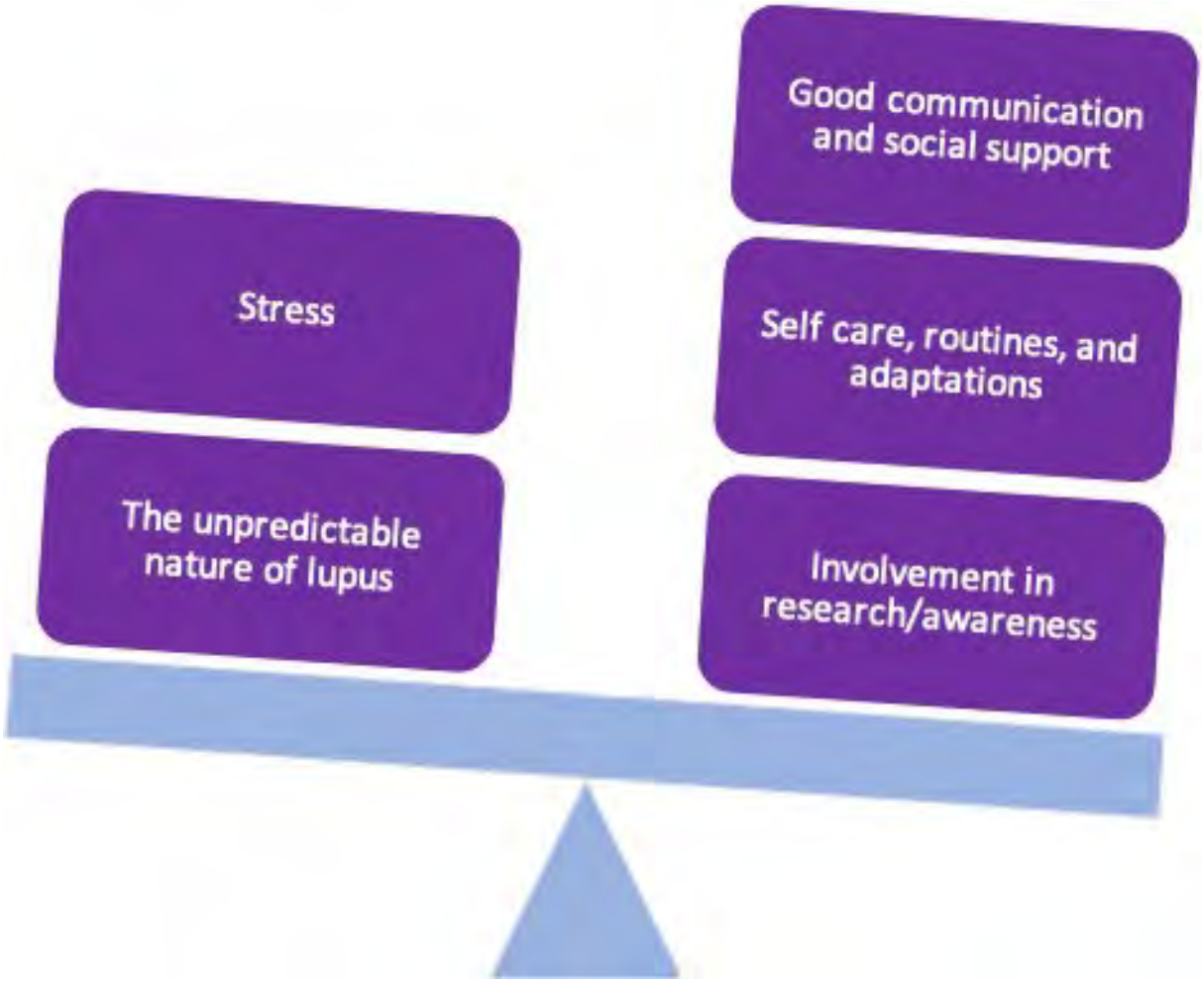
Chieh Lo[1] and Song-Chou Hsieh[2], [1]School of Medicine, I-Shou Univerity, Kaohsiung, Taiwan (Republic of China), [2]Division of Immunology, Allergy and Rheumatology, Department of Medicine, National Taiwan University Hospital, Taipei, Taiwan (Republic of China)

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: A few days after my 18th birthday, I walked into a rheumatology clinic for the first time. I had ulcers in my mouth, felt extremely tired, and my knees were swollen and painful. In just a few years, I went from competing in triathlons to limping around. Leaving the clinic with a prescription of NSAIDs and colchicine, I thought these symptoms would disappear once I was done with stressful college entrance exams. But I had no idea of the journey that lay ahead.



The diagnosis process.



Factors that affect quality of life with lupus.

The author's first ICU clinical rotation.

I ran a low-grade fever for 2 years straight. Sometimes, I felt so sick I couldn't get out of bed. My white blood cell count was often low. Steroids made my face swell, and I felt tempted to stop my medications. At one point, even my own parents accused me of feigning illness-but I didn't have a diagnosis to prove them wrong! Despite all this, I was accepted to medical school. Shortly afterwards, I received a formal diagnosis of SLE. After years of rheumatology appointments, this news did not come as a surprise to me. But as a medical student, I now had to juggle 2 roles: patient and physician-to-be.

Intervention: My illness introduced me to the world of rheumatology. I was fascinated by all the research that was going on in the field, and I wanted to experience the thrill of creating knowledge that will directly help patients like myself. Previously, I was part of an international patient advisory board for lupus research. Currently, I am involved

in several projects ranging from translating an international vaccine survey for people living with rheumatic diseases, to researching HCV clearance and autoimmunity. With help from the rheumatologist who diagnosed me, I am now drafting my first original research article!

Another thing that has inspired me to become more engaged in healthcare is connecting with fellow patients through online groups. As a medical student, I sometimes provide information about lupus, help anxious people who have just been diagnosed, and explain the importance of adhering to treatment. But when things get tough for me, it is also very helpful to talk to people who have been through similar situations. This reciprocal relationship builds a strong sense of support and community.

Maintenance: Stress is a major part of medical school. Sometimes it can be easy to neglect my own health. Forgetting to take steroids in the morning, for example, can lead to an inconvenient bout of arthritis while studying or shadowing in the evening. Prolonged stress and sleep deprivation may also lead to disabling flares. Therefore, I must keep an eye on my mental and physical health, and manage it like any other obligation. This is easier said than done, so I rely on planners and pillboxes to hold myself accountable. Sometimes, I also experience "brain fog" and forgetfulness, so I use digital tools such as phone apps to keep me on track.

Quality of Life: My lupus has now been stable for more than a year. I've become better at recognizing signs of an impending flare and taking action to stop it. With my improved health, I am able to dedicate more of my energy towards academics, research, and having fun. Though I still occasionally worry about what the future holds for me as a physician living with lupus, I remain confident that scientific breakthroughs and advocacy will continue to improve the lives of patients all around the world.

Disclosure: C. Lo, None; **S. Hsieh**, None.

Abstract Number: PP05

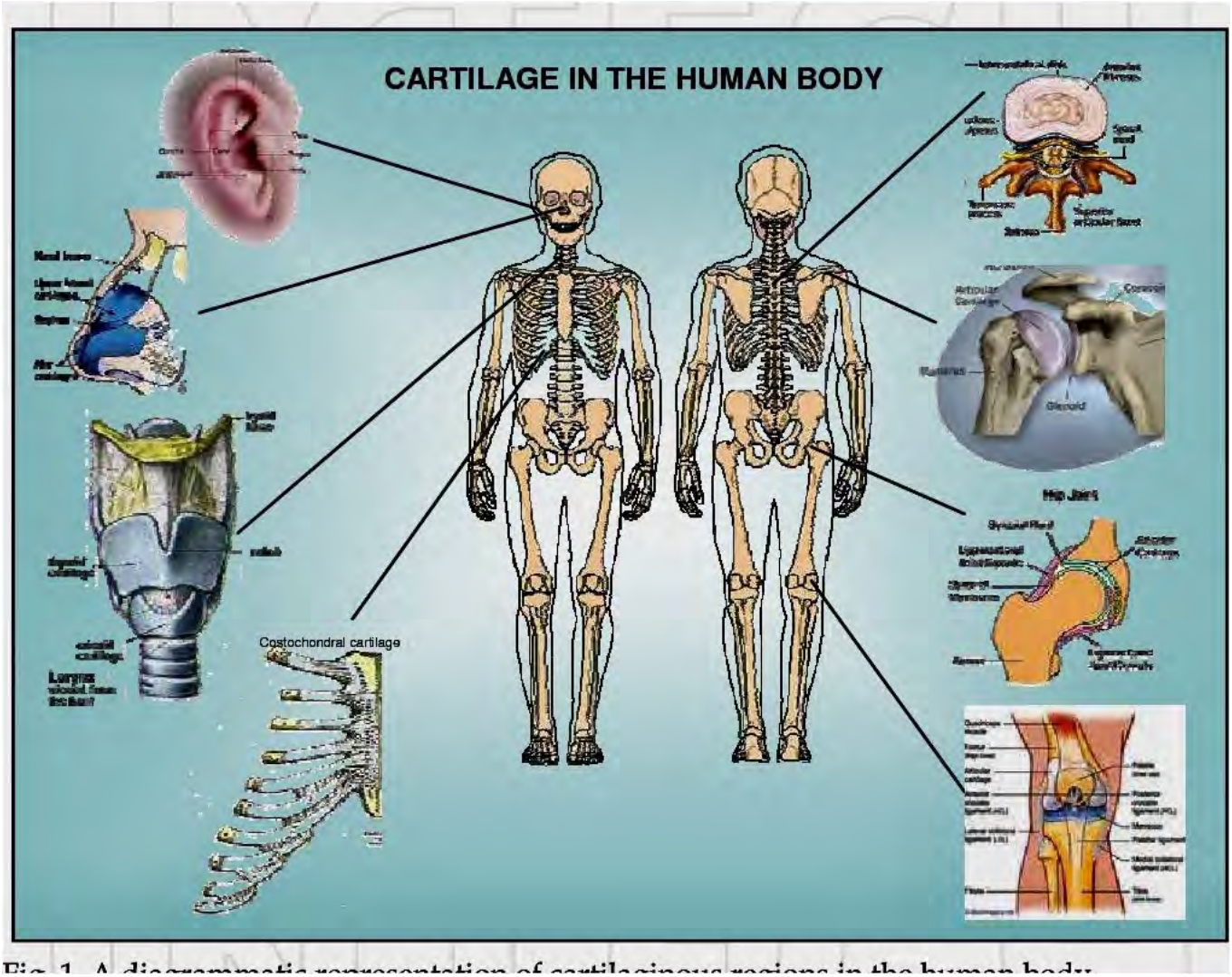
Fighting Health-Related Misinformation Using Social Media / How Creating an Online Group for Patients with Relapsing Polychondritis — and Moderating It with Health Professionals — Helps Spread Reliable and Empowering Information

Michael Linn[1], Spenser Mestel[2] and **Susie Ratledge**[3], [1]Relapsing Polychondritis Foundation, New York, NY, [2]New York, NY, [3]Relapsing Polychondritis: Secular Science and Support group, Chattanooga, TN

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Before I became ill in 2017, I was a registered nurse with a degree in health science who'd often educate patients about how they could better live with their disease by understanding it. In my career, I served as a Health Education Coordinator, for the benefit of patients and communities, and was certified in diabetes education. So, when I was diagnosed with relapsing polychondritis ("RP") in 2018, I began to do my own research.

Unfortunately, RP is a rare disease, and though my rheumatologist was relatively well informed about it, many doctors are unaware of the the case studies and (albeit few) larger population studies. In this vacuum of knowledge, patients



Relapsing Polychondritis: Secular Science and Support Group.

often seek out and fall prey to misinformation. For example, one doctor (commonly found on the internet) touts a diet that "cures" RP. While I certainly encourage others to eat healthy and exercise regularly, there can be significant danger in forgoing legitimate medical treatment in order to pursue unproven cures. Likewise, even well-meaning patients often present their own experiences as if they're proof of the success of a medication or lifestyle change.

Intervention: Troubled by the lack of peer-reviewed science and anecdotal evidence in some other online support groups, I created an online community for RP patients. Along with five other moderators, including two health professionals, we vet the information provided. First and foremost, we ensure that it's coming from a reputable source, and that it's accessible to laypeople. I'll listen to dozens of lectures and comb through pages of results from online archives of biomedical and life science journal literature before I post something to the group.

To provide consistent and practical information, we also do "Monday Meds," where we discuss the different medications for autoimmune disease, and "Favorite Things Friday," where we list what we're grateful for, like pillows with a hole in the center, which helps to relieve the pressure on our ears when sleeping.

However, it's not just about the quality of the information. Given all of us have spent years interacting with fellow RP patients, we've established trust and rapport within the community, allowing us to both highlight reputable sources and to gently discourage misinformation.

Susie Ratledge, Presenting Author.

Maintenance: Through this group, we've been able to equip patients with knowledge to bring to their doctors, empowering them to positively influence their own care. Similarly, we're able to prevent them from getting their hopes up about untested treatments. We offer an evidence-based, community-minded approach that has improved the quality of life for our members and for me.

Quality of Life: By offering both current scientific research and emotional support, our online group addresses the emotional and health-related needs of our community, which would otherwise go unmet for most of us.

Relapsing Polychondritis Foundation.

Disclosure: M. Linn, None; **S. Mestel**, None; **S. Ratledge**, None.

Abstract Number: PP06

Collaborative Advocacy Helps Me and Other Patients With Relapsing Polychondritis (“RP”) / My life improved by helping the RP Foundation and Race for RP facilitate awareness, education, and research to improve the quality of life for patients with RP and advance a cure for this disease

Michael Linn[1] and **Dan Smith**[2], [1]Relapsing Polychondritis Foundation, New York, NY, [2]Relapsing Polychondritis Foundation, Canton, MI

SESSION INFORMATION

Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: In March 2020, I was diagnosed as having relapsing polychondritis ("RP"), an understudied, underdiagnosed, and undertreated debilitating autoimmune disease that can be fatal if left untreated. The disease affects multiple organ, particularly cartilaginous structures such as the ears, nose, airways, joints, as well as the eyes, skin, heart valves, and brain. The cause of RP remains unknown, and consequently, there is not a diagnostic test or targeted treatment options for patients with RP.

Dan & Debbie Smith with Race for RP car.

Race for RP.

Intervention: Since the early stages of my diagnosis, the RP Foundation (www.polychondritis.org) has continued to be a tremendous resource. Soon after my diagnosis, they provided educational materials and introductions to RP experts and an online RP support group. The RP Foundation also connected me to Race for RP (www.RaceForRP.org), which supports research, awareness programs, and care for those who are affected by RP.

From these connections, the importance of working as a team became particularly clear. Celebrating the successes and supporting teammates through the losses applies to sports, managing patient care, conducting research programs, and educating others about autoimmune diseases.

Maintenance: While fighting RP, I was inspired by the RP advocates that I met. So, I volunteered to be the primary liaison between the leading RP social media platforms (including the RP Foundation and Race for RP) and a large, private online support group.

Quality of Life: My life has been significantly improved by being part of a successful team whose purpose is to facilitate awareness, education, and research to improve the quality of life for patients with RP and advance a cure for this disease. It provides me with the opportunity to help others and be excited about the extraordinary advances in patient care and cutting-edge research. I enjoy being an active and helpful member of a successful team.

Relapsing Polychondritis Foundation.

Disclosure: M. Linn, None; **D. Smith**, None.

Abstract Number: PP07

How Online Spanish-Language Resources Got Me and My RA Through the COVID-19 Pandemic

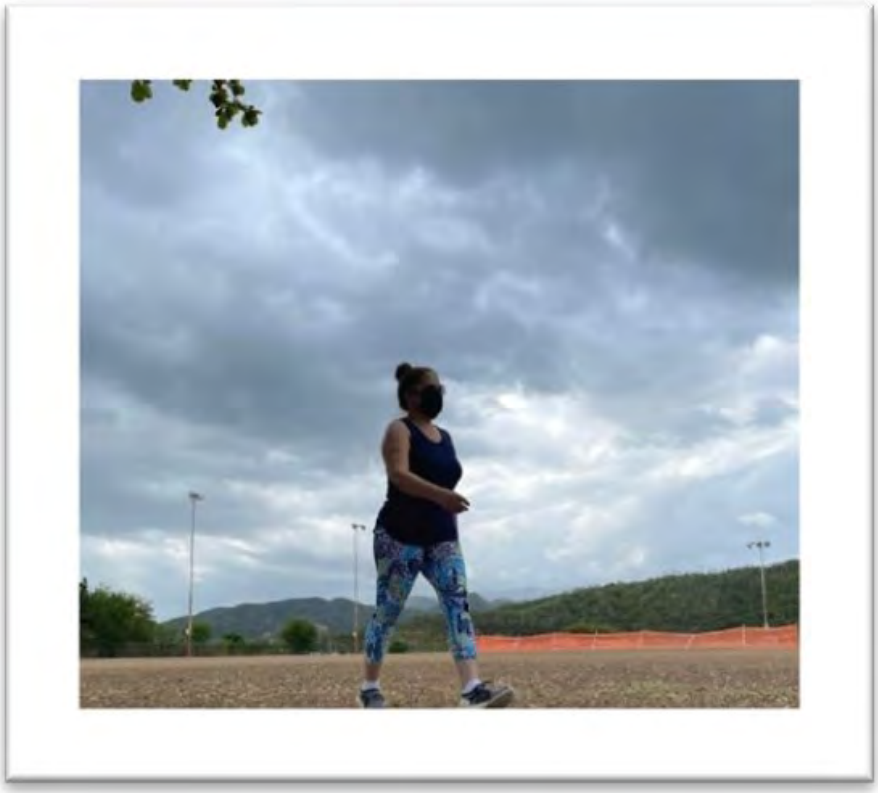
Wigna Cruz, Puerto Rico

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: I was experiencing joint pain especially in my wrists, which led me to see my physician for testing. Initially I was misdiagnosed with lupus. After a few months of seeing my physician and not feeling like I was being heard, I got a second opinion. This led to further testing, and I was then diagnosed with rheumatoid arthritis (RA) in 2014. After attempting a few DMARDs, I was put on a DMARD treatment that works for me. Although I ended up getting the correct treatment for myself, the prior experience of being misdiagnosed and not feeling heard made me feel uncertain of who to trust. During the COVID-19 pandemic, I felt the same uncertainty and fear about who to trust, especially as I was getting so many different suggestions online from different news channels and from peers about what to do to keep safe as an RA patient. For example, was it safer to stop my RA treatment?

Intervention: Interacting with online articles from CreakyJoints Español, and the support I received from other CreakyJoints Español members, made me feel less anxious and more comfortable using the internet. This was es-

Figure 1. Easy-to-Understand COVID-19 Guidance for Patients at CreakyJoints Español.



Taking my daily walk.

pecially true in the beginning of the COVID-19 pandemic when I was getting contradictory information from news outlets and on social media. Luckily, the information I received through CreakyJoints Español was factual and helped me make decisions about my healthcare, including RA treatment decisions, with my doctor (Figure1). It made me feel less anxious and gave me confidence to get outside and walk regularly. Two Spanish-language articles that helped me during this time of uncertainty were:

- ACR guideline updates for patients
- Infographic and information on receiving care during the pandemic

Maintenance: I received COVID-19 information provided by CreakyJoints Español on their webpage and social media channels, and I was able to keep up to date on the ACR's recommendations, including COVID-19 vaccination and treating my RA during the pandemic. CreakyJoints Español gave me a better understanding of how to take into account the CDC COVID-19 guidance while considering trustworthy information that was specific to people with RA. I am continuing to stay informed about any new developments that affect patients like me through CreakyJoints Español.

Quality of Life: I stay physically active for overall health and make sure to attend my telehealth appointments and in-person infusions. I learned the importance of staying healthy physically and mentally and I am comfortable knowing that I can reach out to CreakyJoints Español with questions and for social support. It's important for me to stay informed about things that can affect RA and my quality of life throughout this pandemic and beyond. Having a trusted source of information has proved invaluable during this uncertain time.

Disclosure: W. Cruz, None.

Abstract Number: PP08

Should I Get the COVID-19 Vaccine With My RA? Using Evidence-Based Resources for Decision-Making

Aberdeen Allen, Colgate Palmolive, Parlin, NJ

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Patients with autoimmune rheumatic diseases have concerns about getting the COVID-19 vaccine. As vaccines began to receive emergency use authorization, individuals with conditions like rheumatoid arthritis (RA), looked for information to help make informed decisions. As a patient living with RA for 15 years, and on immunomodulating therapy for it, I was hesitant about getting the COVID-19 vaccine and needed to weigh the risks and benefits to feel confident getting a shot.

Intervention: People living with autoimmune diseases have nearly twice the risk of acquiring severe, vaccine-preventable infections. I was looking for reliable information about the new vaccine's safety and efficacy, and information that would be specific to my needs and experience with RA. I knew that there wasn't much information available on these vaccines that was specific to people with conditions like RA, so I was unsure of whether or when to get vaccinated. My questions were about whether to pause my RA medication, when to do so, and for how long. I wanted to know about possible side effects, like RA flare, and to learn if one of the three available vaccines was best suited for me. I searched online for resources to help me make a decision and gain confidence about my choice.

Given the rapidly changing information about COVID-19, I was anxious to know what was and wasn't evidence-based at every step (Figure 1). In my search, I came across the COVID-19 Patient Support Program offered by the Global Healthy Living Foundation (GHLF). The program shared up-to-date reliable information about COVID-19 through webinars, articles, and a newsletter circulated approximately weekly. Part of keeping up with the rapidly changing informational landscape involved accessing an online collection of fact-checked articles for patients called "COVID-19 Vaccine Information for Immunocompromised Patients" curated by GHLF and informed by medical experts. I learned through an informational webinar organized by GHLF about the American College of Rheumatology (ACR) guidance on COVID-19 vaccination for patients with autoimmune rheumatic diseases that it is important to know what questions to ask, especially when the evidence is changing or incomplete. In addition, after reading a Patient Support Program article called *7 Questions to Ask Your Rheumatologist If You're Nervous About Getting the COVID-19 Vaccine*, I was able to bring questions to with my doctor to help me reach a decision. Ultimately, I decided to get the COVID-19 vaccine (Figure 1).

Maintenance: I continue to have ongoing discussions with my rheumatologist about my concerns despite being fully vaccinated. This means I must stay updated by seeking out information on what experts are learning about COVID-19 as new evidence emerges.

Quality of Life: Being part of an online community like GHLF/CreakyJoints allowed me to voice my concerns and anxieties and to easily find information to address them. This allowed for more meaningful conversations between me and my doctor and helped me make an important decision: whether to get the COVID-19 vaccine. Now that I am fully vaccinated, I feel safer. I am enjoying life outside and socializing after being home for more than a year.

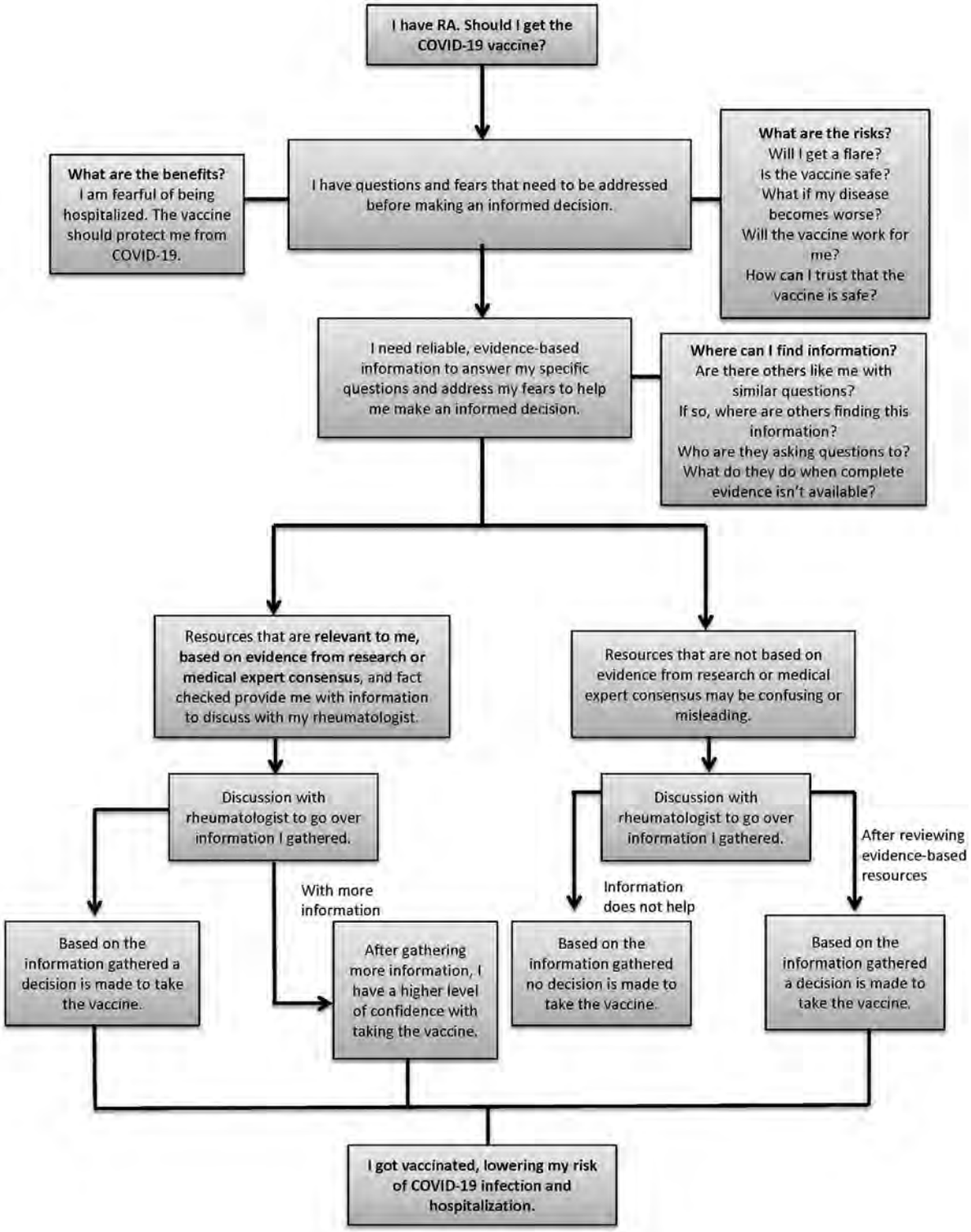


Figure 1. My steps to arrive at an informed decision about the COVID-19 vaccine.

Disclosure: A. Allen, None.

Abstract Number: PP09

Family Planning while Living with Rheumatoid Arthritis

Shannan O'Hara-Levi, Monroe, NY

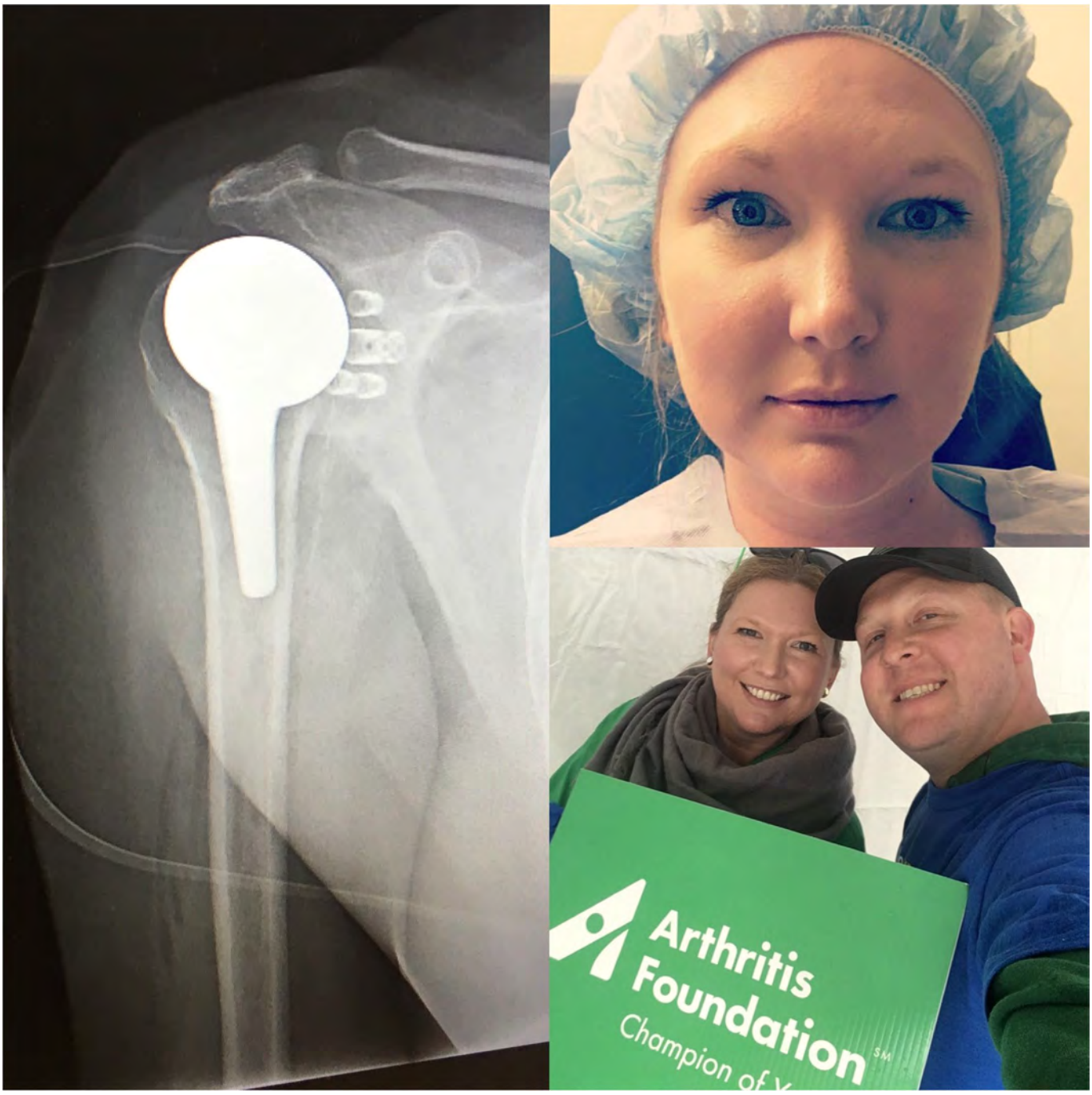
SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives Poster (PP01–PP09)
Session Type: Poster Session B
Session Time: 8:30AM–10:30AM

Background/Purpose: Over the course of my 30+ years living with Polyarticular Juvenile Rheumatoid Arthritis, I have never had long term success on any one biologic treatment, and disease progression continued eventually resulting in a need for a bilateral shoulder replacement surgery which I had in 2018. My husband and I have been hoping to start a family for years but have had to accommodate our plans due to my arthritis. We began seeing a fertility specialist years ago and while my initial fertility lab results were within a normal range, but a major flare prevented us from moving forward with treatments. We are finally in a place now where our family planning conversations can begin again. After an insurance battle early this year, I am now on a biologic that has some data indicating safety and efficacy for women who are pregnant or trying to become pregnant. With the guidance of my fertility specialist, we have added in vitro fertilization (IVF) medications and various supplements, changed my nutritional plan, and incorporated acupuncture into my care plan. Additionally, this May we had our first frozen embryo transfer that we hope to will result in a successful pregnancy.

Intervention: A care plan that empowers me to have a successful pregnancy is my primary focus and goal. In order to do that, careful family planning is essential for my partner and I with my rheumatologist and fertility specialist. Unfortunately, there is not enough data to suggest an ideal care plan for a person like me: someone that grew up with juvenile rheumatoid arthritis and is now of reproductive age hoping to start a family. Neither my fertility doctor nor my rheumatologist has all the answers. I am charged with finding the answers I need, carefully organizing my health information, and coordinating my care between providers.

Maintenance: The onus is on me to explain my arthritis to my fertility specialist and hope that they are able to make informed care plans based on their experience with others in a similar position. Similarly, communicating with my rheumatologist about my family planning is a responsibility that rests on my shoulders. In order to be an effective communicator, I have to organize my life around these two parts of the healthcare world and find ways to bring them together. Being a planner is critical to my care so that I can ensure all aspects of my healthcare team are coordinating to accomplish my care goal: a successful pregnancy while managing my arthritis. Support from other patients like me is essential, and I have found community through social media channels that keep me connected with others in a similar situation.

Quality of Life: We have been working for years to get my arthritis under control to a point where I would be healthy enough to effectively plan our family. I am thankful that we are finally at a point where we can move toward that future based on my medication plan, my successful bilateral shoulder replacements, and my care plan with my fertility specialist. While my juvenile rheumatoid arthritis symptoms are still present, they are maintained, allowing for better function as I pursue IVF treatment and family planning. The peace of mind that we are now able to work toward my ultimate care goal of starting a family has certainly improved my quality of life.


Arthritis
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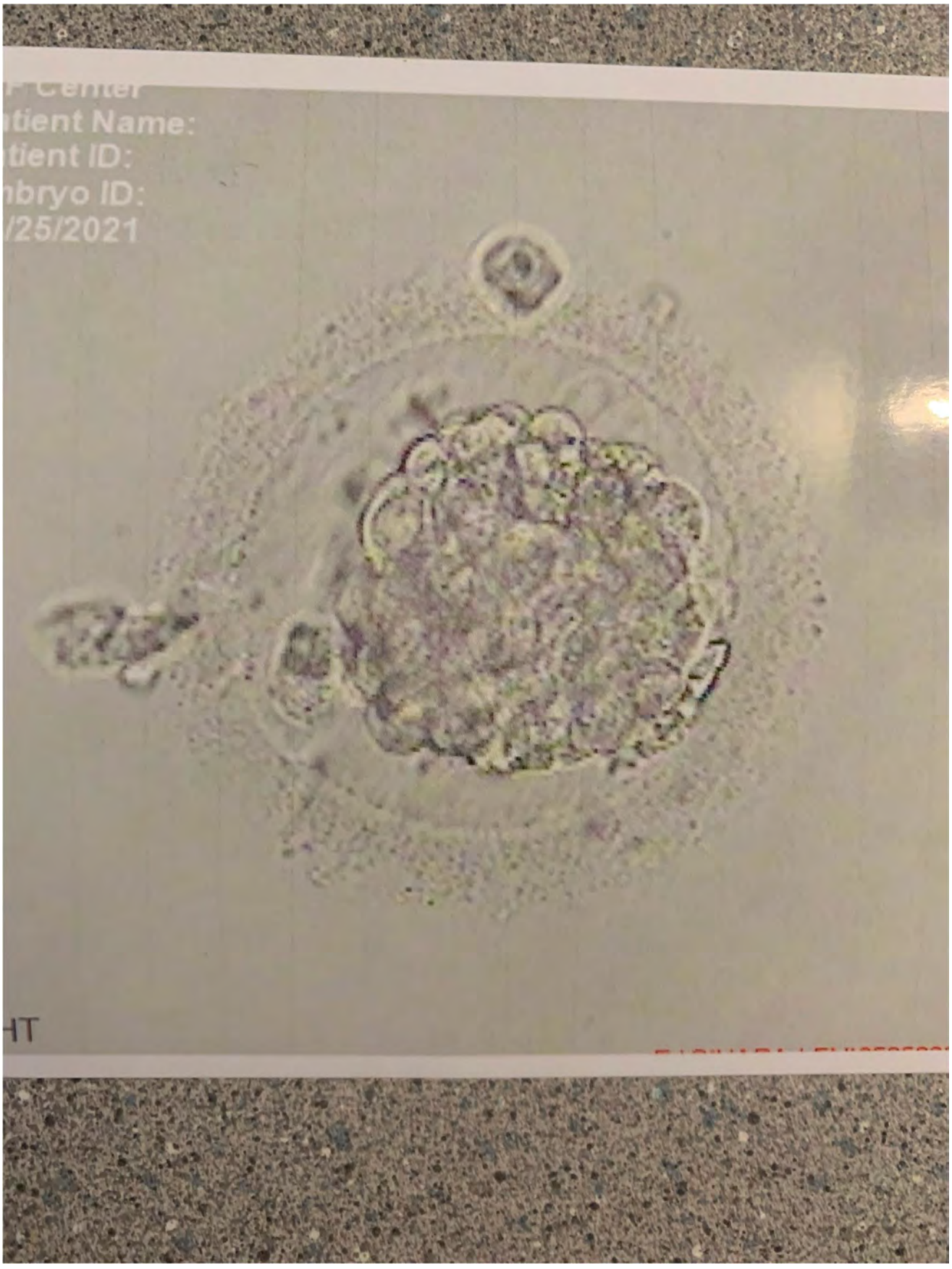
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Disclosure: S. O'Hara-Levi, None.

Abstract Number: PP10

Discovering 'I' Through Interaction with Support Group Members: A Place of Empathy That Transcends the Limitations of Words

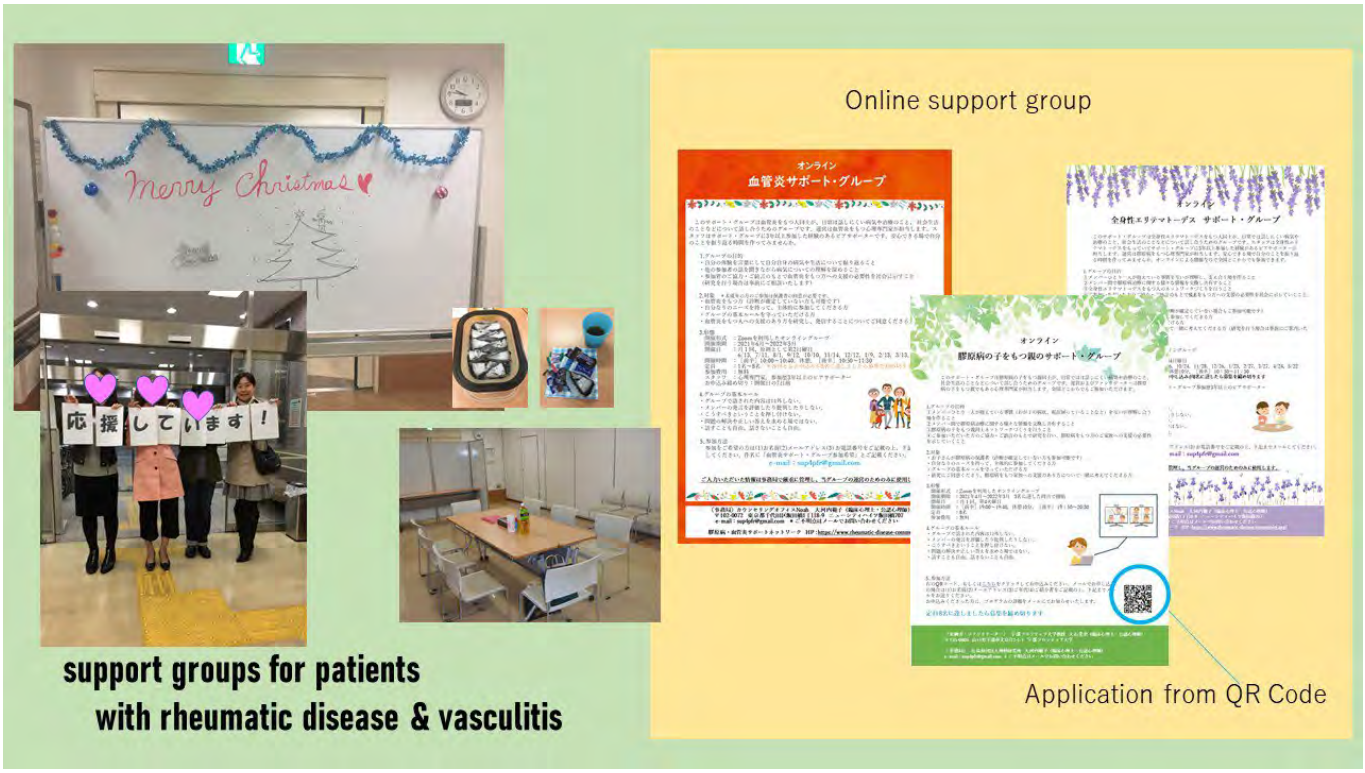
Noriko Okochi[1], Eiji Oishi[2] and Mika Ishiguro[1], [1]Rheumatic Disease and Vasculitis Support Network Japan, Tokyo, Japan, [2]Rheumatic Disease and Vasculitis Support Network Japan, Yamaguchi, Japan

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives (PP10–PP13)
Session Type: Patient Perspectives
Session Time: 3:30PM–4:30PM

Background/Purpose: Since 5-year-old, I have had unexplained symptoms. At the age of 13, my whole body became inflamed. The pain was so intense that I could move just one finger. I could not drink or speak. I found a way to keep from crying because it hurt so much that my parents would pat me on the head. I imagined myself as a log and stopped moving. My world was in my brain. Fortunately, Dr. Tomisaku Kawasaki and other experts in immune diseases helped me to live. I was diagnosed with polyarteritis nodosa around 2000, at the age of 26.

The impact on my personality of living through adolescence without knowing the true nature of my symptoms was immeasurable. Because I felt so close to death, I felt emotionally distant from others. My mind was a mixture of isolation, sadness, confusion, anger, and guilt for having that anger. I found it difficult to understand what was going on inside, even with my family and friends. I became interested in the human mind and became a psychologist. While

Information dissemination via website.



Support groups based on illness and living environment.

practicing psychotherapy in psychiatric, school, and pediatric settings, I was confronted with my habit of suppressing emotions and my tendency to deny my symptoms. I tried to sort out my internal issues through the "language" used by psychologists. However, the more I learned about the language used by psychologists, the more I realized that there were limits to explaining the mind through words.

Intervention: Yalom(1980) says, "Denial is a powerful and ubiquitous defense". For me, living with symptoms, coping with denial, repression, and dissociation was not something that needed to be "treated" but something that was "necessary". In Japan, there are very few opportunities to talk about one's disease. However, I was convinced that the most useful psychological support for a patient with rheumatic disease was the help of fellow patients.

Maintenance: In 2013, I started a support group for patients with rheumatic disease. The purpose of the group was to share experiences and exchange information, to better understand the disease, and to think about facilitating social life. After the corona outbreak, the group moved online and continued. The members who participated in the meeting gradually became staff members to support the participants. Currently, in addition to "the Rheumatic Disease Support Group", "the SLE Support Group", "Vasculitis Support Group", and "Support Group for Parents of Children with Rheumatic Disease" are conducted by these staff members.

Quality of Life: The members are gaining more control over their treatment. Knowing about the prognosis of the disease has led to mental stability. Some members who had lost their sense of self are reaffirming their own value and moving toward self-actualization. A member who lost her eyesight due to the effects of steroids became a swimmer. Some of the members who are inspired by these powerful people turn their introverted viewpoints outward and open themselves up to the hope of self-realization.

Japan is a country where harmony is valued and cooperative behavior is praised, so it is difficult to focus on individual suffering. The fact that members of a support group for people with invisible illnesses have shared their difficulties with the public has caused a stir in the support of people with other kinds of difficulties in Japan.

Disclosure: N. Okochi, None; **E. Oishi**, None; **M. Ishiguro**, None.

Abstract Number: PP11

"Our Arthritis May Be Chronic but We Are Definitely Iconic" - Two Teens Created a National Podcast for Youth with Rheumatic Diseases

Trishtha Peters[1] and **Natasha Trehan**[2], [1]University of Ontario, Toronto, ON, Canada, [2]University of Ottawa, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives (PP10–PP13)
Session Type: Patient Perspectives
Session Time: 3:30PM–4:30PM

Background/Purpose: Trish Peters was diagnosed with JIA at 11. She has been on Methotrexate to lessen disease activity for her knees and hands. She does competitive swimming, running and rugby. It has taken her a long time to understand and accept that she is different from other people in how her body heals, but she has learned to appreciate it as a part of who she is. At 13, Natasha had inflamed fingers, wrists, ankles and feet in which an MRI showed extensive damage due to JIA. She started Prednisone and then switched to Methotrexate. However, six months in, there was no change to her swelling or pain. Natasha took Humira, then Actemra, then Tocilizumab, all of which failed to reduce her disease activity. Finally, ten corticosteroid injections in her joints and triple therapy - a combination of Methotrexate, Sulfasalazine and Plaquenil brought her blood and her inflammation under control. She believes that her healthy eating habits, her regular dance routine, and daily meditation along with the medications have provided her with a pain-free, happy and manageable lifestyle.

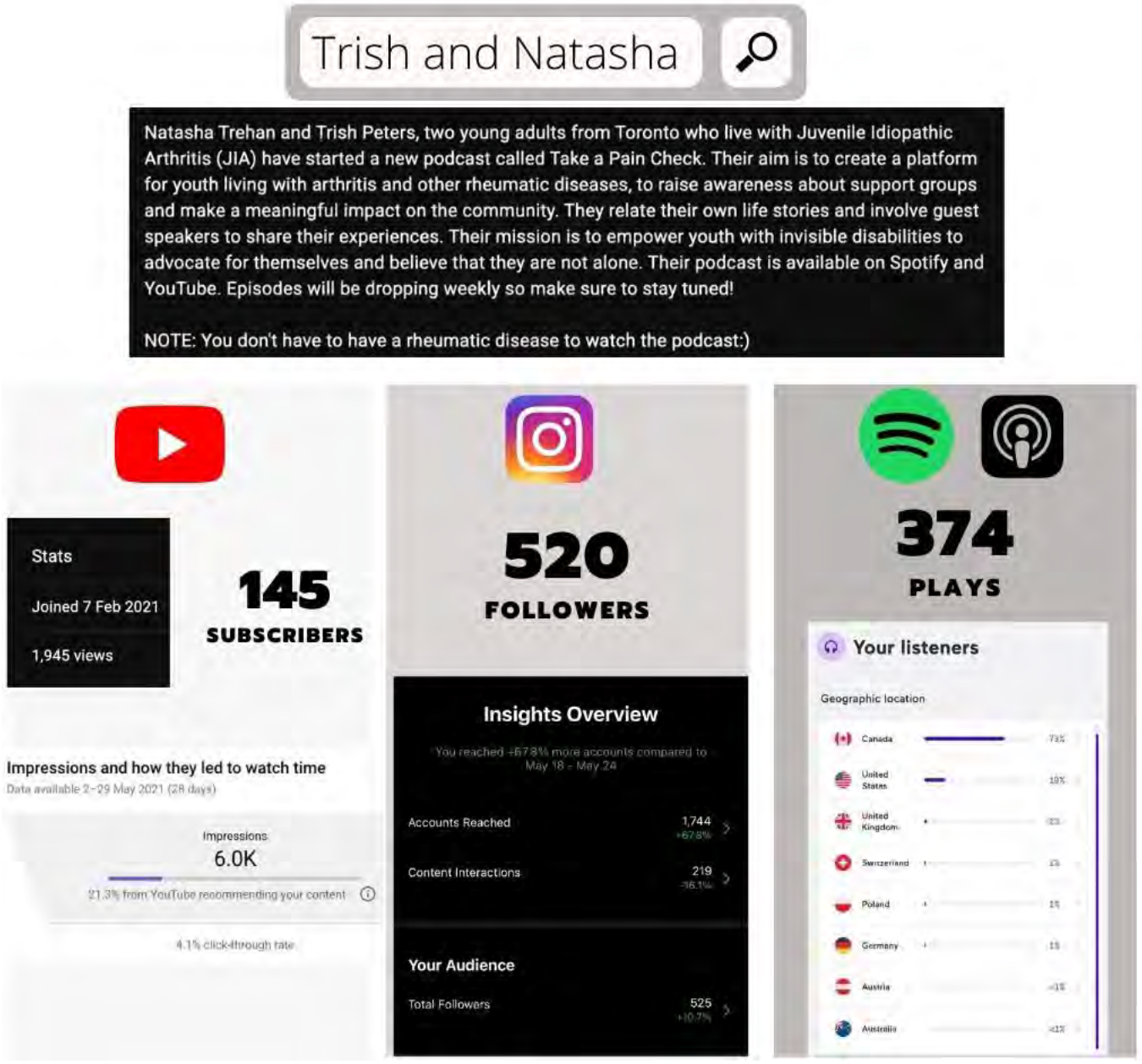
Intervention: Our friendship evolved in January 2020, when we both became leaders at Cassie and Friends. While organizing events for youth together we discussed our stories and realized that we shared similar experiences. We both had struggled to find support and talk to people our age about how we felt. We decided to create a platform to make sure that young patients who are initially diagnosed with any type of rheumatic disease do not go through the same rough journey we did. We co-founded and launched a podcast called Take a Pain Check (TAPC) in March of 2021. It is available on Spotify, YouTube, Apple podcast, and Anchor. Every week, TAPC features a new guest who shares their unique lived experience of rheumatic disease, offering listeners different perspectives to learn from.

Maintenance: TAPC has received amazing feedback from numerous guests - with and without arthritis as well as from hospitals and rheumatology clinics across Canada who have mentioned how youth need the support, moments of laughter, and fun related to their condition. Many guest speakers wished a platform like this existed when they were diagnosed as youth.

Quality of Life: TAPC is currently changing the lives of youth impacted with rheumatic diseases by modelling a wide variety of perspectives and experiences. This is especially important for youth who, like us, may feel too shy or lack the resources to advocate for themselves or meet others. Through TAPC, we have been able to spread the word about research being done. We want to ensure that people don't have to search endlessly for support. We want to actually make a difference in the lives of young people and inspire them to make the best out of this disease.

The accessibility of our podcast. We are available on multiple social media platforms in order to support our audience.

Direct quotes from our Youtube subscribers showing the impact of the podcast to their lives.



Statistics of how the podcast has grown in the past months.

Disclosure: T. Peters, None; **N. Trehan**, None.

Abstract Number: PP12

Fighting for the Care We Deserve: My Experience as a Latina Patient-Researcher During the COVID-19 Pandemic

Guadalupe Torres[1], Courtney Wells[2] and Kristine Carandang[3], [1], [2]University of Wisconsin-River Falls, School of Social Work, St. Paul, MN, [3]Global Healthy Living Foundation, CreakyJoints, San Diego, CA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives (PP10–PP13)
Session Type: Patient Perspectives
Session Time: 3:30PM–4:30PM

Background/Purpose: I am a 23-year-old first generation Latina with rheumatoid arthritis (RA). Despite being disproportionately affected by rheumatic conditions, the perspectives of Latinx remain poorly understood by rheumatology professionals and as such, we are more likely to experience negative health outcomes. I have spent years disengaged with my healthcare, without health insurance or a rheumatology provider. Western medicine and my culture's beliefs are often in conflict. Because I was poorly educated about my disease, I tried so many medications that I was diagnosed with fatty liver disease in 2017. I have felt isolated, without community or support since being diagnosed at 16.

Intervention: In 2020, I was approached by a team of researchers, who also have arthritis, to work as a patient-researcher on a qualitative research project about people's experiences living with rheumatic conditions during the COVID-19 pandemic. This project purposefully recruited Black, Indigenous, People of Color (BIPOC) and others from underrepresented communities. I was excited to bring my unique perspective and expertise and to ensure that Spanish-speaking populations were included. From the news and personal experience, I knew that BIPOC, specifically Latinx, were being hit the hardest by COVID-19 because many were classified as essential workers. Serving as a critical research team member allowed me to practice patient advocacy in the planning, recruitment, data collection, analysis, and dissemination of this project.

Maintenance: Collaborating in this research has helped me build connections with other rheumatology patients, increase my health knowledge, and better manage my mental health during the pandemic. During analysis with the research team, for the first time, I processed my own illness story including the opportunities and barriers that I have faced. In interactions with study participants, I listened to how others were coping and decreasing their risk to COVID-19, which lessened my anxiety as an essential worker and a Person of Color with RA. I also reflected on my own education and personal and professional skills, and felt empowered to help members of my community who continue to lack key health information. These experiences culminated in me fighting to obtain the care I deserve; although it's been years since I last saw my rheumatologist, I am in the process of obtaining health insurance and follow-up care.

Quality of Life: Before this project, I was not an activated patient, nor did I know what I wanted to do after graduating college. Being part of a team of patient-researchers has allowed me to talk about my illness story-in-progress for the first time. I am now actively reflecting on what my role is as a young advocate. This project has shown me how multiple factors (e.g. government response, medical response and cultural/linguistic response) are not in favor of BIPOC and how it affects our financial wellness and physical, mental/emotional, and social health. These lessons have led me to change career paths and work for a Latinx non-profit, and I am reinvigorated to utilize my expertise as a first-generation Latina with a rheumatic condition to fight for my own health as well as for health equity in my community.

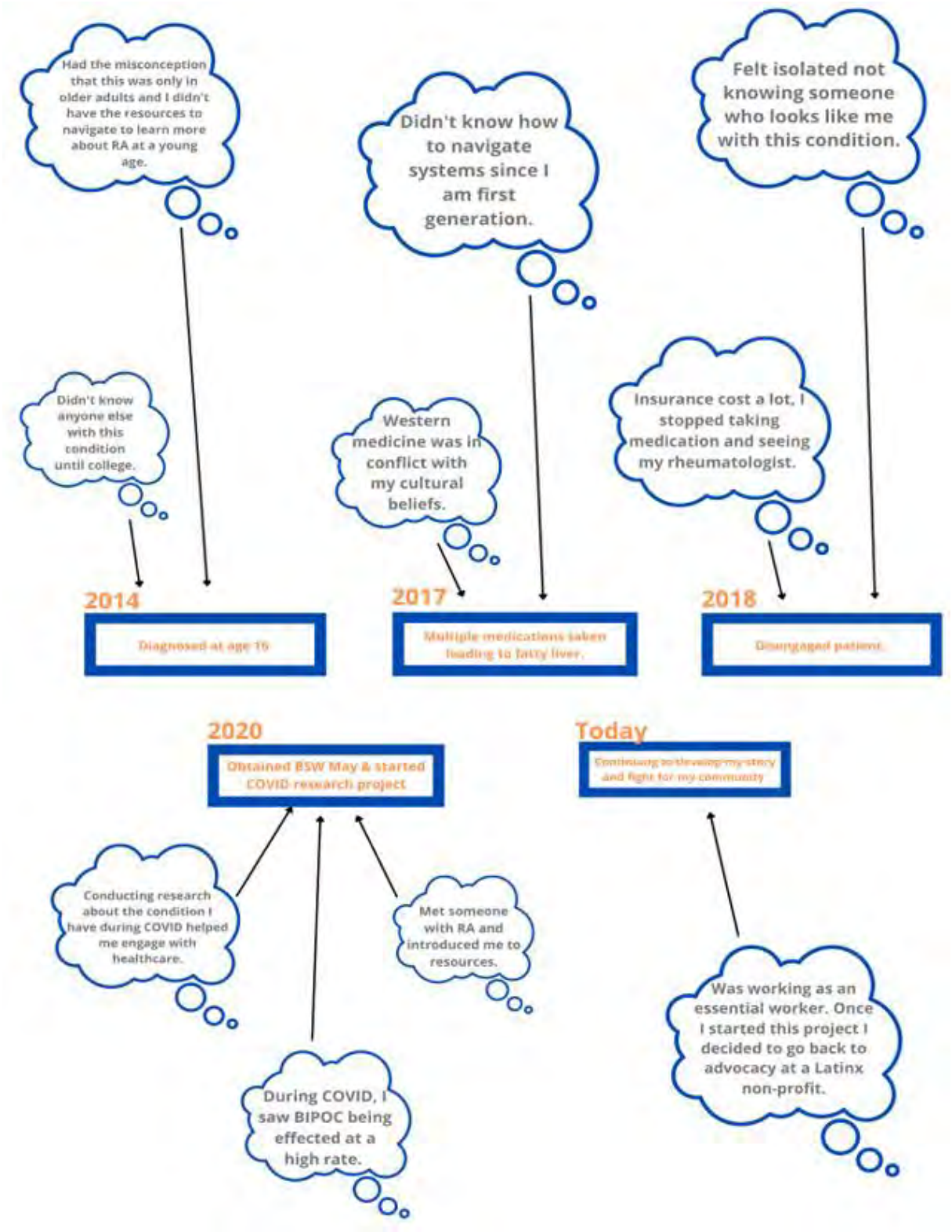


Figure 1. Patient timeline from pediatric diagnosis to adult re-engagement.

Disclosure: G. Torres, None; **C. Wells**, None; **K. Carandang**, None.

Abstract Number: PP13

CreakyKitchen: How the Online Cooking Show I Started is Building Community and Encouraging Better Food Choices for Me and Others Living with Rheumatic and Chronic Disease

Chantelle Marcial, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 7, 2021
Session Title: Patient Perspectives (PP10–PP13)
Session Type: Patient Perspectives
Session Time: 3:30PM–4:30PM

Background/Purpose: At 19, I was mis-diagnosed with Lupus as it was a common condition in my family. My treatment at that time was mainly DMARDs, with little to no results. Approximately six years later, I was connected with my current rheumatologist who did a new panel of testing and accurately diagnosed me with rheumatoid arthritis (RA). I have participated in clinical trials and am currently well-controlled on biologic monotherapy.

Table 1 CreakyKitchen Events, 2020-2021

Recipe	Cooking/Nutrition Tip	Comments from Attendee
Stuffed Mushrooms Topped with Breadcrumbs and Parmesan	To keep your mushrooms fresh, store them in a cool place in their original packaging or a paper bag that breathes; try to use within 3 days.	"This is like being in the studio of a Food Network Show." – Patient living with HIV/AIDS
AppleBerry Slump with Drop Dumplings	Use kitchen tools like dycem to help open jars and make cooking easier.	"Celebrating the Holiday season during the pandemic was definitely isolating, but participating in the CreakyKitchen event allowed me to connect to others and feel excited about little adaptations that make cooking with arthritis easier." – Guest Occupational Therapist
Salad with Herbed Salmon	Look for "snack upgrades" to make healthier choices. Switch chips to whole grain rice cakes, switch salty pretzels to salty kale chips.	"CreakyKitchen Allows members of the community to feel normal, create positive associations with their conditions and have fun along the way." – Guest Registered Dietitian
Berry Chia Jam	Chia seeds are a great way to feed gut bacteria and keep our microbiome healthy.	"CreakyKitchen is such an important tool to have right now. It is giving us tools and bringing us together." – Patient living with Rheumatoid Arthritis
Vegetable Soup	Soups are a great way to use leftover vegetables in the fridge that are close to going bad.	"Having CreakyKitchen and learning new ways to navigate cooking, while chronically ill, is invaluable to the arthritis community because food is medicine for the body and soul." – Guest Body-Centered Psychotherapist and Certified Massage Therapist
Pasta Primavera	If you hate the smell of garlic on your hands, rub them with lemon juice when you're done cutting the garlic.	"Listen to your body, take plenty of breaks, don't push." – Patient living with Psoriatic Arthritis

Figure 1. Graphic created to announce CreakyKitchen events via emails and on social media posts. This graphic depicts a woman cooking with arthritis in her wrists.

Intervention: In 2020 during the COVID-19 pandemic, I was communicating with staff at the Global Healthy Living Foundation, CreakyJoints. During an exchange, I mentioned how a cooking show could be a fun idea to build a sense of community and to share cooking tips and tricks with other patients, and to introduce people to new recipes that are easy, healthy, and delicious. People with chronic disease often go through a trial-and-error process to figure out what foods help them feel good. In collaboration with the Global Healthy Living Foundation, CreakyKitchen was born in November 2020 as a way to come together as a community in a fun and stress-free environment to share strength and experience through cooking and nutrition. We send out email invitations, make announcements on social media using a graphic created to announce CreakyKitchen events (Figure 1), and then come together virtually as a community each month. I share a recipe while people cook and follow along from the comfort of their homes. We are joined by experts and guests in our community who share information about nutrition, along with tips for navigating the kitchen and cooking with arthritis (Table 1).

Maintenance: Our CreakyKitchen community has grown with each monthly streaming event, and now more than 100 people regularly attend in real-time. Being able to connect with members of my CreakyKitchen community has been a huge boost for my mental health. Also, I spend time each month researching healthier recipes to share, which has made an impact on my own meals at home, outside of the show. I have started re-thinking and changing my own go-to recipes and finding ways to alter them to keep the flavors as good as they were, but with a healthier twist. In doing so, I have already shed a few pounds, which is a great relief for my back, knees, and ankles.

Quality of Life: CreakyKitchen gives me a fun, interactive monthly event to look forward to, which has been especially important during the COVID-19 pandemic. I get to connect, share a few laughs and a great recipe (or two) with

other people who are living with rheumatic conditions around the world. Plus I always learn something new about cooking and nutrition thanks to our CreakyKitchen guest co-hosts. I have been able to take information from their segments and apply it in everyday life. From kitchen hacks, to remembering to rest, to finally planning my own herb garden, these have all been great learning moments. Rest has been especially helpful in that I usually push myself to exhaustion and have a hard time getting back to baseline. The reminders to stay mindful of my symptoms and follow their cues has been helpful in better managing my RA.

Disclosure: C. **Marcial**, None.

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